METHAMPHETAMINE USE DISORDERS: EPIDEMIOLOGY, CLINICAL CHALLENGES, AND REVIEW OF TREATMENTS

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Methamphetamine Use Disorders: Epidemiology, Clinical Challenges, and Review of Treatments
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No disclosures
Epidemiology
Types of Stimulant Drugs

Cocaine Products

• Approximately 16-21 million users worldwide
• Cocaine Powder (sniffed, injected, smoked)
• “Crack” (smoked)

Major regions of use:
  – South America
  – North America (predominantly major urban centers disproportionately impacts African American community)
  – Increases in Central and Western Europe
  – Increases in South and Western Africa
Types of Stimulant Drugs

Amphetamine Type Stimulants (ATS)

• Approximately 40-60 million users worldwide

• Methamphetamine
  – Powder: inhaled, smoked, injected
  – Crystal/Ice: smoked
  – Tablets: orally, crushed and inhaled, smoked, injected (e.g., Captagon)

• Amphetamine
  – Powder, Tablets, Liquid: orally, injected, smoked

• Major regions of use:
  – Eastern and SE Asia
  – Australia and Oceania
  – North America
  – Increases in Central, Eastern and Northern Europe
  – Increases in Middle East
  – Increases in South Africa
Cocaine supply increases, price decreases

• After the peace treaty was finalized between the Colombian government and the FARC in 2016, cocaine eradication methods ceased and cocaine production more than quadrupled to the highest levels since 2007 (DEA, 2018).

• The average retail price in the US per pure gram has decreased by 50% (2012-2017) and average gram purity is 85.5% in 2019 (DEA, 2019).
Methamphetamine Availability Reduces 2006

In 2005 Congress passed the Combat Methamphetamine Act, which put pseudoephedrine products behind the counter.

Although some meth makers tried “smurfing,” meth cases plummeted.

• With no more meth lab explosions on the nightly news, the public forgot about the drug.

• Mexican drug cartels stepped in improving production using the P2P Method with higher potency and lower price ($2,000 per pound)
Methamphetamine Today

• The market is inundated with so much pure, low-cost meth that dealers have more of it than they know what to do with.

• 2018 - United States border agents seizing 10 to 20 times the amounts they did a decade ago.

• Methamphetamine, experts say, has never been purer, cheaper or more lethal.

• 2014–2018- Fentanyl-contaminated meth and cocaine
Methamphetamine Seizures and Deaths

![Graph showing the increase in seizures and deaths from methamphetamine use from 2011 to 2017. The graph indicates a steady increase in seizures and a sharp increase in deaths in 2017.]

- **Seizures (kg)**
  - 2011: 5000
  - 2012: 8000
  - 2013: 10000
  - 2014: 15000
  - 2015: 20000
  - 2016: 25000
  - 2017: 30000

- **Deaths (Drug-related Overdoses)**
  - 2011: 1000
  - 2012: 2000
  - 2013: 3000
  - 2014: 4000
  - 2015: 5000
  - 2016: 6000
  - 2017: 12000

NETI 8/8/18

*2017 Overdose death data is provisional*
Drugs Involved in U.S. Overdose Deaths, 1999 to 2017

- Synthetic Opioids other than Methadone, 29,406
- Heroin, 15,958
- Natural and semi-synthetic opioids, 14,958
- Cocaine, 14,556
- Methamphetamine, 10,721
- Methadone, 3,295
Cocaine-Related Deaths

With opioids

Without opioids

Deaths per 100,000 population

Year

2003 2005 2007 2009 2011 2013 2015 2017

2003 2005 2007 2009 2011 2013 2015 2017
Methamphetamine-related Deaths
Twin Epidemics: The surging rise of methamphetamine use in chronic opioid users.

