

HIV Treatment Update and Complications in Long-term Survivors

American Council of Life Insurers (ACLI) Medical Section Annual Program

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February 25th, 2020

Disclosures

- None

Objectives

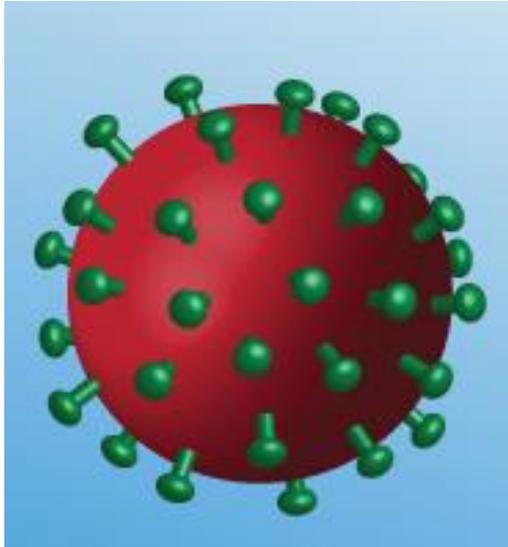
1. Current Treatment and Outlook for a Cure
2. Current Outlook on Prevention
3. Barriers to Treatment and Long-Term Adherence
4. Life Expectancy and Long-Term Mortality of Individuals Currently Living with HIV
5. Illnesses and Complications Associated with Long-Term Survivors of HIV Infection

Typical Cases – A Tale of 2 Syndromes

1. 28-year-old African American male who has sex with men diagnosed 4 years ago but out of care
 - Wasn't on PrEP
 - Thinks infected 4 years before diagnosis
 - Inconsistent visit adherence
 - Parents don't know HIV status or sexual preferences
 - CD4 is less than 35, unintentional weight loss, thrush
2. 62-year-old African American woman with HIV
 - Viral load suppressed for 20 years on medications
 - Acquired from male sexual partner
 - Metabolic syndrome
 - Wonders how cure research is going

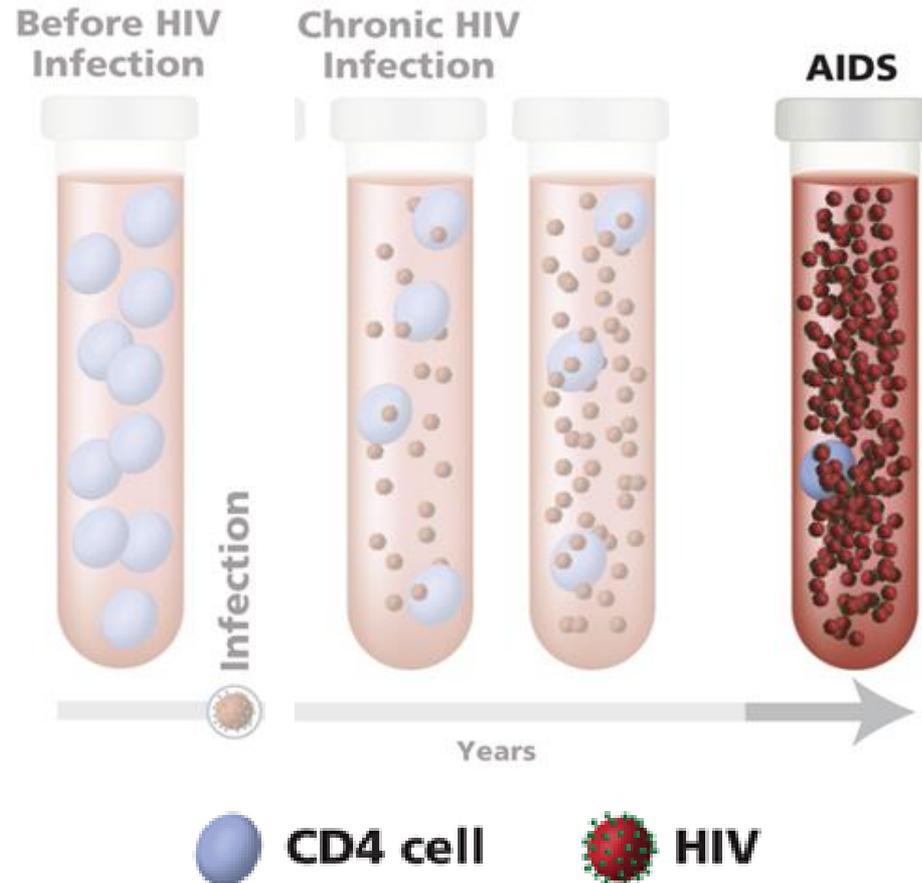
Definitions

HIV

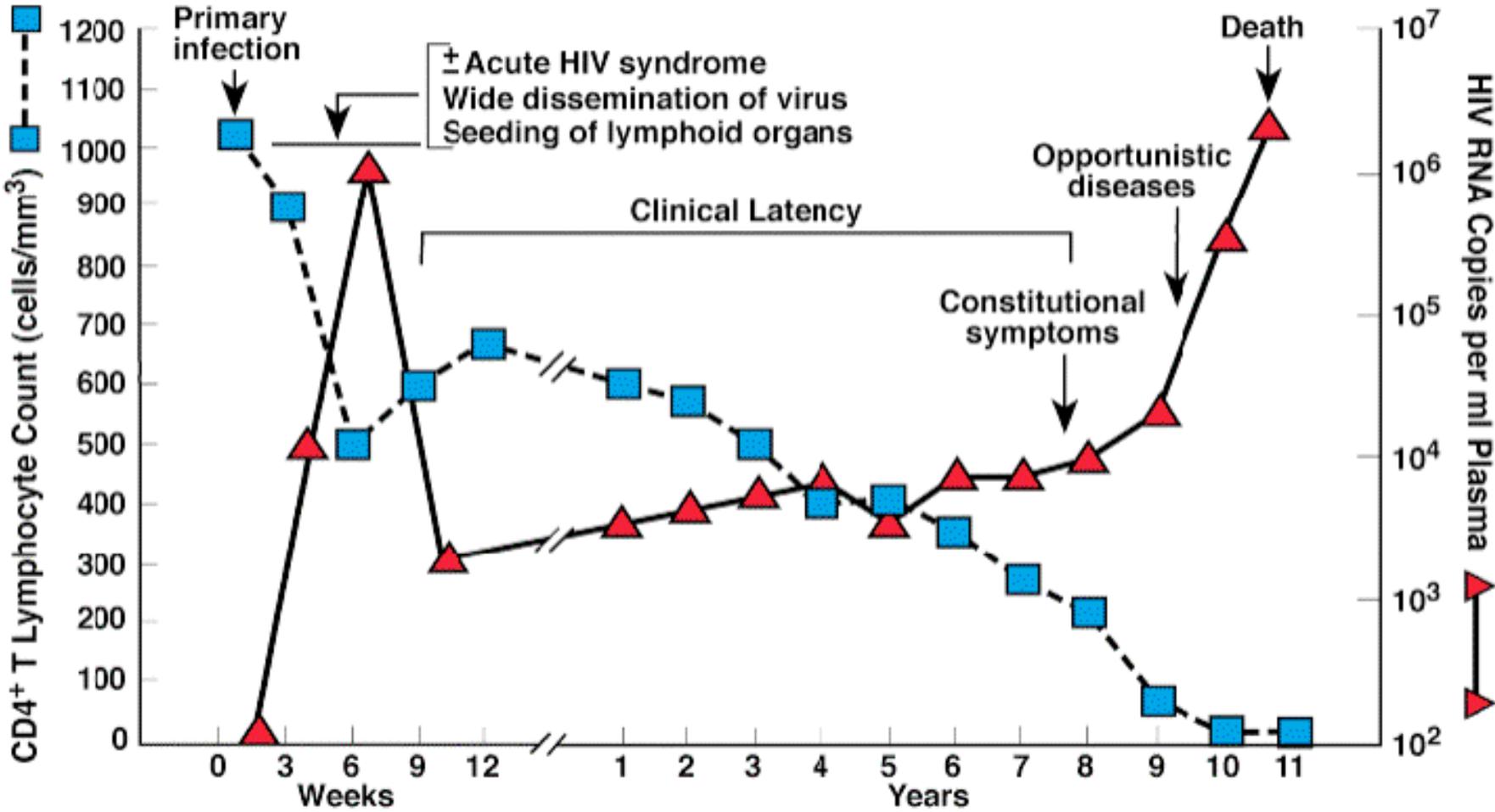


The virus that infects
CD4 cells

AIDS



Typical Course of HIV Infection



Modified From: Fauci, A.S., et al, *Ann. Intern. Med.*, 124:654, 1996

HIV Treatment “Then”



1980s



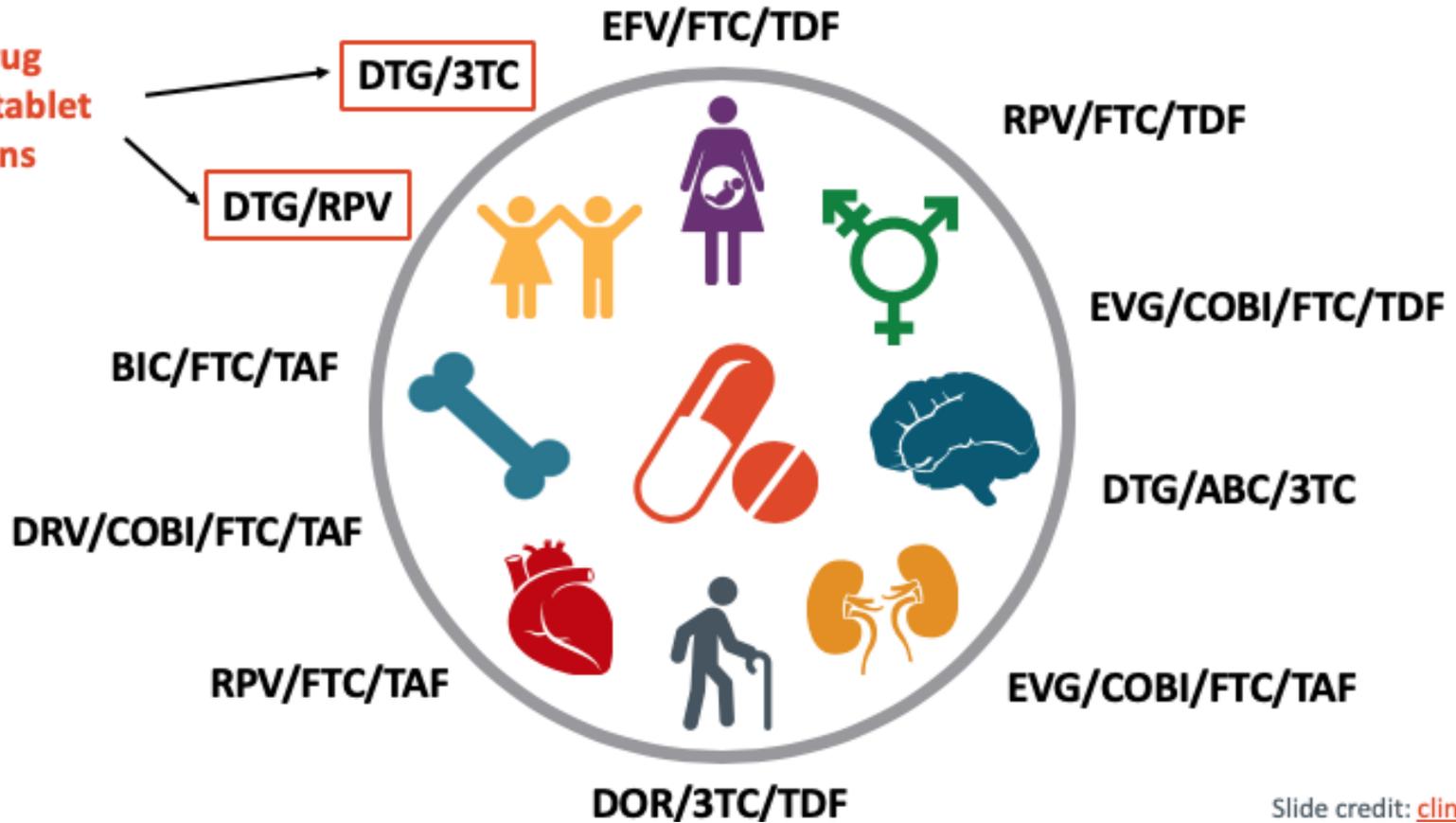
1990s

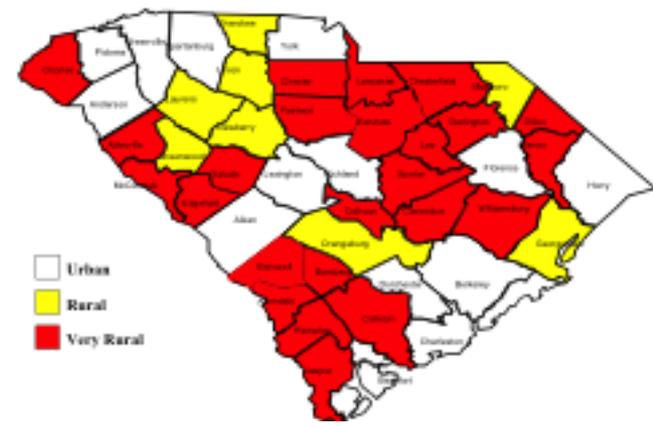
HIV Treatment Today



Fixed-Dose Single Tablet Regimens

Two-drug
single-tablet
regimens

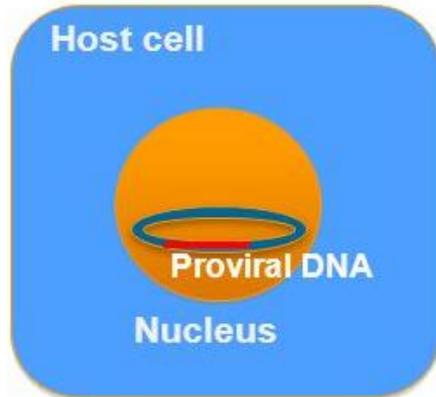




 **RYAN WHITE
WELLNESS CENTER**
ROPER ST. FRANCIS

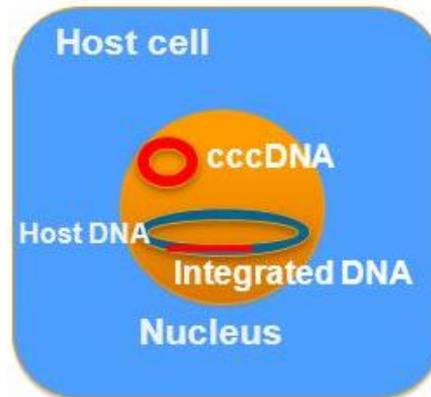


HIV



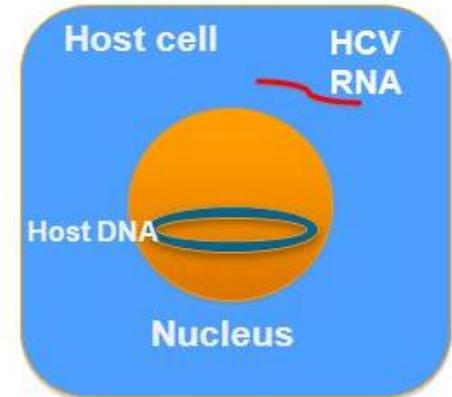
Life-long suppression
of viral replication

HBV



Long-term suppression
of viral replication

HCV



Definitive viral clearance
and SVR

Medical (Pill) "Victories"	"Easy" to Suppress "Easy" to Prevent Normal Lifespan	Kind of easy to suppress 100% Preventable with vaccination	100% curable
Non-Medical "Delivery" Barriers	Undiagnosed Un-linked/Un-retained Stigma/social Economics (prevention) Access/education	Under-diagnosed Patients and providers may be unaware	Undiagnosed Unlinked Access to care Cost (for uninsured) Social/stigma (IVDU)

Typical Cases – A Tale of 2 Syndromes

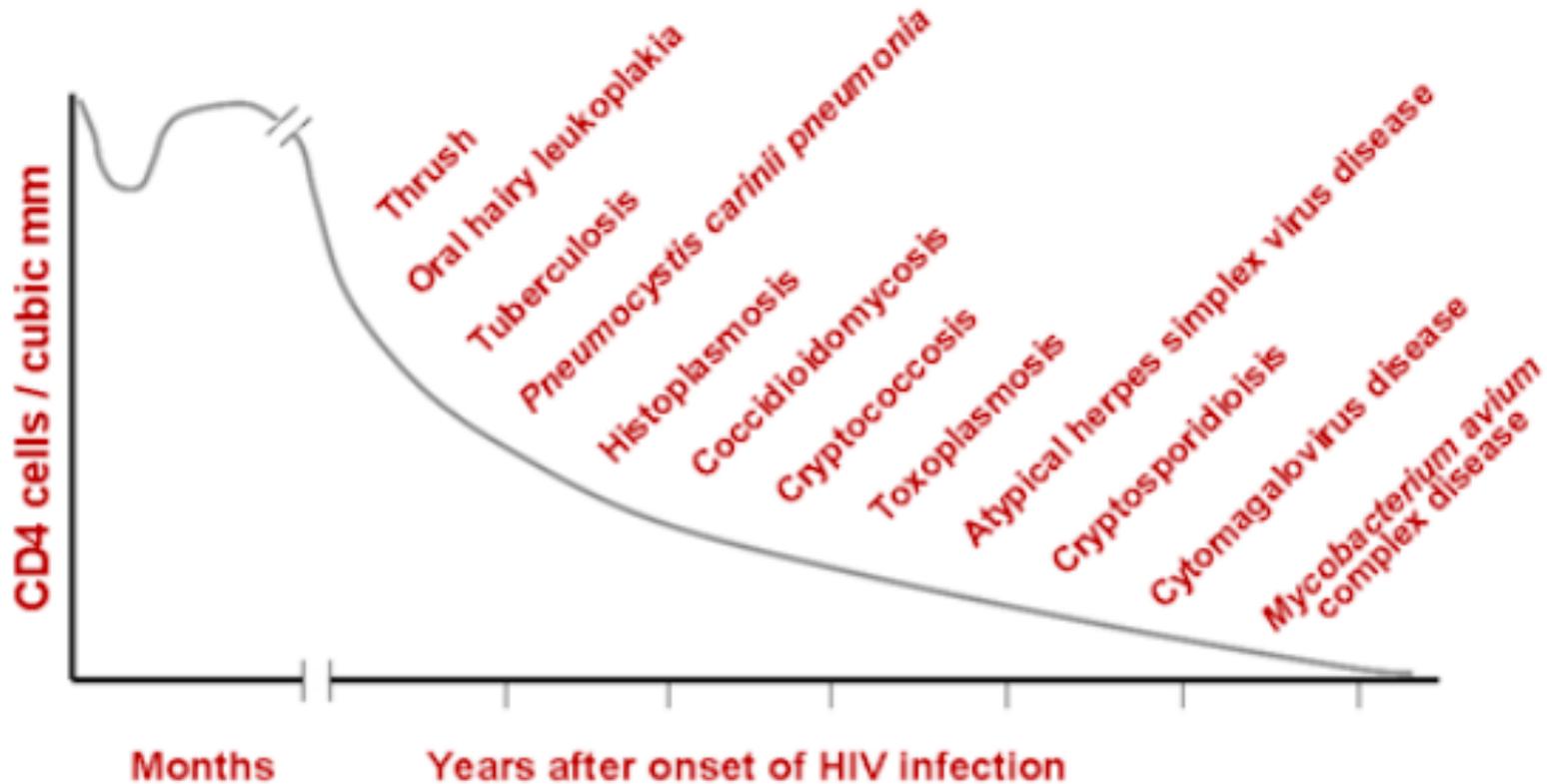
1. 30ish male never HIV diagnosed, CD4 <35
2. 30ish female diagnosed but lost to care, CD4 <35
3. 70ish male diagnosed and in care, CD4 700



