



Providers
Clinical Support
System

Appropriate Interpretation of Urine Drug Screen Results

Emily E. Leppien, PharmD, BCPS, BCPP
Clinical Assistant Professor
Binghamton University School of Pharmacy
and Pharmaceutical Sciences

Mark Garofoli, PharmD, MBA, BCGP, CPE, CTTS
Director of Experiential Learning
Clinical Assistant Professor
West Virginia University School of Pharmacy



Providers
Clinical Support
System

Emily Leppien, PharmD, BCPS, BCPP

Emily Leppien, PharmD, BCPS, BCPP, is a Clinical Assistant Professor at Binghamton University School of Pharmacy and Pharmaceutical Sciences. Dr. Leppien received her Doctor of Pharmacy degree from Albany College of Pharmacy and Health Sciences in 2016. Following graduation, she completed two years of post-graduate residency training at the University at Buffalo School of Pharmacy and Pharmaceutical Sciences and Buffalo Psychiatric Center. Dr. Leppien maintains an ambulatory care clinical practice site at Lourdes Pain Care, where she inaugurated collaborative drug therapy management (CDTM) services.



Dr. Leppien specializes in the treatment of chronic pain, substance use disorder and psychiatric illness. Her professional and research interests include opioid and non-opioid pharmacotherapy, as well as the integration of behavioral health and substance use disorder treatment within pain management services. Dr. Leppien is an active member of the American Pharmacists Association (APhA), currently serving as the Pain, Palliative Care and Addiction SIG Coordinator.

Mark Garofoli, PharmD, MBA, BCGP, CPE, CTTS

Mark Garofoli is a Pitt PharmD graduate, Strayer MBA graduate, Board-Certified Geriatric Pharmacist (BCGP), Certified Pain Educator (CPE), and Certified Tobacco Treatment Specialist (CTTS). His past positions include being a pharmacist leader with CVS Health, Humana, and the WV Safe & Effective Management of Pain (SEMP) Program, along with coordinating the WV SEMP Guidelines Panel.

Today, he is a faculty member of the West Virginia University (WVU) School of Pharmacy, WVU School of Medicine Pain Fellowship Faculty, and a WVU Medicine Pain and Addiction Pharmacist. Mark “Pain Guy” Garofoli has been a 2021 TEDx Talker, CDC grant reviewer, civil/criminal expert witness, seasoned CE developer and presenter, and is the host of the Pain Pod.



Financial Disclosures

Mark Garofoli, PharmD, MBA, BCGP, CPE, CTTS, Emily E. Leppien, PharmD, BCPS, BCPP, and APhA's editorial staff declare no relevant financial relationships or commercial interests in any product or service mentioned in this activity, including grants, employment, gifts, stock holdings, honoraria.

For a complete list of APhA staff disclosures, go to www.pharmacist.com/apha-disclosures.

Conflicts of interest have been resolved through content review by Kieu Nguyen, PharmD, Director of Content Development at the American Pharmacists Association.

Target Audience

The overarching goal of PCSS is to train health care professionals in evidence-based practices for the prevention and treatment of opioid use disorders, particularly in prescribing medications, as well as for the prevention and treatment of substance use disorders.

Educational Objectives

At the conclusion of this application-based activity, participants will be able to:

1. List causes that may lead to unexpected UDS results, specifically false positives and negatives.
2. Explain how opioid and benzodiazepine metabolism impacts UDS results.
3. Interpret a UDS reading based on patient history and reported results.
4. Recommend appropriate monitoring based on patient history and UDS results.
5. Make patient-specific treatment recommendations after analyzing UDS results.

Development and Support

This accredited learning activity for pharmacists, *Appropriate Interpretation of Urine Drug Screen Results*, is developed by the American Pharmacists Association.

This activity is supported by a grant from the Providers Clinical Support System (PCSS).

Funding for this initiative was made possible (in part) by grant no. 6H79TI081968 from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.



Baseline Knowledge Assessment

Pre-Assessment Question 1

Which one of the following medications can possibly produce a false positive urine drug screening for methadone?

- A. Ciprofloxacin
- B. Naproxen
- C. Quetiapine
- D. Cyclobenzaprine

Pre-Assessment Question 2

A patient using morphine may also show a positive result for _____ on a confirmatory urine drug test.

- A. Codeine
- B. Hydromorphone
- C. Oxycodone
- D. Hydrocodone

Pre-Assessment Question 3

Urine drug monitoring should be performed for low-risk patients a minimum of every _____.

- A. 1 month
- B. 3 months
- C. 6 months
- D. 12 months

2022 CDC Opioid Guideline Update

12 Recommendations

1. Nonopioid therapies are effective for many common types of acute pain
2. Nonopioid therapies are preferred for subacute and chronic pain
3. Utilize immediate-release (IR) before extended-release (ER) opioids
4. Start Low, Go Slow, and avoid increasing to high-risk dosage levels
5. For patients already utilizing high-risk opioid dosages: continually and carefully weigh benefits and risk, taper only if risks outweigh benefits, and when tapering ensure a gradual taper unless there is a life-threatening concern
6. When opioids are utilized in acute pain, provide only for expected duration
7. Reevaluate chronic/subacute opioid utilization at least every 3 months (within 1 to 4 weeks initially)
8. Naloxone education
9. Prescription Drug Monitoring Program (PDMP) review initially and periodically
10. **TOXICOLOGY URINE DRUG TESTING (UDT)**
11. Caution with opioid/benzodiazepine combinations (or opioids with any CNS depressant)
12. Treatment with evidenced-based medications to treat patients with opioid use disorder

Urine Drug Monitoring Goals

- Improve proper medication adherence
- Prevent medication misuse/diversion
- Detect medication misuse/diversion