Drug and Alcohol Dependence, 2018, 14-20

Past month use of methamphetamine significantly increased among treatment-seeking opioid users (+82.6%, p < .001), from 18.8% in 2011 to 34.2% in 2017.
% of Respondents reporting use of meth in past 30 days
Ellis et al 2018

Prevalence of Past Month Use of Methamphetamine

- 2011q2-4: 18.8% (n=1653)
- 2012q1-4: 23.8% (n=2475)
- 2013q1-4: 26.2% (n=2369)
- 20141-4: 29.9% (n=2222)
- 2015q1-4: 30.1% (n=1933)
- 2016q1-4: 31.5% (n=2285)
- 2017q1: 34.2% (n=584)
Cocaine and Methamphetamine Neurobiology

COCAINEx

CRACK

METHAMPHETAMINE

ICE
Cocaine vs Methamphetamine

Cocaine
- plant-derived
- high lasts 20-30 minutes
- T ½: 1 hour
- mechanism: mainly DA reuptake
- used medically
- not directly neurotoxic

Methamphetamine
- synthetic
- high lasts 8-24 hours
- T ½: 12 hours
- mechanism: mainly DA release
- medical use less common (Rx as Desoxyn)
- Greater neurotoxicity in commonly used doses
Methamphetamine Neurobiology
Decreased dopamine transporter binding in METH users resembles that in Parkinson’s Disease.
Partial Recovery of Brain Dopamine Transporters in Methamphetamine Abuser After Protracted Abstinence

Clinical Challenges
Special Treatment Consideration Should Be Made for the Following Groups

• Injection users
• Users who take stimulants daily or in very high doses.
• Homeless, chronically mentally ill and/or individuals with high levels of psychiatric symptoms at admission.
• Men who have sex with men (MSM)
• Users under the age of 21.
• **Individuals in medication treatment for OUD**
Clinical Challenges with Stimulant Dependent Individuals

- Limited understanding of stimulant addiction
- Ambivalence about need to stop use
- Impulsivity/Poor judgement
- Cognitive impairment and poor memory
- Anhedonia
- Hypersexuality*
- Violence and psychosis*
- Powerful Pavlovian trigger-craving response
- **Very poor retention in outpatient treatment**
- Elevated rates of psychiatric co-morbidity
  
* especially meth users
Clinical Management of Stimulant Users: Acute Psychosis

• Symptoms of acute psychosis: Auditory hallucinations, and visual (flashing lights, peripheral artifacts), olfactory, and tactile sensations. In addition, powerful paranoia and persecutory delusions are extremely common, along with ideas of reference, stereotypy and compulsive acts, blunt affect, poverty of speech, delirium, and violence.

• Stimulant-induced psychosis is generally transient and may require use of either a benzodiazepine or an antipsychotic, both of which should be discontinued when acute symptoms have resolved. Risperidone and olanzapine are less likely to cause extrapyramidal symptoms and their sedative properties may ameliorate psychomotor agitation. Monitor for hyperthermia and dehydration when antipsychotics are used in patients with acute stimulant intoxication.
Clinical Management of Stimulant Users

Intoxication

• Symptoms include: Euphoria, hyperexcitability, hypersexuality, increased locomotor activity, agitation, and psychotic symptoms, including paranoia and hallucinations. Objective findings of hypertension, tachycardia, and arrhythmias that present on EKGs of users reflect sympathetic overdrive.

• Acute agitation from MA intoxication is most often the condition that leads users to seek medical attention, and “talking down” the patient in a calm environment is the first course of action. Addressing possible cocaine/MA toxicity may involve emetics or lavage to remove MA pills. Benzodiazepines may be effective in acute management of agitation and distress and may reduce seizure potential in patients.
Clinical Management of Stimulant Users: *Withdrawal*

- Stimulant withdrawal symptoms consist of severe fatigue, cognitive impairment, feelings of depression and anxiety, anergia, confusion, and paranoia. For the majority of patients experiencing acute withdrawal/early-phase abstinence, most symptoms resolve within 2 to 10 days.

- Rest, exercise, and a healthy diet may be the best management approach for most people in withdrawal. Those with heightened agitation and sleep disturbance may respond to benzodiazepines, but acute depression and anhedonia associated with early abstinence generally resolve without intervention.
Craving for stimulants is a central and very powerful component of stimulant dependence

A Key Premise

– Classical conditioning and craving
– The brain and addiction
– Craving is automatic and creates a powerful push to use
– For many, the craving seems overpowering and uncontrollable.
– The craving is triggered by external (people, places, things, times of day) and internal (emotional states) stimuli.
– Managing exposure to triggers and responses to triggers is important
Insight is not enough…

“And then it hit me: I’m salivating over a goddam bell.”
Do Methamphetamine Users Respond Differently to Treatment than Cocaine Users?
Response to Behavioral Treatments: Cocaine vs Meth

- In published research studies where treatment response to behavioral treatments have been compared with cocaine users vs meth users, there has been no evidence of differential response.

