



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

METHAMPHETAMINE AND PSYCHOSIS: DIAGNOSIS AND TREATMENT

JONATHAN BUCHHOLZ, MD
VA PUGET SOUND HEALTH CARE SYSTEM



SPEAKER DISCLOSURES

- ✓ Any conflicts of interest?

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose; other disclosures have been mitigated.

Mark Duncan MD

Barb McCann PhD

Matt Iles-Shih, MD, MPH

Kari Stephens PhD

Jen Jepsen, PharmD

Justin C Bayley, DNP

Trudy Mossop MS

Betsy Payn MA PMP

Anna Ratzliff MD PhD

Esther Solano

OBJECTIVES

1. Understand the key DSM5 clinical criteria differentiating substance induced psychosis from primary psychotic illnesses
2. Name 2 types of psychosis associated with amphetamine use and identify one way to differentiate these diagnostically
3. Name 2 treatment modalities associated with improvement in substance induced psychosis

Drugs involved in overdose deaths in King County

Data Source: King County Medical Examiner’s Office

← Return to summary

→ Next tab: Trends

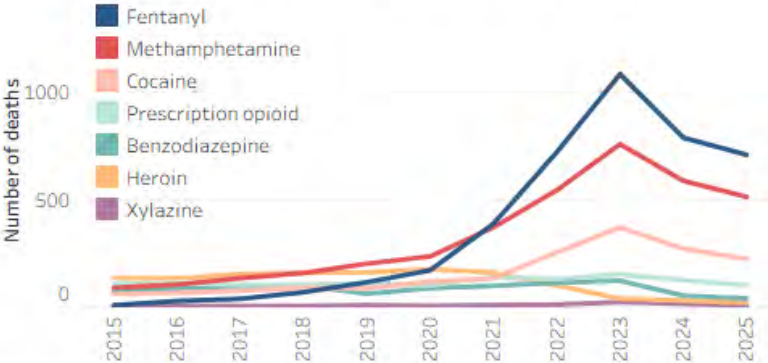
Click to view interpretation of the data

Drugs Involved in King County Overdose Deaths, 2015-2025

Drug overdose deaths typically involve multiple drug classes - most commonly opioids and stimulants.

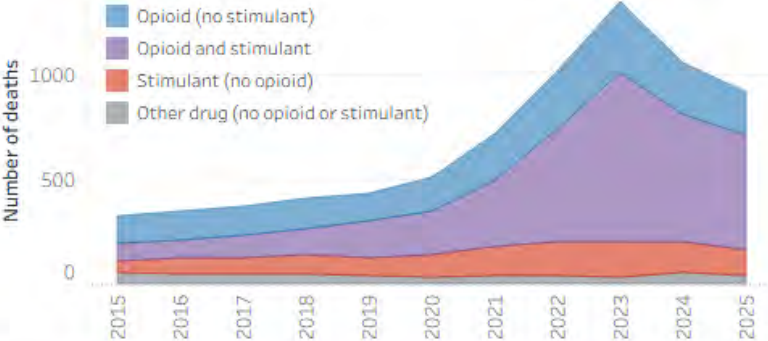
Specific drug classes involved in overdose deaths

Note: Individuals can be represented in more than one line



Number of Overdose Deaths Involving Opioids and/or Stimulants

Note: Individuals are represented only once; Opioid = Fentanyl, Heroin, an/or Prescription Opioids; Stimulant = Methamphetamine and/or cocaine



Drug combinations in 2025 overdose deaths

This bar chart enables viewers to see which drug combinations cause overdose deaths. Click on a drug listed on the left-hand side to see the other drugs also present at time of death.

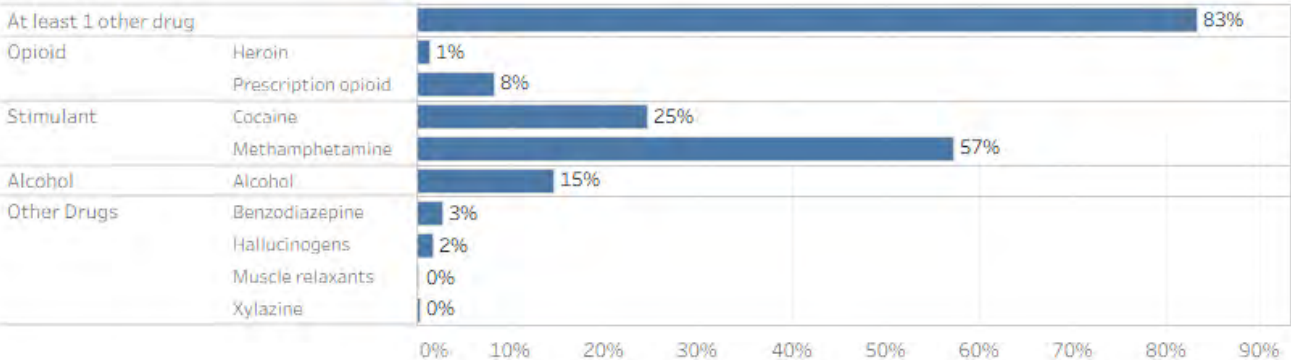
Select drug to view:

- ☒ Fentanyl
- ☐ Methamphetamine
- ☐ Cocaine
- ☐ Prescription opioid
- ☐ Benzodiazepine
- ☐ Heroin
- ☐ Xylazine

Drugs detected in: Fentanyl-involved deaths

In 2025, there were 708 overdose deaths that involved Fentanyl, representing 77% of all overdose deaths in King County. These deaths also involved:

*Cocaine: this includes both powder cocaine and rock-like cocaine, commonly referred to as crack.
Note: Drugs are included here if they were indicated on the death certificate as a cause of death.



