WELCOME TO THE ADDICTION ALLIANCE OF GEORGIA'S

COMPREHENSIVE OPIOID RESPONSE SYMPOSIUM

Scan the QR code to check in for CME/CE credits.

Addiction Alliance of Georgia

EMORY HEALTHCARE | Hazelden Betty Ford Foundation

HOUSEKEEPING

- 9am – 4pm EST
- Breaks & Lunch
- Panel Session & Sticky Notes
- CME / CE

Joint Providership Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Emory University School of Medicine, the Addiction Alliance of Georgia and the Hazelden Betty Ford Foundation.
The Emory University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Physician designation statement
The Emory University School of Medicine designates this live activity for a maximum of 4 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Neurobiology of Substance Use Disorder

Using science to reduce stigma

Stephen M. Delisi, MD

YourPath Care, PLLC

Hazelden Betty Ford Graduate School of Addiction Studies

Hazelden Betty Ford Foundation

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Disclosures and Contact Info

- Employee of YourPath, Inc and YourPath, PLLC
- Adjunct Assistant Professor – Hazelden Betty Ford Graduate School of Addiction Studies
- On-Call Physician Consultant Trainer - HBFF

- Stephen M Delisi, MD
- Steve@yourpathhealth.org
- SDelisi@hazeldenbettyford.edu

Learning Objectives

- Reduce stigma related to substance use disorders (SUDs)
- Describe three primary reinforcements associated with the initial use of addictive substances
- Illustrate neurobiological underpinnings to the three stages of substance use disorders
- Apply this neurobiology to direct clinical interactions with patients with SUDs
- Explore how attachment and trauma play a role in the development and maintenance of SUDs

Bias – Substance Use Disorders

Did the person **CAUSE** it?

The appearance of intentional participation in the development of a condition.

Can the person **CONTROL** it?

Are there factors within a person's abilities to interrupt the course of illness?

"They found a way to get drugs, why can't they find their way to get treatment?"

Kelly JF, Dow SJ, Westerhoff C. Does Our Choice of Substance-Related Terms Influence Perceptions of Treatment Need? An Empirical Investigation with Two Commonly Used Terms. Journal of Drug Issues. 2010;40(4):805-818.

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Neurobiology of Substance Use Disorders

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Initial Reinforcements

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Intersection of ACEs/Trauma and SUD

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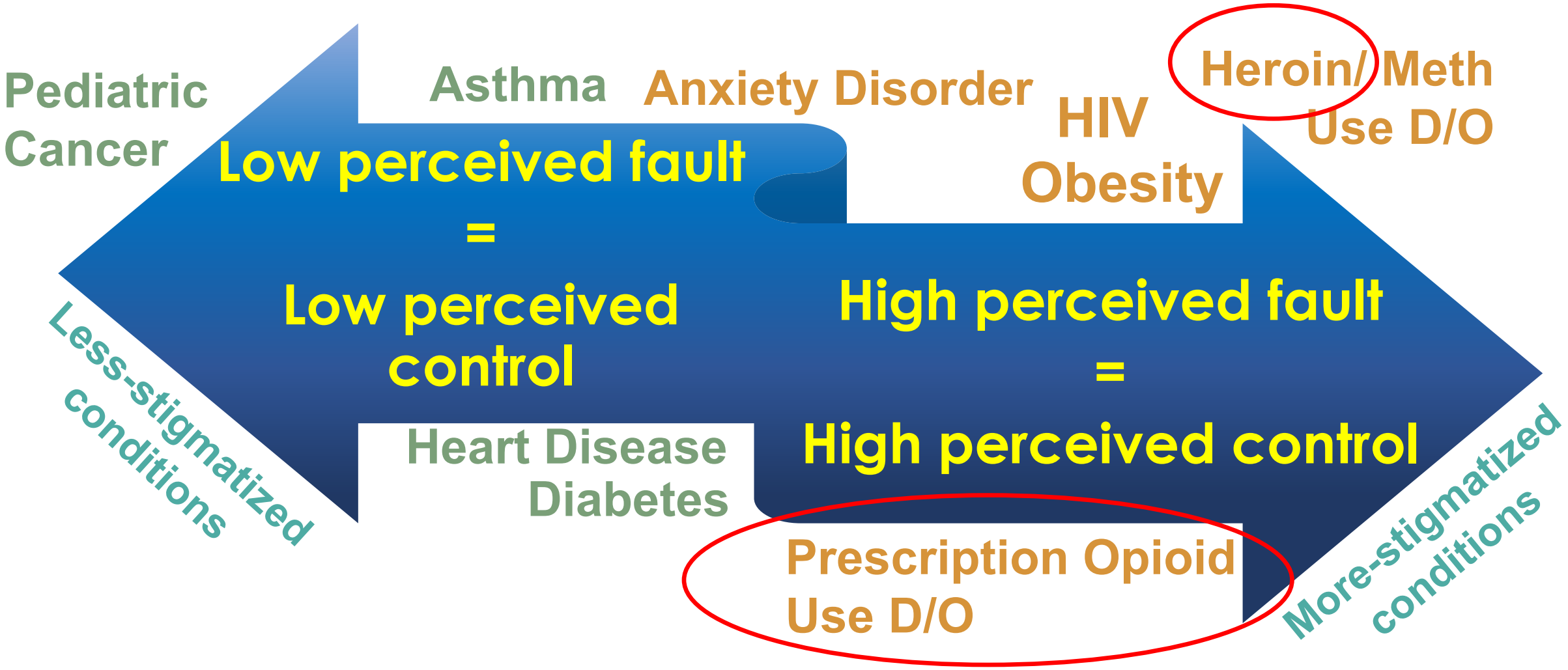
Cause and Control Continuum



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Neurobiology of Substance Use Disorders

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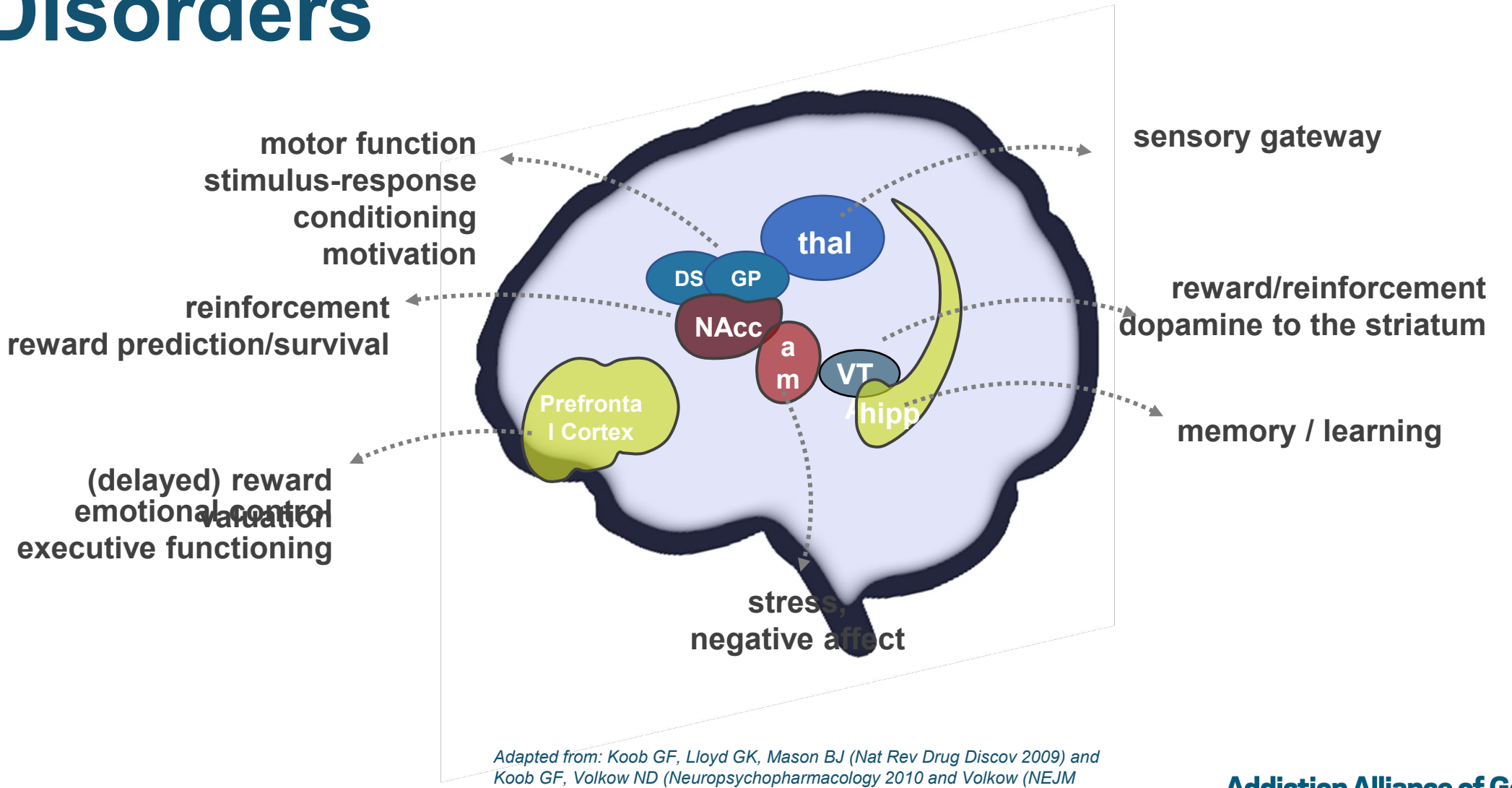
Pathophysiology

While there are some unique features at the molecular, cellular, and behavioral levels,

all substance use disorders share aberrations in the same CNS pathways

So, the Golden Rule is that multiple substance use disorders at the same time is the NORM, not the exception

Neurobiology of Substance Use Disorders



Adapted from: Koob GF, Lloyd GK, Mason BJ (Nat Rev Drug Discov 2009) and Koob GF, Volkow ND (Neuropsychopharmacology 2010 and Volkow (NEJM 2016)) and Volkow ND, et al. (2019). The Neuroscience of Drug Reward and Addiction. Physiol Rev, 99: 2115–2140.

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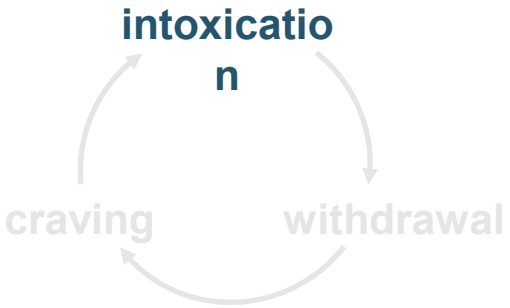
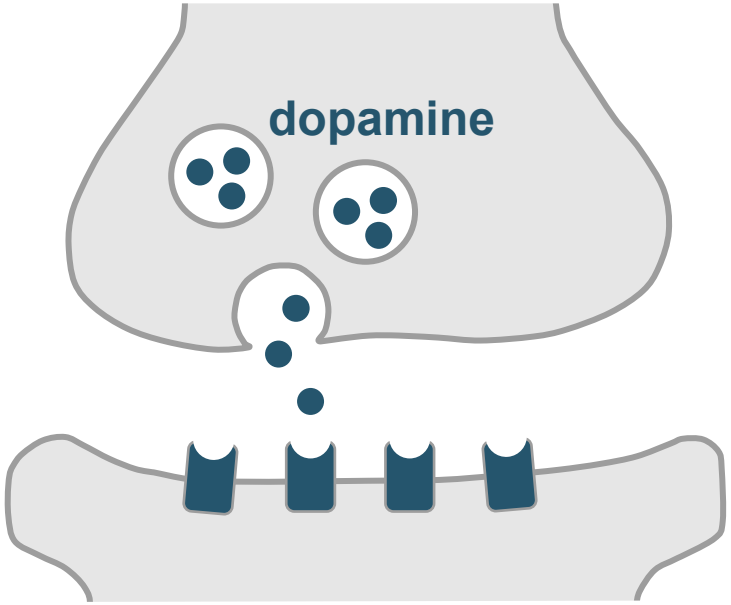
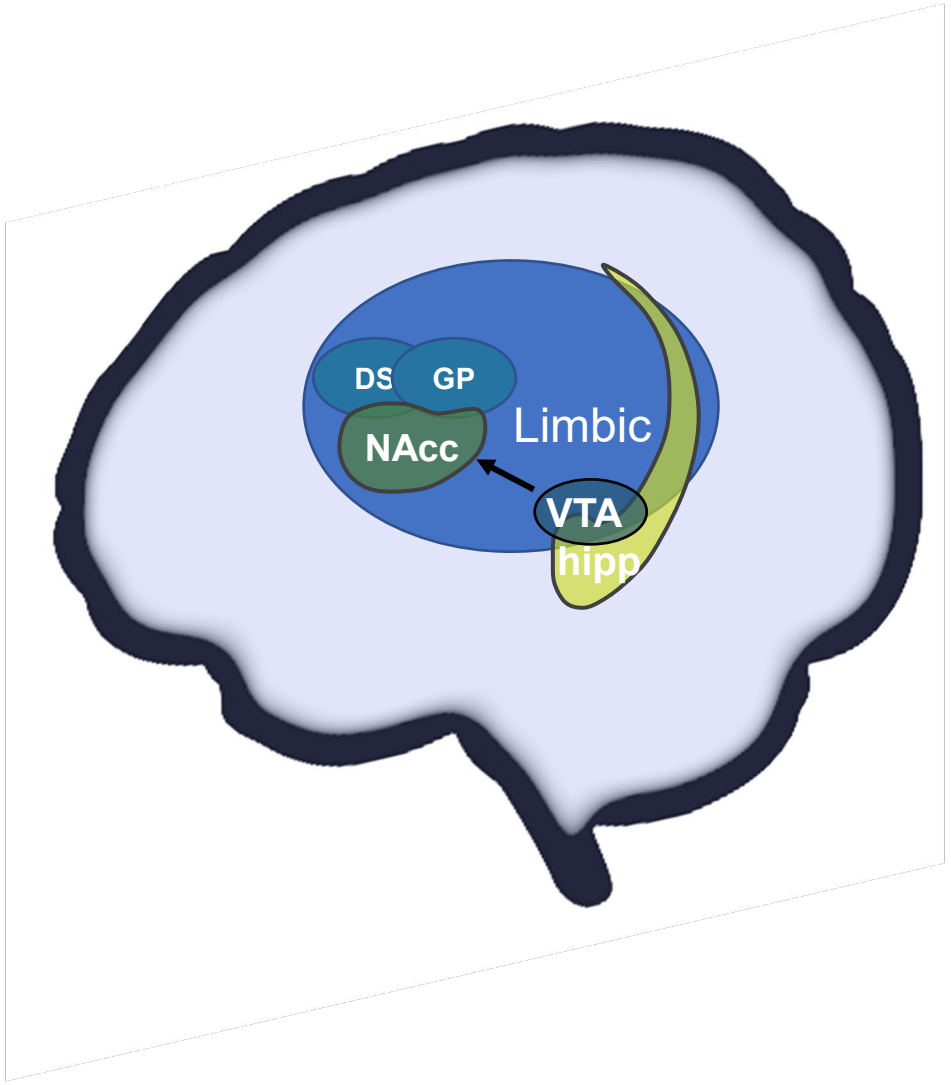
Intoxication & Reward







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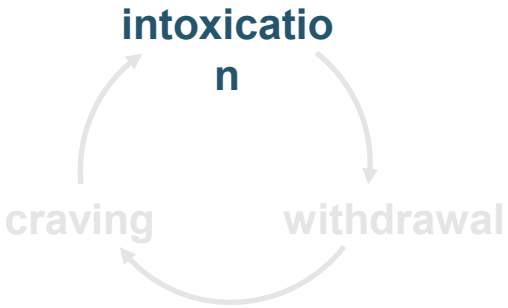

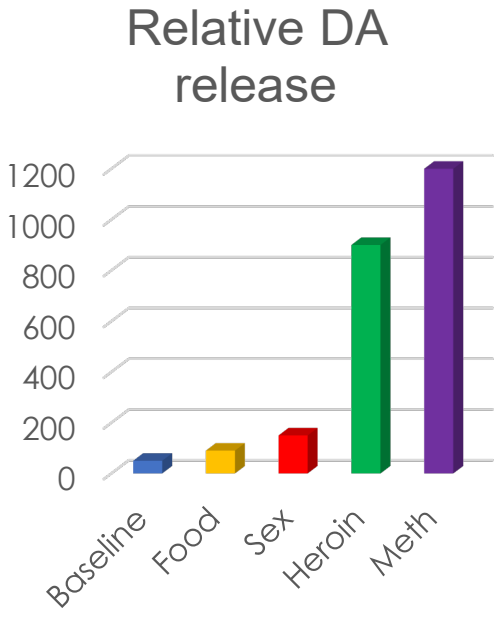

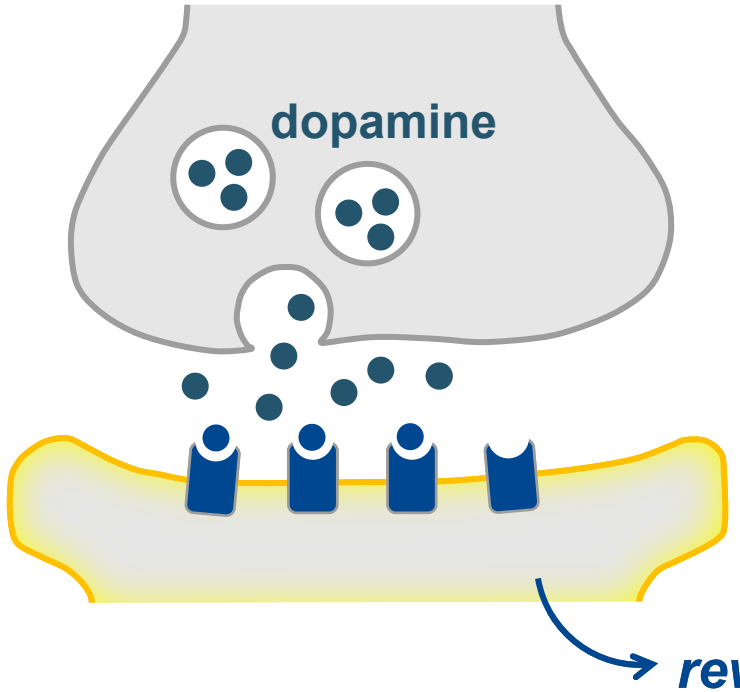

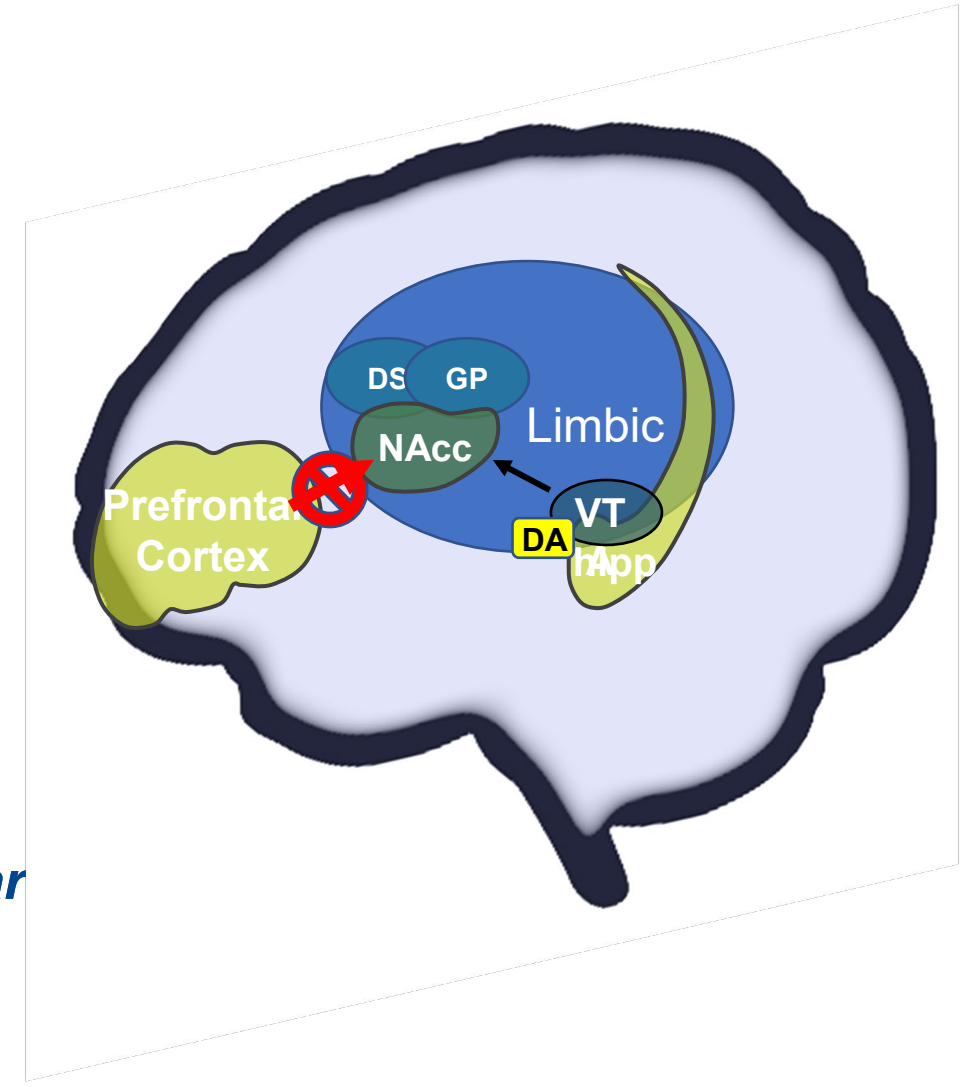

Source: Excerpt of a 2015 presentation for CHCF by addiction specialist R. Corey Waller, MD, medical director of the Center for Integrative Medicine at Spectrum Health Medical Group in Michigan. National Institute on Drug Abuse

Adapted from: Koob GF, Lloyd GK, Mason BJ (Nat Rev Drug Discov 2009) and Koob GF, Volkow ND (Neuropsychopharmacology 2010 and Volkow (NEJM 2016)) and Volkow ND, et al. (2019). The Neuroscience of Drug Reward and Addiction. Physiol Rev, 99: 2115–2140.

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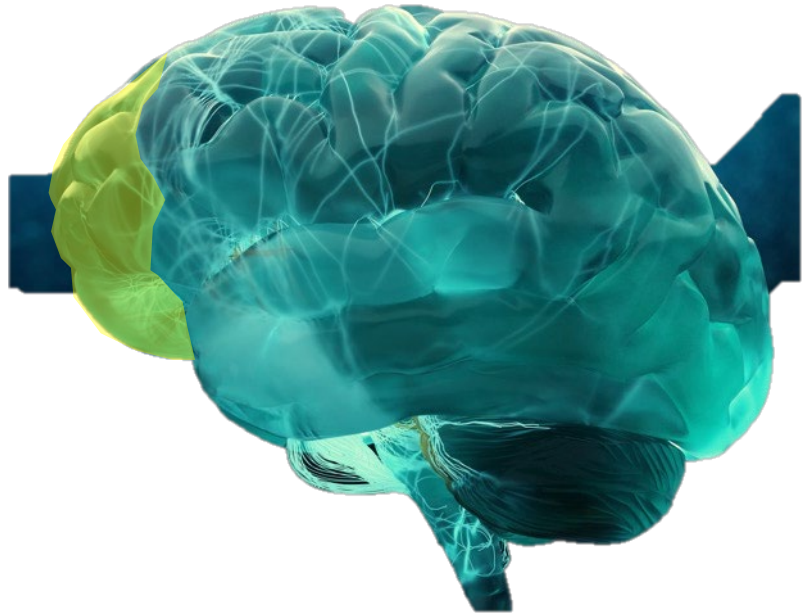
Signs of prefrontal cortex deficits

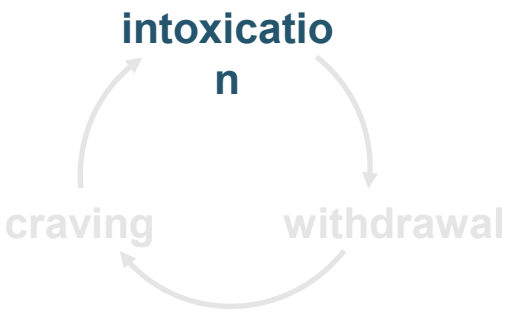
NON-CLINICAL TERMS
(what we all see lived out, stigmatizing):

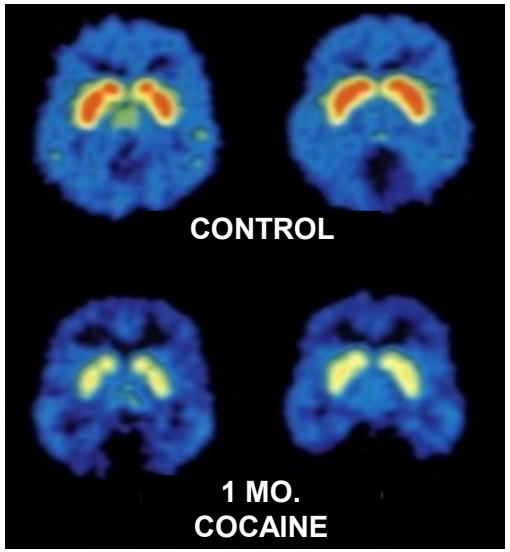


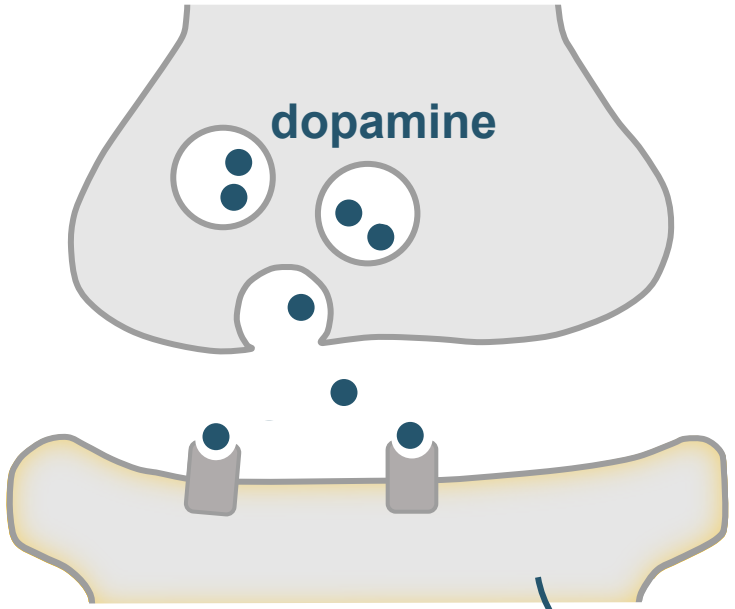
- **Inability to objectively assess oneself**
- **Poor judgment**
- **Inability to learn from experience**
- **Decreased attention span**
- **Becoming easily bored**
- **Argumentative**
- **Thin skinned**
- **Self-centered**
- **Disorganized**

(We need to check our own reactions)

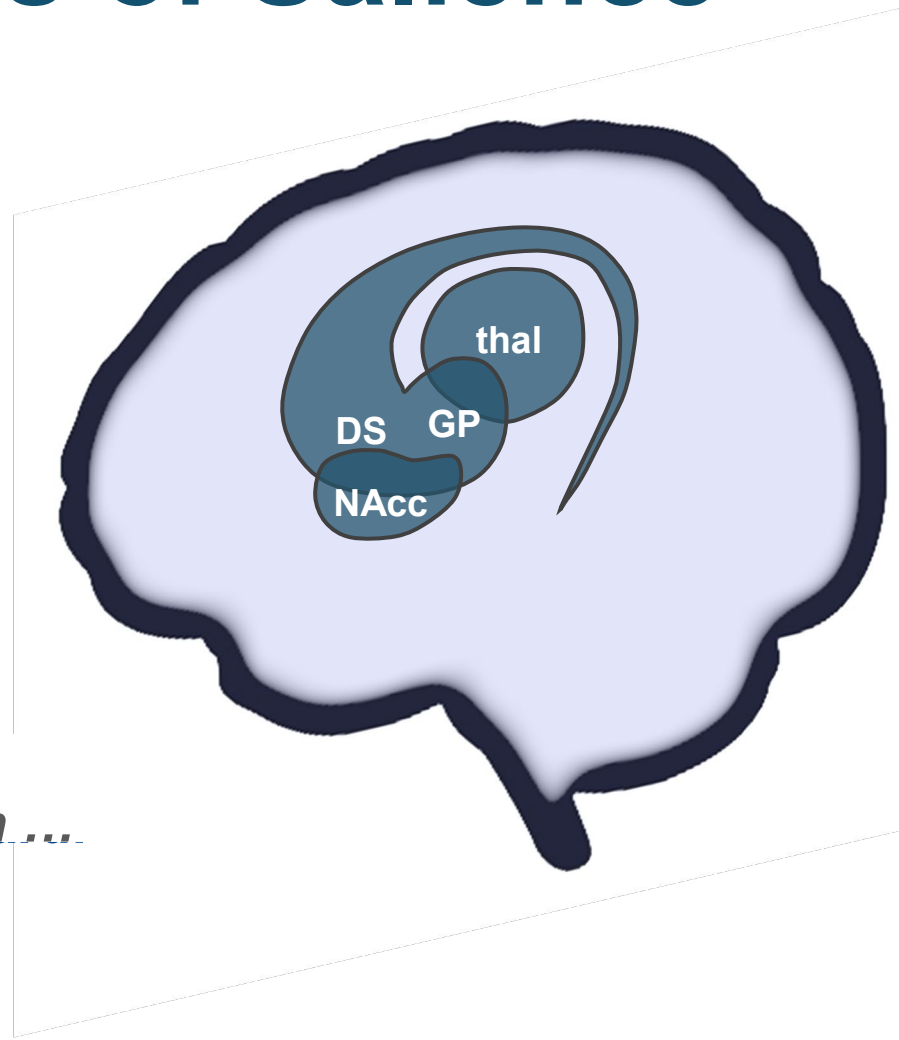
Neuroadaptation & Loss of Salience







blah …



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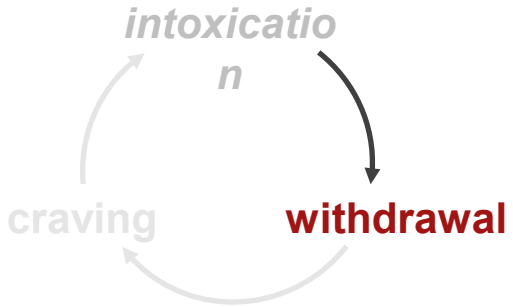
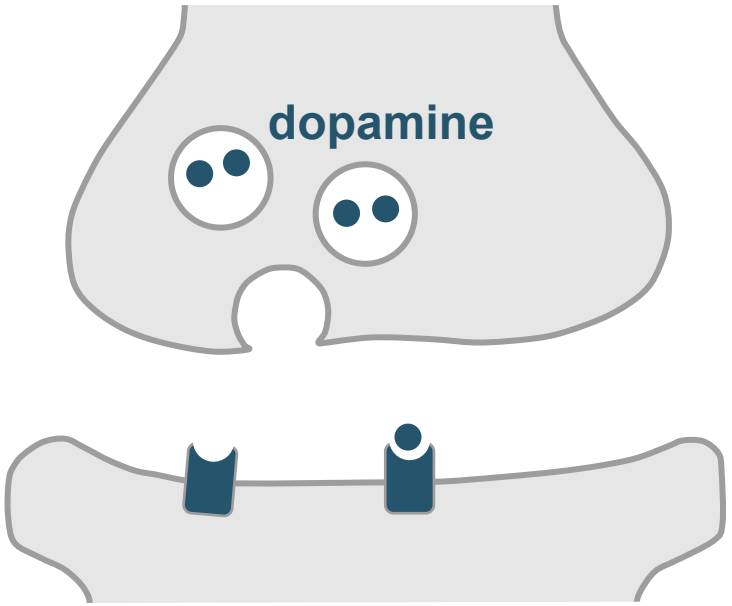
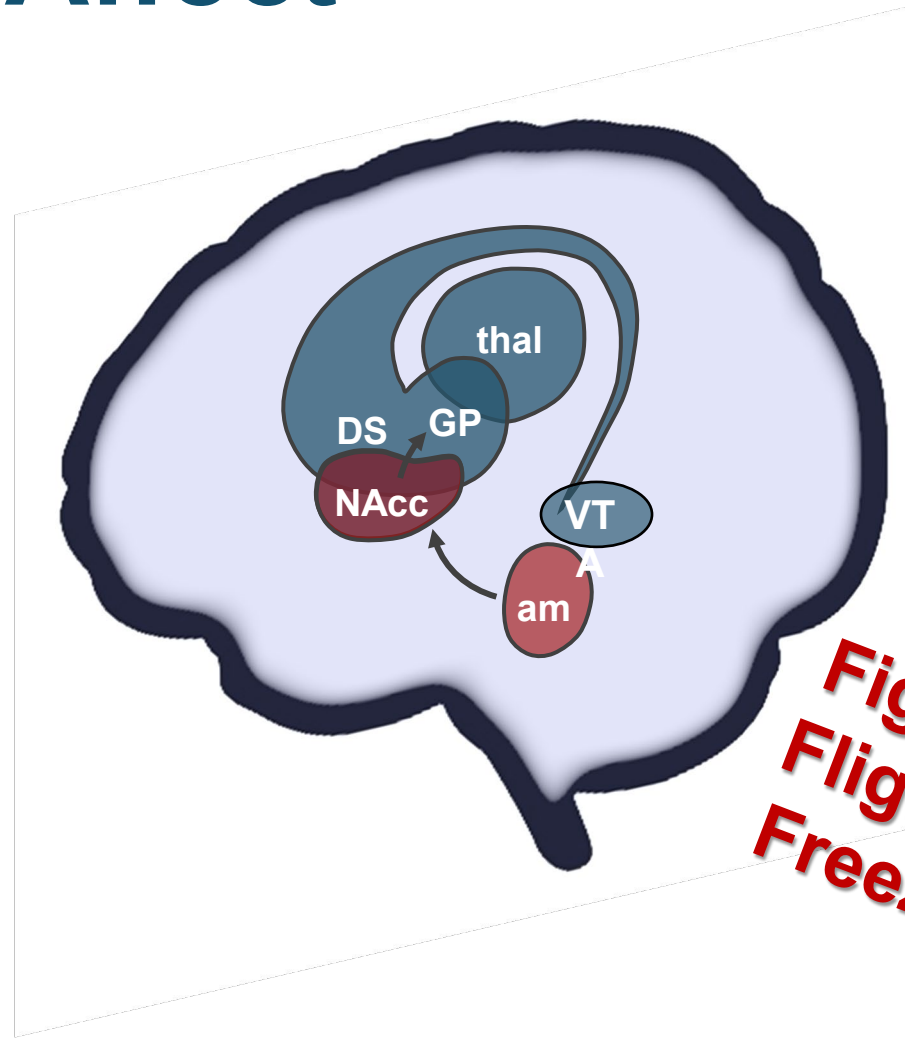
Withdrawal & Negative Affect





GABA
Glutamate
DA
KAPPA



Fight,
Flight,
Freeze

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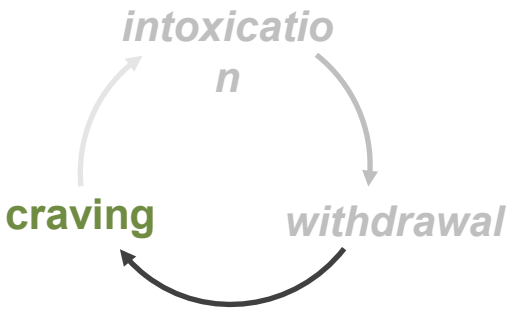
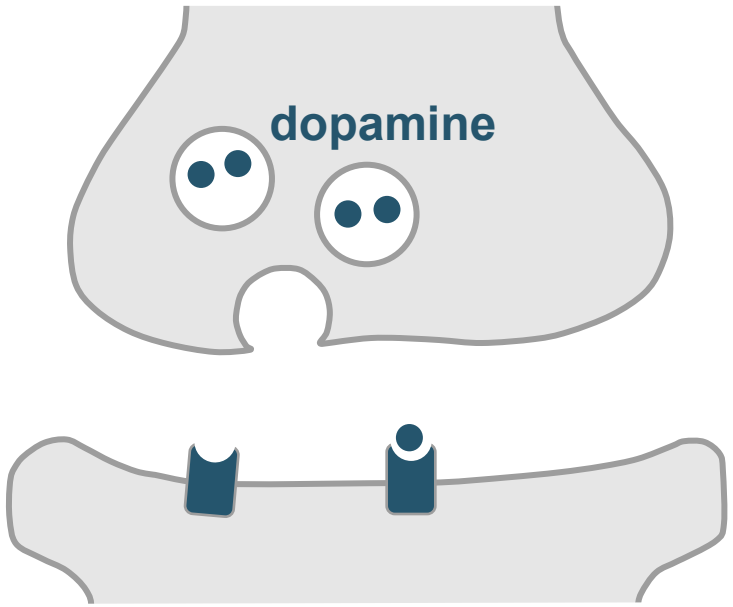
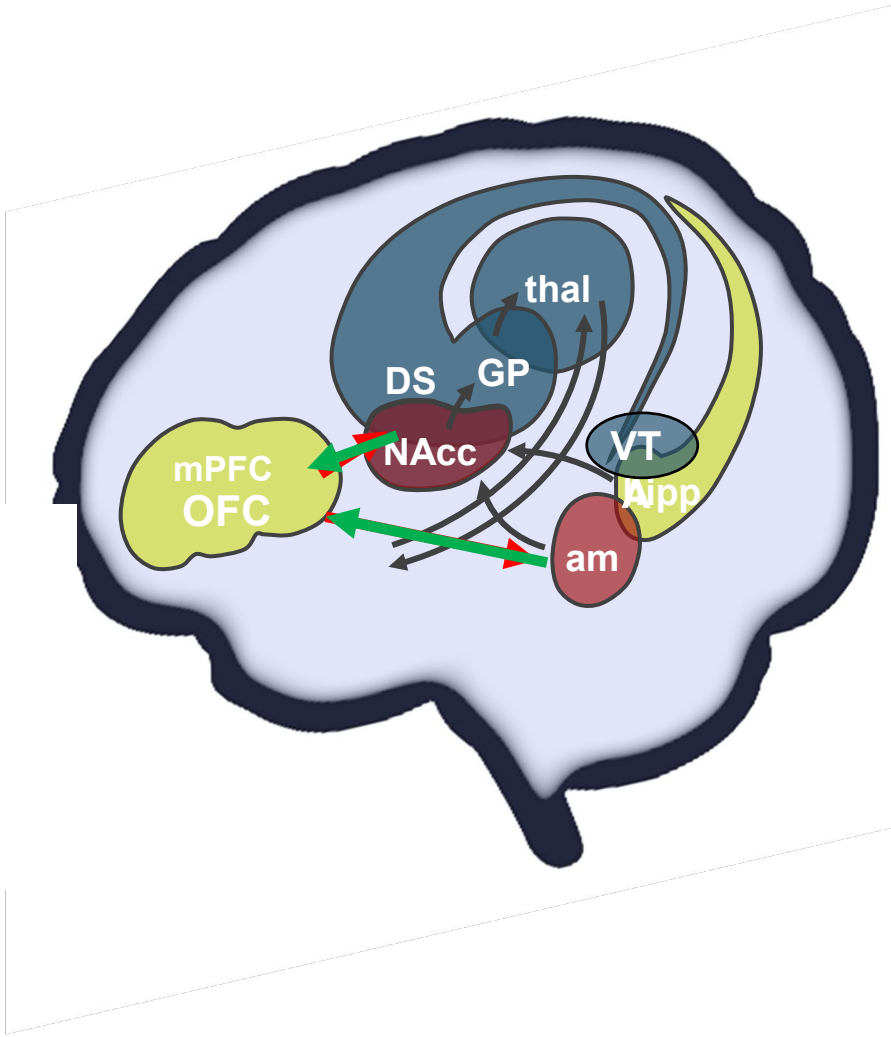
Craving / Preoccupation





LTP - Glutamate



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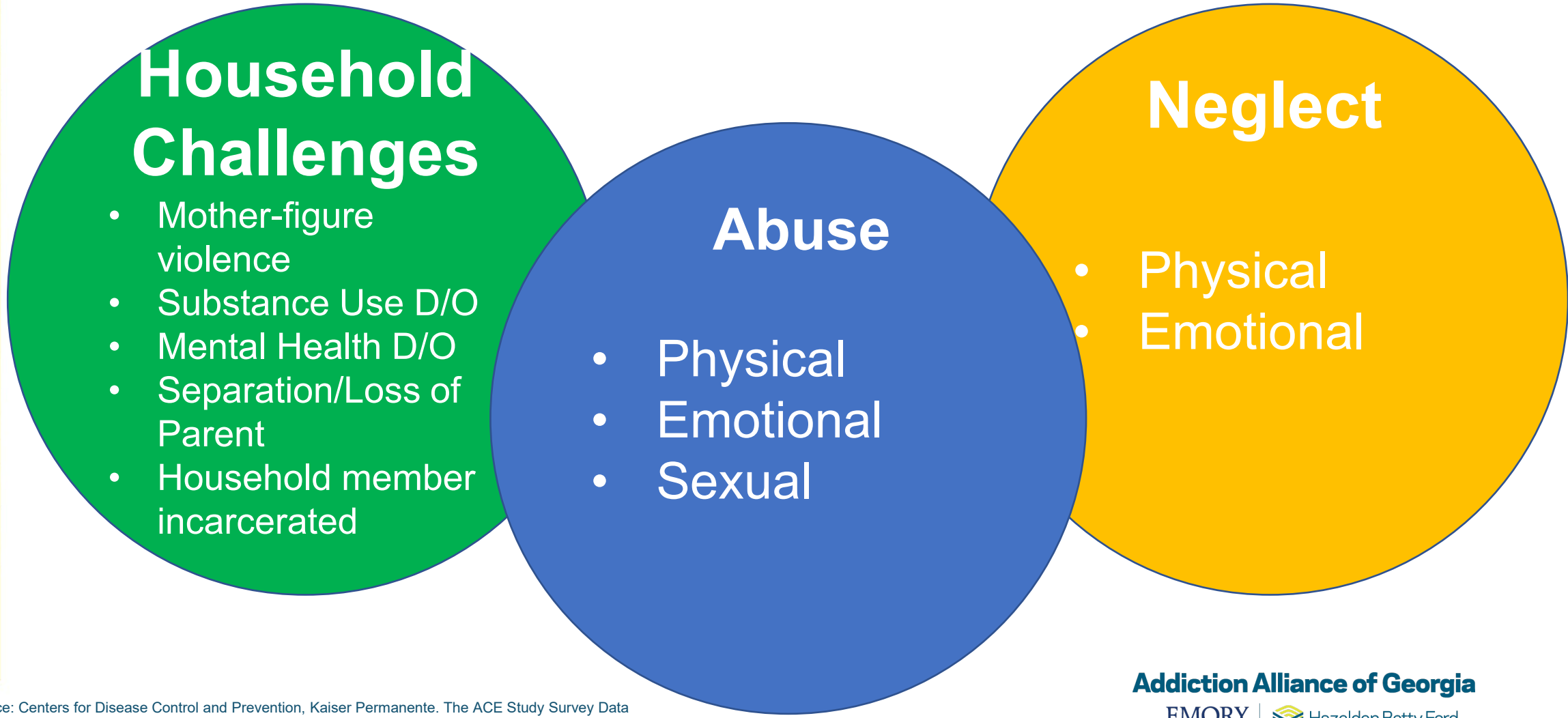
Adverse Childhood Experiences (ACEs)



Source: Centers for Disease Control and Prevention, Kaiser Permanente. The ACE Study Survey Data [Unpublished Data]. Atlanta, Georgia: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2016.