1. HIV/AIDS-related heart condition
2. HIV/AIDS-related infection
3. Non-HIV related stroke

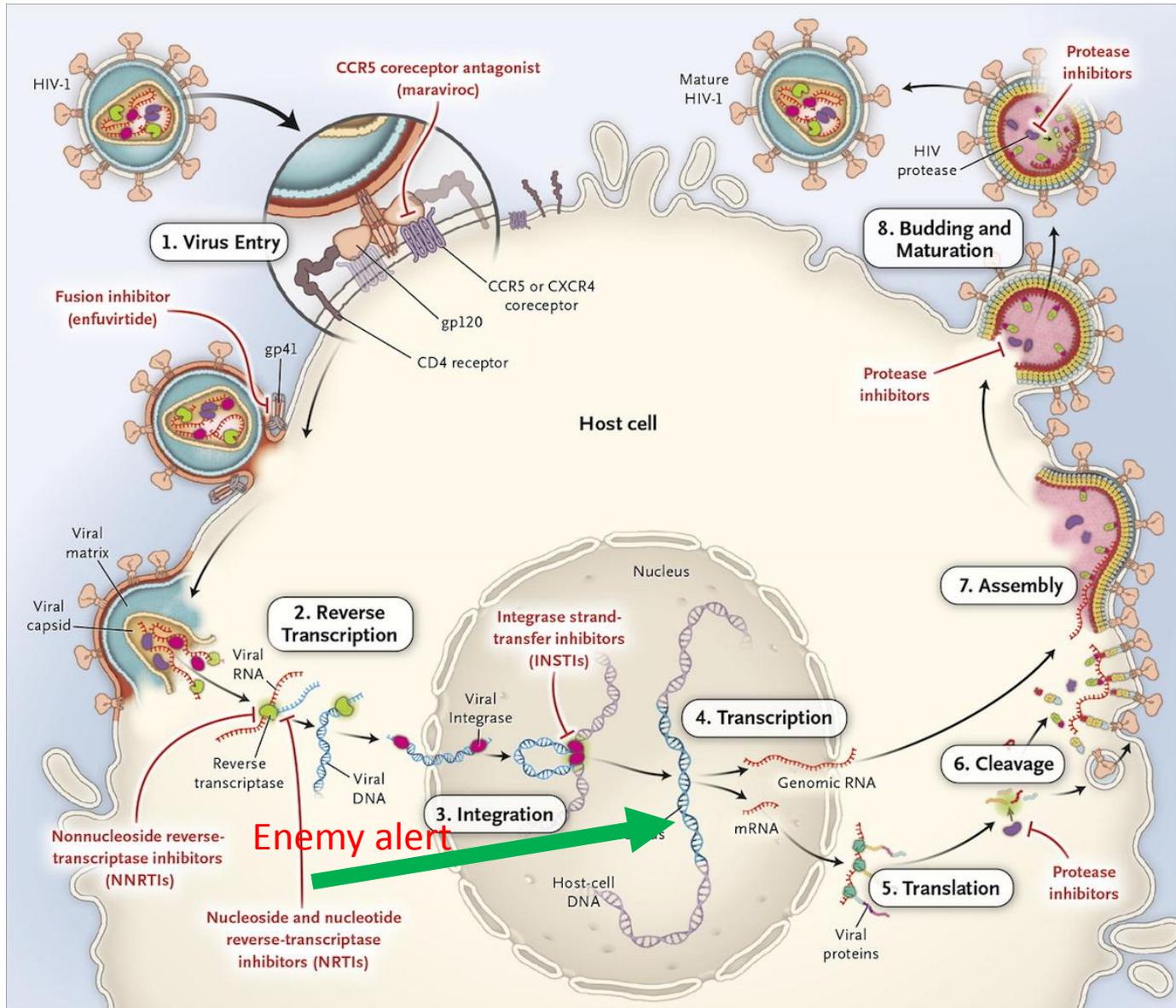
Complications of HIV (AIDS) Still Occurring as we Speak

Natural History of HIV-1 Infection

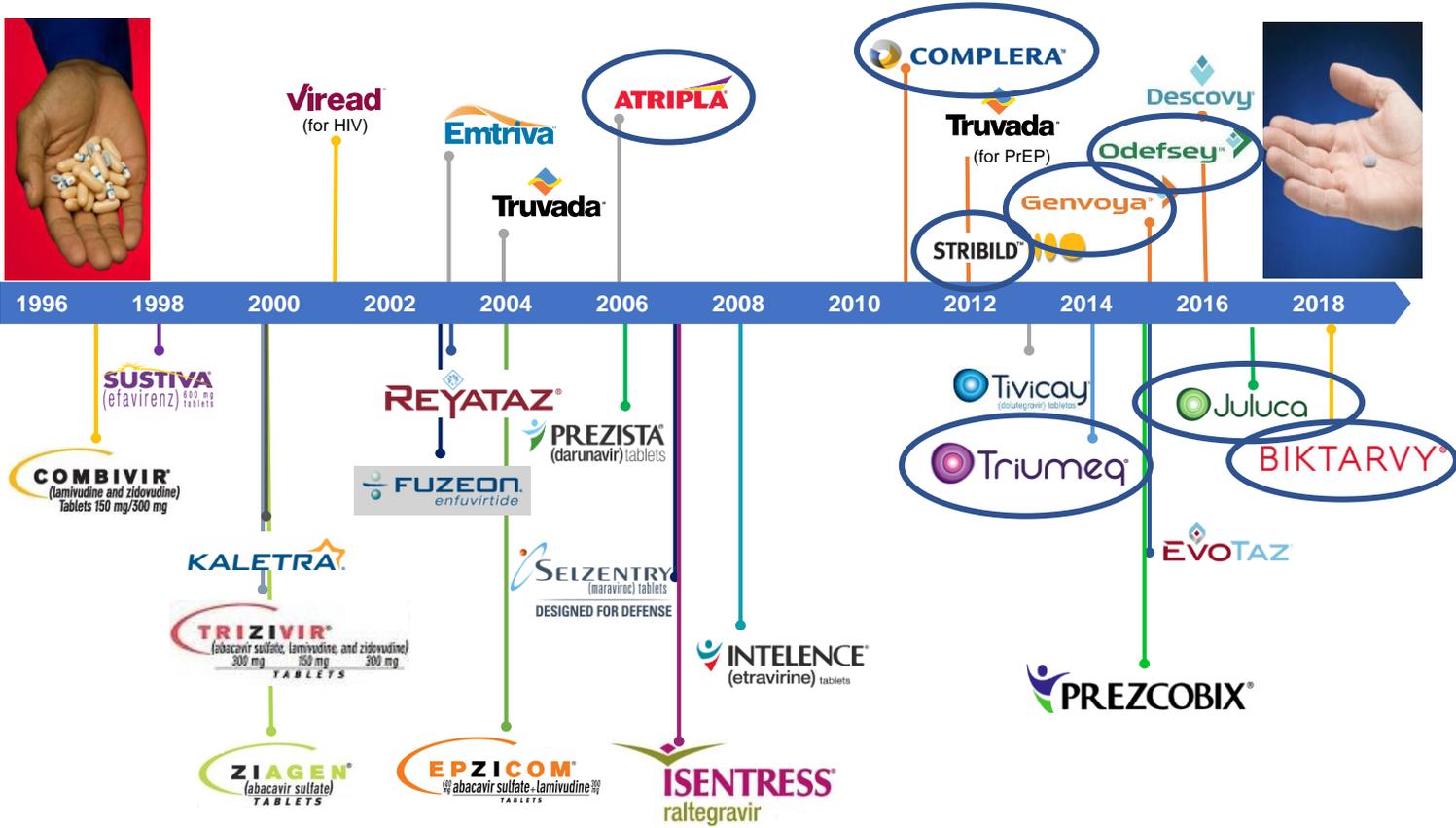


Current Treatment and Outlook for a Cure

HIV Therapy: A Large and Expanding Toolkit

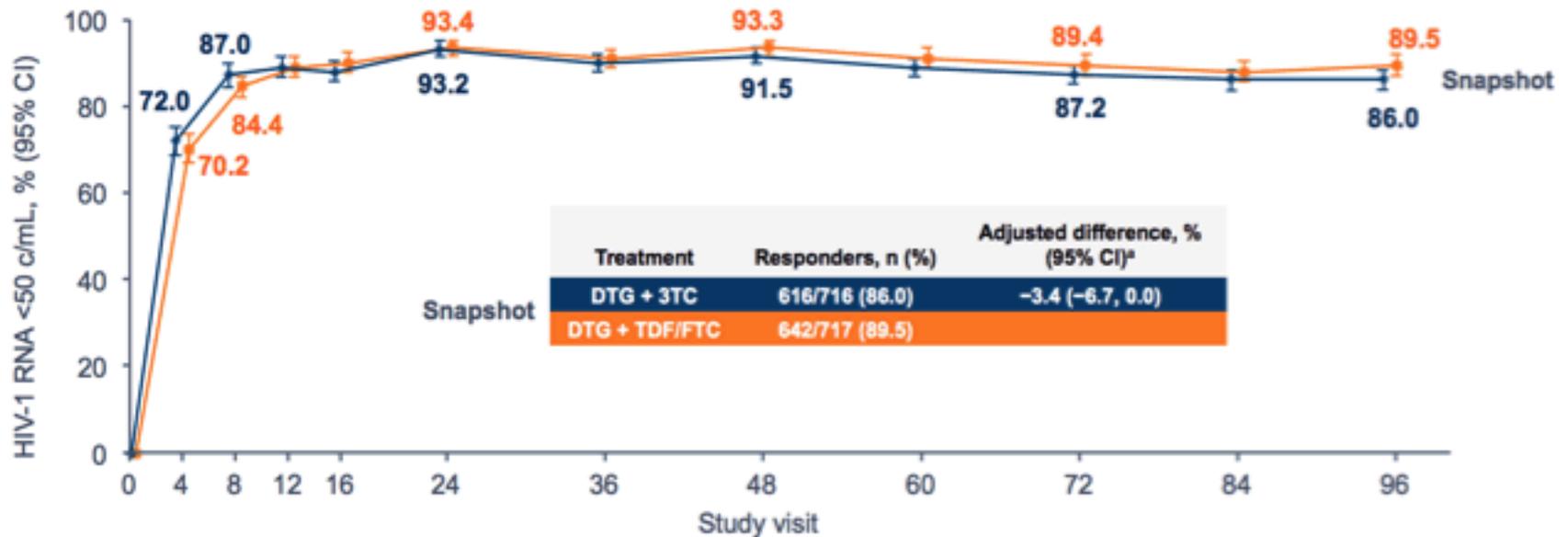


20 Years of Progress in HIV Treatment and Prevention



HIV Therapy: 2 Drugs a Viable Option

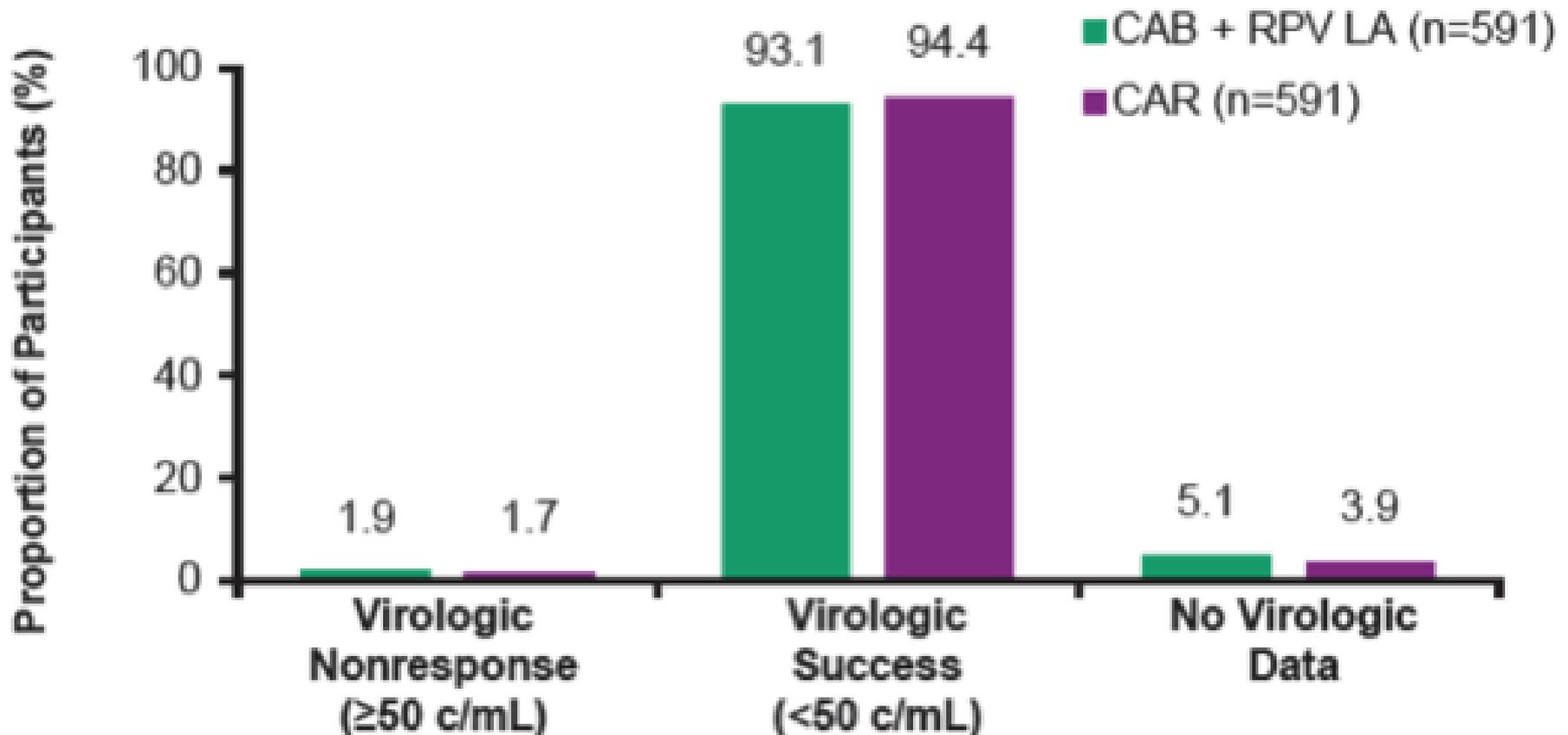
DTG + 3TC IS NON-INFERIOR TO DTG + TDF/FTC IN SNAPSHOT HIV-1 RNA <50 C/ML AT WEEK 96



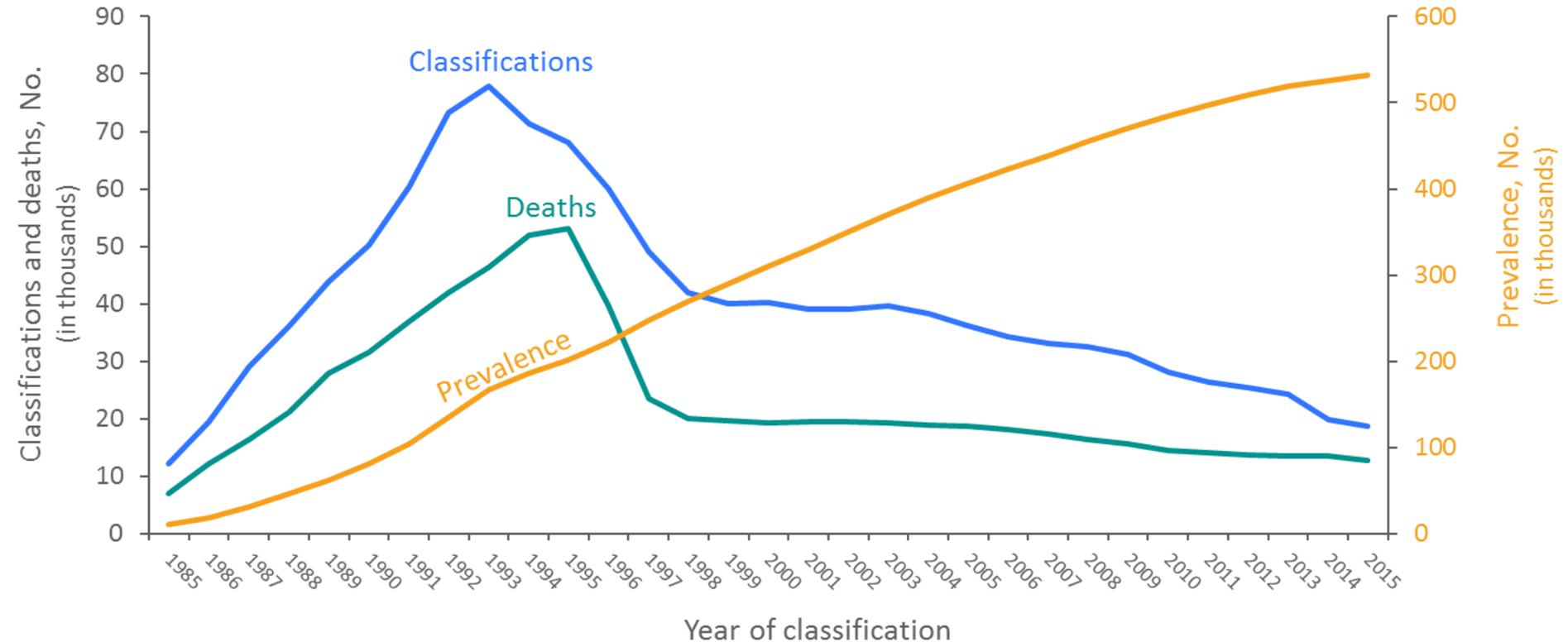
Non-inferiority criteria were met for GEMINI-1, GEMINI-2, and the pooled analysis^b

HIV Therapy: Monthly Injectable Therapy on the Horizon (Not yet Approved)

Virologic Outcomes



Changing Trends in HIV



Slide Credit – Allison Eckard

Source: Centers for Disease Control and Prevention

Life expectancy for HIV patients approaches that of general population

HIV patients:
74 years

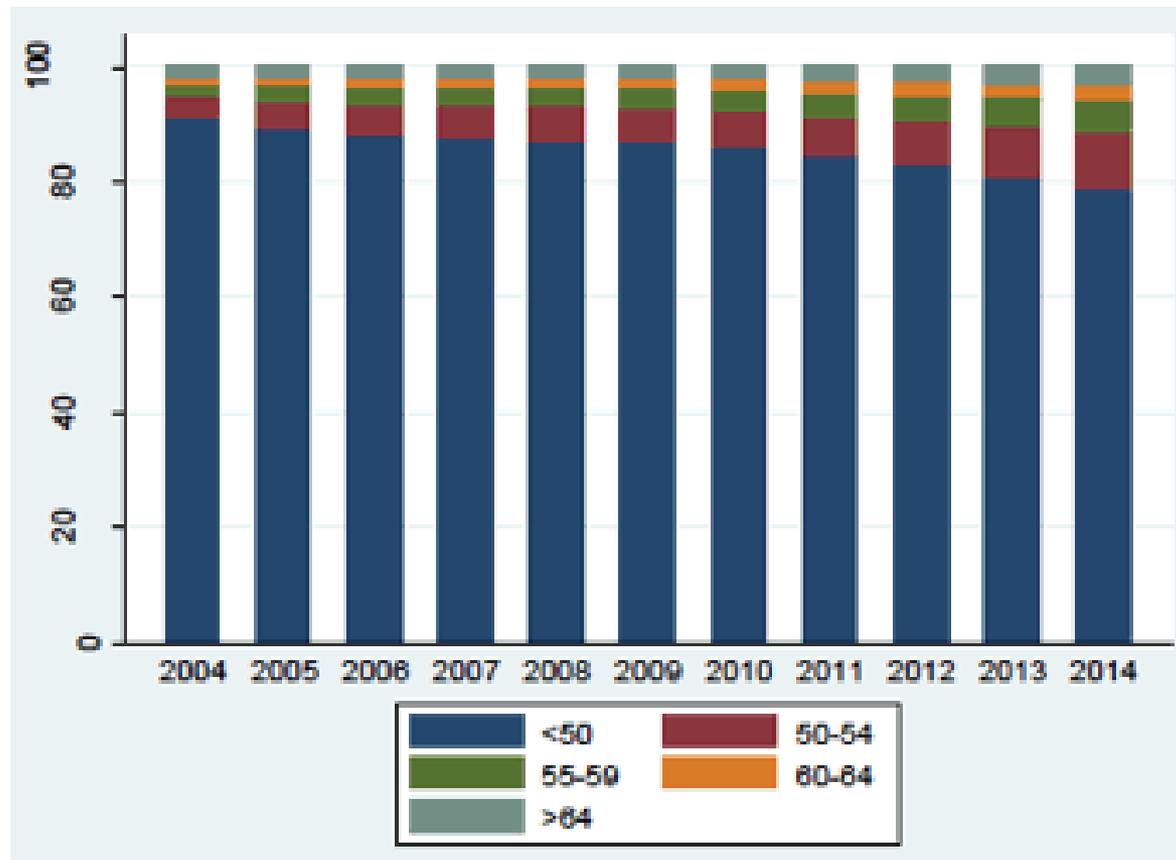
General population:
80 years

Source: Lohse N, Obel N. *Ann Intern Med*. 2016;doi:10.7326/L16-0091.

