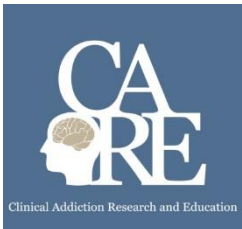


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# Stimulants: Cocaine and Methamphetamine

CRIT/FIT program – April 2016

Alex Walley, MD, MSc

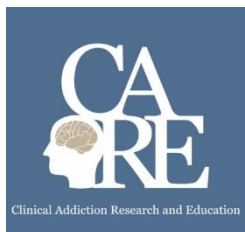


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# Learning objectives

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



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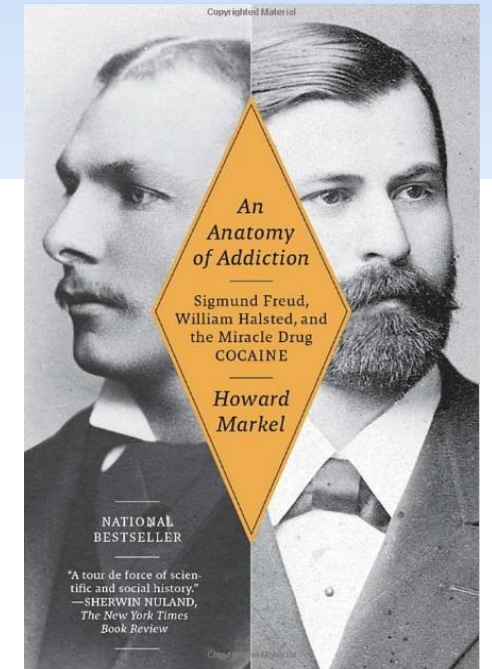
# History: Cocaine



- From erythroxyton 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*



1885 Advertisement for Cocaine Toothache Drops



# 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*





When he sits before Temptation



...prescribe Desoxyn HYDROCHLORIDE (Methamphetamine Hydrochloride, Abbott)

THE SYMPTOMOTIC AMENES HAVE BEEN found to be... when administered... the experience of a placebo... in an effort to determine management of obesity...

SMALLER DOSEAGE LONGER EFFECT. IT IS CON- sidered... that... administration... of the drug... is advised... with a smaller dose...

DOSEAGE AND EFFECTS. THE DOSE OF DESOXYN must be adjusted... in accordance with the requirements and response of the individual patient...

OTHER INDICATIONS. DEPRESSIVE STATES. Desoxy Hydrochloride is indicated for the administration of moderate and more or mild depressive states...

CONTRAINDICATIONS. DESOXYN HYDROCHLORIDE should not be used... in patients with... severe... depression...

PRECAUTIONS. DESOXYN HYDROCHLORIDE should be used... with caution... in patients with... cardiovascular... disease...

ADVERSE REACTIONS. DESOXYN HYDROCHLORIDE... may cause... nervousness... insomnia... and... loss of appetite...

PHYSIOLOGICAL EFFECTS. DESOXYN HYDROCHLORIDE... increases... heart rate... blood pressure... and... respiratory rate...

ONSET OF EFFECT. WITH DESOXYN... the onset of effect... is usually... within... 15 to 30 minutes...

BLOOD PRESSURE, PULSE RATE AND RESPIRATORY rate usually are only slightly or moderately affected...

THE PARENTERAL ADMINISTRATION OF DESOXYN Hydrochloride is suggested for... patients who... are unable... to take... oral... medication...

TOLERANCE NOT DEVELOPED. WHILE THE DRUG is not habit forming... tolerance... is not... developed... because... of... its... short... duration... of... action...

Advertisement for AMBAR TABLETS AND EXTENTABS. Features a man's face in a glass sphere and a man's torso in a wire mesh sphere. Text includes 'WEIGHT REDUCTION WITHOUT JITTERS' and 'AMBAR TABLETS AND EXTENTABS'. Includes a table of drug specifications and a list of distributors.



1957

1959

MEDICAL

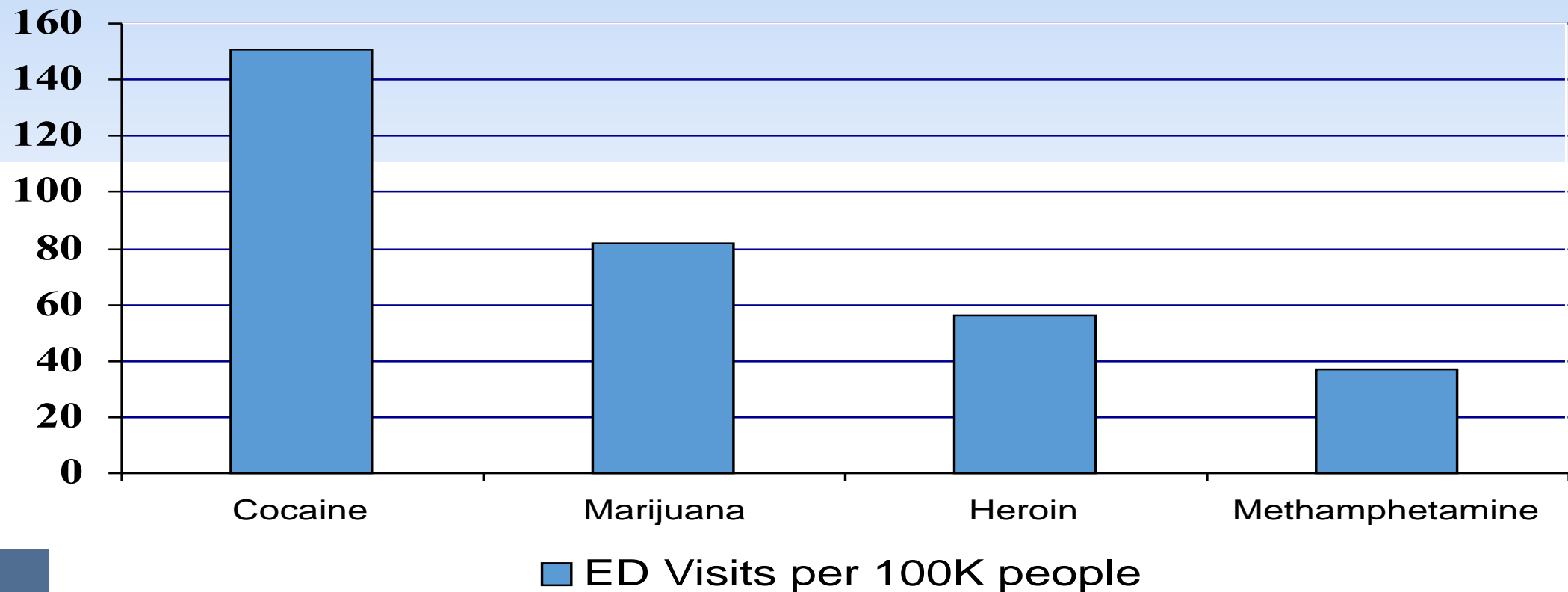
EXCEPTIONAL CARE. WITHOUT EXCEPTION.

# Epidemiology

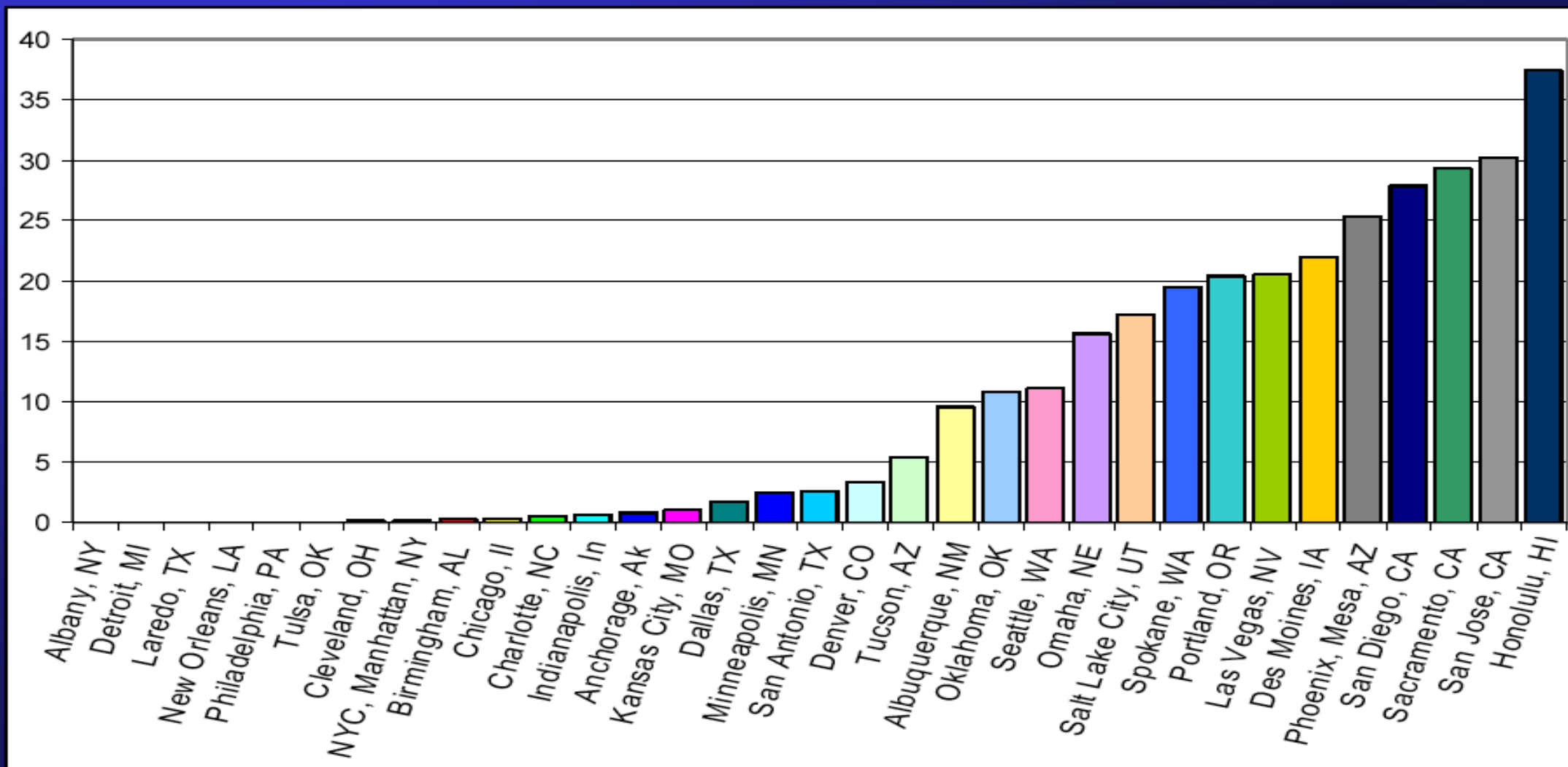


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# 2005 drug-related ED visits



