




# HIV/AIDS 2025



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## Disclosures

- No pharmaceutical or device company relationships
- Co-Chair, U.S. DHHS Adult and Adolescent ART Treatment Guidelines Panel

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## ID Boards – Medical Content: 15% HIV

- Epidemiology (<2%)
- Pathogenesis (<2%)
- Lab testing (<2%)
- HIV Treatment Regimens (4.5%)
- Opportunistic Infections (5%)
- Malignancies (<2%)
- Other complications of HIV (2%)
- Related issues (<2%)

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## Morbidity and Mortality Weekly Report (MMWR): 1981

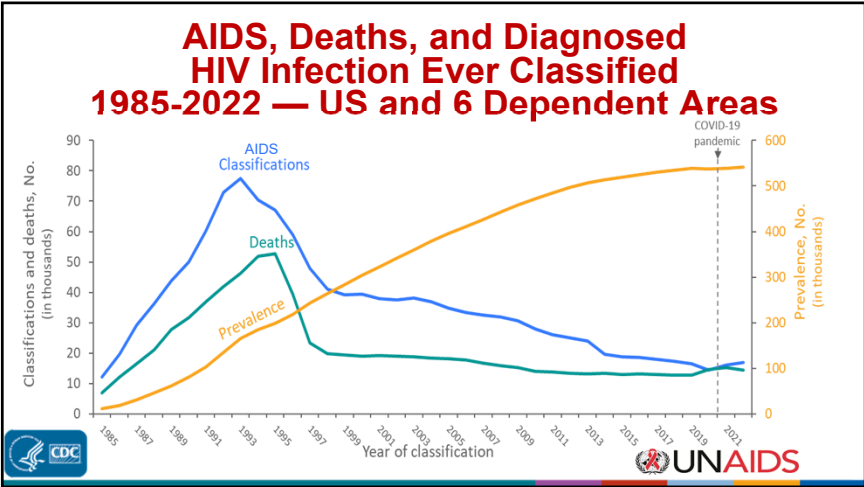
1981 June 5;30:250-2

*Pneumocystis Pneumonia – Los Angeles*

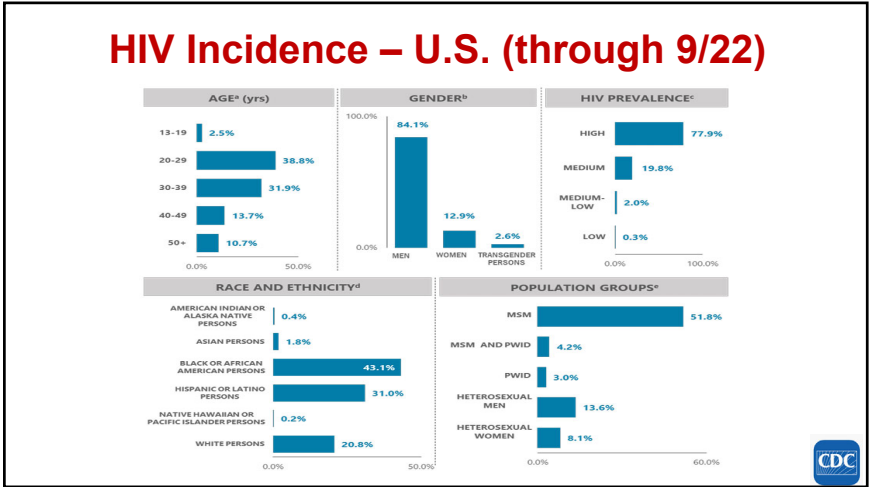
In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

2024: >88 million people infected globally; over 1/2 have died

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### Human Immunodeficiency Virus (HIV)

- Formerly HTLV-III; isolated 1983-4
- Human retrovirus – outer glycoprotein coat, inner protein coat and genetic material: RNA (2 strands)
- Types: HIV-1 and HIV-2
- Subtypes (clades): B most common in North America and Europe
- Zoonosis from primates (~1900)
- Target cell: CD4+ T-lymphocyte

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### Question #1

Which is the current sequence of initial and confirmatory HIV diagnostic testing?

