Everything You Wanted to Know About Medication-Assisted Treatment (But Were Afraid to Ask)

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Disclosure of Relevant Financial Relationships

Name	Commercial Interests	Relevant Financial Relationships: What Was Received	Relevant Financial Relationships: For What Role	No Relevant Financial Relationships with Any Commercial Interests
Indivior		Honorarium	Speaker's Bureau	
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Objectives

- 1. Describe the mechanisms, side effects, and treatment goals of at least three FDA-approved medications for addictive disorders.
- 2. Discuss at least two advantages and disadvantages of employing medicines in a recovery treatment program
- 3. Review three case studies on how effective use of medicines can improve treatment outcomes.
- Explain at least three administrative protocols and processes that are required to implement medicationassisted treatment into a variety of healthcare settings.

Overview

Part I

- Review of MAT Principles
- FDA-approved meds
- Pros and Cons
- Part II
 - Case Studies
 - Implementing MAT
 - Potpourri

What is Medication Assisted Treatment (MAT)?

- MAT is the use of FDA-approved medications, in combination with counseling and behavioral therapies, to provide a wholeperson approach to the treatment of addictive disorders.
- Research shows that medication and behavioral therapies works best!
- MAT is clinically driven with a focus on individualized client care

SAMHSA TIP for MAT

Medication-Assisted Treatment For Opioid Addiction in Opioid Treatment Programs

> A Treatment Improvement Protocol TIP 43





Key Components to MAT

pharmacological therapy
 psychosocial services
 integration of care
 education and outreach

Expectations of Medications

- Manage detoxification
- Target urges / cravings
- Increase likelihood of abstinence
- Reduce harm from addictive behavior
- Lay the groundwork to do recovery

How did MAT happen?

History of MAT

- 1972: Methadone approved
- 1980s: War on Drugs
- 1990s: "Addiction as a brain disease"
 - Advances in genetic, neuroimaging, animal models, slow medication development
- 2000s: Buprenorphine approved
- 2010s: Steadier Growth of Meds

History of Physicians and MAT

• 1990-2000

- MDs had limited choices, trainings to prescribe MAT from office-based settings
- 2000 present
 - DATA 2000 opens doors but capacity low
 - Addiction Psychiatrists
 - Addition Medicine (FP, IM)
 - MDs usually separated from SUD/MH providers

My Own Experience With MAT

- 1998: Graduate Medical School
- 2002: Graduate Residency
- 2003: Complete Addiction Fellowship
- 2004: Obtain "Bup Waiver"
- 2004 Present: Office-based MAT

Overarching Principle of MAT

"Drugs are substances that change body's functioning. Medications are drugs that restore normal functioning"

Recovery

• " A voluntarily maintained lifestyle characterized by sobriety, personal health and citizenship"

J.Substance Abuse Treatment 2008

What are the FDA-approved medications for addictive disorders?

Medication Approaches

 Mechanism of Action -(Full) Antagonist: Naltrexone, Naloxone -(Partial) Agonist/Antagonist Buprenorphine, Varenicline -(Full) Agonist Methadone, NRT

Abused Opiates

Prescription Pills Heroin

FDA-Approved Medications

Drug of Abuse	Brand Name	Generic
Opiates	Suboxone	Buprenorphine/ Naloxone
	Subutex	Buprenorphine
		Methadone
	Revia	Naltrexone
	Vivitrol	Naltrexone

Buprenorphine

How it Works

- Office-based treatment
- Physicians prescribing must have certification from DEA (100 pt. Limit)
- Manages withdrawal
- Used as a maintenance therapy
- Limited abuse potential

Buprenorphine's Properties

- Modest μ agonist activity with ceiling
- Long half life
- Precipitated withdrawal if taken after full agonist
- Decreased risk of respiratory, CNS depression
- Sublingual route of administration
- "Combo" tablet with naloxone limits abuse by injection

Buprenorphine Safety

- No alteration of cognitive functioning – feel "normal"
- No organ damage
 - Early concern of hepatic toxicity unconfirmed
 - No evidence of QT prolongation
- Ceiling prevents respiratory depression, OD (Overdose reports with combining use with benzodiazepines)
- No clinically significant interactions with other drugs

