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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

CARING FOR PEOPLE LIVING WITH HIV (PLWH) AND SUBSTANCE USE

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UW Medicine
UW SCHOOL OF MEDICINE

Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

CASE STUDY

- A 28 yo bisexual cisgender man (he/him) with a PMH of MDD and GERD comes to your clinic for an annual exam.
- He drinks “a few beers” every day with dinner to help “wind down,” and binge-drinking 10-12 beers on Saturdays and Sundays partying with his friends.
- He often vapes nicotine when drinking. He reports cocaine and methamphetamine use once to twice yearly at music festivals with his best friend. They shared needles once four months ago because “I know him, and he’s healthy.” He denies cannabis or opioid use.
- He doesn’t have a partner right now but is sexually active. He uses condoms “most of the time.”
- He takes 20 mg escitalopram daily.

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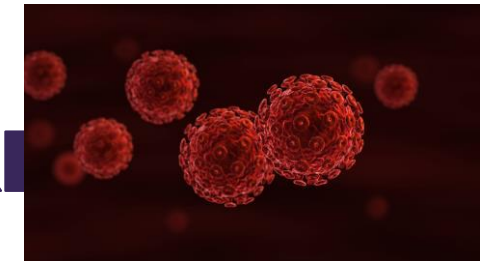
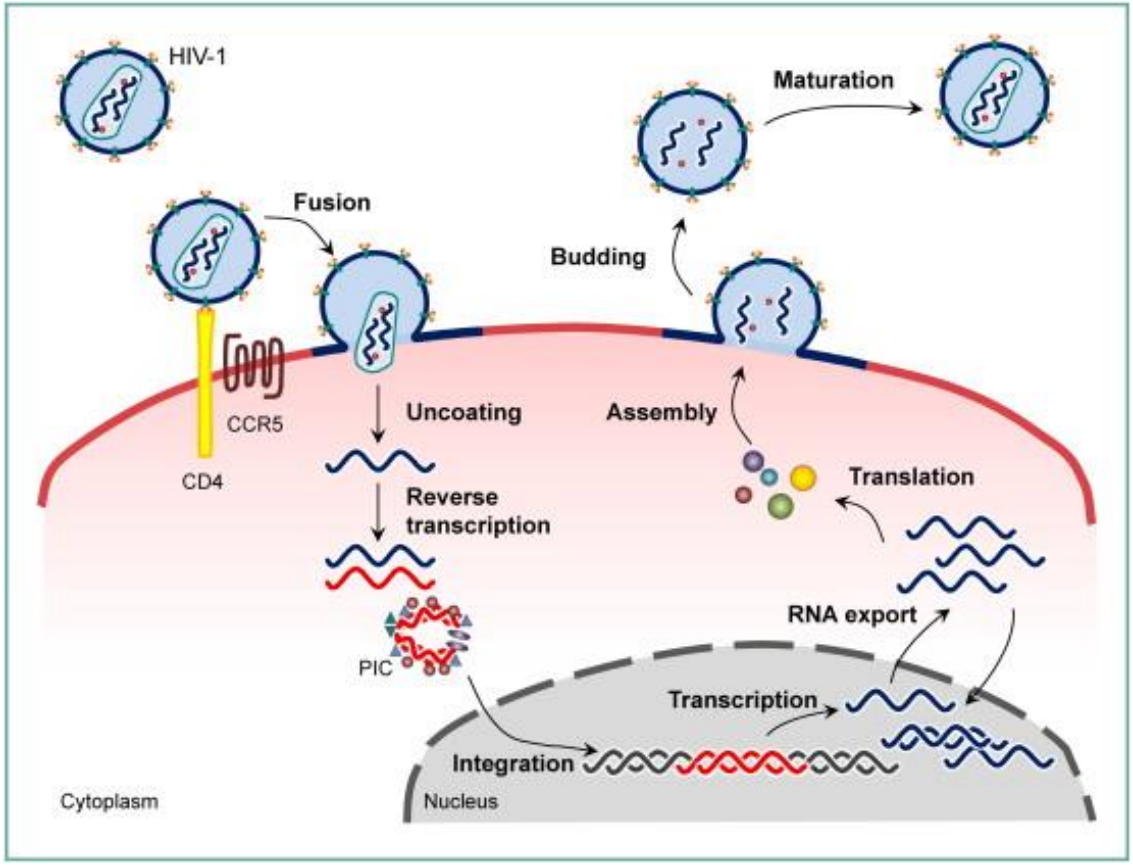
WHAT IS HIV? (A FRIENDLY RI



- Retrovirus
- Attacks the immune system
- Flu-like symptoms within 2 to 4 weeks after infection



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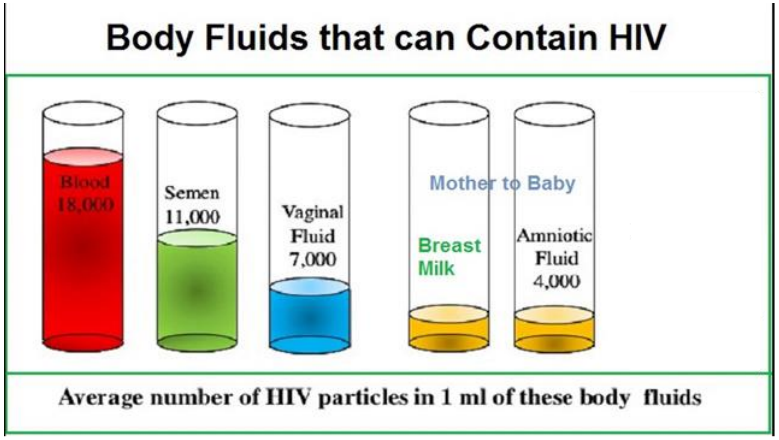
WHAT IS HIV? (A FRIENDLY REVIEW)

- Only certain body fluids can transmit HIV:
  - Blood
  - Semen/pre-seminal fluid
  - Rectal and vaginal fluids
  - Breastmilk
- If untreated, can progress to AIDS
  - CD4 < 200 or presence of opportunistic infections



