NATIONAL ACADEMY OF SCIENCES

- Conclusive evidence regarding the short- and long-term health effects (harms and benefits) of cannabis use remains elusive.
- A lack of scientific research has resulted in a lack of information on the health implications of cannabis use,

RESEARCH CHALLENGES

- Despite ongoing federal funding for cannabinoid research ($111 million in 2015 alone), cannabis researchers have found federal research funds to be restricted and limited.
- Specific regulatory barriers, including the classification of cannabis as a Schedule I substance, that impede the advancement of cannabis and cannabinoid research
- Research proposals were required to undergo a thorough and rigorous assessment by the DEA, NIDA, the FDA, and the U.S. Department of Health and Human Services (HHS).
- It is often difficult for researchers to gain access to the quantity, quality, and type of cannabis product necessary to address specific research questions on the health effects of cannabis use
- If they were federally approved, researchers were limited in the type and quantity of cannabis available from the University of Mississippi, which was contracted by NIDA to act as the only licit supply of the drug for research.
- A diverse network of funders is needed to support cannabis and cannabinoid research that explores the harmful and beneficial health effects of cannabis use
- To develop conclusive evidence for the effects of cannabis use on short and long-term health outcomes, improvements and standardization in research methodology (including those used in controlled trials and observational studies) are needed

CONCLUSIVE EVIDENCE

- For therapeutic effects: There is strong evidence from r**andomized controlled trials** to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.
- For other health effects: There is strong evidence from randomized controlled trials to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.
- For this level of evidence, there are many supportive findings from **good-quality studies with no credible opposing findings**. A firm conclusion can be made, and the limitations to the evidence, including chance, bias, and confounding factors, can be ruled out with reasonable confidence.

SUBSTANTIAL EVIDENCE

- For therapeutic effects: There is strong evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.
- For other health effects: There is strong evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.

- For this level of evidence, there are several supportive findings from good quality studies with very few or no credible opposing findings. A firm conclusion can be made, but minor limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.

MODERATE EVIDENCE

- For therapeutic effects: There is some evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.
- For other health effects: There is some evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.
- For this level of evidence, there are several supportive findings from good- to fair-quality studies with very few or no credible opposing findings. A general conclusion can be made, but limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.

LIMITED EVIDENCE

- For therapeutic effects: There is weak evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.
- For other health effects: There is weak evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.
- For this level of evidence, there are supportive findings from fair-quality studies or mixed findings with most favoring one conclusion. A conclusion can be made, but there is significant uncertainty due to chance, bias, and confounding factors.

NO OR INSUFFICIENT EVIDENCE TO SUPPORT THE ASSOCIATION

- For therapeutic effects: There is no or insufficient evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.
- For other health effects: There is no or insufficient evidence to support or refute.a statistical association between cannabis or cannabinoid use and the health endpoint of interest.
- For this level of evidence, there are mixed findings, a single poor study, or health endpoint has not been studied at all. No conclusion can be made becauseof substantial uncertainty due to chance, bias, and confounding factors

THERAPEUTICS: The vast majority of these studies examined the potential therapeutic effect of cannabinoids (e.g., FDA-approved synthetics) rather than smoked cannabis.

- **In adults with chemotherapy-induced nausea and vomiting, oral cannabinoids are effective antiemetics**
- **In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms.**
- **In adults with multiple sclerosis (MS)-related spasticity, short term use of oral cannabinoids improves patient-reported spasticity symptoms.**

- **For these conditions the effects of cannabinoids are modest; for all other conditions evaluated there is inadequate information to assess their effects.**

There is conclusive or substantial evidence that cannabis or cannabinoids are effective:

- For the treatment of chronic pain in adults (cannabis)
- As antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids)
- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids)

There is moderate evidence that cannabis or cannabinoids are effective for:

- Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols – mix of THC- tetrahydrocannabinol and and CBD - cannabidiol)