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





# From where do these drugs come?

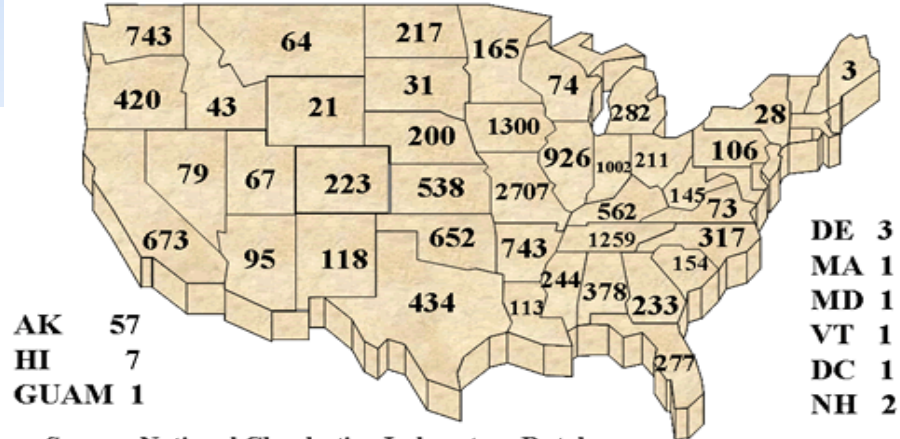


<http://www.colombiajournal.org/cocainephotos.htm>

- Methamphetamine
  - Super labs – Primarily Mexico
  - 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

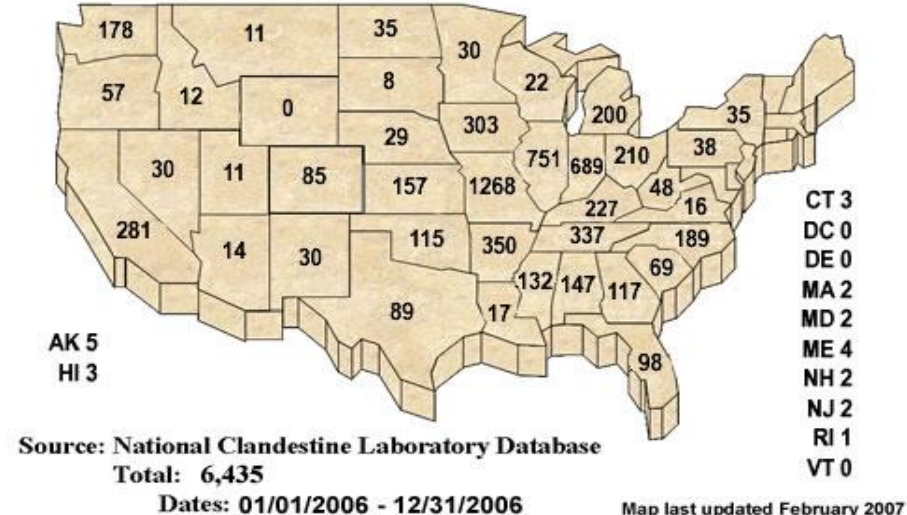
# Clandestine lab incidents

**Total of All Meth Clandestine Laboratory Incidents  
Including Labs, Dumpsites, Chem/Glass/Equipment  
Calendar Year 2004**



Source: National Clandestine Laboratory Database  
Total: 15,994 / 49 States Reporting  
Dates: 01/01/04 to 12/31/04

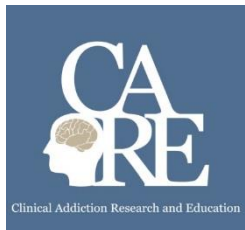
**Total of All Meth Clandestine Laboratory Incidents  
Including Labs, Dumpsites, Chem/Glass/Equipment  
Calendar Year 2006**



Source: National Clandestine Laboratory Database  
Total: 6,435  
Dates: 01/01/2006 - 12/31/2006

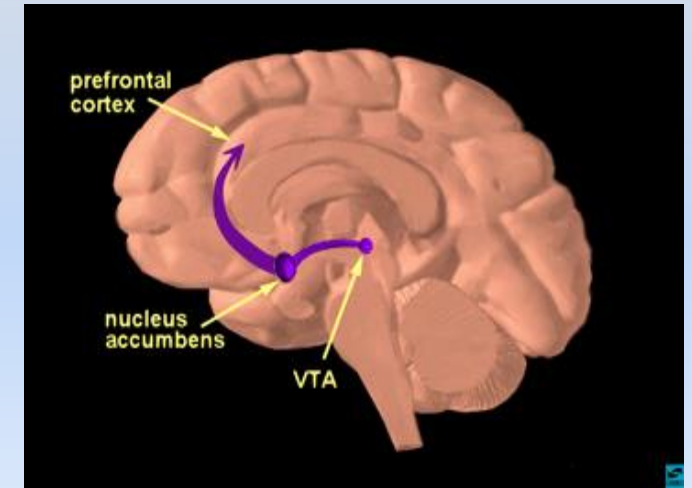
Map last updated February 2007

# Stimulant Effects



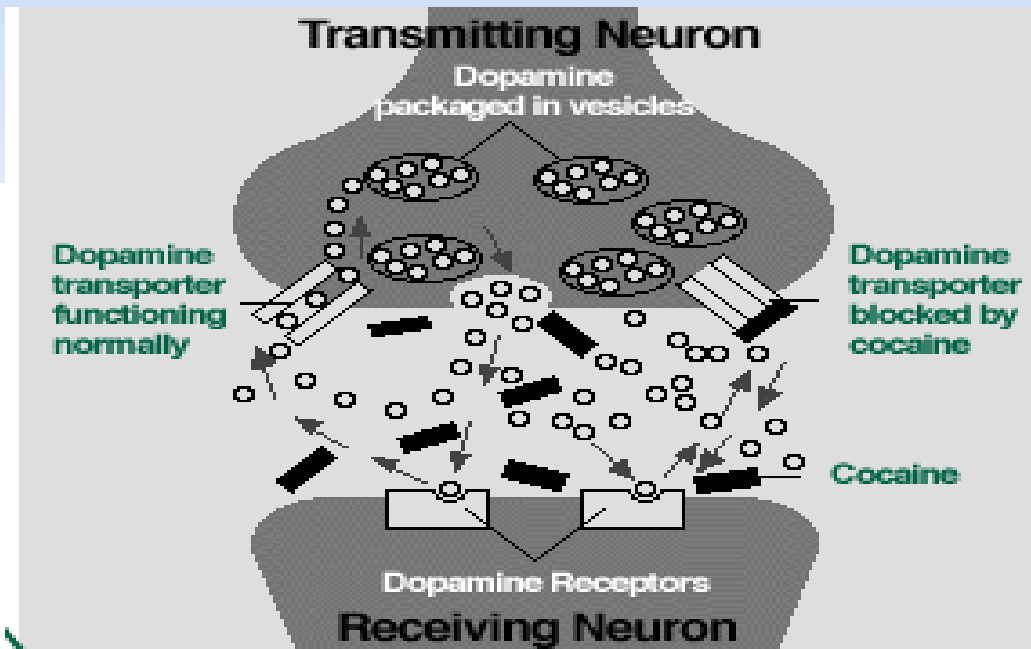
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# Why do people use stimulants?

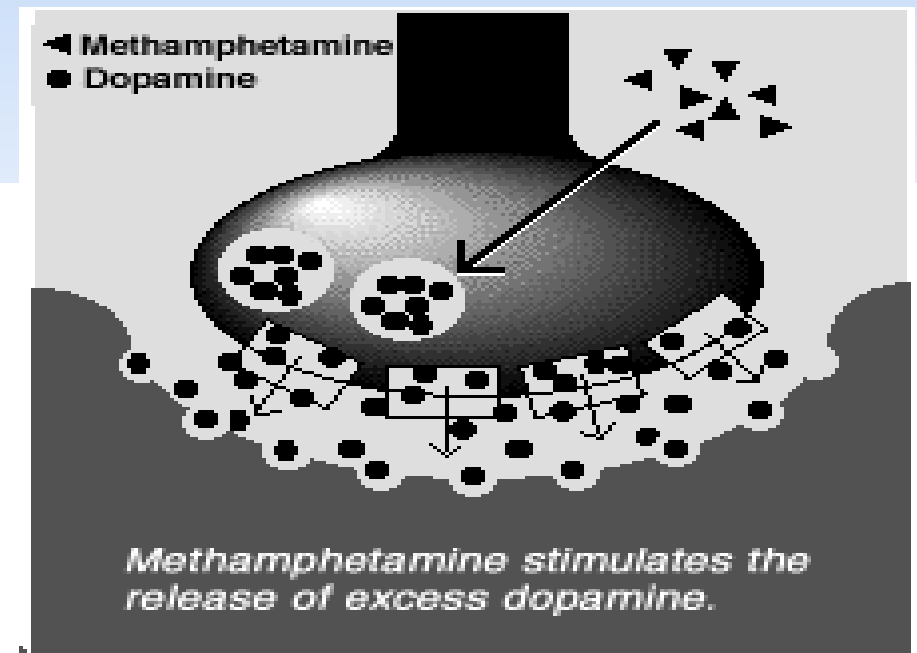


- Euphoria - Rush
  - Onset and intensity depends on delivery method
- Increased energy, alertness, libido
- Diminished social inhibition
- Decreased appetite

# Cocaine



# Methamphetamine



## PK: Cocaine

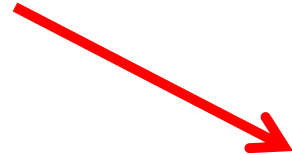
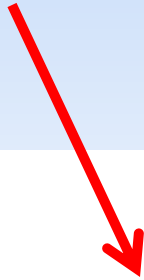
	IV	Smoked	Snorted
Time to effect	10-60sec	3-5sec	1-5min
Peak concent.	3-5min	1-3min	15-20min
Half-life	20-60min	5-15min	60-90min

