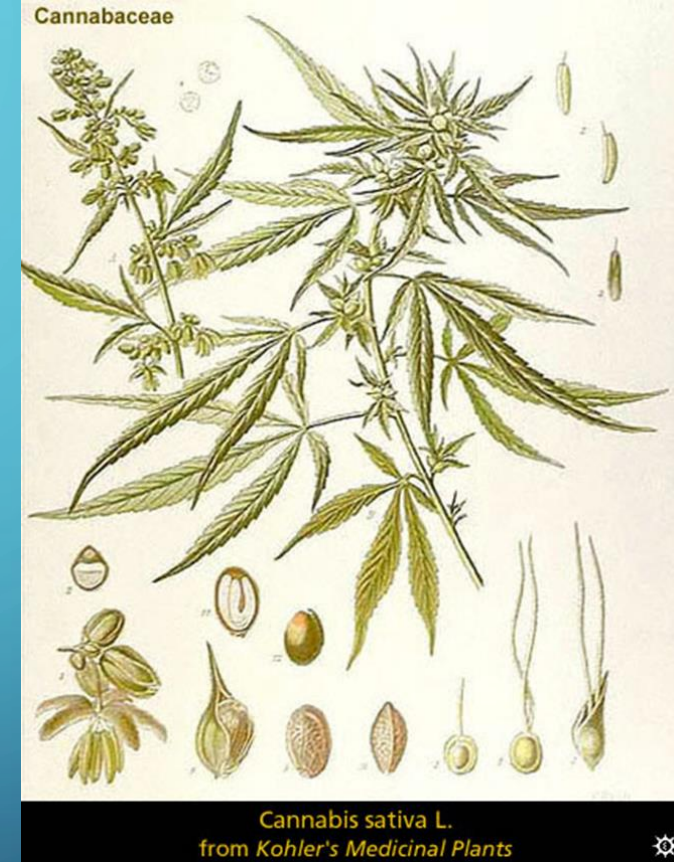


MARIJUANA: IS IT MEDICINE YET?



Donald I. Abrams, MD
Immediate Past Chief, Hematology-Oncology
Zuckerberg San Francisco General Hospital
Professor Emeritus of Medicine, UCSF

DONALD I. ABRAMS' DISCLOSURES

- Scientific Advisor to:
 - Cannformatics
 - Lumen
 - Maui Grown Therapies
- And I did go to college in the '60's

RESEARCH PAPER

Phytochemical and genetic analyses of ancient cannabis from Central Asia

Ethan B. Russo^{1,2,3,*}, Hong-En Jiang^{4,5}, Xiao Li⁵, Alan Sutton², Andrea Carboni⁶, Francesca del Bianco⁶, Giuseppe Mandolino⁶, David J. Potter², You-Xing Zhao⁷, Subir Bera⁸, Yong-Bing Zhang⁵, En-Guo Lü⁹, David K. Ferguson¹⁰, Francis Hueber¹¹, Liang-Cheng Zhao¹², Chang-Jiang Liu⁴, Yu-Fei Wang⁴ and Cheng-Sen Li^{5,13,*}

¹ Visiting Professor, Institute of Botany, Chinese Academy of Sciences, erusso@gwpharm.com

² Wiltshire SP4 OJQ, UK

³ University of Montana, Missoula, MT, USA

⁴ Institute of Botany, Chinese Academy of Sciences, Beijing

A



B

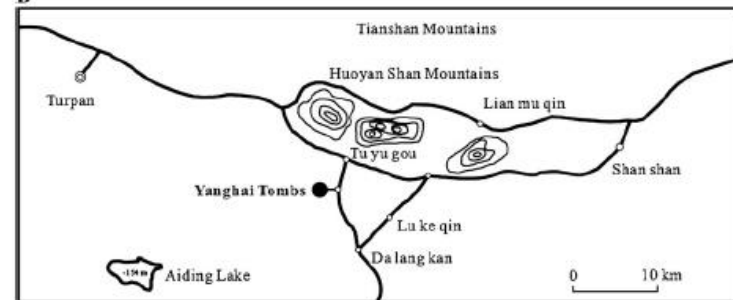


Fig. 1. Area maps. (A) Map of Turpan, Xinjiang, China and its location in Central Asia. (B) Map of Yanghai Tombs site and surrounding area (adapted from Xinjiang Institute of Cultural Relics and Archaeology, 2004).