DSM CRITERIA – SUBSTANCE INDUCED PSYCHOSIS

- During or soon after ingested substance
 - *Should not persist beyond one month
- Not better accounted for by pre-existing mental disorder
- Not a medical disorder (Delirium)
 - Orientation/consciousness intact

HISTORY, HISTORY, HISTORY

- No specific lab values or tests aside from urine toxicology
- Linear history of patient's development and mental health history
 - Family History
 - Developmental history – school, relationship, work
 - Substance use history

TYPICAL SYMPTOMS¹

	Substance Induced Psychosis	Schizophrenia	Bipolar Mania	Depression w/Psychosis
Hallucinations	++++	++++	+++	++
Psychomotor Agitation	++++	++	+++	+/-
Disorganization of Thought	+++	++++	++++	++++
Grandiosity	+++	+/-	+++	+/-
Compulsive Thoughts	+	++++	+++	++++
Poverty of Speech	+/-	++++	+/-	+++
Psychomotor Retardation	+/-	++++	+/-	+++
Flat affect	+/-	++++	+/-	+/-

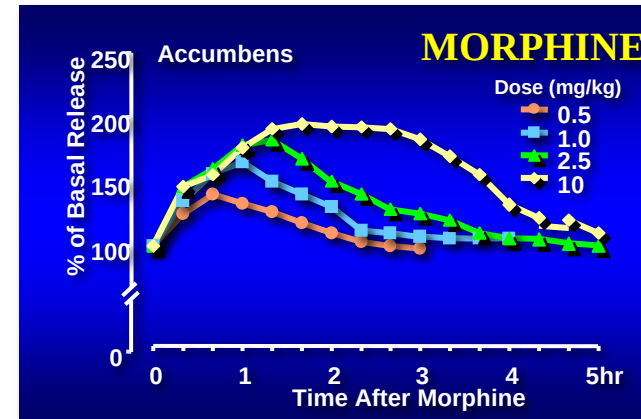
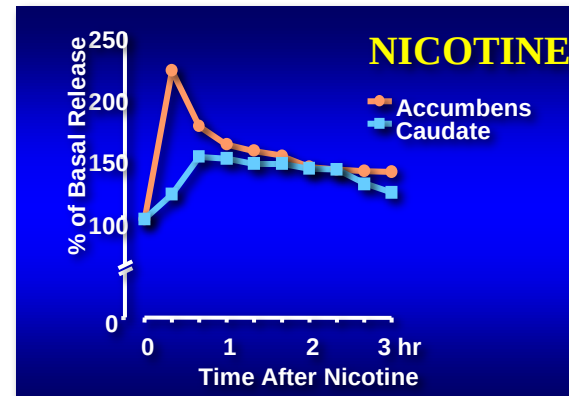
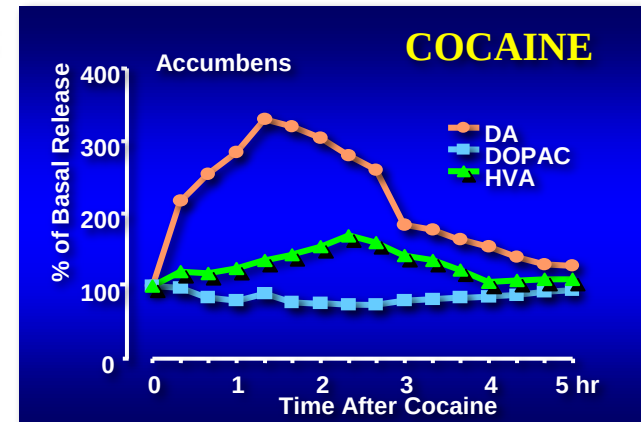
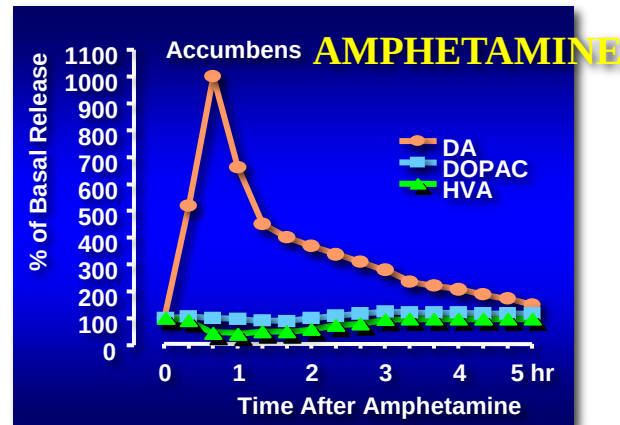
COMMON SUBSTANCES ASSOCIATED WITH PSYCHOSIS¹

- Cannabis – 0.8-10%
- Cocaine – Across the lifespan: 60.0–86.5%
- Methamphetamine - 17–37.1%

METHAMPHETAMINE ASSOCIATED PSYCHOSIS³

- Transient Psychosis
 - 1 cross-sectional study, more than half (52%) of patients with MAP saw a remission of their psychotic symptoms within a week of abstinence from methamphetamines.
- Persistent
 - Psychotic symptoms remained in 26% of patients after 1 month and in 16% of patients after 3 months.
 - Remains unclear if they are already genetically vulnerable, and methamphetamine use triggers the development of a psychotic disorder.