Urine Drug Screen POC results log

Date:	Patient ID	Cutoff (ng/mL)	Result		Note:	
NexScreen UDS Lot#	Amphetamine (AMP)	500	Positive	Negative		
	Barbiturates (BAR)	300	Positive	Negative		
	Buprenorphine (BUP)	10	Positive	Negative		
	Exp date:	Benzodiazepines (BZO)	300	Positive	Negative	
		Cocaine (COC)	150	Positive	Negative	
		Ecstasy (MDMA)	500	Positive	Negative	
		Methamphetamine (MET)	500	Positive	Negative	
		Methadone (MTD)	300	Positive	Negative	
		Opiate (OPI300)	300	Positive	Negative	prescribed
		Oxycodone (OXY)	100	Positive	Negative	
		Phencylidine (PCP)	25	Positive	Negative	
		Tricyclic Antidepressants (TCA)	1000	Positive	Negative	
		Cannabinoids (THC)	50	Positive	Negative	
	Internal QC **		Positive	Negative		
Test performed by:						

Urine Drug Monitoring Frequency

Risk	Frequency
Low	Annual
Moderate	$\geq 2x/\text{year}$
High	$\geq 3x/\text{year}$
Any	? Every Appointment ?

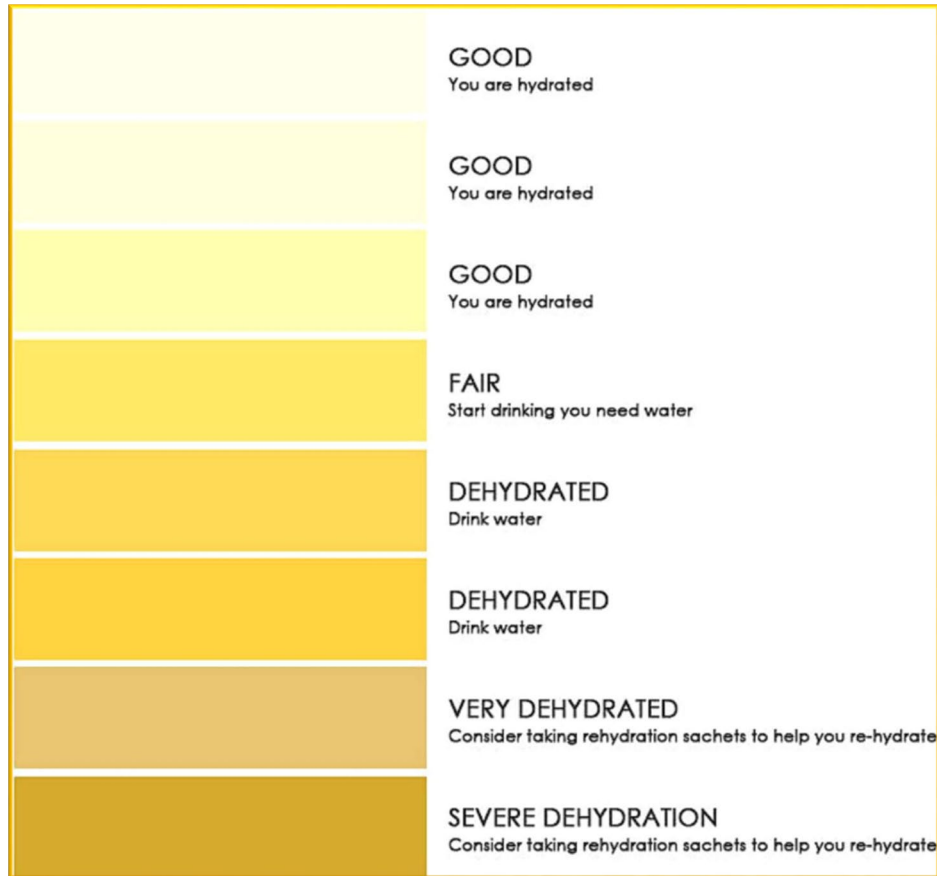
How to Assess Risk?

- Physical examination and detailed medication history
 - Past or current use of illicit substances
 - Specific opioid medications used
- Review of Prescription Drug Monitoring Program (PDMP)
- Use of concomitant medications
 - Benzodiazepines
 - Non-Benzodiazepine Receptor Agonists (NBRAs, Z-Drugs)
- Screening tools:
 - Drug Abuse Screening Test (DAST-10)
 - Opioid Risk Tool (ORT)
 - Screener and Opioid Assessment for Patients with Pain Revised (SOAPP-R)

