The Evolving Landscape of HIV/AIDS: Updates on Antiretroviral Therapy, PrEP, and PEP for Pharmacists

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iCare Infectious Disease Conference 2025

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Learning Objectives

- Interpret current Florida law on HIV/AIDS and its impact on testing, reporting, confidentiality, procedures for pregnant women and partner notification
- Describe the epidemiology of HIV and the importance of infection control procedures
- Identify modes of HIV transmission
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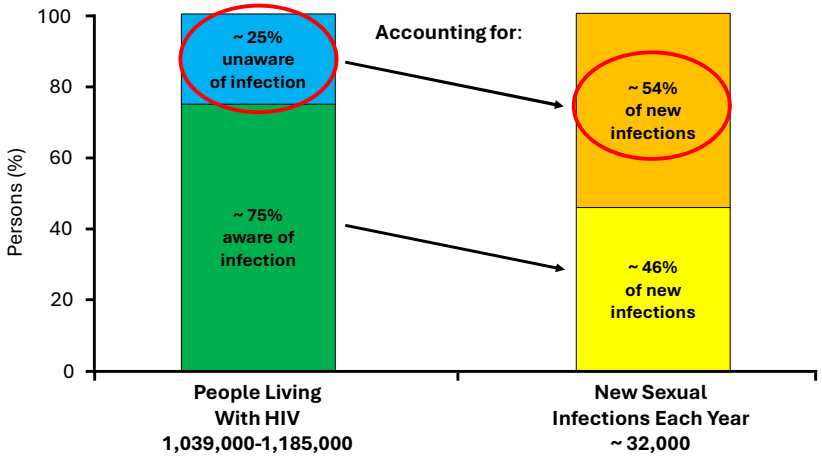
Scope of the Problem: Burden of HIV Infection in the US

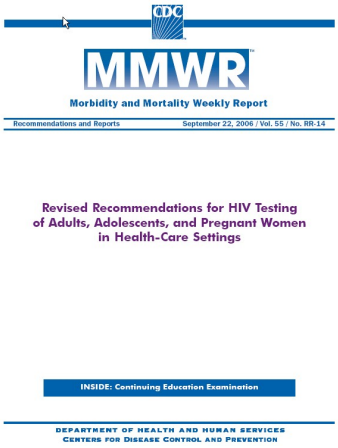


Marks G, et al. AIDS. 2006;20:1447-50.
Campsmith ML, et al. J Acquir Immune Defic Syndr. 2010;53:619-24.

4

Routine HIV Testing Recommended by CDC & USPSTF

- Routine voluntary testing in healthcare settings for patients aged 13-64 years old, **including pregnant women**
- HIV testing **not** based on patient risk
- Repeat HIV testing at discretion of provider, based on patient risk



MMWR Recomm Rep. 2006;55(RR-14):1-17.
USPTF. Ann Intern Med. Published online 30 April 2013.

5

Changes to Florida's HIV Testing Law (381.004, F.S.)

- Amends 381.004, F.S. **removing the requirement for informed consent** prior to HIV testing in health care settings

  381.004(2)(a)1. In a health care setting, a person to be tested shall be notified orally or in writing that the test is planned. A person who has signed a general consent form for medical care is not required to sign or otherwise provide a separate consent for an HIV test. If the person declines the test, it shall be documented in the medical record.

- Intent of legislation: Normalize HIV testing and address CDC recommendations published in 2006

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Changes to Florida's HIV Testing Law (381.004, F.S.)

- Opt-out approach to HIV testing in health care settings
  - ***Written*** informed consent eliminated
  - Patient must be notified that they will be tested for HIV and that they have the right to decline testing
  - Notification of HIV test can be oral or in writing
  - Refusal must be noted in patient's medical record
- No change in law for testing in non-health care settings
  - Health care settings: a setting devoted to the diagnosis and care of persons or the provision of medical services to persons (e.g., hospitals, primary care settings, clinics, blood banks)
  - Non-health care settings: no medical treatment; conducts HIV testing for sole purpose of identifying HIV infection (e.g., outreach settings, mobile vans)

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HIV Testing and Partner Notification

- **Current law: Test results reporting required; requirement for notification to patient**

  *Notification of a person with a positive test result shall include information on the availability of appropriate medical and support services, the importance of **notifying partners** who may have been exposed, and preventing transmission of HIV*
- After diagnosis, health-care providers should:
  - Encourage patients to disclose HIV status to partners
  - Recommend partners be tested for HIV
- **Voluntary & confidential partner notification services offered by Department of Health**
- Florida AIDS Hotline **(800) FLA-AIDS**

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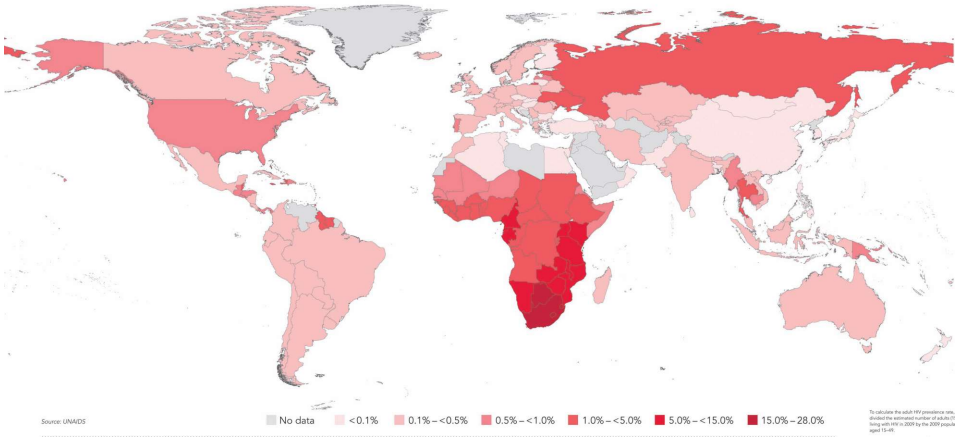
Global View: 33.3 Million People Living with HIV



http://www.unaids.org/documents/20101123_2010_HIV_Prevalence_Map_em.pdf

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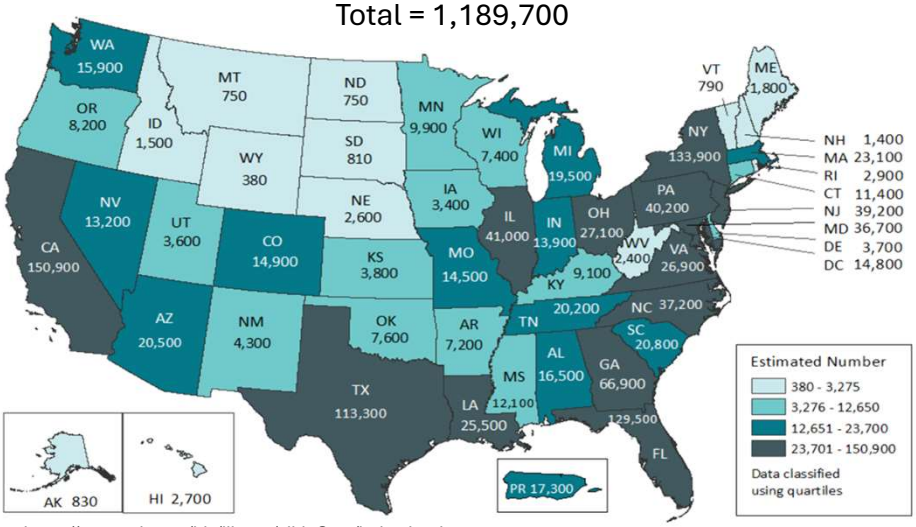
HIV Prevalence in the US: 1.2 Million People

Total = 1,189,700

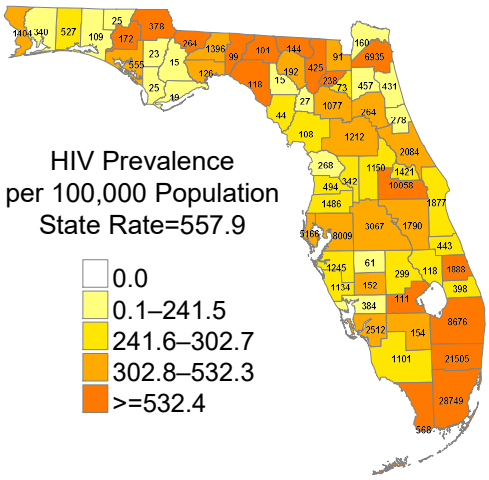


https://www.cdc.gov/hiv/library/slideSets/index.html

11

HIV Epidemic in Florida

- Florida ranks #3 in state HIV rates (Washington DC #1, Georgia #2)
- By metropolitan area, Miami/Ft. Lauderdale/ West Palm #1 for countrywide HIV rates
- One in 154 adults in FL known to be living with HIV

