MNCAMH Webinar

Can We Stop Calling It, "Medication-Assisted Treatment"?

Anti-relapse Medications For
Substance Use Disorders

Ian McLoone, LPCC, LADC

Agenda

1. The Importance of Language
2. Neurobiology of Addiction: Anti-relapse Medication Targets
3. Alcohol
4. Opioids
5. Promising future directions

Contact Information

I am happy to discuss any of this information later/between workshops

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Transforming addiction treatment for the 21st Century

Language Matters!

Changing the Language of Addiction

- We are increasingly moving in the direction of less-stigmatizing, non-judgmental language in our field.
- The DSM-5 changes in 2013 eliminated the terms, “abuse” and “dependence”
- In 2017, the US Drug Czar, Michael Botticelli, disseminated a government-wide memo changing federal terminology regarding substance use, Substance Use Disorders, and people in recovery. The Associated Press (AP Stylebook) followed suit.
- Medications play an important role in recovery for many people, yet their use remains taboo in many circles.

Wise Words

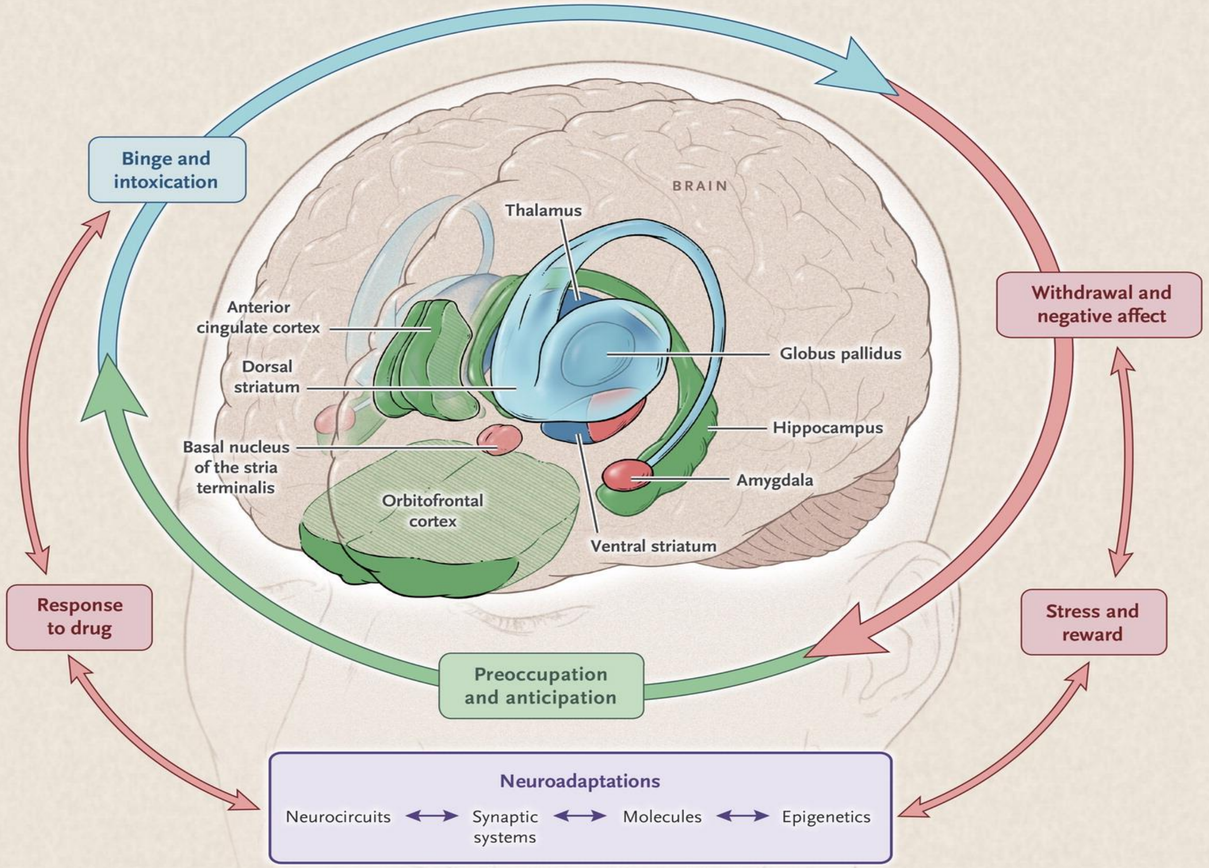
“Language matters. It is far more than superficial concerns about political correctness. The labels applied to individuals affect how they are perceived by others and how they perceive themselves. Stigma and discrimination are couched in a language that reinforces stereotypes and elicits fear. Language that focuses on the person is more respectful and less stigmatizing than language that defines a person in terms of an illness.”

-William L White

Less Helpful	More Helpful
Alcoholic, addict	Person with a substance use disorder
Alcohol/drug abuse	Risky/heavy drinking/use
Slip, lapse	Use episode
Relapse	Recurrence
Harm Reduction	Meeting a person where they’re at, Tx/care
Unmotivated, resistant	Ambivalent about change, non-adherent
Enabler/enabling	Loved one, unskillful support
In denial	Ambivalent about change
Compliant/Non-compliant	Adherent/Non-adherent
Medication-assisted treatment	Pharmacotherapy, anti-relapse medications, treatment