Urine Drug Screening Strategies: Trust, But Verify

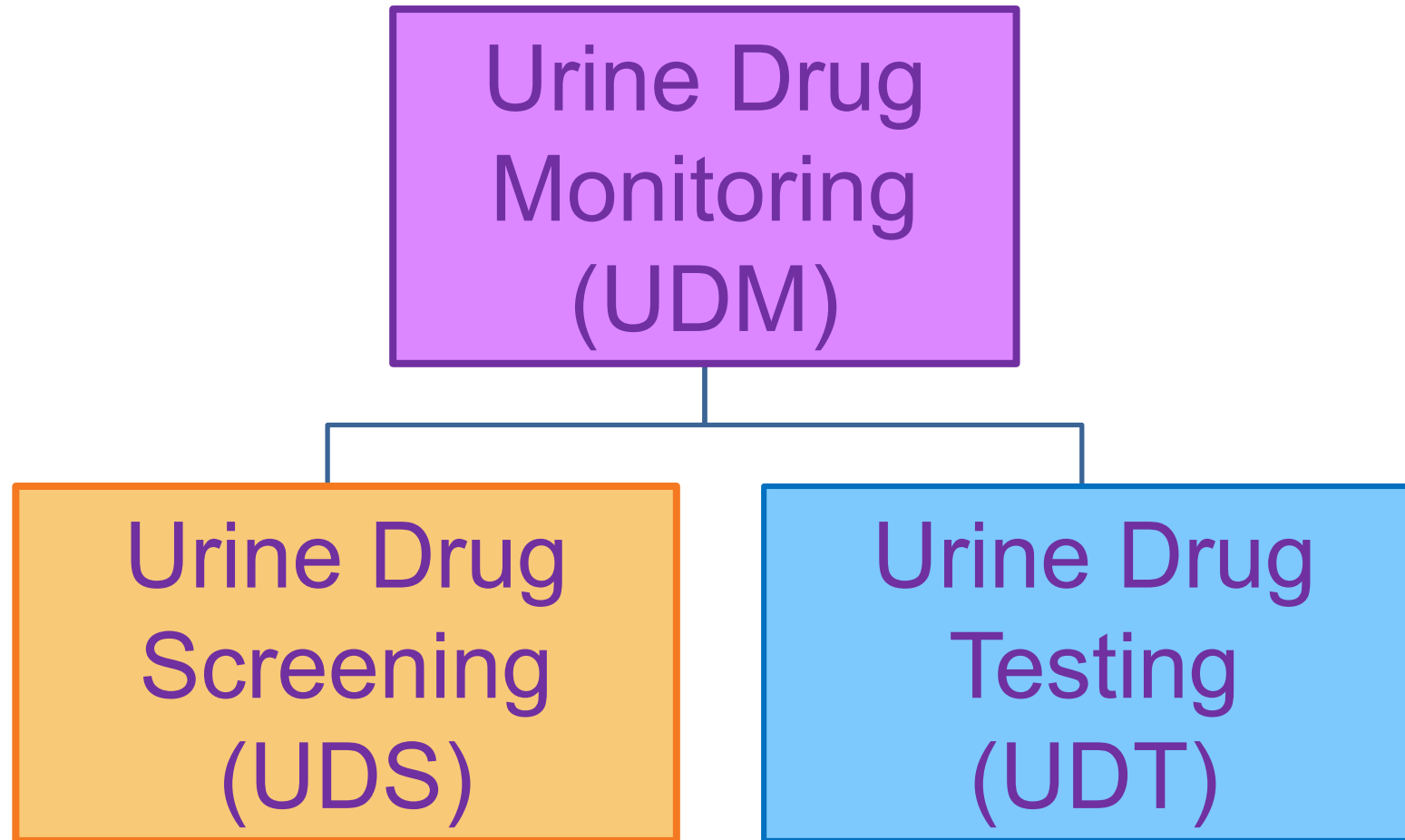
- Patient and Provider Agreement → UDM Procedures
- Random or scheduled (e.g., appointments)
- Urine samples collected in a private bathroom without running water, soap, hand sanitizer or other liquids – and with toilet water stained blue
- Urine specimen cups with temperature strips that fluoresce between 90°F to 100°F
- Urine creatinine and specific gravity can be ordered together with a drug test panel

Urine Color



- The yellow color of urine results from urobilin that is produced as a product of bilirubin degradation
- Normal urine color → light yellow

Toxicology Testing



Urine Drug Testing Versus Screening

Urine Drug Monitoring	
Urine Drug Screening (UDS)	Urine Drug Testing (UDT)
Immunoassay screen (e.g., cup)	GC-MS or LC-MS
PRESUMPTIVE	DEFINITIVE
In-office, point-of-care, or lab-based	Laboratory, highly specific and sensitive
Results within minutes	Results in hours or days
Various cups detect a majority of legal and illicit medications by structural class	Measures all drug/metabolite concentrations
Guidance for preliminary treatment decisions	Definitive identification and analysis
Cross-reactivity common: more false positives	False-positive results are rare
Higher cutoff levels: more false negatives	False-negative results are rare
\$	\$\$\$

GC-MS: gas chromatography-mass spectrometry
 LC-MS: liquid chromatography-mass spectrometry

Moeller KE, Lee KC, Kissack JC. Urine drug screening: practical guide for clinicians. *Mayo Clin Proc.* 2008;83(1):66-76.



Providers
 Clinical Support
 System

Urine Drug Monitoring Cut-Off Levels (SAMHSA)

Chemical	UDS Cut-Off (ng/mL)	UDT Cut-Off (ng/mL)
Tetrahydrocannabinol (THC)	50	15
Opiates	2,000	2,000
Hydrocodone/Hydromorphone	300	100
Oxycodone/Oxymorphone	100	100
6-Monoacetylmorphine (6-MAM)	10	10
Amphetamines/Methamphetamine 3,4-Methylenedioxymethamphetamine (MDMA)	500	250
Cocaine (Benzoylecgonine)	150	100
Phencyclidine (PCP)	25	25

Urine Drug Detection Times

Urine Drug Detection Times	
Drug	Detection Time After Ingestion
Alcohol	7 to 12 Hours
Amphetamines	2 to 3 Days
Benzodiazepines (Short-Acting)	3 Days
Benzodiazepines (Long-Acting)	30 Days
Marijuana (Single Dose)	3 Days
Marijuana (4x/Week)	5 to 7 Days
Marijuana (Daily)	10 to 15 Days
Marijuana (Long-Term)	>30 Days
Codeine	2 Days
Heroin	2 Days
Hydromorphone	2 to 4 Days
Methadone	3 Days
Morphine	2 to 3 Days
Oxycodone	2 to 4 Days

