


# PSYCHOSIS AMONG PEOPLE WHO USE SUBSTANCES

Julius Elefante, MD, FRCPC, ISAM (Cert.)  
Clinical Instructor, UBC  
Staff Psychiatrist, SPH & VGH



I respectfully acknowledge the land on which I work is the unceded traditional territory of the Coast Salish Peoples, including the traditional territories of the Musqueam, Squamish, and Tsleil-Waututh Nations

- 
- I have no financial disclosures to declare
  - To mitigate bias:
    - I will only use generic names in this presentation
    - Where medications are recommended for off-label indications, this would be explicitly stated
    - Both positive and negative trials will be presented

# OBJECTIVES

1. Discuss the relationship between cannabis and psychosis
2. Describe methamphetamine-induced psychosis
3. Summarize the different management and psychosocial issues around substance induced psychosis

# OUTLINE

Background

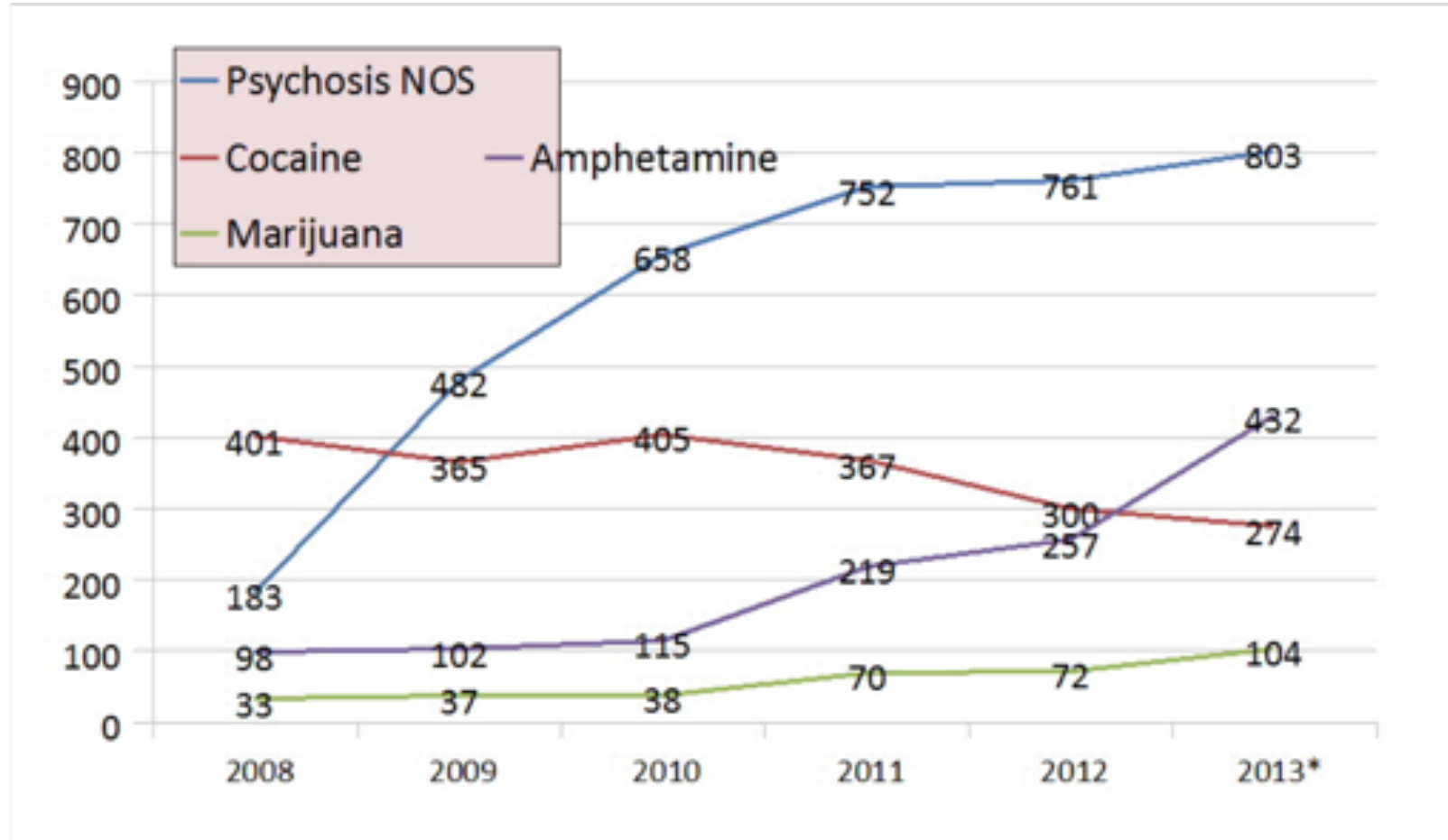
Cannabis

Stimulants

Management  
considerations

Discussion

# DRUG RELATED EMERGENCY ROOM VISITS AT SAINT PAUL'S HOSPITAL 2006 - 2013

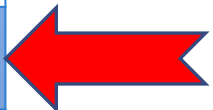
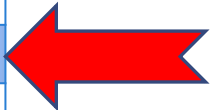


# SUBSTANCES AND PSYCHOSIS: THREE GROUPS OF PATIENTS

1. Transient perceptual disturbances in intoxication do not necessarily constitute a diagnosable psychotic disorder
2. Substance-induced psychotic disorder
3. Primary psychotic disorder and exacerbation with substance use

# SUBSTANCES OR MEDICATIONS THAT CAN BE MISUSED AND CAUSE PSYCHOSIS

| Substance or medication                | Examples  |
|--|---|
| <b>Alcohol and sedatives/hypnotics</b> | Alcohol (intoxication or withdrawal), barbiturates and benzodiazepines (particularly withdrawal)  |
| <b>Anabolic steroids</b>               | Testosterone, methyltestosterone  |
| <b>Analgesics</b>                      | Meperidine, pentazocine, indomethacin   |
| <b>Antidepressants</b>                 | Bupropion, others if triggering a manic switch  |
| <b>Cannabinoids</b>                    | Marijuana, synthetic cannabinoids (ie, "spice"), dronabinol   |
| <b>Hallucinogens</b>                   | LSD, PCP (phencyclidine), ketamine, psilocybin-containing mushrooms, mescaline, synthetic "designer drugs" (eg, 2-CB, "N-Bomb" [25I-NBOMe]), salvia divinorum |
| <b>Inhalants</b>                       | Toluene, butane, gasoline   |
| <b>Over-the-counter (OTC)</b>          | Dextromethorphan (DXM), diphenhydramine, some decongestants   |
| <b>Stimulants</b>                      | Cocaine, amphetamine/methamphetamine, methylphenidate, certain diet pills, "bath salts" (MDPV, mephedrone), MDMA/ecstasy                                      |





# EPIDEMIOLOGY: CANNABIS USE

| Drug Category              | Overall              |
|----------------------------|----------------------|
| Population estimate ('000) | 30,291               |
| <b>Cannabis use</b>        |                      |
| Cannabis - lifetime        | 46.6<br>[44.3 -48.8] |
| Cannabis - past year       | 14.8<br>[13.2 -16.4] |

<https://www.canada.ca/en/health-canada/services/canadian-tobacco-alcohol-drugs-survey/2017-summary.html>

# EPIDEMIOLOGY: CANNABIS USE DISORDER

- Lifetime prevalence: 6.3%
- 12-month prevalence: 2.5%

Hasin DS et al., Am J Psychiatry. 2016

- Increasing rates of individuals in treatment for cannabis use disorder in the US and Europe

Hasin DS et al., Am J Psychiatry. 2016

## According to the Government of Canada, what is the average THC content in dried cannabis in the 1980's compared to nowadays?

A. 3% in 1980's,  
15% these days

✓ 33%

B. 1% in 1980's,  
10% these days

C. 3% in 1980's,  
50% these days


56%

D. 1% in 1980's,  
50% these days

11%

# INTERACTIVE QUIZ

According to the Government of Canada, what is the average THC content in dried cannabis in the 1980's compared to nowadays?

