



Stimulants: Cocaine and Methamphetamine

CRIT/FIT/JFIT/AFIT program – April 2018

Alex Walley, MD, MSc

Learning objectives

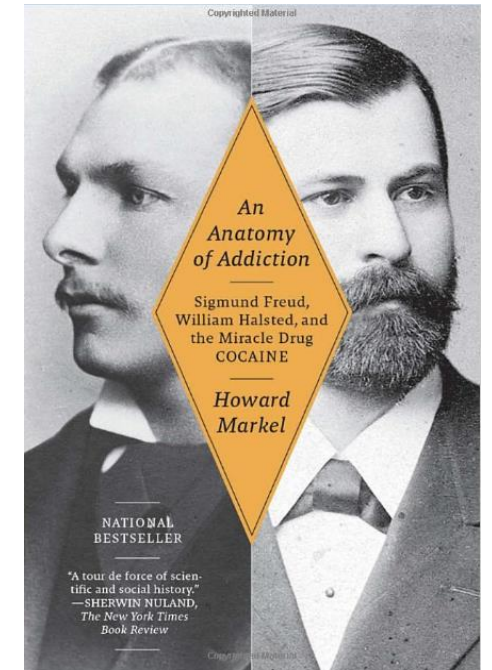
At the end of this session, participants will be able to:

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



- 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*



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*



73

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

THE SYMPTOMATOMIC AMENOR HAVE BEEN found of value, when administered, under the supervision of a physician, in an effort to liberate management of obesity. The chief action of these drugs is their stimulation of the production of adipose tissue in the adipose tissue of the body. In addition to relieving the appetite, Desoxyn imparts a feeling of well-being and increases mental and physical activity in such a way as to relieve the feeling of lassitude and boredom which is often the underlying factor in overeating.

SMALLER DOSEAGE, LONGER EFFECT. IT IS CON- siderably agreed that amphetamine, followed by meth- amphetamine, is more potent than amphetamine in the stimulation of adipose tissue. In a similar way, the amount of effect is more rapid, and the duration longer. Even exceeding doses recommended may produce the effects that characterize the benefits of amphetamine. With ordinary doses, there is no significant increase that has been observed.

Desoxyn should not be relied upon to induce weight reduction but should be used only under the direction of a physician in conjunction with the prescription of a general hygienic regimen and a special diet.

DOSEAGE, SIDE EFFECTS.—THE DOSE OF DESOXYN must be adjusted in accordance with the requirements and response of the individual patient. When the stimulant effect of the drug is desired, an adequate dosage is an average of 10 mg. per day. In the treatment of obesity, the stimulant effect of the drug should not be desired, in those cases. Dosage should be administered with meals or immediately after meals.

Usually the initial dose should be 2 to 4 mg. two to three times daily. Larger doses may be required in some cases, and should be adjusted accordingly. They may be continued as long as the desired beneficial results are obtained and no untoward effects. Individual oral doses in doses of 10 mg. per hour to produce sustained central stimulation. Moderate is not recommended after 4 p.m. or at night. Because of the possibility that the drug may interfere with sleep if the patient is unable to sleep at night, the symptoms may be relieved by the use of effective sedatives such as barbiturates.

OTHER INDICATIONS.—DEPRESSIVE STATES. Desoxyn Hydrochloride is indicated for the relief of depression of moderate to severe degree, and for the relief of depression of moderate to severe degree, and for the relief of depression of moderate to severe degree. This means can be used with great effectiveness in the treatment of depression.

Amphetamine salts have also been reported following the use of desoxyphenone hydrochloride, as well as to the treatment of postoperative depression, postoperative depression, and generally in conditions for which amphetamine salts are indicated.

In the treatment of depression, amphetamine salts are used in the treatment of depression, amphetamine salts are used in the treatment of depression, amphetamine salts are used in the treatment of depression.

INDICATIONS.—DESOXYN HYDROCHLORIDE is indicated for the relief of depression of moderate to severe degree, and for the relief of depression of moderate to severe degree. This means can be used with great effectiveness in the treatment of depression.

DESOXYN HYDROCHLORIDE is indicated for the relief of depression of moderate to severe degree, and for the relief of depression of moderate to severe degree. This means can be used with great effectiveness in the treatment of depression.

ONSET OF EFFECT.—ONSET OF EFFECT WITH DESOXYN occurs in from 20 minutes to one hour. The duration of action of a single dose of 10 mg. usually ranges from one to 12 hours, though in exceptional cases it may be longer. The duration of action of a single dose of 10 mg. usually ranges from one to 12 hours, though in exceptional cases it may be longer.

BLOOD PRESSURE, PULSE RATE AND RESPIRATORY rate usually are only slightly or temporarily affected, unless large doses exceeding 10 to 15 mg. daily are taken.

THE PARENTERAL ADMINISTRATION OF DESOXYN Hydrochloride is suggested for patients and conditions. Blood pressure during operative procedures, particularly during spinal or regional block anesthesia, for use in the treatment of obesity, or in the treatment of obesity, or in the treatment of obesity.

TOLERANCE NOT DEVELOPED, WHILE THE DRUG is not habit forming in the case of the vast majority of patients. Tolerance is not developed, while the drug is not habit forming in the case of the vast majority of patients.

1957

31

WEIGHT REDUCTION WITHOUT JITTERS

AMBAR™ TABLETS AND EXTENTABS™

Weight Reduction: Obese patients may resist weight reduction because they fear losing the emotional security involved in overeating. **AMBAR** Tablets or Tablets help them hold the diet line by giving them a more alert, brighter outlook. **AMBAR** adds incentive to weight reduction, gives the patient a better chance of holding off the disabling effects of continued overweight.

Without Jitters: Methamphetamine, a more potent CNS stimulant than amphetamine, but producing less cardiovascular effect, is combined in **AMBAR** with phenobarbital. The combination subdues CNS effects just enough to protect the patient from overstimulation. Result: mood elevation with no undesirable excitation—weight reduction without jitters.

AMBAR Tablets: 10 to 12 hours of appetite suppression in the controlled release, controlled release tablets.
Methamphetamine hydrochloride . . . 30.0 mg.
Phenobarbital 15 gr. 64.8 mg.

AMBAR Tablets for controlled dosage of lower strength tablets.
Methamphetamine hydrochloride . . . 15.0 mg.
Phenobarbital 7 1/2 gr. 32.4 mg.

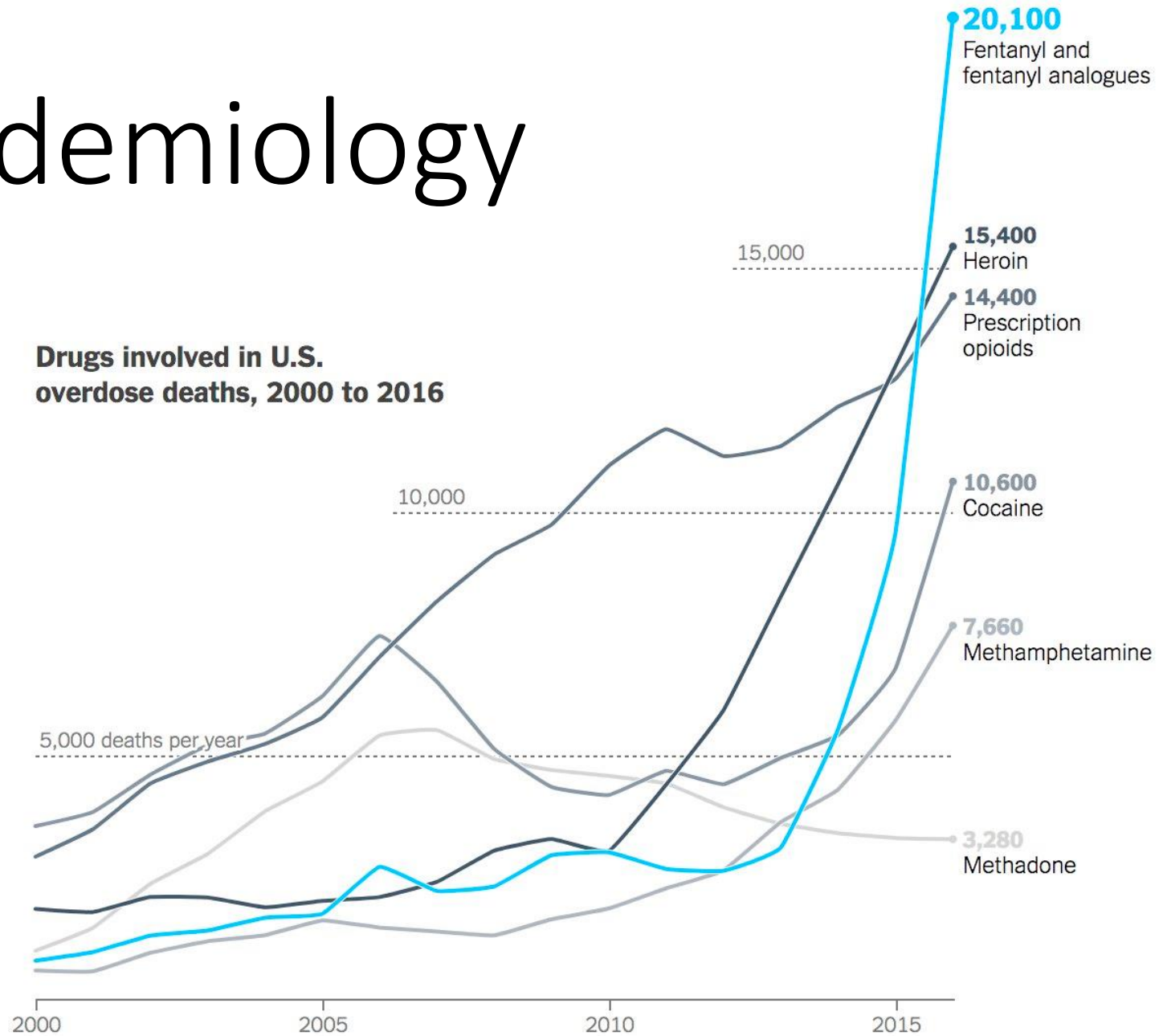
A. H. ROBINS CO., INC.
Rushmore 20, Virginia
Robins Pharmacy
of Mark House 1878.

