Urine Drug Monitoring:
Access and Accountability

Panel Discussion

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Disclosure Information (Required)

- Dr. Alaina Steck, MD, FASAM
  - No Disclosures

- Dr. Stephanie Carreiro, MD
  - No Disclosures

- Dr. Rachel Haroz, MD
  - No Disclosures

- Dr. JoAn Laes, MD, FASAM
  - No Disclosures

Learning Objectives

At the completion of this activity, participants will be able to:

◆ Discuss a variety of approaches to drug monitoring during COVID-19 induced changes in outpatient treatment operations.

◆ Select appropriate testing methods for novel or uncommon substances of abuse.

◆ Identify the benefits and drawbacks of alternative technologies available for drug monitoring.

Case 1

Mr. Jones is a 38-year-old male who began treatment at your OTP in January 2020. He intermittently tests positive for benzodiazepines and methamphetamine but has not used illicit opioids for the past 45 days.

Social distancing measures are enacted in your state in mid-March 2020.

How do you manage Mr. Jones' drug monitoring?

Drug Testing During COVID

- In March, drug testing fell by 70%
- Back to 45% at the end of May
    - MAT and SUD treatment facilities
    - Positivity for non-prescribed fentanyl increased by 35% during pandemic period

- Efficacy of routine drug testing in treatment goals?
- Limitations of immunoassays and confirmatory testing

Audience Question

What methods of drug testing have you been using during COVID?

a. None
b. Urine
c. Saliva

Case 2

Ms. Smith is a 19-year-old college sophomore who is majoring in mathematics. She first began drinking alcohol in her mid-teens because it helped her relax before exams. Last year a friend introduced her to ketamine because "studies show it helps with depression."

Over the past 6 months she has started a variety of "legal highs" and finds that her academic performance is suffering. She presents for treatment because she is worried about losing her scholarship.

How do you monitor her substance use during treatment?

Novel Drugs of Abuse

- ◆ New compounds being synthesized continually
  - ◆ Majority of novel psychoactive substances without established analytical methods

ketamine   methoxetamine
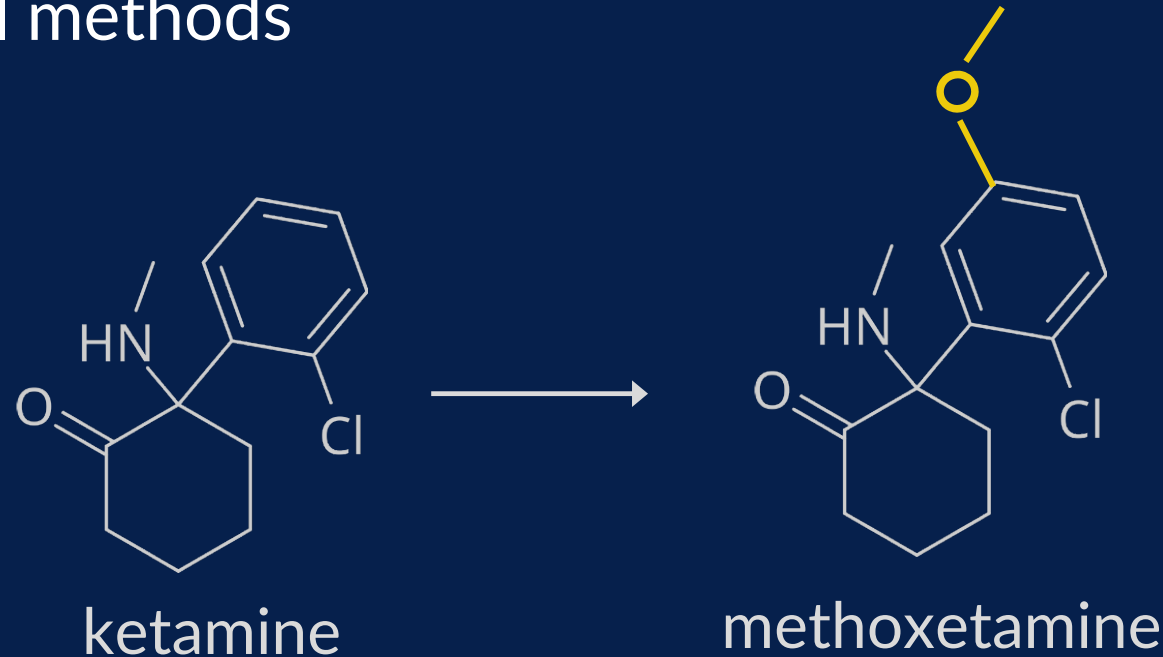
- ◆ Evade detection on standard drug tests

