

Considerations for Stimulant Use Disorder Care

Nickie Mathew, MD, FRCPC, ABPN, ABPM
Clinical Associate Professor, UBC
Medical Director, Complex Concurrent Disorders



Disclosure: Dr. Nickie Mathew

- I do not have a financial interest, arrangement or affiliation to disclose



Learning Objectives

- Recognize the increasing risk of stimulant use
- Discuss evidence-based psychosocial treatment options for stimulant use disorder and how to apply clinical judgement to determine the best course of treatment
- Describe pharmacological interventions that have been studied in the academic literature



Stimulants



Methamphetamine



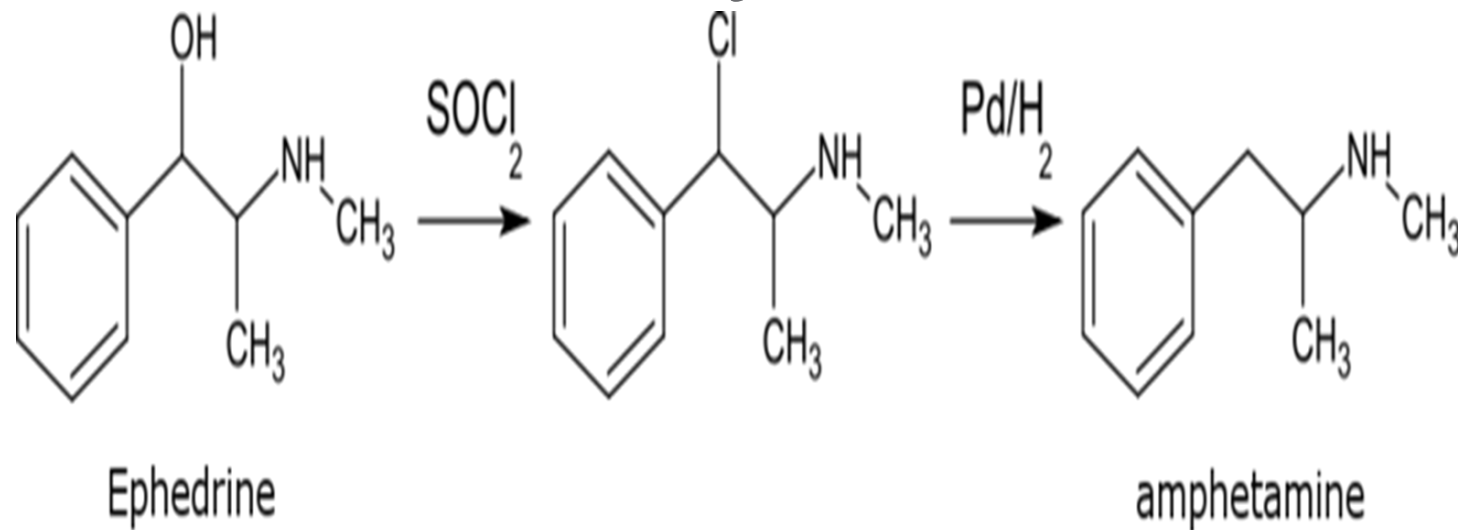
Cocaine



Other amphetamine-type substances



The Rise of P2P Crystal Meth I

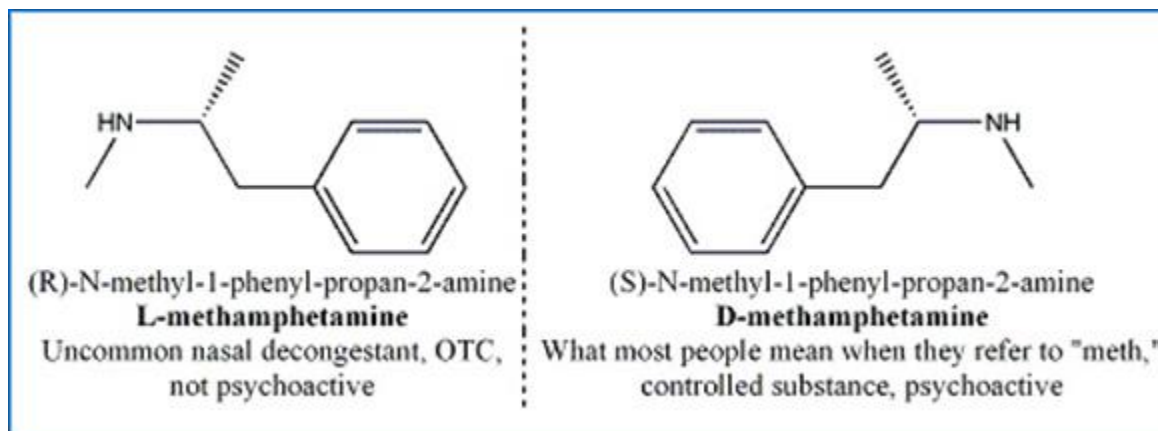
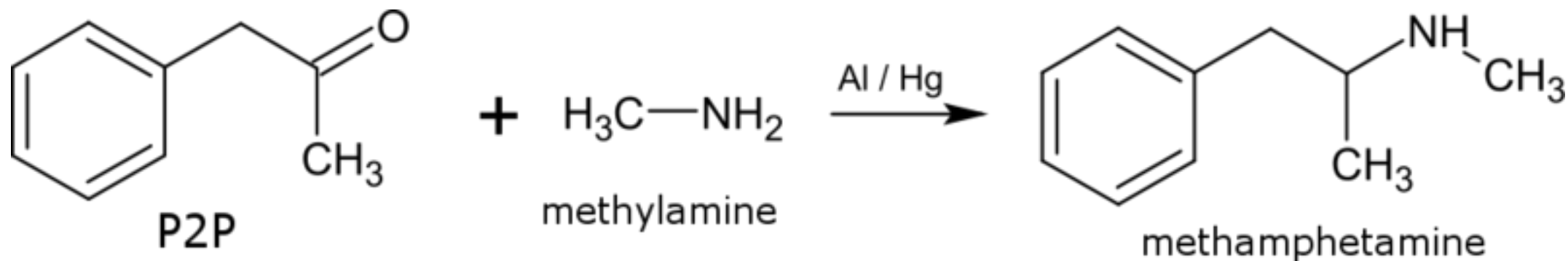