Neurobiology of Addiction and Targets of Anti-Relapse Medications

Implications of Neuroscience

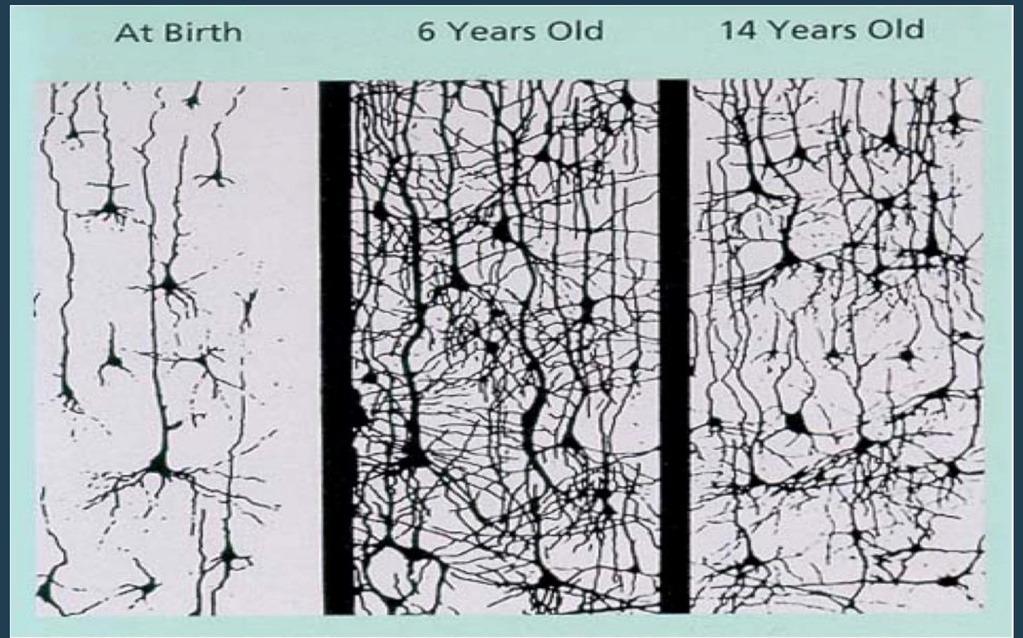


Stage of Addiction	Shifting Drivers Resulting from Neuroadaptations		
Binge and intoxication	Feeling euphoric	Feeling good	Escaping dysphoria
Withdrawal and negative affect	Feeling reduced energy	Feeling reduced excitement	Feeling depressed, anxious, restless
Preoccupation and anticipation	Looking forward	Desiring drug	Obsessing and planning to get drug

Behavioral Changes		
Voluntary action Abstinence Constrained drug taking	Sometimes taking when not intending Sometimes having trouble stopping Sometimes taking more than intended	**Impulsive action** Relapse Compulsive consumption

The field of neuroscience has yielded incredible new findings which are working their way into clinical practice

- Brain anatomy - 100 billion neurons - & genes
- Pharmacological effects of drugs, alcohol and medications
- The importance of the different brain regions in the development and maintenance of addiction
- “Stages of the Addiction Cycle”



Neuroscientific Insights

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Surgeon General Report on Addiction

CHAPTER 2.
THE NEUROBIOLOGY OF SUBSTANCE USE, MISUSE, AND ADDICTION

Chapter 2 Preview

A substantial body of research has accumulated over several decades and transformed our understanding of substance use and its effects on the brain. This knowledge has opened the door to new ways of thinking about prevention and treatment of substance use disorders.

This chapter describes the neurobiological framework underlying substance use and why some people transition from using or misusing alcohol or drugs to a substance use disorder—including its most severe form, addiction. The chapter explains how these substances produce changes in brain structure and function that promote and sustain addiction and contribute to relapse. The chapter also addresses similarities and differences in how the various classes of addictive substances affect the brain and behavior and provides a brief overview of key factors that influence risk for substance use disorders.

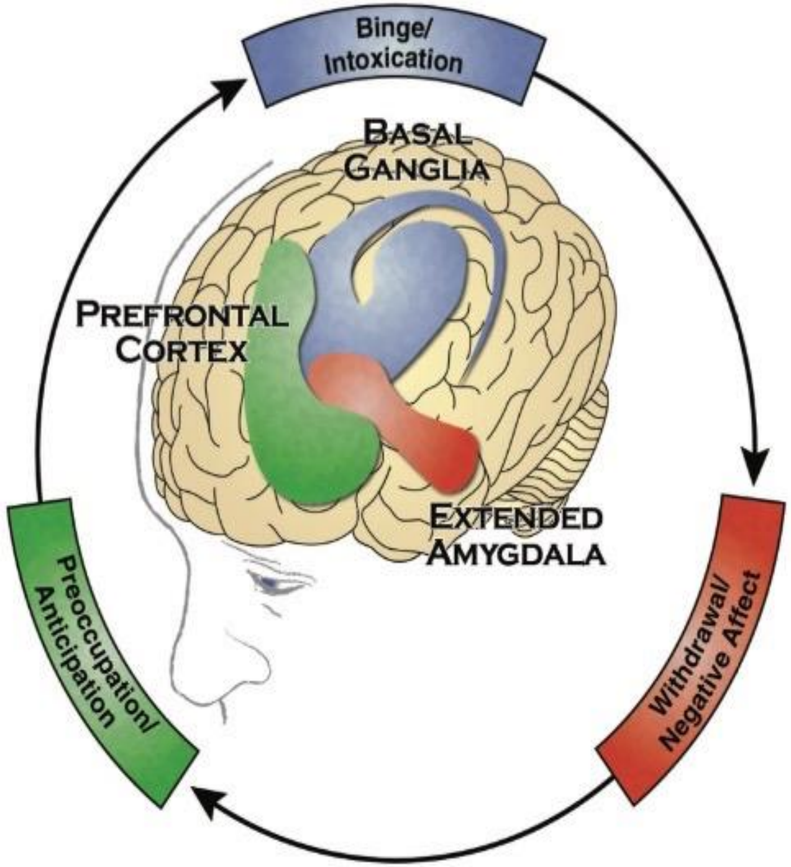
An Evolving Understanding of Substance Use Disorders

Scientific breakthroughs have revolutionized the understanding of substance use disorders. For example, severe substance use disorders, commonly called *addictions*, were once viewed largely as a moral failing or character flaw, but are now understood to be chronic illnesses characterized by clinically significant impairments in health, social function, and voluntary control over substance use.[3] Although the mechanisms may be different, addiction has many features in common with disorders such as diabetes, asthma, and hypertension. All of these disorders are chronic, subject to relapse, and influenced by genetic, developmental, behavioral, social, and environmental factors. In all of these disorders, affected individuals may have difficulty in complying with the prescribed treatment.[4]

This evolving understanding of substance use disorders as medical conditions has had important implications for prevention and treatment. Research demonstrating that addiction is driven by changes in the brain has helped to reduce the negative attitudes associated with substance use disorders and provided support for integrating treatment for substance use disorders into mainstream health care. Moreover, research on the basic neurobiology of addiction has already resulted in several effective