Fig S5. Containers in which cannabis was stored in tomb (previously published in Mandarin



Fig S3B.



Cannabis May Have Eased Breast Cancer Symptoms of Siberian Ice Princess

October 17, 2014 | by Lisa Winter



photo credit: Kobsev via Wikimedia Commons

ANTHROPOLOGY

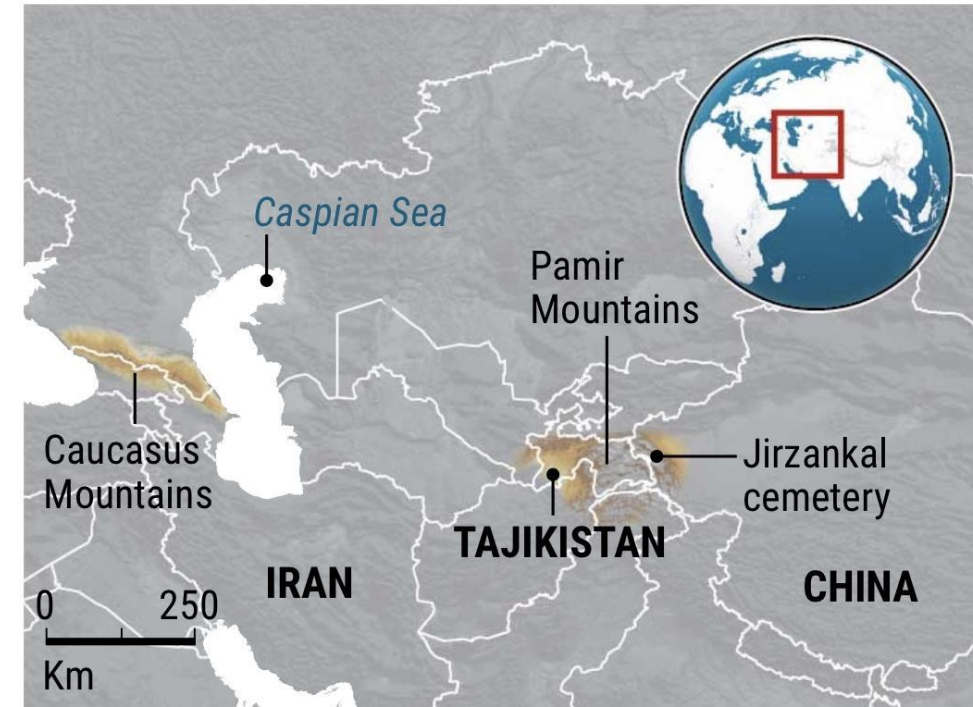
The origins of cannabis smoking: Chemical residue evidence from the first millennium BCE in the Pamirs

Meng Ren^{1,2}, Zihua Tang³, Xinhua Wu⁴, Robert Spengler⁵, Hongen Jiang², Yimin Yang^{2,5*}, Nicole Boivin^{5,6}

Cannabis is one of the oldest cultivated plants in East Asia, grown for grain and fiber as well as for recreational, medical, and ritual purposes. It is one of the most widely used psychoactive drugs in the world today, but little is known about its early psychoactive use or when plants under cultivation evolved the phenotypical trait of increased specialized compound production. The archaeological evidence for ritualized consumption of cannabis is limited and contentious. Here, we present some of the earliest directly dated and scientifically verified evidence for ritual cannabis smoking. This phytochemical analysis indicates that cannabis plants were burned in wooden braziers during mortuary ceremonies at the Jirzankal Cemetery (ca. 500 BCE) in the eastern Pamirs region. This suggests cannabis was smoked as part of ritual and/or religious activities in western China by at least 2500 years ago and that the cannabis plants produced high levels of psychoactive compounds.

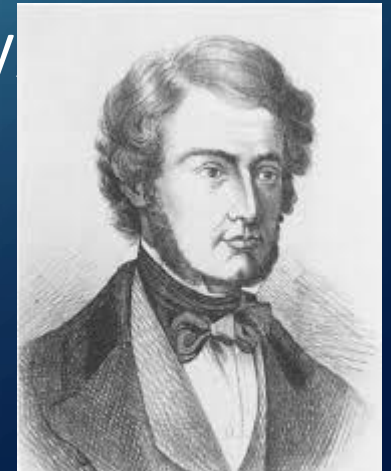
- Ten wooden braziers exhumed from 8 tombs
- Cannabinol, oxidative product of THC, found on the wooden vessels and stones
- Cannabis was of high THC concentration suggesting possible cultivation
- Cannabis used as part of ritual and/or religious activities

Archaeologists have spotted signs of ancient cannabis use from western China to the Caucasus.



