A Comprehensive Look at Cannabis Use Disorder

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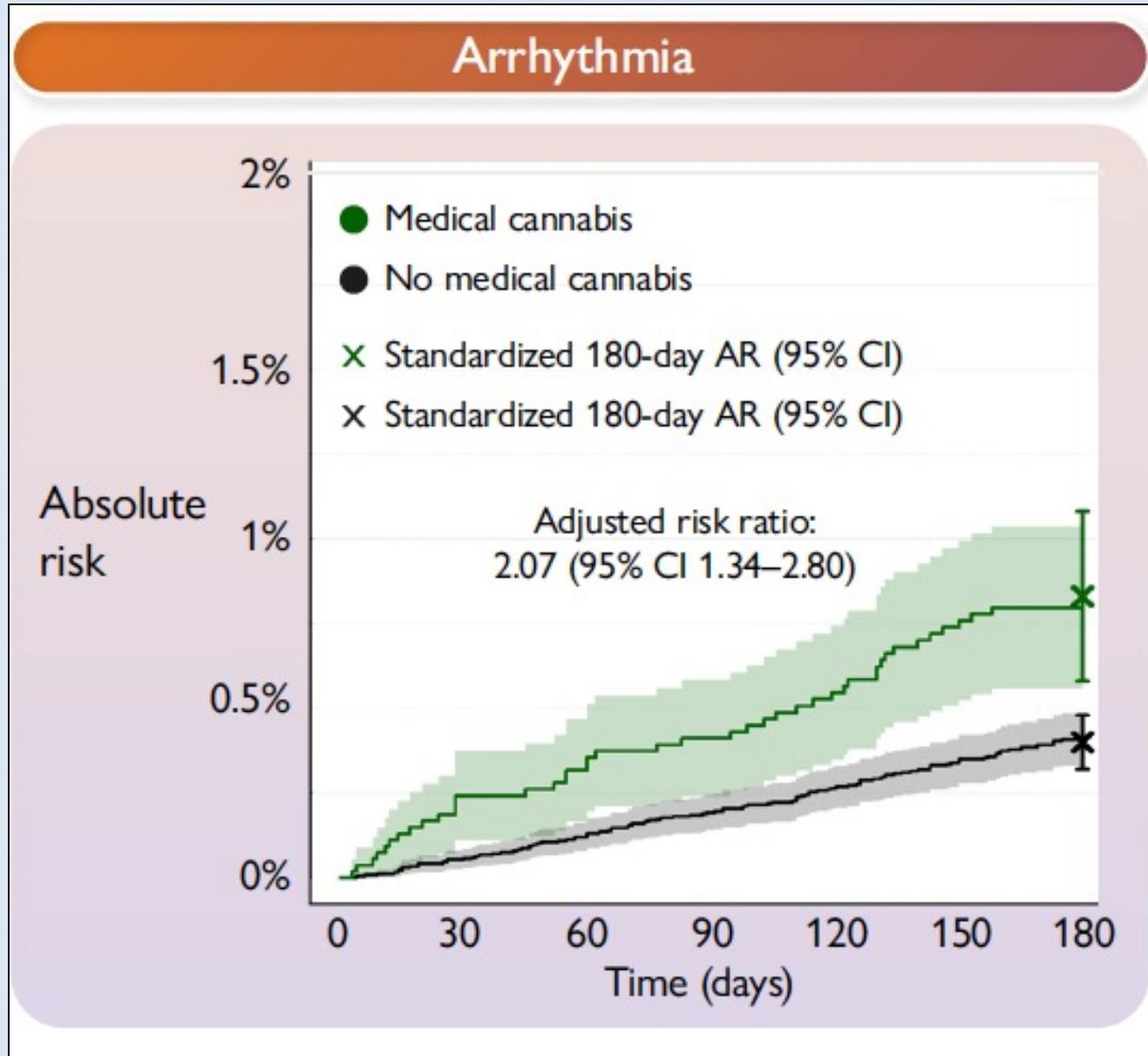January 12, 2024

Presentation overview

- Potential harms of adult cannabis use
- Cannabis Use Disorder (CUD)
  - Definitions
  - Clinical and psychosocial correlates
- Time trends in CUD prevalence
  - Overall
  - By Chronic pain
  - By Psychiatric disorders

Cannabis: potential harms

- First things first: cannabis does not have the same morbidity/mortality profile of opioids
- However, cannabis is not a harmless substance

Cannabis: elevated risk for first-time arrhythmia

Arrhythmia

- Medical cannabis
- No medical cannabis
- X Standardized 180-day AR (95% CI)
- X Standardized 180-day AR (95% CI)

Adjusted risk ratio:
2.07 (95% CI 1.34–2.80)
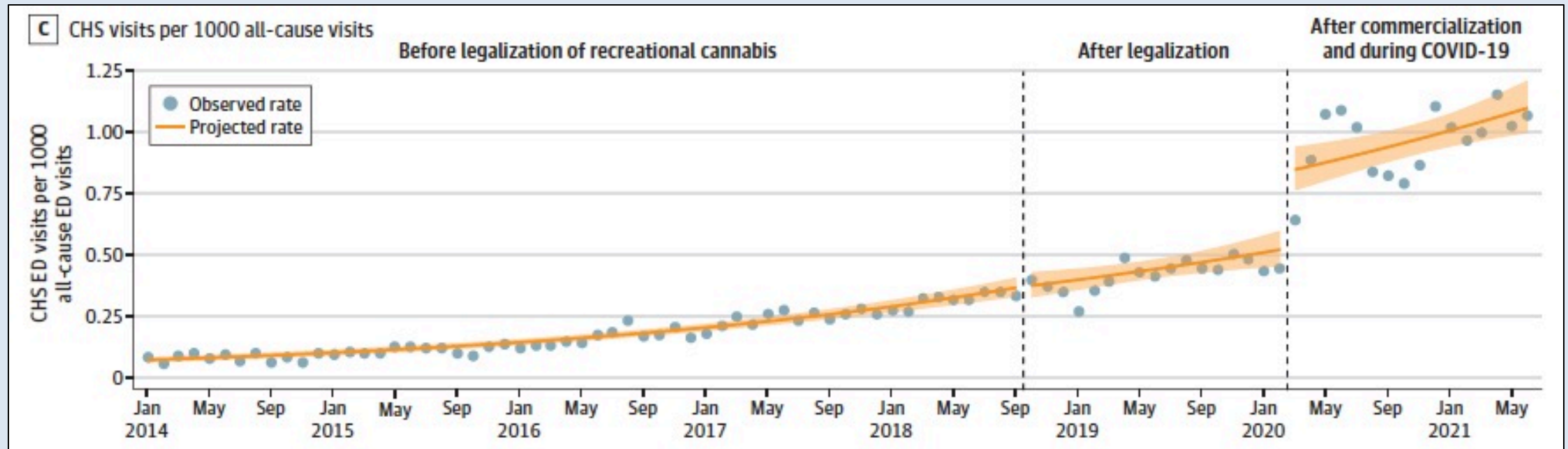
Absolute risk — Time (days)

- Registry study of 1.8 million Danish patients with chronic pain, median age 59 years
- Those with medical cannabis prescription compared to all others.
- 2-fold increased risk found for first-time arrhythmia (atrial fibrillation, condution disorders, paroxysmal tachycardias, ventribular arrhythmias)
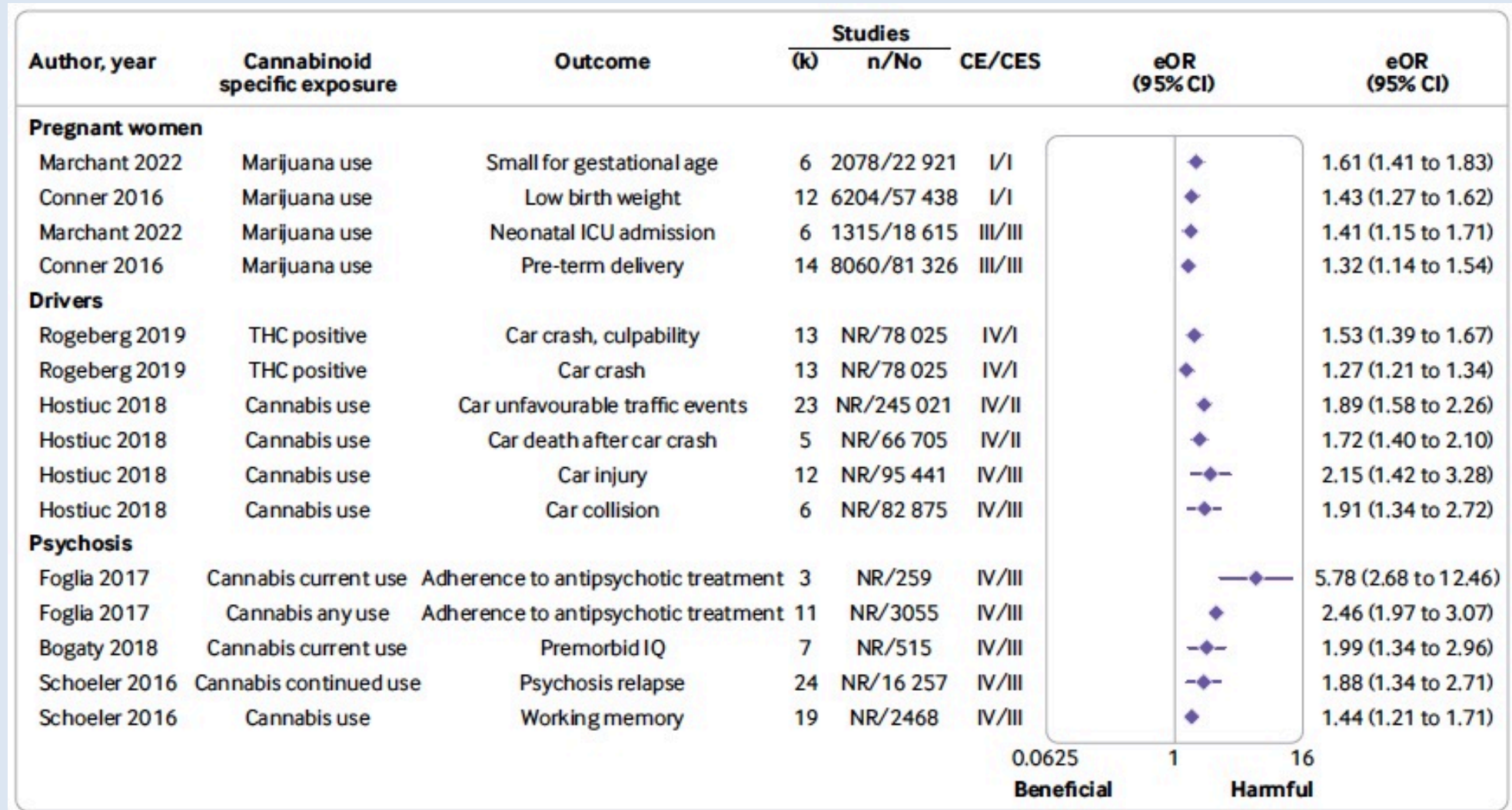
Holt et al., Eur Heart J 2023