A. 3% in 1980's, 15% these days 

B. 1% in 1980's, 10% these days

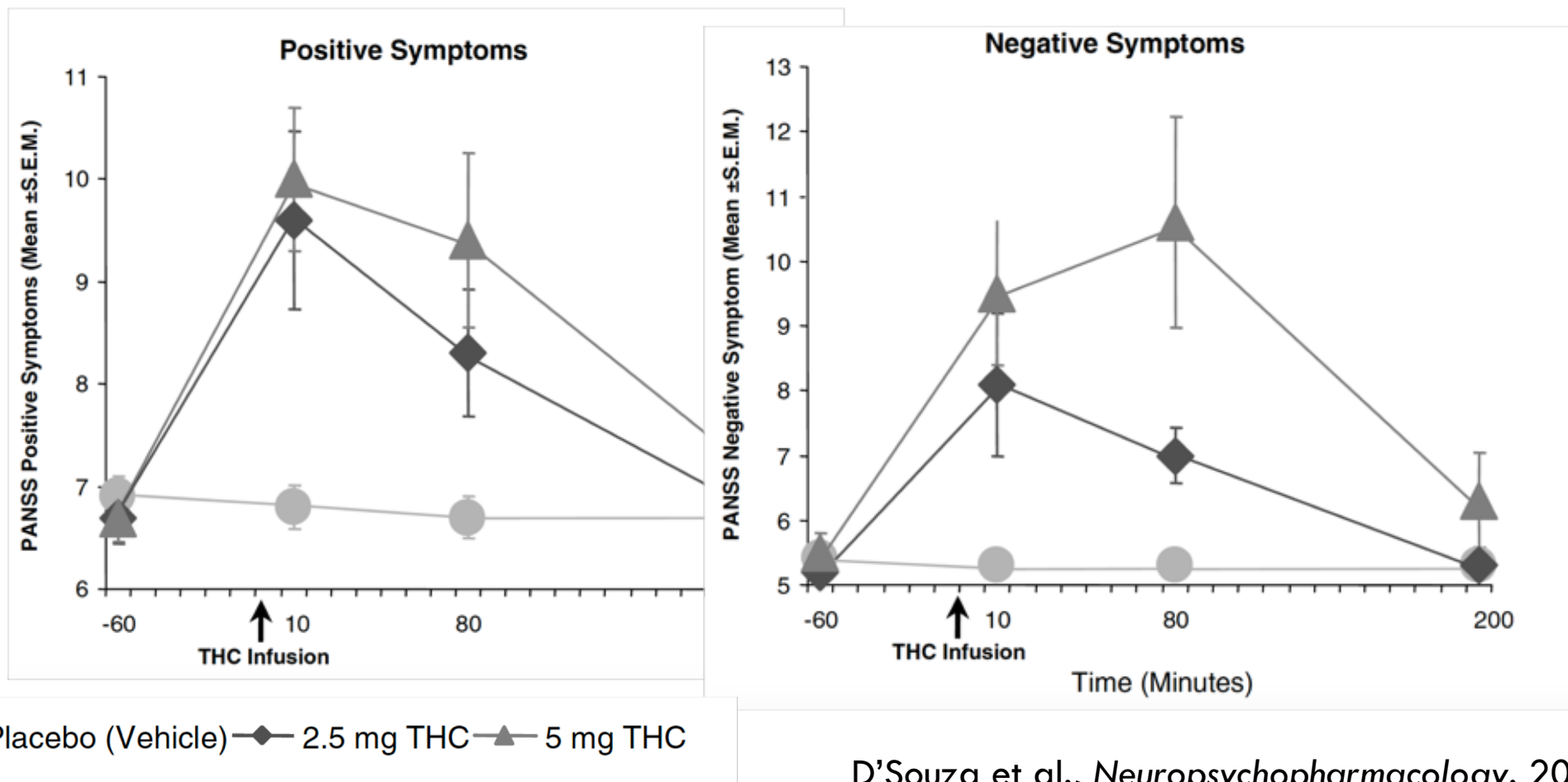
C. 3% in 1980's, 50% these days

D. 1% in 1980's, 50% these days

• For various products in the legal Canadian market: 0 – 30%

BCCSU ACTOC through UBC CPD

# CAN CANNABIS CAUSE TRANSIENT PSYCHOSIS?



D'Souza et al., *Neuropsychopharmacology*. 2004

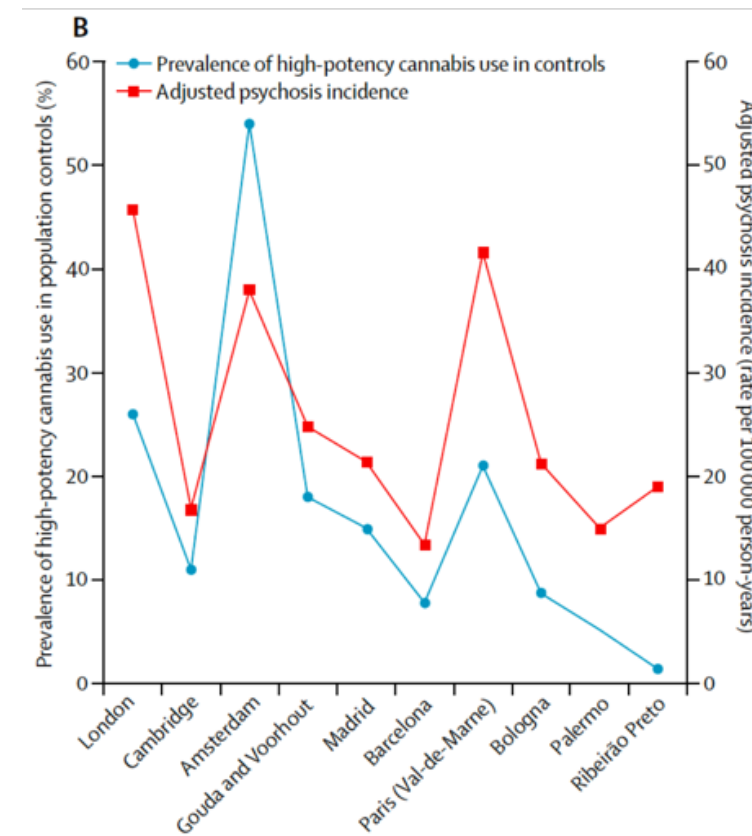
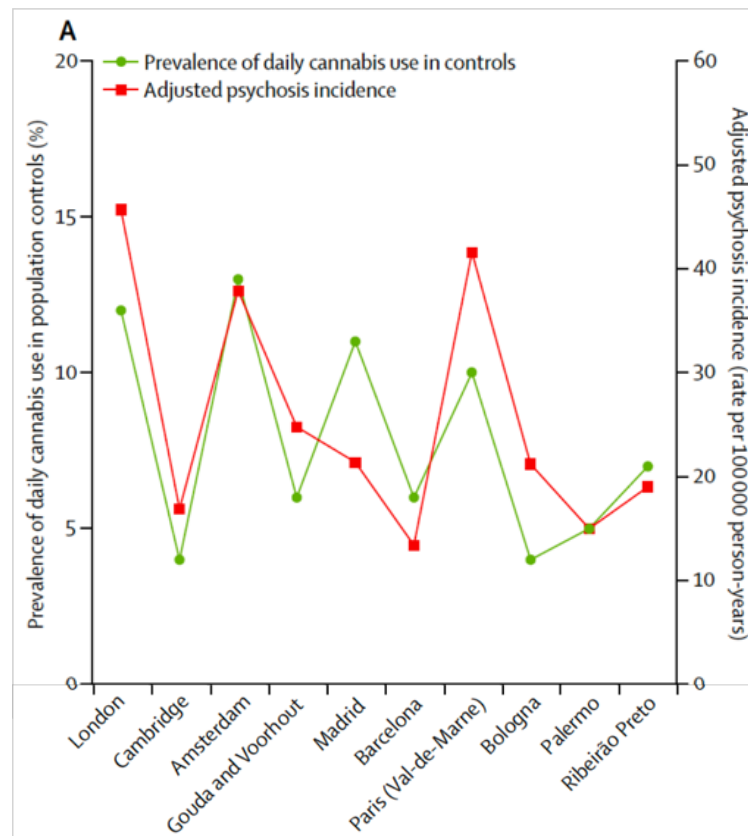
# CAN CANNABIS CAUSE SCHIZOPHRENIA?

- Population rates of schizophrenia have remained stable though the prevalence of cannabis use disorder has increased over the last decade

Caspi A et al., Biol Psychiatry 2005

# SCHIZOPHRENIA AND CANNABIS

- However, Marta Di Forti and colleagues explored this paradox in more detail



Di Forti et al.,  
Lancet Psychiatry,  
2019

# DAILY USE OF HIGH-POTENCY CANNABIS CARRIED MORE THAN A FOUR-TIMES INCREASE IN THE RISK OF PSYCHOTIC DISORDER

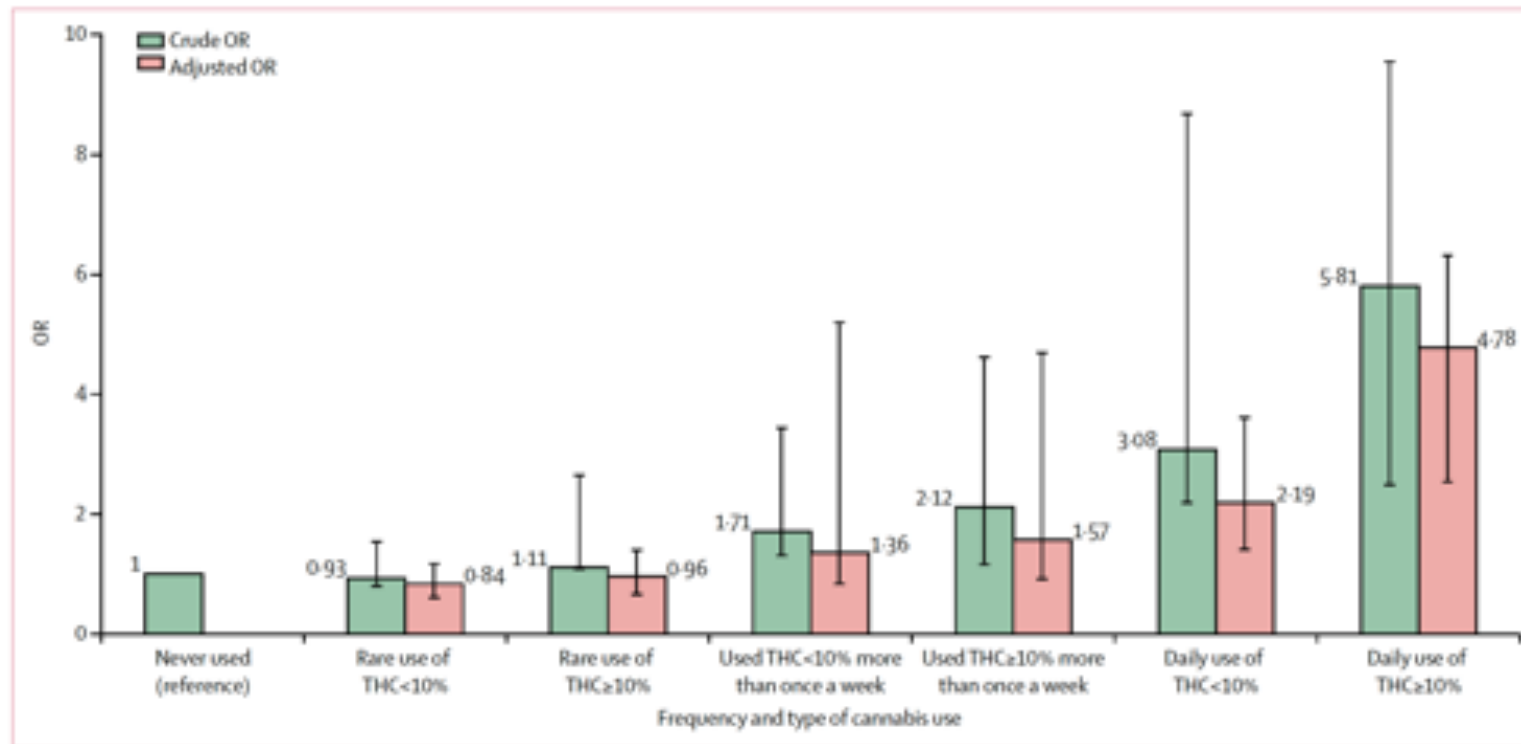


Figure 1: Crude and fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in the whole sample. Crude ORs are adjusted only for age, gender and ethnicity and fully adjusted ORs are additionally adjusted for level of education, employment status, and use of tobacco, stimulants, ketamine, legal highs, and hallucinogenics. Error bars represent 95% CIs. OR=odds ratio.



