HIV/AIDS 2026

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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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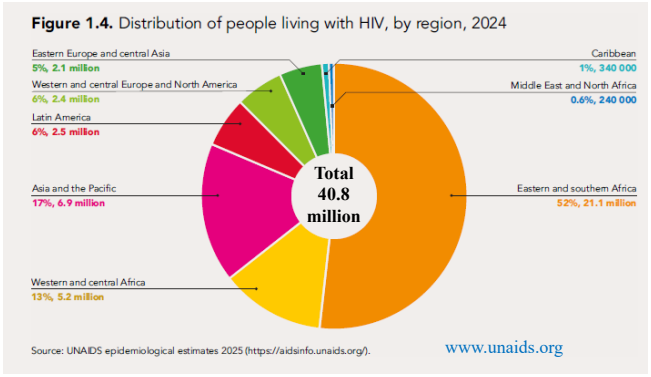
People with HIV (PWH): Global



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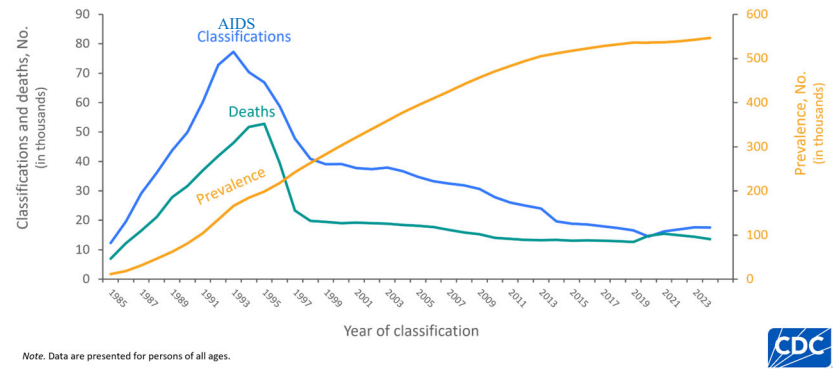
AIDS, Deaths, and Prevalence 1985–2024 — US and 6 Dependent Areas



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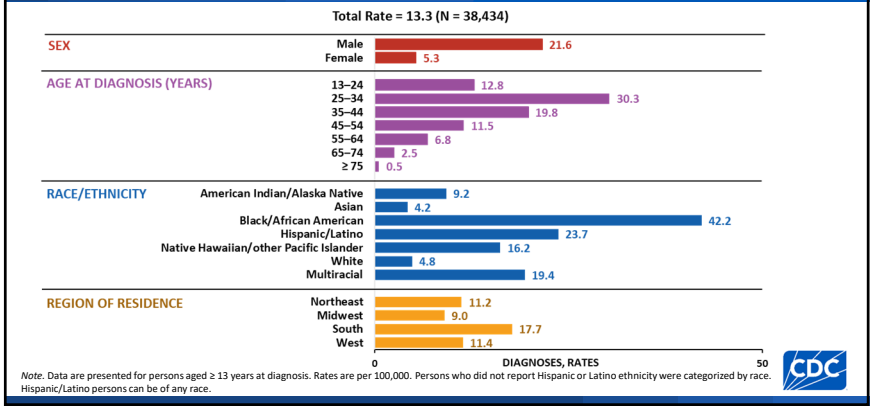
HIV diagnoses rates, by selected characteristics, 2024—United States



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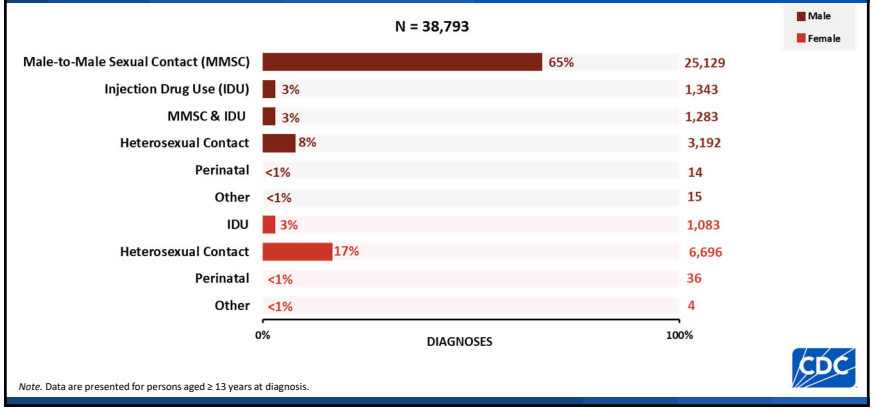
HIV diagnoses, by transmission category and sex, 2024—United States and 7 territories and freely associated states