Drug testing Novel Drugs of Abuse

◆ Triple-quadrupole mass spectrometry with multiple reaction monitoring[1]

  ◆ Don't detect substances not included in the reference standards[2]

  ◆ Every new substance requires development of new assays

◆ High-resolution mass spectrometers (HRMS), Time-Of-Fight (TOF) and Orbitrap[1]

  ◆ Unknown compounds can be identified retrospectively

[1]Conchiero M, et al. (*J Chromatogr 2015*); [2]Liu L, et al. (*Am J Clin Pathol* 2018)
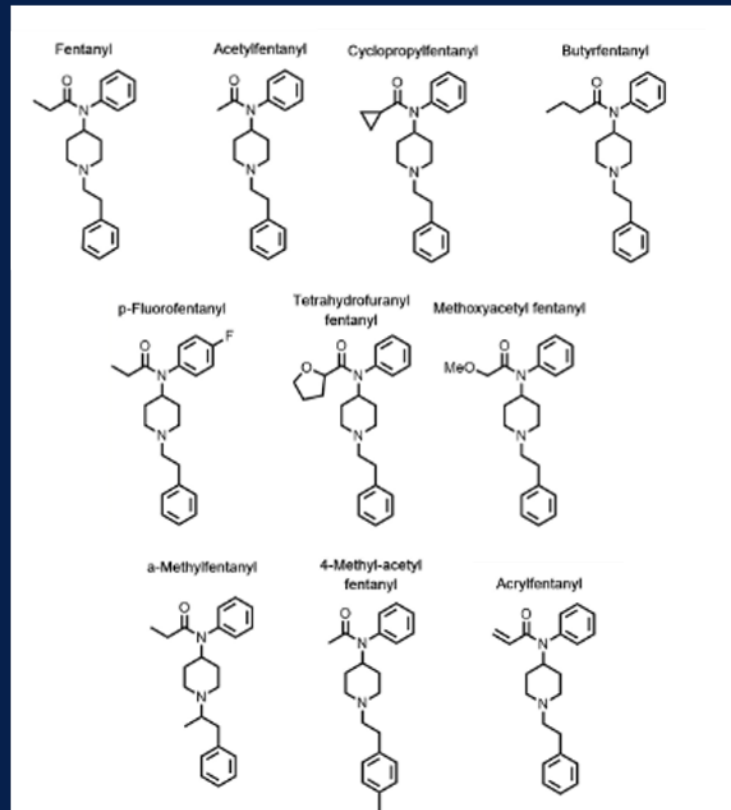
Fentanyl Analogues

- Commercial immunoassay kits[1-3]
  - Lateral Flow Assay (LFA)
  - Capillary action to move liquid sample across different zones
  - Enzyme-linked immunosorbent assays (ELISA)
    - Antibody and enzymed labeled fentanyl: measure enzyme activity following addition of substrate of interest
  - Enzyme multiplied immunoassay technique (EMIT)
    - Enzyme conjugated fentanyl competes with unlabeled fentanyl for antibody binding: measure the rate of enzyme activity change

