Understanding Health Inequities in HIV Outcomes

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Learning Objectives

After attending this presentation, learners will be able to:

- Provide an overview of the HIV Epidemic in the United States
- Review the existing health inequities in HIV Care Outcomes
- Explore the role of Rapid ART initiation and Long-Acting Art in addressing inequities in HIV Care outcomes

HIV IN THE U.S.

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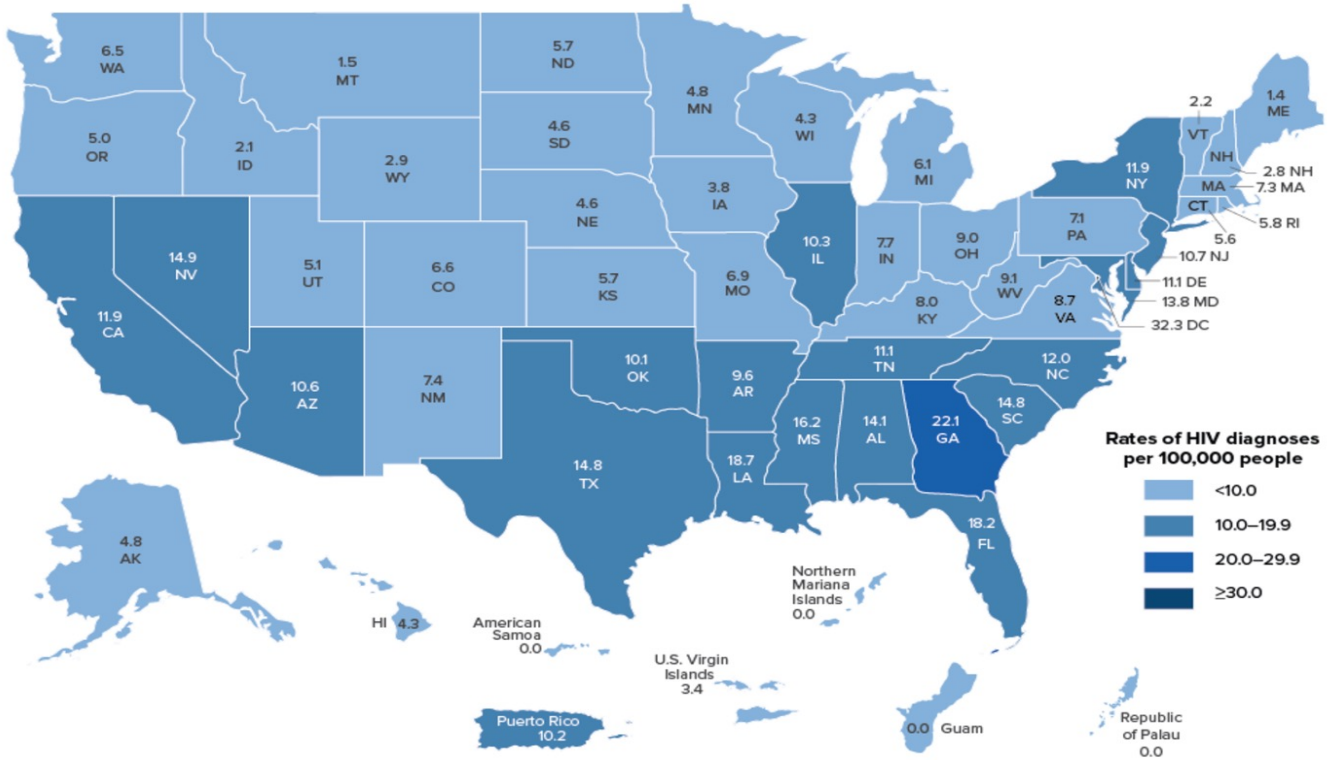
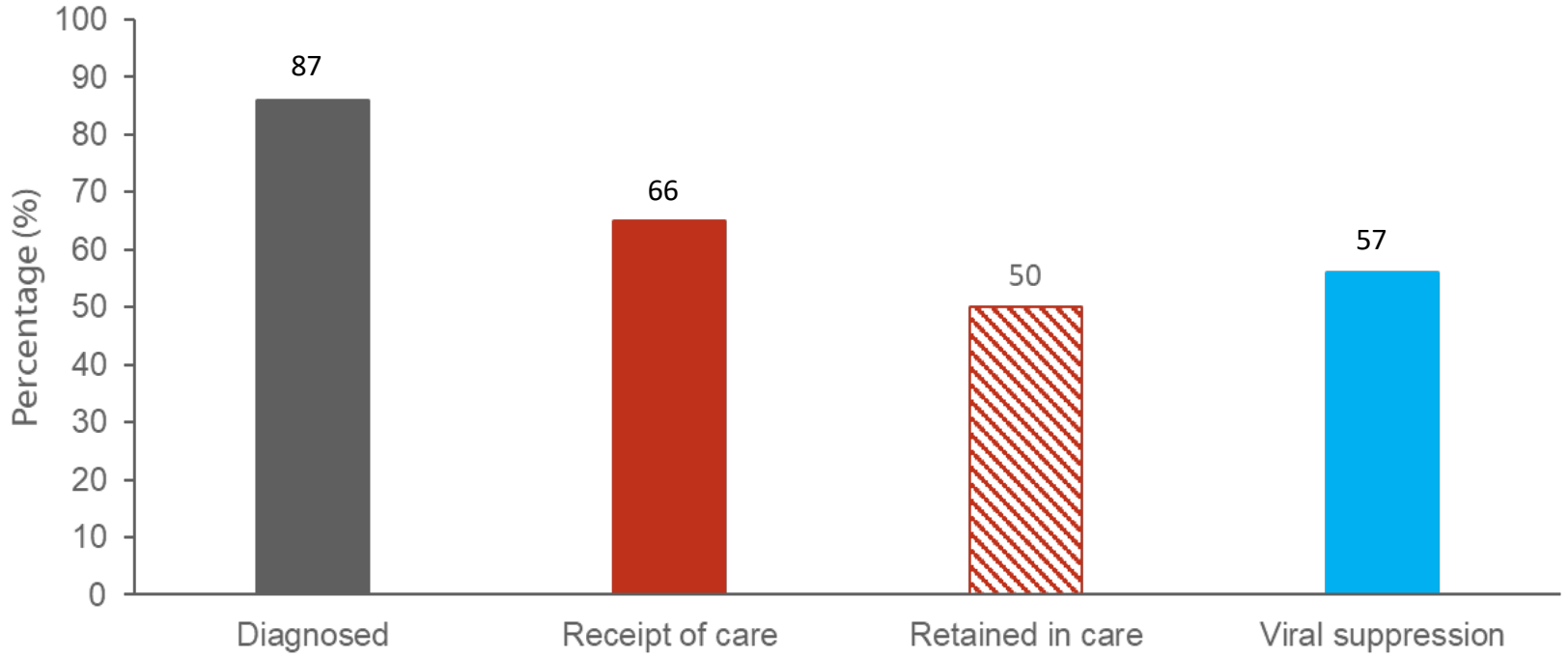
HIV Epidemic in the United States, 2020



Source: CDC. [Diagnoses of HIV infection in the United States and dependent areas, 2020](). *HIV Surveillance Report* 2022;33

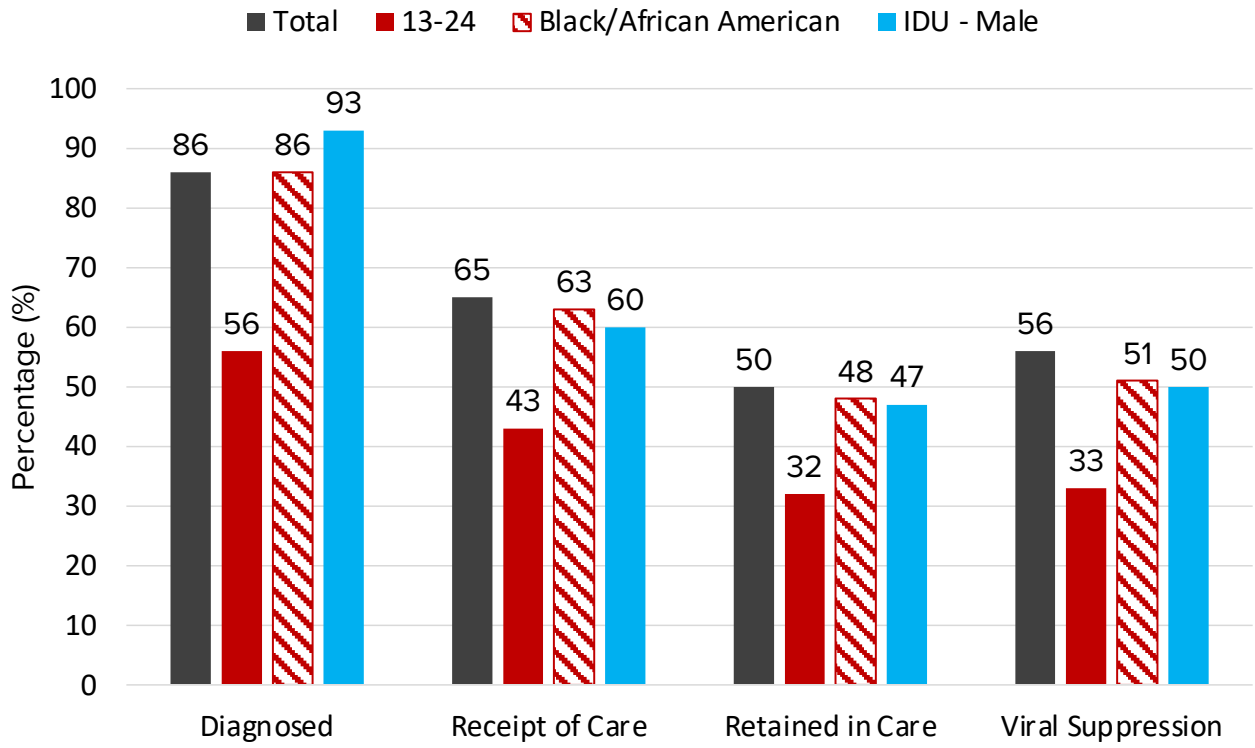
Persons Living with Diagnosed or Undiagnosed HIV Infection

HIV Care Continuum Outcomes, 2019—United States



Note. Receipt of medical care was defined as ≥1 test (CD4 or VL) in 2018. Retained in continuous medical care was defined as ≥2 tests (CD4 or VL) ≥3 months apart in 2018. Viral suppression was defined as <200 copies/mL on the most recent VL test in 2019. CDC, Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2019. HIV Surveillance Supplemental Report 2021; 26(No. 2). Published May 2021.