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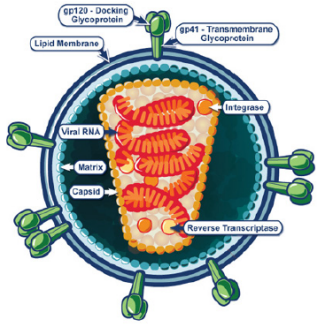
Human Immunodeficiency Virus (HIV)



- 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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HIV Testing

- HIV antibody testing (indirect)
  - Screening test: HIV-1, HIV-2 antibodies by ELISA
  - If repeatedly positive, proceed to confirmatory test
    - Immunoblot (or 2nd HIV rapid test)
  - 20-minute oral test and 1-minute blood test available
- 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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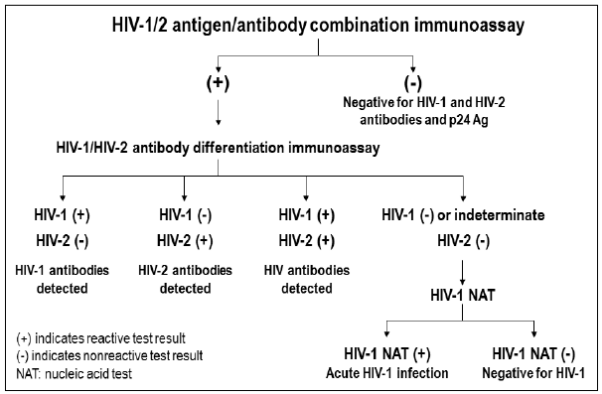
Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens



CDC 2014

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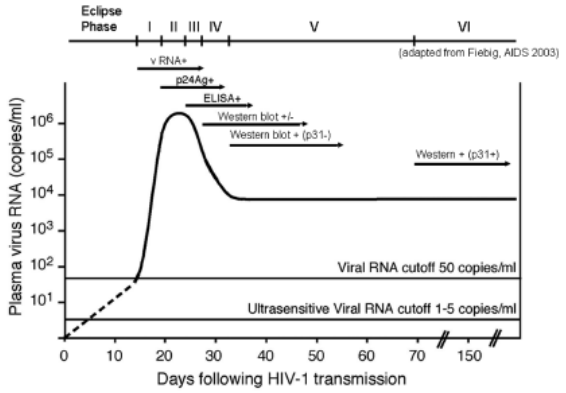
Natural History and Laboratory Staging of HIV Infection



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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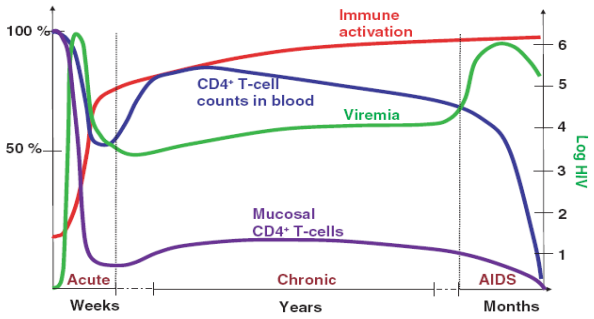
Time Course of HIV Infection



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: Pneumocystis, Cryptococcus, Histoplasma
  - Viral: CMV
  - Parasitic: Toxoplasma
  - Malignancies: Kaposi's sarcoma, Non-Hodgkin's-lymphoma

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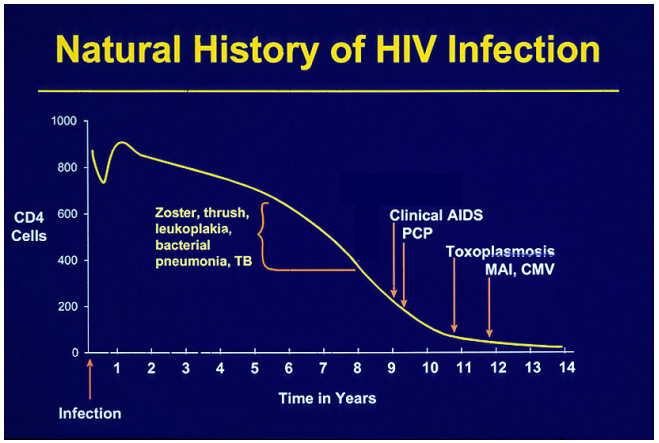
Natural History of HIV Infection



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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/ symp-toms	CD4 <200	CD4 200-350	CD4 350-500	CD4 >500
		←asymptomatic→			
US DHHS '25 www.clinicalinfo.hiv.gov	treat	treat	treat	treat	treat
IAS-USA '24 JAMA 2025;333:609-628	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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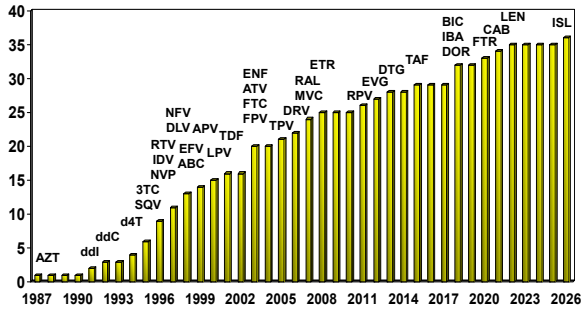
Antiretroviral Drug Approval: 1987 - 2026