- Matrix Model  Huber, Ling and Rawson, 1997
- Contingency Management. Roll et al, 2006
- Community Treatments. Copeland and Sorenson, 2001
- Community Treatments. Luchansky, Krupski and Stark, 2001
Treatment for Individuals with Stimulant Dependence
Meta-analysis of Treatment Efficacy for Individuals with Stimulant Use Disorders

Meta-Analysis Findings

Network meta-analysis was used to analyze 50 clinical studies (6,943 participants) on 12 different psychosocial interventions for cocaine and/or amphetamine addiction.

The combination of 2 different psychosocial interventions, namely contingency management and community reinforcement approach, was the most efficacious and most acceptable treatment both in the short and long term.
Main results

Twenty-seven randomized controlled studies (3663 participants) fulfilled inclusion criteria and had data that could be used for at least one of the main comparisons.

The comparisons between different type of behavioral interventions showed results in favor of treatments with some form of contingency management in respect to both reducing dropouts and lowering cocaine use.
A meta-analysis reports that contingency management results in a successful treatment episode 61% of the time while other treatments with which it has been compared result in a successful treatment episode 39% of the time.
Treatments for Stimulant Use Disorders (SUDs) with Empirical Support

- Contingency Management/Incentives (CM/I)
- Community Reinforcement Approach (CRA)
- Cognitive-Behavioral Therapy (CBT)
- Other approaches with interest
  - Matrix Model
  - Motivational Interviewing
  - Physical Exercise
  - Mindfulness Meditation
Contingency Management

(Also known as Motivational Incentives)
Contingency Management

(Also known as Motivational Incentives)
Contingency Management

A technique employing the systematic delivery of positive reinforcement for desired behaviors. In the treatment of methamphetamine dependence, vouchers or prizes can be “earned” for submission of methamphetamine-free urine samples.
Contingency Management for the Treatment of Methamphetamine Dependence.


• **METHOD:** The authors report data on 113 participants who were diagnosed with methamphetamine abuse or dependence. They were randomly assigned to receive 12 weeks of either treatment as usual (Matrix) or treatment as usual plus contingency management. The reinforcers for drug-negative samples were plastic chips, some of which could be exchanged for prizes.

• **RESULTS:** The participants in both groups remained in treatment for equivalent times, but those receiving contingency management in addition to usual treatment submitted significantly more negative samples, and they were abstinent for a longer period of time (5 versus 3 weeks).
Contingency Management: Fish-Bowl/Prize/Variable Magnitude of Reinforcement Procedure

• Developed by Petry
• Participants earn draws from a container containing 500 chips. Some of these chips can be exchanged for prizes
  • 50% (250) are labeled “Good Job” - No monetary value
  • 41.8% (209) are labeled “Small” - $1 -5.00
  • 8% (40) are labeled “Large” - $20.00
  • 0.02% (1) are labeled “Jumbo” - $80-100.00
Meth Negative Samples: Roll et al 2006

Mean Number of Negative Samples

<table>
<thead>
<tr>
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<th>CM+TAU</th>
<th>TAU</th>
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- CM+TAU: 16
- TAU: 8
Longest Duration of Abstinence: Roll et al 2006

- Mean Weeks of Abstinence

- CM+TAU

- TAU
Retention Rate: Roll et al 2006

A line graph showing the percent of negative samples over weeks. The graph compares two conditions: Incentive and Treatment as usual. The Incentive line starts at approximately 70% and decreases gradually, while the Treatment as usual line starts at around 50% and also decreases over time.
Cognitive Behavioral Therapy and Contingency Management for Stimulant Dependence.

