

SUBSTANCE USE DISORDERS AND TREATMENTS









Continuing Medical Education (CME) & Pharmacy Continuing Education (ACPE) Seminar

Substance Use Disorders and Treatments

Virtual Live Program
on
Saturday, April 30, 2022

8:30 am - Registration

8:45 am – Introductions Maryland Department of Health

Office of Pharmacy Services

9:00 am - Medications for Opioid Use Disorder-

A Patient Centered Approach

Michael I. Fingerhood, MD, FACP, DFASAM, AAIVS

Johns Hopkins University School of Medicine

10:30 am – Alcohol Use Disorder: Recognition

Treatment, and Implications

Vincent Cavaliere, PharmD, BCPP

Luminis Health

11:30 am – Harm Reduction- Not Dirty

Words Anymore

Christopher J. Welsh, MD

University of Maryland School of Medicine

1:00 pm – Closing Remarks Maryland Department of Health

Office of Pharmacy Services

1:15 pm - Adjourn

The views and opinions expressed by the speakers are not necessarily the views and opinions of the State of Maryland Department of Health.

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- Dr. Fingerhood states that he does not have relevant financial relationship with commercial interests and will not be discussing "Off-Label" uses of products or devices. This information is on file with Kepro.
- Dr. Cavaliere states that he does not have relevant financial relationship with commercial interests and will be discussing "Off-Label" uses of products or devices. This information is on file with Kepro.
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Support provided by Kepro.

Activity Type: Knowledge-Based

MACS Medications for Opioid Use Disorder-A Patient Centered Approach Michael Fingerhood MD FACP DFASAM AAHIVS Johns Hopkins University

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Conflict of Interest • No commercial, financial or advisory relationships

Some reasons why everyone should have x waiver

- Caring for patient in opioid withdrawal
- · Patient needs urgent refill for buprenorphine
- · Covering for provider who has patient on buprenorphine
- · Patient doing well on buprenorphine and wants all care integrated
- · Patient had surgery and is having difficulty coming off full opioid agonist
- Patient recovered from major trauma and needs help stopping opioid agonist after 4 weeks of use
- Patient has been on opioid agonist for chronic pain for many years and inquires about switching to buprenorphine (theoretically do not need x number)
- · Caring for patient with opioid use disorder who asks for help
- Diagnosed patient with opioid use disorder and you want to immediately help and prevent an overdose death

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Integration of substance use disorder treatment and primary care

- ➤ In 2006, the IOM released a report recommending improvement in coordination of mental health and substance-related services into general health care services:
- "Available evidence suggests that integration of mental health and primary care may lead to improved care and quality of life"
- Studies of health delivery, process of care, and health outcomes in integrated clinical settings will be critical to inform the process

What should providers expect from their patients with addiction?

- Desire to receive care that will improve health
- Engagement in care based on trust and rapport

Press K, Zornberg G, Geller G, Carrese J, Fingerhood M. What patients with addiction disorders need from their primary care physicians: a qualitative study. Substance Abuse 2016; 37:349-55.

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What do patients with addiction need from their providers

- Knowledge about addiction
- Duty to treat
- · Focus on overall health
- Engage patients in care
- Treat the full scope of illness (isolation, rejection, creating hope)

The sap is extracted by slitting the pod

Highly refined Southwest Asian heroin or Southeast Asian heroin



Opiates & Opioids

Opiates = naturally present in opium
•e.g. morphine, codeine, thebaine

Opioids = manufactured

- •Semisynthetics are derived from an opiate
 - -Heroin from morphine
 - -Buprenorphine, oxycodone from thebaine
- •Synthetics are completely man-made to work like opiates
 - -Methadone
 - -Fentanyl

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Narcotic Regulation in US

- 1914- Harrison Narcotics Tax Act
- 1925- Linder vs United States
- 1964- Methadone introduced as experimental treatment for opioid addiction
- 1968- Bureau of Narcotic and Dangerous Drugs formed (changed to DEA in 1973)

DSM5- Opioid Use Disorder

- Group 1- Impaired control- larger amounts and longer; desire to cut down; great deal
 of time spent related to using; craving
- Group **2-Social impairment** failure to fulfill obligations; interpersonal problems; reduction in social, occupational or recreational activities
- Group 3- Risky use- use in hazardous situations; continued use despite negative consequences
- Group 4- **Pharmacologic dependence** tolerance; withdrawal with cessation

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Management of OUD • Management = Treatment + Prevention • Management = can be utilized across patient goal Minimization of harms from ongoing use Sustained recovery with abstinence from all substances

Options for Treatment

- Medication (MOUD)- methadone, buprenorphine or naltrexone
- Simple detoxification and no other treatment
- Counseling and/or peer support without MOUD
- Referral to short or long term residential treatment

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But here is my bias:

SBIRT

VS

SIT (screen, intervene and treat)

Intervention- "I have joined your fan club"

- Interventions and education are effective
- Interventions should emphasize health and relationship benefits
- Use family/friends in a positive way
- Avoid threats- "If you use, you will die"
- Give hope that life can improve
- Acknowledge reasons for use, but...
- Work together to define the benefits of change

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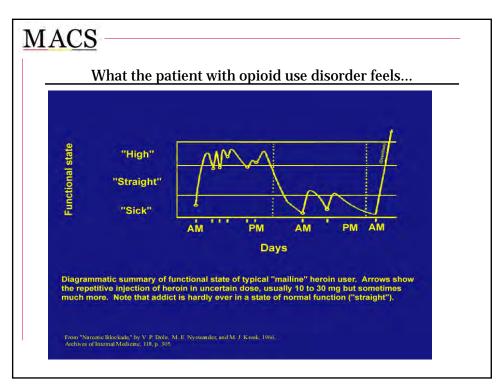
Effective Treatment of Opiate Addiction NIH Consensus Development Conference November 17-19, 1997

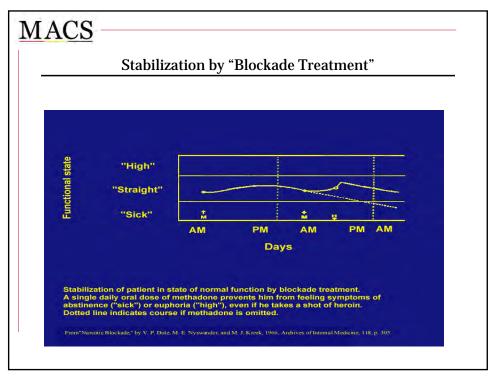
- Opiate dependence is a brain-related medical disorder
- **■** Treatment is effective-
 - "'Although a drug-free state represents an optimal treatment goal, research has demonstrated that this goal cannot be achieved or sustained by the majority of opiate-dependent people."
- Reduce unnecessary regulation of long-acting agonist treatment programs
- Improve training of health care professionals in treatment of opiate dependence

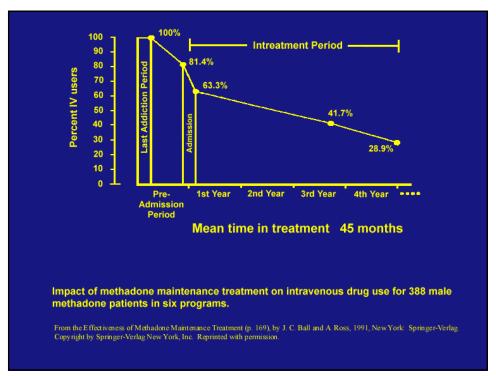
MEDICATIONS

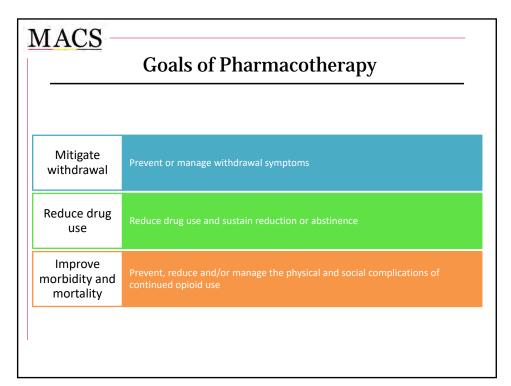
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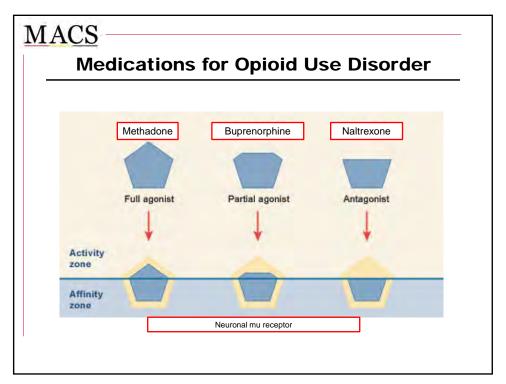
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Drug Abuse Treatment Act (DATA) of 2000

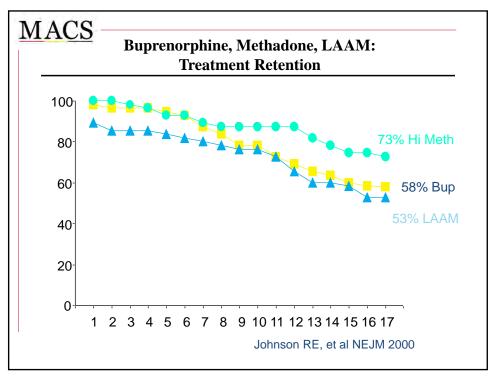
- Allowed "Qualified" physicians to treat opioid dependence outside methadone facilities
 - 1. Addiction certification from approved organization, or
 - 2. Physician in clinical trial of qualifying medication, or
 - 3. Complete 8-hour course from approved organization
- ▶ DEA issues (free) to qualifying physicians a new DEA number to use medication for opioid dependence
- As of today, only one medication formulation is approved for this use

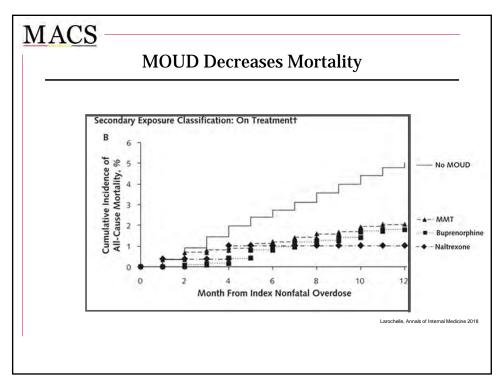
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Opioid Treatment: Changing Approach

Methadone Clinic	Buprenorphine
• Criteria:	• Criteria:
Withdrawal	DSM IV
12 months use	No time criteria
 Dose regulated 	 MD sets dose
• Age > 18	• Age > 16
• Limited take homes	• Take homes (30 days)
• Services "required"	• Services must be "available'





Major Features of Methadone

Full Agonist at mu receptor

Long acting

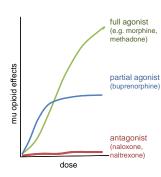
Half-life ~ 15-60 Hours

Weak affinity for mu receptor

 Can be displaced by partial agonists (e.g. burprenorphine) and antagonists (e.g.naloxone, naltrexone), which can both precipitate withdrawal

Monitoring

- Significant respiratory suppression and potential respiratory arrest in overdose
- QT prolongation



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Methadone Initiation

- Require dispensing at "Opioid Treatment Program"
 - -Medical assessment
- Dosing
 - -Starting dose of 30mg
 - -Liquid
 - -Federal law requires that the initial dose be \leq 30 mg and not exceed 40 mg in 1st day