Cannabis Hyperemesis Syndrome (CHS): Emergency Department Visits in Canada, 2014-2021
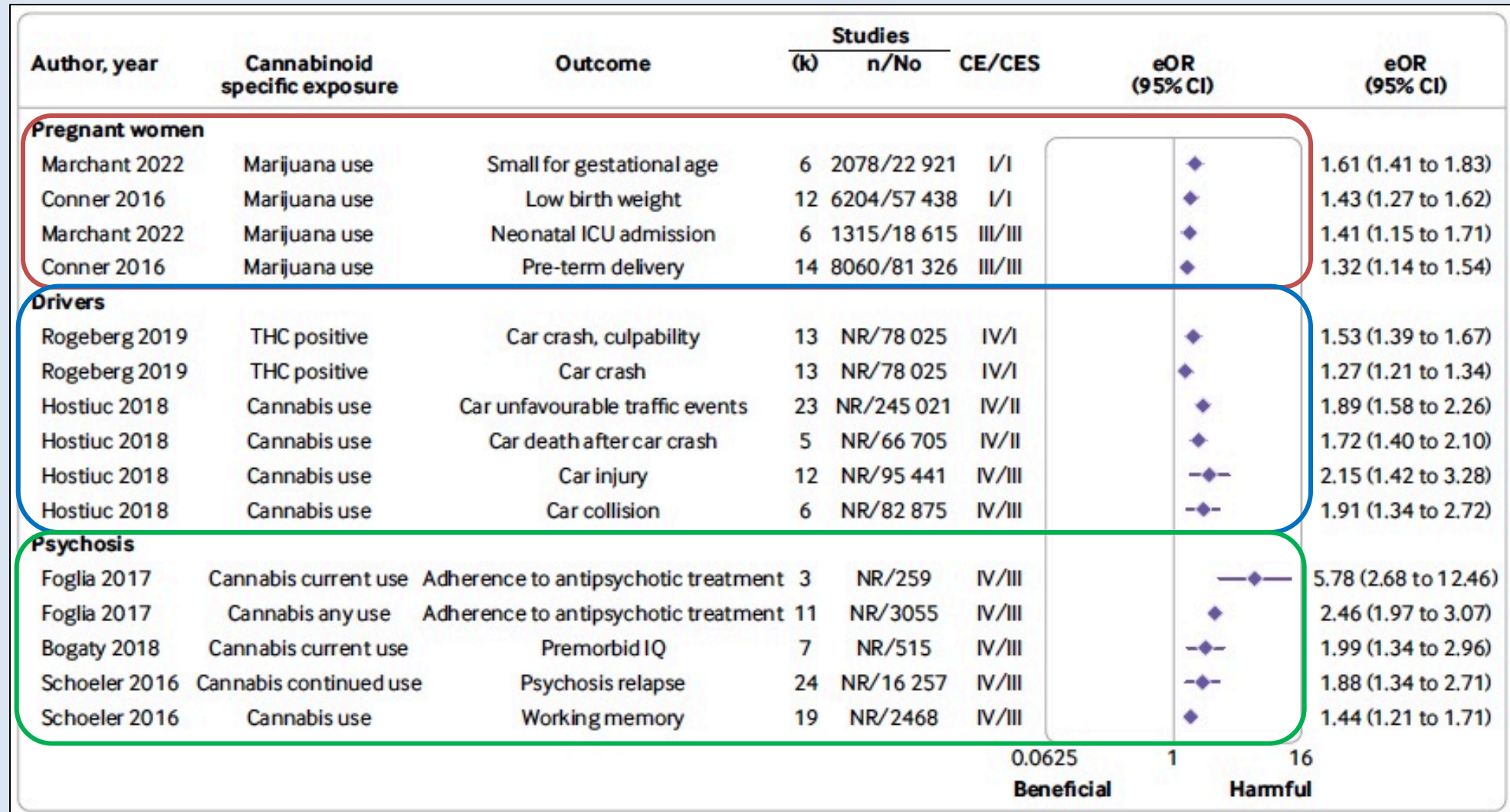
- Cannabis Hyperemesis Syndrome: repeated severe bouts of vomiting
- From 2014 – 2021, rates increased 13-fold
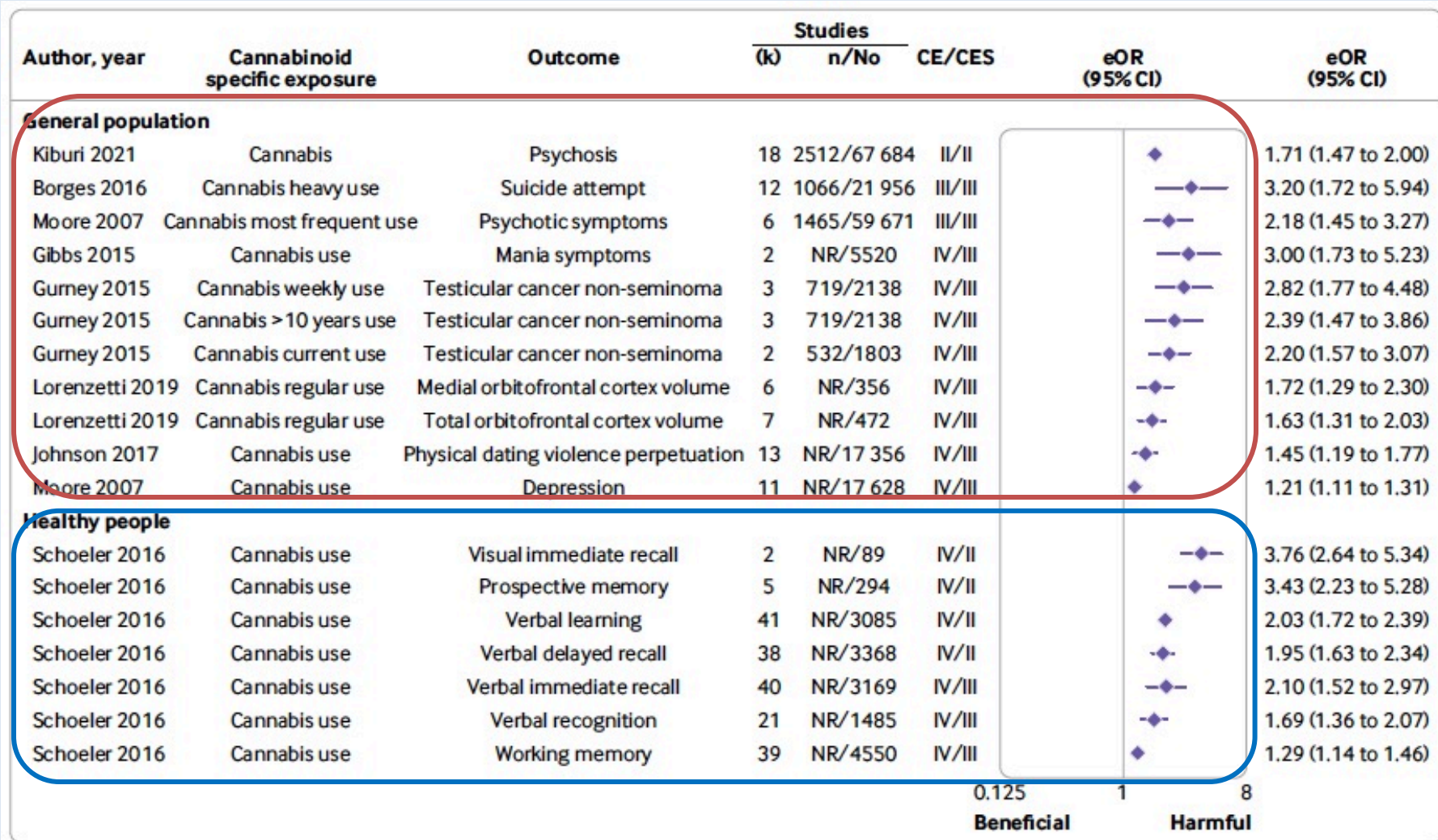- Increases since 2020 specific to CHS, not found for mental health, other substance use.

Myran et al., JAMA Network Open 2022

Meta-analysis: observational studies of harms of cannabis in pregnant women, drivers, & patients with psychosis

Author, year	Cannabinoid specific exposure	Outcome	Studies (k)	n/No	CE/CES	eOR (95% CI)	eOR (95% CI)
Pregnant women							
Marchant 2022	Marijuana use	Small for gestational age	6	2078/22 921	I/I		1.61 (1.41 to 1.83)
Conner 2016	Marijuana use	Low birth weight	12	6204/57 438	I/I		1.43 (1.27 to 1.62)
Marchant 2022	Marijuana use	Neonatal ICU admission	6	1315/18 615	III/III		1.41 (1.15 to 1.71)
Conner 2016	Marijuana use	Pre-term delivery	14	8060/81 326	III/III		1.32 (1.14 to 1.54)
Drivers							
Rogeberg 2019	THC positive	Car crash, culpability	13	NR/78 025	IV/I		1.53 (1.39 to 1.67)
Rogeberg 2019	THC positive	Car crash	13	NR/78 025	IV/I		1.27 (1.21 to 1.34)
Hostiuc 2018	Cannabis use	Car unfavourable traffic events	23	NR/245 021	IV/II		1.89 (1.58 to 2.26)
Hostiuc 2018	Cannabis use	Car death after car crash	5	NR/66 705	IV/II		1.72 (1.40 to 2.10)
Hostiuc 2018	Cannabis use	Car injury	12	NR/95 441	IV/III		2.15 (1.42 to 3.28)
Hostiuc 2018	Cannabis use	Car collision	6	NR/82 875	IV/III		1.91 (1.34 to 2.72)
Psychosis							
Foglia 2017	Cannabis current use	Adherence to antipsychotic treatment	3	NR/259	IV/III		5.78 (2.68 to 12.46)
Foglia 2017	Cannabis any use	Adherence to antipsychotic treatment	11	NR/3055	IV/III		2.46 (1.97 to 3.07)
Bogaty 2018	Cannabis current use	Premorbid IQ	7	NR/515	IV/III		1.99 (1.34 to 2.96)
Schoeler 2016	Cannabis continued use	Psychosis relapse	24	NR/16 257	IV/III		1.88 (1.34 to 2.71)
Schoeler 2016	Cannabis use	Working memory	19	NR/2468	IV/III		1.44 (1.21 to 1.71)

0.0625 — 1 — 16
Beneficial | Harmful

Meta-analysis – adverse outcomes of cannabis in pregnant women, drivers, & patients with psychosis

Author, year	Cannabinoid specific exposure	Outcome	Studies (k)	n/No	CE/CES	eOR (95% CI)	eOR (95% CI)
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0.0625   1   16

Beneficial   **Harmful**

Solmi M et al., Brit Med J 2023

Meta-analysis – adverse outcomes of cannabis use in the general population and in healthy individuals