• **DESIGN:** Randomized clinical trial
• **PARTICIPANTS:** Stimulant-dependent individuals \((n = 171)\)
• **INTERVENTION:** CM, CBT, or combined CM and CBT, 16-week treatment conditions. CM condition participants received vouchers for stimulant-free urine samples. CBT condition participants attended three 90-minute group sessions each week. CM procedures produced better retention and lower rates of stimulant use during the study period.
• **RESULTS:** CM produced evidence of efficacy during treatment. There was no evidence of an additive effect when the two treatments were combined. The response of cocaine and methamphetamine users was comparable.
• **CONCLUSIONS:** This study suggests that CM is an efficacious treatment for reducing stimulant use and is superior during treatment to a CBT approach. CM is useful in engaging substance abusers, retaining them in treatment, and helping them achieve abstinence from stimulant use.
Stimulant-free Uas Rawson et al 2004

Group ($F = 10.2, df = 2, p < 0.0001$)
A Comparison of Contingency Management and Cognitive-Behavioral Approaches During Methadone Maintenance Treatment for Cocaine Dependence.  

- **DESIGN:** Randomized clinical trial.
- **PARTICIPANTS:** Patients with cocaine dependence receiving methadone maintenance treatment (n=120).
- **INTERVENTIONS:** Participants were randomly assigned to 1 of 4 conditions: CM, CBT, combined CM and CBT or methadone treatment as usual. The active study period was 16 weeks, requiring 3 clinic visits per week.
- **RESULTS:** Urinalysis results during the 16-week treatment period show that participants assigned to the 2 groups featuring CM had significantly superior in treatment urinalysis results, whereas urinalysis results from participants in the CBT group were not significantly different than those from the MMTP-only group.
- **CONCLUSIONS:** Study findings during treatment provide solid evidence of efficacy for CM (with and without CBT. There was no evidence of a combined effect.
Stimulant-Free Uas Rawson et al, 2002

Mean # Cocaine-free Urine Samples

Group ($F = 6.8$, $df = 3$, $P < 0.0001$)
Contingency Management Apps

- **reSET** is a 90-day Prescription Digital Therapeutic (PDT) for Substance Use Disorder (SUD) intended to provide cognitive behavioral therapy (CBT), as an adjunct to a contingency management system, for patients 18 years of age and older who are currently enrolled in outpatient treatment. FDA approved. [https://peartherapeutics.com/products/reset-reset-o/](https://peartherapeutics.com/products/reset-reset-o/)

- **DynamiCare** Health is a platform for families and individuals that reinforces a person’s recovery from addiction and rewards healthy behavior. DynamiCare’s easy-to-use technology includes random breath and saliva tests submitted through the app, verified treatment attendance check-ins, a supportive Recovery Coach, rewards for healthy progress, and a dashboard for supporters.

  - [www.dynamicarehealth.com](http://www.dynamicarehealth.com).
The 3 Essential Elements

1. Target behaviors must be readily detected
2. Tangible reinforcers are provided whenever the targeted behavior is demonstrated
3. When the target behavior does not occur, the reinforcers are withheld
Founding Principles

1. Identify Target Behavior
2. Choice of Target Population
3. Choice of Reinforcer
4. Incentive Magnitude
5. Frequency of Incentive Distribution
6. Timing of Incentive
7. Duration of Intervention
1. Identify Target Behavior

A target behavior should be:

• Problematic and in need of change
• Observable
• Measurable
• Relatively easy for the patient to accomplish (at least initially)
2. Choice of Target Population

EXAMPLES:

• Patients not responding to treatment

• Newly enrolled patients

• Users of a specific substance (e.g., patients enrolled in a methadone program and continuing to use cocaine)

• Vulnerable population (e.g., pregnant women)

Who will you target with reinforcement-based interventions?

MAXINE STITZER, PH.D.
3. Choice of Reinforcer

- May be different from what you want or like to do—and it is not what you think is good for the patient.

- Critical to view from patients’ perspectives, or you will compromise effectiveness.

It must be something the patient wants or likes to do.
FOUNDED PRINCIPLES

3. Choice of Reinforcer continued

Three major types of incentive programs

• Access to clinic privileges
  Example: Take-home dose of methadone

• On-site prize distribution
  Example: A prize cabinet contains many small prizes, some large prizes and a few jumbo prizes

• Vouchers or other token economy systems
  Example: Points or vouchers are accumulated in an account and redeemed for retail goods or services
FOUNDING PRINCIPLES

4. Incentive Magnitude

- Will determine the degree to which the intervention is effective
- Should be able to compete with reinforcement derived from the behavior targeted for change
- Increases as the desired behavior is repeated

The Fishbowl Method gives patients the opportunity to win prizes of varying magnitude.