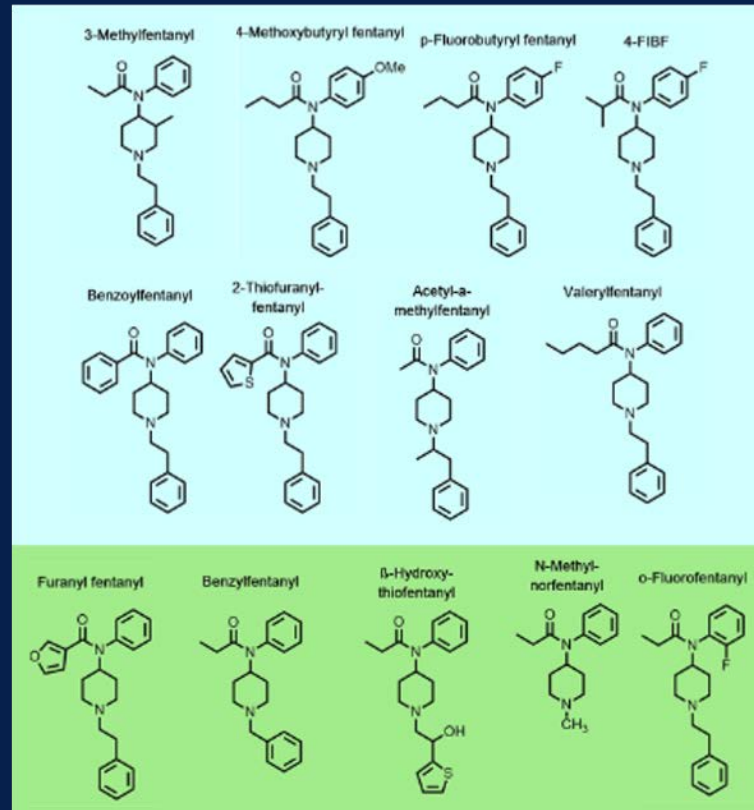[1]Wharton RE, et al. (*J Analytical Toxicol 2021*); [2]Feng S, et al. (*J Anal Toxicol* 2021); [3]Kennedy JH, et al. (*Rapid Comm Mass Spec* 2018)
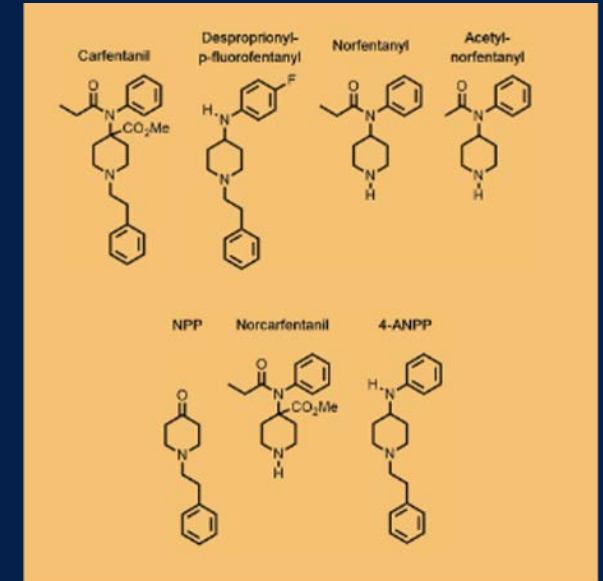
Fentanyl Analogues

Detected   Moderate-to-fair detection   Poor detection

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Fentanyl Analogues

- Pilot study[1]: 30 fentanyl analogues an metabolites by 19 commercially available kits
  - Immunoassays tested were able to detect their intended fentanyl analog and some closely related analogs
    - Structurally diverse analogs, 4-methoxy-butyryl fentanyl and 3-methylfentanyl, less detectable
    - Carfentanil only detected by kits with a specific immunoassay

[1]Wharton RE, et al. (*J Analytical Toxicol 2021*)

Synthetic Cathinones

- ◆ Randox Drugs of Abuse V (DOA-V) Biochip Array Technology[1]

  - ◆ First fully validated immunoassay for preliminary detection of synthetic cathinones in urine.

