- "The idea that some lives matter less is the root of all that is wrong with the world.“
- Dr. Paul Farmer

# How Did I End Up Here?

https://bryankramer.com/tell-unique-story/

- I'm not an Infectious Disease Doctor
- I'm not an Addiction Medicine Specialist

# Back in 2017… Rural Eastern Kenya

Estimated duration (days) of hospital stay: 4.

IP NO: ________ Temp: 39.2 °C Pulse: 146 b/m BP: 108/60 Weight: 47 kg

HIV Status: Known/Unknown (Circle one) Discharge Diagnosis: ________

History, Examination, Findings and Treatment: Date of Discharge ________

| Date: | | Name of C.O/M.O |
|---|---|---|
| | 40 cough x10/7, productive cough, hotness of the body<br>wt loss<br>heavy smoker / takes alcohol<br>has been on drugs unknown to him c̄ no improvement<br>O/E sick looking / febrile<br>pallor<br>RS - bronchial breath sounds (L)<br>- reduced air entry (R) | |

6/9/018 PITC - Client is already known KP who is under care at Mbitini health centre CCC. He started ART on 3/9/018

# 2019- Doctors Without Borders in South Sudan

# 2020-Covid Pandemic- Navajo Reservation

# 2021

*Building the Future of HIV Care through Clinical Excellence and Health Equity Leadership*

Class of 2023

Earl Gerald (EG) Carlos, DO, AAHIVS

*(He/Him)*

Rebecca Lee, DO, AAHIVS

*(She/Her)*

Oliver Refugio, MD, MPH, AAHIVS

*(He/Him)*

# 2023- Democratic Republic of Congo

# HIV and Pain Management

Earl Gerald Garcia Carlos, DO, MPH, AAHIVS

Director of Primary Care- Detroit Community Health Connection
HIV Specialist, Family Medicine

# Learning Objectives

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

1. Define pain management strategies that are supported by guidelines
2. Describe the relation between HIV infection and the Opioid Epidemic
3. Summarize common mistakes in interpretation of toxicology tests
4. Know the indications and contraindications for the use of Medication Assisted Therapy in People Live with HIV (PLH)

# Polling Question

Recent studies that estimate the prevalence of “Chronic Pain” associated with HIV has been found to range

A. 0-5%
B. 5-15%
C. 15-25%
D. Up to 90%

# Polling Question

Recent studies that estimate the prevalence of “Chronic Pain” associated with HIV has been found to range

A. 0-5%

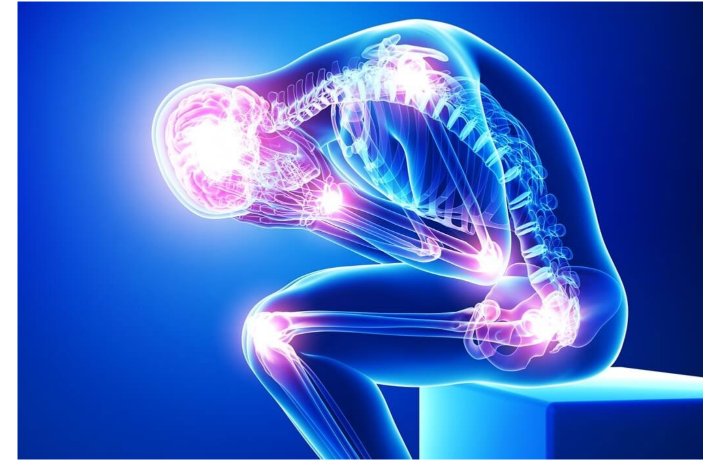
B. 5-15%

C. 15-25%

**D. Up to 90% (Addis, Deberry et. al, 2020)**

# Chronic Pain and HIV

- Chronic pain
  - Defined as lasting at least three months and not associated with ongoing tissue injury
  - Contributes to high rate of disability and decreased quality of life
- Per studies noted
  - 25-90% of PWH are living with "Chronic Pain"(**Addis, Deberry et. al, 2020**)

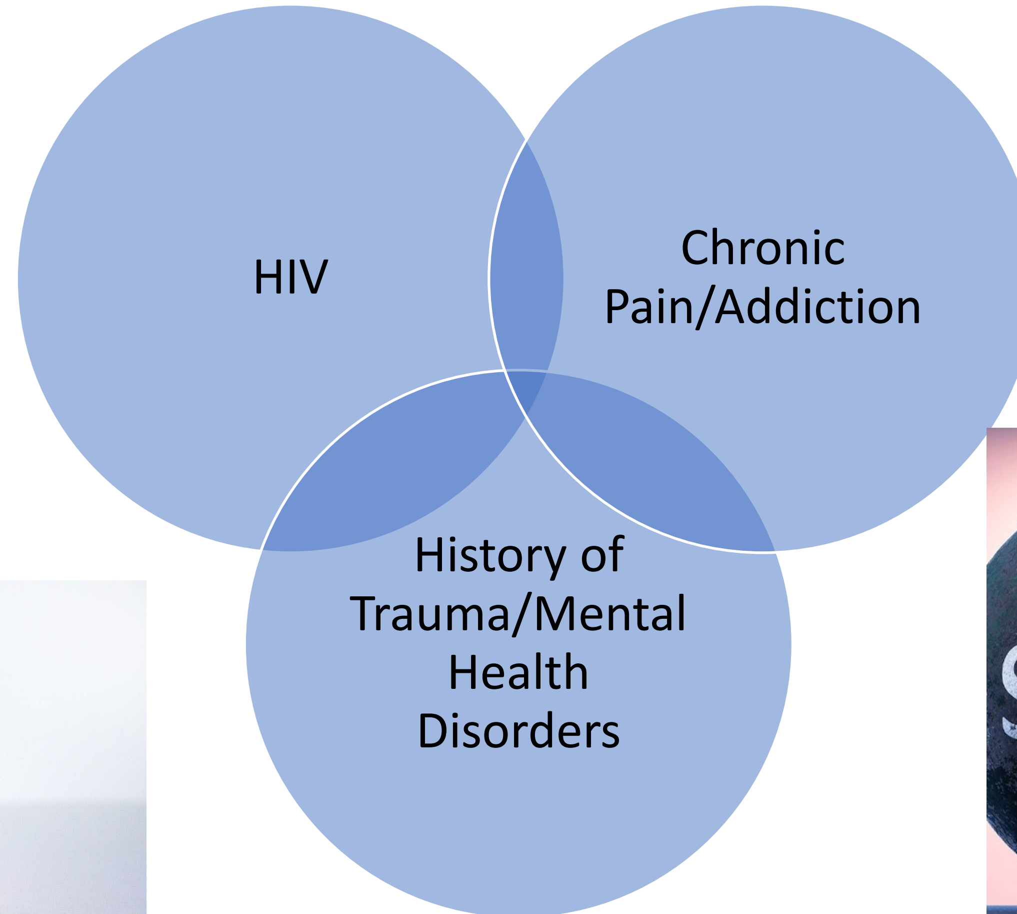


https://images.app.goo.gl/WtrSPmLAnsxd3g2B6

# International Task Force on Pain and AIDS

- 1994- International task Force on Pain and AIDS was created to address this problem
  - In a review article by the IASP, they emphasized the prevalence of pain and its undertreatment (Breibart, Passik 1996)
- Women are more likely than men to have chronic HIV-related pain
  - Women were also at higher risk for being under-treated for their pain
- Etiology of the pain can vary
  - Viral and drug-induced peripheral neuropathies
  - Joint, head, legs and back pain

# Stigma



https://chphealthmt.org/news/5-facts-that-challenge-the-stigma-around-mental-health-issues

