Stimulants: Cocaine and Methamphetamine

CRIT program – April 2014

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Learning objectives

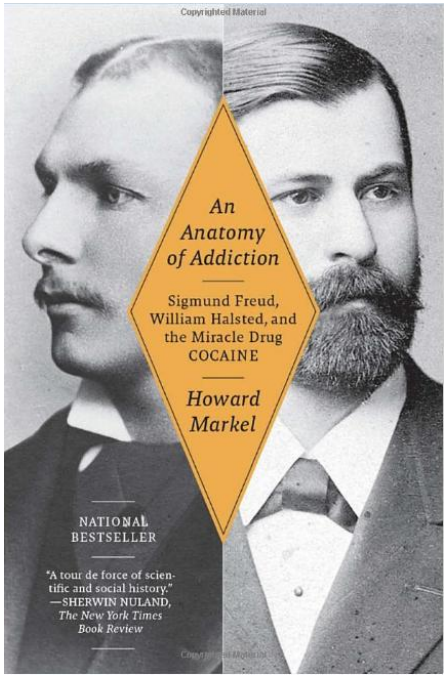
At the end of this session, participants will be able to:

1. Understand how and why people use stimulants
2. Know the characteristics of stimulant intoxication and withdrawal syndromes
3. Understand the consequences of these drugs
4. Know the current options for treatment of stimulant dependence

History: Cocaine

1885 Advertisement for Cocaine Toothache Drops

- From erythroxylon coca leaves in Andes
- Leaves chewed for thousands of years as stimulant
- 1884 Freud published, *Uber Coca*, describing cocaine's effects on Freud and its potential to treat opiate addiction
- 1885 Halsted published study about anesthetic uses
- 1886 Halsted raided ship medicine cabinet for fix
- Used in medicines and beverages until early 1900s
- Street preparations 10-50% cocaine
  - Hydrochloride powder is snorted or injected
  - Alkaline rocks (aka crack) are smoked
  - *Crack, Rock, Base*



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History: Methamphetamine

- 1893 methamphetamine first synthesized in Japan as decongestant
- Used by German, English, American, and Japanese military in WWII for performance enhancement.
- First epidemic occurred in Japan when the military dumped large quantities into the civilian market
- Popular among truckers and west coast bikers in 1970s
- DESOXYN to treat ADHD and obesity
- *Speed, Crystal, Crank, Ice, Meth, Tina*

Lineberry 2006

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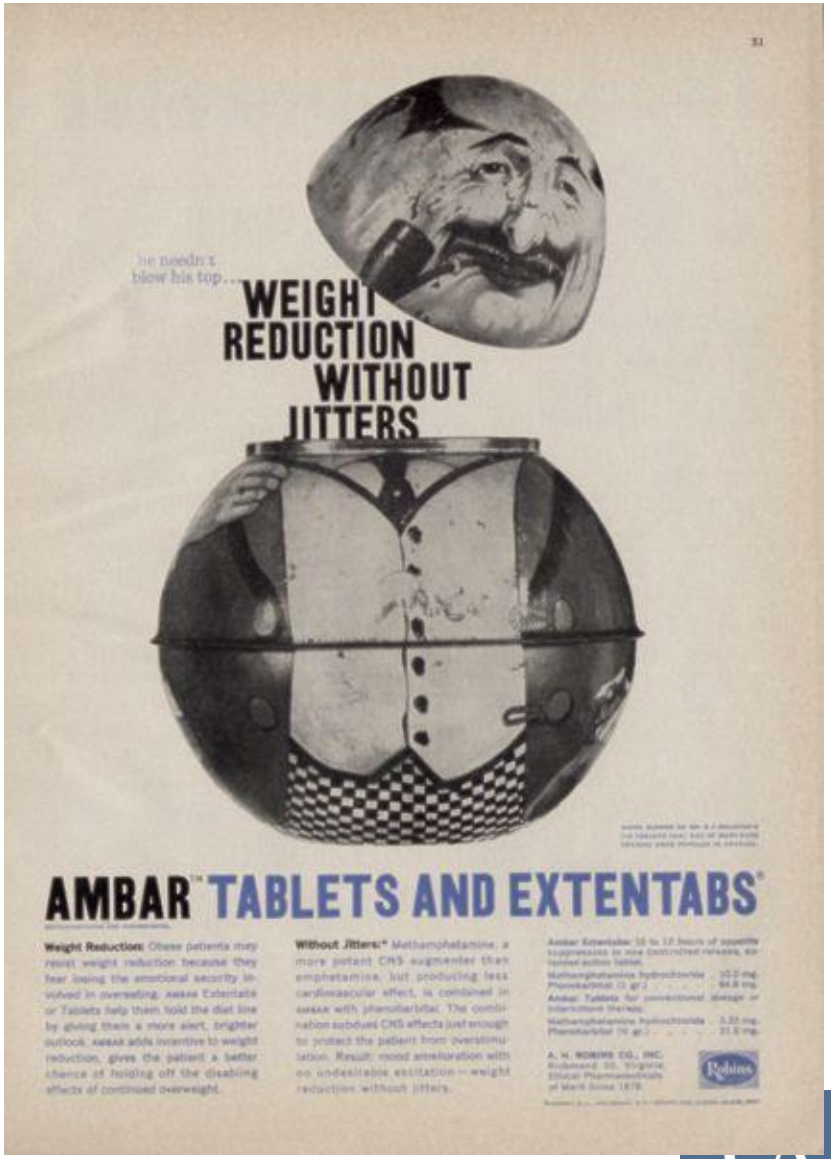
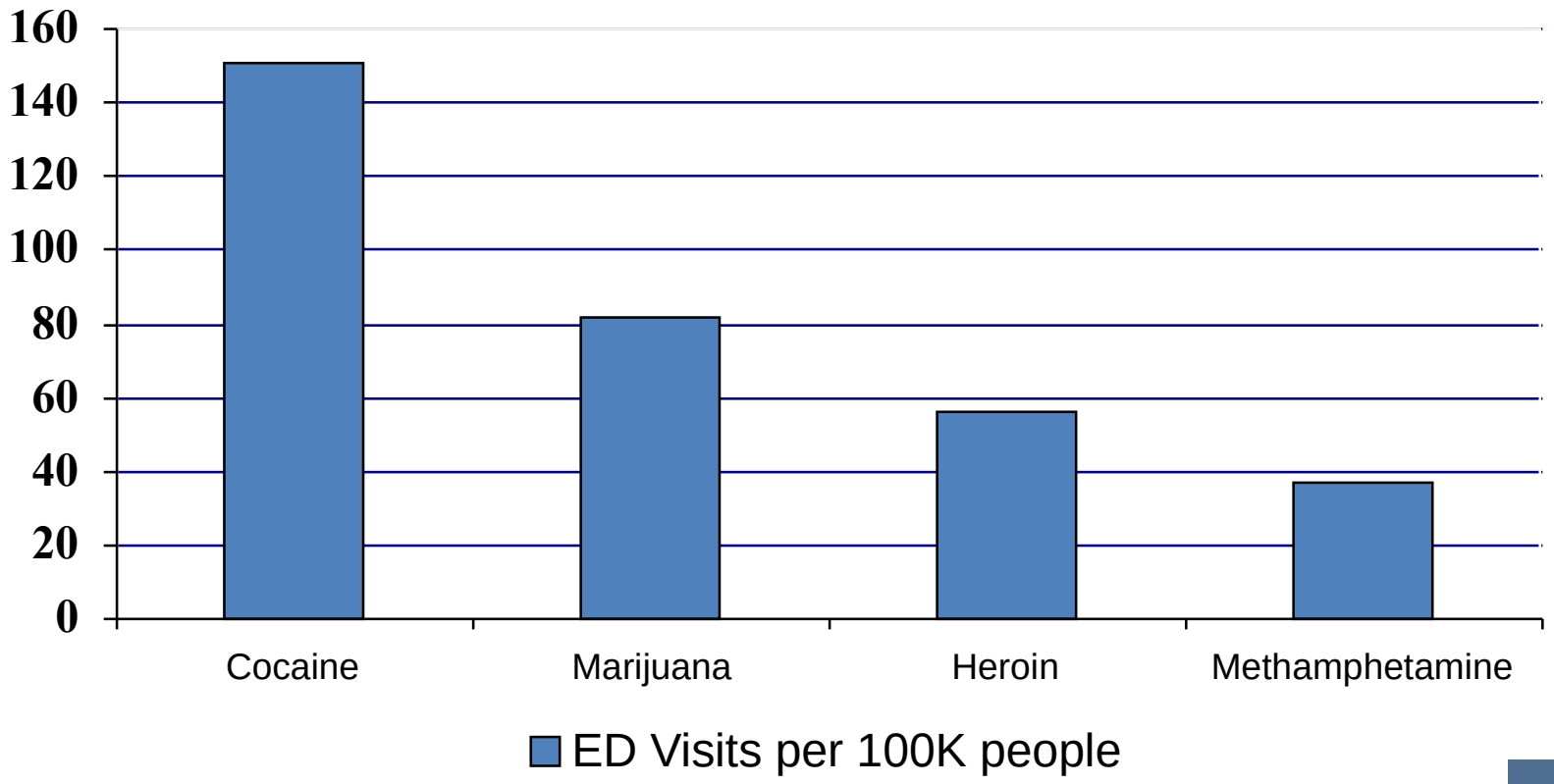
1957