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

## PK: Methamphetamine

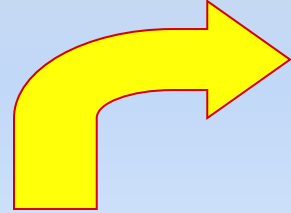
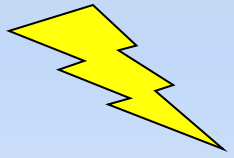
	IV	Smoked	Snorted	Ingested
Time to effect	15-30 sec	Immediate	3-5 min	15-20 min
Peak concent.	2-4 h	2-4 h	2-4 h	2-4 h
Half-life	10-12 h	10-12 h	10-12 h	10-12 h



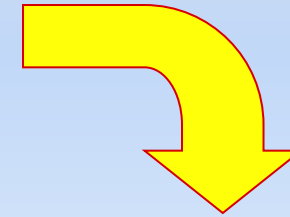


# Dynamic Cycle of Cocaine Addiction

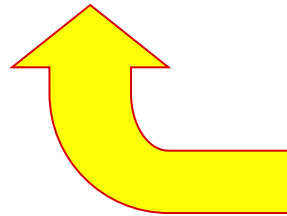
Cocaine



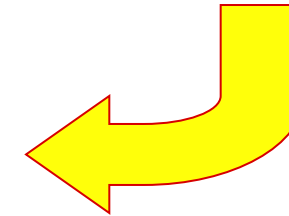
**Cocaine Euphoria**  
**Positive Reinforcement**  
Activated Reward Pathways  
↑DA/Glutamate



**Reward Dysregulation**  
**Cocaine Withdrawal**  
↓DA/Glutamate  
↑Dynorphin/GABA



**-**  
**Cocaine Craving**  
**Negative Reinforcement**  
↓DA/Glutamate

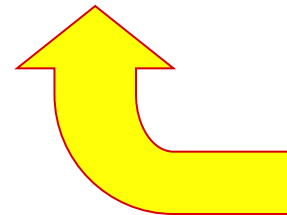


**Cocaine Cues**  
Limbic Activation  
↑DA/Glutamate

**Cocaine Administration**  
Drug-Seeking Behavior  
Failed Impulse Suppression  
Multiple Risks/Hazards

**Loss of Control**

Denial / Poor Decision-Making  
Hypofrontality / Low D2  
Reduced Gray Matter Density



**Stress**

# 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
- Arrhythmia
- Vasoconstriction
- Hyperthermia
- Agitation
- Rhabdomyolysis
- Seizure
- Acute psychosis → prolonged psychosis
  - Paranoid delusions
  - Visual, sensory, and auditory hallucinations
    - ie formications

# Intoxication Treatment

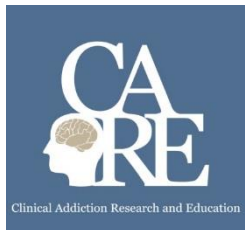
- Minimize sensory stimulation
- Neuroleptics (ie haldol) for agitation
- Benzos to control seizures
- Treat hyperthermia (external cooling)
- For increased BP+HR, use vasodilators and CCB or non-selective beta-blockers

# 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



# Health Consequences



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## Dental

- Darkened teeth
- Caries
- Periodontal disease

## Pulmonary

- Acute pulmonary edema
- Pulmonary HTN
- Inhalation injury

## Cardiovascular

- Hypertension
- DCM
- Arrhythmia/ 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

- Rhabdomyolysis
- Dehydration
- Acute Renal Failure
- Acidosis
- Hyperthermia

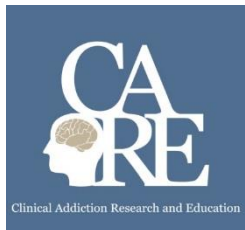
## Skin

- Cellulitis/ abscess
- Excoriations
- Chemical burns

# ETOH + Cocaine >> 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



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## **Anticonvulsants for cocaine dependence (Review)**

Minozzi S **Efficacy of Psychostimulant Drugs for Cocaine Dependence (Review)**

**Efficacy of psychostimulant drugs for amphetamine abuse or dependence (Review)**

Castells X,

I **Dopamine agonists for the treatment of cocaine dependence (Review)**

Minozzi S, Amato L **Antipsychotic medications for cocaine dependence (Review)**

**Disulfiram for the treatment of cocaine dependence (Review)**

**Antidepressants for cocaine dependence and problematic cocaine use (Review)**

Pani PP, Trogu E, Vecchi S, Amato L

Original Investigation

# Topiramate for the Treatment of Cocaine Addiction A Randomized Clinical Trial

Bankole A. Johnson, DSc, MD; Nassima Ait-Daoud, MD; Xin-Qun Wang, MS; J. Kim Penberthy, PhD;  
Martin A. Javors, PhD; Chamindi Seneviratne, MD; Lei Liu, PhD

**IMPORTANCE** No medication has been established as an efficacious treatment for cocaine dependence. We hypothesized that dual modulation of the mesocorticolimbic dopamine system by topiramate—a glutamate receptor antagonist and  $\gamma$ -aminobutyric acid receptor agonist—would result in efficacious treatment for cocaine dependence compared with placebo.

**OBJECTIVE** To determine the efficacy of topiramate vs placebo as a treatment for cocaine dependence.

**DESIGN, SETTING, AND PARTICIPANTS** Double-blind, randomized, placebo-controlled, 12-week trial of 142 cocaine-dependent adults in clinical research facilities at the University of Virginia between November 22, 2005, and July 25, 2011.

**INTERVENTIONS** Topiramate ( $n = 71$ ) or placebo ( $n = 71$ ) in escalating doses from 50 mg/d to the target maintenance dose of 300 mg/d in weeks 6 to 12, combined with weekly cognitive-behavioral treatment.

**MAIN OUTCOMES AND MEASURES** For the efficacy period, weeks 6 to 12, the primary outcome was the weekly difference from baseline in the proportion of cocaine nonuse days; the secondary outcome was urinary cocaine-free weeks, and exploratory outcomes included craving and self- and observer-rated global functioning on the Clinical Global Impression scales.

**RESULTS** Using an intent-to-treat analysis, topiramate was more efficacious than placebo at increasing the weekly proportion of cocaine nonuse days, irrespective of whether missing data were not or were imputed conservatively to the baseline value (13.3% vs 5.3%, 95% CI for the estimated mean difference, 1.4%-14.6%,  $P = .02$  or 8.9% vs 3.7%, 95% CI for the estimated mean difference, 0.2%-10.1%,  $P = .04$ , respectively). Topiramate also was associated, significantly more than placebo, with increasing the likelihood of urinary cocaine-free weeks (16.6% vs 5.8%; odds ratio, 3.21; 95% CI, 1.24-8.32;  $P = .02$ ), as well as decreasing craving and improving observer-rated global functioning (all  $P < .05$ ).

**CONCLUSIONS AND RELEVANCE** Topiramate is more efficacious than placebo at increasing the mean weekly proportion of cocaine nonuse days and associated measures of clinical improvement among cocaine-dependent individuals.

**TRIAL REGISTRATION** [clinicaltrials.gov](https://clinicaltrials.gov) Identifier: NCT00249691

**Author Affiliations:** Department of Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville (Johnson, Ait-Daoud, Penberthy, Seneviratne); now with Department of Psychiatry, University of Maryland School of Medicine, Baltimore (Johnson); Department of Public Health Sciences, University of Virginia, Charlottesville (Wang); Department of Psychiatry, The University of Texas Health Science





## Topiramate for the treatment of methamphetamine addiction: a multi-center placebo-controlled trial

Ahmed Elkashef<sup>1</sup>, Roberta Kahn<sup>1</sup>, Elmer Yu<sup>2</sup>, Erin Iturriaga<sup>1</sup>, Shou-Hua Li<sup>1</sup>, Ann Anderson<sup>1</sup>, Nora Chiang<sup>1</sup>, Nassima Ait-Daoud<sup>3</sup>, David Weiss<sup>4</sup>, Frances McSherry<sup>4</sup>, Tracey Serpi<sup>4</sup>, Richard Rawson<sup>5</sup>, Mark Hrymoc<sup>5</sup>, Dennis Weis<sup>6</sup>, Michael McCann<sup>7</sup>, Tony Pham<sup>7</sup>, Christopher Stock<sup>8</sup>, Ruth Dickinson<sup>8</sup>, Jan Campbell<sup>9</sup>, Charles Gorodetzky<sup>9</sup>, William Haning<sup>10</sup>, Barry Carlton<sup>10</sup>, Joseph Mawhinney<sup>11</sup>, Ming D. Li<sup>3</sup> & Bankole A. Johnson<sup>3</sup>

National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD, USA,<sup>1</sup> Veterans Administration Medical Center, Philadelphia, PA, USA,<sup>2</sup> Department of Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville, VA, USA,<sup>3</sup> Department of Veterans Affairs Cooperative Studies Program Coordinating Center, Perry Point, MD, USA,<sup>4</sup> UCLA Integrated Substance Abuse Programs, Los Angeles, CA, USA,<sup>5</sup> Lutheran Hospital Office of Research, Des Moines, IA, USA,<sup>6</sup> Matrix Institute on Addictions, Costa Mesa, CA, USA,<sup>7</sup> Department of Veterans Affairs, Salt Lake City Health Care System, Salt Lake City, UT, USA,<sup>8</sup> Department of Psychiatry, University of Missouri, Kansas City, MO, USA,<sup>9</sup> Pacific Addiction Research Center, Honolulu, HI, USA<sup>10</sup> and South Bay Treatment Center, San Diego, CA, USA<sup>11</sup>

### ABSTRACT

**Aims** Topiramate has shown efficacy at facilitating abstinence from alcohol and cocaine abuse. This double-blind, placebo-controlled out-patient trial tested topiramate for treating methamphetamine addiction. **Design** Participants ( $n = 140$ ) were randomized to receive topiramate or placebo (13 weeks) in escalating doses from 50 mg/day to the target maintenance of 200 mg/day in weeks 6–12 (tapered in week 13). Medication was combined with weekly brief behavioral compliance enhancement treatment. **Setting** The trial was conducted at eight medical centers in the United States. **Participants** One hundred and forty methamphetamine-dependent adults took part in the trial. **Measurements** The primary outcome was abstinence from methamphetamine during weeks 6–12. Secondary outcomes included use reduction versus baseline, as well as psychosocial variables. **Findings** In the intent-to-treat analysis, topiramate did not increase abstinence from methamphetamine during weeks 6–12. For secondary outcomes, topiramate reduced weekly median urine methamphetamine levels and observer-rated severity of dependence scores significantly. Subjects with negative urine before randomization ( $n = 26$ ) had significantly greater abstinence on topiramate versus placebo during study weeks 6–12. Topiramate was safe and well tolerated. **Conclusions** Topiramate does not appear to promote abstinence in methamphetamine users but can reduce the amount taken and reduce relapse rates in those who are already abstinent.