- 1919 Japanese scientists synthesized methamphetamine from the ephedra plant
 - Hiropon → soldiers and kamikaze pilots in WWII
- Branded as Pervitin by Temmler during the Third Reich
 - Pervitin → soldiers in WWII
- Ephedra method was forgotten
 - Biker gangs
- Ephedrine method was rediscovered in the early 1980's
- Ephedrine was banned in the US in 2004 and sales restricted in Canada in 2006

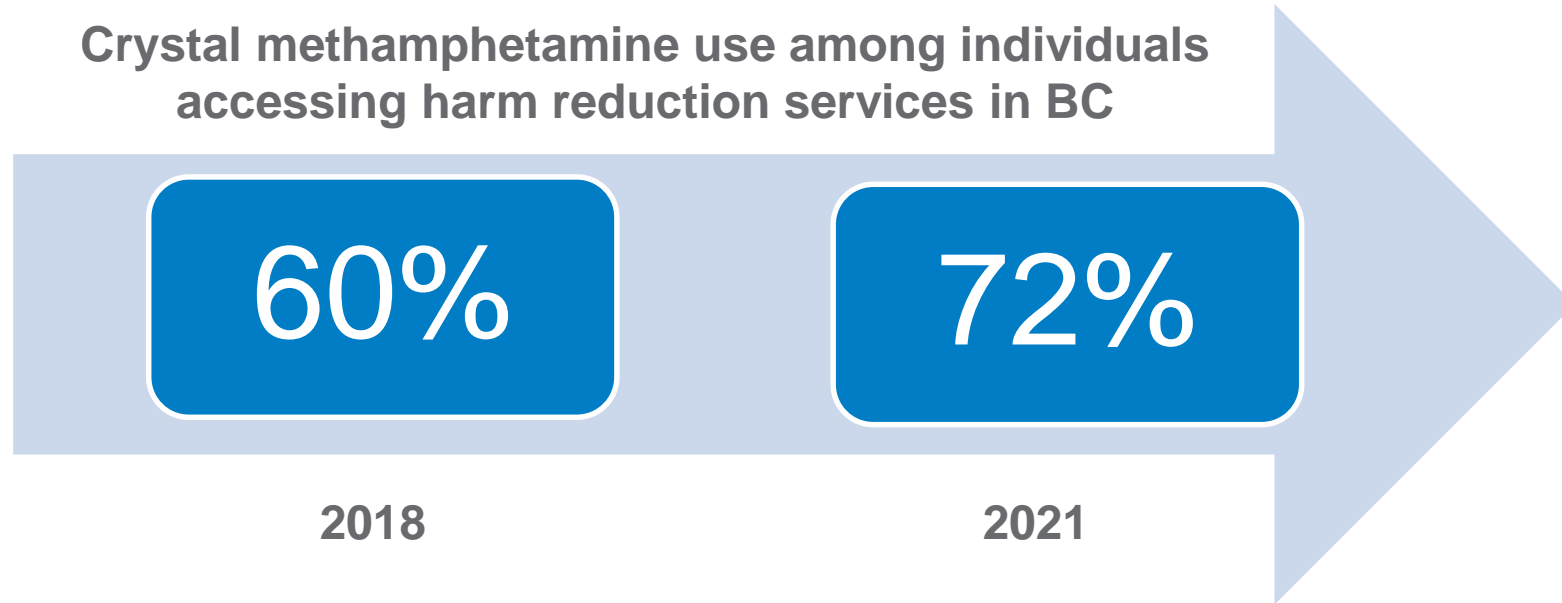


The Rise of P2P Crystal Meth II

- By 2006, Mexican Cartels had rediscovered and perfected the P2P method
 - Not limited by Ephedrine supply
 - Using tartaric acid was stereoselective



Increasing Stimulant Use in BC



Stimulants are among the **most commonly used** unregulated psychoactive substances^{1,2}



Stimulant Associated Risks

BC Coroners Service Unregulated Drug Toxicity Deaths in BC: 2019 - 2022

45%
Cocaine

42%
Methamphetamine

- Increasing unregulated **drug toxicity deaths**³
- Stimulants may be **adulterated**⁴