1959

Epidemiology

2005 drug-related ED visits



Drug Abuse Warning Network 2005 Report

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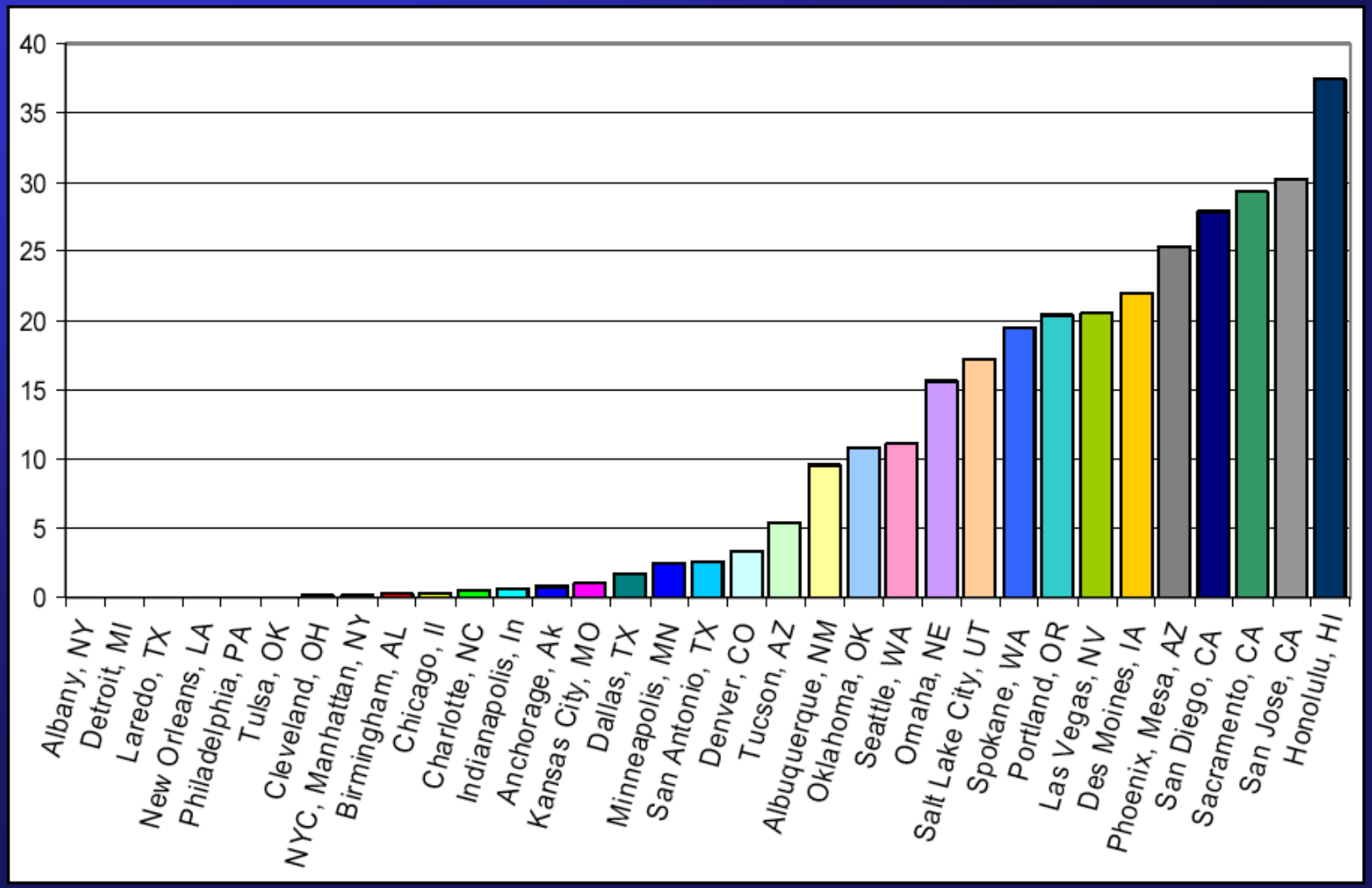
Percent Male Arrestees Testing Positive for Meth (for 33 ADAM sites, 2001)



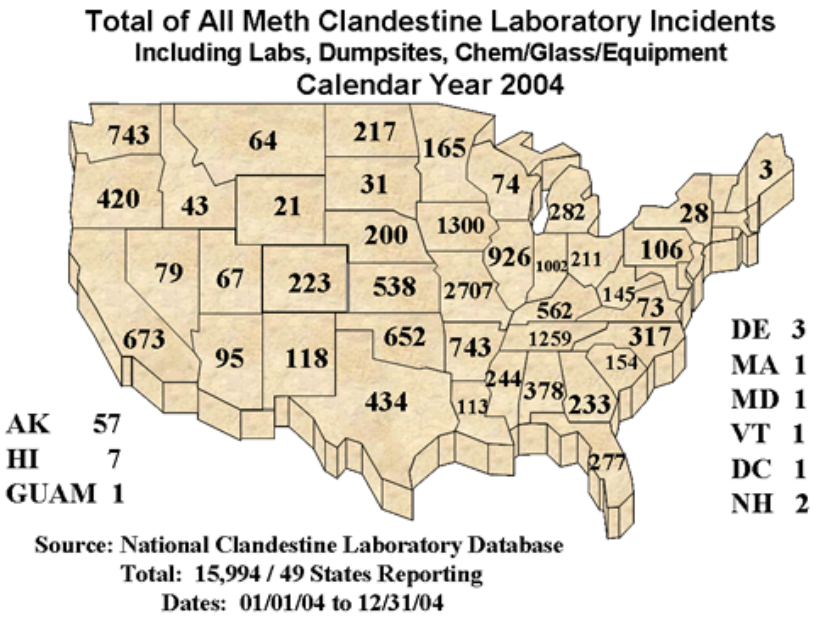
From where do these drugs come?

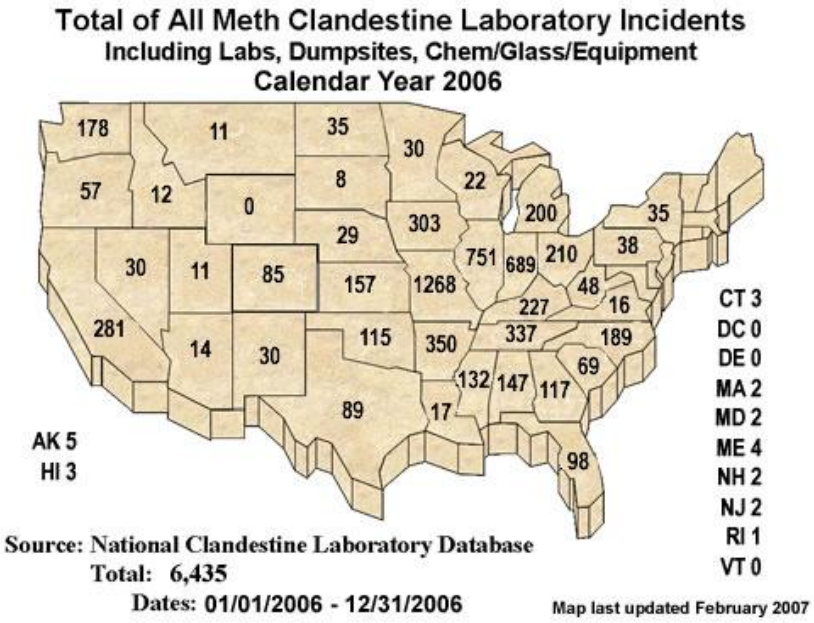
- Methamphetamine
  - Super labs – Primarily Mexico and California
  - Local clandestine labs - 1 pound of MA creates 6 pounds of toxic waste
    - Holton WC. Unlawful lab leftovers. *Environ Health Perspect.* 2001;109:A576
- Cocaine -
  - 75% grown in Colombia with