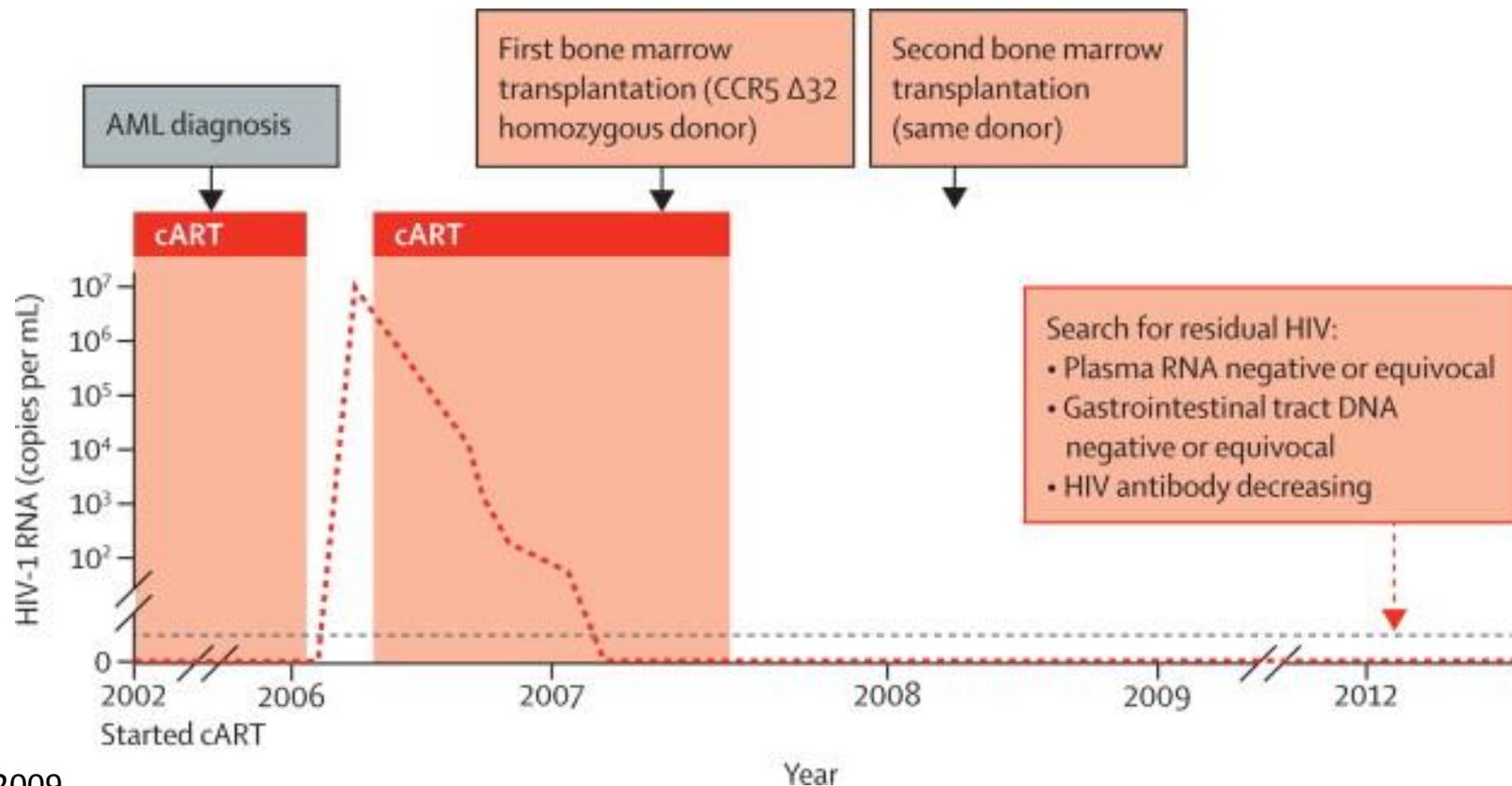
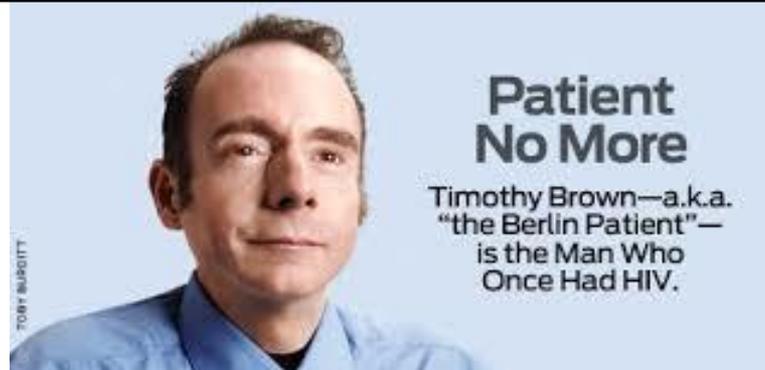
Healio 

Evolution of HIV Infection from a Potentially Fatal to a Potentially Chronic Medical Condition

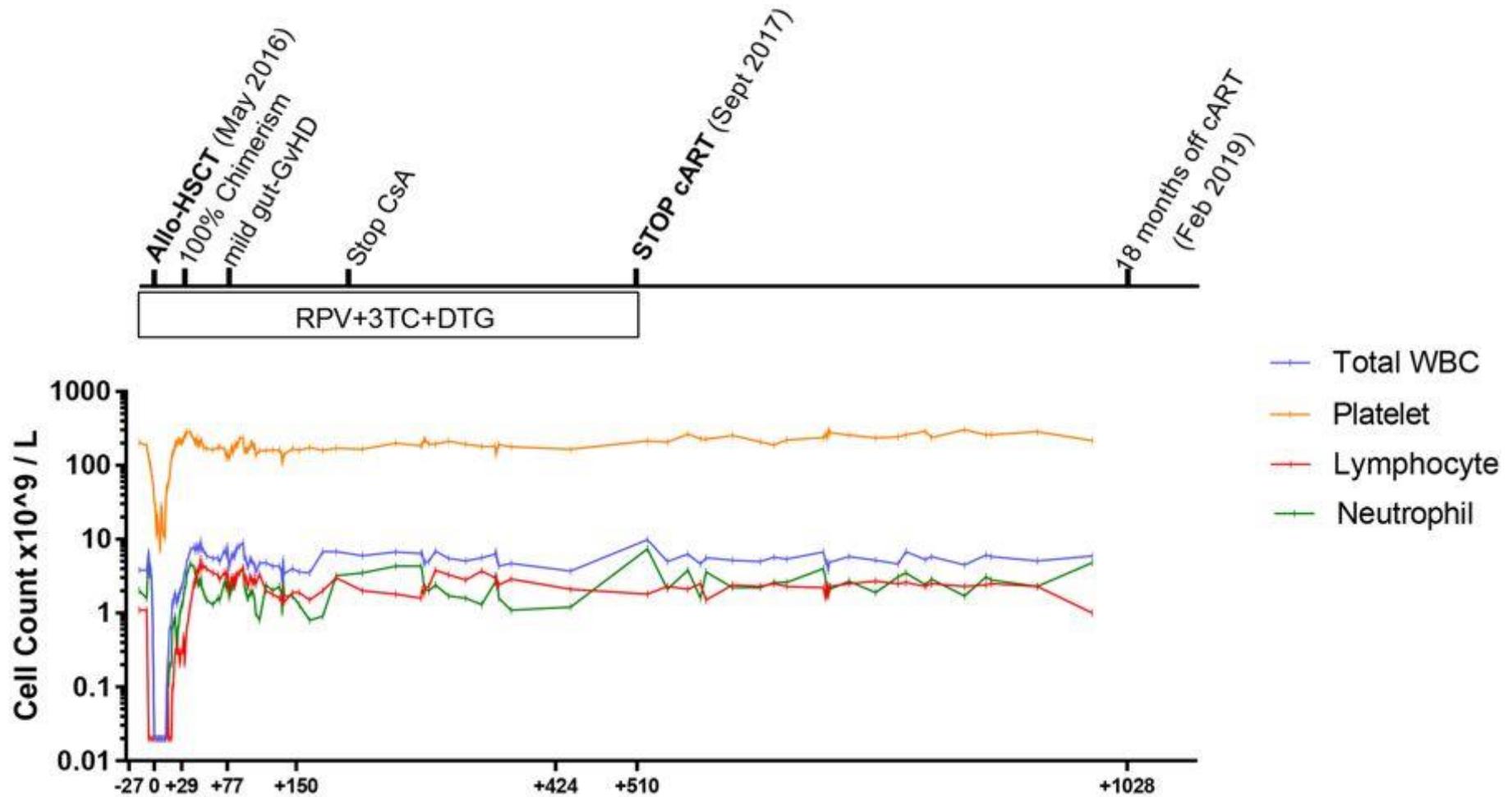
Impact of Aging on non-AIDS Comorbidity in Large Spanish HIV Cohort



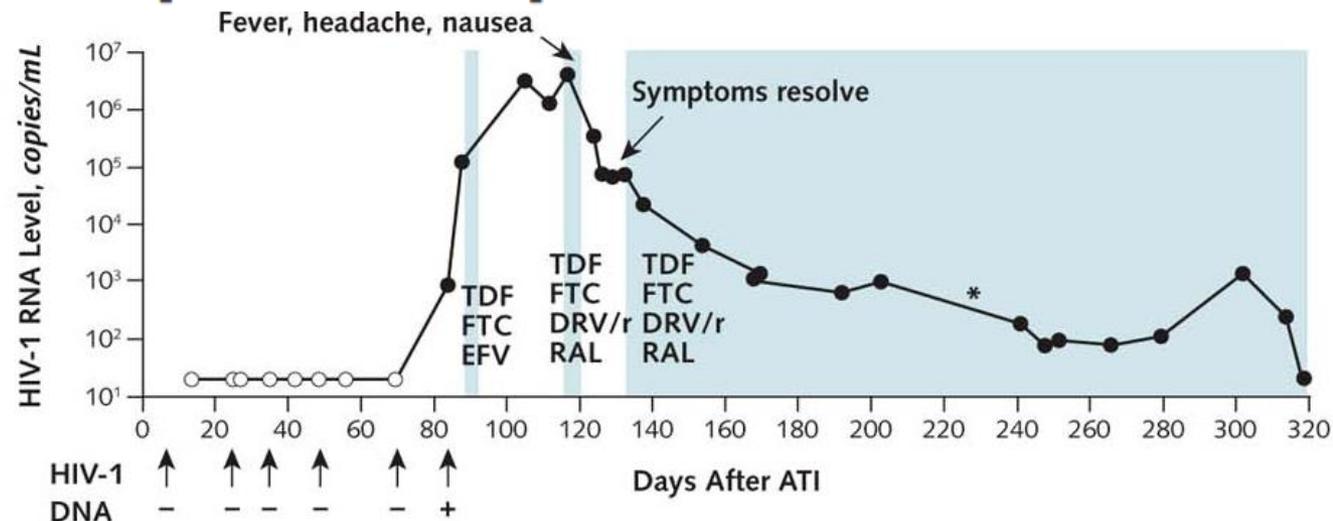
The First Cure: The “Berlin” Patient



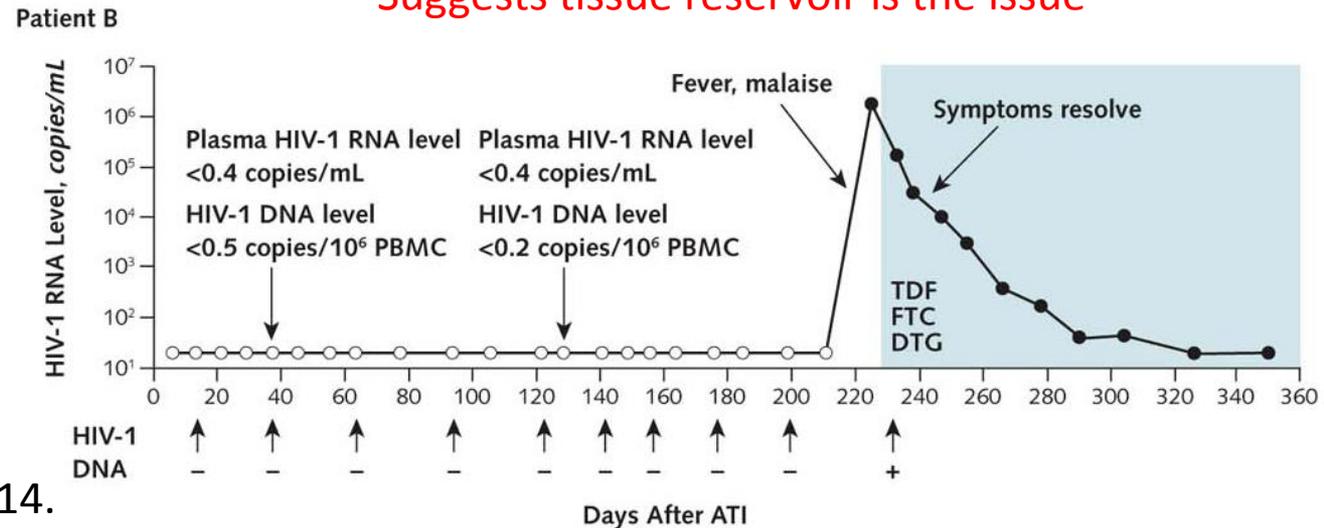
The 2nd Cure: The “London” Patient



Antiretroviral-Free HIV-1 Remission and Viral Rebound After Allogeneic Stem Cell Transplantation: Report of 2 Cases

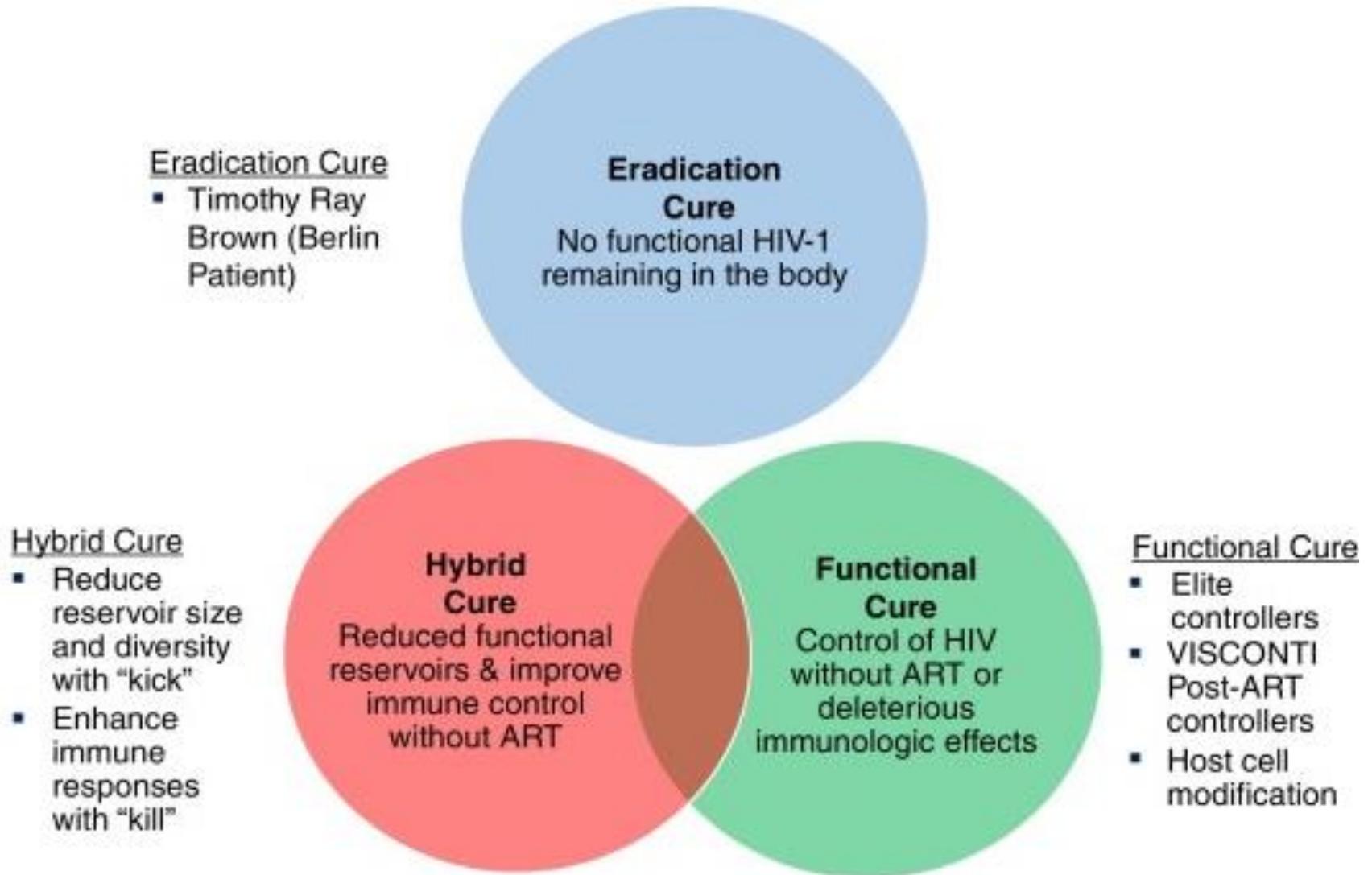


1000-10,000 fold reduction in reservoir size
 No detectable virus in blood or rectal mucosa before ATI
 Single virus accounted for recrudescence
 Suggests tissue reservoir is the issue



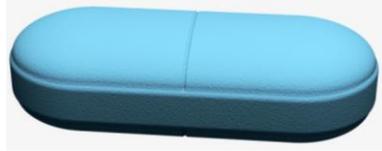
Hill, PNAS, 2014.

Multiple Pure Strategies Being Pursued



Current Outlook on Prevention

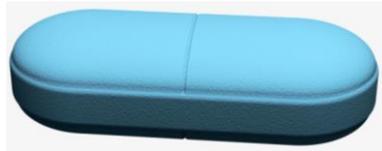
HIV Treatment Now = Available Meds Offer Near Complete Prevention



=

Prevent
Infection

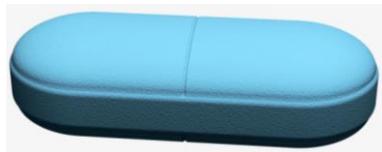
PrEP



=

Prevent
Transmission

U=U



=

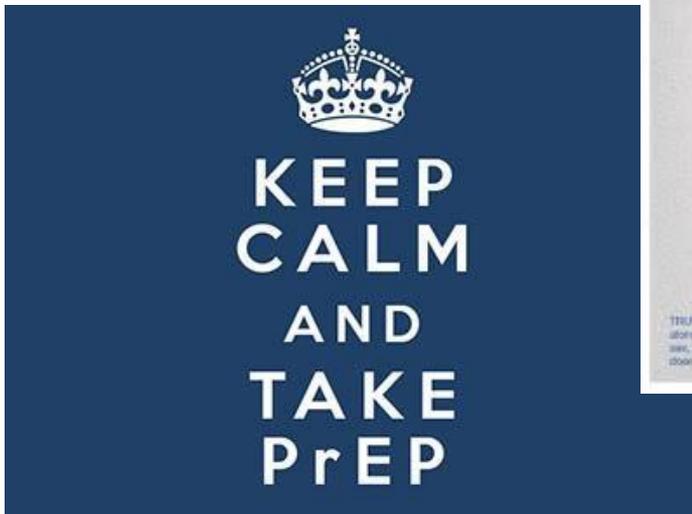
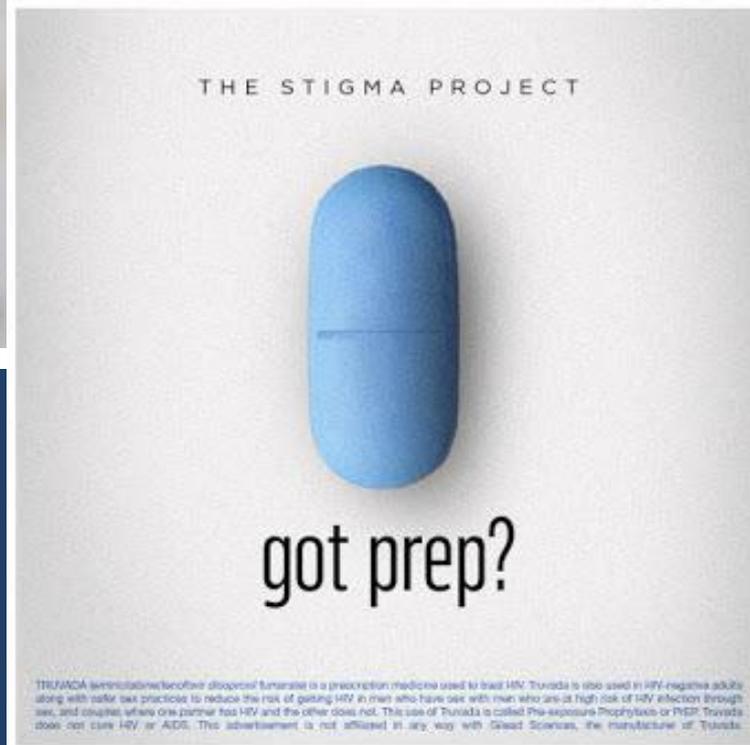
Prevent
AIDS

Normal
Lifespan

Unlike HCV, HIV is well-financed for the uninsured thanks to Ryan White.

