


HIV Update

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MedNet21
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 THE OHIO STATE UNIVERSITY
 WEXNER MEDICAL CENTER

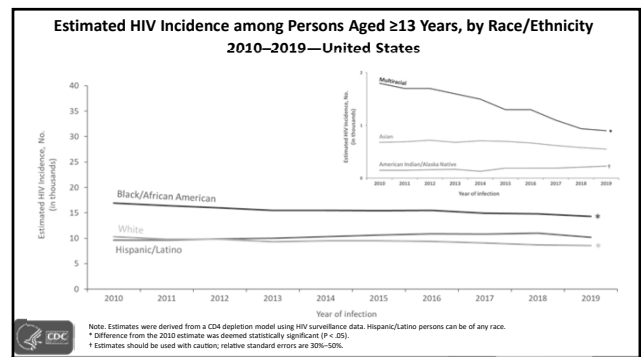
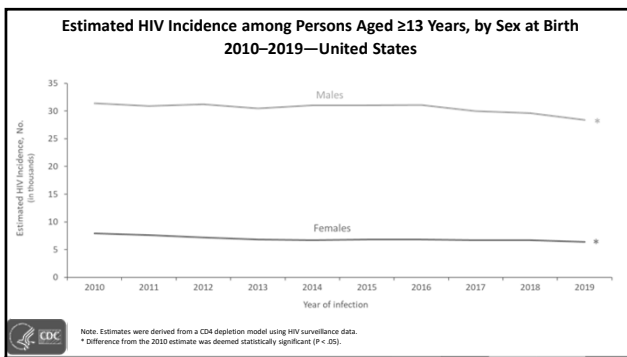
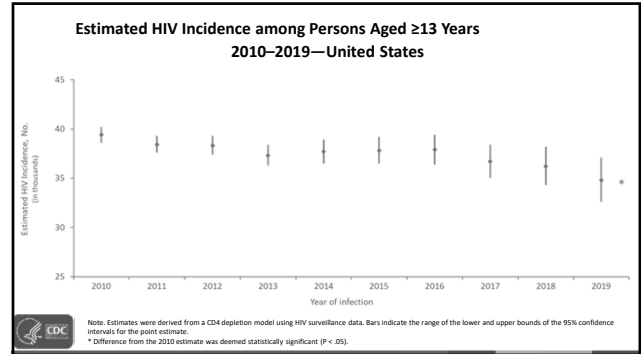
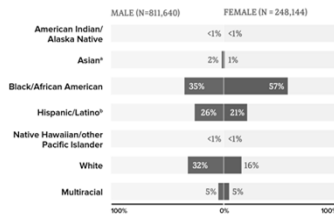


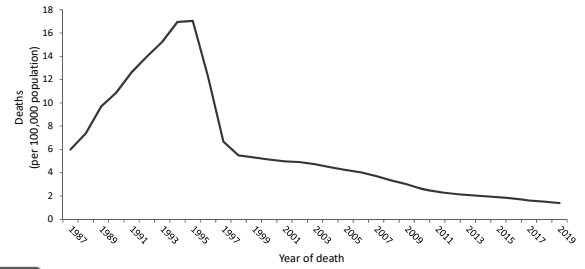
Figure 10. Percentages of Adults and Adolescents Living with Diagnosed HIV Infection, by Sex at Birth and Race/Ethnicity, Year-end 2019—United States and 6 Dependent Areas



Note: Data have been statistically adjusted to account for missing transmission category. See section D4 in the Technical Notes for more information on transmission categories.
 *Includes Asian/Pacific Islander legacy cases.
 **Hispanic/Latino persons can be of any race.