  - ◆ Bath Salt I (BSI) targets mephedrone/methcathinone and Bath Salt II (BSII) targets 3',4'-methylenedioxypyrovalerone (MDPV)/3',4'-methylenedioxy-α-pyrrolidinobutiophenone (MDPBP)

- ◆ Immunoassay performance vs LC-HRMS[2]

  - ◆ poor (<1%) detection on immunoassay

  - ◆ standards for new compounds / metabolites

[1]Ellefsen KN, et al. (*Drug Test Anal 2014*); [2]Belsey SL and Flanagan RJ (*J Anal Toxicol* 2020)

Synthetic Cannabinoids

- Retrospective studies[1]
  - Two homogenous enzyme IAs: JWH-018' kit and a 'UR-144' kit
    - To evaluate detection of currently prevalent synthetic cannabinoids
    - Authentic urine samples
  - Combined application of both IAs (recommended IA cut-offs)
    - Sensitivity of 2%
    - Diagnostic accuracy of 51%

[1]Franz F, et al. (*Clin Chem Lab Med 2017*)   #ASAM2021

Dissociatives

- variable detection on standard PCP immunoassays[1]
    - most cross-reactivity for 3-MeO-PCP and 4-MeO-PCP
    - MXE nearly negligible (<0.25%) cross-reactivity
    - ketamine not detected

[1]Gomila I, et al. (*J Analytical Toxicol 2019*) #ASAM2021

Novel Benzodiazepines

- ◆ 13 designer benzos in 4 commercial immunoassays
    - ◆ variable rates of detection (cross-reactivity) between commercial assays (KIMS II, CEDIA, EMIT II Plus, HEIA)
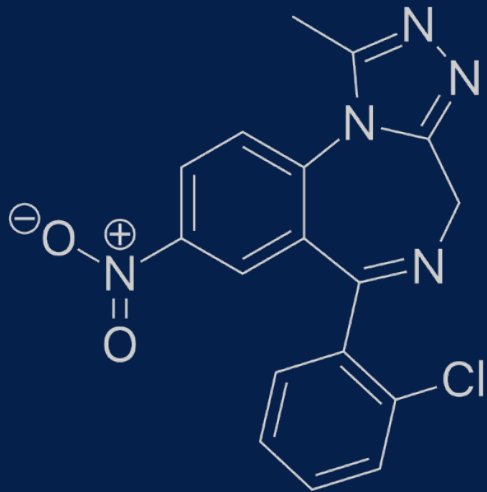
clonazolam
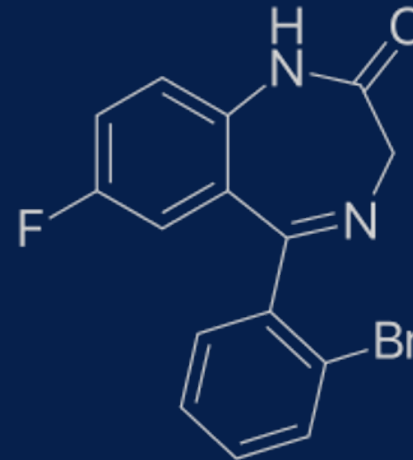
flubromazepam

[1]Pettersson Bergstrand M, et al. (*J Analytical Toxicol 2017*)   #ASAM2021

Case 3

Ms. Parker is a 21-year-old female who enters outpatient treatment for OUD. As part of her (forward thinking) program, she downloads a mobile app to locate NA meetings, one to track geolocation for accountability, and one to track sleep quality through her smart watch. When told she would need to submit a weekly UDS she replies, "Why don't you just use my phone to track sobriety like you track everything else?"

Is there a role for mobile health devices in drug detection and monitoring?

Wearables for Drug Use Physiology...