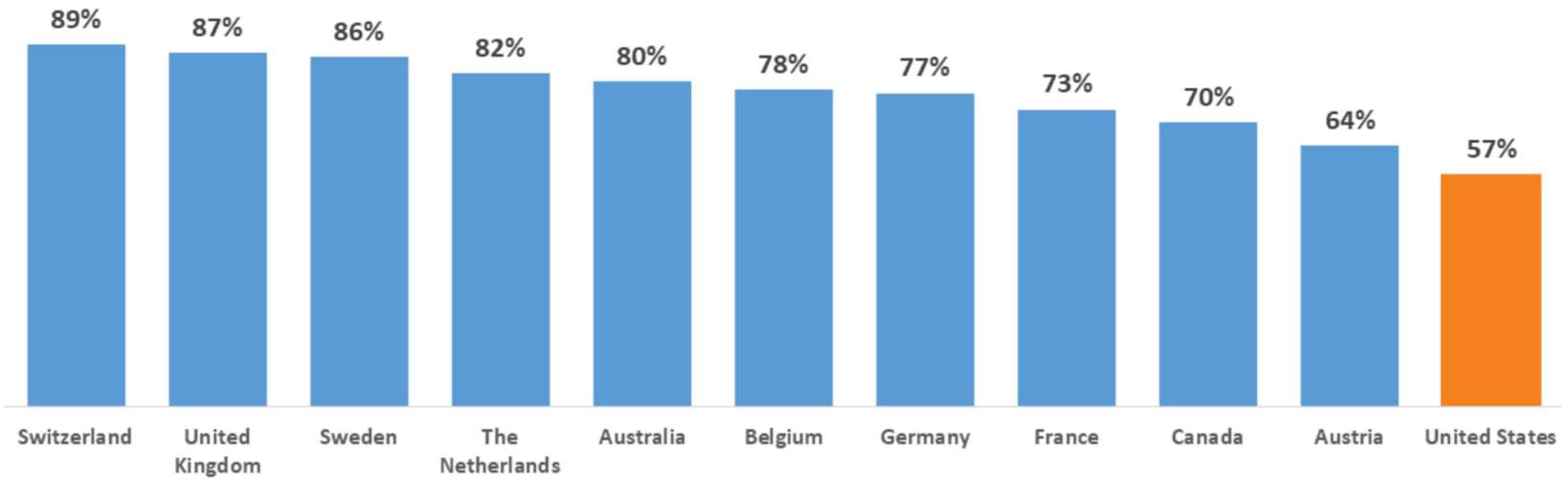
Persons Living with Diagnosed or Undiagnosed HIV Infection, HIV Care Continuum Outcomes, 2018



https://www.cdc.gov/hiv/pdf/library/slidesets/cdc-hiv-prevention-and-care-outcomes-2018.pdf

HIV Viral Suppression Rate in U.S. Lowest Among Comparable High-Income Countries, 2020 or Latest Year

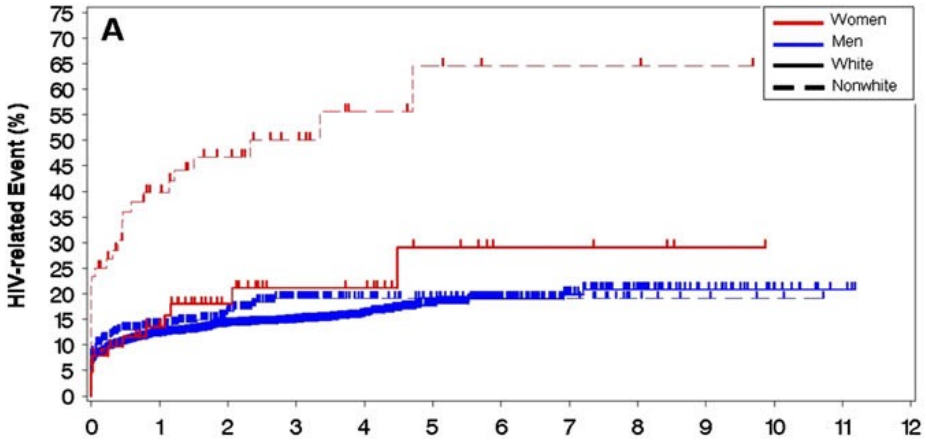
Rates of Viral Suppression Among People with HIV, by Country



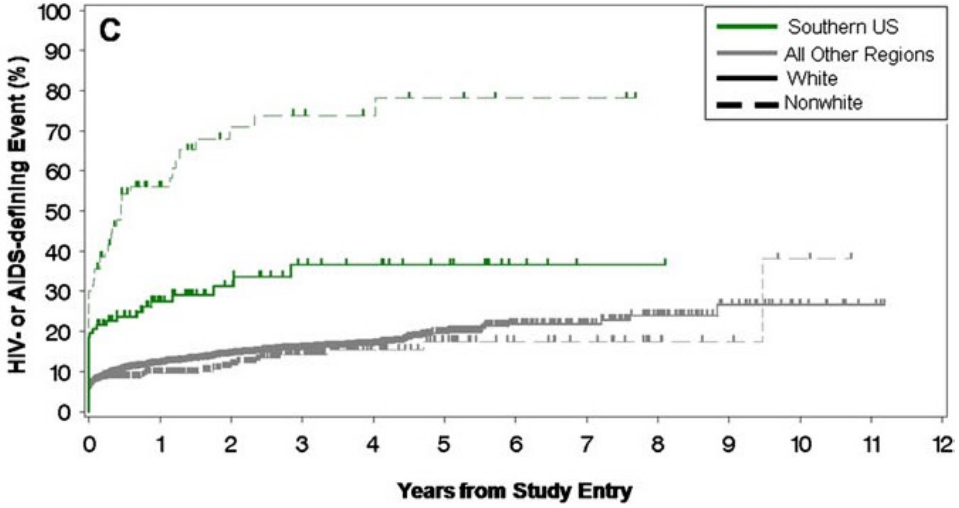
SOURCES: Australia: https://kirby.unsw.edu.au/sites/default/files/kirby/report/Annual-Suveillance-Report-2021_HIV.pdf; Canada: https://www.canada.ca/en/public-health/services/publications/diseases-conditions/summary-estimates-hiv-incidence-prevalence-canadas-progress-90-90-90.html#c; Europe: https://www.ecdc.europa.eu/sites/default/files/documents/hiv-continuum-of-care-dublin-declaration-2021.pdf; United States: Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 dependent areas, 2019. HIV Surveillance Supplemental Report 2021;26(No. 2), 2021. https://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-vol-26-no-2.pdf
NOTE: All data for 2020 except Canada which is for 2018 and U.S. which is for 2019.

KFF

Sex, race, and geographic region influence clinical outcomes following primary HIV-1 infection.