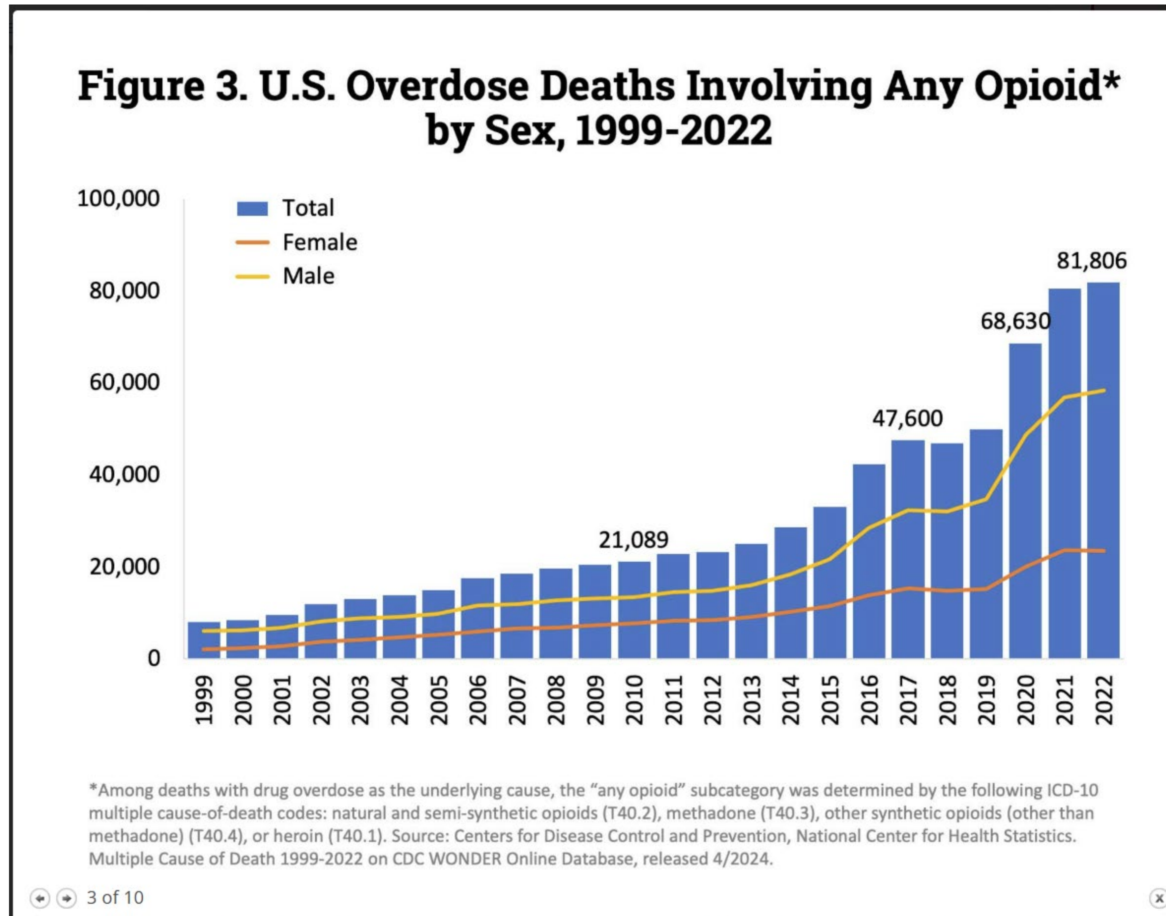
https://www.menningerclinic.org/news-resources/bloggers-confront-the-stigma-of-mental-illness

# Our Tools?

- We don’t have the magic pill
- Interdisciplinary Care
  - Mental/Behavioral Health
  - Non-opioid therapy
    - Physical Therapy
    - Muscle Relaxants
    - NSAIDs
    - Movement/Exercise Programs
- Opioid Therapy→ They ALL are not the best either
  - Full Agonists
  - Partial Agonist
    - Buprenorphine
  - Antagonist
    - Naltrexone

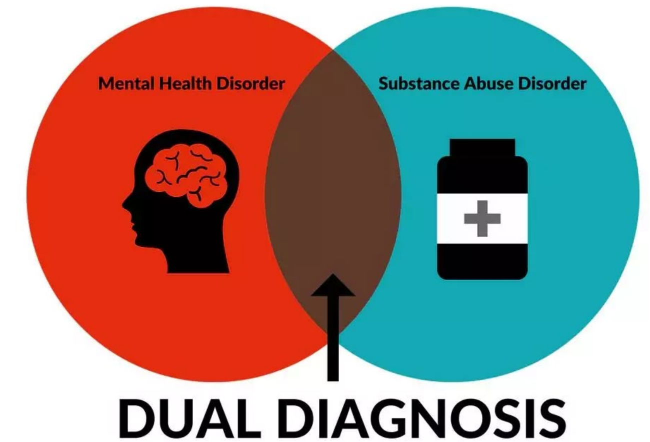
# Opioids and HIV

# Opioid Deaths in the United States



# Pain, Opioids and HIV

- Opioids are commonly prescribed to PWH
  - 21-53% (Cunningham 2018)
- HIV infected persons also receive higher doses of opioids and are more likely to have substance use disorder and mental illness (Cunningham 2018)




https://images.app.goo.gl/DgjGwrP7sqwwRNA99

# 55-year-old male w/ Chronic Pain/HIV

- 55-year-old male with a PMH of HIV presenting for primary care
- Chronic back and shoulder pain
  - MVA about 15 years ago
  - Repeated sessions of physical therapy, last session was about 1 year ago
  - He says that his pain today is a 10/10
- Pain medication
  - Non-opioids
    - Cyclobenzaprine 10 mg at night
  - Opioids
    - Oxycodone ER 60 mg BID
    - Oxycodone IR 10 mg Every 6 hours for breakthrough pain

https://images.app.goo.gl/p23dWnyFsXnqAHRY8

# Case- continued

https://images.app.goo.gl/56owevypivYhhwnp8

- Past Medical History
  - Diabetes
    - Metformin 500 mg BID
    - Pitavastatin 2 mg nightly
    - Olmesartan 20 mg daily
  - Depression
    - Sertraline 100 mg daily
- HIV
  - Diagnosed in 2020, history of injection drug use and partner with HIV
  - Viral Load < 20
  - CD 4 500/30%
  - TAF/FTC/DRV/c + DTG

# Case- ER Visit

- Presented to the emergency department twice the past 2 months because he ran out of pain medication
- Admits to buying oxycodone on the street and to resorting back to injecting heroine when pain is severe
- Last injection drug use was 3 weeks ago

# Social History

- Social history
  - Chronic pain for 15 years s/p MVA
  - Divorced
    - Married with 2 children, divorced 10 years ago
    - Currently with male partner
    - Acquired HIV after divorce
  - History of depression since adolescent years
    - Father was present, but verbally abusive
    - Ran away from home several times growing up
  - High school education
    - Works in a car factory

https://images.app.goo.gl/85h6deKiCFt82RRj9

# Question

- What should you do?
  - 55-year-old male, virologically suppressed TAF/FTC/DRV/c+DTG, history of IVDU and opioid overdose
    a) Re-prescribe original pain regimen
    b) Have him referred to pain management
    c) Have him referred to orthopedic surgery
    d) Have him referred to physical therapy
    e) Ask him more about his pain experience

# Question

- What should you do?
  - 55-year-old male, virologically suppressed TAF/FTC/DRV/c+DTG, history of IVDU and opioid overdose
    a) Re-prescribe original pain regimen
    b) Have him referred to pain management
    c) Have him referred to orthopedic surgery
    d) Have him referred to physical therapy
    **e) Ask him more about his pain experience**

# Pain experience

- Key questions
  - What does a typical day look for you?
  - How does pain limit you throughout the day
  - How has your pain and function changed over time?
- Is the patient currently receiving **benefit** from their opioid therapy?
- Is the patient’s quality of life improved?

