CSAM ADDICTION MEDICINE BOARD EXAM REVIEW COURSE

for the

ABPM Addiction Medicine Certification Examination

August 13, 2025

Anaheim, CA

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CSAM ADDICTION MEDICINE BOARD REVIEW COURSE FACULTY 2025

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Introduction to the ABPM Examination

2007 → American Board of Addiction Medicine (ABAM) → American Board of Medical Subspecialties → American Board of Preventive Medicine → Addiction Medicine **2016**

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Introduction to the ABPM Examination

What ABPM Certification Means

The Addiction Medicine Physician is specifically trained in a wide range of **prevention**, **evaluation**, and **treatment** modalities addressing substance use and addiction disorders.

SETTING
Ambulatory
Acute Care
Long-term Care
Psychiatric
Residential

PATIENTS
Unhealthy Substance Use
Process and Substance Addictions
Co-occurring medical conditions
Co-occurring psychiatric conditions

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Pathways to the ABPM Examination

- There are now only **TWO (2) main pathways** to become certified by the ABPM certification, all culminating in a rigorous test designed and administered by specialists in the field of Addiction Medicine
  - **Practice Pathway** (available through **2025**)
    - Time in practice pathway
    - Non-ACGME Accredited Addiction Medicine Fellowship completion
  - **ACGME Accredited Pathway** (Eventually the only pathway)
    - 12-month minimum **Fellowship**

    ~ ~ ~ ~ ~
  - *RETIRED PATHWAY*
    - *ABAM Diplomate Pathway (available through **2021**)*
    - *For those holding certification through American Board of Addiction Medicine*

If registered in 2025 may sit thru 2027 examination cycle; 2023-->2025; 2024-->2026

Source: https://www.theabpm.org/become-certified/subspecialties/addiction-medicine/table/

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Pass Rates for the ABPM Examination

Exam Date	Examinees #	Pass #	Pass Rate %
Oct 2017	1112	987	89%
Oct 2018	766	590	77%
Oct 2019	883	644	73%
Oct 2020	1028	728	71%
Oct 2021	766	626	82%
Oct 2022	599	497	83%
Oct 2023	501	413	82%
Oct 2024	605	509	84%

Source: https://www.theabpm.org/become-certified/exam-pass-rates/

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Timeline to the ABPM Examination

☐	March 12	Application Opens for APBM Exam
☐	May 22	Initial Certification Exam Registration and Payment Opens
☐	June 30	Application closes 11:59 pm Central Time
☐	July 1	Late Application Opens
☐	July 14	Testing Accommodations Due
☐	July 15	Late application closes 11:59 pm Central Time
☐	July 31	Documentation deadline
☐	Sept 12	Last day to Register and Pay for Initial Certification Exam
☐	Sept 26	Last day to Request Withdraw & Receive Refund (Less Admin Fee)
☐	Oct 13-Nov 2	Pearson Vue Testing Administrations

Source: https://www.theabpm.org/become-certified/dates-fees/

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Fees for the ABPM Examination

	Application Fee*	Late Application Fee**	Examination Fee
Subspecialty Certification: Addiction Medicine	$500	$1000	$2,150

**Application fees are non-refundable.*
***The late application fee is in addition to the application fee.*

Source: https://www.theabpm.org/become-certified/dates-fees/

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Introduction to the ABPM Examination

- ✓ The 2024 Initial Certification Examination is a closed-book, multi-choice Examination. The Examination will be offered 7 days a week, from **Monday, October 13 through Sunday, November 2, 2025**
- ✓ **200** items delivered in four one-hour time blocks administered over four hours and thirty minutes
- ✓ Includes a 15-minute tutorial and a 15-minute break
- ✓ Examination questions are all multiple-choice, best-single-answer with four or five possible responses.

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Introduction to the ABPM Examination

- ✓ The question may contain:
  - a clinical vignette
  - an experimental or epidemiological observation,
  - a definition or classification,
  - an administrative problem,
  - an application of a principle or regulation, or
  - any situation which might be faced by a specialist in practice.
- ✓ All questions are **weighted equally**. Candidates will find it of advantage to answer all questions, and there is no penalty for an incorrect answer, i.e., wrong answers are not subtracted from right answers and there is **no advantage in leaving a question unanswered**.

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ABPM Addiction Medicine Content Areas

Percent of Exam	Core Content Area
25%	01 Definitions 02 Genetics 03 Pharmacokinetic and Pharmacodynamic Principles 04 Pharmacology 05 Neurobiology of Addiction
20%	06 Epidemiological Concepts 07 Epidemiological Trends of Substance Use Disorders 08 Prevention
40%	09 Screening, Assessment, and Brief Intervention 10 Overview of Addiction Treatment 11 Management of Inpatient/Outpatient Intoxication and Withdrawal 12 Pharmacologic Interventions for Addictions 13 Behavioral Interventions 14 Co-Occurring Medical Disorders among Patients with AOD 15 Co-Occurring Psychiatric Disorders among Patients with AOD 16 Pain and Addiction
15%	17 Ethical, Legal and Liability Issues in Addiction Practice

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ABPM Addiction Medicine Content Areas

Substance	Percent of Exam
Alcohol	15-20%
Sedatives	7-10%
Stimulants	7-10%
Opioids	10-15%
Cannabinoids	7-10%
Nicotine	15-20%
Hallucinogens	0.5-3%
Dissociative substances	0.5-3%
Inhalants	0.5-3%
Anabolic steroids	0.5-3%
Other substances	1-3%
Nonsubstance addiction	1-3%
General/All substances combined	1-5%

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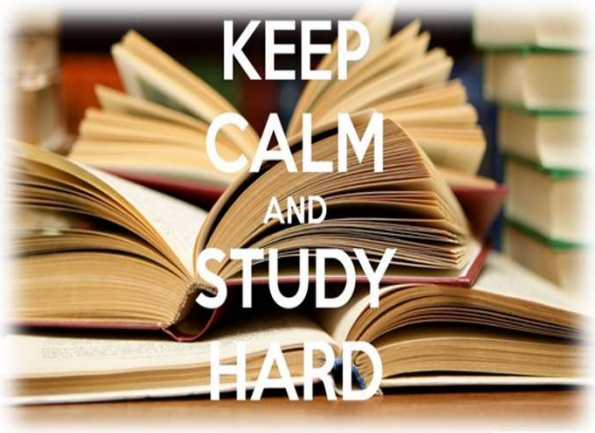
Test Taking Strategies

- Choose a comprehensive source as your core study guide.
- Your study plan should include review of as many topics/chapters per day as needed to complete your test prep about one week prior to the test.
- Continuously assess your progress and change your schedule accordingly.
- Use the last week or two to review test questions and cover areas where you may need more time.
- Wikipedia can be a good resource.
- Do not rest on your laurels. Everyone needs to prepare



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Test-Taking Strategies

- ✓ **Approach the test as a positive challenge and remain optimistic and confident of your skills.**
- ✓ **Majority pass the exam.**
- ✓ **Feel your best: Get a good night's sleep; eat breakfast; dress comfortably.**
- ✓ **Plan transportation to the testing center:**
  - ✓ **Check weather and road conditions several days before the test.**
  - ✓ **Or plan an exact route using public transportation.**
  - ✓ **Plan to arrive very early in order to avoid unanticipated delays.**
- ✓ **If choosing the remotely proctored option, make sure you understand the procedures and ensure your testing environment is distraction free**

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Test-Taking Strategies

- ✓ **Know the exam format and study tutorials related to the construction of the exam. Much time can be lost trying to understand the structure during the test.**
- ✓ **Pace yourself during the exam: Estimate where you should be after half of the time.**
- ✓ **Check exam to ensure all questions are answered.**
- ✓ **Immediately eliminate distractors you know are not correct.**
- ✓ **Change an answer very rarely once selected: Your initial answer is usually the correct one.**
- ✓ **If you do not have a clue as to the correct answer for a particular item, skip it and return to it later.**
- ✓ **WHEN YOU HEAR THE SOUND OF HOOFBEATS, DON'T LOOK FOR ZEBRAS.**

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The Basic Rules for Case Format Questions

- ✓ Avoid reading questions or distractors before the case. This may interfere with your critical, clinical thinking.
- ✓ Read the **entire** case and understand the presenting issues, and as applicable, the presumptive diagnosis before reading the questions.
- ✓ Recognize that portions of the case presentation may be irrelevant to the questions asked and provide context only. Some questions will reflect basic knowledge questions that while related to the case, are not dependent on it.
- ✓ Be aware of additional information in questions that may change the diagnosis or treatment recommendations you formulated upon initial review. Think of the questions as providing additional clinical information that helps to refine the situation.
- ✓ Case format questions are **usually** written for the purpose of testing clinical reasoning not necessarily content knowledge. **Think like a physician when responding.**

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CSAM's Board Review Course

Goal: *To improve pass rates by helping test takers focus on high-yield concepts and successful study methods.*

- ✓ In question format for better retention
- ✓ Topics not covered in presentations will be identified
- ✓ Focus less on the content of the question stems and more on the reasons **why** the answer is correct, and the distractors are incorrect.

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CSAM Board Review Course: Agenda*

7:30 am – 7:45 am	Introduction	Chwen-Yuen Angie Chen, MD
7:45 am – 8:15 am	Adolescence and Special Populations	Jessica Wang, MD, MPH
8:15 am – 8:45 am	Hallucinogens, Psychedelics, Stimulants	Jessica Wang, MD, MPH
8:45 am – 9:15 am	Basic Science (Neurobiology)	Brian Harris, MD
9:15 am – 9:45 am	Legal Aspect of Addiction Medicine	Brian Harris, MD
9:45 am – 10:00 am	BREAK	//
10:00 am – 10:30 am	Epidemiology & Preventive Medicine	Lakai, Banks –Dean, MD
10:30 am – 11:00am	Nicotine	Lakai, Banks –Dean, MD
11:00 am – 11:30 am	Benzodiazepines	Jeremy Flores, MD
11:30 am – 12:00 pm	Cannabis	Jeremy Flores, MD
12:00 pm – 1:15 pm	LUNCH ON YOUR OWN	//
1:15 pm – 1:45 pm	Medical Complications	John Nunes, MD
1:45 pm – 2:15 pm	Maternal Fetal	John Nunes, MD
2:15 pm – 2:45 pm	Opioids	Samantha Ayoub, MD, MS
2:45 pm – 3:00 pm	BREAK	//
3:00 pm – 3:30 pm	Alcohol	Samantha Ayoub, MD, MS
3:30 pm – 4:00 pm	Co-Occurring Disorders	Natassia Gaznick, MD, PhD
4:00 pm – 4:30 pm	Psychosocial Treatments	Natassia Gaznick, MD, PhD

*Subject to modifications

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SAMPLE QUESTION

The Drug Addiction Treatment Act (DATA 2000) permitted qualified physicians to obtain a special X-waiver from separate registration requirements of the Narcotic Addict Treatment Act to treat patients with opioid use disorders in their private offices:

A. With schedule II, III, IV or V controlled substances.
B. With schedule III, IV or V controlled substances.
C. With schedule IV or V controlled substances.
D. With buprenorphine.

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Answer: B

DATA 2000 approved the use of Schedule III, IV or V controlled substances by qualified physicians to treat opioid detoxification and maintenance. Buprenorphine was changed to a schedule III agent to be included in this law. In addition, the act limited the number of patients a practitioner could treat at one time to 30, unless after one year from when the practitioner submitted the initial notification, a second notification was submitted to the Secretary explaining the need and intent of the practitioner to treat up to 100 patients. This was later revised to 275 patients under certain circumstances and then eventually in 2023 these requirements were eliminated.

- Answer A is not correct as DATA 2000 ***did not*** address schedule II substances.
- Answer C is not correct as DATA 2000 ***did*** address schedule III substances by placing buprenorphine on that schedule.
- Answer D is not the best answer as the act was broader than just buprenorphine.

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ABPM Website for More Information

- https://www.theabpm.org/become-certified/exam-content/addiction-medicine-content-outline/
- https://www.theabpm.org/become-certified/exam-information/

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High Yield Topics: Adolescents, Gender, LGBTQ

CSAM Addiction Medicine Board Review Course 2025

Jessica A. Wang, MD, MPH
Health Sciences Clinical Instructor, UCLA
Contents modified from Past Presentation by Waseem Khader, DO, FASAM

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CONFLICT OF INTEREST DISCLOSURE

I, Jessica Wang, have no financial interests to disclose.

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EDUCATIONAL OBJECTIVES

- Develop a treatment approach for opioid use disorders in adolescents
- Differentiate primary mood disorders from substance-induced disorders in adolescents
- Outline the unique issues in diagnosing and treating gambling disorders among different genders
- Understand the unique risks for SUD relevant to LGBTQ populations

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Adolescent SUD

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Case 1

A 16 year-old male is brought in by his grandmother to your addiction medicine clinic. You review the chart before the visit and find that the patient was recently arrested for possession of an illegal substance and sent to juvenile jail, where he was given probation on condition that he seek substance use treatment.

You meet the patient, who is withdrawn, grumpy, and doesn't make eye contact. Grandmother shares that there is a strong family history of substance use. Unfortunately, both parents are still actively using and so grandmother (who has been in recovery herself for 30 years) has custody. The patient's parents have gang ties, and so grandma is worried that the patient may have been involved with a gang as well.

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Case 1 Cont.

You have the grandmother step out of the room and ask the patient what substances he is using. He initially says, "none of your business!" You affirm his autonomy but gently remind him of his probation. After a moment of silence, he shares he has been using fentanyl, inhaled or smoked, sometimes up to 1g a day. He had been working for a dealer transporting the substance to sell, and part of his compensation was free access to the drug.

You perform a physical exam and notice the patient is diaphoretic, appears fidgety, has rhinorrhea, and has dilated pupils. His heart rate is 122, blood pressure 132/86. He reports he is having muscle cramps and has had a couple bouts of diarrhea, nausea but no vomiting. His last reported fentanyl use was approximately 3 days ago, before he was arrested.

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Case 1 Question 1

What medication options are FDA-approved for treatment of OUD in adolescents?

A) There are no FDA-approved medications for OUD in adolescents
B) Buprenorphine SL
C) Methadone
D) Naltrexone
E) Only B and C

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Case 1 Question 1

What medication options are FDA-approved for treatment of OUD in adolescents?

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D) Naltrexone
E) Only B and C

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MOUD for adolescents

- Buprenorphine is FDA-approved for use in patients **aged 16 and older** - should be included in comprehensive treatment plan
- Methadone is technically "off label"
- High risk adolescents
  - *Escalating disruptive behavior*
  - *Fentanyl use*
  - *First time in treatment*
  - *Gender minority stress*

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Case 1 Cont.

You assess that the patient is in moderate withdrawal. After discussion about medication with the grandmother, you give a dose of buprenorphine 4 mg in clinic and the patient has improvement in symptoms. Repeat vitals show HR of 110, BP 119/74. You make arrangements with your community adolescent rehab and the patient goes to treatment the next day.

He does 4 weeks of treatment. The patient's buprenorphine is titrated to 12 mg daily. He is discharged and to follow up with you in clinic in two days.

The patient returns to clinic with his grandmother. He reports since being discharged from rehab, he has used fentanyl a couple times. The second time he used he remembers "passing out" and "waking up" to his grandmother shaking him vigorously.

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Case 1 Question 2

What is the most appropriate next step for treatment of this teen?

A) Recommend tapering off buprenorphine because the patient had an opioid overdose, therefore he shouldn't be on chronic opioids.
B) Recommend increasing buprenorphine from 12 mg to 16 mg daily, because a higher dose will help decrease cravings and protect against overdose.
C) Recommend the patient transition to methadone 30-40 mg, since the buprenorphine doesn't seem to be strong enough and a full mu agonist would be more effective.
D) Recommend naltrexone 50 mg because the buprenorphine isn't working and naltrexone protects against overdose.

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Case 1 Question 2

What is the most appropriate next step for treatment of this teen?

A) Recommend tapering off buprenorphine because the patient had an opioid overdose, therefore he shouldn't be on chronic opioids.
B) Recommend increasing buprenorphine from 12 mg to 16 mg daily, because a higher dose will help decrease cravings and protect against overdose.
C) Recommend the patient transition to methadone 30-40 mg with the local OTP, since the buprenorphine doesn't seem to be strong enough and a full mu agonist would be more effective.
D) Recommend naltrexone 50 mg because the buprenorphine isn't working and naltrexone protects against overdose.

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Case 1 Question 2

Return to use while on buprenorphine treatment is usually not an indication of buprenorphine failure. Is more likely an indication that the dose is not enough.

Especially in the era of fentanyl, doses of 16 mg or higher are becoming not uncommon.

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Methadone Use in Adolescents

- There is no evidence to suggest methadone is superior to buprenorphine for adolescents
- Prior federal regulations required youth under the age of 18 to have a 1-year opioid addiction history, two previous drug-free/withdrawal management attempts, and written consent from a parent or guardian before initiating methadone agonist treatment.
- Part 8 of Title 42 of the Code of Federal Regulations (CFR) published on 02/24/2024 aka "**The Final Rule**" removes unnecessary barriers to medication access by focusing on individual patient needs and adds protections for vulnerable groups.
  - *Eliminates the 1-year opioid addiction history requirement*
  - *Removes the requirement for two documented instances of unsuccessful treatment for people under age 18.*
  - *Allows consent to be obtained electronically.*

Department of Health and Human Services, Substance Abuse and Mental Health Services Administration, SAMHSA, & Baillieu, R. (2024). Medications for the Treatment of Opioid Use Disorder. *Federal Register*, *89*, 7528–7538. https://www.govinfo.gov/content/pkg/FR-2024-02-02/pdf/2024-01693.pdf

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Case 1 Cont.

The patient does well on buprenorphine 16 mg daily. He enrolls in an intensive outpatient program for adolescents with SUD and does well with this treatment. He continues to come to see you in clinic too on a regular basis.

With the help of his grandmother and probation officer, he gets approval to start working at the local gym as a gym assistant. His attendance and performance at school improve.

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Case 1 Cont.

Shortly after his 17th birthday, the grandmother brings him in for an appointment with you and he appears more withdrawn and irritable than prior. Grandmother reports worsening mood swings over the past 2 months and is concerned he may have returned to use.

The patient shares he has started vaping 2 weeks ago on some days because he felt like he needed something to "relax." He alternates between using nicotine and cannabis, whatever he can get ahold of. He denies returning to fentanyl use or interfacing with the dealers he was working for prior.

He has had outbursts at home that led to punching a hole in the wall, breaking a lamp, throwing dishware in anger.

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Case 1 Question 3

What is the best course of action now?

A) Reassurance, he hasn't returned to opioid use so no further intervention is necessary.
B) This is prolonged opioid withdrawal, we should increase the dose buprenorphine to 20-24 mg.
C) Diagnose him with substance-induced mood disorder (cannabis and/or nicotine) and recommend return to residential therapy.
D) Diagnose him with major depression and consider starting an SSRI and refer for psychological support.

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Case 1 Question 3

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Depression/Anxiety in Adolescents

Depression in adolescents is more likely to present as mood swings and irritability.

Nicotine and cannabis can induce mood symptoms however given the chronicity of the presentation, these substances are less likely the cause.

SSRIs and other antidepressants are indicated in the treatment of major depression in adolescents, especially in teens with other high-risk features such as substance use and history of overdose.

Monitor for symptoms that would be more consistent with bipolar disorder.

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Case 2

A 12 year-old child is brought in by their parents for a well-child visit. They share that their child has lately had issues in school and at home that make them suspect they have ADHD.

You give the parents Vanderbilt surveys to complete at home and school. The results are floridly positive and so you diagnose ADHD.

The parents are hesitant to start medication and opt for a trial of therapy. However, issues with disruption at school and poor performance on school work continue.

The child is currently not using any substances.

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Case 2 Question 4

Which of the following is correct regarding co-occurring ADHD and substance use disorders in adolescents?

A. ADHD is not more common among adolescents who also have diagnosis of SUD compared to those without SUD
B. Substance use in childhood or early adolescence predisposes patients to development of ADHD in later adolescence
C. Adolescents who have ADHD and SUD often need higher doses of prescription stimulant medication to treat their ADHD compared to those with no SUD
D. Given the high risk of misuse of psychostimulants, only psychosocial treatment options should be offered initially to adolescents in early recovery from substance use disorders.

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Case 2 Question 4

Which of the following is correct regarding co-occurring ADHD and substance use disorders in adolescents?

A. ADHD is not more common among adolescents who also have diagnosis of SUD compared to those without SUD
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D. Given the high risk of misuse of psychostimulants, only psychosocial treatment options should be offered initially to adolescents in early recovery from substance use disorders.

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ADHD and SUD in adolescents

- Strong evidence indicates that early ***and*** adequate treatment of ADHD in childhood is a prevention strategy for reducing the risk of development of substance use disorders in adolescence and reduces the overall severity of substance use disorders once they manifest.
- Evidence suggests that treatment with stimulants, regardless of whether the adolescent also has a substance use disorder, is the most effective treatment. Data also indicates that treating ADHD in the presence of an SUD is challenging and often results in diminished response to medication.
- Likely, this difference in efficacy is related to disruption of steady state brain dopamine function inherent in both ADHD and SUDs, and evidence supports that higher doses of psychostimulants may need to be used when treating ADHD in the presence of addictive disease.

Heval Özgen, Renske Spijkerman, Moritz Noack, Martin Holtmann, Arnt Schellekens, Søren Dalsgaard, Wim van den Brink, and Vincent Hendriks. *Treatment of Adolescents with Concurrent Substance Use Disorder and Attention-Deficit/Hyperactivity Disorder: A Systematic Review*. J Clin Med. 2021 Sep; 10(17): 3908.

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ADHD and SUD in adolescents

- Answer A is **incorrect** because the rate of ADHD in adolescents with SUDs (24%) is over twice that of those without SUDs (approximately 11.5%)
- While ADHD does predict a higher risk of development of addictive disease, the reverse is not true as typically symptoms of ADHD will appear prior to initiation of substance use. Therefore, answer B is incorrect. However, many substances can lead to symptoms that mimic ADHD and will resolve with ongoing abstinence.
- **The efficacy of psychosocial treatments for ADHD symptoms and behaviors in the adolescent and pediatric population is not well established**. Given the demonstrated benefits of pharmacotherapy for ADHD treatment in adolescents with SUDs, monotherapy with psychosocial treatments is not appropriate.

Vacher C, Goujon A, Romo L, Purper-Ouakil D. Efficacy of psychosocial interventions for children with ADHD and emotion dysregulation: a systematic review. Psychiatry Res. 2020 Sep;291:113151. doi: 10.1016/j.psychres.2020.113151. Epub 2020 May 30. PMID: 32619822.

Tourjman V, Louis-Nascan G, Ahmed G, DuBow A, Côté H, Daly N, Daoud G, Espinet S, Flood J, Gagnier-Marandola E, Gignac M, Graziosi G, Mansuri Z, Sadek J. Psychosocial Interventions for Attention Deficit/Hyperactivity Disorder: A Systematic Review and Meta-Analysis by the CADDRA Guidelines Work GROUP. Brain Sci. 2022 Aug 1;12(8):1023. doi: 10.3390/brainsci12081023. PMID: 36009086; PMCID: PMC9406006.

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Case 3 Question 5

A 14-year-old cis-gendered male is brought to your office by his mother for a routine annual examination. He has a history of asthma and eczema and is otherwise healthy. As part of your thorough questioning, the patient reveals that his friends smoke marijuana at school. **Which of the following would be accurate advice to give this patient?**

A. "Cannabis use in youth has been associated with increased risk of psychosis that is sometimes irreversible and can develop into a chronic psychotic disorder."
B. "It is okay to use cannabis in small amounts because it is generally considered safe and natural. Just stay away from wax pens."
C. "Driving while smoking marijuana isn't considered driving under the influence because marijuana tends to make you drive slower."
D. "You shouldn't smoke cannabis yourself because of your asthma, but it is probably fine to be around your friends who are smoking and be exposed to secondhand cannabis smoke."

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Case 3 Question 5

A 14-year-old cis-gendered male is brought to your office by his mother for a routine annual examination. He has a history of asthma and eczema and is otherwise healthy. As part of your thorough questioning, the patient reveals that his friends smoke marijuana at school. **Which of the following would be accurate advice to give this patient?**

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Cannabis and psychosis

- Cannabis use is associated with an increased risk of psychosis. High potency cannabis and synthetic cannabinoids carry the greatest risk as the active ingredient in cannabis, delta-9-tetrahydrocannabinol (THC), can produce transient, **dose-dependent**, psychosis. The psychotogenic effects of THC can be ameliorated by cannabidiol (CBD).
- Marijuana can be extracted from the cannabis plant in the form of potent concentrates. Solvent-based products contain THC levels averaging 54-69% and reported to exceed 80%.

Murray, R.M., Quigley, H., Quattrone, D., Englund, A. and Di Forti, M. (2016), Traditional marijuana, high-potency cannabis and synthetic cannabinoids: increasing risk for psychosis. World Psychiatry, 15: 195-204. https://doi.org/10.1002/wps.20341

NIDA. 2020, June 25. Cannabis (Marijuana) Concentrates DrugFacts. Retrieved from https://nida.nih.gov/publications/drugfacts/cannabis-marijuana-concentrates on 2024, July 28

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Cannabis and psychosis

- Genetic variation at rs2494732 of AKT1 influences the risk of developing a psychotic disorder in cannabis users.
- The AKT1 gene governs an enzyme that affects brain signaling involving the neurotransmitter dopamine in the striatum. Altered dopamine signaling is known to be involved in schizophrenia.
- Those who use marijuana daily (green bars) with the C/C variant have a **seven times higher risk** of developing psychosis compared to non or infrequent users

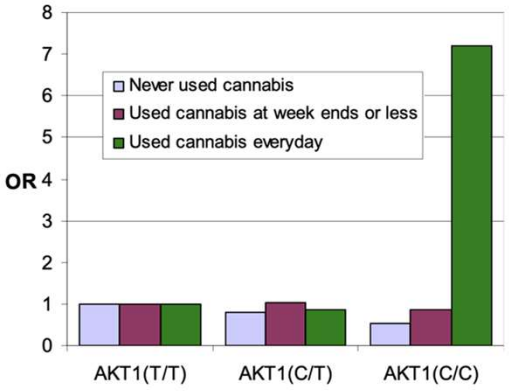

Figure 3. Odds ratio (OR) of psychosis for *AKT1* rs 2494732 C/T or C/C carriers compared to subjects with the T/T genotype depending on lifetime frequency of cannabis use.

NIDA. 2024, May 25. Letter From the Director. Retrieved from https://archives.nida.nih.gov/publications/research-reports/cannabis-marijuana-research-report/letter-director on 2024, July 28

Di Forti, M., Iyegbe, C., Sallis, H., Kolliakou, A., Falcone, M. A., Paparelli, A., Sirianni, M., La Cascia, C., Stilo, S. A., Marques, T. R., Handley, R., Mondelli, V., Dazzan, P., Pariante, C., David, A. S., Morgan, C., Powell, J., & Murray, R. M. (2012). Confirmation that the AKT1 (rs2494732) genotype influences the risk of psychosis in cannabis users. *Biological psychiatry*, *72*(10), 811–816. https://doi.org/10.1016/j.biopsych.2012.06.020

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Question 6

Which of the following statements best reflects the most recent Monitoring the Future (MTF) data on patterns of **nicotine** use among U.S. adolescents (grades 8, 10, and 12) from 2017 to 2020?

A. Exclusive combustible tobacco use (cigarettes or cigars) is the most prevalent pattern of nicotine use among adolescents in all grades.

B. Dual use of e-cigarettes and combustible tobacco is more common than exclusive e-cigarette use in all adolescent grades.

C) Exclusive e-cigarette use is the most prevalent pattern of nicotine/tobacco use among U.S. adolescents, followed by dual use, and then exclusive combustible use.

D) There are no significant differences in nicotine use patterns by parental education level.

Usidame, Bukola, et al. "Sociodemographic patterns of exclusive and dual combustible tobacco and E-cigarette use among US adolescents—a nationally representative study (2017–2020)." *International journal of environmental research and public health* 19.5 (2022): 2965.

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Question 6

Which of the following statements best reflects the most recent Monitoring the Future (MTF) data on patterns of **nicotine** use among U.S. adolescents (grades 8, 10, and 12) from 2017 to 2020?

A. Exclusive combustible tobacco use (cigarettes or cigars) is the most prevalent pattern of nicotine use among adolescents in all grades.

B. Dual use of e-cigarettes and combustible tobacco is more common than exclusive e-cigarette use in all adolescent grades.

C) Exclusive e-cigarette use is the most prevalent pattern of nicotine/tobacco use among U.S. adolescents, followed by dual use, and then exclusive combustible use.

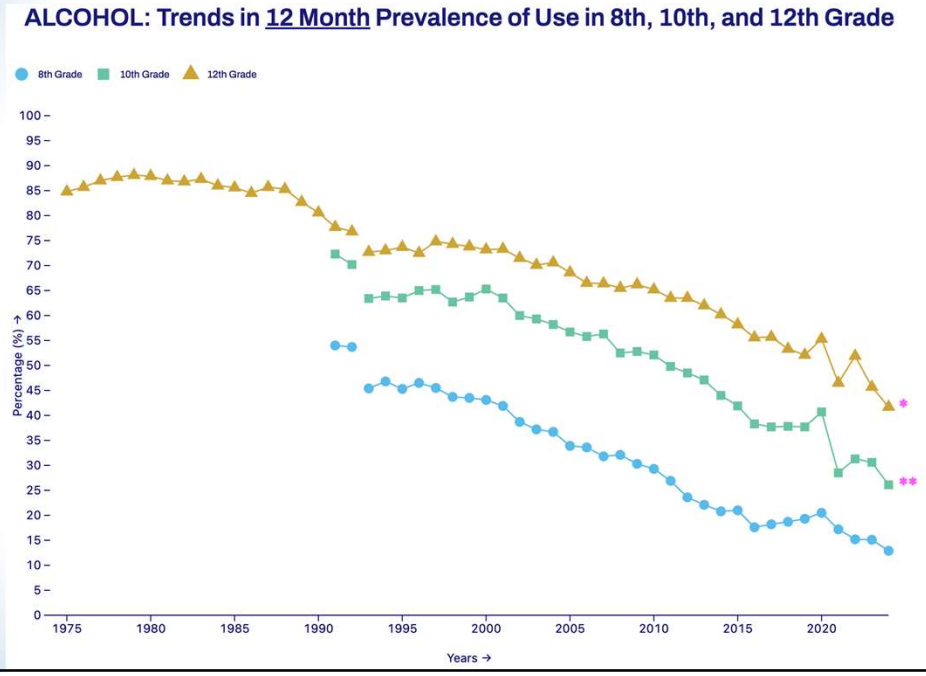
D) There are no significant differences in nicotine use patterns by parental education level.

Usidame, Bukola, et al. "Sociodemographic patterns of exclusive and dual combustible tobacco and E-cigarette use among US adolescents—a nationally representative study (2017–2020)." *International journal of environmental research and public health* 19.5 (2022): 2965.

CSAM

52

Monitoring the Future Study



Miech, R. A., Johnston, L. D., Patrick, M. E., & O'Malley, P. M. (2025). Monitoring the Future national survey results on drug use, 1975–2024: Overview and detailed results for secondary school students. Monitoring the Future Monograph Series. Ann Arbor, MI: Institute for Social Research, University of Michigan. Available at https://monitoringthefuture.org/results/annual-reports/

53

Minorities and LGBTQ Populations

54

Case 4 Question 7

58 y/o F presents for follow up in addiction medicine clinic. She has a history of alcohol and cocaine use disorder now both in sustained remission. You're wrapping up the visit with her, offering positive affirmations for her abilities to maintain recovery, when she suddenly bursts into tears. "Doc, I haven't been able to admit this to anyone, but I think I have an issue with money."

She shares she has been using phone apps for stock trading, focusing on the high-risk, high-reward profiles. She sometimes can make up to $1000 a day, but she has also lost $10,000's overall and keeps trading in hopes she can make up money lost. She is spending increasingly more time on trading such that she is lying to her family about where she is on the weekends. She feels great when she makes profit, but when she is not on her phone looking at stocks, she feels restless. She has tried to stop before, but she can't help but open her app the very next time her phone lights up. She also doesn't know how to explain to her family where her lost money has gone.

55

Case 4 Question 7

Which of the following are criterion for DSM-5 diagnosis of Gambling Disorder?

A. Feelings of irritability or restlessness when trying to cut back on gambling
B. Need to spend more time/money on gambling
C. Lying to conceal gambling
D. Having spent the equivalent of $10,000 USD (as of 2013) or be in debt
E. All the above except D

56

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57

Case 4 Question 8

How many of the DSM-5 criterion does someone have to meet within the past 12 months to qualify for the diagnosis?

A. 4
B. 3
C. 2
D. 1

58

Case 4 Question 8

How many of the DSM-5 criterion does someone have to meet within the past 12 months to qualify for the diagnosis?

A. **4**
B. 3
C. 2
D. 1

This is different from the other SUD dx's, which only require 2 criteria met.

59

Case 4 Question 7-8

Unlike criterion A of other SUDs, which require at least two criteria occurring within a 12-month period, gambling disorder **requires four (or more)** of these criteria during the same duration:

- Need to gamble with increasing amount of money to achieve the desired excitement (tolerance)
- Restless or irritable when trying to cut down or stop gambling (withdrawal)
- Repeated unsuccessful efforts to control, cut back on or stop gambling
- Frequent thoughts about gambling (such as reliving past gambling experiences, planning the next gambling venture, thinking of ways to get money to gamble)
- Often gambling when feeling distressed
- After losing money gambling, often returning to get even (referred to as "chasing" one's losses)
- Lying to conceal gambling activity
- Jeopardizing or losing a significant relationship, job or educational/career opportunity because of gambling
- Relying on others to help with money problems caused by gambling

Source: Diagnostic and Statistical Manual of Mental Disorder (DSM-5)-Fifth Edition. Arlington, VA. American Psychiatric Association, 2013.

60

Case 4 Question 9

Which of the following characteristics of gambling disorder in women is ***false*** compared to men?

A. Women progress to pathologic gambling more slowly than men
B. Compared to men, women have higher rates of "non-strategic" versus "strategic" gambling
C. Most women with gambling disorder are married
D. The prevalence of gambling disorder is lower in women as compared to men

61

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C. Most women with gambling disorder are married
D. The prevalence of gambling disorder is lower in women as compared to men

62

Women and gambling disorder

- Women, who constitute approximately 32% of disordered gamblers in the United States, seem to progress ***more quickly*** than do men, a phenomenon known as **"telescoping."** The lifetime prevalence is about 0.2% for females and 0.6% for males.
- The other answers represent typical characteristics of gambling disorders in women.

Sources: The ASAM Essentials of Addiction Medicine/[edited by] Abigail J. Herron, Timothy Koehler Brennan, Second Edition 2015. Diagnostic and Statistical Manual of Mental Disorder (DSM-5)-Fifth Edition. Arlington, VA. American Psychiatric Association, 2013.

63

Question 10

Which of the following can mimic a gambling use disorder?

A. Treatment of a seizure disorder in a 27-year-old male patient with gabapentin
B. Treatment of multiple sclerosis in a 42-year-old female patient with β-interferon
C. Treatment of attention-deficit hyperactivity disorder in an 18-year-old with dextroamphetamine-amphetamine (Adderall)
D. Treatment of Parkinson's disease in a 56-year-old male patient with dopamine agonists

64

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D. Treatment of Parkinson's disease in a 56-year-old male patient with dopamine agonists

65

Dopamine agents and Gambling

- Patients taking dopaminergic medication for Parkinson's disease may experience urges to gamble. If such symptoms dissipate when the medication dose is reduced or stopped, diagnosis of gambling disorder would not be indicated.
- Although psychostimulant medication increases dopamine levels as well, it has not been classically associated with increased gambling. The other options are not known to affect gambling behavior.

Source: Diagnostic and Statistical Manual of Mental Disorder (DSM-5)-Fifth Edition. Arlington, VA. American Psychiatric Association, 2013.

66

Question 11

Which subgroup within the LGBTQ population demonstrates the highest rates of SUD?

A. Gay men
B. Lesbian women
C. Bisexual women
D. Bisexual men

67

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68

LGBTQI and SUD (Open Evidence)

There are clear differences in the prevalence of substance use disorders among subgroups within the LGBTQ population. **Bisexual women consistently exhibit the highest rates of substance use disorders across multiple substances and age groups**, followed by gay/lesbian individuals and bisexual men.

Among men, gay and bisexual men have higher rates of nearly all substance use disorders compared to heterosexual men, with disparities particularly notable for tobacco, alcohol, cannabis, and several illicit drugs.

Among women, both lesbian and bisexual individuals have elevated risks for alcohol, tobacco, cannabis, and illicit drug use, but the risk is especially pronounced among bisexual women, who also have higher rates of comorbid psychiatric disorders

Sexual Orientation Disparities in Substance Use: Investigating Social Stress Mechanisms in a National Sample.Krueger EA, Fish JN, Upchurch DM. American Journal of Preventive Medicine. 2020;58(1):59-68. doi:10.1016/j.amepre.2019.08.034.

Disparities in Substance Use Behaviors and Disorders Among Adult Sexual Minorities by Age, Gender, and Sexual Identity.Schuler MS, Rice CE, Evans-Polce RJ, Collins RL. Drug and Alcohol Dependence. 2018;189:139-146. doi:10.1016/j.drugalcdep.2018.05.008.

Disparities in Self-Reported Mental Health, Physical Health, and Substance Use Across Sexual Orientations in Canada.Bellows Z, Kim C, Bai Y, Cao P, Chum A. PloS One. 2025;20(3):e0305019. doi:10.1371/journal.pone.0305019.

Disparities in Use/Misuse of Specific Illicit and Prescription Drugs Among Sexual Minority Adults in a National Sample.Schuler MS, Collins RL, Ramchand R. Substance Use & Misuse. 2022;57(3):461-471. doi:10.1080/10826084.2021.2019776.

Alcohol, Tobacco, and Comorbid Psychiatric Disorders and Associations With Sexual Identity and Stress-Related Correlates.Evans-Polce RJ, Kcomt L, Veliz PT, Boyd CJ, McCabe SE. The American Journal of Psychiatry. 2020;177(11):1073-1081. doi:10.1176/appi.ajp.2020.20010005.

69

Stimulants, Hallucinogens, Psychedelics

CSAM Board Exam Review Track 2025

Jessica A. Wang, MD, MPH
Health Sciences Clinical Instructor, UCLA
Modified from past presentation by Amy de la Garza, MD, FASAM

70

CONFLICT OF INTEREST DISCLOSURE

I, Jessica Wang, have nothing to disclose, and I will not be discussing “off label” use of drugs or devices in this presentation.

71

Learning Objectives

After attending this presentation, learners will be able to:

- Explain the mechanism of action
- Describe the clinical presentations
- Identify common toxicities

Of common stimulants, hallucinogens, dissociative anesthetics, and psychedelics

72

Stimulants

This presentation is focused on:

- Cocaine
- Amphetamine/Methamphetamine
- Cathinones/Khat/Bath Salts
- Caffeine

73

Regarding cocaine and amphetamine which of the following statements is false?

A. Amphetamine blocks the reuptake of dopamine to the presynaptic neuron.
B. Cocaine is primarily metabolized in the liver to benzoylecgonine and can be detected in the urine for 2-4 days.
C. Amphetamine can cause persistent psychotic syndromes
D. Cocaine toxicity presents with mydriasis, hyperthermia and paranoia
E. None of the above

74

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E. None of the above

75

Cocaine and Amph - Mechanism of Action

- Cocaine is a **Transporter Blocker/Reuptake blocker**
- Amphetamine is a transport/reuptake blocker AND a transporter **releasers**
  - *Inhibits MAO reuptake transports*
  - *Bind to intracellular vesicular transporters, causing release of stored monoamines into the cytoplasm for delivery to the synapse = MORE dopamine INTO the synapse*

76

Cocaine:

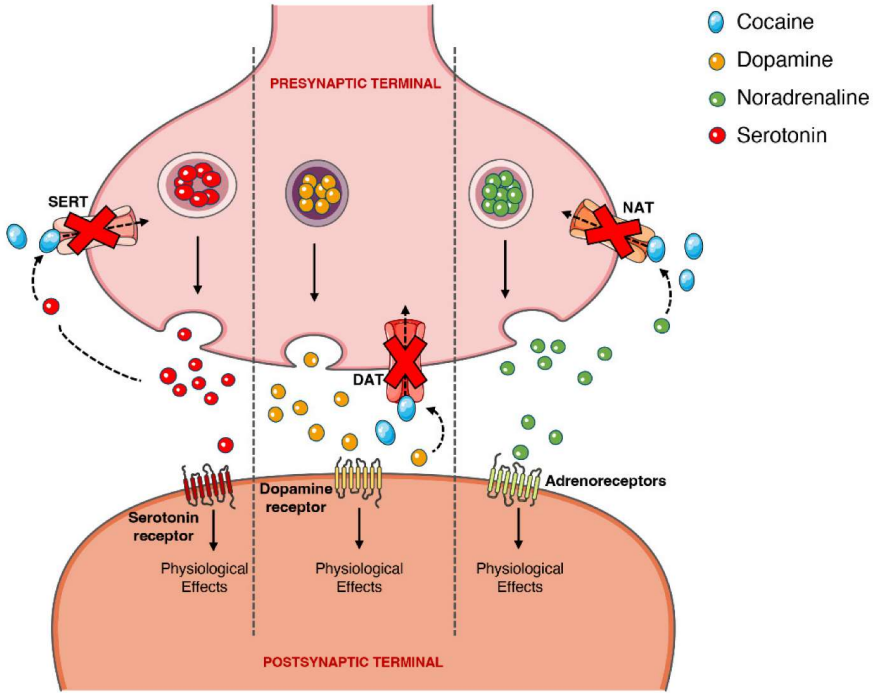

Figure 4 from Roque Bravo, R.; Faria, A.C.; Brito-da-Costa, A.M.; Carmo, H.; Mladěnka, P.; Dias da Silva, D.; Remião, F.; on behalf of The OEMONOM Researchers. Cocaine: An Updated Overview on Chemistry, Detection, Biokinetics, and Pharmacotoxicological Aspects including Abuse Pattern. *Toxins* **2022**, *14*, 278.

77

Amphetamine:

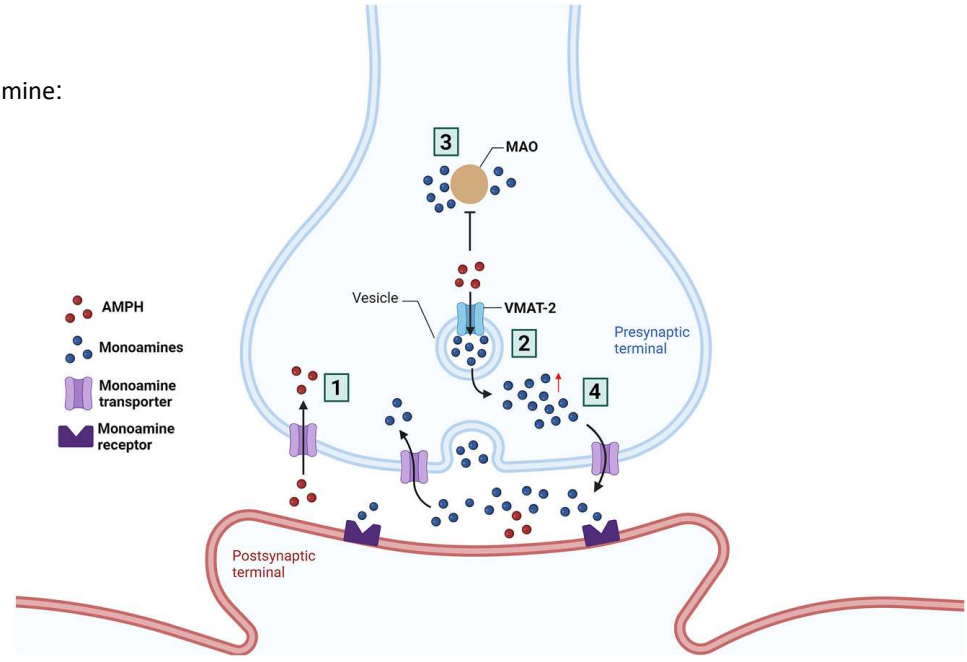

Figure 3 from Ferreira, Mariana, Carneiro, Patrícia, Costa, Vera Marisa, Carvalho, Félix, Meisel, Andreas and Capela, João Paulo. "Amphetamine and methylphenidate potential on the recovery from stroke and traumatic brain injury: a review" *Reviews in the Neurosciences*, vol. 35, no. 7, 2024, pp. 709-746.

78

Cocaine Toxicity

- Result of heavy use or consistent use
- Features: HTN, seizures, diaphoresis, hyperthermia, paranoia, chest pain, dyspnea, paranoia, delirium, epistaxis, arrhythmias, mydriasis
  - *Can look very similar to other hallucinogenic and dissociative intoxication and toxicity.*
- Beta blockers in cocaine toxicity (*)
  - ***Labetalol*** *– mixed alpha and beta-adrenergic receptor blocker, preferred for stimulant-induced hypertension and tachycardia*
  - *Pure beta blockers like metoprolol can cause increased blood pressure and coronary vasoconstriction –* ***unopposed alpha stimulation***
- Benzodiazepines and antipsychotics can be used to reduce agitation and psychosis/paranoia

RichardsJR, Le JK. Cocaine Toxicity. [Updated 2023 Jun 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430976/

79

Methamphetamine Psychosis

- Can be persistent even after cessation of use
- Looks a lot like schizophrenia
- Manage with antipsychotics

Glasner-Edwards S, Mooney LJ. Methamphetamine psychosis: epidemiology and management. CNS Drugs. 2014 Dec;28(12):1115-26.

80

An 18-year-old patient presents to the ED with paranoia, dilated pupils, BP 158/108, HR of 119, His UDS is negative, but his friend tells you that he had been using bath salts from a headshop near his apartment. Which of the following is FALSE regarding bath salts?

A. Bath salts are synthetic cathinones, which stimulate release and inhibit reuptake of dopamine, serotonin, and norepinephrine.

B. Cathinone is a monoamine alkaloid found in the khat plant which is native to East Africa.

C. Medical complications of synthetic cathinone intoxication can include disseminated intravascular coagulation, acute kidney injury, serotonin syndrome and seizures.

D. Bath salt intoxication can be reversed with flumazenil.

81

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Bath Salts

Synthetic cathinones

- *Cathinones = monoamine alkaloids, naturally found in khat plant in E Africa*
- *Stimulate release and inhibit reuptake of dopamine, serotonin, and norepinephrine.*

Intoxication:

- *Euphoria, increased alertness and energy, agitation, psychosis*

Complications can include

- *DIC, AKI, serotonin syndrome and seizures*

Banks, M. L., Worst, T. J., Rusyniak, D. E., & Sprague, J. E. (2014). Synthetic cathinones ("bath salts"). *The Journal of emergency medicine*, *46*(5), 632–642.

83

Caffeine

- Adenosine receptors
- Intoxication/withdrawal – have been in DSM-5

Restlessness, nervousness, excitement	**Headache**
Insomnia	**Fatigue**
Flushed face	**Decreased alertness**
Diuresis	**Irritability**
GI upset	**Depression**
Muscle twitching, psychomotor agitation	**Flu-like symptoms**
Tachycardia or arrhythmia	**Nausea/vomiting**
	Muscle aches

- Caffeine use disorder – not formally in DSM-5 but recognized as needing further study

84

Hallucinogens

- LSD
- Mescaline
- Psilocybin
- DMT, AMT
- MDMA
- Salvia

85

A 33-year-old patient presents to the emergency room with concern for symptoms starting after ingestion of LSD at a party. Other than visual hallucinations, what other clinical findings is this patient most likely to have?

A) Severe respiratory depression and pinpoint pupils

B) Mydriasis and tachycardia

C) Profound bradycardia and hypothermia

D) Hyperreflexia and muscle rigidity without altered perception

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87

Hallucinogens – Intoxication Presentations

- Visual hallucinations (duh)
- Enhanced capacity for introspection, illusions, alterations of time perception
- Sympathomimetic effects (including mydriasis and tachycardia)
- Psychological symptoms such as anxiety, agitation, and altered sense of reality.
- Less common features:
  - Hypertension
  - Increased body temperature
  - Nausea or vomiting

Bogenschutz MP & Nichols D (2019). The pharmacology of hallucinogens. In *ASAM Essentials of Addiction Medicine (6th edition)* pp. 230-245

88

Mechanism of Action

- LSD, mescaline, DMT, and psilocybin are all **5-HT2A partial agonists**
- LSD's duration of action is 8-14 h, compared to 4-8 h for psilocybin and 30-60 min for DMT. DMT is typically smoked or inhaled.
- Tolerance develops quickly with use of hallucinogens though physical withdrawal symptoms typically do not occur. Use of the classical hallucinogens rarely meets criteria for DSM-5 SUD.

Bogenschutz MP & Nichols D (2019). The pharmacology of hallucinogens. In *ASAM Essentials of Addiction Medicine (6th edition)* pp. 230-244

89

A 20-year-old patient presents to clinic with low mood for 5 days after taking a "love drug" at a rave. He says that while intoxicated, it caused increased energy and empathy, euphoria, and emotional closeness. Which of the following is FALSE about the drug he most likely used?

A. It causes release of serotonin, dopamine and norepinephrine and can also cause reuptake inhibition.

B. Agitation or anxiety from intoxication should not be treated with a benzodiazepine such as diazepam.

C. Common clinical symptoms of intoxication include dry mouth, sweating, mydriasis, bruxism, tachycardia.

D. Severe toxicities can include hyperpyrexia leading to multi-organ failure and rhabdomyolysis; serotonin syndrome; hyponatremia and cerebral edema.

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91

MDMA – “Ecstasy” or ”Molly”

- MOA:
  - *Reuptake inhibition*
  - *Release of serotonin, DA and NE.*
- MDMA is an entactogen, not a classic hallucinogen
  - *minimal sensory effects*
  - *increased feelings of elation - 5HT*
  - *some stimulant-like effects.*
- Intoxication: elevated mood, dry mouth, sweating, mydriasis, bruxism, tachycardia.

Hall, A. P., and J. A. Henry. "Acute toxic effects of ‘Ecstasy’(MDMA) and related compounds: overview of pathophysiology and clinical management." *BJA: British Journal of Anaesthesia* 96.6 (2006): 678-685.

92

MDMA

Agitation or anxiety

- *First line: place the patient in a quiet environment with minimal sensory stimulation*
- *Second line: benzodiazepines*

Toxicity

- *Hyperpyrexia - multi-organ failure and rhabdomyolysis. More common in situations where patient is prone to dehydration (dancing all night, alcohol, no hydration)*
- *Serotonin syndrome*
- *Hyponatremia and cerebral edema*

Wilkins JN, Danovitch I, Gorelick D (2019). Management of stimulant, hallucinogen, PCP and club drug intoxication and withdrawal In *ASAM principles of Addiction Medicine*, 6th edition, p 770.

93

Which of the following is part of the mint family and long recognized for its hallucinogenic properties, used in healing ceremonies?

A. Salvia

B. Kratom

C. Ayahuasca

D. Ibogaine

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Salvia

Salvia divinorum, member of the mint family

- Salvinorin A
  - *Kappa opioid receptor agonist - hallucinations, diuresis, analgesia, and altered state of consciousness often called "trance-like"*
- Originates from Mexico, Oaxacan state
- Chewed, smoked, oral ingestion
- No reported cases of withdrawal

Miller, Fiellin et al (2019). Pharmacological Treatment of Stimulant Use Disorders. *ASAM Principles of Addiction Medicine (6th edition) eBook.* pp. 244-245

96

Kratom

Mitragyna speciosa Korth, plant in coffee family

- Mitragynine
  - *Opioid mu and delta agonist*
  - *Alpha-adrenergic, dopamine, serotonin receptor activity*
- From SE Asia, now popularized – "gas station heroin"
- Originally used for euphoria, analgesia, opium withdrawal treatment
  - *Low doses: stimulant*
  - *Higher doses: opioid*
- Chewed leaves or tea, rarely smoked

Miller, Fiellin et al (2019). Pharmacological Treatment of Stimulant Use Disorders. *ASAM Principles of Addiction Medicine (6th edition) eBook.* pp. 782-784

97

Ayahuasca

Plant source for *N*,*N*-dimethyltryptamine (DMT)

- DMT
  - *Serotonin*
  - *Metabolized by MAO*
- S America, Amazon basin
- Smoked, IV, brew

Miller, Fiellin et al (2019). Pharmacological Treatment of Stimulant Use Disorders. *ASAM Principles of Addiction Medicine (6th edition) eBook.* pp. 615, 632-634

98

Ibogaine

Tabernanthe iboga

- Indole alkaloid
  - *Serotonin, NMDA, mu and kappa opioid, nicotinic receptor activity*
- Western/Central Africa – used in rituals

Miller, Fiellin et al (2019). Pharmacological Treatment of Stimulant Use Disorders. *ASAM Principles of Addiction Medicine (6th edition) eBook.* pp. 2022

99

Dissociative Anesthetics

- PCP
- Ketamine
- Dextromethorphan
- Methoxetamine

100

Which of the following best describes the primary mechanism of action of the dissociative anesthetics (ketamine, PCP, etc.)?

A) Selective serotonin reuptake inhibition

B) Non-competitive antagonism of the N-methyl-D-aspartate (NMDA) receptor

C) Direct agonism of μ-opioid receptors

D) Inhibition of voltage-gated calcium channels

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102

Which of the following is FALSE regarding methoxetamine (MXE)?