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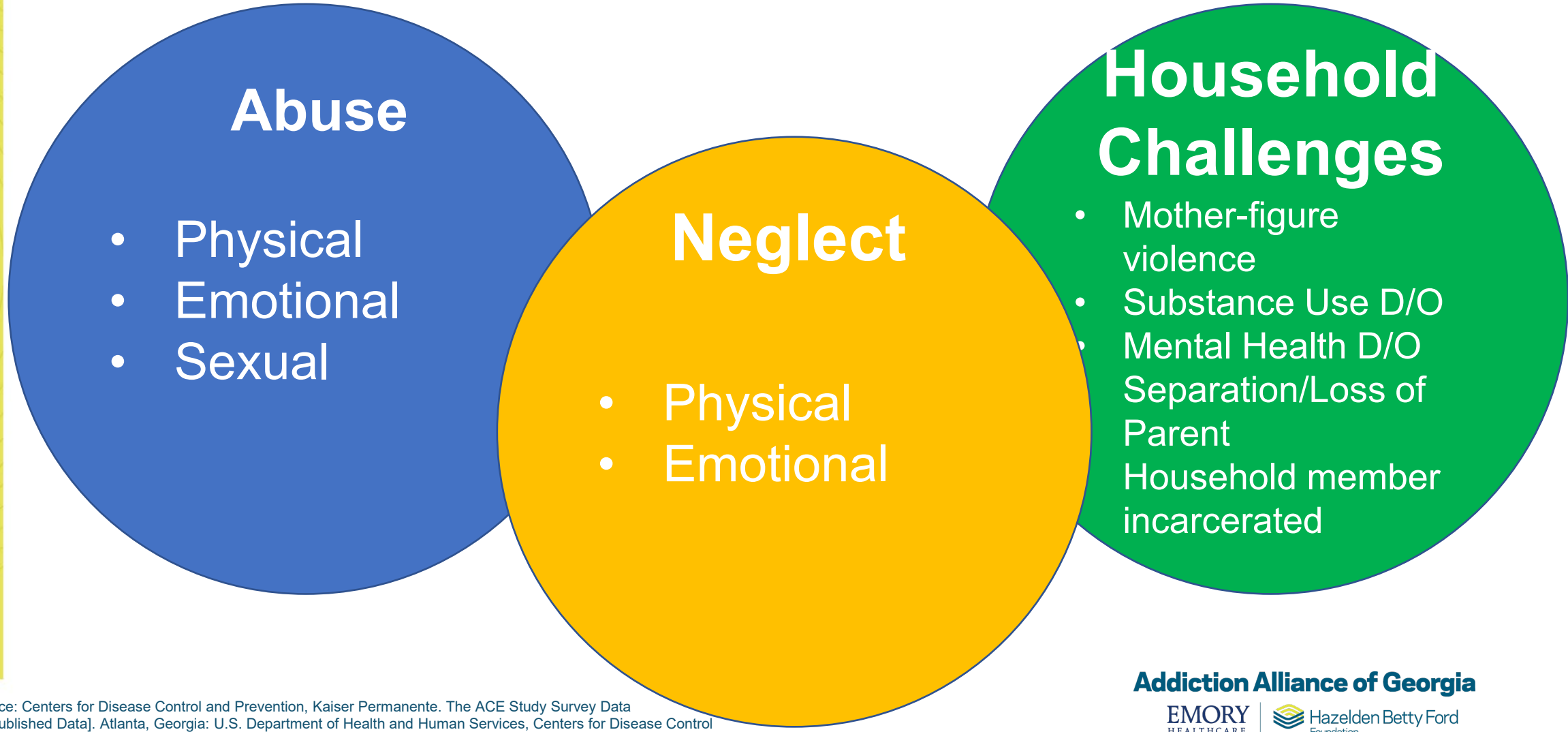

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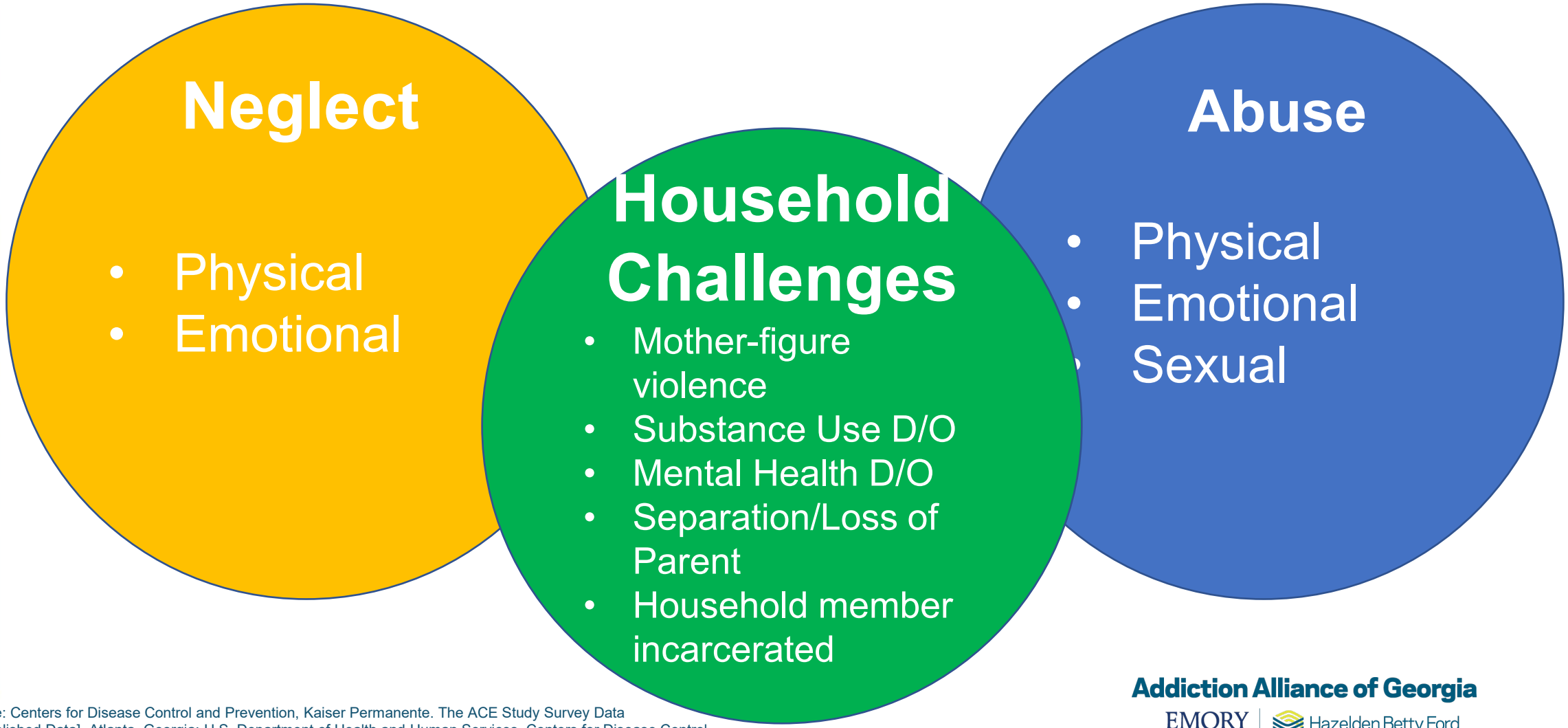

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Three Realms of Adverse Childhood Experiences

Thanks to **Building Community Resilience Collaborative and Networks** and the **International Transformational Resilience Coalition** for inspiration and guidance.
Please visit **ACEsConnection.com** to learn more about the science of ACEs and join the movement to prevent ACEs, heal trauma and build resilience.

ACEs Connection

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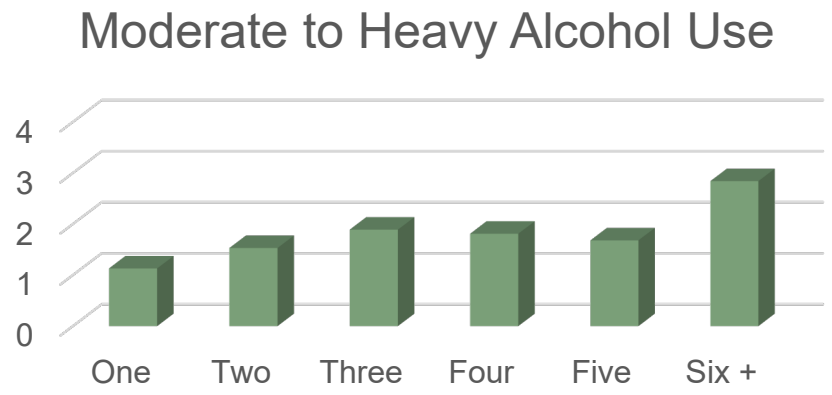
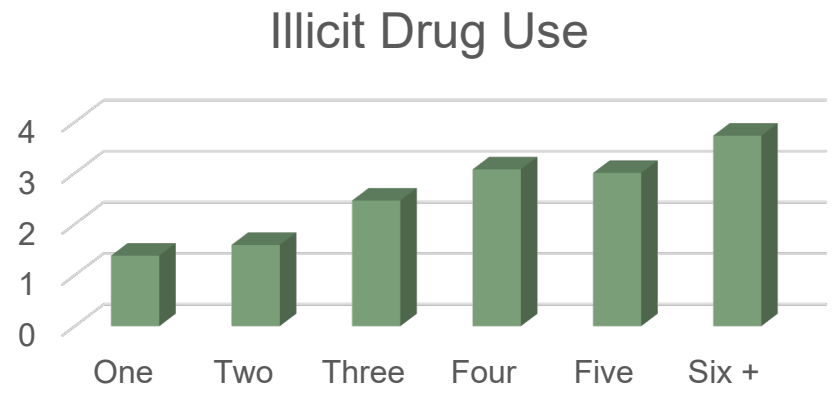
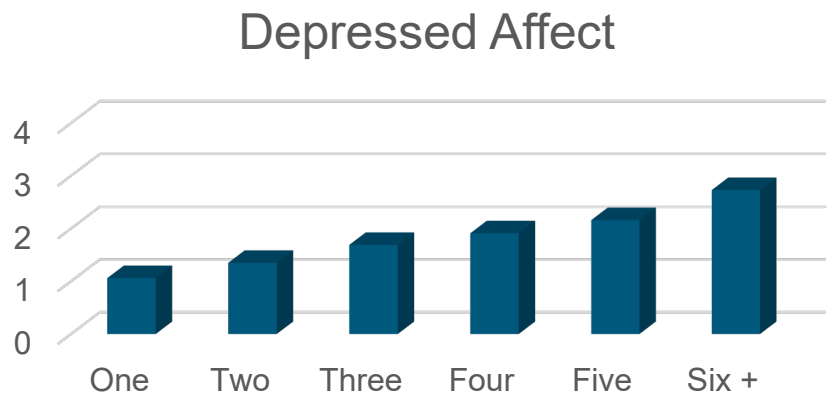
“Dose-responses” with Mental Health/SUD and ACEs





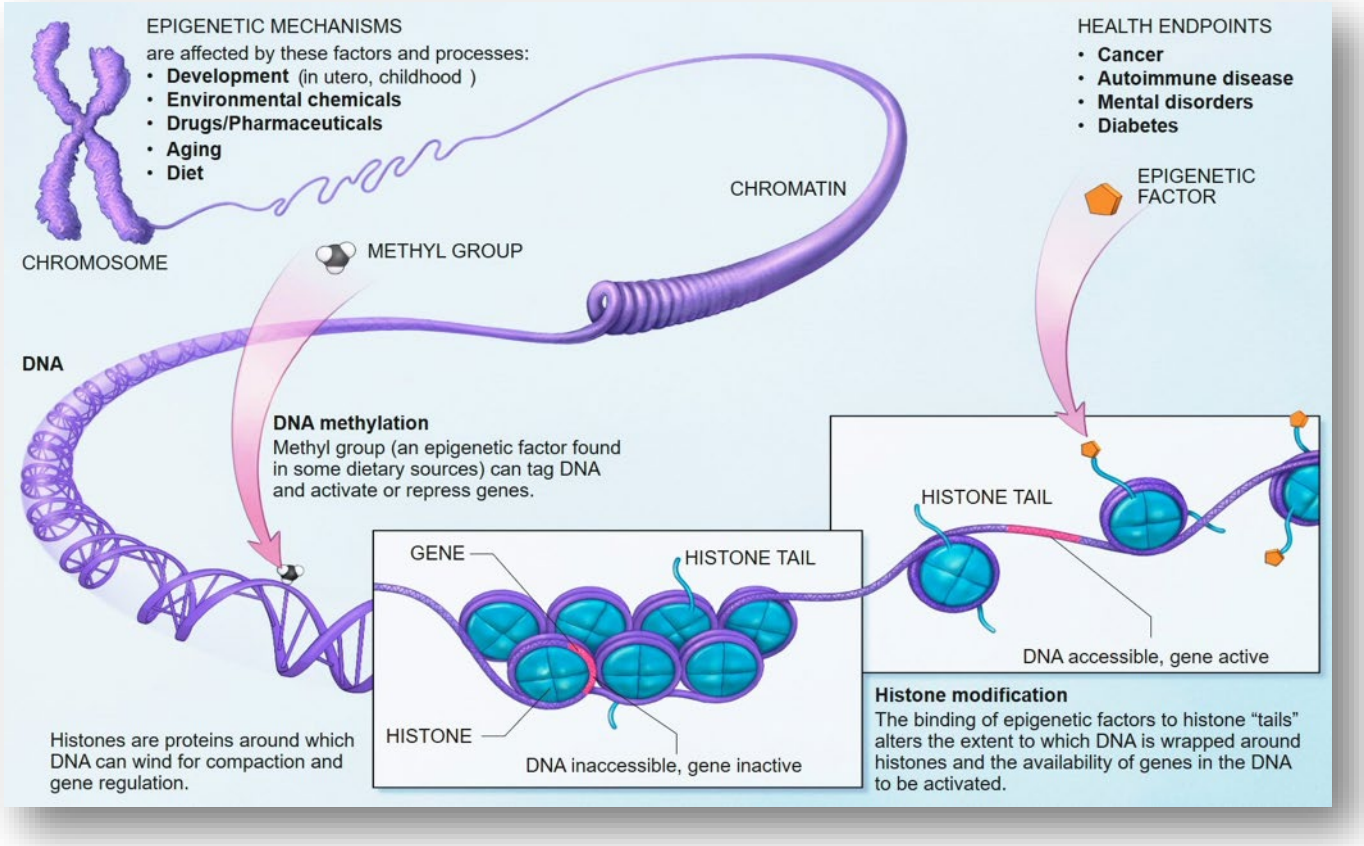


Merrick MT, Ports KA, Ford DC, Afifi TO, Gershoff ET, Grogan-Kaylor A. Unpacking the impact of adverse childhood experiences on adult mental health. Child Abuse Negl. 2017;69:10–19. doi:10.1016/j.chiabu.2017.03.016

Epigenetic Effects = Genetics + Experiences

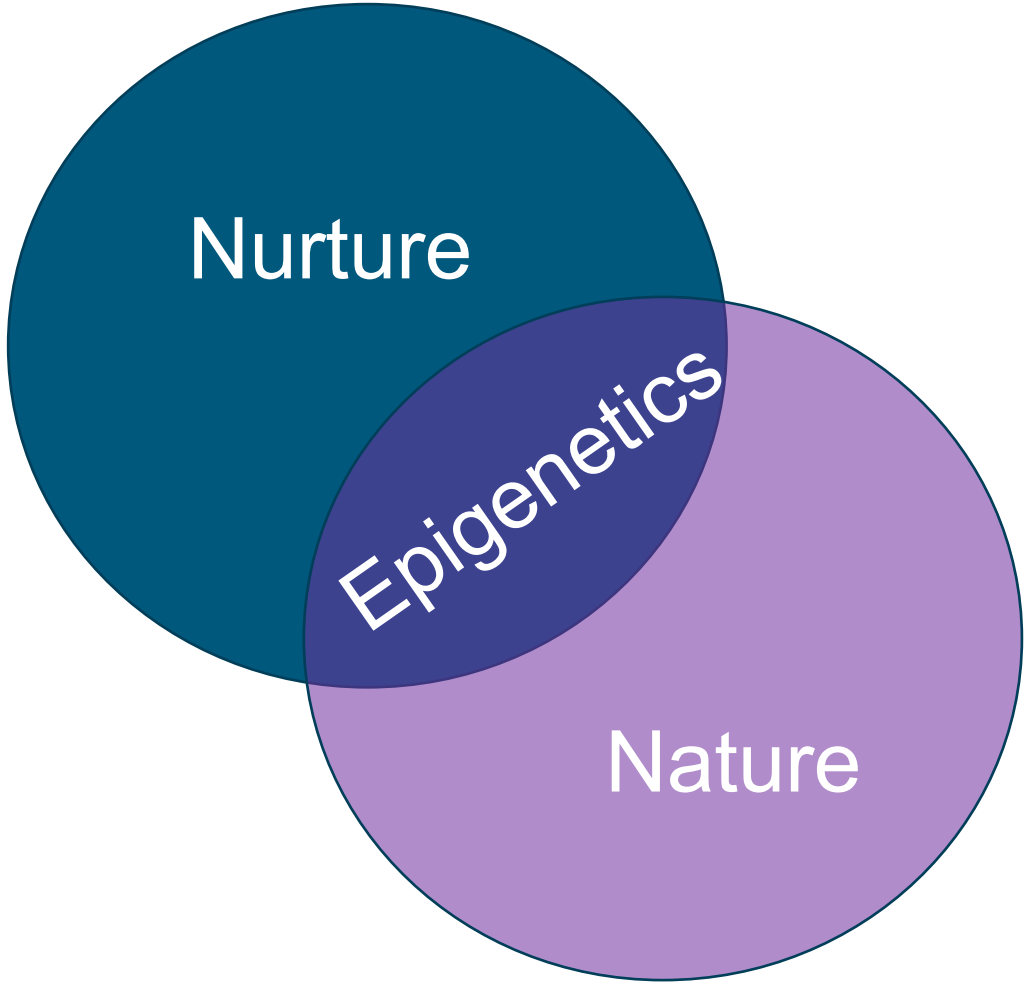
Nurture

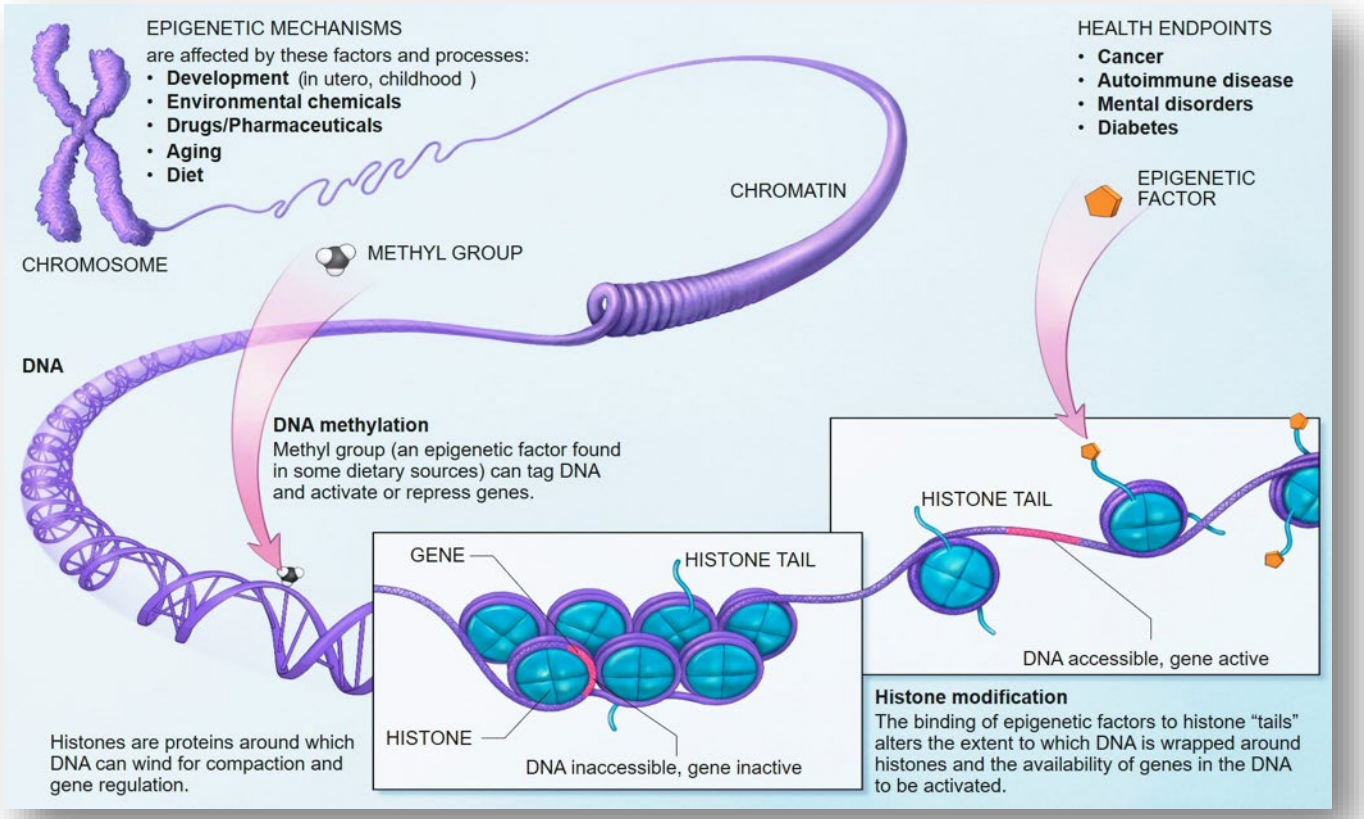
Nature



National Institutes of Health - http://commonfund.nih.gov/epigenomics/figure.aspx

Epigenetic Effects = Genetics + Experiences





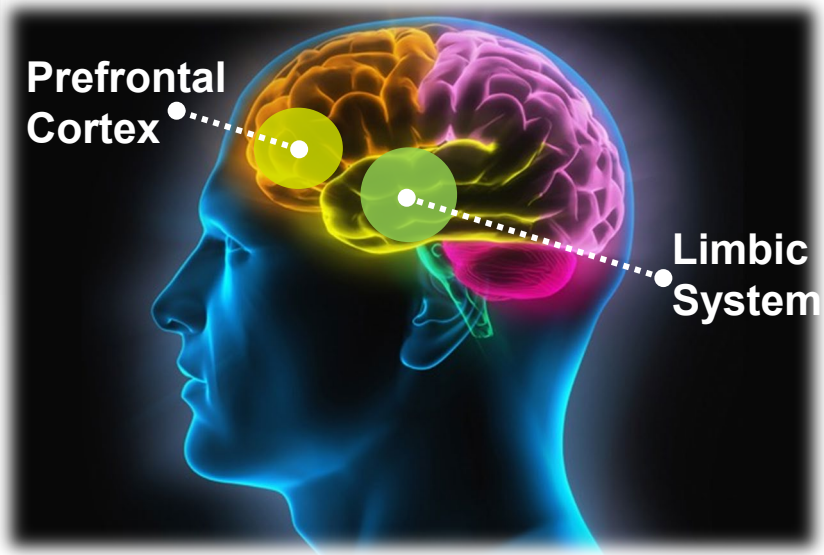
National Institutes of Health - http://commonfund.nih.gov/epigenomics/figure.aspx

Effects of ACEs and trauma (focus on SUD/MH)

Inflammation

Depression

Brain Changes



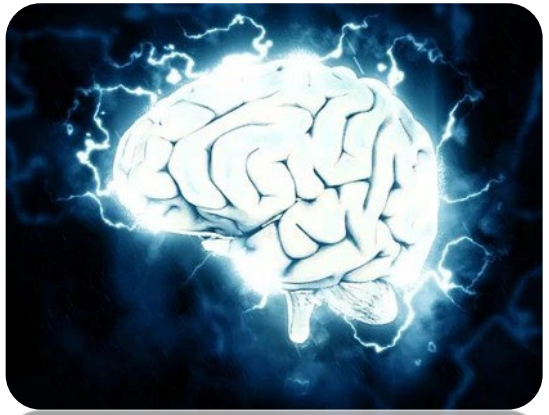
Addiction

Chronic

Pain

Stress

Fight



Freeze

Flight

Herzog JI, Schmahl C. Adverse Childhood Experiences and the Consequences on Neurobiological, Psychosocial, and Somatic Conditions Across the Lifespan. Front Psychiatry. 2018;9:420. Published 2018 Sep 4. doi:10.3389/fpsyt.2018.00420, and Volkow et al. NEJM Neurobiologic Advances from the Brain Disease Model of Addiction2016.

Moderating ACEs with Attachment

- Increased Oxytocin related to social pair bonding
- Oxytocin has also been shown to enhance trust between individuals
- Endogenous opioids regulate the maintenance of social attachment
  - Decreased β-endorphin levels lead to increased seeking of social connections
  - Social play, grooming, and **touch** – incr. β-endorphin (esp. amygdala, nuc. accumbens)
  - Social seeking enhanced with naltrexone, but inhibited by morphine
- Positive Emotions associated with increased activation of the opioid system in the amygdala and hippocampus
- Social support can moderate the association between ACEs and maternal HPA axis function during pregnancy (infant HPA axis too!)

Fineber S. Biol Psychiatry. 2017. 81(3): e19-e21, Machin A. Behaviour. 148(9/10). 2011: 985-1025
Thomas J. Dev Psychopathol. 2018 Aug;30(3):921-939.

Trauma-Informed Care Approach (for entire team)

↓Fight or Flight

SAFETY

- Both an intervention and an organizational orientation that:
- **REALIZES** how prevalent trauma is in our population
- **RECOGNIZES** the neurobiology of trauma and how trauma affects individuals and influences the course of illness and engagement
- **RESPONDS** to the needs of individuals with trauma in manner that focuses on strengths and acknowledges adaptation
- Being trauma-informed is critical for anyone engaging with and working to support individuals with trauma histories
- Fundamental way to directly address effects of ACEs
- This is about human **CONNECTION** and **ATTACHMENT**

HOPE

AUTONOMY

Source: SAMHSA TIP Series 57. HHS Publication No. (SMA). 2014: 13-4801

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Thank you!

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Intersection of Chronic Pain and Opioid Use Disorder

Elizabeth McCord, MD
Joseph Mathias, MD

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Learning Objectives

Understand the importance of treating opioid use disorder with FDA approved Medications

Review chronic pain pathophysiology and evidence for opioids

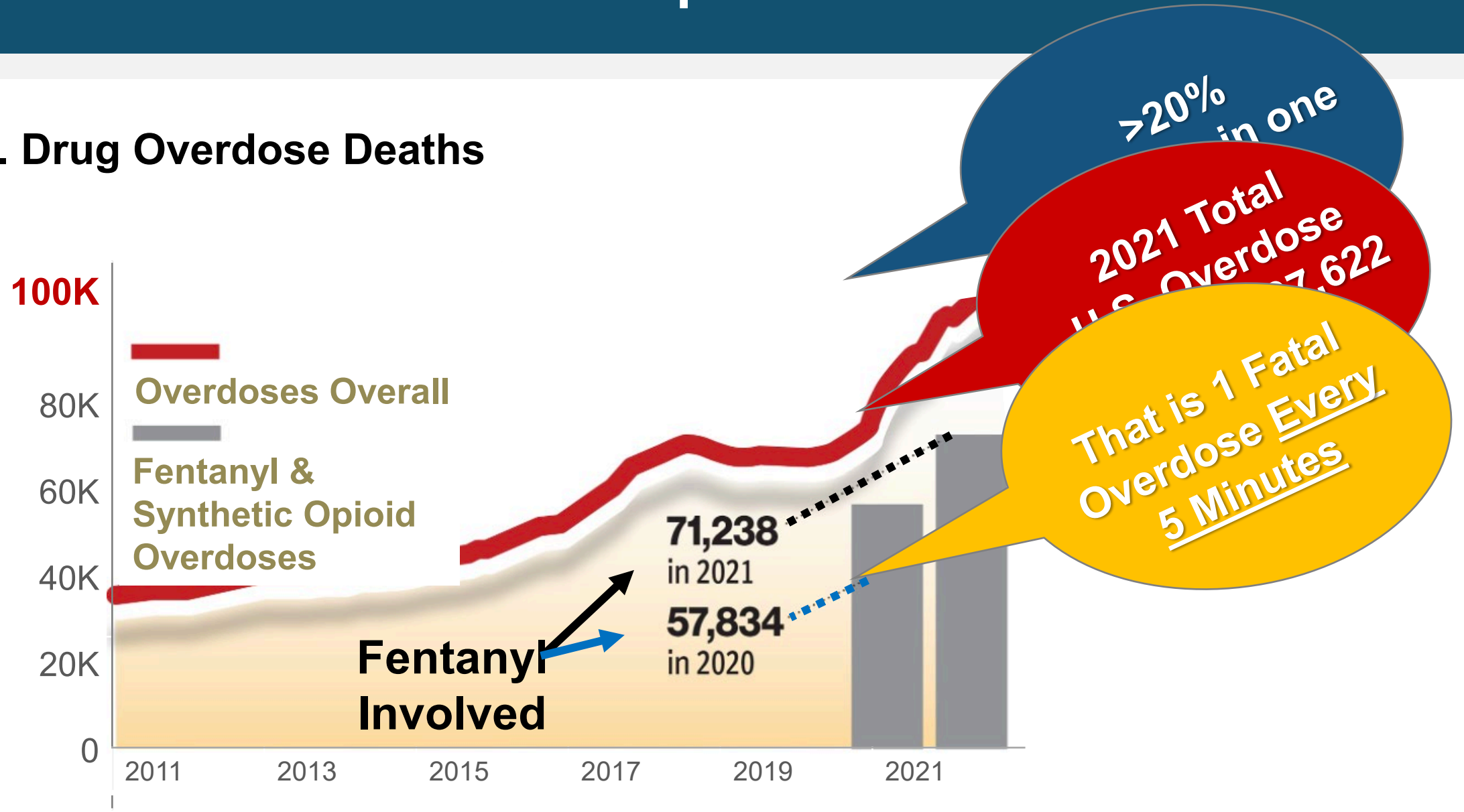
Discuss approaches to mitigating opioid risk while managing pain humanely

Describe basic pharmacology of buprenorphine

Review buprenorphine's role in pain management

A quick WHY for the need to expand Medications for OUD

2021 U.S. Drug Overdose Deaths



Ahmad FB, Cisewski JA, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2022.

Opioid Prescribing Trends

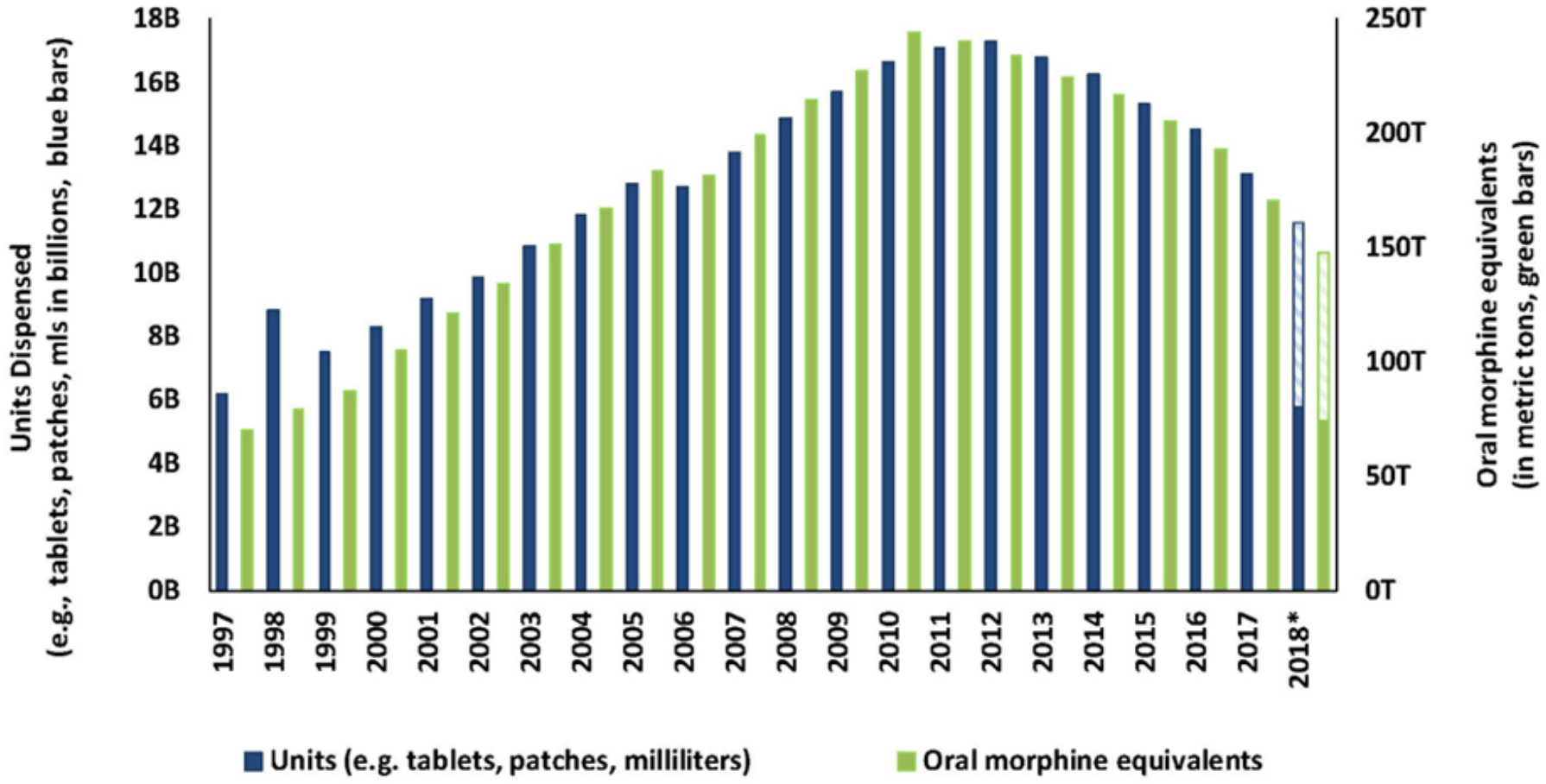
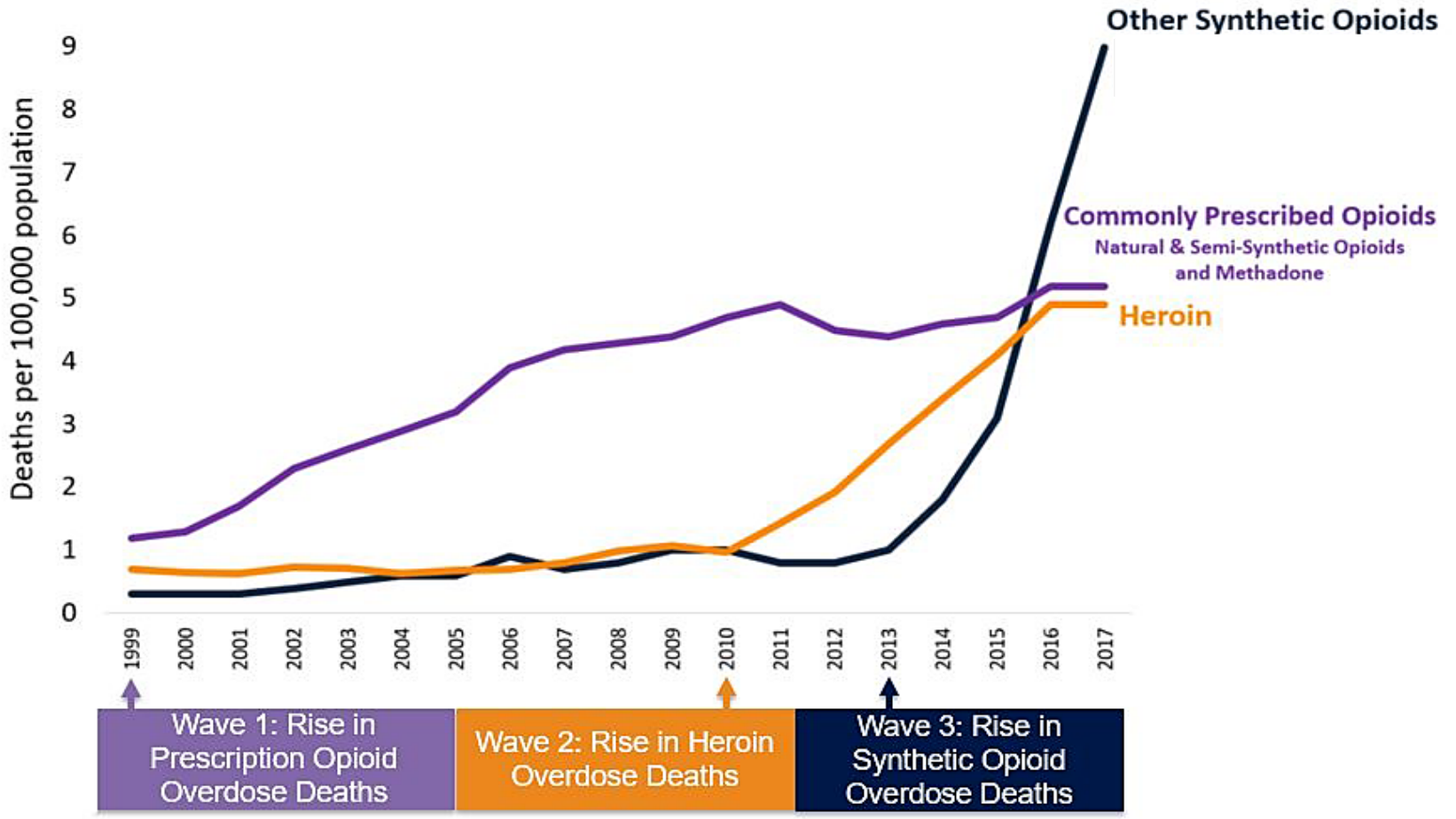


Figure 1: Estimated number of units (e.g., tablets, patches, milliliters) and calculated oral morphine equivalents (in metric tons) dispensed for opioid analgesic products from U.S. outpatient retail pharmacies, 1997 through projected year 2018*

Since 2011, MME declined by 43%

2018 had largest MME decline at 17%

Overdoses by Specific Opioid



SOURCE: National Vital Statistics System Mortality File.

Know the Facts

Prior to the 1990s, opioids rarely prescribed outside of oncological or surgical care (just wouldn't see it for chronic musculoskeletal)

- ***In 150 countries, morphine and opioids are not available at all***

A large percentage of drug related overdose deaths in the United States are categorized as **accidental (74%)**, while **17%** are **intentional** in nature

As many as **one in five** patients currently receiving long-term opioid therapy in a primary care setting struggles with **opioid addiction**

5% of non-cancer chronic pain patients use **70%** of total opioids (in Morphine Equivalent Dosing)

The NEW ENGLAND JOURNAL of MEDICINE

Perspective

The Public and the Opioid-Abuse Epidemic

Robert J. Blendon, Sc.D., and John M. Benson, M.A.

53% of Americans think the opioid epidemic is a major problem while **28%** think it's a national emergency

Of the **64%** of Americans prescribed an opioid, **7%** worry about developing an addiction

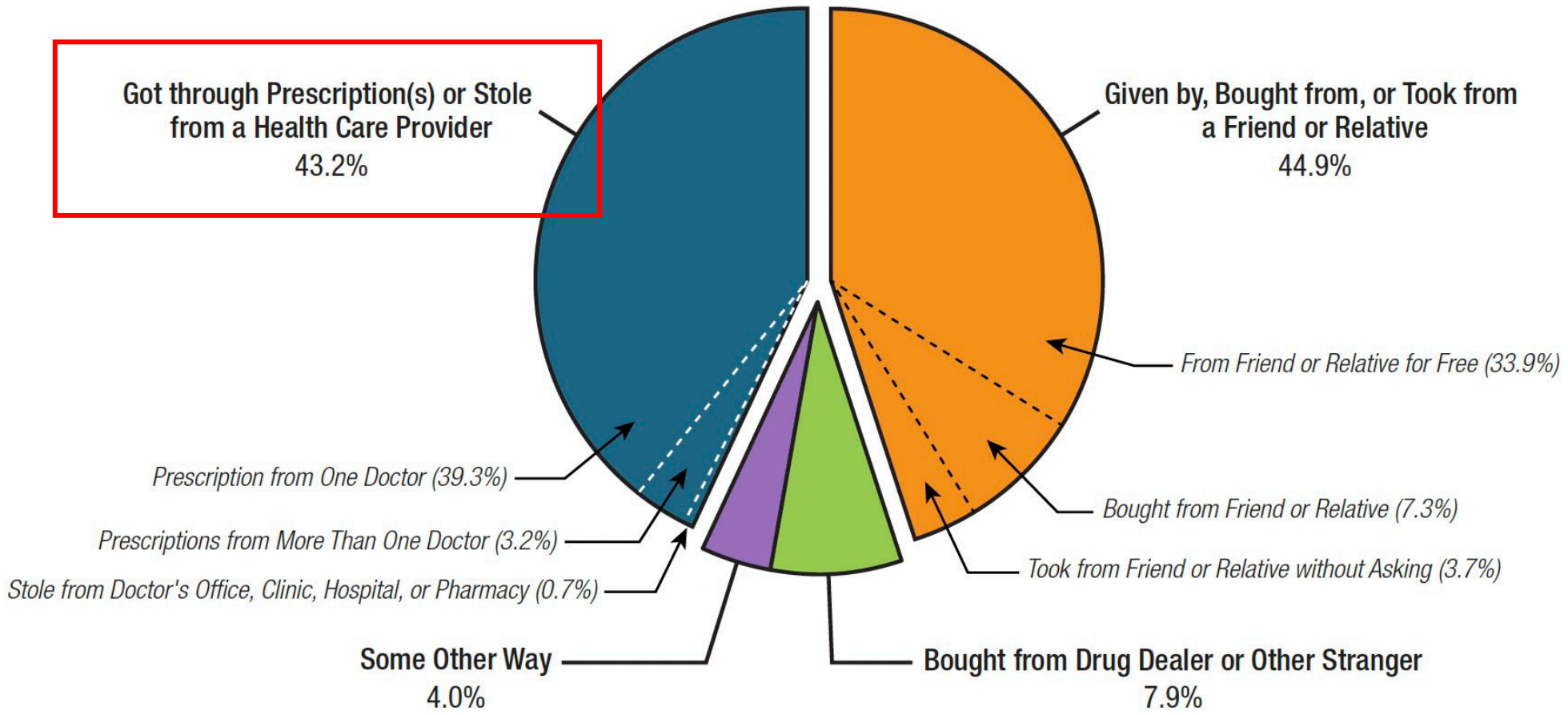
Healers or Dealers?