# SCHIZOPHRENIA AND CANNABIS

- From comparing 83 relevant studies Large et al. found that the age at onset of psychosis compared to non-substance using controls:

- 2.70 years earlier among cannabis users
- 2.00 years earlier in people with unspecified substance use

Large M et al., Arch Gen Psychiatry. 2011 Jun

- Prior cannabis use is associated with a 2-3 times increased risk of later psychosis, though most studies cannot determine if a subtle form of psychosis existed prior to the onset of cannabis use

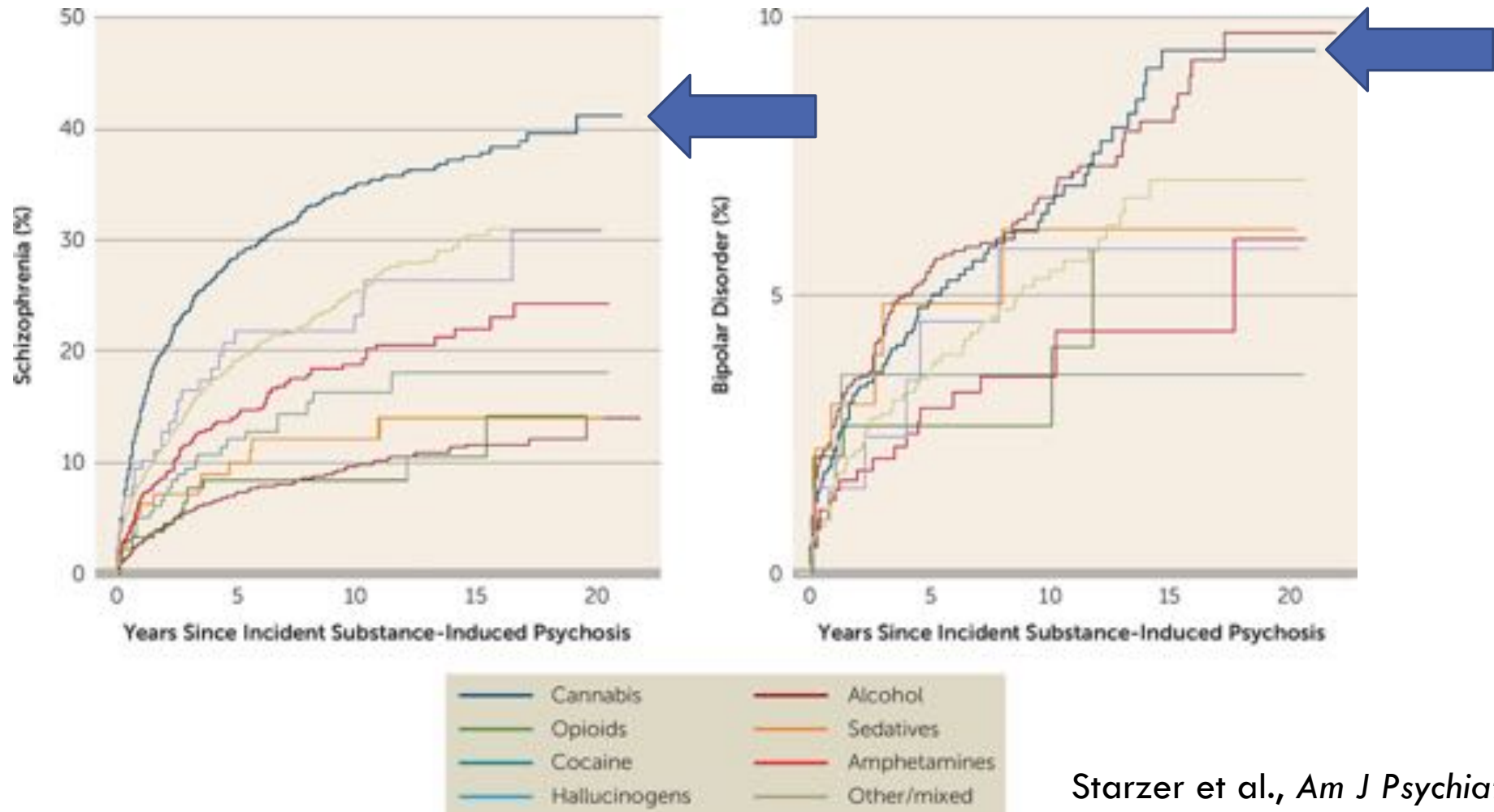
Ehmann, BC EPI Advanced Practice, 2018

# YOUTH ARE THE MOST VULNERABLE

- Prospective longitudinal study of 6534 individuals born in northern Finland in 1986, evaluated at age 15-16, and at 30yrs:
  - 5x higher risk if they started to use marijuana by age 15-16

Mustonen A et al., Br J Psychiatry 2018

# CONVERSION TO SCHIZOPHRENIA OR BIPOLAR DISORDER



[Back to table of contents](#)[Previous Article](#)[Next Article](#)

Articles

[Full Access](#)

## Prediction of Onset of Substance-Induced Psychotic Disorder and Its Progression to Schizophrenia in a Swedish National Sample

Kenneth S. Kendler, M.D., Henrik Ohlsson, Ph.D., Jan Sundquist, M.D., Ph.D., Kristina Sundquist, M.D., Ph.D.

Published Online: 6 May 2019 | <https://doi-org.ezproxy.library.ubc.ca/10.1176/appi.ajp.2019.18101217>

| Familial Risk Score    |       |              |
|------------------------|-------|--------------|
| Nonaffective Psychosis |       |              |
| Schizophrenia          |       | $p = 0.1676$ |
| Without SIPD           | +0.77 | 0.73, 0.82   |
| With SIPD              | +0.66 | 0.51, 0.80   |

- Schizophrenia following substance-induced psychosis is likely a drug-precipitated disorder in highly vulnerable individuals, not a syndrome predominantly caused by drug exposure

# THERAPEUTIC BENEFITS



Government  
of Canada

Gouvernement  
du Canada

[Français](#)

Search Canada.ca



MENU ▾

[Home](#) > [Health](#) > [Drug and health products](#) > [Drugs and medication](#) > [Cannabis](#)  
> [Information for Health Care Practitioners - Medical Use of Cannabis](#)

## Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids

---

[\(PDF Version - 2.236 K\)](#)

Dried or fresh plant and oil for administration by ingestion or other means

Psychoactive agent

# THERAPEUTIC BENEFITS

## Do Cannabinoids Work (Medicinally)?

Note: See "C..."

Generic/TRADE

Indications & Comments

Compared to placebo

- **Smoked vs vaped:** smoking speculated to have more respiratory risk (but data limited). Vaping ~2x more potent (smoking destroys some drug via combustion).
- **Vaping devices:** Consider a Health Canada approved vaporizer.

### "Marijuana Math"

*note: estimate only – some uncertainty!*

What is the estimated THC dose if **1 joint**, containing 0.5 grams of 10% THC dried cannabis, is smoked?

**Answer:** 500mg cannabis x 10% THC x 50% loss to combustion ≈ **25mg THC**

smoked cannabis.<sup>2,7</sup>

**Initial:** 1-2 puffs inhaled HS.  
(1 puff of joint ≈ 1-10mg THC. Variation is due to inhalation depth, puff size, THC potency, smoked vs vaped, joint size, etc.)