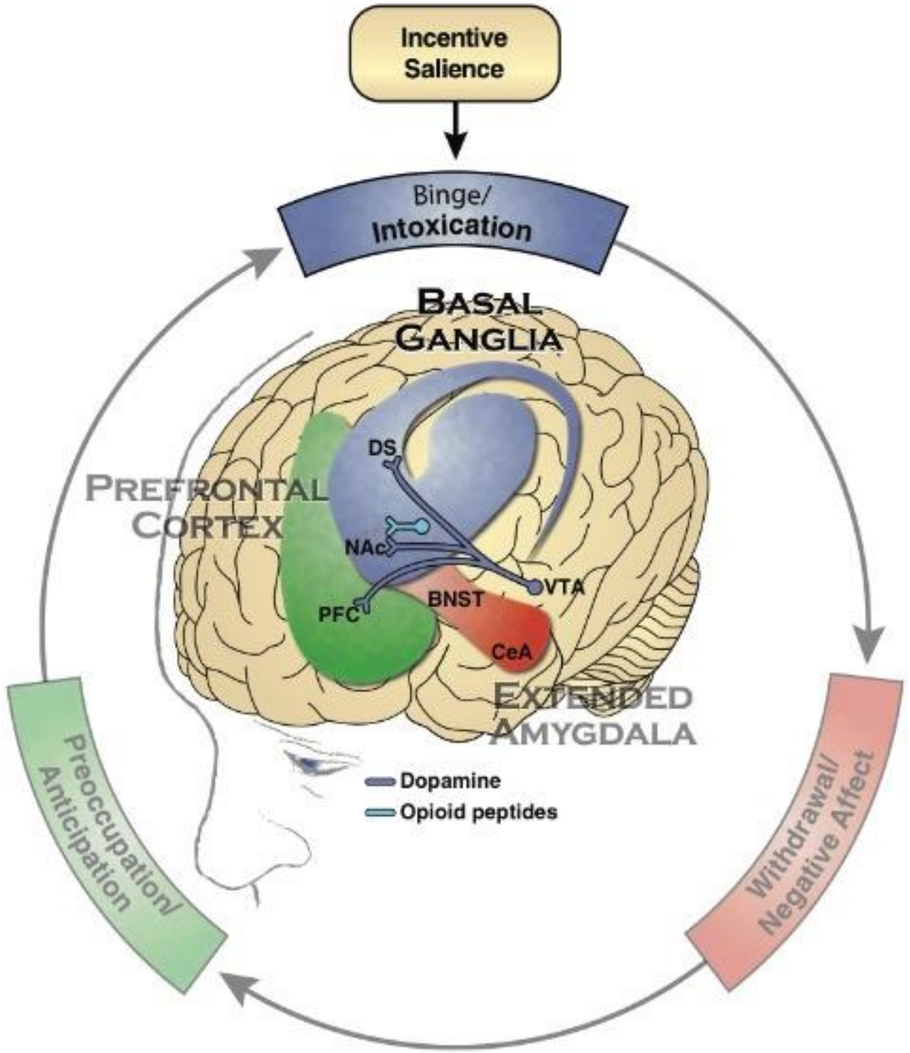
The 3 Stages of the Addiction Cycle

Figure 2.3: The Three Stages of the Addiction Cycle and the Brain Regions Associated with Them



Binge/Intoxication Stage

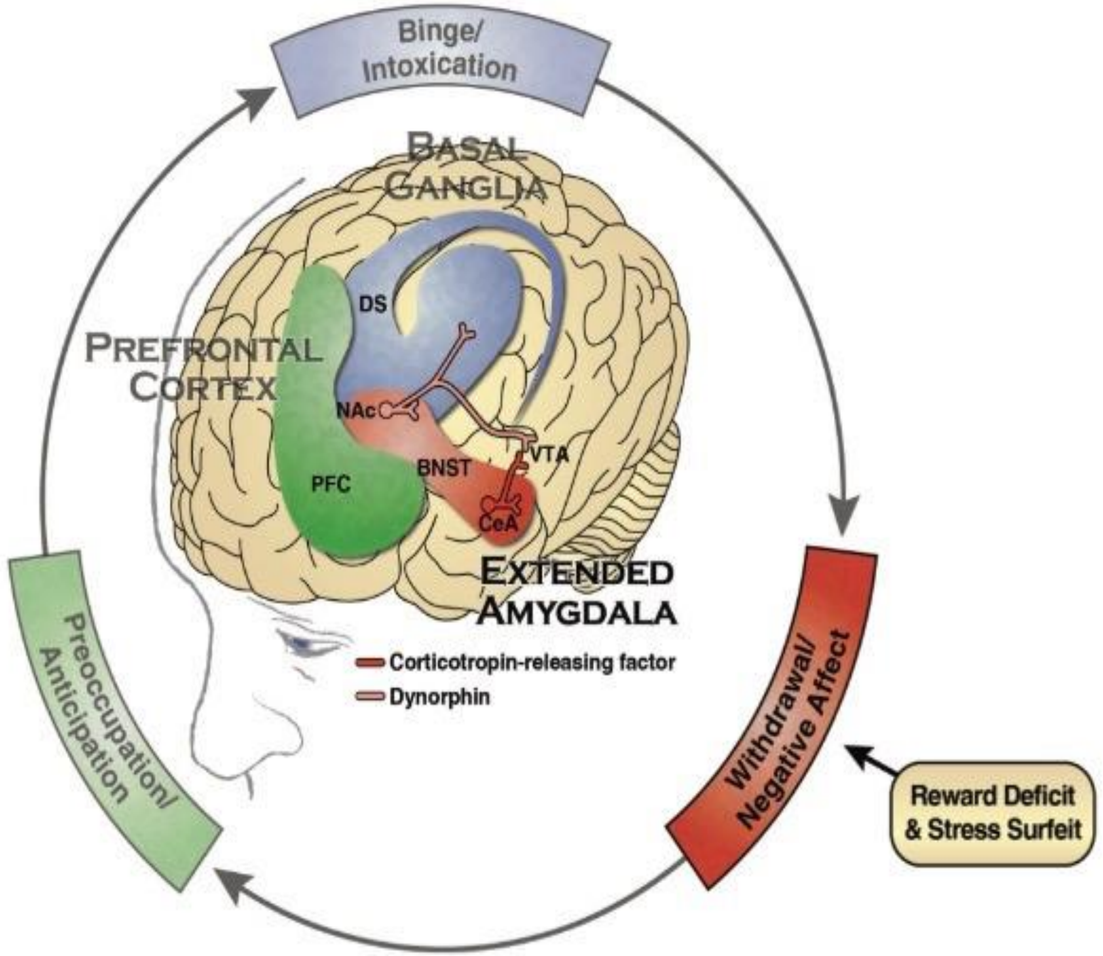
Figure 2.6: Major Neurotransmitter Systems Implicated in the Neuroadaptations Associated with the Binge/Intoxication Stage of Addiction