# Pain experience

- Looking for any sign that they may be looking for an alternative

https://robodk.com/blog/incremental-sheet-forming-guide/an-alternative-etf-play-for-rising-interest-rate-risks/

# Case

- He tells you that he has been on this regimen for about 10 years
- He believes that it is helping out with his pain, but he does feel concerned about the high doses he has to take
- He says that at times he feels "stuck" with his opioid therapy
  - He cannot function with or without his medication

https://tinybuddha.com/blog/feel-stuck-life-secret-dealing/

# Guidelines from CDC for Prescribing Opioids

# Guidelines from CDC for Prescribing Opioids

- Prior to initiating Treatment with Opioids
  - Choose non-pharm and non-opioid therapies
    - NSAIDs, Acetaminophen
    - Muscle relaxants(?), nerve pain medication
    - Physical therapy
  - Establish treatment goals
    - Chronic pain is chronic
      - No magic pill
  - Discuss risks and benefits of opioid use and patient/practitioner responsibilities
    - Pain contract

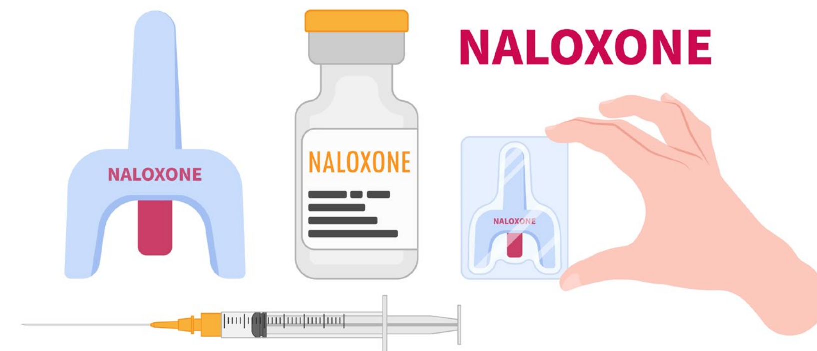
https://images.app.goo.gl/Q1vJLzPQnhTSyMaC7

# Opioid Selection

- Determining Opioid Selection, Dose and Duration
- Prescribe immediate release formulations
  - Lowest effective dose
    - **<50 Morphine Milligram Equivalents**
  - No greater than 3-7 days
  - Revaluate after 3-7 days

# Risks and Harms

- Assessing Risks and Harms
  - Naloxone
  - Prescription drug monitoring program
  - Avoid prescribing both opiates and benzodiazepines
  - **Consider buprenorphine/naloxone or other forms of medication assisted therapy**




https://images.app.goo.gl/Wd6zxV438zNfuEdG6

# Morphine Milligram Equivalents

**Opioid Conversions:**
**Calculating Morphine Milligram Equivalents (MME)**

| Opioid | Morphine Equivalent | Conversion Factor | Divide | Multiply |
|---|---|---|---|---|
| Morphine | 30mg | 1 | | |
| Hydrocodone | 30mg (6 tabs of 5/325) | 1 | | |
| Hydromorphone | 7.5mg | 4 | | |
| Oxycodone | 20mg | 1.5 | | |
| Fentanyl | 12mcg (Never 12.5mcg) | 2 (Safe/Easy) | | |
| Codeine | 200mg | 0.15 (Not Effective) | | |
| Tramadol | 300mg | 0.10 (Not Effective) | | |

https://www.youtube.com/watch?v=xLfRqYSISv0

# MME Chart

| Opioid | MME | Typical Dose | MME per day |
|---|---|---|---|
| Morphine | 1 | 5-15 mg every 4 hours | 30 – 90 MME |
| Hydrocodone | 1 | 5 – 10 mg every 4 to 6 hours | 20 MME – 60 MME |
| Oxycodone | 1.5 | 2.5 mg to 10 mg every 4 to 6 hours | 15 – 90 MME |
| Tramadol | 0.1 | 25 mg – 100 mg every 4 to 6 hours (Max 400 mg/day) | 10 – 40 MME |
| Codeine | 0.15 | 15 mg to 60 mg every 4 hours | 13.5 – 54 MME |
| Hydromorphone | 4 | 1 mg to 2 mg every 4 hours | 24-48 MME |

# Represcribe?

# Re-prescribe?

- What should you do?
  - 55-year-old male, virologically suppressed TAF/FTC/DRV/c+DTG, history of IVDU and opioid overdose
    a) Re-prescribe original pain regimen*

    Oxycodone 60 mg ER BID, Oxycodone 10 mg every 6 hours for breakthrough

    MME= 180 + 60➔ **240**

    **I may re-prescribe his regimen for at least another 7-28 days**

    **I would have been come back within the next 1-2 weeks for further discussion**

# Case Continued

- You prescribe 7 days of the original pain regimen and have him follow up in 1 week
- He comes back in 7 days and you decide to do a **Point of Care** Urine Drug Screen
  - Test was positive for **opioids** and **benzodiazepines**

# Opioids and Benzodiazepines?

- Besides asking the patient about the findings on the initial urine drug screen, what else should you do?
  A. Send him off to pain management
  B. Switch him to another provider
  C. Prescribe him another 7 days of original pain regimen
  D. Evaluate and determine whether the initial urine findings are appropriate

# Answer to Unexpected UDS findings

- Besides asking the patient about the findings on the initial urine drug screen, what else should you do?
  A. Send him off to pain management
  B. Switch him to another provider
  C. Prescribe him another 7 days of original pain regimen
  **D. Evaluate and determine whether the initial urine findings are appropriate**

# Urine Drug Screening

…And some of its pitfalls

# Why should we do urine drug testing?

- Harm reduction tool
  - Patient and provider can be sure that patient is not being unintentionally exposed to any other substances they do not know
  - Fentanyl
- Ensure patient safety and adherence to medication
  - Drug diversion

# Communication Tips

- Always inform a patients **why** you are performing urine drug screening
- Be supportive even when unanticipated results occur
- Avoid saying:
  - “Your urine drug screen was not clean”
- Emphasize that this is an INITIAL urine drug screen
  - Confirm if there are questions/concerns

https://images.app.goo.gl/5KvDeKhZXgrWLknE9

# Initial urine drug screen

- Immunoassay
  - Utilizes antibody  technology to detect drug metabolites
  - Cheap and easy to use
  - Cons-
    - prone to false positives and misinterpretation

https://www.toxtests.com/products/7-panel-first-sign-urine-drug-test-cup-fsccup-174

# Confirmatory testing

- Gas or liquid chromatography paired with mass spectroscopy
  - Confirm all initial urine drug screening tests with a confirmatory test if necessary and if it will impact patient care
- Positive test in confirmatory testing is a **true positive** (Moehler, 2017)

https://images.app.goo.gl/pzU38g5R4ZwZ146s9

# Urine Drug Detection Times

- Detection time in urine is dependent on both patient and drug characteristics
  - Examples
    - Alcohol
      - 7-12 hours in urine
    - Benzodiazepines
      - 3 days in urine for short acting- lorazepam
      - 30 days in urine for long acting- diazepam
    - Marijuana
      - Single use- 3 days in urine
      - Heavy use- 10-30 days in urine
    - Opiates
      - Heroin (morphine) 48 hours in urine

**Clarity CLIA Waived Multi-Drug Urine Test Cup** is competitive binding, lateral flow immunochromatographic assay for qualitative and simultaneous detection of Amphetamine, Oxazepam, Cocaine, Cannabinoids, Methamphetamine, Morphine, Oxycodone, EDDP, Secobarbital, Buprenorphine, Methylenedioxymethamphetamine, Phencyclidine, Propoxyphene , Nortriptyline and Methadone in human urine at the cutoff concentrations of:

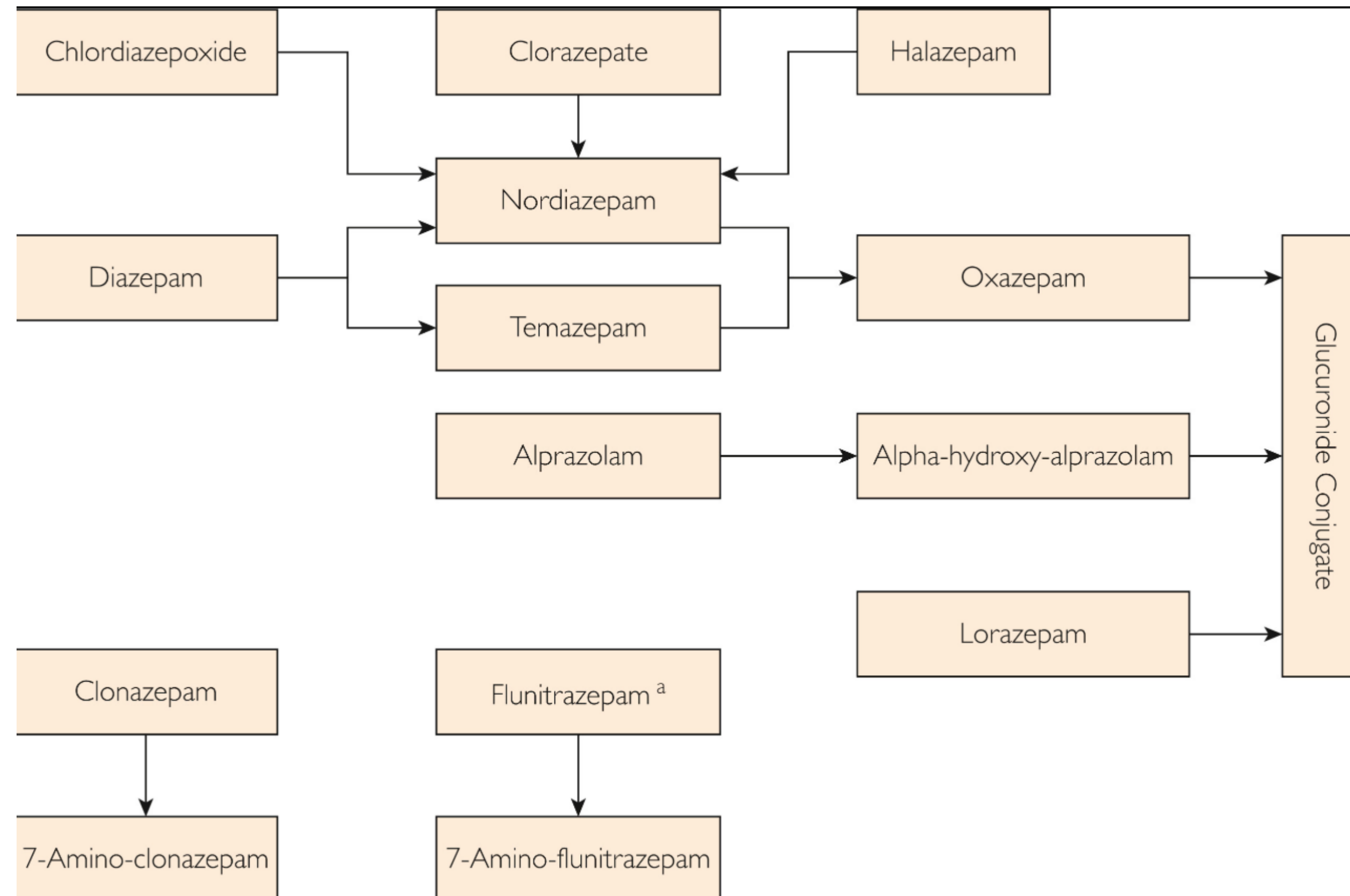
| Test | Calibrator | Cut-off (ng/ml) |
|---|---|---|
| AMP | d-Amphetamine | 1000 ng/mL |
| BAR | Secobarbital | 300 ng/mL |
| BUP | Buprenorphine | 10 ng/mL |
| BZO | Oxazepam | 300 ng/mL |
| COC | Benzoylecgonine | 300 ng/mL |
| MDMA | 3,4-Methylenedioxy-methamphetamine | 500 ng/mL |
| MET | D-Methamphetamine | 1000 ng/mL |
| MTD | Methadone | 300 ng/mL |
| MOP | Morphine | 300 ng/mL |
| OPI | Morphine | 2000 ng/ml |
| OXY | Oxycodone | 100 ng/mL |
| EDDP | 2-Ethylidene-1,5-dimethyl-3,3-dipheylpyrolidine (EDDP) | 300 ng/ml |
| PCP | Phencyclidine | 25 ng/mL |
| TCA | Nortriptyline | 1000 ng/ml |
| THC | 11-nor-$\Delta^9$-THC-9-carboxylic acid | 50 ng/mL |
| PPX | Propoxyphene | 300 ng/ml |

https://claritydiagnostics.com/wp-content/uploads/2022/11/clarity_clia_waived_doa_cup_package_insert.pdf

# Common Initial Drug Monitoring Panel (POC)

- Amphetamines
- Barbiturates
- **Benzodiazepines**
  - **Oxazepam or nordiazepam**
- Marijuana
- Cocaine
- **Opioids (Methadone, oxycodone)**
  - **Oxycodone**
- **Opiates (morphine, codeine)**
  - **Morphine**
- Phencyclidine

# Benzodiazepines Metabolism




https://www.mayoclinicproceedings.org/cms/10.1016/j.mayocp.2016.12.007/asset/68a0e256-ec23-45ec-90ec-7d4ca700719b/main.assets/gr2_lrg.jpg

# Benzodiazepines

- Immunoassays for benzodiazepines detect **Oxazepam or Nordiazepam**
- Diazepam, chlordiazepoxide **will be detected on initial UDS**
- Order confirmatory urine testing for:
  - Alprazolam or Lorazepam
    - will NOT BE detected on initial POC testing
  - Clonazepam
    - will NOT BE detected on initial POC testing

https://images.app.goo.gl/vERQwQ8AdTeG3qFh9

# Which benzodiazepine is the patient taking?

| | | | | | |
|---|---|---|---|---|---|
| Benzodiazepines [82000090] | A | POSITIVE | ng/mL | <100 | F |
| Alphahydroxyalprazolam [82000130] | H | 670 | ng/mL | <25 | F |
| Alphahydroxymidazolam [86011279] | N | NEGATIVE | ng/mL | <50 | F |
| Alphahydroxytriazolam [82000150] | N | NEGATIVE | ng/mL | <50 | F |
| Aminoclonazepam [86011280] See Note A | A | INTERFERENCE | ng/mL | <25 | F |
| Hydroxyethylflurazepam [86011281] | N | NEGATIVE | ng/mL | <50 | F |
| Lorazepam [82000120] | N | NEGATIVE | ng/mL | <50 | F |
| Nordiazepam [82000100] | N | NEGATIVE | ng/mL | <50 | F |
| Oxazepam [82000110] | N | NEGATIVE | ng/mL | <50 | F |
| Temazepam [82000158] | N | NEGATIVE | ng/mL | <50 | F |

# Alprazolam 2 mg TID

| | | | | | |
|---|---|---|---|---|---|
| Benzodiazepines [82000090] | A | POSITIVE | ng/mL | <100 | F |
| Alphahydroxyalprazolam [82000130] | H | 670 | ng/mL | <25 | F |
| Alphahydroxymidazolam [86011279] | N | NEGATIVE | ng/mL | <50 | F |
| Alphahydroxytriazolam [82000150] | N | NEGATIVE | ng/mL | <50 | F |
| Aminoclonazepam [86011280]<br>See Note A | A | INTERFERENCE | ng/mL | <25 | F |
| Hydroxyethylflurazepam [86011281] | N | NEGATIVE | ng/mL | <50 | F |
| Lorazepam [82000120] | N | NEGATIVE | ng/mL | <50 | F |
| Nordiazepam [82000100] | N | NEGATIVE | ng/mL | <50 | F |
| Oxazepam [82000110] | N | NEGATIVE | ng/mL | <50 | F |
| Temazepam [82000158] | N | NEGATIVE | ng/mL | <50 | F |

# Which benzodiazepine is the patient taking?

| | | | | | |
|---|---|---|---|---|---|
| Benzodiazepines [82000090] | A | POSITIVE | ng/mL | <100 | F |
| Alphahydroxyalprazolam [82000130] | H | 26 | ng/mL | <25 | F |
| Alphahydroxymidazolam [86011279] | N | NEGATIVE | ng/mL | <50 | F |
| Alphahydroxytriazolam [82000150] | N | NEGATIVE | ng/mL | <50 | F |
| Aminoclonazepam [86011280] | N | NEGATIVE | ng/mL | <25 | F |
| Hydroxyethylflurazepam [86011281] | N | NEGATIVE | ng/mL | <50 | F |
| Lorazepam [82000120] | H | 166 | ng/mL | <50 | F |
| Nordiazepam [82000100] | H | 121 | ng/mL | <50 | F |
| Oxazepam [82000110] | H | 162 | ng/mL | <50 | F |
| Temazepam [82000158] | H | 212 | ng/mL | <50 | F |
| Benzodiazepines Comments | | | | | F |

# Diazepam 5 mg BID, recently switched from Lorazepam (why is there alprazolam?)

| | | | | | |
|---|---|---|---|---|---|
| Benzodiazepines [82000090] | A | POSITIVE | ng/mL | <100 | F |
| Alphahydroxyalprazolam [82000130] | H | 26 | ng/mL | <25 | F |
| Alphahydroxymidazolam [86011279] | N | NEGATIVE | ng/mL | <50 | F |
| Alphahydroxytriazolam [82000150] | N | NEGATIVE | ng/mL | <50 | F |
| Aminoclonazepam [86011280] | N | NEGATIVE | ng/mL | <25 | F |
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| Lorazepam [82000120] | H | 166 | ng/mL | <50 | F |
| Nordiazepam [82000100] | H | 121 | ng/mL | <50 | F |
| Oxazepam [82000110] | H | 162 | ng/mL | <50 | F |
| Temazepam [82000158] | H | 212 | ng/mL | <50 | F |
| Benzodiazepines Comments | | | | | F |