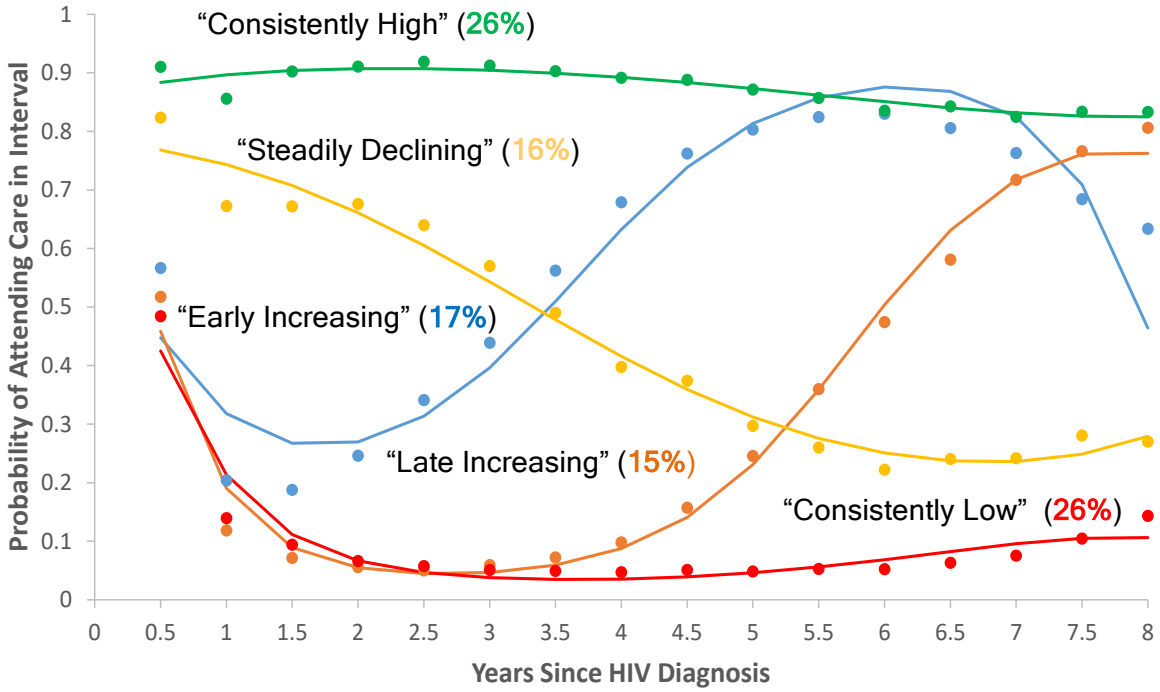


HIV-infected women had less favorable long-term clinical outcomes compared with men, **particularly among non-white women residing in the southern United States**



Meditz AL et al. *JID Feb 15 2011;203(4):442-451*

Engagement in Care is Dynamic



Powers et al, Longitudinal HIV Care Trajectories in North Carolina *JAIDS* 2017; 74(S2)

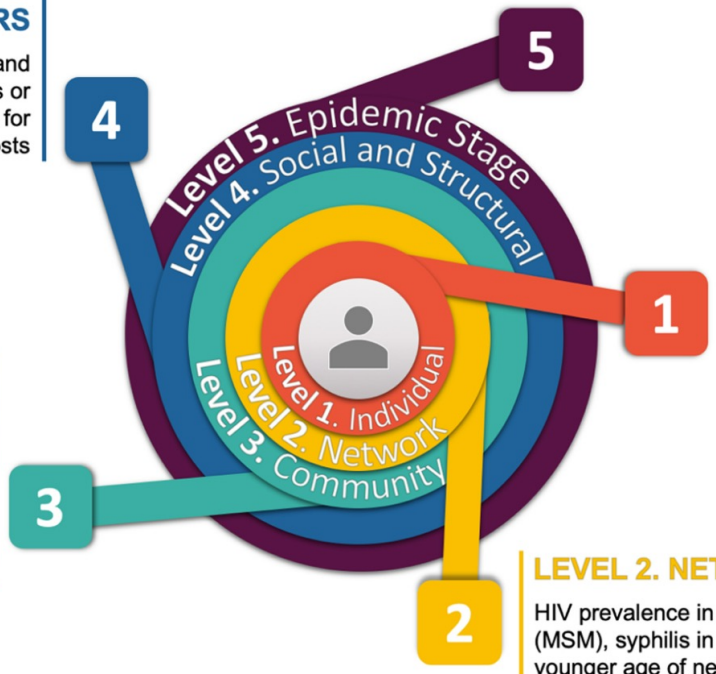
Social-ecological Model of HIV risk and vulnerability in the US

LEVEL 5. EPIDEMIC STAGE

Prevalence, population levels of viremia, force of infection

LEVEL 4. SOCIAL AND STRUCTURAL-LEVEL FACTORS

Medicaid expansion, illicit drug laws and policies, LGBTQ protections or discrimination, educational policies for HIV, PrEP availability, ARV drug costs



LEVEL 1. INDIVIDUAL-LEVEL FACTORS

- **Correlates of viremia**
  Mental health, substance use, unstable housing, criminal justice involvement, self stigma, poverty, younger age
- **Correlates of acquisition risk**
  Status awareness, substance use, low condom use, STI, PrEP adherence

LEVEL 3. COMMUNITY-LEVEL FACTORS

Stigma (HIV, LGBTQ, intersectional), poverty, racism, level of services provision, enabling environments for prevention, needle and syringe exchange, policing.

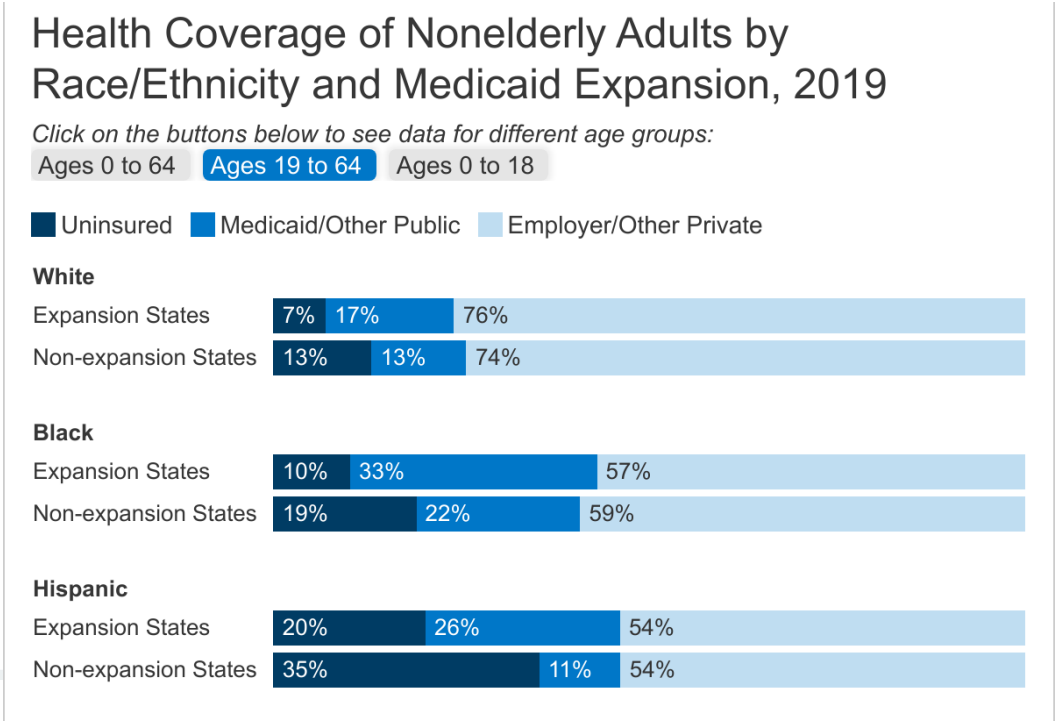
LEVEL 2. NETWORK-LEVEL FACTORS

HIV prevalence in network, viremia, role versatility (MSM), syphilis in network, high levels of association, younger age of network members, rates of acute/recent infection

Beyrer C et al. Call to action: how can the US Ending the HIV Epidemic initiative succeed? Lancet. 2021 Mar 20;397(10279):1151-1156.

Fragmented Health Care Delivery in the U.S.

- HIV Testing, Prevention, and Care:
  - Private Clinics
  - Public Health Clinics
  - Federally Qualified Health Centers (Primary Care)
  - Academic Health Centers
  - Pregnancy care, HIV care, Infant care in 3 different locations
- Funded by:
  - Private Insurance
  - Medicare >65 years
  - Medicaid – state determines eligibility
  - Federal Ryan White Program Clinics
    - Only covers HIV Care; program can be used to purchase private health insurance but regular certifications required.
    - Ryan White Clinics CANNOT use funds to provide PrEP services



The Role of Rapid Start in addressing Health Inequities

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On average, how long does it take from time of HIV diagnosis/referral to your clinic to initiation of ART?

