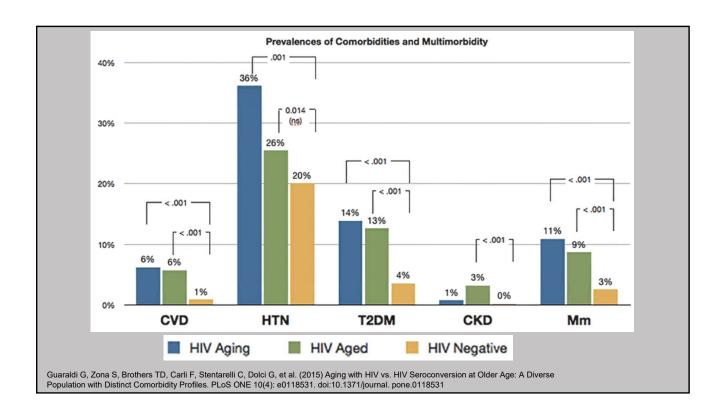


Reported Persons		Living With Diagnosed HIV Infection in 2020			
	Characteristic	Rate	No.	%	
Living with HIV in	Sex at birth				
Ohio, 2020	Males	346.4	19,856	79%	
(n=25,096)	Females	87.9	5,240	21%	
	Age at end of year				
	<13	2.7	49	<1%	
	13-14	7.1	21	<1%	
	15-19	15.3	114	<1%	
	20-24	97.1	726	3%	
	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	380.4	2,634	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%	Ohio Depart
	Black/African American	745.4	11,095	44%	Onio of Hea
	Hispanic/Latino	373.7	1,824	7%	
	White	118.7	10,828	43%	



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 calender 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^
- 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

*Only among adults, adolescents, and children aged ≥ 6 years

^Suggested 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

Ol	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	 TMP-SMX 1 DS tab PO daily TMP-SMX 1 SS tablet daily
Toxoplasma gondii Encephalitis	Toxoplasma IgG positive with CD4 < 100	TMP-SMX 1 DS PO daily
Mycobacterium avium Complex (MAC)	 CD4 < 50 Not recommended for those who immediately start ART Rule out active disease before starting 	 Azithromycin 1200 mg PO once weekly Clarithromycin 500 mg PO BID Azithromycin 600 mg PO twice weekly

Why do we still see Ols?

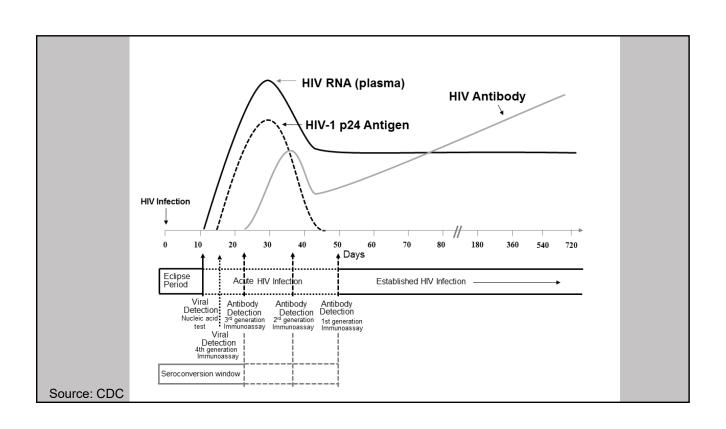
- Undiagnosed or late diagnosis of HIV
- Known HIV infection with poor retention in care
- Not on stable antiretroviral therapy (ART)