Stimulant Associated Risks

- Stimulant use disorder (StUD) is associated with an **increased risk** of health complications and fatal drug poisoning⁵⁻⁸
- Stimulant use may **reduce the effectiveness** of other treatments⁹⁻¹¹



Factors Associated with Stimulant Use^{12,13}



Biological



Psychological



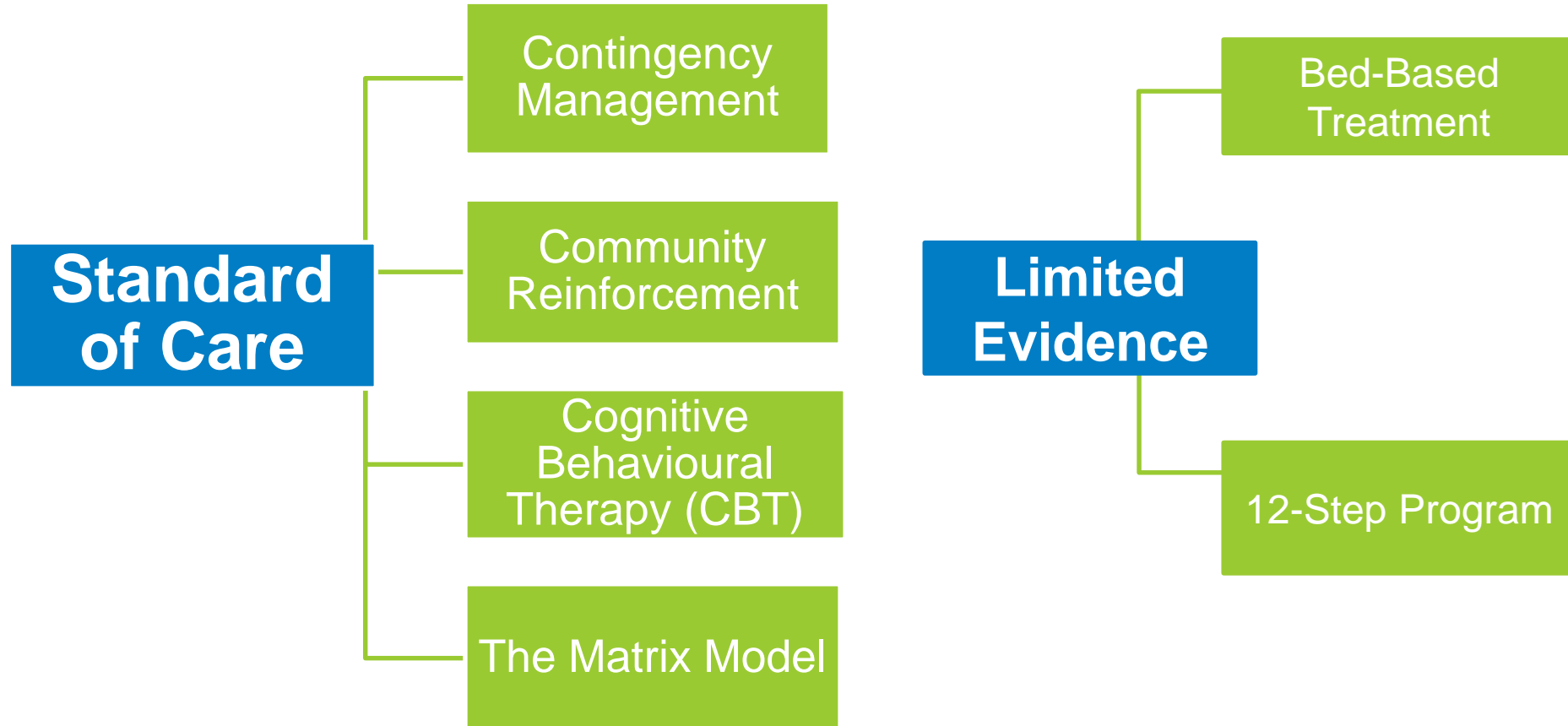
Social



Environmental



Stimulant Use Disorder & Psychosocial Treatment



Contingency Management

- Individuals are **reinforced** for **positive behavioural change**
- Efficacy is supported by a **large body of evidence**¹⁴⁻¹⁷
 - Particularly paired with community reinforcement
- Relatively **poor uptake** due to several **barriers**¹⁸⁻²⁰



Contingency Management

- ← Many clinical trials and several meta-analyses demonstrating CM's efficacy
- ← 12-16 weeks
- ← Reduction in methamphetamine, cocaine, or amphetamine use.
- ← 2.4 times more likely to have –ve UDS
- ← Increased cocaine abstinence during treatment and 1 year of follow-up in contingent group