BLAME

33% - doctors
28% - dealers
10% - users

image by istock.com, aleutie

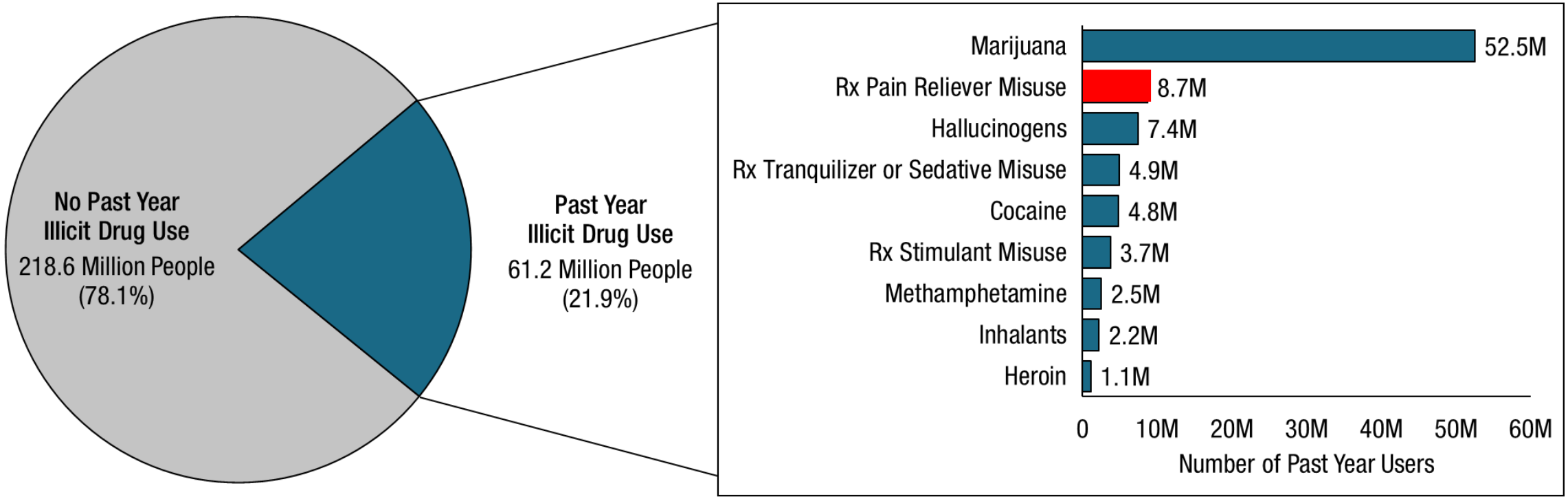
Taking Ownership



8.7 Million People Aged 12 or Older Who Misused Pain Relievers in the Past Year

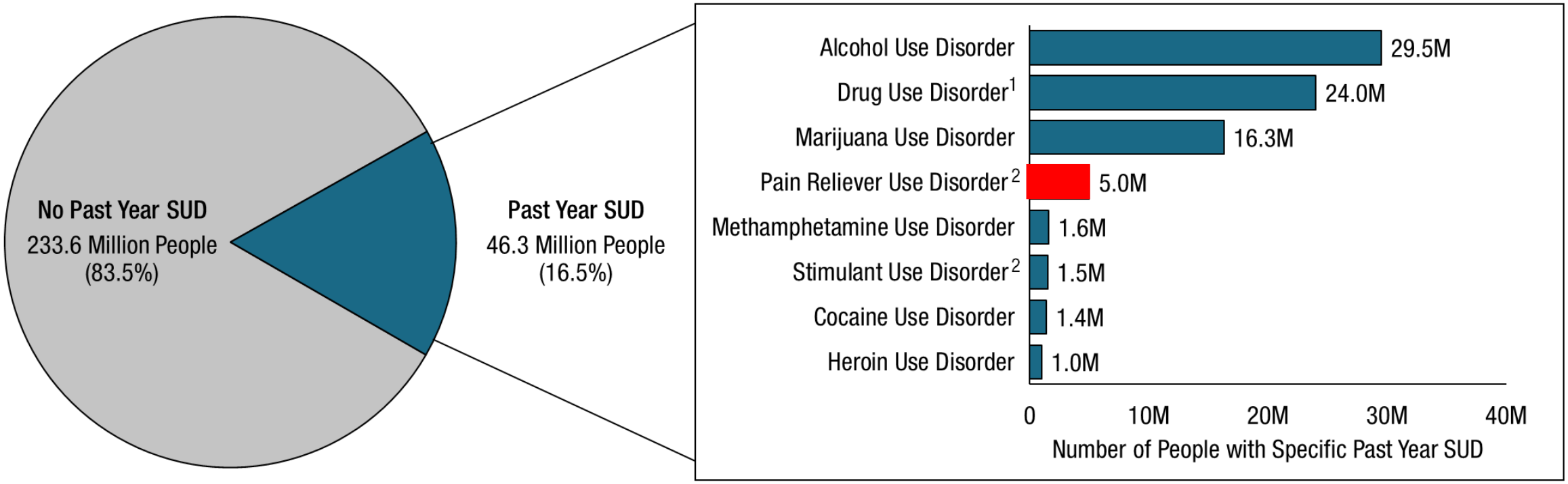
Extracted from: NSDUH (2022)

Past Year Rx Pain Reliever Use



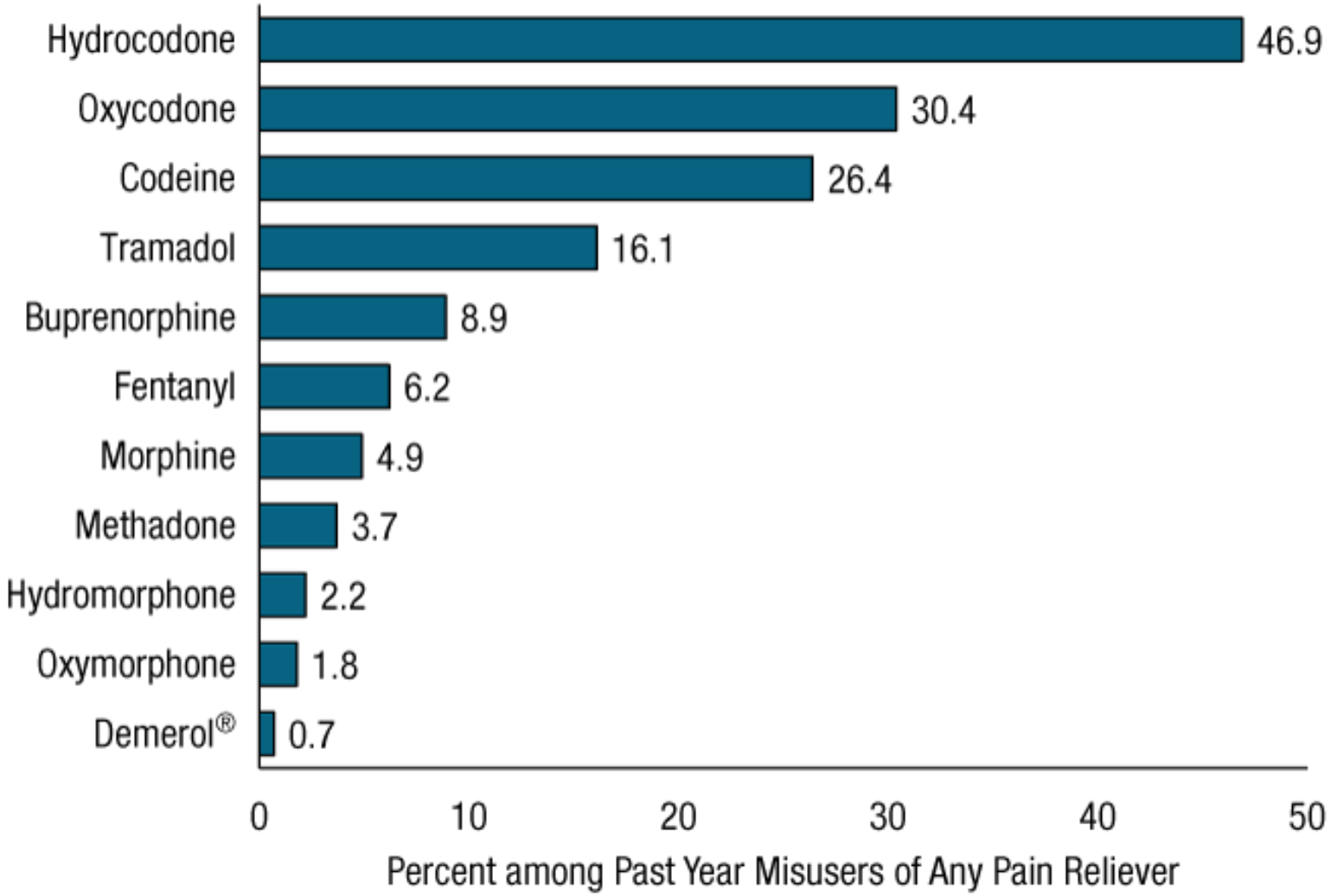
SAMHSA. (2022). 2021 National Survey on Drug Use and Health

Past Year Rx Pain Reliever Use Disorder



SAMHSA. (2022). 2021 National Survey on Drug Use and Health

Past Year Rx Pain Reliever Misuse



Extracted from: NSDUH (2022)

Treatment Gaps Following Opioid Overdoses

Opioids were dispensed to 91% of patients after a nonfatal overdose

n=2848

- **7%** had repeat opioid overdose that year
- At 2 years, cumulative incidence of repeated overdose was **17%** for patients on **high opioid dosages** after the index overdose

Larochelle MR, et al. *Ann Intern Med*. 2016

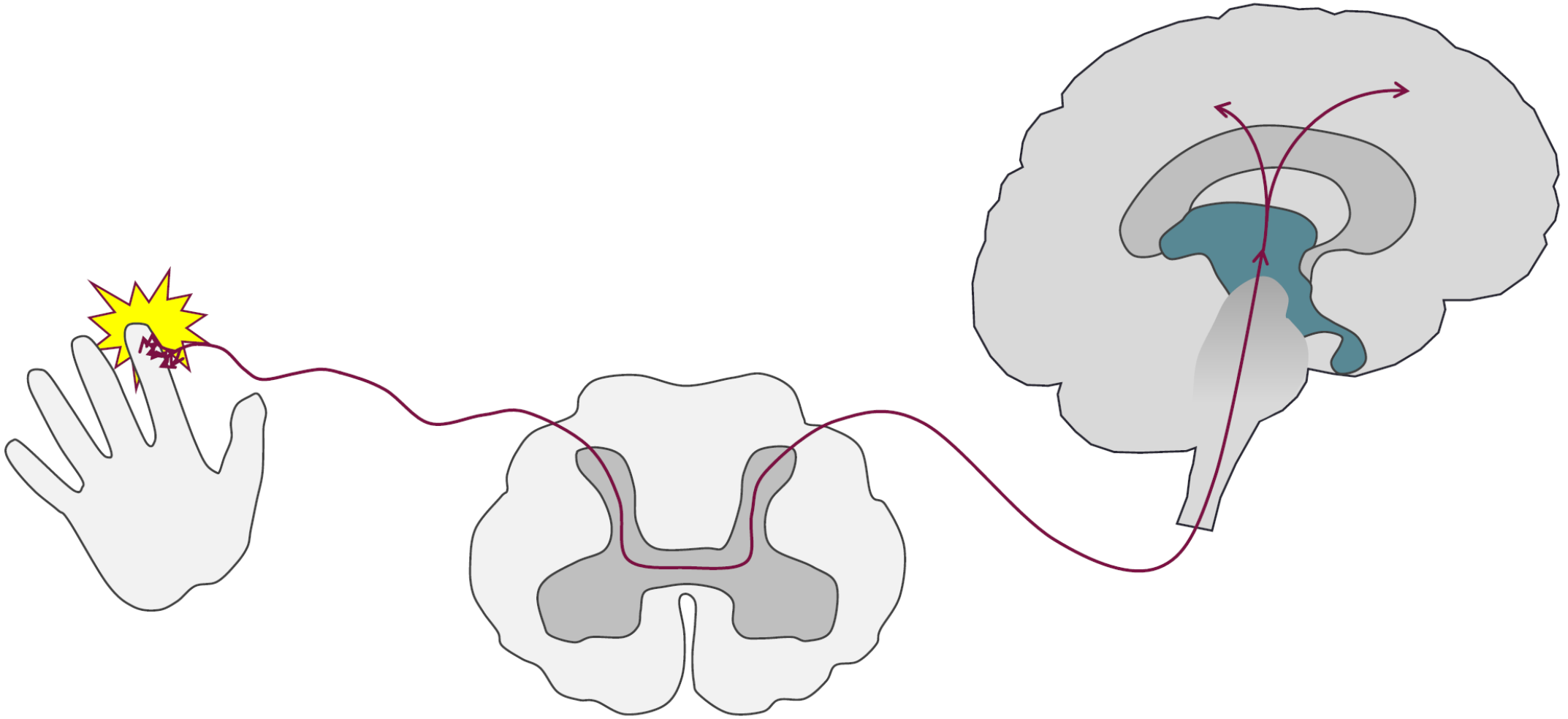
Epidemiology of Chronic Pain

>100 million Americans with chronic pain

- low back pain (27%)
- severe headaches / migraine (15%)
- neck pain (15%)

2/3 of these patients see their primary care/family doctor for management

Pain in the Brain



Pain is Important!

acute pain

- adaptative and life sustaining
- goal is to minimize harm and allow healing

chronic pain

- pain lasting >12 weeks
- can occur without ongoing tissue damage
- disease in and of itself
- maladaptive, pathologic

Chronic Pain in Perspective

Chronic pain is **common** and **subjective**

Barriers to treatment

- *negative attitudes, stigma, financial misalignments, poor support*

Circumstances of injury increase likelihood of developing chronic pain

- *trauma, abuse, sequelae of injury, prior experiences of pain*

Psychiatric co-morbidities are common

- *PTSD, depression, anxiety*

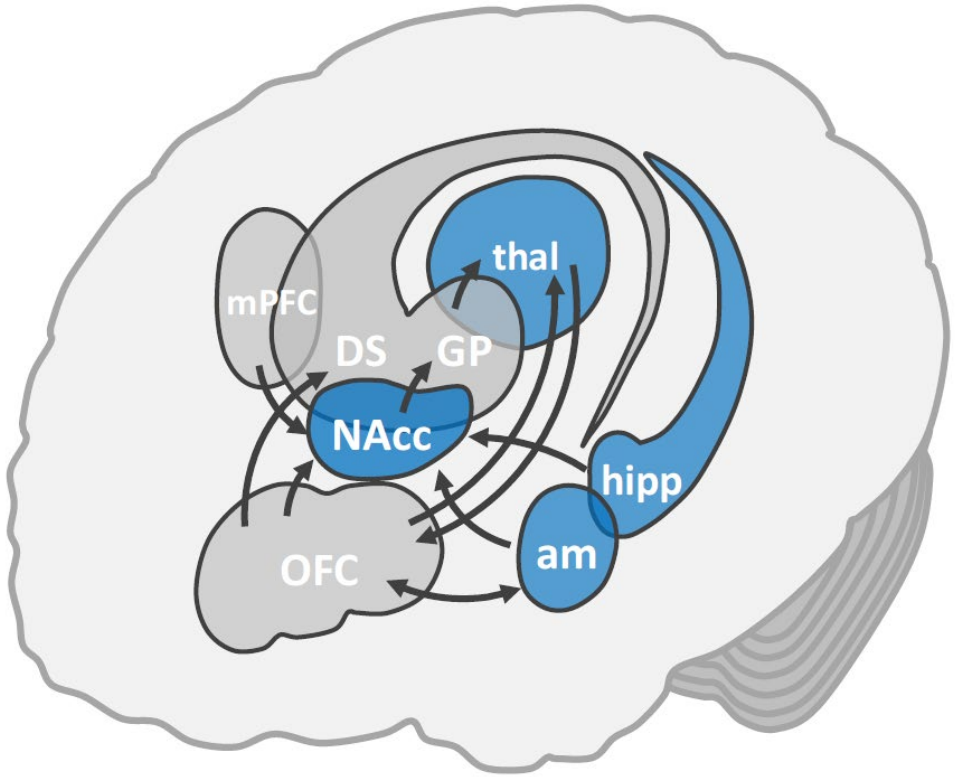
Cheatle M and Gallagher R (Curr Psych Rep 2006); Knaster P, et al. (Gen Hosp Psych 2012); Viana MC, et al. (J Pain 2018)

Chronic Pain and Addiction

Pain, mood, and substance use pathways all **overlap**

OUD risk factors:

- ***trauma****
- ***adverse childhood experiences****
- prior substance use disorder
- ***psychological comorbidities****



The Four A's of Pain Treatment Outcomes

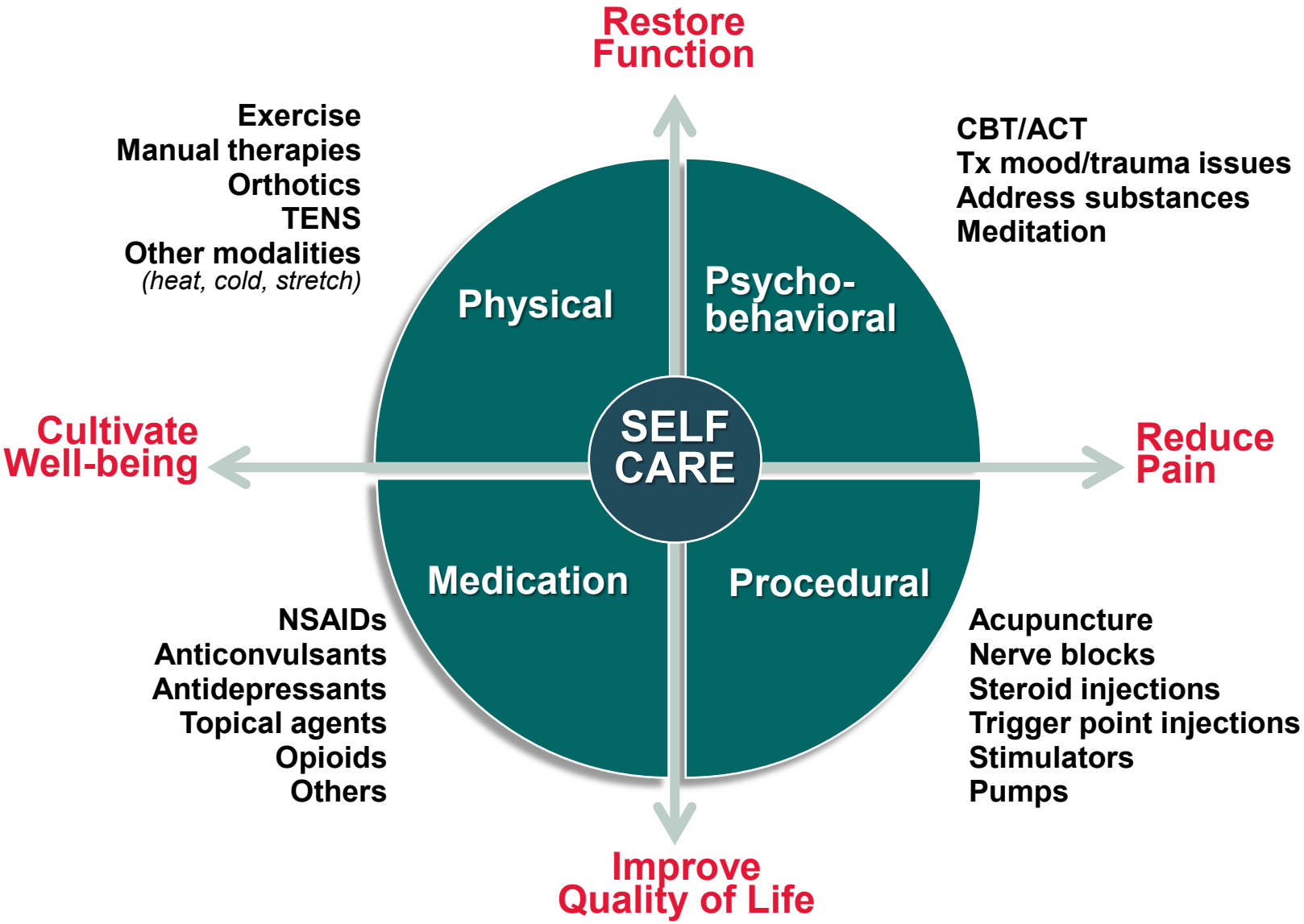
Analgesia
Pain relief

Adverse Effects
Side effects

Activities of Daily Living
Psychosocial functioning

Aberrant Drug Taking
Addiction related outcomes

Multidimensional Care



Studies on all pharmacologic and nonpharmacologic treatments for chronic pain are ≤ 12 m, vast majority are ≤ 12 w

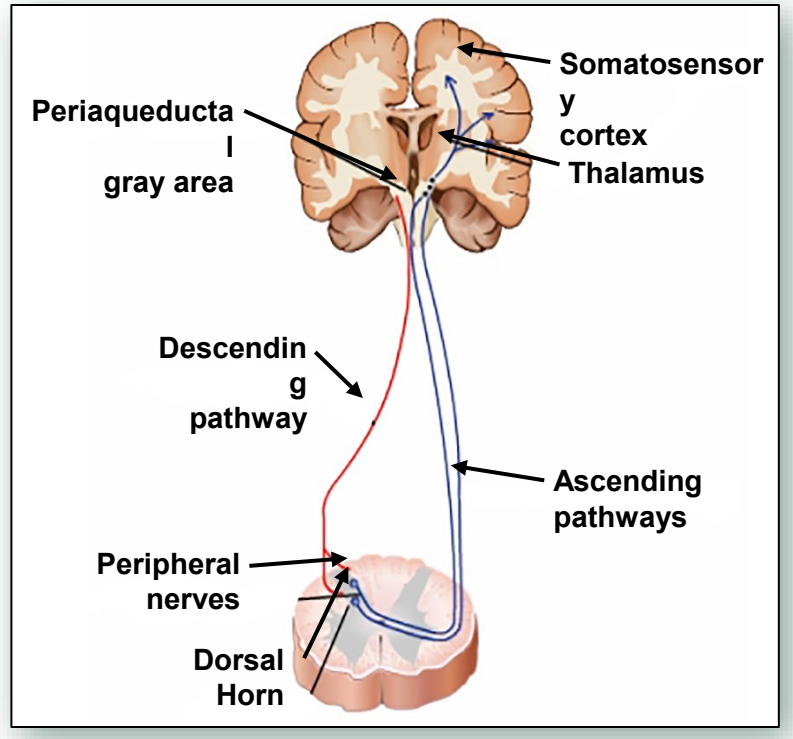
Tayeb BO, et al. *Pain Med.* 2016

Multimodal approaches are more cost-effective than single modality options

Flor H, et al. Pain 1992
Roberts AH, et al. Clin J Pain. 1993
Patrick LE, et al. Spine. 2004
Kamper SJ, et al. Cochrane Review. 2014

Opioid Analgesia

Turn on descending inhibitory systems
Prevent ascending transmission of pain signal
Inhibit terminals of C-fibers in the spinal cord
Inhibit activation of peripheral nociceptors



Variable response

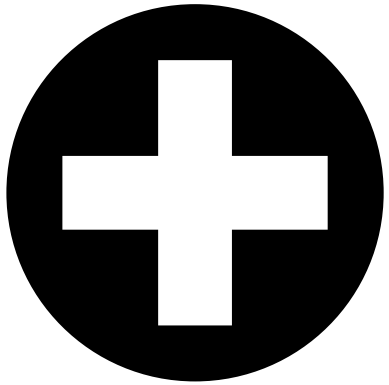
- >3,000 polymorphisms in the human MOR gene
- Differences in pharmacokinetics (opioid metabolism)

***Activate the reward pathway**

McCleane G, Smith HS. *Med Clin N Am.* 2007
Smith HS. *Pain Physician.* 2008

Opioid Side Effects

1. Tolerance
2. Physical Dependence
3. Increased sensitivity to pain
4. Sleepiness and dizziness
5. Addiction
6. Depression
7. Constipation
8. Immune suppression/cancer?



Dunn KM et al. *Ann Intern Med* 2010
Li X et al. *Brain Res* 2001
Doverty M et al. *Pain* 2001

Opioid Efficacy in Chronic Pain

Meta-analyses (3-6 m f/u)

- **Opioids vs placebo** *(high quality studies)* Opioids with statistically significant, but small, improvements in pain[1,2] and physical functioning.[2]
- **Opioids vs nonopioids**

(low-mod quality studies) Similar benefits[2]

RCT[3] found opioids **not superior** to nonopioids for improving musculoskeletal pain-related function over 12 months

Study limitations: [4]

- *Excluded patients already on long-term opioids*
- *89% of eligible patients declined to be enrolled*

Two longer term follow-up studies found **44.3%** on chronic opioids for chronic pain had **at least 50% pain relief** [5]

1. Meske DS, et al. *J Pain Res.* 2018
2. Busse JW, et al. *JAMA*. 2018
3. Krebs EE, et al. *JAMA*. 2018
4. Webster L. *Pain Med.* 2019
5. Noble M, et al. *Cochrane Syst Rev.* 2010

Evidence for Opioid Therapy

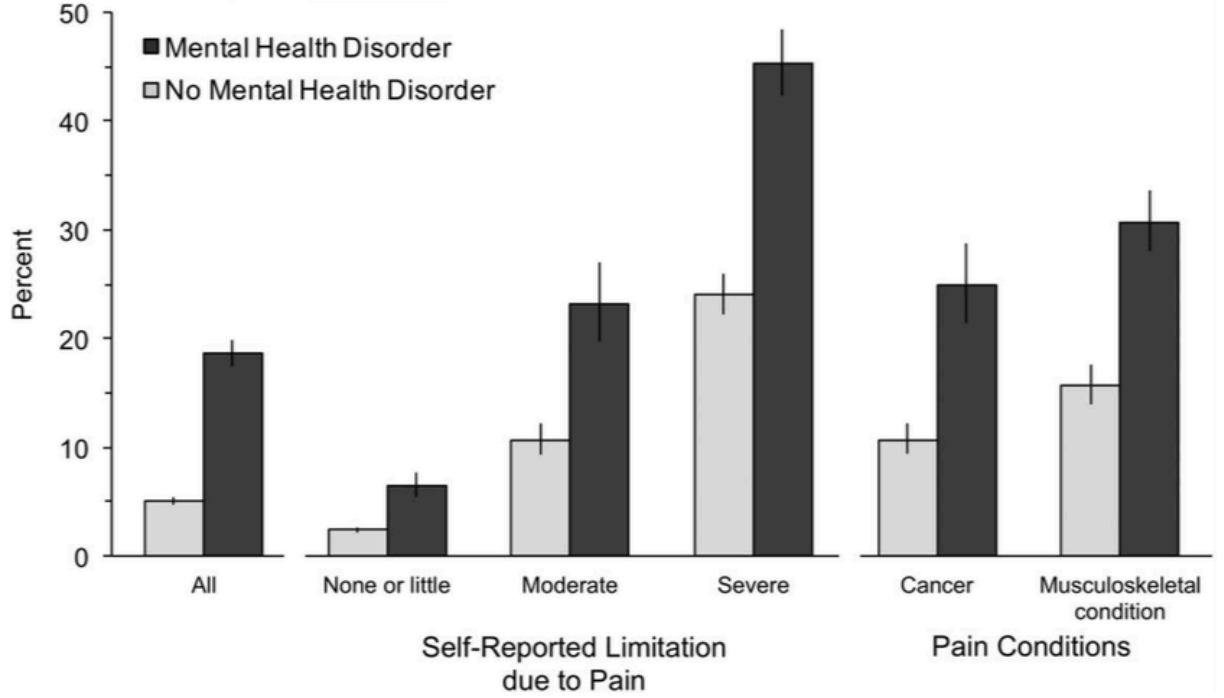
Benefits of long-term opioid therapy for chronic pain **not well supported** by evidence.

Short-term benefits **small to moderate** for pain; inconsistent for function.

Insufficient evidence for long-term benefits in low back pain, headache, and fibromyalgia.

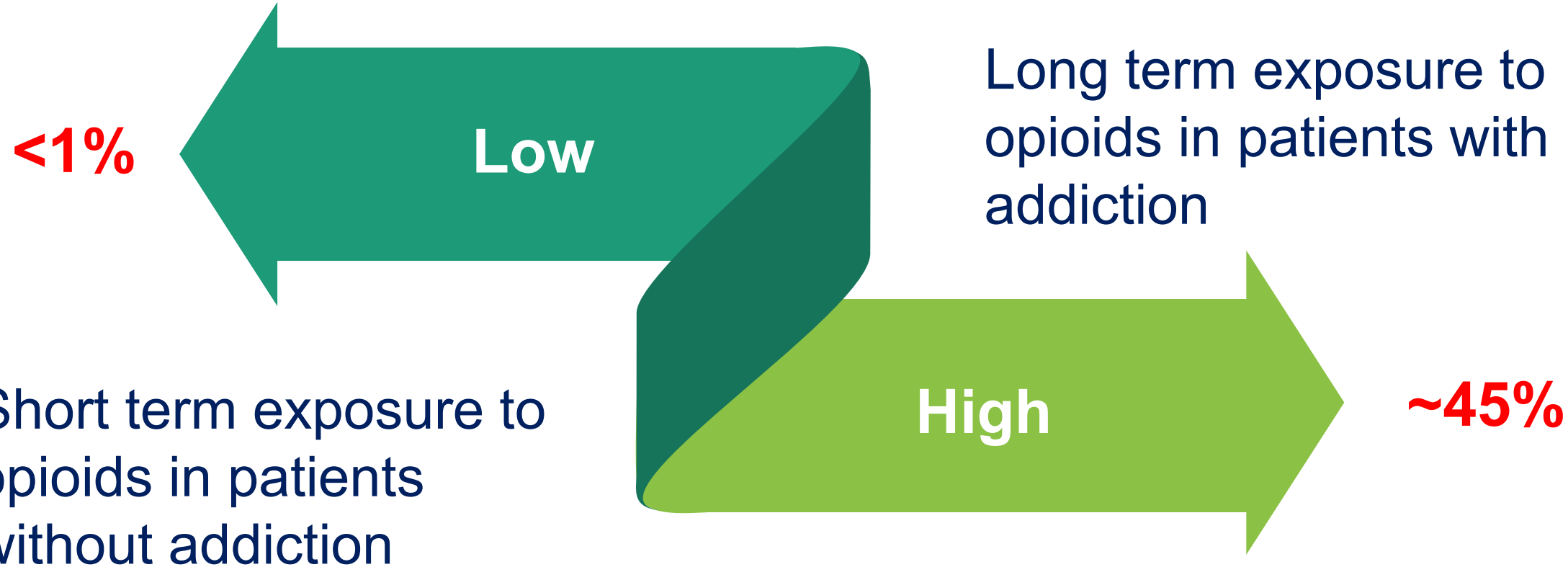
Who is likely to be prescribed opioids?

Figure 2. Estimated percentages of U.S. adults with and without mental health disorders who use prescription opioids, according to selected characteristics. All estimates are weighted to represent the U.S. noninstitutionalized population. Error bars represent 95% confidence intervals. Musculoskeletal conditions include all forms of arthritis, and other pain-related conditions.



Source: Davis et al. (2017)

Risk of developing an addiction with Opioid Rx



Risk Factors for Prescription OUD

Obtaining overlapping prescriptions from multiple providers and pharmacies

Living in a rural area and having low income

Taking high daily dosages of prescription opioids

Having mental illness or a history of alcohol or other substance use disorder

Is my patient addicted?

A clinical syndrome presenting as…
- Loss of **C**ontrol
- **C**ompulsive use
- **C**ontinued use despite harm

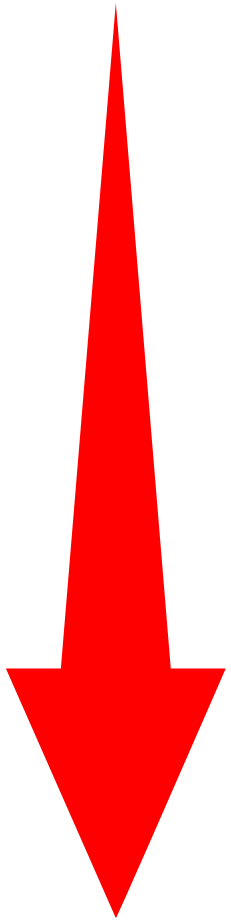
} **Aberrant Medication Taking Behaviors**

Addiction is a **behavioral maladaptation**

Physical Dependence is a **physiologic adaptation**

Savage SR et al. *J Pain Symptom Manage* 20

Red Flags for Prescription Misuse



- Requests for increased opioid dose
- Requests for specific opioid by name, “brand name only”
- Non-adherence w/ other recommended therapies (e.g. PT)
- Running out early (i.e. unsanctioned dose escalation)
- Resistance to change therapy despite side effect (e.g. over-sedation)
- Deterioration in function at home and work
- Non-adherence with monitoring (e.g. pill counts, UDT)
- Multiple “lost” or “stolen” opioid prescriptions
- Illegal activities – forging scripts, selling opioid prescription

DSM-5 TR Criteria of an SUD

Loss of control

- Larger amounts, longer time
- Inability to cutback
- More time spent, getting, using, recovering
- Activities given up to use
- Craving

- **Physiologic Dependence**
- Tolerance**
- Withdrawal**

Consequences

- Hazardous use
- Social or interpersonal problems related to use
- Neglected major roles to use
- Continued use after significant problems

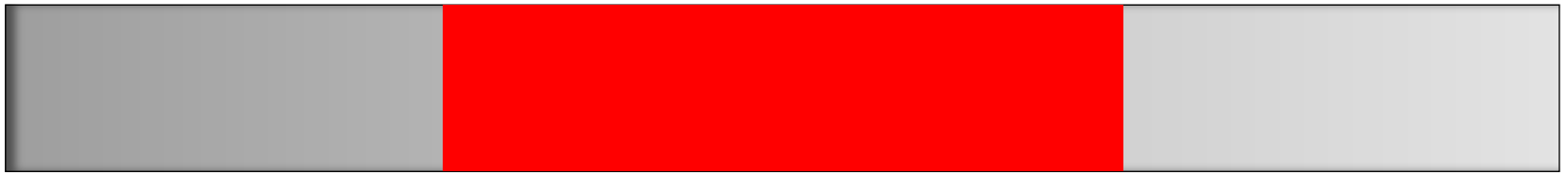
Problematic pattern of substance use that leads to serious impairment or distress.

2 or more of the DSM-5-TR symptoms within 12 months.

Addiction is often synonymous with, "**moderate to severe Substance Use Disorder.**"

2-3 = mild
4-5 = moderate
6+ = severe

The Gray Zone



Addiction

Meets DSM5 criteria

Does not have an Addiction

No lost prescriptions
No ER visits
No early prescriptions
No requests for dose escalation
No UDT aberrancies
No doctor shopping (PDMP)

Continuing Opioids

Before writing the next opioid prescription…you should be convinced that there is…

…benefit (pain, function, QOL) and …

…absence of harm

Despite subjective assessments (benefits/harms), **it should be documented at each visit**

Urine Drug Testing

Objective information that can provide:

- Evidence of therapeutic adherence
- Evidence of use or non-use of illicit drug

Discuss urine drug testing openly with patient

One medical data point to integrate with others

Urine drug screens are usually immunoassays (Risk of false negatives and false positives)

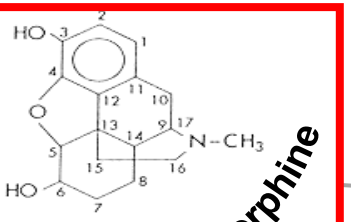
Unexpected findings can be verified with Gas Chromatography (GC) or Liquid Chromatography (LC) and Mass Spectroscopy (MS) (need to know expected metabolites)

Argoff CE, Alford DP, Fudin J et al. *Pain Med.* 2018, Nagpal G et al. *JAMA*. 2017, Christo PJ, et al. *Pain Physic*

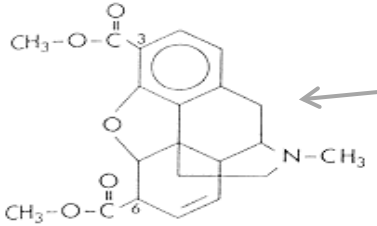
Urine Drug Testing Pearl

Negative drug screens means *no drug or metabolites were detected* in the drug screen **AT OR ABOVE THE CUTOFF**

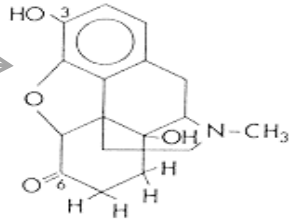
Opiates: Codeine and Morphine



Morphine

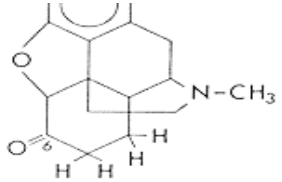


Diacetylmorphine (Heroin)

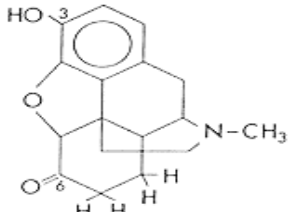


Oxymorphone

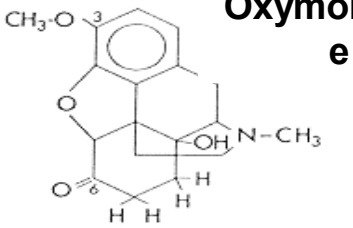
Semisynthetic



Hydrocodone

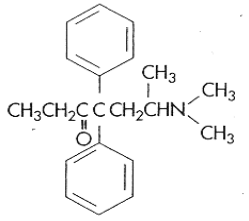


Hydromorphone

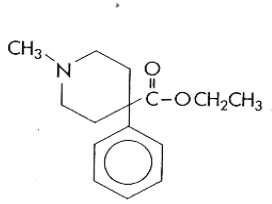


Oxycodone

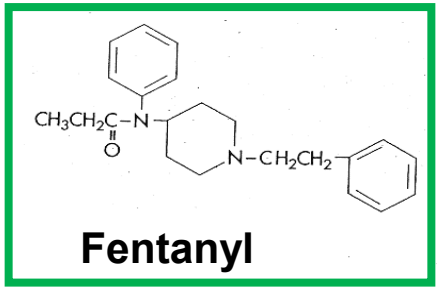
Synthetic



Methadone



Meperidine



Fentanyl

What is your role?

VS

Use a **risk-benefit** framework
Judge the opioid treatment, not the patient

Nicolaidis C. *Pain Medicine* 2011

Discontinuing Opioids?

- Do not have to prove addiction or diversion - only assess and reassess the risk-benefit ratio
- If patient is unable to take opioids safely or is nonadherent with monitoring then discontinuing opioids is appropriate even in setting of benefits
- Need to determine how urgent the discontinuation should be based on the severity of the risks and harms

You are NOT abandoning the patient.
You are abandoning the opioid therapy.

Conversation with the Patient?

Have a frank discussion about the aberrant opioid use

Discuss treatment goals
- Pain relief or euphoria?

