

IMPACT-XII

Urine Drug Screening in Analgesic Clinical Trials

Gary M. Reisfield, M.D.

Departments of Psychiatry and
Community Health & Family Medicine
University of Florida College of Medicine

SUDs and core outcome domains

- Pain
- Physical functioning
- Emotional functioning
- Participant ratings of global improvement and satisfaction with treatment
- Symptoms and adverse events
- Participant disposition
- Supplemental domains

Turk DC, Dworkin RH, Allen RR, et al. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2003;106:337-345.

Why drug test?

- Self-reported drug use among pain patients is unreliable.
 - Fishbain DA, Cutler RB, Rosomoff HL, Rosomoff RS. Validity of self-reported drug use in chronic pain patients. *Clin J Pain* 1999;15:184-191.
 - Berndt S, Maier C, Schultz HW. Polymedication and medication compliance in patients with chronic nonmalignant pain. *Pain* 1993;52:331-339.
 - Ready LB, Sarkis E, Turner JA. Self-reported vs. actual use of medications in chronic pain patients. *Pain* 1982;12:285-294.
- Behavioral observation captures only some problems.
 - Wasan AJ, Butler SF, Budman SH, et al. Psychiatric history and psychological adjustment as risk factors for aberrant drug-related behavior among patients with chronic pain. *Clin J Pain* 2007;23:307-315.
 - Katz NP, Sherburne S, Beach M, et al. Behavioral monitoring and urine toxicology testing in patients receiving long-term opioid therapy. *Anesth Analg* 2003;97:1097-1102.

The role of clinical urine drug testing

The Clinical Journal of Pain
18:S76-S82 © 2002 Lippincott Williams & Wilkins, Inc., Philadelphia

Role of Urine Toxicology Testing in the Management of Chronic Opioid Therapy

*Nathaniel Katz, M.D., and †Gilbert J. Fanciullo, M.D., M.S.

**Pain Trials Center, Brigham and Women's Hospital, Boston, Massachusetts; and †Department of Anesthesiology,
Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, U.S.A.*

“Problems” and urine toxicology

n = 122	Behavioral issues Present	Behavioral issues Absent
Urine toxicology Positive	10 (8%)	26 (21%)
Urine toxicology Negative	17 (14%)	69 (56%)

Katz N, Fanciullo GJ. Role of urine toxicology testing in the management of chronic opioid therapy. *Clin J Pain* 2002;18:S76-S82.

ORIGINAL ARTICLE

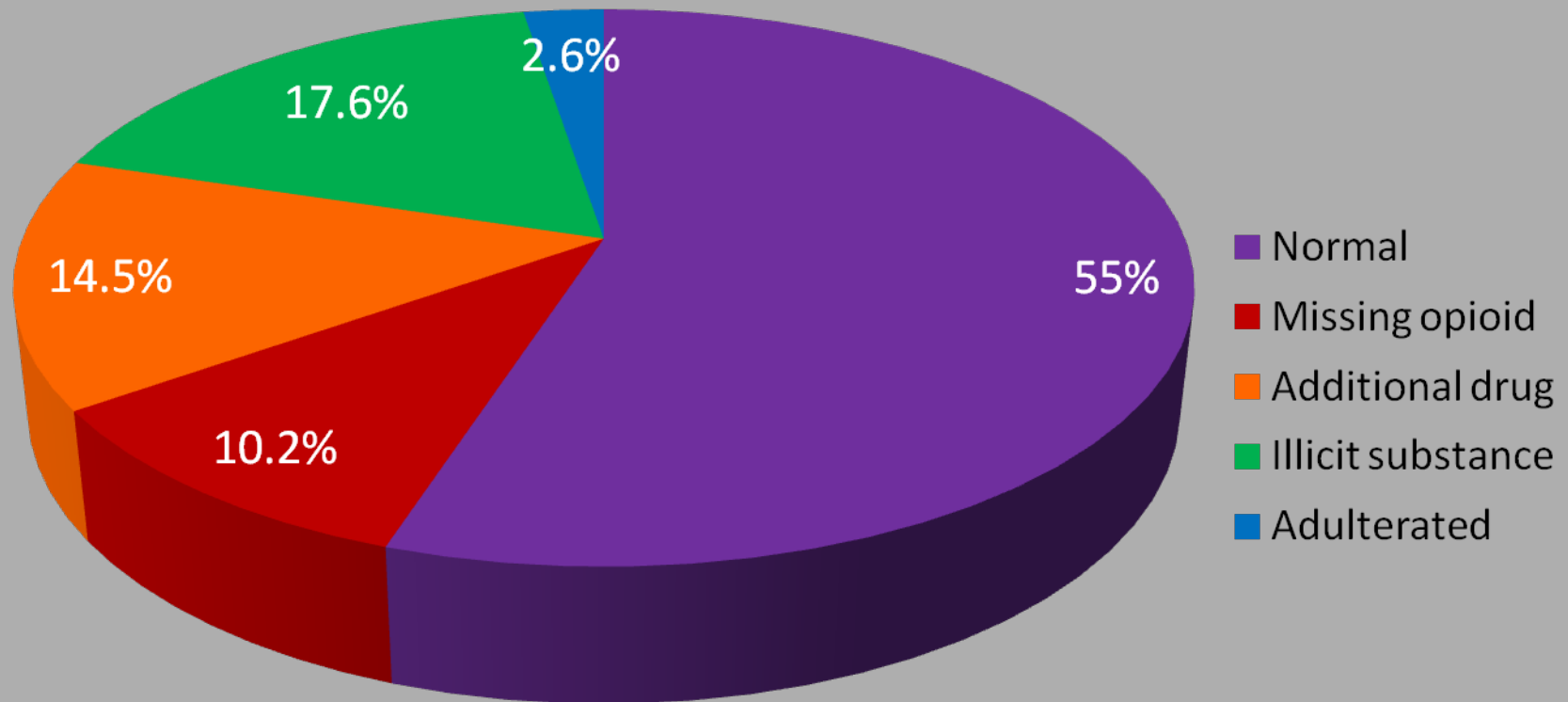
Urine Toxicology Screening Among Chronic Pain Patients on Opioid Therapy: Frequency and Predictability of Abnormal Findings