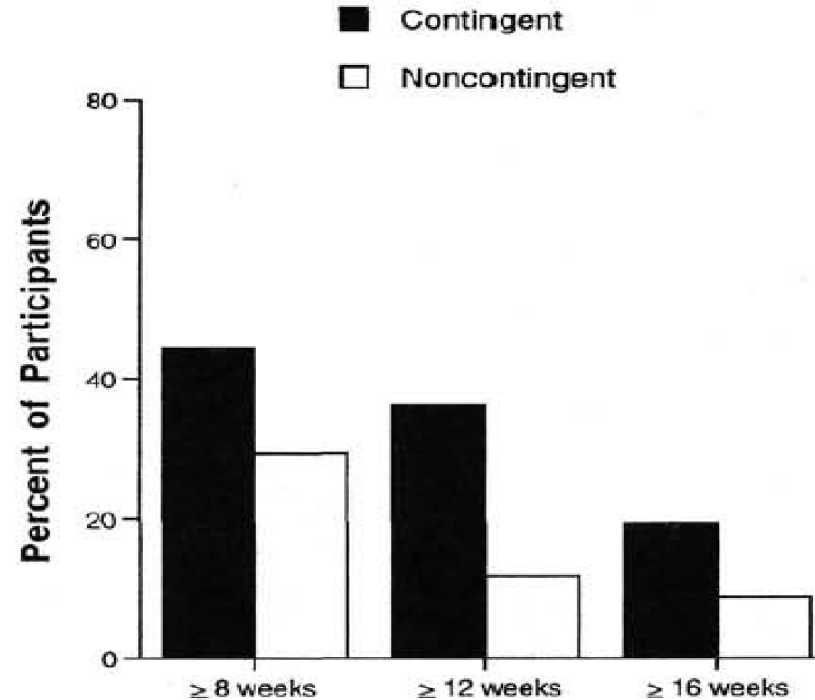


Figure 1. Percentage of participants in the contingent and noncontingent conditions who were documented using urinalysis testing to have achieved durations of 8 or more, 12 or more, and 16 or more weeks of continuous cocaine abstinence during the 24-week treatment period. Condition differences were significant at the .05 level for the 12-or-more-week duration only.

Higgins, S. T., Wong, C. J., Badger, G. J., Ogden, D. E. H., & Dantona, R. L. (2000). Contingent reinforcement increases cocaine abstinence during outpatient treatment and 1 year of follow-up. *Journal of Consulting and Clinical Psychology*, 68(1), 64.



Cognitive Behavioural Therapy (CBT)

- Focuses on modifying **thoughts and behaviours**
- **Specialist-led, manualized** CBT has shown effectiveness in reducing both cocaine and methamphetamine use post-treatment^{16,17}
- Requires a specialist with training in manualized CBT techniques



Matrix Model

- 16-week, **outpatient or inpatient treatment** that integrates CBT, family education, individual counselling, and 12-step fellowship participation
- Promising evidence for:²¹⁻²³
 - Treatment retention
 - Abstinence
 - Reductions in use
 - Reducing high-risk behaviour
 - Improvements in craving management and control



Peer-led Support Groups

12-step programs²⁴

- May provide **some benefit** to those with previous experiences of success in 12-step programs

SMART Recovery, LifeRing^{25,26}

- **No evidence** specific to stimulant use disorder
- Studied mostly for alcohol use disorder



Bed-based Treatment Models

- **Limited evidence** around efficacy for StUD
- **Lack of standardization** on what bed-based programs offer
- **Frequently requested** option
- May be **beneficial for some** people



Choosing a Psychosocial Treatment Intervention

No guidance as to which intervention should be considered first

Include a **physical and psychosocial** assessment to help inform options

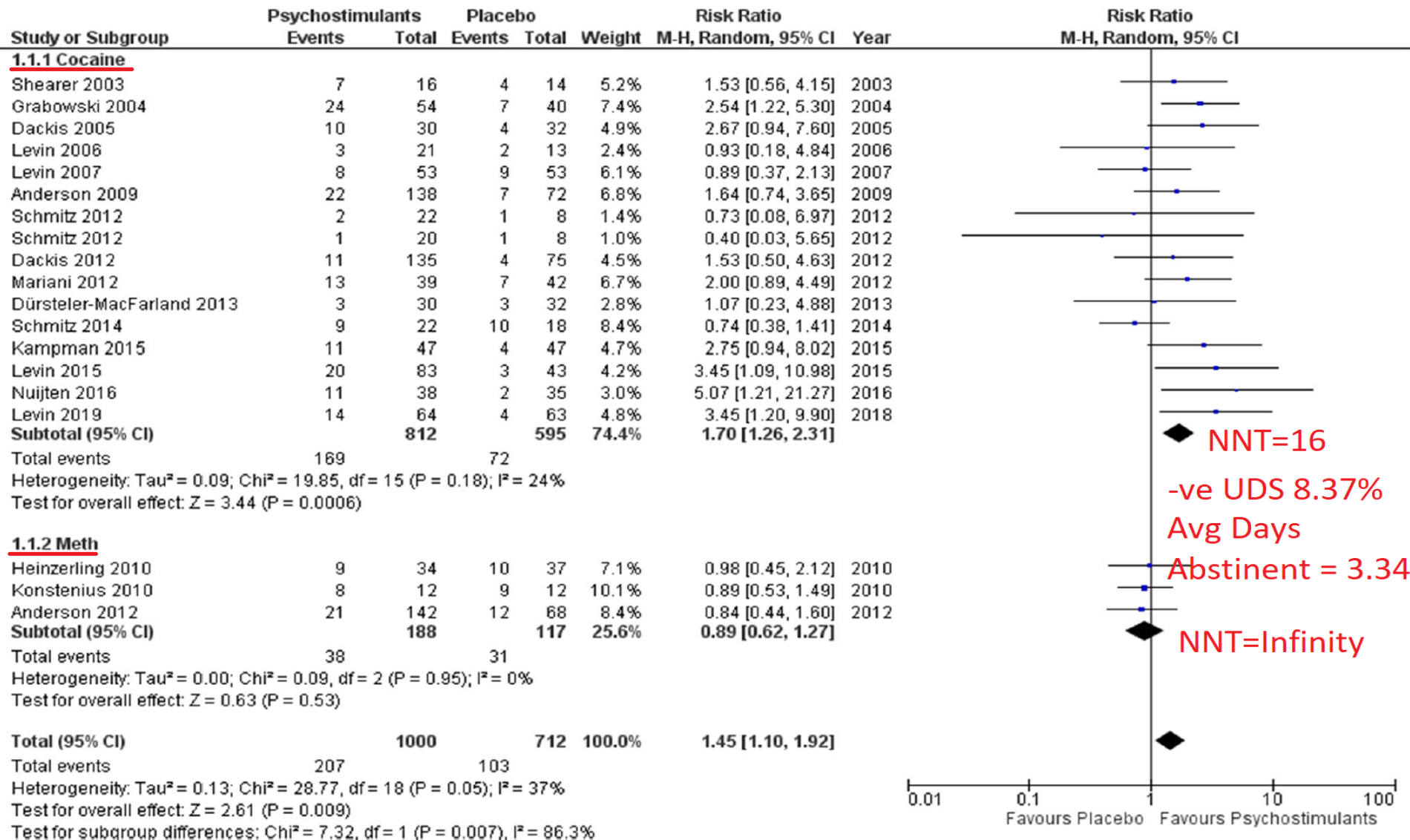
Discuss treatment options and rationale, including weighing of **risks and benefits**