Discuss the lack of benefit despite increased opioid dose

Outline your intent to discontinue opioid therapy
- Determine mutual strategies for tapering
- Clarify that you will use non-opioids for pain control in the future
- Reassure the patient

Key CDC Guidelines for Opioid Prescribing

- Do **not** use opioids as 1st-line therapy → combine w/ other therapies
- Before starting opioids, establish realistic goals. Continue opioids only if meaningful improvements outweighs risks
- Discuss risks and benefits of opioids
- Prescribe the lowest effective opioid dose. Avoid doses ≥ 90 mg morphine equivalents
- Offer/arrange treatment for patients with an OUD

Dowell D et al. MMWR 2016

Treatment Gaps Following Opioid Overdoses

Less than a third of opioid overdose survivors receive MOUD in the subsequent 12 months

n= 17,568

Receipt of MOUD was associated with **decreased** all-cause and opioid-related mortality

Larochelle MR , et al. *Ann Intern Med.* 2018

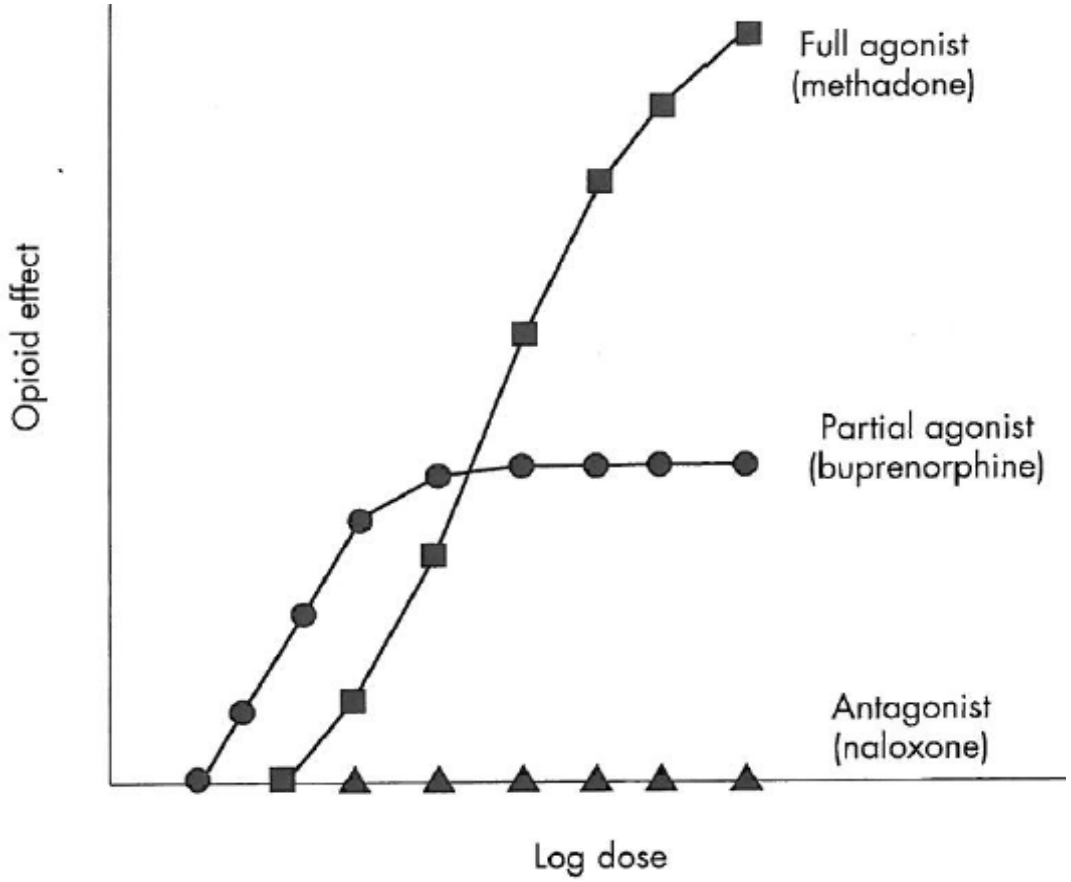
Types of MOUD

Opioid Antagonists

- **Naltrexone** (full antagonist)
- **Naloxone** (full antagonist)

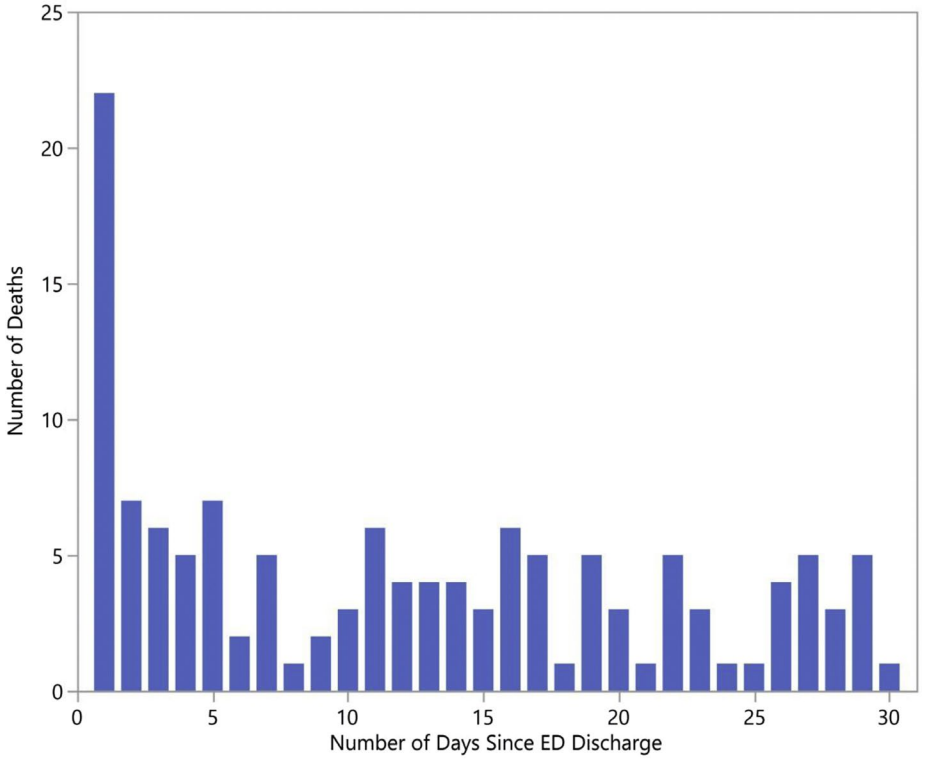
Opioid Agonist Therapy (OAT)

- **Methadone** (full agonist)
- **Buprenorphine** (partial agonist)



One-Year Mortality of Patients After Emergency Department Treatment for Nonfatal Opioid Overdose

Scott G. Weiner, MD, MPH*; Olesya Baker, PhD; Dana Bernson, MPH; Jeremiah D. Schuur, MD, MHS



N=12,000, 1 year outcomes of patients discharged from ED after an overdose without MOUD

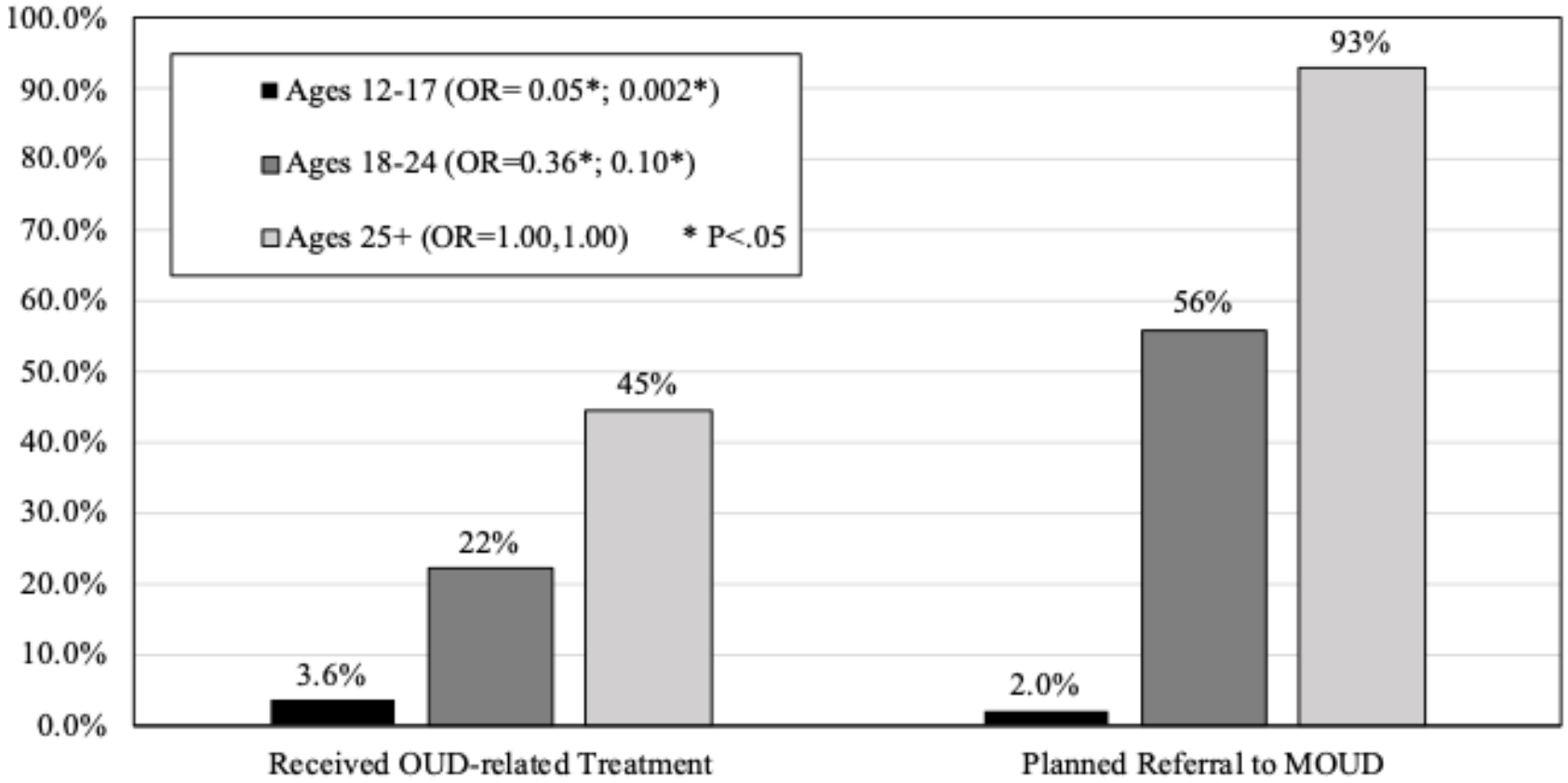
6% of those who survived an overdose died within one year

130 died within first month of ED visit

Weiner SG et al, *Ann Emerg Med*. 2020;75(1):13-17.

MOUD Access

Age Disparity in Access to OUD and MOUD Treatment in 2017



Extracted from: Welsh et. Al., (2021)

Buprenorphine (with or without naloxone)

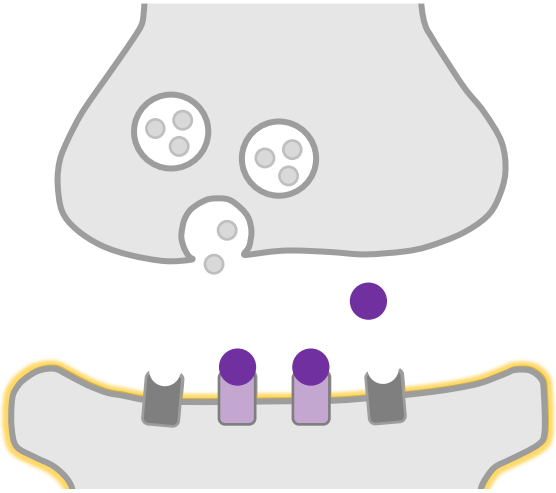
Schedule III (2002)

Semi-synthetic analogue of thebaine

Metabolized in the liver (CYP3A4)

Has a less-active metabolite → ***norbuprenorphine***

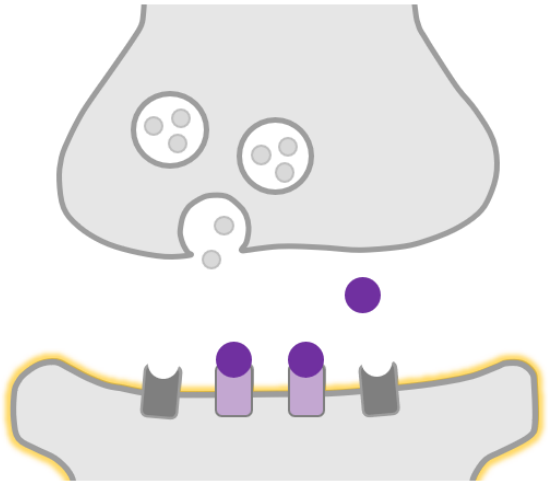
Excreted into the biliary tract, but small % enters the urine



partial μ agonist

Buresh M, et al. (J Gen Int Med 2020)

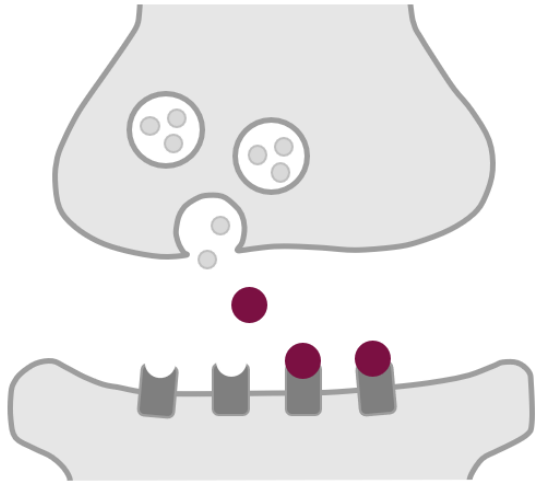
Buprenorphine Receptor Activity



partial μ agonist

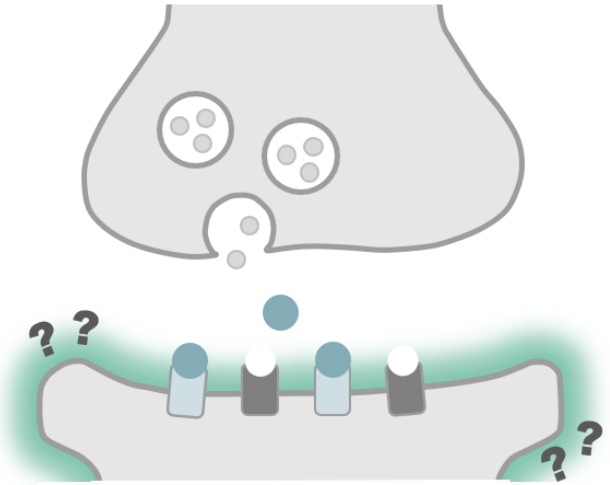
respiratory depression

euphoria



κ antagonist

anxiolysis
mitigates OIH (?)



ORL-1 agonist

pain processing
blunts reward

Formulations

Buprenorphine

Generic (SL tabs)

Probupine (SD implant)

Sublocade (SQ inj)

Butrans (transdermal patch)

Buprenex (IV or IM)

Belbuca (buccal film)

Subutex (SL film)

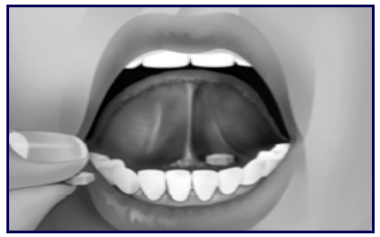
Buprenorphine/Naloxone

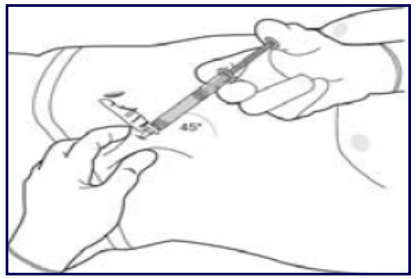
Generic (SL tabs)

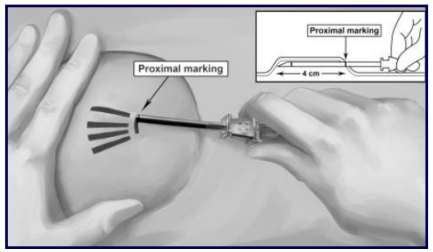
Bunavail (buccal film)

Suboxone (SL film)

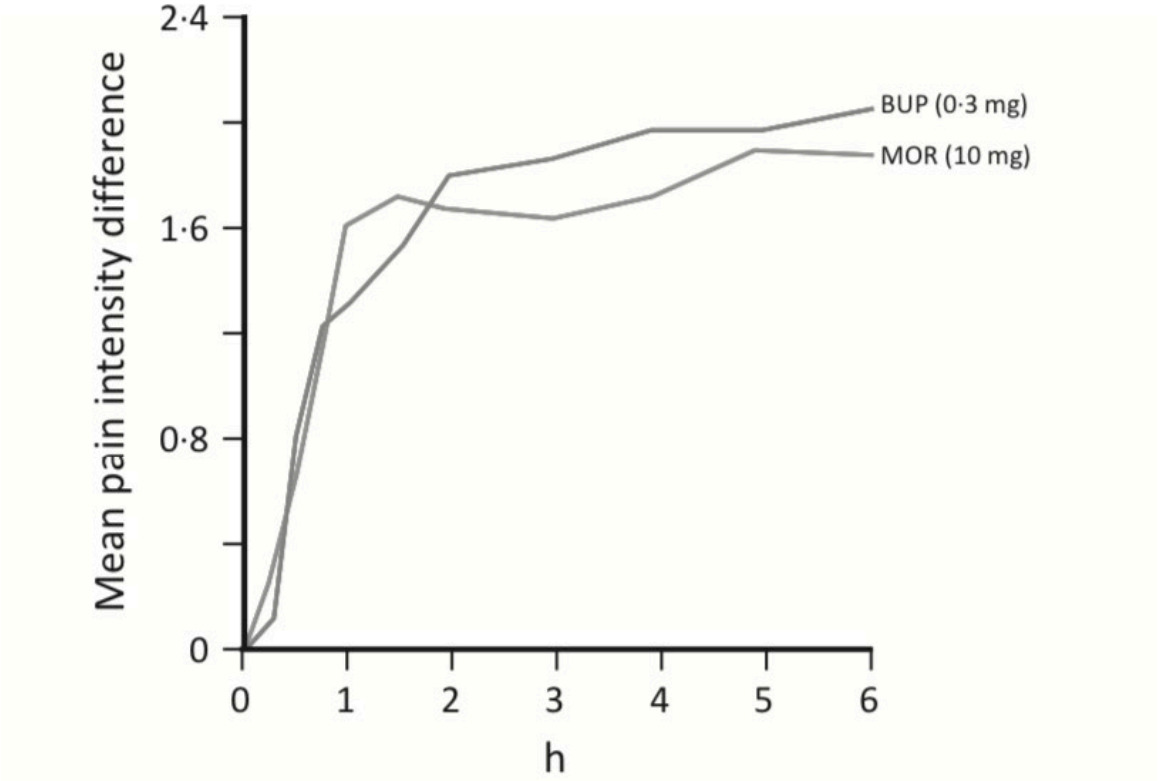
Zubsolv (SL tab)

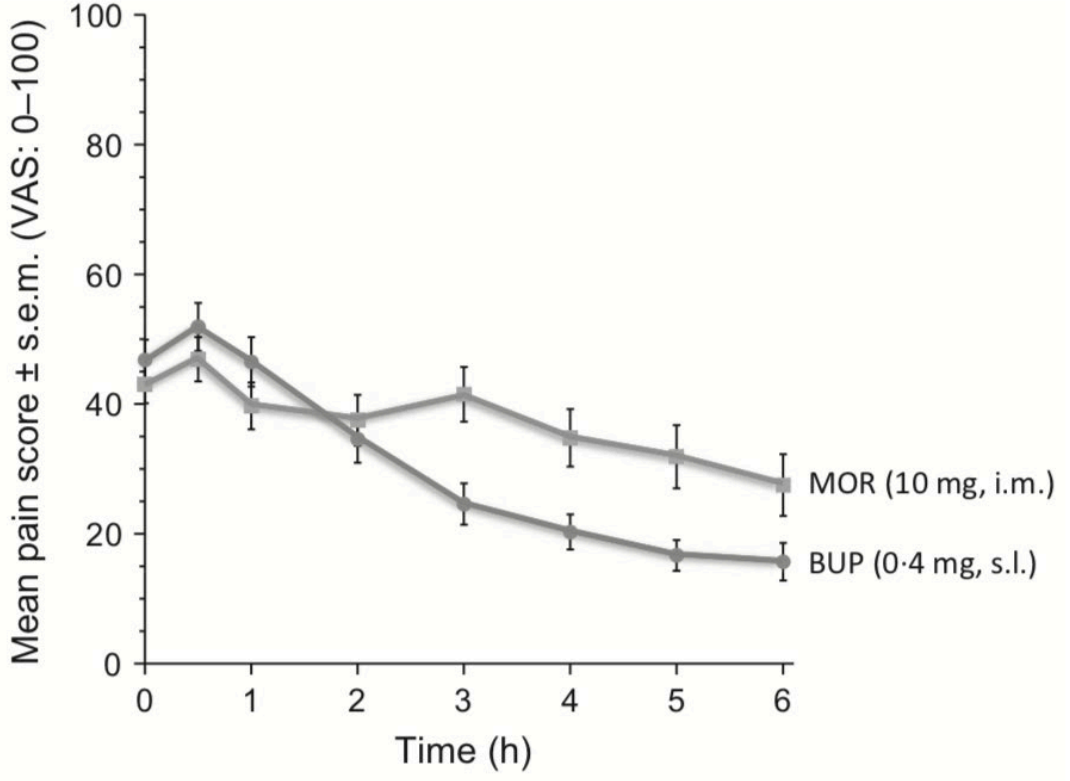






Buprenorphine is an effective analgesic!





Raffa RB (J Clin Pharmacy Therapeutics 2014)

Pain Medicine

Pain Medicine 2014; 15: 2087–2094
Wiley Periodicals, Inc.

Conversion from High-Dose Full-Opioid Agonists to Sublingual Buprenorphine Reduces Pain Scores and Improves Quality of Life for Chronic Pain Patients

Danielle Daitch, MD,* Jonathan Daitch, MD,[†,‡] Daniel Novinson, MPH,[§] Michael Frey, MD,[†,¶] Carol Mitnick, ARNP,[†,‡] and Joseph Pergolizzi, Jr MD[,††,‡‡]**

Subjects. Thirty-five chronic pain patients (age 24–66) were previously treated with high-dose opioid-agonist drugs and converted to SL buprenorphine. Patients' daily morphine equivalents ranged from

12 Reasons to use Buprenorphine for pain

1. Effective in treating cancer pain
2. Effective in treating neuropathic pain
3. Less tolerance, can be combined w/ other opioids
4. Less constipation
5. Ceiling effect on respiratory depression, but not analgesia
6. Less cognitive impairment
7. Not immunosuppressive
8. Does not adversely impact HPA axis
9. Does not significantly prolong QTc
10. Safer in the elderly
11. Safer in liver, renal disease including dialysis
12. Milder withdrawal and less dependence

Bonus reason: decreases OIH & central sensitization! – KOR antagonist, competes w/ spinal dynorphin

Davis MP. Twelve reasons for considering buprenorphine as a frontline analgesic in the management of pain. J Support Oncol. 2012;10(6):209-219.
Khanna IK, Pillarisetti S. Buprenorphine - an attractive opioid with underutilized potential in treatment of chronic pain. J Pain Res. 2015 Dec 4;8:859-70.
Butler S. Buprenorphine-Clinically useful but often misunderstood. Scand J Pain. 2013 Jul 1;4(3):148-152.

Buprenorphine (with or without naloxone)

for pain: any licensed DEA provider

0.075 – 3.2 mg/day (buccal film)

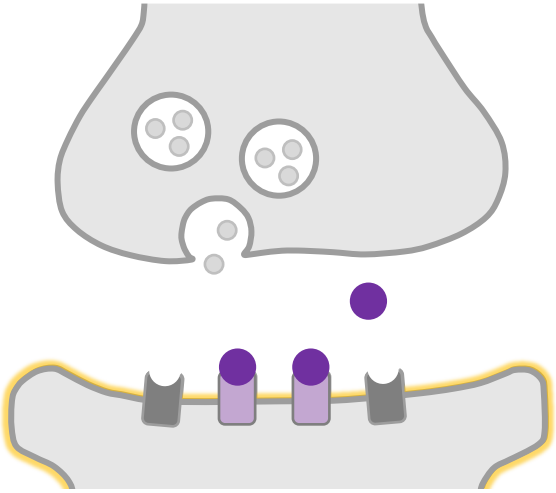
0.8 – 1.7 mg/day (transdermal patch)

analgesic effect: **6 – 8 hours**

for OUD: ~~need an X-waiver~~ !!!

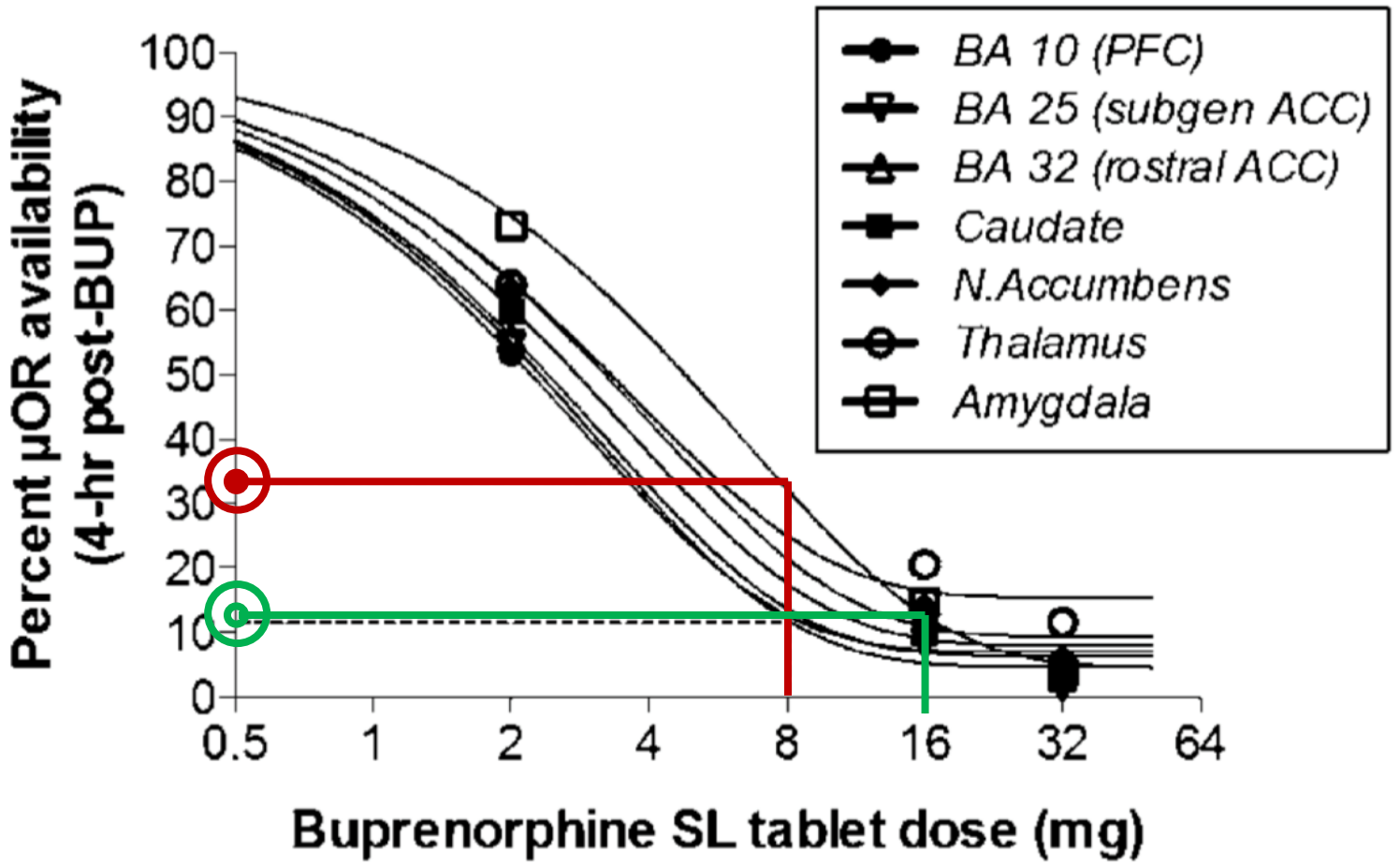
16 – 24 mg/day (sublingual tablet)

withdrawal suppression: **12-36 hours**



partial μ agonist

mu opioid receptor saturations by dose



30-40% blockade for pain suppression

50-60% blockade to suppress withdrawal

80% blockade to suppress reinforcing effects of opioids

>90% blockade to suppress cravings

Greenwald MK, et al. (Drug Alc Dep 2014)

Dosing Buprenorphine as an Analgesic

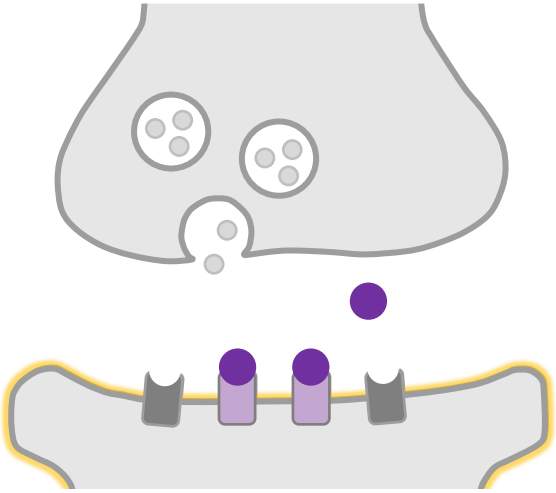
Wide variety of conversion factors from full agonists

Most common: 30-100x OME depending on formulation

Starting Doses:

30-80 MME = 10 mcg/h (TD)

- 90-160 MME = 300 mcg BID (buccal)
- SL?



partial μ agonist

Gudin, J., & Fudin, J. (2020, 2020/06/01). A Narrative Pharmacological Review of Buprenorphine: A Unique Opioid for the Treatment of Chronic Pain. *Pain and Therapy, 9*(1), 41-

Or just use this...

Equianalgesic Conversion Table

Buprenorphine	Oral Morphine Equivalent/24hrs (OME)							
	12	24	48	60	80	100	150	300
Transdermal (TD) patch	5mcg/hr q7days	10mcg/hr q7days	20mcg/hr q7days					
Buccal patch	75mcg daily	75mcg q12hrs	150mcg q12hrs		300mcg q12hrs		450mcg q12hrs	
Sublingual (SL) tabs					1mg BID (split 2mg tabs)		1mg TID	2mg TID

Case AA. et al. Treating Chronic Pain with Buprenorphine—The Practical Guide.Curr Treat. Options in Oncol.

Low (Cross-titration) and High-dose Inductions

Necessitated by the ubiquitous presence of fentanyl

Low-dose induction = cross titration with full agonist

- ↓ Precipitated W/D
- Rapid Engagement
- Accommodates continued use

High-dose induction = using higher doses initially and increasing to address the precipitated withdrawal

- Rapid Induction & Stabilization
- Requires Structure & Support

Initiatives at Emory Healthcare

Addiction Alliance of Georgia

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Emory's Addiction Training Team

Available to provider, units, divisions, and departments in the EHC to promote de-stigmatization of substance use disorders among healthcare providers and assist with implementation of addiction-related treatment protocols

The training team is composed of:
Justine W. Welsh, MD
Elizabeth McCord, MD
Joseph E. Mathias, MD
Noreen Peyatt, APRN, AP-PMN

To request training support, please email the team at addictionservices@emory.edu

Harm Reduction

Contains Free Supply of:

- Narcan Opioid Reversal Kits
- RX Destroyer
- Fentanyl Test Strips

In collaboration with **AWARE:** the **Wa**ronker **A**ddiction and **R**ecovery **E**ndowment

Key Points

- Initiation of opioid therapy for patients with chronic pain should be a deliberate and well-informed choice
- As part of informed consent, discuss pain management goals, functional goals, the length of opioid trial, and the plan for discontinuation
- Monitor for signs of addiction when treating chronic pain with opioids
- Diagnosing opioid use disorder during pain management is difficult and requires a thorough evaluation
- All patients with OUD should be offered maintenance medication due to risk of return to use, overdose death and other bad outcomes
- Buprenorphine can be a viable option in patients on high dose opioids with persistent pain and functional impairment

Thank you!
Questions?

Addiction Alliance of Georgia

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BREAK

Joint Providership Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Emory University School of Medicine, the Addiction Alliance of Georgia and the Hazelden Betty Ford Foundation.
The Emory University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Physician designation statement
The Emory University School of Medicine designates this live activity for a maximum of 4 *AMA PRA Category 1 Credit(s)™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Evidence Based Psychotherapy for Opioid Use Disorder

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Addiction Alliance of Georgia
EMORY HEALTHCARE | Hazelden Betty Ford Foundation

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- MI/MET training completed through the Veterans Affairs healthcare system
- Justine Welsh, MD

Objectives

- Participants will be able to identify Evidence Based Psychotherapies (EBPs) for OUDs/Substance Use Disorders (SUDs)
- Participants will be able to recognize common psychiatric disorders that co-occur with OUDs
- Participants will be able to describe techniques used in EBPs for OUD.

First thoughts on therapy for SUDs

A&E “Intervention”

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“ People are generally better persuaded by the reasons which they have themselves discovered than by those which have come into the mind of others. ”

-Blaise Pascal, Pensees de Pascal, #10, written in 1660

Evidence Based Practice: Application to Substance-Focused Treatment

- Emphasis on shared decision making and individualized treatment plans
- Team based approach
- What are the goals?
  - Complete abstinence
  - Abstinence from most harmful substance
  - Reduction of use
  - Reduction of most harmful behaviors

Glasner & Drazdowski, 2019

Evidence Based Practice: a Focus on Opioid Use Disorder

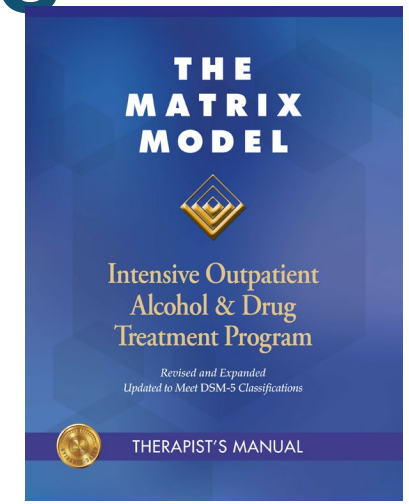
- **Medical management is an essential part of treatment**
  - Detox
  - Maintenance therapy
- **Standard of Care includes medication management for maintenance and behavioral therapy following stabilization**
- **For OUDs, goals include:**
  - Improving adherence to medication
  - Relapse prevention
  - Addressing co-occurring disorders

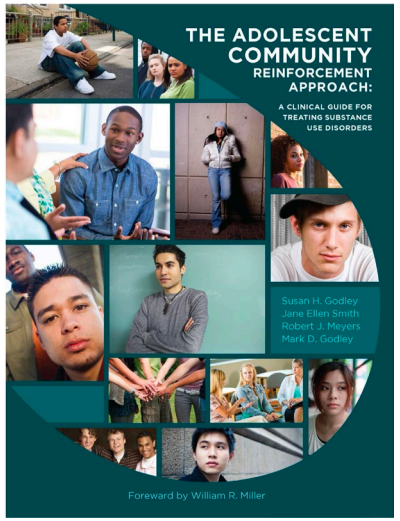
American Psychological Association, 2019

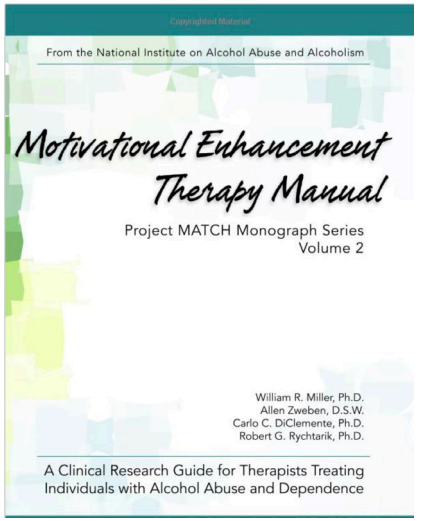
Psychosocial Treatment for SUDs

Evidence Based Individual or Group Therapy:

- ***Cognitive-behavioral therapies***
- ***Contingency management***
- ***Motivational enhancement therapy*** *(MET)*







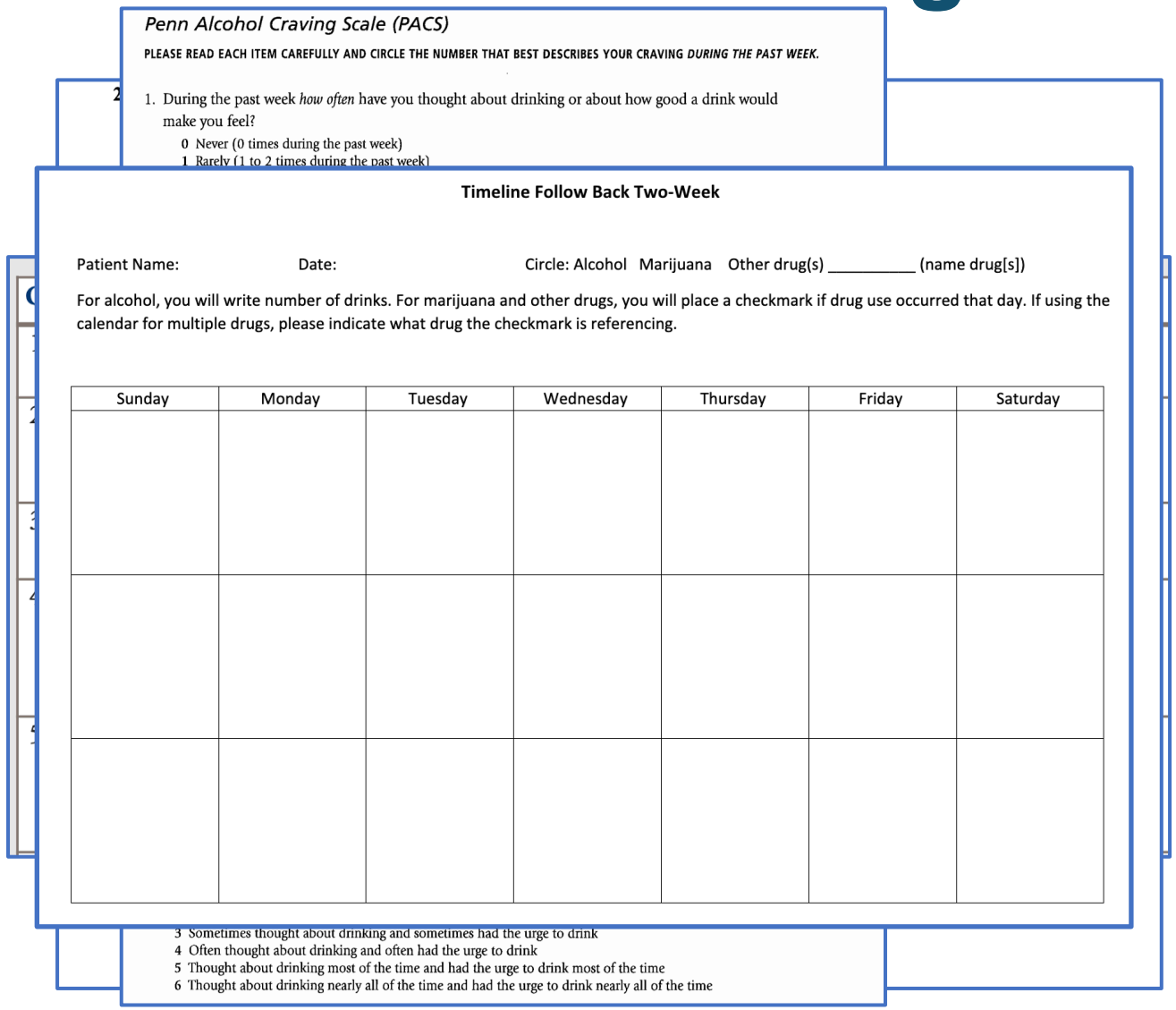
Additional Psychosocial Components

- Self-help groups (e.g., NA/AA, SMART recovery)
- Case management
- Couples/Marital therapy
- ***Family therapies***

(APA Practice Guidelines, 2010; APA, 2019; Glasner, S., & Drazdowski, 2019; VA DOD clinical practice guidelines, 2021)

Symptom Assessment and Tracking

- AUDIT, Drug Abuse Screening Test (DAST)
- Brief Addiction Monitor (BAM-R)
- Penn Alcohol Craving Scale
- Timeline follow back method



Penn Alcohol Craving Scale (PACS)

PLEASE READ EACH ITEM CAREFULLY AND CIRCLE THE NUMBER THAT BEST DESCRIBES YOUR CRAVING *DURING THE PAST WEEK.*

1. During the past week *how often* have you thought about drinking or about how good a drink would make you feel?
   - 0 Never (0 times during the past week)
   - 1 Rarely (1 to 2 times during the past week)
   - 3 Sometimes thought about drinking and sometimes had the urge to drink
   - 4 Often thought about drinking and often had the urge to drink
   - 5 Thought about drinking most of the time and had the urge to drink most of the time
   - 6 Thought about drinking nearly all of the time and had the urge to drink nearly all of the time

Timeline Follow Back Two-Week

Patient Name: Date: Circle: Alcohol Marijuana Other drug(s) _____ (name drug[s])

For alcohol, you will write number of drinks. For marijuana and other drugs, you will place a checkmark if drug use occurred that day. If using the calendar for multiple drugs, please indicate what drug the checkmark is referencing.

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday

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Cognitive Behavioral Treatment for SUDs

- **Treatment based on cognitive behavioral case conceptualization**
- **Identifying the function of the substance use behavior**
  - Antecedents/triggers
  - Contextual factors
  - Rewards
  - Consequences
- **Setting goals around substance reduction/abstinence**
- **Using the functional analysis/case conceptualization and pt goals to design a treatment plan**
- **Use of self-monitoring, symptom tracking to gather data about progress towards goals**
- **Homework/ “at home practice” to generalize skills outside of therapy session**

Functional Analysis of Substance Use

External Triggers	Internal Triggers	Using Behavior	Short-Term Positive Consequences: Good Things (rewards)	Long-Term Negative Consequences: Not So Good Things
1. Who are you usually with when you use?	**1. What are you usually thinking about right before you use?**	**1. What do you usually use?**	**1. What do you like about using (by yourself)?** "Its relaxing, its rewarding myself, this is time to relax	**1. Negative results of using in each of these areas:**
Usually alone, after school, sometimes roommate is there	"I just want to relax" "I deserve it, I had a stressful day"	Marijuana, usually vape sometimes edibles	**2. What do you like about using (at home)?** "It makes the evening go by faster, adds to boring activities"	**a) Interpersonal:** affected relationships when I stayed home to smoke (missed out on social stuff); also, people tell me I'm not as social as I think I am; probably forget conversations
2. Where do you usually use?	**2. What are you usually feeling physically right before you use?**	**2. How much do you usually use?**	**3. What do you like about using (in the evening)?** "Its something to look forward to, unwinding after a day at work, [beliefs about] 'this is how I relax'"	**b) Physical:** weight gain when I eat too much, also "lazier" so less likely to exercise or do active things, may be groggy the next day
At home	Mild jitteriness, difficulty staying still	6 hits total	**4. What are the pleasant thoughts you have while using?** "Absence of worry thoughts, avoidance of or distraction from thinking about responsibilities"	**c) Emotional:** probably impacts motivation and desire to do things outside of smoking weed
				d) Legal: some risk in obtaining it/using it since its illegal
			5. What are the pleasant physical feelings you have while using?	**e) Job:** n.a – does affect school productivity
3. When do you usually use?	**3. What are you usually feeling emotionally right before you use?**	**3. Over how long a period of time do you usually use?**	"Lack of tension, opposite of tightness, looseness"	**f) Financial:** spend quite a bit on it, $300/month
After school, in the afternoon/ evenings	Mild excitement, looking forward to it	5pm-11pm	**6. What are the pleasant emotions you have while using?** Relaxation, calm, playfulness (especially socially)	**g) Other:** though it takes my mind off stress, I end up not getting things done which adds more stress in the long run (e.g., not doing school assignments, not completing student loan app, etc)

Adapted from A-CRA manual (2016)

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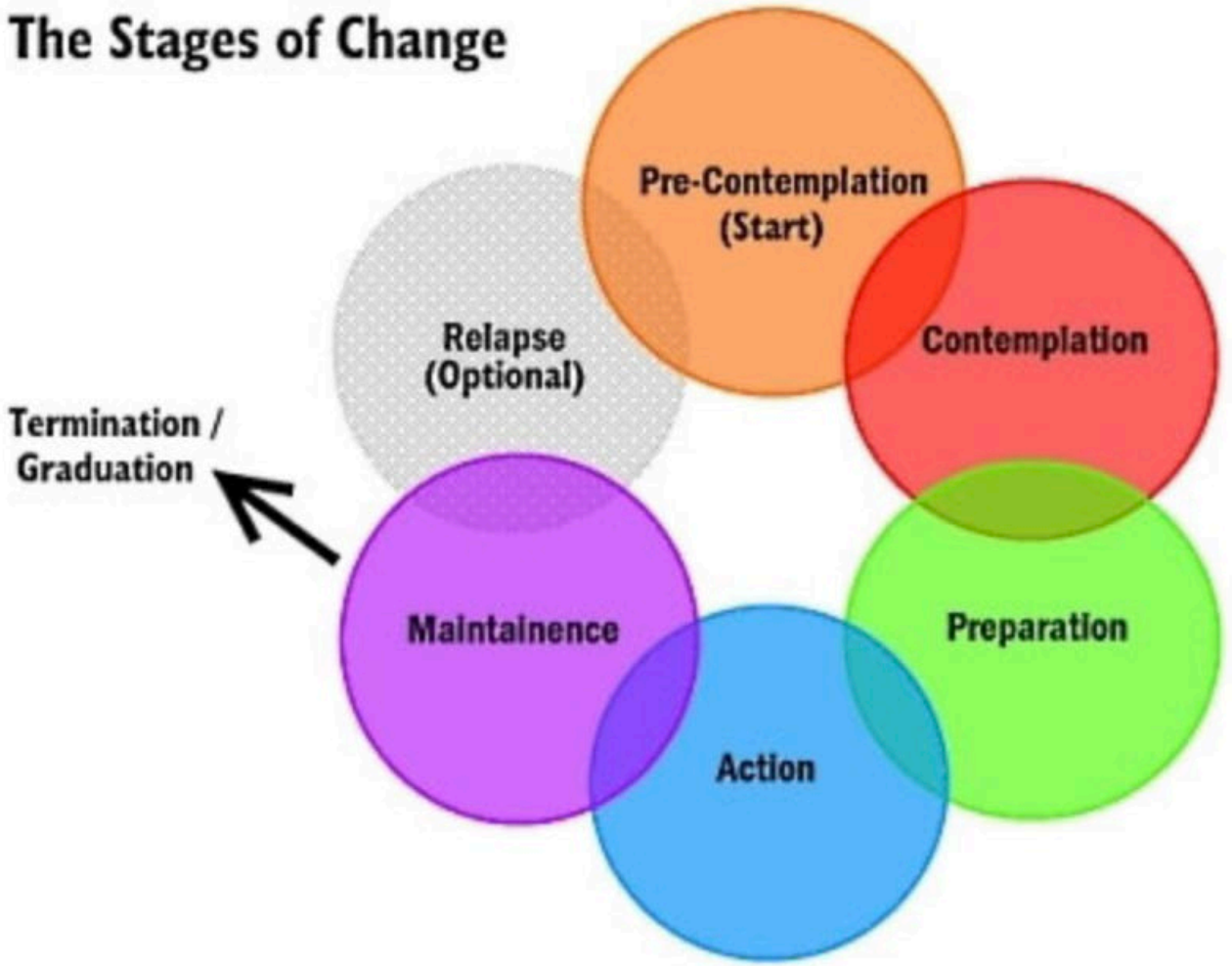
Motivational Interviewing/ Motivational Enhancement Therapy

Technical Definition

- MI is a collaborative, goal-oriented style of communication with particular attention to the language of change.
- MI is designed to strengthen personal motivation for and commitment to a specific goal by eliciting and exploring *the person's own reasons for change* within an atmosphere of acceptance and compassion

MI Stance

Image credit Matrix Counselor manual (2016)



Prochaska and DiClemente, 1983

MI/MET Strategies

- Using OARS to engage and focus the patient, and elicit change talk
- **O: Open-ended questions**
- **A: Affirmation**
- **R: Reflection**
- **S: Summary**

MI Stance: Traps to avoid

- Ordering, directing
- Warning, threatening
- Giving advice, solutions
- Persuading with logic
- Telling people what to do
- Judging, blaming

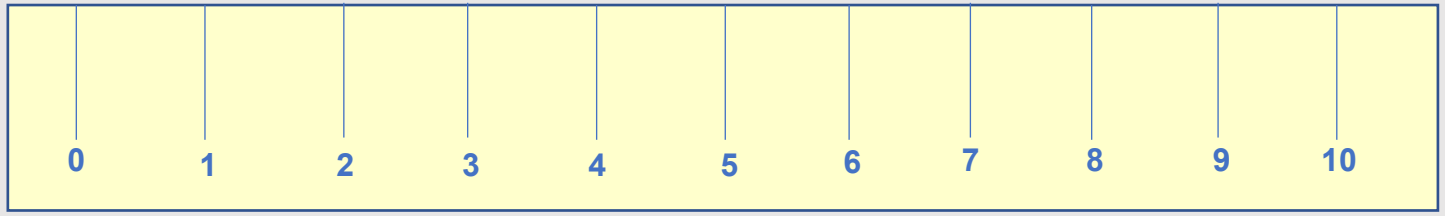
Experiential Exercise Using OARS

Motivational Interviewing technique: assessing pros and cons of changing/ staying the same

List: [Behavior I Want to Change]		
	Staying the Same	**Changing**
Benefits		*[positive effects on life for changing behavior/substance use]*
Costs	*[negative impact of behavior/substance use on life]*	

Motivational Interviewing Technique: Assessing Importance and Confidence of Change

How important would you say it is for you to [*make ** behavior change*]? On a scale from 0 to 10 where 0 is not at all important, and 10 is extremely important, where would you say you are?