1959



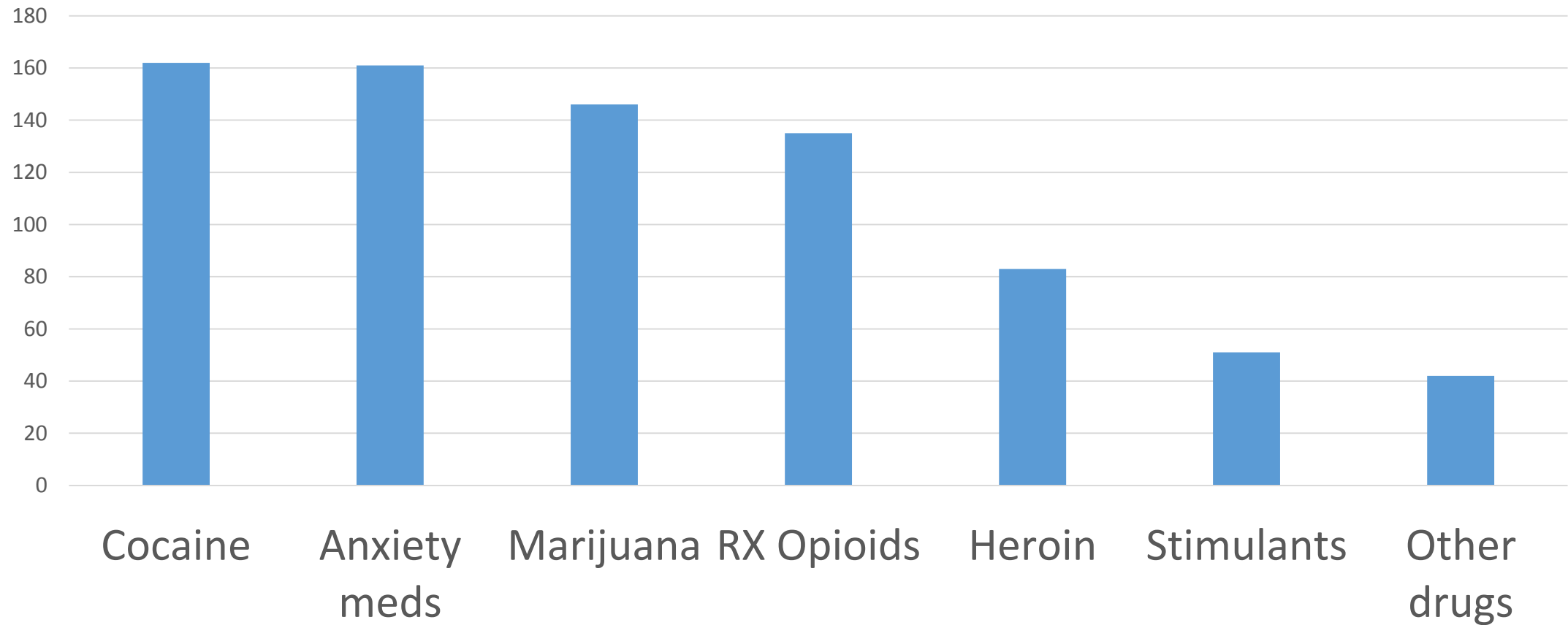
Epidemiology

Drugs involved in U.S. overdose deaths, 2000 to 2016



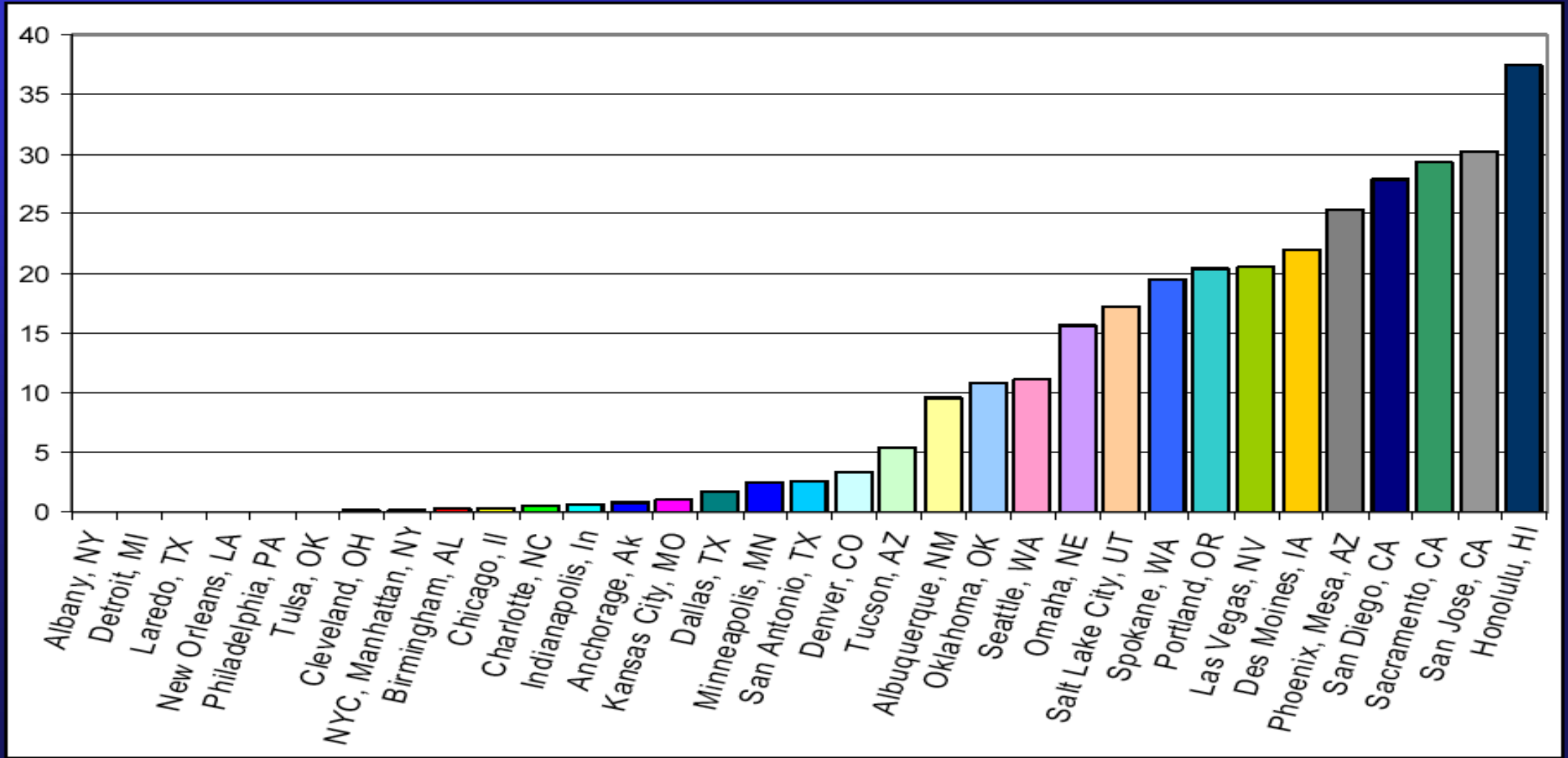
[Katz, J. The First Count of Fentanyl Deaths in 2016: Up 540% in Three Years. NYT – The UpShot 9/2/2017.](#)

2011 Emergency Department visits per 100,000 people



Drug Abuse Warning Network 2011 Report:
www.samhsa.gov/data/sites/default/files/DAWN127/DAWN127/sr127-DAWN-highlights.htm

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



Multiple Fentanyl Overdoses — New Haven, Connecticut, June 23, 2016

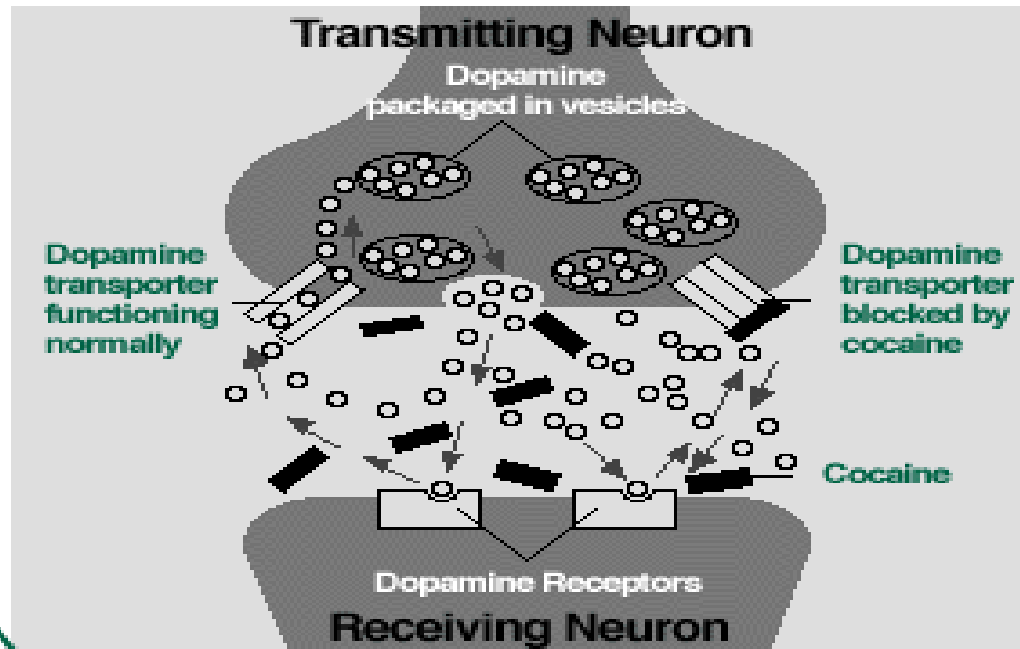
Anthony J. Tomassoni, MD¹; Kathryn F. Hawk, MD¹; Karen Jubanyik, MD¹; Daniel P. Noguee, MD¹; Thomas Durant, MD²; Kara L. Lynch, PhD³; Rushaben Patel, PharmD²; David Dinh, PharmD²; Andrew Ulrich, MD¹; Gail D'Onofrio, MD¹

Over 8 hours at the ED of Yale Hospital, white powder advertised as cocaine resulted in 12 patients for signs of opioid overdose, presumed from snorting