Follow a **person-centred** and evidence-informed approach

Should be informed by the **individual's treatment goals and preferences**



Evidence for the Use of Prescription Stimulants to Treat Stimulant Use Disorder



Tardelli, V. S., Bisaga, A., Arcadevani, F. B., Gerra, G., Levin, F. R., & Fidalgo, T. M. (2020). Prescription psychostimulants for the treatment of stimulant use disorder: a systematic review and meta-analysis. *Psychopharmacology*, 1-23.



Fig. 2. Overall and by dependence drug effect of prescription psychostimulants compared to placebo for outcome sustained abstinence

Takeaways Regarding Prescribing Stimulants for Stimulant Use Disorder

- Some evidence for cocaine use disorder. Does harm outweigh benefit?
- Overall evidence is lacking for amphetamine use disorder. Some possibility for high dose methylphenidate.
- No evidence for those with concurrent severe mental illness (depression, schizophrenia, bipolar disorder, on antipsychotic medication).



Evidence-Based Guidelines for the Pharmacologic Management of Methamphetamine Dependence, Relapse Prevention, Chronic Methamphetamine-Related, and Comorbid Psychiatric Disorders in Post-Acute Settings

Authors

Roland Härtel-Petri^{1*}, Anne Krampe-Scheidler^{2*}, Wolf-Dietrich Braunwarth³, Ursula Havemann-Reinecke⁴, Peter Jeschke⁵, Winfried Looser⁶, Stephan Mühlig⁷, Ingo Schäfer⁸, Norbert Scherbaum⁹, Lydia Bothe¹⁰, Corinna Schaefer¹⁰, Willem Hamdorf¹¹

Bibliography

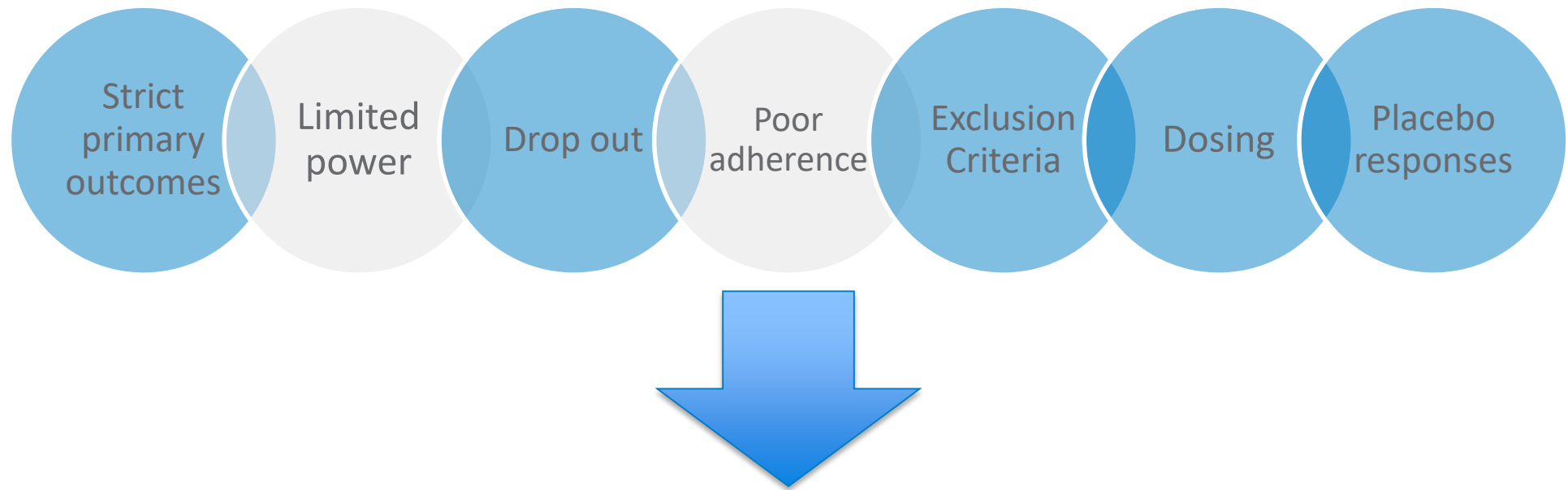
DOI <http://dx.doi.org/10.1055/s-0043-105500>
Published online: 26.4.2017 | Pharmacopsychiatry 2017; 50: 96–104
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► **Table 1** Short summary of recommendations concerning the pharmacological management of chronic methamphetamine use.

