


Trends in Opioid Misuse and Abuse

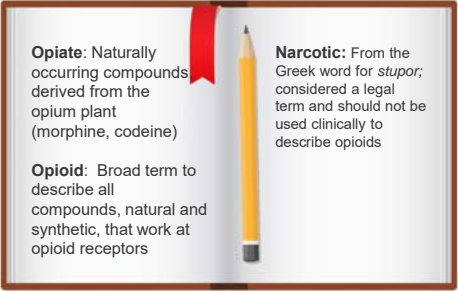
Objectives

- Describe landscape and trends in opioid misuse and abuse
- Identify pharmacology and physiologic effects of opioids
- Discuss consequences of misuse, abuse, and addiction
- Discuss efforts designed to mitigate the risk of opioid use



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Opioid Terminology

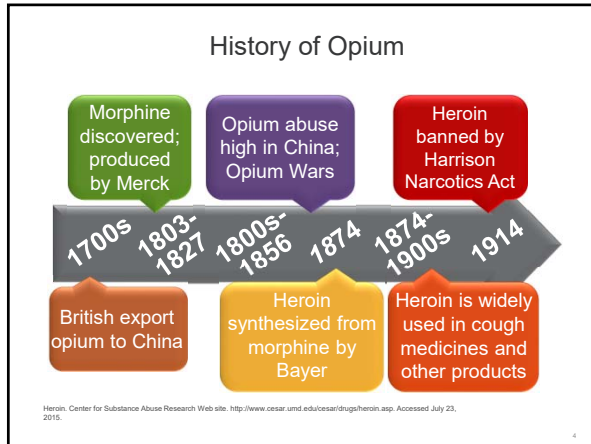


Opiate: Naturally occurring compounds derived from the opium plant (morphine, codeine)

Opioid: Broad term to describe all compounds, natural and synthetic, that work at opioid receptors

Narcotic: From the Greek word for *stupor*; considered a legal term and should not be used clinically to describe opioids

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Opioid Mechanism of Action and Effects

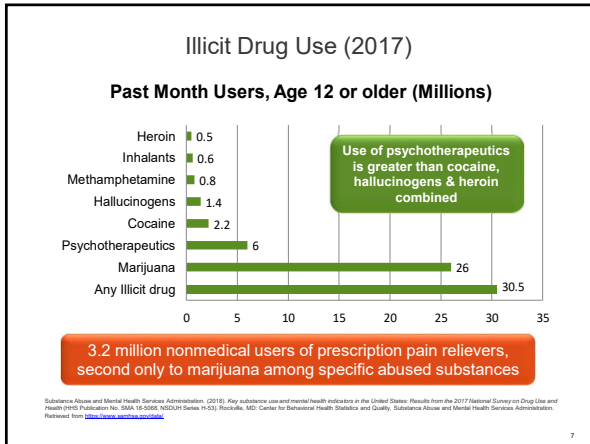
- Central nervous system depressants bind to opioid receptors
- Effects
 - Reduced perception of pain
 - Drowsiness, mental confusion, nausea, constipation, slowed breathing
 - Potential for euphoria

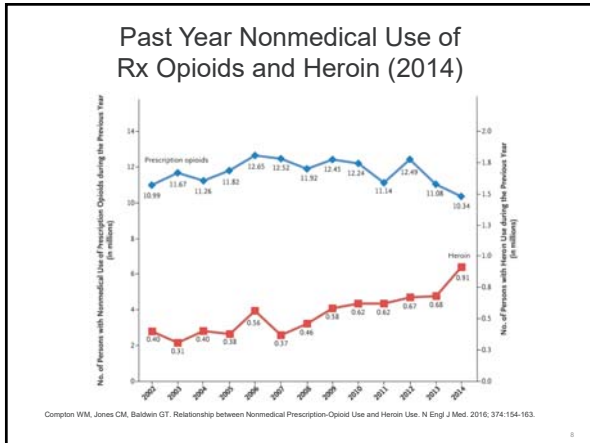
The diagram shows a human silhouette with the brain, spinal cord, and internal organs highlighted in red and blue, representing the central nervous system.