NANCY PETRY, PH.D.
5. Frequency of Incentive Distribution

- Can the targeted behavior be reinforced frequently?
- What method will be used to distribute incentives?
- How often will the incentive be distributed?
6. Timing of Incentive

- Immediacy is important
- Poor timing can undermine the most well-planned intervention

I earn a point for each recovery meeting I attend weekly.
7. Duration of Intervention

How long?

Until the patient...

- Internalizes the recovery process
- Develops naturally-occurring reinforcers that support recovery
LOW COST INCENTIVES

Challenges

- Cost of incentives
- On-site testing
- Counselor resistance
LOW COST INCENTIVES

Challenges

Motivational Incentives are a clinical practice with therapeutic guidelines*:

- Never take the form of cash (instead would be given as gift cards to stores, gas stations, etc.);
- Low in value (not to exceed $200/month or last for more than 3 months);
- Introduced as clinically indicated and as part of an established treatment plan;
- Not advertised and are not offered to all participants.

*OIG Opinion on Motivational Incentives, 2008
LOW COST INCENTIVES

Challenges

Isn’t this just rewarding patients for what they should be doing anyway?

That’s a common concern. But sometimes the problem is that patients are not doing the things that are good for them and need a motivational boost!
LOW COST INCENTIVES

Challenges

How do I set up a Prize Cabinet to deliver prizes (incentives)?

For tools and ideas, visit the Motivational Incentive Web-Portal @ www.attcnetwork.org or www.bettertxoutcomes.org.
LOW COST INCENTIVES

Challenges

Can Motivational Incentives be used with adolescents or patients with co-occurring disorders?

Several studies suggest “yes!” Check out the resource bibliography on the Motivational Incentive Web-Portal.

Higgins, Alessi, & Dantona, 2002
Community Reinforcement Approach (CRA)
Community Reinforcement Approach

- Community Reinforcement Approach (CRA) is a combination of behavioral strategies that address the role of environmental contingencies in encouraging or discouraging drug use, and attempts to rearrange these contingencies so that a non-drug using lifestyle is more rewarding than a using one.
Components of CRA

• CRA Components include:
  – behavioral skills training
  – social and recreational counseling
  – marital therapy
  – motivational enhancement
  – job counseling
  – relapse prevention

• For application to the treatment of cocaine dependence, a voucher based reinforcement program is added.

**METHOD:** The 38 patients were enrolled in outpatient treatment and were randomly assigned to the two treatments. Counseling in the behavioral treatment was based on the community reinforcement approach, while the drug abuse counseling was based on the disease model of dependence and recovery. Patients in the behavioral, but not the drug counseling, treatment also received incentives contingent on submitting cocaine-free urine specimens.

**RESULTS:** Of the 19 patients who received CRA, 58% completed 24 weeks of treatment, versus 11% of the patients who received counseling. In the CRA group 68% and 42% of the patients achieved at least 8 and 16 weeks of documented continuous cocaine abstinence, respectively, versus 11% and 5% in the drug abuse counseling group.
CRA and Contingency Management: Higgins et al., 1993

Completed Treatment: 11%
8 weeks continuous abstinence: 11%
16 weeks continuous abstinence: 5%

- Standard Treatment
- CRA & CM
Community Reinforcement Therapy for Cocaine-Dependent Outpatients


**Method:** One hundred cocaine-dependent outpatients were randomly assigned to one of 2 treatment conditions: CRA + vouchers or vouchers only. All patients earned incentives in the form of vouchers exchangeable for retail items contingent on cocaine-free urinalysis results during treatment weeks 1 to 12. Incentives were combined with a 24-week course of CRA therapy in the CRA + vouchers condition, while incentives represented the primary treatment in the vouchers-only condition.

