OUTLINE

• Cannabis: Patterns of Use
• Health Effects
• Therapeutic Uses
• Changing Policy Landscape
Terminology

- Cannabis: marijuana plant
  - sativa, indica, ruderalis

- Hemp: sativa (low THC/high CBD)

- “Recreational” use: use

- “Medical” marijuana: use for (perceived) therapeutic value
CANNABIS: PATTERNS OF USE
Cannabis: Most Commonly Used Federally Illicit Drug In the U.S.

- Over 26 million Americans 12 and older report past month cannabis use.
- Approximately 4.0 million Americans met criteria for cannabis use disorders in 2017.
- An estimated 3.0 million Americans used cannabis for the first time; 1.2 million were between the ages of 12 and 17.

Tetrahydrocannabinol (THC)
Psychoactive Ingredient in Marijuana

Source: 2017 National Survey on Drug Use and Health, SAMHSA
PAST MONTH MARIJUANA USE IS INCREASING IN ADULTS

10% Increase

23% Increase

National Survey on Drug Use and Health, SAMHSA
PAST MONTH USE OF CIGARETTES, MARIJUANA, AND ALCOHOL IN 12TH GRADERS

nearly 6% report daily use of marijuana

Source: University of Michigan, 2017 Monitoring the Future Study
AMONG CURRENT MARIJUANA USERS, MORE THAN TWO IN FIVE ARE DAILY OR ALMOST DAILY USERS

Number of Days Used Marijuana in the Past Month

**2002**
- 1 to 2 Days: 24%
- 3 to 5 Days: 18%
- 6 to 19 Days: 25%
- 20 or More Days: 33%

**2017**
- 1 to 2 Days: 22%
- 3 to 5 Days: 16%
- 6 to 19 Days: 20%
- 20 or More Days: 42%

14.6 Million Past Month Users of Cannabis in 2002

26.0 Million Past Month Users of Cannabis in 2017

Source: SAMHSA, 2017 National Survey on Drug Use and Health (September 2018).
MARIJUANA POTENCY (% Δ-9 THC) QUADRUPLED IN PAST 20 YEARS

THC Potency of Domestic and Non-Domestic Cannabis Samples Provided by the DEA, Percent Averages from 1995 to Present, by Year.

Source: Potency Monitoring Program, Quarterly report Number 138, NIDA Contract Number: N01DA-15-7793
HEALTH EFFECTS
CANNABIS’ ACUTE EFFECTS (INTOXICATION PHASE)

- Euphoria
- Calmness
- Appetite stimulation
- Altered perception of time
- Heightened sensation
- Impairs coordination and balance
- Increased heart rate: 20 - 100%
  - Some evidence for increased risk of heart attack, may be exacerbated in vulnerable individuals (e.g., baby boomers?)
- Orthostatic (postural) hypotension
- Increased risk of accidents (~2 fold), higher when combined with alcohol
- Hyperemesis (abdominal pain and vomiting)
CANNABIS’ ACUTE EFFECTS (INTOXICATION PHASE)

➢ Cognition
  • Impaired short-term memory
  • Difficulty with complex tasks
  • Difficulty learning

➢ Executive Function
  • Impaired decision-making
  • Increased risky behavior – STDs, HIV?

➢ Mood (especially after high doses or edibles)
  • Anxiety – panic attacks
  • Psychosis – paranoia
Long Term Outcomes:

WE KNOW LESS ABOUT THE LONG TERM HEALTH IMPACT FOLLOWING CHRONIC CANNABIS USE, PARTICULARLY WITH RESPECT TO CAUSALITY.
Cannabis And Brain Development: Most Vulnerable Populations

Prenatal

Adolescent

Older Adults?
CANNABIS USE DURING PREGNANCY HAS DOUBLED SINCE 2002
GREATEST USE DURING FIRST TRIMESTER

Adjusted prevalence of past-month cannabis use

Adjusted prevalence of past-month daily/near daily cannabis use

Source: Volkow et al, JAMA, 2019
FIRST TRIMESTER CANNABIS USE:
RECOMMENDATIONS FROM CANNABIS DISPENSARIES IN COLORADO

- 277 of 400 dispensaries recommended cannabis products for “morning sickness” (71% urban; 63% rural)
- 275 of 277 recommended a specific cannabis type (26% CBD-only; 17% THC-only; 56% both CBD & THC)