Author, year	Cannabinoid specific exposure	Outcome	Studies (k)	n/No	CE/CES	eOR (95% CI)	eOR (95% CI)
General population							
Kiburi 2021	Cannabis	Psychosis	18	2512/67 684	II/II		1.71 (1.47 to 2.00)
Borges 2016	Cannabis heavy use	Suicide attempt	12	1066/21 956	III/III		3.20 (1.72 to 5.94)
Moore 2007	Cannabis most frequent use	Psychotic symptoms	6	1465/59 671	III/III		2.18 (1.45 to 3.27)
Gibbs 2015	Cannabis use	Mania symptoms	2	NR/5520	IV/III		3.00 (1.73 to 5.23)
Gurney 2015	Cannabis weekly use	Testicular cancer non-seminoma	3	719/2138	IV/III		2.82 (1.77 to 4.48)
Gurney 2015	Cannabis >10 years use	Testicular cancer non-seminoma	3	719/2138	IV/III		2.39 (1.47 to 3.86)
Gurney 2015	Cannabis current use	Testicular cancer non-seminoma	2	532/1803	IV/III		2.20 (1.57 to 3.07)
Lorenzetti 2019	Cannabis regular use	Medial orbitofrontal cortex volume	6	NR/356	IV/III		1.72 (1.29 to 2.30)
Lorenzetti 2019	Cannabis regular use	Total orbitofrontal cortex volume	7	NR/472	IV/III		1.63 (1.31 to 2.03)
Johnson 2017	Cannabis use	Physical dating violence perpetuation	13	NR/17 356	IV/III		1.45 (1.19 to 1.77)
Moore 2007	Cannabis use	Depression	11	NR/17 628	IV/III		1.21 (1.11 to 1.31)
Healthy people							
Schoeler 2016	Cannabis use	Visual immediate recall	2	NR/89	IV/II		3.76 (2.64 to 5.34)
Schoeler 2016	Cannabis use	Prospective memory	5	NR/294	IV/II		3.43 (2.23 to 5.28)
Schoeler 2016	Cannabis use	Verbal learning	41	NR/3085	IV/II		2.03 (1.72 to 2.39)
Schoeler 2016	Cannabis use	Verbal delayed recall	38	NR/3368	IV/II		1.95 (1.63 to 2.34)
Schoeler 2016	Cannabis use	Verbal immediate recall	40	NR/3169	IV/III		2.10 (1.52 to 2.97)
Schoeler 2016	Cannabis use	Verbal recognition	21	NR/1485	IV/III		1.69 (1.36 to 2.07)
Schoeler 2016	Cannabis use	Working memory	39	NR/4550	IV/III		1.29 (1.14 to 1.46)

0.125   1   8

Beneficial   Harmful

Solmi M et al., Brit Med J 2023

Increased risk found for other potential adverse outcomes of CUD or cannabis use

Outcome	Population	Citation
Cardiovascular events	59,528 Canadian residents	Bahji et al., Addiction 2023
Cannabinoid hyperemesis syndrome	55,549 U.S. inpatients	Patel et al., Psychosomatics 2019
Perioperative morbidity & mortality	12,422 U.S. non-cardiac inpatients	Potnuru et al., JAMA Surgery 2023
Psychotic and non-psychotic bipolar and unipolar disorder	6,651,765 Danish adults	Jefsen et al., JAMA Psychiatry 2023
Psychosocial problems	36,309 U.S. adults	Gutkind et al., Drug Alch Depen 2021
Cannabis use disorder, cannabis dependence	Multiple clinical and general population studies	Hasin et al., Am J Psychiatry 2013

Substance use disorders, defined: DSM-IV, DSM-5 criteria

- DSM-IV criteria published in 1994

- DSM-5 criteria published in 2013

- Criteria largely overlapped but structure was different

- DSM-5-TR (Text Revision) published in 2022

- DSM-5-TR updated text but did not change diagnostic criteria
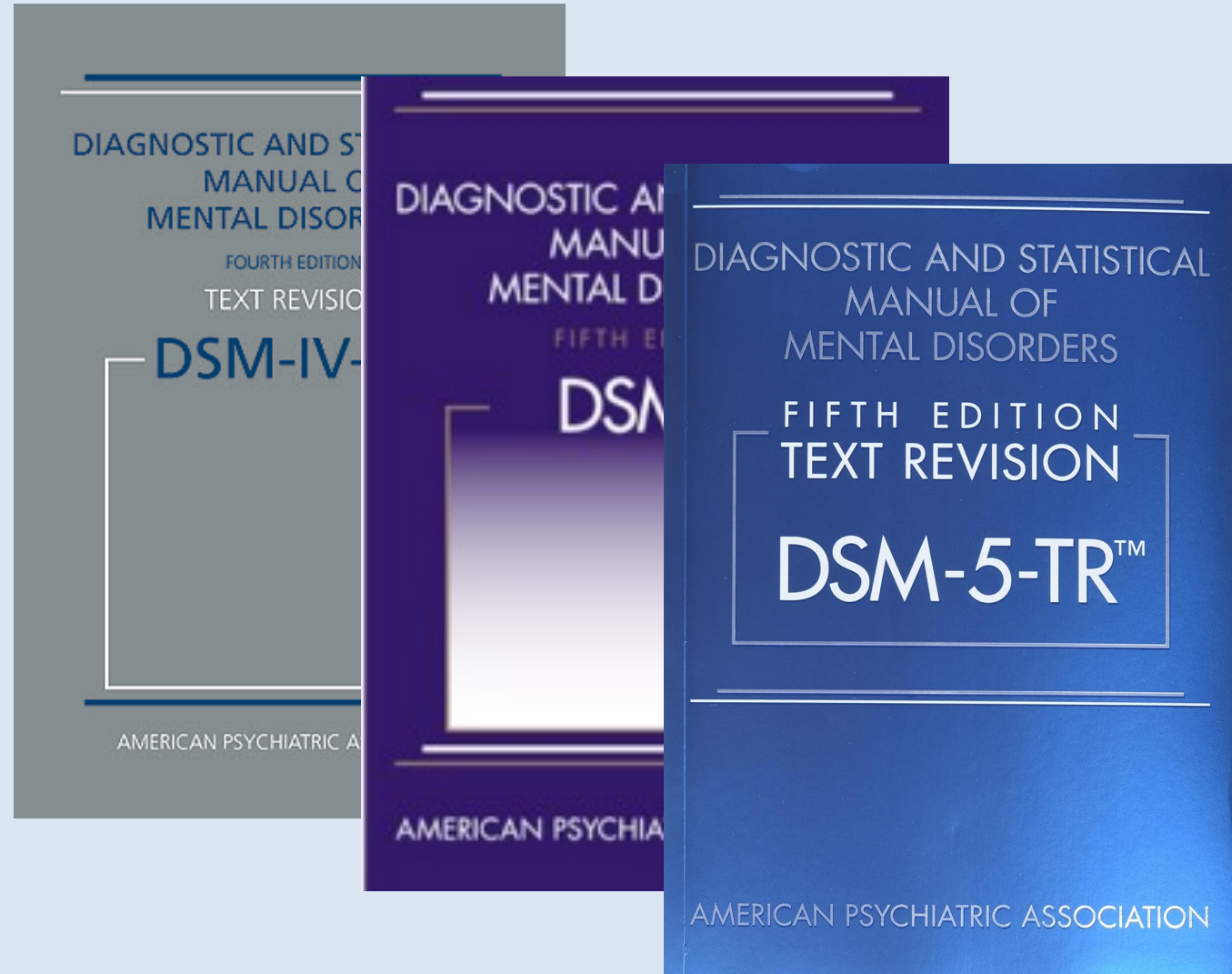
Substance Use Disorder Criteria: DSM-IV

Diagnostic Criteria	Abuse	Dependence
Failure to fulfill major role obligations	X	--
Hazardous use	X	--
Substance-related legal problems	X	--
Social/interpersonal substance-related problems	X	--
Tolerance	--	X
Withdrawal	--	X
Persistent desire/unsuccessful efforts to cut down	--	X
Using more or over for longer than was intended	--	X
Neglect of important activities	--	X
Great deal of time spent in substance activities	--	X
Psychological/Physical use-related problems	--	X
Diagnostic Threshold	**1+ criteria**	**3+ criteria**

(Abuse: 1+) (Dependence: 3+)

American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC, American Psychiatric Association, 2000.

DSM-5 Criteria for Substance Use Disorders: Recommendations and Rationale

Deborah S. Hasin, Ph.D.

Charles P. O'Brien, M.D., Ph.D.

Marc Auriacombe, M.D.

Guilherme Borges, Sc.D.

Kathleen Bucholz, Ph.D.

Alan Budney, Ph.D.

Wilson M. Compton, M.D., M.P.E.

Thomas Crowley, M.D.

Walter Ling, M.D.

Nancy M. Petry, Ph.D.

Marc Schuckit, M.D.

Bridget F. Grant, Ph.D.

Since DSM-IV was published in 1994, its approach to substance use disorders has come under scrutiny. Strengths were identified (notably, reliability and validity of dependence), but concerns have also arisen. The DSM-5 Substance-Related Disorders Work Group considered these issues and recommended revisions for DSM-5. General concerns included whether to retain the division into two main disorders (dependence and abuse), whether substance use disorder criteria should be added or removed, and whether an appropriate substance use disorder severity indicator could be identified. Specific issues included possible addition of withdrawal syndromes for several substances, alignment of nicotine criteria with those for other substances, addition of biomarkers, and inclusion of nonsubstance, behavioral addictions.

This article presents the major issues and evidence considered by the work group, which included literature reviews and extensive new data analyses. The work group recommendations for DSM-5 revisions included combining abuse and dependence criteria into a single substance use disorder based on consistent findings from over 200,000 study participants, dropping legal problems and adding craving as criteria, adding cannabis and caffeine withdrawal syndromes, aligning tobacco use disorder criteria with other substance use disorders, and moving gambling disorders to the chapter formerly reserved for substance-related disorders. The proposed changes overcome many problems, while further studies will be needed to address issues for which less data were available.

Cannabis Use Disorder Criteria: DSM-IV and DSM-5

	DSM-IV		DSM-5
	~~Abuse~~	~~Dependence~~	Cannabis Use Disorder
Diagnostic Criteria			
Failure to fulfill obligations	X	--	X
Hazardous use	X	--	X
~~Substance-related legal problems~~	X	--	--
Social/interpersonal substance-related problems	X	--	X
Tolerance	--	X	X
Withdrawal	--	X	X
Persistent desire/unsuccessful efforts to cut down	--	X	X
Using more or over for longer than was intended	--	X	X
Neglect of important activities	--	X	X
Great deal of time spent in substance activities	--	X	X
Psychological/Physical use-related problems	--	X	X
Craving	--	--	X
Diagnostic Threshold	**1+ criteria**	**3+ Criteria**	**Mild: 2-3 Moderate: 4-5 Severe: ≥6**

