

Drug Monitoring Podcast Series
Prescription and Illicit Drug Testing:
What You Need to Know,
Presumptive and Definitive Testing

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Welcome!

Thank you for joining us today

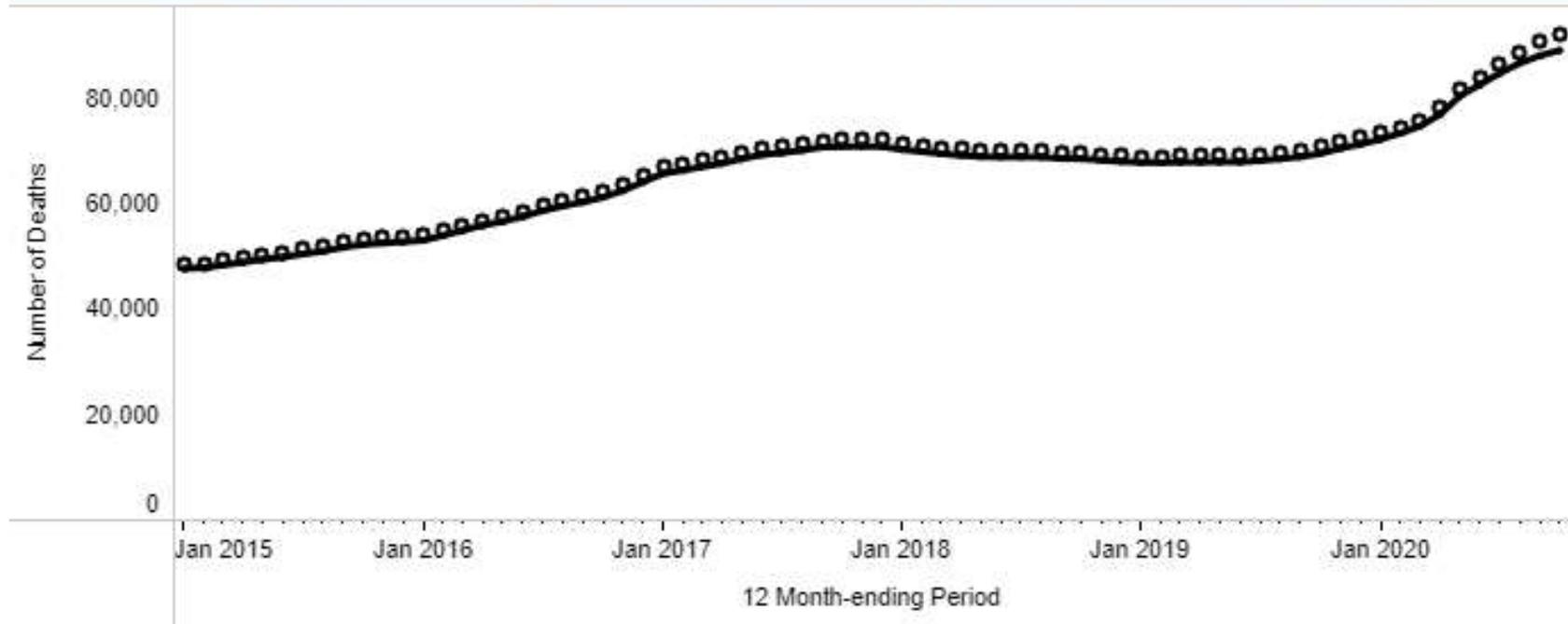
- During today's podcast we will discuss the value of prescription and illicit drug testing and provide insight on the different testing methodologies
- Will discuss and share information regarding:
 1. Current state of the drug misuse epidemic in the US
 2. The value and clinical utility of drug testing
 3. Overview of the 2 main methodologies of drug testing, presumptive testing, and definitive testing

The current state of the drug misuse epidemic in the US

The drug misuse epidemic in the US

Drug overdose deaths at an all-time high

12 Month-ending provisional counts of drug overdose deaths: United States



CDC, *National Vital Statistics System Rapid Release*, accessed June 7, 2021, www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

Quest Health Trends™ publication— The Opioid Epidemic Within the COVID-19 Pandemic: Drug Testing in 2020

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The Opioid Epidemic Within the COVID-19 Pandemic: Drug Testing in 2020

Justin K. Niles, MA, Jeffrey Gudim, MD, Jeff Radcliff, BS, and Harvey W. Kaufman, MD