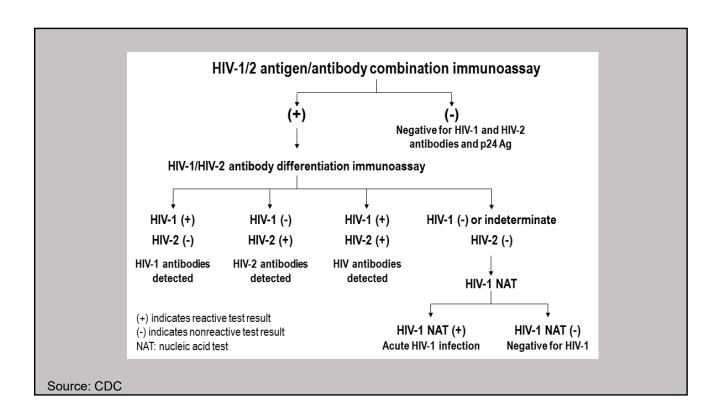
HIV testing in the US

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

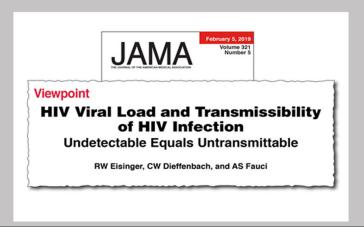
CDC: Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations June 27, 2014