It’s Not Just Dopamine!
*In drugs other than meth & cocaine, dopamine is likely more involved in the “wanting” than in the pleasure.

Withdrawal/Negative Affect Stage

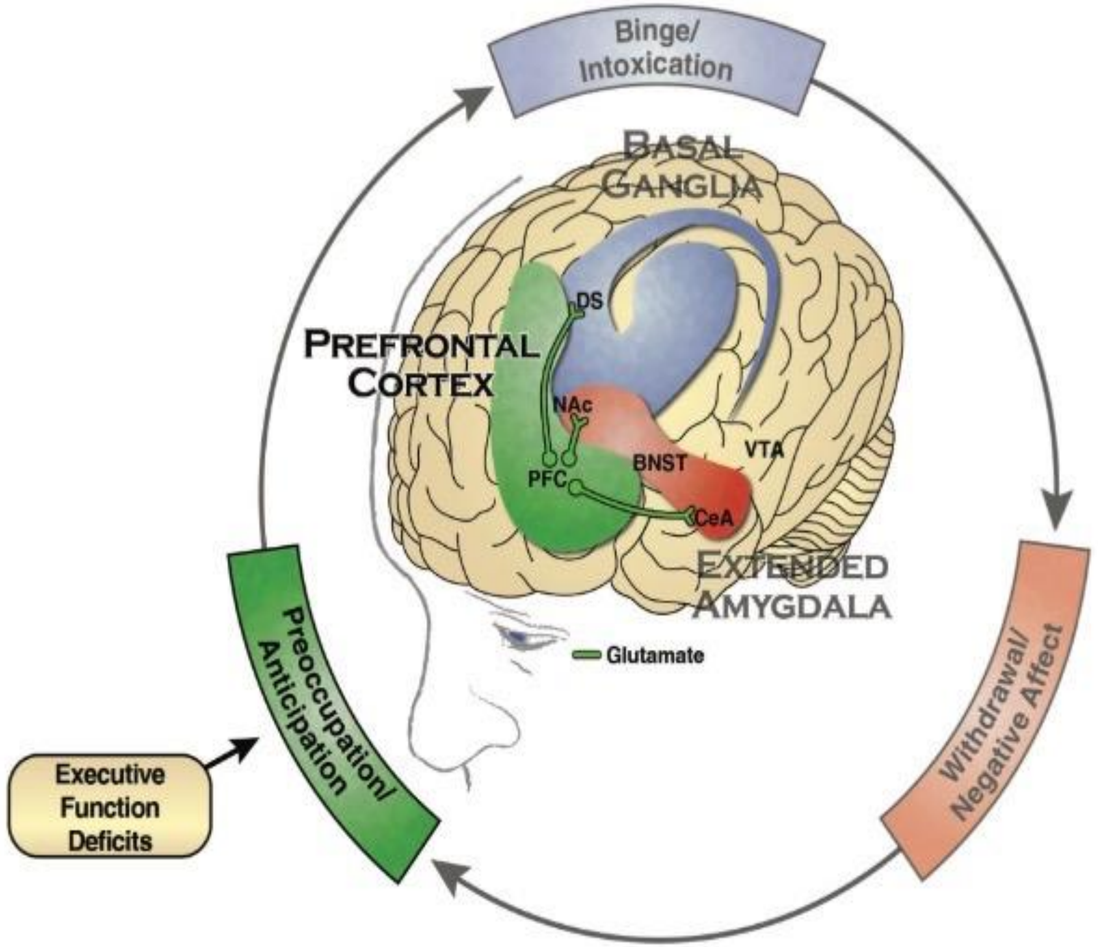
Figure 2.9: Major Neurotransmitter Systems Implicated in the Neuroadaptations Associated with the Withdrawal/Negative Affect Stage of Addiction



As the same system involved in fight/flight gets stressed due to heavy use, a person's ability to tolerate discomfort becomes greatly diminished.