A. Methoxetamine is a synthetic analog of ketamine with longer duration of action.

B. Methoxetamine is now being used to treat opioid use disorder

C. Methoxetamine is an NMDA receptor antagonist which inhibits reuptake of serotonin and dopamine

D. Effects of methoxetamine include hallucinations, euphoria, dissociation, rotatory nystagmus, and confusion.

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104

Methoxetamine

- Methoxetamine is a synthetic analog of ketamine with longer duration of action.
- It is an NMDA receptor antagonist which inhibits reuptake of serotonin and dopamine.
- Effects of methoxetamine include hallucinations, euphoria, dissociation; rotatory nystagmus, tachycardia, and confusion; N/V/D, paranoia and anxiety.

Coppola, M., & Mondola, R. (2012). Methoxetamine: from drug of abuse to rapid-acting antidepressant. *Medical hypotheses*, *79*(4), 504–507.

105

Which of the following is FALSE about PCP, dextromethorphan (DXM) and ketamine?

A. At one point, they were all available as FDA approved medications.

B. Hallucinations and vital sign changes are extremely rare with use at moderate-high doses.

C. They are all considered dissociative anesthetics and NMDA antagonists.

D. They have similar pharmacodynamics to nitrous oxide (NO).

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107

PCP, DXM, Ketamine

- Dissociative anesthetics, NMDA antagonists
- DXM, when taken as directed, has low toxicity and a high therapeutic index
  - *Cough, cold, or flu relief*
  - *One of the most abused OTC medications*
- PCP was developed as an IV anesthetic
  - *Discontinued due to high incidence of post-op emergency reactions*
  - *Only illicit sources now*
  - *Intoxication: confusion, delirium, psychosis, and can include severe agitation and nystagmus*

Domino EF & Miller SC (2019). The pharmacology of dissociatives. In *ASAM Essentials of Addiction Medicine (6th edition)* pp. 252-262

108

PCP, DXM, Ketamine cont.

- Ketamine
  - *Clinical uses: general anesthesia and conscious sedation*
  - *Clinical effects of ketamine are similar to PCP though it is less potent (less agitation and sympathomimetic effects)*
- Nitrous oxide
  - *Also an NMDA antagonist and has dissociative-like clinical effects*
  - *Hypoxia with use, which contributes to feelings of intoxication, and euphoria, which occur rapidly and last for a short time*
  - *Inhalants like NO are most used among 12–17-year-olds*

Domino EF & Miller SC (2019). The pharmacology of dissociatives. In *ASAM Essentials of Addiction Medicine (6th edition)* pp. 252-262

109

A 25-year-old man with a history of OUD on buprenorphine and MDD presents to your office with memory difficulties, worsening anxiety and persistent painful urination. He reports that last year he started receiving weekly ketamine treatment for his depression and has been using illicit ketamine daily for the last 3 months. Which of the following statements regarding ketamine is FALSE?

A. Ketamine intoxication can lead to elevated blood pressure, arrythmia and angina.

B. Psychosis can occur with frequent, long-term use of ketamine.

C. Ketamine-induced cystitis always resolves with cessation of use.

D. Cognitive deficits have been observed in patients with frequent long term ketamine use.

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111

Ketamine-induced cystitis

- Duration and frequency of ketamine use does not always correlate with develop of lower urinary tract symptoms
- Continued ketamine use after the development of symptoms, long duration of use, and severe symptoms may increase risk of long- term symptoms that do not resolve or respond to treatment
- End stage disease may include hydronephrosis, chronic kidney disease or kidney failure

Jhang, JF, Birder LA, Kuo H. Pathophysiology, clinical presentation, and management of ketamine-induced cystitis. *Tzu Chi Med J.* 2023;35(3):205-212.

112

Ketamine Intoxication

- Sedation, impaired consciousness
- Mydriasis and nystagmus, excess salivation (laryngospasm)
- Hypertension (especially in patients with cardiovascular disease)
- Tachycardia, arrythmias, angina
- Abdominal pain, nausea and vomiting (K-cramps)
- Delusions, paranoia, ataxia, dysarthria, dysphoria – prolonged symptoms greater than 24 hours

Ketamine Toxicity Stat Pearls https://www.ncbi.nlm.nih.gov/books/NBK541087/

113

Other Club Drugs

- Gamma-hydroxybutyrate (GHB)
- Spice/K2

114

A 23-year-old patient tells you that during his medical residency he began using GHB before going clubbing with friends. Which of the following is FALSE regarding GHB?

A. GHB has a short half-life of around 20-30 min with a narrow margin of safety.

B. GHB has been used as a muscle developer and fat burner, as a party drug for its euphoric effects, and is FDA approved for the treatment of narcolepsy-associated cataplexy.

C. GHB overdose is often brief with rapid recovery.

D. GHB intoxication typically causes hypertension, tachycardia and violent behavior.

115

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Gamma-hydroxybutyrate (GHB)

Uses

- Clinical: FDA approved for narcolepsy with cataplexy
- Recreational: muscle developer and fat burner
- Party drug for its euphoric effects

Intoxication

- Hypotension, hypoventilation, bradycardia, sedation/LOC, amnesia

Rapidly metabolized – short-lived

Busardò, F. P., & Jones, A. W. (2015). GHB pharmacology and toxicology: acute intoxication, concentrations in blood and urine in forensic cases and treatment of the withdrawal syndrome. *Current neuropharmacology*, *13*(1), 47–70.

117

GHB

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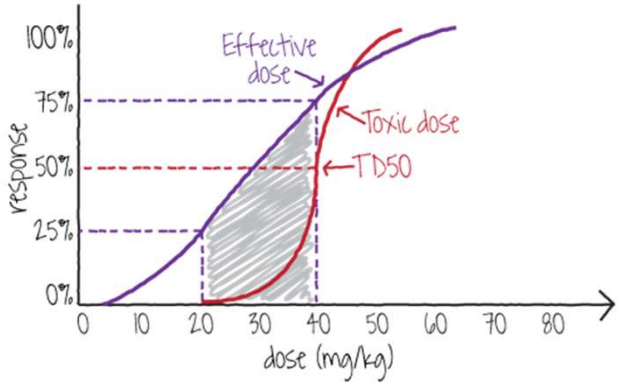
- GHB overdose is often brief with rapid recovery.



Busardò, F. P., & Jones, A. W. (2015). GHB pharmacology and toxicology: acute intoxication, concentrations in blood and urine in forensic cases and treatment of the withdrawal syndrome. *Current neuropharmacology*, *13*(1), 47–70.

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Your patient tells you “I love smoking weed, but I had to stop because I was getting tested at my job. Now I go to my local headshop and get weed from there, but it doesn’t show up on my drug tests. I like it but sometimes I get even more paranoid than when I was just buying it from my dealer.” What substance is he most likely using?

A. Synthetic cathinone

B. Synthetic cannabinoid

C. Methoxetamine

D. Dextromethorphan

119

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A. Synthetic cathinone

B. Synthetic cannabinoid

C. Methoxetamine

D. Dextromethorphan

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Synthetic cannabinoids (AKA SPICE/K2)

- Full CB1 receptor agonists (vs THC which is a partial agonist)
  - *Up to 100 times more potent than THC*
- Do not show up on routine UDS
- Peak effects are around 2-5 hrs, though effects can last for days
- Intoxication: diaphoresis, conjunctival injection, tachycardia & psychosis
- Treatment of intoxication generally centers around supportive care
- Higher use among LGB vs heterosexual adolescents

Castaneto, M. S., Gorelick, D. A., Desrosiers, N. A., Hartman, R. L., Pirard, S., & Huestis, M. A. (2014). Synthetic cannabinoids: epidemiology, pharmacodynamics, and clinical implications. *Drug and alcohol dependence*, *144*, 12–41.
Goldbach, Jeremy T., Ethan H. Mereish, and Claire Burgess. "Sexual orientation disparities in the use of emerging drugs." *Substance use & misuse* 52.2 (2017): 265-271.

121

Last note: Hallucinogen Persisting Perception Disorder

- When a person re-experiences perceptional disturbances that were initially felt under the influence of a hallucinogen when no longer using.
- Most commonly visual
- Episodic or continuous for weeks, months years
- MUST be distressing or impairing functioning
- Other causes (migraine with aura, seizure, psychosis, etc.) must be excluded

APA, DSM, Feb 2022

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SUMMARY/TAKEAWAYS

- Cocaine is a dopamine, serotonin, noradrenaline transport inhibitor
- Methamphetamines are dopamine transport inhibitors AND monoamine/dopamine releasers
- Caffeine works on adenosine receptors

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SUMMARY/TAKEAWAYS

- Classical Hallucinogens (LSD, psilocybin, Mescaline) are 5-HT2A partial agonists, which have low risk of progression to a substance use disorder.
- MDMA is an entactogen, which causes reuptake inhibition and release of serotonin, DA and NE, leading to euphoria and emotional closeness.
- Synthetic drugs like K2 and bath salts escape detection on routine UDS, and are more potent and can lead to various medical & psychiatric complications.
- Dissociative anesthetics (DXM, PCP, Ketamine) are NMDA antagonists, with differing duration of action but which cause feelings of disconnection and distorted sensory perceptions.

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Busardò, F. P., & Jones, A. W. (2015). GHB pharmacology and toxicology: acute intoxication, concentrations in blood and urine in forensic cases and treatment of the withdrawal syndrome. *Current neuropharmacology*, *13*(1), 47–70.

Castaneto, M. S., Gorelick, D. A., Desrosiers, N. A., Hartman, R. L., Pirard, S., & Huestis, M. A. (2014). Synthetic cannabinoids: epidemiology, pharmacodynamics, and clinical implications. *Drug and alcohol dependence*, *144*, 12–41.

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Goldbach, Jeremy T., Ethan H. Mereish, and Claire Burgess. "Sexual orientation disparities in the use of emerging drugs." *Substance use & misuse* 52.2 (2017): 265-271.

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Michaels, Timothy I., et al. "Inclusion of people of color in psychedelic-assisted psychotherapy: A review of the literature." *BMC psychiatry* 18.1 (2018): 1-14

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Roque Bravo, R.; Faria, A.C.; Brito-da-Costa, A.M.; Carmo, H.; Mladěnka, P.; Dias da Silva, D.; Remião, F.; on behalf of The OEMONOM Researchers. Cocaine: An Updated Overview on Chemistry, Detection, Biokinetics, and Pharmacotoxicological Aspects including Abuse Pattern. *Toxins* **2022**, *14*, 278.

CSAM

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BASIC SCIENCES & ADDICTION

AUGUST 13, 2025

CSAM Addiction Medicine Review Course

Brian Harris, MD, D.ABA, D.ABPM, Owner, EusomniaMD, PC
Revised from Waseem Khader, DO

CSAM

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CONFLICT OF INTEREST DISCLOSURE

I, Brian Harris, MD have nothing to disclose. I will not be discussing the “off-label” use of any treatments.

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EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Describe neurobiological substrates of addiction.
2. Explain basic pharmacological principles related to addiction
3. Summarize 3 phases in the prevailing neurobiological model of addiction
4. Identify genetic factors that influence risk for addiction

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BASIC SCIENCES: NEED TO KNOW

- Neural pathways and CNS regions implicated in or affected by addiction
  - *Including prevailing model of 3 phases of addiction neurobiology*
- Neurotransmitters:
  - *How they mediate effects of various substances*
  - *How they are affected by various substances*
- Hereditary & Epigenetic factors related to addiction
- Basics of pharmacokinetics as they pertain to addictive substances

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QUESTION 1

The heritability of most substance use disorders falls in the range of….?

a) 10-20%

b) 30-40%

c) 40-60%

d) 60-75%

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QUESTION 1

ANSWER: c) 40-60%

- **Heritability describes the proportion of phenotypic variability (e.g. DSM5 substance use disorder -vs- not) in a population that is attributable to genetic variation (as opposed to environmental factors).** A **2021** review indicated heritability for substance use disorders is around 50%.
- **Studies of heritability are most often twin or adoption studies, which allows correction for the confound of postnatal exposure to parental psychopathology/substance use.**

Deak JD, Johnson EC. Genetics of substance use disorders: a review. Psychol Med. 2021 Oct;51(13):2189-2200.
Ducci, F., & Goldman, D. (2012). The Genetic Basis of Addictive Disorders. *The Psychiatric Clinics of North America*, *35*(2), 495–519. http://doi.org/10.1016/j.psc.2012.03.010

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QUESTION 2

A first-time user of cocaine reports a sudden rush of euphoria and energy. Which of the following neurological pathways is primarily responsible for this effect?

a. dorsal raphe nucleus' serotonin neurons projecting to ventral striatum

b. nucleus accumbens' dopamine neurons projecting to the extended amygdala

c. ventral tegmental area's dopamine neurons projecting to dorsal raphe nucleus

d. ventral tegmental area's dopamine neurons projecting to the nucleus accumbens

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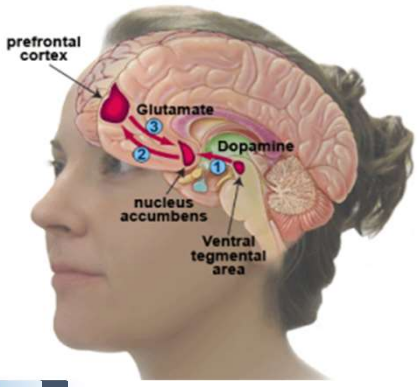
QUESTION 2

ANSWER: d) ventral tegmental area's dopamine neurons projecting to the nucleus accumbens



- The **positive reinforcing effects of substances** and pleasurable sensations due to **dopaminergic projections from the ventral tegmental area (VTA) to the nucleus accumbens (Nacc) [located in the ventral striatum] represents the neural mechanism most consistently implicated in the development of addiction**, especially in early **binge-intoxication** stages.
- The dorsal raphe nucleus is a midbrain cluster of serotonergic neurons, which may be relevant for the effects of certain substances such as hallucinogens and MDMA but is not universally implicated in substance and behavioral positive reinforcement.
- While cocaine can inhibit reuptake of multiple monoamines, its principle euphorigenic and reinforcing effects are attributed to elevations in synaptic dopamine levels.

Koob GF(1), Volkow ND(2). Neurobiology of addiction: a neurocircuitry analysis. Lancet Psychiatry. 2016 Aug;3(8):760-73. doi: 10.1016/S2215-0366(16)00104-8.

133

QUESTION 3

A 24 yo female presents to your outpatient clinic requesting help with her fentanyl addiction. She is currently smoking 1g daily. She agrees to start buprenorphine agonist treatment. In addition to its partial agonist activity at the μ-Or (Opioid Receptor), buprenorphine's therapeutic effect is mediated by:

a) **κ**-Or antagonism, **δ**-Or agonism, γ-Or agonism
b) **κ**-Or antagonism, **δ**-Or antagonism, Opioid receptor-like 1 agonism
c) **κ**-Or agonism, **δ**-Or agonism, γ-Or antagonism
d) **κ**-Or antagonism, γ-Or antagonism, **δ**-Or agonism

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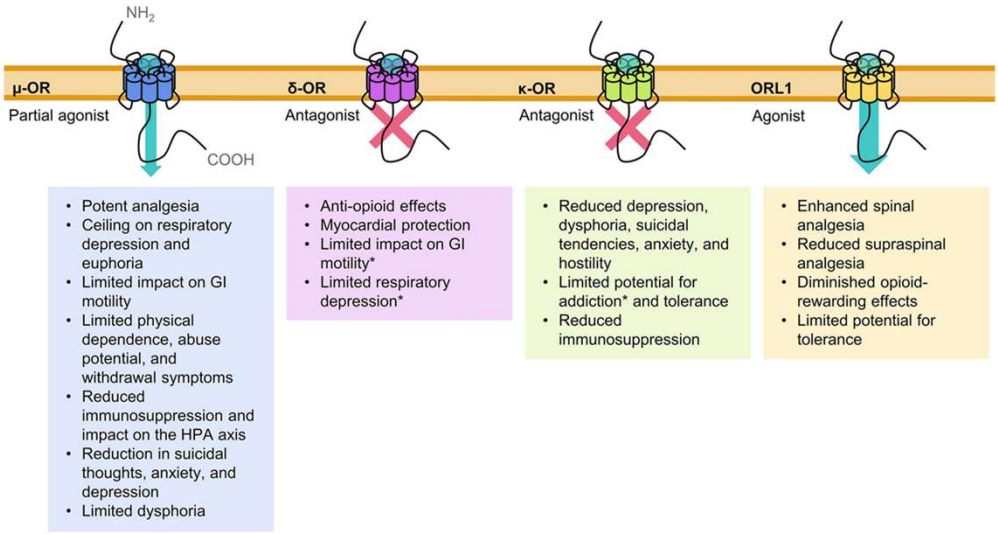
QUESTION 3

ANSWER: b) κ-Or antagonism, δ-Or antagonism, Opioid receptor-like 1 agonism



Gudin, J., Fudin, J. A Narrative Pharmacological Review of Buprenorphine: A Unique Opioid for the Treatment of Chronic Pain. Pain Ther 9, 41–54 (2020). https://doi.org/10.1007/s40122-019-00143-6

135

QUESTION 4

During the initiation phase of buprenorphine treatment, your patient experiences withdrawals and an overall negative emotional state. If you had a medication to make her more resistant to cravings driven by dysphoria, which of the following would be the best potential neurotransmitter target to <u>antagonize</u>?

a) Dopamine
b) Dynorphin
c) Gamma-aminobutyric acid (GABA)
d) Neuropeptide Y

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QUESTION 4

ANSWER: b) Dynorphin

Dynorphin is a κ-opioid, dysphoria inducing substrate whose expression can be modulated by dopamine.

Neurotransmitter	Activity level in withdrawal-negative affect stage
Dopamine	↓
Norepinephrine	↑
GABA	↓
Neuropeptide Y	↓
Dynorphin	↑
CRF	↑

Neural adaptations that occur in response to excessive activation of the reward system during chronic substance use have been described as an **"anti-reward system".**

- A **loss** in function in the brain's **reward system** can lead to **increased** activation of its **stress system**.
- **Dynorphin** levels **increase** in the nucleus accumbens and amygdala → triggers decreased dopamine production in the nucleus accumbens → **Dysphoria**
- **CRF levels increase** in the amygdala, prefrontal cortex, and VTA → **stress-like response and negative emotional state** → negatively reinforces compulsive drug use
- Stress driven negative emotional state creates motivation for negatively reinforced drug seeking known as "**the dark side of addiction.**"

Koob GF(1), Volkow ND(2). Neurobiology of addiction: a neurocircuitry analysis. Lancet Psychiatry. 2016 Aug;3(8):760-73. doi: 10.1016/S2215-0366(16)00104-8.

Koob GF, Volkow ND. Neurocircuitry of addiction. Neuropsychopharmacology. 2010 Jan;35(1):217-38. doi: 10.1038/npp.2009.110. Erratum in: Neuropsychopharmacology. 2010 Mar;35(4):1051. PMID: 19710631; PMCID: PMC2805560.

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QUESTION 5

Case:
A 34-year-old man presents for evaluation of kratom use. He reports daily ingestion of kratom tea to "manage pain" and "boost energy." He recently developed nausea, diarrhea, and mild withdrawal symptoms when he tried to stop. You counsel him about kratom's neuropharmacologic profile and risks.

QUESTION:
Which of the following best describes the principal mechanism of action for kratom's primary alkaloid at therapeutic doses?

A) Full μ-opioid receptor agonism with high intrinsic activity

B) Partial μ-opioid receptor agonism and κ-opioid receptor antagonism

C) Full κ-opioid receptor agonism and norepinephrine reuptake inhibition

D) Mixed μ-opioid receptor agonism and NMDA receptor antagonism

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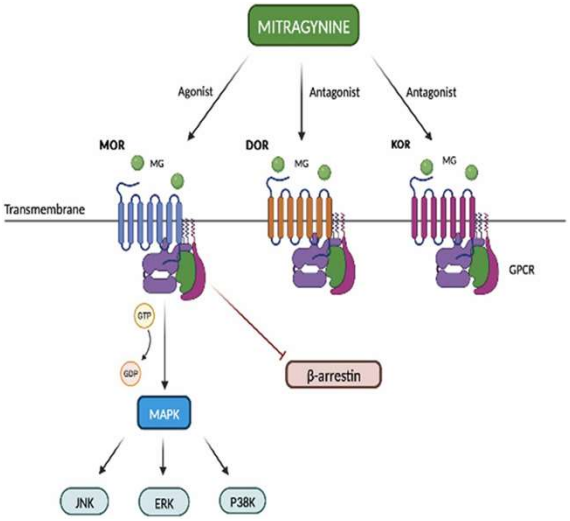
QUESTION 5

ANSWER: B) Partial μ-opioid receptor agonism and κ-opioid receptor antagonism

Mitragynine, kratom's primary alkaloid, functions primarily as a **partial** μ-opioid receptor **agonist** and a κ-opioid receptor **antagonist**. This dual action explains its analgesic properties, milder euphoria, and reduced respiratory depression risk compared to full μ-opioid agonists. Its κ-antagonism helps counteract dysphoria linked to κ receptor activation.

Detractors:
A) Mitragynine: not a full, but partial μ agonist; ceiling effect for respiratory depression.
C) Primary effects aren't via full κ agonism; NE reuptake is mild and incidental
D) Doesn't block NMDA receptors (think ketamine, methadone, magnesium)



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QUESTION 6

A 30 yo male presents to the inpatient substance use recovery unit for acute withdrawal management of alcohol intoxication in the presence of severe alcohol use disorder. He reports his last drink was 5 hours ago and his BAC at the time of admission is 350 mg/dL. You expect his BAC to be approximately_____ 10 hours later, putting him at increased risk for which of the following complications_____?

a) 250 mg/dL; delirium tremens

b) 25 mg/dL; alcohol withdrawal seizures

c) 150 mg/dL; alcohol withdrawal seizures

d) 150 mg/dL; delirium tremens

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QUESTION 6

ANSWER: c) 150mg/dL (0.15mg%); alcohol withdrawal seizures

- The rate of alcohol metabolism varies between individuals but is about 10-15mg/dL/hr and as high as 20-30mg/dL/hr for individuals who drink large quantities of alcohol chronically
- 90% of people do not progress beyond mild-moderate symptoms of alcohol withdrawals (i.e. tachycardia, elevated blood pressure, nausea, headaches, sleep disturbance, anxiety)
- Alcohol withdrawal seizures begin about 8-24 hours and peak about 24-48 hours after the last drink.
- Delirium tremens (DTs) appear about 72-96 hours after the last drink. DTs is characterized as severe delirium that is accompanied with an autonomic storm (i.e. marked tachycardia, tremors, diaphoresis, and fevers) as well as auditory and visual hallucinations

Herron, A., & Brennan, T. K. (2019). The ASAM Essentials of Addiction Medicine. LWW.

141

QUESTION 7

Which of the following is an example of an epigenetic phenomenon?

a) Exposure to chronic neighborhood violence in childhood causes DNA methylation and deactivation of a gene encoding a neuronal growth factor

b) Exposure to a substance causes a DNA mutation in a gene encoding the serotonin transporter

c) Mitochondrial disorders are inherited exclusively from the mother of offspring

d) People in a certain country have exceedingly low risk for alcohol use disorder because alcohol is illegal and very difficult to access

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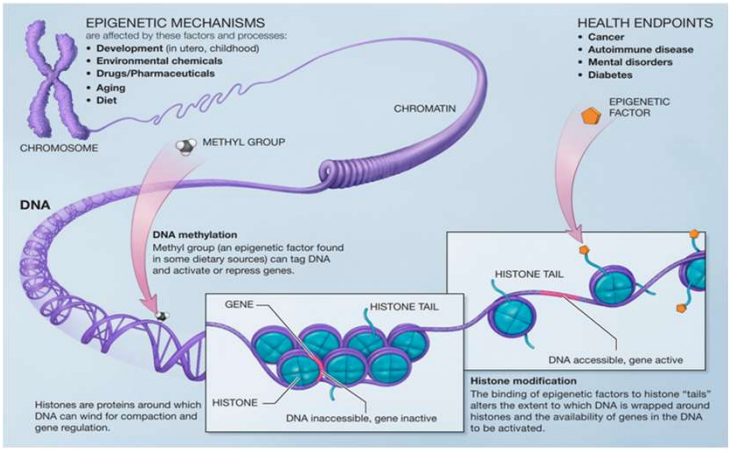
QUESTION 7

ANSWER: a) Exposure to chronic neighborhood violence in childhood causes DNA methylation and deactivation of a gene encoding a neuronal growth factor

EPIGENETICS

- Alterations in expression of the genome that do not alter the DNA base pair sequence
- Common examples involve **DNA methylation** (which can turn on/off gene expression) and **histone modification** that affects how DNA is coiled
- Such epigenetic changes are often heritable to daughter cells and sometimes to offspring
- Epigenetics may play a role in mediating the effects of certain environmental risk factors for addiction (especially adverse childhood events). Such risk factors (e.g. poverty, unsafe neighborhoods) are often disproportionately present in minoritized communities.



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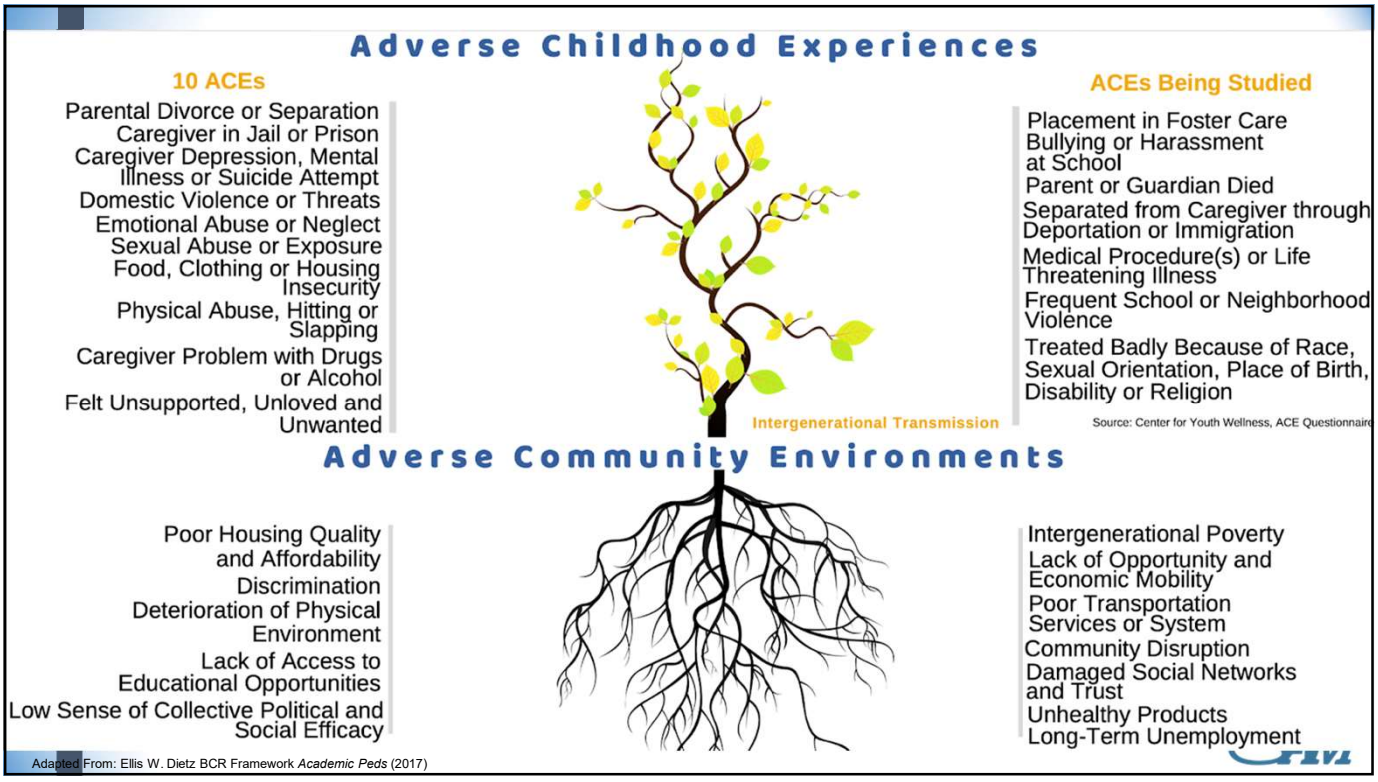

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QUESTION 8

Which of the following <u>INCORRECTLY</u> pairs a neuroanatomical region with one of its putative roles in the risk and/or protection from substance use disorders?

a) Dorsal striatum → Executing habitual substance use behaviors
b) Dorsolateral prefrontal cortex → Cognitive flexibility and planning
c) Extended amygdala → Positive reinforcement & euphoria
d) Orbitofrontal cortex → Processing motivational salience of stimuli

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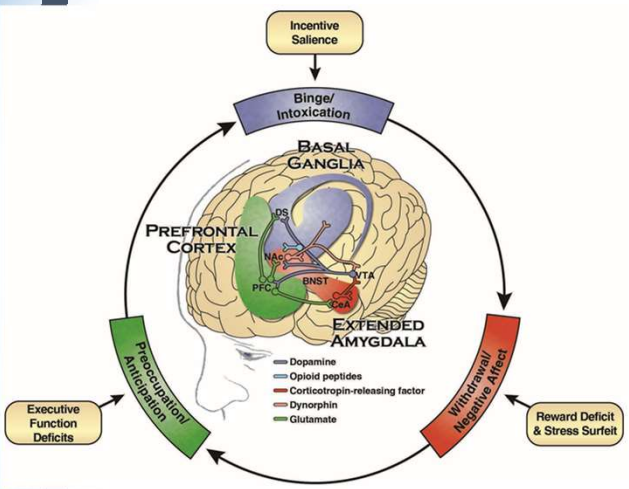
QUESTION 8

ANSWER: c) Extended amygdala → Positive reinforcement & euphoria



BRAIN REGION	ROLE IN ADDICTION
Ventral striatum	<u>Reward</u> processing & prediction, <u>euphoria</u>
Dorsal striatum	<u>Habitualization</u> of drug seeking & taking
Dorsolateral PFC	(malfunctioning) Preoccupation, <u>craving</u>, lack of planning, delay discounting, <u>poor executive functions</u>, poor impulse control
Extended amygdala & Habenula	Withdrawal related stress/dysphoria; encoding negative feedback
Orbitofrontal cortex	Salience attribution (learning, predicting & decision making for emotional & reward related behaviors)

Koob, G. F. (2021). Drug addiction: hyperkatifeia/negative reinforcement as a framework for medications development. *Pharmacological reviews*, *73*(1), 163-201.

146

QUESTION 9

Which of the following is a <u>TRUE</u> statement about genetic and environmental influences on the development of addiction?

a) Both genetic & environmental factors are equally influential on risk for substance initiation and substance addiction

b) Environmental factors exert a greater influence on risk for substance initiation than for substance addiction

c) Genetic factors exert a greater influence on risk for substance initiation than for substance addiction

d) Genetic factors have no influence on substance initiation.

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QUESTION 9

ANSWER: b) Environmental factors exert a greater influence on risk for substance initiation than for substance addiction

- Given the average heritability of addiction is 50%, one can infer about a 50-50 split for genetic vs environmental influence on the development of substance use disorders.
- Genetics also influence substance initiation (thus also indirectly influencing addiction risk) since genetics influences personality traits such as impulsivity & reward dependence as well as psychiatric disorders that influence drug initiation risk, but environmental factors are stronger in determining initiation of substance use (e.g., never use, early-onset use, late-onset use).
- Genetics, however, plays a bigger role in determining risk among those who initiate a substance to go on to development unhealthy use/addiction, especially as adolescents transition into adulthood.

Rhee SH, et al. Genetic and environmental influences on substance initiation, use, and problem use in adolescents. Arch Gen Psychiatry. 2003 Dec;60(12):1256-64.
Fowler T, et al. Exploring the relationship between genetic and environmental influences on initiation and progression of substance use. Addiction. 2007 Mar;102(3):413-22.
Meyers JL, Dick DM. Genetic and environmental risk factors for adolescent-onset substance use disorders. Child Adolesc Psychiatr Clin N Am. 2010 Jul;19(3):465-77.

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QUESTION 10

Which of the following correctly matches the primary inhibitory neurotransmitter system in the CNS to the pharmacologic characteristics of its receptor?

a) $GABA_A$ receptor → Metabotropic heterodimer composed of R1 and R2 heptahelical membrane protein subunits

b) $GABA_A$ receptor → Ionotropic transmembrane pentamer consisting of 2α, 2β, 1γ subunits

c) Glutamate NMDA receptor → Ionotropic assembly of seven subunits (GluN1, GluN2A-D, GluN3A-B) into tetrameric receptor complexes

d) Serotonin 5HT-1A receptor → Metabotropic polypeptide chain of 422 amino acids with an α-helical structure, forming 7 transmembrane domains

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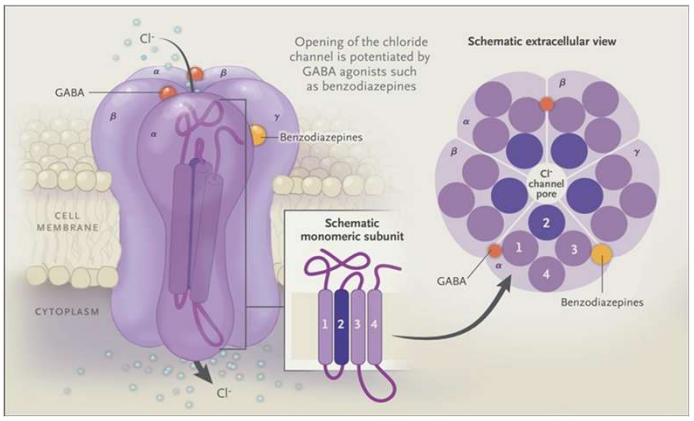
QUESTION 10

ANSWER: b) $GABA_A$ receptor → Ionotropic transmembrane **pentamer** consisting of 2α, 2β, 1γ subunits

RECEPTOR	TYPE
D1-D5	Metabotropic
Nicotinic Ach	Ionotropic
Muscarinic Ach	Metabotropic
5HT 1, 2, 4-7	Metabotropic
5HT3	Ionotropic
α & β adrenergic	Metabotropic
Glu NMDA, AMPA	Ionotropic
GABA-A	Ionotropic
GABA-B	Metabotropic



The ASAM Principles of Addiction Medicine, 6th edition
Soyka M. N Engl J Med 2017;376:1147-1157.

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QUESTION 11

Which of the following neurotransmitters is primarily responsible for the increase in blood pressure and heart rate during substance withdrawal?

a) Glutamate

b) GABA

c) Dopamine

d) Norepinephrine

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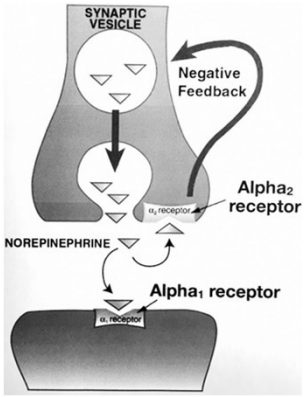
QUESTION 11

ANSWER: d) Norepinephrine

Receptor	*Physiologic Action (Agonism)*
α1	Constriction of vascular smooth muscle Contraction of radial muscle of the eye Contraction of the vas deferens smooth muscle
α2	Inhibition of norepinephrine release from presynaptic neuron Centrally induced sedation via locus ceruleus Centrally mediated pain modification via dorsal horn Inhibition of insulin release from pancreatic β cells
β1	Increased cardiac output (increased chronotropy, dromotropy, inotropy) Increased renin release from kidney
β2	Bronchial smooth muscle relaxation Vascular smooth muscle relaxation (vasodilation) Reduction of mast cell degranulation and histamine release
β3	Increased adipose tissue lipolysis



Giovannitti, J. A., Jr, Thoms, S. M., & Crawford, J. J. (2015). Alpha-2 adrenergic receptor agonists: a review of current clinical applications. *Anesthesia progress*, *62*(1), 31–39. https://doi.org/10.2344/0003-3006-62.1.31

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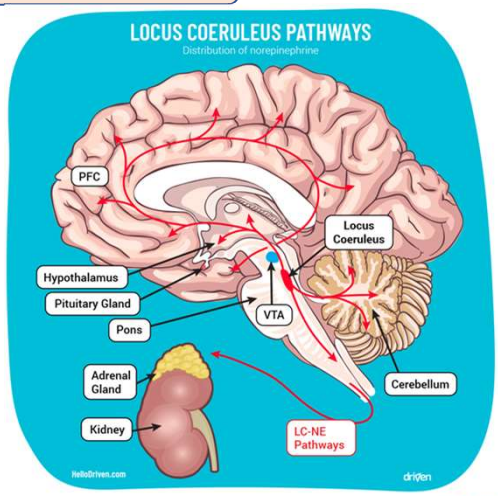
QUESTION 11

ANSWER: d) Norepinephrine

- NE plays a significant role in stress-induced reinstatement of drug-seeking behaviors as well as withdrawal processes
- In an acute setting, peripheral NE signaling via the sympathetic nervous system, in concert with central NE signaling upon the HPA axis, instigate the “flight or fight” response.
- Locus Coeruleus contains the largest number of central noradrenergic neurons and they project to almost all areas of the forebrain
- Noradrenergic drugs such as the α2 agonists clonidine and lofexidine are effective at reducing opioid withdrawal symptoms



Downs, A. M., & McElligott, Z. A. (2022). Noradrenergic circuits and signaling in substance use disorders. *Neuropharmacology*, *208*, 108997. https://doi.org/10.1016/j.neuropharm.2022.108997

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QUESTION 12

A 29-year-old man presents for evaluation of daily cannabis use. He reports smoking high-potency marijuana to "calm down" but notes increasing anxiety and irritability without it. You counsel him about the neurobiology of cannabis dependence.

THC’s psychoactive effects are primarily mediated by which of the following mechanisms?

A) Direct activation of ionotropic cannabinoid receptors on presynaptic terminals

B) Mimicry of endocannabinoid retrograde signaling at CB1 receptors

C) Inhibition of postsynaptic serotonin reuptake

D) Stimulation of nicotinic acetylcholine receptors in the ventral tegmental ar

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QUESTION 12

ANSWER: B) Mimicry of endocannabinoid retrograde signaling at CB1 receptors.
THC mimics endogenous cannabinoids (e.g., anandamide) and binds CB1 receptors, inhibiting neurotransmitter release via retrograde signaling—In this process, postsynaptic activity regulates presynaptic neurotransmitter release.

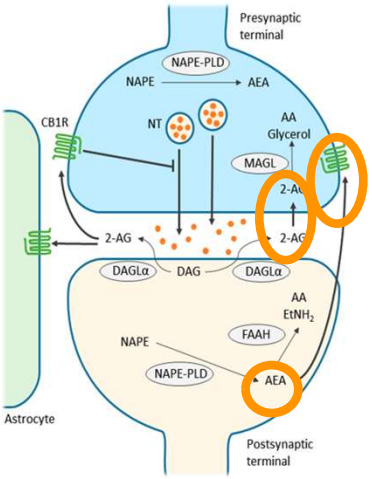
Retrograde signaling

- Post-synaptic neurons communicate to pre-synaptic neurons
- Classic examples are **endocannabinoids** and nitrous oxide

A) CB1 receptors are metabotropic, not ionotropic.

C) THC doesn't modulate serotonin reuptake.

D) Nicotinic receptors in the VTA are key in nicotine dependence, not THC.



AEA = anandamide
AA = arachidonic acid
DAG = diacylglycerol
2-AG – 2-arachodonal glycerol
FAAH = fatty acid amide hydrolase
MAG = monoacylglycerol lipase

Zou S, Kumar U. Cannabinoid Receptors and the Endocannabinoid System: Signaling and Function in the Central Nervous System. Int J Mol Sci. 2018 Mar 13;19(3):833.

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QUESTION 13

A 28-year-old woman with opioid use disorder is enrolled in a medication-assisted treatment program. She has been abstinent from heroin for several months while on buprenorphine-naloxone. During a counseling session, she reports that visiting a neighborhood where she used to obtain heroin triggered intense cravings despite her abstinence. She asks about the neurobiological reason why certain places or situations make her feel a sudden urge to use again.

Which of the following best explains the neurobiological mechanism underlying her cue-induced craving?

A) Chronic opioid exposure leads to permanent depletion of dopamine in the ventral tegmental area, causing persistent anhedonia that drives drug-seeking behavior

B) Repeated drug use strengthens glutamatergic projections from the prefrontal cortex to the nucleus accumbens, sensitizing the reward system to conditioned environmental cues

C) Environmental cues associated with drug use activate learned associations in the amygdala and hippocampus, which send glutamatergic projections to the nucleus accumbens core, triggering dopamine release and craving

D) Chronic opioid exposure upregulates GABA receptors in the locus coeruleus, leading to enhanced noradrenergic activity during withdrawal rather than in response to environmental cues

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QUESTION 13

Explanation (Correct Answer: C)

Cue-induced craving arises when environmental cues activate learned associations in the amygdala and hippocampus. These regions send glutamatergic projections to the nucleus accumbens core, triggering dopamine release and craving.

Detractors:

A) Dopamine is not permanently depleted; the reward system is dysregulated but not irreversibly damaged.

B) While glutamatergic sensitization occurs, the critical projections for cue-induced craving are from the amygdala/hippocampus rather than primarily the prefrontal cortex.

D) Noradrenergic activity from the locus coeruleus is relevant to withdrawal, not cue-induced craving.

Koob GF, Volkow ND. *Lancet Psychiatry.* 2016;3(8):760-773.
Kalivas PW, Volkow ND. *Am J Psychiatry.* 2005;162(8):1403-1413.
Volkow ND, Morales M. *Cell.* 2015;162(4):712-725.

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Fin

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Need To Know High-Yield Pearls: Basic Sciences of Addiction Medicine

1) Neurobiological Substrates of Addiction

- Core addiction circuitry: VTA dopamine projections → nucleus accumbens mediate reinforcement in binge/intoxication phase.
- Extended amygdala mediates negative affect and stress in withdrawal/negative affect phase ("anti-reward" system).
- Dorsal striatum contributes to habit formation in the preoccupation/anticipation phase.
- Orbitofrontal cortex processes motivational salience of drug cues; amygdala/hippocampus form cue associations triggering craving.
- Cue-induced craving: Glutamatergic projections from amygdala/hippocampus → nucleus accumbens core → dopamine release → craving.

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2 Basic Pharmacological Principles Related to Addiction

- Buprenorphine: Partial μ-opioid agonist + κ-opioid antagonist + ORL-1 agonist → analgesia with ceiling effect on respiratory depression.
- Kratom (mitragynine): Partial μ-opioid agonist + κ-opioid antagonist → analgesia, mild euphoria, reduced respiratory depression risk.
- Alcohol metabolism: ADH saturation → zero-order kinetics → constant amount metabolized per hour.
- Norepinephrine: Key driver of autonomic symptoms in withdrawal; α2-agonists (clonidine, lofexidine) mitigate symptoms.
- GABA-A receptor: Ionotropic pentamer (2α, 2β, 1γ); primary inhibitory receptor targeted by substances like alcohol and benzodiazepines.
- THC: Mimics endocannabinoids → binds CB1 receptors → retrograde inhibition of neurotransmitter release.

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3 Three Phases of Addiction Neurobiology

- Binge/intoxication: VTA → nucleus accumbens dopamine surge, driving reinforcement.
- Withdrawal/negative affect: Extended amygdala, dynorphin (κ-opioid agonism), CRF drive dysphoria, stress, negative reinforcement.
- Preoccupation/anticipation: Prefrontal cortex, amygdala, hippocampus activate craving and planning for drug use.

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4 Genetic Factors Influencing Risk

- Heritability of SUDs: ~40–60% across substances.
- Genetic influence: Greater on progression to addiction than on initiation.
- Epigenetics: Adverse childhood environment → DNA methylation of neuronal genes → altered expression without DNA sequence change.

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Neurotransmitters, Substances, and Pharmokinetics

Neurotransmitters – Mediation of Effects

- **Glutamate:** Central in neuroplasticity of addiction; chronic substance use strengthens glutamatergic projections (amygdala/hippocampus → NAc), promoting sensitization and relapse vulnerability.
- **Serotonin:** Modulates mood and impulsivity; hallucinogens (LSD, psilocybin) and MDMA primarily act via serotonin receptor agonism or serotonin release, contributing to their psychoactive effects.

Neurotransmitters – Alterations by Substances

- **Stimulants (e.g., cocaine, methamphetamine):** Lead to dopamine transporter dysfunction and downregulation of postsynaptic dopamine receptors → blunted reward responsiveness.
- **Chronic alcohol use:** Upregulates NMDA glutamate receptors and downregulates GABA-A receptor function → contributes to excitatory-inhibitory imbalance and withdrawal hyperexcitability.
- **Chronic opioid use:** Suppresses endogenous opioid peptide production → enhances dependence on exogenous opioids for normal function.

Pharmacokinetics

- **Lipid solubility:** Highly lipophilic substances (e.g., THC, fentanyl) rapidly cross the blood-brain barrier, leading to quick onset of CNS effects.
- **First-pass metabolism:** Orally ingested substances (e.g., alcohol, methadone) undergo hepatic metabolism before reaching systemic circulation, affecting bioavailability.
- **Active metabolites:** Some substances (e.g., diazepam, methadone) have metabolites that contribute to prolonged duration of action and potential accumulation with chronic use.

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Legal Aspects of Addiction Medicine

August 13, 2025
2025 CSAM Conference - Test Taking Track

Brian Harris, MD, D.ABA, D.ABPM, Owner, EusomniaMD, PC
Revised from Takeo Toyoshima, MD, MRO

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Educational Objectives

After attending this presentation, participants will be able to:

- Describe key relevant aspects of federal legislation 42 CFR Part 2 which regulates privacy and confidentiality in the practice of addiction medicine
- Name other key landmark legislation that applies to addiction medicine in the US
- Understand key ethical and legal principles that might present in the practice of addiction medicine

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Conflicts of Interest

- None pertinent to this presentation

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1. 42 CFR Part 2 protects patient privacy in relation to:

A. Substance use disorders

B. Genetic diseases

C. HIV/AIDS

D.Psychiatric Treatment

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Correct: A. Substance use disorder diagnosis, treatment, or referral

Explanation:

42 CFR Part 2 applies solely to records related to SUD care in federally assisted programs.

Why detractors are wrong:

B. Genetic diseases fall outside Part 2; HIPAA may apply.

C. HIV/AIDS records are not addressed by Part 2.

D. General psychiatric records are outside its scope unless tied to SUD services.

References:

42 CFR §2.1–2.3
ASAM Principles of Addiction Medicine, 6th ed, p. 1535

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2. Which of the following is not covered under 42 CFR Part 2?

A. A private, for-profit opioid treatment program that administers buprenorphine

B. A family medicine physician who practices as a generalist and occasionally treats SUDs, including prescribing buprenorphine for OUD

C. An addiction physician employed by a large hospital system

D. A non-profit, 501(c)(3) residential SUD treatment program

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Correct: B. A family physician who occasionally treats SUDs in general practice

Explanation:

Part 2 applies to entities or individuals who hold themselves out as primarily providing SUD care, not generalists treating SUDs sporadically.

Why detractors are wrong:

A, C, D, These are "programs" under Part 2 or federally assisted entities.

References:

42 CFR §2.11
ASAM Principles, p. 1535

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Title 42 of the Code of Federal Regulations

"Program" (42 CFR§2.11)

- *"Federally assisted"*
- *"Hold itself out"* as providing/primarily providing SUD diagnosis, treatment, referral
- Individual, entity, unit within a hospital/clinic, etc.

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3. Which of the following **IS NOT necessarily "federally assisted"** under 42 CFR Part 2?

A. A private, for-profit addiction treatment program

B. A SAMHSA-certified opioid treatment program

C. A private practice physician who prescribes scheduled substances for SUD treatment

D. A non-profit, 501(c)(3) residential SUD treatment program

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Correct: A) Private, for-profit SUD program without federal funding or certifications

Why correct:

Lacks federal assistance, tax benefits, or certification.

Why detractors are wrong:

B, C, D. All meet criteria for federal assistance (certifications, licenses, or tax benefits).

References:

42 CFR §2.12(b)
ASAM Principles, p. 1535

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42 CFR Part 2: "*Federally assisted*"

1. Authorized, licensed, certified, or registered by federal department or agency
   - Medicare
   - SAMHSA certification
   - DEA license
2. Receives federal funds including financial assistance, revenue sharing
3. Assisted by Internal Revenue Service (IRS) of the Department of Treasury
   - Income tax deductions
   - Tax exempt status
4. Managed by a federal agency or office
   - Exceptions: Veterans Affairs, Armed Forces

A private, for-profit treatment program that does not prescribe medications, not reimbursed by CMS programs, without federally-supported certifications, etc., may be exempt from 42 CFR Part 2, but these are far and few between.

Department of Health and Human Services. Confidentiality of Substance Use Disorder Patient Records, Title 42, Code of Federal Regulations, Part 2. Available at: https://www.ecfr.gov/current/title-42/chapter-I/subchapter-A/part-2

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4. Which of the following is ***NOT*** required as part of a patient's written consent under 42 CFR Part 2?

A. Full name and signature of the patient with date of signature

B. Conditions under which consent will expire

C. Purpose of the disclosure

D. A specific form approved by Substance Abuse and Mental Health Services Administration (SAMHSA)

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Correct: D. A SAMHSA-approved specific form

Why correct:

No mandated form; required elements can appear on any form.

Why detractors are wrong:

A, B, C. All required under 42 CFR §2.31

References:

42 CFR §2.31
ASAM, p. 1536

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42 CFR Part 2: Consent Requirements

1. **Name**
2. **Who is permitted** to make disclosure from Part 2 program
3. **How much and what kind of information** is to be disclosed
4. Names of the **individuals/entities to which a disclosure** is to be made
5. The **purpose of the disclosure**, with information limited to what is necessary for this purpose
6. A **statement that the consent is subject to revocation** at any time
   - Exception to PHI that has already been disclosed in reliance of existing consent

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42 CFR Part 2: Consent Requirements

7. The date, event, or condition upon which the **consent will expire**
8. The **signature** of the patient
   - For minor, the signature of individual(s) authorized to give consent on behalf
   - Electronic signatures as long as not prohibited by other laws
9. The **date** on which the consent is signed

If these required elements are on an organization's form, 42 CFR Part 2 does not require use of a standardized form.

Department of Health and Human Services. Confidentiality of Substance Use Disorder Patient Records, Title 42, Code of Federal Regulations, Part 2. 2023. Retrieved from: https://www.ecfr.gov/current/title-42/chapter-I/subchapter-A/part-2

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5. Under 42 CFR Part 2, disclosure without patient consent is allowed except for:

A. Medical emergency

B. A subpoena by a lawyer

C. A crime on a Part 2 program premise

D. A report of child abuse/neglect

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Correct: B. Subpoena by attorney

Why correct:

A subpoena alone is insufficient; requires court order.

Why detractors are wrong:

A, C, D. Explicit exceptions under Part 2.

References:

42 CFR §2.12(c)
ASAM, p. 1537

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42 CFR Part 2: Disclosures without Consent

1. Medical emergencies
2. Child abuse or neglect reports required by state law
3. Crime committed by patient on program premises or against personnel
4. Court orders authorizing disclosure and use of Part 2 records*
5. Research and Qualified Audits/Evaluations
6. Internal communications
7. To other local programs to prevent multiple enrollments and to prescription database monitoring programs

*Court order is different from subpoena drafted by attorney. Latter can be quashed (i.e., cancelled), modified, etc. But DO NOT IGNORE A SUBPOENA.

Department of Health and Human Services. Confidentiality of Substance Use Disorder Patient Records, Title 42, Code of Federal Regulations, Part 2. Retrieved from: https://www.ecfr.gov/current/title-42/chapter-I/subchapter-A/part-2

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6. A 43-year-old man with severe alcohol use disorder is brought to the emergency department after a suicide attempt. He denies suicidal intent on interview but appears disoriented and repeatedly expresses hopelessness. The physician decides to place the patient on an involuntary psychiatric hold for further evaluation. Under California law, which legal mechanism is most applicable?

A. Tarasoff duty
B. 5150 hold
C. Court-ordered guardianship
D. Ryan Haight Act

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Correct: B. 5150 hold: Under California law, a 5150 hold allows for a 72-hour involuntary psychiatric hold for individuals with a mental disorder who are a danger to self, others, or gravely disabled. SUD-related suicidality would meet this requirement.

Incorrect choices:

- **A. Tarasoff duty:** This applies to duty to warn/protect identifiable third parties from patient threats—not to initiate involuntary holds.
- **C. LPS/Court-ordered conservatorship:** This is a civil process specific to California for appointing someone to make decisions for an incapacitated individual, not an emergent involuntary detention tool. In other states, this may be referred to as either guardianship or conservatorship.
- **D. Ryan Haight Act:** This regulates online prescribing of controlled substances; irrelevant to involuntary psychiatric holds.

Reference:

- California Welfare and Institutions Code §5150
- Mental Health Professionals' Duty to Warn. National Conference of State Legislatures. https://www.ncsl.org/health/mental-health-professionals-duty-to-warn
- Miller SC, Fiellin DA, Rosenthal RN, Saitz R. *ASAM Principles of Addiction Medicine*, 6th ed. Wolters Kluwer; 2019.

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7. A 32-year-old woman with opioid use disorder brings her 2-year-old to clinic. The child appears malnourished, unkempt, and lethargic. The mother discloses that she has been using heroin daily and struggling to care for the child. What is the physician's legal obligation in most U.S. jurisdictions?

A. File a mandatory report with child protective services

B. Refer the patient to a social worker while maintaining confidentiality

C. Encourage the mother to self-report

D. Obtain a court order before breaching confidentiality

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Correct: A. File a mandatory report with child protective services- In nearly all U.S. states, physicians are mandated reporters when they suspect child abuse or neglect, including situations where parental substance use jeopardizes child welfare. 42 CFR Part 2 does *not* override these obligations.