# Benzodiazepines in UDS

- False positives (Moehler, 2017)
  - Sertraline
    - Widely reported to cause false-positives with benzodiazepine immunoassays
  - Efavirenz
    - TAF/FTC/EFV (Atripla)
    - It may cross-react with Cannabinoid immunoassays

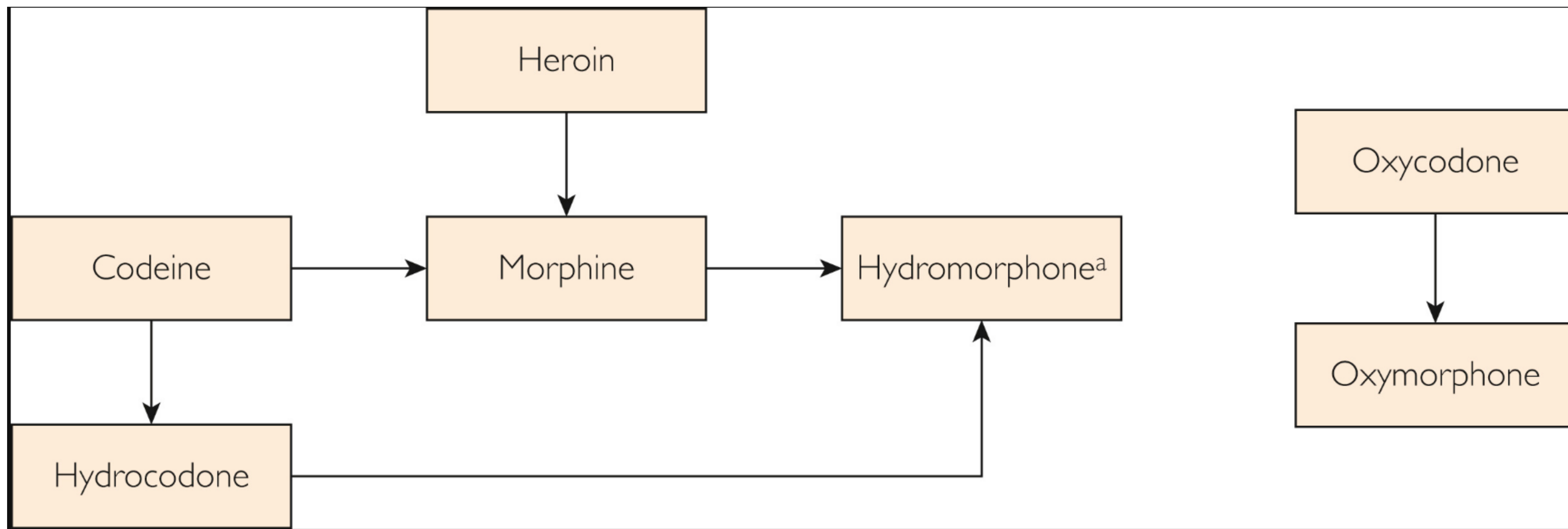
# Opioids/Opiates

# Opioids/Opiates

- "Opioids"
  - Synthetic/semi-synthetic (lab-made)
  - Morphine
  - Hydromorphone/hydrocodone
  - Oxycodone
  - Fentanyl
  - Tramadol
- "Opiates"
  - Derived from opium poppy seed
  - Morphine and codeine
- All opiates are opioids, not all opioids are opiates

https://fox59.com/news/poppy-seed-bagel-leads-to-traumatizing-drug-test-result-for-expectant-mom/

# Opioids/Opiate Metabolism Chart




https://www.mayoclinicproceedings.org/cms/10.1016/j.mayocp.2016.12.007/asset/807e5e88-eea9-4b18-bddb-e6d55f21a1d4/main.assets/gr1_lrg.jpg

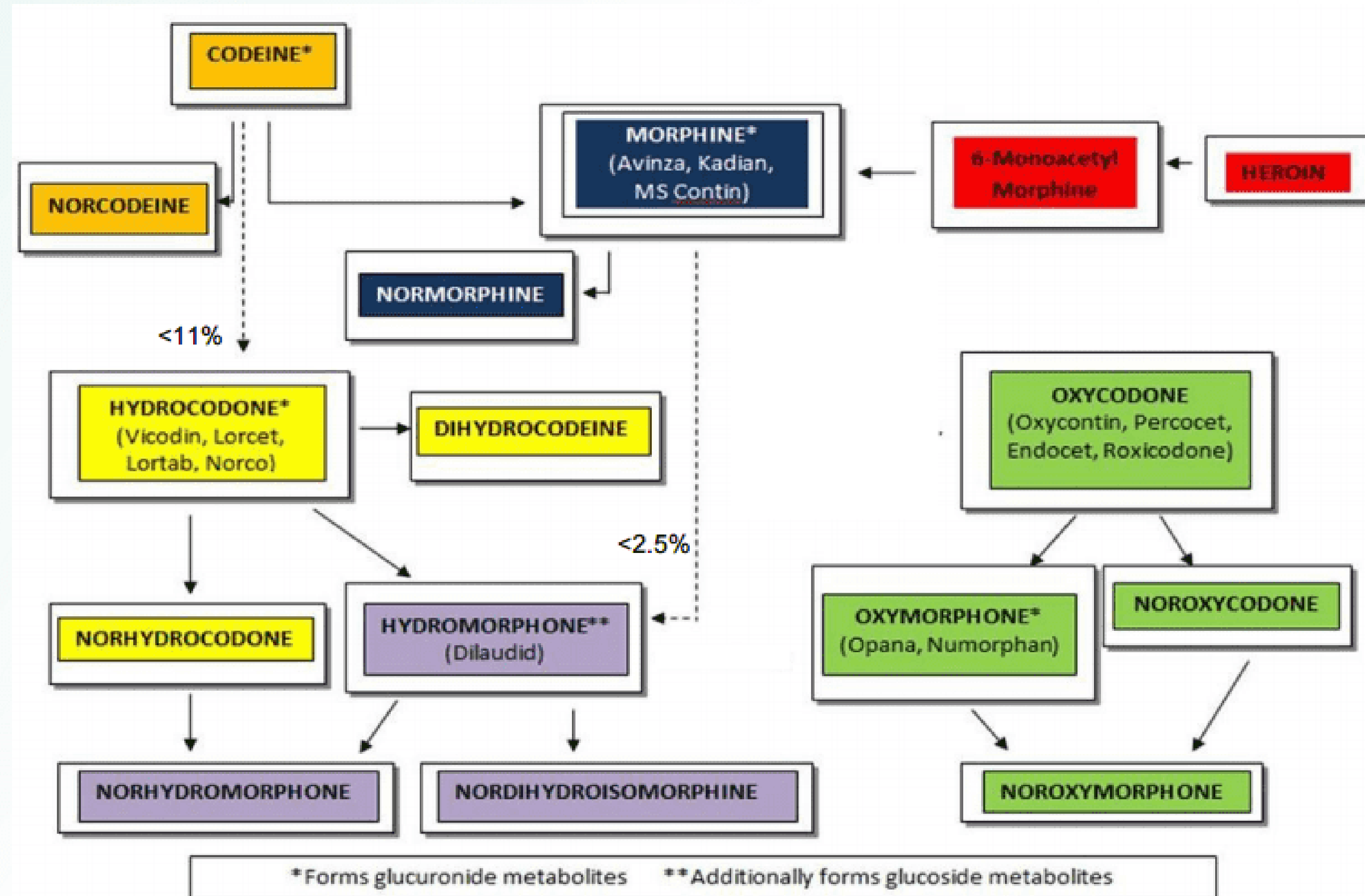
# Opioids/Opiates- UDS

- Urine drug screening may not detect all opioid/opiate drugs equally
- False negatives are common
  - Immunoassays use **oxycodone** to react to **opioids**
    - Hydrocodone, hydromorphone
  - Immunoassays use **morphine** to react to **opiates**
    - Heroine, Codeine
- Fentanyl, methadone and buprenorphine (synthetic opioids) have different chemical structures
  - Will not react to morphine POC immunoassays

