Drug testing for patients with substance use disorders in medication assisted treatment (MAT)

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Drug misuse and abuse

- Abuse of tobacco, alcohol, and prescription and illicit drugs is costly to our nation, estimated at more than $740 billion annually
  - Costs related to crime, lost work productivity, and health care
  - OUD (opioid use disorder) is a medical condition with substantial morbidity and mortality
- More than half of new illicit drug use begin with marijuana. Next most common are prescription pain relievers, followed by inhalants (which is most common among younger teens)[1]
- Most guidelines recommend screening patients to determine risks of drug abuse
  - Tools include questionnaires: PDMPs and urine (or other) drug testing
- Urine drug testing provides objective evidence for medication compliance and aberrant drug behavior
  - May be the only objective tool that informs clinicians what drugs or substances a patient has consumed
  - Detects and confirms presence of prescribed and illicit drugs

Medication assisted treatment

- Medication-assisted treatment (MAT) is the use of medications with counseling and behavioral therapies to treat substance use disorders (SUDs) and prevent overdose[2]
  - Research shows that a combination of medication and therapy can effectively treat these disorders and help sustain recovery
- The prescribed medications in MAT may block the euphoric effects of opioids, relieve physiological cravings, and normalize body functions without the negative effects of the abused drug
- MAT Rx includes methadone, buprenorphine, and naltrexone
  - People may safely take medications used in MAT for months, years, several years, or even a lifetime

Goals of MAT (optional)

- MAT usually provided at opioid treatment programs (OTPs)
  - Federal law requires patients to also receive medical, counseling, vocational, educational, and other assessment and treatment services
- MAT has proven to be clinically effective and to significantly reduce the need for inpatient detoxification services
- The ultimate goal of MAT is full recovery, including the ability to live a self-directed life. This treatment approach has been shown to:
  - Improve patient survival
  - Increase retention in treatment
  - Decrease illicit opiate use and other criminal activity among people with substance use disorders
  - Increase patients' ability to gain and maintain employment
  - Improve birth outcomes among women who have substance use disorders and are pregnant

MAT medications

- Methadone – opioid agonist that prevents withdrawal; dispensed only in specialty regulated clinics
- Naltrexone – office-based opioid antagonist that blocks the effects of opioids; daily (or QoD) pill or monthly injection
- Buprenorphine – office-based opioid partial agonist that reduces withdrawal risks while potentially blocking other opioids; daily dissolving sublingual tablet, cheek film, or 6-month implant under the skin
  - Available as buprenorphine (subutex) or buprenorphine/naloxone (suboxone)
- For a clinician to treat SUD/OUD from their office using buprenorphine, a “waiver” is required from SAMHSA
  - Usually drug abuse treatment occurs in licensed outpatient/inpatient facilities
  - Clinicians can be “waived” from this requirement with education (CMEs)
  - Limits to number of patients who can be maintained on buprenorphine

Drug testing for MAT

- Patient self-report is often insufficient to determine status of substance use
  - Drug testing provides another source of information to complement self-report, collateral report, and provider assessment
- The primary purposes of drug testing in the context of MAT are:
  - Detecting substance use that could complicate treatment
  - Monitoring adherence with the prescribed medication
  - Monitoring possible diversion
- Urine drug testing (UDT) is important when conducting initial comprehensive evaluation and for monitoring compliance with prescribed MAT (methadone or buprenorphine)
- Drug tests play an important role in patient safety because they can identify potentially lethal drug combinations, such as benzodiazepines, alcohol, and opioids
- UDT must be interpreted in context of overall clinical presentation and is not a replacement for clinical judgment
  - Even observed tests are subject to manipulation

Drug testing

- Typically drug testing is performed in one of two ways:
  - Presumptive: usually by immunoassay
    - Rapid; “point-of-care” or lab-based; qualitative;
    - Susceptible to false-positive reactions, eg, reacts to lookalike compounds, as well as false-negatives based on cut-off values
  - Definitive: usually GC or LC-MS: lower incidence of false negatives compared to traditional tests
    - Lower screening cutoffs afforded by sensitive instrumentation
    - Selective detection by MS technology not dependent on cross-reactivity
- Clinicians should have a basic understanding of drug testing, what to order, basic result interpretation and understand the limitations of the tests available
  - For example, what substances are detected by a specific test, and the reasons for false-positive and false-negative reports
- Prior to drug testing, patients should be informed of the reason(s) for testing, how often they will be tested, and what the results might mean
  - Gives them an opportunity to disclose drug use (obviating need for further testing) and identify any additional drug or substance use which may cause a false-positive

Drug testing for MAT (optional)

- Drug tests are designed to detect whether a substance has been used within a precise window of time. The biological sample or specimen can be various matrices: urine, saliva, blood, and hair are some examples
  - Drug testing should be used as a tool for supporting recovery rather than as a punishment. Every effort should be made to persuade patients that drug testing is a therapeutic, rather than punitive, component of treatment
- What to test for is also important
  - A 2017 ASAM white paper states: ‘‘The most important challenge in drug testing today is not the identification of every drug we are technologically capable of detecting, but to do medically necessary and accurate testing for those drugs that are most likely to impact clinical outcomes.’’
- Due to its inherent limitations, drug testing should not be relied upon as the sole measure of a patient’s substance use

