Cannabis and psychiatric outcomes, including psychotic disorders and potency

Deborah Hasin, Ph.D.
Columbia University
High THC-potency in legal markets
September 16, 2022

Measurement issues for cannabis

Quantity of ETOH consumption in beverages containing alcohol, a legal substance

https://www.niaaa.nih.gov/guide

Potency of cannabis products and thereby THC exposure: a measurement challenge

- Unlike alcohol in the U.S., cannabis products are not standardized

- Potency of THC in cannabis products can vary widely by product (plant/flower, vaped oil, wax, shatter), where bought, etc.

- Consumer knowledge of THC levels in the products they use is low *(Hammond & Goodman, 2020)*

State laws and cannabis potency

RCL, MCL and use of potent concentrate cannabis products in past 30 days
2017, n=4,064

	Odds ratio	
2-level cannabis law variable	**Unadjusted**	**Adjusted**
RCL[b]	**1.94**	**1.61**
No RCL	reference	reference
3-level cannabis law variable		
RCL[b]	**2.41**	**2.61**
MCL-only[c]	**1.48**	**1.55**
No-CL (no RCL or MCL)	reference	reference
	Wald c^2 (dof=1), p-value	
Contrast between RCL & MCL effect	36.38, <0.0001	13.24, 0.0003

Hasin D et al., Drug Alch Dep 2021

RCL, MCL and use of potent concentrate cannabis products, past 7 days
2021, n=4,328

	Odds ratio	
2-level cannabis law variable	**Unadjusted**	**Adjusted**
RCL[b]	**1.30**	**1.20**
No RCL	reference	reference
3-level cannabis law variable		
RCL[b]	**1.45**	**1.47**
MCL-only[c]	**1.18**	**1.29**
No-CL (no RCL or MCL)	reference	reference
RCL vs MCL-only	**1.23**	1.14
	Wald c^2 (dof=1), p-value	
Contrast between RCL & MCL effect	**7.67**, 0.0055	1.91, 0.1655

Hasin D et al., Under review

Relationship of cannabis use to other mental disorders/conditions

Adolescent Cannabis Use:
Meta-analysis of risk of depression & anxiety in young adulthood

Figure 2. Forest Plot Showing Adjusted Odds Ratio (OR) and 95% CIs for Depression and Anxiety in Young Adulthood According to Cannabis Use in Individual Studies

Gobbi et al., JAMA Psychiatry 2019
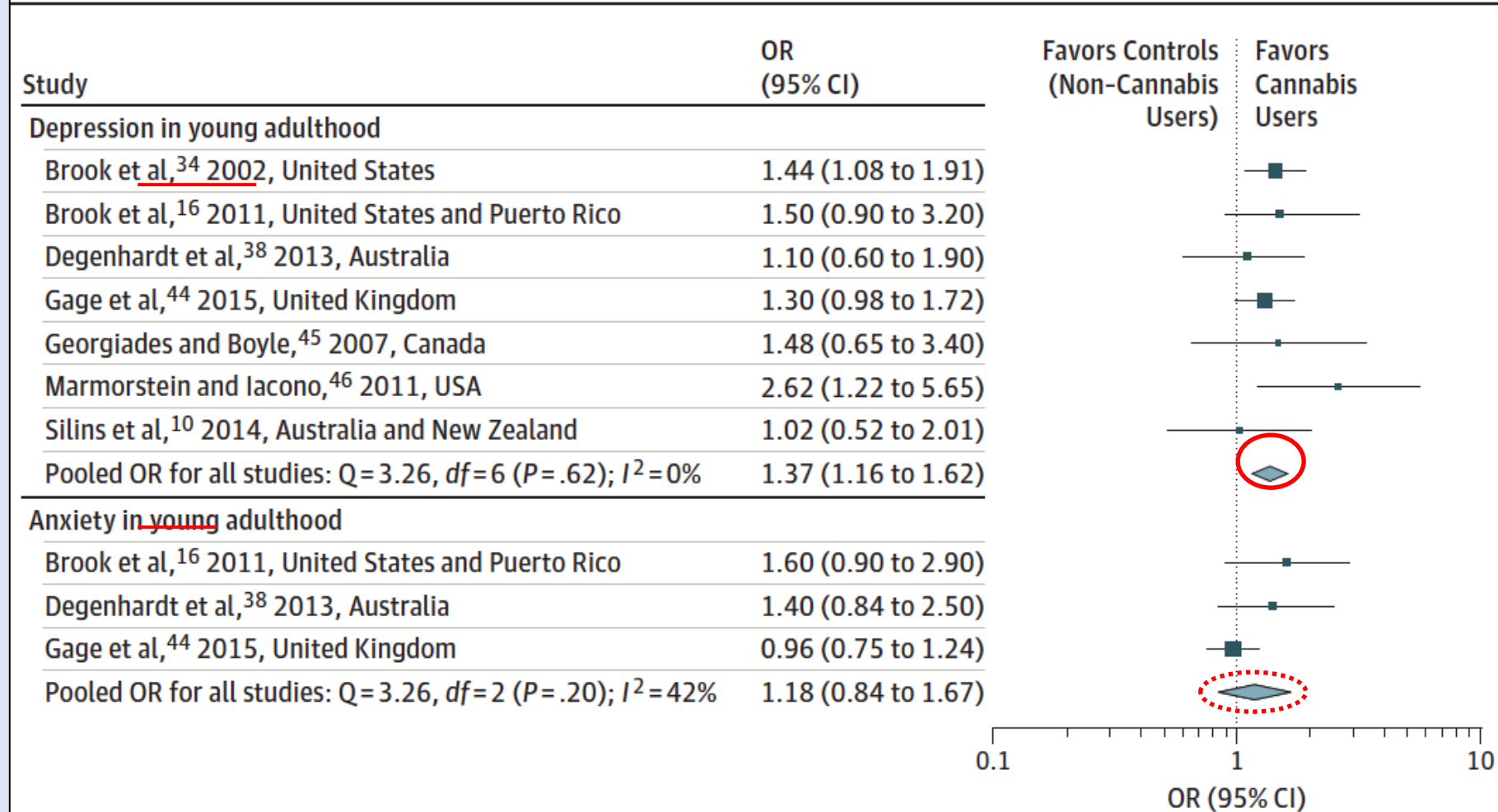
Adolescent Cannabis Use:
Meta-analysis of risk of suicidality in young adulthood