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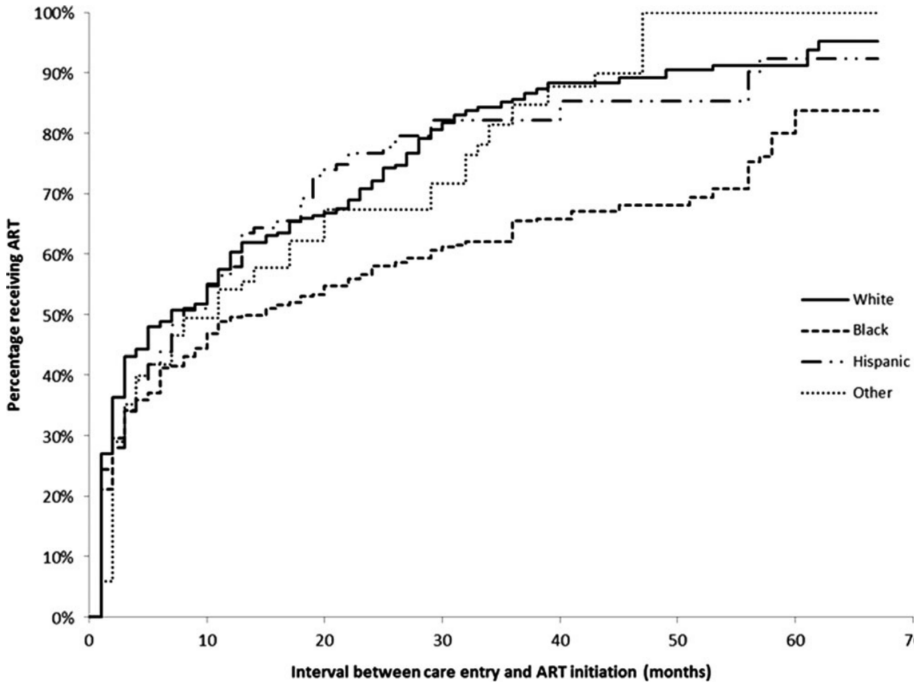
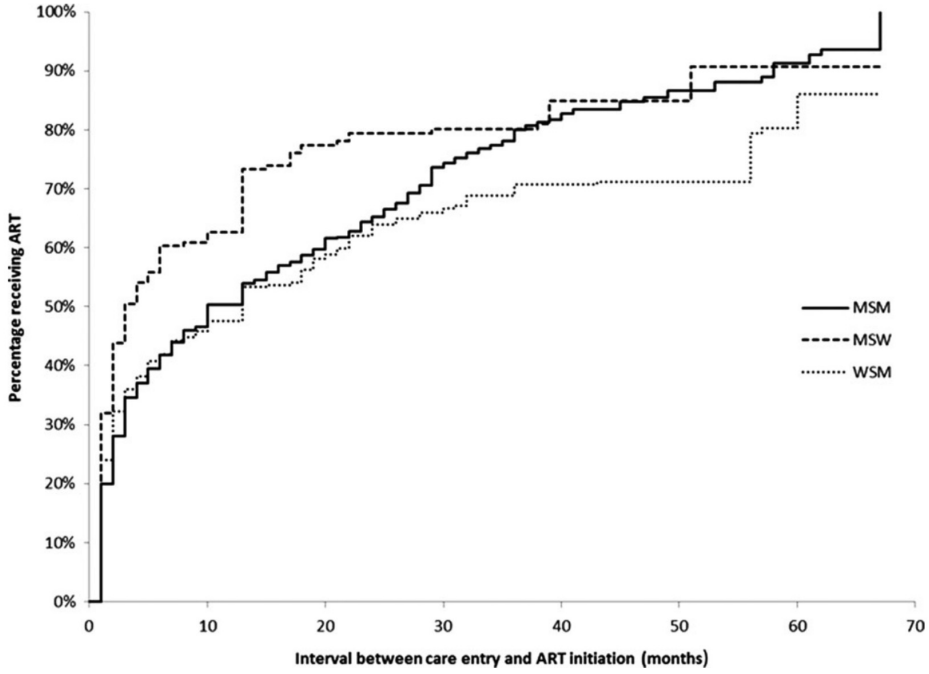
Do We Have Equity in Initiation of ART?





Black MSM patients and have an increased rate of transmission and equivalent linkage to care, yet are less likely than MSM to receive an ART prescription[2]

Adedinsewo DA et al. Timing of antiretroviral therapy initiation in a nationally representative sample of HIV-infected adults receiving medical care in the United States. *AIDS Pt Care STDS*. 2014
[2]Hoots BE, et al. Updated Data on Linkage to Human Immunodeficiency Virus Care and Antiretroviral Treatment Among MSM—20 Cities, United States *J Infect Dis*. 2017

Does Early ART Initiation Work?

- **2011[1,2]**
  - Prevention of HIV-1 Infection With Early ART
    - Final results in 2016
    - Early ART → 93% lower risk of transmission
    - No linked infections with VS index patient
- **2015[3]**
  - Initiation of ART in Early Asymptomatic HIV Infection
    - The INSIGHT START Study Group
    - Early ART led to HR of 0.43 for death, AIDS- related events, or serious non–AIDS-related events
- **2015[4]**
  - A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa[4]
    - Earlier ART resulted in HR of 0.56 for death or severe HIV-related illness
- **Meta-analysis of rapid ART[5]**
  - Likely results in greater viral suppression and better ART uptake at 12 months
  - May improve retention in care
  - Lower mortality estimate

HR, hazard ratio; VS, virologically suppressed.

1. Cohen MS, et al. *N Engl J Med*. 2011;365(6):493-505; 2. Cohen MS, et al. *N Engl J Med*. 2016;375(9):830-839; 3. INSIGHT START Study Group. *N Engl J Med*. 2015;373(9):795-807; 4. TEMPRANO ANRS 12136 Study Group. *N Engl J Med*. 2015;373(9):808-822; 5. Mateo-Urdiales A, et al. *Cochrane Database Syst Rev*. 2019;6(6):CD012962.

Addressing Inequities in Access to ART Across Different Populations

- The clinical encounter may be a major source of disparities[1]
  - Miscommunication, misunderstandings, biases, and stereotypes—especially concerning adherence—affect providers' treatment decisions
  - Stereotyping may be unconsciously utilized—as an outgrowth of learned pattern recognition skills—even by providers with egalitarian and nondiscriminatory views
  - Strategies that build communication and trust and ensure patient participation in clinical decision-making are needed
- Cultural humility is key

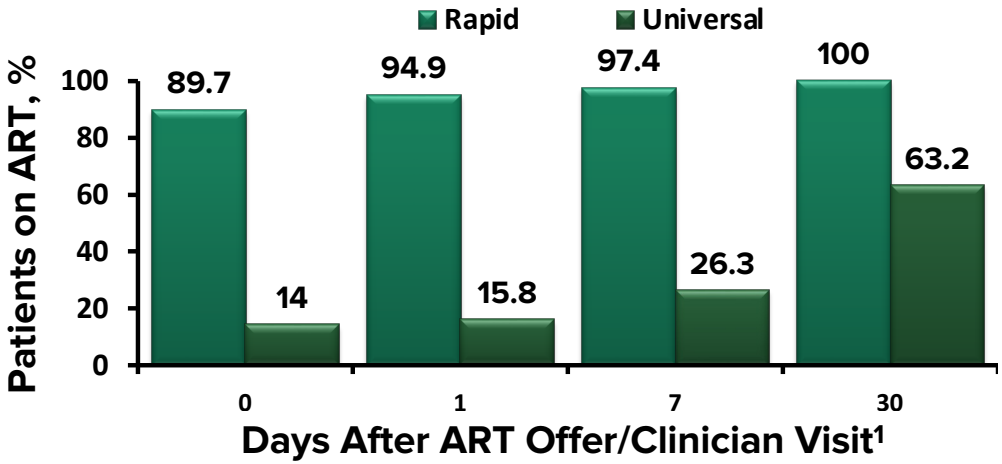
Rapid ART lends a humanistic approach to the *Treat All* philosophy that is essential to mitigating health disparities.[2]

17

1. Stone. VE. *Curr HIV/AIDS Rep.* 2005;2(4):189-193; 2. Coffey S, et al. *Clin Infect Dis*. 2020 (Epub ahead of print).

Rapid ART Works in the Face of Social Challenges

RAPID Model in San Francisco



Key Sociodemographics[1]

	RAPID n=39	Universal n=47
Homelessness	11 (28%)	13 (25%)
Uninsured	39 (100%)	47 (100%)
Illicit substance use	18 (46%)	18 (38%)
Major mental health disorders	21 (54%)	15 (32%)

In the Atlanta REACH cohort, the overwhelming majority were Black men in their mid 30s, and over half were uninsured with a median income of $8800. Nearly half used substances and 26% had a mental health disorder. The median CD4 count was 146 cells/μL. These patients still benefited from the REACH program.[2]

1. Pilcher CD, et al. *J Acquir Immune Defic Syndr*. 2017;74(1):44-51; 2. Colasanti J, et al. *Open Forum Infect Dis*. 2018;5(6):ofy104.

Rapid ART — Today's Standard of Care

DHHS' Formal Endorsement, December 2019

- The Panel recommends that ART be **started immediately or as soon as possible after diagnosis** to
  - Increase the uptake of ART
  - Decrease the time to linkage to care and VS
  - Reduce the risk of HIV transmission
  - Improve the rate of virologic suppression among persons with HIV
- Level of evidence: AII

DHHS. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV.

National HIV/AIDS Strategy

2022-2025

- Goal 2: Improve HIV-Related Health Outcomes of People with HIV
- 2.1.1 Provide same-day or rapid (within 7 days) start of antiretroviral therapy for persons who are able to take it; increase linkage to HIV health care within 30 days for all persons who test positive for HIV.

https://www.whitehouse.gov/wp-content/uploads/2021/11/National-HIV-AIDS-Strategy.pdf

Rapid ART

What to Start

- **DHHS Recommendations**
  - *Avoid*
    - NNRTI-based regimens
    - DTG/3TC
    - ABC
  - *Recommended regimens*[a]
    - BIC/FTC/TAF
    - DRV/r or DRV/c[b] (TAF or TDF)[c] plus (3TC or FTC)
    - DTG + (TAF or TDF) plus (3TC or FTC)

- **Rationale for Recommendations**
  - Transmitted mutations conferring NNRTI and NRTI resistance are more likely than mutations associated with PI or INSTI resistance
  - HLA-B*5701 results may not be available rapidly
  - Transmitted resistance to DRV, BIC, and DTG is rare, and these drugs have high barriers to resistance

ABC, abacavir; BIC, bictegravir; DRV/c, darunavir/cobicistat; DRV/r, darunavir/ritonavir; DTG/ABC/3TC, dolutegravir/abacavir/lamivudine; IAS, International Antiviral Society; NRTI, nucleoside/tide reverse transcriptase inhibitor; PI, protease inhibitor.

