

Testimony by Sean Hennessy before the Senate Caucus on International Narcotics Control
October 23, 2019

Good afternoon. My name is Sean Hennessy and I am a pharmacist-epidemiologist and faculty member at the University of Pennsylvania. I was a member of the 16-person committee that wrote the report entitled *The Health Effects of Cannabis and Cannabinoids*¹ that the National Academies of Science, Engineering and Medicine released in January 2017.

More than 150 years ago, the National Academy of Sciences was created through a congressional charter signed by Abraham Lincoln to serve as an independent, authoritative body outside the government that could advise the nation on matters pertaining to science and technology. It later expanded to include engineering and medicine. Every year, approximately 6,000 National Academies members and volunteers serve pro bono on consensus study committees or convening activities. The National Academies' consensus study process is considered the gold standard of independent, nonpartisan, evidence-based advice.

Our committee conducted a comprehensive review and synthesis of the existing evidence regarding the potential health effects—both therapeutic and harmful—of cannabis and cannabis-derived products. Our 487-page report lists nearly 100 different conclusions about these effects. It also lists four recommendations to address research gaps, improve research quality, improve surveillance capacity, and address research barriers. I'd like to briefly summarize what our committee found and recommended. I have attached a copy of the report's highlights for your reference.

For each potentially therapeutic or harmful health effect that we examined, our committee classified the evidence as either *conclusive*, *substantial*, *moderate*, *limited*, or as *no or insufficient evidence*.

Potential Therapeutic Effects

We found *conclusive evidence* that orally administered tetrahydrocannabinol (THC) is effective in treating chemotherapy-induced nausea and vomiting. Synthetic THC (dronabinol) and a synthetic analogue of THC (nabilone) are both FDA-approved for this use.

We found *substantial evidence* that some cannabis products are effective for the treatment of chronic pain in adults. Of the trials examined, 13 studied a product called *nabiximols* (an oral-mucosal cannabis extract containing equal amounts of THC and CBD), 7 studied cannabis flower that was either smoked or vaped, 5 studied orally administered synthetic THC, and 3 studied THC oramucosal spray.

We found *substantial evidence* that orally administered cannabinoids (nabiximols and nabilone) can improve patient-reported symptoms of muscle spasticity in persons with multiple sclerosis.

We found *moderate evidence* that cannabis-derived products, primarily nabiximols, can improve short-term sleep in persons with sleep disturbance associated with obstructive sleep apnea, fibromyalgia, chronic pain, and multiple sclerosis.

¹ 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. doi:10.17226/24625.

We found only *limited evidence* that cannabis and oral cannabinoids can increase appetite and reduce weight loss associated with HIV/AIDS; that oral cannabinoids can improve clinician-measured muscle spasticity in persons with multiple sclerosis; that oral THC can improve symptoms of Tourette syndrome; that oral CBD can improve anxiety symptoms in individuals with social anxiety disorders; and that nabilone can improve symptoms of posttraumatic stress disorder.

There were many conditions for which we found *no or insufficient evidence* that cannabis or cannabis-derived products were effective, including cancers, irritable bowel syndrome, and Parkinson disease.

After we issued our report, the results of clinical trials were made available that served as the basis for the approval by the US Food and Drug Administration of concentrated CBD oil (Epidiolex®) for use as part of a multi-drug treatment for two rare and severe forms of epilepsy.² For reasons of transparency, I note that I served as a consultant for Greenwich Biosciences, Inc. in 2018 and received consulting fees that were less than the \$5000 threshold for a “significant financial interest” set by the US Department of Health and Human Services.

Potential Harmful Health Effects

We found *substantial evidence* of a statistical association between recent cannabis use and an increased risk of motor vehicle crashes.

We found *substantial evidence* of a statistical association between maternal cannabis smoking and lower birth weight of the offspring.

We found *substantial evidence* of a statistical association between long-term cannabis smoking and worse respiratory symptoms including cough, increased sputum production, wheeze, and more frequent chronic bronchitis episodes.

We found *substantial evidence* that initiating cannabis use at an earlier age is a risk factor for the development of problem cannabis use.

We found *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. However, there is reason to question about the directionality of this association.

We found *moderate evidence* of a statistical association between acute cannabis use and impairment in learning, memory, and attention.

We found *moderate evidence* of a statistical association between regular cannabis use and increased symptoms of mania and hypomania in individuals diagnosed with bipolar disorders.

We found *moderate evidence* of a statistical association between cannabis use and a small increased risk for the development of depressive disorders.

We found *moderate evidence* of a statistical association between cannabis use and increased incidence of suicidal ideation, suicide attempts, and completed suicide.

² <https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-comprised-active-ingredient-derived-marijuana-treat-rare-severe-forms>, accessed 16 October 2019.

We found *moderate evidence* of a statistical association between regular cannabis use and increased incidence of social anxiety disorder.