# Non-medical treatment for addiction

- Physician advice and brief intervention
  - Evidence is limited to non-dependent, risky alcohol use
  - Except Bernstein et al. DAD 2005: 77; 49
- Motivational enhancement therapy
- Cognitive behavior therapy
- Community Reinforcement Approach/ Community Reinforcement and Family Therapy (CRAFT)
- 12-step facilitation
- Contingency management

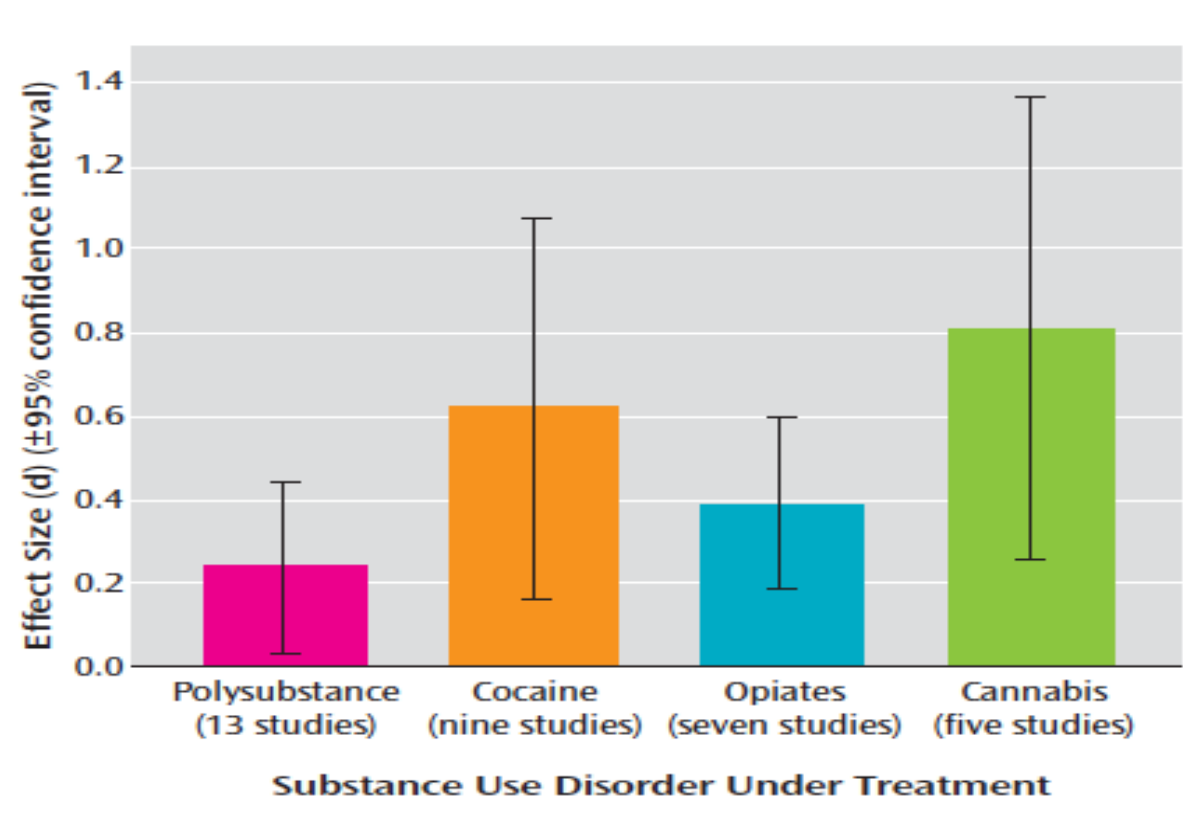
All treatments require adherence



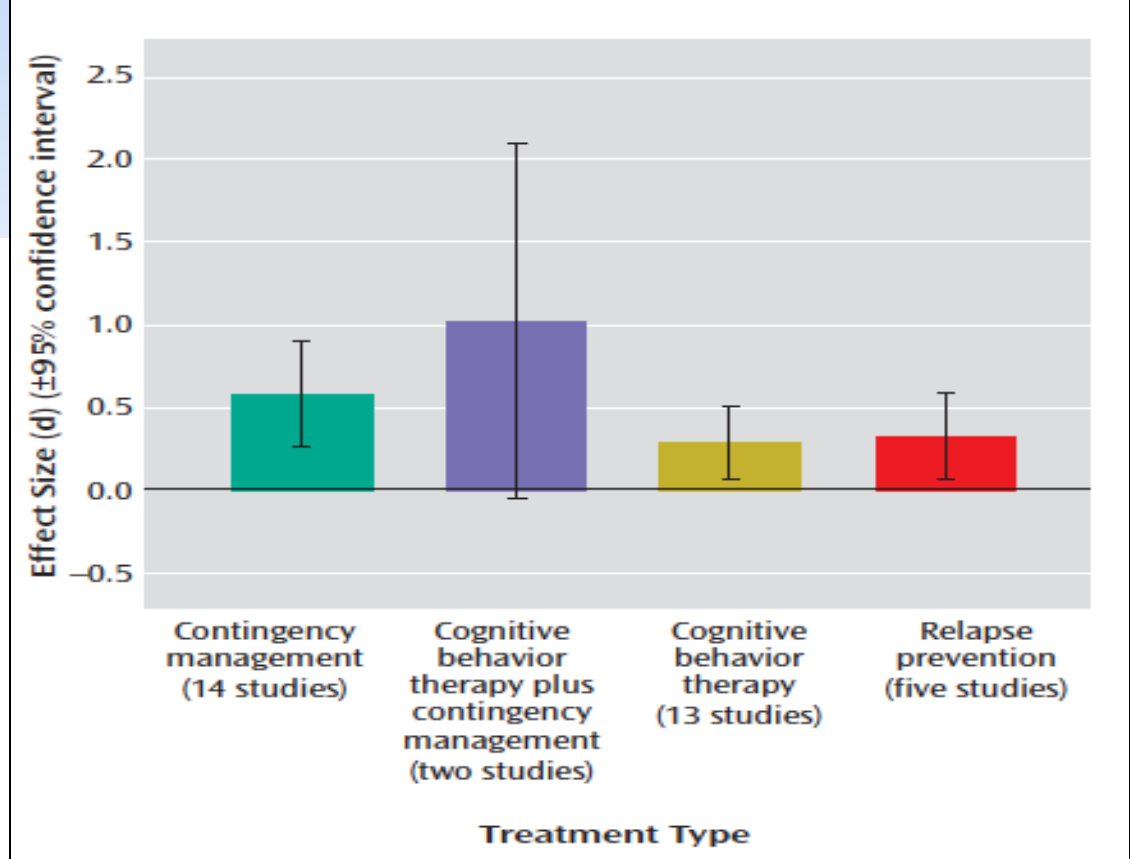
EXCEPTIONAL CARE. WITHOUT EXCEPTION.

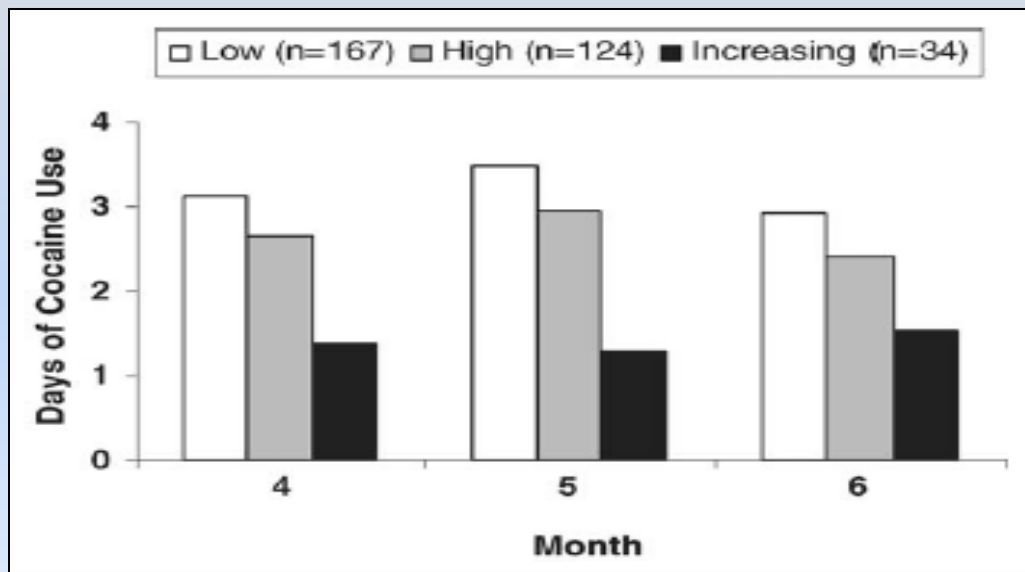
# A Meta-Analytic Review of Psychosocial Interventions for Substance Use Disorders

**FIGURE 1. Mean Effect Sizes Across Substance Use Disorders Under Treatment**



**FIGURE 2. Mean Effect Sizes Across Treatment Types**





- 487 cocaine-dependent outpatients.
- 12-step active participation (i.e. speaking at meetings, working the steps, having a sponsor) predicted reduced cocaine use in the following month.
- 12-step meeting attendance did not predict subsequent drug use.



