

## EMCDDA Symposium at Lisbon Addictions 2022

Emerging changes in Europe's cannabis situation: policy preparedness and responses to a dynamic situation

### Cannabis-related effects and harms: a scientific overview

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# DISCLOSURE

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## **Author disclosure:**

### **JM**

- has worked as consultant for public health agencies (e.g. World Health Organization; European Monitoring Centre for Drugs and Drug Addiction);
- has received honoraria for presentations/workshops/manuscripts funded by various public health agencies;
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**There are no industry links for any author.**

# METHODS

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## (non-systematic) literature review based on the following sources:

1) Comprehensive **overviews** published by national or international health agencies

*WHO 2016; German Ministry of Health 2017; US-based National Academies of Sciences, Engineering, and Medicine 2017*

2) Peer-reviewed **systematic review** on *all* cannabis-related outcomes *Campeny et al., 2020*

3) Additional **PubMed searches** for systematic reviews on *specific* outcomes

## Selection of key harms:

A) 100% attributable to cannabis use (e.g., cannabis use disorder)

B) Other harms:

- At least 3 high-quality primary studies (i.e., longitudinal, case-control, or experimental)
- Adjustment for important confounders
- Consistent effects demonstrated in at least 1 meta analysis

# Conceptual overview of different type of cannabis-related harms

## Harms experienced by the user

PHYSICAL HEALTH

MENTAL HEALTH

COGNITIVE

SOCIAL

LEGAL

## Harms experienced by others

Cannabis exposure during pregnancy

## Many meta-analyses but some have (serious) methodological flaws

### Meta analysis 1 *Rogeberg and Elvik 2016*

- Pooled Odds Ratio from 17 case-control studies: **1.60 (1.19-2.15)** but lower when analysing only high-quality and studies with control for confounders

### Meta analysis 2 *Hostiuc et al., 2018*

- Pooled Odds Ratio for injury or death from 10 case-control studies with blood testing to determine cannabis exposure: **1.97 (1.35-2.87)**



## 2 Meta analyses *Guernsey et al. 2015; Ghasemiesfe et al. 2019*

- Three US-based case-control studies on non-seminoma testicular germ cell tumor:
- Dose-response relationship possible: Pooled Odds Ratios for
  - Current use: **2.09 (1.29-3.37)**
  - At least weekly use: **2.59 (1.60-4.19)**
  - At least ten years of use: **2.40 (1.52-3.80)**

## 1 Meta analysis *Song et al. 2020*

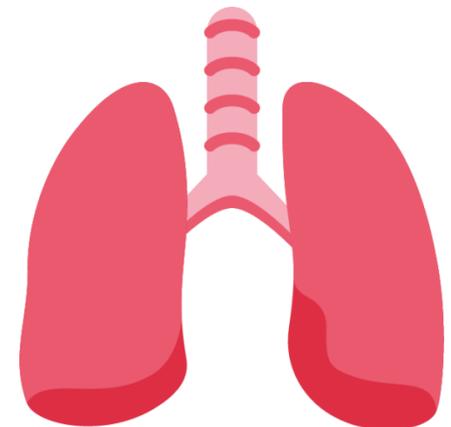
- One additional prospective study (Swedish conscripts): confirmed link to cannabis use

**Biological pathway:** not clear

**High rates of cannabis and tobacco co-use in Europe (77-91%)** *Hindocha 2016*

**3 Systematic reviews** *Mehra et al., 2006; Huang et al., 2015; Ghasemiesfe et al. 2019*

- **No** consistent relationship in cohort and case-control studies (total: 8 studies) *after* adjustment for tobacco use
- No dose-response relationship observable in most studies
- Despite biological plausibility (e.g., tar in cannabis smoke), smoking cannabis (without tobacco) is **unlikely** to increase the risk for lung cancer



**Meta analysis 1** *Moore et al., 2007*

- Pooled Odds Ratio from 6 prospective cohorts comparing heavy (weekly or dependence) cannabis use to non-users for psychotic outcomes: **2.09 (1.54-2.84)**
- 3 studies for psychotic disorders: **2.58 (1.08-6.13)**

**Meta analysis 2** *Robinson et al., 2022*

- Pooled Relative Risk from 8 case-control and 2 prospective studies:
  - Monthly use: **1.07 (0.88-1.31)**
  - Weekly use: **1.29 (1.08-1.54)**
  - (near) daily use: **1.69 (1.34-2.13)**



**Additional systematic reviews:** earlier age of onset (*Large et al., 2011*) and worse prognosis for people with psychosis who keep using cannabis (*Schoeler et al., 2016*)



### **Depression: 2 Meta analyses** *Moore et al., 2007; Lev-Ran et al., 2014*

- Pooled Odds Ratio from 8 prospective cohorts comparing heavy (weekly or dependence) to infrequent cannabis use: **1.49 (1.15-1.94)**
- Pooled Odds Ratios from 10 prospective cohorts for any use (**1.17; 1.05–1.30**) and heavy use (**1.62; 1.21–2.16**)