CANNABIS AS MEDICINE

- Marijuana (cannabis, hemp) is one of the oldest known psychoactive plants
- First reported use as medicine ~ 3000 years ago
- Introduced into Western medicine in 1840's by Dr. W.B. O'Shaughnessy
- Promoted for putative analgesic, sedative, anti-inflammatory, antispasmodic and anticonvulsant properties

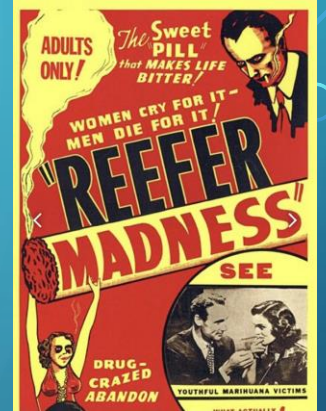




Additional products available in 1906 manufactured by Eli Lilly, Wyeth, Sharp & Dohme

CANNABIS AS *NOT* MEDICINE

- Early 1900's: Interest waned with advent of opiates, barbiturates, chloral hydrate, aspirin and syringes
- 1937: First US restrictions with Marihuana Tax Act (\$1/oz for medical use, \$100/oz for recreational users)
- 1942: Removed from US Pharmacopoeia
- 1951: Boggs Act includes cannabis with narcotics
- 1961: United Nations Single Convention Treaty classified cannabis as a dangerous narcotic
- 1970: US Controlled Substances Act placed cannabis in Schedule I



Harry Jacob Anslinger, zealous man

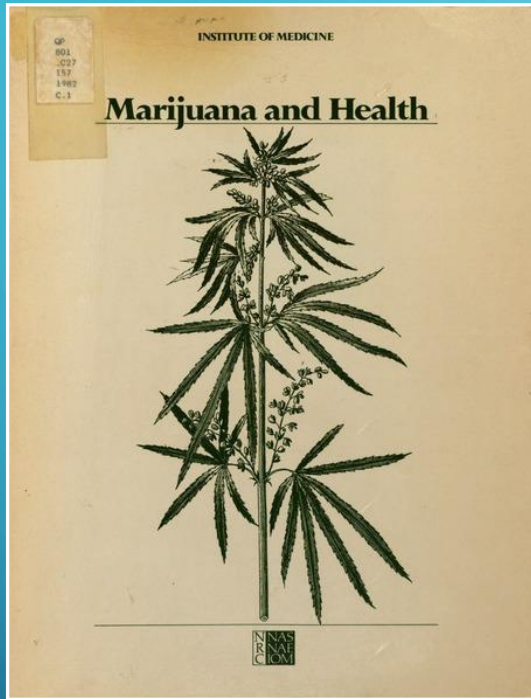
CONTROLLED SUBSTANCES ACT OF 1970

SCHEDULE I SUBSTANCES

HIGH POTENTIAL FOR ABUSE AND NO ACCEPTED MEDICAL USE

- Marijuana
- Heroin
- LSD
- Mescaline
- Other hallucinogenic amphetamine derivatives
- Methaqualone
- Illicit fentanyl derivatives
- Gammahydroxybutyrate (GHB)

THE EIGHTIES



Marijuana and Health
(1982)

INTRODUCING **MARINOL**® (II)
(dronabinol) **Warning: May be habit forming**
capsules 2.5 mg

FOR THE TREATMENT OF ANOREXIA ASSOCIATED WITH WEIGHT LOSS IN PATIENTS WITH AIDS

Week	MARINOL 2.5 mg	Placebo
Week 2 (n=12)	~10	~5
Week 4 (n=10)	~15	~8
Week 6 (n=10)	~18	~10

A significant appetite improvement was achieved at week 4 of a 6-week study.¹ Trends toward improved body weight and mood, and decreases in nausea were also seen during the same 6-week study, but these results were not statistically significant.¹

MARINOL was well tolerated. Side effects were generally mild and reversed by dosage reduction. The most frequent adverse reactions included: euphoria (13%), dizziness (7%), thinking abnormal (7%), sinusitis (6%), somnolence (6%).¹ Although no drug/drug interactions were discovered during clinical trials of MARINOL, cannabinoids

may interact with other drugs, including amphetamines, atropine, and amitriptyline.