Incorrect choices:

- **B. Refer + maintain confidentiality:** Referral is helpful, but does not satisfy legal duty. Reporting is mandatory once neglect is reasonably suspected.
- **C. Encourage self-report:** Ethically desirable, but does not fulfill the physician's independent legal obligation to report.
- **D. Obtain court order:** Not required; mandated reporting laws provide the legal authority for disclosure.

Reference:

- 42 CFR §2.12(c)(6) – disclosures for child abuse/neglect permitted without consent
- Child Welfare Information Gateway. *Mandatory reporters of child abuse and neglect.* U.S. Department of Health and Human Services. https://www.childwelfare.gov/pubPDFs/manda.pdf
- ASAM Principles of Addiction Medicine, 6th ed.

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8. A 38-year-old man with opioid use disorder is treated with methadone. His EKG shows QTc 540 ms after dose escalation. Despite counseling on risk, the patient refuses dose reduction, fearing relapse. The physician reduces the dose to mitigate cardiac risk. Which ethical principle most justifies the physician's decision?

A. Autonomy

B. Beneficence

C. Non-maleficence

D. Justice

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Correct Answer: C. Non-maleficence The primary ethical driver was avoiding harm (i.e., preventing torsades de pointes and sudden death). This principle outweighed respect for the patient's preference.

Detractors:

A. Autonomy: Important, but not absolute; can be overridden to prevent significant harm.

B. Beneficence: The physician acted to benefit the patient, but the overriding concern was harm prevention, making non-maleficence the stronger justification.

D. Justice: Unrelated; justice pertains to fair treatment and distribution of resources, not individual risk mitigation.

References

- Miller SC, Fiellin DA, Rosenthal RN, Saitz R. *ASAM Principles of Addiction Medicine*, 6th ed.
- Beauchamp TL, Childress JF. *Principles of Biomedical Ethics*, 7th ed.

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Basic Principles of Medical Ethics

Beneficence: for the benefit of the patient

Nonmaleficence: obligation to not harm

Autonomy: right to self-determination, free of coercion

Justice: fair, equitable, and appropriate treatment, including appropriation of resources

Miller SC Fiellin DA Rosenthal RN Saitz R American Society of Addiction Medicine. The ASAM Principles of Addiction Medicine. Sixth ed. Philadelphia: Wolters Kluwer; 2019.

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9. *Your patient discloses thoughts of wanting to kill their partner. They also disclose a plan and access to means. With clinic staff, you decide to break confidentiality and call the partner and law enforcement. Which of the following legal/ethical principles was applied?*

A. Duty to Warn/Protect (Tarasoff)

B. Beneficence

C. Justice

D. Duty to treat

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Correct: A. Duty to warn/protect

Why correct:

Tarasoff v. Regents of UC established the precedent for the duty to warn/protect. In California (and many other states), this duty is now codified in statute. Depending on jurisdiction, Tarasoff statutes may impose a duty to warn and/or protect when there is a serious threat to identifiable person(s)

Why detractors are wrong:

B, C, D. General ethics, but not specific duty in this context.

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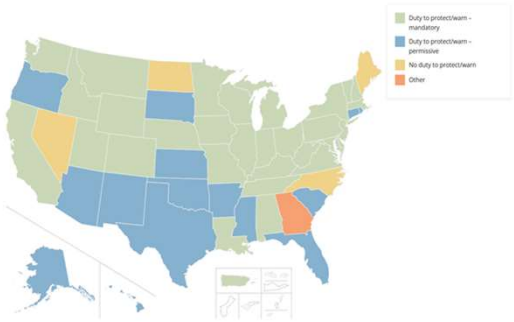
Duty to Warn/Protect

- *Tarasoff v. Regents of the University of California*, CA Supreme Court, 1976
- Duty to Warn v Protect
  - (Potentially) identifiable targets
  - Protect = hospitalize, tx adjustment, etc.
- Jurisdiction-dependent
- Discipline/practice-dependent
  - In CA, Tarasoff applies only to "psychotherapists"



Mental Health Professionals' Duty to Warn. National Conference of State Legislatures. Available at: https://www.ncsl.org/health/mental-health-professionals-duty-to-warn

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10. A 38-year-old man with severe opioid use disorder dies of an opioid overdose three weeks after his final visit with you. The patient had declined buprenorphine despite your repeated offers but was receiving supportive care and frequent follow-up. His spouse files a malpractice suit, alleging negligence in the patient's death. Which element of malpractice will most likely become the central focus of litigation?

A. Duty

B. Dereliction/Deviation from Standard of Care

C. Direct Cause

D. Damages

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Correct Answer: B. Dereliction/Deviation from Standard of Care

Why B is correct:
In most malpractice cases, the focal dispute is whether the physician *breached* the standard of care. The plaintiff must show not just that harm occurred, but that the provider *acted negligently* or omitted appropriate action. In addiction medicine, this often centers on whether the provider should have escalated care, coerced treatment, or intervened more aggressively in the setting of known overdose risk.

Why the others are incorrect:

- **A. Duty** is usually straightforward to establish when a treatment relationship exists.
- **C. Direct Cause** can be debated, but without a breach of duty, causation alone doesn't suffice for liability.
- **D. Damages** (death) are present and rarely contested—malpractice suits almost never hinge on this element.

Pearl:

Malpractice requires all four D's: Duty, Dereliction, Direct Cause, and Damages. But the element that's most often litigated—and most under physician control—is **Dereliction**. Even in emotionally charged overdose cases, if standard of care was followed and documented, liability is difficult to prove.

References:

ASAM Principles of Addiction Medicine, 6th ed., p. 1528
Bal BS. *An Introduction to Medical Malpractice in the United States*. Clin Orthop Relat Res. 2009

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The 4 D's of Medical Malpractice

Duty A patient-physician relationship existed, establishing a legal obligation to provide care.

- *Example:* Giving clinical advice after assuming care, even informally, establishes duty.

Dereliction (Deviation from Standard of Care): The physician failed to act as a reasonably competent peer would in similar circumstances.

- *Example:* Not offering naloxone to a high-risk patient may be a breach.

Direct Cause: The breach led directly to the harm—i.e., but for the dereliction, injury would not have occurred.

- *Example:* Failure to act on signs of overdose risk results in a preventable death.

Damages: Actual harm occurred—physical, emotional, or financial. No harm, no malpractice.

- *Example:* A documentation error without resulting injury doesn't meet this threshold.

Bal BS. An introduction to medical malpractice in the United States. Clin Orthop Relat Res. 2009;467(2):339-347.

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Fin

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Need To Know High-Yield Pearls – Legal Aspects of Addiction Medicine

42 CFR Part 2 & Confidentiality

- **42 CFR Part 2 applies to "federally assisted" programs providing SUD diagnosis, treatment, or referral** — includes those with federal funding, DEA registration, or tax-exempt status (ASAM p. 1535).
- **Disclosure without consent under 42 CFR Part 2 is permitted** for medical emergencies, mandatory child abuse/neglect reporting, crimes on program premises, and via court order — *not* for subpoenas alone (ASAM pp. 1536-1537).
- **A valid 42 CFR Part 2 consent must specify**: patient name, disclosure purpose, recipient, info type, revocation rights, expiration condition/date, patient signature — no specific SAMHSA form required (ASAM p. 1535).

Duty to Warn / Protect

- **Tarasoff v. Regents of UC established the duty to warn/protect identifiable third parties at risk from a patient** — applies to psychotherapists, varies by state (ASAM p. 1537).

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Involuntary Treatment / Civil Commitment

- **A 5150 hold in California authorizes up to 72-hour involuntary hospitalization** for danger to self/others or grave disability due to mental disorder, including SUD-related suicidality (ASAM pp. 1540–1542).
- **5250 hold extends hospitalization beyond 72 hours (up to 14 days)**, but requires prior 5150 evaluation (ASAM p. 1542).

Mandatory Reporting

- **Physicians are mandated reporters of suspected child abuse or neglect in all U.S. jurisdictions** — 42 CFR Part 2 does not override this obligation (ASAM p. 1536).

Medical Ethics in Addiction Medicine

- **Non-maleficence (do no harm) may override autonomy when patient decisions risk serious harm** (e.g., methadone QT prolongation) (ASAM p. 1525).
- **Beneficence means acting for the patient's benefit; justice concerns fairness and equitable distribution of resources** (ASAM p. 1525).

Medical Malpractice

- **The most contested element in malpractice cases is often "dereliction" or deviation from the standard of care** — causation and damages must also be proven (ASAM p. 1528).

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Drug Laws & Regulation

- **Controlled Substances Act of 1970 created Schedules I–V for classifying drugs by abuse potential and medical use** (ASAM p. 1515).
- **Ryan Haight Act regulates online prescribing of controlled substances; telemedicine exceptions are tightly defined** (ASAM p. 1516).

Landmark Cases

- **Powell v. Texas upheld the criminality of public intoxication despite SUD status** (ASAM p. 1539).
- **Robinson v. California prohibited criminalizing the status of addiction under the 8th Amendment** (ASAM p. 1539).

Additional High-Yield Pearls

- **DATA 2000 authorized qualified physicians to prescribe buprenorphine for OUD (X-waiver requirement since repealed by Consolidated Appropriations Act of 2023)** (ASAM p. 1516).
- **Veterans Affairs and military SUD programs are exceptions to certain 42 CFR Part 2 requirements** (ASAM p. 1535).

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Landmark Cases and SUDs

Robinson v. California (USSC, 1962)

- Overturned California law that criminalized being 'addicted to a narcotic' as a violation of the Eighth Amendment

Powell v. Texas (USSC, 1968)

- Upheld Texas statute prohibiting public intoxication as constitutional and not violating the Eighth Amendment

Sell v. US (USSC, 2003)

- Defined criteria for involuntary psychotropic medications for competency restoration in a federal criminal case

In re Lifschutz (CA Supreme Court, 1970)

- Patient-psychotherapist privacy/confidentiality

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SUDs and Laws

- Harrison Narcotics Tax Act of 1914: taxation on opium and coca derivatives in attempt to curb sale/use
  - Chinese and opium; blacks and cocaine
- Eighteenth Amendment (1919): prohibition of alcohol
- Twenty-first Amendment (1933): repealed Eighteenth Amendment
- Marihuana Tax Act of 1937: taxation on sale and distribution of cannabis in attempt to curb sale/use
  - Harry Jacob Anslinger, Bureau of Narcotics

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SUDs and Laws

- Controlled Substances Act of 1970: created drug scheduling, e.g., Schedules I through V
- The Narcotic Addict Treatment Act of 1974: methadone treatment of OUD requires annual DEA registration
- Anti-Drug Abuse Act of 1986: "mandatory minimums" on prison sentences for various drug offenses as part of "War on Drugs"
  - Powder cocaine v. crack cocaine, systemic racism
  - Fair Sentencing Act of 2010 reduced the discrepancy

Sacco LN. Drug Enforcement in the United States: History, Policy, and Trends. Congressional Research Service. October 2, 2014.
Institute of Medicine (US) Committee for the Substance Abuse Coverage Study; Gerstein DR, Harwood HJ, editors. Treating Drug Problems: Volume 2: Commissioned Papers on Historical, Institutional, and Economic Contexts of Drug Treatment. Washington (DC): National Academies Press (US); 1992. A Century of American Narcotic Policy.

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SUDs and Laws

- Ryan Haight Online Pharmacy Consumer Protection Act of 2008: online prescribing of controlled substances, enforced by the DEA,
- Drug Addiction Treatment Act of 2000 (DATA 2000 and X-waiver): treatment of OUD with Schedule III-V narcotic medications approved by the FDA for that specific purpose, i.e., buprenorphine
- Consolidated Appropriations Act of 2023: removed DATA 2000 X-waiver requirement

Sacco LN. Drug Enforcement in the United States: History, Policy, and Trends. Congressional Research Service. October 2, 2014.

Institute of Medicine (US) Committee for the Substance Abuse Coverage Study; Gerstein DR, Harwood HJ, editors. Treating Drug Problems: Volume 2: Commissioned Papers on Historical, Institutional, and Economic Contexts of Drug Treatment. Washington (DC): National Academies Press (US); 1992. A Century of American Narcotic Policy. Available from: https://www.ncbi.nlm.nih.gov/books/NBK234755/

202

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2. **Bal BS.** An introduction to medical malpractice in the United States. *Clin Orthop Relat Res.* 2009;467(2):339-347. doi:10.1007/s11999-008-0636-2
3. **National Conference of State Legislatures.** Mental Health Professionals' Duty to Warn. Accessed June 24, 2023. https://www.ncsl.org/health/mental-health-professionals-duty-to-warn
4. **Miller SC, Fiellin DA, Rosenthal RN, Saitz R, eds.** *The ASAM Principles of Addiction Medicine.* 6th ed. Wolters Kluwer; 2019.
5. **Beauchamp TL, Childress JF.** *Principles of Biomedical Ethics.* 7th ed. Oxford University Press; 2013.
6. **Sacco LN.** Drug Enforcement in the United States: History, Policy, and Trends. *Congressional Research Service.* October 2, 2014.
7. **Institute of Medicine (US) Committee for the Substance Abuse Coverage Study; Gerstein DR, Harwood HJ, eds.** *Treating Drug Problems: Volume 2: Commissioned Papers on Historical, Institutional, and Economic Contexts of Drug Treatment.* National Academies Press; 1992. https://www.ncbi.nlm.nih.gov/books/NBK234755/
8. **California Welfare and Institutions Code §5150.**
9. **42 CFR §2.12(c)(6).** Disclosures for child abuse/neglect permitted without consent.
10. **Child Welfare Information Gateway.** Mandatory reporters of child abuse and neglect. U.S. Department of Health and Human Services. Accessed June 24, 2023. https://www.childwelfare.gov/pubPDFs/manda.pdf

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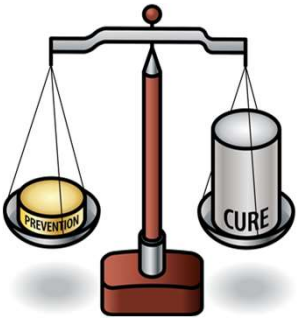
Preventive Medicine & Epidemiology



CSAM Addiction Medicine Board Review

August 13, 2025

Lakai Banks-Dean, MD

Interim Medical Director, New Life Clinic

Updated from past content by Amy de la Garza, MD, FASAM, IFMCP & C.Y Angie Chen, MD, FACP, FASAM

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CONFLICT OF INTEREST DISCLOSURE

I, Lakai Banks-Dean, have nothing to disclose and I will not be discussing “off label” use of drugs or devices during this presentation

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EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Identify conditions and risk factors that require screening and preventative measures
2. Interpret common epidemiologic concepts and their associated equations

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PREVENTIVE MEDICINE

Question 1: The Institute of Medicine classifies prevention strategies based on the targeted population. All the following prevention strategies are correctly paired, **except**:

a) Selective Prevention – HCV screening at a MOUD clinic for patients with Opioid Use Disorder
b) Selective Prevention – Substance use education in primary schools
c) Universal Prevention – Public smoking bans
d) Indicated Prevention – Drug treatment for youth involved with the juvenile justice system

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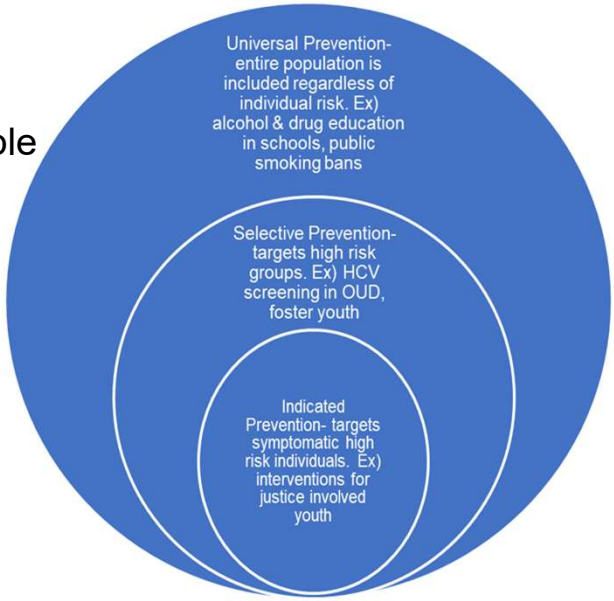
PREVENTIVE MEDICINE

Question 1. The answer is b) Selective Prevention – Substance use education in primary schools

Substance use education in primary schools is an example of universal prevention.



Institute of Medicine (IOM) Classifications for Prevention.
https://dpbh.nv.gov/uploadedFiles/mhnvgov/content/Meetings/Bidders_Conference/Institute%20of%20Medicine%20Prevention%20Classifications-rev10.20.14.pdf.

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PREVENTIVE MEDICINE

Question 2: A 48-year-old man with compensated liver cirrhosis due to alcohol use and a 35 pack-year smoking history presents to the office for his annual physical exam. He received TDaP two (2) years ago after an injury to his left foot. Upon review of his chart, you note he has no history of ever receiving a pneumonia vaccine. According to ACIP guidelines which of the following regimens can bring this patient up to date?

a) PPSV23 followed by PCV15 1 year later
b) This patient does not need any pneumonia vaccine until age 65
c) PCV20 only
d) PCV 13 only

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PREVENTIVE MEDICINE

Question 2. The answer is c) PCV20 only. This patient could have also received PCV 21 or PCV 15 followed by PPSV23 1 year later

Adults 19–49 years old with chronic health conditions
Complete pneumococcal vaccine schedules

Prior vaccines	Option A	Option B
None*	PCV20 or PCV21	PCV15 → ≥1 year → PPSV23†
PCV15 only at any age	≥1 year → PPSV23†	NO OPTION B
PCV15 & **PPSV23** OR **PCV20** OR **PCV21** at any age	**No vaccines** recommended at this time. Review pneumococcal vaccine recommendations again when your patient turns 50 years old.	
PPSV23 only at any age	≥1 year → PCV20 or PCV21	≥1 year → PCV15
PCV13‡ only at any age	≥1 year → PCV20 or PCV21	NO OPTION B
PCV13‡ and **PPSV23** at any age	**No vaccines** are recommended at this time. Review pneumococcal vaccine recommendations again when your patient turns 50 years old.	
Chronic health conditions	• Alcoholism • Chronic heart disease, including congestive heart failure and cardiomyopathies • Chronic liver disease	• Chronic lung disease, including chronic obstructive pulmonary disease, emphysema, and asthma • Cigarette smoking • Diabetes mellitus

* Also applies to people who received PCV7 at any age and no other pneumococcal vaccines
† If PPSV23 is not available, PCV20 or PCV21 may be used
‡ Adults with chronic medical conditions were previously not recommended to receive PCV13

Centers for Disease Control and Prevention. (2025). Pneumococcal vaccine recommendations. Centers for Disease Control and Prevention. https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/index.html
Kobayashi M, Leidner AJ, Gierke R, et al. Expanded Recommendations for Use of Pneumococcal Conjugate Vaccines Among Adults Aged ≥50 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024. MMWR Morb Mortal Wkly Rep 2025;74:1–8. DOI: http://dx.doi.org/10.15585/mmwr.mm7401a1

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PREVENTIVE MEDICINE

Pneumococcal Vaccine Timing for Adults

Make sure your patients are up to date with pneumococcal vaccination.

Adults ≥50 years old
Complete pneumococcal vaccine schedules

Prior vaccines	Option A	Option B
None*	PCV20 or PCV21	PCV15 → ≥1 year† → PPSV23¶
PCV15 only at any age	≥1 year† → PPSV23¶	NO OPTION B
PCV15 & **PPSV23** OR **PCV20** OR **PCV21** at any age	**No vaccines** recommended; schedule is complete.	
PPSV23 only at any age	≥1 year → PCV20 or PCV21	≥1 year → PCV15
PCV13 only at any age	≥1 year → PCV20 or PCV21	NO OPTION B
PCV13 at any age & **PPSV23** at <65 yrs	≥5 years → PCV20 or PCV21	

* Also applies to people who received PCV7 at any age and no other pneumococcal vaccines
¶ If PPSV23 is not available, PCV20 or PCV21 may be used
† Consider minimum interval (8 weeks) for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak (CSF) leak
§ For adults with an immunocompromising condition, cochlear implant, or CSF leak, the minimum interval for PPSV23 is ≥8 weeks since last PCV13 dose and ≥5 years since last PPSV23 dose; for others, the minimum interval for PPSV23 is ≥1 year since last PCV13 dose and ≥5 years since last PPSV23 dose

Shared clinical decision-making for those who already completed the series with PCV13 and PPSV23

Prior vaccines	Shared clinical decision-making option for adults ≥65 years old	
Complete series: PCV13 at any age & **PPSV23** at ≥65 yrs	≥5 years → PCV20 or PCV21	Together, with the patient, vaccine providers **may choose** to administer PCV20 or PCV21 to adults ≥65 years old who have already received PCV13 (but not PCV15, PCV20, or PCV21) at any age and PPSV23 at or after the age of 65 years old.

Note: If the immunization status of a patient 50 years or older is unknown, PCV20 or PCV21 are acceptable options

Centers for Disease Control and Prevention. (2025). Pneumococcal vaccine recommendations. Centers for Disease Control and Prevention. https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/index.html
Kobayashi M, Leidner AJ, Gierke R, et al. Expanded Recommendations for Use of Pneumococcal Conjugate Vaccines Among Adults Aged ≥50 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024. MMWR Morb Mortal Wkly Rep 2025;74:1–8. DOI: http://dx.doi.org/10.15585/mmwr.mm7401a1

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PREVENTIVE MEDICINE

General considerations for pneumococcal vaccinations:

1. Anytime you give PCV 15, in 1 year, you should give PPSV23
2. "Give PCV20 or PCV21, and the job is done"

- Example A: If you give a 35-year-old patient with asthma PCV 20 or PCV 21, at 50-years-old no further pneumococcal vaccination is needed
- Example B: If your 67-year-old diabetic patient received PCV 20 or PCV 21 when they were 25, no further pneumococcal vaccination is needed

3. If an adult patient states they were given their pneumonia vaccine less than 1 year ago and there is no way to verify which vaccine they were given → in 1 year give PCV20 or PCV21

Centers for Disease Control and Prevention. (2025). Pneumococcal vaccine recommendations. Centers for Disease Control and Prevention. https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/index.html
Kobayashi M, Leidner AJ, Gierke R, et al. Expanded Recommendations for Use of Pneumococcal Conjugate Vaccines Among Adults Aged ≥50 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024. MMWR Morb Mortal Wkly Rep 2025;74:1–8. DOI: http://dx.doi.org/10.15585/mmwr.mm7401a1

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PREVENTIVE MEDICINE

CC1

Question 3: A 41-year-old woman with alcohol use disorder in sustained remission presents for routine follow up. Her medical history is significant for hypertension and type 2 diabetes mellitus, both of which are controlled. She had a pap smear with HPV co-testing 2 years ago that showed no evidence of intraepithelial lesion or malignancy and was negative for HPV. She has a copper IUD from 2 years ago, has a regular menstrual cycle every 28 days, and is sexually active with a male partner for the past 5 years. She is up to date on all appropriate vaccinations.

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PREVENTIVE MEDICINE

Question 3: Continued

Her vital signs are: T- 98.3 F HR-72 BPM BP-131/79 RR-14 O2-98% on room air. Physical exam is unremarkable and HIV, RPR, Hep C, Gonorrhea & chlamydia testing are all non-reactive or not detected. According to the USPSTF, which screening should this patient receive?

a) No screening is recommended
b) Screening mammography
c) Low-dose computed tomography (LDCT)
d) DEXA scan

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Slide 213

CC1 This font looks squished
Chen, Chwen-Yuen, 2025-07-02T02:59:20.901

PREVENTIVE MEDICINE

Question 3. The answer is b) Screening mammography

Recommendation Summary

CC1

Population	Recommendation	Grade
Women aged 40 to 74 years	The USPSTF recommends biennial screening mammography for women aged 40 to 74 years.	B

"Breast Cancer: Screening." *Recommendation: Breast Cancer: Screening | United States Preventive Services Taskforce*, US Preventive Services Taskforce, 30 Apr. 2024, www.uspreventiveservicestaskforce.org/uspstf/recommendation/breast-cancer-screening.

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PREVENTIVE MEDICINE

USPSTF Grading Definitions

Grade	Definition	Suggestions for Practice
A	The USPSTF recommends the service. There is high certainty that the net benefit is substantial.	Offer or provide this service.
B	The USPSTF recommends the service. There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial.	Offer or provide this service.
C	The USPSTF recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small.	Offer or provide this service for selected patients depending on individual circumstances.
D	The USPSTF recommends against the service. There is moderate or high certainty that the service has no net benefit or that the harms outweigh the benefits.	Discourage the use of this service.
I Statement	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of the service. Evidence is lacking, of poor quality, or conflicting, and the balance of benefits and harms cannot be determined.	Read the clinical considerations section of USPSTF Recommendation Statement. If the service is offered, patients should understand the uncertainty about the balance of benefits and harms.

https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/grade-definitions

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Slide 215

CC1 Explain Ratings, in this Grade B

Chen, Chwen-Yuen, 2025-07-02T03:11:51.968

PREVENTIVE MEDICINE

Chlamydia and Gonorrhea Screening Guideline

Recommendation Summary

Population	Recommendation	Grade
Sexually active women, including pregnant persons	The USPSTF recommends screening for chlamydia in all sexually active women 24 years or younger and in women 25 years or older who are at increased risk for infection.	B
Sexually active women, including pregnant persons	The USPSTF recommends screening for gonorrhea in all sexually active women 24 years or younger and in women 25 years or older who are at increased risk for infection.	B

- Screen sexually active women 24 years old or younger
- Screen women 25 and older if they have:
  - they have a previous or coexisting STI
  - A new or >1 sex partner
  - A sex partner with an STI
  - A sex partner having sex with other partners at the same time
  - Inconsistent condom use when not in a mutually monogamous relationship
  - History of incarceration
  - History of exchanging sex for money or drugs

Screening for chlamydia and gonorrhea. US Preventative Services Task Force Recommendation Statement. JAMA. 2021;326(10):949-956. doi:10.1001/jama.2021.14081

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PREVENTIVE MEDICINE

Cervical Cancer Screening Recommendation

Population	Recommendation	Grade
Women aged 21 to 65 years	The USPSTF recommends screening for cervical cancer every 3 years with cervical cytology alone in women aged 21 to 29 years. For women aged 30 to 65 years, the USPSTF recommends screening every 3 years with cervical cytology alone, every 5 years with high-risk human papillomavirus (hrHPV) testing alone, or every 5 years with hrHPV testing in combination with cytology (cotesting). See the Clinical Considerations section for the relative benefits and harms of alternative screening strategies for women 21 years or older.	A

- Women 21-29 years old: cytology every 3 years
- Women 30-65 years old: cytology every 3 years, high risk HPV testing alone every 5 years, or cytology with high risk HPV testing every 5 years

US Preventive Services Taskforce. (2018, August 21). *Cervical cancer: Screening*. Recommendation: Cervical Cancer: Screening | United States Preventive Services Taskforce. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/cervical-cancer-screening

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PREVENTIVE MEDICINE

Question 4: Marcus is a 23-year-old transgender man presenting to establish care with you. He would like to get a "check up" and learn how to start gender-affirming hormone therapy to start a female to male transition. He has no chronic medical conditions, has no surgical history, and did not receive vaccinations after 5 years old due to his parents' beliefs. His menses occurs every 28 days and he's had unprotected intercourse with 2 partners in the past year whose HIV status he is not certain of. He currently smokes 15 cigarettes a day and has been doing so for the last 2 years. A rapid point-of-care HIV test is negative. You develop a plan with him to incorporate recommended screenings and preventative care. Which of the following is not a recommended preventative measure for this patient?

a) Doxycycline 100 mg twice daily for 10 days after unprotected intercourse
b) Emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg daily
c) 9-valent human papillomavirus vaccination
d) Pneumococcal 20-valent vaccine

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PREVENTIVE MEDICINE

Question 4: The answer is a)Doxycycline 100 mg twice daily for 10 days after unprotected intercourse

- Doxycycline 100 mg twice daily is not a preventative dose. The CDC recommends 200 mg of doxycycline 72 hours after oral, vaginal, or anal sex for gay, bisexual, and other men who have sex with men and transgender women at increased risk for STIs. (DoxyPEP or Doxy postexposure prohylaxis)
- Answer b) Emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg daily is one regimen for HIV prep and since he is negative for HIV, this preventative measure is recommended
- Answer c) 9-valent human papillomavirus vaccination is recommended in adults through 26 years of age according to ACIP recommendations
- Answer d) Pneumococcal 20-valent vaccine is recommended if no previous pneumococcal vaccine has been given in this patient due to his age and smoking history

Bachmann LH, Barbee LA, Chan P, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. MMWR Recomm Rep 2024;73(No. RR-2):1–8. DOI: http://dx.doi.org/10.15585/mmwr.rr7302a1

"HPV Vaccination Recommendations." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 16 Nov. 2021, www.cdc.gov/vaccines/vpd/hpv/hcp/recommendations.html#schedules.

Centers for Disease Control and Prevention. (2025). Pneumococcal vaccine recommendations. Centers for Disease Control and Prevention. https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/index.html

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PREVENTIVE MEDICINE

HPV Vaccination- Gardasil 9

1. **Series initiated BEFORE 15th birthday (11 or 12 years old, earliest start is 9 years old)**
   - Two doses of HPV vaccine
   - Second dose 6-12 months after the first dose
2. **Series initiated AFTER 15th birthday AND for immunocompromised children/adults**
   - Three doses of HPV vaccine
   - Three-dose schedule is 1-2 months after the first vaccine, 6 months after the second vaccine
   - Three doses are recommended for immunocompromised persons (including those with HIV infection) aged 9 through 26 years.
   - ACIP also recommends vaccination for everyone through age 26 years if not adequately vaccinated when younger.
   - HPV vaccine should not be given during pregnancy

"HPV Vaccination Recommendations." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 16 Nov. 2021, www.cdc.gov/vaccines/vpd/hpv/hcp/recommendations.html#schedules.

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PREVENTIVE MEDICINE

HIV PrEP Guidelines

CC1

Recommendation Summary

Population	Recommendation	Grade
Adolescents and adults at increased risk of HIV	The USPSTF recommends that clinicians prescribe preexposure prophylaxis using effective antiretroviral therapy to persons who are at increased risk of HIV acquisition to decrease the risk of acquiring HIV. See the Practice Considerations section for more information about identification of persons at increased risk and about effective antiretroviral therapy.	A

What additional information should clinicians know about this recommendation?	PrEP is underutilized, particularly for Black and Hispanic/Latino persons with indications for PrEP.

"Prevention of Acquisition of HIV: Preexposure Prophylaxis." *Recommendation: Prevention of Acquisition of HIV: Preexposure Prophylaxis | United States Preventive Services Taskforce*, US Preventive Services Taskforce, 22 Aug. 2023, www.uspreventiveservicestaskforce.org/uspstf/recommendation/prevention-of-human-immunodeficiency-virus-hiv-infection-pre-exposure-prophylaxis.

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Slide 222

CC1 PrEP is an important preventive measure but doesn't fall under SCREENING theme of this question stem

Chen, Chwen-Yuen, 2025-07-02T03:14:34.227

PREVENTIVE MEDICINE

HIV PrEP Guidelines

The USPSTF recommends that the following persons be considered for HIV PrEP:

1. Sexually active adults and adolescents weighing at least 35 kg (77 lb) who have engaged in anal or vaginal sex in the past 6 months and have any of the following:
   - A sexual partner who has HIV (especially if the partner has an unknown or detectable viral load).
   - A bacterial sexually transmitted infection (syphilis, gonorrhea, or chlamydia for men who have sex with men and transgender women; gonorrhea and syphilis for heterosexual women and men) in the past 6 months.
   - A history of inconsistent or no condom use with sex partner(s) whose HIV status is not known
2. Persons who inject drugs and have a drug injecting partner who has HIV or who shares injection equipment.

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PREVENTIVE MEDICINE

Question 5: Mr. Johnson is a 70-year-old heterosexual, cisgendered male with a past medical history of opioid use disorder sees you for a follow up for his buprenorphine-naloxone treatment. He is stable on 12 mg of buprenorphine daily. He asks you if he needs any cancer screening although he quit smoking 5 years ago. Upon further history, he shares that he started smoking at age 20 and smoked 5 cigarettes per day on average until he quit. According to the United States Preventive Services Task Force, you recommend:

a) No recommendation because he quit smoking 5 years ago
b) Yearly low dose computed tomography
c) Yearly PSA screening for prostate cancer
d) 1-time abdominal ultrasound

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Slide 224

CC1 Typo? 5 years or 2 years?
Chen, Chwen-Yuen, 2025-07-02T03:21:03.245

PREVENTIVE MEDICINE

Question 5. The Answer is d) 1-time abdominal ultrasound

- USPSTF recommendations related to smoking should be expected
- D is the correct answer because USPSTF recommends a **1-time screening for abdominal aortic aneurysm (AAA) with ultrasonography in men aged 65 to 75 years who have ever smoked (Grade B)**.
- This question also reviews 2 additional USPSTF guidelines

CC1

Prostate Cancer Screening:

- Individualized decision making for men aged 55-69 years old with periodic PSA-based screening (Grade C).
- USPSTF Recommends against PSA-based screening in men over 70 years and older (Grade D).

"Abdominal Aortic Aneurysm: Screening." *Recommendation: Abdominal Aortic Aneurysm: Screening | United States Preventive Services Taskforce*, US Preventive Services Taskforce, 10 Dec. 2019, https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/abdominal-aortic-aneurysm-screening.

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PREVENTIVE MEDICINE

Question 5. The Answer is d) 1-time abdominal ultrasound

Lung Cancer Screening Recommendation

Recommendation Summary

Population	Recommendation	Grade
Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

US Preventive Services Taskforce. (2021, March 9). *Lung cancer: Screening*. Recommendation: Lung Cancer: Screening | United States Preventive Services Taskforce. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/lung-cancer-screening#:~:text=The%20USPSTF%20recommends%20annual%20screening%20for%20lung%20cancer,or%20have%20quit%20within%20the%20past%2015%20years.

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Slide 225

CC1 Busy slide please cut into 2 slides
Chen, Chwen-Yuen, 2025-07-02T03:22:20.685

PREVENTIVE MEDICINE

Question 5. The Answer is d) 1-time abdominal ultrasound

- Answer b) yearly low dose computed tomography is incorrect because he does not have the pack-year history for this screening.
- Annual screening for lung cancer with low-dose computed tomography (LDCT) in recommended in adults **aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years.** (Max pack year for this patient: 5 cigs = 0.25 ppd x 50 yrs (age 20-70) = **12.5** pack-year)
- Lung cancer is the **2nd most common** cancer.
- Lung cancer leading cause of cancer death among both men and women: **25% of all cancer deaths**. Each year, more people die of lung cancer than of colon, breast, and prostate cancers combined.
- 80%-90% of lung cancer cases are the result of smoking; increasing age & cumulative exposure to tobacco smoke are the 2 most common risk factors.

US Preventive Services Taskforce. (2021, March 9). *Lung cancer: Screening*. Recommendation: Lung Cancer: Screening | United States Preventive Services Taskforce. https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/lung-cancer-screening#:~:text=The%20USPSTF%20recommends%20annual%20screening%20for%20lung%20cancer,or%20have%20quit%20within%20the%20past%2015%20years.

https://www.cancer.org/cancer/types/lung-cancer/about/key-statistics.html

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PREVENTIVE MEDICINE

Question 6: The rate of tuberculosis (TB) infection in the U.S. is 2.9/100,000. The prevalence of tuberculosis in persons who inject drugs (PWID) has been estimated to be 15,000-39,000/100,000. Which of the following is ***true*** regarding TB prevention?

a) Many countries with higher rates of endemic TB do not utilize vaccinations for TB prevention.

b) Treating patients for latent TB is SECONDARY prevention, because it provides treatment before TB progresses from latent to active.

c) Treating patients with active TB is PRIMARY prevention, stopping disease progression & limiting the spread of new infection to others.

a) Screening for TB using the tuberculin skin test or QuantiFERON-TB Gold is an example of TERTIARY prevention, identifying people at risk of active TB before they are sick.

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PREVENTIVE MEDICINE

Question 6. The Answer is b) Treating patients for latent TB is SECONDARY prevention, because it provides treatment before TB progresses from latent to active.

	PRIMARY Prevention	SECONDARY Prevention	TERTIARY Prevention
Definition	Action implemented before disease onset through behavior modification, policy, or medical intervention, such as vaccines.	Screening to detect diseases early before onset of signs and symptoms.	Disease management post diagnosis or to stop disease progression and screen for complications.
Goal	Risk Reduction	Screening	Diagnosis and Treatment
Example	**PRIMARY TB prevention:** environmental controls, such as use of adequate ventilation and decreasing overcrowding. Countries with high rates of infection vaccinate with BCG. 25% of the world's population is infected with TB.	Screening for latent TB infection & treatment of latent TB infection are both examples of **SECONDARY** prevention—the infection has already occurred—it has not been prevented.	**TERTIARY** PREVENTION is what we often think of as medical treatment, decreasing morbidity/mortality of diseases which are already symptomatic

"Picture of America." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 6 Apr. 2017, https://www.cdc.gov/pictureofamerica/index.html.

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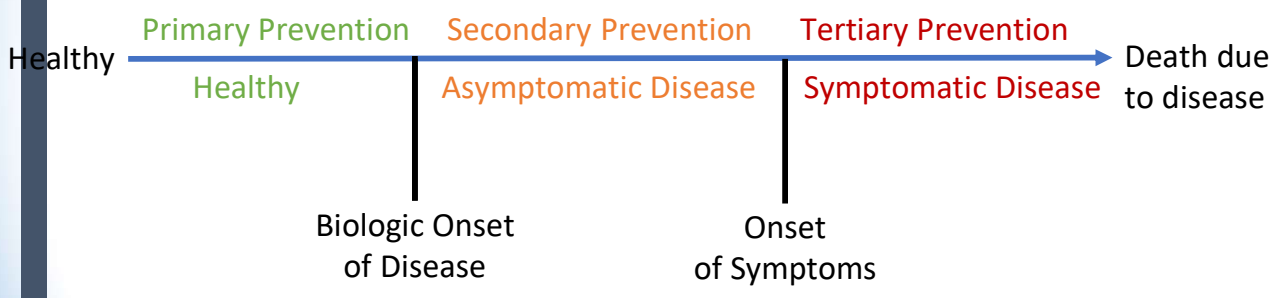
PREVENTIVE MEDICINE

Primary, Secondary, and Tertiary Prevention in relation to disease status



"Picture of America." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 6 Apr. 2017, https://www.cdc.gov/pictureofamerica/index.html.

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Epidemiology Calculations and Concepts

231

Question 7: Given the table below, what is the SENSITIVITY of the test?

	Disease Present (+)	Disease Absent (-)	Total
Test Result (+)	25	10	35
Test Result Negative (-)	5	60	65
Total	30	70	100

a) 5 divided by 35
b) 5 divided by 65
c) 25 divided by 30
d) 25 divided by 35

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Question 7. The answer is c) 25 divided by 30 (.83)

	Disease +	Disease -	Total
Test +	25=TP	FP	TP + FP
Test -	5=FN	TN	TN + FN
Total	30=25TP + 5FN	FP + TN	

25 TP / 30 TP+FN

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Sensitivity

- Mathematically Sensitivity is: **True Positives/(True Positives + False Negatives)**
- Highly **S**e**N**sitive tests when Negative (-) rule OUT disease or use: "SN(-)OUT"
- Sensitivity is the ability of a test to detect disease in all those who have the disease and is expressed as the proportion of those **with disease** correctly identified by a positive screening test result.
- The measure of sensitivity describes how well the proposed screening test performs against an agreed "Gold Standard" test, Gold Standard, meaning a diagnostic test that is regarded as definitive.
- In drug testing, sensitivity is the ability of the test to detect those who have consumed the substance. For instance, if I know that a patient used cocaine, how likely is that test going to come back positive for cocaine? If it were a perfectly sensitive test, it would 100% pick up every person tested who used cocaine.

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Sensitivity

- The measure of sensitivity describes how well the proposed screening test performs against an agreed “Gold Standard” test, Gold Standard, meaning a diagnostic test that is regarded as definitive.
- In drug testing, sensitivity is the ability of the test to detect those who have consumed the substance. For instance, if I know that a patient used cocaine, how likely is that test going to come back positive for cocaine? If it were a perfectly sensitive test, it would 100% pick up every person tested who used cocaine.

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Question 8: Given the table below, what is the SPECIFICITY of the test?

	Disease +	Disease -	Total
Test +	25	10	35
Test -	5	60	65
Total	30	70	100

a) 60 divided by 70
b) 60 divided by 65
c) 25 divided by 70
d) 5 divided by 65

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Question 8. The answer is a) 60 divided by 70 (.86)

	Disease +	Disease -	Total
Test +	TP	10= FP	TP + FP
Test -	FN	60=TN	TN + FN
Total	TP + FN	70=10FP + 60TN	**60 TN / 70 FP+TN**

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Specificity

- Mathematically, specificity is **True Negatives/(True Negatives + False Positives)**
- Specificity is the ability of the test to identify correctly those free of disease in the screened population and is expressed as the proportion of those without disease correctly identified by a negative screening test.
- The measure of specificity describes how well the proposed screening test performs against an agreed "Gold Standard" test, meaning a diagnostic test that is regarded as definitive.
- In drug testing, **specificity is the reliability of the test to be negative in those who have not used the tested drug.**
- The sensitivity and specificity reflect the **TEST** and is **NOT dependent on the population**. Prevalence and incidence do not change how the test performs.
- Highly **SP**ecific tests when POSITIVE (+) rule **IN** disease or use: "SP(+)IN"

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Question 9: A new retrospective trial has been published that examined the relationship between smoking cigarettes and diagnosing a myocardial infarction (MI). According to the data below, what are the odds of having an MI diagnosed in person who smokes cigarettes compared to a person that does not smoke cigarettes?

	MI Diagnosed	No MI Diagnosed
Persons that smoke cigarettes	90	10
Persons that do not smoke cigarettes	75	25

a) 5
b) 1.2
c) 0.48
d) 3

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Question 9. The answer is d) 3

- **Odds Ratio (OR) = (odds of the event in the exposed group) / (odds of the event in the non-exposed group)**

		Event	
		Yes	No
Exposure	Yes	a	b
	No	c	d

$$\text{Odds Ratio} = \frac{a/b}{c/d} = \frac{ad}{bc}$$

$$= \frac{90/10}{75/25} \quad = \frac{90*25}{75*10} \quad = 3$$

	MI Diagnosed	No MI Diagnosed
Persons that smoke cigarettes	90 (a)	10 (b)
Persons that do not smoke cigarettes	75 (c)	25 (d)

Tenny S, Hoffman MR. Odds Ratio. [Updated 2023 May 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK431098/

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Odds Ratios (OR)

- "How strongly an event is associated with an exposure"
- OR >1 means there are greater odds that the event will occur with exposure
- OR<1 means there a fewer odds the event will occur with exposure
- Used in retrospective and case control studies
- Video explaining odds ratio: https://youtu.be/yWf9Zi8OzV8?si=KH3V6-U0fuyp4KfN

Tenny S, Hoffman MR. Odds Ratio. [Updated 2023 May 22]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK431098/

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Question 10: Given the table below, what is the POSITIVE PREDICTIVE VALUE of the test?

	Disease +	Disease -	Total
Test +	25	10	35
Test -	5	60	65
Total	30	70	100

a) 25 divided by 30
b) 25 divided by 35
c) 35 divided by 65
d) 25 divided by 70

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Question 10. The answer is b) 25/35 (.71) PPV

	Disease +	Disease -	Total	
Test +	**25** TRUE POS	10 FALSE POS	**35** Total Test POS	**25/35 (.71) PPV**
Test -	5	60	65	
Total	30	70	100	

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Positive Predictive Value (PPV)

- The positive predictive value (PPV) describes the probability or odds of having the disease given a positive screening test result in the screened population.
- This is expressed as the proportion of those with disease among all screening test positives.
- Mathematically, it is **True Positives/(True Positives + False Positives)**

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Question 11: Given the table below, what is the NEGATIVE PREDICTIVE VALUE of the test?

	Disease +	Disease -	Total
Test +	25	10	35
Test -	5	60	65
Total	30	70	100

a) 60 divided by 65
b) 60 divided by 70
c) 65 divided by 70
d) 70 divided by 100

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Question 11. The answer: a) 60/65 (.92) NPV

	Disease +	Disease -	Total	
Test +	25	10	35	
Test -	5 FALSE NEG	**60** TRUE NEG	**65** Total Test NEG	60/65 (.92) **NPV**
Total	30	70	100	

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Negative Predictive Value (NPV)

- The negative predictive value (NPV) describes the probability or odds of not having the disease given a negative screening test result in the screened population.
- This is expressed as the proportion of those without disease among all screening test negatives.
- Mathematically, it is **True Negatives/(True Negatives + False Negatives)**

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Question 12: Does the prevalence of the disease in the population being screened affect the positive predictive value (PPV) & negative predictive value (NPV) of the screening test?

a) No. PPV & NPV are independent of the prevalence of disease.
b) Yes. As the prevalence of the disease increases, the PPV decreases, & the NPV increases.
c) Yes. As the prevalence of the disease increases, the PPV increases, & the NPV decreases.
d) As the prevalence of the disease increases, PPV & NPV increase, & as the prevalence of the disease decreases, PPV & NPV decrease.

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Question 12. The answer is c) Yes. As the prevalence of the disease increases, the PPV increases & the NPV decreases.

- Positive predictive value (PPV) & negative predictive value (NPV) are disease prevalence dependent, meaning they are population specific. The denominator is the entire population of those with and without disease.
- PPV & NPV give information on how well a screening test will perform in each population with a known prevalence.

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Prevalence = Disease+ / (Disease+ plus Disease-) = 50/1000 = 5%

	Disease +	Disease -	Total
Test +	40	95	135
Test -	10	855	865
Total	50	950	1000

PPV = 40/135 = 29.6%

NPV = 855/865= 98.8%

Sensitivity = 40/50 = 80%

Specificity = 855/950 = 90%

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Prevalence = Disease+ / (Disease+ plus Disease-) = 200/1000 = 20% goes up

	Disease +	Disease -	Total
Test +	160	80	240
Test -	40	720	760
Total	200	800	1000

PPV = 160/240 = **66.6%**
Goes up as well

NPV = 720/760= 94.7%
Goes down slightly

Sensitivity = 160/200 = 80%

Specificity = 720/800 = 90%

Shreffler J, Huecker MR. Diagnostic Testing Accuracy: Sensitivity, Specificity, Predictive Values and Likelihood Ratios. [Updated 2023 Mar 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557491/

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Question 13: A 55-year-old male with controlled hypertension and chronic back pain presents to your office for an annual physical. He has a 20 pack-year smoking history and has no complaints today. He walks 3-4 miles daily, follows a vegan diet, and practices intermittent fasting. He is worried that despite his "pretty healthy" lifestyle that he will still get COPD like his father did. He is adamant that he will not make any changes to his cigarette use but wants to know what his risk of developing COPD is. If the incidence of developing COPD is 5% in the general population and 20% in people who smoke cigarettes, what is relative risk of your patient developing COPD?

a) 0.25
b) 20
c) 4
d) 0.15

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Question 13. The answer is c) 4

- The relative risk (RR) is a ratio of the probability that an event will occur in an exposed group compared to the probability that event will occur in a non-exposed group
- RR= incidence of condition in exposure group / *incidence of condition in group without exposure*
- RR= .20(incidence in people who smoke)/.05(incidence in people who don't smoke)= 4
- RR> 1= increased risk with exposure. RR<1 = decreased risk with exposure
- Can be used in prospective and cohort studies
- Video Explanation of Relative Risk: https://youtu.be/ZjhjHfHn_eY?si=7c6dZaROLZhxJM_j

Tenny S, Hoffman MR. Relative Risk. [Updated 2023 Mar 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430824/

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PREVENTIVE MEDICINE: NEED TO KNOW

- ❑Preventive health issues
  - ❑*Know the difference between universal, indicated, and selective prevention and* ***primary, secondary, and tertiary preventions***
  - ❑*USPSTF screening recommendations (Grade A & B)*
  - ❑*Common health conditions related to specific substance use and modality of use*
    - ❑ID: Hepatitis, TB, HIV, STDs, skin and soft tissue infections
    - ❑Tobacco use: lung cancer (pack-year calculation), abdominal aortic aneurysm
    - ❑Medical: Poor dentition, reactive airway, unplanned pregnancy, Cardiomyopathy, QTc prolongation, COPD, cervical cancer, laryngeal cancer

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Epidemiology Calculations and Concepts: Need to Know

- ❑TIP: write out equations you're not 100% confident about on the scratch paper at the beginning of the test
- ❑Label any 2x2 table to ensure your calculations are correct
- ❑ Basic principles of epidemiology
  - ❑ *Be ready to calculate and interpret:*
    - ❑ Confidence intervals
    - ❑ Positive & Negative predictive value
    - ❑ Incidence & Prevalence
    - ❑ Specificity & Sensitivity
    - ❑ Absolute risk reduction & number needed to treat
    - ❑ Relative risk & odds ratio

- ❑Risk factors for developing substance use disorder (i.e. gender, age, family history, education level, etc)
- ❑General trends from the national surveys about substance use (NESARC III, NSDUH, MTF)

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References

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Question 3: "Breast Cancer: Screening." *Recommendation: Breast Cancer: Screening | United States Preventive Services Taskforce*, US Preventive Services Taskforce, 30 Apr. 2024, www.uspreventiveservicestaskforce.org/uspstf/recommendation/breast-cancer-screening. \

Question 4: Bachmann LH, Barbee LA, Chan P, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. MMWR Recomm Rep 2024;73(No. RR-2):1–8. DOI: http://dx.doi.org/10.15585/mmwr.rr7302a1
"HPV Vaccination Recommendations." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 16 Nov. 2021, www.cdc.gov/vaccines/vpd/hpv/hcp/recommendations.html#schedules.
Centers for Disease Control and Prevention. (2025). Pneumococcal vaccine recommendations. Centers for Disease Control and Prevention. https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/index.html
Question 5: "Abdominal Aortic Aneurysm: Screening." *Recommendation: Abdominal Aortic Aneurysm: Screening | United States Preventive Services Taskforce*, US Preventive Services Taskforce, 10 Dec. 2019, https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/abdominal-aortic-aneurysm-screening.

Question 6: Armenta RF, Collins KM, Strathdee SA, et al. Mycobacterium tuberculosis infection among persons who inject drugs in San Diego, California. Int J Tuberc Lung Dis. 2017;21(4):425-431. doi:10.5588/ijtld.16.0434.
Global Prevention and Elimination of Tuberculosis
New Jersey Medical School Global Tuberculosis Institute./Incorporating Tuberculosis into Public Health Cor Curriculum./2009: Epidemiology Fact Sheet 1: Primary, Secondary, and Tertiary Prevention Fact Sheet – TB Examples INSTRUCTOR"S GUIDE Version 1.0.
RG Deiss, TC Rodwell, RS Garfein. Tuberculosis and Drug Use: Review and Update. Clin Infect Dis. 2009 January 1;48(1): .doi10.1086/594126.

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Tenny S, Hoffman MR. Relative Risk. [Updated 2023 Mar 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430824/

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https://www.thennt.com/thennt-explained/
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Tenny S, Hoffman MR. Relative Risk. [Updated 2023 Mar 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430824/

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Thank you! I trust everyone will do well!
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Nicotine and Nicotine Use Disorder
CSAM Addiction Medicine Board Review Course
August 13, 2025
Lakai Banks-Dean, MD
Interim Medical Director, New Life Clinic
Modified from Daniel Cox, MD and Amy de la Garza, MD, FASAM past presentation
CSAM

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CONFLICT OF INTEREST DISCLOSURE

I, Lakai Banks-Dean, have nothing to disclose, and I will not be discussing "off label" use of drugs or devices in this presentation.

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1. Neurobiology of nicotine addiction
2. Nicotine metabolism via CYP2A6 + pharmacokinetics
3. Nicotine cholinergic receptor subunits
4. Psychoactive effects of nicotine
5. Role of nicotine metabolism as determinant of tobacco use and dependence
6. Pharmacotherapy for smoking cessation
    a. Doses of NRT used for number of cigarettes smoked/day
    b. Mechanism of action for smoking cessation drugs, including receptors and neurotransmitters
    c. Combination pharmacotherapy
    d. Adverse effects and contraindications
    e. Comparative efficacy

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7. Cotinine: Levels for light, moderate, heavy smoking
8. 5 A's for screening and counseling of tobacco use: "Ask, Advise, Assess, Assist, Arrange"
9. Efficacy of telephone quit lines
10. Fagerström test for nicotine dependence
11. Effect of nicotine on metabolism
12. E-Cigarettes/Vaping

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Vignette for Q1:

A 24 year old man establishes care with you after discharging from a residential treatment program for alcohol use disorder. He is worried because his cigarette use increased during his treatment episode and he expresses a desire to stop smoking entirely. He currently consumes 30 hand-rolled cigarettes per day, using an organic, high-nicotine containing tobacco. Although you initially recommend varenicline, he is resistant to using any medications to help him quit.

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Vignette Q1 (continued):

He asks you about switching to light cigarettes as a means of quitting smoking. “That just makes sense to me. I’ll keep smoking the same amount of cigarettes, but since they are light cigarettes with less nicotine, it will help me reduce my use. Then, I’ll just stop from there over the next couple of months. Maybe reduce 1-2 cigarettes every week or something? Plus, using light cigarettes will keep me from missing having a cigarette in my mouth.”

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Q1. Which of the following statements about light cigarettes is most supported by scientific evidence?