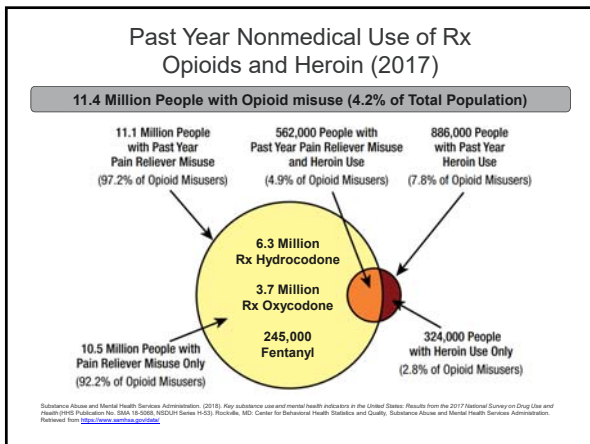
Concerns Related to Opioid Therapy

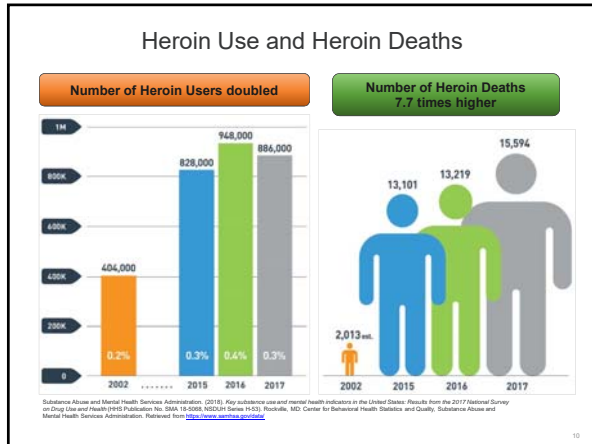
Misuse¹ Use of medication for purposes other than as directed or indicated	Abuse¹ Use of any illicit drug with intentional self-administration of medication for nonmedical purposes, such as altering consciousness
Addiction² A primary, chronic, neurobiological disease with genetic, psychosocial & environmental factors influencing its development and manifestations; characterized by one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving	Diversion¹ Intentional removal of medication from legitimate distribution and dispensing channels for illicit sale or distribution

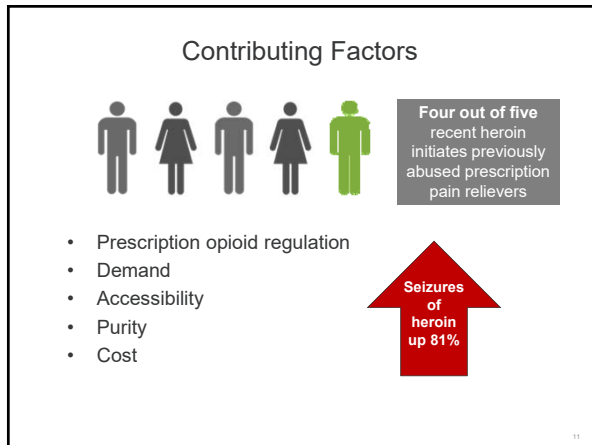
1. Katz N, et al. Challenges in the development of prescription opioid abuse-deterrent formulations. Clin J Pain. 2007;23(7):648-656.
2. American Society of Addiction Medicine (ASAM) Public Policy Statement: Definition of Addiction. http://www.asam.org/docs/public-policy-statements/definition_of_addiction_long_4-11.pdf?shvsn=2. Published August 15, 2011. Accessed October 1, 2012.











Heroin

- Chemical Name: Diacetylmorphine
- Schedule I in US
- Typically injected but may also be snorted or smoked
- Street Names:

❖ Smack	❖ Brown	❖ China White
❖ Dope	❖ 'H'	❖ Boy
❖ Junk	❖ Big H	❖ Harry
❖ Mud	❖ Horse	❖ Mr. Brownstone
❖ Skag	❖ Charley	❖ Dr. Feelgood
❖ Brown Sugar		
- Speedball = heroin + cocaine

Heroin. Center for Substance Abuse Research Web site. <http://www.cesar.umt.edu/cesar/drugs/heroin.asp>. Accessed July 23, 2015.

