UPDATE ON CANNABIS

CANNABIS, CANNABINOIDS, AND MEDICINE: WHAT DOES THE EVIDENCE TELL US?

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DISCLOSURE STATEMENT

- Potential Conflict of Interest:
  - Own Stock Options in GW Pharmaceuticals

- Financial Interests:
  - Own Stock in GW Pharmaceuticals in Retirement IRA Account.
  - Own Bond in Pfizer, Inc. in Retirement IRA Account.
  - Spouse Owns Stock Options in Abbott, Abbvie, and Hospira

OBJECTIVES

- Identify the Clinical Indications for Which Cannabis and Cannabinoids Appear to have Some Data Supporting their Use as Medicine.
- Identify the Potential Side Effects and Harms of Cannabis Use and Briefly Discuss the Evidence Supporting these Claims.
- Understand the Rationale for the Recommendations from SCAODA Regarding Cannabis and Cannabinoids in Wisconsin in the Context of the Evidentiary Science Discussed.
- Be able to describe the legal status of cannabis in Wisconsin.
Legal Status of Cannabis and Cannabinoids in Wisconsin

- Cannabidiol (CBD) Products permitted by Lydia’s Law enacted in 2014 for patients with documentation of a seizure disorder.
- Did NOT legalize the production of CBD Products in the State.
- Did NOT legalize distribution of CBD Products in the State.
- On April 17, 2017, Gov. Scott Walker signed Act 4 which expands the original 2014 law to protect ALL patients who possess CBD and have a letter from their physician.
- It remains illegal to produce or distribute CBD products.

In June 2017, a bipartisan group of lawmakers introduced S 318/A 409, which would reduce the penalty for possessing under 10 grams of marijuana from up to six months in jail and/or a fine of up to $1,000 to a $100 civil fine.

Rep. Melissa Sargent has introduced a bill (third time) to legalize, tax, and regulate marijuana for adult use in Wisconsin.

- Would provide legal protection to employees who test positive for cannabis.
- Would make legal age for use 18.

BEFORE WE BEGIN, LET’S BE HONEST: CANNAISS = $$$$
GOALS OF MOST RECENT IOM REPORT ON CANNABIS AND CANNABINOIDS

- Develop a comprehensive, in-depth review of existing evidence regarding the health effects (both harms and benefits) of cannabis and cannabinoids use.
- Make short- and long-term recommendations regarding a research agenda to identify the most critical research questions and advance the cannabis and cannabinoid research agenda.
- These were the same goals of the SCADAD MARIJUANA AD HOC COMMITTEE'S CANNABIS RESEARCH WORK GROUP.

STUDY APPROACH OF MOST RECENT IOM REPORT ON CANNABIS AND CANNABINOIDS

- Five Levels of Evidence in IOM Report
  - Conclusive Evidence
  - Substantial Evidence
  - Moderate Evidence
  - Limited Evidence
  - No or Insufficient Evidence

RESULTS FROM IOM REPORT ON CANNABIS AND CANNABINOIDS

- Therapeutic Evidence for Cannabis and Cannabinoids
  - In adults with chemotherapy-induced nausea and vomiting, oral cannabinoids are effective antiemetics.
  - Not compared directly to newer antiemetics.
  - Limited by side effects.
  - 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. (Moderate Evidence)
  - 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.
Hot Off the Press: Cannabis for Chronic Pain

A Systematic Review Published in Annals of Internal Medicine in August 2017 demonstrated Limited Evidence of Efficacy for Neuropathic Pain and Insufficient Evidence for Other Types of Pain

Limitations:
1) Few methodologically rigorous trials
2) Cannabis formulations studied may not reflect commercially available products
3) Limited applicability to older, chronically ill populations and patients who use cannabis heavily


RESULTS FROM IOM REPORT ON CANNABIS AND CANNABINOIDS

- Respiratory Adverse Effects
  - There is substantial evidence of a statistical association between long-term cannabis smoking and worse respiratory symptoms and more frequent chronic bronchitis episodes.
  - There is moderate evidence of a statistical association between cannabis smoking and improved airway dynamics with acute use, but not with chronic use.
  - There is moderate evidence of a statistical association between cessation of cannabis smoking and improvements in respiratory symptoms.