# Opiate- Metabolism

- Codeine and hydrocodone metabolism can produce small amounts of hydromorphone
- Codeine is metabolized to morphine and norcodeine
  - In urine, all 3 compounds (morphine, codeine and norcodeine) may be detected
- Heroin is metabolized to 6-acetylmorphine→ 6-monoacetylmorphine (6-MAM)→**morphine**
  - **6-MAM**← more specific for heroin

# Opiate Metabolism



# Which opiate/opioid is the patient taking?

| | | | | | |
|---|---|---|---|---|---|
| Opiates [82000230] | A | POSITIVE | ng/mL | <100 | F |
| Codeine [82000240] | H | >10000 | ng/mL | <50 | F |
| Hydrocodone [82000260] | H | 52 | ng/mL | <50 | F |
| Hydromorphone [82000270] | N | NEGATIVE | ng/mL | <50 | F |
| Morphine [82000250] | H | 221 | ng/mL | <50 | F |
| Norhydrocodone [86011282] | H | 57 | ng/mL | <50 | F |
| Opiates Comments [86025919] | | | | | F |
| See Opiates Notes, LDT Notes | | | | | |
| Oxycodone [82000280] | N | NEGATIVE | ng/mL | <100 | F |

# Acetaminophen w/ Codeine 60 mg QID

| | | | | | |
|---|---|---|---|---|---|
| Opiates [82000230] | A | POSITIVE | ng/mL | <100 | F |
| Codeine [82000240] | H | >10000 | ng/mL | <50 | F |
| Hydrocodone [82000260] | H | 52 | ng/mL | <50 | F |
| Hydromorphone [82000270] | N | NEGATIVE | ng/mL | <50 | F |
| Morphine [82000250] | H | 221 | ng/mL | <50 | F |
| Norhydrocodone [86011282] | H | 57 | ng/mL | <50 | F |
| Opiates Comments [86025919] | | | | | F |
| See Opiates Notes, LDT Notes | | | | | |
| Oxycodone [82000280] | N | NEGATIVE | ng/mL | <100 | F |

# Which opiate/opioid is the patient taking?

| Component | Flag | Result | Units | Range | Status |
|---|---|---|---|---|---|
| Amphetamines [82000000] | N | NEGATIVE | ng/mL | <500 | F |
| Barbiturates [82000030] | N | NEGATIVE | ng/mL | <300 | F |
| Benzodiazepines [82000090] | N | NEGATIVE | ng/mL | <100 | F |
| Cocaine Metabolite [82000180] | N | NEGATIVE | ng/mL | <150 | F |
| Marijuana Metabolite [82000160] | N | NEGATIVE | ng/mL | <20 | F |
| Methadone Metabolite [82000200] | N | NEGATIVE | ng/mL | <100 | F |
| Opiates [82000230] | N | NEGATIVE | ng/mL | <100 | F |
| Oxycodone [82000280] | N | NEGATIVE | ng/mL | <100 | F |
| Phencyclidine [82000310] | N | NEGATIVE | ng/mL | <25 | F |
| Creatinine [84002730] | N | 51.6 | mg/dL | > or = 20.0 | F |
| pH [84002720] | N | 5.1 | | 4.5-9.0 | F |
| Oxidant [84002740] | N | NEGATIVE | mcg/mL | <200 | F |

# Buprenorphine/Naloxone 4 mg BID

**DRUG MONITOR, BUP, W/CONF,W/NALOXONE,URINE** Reviewed: **07/16/25**

-Specimen Information-

Specimen ID: 1
Collection Start Date: 07/14/2025 11:05 A

| Component | Flag | Result | Units | Range | Status |
|---|---|---|---|---|---|
| Buprenorphine [82000420] | A | POSITIVE | ng/mL | <5 | F |
| Buprenorphine [82000430] | H | 428 | ng/mL | <2 | F |
| Norbuprenorphine [82000490] | A | INTERFERENCE | ng/mL | <2 | F |
| See Note A | | | | | |
| Naloxone [86013545] | H | 1454 | ng/mL | <2 | F |
| Buprenorphine Comments [86025923] | | | | | F |
| See Buprenorphine Notes, LDT Notes | | | | | |

# Back to the case

# Case - 55-year-old male w/ Chronic Pain/HIV

- He has been taking sertraline 100 mg daily as prescribed
- Since this is the first time you are seeing the patient, you confirm the initial urine drug screen to include all forms of benzodiazepines (results come back negative a few days later)
- At this visit, he asks you whether you can keep prescribing oxycodone ER 60 mg BID, along with oxycodone 10 mg every 6 hours for breakthrough pain

# Case

- What should you do?
  A. Have a discussion about the risks of consistent full agonist opioid use
  B. Prescribe oxycodone ER 60 mg BID, along with oxycodone 10 mg every 6 hours for breakthrough pain
  C. Prescribe non-opioid prescription medication (NSAIDs and muscle relaxants)
  D. Tell him about the benefits of going back into physical therapy
  E. Have a discussion about Buprenorphine
  F. A, C, D and E

# Putting it all together

- What should you do?
  A. Have a discussion about the risks of consistent full agonist opioid use
  B. Prescribe oxycodone ER 60 mg BID, along with oxycodone 10 mg every 6 hours for breakthrough pain
  C. Prescribe non-opioid prescription medication (NSAIDs and muscle relaxants)
  D. Tell him about the benefits of going back into physical therapy
  E. Have a discussion about Buprenorphine
  **F. A, C, D and E**

# Buprenorphine

# Buprenorphine for Chronic Pain

- Evaluation of Buprenorphine Rotation in Patients Receiving Long-Term Opioids for Chronic Pain: Systemic Review (Powell, Rosenberg 2021)
  - 22 studies
    - 5 RCTs
    - 7 case-control or cohort studies
    - 10 uncontrolled pre-post studies
  - 1616 unique individuals

# Buprenorphine for Chronic Pain- Evidence

- Evaluation of Buprenorphine Rotation in Patients Receiving Long-Term Opioids for Chronic Pain: Systemic Review (Powell, Rosenberg 2021)
- "In this systemic review, buprenorphine was associated with **reduced chronic pain intensity without precipitating opioid withdrawal in individuals** with chronic pain receiving long term opioid therapy"

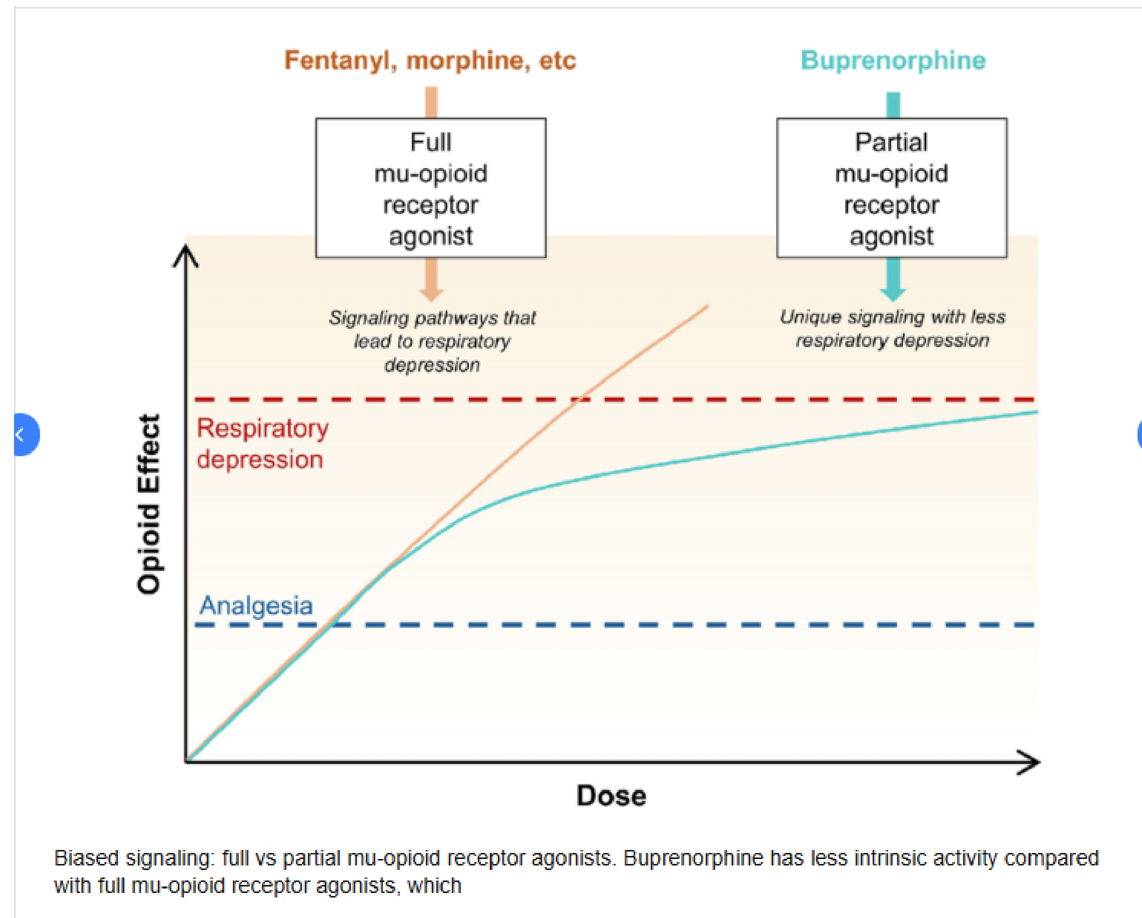
# Partial Opioid Agonist?