PrEP for Prevention

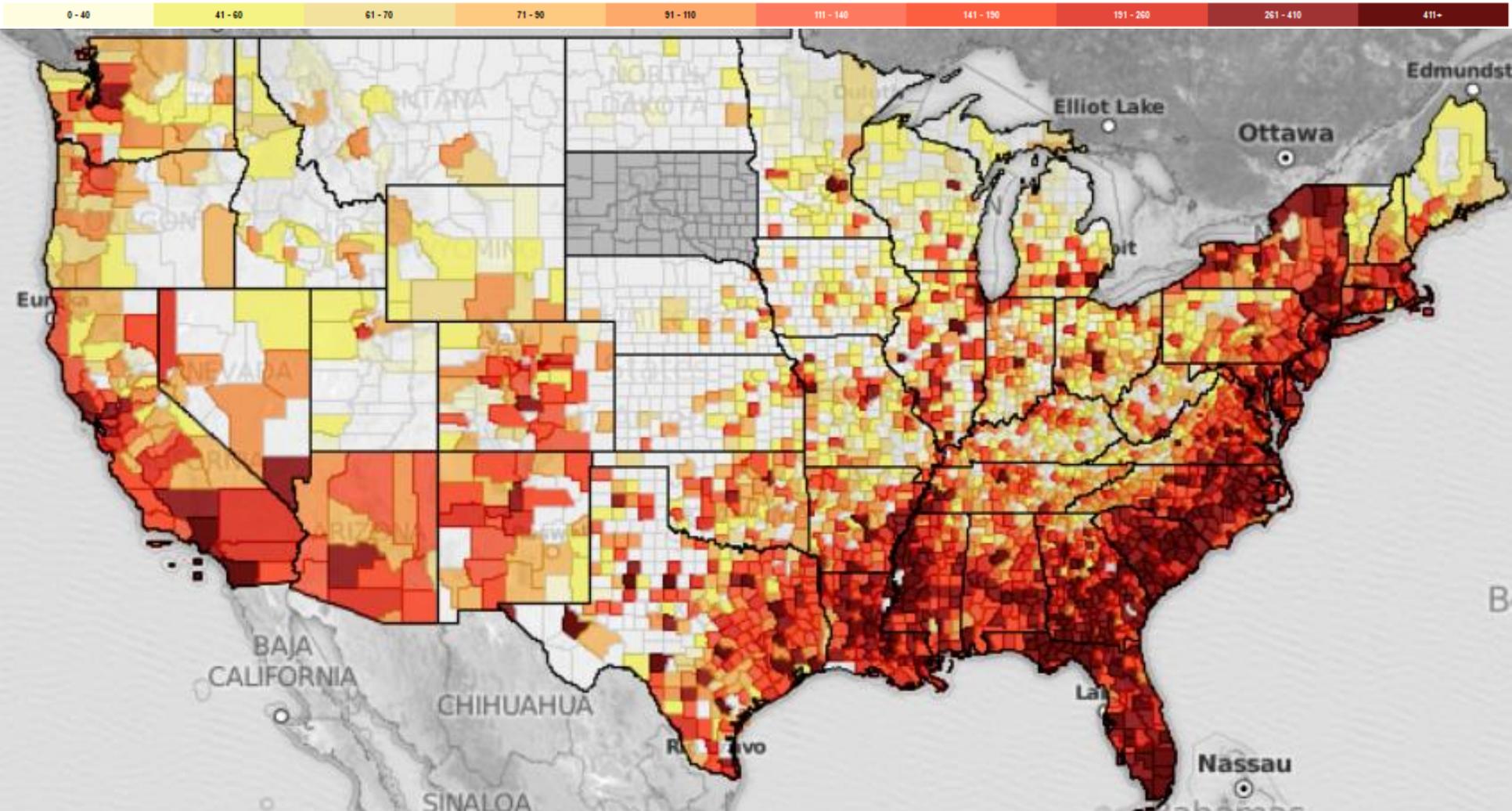
- Pre-exposure prophylaxis (PrEP)



The time for debate on the effectiveness of PrEP is over.

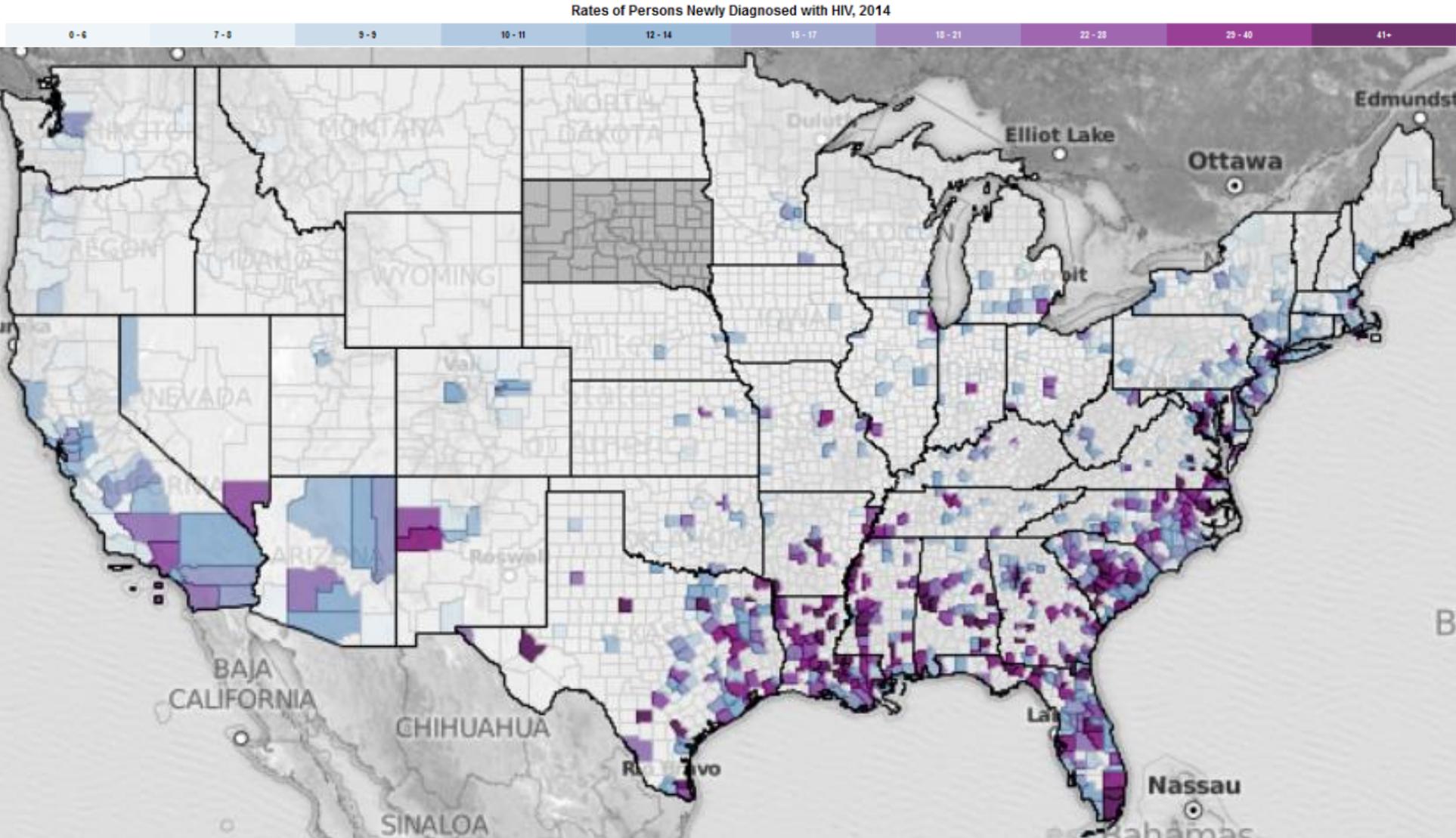
HIV Prevalence is Highest in Southern States

Rates of Persons Living with Diagnosed HIV, 2013



44% of all persons living with HIV live in Southern states (CDC: *HIV in the Southern United States*. May 2016.)

HIV Incidence is Highest in Southern States

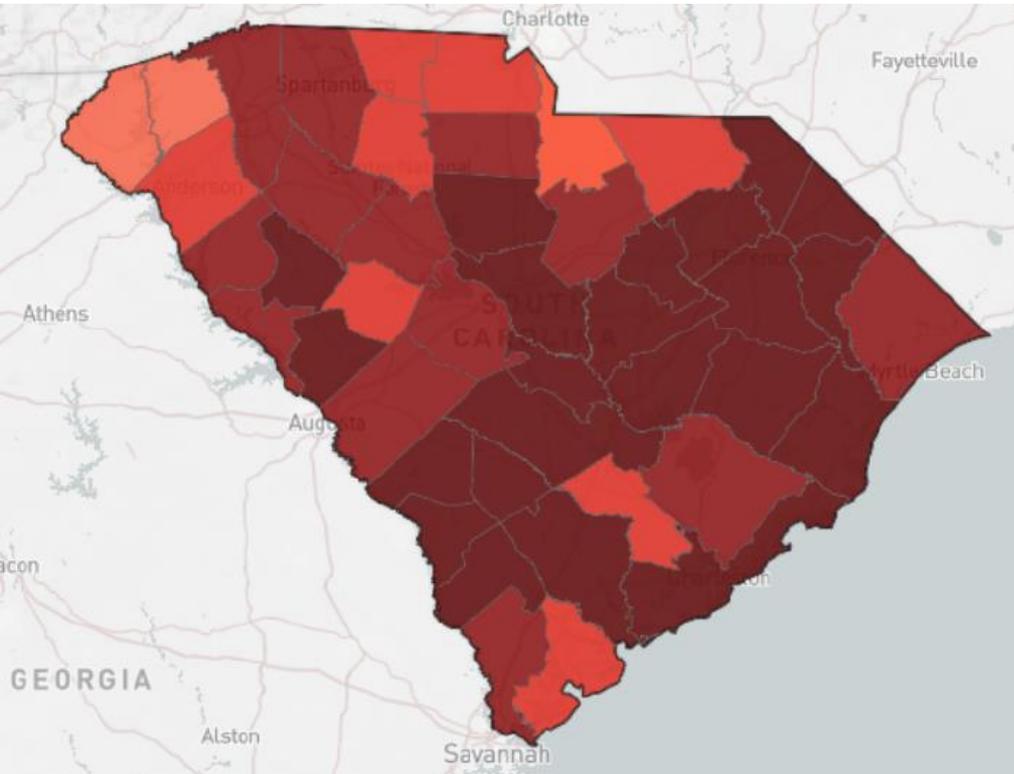


54% of all new HIV diagnoses occur in southern states (CDC: *HIV in the Southern United States*. May 2016.)

Source: Aidsvu.org, 2013 data

Units: Persons per 100,000

HIV in South Carolina



- ~20,000 persons living with HIV
- 69% African American
 - 70% Male
- ~750 new cases/year
(we know how to prevent)
- ~300 deaths/year
(avoidable with treatment)

End the HIV Epidemic: A Plan for America

Ending
the
HIV
Epidemic

GOAL:

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



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



Diagnose all people with HIV as early as possible.

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

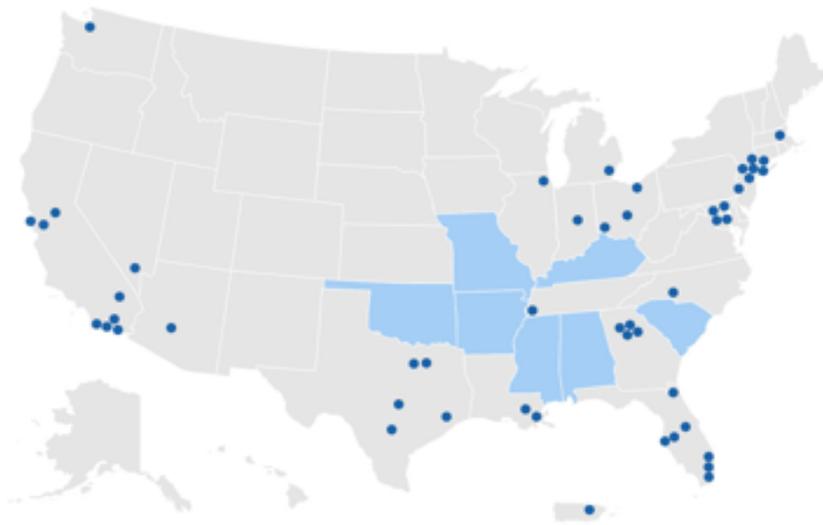


Prevent new HIV transmissions by using proven interventions, including pre-exposure prophylaxis (PrEP) and syringe services programs (SSPs).

Respond quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them.



End the HIV Epidemic: Focus on Areas with Highest Rates of New Infections

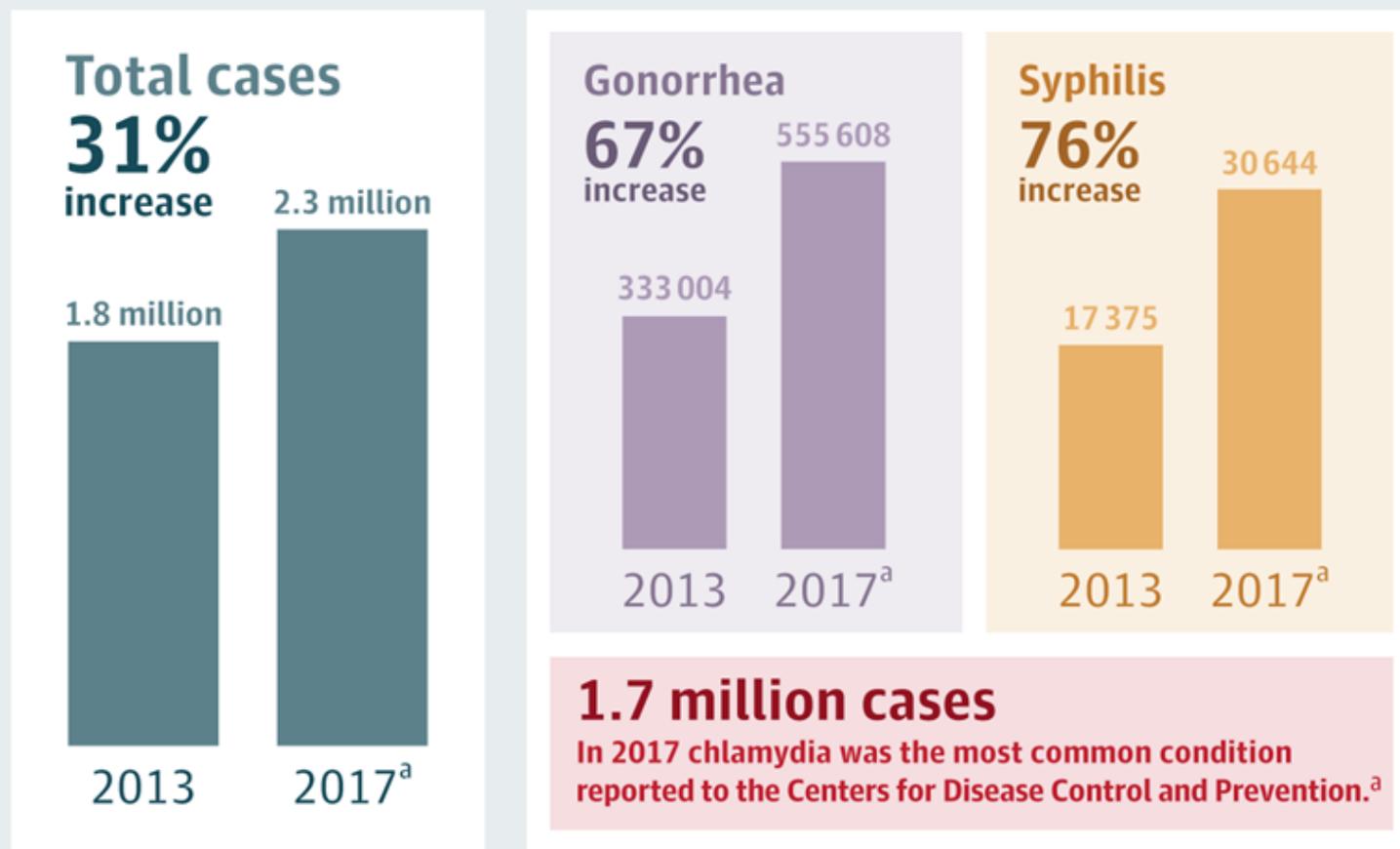


- In 2016-2017, > 50% of new HIV diagnoses occurred in 48 counties; Washington, DC; and San Juan, Puerto Rico
- 7 states have high rural burden: > 75 cases and $\geq 10\%$ of diagnoses in rural areas

This is in Context Where STD Rates are on the Rise

The United States is experiencing steep, sustained increases in sexually transmitted diseases.

Combined diagnoses of chlamydia, gonorrhea, and syphilis increased sharply over the past 5 years.