Not at all Important

Extremely Important

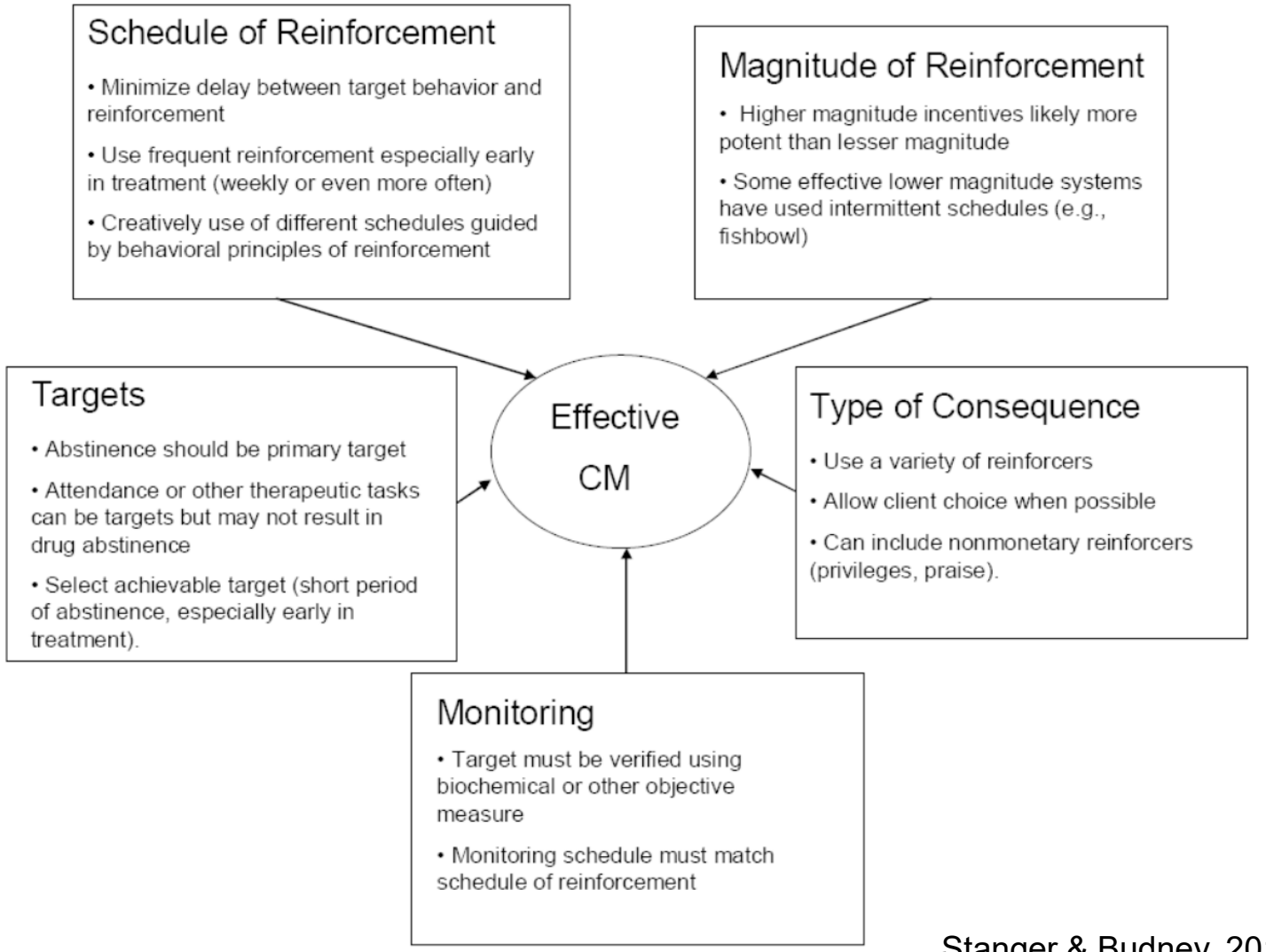
And how confident are you that if you decided to [*make ** behavior change*], you could do it? On the same scale, where 0 is not at all confident and 10 is extremely confident.

Community Reinforcement/Contingency Management

- **<u>Community Reinforcement Approach</u> focuses on environmental contingencies that impact the patient's behavior**
  - Uses family, social, recreational, and occupational events to support the individual in changing their substance using behaviors
  - Goal to make a sober life more rewarding
- **<u>Contingency Management</u> is based on behavioral principles of reinforcement that reward specific behavioral goals related to recovery**
  - Can include monetary or nonmonetary rewards
  - Usually contingent on negative toxicology results, treatment adherence, or progress towards treatment goals

VA DOD clinical practice guidelines, 2021

Key Principles in Contingency Management



Stanger & Budney, 2010

Sample Contingency Management Contract

Substance Monitoring Contract

If _____'s urine drug screen is negative (no drugs detected or reported) and there were no positive or refused alcohol breath tests since the last drug screen, I will:

1. Praise their progress!
2. Ask how I can help them keep up the good work.
3. Celebrate their progress by:

_____
_____
_____

If _____'s urine drug screen is positive (drugs detected or reported) and/or there were positive or refused alcohol breath tests since the last drug screen, and/or urine screen is refused, I will:

1. Remain calm!
2. Not give a lecture
3. Ask how I can help them
4. Express confidence that they can do better next time
5. Use the following consequence:

_____

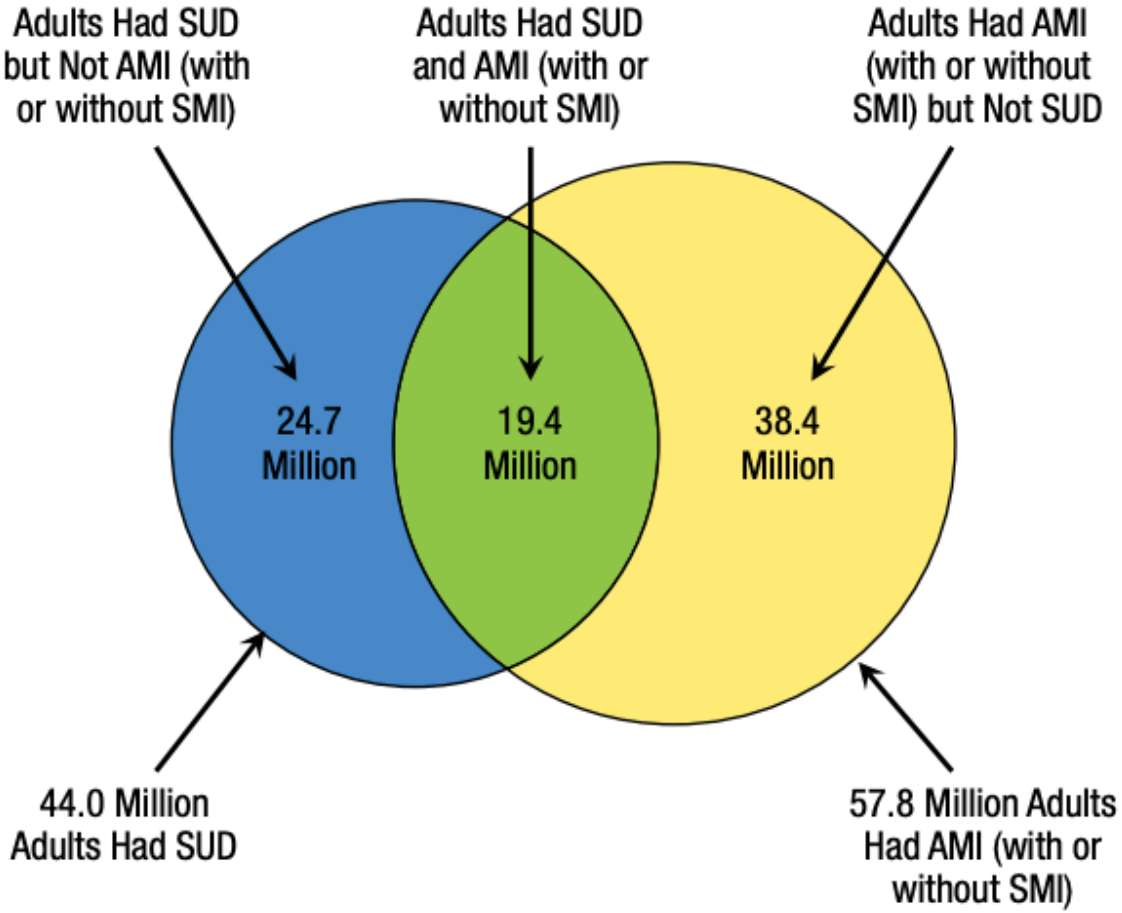
_____ _____
Parent Signature Date

_____ _____
Teen Signature Date

_____ _____
Therapist Signature Date

Stanger & Budney, 2010

Co-Occurring Disorders



SAMHSA, 2021

Opioid Use Disorder and Co-occurring Disorders

- 77 percent also had another SUD or nicotine use disorder in the past year
- 64 percent also had any co-occurring mental illness in the past year.
- 27 percent had a past-year comorbid SMI.
- **Only ¼ of individuals with an OUD and co-occurring disorder received treatment for both disorders**

SAMHSA, 2020

Co-Occurring Disorders (cont.)

- **Stressful experiences such as childhood trauma have been implicated in the initiation of substance use.**
- **PTSD and SUDs are highly comorbid**
  - Associated with worse treatment outcomes and more severe clinical course
- **Drug use and its effects can mimic other mental health disorders**
  - Withdrawal
  - Intoxication
- **Substance induced mood disorders**
- **SUDs during pregnancy and postpartum**

Treatment Approaches for Co-Occurring Disorders

- **Integrated Treatment associated with better outcomes**
- **Some exist, particularly for trauma/PTSD:**
  - Seeking Safety (trauma and SUDs)
  - Concurrent Treatment of PTSD and Substance Use Disorders using Prolonged Exposure (COPE): PTSD and SUDs
- **Unified Protocol is also a transdiagnostic treatment approach**
- **Cognitive Behavioral Therapy principles can be applied to comprehensive treatment of the SUD and co-occurring psychiatric problems**

SAMHSA, 2020; Barlow 2017

The Role of Self Help Groups in Recovery

	Pros	Cons
AA/NA	Education and Instillation of hope —learn about recovery from others, others experiences can inspire hope.	"War stories"—members' stories could be depressing and not inspiring or too "heavy"; language used can be also be offensive
	Spirituality—appeals to a Higher Power if this is consistent with pt beliefs.	Spirituality—may not be consistent with pt beliefs.
	Support—gain support from other members or sponsor	Unwanted familiarity could cause discomfort
	Availability—usually available 24/7/365 worldwide	
SMART Recovery	Group size—generally small group.	Support—not as much of an emphasis on using group for support
	CB approach—uses cognitive-behavioral approach to change cognitions and behaviors.	Effectiveness—no studies of effectiveness.
	No focus on a Higher Power-which may align with beliefs	Availability— fewer in person groups available, virtual groups fairly common (not necessarily 24 hrs/day), no sponsor option
	Not always abstinence-focused—sometimes focused on moderation, may or may not align with treatment goals	Not always abstinence-focused—sometimes focused on moderation.

Adapted from Women's Recovery Group manual, Sugarman et al, 2016

Summary

- **Evidence Based Behavioral Treatment for SUDs exists**
- **Best to formulate individualized treatment plans in a collaborative, patient centered manner**
- **Team-based approach is gold standard**
- **For OUDs, first line treatment is medication management, with psychotherapy added for relapse prevention and co-occurring problems**
  - Co-occurring disorders are the norm; important to treat in an integrated way if possible
- **Couples/Family therapy, and community support, are helpful additions**

Questions, Comments, Discussion

LUNCH

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Gish Placeholder

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Overdose Prevention & Georgia's Medical Amnesty Law

Andy Gish RN, BSN, CEN
Director, Georgia Overdose Prevention

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GEORGIA OVERDOSE PREVENTION

GEORGIA HARM REDUCTION COALITION

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How Harm Reduction made me a better nurse.

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In 2014, Georgia became the 15th state to pass a Medical Amnesty Law: Don't Run, Call 911

The law provides limited immunity from arrest, charge and prosecution for possession of drugs and drug paraphernalia when someone is experiencing a suspected overdose

Access to Naloxone/Narcan (the antidote to opioid overdoses) to anyone in Georgia without a prescription

What is your state's Medical Amnesty Law?

Why are opioids dangerous?

When opioid receptors are flooded with opioids, they decrease or turn off the functions of those organs

In the brainstem this causes respiratory depression or failure

This shuts down automatic breathing

How does someone die from an overdose?

1st - Respiratory Arrest (stops breathing)

2nd - Brain injury occurs before death

3rd - Cardiac Arrest (heart stops)

At any stage in this process this can be reverse, sometimes even after cardiac arrest.

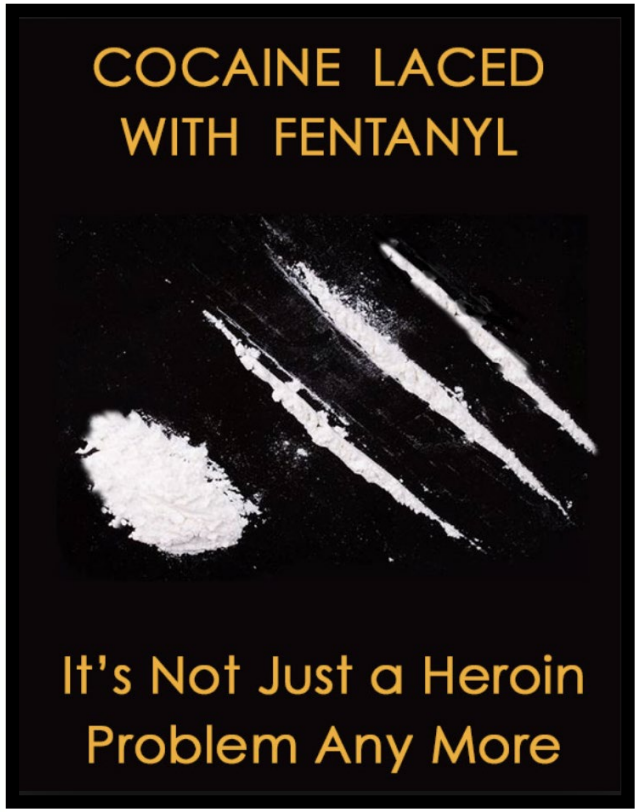
Remember many overdoses occur from legally prescribed medications that are given to treat real diseases and real chronic pain

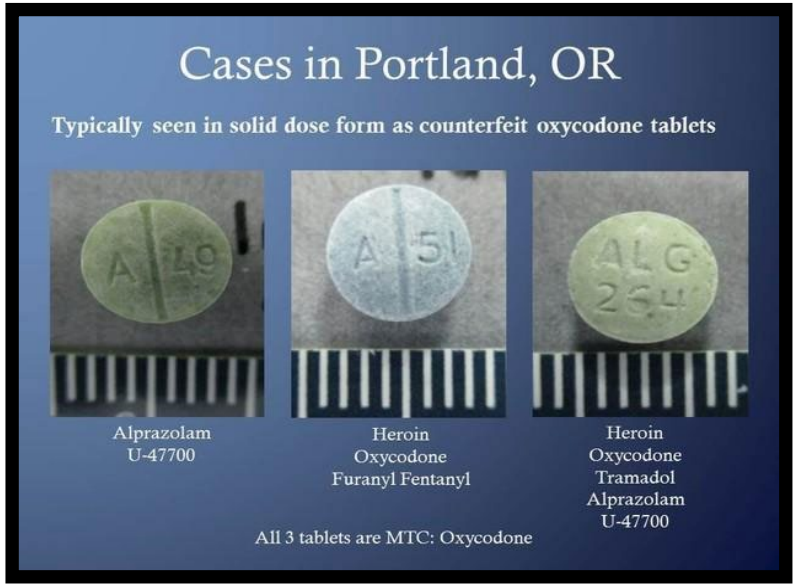
What kinds of opioids are we seeing?

Heroin is not heroin anymore

98% of heroin in a Massachusetts study was positive for fentanyl

Fentanyl laced pressed pills





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Recognizing and Treating an Overdose

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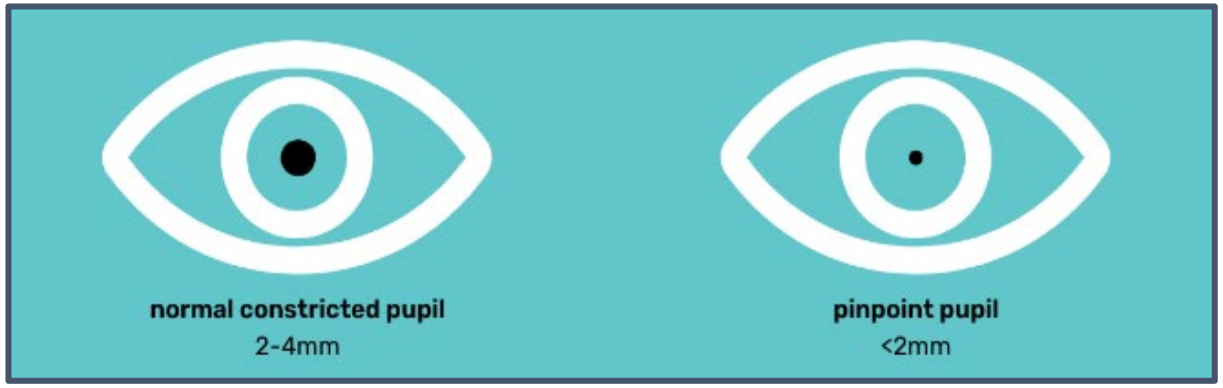
Recognizing an overdose



- Pinpoint Pupils (classic sign)
- Blue lips, nails, and skin
- Limp limbs
- Pale face or skin
- Passing out or “nodding off”, "frozen stance"
- Ineffective breathing (slow, irregular, choking, gurgling, snoring, apnea)
- Awake, but unable to respond

A person nodding off with little verbal response may be on the precipice of respiratory failure!

Caring for an overdose victim

Assess for responsiveness (Shout/Shake/Sternal Rub)

<u>Administer the antidote Narcan/naloxone</u>

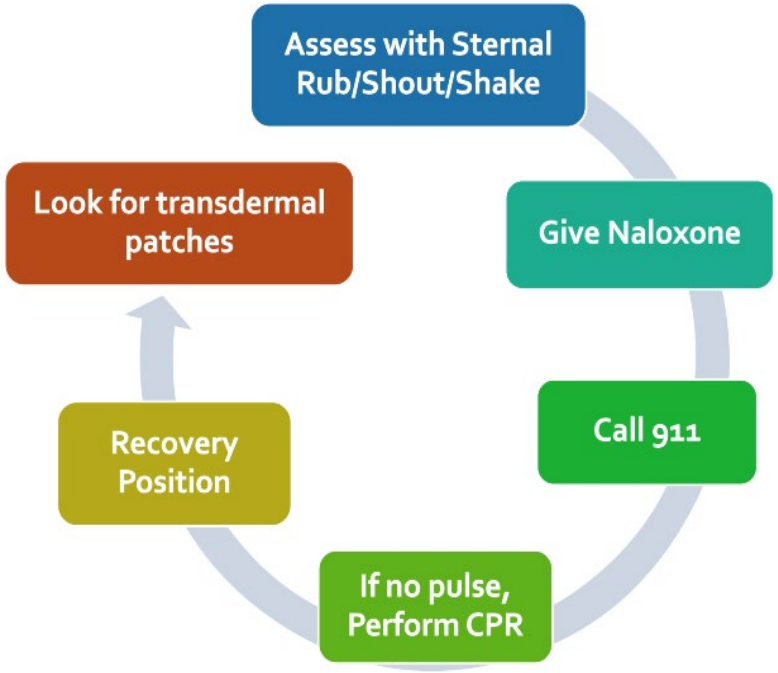
Call 911

Perform CPR if needed ***Rescue breathing is essential!***

Turn them on their side if CPR is not needed ***Recovery position***

Look for transdermal patches (remove with gloves only)

If pulseless, CPR moves naloxone around!



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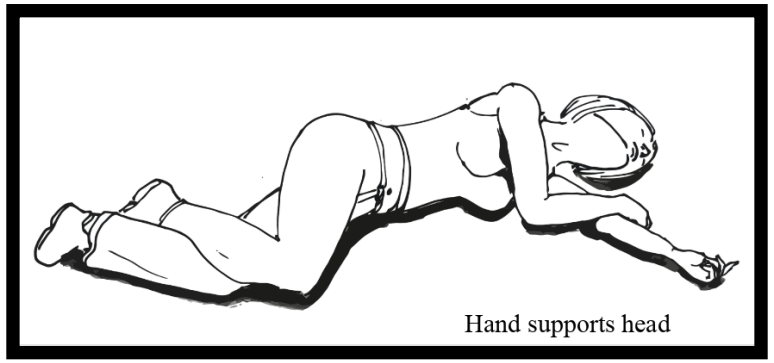
Caring for an overdose victim

Protect Yourself!

- Always wear PPE if available
- Consider any powder may be residual opioids (mask/gown)
- Consider their may be sharps around

Important

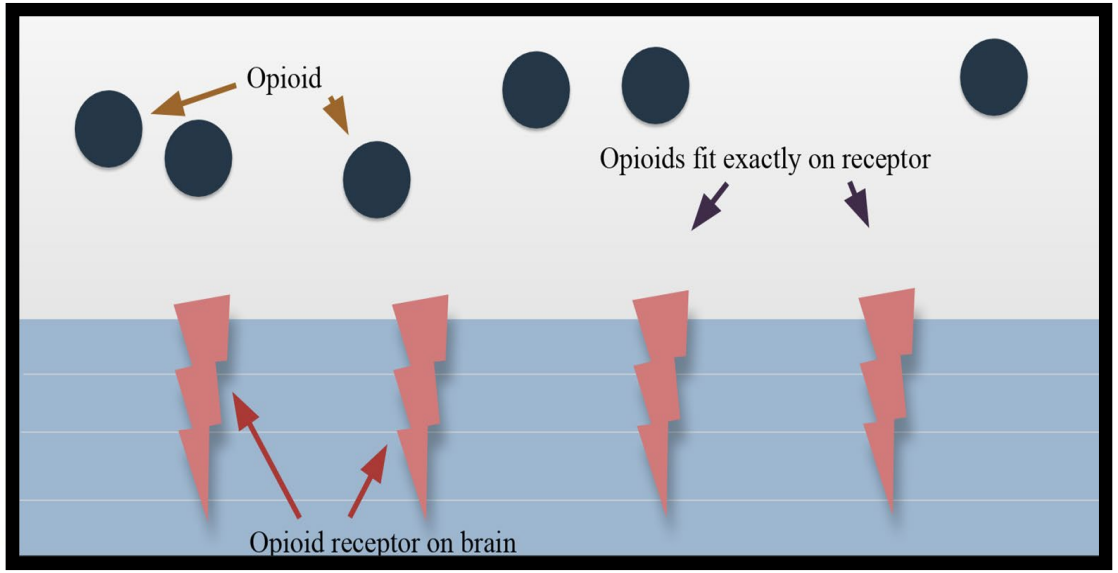
- As someone is waking up, if you feel unsafe – sit behind the victim
- Remember this can be unsettling – be kind to yourself.

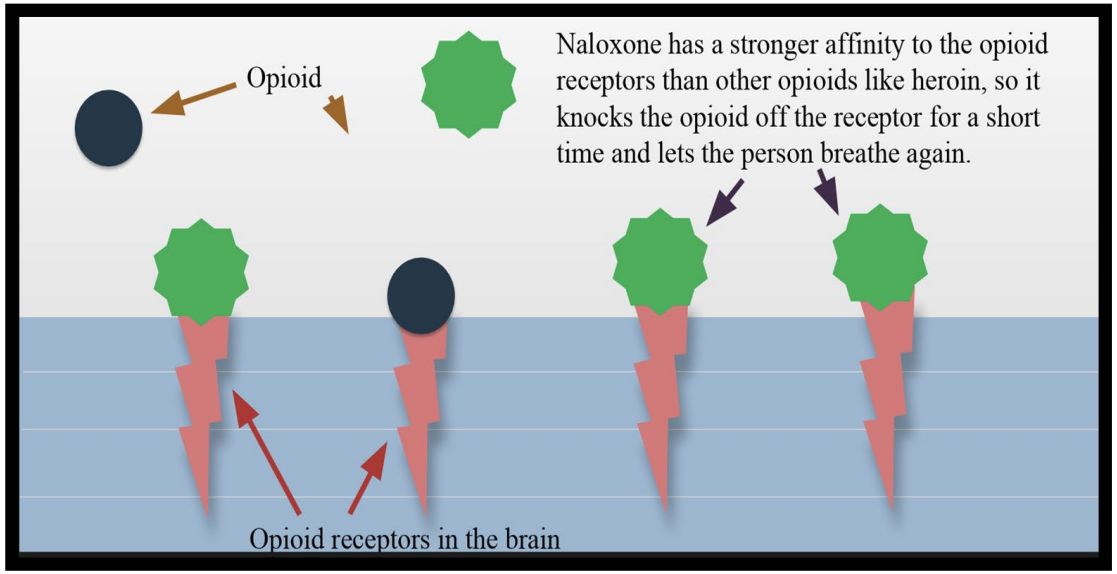


Naloxone AKA Narcan

The Antidote!

How does naloxone work?





Graphic: Georgia Department of Public Health

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Naloxone (Est. 1971)

Onset: 2-4 minutes

Safety: Only reverses opioid overdoses. Won't cause harm in other medical emergencies

Stability: Temperature stable (keep it where you will use it!)

Expiration: Works at least 28 YEARS after expiration

Duration of Effect/Half Life: 30-90 minutes to an hour. People can have a recurring overdose without ingesting more opioids.

Side effects: Withdrawal symptoms: nausea, vomiting, body aches, "lights off, lights on

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Narcan (4mg/0.1ml) Nasal

Very strong dose in small amount of fluid

2 doses per box

Cost: $45 (copay is often low)

How to give:

- Tilt head back (supine)
- Alternate nostrils every 2 minutes until person is breathing or EMS arrives
- They do not have to be breathing! The liquid just has to touch the mucosal membrane

There is no “priming” of the nasal delivery device. One Step Only!

Quick guide inside cover of box

If not giving CPR, place them in recovery position between doses. ***WHY is this?***

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Naloxone (0.4mg/1 ml) IM

Intramuscular Injection

Preferred location: deltoid (upper shoulder) or thigh

Most kits have 2 syringes and 2 vials

Most syringes can go through jeans

No need to clean off with an alcohol swab

After injection YOUR safety is the most important. Push the safety cap or safely cap the needle so you don't accidentally get stuck

Cost: $2-$30

Easily portable. Cost Effective. Preferred by active people who use IV, Harm Reduction groups.

Narcan OTC Nasal

HARM REDUCTION THERAPEUTICS

FDA has approved Nasal Naloxone to be OTC!

First company “Narcan” expected to be on shelves Oct 2023 at “under $50”

High dose and long acting versions of naloxone or nalmefene are not supported by Harm Reduction

Higher, longer-acting doses are not better! You can throw people into precipitated withdrawals and keep them there.

- Painful
- Unnecessary
- Punitive
- More likely to use
- ***This is stigma in practice***

Discussion: Naloxone given in the community

What do you notice?

What does this mean for the EMS/ER/Hospital?

What does this mean for the patient/family/community?

Is there anything you would have done differently?

What other outcomes could have happened?

MEDIA: Officer giving Naloxone to overdose victim

Common questions about Naloxone

But what if it is a mixed overdose?
Naloxone can help them breathe again but they may still be altered. Ie: intoxicated

What if it is not an overdose, what if it's a STROKE, SEIZURE?
Naloxone WILL NOT hurt them

Doesn't Narcan encourage addiction?
No! Naloxone does not encourage addiction! No one wants "Narcaned"

Is it really legal to carry naloxone?
YES! In Georgia and in almost all states!

Am I really protected if I give it to an unconscious stranger?
YES! In Georgia and in almost all states!

Who is at biggest risk of an overdose?

Just out of treatment or incarceration (low tolerance)

New cities (new kinds of street opioids)

Newly experimenting (less knowledge, less tolerance)

Obtaining pills/drugs from unknown sources

Using alone

Mixing substances

Elderly (polypharmacy, forgetting if they took meds)

What are some common overdose myths?

You can only overdose if you are using intravenously

Overdoses occur immediately after using
- They can occur over hours
- They can start hours after consumption

Overdoses happen at night (they happen everywhere, at all times of day)

Overdoses only happen to young people, people who look a certain way… (continue to check your bias)

You can counteract an overdose with coffee, ice baths, milk, salt, cocaine

The only effective way to counteract an opioid overdose is with naloxone/narcan.

The sooner naloxone is administered, the sooner the brain will get oxygen and the less brain injury occurs. Every second counts!

Where might you see an overdose in the community?

Anywhere. Any time of day. Any person

Targeted Areas:

- Busy parking lots (assess people sleeping in a car)
- Single use bathrooms
- Places with baby changers

Remember “nodding off” is a symptom of overdose. Don’t leave someone.

Reminder: Naloxone is ***short-acting***. If someone gets reversed, they still need medical help.

Call 911 and let EMS take over.

Over 9,400 Community Reversals

GEORGIA OVERDOSE PREVENTION

AHRC
Atlanta Harm Reduction Coalition

Please Report Reversals!

Every single reversal is a save for us, we keep close to our hearts

georgiaoverdoseprevention.org

Call/text GOP Report a Reversal Hotline
404-919-4812

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TRAUMA INFORMED CARE & INTEGRATED TREATMENT FOR PTSD AND SUBSTANCE USE DISORDERS

Recognizing The Impact of Trauma to Increase Safety, Trust and Hope

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WELCOME AND INTRODUCTIONS

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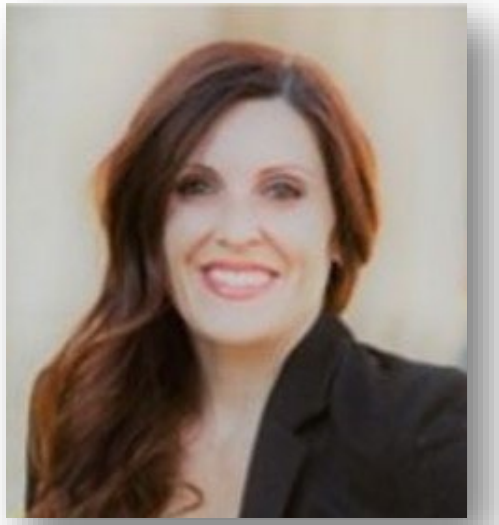

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OBJECTIVES

- Identify the core principals of trauma informed care and discuss strategies to promote these core principals at the individual and organizational levels to increase access to care.
- Examine the neurobiology of trauma to effectively engage patients with substance use disorders and histories of trauma.
- Review Evidence Based integrated psychotherapies for trauma and substance use disorders to effectively engage patients with substance use disorders and histories of trauma.

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SAFETY

Things you can do:

- Breathe
- Imagine a safe space
- Stretch
- Joyful Movement
- Count Backwards
- Massage your hands
- Meditation
- Prayer
- Mantra

WHAT IS TRAUMA INFORMED CARE?

Organizational and systems change

A paradigm shift

Evaluating our policies, processes, procedures to ensure safety for everyone involved in our system.

Taking care of the people, that take care of people

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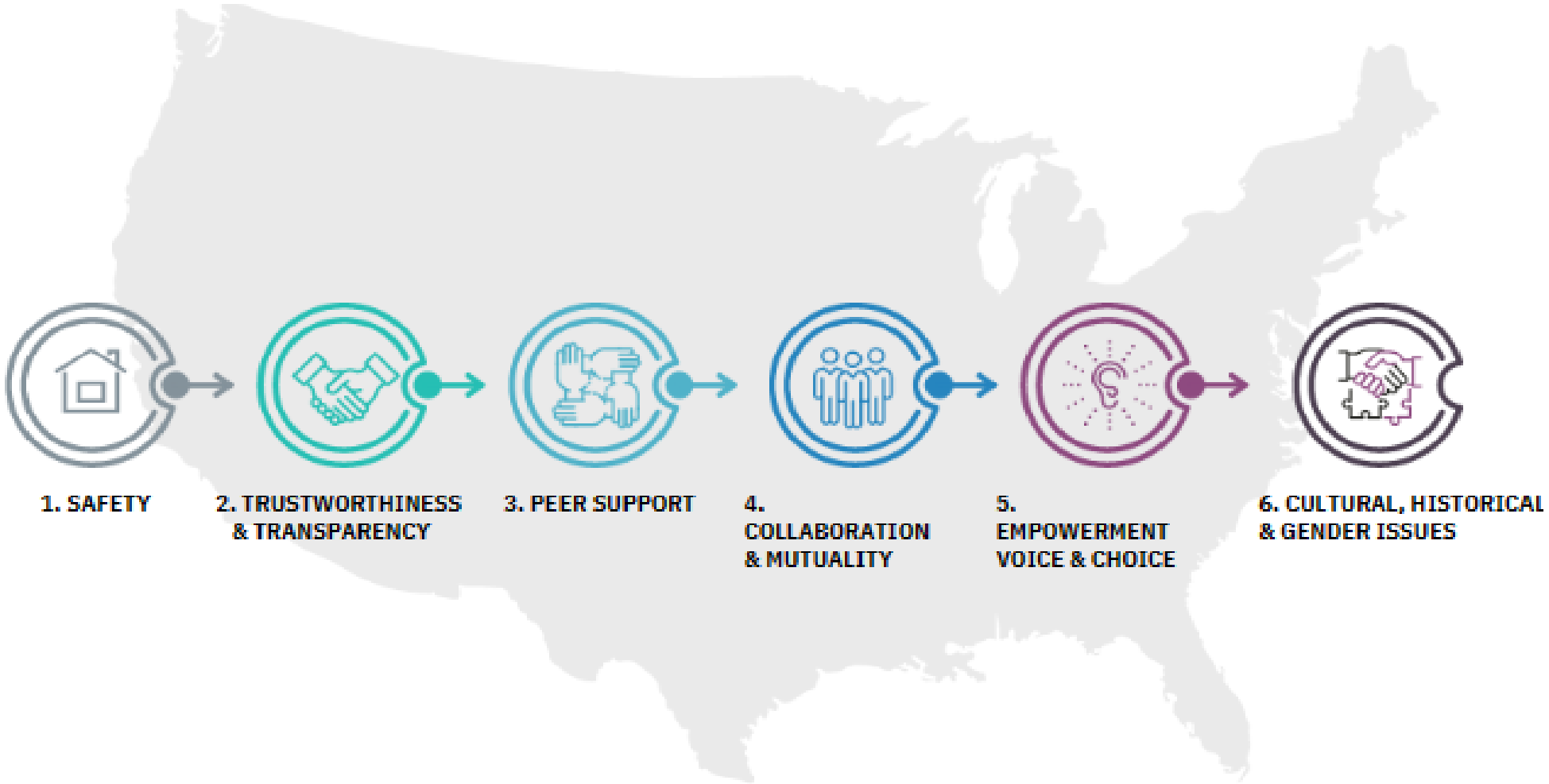
4 R's OF A TRAUMA INFORMED APPROACH

Realizes	• The widespread prevalence of trauma individually and collectively and the presence of strength, resilience and paths for recovery.
Recognizes	• Signs and symptoms of trauma in individual patients, families and staff
Responds	• By integrating knowledge about trauma into polices, procedures, practices; and
Resists	• Seeks to actively resist re-traumatization by seeking to eliminate procedures or policies that have been activating or traumatizing in the past.

6 CORE PRINCIPALS OF TRAUMA INFORMED CARE



1. SAFETY
2. TRUSTWORTHINESS & TRANSPARENCY
3. PEER SUPPORT
4. COLLABORATION & MUTUALITY
5. EMPOWERMENT VOICE & CHOICE
6. CULTURAL, HISTORICAL & GENDER ISSUES

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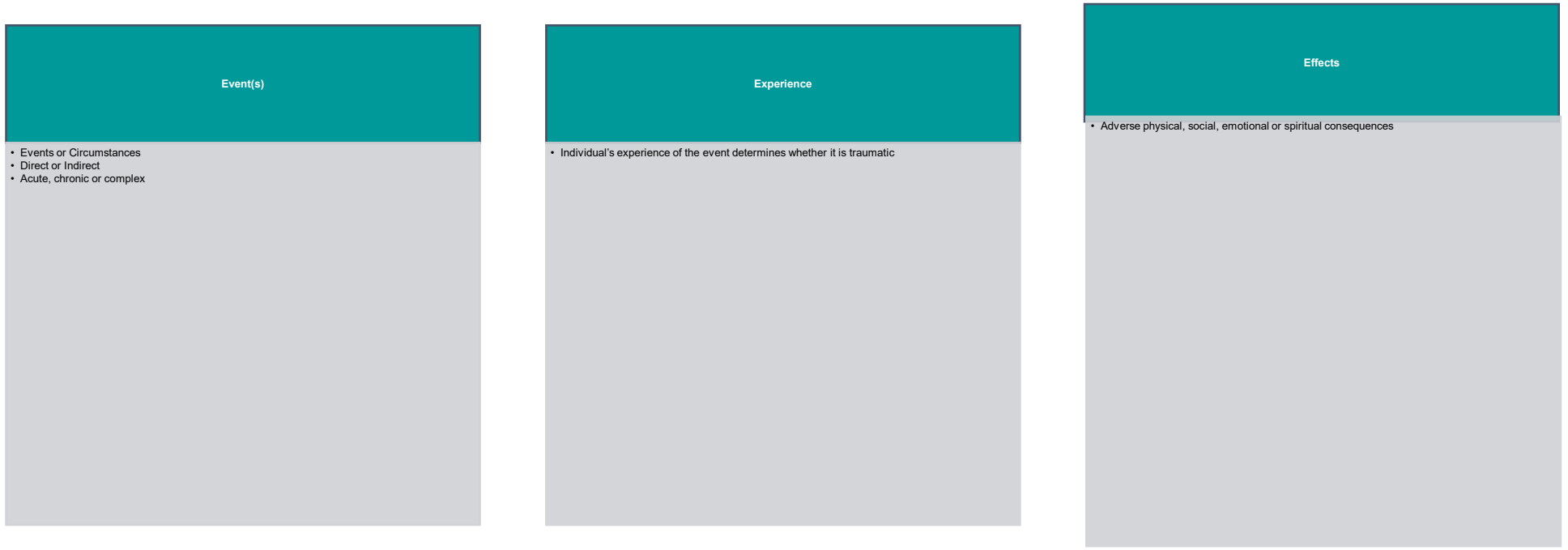
DEFINING TRAUMA: THE THREE E's

EXPERIENCES THAT OVERWHELM AN INDIVIDUAL'S CAPACITY TO COPE.



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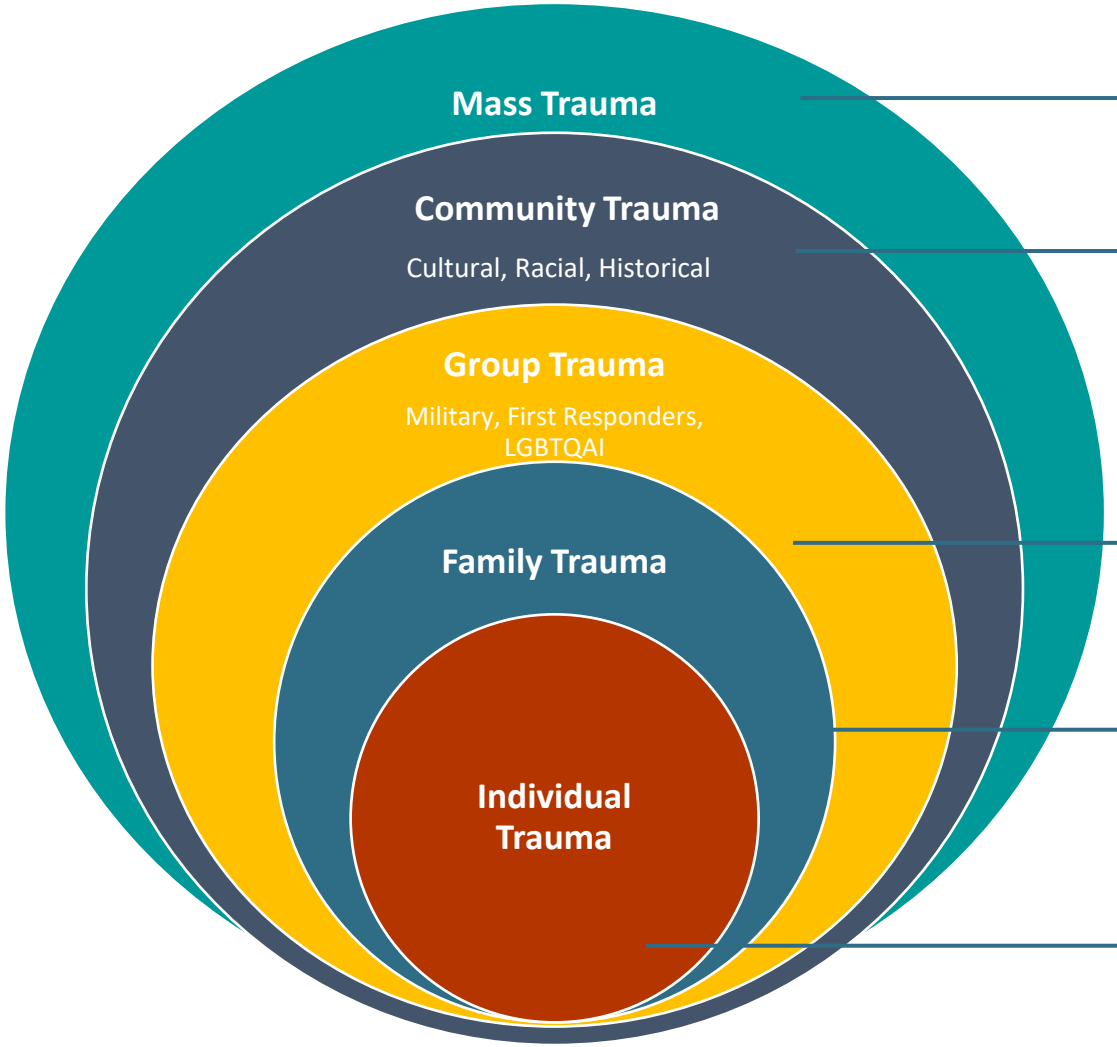
DEFINING TRAUMA: THE THREE E's



Affects large numbers of people

Impacts a few people but has structural or social traumatic consequences.