**Results:** Patients treated with **CRA + vouchers were retained better in treatment, used cocaine at a lower frequency during treatment but not follow-up compared with patients treated with vouchers only.**

Patients treated with **CRA + vouchers also reported a higher frequency of days of paid employment during treatment and the initial 6 months of follow-up, decreased depressive symptoms during treatment only, and fewer hospitalizations and legal problems during follow-up**
Manual 2

A Community Reinforcement Plus Vouchers Approach: Treating Cocaine Addiction
Cognitive Behavioral Therapy (CBT)
Research on CBT for SUD


• CBT for CBT Website: [http://www.cbt4cbt.com/](http://www.cbt4cbt.com/)
Matrix Model
Matrix Model

• Is a manualized, 16-week, psychosocial approach used primarily in outpatient settings for the treatment of drug dependence.

• Manuals Can be downloaded at SAMHSA.gov

• Designed to integrate several interventions into a comprehensive approach. Elements include:
  – Individual counseling
  – Cognitive behavioral therapy
  – Motivational interviewing
  – Positive reinforcement for behavior change
  – Family education groups
  – Urine testing
  – Participation in 12-step programs
Matrix Model: Components

- Cognitive Behavioral Therapy
- Motivational Interviewing
- Family Therapy
- Psycho-education
- Contingency Management
- 12 Step Facilitation
- Urine Testing
MATRIX MODEL
Organizing Principles

Create explicit structure and expectations
Establish positive, collaborative relationship w/ clients
Teach information and cognitive-behavioral concepts
Positively reinforce positive behavior change
Provide corrective feedback when necessary
Educate family regarding stimulant abuse recovery
Introduce and encourage self-help participation
Use urinalysis to monitor drug use
MATRIX MODEL
Organizing Principles

Nonjudgmental, supportive attitude
Engagement & Retention
Strong bond with individual counselor or group
Minimal use of confrontation
Use of recovering staff and/or role models
Ability to work with relapse
EVIDENCE BASED THERAPIES (EBT’S) THAT ARE INCORPORATED IN THE MATRIX MODEL

- Cognitive Behavioral Therapy
- Motivational Interviewing
- Family Therapies
- Contingency Management
- 12-Step Facilitation
Encouraging and reinforcing behavior change
Recognizing and avoiding high risk settings
Behavioral planning (scheduling)
Coping skills
Conditioned “triggers”
Understanding and dealing with craving
Understanding basic psychopharmacology principles
Self-efficacy (MI Concept)
Study Design

• 1016 treatment seeking individuals dependent upon methamphetamine were randomly assigned into Treatment as Usual (TAU) or the Matrix Model (MM).
• Study was conducted at 6 sites in California and sites in Montana and Hawaii.
• Each condition provided treatment for 4 months.
Mean Number of UA’s That Were MA-Free During Treatment

- Billings
- Concord
- Costa Mesa
- Hayward
- Honolulu
- San Diego
- San Mateo Pyra
- San Mateo ODAS

The graph compares the mean number of MA-free UA’s for different locations under Matrix and TAU treatments.
Exercise as a Treatment Intervention for Methamphetamine Dependence
Exercise Is Effective for Medical Conditions

• Improvements from regular exercise at moderate levels for adults include:
  – Lower risk of early death, heart disease, stroke, type II diabetes, high blood pressure, adverse blood lipid profile, metabolic syndrome, colon and breast cancers
  – Prevention of weight gain
  – Weight loss when combined with diet
  – Improved cardio-respiratory and muscular fitness
  – Reduced depression and improved cognition
Exercise Is Good For You

• Reduces Depression
• Reduces Anxiety
• Improves Medical Conditions (heart disease, stroke, diabetes, etc)
• Improves Cognition (executive functioning)
Primary Aims

• Characterize effects of an aerobic and resistance exercise intervention ("Exercise") compared to health education ("Education")
• Characterize effects of Exercise on MA craving and negative affective states, including anxiety, depression, and anhedonia
• Characterize variations in health-related outcomes among participants in the Exercise condition compared with those in the Education condition (BMI, strength, blood pressure)
• Examine changes in dopamine D_2/D_3 receptor availability in abstinent MA-dependent participants assigned to the Exercise group compared to a subsample of participants in the Education (control) group (n = 15 per group)
• Assess impact on relapse to methamphetamine after discharge from residential treatment
Study Interventions

- Participants randomized to 1 hour, 3 d/wk of exercise training (EX) or education (ED) over the 8-wk study period (24 sessions)
  - **EX**: 5 minutes warm-up followed by 30 minutes aerobic exercise on treadmill at 65%-85% max heart rate, followed by 15 minutes circuit-style resistance training of major muscle groups, 5 minute cool-down (light stretching)
  - **ED**: equal attention via health and wellness education sessions delivered by counselor. Topics include nutrition, health screening, meditation, acupressure, dental care, stress relief
Exercise Testing & Fitness Data

• Assessed at baseline and for aerobic fitness (V02 Max) with a maximal cardiopulmonary exercise test (CXT) using a novel treadmill ramp protocol.