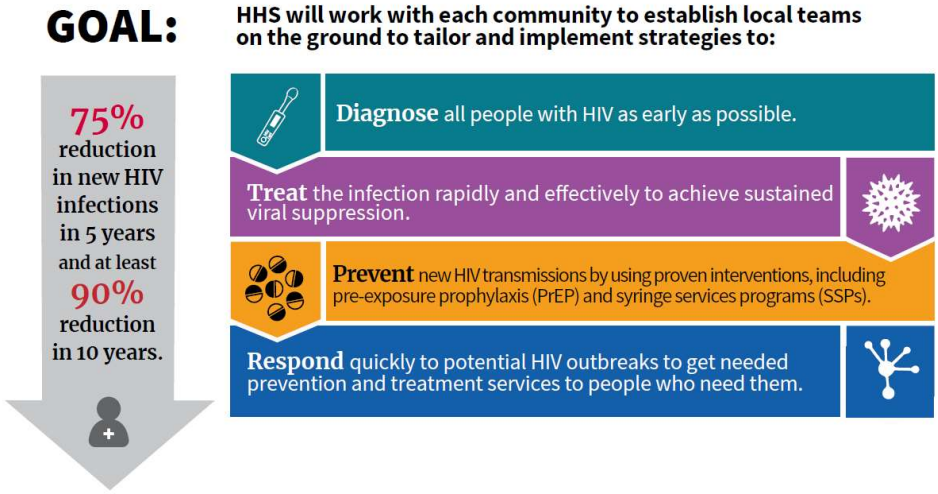


http://www.floridahealth.gov/diseases-and-conditions/aids/surveillance/epi-slide-sets.html

12

Ending the HIV Epidemic: A Plan for America

Ending the HIV Epidemic



https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview

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Modes and Risk of HIV Transmission

- An exposure must meet two criteria:
  - Portal of entry
  - Contaminated body fluid
- Types of exposures:

Occupational Exposures	
Percutaneous	0.3%
Mucocutaneous	0.09%

Non-Occupational Exposures	
Vertical birth	24%
Needle-sharing IVDU	0.67%
Receptive anal	0.1 – 5%
Receptive vaginal	0.1 – 0.2%
Insertive anal	0.065%
Insertive vaginal	0.05%
Receptive oral- ♂	0.01%
Insertive oral	0.005%
♀-♀ orogenital contact	Case reports

Centers for Disease Control and Prevention. MMWR 2005;54:RR-2.
Landovitz RJ. Top HIV Med 2009;17:104-8.

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OSHA: Universal Precautions

Employees who come into contact with HIV-infected materials:

- Wear protective equipment (gloves, gowns, masks, and goggles)
- Wash hands with antimicrobial soap before and after wearing gloves
- Properly dispose of needles and other sharps
- Avoid recapping needles, or use needleless devices, to prevent needle sticks

Center for Disease Control and Prevention. MMWR 2006;55(RR-14)

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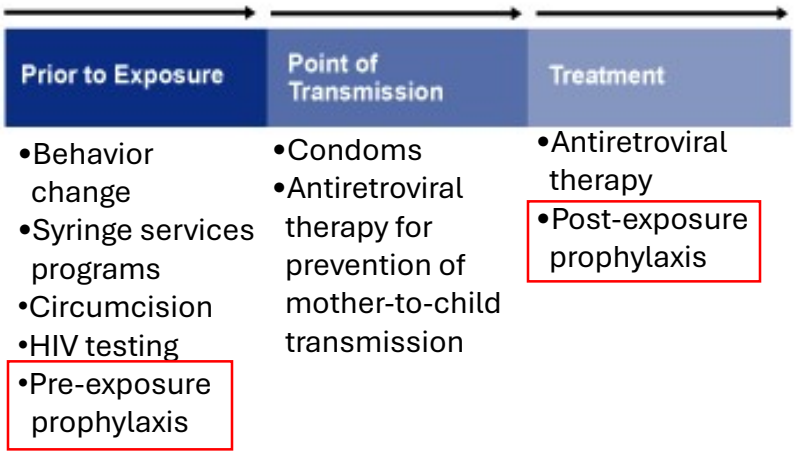
Spectrum of HIV Prevention Strategies



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Pre-**E**xposure **P**rophylaxis (PrEP) for HIV Prevention

- Use of antiretroviral medications by *uninfected* patients to prevent HIV infection
- Used before and during periods of risk
  - Heterosexually active men and women, men who have sex with men, people who inject drugs
- Antiretrovirals approved for PrEP are 99% effective at reducing risk of sexual transmission of HIV
  - Emtricitabine/tenofovir (Truvada® or Descovy®) PO
  - Cabotegravir (Apretude®) IM
- Additional antiretrovirals & dosage forms in clinical trials

Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. https://stacks.cdc.gov/view/cdc/112360.

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Recommended PrEP Regimens

	Patient Population	Emtricitabine/ tenofovir disoproxil fumarate (FTC/TDF) (Truvada®)	Emtricitabine/ tenofovir alafenamide (FTC/TAF) (Descovy®)	Long-acting cabotegravir (Apretude®)
		200 mg/300 mg by mouth once **daily**	200 mg/25 mg by mouth once **daily**	600 mg IM once monthly for 2 doses, then once **every 2 months**
People born male	Men who have sex with men	FDA-approved, guideline recommended	FDA-approved, guideline recommended	FDA-approved, guideline recommended
People born male	Transgender women			
People born male	Heterosexual men			
People born female	Heterosexual women		Off-label, not recommended	FDA-approved, guideline recommended (except in pregnancy)
People born female	Transgender men		Off-label, not recommended (unless likelihood from anal sex only)	

Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. https://stacks.cdc.gov/view/cdc/112360.

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Stopping Long-Acting CAB for PrEP

- LA CAB has a prolonged pharmacokinetic tail
  - Median time to undetectable CAB: 44 weeks in men, 67 weeks in women
- Discontinued LA CAB (in the event of HIV acquisition) equivalent to low-level monotherapy
- PrEP continuation based on ongoing risk of HIV exposure
  - **At-risk: oral FTC/TDF or FTC/TAF** within 8 weeks after last injection
  - **No longer at-risk: no PrEP required**
  - Quarterly follow-up visits with HIV testing for 12 months after CAB discontinuation

Centers for Disease Control and Prevention: US Public Health Service: Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 Update: a clinical practice guideline. https://stacks.cdc.gov/view/cdc/112360.

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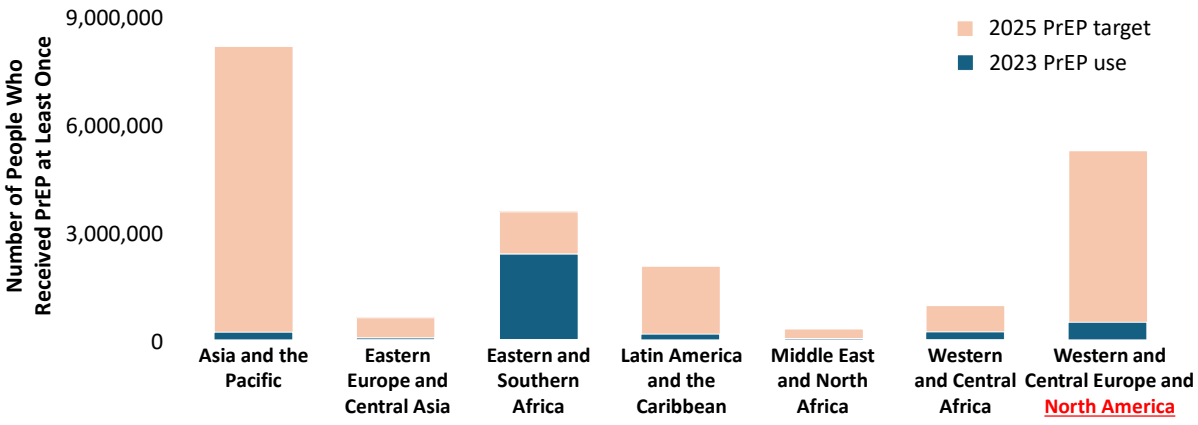
Full Potential of PrEP is Not Being Realized