- A. ELISA, followed by Western Blot
- B. ELISA, followed by HIV RNA
- C. ELISA, followed by immunoassay
- D. HIV RNA, followed by Western Blot
- E. HIV RNA, followed by ELISA
- F. HIV RNA, followed by immunoassay

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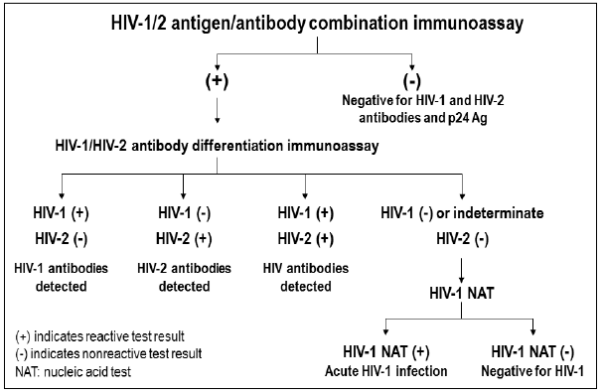
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HIV Testing

- HIV antibody testing (indirect)
  - Screening test: HIV-1, HIV-2 antibodies by ELISA
  - If repeatedly positive, proceed to confirmatory test
    - Immunoblot (or 2<sup>nd</sup> HIV rapid test)
  - 20-minute oral test and 1-minute blood test
- HIV viral testing (direct)
  - p24 antigen
  - viral culture
  - HIV RNA (viral load)
- Combination antibody + antigen test
  - window period ↓ 3 months → 2 weeks

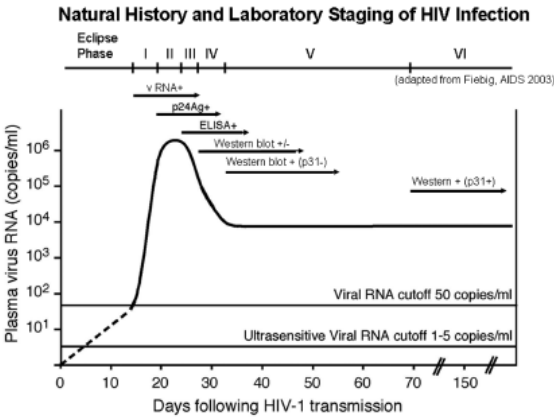
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Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens



CDC 2014

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Cohen JID 2010;202:S270

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Question #2

Who should NOT be routinely offered HIV testing?

- A. 32-year-old pregnant woman in a stable relationship
- B. 23-year-old sexually active monogamous gay man
- C. 75-year-old former injection drug user
- D. 10-year-old pre-pubescent girl
- E. All of them should be routinely offered HIV testing

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Question #2

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U.S. Preventive Services Task Force (UPSTF)  
Recommendations

- Screen adolescents and adults ages 15 to 65 for HIV infection
- Screen all pregnant women
- Younger adolescents and older adults who are at increased risk should also be screened
- This is a grade A recommendation (“high certainty that the net benefit is substantial”)
- Federal Rule: Private Insurance and Medicare must offer A or B services without a co-pay

Ann Intern Med 2013;159:1-36

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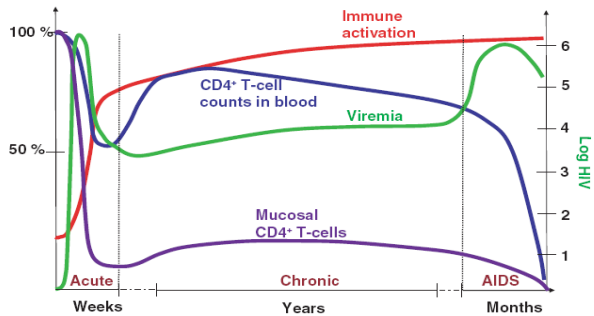
HIV Transmission Risks

Exposure from HIV+ source	Risk per exposure (%)	Risk per exposure (number)
Blood transfusion	93%	9/10
Needle-sharing injection drug use	0.6%	1/167
Percutaneous needle stick	0.2%	1/500
Receptive anal sex	1.4%	1/70
Insertive anal sex	0.1%	1/1000
Receptive penile-vaginal sex	0.08%	1/1250
Insertive penile-vaginal sex	0.04%	1/2500
Oral sex	low	very low
Mother-to-child	23%	1/4

Patel AIDS 2014;28:1509

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**Time Course of HIV Infection**



Grossman Nature Medicine 2006;12:289-295

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**CDC Adult AIDS Case Definition**

- 1982: “AIDS” -- list of diseases (definitive diagnosis) and disqualifying conditions
- 1985: HIV antibody testing added to definition
- 1987: presumptive diagnoses with a positive HIV antibody added
- 1993: CD4 <200 (without symptoms) and other diagnoses added

