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Disclosures

- No financial conflicts of interest
- Receive grant funding from NIH for two clinical trials using injectable buprenorphine for opioid use disorder (CTN-0099), and methamphetamine use disorder (CTN-0110)

Learning Objectives

- Understand burden and complexity of clinical care in the ED related to methamphetamine use disorder
- Develop strategies to manage complications, including agitation and psychosis, from methamphetamine use
- Integrate treatment strategies for methamphetamine use disorder for ED patients

24 year old male presents to the ED agitated after using meth

He was placed on a 5150 hold for "grave disability"

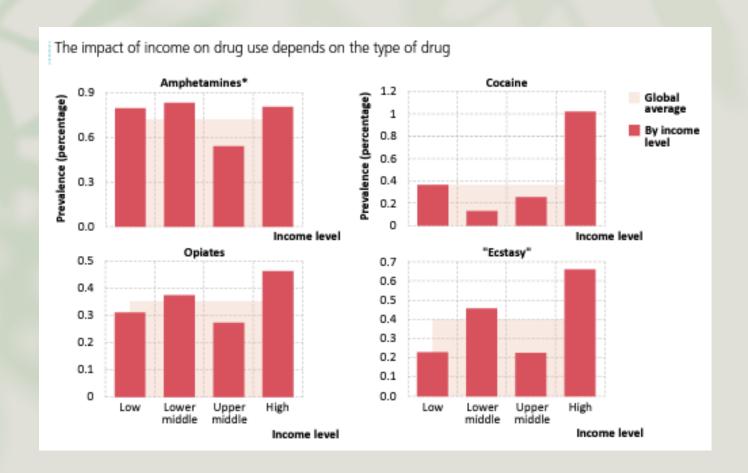
He is disorganized and combative with staff, several prior ED visits for meth use

Case

Background

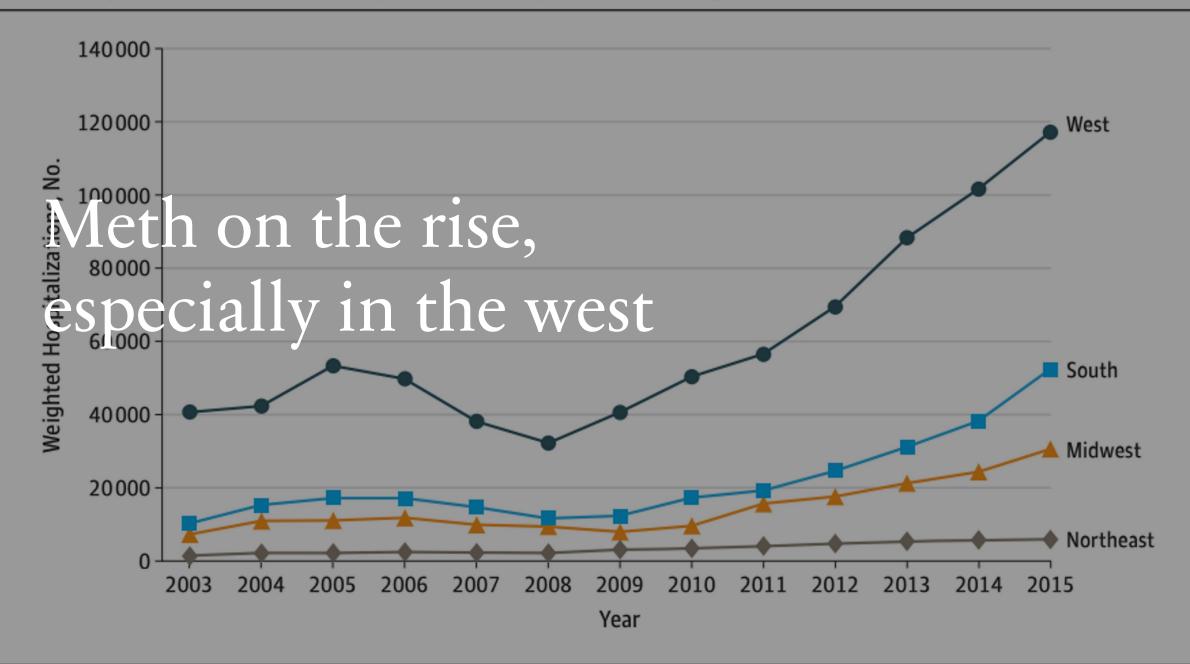
Meth is causing some problems, to put it mildly