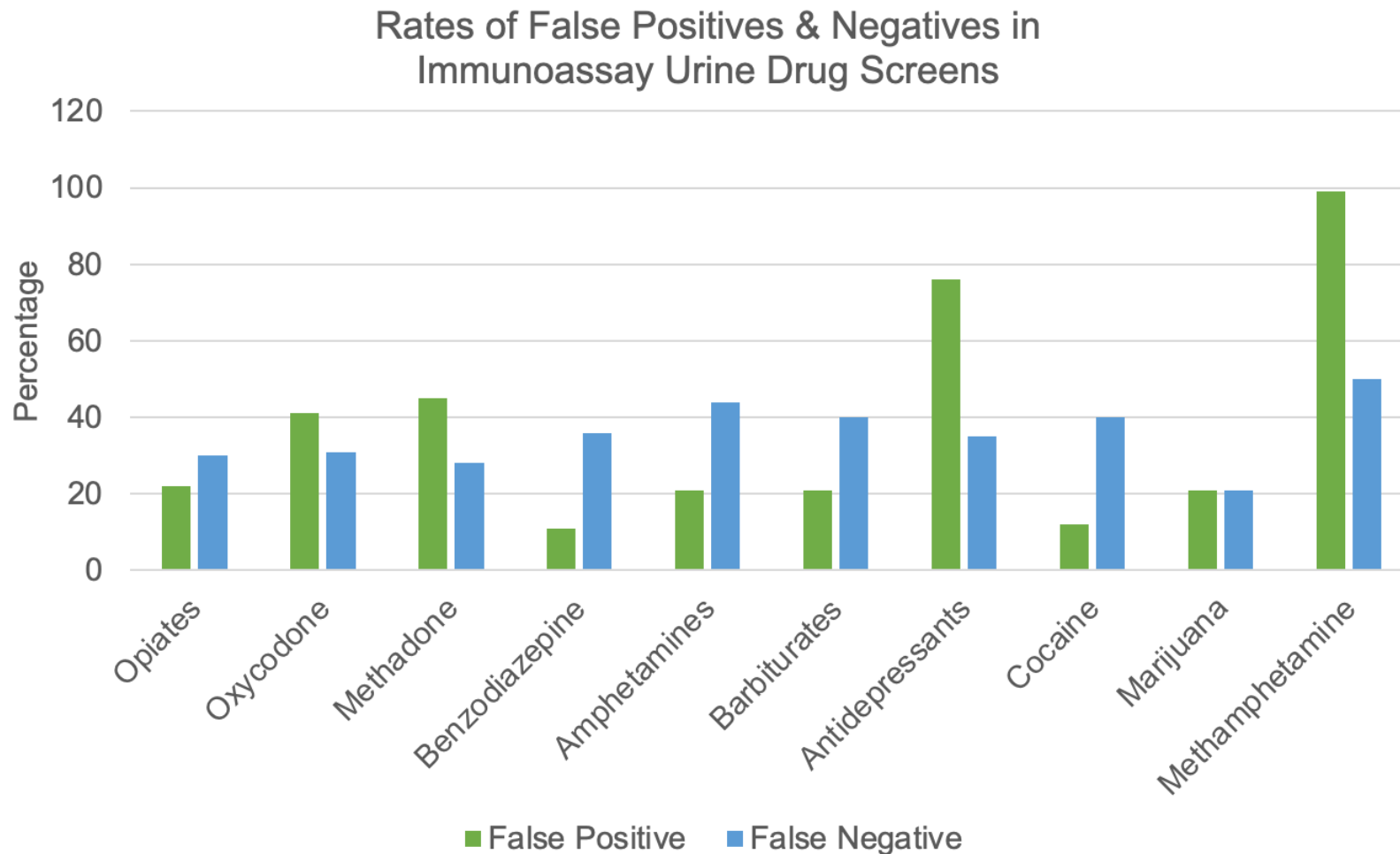
Schwebach A and Ball J. Urine drug screening: minimizing false-positives and false-negatives to optimize patient care. *US Pharm.* 2016;41(8):26-30.

UDS Different Drug Panels

URINE DRUG SCREENS						
SUBSTANCE	5 Panel	7 Panel	10 Panel	12 Panel	13 Panel	14 Panel
THC	X	X	X	X	X	X
Cocaine	X	X	X	X	X	X
Opiates	X	X	X	X	X	X
PCP	X	X	X	X	X	X
Amphetamines	X	X	X	X	X	X
Benzodiazepines		X	X	X	X	X
Barbiturates		X	X	X	X	X
Methadone			X	X	X	X
Propoxyphene			X	X	X	X
Quaaludes			X	X	X	X
Ecstasy				X	X	X
Oxycodone				X	X	X
Fentanyl					X	X
Meperidine					X	X
Buprenorphine						X

Moeller, K, Lee KC,
Kissack JC. Urine drug
screenings: practical
guide for clinicians.
Mayo Clin Proc.
2008;83(1)66-76.

False Positives and Negatives



UDS False Positives

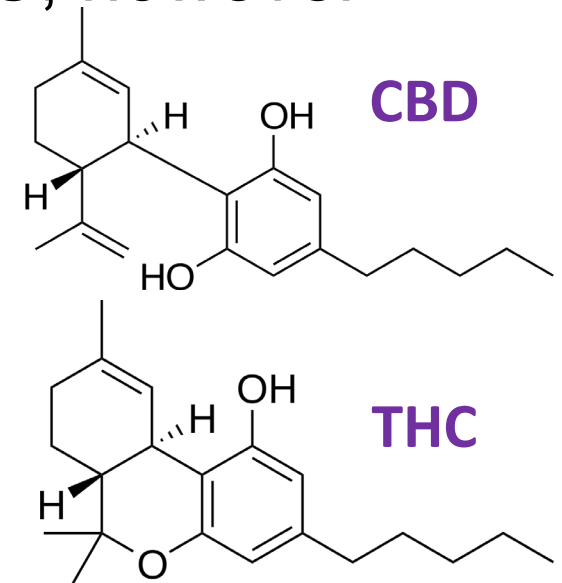
Urine Drug Screening False Positives	
Substance	UDS Cross-Reactant
Alcohol	asthma inhalers and isopropyl alcohol
Amphetamine Methamphetamine	amantadine, bupropion, chlorpromazine, desipramine, labetalol, phentermine, phenylephrine, promethazine, pseudoephedrine, selegiline, trazodone
Barbiturates	ibuprofen and naproxen
Benzodiazepines	oxaprozin, sertraline and some herbals
Cannabinoids	dronabinol (synthetics), NSAIDs (ibuprofen/naproxen), efavirenz, PPIs (pantoprazole), promethazine
Opioids	chlorpromazine, dextromethorphan, diphenhydramine, doxylamine, poppy seeds, quinine, quinolones, rifampin, verapamil
Methadone	quetiapine
Tricyclic antidepressants (TCAs)	carbamazepine, cyclobenzaprine, quetiapine

Moeller KE, Lee KC, Kissack JC. Urine drug screening: practical guide for clinicians. *Mayo Clin Proc.* 2008 Jan;83(1):66-76.