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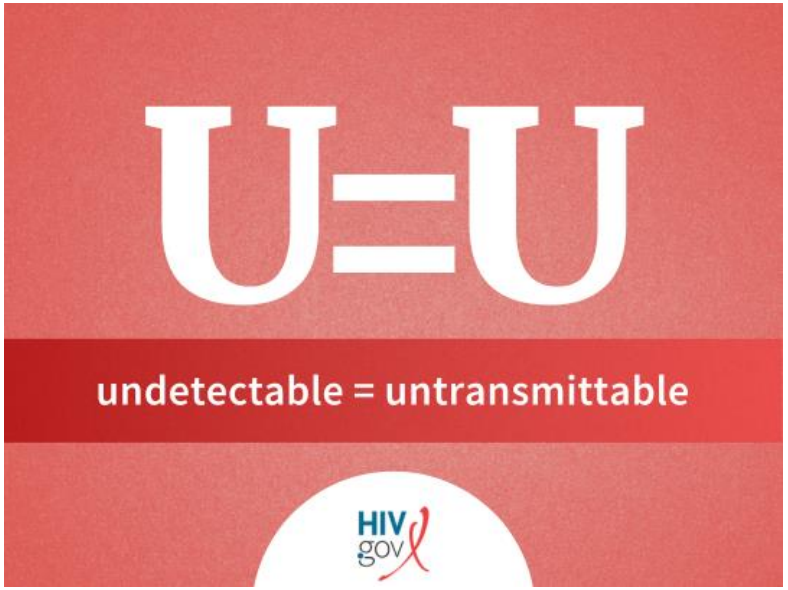
PLWH who take HIV medicine as prescribed and keep an undetectable viral load can live long, healthy lives and cannot transmit HIV to others.



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EPIDEMIOLOGY: HIV

- 1.2 million people in the U.S. have HIV
  - 13% are undiagnosed
  - 76% received some HIV care, 54% were retained in care, and 65% were virally suppressed
  - 19,310 deaths
- New infections decreased 12% from 36,300 in 2018 to 31,800 in 2022
- Disproportionately impacts racial and ethnic minorities, men who have sex with men and those living in the South

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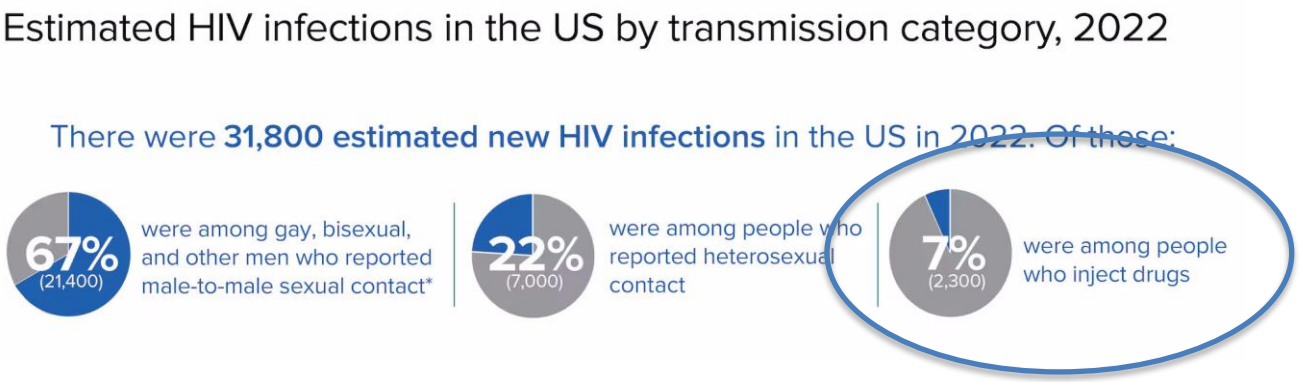
EPIDEMIOLOGY: HIV AND IVDU

> **People who inject drugs accounted for 7% (2,300)** of the 31,800 estimated new HIV infections in 2022



EPIDEMIOLOGY: HIV AND SUD

- Prevalence of SUDs is higher among PLWH
- Polysubstance use is common
- 30 - 50% of PLWH report current or past SUD
- PLWH who use drugs have higher matched morbidity and mortality compared to non-drug using PLWH

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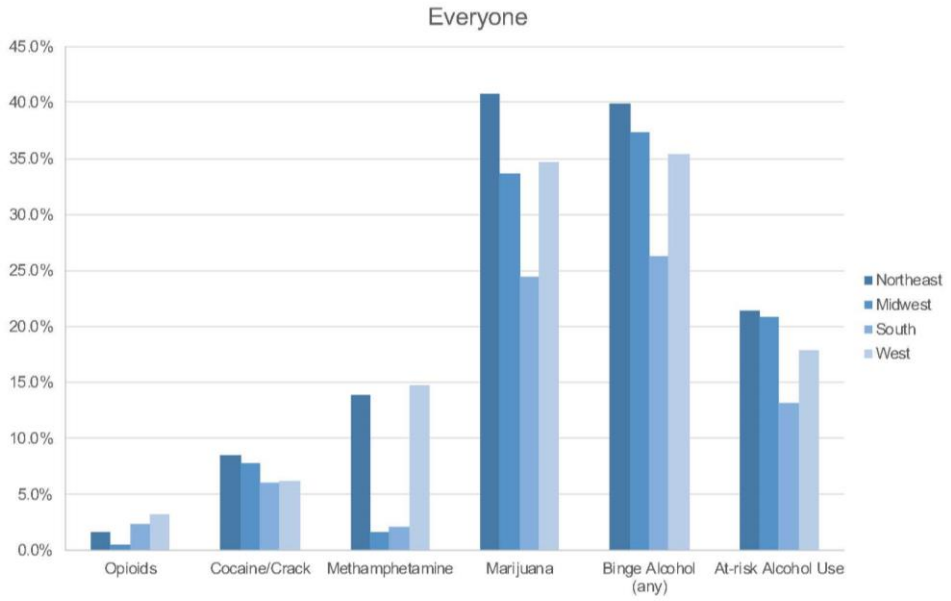
EPIDEMIOLOGY: HIV AND SUD

- Difficult to find data on prevalence of active substance use disorders in PLWH
- Some ***estimates*** of ***use***
  - Nicotine: 40%
  - Alcohol: 30%
  - Cannabis 30%
  - Stimulants: 10%
  - Opioids: 3%



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Substance use treatment services represent a rich opportunity to:

1. **Reduce incident infections** for high-risk patients
2. **Improve outcomes** for HIV+ patients

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HOW DOES SUBSTANCE USE INCREASE HIV TRANSMISSION?