**Usual:** Uncertain due to poor quality evidence. Titrate slowly. Based on market data for 2017 in Canada, medical cannabis patients titrated themselves to an average dose of **750mg** dried cannabis per day.<sup>16</sup>

cannabis.<sup>CFP'18</sup>  
 ting from  
 y  
 anorexia  
 pain  
 line drug screen  
 cannabis.<sup>CFP'18</sup>  
 n (adjunctive)  
 neuropathic pain  
 tive)  
 e lower doses  
 rays vs  
 s associated

Adverse effects  
 patients out  
 ~1 patient in  
 adverse effects  
 disorders NN  
 Additional co  
 psychosis. Se  
 unstudied (ir

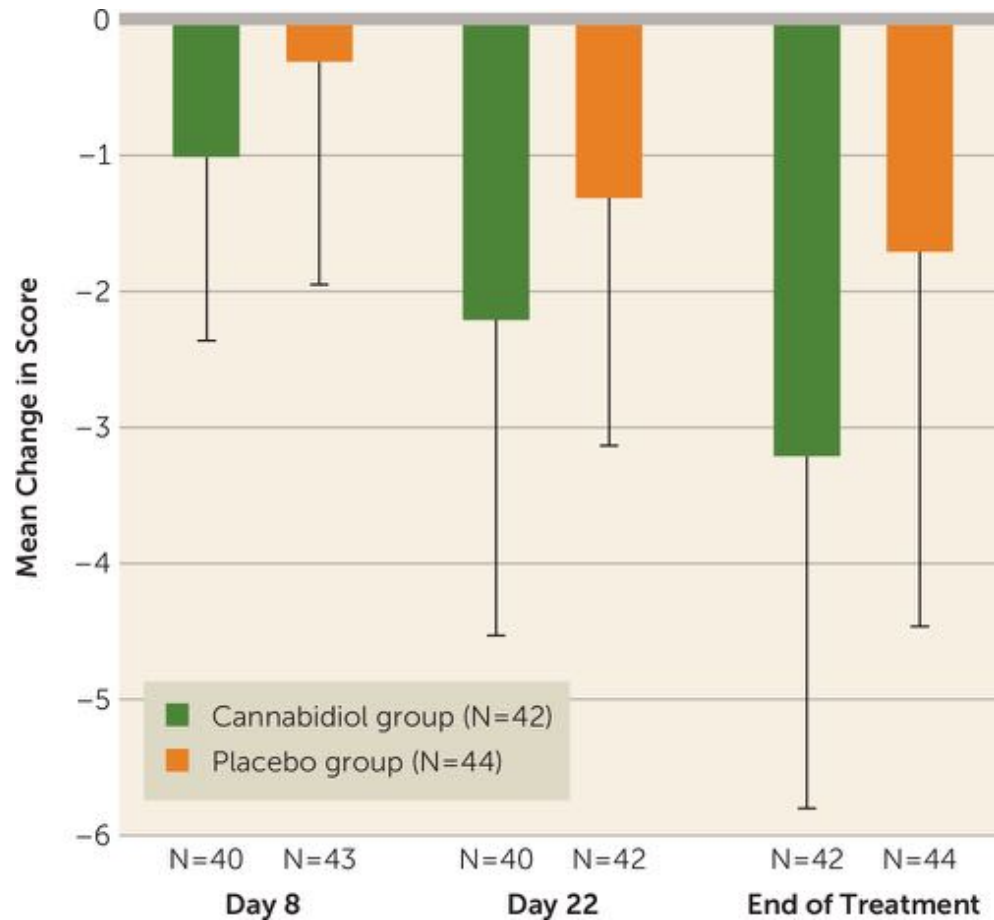
Canadians reported using  
 recreationally

with Lennox-Gastaut syndrome or

# CANNABIS FOR PSYCHIATRIC CONDITIONS?

- THC exhibits biphasic effects on mood with low doses having anxiolytic and mood-elevating effects and high doses the opposite effect
- Limited evidence that preparations with higher proportions of CBD may attenuate perturbations in mood seen in THC predominant preparations
- Emerging evidence from pre-clinical, clinical, and epidemiological studies suggests CBD may attenuate THC-induced psychosis

# CBD AS A NEW CLASS OF TREATMENT FOR SCHIZOPHRENIA?



- Exploratory double-blind parallel-group trial, patients with schizophrenia were randomized in a 1:1 ratio to receive CBD (1000 mg/day; N=43) or placebo (N=45) alongside their existing antipsychotic medication
- After 6 weeks of treatment, compared with the placebo group, the CBD group had lower levels of positive psychotic symptoms

McGuire et al., *Am J Psychiatry*, 2017



# CRYSTAL METHAMPHETAMINE USE EPIDEMIOLOGY

| Drug Category                      | Overall |
|------------------------------------|---------|
| Cannabis - lifetime                | 46.6    |
| Cannabis - past year               | 14.8    |
| <b>Lifetime illegal drug use</b>   |         |
| Cocaine/Crack                      | 10.4    |
| Speed/Methamphetamine/Crystal meth | 3.7     |
| <b>Illegal drug use past year</b>  |         |
| Cocaine/Crack                      | 2.5     |
| Speed/Methamphetamine/Crystal meth | *       |

# CRYSTAL METHAMPHETAMINE USE EPIDEMIOLOGY

- Methamphetamine use is more prevalent among street-involved youth and gay, bisexual, men who have sex with men (GBMSM)
- Vancouver At-Risk Youth Study
  - 1019 street-involved youth (age 14-26) surveyed between 2005 and 2012
  - 69% reported any prior crystal methamphetamine use

Uhlmann et al., *Am J Drug & Alcohol Abuse*, 2014

# CRYSTAL METHAMPHETAMINE USE AMONG SEXUALLY ACTIVE GBM (VANCOUVER)

## Crystal Methamphetamine Initiation Among HIV-Positive and HIV-Negative Men Who Have Sex With Men in Vancouver, Canada: A Longitudinal Analysis

N.J. Lachowsky<sup>1,2</sup>, M. Hull<sup>2,3</sup>, S. Colyer<sup>2</sup>, Z. Cui<sup>2</sup>, J. Zhu<sup>2</sup>, H.L. Armstrong<sup>2,3</sup>, M. Taylor<sup>4</sup>, J. Edwards<sup>4</sup>, G. Olarewaju<sup>2</sup>, R. Hogg<sup>2,5</sup>, E.A. Roth<sup>6</sup>, D.M. Moore<sup>2,3</sup>, Momentum Health Study

1. School of Public Health & Social Policy, University of Victoria, Victoria, Canada  
2. British Columbia Centre for Excellence in HIV/AIDS, Vancouver, Canada  
3. Faculty of Medicine, University of British Columbia, Vancouver, Canada

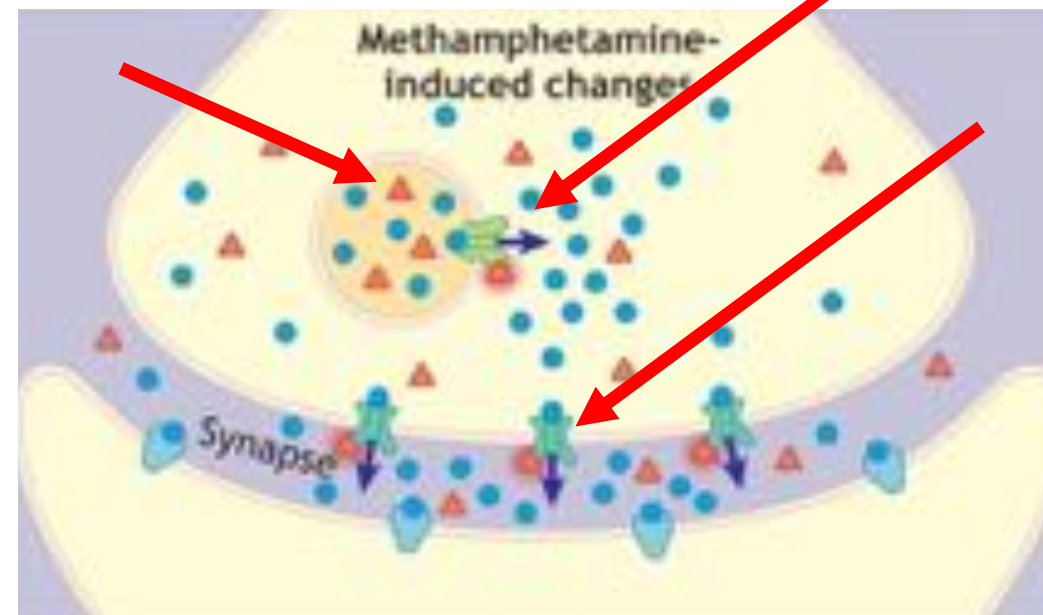
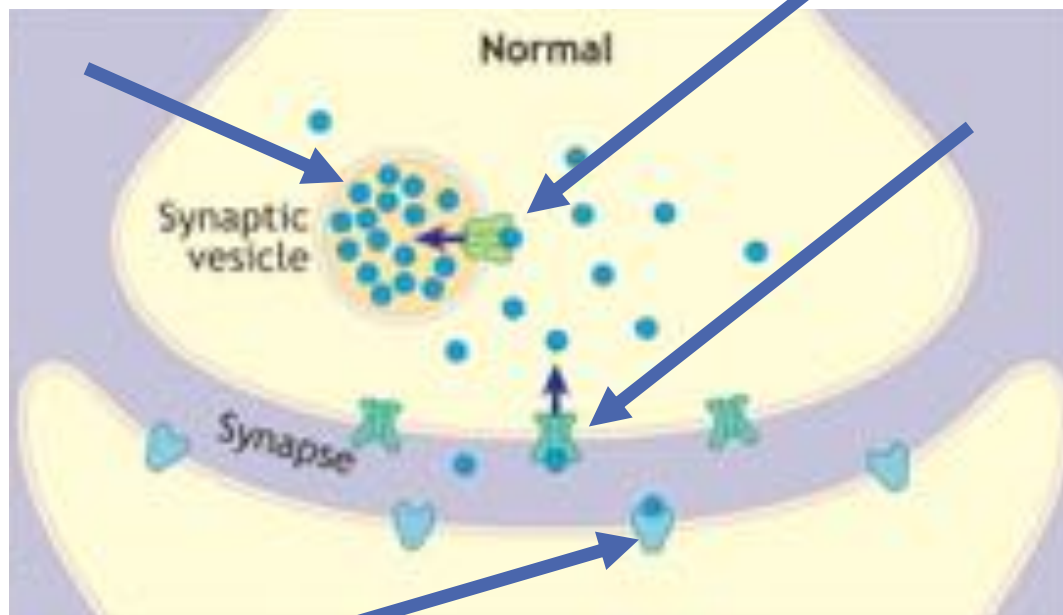
4. Health Initiative for Men, Vancouver, Canada  
5. Faculty of Health Science, Simon Fraser University, Burnaby, Canada  
6. Department of Anthropology, University of Victoria, Victoria, Canada