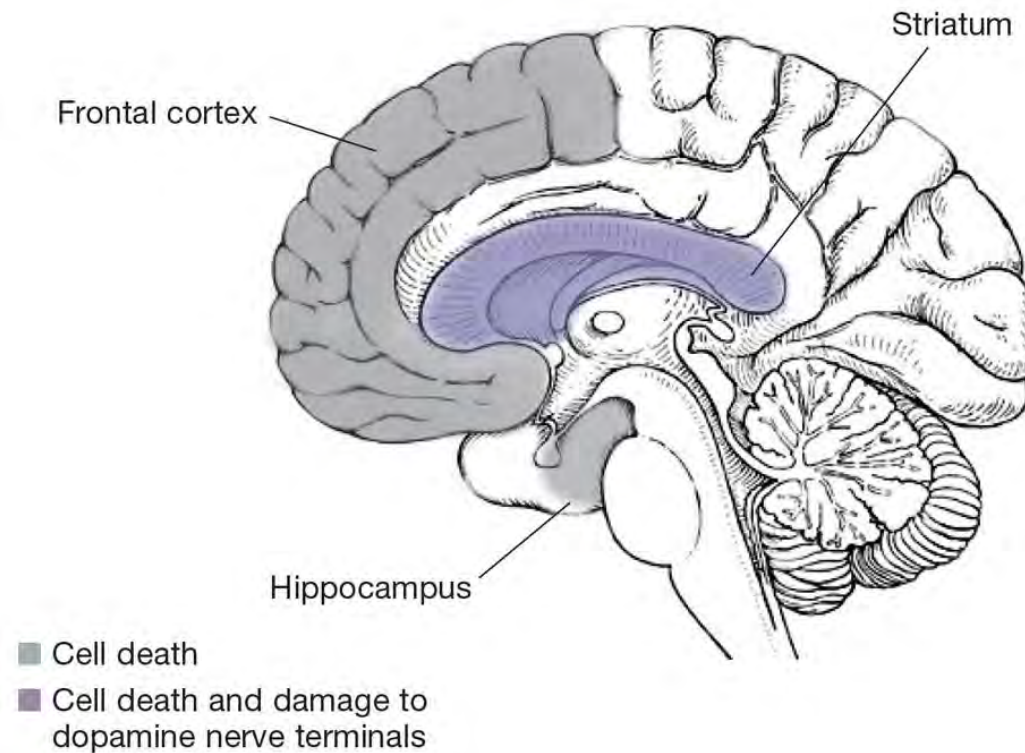
Effects of drugs on dopamine levels



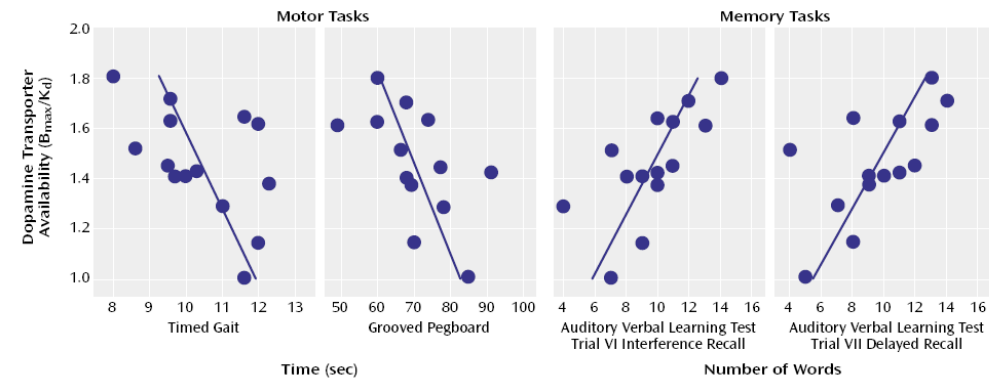
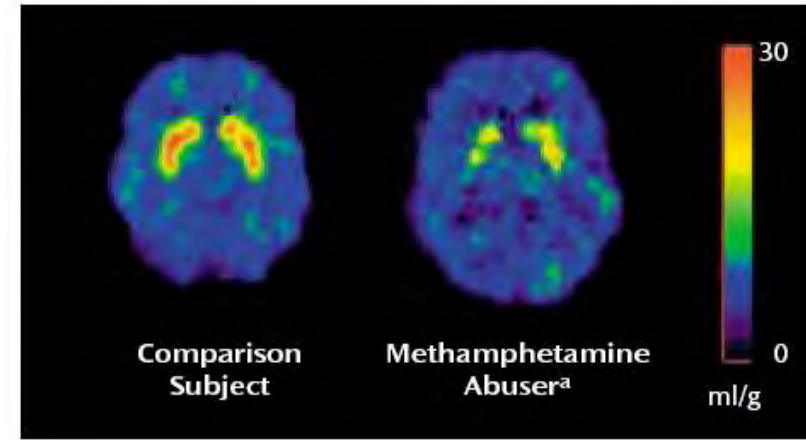
Source: Di Chiara and Imperato

METHAMPHETAMINE NEUROTOXICITY

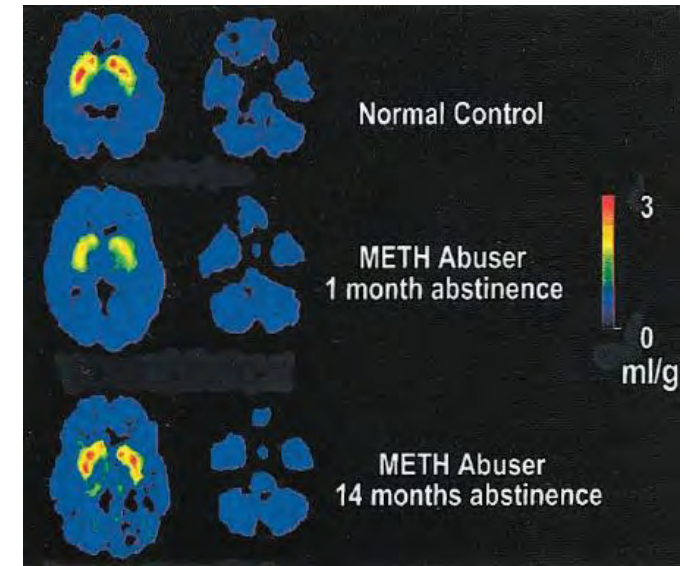
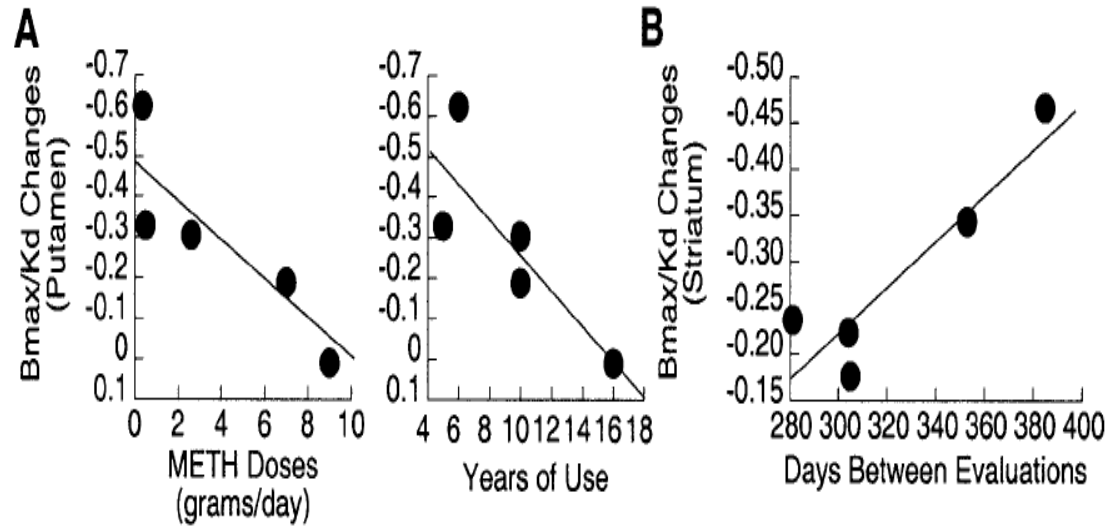
- Meth → ROS → neuron damage
- Less damage on 5-HT system
- Dose-dependent destruction of striatal dopamine nerve terminals
- Behavior changes partially reversible with time



- Decreased dopaminergic function → worse cognition
- Dose-dependent damage
- Cognition slowly improves with abstinence
- 5HT transporter decline → increased aggression



METHAMPHETAMINE NEUROTOXICITY



METHAMPHETAMINE NEUROTOXICITY

CASE

- 24 y.o. man who presents to the ED in severe distress stating that his roommates are poisoning him through the heating ducts.
- Patient has been using methamphetamine in binge fashion for 3 years. He usually uses stimulants partying with friends. Patient last used 2 days ago but was “passed out for the last day” prior to coming into the hospital because “they are pumping toxic gas into my room.”