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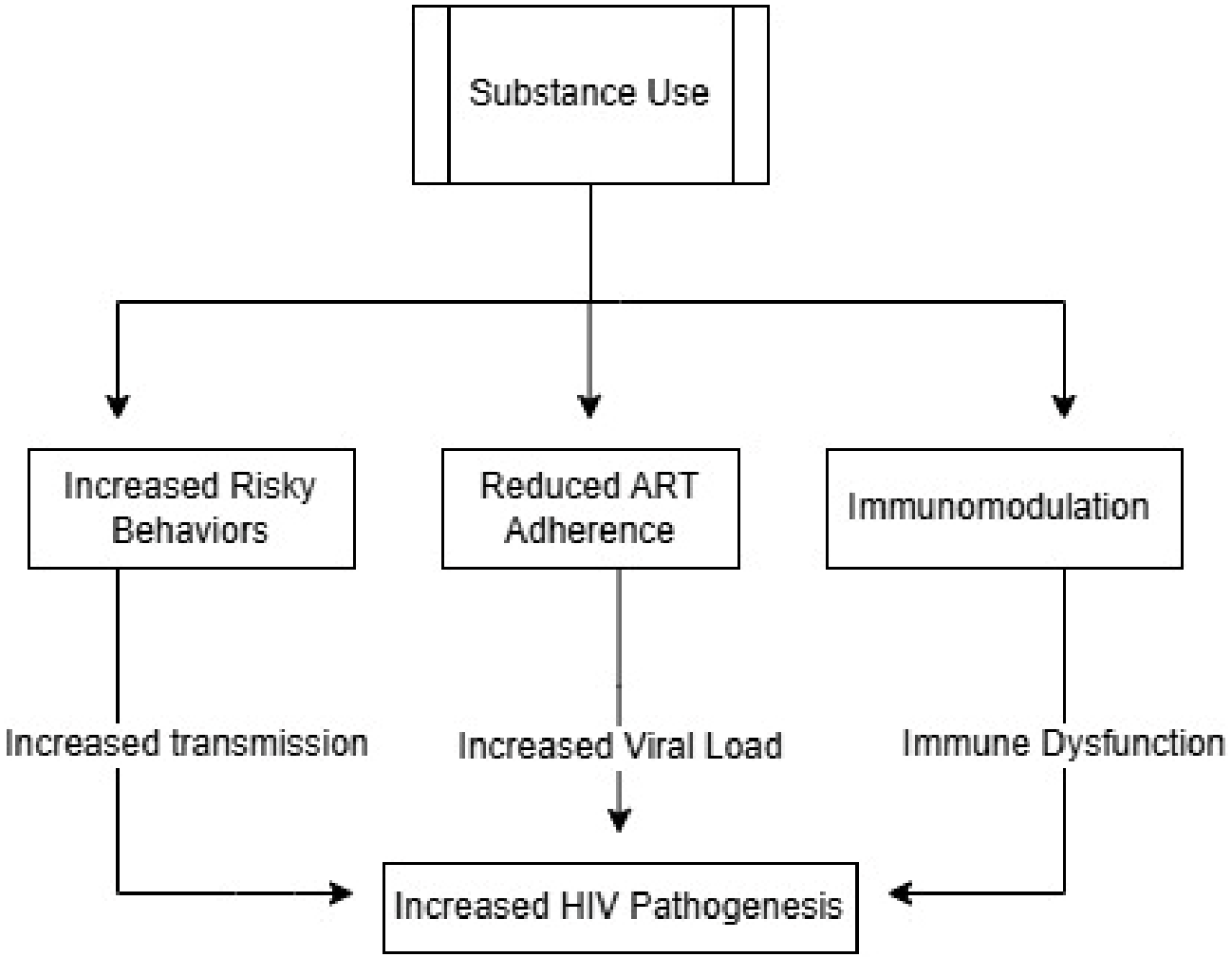

INCREASED HIGH-RISK BEHAVIORS

- Sexual
  - –Unprotected sex
  - –Multiple partners
  - –Anal sex
- Needle sharing

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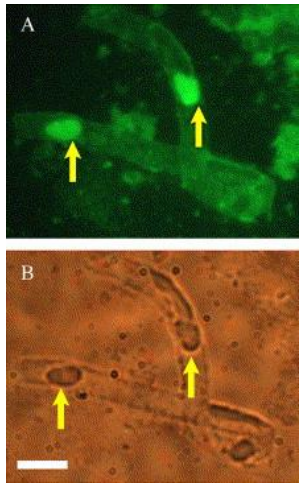
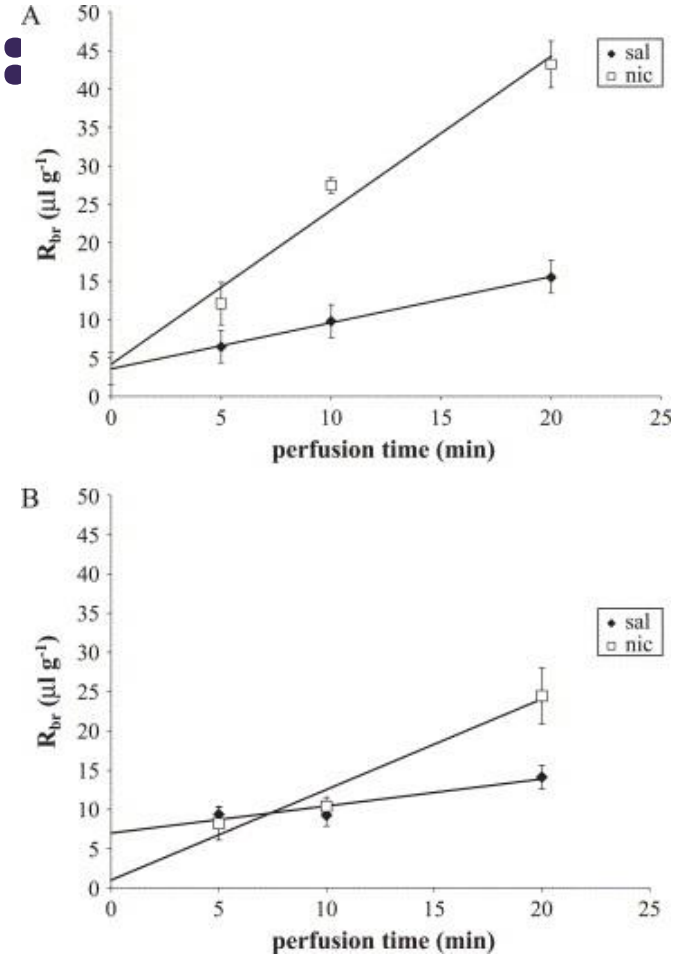
IMMUNOMODULATION:

- Metabolized by CYP enzymes (mostly 2A6) to generate ROS reactive metabolites
  - Macrophages
- Nicotine increase BBB permeability





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IMMUNOMODULATION: ALCOHOL

> Intoxicating doses are immunosuppressive
> Chronic consumption is immune-activating

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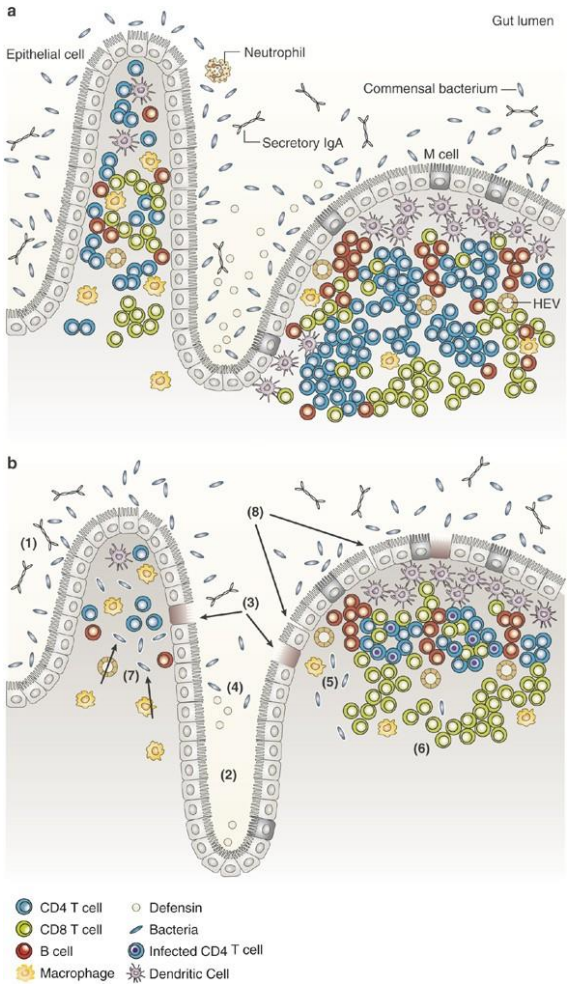
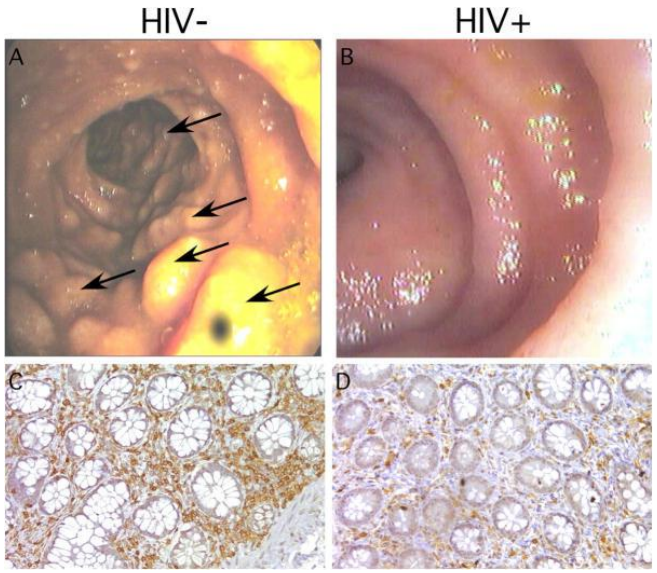
IMMUNOMODULATION: ALCOHOL



- Intestinal mucosal damage
- Intestinal lymphocytic depletion
- Microbial translocation
- Genital mucosal damage?



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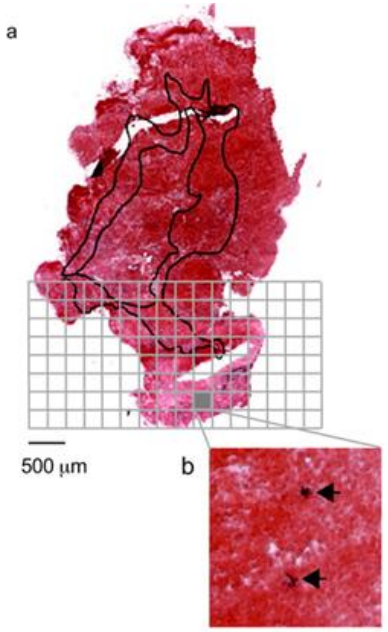
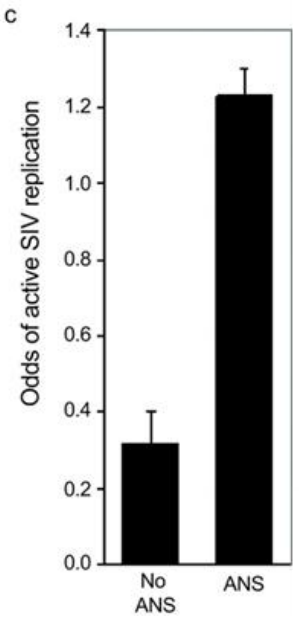
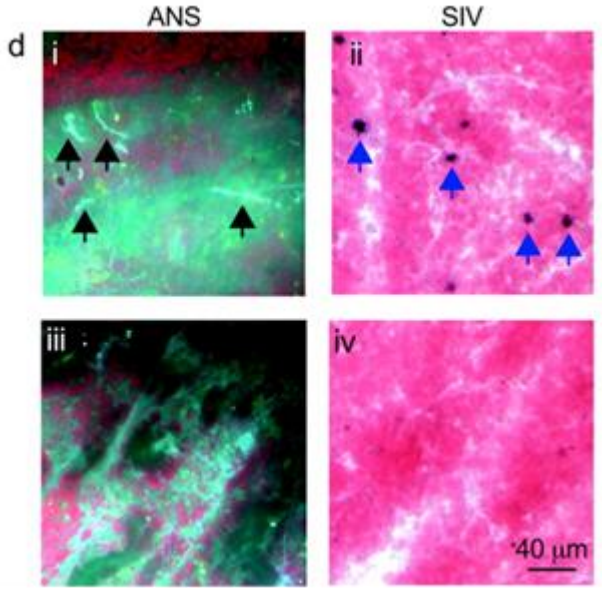
IMMUNOMODULATION: STIMULANTS