How to drug test for methadone or buprenorphine

- Methadone is metabolized primarily to 2 pharmacologically inactive metabolites: (EDDP and EMDP). Monitoring for the presence of EDDP by drug testing is a means to determine compliance with methadone treatment
  - Drug testing looks for both parent drug (methadone) and metabolite (EDDP)
- Buprenorphine is metabolized to a pharmacologically active metabolite, norbuprenorphine
- Buprenorphine and norbuprenorphine are excreted in urine almost exclusively as glucuronides with very little free drug being detected
  - Urine drug testing assesses both the parent (buprenorphine) and metabolite (norbuprenorphine) to ensure no “pill shaving” has occurred

Specimen collection

- Proper specimen collection procedures are critical for ensuring an adequate urine sample for drug testing
- The internet provides advice on a host of mechanisms for defeating urine drug tests that range from simple to sophisticated. The most easily accomplished methods for tampering with a urine sample are:
  - Adding water or other fluids or substituting a previously collected sample.
  - Simple specimen validity checks (described below) can identify most samples that have been adulterated
- Supervised sample collection is recommended to discourage tampering and increase the utility of testing
  - Direct observation of the specimen is optimal but invasive and often not practical in a clinical office setting
- Urine samples are collected in a private bathroom without running water, soap, or other liquids, and with toilet water stained blue. No outer clothing, bags, or brief cases are permitted in the bathroom

Specimen validity

- Regardless of collection procedures, validity checks are recommended for all urine specimens
  - Temperature checked immediately after voiding (temperature strips that fluoresce between 90-100^{0} degrees F)
  - Creatinine is a product of muscle metabolism that can be used as a marker of urine concentration
    - Urine samples with a random creatinine between 2 and 20 mg/mL should be considered dilute; a specimen with a creatinine less than 2 mg/mL should be considered substituted (not urine) or artificially diluted (water has been added)
  - Specific gravity
  - pH
  - Nitrites

Ways to tamper with urine specimen

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Confirmation

- Enzyme-linked IA tests are relatively quick, inexpensive, and easy to perform and as such are often used by laboratories as a first-line screen
  - This testing format identifies drugs or metabolites above a certain threshold concentration in the urine
  - Typically the threshold concentration is set high enough to limit detection of low levels of drugs or metabolites that may be found in foods
- IA is non-specific and cross-reactions can occur. As an example:
  - Quinolone antibiotics can cross-react with an opioid panel yielding a false-positive test result
  - To eliminate this type of error, IA tests should be confirmed with a more definitive chromatographic test (eg, GC-MS), particularly if a test result is unexpected and does not correlate with a patient's history

A drug test will be negative despite ongoing drug use when:

- The window of detection has passed
  - The window of detection for most substances is 2-3 days and drug use will not be detected after this period. One notable exception: heavy, chronic use of cannabis, which can result in prolonged excretion for up to 4 weeks, complicating interpretation during this period
- The patient has used a substance not detected by the testing panel
  - While nearly any substance can be tested for in urine, standard test panels are limited to commonly used substances. For example, synthetic cannabinoids are not detected by standard tests for cannabis and should be ordered separately if use is suspected. Inhalants are excreted by the lungs and cannot be detected in a urine specimen
- The concentration of the substance is below the detection limit of the test
  - This is uncommon with definitive tests which are typically very sensitive but may occur with POC IA tests which typically have a set cut-off threshold. Intentional urine dilution may result in a falsely negative test
- The specimen has been substituted or adulterated
  - Proper specimen collection techniques (see above), use of temperature testing, and adulterant panels can minimize opportunities for interfering with testing

Summary: Quest Diagnostics

- The abuse and misuse of prescription drugs remans an epidemic in the US
- Quest serves 1 in 3 adult Americans and half the physicians and hospitals in the United States
  - Quest Diagnostics has the world's largest database of clinical lab results; our diagnostic insights help improve healthcare management
- A properly implemented drug testing program is an important step in tackling drug misuse and abuse
- By performing more than 10 million drug tests annually, Quest Diagnostics has the experience to help you implement a successful PDM program—one that helps protect your practice, safeguards your patients, and keeps your community safe
  - Rx Tox Line available to help clinicians with test ordering or result interpretation

References

1 National Institute on Drug Abuse. Nationwide Trends. Published June 25, 2015. Accessed December 17, 2019. https://www.drugabuse.gov/publications/drugfacts/nationwide-trends

2 Substance Abuse and Mental Health Services Administration. Medication-assisted treatment overview. Published May 7, 2019. Accessed December 17, 2019. https://www.samhsa.gov/medication-assisted-treatment/treatment#medications-used-in-mat