Available online at [www.sciencedirect.com](http://www.sciencedirect.com)



Drug and Alcohol Dependence 77 (2005) 177–184



[www.elsevier.com/locate/drugaldep](http://www.elsevier.com/locate/drugaldep)

## The effect of 12-step self-help group attendance and participation on drug use outcomes among cocaine-dependent patients<sup>☆</sup>

Roger D. Weiss<sup>a,b,\*</sup>, Margaret L. Griffin<sup>a,b</sup>, Robert J. Gallop<sup>c</sup>, Lisa M. Najavits<sup>a,b</sup>, Arlene Frank<sup>d</sup>, Paul Crits-Christoph<sup>c</sup>, Michael E. Thase<sup>e</sup>, Jack Blaine<sup>f</sup>, David R. Gastfriend<sup>a,g</sup>, Dennis Daley<sup>e</sup>, Lester Luborsky<sup>c</sup>



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# Contingency Management

Systematic Review – Schierenberg 2012 – 19 studies

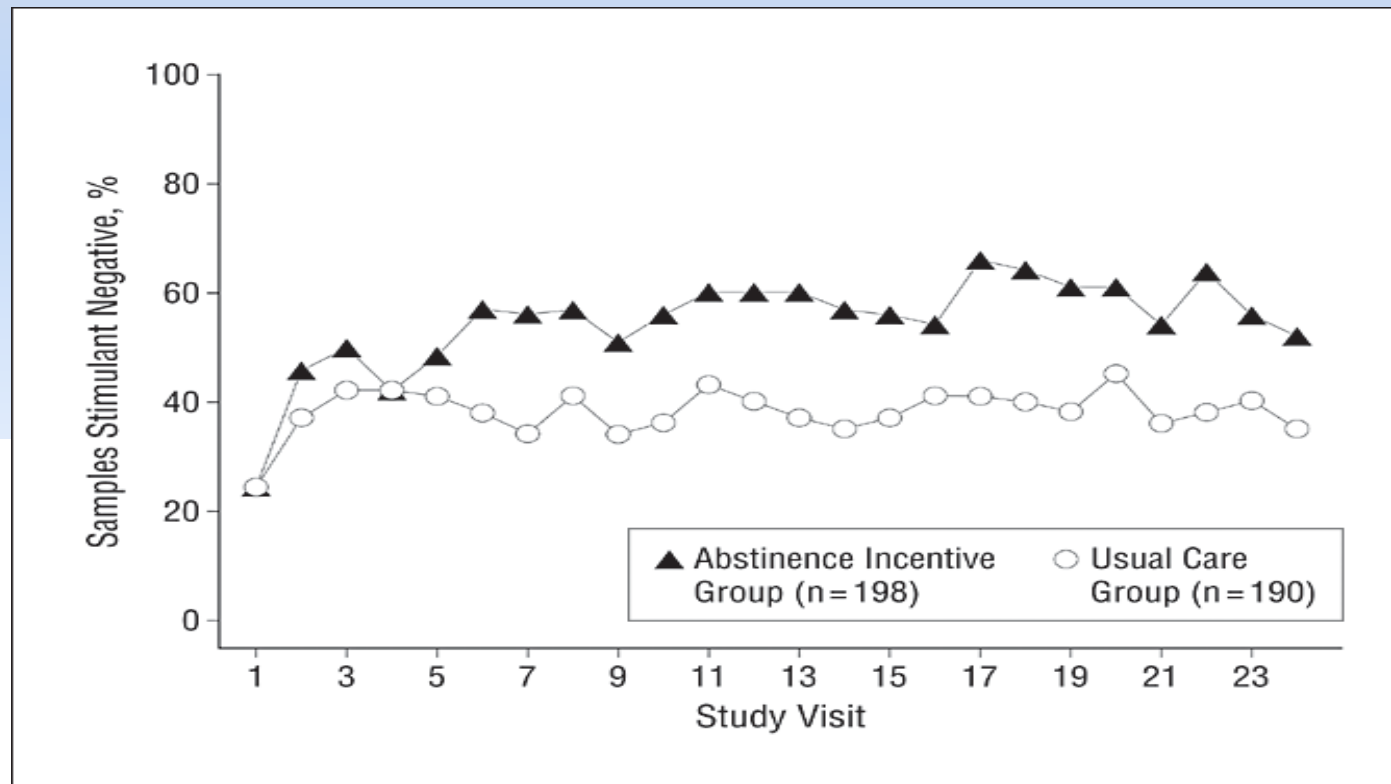
- CM in combination with other treatment
  - Increases cocaine abstinence
  - Improves treatment retention
  - May act synergistically with medications

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.

# Contingency Management



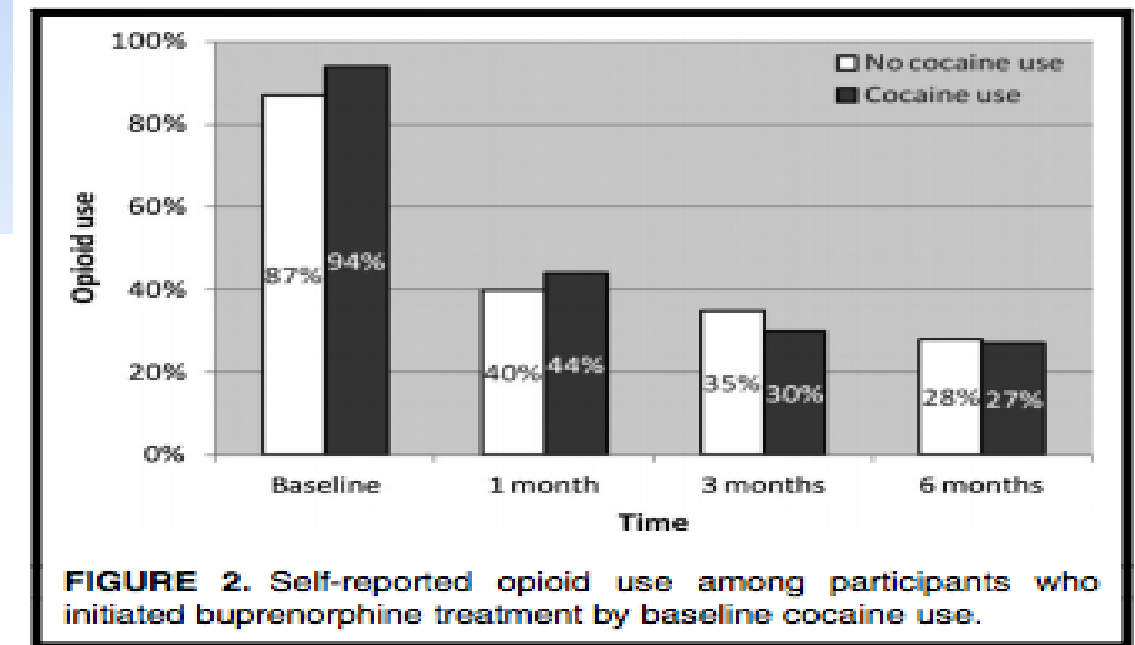
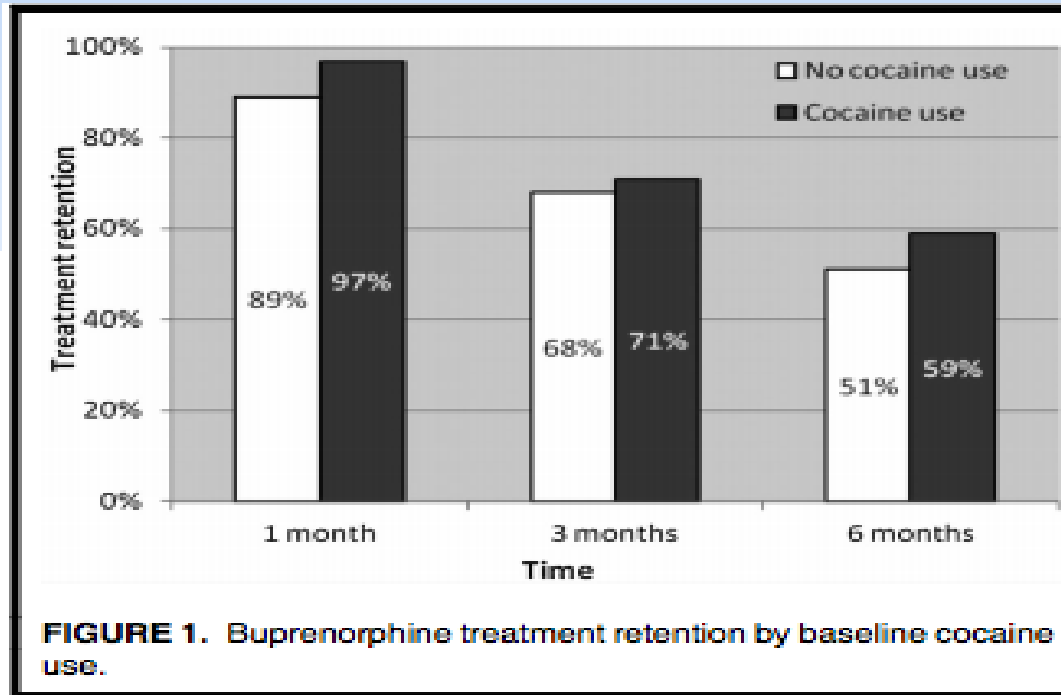
The mean percentage of submitted samples testing negative for target drugs (stimulants and alcohol) is shown for abstinence incentive and usual care participants at each of 24 study visits.

Average cost = \$1.46 per person/day





# Cocaine use at beginning of buprenorphine treatment



# What should we do with our stimulant-using patients?

- Ask and educate about medical complications, overdose
- Harm reduction – safer use techniques
- Recommend psychosocial treatment, especially contingency management
- Methylphenidate, topiramate and naltrexone have shown some promise, but no medications have shown consistent, convincing evidence for effectiveness
- Advocate, research and develop novel strategies in the treatment of stimulant use disorders

# 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

# Thanks!

Alex Walley, MD, MSc  
awalley@bu.edu



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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 cath if ST remain elevated after NTG and CCB (Level C)
      - Fibrinolytics if cath not available
- **Class Ila: 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  $\geq$  Risk**
  - Non-selective beta-blockers for bp > 150/100 or HR > 100 after NTG or CCB
- **Class III: Risk  $\geq$  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



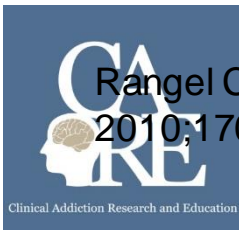
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# Beta-Blockers in Cocaine Chest Pain

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.



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# 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

# Does crack make people more violent than powder cocaine?

TABLE 2.  
Violent behaviors of adults with a lifetime history of crack cocaine or powder cocaine use.