> Sympathetic nervous system innervates lymphoid organs
> More immune cells = more targets to infect
> Mostly *in vitro* evidence







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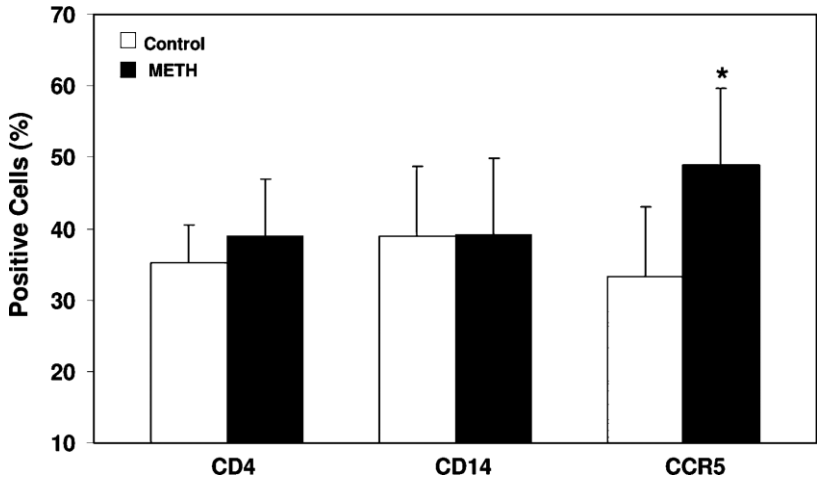
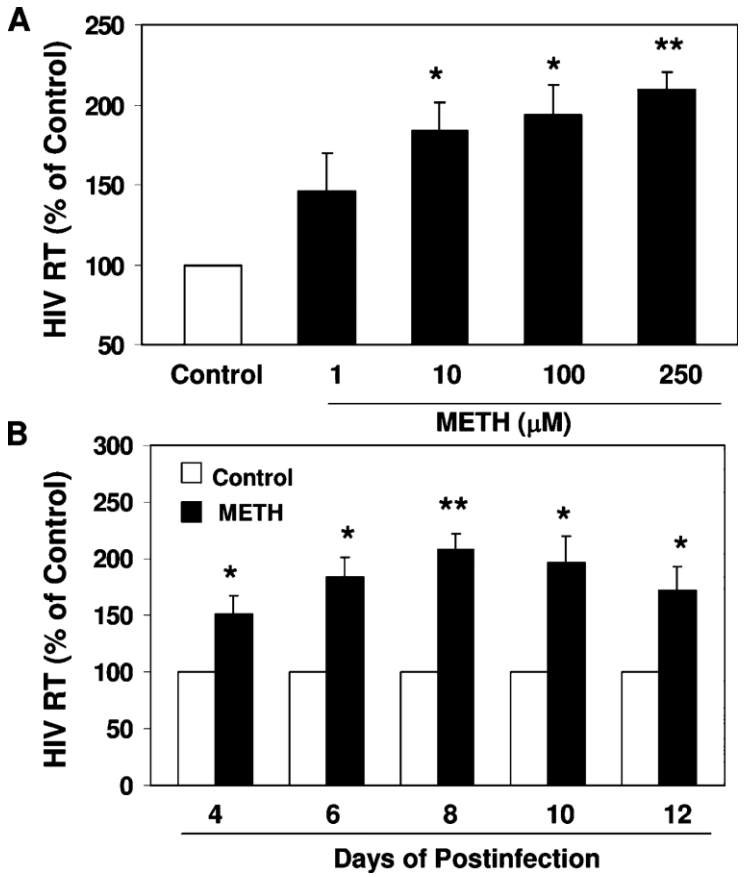
IMMUNOMODULATION: STIMULANTS





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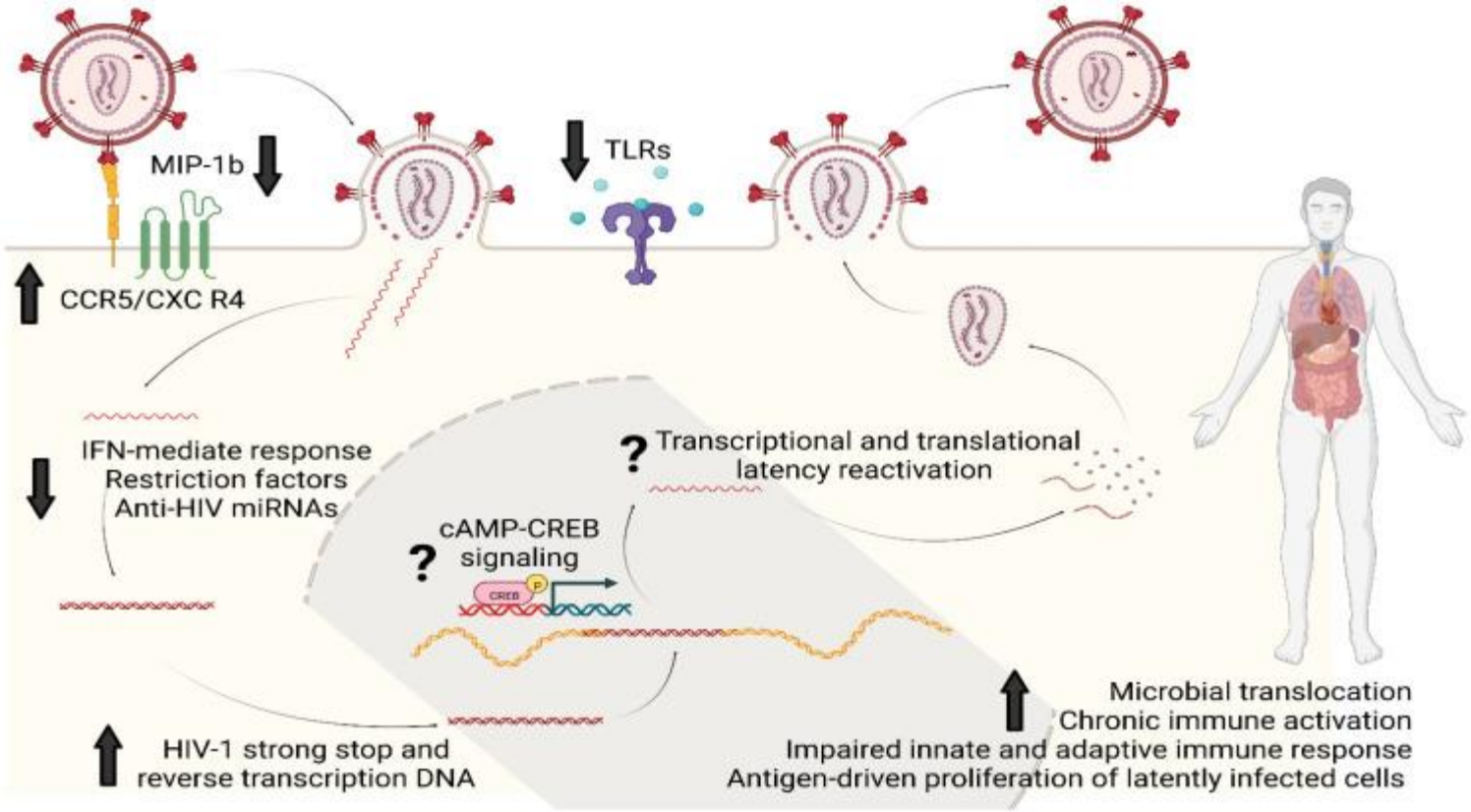
IMMUNOMODULATION: OPIOIDS