Methadone Maintenance

- Initial Dose Increase
 - Doses ↑ 5-10 mg every 7d
 - Can take 4d for full effect
- Maintenance Dosing
 - ↑ 60-120mg/d based on response (no craving, withdrawal, euphoria)
 - Higher dosing associated with better efficacy
 - Can go up to >200mg
- · Federal law regulates take-home schedule in first two years of therapy

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Methadone Safety



Side effects:

Common: constipation, lightheadedness, dizziness, sedation, nausea, vomiting, sweating

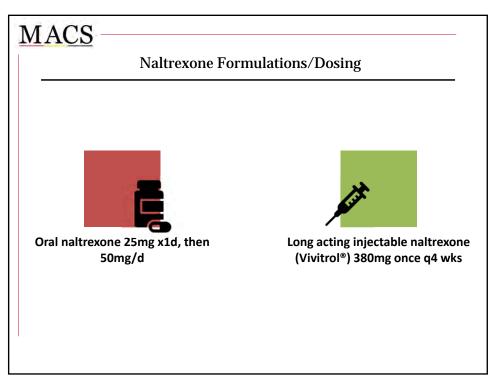
Rare: EKG abnormalities, psychosis, pruritis, sexual dysfunction or decreased libido, amenorrhea, weight gain, edema, seizures, hypotension



Drug Interactions:

Metabolized primarily by CYP3A4
Inducers ↓ methadone effect
Inhibitors ↑ toxicity

MACS **Major Features of Naltrexone** Full Antagonist at mu receptor Competitive binding at mu receptor full agonist (e.g. morphine, methadone) Long acting Half-life: • Oral ~ 4 Hours mu opioid effects partial agonist (buprenorphine) • IM ~ 5-10 days High affinity for mu receptor Blocks other opioids Displaces other opioids · Can precipitate withdrawal antagonist (naloxone, **Formulations** Tablets: Revia®: FDA approved in 1984 naltrexone) dose Extended-Release intramuscular injection: Vivitrol®: FDA approved in 2010 SAMHSA, 2018



Naltrexone Initiation

- Start \geq 7 days after last opioid use
 - −≥14 days with long acting opioids (buprenorphine, methadone)
 - -Can precipitate severe opioid withdrawal
- Strategies
 - -Negative urine screen
 - -Challenge with naloxone before administering XR-NTX

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Major Features of Buprenorphine

Partial agonist at mu receptor

 Comparatively minimal respiratory suppression and no respiratory arrest when used as prescribed

Long acting

Half-life ~ 24-36 Hours

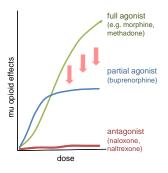
High affinity for mu receptor

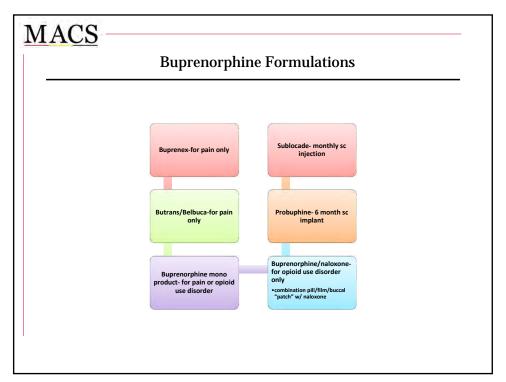
- Blocks other opioids
- Displaces other opioids
 - Can precipitate withdrawal

Slow dissociation from mu receptor

Stays on receptor for a long time

SAMHSA, 2018 Orman & Keating, 2009







Buprenorphine Common Adverse Effects

- Headaches
 - Management: aspirin, ibuprofen, acetaminophen (if there are no contra-indications)
- Nausea
 - Management: Consider spitting the saliva out after adequate absorption instead of swallowing.
- Constipation
 - Management: Stay well-hydrated, Consume high-fiber diet, Consider stool softeners, laxatives, naloxegol
- Xerostomia (Dry mouth)
 - Complications: Gingivitis, Periodontitis
 - Management: Stay well-hydrated, Maintain good oral hygiene

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Precipitated Withdrawal

- Because of its high affinity for mu opioid receptors, buprenorphine can displace other agonists (such as heroin, methadone) that are already present and occupying the receptors
- The sudden change from full-agonist to partial-agonist activation of opioid receptors can cause sudden and severe withdrawal symptoms (precipitated withdrawal)

MACS MOUD Methadone **Buprenorphine (Oral)** Naltrexone (IM) Mechanism Full Agonist Partial Agonist Antagonist on Opioid Receptor on Opioid Receptor on Opioid Receptor of Action Dosing 80mg-100mg 4-32mg 380mg Depot Injection (Usual Dose) No addictive potential or Provided in a highly Improved safety due Advantages • structured supervised to partial agonism diversion risk setting where additional Availability in office-Available in office-based services can be provided based settings settings on-site and diversion is Option for individuals unlikely seeking to avoid any Maybe effective for opioids individuals who have not benefited sufficiently from partial agonists or antagonists Schuckit, 2016

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	STARTING BUPRENORPHINE

Obtaining History









Ask about all substances:

Age at first use

Determine patterns of use over time:

Assess recent use

Prescribed and non-prescribed

Frequency Amount In the last 2 weeks

Most recent use

Route

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Previous Treatment

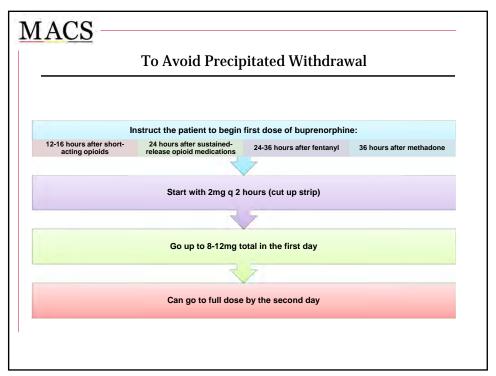
- Prior treatment attempts
 - -What type?
 - -What age?
 - -What happened?
 - -What was your experience?
 - -What was the outcome?

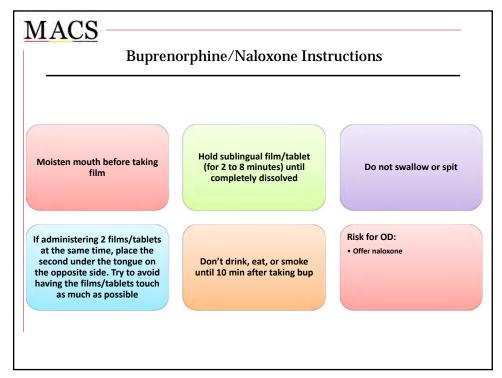
Clinical Opiate Withdrawal Scale (COWS)

- Resting Pulse
- Sweating
- Restlessness
- GI Upset
- Tremor
- Pupil Size
- Bone or Joint Aches
- Yawning
- · Anxiety or Irritability
- Gooseflesh
- Runny Nose or Tearing Eyes

Wesson and Ling, 2003

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MACS MAINTAINING BUPRENORPHINE

Treatment Duration

Evidence supports long term maintenance

- Studies up to 16 weeks show high relapse rates with medication withdrawal
- Improved retention rates in treatment with extended buprenorphine maintenance



Continue maintenance as long as patient is benefitting from treatment

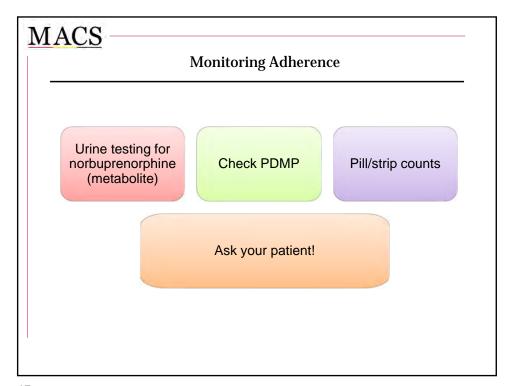
Kakko et al., 2003 Weiss et al., 2011

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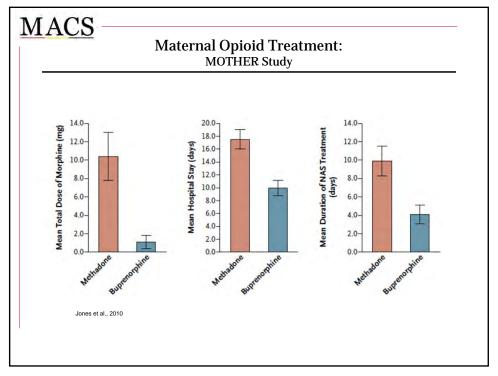
Monitoring Efficacy

- Urine toxicology
 - Testing is not meant to "catch" the patient
 - Positive UDS results
 - Reflect only recent drug use
 - Cannot determine exposure time, dose, or frequency of use
 - Should not lead to a discharge from treatment
 - Opportunity for discussion



Amphetamine	2-4 days
Benzodiazepines	1-10 days
Cocaine	1-3 days
Heroin/morphine	1-3 days
Methadone	1-4 days
Marijuana	1-30 days
PCP	3-30 days

MACS **MOUD** in Pregnancy Buprenorphine Similar efficacy as methadone More structure- better for patients in Same rates of adverse events, NAS, as unstable situations methadone Decreased risk of diversion Improvement over methadone: More long-term data on outcomes Lower risk of overdose Fewer drug interactions Milder withdrawal symptoms in Reduced morphine dosing for NAS Significantly shorter hospital stay Fischer et al., 1998, 1999 Jones et al., 2010; Kakko et al., 2008; Kraft et al., 2017



Optimal Management

Medications alone are efficacious and should never be delayed for individuals without access to counseling or therapy

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But don't I need to provider a counselor?

Adjunctive Counseling During Brief and Extended Buprenorphine-Naloxone Treatment for Prescription Opioid Dependence: *A 2-Phase Randomized Controlled Trial*

Roger D. Weiss, MD; Jennifer Sharpe Potter, PhD; David A. Fiellin, MD et. al. Arch Gen Psych 2011; 68:1238-1246

• Multicenter randomized clinical trial- n=653

In both phases patients randomized to standard medical management(SMM) or SMM plus counseling

In both phases (3 &12 weeks of buprenorphine), separate counseling did not change outcomes

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Support groups?

"You're not in recovery if you're on medication"

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So now I am convinced (maybe) I should prescribe in my primary care setting...

- •Prescribing is the easy part
- •The conversation is the art of medicine (and the fun)

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SHAME



Self-esteem

- You- "The best thing you can do for yourself is stop using drugs"
- Patient- "I don't deserve the best, what else can I do?"

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Coping



Visit openers:

What have you done today to make the world a better place?

What have you done today to make today better than yesterday?

Give me an update for your fan club

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What if?