Substance/Class	Recommendation	Grade
Antidepressants		
Sertraline	Sertraline should not be administered to patients with a methamphetamine-related disorder to achieve abstinence (LoE 2; ↓↓↓).	↓↓↓
Bupropion	Bupropion may be considered in patients with moderate, non-daily methamphetamine use in order to support achievement of abstinence (LoE 2; ↔).	↔
Mirtazapine	Mirtazapine should be offered to men who have sex with men (MSM) to reduce consumption and risky sexual behaviour (LoE 2; ↑↑↑)	↑↑↑
Imipramine	Imipramine may be considered to increase the retention rate (LoE 2; ↔)	↔
Neuroleptics	No positive recommendation for this group in this treatment goal	
Psychostimulants		
Controlled substances such as d-amphetamine, methylphenidate, and the like	Any treatment beyond acute withdrawal involving dopaminergic amphetamine-like analogues ("replacement therapies") should not be offered unless as part of a registered clinical trial (LoE 2; ↓↓↓).	↓↓↓
Modafinil	Modafinil ought not be administered in the post-acute phase (LoE 2; ↓)	↓
Combined pharmacological treatments	A combined intravenous treatment with flumazenil, gabapentin and hydroxyzine (PROMETA®) should not be administered (LoE 2; ↓↓↓).	↓↓↓



Current evidence is impacted by:



Conclusions are **limited**





Reducing Stigma and Discrimination

Mitigate stigma by:

- **Using respectful**, non-judgmental, and non-stigmatizing **language**
- **Offering harm reduction** services, supplies, and education
- **Participating** in self-reflection, education and cultural safety trainings
- **Removing** pre-conceived assumptions about individuals



Amphetamine Use Disorder and Psychosis

- 1 in 660 people in the general population with ADHD who are prescribed psychostimulants will develop psychosis
- However, 40% of people with amphetamine use disorder will develop amphetamine induced psychosis
- Ranged from 30.8% with abuse and 100% with severe dependence

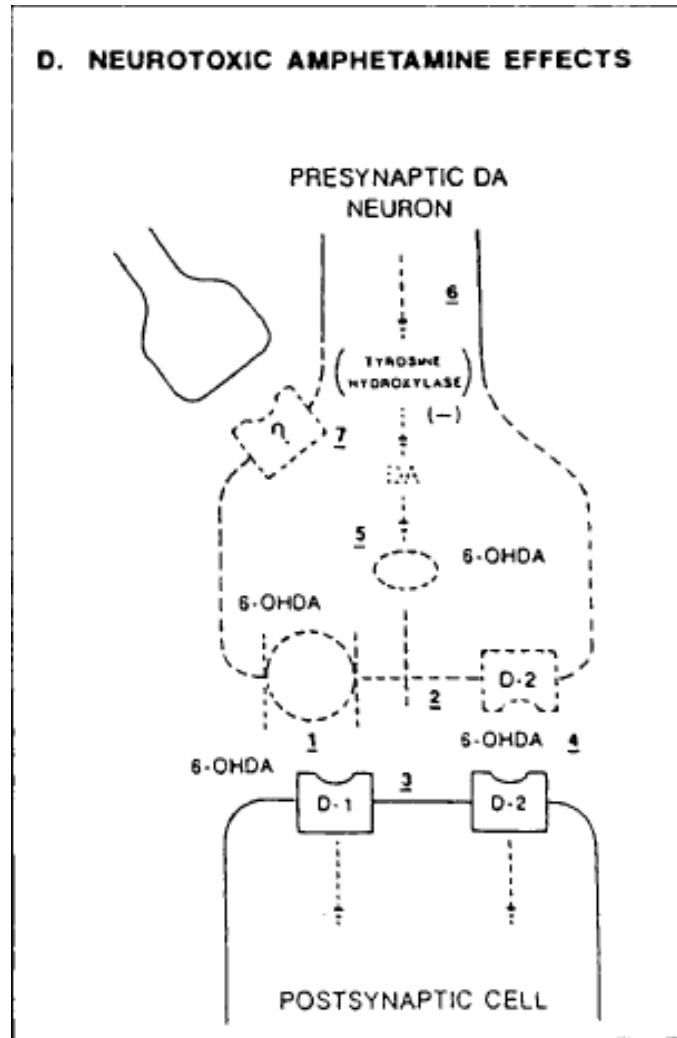
Moran, L. V., Ongur, D., Hsu, J., Castro, V. M., Perlis, R. H., & Schneeweiss, S. (2019). Psychosis with methylphenidate or amphetamine in patients with ADHD. *New England Journal of Medicine*, 380(12), 1128-1138.

