Interpretation of Drug Testing Results in Medication Assisted Treatment

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What Does This Result Mean?

Two-Step Testing Approach

- screening test designed to separate negative samples from samples that are "presumptively" positive
- confirmation test follow-up procedure designed to validate positive test results
- why can't you adjudicate based on the screening test results?
- FALSE POSITIVES

- screening tests can and do react to "non-target" compounds
 - amphetamines
 - benzodiazepines
- obtain list of interfering compounds from lab or on-site test vendor
- study results have demonstrated accuracy rates for initial screening tests as low as 70%
- confirm positive results

Typical Cutoff Levels screening & confirmation

- amphetamines *
- benzodiazepines
- cannabinoids *
- cocaine (crack)*
- opiates (heroin) *
- phencyclidine (PCP) *
- alcohol

500 ng/mL 300 ng/mL 20 & 50 ng/mL 150 ng/mL 300/2000 ng/mL 25 ng/mL 20 mg/dL 250 ng/mL variable 15 ng/mL 100 ng/mL variable 25 ng/mL 10 mg/dL

* SAMHSA (formerly NIDA) drugs

What is a "cutoff" level ?

- cutoffs are not designed to frustrate CJ professionals
- a drug concentration, *administratively* established for a drug test that allows the test to distinguish between negative and positive sample - "threshold"
- cutoffs provide important safeguards:
 - scientific purposes (detection accuracy)
 - legal protections (evidentiary admissibility)
- measured in ng/mL = ppb

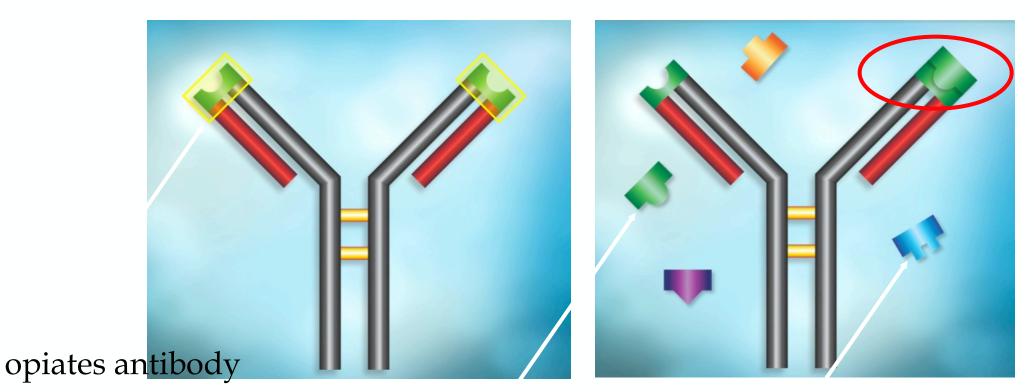
Cutoffs and False Positives

as you lower the cutoff level of a drug test

you increase the potential for false positive test results

How Do Drug Tests Work?

Immunoassay screening tests



opiates fit = positive test

methadone doesn't fit = negative test

100%
200%
80%
75%
45%
20%





(300 ng/mL opiate cutoff test)





If oxycodone is a major substance of abuse in your jurisdiction, you should consider a separate drug test for oxycodone as part of your initial screening analysis.

Result Interpretation for MAT Drugs

Medication-Assisted Treatment (MAT) is a form of pharmacotherapy and refers to any treatment for a substance use disorder that includes a pharmacologic intervention as part of a comprehensive substance abuse treatment plan with an ultimate goal of participant recovery with full social function.

Medication-Assisted **Treatment in Drug Courts**

Recommended Strategies





LEGAL

ACTION

Conclusions

- Scientific evidence overwhelmingly shows that MAT is a critical tool in the treatment of opioid addiction and essential in fighting the opioid epidemic.
- Drug treatment courts can play a key role in ensuring that participants have access to this effective, evidence-based treatment.