- Over the 4-year study period, 698 GBM completed 3,085 study visits (median follow-up of 2.49 years)
  - **20.1% of GBM reported crystal methamphetamine use in the six months prior to survey**
  - **HIV-positive GBM 44.3%**
  - **HIV-negative GBM 10.3%**

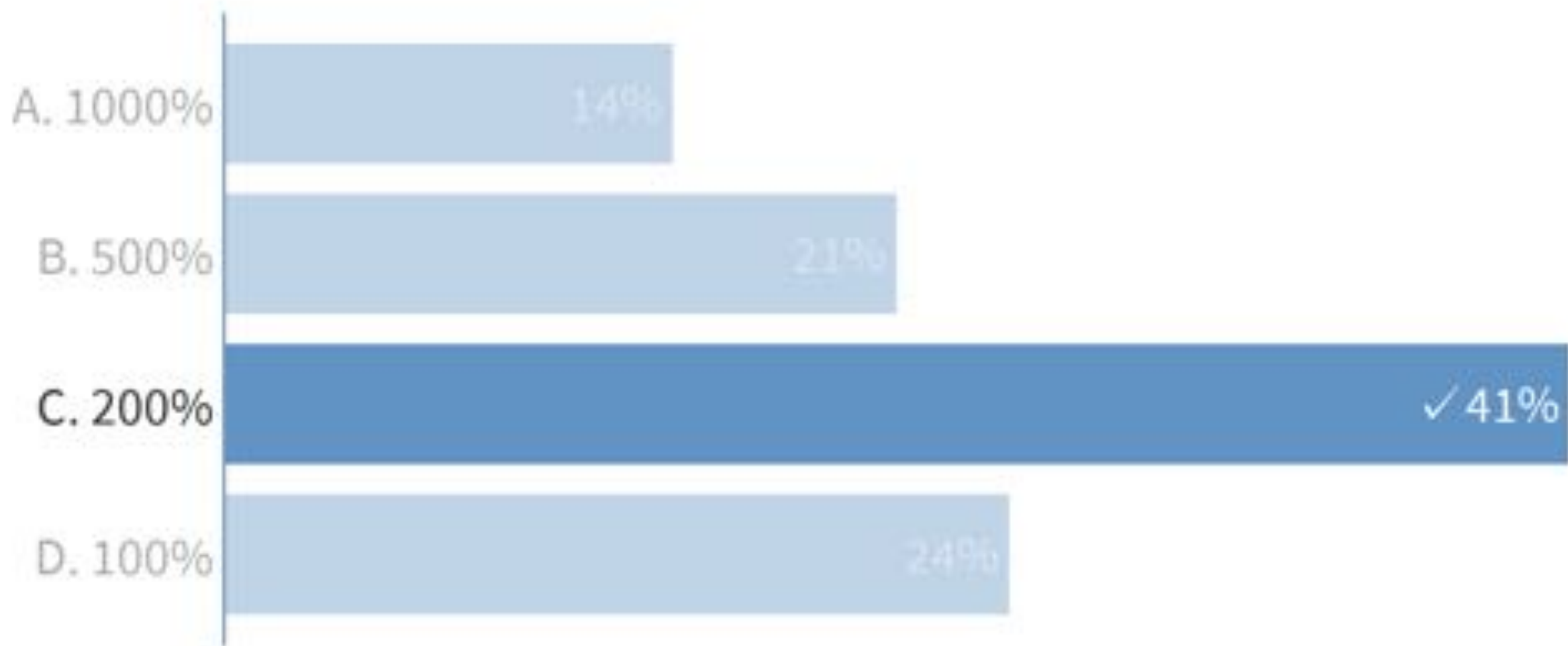
*With permission from the authors*

# CRYSTAL METHAMPHETAMINE

- ▲ Methamphetamine
- Dopamine
- ⌘ Dopamine transporter
- ⌘ Vesicular monoamine transporter 2
- ⌘ Dopamine receptor



**In a study of rats by Fiorino and Phillips (1999), what % over basal release did dopamine levels rise in the nucleus accumbens after sex?**



# INTERACTIVE QUIZ

In a study in rats by Fiorino and Phillips, what % over basal release did dopamine levels rise in the nucleus accumbens after sex?

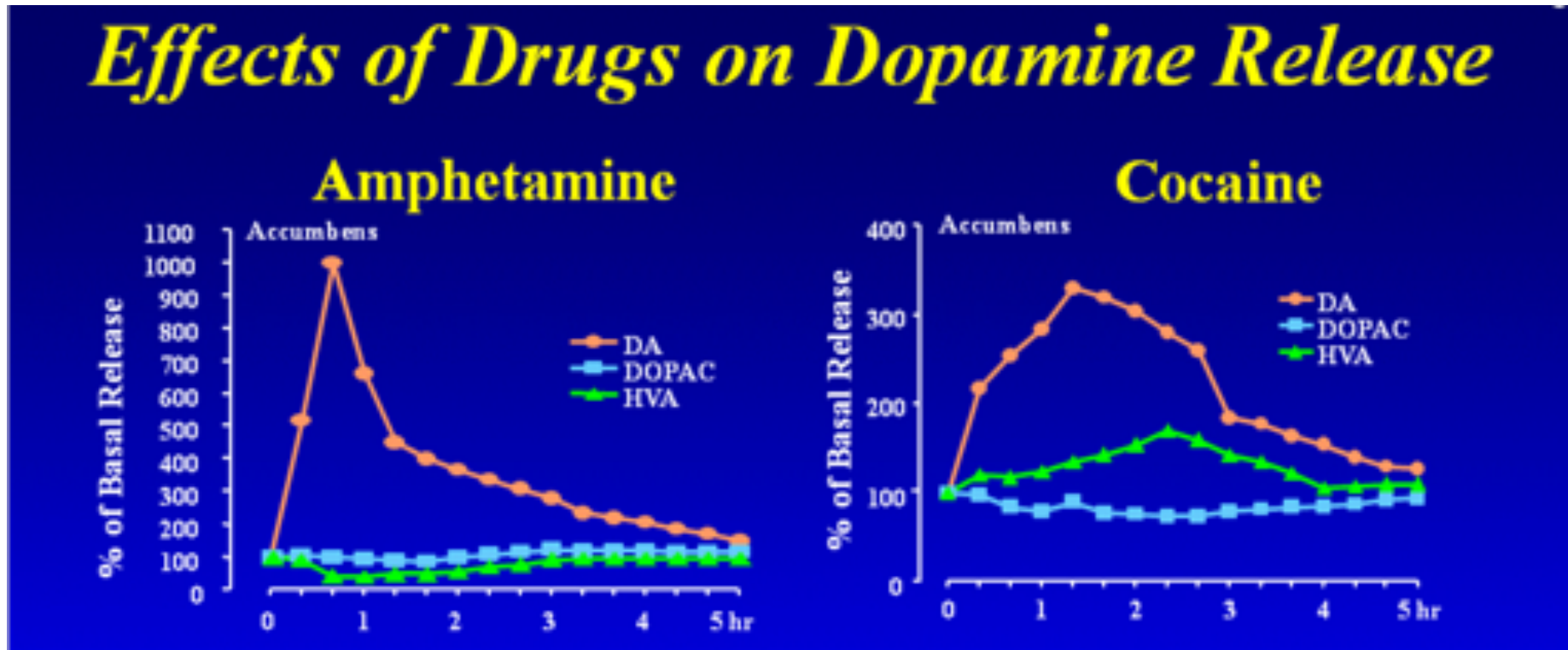
- A. 1000%
- B. 500%
- C. 200%
- D. 100%



For food, it was about 150%



# HIGH ADDICTION POTENTIAL



Di Chiara G and Imperato A. *Proc Natl Acad Sci USA*. 1988 Jul



# HIGH ADDICTION PERSISTENCE

- 61% of individuals treated for addiction relapsing within one year
- Nearly half of those with methamphetamine addiction continue with use over a ten-year period