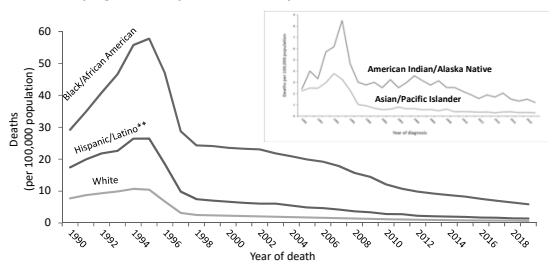
HIV Surveillance Report: CDC

Trends in Annual Age-Adjusted* Rates of Death with HIV Disease as the Underlying Cause, 1987–2019—United States



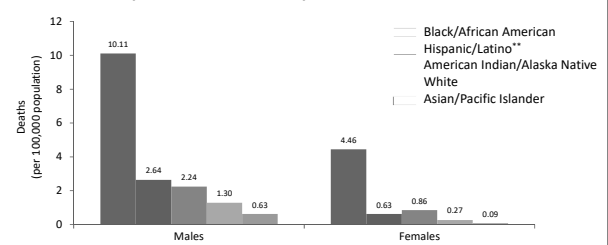
Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for ICD-10 rules instead of ICD-9 rules.
 *Standard: age distribution of 2000 US population.

Trends in Age-Adjusted* Annual Rates of Death with HIV Disease as the Underlying Cause, by Race/Ethnicity, 1990–2019—United States

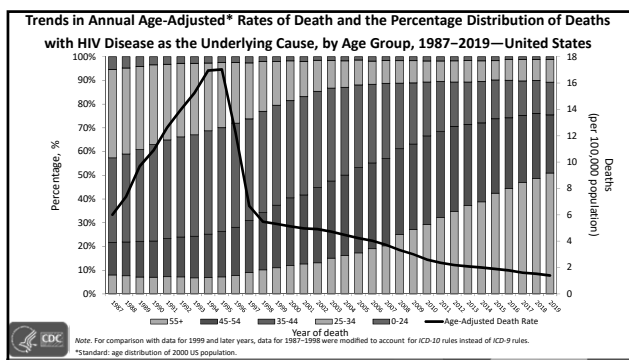


Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for ICD-10 rules instead of ICD-9 rules.
 *Standard age distribution of 2000 US population.
 **Hispanic/Latino persons can be of any race.

Age-Adjusted* Average Annual Rate of Death with HIV Disease as the Underlying Cause by Sex and Race/Ethnicity, 2015–2019 — United States



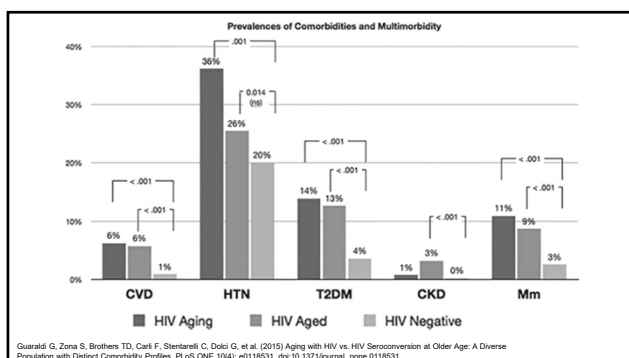
*Standard age distribution of 2000 US population.
 **Hispanic/Latino persons can be of any race.



Reported Persons Living with HIV in Ohio, 2020 (n=25,096)

Characteristic	Living With Diagnosed HIV Infection in 2020	
	Rate ^a	No. %
Sex at birth		
Males	346.4	19,856 79%
Females	87.9	5,240 21%
Age at end of year		
<13	2.7	49 <1%
13-14	7.1	21 <1%
15-19	15.3	114 <1%
20-24	97.1	726 3%
25-29	243.0	1,927 8%
30-34	350.2	2,693 11%
35-39	322.4	2,339 9%
40-44	346.9	2,377 9%
45-49	390.4	2,834 10%
50-54	474.5	3,452 14%
55-64	400.9	6,362 25%
65+	114.5	2,402 10%
Race/Ethnicity^b		
American Indian/Alaska Native	66.3	15 <1%
Asian/Pacific Islander	56.7	173 1%
Black/African American	745.4	11,095 44%
Hispanic/Latino	373.7	1,824 7%
White	118.7	10,826 43%

Ohio Department of Health



Trends in MI Risk in 2 United States Healthcare Systems

Cohort study (2005-2010)

- Kaiser Permanente Northern California (n=4.5 million)
- Partners cohort (Massachusetts General Brigham) (n=1.5 million)

Similar CVD risk profiles at baseline

- Outcomes during calendar era 2005-2009 and 2010-2017

- New MI diagnosis by HIV status

MI risk (HIV versus no HIV)

- 2005-2009: no difference (aHR 1.1 95% CI 0.8, 1.5)
- 2010-2017: higher in HIV (aHR 1.6 95% CI 1.1, 2.4; P=0.007)
- HIV-specific factors, such as longer HIV duration and newer ART, may have prevented PWH from realizing the same improvements in MI risk as person without HIV

Cumulative Incidence of MI

	With HIV	No HIV
2005-2009 (%)	1.1	1.1
2010-2017 (%)	1.2	0.9

*P=0.03 versus no HIV.