    75% via Mexico/ Central America

http://www.colombiajournal.org/cocainephotos.htm

Clandestine lab incidents





www.dea.gov

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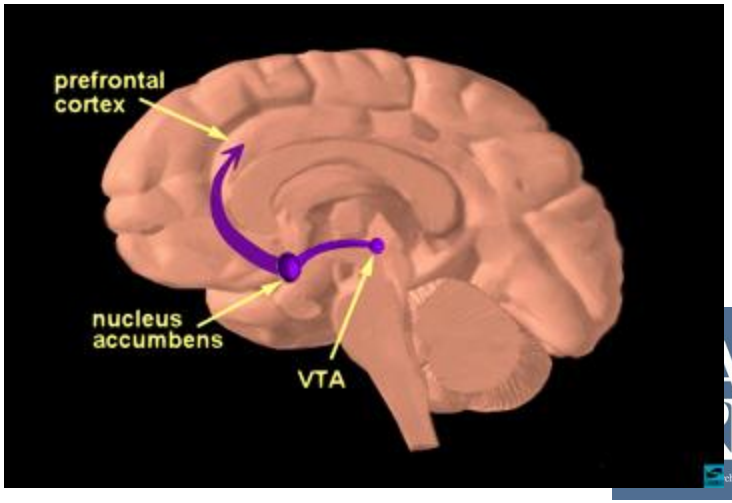
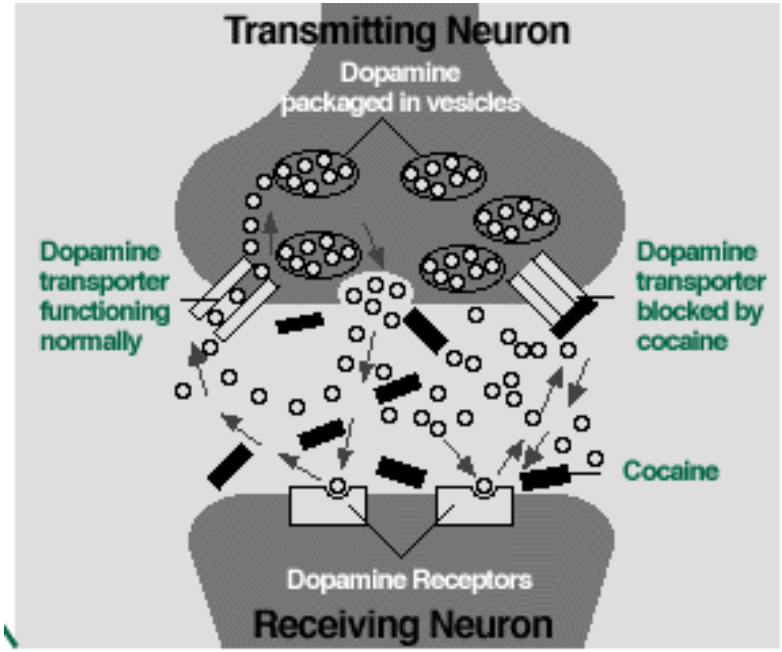
Stimulant Effects

Why do people use stimulants?

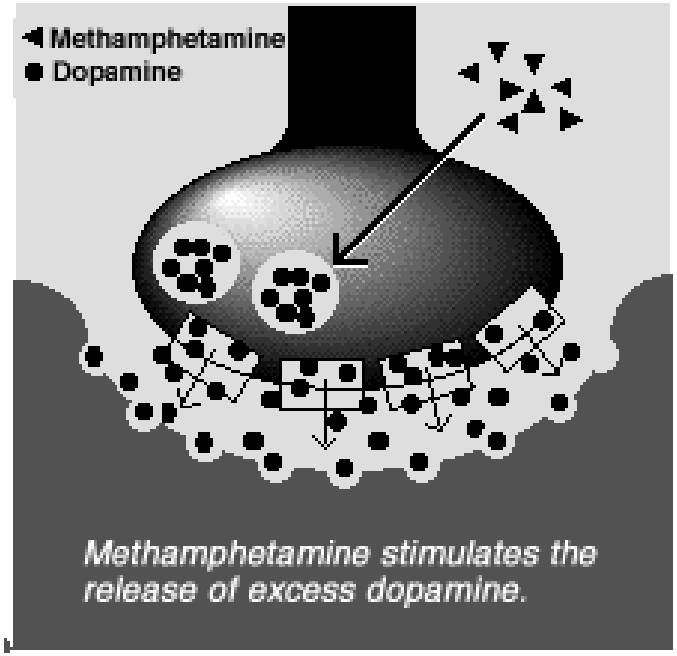
- Euphoria - Rush
  - Onset and intensity depends on delivery method
- Increased energy, alertness, libido
- Diminished social inhibition
- Decreased appetite



Cocaine



Methamphetamine



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PK: Cocaine

	IV	Smoked	Snorted
Time to effect	10-60sec	3-5sec	1-5min
Peak concent.	3-5min	1-3min	15-20min
Half-life	20-60min	5-15min	60-90min

Lange, R. A. and L. D. Hillis (2001). "Cardiovascular complications of cocaine use." N Engl J Med **345**(5): 351-8.

PK: Methamphetamine

	IV	Smoked	Snorted	Ingested
Time to effect	15-30 sec	Immediate	3-5 min	15-20 min
Peak concent.	2-4 h	2-4 h	2-4 h	2-4 h
Half-life	10-12 h	10-12 h	10-12 h	10-12 h

Lineberry 2006

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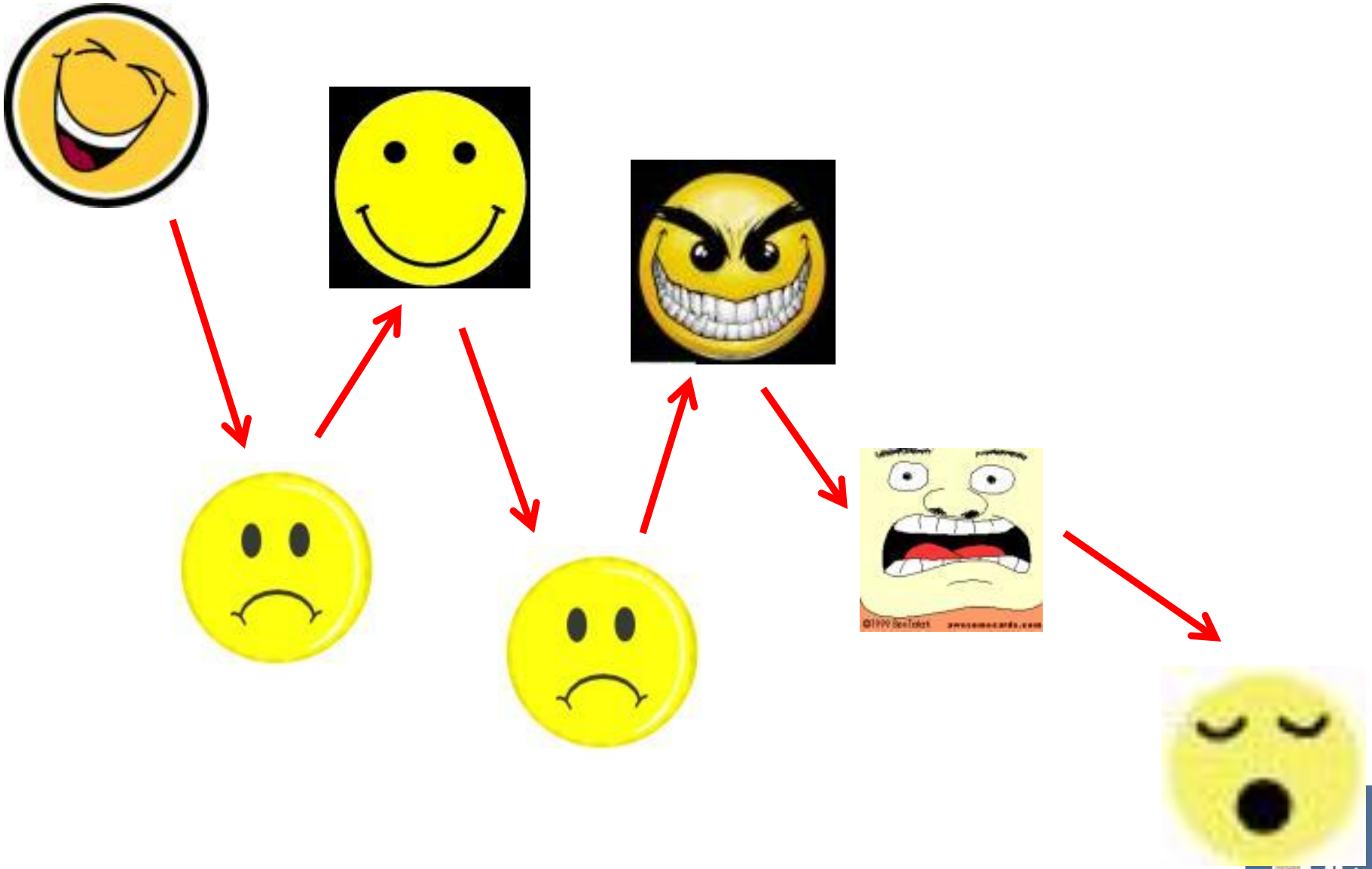

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Binges

- 2-3 day binges are typical, called runs
- Regular re-dosing to maintain rush or high in setting of acute tolerance
- Ends when drug or money runs out, or paranoia/ disorganized thinking sets in

Acute Toxicity

- Elevated BP and HR
- Arrythmia
- Vasoconstriction
- Hyperthermia
- Agitation
- Rhabdomyolysis
- Seizure

- Acute psychosis → prolonged psychosis
  - –Paranoid delusions
  - –Visual, sensory, and auditory hallucinations
    - – ie formications

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Intoxication Treatment

- Minimize sensory stimulation
- Neuroleptics (ie haldol) for agitation
- Benzos to control seizures
- Treat hyperthermia (external cooling)
- For increased BP+HR, use vasodilators and CCB or non-selective beta-blockers

Is there stimulant withdrawal?