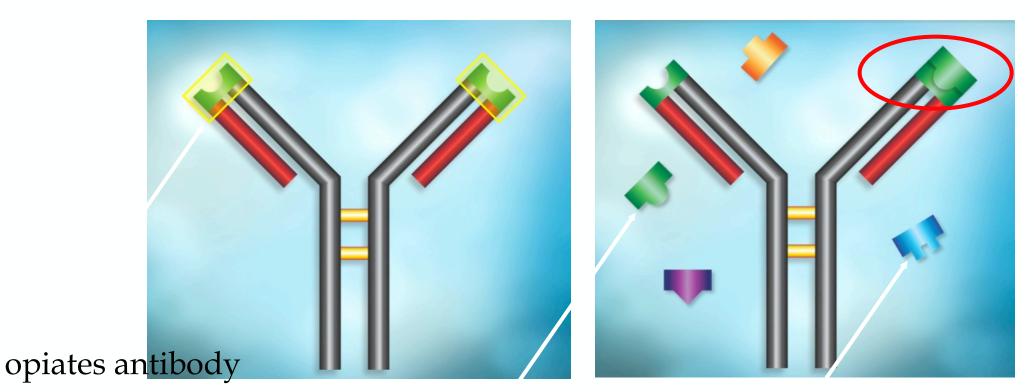
MAT Drugs

- Medications for Alcohol Dependence
 - Naltrexone: (ReVia[®], Vivitrol[®], Depade [®])
 - Disulfiram: (Antabuse[®])
 - Acamprosate: (Campral[®])
- Medications for Opioid Dependence
 - Methadone:
 - Buprenorphine: (Suboxone[®] and Subutex[®])
 - Naltrexone: (ReVia[®], Vivitrol[®], Depade [®])

What is Naltrexone?

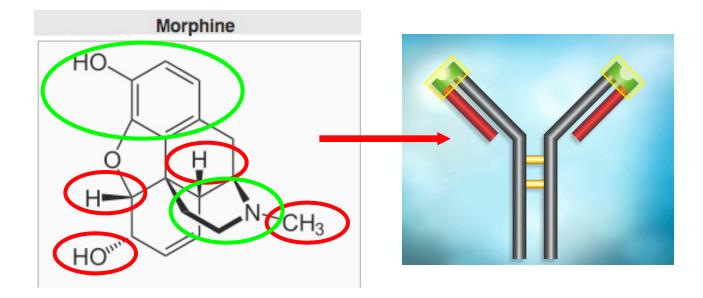
- belongs to a class of drugs known as opiate antagonists
- block the brain's neurotransmitters
- displaces opiates from their binding site
- diminishes physical effects of opiates
- will naltrexone test positive on an opiate drug test?

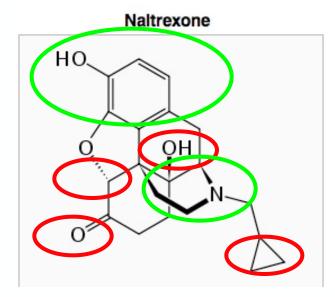
Immunoassay screening tests



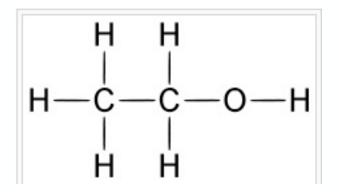
opiates fit = positive test

methadone doesn't fit = negative test





Ethanol



EMIT[®] II PLUS - OPIATE

Negative

The compounds below were negative for the Opiate 300 and 2000 cutoffs at the concentrations shown except where noted. Concentrations listed are in µg/mL.

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Nylidrin 1000				
			Nylidrin	1000

Siemens EMIT Assay Cross-Reactivity Data

Myoglobin	287
Naltrexone	1000
NAPA (N-Acetylprocainamide)	400
Naproxen	1000

= 1,000,000 ng/mL

CEDIA® Opiate Cross-Reactivity Table For catalog #s 100089, 100098 & 1661248

POSITIVE COMPOUNDS

The following compounds tested POSITIVE on the CEDIA® DAU Opiate assay at the 300 ng/mL cutoff.

Positive Compounds	Trade Name	Concentration Tested (ng/mL)
6-Monoacetylmorphine		370
Clomipramine HCI	Anafranil	500,000
Codeine		240
Cyclazocine		500,000
Cyamemazine		31,125
Diacetylmorphine	Heroin	570
Dihydrocodeine	DHC Plus, Synalgos-DC	600
Hydrocodone	Lortab, Vicodin	625
Hydromorphone	Dilaudid	530
Levorphanol tartrate	Levo-Dromoran	100,000
Morphine		300
Morphine SO4	MS Contin, MSIR, Oramorph SR, Roxanol	100,000
Morphine-3-glucuronide		370
Morphine-6-glucuronide		640
Nalorphine HCI		100,000
Naloxone	Narcan	6,000
Naltrexone HCI	Depade, ReVia	50,000
Ofloxacin	Floxin	100,000
Oxycodone	OxyContin	320,000
Pholcodine		500
Rifampin	Rifadin	65,000
Thebaine		1,250

Abstract: A clinical evaluation of the naltrexone, a biodegradable sustained-release dosage was carried out in 4 healthy normal males.