- My patient's urine drug screen is positive for...
- My patient's urine drug screen is negative for buprenorphine
- My patient misses an appointment
- My patient asks for a refill early
- My patient has an overdose

Recovery is about progression (not linear), not perfection

Components of Recovery



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Quotes from patients on buprenorphine

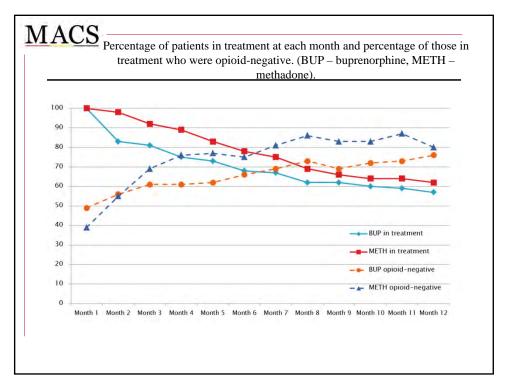
"I feel normal"
"I wake up not sick"
"I have my life back"

- Treatment in normal medical settings:
 - -Encourages continuity of medical care
 - -Encourages relationship building
 - -Legitimizes opioid use disorder as a treatable, chronic illness

Fingerhood M, King V, Brooner R, Rastegar D. A comparison of characteristics and outcomes of opioid dependent patients initiating office-based buprenorphine or methadone maintenance treatment.

Substance Abuse. 2014; 35:122-6.

Characteristic	BUP n=252	METH n=252	P value
Abused Substances			
Heroin	83%	86%	0.39
Opioid Rx	29%	9%	<0.001
Cocaine	53%	55%	0.73
Benzodiazepines	9%	23%	<0.001
Injection drug use	61%	69%	0.051
HIV infection	14%	8%	0.023
Chronic pain	18%	12%	0.063
Recent criminal charges	43%	50%	0.129



Integrated buprenorphine cost study

Hsu YJ, Marsteller JA, Kachur SG, Fingerhood MI. Integration of buprenorphine treatment with primary care: Comparative effectiveness on retention, utilization and cost. Pop Health Managem. 2019; 22:292-9.

- Maryland Medicaid Priority Partners beneficiaries who received a script for buprenorphine and no buprenorphine script in previous 3 months
- Only first episodes analyzed

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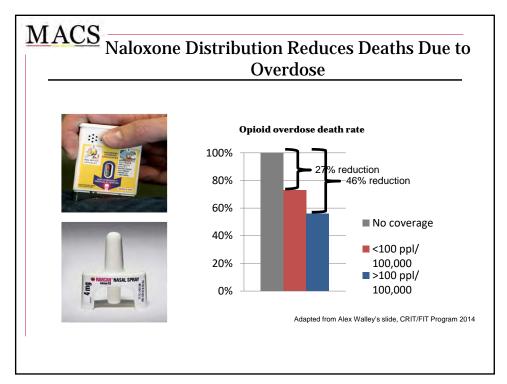
Buprenorphine cost study

	CCP n=137	Non-CCP n=992	
6 month retention	80.3%	59.2%	p<.001
Any ED visit 12 months	63.5%	60.4%	NS
Any acute hospital stay 12 months	15.3%	18.9%	NS
Total cost 12 months mean	\$10,785	\$12,210	P<.001

Harm Reduction

- The practice of reducing the negative consequences of drug use in people who are not ready, or not able to abstain from drug use completely
 - -Needle and syringe programs
 - -Safe injection practice counseling
 - -Overdose education and naloxone distribution

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MACS Alternatives Why? Terms to avoid Addict User Person-first language • Person with...(OUD, AUD, SUD) Shows that a person "has" a medical problem, rather than "is" the problem Substance or Drug Abuser • Person with opioid addiction... Junkie • Patient • Avoids negative associations, punitive attitudes, Alcoholic/Drunk Substance Dependence • Person in recovery and blame For toxicology screen results: Accurate terminology consistent with a medical Clean/Dirty • Testing negative/positive disorder Opioid agonist therapy Evidence-Based medication for OUD Opioid Substitution Therapy/ • Avoid misconception medications substitute for another drug/addiction Pharmacotherapy • "Assisted treatment" • Medication to treat OUD Medication Assisted Treatment (MAT) -undervalues the role of medication -unlike other medical disorders • Pharmacotherapy for OUD

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Patient vignette 1

- EB is a 72 F seen for initial visit. She has a history of chronic pain in hips and knees. Her previous provider will no longer prescribe oxycodone as for the past 2 months her 30 day script ran out after 2 weeks. Tearful and fearful that providers won't help her. Cannot take NSAIDs. She admits that she often takes oxycodone when she is upset.
- She lives alone in senior housing apartment; 2 daughters- both with difficulties (medical and social). Non-smoker; no alcohol.

Patient vignette 1 outcome

- After spending time building rapport and making sure she knew my goal was to work with her, I explained I would not prescribe her oxycodone.
- She was open to undoing isolation, treating mood and trying buprenorphine.
- Almost immediately, physically more active (no longer dwelling on when next dose of pain medication is and does she have enough), remains on low dose buprenorphine, never running out before she should, with improved pain.

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Patient vignette 2

- KL is a 65F retired nurse who had right total knee replacement complicated by joint infection requiring prolonged course of antibiotics, hardware removal with spacer and finally replacement of hardware. She has been on oxycodone 15 mg four times daily for 4 months.
- She sees orthopedics in f/u and is told she should not be on any further opioids as she is now 2 weeks out since the last surgery. She is told to take ibuprofen.

Patient vignette 2 outcome

- I receive a call from the police that KL had died from an apparent opioid overdose
- I find out from her son that she had gone into severe opioid withdrawal and bought opioids on the street.

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Patient vignette 3

- 28F seen for first visit. Able to review in CRISP/PDMP- multiple ER visits for back pain and one opioid overdose, and many filled scripts for oxycodone from many providers. Had abnormal PAP 3 years ago. History of HIV (not addressed) and hypertension (has elevated BP today)
- Her agenda- getting script for oxycodone. My agenda- getting her engaged in medical care and treatment for opioid use disorder

Patient vignette 3 outcome

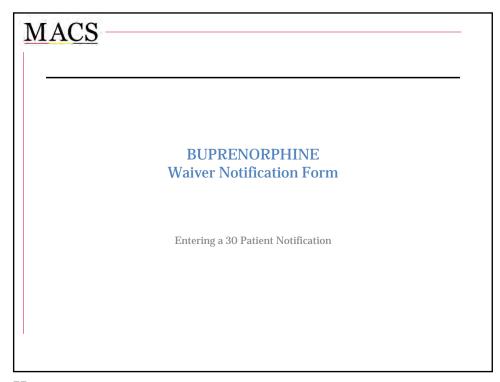
- After 3 months seen her 7 times
- Doing well on buprenorphine/naloxone. No back pain. Urine drug screens all negative since the first visit.
- On medication for hypertension; adherent with HAART for HIV; had PAP done. No ER visits.
- Mood/self-esteem much improved. Better relationship with family. Working part-time.

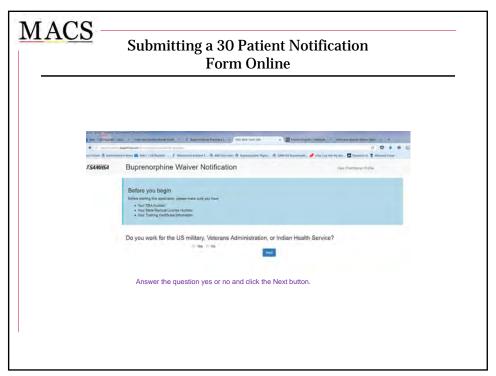
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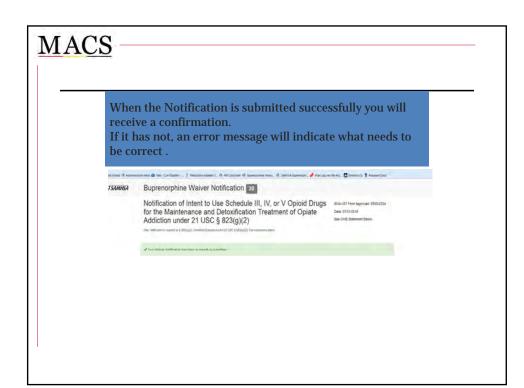
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X waiver by the numbers

- 30- how many patients can be treated with taking 5 minutes to apply
- 100- how many patients can be treated if you have taken 8 hour training for physicians or 24 hours for non-physicians
- 275- how many patients can be treated after one year of being able to prescribe for 100
 patients







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Provides support to prescribers and their practices, pharmacists, and healthcare teams in addressing the needs of their patients with substance use disorders and chronic pain management.

All Services are FREE

- Phone consultation for clinical questions
- Education and training opportunities related to substance use disorders and chronic pain management
- Assistance with addiction and behavioral health resources and referrals
- Technical assistance to practices implementing or expanding office-based addiction treatment services
- MACS TeleECHO™ Clinics: collaborative medical education through didactic presentations and case-based learning

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Notes

Alcohol Use Disorder: Recognition, Treatment, and Implications

Vincent Cavaliere, PharmD, MM, BCPP vcavaliere@luminishealth.org

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Conflict of Interests

No conflicts of interest to disclose

Will be discussing the off-label use of gabapentin and topiramate for alcohol use disorder

Learning Objectives

- 1. Recognize signs, symptoms, risk factors, diagnostic criteria, disease course, and treatment options for:
 - Acute alcohol withdrawal
- > Wernicke-Korsakoff syndrome (WKS)
- > Delirium tremens (DTs)
- ➤ Alcohol use disorder (AUD)
- 2. Identify guideline-recommended agents for the treatment of AUD
 - Dosing

- Common adverse effects
- Contraindications

> Serious adverse effects

> Precautions

> Patient counseling

2

QUESTIONS TO CONSIDER

Δ

Question 1

A patient that has been stable on naltrexone 50 mg PO daily mentions that they have been forgetting to take the tablet everyday since working nights. What do you recommend?

- A. Continue naltrexone 50 mg PO daily
- B. Recommend switching to acamprosate 666 mg PO TID
- C. Recommend switching to topiramate 100 mg PO BID
- D. Recommend switching to Vivitrol® 380 mg IM monthly

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Question 2

Which of the following treatment options for AUD does not require dose adjustments in patients with renal impairment?

- A. Gabapentin
- B. Acamprosate
- C. Naltrexone
- D. Topiramate

Question 3

Which FDA-indicated treatment for AUD can cause serious harm if the user ingests alcohol after taking their dose?

- A. Naltrexone
- B. Acamprosate
- C. Disulfiram
- D. Topiramate
- E. Gabapentin

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DEFINING "ADDICTION"

Addiction



Terminology varies:

American Psychiatric Association (APA)

Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5)

 Substance use disorders (alcohol use disorder [AUD], opioid use disorder [OUD], cannabis use disorder, etc.)

National Institute of Drug Abuse (NIDA)

Addiction is widely accepted as a DISEASE

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). https://doi.org/10.1176/appii.books.978089042555

NIDA. Understanding Drug Use and Addiction. National Institute on Drug Abuse website. https://www.drugabuse.gov/publications/drugfacts/understanding-drug-use-addiction. June 6, 201

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Addiction (NIDA)

A chronic, relapsing disease characterized by compulsive drug seeking and use despite harmful consequences as well as neurochemical and molecular changes in the brain

NIDA. https://www.drugabuse.gov/publications/drugfacts/understanding-drug-use-addiction. June 6, 2018

Recommended Limits for Alcohol Consumption

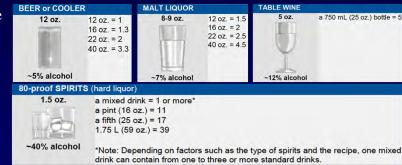
Men ≤ 65 years

- \leq 2 drinks per day on average
- \leq 4 drinks in one day
- ≤ 14 drinks per week

Men > 65 or Women

- ≤ 1 drink per day on average
- \leq 3 drinks in one day
- \leq 7 drinks per week

"Standard" Drinks



VA / DoD Clinical Practice Guideline for the Management of Substance Use Disorders. 2021

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SCREENING TOOLS

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Screening, Brief Intervention, and Referral to Treatment (SBIRT)

Screening

Assesses severity of substance use Identifies appropriate level of treatment

Brief Intervention

Express concern and advise to abstain or decrease drinking Explain alcohol-related risks and links to heath outcomes

Referral to Treatment

Recommend specialty care or treatment options

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SAMHSA, SBIRT, https://www.samhsa.gov/sbirt, Published September 15, 201

CAGE

C: Have you ever felt the need to CUT DOWN on your alcohol or drug use?