INITIAL SCREEN

- HR: 108, BP: 158/94, RR:14, Temp: 37.8, 99% RA
 - Chem panel normal aside from Cr of 2.1
 - CBC normal aside from white count of 12
 - Utox is negative for everything aside from methamphetamine
-
- As you consider follow up labs, pt becomes increasingly agitated screaming that he's being poisoned. What is the next step in management?

NEXT STEP IN MANAGEMENT OF AGITATION

- A. Haldol 5mg
- B. Ativan 2mg
- C. Olanzapine 10mg
- D. Restraints

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MANAGEMENT OF ACUTE AGITATION

- Medication
 - Benzodiazepines
 - Antipsychotics: avoid in patients with evidence of Rhabdomyolysis and those with prolonged QTc
- Supportive Care
- Ongoing medical workup
 - Continue to monitor for delirium
- Reassurance/low stimulation

CASE CONTINUED

- Patient found to have CK of 2200 admitted for treatment of Rhabdomyolysis and secondary AKI. After 2 days of supportive care, aggressive fluid resuscitation and monitoring, CK is normalized, creatinine is down trending. Patient remains convinced that his roommates are poisoning him. What questions do you have next?

TREATMENT OF STIMULANT INDUCED PSYCHOSIS ⁴

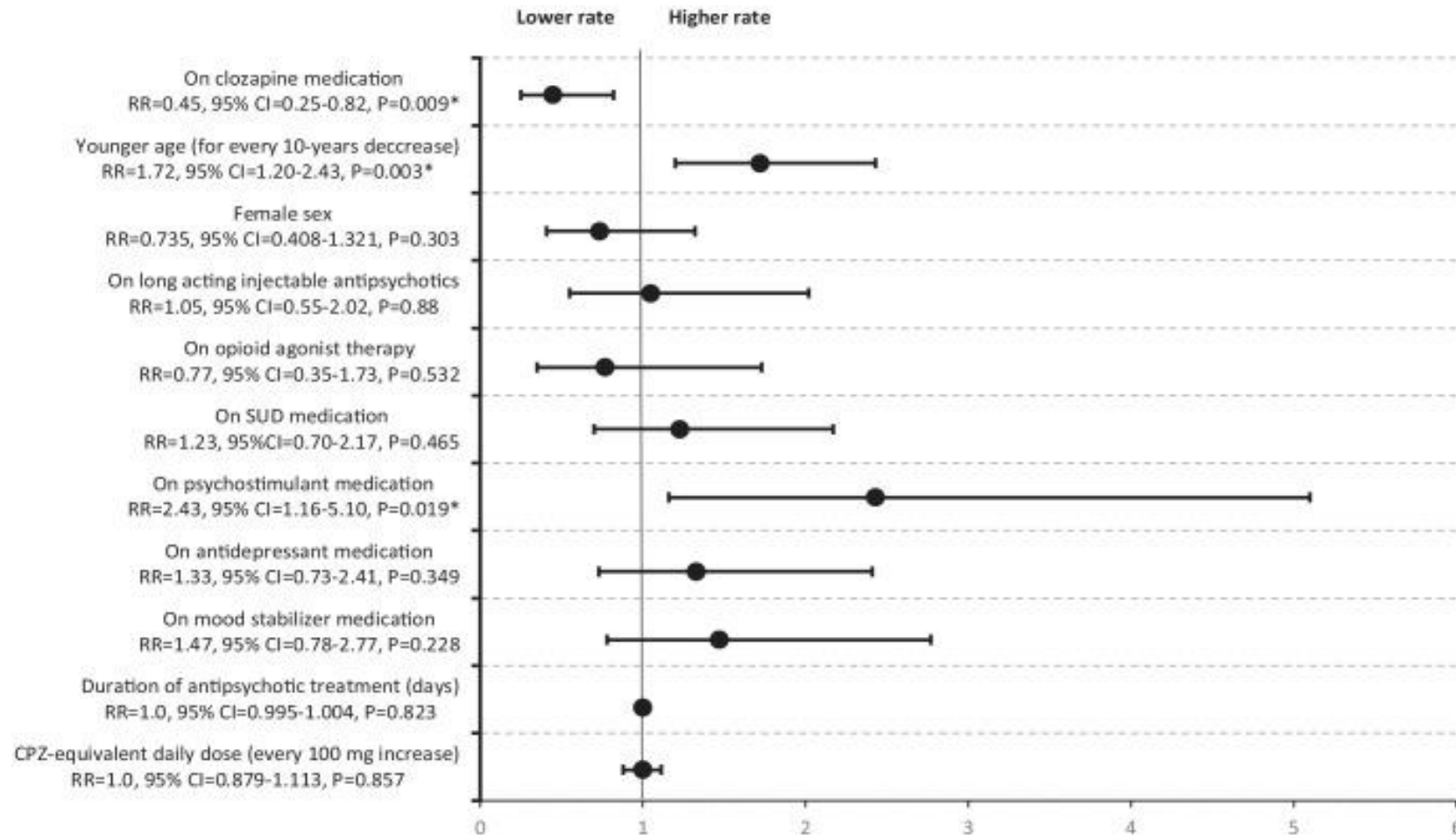
- Antipsychotics with evidence:
 - Aripiprazole, haloperidol, quetiapine, olanzapine, and risperidone
- No clear/consistent evidence favoring one agent
- Reduced side effects with 2nd generation medications
- No consistent time frame for treatment – until symptoms abate
- Side effect profile can help guide tx
- Unclear benefit from long-acting injectables

Table. Pharmacologic Treatment Recommendations for Methamphetamine-Associated Psychosis