A. Smoking light cigarettes will not help. Smokers adjust their nicotine level by adjusting puffing habits.

B. If the patient is unable to quit, the fact that he initially tried light cigarettes will allow him to use a lower dose of nicotine replacement therapy if that is later indicated.

C. Using light cigarettes to quit helps to address the behavioral aspects of smoking while delivering less nicotine.

D. The patient is right: Reduction in the total amount of nicotine smoked on a daily basis allows the patient to gradually withdraw from nicotine, facilitating the quitting process.

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Answer: A. Smoking light cigarettes will not help. Smokers adjust their nicotine level by adjusting puffing habits.

Much evidence has refuted decades-old claims that light or ultra-light cigarettes help to improve the chances of success with smoking cessation among heavy smokers.

While it is true that patients who smoke primarily light cigarettes will potentially require lower doses of nicotine replacement therapy, in this patient with heavy tobacco use, he will probably adjust his puffing habits (puff volume, number of puffs, intensity of puffing, and depth of inhalation) and potentially, increase the number of cigarettes smoked to maintain his baseline nicotine level.

Reference:
Benowitz NL, Henningfield JE Reducing the nicotine content to make cigarettes less addictive *Tobacco Control* 2013;**22**:i14-i17.

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Q2. The previous patient returns to the office after attempting to smoke light cigarettes for one month to quit smoking and has increased his use of cigarettes to 3 packs per day. He is ready to try anything to quit smoking and has even set a quit date. He mentions wanting the same medication his father has been taking to help stop cigarettes. He cannot recall the name of the medication but knows it was recommended to his father's depression as well. The mechanism by which this medication decreases tobacco use is:

A. Partial agonism and antagonism at the alpha-4, beta-2 nicotinic receptor
B. Full agonism at the apha-4, beta-2 nicotinic receptor
C. Inhibition of opioid receptors
D. Inhibition of dopamine and norepinephrine reuptake

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Answer: D. Inhibition of dopamine and norepinephrine reuptake

"Bupropion blocks nicotine activation of $\alpha_3\beta_2$, $\alpha_4\beta_2$, and α_7 neuronal acetylcholine nicotinic receptors (nAChRs) with some degree of selectivity"- Slemmer, et al., 2000

This blockade leads to inhibition of dopamine and norepinephrine reuptake (functionally increasing dopamine and norepinephrine in regions such as the nucleus accumbens and ventral tegmental area)

Decreases nicotine withdrawal symptoms, cravings, and nicotine reinforcement

- Slemmer, J. E., Martin, B. R., & Damaj, M. I. (2000). Bupropion is a nicotinic antagonist. *The Journal of Pharmacology and Experimental Therapeutics, 295*(1), 321–327
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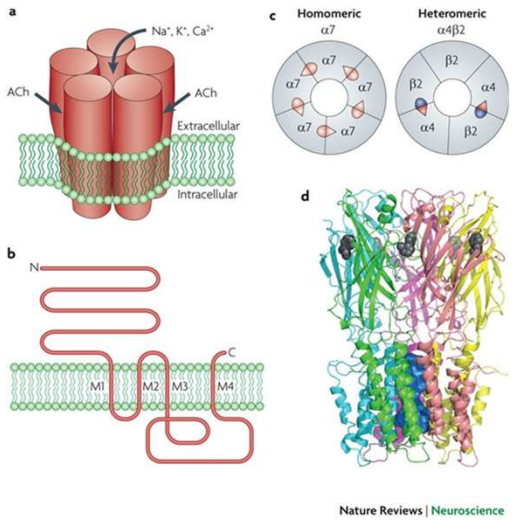
Answer: D. Inhibition of dopamine and norepinephrine reuptake

- Choice A is the mechanism of action of varenicline
- **Partial agonist** at the alpha-4, beta-2 nicotinic receptor
  - Reducing craving and withdrawal
- **Competitive antagonist** at the same receptor
  - Blocking rewarding effects of nicotine



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EAGLES STUDY

Randomized Controlled Trial > Lancet. 2016 Jun 18;387(10037):2507-20.
doi: 10.1016/S0140-6736(16)30272-0. Epub 2016 Apr 22.

Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial

Robert M Anthenelli [1], Neal L Benowitz [2], Robert West [3], Lisa St Aubin [4], Thomas McRae [4], David Lawrence [4], John Ascher [5], Cristina Russ [4], Alok Krishen [6], A Eden Evins [7]

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EAGLES Study

- Randomized trial of participants who wanted to quit smoking, with and without psychiatric conditions
- Randomized to nicotine patch, varenicline, bupropion, placebo for 12 weeks
- Primary endpoint: incidence of moderate to severe neuropsychiatric adverse events
- Main efficacy endpoint: continuous nicotine abstinence weeks 9-12

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EAGLES Study

Results

- Varenicline and bupropion **did not** show significant increase in adverse neuropsychiatric events
- Varenicline more effective than placebo, patch or bupropion
- Bupropion and nicotine patch were each more effective than placebo

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Results from 2013 Cochrane Review

Medication	Versus Placebo OR (95% Credible Interval)	Versus other medication OR (95% Credible Interval)
NRT	1.84 (1.71-1.99)	Combination outperformed single formulations
Bupropion	1.82 (1.60-2.06)	NRT: 0.99 (0.86-1.13)
Varenicline	2.88 (2.40-3.47)	Nicotine patches: 1.51 (1.22-1.87) Nicotine gums: 1.72 (1.38-2.13) Other NRT: 1.42 (1.12-1.79) Combination NRT: 1.06 (0.75-1.48)

Cahill K. et al. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane database of systematic reviews. 2013.

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Things to Consider Regarding Pharmacotherapy for Smoking Cessation

- **Varenicline is more effective than both monotherapy with nicotine replacement and bupropion.**
- Combination nicotine replacement therapy may be as effective varenicline
- Varenicline with nicotine replacement therapy appears to improve abstinence rates over varenicline alone
- Bupropion and varenicline may be more effective than varenicline alone

Livingstone-Banks J, Fanshawe TR, Thomas KH, Theodoulou A, Hajizadeh A, Hartman L, Lindson N. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev. 2023 May 5;5(5):CD006103. doi: 10.1002/14651858.CD006103.pub8. PMID: 37142273; PMCID: PMC10169257.

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TABLE 65-1 FDA-Approved Medications for Tobacco Dependence

Medication	Recommended duration and dose[a]	Odds ratio[a] (95% CI) Number of studies	Considerations
Nicotine gum	Up to[b] 12 weeks; 2 mg (for those who smoke < 25 cigarettes per day; 4 mg (for those who smoke > 25 cigarettes per day	1.49 (1.40-1.60) 56 trials	Addresses cue-elicited craving and affordable; lower compliance
Nicotine patch	Up to 10 weeks; dose duration (7, 14, 21 mg) varies by cigarettes per day	1.64 (1.53-1.75) 51 trials	Better compliance, few side effects, affordable; does not address cue-elicited craving
Nicotine spray	Up to 6 mo; 8-40 sprays per day	2.02 (1.49-2.73) 4 trials	Rapid nicotine absorption and addresses cue-elicited craving; higher side effects and poor adherence
Nicotine inhaler	Up to 6 mo; 6-16 cartridges per day	1.90 (1.36-2.67) 4 trials	Address cue-elicited craving; higher side effects and poor adherence
Nicotine lozenge	Up to 12 weeks; 2 mg (for those who smoke their first cigarette >30 min after waking) and 4 mg (for those who smoke their first cigarette <30 min of waking)	1.52 (1.32-1.74) 8 trials	Address cue-elicited craving and affordable; lower compliance
Bupropion	12-24 weeks; 300 mg/d; 150 mg/d for 3 d then 300 mg/d from day 4 to end of treatment	1.85 (1.63-2.10) 36 trials	More contraindications and more expensive; can mitigate abstinence-induced weight gain
Varenicline	12-24 weeks; 2 mg/d; 0.5 mg for days 1-3, 0.5 mg twice daily for 4 d, and 1 mg twice daily from day 8 to end of treatment	2.24 (2.06-2.43) 27 trials	Well-tolerated; reduces withdrawal and reinforcing effects of nicotine; can cause nausea

Table 1 From The ASAM Principles of Addiction Medicine 7th Edition. 2024 Chapter 65. Pharmacological Interventions for Ncotine and Tobacco Use. p 1032

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Q3. The patient successfully quits smoking using bupropion. He asks you "What is my chance of being off cigarettes at one year?"

Which of the following is the most accurate statement?

A. Rates of recurrent use are high, with 40% of smokers returning to use in the first year.

B. The highest rates of abstinence are achieved in the first year, during which almost 75% of smokers will achieve abstinence. Rates of longer-term abstinence continue to steadily increase.

C. Return to use is extremely common in the first 3-6 months after a quit attempt, but the rates of recurrent use drop significantly after 6 months.

D. Former cigarette smokers who remain abstinent for at least two years return to use at a rate of 2% - 4 % each year within the second through sixth years, but this risk decreases to less than 1% annually after 10 years of abstinence.

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D. Former cigarette smokers who remain abstinent for at least two years have a risk of recurrent use of 2% - 4% each year within the second through sixth years, but this risk decreases to less than 1% annually after 10 years of abstinence.

Return to use is a major problem with nicotine use disorders, particularly in the first two years after a quit attempt and in spite of treatment.

Up to 90%, not 40%, of patients will return to use annually in the first two years, but once **two** years of abstinence is achieved, this rate diminishes substantially and decreases to less than 1% annually after 10 year of abstinence.

Efforts to enhance abstinence can be achieved through supportive psychotherapy and techniques for preventing return to use.

John R. Hughes, Erica N. Peters, and Shelly Naud. Relapse to Smoking After 1 Year of Abstinence: A Meta-analysis. Addict Behav. 2008 Dec; 33(12): 1516–1520
https://www.eurekalert.org/pub_releases/2002-02/cfta-srr022702.php

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Factors Associated with Odds of Relapsing on Cigarette Smoking

- Smoking being allowed in the home
- Married status decreased odds of relapse compared to single, divorced, widowed, never married, and separated statuses
- Older age decreased odds, Younger age (18-24) had the highest odds of relapse
- Continuous smoking cessation of less than 6 months
- Hispanic persons had higher odds of relapse compared to White (non-Hispanic) persons

Aboksmaty A, Agaku IT, Odani S, *et al*
Prevalence and determinants of cigarette smoking relapse among US adult smokers: a longitudinal study. *BMJ Open* 2019;**9:**e031676. doi: 10.1136/bmjopen-2019-031676

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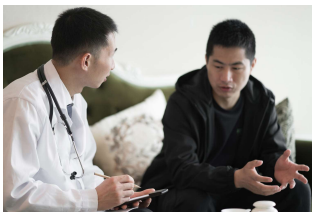
Vignette for Q4:

You see the patient one year later for his yearly physical. While he has not resumed smoking cigarettes, he has started to use e-cigarettes, noting that his girlfriend had started vaping and when he told her he was really craving cigarettes that it would be a good way for him to avoid returning to them.



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Q4. Regarding the use of vaping, which of the following is not true?

A. Most people who use vapes to stop smoking tobacco cigarettes are successful and do not use tobacco cigarettes at the same time they are vaping.

B. Levels of nicotine vaping amongst high school students rose dramatically from 2017 to 2019, peaking historically, before declining significantly during the COVID pandemic.

C. Nicotine vapes are equally as addictive as tobacco cigarettes.

D. Many users of vapes have greater nicotine exposure than when they were smoking tobacco cigarettes.

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A. Most people who use vapes to stop smoking tobacco cigarettes are successful and do not use tobacco cigarettes at the same time they are vaping **NOT TRUE**

- Most people who vape to quit smoking tobacco cigarettes end up using both products simultaneously, which renders their use in smoking cessation questionable. A 2022 meta-analysis deemed efficacy estimates of e-cigarettes for tobacco cessation to be uncertain/imprecise despite some positive RCTs and some signal for efficacy. Estimates of relative harm are even less well-known.

Thomas KH, et al. Comparative clinical effectiveness and safety of tobacco cessation pharmacotherapies and electronic cigarettes: a systematic review and network meta-analysis of randomized controlled trials. Addiction. 2022 Apr;117(4):861-876.

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A. Most people who use vapes to stop smoking tobacco cigarettes are successful and do not use tobacco cigarettes at the same time they are vaping **NOT TRUE**

- Although e-cigarettes have been associated with a number of different pulmonary and cardiac issues, regular tobacco cigarettes contain over 7000 chemicals and cause a greater burden of disease.
- Because of the ease of increasing nicotine with use of e-cigarettes, many users end up using more nicotine when they switch.
- Decreases in vaping amongst HS students during the COVID pandemic likely reflected constraints in supply chains for e-devices as well as changes in school and social structure related to the pandemic.

https://www.hopkinsmedicine.org/health/wellness-and-prevention/5-truths-you-need-to-know-about-vaping
Johnston, et al. Monitoring the Future, National Survey Results on Drug Use, 1975-2021. 2021 Overview. Key Findings on Adolescent Drug Use.
Thomas KH, et al. Comparative clinical effectiveness and safety of tobacco cessation pharmacotherapies and electronic cigarettes: a systematic review and network meta-analysis of randomized controlled trials. Addiction. 2022 Apr;117(4):861-876.

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Q5. A 75-year-old Caucasian male with COPD and hypertension presents to your primary care office to establish care. He takes lisinopril 20 mg and 2 inhalations of tiotropium bromide-olodaterol daily. He has a 40 pack/year smoking history and has not smoked a cigarette in 20 years. He shares his previous physician used to test him for cancer every year and wants to restart that testing as soon as possible. What is the most appropriate recommendation regarding cancer screening for this patient?

A. Low-dose CT scan every year for the next 5 years
B. No lung cancer screening due to patient's age
C. Low-dose CT scan every year for the next 10 years
D. No lung cancer screening due to duration of abstinence from cigarettes

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D. No lung cancer screening due to duration of abstinence from cigarettes

While this patient is in the correct age range to be screened, 50-80 years old, he stopped smoking 20 years ago and annual screening for lung cancer is no longer recommended

Recommendation Summary

Population	Recommendation	Grade
Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

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USPSTF Recommendations for Tobacco Screening

Screening ALL adults & pregnant persons for tobacco use is recommended

Recommendation Summary

Population	Recommendation	Grade
Nonpregnant adults	The USPSTF recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and US Food and Drug Administration (FDA)--approved pharmacotherapy for cessation to nonpregnant adults who use tobacco.	A
Pregnant persons	The USPSTF recommends that clinicians ask all pregnant persons about tobacco use, advise them to stop using tobacco, and provide behavioral interventions for cessation to pregnant persons who use tobacco.	A
Pregnant persons	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of pharmacotherapy interventions for tobacco cessation in pregnant persons.	I
All adults	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of electronic cigarettes (e-cigarettes) for tobacco cessation in adults, including pregnant persons. The USPSTF recommends that clinicians direct patients who use tobacco to other tobacco cessation interventions with proven effectiveness and established safety. See the Practice Considerations section for more information on recommended behavioral interventions and pharmacotherapy and for suggestions for practice regarding the I statements.	I

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USPSTF Recommendations for Tobacco Screening

There are currently NO USPSTF Guidelines for SCREENING children and adolescents for tobacco and nicotine use. There ARE recommendations for providing education and counseling.

"The US Preventive Services Task Force (USPSTF) recommends in its 2020 recommendation statement that pediatricians provide education or brief counseling to prevent initiation of tobacco use among school-aged children and adolescents."

The USPSTF Tobacco Use Prevention and Cessation in Children and Adolescents is still being updated

Reference:
https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions#:~:text=Recommendation%20Summary&text=The%20USPSTF%20recommends%20that%20clinicians%20ask%20all%20pregnant%20persons%20about,pregnant%20persons%20who%20use%20tobacco.

Recommendation: Tobacco Use in Children and Adolescents: Primary Care Interventions | United States Preventive Services Taskforce

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Tobacco Screening for Adolescents

CLINICAL REPORT| APRIL 17 2023

Protecting Children and Adolescents From Tobacco and Nicotine

The American Academy of Pediatrics DOES however recommend SCREENING adolescents for tobacco and nicotine use at routine health maintenance visits.

Screening tools for adolescent substance use, including tobacco and nicotine include:

- The Car-Relax-Alone-Forget-Friends-Trouble 2.1+N
- Brief Screener for Tobacco, Alcohol, and other Drugs
- Screening to Brief Intervention

References:
Jenssen, BP et al. Protecting children and adolescents from tobacco and nicotine. *Pediatrics.* 2023;151(5): e2023061805. https://doi.org/10.1542/peds.2023-061805

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Q6. Regarding the use of smokeless chewing tobacco and cigars, which of the following statements is *false* regarding the use of non-cigarette forms of tobacco delivery?

A. Men are four times more likely to use smokeless tobacco than women.
B. Evidence has demonstrated that non-cigarette tobacco users who use those products in combination with cigarettes have a more difficult time quitting either.
C. The use of cigars and pipes is associated with cancers of the lung, stomach, oral cavity, larynx, and esophagus.
D. E-cigarettes with nicotine improve quit rates compared to NRT for people who smoke tobacco

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B. Evidence has demonstrated that non-cigarette tobacco users who use those products in combination with cigarettes have a more difficult time quitting either.

Evidence is actually mixed and has not definitively demonstrated comparative successes (or failures) in quitting when non-cigarette tobacco products are used in conjunction with cigarettes (or alone).

Smokeless tobacco is used by 4% of men and 1% of women according to the most recent population estimates.

The use of cigars and pipes is associated with cancers of the lung, stomach, oral cavity, larynx, and esophagus. Smokeless tobacco on the other hand is typically associated with oral, pancreatic and esophageal cancer, but no clear evidence has associated use with stomach cancer.

Tobacco Use and Dependence Guideline Panel. Treating Tobacco Use and Dependence: 2008 Update. Rockville (MD): US Department of Health and Human Services; 2008 May. Available from: https://www.ncbi.nlm.nih.gov/books/NBK63952/

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B. Evidence has demonstrated that non-cigarette tobacco users who use those products in combination with cigarettes have a more difficult time quitting either.
NOT TRUE

Cochrane Review January 2024

Living systematic review - will continue to be updated as new evidence is available

- High certainly evidence that nicotine EC increase quit rates compared to NRT
- Moderate-certainty evidence that nicotine EC increase quit rates compared to non-nicotine EC
- No evidence of serious adverse events from nicotine EC but limited by follow-up of only 2 years and small number of studies

Reference:

Lindson, N et al. Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev.* 2024;1(1):CD010216.

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Q7. Which of these is *not* part of the Fagerström test for nicotine dependence?

A. How soon after you wake up do you smoke your first cigarette?

B. Do you find it difficult to refrain from smoking in places where it is forbidden (e.g., in church, at the library, in cinema, etc)?

C. Which cigarette would you hate most to give up?

D. How often have you attempted to quit smoking?

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D. How often have you attempted to quit smoking?
Fägerstrom Test for Nicotine Dependence (FTND)

- How soon after you **wake up** do you smoke your 1st cigarette?
  - *> 60 min (0)*
  - *31-60 min (1)*
  - *6-30 min (2)*
  - *Within 5 min (3)*
- Is it difficult to not smoke in places where it is **forbidden** (e.g., church, school, hospital)?
  - *No (0)*
  - *Yes (1)*
- Which cigarette would you **hate** most to **give up**/treasure the most?
  - *First morning cigarette (1)*
  - *Any other one (0)*
- **How many** cigarettes/day?
  - *≤ 10 (0)*
  - *11-20 (1)*
  - *21-30 (2)*
  - *≥ 31 (3)*
- Smoke more **during first few hours** after waking up than the rest of the day?
  - *No (0)*
  - *Yes (1)*
- Do you **still smoke if you are sick** (have a cold or the flu, difficulty breathing, in bed all day, etc.)?
  - *No (0)*
  - *Yes (1)*

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Vignette for Q8:

A local obstetrician refers to your clinic a new patient, a 26 year-old G1P0 at 13 weeks into her pregnancy who smokes 15 cigarettes per day and who twice during pregnancy already has had unsuccessful quite attempts despite behavioral counseling. The OB and patient both are hoping that you, as an addiction medicine specialist, can recommend safe and effective medications for this patient to augment the behavioral counseling that she has already undertaken.

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Q8. Which of the following statements about medications for tobacco use in pregnancy is most appropriate?

A. Continued behavioral counseling and no medication as the certain harms of medications on the developing fetus should be avoided.
B. Initiation of varenicline, which has the best efficacy of treatment options in pregnancy and has been shown to be safe.
C. Patient-centered selection between nicotine-replacement therapy and bupropion, which have more extensive safety data than varenicline and may benefit expectant mothers in their desire for smoking cessation.
D. Patient-centered selection amongst varenicline, bupropion, or nicotine-replacement therapy (NRT), which are all considered safe in pregnancy when balanced against the known harms of continued smoking.

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Answer: C. Patient-centered selection between nicotine-replacement therapy and bupropion, which have more extensive safety data than varenicline and may benefit expectant mothers in their desire for smoking cessation.

Smoking cessation counseling is the first-line gold standard intervention for all pregnant persons who wish to stop smoking. However, counseling is insufficient for some patients. Given the known harms of continued smoking during pregnancy, additional safe pharmacotherapy may be offered.

Risk factors for inability to quit include heavy smoking (>10 cig/day), prior unsuccessful quit attempts during pregnancy, and smoking later in pregnancy.

Tobacco and Nicotine Cessation During Pregnancy: ACOG Committee Opinion, Number 807. Obstet Gynecol. 2020;135(5):e221.

Hegaard HK, et al. "Multimodal intervention raises smoking cessation rate during pregnancy." Acta Obstet Gynecol Scand. 2003 Sep;82(9):813-9.

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Adverse pregnancy outcomes associated with smoking include:

- Placental abruption, preterm premature rupture of membranes (PPROM), placenta previa, preterm labor and delivery, low birth weight (LBW), and ectopic pregnancy.
- Possible mechanisms for these include impaired fetal oxygenation, altered fetal development and physiologic response, and toxin exposure.
- Postnatal morbidities that have been associated with maternal smoking include sudden infant death syndrome (SIDS), respiratory infections, asthma, infantile colic, bronchiolitis, short stature, lower reading and spelling scores, shorter attention spans, hyperactivity, childhood obesity, and decreased school performance.

Castles A, et al. "Effects of smoking during pregnancy. Five meta-analyses." Am J Prev Med. 1999;16(3):208.
Tobacco and Nicotine Cessation During Pregnancy: ACOG Committee Opinion, Number 807. Obstet Gynecol. 2020;135(5):e221.

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Answer: C. Patient-centered selection between nicotine-replacement therapy and bupropion, which have more extensive safety data than varenicline and may benefit expectant mothers in their desire for smoking cessation.

- The benefits of quitting with specific pharmacotherapy outweighs the potential risks of pharmacotherapy when balanced against the risks of continued smoking.
- As with all safe prescribing practices during pregnancy, using the lowest effective dose to minimize fetal exposure and titrating up as necessary is recommended.
- Because of the paucity of safety data for varenicline in human pregnancy, its use is avoided.
- NRT and bupropion both have reasonable safety data in pregnancy when compared to ongoing combustible tobacco use, though there are no direct head-to-head trials to recommend one over the other and patient-centered decision-making should be employed. Timing of initiation relative to key growth scan ultrasounds is also a consideration.

Chan B, et al. "Effectiveness of bupropion for smoking cessation during pregnancy." J Addict Dis. 2005;24(2):19.
Bérard A, et al. "Success of smoking cessation interventions during pregnancy." Am J Obstet Gynecol. 2016;215(5):611.e1.
Tobacco and Nicotine Cessation During Pregnancy: ACOG Committee Opinion, Number 807. Obstet Gynecol. 2020;135(5):e221.

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Q9. A 54-year-old female with tobacco use and osteoarthritis of her right knee presents to your office for a pre-operative evaluation for an upcoming knee arthroplasty. She tells you the surgeon advised her to stop smoking or her surgery will be delayed. She reports smoking 1-2 cigarettes per day which has been her pattern for 10 years. She has no other chronic medical conditions and as a part of the evaluation you order a plasma cotinine level which returns at 120 ng/mL. Based off this cotinine level, how many cigarettes is the patient possibly smoking on average in a day?

A. 1-2 cigarettes
B. 12-15 cigarettes
C. 18-20 cigarettes
D. 8-10 cigarettes

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Q9. The answer is B.12-15 cigarettes.

- 1 cigarette produces a cotinine level between 8-10 ng/mL
- 120 ng/mL divided by 10 is 12. 120 divide by 8 is 15. So a cotinine level of 120 ng/mL may indicate 12-15 cigarettes are being smoked
- 80% of nicotine is metabolized to cotinine by CYP2A6. Cotinine can be found in serum, urine, and saliva. Variability in metabolism limits its ability as a definitive quantitative marker of nicotine use by itself
- Cotinine levels greater than 5 ng/mL may indicate smoking and can range between 250-300 ng/mL in daily smokers

Dani, J. A., Kosten, T. R., & Benowitz, N. (2024). The Pharmacology of Nicotine and Tobacco. In *The ASAM Principles of Addiction Medicine* (7th ed., pp. 230–234). essay, Wolters Kluwer.

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Q10. You are speaking at a PTA meeting to educate parents about teenage substance use including cigarette use. One parent states she is worried that her 16-year-old son can just walk into any store to buy cigarettes. You tell her which of the following true statements about purchase of tobacco products?

A. The minimum age for the sale of all tobacco products is 18.
B. The minimum age for the sale of cigarettes is 21, whereas electronic nicotine delivery systems, hookah tobacco, and smokeless tobacco products can be sold to those who are 18 and above.
C. The minimum age for the sale of all tobacco products is 21.
D. A recent law raised the age for the sale of cigarettes from 18 to 21, and a sunset provision will go into effect in 2036 returning the minimum age to 18 and allow for re-assessment of the impacts of age requirements on the sale of cigarettes.

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Answer: C. The minimum age for the sale of all tobacco products is 21.

- Effective immediately on December 20, 2019 as signed by the President into US federal law, the minimum age for the sale of all tobacco products, including cigarettes, smokeless tobacco, hookah tobacco, cigars, pipe tobacco, electronic nicotine delivery systems including e-cigarettes and e-liquids, was raised from 18 to 21. There was no delay in enforcement, with no carve-outs for military personnel or certain types of tobacco products, and without a sunset provision.

Reference:
https://www.fda.gov/tobacco-products/retail-sales-tobacco-products/tobacco-21

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The Five A's

- Ask- inquire about patient's smoking or tobacco use. (ideally a validated screen would be used)
- Advise- direct, non-judgmental, personalized advice about smoking
- Assess- severity of use and readiness of patient to change
- Assist- help patients interested in change identify goals and a plan
- Arrange- follow up visit or even specialty referrals if needed

Video reviewing the 5 A's: https://www.youtube.com/watch?v=iYCMIuD6djc

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BENZODIAZEPINES

CSAM Addiction Medicine Board Review Course

August 13, 2025

Slides revised from Dr. Steven Tate, MD MSc

Jeremy Flores, MD

Health Sciences Clinical Instructor - UCLA Dept of Psychiatry, Addiction Division

Behavioral Health Services Lead- UCLA Homeless Healthcare Collaborative

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CONFLICT OF INTEREST DISCLOSURE

I, *Jeremy Flores,* have nothing to disclose, and I will not be discussing "off label" use of drugs or devices in this presentation.

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EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Discuss the neurobiology and pharmacology of benzodiazepines
2. Understand the prescribing history and epidemiology of benzodiazepine use
3. Discuss the management of intoxication and withdrawal, including benzodiazepine tapers
4. Recognize drug-drug interactions, toxicity and drug testing discrepancies

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Benzodiazepines: Need to Know

- The basic **structure** of benzodiazepines and the Z-Drugs
- History of development – background in relation to barbiturates
- **Epidemiology** of unhealthy use; use in pregnancy
- **Pharmacokinetics** – relative potencies, time of onset, half-lives; the parent drug and elimination half-life and excretion; CYP450 hepatic **metabolism** versus glucoronidation, onset of action and active metabolites
- **Pharmacodynamics** – development of physiologic dependence; GABA receptor characteristics, activity at the GABA receptor and antagonism
- **Drug-Drug interactions** and concomitant opioid and alcohol use
- **Toxicity** and how to treat benzodiazepine overdose and withdrawal syndromes
- **Addiction** liability and how to **taper**

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Principles of Addiction Medicine 6th Edition

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Benzodiazepines

Question 1: Which Benzodiazepine is commonly undetected on urine immunoassay?

a) Temazepam
b) Clonazepam
c) Diazepam
d) Oxazepam

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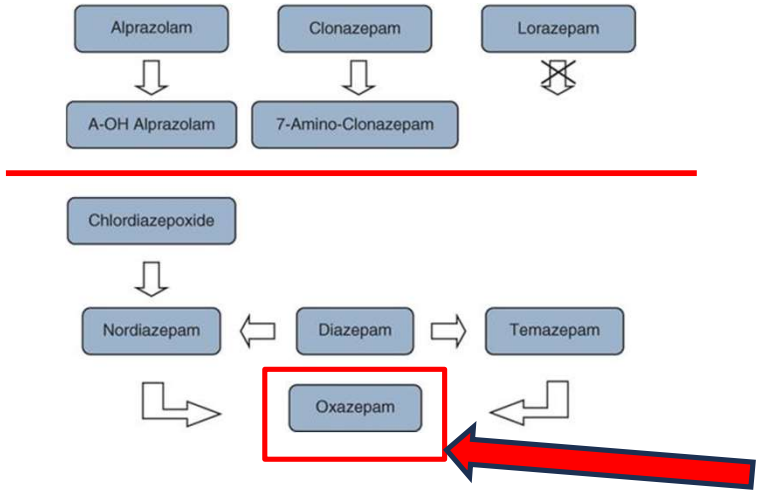
1) Answer: B - Clonazepam



Metabolite generally tested for on immunoassays

Sarah E. Wakeman, Joshua D. Lee, Anika A. H. Alvanzo. Pocket Addiction Medicine, 1e

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Benzodiazepines

Question 2: Paul is a 32-year-old with generalized anxiety disorder who has a fear of flying and requests an alprazolam prescription for an upcoming transcontinental flight to visit an ailing father with end-stage liver disease and a history of alcohol use disorder. Paul notes that he "tried a friend's xanax" and felt it was more effective than clonazepam and oxazepam which he had previously been prescribed for anxiety. What property of alprazolam explains this subjective effect that Paul is reporting?

a) Alprazolam has a rapid onset of action
b) Alprazolam has a greater duration of action than clonazepam and oxazepam
c) Alprazolam has greater anxiolytic effect than most other benzodiazepines
d) Alprazolam has less cognitive side effects than a long-acting benzodiazepine

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2) Answer: A - Alprazolam has a rapid onset of action

Most benzodiazepines have comparable sedative, anxiolytic, hypnotic, cognitive, and psychomotor performance effects (considering relative potency), but onset of action and duration of effects vary.

Alprazolam is highly potent, with a greater rate of absorption, a rapid onset contributing to increased euphoria, and a short half-life contributing faster withdrawal onset. These are all **pharmacokinetic** properties.

Pharmacokinetics determine drug onset and duration of effect.

Charles E. Griffin, III, MD, Adam M. Kaye, Pharm D, Franklin Rivera Bueno, MS,and Alan D. Kaye, MD, PhD, Benzodiazepine Pharmacology and Central Nervous System–Mediated Effects Ochsner J. 2013 Summer; 13(2): 214–223.

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2) Answer: A - Alprazolam has a rapid onset of action

Pharmacokinetic and Pharmacodynamic Properties of Commonly Used Benzodiazepines

Generic Drug	Approximate Dosage Equivalents (mg)	Time to Peak Plasma Level (Hours)	Elimination Half-Life (Hours)	Metabolite Activity
Alprazolam	0.5	1–2	12–15	Inactive
Chlordiazepoxide	10–25	2–4	24–48 (>96*)	Active
Clonazepam	0.25–0.5	1–4	30–40	Inactive
Diazepam	5	1–2	44–48 (50–100*)	Active
Lorazepam	1	1–6	10–20	Inactive
Oxazepam	15	2–4	5–20	Inactive
Temazepam	15	2.5	10–20	Active

**Denotes prolonged half-life due to active metabolites. (Sources: Peng et al, 2022; Management of Substance Use Disorders Work Group.* VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. *Washington, DC: Department of Veterans Affairs and Department of Defense; 2021.)*

Abelleria, A. *Benzodiazepines: The Basics and Beyond.* The Carlat Addiction Treatment Report. 2023

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Benzodiazepines

Question 3: What component of Paul's history likely places him at higher risk for problematic benzodiazepine use?

a) Paul's generalized anxiety disorder
b) Paul's previous exposure to multiple benzodiazepines
c) Paul's family history of alcohol use disorder
d) Paul's request of benzodiazepines for anxiety related to flying

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3) Answer: C- Patients with alcohol-use-disorder and a family history of alcohol use disorder are likely at greater risk for benzodiazepine misuse.

(1) moderate to heavy drinkers, (2) people with alcohol use disorder, even if abstinent, and (3) people with a family history of alcohol use disorder are at greater risk for problematic benzodiazepine use compared to those with anxiety disorders.

In addition, patients with opioid use disorder, including those on mOUD are at increased risk of problematic benzodiazepine use.

"In one report, 47% of patients in a methadone [opioid treatment program] reported having a history of benzodiazepine use, with more than half of these patients starting the use of benzodiazepines after entering the methadone maintenance program" - ASAM Essentials

ASAM Essentials, Chap 52

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Benzodiazepines

Question 4: Which of the following statements about interaction between BZDs and the GABA receptor is **False**?

a) BZD require the presence of GABA at the receptor
b) BZD increase the duration of the opening of the receptor
c) BZD bind at the cleft between the alpha and gamma subunits
d) BZD potentiate the inhibitory effects of GABA in the CNS

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4) Answer: B- BZD increase the duration of the opening of the receptor

- The GABA receptor consists of 5 transmembrane glycoprotein subunits around a Chloride channel pore.
- BZD increase the **frequency** of the chloride-channel opening, Barbiturates increase the **duration** and do NOT require the presence of GABA
- They both potentiate the inhibitory effects of GABA in the CNS
- Together Benzodiazepines and Barbiturates have a synergistic effect and use of them together increases the risk for respiratory depression especially with other CNS depressants like alcohol

Soyka. The Treatment of Benzodiazepine Dependence. NEJM 2017, 376;12

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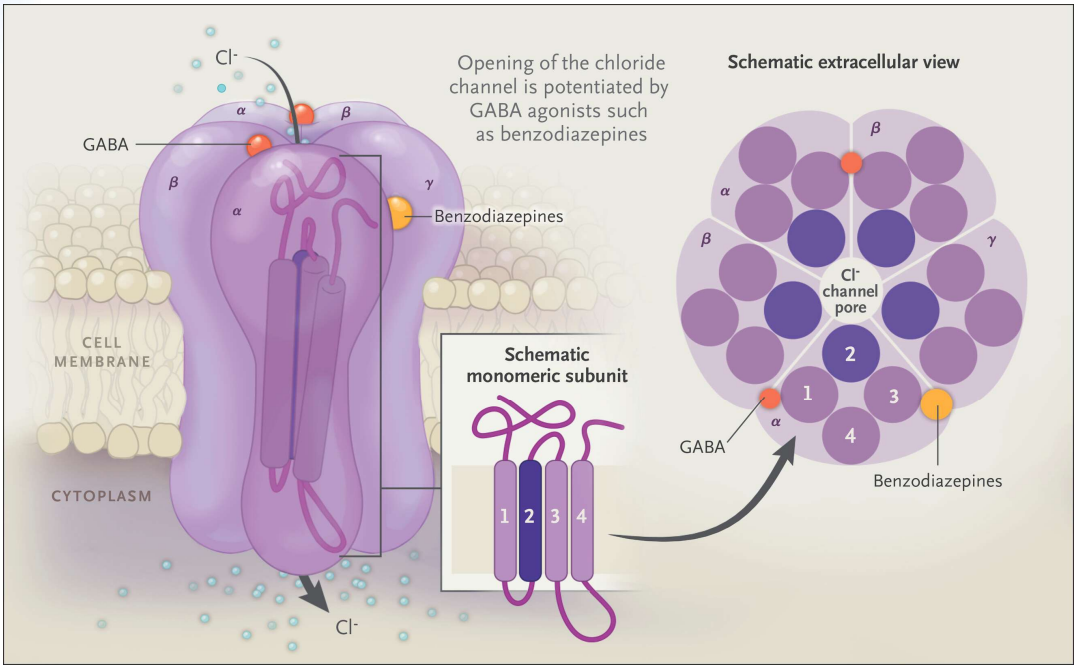

Soyka. The Treatment of Benzodiazepine Dependence. NEJM 2017, 376;12

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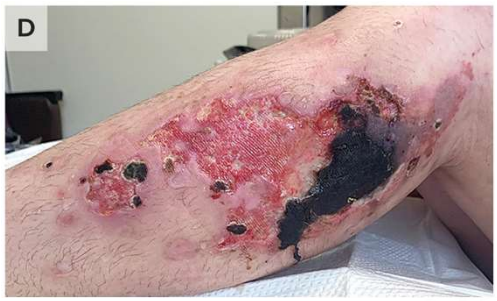
Benzodiazepines

Question 5: A 45-year-old man experiencing homelessness was found unresponsive by EMTs. He responded to naloxone on route to the emergency department and found to have significant extremity wounds similar to the figure below. The patient told the team that he has only been using "Xanax bars" but his urine drug screen was positive for fentanyl. Approximately what percentage of fentanyl overdoses involve benzodiazepines?

a) 10%
b) 20%
c) 30%
d) 50%



O'Neil, J., & Kovach, S. (2023). Xylazine-Associated Skin Injury. *The New England journal of medicine*, *388*(24), 2274. https://doi.org/10.1056/NEJMicm2303601

316

5) Answer: C – 30%

In a multicenter U.S. emergency department study (2020–2023), **29.0% of patients** with confirmed opioid overdose (the majority of which involved fentanyl) had detectable benzodiazepines, including both prescription (20.5%) and novel (8.5%) agents. A forensic toxicology review found that after opioids, **benzodiazepines were among the most frequently detected drug classes in cases where xylazine was present with fentanyl**

In 2022, the U.S. Drug Enforcement Agency (DEA) Laboratory found that **six in ten** illicitly manufactured benzodiazepines contained a potentially fatal dose of fentanyl.

Hughes, A., Spungen, H., Culbreth, R., Aldy, K., Krotulski, A., Hendrickson, R. G., Amaducci, A., Judge, B., Meaden, C., Calello, D. P., Buchanan, J., Carpenter, J., Shulman, J., Brent, J., Wax, P., Campleman, S., Levine, M., Schwarz, E., & Manini, A. F. (2025). Benzodiazepine Co-Exposure Among Patients Presenting to the Emergency Department With a Confirmed Opioid Overdose. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine, 10.1111/acem.70104. Advance online publication. https://doi.org/10.1111/acem.70104

Liu S, O'Donnell J, Gladden RM, McGlone L, Chowdhury F. Trends in Nonfatal and Fatal Overdoses Involving Benzodiazepines — 38 States and the District of Columbia, 2019–2020. MMWR Morb Mortal Wkly Rep 2021;70:1136–1141. DOI: http://dx.doi.org/10.15585/mmwr.mm7034a2external icon

Drug Enforcement Administration. *"DEA Laboratory Testing Reveals that 6 out of 10 Fentanyl-Laced Fake Prescription Pills Now Contain a Potentially Lethal Dose of Fentanyl"* Public Safety Alert. https://www.dea.gov/alert/dea-laboratory-testing-reveals-6-out-10-fentanyl-laced-fake-prescription-pills-now-contain

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Benzodiazepines

Question 6: A 32 y/o female presents to your treatment program for help in getting off alprazolam. The patient has been prescribed three to four 2 mg alprazolam tabs (6-8 mg) daily as needed for the past 6 years. She gets anxiety with tremors when she tries to stop. After drug screens are negative for other substances besides alprazolam, all the following would be acceptable treatment options ***except***:

a) Assess for seizure risk and consider inpatient treatment
b) Switch to diazepam and provided a short, fixed dose taper over the course of a week
c) Continue with current alprazolam and begin gradual taper
d) Switch to chlordiazepoxide and taper slowly over several months

CSAM

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6) Answer: B - Switch to diazepam and provided a short, fixed dose taper over the course of a week

Table 3. Risk for Clinically Significant BZD Withdrawal*

Duration of BZD Use	Frequency of BZD Use	Total Daily BZD Dose	Risk for Clinically Significant Withdrawal†
Any	≤3 days per week	Any	Rare
<1 month	≥4 days per week	Any	Lower risk, but possible
1–3 months	≥4 days per week	Low‡	Lower risk, but possible
1–3 months	≥4 days per week	Moderate§ to high**	Yes, with greater risk with increasing dose and duration
≥3 months	≥4 days per week	Any	Yes, with greater risk with increasing dose and duration

Brunner, E., Chen, C. A., Klein, T., Maust, D., Mazer-Amirshahi, M., Mecca, M., Najera, D., Ogbonna, C., Rajneesh, K. F., Roll, E., Sanders, A. E., Snodgrass, B., VandenBerg, A., Wright, T., Boyle, M., Devoto, A., Framnes-DeBoer, S., Kleykamp, B., Norrington, J., & Lindsay, D. (2025). Joint Clinical Practice Guideline on Benzodiazepine Tapering: Considerations When Risks Outweigh Benefits. Journal of general internal medicine, 10.1007/s11606-025-09499-2. Advance online publication. https://doi.org/10.1007/s11606-025-09499-2

CSAM

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6) Answer: B - Switch to diazepam and provided a short, fixed dose taper over the course of a week

A Cochrane Review in 2006 failed to find any convincing evidence for one treatment strategy over another. **However, a rapid taper is rarely tolerated, especially in the outpatient setting.**

If there is a need for a rapid taper such as with "high dose + erratic-dose, illicit source, “polysubstance,” or alcohol plus sedative-hypnotic use, then patients will likely need to be in a medically monitored setting. Agents such as phenobarbital can be considered.

Gradual taper of same benzodiazepine, switching to a longer acting benzodiazepine and using other agents such as carbamazepine are probably all acceptable methods of taper, given current limited state of knowledge.

Tapering will usually take months. One possibility: Reduce dose initially by 5-10% every 2-4 weeks (even longer). Usually no more than 25% every two weeks. Anticipate rebound anxiety and insomnia

Additional **psychosocial support and education** are the most helpful things you can offer patients.

Brunner, E., Chen, C. A., Klein, T., Maust, D., Mazer-Amirshahi, M., Mecca, M., Najera, D., Ogbonna, C., Rajneesh, K. F., Roll, E., Sanders, A. E., Snodgrass, B., VandenBerg, A., Wright, T., Boyle, M., Devoto, A., Framnes-DeBoer, S., Kleykamp, B., Norrington, J., & Lindsay, D. (2025). Joint Clinical Practice Guideline on Benzodiazepine Tapering: Considerations When Risks Outweigh Benefits. Journal of general internal medicine, 10.1007/s11606-025-09499-2. Advance online publication. https://doi.org/10.1007/s11606-025-09499-2

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Benzodiazepines

Question 7: Sally is a 54-year-old woman with alcohol-associated cirrhosis and is admitted for alcohol withdrawal. Which benzodiazepine would be the best option to manage alcohol withdrawal symptoms and why?

a) Clonazepam– because it is not metabolized by cytochrome P-450 enzymes
b) Chlordiazepoxide—because an end metabolite is oxazepam
c) Oxazepam– because it is not metabolized by cytochrome P-450 enzymes
d) Alprazolam – because of its half-life

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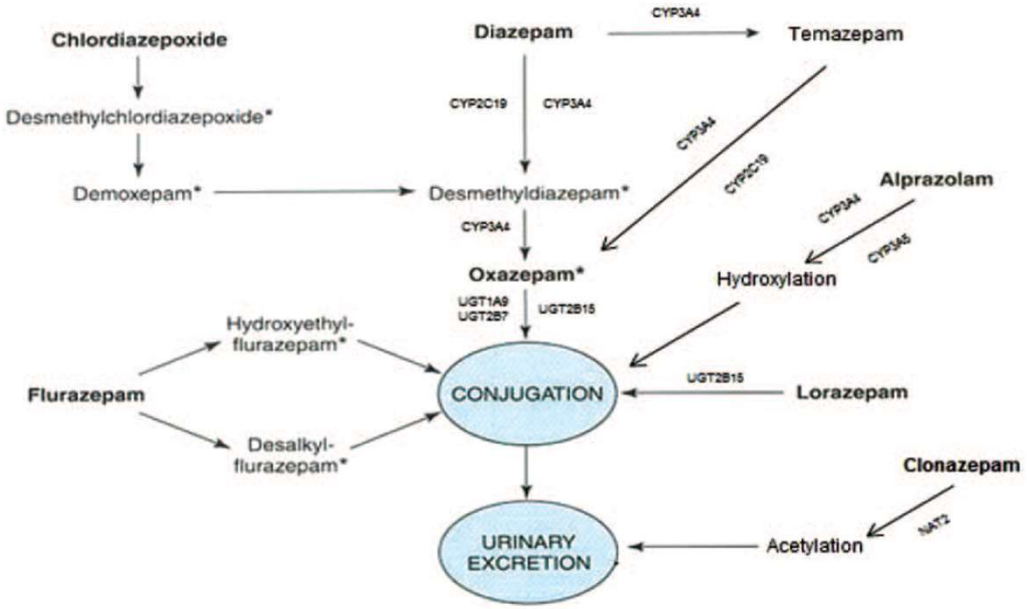
7) Answer: C - not metabolized by cytochrome P-450 enzymes



Behnoush B, Sheikhazadi A, Bazmi E, Fattahi A, Sheikhazadi E, Saberi Anary SH. Comparison of UHPLC and HPLC in benzodiazepines analysis of postmortem samples: a case-control study. Medicine (Baltimore). 2015 Apr;94(14):e640.

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Benzodiazepines

Question 8: A 33-year-old woman presents to the clinic requesting to stop her Lorazepam that she had been taking daily for 3 years. Which of the following symptoms of benzodiazepine withdrawal would you not expect to see?

A. Tachycardia/Hypertension

B. Agitation/Hallucinations/Seizures

C. Nausea/Diarrhea

D. Piloerection, diaphoresis, and temperature dysregulation

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Answer: D- Piloerection, diaphoresis, and temperature dysregulation

- Symptoms of benzodiazepine discontinuation fall into 4 categories
  - *Symptom recurrence or relapse* – recurrence of symptoms such as anxiety or insomnia for which the BZD was initially intended to treat.
  - *Rebound* – symptoms within hours to days of medication discontinuation that are similar but more intense than before treatment
  - *Psychological withdrawal* – occurs when the expectations of withdrawal lead to the experience of withdrawal symptoms, without any reduction in the medicine (fear, anticipation)
  - *Physical withdrawal* – occurs when a BZD is stopped in an individual with physical dependence on the medication, symptoms are psychological and somatic, can use CIWA – Ar scale to monitor/follow symptoms

ASAM Essentials, Chap 52

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Answer: D- Piloerection, diaphoresis, temperature dysregulation

Table 4. Common Benzodiazepine Withdrawal Signs and Symptoms*

General	Affective	Cardiovascular	Gastrointestinal
• Elevated blood pressure • Headaches • Sweating, night sweats	• Anxiety, panic attacks • Depression, dysphoria • Irritability, agitation, aggression	• Chest pain • Palpitations • Tachycardia	• Abdominal cramps • Diarrhea • Nausea and vomiting
Neurological	**Neuromuscular**	**Neuropsychiatric**	**Sleep**
• Cognitive impairment (eg, poor memory, reduced concentration) • Confusion, delirium† • Perceptual disturbance • Seizures† • Sensory hypersensitivity (ie, to light, sound, taste, and smell) • Tingling, numbness, altered sensation • Tinnitus	• Coordination, balance problems • Dysesthesia, kinetic disorders • Muscle pain (eg, tension, weakness, spasms) • Muscle twitches, jerks, and fasciculations • Tremors	• Akathisia, restlessness • Depersonalization, derealization • Psychosis (eg, paranoia)† • Suicidality and self-harm	• Hypersomnia • Insomnia • Nightmares

Brunner, E., Chen, C. A., Klein, T., Maust, D., Mazer-Amirshahi, M., Mecca, M., Najera, D., Ogbonna, C., Rajneesh, K. F., Roll, E., Sanders, A. E., Snodgrass, B., VandenBerg, A., Wright, T., Boyle, M., Devoto, A., Framnes-DeBoer, S., Kleykamp, B., Norrington, J., & Lindsay, D. (2025). Joint Clinical Practice Guideline on Benzodiazepine Tapering: Considerations When Risks Outweigh Benefits. Journal of general internal medicine, 10.1007/s11606-025-09499-2. Advance online publication. https://doi.org/10.1007/s11606-025-09499-2

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Benzodiazepines

Question 9: A 43 y/o female with history of panic disorder presents to the ED after a seizure. Her CT head is within normal limits and urine immunoassay is negative. A few days later her confirmatory test detects 7-amino-clonazepam at 215 ng/ml. The patient admits to taking 7-9 mg clonazepam daily, self-obtained. What is the next best step?

a) Prescribe alprazolam and refer to residential treatment
b) Coordinate outpatient care for chlordiazepoxide taper along with psychotherapy services.
c) Add levetiracetam (Keppra®) 500 mg twice a day to clonazepam taper
d) Add quetiapine 50 mg as needed for anxiety

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9) Answer: B - Coordinate outpatient care for chlordiazepoxide taper along with psychotherapy referral.

The patient's urine clonazepam metabolite levels are low which accounts for the seizure. One option is to begin taper with a long-acting agent such as chlordiazepoxide. Changing from a long-acting to short-acting agent such as alprazolam offers no advantage, only potential complications for inter-dose rebound withdrawal.

Patients with Sedative, Hypnotic or Anxiolytic Use Disorders should receive additional psychosocial intervention and treatment in addition to medically supervised tapers.

The seizure is most likely due to known benzodiazepine withdrawal; therefore, **anti-epileptic and antipsychotic medications are not usually standard of care in acute benzodiazepine withdrawal**. However, the use of other anti-convulsive medications such as gabapentin could be used for post acute withdrawal syndrome (PAWS)

Darker CD, Sweeney BP, Barry JM, Farrell MF, Donnelly-Swift E. Psychosocial interventions for benzodiazepine harmful use, abuse or dependence. Cochrane Database Syst Rev. 2015;(5):CD009652. doi: 10.1002/14651858.CD009652.pub2. PMID: 26106751.

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Benzodiazepines

Question 10: Phil is a 73-year-old male retiree who takes care of his school-aged grandchildren and is establishing care with you, requesting that you continue his previous lorazepam 0.5 mg bedtime prn dose that he only uses on rare occasions and may only need #30 tabs every 6 months. What aspect of Phil's history is typical for a patient who uses benzodiazepines?

a) His sex
b) His age
c) Lorazepam use
d) His long-term use

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10) Answer: B - His age

- Approximately **12.5% of adults** in the United States use benzodiazepines, 2.1% have misuse, and 0.2% meet criteria for a use disorder.
- The prevalence of use increases as people age.
- National Survey on Drug Use and Health

	NSDUH respondents overall (n=86,186) Weighted %[a]	BZD use				
		None (n=75,896) Weighted %	Any (n=10,290) Weighted %	F[b]	df	p-value
Overall	100.0	87.5	12.6	—	—	—
Demographic Characteristics						
Age				18.2	3, 138	<.001
18-25	14.3	89.8	10.2			
26-34	15.8	88.3	11.7			
35-49	24.9	87.6	12.4			
50-64	25.6	85.7	14.3			
≥65	19.4	87.1	12.9			

Maust, D. T., Lin, L. A., & Blow, F. C. (2019). Benzodiazepine Use and Misuse Among Adults in the United States. Psychiatric services (Washington, D.C.), 70(2), 97–106. https://doi.org/10.1176/appi.ps.201800321

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10) Answer: B - His age

- The prevalence of use increases as people age. Use ranged from:
  - *2.6% (18-35)*
  - *5.4% (36-50)*
  - *7.4% (51-64)*
  - ***8.7% (65-80)***
- Benzodiazepine use is twice as prevalent in **women** >> as in men.
- In the oldest age group (65-80), **31.4%** of those using benzodiazepines are using them long term (>120 days).
- In 1970 BZD accounted for 10 % of all prescriptions written in the US.

The Journal of Clinical Psychiatry. 2018;79(6):18m12174. doi:10.4088/JCP.18m12174.

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Benzodiazepines

Question 11: Jane is a 27-year-old G1P0 who is 10 weeks pregnant and has been referred to you by high-risk OB, because she is taking diazepam 20 mg daily for back spasms and insomnia, along with buprenorphine 10mg sublingual daily. Which of the following is **False**?

a) Prenatal benzodiazepine use can exacerbate neonatal abstinence syndrome (NAS) in the presence of opioid use disorder and can cause seizures in the newborn.
b) Diazepam is highly teratogenic, and the patient should switch to temazepam.
c) While medically assisted opioid tapering is contraindicated in pregnancy, sedative–hypnotic–anxiolytic tapering can be accomplished with caution and regular monitoring.
d) Possible neonatal benzodiazepine effects include neonatal withdrawal symptoms and floppy infant syndrome.

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11) Answer: B- Diazepam is highly teratogenic therefore switch to temazepam.

- In the FDA's previous pregnancy risk categories most benzodiazepines were **Category D** rating (positive evidence of human fetal risk), more current recommendations state to weigh risk versus benefit. However, four sedative-hypnotics (flurazepam, estazolam, **temazepam**, and quazepam) had a Category X rating and are contraindicated in pregnancy. **Do Not switch her to temazepam – at best the risk is not lessened.**
- Prenatal benzodiazepine use can exacerbate neonatal abstinence syndrome (NAS) **in the presence of opioid use disorder** and can cause seizures in the newborn.
- While medically assisted opioid withdrawal is contraindicated in pregnancy, one could perform sedative–hypnotic–anxiolytic tapering slowly and regular monitoring.