Edward Michna, MD, JD, Robert N. Jamison, PhD,*† Loc-Duyen Pham, BS,*
Edgar L. Ross, MD,* David Janfaza, MD,* Srdjan S. Nedeljkovic, MD,* Sanjeet Narang, MD,*
Diane Palombi, RN,* and Ajay D. Wasan, MD, MSc*†*

Clin J Pain • Volume 23, Number 2, February 2007

What is (and isn't) in the urine

$n = 470$



Michna E, Jamison RN, Pham LD, et al. Urine toxicology screening among chronic pain patients on opioid therapy: frequency and predictability of abnormal findings. *Clin J Pain* 2007; 23: 173-179.

Why urine?

- Plentiful
- Easy to collect
- Noninvasive collection
- Concentrated ultrafiltrate of blood
- Useful frame of detection (usually days)
 - Longer than blood; shorter than hair
- Deepest and broadest scientific base

What do
“positive” and “negative”
urine drug test results mean?

Potentially inappropriate positive and negative test results

- Positive

- Unauthorized drug administration
- Metabolic conversions
- Exposure to licit sources of drug
- Laboratory error
 - Preanalytical
 - Analytical :cross-reactivity
 - Postanalytical

- Negative

- Drug is absent
- Limited test specificity
- Drug is present, but below cutoff
 - Lack of recent use
 - Pharmacologic induction
 - Genetic polymorphism
- Specimen manipulation
- Laboratory error
 - Preanalytical
 - Analytical
 - Postanalytical

Reisfield GM, Goldberger BA, Bertholf RL. “False-positive” and “false-negative” test results in clinical urine drug testing. *Bioanalysis* 2009;1(5):937-952

What a potentially inappropriate UDT result does *not* tell you

- Pattern of recent use
 - Dose
 - Frequency
- Impairment
- What the exposure means
 - Abuse
 - Addiction
 - Misuse

Urine Drug Testing of Chronic Pain Patients: Licit and Illicit Drug Patterns

Edward J. Cone*

Johns Hopkins School of Medicine, Baltimore, Maryland

Yale H. Caplan

National Scientific Services, Baltimore, Maryland

David L. Black, Timothy Robert, and Frank Moser

Aegis Sciences Corp., Nashville, Tennessee

Prevalence of urinary opioids ($n=10,922$)

Opioid	# positive	% positive
Hydrocodone	5,748	52.6
Hydromorphone	3,695	33.8
Dihydrocodeine	2,280	20.9
Oxycodone	2,068	18.9
Oxymorphone	1,629	14.9
Methadone/EDDP	1,209	11.1
Morphine	1,060	9.7
Fentanyl	458	4.2
Propoxyphene/NP	385	3.5
Codeine	135	1.2
Meperidine/NM	58	0.5

$n = 10,922$

Cone EJ, Caplan YH, Black DL, et al. Urine drug testing of chronic pain patients: licit and illicit drug patterns. *J Anal Toxicol* 2008;32:530-543.

A proposed minimum screening panel

Opioids

- Opiates
 - Morphine
 - Codeine
 - Verify sensitivity for:
 - Hydrocodone
 - Hydromorphone
- Opioids
 - *Buprenorphine*
 - Dihydrocodeine
 - Fentanyl
 - *Meperidine*
 - Methadone/EDDP
 - Oxycodone
 - Oxymorphone
 - Propoxyphene
 - 6-AM
- Atypical opioids
 - *Tapentadol*
 - *Tramadol*

Non-opioids

- Amphetamines
- Barbiturates
- Benzodiazepines
- Cannabinoids
- Cocaine metabolite
- Ethanol
- *Others*
 - *Carisoprodol/meprobamate*
 - *MDMA/MDEA/MDA*
 - *Phencyclidine (PCP)*

Note: drugs in italics optional

Possible guidelines

- Comprehensive initial urine drug screening, including:
 - Suggested (minimum) screening panel
 - Additional drugs at discretion of investigators
 - SVT: temperature, pH, specific gravity, [creatinine] , adulterants
- Follow-up drug screening
 - At each scheduled visit?
 - At specified intervals, e.g. quarterly? + for cause
 - At random? + for cause
 - ~~For cause only?~~
- Potentially inappropriate positive or negative results should be subjected to confirmatory testing (i.e. GC-MS or LC-MS-MS) for parent drug and/or metabolite(s)
- Caution in inferring adherence based on urine [drug] and/or [metabolite]
- Knowledgeable interpreter