A: Have you ever been **ANNOYED** by criticism of your alcohol or drug use?

G: Have you ever felt GUILTY about your alcohol or drug use?

E: Have you ever needed an EYE OPENER to get started at the beginning of the day?

One "Yes" answer may indicate need for further screening Two or more "Yes" answers is considered clinically significant

Ewing JA. Detecting alcoholism. The CAGE questionnaire. JAMA. 1984;252(14):1905–1907. doi:10.1001/jama.252.14.1905

Alcohol Use Disorders Identification Test (AUDIT)

Developed by the World Health Organization (WHO)

10-question self- or clinician-administered survey

Scores ≥ 8 indicate harmful drinking (≥ 7 in elderly)

Abbreviated version (AUDIT-C) – seen below

Administer annually

Questions	Scoring System					Score
	0	1	2	3	4	
How often do you have a drink containing alcohol?	Never	Monthly or less	2-4 times per month	2-3 times per week	4+ times per week	
How many units of alcohol do you drink on a typical day when you are drinking?	1-2	3-4	5-6	7-9	10+	
How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in the last year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	

Babor T.F., de la Fuente J.R., Saunders J.B. and Grant M. AUDIT. The Alcohol Use Disorders Identification Test; Guidelines for Use in Primary Health Care, Geneva; WHO, 1992

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Single Item Alcohol Screening Questionnaire (SASQ)

- 1. Do you sometimes drink beer, wine, or other alcoholic beverages?
- 2. How many times in the past year have you had...

Men: five or more drinks in a day?

Women: four or more drinks in a day?

Screen is positive if the answer to #2 is one or more

VA / DoD. 2021.

Alcohol Intoxication (DSM-5)

Recent ingestion of alcohol (EtOH)

Significant problematic behavior or psychological changes developed during, or shortly after, ingestion

Symptoms are not due to another medical condition or mental disorder \geq 1 of the following:

Slurred speech

Incoordination

Unsteady gait

Nystagmus

Impairment in attention or

memory

Stupor or coma

DSM-5. 2013.

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ALCOHOL WITHDRAWAL

18

Alcohol Withdrawal (DSM-5)

Reduction in heavy and prolonged EtOH use

Significant impairment in everyday functioning

Not better explained by another medical or psychological condition

\geq 2 symptoms, hours to days after cessation:

Autonomic hyperactivity (e.g., ↑ HR/BP, sweating)

Hand tremor

Insomnia

Nausea/vomiting

Transient hallucinations (audio, visual, or tactile)

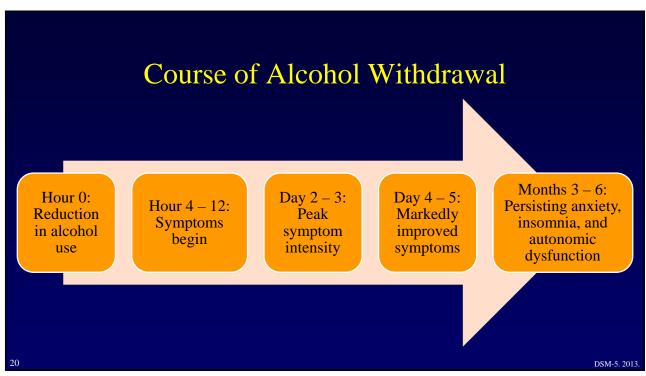
Psychomotor agitation

Anxiety

Generalized tonic-clonic seizures

DSM-5. 2013.

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Monitoring Withdrawal

Clinical Institute Withdrawal Assessment for Alcohol (CIWA-A)

Often use 10-item revised version (CIWA-Ar)

Mainly objective measures

Quick administration (~ 2 mins)

Measures withdrawal severity

Absent or Minimal ≤ 8

Mild to Moderate 9 – 19

Severe ≥ 20

NOT a diagnostic tool

Others (less common):

Alcohol Withdrawal Scale (AWS)

Short Alcohol Withdrawal Scale (SAWS)

Alcohol Use Disorders Identification Test-Piccinelli Consumption (AUDIT-PC)

Luebeck Alcohol Withdrawal Risk Scale-11 (LARS-11)

Prediction of Alcohol Withdrawal Severity Scale (PAWSS)

VA / DoD. 2021

Sullivan JT, et al. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). Br J Addict. 1989;84:1353-7
The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management. J Addict Med. 2020 May/Jun;14(3S Suppl 1):1-72. doi: 10.1097/ADM.0000000000000668

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Risk Factors for Severe or Complicated Withdrawal

- 1. History of delirium tremens or withdrawal seizure
- 2. Numerous prior withdrawal episodes
- 3. Comorbid medical/surgical illness
 - a. Especially traumatic brain injury
- 4. Increased age (> 65)

- 5. Long duration of heavy and regular alcohol consumption
- 6. Seizure during current episode
- 7. Marked autonomic hyperactivity on presentation
- 8. Physiological dependence on GABAergic agents
 - a. Benzodiazepines, barbituates

ASAM, 2020.

Inpatient Withdrawal Management

- 1. CIWA-Ar > 20 (severe)
- 2. History of delirium tremens or withdrawal seizures
- 3. Unable to tolerate oral medications
- 4. Co-occurring medical conditions posing risk if managed outpatient (e.g. pregnancy)
- 5. Co-occurring substance withdrawal (e.g., sedative-hypnotics)

- 6. CIWA-Ar > 10 (moderate) PLUS any of the following:
 - a. Recurrent unsuccessful outpatient attempts
 - b. Reasonable likelihood patient will not complete outpatient program (e.g., homelessness)
 - c. Active psychosis or severe cognitive impairment

VA / DoD. 2021. ASAM. 2020.

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Acute Withdrawal Pharmacotherapy Options Supportive Supportive First-Line Second-Line Treatment Treatment Benzodiazepines Carbamazepine Supplements Antipyretics (BZD) (CBZ) Valproic Acid Antipsychotics Antihypertensives (VPA) Gabapentin VA / DoD. 2021. ASAM. 2020.

Benzodiazepine Options

Drug	Form	t _{1/2} (hours)	Active Metabolites	Rate of Onset
Chlordiazepoxide* (Librium)	Cap	10–48 (parent) 14–95 (metab)	Yes (2)	Intermediate (30 min – 2 hr)
Diazepam (Valium, Diastat)	IM, IV, Liq, Tab, Nasal, Rectal	48 (parent) 100–194 (metab)	Yes (3)	Very fast (15–30 mins)
Lorazepam** (Ativan)	IV, IM, Liq, Tab	12	No	Intermediate (20–30 min)

*Slower onset: less abuse potential

Benzodiazepines reduce:

Withdrawal severity

Incidence of delirium tremens

Incidence of withdrawal seizures

"LOT" (lorazepam, oxazepam, temazepam)

Bypass phase I metabolism (i.e. bypass the liver)

Ideal for elderly, over-sedated, or liver impairment

VA / DoD. 2021

Chlordiazepoxide, Diazepam, Lorazepam. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. htt

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Dosing Regimens

- 1. Fixed-dose taper
- 2. Symptom Triggered
 - 3. Front Loading

^{**}Can be administered IV, IM, PO with predictable results (IM diazepam is variable)

Fixed-dose Taper

Advantages:

Patient should receive adequate medication

Less monitoring / lower staff burden

Disadvantages:

May receive more medication than necessary († side effects)

Should not be used for delirium tremens management

Examples:

Chlordiazepoxide 100 mg Q6H x 4 doses (with PRN), then

Chlordiazepoxide 50 mg Q8H x 8 doses (with PRN), then

Chlordiazepoxide 25–100 mg Q1H PRN CIWA-Ar ≥ 10

VA / DoD. 2021

Grover S, Ghosh A. Delirium Tremens: Assessment and Management. J Clin Exp Hepatol. 2018. doi:10.1016/j.jceh.2018.04.012

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Symptom Triggered Dosing

Advantages:

Only give amount of drug needed to control symptoms

Less medication use

Shorter duration of treatment

Disadvantages:

Requires trained staff to assess

Examples:

Chlordiazepoxide 25–100 mg Q1H PRN CIWA-Ar \geq 10, or

Diazepam 5–20 mg Q1–4H PRN CIWA-Ar \geq 10, or

Lorazepam 4 mg every 10 mins until CIWA-Ar < 10 or sedation

VA / DoD. 2021. Grover S, et al. *J Clin Exp Hepatol*. 2018

Front Loading

Slowly titrate dose upwards until one of the following: Light sedation is reached (can be aroused with verbal stimulation) CIWA-Ar < 10

Preferred treatment regimen for delirium tremens

Not favored in suspected head injury and liver dysfunction

Example:

Diazepam 10 mg \rightarrow 20 mg \rightarrow 30 mg \rightarrow 40 mg \rightarrow 50 mg \rightarrow 60 mg Repeat each strength dose once (10 mg, 10 mg, 20 mg, 20 mg...) 10 mins apart Continue administration until 320 mg total, light sedation, or CIWA-Ar < 8

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Grover S, et al. J Clin Exp Hepatol. 2018

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Second-Line Agents

Mild-moderate withdrawal when BZD risk outweighs benefits Less abuse potential

Outpatient withdrawal management

Adjunctive treatment

Efficacy comparable to BZDs

Reduction of withdrawal symptoms

Time to withdrawal completion

Adverse effects

Evidence limited to small, single-site randomized trials

VA / DoD. 2021. Brathen G, et. al. Eur J Neurol. 2005;12(10):575-581. CPNP. Pharmacist Toolkit: Alcohol Use Disorder.

Second-Line Agents (Antiepileptics)

	Gabapentin	Valproic Acid	Carbamazepine
Daily dose	1200 mg (divided BID – TID)	15 mg/kg	800 mg
Taper duration	4 – 6 days	4 days	4 – 9 days
Comments	Possible abuse potential	May use as adjunct to BZDs Not recommended by ASAM as monotherapy	Common: dizziness, N/V Serious: neutropenia, SJS

Phenytoin is **NOT** effective in preventing withdrawal seizures

VA / DoD. 2021. ASAM. 2020. Brathen G, et. al. *Eur J Neurol*. 2005;12(10):575-581. CPNP. Pharmacist Toolkit: Alcohol Use Disorder.

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Supportive Care Antihypertensive Dietary Antipsychotics Antipyretics Supplements Agents Clonidine • Multivitamin • Consider in • Ibuprofen Anti-anxiety severely agitated • Thiamine • Acetaminophen patients • Folic acid • Beta-blockers • Pain relief (propranolol) • May help with • Fever • During • Anti-tremor hallucinations in withdrawal and Headaches delirium tremens for \geq 30 days • ↓ HR, ↓ BP after Brathen G, et. al. *Eur J Neurol*. 2005;12(10):575-581. CPNP. Pharmacist Toolkit: Alcohol Use Disorder.