- Intense craving
- Depression
- Fatigue
- Unpleasant dreams
- Hypersomnia, then insomnia
- Increased appetite
- Limited ability to experience pleasure

>> All results of relative dopamine depletion

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Health Consequences

Dental

- Darkened teeth
- Caries
- Periodontal disease

Pulmonary

- Acute pulmonary edema
- Pulmonary HTN
- Inhalation injury

Cardiovascular

- Hypertension
- DCM
- Arrythmia/ Tachycardia
- Acute Coronary Syndrome
- Aneurysm/ dissection
- Erectile dysfunction

Infectious

- HIV risk
- HCV/ HBV
- STDs

Neuro-psychiatric

- Stroke
- Seizure
- Depression
- Anxiety
- Mania
- Impulsivity
- Paranoia
- Auditory/ visual hallucinations + formications
- Violence

Renal/Metabolic

- Rhabdomyolisis
- Dehydration
- Acute Renal Failure
- Acidosis
- Hyperthermia

Skin

- Cellulitis/ abscess
- Excoriations
- Chemical burns

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Cocaethylene

- Psychoactive substrate from EtOH+cocaine
- ETOH commonly used as “landing gear”
- ETOH before cocaine inhibits cocaine metabolism, producing cocaethylene
- 60-90% of cocaine abusers abuse ETOH
- Greater cardiac toxicity
- Greater rates of seizures, hepatic damage

Treatment

Pharmacologic Treatment

- Antipsychotics
  - Amato. Cochr Database Syst Rev. 2007 Jul 18;(3):
- Anticonvulsants - GABA modulators
  - Carbamazepine, Phenytoin, Valproic Acid, Tigabine, Gabapentin, Lamotrigine – Alvarez. JSAT 2010: 38; 66-73.
  - Baclofen – Heinzerling. Drug Alcohol Depend. 2006 Dec 1;85(3):177-84.
  - Vigabatrin – Brodie. Am J Psychiatry. 2009;166:1269-77.
  - Topiramate – Ekashef Addiction 2012: 107;1297-1306.
- Stimulant replacement
  - Modafinil – Shearer. Addiction. 2009 Feb;104(2):224-33.
  - Dexamphetamine – Longo. Addiction 2009, 105, 146–154
- Vaccine
  - Martell. Arch Gen Psychiatry. 2009 Oct;66(10):1116-23.
- Disulfiram – Pani. Cochr Database Syst Rev. 2010. Oliveto. Drug Alcohol Depend 2010

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Non-Pharma Treatment

- Brief Intervention?
  - Bernstein et al. DAD 2005: 77; 49.
- Cognitive behavioral therapy
- Community Reenforcement Approach
- Contingency management
  - Schierenberg et al. Current Drug Abuse Reviews 2012: 5; 320-331.
- Self-help/ 12 step facilitation

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Contingency Management

Method	Positive Stimulus	Negative Stimulus
Reinforcement: Increase desirable behavior	Positive *Reinforcement*: Delivery of a desired consequence contingent on desirable behavior	Negative *Reinforcement*: Removing an aversive or confining circumstance contingent on desirable behavior
Punishment: Decrease undesirable behavior	Positive *Punishment*: Punishing consequence contingent on evidence of undesirable behavior	Negative *Punishment*: Removing a positive circumstance or condition contingent on evidence of undesirable behavior

RCT in 6 community methadone programs of CM among stimulant users

- Usual Care vs.
- Intermittent, escalating re-enforcement
  - 1000 chips
    - 500 “Good job”
    - 250 “Small” - $1 value – i.e. toiletries
    - 209 “Large” - $20 value – i.e. kitchenware
    - 1 “Jumbo” – $80-100 value – tv, stereo
  - # of draws = # of weeks with clean urine

Peirce et al. Arch Gen Psychiatry. 2006;63:201-208.

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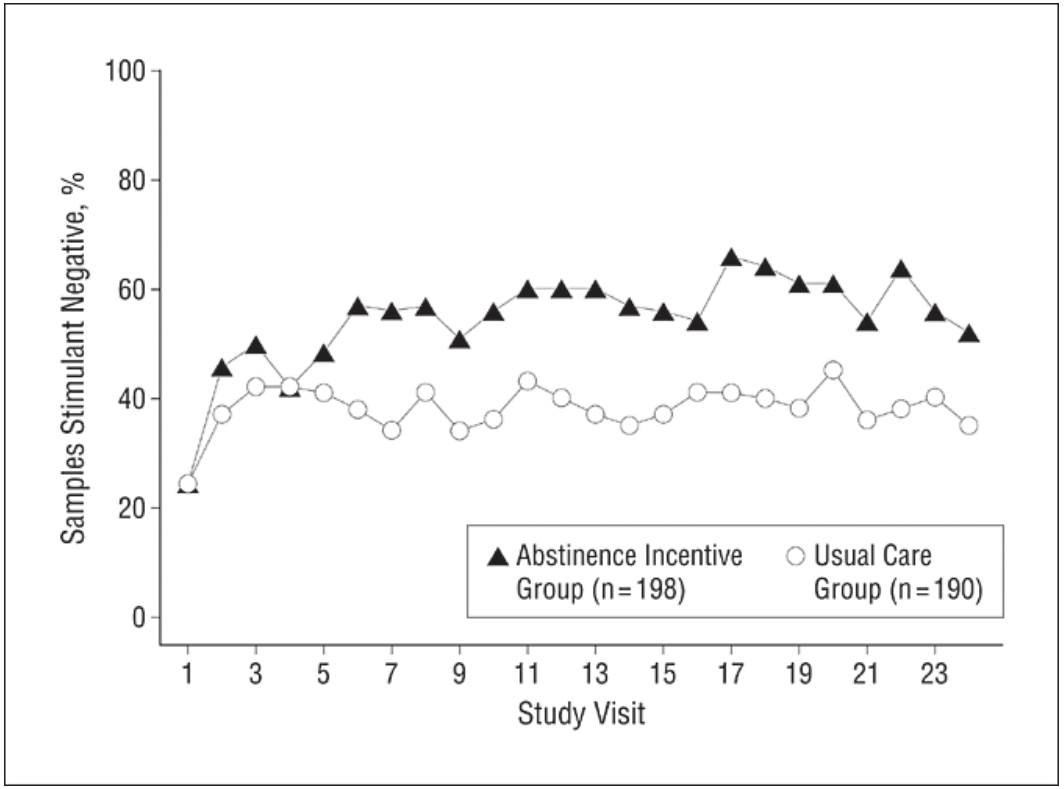
Contingency Management



The mean percentage of submitted samples testing negative for target drugs (stimulants and alcohol) is shown for abstinence incentive and usual care participants at each of 24 study visits.

Average cost = $1.46 per person/day

Peirce et al. Arch Gen Psychiatry. 2006;63:201-208

What should we do with our stimulant-using patients?

- For both inpatients and outpatients
  - Ask about medical complications, overdose
  - Harm reduction – safer use techniques
  - Motivational interviewing to develop a decisional balance that favors safer use, quitting and engaging in available treatment
- Refer or provide
  - Cognitive Behavioral Therapy
  - Community Reenforcement Approach
  - Contingency Management
  - 12 step facilitation

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Cocaine use at beginning of buprenorphine treatment

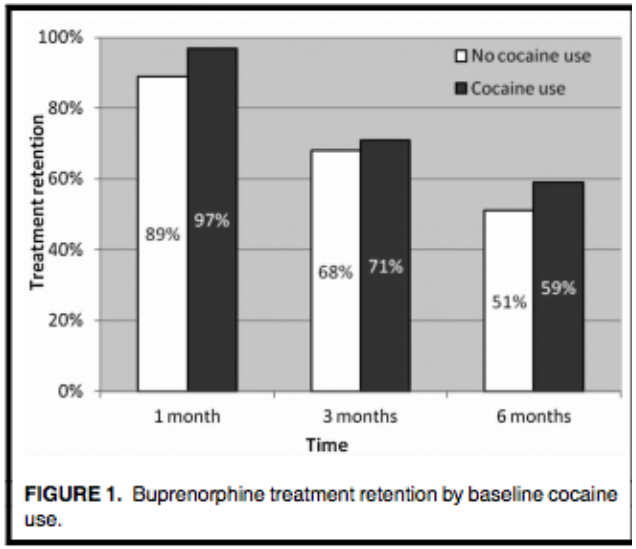

FIGURE 1. Buprenorphine treatment retention by baseline cocaine use.

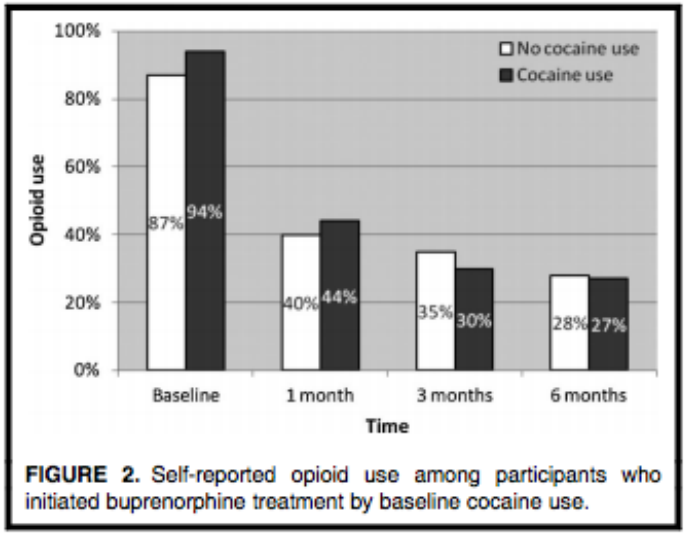

FIGURE 2. Self-reported opioid use among participants who initiated buprenorphine treatment by baseline cocaine use.

Cunningham et al. Am Journal Addictions 2013: 22; 352-357.