unaids.org/sites/default/files/media_asset/2024-unaids-global-aids-update_en.pdf

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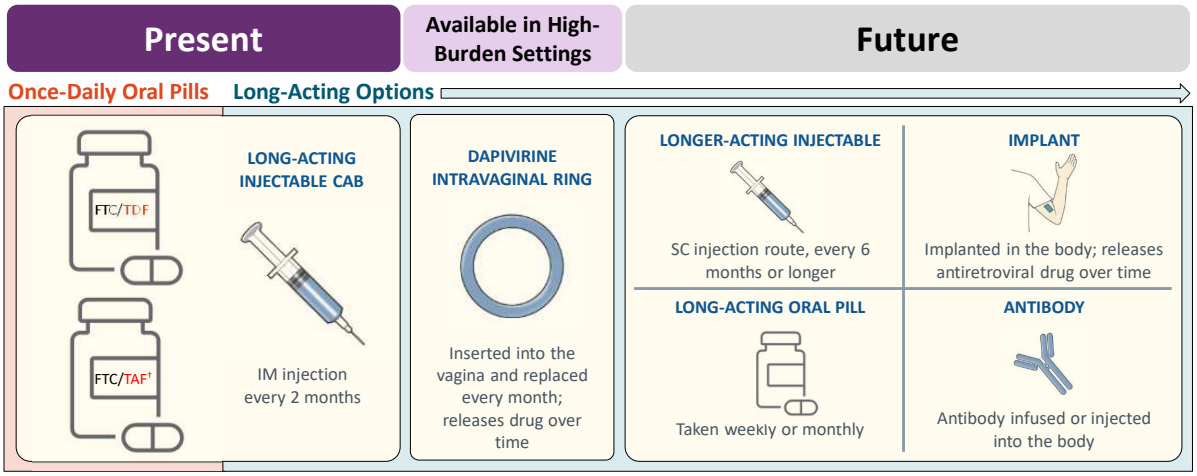
Expanding PrEP Options: Today and the Future



†Currently for cisgender men and transgender women only.

hiv.gov/hiv-basics/hiv-prevention/potential-future-options/long-acting-prep

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Future HIV PrEP Medication: Long-acting Lenacapavir Injections q6 Months

- Lenacapavir is currently FDA-approved for HIV treatment only
  - HIV capsid inhibitor – unique mechanism of action
  - Reserved for treatment-experienced adults with multidrug resistance
  - Dosed as two 1.5 mL subcutaneous injections into the abdomen q6 months by a healthcare provider
- Two large clinical trials published in 2024 demonstrate lenacapavir's remarkable efficacy when used for PrEP
  - PURPOSE1: Heterosexual women (n=5,368)
  - PURPOSE2: Men who have sex with men (n=3,295)
  - NDA submitted to FDA; PDUFA date June 2025

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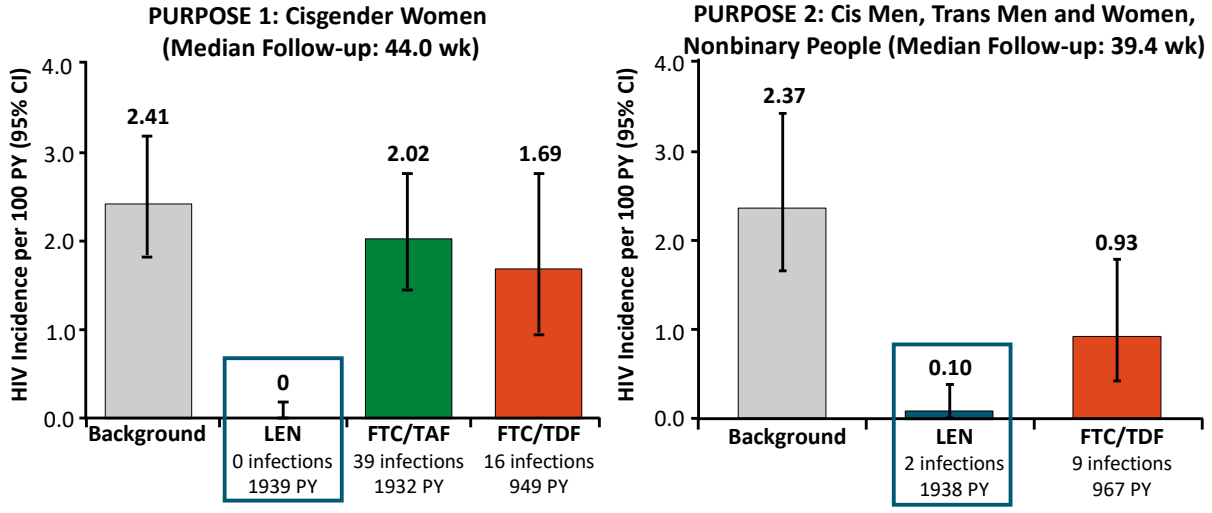
PURPOSE 1 and 2: Lenacapavir HIV Incidence

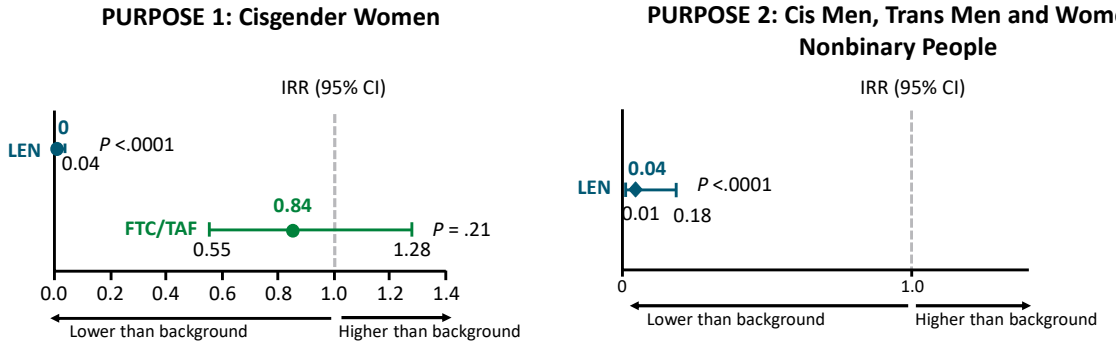


Bekker LG, et al. N Engl J Med. 2024 Oct 3;391(13):1179-1192.
Kelley CF. N Engl J Med. 2025 Apr 3;392(13):1261-1276.

25

PURPOSE 1 and 2: Primary and Secondary Analyses of Lenacapavir Efficacy

Primary Endpoint: HIV Infection Incidence Rate Ratio (IRR) vs Background



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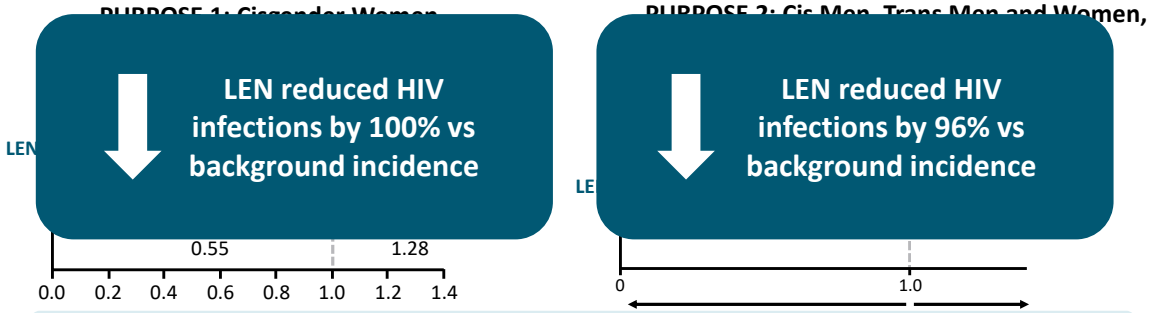

Secondary Endpoint: LEN reduced HIV infections by 100% in PURPOSE 1 and 89% in PURPOSE 2 vs daily oral FTC/TDF

Bekker LG, et al. N Engl J Med. 2024 Oct 3;391(13):1179-1192.
Kelley CF. N Engl J Med. 2025 Apr 3;392(13):1261-1276.