Figure 3. Forest Plot Showing Adjusted Odds Ratio (OR) and 95% CIs for Suicidal Ideations and Attempts According to Cannabis Use in Individual Studies

Study	OR (95% CI)	
Suicide ideations		
Fergusson et al,[41] 1996, New Zealand	1.40 (0.70 to 2.80)	
McGee et al,[47] 2005, New Zealand	1.10 (0.58 to 2.07)	
Weeks and Colman,[57] 2016, Canada	1.74 (1.16 to 2.60)	
Pooled OR for all studies: Q = 1.49, df = 2 (P = .48); I^2 = 0%	1.50 (1.11 to 2.03)	
Suicide attempts		
Roberts et al,[54] 2010, United States	4.81 (1.82 to 12.66)	
Silins et al,[10] 2014, Australia and New Zealand	6.83 (2.04 to 22.90)	
Weeks and Colman,[57] 2016, Canada	1.87 (1.09 to 3.22)	
Pooled OR for all studies: Q = 5.38, df = 2 (P = .07); I^2 = 61.3%	3.46 (1.53 to 7.84)	

Favors Controls (Non–Cannabis Users) — Favors Cannabis Users

OR (95% CI)

Gobbi et al., JAMA Psychiatry 2019

Cannabis use and psychosis, regardless of potency

Cannabis as a risk factor for psychosis: meta-analytic results

Marconi A et al., Schizophrenia Bull 2016
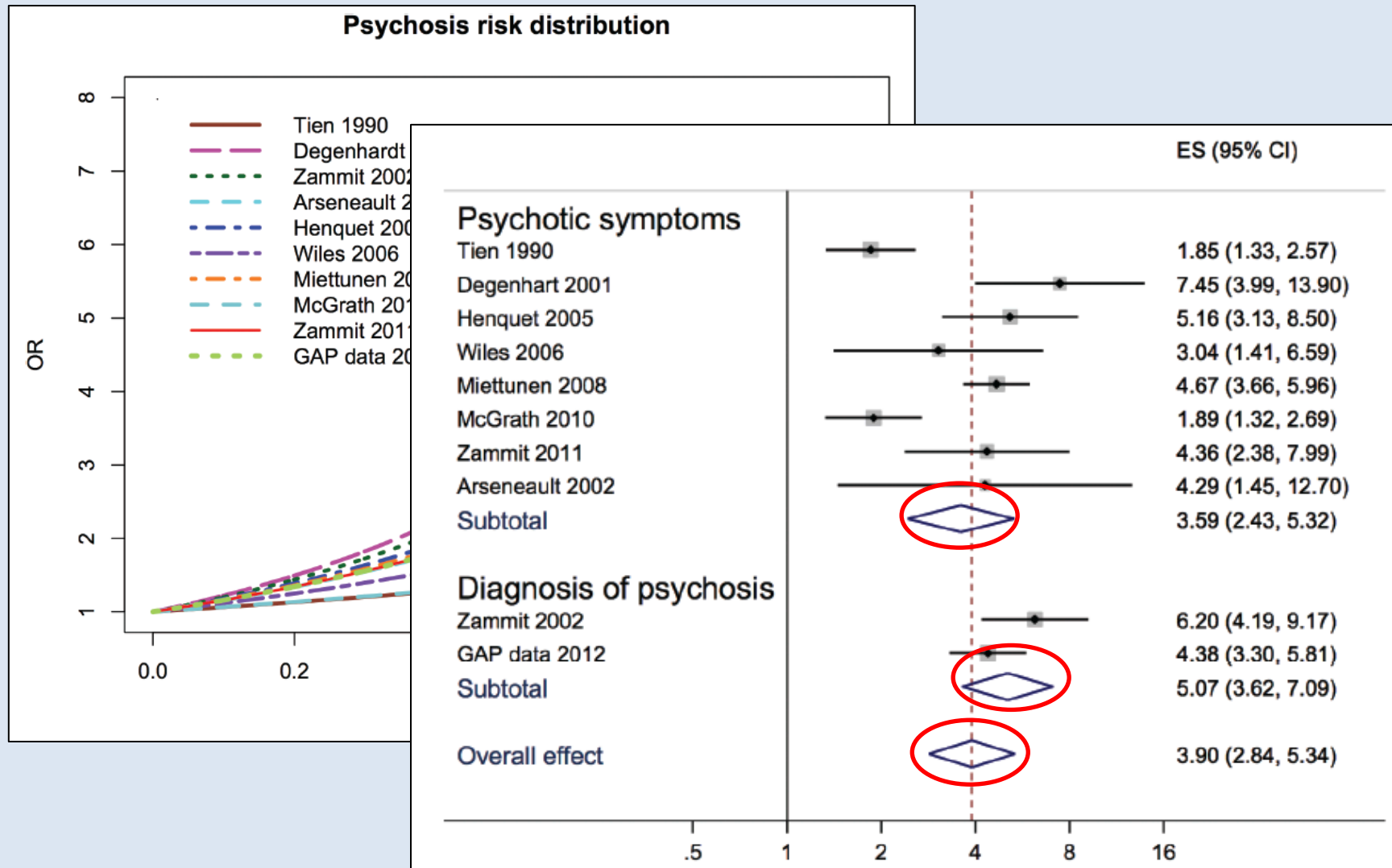
Among patients with psychosis, continued cannabis use and psychosis relapse