11 criteria

Example of pre-DSM-5 psychometric analysis of Cannabis Use Disorder criteria
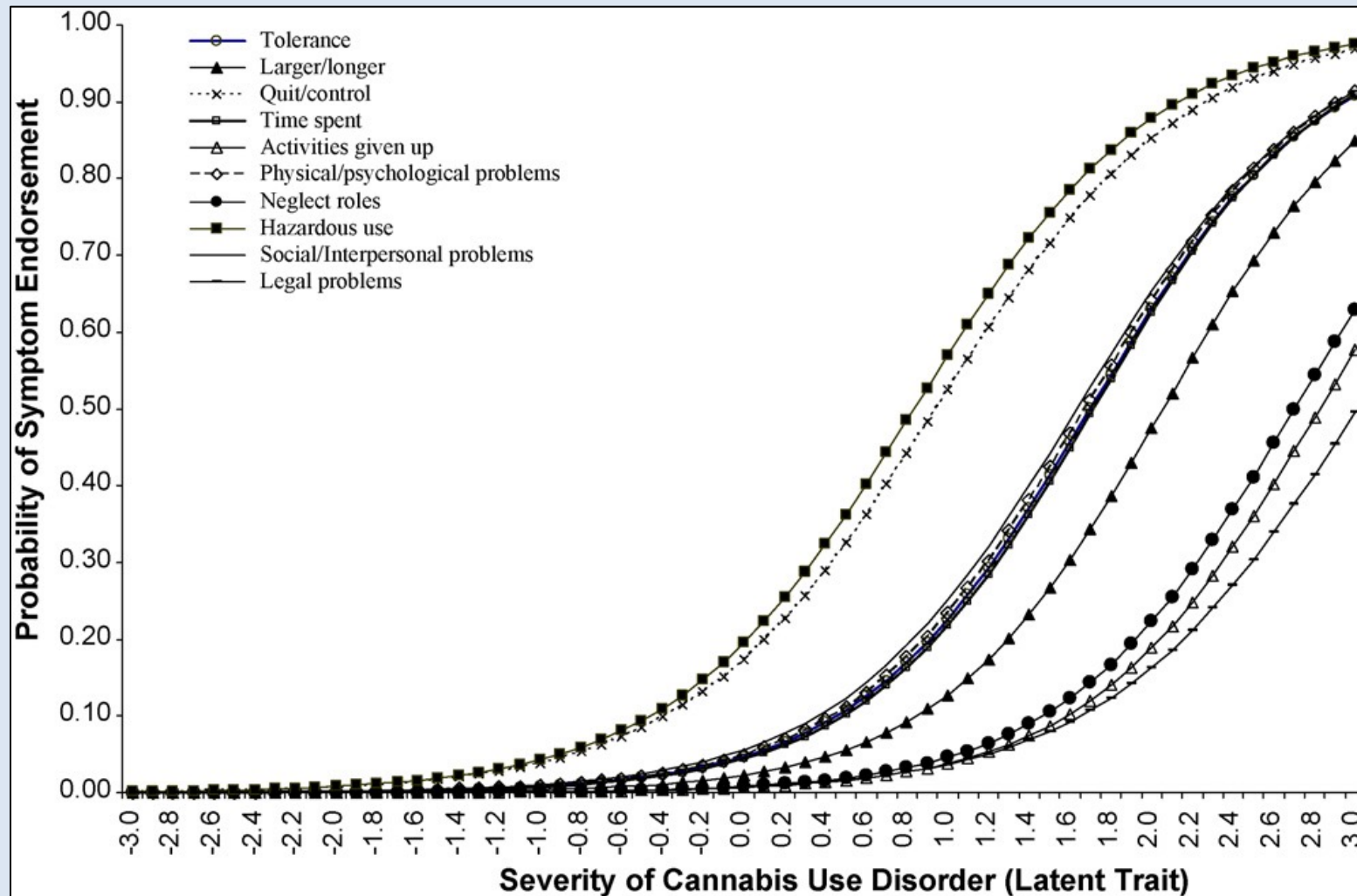
Compton et al., Drug Alch Dep 2009

Risk of Cannabis Use Disorder Among Individuals Who Use Cannabis

What is the prevalence and risk of cannabis use disorders among people who use cannabis? a systematic review and *meta*-analysis

Janni Leung[a,b,*], Gary C.K. Chan[b], Leanne Hides[a,b], Wayne D. Hall[b]

[a] School of Psychology, Lives Lived Well Group, The University of Queensland, Australia
[b] Centre for Youth Substance Abuse Research, The University of Queensland, Australia

HIGHLIGHTS

- There is a global shift towards cannabis legalization and underestimation of harms.
- A systematic review *meta*-analysed the risk of cannabis use disorders (CUD) from use.
- People who use cannabis have a 1 in 5 risk of developing a CUD.
- Risks increase if cannabis is initiated early and used frequently.
- The public needs to be informed about the risks of developing CUD from cannabis use.

Meta-analysis of risk for Cannabis Use Disorder[1] 3-17 years later, by frequency of use at initial assessment: 6 studies, 40,984 participants

Baseline cannabis use frequency	Relative Risk (RR) of follow-up Cannabis Use Disorder
Never	reference
1-11 days/year (yearly)	2.03
1-3 days/month (monthly)	4.12
1-4 days/week (weekly)	8.37
5-7 days/week (daily)	16.99

1 DSM-IV or DSM-5 CUD.
Significance of overall model: p<0.0001

Robinson T et al., Drug Alch Depend, 2022

DSM-5 Cannabis Use Disorder: Association with Other SUDs NESARC-III (2012-2013), N = 36,309

Comorbid DSM-5 Disorder	Adjusted Odds ratios 12-month DSM-5 Cannabis Use Disorder			
	Any	Mild	Moderate	Severe
Any other SUD	9.3	7.4	12.2	13.1
Alcohol use disorder	6.0	5.1	7.7	6.8
Other drug use disorder	9.0	6.6	11.5	13.4
Nicotine use disorder	6.2	4.8	7.3	10.5

Hasin et al., Am J Psychiatry 2016

DSM-5 Cannabis Use Disorder and psychiatric disorders:
NESARC-III (2012-2013), N = 36,309

Comorbid Disorder	Adjusted Odds Ratios 12-month DSM-5 Cannabis Use Disorder			
	Any	**Mild**	**Moderate**	**Severe**
Any mood disorder	3.8	2.8	3.5	8.1
Major depressive disorder	2.8	2.2	3.1	4.2
Bipolar I	5.0	3.4	4.1	10.1
Bipolar II	2.7	2.7	3.4	1.9
Any anxiety disorder	2.8	2.2	2.9	4.4
Panic Disorder	3.3	2.5	2.8	6.6
Agoraphobia	2.6	2.4	3.5	2.0
Social phobia	2.3	1.3	3.5	3.9
Specific phobia	1.7	1.4	2.2	1.9
Generalized anxiety	3.7	3.0	3.6	6.3
PTSD	4.3	2.1	6.2	9.5

Hasin et al., Am J Psychiatry 2016

Impaired functioning in adults with DSM-5 CUD NESARC-III, 2012-2013
≥ 0.5 S.D. below population norm
SF-12v2 functioning scale
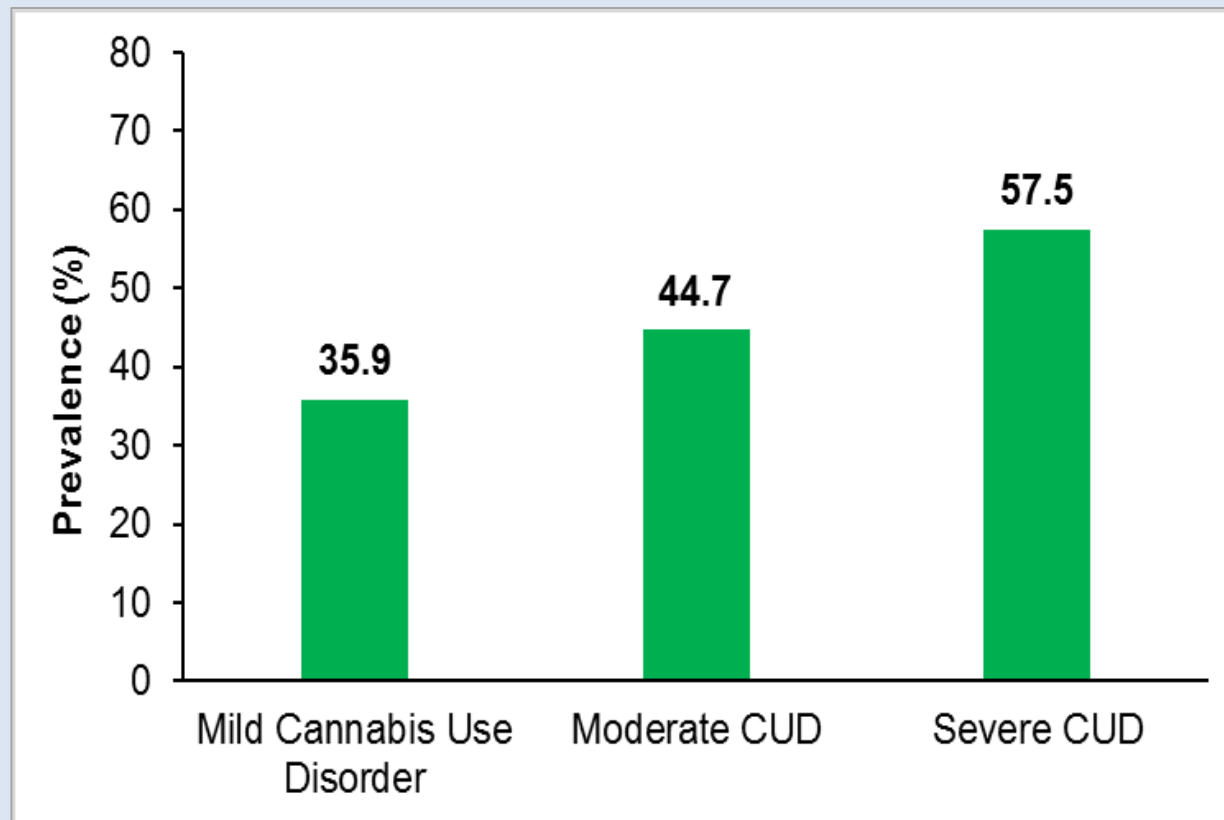
Hasin et al., Am J Psychiatry 2017

Problems associated with Alcohol Use Disorder (AUD) and Cannabis Use Disorder (CUD) in the U.S.

	AUD only vs. No AUD or CUD	CUD only vs. No AUD or CUD
Problems	aOR[a]	aOR[a]
Interpersonal		
Trouble with boss or co-workers	**1.87**	- -
Prob's with neighbor, relative, friend	**2.04**	**3.97**
Broke up major relationship	**2.37**	**2.42**
Financial and Legal		
Fired or laid off	**1.69**	**2.02**
Unemployed	**1.53**	**2.75**
Homeless	**2.78**	**4.26**
Declared bankruptcy	1.04	- -
So much debt couldn't repay	**1.90**	**2.33**
Trouble with law/police	**3.34**	**3.62**
Health-related		
Hospitalized	**1.13**	- -
Emergency treatment	**1.29**	**1.74**
Suicide attempt at current age	**3.48**	--
a adjusted for age, sex, ethnicity/race, and education		

Gutkind S et al., NESARC-III data, DAD 2021

Problems associated with Alcohol Use Disorder (AUD) and Cannabis Use Disorder (CUD) in the U.S.

Problems	AUD only vs. No AUD or CUD	CUD only vs. No AUD or CUD
	aOR[a]	aOR[a]
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Gutkind S et al., NESARC-III data, DAD 2021