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11) Answer: B- Diazepam is highly teratogenic therefore switch to temazepam.

- Newborns exposed to benzodiazepines in utero in the 3rd trimester or during delivery may present with floppy infant syndrome (low Apgar score, poor sucking, hypotonia, diminished reflexes, and/or apnea). Neonatal withdrawal syndromes have also been described.
- Severe benzodiazepine withdrawal symptoms during pregnancy can place the fetus in distress, potentially causing miscarriage, and may induce preterm labor.
- All classes of benzodiazepines (and phenobarbital) cross the placenta and are excreted in breast milk

Pg. 731 Principles of Addiction Medicine 6th Edition

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Benzodiazepines

Question 12: Tiffany is a 26-year-old post-graduate student from Singapore who comes to you during a student health clinic visit asking for zolpidem because of insomnia and alprazolam for panic attacks. The risks of this request for zolpidem and alprazolam include all of the following ***except***:

a) Suicide
b) Mortality
c) Motor Vehicle Accidents
d) Cerebrovascular Accident

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12) Answer: D - Cerebrovascular Accident

- Benzodiazepines appear to cause an overall **increase in the risk of attempting or completing suicide**. Possible mechanisms of pro-suicidal effects may include increases in impulsivity or aggression, rebound or withdrawal symptoms, and toxicity in overdose.

- **Subgroup analyses showed that the exposure to zolpidem consistently increased the OR of suicide and suicide attempt** in different age groups, sex, urbanization level, occupation, mental disorders, and comorbidity index levels and in groups of people with or without the presence of insomnia.

Dodds TJ. Prescribed Benzodiazepines and Suicide Risk: A Review of the Literature. Prim Care Companion CNS Disord. 2017
Sun Y, et al Association Between Zolpidem and Suicide: A Nationwide Population-Based Case-Control Study. Mayo Clin Proc. 2016
Weich S, et al. Effect of anxiolytic and hypnotic drug prescriptions on mortality hazards: retrospective cohort study BMJ 2014
Brandt J, et l Benzodiazepines and Z-Drugs: An Updated Review of Major Adverse Outcomes Reported on in Epidemiologic Research. Drugs R D. 2017
https://www.mdcalc.com/charlson-comorbidity-index-cci

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12) Answer: d) Cerebrovascular Accident

BMJ study, published in 2014, retrospective cohort study of over 100 K patients

- Patients were followed for a mean **of 7.6 years**
- Age adjusted hazard ratio for **mortality** during the entire follow-up period for use of any benzodiazepine or Z drug in the first year
  - *after adjusting for potential confounders* ***3.32*** *(3.19 to 3.45).*

- There is an **overwhelming degree of evidence, both experimental and epidemiological, implicating benzodiazepines and Z-drugs, with fatal and non-fatal motor vehicle accidents.**

Weich S, et al. Effect of anxiolytic and hypnotic drug prescriptions on mortality hazards: retrospective cohort study BMJ 2014
Dodds TJ. Prescribed Benzodiazepines and Suicide Risk: A Review of the Literature. Prim Care Companion CNS Disord. 2017
Sun Y, et al Association Between Zolpidem and Suicide: A Nationwide Population-Based Case-Control Study. Mayo Clin Proc. 2016
Brandt J, et l Benzodiazepines and Z-Drugs: An Updated Review of Major Adverse Outcomes Reported on in Epidemiologic Research. Drugs R D. 2017

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Benzodiazepines

Question 13: Alex is a 28-year-old graduate student who was originally prescribed sodium oxybate (the sodium salt of γ-hydroxybutyric acid [GHB]) for narcolepsy 5 year prior until they had escalating doses and transitioned to procuring and using illicit GHB to promote sleep and prevent withdrawal. They now present to the ED requesting GHB withdrawal management. All of the following are true about GHB withdrawal ***except***:

a) GHB withdrawal can include diaphoresis, tremors, and anxiety
b) GHB withdrawal has a slower onset than alcohol and benzodiazepine withdrawal due to its long half life
c) GHB withdrawal has more prominent neuropsychiatric symptoms than benzodiazepines
d) Benzodiazepines are commonly used for treatment of withdrawal

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13) Answer: B - GHB withdrawal has a slower onset than alcohol and benzodiazepine withdrawal due to its long half life

- GHB has a short half-life and dependent patients often need to dose frequently with multiple doses a day and often waking at night to use
- GHB withdrawal is similar to benzodiazepine and alcohol withdrawal though has a faster onset (due to this short half life) and often has more prominent neuropsychiatric symptoms (psychosis, delirium)
- Benzodiazepines are the mainstay of treatment despite GHB primarily acting at the GABA-B receptors. Baclofen may be added as an adjunct (acts at GABA-B).

Karila, Laurent & Angerville, Bernard & Amine, Benyamina & Billieux, Joel. (2024). Pharmacological Treatment of GHB Withdrawal Syndrome. Current Addiction Reports. 11. 1-9. 10.1007/s40429-023-00531-1.

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Benzodiazepines: Need to Know

- The basic **structure** of benzodiazepines and the Z-Drugs
- History of development – background in relation to barbiturates
- **Epidemiology** of unhealthy use; use in pregnancy
- **Pharmacokinetics** – relative potencies, time of onset, half-lives; the parent drug and elimination half-life and excretion; CYP450 hepatic **metabolism** versus glucoronidation, onset of action and active metabolites
- **Pharmacodynamics** – development of physiologic dependence; GABA receptor characteristics, activity at the GABA receptor and antagonism
- **Drug-Drug interactions** and concomitant opioid and alcohol use
- **Toxicity** and how to treat benzodiazepine overdose and withdrawal syndromes
- **Addiction** liability and how to **taper**

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Thank you!

2025 CSAM Conference – BEPT Track – Benzodiazepines

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CANNABIS

August 13, 2025

2025 CSAM Conference – BEPT Track

Slides Revised From Takeo Toyoshima, MD, MRO

Jeremy Flores, MD
Health Sciences Clinical Instructor - UCLA Dept of Psychiatry, Addiction Division
Behavioral Health Services Lead- UCLA Homeless Healthcare Collaborative

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Educational Objectives

After attending this presentation, participants will be able to:

1. Summarize the clinical manifestations and diagnostic criteria for cannabis use disorder, cannabis withdrawal, and cannabis intoxication
2. Understand the basic pharmacology of cannabinoids, in particular THC and CBD
3. Describe current epidemiologic trends in cannabis use and cannabis use disorder

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Conflicts of Interest

I, *Jeremy Flores,* have nothing to disclose, and I will not be discussing "off label" use of drugs or devices in this presentation.

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Need To Know

1. Function of the endocannabinoid system
2. Cannabis pharmacology
3. Epidemiology of cannabis use
4. Cannabis intoxication and withdrawal
5. Cannabis drug testing
6. Synthetic cannabinoids
7. Negative effects from cannabis use
8. FDA-approved cannabinoids

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Question 1

A 22-year-old patient has been smoking cannabis almost daily since he was 18 years old. He has experienced mood symptoms and worsening anxiety for the last year. Which of the following statements is true regarding the endocannabinoid system?

A. Δ^9-tetrahydrocannabinol (THC) is the main psychoactive component of cannabis and exerts its behavioral effects through the CB_2 receptor.

B. Cannabidiol (CBD) is the main psychoactive component of cannabis and exerts its behavioral effects through the CB_2 receptor.

C. Cannabidiol (CBD) is the main psychoactive component of cannabis and exerts its behavioral effects through the CB_1 receptor.

D. Δ^9-tetrahydrocannabinol (THC) is the main psychoactive component of cannabis and exerts its behavioral effects through the CB_1

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D. **Δ^9-tetrahydrocannabinol (THC) is the main psychoactive component of cannabis and exerts its behavioral effects through the CB_1**

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Cannabinoids and the Endocannabinoid System

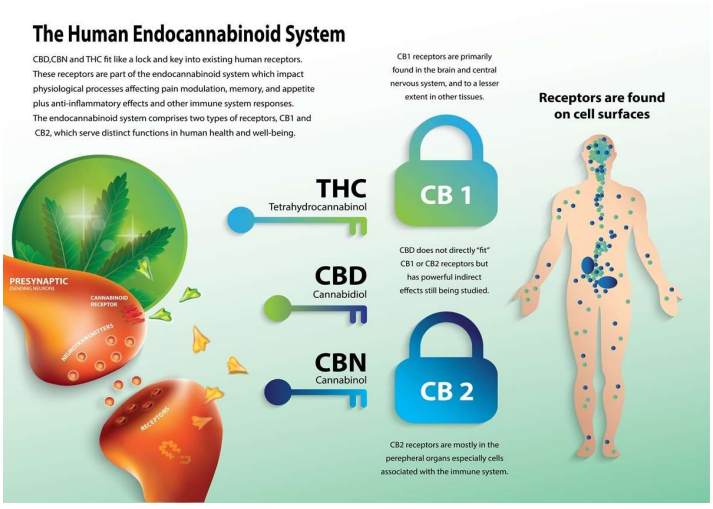

Image from News-Medical.net

Cannabis sativa and indica

113 cannabinoids *Gulk and Moller, 2020*

- ***Δ9-THC***
- Δ8-THC
- **Cannabidiol (CBD)**
- Cannabinol (CBN)

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Question 2

Which of the following is true regarding the endocannabinoid system?

A. The CB1 receptor is tonically inactive
B. The CB1 receptor is a G-protein coupled receptor
C. The CB1 receptor is a voltage gated sodium channel
D. THC is a full agonist with a high binding affinity at the CB1 receptor

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Question 2

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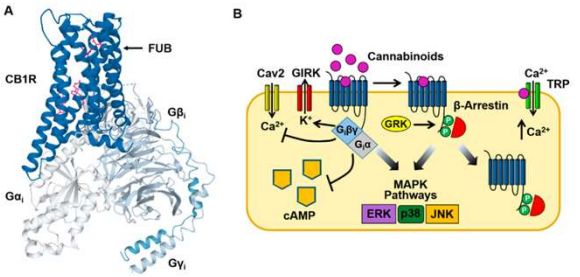
350

Cannabinoid Pharmacology



Walsh and Andersen, Int. J. Mol. Sci. 2020

- CB1 receptor is a **GPCR**
  - EC activation decreases cAMP → decrease neuronal excitability
- Intrinsic activity, **tonically active**
  - Off-balance by exogenous cannabinoids
- THC: **partial agonist** → ~20% CB1R activation
  - Synthetic cannabinoids are often full agonists, activate CB1R ~100%

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Question 3

A 16-year-old boy presents to his primary care doctor brought in by his parents concerned about his marijuana use and seeking psychoeducation. According to the 2023 National Survey on Drug Use and Health (NSDUH), which age group had highest percentage of past 12-month cannabis use?

A. 12-17
B. 18-25
C. 35-49
D. 65 and older

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Question 3

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A. 12-17

B. 18-25

C. 35-49

D. 65 and older

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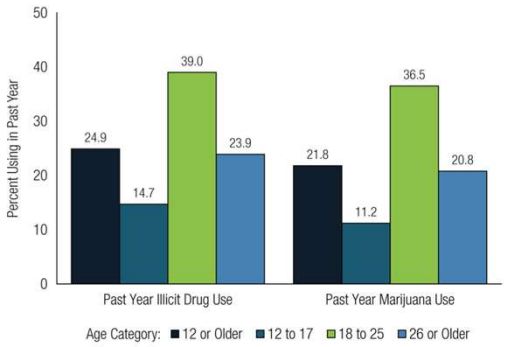
Cannabis Use and Use Disorder Epidemiology

- Past year cannabis use, 2023 NSDUH



SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2023.

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Cannabis Use and Use Disorder Epidemiology

- Cannabis Use Disorder Past Year Prevalence Estimates, 2023
  - **Young adults (18-25): 16.6%, 5.6 million** (2022, 16.5%, 5.7 million)
  - Adults (26+): 5.5%, 12.3 million (2022, 5.4%, 11.9 million)
  - Adolescents (12-17): 4.7%, 1.2 million (2022, 5.1%, 1.3 million)
- CUD risk factors include patterns of use (early onset, heavy/frequent use, potent forms); genetics; psychiatric and SUD comorbidities; male sex; less education; certain racial/ethnic groups

SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2022 and 2023.
https://www.samhsa.gov/data/report/2023-nsduh-detailed-tables

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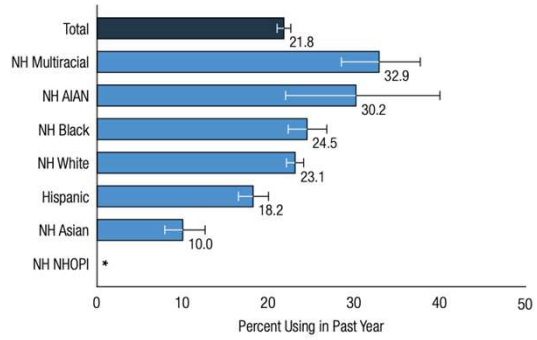
Cannabis Use and Use Disorder Epidemiology

- Subpopulation differences
- Multiracial and Native American/Alaskan Native have highest prevalence
- In comparing 2022 to 2023 data,
  - Multiracial and NA-AN: decrease in prevalence
  - All others: increase in prevalence (Black from 21.3%, White from 22.9%, Hispanic from 15.8%, and Asian from 8.6%)

Figure 15. Past Year Marijuana Use: Among People Aged 12 or Older; by Race/Ethnicity, 2023



* Low precision; no estimate reported.

AIAN = American Indian or Alaska Native; Black = Black or African American; Hispanic = Hispanic or Latino; NH = Not Hispanic or Latino; NHOPI = Native Hawaiian or Other Pacific Islander.

Note: Error bars were calculated as 99 percent confidence intervals. Wider error bars indicate less precise estimates. Large apparent differences between groups may not be statistically significant.

SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2023

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Question 4

A new patient was referred for evaluation of their cannabis use at the behest of their family. Your evaluation identifies five DSM-5 cannabis use disorder criteria. What is the appropriate diagnosis?

A. Problematic cannabis use
B. Mild cannabis use disorder
C. Moderate cannabis use disorder
D. Severe cannabis use disorder

357

Question 4

A new patient was referred for evaluation of their cannabis use at the behest of their family. Your evaluation identifies five DSM-5 cannabis use disorder criteria. What is the appropriate diagnosis?

A. Problematic cannabis use
B. Mild cannabis use disorder
C. Moderate cannabis use disorder
D. Severe cannabis use disorder

358

DSM-IV to DSM-5

DSM-IV

DSM-5

Abuse

Dependence

Substance Use Disorder

Clinically, still may address binge v heavy continuous use differently

359

DSM-5 Criteria for SUD

1. Larger amount or longer period than intended
2. Persistent desire or failure to cut down or control use
3. Great deal of time spent to obtain, use, or recover
4. Craving
5. Recurrent use despite failure to fulfill role obligations
6. Persistent/recurrent social or interpersonal problems
7. Activities given up
8. Using in dangerous situations
9. Continued use despite knowledge of risks/harm
10. Tolerance
11. Withdrawal

APA. Diagnostic and Statistical Manual of Mental Disorders (5th ed., text rev.).

360

DSM-5 Cannabis Use Disorder

A. Problematic pattern of cannabis use causing impairment/distress
   1. ***11 possible criteria****, e.g., using larger amount/for longer periods, difficulty cutting down or controlling use, cravings, social problems, physically hazardous use, tolerance, withdrawal, etc.*
   2. ***3 C's: control, consequences, cravings***
   3. ***D: dependency (withdrawal and tolerance)***
B. Severity: 2-3 = mild, 4-5 = moderate, 6+ = severe
C. Remission: 3 month = early, 12 month = sustained

APA. Diagnostic and Statistical Manual of Mental Disorders (5th ed., text rev.).

361

Question 5

A 60-year-old patient smoked cannabis today for the first time in three decades and presents to your urgent care clinic. He bought the cannabis from a local dispensary. After smoking, he felt panicked, paranoid, disoriented, and physically ill. After examination, you inform him that greatest reason why he experienced intense and less-desired cannabis intoxication symptoms is because:

A. He lost tolerance to cannabis
B. Today's cannabis has higher THC concentrations
C. Today's cannabis has higher CBD concentrations
D. His cannabis supply was contaminated with stimulants

362

Question 5

A 60-year-old patient smoked cannabis today for the first time in three decades and presents to your urgent care clinic. He bought the cannabis from a local dispensary. After smoking, he felt panicked, paranoid, disoriented, and physically ill. After examination, you inform him that greatest reason why he experienced intense and less-desired cannabis intoxication symptoms is because:

A. He lost tolerance to cannabis

B. **Today's cannabis has higher THC concentrations**

C. Today's cannabis has higher CBD concentrations

D. His cannabis supply was contaminated with stimulants

363

DSM-5 Cannabis Intoxication

A. Recent cannabis use

B. Clinically significant problematic behavior or psychological changes (motor incoordination, euphoria, anxiety, changes in time perception, impaired judgment, social withdrawal)

C. Two or more of following signs or symptoms within 2 hours of use:
   1. Conjunctival injection
   2. Increased appetite
   3. Dry Mouth
   4. Tachycardia

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Cannabis Preparations and Intoxication

- Cannabis plant (5-30+% THC) < concentrates (as high as 90+% THC)
  - Potency today far greater than in the 90s (4% vs 17-28%) *ElSohly Biol Psychiatry 2016*
- Smoked/vaped cannabis: faster onset, more intense hig
- Edible cannabis: slower onset, longer duration
- Potency of THC associated with adverse neuropsychiatri effects in a dose dependent manner
- Treatment of intoxication: supportive and symptom-targeted

ASAM Principles of Addiction Medicine, 6th Ed.

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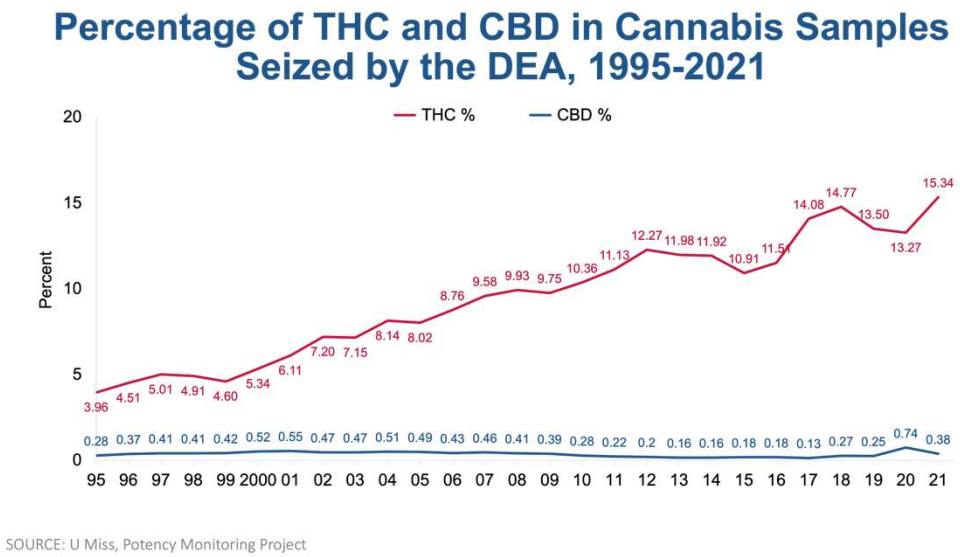
Cannabis and THC/CBD potency over time

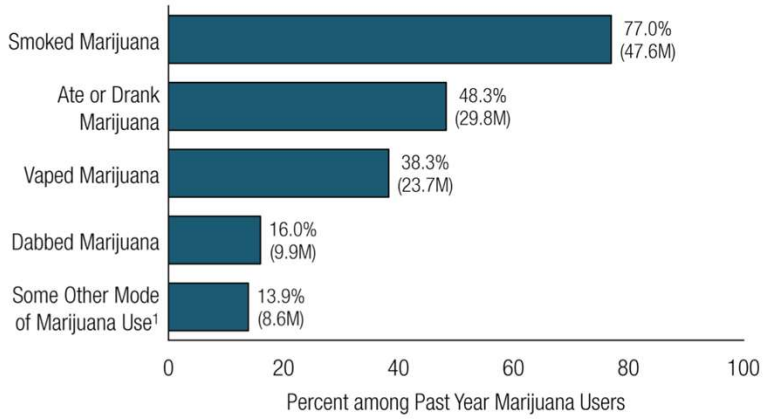


SOURCE: U Miss, Potency Monitoring Project

NIDA, 2022

366

Differences in Modes of Use



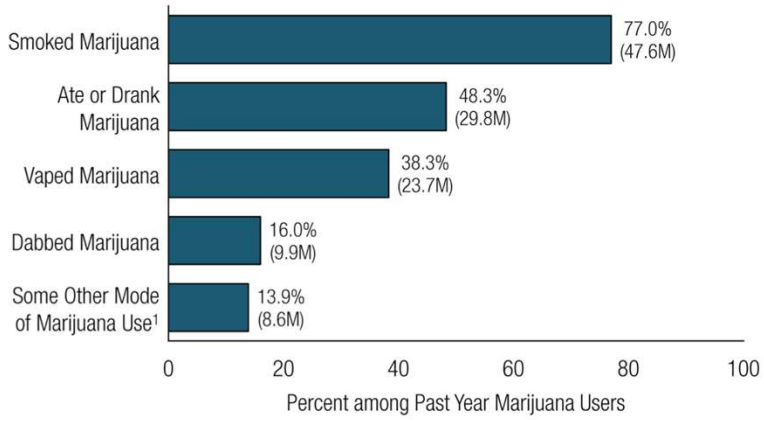
Note: Respondents could indicate multiple modes of marijuana use; thus, these response categories are not mutually exclusive.

[1] Includes applying lotion, cream, or patches to skin; putting drops, strips, lozenges, or sprays in mouth or under tongue; taking pills; or some other way not already listed in this figure.

SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2023

367

Differences in Modes of Use



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SAMHSA, Center for Behavioral Health Statistics and Quality, National Survey on Drug Use and Health, 2023

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Question 6

Regarding cannabis withdrawal, which of the following is FALSE?

A. Cannabis withdrawal is defined in the DSM-5
B. Chronic heavy cannabis use causes a reduction in CB1 receptors that reverses as cannabis withdrawal resolves
C. Cannabis withdrawal is equally likely to occur from use of CBD as it is from use of THC
D. There are no FDA-approved treatments for cannabis withdrawal

369

Question 6

Regarding cannabis withdrawal, which of the following is FALSE?

A. Cannabis withdrawal is defined in the DSM-5
B. Chronic heavy cannabis use causes a reduction in CB1 receptors that reverses as cannabis withdrawal resolves
C. **Cannabis withdrawal is equally likely to occur from use of CBD as it is from use of THC**
D. There are no FDA-approved treatments for cannabis withdrawal

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DSM-5 Cannabis Withdrawal

A. Cessation of heavy and prolonged cannabis/THC use (daily to near-daily)

B. 3+ of following within 1 week of cessation:
   1. Irritability, anger, or aggression
   2. Nervousness or anxiety
   3. Sleep difficulty
   4. Decreased appetite or weight loss
   5. Restlessness
   6. Depressed mood
   7. At least 1 physical symptom: abdominal pain, tremors, sweating, fever, chills, headaches

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Cannabis Withdrawal

- Prevalence 47% with cessation of daily cannabis/THC use *Bahji et al 2020*
- Peaks at day 4 in most, resolves by day 16
- On PET, CB1R expression reduced with chronic heavy use *D'Souza et al 2017*
  - *Reverses with abstinence*
- Time-limited, symptom-targeted pharmacotherapy
  - *No FDA-approved options*
  - *Some evidence for dronabinol, gabapentin* *Werneck et al., 2018; Brezing and Levin, 2017; Mason et al., 2012*
- Rule out other substance use/withdrawal, psychiatric comorbidities
  - *Those with co-occurring depression and anxiety may have a prolonged course*

ASAM Principles of Addiction Medicine, 6th Ed.

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Question 7

A patient with a history of heavy, daily cannabis use reports abstinence for three weeks. His urine drug screen results as +cannabinoid. The patient adamantly denies use.

Which of the following is true?

A. With heavy cannabis use, THC metabolites can be detected for weeks or even a month after last use.
B. Cannabinoid urine drug screens are prone to false positive results.
C. If the patient was poorly hydrated, urine THC metabolite concentration would decrease.
D. Pure CBD would be expected to yield a positive cannabinoid urine drug screen.

373

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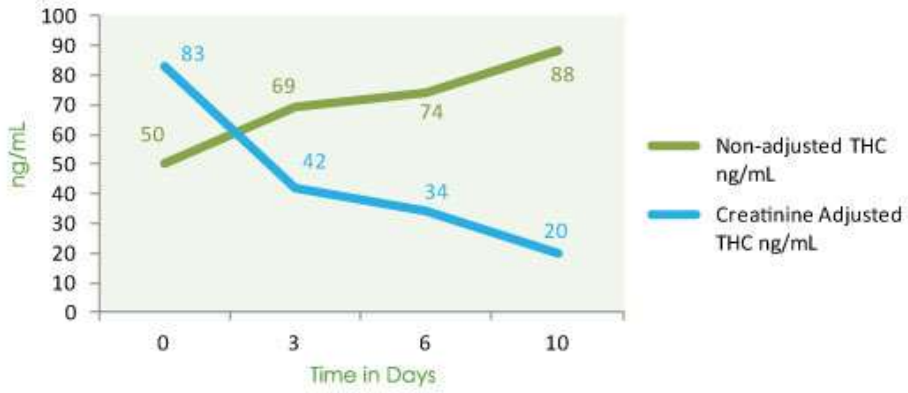
Cannabis Drug Testing

- Detection of THC/metabolites, 11-nor-9-carboxy-Δ-9-THC (carboxy THC)
- Urine Immunoassay (urine)
  - *Sensitive and specific*
  - *Single use detected 2-4 days*
  - *More frequent use 1-2 weeks*
  - *Chronic heavy use 20-30 days, rarely longer*
  - *THC concentrations in hemp (CBD products) too low, as is passive/ second-hand inhalation*
  - *Rare false positives: efavirenz, PPIs (pantoprazole)*

ASAM Principles of Addiction Medicine, 6th Ed.
URUP Laboratories. (2019). Drug Plasma Half Life and Urine Detection Window.

375

THC:Creatinine Ratio



- Can test levels over time to monitor abstinence
- Corrects for hydration status

Dominion Diagnostics

376

Question 8

A teenage patient presents with altered mental status. Family witnessed him smoke from a pipe. Shortly after, he became agitated and began shouting to himself. His vital signs are HR 111 bpm, BP 142/88 mmHg; RR 22/min, and temperature 37.7 °C. The drug screen result is pan-negative including for cannabinoids and stimulants.

Which of the following would be the most plausible explanation?

A. He submitted a false urine sample
B. He used synthetic cannabinoids
C. He used gamma hydroxybutyrate (GHB)
D. He has schizophrenia

377

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B. He used synthetic cannabinoids
C. He used gamma hydroxybutyrate (GHB)
D. He has schizophrenia

378

Synthetic Cannabinoids

- Over 180 known compounds manufactured in illicit drug labs
  - *Sprayed onto herbs and smoked, insufflated, orally ingested*
  - *K2, Spice, various names/brands*
  - *"Herbal incense" or "fragrant potpourri"*
- Potent full CB1 agonists (2-800x more potent than THC)
- Generally decreasing rates: adolescents (1.6% of high school students in 2021), forensic settings, military

NPR

Monitoring the Future 2021
Tait et al. 2015

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Synthetic Cannabinoids

- Intoxication similar to cannabis, e.g., tachycardia, conjunctival injection, increased appetite, ataxia
- Higher risk of serious neuropsychiatric toxicity: agitation, delirium, hallucinations, psychosis, seizures, coma
- Diagnosis
  - *Not on standard UDS, typically not cross reactive with THC*
  - *Can get confirmatory testing*
- Treatment largely supportive: IV fluids (high risk of rhabdo) , quiet room
  - *Sedatives, antipsychotics for severe anxiety or agitation*

Tait et al. 2015

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Question 9

A 17-year-old high school student is brought to your clinic by his parents due to concerns about his daily cannabis use. The patient says he heard from friends that "weed is safe to use" and wants to know if there are any risks to his use. ***Which of the following is False?***

A. Chronic cannabis use is associated with decreased sperm count and motility
B. Regular cannabis use is not associated with higher risk of being diagnosed with schizophrenia
C. Cannabis use, especially with alcohol, is linked with hepatic steatosis
D. Smoking cannabis is not associated with chronic obstructive pulmonary disease (COPD)

381

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Adverse Effects of Cannabinoids

- Cardiovascular: increased heart rate, orthostatic hypotension
- Pulmonary: smoked cannabis associated with increased resp illness, upper airway inflammation/edema, NOT with small airway disease (e.g., COPD)
- Liver: contributes to steatosis=>cirrhosis risk
- Endocrine/reproductive effects: reduced pregnancy and IVF success, lower sperm count/motility, sex hormone effects
  - *ACOG: recommends peripartum abstinence, crosses placenta (endocannabinoids involved in normal development), enters breastmilk*
- Oncologic risks inconclusive

ACOG, Marijuana Use During Pregnancy and Lactation, 2017.
National Academies, 2017
ASAM Principles of Addiction Medicine, 6th ed.

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Neuropsychiatric Effects

- Risk worse with earlier onset use (before 16), higher THC potency, and frequent/daily use
- Neuropsychiatric
  - *APA: Position Statement in Opposition to Cannabis as Medicine*
  - *Psychosis and bipolar disorder with strongest risk of onset/worsening*
  - *Anxiety disorders, depressive disorders, PTSD*
  - *Impaired attention, working memory* *Crean, J Addict Med, 2012*
  - *Persistent cannabis use associated with IQ drop from childhood to adulthood* *Meier, Proc Natl Acad Sci, 2012*
    - Adolescent-onset use did not recompensate IQ after cessation; adult-onset did
  - *"Gateway drug" hypothesis simplistic but associations valid* *Jorgensen and Wells, 2021*

National Academies, 2017
ASAM Principles of Addiction Medicine, 6th ed.

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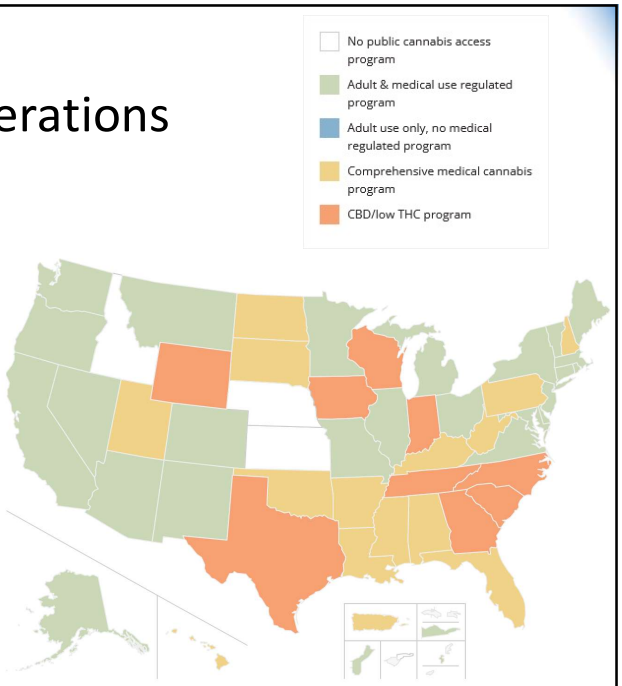
Other considerations

- DEA Schedule I (federally illegal)
- Workplace testing
  - *Drug-Free Workplace Act (1988)*
  - *State-specific laws*
- Current use/impairment not protected under ADA
- Acute intoxication and DUI/DWI
  Brubacher et al., 2019; Rogeberg and Elvik, 2016
- Pediatric/accidental exposures
  Wang et al., 2016; Whitehill et al., 2019; Dilley et al., 2021



National Conference of State Legislatures

CSAM

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Question 10

A 65-year-old patient is currently prescribed an FDA-approved cannabinoid medication. ***For which condition is this medication prescribed?***

A. Fibromyalgia
B. Post operative nausea and vomiting
C. Chemotherapy-induced nausea and vomiting
D. Muscle spasticity related to multiple sclerosis

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B. Post operative nausea and vomiting
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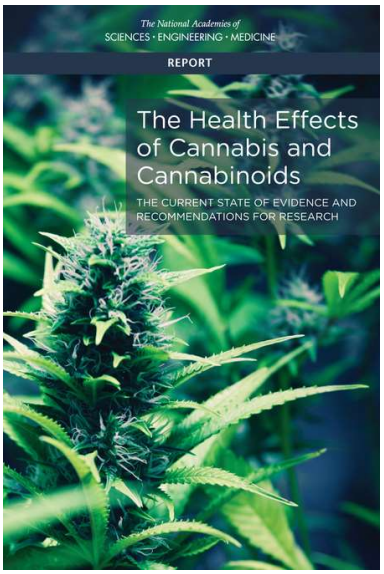
Only 3 FDA-Approved Cannabinoids as Medicine

- Dronabinol (THC)
  - *Anorexia/cachexia due to AIDS*
  - *Chemotherapy-induced nausea/vomiting*
- Nabilone (THC) [Discontinued]
  - *Chemotherapy induced nausea and vomiting*
- Cannabidiol (cannabis derived CBD)
  - *Seizures due to Lennox-Gastaut syndrome, Dravet Syndrome, tuberous sclerosis*



Uptodate
National Academies, 2017
ASAM Principles of Addiction Medicine, 6th Ed.

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Thank you!

2025 CSAM Conference – BEPT Track – Cannabis

Jeremy Flores, MD
Jeremyflores@mednet.ucla.edu

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Medical Presentations & Complications of Substance Use

CSAM Addiction Medicine Board Review Course

August 13, 2025

John Nuhn, MD
Core Faculty, Family Medicine Residency and
Addiction Medicine Fellowship
Ventura County Medical Center
Presentation updated from 2024 Thomas Meeks, MD

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CONFLICT OF INTEREST DISCLOSURE

I, John Nuhn MD, have nothing to disclose, and any off-label use of medications will be disclosed in the slides.

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EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Recognize medical presentations of substance use including toxidromes and withdrawal syndromes.
2. Diagnose and manage several common medical complications of substance use.
3. Target screening for infectious complications of substance use for highest risk patients including sexual and gender minorities.

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Need To Know

1. Toxidromes (clinical symptoms & management)
2. Withdrawal syndromes (clinical symptoms & management)
3. Cardiovascular morbidity: ischemia, arrhythmia, CHF
4. Pulmonary morbidity: COPD, cancer, pulmonary hypertension
5. GI morbidity: hepatitis, cirrhosis, malignancy associated with AUD
6. Infectious disease morbidity: Endocarditis, soft tissue infections, sexually transmitted infections
7. Common drug interaction concerns: serotonin syndrome, cytochrome P-450 enzyme inducer/inhibitors

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Question 1

A 32-year-old man with IV drug use presents to the emergency room. He has a runny nose, complains of diffuse myalgia, has 5 mm pupils bilaterally, and states that he has had no injection drug use in 2 days because of about 10 days of malaise and fatigue. His girlfriend told him his eyes were starting to look yellow. On exam, his temperature is 38.0°C (100.4°F), HR 97, BP 128/70, and RR 14/min. He has mild scleral icterus, scattered non-tender firm nodules in the muscles of bilateral arms and legs, and hepatomegaly, but no splenomegaly, asterixis, or ascites.

394

Question 1 (cont.)

Blood chemistry shows:

Total bilirubin 4.4 mg/dL (*H)

AST 580 (*H)

ALT 750 (*H)

Alk phos 145

Albumin 4.2

INR 1.3 (*H)

Urine drug screen: **THC** positive, otherwise negative

Ultrasonography shows:

Hepatomegaly and diffusely decreased echotexture

Viral testing:

HIV ELISA antibody: negative

HIV p24 antigen: negative

HIV viral load: negative

Hep B surface antigen: negative

Hep B surface antibody: negative

Hep B core IgM: negative

Hepatitis C antibody: negative

Hepatitis A IgG and IgM: negative

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Question 1 (cont.)

Which test is the most appropriate next step in this patient's evaluation?

A. Ethyl glucuronide urine testing
B. Hepatitis C virus RNA
C. Liver biopsy
D. MRI abdomen

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1. Answer: **B. Hepatitis C virus RNA**

- The most sensitive diagnostic test for acute viral HCV is measurement of HCV RNA. If positive, suggests active infection.
- Patient has signs of acute hepatitis, including moderately elevated liver tests, jaundice, nausea, dark urine, fatigue, malaise, fever, chills.
- These can develop 2-12 weeks after exposure.
- Possible exposure through injection drug use. The *incidence of HCV is approximately 20% for each year* of injection drug use, and a review estimated overall hepatitis C prevalence of about *53% among people who inject drugs* in the US.
- *Acute hepatitis C virus may remain seronegative for longer than 8 weeks. So, in cases of high risk, testing HCV RNA is appropriate.* Only about 20% of new hepatitis C infections are acutely symptomatic, which contributes to fact that many cases go undetected without routine testing.

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1. Answer: **B. Hepatitis C virus RNA**

GU2 Update: **As of 2020, CDC now recommends:**

- **Universal one-time hepatitis C screening for all U.S. adults**
- **Screening pregnant women during every new pregnancy.**
- **At anytime for those with ongoing risk factors such as injection drug use or risky sexual behaviors**

- Injection drug use accounts for the *majority of new HCV infections* (70%), and is a driving force behind this recommendation since testing with *linkage to antiviral treatment* has the potential to decrease HCV infections
- Injection-related infections can also include skin and soft tissue infections, bloodstream and endovascular infections, epidural abscess, spinal osteomyelitis, transmission of viruses (HIV, HBV, HCV – consider prevention with *HIV PREP/PEP* and HBV & HAV vaccination)

https://www.cdc.gov/hepatitis/hcv/guidelinesc.htm

398

Slide 398

GU1 need to clarify this universal HCV screening is a "one-time" event in general population, while it is for every pregnancy.
Guest User, 2023-06-24T23:18:47.403

GU1 0 I changed formating. Not sure how to make it more clear.
Guest User, 2023-06-26T20:21:09.750

GU2 There are also new 2023 Hepatitis B guidelines::
Screen all adults aged 18 years and older at least once in their lifetime using a triple panel test
Screen pregnant people for hepatitis B surface antigen (HBsAg) during each pregnancy regardless of vaccination status and history of testing
Expand periodic risk-based testing to include people incarcerated, people with a history of sexually transmitted infections or multiple sex partners, and people with hepatitis C virus infection
Test anyone who requests HBV testing regardless of disclosure of risk
Guest User, 2023-06-24T23:19:48.314

GU2 0 https://www.cdc.gov/hepatitis/hbv/testingchronic.htm
Guest User, 2023-06-24T23:20:37.927

1. Answer: **B. Hepatitis C virus RNA**

GU2 2023 CDC Guideline Hepatitis B:

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https://www.cdc.gov/hepatitis/hbv/testingchronic.htm

399

1. Answer: **B. Hepatitis C virus RNA**

- **Liver biopsy** may show histopathological features, including steatosis, lymphoid aggregates, and bile duct damage. However, these findings are not specific for Hepatitis C (HCV) and similar findings are associated with several forms of acute hepatitis.
- **MRI of the liver** will detail hepatic morphology but will not contribute any more to the diagnosis than the ultrasonography.
- Alcohol can cause of acute hepatitis, though this case does not suggest its role. **Ethyl glucuronide** (EtG) is a metabolite of alcohol that can be tested in urine or hair but is generally not used in this clinical setting.

https://www.aasld.org/sites/default/files/2022-07/PracticeGuidelines-HCV-November2018.pdf

400

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Guest User, 2023-06-24T23:20:37.927

GU2 1 Slide added
Guest User, 2023-07-25T15:31:21.094

Question 2

45-year-old male is found to have positive HCV antibodies and high HCV RNA viral load suggesting active, chronic HCV infection. He has alcohol use disorder and is interested in treatment with direct-acting antiviral therapy. **Which of the following is true regarding treatment of HCV in patients with ongoing substance use?**

A. Alcohol is not a contraindication to starting antiviral therapy
B. Buprenorphine should be avoided for persons with HCV because of liver toxicity concerns
C. The risk of hepatocellular carcinoma for persons with HCV is not affected by alcohol use
D. Treating patients with HCV who are actively using substances causes high rates of viral resistance and yields low HCV cure rates

401

2. Answer:

A. Alcohol is not a contraindication to starting antiviral therapy

- *60-75% of patients infected with hepatitis C will fail* to clear the virus and go on to develop chronic HCV, and 16% of those will develop cirrhosis
- **Alcohol and other substance use is not a contraindication** to starting antiviral therapy. Treatment success rates appear similar to patients who do not drink alcohol or use drugs. Drug resistance (e.g. from more erratic adherence) has not emerged as a concern that would warrant withholding treatment in this population.
- While of some initial concern, there does not appear to be any reason to avoid buprenorphine in persons with OUD and viral hepatitis. A notable study found no significantly different liver outcomes compared to methadone in this population
- Alcohol is associated with increased hepatitis C viral load, progression of liver fibrosis and risk of developing hepatocellular carcinoma

ASAM Principles of Addiction Medicine, 6th edition. Chapter on Liver Disorders Related to Alcohol and Other Drug Use
http://www.hcvguidelines.org/full-report/hcv-testing-and-linkage-care.
Saxon AJ, et al. Buprenorphine/Naloxone and methadone effects on laboratory indices of liver health: a randomized trial. Drug Alcohol Depend. 2013 Feb 1;128(1-2):71-6.

402

Question 3

A 25-year-old woman comes to clinic. Six months ago, she had an episode of syncope and was hospitalized and given a new diagnosis of Hypertrophic Obstructive Cardiomyopathy (HOCM). One week after hospitalization, she failed her bar exam to practice law in California, and has been struggling with depressed mood, insomnia, and anxiety ever since.

PDMP report reveals monthly refills of lorazepam 1 mg, which she states she takes only once or twice a week on the weekends (4-6 tabs at a time). Since her HOCM diagnosis, she has also been drinking 1 glass of alcohol daily during the week and 6-10 drinks daily on the weekends, as well as using marijuana every evening (previously only occasionally). She states that her biggest source of anxiety is concern over her heart condition.

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Question 3 (cont.)

In counseling this patient, which potential complication of her substance use would you consider the most immediately likely and most concerning?

A. Atrial fibrillation
B. Cerebrovascular accident
C. Endocarditis
D. Myocardial infarction

404

3. Answer: **A. Atrial fibrillation**

• Atrial fibrillation (AF) is the most common arrhythmia in adults and is associated with heavy alcohol use.

• AF occurs at some point in up to 60% of people with binge drinking (> 3 drinks at a time in women or > 4 drinks at a time in men). This most commonly presents during or after holidays or weekends when patients have consumed more than usual, earning the term "holiday heart." It can occur in persons who are not otherwise heavy or frequent users after binges.

• A recent trial study reported atrial fibrillation burden was lower in abstinence/reduced drinking group vs heavier drinking. *Alcohol use is a modifiable risk factor in management of atrial fibrillation.*

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3. Answer: **A. Atrial fibrillation**

- Patients with **hypertrophic obstructive cardiomyopathy (or any heart disease) are also at increased risk of atrial fibrillation** which puts them at risk of worsening cardiomyopathy, outflow obstruction, and more malignant arrhythmias including ventricular fibrillation.
- Although there is a slightly increased risk of endocarditis in HOCM patients, none of this patients' substance use patterns substantially increases that risk. You can review the *Duke Criteria* for endocarditis probability and diagnosis.
- Alcohol increases *cardiovascular risks* such as myocardial infarction and cerebrovascular accident, though less immediately likely since this risk develops with more chronic use.

Voskoboinik A, Kalman JM, De Silva A, et al. Alcohol abstinence in drinkers with atrial fibrillation. N Engl J Med 2020;382:20-28.
Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, Bashore T, Corey GR. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis. 2000 Apr;30(4):633-8.

406

Question 4

A 62-year-old man is found down on the sidewalk and brought to your emergency department. Blood testing reveals a pH of 7.1 and an anion gap of 26, and an elevated serum osmolal gap. Creatinine is 3.2. Blood-alcohol level is 245 mg/dL. There are calcium oxalate crystals in his urine. He has a history of suicide attempts.

What is your first step in treating this patient?

A. Administer fomepizole first

B. Arrange dialysis first

C. Give IV fluids and thiamine until anion gap closes

D. Wait for blood alcohol level to decrease and then proceed with dialysis

CSAM

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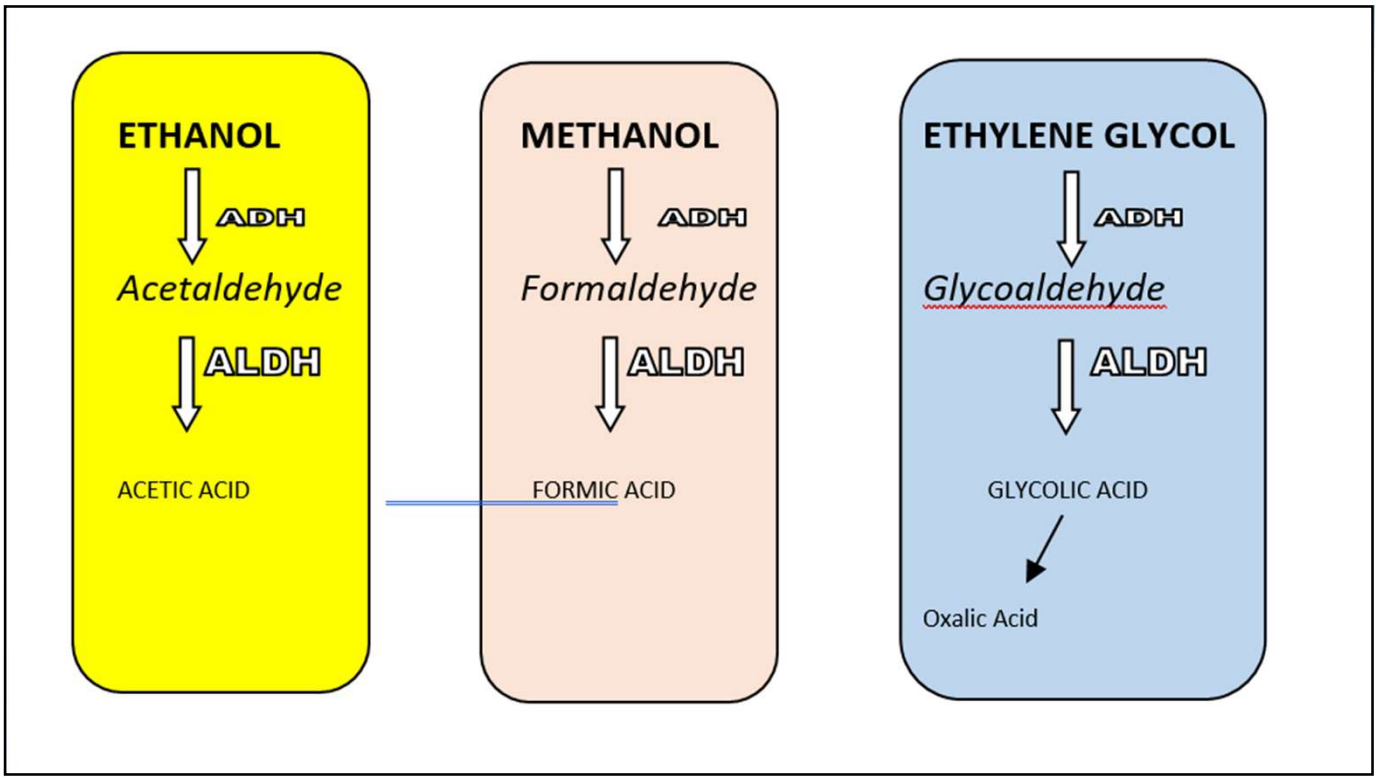
4. Answer: **B. Arrange dialysis first**

- Toxic alcohols (methanol, ethylene glycol, isopropyl alcohol) are occasionally ingested as a substitute for ethanol, or intentionally in a suicide attempt.
- Metabolized by *alcohol dehydrogenase*
- Metabolites can cause anion gap acidosis, osmolal gap* and organ damage such as kidney failure.
- Patient has signs and symptoms consistent with ethylene glycol (antifreeze) toxicity, including **calcium oxalate crystals in the urine & osmole gap metabolic acidosis**.

CSAM

408



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	ETHANOL	ISOPROPYL ALCOHOL	METHANOL	ETHYLENE GLYCOL
SOURCE	Beverages, cough med, mouthwash	"rubbing alcohol", solvents	Paint thinner, windshield or copier fluid, moonshine	Antifreeze (most often in intentional poisoning or suicide)
CLINICAL	CNS depression	CNS depression "fruity" breath smell	Visual disturbance, CNS depression	Renal failure w/ calcium oxalate crystals in urine
METABOLITE	Acetyl coA	Acetone	Formic Acid	Glycolic acid→ oxalic acid
METABOLIC ACIDOSIS	Indirectly (lactic acidosis) is possible	NO	Yes	Yes
INCREASED ANION GAP	If lactic acidosis occurs, yes	NO	Yes	Yes
OSMOLAL GAP	Usually yes	Usually yes	Usually yes	Usually yes
MANAGEMENT	Supportive	Supportive	Dialysis Fomepizole	Dialysis Fomepizole

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4. Answer: **B. Arrange dialysis first**

- Fomepizole is a treatment that **inhibits alcohol dehydrogenase and prevents metabolism of the ethylene glycol (and methanol) to harmful metabolites**.
- However, if ethanol is co-ingested along with ethylene glycol, alcohol dehydrogenase will preferentially *metabolize ethanol first (historical treatment).*
- *If serum alcohol concentration is sufficiently high (>100 mg/dL), then there is some time before fomepizole administration is necessary*, since the alcohol dehydrogenase will first be occupied with ethanol metabolism. In this case, with a very elevated serum BAL, the first and **most important step is arranging hemodialysis** to remove ethylene glycol and its metabolites. Once these arrangements have been made, treatment with fomepizole could begin.

411

Question 5

CC1

A 32-year-old man with a history of opioid use disorder presents to the emergency department with severe agitation, vomiting, abdominal cramps, sweating, and muscle aches. His partner reports that the patient has been using illicit fentanyl daily for the past 2 years and has been wanting to stop fentanyl use but has been unable to tolerate withdrawal symptoms and returns to use quickly. Partner reports he last saw the patient use fentanyl early this morning. On arrival vitals include temp 37.8°C, HR: 122 bpm, BP: 152/92 mmHg, RR: 24/min, Pupils: 6 mm and reactive. Calculated a COWS of 26.

Which of the following is the most likely cause of this patient's presentation?

A. Acute opioid overdose
B. Spontaneous opioid withdrawal
C. Precipitated withdrawal due to buprenorphine administration
D. Serotonin syndrome from fentanyl adulteration

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Slide 412

CC1 Consider “returns to use” quickly
Chen, Chwen-Yuen, 2025-07-05T05:54:56.870

JN1 0 Thank you, nomenclature updated as requested
Nuhn, John, 2025-07-06T20:44:12.023

5. Answer:
C. Precipitated withdrawal due to buprenorphine administration

CC1 Buprenorphine is not difficult nor uncommon to find without a prescription and many patients will attempt to transition from fentanyl to buprenorphine without guidance from a prescriber.

Patient is experiencing **precipitated opioid withdrawal**, a well-known complication when **buprenorphine** (partial mu-opioid agonist with high receptor affinity) is given too soon after full agonist use.

Fentanyl is **highly lipophilic**, **accumulates in adipose tissue**, and can remain bound to receptors **longer than expected**, even when the patient appears to be in withdrawal. Administering buprenorphine displaces fentanyl from the mu-opioid receptors, but since buprenorphine does not stimulate the receptor to the same degree, this causes a **sudden drop in receptor activation** — resulting in **acute, severe withdrawal symptoms** (the toxidrome seen here).

ASAM Principles of Addiction Medicine, 6rh ed.

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5. Answer:
C. Precipitated withdrawal due to buprenorphine administration

A. Acute opioid overdose – opposite presentation
- patients typically appear somnolent with low respiratory rate

B. Spontaneous opioid withdrawal – unlikely in this setting
- partner noticed last use of fentanyl today
- spontaneous withdrawal not expected for another 12-24 hours

D. Serotonin syndrome from fentanyl adulteration – symptoms of serotonin syndrome include tremor, diaphoresis, rigidity. Not consistent with this presentation.

414

Slide 413

CC1 May want to open by saying that it is not uncommon for patients to find unprescribed buprenorphine to manage their symptoms and self transition to buprenorphine. When done too quickly this is what happens. Then we need to explain why all the other choices are wrong.

Chen, Chwen-Yuen, 2025-07-05T05:56:38.826

5. Answer:
C. Precipitated withdrawal due to buprenorphine administration

- Precipitated withdrawal is common with fentanyl due to long depot effect, potentially even after a short period of abstinence.
- Can occur with partial agonist (buprenorphine) or full antagonist (naloxone or naltrexone) use.

To reduce precipitated withdrawal risk, consider initiation of buprenorphine only after:

- clear, moderate withdrawal (e.g. COWS ≥ 13)
- use microdosing protocols, consider continued full agonist at initiation
- consider use of long-acting injectable buprenorphine with emerging protocols.

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5. Answer:
C. Precipitated withdrawal due to buprenorphine administration

- Naloxone can cause symptoms of precipitated withdrawal but due to short half life is indicated for the management of overdose and can be used to check if someone is as risk for withdrawal symptoms days or even weeks out from fentanyl use.
- Naltrexone is contraindicated until patients are no longer at risk of precipitated withdrawal, typically at least 7 days after last use of an opioid, though withdrawal symptoms have been reported even after longer periods since last use of fentanyl.
- Consider use of naloxone and monitor for signs of withdrawal if considering use of naltrexone but there is concern for withdrawal symptoms (i.e naloxone challenge).