Effects of Heroin

Onset

}

IV
7-8 seconds

IM
5-8 minutes

Smoked or Snorted
10-15 minutes

- Acute Effects:** Euphoria, skin flushing, dry mouth, heavy extremities, impaired mental function, slowed breathing
- Long-Term Effects:** Collapsed veins, abscesses, infections, liver disease, lung complications

Addiction, overdose, death

Heroin, Center for Substance Abuse Research Web site: <http://www.oesar.umd.edu/oesar/drugs/heroin.asp>. Accessed July 23, 2015.

Who Is Using?

Opioid Pain Relievers

Heroin

1. Increases in Heroin Overdose Deaths — 29 States, 2010 to 2012. Morbidity and Mortality Weekly Report. Centers for Disease Control and Prevention Web site, October 3, 2014. http://www.cdc.gov/mmwr/mmwr/mortmorbidity0416a4.htm?_id=m416a4_w

2. Stabli L. Heroin, C. Infections caused by prescription painkiller abuse, USA. Today May 8, 2015. <http://www.usatoday.com/story/news/2015/05/07/heroin-cause-infections-painkiller/2807748/>

3. U.S. Dept. of Health and Human Services. Addressing Prescription Drug Abuse in the United States. Sept. 2013. <http://www.hhs.gov/ondcp/prescription-drug-abuse-report-09-2013.pdf>

4. Hansen RN, Oster G, Eisenberg J, Wooley GE, Sullivan SD. Economic costs of nonmedical use of prescription opioids. Clin J Pain. 2011;27(3): 194-202.

Public Health Consequences¹⁻⁴

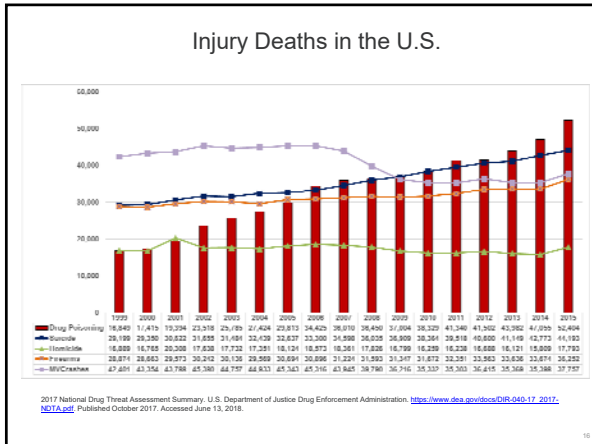
- HIV, Hepatitis B and C and other blood borne pathogens
- Increased utilization of healthcare, lost productivity and crime
- Treatment center admissions
- Overdose
- Death

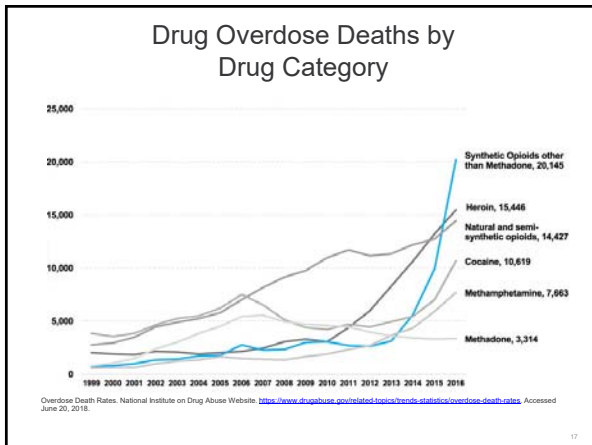
1. Community Outbreak of HIV Infection Linked to Injection Drug Use of Opiomorphine — Indiana, 2015. Morbidity and Mortality Weekly Report. Centers for Disease Control and Prevention Web site. May 1, 2015. http://www.cdc.gov/mmwr/mmwr/mortmorbidity0516a4.htm?_id=m416a4_w