Schuckit, M. A. (2006). Comorbidity between substance use disorders and psychiatric conditions. *Addiction*, 101, 76-88.

Smith, M. J., Thirhalli, J., Abdallah, A. B., Murray, R. M., & Cottler, L. B. (2009). Prevalence of psychotic symptoms in substance users: a comparison across substances. *Comprehensive psychiatry*, 50(3), 245-250.



Pathophysiology of Substance Induced Psychosis

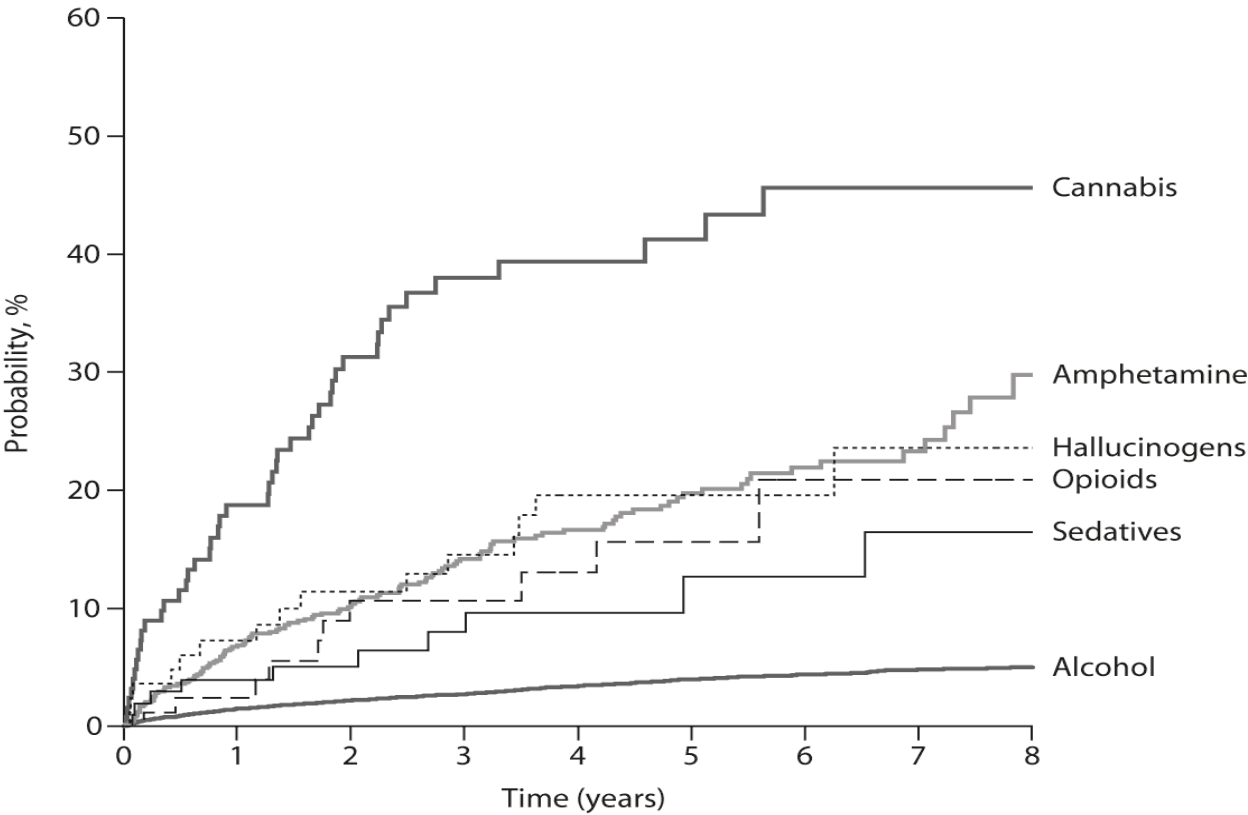


- Neurotoxic event
- Kindling effect
- Antipsychotics will not prevent



Probability of Those With Substance Induced Psychosis Later Being Diagnosed With Schizophrenia

Figure 1. Cumulative Probability of Receiving a Schizophrenia Spectrum Disorder Diagnosis (N = 18,478)



Substance	% of Total	% Diagnosis Conversion
Cannabis	0.7	46%
Amphetamines	4.5	30%
Hallucinogens	0.45	24%
Opioids	0.5	21%
Sedatives	0.66	15%
Alcohol	85.4	5%

Niemi-Pynttari, J. A., Sund, R., Putkonen, H., Vorma, H., Wahlbeck, K., & Pirkola, S. P. (2013). Substance-induced psychoses converting into schizophrenia: a register-based study of 18,478 Finnish inpatient cases. The Journal of clinical psychiatry, 74(1), 94-99.