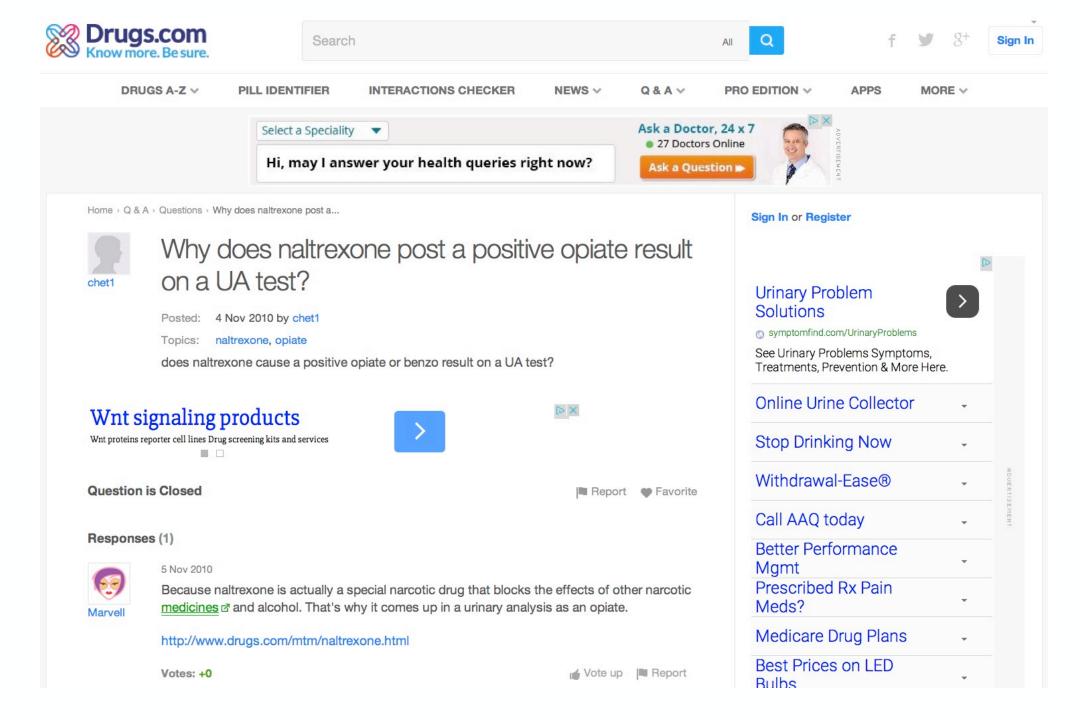
Subjects were given an intravenous dose of 10 mg naltrexone and approximately 1 week later a 63-mg dose of naltrexone by subcutaneous administration.

Urine levels for naltrexone were 79-215 ng/mL.

Naloxone	Narcan	6,000
Naltrexone HCI	Depade, ReVia	50,000
Ofloxacin	Ploxin	100,000

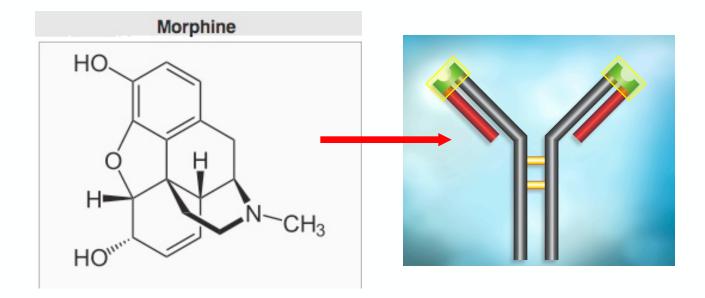
MAT Drugs

- Medications for Alcohol Dependence
 - Naltrexone: False Positive with Opiate Assay -NO!
 - Disulfiram: (Antabuse[®])
 - Acamprosate: (Campral[®])
- Medications for Opioid Dependence
 - Methadone:
 - Buprenorphine: (Suboxone[®] and Subutex[®])
 - Naltrexone: False Positive with Opiate Assay -NO!