Abstract

The convergence of the opioid epidemic and the coronavirus disease 2019 (COVID-19) pandemic has created new health care challenges. The authors analyzed changes in clinical drug testing patterns and results at a national clinical laboratory, comparing data obtained before and during the pandemic. Testing for prescription and illicit drugs declined rapidly during the pandemic, with weekly test volumes falling by approximately 70% from the baseline period to the trough (the week beginning March 29) before rising in subsequent weeks. Among individuals tested, positivity increased by 35% for non-prescribed fentanyl and 44% for heroin during the pandemic. Positivity for non-prescribed fentanyl increased significantly among patients positive for other drugs; by 89% for specimens positive for amphetamines; 48% for benzodiazepines; 34% for cocaine; and 39% for opiates ($P < 0.01$ for all comparisons). These findings suggest significant increases in dangerous drug combinations. Positivity for non-prescribed use of many other drugs remained consistent or declined for some drugs, relative to pre-pandemic patterns. Models adjusting for potential confounding variables, including medication-assisted treatment and treatment at a substance use disorder facility indicated that the risk for non-prescribed fentanyl positivity rose by more than 50% during the pandemic. In summary, these findings demonstrate decreased drug testing overall, with increased positivity for high-risk drugs and dangerous drug combinations. The convergence of the drug abuse epidemic and COVID-19 pandemic has led to an increased need for health care and public health resources dedicated to supporting vulnerable patients and addressing the underlying causes of these disturbing trends.

Keywords: clinical drug testing, substance use disorder, COVID-19, SARS-CoV-2, opioid, fentanyl

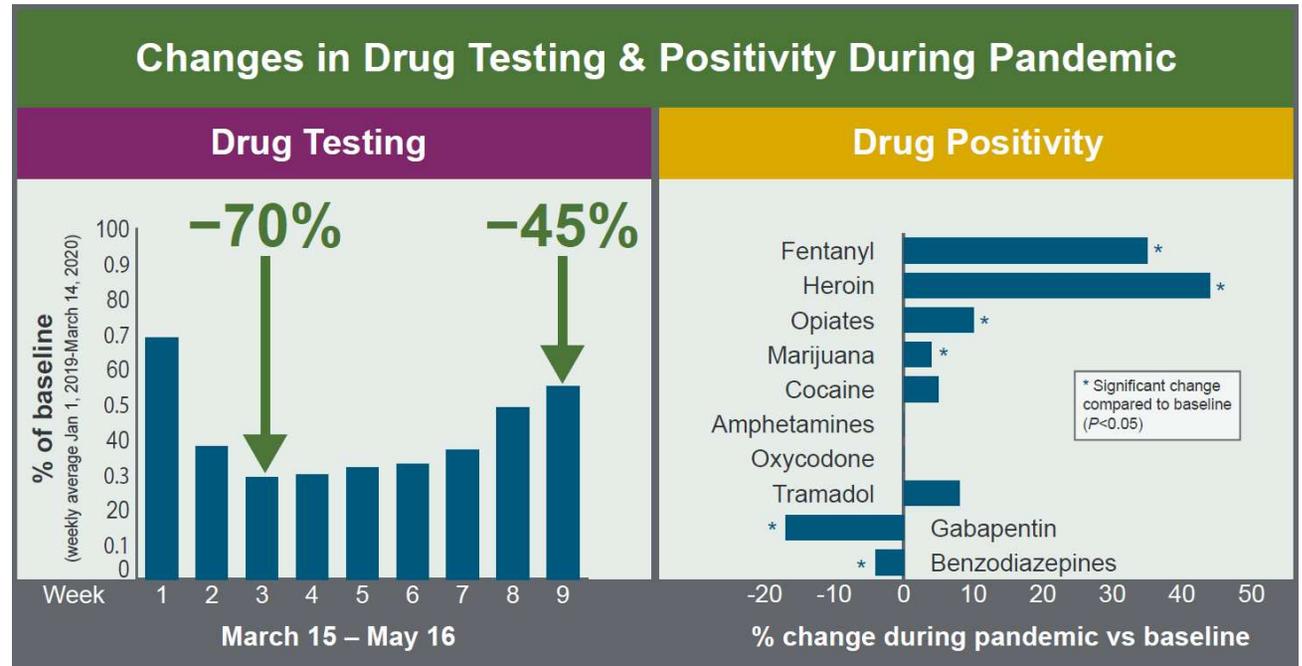
Introduction

The drug epidemic transformed daily life in the United States in innumerable ways. Stay-at-home orders began in various states in March, and by the end of April nearly all states warned their residents to stay home. To help prevent the spread of COVID-19, the Centers for Disease Control and Prevention (CDC) also recommended postponement of medical prevention services that could not be performed virtually.¹ An unfortunate consequence of these measures was a large decline in clinical drug testing (drug testing to assess compliance with prescribed drugs and/or use of non-prescribed/illicit drugs). Despite the mitigation efforts advocated by medical scientists, businesses, and government agencies, COVID-19 has spread rapidly across the United States, with more than 4.3 million confirmed cases resulting in more than 150,000 deaths as of late July 2020.²