MARINOL has the potential for abuse. The same care in prescribing and accounting for MARINOL should be used as for other Schedule II drugs. Prescriptions should be limited to the amount necessary for the period between visits.

A Patient Assistance Program is available. For information call: 1-800-274-8651.

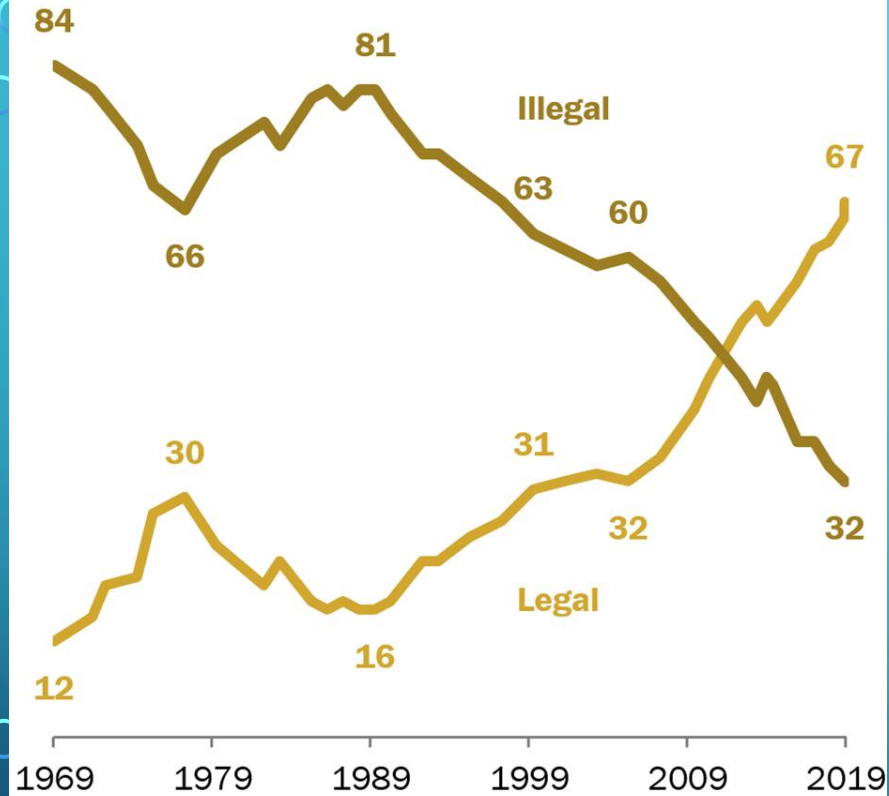
*The USAN name for delta-9-tetrahydrocannabinol (THC). Please see Brief Summary of Full Prescribing Information on adjacent page.



Approved 1986 for CINV; expanded 1992

U.S. public opinion on legalizing marijuana, 1969-2019

Do you think the use of marijuana should be made legal, or not? (%)



Note: No answer responses not shown. 2019 data from Pew Research Center's online American Trends Panel; prior data from telephone surveys. Data from 1969-1972 from Gallup; data from 1973-2008 from General Social Surveys.