Varshneya NB, Thakrar AP, Hobelmann JG, Dunn KE, Huhn AS. Evidence of Buprenorphine-precipitated Withdrawal in Persons Who Use Fentanyl. J Addict Med. 2022 Jul-Aug 01;16(4):e265-e268. doi: 10.1097/ADM.0000000000000922. Epub 2021 Nov 23. PMID: 34816821; PMCID: PMC9124721.
The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. Journal of Addiction Medicine 14(2S):p 1-91, March/April 2020. | DOI: 10.1097/ADM.0000000000000633

416

Question 6

A local hospitalist calls you for history about your 24-year-old non-binary patient (they/them) who is being admitted and is too altered to provide much history. The patient has chronic epigastric pain, nausea, and vomiting. As their addiction medicine doctor, you have been working with their primary care physician to taper their medications. They have a history of club drug (i.e., MDMA, ketamine, GHB) use as well as sedative/hypnotic and opioid use disorders.

They have been taking tramadol for pain, duloxetine for pain and depression, metoclopramide and ondansetron for nausea, trazodone for insomnia. You have transitioned from alprazolam to diazepam for taper.

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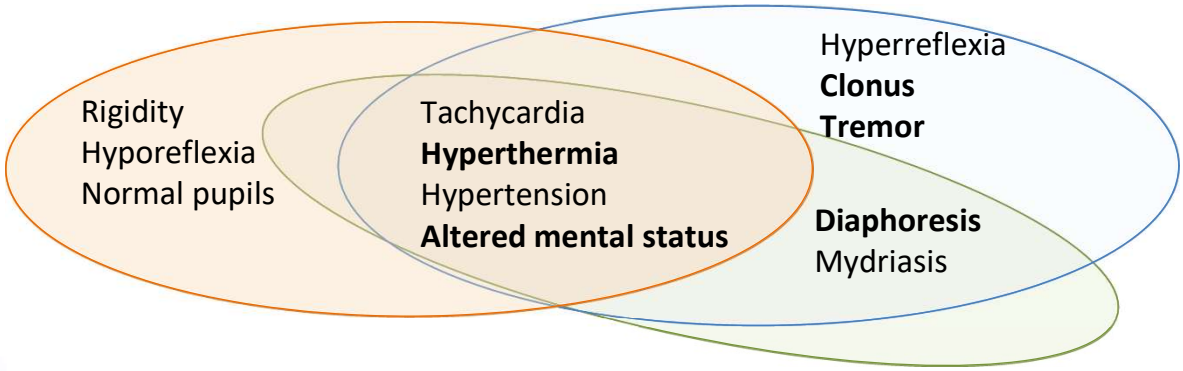
Question 6 (cont.)

They initially presented to the ER with tremor, diaphoresis, fever of 102°F, clonus in bilateral lower extremities, and agitation.
What do you suspect is the diagnosis, and how will you confirm it?

A. MDMA (Ecstasy) intoxication, by urine drug testing
B. Meningitis, by lumbar puncture
C. Neuroleptic Malignant Syndrome, by clinical presentation and CK level
D. Serotonin syndrome, by clinical presentation

418

6. Answer: **D. Serotonin syndrome, by clinical presentation**

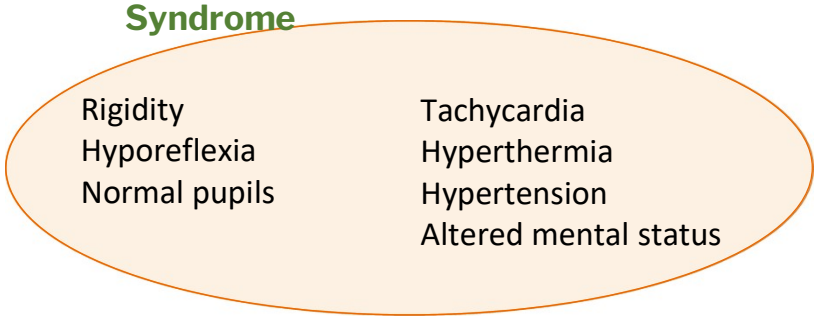


Serotonin Syndrome. *Uptodate.com*. 2023FEB16.

419

6. Answer: **D. Serotonin syndrome, by clinical presentation**

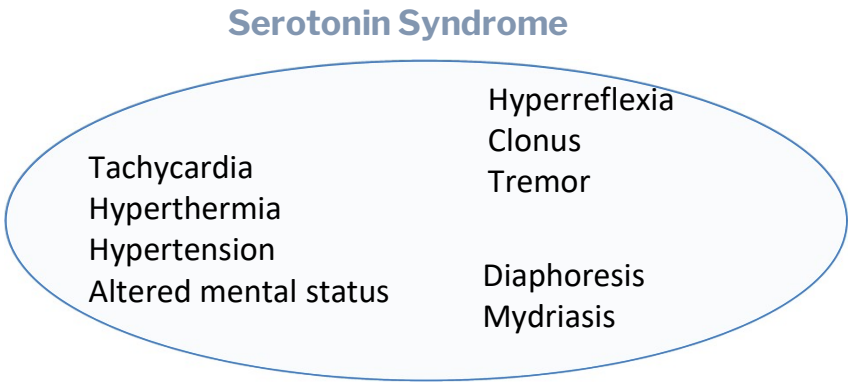
Neuroleptic Malignant Syndrome



Perry PJ, Wilborn CA. Serotonin syndrome vs neuroleptic malignant syndrome: a contrast of causes, diagnoses, and management. *Ann Clin Psych.* 2012; 24(2) 155-162.

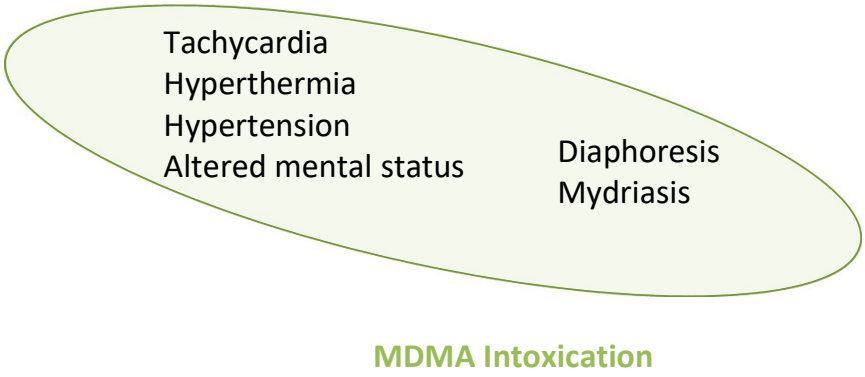
420

6. Answer: **D. Serotonin syndrome, by clinical presentation**



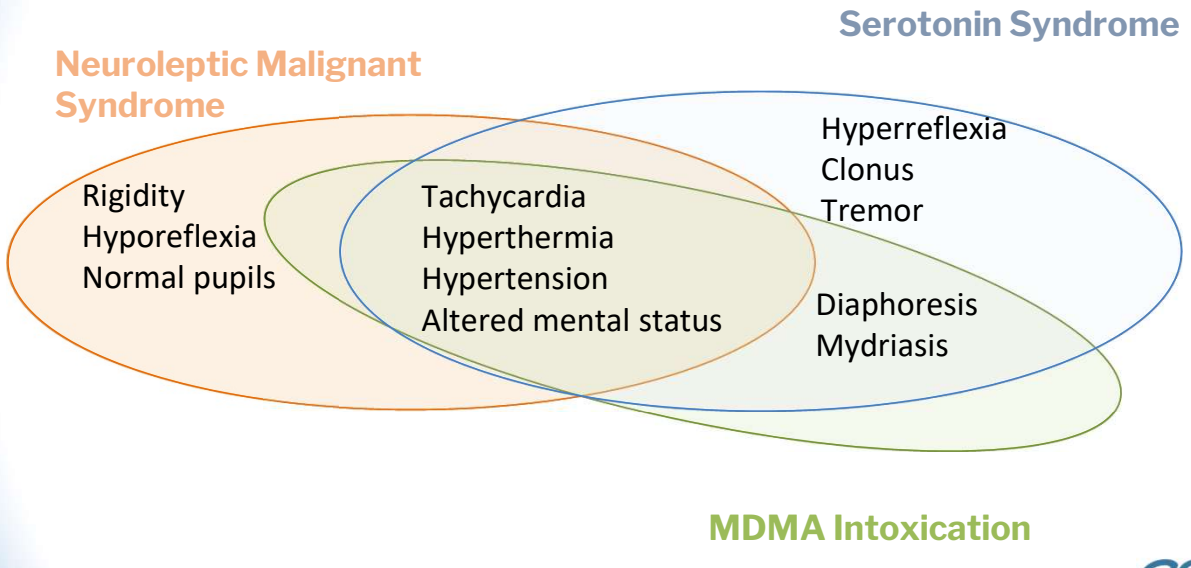
421

6. Answer: **D. Serotonin syndrome, by clinical presentation**



422

6. Answer: **D. Serotonin syndrome, by clinical presentation**



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Potential combos to provoke Serotonin Syndrome

SSRI + other serotonergic antidepressant (trazodone, mirtazapine, TCA, MAOI)

SSRI + triptans for migraine

SSRI + serotonin receptor agonists (hallucinogens, buspirone, some antipsychotics)

SSRI + non-prescribed psychoactives (amphetamines, dextromethorphan, MDMA)

SSRI + medications that inhibit their CYP450 metabolism

SSRI + opioids

- Lower risk: morphine, (codeine), buprenorphine, oxycodone, hydrocodone
- Medium risk: fentanyl & methadone
- Higher risk: tramadol

Opioids and serotonergic medications. *Medsafe*. https://www.medsafe.govt.nz/profs/PUArticles/September2022/Opioids-and-serotonergic%20medicines-risk-of-serotonin-syndrome.html. *Prescriber Update 43 (3):32-34.*

424

Question 7

A 23-year-old man presents to a primary care clinic with complaints of burning on urination as well as increased urinary frequency and urgency. He has a history of severe depression and reports he feels much better after starting a new treatment he ordered online, although he is starting to get more anxious about his urinary symptoms. Urinalysis results are below. Bladder ultrasound shows diffuse bladder wall thickening and reduced bladder capacity.

Color	Yellow
Specific gravity	1.062
pH	6.4
Protein	Negative
Glucose	Negative
Nitrite	Negative
Leukocyte Esterase	negative

RBCs	50/hpf
Bilirubin	Negative
Urobilinogen	Negative
Ketones	Negative
WBC	3/hpf
Bacteria	Absent
Blood	2+

425

Question 7 (continued)

Which of the following is the most likely diagnosis?

A. Chlamydia due to methamphetamine-associated high risk sexual behavior
B. Ketamine-associated cystitis
C. Levamisole-induced nephropathy
D. Tianeptine-induced urinary retention

426

7. Answer: **B. Ketamine-associated uropathy (KAU)**

- Ketamine now popularized as treatment of major depression
- Studies show some efficacy in depression (esketamine nasal spray is FDA-approved).
- Is marketed for use via telehealth in “at-home” sessions
- Patient’s lower urinary tract symptoms consistent with cystitis has been reported with ketamine use
- Common symptoms include urinary frequency/urgency, suprapubic pain, dysuria, hematuria, and incontinence.

Chan EOT, Chan VWS, Tang TST, Cheung V, Wong MCS, Yee CH, Ng CF, Teoh JYC. Systematic review and meta-analysis of ketamine-associated uropathy. Hong Kong Med J. 2022 Dec;28(6):466-474.

427

7. Answer: **B. Ketamine-associated uropathy (KAU)**

- Urinalysis can evaluate for other pathologies (UTI, heamturia).
- If etiology in doubt, bladder ultrasound is a common next step in evaluation

KAU often demonstrates:
- Bladder wall thickening
- Reduced bladder capacity (from fibrosis decreasing bladder elasticity).

Chan EOT, Chan VWS, Tang TST, Cheung V, Wong MCS, Yee CH, Ng CF, Teoh JYC. Systematic review and meta-analysis of ketamine-associated uropathy. Hong Kong Med J. 2022 Dec;28(6):466-474.

428

7. Answer: B. **Ketamine-associated uropathy (KAU)**

A. Chlamydia is not the best answer:

- Dysuria and urinary frequency/urgency could be caused by a variety of other more common causes, such as UTI or sexually transmitted infections such as Gonorrhea or Chlamydia.
- Absence of bacteria, minimal WBCs, and lack of leukocyte esterase and nitrites make UTI less likely.
- Gonorrhea and Chlamydia would not usually cause microscopic hematuria and would not cause the bladder wall thickening or reduced bladder capacity.

Solomon N, Hayes J. Levamisole: A High Performance Cutting Agent. Acad Forensic Pathol. 2017 Sep;7(3):469-476.

429

7. Answer: **B. Ketamine-associated uropathy (KAU)**

C. Levamisole is a veterinary anti-helminthic agent used as an adulterant to cocaine, possibly due to its similar appearance, lower cost, and mild potentiation of stimulant effects in the brain.

- Complications include agranulocytosis, rash, and vasculitis, including glomerulonephritis.
- However, upper urinary tract effect (not one causing LUTS and bladder changes).

D. Tianeptine is a mu-opioid receptor agonist used as an antidepressant in other countries.

- Known as “gas station heroin” - it is not a federally controlled substance.
- Like all opioids, it can cause urinary retention, but that would not usually cause dysuria or hematuria
- ultrasound should reveal a distended bladder (not reduced capacity as seen here).

Solomon N, Hayes J. Levamisole: A High Performance Cutting Agent. Acad Forensic Pathol. 2017 Sep;7(3):469-476.

430

Question 8

34-year-old patient presents with a rash on the flank consistent with herpes zoster which has recurred for a second time this year. She identifies as transgender woman and attends a clinic specializing in gender-affirming care. While at the clinic, she asks the clinician on duty about medications to cut back on methamphetamine use.

The clinician should order testing for which of the following conditions:

A. Diabetes
B. HIV
C. Psoriasis
D. Skin allergies

431

8. Answer: **B. HIV**

- Methamphetamine use may increase high risk sexual behaviors that can lead to HIV transmission
- Herpes zoster (shingles) is more common with immunodeficiencies, including age-related and HIV.
- VZV reactivation triggers a painful vesicular rash in a dermatomal distribution.
- Shingles may be an initial presentation in unrecognized HIV infection and is 12 times or more common in persons with HIV

Zachariah S, Sullivan A, Donato A. Shingles: a harbinger of chronic HIV infection. J Community Hosp Intern Med Perspect. 2021 Nov 15;11(6):871-873.

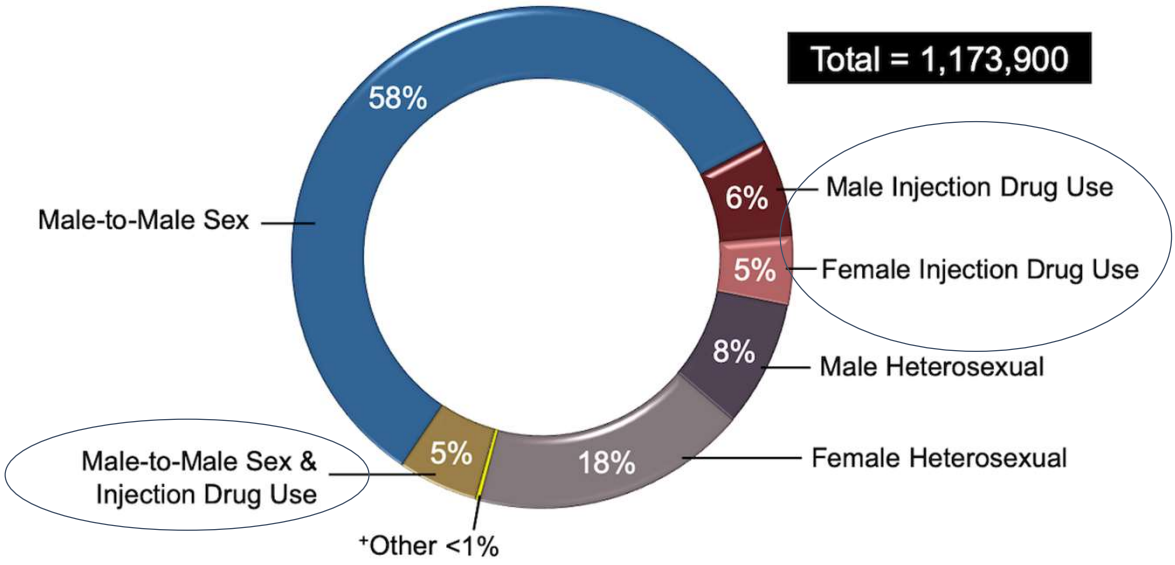
432

8. Answer: **B. HIV**

- HIV seroconversion rates are high among sexual and gender minorities (in this case a transgender woman)
- Regularly test for HIV infection in anyone with risk factors on history
- Offer pre- and post- exposure prophylaxis (PrEP) in persons at elevated risk
- If high suspicion for acute infection, check **HIV viral load**.
- Offer PreP: emtricitabine/tenofovir or cabotegravir (Apretude)

Zachariah S, Sullivan A, Donato A. Shingles: a harbinger of chronic HIV infection. J Community Hosp Intern Med Perspect. 2021 Nov 15;11(6):871-873.

433



+Other = perinatal, hemophilia, blood transfusion, and risk factor not reported or identified.

*Estimate for persons ≥13 years of age living with diagnosed or undiagnosed HIV infection

Figure 6 - Estimated Number of Persons Living with HIV in United States, by Transmission Category, 2018

Source: Centers for Disease Control and Prevention. Estimated HIV Incidence and Prevalence in the United States, 2014–2018. HIV Surveillance Supplemental Report. 2020;25(No. 1):1-77. Published May 2020.

434

Question 9

37-year-old male visits a primary care clinic affiliated with an outpatient opioid treatment program. He reports a single painless ulcer on his penis. Which test is most appropriate?

A. Gonorrhea/Chlamydia Urine PCR
B. PPD Skin Testing
C. RPR or VDRL serum test
D. Tzanck smear

435

9. Answer: **C. RPR or VDRL Serum test**

- A single painless ulcer (typically on penis or labia) is a classic presentation of primary syphilis and is **called a chancre**
- Gonorrhea & chlamydia usually present with dysuria +/- purulent discharge, but vesicular/ulcerative lesions are not typical. Testing is warranted when other STIs are present but it's not the most relevant answer to this presentation
- PPD is used for tuberculosis testing but nothing in this presentation is acutely concerning for TB
- HSV can sometimes be detected by a Tzank smear but current preferred test is PCR using fluid/material from a lesion and/or viral culture of the lesion. HSV typically manifests as multiple painful blisters/sores.

Kidd SE, Grey JA, Torrone EA, Weinstock HS. Increased Methamphetamine, Injection Drug, and Heroin Use Among Women and Heterosexual Men with Primary and Secondary Syphilis — United States, 2013–2017. MMWR Morb Mortal Wkly Rep 2019;68:144–148.

436

9. Answer: **C. RPR or VDRL Serum test**

- Syphilis transmission and drug use, particularly methamphetamine use, are intersecting epidemics
- Until 2013, the increase was primarily among MSM
- During 2013–2017, syphilis rate increased 72.7% nationally and 155.6% among **women**. Reported methamphetamine, injection drug, and heroin use increased substantially among women and heterosexual men with syphilis.
- File a Communicable Disease Report (state dependent)

Kidd SE, Grey JA, Torrone EA, Weinstock HS. Increased Methamphetamine, Injection Drug, and Heroin Use Among Women and Heterosexual Men with Primary and Secondary Syphilis — United States, 2013–2017. MMWR Morb Mortal Wkly Rep 2019;68:144–148.

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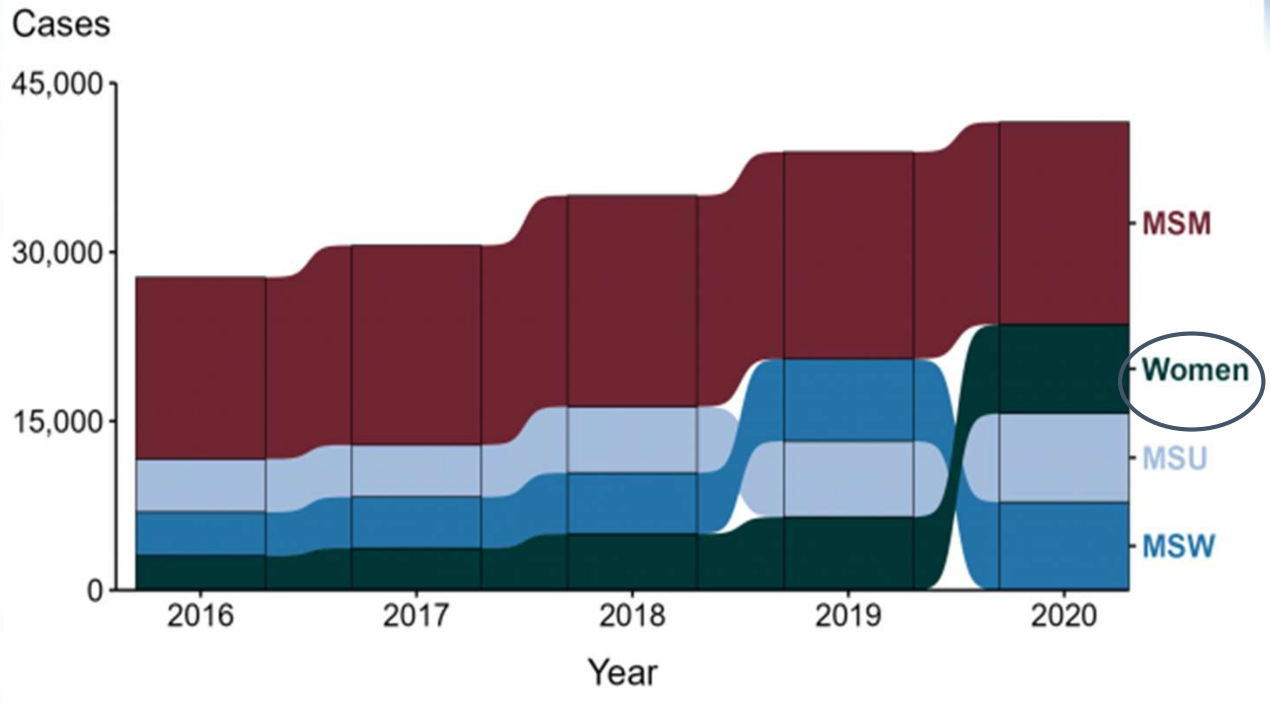
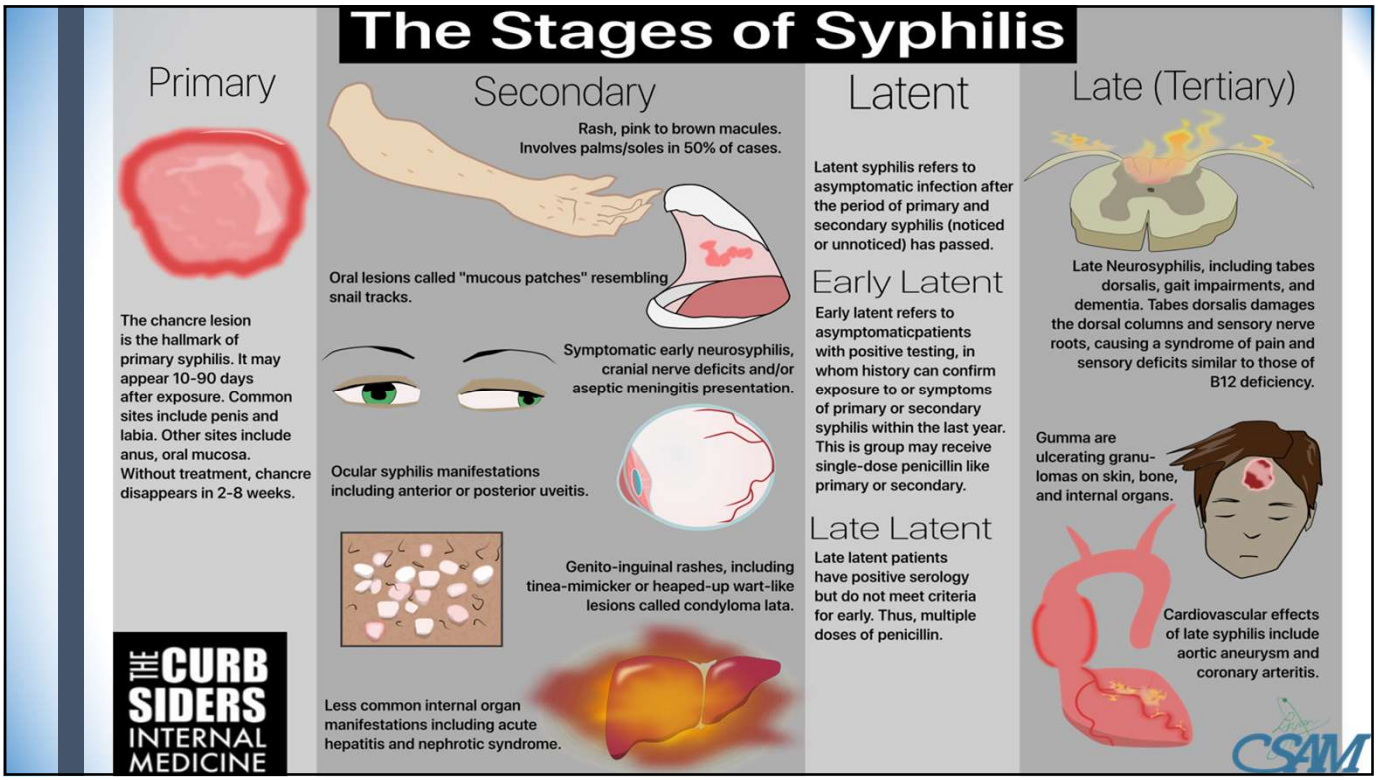


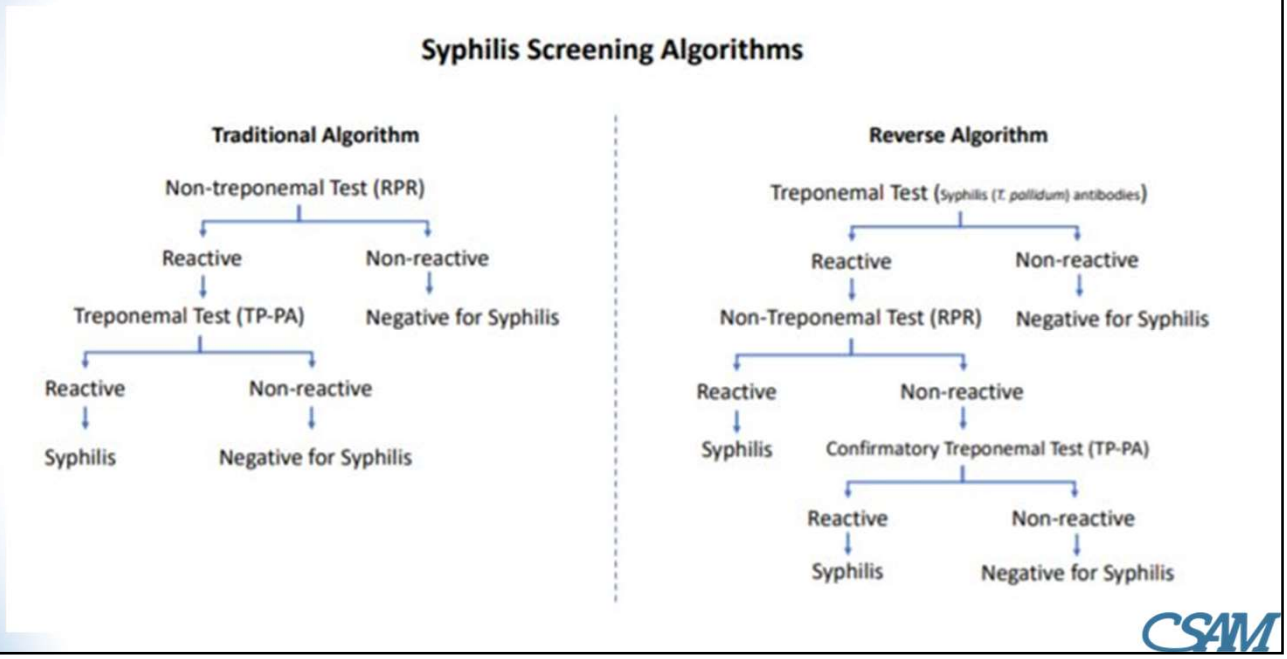
https://www.cdc.gov/std/syphilis/stats.htm

438



439

9. Answer C. RPR, VDRL Testing



440

Question 10

A 32-year-old woman presents to the clinic with progressive shortness of breath, fatigue, and occasional dizziness over the past several months. She has no significant past medical history but admits to using methamphetamine regularly for the past 3 years.

Vital signs are notable for a blood pressure of 118/72 mmHg, heart rate of 92 bpm, and oxygen saturation of 94% on room air.

Physical examination reveals jugular venous distension, a loud P2 component of the second heart sound, and peripheral edema. Echocardiogram is most likely to reveal:

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Question 10 (continued)

Echocardiogram is most likely to reveal:

A. Evidence of right heart strain
B. Ejection fraction of 20%
C. Right ventricular hypertrophy and elevated pulmonary artery pressures
D. Chronic obstructive pulmonary disease

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10 Answer: **C. Right ventricular hypertrophy and elevated pulmonary artery pressures**

- This presentation — progressive dyspnea, fatigue, elevated JVP, loud P2, peripheral edema, and history of methamphetamine use — is classic for **Group 1 pulmonary arterial hypertension**, most likely **drug-induced (methamphetamine)**. Important to screen in those who use MA
- On echocardiogram, the most expected findings include:
  - *Right ventricular hypertrophy*
  - *Dilated right atrium and ventricle*
  - *Elevated estimated pulmonary artery systolic pressure (PASP)*
  - *Possibly flattening of the interventricular septum ("D-shaped septum")*

Yuan JX, et al. Pathogenesis of pulmonary arterial hypertension: role of serotonin, methamphetamines, and BMPR2. *Circ Res.* 2007;100(7):918-927.

443

10 Answer: **C. Right ventricular hypertrophy and elevated pulmonary artery pressures**

A. Evidence of right heart strain *Partially correct though too vague.*

- *Right heart strain may be seen, but this answer lacks specificity. Choice 3 is more accurate because it directly describes the structural and hemodynamic findings you expect in this condition.*

B. Ejection fraction of 20% *which would indicate* ***severe left ventricular systolic dysfunction***

- *This is not supported by the history, exam, or likely cause (methamphetamine-induced PAH, not cardiomyopathy).*

D. Chronic obstructive pulmonary disease (COPD)

- *This is not an echocardiographic finding*
- *Also,* ***no clinical history*** *of smoking, wheezing, or chronic respiratory symptoms to support COPD and the patient is young, though that does not rule it out*

*** In addition: Atrial fibrillation** *is typically an EKG finding, though can be seen on ECHO*

- *While it can be seen in advanced pulmonary hypertension, it is not generally the primary finding on echocardiogram.*

444

10 Answer: **C. Right ventricular hypertrophy and elevated pulmonary artery pressures**

- Methamphetamine use is a known but under-recognized cause of pulmonary arterial hypertension (PAH).
- Classified as Group 1 pulmonary hypertension and associated with poor prognosis.
- Exact mechanism is not fully understood, but proposed mechanisms include:
  - *Pulmonary vascular remodeling*
  - *Oxidative stress and inflammation*
  - *Increased serotonin signaling promoting smooth muscle proliferation*
  - *Direct toxic effects on pulmonary endothelial cells*
  - *Patients with methamphetamine-associated PAH tend to present at a **younger age** and may have more **severe hemodynamic compromise** at diagnosis compared to idiopathic PAH.*

American Heart Association and WHO Classification of Pulmonary Hypertension, which now includes drug-induced PAH (including methamphetamine) under Group 1.

445

Need to Know

1. Toxidromes (clinical symptoms & management)
2. Withdrawal syndromes (clinical symptoms & management)
3. Cardiovascular morbidity: ischemia, arrhythmia, CHF
4. Pulmonary morbidity: COPD, cancer, pulmonary hypertension
5. GI morbidity: hepatitis, cirrhosis, cancer
6. Infectious disease morbidity: Endocarditis, soft tissue infections, sexually transmitted infections
7. Common drug interaction concerns: serotonin syndrome, cytochrome P-450 enzyme inducer/inhibitors

446

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Degenhardt L, Peacock A, Colledge S, Leung J, Grebely J, Vickerman P, Stone J, Cunningham EB, Trickey A, Dumchev K, Lynskey M, Griffiths P, Mattick RP, Hickman M, Larney S. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. Lancet Global Health. 2017;5(12):e1192-1207.

Havens PL, Anderson JR. Updated CDC Recommendations for Universal Hepatitis C Virus Screening Among Adults and Pregnant Women: Implications for Clinical Practice. *JAMA.* 2020;323(22):2258–2259. doi:10.1001/jama.2020.3693

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American Heart Association and WHO Classification of Pulmonary Hypertension, which now includes drug-induced PAH (including methamphetamine) under Group 1.

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448

Maternal-Fetal Substance Use Disorder

CSAM Addiction Medicine Board Review Course
August 13, 2025

John Nuhn, MD
Core Faculty, Family Medicine Residency and
Addiction Medicine Fellowship
Ventura County Medical Center
Presentation updated from 2024 Katherine Pier, MD

449

CONFLICT OF INTEREST DISCLOSURE

I, John Nuhn, have nothing to disclose.

I will be discussing “off label” use of drugs or devices in this presentation.

450

EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Explain the impact of maternal substance use on pregnancy and fetal development
2. Evaluate psychosocial and pharmacologic approaches to the treatment of expectant mothers with substance use disorders
3. Identify best practices for managing neonates and mothers with substance use disorders and withdrawal syndromes in the postpartum period
4. Describe barriers to accessing pharmacotherapy for SUDs among pregnant women

CSAM

451

1. A 28-year-old pregnant woman presents with premature rupture of membranes and discloses use of fentanyl and methamphetamine during her pregnancy. She has missed prenatal appointments due to fear of treatments that would cause withdrawal. Which of the following is most accurate about the barriers faced by pregnant patients with addictions?

A. CPS removal of neonates deters mothers from substance use during subsequent pregnancies.

B. Limited safety data for use of buprenorphine and methadone in pregnancy is a major reason to recommend medication-assisted withdrawal

C. A benefit of CPS taking custody of neonates who test positive for substances is that mothers are then enrolled in state-funded addiction care.

D. Physician stigma and patient fear of CPS involvement are commonly cited reasons pregnant patients with addictions avoid prenatal care.

CSAM

452

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D. Physician stigma and patient fear of CPS involvement are commonly cited reasons pregnant patients with addictions avoid prenatal care.

453

1. Answer: **D - Physician stigma and patient fear of CPS involvement are commonly cited reasons pregnant patients with addictions avoid prenatal care.**

Fear of CPS involvement and legal repercussions deter pregnant individuals from seeking prenatal care and substance use treatment.

Studies have shown that such fears contribute to delayed prenatal care initiation, reduced engagement in substance use treatment, and increased risks of adverse birth outcomes.

Physician stigma is a commonly cited deterrent to disclosing perinatal substance use and accessing treatment.

CPS removal of neonates is associated with **shorter intervals** to subsequent pregnancies and increased risk that those fetuses will be exposed to substances in utero

ACOG 2017. Terplan et al 2017. Krans et al 2016. Reddy et al 2024.

454

1. Answer: **D - Physician stigma and patient fear of CPS involvement are commonly cited reasons pregnant patients with addictions avoid prenatal care.**

Evidence is clear - maternal and fetal outcomes are superior with methadone or buprenorphine vs medication-assisted withdrawal alone.

Addressing pregnant patients with **supportive** and **non-punitive** approaches is crucial in promoting maternal and infant well-being.

ACOG 2017. Terplan et al 2017. Krans et al 2016. Reddy et al 2024.

455

2. Which is **not** a known complication of methamphetamine or cocaine use in pregnancy?

A. Preterm labor
B. Premature rupture of membranes
C. Large for gestational age
D. Placental Abruption

456

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Kalaitzopoulous et al, 2018. Smid et al, 2019. ASAM Essentials of Addiction Medicine, 3rd Ed

457

2. Answer **C - Large for gestational age**

Newborns exposed to methamphetamine and cocaine are at risk for intrauterine growth restriction, preterm labor and small for gestational age. Methamphetamine use can contribute to placental insufficiency and abruption.

Mechanisms by which stimulants contribute to adverse neonatal and fetal outcomes include poor maternal nutrition, vasoconstriction, maternal HTN, and trauma.

Large for gestational age is associated with maternal diabetes, not substance use disorders.

Kalaitzopoulous et al, 2018. Smid et al, 2019. ASAM Essentials of Addiction Medicine, 3rd Ed

458

3. A 28 yo woman presents to Labor & Delivery at 38 weeks gestation with a history of opioid use disorder, currently on methadone therapy. She delivers a healthy infant with an Apgar score of 8 and 9 at 1 and 5 minutes, respectively. The neonate is at risk for Neonatal Opioid Withdrawal Syndrome (NOWS). Which of the following management strategies is most supported by recent research for treating neonates with NOWS?

A. Immediate transfer to the neonatal intensive care unit and initiation of a standardized opioid tapering protocol.

B. Use of a Eat, Sleep, Console (ESC) approach combined with rooming-in, regardless of initial NOWS severity.

C. Strict adherence to the Finnegan Neonatal Abstinence Scoring System (FNASS) to guide initiation and escalation of pharmacologic treatment.

D. Early discharge with outpatient follow-up and support, minimizing the duration of hospital stay.

459

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460

3. Answer **B - Use of a Eat, Sleep, Console (ESC) approach combined with rooming-in, regardless of initial NOWS severity.**

- ESC is an emerging, evidence-based, parent-centered model of care shown to decrease hospital length of stay and need for pharmacological treatment, without increasing adverse events or readmission.
- It is a function-based assessment focusing on the infant's ability to do the following 3 elements of care:
- **Eat:** Breastfeed or take adequate volumes
- **Sleep:** At least 1 hr undisturbed
- **Be Consoled**: Within 10 mins

Grossman et al, 2018. Grossman et al, 2017. MacMillan et al, 2018. Wachman et al, 2017. Young et al 2023. Devlin et al, 2024.

461

3. Answer **B - Use of a Eat, Sleep, Console (ESC) approach combined with rooming-in, regardless of initial NOWS severity.**

- ESC promotes:
  - *shorter hospital lengths of stay for infants*
  - *less medication to treat NOWS*
  - *lower hospital costs*
  - *less NICU time in favor of rooming-in with their parents*
- NICU stays following immediate transfer are much longer than when ESC is used: 22.5 days vs 5.9 days in one study
- Use of FNASS associated with longer NICU stays and more morphine use
- NOWS can be life-threatening and requires inpatient observation

Grossman et al, 2018. Grossman et al, 2017. MacMillan et al, 2018. Wachman et al, 2017. Young et al 2023. Devlin et al, 2024.

462

4. A 3-day-old neonate born at 39 weeks gestation to a mother with a history of heroin and methadone use during pregnancy is being treated for neonatal opioid withdrawal syndrome (NOWS) with oral morphine. Despite optimized dosing, the infant continues to exhibit symptoms of withdrawal including high-pitched crying, tremors, poor feeding, and frequent loose stools. What is the most appropriate next step in pharmacologic management?

A. Switch from morphine to phenobarbital
B. Add clonidine to the current morphine regimen
C. Increase the morphine dose beyond recommended limits
D. Initiate naloxone therapy
E. Discontinue morphine and start buprenorphine

463

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464

4. Answer **B - Add clonidine to the current morphine regimen**

- When NOWS symptoms are not adequately controlled with morphine monotherapy, an adjunct medication is often added.
- Clonidine, an alpha-2 adrenergic agonist, or phenobarbital, a GABA agonist, can help control autonomic symptoms and reduce total opioid requirements.
- Abruptly switching from morphine to phenobarbital may worsen withdrawal symptoms. Phenobarbital should be added as an adjunct if neurologic symptoms persist (tremors, poor sleep pattern) or weaning morphine is unsuccessful despite non-pharmacologic measures.
- Naloxone is contraindicated due to risk of acute withdrawal
- Increasing morphine beyond safe dosing is not appropriate
- Buprenorphine is not standard second-line therapy in neonates, especially along with morphine

465

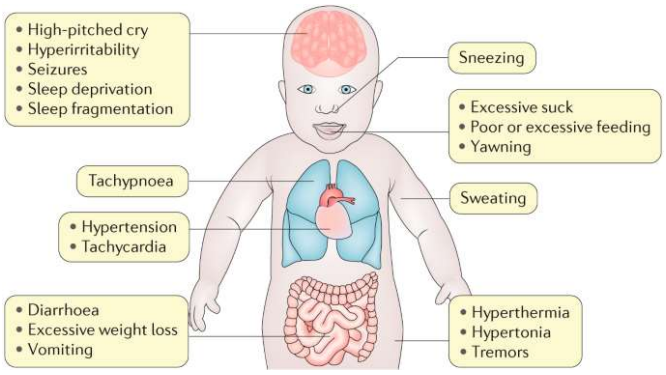
Neonatal Opioid Withdrawal Syndrome

- Observation of infants recommended for 4-7 days if in-utero exposure to opioids is suspected, regardless of opioid.
- Withdrawal syndromes in neonates occur in similar timeframes as they do in non-pregnant individuals

→ fentanyl: variable (hrs-days),

→ oxy & heroin: 1-3 days

→ methadone & bup: within 4



Coyle *et al, 2018*

466

4. Answer **B - Add clonidine to the current morphine regimen**

Clonidine or phenobarbital are appropriate as first-line adjunct for persistent severe withdrawal at maximum opioid dosing

Clonidine is an effective adjunctive therapy to morphine in NOWS, improving outcomes by:

- Reducing total morphine exposure
- Shortening hospital stay
- Managing autonomic symptoms

467

4. Answer **B - Add clonidine to the current morphine regimen**

- In neonates treated with morphine, adding clonidine (1 µg/kg q4h) reduced median length of stay – 15 to 11 days and total morphine use (19.2 mg → 7.7 mg)
- Comparing morphine + clonidine vs. morphine + phenobarbital, the clonidine group had shorter total treatment duration and was weaned before discharge, whereas phenobarbital led to shorter inpatient opioid duration but often required longer outpatient tapers.
- Clonidine, an α_2-adrenergic agonist, diminishes sympathetic overactivity (e.g., tachycardia, tremors, diarrhea) by reducing norepinephrine release—reversing many withdrawal symptoms
- CHOP protocol : Consider adding adjunct medication, if > 1 mg/kg/day of morphine, initiate clonidine at1 mcg/kg/dose every 6 hours. No loading dose. Check BP before 1st dose.

Surran et al, 2013. Brusseau et al, 2020. Cochran review, 2021.
https://www.chop.edu/clinical-pathway/neonatal-abstinence-syndrome-nas-neonatal-opioid-withdrawal-syndrome-nows-clinical-pathway

468

5. A patient presents to your practice at 10 weeks gestation with opioid withdrawal. She expresses interested in beginning medication to assist with her recovery. Compared to methadone, you counsel her that the following is true about buprenorphine:

A. Associated with a clinically meaningful reduction in the severity of NOWS.
B. Associated with higher treatment retention rates than methadone.
C. Safer in pregnancy when combined with naloxone rather than used as monoproduct.
D. Associated with higher doses of morphine for the treatment of neonatal abstinence syndrome.

469

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D. Associated with higher doses of morphine for the treatment of neonatal abstinence syndrome.

Jones et al, 2010. Link et al, 2020. Suarez et al, 2022. SAMHSA 2022.

470

5. Answer: **A. Associated with a clinically meaningful reduction in the severity of NOWS**

- The MOTHER trial demonstrated buprenorphine is an acceptable treatment alternative to methadone for managing opioid use disorder in pregnant women
- Neonates of mothers treated with buprenorphine in pregnancy required **less morphine,** had **shorter hospital stays** and **shorter duration of treatment for NOWS** than neonates of mothers treated with methadone.
- Large cohort study since showed lower rates of NOWS in buprenorphine vs methadone exposed neonates, **and** lower relative risk of SGA, LBW and preterm birth while maternal outcomes (rates of c-section and severe maternal complications) were similar for mothers exposed to buprenorphine and methadone

Jones et al, 2010. Link et al, 2020. Suarez et al, 2022. SAMHSA 2022.

471

5. Answer: **A. Associated with a clinically meaningful reduction in the severity of NOWS**

- Retention was a problem in the buprenorphine arm of the MOTHER study, about 33% dropped out, most citing dissatisfaction with the medication. Possible that induction was too slow or withdrawal was incomplete.
- Findings on retention since the MOTHER study have been mixed.

Dosing of bup and methadone in pregnancy:

- Buprenorphine doses often need to be increased as pregnancy progresses. As volume of distribution increases, pregnant women sometimes require twice daily or more frequent dosing.
- Metabolic rates of methadone generally increase during pregnancy, sometimes dramatically. Most women require twice daily dosing regimens, some more frequent.

Jones et al, 2010. Link et al, 2020. Suarez et al, 2022. SAMHSA 2022.

472

5. Answer: **A. Associated with a clinically meaningful reduction in the severity of NOWS**

Buprenorphine Monoproduct vs Buprenorphine/Naloxone:

- While bup/nx is recommended over monoproduct in non-pregnant patients with IV opioid use, theoretical risk of precipitating withdrawal in pregnancy among reasons monoproduct was previously preferred for new buprenorphine inductions or in unstable patients
- Recent studies show equivalent pregnancy and neonatal outcomes in women treated with buprenorphine-naloxone compared with buprenorphine alone
- Consider continuing buprenorphine-naloxone for patients who are successful with it
- General expert consensus presently is that use of combine product does not increase risk in pregnancy

473

6. A 24-year-old woman presents to your office with a 6-week history of nausea/vomiting & reports drinking a 12-pack of beer daily for the past year. A routine pregnancy test is positive. The patient is motivated to stop drinking to protect the baby. History is positive for severe alcohol withdrawal symptoms with prior cessation attempts but negative for delirium tremens & seizures. In addition to psychosocial treatment, you recommend:

A. Admission and treatment with an anticonvulsant, such as carbamazepine.
B. Careful monitoring, but medication management likely will not be necessary since patient's history is negative for seizures & delirium tremens.
C. Admission and treatment with a benzodiazepine.
D. Admission and treatment with clonidine and gabapentin

474

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CSAM

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6. Answer **C - Admission and treatment with a benzodiazepine.**

- Given the patient's history of severe alcohol withdrawal, medical management is appropriate.
- Of the choices listed, a benzodiazepine is most appropriate.
- Most anticonvulsants are relatively contraindicated in pregnancy
- Phenobarbital linked to cardiovascular defects, cleft palate, skeletal abnormalities, fetal growth restriction and developmental delays
- Clonidine and gabapentin, while becoming more widely used and studied, are still not first line monotherapy for alcohol withdrawal and are not well studied in pregnancy.

CSAM

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7. A 32-year-old woman in her first trimester of pregnancy presents for routine prenatal counseling. She mentions that she recently read an article suggesting that small amounts of alcohol during pregnancy may be safe and asks whether it is acceptable for her to have an occasional glass of wine. She reports no history of alcohol use disorder. What has happened to alcohol use during pregnancy in recent years?

A. Alcohol use has slightly decreased
B. Alcohol use has remained consistent
C. Alcohol use has increased slightly
D. Alcohol use has increased a lot with information regarding the safety of alcohol during pregnancy circulating

477

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478

7. Answer **C - Alcohol use has increased slightly**

Alcohol use during pregnancy has **slightly increased** in recent years
- current drinking is reported by 13–14% of pregnant women
- 5% report binge drinking in the past month

From 2011 to 2018 pregnant women reported
- *any alcohol use* rose from ~9% to ~11%
- *binge drinking* also increased

Between 2018 and 2020:
- 13.5% of pregnant individuals reported current drinking
- 5.2% reported binge drinking.

CDC and NIAA June 2024 data

479

7. Answer **C - Alcohol use has increased slightly**

Though most women discontinue alcohol use upon discovering they are pregnant or when trying to become pregnant, a significant subset of pregnant women continue to drink, especially in the first trimester.

Correlations with continued alcohol use include:
- Mental health issues
- Lack of consistent healthcare
- Socioeconomic stress

Denny et al, 2020. Gosdin et al, 2022. Howard et al, 2022.

480

7. Answer **C - Alcohol use has increased slightly**

Any alcohol use can lead to **Fetal Alcohol Syndrome:**

- Facial abnormalities (short palpebral fissure, smooth philtrum, thin upper lip)
- Poor growth
- Neurodevelopmental and behavioral issues

Fetal Alcohol Spectrum Disorders effect 1-5% of first graders in one major study

Appropriate counseling is for complete abstinence during pregnancy.

Denny et al, 2020. Gosdin et al, 2022. Howard et al, 2022.

481

8. A G1P0 woman presents to your office 14 weeks pregnant to discuss insomnia. She says that she tried diphenhydramine as you had recommended but has found the cannabis works much better with fewer side effects. Which of the following statements about cannabis use during pregnancy is most accurate:

A. Rates of maternal cannabis use during pregnancy have decreased in recent years, aligning with broader public health efforts to reduce substance use among pregnant individuals.
B. Emerging research suggests that maternal cannabis use during pregnancy may have protective effects on fetal development, potentially reducing the risk of preterm birth and low birth weight.
C. Advanced neuroimaging studies have not corroborated evidence that prenatal cannabis exposure correlates with increased aggressive behavior, suggesting bias in the previous studies
D. Pregnant patients should be advised to avoid cannabis entirely during pregnancy because of evidence that intrauterine exposure to cannabis correlates with attention, social and behavioral problems in offspring

482

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Ryan et al, 2018. Volkow et al, 2019. Young-Wolff et al, 2022.

483

8. Answer **D - Pregnant patients should be advised to avoid cannabis entirely during pregnancy because of evidence that intrauterine exposure to cannabis correlates with attention, social and behavioral problems in offspring**

- Evidence suggests that prevalence of maternal cannabis use in pregnancy has increased over the last decade
- delta-9-tetrahydrocannabinol (THC) crosses the placenta and can affect brain development, causing cognitive, social-emotional and behavioral problems that persist at least until adolescence. These include increased aggression, problems in attention, memory, learning, psychological problems and substance use. This is supported by evidence integrating advanced neuroimaging techniques
- Evidence suggests an association between prenatal cannabis use and preterm labor, small for gestational age and stillbirth
- ACOG recommends against the use of cannabis in pregnancy and lactation

Ryan et al, 2018. Volkow et al, 2019. Young-Wolff et al, 2022.

484

9. During a monthly follow-up visit with a 24-year-old pregnant woman on opioid agonist treatment with methadone for management of opioid use disorder secondary to heroin, she asks whether it would be okay for her to breastfeed. Which aspect of this patient's case would cause you to recommend **against** breastfeeding?

A. Patient's methadone dose is 140 mg at the time of delivery.
B. Patient has had two brief relapses to binge drinking, but none since starting on escitalopram for treatment of her anxiety.
C. Patient's partner just tested positive for HIV, and her own confirmatory test comes back positive.
D. Patient has hepatitis C.

485

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D. Patient has hepatitis C.

ABMPC guideline, 2009. Chen et al, 2013. Carneiro-Proietti et al, 2014.

486

9. Answer **C - Patient's partner just tested positive for HIV, and her own confirmatory test comes back positive.**

- ACOG & the AAP agree that methadone and buprenorphine, including with naloxone, at **any** therapeutic dose, is compatible with breastfeeding.
- **HIV is a contraindication to breastfeeding**, BUT Hepatitis B & C are not. Hepatitis C is not found in breastmilk. Hepatitis B DNA can be detected in breast milk, but breastfeeding has not been found to be a risk factor for mother-to-child transmission. Newborns are further protected from Hepatitis B by beginning the vaccination series at delivery. Mothers with Hepatitis B &/or C should pump & discard in the event of cracked & bleeding nipples, until the condition resolves.
- Escitalopram is compatible with breastfeeding.
- Rare past binge drinking episodes are not a contraindication to breastfeeding, with ongoing monitoring.

ABMPC guideline, 2009. Chen et al, 2013. Carneiro-Proietti et al, 2014.

487

10. A 36-year-old G3P2 presents to your clinic for her first prenatal care visit at 5 weeks and 4 days. She has been smoking cigarettes on and off since age 14. Prior to this pregnancy, she participated in your clinic's smoking cessation program but stopped going after 3 sessions stating she didn't like it. She was unable to abstain from cigarettes using behavioral modification in her last pregnancy. Which of the following options describes the best management of this patient's nicotine use disorder in pregnancy?

A. Prescription of nicotine-replacement therapy, after discussion of the risks and benefits.
B. Prescription of bupropion, after discussion of the risks and benefits
C. Prescription of varenicline, after discussion of the risks and benefits
D. Recommendation to switch to e-cigarettes to avoid prenatal exposure to tar in cigarettes, after discussion of the risks and benefits

488

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Claire et al, 2020. Kranzier et al, 2021. Patnode et al, 2021. Taylor et al, 2021.

