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An HIV Update: The Care Continuum, Prophylaxis, Diagnostics, and Treatment



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Disclosure

We have no conflicts of interest to disclose.



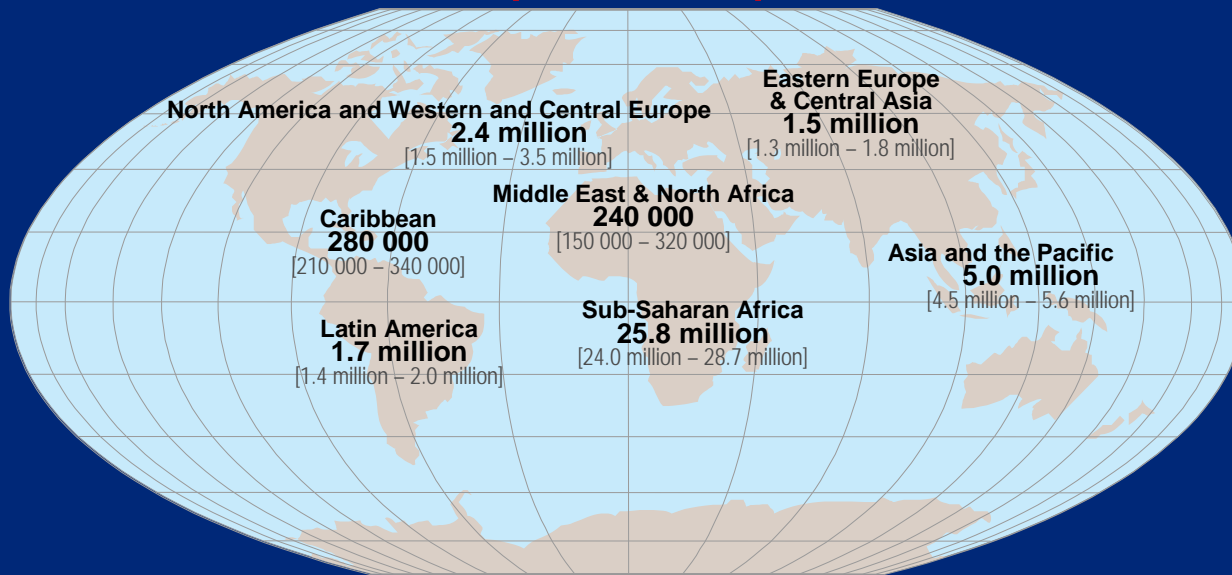
Learning Objectives

- Describe the importance of the HIV care continuum in the context of the global and local HIV epidemic
- Review evidence and recommendations regarding use of pre-exposure prophylaxis (PrEP) to prevent HIV infection
- Understand advantages and limitations of 4th generation HIV diagnostic tests in clinical care
- Summarize new antiretroviral treatment guidelines



Adults and children estimated to be living with HIV

2014

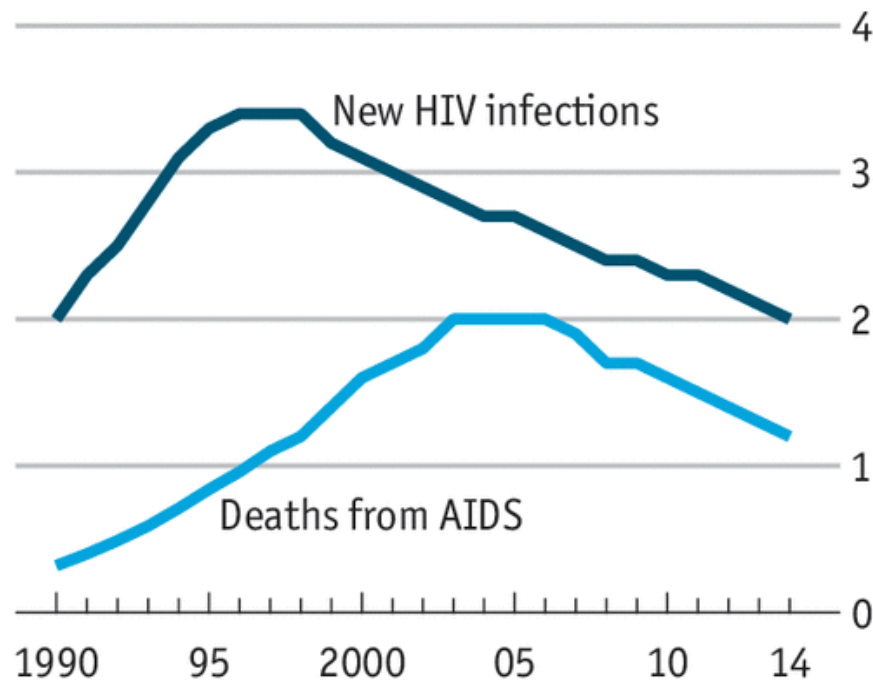


Total: 36.9 million [34.3 million – 41.4 million]