- **Cultural Trauma**
- **Racial Trauma**
- **Historical Trauma**

Affects a particular group

Affects Multiple members within a family

Affects one person

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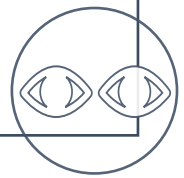
POST TRAUMATIC STRESS DISORDER

Criterion A: Exposure to actual or threatened death serious injury, or sexual violence in one or more of the following ways:

- Directly experiencing the traumatic event
- Witnessing an event as it occurs to others.
- Learning that a traumatic event occurred to a close family member or close friend.
- Experiencing repeated or extreme exposure to aversive details of the traumatic event (first responders, police officers, child welfare workers)

RE-EXPERIENCING THE TRAUMA

- Involuntary Memories
- Nightmares and Flashbacks
- Illusions or Hallucinations
- Psychological Distress

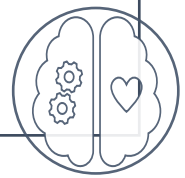


AVOIDANCE OF STIMULI

- Avoiding Trauma related:
  - Thoughts and feelings
  - Conversations and Activities
  - People and Places

CHANGES IN THOUGHTS OR MOOD

- Inability to remember aspects of the event
- Distorted beliefs about self and others
- Lack of interest in activities
- Detachment from others
- Difficulty experiencing joy



REACTIVITY AND AROUSAL

- Irritable behavior
- Reckless or self-destructive behavior
- Hyperarousal & hypervigilance
- Exaggerated startle response
- Sleep & concentration problems

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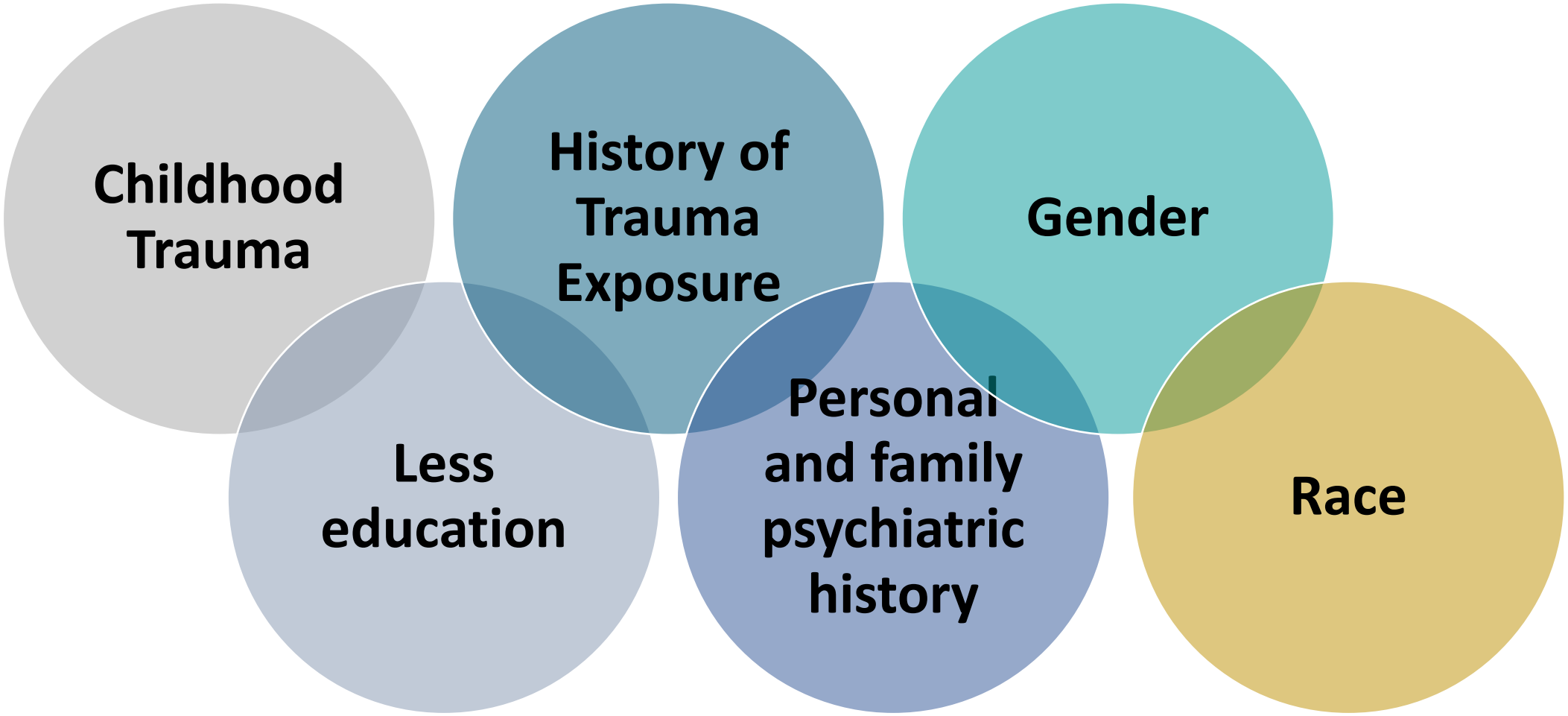
PTSD RISK FACTORS



PREVALANCE OF TRAUMA AND POST TRAUMATIC STRESS DISORDER

- 70% of US Americans have experienced a traumatic event in their lifetime.
- Studies show between 6 and 9% of American adults will have experienced Post Traumatic Stress Disorder at some point in their lives.
- The leading cause of PTSD is sexual violence at 33% following with 30% interpersonal network traumatic experiences **(loss of a loved one, life-threatening illness of a child, or other traumatic event of a loved one.)**

HUMANS ARE RESILIENT

Individual Strengths	Social Support
RESILIENCY FACTORS	
Cultural Supports	Community Supports

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Neurobiology of Trauma

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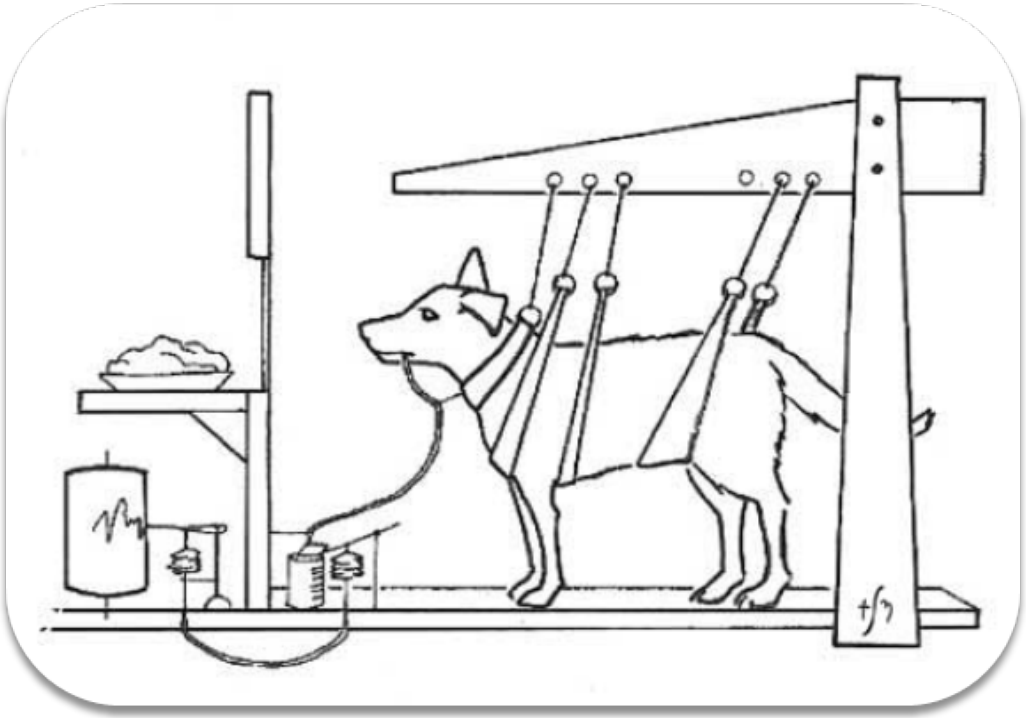
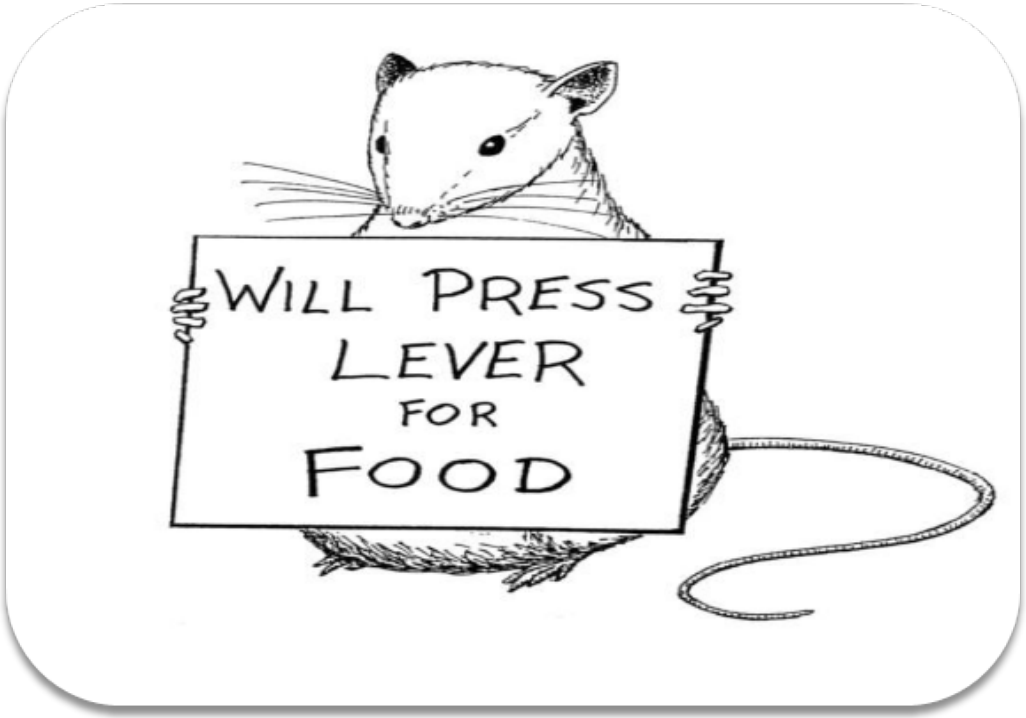
CLASSICAL AND OPERANT CONDITIONING





Classical

Operant

CLASSICAL CONDITIONING

Neutral Stimulus + Aversive Stimulus

Conditioned Stimulus

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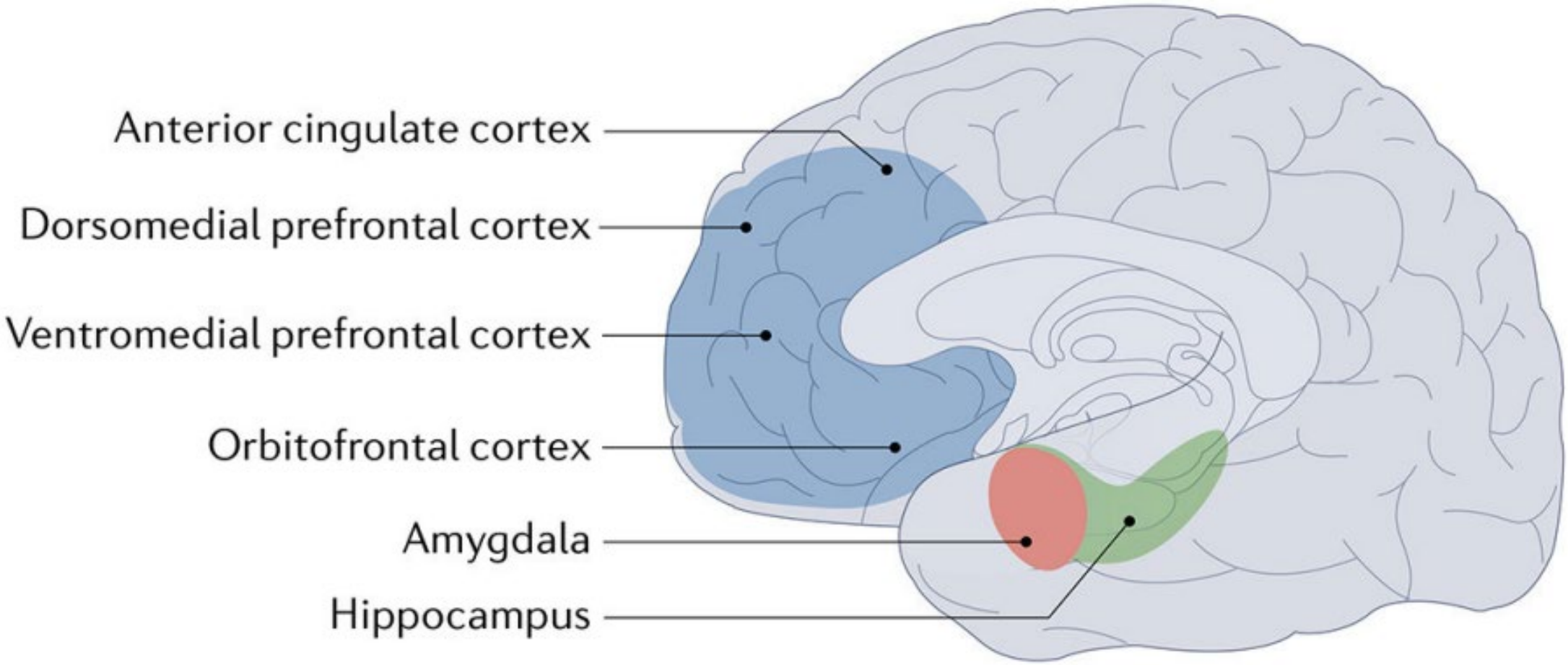
TRAUMA AND THE BRAIN



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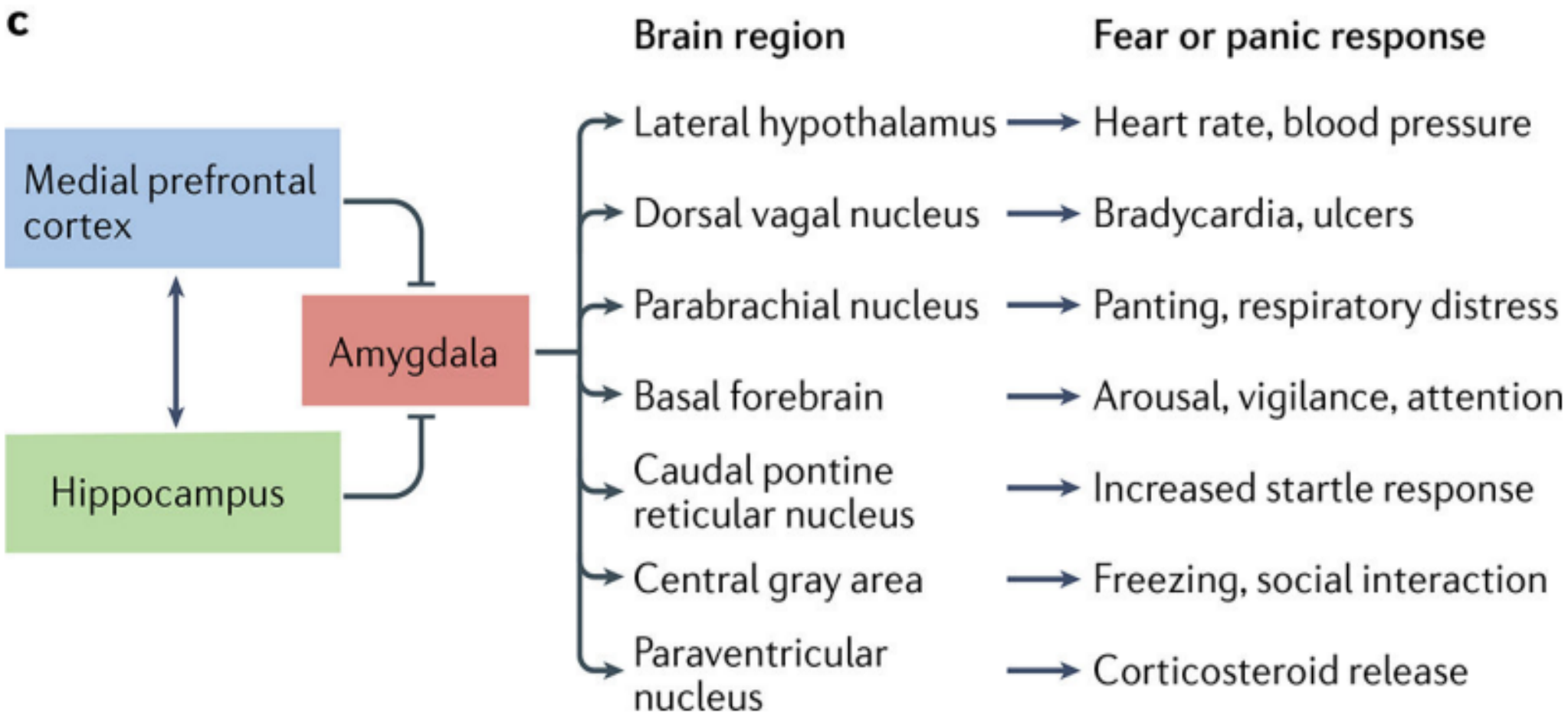
TRAUMA AND THE BRAIN



From "Post-traumatic stress disorder: clinical and translational neuroscience from cells to circuits," by Ressler, K.J., et al., 2022, Nature review Neurology, 18(5), 273-288.

OPERANT CONDITIONING

	Add or Give	Subtract or Take
Behavior Happens More	Positive Reinforcement	Negative Reinforcement
Behavior Happens Less	Positive Punishment	Negative Punishment

OPERANT CONDITIONING

	Add or Give	Subtract or Take
Behavior Happens More	Positive Reinforcement	**Negative Reinforcement**
Behavior Happens Less	Positive Punishment	Negative Punishment

INTEGRATED PSCYCHOTHERAPIES FOR POST TRAUMATIC STRESS AND SUBSTANCE USE DISORDERS

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HISTORY OF TRAUMA AND SUBSTANCE USE DISORDER TREATMENT

- Trauma was ignored, not an issue.
- Trauma was acknowledged but not discussed as part of treatment.
- Substance use took primary focus even when there was a diagnosis of PTSD or history of trauma.
- **Mantra: "You can address your trauma once you've had a year of recovery"**

THEORIES OF PTSD AND SUBSTANCE USE DISORDERS

Shared vulnerability

Self-medication

Mutual maintenance

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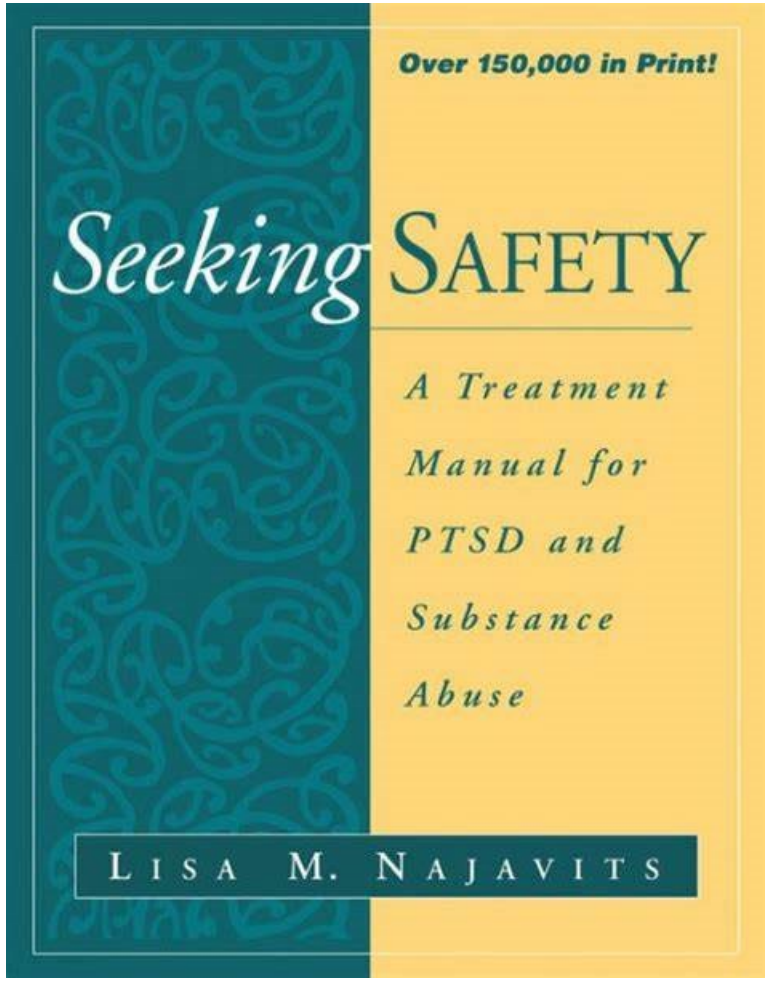
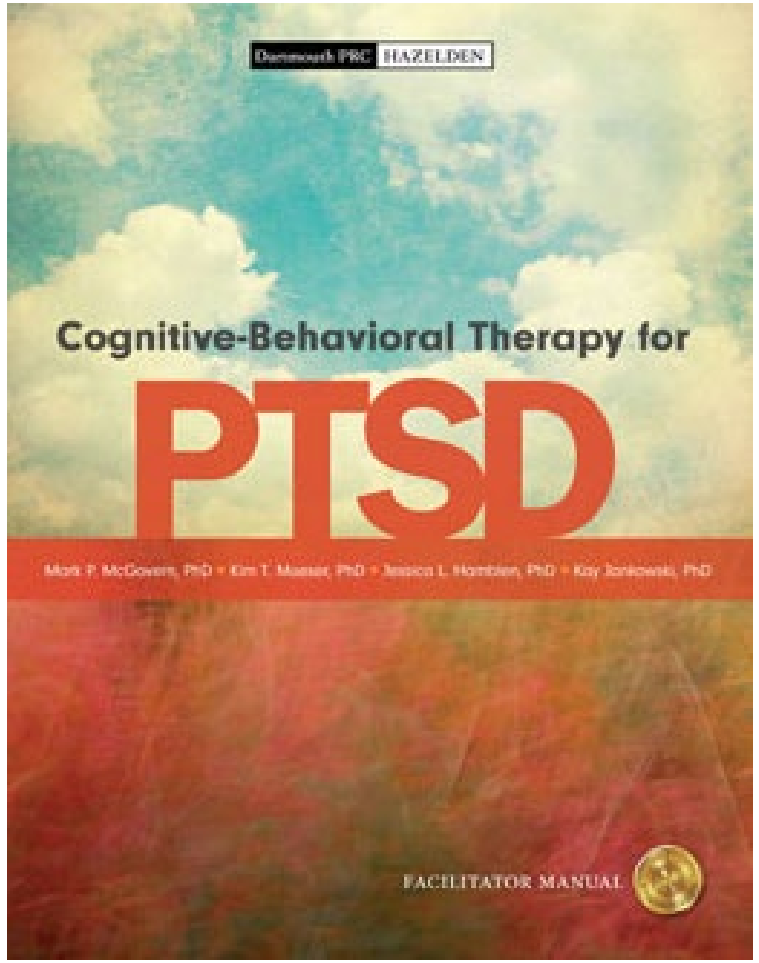
SEEKING SAFETY



- 25: 60–90-minute sessions
- Decreasing risky behaviors, setting boundaries, coping with triggers
- Goal is to establish safety, present-focused
- No clear evidence to say that it outperforms substance use treatment alone

INTEGRATED CBT



- 8-12: 60-minute sessions
- Breathing retraining, psycho-education, CBT coping skills
- Research

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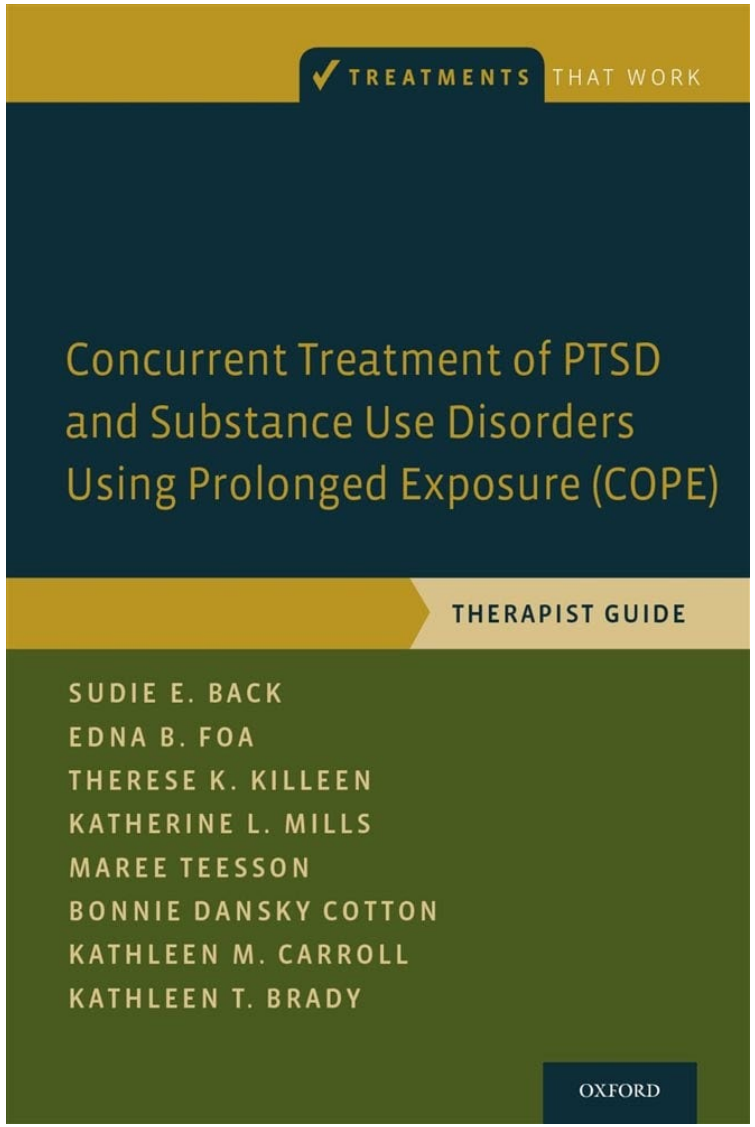
COPE



12: 90-minute sessions

- 30 min substance focused
- 45-60 minutes PTSD focused

Integrates prolonged exposure and relapse prevention

- Psychoeducation
- in vivo hierarchy
- imaginal exposure
- craving management

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STRATEGIES FOR MOVING FROM TRAUMA AWARE TO TRAUMA INFORMED

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“You deserve to be in environments that bring out the softness in you, not the survival in you.”

— ***Ronne Brown***

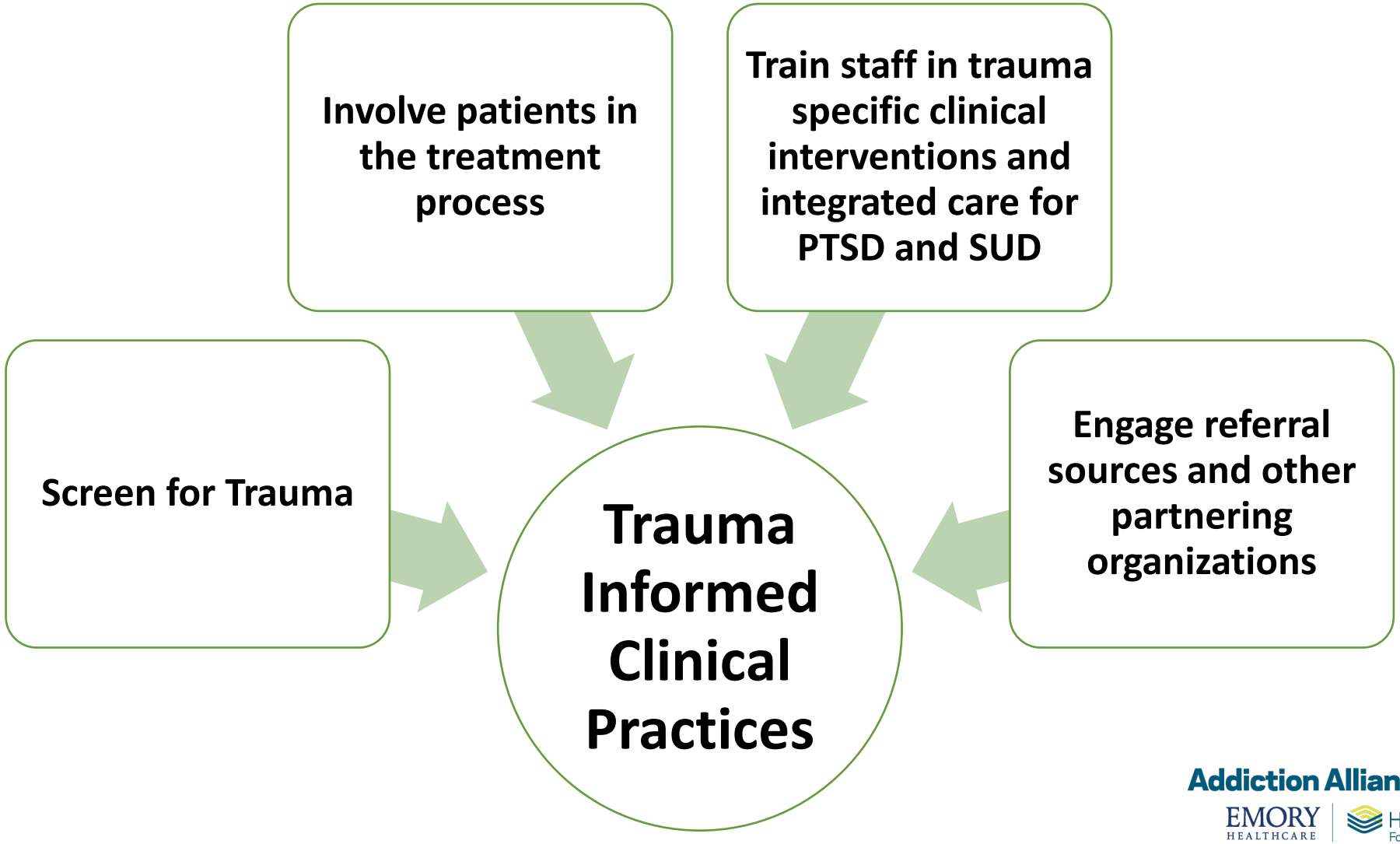
SAFETY CONCERNS

Chaotic treatment environments (noisy, messy areas)	Stigmatizing language	Lack of Gender Responsive Care	Non-welcoming staff processes and procedures
Privacy and confidentiality concerns	Security concerns	Invasive procedures without collaboration or transparency (urine drug screens, blood draws, physical exams)	Lack of diversity, no representation of identities
	Lack of transparency and collaboration on what to expect during treatment	No group rituals, or group norms to provide structure and containment	

KEY INGREDIENTS: TRAUMA INFORMED ORGANIZATIONS

Leading and communicating the organizational transformation process	**Engaging patients in organizational planning**	**Training clinical and non-clinical staff on trauma and trauma informed care**
Creating a safe environment	**Preventing secondary traumatic stress in staff**	**Hiring a trauma informed workforce**

KEY INGREDIENTS: TRAUMA INFORMED CLINICAL PRACTICES



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THE 4 R's REVISITED

Realizes	• The prevalence of trauma in the people we serve and the belief in resiliency.
Recognizes	• Symptoms as someone's most resilient attempt to cope with the symptoms of trauma.
Responds	• With our whole hearts, with love and compassion and recognizing the humanity of others at all times.
Resists	• Re-traumatization by going back, and humbly re-evaluating our policies and procedures to ensure safety for clients, staff and families.

“Regardless of the pain, challenges or wounds that we carry, there is always potential for healing and transformation.”

—Gabor Mate

THANK YOU

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ADVANTAGE
BEHAVIORAL HEALTH SYSTEMS

Peers in Recovery from Opioid Use and Dependency

PROUD Program

Catherine Mills
Director of Addictive Disease
CAC-I, CPRP, CPS-AD

Jonathan Barr
Program Manager
CADC, CPS-AD, MATS

ADVANTAGE
BEHAVIORAL HEALTH SYSTEMS

TERMINAL OBJECTIVE

This presentation will inform treatment providers of the change that results from creating a ***culture of person-centered care***. The emphasis is on the power of the certified peer specialist to ***develop rapport***, to advocate for ***best practice***, and to connect clients with ***clinical, community,*** *and* ***natural supports*** *that* ***enrich the recovery process*** *and* ***improve treatment outcomes***.

ADVANTAGE
BEHAVIORAL HEALTH SYSTEMS

WHAT WE DO

Medication **Assisted** **Treatment**

Peer Support in a comprehensive system of care

Transcending all ASAM Levels

ADVANTAGE
BEHAVIORAL HEALTH SYSTEMS

WHAT WE DO

- Crisis Stabilization
- Intensive SA Residential Programs
- WTRS (Women and Children) Programs
- THOR and GARR / Long Term Residential Programs
- Transitional Housing and Sober Living Houses
- Accountability Courts
- Intensive/Non-Intensive Outpatient
- After Care and Med Management
- Mental Health Providers
- Recovery Community Organizations
- Medical Providers

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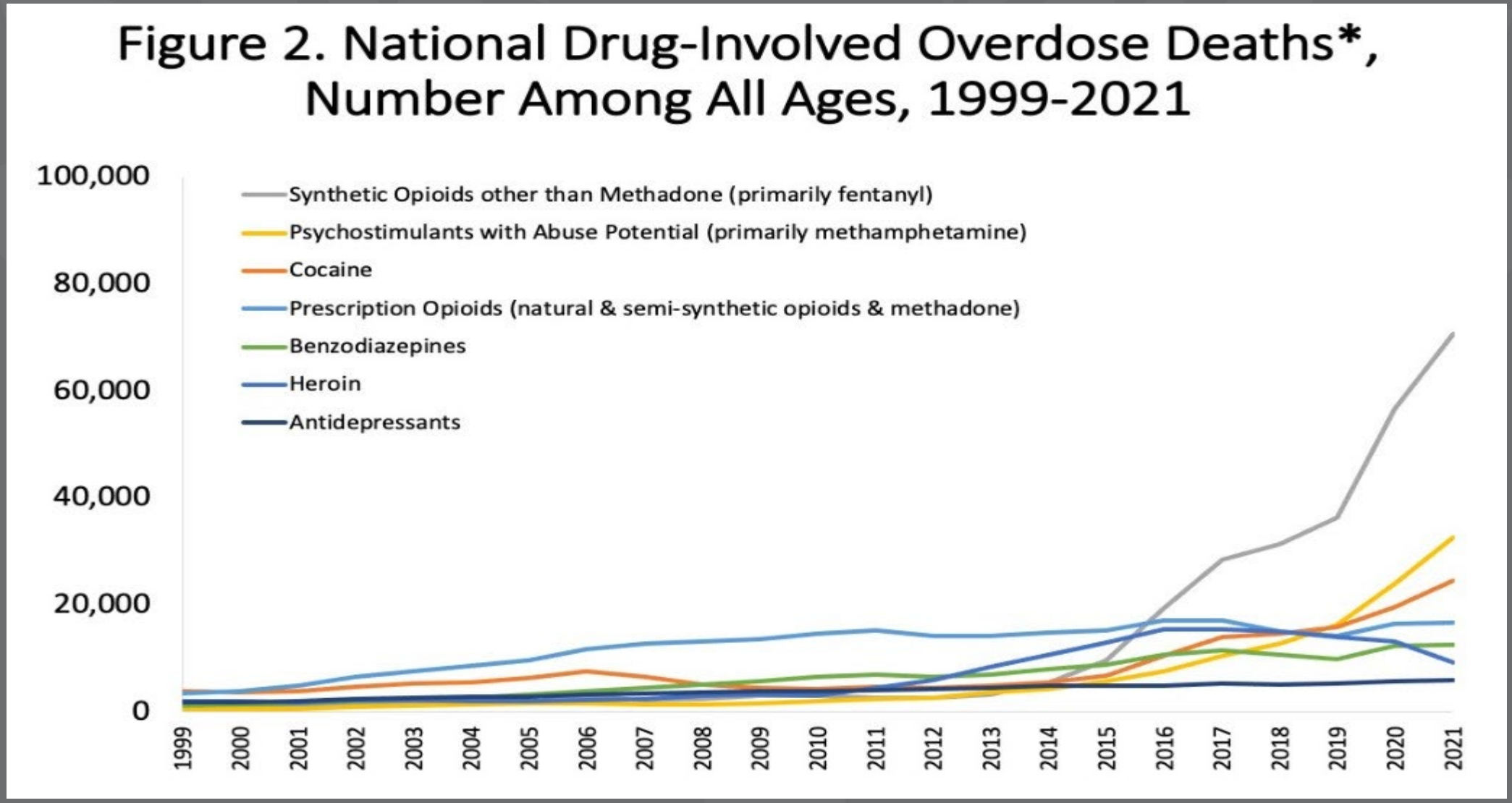
BEHAVIORAL HEALTH SYSTEMS

WHY WE DO



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WHY WE DO

- Still in Active Misuse or Withdrawing
- Unmanaged Mental Health Challenges
- Unaddressed Co-Morbidity
- Trauma History
- Extensive Losses
- Family Estrangement
- Poor ADLs
- Financially Unstable
- Historically Homeless
- Ongoing Legal Issues
- Open DFACs Case

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BEHAVIORAL HEALTH SYSTEMS

HOW WE DO

Hope is at the very heart of peer support.
Hope is the catalyst for change.

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HOW WE DO

"The opposite of addiction isn't sobriety- it is human connection."

-Johann Hari

- Compassion
- Empowerment
- Empathy
- Strengths Based
- Collaboration
- Advocacy
- Person Centered
- Self Direction
- Respect
- Autonomy
- Language

Peers in Recovery from Opioid Use and Dependency

PROUD Program

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ADVANTAGE

BEHAVIORAL HEALTH SYSTEMS

QUESTIONS?

The Fiendishness of Fentanyl

Best Practices for buprenorphine using low dose or macro dose induction

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WELCOME AND INTRODUCTIONS

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Disclosures:

- ✓ Training consultant with Hazelden Betty Ford Foundation
- ✓ Medical Director of Gateway Recovery Center
- ✓ Specifics of medication dosing discussed in this presentation is “off-label” use

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OBJECTIVES

- Review the uniquely fatal nature of Fentanyl Use Disorder.
- Learn about low dose induction schedules and macro-dosing schedules with buprenorphine being used to reduce precipitated withdrawal.
- Review importance of using harm reduction principles to reduce overdose, including naloxone at higher doses.

Source: Jetlagged Comic. (n.d.). *Jetlagged comic*. https://www.jetlaggedcomic.com/

DISCLAIMER:
Medications discussed are "off-label" use and this issue is continually evolving with new information emerging. We need to continue to follow and adapt our practices.

Brief Terminology Digression

- **Micro-dosing can be interpreted in a specific way.**

The case of SG

- Patient using primarily injection opioids; comes into recovery facility and reports using 1.5 -2 g of heroin daily; starting to experience withdrawal (last used 12 hours ago), so is given a typical induction protocol with buprenorphine.

- Goes into severe precipitated withdrawal, which he reports he is unable to tolerate, and reports he needs to leave AMA.

- Patient returns to use, and overdoses, his girlfriend reverses him with naloxone, but 4 doses of intranasal naloxone are needed to reverse him, and he ends up on a naloxone drip.

- He then returns to your recovery facility; what can you do differently??

The Problem

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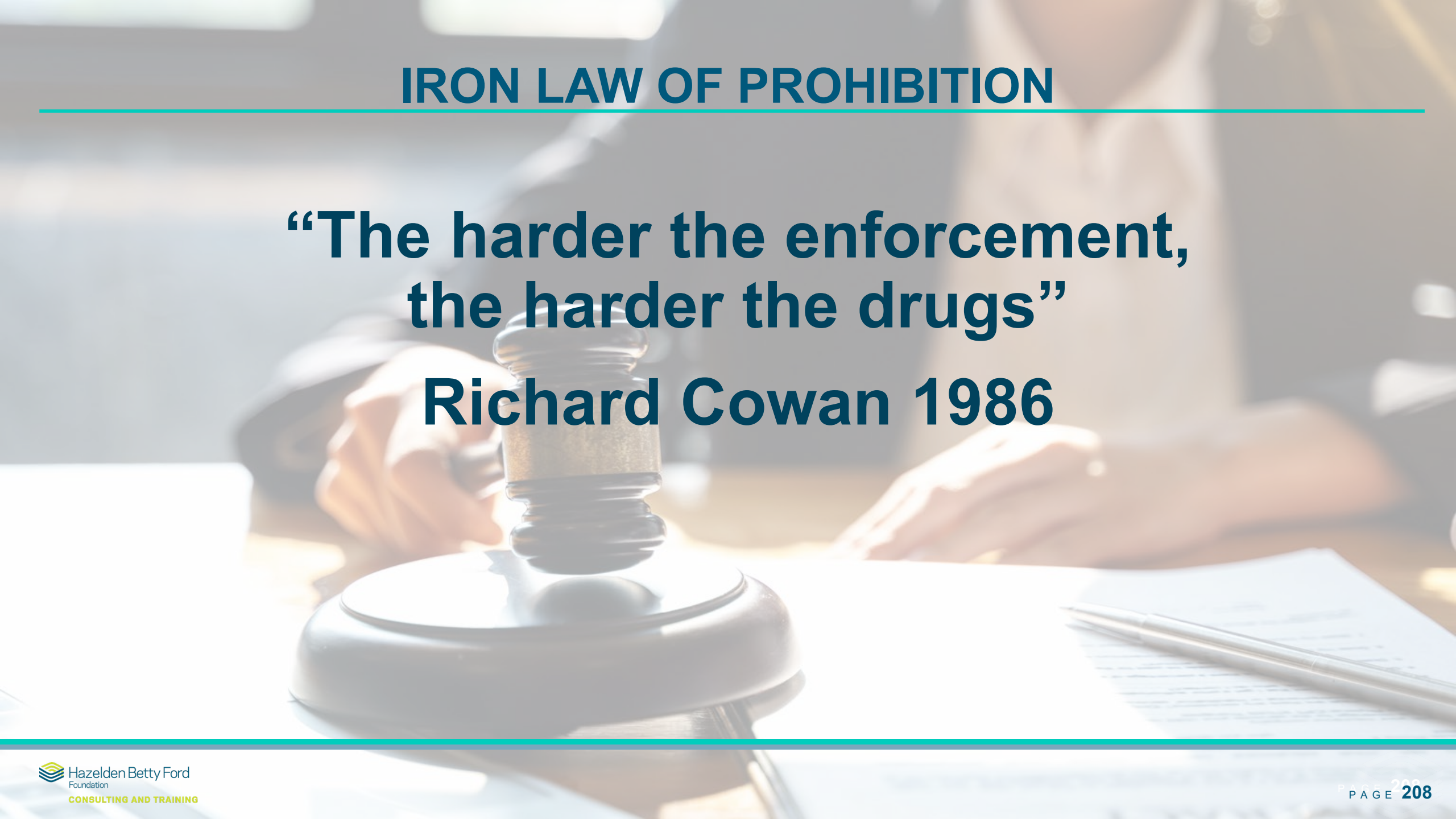
UNINTENDED CONSEQUENCES

Illustration Source: Lee Sauer 2016

THE START

Big Pharma…Oxycodone

IRON LAW OF PROHIBITION



“The harder the enforcement, the harder the drugs”

Richard Cowan 1986

WHAT IS XYLAZINE?