Is cannabis use disorder increasing faster in individuals with known risk factors?
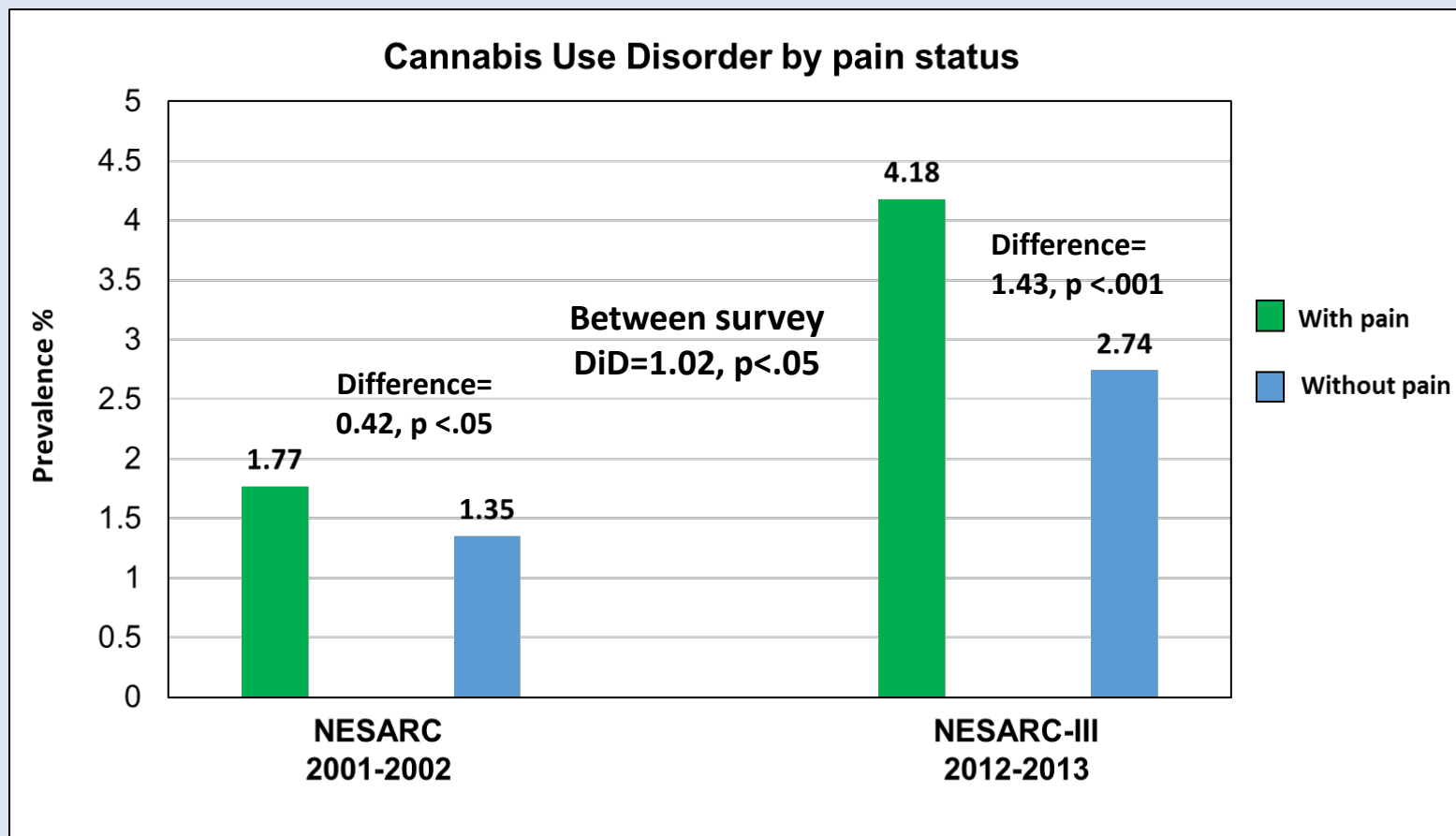# National Surveys on Alcohol and Related Conditions (NESARC)
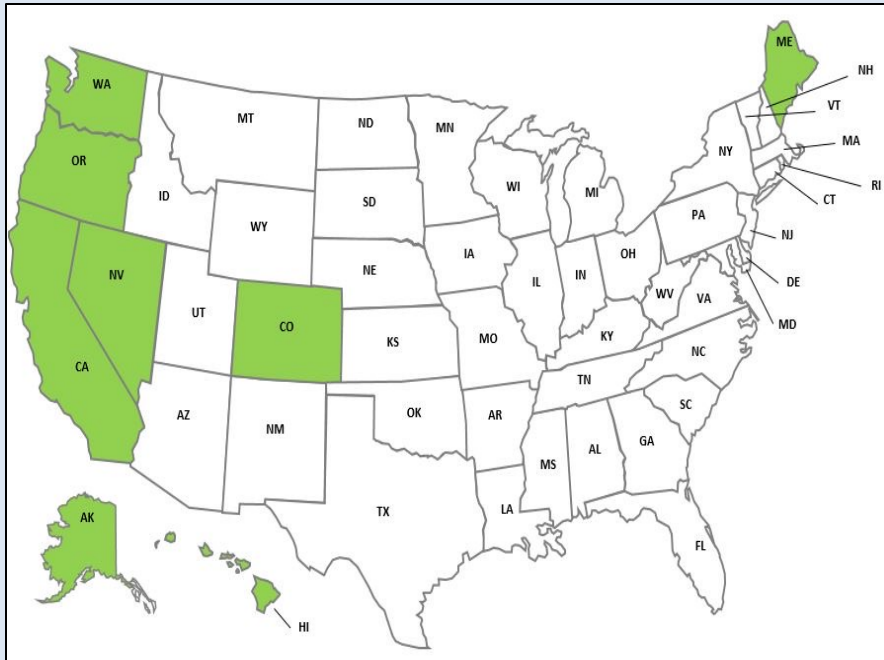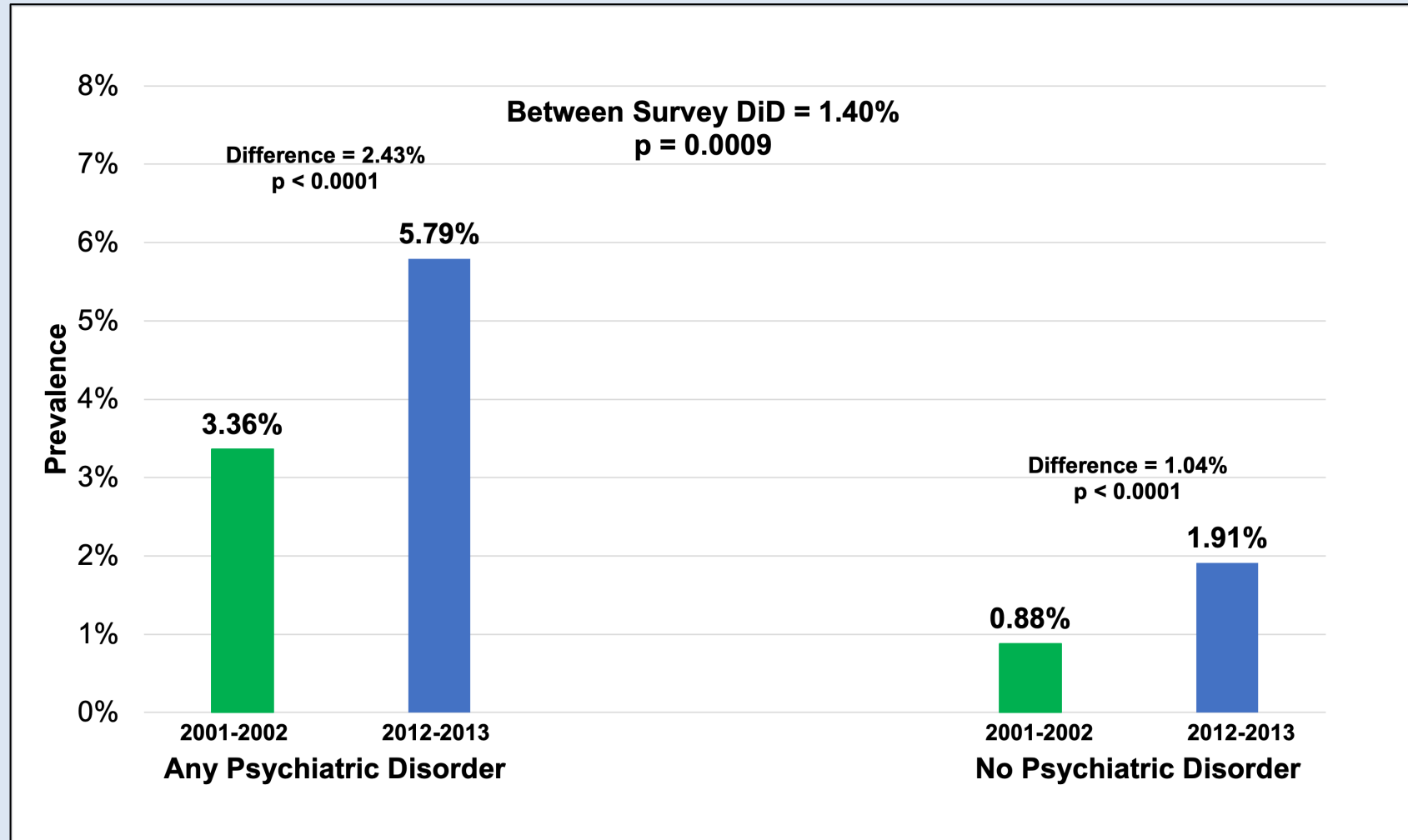

NESARC Wave 1: 2001-2002
_N=43,092_
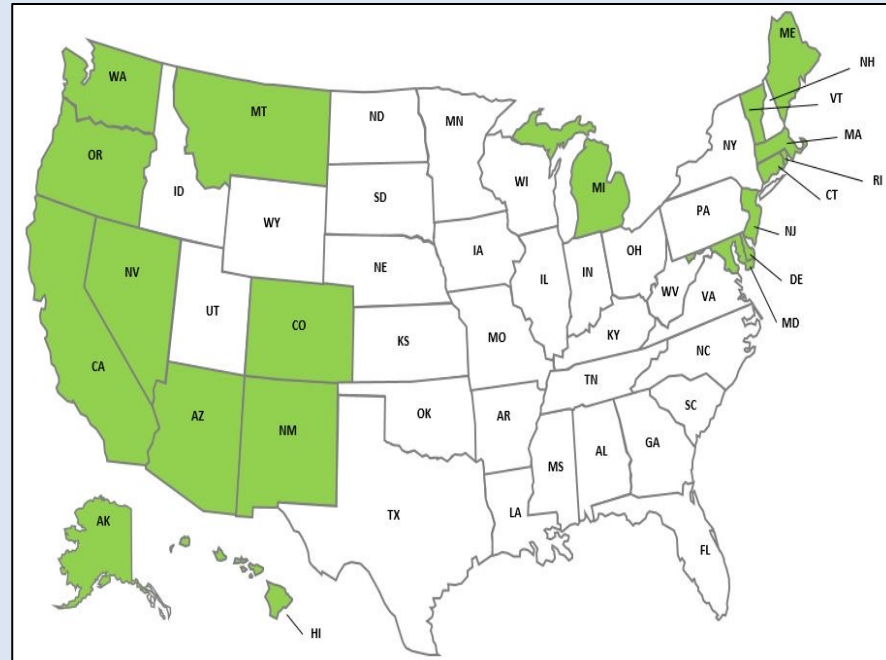
NESARC-III: 2012-2013
_N=36,309_