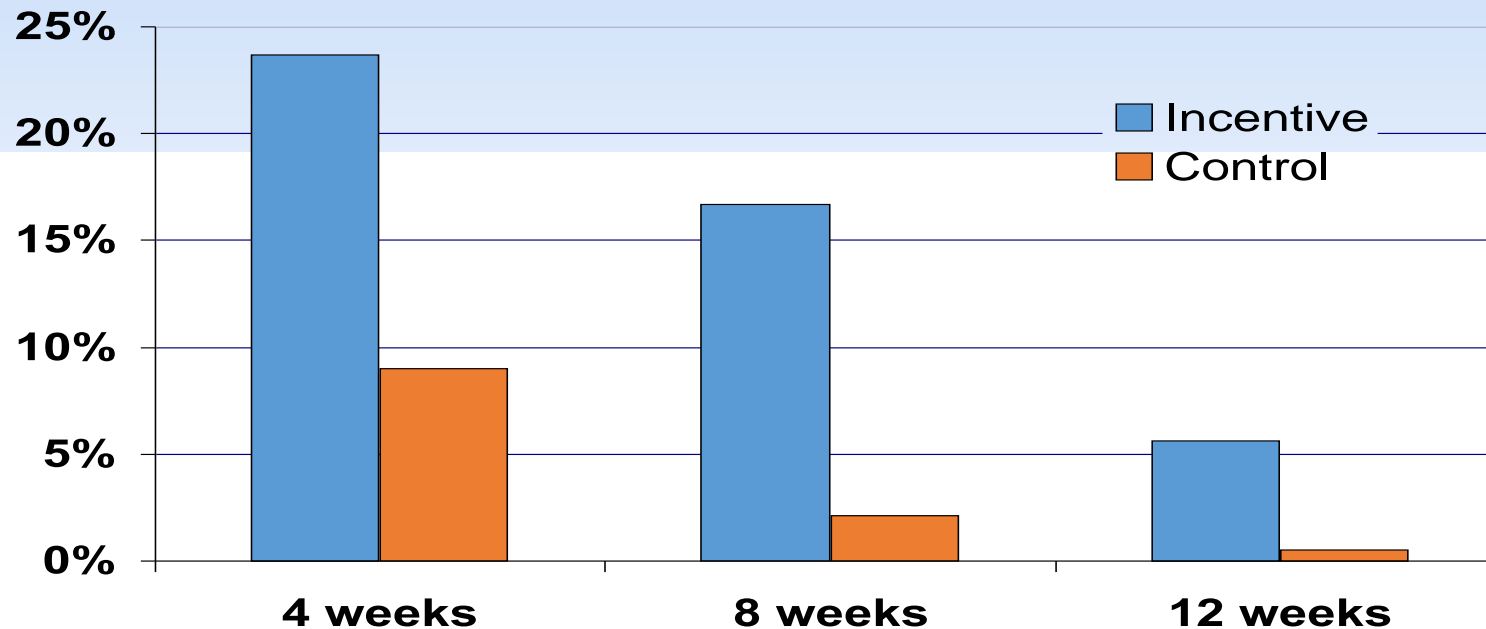
Violent behaviors	Powdered Cocaine % (95% CI) <sup>a</sup>	Crack Cocaine % (95% CI)	Odds Ratio <sup>b</sup> (unadjusted) (95% CI)	Odds Ratio <sup>c</sup> (adjusted) (95% CI)
Bully/push people	17.44(15.26–19.87)	23.27(19.01–28.17)	<b>1.44 (1.04–1.97)</b>	.82(.57–1.19)
Do things that could have easily hurt you/others	46.01(42.66–49.41)	55.26(49.02–61.33)	<b>1.45 (1.07–1.96)</b>	1.24(.84–1.84)
Rob/mug someone or snatch a purse	1.78(1.19–2.64)	4.55(2.66–7.71)	<b>2.63 (1.35–5.12)</b>	.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)	<b>2.40 (1.76–3.27)</b>	<b>1.55 (1.05–2.28)</b>
Use a weapon in a fight	8.92(7.48–10.60)	19.87(15.84–24.63)	<b>2.53 (1.83–3.50)</b>	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)	<b>1.66 (1.23–2.25)</b>	.79(.53–1.18)
Harass/threaten/blackmail someone	6.80(5.56–8.29)	12.27(9.20–16.20)	<b>1.92 (1.34–2.74)</b>	.93(.59–1.46)
Hurt an animal on purpose	5.59(4.44–7.02)	8.78(6.09–12.51)	<b>1.63 (1.04–2.54)</b>	.88(.55–1.40)

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



# 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

# 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

# Which statement is true about stimulants?

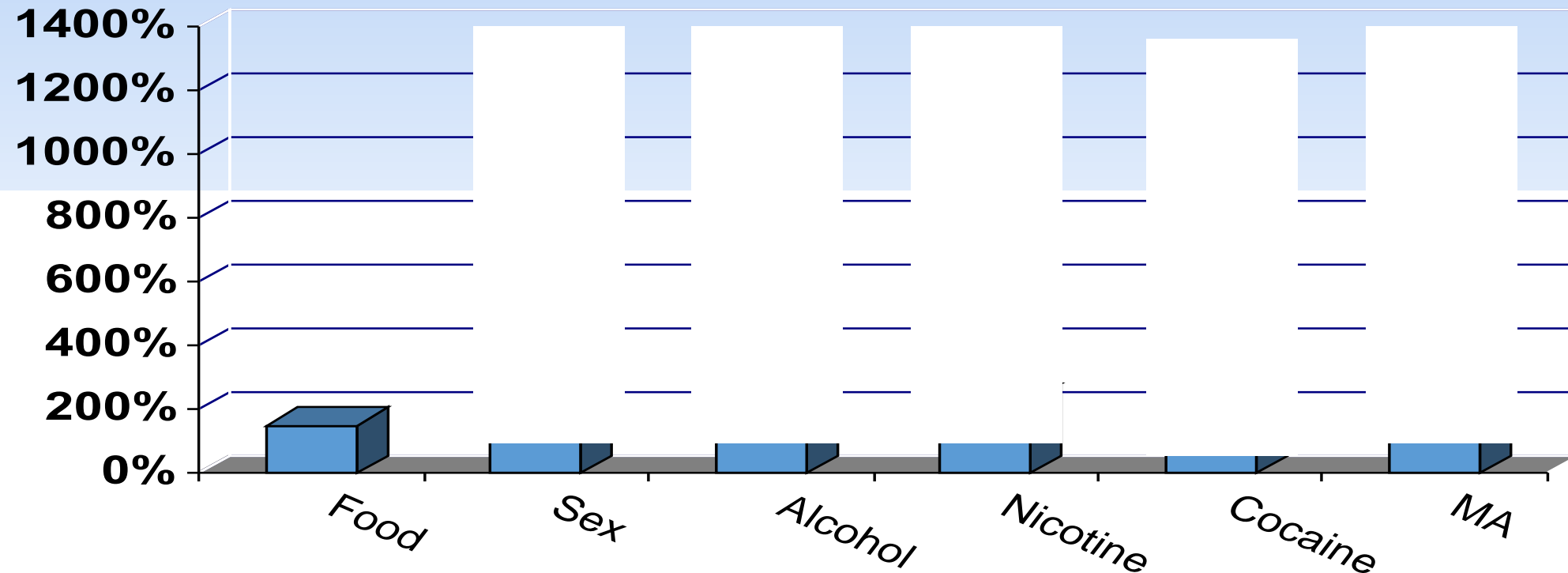
1. Methamphetamine is only used intravenously or smoked
2. Methamphetamine has a longer half-life than cocaine
3. Intravenous injection results in the fastest onset of action
4. Cocaine's peak concentration occurs in about 1 hour