[a]Listed in alphabetical order; [b]Boosted DRV regimens are included in the DHHS guidelines for rapid start but are no longer recommended as first-line regimens for most people with HIV; [c]Consider TAF if serum creatinine level is unknown.

1. Clinical Info HIV.gov. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Last updated December 2019. https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/what-start-initial-combination-regimens-antiretroviral-naive?view=full.

Potential Barriers to Starting ART

- **Structural/systemic**
  - HIV testing/diagnosis occurs off-site; ie, referral to clinic
  - Complex eligibility criteria for some clinics; eg, CD4 count, income, residence
  - Access to medications without payer source
  - Scheduling and provider availability
- **Provider/staff beliefs**
  - "That's how we've always done it"
  - Preparatory lab results must be known; ie, serum creatinine, hepatitis B and C serology, genotype

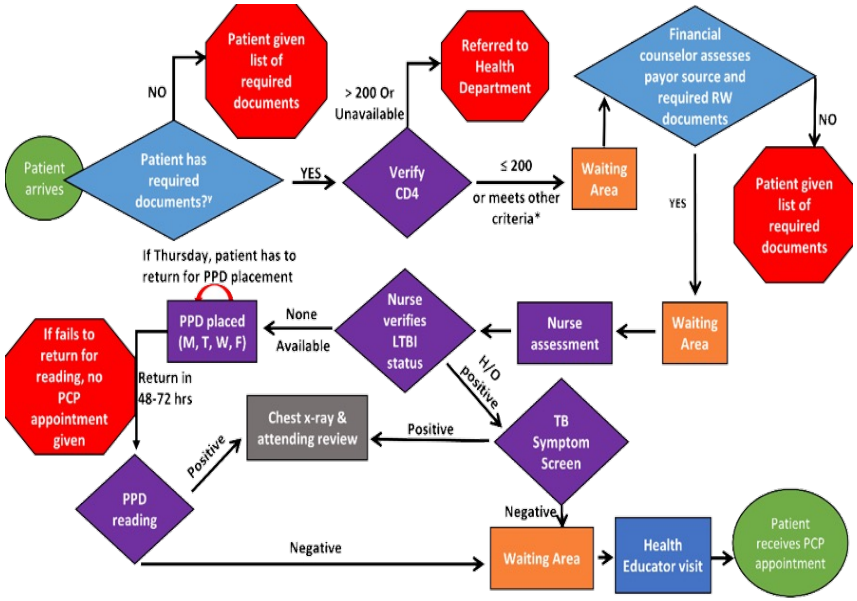
Coffey et al. CID 2021

- **Patients' readiness and psychosocial comorbidities**
  - Coping with HIV diagnosis
  - Housing stability
  - Food insecurity
  - Mental illness
  - Substance use

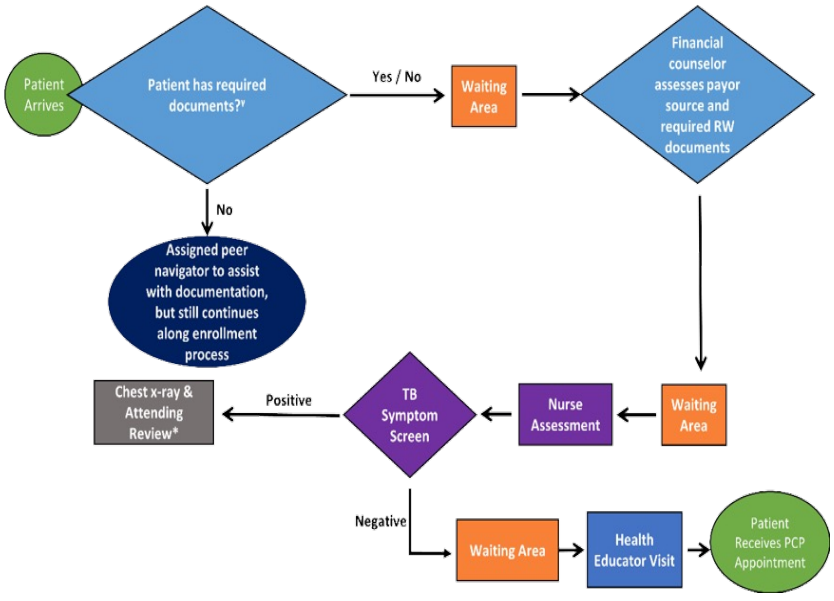
Administrative Barriers

REACH, Atlanta

PRE-REACH



POST-REACH



LTBI, latent tuberculosis infection; H/O, history of; PPD, purified protein derivative; RW, Ryan White.

Colasanti J, et al. *Open Forum Infect Dis*. 2018;5(6):ofy104.

Successful Rapid ART Initiation

An Overview of Key Facilitators and Indicators

- **Key facilitators**[1]
  - Tight working relationships between testing sites and rapid-ART sites
  - Warm hand-offs and accessible linkage coordinators
  - Early and sustained access to ART
  - Expedited insurance/payer source and clinic enrollments
  - Same-day clinician visits
  - Close follow-up, patient navigation, ongoing HIV education, retention services
- **Key indicators**[1–3]
  - Median time to ART initiation
  - Median time to VS

CCSI, CrescentCare Start Initiative; REACH, Rapid Entry and ART in Clinic for HIV.

1. Coffey S, et al. *Clin Infect Dis*. 2020 (Epub ahead of print); 2. Colasanti J, et al. *Open Forum Infect Dis*. 2018;5(6):ofy104;
3. Halperin J, et al. *AIDS Patient Care STDS*. 2018;32(2):39-41.

Is there a Role for Long Acting ART in Addressing Health Inequities?

2022 Ryan White HIV/AIDS Program CLINICAL CONFERENCE

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“I offer injectable cabotegravir + injectable rilpivirine to PWH with adherence challenges.”