Time since last use of methamphetamine	Recommended starting dose	Other considerations
Less than 24 hours	Titrate to resolution of agitation: Lorazepam 2 mg po, IM or IV Midazolam 2.5-5 mg IV, or 5-10 mg IM Ketamine 1-2 mg/kg IV or 3-4 mg/kg IM Haloperidol 5-10 mg po or IM Olanzapine 5-10 mg po, IM, or SL Risperidone 1-2 mg po	Consider transfer to emergency-level room for management. Incorporate IV hydration. Monitor vital signs and consider cardiac sequelae of intoxication. Rule out medical etiology for acute psychotic symptoms.
Less than 7 days	Titrate to resolution of psychotic symptoms: Risperidone 1-2 mg po bid Aripiprazole 10 mg po daily Quetiapine 100 mg po daily Haloperidol 2-5 mg po or IM bid	Evaluate for suicide risk. Evaluate for withdrawal of comorbid substance use.
Less than 30 days	Same as above. If symptoms resolve, slow titrate with frequent monitoring for reemergence of symptoms. If symptoms recur, resume antipsychotic medication. If depressive symptoms, consider bupropion 300-450 mg po daily, if tolerated. Otherwise, use SSRI or SNRI as indicated.	Address extrapyramidal adverse effects promptly. Refer for substance use treatment to prevent resumption of methamphetamine use. Obtain history to rule out premorbid psychotic disorder prior to methamphetamine use.

CONCURRENT SCHIZOPHRENIA AND STIMULANT USE DISORDER – *RAFIZADEH ET AL 2023

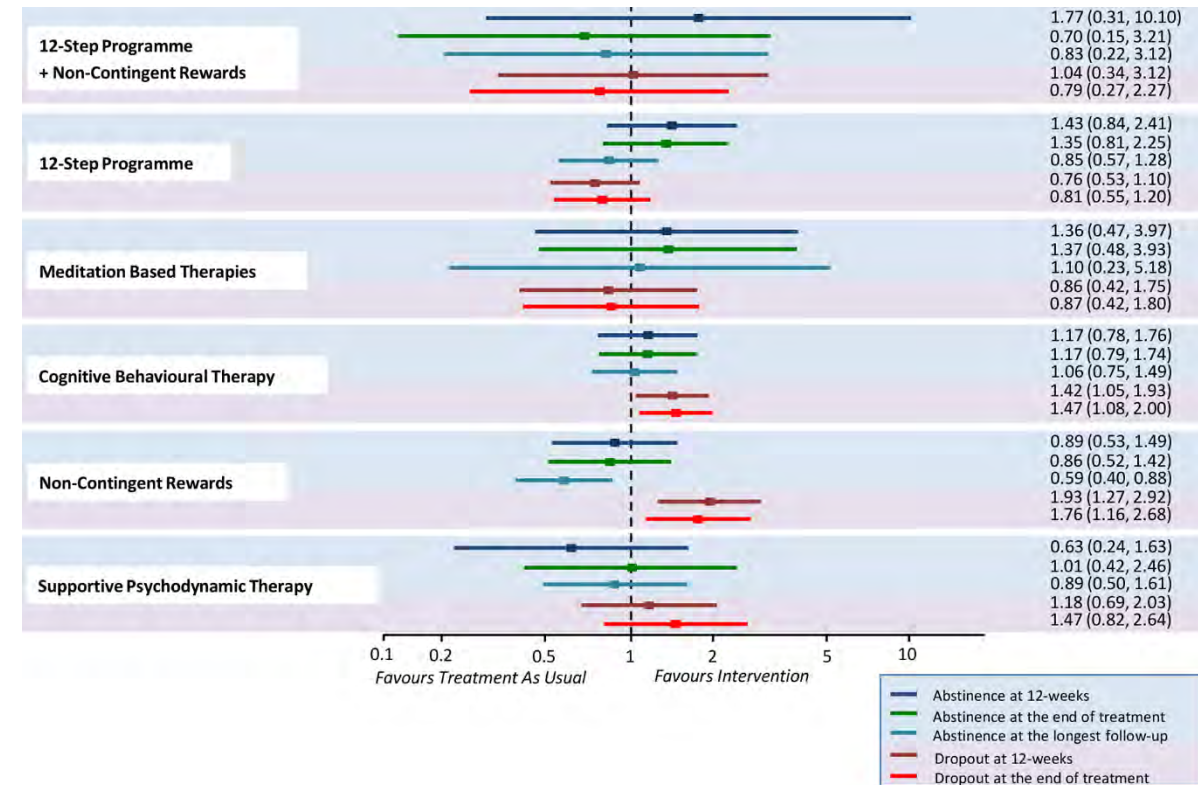
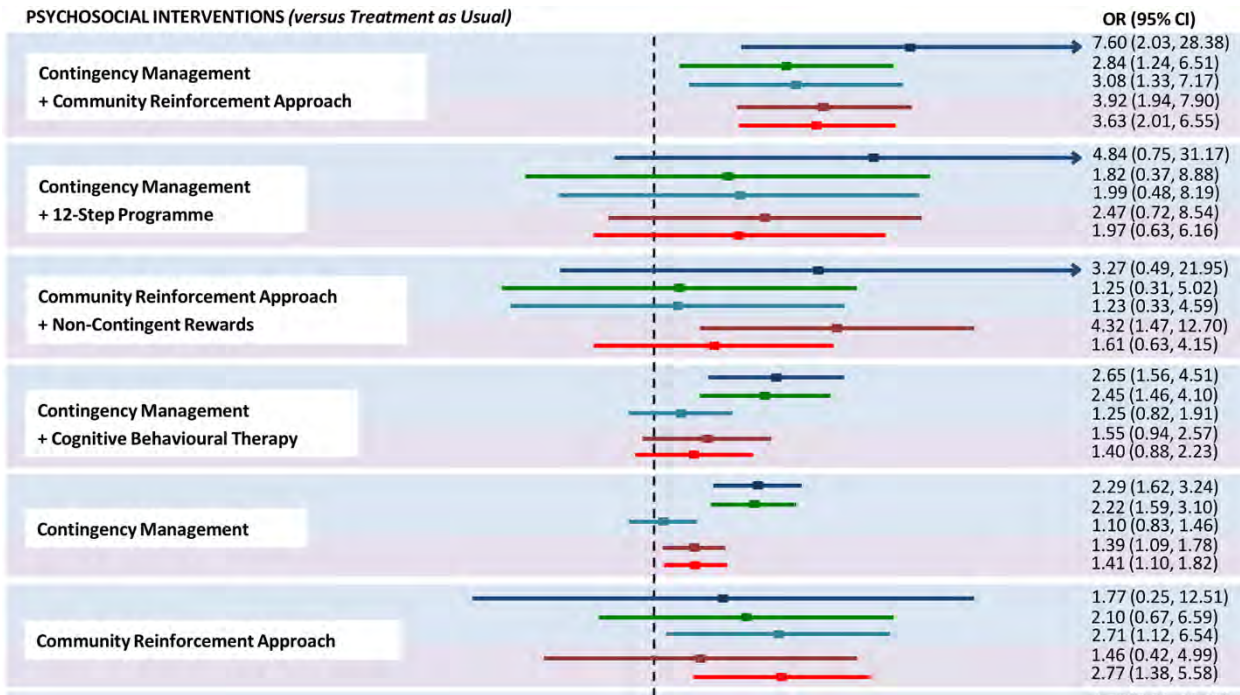
Retrospective cohort study: 87 patients On clozapine n =39; Other antipsychotics n=48