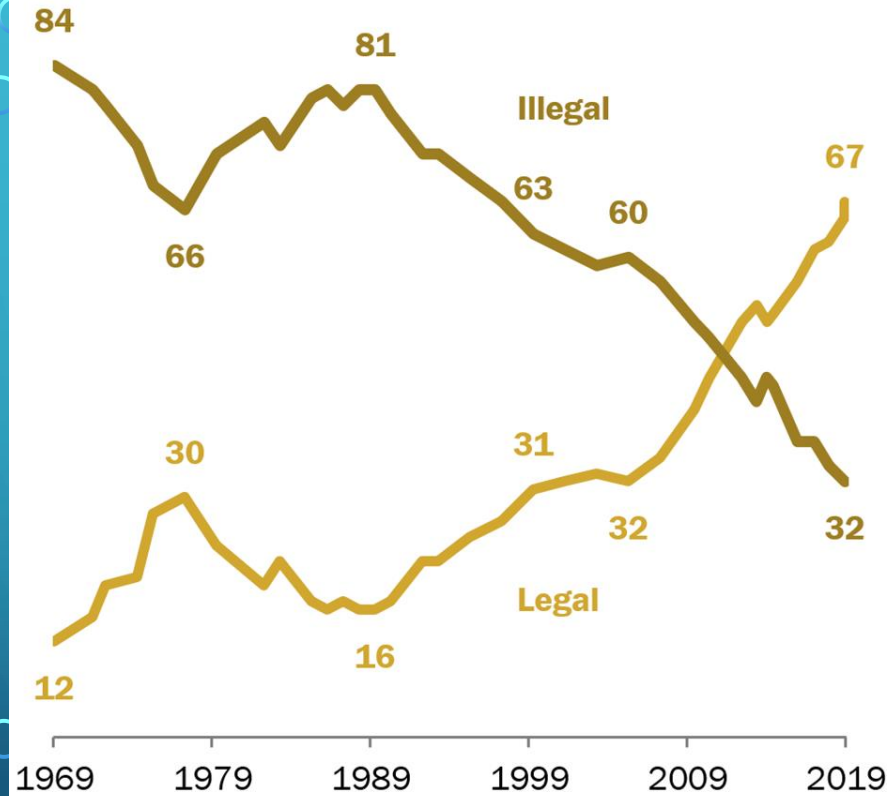
Source: Survey of U.S. adults conducted Sept. 3-15, 2019.

PEW RESEARCH CENTER

JUST SAY NO WORKED FOR AWHILE

U.S. public opinion on legalizing marijuana, 1969-2019

Do you think the use of marijuana should be made legal, or not? (%)



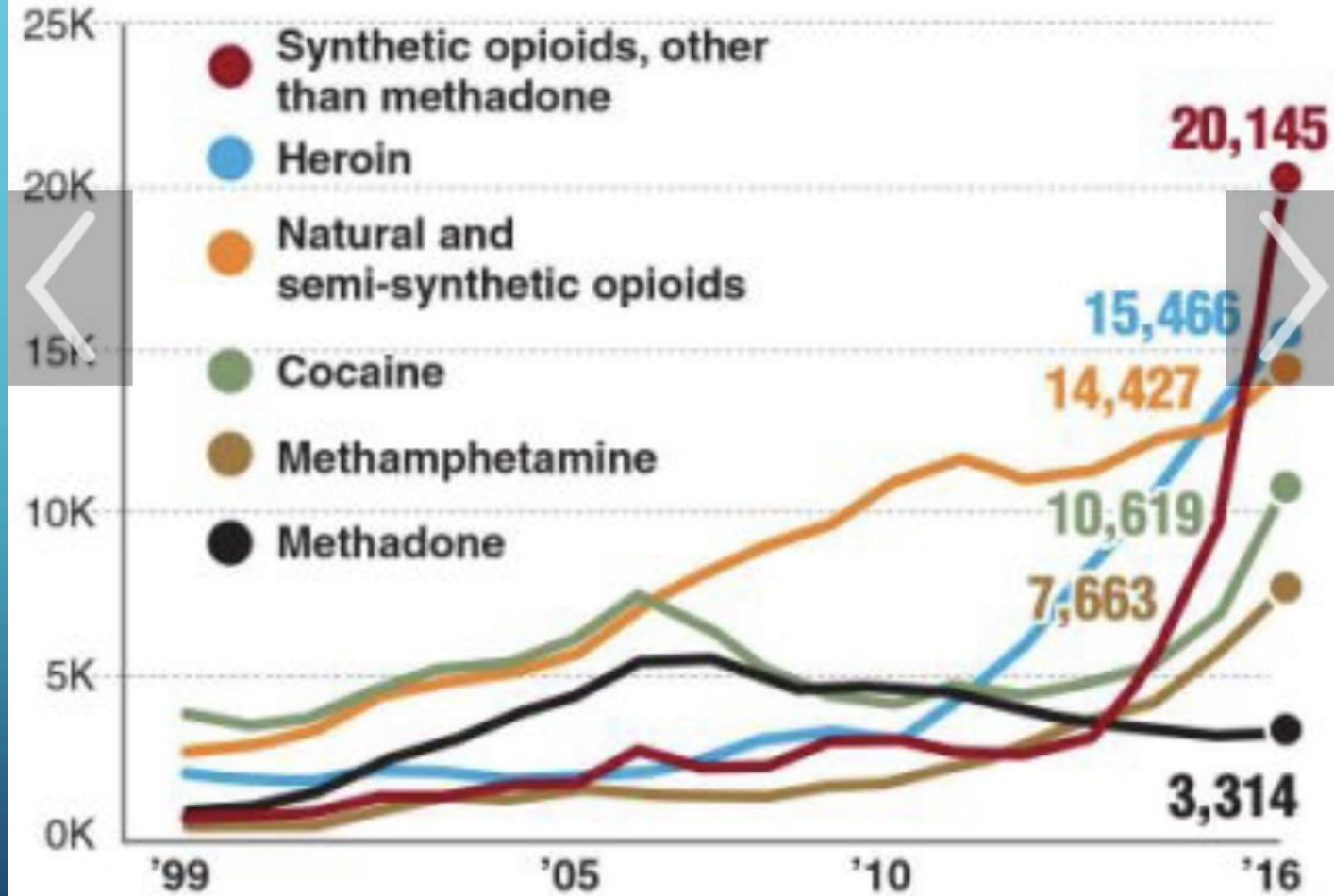
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PEW RESEARCH CENTER