Schwebach A, Ball J. Urine drug screening: minimizing false-positives and false-negatives to optimize patient care. *US Pharm.* 2016 Aug;41(8):26-30.

Cannabinoids: Use Is on the Rise

- THC metabolite: THC-COOH
 - Carboxylic acid group added to allow for kidney excretion
- Cannabidiol (CBD) *should not* screen (+) for THC, however
 - High % of products contain other substances
 - Bonn-Miller et al. *JAMA* 2017 study:
 - 26 of 84 (~30%) CBD extracts had accurate labels
 - CBD and THC structures are very similar



Bonn-Miller MO, Loflin MJE, Thomas BF, et al. Labeling accuracy of cannabidiol extracts sold online. *JAMA*. 2017;318(17):1708-1709.

Schwab J. Can you fail a drug test due to CBD? US Drug Test Centers and SAMHSA.

Available at: <https://www.usdrugtestcenters.com/drug-test-blog/181/can-you-fail-a-drug-test-due-to-cbd.html>.

Accessed January 4, 2023.

Example Patient Case 1

- JP is prescribed **oxycodone ER** and **hydrocodone/acetaminophen**. After review of his medical records, it is noted he is also prescribed **cyclobenzaprine** and **dronabinol** for pain management. Routine 12-panel UDS was positive for opiates, oxycodone, and TCAs.
- **TRUE/FALSE:** UDS results are as expected given the patient's current medication regimen.
- What happens next?

FALSE

UDS False Negatives

- Dilute urine, overhydration
- Low urine drug concentration
- As needed use, with no use prior to screening
- Increased time between administration and screening time

UDS “Work-Arounds”

- Home remedies:
 - Niacin, bleach, vinegar, goldenseal root, cranberry juice
- Synthetic urine
 - Purchasing urine from a smoke shop
- Dilution
 - Decrease amount of drug present in urine
- Substitution
 - Using someone else’s urine

UDT to Confirm Results

- Unexpected or unexplained results should be confirmed with UDT
 - Unexpected positive or negative results

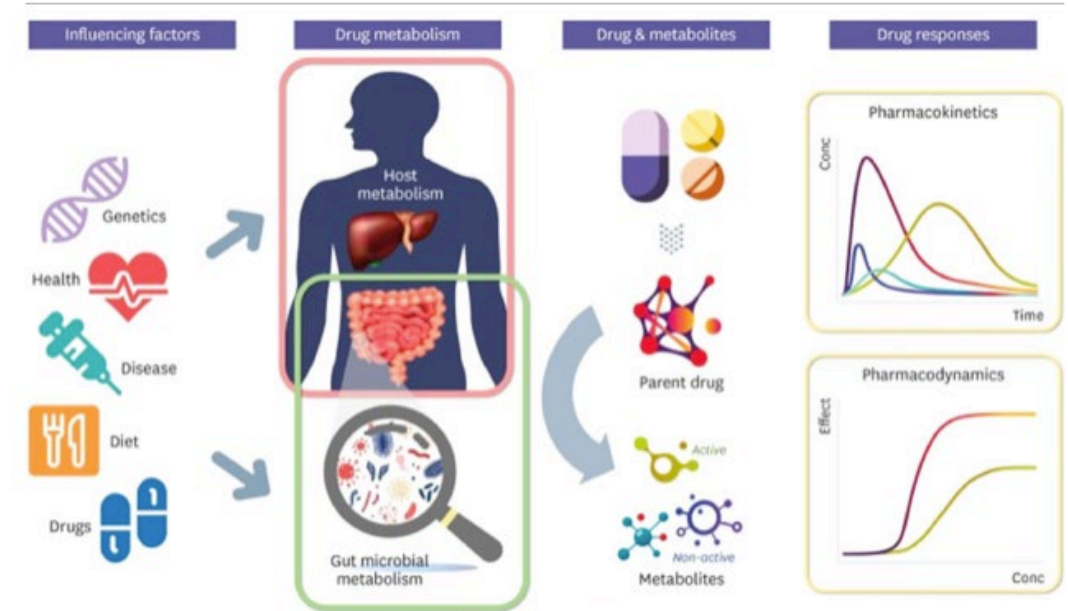


Copyright Permission Allowed:

Image Source: Adashek JJ, Khadilkar A, Enciso J, et al.. A Case of Esmolol-Induced False-Positive Amphetamine Urine Drug Test. Cureus. 2021;13(1):e12429.