Meth is the most commonly used illicit drug in the world – and spans income status

Figure 2. Amphetamine-Related Hospitalizations by US Census Region, 2003 to 2015



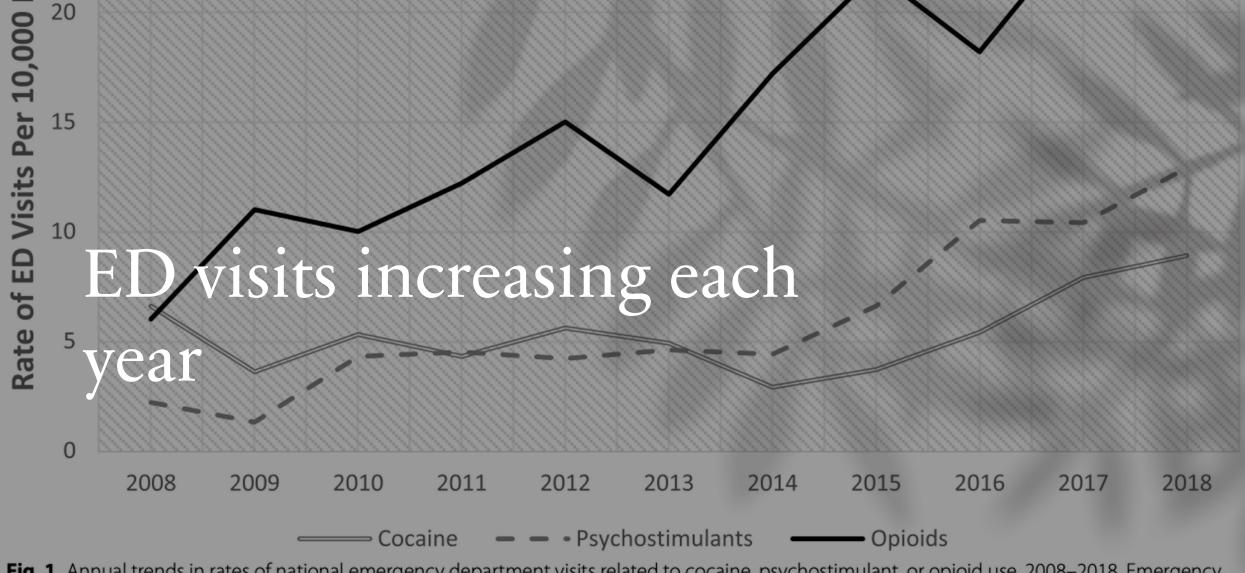
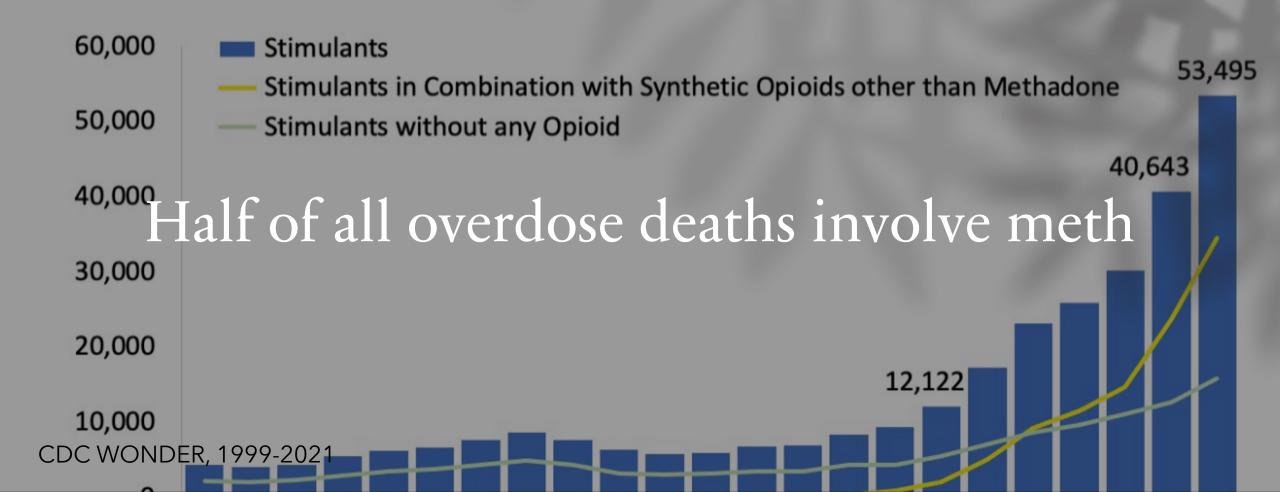