**DSM-IV Cannabis Use Disorder
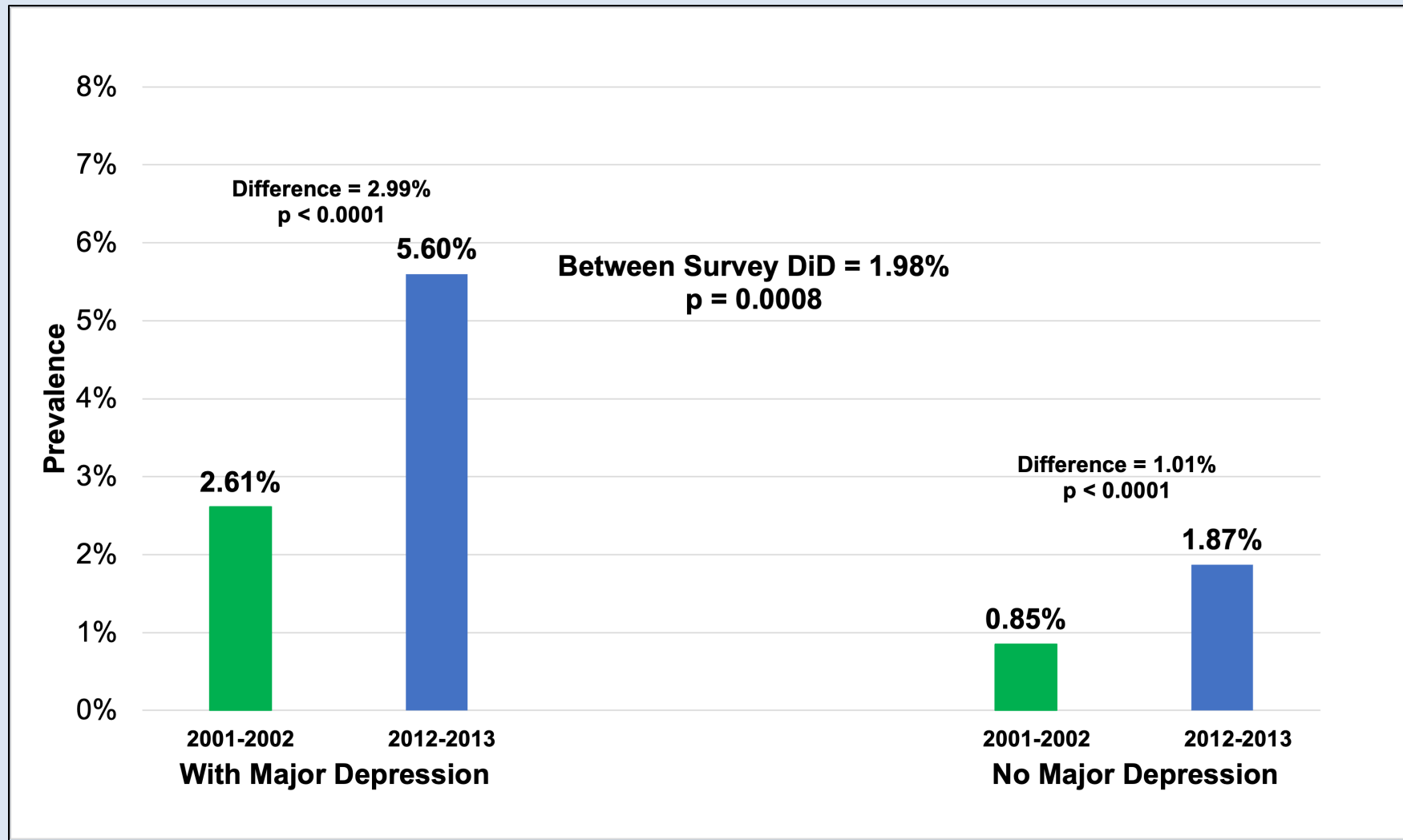in adults with and without chronic pain
2001-2002 and 2012-2013**

Cannabis Use Disorder by pain status

Prevalence %

Difference=
0.42, p <.05

**Between survey
DiD=1.02, p<.05**

Difference=
1.43, p <.001

4.18

2.74

1.77

1.35

■ With pain

■ Without pain

NESARC
2001-2002

NESARC-III
2012-2013

Models adjusted for sociodemographic covariates, covariate x pain interactions
Hasin et al., Am J Psychiatry 2020

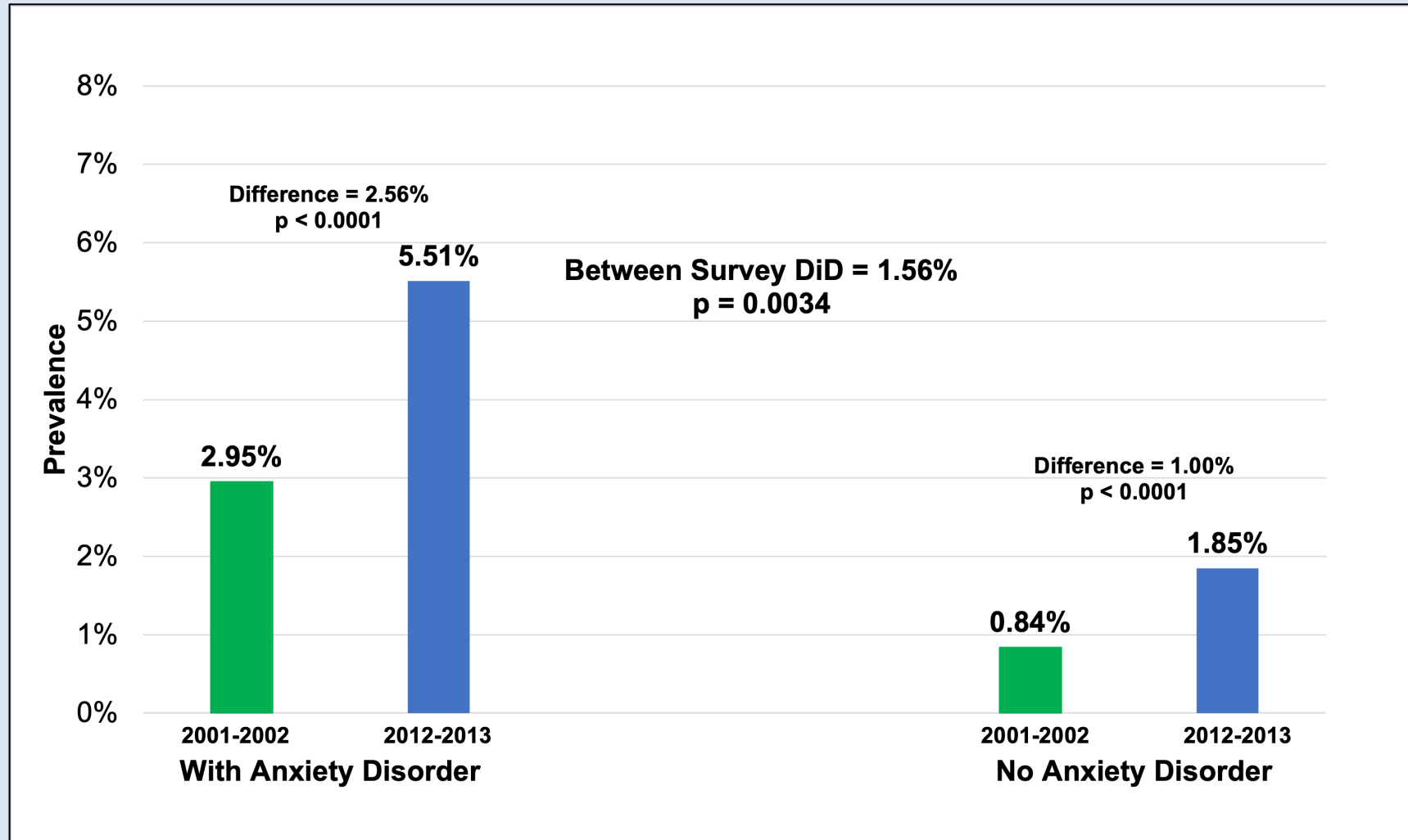**DSM-IV Cannabis Use Disorder, by Any Psychiatric Disorder, NESARC (2001-2002) and NESARC-III (2012-2013)**

Between Survey DiD = 1.40%
p = 0.0009

Difference = 2.43%
p < 0.0001

5.79%

3.36%

Difference = 1.04%
p < 0.0001

1.91%

0.88%

2001-2002   2012-2013
Any Psychiatric Disorder

2001-2002   2012-2013
No Psychiatric Disorder

Prevalence

Models adjusted for sociodemographic covariates
Hasin et al., in preparation

DSM-IV Cannabis Use Disorder, by Major Depressive Disorder, NESARC (2001-2002) and NESARC-III (2012-2013)
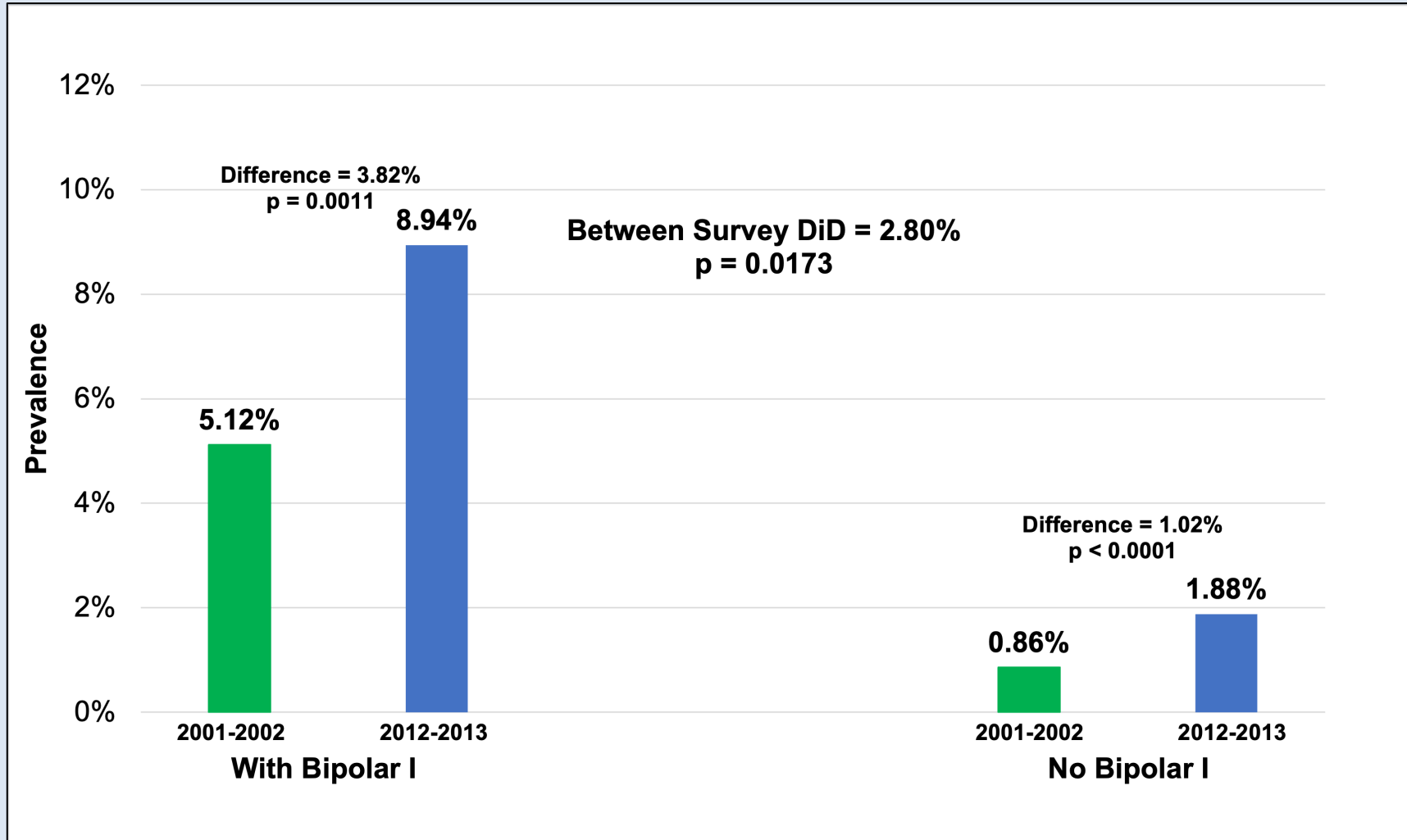
Difference = 2.99%
p < 0.0001

