



Opioid Addiction Treatment ECHO For Providers and Primary Care Teams

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Learning Objectives

1. Discuss common clinic concerns in taking care of patients on buprenorphine
 - Drug testing, the pitfalls
 - Continued use: what next?
 - Diversion





Drug testing

- It is a monitoring tool to see if the treatment plan needs to be improved. The real outcome is RECOVERY

It is not to confirm the patient is telling the truth.

It is not to indicate the patient has failed

A positive does not mean the patient is not making progress

It must always be interpreted in the context of the clinical picture.



State Law Requirements for OBOT providers

- Perform toxicology screening for the following
 - Stimulants, Alcohol, Opioids including oxycodone, methadone and buprenorphine, THC, Benzodiazepines and Cocaine
- If toxicology screening shows the presence of an illegal or nonprescribed drug the provider shall assess the risk of the patient to be successfully treated and document
- The provider may perform a subsequent confirmation toxicology screening if the provider considers it medically necessary
- Rules regarding frequency are to be developed in consultation with the State Dept of Health and office of Secretary of Family and Social Services



Interpretation of drug testing requires:

- Understanding the limitations of the test
 - screening (ELISA)
 - issue of false positives and false negatives
 - what are the detection levels for the screening
- Understanding of the metabolism of the drug
 - half lives, fat solubility (windows of detection)
 - should metabolites be present
- Understanding how to identify appropriate samples
 - when is dilution intentional
 - bringing in other someone else's urine



False positives and negatives

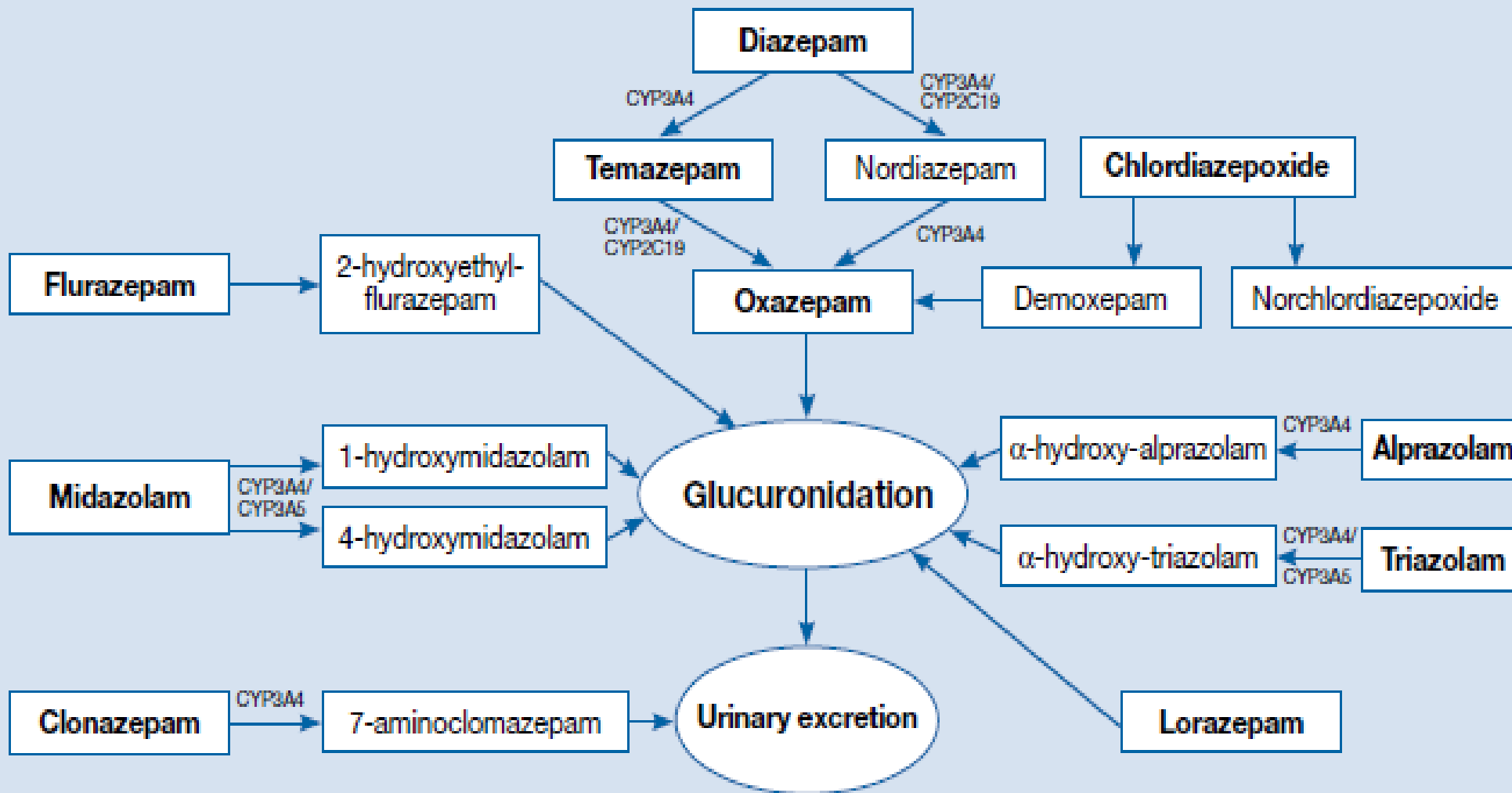
DRUG	FALSE POSITIVES	FALSE NEGATIVES
Amphetamines	Bupropion, trazadone, desipramine, doxepin, labetaolol, metformin, ephedrine, pseudoephedrine, Phentermine, atomoxetine, ranitidine, aripiprazole	
Benzodiazepines	Sertaline, efavirenz	clonazepam
Cocaine	None (medical anesthesia)	
THC	Efavirenz, ibuprofen, naproxenm dronabinol, CBD	Synthetic cannabinoids
Methadone	Quetiapine, verapamil, diphenhydramine, chlorpromazine	
Opioids	Quinolones, naltrexone, diphenhydramine,	Synthetic opioids
PCP	Velafaxine, lamotrigine, ibuprofen, zolpidem, ...	