^aPreliminary data

And the Lifetime Risk for HIV Acquisition in Some Groups Remains High

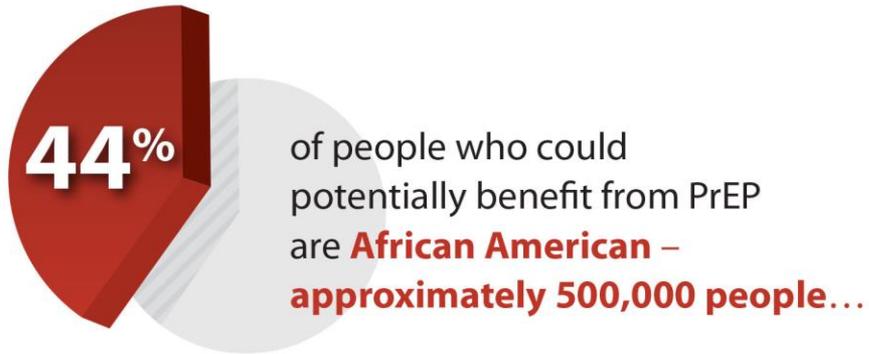
Lifetime Risk of HIV Diagnosis among MSM by Race/Ethnicity



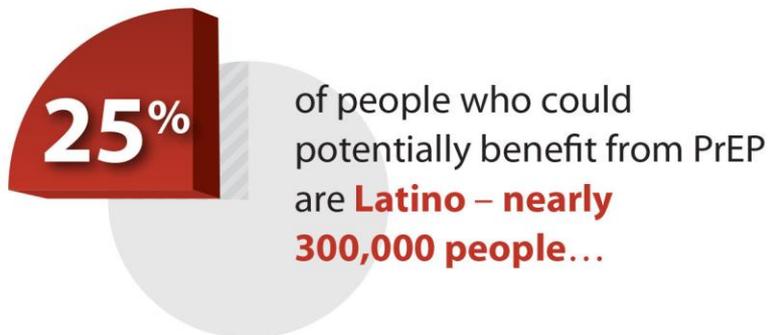
Source: Centers for Disease Control and Prevention

CDC: PrEP Uptake is Too Low

HIV prevention pill is not reaching most who could potentially benefit – especially African Americans and Latinos



...but only **1%** of those – **7,000 African Americans** – were prescribed PrEP*



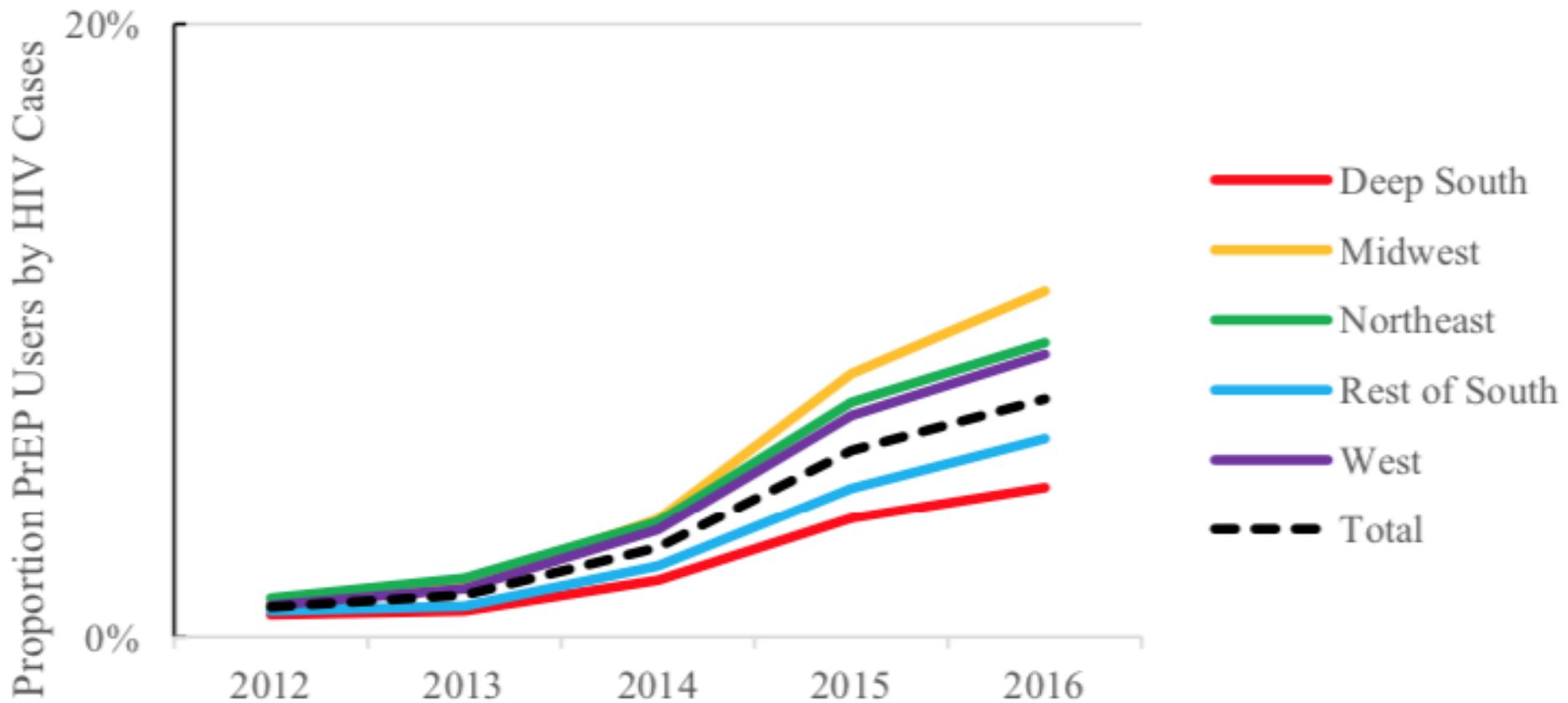
...but only **3%** of those – **7,600 Latinos** – were prescribed PrEP*



*Prescription data in this analysis limited to those filled at retail pharmacies or mail order services from September 2015 – August 2016; racial and ethnic information not available for one-third of the prescription data

PrEP Uptake is the Lowest in the South

Figure 11. Proportion of PrEP Users and Total HIV Cases by Region, 2012-2016



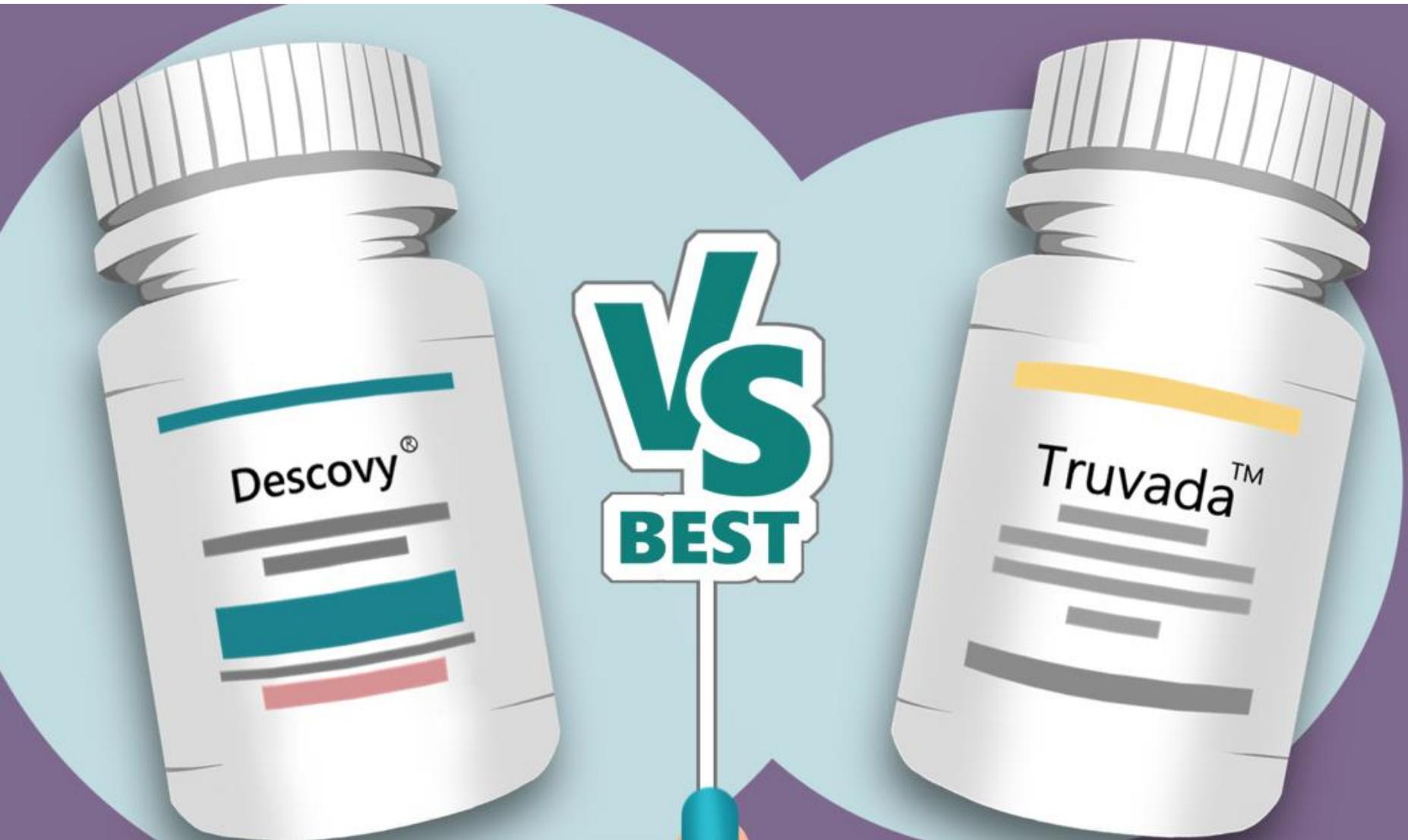
PrEP Use is Rising but Still Plenty of Room for Growth

Measure	2012	2013	2014	2015	2016	2017
HIV incidence rate (new diagnoses)	4.72	4.65	4.18	3.70	3.66	3.46
PrEP use per 100 persons at risk*	1.6	2.2	4.4	9.6	11.9	15.4
PLWH proportion with virologic suppression [†]	79.8	81.9	83.3	84.5	85.7	86.7

*PrEP use calculated as persons receiving FTC/TDF divided by persons with PrEP indication in each MSA.

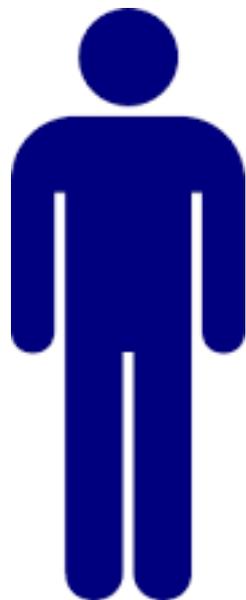
[†]TasP measured by proxy: proportion with HIV-1 RNA < 200 copies/mL among those with ≥ 1 viral load test.

Expanding Medical Toolkit for Prevention



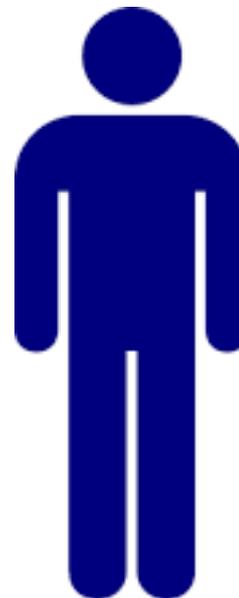
Like HIV Treatment, PrEP for HIV Prevention is a a Major Delivery Issue

At risk



Deliver Prevention
Deliver Education

Infected



Diagnose
Deliver Treatment

One of our main jobs in 2020
Devise and implement novel ways of delivery

HIV Treatment as Prevention



Health » Food | Fitness | Wellness | Parenting | Live Longer

Live TV

U.S. Edition +



40% of people with HIV transmit most new infections in the US, a new analysis says. Here's the plan to stop the spread



By **Susan Scutti**, CNN

Updated 3:33 PM ET, Mon March 18, 2019



1/2

Half of people with HIV know it, are in care, and are virally suppressed or undetectable.

8 in 10

8 in 10 new HIV infections come from people not in HIV care.

90%

New US goal: cut new HIV infections by at least 90% in 10 years. The time is now.

HIV Treatment as Prevention: U = U

Dear Colleague: September 27, 2017



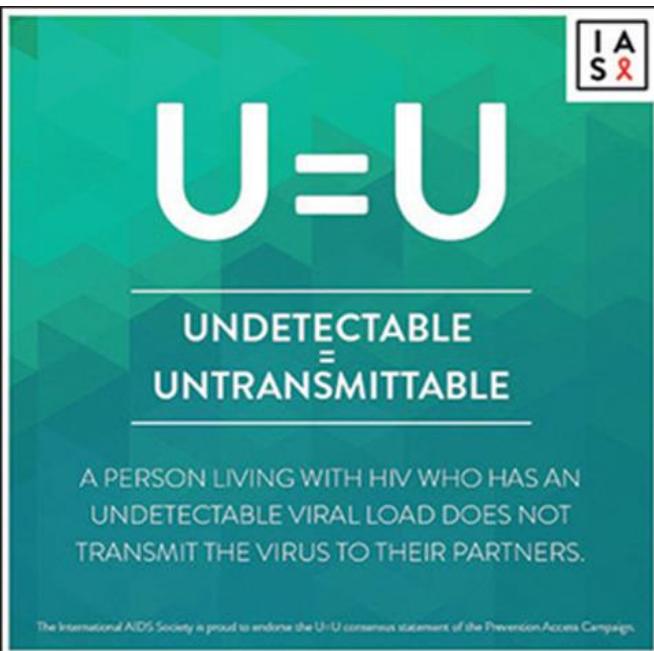
Dear Colleague

INFORMATION FROM CDC'S DIVISION OF HIV/AIDS PREVENTION

September 27, 2017

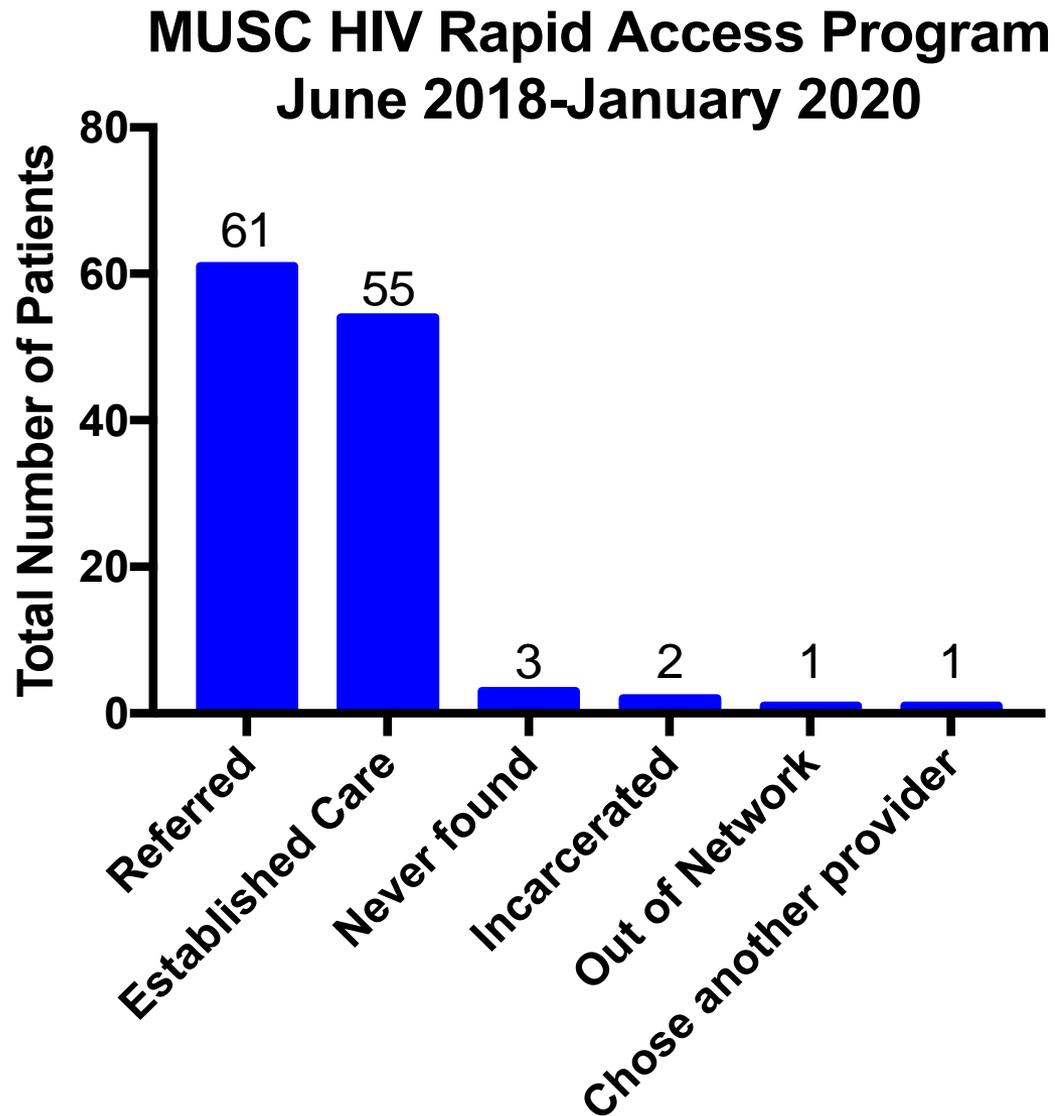
Dear Colleague,

Today is [National Gay Men's HIV/AIDS Awareness Day](#). On this day, we join together in taking actions to prevent HIV among gay and bisexual men and ensure that all gay and bisexual men living with HIV get the care they need to stay healthy. Gay and bisexual men are severely affected by HIV. More than 26,000 gay and bisexual men received an HIV diagnosis in 2015, representing two-thirds of all new diagnoses in the United States, and diagnoses increased among Hispanic/Latino gay and bisexual men from 2010 to 2014.



Across three different studies, including thousands of couples and many thousand acts of sex without a condom or pre-exposure prophylaxis (PrEP), no HIV transmissions to an HIV-negative partner were observed when the HIV-positive person was virally suppressed. **This means that people who take ART daily as prescribed and achieve and maintain an undetectable viral load have effectively no risk of sexually transmitting the virus to an HIV-negative partner.**

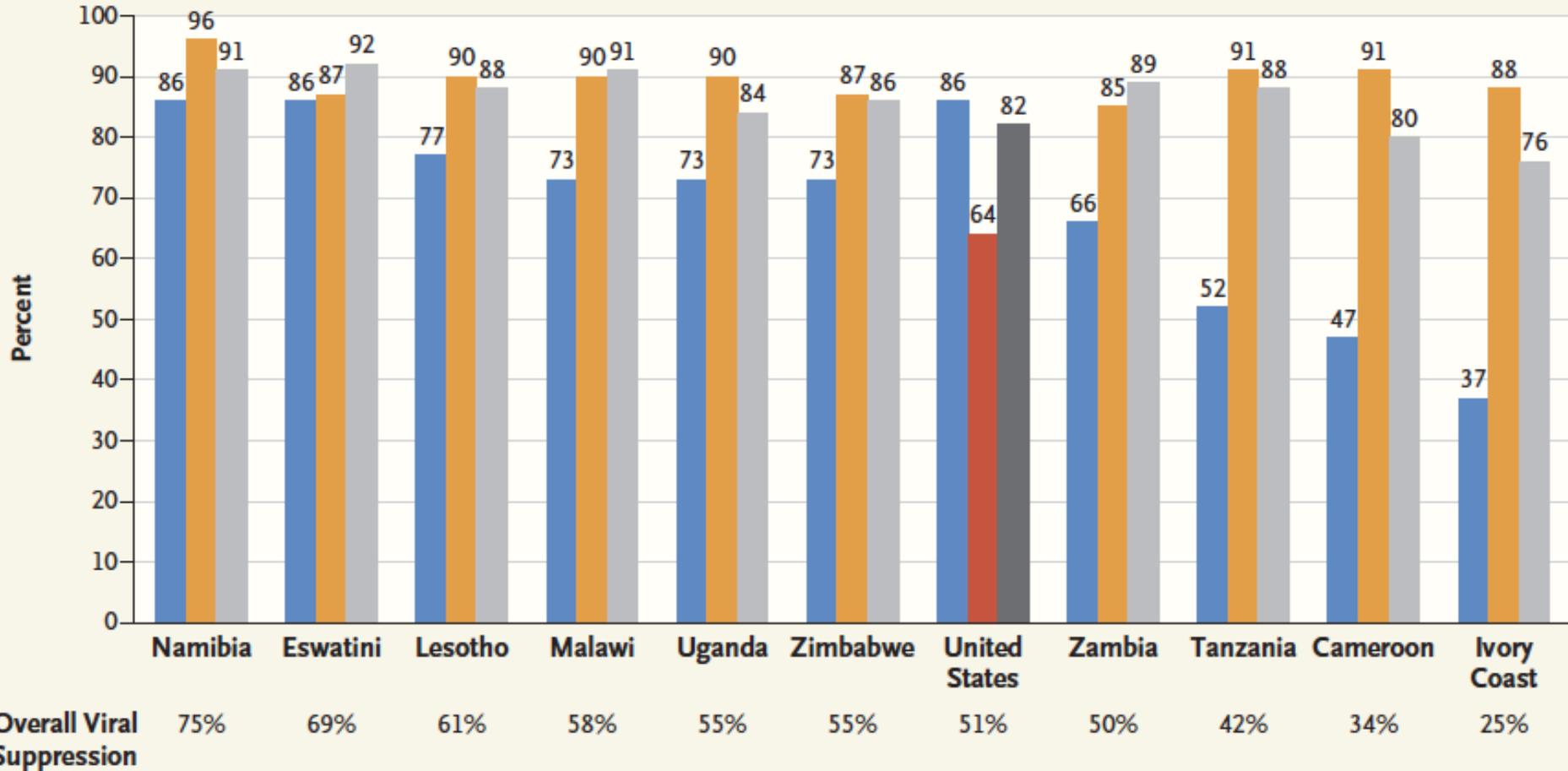
HIV Rapid Access Program- Start ARVs Same Day as Diagnosis (or soon thereafter)