More than 750,000 people have died from a drug overdose in the United States from 1999 to 2018,³ with nearly 450,000 deaths involving prescribed or illicit opioids.⁴ The most recent yearly estimates indicate that the overdose epidemic peaked in 2017, with 70,723 reported deaths, followed by a 4.6% decrease in overdose deaths in 2018.⁵ Although progress has been made overall, fentanyl-related deaths threaten to bring deaths from drug overdoses to tragic new heights. The 12-month rolling count of provisional overdose deaths associated with non-methadone synthetic opioids (likely fentanyl) has increased every month since at least January 2015 (5766) through December 2019 (16,309).⁶

Convergence of an epidemic and pandemic Nationally suspended overdose admissions to the Overdose Mapping Application Program (ODMAP) in 2020 rose

Quest Diagnostics, Secaucus, New Jersey, USA.



The value of drug testing— A critical tool to help guide clinical care decisions

Drug Testing

- Drug testing¹
 - Uses a biological sample (urine, saliva, sweat, or hair)
 - To detect the presence or absence of a specific drug (or drugs) as well as drug metabolites
 - Within a specific window of time
- Drug testing is frequently used in clinical, employment, educational, and legal settings¹
 - Screening and diagnosis
 - Treatment and recovery
 - Chronic care management
- Complements self-report, collateral report, and provider assessment¹
- Urine is the most common specimen for drug testing due to its noninvasive route and ease of sample collection²
 - blood, hair, saliva, sweat, nails, and meconium have been used as well
- Clinicians need a basic understanding of drug testing and interpretation²
- Aids in clinical and pharmacological decision making²

1. ASAM Consensus Statement: [https://www.asam.org/docs/default-source/quality-science/appropriate_use_of_drug_testing_in_clinical-1-\(7\).pdf?sfvrsn=2](https://www.asam.org/docs/default-source/quality-science/appropriate_use_of_drug_testing_in_clinical-1-(7).pdf?sfvrsn=2) Clinical and Public Health Considerations in Urine Drug Testing to Identify and Treat Substance Use: <https://doi.org/10.3109/10826084.2015.1135953>

2. Moeller K, et al. Mayo Clin Proc..May 2017;92(5):774-796

Why should you drug test?

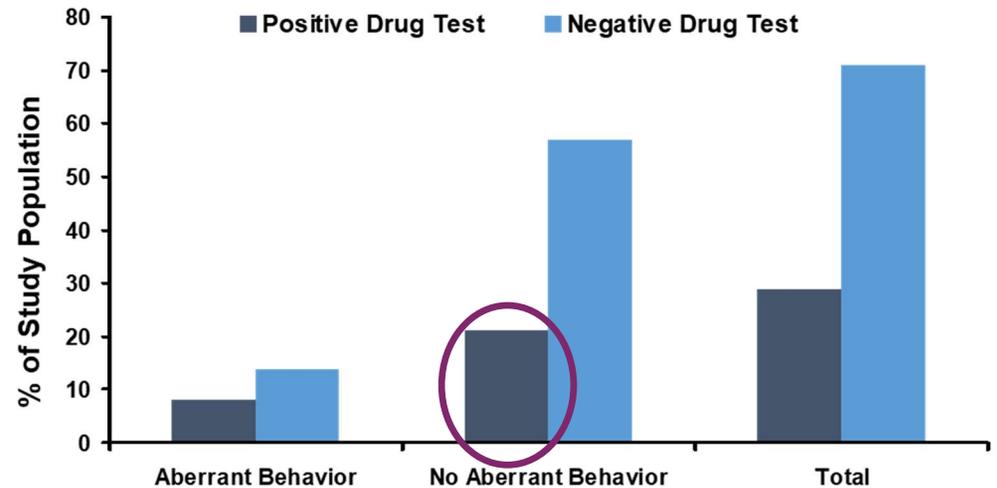
- Manage prescription drug use
 - Positive for prescribed drug(s) of interest
 - Negative for illicit drugs and other prescribed drugs
- Objectively analyze adherence to the plan
- Help diagnosis substance misuse, abuse, and addiction
- Identify patients who may be diverting medications
- Meet expectations of medical boards and regulatory agencies
- Advocate for patients
- PROTECT YOURSELF

Heit HA, Gourlay DL. *J Pain Symptom Manage*. 2004;27:260-267.

Who should be tested?