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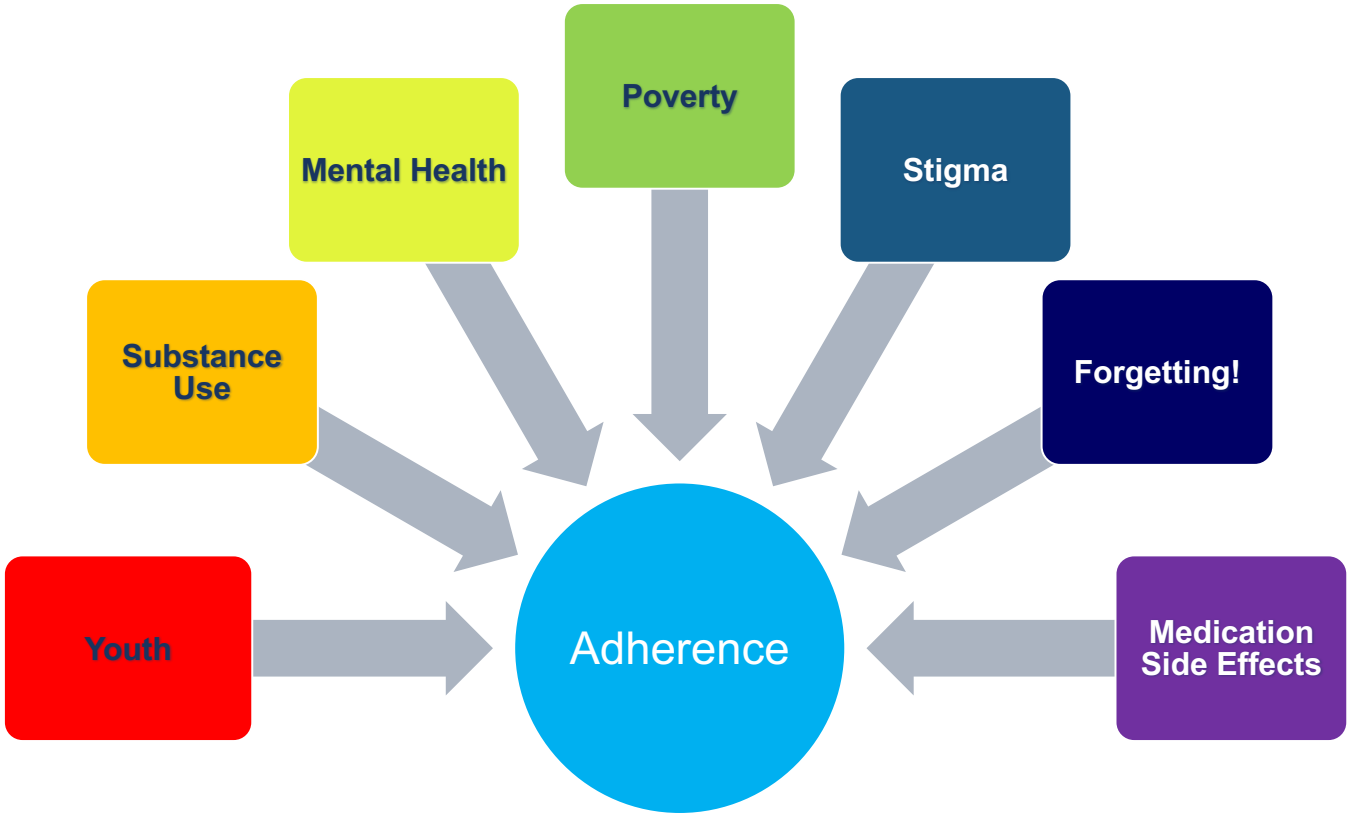
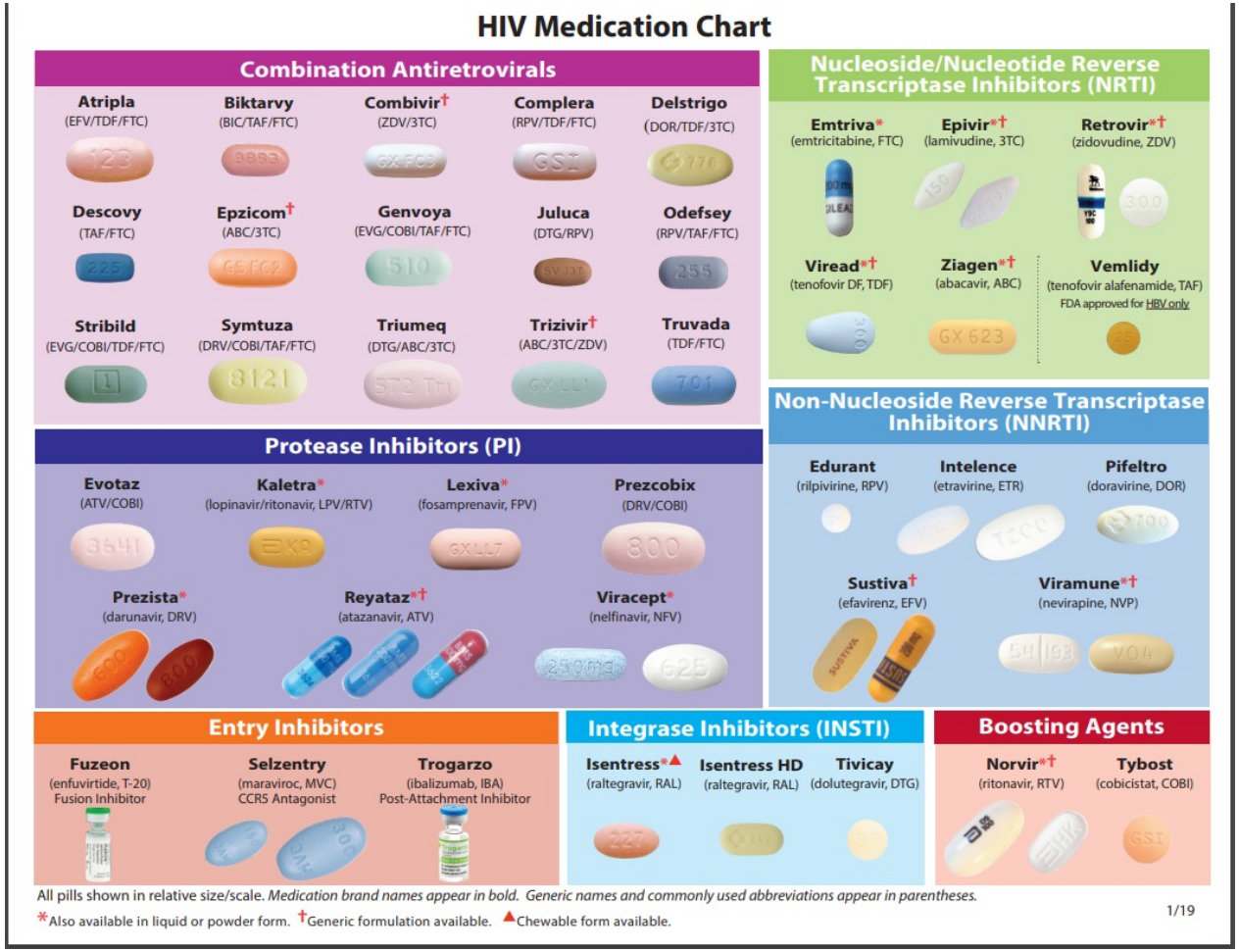
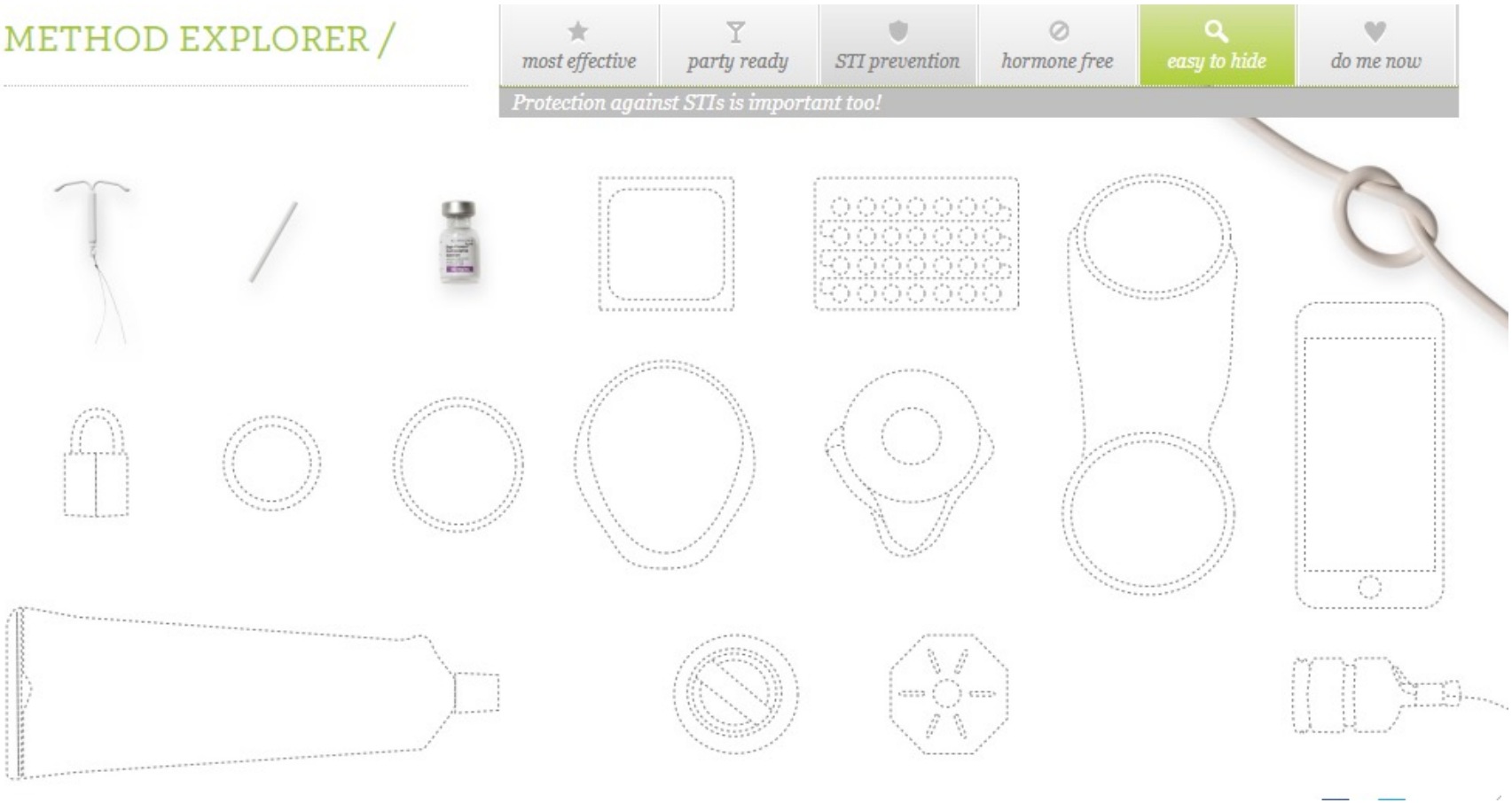
Assessing Individual Barriers to Care and Treatment





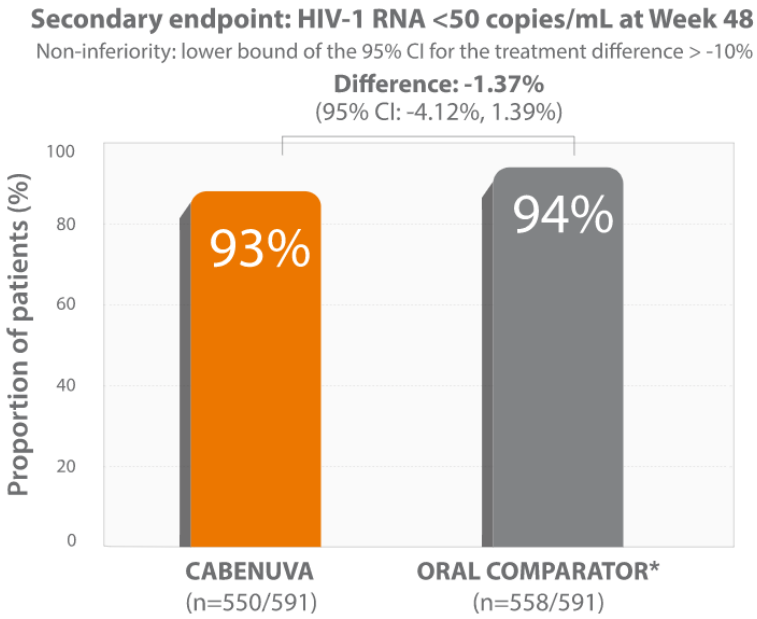
https://aidsetc.org/resource/hiv-medication-chart-pad