Global Decline in New Infections

What's going down

AIDS worldwide, m



Source: UNAIDS Global Report 2015

ART Coverage

Improved, but with work left to do



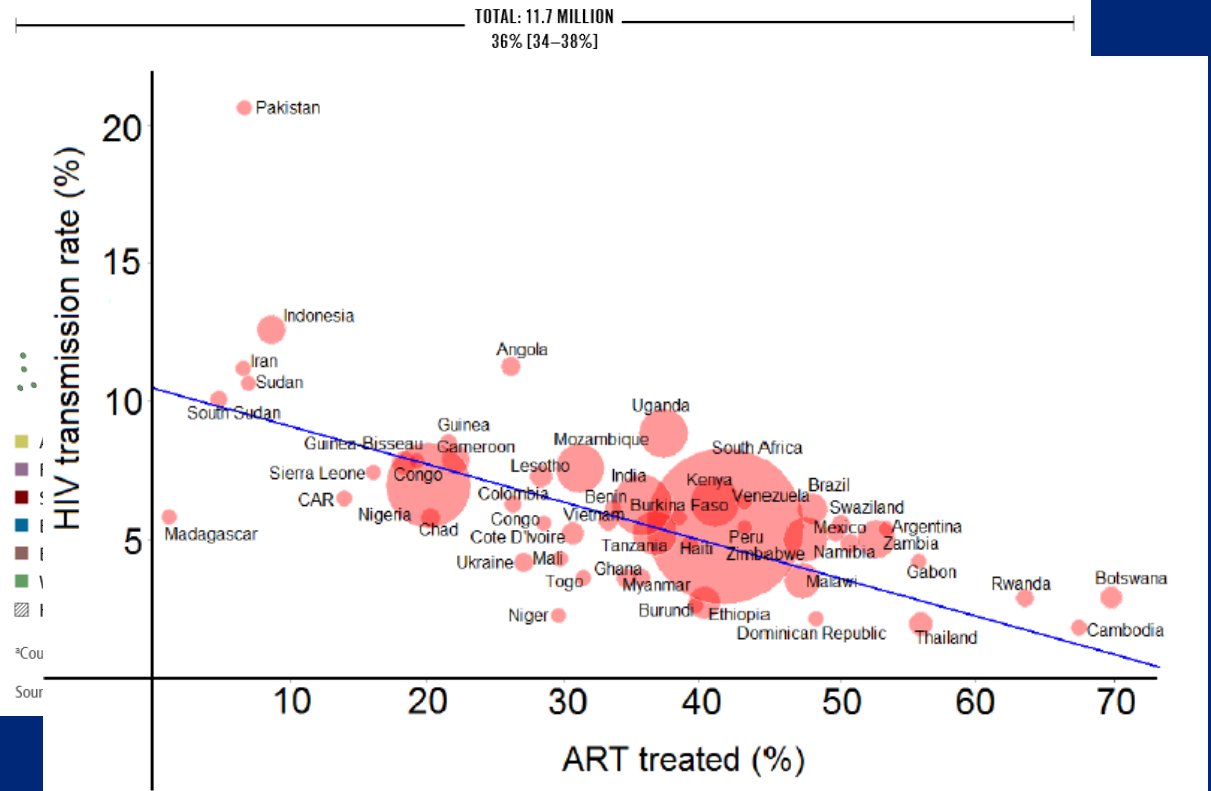
GUIDELINES



GUIDELINE ON WHEN TO START ANTIRETROVIRAL THERAPY AND ON PRE-EXPOSURE PROPHYLAXIS FOR HIV

SEPTEMBER 2015

Number of people receiving ART and percentage of all people living with HIV receiving ART in low- and middle-income countries overall and by WHO region, 2013^a





HIV/AIDS in the United States

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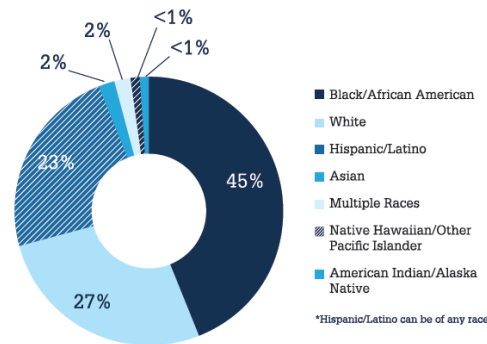
- More than 1.2 million living with HIV infection
 - 50,000 new infections/year
 - almost 1 in 8 (12.8%) don't know it
- An estimated 13,712 people with an AIDS diagnosis died in 2012
 - Number of people living with HIV increasing by about 35,000 each year!

HIV is not going away

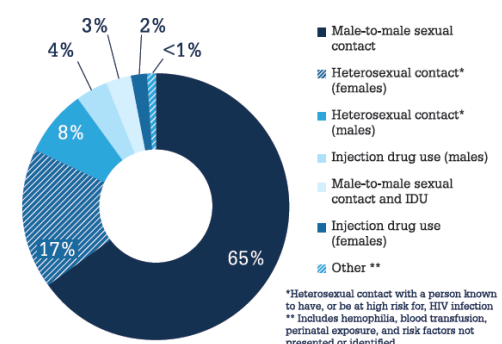
Where is the U.S Epidemic Concentrating?

- 45% Black/African American
- 65% MSM
- 51% < 35 years of age
- 51% in the South