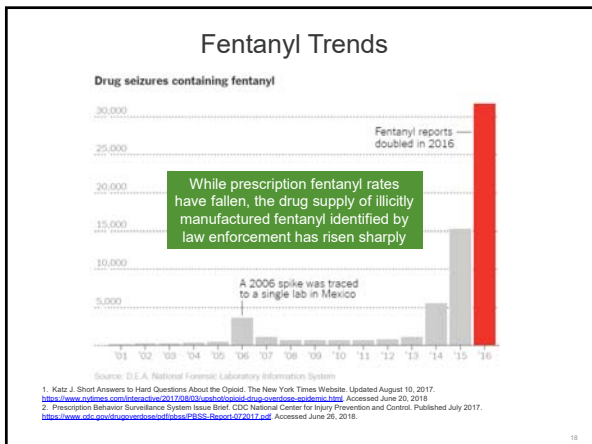
2. Stabli L. Heroin, C. Infections caused by prescription painkiller abuse, USA. Today May 8, 2015. <http://www.usatoday.com/story/news/2015/05/07/heroin-cause-infections-painkiller/2807748/>

3. U.S. Dept. of Health and Human Services. Addressing Prescription Drug Abuse in the United States. Sept. 2013. <http://www.hhs.gov/ondcp/prescription-drug-abuse-report-09-2013.pdf>

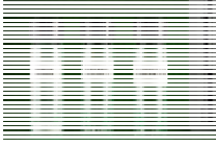
4. Hansen RN, Oster G, Eisenberg J, Wooley GE, Sullivan SD. Economic costs of nonmedical use of prescription opioids. Clin J Pain. 2011;27(3): 194-202.







Fentanyl and Fentanyl Analogues



Credit: Bruce A. Taylor, NH State Police Forensic Lab



- Fentanyl: 50-100 times more potent than morphine
- Fentanyl Analogues (e.g. carfentanil, furanyl fentanyl, acetyl fentanyl): up to 10,000 times more potent than morphine
- Street Names: Apache, China White, Dance Fever, Goodfella, Jackpot, Murder 8, TNT, and Tango and CashChina

1. 2017 National Drug Threat Assessment Summary, U.S. Department of Justice Drug Enforcement Administration. <https://www.dea.gov/docs/DR-046-17-2017-NDTA.pdf> Published October 2017. Accessed June 13, 2018.
 2. Fentanyl, National Institute on Drug Abuse Website. <https://www.drugabuse.gov/drug-abuse/fentanyl> Accessed June 20, 2018.

Photograph used with authors' permission

U-47700



- Schedule I synthetic opioid
- 7.5 times the potency of morphine
- Responsible for at least 80 deaths in 2016
- Street names: U4, Pink, or Pinky

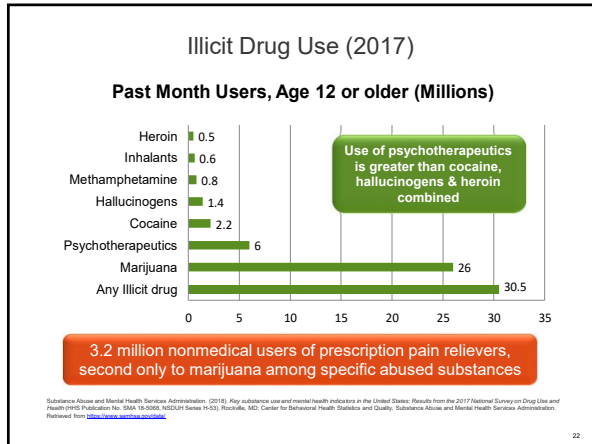
1. 2017 National Drug Threat Assessment Summary, U.S. Department of Justice Drug Enforcement Administration. <https://www.dea.gov/docs/DR-046-17-2017-NDTA.pdf> Published October 2017. Accessed June 13, 2018.
 2. U-47700, Drug Enforcement Agency Website. <https://www.justice.gov/eaad/press-releases/47700> Accessed June 20, 2018.