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Post-Exposure Prophylaxis (PEP) for HIV Prevention

- Use of antiretroviral meds by *uninfected* patients *following an HIV exposure* to prevent HIV infection
  - Needlesticks, blood splashes (occupational)
  - Injection drug use, sexual (non-occupational)
- Antiretrovirals started immediately (ideally 1-2 hrs) after HIV exposure and continued 28 days; Start not recommended beyond 72 hours
  - Preferred PEP regimen: Truvada + Isentress **or** Truvada + Tivicay
- PEPLine provides consultation 888-448-4911

https://stacks.cdc.gov/view/cdc/20711
https://stacks.cdc.gov/view/cdc/38856

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Role of the Pharmacist: Expand PrEP and PEP Uptake

- Initiating PrEP/PEP independently in a pharmacy setting
  - Several states have passed legislation
- Establishing collaborative practice agreements
- Facilitating PrEP awareness among sexually active persons and persons who inject drugs
  - "Do you know about PrEP/PEP and what it does?"
  - [preplocator.org]
- Help patients pay for PrEP and PEP
  - Generic emtricitabine/tenofovir disoproxil fumarate
  - Copay and manufacturer assistance programs

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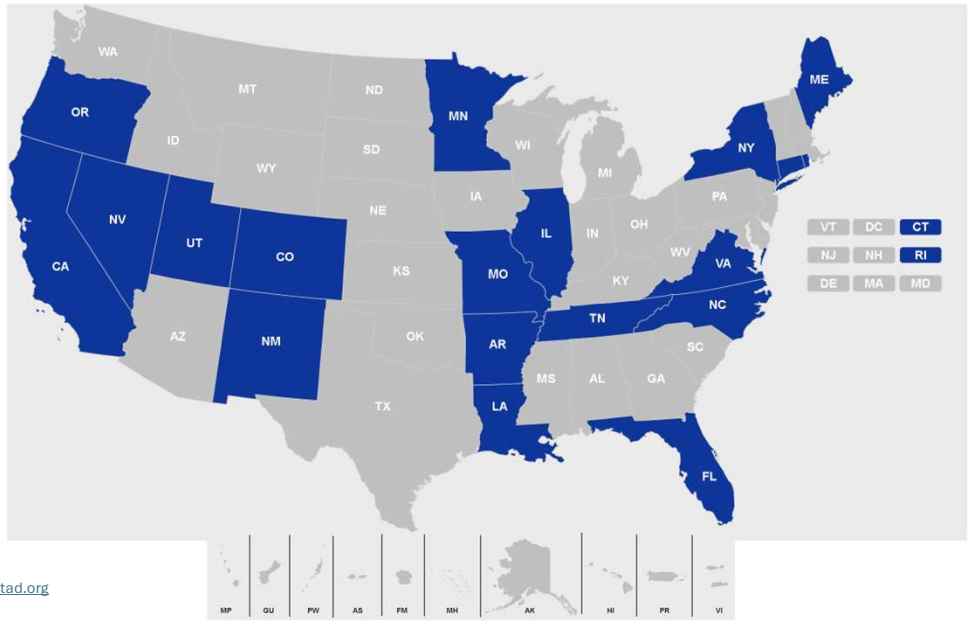
States With PrEP/PEP-Specific Pharmacist Legislation



https://nastad.org

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Florida Pharmacists' Authority: PrEP, PEP, Collaborative Practice

- **PrEP:** ☹
- **PEP**: Pharmacists may prescribe and dispense PEP pursuant to a standing order *(Enacted July 2024)*
  - Must have standing order from a physician provided through a collaborative practice agreement with the same physician
  - No quantity limits on pharmacy-initiated PEP or limitations on frequency with which pharmacists can prescribe PEP
  - Legislation does not address pharmacist's reimbursement
  - Additional board-approved training course required
  - Must have professional liability insurance ≥ $250,000
- **Collaborative practice agreement**: Permits a pharmacist to enter a CPA with a primary care provider to manage chronic health conditions, including HIV

H.B. 159, (Fla. 2024)
Fla. Stat. Ann. § 465.1861

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Recommended HIV Resources

clinicalinfo.hiv.gov

- HHS: Guidelines for the use of antiretroviral agents in adults and adolescents with HIV. September 12, 2024.

www.hiv-druginteractions.org

- University of Liverpool HIV iChart app for iPhone and Android

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HIV Attacks CD4 T Cells

- HIV attacks immune system CD4 T cells
  - HIV uses T cell machinery to replicate
- Depletion of CD4 T cells by HIV impairs immune defenses (leaving host susceptible to opportunistic infection)
- Antiretroviral therapy (ART) suppresses viral load, allowing improvements in immune system functioning

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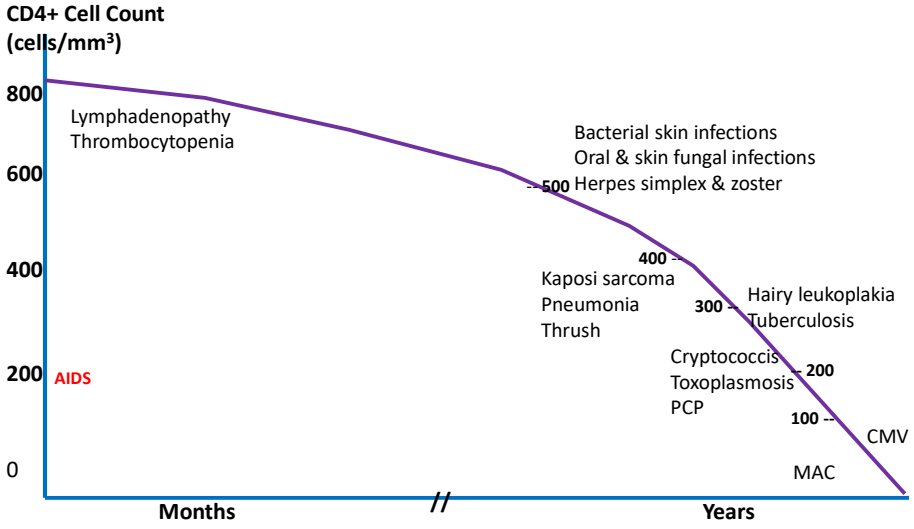
Correlation of Opportunistic Infections with CD4 Count



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Initiation of Antiretroviral Therapy (ART): Current Recommendations

HHS Panel's Recommendations for Initiating Antiretroviral Therapy in Treatment-Naïve Patients
• **Antiretroviral therapy (ART) is recommended for all persons with HIV to reduce morbidity and mortality and to prevent the transmission of HIV to others.** (AI)
• **The Panel recommends initiating ART immediately (or as soon as possible) after HIV diagnosis** in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among persons with HIV. (AII)
• When initiating ART, it is important to educate patients regarding the benefits of ART and to deploy strategies to **optimize care engagement and treatment adherence**. (AIII)

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

US HHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/

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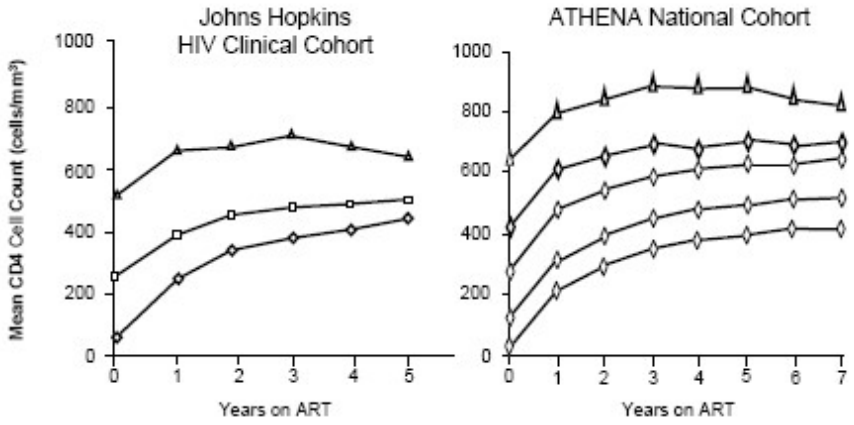
Likelihood of achieving normal CD4 cell count depends where you start



Keruly J, et al. *Clin Infect Dis*. 2007;44(3):441-446.
Gras L, et al. *J Acquir Immune Defic Syndr*. 2007;45(2):183-192.