We found *moderate evidence* that 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.

We found *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.

We found *moderate evidence* of a statistical association between cannabis use and an increased risk of overdose injuries among pediatric populations in U.S. states where cannabis is legal according to state law.

Barriers to Research on the Effects of Cannabis and Cannabis-derived Products

Our committee identified four challenges to conducting research on the health effects of cannabis:

1. There are specific regulatory barriers, including the classification of cannabis as a Schedule I substance, that impede the advancement of cannabis and cannabinoid research.
2. 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.
3. A diverse network of funders is needed to support cannabis and cannabinoid research that explores the beneficial and harmful health effects of cannabis use.
4. To develop conclusive evidence for the effects of cannabis use on short- and long-term health outcomes, improvements and standardization in research methods are needed.

Recommendations

Our committee made the following four recommendations:

1. To develop a comprehensive evidence base on the short- and long-term health effects of cannabis use (both beneficial and harmful effects), public agencies, philanthropic and professional organizations, private companies, and clinical and public health research groups should provide funding and support for a national cannabis research agenda that addresses key gaps in the evidence base.
2. To promote the development of conclusive evidence on the short- and long-term health effects of cannabis use (both beneficial and harmful effects), agencies of the U.S. Department of Health and Human Services should jointly fund a workshop to develop a set of research standards and benchmarks to guide and ensure the production of high-quality cannabis research.
3. To ensure that sufficient data are available to inform research on the short- and long-term health effects of cannabis use, the federal, state, and local health authorities should fund and support improvements to federal public health surveillance systems and state-based public health surveillance efforts.
4. The Centers for Disease Control and Prevention, National Institutes of Health, U.S. Food and Drug Administration, industry groups, and nongovernmental organizations should fund the convening of a committee of experts tasked to produce an objective and evidence-based report that fully characterizes the impacts of regulatory barriers to cannabis research and that

proposes strategies for supporting development of the resources and infrastructure necessary to conduct a comprehensive cannabis research agenda.

Thank you for your attention and the opportunity to discuss these issues. I look forward to answering your questions.

January 2017

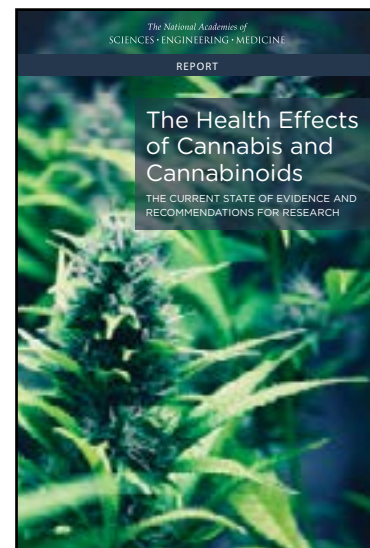
The Health Effects of Cannabis and Cannabinoids

The Current State of Evidence and Recommendations for Research

Recent years have seen a rapid rise in the medical and recreational use of cannabis: a broad term that can be used to describe the various products and chemical compounds (e.g., marijuana, cannabinoids) derived from different species of the cannabis plant. Despite increased cannabis use and a changing state-level policy landscape, conclusive evidence regarding the short- and long-term health effects—both harms and benefits—of cannabis use remains elusive.

A lack of definitive evidence has resulted in insufficient information on the health implications of cannabis use, causing a significant public health concern for vulnerable populations such as adolescents, pregnant women, and others. Unlike with substances such as alcohol or tobacco, no accepted standards exist to help guide individuals as they make choices regarding if, when, where, and how to use cannabis safely and, in regard to therapeutic uses, effectively.

With support from a host of federal, state, philanthropic and nongovernmental organizations, the National Academies of Sciences, Engineering, and Medicine convened an ad hoc, expert committee to develop a comprehensive, in-depth review of the most recent evidence regarding health effects of using cannabis and cannabis-derived products. In the resulting report, *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*, the committee presents nearly 100 research conclusions. The committee also formulated recommendations to expand and improve the quality of cannabis research efforts, enhance data collection efforts to support the advancement of research, and address the current barriers to cannabis research.



Despite increased cannabis use and a changing state-level policy landscape, conclusive evidence regarding the short- and long-term health effects—both harms and benefits—of cannabis use remains elusive.

THE STUDY PROCESS

The committee conducted an extensive search of literature databases to identify relevant articles published since the 1999 release of the National Academies report *Marijuana and Medicine: Assessing the Science Base*. As a result of their search efforts, the committee considered more than 10,000 scientific abstracts for their relevance to the report. Given the large scientific literature on cannabis, the breadth of the statement of task, and other constraints of the study, the committee gave primacy to recently published systematic reviews and high-quality primary research for 11 groups of health topics and concerns, including therapeutic effects for a variety of diseases and conditions; cancer incidence; respiratory disease; prenatal, perinatal, and neonatal outcomes; psychosocial and mental health concerns, and others.