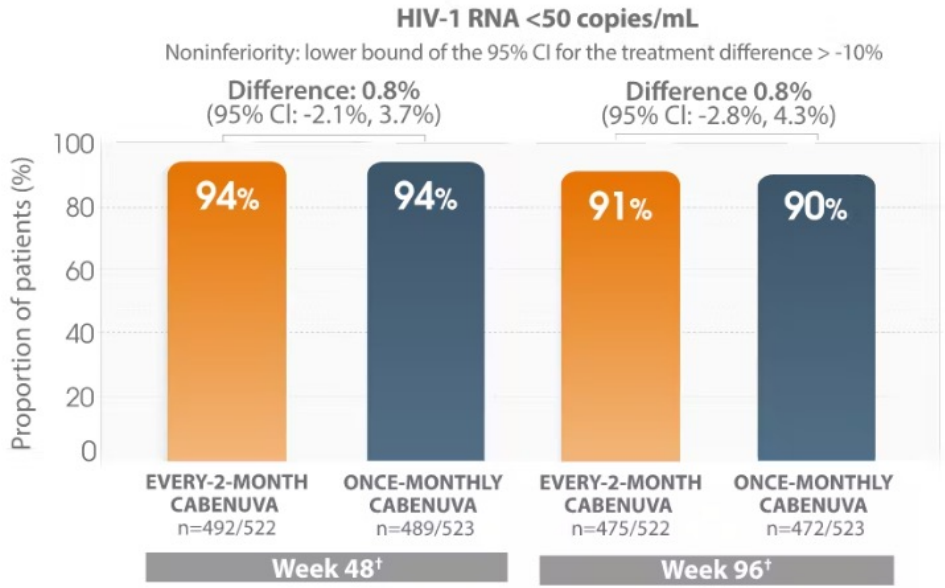
https://www.bedsider.org/methods

Phase III studies of LA-CAB/RPV

Pooled ATLAS/FLAIR



ATLAS-2M



BUT, these studies **did not include** PWH who face adherence barriers.

Orkin C, et al. NEJM 2020. Swindells S, et al. NEJM 2020.
Overton ET, et al. Lancet 2020. Jaeger H, et al. Lancet HIV 2021

DHHS HIV Clinical Guidelines

Long-Acting Antiretroviral Therapy

Updated Sept 21, 2022

A long-acting ART (LA-ART) regimen (intramuscular cabotegravir and rilpivirine) has been studied and approved for use in populations with viral suppression. There are no data on the safety and efficacy of using LA-ART in people who currently do not have suppressed HIV replication. The long pharmacologic tail of LA-ART after last dose raises concerns for the emergence of resistant mutations in people who discontinue therapy without rapidly transitioning to an oral therapy. The Panel on Antiretroviral Guidelines for Adults and Adolescents, therefore, **recommends against** the use of LA-ART in people who have detectable viral load due to suboptimal adherence to ART and in people who have ongoing challenges with retention in HIV care except in the context of a clinical trial **(AIII).**

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/adherence-continuum-care?view=full

Challenges with the uptake and use of LA ART

- Requires adherence / retention
- Resistance
  - 2 drug ART regimen CAB/RPV
    - limited to those WITHOUT an extensive history of resistance
  - Long half-life of injectables: Risk of development of resistance
- Side-effects to Injections
- Unstudied populations
  - Women of Child Bearing Potential, Youth
- Cost and Equity

What do patients say about LA-ART?

At the beginning I thought…Oh my God…I hope I get over this depression. But, my God…I hope I won't be taking these pills all my life. Then I went on to the injectable phase…and it was like I saw the light. And I said, God…how easy and convenient this is. It was like seeing the light.
-Spain, Male trial participant

that's just one less thing on my plate that I have to worry about… I definitely feel there's less pressure. I like the injection because it's not a daily, in my face, I have to do this.
- U.S., Female trial participant-

In reality, taking the pill everyday keeps it [HIV] present …and the shot is just once a month…you remember it when you come in and the rest of the time you can basically forget it.
–Spain, Male trial participant

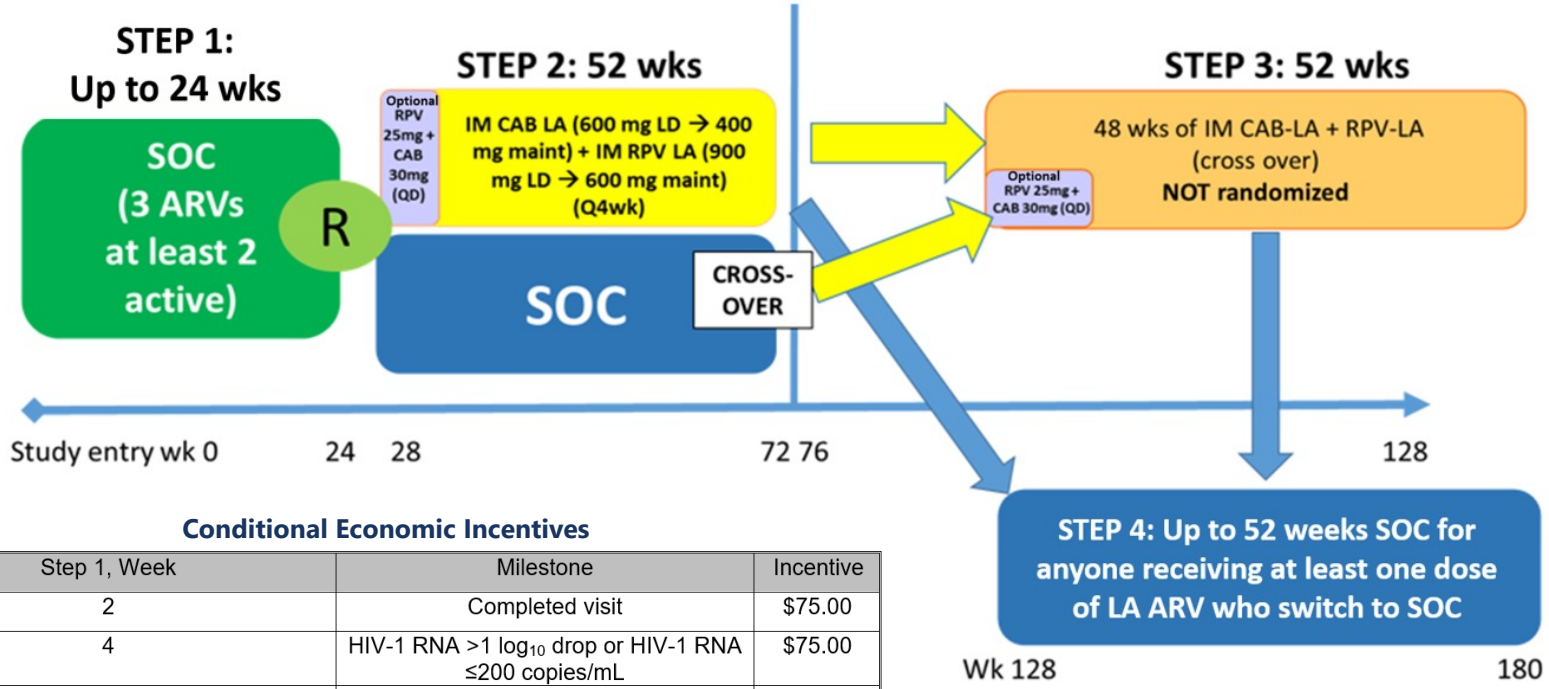
Kerrigan D et al. Experiences with LA ART: A qualitative study among PLHIV participating in Latte-2 in the US and Spain. PLOS One. 2018.

ACTG Protocol 5359

LATITUDE : Long-Acting Therapy to Improve Treatment sUccess in Daily LifE

- ART-experienced, HIV-infected, males and non-pregnant females ≥18 years of age with:
  - HIV-1 RNA >200 copies/mL
  - Evidence of non-adherence according to at least one of the following criteria:
    - Poor virologic response to prescribed ART for at least 6 months
    - Loss to clinical follow-up for >6 months with ART non-adherence
  - Negative for Hepatitis B

LATITUDE (A5359) Study Design (V2.0)



Conditional Economic Incentives

Step 1, Week	Milestone	Incentive
2	Completed visit	$75.00
4	HIV-1 RNA >1 $\log_{10}$ drop or HIV-1 RNA ≤200 copies/mL	$75.00
8	HIV-1 RNA >2 $\log_{10}$ drop or HIV-1 RNA ≤200 copies/mL	$75.00
12	HIV-1 RNA ≤200 copies/mL	$150.00*
16 (if needed)	HIV-1 RNA ≤200 copies/mL	$150.00*
20 (if needed) or Confirmation viral load after week 20 (but prior to week 24)	HIV-1 RNA ≤200 copies/mL	$150.00

ATLAS baseline characteristics

ACTG Protocol 5359 — ACTG LATITUDE

- Registered Sites: 31 ACTG, 4 IMPAACT – U.S + Puerto Rico
- Screened: 617
- Enrolled in Step 1: 292
- Randomized in Step 2: 175 (55%)
  - 63% Black/African-American
  - 18% Hispanic/Latinx Ethnicity
  - 30% Female Sex at Birth
  - 6% Age 18-24 years
  - 7% Transgender
  - 5% current injection substance use
  - Median CD4 count 263 cells/mm3
  - Median time since HIV diagnosis 13 years