5.60%

Between Survey DiD = 1.98%
p = 0.0008

Difference = 1.01%
p < 0.0001

2.61%

1.87%

0.85%

Prevalence

8%
7%
6%
5%
4%
3%
2%
1%
0%

2001-2002   2012-2013
With Major Depression

2001-2002   2012-2013
No Major Depression

Models adjusted for sociodemographic covariates
Hasin et al., in preparation

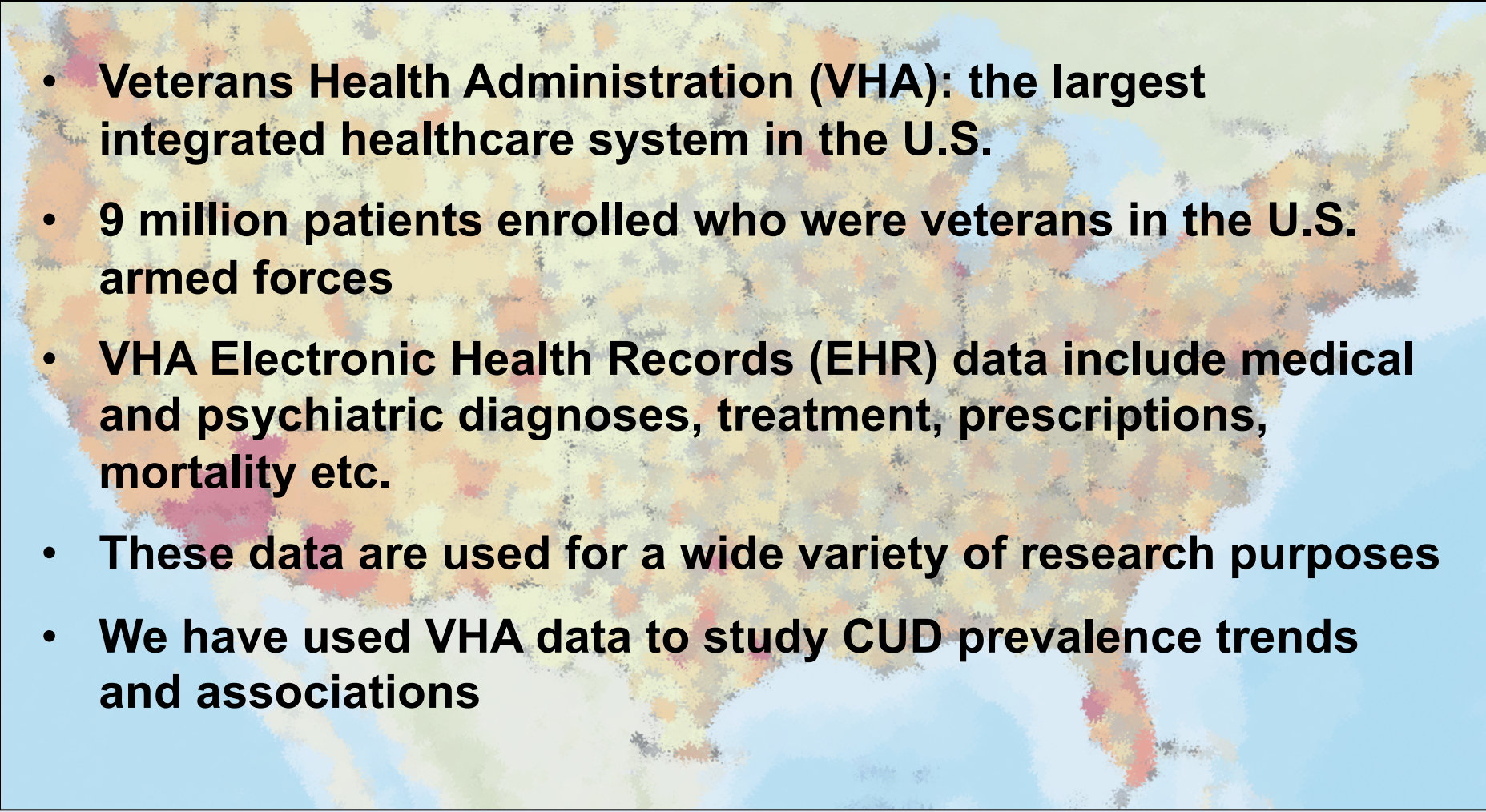# DSM-IV Cannabis Use Disorder by Any Anxiety Disorder, NESARC (2001-2002) and NESARC-III (2012-2013)

Prevalence

Difference = 2.56%
p < 0.0001

5.51%

Between Survey DiD = 1.56%
p = 0.0034

2.95%

Difference = 1.00%
p < 0.0001

1.85%

0.84%

2001-2002   2012-2013
With Anxiety Disorder

2001-2002   2012-2013
No Anxiety Disorder

Models adjusted for sociodemographic covariates
Hasin et al., in preparation

DSM-IV Cannabis Use Disorder by Bipolar I Disorder, NESARC (2001-2002) and NESARC-III (2012-2013)

With Bipolar I

Difference = 3.82%
p = 0.0011

5.12%
8.94%

Between Survey DiD = 2.80%
p = 0.0173

No Bipolar I

Difference = 1.02%
p < 0.0001

0.86%
1.88%

Prevalence

2001-2002   2012-2013   2001-2002   2012-2013

Models adjusted for sociodemographic covariates
Hasin et al., in preparation

# Time trends in adult DSM-5 cannabis use disorders 2002-2017, NSDUH

Cannabis use disorders among adults in the United States during a time of increasing use of cannabis

Wilson M. Compton[a],*, Beth Han[b], Christopher M. Jones[c], Carlos Blanco[a]

[a] National Institute on Drug Abuse, National Institutes of Health, 6001 Executive Blvd., Bethesda, MD, 20892, USA
[b] Substance Abuse and Mental Health Services Administration, 5600 Fishers Lane, Rockville, MD, 20857, USA
[c] Centers for Disease Control and Prevention, Atlanta, GA, 30341, USA

- DSM-IV CUD remained stable, while use and daily use increased

- **DSM-5 CUD (proxy; 2 of 9 criteria) increased**, with increases seen in the mild category; DSM-5 considered "more sensitive"

- DSM-5 craving and withdrawal missing in NSDUH, so unclear how results would have looked if these were included

Veterans Health Administration: Health Data

- **Veterans Health Administration (VHA): the largest integrated healthcare system in the U.S.**

- **9 million patients enrolled who were veterans in the U.S. armed forces**

- **VHA Electronic Health Records (EHR) data include medical and psychiatric diagnoses, treatment, prescriptions, mortality etc.**

- **These data are used for a wide variety of research purposes**

- **We have used VHA data to study CUD prevalence trends and associations**

ICD-9-CM and ICD-10-CM Cannabis Use Disorder: Veterans Administration Patients, 2005-2019

Hasin et al, Am J Psychiatry 2022
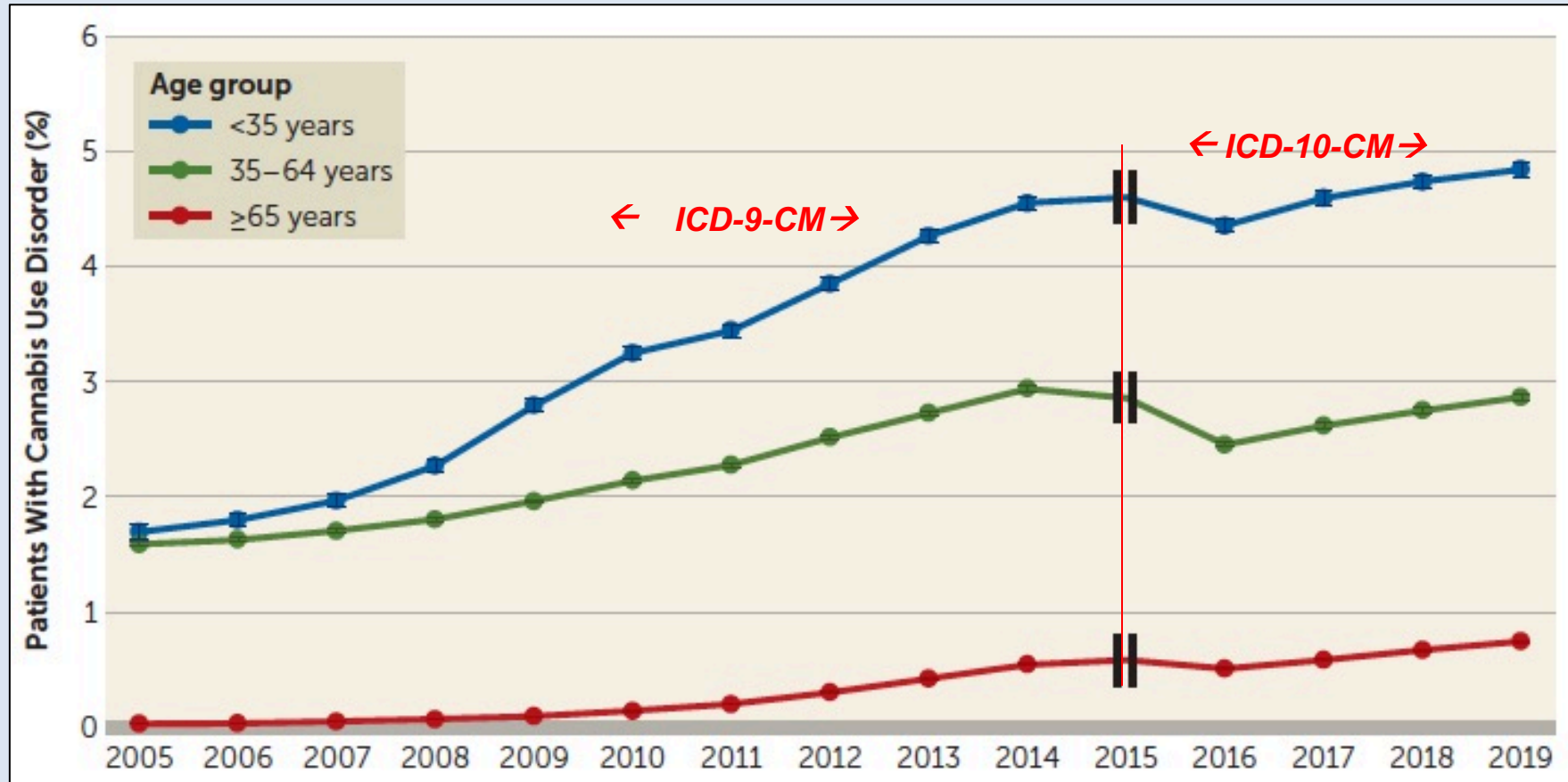
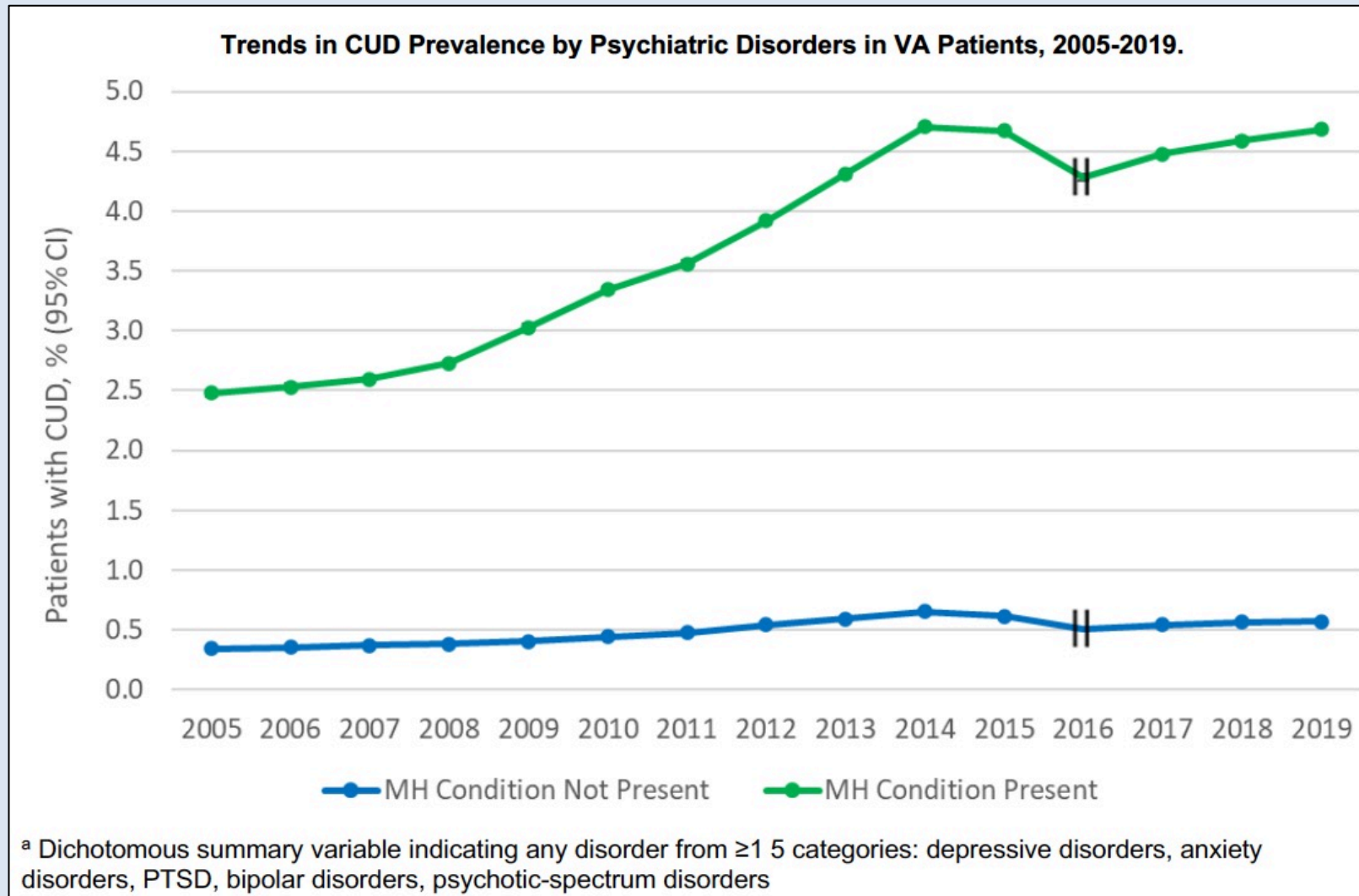**Trends in CUD prevalence in VHA patients by clinical comorbidity**