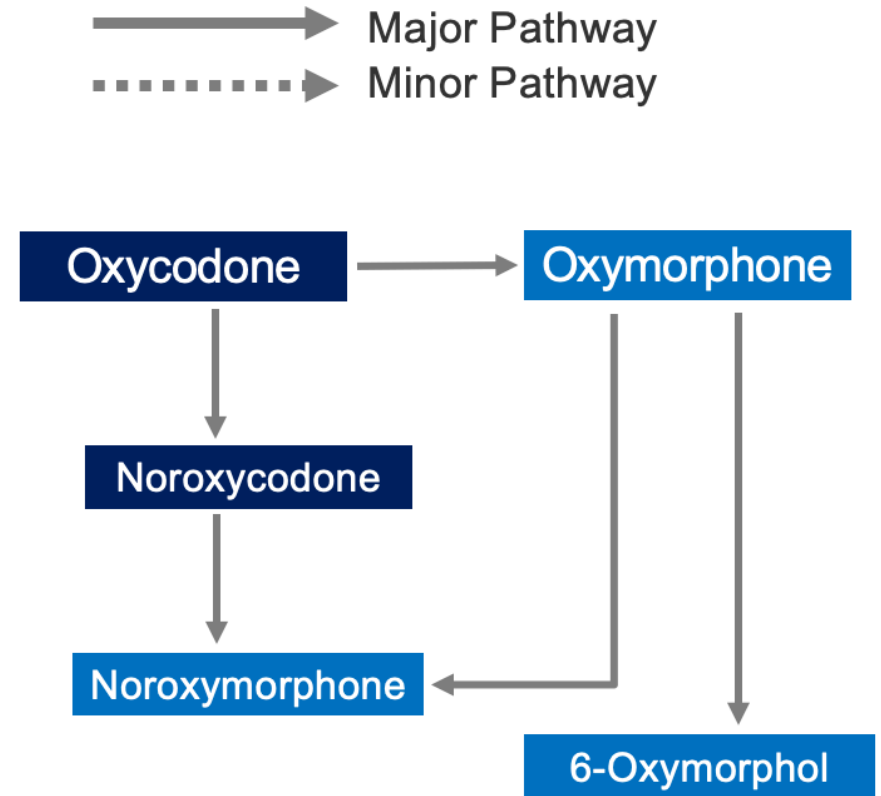
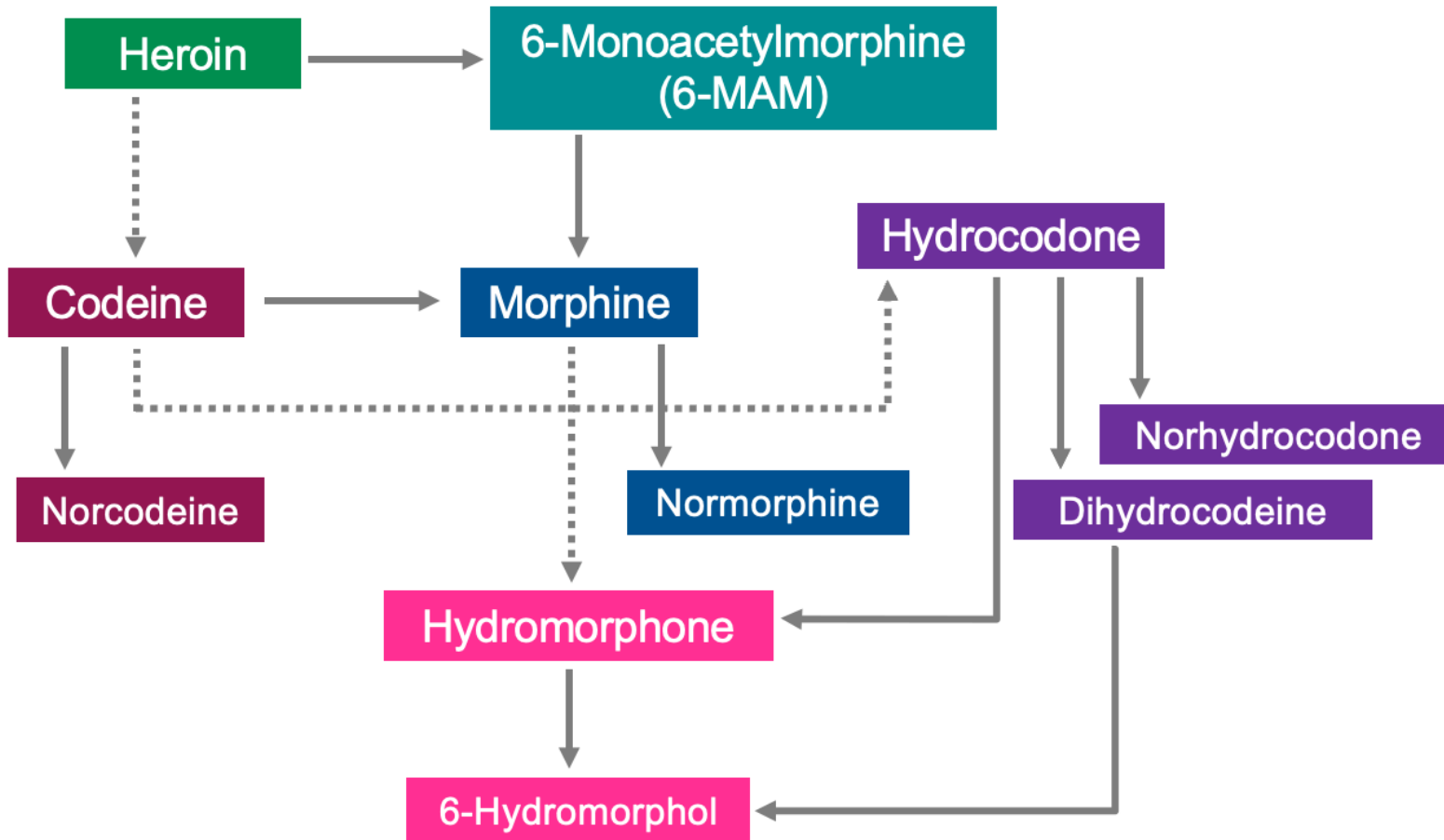
UDT Negative Result: Possible Causes

- Never took medication
- ↓ oral absorption of medication
- ↓ urinary excretion of medication metabolites
- Medication taken too many hours before test for detectable level to be present
- Medication was stolen, sold, or otherwise illicitly distributed



What to Expect on UDT?