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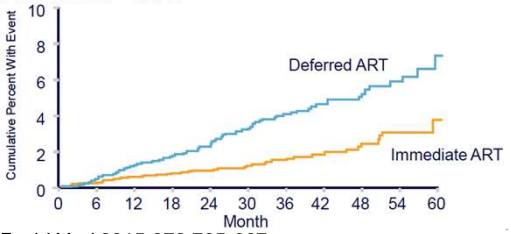
START (Strategic Timing of AntiRetroviral Treatment) Trial: ↓Death Associated with Starting ART at CD4 > 500

- N=4,685; 215 sites in 35 countries; 3 years follow-up
- Inclusion: HIV+, ART naïve with CD4 > 500
- Comparison: Initiate ART immediately (early arm) vs. wait until CD4 declined to <350 (deferred arm)
- Results: Study stopped early by DSMB
  - **Risk of serious illness or death reduced by 57% with immediate ART** [1.8% vs. 4.1%, HR 0.43, 95% CI: 0.3-0.62; *P*<.001]



Lundgren J, et al. N Engl J Med 2015;373:795-807.

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Undetectable = Untransmittable (U = U)

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

People who take ART daily as prescribed and achieve and maintain an undetectable viral load have effectively no risk of sexually transmitting the virus to an HIV-negative partner.

September, 2017

www.preventionaccess.org and www.cdc.gov/hiv/risk/art/index.html

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Evidence Supporting U=U

Study	Enrolled Sample	Number of condomless sex acts	Number of New HIV Infections		
			Total	Phylogenetically Linked	**Phylogenetically Linked When HIV+ Partner Stably Virally Suppressed**
HPTN 052 Cohen et al., 2016	1,763 mixed status couples • 98% male-female couples	Not reported	78 • 19 in early ART group • 59 in delayed ART group	46 • 3 in early ART group • 43 in delayed ART group	**0**
PARTNER1 Rodger et al., 2016	~900 mixed status couples • 62% male-female couples	55,193 • 34,214 among male-female couples • 20,979 among male-male couples	11	0	**0**
Opposites Attract Bavinton et al., 2018	358 mixed status male-male couples	12,447	3	0	**0**
PARTNER2 Rodger et al., 2019	972 mixed status male-male couples	76,991	15	0	**0**

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Overview of ART Drug Classes

- Classification based on where in the viral life cycle each drug acts
- 6 Antiretroviral Classes
  - **Nucleos(t)ide reverse transcriptase inhibitors (NRTI)***
  - **Integrase strand transfer inhibitors (INSTI)***
  - Protease inhibitors (PI)†
  - Non-nucleoside reverse transcriptase inhibitors (NNRTI)†
  - Entry inhibitors††
  - Capsid inhibitor††

***Recommended in initial regimens for most people with HIV**
†Recommended only in certain clinical scenarios
†† Not recommended for initial therapy

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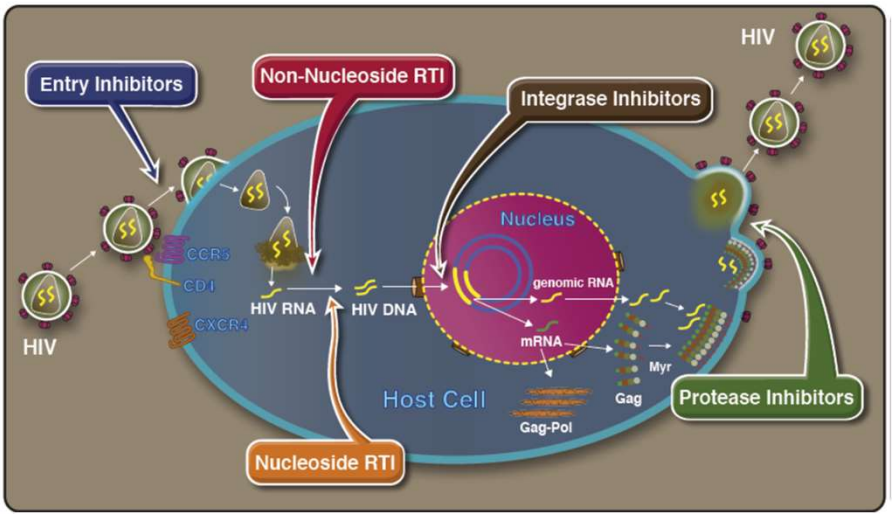
HIV Life Cycle & ARV Drug Classes



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Antiretroviral Medications

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

Abacavir (ABC) (Ziagen®)
Didanosine (ddI) (Videx®)
Emtricitabine (FTC) (Emtriva®)
Lamivudine (3TC) (Epivir®)
~~Stavudine (d4T) (Zerit®)~~ *withdrawn 2020*
Tenofovir (TDF or TAF) (Viread® or Vemlidy®)
~~Zalcitabine (ddC) (Hivid®)~~ *withdrawn 2005*
Zidovudine (ZDV, AZT) (Retrovir®)
3TC/ABC (Epzicom®)
~~3TC/ABC/ZDV (Trizivir®)~~ *discontinued 2024*
3TC/ZDV (Combivir®)
3TC/TDF (Cimduo®, Temixys®)
FTC/TDF (Truvada®)
FTC/TAF (Descovy®)

Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

~~Delavirdine (DLV) (Rescriptor®)~~ *Discontinued 2018*
Doravirine (DOR) (Pifeltro®)
Efavirenz (EFV) (Sustiva®)
Etravirine (ETR) (Intelence®)
Nevirapine (NVP) (Viramune®)
Rilpivirine (RPV) (Edurant®)

Integrase Inhibitors (INSTIs)

Bictegravir (BIC)
Cabotegravir (CAB) (Vocabria®)
Dolutegravir (DTG) (Tivicay®)
Elvitegravir (EVG)
Raltegravir (RAL) (Isentress®)

Pharmacokinetic Enhancers "Boosters"

Cobicistat (cobi) (Tybost®)
Ritonavir (r) (Norvir®)

Protease Inhibitors (PIs)

~~Amprenavir (APV) (Agenerase®)~~ *discontinued 2004*
Atazanavir (ATV) (Reyataz®)
Atazanavir/cobicistat (ATV/c) (Evotaz®)
Darunavir (DRV) (Prezista®)
Darunavir/cobicistat (DRV/c) (Prezcobix®)
Fosamprenavir (FPV) (Lexiva®)
~~Indinavir (IDV) (Crixivan®)~~ *discontinued 2020*
Lopinavir/ritonavir (LPV/r) (Kaletra®)
Nelfinavir (NFV) (Viracept®)
Ritonavir (RTV) (Norvir®)
~~Saquinavir (SQV) (Invirase®)~~ *discontinued 2006*
Tipranavir (TPV) (Aptivus®)

Entry Inhibitors

~~Enfuvirtide (ENF, T20) (Fuzeon®)~~ *discontinued 2025*
Ibalizumab (Trogarzo®)
Maraviroc (MVC) (Selzentry®)
Fostemsavir (Rukobia®)

Single Tablet Regimens

BIC/FTC/TAF (Biktarvy®)
DRV/cobi/FTC/TAF (Symtuza®)
DTG/3TC/ABC (Triumeq®)
DTG/RPV (Juluca®)
DTG/3TC (Dovato®)
DOR/3TC/TDF (Delstrigo®)
EFV/FTC/TDF (Atripla®)
EFV/3TC/TDF (Symfi® or Symfi Lo®)
EVG/cobi/FTC/TAF (Genvoya®)
EVG/cobi/FTC/TDF (Stribild®)
RPV/FTC/TAF (Odefsey®)
RPV/FTC/TDF (Complera®)

Long acting injectable ART

CAB/RPV (Cabenuva®)

Capsid inhibitor

Lenacapavir (LEN) (Sunlenca®)

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Initial HIV Management Principles

- Initiate ART with 1 of 3 types of regimens
- Most regimens include **1-2 NRTIs plus 1 drug from a separate class**:
  - **1-2 NRTIs + 1 INSTI***
  - 2 NRTIs + NNRTI†
  - 2 NRTIs + 1 PI (boosted PI) †