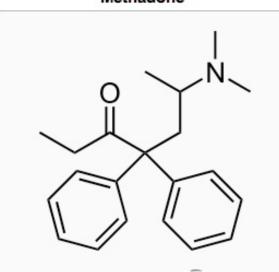
Opiates - Results Interpretation

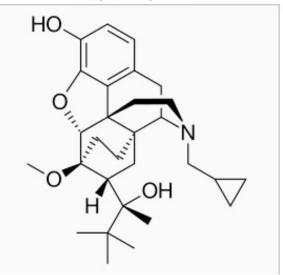
- all opiates are narcotic analgesics
 relieve pain & controlled substances
- not all narcotic analgesics are opiates
 - meperidine (Demerol[®])
 - propoxyphene (Darvon[®])
 - methadone
 - pentazocine (Talwin[®])
 - fentanyl (Sublimaze[®])
 - buprenorphine:_(Suboxone^{®)}
 - naltrexone: (ReVia[®], Vivitrol[®], Depade [®])



Methadone

Buprenorphine





Siemens Negative Reactivity Data

Azithromycin	1000
AZT (Zidovudine)	2000
Benazepril	1000
Benzoylecgonine	1000
Buprenorphine	1000
Bupropion	1000
Caffeine	1000

Thermo-Fisher Negative Reactivity Data

Negative Compounds	Trade Name	Concentration Tested (ng/mL)
Bromocriptine mesylate	Ergoset, Parlodel	500,000
Brompheniramine	Dimetane, Dimetapp, Nasahist, ND- Stat, Oraminic II	500,000
Bupivacaine	Marcaine, Ochsoreaine	500,000
Buprenorphine	Buprenex	100,000
Bupropion	Wellburn, Zyban	100,000

Siemens Negative Reactivity Data

Metaproterenol	1000
Metformin	1000
Methadone	100
d-Methamphetamine	35
Methaqualone	1500

Thermo-Fisher Negative Reactivity Data

Metaproterenol hemisulfate salt	Alupent, Metaprel	500,000	
Metaraminol bitartrate	Aramine	500,000	
Methadone HCI	Dolophine	500,000	
Methamphetamine	Desoxyn	500,000	
Methaqualone HCI	Normi-Nox, Pallidan, Somnomed, Quaalude	100,000	

MAT Drugs

- Medications for Alcohol Dependence
 - Naltrexone: False Positive with Opiate Assay -NO!
 - Disulfiram: (Antabuse[®])
 - Acamprosate: (Campral[®])
- Medications for Opioid Dependence
 - Methadone: NO! with Opiate Assay
 - Buprenorphine: NO! with Opiate Assay
 - Naltrexone: False Positive with Opiate Assay -NO!



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MAT Drugs

- Medications for Alcohol Dependence
 - Naltrexone: False Positive with Opiate Assay -NO!
 - Disulfiram: NO! with drug tests reviewed
 - Acamprosate: NO! with drug tests reviewed
- Medications for Opioid Dependence
 - Methadone: NO! with Opiate Assay
 - Buprenorphine: NO! with Opiate Assay
 - Naltrexone: False Positive with Opiate Assay -NO!

Result Interpretation for Therapeutic/OTC Drugs

Very Difficult Task

not all drug tests are created equal

 laboratory-based tests (numerous products)
 on-site, instant, POC tests (dozens of products)
 each test has unique selectivity (i.e. ability to distinguish between similar compounds

 hundreds of therapeutic drugs
 hundreds of OTC medications

Court's Obligation

- limit use of therapeutic drugs
 - court must be notified
- prohibit the use of OTC medications without prior approval
- prohibit the use of dietary supplements, energy drinks, homeopathic substances, herbal products, sports nutrition powders, anything not regulated by FDA (anything from GNC)

An Interpretational Gift!