Confirmation testing

- Eliminates the doubt (unless the collection or lab processing is in error)
- It allows evaluation of metabolites
 - The lower cut offs mean the drug use may have been earlier (weeks before) if the levels come back very low
 - The lower cut offs expand the possibility of unknowing exposure
 - poppy seeds
 - passive inhalation
 - skin exposure



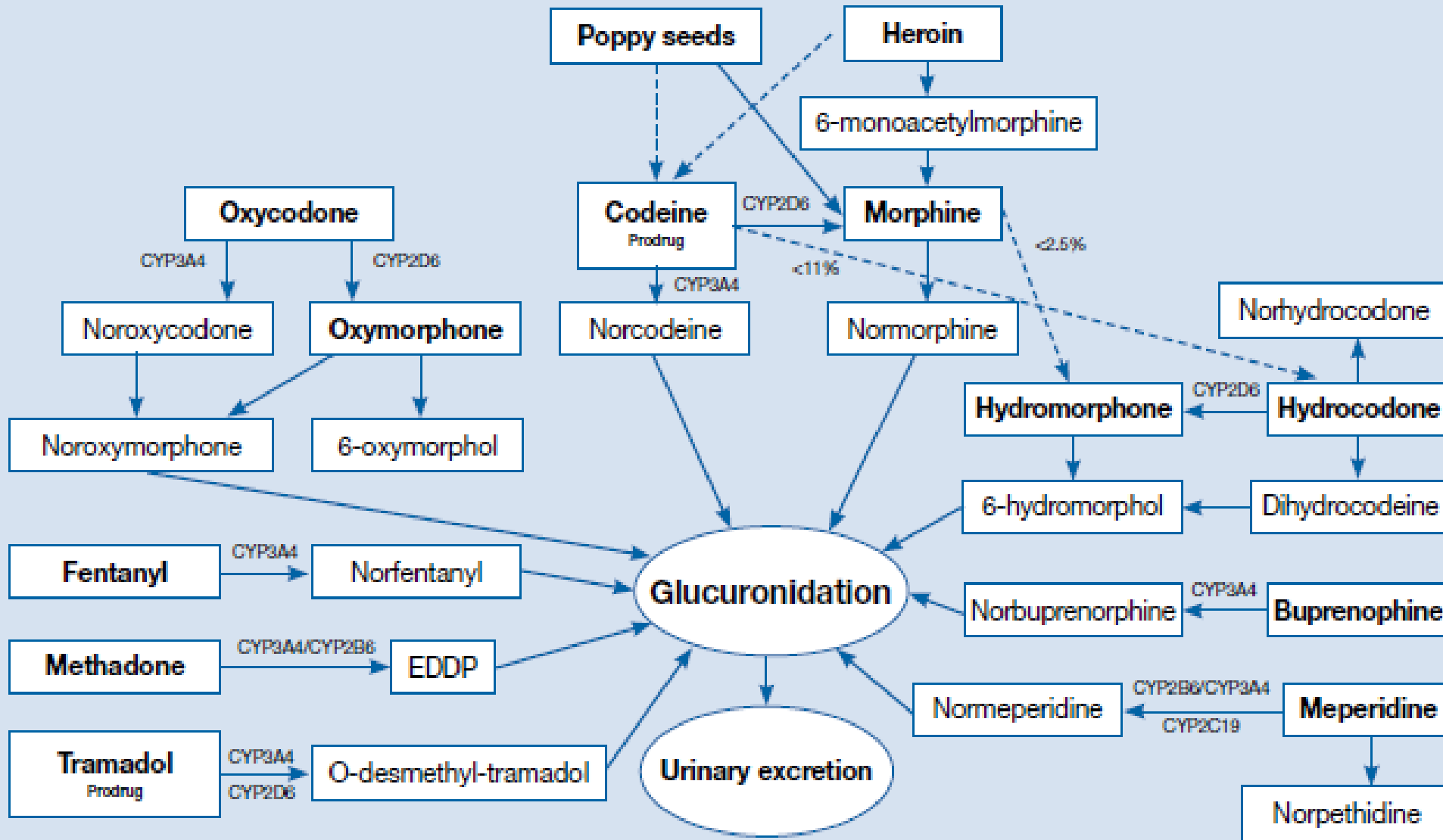
*Drugs in bold are commonly used benzodiazepines