Silverberg MJ, et al. CROI 2022. Abstract 53.

2014 CDC Revised Classification System: Stage 3-Defining Opportunistic Illnesses in HIV Infection

- Bacterial infections, multiple or recurrent*
- Candidiasis of bronchia, trachea, or lungs
- Candidiasis of esophagus
- Cervical cancer, invasive*
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month)
- Cytomegalovirus disease (other than liver, spleen, or nodes), onset age > 1 month
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy attributed to HIV^A
- Herpes simplex: chronic ulcers (present for >1 month) or bronchitis, pneumonitis, or esophagitis (onset at age > 1 month)
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (> 1 month's duration)
- Kaposi's sarcoma
- Lymphoma, Burkitt's (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary of brain
- *Mycobacterium avium* complex or *Mycobacterium kansasii*, disseminated or extrapulmonary
- *Mycobacterium tuberculosis* of any site, pulmonary*, disseminated, or extrapulmonary
- *Mycobacterium*, other species or unidentified species, disseminated or extrapulmonary
- *Pneumocystis jirovecii* (previously known as "*Pneumocystis carinii*") pneumonia
- Pneumonia, recurrent*
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain, onset at age > 1 month
- Wasting syndrome attributed to HIV

*Only among children aged < 6 years

^AOnly among adults, adolescents, and children aged ≥ 6 years

^BSuggested diagnostic criteria for these illnesses are defined in prior surveillance case definitions

CDC.gov. Revised surveillance case definition for HIV Infection – United States, 2015. MMWR Recomm Rep. 2014;63(RR-03):1-10.

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV


Recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America

<https://aidsinfo.nih.gov/guidelines>

Last update: February 17, 2022

Primary Prophylaxis

OI	Indication	Preferred
Pneumocystis Pneumonia (PCP)	CD4 < 200 CD4 < 14% If ART initiation has to be delayed, CD4 ≥ 200, but < 250 and can't monitor every 3 mos	1. TMP-SMX 1 DS tab PO daily 2. TMP-SMX 1 SS tablet daily
<i>Toxoplasma gondii</i> Encephalitis	Toxoplasma IgG positive with CD4 < 100	TMP-SMX 1 DS PO daily
<i>Mycobacterium avium</i> Complex (MAC)	CD4 < 50 • Not recommended for those who immediately start ART • Rule out active disease before starting	1. Azithromycin 1200 mg PO once weekly 2. Clarithromycin 500 mg PO BID 3. Azithromycin 600 mg PO twice weekly

Excerpted from Table 1

Why do we still see OIs?

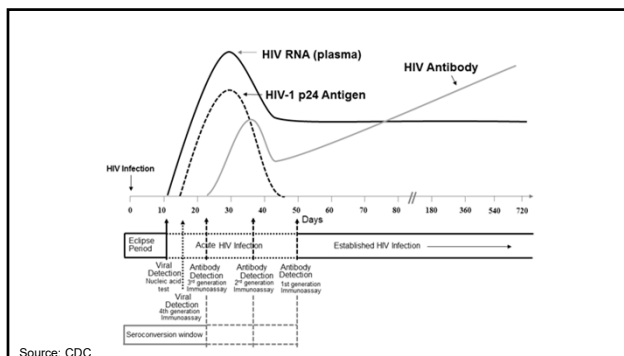
- Undiagnosed or late diagnosis of HIV
- Known HIV infection with poor retention in care
- Not on stable antiretroviral therapy (ART)

HIV testing in the US

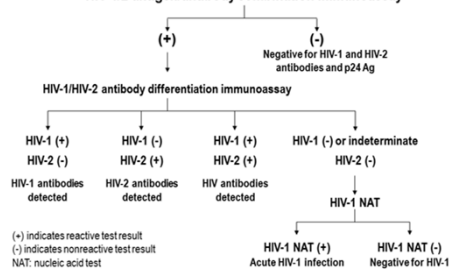
4 generations of assays to test for HIV:

- 1st: detects IgG (examples: Western Blot, IFA)
- 2nd: detects IgG (examples: HIV-1 EIA, rapid HIV Ab tests)
- 3rd: detects IgM & IgG (examples: HIV-1/2 immunoassay and HIV1/2 chemiluminescent immunoassays)
- 4th: detects IgM & IgG and p24 Antigen (example: combination test - 3rd gen plus one rapid test that uses separate indicators for HIV-1/2 antigen and antibodies)

CDC: Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations June 27, 2014



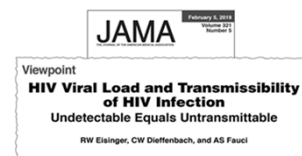
HIV-1/2 antigen/antibody combination immunoassay

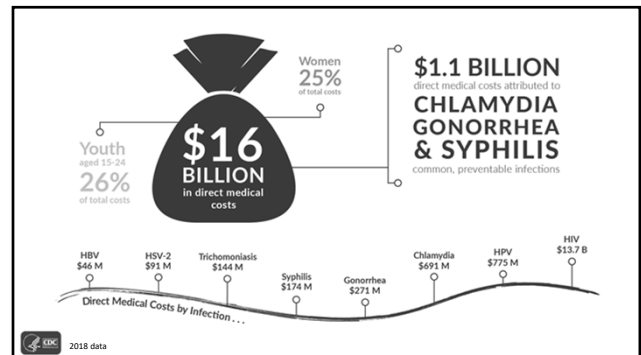
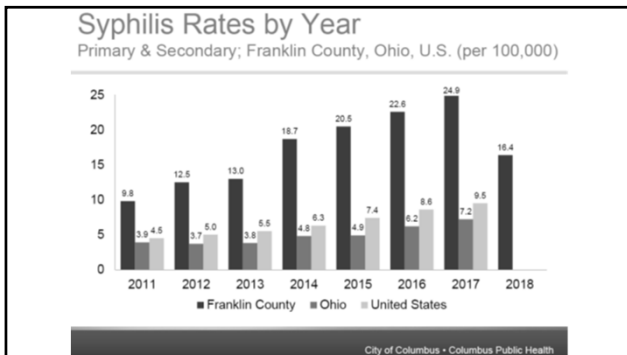
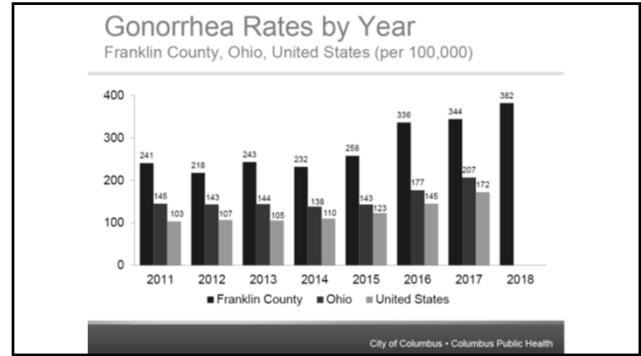
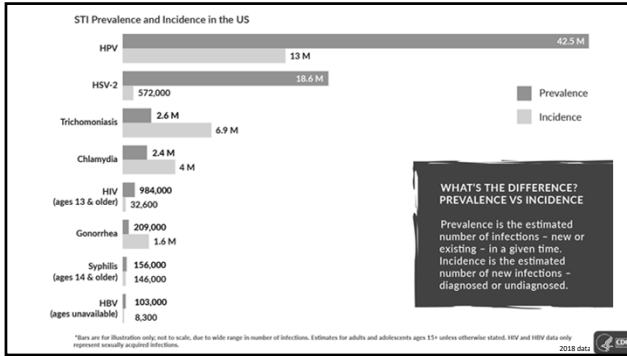