Opiate Metabolites

Parent Drug: Codeine Metabolites: Norcodeine,Morphine, (hydrocodone potential minor metabolite in high codeine doses)

Parent Drug: Morphine Metabolites: Normorphine

Parent Drug: Heroin Metabolites: 6-monoacetyl morphine (6-AM), Normorphine, Morphine

Parent Drug: Oxycodone Metabolites: Oxymorphone, Noroxycodone, Noroxymorphone

Opiate Metabolites

Parent Drug: Hydrocodone Metabolites: Hydromorphone, Norhydrocodone

Parent: Hydromorphone (may only as parent drug) Metabolites: undetectable conjugated metabolites

Benzo Metabolites

Parent: Alprazolam Metabolites: alpha-hydroxyalprazolam

Parent: Lorazepam Metabolites: Detected as parent drug; undetectable metabolites

Parent: Clonazepam Metabolites: 7-aminoclonazepam

Parent: Diazepam Metabolites: Temazepam, Nordiazepam, Oxazepam

Benzo Metabolites

Parent: Temazepam Metabolites: Oxazepam

Parent: Chlordiazepoxide Metabolites: Norchlordiazepoxide, Nordiazepam, Oxazepam

Parent: Triazolam Metabolites: only as parent drug; undetectable metabolites

Parent: Clorazepate Metabolites: Nordiazepam, Oxazepam

Therapeutic/OTC Drugs

Drug/Class

Potential F/P Results

- antihistamines/decongestants
- Adderall

amphetamines

amphetamines

- confirm by GC/MS ensure no methamphetamine
- chlordiazepoxide

benzodiazepine

- confirm by GC/MS look for other benzos not metabolites of chlordiazepoxide
- dextromethorphan
- *l*-methamphetamine (OTC nasal inhaler)
 Vick's
- diet pills (eg, clobenzorex, fenproporex)
- quinolone antibiotics (eg, levofloxacin)
- antidepressants (Stertraline)

phencyclidine (PCP) amphetamines

amphetamines opiates benzodiazepine

How to Drive a Toxicologist Crazy

My client claims he is testing positive for THC because he takes ibuprofen (Advil).

REVIEW

Urine Drug Screening: Practical Guide for Clinicians

KAREN E. MOELLER, PHARMD, BCPP; KELLY C. LEE, PHARMD, BCPP; AND JULIE C. KISSACK, PHARMD, BCPP

Drug testing, commonly used in health care, workplace, and criminal settings, has become widespread during the past decade. Urine drug screens have been the most common method for analysis because of ease of sampling. The simplicity of use and access to rapid results have increased demand for and use of immunoassays; however, these assays are not perfect. Falsepositive results of immunoassays can lead to serious medical or social consequences if results are not confirmed by secondary analysis, such as gas chromatography-mass spectrometry. The Department of Health and Human Services' guidelines for the workplace require testing for the following 5 substances: amphetamines, cannabinoids, cocaine, opiates, and phencyclidine. This article discusses potential false-positive results and false-negative results that occur with immunoassays of these substances and with alcohol, benzodiazepines, and tricyclic antidepressants. Other pitfalls, such as adulteration, substitution, and dilution of urine samples, are discussed. Pragmatic concepts summarized in this article should minimize the potential risks of misinterpreting urine drug screens.

Mayo Clin Proc. 2008;83(1)66-76

Our goal is to provide clinically relevant information that can be used to interpret urine drug screens (UDSs) for commonly abused drugs (ie, alcohol, amphetamines, benzodiazepines, opioids, marijuana, cocaine, phencyclidine [PCP], and tricyclic antidepressants [TCAs]). Proper evaluation of urine specimens, including detection times, are discussed, as well as false-positive results and potential false-negative results. Interpretation of tests for performance-enhancing drugs is beyond the scope of this article and is not discussed.

METHODS OF DRUG TESTING

Urine, blood, hair, saliva, sweat, and nails (toenails and fingernails) are some biological specimens used to perform laboratory drug testing, and they provide different levels of

URINE DRUG SCREENING

Substance tested via immunoassay	Potential agents causing false-positive result	Substance tested via immunoassay	Potential agents causing false-positive result	
Alcohol ²⁰	Short-chain alcohols (eg, isopropyl alcohol)	Cannabinoids ^{1,8,43-48}	Dronabinol Efavirenz	
Amphetamines ²¹⁻⁴⁰	Amantadine Benzphetamine Bupropion Chlorpromazine	adine H hetamine H bion H		

TABLE 3. Summary of Agents Contributing to Positive Results by Immunoassay^a

URINE DRUG SCREENING

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Investigation of Interference by Nonsteroidal Anti-Inflammatory Drugs in Urine Tests for Abused Drugs

Douglas E. Rollins,¹ Thomas A. Jennison,² and Graham Jones³

Anecdotal and uncontrolled studies have suggested that nonsteroidal anti-inflammatory drugs produce false-positive results in immunoassay urine tests for some drugs of abuse. This study was performed in 60 volunteers who took ibuprofen as either a single 400-mg dose, or 200 mg three times a day, or 400 mg three times a day, and in 42 patients taking ibuprofen, naproxyn, or fenoprofen in therapeutic regimens for more than 30 days. Of the 510 urines collected from 102 individuals during these dosage regimens, two gave falsepositive tests for cannabinoid by enzyme-mediated immunoassay (EMIA), one after 1200 mg of ibuprofen in three divided doses for one day and one in a patient taking naproxyn on a chronic basis; none was falsely positive for falsely positive report.