DELIRIUM TREMENS

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Timeline of Alcohol Withdrawal Symptoms - 6 hr - Cravings, tremor, autonomic hyperactivity (HTN, ↑ HR), sweating, hyperthermia, N/V, anxiety, insomnia, hyperreflexia 12–24 hr - Hallucinations (visual > auditory/tactile) - 24 hr - Withdrawal seizures (generalized, tonic-clonic) - Withdrawal seizures (generalized, tonic-clonic) - Belirium Tremens (DTs)

Delirium Tremens (DT)

Two distinct aspects: delirium & severe alcohol withdrawal

Increases length of hospital stay, stay in the ICU, and mortality

Overall mortality 1–4%

Increases to 5–15% in those untreated

Due to hyperthermia, cardiac arrhythmias, complications of withdrawal seizures, or concomitant medical disorders

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Grover S, et al. J Clin Exp Hepatol. 2018

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Course of DT

Duration: 3–4 days (up to 8 days)

Ends with a prolonged sleep

Rapid onset & fluctuating course,

with disturbances in:

Level of consciousness

Cognition

Psychomotor activity

Sleep-wake cycle

Symptoms:

Confusion

Hallucinations

Agitation

Tachycardia

Mydriasis (pupil dilation)

Fever

Grover S, et al. J Clin Exp Hepatol. 2018.

Risk Factors for DT

History of DT

Long history of drinking

History of withdrawal seizures

Concurrent acute illness

Especially infection, respiratory, and cardiac disease

Early withdrawal symptoms

Severity of early withdrawal symptoms (SBP > 150, DBP > 100)

Older age

Structural brain lesion

↑ [ALT], [GGT]

↓ [Platelets]

 \downarrow [K], \downarrow [Mg]

 \downarrow [pyridoxine] (B₆)

↑ [Homocysteine]

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Grover S, et al. J Clin Exp Hepatol. 2018

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Treatment of DTs

The best treatment is prevention with long-acting BZDs, using a front-loading strategy

Thiamine replacement (high rates of deficiency in DT)
Will NOT treat DT or symptoms of DT

Treatment refractory: phenobarbital, propofol (ICU), dexmedetomidine (ICU)

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Grover S, et al. J Clin Exp Hepatol. 2018.

WERNICKE-KORSAKOFF SYNDROME

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Wernicke-Korsakoff Syndrome

Wernicke Encephalopathy

Caused by thiamine (Vit B₁) deficiency

Acute and reversible

Caine's Criteria

Eye signs

Cerebellar dysfunction

Mild memory impairment or AMS

Signs of malnutrition

> 2 out of 4 is used to 'make a case'

Korsakoff Syndrome

Long-term B₁ deficiency leads to permanent neuronal damage

Mainly in the mamillary bodies

Chronic and irreversible

No diagnostic criteria

Severe memory problems

Confabulation

Normal cognition otherwise

Isenberg-Grzeda E, Kutner HE, Nicolson SE. Wernicke-Korsakoff-Syndrome: Under-Recognized and Under-Treated. *Psychosomatics*. 2012. doi:10.1016/j.psym.2012.04.008 Johnson JM, Fox V. Beyond Thiamine: Treatment for Cognitive Impairment in Korsakoff's Syndrome. *Psychosomatics*. 2018. doi:10.1016/j.psym.2018.03.011

Wernicke's Encephalopathy

Classical Triad

Mental status changes (82%)

Confusion

Memory disorder

Anxiety / Fear

Coma / Stupor

Ophthalmoplegia (29%)

Nystagmus / Retinal hemorrhages

Ptosis / Photophobia

Diplopia / Blurred vision

Ataxia (23%)

Unsteady gait / Dysarthria

Severity of Illness

Mild Disease

Anorexia, followed by N/V, nystagmus, and subjective eye sx

Moderate Disease

Insomnia and emotional changes (anxiety, apathy, apprehension)

Progressive loss of recent memory occurs over 2–3 weeks

Severe Disease

Disorientation, confabulation, coma

Isenberg-Grzeda E, et al. Psychosomatics. 2012.

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Thiamine Deficiency

Reasons for deficiency in AUD

Poor diet

↓ absorption in the setting of EtOH

↑ thiamine loss in kidneys

↓ metabolism to active thiamine

↓ absorption of colonic bacterial thiamine

↓ Mg, which is a necessary cofactor in thiamine utilization

Treatment

Parenteral Thiamine

Thiamine IV 200–500 mg TID x 3–5 days or until improvement

Improvement occurs within 6 hours -3 days NO ROLE for oral B_1 during acute deficiency

Oral thiamine and multivitamin can be given at discharge to prevent deficiency

Patients shouldn't receive carbohydrates (PO / IV) before thiamine replacement

Isenberg-Grzeda E, et al. Psychosomatics. 2012.

Symptoms of Korsakoff's Syndrome

Progression occurs in 56–84% of patients, regardless of thiamine replacement

Prognosis

Recover promptly: 25%

Improvement over time: 50%

Unchanged, permanently impaired, requiring LTC: 25%

Prevention is critical

No treatment for KS

Symptoms

Anterograde amnesia

Inability to form new memories

Confabulation

Replacing memory gaps with seemingly reasonable, but untrue, information

Retrograde amnesia

Episodic memory (events from the past) severely affected
Semantic memory (facts, concepts, language) is variably affected
Implicit memory (muscle memory) spared

Johnson JM, et al. Psychosomatics. 2018.

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ALCOHOL USE DISORDER

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Epidemiology

12-month prevalence (US)

12–17 y/o: 4.6% ≥ 18 y/o: 8.5%

Age of onset

Late adolescence-early adulthood

Costs US \$223.5 billion yearly Lost productivity, crime, health

Undertreated (< 20%)

↑ Mortality

Comorbid conditions (e.g., liver disease, CVD, GI effects)

EtOH accounts for 55% of fatal driving events

Increased suicidal behavior and completion rate

45 45 VA / DoD. 2021

Risk Factors for AUD

Race

Native American/Alaskan: 12.1%

White: 8.9%

↑ availability/peer use/stress

Poor coping skills

Comorbid psychiatric illness Schizophrenia, bipolar disorder

Genetics

3–4x risk if close relative has AUD Children of AUD parents at risk, even if adopted at birth

Age

18–29 y/o: 16.2% ≥ 65 y/o: 1.5%

Gender

Males (12.4%) > females (4.9%)

DSM-5

Course of Illness

Characterized by periods of remission and relapse

Relapse does **NOT** mean treatment failure!

Common Scenario:

Decision to stop drinking (often a response to a crisis) \rightarrow

Period of abstinence (weeks or more) →

Limited periods of controlled, nonproblematic drinking \rightarrow

Consumption rapidly escalates to severe problems, again

DSM-5 VA / DoD. 2021.

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Age-related Physical Changes

CNS depression

† brain susceptibility
Concomitant medications

↓ liver metabolism

↓ body water

More severe intoxication

† problems at lower levels

of consumption

Comorbid medical conditions

DSM-5

DIAGNOSTIC CRITERIA

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Alcohol Use Disorder (DSM-5)

Significant impairment or distress caused by a problematic pattern of alcohol use with ≥ 2 of the following within a 12-month period:

Using ↑ amounts over longer time periods

Difficulty cutting down

↑ time spent seeking EtOH/recovering

Craving EtOH

Failing to fulfill obligations

Continued use despite social problems

↓ in other activities

Use in hazardous situations

Using despite knowledge of physical or psychological problems

Tolerance (one or both):

↑ amounts needed to produce desired effect

 \downarrow effect with use of the same amount

Withdrawal (one or both):

Symptoms of withdrawal (slide 10)

EtOH used to relieve or avoid symptoms

DSM-5

Alcohol Use Disorder (DSM-5)

Most who consume EtOH do not meet AUD criteria

Severity determined by number of symptoms displayed

Mild: 2–3 symptoms

Moderate: 4–5 symptoms

Severe: \geq 6 symptoms

Many individuals have a promising prognosis

DSM-5

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AUD TREATMENT

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Goals of Pharmacotherapy



Develop goals with the patient (goals may vary for each) Achieve and sustain abstinence from alcohol ↓ use, prevent long-term complications, etc.

Minimize and manage alcohol withdrawal symptoms

Prevent and/or manage the physical and social complications of continued alcohol use

Minimize or prevent relapses

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Comparing Guidelines

	VA/DOD (2021)	APA (2018)	NIH/SAMHSA (2015)	
1 st line	Naltrexone (PO/IM) Topiramate	Naltrexone (PO/IM) Acamprosate	Naltrexone (PO/IM) Acamprosate Disulfiram	
2 nd line	Acamprosate Disulfiram	Disulfiram Gabapentin Topiramate	N/A	
3 rd line	Gabapentin	N/A	N/A	
Duration of Treatment	No recommendations	No recommendations	6 months – 1 year	
Non- Pharm	All guidelines suggest that pharmacologic therapy be supplemented with non-pharmacologic therapy (e.g., psychosocial therapy, 12-step programs)			

Reus VI, et al. Am J Psychiatry. 2018 SAMHSA/NIAAA, Medication for the Treatment of Alcohol Use Disorder: A Brief Guide. HHS Publication No. (SMA) 15-4907. Rockville, MD: SAMHSA, 2015

Nonpharmacologic Therapy

Psychosocial interventions

Behavioral Couples Therapy (BCT)

Cognitive Behavioral Therapy (CBT)

Community Reinforcement Approach (CRA)

Motivational Enhancement Therapy (MET)

12-Step Facilitation (TSF): <u>Alcoholic's Anonymous</u> (AA), etc. "Ninety-day rule"

Medications may help patients be more receptive to therapy

VA / DoD. 2021 SAMHSA/NIAAA. 2015

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Naltrexone (ReVia, Vivitrol)

Mechanism

Opioid antagonist

May block reward signals

Dosing

ReVia: 50 mg PO every morning

Vivitrol: 380 mg IM every 4 weeks (deep gluteal muscle)

Efficacy

Outcomes

↓ relapses to dependence

↓ returning to drinking

↓ cravings

↓ drinking days

↓ relapse to heavy drinking

COMBINE (US)

Naltrexone > acamprosate

PREDICT (Germany)

Naltrexone = acamprosate

Reus VI, et al. Am J Psychiatry. 2018.

Naltrexone (ReVia, Vivitrol)

Contraindications

Opioid use within the past 7 days Acute hepatitis or liver failure

Precaution

Hepatotoxicity (dose-dependent)

Adverse Effects

GI upset

Dizziness / anxiety

Injection site reaction (LAI)

Patient Education

Maintain abstinence for 5 days prior to initiation

Not necessary, but improves outcomes

Must be opioid-free for 7 days

Lower dose may ↓ GI upset

Medical bracelet / dog tags

Alert paramedics to use non-opioids for pain relief

Opioid tolerance will drastically decrease in OUD patients

High risk of overdose

Reus VI, et al. Am J Psychiatry. 2018 SAMHSA/NIAAA. 2015

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Acamprosate (Campral)

Mechanism

Unclear

Glutamate modulator thought to counteract the GABA-glutamate imbalance associated with prolonged EtOH use

Dosing

Two 333 mg (666 mg/dose) DR tabs PO TID

Efficacy

Outcomes

Reduced number of drinking days Increased abstinence

Lengthens time to relapse

European studies
Positive outcomes

US studies

No benefit

VA / DoD. 2021. Reus VI, et al. Am J Psychiatry. 2018. SAMHSA/NIAAA. 2015.