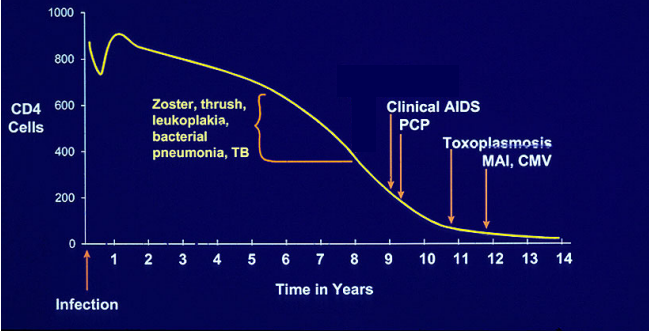
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**Opportunistic Infections (OI)**

- Definition: Infection caused by an organism capable of causing disease only in a host whose resistance is lowered (by other diseases or by drugs)
- AIDS-related:
  - Bacterial: MAC, tuberculosis
  - Fungal: PCP, Cryptococcus, Histoplasma
  - Viral: CMV
  - Parasitic: Toxoplasma
  - Malignancies: Kaposi’s sarcoma, Non-Hodgkin’s-lymphoma

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**Natural History of HIV Infection**



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Goal of Antiretroviral Therapy

- To suppress HIV RNA (viral load level) as low as possible, for as long as possible
- To preserve or enhance immune function
- To delay clinical progression of HIV disease and prolong healthy survival

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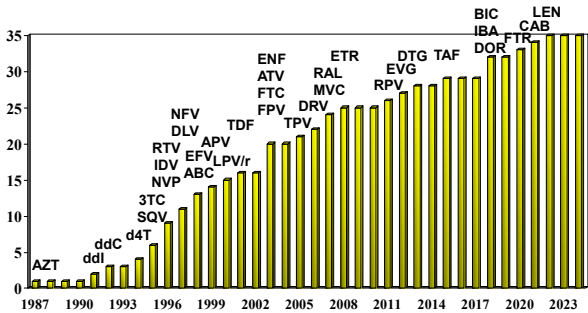
When to Start ART?

Guidelines	AIDS/ symptoms	CD4 <200	CD4 200-350	CD4 350-500	CD4 >500
		← asymptomatic →			
US DHHS '24 <a href="http://www.clinicalinfo.hiv.gov">www.clinicalinfo.hiv.gov</a>	treat	treat	treat	treat	treat
IAS-USA '24 <a href="https://doi.org/10.1093/infdis/jiaa001">JAMA 2025;333:609-628</a>	treat	treat	treat	treat	treat

- U.S. DHHS HIV Treatment Guidelines:
- ART is recommended for all persons with HIV to ↓ morbidity and mortality (**AI**) and to prevent transmission of HIV to others (**AI**).
  - Initiate ART immediately (or as soon as possible) after HIV diagnosis.

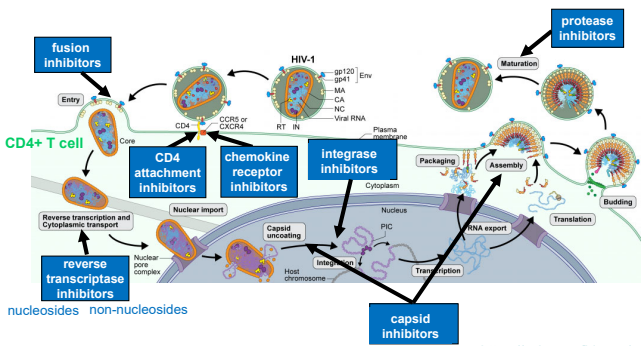
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Antiretroviral Drug Approval: 1987-2025



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Life Cycle of HIV



<https://scienceofhiv.org/wp/animations/>

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Approved ART: 2025\*

Nucleoside/tide RTIs (NRTIs)

- zidovudine (ZDV, AZT)
- lamivudine (3TC)
- abacavir (ABC)
- emtricitabine (FTC)
- tenofovir (TAF, TDF)

NNRTIs

- nevirapine (NVP)
- efavirenz (EFV)
- etravirine (ETR)
- rilpivirine (RPV)
- doravirine (DOR)

Protease inhibitors (PIs)

- saquinavir (SQV)
- ritonavir (RTV)
- indinavir (IDV)
- nelfinavir (NFV)
- lopinavir/r (LPV/r)
- atazanavir (ATV)
- tipranavir (TPV)
- darunavir (DRV)