Preoccupation/Anticipation Stage

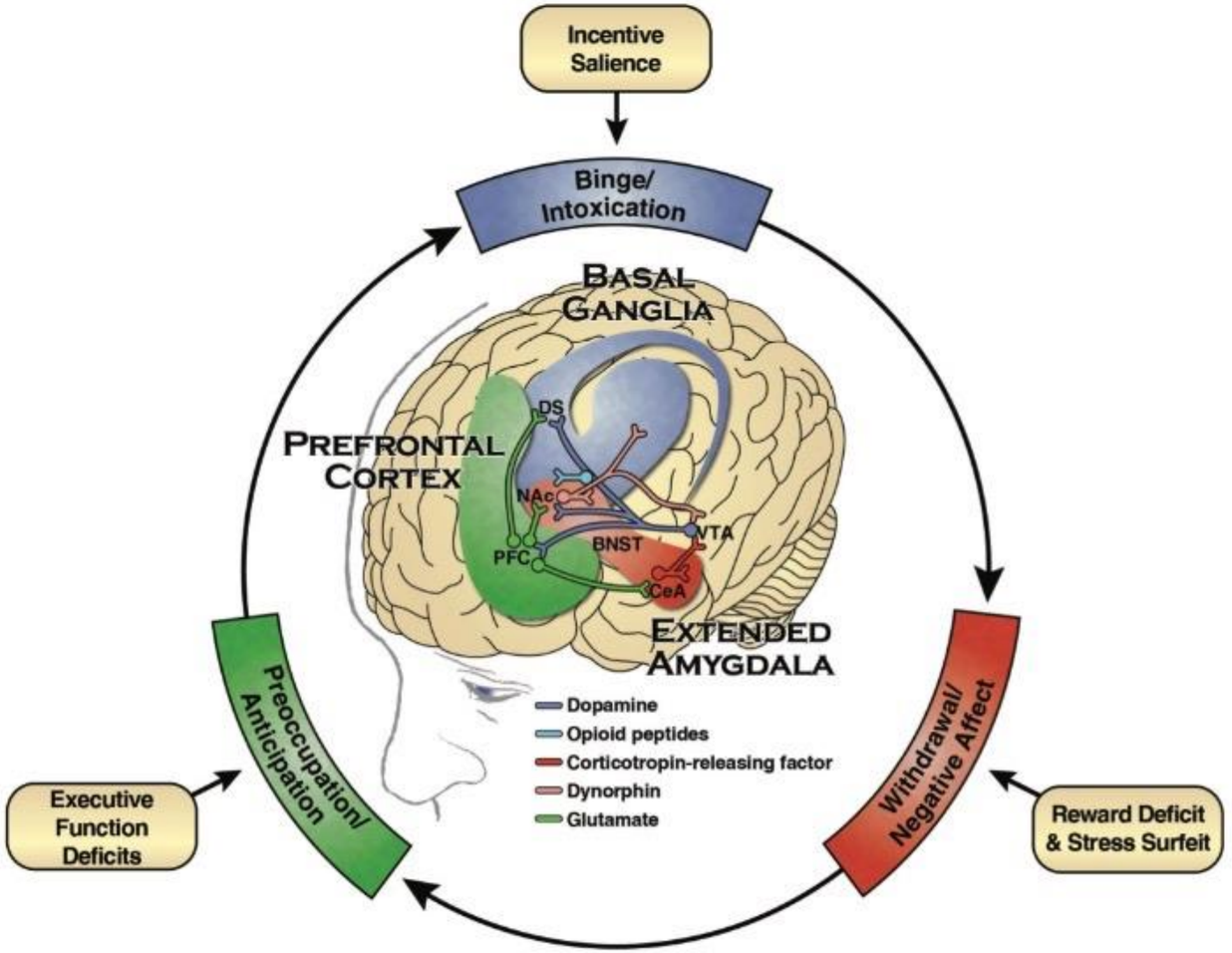
Figure 2.11: Major Neurotransmitter Systems Implicated in the Neuroadaptations Associated with the Preoccupation/Anticipation Stage of Addiction



"This time is gonna be different"
The process of anticipation is a key motivator of continued use, characterized by executive function deficits.

Targets of Anti-relapse Medications

Figure 2.12: The Primary Brain Regions and Neurotransmitter Systems Involved in Each of the Three Stages of the Addiction Cycle



Based on this cycle, what might be ideal targets of anti-relapse medications?

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Why Use ARMs?

- Improve outcomes
- Improve retention
- Reduce risk of recurrences
- Reduce ODs

Anti-Relapse Medications

Anti-relapse Medications

Naltrexone

Disulfiram/
Antabuse

Gabapentin

Baclofen

Anti-relapse Medications

Suboxone/
Buprenorphine

Methadone

Naltrexone

Vivitrol

Medications for Alcohol use Disorder

Naltrexone

Gabapentin

Baclofen

Disulfiram (Antabuse)

Acamprosate (Campral)

Naltrexone

Mechanism of action: mu-Opioid Antagonist

Blocks the initial buzz, reduces craving, helps reduce drinking

Dosing: 50mg tablet 1-2 hours before “witching hour”

Can add additional tablet in AM, also effective PRN dosing

Pros: Great for at-risk drinkers, those with goal to moderate

Safe, few side-effects/drug interactions, quite effective

Cons: Doesn’t work in everyone, contraindicated in opioid therapy, requires good adherence

After first dose, ask if it *changed their experience of drinking*, if not, it doesn’t work

Gabapentin

Mechanism of action: Unclear

Appears to restore GABA-Glutamate balance, reducing “protracted abstinence syndrome”

Dosing: 300mg twice/day and 600mg at night

Can increase as needed. Works best with another ARM, like naltrexone.

Pros: Very helpful reducing anxiety, irritability and insomnia in early abstinence

Very benign, forgiving med with few side effects; well tolerated.

Cons: Not FDA-approved, so lack of significant empirical data. May cause sedation at first.

Can decrease initial dose if sedating. Few, if any, withdrawal risks.

Baclofen

Mechanism of action: GABA-B agonist

Also restores GABA-Glutamate balance, reducing craving and preoccupation.

Dosing: 10mg tid x 7 days, then 20mg tid

Especially indicated in patients with co-existing anxiety disorder. Best in combination with Naltrexone.

Pros: Often helpful reducing anxiety, irritability; improves wellbeing in some patients.

Safe at doses <100mg/day. Can reduce certain types of pain.

Cons: Not FDA-approved, so lack of significant empirical data and no clear dosing guidelines.

May cause sedation at first; high dose safety and efficacy unknown.

Antabuse/Disulfiram

Mechanism of action: Irreversible inhibitor of acetaldehyde dehydrogenase

Leads to build up of acetaldehyde, acting as deterrent.

Pros: Arguably the best medication available for goal of complete abstinence.

Because drinking is not an option, tends to be a significant reduction in craving, preoccupation

Dosing: Usual dose is 250mg/day. Can increase to 500mg/day

Adverse effect is dose-dependent, so the more a patient drinks, the worse they feel.

Cons: Several contraindications (CV disease, previous DER, cirrhosis)

Have seen 2 severe types of adverse reactions: hepatitis, neuropathy

Campral/Acamprosate

Mechanism of action:
Unclear. May reduce hyperglutaminergic state

“Reduces craving”

Dosing:
666mg tid (2 333mg capsules 3x/day)

Can be difficult to ensure adherence.

Pros:
Low side effect, interaction profile.

Diarrhea is common side effect.

Cons:
By far, least persuasive evidence of efficacy.