Acamprosate (Campral)

Contraindications

CrCl < 30 mL/min (severe renal impairment)

Precaution

CrCl 30–50 mL/min: reduce dose to 333 mg PO TID

Adverse Effects

Diarrhea (transient)

HA, changes in libido, insomnia, anxiety, muscle weakness, dizziness, and suicidality

Patient Education

Swallow pill whole, do not crush/chew

Best results if taken 5 days after quitting (can start earlier if needed)

Full effect may take 5-8 days

Continue therapy even through relapse

Report any changes in mood or suicidal ideation

Can safely take with EtOH or opioids

Reus VI, et al. *Am J Psychiatry*. 2018 SAMHSA/NIAAA. 2015

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Disulfiram (Antabuse)

Mechanism

Irreversible inhibitor of acetaldehyde

de hydrogen as e

Acetaldehyde buildup causes flushing, N/V, ↑ HR, CV collapse,

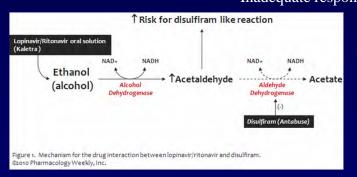
death

Dosing

500 mg PO daily x 1–2 weeks, then

250 mg PO daily

Significant ADRs: 125 mg daily Inadequate response: 500 mg daily



Reus VI, et al. Am J Psychiatry. 2018 SAMHSA/NIAAA. 2015.

Disulfiram (Antabuse)

Efficacy

Ideal in highly motivated patients Conflicting results in study data High dropout rates within studies (i.e., poor adherence)

May be beneficial in patients court—ordered to take medication

Drug-Drug Interactions

Foods/drinks/medications with EtOH

Elixirs, mouthwash, etc.

Metronidazole/ketoconazole

Produce similar effect

Inhibits CYP 3A4

May interact with warfarin, phenytoin, rifampin, etc.

Reus VI, et al. Am J Psychiatry. 2018 SAMHSA/NIAAA. 2015

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Disulfiram (Antabuse)

Contraindications

Severe respiratory, CV, renal, or hepatic disease

Metronidazole/ketoconazole therapy
Produce disulfiram-like reaction

Patient Education

Reaction lasts 30–60 mins to several hrs Can use as PRN for difficult scenarios Holidays, gatherings with EtOH, etc. Consuming large amounts of EtOH can lead to coma/death

Adverse Effects

Transient:

Skin/acneiform eruptions/dermatitis HA, drowsiness/fatigue
Impotence
Metallic or garlic-like after taste

Serious (D/C disulfiram):

Optic neuritis Peripheral neuritis, polyneuritis, peripheral neuropathy Hepatitis and hepatic failure

> Reus VI, et al. Am J Psychiatry. 2018. SAMHSA/NIAAA. 2015.

Topiramate (Topamax)

Mechanism

Believed to antagonize glutamate receptors, inhibiting dopamine release in the reward center

Dosing

Initial: 50 mg PO daily May need 100 mg PO BID Maximum: 300 mg daily Titrate over several weeks

Efficacy

Outcomes

Reduced drinks per drinking day Reduced % of heavy drinking days Reduced % of drinking days

NOT FDA-approved for AUD

VA / DoD. 2021 Reus VI, et al. Am J Psychiatry. 2018

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Topiramate (Topamax)

Precautions

CrCl < 70 mL/min: reduce dose by 50% and titrate slowly

Dose adjustment may be needed in hepatic impairment

Adverse Effects

CNS: Cognitive dulling, psychiatric disturbances, sedation, paresthesia, nervousness, ataxia, lack of concentration

GI: abdominal pain, anorexia

Patient Education

Do not stop taking abruptly

Gradually taper

Topiramate may decrease efficacy of contraceptives

Consider using back up method while on this medication

Crushing/chewing the tablet may produce a bitter taste

VA / DoD. 2021. Reus VI, et al. Am J Psychiatry. 2018.

Gabapentin (Neurontin)

Mechanism

Unclear

Likely through modulation of GABA activity in the amygdala

Dosing

Initiate at 300 mg PO daily

↑ by 300 mg daily, as tolerated

Target dose: 1800 mg PO daily

Three divided doses

Efficacy

Outcomes

↑ rates of abstinence

↑ abstinence from heavy drinking

Possible useful in cooccurring neuropathic pain

Possible adjunct to naltrexone

NOT FDA-approved for AUD

VA / DoD. 2021. Reus VI, et al. Am J Psychiatry. 2018.

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Gabapentin (Neurontin)

Precautions

Possible ↑ in suicide risk CrCl < 60 mL/min: consider target dose < 1800 mg daily

Adverse Effects

CNS: dizziness, drowsiness, somnolence, ataxia, fatigue GI: N/V/D, abdominal pain

Patient Education

Do not stop taking abruptly Taper gradually

Avoid CNS depressants

Alcohol, opioids, BZDs ↑ risk of respiratory depression

Antacids may decrease levels

VA / DoD. 2021. Reus VI, et al. Am J Psychiatry. 2018.

Pharmacotherapy Basics

Generic	Brand	Dose (or range)	Dose Adj.	Common ADRs
Naltrexone (oral)	ReVia®	50 mg daily	N/A	GI upset
Naltrexone (IM)	Vivitrol®	380 mg monthly	N/A	Injection site reaction
Acamprosate	Camprol [®]	Two 333 mg tabs TID	Renal	Diarrhea
Disulfiram	Antabuse®	125-500 mg daily	Hepatic	Metallic/garlic taste; HA; fatigue
Topiramate	Topamax [®]	50–300 mg daily (divided)	Renal Hepatic	Cognitive dulling
Gabapentin	Neurontin®	1800 mg daily (divided TID)	Renal	Drowsiness

AUD treatment works best if started *after* withdrawal symptoms subside

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QUESTION REVIEW

Question 1

A patient that has been stable on naltrexone 50 mg PO daily mentions that they have been forgetting to take the tablet everyday since working nights. What do you recommend?

- A. Continue naltrexone 50 mg PO daily
- B. Recommend switching to acamprosate 666 mg PO TID
- C. Recommend switching to topiramate 100 mg PO BID
- D. Recommend switching to Vivitrol® 380 mg IM monthly

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Question 2

Which of the following treatment options for AUD does not require dose adjustments in patients with renal impairment?

- A. Gabapentin
- B. Acamprosate
- C. Naltrexone
- D. Topiramate

Question 3

Which FDA-indicated treatment for AUD can cause serious harm if the user ingests alcohol after taking their dose?

- A. Naltrexone
- B. Acamprosate
- C. Disulfiram
- D. Topiramate
- E. Gabapentin

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Key Takeaways Withdrawal Alcohol use ↑ WKS: parenteral management: thiamine mortality **BZD** FDA-approved: Non-approved: AUD treatment: naltrexone, non-pharm + topiramate & acamprosate, & gabapentin pharm disulfiram

Alcohol Use Disorder: Recognition, Treatment, and Implications

Vincent Cavaliere, PharmD, MM, BCPP vcavaliere@luminishealth.org

Notes



"HARM REDUCTION" Not Dirty Words Any More



Christopher Welsh M.D.

Associate Professor

Division of Addiction Research & Treatment

Department of Psychiatry

University of Maryland School of Medicine



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OBJECTIVES

- Learners will be able to state 3 principles of harm reduction.
- Learners will be able to list 3harm reduction measures used to help decrease blood-borne infections.
- Learners will be able to list 3 harm reduction measures that are being used to help decrease fatal opioid overdose.



WHAT IT IS

- AKA: "Risk reduction", "Harm minimization"
- "Normalization"
- An attitude
- Secondary & Tertiary Prevention
- A difference in emphasis
- A difference in threshold- "Pre-Treatment"
- An acceptable outcome of all treatment
- An acceptable outcome even without treatment
- A means to an end and an end in itself
- It is NOT (necessarily) pro drug use or anti abstinence
- It is NOT "The lesser of two evils."

3



DEFINITION (Harm Reduction International)

- Harm reduction refers to policies, programs and practices that aim to minimize negative health, social and legal impacts associated with drug use, drug policies and drug laws.
- Harm reduction is grounded in justice and human rights. It focuses on positive change and on working with people without judgement, coercion, discrimination, or requiring that they stop using drugs as a precondition of support.



NO EXCESSIVE HARM

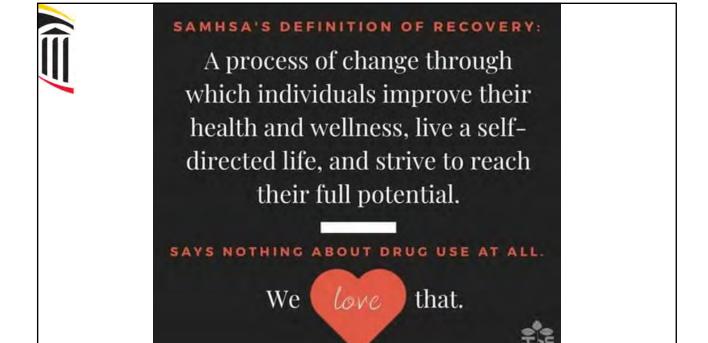
Absolute use may or may not correlate with this

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"Any Positive Change"

Isn't this just the treatment of any chronic disorder?





"...to heal is always a matter of time, but it is also sometimes a matter of opportunity..."

Hippocrates



- A public health alternative to traditional models of substance use & treatment
- Sees improved quality of life & well-being as main criteria for success
- Focus on individual & community
- Person-centered- recognizing strengths & need for input from persons engaging in substance use
- Acknowledges that reducing substance use may not be feasible or desired nor the only way to reduce harm



BASIC PRINCIPLES

- Non-judgmental
- Pragmatic
 - "compassionate pragmatism"
- "Meet the person where they are"
 - Both figuratively and literally
 - "Low-threshold"
- De-medicalization vs Medicalization ("client" vs "patient")
- Address service needs of users, not priorities of providers

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ZERO ZERO TOLERANCE + COMPASSION = ZERO



BASIC STRATEGIES

- Working with individuals and groups to reduce harmful behaviors
- Modifying the environment to enhance safety and reduce risk
- Implementing public policy changes to reduce harm to individuals and society
- Establishing a and addressing the more immediate and realistic first

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WHY HARM REDUCTION?

"Nothing strikes fear in my heart more than seeing someone coming to do me good against my will."

Thoreau

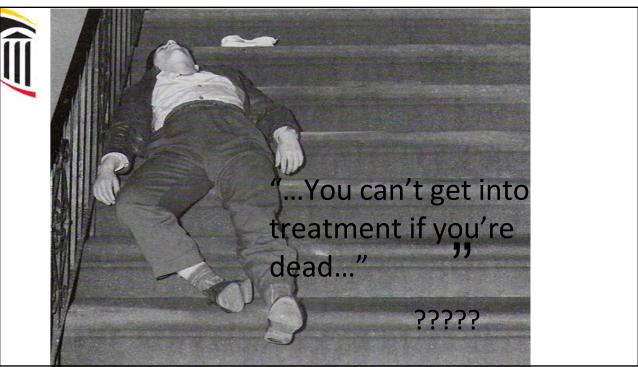


STAGES OF CHANGE

(Prochaska & DiClemente)

- Precontemplation
- Contemplation
- Preparation
- Action
- Maintenance
- Termination

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AREAS OF APPLICATION

What happened you don't

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What you should do...