Antipsychotics and Acute Psychosis in the Setting of Meth Use

- In a double-blind study, 45 participants were randomly allocated to either aripiprazole 15 mg or risperidone 4 mg daily over a six-week trial
 - Both aripiprazole and risperidone were effective for patients diagnosed with amphetamine-induced psychotic disorder



Long-Term Antipsychotics and Methamphetamine Induced Psychosis

Review

 Thieme

Evidence-Based Guidelines for the Pharmacologic Management of Methamphetamine Dependence, Relapse Prevention, Chronic Methamphetamine-Related, and Comorbid Psychiatric Disorders in Post-Acute Settings

- The indication for the continuation of neuroleptic therapy ought to be reviewed at the latest after 6 months of treatment in individuals presenting with a methamphetamine-associated psychosis



For Those with Schizophrenia

Short Report

Association of clozapine treatment and rate of methamphetamine or amphetamine relapses and abstinence among individuals with concurrent schizophrenia spectrum and amphetamine use disorder: A retrospective cohort study

Reza Rafizadeh^{1,2,3,5,6} , Laura Frankow^{3*}, Hajer Mahmood^{3*}, Sukhpreet Poonia^{3,6}, Nickie Mathew^{2,5}, Marlon Danilewitz¹⁰, Chad A Bousman^{7,8,9}, William G Honer^{2,4} and Christian G Schütz^{2,4,5}



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- **Results:** Clozapine use was both associated with increased likelihood of maintaining abstinence from MA use (adjusted odds ratio (aOR) = 3.05, 95% confidence intervals (CI) = 1.15–8.1, $p = 0.025$), and decreased rate of MA relapses (aRR = 0.45, 95% CI = 0.25–0.82, $p = 0.009$) for the duration of antipsychotic exposure. Co-prescription of psychostimulants was associated with increased rate of MA relapses (aRR = 2.43, 95% CI = 1.16–5.10, $p = 0.019$).



Prescribing Prescription Stimulants To Patients with Psychosis

- Cressman (2015)
 - This looked at people who were admitted to the ER with substance induced psychosis.
 - Of that group, about a third were prescribed psychostimulants on discharge.
 - Of the people that were prescribed psychostimulants after being admitted for substance induced psychosis, 45% were readmitted to hospital within 18 days for substance induced psychosis.



ADHD and Stimulant Use Disorder

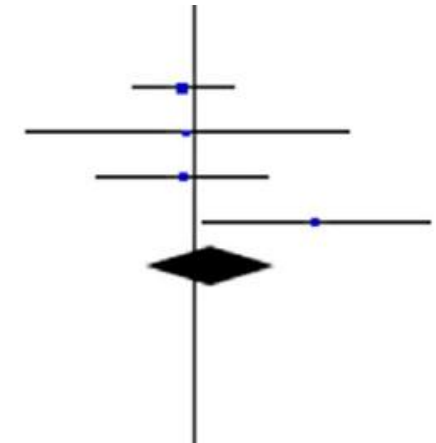
1.21.2 ADHD

Konstenius 2010	8	12	9	12	10.1%	0.89 [0.53, 1.49]
Levin 2006	3	21	2	13	2.4%	0.93 [0.18, 4.84]
Levin 2007	8	53	9	53	6.1%	0.89 [0.37, 2.13]
Levin 2015	20	83	3	43	4.2%	3.45 [1.09, 10.98]
Subtotal (95% CI)		169		121	22.9%	1.17 [0.61, 2.25]

Total events 39 23

Heterogeneity: $\text{Tau}^2 = 0.21$; $\text{Chi}^2 = 5.78$, $\text{df} = 3$ ($P = 0.12$); $I^2 = 48\%$

Test for overall effect: $Z = 0.48$ ($P = 0.63$)



Tardelli, V. S., Bisaga, A., Arcadepani, F. B., Gerra, G., Levin, F. R., & Fidalgo, T. M. (2020). Prescription psychostimulants for the treatment of stimulant use disorder: a systematic review and meta-analysis. *Psychopharmacology*, 1-23.





Original Investigation | Substance Use and Addiction

Analysis of Stimulant Prescriptions and Drug-Related Poisoning Risk Among Persons Receiving Buprenorphine Treatment for Opioid Use Disorder

Carrie M. Mintz, MD; Kevin Y. Xu, MD, MPH; Ned J. Presnall, MSW; Sarah M. Hartz, MD, PhD; Frances R. Levin, MD; Jeffrey F. Scherrer, PhD; Laura J. Bierut, MD; Richard A. Grucza, PhD

Key Points

Question How are use of prescription stimulants associated with treatment outcomes in persons with opioid use disorder (OUD)?

Findings In this cohort study of 22 946 persons with OUD receiving buprenorphine treatment, stimulant treatment days were associated with 19% increased odds of drug-related poisoning and 36% decreased risk of attrition from buprenorphine treatment.



Summary

- Individuals face **increasing risk** of stimulant-related harms
- Psychosocial treatment is the **standard of care** for StUD
 - Treatment *should* be **person-centered, trauma-informed** and **evidence-based**
- Evidence supporting pharmacotherapy for StUD is **limited and inconclusive**
- **Harm reduction** practices focus on **offering support** and **education**
- **Consider concurrent disorders**

