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Disclosures

- I am paid presenter for Alkermes: Vivitrol

2

"Most middle- and high-income countries globally have become largely inured to the endemic premature mortalities related to more commonly used substances such as alcohol and tobacco. While these account for a much larger number of deaths and economic and social harms than opioids each year, the devastation wreaked by these substances, their casualties, and the associated blood and tears are all relatively willingly absorbed into the social fabric."

John F. Kelly and Sarah E. Wakeman, 2019

Perspective

3

Oral Fluids Testing

"Oral Fluid testing, with its many advantages over urine should be endorsed on an equal if not higher basis, than urine."

Edward Cone, PhD, Conechem Research

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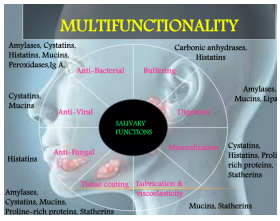
Conclusion

Saliva lacks the drama of blood, the emotion of tears and toil of sweat but it still remains one of the most important fluids in the human body

What is Saliva?



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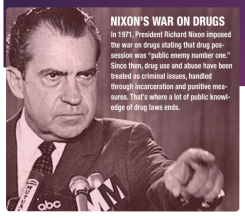

War On Drugs

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Factors influencing OFT

- Passive Diffusion
- Salivary Gland Secretion
  - Saliva flow rate
- Drug use and Consumption
- Drug properties
  - Lipid solubility
  - Molecular Weight
  - pH

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Back to OFT: Makes sense

- Non-invasive
- Difficult to adulterate
- Useful for therapeutic drug monitoring and forensic analysis
- Provides a window into recent drug use

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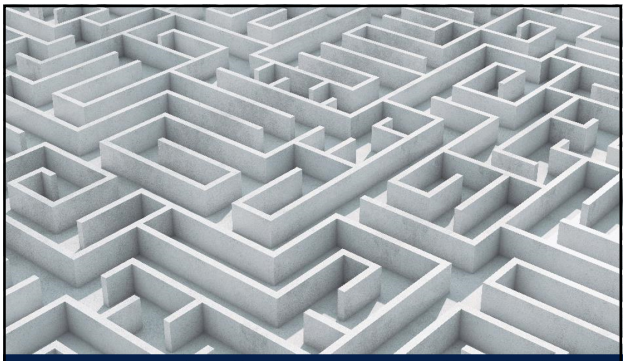

Until now, there has been **no specific guidance** about how to effectively utilize drug testing in clinical settings to help identify, treat, and support the recovery of patients with addictions.

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Purpose of Discussion

- Provide clinical guidance about the effective use of drug testing in the identification, diagnosis, treatment and promotion of health for patients at risk
  - Current clinical practice standards and disagreements
  - RAND/UCLA research recommendations
  - Expert opinion

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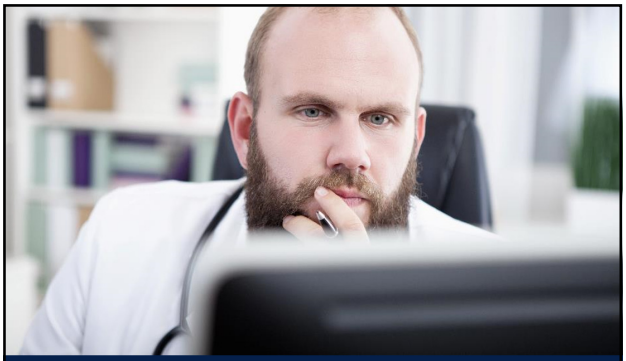

Clinicians **need guidance**. Currently, there is a lack of understanding of methodological limitations, interpretation, and application of drug test results among clinicians.

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Drug testing

Using biological sample to detect presence of absence of a specific drug or metabolite within a specific window or time.

No Universal standard exists in clinical drug testing for Addiction Medicine (MAT), Primary Care Screening, Chronic Pain Management, Hospice / Palliative care

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SMART drug testing: Is Recommended

- Increased use of random drug testing vs scheduled testing.
- Expanding matrices beyond urine (oral fluids)
- Expanded drug testing beyond of the SAMSHA 5 panel: THC, cocaine, opiates, amphetamines and phencyclidine
- Efforts to decrease adulteration and substitution
- Financial cost of testing in relationship to value provided.