TREATMENT INTERVENTIONS FOR MUD

- Behavioral treatment for MUD is considered to be an optimal first-line treatment approach to reduce rates of psychosis in MA using populations
 - Contingency Management
 - Community Reinforcement Approach
 - Cognitive Behavioral Therapy
 - Motivational Enhancement

PSYCHOSOCIAL TREATMENTS FOR STIMULANT USE DISORDER



MEDICATIONS FOR MUD

No FDA approved medications

Dozens of medications with a variety of mechanisms have been studied

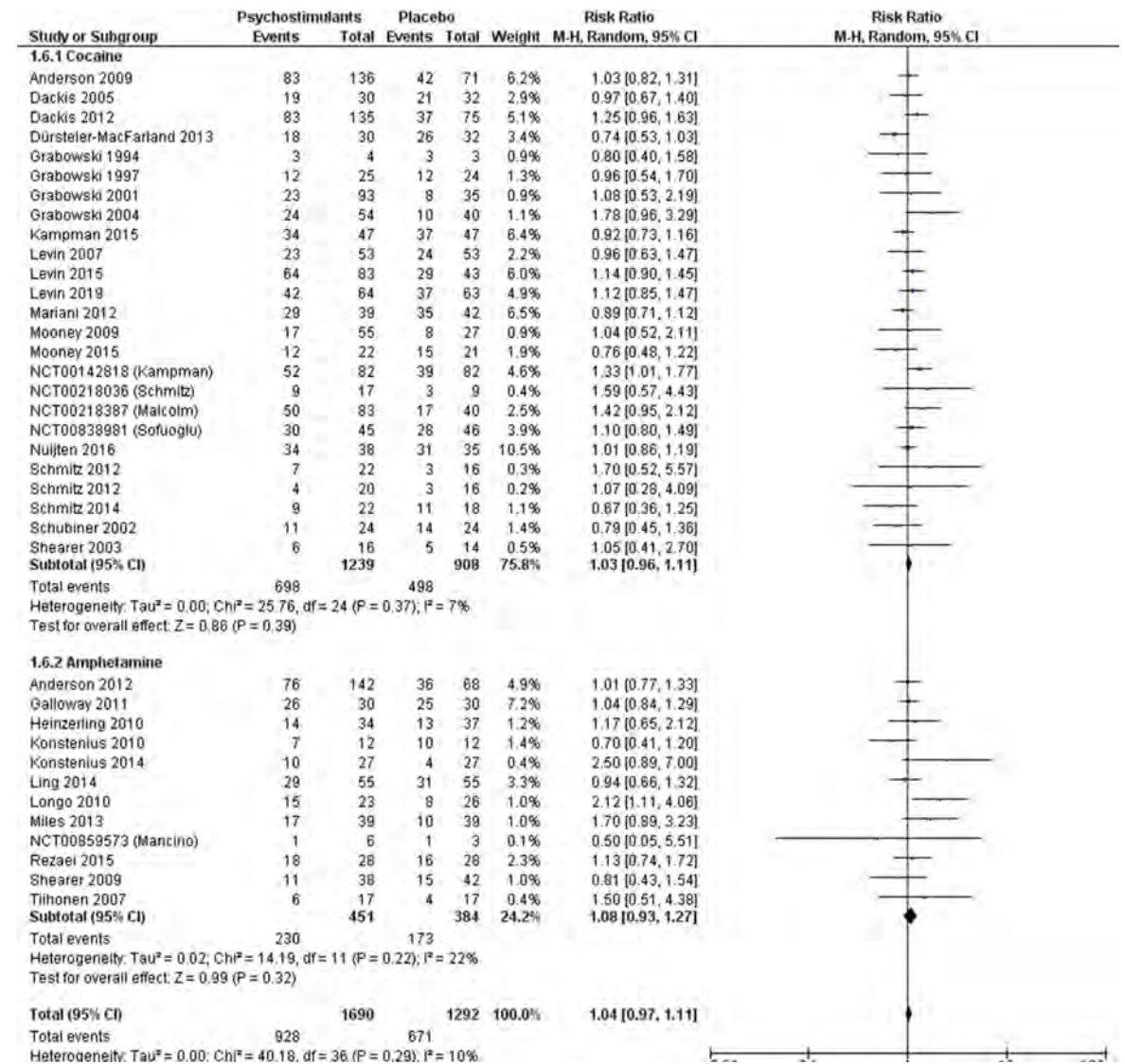
- Aripiprazole, baclofen, bupropion, buspirone, citicoline, creatine, dextro-amphetamine, dextro-methamphetamine, gabapentin, ibudilast, methylphenidate, mirtazapine, modafinil, N-acetyl cysteine, naltrexone, ondansetron, perindopril, pexacerfont, prazosin, sertraline, risperidone, rivastigmine, topiramate, varenicline, vigabatrin, vortioextine

Medications with evidence

- Psychostimulants
- Naltrexone
- Mirtazapine
- Bupropion +Naltrexone

MEDICATIONS CONTINUED

- Psychostimulants for Stimulant use disorder (cocaine and methamphetamine)
 - Systematic review and Meta Analysis -Tardelli et. al. 2020
 - 38 trials included, 2889 patients, Randomized, Double-blind, Placebo controlled, parallel-design for cocaine and amphetamine UD
 - Engagement not improved