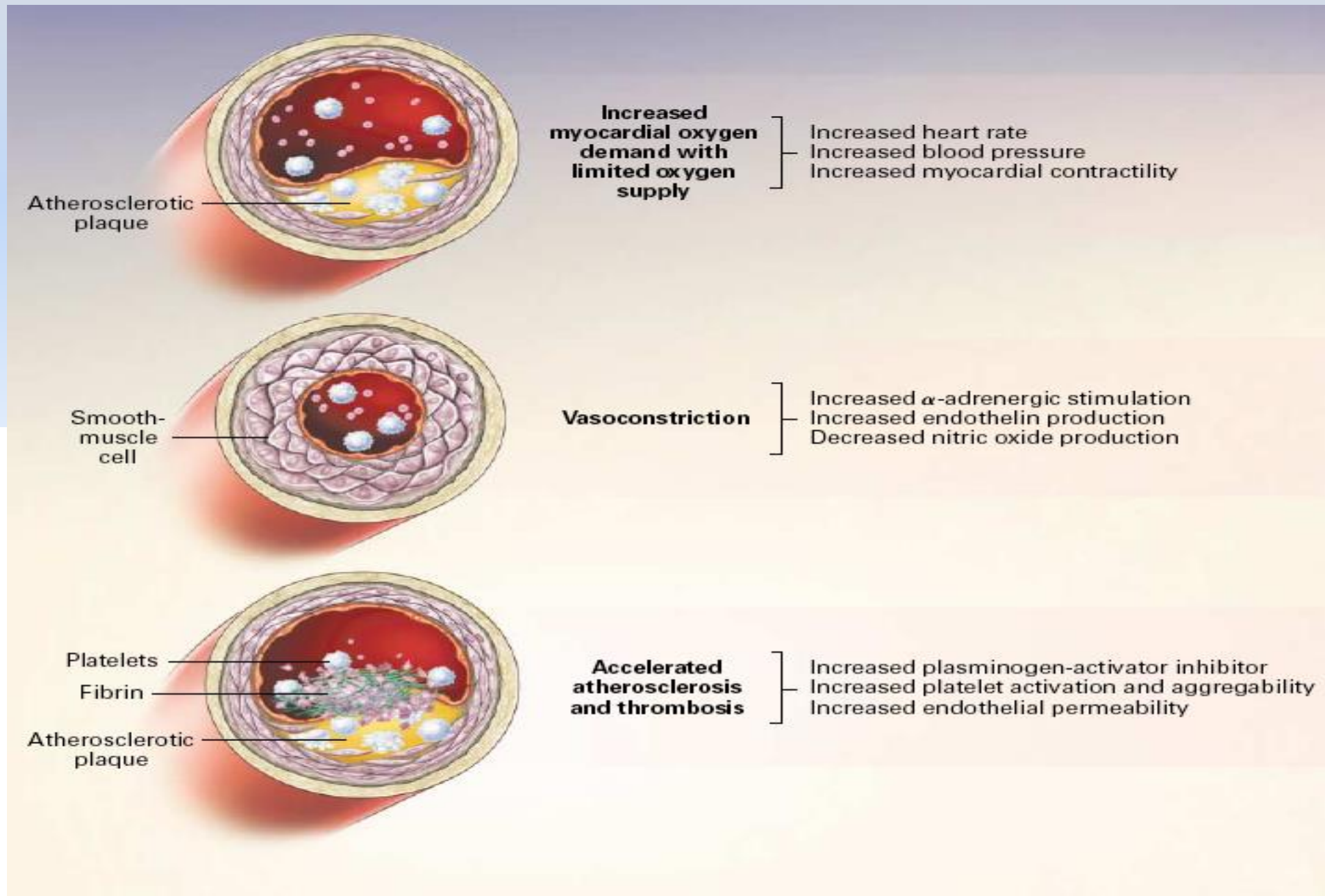
# 5 things about stimulants

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

# Dopamine release: nucleus accumbens

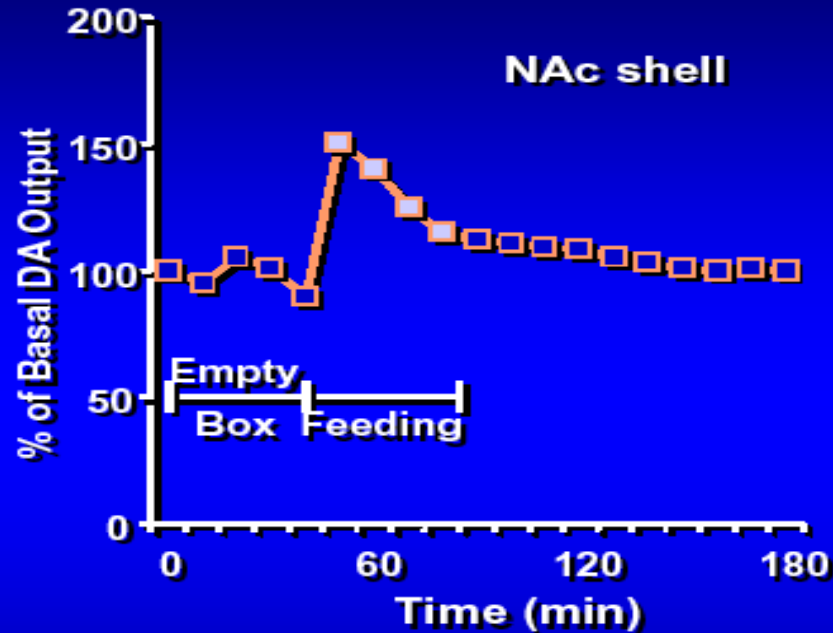


■ % basal dopamine in rat/ mouse NA after...



# Natural Rewards Elevate Dopamine

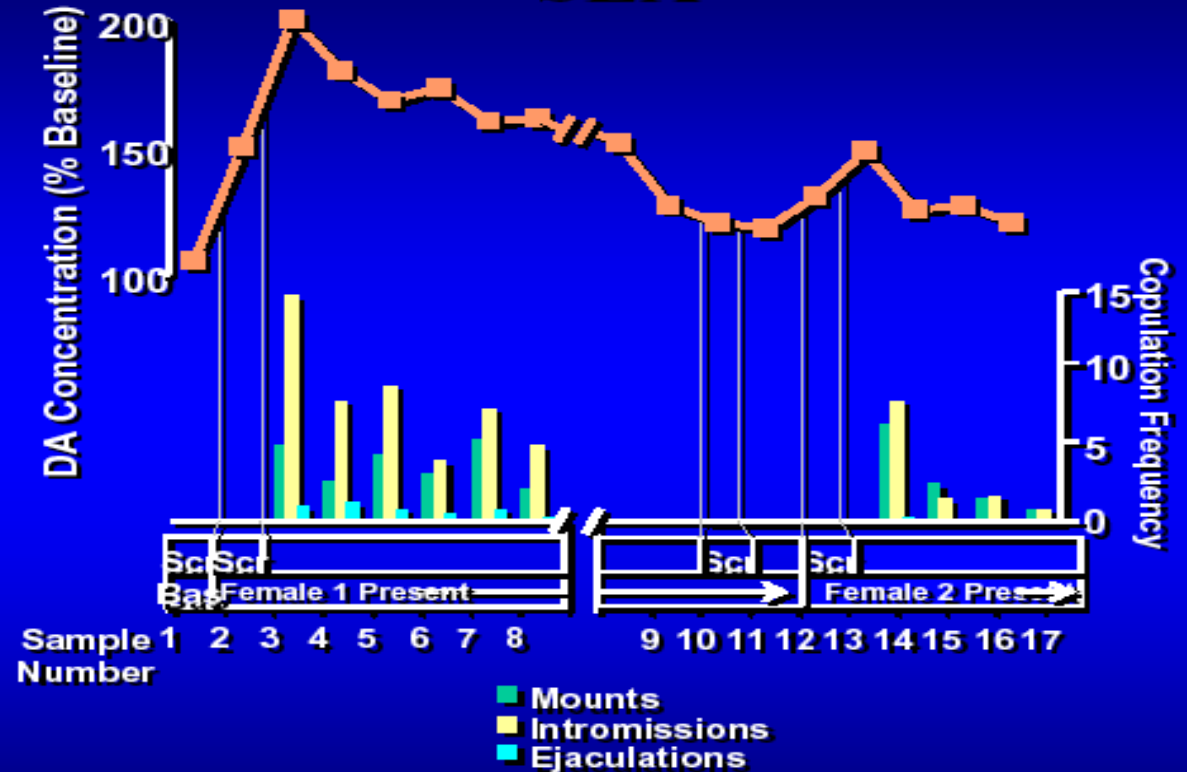
## FOOD



Source: Di Chiara et al.

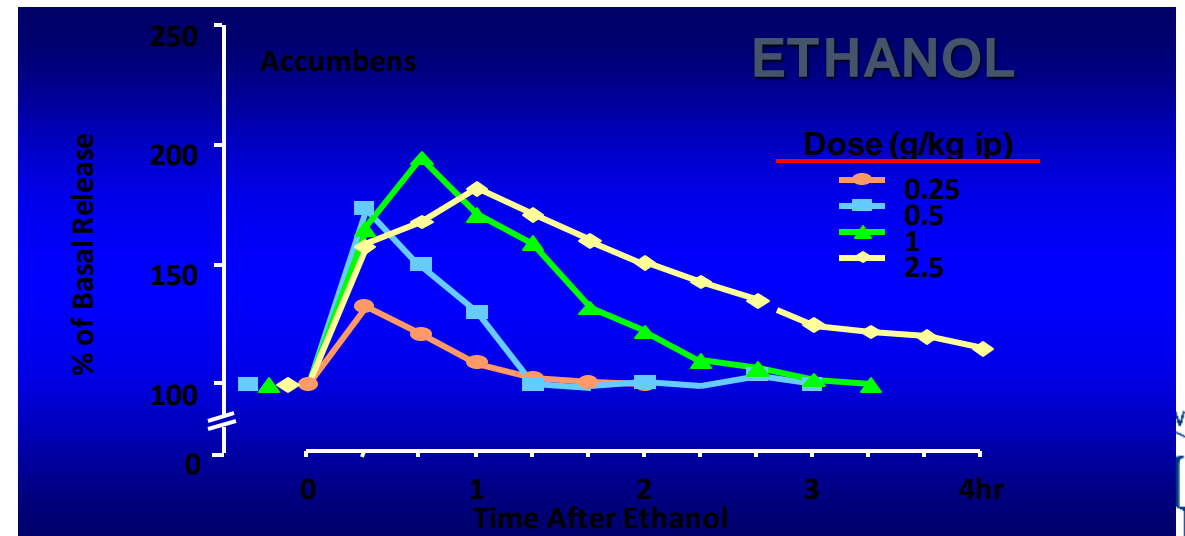
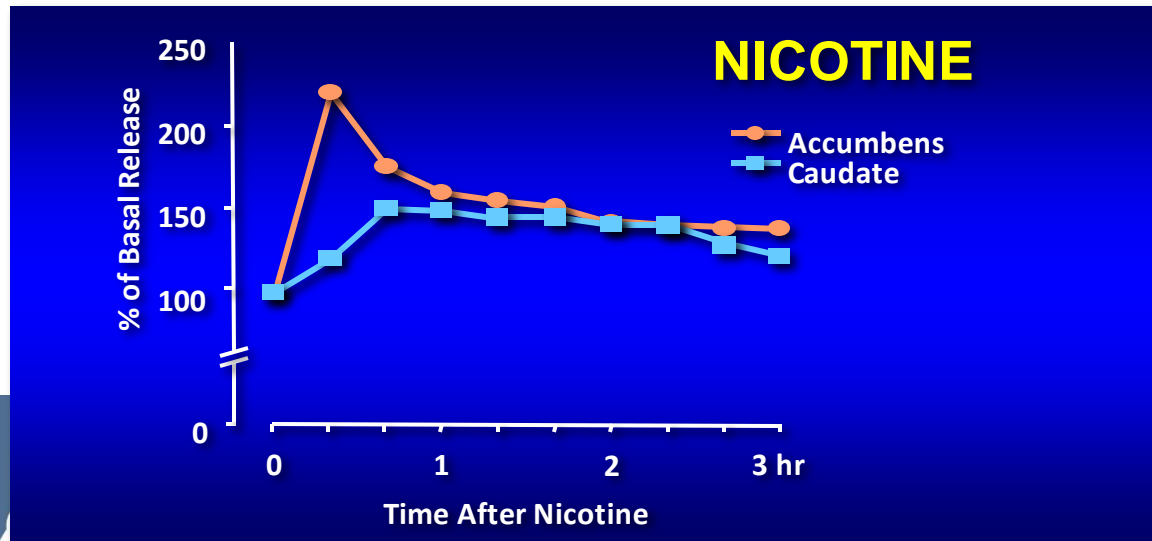
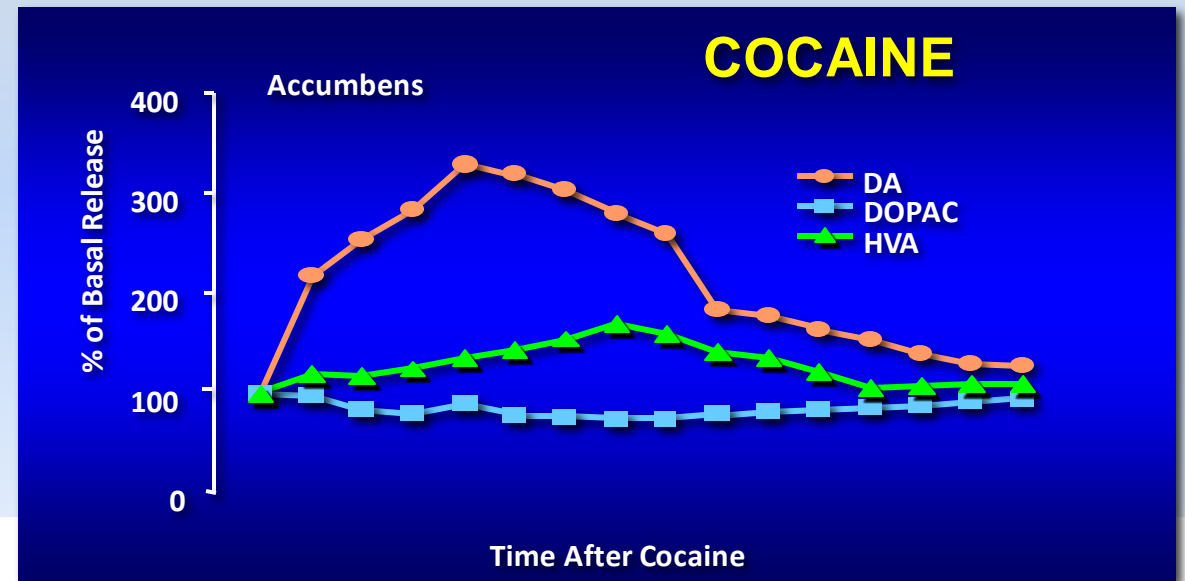
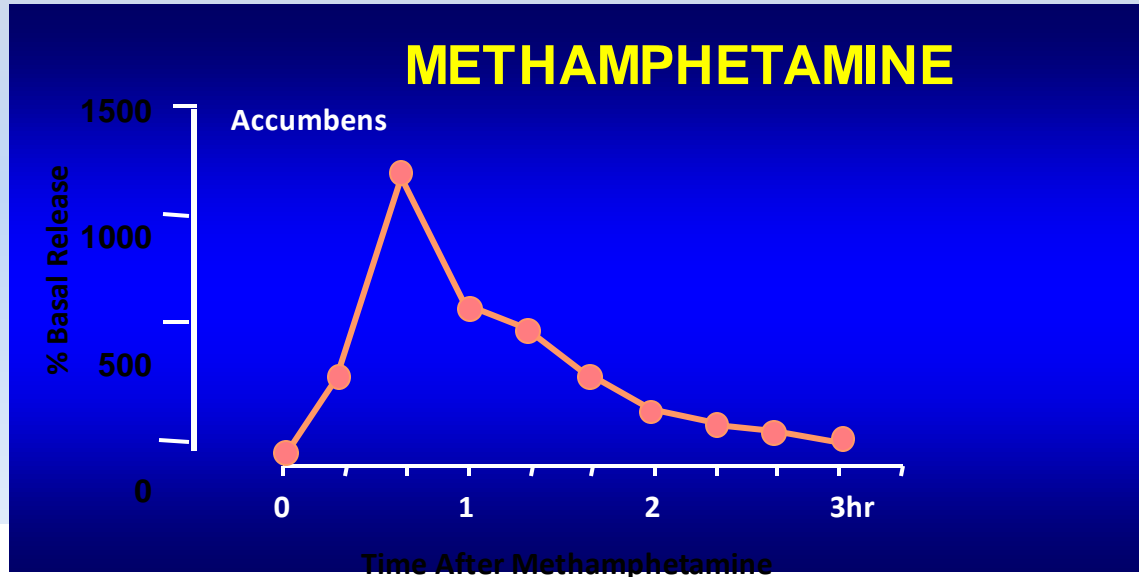
## Levels