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AHA 2011 Updated Scientific Statement on cocaine and methamphetamine unstable angina/NSTEMI

- Class I: Benefit >>> Risk
  - NTG and CCB for ST changes (Level C)
    - Immediate cathif ST remain elevated after NTG and CCB (Level C)
      - Fibrinolytics if cath not available
- Class IIa: Benefit >> Risk
  - NTG + CCB for normal ECGs or minimal ST changes (Level C)
  - Cath for new persistent ST changes after NTG + CCB (Level C)
  - Manage methamphetamine similarly to cocaine UA
- Class IIb: Benefit ≥ Risk
  - Non-selective beta-blockers for bp > 150/100 or HR > 100 after NTG or CCB
- Class III: Risk ≥ Benefit
  - Cath with no ST changes and negative stress test and troponins

Wright et al. JACC. 2011: 57; e215-367

All guidelines are Class 3 LIMITED evidence

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Beta-Blockers in Cocaine Chest Pain

331 patients with chest pain and cocaine-positive urine test results admitted to San Francisco General Hospital between 2001-05

- 151 patients received a beta-blocker in ED
  - 85% received metoprolol
- During the hospitalization
  - SBP decreased more in ED beta-block group
  - No differences in ECG results, troponin levels, intubation rates, vasopressor use, malignant ventricular arrhythmia rates, or death were found.
- 45 deaths over a median follow-up of 972 days
  - Discharge on a beta-blocker regimen was associated with a lower risk of cardiovascular-specific death but not all-cause mortality

Rangel C, Shu RG, Lazar LD, et al. Beta-blockers for chest pain associated with recent cocaine use. *Arch Intern Med.* 2010;170(10):874–9.

Thanks!

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Does crack make people more violent than powder cocaine?

Violent behaviors of adults with a lifetime history of crack cocaine or powder cocaine use.

Violent behaviors	Powdered Cocaine % (95% CI[a])	Crack Cocaine % (95% CI)	Odds Ratio[b] (unadjusted) (95% CI)	Odds Ratio[c] (adjusted) (95% CI)
Bully/push people	17.44(15.26–19.87)	23.27(19.01–28.17)	**1.44 (1.04–1.97)**	.82(.57–1.19)
Do things that could have easily hurt you/others	46.01(42.66–49.41)	55.26(49.02–61.33)	**1.45 (1.07–1.96)**	1.24(.84–1.84)
Rob/mug someone or snatch a purse	1.78(1.19–2.64)	4.55(2.66–7.71)	**2.63 (1.35–5.12)**	.89(.41–1.93)
Force someone to have sex	.63(.33–1.20)	2.36(.91–5.93)	3.78(1.19–12.00)	2.56(.71–9.21)
Get into lots of fights that you started	9.42(7.90–11.20)	15.36(12.01–19.44)	1.74(1.24–2.45)	.85(.56–1.29)
Get into a fight that came to swapping blows with husband/wife or boyfriend/ girlfriend	17.98(15.59–20.66)	34.47(29.19–40.16)	**2.40 (1.76–3.27)**	**1.55 (1.05–2.28)**
Use a weapon in a fight	8.92(7.48–10.60)	19.87(15.84–24.63)	**2.53 (1.83–3.50)**	1.18(.80–1.73)
Hit someone so hard that you injure them	20.48(18.16–23.01)	30.01(24.57–36.07)	**1.66 (1.23–2.25)**	.79(.53–1.18)
Harass/threaten/blackmail someone	6.80(5.56–8.29)	12.27(9.20–16.20)	**1.92 (1.34–2.74)**	.93(.59–1.46)
Hurt an animal on purpose	5.59(4.44–7.02)	8.78(6.09–12.51)	**1.63 (1.04–2.54)**	.88(.55–1.40)

Note: [a]CI: confidence interval, [b]OR: odds ratio, [c]Odds ratios adjusted for sociodemographic characteristics, lifetime mood and alcohol and substance use disorders, OR values in bold are statistically significant.

Vaughn et al. AM J Drug Alc Abuse 2010: 36; 181-186.

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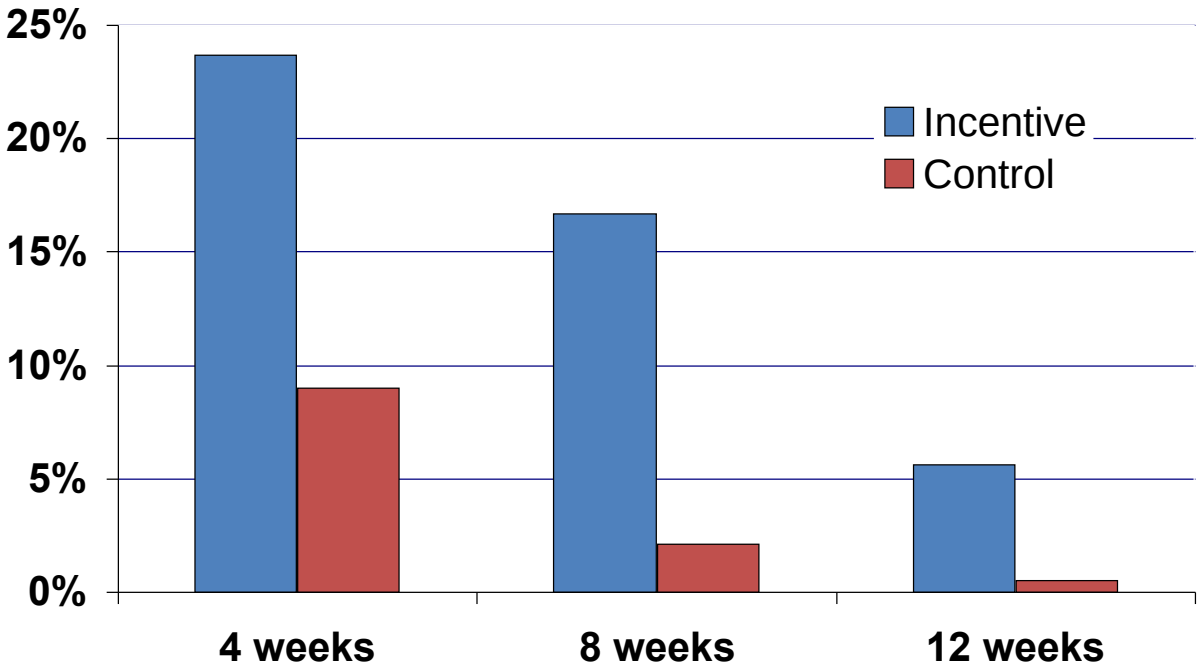
Contingency Management

Methadone Maintenance Patients With Specified Weeks of Continuous Stimulant/Alcohol-Negative Samples (n=388)



Average cost = $1.46 per person/day

Pierce et al. Arch Gen Psychiatry. 2006;63:201-208.

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Studies of the treatment for cocaine-related unstable angina with beta-blockers…

1. include randomized controlled trials that demonstrate that they save lives
2. include randomized controlled trials that demonstrate that they cause harm
3. include catheter studies in humans that show improved vasospasm with propranolol
4. include observational studies that show no increased adverse events among people receiving beta-blockers in the ED

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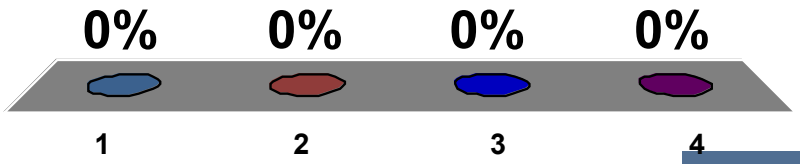
Which statement is true about stimulants?

1. Methamphetamine is only used intravenously or smoked
2. Methamphetamine has a longer half-life than cocaine
3. Intravenous injection results in the fastest onset of action
4. Cocaine's peak concentration occurs in about 1 hour



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5 things about stimulants

1. Easily available
2. Directly activate the mesolimbic pleasure center
3. Binge use often ends with dysphoria or lack of funds
4. Social and medical consequences
5. Treatment can work if you can find it