Figure 2: Random effects model of relapse and continued cannabis use versus non-use

Schoeler et al., Lancet Psychiatry 2016
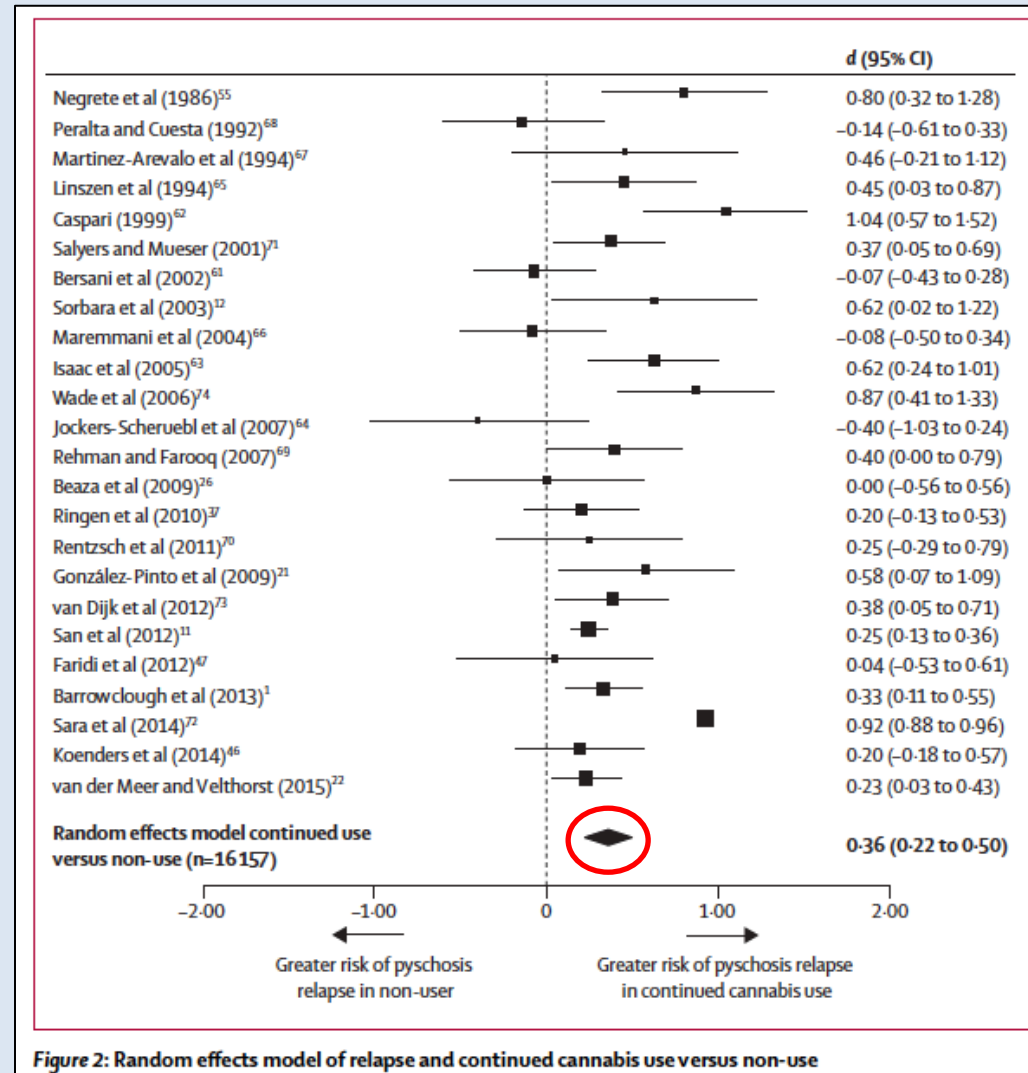
Cannabis use and self-reported psychotic disorders, National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) and NESARC-III
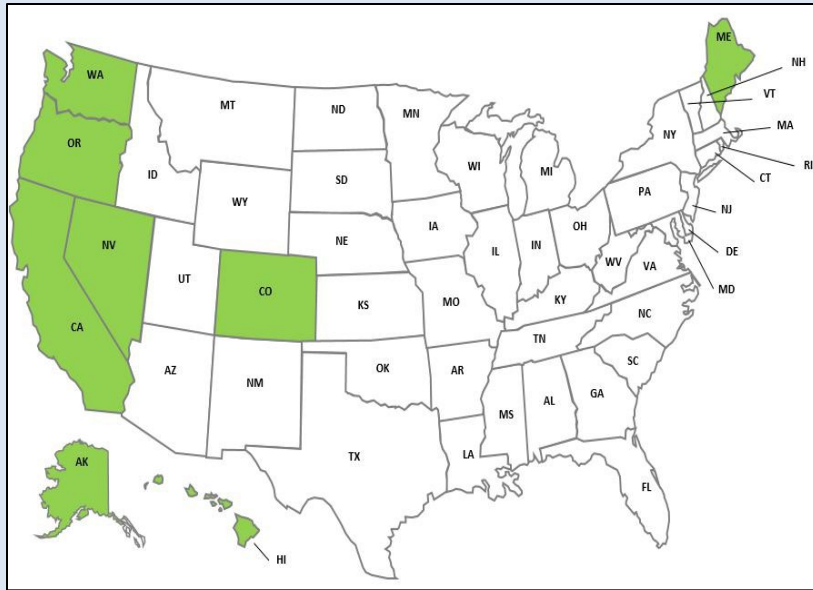
NESARC: 2001-2002
N=43,092