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WHAT SPECIAL CONSIDERATIONS ARE THERE FOR TREATING SUBSTANCE USE IN PLWH?

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DECREASED ART ADHERENCE

- Decreased medication compliance
- Decrease engagement in medical care

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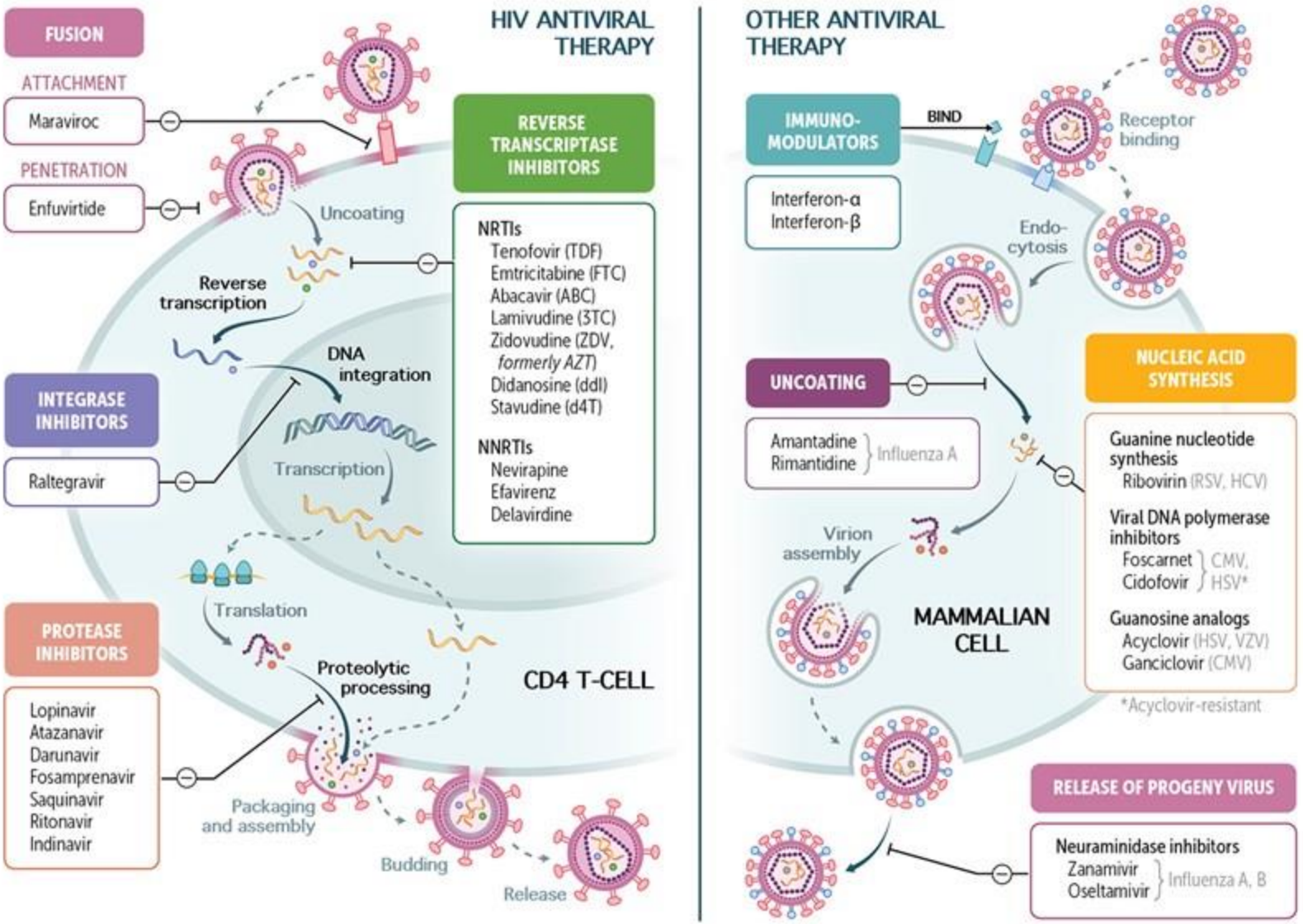