Source: CDC

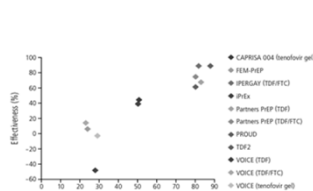
Benefits of Testing/Knowing HIV Status

- Individual health
- Public Health

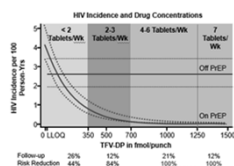




Adherence is Important for Oral PrEP



Buchbinder. *Top Antivir Med.* 2018;25(4):138-142



- In Men Who have Sex With Men 100% adherence was not required to attain full benefit from PrEP

- Benefit of 4-6 tablets/wk similar to 7 tablets/wk

1. Grant R, et al. *IAC* 2014. Abstract TUAC0105LB.

Oral PrEP Safety

TDF/FTC is well tolerated

Start-up syndrome

- 1-18.5% with nausea, vomiting \pm dizziness

Renal safety

- 0.2% Grade 2-4 elevations in creatinine among 5469 participants randomized to TDF/FTC

Bone safety

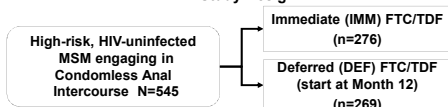
- 0.4 to 1.5% loss of BMD across total hip, spine
- Return to baseline after discontinuation
- Not associated with increased fracture risk

- Grant RM, et al. *N Engl J Med.* 2010;363:2587-2599.
- Van Damme. *N Engl J Med* 2012; 367:411-422
- Thigpen MC, et al. *N Engl J Med* 2012; 367:423-434
- Grant, et al. Abstract 48 LB. *CROI* 2016. Boston, MA
- Beeten JM, et al. *N Engl J Med.* 2012;367:399-410.

PrEP Highly Effective in “Real World” Evaluation

PROUD Trial: Randomized, multi-center, open-label pilot study in London

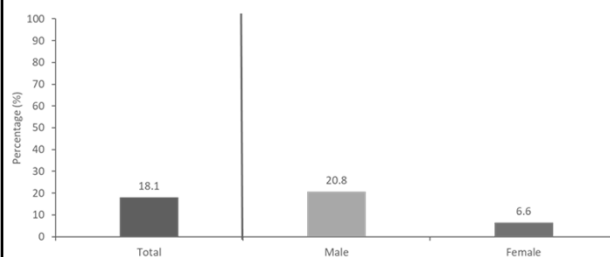
Study Design



- DSMB stopped study early due and recommended that all participants be offered PrEP
- 86% reduction in risk seen over 60 wks with immediate PrEP (90% CI: 58% to 96%, $P = .0002$)
 - Rate difference: 7.6 (90% CI: 4.1-11.2)
 - Number needed to treat to prevent 1 infection: 13 (90% CI: 9-25)

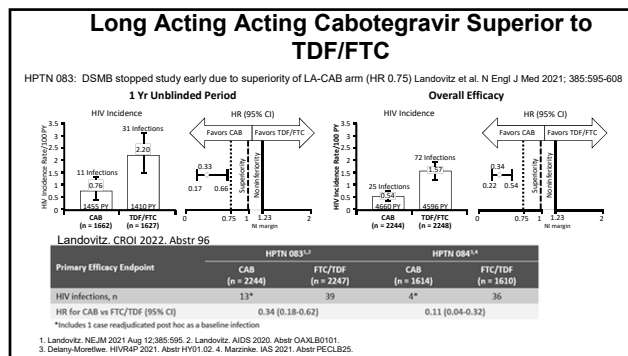
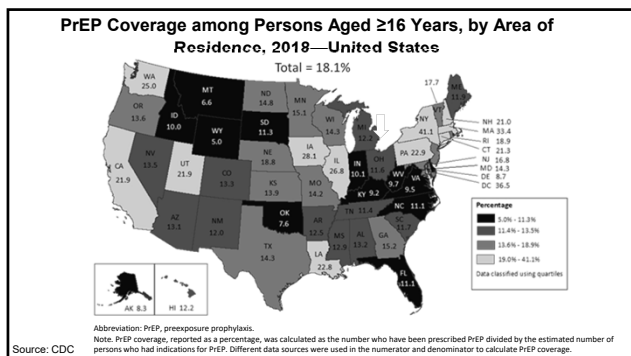
McCombs S, et al. *CROI* 2015. Seattle, WA #523B

PrEP Coverage among Persons at Risk Remains Very Low



Abbreviation: PrEP, preexposure prophylaxis.