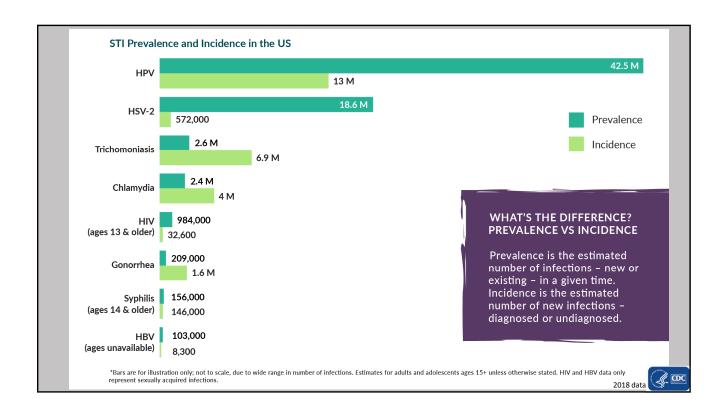


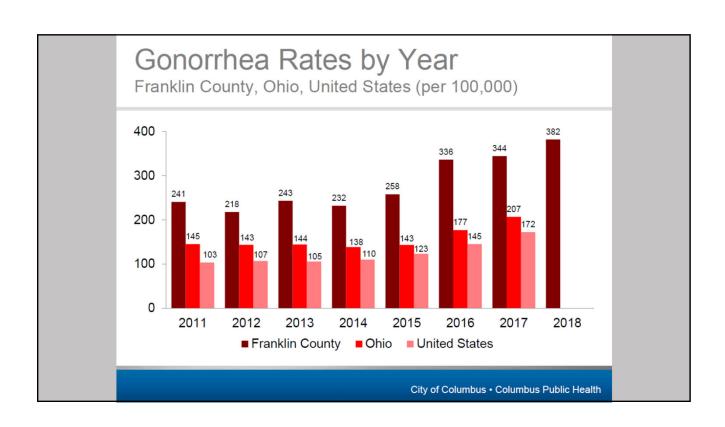


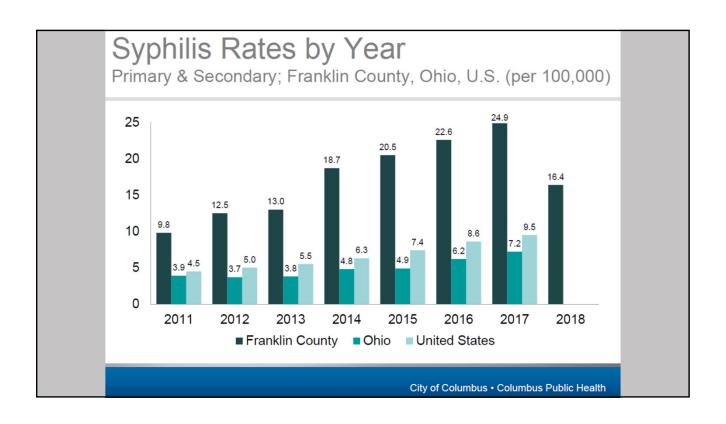
Benefits of Testing/Knowing HIV Status

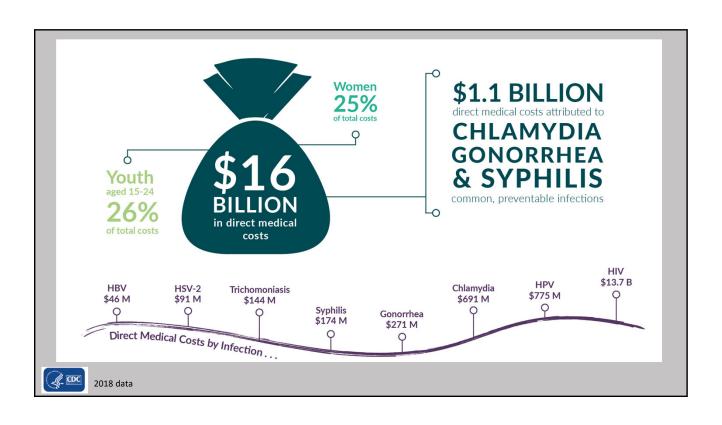
- · Individual health
- Public Health

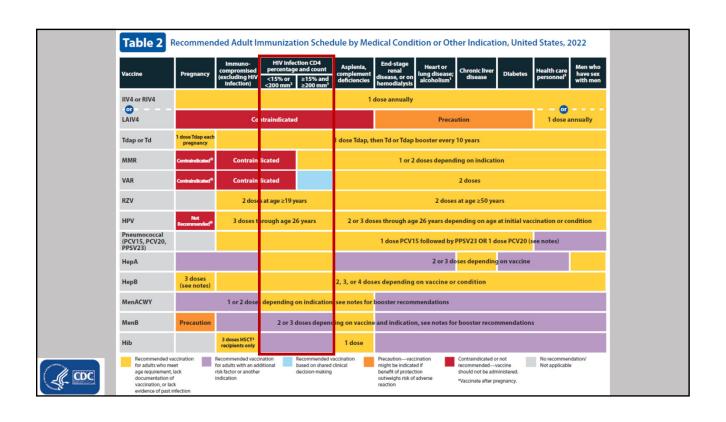


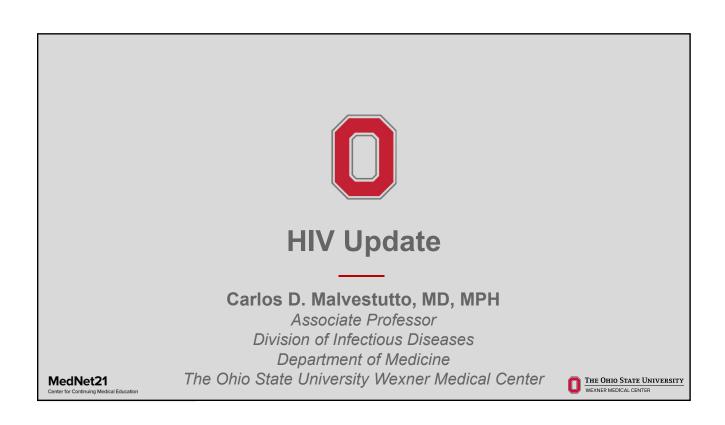












PrEP

Pre-Exposure Prophylaxis

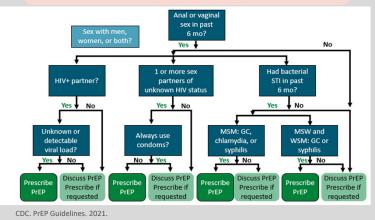
Pre-exposure Prophylaxis: A pharmacologic HIV prevention intervention for persons at high risk of acquiring HIV.