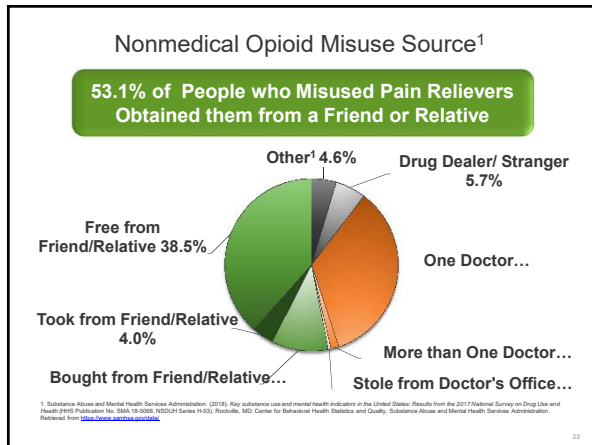
Prevention and Treatment Strategies

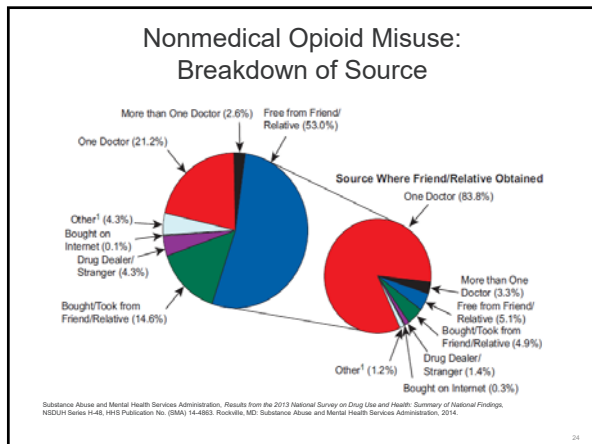
- Responsible opioid prescribing
- Substance use disorder treatment access and research
- Overdose prevention measures
- Education and social awareness

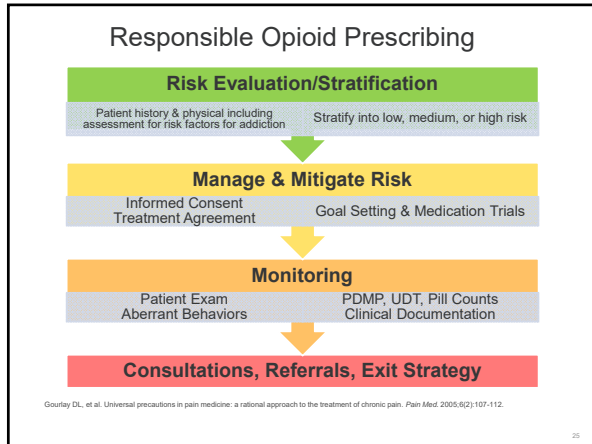


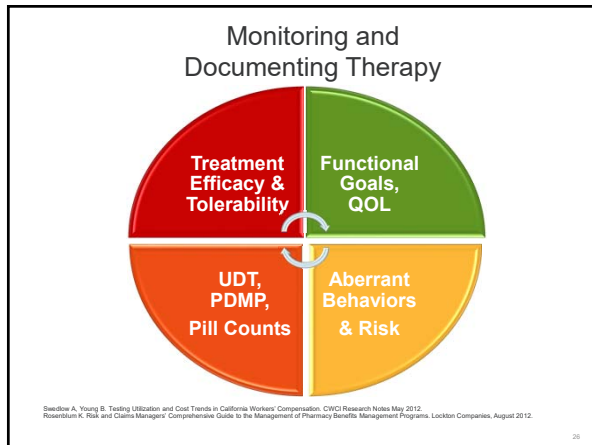
Not an actual patient or clinician

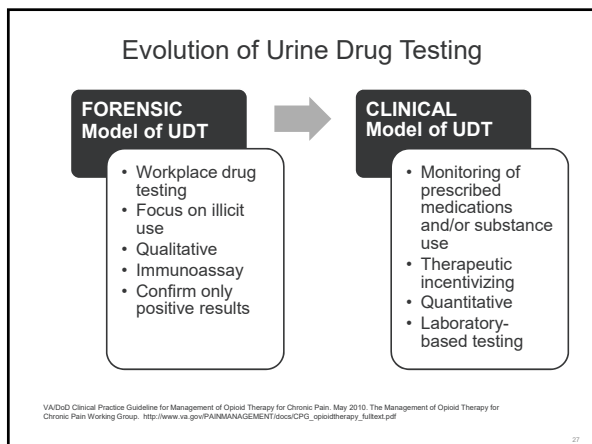













Clinical Settings

Urine Drug Testing is utilized in numerous settings:

- Pain Management/Chronic Opioid Therapy (COT)
- Substance Use Treatment
 - Office-Based Treatment
 - Addiction Treatment Facilities
- Primary Care
- Psychiatry
- Obstetrics



Urine Drug Testing (UDT) Rationale

UDT provides objective information to support improved clinical decision making.