***Recommended for most patients**
†Recommended in certain clinical scenarios

US HHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/

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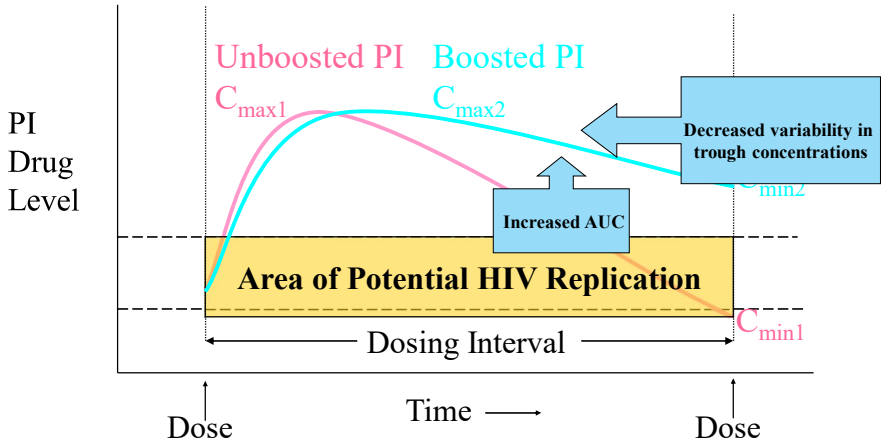
Boosting a Protease Inhibitor (PI) With Ritonavir or Cobicistat



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Goals of Antiretroviral Therapy

- Decrease HIV RNA
  - Goal HIV RNA or "viral load" <20-75 copies/mL or "undetectable"
- Increase CD4 count
  - 500-1500 cells/mm^3 is normal CD4 range
  - AIDS diagnosis is CD4 < 200 or CD4% < 14% (or AIDS defining illness)
- Improve quality of life and reduce HIV-related morbidity & mortality
- Prevent HIV transmission to others

US HHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/

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Laboratory Monitoring Schedule for ART Adverse Effects

	Entry into care	ART initiation or modification	4-8 weeks after ART initiation or modification	Every 3 mo.	Every 6 mo.	Every 12 mo.	When clinically indicated
Basic metabolic panel	√	√	√		√		√
AST, ALT, T. bili	√	√	√		√		√
CBC with differential	√	√		√ If CD4 testing is done	√ If CD4 testing is done	√ When no longer monitoring CD4 count	√
Lipid profile	√		Consider 1-3 months after ARV initiation or modification			√ If normal at baseline but with CV risk	√
Glucose	√	√					√
Urinalysis	√						√

US HHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/

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Monitoring for Drug Interactions

- Common drug interactions occur between ART and medications used to manage common comorbidities
- Drug interactions range from mild to severe (and even potentially fatal, requiring FDA labeling to prohibit co-administration)
- Any changes to a patient's medication list requires careful consideration of potential drug interactions
- Ask about all medications: prescription, over-the-counter, herbal, recreational
  - The INSTIs bictegravir, dolutegravir, & raltegravir have the fewest drug interactions
  - Regimens containing cobicistat or ritonavir as boosters have a high potential for drug interactions

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Adherence Interventions

- Provide accessible, trustworthy, nonjudgmental multidisciplinary health care team
- Find resources to assist with treatment costs to maintain uninterrupted access to both ART and appointments
  - Resources to obtain prescription drug coverage
    - AIDS Drug Assistance Program (ADAP)
    - Pharmaceutical company HIV patient assistance programs and cost-sharing assistance programs
- Allow flexible appointment scheduling
- Assist with transportation to clinic and pharmacy
- Link patients to counseling to overcome stigma, substance use, or depression
- Medication scheduling reminders
- Change ART to simplify dosing or reduce side effects

US HHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/

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Simplified ART Regimens

- Use of single-tablet regimens (STRs) vs. multi-tablet regimens
- Co-formulated antiretroviral agents and once-daily dosing can reduce pill burden and simplify dosing schedules
- Simplified treatment regimens
  - Effective
  - Favored by patients and providers
  - Associated with better adherence

Yang T, Oliyai R, Kent KM. *Antiviral Therapy*. 2022;27(2).

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Single Tablet Regimens (STRs)

Year of FDA Approval	Brand Name	Generic Name	Antiretroviral Drug Classes
2006	Atripla	Efavirenz/tenofovir DF/emtricitabine	NNRTI + dual NRTI
2011	Complera	Rilpivirine/tenofovir DF/emtricitabine	NNRTI + dual NRTI
2012	Stribild	Elvitegravir/cobicistat/tenofovir DF/emtricitabine	INSTI + booster + dual NRTI
2014	Triumeq	Dolutegravir/abacavir/lamivudine	INSTI + dual NRTI
2015	Genvoya	Elvitegravir/cobicistat/tenofovir AF/emtricitabine	INSTI + booster + dual NRTI
2016	Odefsey	Rilpivirine/tenofovir AF/emtricitabine	NNRTI + dual NRTI
2017	Juluca	Dolutegravir/rilpivirine	INSTI + NNRTI
2018	Biktarvy	Bictegravir/tenofovir AF/emtricitabine	INSTI + dual NRTI
2018	Symtuza	Darunavir/cobicistat/tenofovir AF/emtricitabine	PI + booster + dual NRTI
2018	Delstrigo	Doravirine/tenofovir DF/emtricitabine	NNRTI + dual NRTI
2019	Dovato	Dolutegravir/lamivudine	INSTI + NRTI

Key: DF = disoproxil fumarate; AF = alafenamide; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucelos(t)ide reverse transcriptase inhibitor; INSTI = integrase strand transfer inhibitor; PI = protease inhibitor

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Food Considerations with STRs

STR Brand Name	STR Generic Name	Food Considerations
Atripla	Efavirenz/tenofovir DF/emtricitabine	Empty stomach
Biktarvy	Bictegravir/tenofovir AF/emtricitabine	With or without food
Complera	Rilpivirine/tenofovir DF/emtricitabine	With a full meal (not a protein drink)
Delstrigo	Doravirine/tenofovir DF/emtricitabine	With or without food
Dovato	Dolutegravir/lamivudine	With or without food
Genvoya	Elvitegravir/cobicistat/tenofovir AF/emtricitabine	With food
Juluca	Dolutegravir/rilpivirine	With a full meal (not a protein drink)
Odefsey	Rilpivirine/tenofovir AF/emtricitabine	With a full meal (not a protein drink)
Stribild	Elvitegravir/cobicistat/tenofovir DF/emtricitabine	With food
Symtuza	Darunavir/cobicistat/tenofovir AF/emtricitabine	With food
Triumeq	Dolutegravir/abacavir/lamivudine	With or without food

Key: DF = disoproxil fumarate; AF = alafenamide

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What exactly does empty stomach, with food, or with a full meal mean?

- Empty stomach: 1 hour before a meal or 2 hours after a meal
- With food: Within 2 hours after eating
- With a full meal: At least 390 calories

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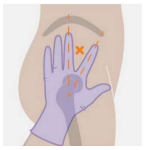
Simplified Regimen: Long-acting cabotegravir/rilpivirine (LA CAB/RPV)



- Intramuscular gluteal injections every 4 weeks or every 8 weeks, administered by healthcare provider
- FDA approved to replace ART in persons with HIV RNA <50 copies/mL, and:
  - Taking stable ARV regimen
  - No history of treatment failure
  - No known/suspected resistance to CAB or RPV
  - Not pregnant or planning to become pregnant
  - No hepatitis B virus
  - No drug interactions

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Process for Selecting an Initial ART Regimen

- Regimen efficacy
  - Standard therapy for HIV typically consists of 2-3+ drugs from 2+ classes (no monotherapy)
- Comorbidities
  - Potential adverse effects or drug-drug interactions
- Drug resistance
  - Presence of transmitted drug resistance or development of drug resistance on failure
- Adherence potential
  - Pill burden, dosing frequency, food restrictions

US HHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/

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Recommended Initial Regimens for Most People with HIV

1-2 NRTIs		INTEGRASE INHIBITOR
Emtricitabine + Tenofovir **OR** Lamivudine *only with dolutegravir and when HIV RNA < 500,000, no HBV, and no resistance	+	Bictegravir Dolutegravir

Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are two forms of tenofovir approved by the FDA. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

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Recommended Initial Regimens in Certain Clinical Scenarios

2 NRTIs

Emtricitabine + Tenofovir
OR
Lamivudine + Abacavir

+

PROTEASE INHIBITOR
(boosted with ritonavir or cobicistat)

Darunavir + RTV or Darunavir + COBI

OR

NNRTI

Doravirine
Rilpivirine

OR

INTEGRASE INHIBITOR

Dolutegravir

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Selecting an Initial HIV Regimen: The "Chinese Food Rule"