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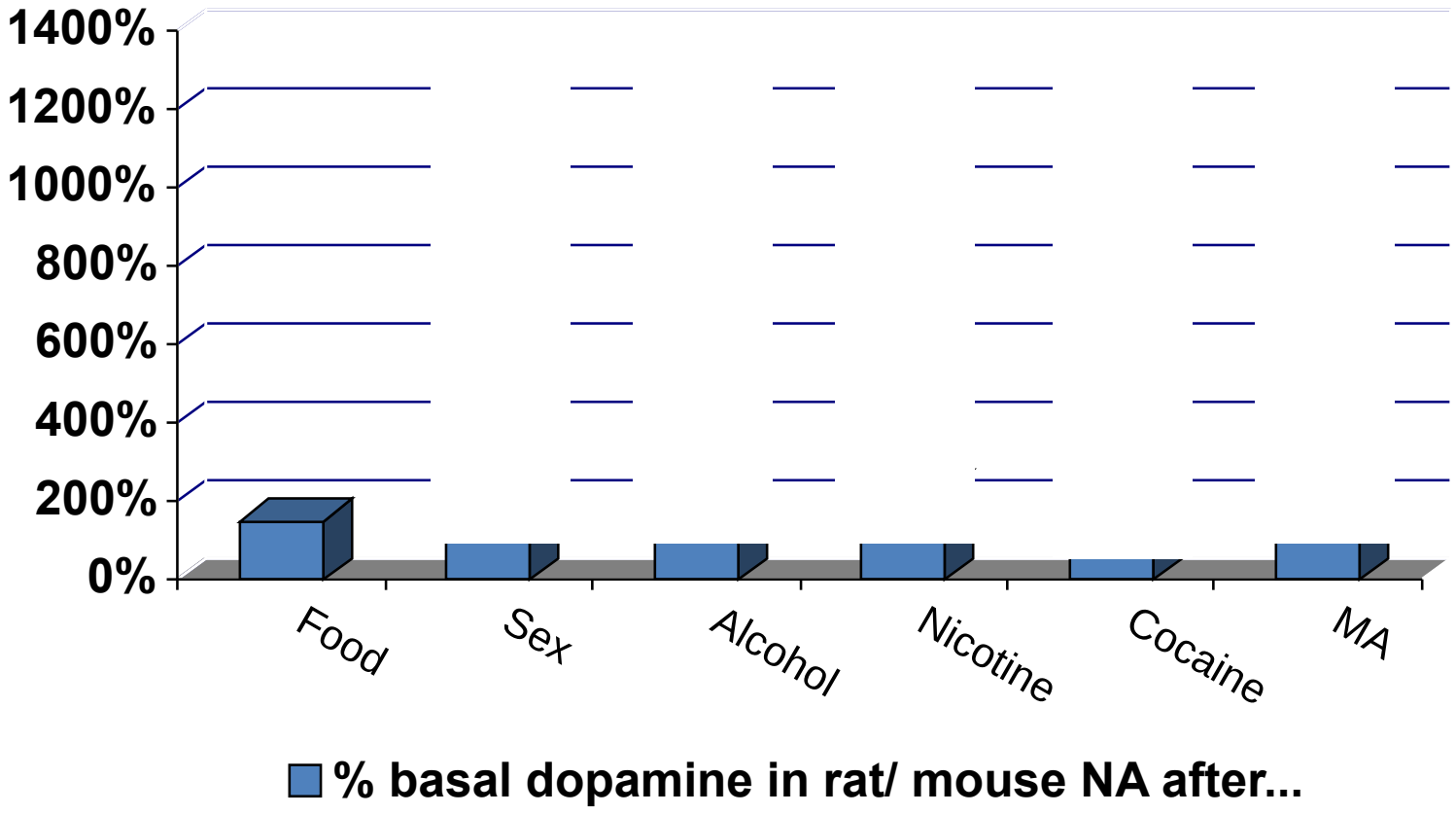
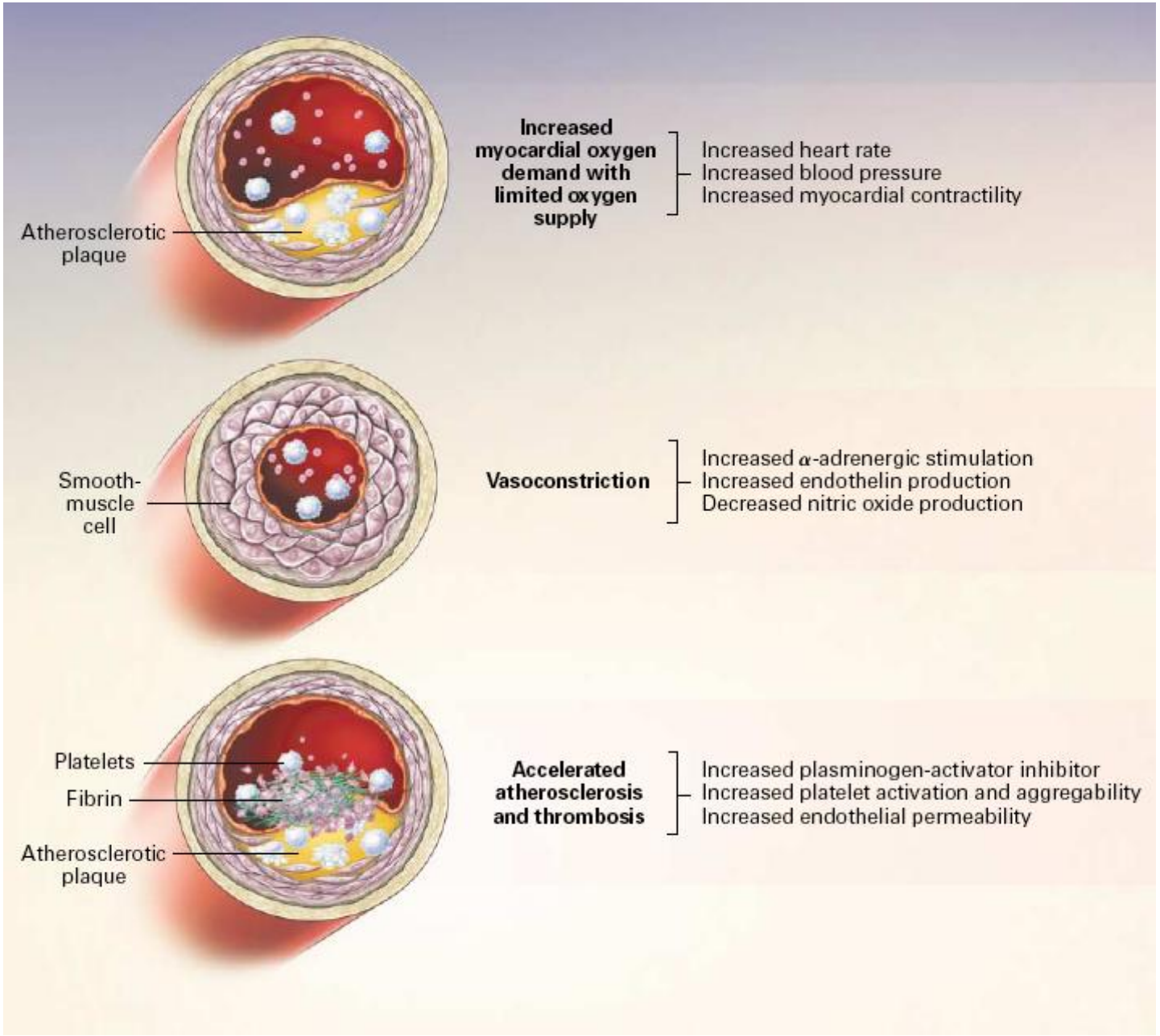
Learning objectives

At the end of this session, participants will be able to:

1. Understand how and why people use stimulants
2. Know the characteristics of stimulant intoxication and withdrawal syndromes
3. Understand the consequences of these drugs
4. Know the current options for treatment of stimulant dependence