UDT helps clinicians to:

- Monitor and support decisions about medication therapy, particularly controlled substances
- Identify recent use of prescription medications, non-prescribed medications, and illicit substances
- Detect medications that may result in drug-drug interactions
- Advocate for and communicate with patients about individual treatment plans
- Identify possible illicit drug or medication abuse, misuse, or diversion

Types of UDT

Presumptive Immunoassay Screen	Definitive Mass Spectrometry
In-office Point-of-Care (POC), or Laboratory Qualitative	Laboratory Quantitative (GC-MS or LC-MS/MS)
Minutes (POC) or days (Lab)	Hours to days
Drug classes and some select meds/substances	Specific medications, substances, and metabolites
Guidance for preliminary treatment decisions	Definitive quantitative results
Higher cutoff levels and cross-reactivity common; more false positives and false negatives	Lower cutoff levels. False positive and false negative results are rare

The clinician must choose testing method based on the needs dictated by the patient's history, presentation, community factors and treatment plan goals. The clinician's rationale for test and the analytes ordered must be documented in the patient's medical record.

False Negative vs. False Positive Most Common with Presumptive/Immunoassay-based Tests

False Negative: <i>The test fails to detect the presence of the drug or metabolites!</i>	False Positive: <i>The test incorrectly detects the presence of the drug when none is present!</i>
Primary Reasons Include: <ul style="list-style-type: none"> Higher cutoffs compared to mass spec. IAs unable to effectively identify some substances (e.g., lorazepam) 	Primary Reason: <ul style="list-style-type: none"> Cross-reactivity
Potential Adverse Impact on Patient: <ul style="list-style-type: none"> Undetected illicit use Accused of drug diversion Not receive ongoing meds Drug interactions 	Potential Adverse Impact on Patient: <ul style="list-style-type: none"> Discharged from practice Not having access to care Legal decisions – lose family, return to jail

¹ Center for Substance Abuse Treatment. (2012). Clinical drug testing in primary care. Technical Assistance Publication (TAP) Series, 32. DHS Publication No. (SMA) 12-4668. Rockville, MD: Substance Abuse and Mental Health Services Administration. Available: <http://www.kap.samhsa.gov/products/manuals/pdf/TAP32.pdf>.

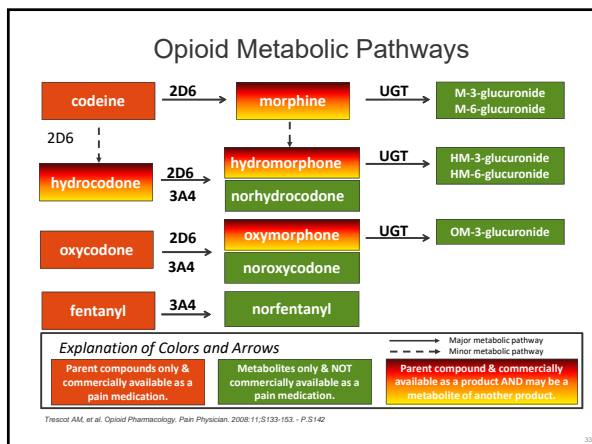
Addressing Unexpected Results

Providers should not always interpret unexpected results as abuse, misuse, or diversion

Numerous factors may contribute to unexpected UDT results¹⁻³:

- Patient medication use
- Time of the last dose
- Undiscovered or unknown over-the-counter or prescription medication use
- Type of testing
- Pharmacogenetics
- Drug-drug interactions

¹ Sourley DL, Heit HA, Caplan YH. Urine Drug Testing in Clinical Practice: the Art and Science of Patient Care. PharmaCom Group, Inc. <http://www.pharmacomgroup.com/udt/udt.pdf>. Accessed March 14, 2013.
² Christo PJ, Manoharan L, Buan X, Bottros M, et al. Urine Drug Testing in Chronic Pain. Pain Physician 2011; 14: 123-143.
³ Reisdorf GM, Goodberger, BA, Birchhoff RL. False-positive and false-negative test results in clinical urine drug testing. Bioanalysis 2009; 1(5): 937-52.