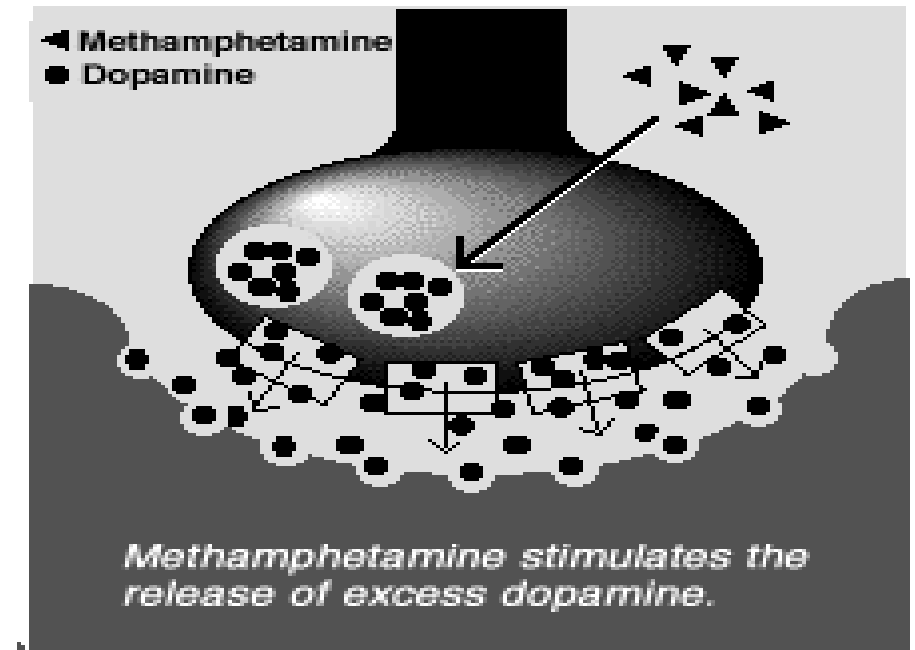
- 9 admitted, 4 to ICU, 3 intubated, 1 on naloxone gtt, 3 died
- High doses of naloxone required: 4mg and higher
- Drug sample tested had 6.6% fentanyl by weight and trace amounts of cocaine + inert adulterant

Stimulant Effects

Cocaine



Methamphetamine



PK: Cocaine

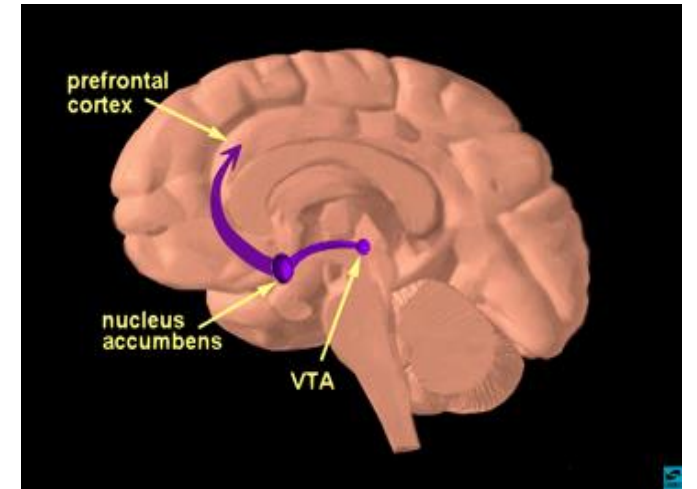
	IV	Smoked	Snorted
Time to effect	10-60sec	3-5sec	1-5min
Peak concent.	3-5min	1-3min	15-20min
Half-life	20-60min	5-15min	60-90min

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

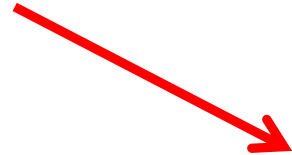
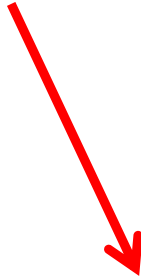
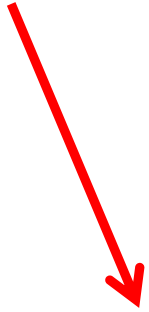
PK: Methamphetamine

	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

Why do people use stimulants?



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



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

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

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,

Dopamine agonists for the treatment of cocaine dependence (Review)

Antipsychotic medications for cocaine dependence (Review)

This review found mixed results. Psychostimulants improved cocaine abstinence compared to placebo in some analyses but did not improve treatment retention. Since treatment dropout was high, we cannot rule out the possibility that these results were influenced by attrition bias. Existing evidence does not clearly demonstrate the efficacy of any pharmacological treatment for cocaine dependence, but substitution treatment with psychostimulants appears promising and deserves further investigation.

Sustained-release dexamfetamine in the treatment of chronic cocaine-dependent patients on heroin-assisted treatment: *Lancet* 2016; 387: 2226–34

a randomised, double-blind, placebo-controlled trial

Published **Online**

March 22, 2016

[http://dx.doi.org/10.1016/S0140-6736\(16\)00205-1](http://dx.doi.org/10.1016/S0140-6736(16)00205-1)

Mascha Nuijten, Peter Blanken, Ben van de Wetering, Bastiaan Nuijen, Wim van den Brink, Vincent M Hendriks

- 73 Dutch patients with co-occurring heroin and cocaine UD on heroin/methadone maintenance and unable to stop cocaine despite 2 efforts
- Received dexamphetamine SR 60mg once daily observed vs. placebo
- At 12 weeks
 - 45 versus 61 days self-reported days of cocaine use
 - 21% versus 8% with at least one cocaine-negative urine test in last 4 weeks
 - No significant differences in craving, use of other substances, or criminality

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 Training (CRAFT)
- 12-step facilitation
- Contingency management

All treatments require adherence

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

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

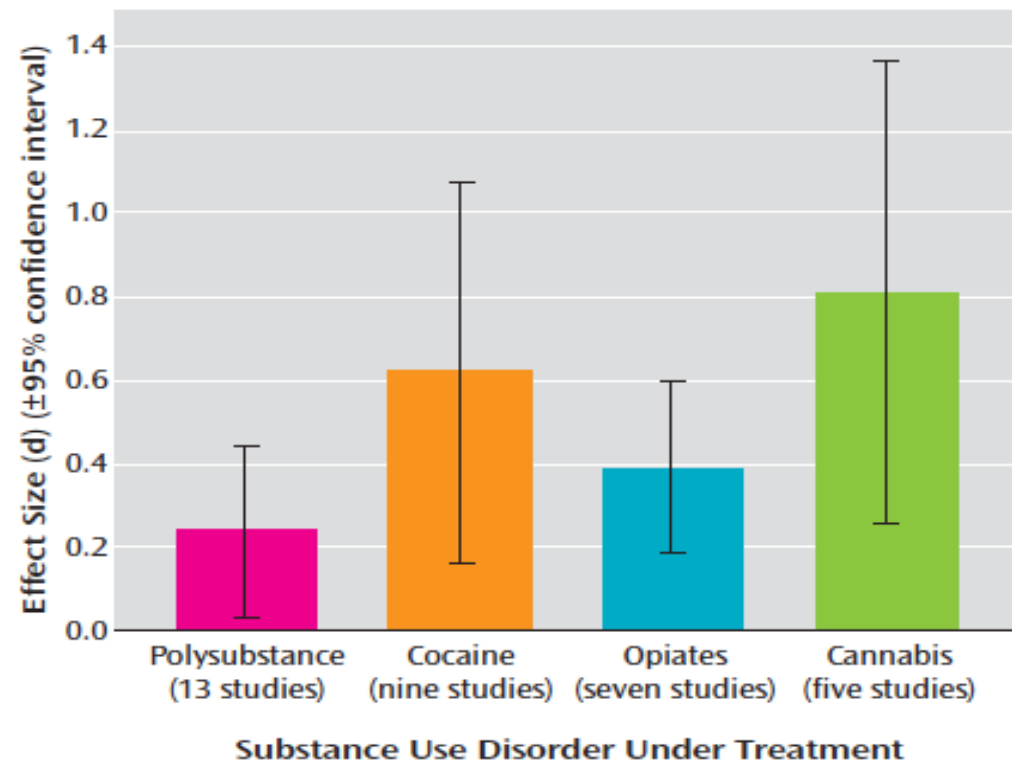
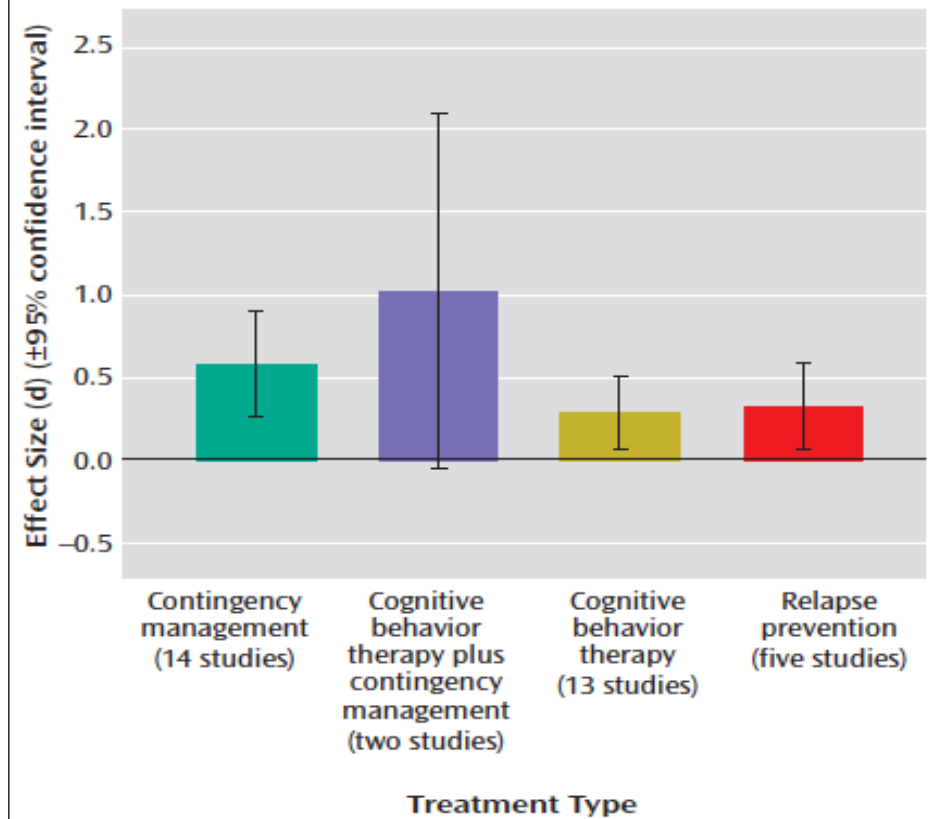