Works great in rats - if you know any alcoholic rats, they’re in luck!

ARMs for Alcohol

Research into the effect of these medications has shown the following:

- Reduction in total number of drinking days.
- Reduction in number of heavy drinking days.
- Increase in likelihood of abstinence.
- Prevention of relapse/recurrence.
- Reduction in criminal recidivism

Medications for Opioid use Disorder

Methadone

Naltrexone/Vivitrol

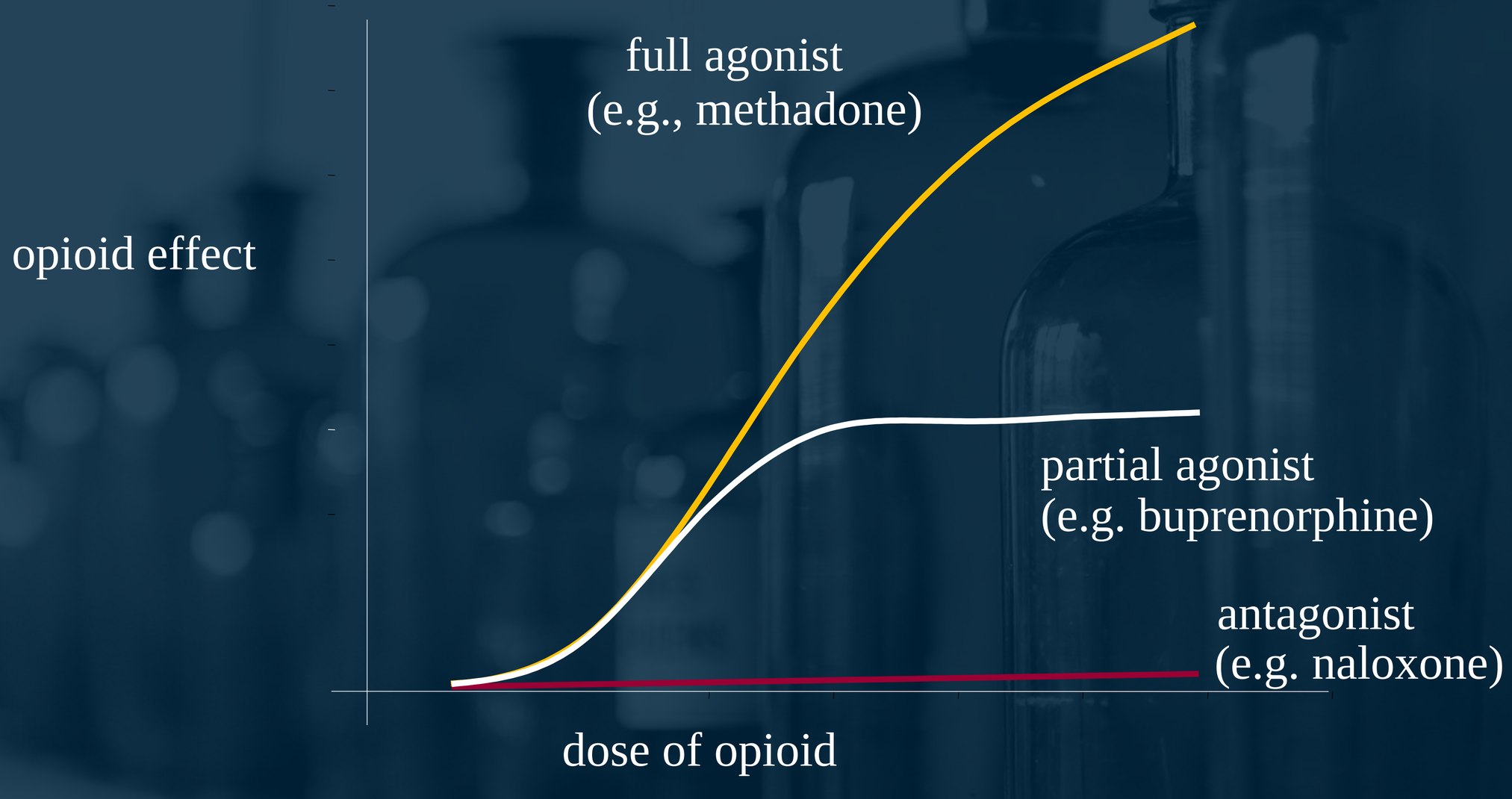
Buprenorphine

Opioids

“Are a class of drugs that include the illicit drug heroin as well as the licit prescription pain relievers oxycodone, hydrocodone, codeine, morphine, fentanyl and others.”
“Are chemically related and interact with opioid receptors on nerve cells in the brain and nervous system to produce pleasurable effects and relieve pain.”

- ASAM, 2016 Opioids Facts and Figures

How do Opioids Work?



Slides adapted from
Adrienne C. Lindsey, MA, DBH

Methadone

The “gold standard” in opioid addiction treatment. Introduced in US in 1960s

Full agonist, once-daily dosing, also used to treat moderate-severe pain

Dosing: Average effective dose 80-120 mg/day

Dose begins @ 30mg, then titrates up 3mg or more/day

Pros: Affordable, highly effective, safe in pregnancy, convenient once-daily dosing

Research consistently shows methadone is cost-effective, increases employment and reduces criminal activity

Cons: Must be dispensed in OTP, strict regulations, burdensome attendance requirements

Common side effects: constipation, excessive sweating, risk of overdose esp w/alcohol

Naltrexone, Vivitrol

Opioid antagonist: binds to opioid receptors, maintains state, blocks other opioids

Prevents user from getting high in event of recurrence

Dosing
Tablets: 50mg once/day
Vivitrol: 380mg monthly intramuscular injection

Dose begins @ 30mg, then titrates up 3mg or more/day

Pros: Blocks the high of opioids, non-addictive, no risk of misuse, monthly injection very convenient

Probably most effective when agonist medications are unavailable

Cons: No effect on craving or withdrawal, very hard to maintain adherence, high risk of OD, not much evidence

Anecdotal reports that by day 21 or so after injection, the full effect wears off

Buprenorphine

Opioid partial-agonist: binds to opioid receptors, partially activates them

Provides craving relief AND blocks additional opioids

Dosing: 16mg or higher 1x/day Available in film, tablet, buccal film, and implant