43% had a "problem" (either positive urine toxicology or one or more aberrant drug-taking behaviors)

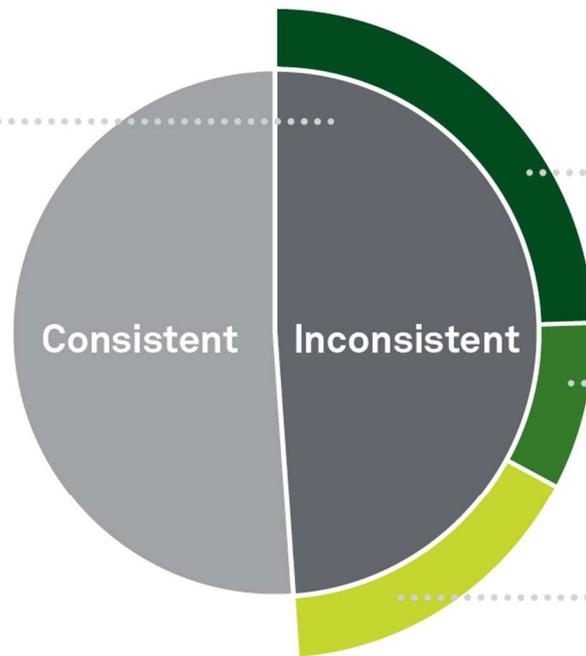
- Of patients with no behavioral issues, 21% had a positive urine screen for either an illicit drug or a nonprescribed controlled medication
- Of patients with a negative urine screen, 14% had 1 or more behavioral issues



N=122 patients on chronic opioid therapy monitored over a 3-year period

Quest drug testing data shows that nearly half of patients misuse their medications¹

48%
of Quest's drug monitoring tests showed signs of misuse



Additional drugs are found

49% combined prescribed drug(s) with at least one other nonprescribed or illicit drug

Different drugs are found

18% did not show prescribed drugs, but were positive for at least one other nonprescribed or illicit drug

No drugs are found

33% did not show the prescribed drugs or any other tested drug

1. Quest Diagnostics Health Trends™, January 2020– December 2020

Drug testing data shows that anyone is at risk

Regardless of gender or age¹

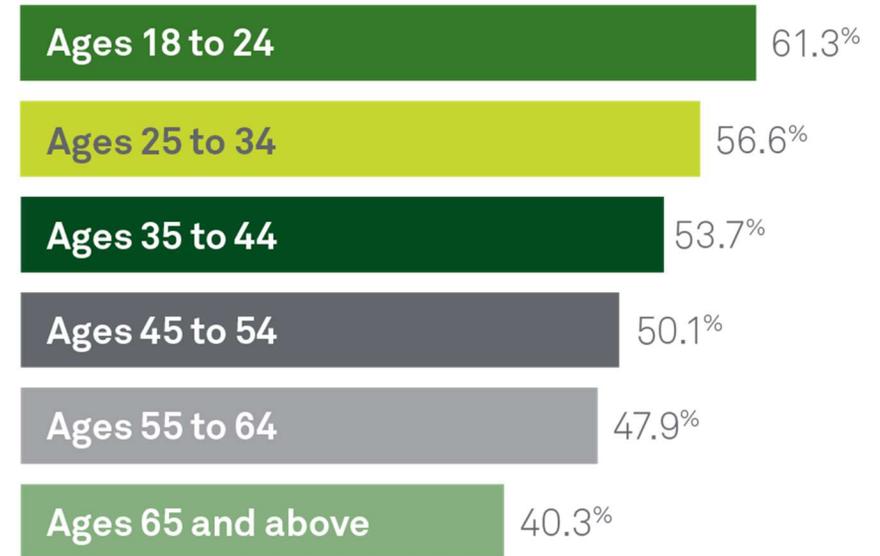
Rates of misuse were virtually identical for males and females



Misuse rates were higher for men and women of reproductive age (15-45)



Misuse remains high across all age groups



Medical and public health organizations support drug testing

- *CDC Guidelines for Prescribing Opioids for Chronic Pain (March 2016)*¹
 - *“When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.”*
- *The American Association for Clinical Chemistry (AACC) Academy–Laboratory Medicine Practice Guidelines: Using Clinical Laboratory Tests to Monitor Drug Therapy in Pain Management Patients (November 2017)*²
 - *“Based on level II evidence, baseline drug testing should be performed prior to initiation of acute or chronic controlled substance therapy. In addition, random drug testing should be performed at a minimum of one to two times a year for low-risk patients (based on history of past substance abuse/addiction, aberrant behaviors, and opioid risk screening criteria), with increasing frequency for higher-risk patients prescribed controlled substances.”*
- *The American Society of Addiction Medicine (ASAM) Appropriate Use of Drug Testing in Clinical Addiction Medicine, consensus statement (April 2017)*³
 - *“Drug testing should be a routine part of initial and ongoing patient assessment of recent substance use in all addiction treatment settings.”*

1. CDC Guidelines for Prescribing Opioids for Chronic Pain: <https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm>

2. AACC: <https://www.aacc.org/science-and-practice/practice-guidelines/using-clinical-laboratory-tests-to-monitor-drug-therapy-in-pain-management-patients>

3. ASAM: https://journals.lww.com/journaladdictionmedicine/Fulltext/2017/06000/Appropriate_Use_of_Drug_Testing_in_Clinical.1.aspx

Types of drug testing / monitoring

Qualitative – result that tells you if a substance or drug is present in the specimen (positive, negative, trace amount)

Quantitative – result that identifies the presence of a substance along with the numerical amount of that drug or substance present (2 mg/dl, 120 mcg/dl)

Presumptive – Identifies possible use or non-use of a drug or drug class. May be followed by definitive drug identification

Definitive – Drug identification is able to identify individual drugs. It can be qualitative or quantitative.

