Marijuana Research: Evaluation, Conclusions and Gaps

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Retail marijuana shops open in Colorado
Marijuana Use in Colorado

- 14% of all adults are current users¹
- One-in-eight 18-25yr olds use daily or near daily¹
- Many adults use three or more times per day²
- Top reasons for use: sleep, anxiety and feel good²
- 25% of HS juniors and seniors are current users³
- Smoking remains the most common method of use¹,²,³

1. Behavioral Risk Factor Surveillance System
2. Cannabis Users Survey on Health
3. Healthy Kids Colorado Survey
Yes, it’s bad for you
Don’t lie to yourself

Although legalization activists and many marijuana users believe smoking pot has no negative effects, scientific research indicates that marijuana use can cause many different health problems.

- Distorted perception (sights, sounds, time, touch)
- Problems with memory and learning
- Loss of coordination
- Trouble with thinking and problem-solving
- Increased heart rate, reduced blood pressure
- Hallucinations
- Delusions
- Impaired memory
- Disorientation
- Daily cough and phlegm production
- More frequent acute chest illnesses
- Increased risk of lung infections
- Obstructed airways

Summarizing and improving cannabis research is more important than ever

Let’s talk about:

• Colorado’s marijuana literature review
• Important considerations when evaluating marijuana research
• Comparison of our findings with the NAM report
• Research gaps
Introduction
1. Review existing and emerging research on health effects of marijuana and report
   a) With the Retail Marijuana Public Health Advisory Committee

2. Data monitoring
   a) Monitor patterns of use
   b) Monitor health impacts

3. Marijuana research grants
   a) Medical efficacy
   b) Public health concerns
Marijuana and Health

• [www.colorado.gov/cdphe/marijuana-health-report](http://www.colorado.gov/cdphe/marijuana-health-report)

• OR search “monitoring marijuana CO” and select the first link (“trends and health effects”)
Retail Marijuana Public Health Advisory Committee - Structure

- Was convened by statutory requirement, to monitor the science on marijuana’s health effects
- Responsible for ongoing review of published research and updating evidence summaries
- Made up of physicians, pharmacologists, behavioral health experts and epidemiologists
- Met monthly in 2014 and now meet five times each year to update reviews
Retail Marijuana Public Health Advisory Committee - Systematic Review Process

- Use standardized criteria and language for weight of evidence - 5 levels: Substantial, Moderate, Limited, Insufficient and Mixed
- Searches include research published from 2005 forward, or older for some topics
- Include all relevant primary research and meta-analyses identified for each topic
Topics Evaluated

- Cancer
- Cardiovascular
- Respiratory
- Injury
- Driving
- Unintentional Exposure in Children
- Pregnancy and Breast Feeding
- Cognitive
- Mental Health
- Gastrointestinal
- Reproductive
- Dose, Metabolism and Drug Interactions
- Adolescents and Young Adults
Evaluating Cannabis Research

Translate Science into Public Health

1. Broad Literature Search
2. Relevant Literature Review
3. Group Findings (Pop, Exp, Outcome)
4. Rate Quality of Findings; High, Medium, Low
5. Draft Evidence Statements based on 'Weight of Evidence'
6. Draft Public Health Statements
7. Prevention Messaging & Education Resources
Evaluation resources

- Newcastle-Ottawa Scale for evaluating observational studies
  - Meta-analysis Of Observational Studies in Epidemiology (MOOSE)

- Grading of Recommendations Assessment, Development and Evaluation (GRADE)
  - More focused on randomized trials
  - http://training.cochrane.org/path/grade-approach-evaluating-quality-evidence-pathway
Common Limitations of Cannabis Research

Population

▪ Consider the final study population
  ○ Example: a study designed to evaluate all adults ended up recruiting very few subjects over age 30

▪ . . . especially if subgroup-specific findings are reported
  ○ Example: decreased IQ was found among those with multiple years of cannabis use disorder, and not among the more general study population
Common Limitations of Cannabis Research

Exposure

- “Marijuana use” is often defined with a relatively low amount of exposure
  - Example: an “ever used” group compared with “never used”

- Self-report is the primary method of measuring use
  - Possible underreporting of use in general
  - Possible recall bias in case-control studies