FIGURE 2. Mean Effect Sizes Across Treatment Types



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

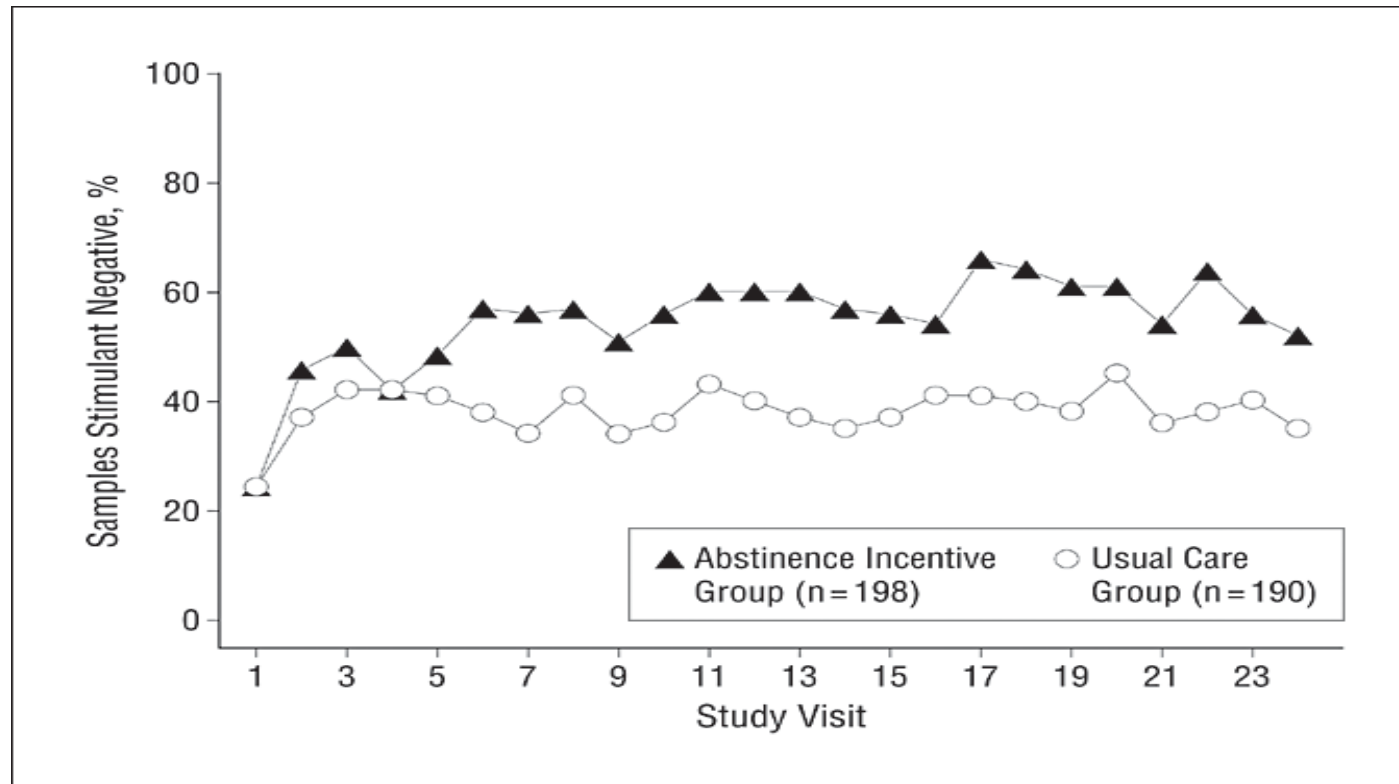
RCT in 6 community methadone programs of CM among stimulant users

- 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

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

How can we help our stimulant-using patients?

- Ask and educate about medical complications, overdose
- Harm reduction – safer use techniques
- Recommend psychosocial treatment, especially contingency management
- Stimulants have shown some promise for cocaine, 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

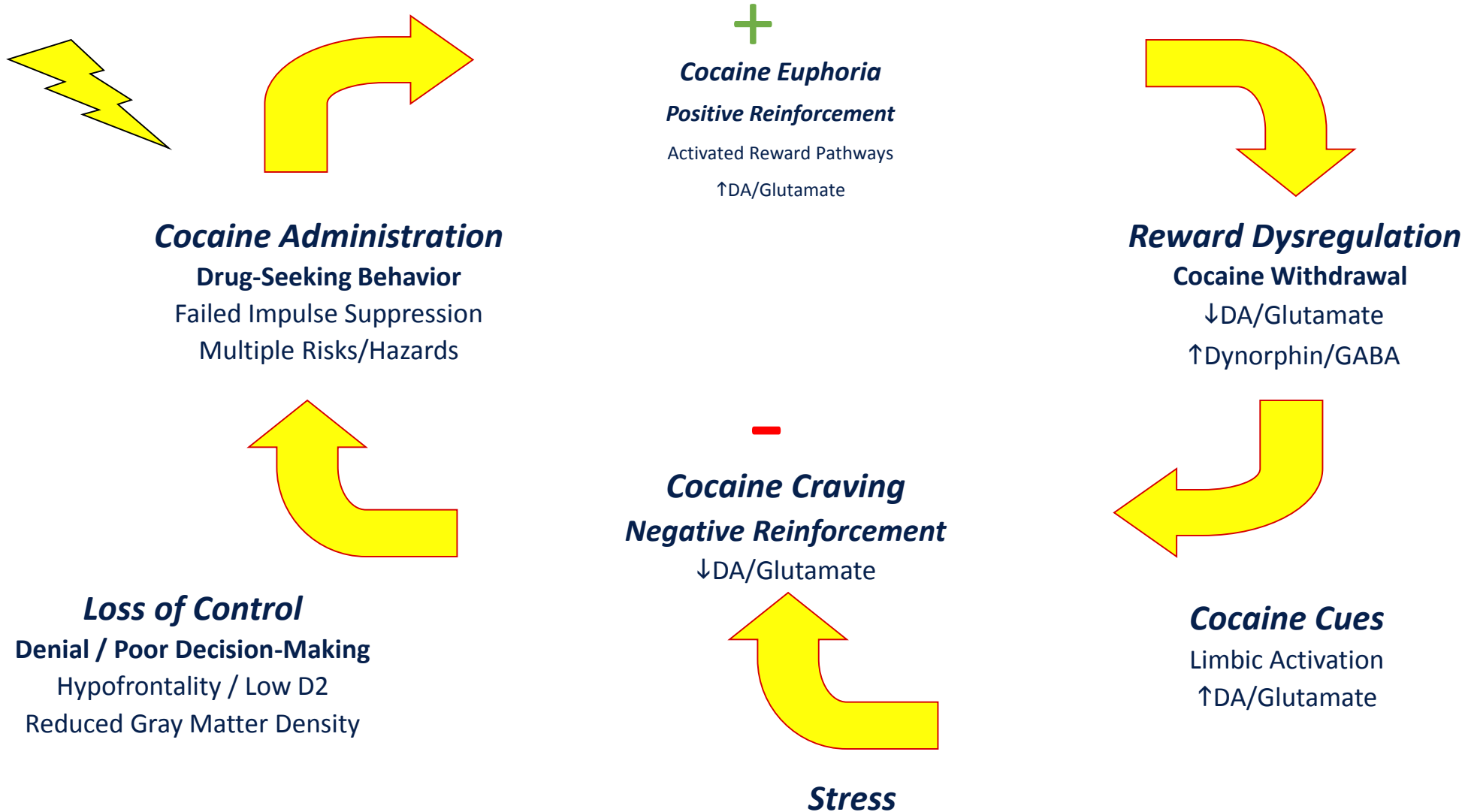
Thanks!