Fig. 1 Annual trends in rates of national emergency department visits related to cocaine, psychostimulant, or opioid use, 2008–2018. Emergency department visits categorized by drug-type if any of the top three *ICD9-CM/ICD10-CM* diagnoses codes were related to opioid, cocaine, or psychostimulant use. Visits were mutually exclusive for drug type, as visits associated with two or more drug-categories were excluded. Rates were calculated by dividing weighted number of visits in each year by US Census Bureau estimates of civilian, noninstitutionalized adults aged 18 and older for that year. All rates per 10,000 population. Source: National Hospital Ambulatory Medical Care Survey

Suen et al.

Figure 6. National Overdose Deaths Involving Stimulants (Cocaine and Psychostimulants*), by Opioid Involvement, Number Among All Ages, 1999-2021





Co-Use with opioids is the RULE (and much more complicated)

- Highest rates of:
 - Overdose
 - Unstable housing
 - Serious mental illness
 - Injection drug use
 - Blood born viral infections
- Lowest rates of:
 - Treatment engagement and retention

Meth complication categories in the ED

- Psychiatric (agitation)
- Cardiovascular/neurologic
- Trauma
- Overdose (usually opioid related)

Psychiatric complications of methamphetamine use

- What are some pharmacologic strategies for sedation?
- Is there any evidence for these strategies in this population?

De-escalation strategies

- Reasonable to attempt for any patient with agitation or psychosis
- No data to suggest this is easier or harder with meth vs. primary psychosis

Miller's Law

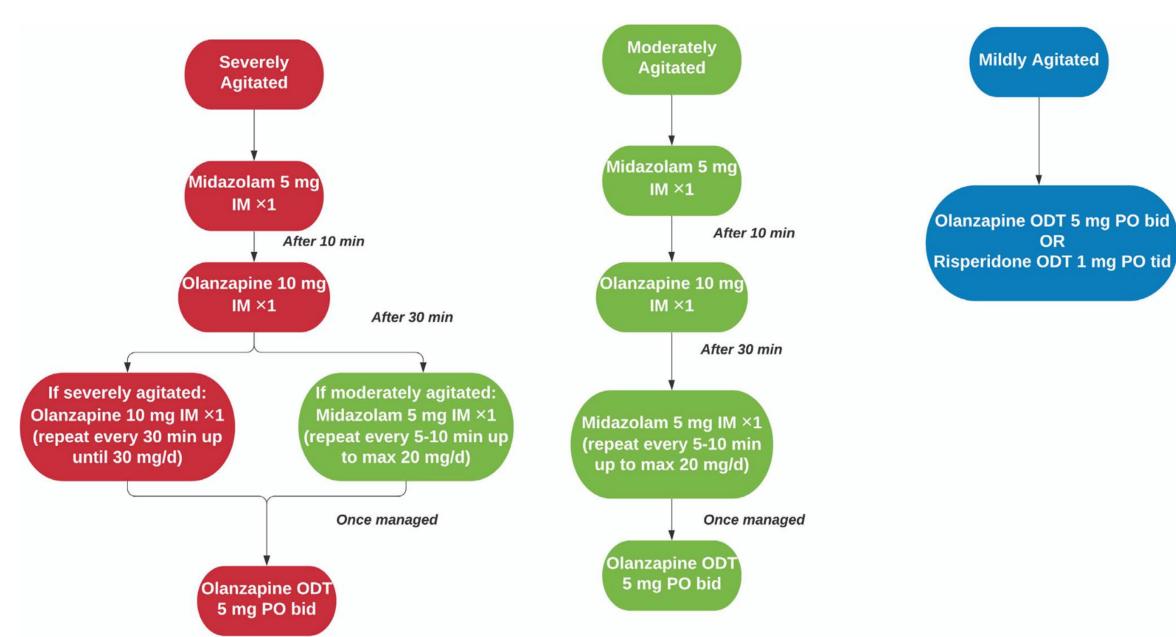
"To understand what another person is saying, you must assume that it is true and try to imagine what it could be true of."