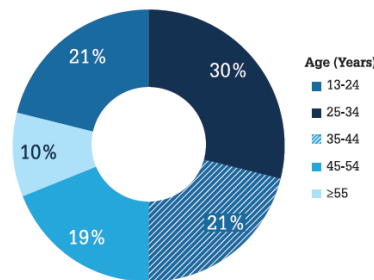
DIAGNOSES OF HIV INFECTION BY RACE/ETHNICITY - 2013



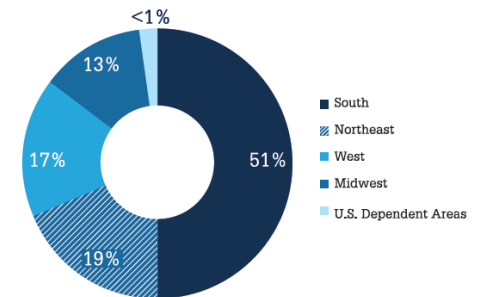
DIAGNOSES OF HIV INFECTION BY TRANSMISSION CATEGORY - 2013



DIAGNOSES OF HIV INFECTION BY AGE AT DIAGNOSIS - 2013



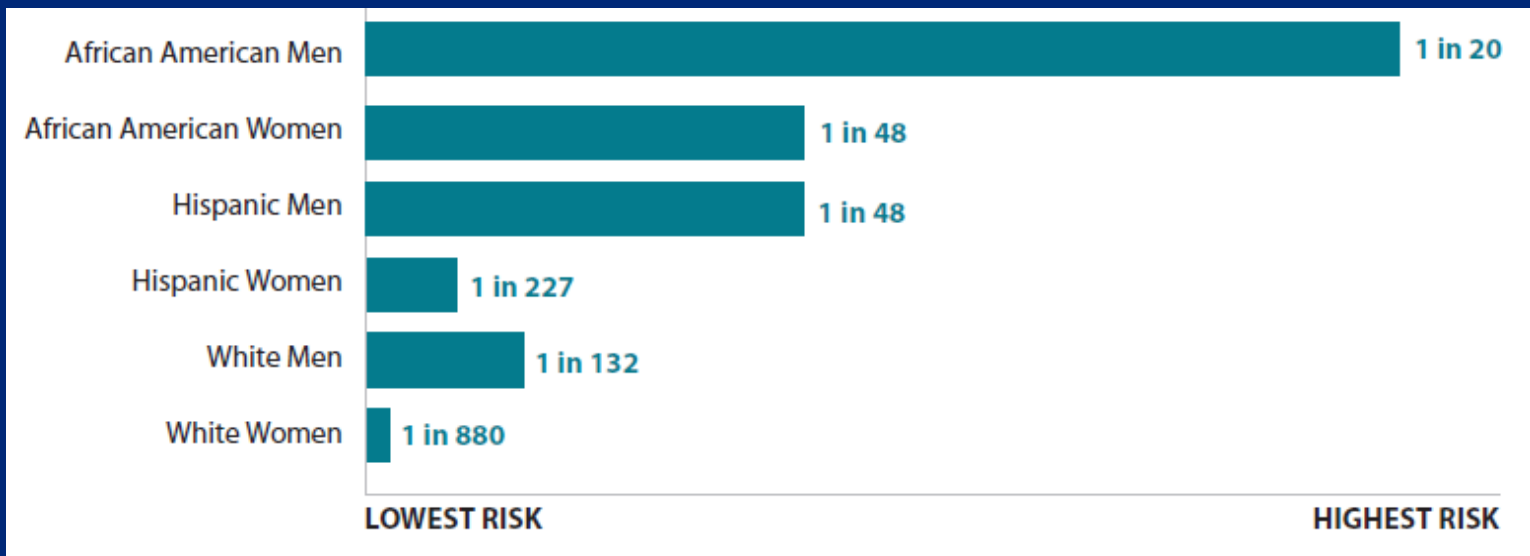
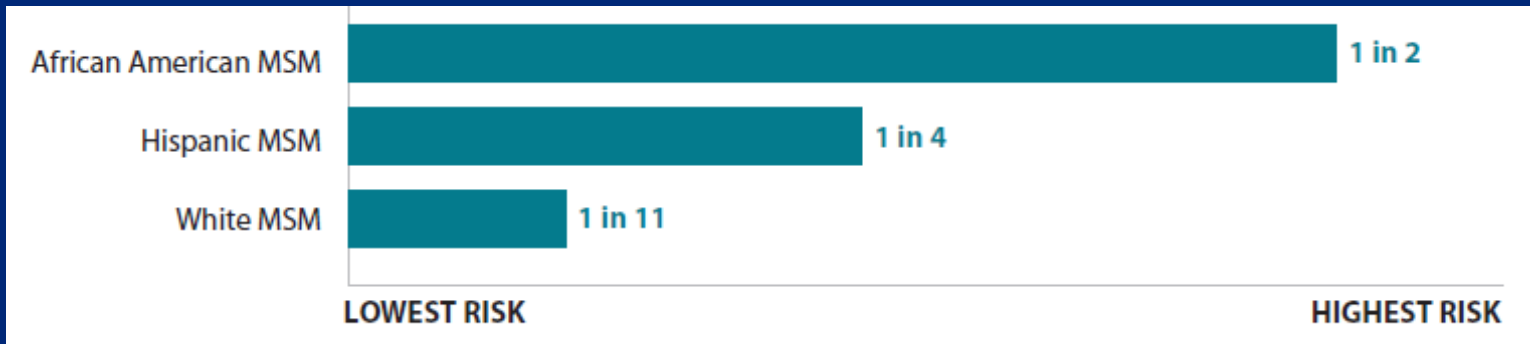
DIAGNOSES OF HIV INFECTION BY REGION - 2013





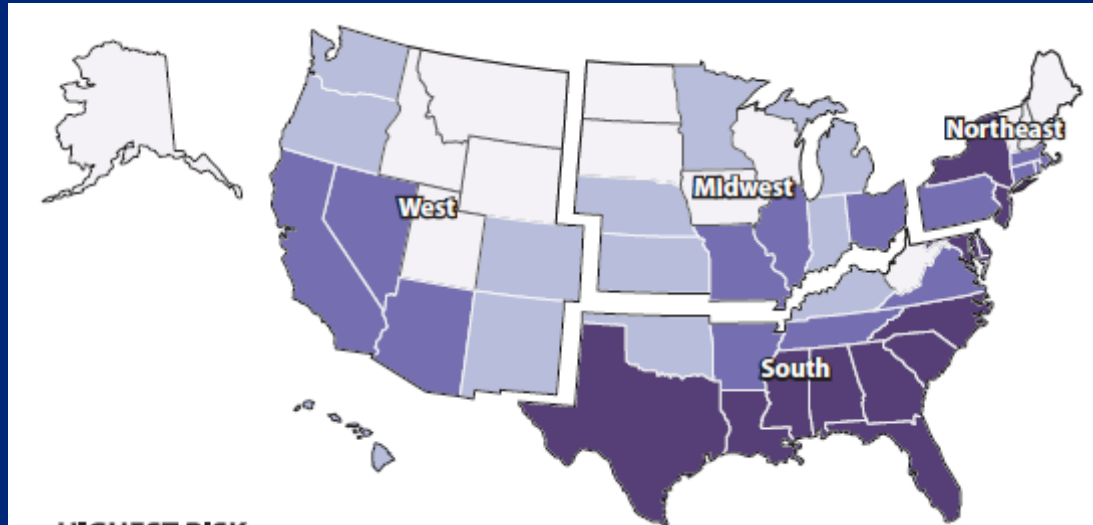
Who is at risk of HIV infection in the US?

Lifetime risk of HIV infection is.....