Brecht ML et al., *Drug Alcohol Depend*, 2014

Brecht ML et al., *J Subst Abuse Treat*, 2013

- Epigenetic changes in reward regions may contribute to longterm addiction

Nestler EJ, *Neuropharmacology*, 2014

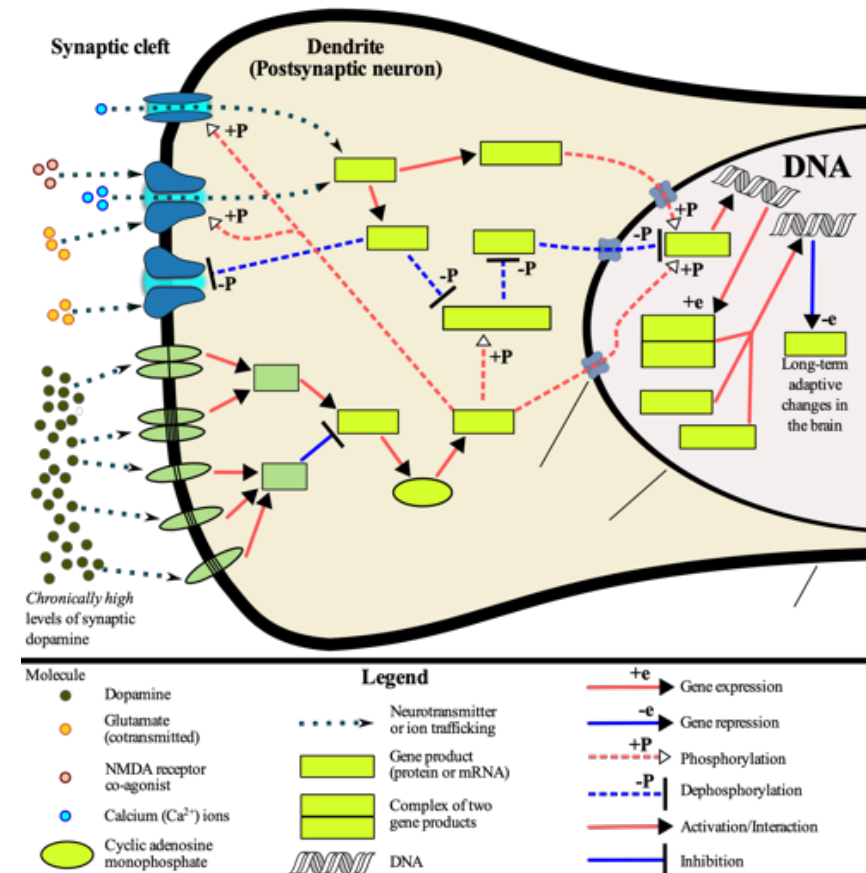
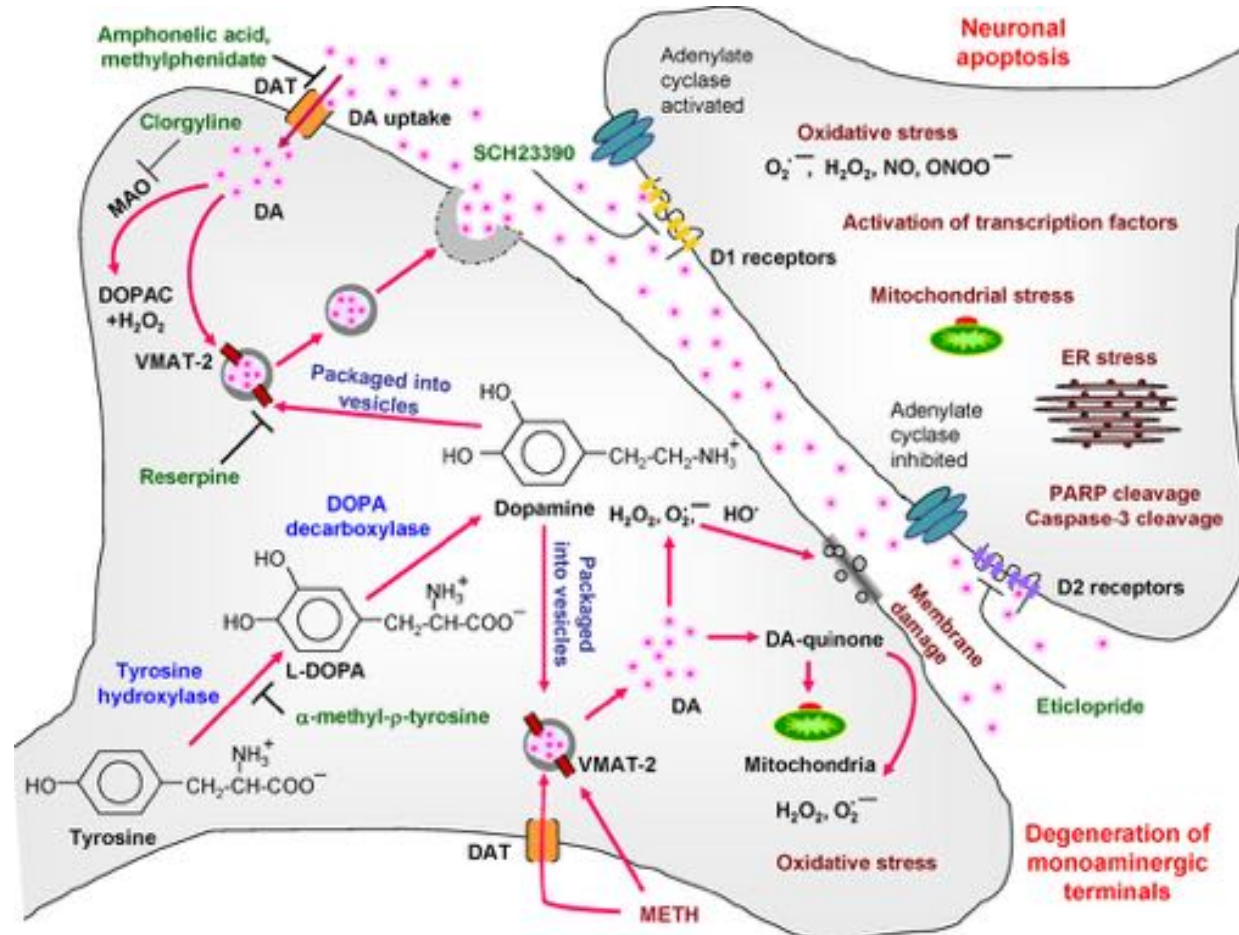


Image from: Wikipedia



# METHAMPHETAMINE NEUROTOXICITY

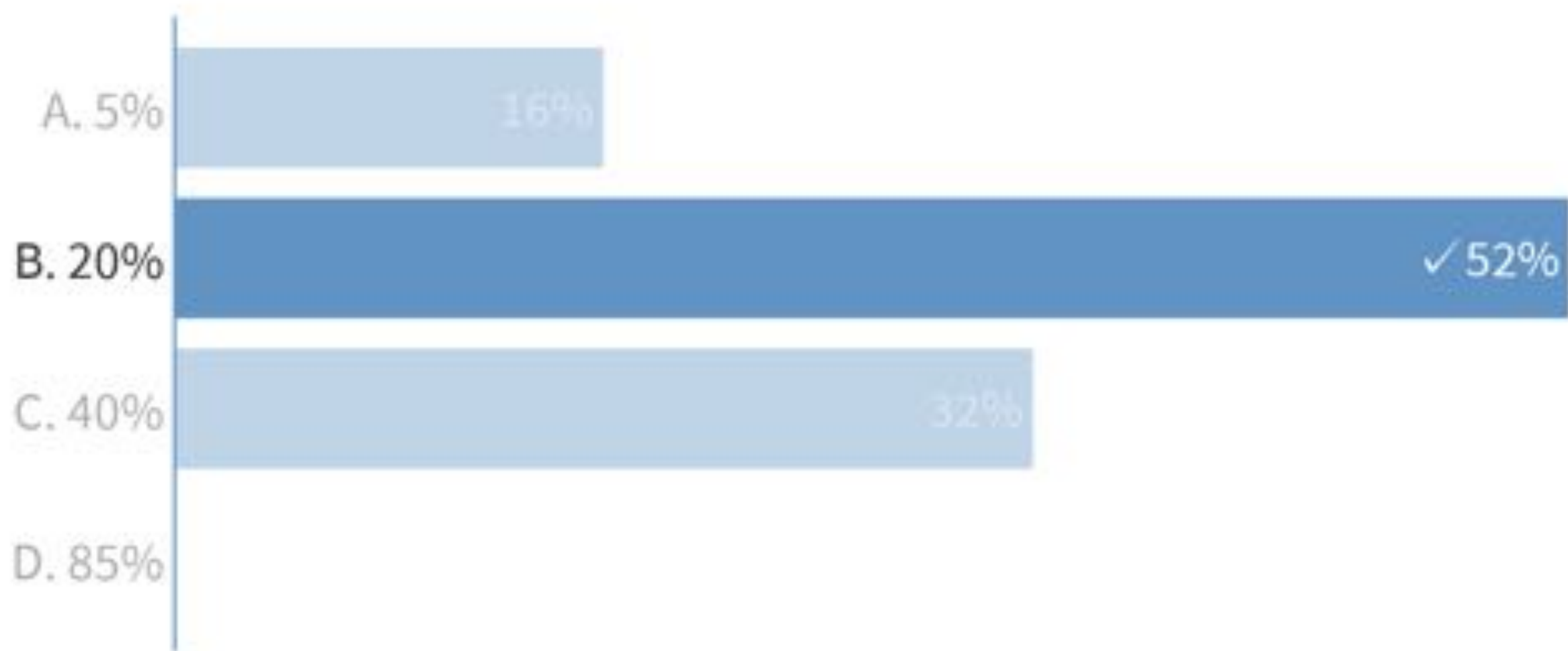


# COURSE

- A Japanese study of recovery from methamphetamine psychosis reported a 64% recovery rate within 10 days rising to an 82% recovery rate at 30 days after methamphetamine cessation

Sato M et al., *Schizophr Bull*, 1992

**What percent of those initially diagnosed with methamphetamine induced psychosis eventually receive a diagnosis of schizophrenia?**



# INTERACTIVE QUIZ

What percent of those initially diagnosed with methamphetamine induced psychosis eventually receive a diagnosis of schizophrenia?