Integrase inhibitors (IIs)

- raltegravir (RAL)
- elvitegravir (EVG)
- dolutegravir (DTG)
- bictegravir (BIC)
- cabotegravir (CAB)

Entry inhibitors (EIs)

- enfuvirtide (T-20, fusion inhibitor)
- maraviroc (MVC, CCR5 antagonist)
- ibalizumab (IBA, CD4 post-attachment inhibitor)
- fostemsavir (FTR, CD4 attachment inhibitor)

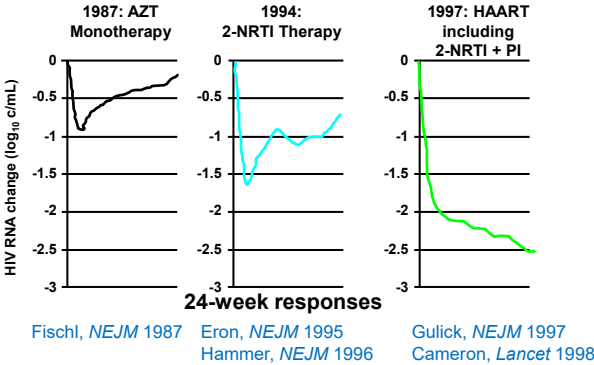
Capsid inhibitors (CIs)

- lenacapavir (LEN)

\*ddi, ddC, d4T, DLV, APV, FPV, and ENF (T-20) discontinued from market

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Antiretroviral Activity: 1987-1997



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Question #3

Which class of ART is recommended for initial HIV treatment for most patients?

- A. All nucleoside analog (NRTI) regimen
- B. Non-nucleoside (NNRTI)-based regimen
- C. Protease inhibitor (PI)-based regimen
- D. Integrase inhibitor (INSTI)-based regimen
- E. Entry inhibitor (EI)-based regimen

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Question #3

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- E. Entry inhibitor (EI)-based regimen

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## What to Start?

### Recommended Regimens:

**1 or 2 nucleoside analogues + integrase inhibitor**

- Bictegravir/tenofovir alafenamide (TAF)/emtricitabine (FTC)
- Dolutegravir + (FTC or lamivudine [3TC]) + (TAF or tenofovir disoproxil fumarate [TDF])
- Dolutegravir/3TC
- With prior cabotegravir (CAB) for PrEP: darunavir/booster (cobicistat or ritonavir) + [(TAF or TDF) + (FTC or 3TC)]

**Alternative regimens:** abacavir-containing, non-nucleoside (NNRTI)-based, protease inhibitor (PI)-based

U.S. DHHS HIV Treatment Guidelines 9/24

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## Approved Single-Tablet ART Regimens

TDF/FTC/EFV (2006)		DTG/RPV (2017)*	
TDF/FTC/RPV (2011)		TAF/FTC/BIC (2018)	
TDF/FTC/EVG/c (2012)		TAF/FTC/DRV/c (2018)	
ABC/3TC/DTG (2014)		TDF/3TC/DOR (2018)	
TAF/FTC/EVG/c (2015)		DTG/3TC (2019)	
TAF/FTC/RPV (2016)			

\*FDA approved for maintenance therapy

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## Cabotegravir (CAB)

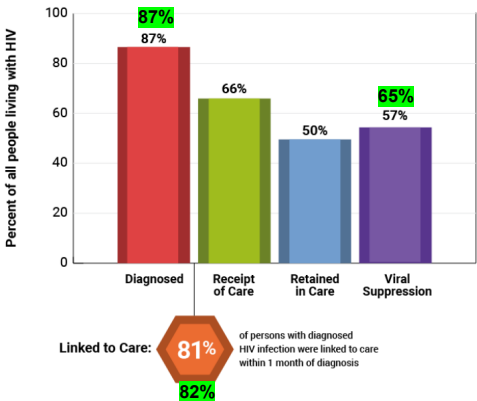
- Integrase inhibitor similar to dolutegravir
- Potent in people with HIV (5, 10, 30, 60 mg oral)
  - Spreen HIV Clin Trials 2013;14:192
- Nanotechnology formulation; injectable
- Phase 3 studies of IM CAB/rilpivirine (RPV) for treatment switch demonstrated **non-inferiority** to standard oral treatment regimens
  - Orkin NEJM 2020;382:1124
  - Swindells NEJM 2020;382:1112
- U.S. FDA approved the combination of IM CAB + RPV monthly for switch treatment in 2021
  - For patients undetectable on ART without a history of virologic failure, drug resistance, or chronic HBV infection
  - 2022 FDA label amended for every other month dosing and optional lead-in dosing