Alex Walley, MD, MSc

awalley@bu.edu

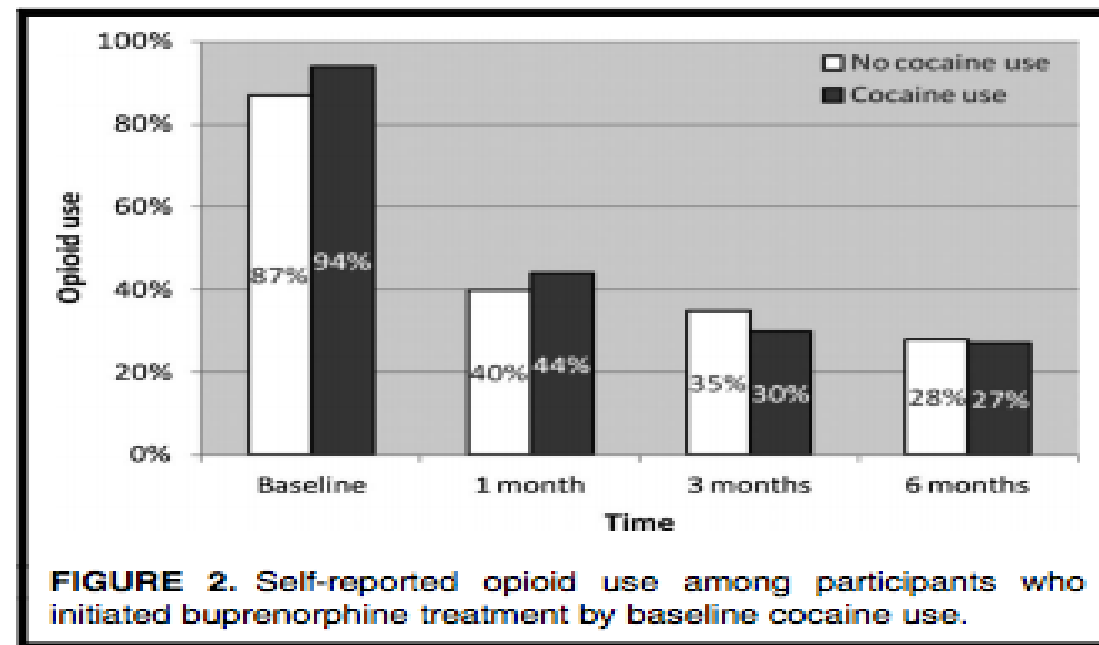
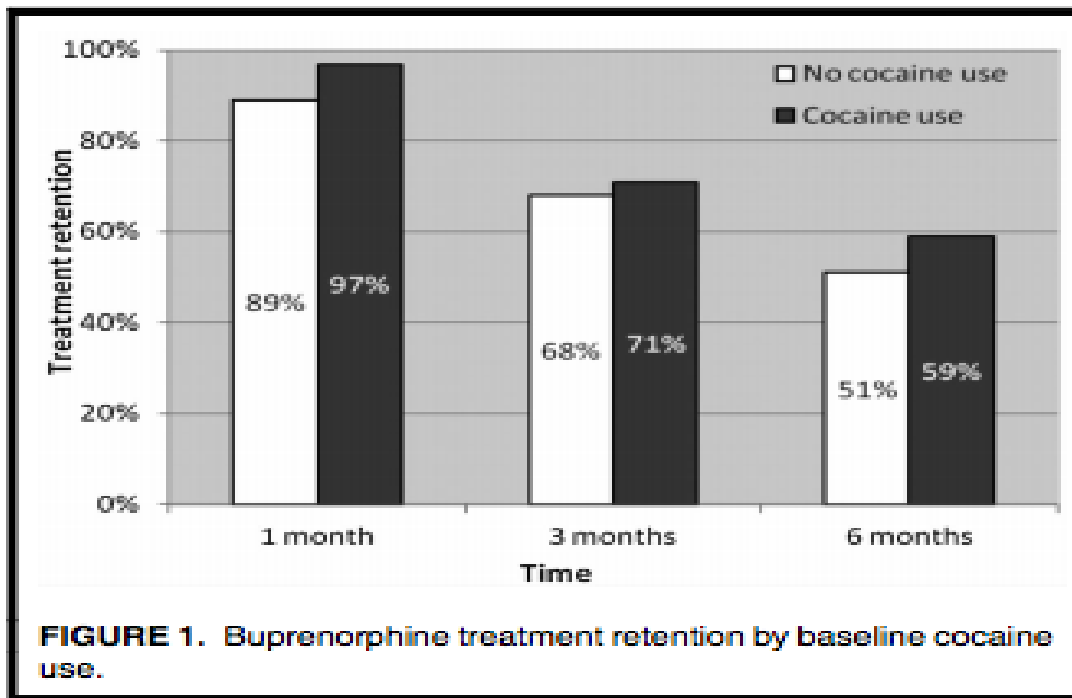
Dynamic Cycle of Stimulant Addiction

Cocaine

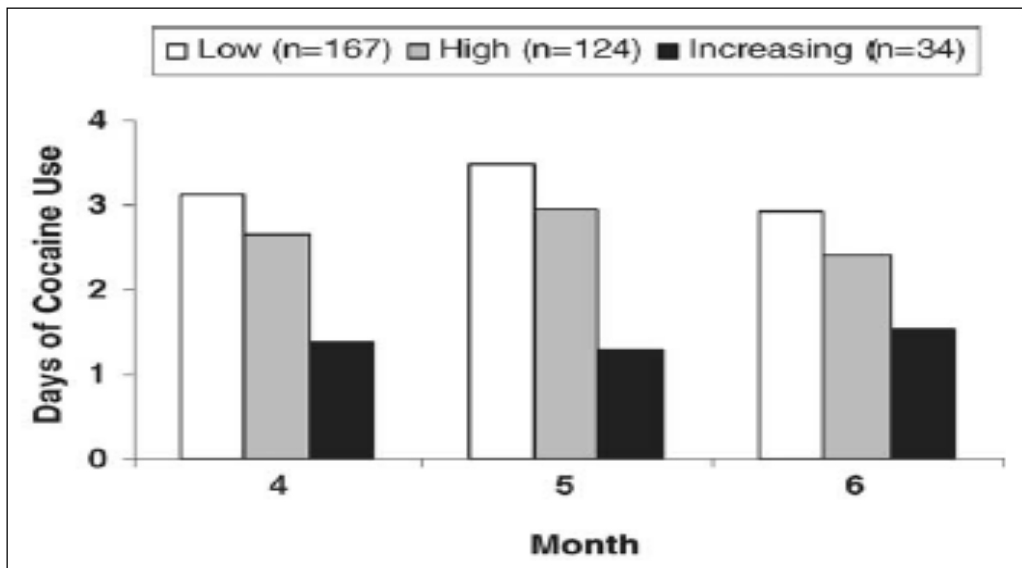


Slide from Nadia Fairbairn

Cocaine use at beginning of buprenorphine treatment



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



- 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

SCIENCE @ DIRECT®

Drug and Alcohol Dependence 77 (2005) 177–184



www.elsevier.com/locate/drugalcddep

The effect of 12-step self-help group attendance and participation on drug use outcomes among cocaine-dependent patients[☆]

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

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 γ -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 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 Elkashef¹, Roberta Kahn¹, Elmer Yu², Erin Iturriaga¹, Shou-Hua Li¹, Ann Anderson¹, Nora Chiang¹, Nassima Ait-Daoud³, David Weiss⁴, Frances McSherry⁴, Tracey Serpi⁴, Richard Rawson⁵, Mark Hrymoc⁵, Dennis Weis⁶, Michael McCann⁷, Tony Pham⁷, Christopher Stock⁸, Ruth Dickinson⁸, Jan Campbell⁹, Charles Gorodetzky⁹, William Haning¹⁰, Barry Carlton¹⁰, Joseph Mawhinney¹¹, Ming D. Li³ & Bankole A. Johnson³

National Institute on Drug Abuse, National Institutes of Health, Bethesda, MD, USA,¹ Veterans Administration Medical Center, Philadelphia, PA, USA,² Department of Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville, VA, USA,³ Department of Veterans Affairs Cooperative Studies Program Coordinating Center, Perry Point, MD, USA,⁴ UCLA Integrated Substance Abuse Programs, Los Angeles, CA, USA,⁵ Lutheran Hospital Office of Research, Des Moines, IA, USA,⁶ Matrix Institute on Addictions, Costa Mesa, CA, USA,⁷ Department of Veterans Affairs, Salt Lake City Health Care System, Salt Lake City, UT, USA,⁸ Department of Psychiatry, University of Missouri, Kansas City, MO, USA,⁹ Pacific Addiction Research Center, Honolulu, HI, USA¹⁰ and South Bay Treatment Center, San Diego, CA, USA¹¹

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.

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 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 \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

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.

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?

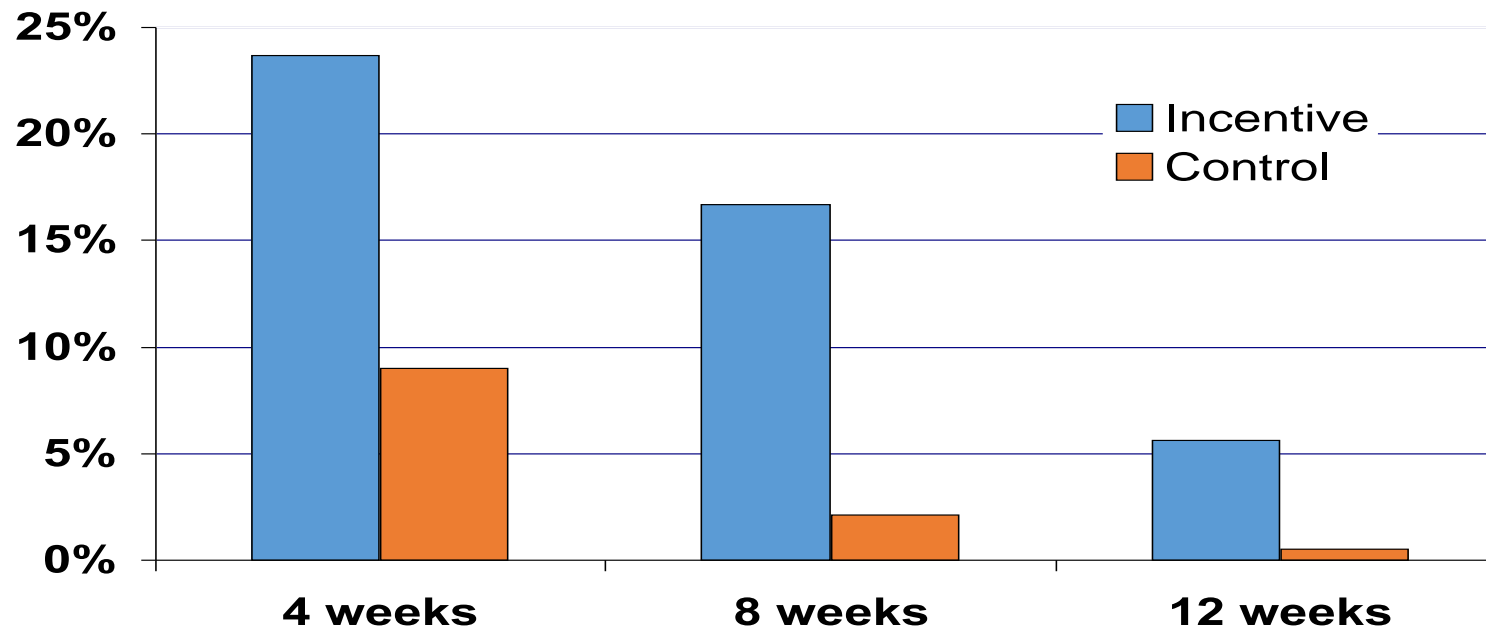
TABLE 2.
Violent behaviors of adults with a lifetime history of crack cocaine or powder cocaine use.