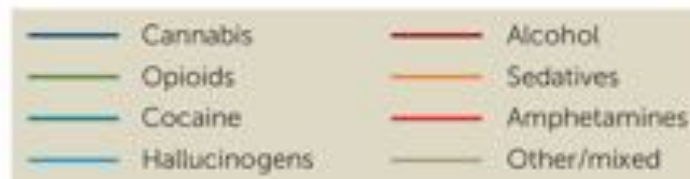
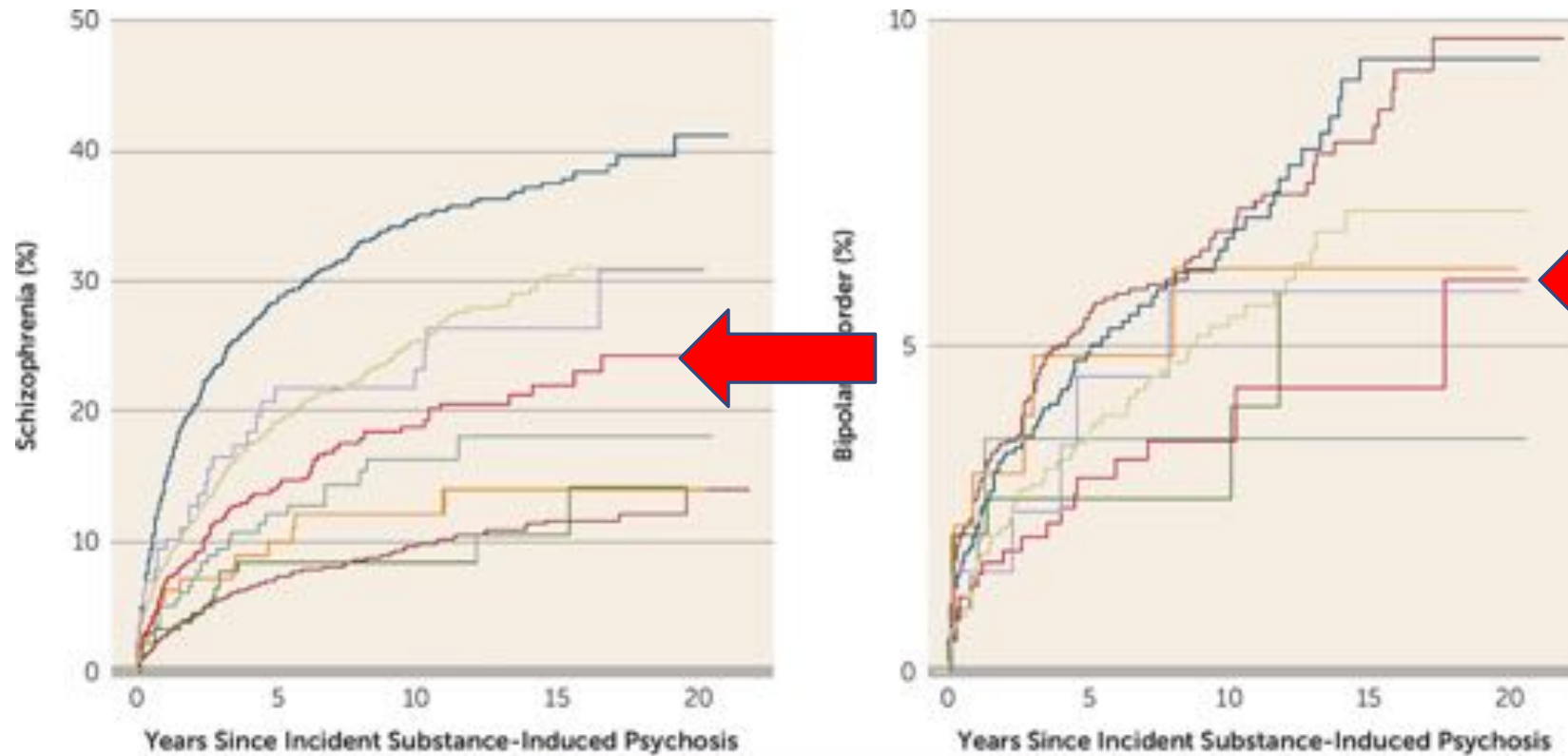
- A. 5%
- B. 20%
- C. 40%
- D. 85%

• 15-23% of those initially diagnosed with amphetamine-induced psychosis eventually receive a diagnosis of schizophrenia

Kittirattanapaiboon P et al., *Drug Alcohol Rev*, 2010

Niemi-Pynttari JA et al., *J Clin Psych*, 2013

# CONVERSION TO SCHIZOPHRENIA OR BIPOLAR DISORDER



# OUTLINE

Background

Cannabis

Stimulants

Management  
considerations

Discussion

# 1. PHARMACOLOGICAL TREATMENT TRIALS FOR METHAMPHETAMINE USE DISORDER ARE DISAPPOINTING

- Dexamphetamine
- Methylphenidate
- Modafinil

- Bupropion

- Mirtazapine

- Sertraline

- Fluoxetine

- Flumazenil + gabapentin

- Topiramate

- Gabapentin

- Vigabatrin

- Risperidone

- Aripiprazole

- Buprenorphine

- Naltrexone

- Baclofen

- Ondansetron

- Varenicline

- Amlodipine

## **More investigation:**

- Glutamate modulators

- Cannabidiol

- Lisdexamfetamine

- N-acetylsteine

# EARLIER TRIALS WERE OPTIMISTIC

Addiction



RESEARCH REPORT

doi:10.1111/j.1360-0443.2009.02717.x

## Randomized controlled trial of dexamphetamine maintenance for the treatment of methamphetamine dependence

Marie Longo<sup>1</sup>, Wendy Wickes<sup>1</sup>, Matthew Smout<sup>1</sup>, Sonia Harrison<sup>1</sup>, Sharon Cahill<sup>1</sup> & Jason M. White<sup>1,2</sup>

Pharmacotherapies Research Unit, Drug and Alcohol Services South Australia, Norwood, South Australia, Australia<sup>1</sup> and Discipline of Pharmacology, University of Adelaide, Adelaide, South Australia, Australia<sup>2</sup>

Longo et al., *Addiction*. 2010 Jan





Trusted evidence.  
Informed decisions.  
Better health.

[Our evidence](#)[About us](#)[Join Cochrane](#)[News and jobs](#)[Cochrane Library](#)

## Efficacy of psychostimulant drugs for amphetamine abuse or dependence

We found eleven studies enrolling 791 amphetamine-dependent participants and assessing the effects of four different psychostimulants: dexamphetamine, bupropion, methylphenidate and modafinil. Psychosocial interventions were additionally provided to all participants. The studies were conducted in the USA, Australia or Northern Europe, and study length ranged from 8 to 20 weeks.

**Psychostimulants did not reduce amphetamine use or amphetamine craving and also did not increase sustained abstinence in comparison with placebo.**

**Retention in treatment was similar and low with both treatments.**

# THE LATEST SYSTEMATIC REVIEW AND META-ANALYSIS

ADDICTION

SS

A SOCIETY FOR THE  
STUDY OF  
ADDICTION

REVIEW

doi:10.1111/add.14755

## Pharmacotherapy for methamphetamine/amphetamine use disorder—a systematic review and meta-analysis

Brian Chan<sup>1,2</sup>, Michele Freeman<sup>3</sup> , Karli Kondo<sup>3</sup>, Chelsea Ayers<sup>3</sup>, Jessica Montgomery<sup>3</sup>,  
Robin Paynter<sup>3</sup> & Devan Kansagara<sup>1,3,4</sup>

Division of General Internal Medicine and Geriatrics, Oregon Health and Science University, Portland, OR, USA,<sup>1</sup> Central City Concern, Portland, OR, USA,<sup>2</sup> Evidence-based Synthesis Program Center, VA Portland Health Care System, Portland, USA,<sup>3</sup> and Department of Medicine, VA Portland Health Care System, Portland, OR, USA<sup>4</sup>

# THE LATEST SYSTEMATIC REVIEW AND META-ANALYSIS

Table 3 Brief summary of findings.

|   | Abstinence | Use | Retention | Harms |
|---|------------|-----|-----------|-------|
| <b>All Antidepressants</b>  | ★★         | ∅   | ★★        | ★     |
| <b>Aminoketone:</b> Bupropion   | ★          | ★   | ★★        | ∅     |
| <b>Atypical Antidepressant:</b> Mirtazapine   | NA         | ∅   | ∅         | ∅     |
| <b>SSRI:</b> Sertraline   | ∅          | NA  | ∅         | NA    |
| <b>Atypical Antipsychotics:</b> Aripiprazole  | ∅          | ★   | ∅         | ∅     |
| <b>Psychostimulants and Other Medications for ADHD</b>                              |            |     |           |       |
| <b>All Psychostimulants:</b><br>Modafinil, Dexamphetamine, Methylphenidate          | ★          | ∅   | ★         | NA    |
| Methylphenidate   | NA         | ★   | ★         | NA    |
| Atomoxetine   | NA         | ∅   | ∅         | ∅     |
| <b>All Anticonvulsant and Muscle Relaxants:</b><br>Baclofen, Gabapentin, Topiramate | ∅          | ∅   | ∅         | ∅     |
| Topiramate  | NA         | ★   | ★         | ★     |
| <b>Medications used for other substance use disorders</b>                           |            |     |           |       |
| Naltrexone  | ∅          | ★   | ★         | ★★    |
| Varenicline   | NA         | ∅   | ∅         | ∅     |