Opiate Metabolism



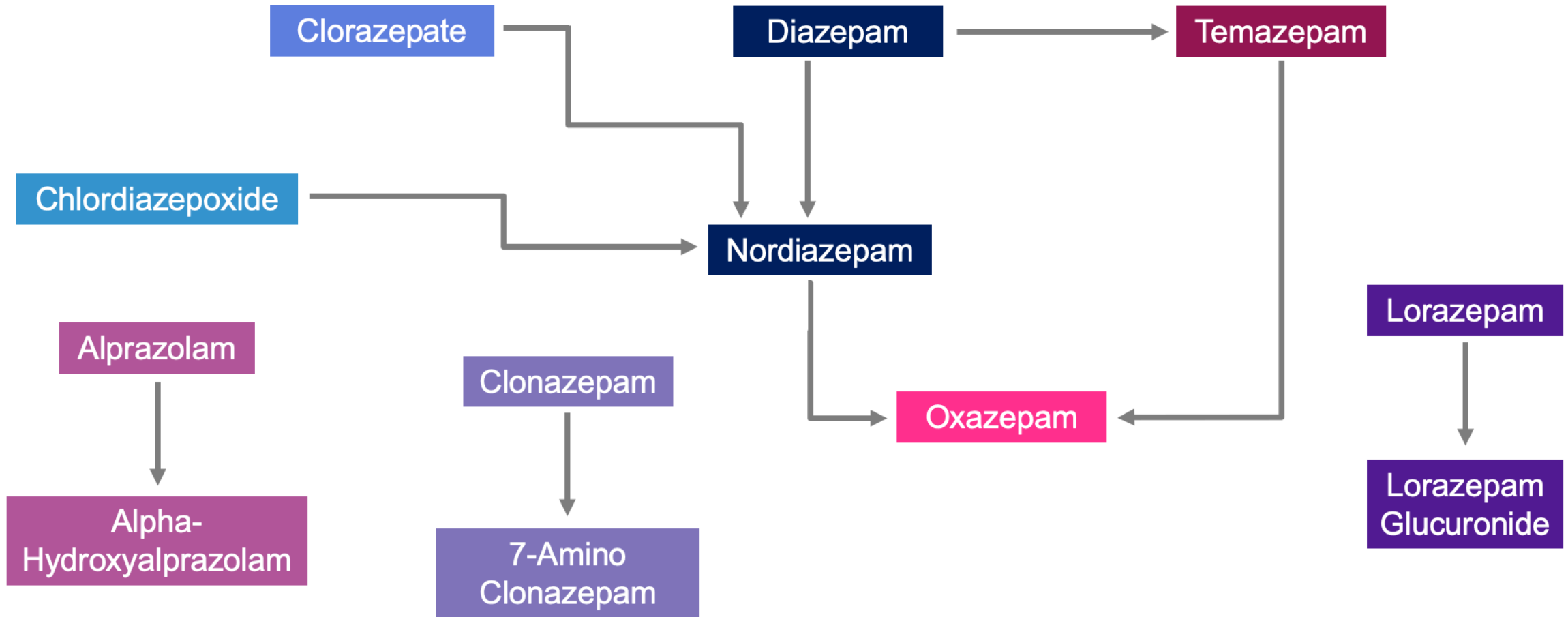
—————> Major Pathway
> Minor Pathway

CYP450 Opioid Metabolism

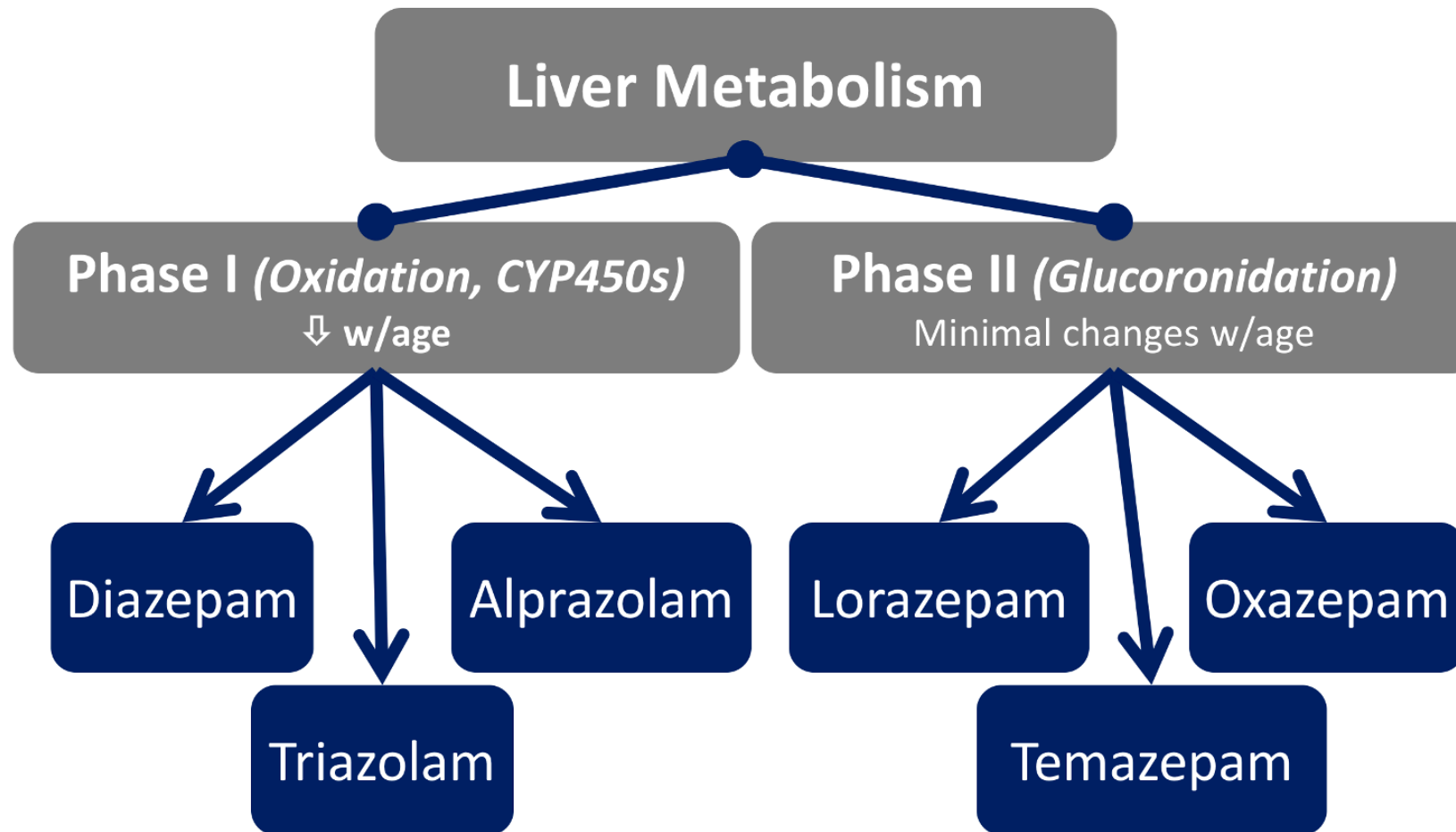
Drug	CYP Metabolism	Primary Active Metabolite
Codeine	2D6	Morphine
Fentanyl	3A4	--
Hydrocodone	3A4, 2D6	Hydromorphone
Methadone	3A4, 2D6 2C8, 2C9, 2C19, 2B6, 1A2	Oxymorphone
Oxycodone	3A4, 2D6	Oxymorphone
Tramadol	2D6	--