NESARC-III: 2012-2013
N=36,309

Livne O et al., Am J Psychiatry 2022
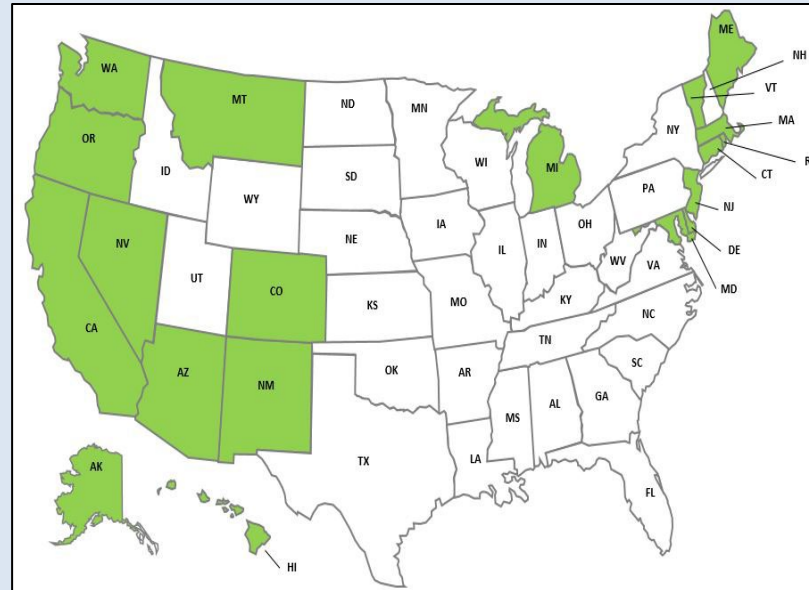
**Self-reported psychotic disorders,
NESARC and NESARC-III**

Did a doctor or other health professional tell the respondent they had schizophreniaor psychotic illness or episode in the past year?

NESARC (2001-2002)	NESARC-III (2012-2013)	Increase
0.33%	0.80%	0.47% (95% CI = 0.33, 0.61)

Research questions:
1. **Were self-reported psychotic disorders associated with non-medical cannabis use or Cannabis Use Disorder (CUD)?**
2. **Did associations change over time?**

Livne O et al., Am J Psychiatry 2022

Self-reported psychotic disorders by past-year cannabis variables (non-medical use) NESARC-III (2012-2013)

	N	Prevalence %
Total sample	36,309	**0.80**
Cannabis use groups		
No cannabis use	32,608	**0.68**
Any cannabis use	3,701	**1.89**
Frequent cannabis use	1,527	**2.79**
Daily/near-daily cannabis use	1,161	**2.52**
DSM-IV Cannabis Use Disorder	1,086	**3.38**
DSM-5 proxy Cannabis Use Disorder	1,104	**3.33**
Non-medical cannabis use: without a prescription or other than prescribed, e.g., to get high. **Self-reported psychotic disorders:** respondent-reported as diagnosed by MD or other health professional		

Livne O et al., Am J Psychiatry 2022

Self-reported psychotic disorders by past-year cannabis variables (non-medical use) NESARC-III (2012-2013)

	N	Prevalence %
Total sample	36,309	0.80

Self-reported psychotic disorders by past-year cannabis variables (non-medical use) NESARC-III (2012-2013)

	N	Prevalence %
Total sample	36,309	**0.80**
Cannabis use groups		
No cannabis use	32,608	**0.68**
Any cannabis use	3,701	**1.89**
Frequent cannabis use	1,527	**2.79**
Daily/near-daily cannabis use	1,161	**2.52**
DSM-IV Cannabis Use Disorder	1,086	**3.38**
DSM-5 proxy Cannabis Use Disorder	1,104	**3.33**
Non-medical cannabis use: without a prescription or other than prescribed, e.g., to get high **Self-reported psychotic disorders: respondent-reported as diagnosed by MD or other health professional**		

Livne O et al., Am J Psychiatry 2022

Association of self-reported psychotic disorders with past-year non-medical cannabis variables: odds ratios NESARC-III (2012-2013), N = 36,309

	Adjusted Odds Ratio
No cannabis use	*Reference group*

Livne O et al., Am J Psychiatry 2022

Association of self-reported psychotic disorders with past-year non-medical cannabis variables: odds ratios NESARC-III (2012-2013), N = 36,309

	Adjusted Odds Ratio
No cannabis use	*Reference group*
Any cannabis use	2.83
Frequent cannabis use	4.25
Daily/near-daily cannabis use	3.82
Cannabis Use Disorder	5.19
DSM-5 proxy Cannabis Use Disorder	5.12