Pharmacology

- Semi-synthetic morphine alkaloid
- Partial agonist at mu receptor
 Ceiling effects
- Antagonist at kappa receptor
- Schedule III
- Over 20 years of research

Opioid Receptors

Drugs and medications that activate mu receptors:

- Morphine
- Hydromorphone
- Oxymorphone
- Fentanyl
- Methadone

Codeine Hydrocodone Oxycodone LAAM Buprenorphine

Function at Receptors: Full Opioid Agonists



• activates the mu receptor

Is highly reinforcing

③ is the most abused opioid type

Includes heroin, codeine, & others



• activates the receptor at lower levels

Is relatively less reinforcing

③ is a less abused opioid type

Includes buprenorphine

Function at Receptors: Opioid Antagonists Mu receptor Antagonist binding ...

Occupies without activating

Is not reinforcing

B blocks abused agonist opioid types

Includes naloxone and naltrexone

Full vs. Partial Agonist



Dose

Buprenorphine/Naloxone Tablets



2mg/0.5mg

8mg/2mg

.6/ -....6





SUBOXONE Film



For complete Prescribing Information, visit suboxone.com. SUBOXONE[®] Sublingual Film is a registered trademark of Reckitt Benckiser (UK) Ltd.





Zubsolv Sublingual Tablets



Available doses (BUP/NX): 1.4 mg / 0.36 mg; 5.7 mg / 1.4 mg

Recommended maintenance dose: 11.4 mg/ 2.8 mg

Bunavail Buccal Film



Available dosages (BUP/NX): 2.1 mg / 0.3 mg; 4.2 mg/0.7 mg; 6.3 mg/ 1.0mg

Recommended maintenance dose: 8.4mg / 1.4mg

Buprenorphine, Methadone, LAAM: Treatment Retention





Kakko J, Lancet 2003

Most often heard quotes with Buprenorphine "Doc, I feel normal" "I wake up not sick" "I have my life back"

- Treatment in normal medical settings:
 - Encourages continuity of medical/specialty care
 - Encourages relationship building with clinicians
 - Legitimize opioid dependence as a normal, treatable, chronic illness
Overdose Education and Naloxone Distribution (OEND)

- ~20,000 deaths / yr
- Naloxone (injectable and nasal spray)
 Reverses opiate overdoses
- In early 2015, California law allows pharmacists to distribute naloxone directly to patients

How to identify an opioid overdose:

Look for these common signs:

- The person won't wake up even if you shake them or say their name
- Breathing slows or even stops
- Lips and fingernails turn blue or gray
- Skin gets pale, clammy

In case of overdose:

1 Call 911 and give naloxone If no reaction in 3 minutes, give second naloxone dose

2 Do rescue breathing or chest compressions Follow 911 dispatcher instructions

3 After naloxone

Stay with person for at least 3 hours or until help arrives

How to give naloxone:

There are 3 ways to give naloxone. Follow the instructions for the type you have.

Nasal spray naloxone



Injectable naloxone



Auto-injector

The naloxone auto-injector is FDA approved for use by anyone in the community. It contains a speaker that provides instructions to inject naloxone into the outer thigh, through clothing if needed.

Naloxone Formulations

Generic Injection Solution: 0.4 MG/1 ML, 1 MG/1 ML

Evzio Injection Solution: 0.4 MG/0.4 ML

Narcan Nasal Spray: 4 MG/0.1 ML

Opioid Antagonist: Naltrexone

Opioid Blockade FDA Approved for Alcohol Prevents relapse Strong Anti-Craving Minimized overdose risk; especially after detox **Highly Motivated** Does not want agonist therapy

Injectable NTX Provides a Sustained-Release of Medication



IM Naltrexone Eliminates Daily Adherence Decisions¹

- Naltrexone utilizes a delivery system that
 Provides a month of medication in a single dose
- Adherence to any treatment program is essential for successful outcomes
- Administration by a healthcare provider ensures that the patient receives the medication as directed

"...addressing patient adherence systematically will maximize the effectiveness of these medications."²