• Body composition assessed with skinfold technique.

• Muscle strength measured by 1-rep maximum (1-RM) for the leg press (LP) and chest press (CP) exercises; muscle endurance determined by the number of repetitions to failure in the LP and CP exercises using 85% of baseline 1-RM values.

• Individualized programs for endurance and resistance exercise training developed from baseline CXT and 1-RM tests as well as subsequent assessments during training.
Exercise Testing & Fitness Data (8 weeks)

Exercise Group:
1h, 3 days/wk

Health Education Group:
1h, 3 days/wk

Assessments: cardiopulmonary exercise test, body composition, muscle strength & endurance

N=15

N=14
Change in VO\textsubscript{2} max (L/min) after 8 wk Exercise or Education

- Exercise (N = 15): +21%
- Education (N = 14): -1%

$P < 0.001$
Change in relative body fat % after 8 wk
Exercise Training or Education

- Exercise (N = 15): -15%
- Education (N = 14): +3%

P < 0.001
Change in CP & LP strength after 8 wk Exercise Training or Education

- Chest Press: 49% change
- Leg Press: 40% change

Exercise: P < 0.001
Education: 3% change
Change in repetitions to failure 85% baseline 1-RM for CP & LP after 8 wk Exercise or Education

![Graph showing change in repetitions to failure 85% baseline 1-RM for CP & LP after 8 wk Exercise or Education.]

- **Chest Press**
  - Exercise: 96%
  - Education: -1%

- **Leg Press**
  - Exercise: 120%
  - Education: 7%

*P < 0.001*
Mood Data (Anxiety & Depression) N=135

Exercise Group:
1h, 3 days/wk
N=69

Health Education Group:
1h, 3 days/wk
N=66

Assessments: Beck Anxiety and Depression Indices
Change Scores in Depression (BDI)

Week 1 2 3 4 5 6 7 8

Change Score in BDI

Exercise
Education
MA-dependent participants in a residential treatment program (8 weeks)

Exercise Group:
1h, 3 days/wk
N=10

Health Education Group:
1h, 3 days/wk
N=9

D2-like receptor assay with $^{18}$F-fallypride and PET: before & after intervention
Exercise group shows increases in striatal $BP_{ND}$
Figure 2a: Percent MA-positive urine samples by treatment condition at 1- and 3-months post-discharge
Figure 3a. UA test results at 1- and 3-months post-discharge by MA use severity subgroups

*P < 0.05
Figure 3b: Self-reported days of MA use by severity subgroups at 1 and 3 months post-discharge

*Significant at P <0.05

- Exercise MA ≤ 18
- Education MA ≤ 18
- Exercise MA > 18
- Education MA > 18
Summary

- MA users can engage in exercise
- Resistance and aerobic exercise delivered 3 Xs/week over just 8 weeks confers benefits to physical health, mood, and dopamine receptor availability and post-discharge relapse in MA users
- Limitations: supervised administration in residential facility limits generalizability
- Optimal type and duration of exercise unknown
- Mechanism of action in effect on drug use unknown: changes in neurotransmitters (serotonin, dopamine), BDNF, sleep, mood?
- Further exploration of exercise in conjunction with other forms of therapy as well as effects on drug use is warranted
Medications for Stimulant Use Disorders
Medications Considered for Cocaine Use Disorder

Positive/Under Consideration

- topiramate*
- modafinil*
- bupropion*
- amphetamine salts*
- disulfiram (mixed, worse retention)
- propranolol (WD)
- buprenorphine+naltrexone
Medications Considered for Cocaine Use Disorder

**Mostly) Negative**
- Gabapentin
- Aripiprazole
- Olanzapine
- Tiagabine
- Buspirone
- Desipramine*
- Amantadine*
- TA-CD Vaccine
- Baclofen*
- GVG (vigabatrin)
- N-acetylcystine
Medications for Methamphetamine Use Disorder