Non-medical cannabis use: without a prescription or other than prescribed, e.g., to get high
Self-reported psychotic disorders: respondent-reported as diagnosed by MD or other health professional
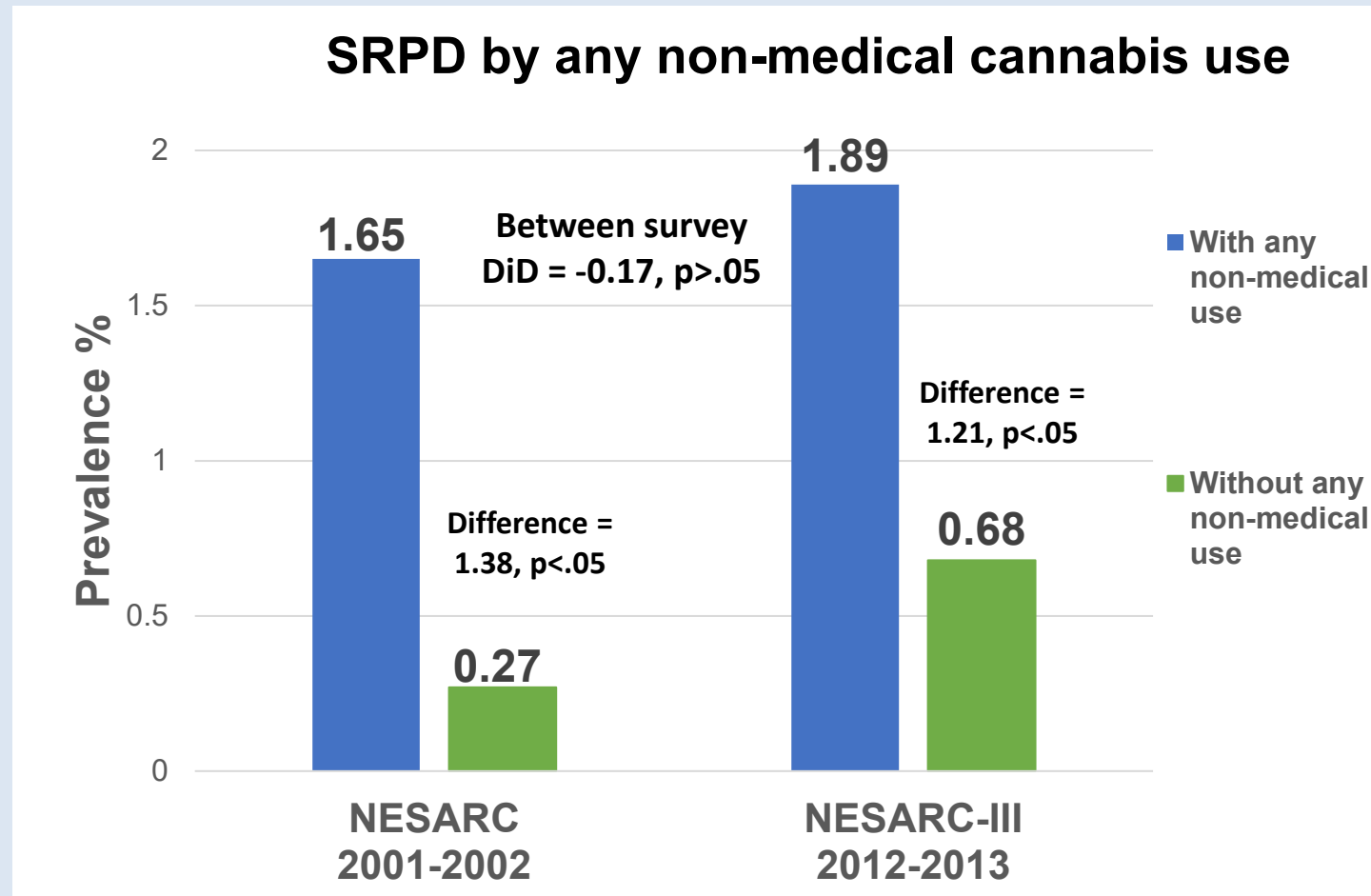Models adjusted for age, race/ethnicity, gender, education, and urbanicity

Livne O et al., Am J Psychiatry 2022

Did self-reported psychotic disorders (SRPD) differ between adults with and without non-medical cannabis use, 2001-2002 and 2012-2013?

SRPD by any non-medical cannabis use

- With any non-medical use
- Without any non-medical use

1.65

1.89

Between survey DiD = -0.17, p>.05

Difference = 1.21, p<.05

Difference = 1.38, p<.05

0.27

0.68

Prevalence %

NESARC 2001-2002

NESARC-III 2012-2013

Models adjusted for sociodemographic covariates

Livne O et al., Am J Psychiatry 2022

Did self-reported psychotic disorders (SRPD) differ between adults with daily/near daily cannabis use vs. no use, 2001-2002 and 2012-2013?

SRPD by daily/near daily use vs. no use

Between survey
DiD = 1.23, p>.05

2.52

Difference =
1.84, p<.05

0.88

Difference =
0.61, p>.05

0.68

0.27

Prevalence %

NESARC
2001-2002

NESARC-III
2012-2013

■ With daily/near daily cannabis use

■ Without any non-medical use
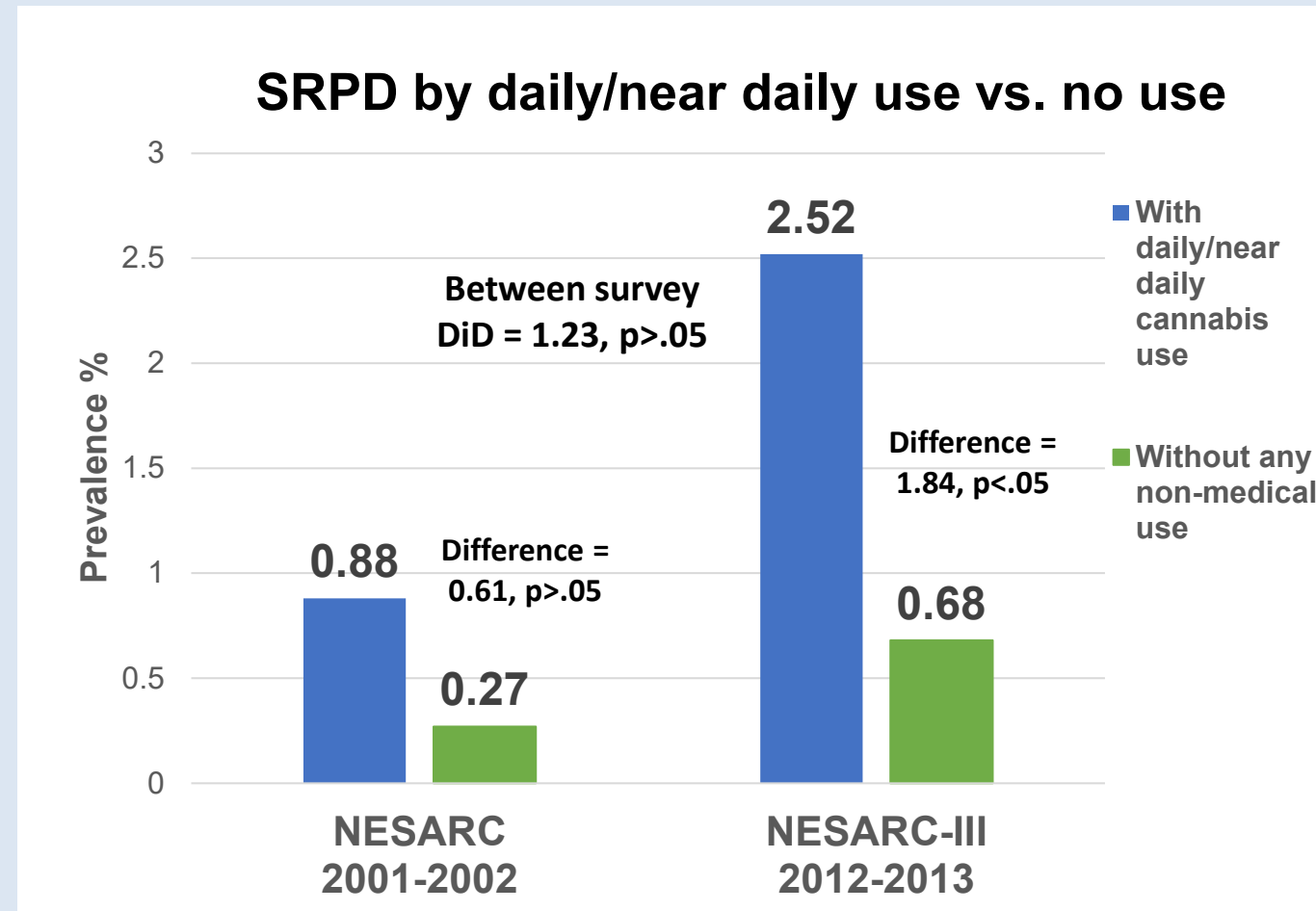
Models adjusted for sociodemographic covariates
Livne O et al., Am J Psychiatry 2022