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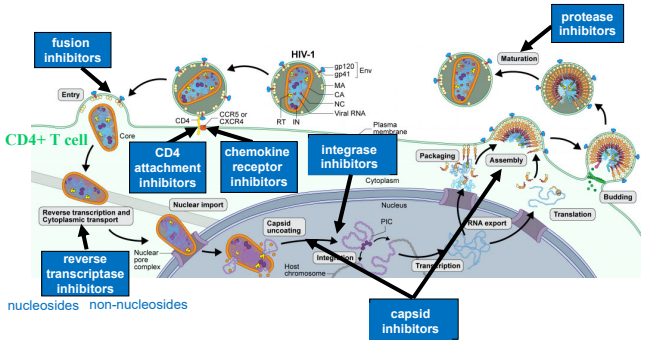
Life Cycle of HIV



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

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Approved ART: 2026*

nucleoside/tide RTIs (NRTIs)
- zidovudine (ZDV, AZT)
- lamivudine (3TC)
- abacavir (ABC)
- emtricitabine (FTC)
- islatravir (ISL)
- tenofovir (TAF, TDF)

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

protease inhibitors (PIs)
- ritonavir (RTV)
- 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)
- maraviroc (MVC, CCR5 antagonist)
- ibalizumab (IBA, CD4 post-attachment inhibitor)
- fostemsavir (FTR, CD4 attachment inhibitor)

capsid inhibitors (CIs)
- lenacapavir (LEN)

*ddI, ddC, d4T, DLV, SQV, IDV, APV, FPV, + ENF (T-20) discontinued

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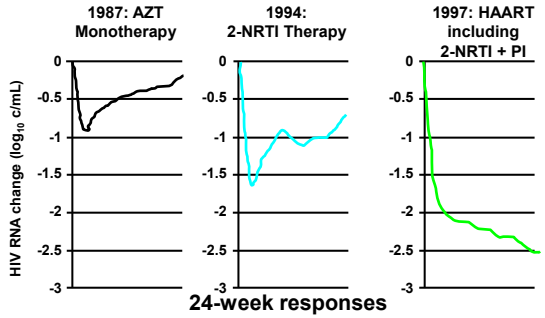
Antiretroviral Activity: 1987-1997



Fischl, *NEJM* 1987
Eron, *NEJM* 1995
Hammer, *NEJM* 1996
Gulick, *NEJM* 1997
Cameron, *Lancet* 1998

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Question 3

Which class of ART is recommended as the basis 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
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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 9/25

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Approved Single-Tablet ART Regimens

TDF/FTC/EFV (2006)
TDF/FTC/RPV (2011)
TDF/FTC/EVG/c (2012)
ABC/3TC/DTG (2014)
TAF/FTC/EVG/c (2015)
TAF/FTC/RPV (2016)
DTG/RPV (2017)*
TAF/FTC/BIC (2018)
TAF/FTC/DRV/c (2018)
TDF/3TC/DOR (2018)
DTG/3TC (2019)
ISL/DOR (2026)*

*FDA approved only for maintenance therapy

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Cabotegravir (CAB)

- Integrase inhibitor similar to dolutegravir
- Nanotechnology formulation; injectable
- Phase 3 studies of IM CAB/IM 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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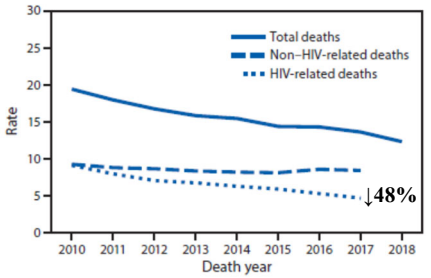
U.S. HIV Deaths: 2010-2018

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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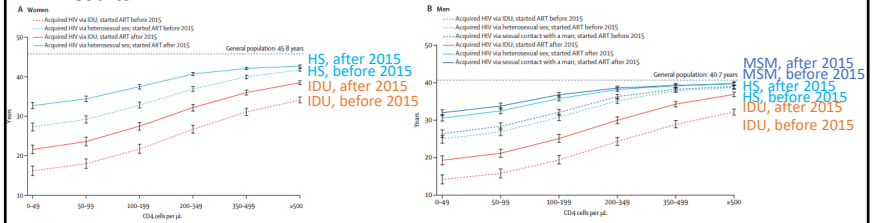
Life Expectancy of HIV on ART