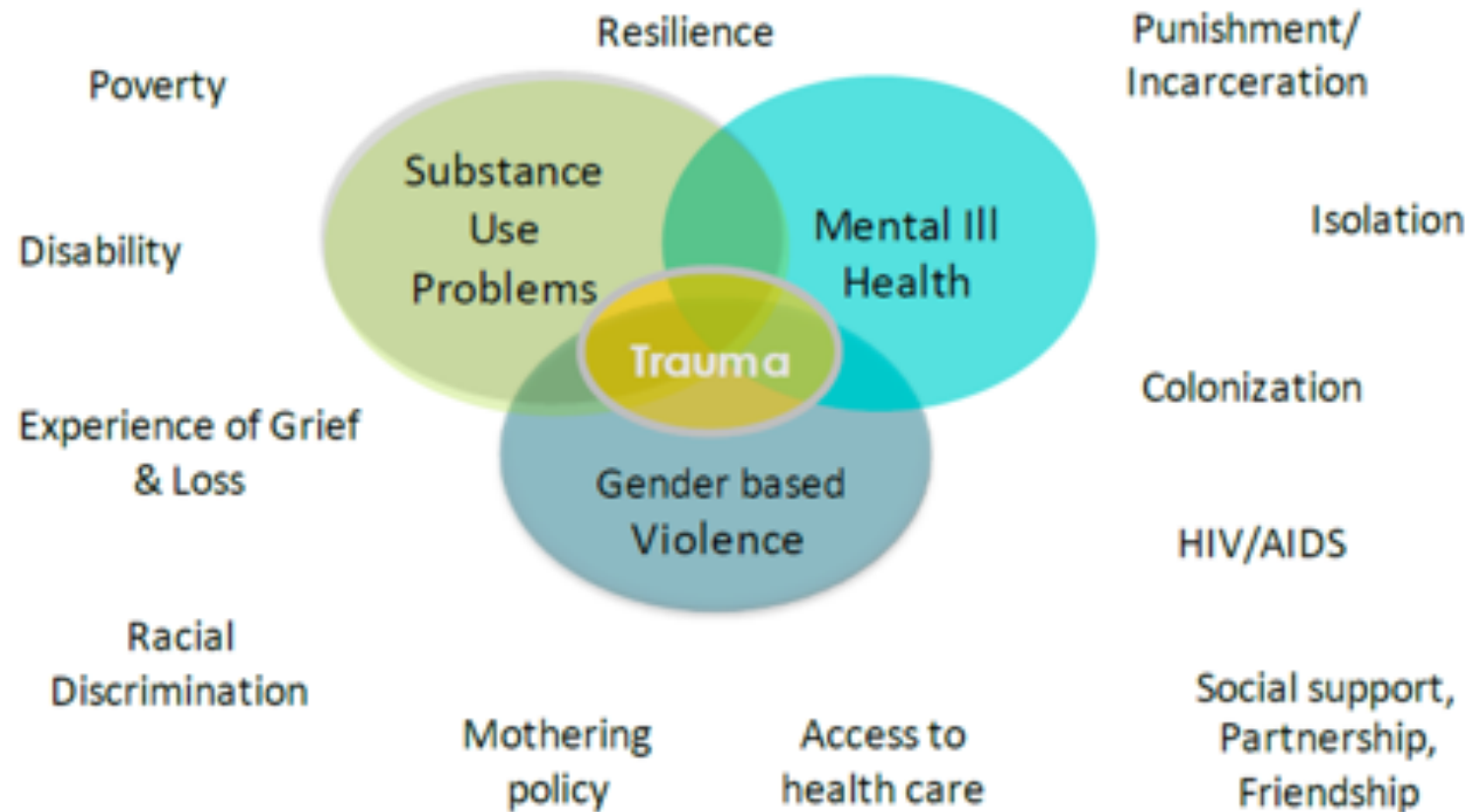
Shading represents the direction of effect:

|            |                     |
|------------|---------------------|
| (No color) | Unclear             |
| Grey       | No difference       |
| Green      | Evidence of benefit |
| Red        | Favors placebo      |

Symbols represent the strength of the evidence:

|     |                               |
|-----|-------------------------------|
| NA  | No evidence or not applicable |
| ∅   | Insufficient                  |
| ★   | Low                           |
| ★★  | Moderate                      |
| ★★★ | High                          |

## 2. SOCIAL DETERMINANTS OF HEALTH MATTER



IMPACTS OF  
METHAMPHETAMINE  
ABUSE IN CANADA  
Report of the Standing  
Committee on Health  
House of Commons  
June 2019

### 3. EVALUATE FOR SEXUALIZED DRUG USE

- The practice of intentionally using drugs before or during sex to increase both sexual pleasure and arousal
- “Chemsex,” “party and play,” “Slamsex,” “H and H”
- Crystal meth, GHB, mephedrone, ketamine
- Sex is often prolonged, mechanically intense (mucosally damaging), condomless, with involvement of groups, and casual or anonymous partners



[HTTP://DEAN.ST/CHEMSEX-SUPPORT](http://dean.st/chemsex-support)



The screenshot shows the top navigation bar of the Dean Street website. It features four service icons: '56 DEAN STREET' (blue), 'DEAN STREET BOOK APPOINTMENTS' (orange), 'DEAN STREET WELLBEING' (green), and 'DEAN STREET PrEP SHOP' (blue). The navigation menu includes: HOME, STD AND HIV TESTING, CONTRACEPTION, HIV SERVICES, PREP SHOP, APPOINTMENTS, CLINIC, CHEMSEX, PLAN ZERO, PSYCHOSEXUAL, UNDER 20, GETTING HERE, and FEEDBACK/COMPLAINTS. Below the navigation is a blue banner with the text 'Chemsex support at 56 Dean Street'. The main content area features a teal text box on the left and a background image of a man's profile on the right.

**Chemsex support at 56 Dean Street**

Chems can be manageable for some, but for others they can become problematic. We are here to help you maintain control if

## 4. TREATMENT FOR STIMULANT INDUCED PSYCHOSIS — SHORT TERM

- First: consider risks versus benefit of antipsychotic treatment
- If deciding to use antipsychotic medication:
  - Olanzapine and haloperidol were efficacious in resolving psychotic symptoms. Olanzapine had greater safety and tolerability (Cochrane, 2009)
  - Aripiprazole and risperidone were effective for patients diagnosed with amphetamine-induced psychotic disorder (Farnia et al., *Am J Drug Alcohol Abuse*, 2014)
  - Haloperidol and quetiapine had similar efficacy and no difference in adverse effects (Verachai V et al., *Psychopharmacology*, 2014)

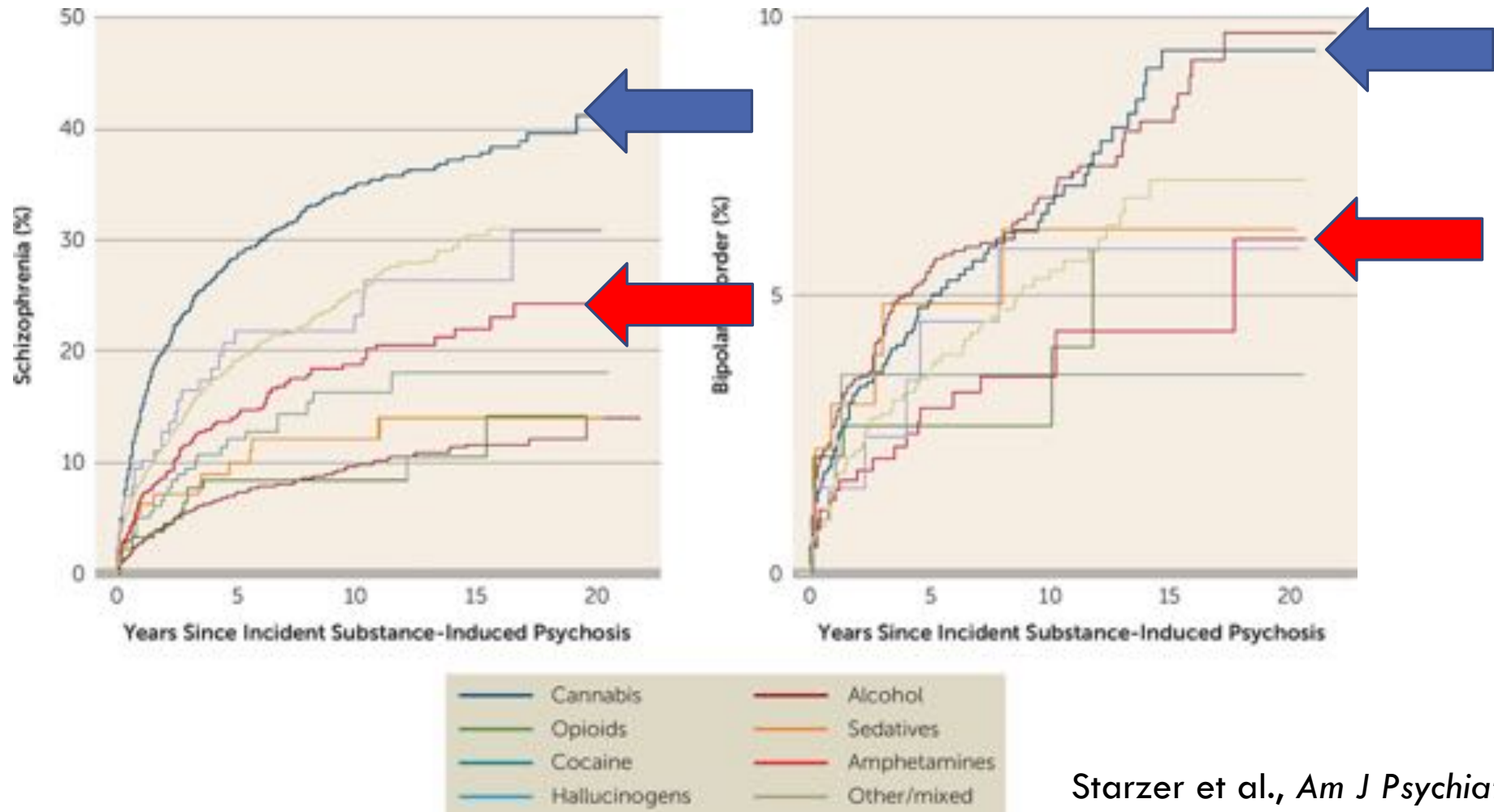
## 5. TREATMENT FOR STIMULANT INDUCED PSYCHOSIS — REFRACTORY CASES

- There is some evidence that dual diagnosis patients might do better on clozapine, with less relapse into abuse of drugs or alcohol
- Comprehensive services and case management are important

Buckley et al., Schizophr Bull, 2008



## 6. LONG-TERM FOLLOW-UP IS ADVISED FOR PATIENTS WHO HAVE PRESENTED WITH SUBSTANCE INDUCED PSYCHOSIS



# THANK YOU

JULIUS.ELEFANTE@UBC.CA



@RJELEFANTE

Comments,  
questions and  
suggestions