The committee was charged to conduct a comprehensive, in-depth review of health topics with the greatest public health impact rather than to conduct multiple systematic reviews, which would have required a lengthy and robust series of processes. The committee did, however, adopt key features of that process: a comprehensive literature search, assessments by more than one person of the quality of the literature and the conclusions, pre-specification of the questions of interest before conclusions were formulated, standard language to allow for comparisons between conclusions, and declarations of conflict of interest via the National Academies conflict-of-interest policies.

Because of the practical steps taken to narrow a very large literature to one that was manageable within the timeframe available to the committee, there is a possibility that some literature was missed. Furthermore, some research may not be reflected in this report if it did not directly address the health endpoint research questions that were prioritized by the committee.

THE COMMITTEE'S CONCLUSIONS

The committee arrived at nearly 100 different research conclusions related to cannabis or cannabinoid use and health, organizing these into 5 categories: conclusive, substantial, moderate, limited, and no/insufficient evidence.

For a definition of these levels of evidence and a full listing of the conclusions, please see the "Committee's Conclusions" document by visiting the report's website at [nationalacademies.org/CannabisHealthEffects](https://www.nationalacademies.org/CannabisHealthEffects).

THE COMMITTEE'S RECOMMENDATIONS

Based on their research conclusions, the committee members formulated four recommendations that outline priorities to inform a research agenda. The recommendations prioritize research approaches and objectives to:

- address current research gaps, highlighting the need for a national cannabis research agenda that includes clinical and observational research, health policy and health economics research, and public health and public safety research;
- identify actionable strategies to improve research quality and promote the development of research standards and benchmarks;
- highlight the potential for improvements in data collection efforts and the enhancement of surveillance capacity; and
- propose strategies for addressing the current barriers to the advancement of the cannabis research agenda.

The full text of the committee's recommendations appears on the pages that follow.

CONCLUSION

This is a pivotal time in the world of cannabis policy and research. Shifting public sentiment, conflicting and impeded scientific research, and legislative battles have fueled the debate about what, if any, harms or benefits can be attributed to the use of cannabis or its derivatives. This report provides a broad set of evidence-based research conclusions on the health effects of cannabis and cannabinoids and puts forth recommendations to help advance the research field and better inform public health decisions.

To read the full report, please visit [nationalacademies.org/CannabisHealthEffects](https://www.nationalacademies.org/CannabisHealthEffects).

RECOMMENDATIONS

Recommendation 1: To develop a comprehensive evidence base on the short- and long-term health effects of cannabis use (both beneficial and harmful effects), public agencies, philanthropic and professional organizations, private companies, and clinical and public health research groups should provide funding and support for a national cannabis research agenda that addresses key gaps in the evidence base.

Prioritized research streams and objectives should include, but need not be limited to:

Clinical and Observational Research

- Examine the health effects of cannabis use in at-risk or under-researched populations, such as children and youth (often described as less than 18 years of age) and older populations (generally over 50 years of age), pregnant and breastfeeding women, and heavy cannabis users.
- Investigate the pharmacokinetic and pharmacodynamic properties of cannabis, modes of delivery, different concentrations, in various populations, including the dose–response relationships of cannabis and THC or other cannabinoids.
- Determine the benefits and harms associated with understudied cannabis products, such as edibles, concentrates, and topicals.
- Conduct well-controlled trials on the potential beneficial and harmful health effects of using different forms of cannabis, such as inhaled (smoked or vaporized) whole cannabis plant and oral cannabis.
- Characterize the health effects of cannabis on unstudied and understudied health endpoints, such as epilepsy in pediatric populations; symptoms of posttraumatic stress disorder; childhood and adult cancers; cannabis-related overdoses and poisonings; and other high-priority health endpoints.

Health Policy and Health Economics Research

- Identify models, including existing state cannabis policy models, for sustainable funding of national, state, and local public health surveillance systems.
- Investigate the economic impact of recreational and medical cannabis use on national and state public health and health care systems, health insurance providers, and patients.

Public Health and Public Safety Research

- Identify gaps in the cannabis-related knowledge and skills of health care and public health professionals, and assess the need for, and performance of, continuing education programs that address these gaps.
- Characterize public safety concerns related to recreational cannabis use and evaluate existing quality assurance, safety, and packaging standards for recreational cannabis products.

Recommendation 2: To promote the development of conclusive evidence on the short- and long-term health effects of cannabis use (both beneficial and harmful effects), agencies of the United States Department of Health and Human Services, including the National Institutes of Health and the Centers for Disease Control and Prevention should jointly fund a workshop to develop a set of research standards and benchmarks to guide and ensure the production of high-quality cannabis research. Workshop objectives should include, but need not be limited to:

- The development of a minimum dataset for observational and clinical studies, standards for research methods and design, and guidelines for data collection methods.
- Adaptation of existing research-reporting standards to the needs of cannabis research.
- The development of uniform terminology for clinical and epidemiological cannabis research.
- The development of standardized and evidence-based question banks for clinical research and public health surveillance tools.