MEDICATIONS CONTINUED

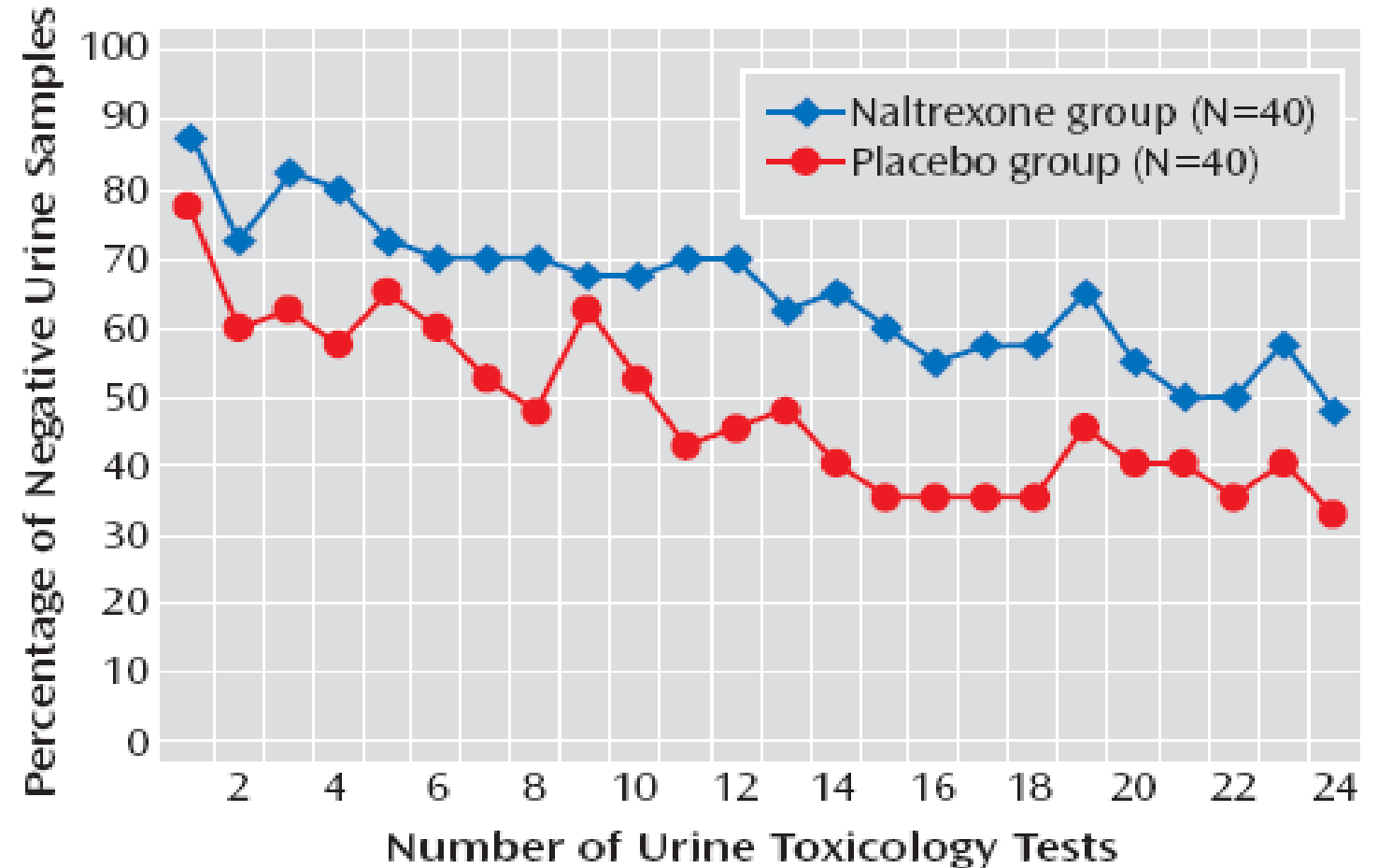
- Psychostimulants for Amphetamine like stimulants
 - Sharafi et al. Addiction. 2024. Systematic review and Meta Analysis
 - Removed modafinil and bupropion from analyses
 - Ten RCTs (n = 561 participants)
- Results:
 - No robust differences on initial comparisons
- **Subgroup analysis**
 - High dose methylphenidate >162mg superior to lower dose methylphenidate or dextroamphetamine
 - # of UAs positive for amphetamines
 - Engagement in treatment
- ADHD co-occurrence in positive studies
- Generally max dosing for ADHD alone is 108mg for methylphenidate and 50mg for dextroamphetamine

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NALTREXONE FOR METHAMPHETAMINE

JAYARAM-LINDSTROM ET
AL, AM J PSYCHIATRY
2008



ORIGINAL ARTICLE

Bupropion and Naltrexone in Methamphetamine Use Disorder

M.H. Trivedi, R. Walker, W. Ling, A. dela Cruz, G. Sharma, T. Carmody, U.E. Ghitza,
A. Wahle, M. Kim, K. Shores-Wilson, S. Sparenborg, P. Coffin, J. Schmitz, K. Wiest,
G. Bart, S.C. Sonne, S. Wakhlu, A.J. Rush, E.V. Nunes, and S. Shoptaw

12-week study, 403 participants, randomized, double-blind trial, which used a sequential parallel comparison design

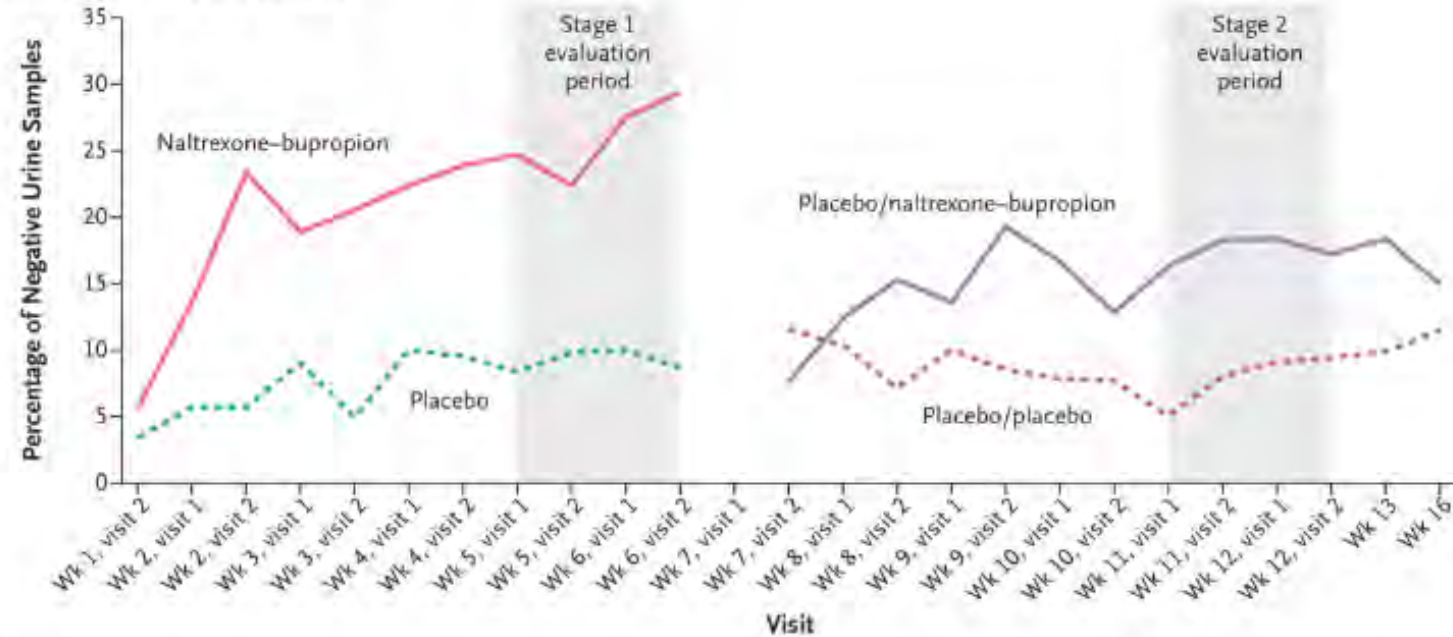
13.6% of the group receiving 380mg naltrexone-extended release (XR) plus 450mg bupropion-XR versus 2.5% of the placebo group had at least three methamphetamine-negative urine samples out of four samples at the end of the 6-week trial (an overall treatment effect of 11.1 percentage points).