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FIRST LINE HIV+ PREP PEP

HIV Medication Chart

Combination Antiretrovirals

Single-Tablet Regimens

- **Atripla**† (EFV/TDF/FTC)
- **Biktarvy** (BIC/TAF/FTC)
- **Complera** (RPV/TDF/FTC)
- **Delstrigo** (DOR/TDF/3TC)
- **Dovato** (DTG/3TC)
- **Genvoya** (EVG/COBI/TAF/FTC)
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- **Odefsey** (RPV/TAF/FTC)
- **Stribild** (EVG/COBI/TDF/FTC)
- **Symtuza** (DRV/COBI/TAF/FTC)
- **Triumeq** (DTG/ABC/3TC)

Long-Acting Injectable Regimens

- **Cabenuva** (CAB/RPV)

Regimens Used in Combination with Other HIV Medications

- **Combivir**† (ZDV/3TC)
- **Descovy** (TAF/FTC)
- **Epzicom**† (ABC/3TC)
- **Truvada**† (TDF/FTC)

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTI)

- **Emtriva***† (emtricitabine, FTC)
- **Epivir***† (lamivudine, 3TC)
- **Viread***† (tenofovir DF, TDF)
- **Ziagen***† (abacavir, ABC)
- **Vemlidy** (tenofovir alafenamide, TAF) FDA approved for HBV only

Protease Inhibitors (PI)

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- **Kaletra*** (lopinavir/ritonavir, LPV/RTV)
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- **Prezista*** (darunavir, DRV)
- **Reyataz***† (atazanavir, ATV)

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)

- **Edurant** (rilpivirine, RPV)
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- **Pifeltro** (doravirine, DOR)
- **Sustiva**† (efavirenz, EFV)
- **Viramune***† (nevirapine, NVP)

Entry Inhibitors

- **Rukobia** (fostemsavir, FTR) gp120 Attachment Inhibitor
- **Selzentry*** (maraviroc, MVC) CCR5 Antagonist
- **Trogarzo** (ibalizumab, IBA) Post-Attachment Inhibitor

Boosting Agents

- **Norvir***† (ritonavir, RTV)
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Integrase Inhibitors (INSTI)

- **Isentress***▲ (raltegravir, RAL)
- **Isentress HD** (raltegravir, RAL)
- **Tivicay*** (dolutegravir, DTG)
- **Vocabria** (cabotegravir, CAB)

All pills shown in relative size/scale. *Medication brand names appear in bold. Generic names and commonly used abbreviations appear in parentheses.*

*Also available in liquid or powder form. †Generic formulation available. ▲Chewable form available.

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SUBSTANCES EFFECTS ON ART AND VICE VERSA

- No absolute contraindications between substances and HIV medications given benefits >> risks
- MDMA, GHB, ketamine, and methamphetamine metabolized extensively by CYP system
  - One case report: ritonavir raised MDMA to fatal level (1998)
- **Prescribe ART, even if patients are using!**

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SPECIAL TREATMENT CONSIDERATIONS IN PLWH

- Nicotine
  - Varenicline* > bupropion > NRT alone
- Alcohol
  - Naltrexone*
- Methamphetamines
  - Mirtazapine in MSM*
- Opioids
  - Methadone*, buprenorphine* > naltrexone

*has been studied specifically in PLWH

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ALCOHOL USE DISORDER MEDICATIONS AND ART: DRUG–DRUG INTERACTIONS

Medication	Dose and Recommendations	Potential Interaction with ARV Drugs	Comments
Alcohol Use Disorder			
Acamprosate	666 mg PO three times a day *or* 333 mg PO three times a day for people with CrCl 30–50 mL/min	No significant interaction with ARV drugs expected.	**Contraindicated** in people with CrCl <30 mL/min
Disulfiram	250 mg PO once daily	Use with caution when prescribing an ARV oral solution that contains ethanol and/or propylene glycol (e.g., FPV, LPV/r, RTV).	Counsel people regarding disulfiram reaction when taken with alcohol; symptoms for the reaction may include flushing, tachycardia, nausea, vomiting, or hypotension.
Naltrexone	50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.	No significant interaction with ARV drugs expected.	Has the greatest efficacy of all FDA-approved medications for AUD.

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NICOTINE USE DISORDER AND ART: DRUG-DRUG INTERACTIONS

Medication	Dose and Recommendations	Potential Interaction with ARV Drugs	Comments
Nicotine Use Disorder			
Nicotine Replacement Therapy	The FDA has approved a wide variety of nicotine replacement products. All formulations are effective.	No significant interaction with ARV drugs expected.	Work with the person to identify the route of delivery that they will use and find most helpful.
Bupropion	Start at 150 mg PO daily for 3 days, then increase to either 150 mg twice daily or 300 mg once daily (use only formulations that are approved for once-daily dosing).	Concentration may be reduced when used with ARV drugs that are CYP2D6 inducers	For optimal results, tobacco quit date should occur 1 week after starting therapy.
Varenicline	Titrate the dose based on tolerability until the desired effect is achieved. The goal is to reach a dose of 1 mg PO twice daily. Requires dose adjustment in people with CrCl <30 mL/min.	No significant interaction with ARV drugs expected.	For optimal results, tobacco quit date should occur 1 week after starting therapy.

Substrate of CYP2B6
Inhibitor of CYP2D6

- Bupropion ↓
- ART ↑
- Not usually clinically significant

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METHAMPHETAMINE USE DISORDER MEDICATIONS AND ART: DRUG-DRUG INTERACTIONS

- Mirtazapine: no interactions
- Naltrexone: see previous slide
- Bupropion: see previous slide

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OPIOID USE DISORDER MEDICATIONS AND ART: DRUG-DRUG INTERACTIONS

Medication	Dose and Recommendations	Potential Interaction with ARV Drugs	Comments
Opioid Use Disorder			
Buprenorphine	Individualize buprenorphine dosing based on the person's opioid use. The dose range is 4–24 mg sublingually. Dosing is once daily or twice daily.	Potential interaction with ARV drugs that are CYP inhibitors or inducers.	Buprenorphine has 90% first-pass hepatic metabolism. Verify that the person is using the appropriate technique for sublingual administration before adjusting the dose, because improper administration will result in poor absorption and low drug levels.
Methadone	Individualize the dose. People who receive higher doses (>100 mg) are more likely to remain in treatment.	Potential interaction with ARV drugs that are CYP inhibitors or inducers.	QTc prolongation is a concern at higher doses. Methadone can be prescribed for OUD only by a licensed OTP.
Naltrexone	50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.	No significant interaction with ARV drugs expected.	Longer time of continuous abstinence in those who received depot formulation naltrexone compared with placebo after transition from prison to community.