Overton Lancet 2021;396:1994 + Orkin Lancet HIV 2021;8:e668

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## Prevalence-based HIV Care Continuum, U.S. and 6 Dependent Areas, 2019



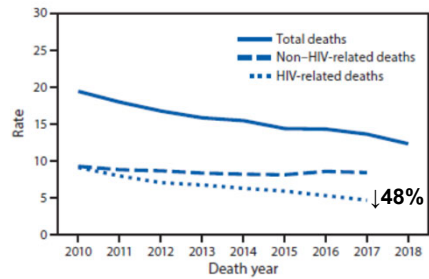
www.hiv.gov  
CDC 2021

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U.S. HIV Deaths: 2010-2018

FIGURE 1. Age-adjusted rates\* of total deaths,† human immunodeficiency virus (HIV)-related deaths,‡ and non-HIV-related deaths among persons aged ≥13 years with diagnosed HIV infection — United States, 2010–2018§

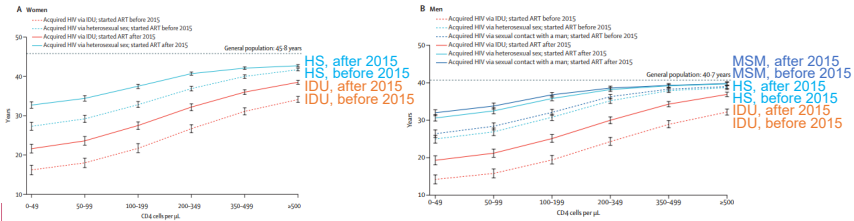


Bosh, MMWR 2020;69:1717-24

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Life Expectancy of HIV on ART

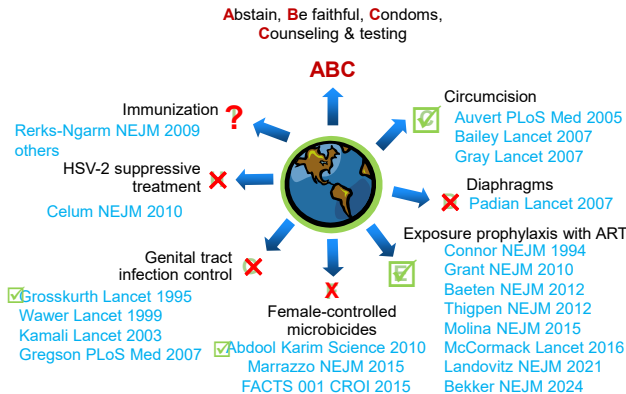
- Goal: To estimate life expectancy of people with HIV on ART for ≥1 year after 2015 at age 40 in North America / Europe
- Study population: ART Cohort Collaboration + UK CHIC Cohort Study (N=206,891 with 5780 deaths)
- Results:



Trickey Lancet HIV 2023;10:e295-e307

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HIV Prevention Strategies



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Question #4

Which PrEP regimen is FDA-approved for at-risk men and women?

- A. Daily tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC)
- B. Daily tenofovir alafenamide (TAF)/FTC
- C. On-demand TDF/FTC
- D. On-demand TAF/FTC
- E. All of the above

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Question #4

Which PrEP regimen is FDA-approved for at-risk men and women?

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- B. Daily tenofovir alafenamide (TAF)/FTC
- C. On-demand TDF/FTC
- D. On-demand TAF/FTC
- E. All of the above

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HIV Prevention Strategy: PrEP

- Pre-exposure prophylaxis
- Strategy of administering HIV medications to uninfected, at-risk individuals
- Optimal drug candidates:
  - potent, safe, tolerable, and convenient
  -  = co-formulated tenofovir/FTC
- 2012: FDA approves TDF/FTC for PrEP
- 2019: FDA approves TAF/FTC for PrEP
- 2021: FDA approves injectable CAB for PrEP
- 2024: Subcutaneous lenacapavir (LEN) studies

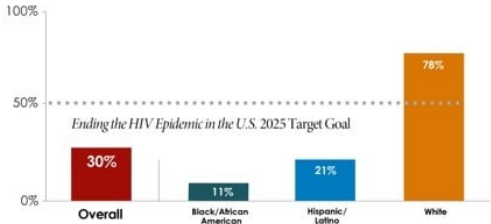
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Recent PrEP Studies