### **Suicide attempts: 3 meta analyses** *Fresán et al., 2022; Borges et al., 2016; Silins et al., 2014*

- Pooled Odds Ratio from 20 studies (mostly cross-sectional but 7 cohort studies) for any cannabis smoking before age 22: **2.33 (1.78-3.05)**
- Dose response relationships also identified

**Caveat:** common genetic heritability of cannabis use disorder, depression and suicidality

## 1 Meta analysis *Power et al., 2021*

- 7 cohort studies: reduction of Intelligence Quotient by 2 (0.99–2.97) points for frequent or dependent cannabis use during adolescence

## Learning and Memory/Decision making/Executive Functioning *Lovell et al. 2020*

- Acute effects: clear impairment from experimental studies
- Chronic effects: worse among cannabis users in cross-sectional studies
  - Meta-analysis of prospective studies not available



## Education: 1 Meta analysis *Horwood et al., 2010*

- 3 cohort studies from Australia and New Zealand: higher rates of educational attainment for early onset cannabis use
- Odds ratios for no cannabis use before age 18 vs. cannabis use before age 15:
  - High school completion: **3.6 (2.6-4.9)**
  - University enrolment: **2.3 (1.8-3.1)**
  - University degree attained: **3.7 (2.8-4.9)**
- Findings confirmed in meta analysis with 1 other cohort *Silins et al 2014*

## Economic achievements

- Plausible given lower educational achievements
- meta-analysis of high-quality studies not available



## Arrests and imprisonment

- 100% cannabis-attributable
- Consequences are hardly studied (e.g., disadvantages for employment)

## Adulterations

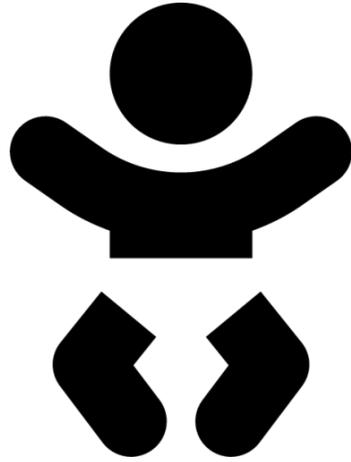
For example: *involuntary* consumption of synthetic cannabinoids; EVALI (vitamin E acetate in illegally sold THC cartridges)

- Occurrence of deaths and severe injuries linked to illegal status of cannabis
- Evidence mostly based on poor-quality studies (e.g. case control) with unknown ascertainment of exposure

# HARM TO OTHERS

## 1 Meta analysis *Duko et al., 2022*

- Pooled Odds Ratio of 27 (mostly prospective) studies for pre-term delivery related to cannabis use during pregnancy: 1.35 (1.24–1.48)



## Other plausible detrimental effects but quality criteria not met:

- Low birth weight in offspring of mothers with continued cannabis use during pregnancy
  - lower birthweight found (*Marchand et al., 2022*) but not when controlling for confounders (*Conner et al., 2016*)
- Respiratory & cardiovascular problems from exposure to second-hand cannabis smoke
  - No high-quality studies identified
- Physical harms to innocent persons involved in cannabis-attributable car accident
  - No high-quality studies identified

# Conceptual overview of different type of cannabis-related harms

## Harms experienced by the user

### PHYSICAL HEALTH

Injuries and deaths from motor vehicle accidents

Testicular Cancer

Lung cancer

### MENTAL HEALTH

Cannabis Use Disorder

Psychosis

Depression

Suicide

### COGNITIVE

Intelligence

Learning and Memory

Decision Making

### SOCIAL

Educational attainment

Economic achievements

### LEGAL

Consequences of arrests and imprisonment

Consequences of using adulterated products

## Harms experienced by others

Physical harms for being innocently involved in cannabis-attributable motor vehicle crashes

Physical health problems for people exposed to second-hand smoke

Cannabis exposure during pregnancy

Premature birth for offspring

Other adverse birth outcomes

## LEGEND

100% cannabis-attributable or high level of evidence available

Plausible but (high-level) of evidence is lacking

# CONCLUSIONS

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- Cannabis use is related to harms across various domains (not only health)
  - **Rule of thumb:** (Heavy) cannabis use doubles the risks for most outcomes
  
- Cannabis use during adolescence more risky than during later life
  - e.g., intelligence, educational attainment, depression/suicide
  
- Further research required
  - For exposure to higher levels of THC (most primary studies are at least 10 years old)
  - For outcomes with low-quality evidence (e.g. cardiovascular problems)
  - For outcomes with high-quality evidence but unclear causal pathways (e.g. testicular cancer)
  - For outcomes with plausible causal pathways but no association (e.g. lung cancer)