Benzos should be first line

Pharmacologic sedation for meth intoxication

Okay to treat psychosis with anti-psychotics

Specific literature about meth is unrevealing



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385, OCTOBER 01, 2018

Intramuscular Midazolam, Olanzapine, Ziprasidone, or Haloperidol for Treating Acute Agitation in the Emergency Department

Lauren R. Klein, MD, MS <a> □ • Brian E. Driver, MD • James R. Miner, MD • ... Erik Fagerstrom, BS •

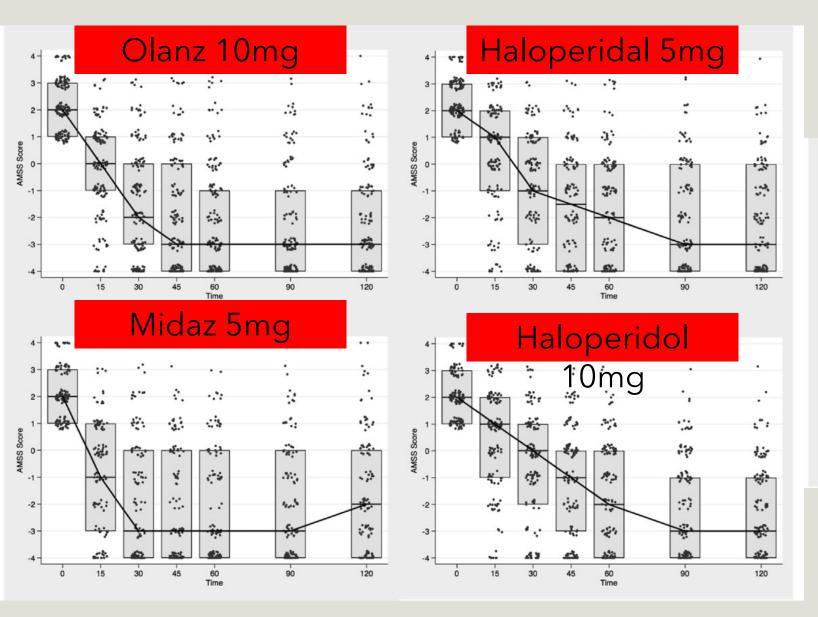
Rajesh Satpathy, BA • Jon B. Cole, MD • Show all authors

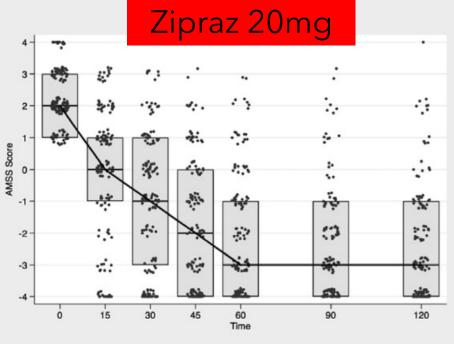
Published: June 06, 2018 • DOI: https://doi.org/10.1016/j.annemergmed.2018.04.027 •



Medications

- Olanzapine 10mg IM
- Haloperidol 5mg IM
- Haloperidol 10mg IM
- Midazolam 5mg IM
- Ziprazadone 20mg IM





Take away

- Midaz and Olanzapine both worked well
- Didn't look at combination meds
- All similarly low adverse events
- Low rates of stimulant use in this population

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A Prospective Study of Intramuscular Droperidol or Olanzapine for Acute Agitation in the Emergency Department: A Natural Experiment Owing to Drug Shortages