Note: PrEP coverage, reported as a percentage, was calculated as the number who have been prescribed PrEP divided by the estimated number of persons who had indications for PrEP. Different data sources were used in the numerator and denominator to calculate PrEP coverage.



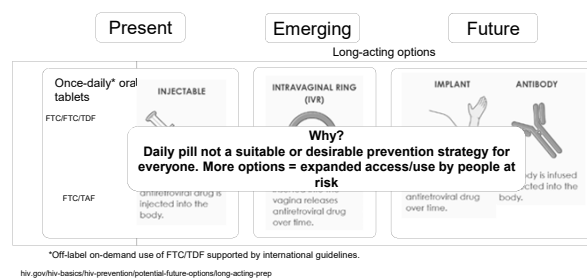
New Long-Acting Option for PrEP

Long-acting cabotegravir (IM injection every 2 months)

- For use as PrEP in at-risk adults and adolescents weighing ≥35 kg to reduce the risk of sexually acquired HIV
- Initiated as 2 injections administered 1 mo apart, and then every 2 mo thereafter
- Patients can either start with cabotegravir injections or take oral cabotegravir for 4 wk to assess how well they tolerate the drug

Cabotegravir extended-release injectable suspension PI.

HIV PrEP: Present, Emerging, and Future



Resources

Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents

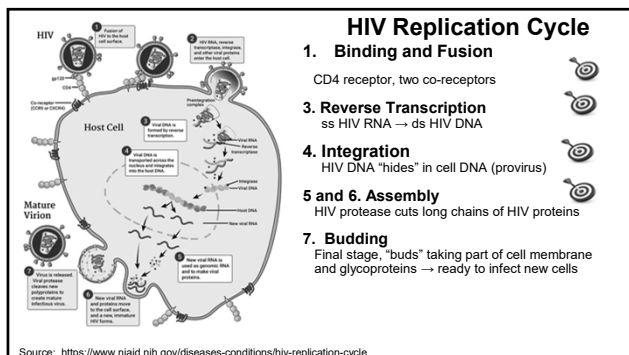
<http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf>

PrEP Guideline 2021 Update-CDC

<https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf>

Primary Care Guidelines for the Management of Persons Infected With HIV: 2020 Update by the HIV Medicine Association of the Infectious Diseases Society of America
<https://academic.oup.com/cid/article-lookup/doi/10.1093/cid/ciaa1391>

Antiretroviral Treatment (ART)



Current ARV Medications 2022

NRTIs (Nucleoside RTIs)

- abacavir (ABC)
- didanosine (ddI)
- emtricitabine (FTC)
- lamivudine (3TC)
- stavudine (d4T)
- tenofovir (TDF/TAF)
- zidovudine (AZT, ZDV)

Integrase Inhibitor

- raltegravir (RAL)
- elvitegravir (ELV)
- dolutegravir (DTG)
- Cabotegravir (CAB)*

Non-NRTIs

- delavirdine (DLV)
- efavirenz (EFV)
- etravirine (ETR)
- nevirapine (NVP)
- rilpivirine (RPV)
- Doravirine (DOR)

Entry Inhibitors

- enfuvirtide (T-20)

CCR5 Antagonist

- maraviroc (MVC)

CD4 Blocker

- Ibalizumab

Protease Inhibitors

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

Current Combination ARV Medications

NRTIs (Nucleoside RTIs)

- abacavir (ABC)/lamivudine (3TC) = **Epzicom**
- zidovudine (ABC)/lamivudine (3TC) = **Combivir**
- abacavir (ABC)/lamivudine (3TC)/zidovudine (AZT) = **Trizivir**
- emtricitabine (FTC)/tenofovir (TDF) = **Truvada** TAF Version: **Descovy**

Protease Inhibitors

- lopinavir (LPV) + ritonavir (r) = **Kaletra**
- atazanavir (ATV) + cobicistat* = **Evotaz**
- darunavir (DRV) + cobicistat = **Prezcobix**