The National Academy of SCIENCES-ENGINEERING-MEDICINE

9/13/2017
Results from IOM Report on Cannabis and Cannabinoids

Respiratory Adverse Effects

- There is limited evidence of a statistical association between occasional cannabis smoking and an increased risk of developing chronic obstructive pulmonary disease (COPD) when controlled for tobacco use.
- There is insufficient evidence to support or refute a statistical association between cannabis smoking and hospital admissions for COPD, asthma development, or asthma exacerbation.

- There is substantial evidence of a statistical association between long-term cannabis smoking and worse respiratory symptoms and more frequent chronic bronchitis episodes.
- There is moderate evidence of a statistical association between cannabis smoking and improved airway dynamics with acute use, but not with chronic use.
- There is moderate evidence of a statistical association between cessation of cannabis smoking and improvements in respiratory symptoms.

Injury and Death

- Cannabis use prior to driving increases the risk of being involved in a motor vehicle accident.
- 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.
RESULTS FROM IOM REPORT ON CANNABIS AND CANNABINOIDS

- **Cancer**
  - There is moderate evidence of no statistical association between cannabis smoking and the incidence of lung cancer.
  - There is moderate evidence of no statistical association between cannabis use and the incidence of head and neck cancers.
  - There is limited evidence of a statistical association between current, frequent, or chronic cannabis smoking and non-seminoma-type testicular germ cell tumors.

- There is insufficient evidence to support or refute a statistical association between cannabis smoking and the incidence of esophageal cancer.
- There is insufficient evidence to support or refute a statistical association between cannabis use and the incidence of prostate cancer, cervical cancer, malignant gliomas, non-Hodgkin lymphoma, penile cancer, and cancer, Kaposi's sarcoma, or bladder cancer.
- There is insufficient evidence to support or refute a statistical association between parental cannabis use and a subsequent risk of developing acute myeloid leukemia/acute non-lymphoblastic leukemia, acute lymphoblastic leukemia, medulloblastoma, or neuroblastoma in offspring.
RESULTS FROM IOM REPORT ON CANNABIS AND CANNABINOIDS

Cardiometabolic Risk

- The evidence is unclear as to whether and how cannabis use is associated with heart attack, stroke, and diabetes.
- At least one recent study suggests that neither cumulative lifetime nor recent use of marijuana is associated with an increased incidence of CVD in middle age.


RESULTS FROM IOM REPORT ON CANNABIS AND CANNABINOIDS

Immune System Function

- 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.

RESULTS FROM IOM REPORT ON CANNABIS AND CANNABINOIDS

Prenatal, Perinatal, and Neonatal Outcomes

- Smoking cannabis during pregnancy is linked to lower birth weight in the infant.
- The relationship between smoking cannabis during pregnancy and other pregnancy and childhood outcomes is unclear.
RESULTS FROM IOM REPORT ON CANNABIS AND CANNABINOIDS

- 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.

- Mental Health
  - 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.
  - 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 disorder, near daily cannabis use may be linked to greater symptoms of bipolar disorder than non-users.
  - Heavy cannabis users are more likely to report thoughts of suicide than nonusers.
  - Regular cannabis use is likely to increase the risk for developing social anxiety disorder.

- 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.
RESULTS FROM IOM REPORT ON CANNABIS AND CANNABINOIDs

- Cannabis Use and Abuse of Other Substances
  - There is limited evidence of a statistical association between cannabis use and the initiation of tobacco use.
  - There is limited evidence of a statistical association between cannabis use and changes in the rates and use patterns of other licit and illicit substances.
  - 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.

CANNABIS GATEWAY EFFECT?

- The “Gateway Effect” suggests that the use of a substance “opens a gate” to the use of “harder” substances.
  - Assumes that the use of these substances in and of themselves is not as dangerous as “harder” substances.
  - Assumes that there is a cause and effect relationship between use of the “gateway substance” and “harder” drugs.
  - Assumes that use of substances progresses in a sequential pattern beginning with alcohol or tobacco, progressing to cannabis, and then to substances like heroin or cocaine.

CANNABIS GATEWAY EFFECT?