CYP: cytochrome P450

Source: Reference 14



Benzodiazepines	Presumptive Positive, Confirmed
NORDIAZEPAM LCMS	171.50
OXAZEPAM LCMS	>800
TEMAZEPAM LCMS	123.76
ALPRAZOLAM LCMS	None Detected
α -OH-ALPRAZOLAM LCMS	None Detected
7-AMINO-CLONAZEPAM LCMS	None Detected
LORAZEPAM LCMS	None Detected



*Dashed lines indicate minor pathways. Drugs in bold are commonly used opioids

CYP: cytochrome P450; EDDP: 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine

Source: Reference 15



Pre and Post Test Probability

Jul 20, 2018 10:14	Opiates	Presumptive Negative
	Oxycodone	Presumptive Negative
	Cocaine	Presumptive Negative
	Amphetamines	Presumptive Positive
	Benzodiazepines	Presumptive Negative
	Methadone	Presumptive Negative
	Phencyclidine	Presumptive Negative
	Cannabinoids	Presumptive Negative
	Barbiturates	Presumptive Negative
	URINE CREATININE	161.3
	CHROMATE(SVT)	<2.00
	NITRITE(SVT)	174
	SPECIFIC GRAVITY(SVT)	1.007
	pH(SVT)	7.6
	OXIDANT(SVT)	<5