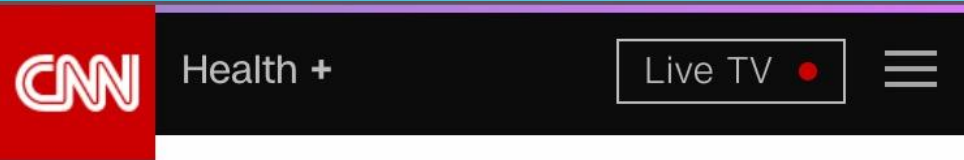
U.S. drug overdose deaths

Among the more than 64,000 drug overdose deaths estimated in 2016, the sharpest increase occurred among deaths related to fentanyl and fentanyl analogs (synthetic opioids), more than 20,000 overdose deaths.



Source: CDC
Graphic: Staff, TNS

SANJAY GUPTA, MD INTRODUCES THE WORLD TO CBD



Marijuana stops child's severe seizures

By Sandra Young, CNN

Updated 4:51 PM ET, Wed August 7, 2013



Photos: Photos: Charlotte's Web



By Sandra Young, CNN

Updated 4:51 PM ET, Wed August 7, 2013



Photos: Photos: Charlotte's Web

C
B
D

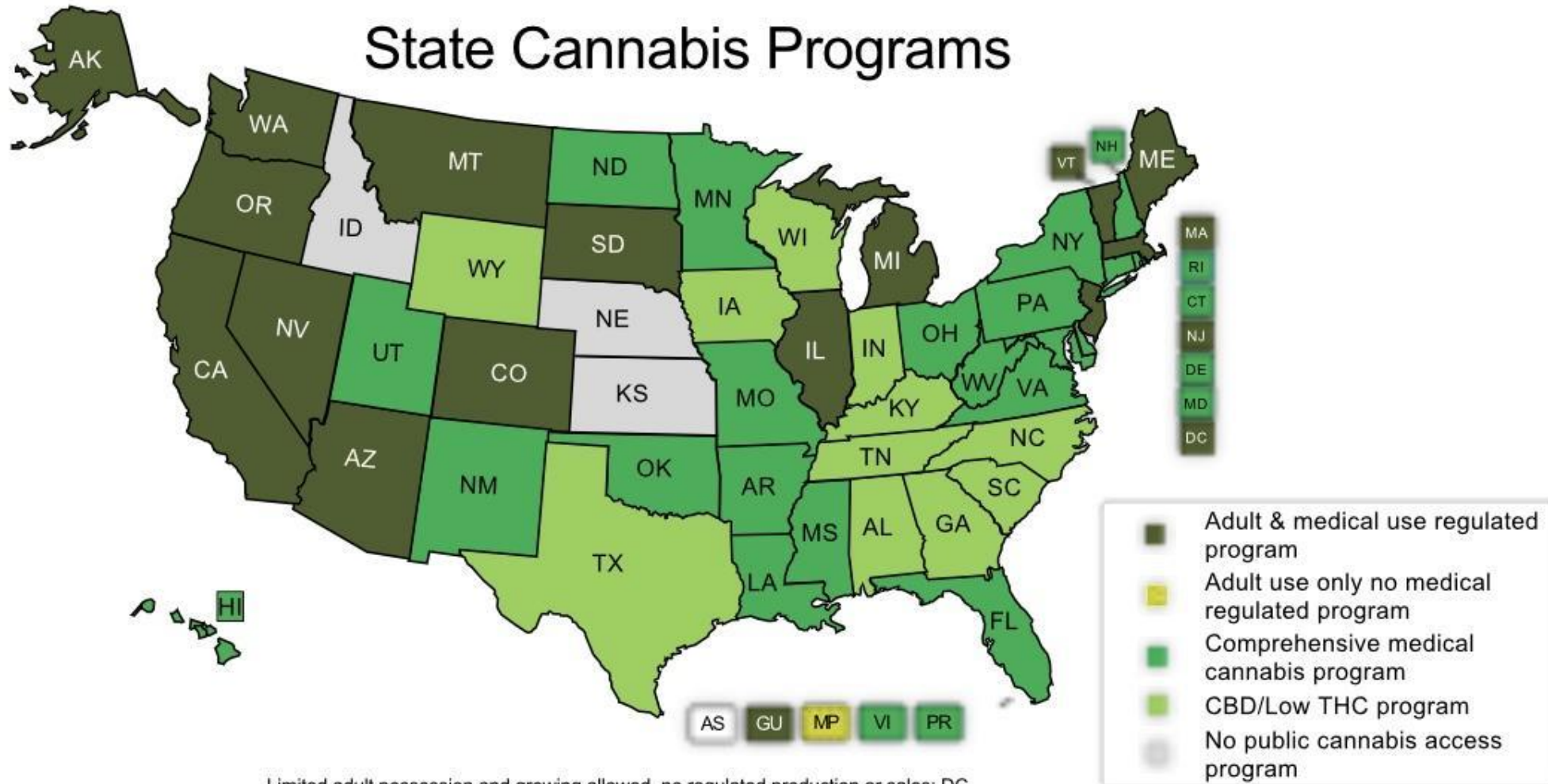
AGRICULTURAL IMPROVEMENT BILL 2018

- Also known as the Farm Bill
- Removed industrial hemp (cannabis with $< 0.3\%$ THC) from the Controlled Substances Act
- Reaffirmed FDA regulatory authority for hemp-derived medications, dietary supplements and food additives
- CBD derived from plant with $>0.3\%$ THC is still Schedule I in the eyes of DEA

WHO EXPERT COMMITTEE ON DRUG DEPENDENCE: 40TH REPORT 2018