-Updated NIAAA Clinician's Guide



Clinical assessment and diagnosis

NIAAA Clinician's Guide

Helping Patients Who Drink Too Much



A CLINICIAN'S GUIDE

2005 Edition

FDA-Approved Medications

Drugs of Abuse	Brand Name	Generic Name
Alcohol	Antabuse	Disulfiram
	Vivitrol	Naltrexone
	Revia	Naltrexone
	Campral	Acamprosate

Disulfiram (Antabuse)

Dosing: 250 mg – 500 mg qd Side effects: Nausea, metallic taste, dysphoria, fatigue, hepatitis, psychosis (dopamine) Effects can last 72 hours after last dose





Naltrexone (Revia)

FDA Approved 1994 MOA: Opiate Antagonist decrease positive, reinforcing effects increase negative aspects of drinking decrease craving from first dose (prime) decrease craving from cues

Naltrexone



Starting: (50 mg tabs) 25 mg and increase by 25 mg week until SE or target dose of 200 mg SE: dysphoria, nausea, increased LFTs, **\$\$\$\$** Modest effect, at best (decreased time to relapse, # of drinks, cravings)

Naltrexone Decreases Relapse



Wilkins, JN. Traditional Pharmacotherapy of Alcohol Dependence J Clin Psychiatry, 2006

Naltrexone Decreases Heavy Drinking Days



Garbutt JC et al. JAMA 2005.

Naltrexone Decreases Hazardous Drinking



Figure 1. Time to termination of hazardous drinking defined by weekly or daily limits.

O'Malley et al. Int J Neuropsychopharm. 2008.

IM Naltrexone (Vivitrol)

- MOA: same as oral naltrexone
- Dose: 380 mg IM q 4 weeks
- No oral lead-in
- Stop drinking 7 days prior (ideal)
- Gluteal IM
- Results: Decrease drinking days and decreases heavy drinking days

Acamprosate (Campral)

MOA: Made from taurine ; restores NMDA receptor tone in the glutamate system; **GABA-properties** FDA approved 2004 **Targets "negative reinforcement"** Efficacy: higher abstinence, higher % of days abstinent and increased time to 1st drink

Acamprosate (Campral)

SE: Diarrhea, rash.

Dosing: 333mg bid – 333mg tid (1,998 mg) Start once detox is complete Continue taking during slips

Topiramate (Topamax)

- FDA-approved for migraines & epilepsy
- Evidence for alcoholism is good
- Promising for stimulant addiction
- Increases GABA & inhibits glutamate activity
- Carbonic anhydrase inhibitor
- Ask about kidney stones, glaucoma
- Start 25 mg daily, titrate to 200-300 mg daily

Kampman, K. A Pilot Trial of Topiramate for Cocaine Dep. Drug & Alcohol Dep, 2004 Johnson, BA. Topiramate for the Treatment of Alcohol Dependence. JAMA, 2007

Topiramate



Johnson BA et al. JAMA 2007.



Smoking in California

- First state to enact
 - Tobacco control program (1988)
 - Smoke-Free workplace (1994)
 - Indoor smoking bans
- Current smoking prevalence for adults 13.3% (2008) 22.7% (1988)

FDA-Approved Medications

Drug of Abuse	Brand Name	Generic Name
Nicotine	Nicotine Replacement Therapies	Patches, Lozenge, Inhalers, Gums
	Chantix	Varenicline
	Zyban	Bupropion

Nicotine Patch

Slow onset **Continuous delivery** 24 or 16 hour dosing Easy compliance With or without taper Side effects- skin reaction, insomnia OTC



Nicotine Gum

Use every 1 hour Bite and "park" Slow, buccal absorption Acidic foods 1 absorption Side effects- mouth, throat burning Dose: 2mg < 25 cpd4mg > 25 cpd





Bupropion SR (Zyban)

Nonsedating/activating Affects NE and DA Side effects- headache, insomnia **Contraindicated: seizures/ eating** disorder Nicotinic receptor antagonist Start 10-14 days prior to guit date 300mg dose has least weight gain



Varenicline (Chantix)