12, 2019 12:06	OXYMORPHONE LCMS	None Detected		ng/mL	Cutoff: 50 ng/mL -
	Cocaine	Presumptive Negative		mAbs	Ref: Presumptive Negative
	BENZOYLECGONINE LCMS	None Detected		ng/mL	Cutoff: 30 ng/mL -
	Amphetamines	Presumptive Negative		mAbs	Ref: Presumptive Negative
	METHAMPHETAMINE LCMS	<50		ng/mL	Cutoff: 50 ng/mL -
	AMPHETAMINE LCMS	None Detected		ng/mL	Cutoff: 100 ng/mL -
	Benzodiazepines	Presumptive Negative		mAbs	Ref: Presumptive Negative
	NORDIAZEPAM LCMS	None Detected		ng/mL	Cutoff: 40 ng/mL -
	OXAZEPAM LCMS	None Detected		ng/mL	Cutoff: 40 ng/mL -
	TEMAZEPAM LCMS	None Detected		ng/mL	Cutoff: 50 ng/mL -
	ALPRAZOLAM LCMS	None Detected		ng/mL	Cutoff: 50 ng/mL -
	a-OH-ALPRAZOLAM LCMS	None Detected		ng/mL	Cutoff: 20 ng/mL -
	7-AMINO-CLONAZEPAM LCMS	None Detected		ng/mL	Cutoff: 20 ng/mL -
	LORAZEPAM LCMS	None Detected		ng/mL	Cutoff: 40 ng/mL -
	Methadone	Presumptive Negative		mAbs	Ref: Presumptive Negative
	METHADONE LCMS	None Detected		ng/mL	Cutoff: 100 ng/mL -
	EDDP LCMS	None Detected		ng/mL	Cutoff: 100 ng/mL -
	Phencyclidine	Presumptive Negative		mAbs	Ref: Presumptive Negative
	PCP LCMS	None Detected		ng/mL	Cutoff: 10 ng/mL -
	Cannabinoids	Presumptive Negative		mAbs	Ref: Presumptive Negative
	THC-COOH LCMS	None Detected		ng/mL	Cutoff: 30 ng/mL -
	Comprehensive LCMS	Complete			
	Barbiturates	Presumptive Negative		mAbs	Ref: Presumptive Negative
	BUTALBITAL LCMS	None Detected		ng/mL	Cutoff: 200 ng/mL -
	PHENOBARBITAL LCMS	None Detected		ng/mL	Cutoff: 200 ng/mL -
	FENTANYL LCMS	None Detected		ng/mL	Cutoff: 2 ng/mL -
	NORFENTANYL LCMS	None Detected		ng/mL	Cutoff: 8 ng/mL -
	MDPV LCMS	None Detected		ng/mL	Cutoff: 50 ng/mL -
	MEPHEDRONE LCMS	None Detected		ng/mL	Cutoff: 50 ng/mL -
	METHYLONE LCMS	None Detected		ng/mL	Cutoff: 50 ng/mL -
	MDMA LCMS	None Detected		ng/mL	Cutoff: 100 ng/mL -
	MEPERIDINE LCMS	None Detected		ng/mL	Cutoff: 50 ng/mL -
	ZOLPIDEM METABOLITE LCMS	None Detected		ng/mL	Cutoff: 10 ng/mL -



DATA FROM DEA AGENTS



- Table II. All Samples Containing Detectable Methamphetamine from the
- 101 Samples Tested*

• Sample Number	Concentration (ng/mL)	Date Sample Collected	Sample Number	Concentration (ng/ml)	Collected
• 1†	9.	5/8/2002	28	27	1/28/2004
• 2	43.	5/8/2002	29	3.	6/15/2004
• 3	15	5/8/2002	30	2.3	6/15/2004
• 4†	16	9/24/2002	31	10.	6/15/2004
• 5	36	9/24/2002	32	11.	6/15/2004
• 6	1.6	9/24/2002	33	2.6	6/15/2004
• 7	11	9/24/2002	34	10.	9/9/2004
• 8	13	9/24/2002	35	5.4	9/9/2004
• 9	6.7	31/2003	36	10.	9/9/2004
• 10	15	1/31/2003	37	12.	9/9/2004
• 11	3.1	1/31/2003			
• 12	4.	1/31/2003			
• 13	12	1/23/2003			
• 14	5	1/23/2003			
• 15	262	1/23/2003			

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- * Note that the limit of quantitation was 15 ng/mL, and the limit of detection was 1 ng/mL. Values less than 15
- ng/mL are given because all chromatographic acceptance criteria were acceptable, indicating the presence



Confirmation shows:

Comprehensive LCMS	Complete
MORPHINE LCMS	None Detected
CODEINE LCMS	None Detected
HYDROCODONE LCMS	None Detected
HYDROMORPHONE LCMS	None Detected
6-ACETYLMORPHINE LCMS	None Detected
OXYCODONE LCMS	None Detected
OXYMORPHONE LCMS	None Detected
BENZOYLECGONINE LCMS	None Detected
METHAMPHETAMINE LCMS	129.49
AMPHETAMINE LCMS	>2000