Source: Dickson et al; 2018 Obstetrics and Gynecology
Prenatal Cannabis Exposure: Overview of Effects*

- **Neonates**: Lower birth weight; smaller head circumference; hyperarousal
- **18 Months**: Lower scores in verbal and memory domains
- **3-4 Years**: Externalizing behaviors (attention, impulsivity); ADHD; depressive symptoms; delinquency; psychosis proneness
- **6 Years**: Lower IQ; decreased verbal/quantitative reasoning; hyperactivity; increased frontal cortical thickness
- **8-10 Years**: Problems with executive function; early onset substance use
- **Young Adult**: Multiple Caveats

THE BRAIN CONTINUES TO MATURE INTO EARLY ADULTHOOD

How does cannabis (and other substances) affect the developing brain and an individual’s trajectory into adulthood?
MULTIPLE STUDIES SHOW ALTERED BRAIN STRUCTURE AND FUNCTION IN YOUTH WHO REGULARLY USE CANNABIS

Early (<18y) Cannabis Use Decreases Axonal Fiber Connectivity

Axonal paths with reduced connectivity (measured with diffusion-weighted MRI) in cannabis users (n=59) than in controls (N=33).

Source: Zalesky et al Brain 2012
NOT ALL STUDIES FIND DIFFERENCES: SUBCORTICAL STRUCTURES

NO DIFFERENCES BETWEEN REGULAR MARIJUANA USERS AND NONUSERS WHEN PARTICIPANTS WERE MATCHED ON ALCOHOL USE

ADDICTION: ABOUT 9% OF USERS BECOME DEPENDENT, 1 IN 6 WHO START USE IN ADOLESCENCE, 25-50% OF DAILY USERS

Estimated Prevalence of Dependence Among Users

Source: Anthony JC et al., 1994

Whole Body Distribution of CB1 Receptors (2, 25, and 100 min after injection of 11C-MePPEP)

Cannabinoid receptors are also located throughout the body.

Therapeutic Uses
CANNABIS/CANNABINOIDs FOR MEDICAL PURPOSES

- Difficult to develop a botanical-based product with accurate and consistent doses
- Medications which use purified chemicals derived from the cannabis plant considered most promising
- Several FDA-approved compounds show medical benefits:
  - Dronabinol (Marinol®) and nabilone (Cesamet®) (synthetic THC): treatment of nausea in patients undergoing cancer chemotherapy and to stimulate appetite in patients with wasting syndrome due to AIDS.
  - Nabiximols (Sativex®) (plant-based THC/CBD) - a mouth spray for treating spasticity and neuropathic pain that may accompany multiple sclerosis (not yet available in US)
### MEDICAL APPLICATIONS:
#### STRENGTH OF THE RESEARCH

<table>
<thead>
<tr>
<th>Strongest Evidence</th>
<th>Moderate Evidence</th>
<th>Weakest Evidence</th>
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<tbody>
<tr>
<td>Nausea (cancer chemotherapy)</td>
<td>Anti-convulsant</td>
<td>PTSD</td>
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<td>Spasticity and pain (MS)</td>
<td>Anti-inflammatory</td>
<td>ADHD</td>
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<tr>
<td>Appetite stimulant (AIDS wasting)</td>
<td>Anti-tumor</td>
<td>Alzheimer’s</td>
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<td>Neuropathic pain</td>
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<td>Anxiety</td>
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<td>Seizures</td>
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</table>

- Strongest Evidence
- Moderate Evidence
- Weakest Evidence
CHANGING POLICY LANDSCAPE
WHERE ARE WE NOW: FEDERAL POLICY

- Cannabis: Schedule I Substance → Controlled Substances Act (1970): high risk for abuse/dependence; no accepted medical use.