There is limited evidence that cannabis or cannabinoids are effective for:

- Increasing appetite and decreasing weight loss associated with HIV/AIDS(cannabis and oral cannabinoids)
- Improving clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids)
- Improving symptoms of Tourette syndrome (THC capsules)
- Improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders (cannabidiol)
- Improving symptoms of posttraumatic stress disorder (nabilone – THC synthetic analog - a single, small fair-quality trial)

There is limited evidence of a statistical association between cannabinoids and:

- Better outcomes (i.e., mortality, disability) after a traumatic brain injury or intracranial hemorrhage

CANCER: like tobacco smoke, MJ smoke contains carcinogens

- **The evidence suggests that smoking cannabis does not increase the risk for certain cancers (i.e., lung, head and neck) in adults.**
- **There is modest evidence that cannabis use is associated with one subtype of testicular cancer.**
- **There is minimal evidence that parental cannabis use during pregnancy is associated with greater cancer risk in offspring.**

There is moderate evidence of *no* statistical association between cannabis use and:

- Incidence of lung cancer (cannabis smoking)
- Incidence of head and neck cancers

There is limited evidence of a statistical association between cannabis smoking and:

- Non-seminoma-type testicular germ cell tumors (current, frequent, or chronic cannabis smoking)

There is no or insufficient evidence to support or refute a statistical association between cannabis use and:

- Incidence of esophageal cancer (cannabis smoking)
- Incidence of prostate cancer, cervical cancer, malignant gliomas, non-
- Hodgkin lymphoma, penile cancer, anal cancer, Kaposi's sarcoma, or bladder cancer
- Subsequent risk of developing acute myeloid leukemia/acute non-lymphoblastic leukemia, acute lymphoblastic leukemia, rhabdomyosarcoma, astrocytoma, or neuroblastoma in offspring (parental cannabis use)
-

CARDIOMETABOLIC RISK:

- **The evidence is unclear as to whether and how cannabis use is associated with heart attack, stroke, and diabetes.**

There is limited evidence of a statistical association between cannabis use and:

- The triggering of acute myocardial infarction (cannabis smoking)
- Ischemic stroke or subarachnoid hemorrhage
- Decreased risk of metabolic syndrome and diabetes
- Increased risk of prediabetes (6-3b)

There is no evidence to support or refute a statistical association between *chronic effects* of cannabis use and:

- The increased risk of acute myocardial infarction

RESPIRATORY DISEASE: 40% of users smoke daily, inhale deeply, hold it in (get more tar and CO, but MJ users smoke fewer MJ cigarettes compared to tobacco users smoke tobacco cigarettes.

- **Smoking cannabis on a regular basis is associated with chronic cough and phlegm production.**
- **Quitting cannabis smoking is likely to reduce chronic cough and phlegm production.**
- **It is unclear whether cannabis use is associated with chronic obstructive pulmonary disorder, asthma, or worsened lung function.**

There is substantial evidence of a statistical association between cannabis smoking and:

- Worse respiratory symptoms and more frequent chronic bronchitis episodes (long-term cannabis smoking)

There is moderate evidence of a statistical association between cannabis smoking and:

- Improved airway dynamics with acute use, but not with chronic use
- Higher forced vital capacity (FVC)

There is moderate evidence of a statistical association between *the cessation*of cannabis smoking and:

- Improvements in respiratory symptoms

There is limited evidence of a statistical association between cannabis smoking and:

- An increased risk of developing chronic obstructive pulmonary disease (COPD) when controlled for tobacco use (occasional cannabis smoking)

There is no or insufficient evidence to support or refute a statistical association between cannabis smoking and:

- Hospital admissions for COPD
- Asthma development or asthma exacerbation

IMMUNITY:

- **There exists a paucity of data on the effects of cannabis or cannabinoid-based therapeutics on the human immune system**
- **There is insufficient data to draw overarching conclusions concerning the effects of cannabis smoke or cannabinoids on immune competence.**
- **There is limited evidence to suggest that regular exposure to cannabis smoke may have anti-inflammatory activity.**
- **There is insufficient evidence to support or refute a statistical association between cannabis or cannabinoid use and adverse effects on immune status in individuals with HIV**

INJURY AND DEATH

- **Cannabis use prior to driving increases the risk of being involved in a motor vehicle accident.**
    - Moreover, the association between THC levels in blood and either acute intoxication or driving impairment remains a subject of controversy, and it could represent an important limitation in the interpretation of findings in culpability studies based on blood THC levels
- In states where cannabis use is legal, there is increased risk of unintentional cannabis overdose injuries among children.
- It is unclear whether and how cannabis use is associated with all-cause mortality or with occupational injury.

There is substantial evidence of a statistical association between cannabis use and:

- Increased risk of motor vehicle crashes (9-3)

There is moderate evidence of a statistical association between cannabis use and:

- Increased risk of overdose injuries, including respiratory distress, among pediatric populations in U.S. states where cannabis is legal

There is no or insufficient evidence to support or refute a statistical association between cannabis use and:

- All-cause mortality (self-reported cannabis use)
- Occupational accidents or injuries (general, nonmedical cannabis use)
- Death due to cannabis overdose

PRENATAL, PERINATAL AND NEONATAL EXPOSURE TO CANNABIS:

- **THC crosses the placenta and is secreted in breast milk**
- **Smoking cannabis during pregnancy is linked to lower birth weight in the offspring.**
- **The relationship between smoking cannabis during pregnancy and other pregnancy and childhood outcomes is unclear.**

There is substantial evidence of a statistical association between maternal cannabis smoking and:

- Lower birth weight of the offspring

There is limited evidence of a statistical association between maternal cannabis smoking and:

- Pregnancy complications for the mother
- Admission of the infant to the neonatal intensive care unit (NICU)

There is insufficient evidence to support or refute a statistical association between maternal cannabis smoking and:

- Later outcomes in the offspring (e.g., sudden infant death syndrome, cognition/academic achievement, and later substance use)

PSYCHOSOCIAL:

- **Recent cannabis use impairs the performance in cognitive domains of learning, memory, and attention. Recent use may be defined as cannabis use within 24 hours of evaluation.**
- **A limited number of studies suggest that there are impairments in cognitive domains of learning, memory, and attention in individuals who have stopped smoking cannabis.**
- **Cannabis use during adolescence is related to impairments in subsequent academic achievement and education, employment and income, and social relationships and social roles.**

There is moderate evidence of a statistical association between cannabis use and:

- The impairment in the cognitive domains of learning, memory, and attention (acute cannabis use)

There is limited evidence of a statistical association between cannabis use and:

- Impaired academic achievement and education outcomes
- Increased rates of unemployment and/or low income
- Impaired social functioning or engagement in developmentally appropriate social roles

There is limited evidence of a statistical association between *sustained abstinence from* cannabis use and:

- Impairments in the cognitive domains of learning, memory, and attention

MENTAL HEALTH:

- **Cannabis use is likely to increase the risk of developing schizophrenia and other psychoses; the higher the use, the greater the risk.**
- **In individuals with schizophrenia and other psychoses, a history of cannabis use may be linked to better performance on learning and memory tasks.**
- **Cannabis use does not appear to increase the likelihood of developing depression, anxiety, and posttraumatic stress disorder.**
- **For individuals diagnosed with bipolar disorders, near daily cannabis use may be linked to greater symptoms of bipolar disorder than for nonusers.**
- **Heavy cannabis users are more likely to report thoughts of suicide than are nonusers.**

- **Regular cannabis use is likely to increase the risk for developing social anxiety disorder.**

There is substantial evidence of a statistical association between cannabis use and:

- The development of schizophrenia or other psychoses, with the highest risk among the most frequent users (12-1)

There is moderate evidence of a statistical association between cannabis use and:

- Better cognitive performance among individuals with psychotic disorders and a history of cannabis use
- Increased symptoms of mania and hypomania in individuals diagnosed with bipolar disorders (regular cannabis use)
- A small increased risk for the development of depressive disorders
- Increased incidence of suicidal ideation and suicide attempts with a higher incidence among heavier users
- Increased incidence of suicide completion
- Increased incidence of social anxiety disorder (regular cannabis use)

There is moderate evidence of *no* statistical association between cannabis use and:

- Worsening of negative symptoms of schizophrenia (e.g., blunted affect)among individuals with psychotic disorders (12-2c)

There is limited evidence of a statistical association between cannabis use and:

- An increase in positive symptoms of schizophrenia (e.g., hallucinations) among individuals with psychotic disorders
- The likelihood of developing bipolar disorder, particularly among regular or daily users
- The development of any type of anxiety disorder, except social anxiety disorder
- Increased symptoms of anxiety (near daily cannabis use)
- Increased severity of posttraumatic stress disorder symptoms among indi- viduals with posttraumatic stress disorder

There is no evidence to support or refute a statistical association between cannabis use and:

- Changes in the course or symptoms of depressive disorders (12-6)
- The development of posttraumatic stress disorder (12-10)

PROBLEM CANNABIS USE:

- **Greater frequency of cannabis use increases the likelihood of developing problem cannabis use.**
- **Initiating cannabis use at a younger age increases the likelihood of developing problem cannabis use.**

There is substantial evidence that:

- Stimulant treatment of attention deficit hyperactivity disorder (ADHD) dur- ing adolescence is *not* a risk factor for the development of problem can- nabis use (13-2e)
- Being male and smoking cigarettes are risk factors for the progression of cannabis use to problem cannabis use (13-2i)

- Initiating cannabis use at an earlier age is a risk factor for the development of problem cannabis use (13-2j)

There is substantial evidence of a statistical association between:

- Increases in cannabis use frequency and the progression to developing problem cannabis use
- Being male and the severity of problem cannabis use, but the recurrence of problem cannabis use does not differ between males and females

There is moderate evidence that:

- Anxiety, personality disorders, and bipolar disorders are *not* risk factors for the development of problem cannabis use
- Major depressive disorder is a risk factor for the development of problem cannabis use
- Adolescent ADHD is *not* a risk factor for the development of problem cannabis use
- Being male is a risk factor for the development of problem cannabis use
- Exposure to the combined use of abused drugs is a risk factor for the development of problem cannabis use
- Neither alcohol nor nicotine dependence alone are risk factors for the progression from cannabis use to problem cannabis use
- During adolescence the frequency of cannabis use, oppositional behaviors, a younger age of first alcohol use, nicotine use, parental substance use, poor school performance, antisocial behaviors, and childhood sexual abuse are risk factors for the development of problem cannabis use

There is moderate evidence of a statistical association between:

- A persistence of problem cannabis use and a history of psychiatric treatment
- Problem cannabis use and increased severity of PTSD symptoms

There is limited evidence that:

- Childhood anxiety and childhood depression are risk factors for the development of problem cannabis use

CANNABIS USE AND THE USE OF OTHER SUBSTANCES:

- **Cannabis use is likely to increase the risk for developing substance dependence (other than cannabis use disorder).**

There is moderate evidence of a statistical association between cannabis use and:

- The development of substance dependence and/or a substance abuse disorder for substances, including alcohol, tobacco, and other illicit drugs

There is limited evidence of a statistical association between cannabis use and:

- The initiation of tobacco use
- Changes in the rates and use patterns of other licit and illicit substances

BOTTOM LINE:

1. More research is needed
2. MJ is a psychoactive substance that is associated with decreased academic performance in children whose brains are still developing
3. Youth use in Clark County has not increased since retail legalization
4. Youth perception of ease of access MJ has decreased since retail legalization
5. We need to support prevention efforts just as we do for alcohol, tobacco and other drugs