Heroin Metabolism

CC(=O)OC1C=CC2C3CC4=C5C2(C1OC5=C(C=C4)OC)C3
Heroin

100%
2-6 minutes

CC1C=CC2C3CC4=C5C2(C1OC5=C(C=C4)OC)C3
6-Monoacetylmorphine
6-MAM

100%
6-25 minutes

CC1C=CC2C3CC4=C5C2(C1OC5=C(C=C4)OC)C3
Morphine

Concentration
Cmax
Tmax
Time

"The Abuse Quotient" = Cmax/Tmax

Cmax: maximum concentration
Tmax: time to max concentration

Yee DA, Hughes MM, Adaya RS, Best BM, Pease AJ. Observations on the Relationship between Opioid Medications, Illicit Drugs and Heroin Use in Pain Patients. *Am. J. Pharm. & Theroc.* 2011; 5 (4): 5-10.
<http://www.ddsmag.com/articles/2009/07/question-opioid-euphoria>

Not an actual patient

Meet "Michael"


- 28-year-old male, history of heroin use disorder and hepatitis C
- Has received office-based treatment for opioid dependence from Dr. Gibbons for 6 months in addition to counseling
- Current medications:
 - Buprenorphine/naloxone (Suboxone®)
 - Ledipasvir-sofosbuvir (Harvoni®)

Substance Use Monitoring *Urine Drug Testing*

- American Society of Addiction Medicine (ASAM) recommends urine drug testing as a key diagnostic and therapeutic tool, useful for patient care and in monitoring the ongoing status of a person treated for addiction¹
- "Drug use during treatment must be monitored continuously"²
 - Awareness of monitoring can be an incentive
 - Monitoring may identify an early indication of a relapse and need to adjust the treatment plan
- Each test should be based on individual patient situation in support of the treatment plan

1. American Society of Addiction Medicine. Public Policy Statement On Drug Testing as a Component of Addiction Treatment and Monitoring Programs and in other Clinical Settings. <http://www.asam.org/docs/public-policy-statements/1drug-testing-clinical-10-10.pdf>?hlrs=0. Adopted July 1, 2002; Revised October 1, 2010; Accessed February 13, 2014.

2. National Institute on Drug Abuse. Principles of Drug Addiction Treatment: A research-based guide, 3rd ed. NIH Publication No. 09-4180. http://www.drugabuse.gov/sites/default/files/principles_1.pdf. Printed October 1999; Revised December 2012. Accessed December 27, 2012.



Not an actual patient


Case: "Michael"

Per published guidelines, Michael's physician utilizes urine drug testing to monitor prescribed drug therapy, as well as monitor for illicit and non-prescribed drug use.

In-Office Test Result	
Test	Result
Buprenorphine	Negative
Opiate	Positive

Based on these results, does it appear Michael is taking his medication?

What might the opiate positive mean on a urine drug screen?