Recommendation 3: To ensure that sufficient data are available to inform research on the short- and long-term health effects of cannabis use, (both beneficial and harmful effects), the Centers for Disease Control and Prevention, the Substance Abuse and Mental Health Services Administration, the Association of State and Territorial Health Officials, National Association of County and City Health Officials, the Association of Public Health Laboratories, and state and local public health departments should fund and support improvements to federal public health surveillance systems and state-based public health surveillance efforts. Potential efforts should include, but need not be limited to:

- The development of question banks on the beneficial and harmful health effects of therapeutic and recreational cannabis use and their incorporation into major public health surveys, including: the National Health and

Committee on the Health Effects of Marijuana

Marie McCormick (Chair),
Harvard T.H. Chan School of
Public Health

Donald I. Abrams
Zuckerberg San Francisco
General Hospital

Margarita Alegría
Massachusetts General Hospital

William Checkley
Johns Hopkins University

R. Lorraine Collins
State University of New York
at Buffalo

Ziva Cooper
Columbia University Medical
Center

Adre J. Du Plessis
Children's National Health
System

Sarah Feldstein Ewing
Oregon Health & Science
University

Sean Hennessy
University of Pennsylvania

Kent Hutchison
University of Colorado Boulder

Norbert E. Kaminski
Michigan State University

Sachin Patel
Vanderbilt University
Medical Center

Daniele Piomelli
University of California, Irvine

Stephen Sidney
Kaiser Permanente Northern
California

Robert B. Wallace
University of Iowa College of
Public Health

John Williams
Duke University Medical Center

Study Sponsors

Alaska Mental Health Trust
Authority

Arizona Department of Health
Services

California Department of
Public Health

CDC Foundation

Centers for Disease Control
and Prevention

Food and Drug Administration

Mat-Su Health Foundation

National Cancer Institute—
National Institutes of Health

National Highway Traffic Safety
Administration

National Institute on Drug
Abuse—National Institutes of
Health

Oregon Health Authority

Robert W. Woodruff
Foundation

The Colorado Health
Foundation

Truth Initiative

Washington State
Department of Health

Study Staff

Leigh Miles Jackson
Study Director

Jennifer Cohen
Program Officer

Kelsey Geiser
Research Associate
(from July 2016)

R. Brian Woodbury
Research Associate

Sara Tharakan
Research Associate
(until July 2016)

Hope Hare
Administrative Assistant

Matthew Masiello
Research Assistant
(from June 2016)

Marjorie Pichon
Senior Program Assistant
(from August 2016)

Kathleen Stratton
Scholar

**Brownsyne
Tucker-Edmonds**
Norman F. Grant/American
Board of Obstetrics and
Gynecology Fellow

Rose Marie Martinez
Senior Board Director, Board
on Population Health and
Public Health Practice

Nutrition Examination Survey, National Health Interview Survey, Behavioral Risk Factor Surveillance System, National Survey on Drug Use and Health, Youth Risk Behavior Surveillance System, National Vital Statistics System, Medical Expenditure Panel Survey, and the National Survey of Family Growth.

- Determining the capacity to collect and reliably interpret data from diagnostic classification codes in administrative data (e.g., International Classification of Diseases-10)
- The establishment and utilization of state-based testing facilities to analyze the chemical composition of cannabis and products containing cannabis, cannabinoids, or THC.
- The development of novel diagnostic technologies that allow for rapid, accurate, and noninvasive assessment of cannabis exposure and impairment.
- Strategies for surveillance of harmful effects of cannabis for therapeutic use.

Recommendation 4: The Centers for Disease Control and Prevention, National Institutes of Health, Food and Drug Administration, industry groups, and nongovernmental organizations should fund the convening of a committee of experts tasked to produce an objective and evidence-based report that fully characterizes the impacts of regulatory barriers to cannabis research and that proposes strategies for supporting development of the resources and infrastructure necessary to conduct a comprehensive cannabis research agenda. Committee objectives should include, but need not be limited to:

- Proposing strategies for expanding access to research-grade marijuana, through the creation and approval of new facilities for growing and storing cannabis.
- Identifying nontraditional funding sources and mechanisms to support a comprehensive national cannabis research agenda.
- Investigating strategies for improving the quality, diversity, and external validity of research-grade cannabis products.

Health and Medicine Division

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

The nation turns to the National Academies of Sciences, Engineering, and Medicine for independent, objective advice on issues that affect people's lives worldwide.

www.national-academies.org