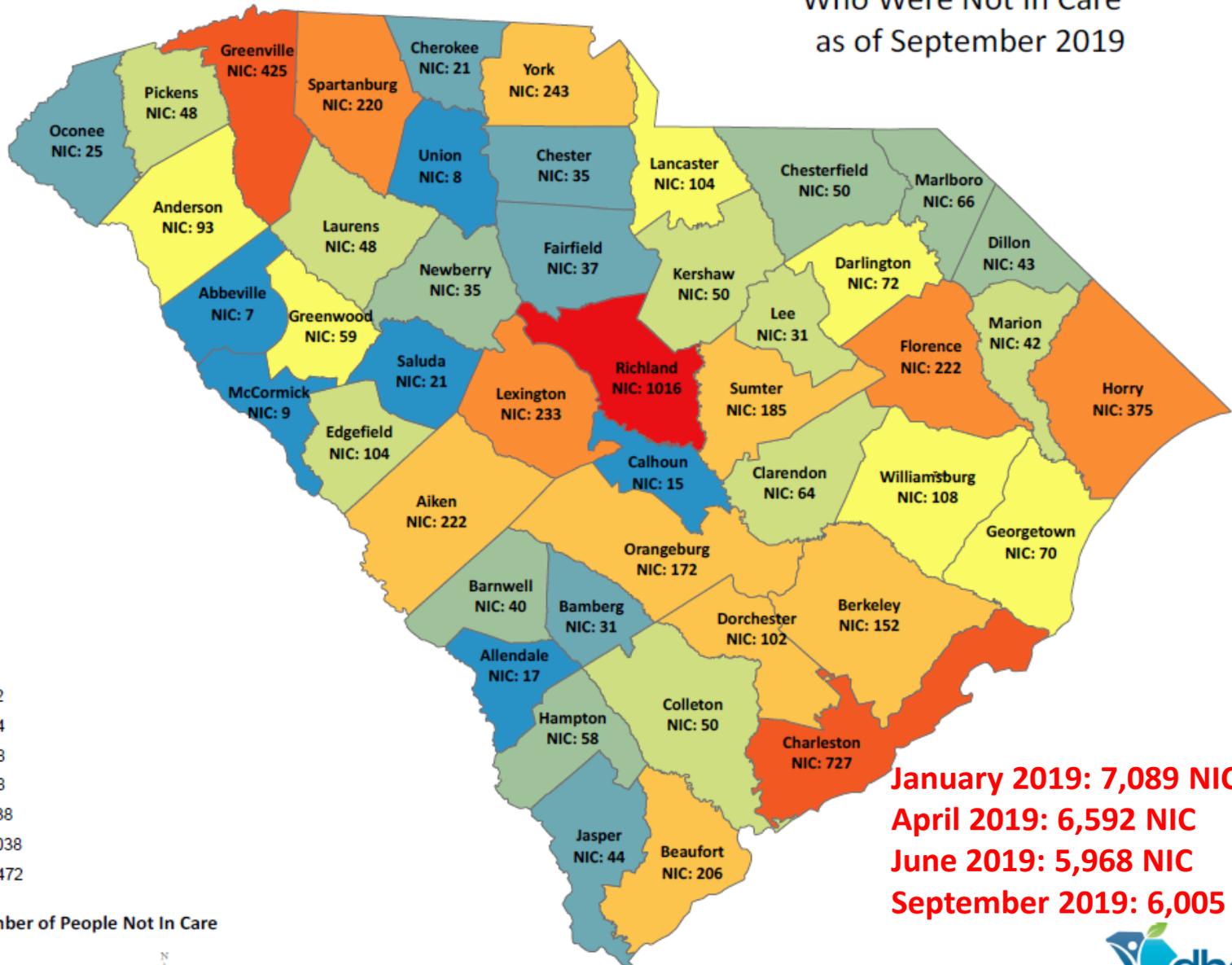
Barriers to Treatment and Long-Term Adherence

HIV in the US: Inadequate Retention in Care

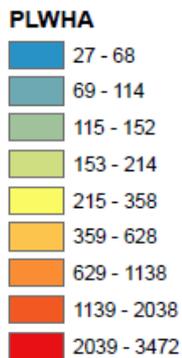
■ Aware of HIV status
 ■ Aware of HIV status and receiving ART
 ■ Receiving ART and achieved viral suppression
■ Aware of HIV status and received HIV care (U.S.)
 ■ Receiving HIV care and achieved viral suppression (U.S.)



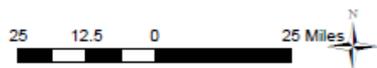
People Living With HIV/AIDS (PLWHA) Who Were Not In Care* as of September 2019



January 2019: 7,089 NIC
April 2019: 6,592 NIC
June 2019: 5,968 NIC
September 2019: 6,005 NIC



NIC: ## = Number of People Not In Care



* Not In Care per Data to Care Program definition

MUSC HIV Clinic

Care for about **~1200** patients each year

3000+ clinic visits/year

400+ females, **800+** males, **9** transgender

800+ African-American, **300+** Caucasian, **40+** Hispanic

Age 13-24 **n=60+**, age 25-44 **n=450+**, age 45-64
n=600+, age > 65 **n=70+**

50% heterosexual, **36%** MSM, **3%** IVDU, **2%** perinatal



- Case management
 - Social work
 - Dental care
 - HIV Pharmacist
 - Outreach team
 - Ryan White Program to cover medical costs
 - ADAP to cover medications
 - Rapid access clinic (treat day of diagnosis)
 - Suboxone therapy
 - Addictions counseling
 - Psychiatric care
 - Gyn care (Wendy Lazenby)
 - Transition Clinic (Allison Eckard)
 - Mental health counseling
 - Same day sick visits (PA Hopkins)
 - Text messaging study
 - STD treatment
 - PrEP/PEP
 - Help with obtaining health insurance
 - ER -> ID Clinic direct referral for STD/PrEP
- Medical care**



Yet the Continuum Still Not Ideal

The U.S. HIV Care Continuum¹

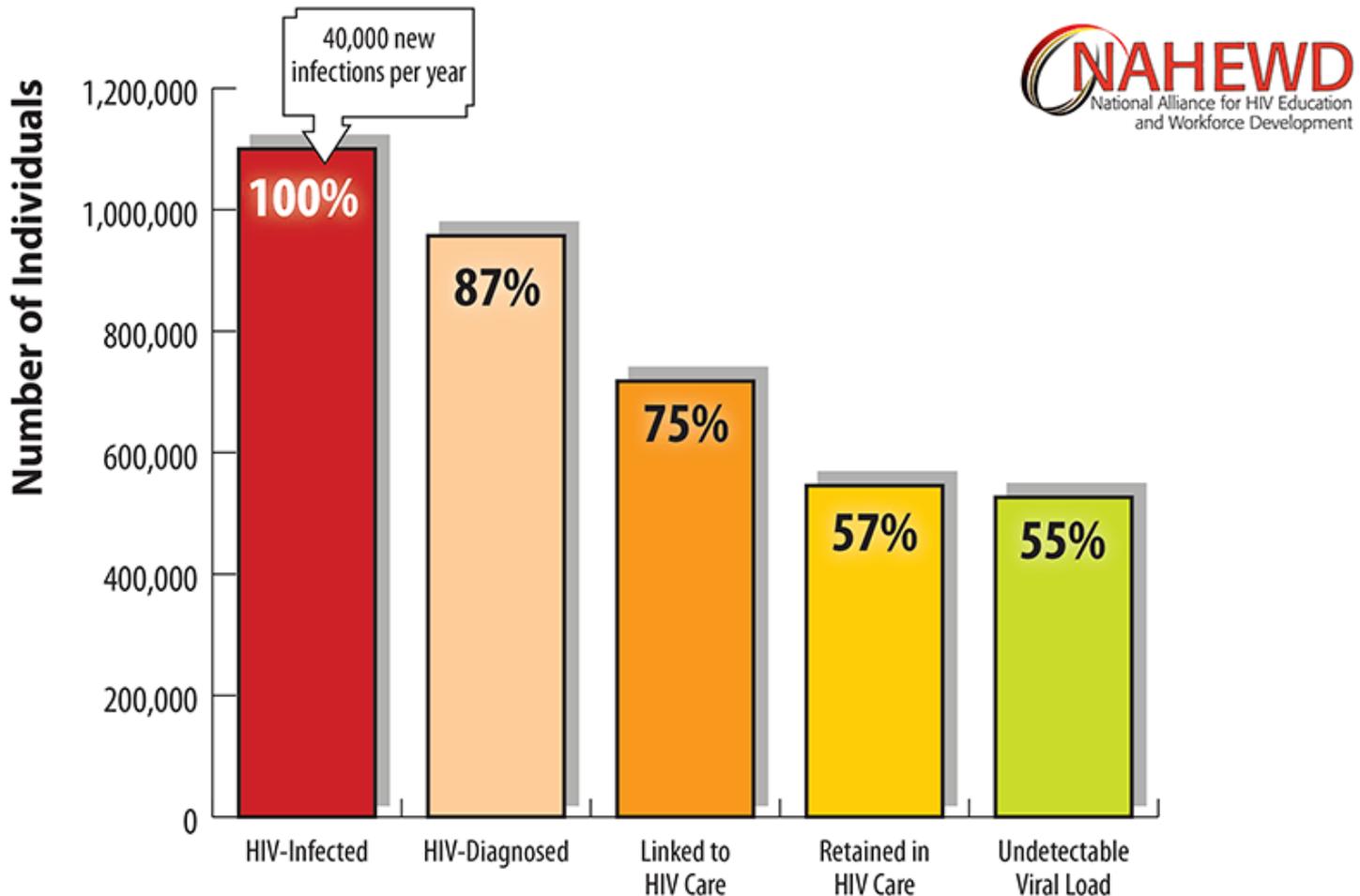
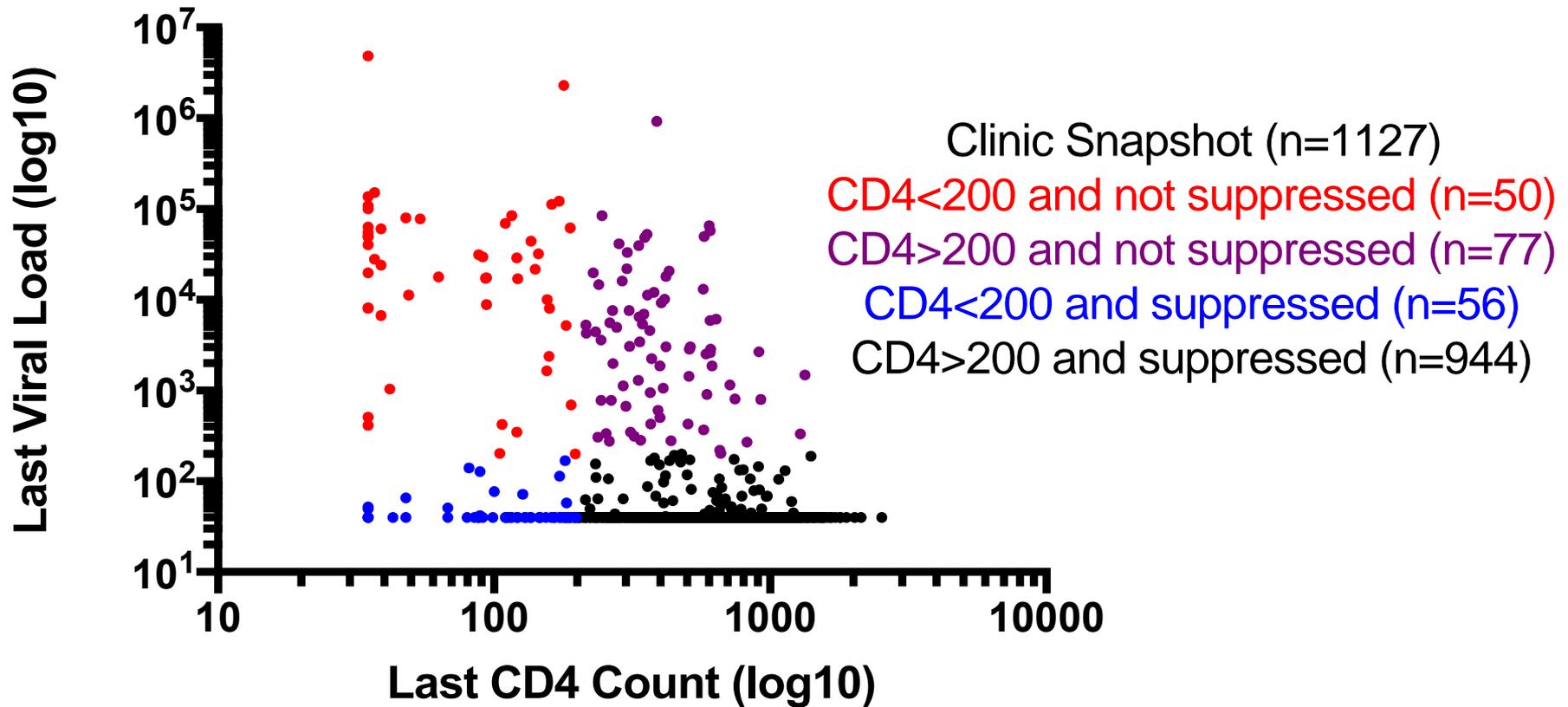


Chart data source: [Indicator Supplement](#), In: National HIV/AIDS Strategy for the United States: Updated to 2020. December 2016.

MUSC Clinic as Seen by Last CD4 Count and Viral Load





Stigma plus Social Determinants of Health

Transportation

Mental Health/Substance Use

Mistrust

Denial

Competing Life Issues

Logistics

Others

Goals of HIV Therapy and Plans to Get There

- Viral suppression
- Restore/preserve immune function
- Reduce HIV-associated morbidity and prolong the duration and quality of survival
- Prevent transmission

«90-90-90» - ambitious target aimed at ending AIDS



diagnosed

In 2020
90% of all people
living with HIV will
know their HIV status



on treatment

In 2020
90% of all people
diagnosed with HIV will
receive sustained
antiretroviral therapy



virally suppressed

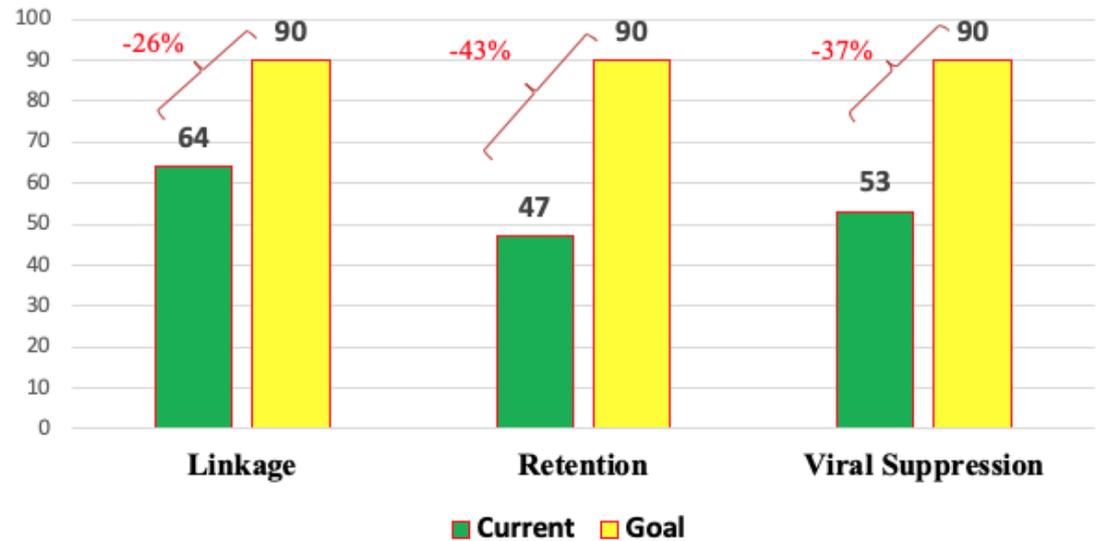
In 2020
90% of all people receiving
antiretroviral therapy will be
virally suppressed

Charleston Joins Fast-Track Cities Network to End HIV

Mayor of South Carolina's Largest City Signs *Paris Declaration* on National HIV Testing Day



Figure 2. Charleston County Current 90-90-90 Status

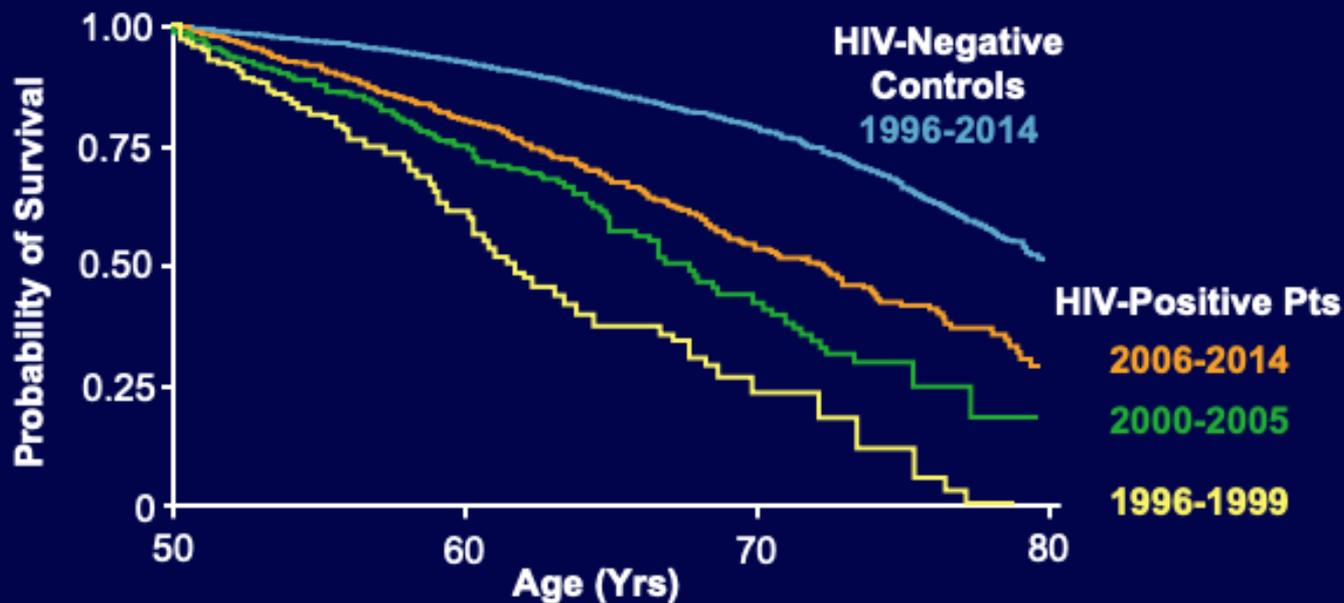


Life Expectancy and Long-Term Mortality of
Individuals Currently Living with HIV

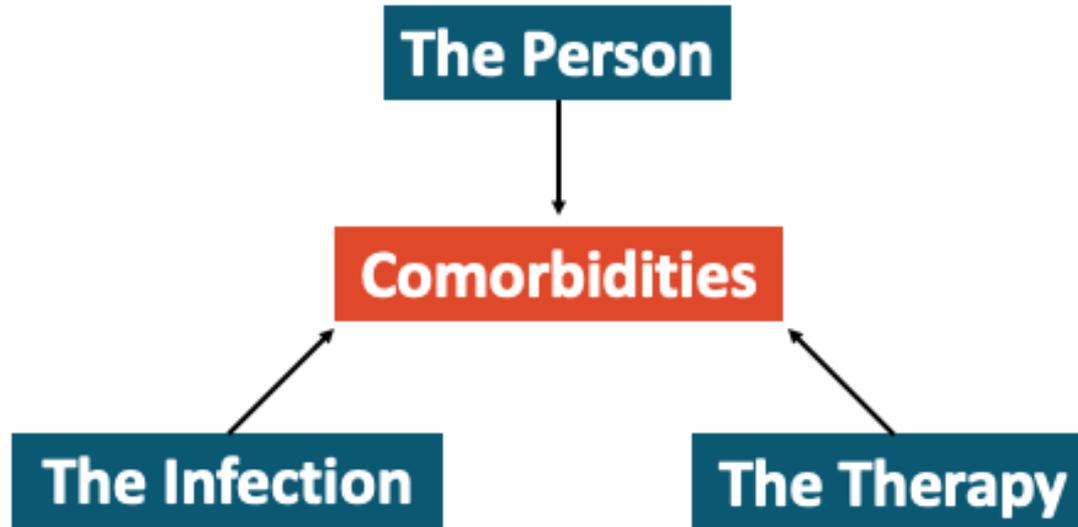
Illnesses and Complications Associated with
Long-Term Survivors of HIV Infection