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Biggest challenge

The most important challenge in drug testing today is not the identification of every drug we are technically capable of detecting, but to do so in a medically necessary, cost effective and accurate manner that is likely to effect clinical outcomes.

Inappropriate testing can have extraordinary costs to third party payers, taxpayers and patients. Undermines physician credibility.

Large, arbitrary panels, unnecessary frequency, confirmation and quantification of all presumptive positives and negatives

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Principles of Detection

- A positive drug test indicates the patient providing the sample had a detectable amount of the target substance in his or her system when the sample was collected. Nothing more nothing less.
  - Timing of sample, matrices used, elimination rate
  - Positive test does not indicate SUD, patterns of use, impairment, aberrant behavior or compliance or noncompliance

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Sources of information

- If interpretation of the drug testing is so narrow: why bother:
  - Complement self report: potential of negative consequences limits self report accuracy
  - Collateral reports
  - Provider assessment
    - Patient reports may be inaccurate, incomplete, limited by memory, social acceptability and missing information

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Patient outcomes

Evidence is limited that it improves outcomes

Us vs them mentality

Therapeutic tool?

Explore denial motivation use

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Choosing a test

- What information do you want to gain?
- Particular substance targeted?
- Matrix sample chosen
- Reliability: usefulness of results
- Cost. Important for clinicians to be aware of cost

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Presumptive and Definitive test

Presumptive: ELISA	• Qualitative, preliminary, immunoassay, POCT, screen, semi-quantitative, simple, class
Definitive: Mass Spec	• Quantitative, confirmatory, chromatography /mass-spectrometry, absolute, complex, specific

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SENSITIVITY	SPECIFICITY
Probability of a positive test among patient with condition	Probability of a negative test among patient without condition
Tests with high sensitivity are used to rule out condition ("snout = rule out")	Tests with high specificity are used to rule in condition ("spin = rule in")
True positive—help identify patients with condition	*True negatives*—help identify patients without condition

Sensitivity vs Specificity

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Sensitivity vs specificity

Sensitivity	Specificity
• The likelihood that a given test is able to detect the presence of a drug or metabolite that is actually in a specimen • Ability to avoid false negatives • Number of false negatives / number of positive samples • Negative is useful for ruling out	• Likelihood that a given test is able to identify the specific drug or metabolite and not to label erroneous drugs or metabolites • Ability of avoid false positives • Number of false positives / number of negative samples • Positive results can help rule in

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Responding to test results

Clinicians should have a plan on what to do with the test results.

Clinicians should attach a meaningful response to test results, both positive and negative and deliver it as quickly as possible.

Non confrontational	Be prepared to make difficult, sometimes irreversible, clinical decisions

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Historically, drug testing in addiction treatment has been wielded as a **tool for control** and punishment.

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Test Frequency: What is the Right Answer

- Individualized
- More frequent testing does not lead to better patient outcome
- In general, more frequent at the beginning of treatment, less frequent with stability

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Documentation and Confidentiality

- CLINICIANS SHOULD PROVIDE WRITTEN TREATMENT AGREEMENTS WHICH CLEARLY EXPLAIN DRUG TESTING PROCEDURES
- RESULTS DOCUMENTED IN THE RECORD
- KEPT CONFIDENTIAL TO THE EXTENT PERMITTED BY LAW

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Clinician knowledge and Proficiency

- Be familiar with limitations of presumptive and definitive testing
- Consider the possibility of tampering
- Providers should understand the potential benefits of alternative matrices of testing
- Providers, within reason, should have a understanding of the cost of the testing
- Providers should have access to MRO or medical toxicologist if assistance is needed in interpretation

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Language and Attitiude

Use positive or negative not clean or dirty

Present a consistent positive attitude about drug testing

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Choosing a laboratory

- Use only labs that are certified by state standards
- Labs that collaborate on interpretation, test panel selection, tampering detection, regional drug trends
- Labs that give clinicians access to expert medical toxicologist for assistance
- Labs that give clinicians options for individualized testing.