Did SPRD differ between adults with DSM-5 cannabis use disorder (CUD) and non-users 2001-2002 and 2012-2013?

SRPD by proxy DSM-5 CUD compared to no use

Between survey DiD = 0.12, p>.05

Difference = 2.53, p<.05

Difference = 2.65, p<.05

3.33

2.8

0.27

0.68

Prevalence %

With Cannabis use disorder

Without any non-medical use

NESARC 2001-2002

NESARC-III 2012-2013
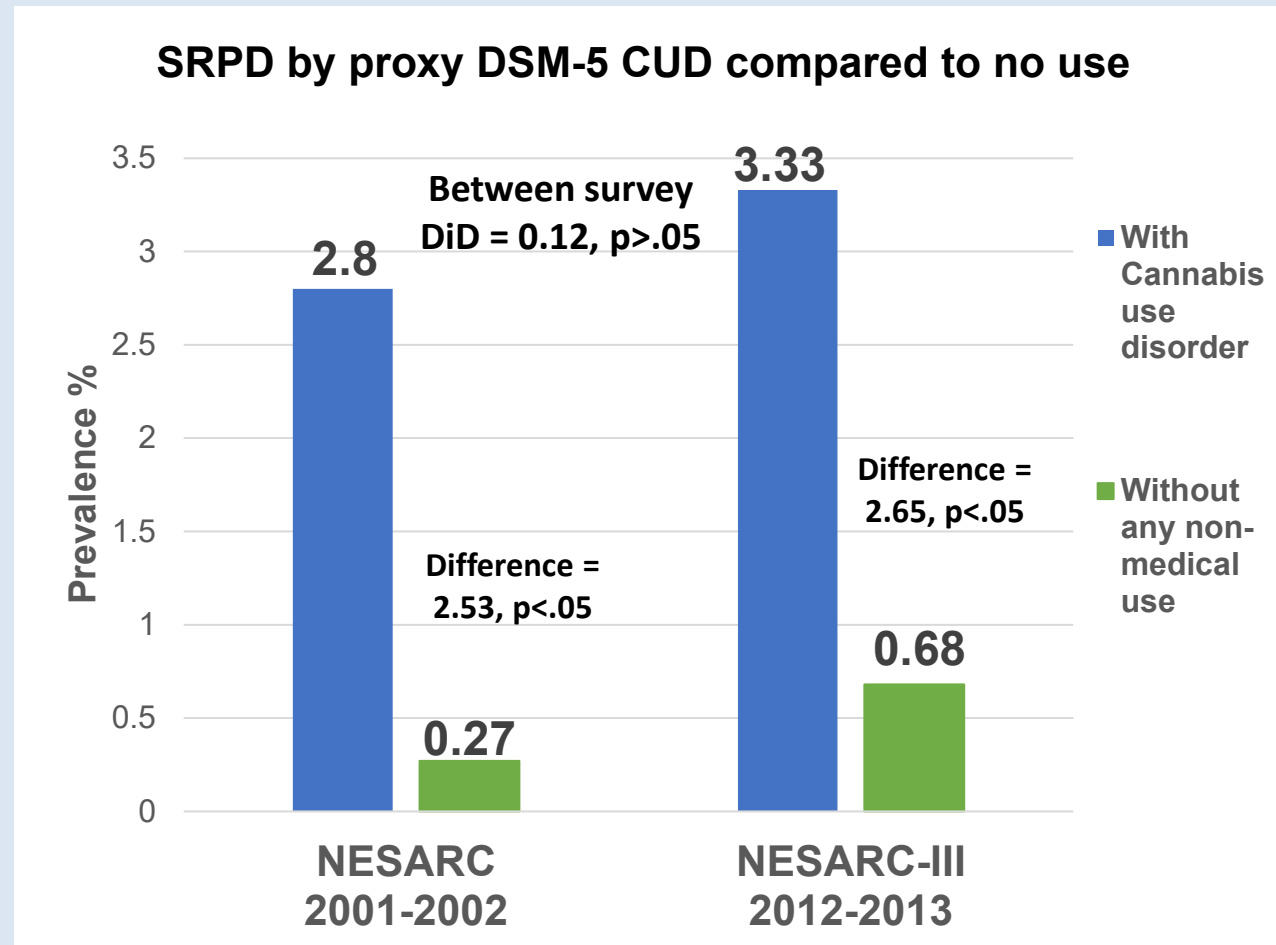
Models adjusted for sociodemographic covariates.
Livne O et al., Am J Psychiatry 2022