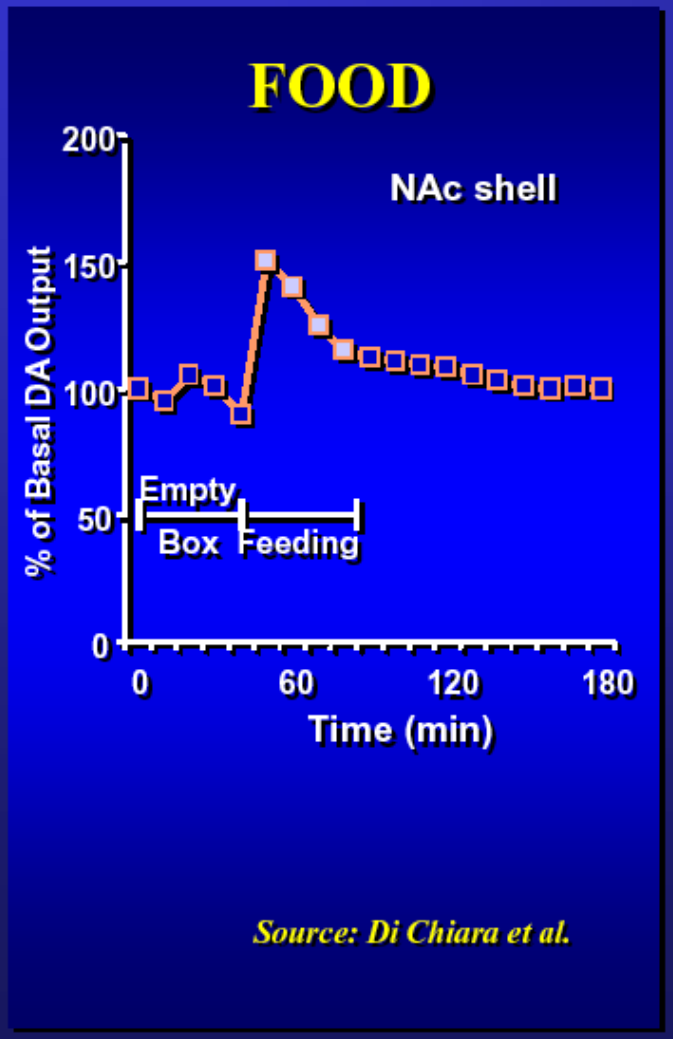
Dopamine release: nucleus accumbens

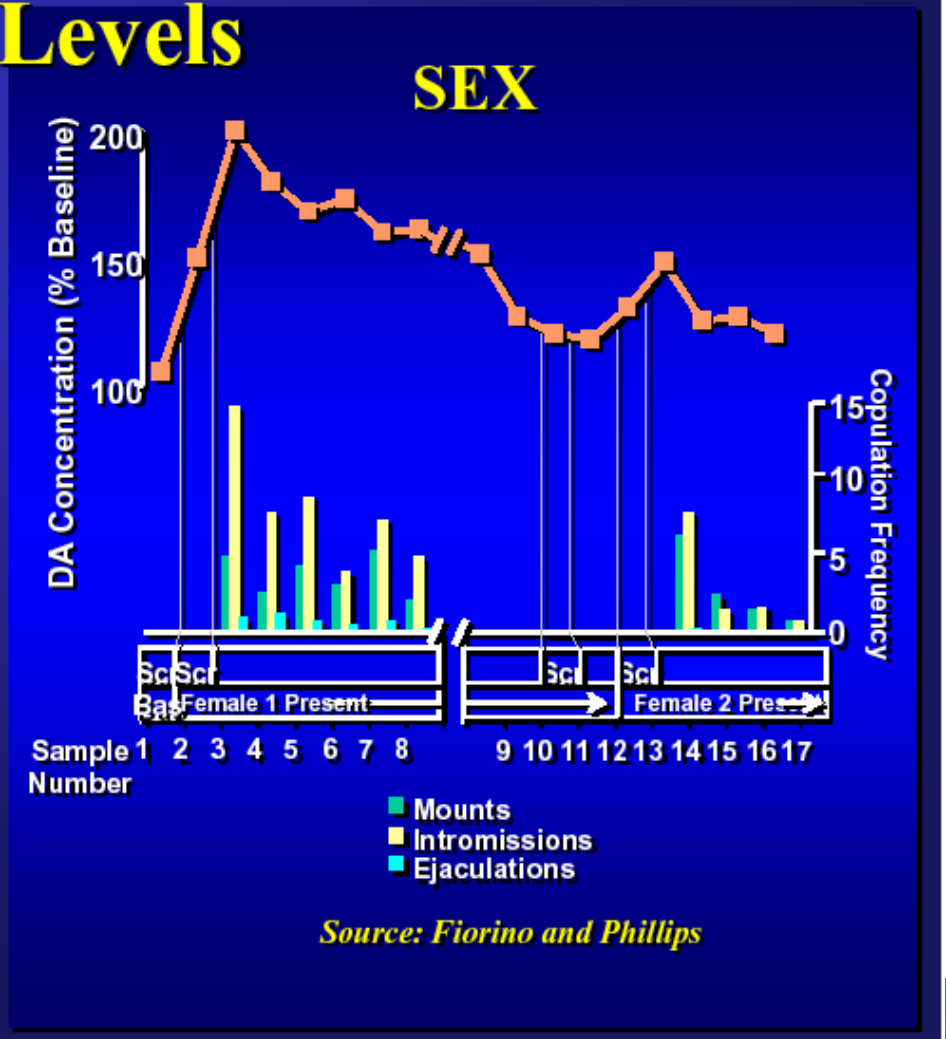




Lange, R. A. and L. D. Hillis (2001). "Cardiovascular complications of cocaine use." N Engl J Med **345**(5): 351-8.

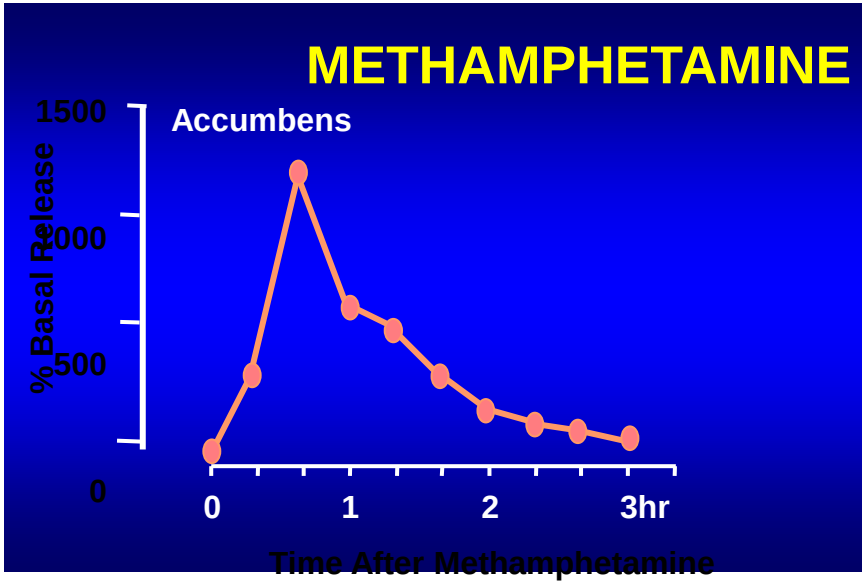
Natural Rewards Elevate Dopamine Levels

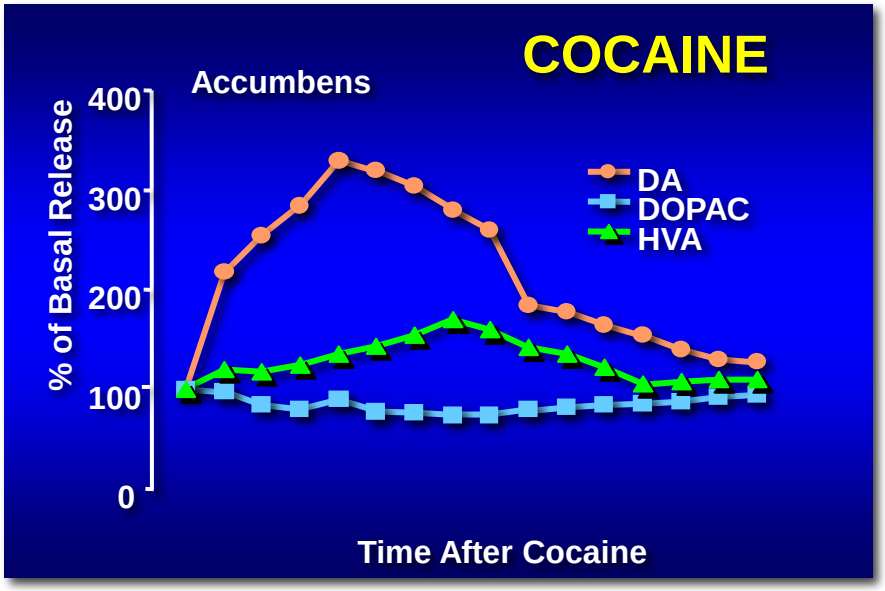


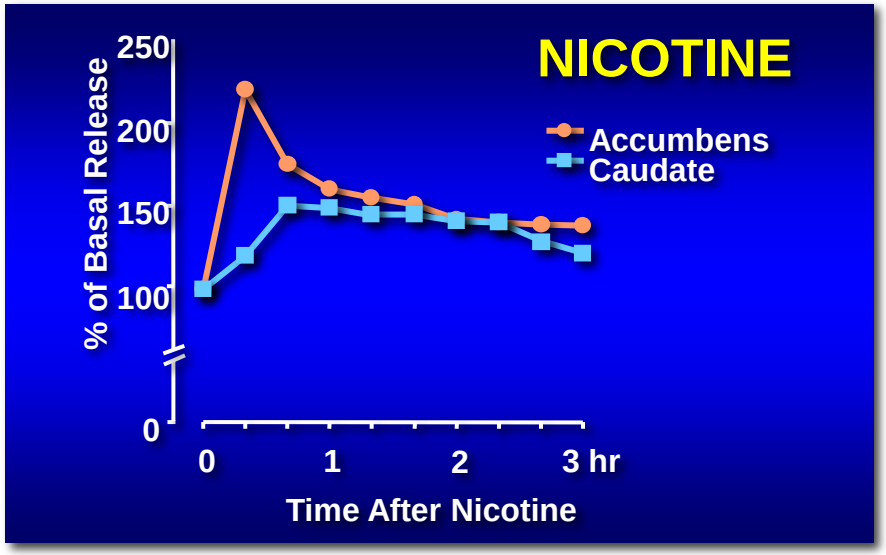


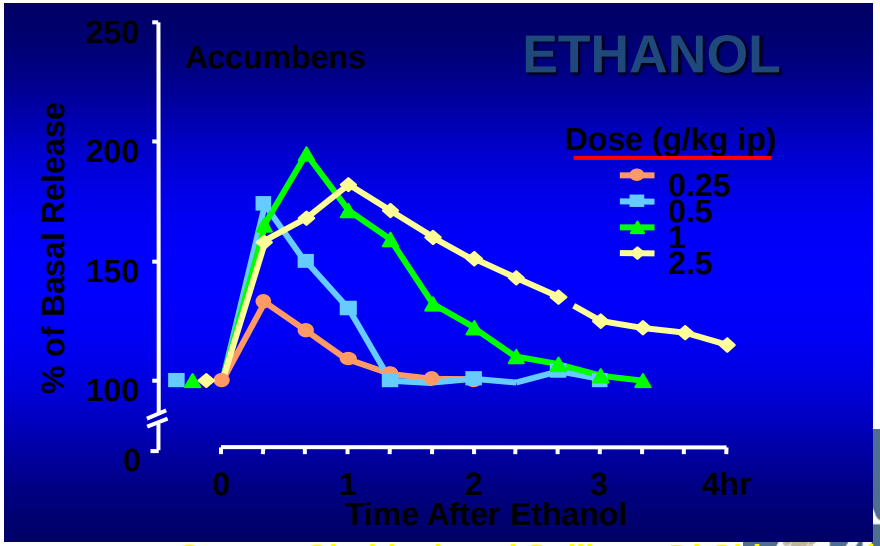
Slide from Richard Rawson

Effects of Drugs on Dopamine Release









Source: Shoblock and Sullivan; Di Chiara and Imperato

Slide from Richard Rawson

Pregnancy

- More common in stimulant users:
  - Mental illness, seizure, injury, hypertension
  - Premature membrane rupture and labor, placenta previa, placental abruption, intrauterine death
- 1998-2004
  - Cocaine-related hosp decreased: 0.74>>0.41 per 100
  - MA-related hosp increased: 0.11>>0.22 per 100
- Cocaine vs. MA related pregnancy
  - More common for cocaine: mental illness, poor fetal growth, and premature delivery
  - More common for MA: hypertension, placenta previa

Cox et al. Obstet Gynecol. 2008;111:341–7.