- Cannabis would meet the conditions for gateway drug if (a) its use was initiated prior to the onset of other illicit drug use; and, (b) cannabis use increased the likelihood of using other illicit drugs.
  - Many substances have been considered to have a gateway effect to “harder” substances:
    - Nicotine/Tobacco Products
    - Cannabis
    - Alcohol
    - Prescription Substances
What about Cannabis?

A recent study suggests that a large proportion (44.7%), but not all, individuals who use cannabis go on to use other substances.\(^1\)

Some individuals where at much higher risk of progression:
- Individuals with psychiatric illness
- Being Male
- Individuals who initiated cannabis use at a younger age
- Family history of Substance Use Disorders
- Being never married, separated, or divorced
- Urban Residence


RESULTS FROM IOM REPORT ON CANNABIS AND CANNABINOIDS

Barriers to Cannabis Research (Conclusions)

- There are specific regulatory barriers, including the classification of cannabis as a Schedule I substance, that impede the advancement of cannabis and cannabinoid research.
- 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.
- A diverse network of funders is needed to support cannabis and cannabinoid research that explores the beneficial and harmful 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

RECOMMENDATIONS FROM IOM REPORT ON CANNABIS AND CANNABINOIDS

Recommendation 1: Address Research Gaps

- 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
  - Health Policy and Health Economics Research
  - Public Health and Public Safety Research
Recommendation 2: Improve Research Quality

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.

Recommendation 3: Improve Surveillance Capacity

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.

Recommendation 4: Address Research Barriers

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.
Under the guidance of the SCAODA Prevention Committee, the Marijuana Ad-hoc Committee was charged with researching, evaluating, and developing recommendations regarding marijuana that best serve the public health and safety of all Wisconsin residents. Established in October 2014 as a result of concerns raised when preparing the Wisconsin’s Heroin Epidemic: Strategies and Solutions (Analysis and Recommendations for Reducing Heroin Abuse in Wisconsin).

Committee Divided into Four Subgroups
- Cannabinoid Research Workgroup
- Legalities and Regulation Workgroup
- Prevention Workgroup
- Treatment and Recovery Workgroup

The Committee Produced a 71 page, Evidence-Based Report with policy recommendations for Wisconsin using the best available research from over 150 references.

A copy of the full report is available through the SCAODA Web Page at: https://scaoda.wisconsin.gov/scfiles/marijuana/marijuana-072216.pdf
Brief review of the history of cannabinoids and cannabis as medicine.
Brief description of the Endocannabinoid System.
Review of evidence for specific clinical indications.
Review of evidence regarding side effects and potential harm of cannabis and cannabinoid use.
Workgroup Recommendations.

CANNABINOID RESEARCH WORKGROUP

- CANNABIS, CANNABINOID PHARMACEUTICALS, AND CANNABIS/CANNABINOID DELIVERY SYSTEMS SHOULD BE SUBJECT TO THE SAME RIGOROUS STANDARDS FOR APPROVAL THAT ARE APPLICABLE TO OTHER PRESCRIPTION MEDICATIONS AND MEDICAL DEVICES AND SHOULD NOT BE MADE AVAILABLE FOR USE BY PATIENTS UNTIL SUCH A TIME AS THEY HAVE BEEN APPROVED BY THE FOOD AND DRUG ADMINISTRATION (FDA).

- THE STATE AND FEDERAL GOVERNMENT SHOULD ENCOURAGE AND PROMOTE FURTHER RESEARCH AND DEVELOPMENT FOCUSED ON THE STUDY OF SPECIFIC PHARMACEUTICAL GRADE CANNABINOID COMPOUNDS AND PREPARATIONS (INCLUDING WHOLE PLANT PREPARATIONS) FOR VARIOUS CLINICAL APPLICATIONS.

- SMOKED CANNABIS IS NOT A SAFE DELIVERY SYSTEM FOR CANNABINOIDS, AND SHOULD NOT BE LEGALIZED IN ANY FORM SINCE IT APPEARS TO HAVE SIMILAR CLINICAL EFFICACY VIA INHALATION (VAPORIZED ROUTE), SUBLINGUAL, AND ORAL ROUTES WHICH ARE SAFER, AND THAT MAY HAVE DECREASED ABUSE POTENTIAL.