- ◆ Wrist worn sensors can detect digital biomarkers of opioid and cocaine used based on:
  - ◆ Accelerometry, skin temperature, heart rate and electrodermal activity
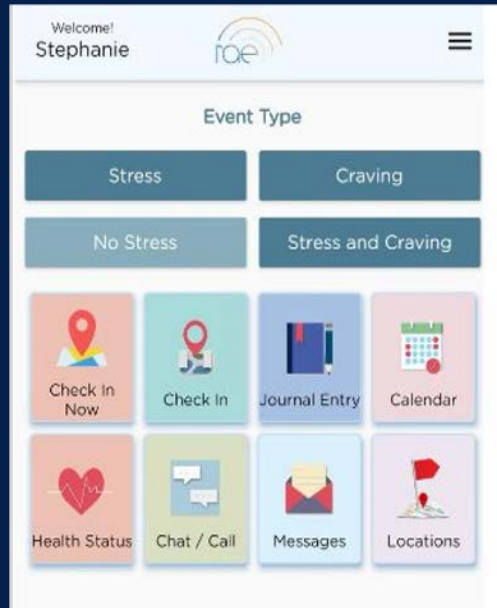
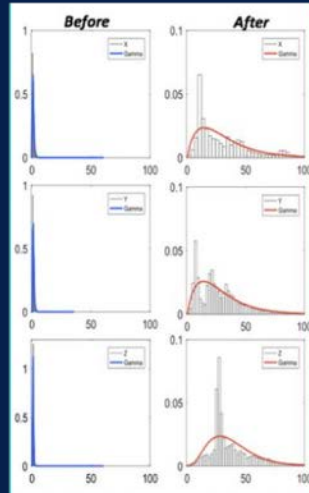- ◆ Digital biomarkers of opioid use differ based on level of opioid tolerance

[1]Carreiro S, et al. (*J Med Syst 2015*);
[2]Carreiro S, et al. (*J Med Toxicol* 2016); [3]Mahmud MS, et al. (*ICNC* 2018)
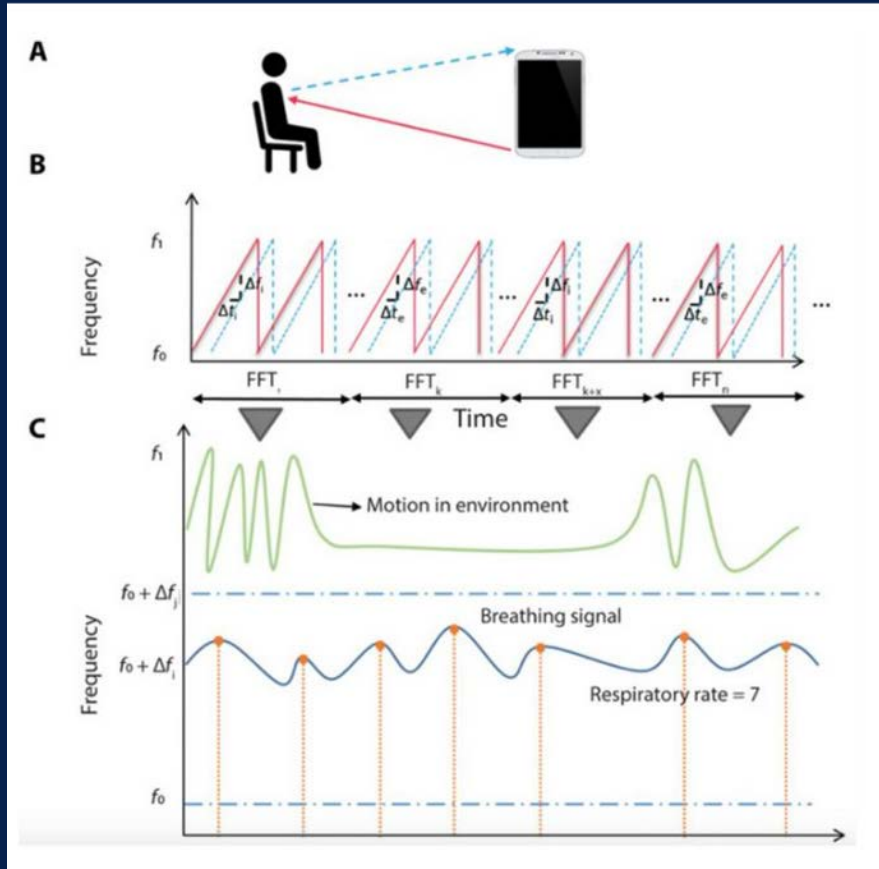
...and beyond

- ◆ Wearables can also be used to detect:
  - ◆ Withdrawal
  - ◆ Craving
  - ◆ Stress

- ◆ Can be integrated into a smart system for patients with active OUD

[1]Kulman E, et al. (*Proc Ann Hawaii Int Conf Syst Sci* 2021);
[2]Carreiro S, et al. (*Drug Alc Dep* 2020)