Study (reference)	Study population	Design	Results: Reduction in HIV Infection
<b>PROUD</b> <a href="#">McCormack Lancet 2015;387:54-60</a>	544 HIV- MSM in UK	TDF/FTC (daily) immediate vs. delayed	TDF/FTC immediate: <b>86% reduction</b>
<b>IPERGAY</b> <a href="#">Molina NEJM 2015;373:2237</a>	400 HIV- MSM in France and Canada	TDF/FTC (on demand) vs. placebo	TDF/FTC: <b>86% reduction</b>
<b>HPTN 083</b> <a href="#">Landovitz NEJM 2022;385:595</a>	4570 HIV- MSM and transgender women globally	TDF/FTC (daily) vs. CAB injections (every other month)	CAB non-inferior and <b>superior</b> to TDF/FTC
<b>HPTN 084</b> <a href="#">Delany-Moretlwe Lancet 2022;399:1779</a>	3224 HIV- at-risk women aged 18-45 in Sub-Saharan Africa	TDF/FTC (daily) vs. CAB injections (every other month)	CAB <b>superior</b> to TDF/FTC

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WHILE NEARLY ONE-THIRD OF PEOPLE ELIGIBLE FOR PREP WERE PRESCRIBED IT IN 2021, STARK DISPARITIES REMAIN  
ESTIMATED PREP COVERAGE IN THE U.S., BY RACE/ETHNICITY, 2021\*



\*Data unavailable for other races/ethnicities.  
Source: Centers for Disease Control and Prevention

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Federal Plan to End AIDS by 2030

**GOAL:** Our goal is ambitious and the pathway is clear – employ strategic practices in the *places* focused on the right *people* to:

75% reduction in new HIV infections in 5 years and at least 90% reduction in 10 years.

Diagnose all people with HIV as early as possible after infection.

Treat the infection rapidly and effectively to achieve sustained viral suppression.

Protect people at risk for HIV using potent and proven prevention interventions, including PrEP, a medication that can prevent HIV infections.

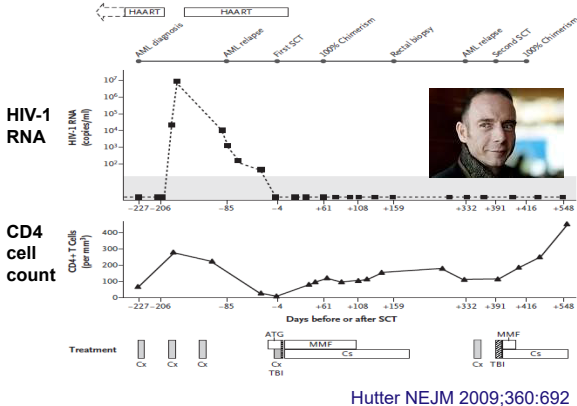
Respond rapidly to detect and respond to growing HIV clusters and prevent new HIV infections.

HIV HealthForce will establish local teams committed to the success of the initiative in each jurisdiction.

<https://www.hiv.gov/> (2019)

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HIV Cure (N=1) 9!



**Cure #2** \*first Latino  
London  
Gupta, Nature 2019;568:244-248  
**Cure #3** \*first woman  
NYC  
Hsu, Cell 2023;186:1115-1126  
**Cure #4**  
Dusseldorf  
Jensen, Nat Med 2023;29:583-587  
**Cure #5**  
City of Hope  
Dickter, NEJM 2024;390:669-671  
**Cure #6** \*wild-type donor  
Geneva  
Saez-Cirion, Nat Med 2024;30:3544-3554  
**Cure #7** \*first Δ32 hetero donor  
Berlin  
Gaebler, et al IAS 2024  
**Cure #8** \*HIV rebound  
Chicago  
Rubinstein CROI 2025 #531  
**Cure #9**  
Oslo  
Troiseid CROI 2025 #532

Hutter NEJM 2009;360:692

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Conclusions

- HIV/AIDS is a worldwide pandemic
- Routine HIV testing should be offered to ALL patients
- Antiretroviral therapy (ART) ↓ HIV RNA, ↑ CD4 cell counts, prevents disease progression, and prolongs healthy survival
- Current ART consists of 2- or 3-drug therapy and is increasingly available worldwide
- Current life expectancy for people with HIV on therapy approaches that of the general population
- Prevention continues to be key
- Cure research is in progress

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Acknowledgments

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- AIDS Clinical Trials Group (ACTG)
- Division of AIDS, NIAID, NIH
- The patient volunteers!



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