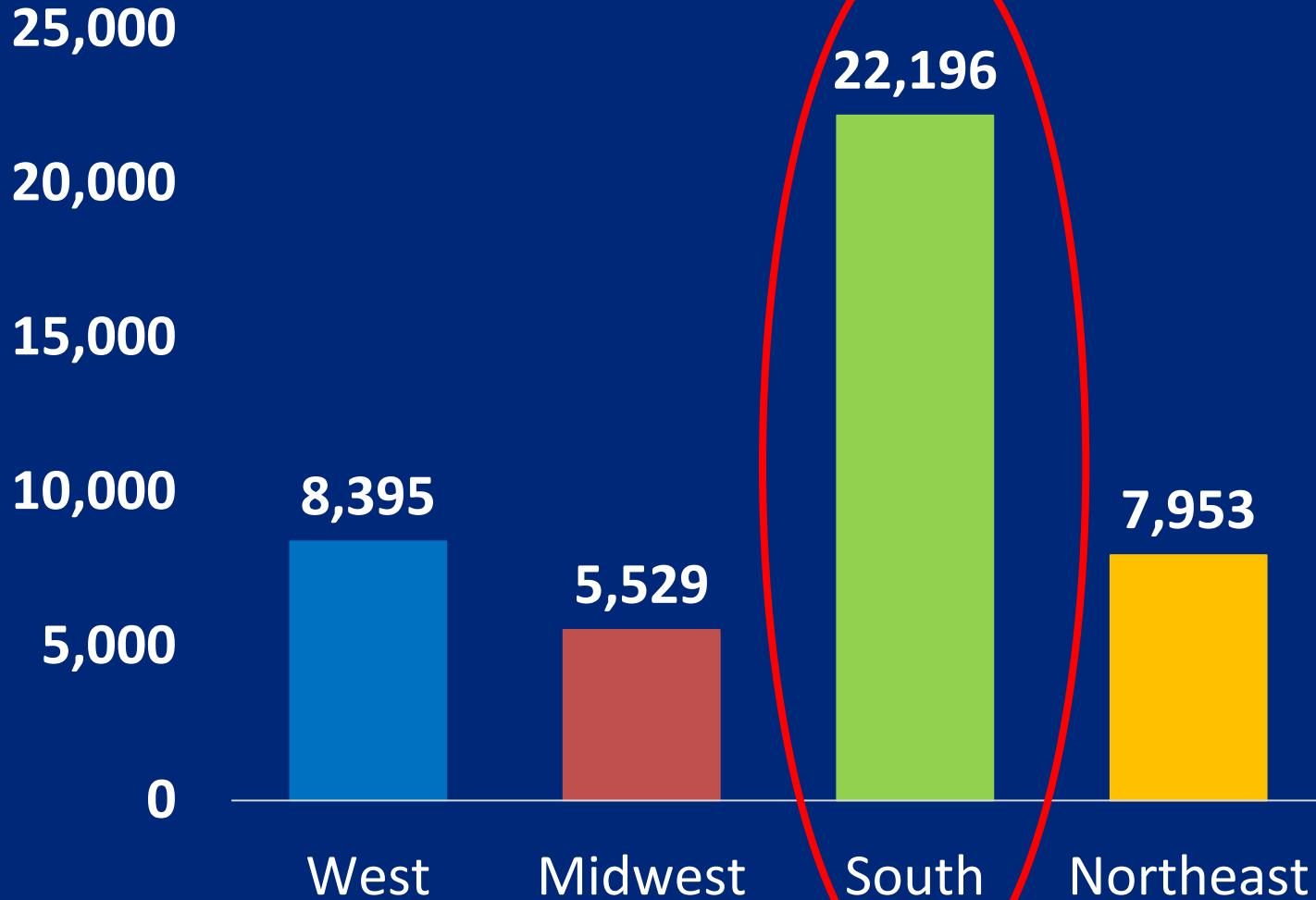
And by region and State....



State	One in "n"	State	One in "n"	State	One in "n"	State	One in "n"
District of Columbia	13	Nevada	98	Michigan	167	West Virginia	302
Maryland	49	Illinois	101	Oklahoma	168	Wisconsin	307
Georgia	51	California	102	Kentucky	173	Iowa	342
Florida	54	Tennessee	103	Indiana	183	Utah	366
Louisiana	56	Pennsylvania	115	Washington	185	Maine	373
New York	69	Virginia	115	Colorado	191	Alaska	384
Texas	81	Massachusetts	121	New Mexico	196	South Dakota	402
New Jersey	84	Arizona	138	Hawaii	202	New Hampshire	411
Mississippi	85	Connecticut	139	Oregon	214	Wyoming	481
South Carolina	86	Rhode Island	143	Minnesota	216	Vermont	527
North Carolina	93	Ohio	150	Kansas	262	Idaho	547
Delaware	96	Missouri	155	Nebraska	264	Montana	578
Alabama	97	Arkansas	159			North Dakota	670



New HIV Diagnoses by Region, 2014

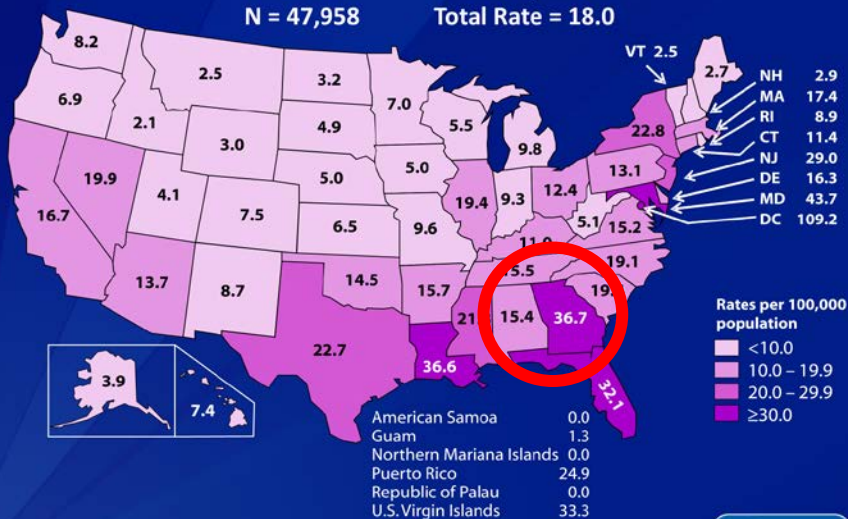


Georgia's Rank Among States?