- There are no case reports of abuse or dependence relating to the use of pure CBD
- No public health problems have been associated with CBD use
- CBD has been found to be generally well tolerated with a good safety profile
- The Committee recommended that preparations considered to be pure CBD should not be scheduled

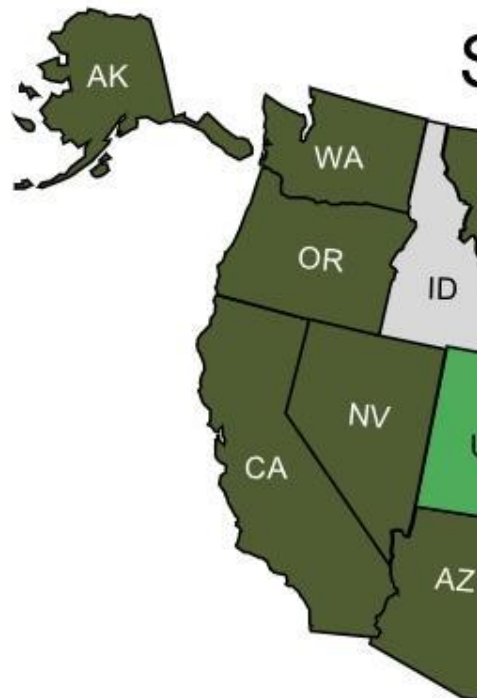
State Cannabis Programs



SOURCE: National Conference of State Legislatures Website

Virginia joins 15 other states in legalizing marijuana

Virginia is the 16th U.S. state to pass an adult-use marijuana legalization law, though sales would not start until 2024.



Limited adult



Adult & medical use regulated program
Adult use only no medical regulated program
Comprehensive medical cannabis program
CBD/Low THC program
No public cannabis access program

November 2020

SOURCE: N

A marijuana plant is visible at a medical marijuana dispensary. | Julio Cortez/AP Photo

Website



LIFE

MARIJUANA

At least 12 million Americans
have now tried it
Are penalties too severe?
Should it be legalized?

OCTOBER 31 • 1969 • 40¢