The number needed to treat for one patient to have a response under the assumptions in this trial is 9.

Adverse events included gastrointestinal disorders, tremor, malaise, hyperhidrosis, and anorexia. Serious adverse events occurred in 8 of 223 participants (3.6%) who received naltrexone–bupropion during the trial.

BUPROPION AND NALTREXONE FOR METHAMPHETAMINE

B Methamphetamine-Negative Urine Samples

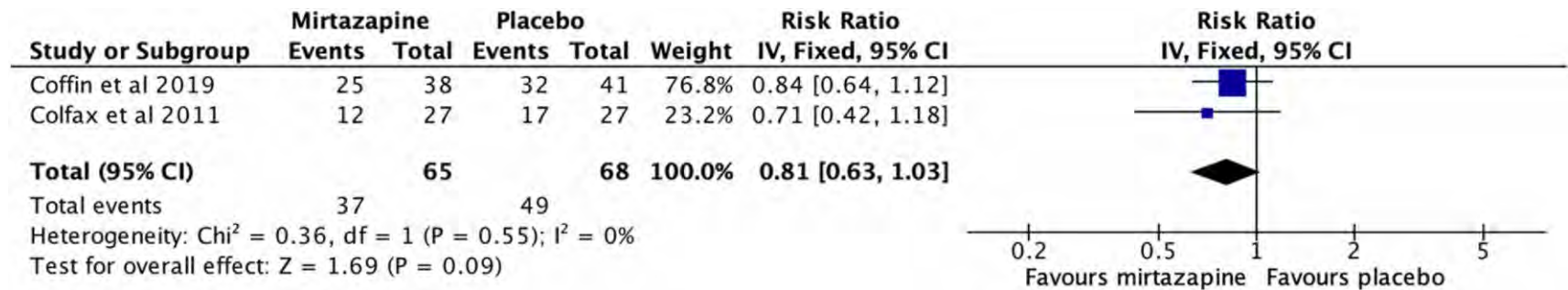


**No. of Urine Samples
Obtained at Each Visit**

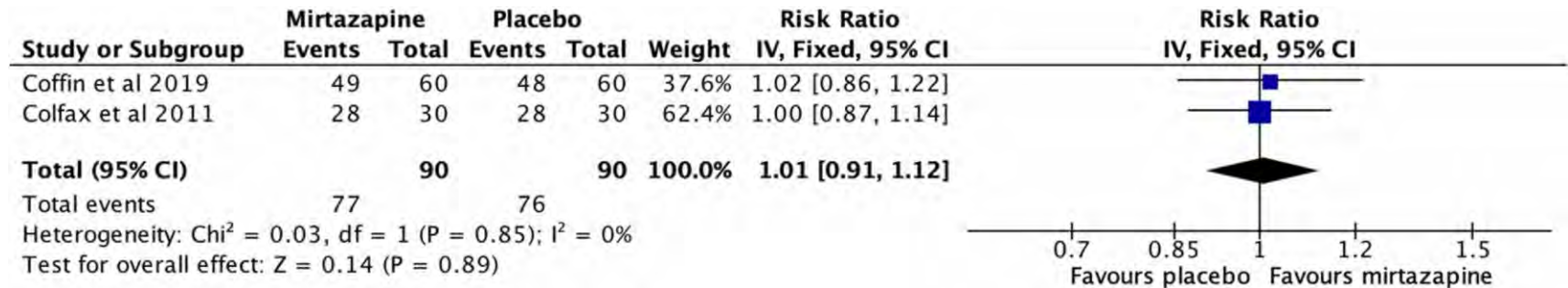
Obtained at Each Visit												Stage 1					Stage 2											
Naltrexone-bupropion	89	96	77	90	73	85	67	81	67	80	68																	
Placebo	265	280	229	266	223	260	210	239	203	240	207																	
Placebo/naltrexone- bupropion													92	97	85	103	83	96	78	98	82	98	93	98	87			
Placebo/placebo													95	106	84	100	82	102	91	99	87	99	85	101	96			

Mirtazapine for the treatment of amphetamine and methamphetamine use disorder: A systematic review and meta-analysis ⁷

Reduction in MA Positive Urine Screens



Retention in Treatment



NEW DATA ON MIRTAZAPINE – RTC FROM AUSTRALIA

- Double-blind, placebo controlled, multi-site across Australia
- General population
- Mirtazapine 30mg daily vs. placebo x 12 weeks
- Monthly dispensing of medication, 86% retention rate
- Participants receiving mirtazapine reduced methamphetamine use by a mean of **7 days** (out of 28), compared to a **5-day reduction** with placebo — a statistically significant **2-day difference** representing an **8% reduction in the risk of methamphetamine use on any given day.**

CITATIONS

1. Fiorentini A, Cantù F, Crisanti C, Cereda G, Oldani L, Brambilla P. Substance-Induced Psychoses: An Updated Literature Review. *Front Psychiatry*. 2021 Dec 23;12:694863. doi: 10.3389/fpsyt.2021.694863. PMID: 35002789; PMCID: PMC8732862.
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