Cardiomyopathy and Methamphetamine

- In a case-control study, researchers examined the association between methamphetamine use and cardiomyopathy (CM).

- Subjects included patients aged 45 years or younger discharged from a tertiary care medical center in Honolulu.

- Through medical record review, researchers identified...
  - 107 cases (had a discharge diagnosis of CM or congestive heart failure) and
  - 114 controls (ejection fraction ≥55% and no wall motion abnormalities).

Yeo K-K, et al. *Am J Med*. 2007;120(2):165–171.

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Cardiomyopathy and Methamphetamine

- 42% of cases and 20% of controls had ever used methamphetamine.
- Methamphetamine use was significantly more common in cases than in controls.
- OR in analyses adjusted for age, body mass index, and renal failure, 3.7

Yeo K-K, et al. *Am J Med*. 2007;120(2):165–171.

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“No lies here folks this recipe will manufacture methamphetamine this will get you into trouble if you do this BE CAREFUL!”
First of all let's talk about supplies:

- 1 Case Regular Pint size Mason Jars (Used for canning)
- 2 Boxes Contact 12 hour time released tablets.
- 3 Bottles of Heet.
- 4 feet of surgical tubing.
- 1 Bottle of Rubbing Alcohol.
- 1 Gallon Muriatic Acid (Used for cleaning concrete)
- 1 Gallon of Coleman's Fuel
- 1 Gallon of Aceton
- 1 Pack of Coffee Filters
- 1 Electric Skillet

- 2 Bottles of Hydrogen peroxide
- 3 20 0z Coke Bottles (Plastic type)(with Lids/caps)
- 1 Can Red Devils Lye
- 1 Pair of sharp scissors
- 4 Boxes Book Matches (try to get the ones with brown/red striker pads)
- 1 pyrodex baking dish
- 1 Box execto razor blades single sided
- 1 digital scale that reads grams
- 2 gallons distilled water
- 1 Roll Aluminum foil tape

“That's what you would have to go buy if you wanted to make meth.”

www.totse.com/en/drugs/speedy_drugs/howtomanufactu172921.html

Cocaine and HIV

- Crack cocaine use is associated
  - increased number of sex partners
  - sex work
  - HIV infection, independent of IVD use
- IV cocaine leads to HIV through frequent injection Chaisson. JAMA. 1989 Jan 27;261(4):561-5.

MA and HIV

- Increased libido, social disinhibition, increased energy >> riskier sex behaviors
- PDE5 inhibitors (sildenafil) can be used to mitigate MA-induced erectile dysfunction

Methamphetamine and Trauma

To assess the prevalence and impact of methamphetamine use (MU) in trauma patients, researchers surveyed the records of…

- 4932 patients who presented to
  - San Diego trauma center between 2003–2005
  - urine toxicology screening during their visit

Swanson SM, et al. *J Trauma*. 2007;63(3):531

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Results

- The rate of MU (defined as a positive urine screen), but not other illicit drug use, increased from 2003 to 2005 (from 9% to 15%).
- In adjusted analyses, patients with MU were more likely to have…
  - been injured in a violent way (OR, 2.0),
  - attempted suicide (OR, 1.7),
  - been a victim of domestic violence (OR, 2.5),
  - required more medical care (e.g., ≥1 operations [OR, 1.5], mechanical ventilation [OR, 1.6]), and
  - died from their injuries (OR, 2.3).

Swanson SM, et al. *J Trauma*. 2007;63(3):531

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16 week RCT of cocaine-dependent methadone patients of:

CBT vs. CM vs. CBT+CM vs. TAU

30 patients per group

Rawson et al. Arch Gen Psychiatry. 20

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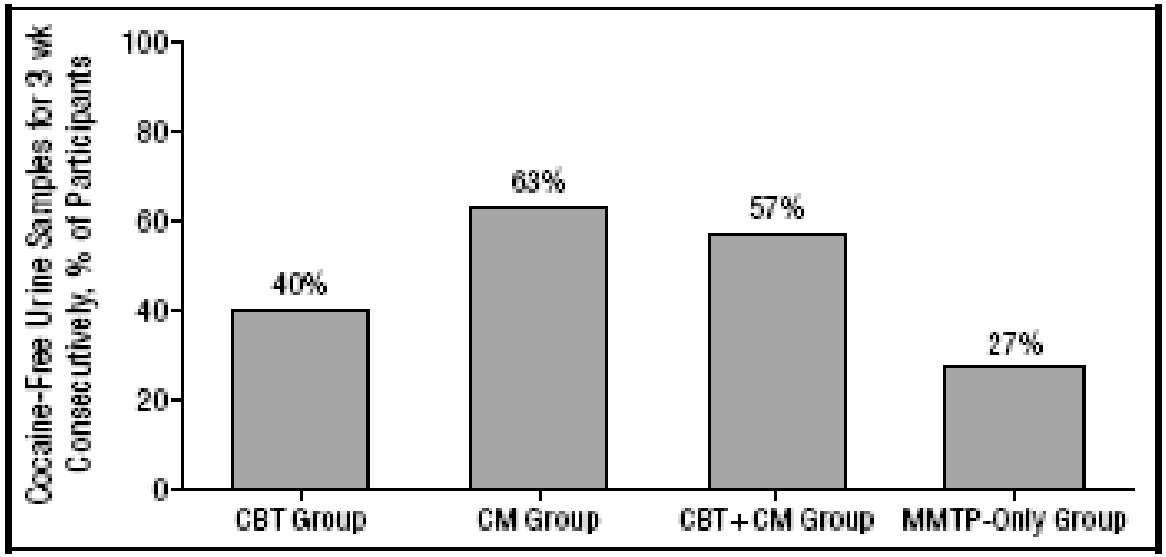

Figure 5. Percentage of patients achieving 3 consecutive weeks of cocaine-free urine samples by group ($\chi^2_3 = 9.9$; $P = .02$). CBT indicates cognitive-behavioral therapy; CM, contingency management; and MMTP, methadone maintenance treatment program.

Rawson et al. Arch Gen Psychiatry. 20

Cognitive Behavioral Therapy

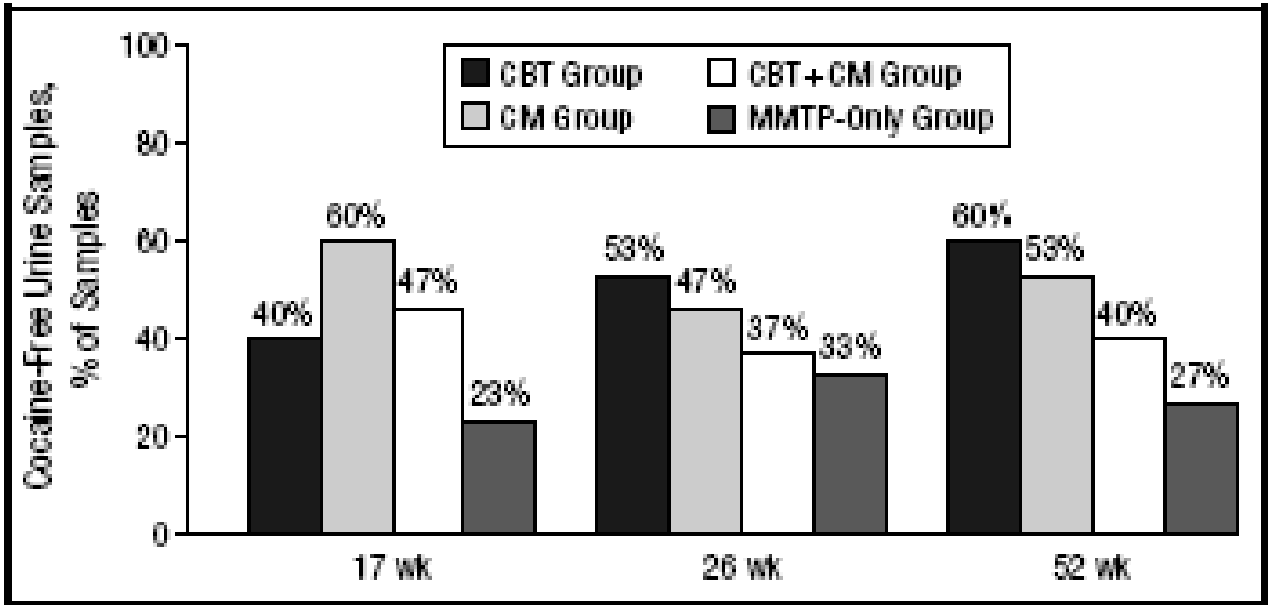

Figure 6. Percentage of 30 possible cocaine-free urine samples at the 17-week, 26-week, and 52-week follow-up points. CBT indicates cognitive-behavioral therapy; CM, contingency management; and MMTP, methadone maintenance treatment program.

Rawson et al. Arch Gen Psychiatry. 2002

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