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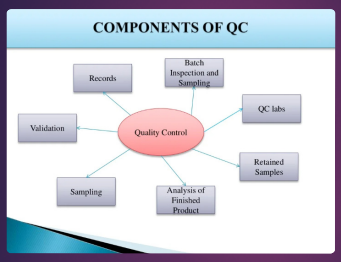
Quality Assurance and control



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Biological Matrices

- URINE
- BLOOD
- BREATH
- ORAL FLUIDS
- SWEAT
- HAIR

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Urine

Mature Technology

Two MAJOR drawbacks:

- Ease of sample tampering through substitution, dilution and adulteration
- Invasiveness and resource intensity of witnessed sample collection, the primary means of countering sample tampering

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Oral Fluids

- Drugs are present through passive diffusion from bloodstream to salivary glands and through absorption and excretion of mucous membranes in the oral cavity during ingestion or inhalation
- Oral fluids generally correlate very well with plasma concentration
- More likely to detect parent compound vs metabolites
- No eating drinking or smoking 15 minutes prior to testing. Prefer 2 hours from last drug ingestion.

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POLICY PROFILE

Drug Toxicology Testing Requirements

RAND-USC SCHAEFFER OPIOID POLICY TOOLS AND INFORMATION CENTER

Mandate that providers of medication treatments for opioid use disorder (OUD) conduct at least six drug screens from patients to guide treatment planning.

A panel of experts rated how they expect this type of policy to affect four outcomes: *OUD treatment engagement, OUD treatment retention, OUD remission*, and *opioid overdose mortality*. Another panel of experts rated the policy on four implementation criteria: *acceptability* to the public, *feasibility* of implementation, *affordability* from a societal perspective, and *equitability* in health effects.

POLICY RECOMMENDATION ACCORDING TO EXPERT RATINGS

OPPOSE	UNCERTAIN	SUPPORT

RAND/UCLA

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SUMMARY OF EXPERT RATINGS

OUTCOMES	EFFECT RATING		
OUD Treatment Engagement	HARMFUL	LITTLE-TO-NO	BENEFICIAL
OUD Treatment Retention	HARMFUL	LITTLE-TO-NO	BENEFICIAL
OUD Remission	HARMFUL	LITTLE-TO-NO	BENEFICIAL
Opioid Overdose Mortality	HARMFUL	LITTLE-TO-NO	BENEFICIAL
CRITERIA	**IMPLEMENTATION RATING**		
Acceptability	LOW	MODERATE	HIGH
Feasibility	LOW	MODERATE	HIGH
Affordability	LOW	MODERATE	HIGH
Equitability	LOW	MODERATE	HIGH

RAND/UCLA

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RAND/UCLA

SUMMARY OF EXPERT COMMENTS

- The panel expects minimal yet negative impacts across all four outcomes because testing may deter patients from treatment and be used by providers as grounds for treatment discharge.
- The panel expects this policy will exacerbate disparities due to inequitable implementation as a punitive measure, the history of systemic racism associated with drug testing as surveillance and grounds for punitive consequences, and disproportionate treatment dropout and low-quality treatment among populations who already experience disparate outcomes.
- The general public views toxicology testing as a standard aspect of care; experts expressed concern that toxicology testing could be used punitively in practice.
- Frequent toxicology testing may be feasible and affordable when used appropriately (i.e., to guide treatment planning rather than discharge patients). However, this policy also depends on political environment, provider willingness to conduct testing, availability of resources for testing, and paying for testing at scale.

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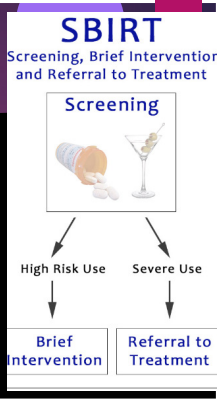
Why Screen?

- Patient safety
  - Overdose risk
  - Polypharmacy Risk
  - Drug Interactions
  - Diagnostic Clarity
- Public Health / Safety
  - Diversion Control
  - Harms Reduction
- Physician Liability
  - Minimal Standards
  - Pain Management / Controlled Agreement
  - MAT standards
  - Psychiatric Standards



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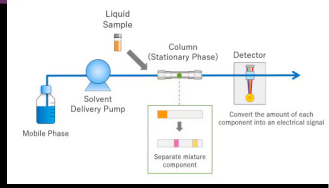
Historical development of drug testing

- 1950s: Formalization began to take shape
- 1960s: Term therapeutic Drug Monitoring began to take shape.
- 1967: Development of High Performance Liquid Chromatography