Not always glamorous at the top

Rate of New HIV Infections: #2

Rates of Diagnoses of HIV Infection among Adults and Adolescents, 2013—United States and 6 Dependent Areas
N = 47,958 Total Rate = 18.0



Rate of AIDS: #3

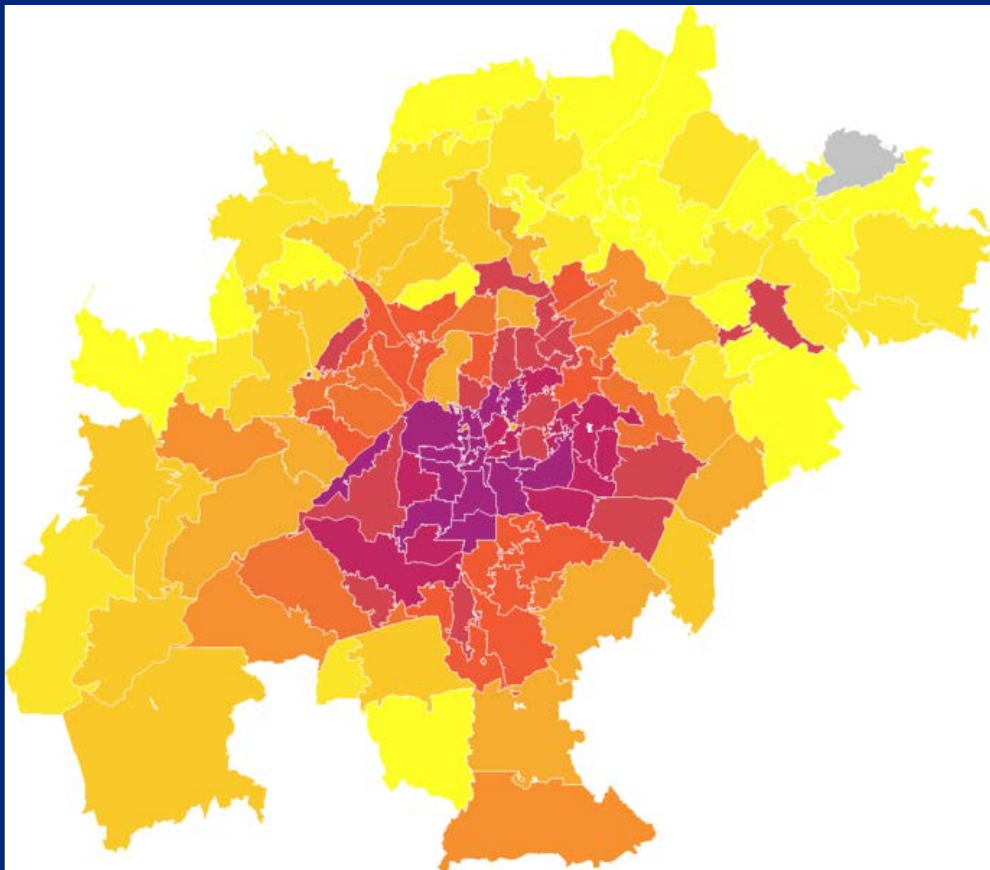
Rates of Stage 3 (AIDS) Classifications among Persons with HIV Infection, 2013—United States and 6 Dependent Areas
N = 27,135 Total Rate = 8.5





HIV/AIDS in Atlanta

Rates of Persons Living with an HIV or AIDS, Atlanta, 2012



Metropolitan area with the 7th highest rate of new diagnoses



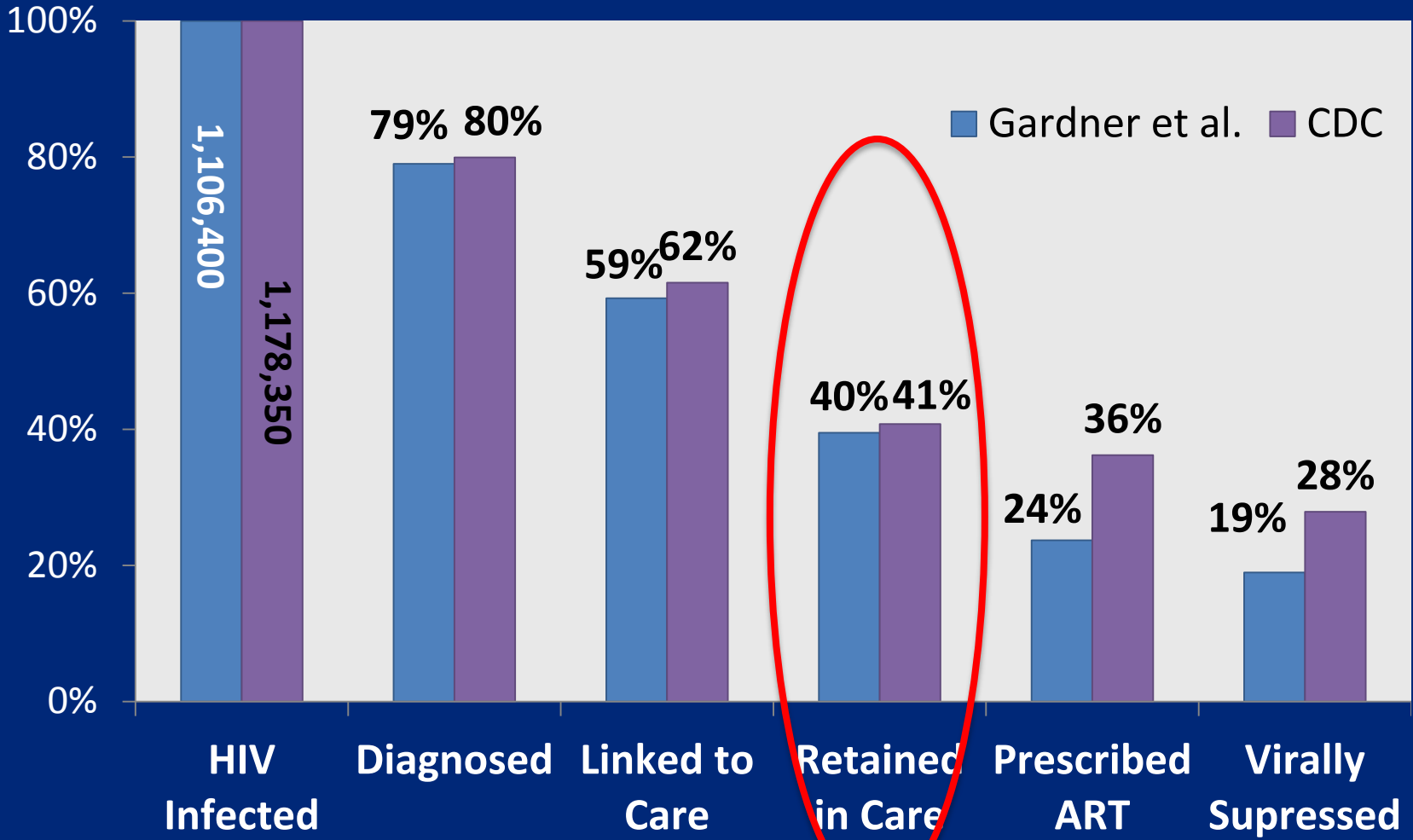
0 - 108 109 - 166 167 - 228 229 - 311 312 - 412 413 - 573 574 - 790 791 - 1,201 1,202 - 1,955 1,956+