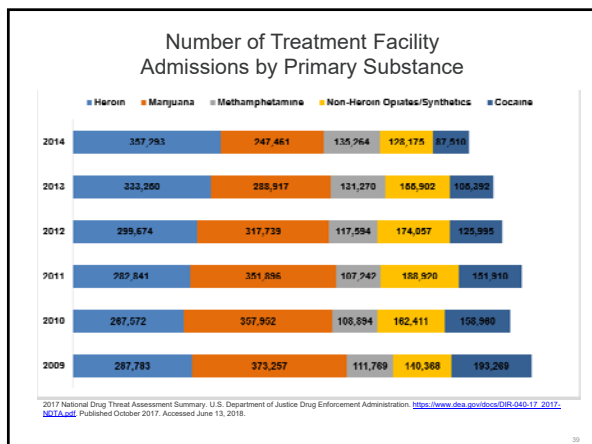


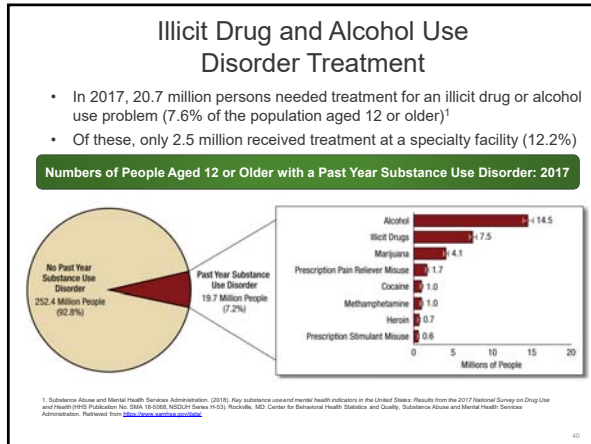
Not an actual patient

Case: "Michael"

LC-MS/MS Laboratory Test Results		
Test	Result	Creatinine Normalized Results (ng/mL)
Buprenorphine	Negative	0
Norbuprenorphine	Positive	86
Naloxone	Negative	0
6-MAM	Positive	163
Codeine	Positive	234
Morphine	Positive	8,536
Fentanyl	Positive	4
Norfentanyl	Positive	26

How might these test results impact Michael's treatment?

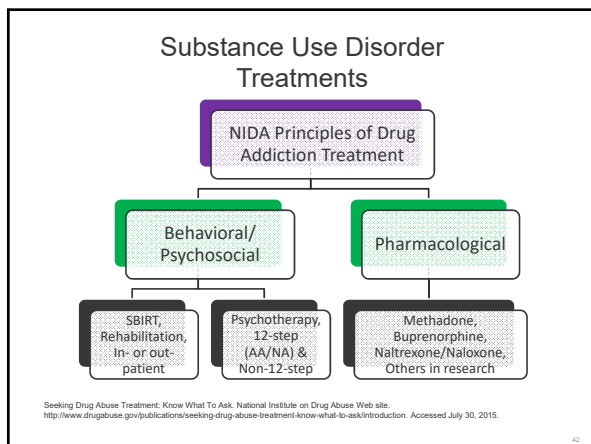




Addiction as a Chronic Disease

Addiction	Hypertension
30-60% Genetic	25-50% Genetic
40-60% Relapse	50-70% Relapse
Initial choices: alcohol/drug	Initial choices: food, activity
Potential permanent physiological changes	Potential permanent physiological changes
Abstinence and medications do not reverse disease	Lifestyle changes and medications do not reverse disease
< 50% adhere to drug abstinence 1 year post-treatment	< 40% adhere to medication, 30% adhere to lifestyle changes

McElran AT, Lewis DC, O'Brien CP, Kieber HD. Drug dependence, a chronic medical illness: implications for treatment, insurance, and outcomes evaluation. JAMA. 2000 Oct; 284(13): 1689-95.



Education

- National Institute on Drug Abuse – www.drugabuse.gov
- Centers for Disease Control and Prevention – www.cdc.gov
- Drug Enforcement Administration – www.justthinktwice.com
- Partnership for Drug Free Kids – www.drugfree.org



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Medical Necessity

Criteria to establish medical necessity must be based on patient-specific elements identified during the clinical assessment and documented in the patient's medical record by the provider.

Documenting Medical Necessity

- Orders must be individualized
- Tests ordered and reasons for testing must be documented in the patient's medical record
- Risk assessment and stage of treatment should match testing frequency

Documenting How the Test Results Were Used

- Review of results and use in the treatment plan

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Summary

- While drug-poisoning deaths involving opioid analgesics has leveled in recent years, the rate for deaths involving heroin is on the rise
- Heroin is widely available and has become increasingly pure while prices drop
- Young adults have the highest rates of heroin overdose deaths and treatment center admissions
- A combination of strategies are being employed to address opioid misuse, abuse, and diversion
- Understanding the benefits and limitations of the various types of UDT is critical for providers to appropriately apply the results

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