  
  - Cannabis is illegal to grow, possess, or distribute
  
  - Each nation can designate a single source of marijuana for research purposes
  
  - The DEA has designated NIDA to be that source using a contract with the University of Mississippi
U.S. STATE CANNABIS LAWS

States with MML vary on:
• Allowable conditions and routes of administration.
• Dispensaries/home growth, registries.
• Testing, regulatory requirements.

States with Adult Use Laws vary on:
• Marketing, product labeling, distribution (home growth, delivery).
• Taxation.
• Public Consumption.
• Expungement.
NEW TERRITORY: AGRICULTURE IMPROVEMENT ACT 2018 (FARM BILL)

- Removed Industrial Hemp (defined as cannabis sativa plant containing less than 0.3% THC) from Controlled Substances Act
- Re-affirms the regulatory role of the FDA for hemp – derived products
  - Medications (to treat illnesses or symptoms)
  - Dietary Supplements (wellness)
  - Food Additives

Public Hearing: May 31; >120 speakers provided input as FDA considers how to go about regulating CBD

- Expected to be a $2B industry by 2020
- Concerns re: current market: Unregulated Products; Unverified Claims; Uninformed Users (e.g., side effects, drug interactions).

The implications for research with CBD are not yet clear.
CONSEQUENCES OF CONFLICTING FEDERAL AND STATE POLICIES

- UNCERTAINTY around what the DOJ will do in way of ENFORCEMENT
- STATES are developing DIFFERENT APPROACHES to TESTING and LABELING of PRODUCTS
  - What are ALLOWABLE products?
- UNEVEN QUALITY CONTROL, including for home grown Cannabis
- No NATIONAL Guidance, Oversight, or Monitoring of what States are dispensing to patients/recreational users
- BANKING Problems
- “Big Marijuana” industry presence
- BARRIERS to RESEARCH
  - SCHEDULE I STATUS
  - SINGLE SOURCE FOR MARIJUANA
CANNABIS RELATED POISON CONTROL CALLS INCREASED IN COLORADO AND WASHINGTON, INCLUDING IN CHILDREN, INFANTS

Colorado: RMPDC, 2017

Washington: WSOFM, 2017
EMERGENCY DEPARTMENT VISITS WITH CANNABIS RELATED DIAGNOSES IN SAN DIEGO COUNTY

The Center for Community Research prepared this analysis for the San Diego County Marijuana Prevention Initiative with data from the California Department of Public Health, March 2016.

mpisdcounty.net
TRAFFIC FATALITIES IN COLORADO

Traffic Deaths Related to Marijuana when a Driver Tested Positive for Marijuana

- Commercialization
- Legalization

<table>
<thead>
<tr>
<th>Year</th>
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<td>2015</td>
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<td>2016</td>
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Caveat: Impairment/time of last use not determined

Source: www.RMHIDTA.org
WHEN CANNABIS SALES WERE RESTRICTED IN THE NETHERLANDS (MAASTRICHT), UNIVERSITY GRADES IMPROVED
CHALLENGES INTERPRETING POLICY RESEARCH

- Lack of accurate baseline data prior to policy enactment
- Much of the research ignores important policy heterogeneity
- It also ignores how laws were implemented; how they have changed over time
- Lack of attention to specificity and timing generates mixed and inconclusive findings
- Many of the measures being collected (prevalence of use) do not necessarily relate to outcomes of interest (e.g., hospitalizations, treatment needs, school outcomes).
- Findings are observational, associative, and cannot account for all confounding factors (esp. pertinent for opioid findings).
- Few/any assess potential benefits: treatment of pain, stress relief, criminal justice, others.

Modified from: Pacula, March 2016
HOW CAN SCIENCE INFORM POLICY?

• Acknowledge the polarized nature of the issue.
• Need to be explicit and clear about what we know, what we think we know, and what we don’t know.
• Try to answer real world questions:
  • Does cannabis legalization impact the opioid epidemic?
  • Is there a potency limit that should be imposed?
  • Should certain products be prohibited.
  • How dangerous is prenatal exposure to cannabis?
• Be precise in use of terminology
• Help ensure that the public health interests are front and
Ten year longitudinal study of ~10,000 children from age 10 to 20 years to assess effects of childhood experiences, including use of cannabis and other substances on individual brain development trajectories.
Thank you!