- NON-PHARMACEUTICAL GRADE ORAL FORMULATIONS (“EDIBLES”) AND ORAL FORMULATIONS NOT APPROVED BY THE FDA SHOULD NOT BE PERMITTED DUE TO VARIABILITY IN DOSAGE BETWEEN SAMPLES, NON-HOMOGENEOUS DISTRIBUTION OF CANNABINOIDS WITHIN NON-STANDARDIZED ORAL FORMULATIONS, AND THE FACT THAT FDA APPROVED ORAL CANNABINOIDS ARE ALREADY AVAILABLE BY PRESCRIPTION IN THE FORM OF DRONABINOL (MARINOL®) AND NABILONE (CESAMET®).
CANNABINOID RESEARCH WORKGROUP

- CANNABIS AND CANNABIS EXTRACTS THAT ARE NOT SPECIFICALLY FDA APPROVED FOR USE IN INDIVIDUALS LESS THAN AGE 21 SHOULD NOT BE LEGALIZED IN ANY FORM FOR USE IN INDIVIDUALS YOUNGER THAN AGE 21 DUE TO A GROWING BODY OF EVIDENCE THAT LINKS EARLY CANNABIS EXPOSURE WITH NEUROBIOLOGICAL BRAIN ABNORMALITIES, AN INCREASED RISK OF ADDICTION, A POTENTIAL TO ACT AS A GATEWAY DRUG, PERMANENT NEUROCOGNITIVE DECLINE, AND LOWER SCHOOL PERFORMANCE/LIFETIME ACHIEVEMENT.

LEGALITIES AND REGULATION WORKGROUP

- Brief introduction including differentiating between the concepts of decriminalization and legalization of marijuana.
- Presentation of current Wisconsin State Law and its enforcement.
- Discussion of the Drug Treatment Court Model.
- Discussion of several decriminalization models including the “Portugal Model.”

LEGALITIES AND REGULATION WORKGROUP

- CANNABIS SHOULD NOT BE LEGALIZED FOR PERSONAL RECREATIONAL USE IN THE STATE OF WISCONSIN.
PREVENTION WORKGROUP

- Community groups, organizations and coalitions should implement evidence-based prevention strategies that address known risk and protective factors for marijuana use.
- Support coalitions as the vehicle through which communities will successfully prevent and reduce marijuana use.
- Work to foster an environment locally that empowers young people not to use marijuana.

- Provide information to employers, and especially supervisors, regarding signs, symptoms and consequences of marijuana use, as well as local resources for obtaining help for cannabis use disorders.
- Make drugged driving prevention and enforcement a priority statewide.
- Incorporate SBIRT (screening, brief intervention and referral to treatment) as a tool for helping clients who may be experiencing problems resulting from marijuana or other substance use.

TREATMENT AND RECOVERY WORKGROUP

- Expand adolescent substance use disorders treatment and recovery options across the state to allow timely access of appropriate level of care for all youth and young adults.
- Expand adult substance use disorders treatment and recovery options across the state to allow timely access of appropriate level of care for all residents.
- Substance use disorders treatment and recovery services for pregnant women should promote abstinence from marijuana during and after pregnancy to protect unborn and developing children and prevent drug-affected newborns and nursing infants.
TREATMENT AND RECOVERY WORKGROUP

- Research, evaluate and implement promising alternative diversion programs including substance use disorders treatment within the legal system.
- Provide substance use disorders treatment for persons while incarcerated and develop better linkages to improve the integration of services between criminal justice, primary medical care and treatment and recovery providers to ensure continuing care.

TREATMENT AND RECOVERY WORKGROUP

- Provide continuing educational opportunities for treatment and recovery providers in an effort to increase understanding of developing science with regard to cannabis use disorders including (but not limited to):
  - Evidence-based treatment options and promising research.
  - Research findings regarding pharmacotherapies to assist in treatment.
  - Clinical innovations to use in the management of withdrawal symptoms.
  - The effect of marijuana use on the developing brain.
  - The impact of adverse childhood experiences and treatment approaches that reflect best practice in trauma-informed care.
  - Emerging research of best practices for adolescent and young adult specific recovery and support programs.

QUESTIONS?