Dose begins @ 8mg, then titrates up to effective dose

Pros: Blocks the high of opioids, provides full craving relief, presence of naloxone prevents IV use

Office-based prescribing helps reduce stigma, does not require daily attendance

Cons: Can be expensive, few doctors accept insurance, fewer structured housing options

Primary side effects: constipation, excessive sweating (though not as bad as methadone)

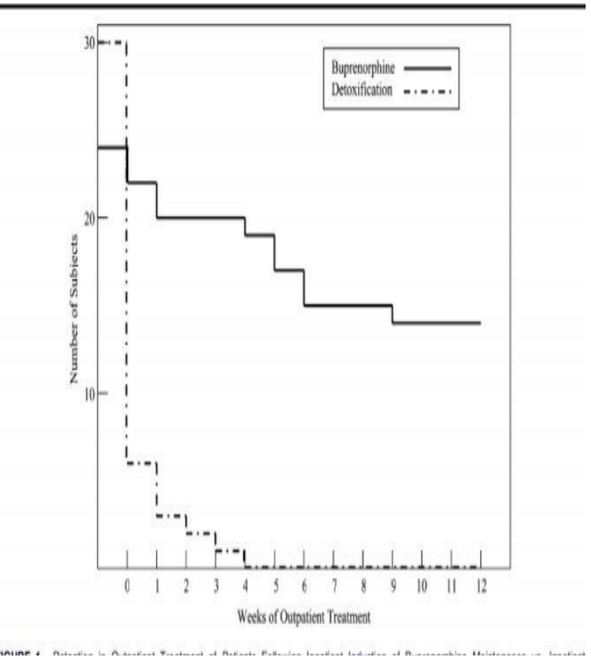
Who is Appropriate for Maintenance Treatment?

- Adults with long-term opioid addiction (arbitrary length of time: >12 m0nths)
- Willingness to use medications
- Especially if previously attempted treatment/recovery
- Is currently abstinent but struggling with cravings, low mood, agitation, etc., all of which are symptoms of opioid deficiency syndrome

What does the research say?

- There has never been a single RCT that showed an abstinence-based treatment could outperform agonist medications.
- At least 80% of patients treated without meds return to opioid use (in some studies, as many as 93-100%). Whereas treatment retention rates are 60-80% with medications while only 15% continue to use opioids.
- Dosing must be adequate.
- Open-ended treatment is key, forced tapers DO NOT WORK
- Patient choice is key. As long as they are well-informed, let them decide!

-Bart G. Maintenance medication for opiate addiction: the foundation of recovery. J Addict Dis. 2012;31:207-225
-Wakeman, S. E. (2016). Using science to battle stigma in addressing the opioid epidemic: opioid agonist therapy saves lives. *The American journal of medicine*, *129*(5), 455-456.



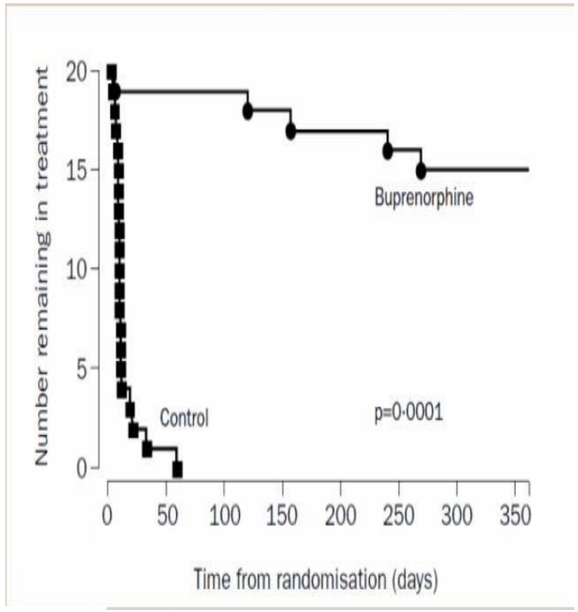
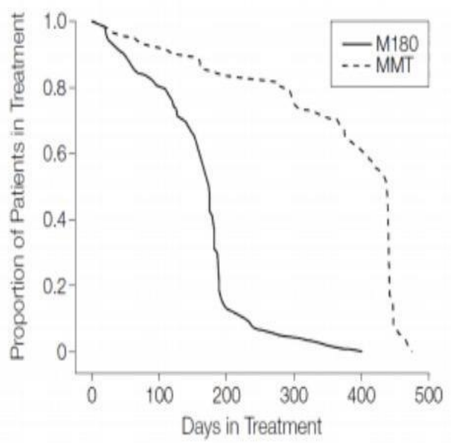
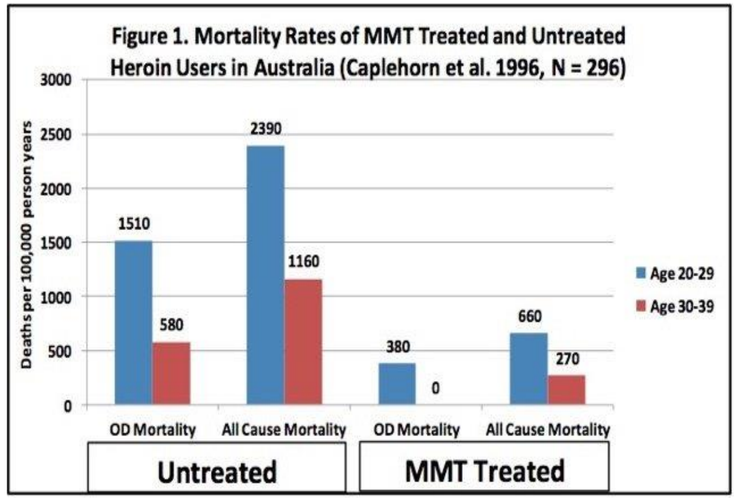


Figure 3. Survival Function by Treatment Group



Proportion of study participants in treatment by group ime. M180 indicates 180-day methadone- d detoxification; MMT, methadone mainte- treatment. For significant differences between ions, Wilcoxon χ^2_1, 85.0 ($P<.001$).