Decreased Life Expectancy in Older HIV-Positive Adults in Modern ART Era

- Population-based cohort study of survival in HIV-infected pts (n = 2440) and uninfected controls matched by age and sex (n = 14,588) in Denmark



Considering Co-morbid Risk Factors

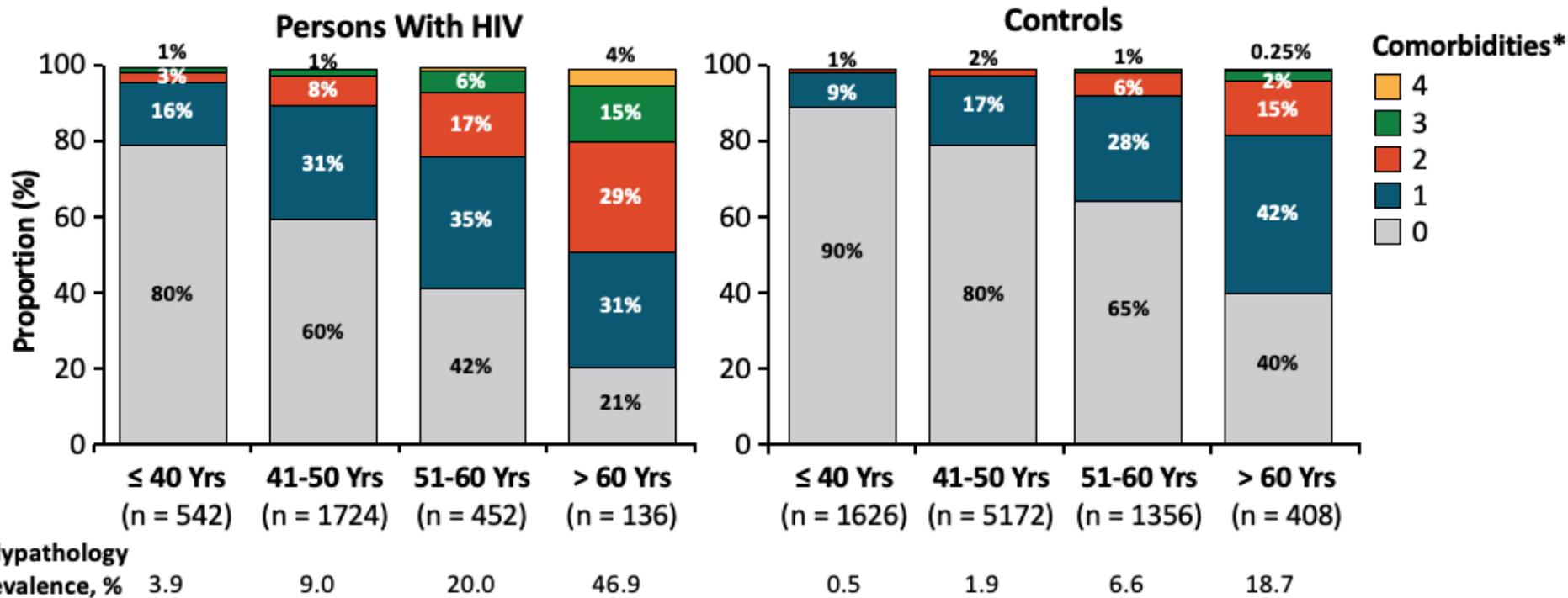


Co-morbid Conditions are More Common in HIV

Table. Comparative Prevalence of Selected Comorbidities Among People With HIV Treated With Antiretroviral Therapy and Matched Controls Without HIV in the United States, 2003-2013^a

	Commercial Insurance, No. (%)		Medicaid, No. (%)	
	HIV Cases (n = 20 519)	Controls (n = 46 763)	HIV Cases (n = 16 020)	Controls (n = 36 791)
Cardiovascular events	1375 (6.7)	1871 (4.0)	1666 (10.4)	2796 (7.6)
Kidney impairment	1806 (8.8)	1309 (2.8)	2435 (15.2)	2171 (5.9)
Fracture or osteoporosis	1559 (7.6)	2993 (6.4)	2083 (13.0)	3679 (10.0)
Liver disease	1272 (6.2)	1122 (2.4)	1810 (11.3)	1656 (4.5)
Cancer	1642 (8.0)	1917 (4.1)	1570 (9.8)	1545 (4.2)

Co-morbid Conditions are More Common in HIV



*Includes evaluation of HTN, diabetes, hypothyroidism, CVD, and bone fracture.
 Guaraldi. Clin Infect Dis. 2011;53:1120.

Factors Related to Non-AIDS Comorbidities in HIV-Infected Patients

Factors

AGING
Chronic HIV infection
ART toxicity
HCV and other coinfections
Genetics
Obesity, exercise, diet,
smoking
Stress
Depression



Conditions

Inflammation and fibrosis
Dyslipidemia
Insulin resistance
Decreased physical functioning

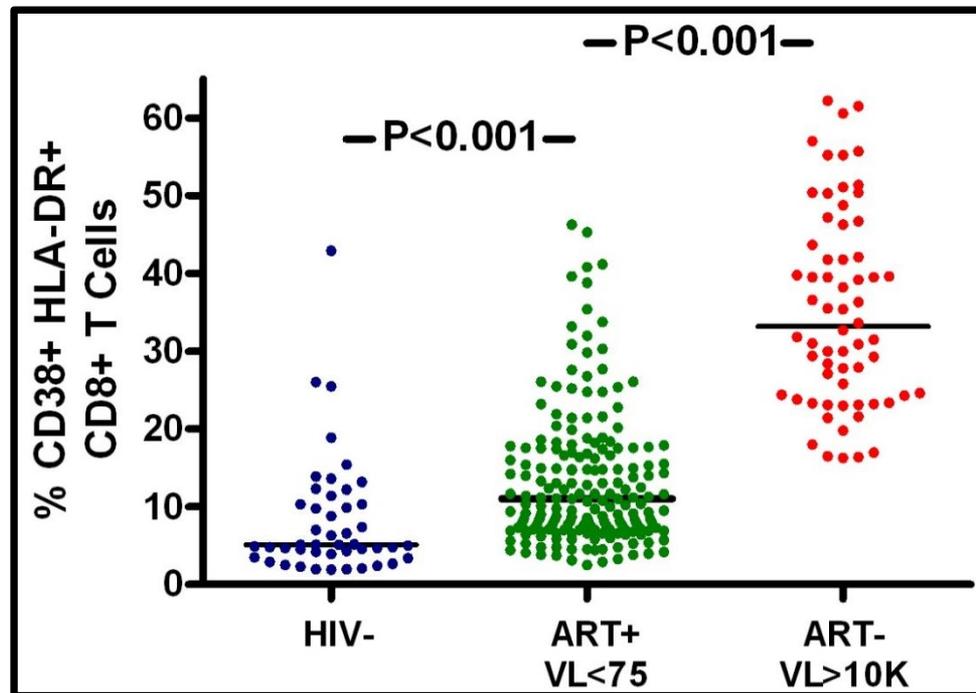


End Organ Disease

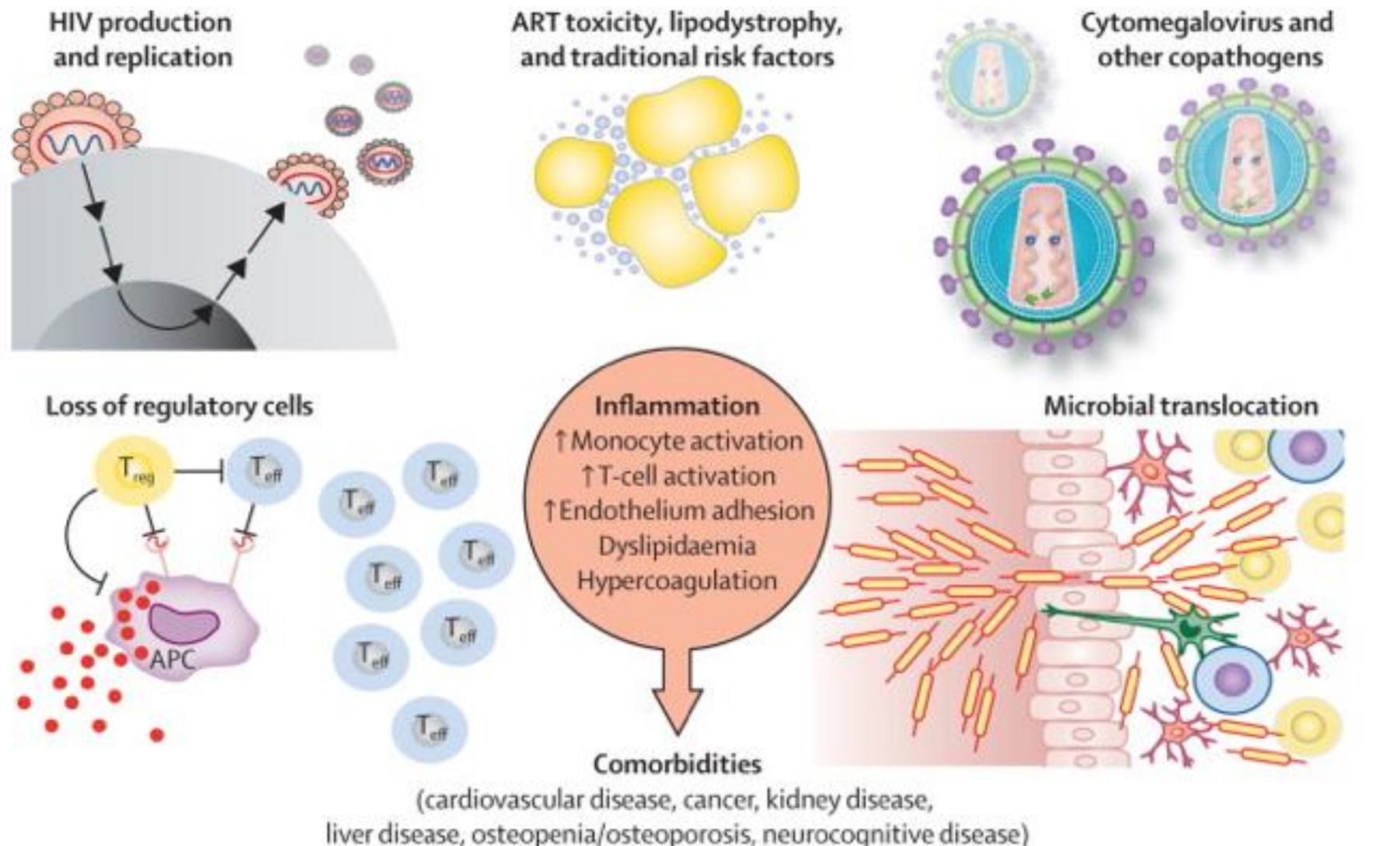
Cardiovascular
Renal
Metabolic
Functional
Neuropsychiatric

Markers of Inflammation are Higher Even in Those with Suppressed HIV Infection

- ❖ Suppressive antiretroviral therapy decreases inflammation and immune activation but does not restore it to normal



Factors Contributing to Persistent Inflammation During HIV Therapy



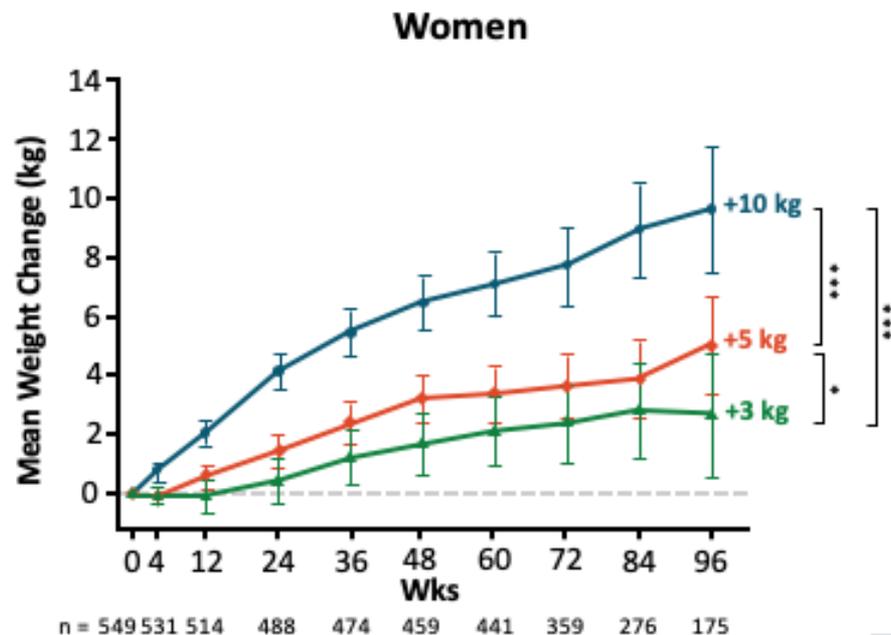
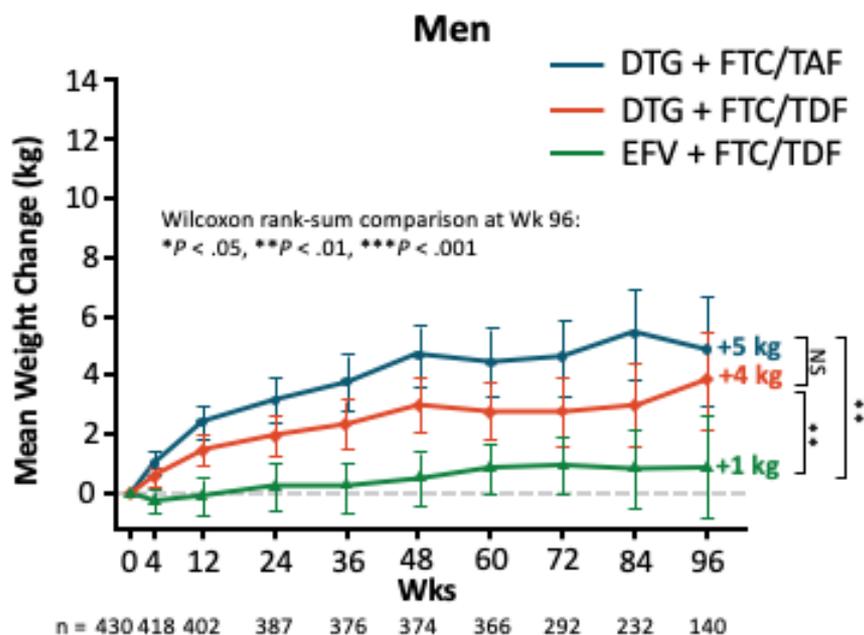
Antiretrovirals, While Fantastic to Suppress the Virus, can Cause Side Effects

Class	Agent	Select AEs
NRTI	ABC	Ischemic heart disease
	TDF	↓ BMD, osteomalacia, ↑ fracture risk, ↓ eGFR, Fanconi syndrome
NNRTI	EFV	Depression, sleep disturbance, headache, suicidal ideation
PI	ATV	↓ eGFR, nephrolithiasis
	DRV	Ischemic heart disease, nephrolithiasis
	LPV	Ischemic heart disease, ↓ eGFR

* New association of TAF and Integrase Inhibitors with Weight Gain Being Explored

ADVANCE: Weight Gain on ART in South African PLWH

- Significantly greater weight increase with DTG vs EFV, with TAF vs TDF; plateauing in weight gain after Wk 48 observed in men but not in women



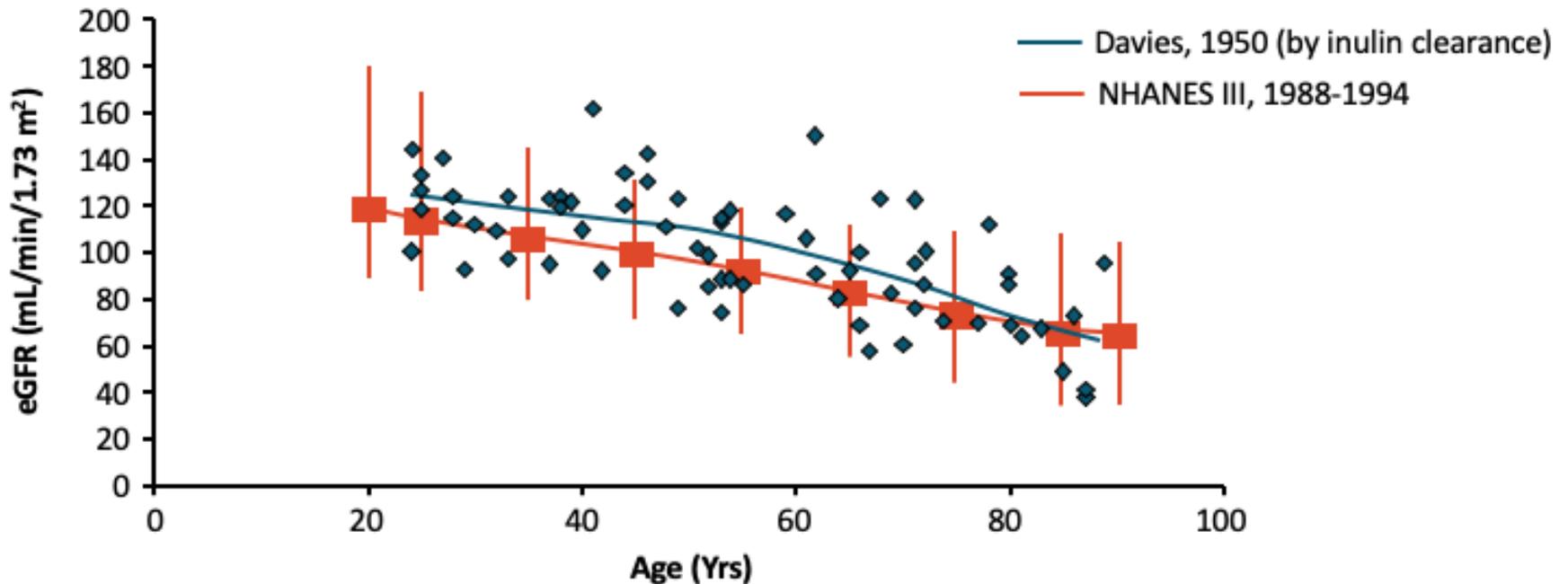
Considerations When Selecting ART in Aging Patients

- How to achieve or maintain undetectable viral load
- How to minimize the effect on comorbidities
- How to avoid drug–drug interactions