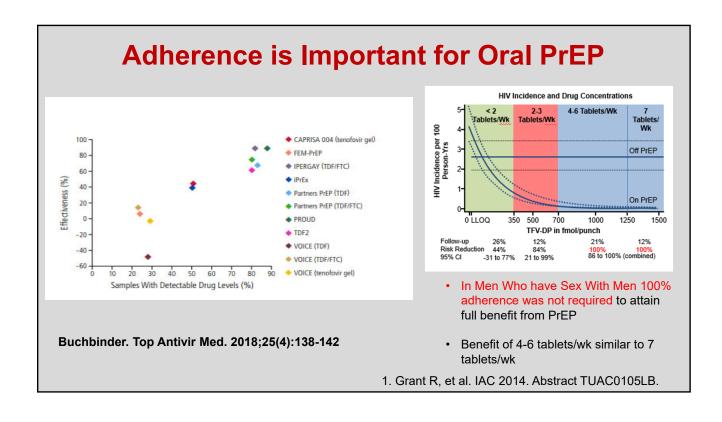
A person without HIV takes antiretroviral medication(s) **before** potential HIV exposure

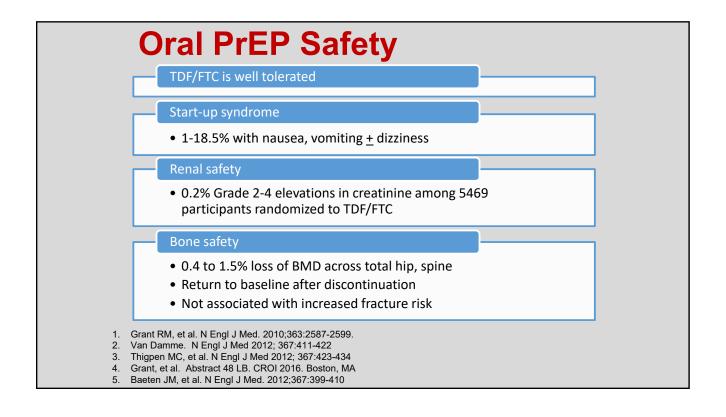
First option was daily oral TDF/FTC (FDA approved in 2012)

TAF/FTC is an alternative oral option (not evaluated in cisgender women)

"All sexually active adults and adolescents should be informed about PrEP for prevention of HIV acquisition"







Pred Highly Effective in "Real World" Evaluation PROUD Trial: Randomized, multi-center, open-label pilot study in London

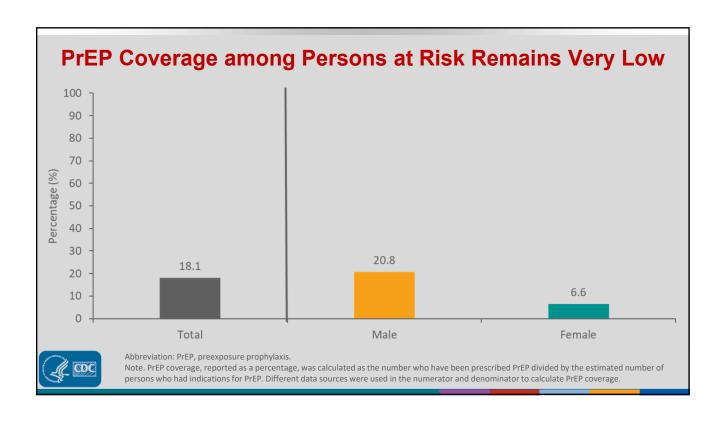
Study Design

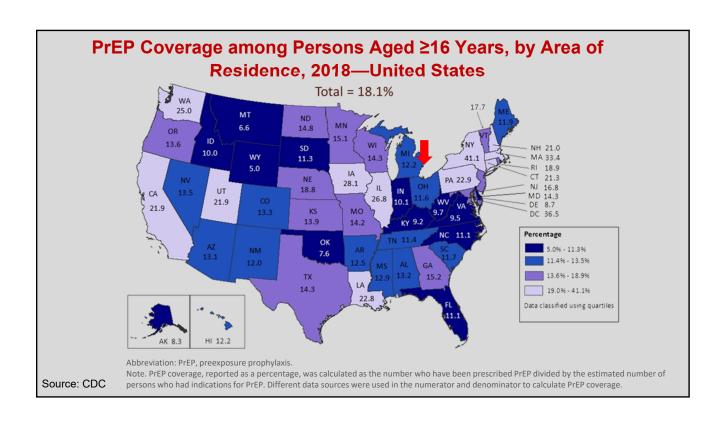
High-risk, HIV-uninfected MSM engaging in Condomless Anal Intercourse N=545 Immediate (IMM) FTC/TDF
(n=276)