Data not shown *



Initial Care Continuum, 2011

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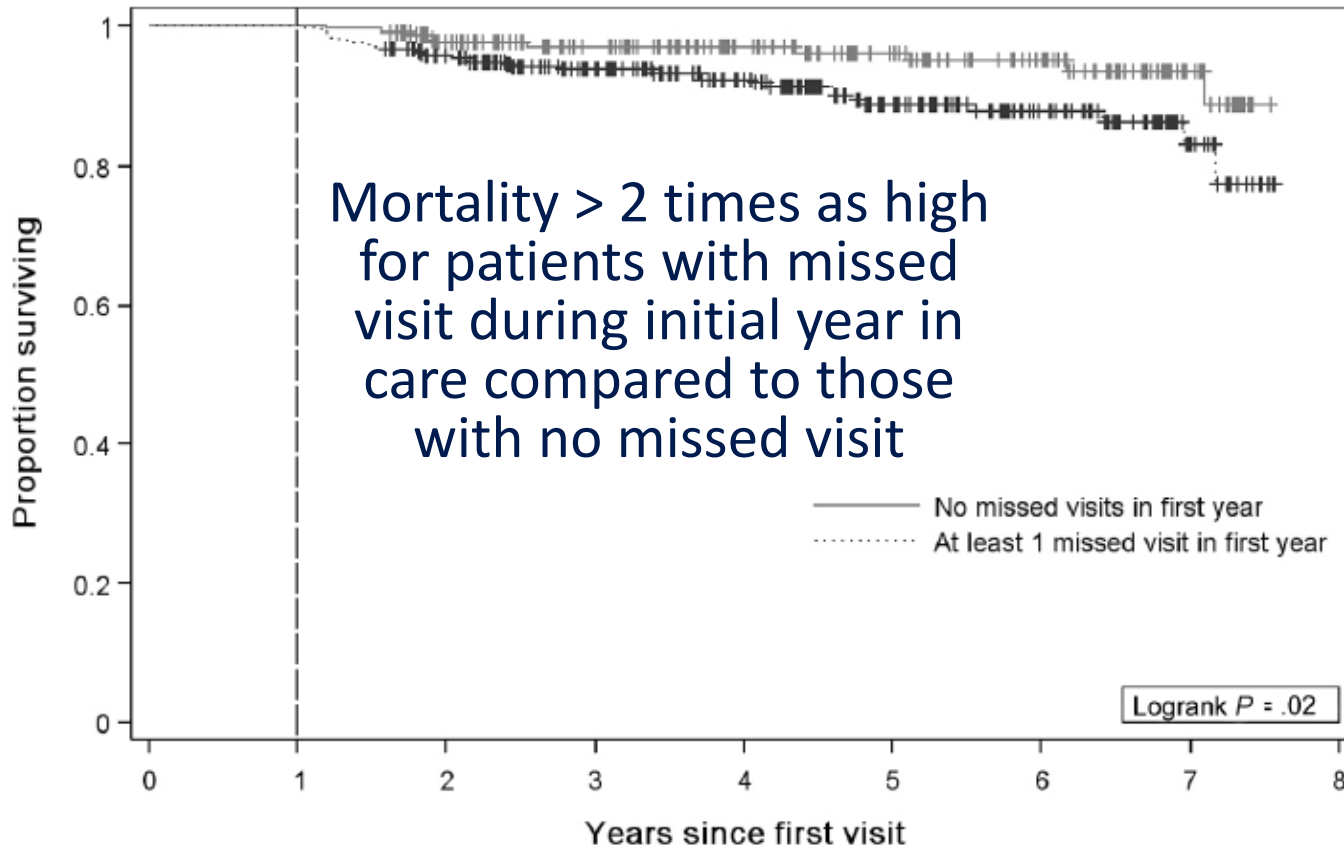


Strengths of Care Continuum as a Public Health Metric

- Powerful visual tool to monitor engagement in care
 - National, state, local and health care system levels
- Valuable insights into where drop-off in engagement occurs
 - Help target programmatic and research activities
- Monitor progress of jurisdictions over time, and between jurisdictions **if** similar definitions and methodologies used