- A true effect should usually be equal or greater in groups with more exposure (in a single study)
  - Example: an effect was statistically significant among less-than-weekly users, but not among weekly users
Common Limitations of Cannabis Research

Analysis

- Tobacco use and alcohol use are common and should be accounted for.
- Most cognitive studies have multiple test types:
  - Often find impairment in some tests but not others.
  - Interpreting the significance of findings is difficult.
  - Multiple comparisons should be statistically corrected for.
- Mental health and marijuana use have many shared predictors that should be accounted for.
Ecological studies

- Studies of the state-level effect of marijuana legalization should consider other policy and social differences
  - Example: policies designed to reduce opioid related outcomes are key in a pre-post MJ legalization analysis
  - Example: increases in hospital screening for marijuana use may increase apparent marijuana-related cases
The CDPHE report and the NAM report:

Comparison of findings
Notes on these comparisons

- Topics are included in these slides if:
  - Topics in the CDPHE report that are not addressed in the NAM report
  - There is an important difference in population, level of exposure or outcome measure
  - Findings are “Limited” or lower in one report and “Moderate” or higher in the other report

- Topics are not included in these slides if:
  - The evidence level is “Substantial” in one report and “Moderate” in the other
  - The evidence level is different, but among “Limited,” “Insufficient,” or “Mixed” in both reports
Respiratory

- We found LIMITED evidence that daily or near-daily marijuana smoking is associated with bullous lung disease leading to pneumothorax in individuals younger than 40 years of age.

- We found LIMITED evidence that after one month, weekly or daily marijuana smokers who switched to vaporizing had fewer respiratory symptoms and improved pulmonary function.
Driving

- Among less-than-weekly cannabis users, there is SUBSTANTIAL evidence of:
  - Driving impairment at blood levels of 2-5ng/ml
  - Smoking more than 10mg THC is likely to impair driving
  - Delaying driving for 6 hrs after smoking 18mg THC or less allows impairment to resolve or nearly resolve (MODERATE evidence of the same for 35mg or less)
  - Ingesting 10mg THC or more is likely to impair driving
  - Delaying driving for 8 hrs after ingesting 18mg or less allows impairment to resolve or nearly resolve

- We found INSUFFICIENT evidence about driving impairment among daily or near-daily cannabis users
Driving

(Both reports: cannabis use increases crash risk)

- We found SUBSTANTIAL evidence that the combined use of marijuana and alcohol increases driving impairment and motor vehicle crash risk more than use of either substance alone
Injury

- We found LIMITED evidence that marijuana use is associated with physical dating violence perpetration by adolescent girls and victimization among adolescent boys. (and not the converse)

- We found a LIMITED body of research that failed to show an association between marijuana use and physical dating violence among young adult men or women.
Cancer

- We found SUBSTANTIAL evidence that marijuana smoke, both mainstream and sidestream, contains many of the same cancer-causing chemicals as tobacco smoke.

- We found SUBSTANTIAL evidence that daily or near-daily marijuana smoking is associated with pre-malignant lesions in the airway.
Cancer

- We found SUBSTANTIAL evidence that daily or near-daily marijuana smoking is associated with pre-malignant lesions in the airway.

- We divided lung cancer evidence at 10 “joint-years” (equivalent to one joint/day for 10 years)
  - We found MIXED evidence for whether or not marijuana smoking greater than 10 joint-years is associated with lung cancer.
  - We found a MODERATE body of research that failed to show an association between marijuana smoking less than 10 joint-years and lung cancer.
Cardiovascular

- We found LIMITED evidence that acute marijuana use increases risk of myocardial infarction.

- We found LIMITED evidence that marijuana use increases risk of ischemic stroke in individuals younger than 55 years of age.
Pregnancy and Breast Feeding

- Biological evidence shows that THC is passed through the placenta of women who use marijuana during pregnancy and that the fetus absorbs and metabolizes the THC.