James R. Miner, MD • Brian E. Driver, MD

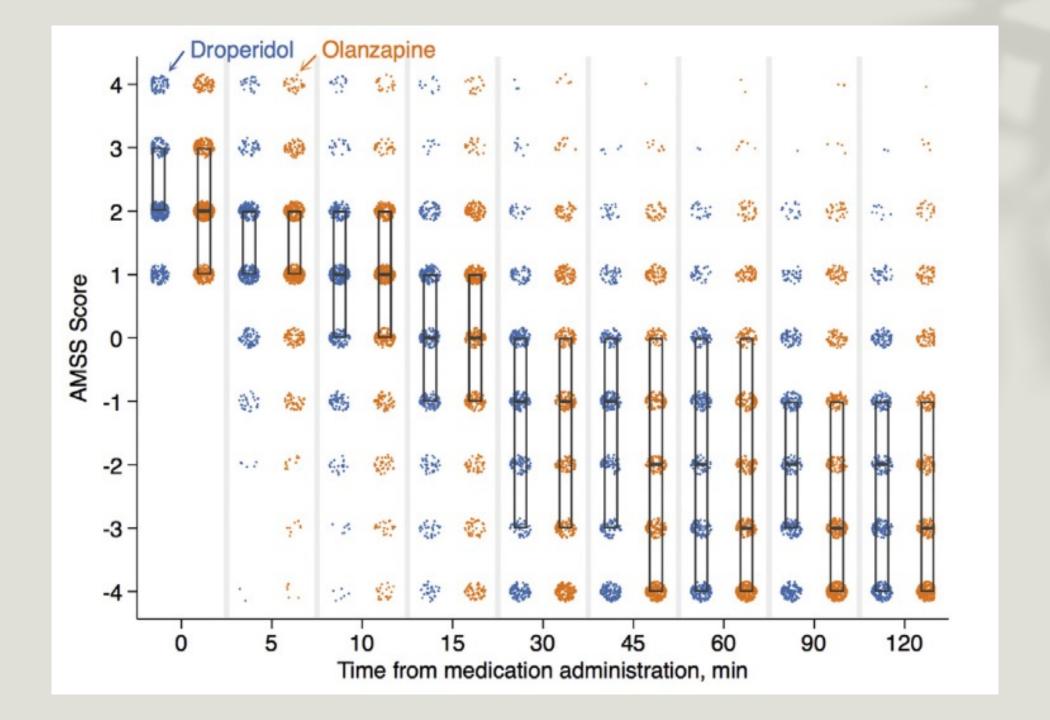
Published: April 09, 2021 • DOI: https://doi.org/10.1016/j.annemergmed.2021.01.005 •



Medications

Olanzapine 10mg IM

Droperidol 5mg IM



Take away

- Olanz 10mg = Droperidol 5mg
- All "intoxicated"
- Institutional preferences at play

General approach

- Most patients will respond to a combination of a combination of:
 - De-escalation
 - Benzos
 - Antipsychotics
- Its reasonable to stick to institutional practice patterns

Additional critical care considerations



Ketamine and sedation

What role (if any) does stimulant intoxication play?

Ketamine vs. Midazolam (5mg)+Haloperidol (5mg)

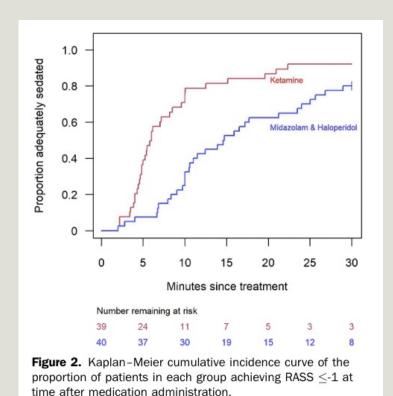


Table 2. Frequency of serious adverse events. Haloperidol and Ketamine Serious Adverse Event Midazolam (n=40) (n=40)1 (2.5) 2 (5.0) Apnea 1 (2.5) Supplemental 1 (2.5) oxygen required 1 (2.5) 0 Laryngospasm 0 1 (2.5) Dystonia 5 (12.5%) Total 2 (5%)