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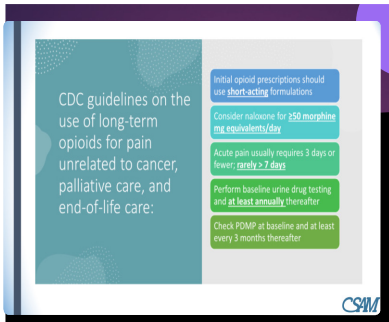

CDC Guidelines

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Consensus: Mitigation Strategies

- CONCLUSION: Despite limited evidence and variable development methods, recent guidelines on chronic pain agree on several opioid risk mitigation strategies:
  - including upper dosing thresholds
  - cautions with certain medications
  - attention to drug–drug and drug–disease interactions
  - and use of risk assessment tools
  - treatment agreements
  - and drug testing (urine/Oral)..

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Results

Participants were mostly women (47 [62%]), White (94 (78 [65%]), and held MD/DO degrees (115 [96%]). For a patient with untreated OUD, regardless of prognosis, it was deemed appropriate to begin treatment with buprenorphine/naloxone and inappropriate to refer to a methadone clinic. Beginning split-dose methadone was deemed appropriate for patients with shorter prognoses and of uncertain appropriateness for those with longer prognoses. Beginning a full opioid agonist was deemed of uncertain appropriateness for those with a short prognosis and inappropriate for those with a longer prognosis. Regardless of prognosis, for a patient with no medical history of OUD taking more opioids than prescribed, it was deemed appropriate to increase monitoring, inappropriate to taper opioids, and of uncertain appropriateness to increase the patient's opioids or transition to buprenorphine/naloxone. For a patient with a urine drug test positive for non-prescribed benzodiazepines, regardless of prognosis, it was deemed appropriate to increase monitoring, inappropriate to taper opioids and prescribe buprenorphine/naloxone.

Cancer and Monitoring

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Harms Reduction

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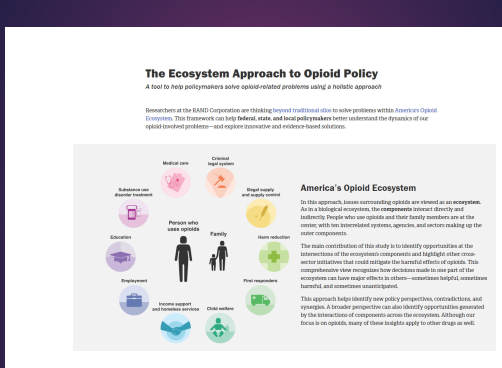

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RAND Expert Panel

- Coercive policies and policies levying additional requirements on individuals with Chronic Malignant and Non-Malignant Pain receiving full agonist and/or OUD receiving treatment (eg, drug toxicology testing, counseling requirements) were viewed as low-value policies (ie, decreasing treatment engagement and retention, increasing overdose mortality, and increasing health inequities).

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Pain Management Consensus

- Therapeutic Drug monitoring is suggested to be performed at baseline for most patients prescribed opioids for chronic pain and at least annually for those at low risk, two or more times per year for those at moderate risk, and three or more times per year for those at high risk. Additional drug testing should be performed as needed on the basis of clinical judgment.

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Annually

As part of this guidance, the CDC stated, "when prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least **annually** to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs."

CDC

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Toxicology Report: Get to know your lab

- Name, address, phone, fax, CLIA:ID of lab performing
- Sample type
- Patient Identifiers
- Date collected, Date Received, Requisition ID
- Drug Class, compounds, Results Screen vs Confirmation LC/MS quantitation, cutoff values, Historical comparisons

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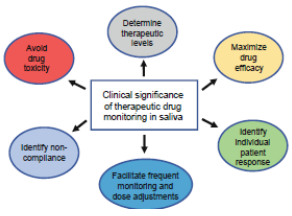
- The potential is very exciting and clinically relevant.



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Summary:

- Oral Fluid Testing is a valuable tool for any clinician prescribing controlled substances regardless of clinical setting.
- Anticipate response to results.
- Use agreements with patients to set the stage for expectations.
- Try to not be punitive with aberrant behavior.
- Get to know your lab and toxicologist.

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