Therapeutic – Therapeutic drug assays are performed to monitor response to prescribed medications. Test can be performed with whole blood, serum, plasma, or spinal fluid.

The 2 main types of drug tests: Presumptive & Definitive

Presumptive Drug Testing

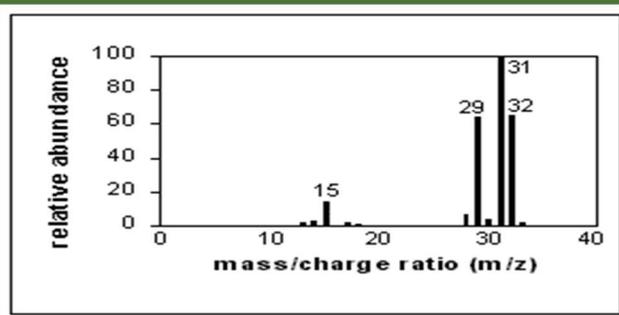


- Initial drug screens (presumptive tests) can be conducted in the laboratory or onsite with point-of-care testing (POCT)
- Presumptive testing typically uses an immunoassay (IA) to differentiate “negative” from “presumptive positive” specimens
- Immunoassays allow for a large number of analytes to be screened and provide relatively rapid results
 - Unfortunately, immunoassays will detect substances with similar characteristics, resulting in cross-reactivity leading to false positive results
- Antibody cross reactivity to the antigen (drug/metabolites) may be broad or narrow and all results that are equal to or greater than the cutoff are considered to be “presumptive”
 - Immunoassays cannot provide definitive identification of what drug/metabolites are present, and
 - False-positive results cannot be distinguished from true-positive results

Example:

- Cross reactivity example: ibuprofen and marijuana

Definitive Drug Testing



- Uses a method with high sensitivity and specificity
- Identifies specific molecules and quantifies the amount of a drug or substance present in the sample
- Definitive assays rule out “false-positive” results and identify “true-positive” drugs/metabolites
- Contemporary methods utilize gas or liquid chromatography combined with mass spectrometry as the “gold standard” method to identify drugs/metabolites

Examples of mass spectrometry include:

- Gas or liquid chromatography-tandem mass spectrometry (GC or LC/MS/MS)
- Liquid chromatography-time of flight mass spectrometry (LC/TOF)

Definitive tests may be qualitative or quantitative

Disclaimer: Confirmatory testing should always be conducted when making legal, forensic, academic, employment, or other decisions that have significant sequelae.

How do clinicians decide which test to choose?

Presumptive Test

Chemistry Instrumentation or Mass Spectrometry

- Testing is performed at the drug class level
- Qualitative results are produced
- If result is negative, testing ends
- If result is presumptive positive, further testing is needed to identify the drugs/metabolites

Presumptive Positives confirmed by Definitive Test (if ordered)

Presumptive positive tests are followed by confirmation testing, if ordered

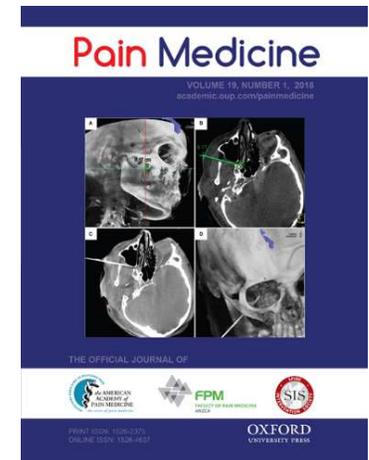
Mass Spectrometry Definitive Test

Definitive test is performed using Mass Spectrometry

- Drug(s) and metabolite(s) are identified
- Qualitative or quantitative results are reported
- Confirmations and Direct-to-Definitive

Rational urine drug monitoring in patients receiving opioids for chronic pain: consensus recommendations (AAPM)