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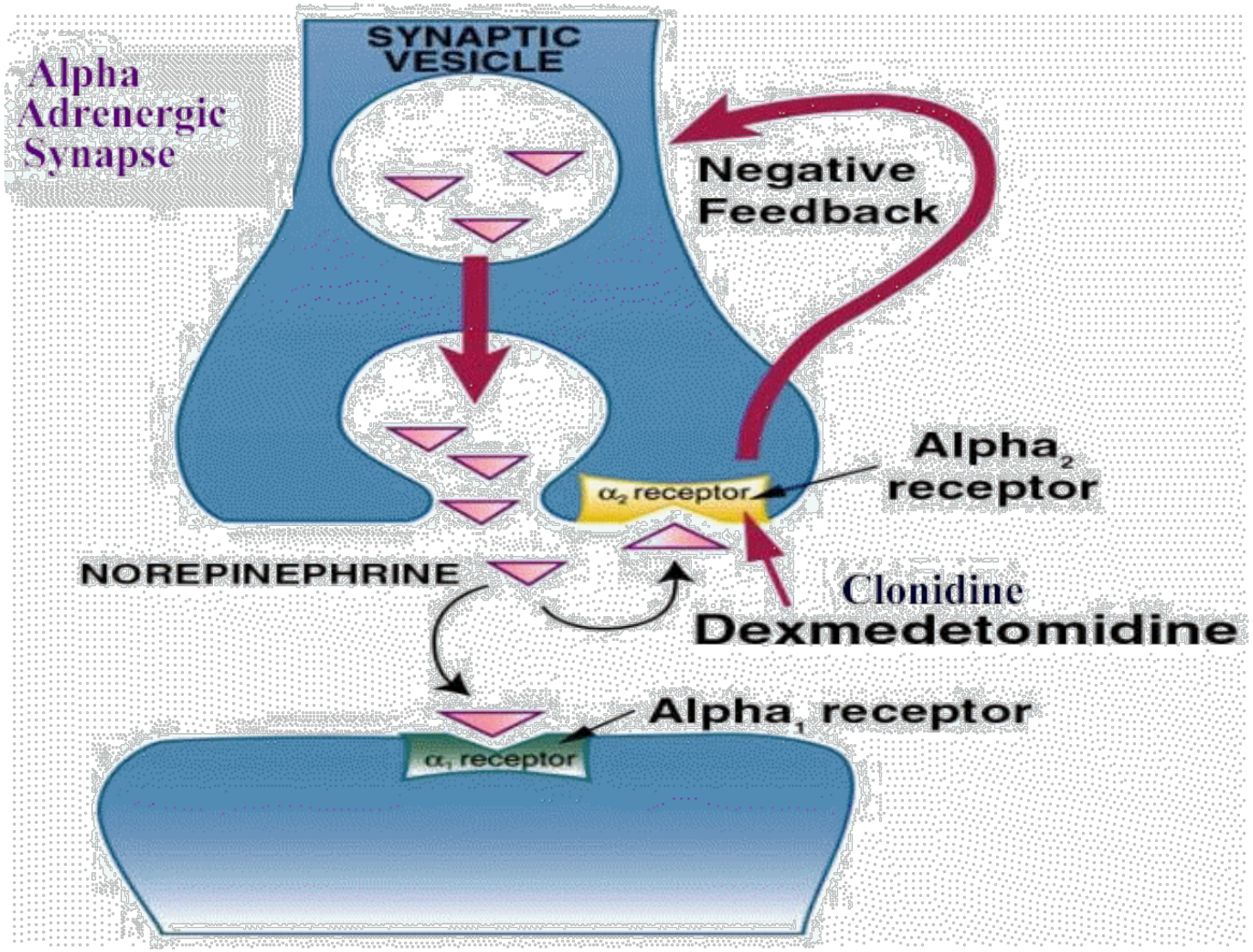
CONSULTING AND TRAINING

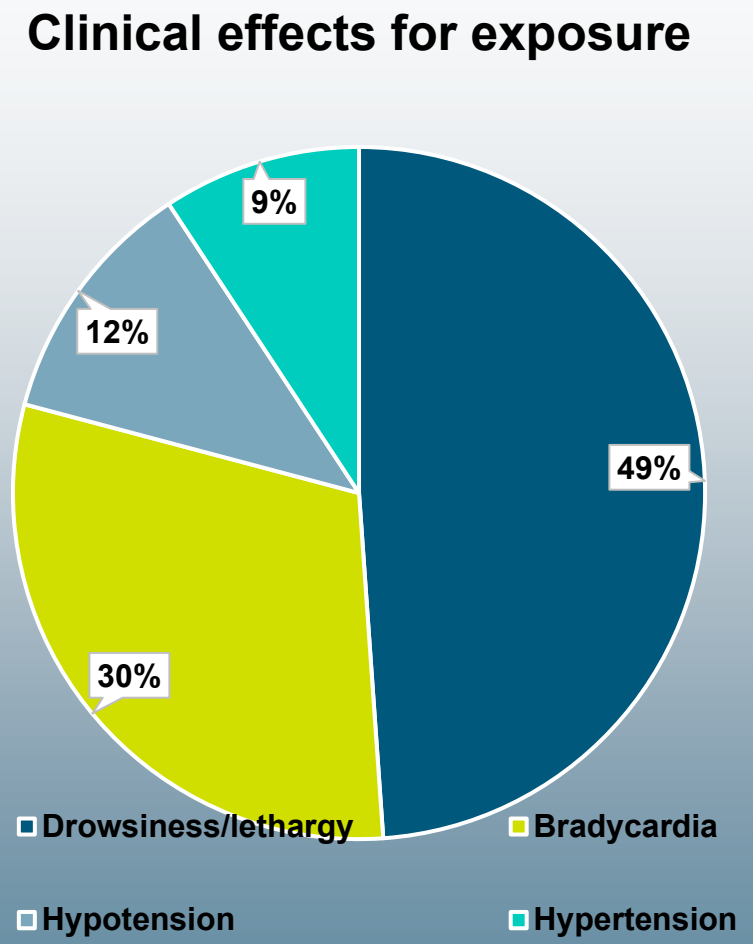
ALPHA-2 AGONIST

- Alpha-2 agonist causes a reduction in presynaptic release of norepinephrine



EFFECTS ON HUMANS

- Xylazine was never approved for human use because it was found to cause profound hypotension and CNS depressant effects in clinical trials.
    - Causes bradycardia, miosis, hypotension, hyperglycemia, respiratory depression and hypothermia.
- Can be an adulterant or be used purposefully (with or without opioids).
- Can be used to lengthen effect of fentanyl.

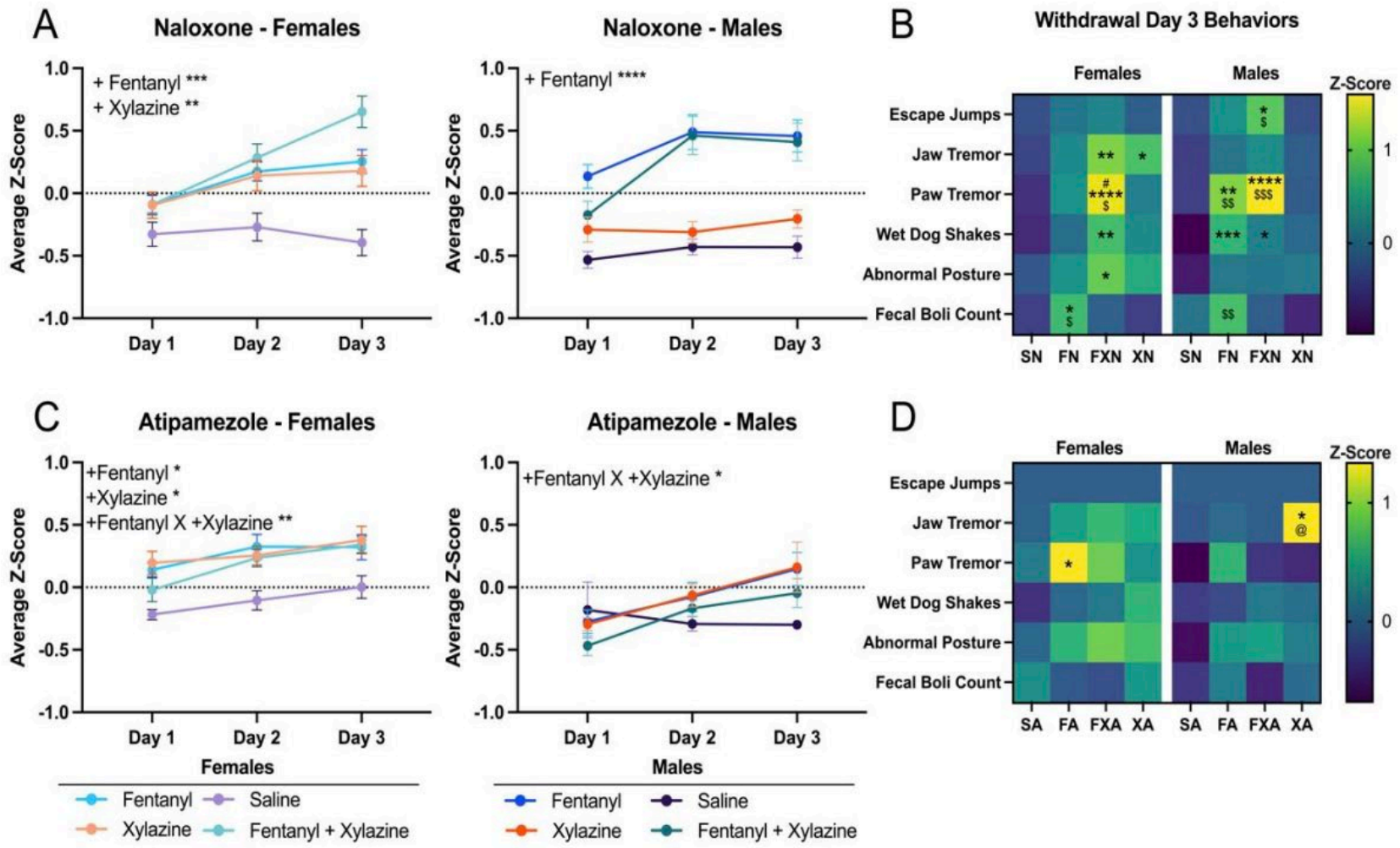


PRE-PRINT ARTICLE RE: KAPPA OPIOID RECEPTOR

- Recent pre-print article reveals evidence that xylazine is a kappa opioid agonist based on mouse studies.
- This helped to explain why in the mouse studies, xylazine was responsive to naloxone, particularly in female mice

This has extremely important healthcare implications for messaging around naloxone use in this population

NALOXONE RESPONSIVENESS
IN MICE EXPOSED TO XYLAZINE



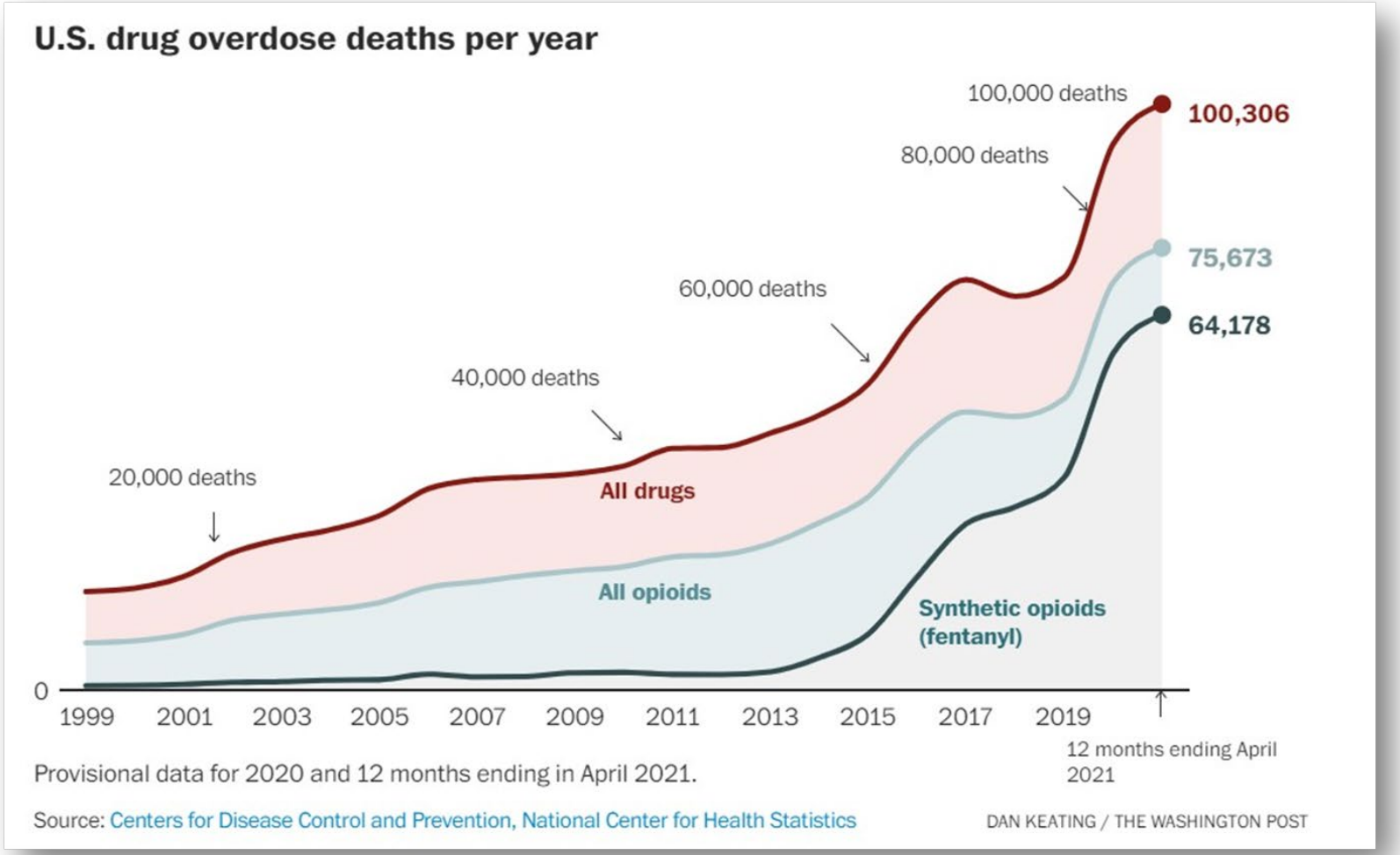
COMMON COMORBID SUBSTANCES

Fentanyl is most common substance found with Xylazine.

In a recent study done in Connecticut, fentanyl was found in >99% of overdose deaths related to Xylazine (Thangada 2021).

- Other substances were also commonly found in:
  - cocaine (34.2%)
  - heroin (30.1%)
  - benzodiazepines (26.0%)
  - ethanol (22.6%)
  - gabapentin (12.3%)
- Xylazine-associated deaths occurred primarily among males (80.9%) and non-Hispanic White persons (74.0%).
- Mortality was highest among persons aged 25–34 years (28.1%), followed by those aged 35–44 (26.7%) and ≥55 years (23.3%).
- Fifty-seven percent of xylazine-associated deaths occurred at home, which was also the predominant location of overdose (75.3%).
- Twenty-six percent of deaths occurred at the hospital; naloxone was administered 18.5% of the time.

Fentanyl
the reason for the high number



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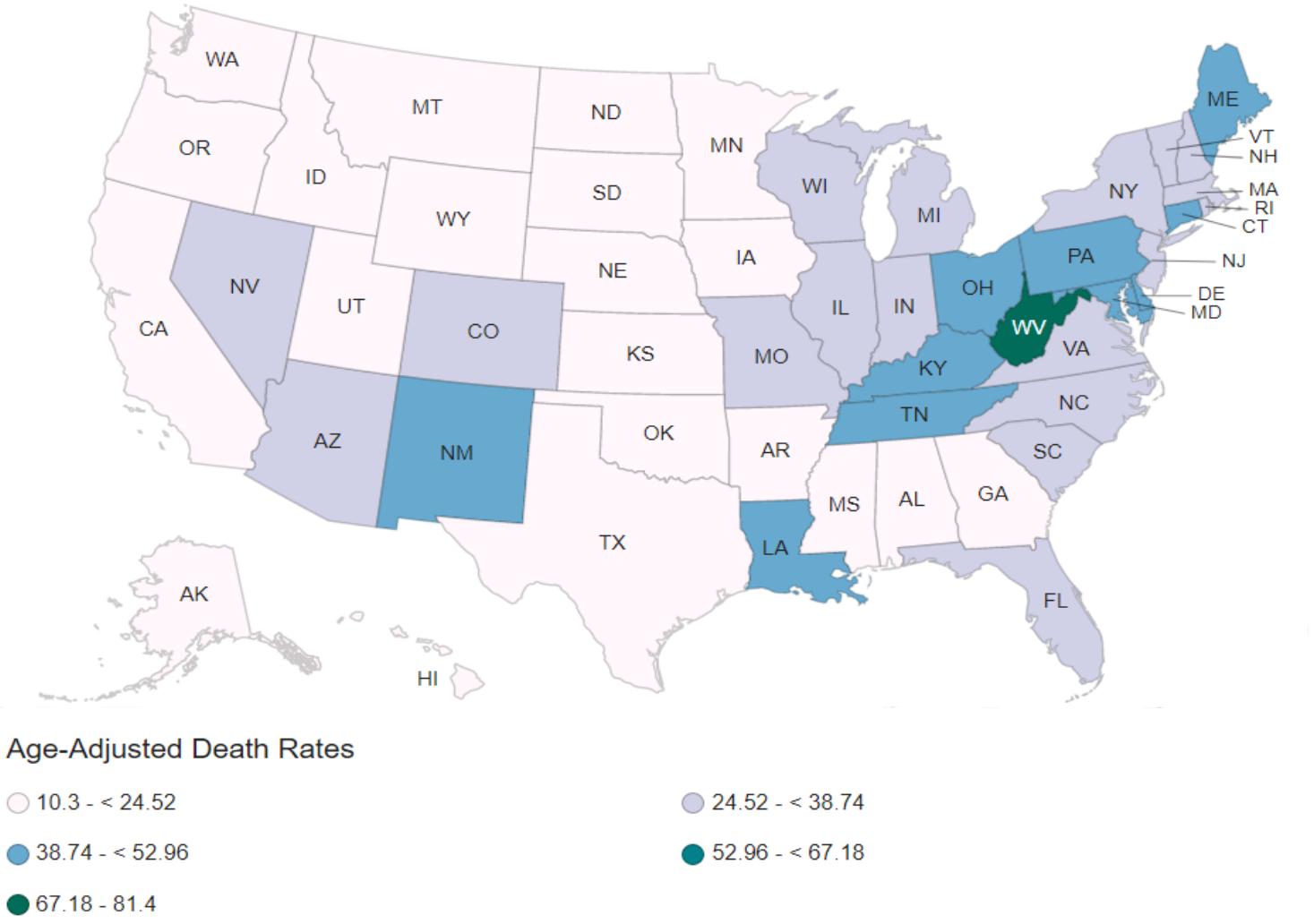
Overdose

Overdose Mortality Rates by State in 2020



https://www.cdc.gov/nchs/pressroom/sosmap/drug_poisoning_mortality/drug_poisoning.htm

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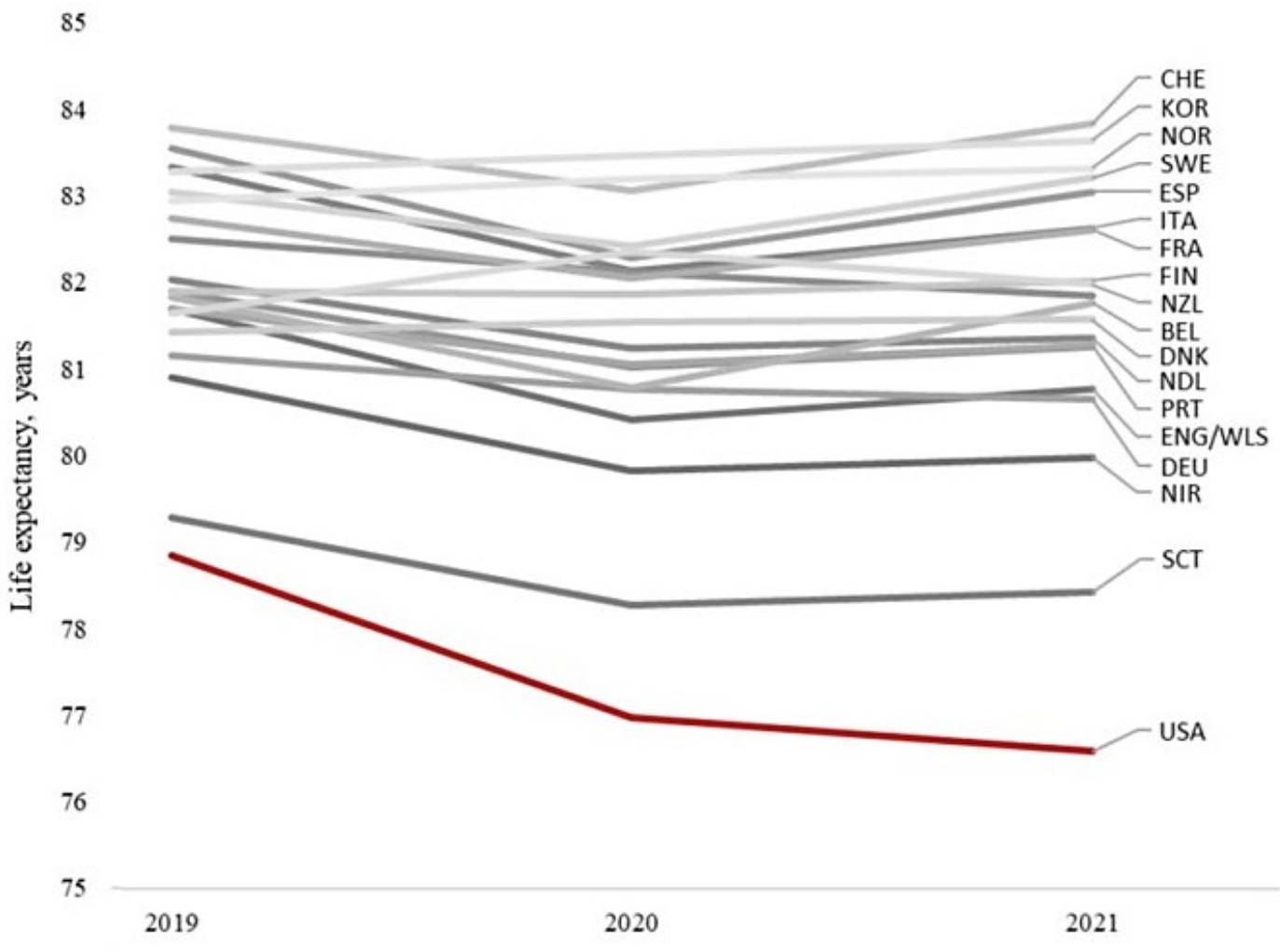
Life Expectancy

- **Life Expectancy 2020: Dropped by over a year**
- **Life Expectancy 2021: Dropped to 76.6 years**



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Medrxiv.org

Fentanyl Analog Potencies
Relative to Morphine

Fentanyl Analog	Relative to Morphine
Fentanyl	80 to 100x
Acetylfentanyl	15x
Valerylfentanyl	15-20x
Furanylfentanyl	20x
Butyrylfentanyl	20-25x
Acrylfentanyl	100x
3-Methylfentanyl	Trans-isomer 400x, cis-somer 6,000x
Carfentanil	10,000-100,000x

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Schueler HE. Emerging Synthetic Fentanyl Analogs. *Acad Forensic Pathol*. 2017;7(1):36-40.

Beyond Fentanyl
Nitazenes

- **Novel ultra-potent opioid that is up to 20x as potent as fentanyl.**
- **Need more data on naloxone dosing**

Fentanyl

- Naloxone has been found to be effective in fentanyl overdose
  - similar affinity to opioid receptors as naloxone.
  - Inconclusive not controlled studies regarding naloxone dosing
  - ? Presence of adulterants such as xylazine
  - When in doubt, consider repeat dosing

- Fentanyl is highly lipophilic and easily crosses the blood-brain barrier
  - May contribute to need for alternative buprenorphine inductions due to potential ongoing fentanyl release from lipid stores

Pergolizzi 2021

Fentanyl
Urine Drug Testing

- Fentanyl is a synthetic opioid, and does NOT show up on typical drug screen panels
- Send out testing or fentanyl test strip screening required
- Currently, there is NOT a CLIA-waivered outpatient test strip available for fentanyl testing
- Because of its lipophilic nature, fentanyl may be found on drug screen over a week after cessation of use
- Note that fentanyl strip may not detect all fentanyls and wont detect Novel Potent Opioids

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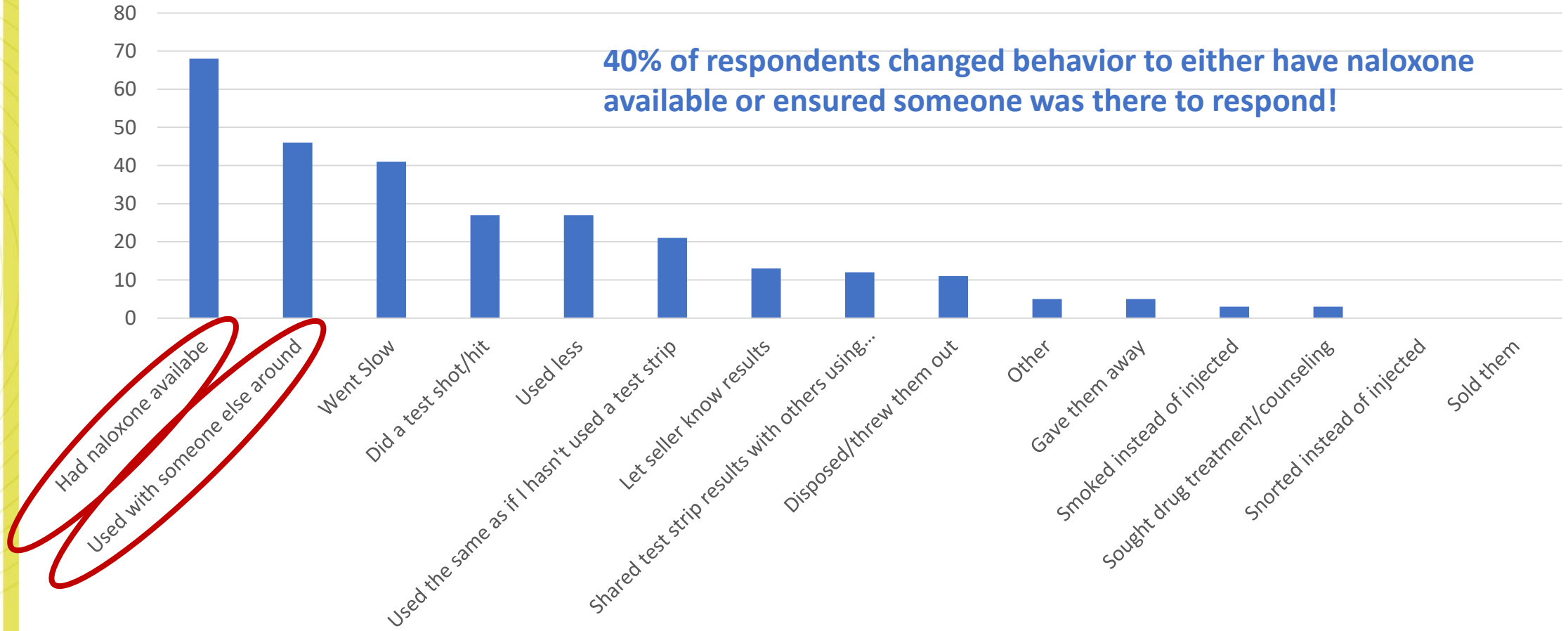
Harm reduction

Changes to Drug use Behavior

Participant Question: Based on test strip results, what did you do differently?



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Utah Department of Health. *Fentanyl Test Strip Pilot Project*

Alternative Induction Strategies:

The more things change, the more they stay the same

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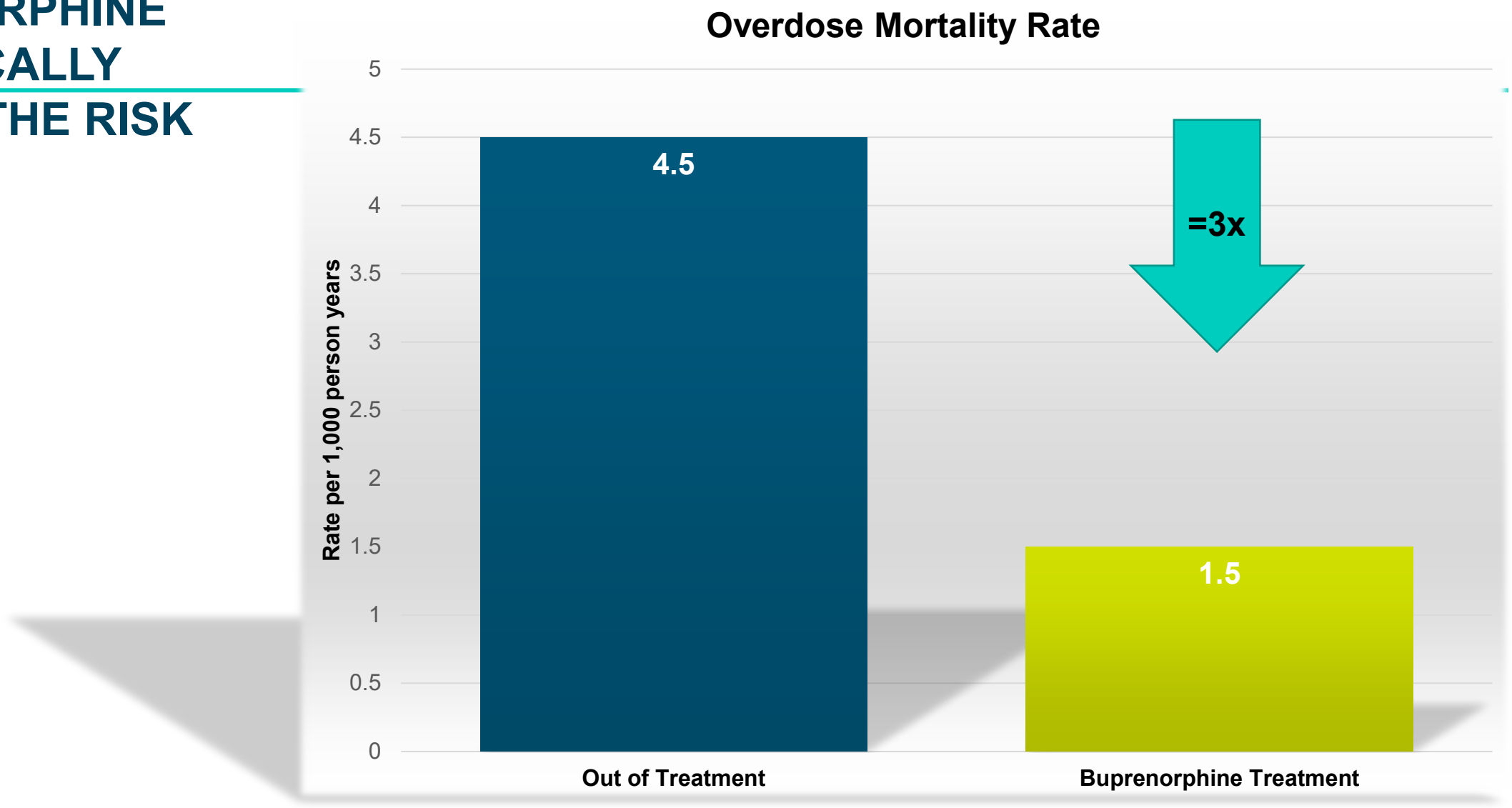
BUPRENORPHINE DRAMATICALLY LOWERS THE RISK OF DEATH



www.va.gov, Emergency Department (ED) and Buprenorphine/Naloxone Treatment, June 2020 IB 10-1496 P97019

WE HAVE 3 FDA-APPROVED MEDICATIONS, UNTIL 2023 ONLY 1 OF THESE COULD BE PROVIDED BY MOST PRESCRIBERS

THE ONE THAT DOES NOT REDUCE MORTALITY….

Back to the case of SG

- **Why did our patient experience precipitated withdrawal during his buprenorphine induction?**
  - Because fentanyl builds up in the lipid system, patients may experience precipitated withdrawal within the first 2-3 days when typical induction is performed; for many patient's, this is intolerable, and they are unable to successfully get onto buprenorphine using this paradigm.
- **How can we help him to avoid this in the future?**

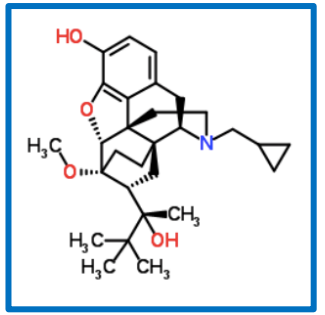
BUPRENORPHINE'S UNIQUE PHARMACOLOGY

Background: Buprenorphine is a Schedule III partial μ-opioid receptor agonist

- Modern atypical opioid - derivative of opium alkaloid thebaine
- Equally effective but potentially safer treatment option for chronic pain than full μ-opioid receptor agonists
- Used as an analgesic since 1981
- Multi-mechanistic effects depending on the receptor subtype provider potent analgesia with less potential for side effects

Mechanism of Action:

- **Partial agonist**: μ-opioid receptor, high affinity, low intrinsic activity, slow dissociation
- **Antagonist:** δ- and κ-opioid receptors
- **Agonist:** ORL-1



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Precipitated Withdrawal with Buprenorphine

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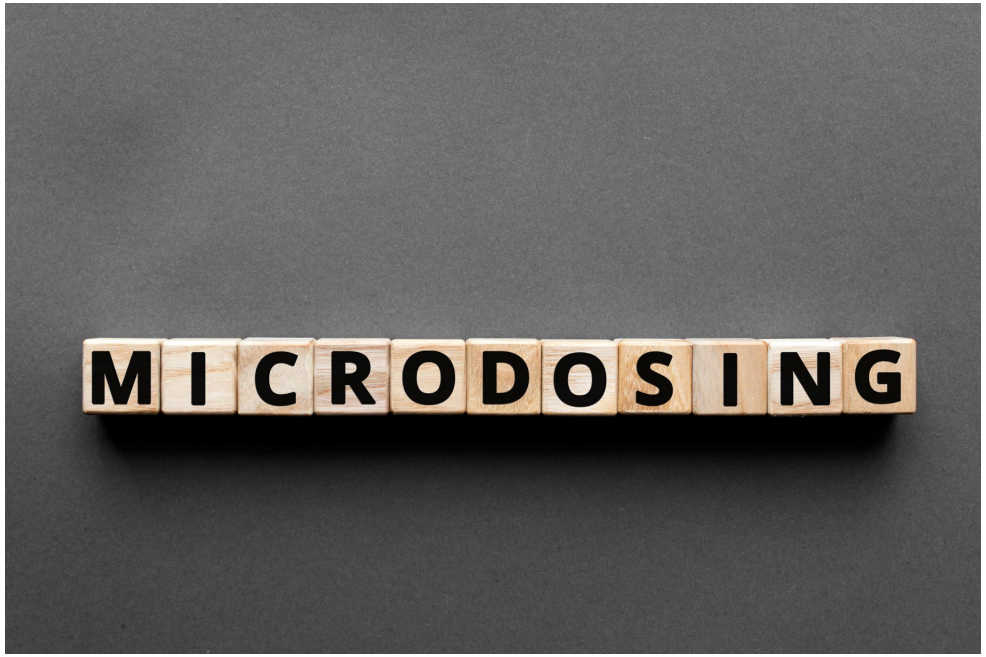
Emerging Induction Strategies for Patients Using Fentanyl

- **Low dose inductions with transdermal and injectable buprenorphine**
- **Various low dose inductions with sublingual buprenorphine**
  - **Micro-inductions at “micro intervals” – q1-4hrs**
  - **Dose intervals can also be daily or twice daily**
- **Macro-induction – For hospital and residential settings**
  - **Large initial doses 8-16 mg buprenorphine for patients in naloxone induced precipitated withdrawal or in abstinence-based withdrawal**
  - **Difficult to implement in the outpatient setting**

The “Bernese” Method historic micro-dosing model

- Long-standing history of doing this for induction of patients on methadone in converting from methadone to buprenorphine

- Because fentanyl stores in the fat deposits, people can experience precipitated withdrawal when starting buprenorphine within the 2-3 days of stopping fentanyl use



Low Dose Induction Protocols (Also termed micro induction) When to consider

- Patients on methadone maintenance
- Patients transitioning from a fentanyl patch
- Significant patient fear of withdrawal
- Can not tolerate routine SL induction
- Patients primarily using fentanyl, via injection or oral use
- Patients continuing on full opioid agonists

Micro-Dosing
Theoretical Basis

- Using small doses of the partial agonist, buprenorphine to displace the full agonist, fentanyl, without causing clinically significant precipitated withdrawal

- Because of the longer receptor binding time of buprenorphine, this would accumulate over time

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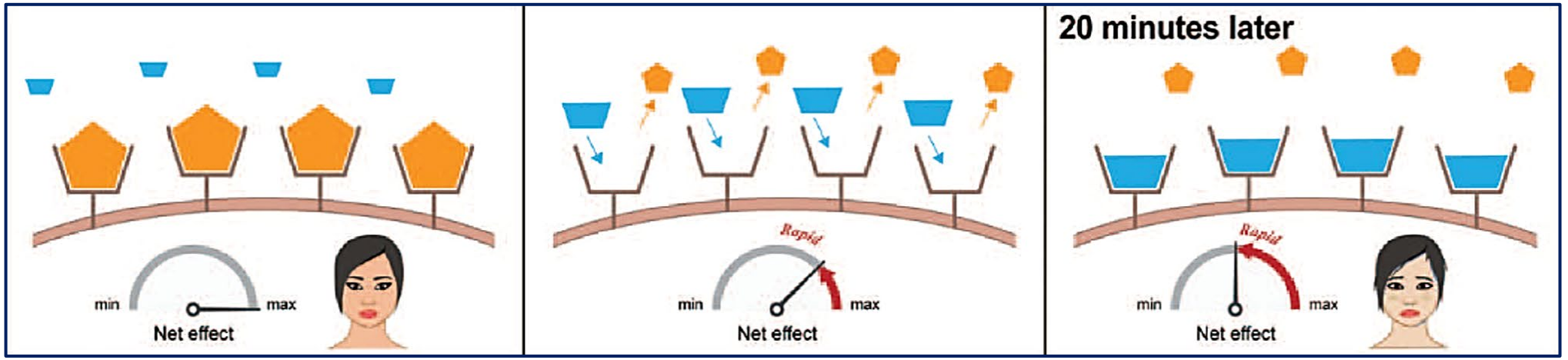
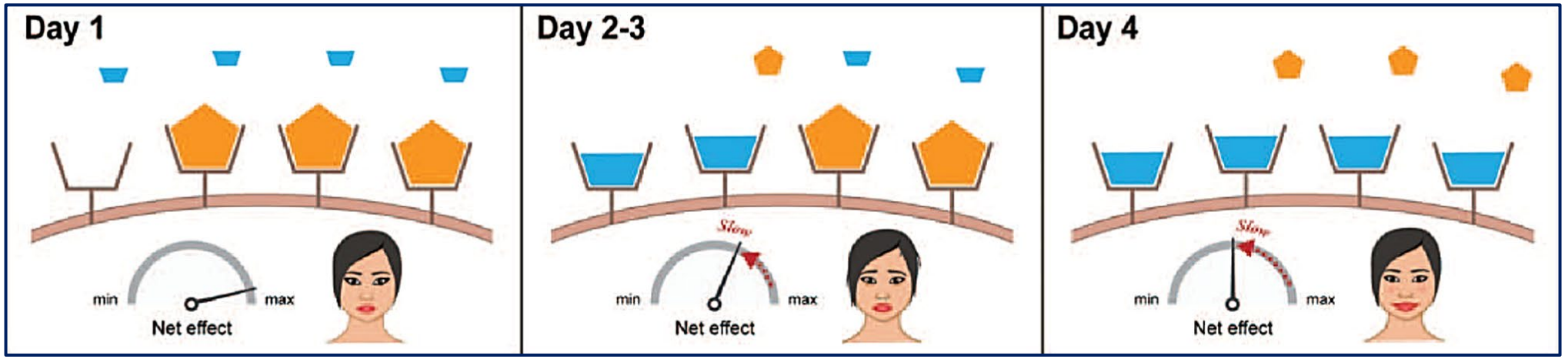
Micro-Induction

Mechanism Behind BUP/NAL

Mechanism of Precipitated Withdrawal



Bridging at a Molecular Level



Ghosh SM, Klaire S, Tanguay R, et al. A Review of Novel Methods To Support The Transition From Methadone and Other Full Agonist Opioids To Buprenorphine/Naloxone Sublingual In Both Community and Acute Care Settings. (2019). *Can Jour of Addict*: 10(4)41-50.

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Micro-Dosing and Macro-Dosing
Cautions

Data is limited to case reports and cases series

Evidence: No RCTs investigating any one BUP or BUP/NAL micro-induction strategy/protocol or a comparisons of strategies or protocols

No outcomes data (i.e., tolerability, treatment retention, etc..)