Violent behaviors	Powdered Cocaine % (95% CI) ^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: ^aCI: confidence interval, ^bOR: odds ratio, ^cOdds 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

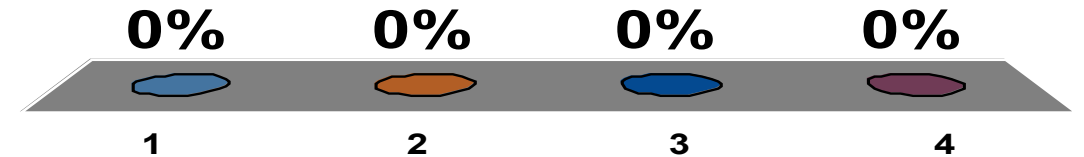
Pierce et al. Arch Gen Psychiatry. 2006;63:201-208.

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?

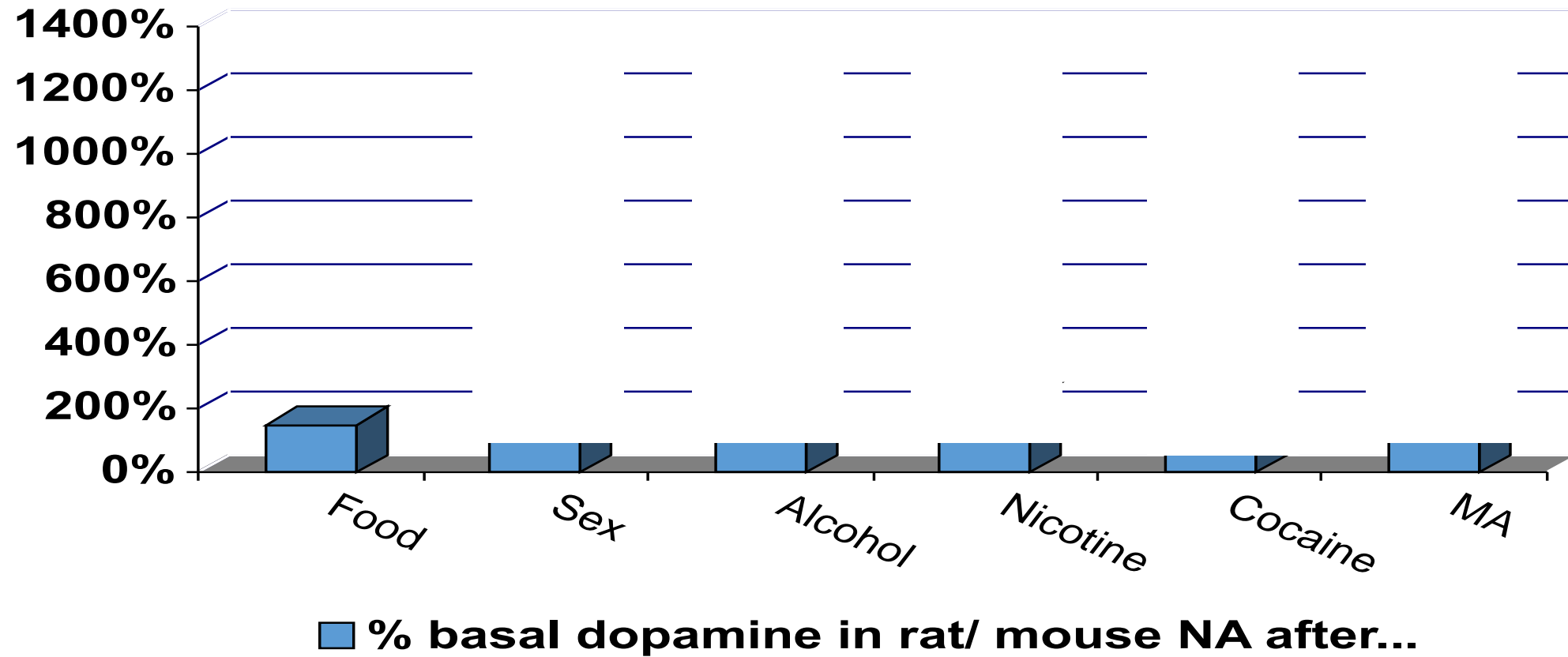
1. Methamphetamine is only used intravenously or smoked
2. Methamphetamine has a longer half-life than cocaine
3. Intravenous injection results in the fastest onset of action
4. Cocaine's peak concentration occurs in about 1 hour