- To develop consensus recommendations on urine drug monitoring (UDM) in patients with chronic pain who are prescribed opioids
- Definitive testing is recommended as most clinically appropriate for UDM because of its accuracy; however, institutional or payer policies may require initial use of presumptive testing (ie, immunoassay)
- The rational choice of substances to analyze for UDM involves considerations that are specific to each patient and related to illicit drug availability
- Appropriate opioid risk stratification is based on patient history (especially psychiatric conditions or history of opioid or substance use disorder), prescription drug monitoring program data, results from validated risk assessment tools, and previous UDM
- Urine drug monitoring is suggested to be performed at baseline for most patients prescribed opioids for chronic pain and at least annually for those at low risk, 2 or more times per year for those at moderate risk, and 3 or more times per year for those at high risk. Additional UDM should be performed as needed on the basis of clinical judgment



Clinicians need to focus on:

Safe use of prescription medications

- Opioids (MOUD)
- Benzodiazepines
- Psychostimulants
- Gabapentinoids
- Muscle Relaxants
- Antidepressants
- Antipsychotics
- ADHD drugs

Detection of illicit drugs and other substances

- Alcohol/Nicotine
- Marijuana
- Cocaine
- Methamphetamine
- Heroin/Fentanyl
- Synthetic and designer drugs
- Kratom
- Bath Salts...

Conclusions

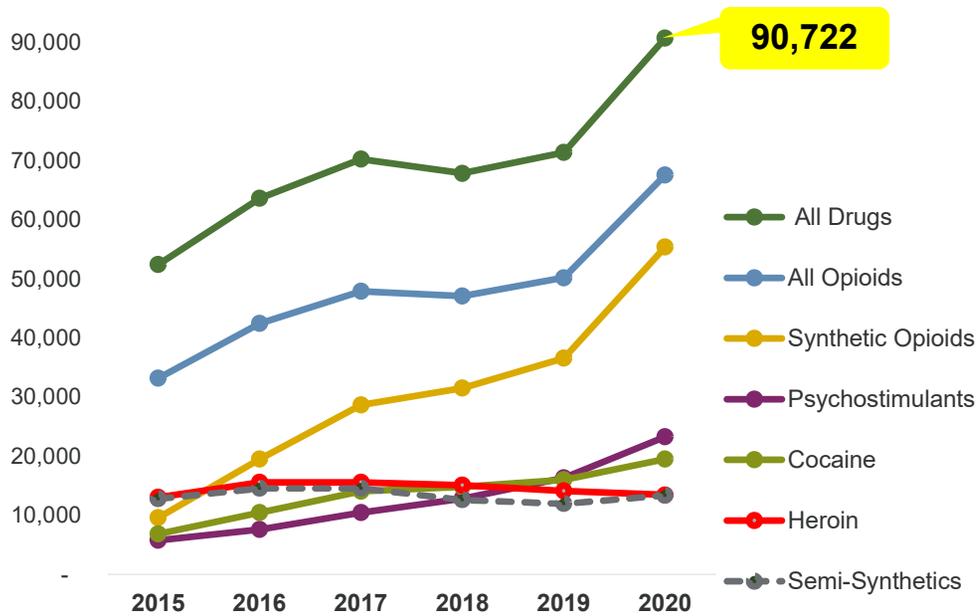
- Clinicians who prescribe controlled substances must develop risk management strategies including skill sets in drug testing as well as mitigation of drug misuse and abuse
- **Drug monitoring is standard of care when managing patients on controlled substances**
- Communicate with your laboratories and toxicologists to ensure proper interpretation of test results
 - 1.877.40.RX.TOX (1.877.407.9869)
- More structured therapy with comprehensive monitoring plans can help patients adhere to opioid-based treatment regimens, especially those who are higher risk or display aberrant behaviors
- Better guidelines for drug monitoring are needed from regulatory agencies and medical societies

BACK UP SLIDES

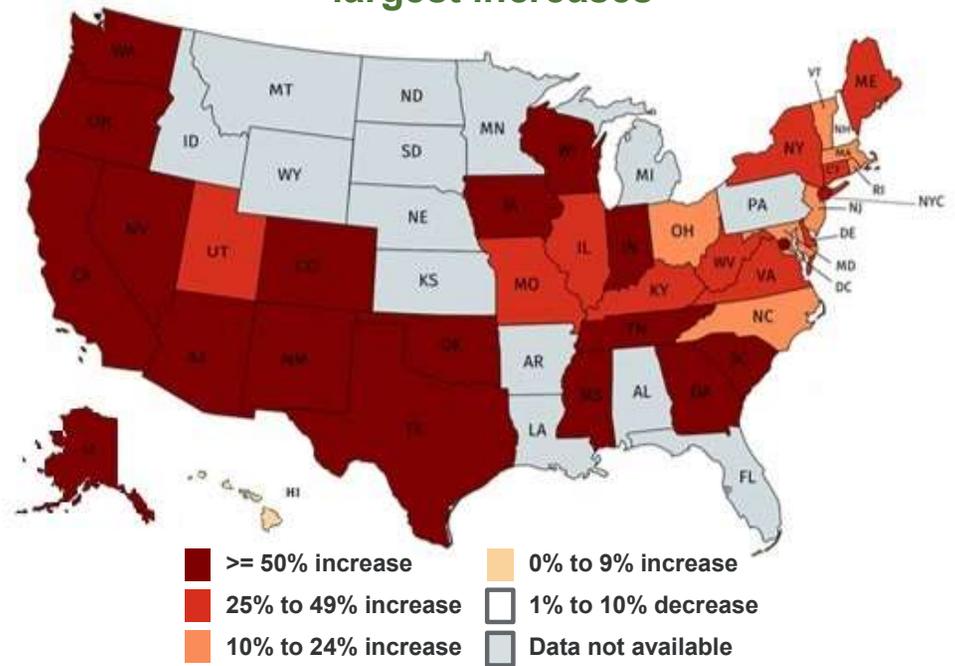
Despite efforts, overdose deaths have exceeded 90,000 in 2020*