489

10. Answer **A -** Prescription of nicotine-replacement therapy, after discussion of the risks and benefits.

- Note that the treatment of choice for smoking cessation in pregnancy would be behavioral therapy, however this patient declined that option.
- NRT in pregnancy may result in higher chance of quitting compared to no medication. Evidence on safety is limited but suggests that there is no increased risk of fetal harm from NRT.
- Consider a trial of NRT for pregnant women who have not been successful in quitting with behavioral support alone and/or when individual risks are especially high from continued smoking

Claire et al, 2020. Kranzier et al, 2021. Patnode et al, 2021. Taylor et al, 2021.

490

10. Answer **A** - continued.

- There is insufficient evidence of efficacy for bupropion for smoking cessation during pregnancy and safety data for bupropion in humans is limited (category C). Could be considered on a case-by-case basis.
- Neither the safety nor efficacy of varenicline during pregnancy has been established.
- There is **inconclusive evidence in adults for the role of e-cigarettes** in smoking cessation, and even less evidence regarding safety and efficacy in pregnant persons.

Claire et al, 2020. Kranzier et al, 2021. Patnode et al, 2021. Taylor et al, 2021.

491

11. A 24-year-old G1P0 presents to L&D in early labor. She appears withdrawn and somewhat somnolent. A urine drug screen is positive for methamphetamine. Which of the following treatment approaches would NOT be recommended?

A. Offer referral to a local residential treatment center for pregnant and postpartum mothers
B. Counsel her about the importance of frequent early breastfeeding to increase maternal-infant bonding and improve newborn outcomes.
C. Offer take-home naloxone at the time of discharge given high probability of encountering methamphetamine laced with fentanyl in many communities.
D. Send urine for confirmatory GC/MS testing to clarify which substances the patient and fetus were exposed to and consider meconium drug testing after delivery.

492

11. A 24-year-old G1P0 presents to L&D in early labor. She appears withdrawn and somewhat somnolent. A urine drug screen is positive for methamphetamine. Which of the following treatment approaches would NOT be recommended?

A. Offer referral to a local residential treatment center for pregnant and postpartum mothers

B. Counsel her about the importance of frequent early breastfeeding to increase maternal-infant bonding and improve newborn outcomes.

C. Offer take-home naloxone at the time of discharge given high probability of encountering methamphetamine laced with fentanyl in many communities.

D. Send urine for confirmatory GC/MS testing to clarify which substances the patient and fetus were exposed to and consider meconium drug testing after delivery.

493

11. Answer **B - Counsel her about the importance of frequent early breastfeeding to increase maternal-infant bonding and improve newborn outcomes.**

- Standard of care for women using methamphetamines during pregnancy is behavioral treatment. Postpartum **residential** treatment allows substance use treatment to occur alongside developmental and parenting interventions for the mother-infant pair.
- Methamphetamine is relatively concentrated in breast milk--to levels even higher than that of the maternal serum level--and therefore **breastfeeding is contraindicated** for mothers with recent or ongoing methamphetamine use.
- Take-home naloxone should be given to patients who use methamphetamine given high frequency of fentanyl co-positivity in urine specimens that are positive for methamphetamine

ACOG 2011. Putnam-Hornstein et al, 2016. Larue et al, 2019.

494

11. Answer **B - Counsel her about the importance of frequent early breastfeeding to increase maternal-infant bonding and improve newborn outcomes.**

- Confirming maternal/fetal exposure to substances through maternal urine drug testing is indicated and should be obtained with informed consent. Meconium testing of the neonate may be considered in this case, but **neither** is required by law in most states including California
- In California, there is **no mandated reporting for prenatal** substance use
- An infant identified as being affected by prenatal substance use or withdrawal should be referred for an **assessment of needs** (usually by hospital social worker) prior to discharge; this assessment usually includes referral to child welfare services (CPS).

ACOG 2011. Putnam-Hornstein et al, 2016. Larue et al, 2019.

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12. A 15-week pregnant woman asks her obstetrician for assistance accessing medication for opioid use disorder during pregnancy. Which of the following responses from her obstetrician most accurately describes barriers pregnant women face in accessing pharmacotherapies for opioid use disorder?

A. Pregnant women paying cash wait longer for appointments than those paying with insurance.

B. When compared to white non-Hispanic women, pregnant women, identifying as Hispanic or Black, are less likely to receive buprenorphine treatment vs methadone treatment

C. Wait times for pregnant women to access office-based buprenorphine treatment are shorter than wait times to access methadone through opioid treatment programs

D. Pregnant women will be able to access buprenorphine and methadone at the same rates as non-pregnant women

CSAM

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Patrick et al, 2019. Patrick et al, 2020. Schiff et al, 2020.

497

12. Answer **B - Pregnant women who identify as Hispanic and blacks have a lower likelihood than white non-Hispanic women of receiving buprenorphine treatment compared with methadone treatment**

- Pregnant women access appointments with buprenorphine prescribers at lower rates than non-pregnant women.
- Pregnant and non-pregnant women access methadone at similar rates
- Those able to pay cash access OTPs and buprenorphine providers at significantly higher rates and with shorter wait times than those using insurance
- Compared with white non-Hispanic women, black and Hispanic women have a substantially lower likelihood of receiving any medication for the treatment of OUD and are more likely to receive methadone than buprenorphine

Patrick et al, 2019. Patrick et al, 2020. Schiff et al, 2020.

498

NEED TO KNOW

1. Effects of the following in-utero exposures on pregnancy and fetal development
   - Nicotine
   - Alcohol
   - Stimulants
   - Barbiturates
   - Benzodiazepines
   - Cannabinoids
   - Opioids & opioid withdrawal
2. Barriers to treatment for pregnant populations
3. Medications used to treat opioid use disorder in pregnancy, including research comparing maternal and neonatal outcomes for buprenorphine vs methadone

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NEED TO KNOW

4. Effects of pregnancy on metabolism of methadone vs. buprenorphine
5. Signs of neonatal opioid withdrawal syndrome and ideal management
6. Timing and onset of neonatal withdrawal after in utero exposure to heroin, methadone, & buprenorphine
7. Compatibility of buprenorphine & methadone with breastfeeding

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Thank you & Good Luck!

501

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OPIOIDS & PAIN

CSAM Addiction Medicine Board Review Course
August 13, 2025

Samantha Ayoub, MD, MS
Addiction Medicine Physician, VA Loma Linda
Assistant Professor
Loma Linda University

Contents modified from Past Presentation by Katherine Pier MD

514

CONFLICT OF INTEREST DISCLOSURE

I, Samantha Ayoub, have nothing to disclose, and I will be discussing “off label” use of drugs or devices in this presentation.

515

EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Master relevant pharmacology related to the therapeutic and addictive properties of opioids
2. Describe the pharmacological properties of specific opioids
3. Review treatment options for opioid use disorder and drug-drug interactions
4. Describe epidemiology & illness course of opioid use disorder
5. Apply treatment guidelines to the management of chronic pain in the setting of opioid use disorder

516

Question#1

Endogenous opioid peptides include the families of dynorphin, endorphin, and _____. These peptides are expressed in brain regions associated with reward, motivation, and pain perception.

A. enkephalin
B. oxytocin
C. peptidoglycan
D. thebaine

517

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B. oxytocin
C. peptidoglycan
D. thebaine

518

Type	Effects	Notable agonists	Notable antagonists
μ	Analgesia, euphoria, respiratory depression , physiologic dependence	Morphine, fentanyl, methadone **Endomorphins, β-endorphins**	Naltrexone, naloxone
δ	Analgesia, nociception, convulsions, antidepressant, respiratory depression	**Enkephalins, β-endorphins**	Naltrexone, naloxone
K	Analgesia, nociception, **dysphoria,** anticonvulsant, dissociative/hallucinogen	Salvia, ibogaine **Dynorphins**	Naltrexone, naloxone, buprenorphine

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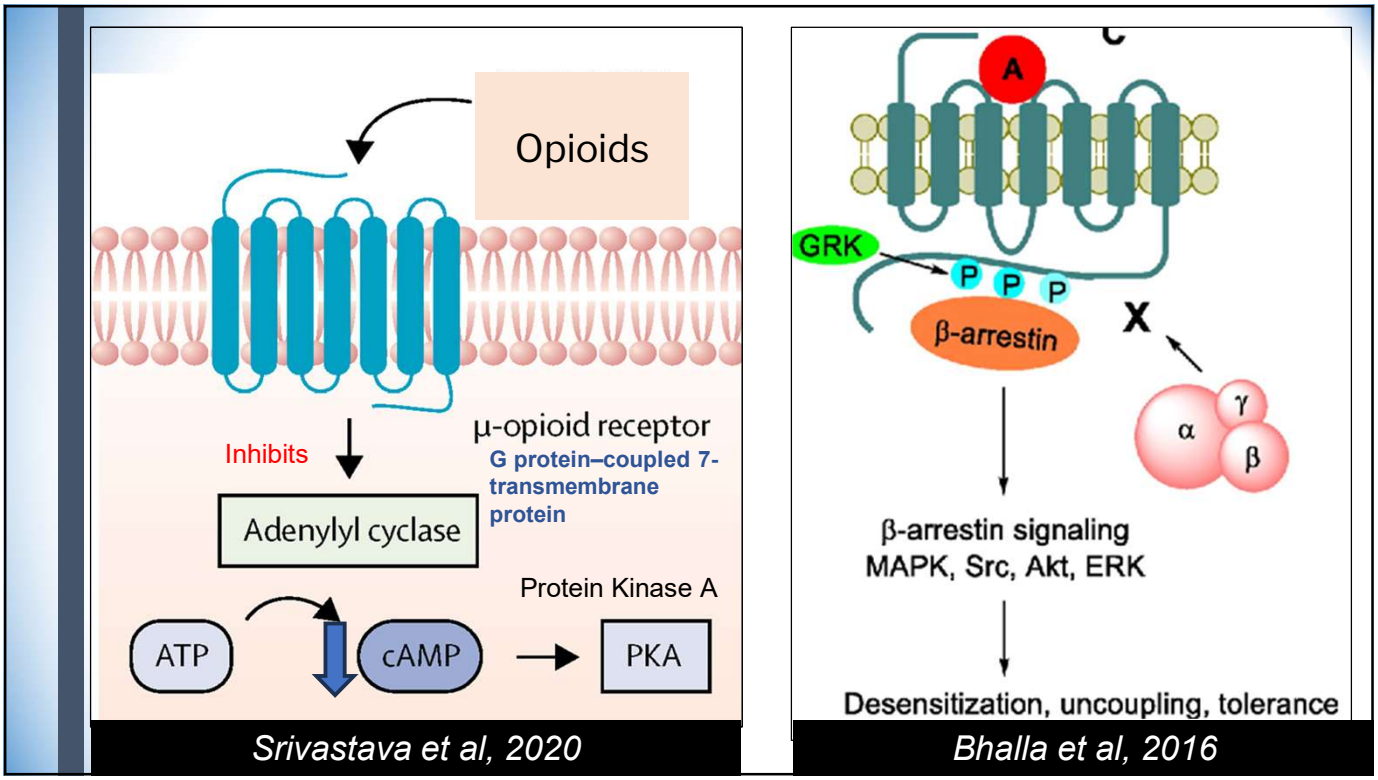

520

QUESTION#2

Which of the following is *incorrectly* paired with one of its purported mechanisms of action?

A. Methadone—NMDA glutamate antagonist

B. Mitragynine—Mu-opioid receptor partial agonist

C. Salvinorin—Kappa-opioid antagonist

D. Tramadol—Serotonin reuptake inhibitor

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521

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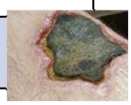
Name	Receptor effects	Highlights
Salvinorin (Salvia)	κ receptor agonist 	• Dissociative/hallucinogen via κ agonism • Hallucinations, analgesia • No respiratory depression
Methadone	μ opioid receptor agonist	
	NMDA receptor antagonist	• Attenuates tolerance, analgesia
Mitragynine (Kratom)	Partial at μ and most likely competitive antagonism of δ opioid receptors	• Very high potency at μ receptor • Low doses- stimulation, Higher- opioid effects • Used by patients to "attenuate" opioid withdrawal
Tramadol	μ opioid receptor partial agonist; SNRI	• Serotonin syndrome • Not detected on drug screens
Desomorphine (Krokodil)	High potency μ opioid agonist	• Easily synthesized from codeine • Extensive skin necrosis 

523

QUESTION#3

Which of the following best describes epidemiologic trends in opioid use disorder (OUD) and opioid-related overdose in the United States?

a. Xylazine adulteration of synthetic opioids has remained confined primarily to the Northeastern United States.
b. Young people who report prescription opioid misuse most often obtain opioids from a physician.
c. Stimulant involvement in opioid-related overdose deaths has been decreasing in recent years.
d. Illicit synthetic opioids have contributed to the largest proportion of all overdose deaths since 2016.

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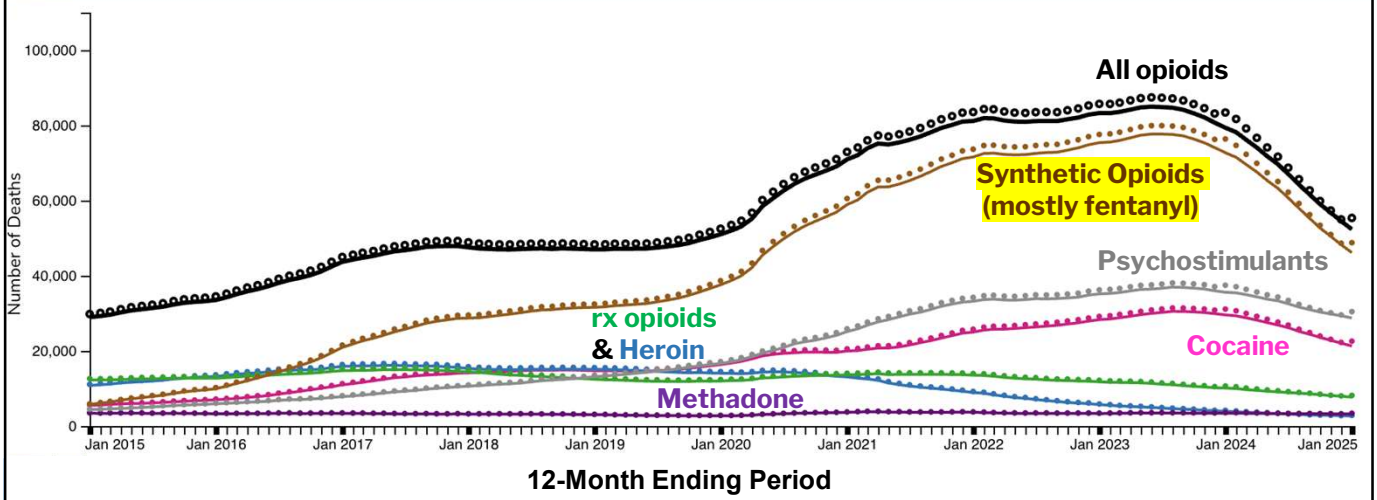
525

12 Month-ending Provisional Number of Drug Overdose Deaths by Drug or Drug Class: United States



Centers for Disease and Prevention. (2025, June 11). *Vital statistics rapid release: Provisional drug overdose death data*. National Center for Health StatisticsControl

Very recent data shows decreasing opioid overdose deaths in 2023 for the first time since 2018. Synthetic opioids are the still most common cause of overdose death (Answer D).

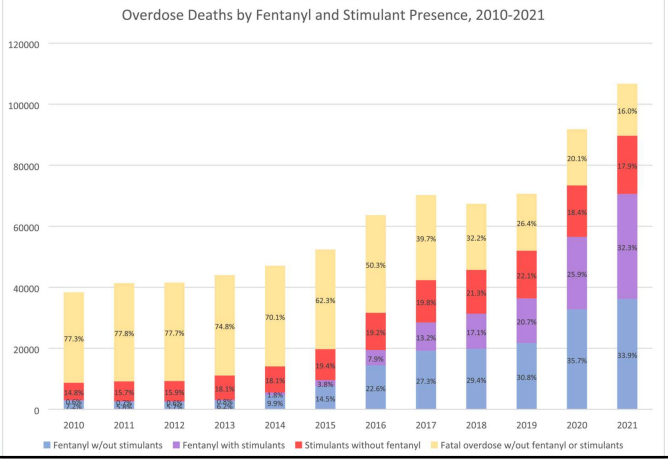
526

a) Xylazine has been detected in 49 out of 50 states as of 2024. Between 2018 and 2021, xylazine-fentanyl overdose deaths increased from 0.36% to 10.9%. Xylazine needs to be considered in overdose response, as it can cause continued sedation despite naloxone administration. It can also increase the need for medical attention for people using drugs, due to overdose, wounds, and infections.

b) Social networks appear to play a major role in how people under 50, especially adolescents and young adults, obtain prescription opioids. Studies generally show that most adolescents and young adults who misuse opioids acquire them from family members or friends—either given for free, by purchasing, or taken without permission.

527

c) Involvement of stimulants has significantly increased in synthetic opioid overdose deaths. This has been a consistent finding when analyzing data between 2010 and 2022 and may be part of a "Fourth wave" of the opioid crisis (synthetic opioids in combination with other substances)

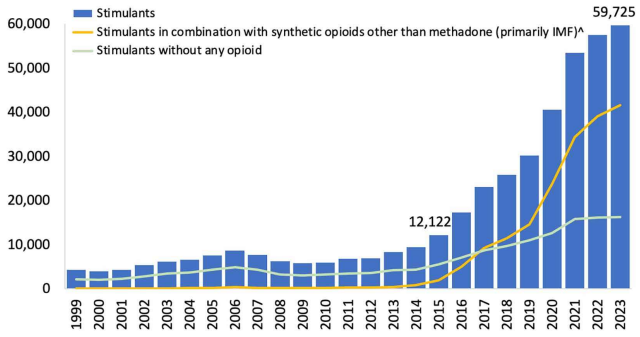


Friedman, J., & Shover, C. L. (2023).

528

c) (cont.) Stimulant overdose deaths alone have also been increasing since 2014, but at a lower rate than stimulants in combination with synthetic opioids.

Figure 6. U.S. Overdose Deaths Involving Stimulants (Cocaine or Psychostimulants with Abuse Potential), 1999-2023



*Among deaths with drug overdose as the underlying cause, the stimulants category included cocaine and psychostimulants with abuse potential (primarily methamphetamine) determined by the T40.5 and the T43.6 ICD-10 multiple cause-of-death codes, respectively. ^illicitly manufactured fentanyl. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2023 on CDC WONDER Online Database, released 1/2025.

Image from: National Institute on Drug Abuse

529

QUESTION#4

Which of the following is a potential benefit of low-dose buprenorphine initiation for the treatment of opioid use disorder?

A. Rapid onset of opioid withdrawal symptoms

B. Buprenorphine can be initiated concurrent with continued fentanyl use

C. Buprenorphine can be initiated once a COWS score reaches 5

D. It allows health care providers to use the lowest effective dose of buprenorphine

2023

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QUESTION#4

Which of the following is a potential benefit of low-dose buprenorphine initiation for the treatment of opioid use disorder?

A. Rapid onset of opioid withdrawal symptoms

B. Buprenorphine can be initiated concurrent with continued fentanyl use

C. Buprenorphine can be initiated once a COWS score reaches 5

D. It allows health care providers to use the lowest effective dose of buprenorphine

531

A Plea From People Who Use Drugs to Clinicians: New Ways to Initiate Buprenorphine are Urgently Needed in the Fentanyl Era

Kimberly L. Sue, MD, PhD, Shawn Cohen, MD, Jess Tilley, and Avi Yocheved

- *Rates of precipitated withdrawal using standard buprenorphine induction protocols are high, especially in patients using fentanyl*
- *Inability to stop using full agonist opioids for a required period*

Sue et al, 2022
Varshneya NB et al, 2022

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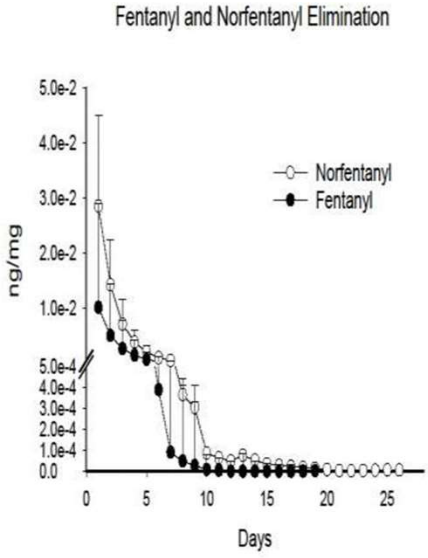
Pharmacological Properties of Fentanyl

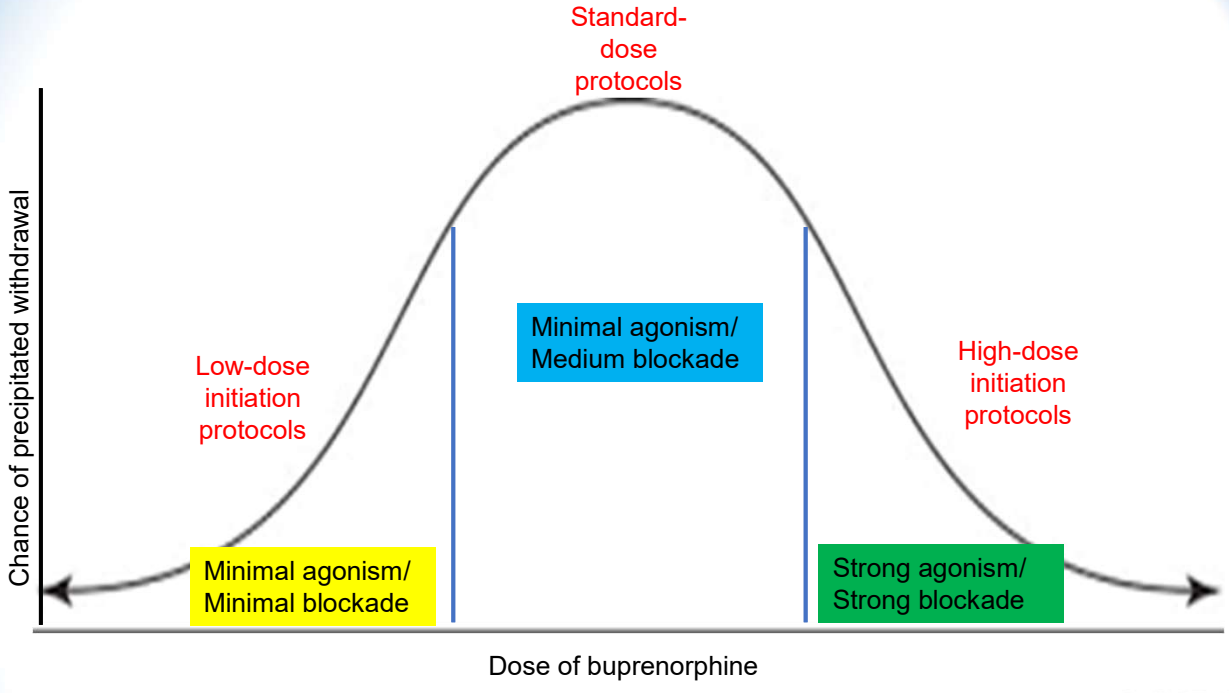
- Fast onset and high potency
  - *50-100x more potent than morphine*
  - *high lipid solubility increases potency*
- Short duration of action due to redistribution in body fat
- Chronic use causes accumulation in adipose tissue and protracted renal clearance
  - *Might partly explain heterogeneous response to traditional buprenorphine induction strategies*



Herron & Brennan, 2019

Huhn et al, 2020

533



Greenwald et al, 2022

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Example protocols

	Low-Dose	Standard-Dose	High-Dose
Optimal time since last use of fentanyl	Concurrent use is acceptable	>72 hrs * patients may not wait that long	Depends on protocol; generally, >6 hours OR use naloxone
Typical starting dose	<2mg	4mg	16mg and up to 32mg on day 1
Time until target dose	2-7 days * risks lost to follow up	2-3 days	1-2 days
Precipitated withdrawal risk	Low	Moderate	Low (<2%) and resolves quickly

Cohen et al, 2021

Herring AA et al, 2021

Randall A et al, 2023

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QUESTION#5

A 45-year-old male with a history of opioid use disorder presents to your clinic seeking treatment. He lives in a rural area and has difficulty attending in-person visits due to transportation issues. Considering the recent regulatory changes, which of the following statements is TRUE regarding his treatment options with methadone and buprenorphine?

A. Screening and initial physical examination by audiovisual telehealth is permitted for admission to an opioid treatment program prescribing methadone.

B. Methadone doses may never exceed 50mg on the first day of methadone treatment.

C. Prescribers are required to obtain a special X-license to prescribe buprenorphine for opioid use disorder

D. Increasingly flexible regulations around methadone prescribing practices during the COVID-19 pandemic contributed to the surge in opioid overdose deaths.

536

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CSAM

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A. Methadone can be initiated by telehealth and opioid treatment programs may expand eligibility for patients to receive take-home doses of methadone earlier in their course of treatment.

Updates in 2024 from the Dept of Health and Human Services (HHS) have significantly changed the regulations governing OTPs, aiming to improve access to medications for OUD. Key updates include:

1) Admission to an OTP program is permitted with an initial telehealth screening and physical examination.
2) Take-home doses - Covid-19 era flexibilities now permanent
3) Elimination of the X-license requirement for buprenorphine

SAMHSA 2024

CSAM

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"The total dose for the first day **should not exceed 50 milligrams unless the OTP practitioner, licensed under the appropriate State law and registered under the appropriate State and Federal laws to administer or dispense MOUD, finds sufficient medical rationale,** including but not limited to if the patient is transferring from another OTP on a higher dose that has been verified, and documents in the patient's record that a higher dose was clinically indicated." 42 CFR § 8.12(h)

Increasingly flexible regulations around methadone prescribing practices during the Covid-19 pandemic were NOT associated with increased rates of overdose and did not reduce retention (Williams et al, 2023)

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QUESTION#6

A 55-year-old woman with opioid use disorder, diabetes mellitus type 2, uncontrolled hypertension, congestive heart failure and HIV is being treated for her opioid use disorder with methadone. The following medications were added in the past 6 months: metformin, carvedilol, efavirenz, and verapamil. She reports new onset episodes of gait instability and slurred speech, and her daughter later found her unresponsive on the floor of her home. Which of the following drug interactions is the *MOST LIKELY* explanation for her symptoms?

A. carvedilol-methadone interaction at cardiac beta-adrenergic receptors

B. efavirenz-methadone interaction at cytochrome P450 2B6 enzyme

C. verapamil-methadone interaction at cytochrome P450 3A4 enzyme

D. metformin-methadone interaction at cytochrome P450 2D6 enzyme

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CSAM

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CYP3A4 INDUCERS	CYP3A4 INHIBITORS
CarbAMAZEpine	Grapefruit + cranberry juice
RifAMPin	azole antifungals (ketoconazole, itraconazole > fluconazole)
St. Johns wort	Macrolide antibiotics: clarithromycin> erythromycin
Phenobarbital	Protease inhibitors: ritonavir, indinavir
Phenytoin	Thyroid hormones
Efavirenz	Calcium channel blockers (verapamil, diltiazem)
Psych: risperidone, modafinil	Cimetidine, omeprazole
Griseofulvin	Psych: fluoxetine, fluvoxamine, valproic acid

CSAM

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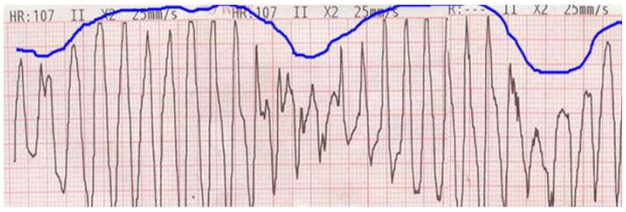
Other tested methadone interactions

- **QTc prolongation & torsade de pointes**
  - Repeat EKG after other QTc prolonging medications are added including TCA antidepressants like imipramine, clomipramine and citalopram
  - *Block K+ efflux from cardiac myocytes during cardiac repolarization*



Kranz et al, 2009

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QUESTION#7

A healthy 23-year-old man last used pure heroin 34 hours ago. Which of the following is the most likely to be the result from a confirmatory gas chromatography/mass spectroscopy urine test?

A. 1200 ng/mL 6-monoacetyl-morphine and 8750 ng/mL of morphine
B. 5430 ng/mL of 6-monoacetyl-morphine
C. 1420 ng/mL of hydromorphone and 4315 ng/mL of morphine
D. 3130 ng/mL of morphine

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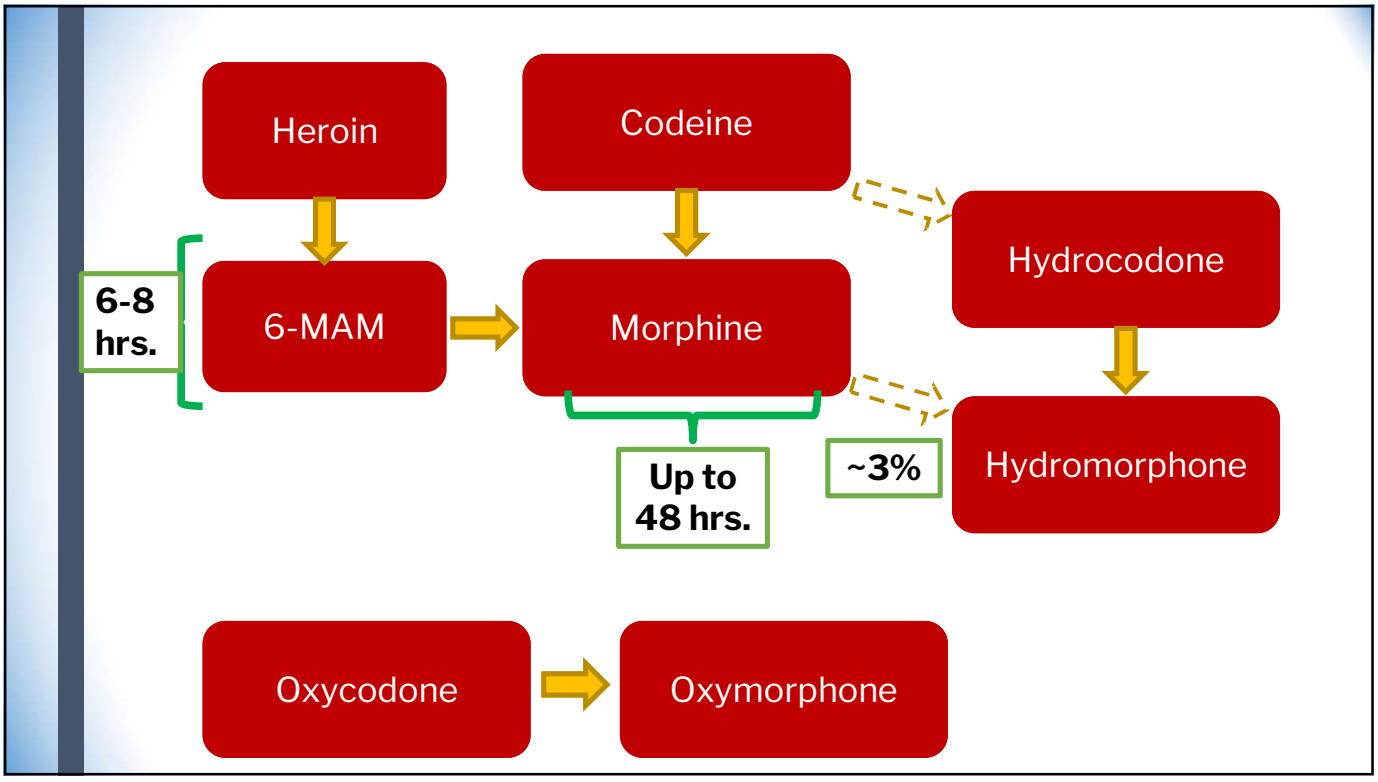

546

QUESTION#8

In 2016 the Center for Disease Control (CDC) published guidelines for the use of opioids in the management of chronic, non-cancer pain. Which of the following was among their recommendations?

A. Acute pain usually requires 3 months or less of opioids
B. Consider prescribing naloxone when daily opioid doses reach 50 morphine milligram equivalents or more
C. New opioid starts should use long-acting formulations when possible
D. Urine drug testing should be performed at least monthly when prescribing long-term opioids

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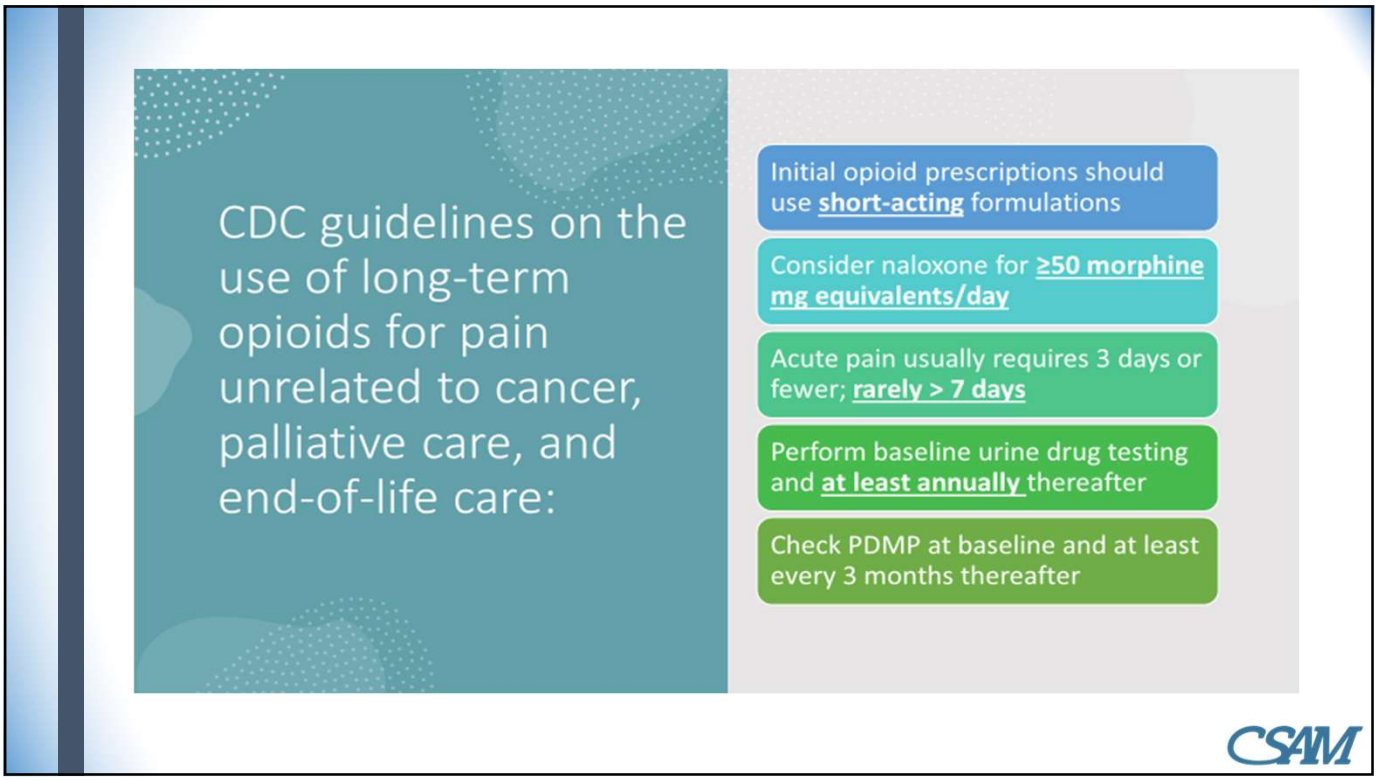

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QUESTION#9

A 53-year-old man with severe hip osteoarthritis is planning to undergo an elective total hip arthroplasty. He has a history of opioid use disorder, in sustained remission on buprenorphine treatment (total daily dose 16 mg). Which of the following *best* presents the expert consensus?

A. Continue buprenorphine and treat postoperative pain with short-acting, full agonist opioids
B. Continue buprenorphine and treat postoperative pain with multimodal analgesia
C. Taper off buprenorphine 3 days prior to surgery and start full agonist opioids postoperatively
D. Taper off buprenorphine 1 week prior to surgery and treat with non-opioid pain treatments postoperatively

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CSAM

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Management of Perioperative Pain for Patients on MOUD

Buprenorphine	Methadone	Naltrexone
• Blocks many effects of additive opioids, but additive analgesia is maintained • Consider TID dosing • Some argue for dropping <16mg below full μ-receptor occupancy	• α –elimination reaction is about 8 hours and affects analgesia, split to TID dosing	• 10-hour half-life, oral should be discontinued 48 hours prior to surgery • Recommend stopping XR-NTX 4th weeks ahead of surgery; reports of analgesic blockade within 1st 2 weeks holding NTX

CSAM

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Several multimodal pain management options, depending on the specific procedure, are possible perioperatively:

- non-opioid medications (gabapentinoids, IV acetaminophen, alpha-2 agonists, ketamine, ketorolac, bupivacaine/lidocaine)
- regional anesthesia (e.g., peripheral nerve catheters, epidural medications)
- psychosocial supports, and…
- …if these options fail, adding full agonist opioids.
  - *While conventional short-acting opioids may benefit some people, others might require higher than normal doses and high potency agents such as fentanyl or hydromorphone.*
  - *When the latter approach is used, care should be in a unit with quick access to emergency airway management in the event of overshooting the full agonist dose*[11]

CSAM

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QUESTION#10

A 29-year-old man presents with restlessness, insomnia, muscle aches, and diarrhea that began two days ago. He is anxious, diaphoretic, and tachycardic on exam. He denies any recent use of prescription or illicit substances. He reports that he has been purchasing an herbal supplement online that is advertised to boost energy and improve mood. He stopped using it recently for financial reasons. A standard urine drug screen is negative.

Which of the following is ***false*** about the substance this patient is using?

A. It is a controlled substance in 6 states.
B. It is a full agonist at the mu opioid receptors
C. Use is most prevalent in males 25 – 44 years old
D. It acts on alpha-adrenergic receptors

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Kratom: Mitragynine & 7-hydroxymitragynine

- Kratom is derived from the Southeast Asian plant Mitragyna speciosa. Mitragynine & 7-hydroxymitragynine are clinically relevant, psychoactive alkaloids.
- It has been used as an herbal remedy for centuries in Southeast Asia, including for pain and fatigue in laborers.
- Mitragynine is measured in much higher concentrations than 7-hydroxymitragynine in the plant itself.
- Both alkaloids are *partial mu receptor agonists*, but 7-hydroxymitragynine is much **more potent.** (answer B is *false)*
- Kratom has also been shown to have agonist effects at the adrenergic receptors and interacts with the serotonergic and dopaminergic receptors. (answer D is *true*). It has both sympathomimetic and opioid effects.

Image from: https://www.chhs.colostate.edu/fsi/food-articles/non-produce-plants/kratom/

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Kratom

Several studies have shown kratom use is more prevalent in men, adults between the ages of 25-44, and those with a high school education and some college. (answer C is true)

Regulation:

Currently regulated at the state or local level. Not classified as a controlled substance under the Controlled Substances Act.

Classified as a controlled substance in six states currently: Alabama, Arkansas, Indiana, Rhode Island, Vermont, and Wisconsin. In 18 other states, kratom products are regulated but not classified as controlled substances.

Treatment: No formal guidelines.

- ***Withdrawal symptoms resemble opioid withdrawal***. Supportive care in withdrawal with evidence for buprenorphine treatment.
- There is also limited evidence supporting the use of long-term medications for opioid use disorder, especially in patients with co-use of illicit/non-medical use of opioids and/or a history of opioid use disorder.

Product image: https://drinkjubi.com/products/jubi-trial-pack

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QUESTION#11

A 38-year-old female with active fentanyl use presents for consultation. Despite prior attempts with daily buprenorphine/naloxone, she reports recurring relapses. Which of the following statements about buprenorphine products is correct?

A. Transdermal buprenorphine is FDA-approved for the treatment of opioid use disorder
B. Long-acting injectable formulations of buprenorphine are non-inferior to sublingual formulations and may improve patient satisfaction.
C. Buccal and sublingual buprenorphine have lower bioavailability than transdermal buprenorphine.
D. Intramuscular injection is the standard route for extended-release buprenorphine used in opioid use disorder treatment.

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B. Long-acting injectable formulations of buprenorphine are non-inferior to sublingual formulations and may improve patient satisfaction.

- Injectable buprenorphine is at least non-inferior to daily oral buprenorphine in promoting opioid-native urine drug screens. Patient satisfaction may also be higher with the injectables.
- The choice between injectable buprenorphine products should be guided by patient preference and weighing risks and benefits.
- Sublocade® is capable of maintaining higher peak concentrations than Brixadi® Brixadi® offers more flexible dosing regimens. Both are FDA-approved for the treatment of opioid use disorder.
- Both injectable buprenorphine products are administered subcutaneously (D)

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Properties of buprenorphine products

Generic name (Brand name)	Formulation / Route	FDA-Approved Indication	Comments
Buprenorphine	Sublingual tablet	OUD	Bioavailability ~30%
Buprenorphine/Naloxone (Zubsolv®)	Sublingual tablet, Rapid dissolve	OUD	Higher bioavailability than buprenorphine/naloxone sublingual films and tablets.
Buprenorphine/Naloxone (Suboxone®)	Sublingual film	OUD	Bioavailability ~30–50%
Buprenorphine/Naloxone (Bunavail®)	Buccal film	OUD	Bioavailability ~46–65% (discontinued by manufacturer)
Buprenorphine (Belbuca®)	Buccal film/tablet	Chronic Pain	Bioavailability ~46–65%
Buprenorphine (Butrans®)	Transdermal patch	Chronic Pain	Lowest bioavailability - 15%
Buprenorphine (Sublocade®)	Extended-release SC injection	OUD	Requires REMS program
Buprenorphine (Brixadi®)	Extended-release SC injection	OUD	Requires REMS program

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OPIOIDS: NEED TO KNOW

- Opioid Use Disorder vs. Opioid Dependence
- Treatment guidelines for OUD
- The role of opioids in the management of chronic and acute pain
- The pharmacokinetics & pharmacodynamics of common opioids
- The epidemiological trends in OUD and opioid overdoses
- OUD treatment in special populations
- Principles of preventive medicine as applied to persons with OUD

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ALCOHOL & ALCOHOL USE DISORDER

CSAM Board Exam Prep Track

August 13, 2025

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Contents modified from Past Presentation by Steven Tate MD

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CONFLICT OF INTEREST DISCLOSURE

I, Samantha Ayoub, have nothing to disclose. Off-label use of gabapentin, baclofen, carbamazepine, and divalproex for treatment of alcohol use disorder/withdrawal will be discussed in this presentation.

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EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Summarize assessment tools & diagnostic aides useful in identifying and treating unhealthy alcohol use and alcohol use disorder.

2. Explain the epidemiology, prevention, and illness course of alcohol use disorder.

3. Describe the effects of alcohol on the human body, including intoxication, withdrawal, biomarkers, and long-term health effects.

4. Demonstrate knowledge about effective pharmacological and non-pharmacological treatments for alcohol use disorder and alcohol withdrawal.

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QUESTION #1

A 36-year-old woman came in for her annual physical. She works full-time as a software designer and reports stopping after work for a glass of wine with a group of friends just about every night. On weekends, she goes out to clubs to dance and drink, and she may have up to 4-5 drinks/night. She denied any negative consequences from alcohol use. Her father quit drinking when she was a teenager and continues to attend Alcoholics Anonymous meetings.
You recommend that she:

a) Abstain from alcohol and start naltrexone

b) Not increase her alcohol use any further

c) Limit her drinking to 3 drinks/day and 7 drinks/week

d) Limit her drinking to 4 drinks/day and 14 drinks/week

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d) Limit her drinking to 4 drinks/day and 14 drinks/week

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QUESTION #1

Answer: c) Limit drinking to 3 drinks/day and 7 drinks/week

National Institute on Alcohol Abuse and Alcoholism (NIAAA) **defines <u>at-risk drinking</u>**, as occurring above the following limits:

	Maximum drinks/day	Maximum drinks/week
Women	3	7
Men	4	14

The Substance Abuse and Mental Health Services Administration defines heavy alcohol use as **<u>binge drinking</u> (women ≥4 and Men ≥5 drinks within 2 hours) on at least one day in the past 30 days**. This pattern of use usually results in BAC of 0.08 g/dL or higher.

Other recommendations, including the U.S. Department of Health and Human Services and the U.S. Department Agriculture, Dietary Guidelines for Americans 2020-2025, have more stringent recommendations (same weekly cap but no more than 2 drinks/day for men & no more than 1 drink/day for women).

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QUESTION #2

Which of the following is most accurate regarding sex-based differences in alcohol use disorder?

A. Women tend to have higher first-pass metabolism of alcohol than men due to increased gastric alcohol dehydrogenase activity.

B. Men have higher rates of alcohol use disorder, and the gap between men and women has been increasing in the United States.

C. Women, on average, have a lower volume of distribution for alcohol than men.

D. Women tend to have fewer medical consequences due to heavy alcohol use and after longer periods of drinking.

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D. Women tend to have fewer medical consequences due to heavy alcohol use and after longer periods of drinking.

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QUESTION #2

Answer: c) Women on average have a lower volume of distribution for alcohol than men.

TRUE: Women on average **have a lower volume of distribution**. On average, they weigh less. Women also on average have higher body fat percentage and lower lean body mass percentage than men.

Alcohol is water-soluble, not fat-soluble, and can only distribute to lean body mass. When there is less lean body mass, the bodily compartment over which alcohol is distributed shrinks, which causes the concentration of anything dissolved in that compartment to increase.

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QUESTION #2

a. FALSE: First-pass metabolism of alcohol is lower in women than in men, in part due to *lower* gastric alcohol dehydrogenase activity. This is generally true in large studies and may contribute to differences in blood alcohol concentration and medical consequences observed between men and women.

b. FALSE: Although men have higher rates of alcohol use disorder, the gap between men and women has been decreasing in the United States in recent decades. According to one study that analyzed data from the National Epidemiologic Survey on Alcohol and Related Conditions between 2001-2002 and 2012-2013, the prevalence of high-risk drinking and AUD increased by 57.9% and 83.7% among women, compared to 15.5% and 34.7% among men in the United States.

d. FALSE: Studies overall support that women, likely due to psychosocial and biological factors, have accelerated medical consequences due to drinking alcohol. This phenomenon is referred to as a telescoped course.

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QUESTION #3

Which of the following public health interventions has the most robust evidence for reducing excessive alcohol use and its associated harms?

a) Increased prices/taxes for alcohol purchase

b) Privatization of alcohol sales

c) Project D.A.R.E. (Drug Abuse Resistance Education)

d) School programs promoting resilience among students

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d) School programs promoting resilience among students

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QUESTION #3

Answer: a. Increased prices/taxes for alcohol purchase

- Meta-analyses across multiple studies in many different locations have demonstrated that **increasing alcohol prices and/or taxation reduces overall alcohol use**, heavy alcohol use, alcohol-related motor vehicle collisions, and both all-cause and liver-related mortality.
- Preventive interventions targeting children and adolescents in school have been studied. One of the most well-known was **Project D.A.R.E.**, which centered around uniformed police officers educating elementary school children about how to resist peer pressure to use alcohol/drugs. Despite substantial financial investment and widespread implementation, it **failed to demonstrate benefits** for substance use outcomes.

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QUESTION #3

Answer: a) Increased prices/taxes for alcohol purchase

- A somewhat more successful approach to school-based interventions to prevent substance use has involved programs to **build emotional resilience among the students**. A recent meta-analysis showed **these can reduce drug use** but they did not clearly reduce alcohol or tobacco use.
- **Privatization of alcohol sales** leads to an increase in alcohol sales outlet density, which **is associated with increased alcohol use/alcohol-related harms.**
- Other interventions that may reduce alcohol use/harm include reduction in sales outlet density, enhanced enforcement prohibiting sales to minors, and holding businesses liable for failing to limit the inappropriate sale or service of alcohol.

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QUESTION #4

A 45-year-old man presents to the emergency department with mild confusion, slurred speech, and an unsteady gait. He attended a party last night and reports that his last alcoholic drink was approximately 3 hours ago. He denies other substance use and has no known history of alcohol use disorder. His vital signs are stable. His blood alcohol concentration (BAC) is measured at 0.157 g/dL.

Which of the following statements is ***most*** accurate?

A. He most likely consumed 2 standard drinks, assuming typical alcohol metabolism.
B. Alcohol is primarily eliminated by first-order kinetics at common intoxication levels.
C. In an average man without tolerance, each standard drink typically raises BAC by approximately 0.02 g/dL.
D. A BAC of 0.157 g/dL is unlikely to cause clinically significant impairment in most individuals.

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QUESTION #4

A 45-year-old man presents to the emergency department with mild confusion, slurred speech, and an unsteady gait. He attended a party last night and reports that his last alcoholic drink was approximately 3 hours ago. He denies other substance use and has no known history of alcohol use disorder. His vital signs are stable. His blood alcohol concentration (BAC) is measured at 0.157 g/dL.

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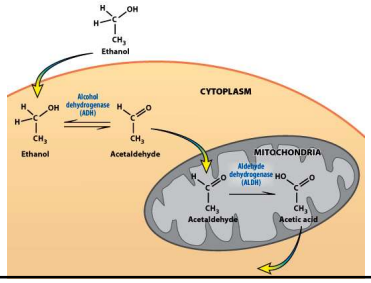
QUESTION #4

Basics of Alcohol Metabolism:

- Estimated elimination rate of alcohol 15mg/dL to 20mg/dL per hour (0.015g/dL to 0.02g/dL per hour) in non-tolerant individuals.
- How are generalized elimination estimates possible?
  - Alcohol dehydrogenase (ADH) is saturated at relatively low blood ethanol concentrations.
  - ADH acts by primarily zero-order kinetics at clinically relevant levels.
- There are variations in elimination rates based on individual factors, genetics, age, medical co-morbidities, and tolerance.
- In people who develop tolerance to alcohol, the elimination rate may be *higher.*



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QUESTION #4

- A standard drink in the United States is 0.6 fluid ounces or 14 grams of pure alcohol.

- In general, even at the same weight, BAC increases more per drink for women compared to men.
- The current legal BAC limit for drivers is 0.08 g/dL (80 mg/dL). Based on studies of impairment at lower BAC's, the National Transportation Safety Board recommended states lower the BAC limit to 0.050 g/dL in 2013.

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QUESTION #4

Clinical signs of impairment and blood alcohol concentration (BAC)

- mg% = mg/dL

Blood Alcohol Level[a] (MG%)	Clinical Manifestations
20-99	Loss of muscular coordination Changes in mood, personality, and behavior
100-199	Neurologic impairment with prolonged reaction time, ataxia, incoordination, and mental impairment
200-299	Very obvious intoxication, except in those with marked tolerance Nausea, vomiting, marked ataxia
300-399	Hypothermia, severe dysarthria, amnesia, stage I anesthesia
400-799	Onset of alcoholic coma, with precise level depending on the degree of tolerance Progressive obtundation, decreases in respiration, blood pressure, and body temperature (hypothermia) Urinary incontinence or retention, reflexes markedly decreased or absent
600-800	Often fatal because of loss of airway-protective reflexes from airway obstruction by the flaccid tongue, from pulmonary aspiration of gastric contents, or from respiratory arrest from profound central nervous system obstruction

[a]Levels of 200-300 mg%, particularly when reached quickly ("chugging"), may result in coma, aspiration, and death in nontolerant individuals, particularly adolescents and young adults. In addition, presence of other depressant drugs, even in therapeutic doses (benzodiazepines, sedative-hypnotics, opioids), may result in respiratory depression, coma, and death at lower levels of alcohol.

Table from:
Wartenberg, A. A. (2018). Clinical effects of alcohol. In S. C. Miller, R. K. Ries, D. A. Fiellin, & R. Saitz (Eds.), *The ASAM principles of addiction medicine* (6th ed,). Wolters Kluwer.

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QUESTION #5

A 63-year-old man is drinking a fifth of liquor daily. His doctor advised him that his drinking was making it difficult to control his blood pressure, diabetes mellitus and acid reflux, as well as putting him at risk for many more adverse health consequences. He presents stating that he cannot imagine stopping alcohol altogether but is open to reducing his alcohol use. He requests a medication to help. Recent lab values are below. **What medication would have the best combination of safety & effectiveness in this case?**

a) Acamprosate
b) Disulfiram
c) Gabapentin
d) Naltrexone

Total Bilirubin	1.4 mg/dL	normal 0.3-1.2 mg/dL
Aspartate aminotransferase	100 U/L	normal < 45 U/L
Alanine aminotransferase	59 U/L	normal < 35 U/L
Estimated glomerular filtration	30 mL/min	normal 60-111 mL/min

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QUESTION #5

Answer: d) Naltrexone

Disulfiram would not be appropriate for someone looking merely to reduce alcohol use. (answer choice B)

Of the remaining medications, **naltrexone has the best evidence for harm reduction outcomes among someone who plans to still consume alcohol**.

Weighing risks and benefits:

- Acamprosate or gabapentin (renally cleared meds) in the setting of moderate to severe renal impairment, as indicated by glomerular filtration rate. The patient also has the top two risk factors for chronic kidney disease: hypertension & diabetes mellitus. (answer choices A and C)
- Naltrexone in the setting of mild liver enzyme elevations ***without evidence*** of severe, decompensated liver disease. (choice D)
- More on these medications in the next question.