Incidence risk ratio of cannabis-induced psychosis and schizophrenia per year in Denmark

Cannabis-induced psychosis

Hjorthøj C et al., Psych Med 2019
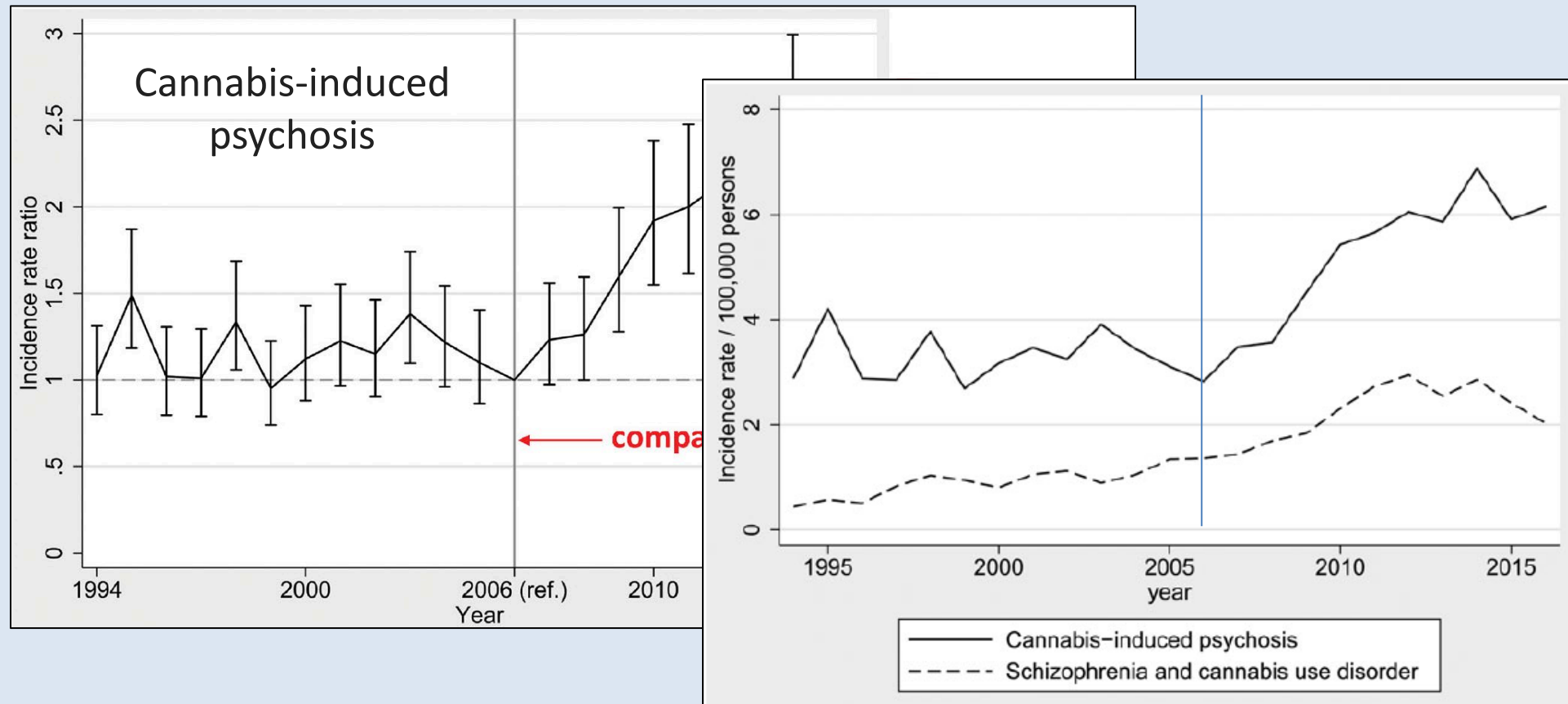
Cannabis potency and risk of psychosis

Genetics and Psychosis (GAP) study, London
Cannabis potency & risk of First-episode psychosis

Exposure: Cannabis & its potency
- **high-potency "Skunk" (12-14% THC)**
- **low-potency other (3.4%)**

Sample size	Comparison	Psychotic patients	Community controls	Adjusted Odds Ratio
N=454[1]	Any lifetime cannabis use	57%	63%	**1.0**
	Among users, those who used skunk	78%	37%	**6.8**

1 DiForti et al, Brit J Psychiatry 2009; 2 DiForti et al, Lancet Psychiatry 2015

Genetics and Psychosis (GAP) study, London
Cannabis potency & risk of First-episode psychosis

Exposure: Cannabis & its potency
- **high-potency "Skunk" (12-14% THC)**
- **low-potency other (3.4%)**

Sample size	Comparison	Psychotic patients	Community controls	Adjusted Odds Ratio
N=454[1]	Any lifetime cannabis use	57%	63%	**1.0**
	Among users, those who used skunk	78%	37%	**6.8**
N=780[2]	Any lifetime cannabis	67%	63%	**--**
	Used skunk	53%	19%	**2.9**
	Used skunk every day	25%	9%	**5.4**

1 DiForti et al, Brit J Psychiatry 2009; 2 DiForti et al, Lancet Psychiatry 2015

Cannabis use and incident psychotic disorder across Europe and Brazil: a multi-center case-control study, n=2138