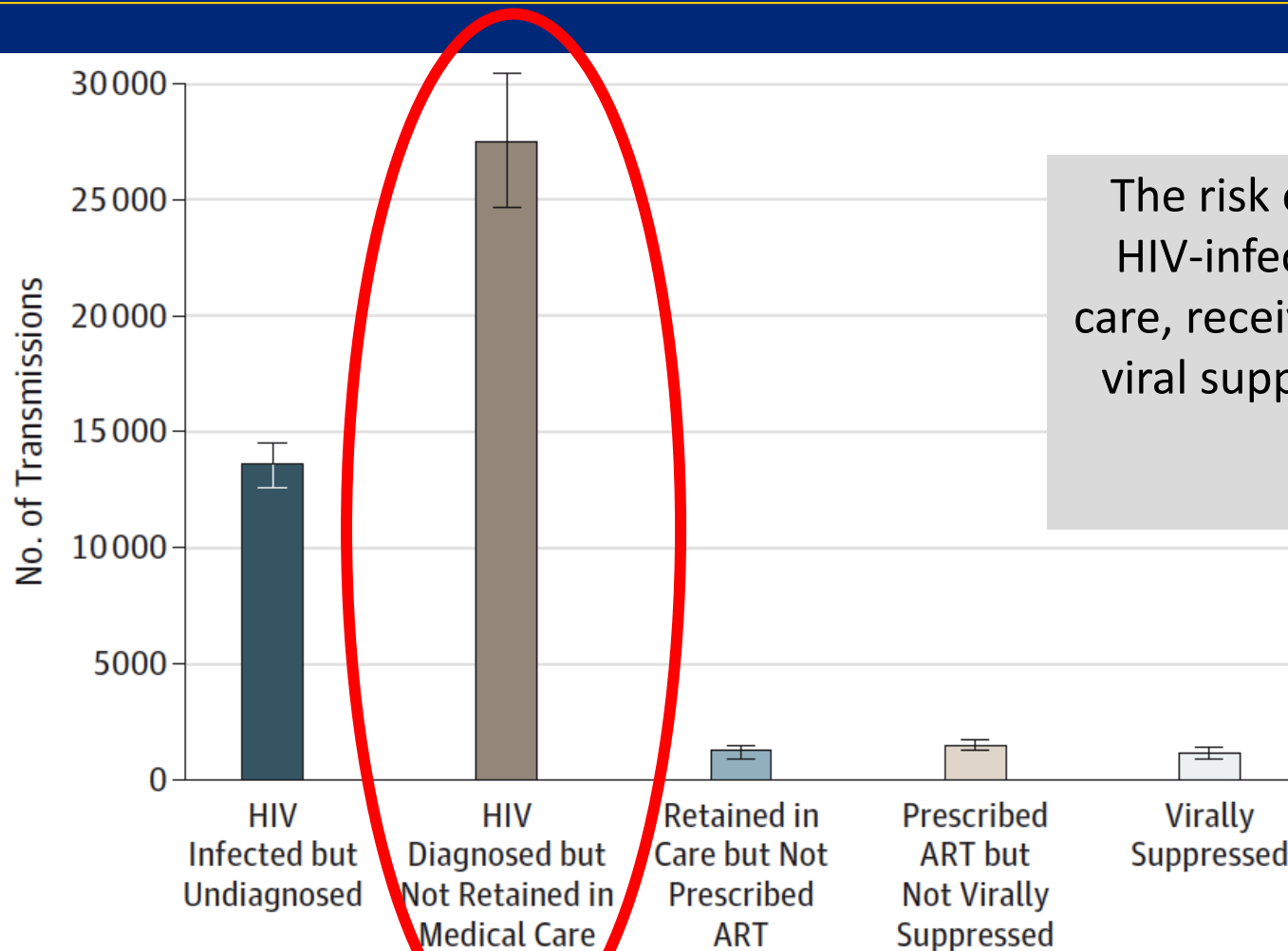


Individual Consequences of Missed Clinic Visits



	Patients	Died	Censored
No missed visits in first year	218	5% (10)	95% (208)
At least 1 missed visit in first year	325	10% (32)	90% (293)

Public Health Importance of Retention and VS

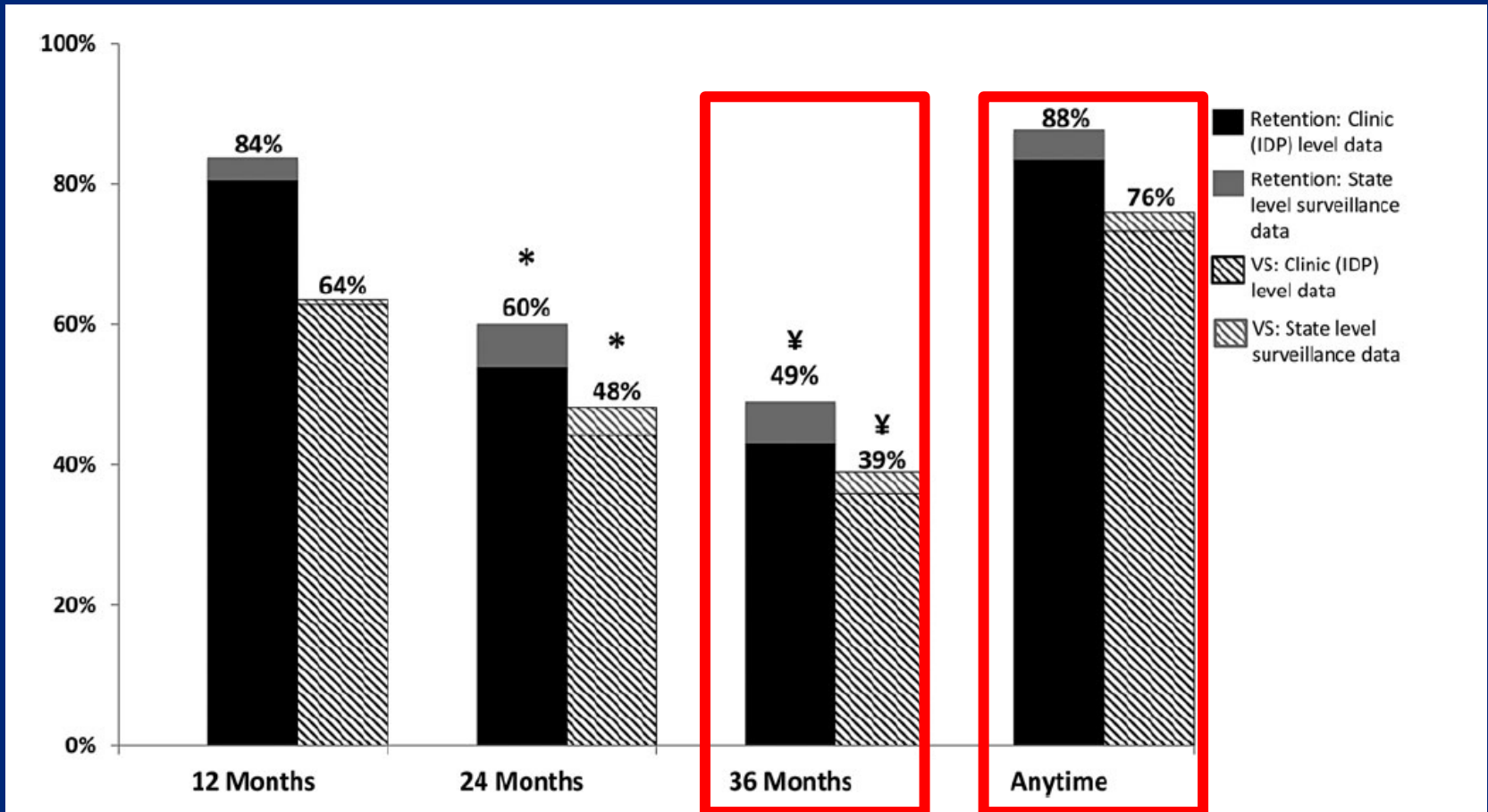


The risk of transmission by HIV-infected individuals in care, receiving treatment with viral suppression is virtually