*Tip of the hat to Royce Lin, MD, Associate Clinical Professor of Medicine, UCSF

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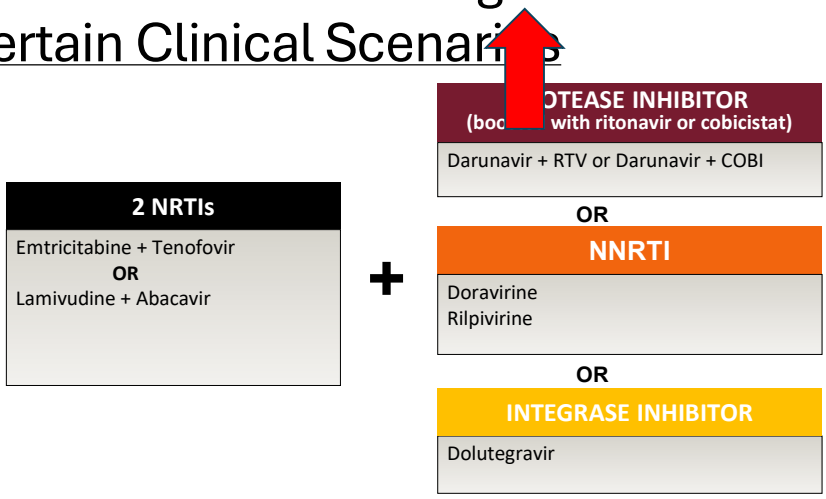
Recommended Initial Regimens in Certain Clinical Scenarios



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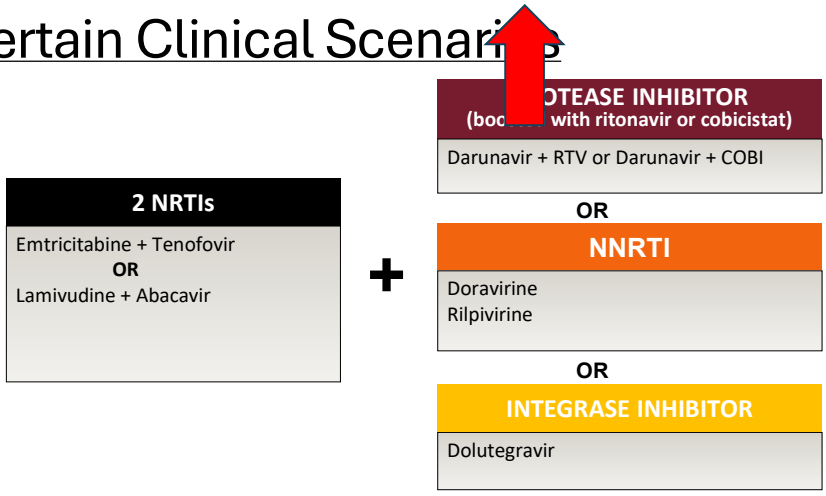
Recommended Initial CHINESE FOOD in Certain Clinical Scenarios



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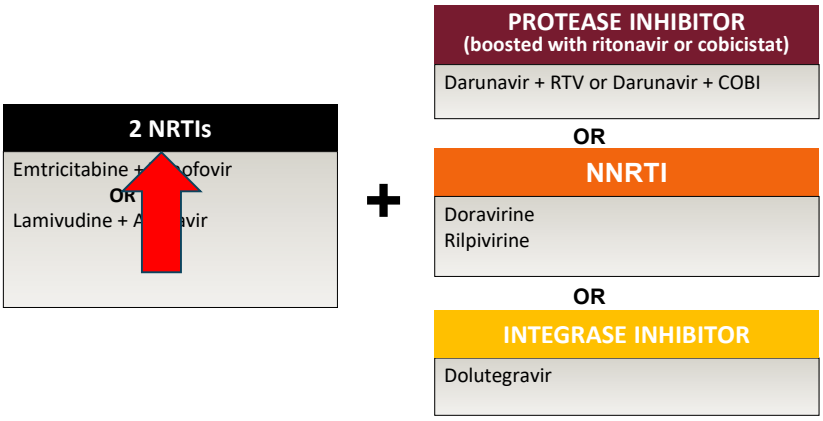
Recommended Initial CHINESE FOOD in Certain Clinical Scenarios



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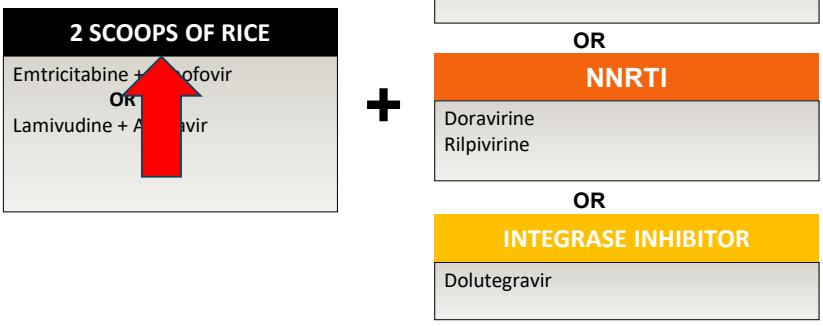

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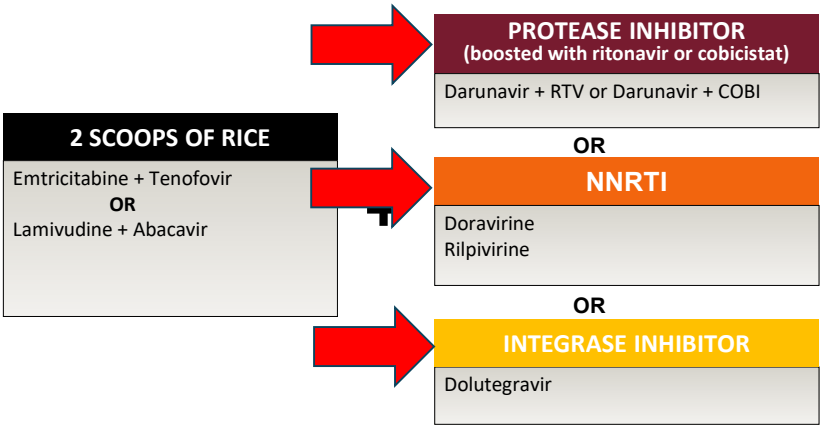
Recommended Initial CHINESE FOOD in Certain Clinical Scenarios



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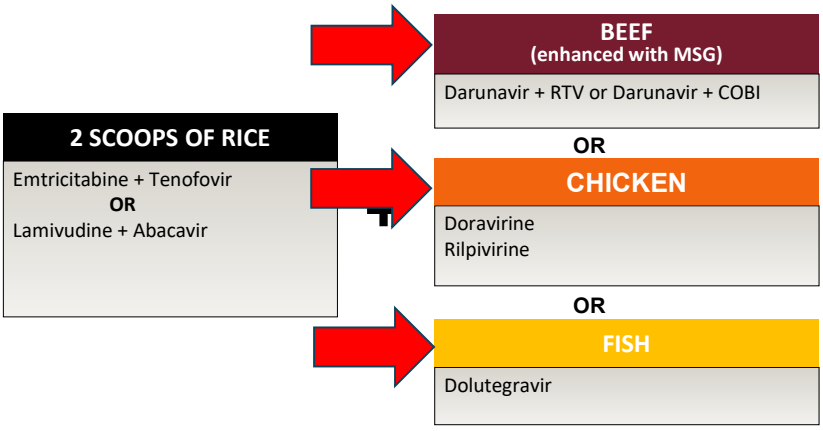

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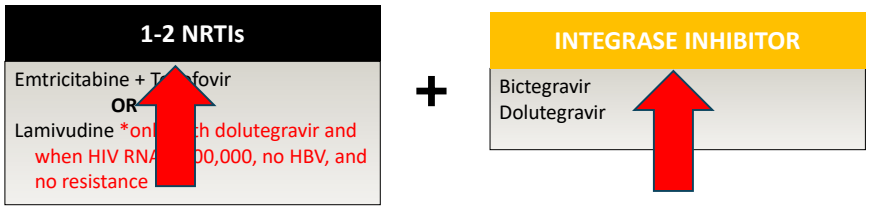
Recommended Initial Regimens for Most People with HIV



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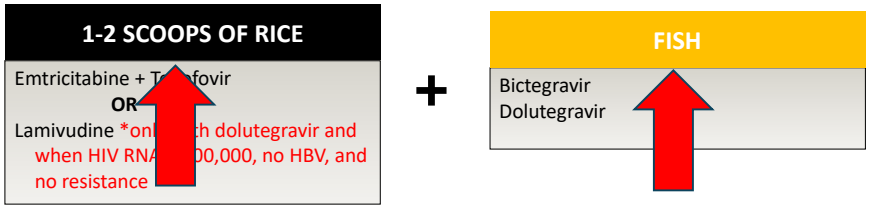