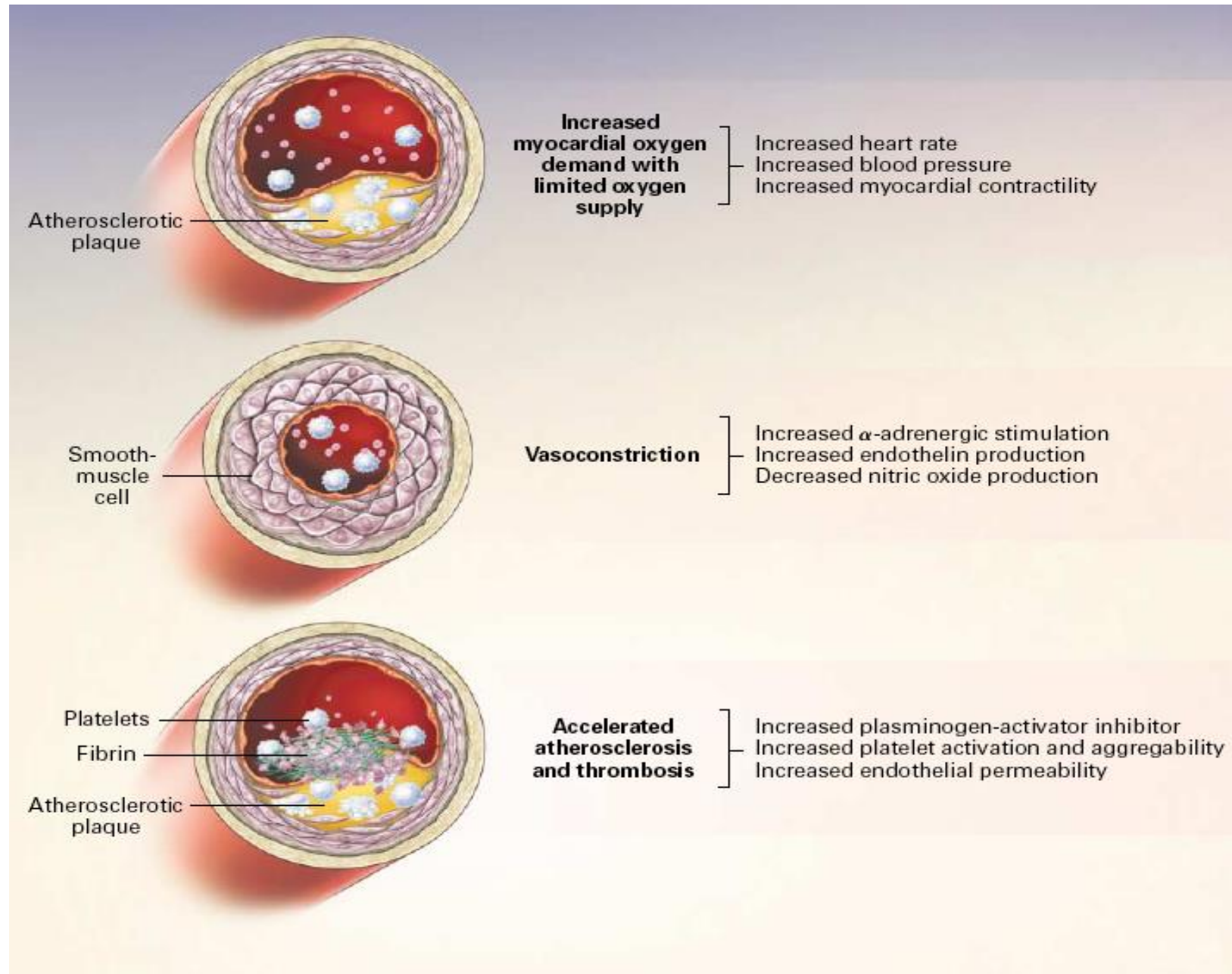


5 things about stimulants

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

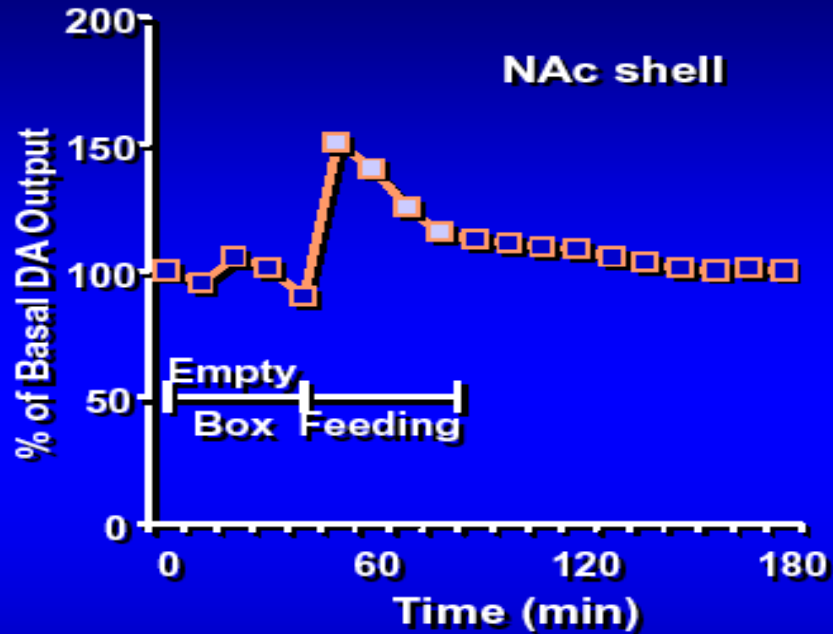
Dopamine release: nucleus accumbens





Natural Rewards Elevate Dopamine

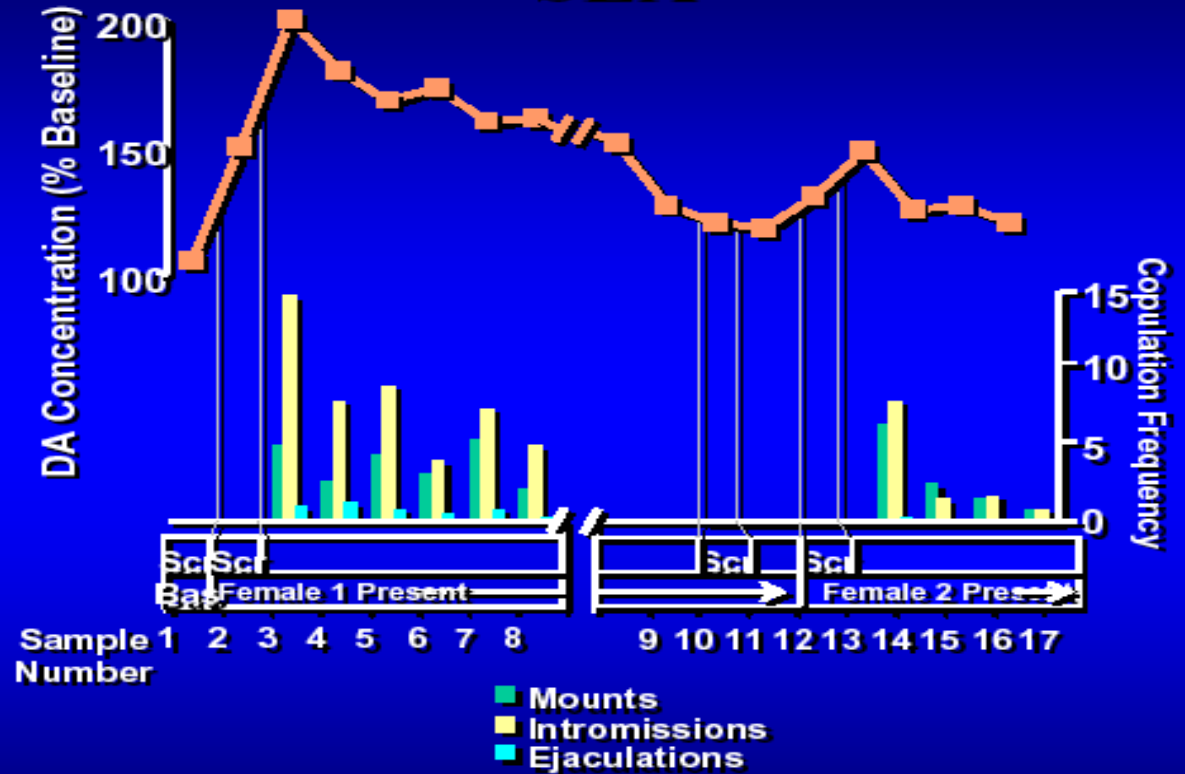
FOOD



Source: Di Chiara et al.

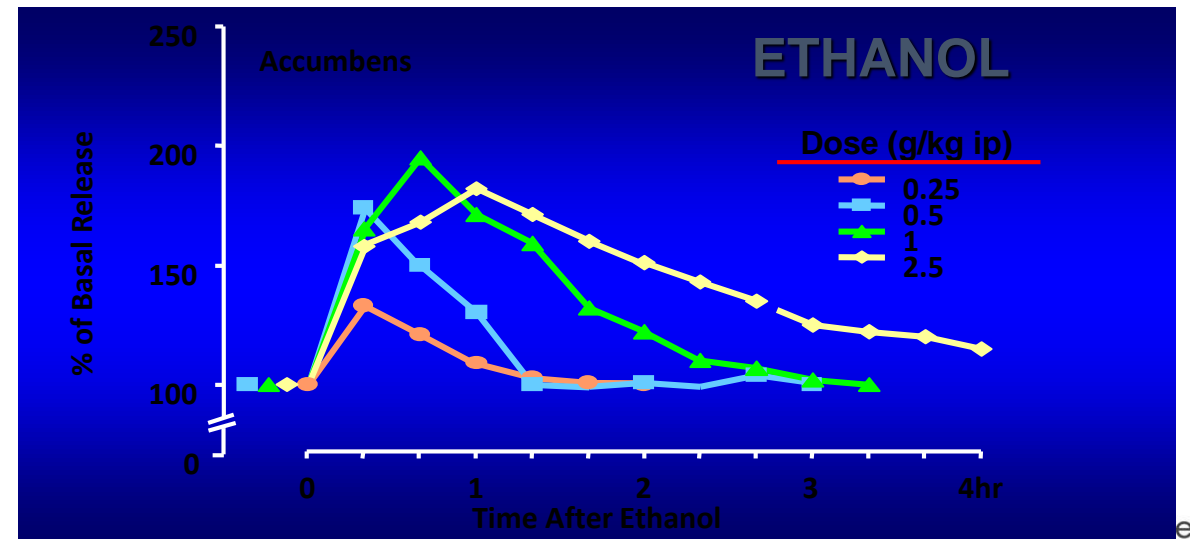
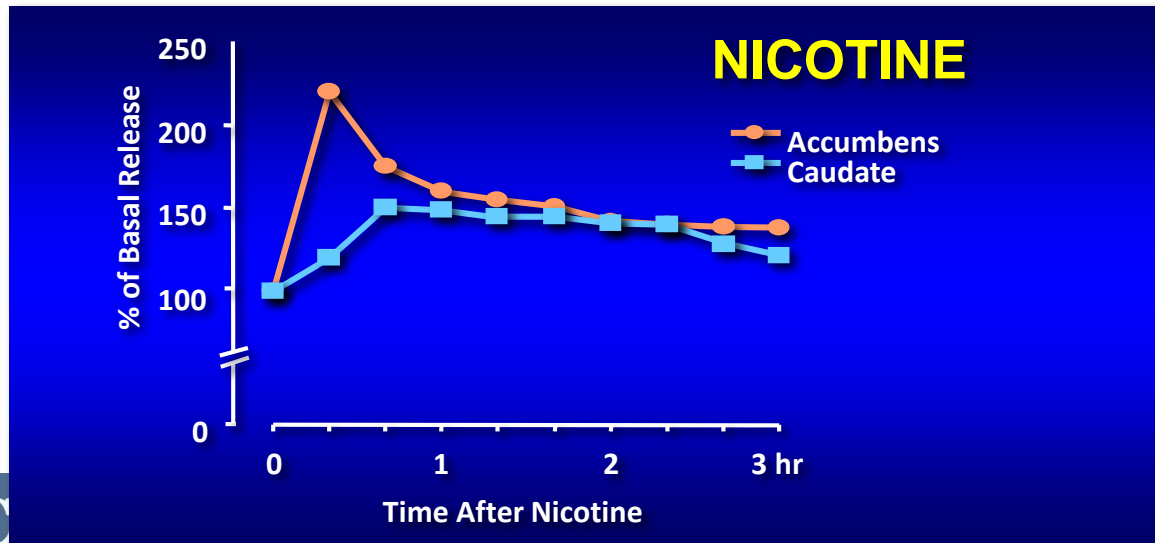
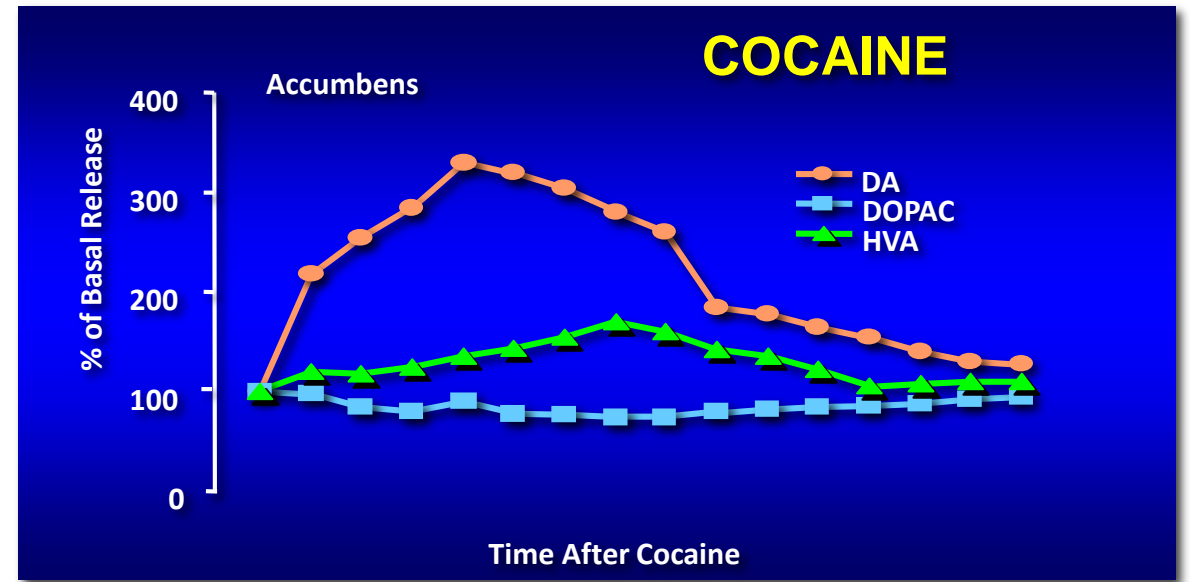
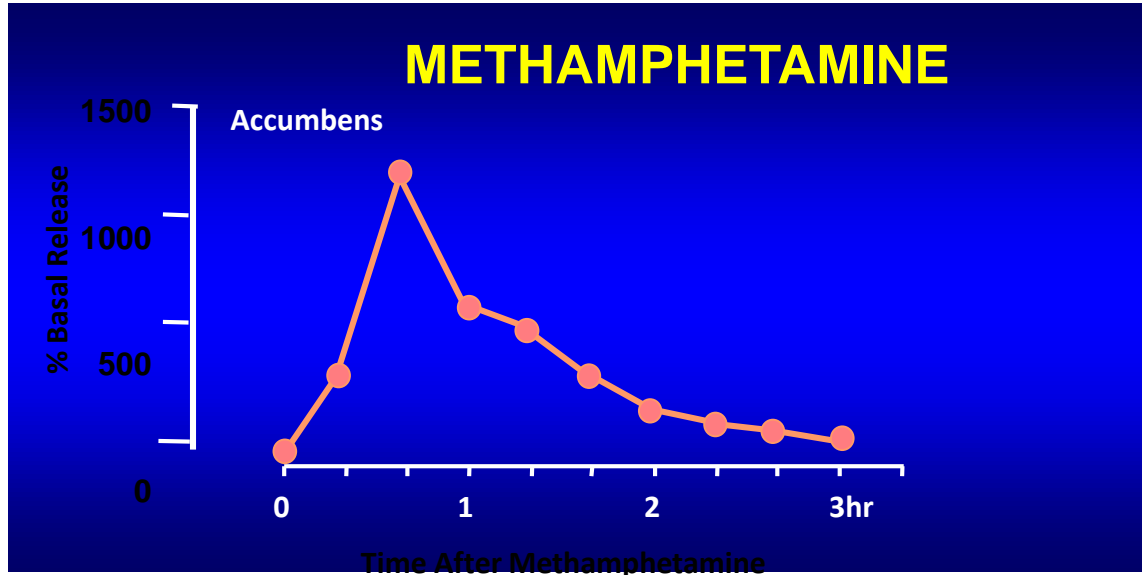
Levels