Methamphetamine--→ Amphetamine



Pre and Post Test Probability

Collection Date/Time	Test	Result / Status	Flag
Dec 27, 2018 13:00	Comprehensive LCMS	Complete	
	MORPHINE LCMS	<50	
	CODEINE LCMS	None Detected	
	HYDROCODONE LCMS	None Detected	
	HYDROMORPHONE LCMS	None Detected	
	6-ACETYLMORPHINE LCMS	None Detected	
	OXYCODONE LCMS	None Detected	
	OXYMORPHONE LCMS	None Detected	
	BENZOYLECGONINE LCMS	None Detected	
	METHAMPHETAMINE LCMS	None Detected	
	AMPHETAMINE LCMS	None Detected	
	NORDIAZEPAM LCMS	None Detected	

SUBSTITUTION





Interpretation of Urine Dilution

- Value < 20 mg/dL suggests water ingestion
- The amount of H₂O required to dilute the urine will vary greatly (can be as little as 16 ounces) – it is not always intentional
- Must interpret with the clinical history
- Ask about diuretics, diabetes, polydipsia
- Value < 20 mg/dl strongly suggest intentional ingestion
- Value < 5 inconsistent with urine
- If dilute a confirmation , which has lower cutoffs, may pick up suspected drugs



SUBJECT	Time	H2O	Creatinine(mg/dl)
D	22.82	12 oz	216
	23.82		157
	24.82		177
D	69.15	12 oz	215
	71.98		119
	72.82		64
	73.85		122
E	22.73	12 oz H2O	49
	23.48		111
	25.37		35
	28.07		45
F	21.68		88
	22.18	12 oz H2O	128
	29.18		105
G	32.93		33
	70.10	12 oz H2O	72
	71.93		28
C	78.27		206
	21.62		66
	22.87	12 oz H2O	109
	24.29		23
	24.62		19



**Okay, one last time:
This is not a urinal.**



Get caught tossing a bottle of urine and you'll pay \$95.
Fines for littering range from \$95 to \$1,000. Remember, Washington
State Patrol has eyes out for violators. (Not to mention their noses).

**Litter and
it will hurt.**

**REPORT VIOLATORS
866-LITTER-1**

For every action on
an object there is
an equal and
opposite reaction

Sir Isaac Newton



How to approach patient who absolutely denies use despite positive urine

- Consider confirmatory testing with quantitative levels
- Do not focus on patient characteristics "this must mean you used" but focus on result "the urine was positive for opioids" and I am concerned about your recovery
- If patient reluctant to intensify treatment, present this as standard care and not a personal decision
- Invite the patient "If you had a patient with this result who denied it what would you do?"





Urine Buprenorphine testing

- Buprenorphine → norbuprenorphine + bup 3 glucuronide
- Urine levels do not correlate well with dose
- Total norbup > buprenorphine but not always (80-100%)
- time of dosing to collection impacts this ratio
- Bup without metabolite - adulterated specimen
Bup > 750-1000 with metabolite- likely adulteration
- 95% is excreted after 144 hours



	TRAMADOL LCMS	None Detected
	NORTRAMADOL LCMS	None Detected
	BUPRENORPHINE LCMS	>400
	NORBUPRENORPHINE LCMS	None Detected
	METHYLPHENIDATE LCMS	None Detected
	RITALINIC ACID LCMS	None Detected
	URINE CREATININE	18.8



Diversion

- Use of non-prescribed buprenorphine on the street is most often to self-treat withdrawal (64% in one study)
- Patients may divert to help another friend/family member
- Educate patients up front about importance of not diverting
- Take steps to minimize the risk but do not become the police
 - communicate, more frequent visits, smallest dose that is effective, monitored urines with bup levels, pill count policy

* A Review of Buprenorphine Diversion and Misuse:
J Addict Medicine 2014 Sep-Oct 8(5)



Addressing Continued Use

- Return to use is expected and will vary in severity
- Do not stop treatment for positive urine alone
- Intensify treatment plan through more frequent visits, urine drug screens, and psychosocial supports
- Have a guide for when you will refer for higher level of care (i.e., IOP, new MAT, more therapy)
- Is the patient on an adequate dose?



Should treatment ever be stopped????

- When there are safety concerns (overdosing on the medications being used to treat)
- Disruptive behaviors to other clients and staff
- Total nonengagement
- Weigh the risk of overdose on the street vs continued treatment
- Some patients require the structure of a choice