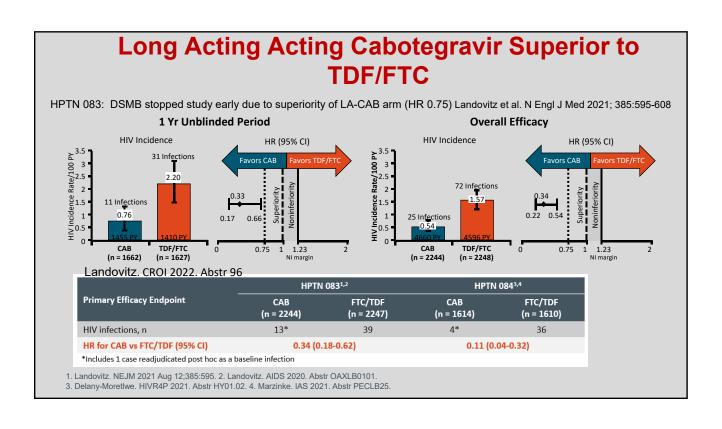
Deferred (DEF) FTC/TDF
(start at Month 12)
(n=269)

- 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)

McCormack S, et al. CROI 2015; Seattle, WA. #22LB





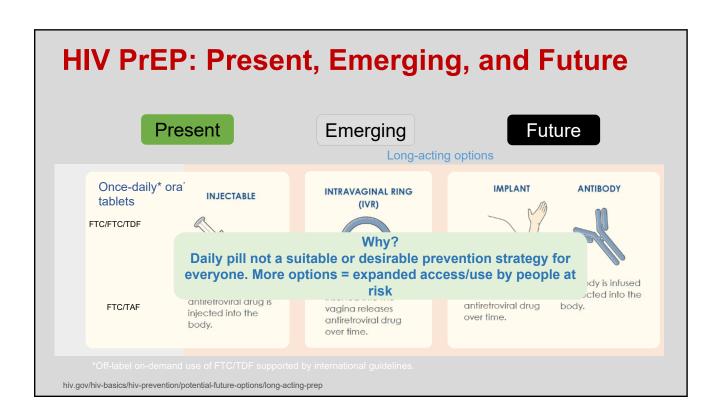


New Long-Acting Option for PrEP

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 PL



Resources

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

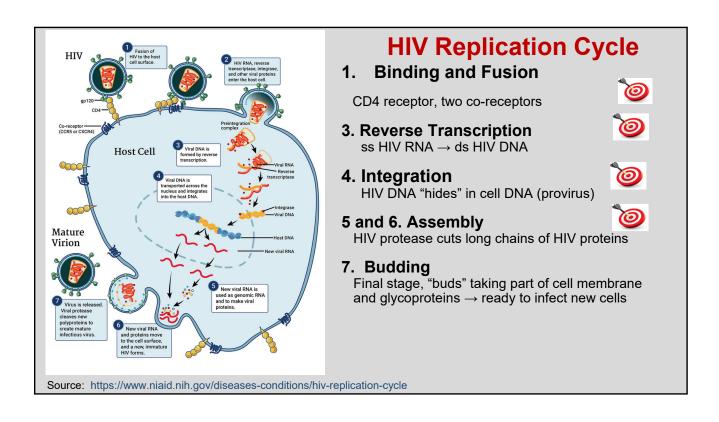
http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf

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 (ddl)
- emtricitabine (FTC)
- lamivudine (3TC)
- stavudine (d4T)
- tenofovir (TDF/TAF)
- zidovudine (AZT, ZDV)