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

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
- 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

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

Cognitive Behavioral Therapy

16 week RCT of cocaine-dependent methadone patients of:

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

30 patients per group

Cognitive Behavioral Therapy

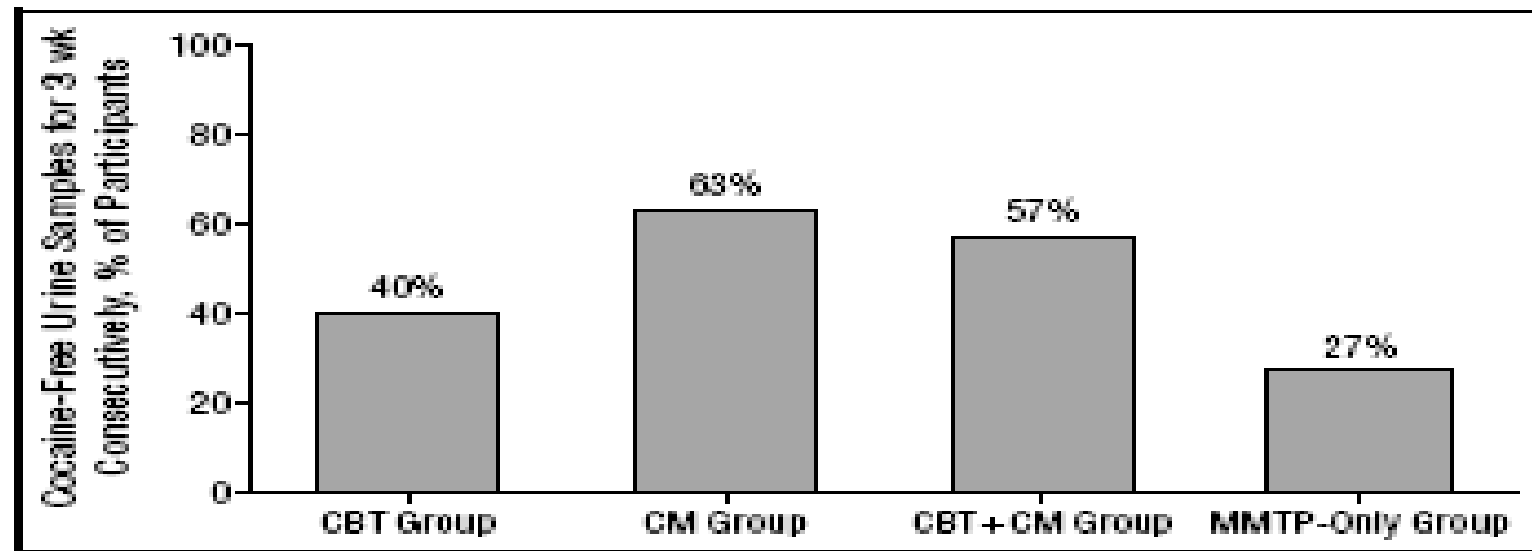


Figure 5. Percentage of patients achieving 3 consecutive weeks of cocaine-free urine samples by group ($\chi^2_3=9.9$; $P=.02$). CBT indicates cognitive-behavioral therapy; CM, contingency management; and MMTP, methadone maintenance treatment program.

Cognitive Behavioral Therapy

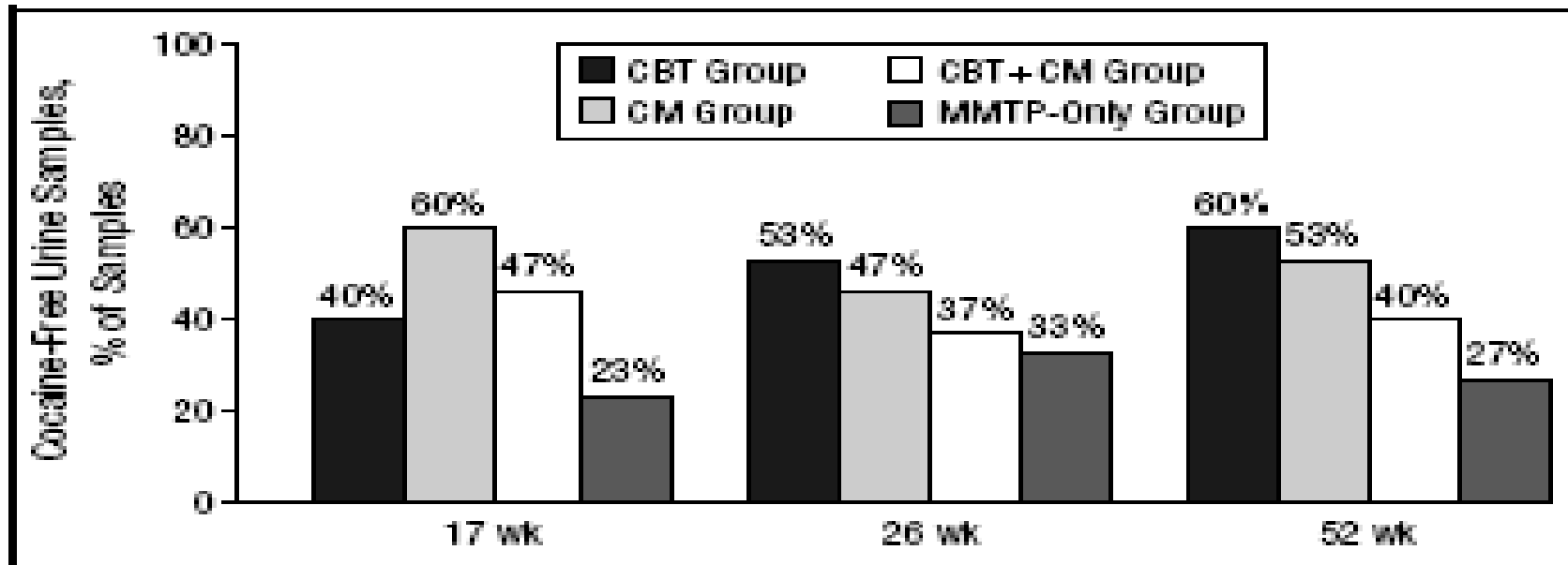
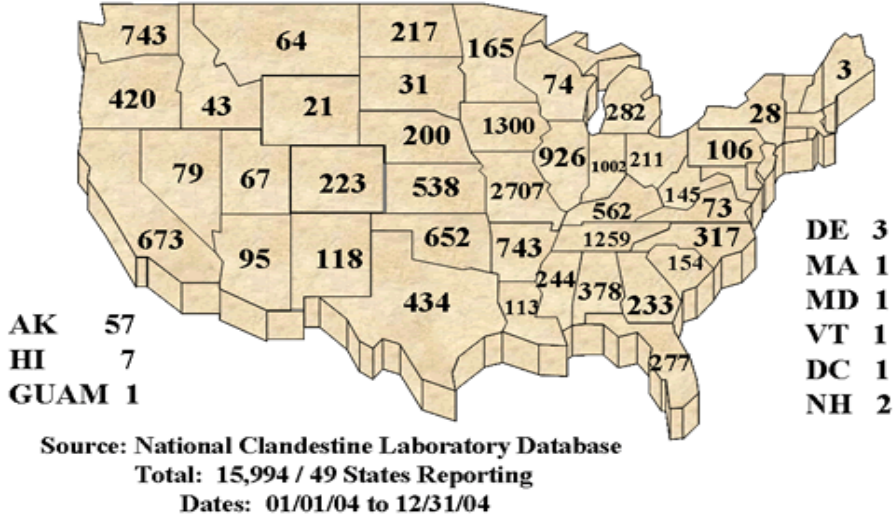


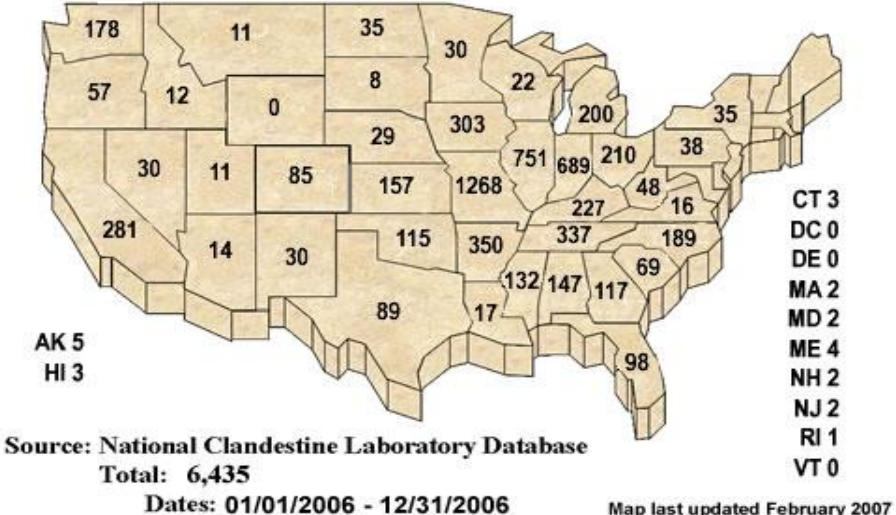
Figure 6. Percentage of 30 possible cocaine-free urine samples at the 17-week, 26-week, and 52-week follow-up points. CBT indicates cognitive-behavioral therapy; CM, contingency management; and MMTP, methadone maintenance treatment program.

Clandestine lab incidents

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



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



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