Current Combination ARV Medications

"Complete" Single Tablet Regimens

- Descovy+BIC=**Biktarvy**
- Truvada + EFV (Sustiva) = **Atripla**
- Truvada + RPV (Edurant) = **Complera** TAF Version: **Odefsey**
- Truvada + EGV/cobi = **Stribild** TAF Version: **Genvoya**
- Epzicom + DTG (Tivicay) = **Triumeq**
- Rilpivirine+DTG (Tivicay)=**Juluca**
- Lamivudine+DTG (Tivicay)=**Dovato**

Principles of HIV Treatment

- 2-3 fully active drugs given together to maintain viral suppression
- Current ART regimens are potent and safe with minimal adverse effects
- ART should be fully suppressive
 - Target HIV RNA<limit of quantification
 - "Detectable HIV RNA on Rx=**Failure**"
- All or none principle (decreases risk of viral resistance)
- Compliance ≥95% with daily oral regimen to achieve goal HIV RNA
- CD4 T cell reconstitution occurs after HIV RNA=undetectable
- We can maintain viral suppression indefinitely but we are not yet able to eradicate long-lived latently infected cells ("HIV reservoir")

Undetectable HIV Viral Load Equals Untransmittable HIV Infection (U=U)

- In 2017, HIV Medical Association officially endorsed the U=U Consensus Statement

– "When a person living with HIV has an undetectable viral load, they will

UNDETECTABLE = UNTRANSMITTABLE



<https://www.hivma.org>

- Supported by data from several studies from 2008-2016 showing zero linked HIV transmissions after > 100,000 condomless sex acts within both female-male and male-male serodiscordant couples in which the partner living with HIV had a **durably undetectable viral load**

HPTN 052

PARTNER

Opposites Attract

PARTNER 2

HIV START Trial

Early vs Delayed ART

CD4>500/mm³ and No Symptoms

Early therapy vs delay until CD4<350/mm³ or AIDS defining illness

Early therapy permits rapid achievement of viral suppression

Early ART prevents

AIDS events

AIDS related cancers

Major cardiovascular, renal and liver disease

Non-AIDS cancer

Death not attributable to AIDS

Serious AIDS events, serious non-AIDS events and death[†]: 57%

START Study Group, Lundgren JD, et al. NEJM. 2015 Aug 27;373(9):795-807

Future of HIV Treatment

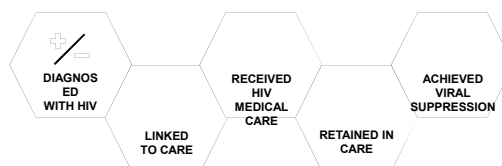
- Recent ART options are potent, well tolerated and safe and permit simplification to single tablet regimens with minimal DDIs
- New drug classes soon to become available (capsid inhibitors, broadly neutralizing antibodies, etc)
- More long-acting options (oral, injectable, implants) dosed every 2-4 months and possibly every 6 months!
- Lots of research ongoing to achieve functional cure

Putting It All Together

PrEP+Treatment as Prevention

HIV Care Continuum

- "The HIV care continuum is a public health model that outlines the steps or stages that people with HIV go through from diagnosis to achieving and maintaining viral suppression"

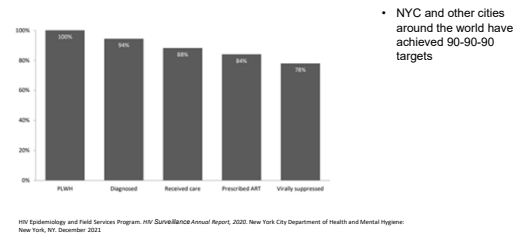


<https://www.hiv.gov/federal-response/policies-issues/hiv-aids-care-continuum>

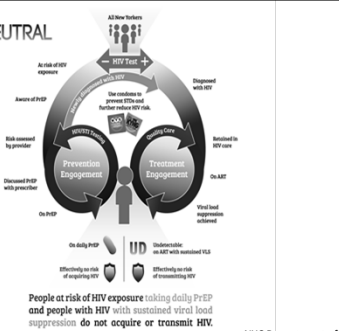
90-90-90 UNAIDS Targets

- By 2020
 - 90% of PLWH will know their HIV status
 - 90% of people with diagnosed HIV will receive ART
 - 90% of people receiving ART will be virally suppressed
- If 90-90-90 targets are achieved, 73% of PLWH would be virally suppressed and the HIV epidemic would end by 2030