Largest increases recorded from March 2020 to May 2020 during the pandemic

Fentanyl is driving the most overdoses



Western half of the country shows the largest increases



<https://emergency.cdc.gov/han/images/HAN-438-figure3.jpg> , <https://emergency.cdc.gov/han/2020/han00438.asp>

*Estimate based on provisional data- through November 2020, CDC: <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>

Drug testing terminology

- Effective 2015, the American Medical Association (AMA) Current Procedural Terminology (CPT) publication defined presumptive and definitive as intuitive terms to describe drug testing for use or non-use of drugs
 - Qualitative and Quantitative were used previously to describe drug testing but are now obsolete
- Presumptive testing is always reported qualitatively as either Negative or Presumptive Positive
- Definitive testing can be reported qualitatively (negative or + drug/metabolite identified) or quantitatively (quantitation of drugs/metabolites)

Drug testing terminology (continued)

- Analyte
 - The component of a sample that is identified and measured, eg, parent drug or metabolite
 - Presence indicates exposure to a substance or family of substances within window of detection
- Presumptive testing
 - Uses a method with lower sensitivity and/or specificity
 - Establishes preliminary evidence regarding the absence or presence of drugs or metabolites in a sample
- Definitive testing
 - Uses a method with high sensitivity and specificity
 - Gas or liquid chromatography combined with mass spectrometry is the “gold standard” method
 - Can identify specific drugs, their metabolites, and/or drug quantities

Other common terminology

Preliminary	Definitive
Immunoassay	Chromatography – mass spectrometry
Presumptive	Confirmatory
Qualitative	Quantitative
Point-of-care / in-office / lab-based	In-office / lab-based
Screen	Confirmation
Semi-quantitative / quasi-quantitative	Absolute level, creatinine corrected
Simple test (cup / strip / dip / cassette)	Complex test

Adulteration / Specimen Validity

- People misusing drugs commonly use various methods (eg, adulteration, urine substitution, diluting urine) to avoid detection
- The temperature of the urine sample should be recorded within the first 4 minutes after collection and is usually between 90F and 100F.¹⁸
- Urine pH ranges between 4.5 and 8
- Specific gravity ranges between 1.002 and 1.030
- Urine creatinine concentrations should be greater than 20 mg/dL
 - concentrations less than 20 mg/dL are indicative of dilute urine, whereas those less than 5 mg/dL combined with a specific gravity of less than 1.001 are not consistent with human urine

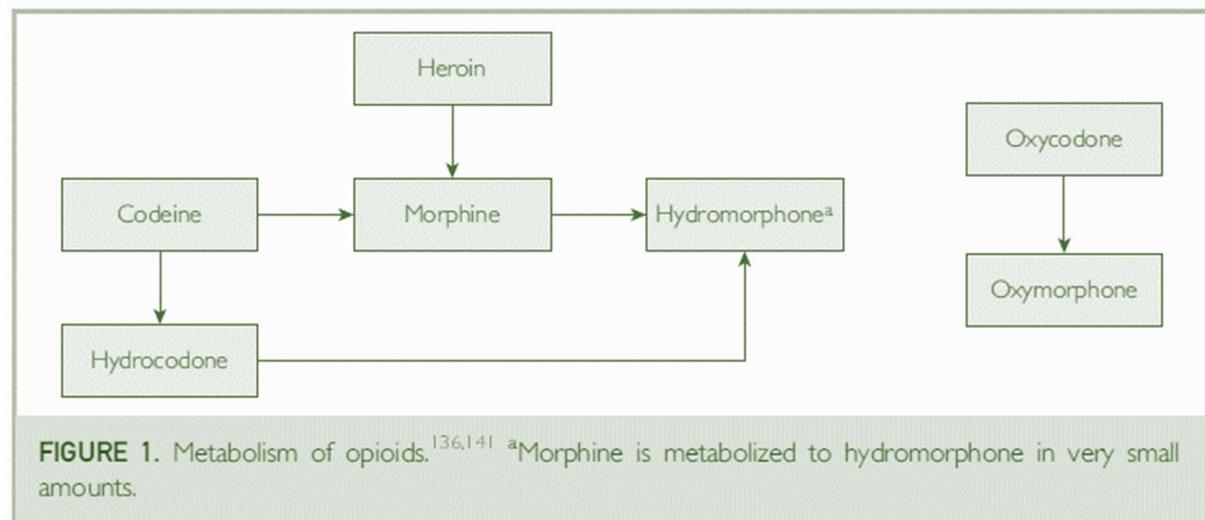
Urine Luck!