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HIV Regimen / Chinese Food Selection: A Stepwise Approach

1. Get 1-2 scoops of rice  
   - Choose 2 NRTIs, co-formulated when possible
     - Example: Tenofovir + emtricitabine
     - Example: Abacavir + lamivudine
   - Only one regimen (lamivudine + dolutegravir) uses 1 NRTI *VL<500,000, no hepatitis B, no resistance
2. Beef, fish, or chicken?   
   - Decide which class to use (PI, INSTI, NNRTI)
   - Choose specific agent based on comorbidities, pill burden, drug interactions, resistance testing

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Choosing NRTI Backbone

Abacavir

- Black box warning: Hypersensitivity reaction
- Use only if HLA-B*5701 negative
- Possible ↑ risk of MI
- Less effective if VL>100K (unless it's paired with both dolutegravir and lamivudine)

Tenofovir disoproxil fumarate (TDF)

- Loss of bone density (osteopenia and osteoporosis)
- Can cause renal impairment (Fanconi's syndrome, acute renal insufficiency)
- More favorable lipid profile compared to TAF

Tenofovir alafenamide (TAF)

- Less bone mineral density loss or adverse impact on renal function vs. TDF
- Has some P-gp mediated drug interactions that TDF does not have (anticonvulsants, rifampin)

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PI, InSTI, or NNRTI? (Beef, Fish, or Chicken?)

PI + RTV or COBI (Beef + MSG)	INSTI (Fish)	NNRTI (Chicken)
PRO •Very strong, potency well established •Harder to get resistance •Best for patients with uncertain adherence or if resistance tests not available •Use darunavir-based ART if prior use of cabotegravir for PrEP and INSTI resistance test result not yet available or INSTI resistance	**PRO** •Highly effective for most patients •Very few side effects •Less drug interactions •Less resistance seen with dolutegravir or bictegravir (strong, potent) •Dolutegravir or bictegravir can be used if resistance tests not available (unless prior use of cabotegravir for PrEP)	**PRO** •Doravirine: less drug interactions, can take with or without food •Rilpivirine is in smallest single tablet regimen 
CON •Boosting required •Many drug interactions (P450 metabolism) •Metabolic effects (↑ cholesterol, glucose) •GI side effects	**CON** •Weight gain (e.g. bictegravir, dolutegravir, especially when used with tenofovir alafenamide) •Dolutegravir and bictegravir cause benign increase in SCr (mean 0.1 mg/dL) •Rarely: insomnia, ↑CPK	**CON** •Doravirine comes co-formulated only with lamivudine/tenofovir disoproxil fumarate •Oral rilpivirine has lower efficacy in some patients (use only if CD4>200 and VL<100,000) and requires acidic environment for absorption

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Despite Extraordinary Efficacy, ART Can Be Improved

- Virologic suppression rates are excellent in adherent patients
- But there is room to improve ART:
  - Convenience
    - Regimen simplification to single tablet regimens or regimens given less often than daily
  - Activity against pan-resistant virus
    - Older people treated in early ART days with less potent regimens that had low resistance barriers
    - Younger people with congenital infection, now young adults

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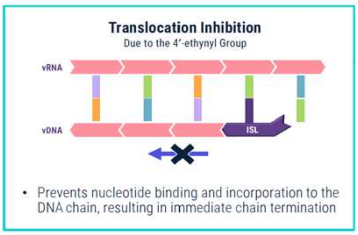
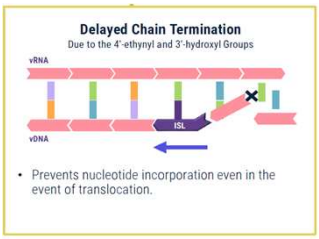
Investigational ART: Islatravir (Phase 3)

Nucleoside reverse transcriptase translocation inhibitor (NRTTI)

- Multiple mechanisms of action





- Potential advantages
  - Potent, long t½, high genetic barrier to resistance
  - Activity against NRTI resistance
  - Low potential for drug interactions

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Select Pipeline Regimens for HIV Treatment

Regimen	Islatravir + Doravirine (ISL + DOR)	Islatravir + Lenacapavir (ISL + LEN)	Bictegravir + Lenacapavir (BIC + LEN)
Indication (Study Phase)	ART naïve & virologically suppressed (III)	Virologically suppressed (II)	Virologically suppressed (III)
Dosing	**Daily oral** ISL 0.25 mg + DOR 100 mg fixed-dose combination	**Weekly oral** ISL 2 mg + LEN 300 mg (after oral LEN loading dose)	**Daily oral** BIC 75 mg + LEN 50 mg (after oral LEN loading dose)

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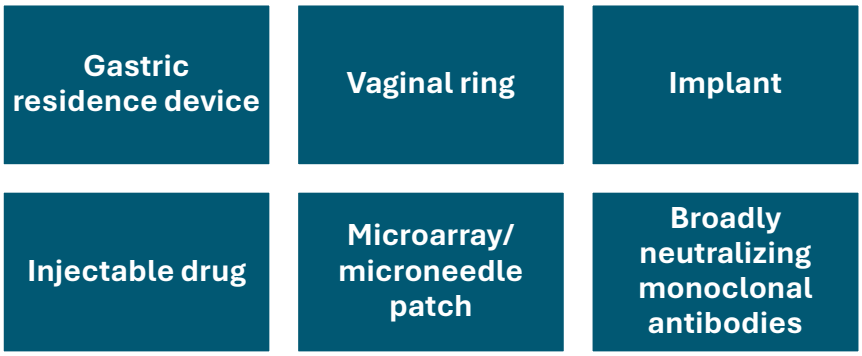
Long-Acting ARV Technologies in the Pipeline



Chandiwana. AIDS. 2021;35:S137.

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Interactive Patient Case

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Patient Case

- Collin is a 43-year-old man who presents to clinic after a recent diagnosis of HIV
- He was diagnosed after routine screening for sexually transmitted infections
- He has been sexually active with five partners in the past 6 months
- He is aware of his diagnosis, has met with a linkage coordinator, and has notified prior partners. He feels well supported and ready to start treatment.
- He has a past medical history of depression treated with escitalopram, diabetes treated with metformin and semaglutide injections, and hypertension treated with lisinopril

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Audience Discussion

- What other information do you want prior to initiating ART?

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Patient Case Continued

- He has completed initial laboratory studies as part of clinic intake as follows:
  - Complete blood count within normal limits
  - Comprehensive metabolic panel within normal limits
  - CD4 count 750 cells/mm3
  - HIV RNA PCR with 39,000 copies/mL
  - Baseline HIV genotype without evidence of resistance
  - Sexually transmitted infection testing without evidence of active infection
  - Hepatitis A & B serologies consistent with prior vaccination
  - Hepatitis C serology negative

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Audience Discussion

- What general counseling regarding ART do you wish to provide at this initial visit?

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Audience Discussion

- What general counseling regarding ART do you wish to provide at this initial visit?
- What factors should you consider when selecting an initial ART regimen?

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Patient Case Continued

- Collin is concerned about side effects with new treatments
- He has seen several advertisements for both single-tablet regimens as well as injectable therapy

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Audience Discussion

- Which antiretroviral regimen would you recommend for Collin?

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Audience Discussion

- Which antiretroviral regimen would you recommend for Collin?
- Which resources can you utilize to assess for drug-drug interactions?

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Audience Discussion

- Which antiretroviral regimen would you recommend for Collin?
- Which resources can you utilize to assess for drug-drug interactions?
- What counseling may be provided regarding adverse effects for this and/or other initial ART regimens?

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Summary

- Number of people with HIV steadily increasing
- HIV transmission risk varies widely depending on the type of exposure or behavior
- Ending the HIV epidemic = Scaling up key HIV treatment and prevention strategies including PrEP (pre-exposure prophylaxis) and PEP (post-exposure prophylaxis) among others
- HIV testing should be routinized
- Antiretroviral therapy recommended for all HIV+
  - Initial ART = 1-2 NRTIs + INSTI or PI or NNRTI

    (1-2 scoops of rice + 1 main entrée)
- Pharmacists play a crucial role in the care of people with HIV and people at risk of HIV acquisition

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