Wearables to detect intoxication

- ◆ Contactless system converts a mobile phone speaker and microphone into short range sonar, uses machine learning to identify:
  - ◆ Respiratory depression (87% sensitivity and 89% specificity)
  - ◆ Opioid Induced Central Apnea (96% sensitivity and 98% specificity)

[1]Nandakumar R, et al. (*Sci Transl Med* 2019)   #ASAM2021

Wearables to detect & <u>treat</u> intoxication
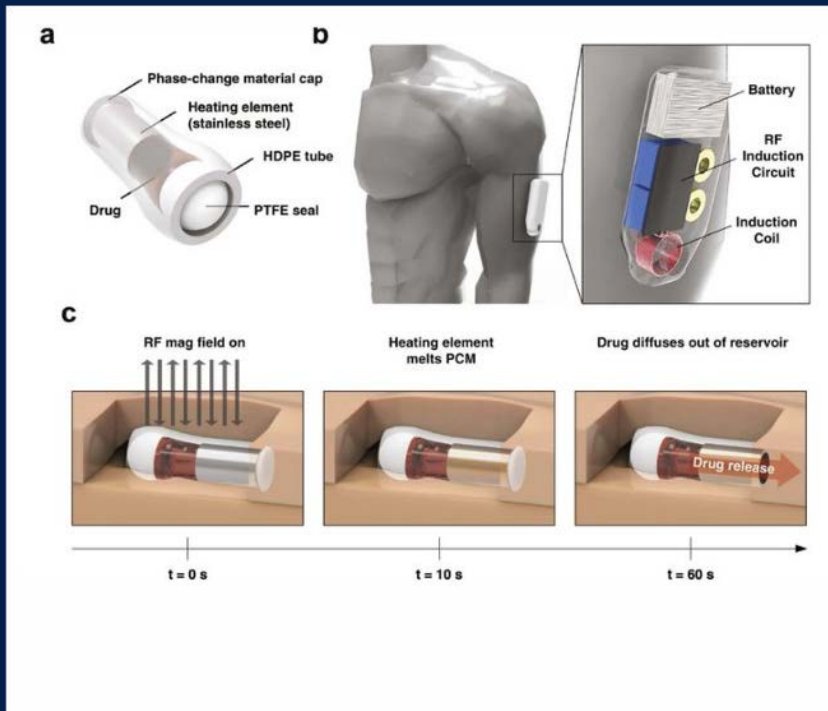
- The "Holy Grail"—everyone wants to do this
- Closed loop delivery system that senses opioid overdose and auto-injects naloxone

- Acceptability is questionable—and critical for success

[1]Dhowan B, et al. (*J Controlled Release* 2019)   #ASAM2021

Mobile Biochemical EtOH Detection

- ◆ Bluetooth breathalyzer + mobile app available
- ◆ Includes digital facial recognition
- ◆ Off-the-shelf technology

[1]https://www.soberlink.com   #ASAM2021

Wearables for Biochemical Detection

- Transdermal alcohol concentration (TAC) can be measured via a wrist (or ankle) worn wearable sensor

- Delay in detection from drinking initiation is approximately half hour

[1]Wang Y, et al. (*Alcohol* 2021)
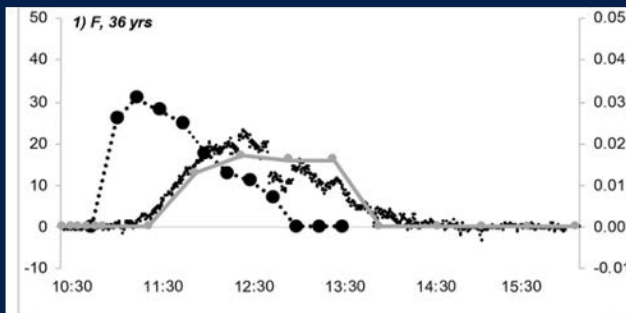
Final Takeaways

◆ Approaches to drug monitoring during COVID-19

◆ Novel / uncommon substances of abuse

◆ Benefits and drawbacks of alternative technologies for drug monitoring

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