Conversely, adulterants (e.g., acids or bases or substances with a high ionic strength) added to a urine specimen may give falsely negative immunoassay results (1). Moreover, the excretion of drugs, drug metabolites, or food substances in the urine could also interfere with immunoassays and cause a false-positive or false-negative result for a urine drug assay. Ibuprofen and other commonly used nonsteroidal anti-inflammatory drugs (NSAIDs) reportedly cause false-positive test results with the EMIA (EMITTH; Syva Co., Palo Alto, CA) for cannabinoids (2-4), false-negative mass-spectrometric confirmation for cannabinoids (5), and false-positive results for barbiturates and benzodiazepines by the FPIA (TDxTH; Abbott oid tests (14).

Brunk (5) describes a false-negative GC/MS cannabinoid confirmation caused by high concentrations of urinary ibuprofen that competed with the analyte for the cannabinoid-derivatizing reagent. This is an unlikely explanation for the data presented in this study. In his GC/MS tests. Brunk extracted 10 mL of urine, which would contain large amounts of potentially competing substances. He used tetramethyl ammonium hydroxide as a derivatizing reagent, and did not use a deuterated internal standard. For cannabinoid confirmation in this study we used only 1 mL of urine, hexafluoroisopropanol and pentafluoropropionic anhydride as the derivatizing reagents, and deuterated COOH-THC as an internal standard. If competition between ibuprofen and COOH-THC for the derivatizing reagents had occurred, no peak for the internal standard would have been observed-a situation that did not occur for any specimen in this study.

In conclusion, these data demonstrate that ibuprofen taken as either a single dose or in acute multiple doses or ibuprofen, naproxyn, or fenoprofen taken as chronic doses is unlikely to result in a positive immunoassay test for urine cannabinoids, benzodiazepines, or barbiturates. All positive immunoassay results should be considered as presumptively positive. A second chemical test such as GC/MS, performed properly, will markedly reduce the possibility of falsely accusing of substance abuse someone who was taking NSAIDs.

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- 1. Article used by the Mayo paper claiming ibuprofen could cause a false positive cannabinoid test is 25 years old.
- 2. Even though the Rollins paper is 25 years old, it concludes "unlikely".
- 3. Assay used to conduct the 25-year old paper has not been available commercially for two decades
- 4. Confirmation testing resolves potential "false positive" concerns.
- 5. Doesn't prohibit Mayo from publishing a misleading paper.

CLINICAL CONSULTATION

Commonly prescribed medications and potential false-positive urine drug screens

NANCY C. BRAHM, LYNN L. YEAGER, MARK D. FOX, KEVIN C. FARMER, AND TONY A. PALMER

he potential for false-positive urine drug screen (UDS) results for substances of abuse presents a therapeutic selection dilemma for the treating health care professional. While this problem is reported with specific medications, the extent of the problem in a clinic serving indigent patients and the medically underserved has not been evaluated. In particular, the use of medications with the potential for false-positive UDS results may present a significant liability for individuals required to undergo random or periodic UDSs as a component of a recovery or courtordered monitoring program^{1,2} or as a condition of employment.1,3,4 In addition, false-positive UDS results may affect the clinician-patient relationship by raising issues of trust.5 This article identifies commonly used medications associated with reports of false-positive UDSs.