- Partial nicotinic agonist $\alpha 4\beta 2$
- Attenuates withdrawal
- Decreases craving
- Dosing: Starter Pak, Continuing Pak
- SE: Nausea, H/A, Insomnia
- Black Box Suicidal Ideation
- \$100 per month

Varenicline



Gonzales D. et al., JAMA 2006 296:47-55

Stimulants





Medications Considered for Cocaine

Negative Results

- Desipramine*
- Amantadine*
- Gabapentin
- Bupropion*
- Aripiprazole
- Olanzapine
- Baclofen*

+/Under Consideration modafinil disulfiram propanolol (WD) GVG (vigabatrin) topiramate DHEA **TA-CD** Vaccine buprenorphine N-acetylcystine d-amphetamine

Medications for Methamphetamine Dependence

Negative Results

- Imipramine
- Desipramine
- Tyrosine
- Ondansetron
- Fluoxetine
- Sertraline, paroxetine
- Aripiprazole
- Gabapentin
- N-acetylcysteine
- Topiramate*
- Modafinil*

+/<u>Under Consideration</u> bupropion mirtazapine naltrexone d-amphetamine* methylphenidate



Medications Under Consideration

- Rimonabant (cannabinoid antagonist)
 Associated with SI
- Marinol + Lofexidine
 - Synthetic THC plus adrenergic modulator
- N-Acetyl Cysteine

FDA-Approved Medications

Addictive Disorder	Brand Name	Generic Name
Cocaine	-	_
Methamphetamine	-	_
Marijuana	_	_
Gambling	-	_
Sexual Addictions	_	_
MAT Advantages

- Uses power of science to improve treatment outcomes
- Uses biopsychosocial approach
- Improve treatment retention
- Target symptoms that were previously not reachable by counseling / therapy

MAT Disadvantages

- "Magic Pills"
- May de-emphasize recovery process

 Home, health, purpose, community
- Expensive, time consuming
- Long-term impact not fully known
- Deepens the "generational gap" among those in recovery

Essential Questions of MAT

Aren't I just substituting one drug for another?

Isn't it better for me to be in recovery without medications?

How long do I need to take medication? Could this be life-long? My sponsor got sober without medications, so why can't l?

Our treatment program will never accept MAT. Short Break . . .

What MAT looks like at UCLA

- Outpatient offices
- Appointments 3 days a week
- Patients / families call
 - 1 week up to 6 week waitlist for appointment
- Must have insurance or ability to selfpay

What MAT looks like at UCLA

- Intake: 60 min with MD
 Laboratory studies available on site
- Monthly visits (with frequent communications)
- Therapy off-site, usually
- 12-step highly recommended
- Solo Practice, for all intents and purposes

What MAT looks Like at UCLA

- Electronic records
- Electronic prescriptions
- Paper prescriptions for buprenorphine
- Follow-up visits: 30 min
- Insurance haggling often occurs Prior Authorizations, Visits,

Case Studies of MAT

Case Study #1: Movie Guy

- 48 year old white male, self-referred, requesting Suboxone.
- Heard about Suboxone from friend and wants to try it himself
- He currently takes 6-8 Vicodins per day, experiences withdrawal, money impact and shame from buying it off-market

Case Study #1: Movie Guy

- Works full-time, ample resources, supportive family
- No health concerns except obesity, high cholesterol
- Past history of depression

- What are his treatment options?
- What else should be done at the first visit?
- What are the potential pitfalls in a case like this?
- What are the next steps?

- Screening and Assessment
 - Confirm diagnosis of Opiate Disorder
 - Screen for other addictive disorders
 - Urine toxicology
 - Basic laboratory studies
 - Brief, physical exam
 - Rule out significant, acute psychiatric issues

- After first visit, he receives one week supply of Suboxone Film
- He stays in contact daily on days 1-7 and his wife also is included in the "detox" phase
- He starts an IOP
- Follows-up in one week

- Over the next 6 months, he comes in monthly, stating that Suboxone helps take away urges for Vicodin
- Continues with therapy
- Collateral from wife supports his recovery story
- Sporadic 12-step attendance