## SEX



Source: Fiorino and Phillips

# 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



EXCEPTIONAL CARE. WITHOUT EXCEPTION.

# 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  $\geq 55\%$  and no wall motion abnormalities).

# Cardiomyopathy and Methamphetamine

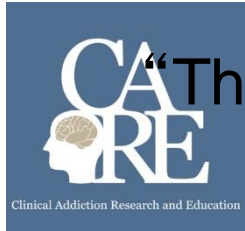
- 42% of cases and 20% of controls had ever used methamphetamine.
- Methamphetamine use was significantly more common in cases than in controls.
- OR in analyses adjusted for age, body mass index, and renal failure, 3.7

“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
- 4 Bottles Iodine Tincture 2%
- 2 Bottles of Hydrogen peroxide
- 3 20 Oz 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.”



# 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.

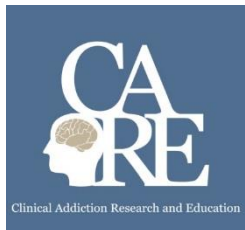
# MA and HIV

- 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



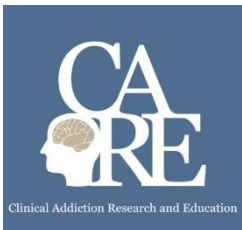
Swanson SM, et al. *J Trauma*. 2007;63(3):531.



EXCEPTIONAL CARE. WITHOUT EXCEPTION.

# 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.,  $\geq 1$  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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# Cognitive Behavioral Therapy

16 week RCT of cocaine-dependent methadone patients of:

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

30 patients per group

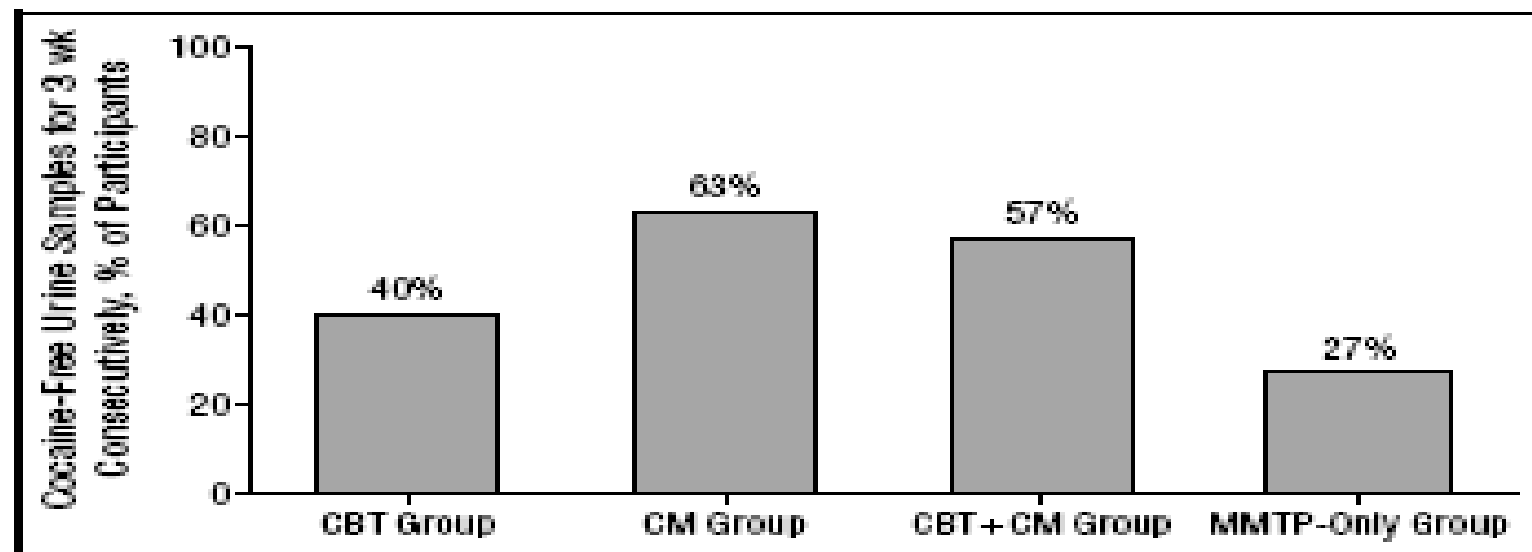


Rawson et al. Arch Gen Psychiatry. 2002



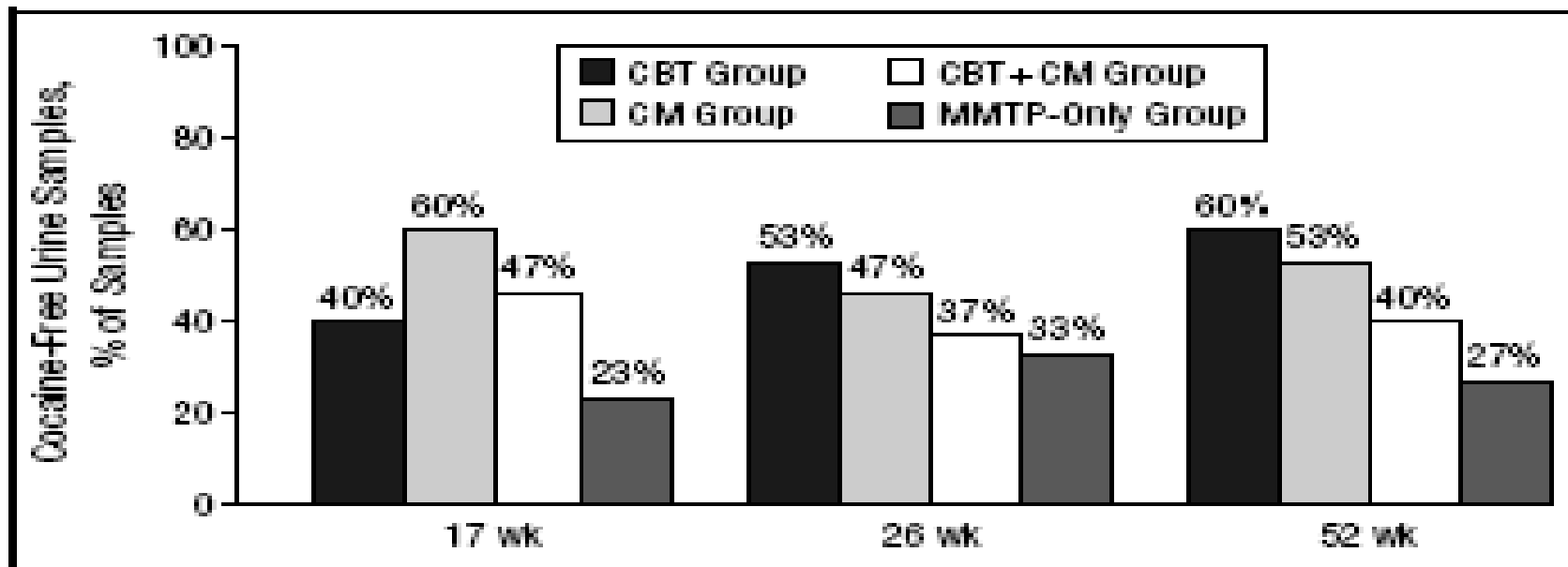
EXCEPTIONAL CARE. WITHOUT EXCEPTION.

# Cognitive Behavioral Therapy



**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.

# 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.