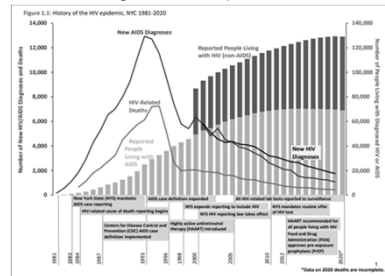
HIV Care Continuum (New York City 2020)



NEW YORK CITY'S HIV STATUS NEUTRAL PREVENTION & TREATMENT CYCLE

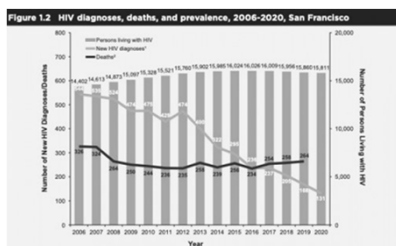


Ending the HIV Epidemic in New York City



HIV Epidemiology and Field Services Program, HIV Surveillance Annual Report, 2020, New York City Department of Health and Mental Hygiene, New York, NY, December 2021

Declining HIV Incidence in San Francisco



San Francisco HIV Epidemiology Report 2020

Ending the HIV Epidemic: We have the tools to do it

Ending the HIV Epidemic: A Plan for America

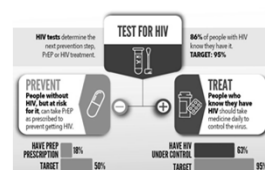
The U.S. Department of Health and Human Services (HHS) has launched Ending the HIV Epidemic: A Plan for America. The cross-agency initiative leverages critical scientific advances in HIV prevention, diagnosis, treatment, and outbreak response by coordinating the highly successful programs, resources, and infrastructure of many HHS agencies and offices.

GOAL:

HHS will work with each community to establish local teams on the ground to tailor and implement strategies for:

- **Prevent** new HIV infections by using proven interventions, including pre-exposure prophylaxis (PrEP) and condom use programs (COPs).
- **Diagnose** all people with HIV as early as possible after infection.
- **Treat** the infection rapidly and effectively to achieve sustained viral suppression.
- **Engage** quickly to potential HIV outcomes to get needed prevention and treatment services to people who need them.

<https://www.hhs.gov/endinghiv/about.html>

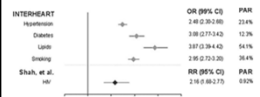


Comorbidities in HIV: Cardiovascular Disease

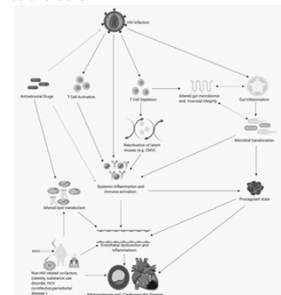
Cardiovascular Disease in HIV

CVD is a leading cause of death for PWH. Associated in part to increased prevalence of traditional risk factors (smoking, HTN, diabetes).

But HIV itself is an independent risk factor for CVD (related to chronic inflammation and immune activation despite viral suppression).



Hsue PY, Waters DD. Time to Recognize HIV Infection as a Major Cardiovascular Risk Factor. Circulation. 2018 Sep 11;138(11):1113-1115.

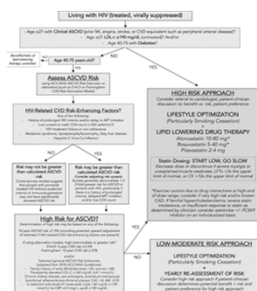


Titani B, et al. J Am Heart Assoc. 2020 Feb 4;9(3):e014873.

Management of CVD Risk in PWH

ACC/AHA and Framingham risk ASCVD risk calculators may underestimate risk in PWH

AHA Guidelines recommend taking into account HIV-related CVD Risk-Enhancing Factors



Feinstein MJ et al. Characteristics, prevention, and Management of CVD in People Living with HIV: A Scientific Statement from the American Heart Association. *Circulation* 2019;140(2):e98-e124.

Statins to Reduce Cardiovascular Events in PWH

The JUPITER trial showed impact of statins on inflammation and mortality in people without HIV (Ridker et al. NEJM 2008;359:2195-2207)

REPRIEVE Trial evaluating use of statin as primary prophylaxis in PWH on ART with mild to moderate ASCVD risk