Cannabis potency exposure:
high-potency: THC $\geq$ 10%
low-potency: THC < 10%

Comparison	Psychotic patients N=901	Community controls N=1237
Any lifetime cannabis use	65%	46%
Among users, those who used "high"-potency	37%	19%

DiForti et al, Lancet Psychiatry 2019

Cannabis use and incident psychotic disorder across Europe and Brazil: a multi-center case-control study, n=2138
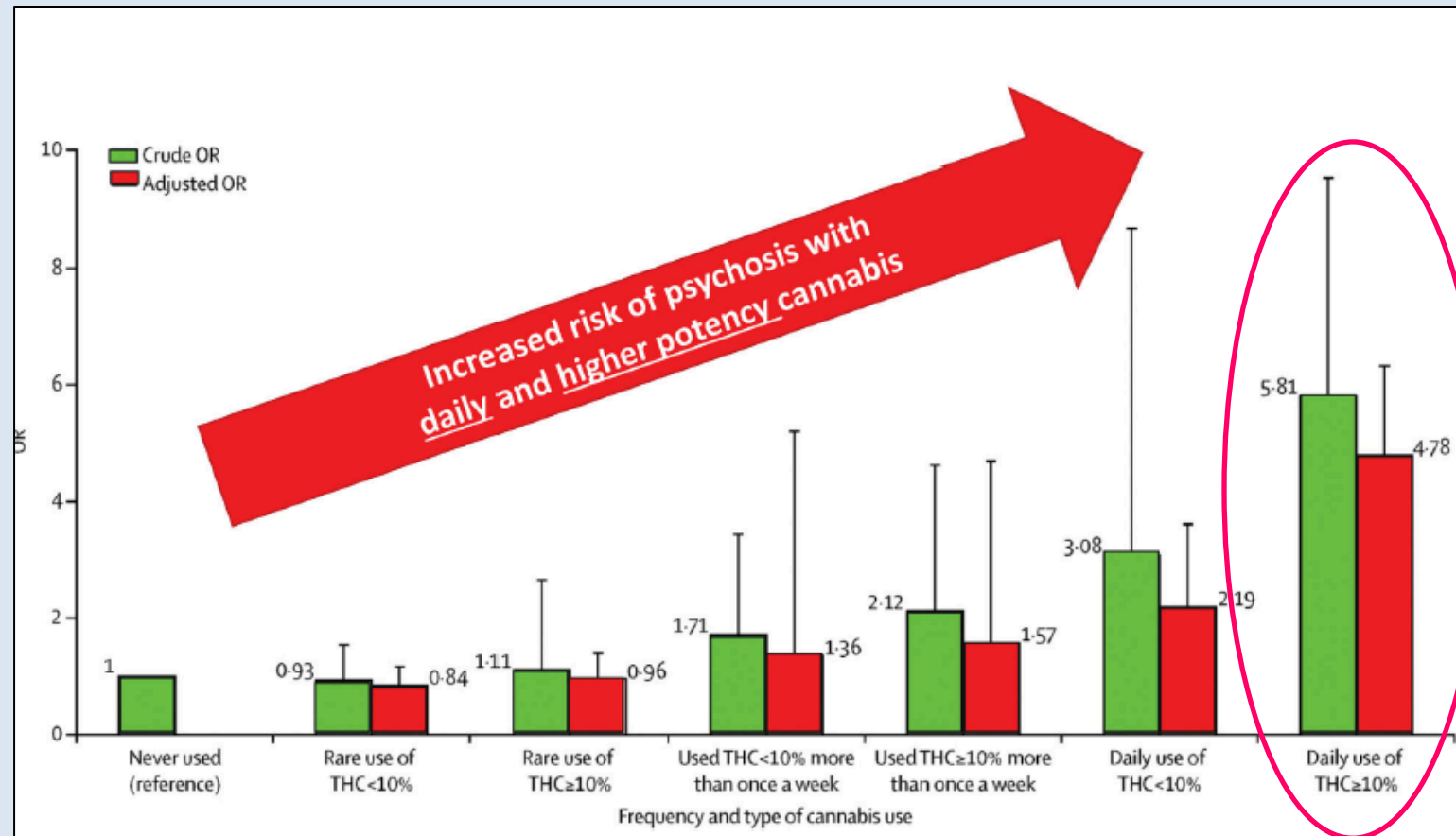
DiForti et al, Lancet Psychiatry 2019; D'Souza et al., World J Bio Psychiatry

Explanation of association of cannabis and psychosis: debate by geneticists

- Genetic researchers (e.g., Gillespie & Kendler, *JAMA Psychiatry* 2021) have suggested
  - Reverse direction: that schizophrenia leads to cannabis use
  - Shared genetic risk: the same factors causing both cannabis use and psychosis
- Classic criteria (Hill AB, *Proc R Soc Med* 1965) to investigate causality in associations:
  - Strength of association, consistency across studies
  - Specificity, temporal ordering
  - Biological gradient, plausibility
- Using these criteria, cannabis is seen by many as one potential cause of psychosis (Ganesh & D'Souza, *Am J Psychiatry* 2022)
- Ultimately, many genetic and environmental factors are likely to be responsible, with cannabis use as one of these factors

Summary and public policy implications

- Cannabis use is highly associated with increased risk for psychotic disorders and increased risk for relapse

- Most research on the effects of cannabis potency was conducted during years when "high"-potency cannabis was only 10%-14%, weak by today's standards

- From a health and prevention standpoint, reasonable to conclude that today's very high-potency cannabis products confer even greater risk for psychosis

- Although psychotic disorders are relatively rare in the general population, they are very debilitating and burdensome to patients and their families

- One public health reason (among many to) limit marketing of very-high potency cannabis products.

- Now that cannabis use is widely seen as harmless, some education for clinicians and the public also appears warranted

Contact information:
Deborah.hasin@gmail.com
dsh2@cumc.Columbia.edu