What to Expect on UDT?

Benzodiazepine Metabolism



Benzodiazepine Metabolism



Conversation Starters

If unexpected results occur when ordering a UDT, remember that the focus is to improve patient safety. Have a plan in place for communicating results and practice the difficult conversations you may have with your patients.

tips

TALKING WITH PATIENTS ABOUT URINE DRUG TESTING RESULTS:

- Always keep the focus on the patient's well-being and safety.
- Do not jump to conclusions about unexpected results; have a candid conversation with the patient about possible explanations.
- Do not dismiss patients from care based on UDT results.
- Consider using the CDC mobile app to practice the types of conversations you may encounter with patients.

Actions to take post-urine drug testing:

- Discuss unexpected results with the local laboratory or toxicologist if assistance is needed with interpretation.
- Inform the patient of the test results.
- Take time to discuss unexpected results with the patient and refer to pre-UDT information the patient may have shared with you.
- Review the treatment agreement and focus conversations around patient safety.
- Determine if frequency and intensity of monitoring should be increased and keep the patient informed.

Example Patient Case 2

- AZ is prescribed **morphine ER 15 mg PO Q8h** and **duloxetine 60 mg PO BID** for chronic pain. Routine 12-panel UDS was **negative** for all substances.
- Urine sample is sent to laboratory for confirmatory UDT.
- UDT reveals **positive** result for morphine, marijuana, and cocaine.
 - Are these results expected?
 - How do we discuss these results with the patient?
 - When should UDM be repeated?

Handling Situations: Confirmed Drug Seeking or Diversion

- Reference the patient and provider agreement/contract
- Treatment can continue with non-controlled substance therapies
- Refer to a substance-use disorder specialist or program
- Contact law enforcement if concern for safety of patient or others
- Respect for all those directly or indirectly involved in the specific patient case should be upheld, while also ensuring both a procession within federal and state laws and an appropriate level of patient care

Avoid Patient Abandonment

- Document patient encounters thoroughly
- Engage in collaborative interprofessional care
- Stress importance of continued patient care
- Submit referrals to additional healthcare professionals as appropriate

Key Messages

- Urine Drug Monitoring (UDM) includes:
 - Urine Drug Screenings (UDS) and Urine Drug Tests (UDT)
- UDS is presumptive with a concerning observed percentage of false positives/negatives
 - UDT is definitive
- To determine if a possible false positive can occur for a given substance on a UDS, one can analyze the chemical structure to review for similarities
 - This is not a concern with UDT
- Many opioids and benzodiazepines are metabolized into active metabolites
 - Metabolites may be commercially available products
- Monitoring frequency can be determined by identifying risk
 - No such thing as too frequent monitoring
 - Can also consider performing random UDM



Audience Questions



Post- Assessment Questions

Post-Assessment Question 1

Which one of the following medications can possibly produce a false positive urine drug screening for methadone?

- A. Ciprofloxacin
- B. Naproxen
- C. Quetiapine
- D. Cyclobenzaprine

Post-Assessment Question 2

A patient using morphine may also show a positive result for _____ on a confirmatory urine drug test.

- A. Codeine
- B. Hydromorphone
- C. Oxycodone
- D. Hydrocodone

Post-Assessment Question 3

Urine drug monitoring should be performed for low-risk patients a minimum of every _____.

- A. 1 month
- B. 3 months
- C. 6 months
- D. 12 months

PCSS Mentoring Program

- PCSS Mentoring Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder (MOUD).
- PCSS mentors are a national network of providers with expertise in **addictions, pain, and evidence-based treatment including MOUD.**
- 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.
- No cost.

For more information visit:

<https://pcssNOW.org/mentoring/>



Providers
Clinical Support
System

PCSS Discussion Forum

Have a clinical question?

Ask a Colleague

A simple and direct way to receive an answer related to medications for opioid use disorder. Designed to provide a prompt response to simple practice-related questions.

<http://pcss.invisionzone.com/register>



Providers
Clinical Support
System

PCSS is a collaborative effort led by the American Academy of Addiction Psychiatry (AAAP) in partnership with:

Addiction Technology Transfer Center	American Society of Addiction Medicine
American Academy of Family Physicians	American Society for Pain Management Nursing
American Academy of Pain Medicine	Association for Multidisciplinary Education and Research in Substance use and Addiction
American Academy of Pediatrics	Council on Social Work Education
American Pharmacists Association	International Nurses Society on Addictions
American College of Emergency Physicians	National Association of Community Health Centers
American Dental Association	National Association of Social Workers
American Medical Association	National Council for Mental Wellbeing
American Osteopathic Academy of Addiction Medicine	The National Judicial College
American Psychiatric Association	Physician Assistant Education Association
American Psychiatric Nurses Association	Society for Academic Emergency Medicine



Providers
Clinical Support
System

Educate. Train. Mentor



[@PCSSProjects](https://twitter.com/PCSSProjects)



www.facebook.com/pcssprojects/

www.pcssNOW.org

pcss@aaap.org

Funding for this initiative was made possible (in part) by grant no. 6H79TI081968 from SAMHSA. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government.