Literature review

A comprehensive literature review

Purpose. The implications of potential false-positive urine drug screen (UDS) results for patients receiving commonly prescribed medications were evaluated. Summary. A comprehensive literature review was conducted to identify falsepositive UDSs associated with all clinic formulary medications, as well as common nonprescription medications. The references of each report describing a medication whose use was associated with false-positive UDS results were also reviewed. If a class effect was suspected. additional agents in the category were searched. A total of 25 reports of falsepositive UDS results were identified. Categories of medications included antihistamines, antidepressants, antibiotics, analgesics, antipsychotics, and nonprescription agents. Reports of falsepositive results were found for the following formulary and nonprescription medications: brompheniramine, bupropion, chlorpromazine, clomipramine, dextromethorphan, diphenhydramine, doxylamine, ibuprofen, naproxen, promethazine, guetiapine, guinolones (ofloxacin and gatifloxacin), ranitidine, sertraline, thioridazine, trazodone, venlafaxine,

verapamil, and a nonprescription nasal inhaler. False-positive results for amphetamine and methamphetamine were the most commonly reported. False-positive results for methadone, opioids, phencyclidine, barbiturates, cannabinoids, and benzodiazepines were also reported in patients taking commonly used medications. The most commonly used tests to screen urine for drugs of abuse are immunoassays, even though false-positive results for drugs of abuse have been reported with a number of these rapid-screening products. Results from such tests should be confirmed using additional analytical methods, including gas chromatographymass spectrometry.

Conclusion. A number of routinely prescribed medications have been associated with triggering false-positive UDS results. Verification of the test results with a different screening test or additional analytical tests should be performed to avoid adverse consequences for the patients.

Index terms: Drug abuse; Drugs, over the counter; Drugs; False positive reactions; Tests, laboratory; Urine levels Am J Health-Syst Pharm. 2010; 67:1344-50

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Table 1.

Reports of False-Positive Results of Urine Drug Screens for Selected Formulary Agents⁶⁻³⁰

	False-Positive Result						
Medication	Amphetamine or Methamphetamine	Phencyclidine	Methadone	Opiates	Benzodia zepines	Cannabinoids	Barbiturates
Antihistamines/decongestants							
Brompheniramine	х						
Diphenhydramine			Х				
Doxylamine			Х				
Phenylpropanolamine	Х						
Nonprescription nasal inhaler	х						
Antidepressants							
Bupropion	x						
Clomipramine			Х				
Sertraline					Х		
Trazodone	Х						
Venlafaxine	2640	Х					
Antibiotics							
Quinolonos (celected agents)				X			
Analgesics							
Ibuprofen		Х				Х	X
Naproxen						Х	Х
Anupsychotics							
Chlorpromazine	A		Х				
Promethazine	Х						
Quetiapine			Х				
Thioridazine			Х				
Other agents							
Dextromethorphan		Х					
Ranitidine	Х						
Verapamil			Х				

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Confirmation: Best Practice

- gas or liquid chromatography-mass spectrometry - GC/MS or LC/MS/MS
 - drug molecules separated by physical characteristics
 - identified based on chemical "finger-print"
 considered "gold standard"
- refer to NADCP Adult Drug Court Best Practice Standards - Volume II

No Substitute for Knowledge/Expertise

- unethical to adjudicate based upon misinformation - violation of due process
- develop a relationship with your laboratory
- develop a relationship with your on-site device vendor
- don't be afraid to "call the company"
- seek expert advice

Prescription Drugs

Challenge with Prescription Drugs

therapeutic use versus abuse



therapeutic use

various stages of misuse

abuse

Drug testing is an excellent tool for the abstinence monitoring of court clients, however it provides limited information for the differentiation between the appropriate therapeutic use of prescribed medications and the misuse/abuse of those same drugs - regardless of the specimen tested.

Client Signed Releases doctors dentists ■other healthcare professionals pharmacies

I (client name), am a participant in drug court. This program is a court monitored recovery program for addicts. As a result, I am subject to frequent and random drug testing. Therefore, I must report to the court my visit today. As I am in recovery, I would respectfully request that you take this into consideration and offer non-narcotic medications, if possible, when drugs are necessary for my medical treatment.

Physician (Name)	
Physician (Signature)	

If you have any questions or concerns, please feel free to call the court and talk to my case specialists.

If this patient fails to present this form to the nurse and physician prior to receiving medication or a prescription for medication, please notify the court.

Please list the medications prescribed today:

Other Control Strategies

- search & seizure (client contract)
 - car, home, possessions
- pill counts
- no out-of-state prescriptions
- use of specified pharmacies
- loss of completion credits/time while on certain prescription meds

Drug Testing is a *TOOL*!

- drug testing, as an abstinence monitoring strategy, is just one assessment option
- don't become myopic regarding drug testing results
- consider all of the client behavioral data
- consider the therapeutic ramifications of results & adjudicate to support recovery

email address:

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