- Sexual Behaviors
- Driving Behaviors
- Sports & Recreation
- Firearms
- Alcohol Use
- Tobacco Use
- Illicit Drug Use





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ANCIENT HISTORY

- Evidence that it has been used for thousands of years
- Opium (Asia), hallucinogens & coca (Central & South America) with rituals & taboos to protect community & individual health
 - Limiting use to certain religious rituals or individuals (e.g. "shaman")
- 1700s- Outreach to "intoxicants" in Europe
- 1700s-1800s- Opium provided to registered opium users in European colonies in Asia





"MODERN" HISTORY

- 1920s- "British System"
 - Rollerston Commission
 - · Concluded that maintenance on drugs may be necessary to help drug users lead useful lives
- 1960s- Methadone Maintenance
- 1980s- Merseyside Model
- 1980s- "Junky Union" in Amsterdam
- 1990- 1st international conference
 - Liverpool, England
- 1996- 1st national conference
 - Oakland, California

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THE U.K. MODEL

- Merseyside Health Authority
 - Outside Lverpool
- "Medicalization"
- Used 1926 Rolleston Committee recommendations to prescribe to addicts
 - Prescribed heroin and cocaine
 - Varied delivery systems
 - "reefers" (injected with Methadone and heroin)
 - Aerosolized formulations
- Provision of other social/medical services
- Close partnership with law enforcement
- Saw significant drop in HIV rates



THE DUTCH MODEL

- 1972-Narcotics Working Party
 - Drug policy should be congruent w risk of drug use
- 1976-revised Dutch Opium Act
 - Distinguished "hard" and "soft" drugs
 - De facto decriminalization of marijuana and hashish
 - Allowed legal "markets" for soft drugs (coffee shops)
 - Does not appear to have led to increased use
- 1980s- Federation of Dutch Junkie Leagues
 - An outgrowth of original "Junkiebond" (Junkie League) established in Rotterdam
- 1985- "Normalization" policy
- 1995- revised policy: "Continuity and Change"
 - To address resale, smuggling and "drug tourists."

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THE DUTCH MODEL

"Increasing encouragement by the Government has been given to forms of aid which are not primarily intended to end addiction as such, but to improve addicts' physical and social well-being and to help them function in society. At this stage, the addicts' inability to give up drug use was accepted as fact."

Engelsman (BMJ; 1989)

"The Dutch policy of normalization seems to have produced a context where the addict more resembles an unemployed Dutch citizen than a monster endangering society."



PLASTZPITZ

- "Needle Park"
- Zurich, Switzerland
- 1987-1992













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THE SWISS EXPERIMENT

- 1993; 8 cities
- Provided
 - Heroin, morphine, IV methadone
 - Social services
 - Medical/psychiatric services
- 1994 Social Welfare Department, Zurich:
 - No black market in diverted heroin
 - Health of drug users significantly improved
 - Heroin prescription alone can't solve problem
 - Heroin, per se, causes few problems if used in a controlled fashion in hygienic conditions



THE FRANKFURT PROGRAM

- Started in 1990
- Model for other European cities
- Provide
 - Mobile vans w counseling & needle exchange
 - Needle exchange in pharmacies
 - Low-threshold methadone programs
 - Emergency shelters
 - Crisis centers w medical care ("contact cafes")
 - "Health care rooms" ("Fixerstuebli")
- Found significant reductions in OD deaths & HIV and other injectionrelated problems

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INTERNATIONAL PERSPECTIVE

- Many countries and organizations have adopted Harm Reduction as policy
 - Dutch Narcotics Working Party (1972) & Opium Act (1976)
 - Dutch Federation of Junkie Leagues (early 1980s)
 - Australian National Campaign Against Drug Abuse (1985)
 - British Advisory Council on the misuse of Drugs (AMCD)
 - World Health Organization
 - Canada's National Drug Strategy (1987)
 - European "alliances" (Zurich, Amsterdam, etc)
 - Swiss "experiment" (1993)
 - U.S. Overdose Prevention Strategy (2021)







ILLICIT DRUG USE

- Needle exchange programs
- Safe injection rooms ("tolerance rooms")
- Opioid substitution therapies
- Prescription heroin
- Decriminalization/legalization of drugs
- Injection education
- Overdose prevention training
- Changing route of administration
- Street outreach/drop-in centers
- Drug Testing
- Legal- (Legalization, Decriminalization, Drug courts)

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BLOOD-BORNE INFECTIONS

- Posters about not sharing needles
- Outreach education about not sharing
- Bleach and cleaning supplies
- Pharmacy sales of syringes
- Needle/syringe exchange programs
- Needle/syringe dispensing machines
- Safe injection facilities



SYRINGE CLEANING & DISPOSAL





Operation Red Box: a pilot project of needle and syringe drop boxes for injection drug users in East Baltimore





SYRINGE SERVICE PROGRAMS (SSP)

- "Needle Exchange"
- Syringe vs Needle
- Exchange vs Distribution
- "SNAP" Syringe-Needle Access Program
- •>85 countries currently have some form of syringe services
- In U.S., @ 500 known needle exchange programs in >200

cities and 42 states



SYRINGE SERVICE PROGRAMS

- 1960s- needles and syringes provided to users getting prescribed heroin in UK
- 1984- 1st program in Amsterdam
 - Started by a users advocacy group ("Junkiebond")
- 1986- John Parker began distributing syringes in New Haven and Boston
- 1987- New Zealand established first national program
- 1988- 1st comprehensive U.S. program-Tacoma, WA
- 1989- Canadian government begins funding HIV prevention programs including NEPs
- 1992- U.S. law prohibits Federal funds for NEPs
- 1996- Syringe "vending machines"-Marseille, France
- 2009-Federal funding band lifted
- 2010- Federal funding ban reinstated
- 2015- Federal funding ban partially lifted in U.S. (All except cost of needles & syringes)
- 2021- American Rescue Plan Act-funding for various herm reduction



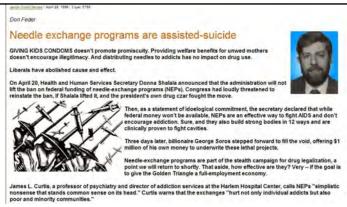
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THE 1^{ST} NEEDLE EXCHANGE







"I'm giving them clean glasses, not whiskey."

Mayor of Tacoma, 1980s

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SSPs-EFFECTIVENESS

- Most studies primarily descriptive
 - Primarily demographics, # of syringes, etc
 - Comment on needle sharing behavior at a fixed point in time
 - @ 90 studies w/ any comparison data
 - >80 different variables in comparison studies
 - Difficult to compare studies
- Major Findings
 - No evidence of increased drug use
 - Decreased rates of HIV infection
 - Reduction in needle sharing
 - Increased HIV/AIDS knowledge



CITY OF BALTIMORE, MARYLAND Mayor Kurt L. Schmoke

1994



Needle Exchange Programs Benefit Everyone



Drug abuse is at the root of a host of problems that threaten the well being of our city, including crime, child neglect, and neighborhood blight. Because 80 percent of new AIDS cases in Baltimore are linked to injection drug use, drug abuse is also the City's biggest public health threat

Health Department officials estimate that there are approximately 43,000 heroin and cocaine addicts in Baltimore. Despite this staggering problem, Baltimore City currently has only 5,700 drug treatment slots. This means that we are only able to help about 16,000 addicts a year. What's more, there is up to a four-month will for drug treatment. And drug addicts are not patient people. When they finally take the step to get help, they need that help now. Clearly, we must do more to meet this pressing need.

The case for drug treatment is strong. Respected research studies have found that treatment is cost-effective and that those who are in treatment or who complete treatment are much less likely to commit crimes or engage in high-risk behavior. Such individuals also are much more likely to become productive members of society than their drug using counterparts.

In addition, we know that it is impractical to jail every person who has a drug habit. Maryland's prisons are already overcrowded with people charged with various drug offenses, and we know that young black men are disproportionately represented in this population. After serving their sentences, these young men not only must forever bear the label "ex-con," they also are likely to leave prison with the yearning for drugs still intact, and the downward spiral of addiction and addiction-related crime begins anew.



Given these harsh realities, Baltimore has been seeking additional drug treatment funds from the federal government for the last three years — to no avail. The problem is too grave for us to wait any longer for outside funding. That's why I recently moved to create a \$5 million pool of funds, drawn from existing City resources, to enable us to expand drug treatment programs.

These reallocated funds will allow us to provide treatment slots for an additional 5,000 addicts. Most importantly, we plan to use these funds to leverage additional money from local and national foundations, as well as through federal grants, to enable us to treat



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SYRINGE SERVICES PROGRAMS MARYLAND 20 approved SSPs and the Baltimore City NEP 14 jurisdictions 2 programs not yet operational 1st multi-county program 9 out of 21 programs are Community Based Orgs Two Pharmacy Voucher Programs: Wicconico County Frederick County mdh.syringeservices@maryland.gov



SYRINGE DISPENSING MACHINES









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SUBSTANCE USE MANAGEMENT

- Using proper injection techniques
- Changing route of administration
- Substitution of less harmful substances
- Education about drug combinations
- Buying drugs from reliable person
- Controlling amount & rate of use
- Using in a familiar setting







SAFE INJECTION FACILITIES

- AKA: Safe(r)/Supervised
 Consumption/Injection/Use
 Facilities/Centers/Rooms/Services/Spaces
 "Overdose Prevention Site"
- Integrated or Specialized
- 1st "sanctioned" one: Berne, Switzerland-1986
 - "Fixerstubli" "IDU's Living Room"
- >170 sanctioned
- >75 cities
- 11 Countries
 - Switzerland, Netherlands, Germany, Spain, Denmark, Norway, Luxembourg, France, Canada, Australia, U.S.



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GOALS of SCFs

- Reducing overdoses, both fatal and non-fatal
- Reducing injection-related health problems such as skin abscesses, heart valve and spinal infections
- Reducing the transmission of viral infections such as Hepatitis B & C & HIV
- Reducing the number of **used syringes/needles** discarded improperly
- Reducing the "nuisance" of public drug use and intoxication
- Reducing interactions with police among people who use drugs
- Connecting individuals who inject drugs with **medical and social services**
- Engaging individuals who inject drugs in more formal substance use treatment???







VANCOUVER

ST. PAUL'S OPENS SUPERVISED INJECTION SITE IN TENT OUTSIDE HOSPITAL (OPS)

DISTER ON THE MAN DA THE WITH THE



St. Paul's Hospital in Vancouver has set up the first overdose prevention site at a hospital in B.C... as new figures show an ever-increasing rise in overdose deaths from Illicit drups.

It is also the first overdose prevention site to be located outside the Downtown Eastside, within the boundaries of the Vancouver Coastal Health region.

As the overdose crisis has fleshed out and spread across Vancouver, a need arose for a site serving the West End and Crainville corridor, said Scott Harrison, director of urban health, indigenous health, substance use, maternify and neonatal intensive care with Providence Health Care.