Integrase Inhibitor

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

Non-NRTIs

- efavirenz (EFV)
- etravirine (ETR)

- rilpivirine (RPV)
- Doravirine (DOR)

Entry Inhibitors

Fusion Inhibitor

CCR5 Antagonist

maraviroc (MVC)

CD4 Blocker

Ibalizumab

Protease Inhibitors

- atazanavir (ATV)
 - · ATV/c
- darunavir (DRV)
 - DRV/c
- fosamprenavir (FPV)
- indinavir (IDV)
- lopinavir/rtv (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

TAF Version: Genvoya

"Complete" Single Tablet Regimens

- Descovy+BIC=Biktarvy
- Truvada + EFV (Sustiva) = Atripla
- Truvada + RPV (Edurant) = Complera TAF Version: Odefsey
- Truvada + EGV/cobi = Stribild
- Epzicom + DTG (Tivicay) = **Triumeg**
- Epzicom · DTG (Tivicay) = Triume
- 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 <u>></u>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")

<u>Undetectable HIV Viral Load Equals</u> <u>Untransmittable HIV Infection (U=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



 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

https://www.hivma.org

HIV START Trial

Early vs Delayed ART

CD4>500/mm3 and No Symptoms
Early therapy vs delay until CD4<350/mm3 or AIDS defining

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-

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

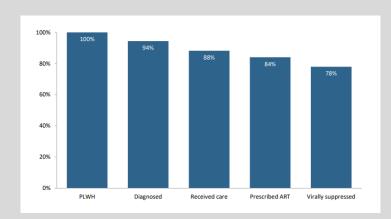
■ "The HIV care continuum is a public health model that outlines the steps or stages that people with HIV go through from diagnosis to achieving and maintaining viral suppression"



90-90-90 UNAIDS Targets

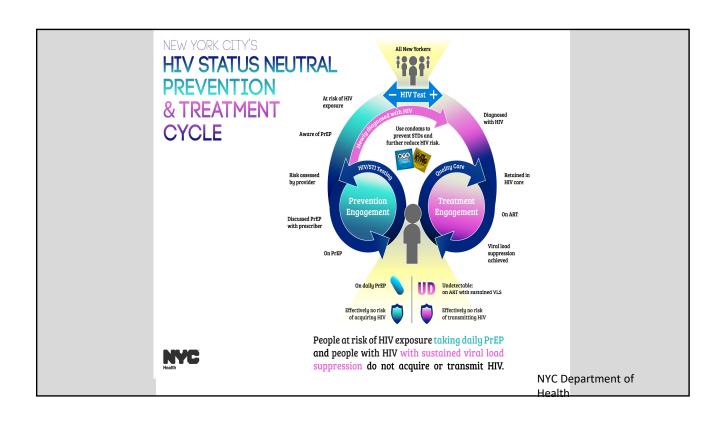
- By 2020
 - 90% of PLWH will know their HIV status
 - 90% of people with diagnosed HIV will receive ART
 - 90% of people receiving ART will be virally suppressed
- If 90-90-90 targets are achieved, 73% of PLWH would be virally suppressed and the HIV epidemic would end by 2030

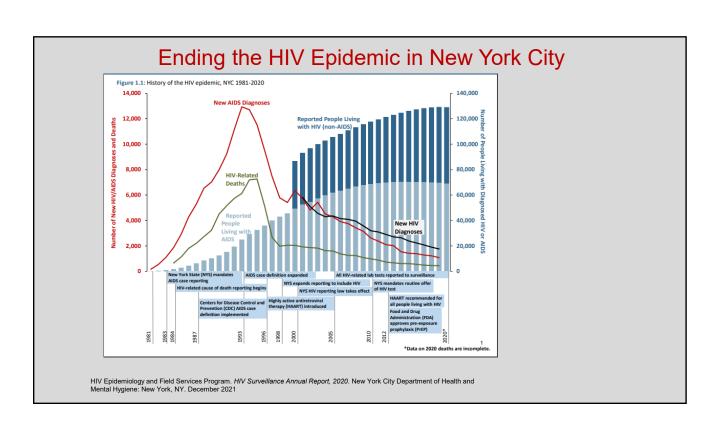
HIV Care Continuum (New York City 2020)