- Biological evidence shows that THC is present in the breast milk of women who use marijuana and that infants who drink breast milk containing THC absorb and metabolize the THC.
Pregnancy and Breast Feeding

- We found MIXED evidence for whether or not maternal use of marijuana during pregnancy is associated with low-birth weight infants.
  - The NAM report found substantial evidence of an association - review included one meta-analysis (Gunn 2016) and 3 primary studies
  - Our review included 6 primary studies, and was prior to Gunn 2016
  - This is the only significant contradiction between the two reports
  - We are currently reviewing newer research
Pregnancy and Breast Feeding

- We found MODERATE evidence that maternal use of marijuana during pregnancy is associated with these outcomes in exposed offspring:
  - Reduced cognitive function
  - Decreased IQ scores
  - Attention problems
  - Decreased growth
Cognitive and Achievement

- We found SUBSTANTIAL evidence that adolescents who use marijuana weekly or more frequently are less likely than non-users to graduate from high school.

- We found MODERATE evidence that adolescents and young adults who use marijuana weekly or more frequently are less likely than non-users to attain a college degree.
Mental Health

- We found SUBSTANTIAL evidence that THC intoxication can cause acute psychotic symptoms, which are worse with higher doses.
Gastrointestinal

- We found MODERATE evidence that long-time, daily or near-daily marijuana use is associated with cyclic vomiting (some medical experts call this cannabinoid hyperemesis syndrome).
Metabolism

THC blood levels after inhaling - peak at 12 minutes

THC blood levels after ingesting - peak at 4 hours
Secondhand Exposure and Testing

- We found INSUFFICIENT evidence to determine the health effects of secondhand marijuana smoke.
- We found SUBSTANTIAL evidence that typical secondhand exposure to marijuana smoke is unlikely to result in a failed workplace urine test or failed driving impairment blood test.
Extreme Secondhand Exposure

Individuals exposed to one hour of secondhand marijuana smoke in an unventilated space may experience:

- Increased heart rate
- Psychomotor impairment
- Can test positive
Opioids - state level comparisons

- We found INSUFFICIENT evidence to determine whether or not there is an association between the availability of legal medical marijuana and the prevalence of opioid use.
- We are currently reviewing studies on rates of opioid overdose, opioid-related hospitalizations, and other severe opioid-related outcomes.
Opioids - individual level comparisons

- We found MIXED evidence for whether or not marijuana use is associated with a reduction in the number of patients using opioids or the amount of opioid use among chronic pain patients.

- We found MIXED evidence for whether or not marijuana use is associated with a reduction in opioid use among individuals with a history of problem drug use (injection drug use or opioid addiction treatment).
Cannabis-Medication Interactions

- There is credible evidence of clinically important drug-drug interactions between cannabis and the following medications:
  - Chlorpromazine
  - Clobazam
  - Clozapine
  - CNS depressants (e.g. barbiturates, benzodiazepines)
  - Disulfiram
  - Hexobarbital
  - Hydrocortisone
  - Ketoconazole
  - MAO inhibitors
  - Phenytoin
  - Protease inhibitors (e.g. indinavir, nelfinavir)
  - Theophylline
  - Tricyclic antidepressants
  - Warfarin
Cannabis Research Gaps
Topics Lacking Research

- Effects of more frequent use, higher quantity of use and higher concentrations of THC
- Driving impairment:
  - In frequent users
  - With higher doses of THC
  - Evaluation methods that more accurately correlate with impairment
- Effects of secondhand cannabis smoke exposure
- Interactions between cannabis and prescription medications (drug-drug interactions)
Topics Lacking Research

- More on effects of prenatal exposure, especially miscarriage, birth weight and early childhood development
- Cannabinoid presence/duration in breastmilk and effects on exposed infants
- Factors related to adolescent initiation, including legalization, perceptions, marketing & merchandising, parental influences and education efforts
Improvements Needed in Research

- More prospective longitudinal studies would be ideal - most likely nested in broader studies
- Better classification of exposure
  - Collect use data on times/day or times/week
  - Separate groups with occasional or heavy use
  - Effects of former use after various periods of abstinence to assess duration
- Improved data collection and analysis for potential confounders
- Trials, such as driving impairment studies, should use doses consistent with current THC
Retail Marijuana Public Health Advisory Committee Members

- Mike Van Dyke, PhD, CIH  
  CDPHE Environmental Epidemiology, Committee Chairman
- Shireen Banerji, PharmD, DABAT  
  Poison Center Representative
- Laura Borgelt, PharmD  
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Thank you!
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