- 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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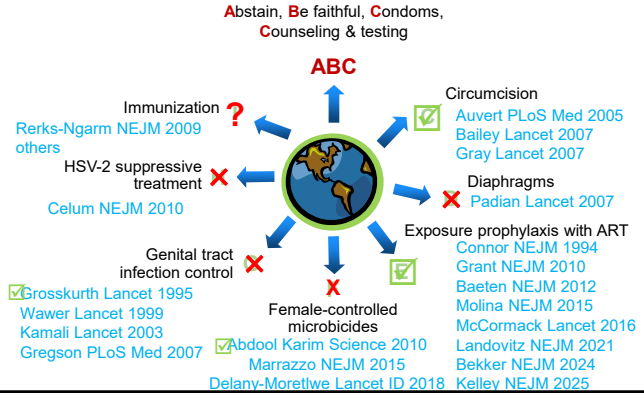
HIV Prevention Strategies



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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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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
  -  = IM CAB or SQ LEN

FDA PrEP approvals:

- 2012: TDF/FTC
- 2019: TAF/FTC (men only)
- 2021: injectable cabotegravir (CAB)
- 2025: subcutaneous lenacapavir (LEN)

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Recent PrEP Studies

Study (reference)	Study population (without HIV)	Design	Results: Reduction in HIV Infection with PrEP
PROUD McCormack Lancet 2015;387:54-60	544 MSM in UK	TDF/FTC (daily) immediate vs. delayed	↓86% 
HPTN 083 Landovitz NEJM 2021;385:595	4566 MSM and TGW globally	TDF/FTC (daily) vs. IM CAB every 2 months	IM CAB: ↓66% vs. TDF/FTC 
PURPOSE 1 Bekker NEJM 2024;391:1179	5338 young women in South Africa and Uganda	TDF/FTC or TAF/FTC (daily oral) vs. SQ LEN every 6 months	SQ LEN: 0 infections! 

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HIV Vaccine Studies

HIV Vaccine	N	Approach	Response	Result
AIDSVAX Pitisuttithum JID 2006	2546	gp120 subunit	antibody	no effect
STEP Buchbinder Lancet 2008	3000	Adenovirus vector + HIV genes	CTL	no effect
RV144 Rerks-Ngarm NEJM 2009	16,402	Canarypox vector + HIV genes + boost with gp120	both	31% ↓ in HIV
HVTN 505 Hammer NEJM 2013	2504	DNA prime + adenovirus boost	CTL	futility
HVTN 702 Gray NEJM 2021	5404	ALVAC-HIV + bivalent sub C gp120	both	no effect
HVTN 705 Gray Lancet ID 2024	2637	Ad26.Mos4.HIV + mosaic GAG/POL /ENV Ag+ C gp140	both	no effect
HVTN 706 Mosaico Buchbinder Lancet HIV 2025	3900	Mosaic adenovirus vector+ mix of soluble proteins	both	no effect

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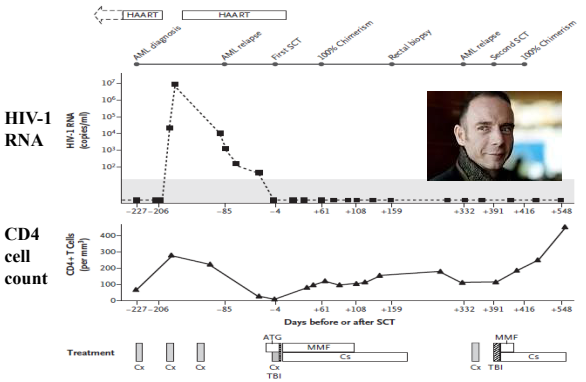
HIV Cure (N=4) 10+!



Hutter NEJM 2009;360:692

Cure #2 *first Latino
London
Gupta, Nature 2019;568:244
Cure #3 *first woman
NYC
Hsu, Cell 2023;186:1115
Cure #4
Dusseldorf
Jensen, Nat Med 2023;29:583
Cure #5
City of Hope
Dickter, NEJM 2024;390:669
Cure #6 *wild-type donor
Geneva
Saez-Cirion, Nat Med 2024;30:3544
Cure #7 *first Δ32 hetero donor
Berlin
Gaebler, Nature 2026;650:701
Cure #8 *HIV rebound
Chicago
Rubinstein CROI 2025 #531
Cure #9
Oslo
Myhre Nat Micro 2026;11:1374
+ more!

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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

- Cornell HIV Clinical Trials Unit (CCTU)
- Division of Infectious Diseases
- Weill Cornell Medicine
- NY Presbyterian
- AIDS Clinical Trials Group (ACTG)
- Division of AIDS, NIAID, NIH
- The patient volunteers!

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