# But doc, I don’t want a medication with only partial effect!

# Why use Buprenorphine?

- **Partial opioid agonist**
- It CAN have less ‘opioid’ burden
  - Decreased sedation
  - Decreased risk of respiratory depression
  - Less risk of **opioid induced hyperalgesia**
    - Paradoxical reaction to too much opioid burden
    - Pain is worse despite being on current pain regimen

# Partial Opioid Agonist




Biased signaling: full vs partial mu-opioid receptor agonists. Buprenorphine has less intrinsic activity compared with full mu-opioid receptor agonists, which

https://www.researchgate.net/figure/Biased-signaling-full-vs-partial-mu-opioid-receptor-agonists-Buprenorphine-has-less_fig5_345322590

# Outcomes in Long-term Opioid Tapering and Buprenorphine Transition: A Retrospective Clinical Data Analysis

- Sturgeon, Sullivan et al 2020 American Academy of Pain Medicine
- Retrospective review of **240 patients with chronic pain** and Long-Term Opioid Therapy (Very High > 90 MME)
- Tried to do 2 things
  - Taper medications to **MME < 90**
  - If unsuccessful, transition to Buprenorphine

https://www.painnewsnetwork.org/stories/2017/1/2/few-pain-patients-become-long-term-opioid-users

# Results

- 44.6% successfully tapered their medications to under 90 MME
  - 107/240
- **18.8%** transitioned to buprenorphine
  - 45/240
- 36.6% dropped out
  - 88/240
    - 11 patients during the taper
    - 8 patients during the transition to buprenorphine
    - 69 patients were lost to follow up before the taper began

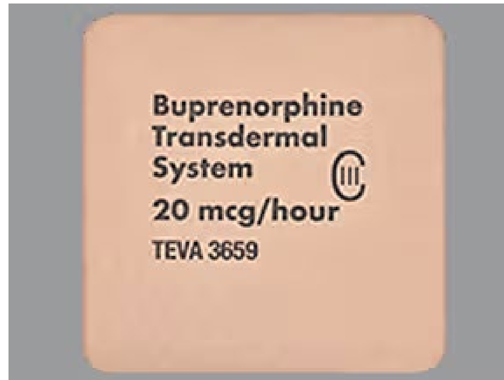
# Conclusion

- Higher initial doses of opioids predicted a higher likelihood of requiring buprenorphine transition
- Co-occurring benzodiazepine or z-drug prescriptions predicted a greater likelihood of dropout with both interventions

# MY Conclusion from this study

- I would consider transitioning to Buprenorphine on those presenting with long-term opioid therapy and high MME (>90)
- If they have low MME (<90), but have co-occurring use of **benzodiazepines or z-drugs**, discussion about Buprenorphine may be appropriate to minimize overall risk

# Formulations

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https://images.app.goo.gl/rViQ2qMKYeJf2vg z5

https://images.app.goo.gl/cghsPhPfyLkcPcat6

# Buccal/Dermal vs Sublingual Tablet/Film

- Dermal
  - 5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, 20 mcg/hr
- Buccal
  - 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, 900 mcg (dosed twice a day)

- Tablet/film
- 2 mg
- 4 mg
- 8 mg

# Buprenorphine

| | | MME | Typical Dose | MME per Day |
|---|---|---|---|---|
| Morphine | | 1 | 5-15 mg every 4 hours | 20-90 MME |
| Burprenorphine | film/tablet | 38.8 | 2-8 mg every 12 hours | 155- 620 MME |
| | | | 2-8 mg every 8 hours | 232- 931 |
| | | | 2-8 mg every 6 hours | 310-1241 |
| | patch | 2.2 | 5-20 mcg per hour | 11- 44 MME |
| | buccal | 0.039 | 75 mcg – 900 mcg every 12 hours | 5.85-23.4 MME |

https://research-mme.wakehealth.edu/main

# Making the Switch

# Making the Switch

- More than one way to do this
- Always… First Do No Harm
- Keep the patient safe and keep the patient comfortable

# Initiation

- Traditional
  - Stop full agonist
    - Await Withdrawal Symptoms
  - Full 24 hours
    - Depending on current opiate regimen
  - 12 hours
    - **COWS**
- Supportive medication to help Withdrawal Symptoms
  - Clonidine
  - Hydroxyzine
  - Tizanidine
  - Trazodone

Wesson & Ling, J Psychoactive Drugs. 2003 Apr-Jun;35(2):253-9.

# COWS Clinical Opiate Withdrawal Scale

| | |
|---|---|
| Resting Pulse Rate: ________ beats/minute<br>*Measured after patient is sitting or lying for one minute*<br>0 Pulse rate 80 or below<br>1 Pulse rate 81-100<br>2 Pulse rate 101-120<br>4 Pulse rate greater than 120 | GI Upset: *over last 1/2 hour*<br>0 No GI symptoms<br>1 Stomach cramps<br>2 Nausea or loose stool<br>3 Vomiting or diarrhea<br>5 Multiple episodes of diarrhea or vomiting |
| Sweating: *over past 1/2 hour not accounted for by room temperature or patient activity.*<br>0 No report of chills or flushing<br>1 Subjective report of chills or flushing<br>2 Flushed or observable moistness on face<br>3 Beads of sweat on brow or face<br>4 Sweat streaming off face | Tremor *observation of outstretched hands*<br>0 No tremor<br>1 Tremor can be felt, but not observed<br>2 Slight tremor observable<br>4 Gross tremor or muscle twitching |
| Restlessness *Observation during assessment*<br>0 Able to sit still<br>1 Reports difficulty sitting still, but is able to do so<br>3 Frequent shifting or extraneous movements of legs/arms<br>5 Unable to sit still for more than a few seconds | Yawning *Observation during assessment*<br>0 No yawning<br>1 Yawning once or twice during assessment<br>2 Yawning three or more times during assessment<br>4 Yawning several times/minute |
| Pupil size<br>0 Pupils pinned or normal size for room light<br>1 Pupils possibly larger than normal for room light<br>2 Pupils moderately dilated<br>5 Pupils so dilated that only the rim of the iris is visible | Anxiety or irritability<br>0 None<br>1 Patient reports increasing irritability or anxiousness<br>2 Patient obviously irritable anxious<br>4 Patient so irritable or anxious that participation in the assessment is difficult |
| Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored*<br>0 Not present<br>1 Mild diffuse discomfort<br>2 Patient reports severe diffuse aching of joints/ muscles<br>4 Patient is rubbing joints or muscles and is unable to sit still because of discomfort | Gooseflesh skin<br>0 Skin is smooth<br>3 Piloerrection of skin can be felt or hairs standing up on arms<br>5 Prominent piloerrection |
| Runny nose or tearing *Not accounted for by cold symptoms or allergies*<br>0 Not present<br>1 Nasal stuffiness or unusually moist eyes<br>2 Nose running or tearing<br>4 Nose constantly running or tears streaming down cheeks | Total Score ________<br>The total score is the sum of all 11 items<br>Initials of person completing Assessment:______________ |