Positive/Under Consideration

bupropion (better in low severity users)
mirtazapine
naltrexone
methylphenidate
d-amphetamine (craving/WD)
topiramate* (better if abstinent at tx entry)
Medications for Methamphetamine Use Disorder

**Negative Results**
- Imipramine
- Desipramine
- Tyrosine
- Ondansetron
- Fluoxetine
- Sertraline, paroxetine
- Aripiprazole
- Gabapentin
- N-acetylcysteine
- Modafinil* (better in hi-severity users)
Stimulant use by patients on OUD Medications
Cocaine Use by Patients on Methadone: We’ve been here before

• In the late 1980s and 1990s, the cocaine epidemic seriously damaged the treatment progress of many patients on methadone.
• In many OTPs, 70% + of UAs were positive of cocaine.
• The treatment progress for many patients on methadone and who had not used illicit drugs for years was seriously degraded by high levels of cocaine use. This was particularly true once crack became available.
• Dramatic increases in injection drug use, HIV, Hep C and drug-related crime were associated with the elevated cocaine use. Premature treatment termination/drop-out rates increased dramatically.
• Many OTPs became locations for cocaine dealing and associated behaviors
Qualitative Interviews with Patients on Medication for OUD

• Estimates from clinicians in Vermont H&S network suggest that 20-40% of individuals on MOUD are using cocaine/methamphetamine.

• Stimulant use is a significant concern to clinicians treating patients with MOUD.

• Interviews with a group of 25 stimulant-using patients in MOUD, suggest that current treatments (increased counseling) are not effective in addressing their ongoing stimulant use.
What did the patients say?

• Reported availability of cocaine (and more recently meth) has greatly increased in past year. Is available from people who previously only sold opioids.

• Drug history: 22 of 24 had used cocaine before using opioids. 6 of those individuals said they started opioids ( pills ) to “mellow out” from cocaine effects.

• 12 reported that they felt the effects of stimulants were more “addicting” than opioids. (They were referring to the fact that their opioid use was driven to avoid withdrawal. Their stimulant use was driven by a response to craving and desire for drug effect.)
What did the patients say?

- What are/were the challenges of stopping stimulant use?
  - Love the drug effect and in a perfect world would use all the time
  - Craving/desire is very powerful and ambivalent about stopping
  - Drug is widely available in inexpensive dosage forms
  - Craving is triggered by many things
    - Coming to the clinic
    - Standing in long dosing lines with drug conversations
    - Parts of town
    - Drug using friends
    - Dealers phone calls
    - Boredom
What did the patients say?

• What helped them with stopping?
  – Group and individual general counseling.. NO
  – Groups discussing stimulant use... NO NO NO
  (not unusual to go and use after group, with other group members)
  – Changing dose...NO
  – Not carrying cash and limiting handling of money...YES
  – Avoiding drug using friends.. YES
  – Avoiding parts of town....YES
  – Changing phone numbers... YES
  – Coming to clinic when less crowded...Yes
  – Staying busy with activities
    • Kids
    • Exercise/sports
    • Animal rescue
What did the patients say?

- Had any form of treatment been useful?
- 2 people reported that drug court was the key to their stopping
- 2 people had previously been in a study of contingency management and found it very useful.
- With both of these “interventions” patients said the immediate certain consequences resulting from the results of a UA gave them something to “hold on to”. Although in drug court the main focus is on the negative contingency, the 2 patients talked about how rewarding it was to get the praise from the drug court folks and the judge for giving stimulant free samples.
Methadone vs Buprenorphine: Is There a Different Response to Stimulant Use?

- Don’t know. We do not have good data on rates of stimulant use comparing patients on methadone with those on buprenorphine.
- Preclinical research in the 80s and 90s suggested that buprenorphine may be useful in reducing stimulant use.
- Several studies compared methadone and buprenorphine for the treatment of individuals who used opioids and cocaine. Both studies showed that both medications reduced opioid use but did not affect cocaine use.
- Ling et al 2016 reported mixed results when buprenorphine was used to treat cocaine dependent individuals. Some measures indicated a reduction of cocaine use, other measures concluded no effect.
Thank you

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