Substrate of CYP3A4

Most induce

Substrate of CYP3A4

Most induce

- Buprenorphine ↓
- Not usually clinically significant

- Methadone ↓
- Can be clinically significant

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WHAT MEDICAL CO-MORBIDITIES ARE EXACERBATED IN PLWH AND SUBSTANCE USE?

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NICOTINE USE AND PLWH: MEDICAL COMORBIDITIES

- Mouth infections
  - Oral candidiasis
  - Hairy leukoplakia
- Lung infections
  - Bacterial pneumonia
  - Pneumocystis pneumonia
- COPD
- Bone disease
- Cardiac disease
- Stroke
- Dental infections
- Cancers
  - Lung
  - Cervical
  - Anal
  - Head and neck

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ALCOHOL USE AND PLWH: MEDICAL COMORBIDITIES

- Liver disease
  - ART has many hepatic adverse effects
  - Co-infection with viral hepatitis
- Cancer
  - Liver
  - Head and neck
- Cardiac disease
- Pulmonary disease
- Bone disease

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STIMULANT USE AND PLWH: MEDICAL COMORBIDITIES

- No increased risk of myocardial infarction or heart disease based on one (one observational case/control study, 2021)
- Dental infections
- Lung infections (if smoked)
- Skin infections (if IVDU)

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OPIOID USE AND PLWH: MEDICAL COMORBIDITIES

- Liver
- Cancer
- Lung infections (if smoked)
- Skin infections (if IVDU)

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HIV HARM REDUCTION: BEHAVIORAL

- Clean needle exchanges
- Sexual protection
  - Condoms
  - Lubricant (water or silicone)
  - Dental dams

HIV HARM REDUCTION: PRE-EXPOSURE PROPHYLAXIS (PREP)

- **IVDU with shared equipment within the past 6 months**
- History: date of most recent exposure, renal disease, bone disease
- Initial labs: HIV antigen/antibody, Cr, other STIs (GC/CT, RPR), hepatitis B and C, pregnancy test
- Options
  - Oral: **TDF-FTC 200/300mg** (Truvada)
    - Avoid in renal/bone disease
  - LA: **Cabotegravir* 600mg** (monthly x2 months, then every 2 months)
    - Risk of resistance
- Maintenance labs: HIV test q 3 months

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HIV HARM REDUCTION: POST-EXPOSURE PROPHYLAXIS (PEP)

- History: known exposure with the past 72 hours
- Initial labs: same as PreP
- Options: same as first-line triple-therapy **x4 weeks**
  - Bictegravir-emtricitabine-tenofovir alafenamide (Biktarvy)
  - Dolutegravir + TDF/FTC (Truvada) or TAF/FTC (Descovy)
- f/u HIV test
- **Transition to PrEP?**

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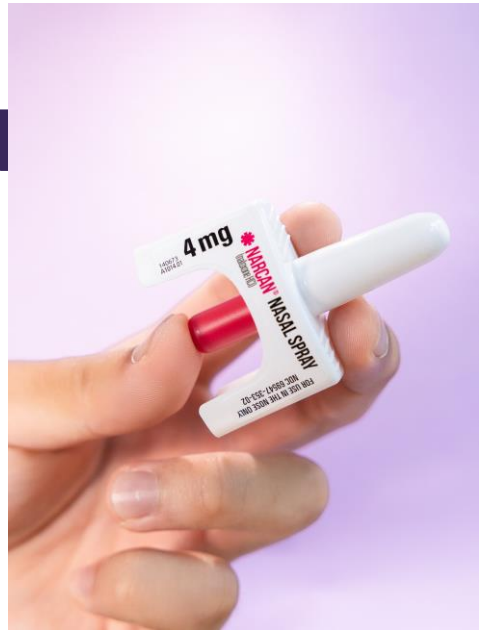
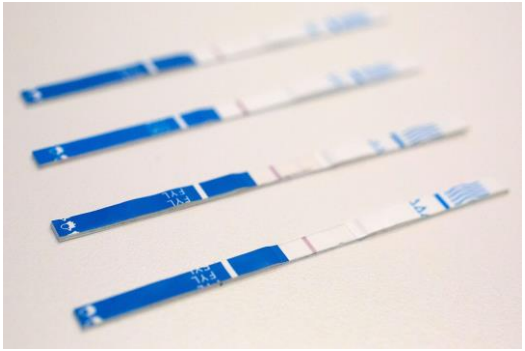
HIV AND SUD HARM REDUCT



- Opioid overdose prevention*
  - Naloxone rescue kits & education
  - Fentanyl test strips
  - Never Use Alone



For anyone who uses opioids **or drugs at risk of contamination!*

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CASE STUDY

- A 28 yo bisexual cisgender man (he/him) with a PMH of MDD and GERD comes to your clinic for an annual exam.
- He drinks “a few beers” every day with dinner to help “wind down,” and binge-drinking 10-12 beers on Saturdays and Sundays partying with his friends.
- He often vapes nicotine when drinking. He reports cocaine and methamphetamine use once to twice yearly at music festivals with his best friend. They shared needles once four months ago because “I know him, and he’s healthy.” He denies cannabis or opioid use.
- He doesn’t have a partner right now but is sexually active. He uses condoms “most of the time.”
- He takes 20 mg escitalopram daily.

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DISCUSSION

- What else do you want to ask the patient?
  - About his mental health?
  - About his substance use?
  - About his sexual health?
- What motivational interviewing strategies do you want to use? Can you give some example statements?
  - For his substance use?
  - For his sexual health?
- What medications, if any, would you offer?
- What harm reduction measures would you discuss?

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SUMMARY

- U = U
- Substance use increases HIV transmission and worsens HIV outcomes due to **increased high-risk behaviors, decreased medication compliance, and immunomodulation**
- There are **no absolute contra**indications between substances and HIV medications given benefits >> risks
- Commonly used medications for substance use that may interact with certain ARTs include **bupropion, methadone and buprenorphine**
- **PrEP** and **PEP** are important harm reduction measures for patients who use substances

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REFERENCES

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RESOURCES

- Clinicalinfo.HIV.gov
  - https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/special-populations-substance-use
- Liverpool Drug Interaction Checker
  - https://www.hiv-druginteractions.org/checker

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