Trends in CUD diagnoses, 2005-2019,
VHA patients, by chronic pain
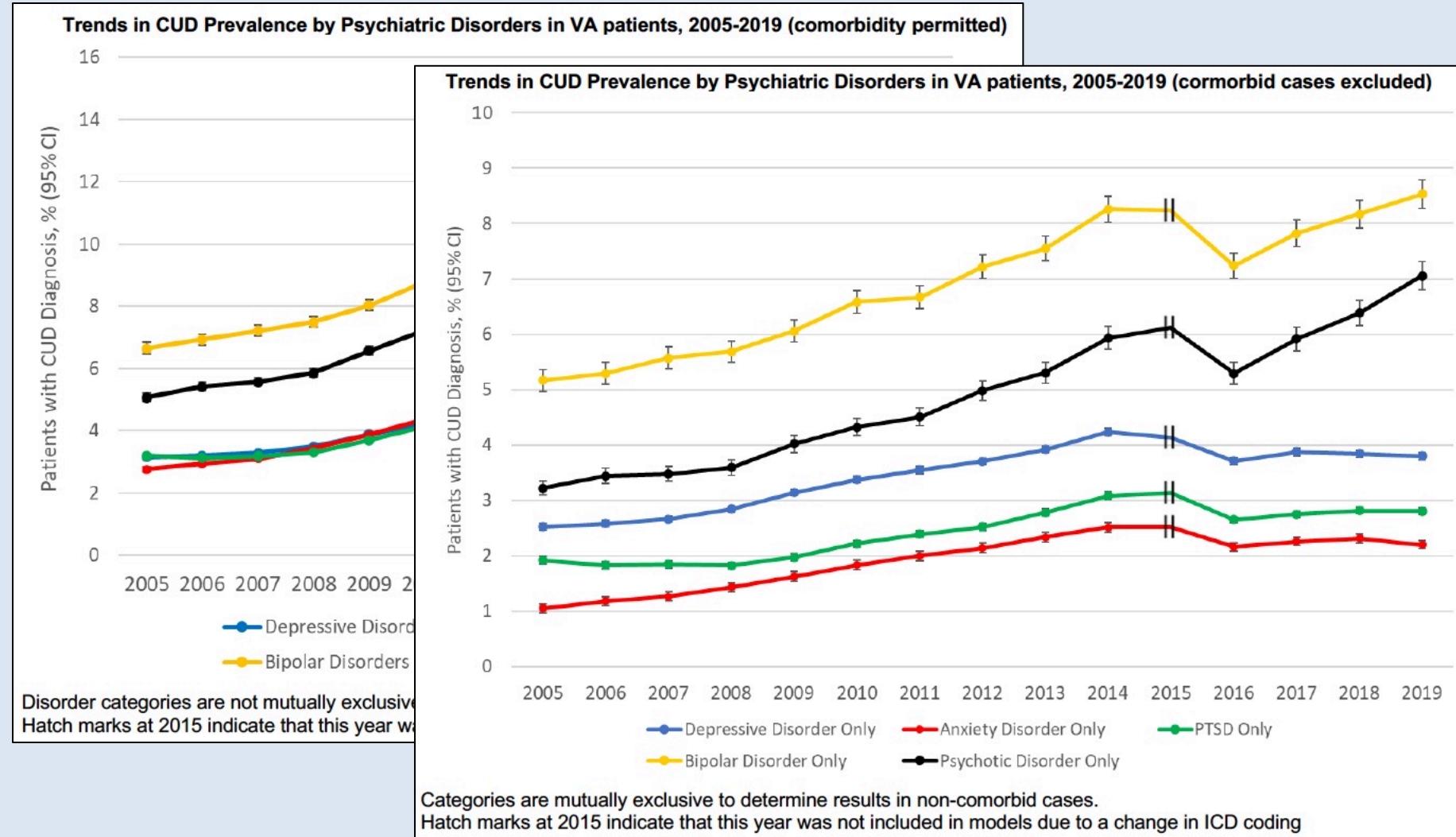# (diagnoses of medical conditions associated with pain)
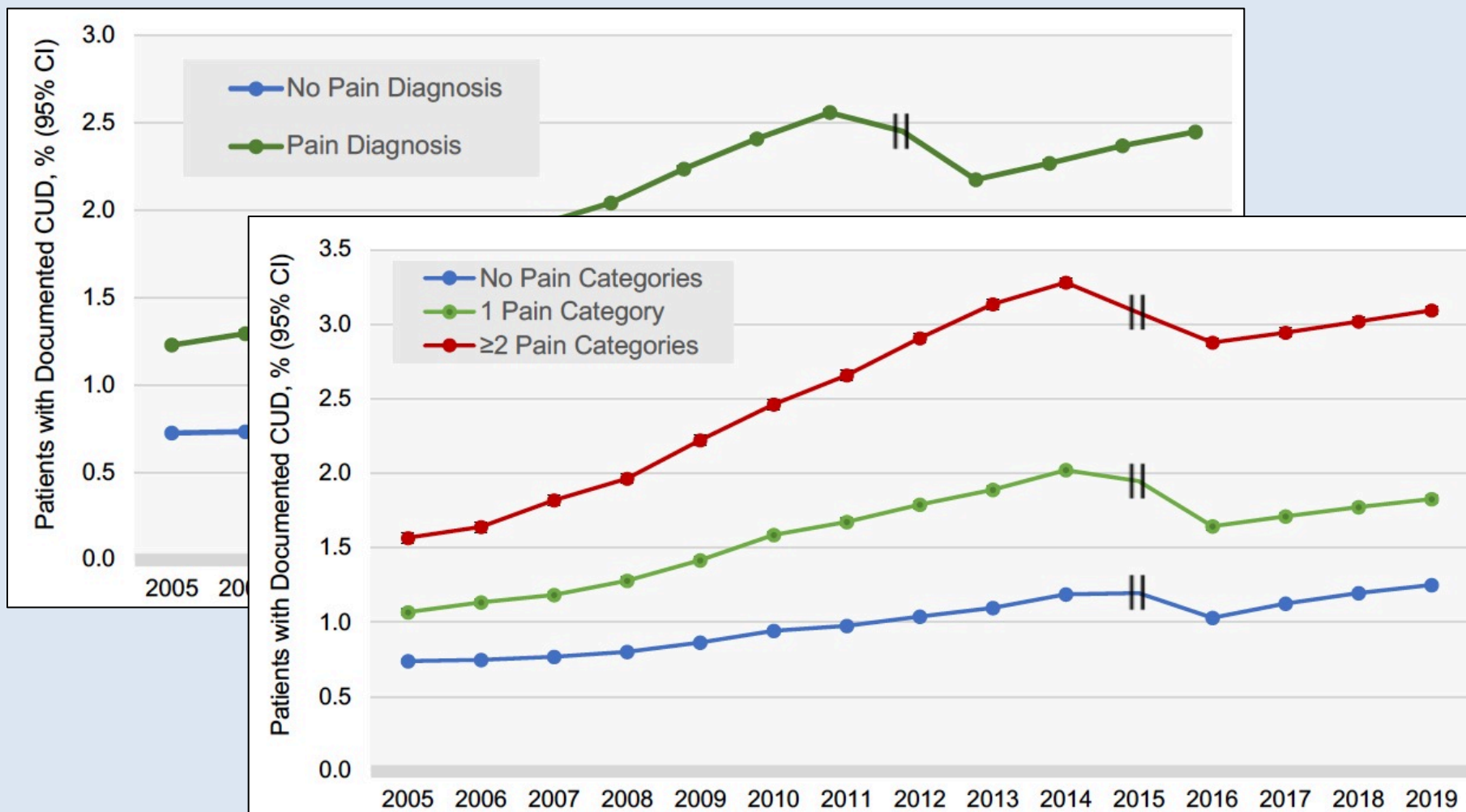
Mannes Z et al., Pain 2023

Trends in CUD diagnoses, VHA patients by most common psychiatric disorders, 2005-2019

Trends in CUD Prevalence by Psychiatric Disorders in VA Patients, 2005-2019.

ᵃ Dichotomous summary variable indicating any disorder from ≥1 5 categories: depressive disorders, anxiety disorders, PTSD, bipolar disorders, psychotic-spectrum disorders

Livne et al., in press, Am J Psychiatry

Trends in CUD diagnoses, VHA patients by most common psychiatric disorders, 2005-2019

Trends in CUD Prevalence by Psychiatric Disorders in VA patients, 2005-2019 (comorbidity permitted)

Patients with CUD Diagnosis, % (95% CI)

Depressive Disord

Bipolar Disorders

Disorder categories are not mutually exclusive
Hatch marks at 2015 indicate that this year wa

Trends in CUD Prevalence by Psychiatric Disorders in VA patients, 2005-2019 (cormorbid cases excluded)

Patients with CUD Diagnosis, % (95% CI)

Depressive Disorder Only   Anxiety Disorder Only   PTSD Only

Bipolar Disorder Only   Psychotic Disorder Only

Categories are mutually exclusive to determine results in non-comorbid cases.
Hatch marks at 2015 indicate that this year was not included in models due to a change in ICD coding

Livne et al., In press, Am J Psychiatry

Summary

- Cannabis use does involve some risk of various health harms

- Cannabis Use Disorder is a valid, evidence-based diagnosis with considerable impairment and comorbidity

- The prevalence of Cannabis Use Disorder is increasing in the general population and in large-scale patient populations

- The increases in CUD prevalence are disproportionately occurring in individuals with chronic pain and with psychiatric disorders

Acknowledgements

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