- 12 months after starting Suboxone, he says he wants to taper off because it is expensive (doesn't want insurance to know)
- Tapers off within one month
- Symptoms of urges, anxiety, thinking about Vicodin, increased stress return
- Goes back on Suboxone and symptoms subside

- 4 years later
- Remains on Suboxone Film daily
- Uses insurance
- Lost weight
- No relapse
- No side effects
- Maintains periodic 12-step and therapy
- Incredible quality of life described

- 22 yo college senior referred by student psychologist for comprehensive addiction treatment
- Heroin, cocaine and alcohol use disorder
- Deals drugs yet never "caught"
- GPA ok, parents have no idea
- Main concern is "I'm gonna OD"

- During intake, denies SI/HI or presence of psychiatric conditions, other than addiction and anti-social behaviors
- Adamantly refuses rehab, inpatient detox or involving his parents
- Firmly requests Suboxone and says "I'll get it even if you don't prescribe it to me"

- What is the best course of action in this case?
- How should boundaries be set?
- What is the role of MAT here?

- After intake, he agrees to Suboxone but only for "a short while", agrees to therapy and agrees to 12-step support
- After successful outpatient detox, he makes 2 appointments and disappears from care, despite efforts to track and find him

- 6 weeks later, he calls, asking for a refill, saying he stretched out Suboxone but is now out and will relapse unless he "gets a refill"
- Parents remain unaware
- He has stopped or refused doing all other recovery activities

- What do you do now?
 - Give MAT = but not they way intended
 - Not Give MAT = possible OD situation
 - Ambivalence, pre-contemplation, reluctance, denial all operating here
 - Naltrexone / Methadone -- refused

So, What Happened?

- As of September 2016,
 - Choppy compliance with Suboxone
 - No OD, in school, parents know about drug use
 - Weekly MAT visits
 - Weekly therapy
 - Weekly medication dispensing

ASAM developed the National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use to provide information on evidencebased treatment of opioid use disorder.



ASAM Guidelines

- ASAM developed this National Practice Guideline to provide information on evidence--based treatment of opioid use disorder (OUD).
- The Practice Guideline contains recommendations for the evaluation and treatment of opioid use disorder, opioid withdrawal management, psychosocial treatment, special populations, and opioid overdose.

ASAM Guidelines

The medications covered are Methadone. Buprenorphine, Naltrexone (in oral and extended-- release injectable formulations), and Naloxone. The National Practice Guideline is intended primarily for clinicians involved in evaluating patients and providing authorization for pharmacological treatments at any level (physicians, prescribing healthcare providers, medical educators, and clinical care managers)

PCSS - MAT

- PCSS-MAT Mentor Program is designed to offer general information to clinicians about evidencebased clinical practices in prescribing medications for opioid addiction.
- PCSS-MAT Mentors comprise a national network of trained providers with expertise in medication-assisted treatment, addictions and clinical education.
- pcssmat.org/mentoring

Obama Administration Announces Additional Actions to Address the Prescription Opioid Abuse and Heroin Epidemic

March 28, 2016

Action List

- Expand access to treatment
- Create MH/SUD Taskforce
- Prevent Overdose Deaths (naloxone)
- SUD Treatment Parity
- Implement Syringe Services Programs
- Medical Schools Mandated Prescriber Education

Five Ways To Address Opioid Epidemic

- Recognize Opioid Use Disorder
- Increase Access To Treatment
- Properly Dispose of Opiates
- Reduce Overprescribing
- Increase partnerships
- 72 yo, retired female stockbroker referred to Addiction Clinic by PCP for MAT for ETOH Use Disorder, moderate
- Drinks up to 4 drinks per night, wine only
- Consequences memory problems, subjective distress, can't reduce on her own, weight gain, insomnia

- Tried AA three times in last 12 months, without connection
- Did one IOP a year ago and did not like the "chatty" part of it
- Describes ETOH use as enjoyable, triggered by boredom, still views it as pleasurable

- Screening and Assessment
 - Mild, AUD
 - No other addictive disorder
 - No depression, dementia
 - Mild, Generalized Anxiety
 - Socially active but psychologically bored