Important to obtain patient consent prior to induction: Requires the patient to continually assess withdrawal over several days

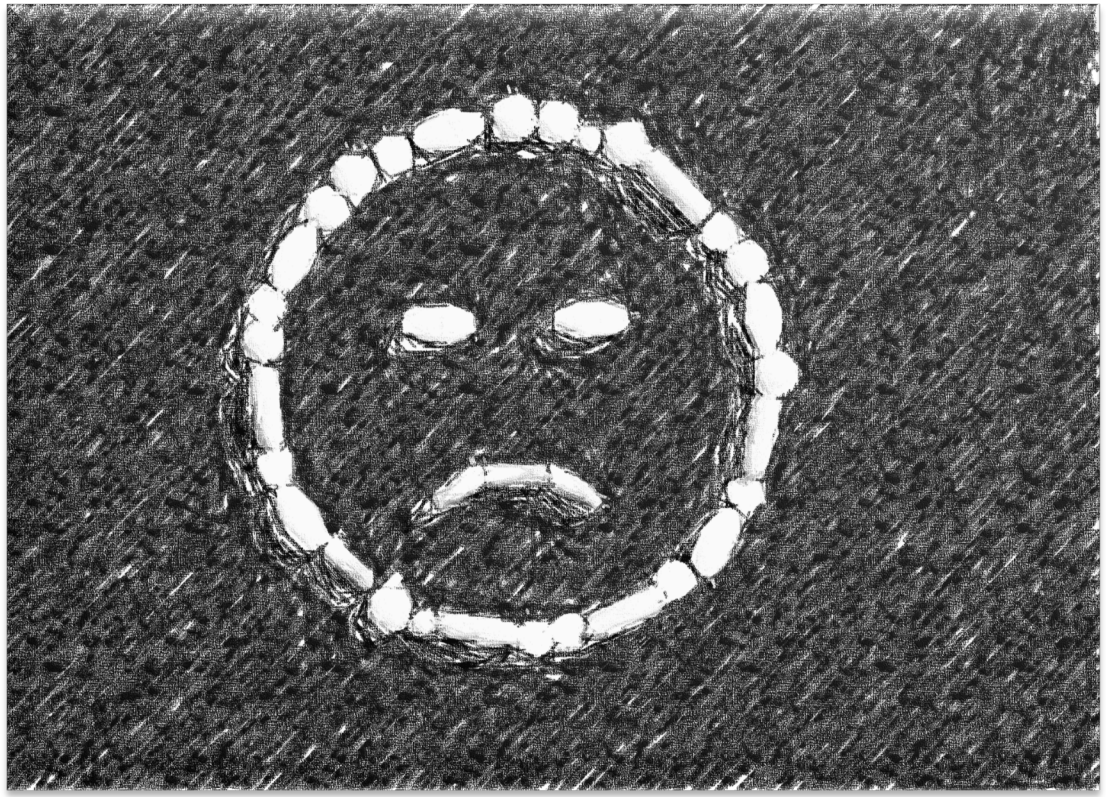
"Off-label" practice; not included in clinical practice guidelines from 2020

Typical Inductions

ASAM OUD Guidelines from 2020

Once objective signs of withdrawal are observed:

- Initiate buprenorphine with a dose of 2 to 4 mg, with dosage increments of 2 to 8 mg every 1-4 hours
- Generally, Day 1 dosing should not exceed 12 mg; Day 2 max dose of 16 mg
- Evidence suggests that 16 mg per day or more may be more effective than lower doses.



Hot off the press! Suggested management of MOUD in high potency synthetic opioids was updated in 2023

- Buprenorphine Treatment of Opioid Use Disorder for Individuals Using High-potency Synthetic Opioids on asam website
- "Case reports and anecdotal experience suggest improvement with rapid dose escalations to 24–32 mg SL per day during initiation. Given the relative safety profile, increasing the buprenorphine dose is the most reasonable first-line treatment of persistent OWS."
  - Successful use of buprenorphine doses during initiation as high as 64 mg SL has been reported
  - For intractable cases of OWS, treatment escalation involves transition to an ED or hospital for additional buprenorphine and consideration of high-affinity FAO, benzodiazepines, ketamine, or dexmedetomidine
- Methadone is also an important and evidence-based option for management of these individuals
- Use of extended release naltrexone is recommended to be only used a highly structured, medically managed inpatient environment, and patients should be counseled on their INCREASED risk of overdose

MEDICATIONS TO CONSIDER IF BUPRENORPHINE DOSE IS MAXED OUT

Consider what "maxed out" means; reasonable to try going up to 32 mg per day.

- **Consider switching to Methadone**

- **Clonidine 0.1 po 1-2 tablets up to three times daily as needed to help with opioid cravings**
- **Gabapentin 300 mg PO tid as needed to start with**

Low Dose/ Micro Inductions

Ranges from one to several days

- Various dosing regimens starting with 150 mcg –1 mg buccal /sublingual/transdermal buprenorphine , then titrating upwards
- Note different bioavailability of different formulations!

Micro-Dosing

Buprenorphine Films/Tablets

- Day 1: 0.5 mg SL daily
  - (This is ¼ of a 2 mg SL buprenorphine tablet/film)
- Day 2: 0.5 mg SL bid for a total of 1 mg SL daily
- Day 3: 1 mg twice per day for a total of 2 mg SL daily
- Day 4: 2 mg SL twice per day for total of 4 mg total
- Day 5: 3 mg SL bid for a total of 6 mg total
  - (This is 1½ of a tablet/film to take twice per day)
- Day 6: 4 mg SL bid for a total of 8 mg total
  - (2 tablet twice per day)
- Day 7: 12 mg SL once daily- all in AM
  - (6 of the 2 mg tablets/films)

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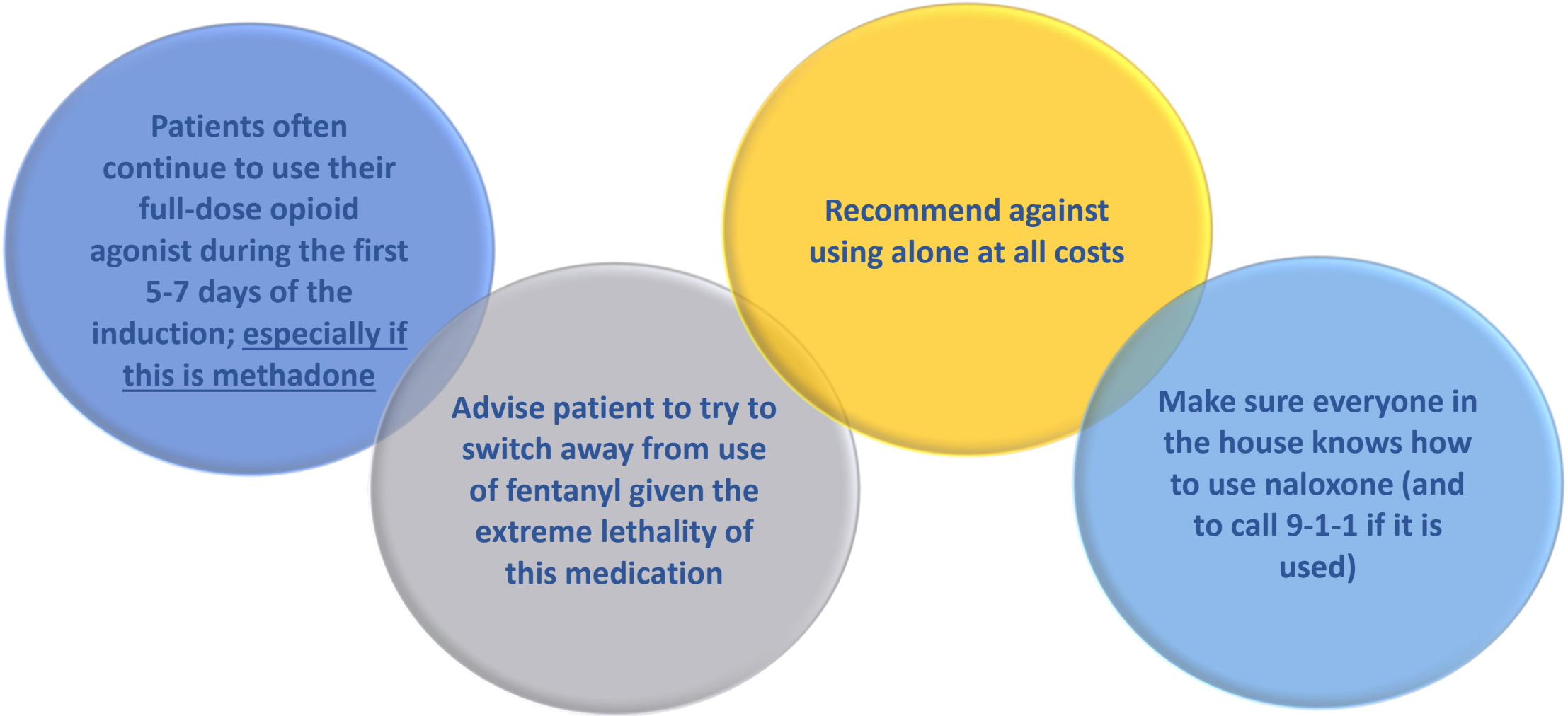
Micro-Dosing
Ongoing Full Opioid Agonist Use



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Sample Micro-Dosing for PB

Get a release to talk to methadone clinic

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Buprenorphine

- Buprenorphine prevents fentanyl-induced respiration depression
- In a recent case study, being on buprenorphine allowed patients to maintain ventilation when infused with fentanyl

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Buprenorphine
Protect Against Fentanyl?

- **Study Question: can sustained BUP plasma concentrations reduce the frequency and magnitude of fentanyl-induced respiratory depression**
- **Primary Endpoint: change in isohypercapnic minute ventilation (V_E).**
- **Study Type: single-center study, (single-blind, randomized)**
- ***n*=14 healthy volunteers and 8 opioid-tolerant patients taking ≥90MME/day**
- **Each group received continuous IV BUP or placebo for 360 minutes**

PLOS ONE

RESEARCH ARTICLE

Published January 27th, 2022

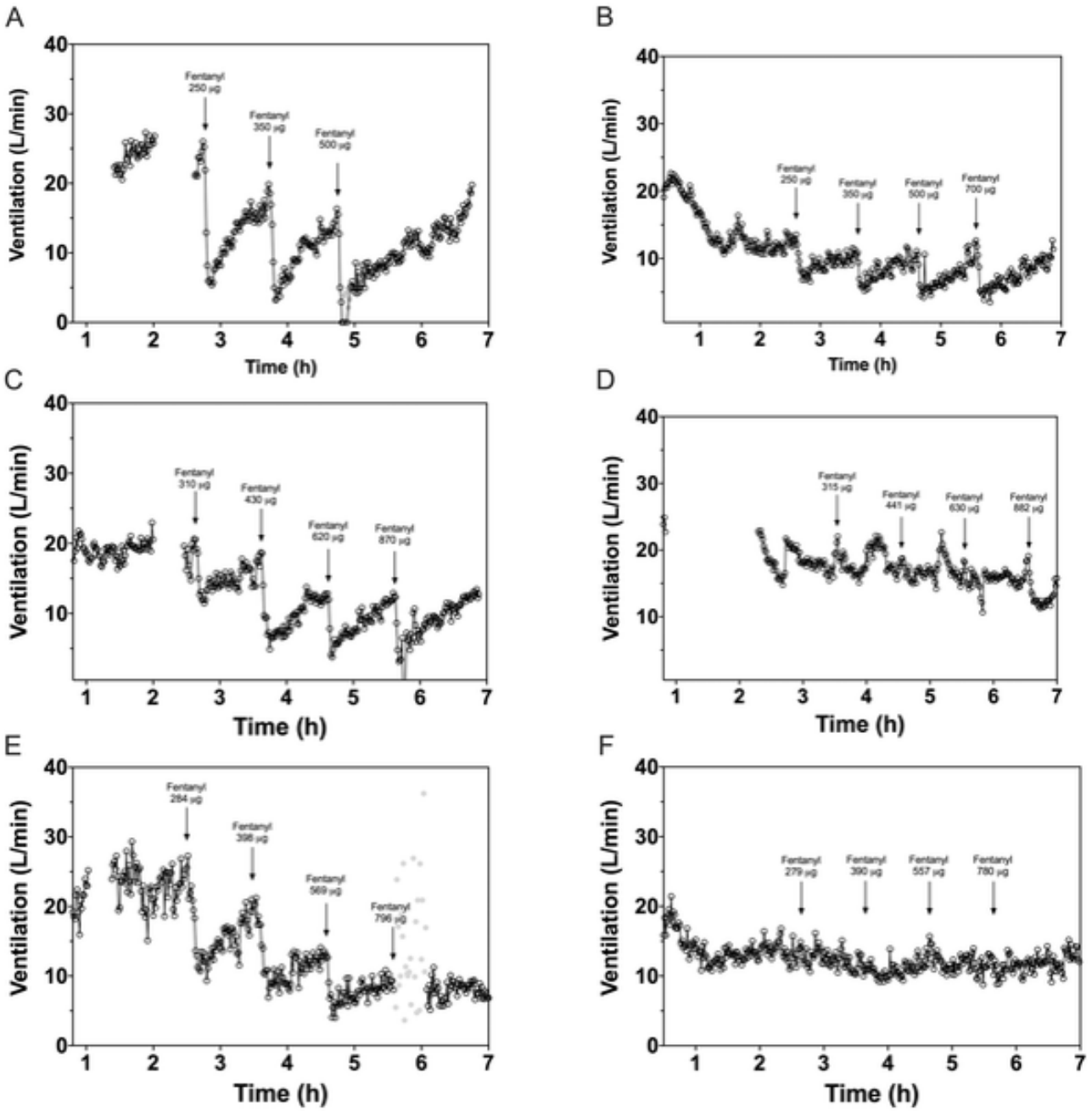
Effect of sustained high buprenorphine plasma concentrations on fentanyl-induced respiratory depression: A placebo-controlled crossover study in healthy volunteers and opioid-tolerant patients

Moss LM, Algera MH, Dobbins R, et al

Results in Opioid-Tolerant Patients:

1. **Reduced fentanyl VE was reduced up to 49% (21-76%)**
2. **Lowered risk of experiencing apnea requiring stimulation**

Moss LM, Algera MH, Dobbins R, et al. Effect of sustained high buprenorphine plasma concentrations on fentanyl-induced respiratory depression: A placebo-controlled crossover study in healthy volunteers and opioid-tolerant patients. *PLoS One*. 2022;17(1):e0256752. Published 2022 Jan 27. doi:10.1371/journal.pone.0256752



Example graphs showing the effect of fentanyl on minute ventilation in three opioid-tolerant patients during placebo infusion and buprenorphine infusion.

Moss LM, Algera MH, Dobbins R, Gray F, Strafford S, et al. (2022) Effect of sustained high buprenorphine plasma concentrations on fentanyl-induced respiratory depression: A placebo-controlled crossover study in healthy volunteers and opioid-tolerant patients. PLOS ONE 17(1): e0256752. https://doi.org/10.1371/journal.pone.0256752
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0256752

Alternate Induction Schedules

Butrans Patch

Belbuca

Buprenorphine infusion via IV

“Combo” Products

BUP “Mono” and BUP/NAL

BUP “Mono” Products:

- Subutex ® (SL tablets) only, generic available
- Probuphine ® subdermal implant (6-month)

  Off market
- Sublocade ® ER SQ injection (monthly)
- Brixadi ® ER SQ injection (weekly and monthly)
- Butrans ® transdermal patch (for pain only)
- Belbucca ® buccal films (for pain only)

BUP/NAL Combo Products:

- ❑ Suboxone ® buccal films, generic available
- ❑ Suboxone ® SL tablets, generic available
- ❑ Zubsolv ® SL tablets
- ❑ ~~Bunavail ® buccal films~~

  (discontinued)

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Induction
Butrans Patch

Day 1: Place one 10 mcg/hour patch x 24 hours

Day 2: Place one 20 mcg/hour patch x 24 hours

Day 3: 1 mg twice per day for a total of 2 mg SL daily

Day 4: 2 mg SL twice per day for total of 4 mg total

Day 5: 3 mg SL bid for a total of 6 mg total

(This is 1½ of a tablet/film to take twice per day)

Day 6: 4 mg SL bid for a total of 8 mg total (2 tablet twice per day)

Day 7: 12 mg SL once daily- all in AM (6 of the 2 mg tablets/films)

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Micro-Induction Initiating Belbuca ®

Day	Belbuca® Buccal Film	Sublingual tablet	Methadone
1	225 mcg once daily (75 mcg+150mcg)		Continue
2	225 mcg twice daily		Continue
3	450 mcg twice daily		Continue
4		2mg SL twice daily	Continue
5		4mg SL twice daily	Continue
6		8mg SL twice daily	Stop
7		8mg-12mg SL twice daily	Stop

- Belbuca is only currently approved for treatment of pain
- Patient may have to pay out of pocket for these first few doses
- Taking it via buccal dosing and then sublingual dosing may be confusing and should be explained

Sample Micro-Induction #2

Buprenorphine Day 1: Buprenorphine 450 mcg buccal q6h OR Buprenorphine 150 mcg q3h
Day 2: Buprenorphine /naloxone 2 mg SL q6h
Day 3: Buprenorphine /naloxone 4 mg SL q6h

https://penncamp.org/clinical/micro-dosing/

Recent Case Reports Published of the Use of IV Buprenorphine as Micro-Dosing (Thakrar 2022)

	Buprenorphine (Amount Given)	Scheduled Full Opioid Agonists	As needed full Opioid Agonists Ordered (Amount Given)
Case 1			
Before admission		PO methadone 65 mg	
Day 0		PO methadone 40mg	
Day 1	IV buprenorphine 0.15 mg q6h	PO methadone 20 mg	IV hydromorphone 1-2 mg q4h (11mg)
Day 2	IV buprenorphine 0.3 mg q6h	PO methadone 20 mg	IV hydromorphone 2 mg q4h (12mg)
Day 3	IV buprenorphine 0.6 mg q6h	PO methadone 20 mg	IV hydromorphone 2 mg q4h (8mg)
Day 4	SL buprenorphine 4-8 mg q4h PRN (28 mg)		IV hydromorphone 2 mg q4h (6mg)
Discharge	SL buprenorphine 12 mg BID		
Case 2			
Day 0			PO oxycodone 20mg q4h (60mg), PO hydromorphone 8mg q4h (24mg), IV hydromorphone 1mg q4h (1mg), PO tramadol 50 mg q4h (100)
Day 1	IV buprenorphine 0.15 mg q6h		PO hydromorphone 6-8 mg q4h 946). tramadol 50mg q4h (50mg)
Day 2	IV buprenorphine 0.3 mg q6h		PO hydromorphone 8mg q4h (48) mg
Day 3	IV buprenorphine 0.6 mg q6h		PO hydromorphone 8mg q4h (48mg)
Day 4	SL buprenorphine 4 mg q4h		PO hydromorphone 4-8 mg q4h 936 mg)
Discharge	SL buprenorphine 8 mg BID		PO hydromorphone 2-4 mg q4h tapered over 3 weeks

Macro-Dosing Buprenorphine

- Goal is to push patient past the point of precipitated withdrawal with saturation of opioid receptors and utilizing opioid agonist effect of buprenorphine
- Sounds paradoxical, but often a good strategy in a highly regulated setting
- Often not an effective outpatient strategy

Macro-Dosing
Sample Protocol

- When patient develops withdrawal (identified by the increase in the COWS score)
  - Naloxone induced precipitated withdrawal
  - Abstinence based withdrawal
  - Buprenorphine induced precipitated withdrawal
- Administer 8-16 mg SL AND use adjunctive prn medications (IV Phenergan, etc.)
- May use additional doses of 8-16 mg sublingual buprenorphine
- In this case, could exceed the 12 mg on the first day, and may go even above 24 mg on the first day to total 32 mg buprenorphine

“Macro-Dosing” of Buprenorphine Case Series

In a case series of 391 patients in ER per Herring in 2021, administered by 54 unique clinicians including 138 doses (28%) of buprenorphine of greater or equal to 28 mg…

- **There was no relationship between reported precipitated withdrawal events and buprenorphine dose**
- **4 of the 5 cases occurred after an 8 mg dose was provided**
    - **(*additional buprenorphine was used to treat the precipitated withdrawal to a dose of 28 mg)**

MACRO-DOSING
*NOTE OF WARNING

- **At this time, would only attempt macro-dosing in a residential setting with clinical staff, inpatient setting or ER**
- **The concern is that in the outpatient setting, the patient would develop withdrawal symptoms of such severity that there is a return to use or medical complications**

Adjunctive Medications

- Ondansetron: 4 mg – 8 mg po or ODT as needed every 6 hours as needed for nausea
- Methocarbamol: 750-1000 mg po tid prn for myalgias
- Ibuprofen: 400-800 mg po q 6 hours as needed for pain/fever; max 3200 mg/day
- Loperamide: 2mg as needed for diarrhea
- Clonidine: 0.1 mg po tid –qid as needed for opioid withdrawal; hold for hypotension (also consider lofexidine)
- Gabapentin: 300 mg po tid prn anxiety; especially helpful if there is a history of alcohol withdrawal
- Trazodone: 50-100 mg po before bed as needed to help with insomnia
- Controlled settings: consider ketamine and benzodiazepines to bridge intractable agitation

MANAGEMENT PARADIGMS

Replacement therapy with alpha-2-adrenergic agonists:

- Clonidine
- Dexmedetomidine
- Tizanidine
- Guanfacine

Symptom management:

- **Pain:** Short acting opioids, Ketamine, Gabapentin, Ketorolac, Acetaminophen, NSAIDs
- **Insomnia:** Trazadone, Quetiapine, Mirtazapine
- **Anxiety:** Hydroxyzine, **Benzodiazepines** (judiciously)

Treating opioid use disorder and opioid withdrawal:

- If a patient is on opioid agonist therapy, then split dosing can increase analgesic effect and improve pain control.

Harm Reduction Measures

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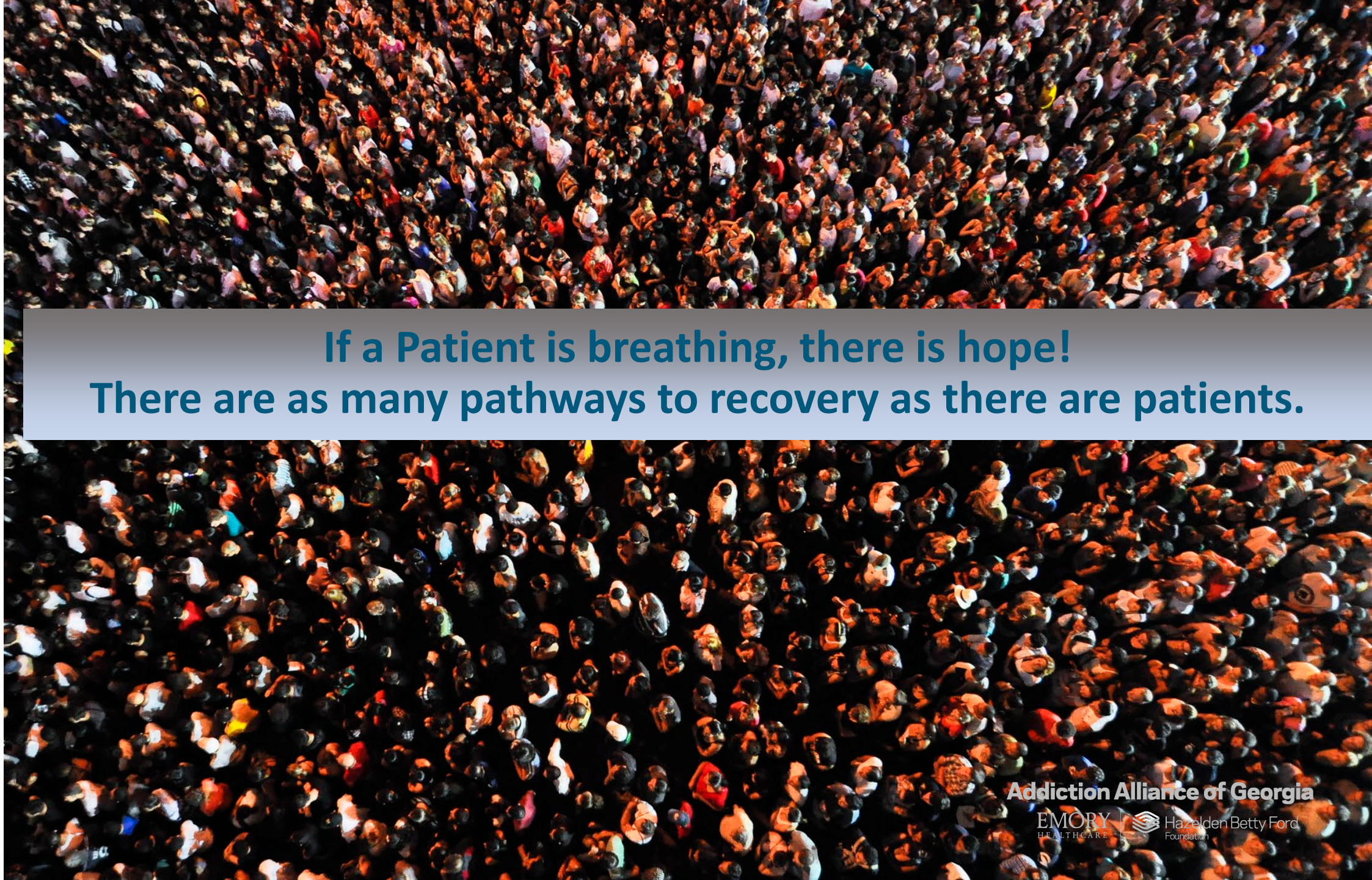

If a Patient is breathing, there is hope!
There are as many pathways to recovery as there are patients.

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Comorbid PTSD

- **Not only do ACEs and trauma predispose to substance use disorder in a hugely significant way, but the lifestyle associated with ongoing use often leads to repeated traumatizing experiences, such as being in jail, being unhoused and violent encounters.**

- **If underlying PTSD is not addressed concurrently, it can be very difficult for a patient to maintain abstinence.**

- **Approaching patients in a non-stigmatizing, trauma-informed way is imperative.**

Universally Provide Trauma Informed Care

Infographic: 6 Guiding Principles to a Trauma-Informed Approach | CDC, n.d.)

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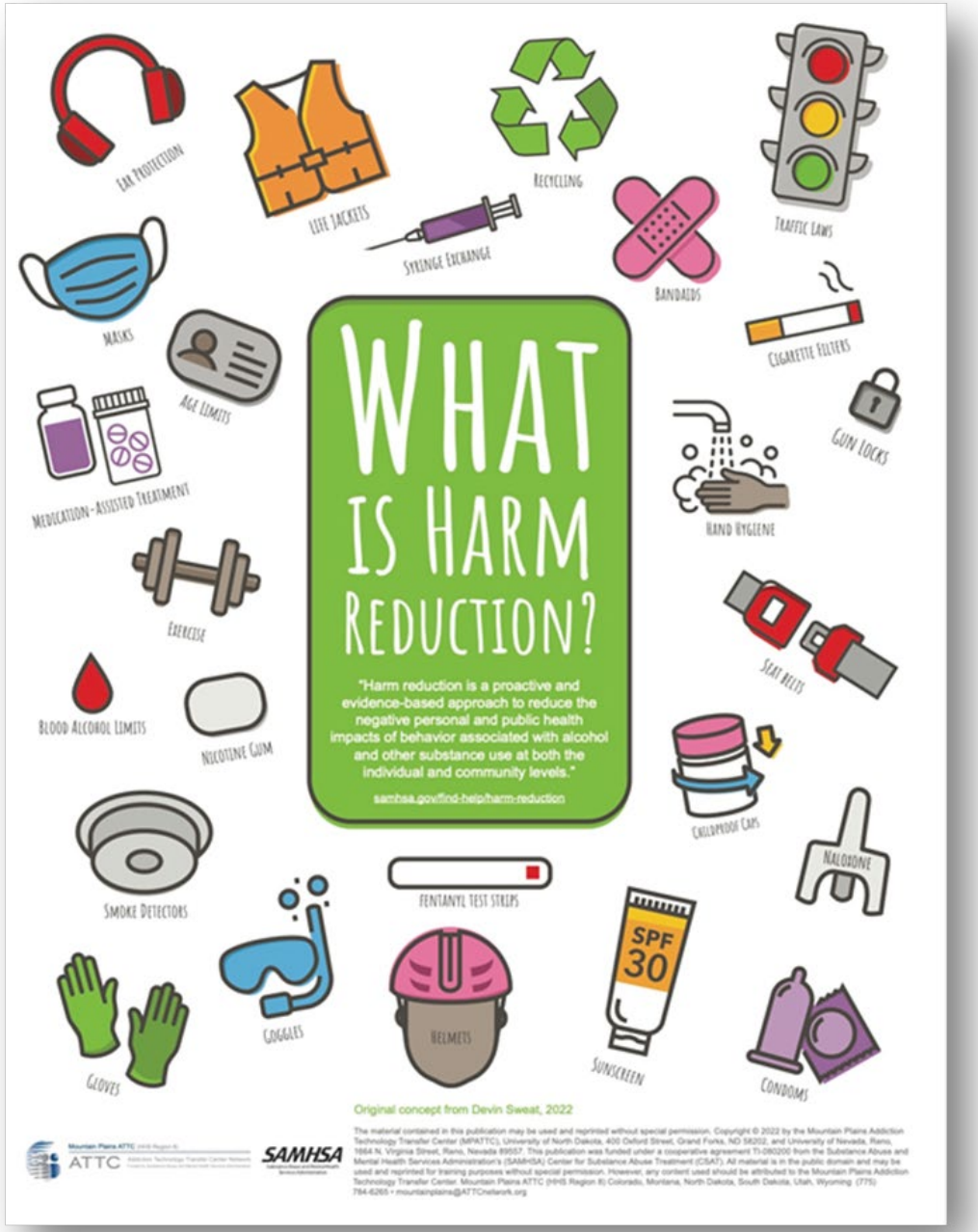

Harm Reduction

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Harm Reduction

- Don’t use alone.
- Carry naloxone.
- If injecting, make sure to use clean supplies.
- Use via smoking/snorting, not injection.
- Use less, esp. after a period of not using.
- Distribution of fentanyl testing strips.
- Be aware, “non-prescribed buprenorphine is almost never used euphorically, rather as a form of self-treatment” (Caroll, Rich & Green 2018).
- In fact, “more frequent use of non-prescribed buprenorphine is associated with a decreased risk of overdose” (Carlson et. Al 2019).

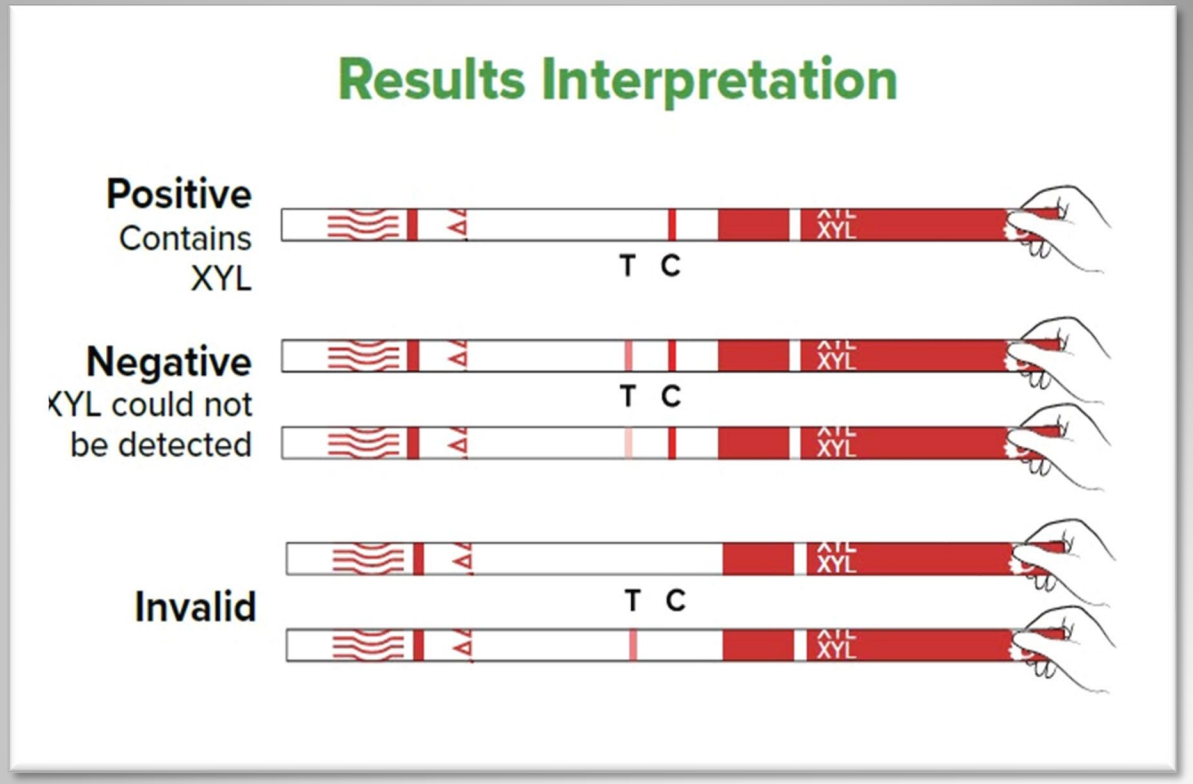
URINE TOXICOLOGY

Harm Reduction test strips available, but

* Not CLIA waived

Some laboratories can test for this chemical, and levels, but at present,

*there is not point-of-care testing available for xylazine in hospitals



Naloxone
Co-Prescribe

FDA-approved naloxone products for community use that are available by prescription

INJECTABLE
Naloxone 0.4mg/1ml
IM injection
(3ml 25g 1” syringes are recommended)

INTRANASAL
Naloxone 4mg/1ml
intranasal spray
Box contains 2 (two) single-spray devices

Now Available!!

Kloxxado™ (naloxone HCl)
nasal spray 8 mg

INTRANASAL
Naloxone 8mg/1ml intranasal spray
Box contains 2 (two) single-spray devices

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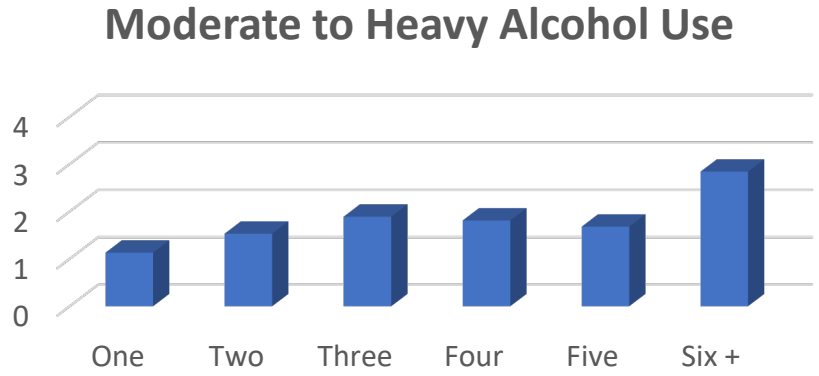
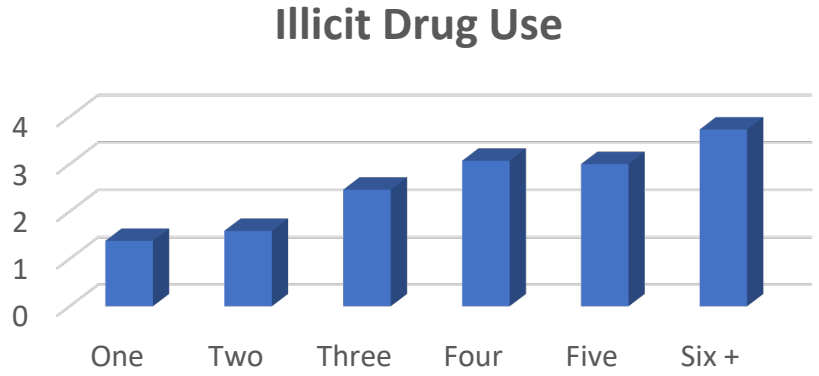
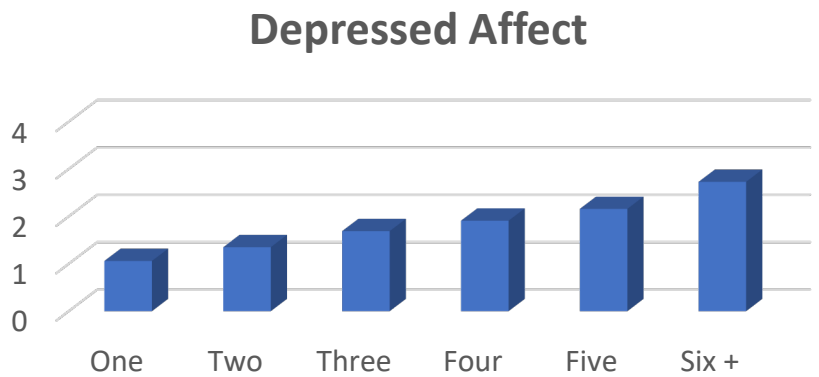
Stigma
Combat it Wherever **YOU** Find It

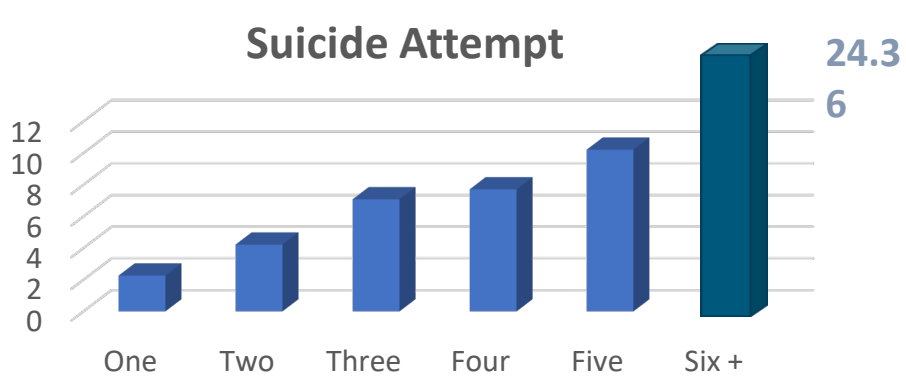
- **This is a daily job!**
- **Use neutral, nonjudgement terminology- review the words matter document**
- **Remind patients and our colleagues how much hope our patients have, and how our goals fit with much of chronic disease management methods we use for treating other diseases**
- **Discuss the connection between substance use disorders and childhood trauma**
- **Remember- this is progress not perfection- for those of us who have been doing this a while, the changing terms can be difficult to keep up with**

Dose Response Curve with MH/SUD and ACEs









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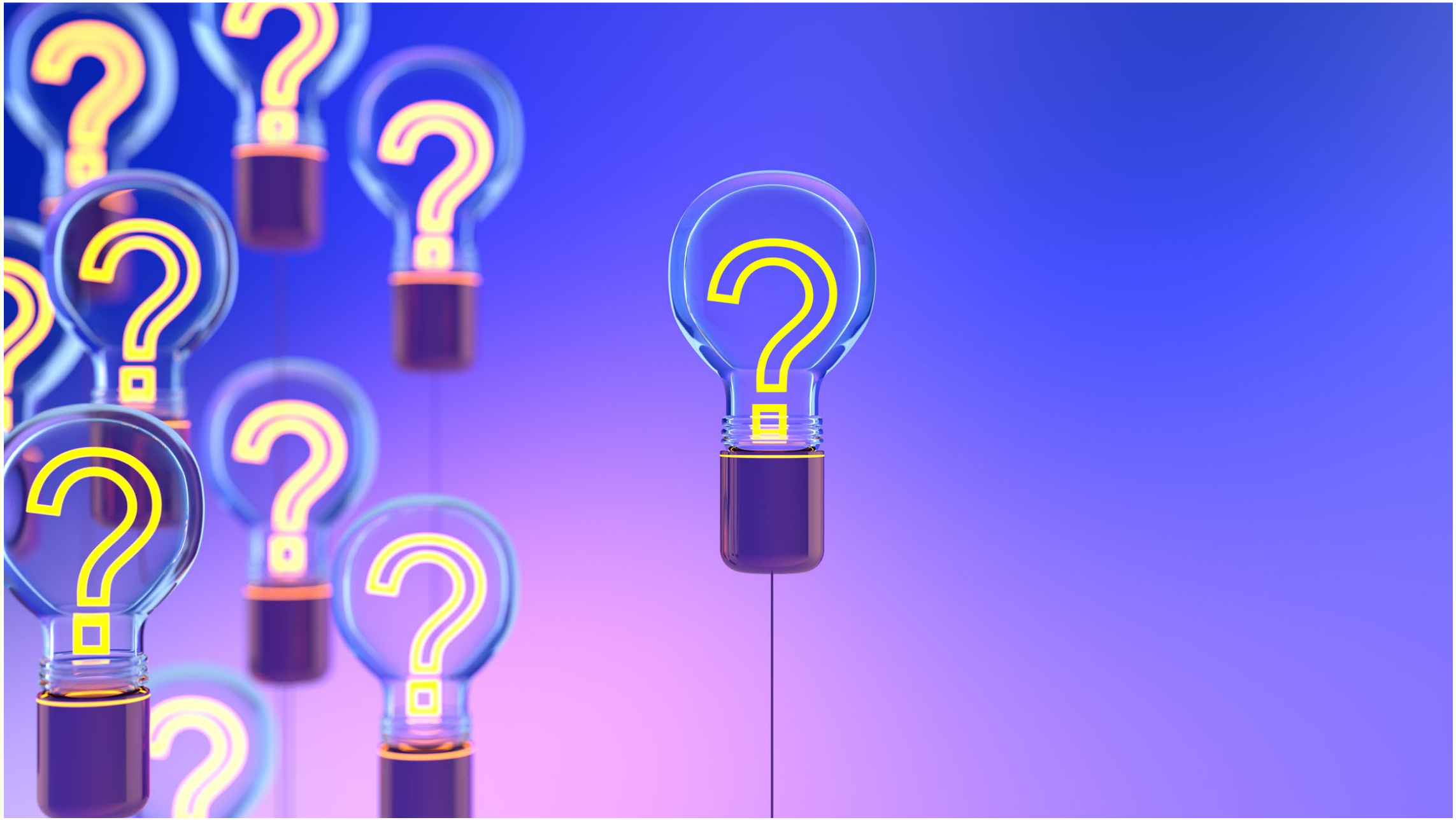
How Can We Apply What We Have Learned to Help SG?

- We can consider use of a low dose outpatient or recovery facility induction for SG using sublingual buprenorphine-naloxone
  - This could take 3-7 days to accomplish
- We can consider having patient present to ER to be given a macro-induction with sublingual buprenorphine
- We can prescribe patient high-dose or multiple dose naloxone
- We can counsel SG on reduction of infectious disease risk AND on the importance of not using alone
- We can provide a safe harbor for SG, and provide information so he feels comfortable returning in the future and understands despite his difficult experience he can still benefit from MOUD treatment

❖ Out of the scope of this talk, but we can consider referral to an OTP to obtain methadone if patient really cannot tolerate buprenorphine induction



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Thanks for your attention

- If you have any questions, please contact me at ebrunner@hazeldenbettyford.org
- Thanks to Kerry Hettinger, Pharm D and Joan Laes, MD DFASAM, who provided many resources on fentanyl, and the many other addiction doctors currently working on this issue

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BREAK

Joint Providership Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Emory University School of Medicine, the Addiction Alliance of Georgia
and the Hazelden Betty Ford Foundation.
The Emory University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Physician designation statement
The Emory University School of Medicine designates this live activity for a maximum of 4 *AMA PRA Category 1 Credit(s)™*.
Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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Panel Q&A

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Addiction Psychologist and Clinical Director, Intensive Outpatient Program – Emory Healthcare

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THANK YOU!

Scan the QR code to check out for CME/CE credits.

An email to the CME questionnaire and/or CE evaluation will be emailed to you by tomorrow, Friday, 11/3.

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