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QUESTION #6

A 63-year-old man with unstable diabetes mellitus and severe coronary artery disease recently completed inpatient treatment for alcohol withdrawal and is abstinent now for 7 days. He presents requesting a medication that might help him abstain from alcohol. His lab results are below. You notice on physical exam some spider angiomas and lower extremity edema. Given the below test results, **What medication would have the best combination of safety & effectiveness in this case?**

a) Acamprosate
b) Disulfiram
c) Gabapentin
d) Naltrexone

Albumin	2.8 g/dL	normal 3.5-5.4 g/dL
Total Bilirubin	4.9 mg/dL	normal 0.3-1.2 mg/dL
INR	2.5	normal 0.8-1.2
Estimated GFR	78 mL/min	normal 60-111 mL/min

CSAM

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QUESTION #6

Answer: a) Acamprosate

The patient in this case has some relative contraindications to use of naltrexone & disulfiram. **Naltrexone relative contraindications** include:

- **Severe liver disease** (e.g. liver enzymes >3-5x ULN, clinical signs of decompensated cirrhosis or significant bilirubin or INR elevation). *This patient's physical exam findings are consistent with cirrhosis, along with markedly elevated INR & bilirubin.*
- Pregnancy
- Taking opioids or imminently will need opioids (absolute contraindication)

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QUESTION #6

Answer: a) Acamprosate

Both **gabapentin** and **acamprosate can be safely used in severe liver disease, as they both are cleared renally. However, there is more evidence supporting efficacy for acamprosate in AUD, especially for abstinence outcomes**. Acamprosate is more effective if, as in this case, the person is already abstinent. Gabapentin has several positive trials for AUD and alcohol withdrawal, though the largest randomized control trial (RCT) for AUD failed to demonstrate efficacy.

The medication with the most RCTs for AUD in alcohol-related liver disease is actually baclofen, but there are safety concerns and the results have also been mixed. *Neither gabapentin nor baclofen is FDA-approved for the treatment of alcohol use disorder.*

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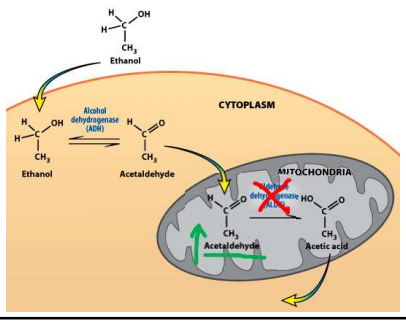
The final FDA-approved medication for AUD

Disulfiram: Inhibits the enzyme aldehyde dehydrogenase

Disulfiram relative contraindications include:

- **Unstable medical illness** (e.g., cardiovascular disease, diabetes mellitus)
- Pregnancy
- Taking paraldehyde, metronidazole, or any alcohol containing product
- Treatment goal is not abstinence from alcohol
- Psychosis



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QUESTION #7

Parker is a 35-year-old patient with moderate alcohol use disorder. You discuss treatment options with them including pharmacologic support, cognitive behavioral therapy, and 12-step based mutual support. Parker is most interested in 12-step based mutual support and contemplative about medications and other psychosocial support. Which of the following is true about 12-step based programs:

a) 12-step programs are only effective if attended in conjunction with manualized professionally led 12-step facilitation (TSF)

b) Pharmacotherapy alone is more effective 12-step programs

c) 12-step programs do not allow patients on medications so Parker must select one or the other

d) 12-step programs are as effective as cognitive behavioral therapy and other forms of treatment

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QUESTION #7

Answer D) 12-step programs are as effective as cognitive behavioral therapy and other forms of treatment

- For answer choice a) 12 step facilitation (TSF) may be ***more*** effective than 12 step programs alone, but 12 step programs alone are still effective.

- Pharmacology for alcohol use disorder has not been shown to be more effective than 12 step programs and 12 step programs do not restrict the use of prescribed medications though this is a common misconception (see: https://www.aa.org/aa-member-medications-and-other-drugs)

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Manualized 12-step facilitation (TSF) more effective than other psychosocial interventions.

Alcoholics Anonymous and other 12-step programs for alcohol use disorder (Review)

Summary of findings 1. Alcoholics Anonymous (AA)/Twelve-Step Facilitation (TSF) (manualized) compared to other clinical interventions for alcohol use disorder (1A)

Alcoholics Anonymous (AA)/Twelve-Step Facilitation (TSF) (manualized) compared to other clinical interventions for alcohol use disorder (RCT/quasi-RCT evidence)

Patient or population: adults (> 18 years) with alcohol use disorder, alcohol abuse, or alcohol dependence
Setting: outpatient treatment
Intervention: AA/TSF (manualized)
Comparison: other clinical interventions (e.g. CBT)

Outcomes		Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
		Risk with other clinical interventions	Risk with AA/TSF				
Abstinence	Proportion of participants (%) completely abstinent Follow-up: 12 months	Study population 345 per 1000	418 per 1000 (356 to 490)	RR 1.21 (1.03 to 1.42)	1936 (2 RCTs)	⊕⊕⊕⊕ High	

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Non-manualized 12-step facilitation as effective as other psychosocial interventions.

Alcoholics Anonymous and other 12-step programs for alcohol use disorder (Review)

Summary of findings 2. Alcoholics Anonymous (AA)/Twelve-Step Facilitation (TSF) (non-manualized) compared to other clinical interventions for alcohol use disorder (1B)

Alcoholics Anonymous (AA)/Twelve-Step Facilitation (TSF) (non-manualized) compared to other clinical interventions for alcohol use disorder (RCT/quasi-RCT evidence)

Patient or population: adults (> 18 years) with alcohol use disorder, alcohol abuse, or alcohol dependence
Setting: outpatient treatment; inpatient/residential facility
Intervention: AA/TSF (non-manualized)
Comparison: other clinical interventions (e.g. CBT)

Outcomes		Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
		Risk with other clinical interventions	Risk with AA/TSF				
Abstinence	Proportion of participants (%) completely abstinent Follow-up: 9 months	Study population 167 per 1000	118 more per 1000 (50 fewer to 530 more)	RR 1.71 (0.70 to 4.18)	93 (1 RCT)	⊕⊕⊖⊖ Low[a]	No data available for 12-month follow-up

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QUESTION #8

You are designing an intake questionnaire for a primary care clinic. You want to screen for problematic alcohol use. **If you were to include only one question, what should you use?**

a) Are you able to stop drinking if you want to?

b) Have you ever felt guilty about drinking?

c) How many drinks containing alcohol did you have on a typical day when you were drinking last year?

d) How many times in the past year have you had more than four drinks (for women) or five drinks (for men) in a day?

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QUESTION #8

You are designing an intake questionnaire for a primary care clinic. You want to screen for problematic alcohol use. **If you were to include only one question, what would you use?**

a) Are you able to stop drinking if you want to? MAST

b) Have you ever felt guilty about drinking? CAGE

c) How many drinks containing alcohol did you have on a typical day when you were drinking last year? AUDIT-C

d) How many times in the past year have you had more than four drinks (for women) or five drinks (for men) in a day? Single Alcohol Screening Question (SASQ)

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QUESTION #8

Answer: d) How many times in the past year have you had more than four drinks (for women) or five drinks (for men) in a day?

The most commonly used brief screening tools to assess for possible unhealthy alcohol use are the **AUDIT-C** (Alcohol Use Disorder Identification Test, the first 3 questions) and **CAGE** (cut back, annoyed, guilty, eye opener). **AUDIT-C is more sensitive than CAGE in detecting at-risk alcohol** use that is not yet an alcohol use disorder. (answer B and C)

A **SINGLE ALCOHOL SCREENING QUESTION** has been developed with a modified version of question 3 from the AUDIT-C, which incorporates a sex-specific definition of binge drinking and the NIAAA-recommended limit of drinks/day for lower-risk alcohol use. Any response other than 0 is considered a positive screen. (answer D)

The Michigan Alcohol Screening Test (MAST) and CAGE are more specific for alcohol use disorder than the AUDIT-C or single-item screening question. (answer a)

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QUESTION #8

Test		Sensitivity (Hazardous drinking)	Specificity (Hazardous drinking)	Sensitivity (AUD)	Specificity (AUD)
AUDIT-C	men	0.86	0.72	0.79	0.56
	women	0.66	0.94	0.80	0.87
CAGE ≥1 HD ≥2 AUD	all	0.47	0.87	0.71	0.90
	Primary care	0.49	0.75	0.85	0.78
Brief-MAST* ≥6 HD ≥13 AUD		0.35	0.97	0.50	0.98
Single Item		0.84	0.78	0.88	0.67

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QUESTION #9

Which of the following statements about Screening and Brief Intervention (SBI) is correct?

a) SBI for alcohol use in primary care is recommended with an evidence grade of B by the US Preventive Services Task Force

b) SBI is more effective for alcohol use disorder than for risky alcohol use.

c) SBI is more effective for reducing opioid use than for reducing alcohol use.

d) The setting with the most robust evidence supporting the efficacy of SBI for alcohol use disorder is the emergency department

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QUESTION #9

Which of the following statements about Screening and Brief Intervention (SBI) is correct?

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c) SBI is more effective for reducing opioid use than for reducing alcohol use.

d) The setting with the most robust evidence supporting the efficacy of SBI for alcohol use disorder is the emergency department

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QUESTION #9

Answer: a) SBI for alcohol use in primary care is recommended with an evidence grade of B by the US Preventive Services Task Force (USPSTF)

- **Decades of research on SBI for alcohol use in primary care settings support the above statement/grading.** More specifically, the recommendation to conduct SBI for alcohol use in primary care is for those with **risky or hazardous alcohol use**. The efficacy for those with alcohol use disorder is not as well established. Also, the **recommendation is specific to adults aged 18 or older**—the evidence was deemed insufficient in adolescents (grade I).
- While one review found some small short-term benefits of SBI for alcohol use in the **ED**, overall, the **evidence is less consistent than in primary care**.
- There is **insufficient evidence to recommend routine use of SBI** for drug use, including opioids, per USPSTF guidelines.

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QUESTION #10

Which of the following correctly describes hazardous, harmful, and unhealthy alcohol use as defined by the American Society of Addiction Medicine (ASAM)?

a) Harmful alcohol use is synonymous with at-risk alcohol use.
b) Harmful and hazardous alcohol use are both forms of unhealthy alcohol use
c) Hazardous alcohol use is a subtype of harmful alcohol use.
d) Unhealthy alcohol use implies that an individual has experienced direct harm to their health as a result of alcohol use.

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QUESTION #10

Category of alcohol use	Subcategory	Organization responsible	Definition
Lower risk use		**ASAM**	**Consumption below amount identified as hazardous and in situations not defined as hazardous**
Risky/at-risk use		**NIAAA**	**Consumption above the daily/per occasion & weekly amounts that does not meet criteria for AUD**
Unhealthy use	Hazardous	**ASAM**	**Use that increases risk for adverse health consequences but no such consequences yet**
	Hazardous	WHO	A pattern of alcohol use that appreciably increases the risk of harmful physical or mental health consequences to the user or to others to an extent that warrants attention and advice from health professionals. (Not a distinct disorder in ICD-11)
	Harmful	**ASAM**	**Use adversely affecting health in the absence of addiction**
	Harmful	WHO	A pattern of alcohol use that has caused damage to a person's physical or mental health or contributed to behavior leading to harm to the health of others. (ICD-11 code)
Dependence		WHO	A disorder of regulation of alcohol use arising from repeated or continuous use, characterized by a strong internal drive to use alcohol, and may include tolerance and withdrawal. (ICD-11 code)
AUD		**DSM-5**	**Diagnosis requires 2 or more of 11 criteria met within a 12-month period, causing clinically significant distress or impairment. AUD is characterized as a spectrum disorder from mild to severe and combines what were previously separate diagnoses of abuse and dependence (per DSM-IV).**

WHO = World Health Organization; DSM-5= The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

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QUESTION #11

A patient is 4 days post-operative from a total hip arthroplasty and starts to exhibit fever, tachycardia, waxing and waning confusion, visual hallucinations, and diaphoresis. **Without knowing additional details, which of the following are the most appropriate next steps in managing this case?**

a) Administer IV diazepam & thiamine, obtain blood cultures
b) Administer IV phenobarbital & folic acid, correct electrolyte derangements
c) Administer oral gabapentin, IV folic acid, and IV haloperidol
d) Administer oral oxazepam, IV thiamine, and place physical restraints

610

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QUESTION #11

Answer: a) Administer IV diazepam & thiamine, obtain blood cultures

- **Benzodiazepines are first-line treatment** for severe alcohol withdrawal.
- Among benzodiazepines, **long-acting agents with active metabolites (e.g. diazepam or chlordiazepoxide) are preferred,** as they have a smoother coverage of symptoms, except in severe liver disease or older adults (lorazepam and oxazepam are preferable). For severe withdrawal, **rapid onset is critical, so intravenous administration is often ideal.**
- **Anticonvulsants** (e.g., gabapentin, divalproex, carbamazepine) may be helpful **adjuncts** to benzodiazepines or effectively treat/prevent mild alcohol withdrawal. **For refractory severe withdrawal, phenobarbital, propofol, or dexmedetomidine may be considered** (usually in an ICU because mechanical ventilation is often needed on these meds). Of these, phenobarbital has the strongest evidence.

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QUESTION #11

Answer: a) Administer IV diazepam & thiamine, obtain blood cultures

- **Antipsychotics have limited benefit** in alcohol withdrawal. They may **lower seizure threshold, prolong QTc intervals, and impair thermoregulation**.
- **Thiamine is the priority to replenish. This is necessary so that glucose in IVF can be administered without risk of precipitating Wernicke-Korsakoff syndrome**. Electrolyte imbalances should be assessed and corrected as needed. Folic acid is not as urgent as thiamine replacement.
- Especially when one is not anticipating alcohol withdrawal (e.g., use was potentially under-reported pre-admission), **it is important to consider other causes**. In a patient presenting with fever, tachycardia, confusion, and hallucinations, infections should be ruled out, including obtaining blood cultures.

CSAM

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QUESTION #12

Jordan is a 46-year-old patient with liver failure who you are asked to see on day 4 of his hospitalization. He is being evaluated for liver transplantation. Two months prior, he was diagnosed with alcohol use disorder during a hospitalization for alcohol-associated hepatitis. Since then, he reports abstinence and regular engagement in mutual support. The primary team wants to know if there is a laboratory test that they can order to further support his history of sobriety in the weeks before admission. You recommend:

a) Phosphatidylethanol (PEth)

b) Serum Ethanol level

c) Urine Ethyl glucuronide

d) Gamma-glutamyl transferase (GGT)

CSAM

614

QUESTION #12

Jordan is a 46-year-old patient with liver failure who you are asked to see on day 4 of his hospitalization. He is being evaluated for liver transplantation. Two months prior, he was diagnosed with alcohol use disorder during a hospitalization for alcohol-associated hepatitis. Since then, he reports abstinence and regular engagement in mutual support. The primary team wants to know if there is a laboratory test that they can order to further support his history of sobriety in the weeks before admission. You recommend:

a) Phosphatidylethanol (PEth)

b) Serum Ethanol level

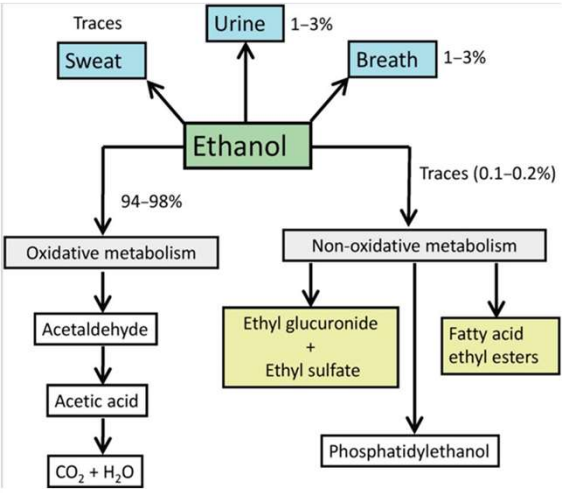
c) Urine Ethyl glucuronide

d) Gamma-glutamyl transferase (GGT)

615

QUESTION #12

Answer: a) Phosphatidylethanol (PEth)



PEth is phospholipid in red blood cell membranes produced in the presence of ethanol. It can identify heavy alcohol use in the prior 2-3 weeks.

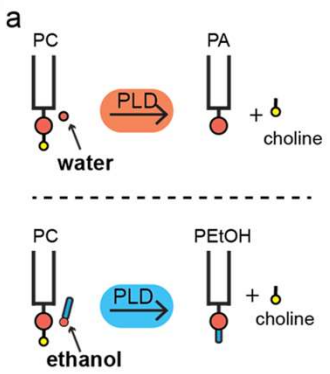
ETG is a **direct** metabolite of ethanol, detectable in urine 1-5 days after ingestion.

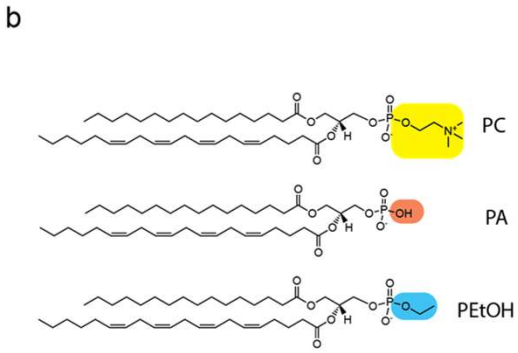
GGT is an **indirect** marker of alcohol use that can be elevated for 2-4 weeks after regular drinking. Non-specific and likely elevated in patients with liver injury, such as this patient.

616

QUESTION #12

Phosphatidyl Ethanol (PEth)





Incorporated into the Red Blood Cell Membrane

Detectable for 2-4 weeks after alcohol consumption

Can be detectable much longer in chronic or heavy drinkers

617

QUESTION #13

A 58-year-old man presents for persistent memory problems. He was hospitalized two months ago for acute confusion, unsteady gait, and abnormal eye movements, which were attributed to a nutritional deficiency. He received treatment and was discharged, but his memory problems have persisted. His daughter reports that he frequently repeats the same questions. On interview, he discusses details about his job as a lawyer, when his daughter confirms he has never been a lawyer. The patient has a 25-year history of heavy alcohol use and has not consumed alcohol since his hospitalization.
On examination, the patient is alert and pleasant. Neurologic exam is notable for mild ataxia.
Which of the following best describes the expected course of this patient's current condition?

A. Persistent anterograde amnesia that is likely irreversible

B. Progressive gait instability and proprioceptive loss

C. Full recovery of memory function with continued abstinence from alcohol

D. Fluctuating levels of consciousness and cognition related to ammonia crossing the blood-brain barrier

618

QUESTION #13

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619

QUESTION #13

Wernicke encephalopathy (WE) is an acute syndrome → unrecognized, undertreated WE → Korsakoff syndrome

Treatment of suspected WE → thiamine (BEFORE glucose to prevent exacerbated thiamine deficiency)

Triad of clinical symptoms:

Altered mental status/ Confusion  +  Ataxia + Ocular abnormalities 

Cleveland Clinic (2023)

An estimated one-third or fewer of patients with WE present with all three hallmark symptoms.

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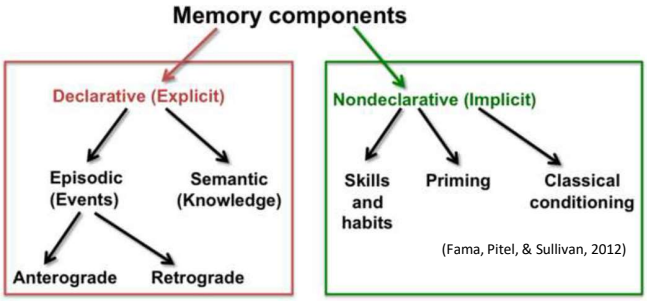
QUESTION #13

Korsakoff Syndrome (KS):

Persistent *anterograde amnesia* is a defining feature.

Retrograde amnesia often with a temporal gradient effect (childhood memories retained).

Confabulations – false memories or statements without the intention to deceive.



Lost memory components in KS = Red
Maintained memory in KS = Green

- Damage to the mamillary bodies, thalamus, hypothalamus, and fornix in KS
- KS, particularly the anterograde amnesia, is usually irreversible despite thiamine treatment and cessation of alcohol use (option C)

621

QUESTION #13

B. This is subacute combined degeneration, caused by vitamin B12 deficiency that affects the dorsal columns and corticospinal tract of the spinal cord. It is more often associated with ***chronic nitrous oxide exposure***, which functionally inactivates B12. It is not typically associated with chronic alcohol use.
Clinically, subacute combined degeneration presents primarily with motor and sensory symptoms, whereas this patient's symptoms are mainly cognitive and memory-related.

D. This is hepatic encephalopathy, which results primarily from ammonia accumulation in the setting of advanced liver disease. Ammonia and other toxins cause astrocyte swelling, oxidative stress, and altered neurotransmission, leading to global cognitive dysfunction and waxing and waning mental status. In contrast, this patient is consistently alert and demonstrates specific and persistent memory deficits with confabulation, which are hallmark features of Korsakoff syndrome.

622

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ALCOHOL: NEED TO KNOW

- Epidemiology of alcohol use & alcohol use disorder
- Prevention, including USPSTF Screening Recommendations & SBIRT
- Differentiate between unhealthy drinking, mild/moderate/severe AUD
- Neurobiology/pharmacology of intoxication, chronic use, and withdrawal
- Laboratory evaluation related to AUD
- Pharmacokinetics & pharmacodynamics of alcohol ingestion
- Evidence-based treatments, pharmacological & otherwise, for intoxication, withdrawal, & AUD
- Medical sequelae of unhealthy alcohol use

CSAM

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Psychosocial Screening Tools & Interventions

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California Society of Addiction Medicine Annual Meeting
Addiction Medicine Board Exam Preparation Workshop
Garden Grove, CA
August 13, 2025
Updated from past content by Lakai Banks-Dean, MD

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DISCLOSURES

I, Natassia Gaznick, have nothing to disclose.

I will not be discussing “off label” use of drugs or devices during this presentation.

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LEARNING OBJECTIVES

1. Determine a patient's readiness for change according to the Transtheoretical Model
2. Utilize appropriate screening and assessment tools
3. Identify the ASAM Criteria Continuum of Care
4. Identify and utilize appropriate psychosocial treatments when treating patients with substance use disorders
5. Describe mutual help groups and how to support a patient's use of them

CSAM

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1. A 24-year-old female patient presents to the clinic informing you that she received a DWI/DUI two weeks ago (her third in 2 years) and admits alcohol use is negatively impacting her life. She wants to know what treatment is available to help her stop drinking and mentions she plans on attending an AA meeting with a friend next week. Regarding her alcohol use, she is at which stage in the Stages of Change model?

A. Preparation
B. Action
C. Contemplation
D. Pre-contemplation

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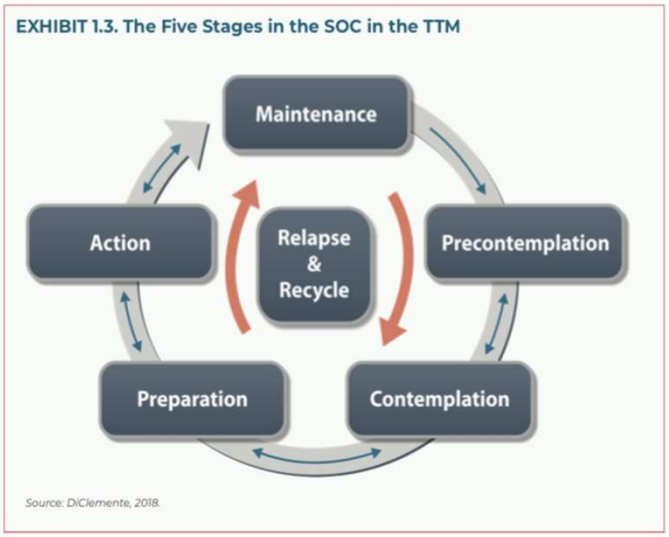
Answer: A. Preparation

Preparation – intends to take action in the immediate future (usually defined as **under 1 month**); generally has plan of action
- She **plans on attending an AA meeting with a friend next week**



Miller et al. (Eds), 2024

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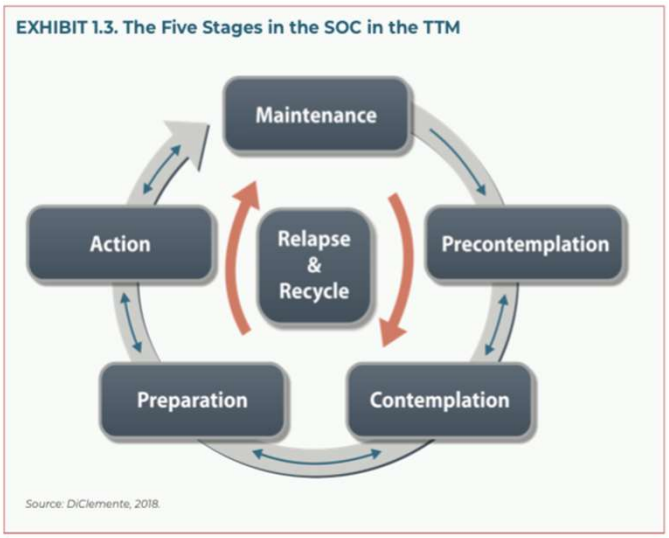
Stages of Change

Pre-contemplation – no intention to take action in the foreseeable future **(6 months)**

Contemplation – aware that a problem exists/seriously thinking about overcoming it but have not yet made a commitment to take action

Preparation *(see last slide)*



Miller et al. (Eds), 2024

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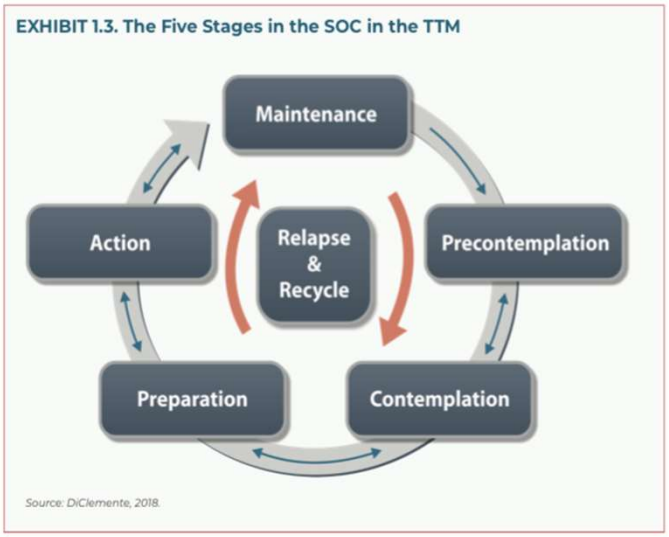
Stages of Change

Action – make specific, overt modifications in lifestyle (within **preceding 6 months**)

Maintenance – working to prevent return to use (without need to apply change processes as frequently); consolidate progress they have made



Miller et al. (Eds), 2024

633

2. **Ms. Jones is a 29-year-old primigravid presenting to the office for an initial prenatal visit. She has no chronic medical conditions and only takes a prenatal vitamin. Social history is significant for cannabis smoking socially (once every 2-3 months) when she was 25 to 27 and denies any use for the past 2 years. You order routine prenatal labs and ultrasonography for dating.**
After Ms. Jones leaves the office, your medical assistant asks if you want to send her urine to the lab to screen for substance use. You tell her no because you already used a screening tool to assess for alcohol and substance use.

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2. **Which of the following screening tools is a 5-item questionnaire used to assess alcohol and substance use during pregnancy?**

A. AUDIT-C
B. TWEAK
C. 4P's Plus
D. DAST 10

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Answer: C. 4P's Plus

4P's Plus is a 5-item questionnaire that screens for tobacco, alcohol, heroin, cocaine, and methamphetamine. Asks about use of substances and alcohol in **P**arents, **P**artners, in the patient's **P**ast and during **P**regnancy

Bertholet N, et al, 2019; Fiellin DA, et al, 2000; Maisto SA, et al, 2003

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Other Screening Tools

AUDIT (Alcohol Use Disorders Identification Test) is the most widely validated instrument to assess for **unhealthy alcohol use**, has 10 items, and takes two to three minutes to complete. It is scored from 0-40.

TWEAK is derived from CAGE questionnaire and stands for Tolerance, Worried, Eye opener, Amnesia, and K (cut down). It is used to assess **alcohol use in pregnancy** but **not tobacco or other substances**.

DAST-10 (Drug Abuse Screening Test-10) takes approximately 5 minutes to administer and may be given in either a self-report or interview format and may be used in a variety of settings to provide a quick index of **drug use problems**, but **not alcohol or tobacco.**

Bertholet N, et al, 2019; Fiellin DA, et al, 2000; Maisto SA, et al, 2003

CSAM

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3. **Many national organizations recommend screening and brief intervention for tobacco, alcohol, and drugs in adolescents. However, according to the United States Preventive Services Task Force (USPSTF), evidence is sufficient to recommend brief interventions only for which of the following in adolescents:**

A. Prevention of tobacco use.

B. Cessation of tobacco use.

C. Prevention of alcohol use.

D. Cessation of alcohol use.

CSAM

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Answer: A. Prevention of tobacco use.

According to the 2018 alcohol recommendations and the 2020 tobacco recommendations, only **behavioral interventions for the prevention of tobacco** use received a grade. **Others (tobacco cessation, alcohol use, and unhealthy drug use) received an insufficiency (I) statement.**

As of June 2025, updates are in progress.

*Remember, a statement of insufficiency (I) does not equate to there being no evidence. It means that evidence is insufficient to assess the balance of benefits and harms. The clinician should read the clinical considerations portion of the statement to explain the uncertainty about the balance of benefits and harms.

Curry et. Al, 2018; Owens et al., 2020; Selph et al, 2020

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4. **A 56-year-old male with severely uncontrolled type 2 diabetes mellitus (T2DM) and hypertension (HTN) is undergoing treatment for alcohol and opioid use. He is receiving as-needed lorazepam, gabapentin, acetaminophen, and ibuprofen, which are administered following nursing evaluations every 4 hours. His vital signs are continuously monitored. He is prescribed a diabetic diet and insulin is administered by nursing staff. He attends daily virtual AA meetings. He is evaluated by a physician each day to monitor his symptoms.**

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4. Which best describes the level of care he is receiving according to the ASAM Criteria Continuum of Care (4th edition)?

A. Level 1 Outpatient
B. Level 2 Intensive Outpatient
C. Level 3 Residential
D. Level 4 Medically Managed Inpatient

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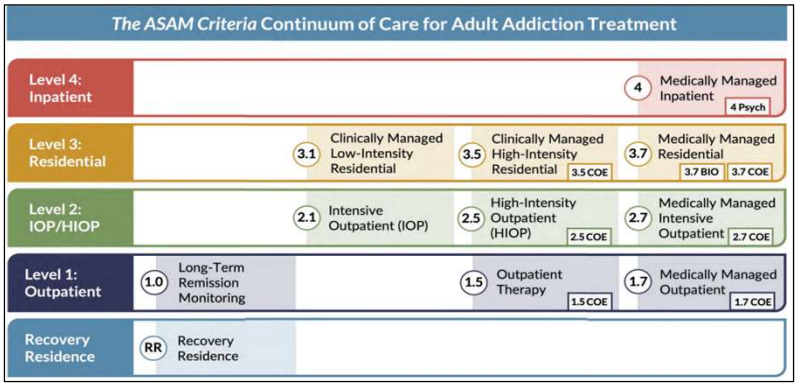
Answer: D. Level 4 Medically Managed Inpatient

Level 4: Medically Managed Inpatient – The highest level of treatment is recommended when physical health is in danger. Attention is aimed towards safety and medical stabilization. It includes medication-assisted treatment and medical detoxification with **daily physician interaction.**



Waller et al, 2023

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4th Edition Continuum of Care

Level 1: Outpatient Treatment – An appropriate first step for people who need addiction treatment but can't miss out on obligations like work or school and are **healthy enough to be unsupervised** throughout the day, or those who are further along in their abstinence.

Outpatient treatment consists of appointments with a medical professional and having access to various therapies or clinical services/medications.

Waller et al, 2023

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4th Edition Continuum of Care

Level 2: Intensive Outpatient/ High-Intensity Outpatient - For patients who **need more frequent outpatient appointments** but still need to attend school, work or other obligations. These programs are beneficial for people with **more complex substance use disorders**, i.e., a high severity of addiction or the presence of co-occurring disorders that require more attention and supervision.

"High-Intensity Outpatient" is analogous to partial hospitalization programs (PHPs). The terminology has changed as most PHPs are not in hospitals.

Waller et al, 2023

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4th Edition Continuum of Care

Level 3: Residential- For patients who will benefit most from having **access to medical staff/mental health professionals** while they **reside at the treatment facility**.
Treatment centers can provide various versions of residential treatment to accommodate multiple types of patients and ensure they have the right resources to provide the best care.

Waller et al, 2023

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Updated Continuum

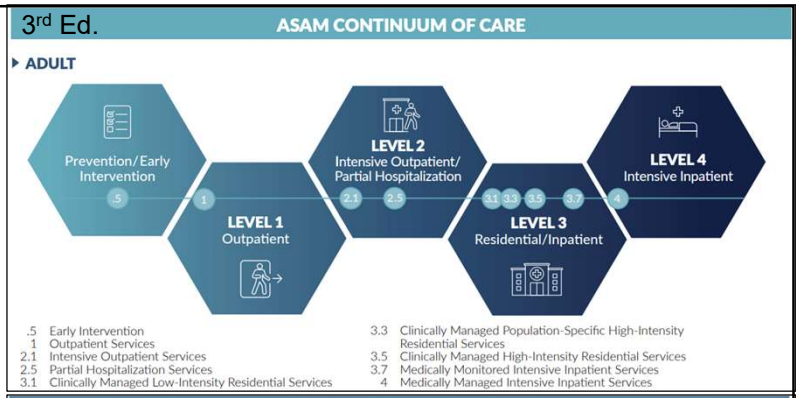
4 broad tx levels with further gradation

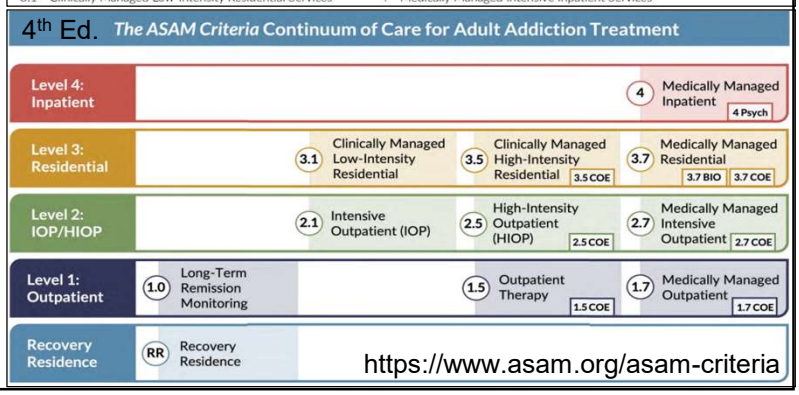
- Medically managed
- Enhanced biomedical (BIO)
- Co-occurring enhanced (COE)

Remission monitoring

Recovery residence

Mee-Lee et al., 2013; Waller et al, 2023





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5. **A 61-year-old male, KH, presents to your clinic with epigastric abdominal pain. After acknowledging his alcohol use has increased, with his permission you share some information about how alcohol use can lead to gastritis/gastric ulcers. He isn't sure what to do about his use. You inquire about his previous experiences cutting back on alcohol use. He tells you that he was able to abstain from alcohol use for a few months last year, which you respond to with encouragement. You acknowledge that while he enjoys relaxation effects of alcohol, he is also aware alcohol may be causing him health problems. When you ask what he wants to do regarding alcohol use, he voices desire to cut back and follow-up with you in 2 weeks.**

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5. **This strategy of engagement is known as which of the following?**

A. Motivational Interviewing
B. Individual Drug Counseling
C. Contingency Management
D. Cognitive Behavioral Therapy

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Answer: A. Motivational Interviewing

It is a directive, **patient-centered counseling approach**.

Developed in part by clinical psychologists William R. Miller, PhD and Stephen Rollnick, PhD, it focuses on helping patients **explore and resolve ambivalence** around their substance use. Each patient may be in differing stages of readiness, and providers need **to act according to the patient's current stage, culture, type of problems, treatment setting, and current needs**.*

Motivational interventions are associated with successful outcomes including adherence to and retention in SUD treatment; reduction in or abstinence from various substances; and reductions in substance misuse consequences and related problems.

DiClemente et al., 2017; Miller and Rollnick, 2023 *4th edition of the Miller and Rollnick book (2023) now available.

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Motivational Interviewing

Motivational interventions have demonstrated efficacy across ages (i.e., adolescents, young adults, and older adults), genders, and racial and ethnic groups.

One study found that MI was one of two evidence-based treatments endorsed as culturally appropriate by a majority of surveyed SUD treatment programs serving American Indian and Alaska Native (AI/AN) clients.

MI's core elements, including its emphasis on collaboration, evoking clients' perspectives, and honoring clients' autonomy, align well culturally with African Americans.

Lenz et al., 2016; Montgomery, Robinson, Seaman, & Haeny, 2017 ; Novins, Croy, Moore, & Rieckmann, 2016

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Other Interventions

Individual Drug Counseling is a manualized approach that focuses on **skills building and promotion of the 12-step ideology** to decrease substance use and make changes in self/lifestyle.

Contingency management is based on **operant conditioning principles, providing tangible reinforcers** for evidence of behavior change (*discussed further in a future question*).

Cognitive behavioral therapy is a structured, multi-session behavioral treatment to help patients understand their ways of thinking/behaving and create **tools to change their maladaptive cognitive and behavioral patterns** (*discussed further in a future question*).

Miller et al. (Eds), 2024

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6. **This is the transcript of the interaction from the prior case:**

KH: I'm worried about my recent stomach pains, and my wife seems to think I'm drinking too much.

MD: You're concerned about your health, and I am glad you came in to speak today. Tell me about your diet and drinking habits.

KH: Being at home, it seems like I am constantly eating and after a full day of video meetings, I need a few beers to unwind, which I didn't think was an issue. However, now I am worried about my stomach.

MD: Your current work situation keeps you at home and having a few beers helps you relax after a stressful day. However, it also seems that you are concerned about stomach pain and your wife's thoughts about your drinking and want to make some positive changes for your health. What areas do you think you can change?

(Continued on next slide)

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6. **Previous Scenario:** ***(continued)***

***KH*:** I know alcohol isn't the best and I need to cut back. I did stop for a few months last year.

MD: You're clearly aware that alcohol isn't helping, and you think you should reduce. You have already shown the ability to stop.

KH: I think I can cut down on my use. I don't need to drink every night.

MD: You're making a commitment to get healthy, and now you have thought of ways to make that happen. You have recognized some concerns about your health, which alcohol may be contributing to, and you plan to reduce your amount.

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6. All of the following Motivational Interviewing technique(s) were utilized in the previous scenario except?

A. Open-ended questions
B. Affirmations
C. Reflections
D. Confrontations

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Answer: D. CONFRONTATIONS

Confrontations are not a tool in motivational interviewing.

OARS is a basic communication style that is used throughout consultation or counseling sessions.

O: open-ended questions

A: affirmations

R: reflective statements

S: summarizations

These techniques are used to elicit **"change talk"** from patients. Using these tools, a clinician **expresses empathy, develops discrepancy, dances with discord, and supports self-efficacy**, which are key principles of MI.

Miller and Rollnick, 2023

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Motivational Interviewing Techniques

KH: I'm worried about recent stomach pains, and my wife seems to think I'm drinking too much.

MD: You're concerned about your health (***reflection***), and I am glad you came in to speak today (***affirmation***). Tell me about your diet and drinking habits (***open-ended question***).

KH: Being at home, it seems like I am constantly eating and after a full day of video meetings, I need a few beers to unwind, which I didn't think was an issue. However, now I am worried about my stomach.

MD: Your current work situation keeps you at home (***reflection***) and having a few beers helps you relax after a stressful day (***reflection***). However, it also seems that you are concerned about stomach pain and your wife's thoughts about your drinking (***reflection***) and want to make some positive changes for your health (***affirmation***). What areas do you think you can change (***open-ended question***)?

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Motivational Interviewing Techniques

***KH*:** I know alcohol isn't the best and I need to cut back. I did stop for a few months last year.

MD: You're clearly aware that alcohol isn't helping, and you think you should reduce (***reflection***). You have already shown the ability to stop (***affirmation***).

KH: I think I can cut down on my use. I don't need to drink every night.

MD: You're making a commitment to get healthy (***affirmation***), and now you have thought of ways to make that happen (***reflection***). You have recognized some concerns about your health, which alcohol may be contributing to and you plan to reduce your amount (***summarization***).

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7. Screening, Brief Intervention, and Referral to Treatment (SBIRT) has shown the most efficacy for what substance?

A. Heroin
B. Alcohol
C. Methamphetamine
D. Cocaine

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Answer: B. ALCOHOL

Several systematic reviews and meta-analyses confirm the efficacy of SBIRT for unhealthy alcohol use in primary care patients; however, this effect was not been consistently replicated in other settings (EDs), with more severe alcohol use, or with other substances (although findings showing the effectiveness of SBIRT for tobacco use and drug misuse are accumulating.)

Babor TF, et al, 2017; Roy-Byrne P, et al, 2014; Saitz R, 2010; Saitz R, et al, 2014

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8. Three brothers ages 17, 15, and 14 present to the clinic for fentanyl use for the past 1.5 years. Their mother has brought them to clinic at the recommendation of child and family services to avoid losing custody. Two of the siblings have had overdose episodes at school requiring narcan in the past 6 months. After assessing and diagnosing each patient, you develop a multidisciplinary treatment plan. One aspect of this plan is a psychosocial intervention that approaches drug use in terms of a network of influences.

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8. The intervention is provided three times a week at home, the office, and school for three to six months with the goal of decreasing unwanted behavior and increasing desirable behavior. What is this intervention?

A. Cognitive Behavioral Therapy
B. Multidimensional Family Therapy
C. Network Therapy
D. Motivational Enhancement Therapy

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Answer: B. Multidimensional Family Therapy (MDFT)

MDFT is an outpatient intervention **designed for youth and young adults**. It is comprised of **1-3 therapy sessions a week over 3-6 months** in a **variety of locations** such as: school, home, office, court, other community areas. Four treatment domains: adolescent, parent, family, and community.

Adolescent drug use is approached in terms of a network of influences. MDFT suggests that reducing unwanted behavior and increasing desirable behavior occurs in multiple ways in different settings."

Adolescents develop skills in stress management, communication of emotions and thoughts, and vocation. **Family members also receive sessions** in parallel with the adolescents.

Barthwell, AG, et al.2019 ; Jaffe, SL, et al 2019.,

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Cognitive Behavioral Therapy (CBT) is a **time limited** (8 – 12 sessions usually), structured, goal-oriented treatment that can be adapted to a variety of substances and settings. Skills taught (and rehearsed) include recognizing triggers for substance use, avoiding high-risk situations, and coping with cravings.

Extensive evidence exists to support **benefit for multiple substance use disorders.**

Data from multiple studies has shown a **"sleeper effect,"** where individuals show greater improvement over time after formal treatment ends.

A computer-based CBT system has also been shown to be effective in helping reduce drug use following standard drug abuse treatment.

Carroll KM, Kiluk BD, 2017; Carroll, KM et al, 2008

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Motivational Enhancement Therapy (MET) is a standardized "**patient-centered counseling approach** that attempts to initiate behavior change." It was developed originally for tobacco use disorder. Its goal is to "**resolve patient ambivalence** about treatment stopping drug use."

Network Therapy stresses a "teamwork" feeling using **cognitive-behavioral relapse prevention** and direct involvement of one's **social network**. The main goal is for the **network to support the patient's treatment and not necessarily to repair relationships**. The **network is part of the team and not a recipient of treatment**. Examples of interventions include medication monitoring, help with homework assignments, and providing social reinforcement contingent on abstinence. This has been used as an effective adjunct to buprenorphine treatment.

Barthwell, Andrea G, et al. 2019; Galanter, M. et al 2004.

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9. A 45-year-old transgender woman comes to your outpatient office asking for help in decreasing her alcohol use, which currently consists of approximately one bottle of wine nightly for the past year. She reports her drinking started following episodes of physical abuse by her now ex-partner in their shared home.
She describes using alcohol to suppress thoughts related to the trauma, manage self-blame, reduce hypervigilance, and cope with the emotional distress of living in the home where the abuse occurred. Her presentation suggests a moderate alcohol use disorder and the presence of another psychiatric diagnosis.

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9. After discussing her possible diagnoses and potential referrals, what type of psychotherapeutic intervention would you recommend to target both her substance use and psychiatric symptoms?

A. Mindfulness based relapse prevention
B. Seeking safety
C. Contingency management
D. Supportive expressive therapy

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Answer: B. Seeking safety

This patient may be dealing with both AUD and PTSD.

Seeking Safety is an integrated treatment **for co-occurring PTSD and SUD**. It is a **manualized CBT model** that includes behavioral, interpersonal, cognitive, and case management components. Originally a group model, it has been implemented in various settings and with both men and women. It has been shown to improve both SUD and PTSD symptoms.

Lopez et al. (2021); Najavits (2002).

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Mindfulness based relapse prevention (MBRP) integrates traditional psychotherapeutic relapse prevention techniques with mindfulness-based practices.

- Mindfulness based interventions aim to **increase self-awareness and self-regulation**.
- While MBRP has shown efficacy in treating numerous SUDs, her **alcohol use appears to be secondary to her PTSD**.

Miller et al. (Eds), 2024

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Contingency management is a behavioral therapy that **reinforces a target behavior through rewards**.
- There is best evidence for stimulant use disorders, especially cocaine, and opioid use disorders, especially heroin. There are some data to suggest CM may be helpful for cannabis, nicotine, and benzodiazepines, with evidence most limited for alcohol.

Supportive expressive therapy focuses on helping patients to feel comfortable **recognizing and expressing their feelings** and understanding the relationship between their emotions, substance use, and problematic relationships

Miller et al. (Eds), 2024

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10. Based on data from Project MATCH, which of the following behavioral interventions would be the most effective for the treatment of alcohol use disorder?

A. Twelve-Step Facilitation Therapy
B. Cognitive Behavioral Coping Skills Therapy
C. Motivational Enhancement Therapy
D. All are equally effective

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Answer: D. All are equally effective

Project MATCH was an eight-year multi-site clinical trial which focused on three common forms of behavioral therapy for alcohol use disorder: Motivational Enhancement Therapy, Cognitive Behavioral Coping Skills Therapy, & Twelve Step Facilitation Therapy. It attempted to determine if varying subgroups of persons with alcohol use disorder respond differently to the three treatments.

Overall, participants showed significant and sustained improvement in increased percentage of abstinent days and decreased number of drinks per drinking days, with **few clinically significant outcome differences among the three treatments** in either treatment arm.

Project MATCH Research Group, 1999

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11. Which of the following statements regarding 12-step programs is true?

A. Abstinence is a requirement for Alcoholics Anonymous (AA) membership.

B. Prayer and meditation is one of AA's 12 steps.

C. Al-Anon members are majority white males.

D. Gamblers Anonymous believes compulsive gamblers can practice moderation.

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Answer: B. Prayer and meditation is one of AA's 12 steps.*

Step 11 of AA states, "Sought through **prayer and meditation** to improve our conscious contact with God as we understood Him, praying only for knowledge of His will for us and the power to carry that out."

*Reference slides are available at the end of the talk

Alcoholics Anonymous. Twelve Steps and Twelve Traditions. Alcoholics Anonymous World Services; 1978.

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Twelve Step programs are peer-led recovery groups that use a structured, step-by-step approach to help individuals overcome addiction, compulsive behaviors, or emotional struggles. They emphasize personal accountability, spiritual growth, and mutual support.

They include well-known groups like Alcoholics Anonymous (AA), Narcotics Anonymous (NA), Al-Anon, and Gamblers Anonymous.

For more information, see:

https://www.aa.org

https://al-anon.org/

https://na.org

https://gamblersanonymous.org/

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Abstinence is NOT a requirement for AA membership. Tradition 11 states, "**The only requirement for AA membership is a desire to stop drinking**."

Al-Anon members are majority **white FEMALES**.

Gamblers Anonymous believes **compulsive gamblers can NOT practice moderation**. This is similar to AA, which notes that while some people with unhealthy use can later practice moderation, "alcoholics" cannot.

Alcoholics Anonymous. Twelve Steps and Twelve Traditions. Alcoholics Anonymous World Services; 1978.
https://al-anon.org/pdf/2024-Membership-Survey.pdf ; https://gamblersanonymous.org/about-gamblers-anonymous/

CSAM

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12. Which of the following mutual-help groups is an evidence-based, secular alternative to AA meetings using a 4-point recovery program?

A. LifeRing
B. Women for Sobriety
C. Secular Organizations for Sobriety
D. SMART Recovery

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Answer: D. SMART Recovery

SMART Recovery is an abstinence-based, secular approach that emphasizes **self-empowerment** and uses **CBT** and **non-confrontational motivation methods** to develop skills in four areas: **Enhancing Motivation, Coping with Urges, Problem Solving, and Lifestyle Balance.** *(https://www.smartrecovery.org)*

Studies have shown that SMART Recovery methods can help to decrease problems related to drinking and increase the number of days a person remains abstinent.

Campbell W, et al, 2016

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Other Mutual Support Groups

LifeRing is a secular, abstinence-oriented group with meetings and doctrine; has no prescribed steps; is open to all addictions; and welcomes significant others to meetings. LifeRing's principles are **Sobriety, Secularity, and Self-Help.** (https://lifering.org/)

Women for Sobriety (WFS) is a secular program engineered to focus on **women's treatment needs** and what will best support their recovery. Groups are led by moderators and promote **emotional and spiritual growth** free from the bounds of unhealthy alcohol use and use disorders. *(https://womenforsobriety.org/)*

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Other Mutual Support Groups

Secular Organizations for Sobriety - is not one specific program, but rather a collection of programs that are autonomous from each other. Also called Save Our Selves, SOS provides alternatives to spirituality-based recovery programs. SOS is not designed for a specific addiction. *(http://www.sossobriety.org/)*

Most organizations have in-person and online meetings.

To find a variety of mutual support secular meetings, *patients can*

- use the AA mobile app and filter using "secular"

- go to https://www.worldwidesecularmeetings.com to find AA, Buddhist, and other groups

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NEED TO KNOW

1. Transtheoretical Model (Stages of Change)
2. Screening/assessment tools and Screening, Brief Intervention, & Referral to Treatment (SBIRT)
3. Matching patients to appropriate levels of care
4. Motivational Interviewing
5. Behavioral and psychotherapeutic treatments
   a) Individual, group, family, and community interventions
   b) When to recommend various approaches (based on substance and psychosocial factors)
6. Mutual Support
   a) Twelve Step groups (Alcoholics Anonymous, including the Twelve Steps Twelve Traditions)
   b) Non 12-step based groups

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Test Taking & Test Preparation Tips

- Go to the end of the question first to identify what is being asked of you, then read the question from the beginning
- Cover the answer choices and produce your own answer before looking at the choices.
- Answer questions you are uncertain about, then mark them for later review if you have time
- Practice test review: focus on concepts from questions you got wrong and questions you had to guess

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TWELVE STEPS OF AA

1. We admitted we were powerless over alcohol—that our lives had become unmanageable.
2. Came to believe that a Power greater than ourselves could restore us to sanity.
3. Made a decision to turn our will and our lives over to the care of God as we understood Him.
4. Made a searching and fearless moral inventory of ourselves.
5. Admitted to God, to ourselves, and to another human being the exact nature of our wrongs.
6. Were entirely ready to have God remove all these defects of character.
7. Humbly asked Him to remove our shortcomings.
8. Made a list of all persons we had harmed, and became willing to make amends to them all.
9. Made direct amends to such people wherever possible, except when to do so would injure them or others.
10. Continued to take personal inventory and when we were wrong promptly admitted it.
11. Sought through prayer and meditation to improve our conscious contact with God as we understood Him, praying only for knowledge of His will for us and the power to carry that out.
12. Having had a spiritual awakening as the result of these steps, we tried to carry this message to alcoholics, and to practice these principles in all our affairs.

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TWELVE TRADITIONS OF NA

1. Our common welfare should come first; personal recovery depends on NA unity.
2. For our group purpose there is but one ultimate authority— a loving God as He may express Himself in our group conscience. Our leaders are but trusted servants; they do not govern.
3. The only requirement for membership is a desire to stop using.
4. Each group should be autonomous except in matters affecting other groups or NA as a whole.
5. Each group has but one primary purpose—to carry the message to the addict who still suffers.
6. An NA group ought never endorse, finance, or lend the NA name to any related facility or outside enterprise, lest problems of money, property, or prestige divert us from our primary purpose.
7. Every NA group ought to be fully self-supporting, declining outside contributions.
8. Narcotics Anonymous should remain forever nonprofessional, but our service centers may employ special workers.
9. NA, as such, ought never be organized, but we may create service boards or committees directly responsible to those they serve.
10. NA has no opinion on outside issues; hence the NA name ought never be drawn into public controversy.
11. Our public relations policy is based on attraction rather than promotion; we need always maintain personal anonymity at the level of press, radio, and films.
12. Anonymity is the spiritual foundation of all our Traditions, ever reminding us to place principles before personalities.

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Motivational Interviewing (MI) Acronyms

Spirit of Motivational Interviewing- P.A.C.E.*

Partnership

Acceptance

Compassion

Evocation (*Empowerment)

Principles of Motivational Interviewing- D.E.A.R.S*

Develop discrepancy (*Planting Seeds)

Express empathy

Amplify ambivalence

Roll with resistance (*Sustain Talk and Discord)

Support self efficacy

*Differences in terminology for 2023 4th edition book. For a brief summary of changes, see: https://motivationalinterviewing.org/sites/default/files/what_new_in_mi-4.pdf

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Motivational Interviewing (MI) Acronyms

Skills of Motivational Interviewing- O.A.R.S

Open-ended questions

Affirmations

Reflections

Summarization

Change Talk (from the patient) - D.A.R.N.C.A.T

Desire

Ability

Reasons

Need

Commitment

Activation

Taking steps

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Thank you!

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