Initial Treatment Plan

- Naltrexone (Injectable)
- No 12-step
- Therapy as option
- Focus on SAMHSA Domain of Recovery
 - Home
 - Health
 - Purpose
 - Community

- One week post intake, difficulties with insurance ensue (won't cover, very costly, pharmacy unclear, who will do the injection?)
- Switches her to oral naltrexone,

- Immediately notices that "alcohol doesn't mean as much" – within 7 days of starting
- Makes a few, small behavioral changes (gets rid of ETOH in house)
- Pledges to come monthly

- 4 months later, no ETOH use reported mainly because of diminished urges, presence in her mind and, noticing other activities more (i.e. improved attention)
- Feels medication has made a difference that she can "feel"

- Would this have happened without MAT?
- Why did this happen now?
- What will the likely outcome of this case be in 5 years?
- How long will she remain on MAT?

Implementing MAT

Implementing MAT

- Many different, empirically tested models of delivery
 - Differs based on staffing, space, provider capacity, payment structures, program philosophies, etc.
- No ONE model is "the best way" of delivering MAT

MAT Procedures

- Complete thorough assessment to determine appropriateness of MAT
- Develop a plan and oversee provision of MAT services in accordance best practices
- Regular and ongoing assessment will be conducted to ensure the continued appropriateness of care throughout the intervention. (weekly, bi-weekly, monthly)

General Policies of MAT Delivery

- in accordance with Good Clinical Practice Guideline for each medication;
- under the supervision of a medical professional working within his/her scope of practice;
- as part of a comprehensive package of services combining the use of medication with
- counseling, behavioral therapies and other supportive services must be delivered simultaneously. MAT NEVER IN ISOLATION.

Principles for Implementation

- Licensed prescribers operating within their scope of practice assist the client in clinical decision-making, assuring awareness of all appropriate therapeutic alternatives.
- Informed consent for all pharmacotherapies must be obtained, including discussion about the advantages and disadvantages of MAT, taking into consideration the benefits, side effects, alternatives, cost, availability, and potential for diversion

Review MAT Policies

- Policies are reviewed at least annually to ensure
- a) consistency with current practice standards in behavioral health care and b) compliance with federal, state, and county regulations, licensure requirements and accreditation standards.

Recent Major Review of MAT

The MAT models of care that were viewed as particularly successful utilized a designated non-physician staff member in the integration/coordination role

Improving MAT Implementation and Outcome

- Education and outreach critical for reducing stigma associated with MAT,
- increasing the pool of prescribing physicians, and increasing uptake, particularly in settings in which stigma is still high.
- Education was also viewed as critical for improving standards and quality of care.

Challenges to MAT

- including methods for measuring quality of care,
- how to assess patients to better individualize care, optimal psychosocial components of
- MAT, effectiveness of mid-level prescribing, enhancing access to and uptake of MAT in primary care settings,
- effectiveness of newer or alternative medications for OUD

Challenges to MAT

- medications dosing strategies, cost and costeffectiveness, methods for reducing diversion,
- effective implementation methods, optimal methods for coordination and integration of care
- effectiveness of telemedicine approaches

Where do I find a physician who can do MAT?

Finding a MAT Physician

- American Academy of Addiction Psychiatry
- American Society of Addiction Medicine
- SAMHA Buprenorphine Locator
- Other searchable databases
 (commercial, social media, journals)

Essential Questions of MAT

Aren't I just substituting one drug for another?

Isn't it better for me to be in recovery without medications?

How long do I need to take medication? Could this be life-long? My sponsor got sober without medications, so why can't l?

Impact of Medication-Assisted Treatment

- Over 900,000 patients were treated with buprenorphine/naloxone in 2010
- MAT is safe and an effective treatment for opioid dependence
- Treatment
 - is cost-effective
 - can improve functioning across several psychosocial parameters
 - Saves lives when used properly

Further Resources

- SAMHSA Treatment Locator
 - <u>http://findtreatment.samhsa.gov</u>
 - 1-800-662-HELP
- PCSS O; PCSS-MAT
- American Academy of Addiction Psychiatry
- American Society of Addiction Medicine



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