Score: 5-12 mild; 13-24 moderate; 25-36 moderately severe; more than 36 = severe withdrawal

# Initiation

- **Microdosing/Overlap Method**
  - Start at low dose of buprenorphine
  - By day 7, full discontinue full agonist
  - Use for patients on initially high MME

https://images.app.goo.gl/m2dq6TG1itZJFWQN8

# Calculate the MME

- Oxycodone ER 60 mg BID, Oxycodone 10 mg every 6 hours PRN
- **MME is High – 240**
- Buprenorphine/Naloxone sublingual film/tablet
- Goal= 6 mg of buprenorphine per day

# Microdosing

| Day | Buprenorphine Dose | Buprenorphine MME | Full Agonist | Full Agonist MME | Total |
|---|---|---|---|---|---|
| 1 | 0.5 mg | 19.4 | Oxycodone ER 60 mg BID, Oxycodone 10 mg every 6 hours PRN | 240 | 259.4 |
| 2 | 0.5 mg BID | 38.8 | Oxycodone ER 60 mg BID, Oxycodone 10 mg every 6 hours PRN | 240 | 278.8 |
| 3 | 1 mg BID | 77.6 | Oxycodone ER 60 mg BID, Oxycodone 10 mg every 6 hours PRN | 240 | 317.6 |

# Microdosing Sample

| Day | Buprenorphine Dose | Buprenorphine MME | Full Agonist | Full Agonist MME | Total |
|---|---|---|---|---|---|
| 4 | 1.5 mg BID | 116.4 | Oxycodone **30** mg BID (90)<br>Oxycodone 10 mg QID (60) | 150 | 266.4 |
| 5 | 2 mg BID | 155.5 | Oxycodone 30 mg once (45)<br>Oxycodone 10 mg BID (30) | 75 | 230 |
| 6 | 4 mg in the AM<br>2 mg in the PM | 310 | 0 | 0 | 232 |

# Sample

- Acetaminophen-codeine 300/60 mg every 6 hours (4 doses per day)
  - 36 MME per day
- Alternatives
  - **Consider Buprenorphine patch 10-20 mcg/hr**
    - 22 MME – 44 MME per day
  - **Consider Buprenorphine buccal film 300 mcg BID**
    - 23.4 MME per day
- Rapid Start
  - Overlap both medications for first 24 hours

# Sample

- Oxycodone/Acetaminophen 10/325 mg every 6 hours (4 doses per day)
  - 60 MME per day
- Alternatives
  - **Consider Buprenorphine buccal film 750 mcg BID**
    - 58.5 MME per day
- Rapid Start
  - Overlap and microdosing is reasonable

# HIV and Buprenorphine

# HIV and Buprenorphine- Evidence (OUD)

- Buprenorphine/Naloxone was associated with better rates of initiation of ART and improved CD4 counts (Altice, Bruce 2011)
- Clinic-based buprenorphine/naloxone maintenance therapy may potentially be effective in ameliorating some of the adverse effects of opioid dependence in HIV infected populations (Korthuis, Tozzi 2011)
- Initiation of buprenorphine results in an increase in probability of viral suppression (Kim, Lesko 2021)

# HIV and Buprenorphine- ART

- NRTIs
  - TDF/TAF, FTC/3TC or ABC
  - No dose adjustment needed
- NNRTIs
  - DOR, RPV IM/PO
    - No dose adjust adjustment
  - EFV/ETR
    - No dose adjustment
      - Can decrease buprenorphine exposure (AUC 25→50%)
      - Watch for withdrawal symptoms

# HIV and Buprenorphine- ART Continued

- INSTI
  - BIC, CAB (PO/IM), DTG, RAL
    - No dose adjustment
  - EVG/c
    - No dose adjustment needed
    - Can increase buprenorphine exposure (AUC 35%)

# HIV and Buprenorphine- ART Continued - PIs

- PIs
  - DRV/c, ATV/c
    - Buprenorphine dose adjustment needed
      - Titrate dose to lowest initial dose
  - DRV/r
    - No dose adjustment needed
  - ATV/r
    - Buprenorphine dose adjustment needed
      - Can increase buprenorphine exposure (AUC 66%)

# Conclusion

# Conclusion

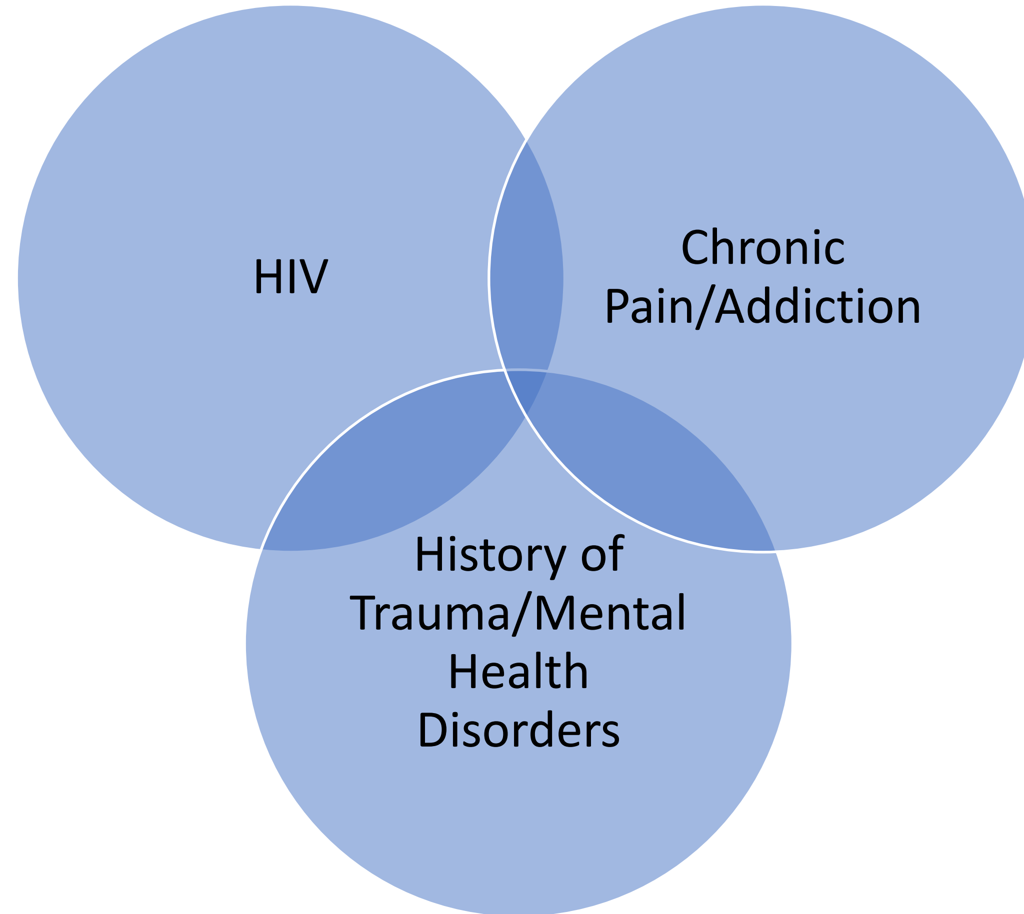
- Patient was successfully switched to Buprenorphine/Naloxone 4 mg in the AM and 2 mg in the PM
  - Microdose Method
- He is doing well
- Viral load continues to be undetectable

https://www.spreadshirt.com.au/shop/design/double+thumbs+up+sloth+funny+encouraging+good+job+sticker-D675029737c95ce06c39e4b3b?sellable=eN9Mpbe1wwh10oxg7Awb-1459-215

# Conclusion

- Patient buy-in is key
  - Answer all their questions, validate their concerns and gain their trust
- Chronic pain management is not easy
  - HIV or non-HIV
  - Know your resources, calculate the MME, look up formularies
- Know where your patient is coming from
  - Opioid use disorder
  - History of Physical/Mental Trauma, Neglect, Abuse

# Conclusion



# Thanks to Everyone for All That You Do

- "The idea that some lives matter less is the root of all that is wrong with the world.“
  - Dr. Paul Farmer

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