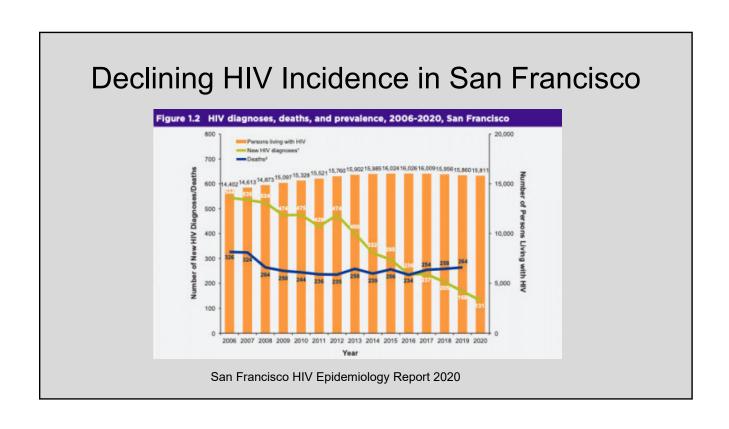


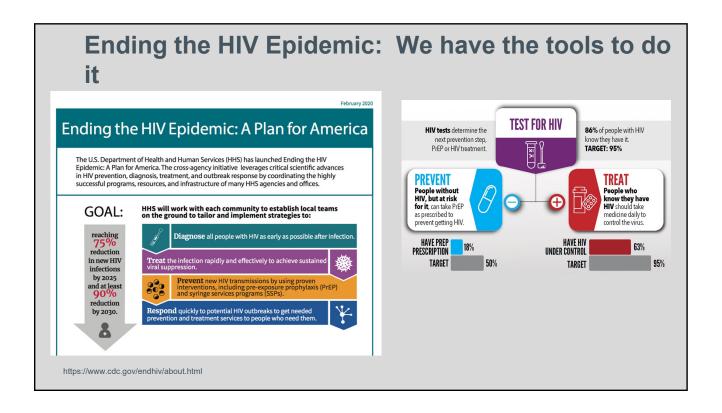
 NYC and other cities around the world have achieved 90-90-90 targets

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









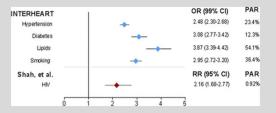
Comorbidities in HIV: Cardiovascular Disease

Cardiovascular Disease in HIV

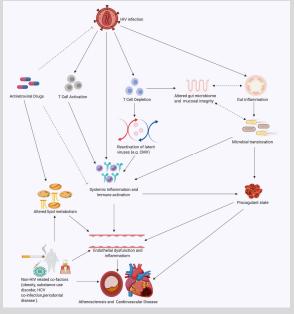
CVD is a leading cause of death for PWH

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



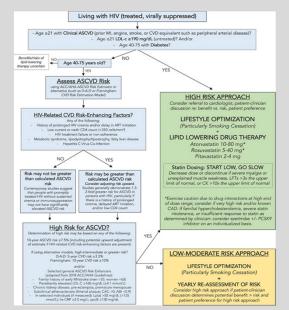
Titanji B, et al. J Am Heart Assoc. 2020 Feb 4;9(3):e014873

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

Triant VA, et al. Circulation 2018;137(19):2203-14



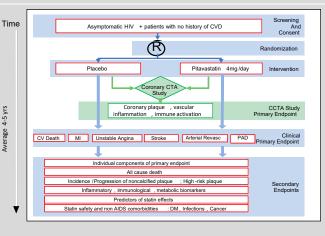
Feinstein MJ et al. Characteristics, prevention, and Management of CVD in People Living with HIV: A Scientific Statement from the American Heart Association. *Circulation* 2019;140(2):e98-e124.

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

REPRIEVE Trial Design N=7700



Source: Steve Grinspoon MD