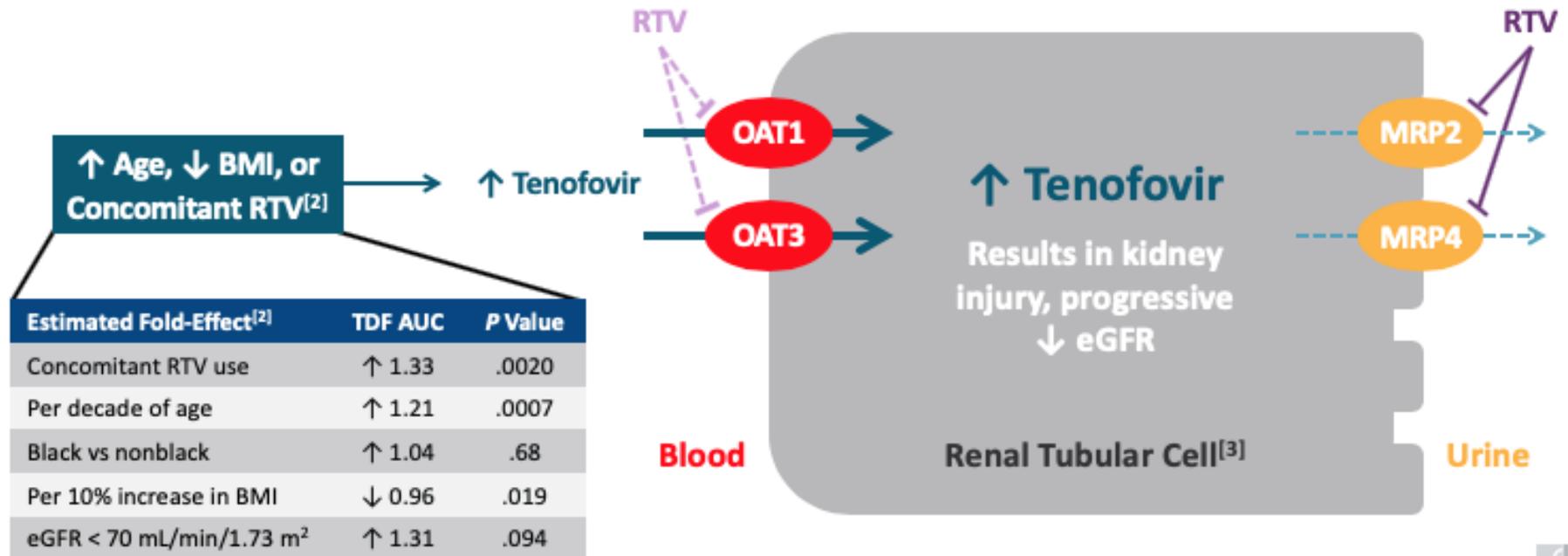
Renal Function Normally Declines with Age to Some Extent

- Annual eGFR decline ($\text{mL}/\text{min}/1.73 \text{ m}^2$): normal, 0.5-1; abnormal, > 3-5



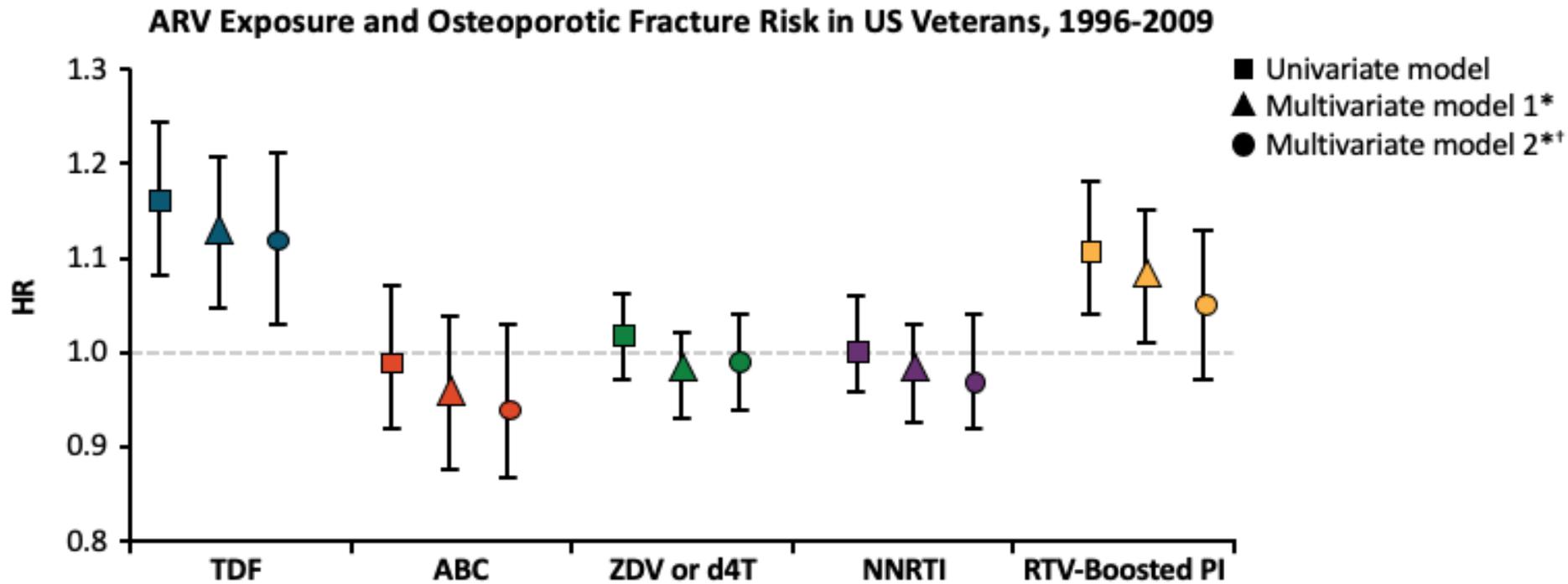
Tenofovir can Impact Renal Function

- Most tenofovir eliminated through glomerular filtration, with 20% to 30% excreted through tubular secretion^[1]



1. Venter. South Afr J HIV Med. 2018;19:817. 2. Baxi. AIDS. 2014;28:59. 3. Yombi. AIDS. 2014;28:621

Tenofovir can Impact Bone Density



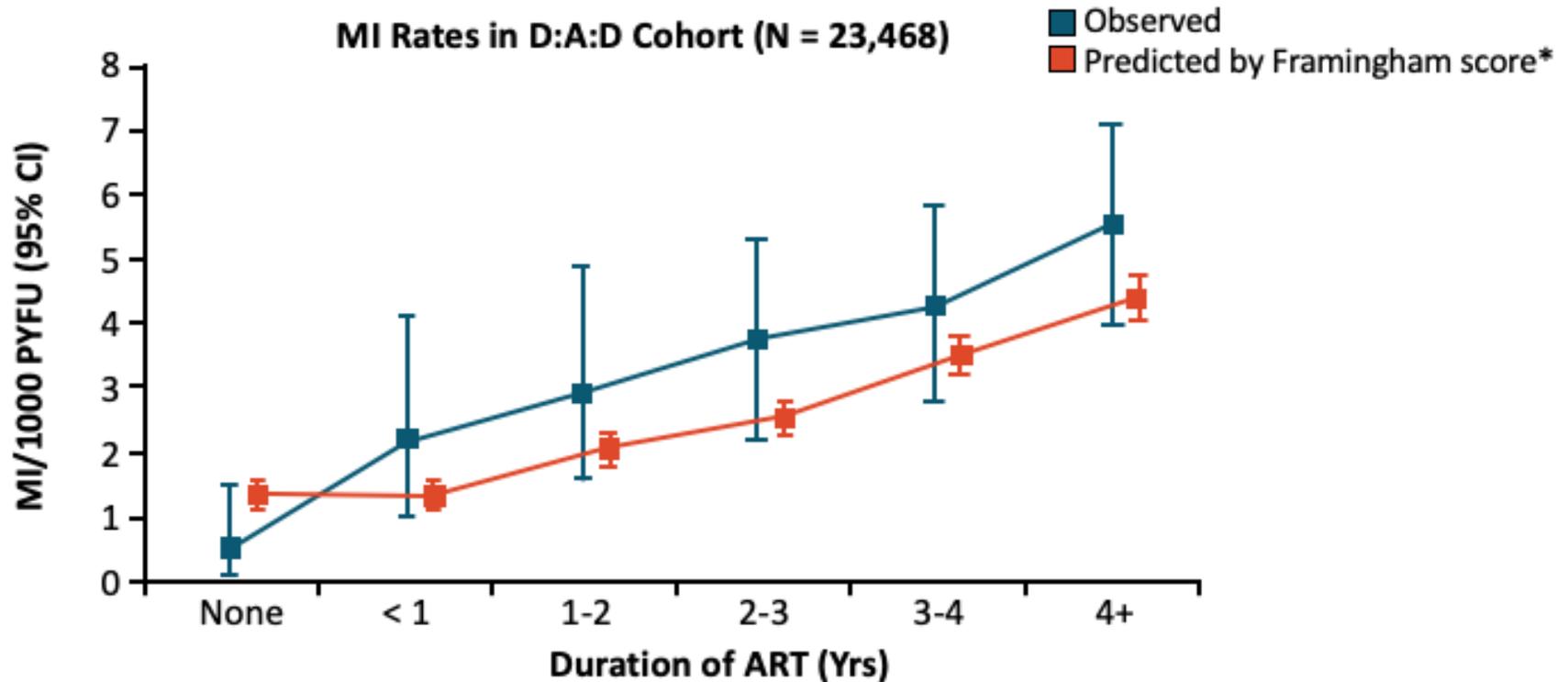
*Controlling for CKD, age, race, tobacco use, diabetes, and BMI. †Controlling for concomitant exposure to other ARVs.

Bone Health is Measured as Part of HIV Care

HIV-Infected Population	Assessment	Monitoring
Men 40-49 yrs of age Premenopausal women ≥ 40 yrs of age	<ul style="list-style-type: none"> Assess risk of fragility fracture using FRAX 	<ul style="list-style-type: none"> For pts with FRAX score ≤ 10%, monitor FRAX in 2-3 yrs For pts with FRAX score > 10%, perform DXA
Men ≥ 50 yrs of age Postmenopausal women Pts with fragility fracture history, receiving chronic glucocorticoids, or at high risk of falls	<ul style="list-style-type: none"> Assess BMD using DXA 	<ul style="list-style-type: none"> For pts with advanced osteopenia, monitor DXA in 1-2 yrs For pts with mild or moderate osteopenia, monitor DXA in 5 yrs For pts started on bisphosphonates (significantly reduced BMD or fracture history), repeat DXA in 2 yrs

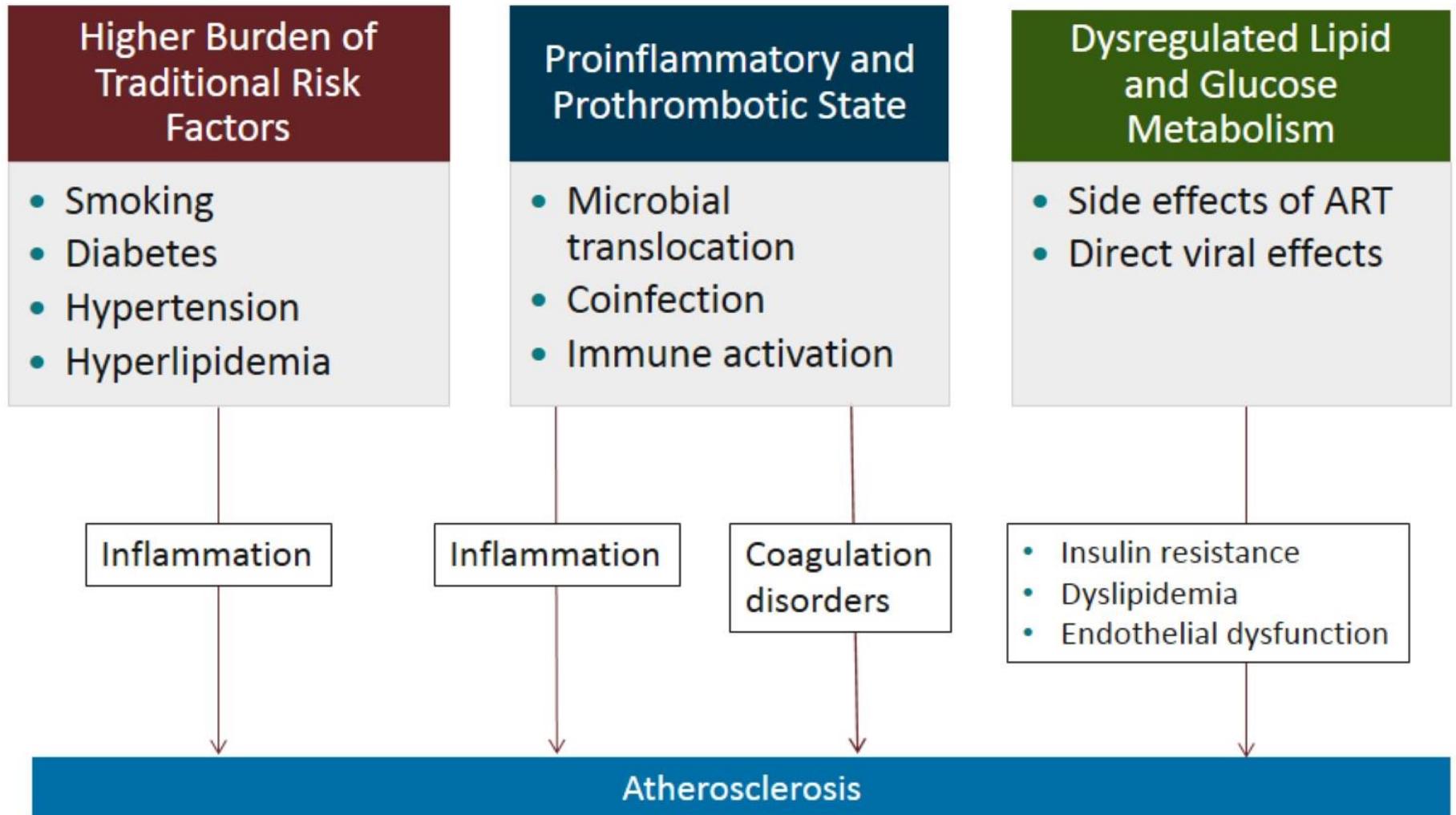
Some Consider Treated HIV a Cardiovascular Risk Factor

Framingham Score Underestimates MI Risk in PLWH



*Controls for sex, smoking, age, systolic blood pressure, diabetes, and TC:HDL-C.

Reasons for Elevated Cardiovascular Risk in HIV



Monitoring for Cholesterol in the MUSC HIV Clinic is Good but Imperfect

	Yes	Total	%
Total Population	701	1170	60%
Age 30 – 75	604	999	60%
Moderate	321	462	69%
High	157	210	75%
Very High	140	188	74%

Monitoring for Cholesterol in the MUSC HIV Clinic is Good but Imperfect

Figure 1. Number of Patients per Framingham Risk Category

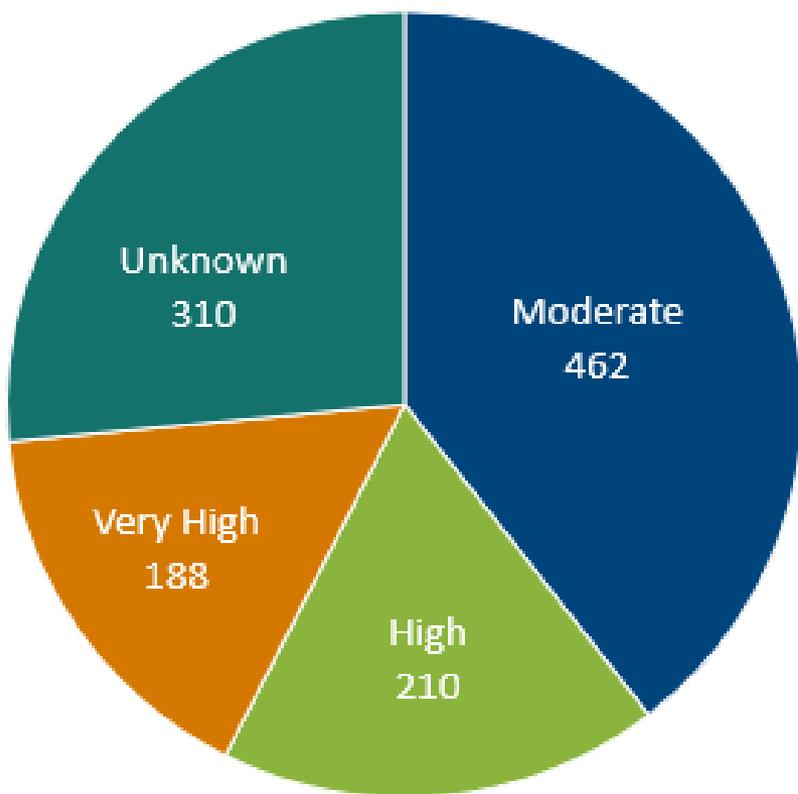
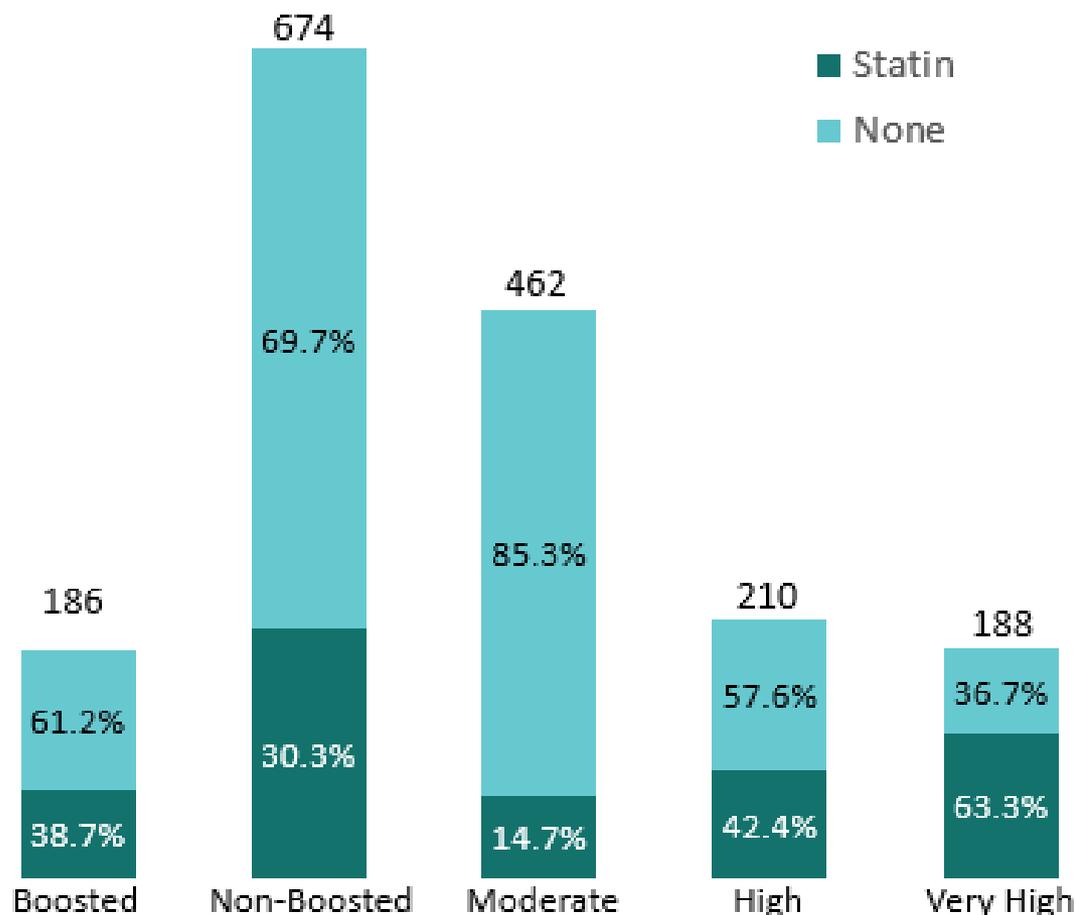


Figure 2. Statin Prescribing per Parameter



Back to Our Examples

1. 30ish male never HIV diagnosed, **CD4 <35**
2. 30ish female diagnosed but lost to care, **CD4 <35**
3. 70ish male diagnosed and in care, **CD4 700**



Needed: Before infection

1. PrEP (+ preventative), U=U
- 2.
- 3.

After infection

1. Diagnosis, linkage/retention
2. Linkage/retention, U=U
3. Optimization of primary care/cure

Conclusions

- We have the medications to achieve 100% treatment for those infected and 100% preventative for those at risks
- Overcoming barriers to delivering these medications (and other interventions) is the key public health prerogative for us today
- Comorbid conditions, the sequelae of chronic inflammation, and aging all need consideration and management as the patients we care for grow older