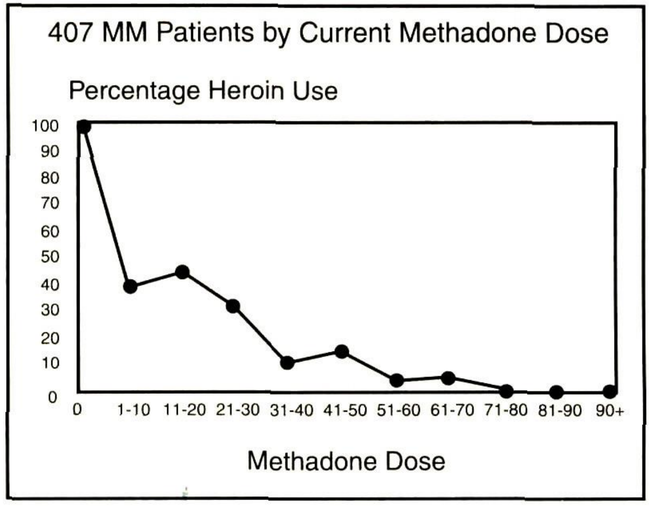
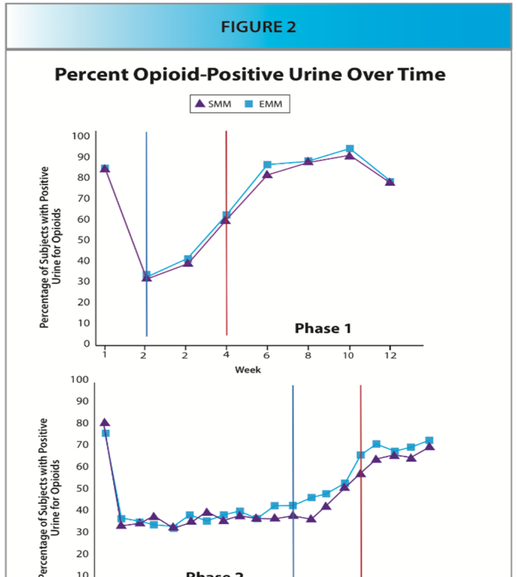


Figure. *Heroin use in past 30 days. From: Payte JT, Khuri ET. Principles of methadone dose determination. In:* State Methadone Maintenance Treatment Guidelines. *Rockville, MD: Center for Substance Abuse Treatment, Substance Abuse and Mental*



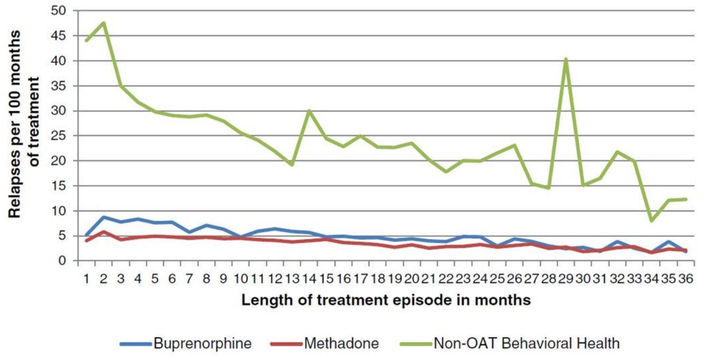


Fig. 1. Relapses during treatment among MassHealth members who received treatment for opioid addiction between 2003 and 2010[1]. [1] N = 18,866 episodes of buprenorphine treatment, 24,309 episodes of methadone treatment and 31,220 episodes of non-OAT behavioral health treatment in month 1. 33% of buprenorphine episodes, 52% of methadone episodes, and 12% of non-OAT treatment episodes lasted 12 months or more. 13% of buprenorphine treatment episodes, 27% of methadone episodes, and 1% of non-OAT treatment episodes lasted 24 months or longer.

Stimulants: Promising Future Directions

Baclofen

Adderall + Topamax

Contingency Management

Psychedelic-Assisted Therapies

Psilocybin

Ibogaine

Ayahuasca

MDMA

LSD

Psychedelic-Assisted Therapies

- https://drive.google.com/file/d/0B5xoah_OJtrORXVwd1lMeWNQcHM/view?usp=sharing
- http://journals.sagepub.com/toc/jopa/30/12
- http://www.slate.com/articles/technology/future_tense/2017/01/the_war_on_drugs_halted_research_into_the_potential_benefits_of_psychedelics.html
- https://www.nytimes.com/2016/12/01/health/hallucinogenic-mushrooms-psilocybin-cancer-anxiety-depression.html
- https://docs.google.com/document/d/14WSmmC_rsMkqTmxnTdoDOezego3jEd_O3EYyH2qb6Pk/edit?usp=sharing

The Role of the Non-Prescriber

What is the Role of the Non-Prescriber?

- Assess adherence and develop strategies to enhance the likelihood of good adherence.
- Assess for side effects or adverse reactions and communicate them to the prescriber.
- Explore and discuss the patient’s feelings (eg, ambivalence, mistrust, idealization, etc.) about their medications and what they mean or do not mean.
- Build on and complement the effects of the medication.

Contingency Management

- The provision of rewards or tangible incentives for desired behavior - ex. $5 gift card for a week of substance-negative UAs
- Draws on application of operant conditioning, using reinforcement to promote behavior change
- Shown to be highly effective for SUD and is the only consistently effective intervention for stimulants
- Rewards and contingencies must be clearly defined, predictable, and consistent

Higgins, S. T., & Petry, N. M. (1999). Contingency management. *Alcohol Research & Health*, *23*, 122-7.

Community Reinforcement and Family Training

- Developed by psychologists at UNM
- An evidence-based approach to training family and concerned others to enhance a loved one's' motivation to enter treatment/get help
- Skills-based program to improve communication and change the way that the family interacts with the substance user
- Uses strategies to reward desired behaviors and disincentivize undesired behaviors
- Shown to be more effective than Johnson Institute-style "intervention" or simply sending the family to Alanon

Source: http://motivationandchange.com/outpatient-treatment/for-families/craft-overview/

Questions and Discussion

THANK YOU!

References (additional provided on request)

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