Prehospital ketamine for agitation in setting of substance use

N=86 patients given ketamine for delirium with agitation

Utox used to classify substance use*

Low rates of meth, high rates of cocaine

Concurrent cocaine use associated with higher rates of intubation

Ketamine and profoundly agitated patients

Profoundly agitated patients have high rates of substance use

Profoundly agitated patients have high rates of intubation

Profoundly agitated patients occasionally receive ketamine

Dexmedetomidine and stimulant use

- Case report of use in benzo refractor patients
- Could this reduce sympathetic drive

Ketamine and catecholamine depletion

- Ketamine induces catecholamine secretion from adrenals
 - Typical increase in blood pressure
- Observational data suggests in catecholamine depleted patients (shock), it can cause hypotension
- Analogies made with stimulant intoxication are these patients catecholamine depleted?

Succinylcholine and meth intoxication

- Succ associated with mild hyperK (idiosyncratic), malignant hyperthermia
- Stimulant use may be complicated by rhabdo or hyperthermia



Complications in critically ill patients more likely related to underlying pathology as opposed to acute intoxication

Intraoperative vasopressor use during emergency surgery on injured meth users

Alexandra Marie Edwards, 1 Eric Gregory Johnson 6, 2,3 Andrew C. Bernard4

Sedation and analgesia needs in methamphetamine intoxicated patients: much ado about nothing

Elaine Chiang ^{a,1,*}, Jon Case ^a, Mackenzie R. Cook ^b, Martin Schreiber ^b, Cody Sorenson ^a, Cassie Barton ^a

Consider substance use disorder

ED episodic care is part of broad opportunity to treat SUDs





Cycle of methamphetamine abuse

THE BAD THINGS HAPPEN HERE

Psychosis

Cadet, Jean Lud, and M. S. Gold.
"Methamphetamine-induced psychosis:
who says all drug use is reversible." Curr.
Psychiatry 16 (2018): 15-20.

Initial drug exposure Increasing methamphetamine use Methamphetamine binges

Abstinence, withdrawal

Affective diatheses

Multiple relapses

Treatment of Methamphetamine / Stimulant Crisis

- 1. Sleep. No sleep = No recovery. They have to sleep.
 - Treat any agitation with benzodiazepine +/- antipsychotic
 - Let them rest. Assist to find shelter.
 - Example: Trazodone 50-100mg nightly x 1 week
- 2. Antipsychotic. Any hint of psychosis
 - Example: Olanzapine 5-10mg twice a day X 1 week
 - Explain it is OK to take as needed to: "slow down your thoughts and help you sleep."
- 3. Mirtazapine May help reduce withdrawal symptoms.

• 30mg at night

General Approach

Agitation without psychosis

BDZ

Psyhosis → BDZ + Antipsyhotic

BEAT Meth –ED-based study

- PES "multimodal" intervention for meth use induced psychosis
- Meds: Antipsychotics and benzos
- Double meal portions
- Discharge planning with goal to engage in outpatient or residential programs
- Higher rates of engagement in outpatient treatment



Medications with some support for reducing meth use

- Mirtazapine
 - 30mg daily, moderate evidence reduces use (mainly 1 RCT)
- Bupropion (high dose) + Naltrexone-XR
 - ADAPT-2 trial with higher rates of abstinence use, multi-center clinical trial
 - Significant cash incentives in both arms
- Agonists treatments (methylphenidate, dexamphetamine,
 - Mixed results, some recent association data

MURB - Bup 4 Meth

- RCT of injectable buprenorphine vs placebo
- Based on kappa opioid antagonism
- Targets a co-using population that doesn't meet moderate-severe
 OUD criteria

Treatments with some support for reducing meth use

- Cognitive behavioral therapy
 - Moderate evidence that can decrease use, even a few sessions
- Contingency management
 - Good evidence CM can decrease meth use
- Psychosocial interventions less effective after treatment over, less effective for more severe disorders

Summary

- Methamphetamine contributes to significant morbidity and mortality
- Agitation and psychosis are common complications when presenting to the ED
- Typical sedation approaches include de-escalation and pharmacotherapy
- Critical care treatment focused on resuscitation
- ED visits are an opportunity consider treatment options