Table 1. Baseline Characteristics of Participants in the Intention-to-Treat Exposed Population.*

Characteristic	Long-Acting Therapy (N=308)	Oral Therapy (N=308)	Overall (N=616)
Median age (range) — yr	40 (21–74)	43 (18–82)	42 (18–82)
Age group — no. (%)			
<35 yr	80 (26)	80 (26)	160 (26)
35–49 yr	162 (53)	132 (43)	294 (48)
≥50 yr	66 (21)	96 (31)	162 (26)
Female sex — no. (%)	99 (32)	104 (34)	203 (33)
Median body-mass index (range)†	26 (15–51)	26 (18–58)	26 (15–58)
Race — no. (%)‡			
White	214 (69)	207 (67)	421 (68)
Black	62 (20)	77 (25)	139 (23)
Asian	22 (7)	13 (4)	35 (6)
Other	10 (3)	11 (4)	21 (3)
CD4+ lymphocyte count — no. (%)			
<350/mm^3	23 (7)	27 (9)	50 (8)
350–499/mm^3	56 (18)	57 (19)	113 (18)
≥500/mm^3	229 (74)	224 (73)	453 (74)
Median time since first ART (range) — mo	52 (7–222)	52 (7–257)	52 (7–257)

LA-CAB/RPV in PWH with viremia-Case Report

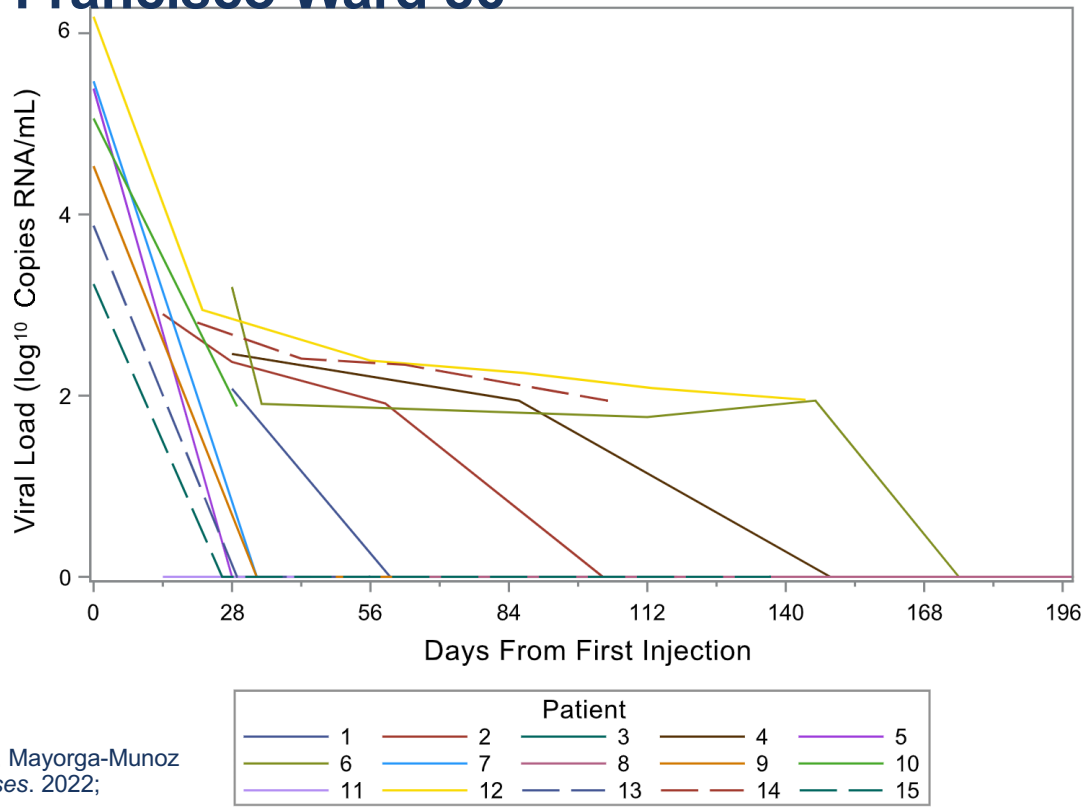
Table 1. Treatment management and HIV outcomes for case patient.

Time	ART	CD4$^+$	VL	Genotype/phenotype	Actions
−96 months	EFV-TDF-FTC	381	7519	RT: K103N	Switch to DTG-ABC-3TC
−60 months	DTG-ABC-3TC	193	244 665	RT: K103N, INSTI: 157Q, S230N	Switch to DRV-COBI+TAF-FTC
−53 months	DRV-COBI+TAF-FTC	166	140 707	No resistance mutations	Switch to DTG+TAF-FTC
−31 months	DTG+TAF-FTC	331	382	No resistance mutations	Switch to BIC-TAF-FTC
−28 months	BIC-TAF-FTC	204	198 185		Directly-observed therapy instituted
−6 months	BIC-TAF-FTC	224	161 000		Switched to DTG-3TC
Time 0	CAB + RPV (oral)	260	341 000	Phenotype-No resistance mutations	Switched to CAB+RPV
+4 weeks	CAB + RPV (injectable)	–	–		
+8 weeks	CAB + RPV (injectable)	–	–		
+12 weeks	CAB + RPV (injectable)	374	<20		
+26 weeks	CAB + RPV (injectable)	445	<20		

EFV: efavirenz. TDF: tenofovir disoproxil fumarate. FTC: emtricitabine. DTG: dolutegravir. ABC: abacavir. 3TC: lamivudine. DRV: darunavir. COBI: cobicistat. TAF: tenofovir alafenamide. BIC: bictegravir.

Barnett SK, et al. AIDS 2022.

First Demonstration Project of Long-Acting Injectable Antiretroviral Therapy for Persons With and Without Detectable Human Immunodeficiency Virus (HIV) Viremia in an Urban HIV Clinic, San Francisco Ward 86



Christopoulos KA, Grochowski J, Mayorga-Munoz F, et al. *Clinical Infectious Diseases*. 2022;

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Pilot Data from the Grady Ponce de Leon Center

Open Forum Infectious Diseases

MAJOR ARTICLE

Early Experience Implementing Long-Acting Injectable Cabotegravir/Rilpivirine for Human Immunodeficiency Virus-1 Treatment at a Ryan White-Funded Clinic in the US South

Lauren F. Collins,[1,2,] Della Corbin-Johnson,[2] Meron Asrat,[2] Zoey P. Morton,[1] Kaylin Dance,[1] Alton Condra,[2] Kimberly Jenkins,[2] Marie Todd-Turner,[2] Jeri Sumitani,[2] Bradley L. Smith,[2] Wendy S. Armstrong,[1,2] and Jonathan A. Colasanti[1,2,3]

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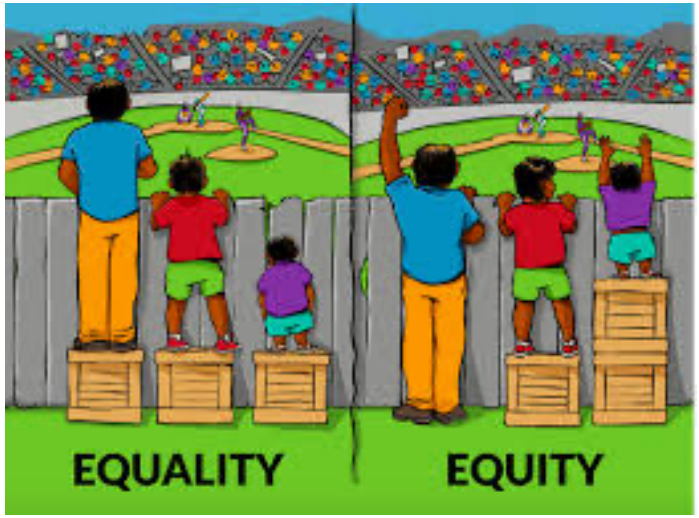
Narrow rather than widen the disparity gap



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A Nudge
Travel Voucher
Appointment Reminders

More Help
Contingency Management

Patient Navigation

Mobile Units

“LAI available in our clinic AND we’ll do what we can to ensure you benefit from it”

Suggested Readings

- Beyrer C et al. Call to action: how can the US Ending the HIV Epidemic initiative succeed? Lancet. 2021 Mar 20;397(10279):1151-1156.
- Brooke E Hoots, Teresa J Finlayson, Cyprian Wejnert, Gabriela Paz-Bailey, for the National HIV Behavioral Surveillance (NHBS) Study Group, Updated Data on Linkage to Human Immunodeficiency Virus Care and Antiretroviral Treatment Among Men Who Have Sex With Men—20 Cities, United States, *The Journal of Infectious Diseases*, Volume 216, Issue 7, 1 October 2017, Pages 808–812,
- Coffey S, Halperin J, Rana AI, Colasanti JA. Rapid Antiretroviral Therapy: Time for a new Standard of Care. Clin Infect Dis. 2021 Jul 1;73(1):134-136.
- Kerrigan D et al. Experiences with LA ART: A qualitative study among PLHIV participating in Latte-2 in the US and Spain. PLOS One. 2018.
- White House National HIV/AIDS Strategy 2022-2025. https://www.whitehouse.gov/wp-content/uploads/2021/11/National-HIV-AIDS-Strategy.pdf

Question-and-Answer Session
Contact: rana@uab.edu

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