

Health and social effects of non-medical cannabis use: An Update

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Disclosure

- WH
 - Consultant to WHO in 2016 and 2019-2022
 - Consultant to EMCDDA in 2018.
 - Consultant to Australian government 2017-2018
 - Member of Australian Advisory Council on Medical Uses of Cannabis 2018-2021

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 - Consultant to WHO in 2019-2022
 - Consultant to EMCDDA in 2015, 2016, 2021-2022
 - Consultant to German Government in 2016-2018 and 2020-2022.

Causal inferences about cannabis harms

- Cannabis use & the adverse effect are associated
- Separating cannabis effects from other variables
 - Alcohol, tobacco and stimulants and other drugs.
 - cognitive ability
 - psychosocial characteristics
 - Genetic risks
 - etc.
- What comes first: cannabis use or adverse effect?
- Is a causal relationship biologically plausible?
- How do the harms of cannabis compare with other drugs?

Acute adverse effects

Acute adverse effects

- **Low acute toxicity**
 - No fatal, unlike opioids (i.e., no respiratory depression)
- **Risk of overdose**
 - Heart attacks and strokes in heavy smokers
- **Acutely impaired cognitive functioning**
- **Anxiety, dysphoria, panic, paranoia, psychosis**
 - Common among naive users and experienced users who take more or higher dose of cannabis than planned.

Accidental injury

- **Impaired psychomotor performance:** Evidence of dose-dependent relationship
 - Supported by complex laboratory tasks & simulated driving studies and small number of on-road driving studies.
- **Risk of accident (RR~ 1.3-2.1)**
 - Among recent cannabis users, larger if alcohol and cannabis are both used.
 - Supported by meta-analyses of case control and culpability studies.
- **Risk of driving fatalities**
 - Supported by larger epidemiological studies, controlling for alcohol.
 - Contribution to fatal accidents (attributable risk) is much smaller than alcohol (2.8% vs 28% in France, 2005).

Adverse effects of long-term regular use

Adverse effects of long-term regular use

- What do we mean by longer term regular use?
 - “Daily or near daily use”
 - “Use over months and years”
 - Most studied pattern: daily use from teens to early 30s

Cognitive impairment

■ Impaired cognitive performance

- There is evidence of a dose-dependent association between cannabis and cognitive functioning.
- Support from cognitive lab tasks.

■ More impairment in long-term daily users

- Support from case-control studies and neuroimaging studies

■ IQ decline

- Longitudinal Dunedin cohort finds an 8-point IQ decline in early cannabis users who used daily throughout 20s into 30s.

=> How reversible are these effects?

Educational attainment

- Meta-analysis of 3 Australasian studies (Horwood et al. 2010):
 - Cannabis use predicted **higher rates school drop out, lower rates of educational achievement, and lower rates of high-school completion**
 - **Poor school performers** were more likely to use cannabis.
 - Associations were small but persisted after statistical adjustment.

What is cause and what is effect?

- poor school performers → use cannabis
- cannabis → impairs school performance
- Probably both are true!

Cannabis dependence

- **Treatment for cannabis-related problems**
 - A substantial number of cannabis users seek help to quit cannabis
 - Cannabis is the primary drug among first-time drug treatment entrants (e.g., EMCDDA 2021).
- **Prevalence of cannabis use disorder in epidemiological studies**
 - 9% of lifetime users (in early 1990s in USA)
 - 16% in adolescent initiators; 33-50% of daily users
 - Meta-analysis updated these risk estimates (Leung et al.; 2020): 20% in past year users.
- **Various consequences ...**
 - respiratory symptoms
 - impaired cognitive and work performance
 - social consequences (e.g., problems with family, job, financial situation)
 - diminished life satisfaction.