- Adulterants that have been used to mask a person's use of a substance include household items such as table salt, laundry bleach, toilet bowl cleaner, vinegar, lemon juice, ammonia, or eye drops
- Several select commercial adulterants containing glutaraldehyde (Clean X), Sodium or potassium nitrite (Klear, Whizzies), pyridinium chlorochromate (Urine Luck), and peroxide/peroxidase (Stealth) are used to mask drug use¹
- Most household adulterants, except for eyedrops, can be detected by routine specimen integrity assessment

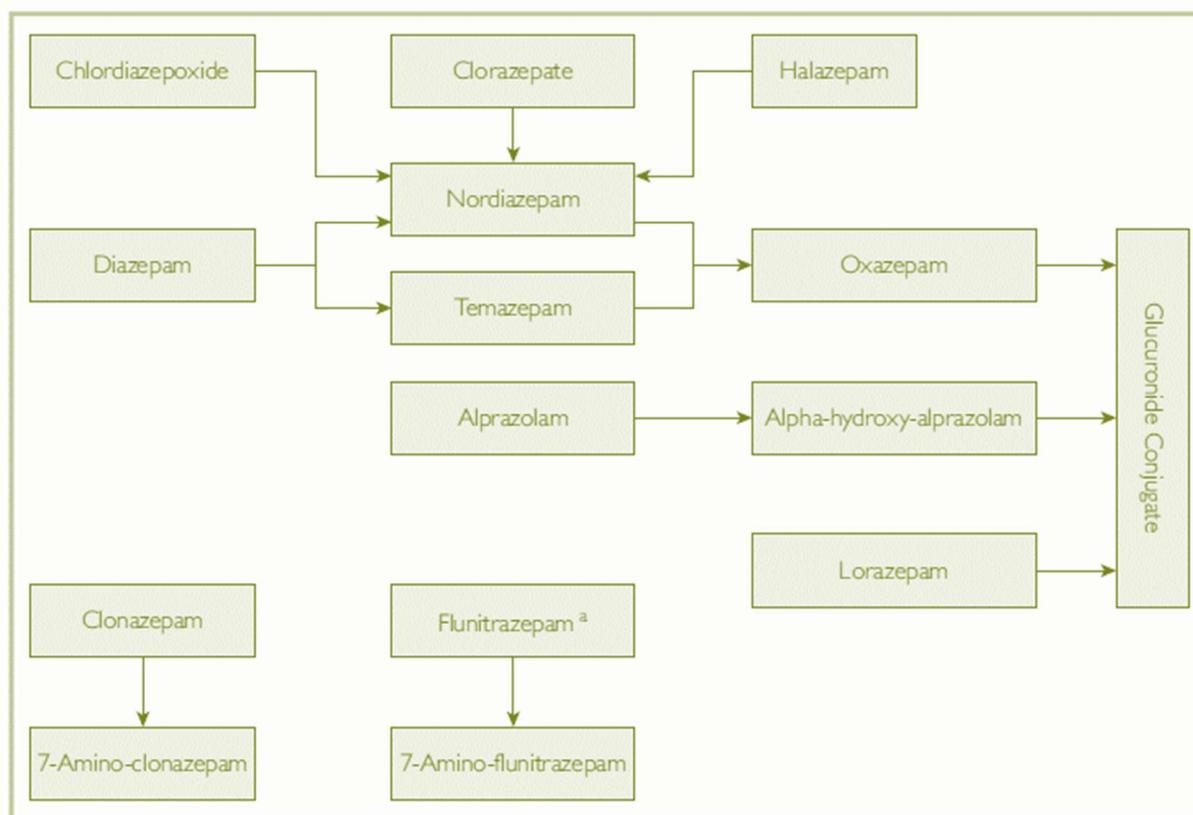
1. Jaffee WB, Trucco E, Levy S, Weiss RD. Is this urine really negative? A systematic review of tampering methods in urine drug screening and testing. *J Subst Abuse Treat.* 2007;33(1):33-42.

Understanding the Results

- UDT can be complex with perplexing results
- Clinicians need a basic understanding of drug metabolism



Benzodiazepine Metabolism



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