News / Local News

Canada's first in-hospital overdose prevention site touts lives saved in first year

Nurses supervised St. Paul's patients as they injected illicit opioids, stimulants in the hospital room this past year

Sarah Grochowski
Feb 01, 2022 • February 1, 2022 • 3 minute read • ☐ Join the conversation



Supervised drug use area as St. Paul's Hospital has been open now for one year. PHOTO BY NICE

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AMSTERDAM

"Medical" vs "Social"



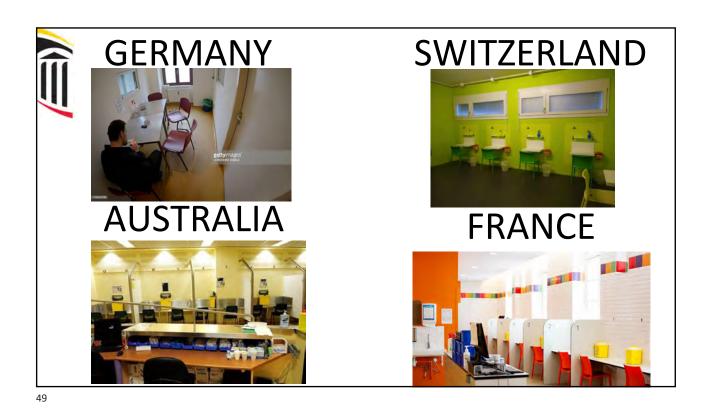




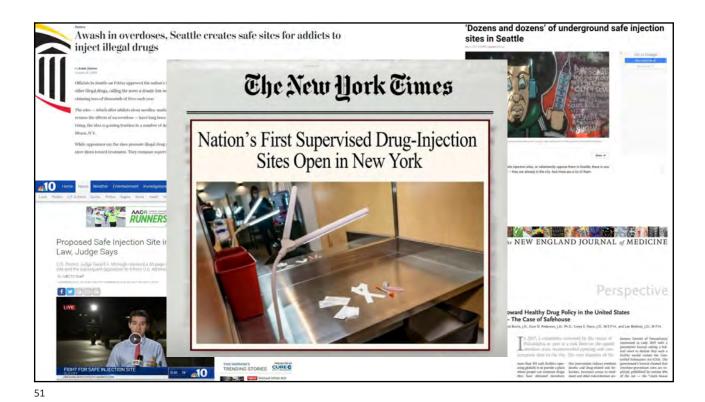














SCFs-EFFECTIVENESS

- Decreased overdoses
 - No overdose deaths at any SCS worldwide (among millions of injections)
 - In the 2 years after Insite opened, there was a 35% reduction in overdose events in the ¼ mile immediately surrounding Insite vs. a 9% reduction in the rest of the city
- Decreased risky injection behaviors
- Decreased HIV & Hepatitis
- Increased engagement in drug treatment
 - After 2 years of attending SCS, 23% ceased injection and 57% reported drug treatment entry among PWIDs who did not report treatment at baseline (n=625)
- No increase in drug use or new injection drug use
- No increase in crime



NOT-QUITE-SCF



- Supportive place for observation & treatment
- Boston Health Care for the Homeless



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HEROIN ASSISTED TREATMENT (HAT)

- Present in Britain since 1920s
 - Primary treatment in UK until late 1960s
- Part of standard practice: Britain, Germany, Netherlands, Denmark, Switzerland
- Ongoing clinical trials: Canada, Spain, Belgium
- Most also give patients methadone
- Some use parenteral & some use oral or inhaled heroin
- PROVE (Switzerland; 1994-1996)
- RIOTT (U.K.; 2004-2009)

AMSTERDAM- HAT













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heroin addicts: two randomised controlled trials

Wim van den Brink, professor¹, Vincent M Hendriks, senior researcher³, Peter Blanken, researcher¹, Maarten W J Koeter, assistant professor², Barbara J van Zwieten, delegate to CPMP⁴, Jan M van Ree, professor⁵

¹ Central Committee on the Treatment of Heroin Addicts (CCBH), Stratenum, Universiteitsweg 100, 3584 CG Utrecht, Netherlands, ² Amsterdam Institute for Addiction Research, Tafelbergweg 25, 1105 BC Amsterdam, Netherlands, ³ Parmassia Addiction Research Centre, PO Box 2505 AA The Hague, Netherlands, ⁴ Netherlands Medicines Evaluation Board, Kalvermarkt 53, The Hague, Netherlands, ⁵ Rudolf Magnus Institute of Neuroscience, Utrecht University, Utrecht, Netherlands

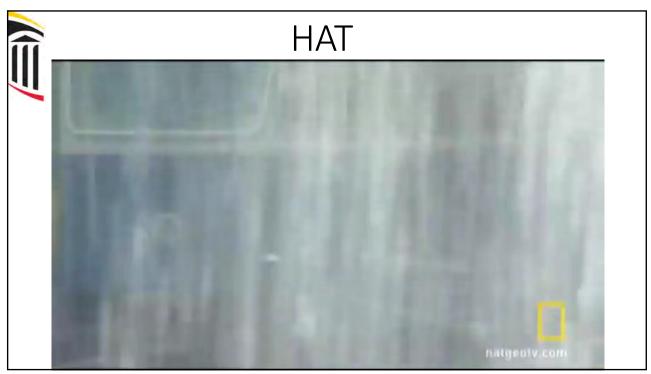


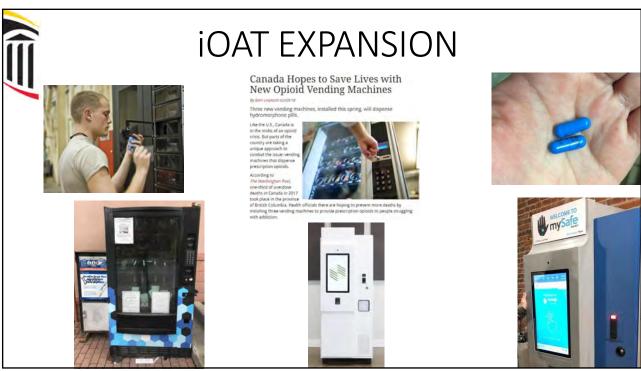
Diacetylmorphine versus Methadone for the Treatment of Opioid Addiction

Eugenia Oviedo-Joekes, Ph.D., Suzanne Brissette, M.D., David C. Marsh, M.D., Pierre Lauzon, M.D., Daphne Guh, M.Sc., Aslam Anis, Ph.D., and Martin T. Schechter, M.D., Ph.D.











MySafe PROJECT- VANCOUVER



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OVERDOSE PREVENTION

- Growing issue with increased fentanyl & newer synthetics
- Multimodal
 - Education of users and public:
 - Recognition
 - Prevention
 - Response
 - Education of healthcare providers
 - Monitoring of healthcare providers
 - Rescue breathing
 - Naloxone
 - Increased treatment





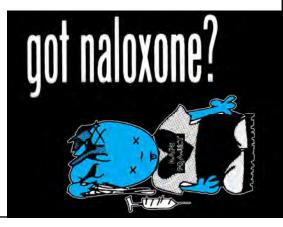


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NALOXONE DISTRIBUTION

- Mid 1990s- 1st program in Australia
- 1996- 1st program in U.S. in Chicago
- 2012- > 50 programs in U.S.(18 states & D.C.)
- Late 2000-teens- programs in every state
- > 25,000 reported reversals
- No evidence that it increases drug use
- Various issues/questions related to:
 - Price
 - Availability
 - Route of Administration
 - Dose needed for higher-potency synthetics
 - FDA status (OTC?)
 - Prescribing
 - Poor public acceptance

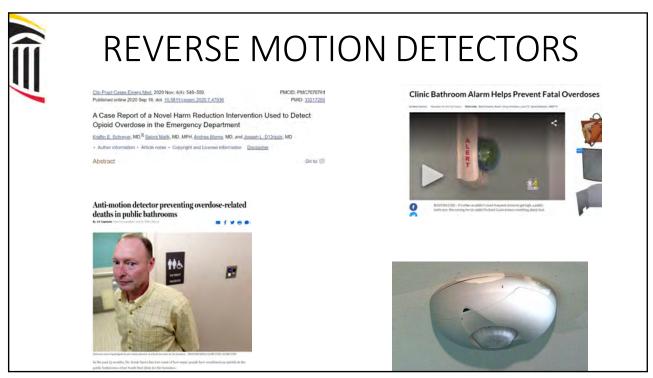














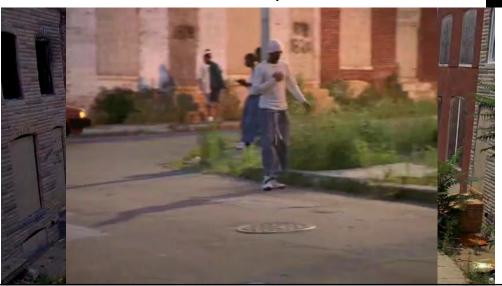






HAMSTERDAM

• Baltimore, Maryland



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ALCOHOL USE

- Drinking and driving laws
- Designated driver campaigns
- Paid Cab/Lyft services
- Sober students at campus parties
- Alcohol percent limits
- Restrictions on advertisement
- Warning labels
- Low threshold shelters/housing ("wet shelters")
- Moderation drinking training
- Thiamine supplementation





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Thiamine Intification of alcoholic beverages

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ALCOHOL GLASSES & BOTTLES

have been sold in plastic bottles with the caps removed, and fan-











TOBACCO USE



- Restrictions on advertisement
- Graphic warning labels
- Nicotine replacement
- Vaping
- Designated smoking areas
- Bans on smoking in certain public areas



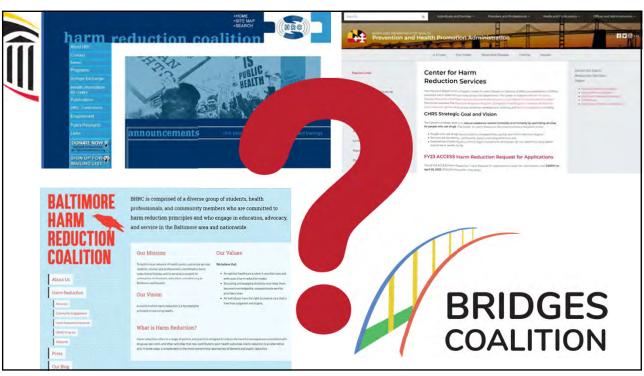








- •The principals of harm reduction should be integrated into all medical settings, addiction treatment programs, social services and law enforcement agencies.
- •The basic philosophy that total abstinence from all substance use is not the only acceptable goal/outcome of successful treatment has become much more acceptable in the current addiction treatment world.
- •Efforts should be made to reduce the barriers to accessing care for individuals using substances.
- •Providers should familiarize themselves with local harm reduction services and refer patients to them readily.







Provides support to prescribers and their practices in addressing the needs of their patients with substance use disorders and chronic pain management.

All Services are FREE

- Phone consultation for clinical questions
- Education and training opportunities related to substance use disorders & chronic pain management
- Assistance with addiction and behavioral health resources and referrals
- Technical assistance to practices implementing or expanding office-based addiction treatment services
- MACS TeleECHO™ Clinics: collaborative medical education through didactic presentations and case-based learning

1-855-337-MACS (6227)

www.marylandMACS.org

Notes





Office of Pharmacy Services 201 W. Preston Street, Baltimore, MD 21201

Toll Free: 1-800-492-5231 TTY: 1-800-735-2258

https://health.maryland.gov/mmcp/pap/pages/paphome.aspx