Cannabis use and schizophrenia

- **Dose-dependent relationship between cannabis use and symptoms of psychosis.**
 - is supported by cohort studies in Australia, NZ, NL, and Germany
 - 27 year follow up of Swedish cohort (N = 50,000): RR = 3, dose response that persisted after statistical adjustment.
- **Use of higher THC products** is associated with more cases of psychosis
 - Meta-analysis: RR=3.9
- **Shared genetic risks** for cannabis use and psychosis
- **Biologically plausible causal relationship**
 - Cannabinoid-dopamine interaction
 - provocation studies using THC in normal and affected persons
- **Comparative evaluation: better evidence than alcohol and stimulants**

Mood Disorders and Suicide

- **Dose-dependent relationship**
 - **Depression** (RR ~ 1.6 in cross sectional and longitudinal studies)
 - **Bipolar disorder**
 - **Anxiety disorders**
 - **Higher suicide risks** (some studies, including prospective studies with limited statistical power).
- Causality less clear
 - Control of confounders?
 - Self-medication?
 - Does cannabis worsen symptoms and course of disease?

Cannabis use during pregnancy

- **Lower birth weight** and increased **prematurity** of newborn
- **Birth defects, cognitive impairment in childhood and adolescence**
- Limitations:
 - Most studies rely on self-reported cannabis use
 - Low statistical power
 - Confounding

=> Because of potential risks, cannabis use during pregnancy or breastfeeding should be discouraged !

Respiratory effects and cancers

Respiratory effects

- Increased cough, sputum, wheeze
- Impaired immunological responses
- Conflicting evidence on respiratory function

Risk reduction?

- vaporizers

- ingestible cannabis

Cancer

- Case reports of histopathological changes and lung cancer.
- Composition of cannabis smoke: tar, carcinogens and particulates.

=> *Conflicting epidemiological evidence, confounded by tobacco smoking*

Other cancers

- **Childhood cancers**
 - Old case control studies of 3 different cancers
 - Cannabis use measured as a possible confounder
 - Results not replicated and no trends in their incidence
- **Prostate cancer**
 - Single cohort study: modest RR
 - Confounding a risk: AIDS deaths in cohort
- **Testicular cancer**
 - Three case-control studies and two replications
 - Cannabis use and dose related risk of non-seminomas
 - Further studies needed: CB receptors in testes

Cardiovascular effects

- **THC is a potent cardiovascular stimulant**
 - Increases heart rate acutely and has complex effects on BP
 - Case reports of myocardial infarction and strokes in young users.
 - Concern about cardio-vascular risks in older (medical) cannabis users.

- **Myocardial infarction**
 - Case-crossover study found a doubling of MI risk in hours after *smoking* cannabis, consistent with provocation studies.
 - Longitudinal study indicates higher mortality in cannabis *smokers*.

Conclusions

- **Major adverse mental and social effects of non-medical cannabis:**
 - Acute risks, overdoses and accidental injury
 - Cannabis dependence
 - Poorer cognition and educational attainment
 - Impaired reproductive outcomes
 - Worsening of mental health
 - Physical health effects are likely (respiratory, cardiovascular, cancer), but evidence is unclear.
- **Limitations**
 - Cannabis is under-studied compared to alcohol, tobacco, opioids or stimulants
 - Number users, who used cannabis “near daily” for decades in studies is small.
 - Measuring “cannabis dose” is a challenge.

Thank you!

Contributing experts

- Wayne Hall: introduction and epidemiology of cannabis use, scientific editing of the report
- Susan Weiss and Janny Leung: epidemiology of cannabis use
- Marylin Huestis: neurobiology and pharmacology
- Eva Hoch: adverse effects of acute and chronic health and psychological effects
- Jason Connor and Daniel Stépjanovic: treatment of cannabis dependence
- David Jernigan: prevention
- Sarah Yeats: Formatting and Proofreading

WHO

- Vladimir Poznyak & Team
- TECHNICAL EXPERTS ON PUBLIC HEALTH RESPONSES TO PUBLIC HEALTH RISKS ASSOCIATED WITH CANNABIS USE AND CANNABIS USE DISORDERS, MEETING on 18-20 DECEMBER 2019
WHO HEADQUARTERS, GENEVA, SWITZERLAND