ZERO

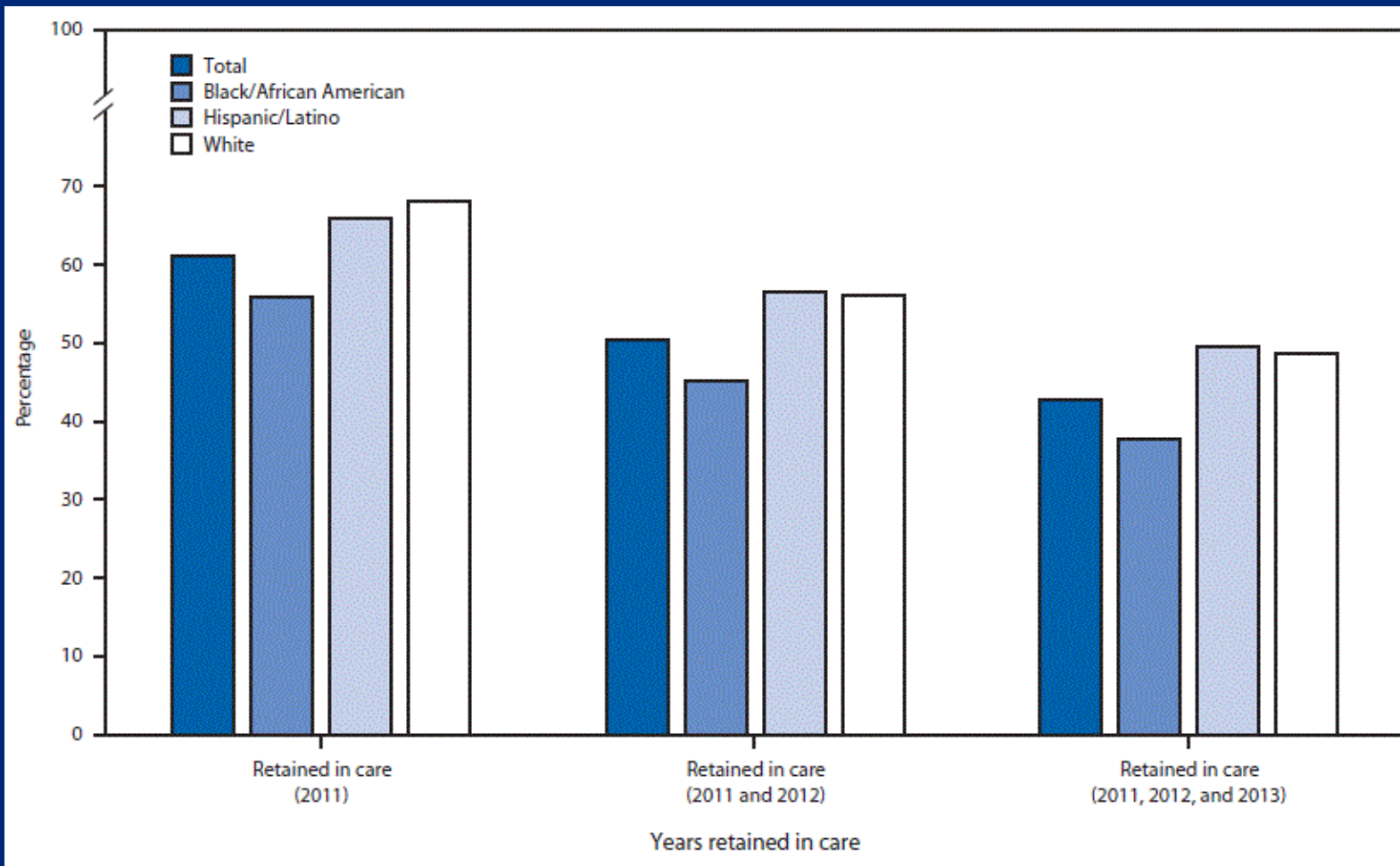


Poor Long Term Outcomes in a Chronic Disease





Same Story in 12 Jurisdictions



National HIV/AIDS Strategy: Indicators Based on Care Continuum

90% Diagnosis

Indicator 1: ↑ % of people living with HIV who know serostatus to 90%

85% Linkage to Care

Indicator 4: ↑ % of newly diagnosed persons linked to care within 30 days of diagnosis to 85%

90% Retention

Indicator 5: ↑ % of persons with diagnosed HIV who are retained to care to 90%

80% Viral Suppression

Indicator 6: ↑ % of persons with diagnosed HIV who are virally suppressed to 80%



The Implementation Gap

Antiretroviral Therapy
=
Viral Suppression

Implementation

Sustained Virologic
Suppression in Real
World Settings

1. Health System Challenges
2. Bio-psycho-social Challenges

- Mental illness
- Substance use
- Poverty
- Transportation
- Jail/prison
- Stigma
- Low social support
- Food insecurity



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HIV PREVENTION

What is Pre-Exposure Prophylaxis (PrEP)?

The use of antiretroviral medications in HIV negative patients to prevent HIV acquisition.

What's the Evidence Behind PrEP?

		OUTCOME – Efficacy in % reduction in risk of HIV acquisition	
<u>STUDY</u>	Agent vs Control	ITT group	Subgroup with high adherence rates
Men Who Have Sex with Men (MSM)			
iPrEX	TDF/FTC vs Placebo	44%	>90%
Heterosexual Men and Women			
Partners PrEP	TDF vs Placebo	67%	90%
	TDF/FTC vs Placebo	75%	
TDF2	TDF/FTC vs Placebo	62%	Not reported
IV Drug Abusers			
Bangkok	TDF vs Placebo	49%	73.5%

Does PrEP work in “real life”?

PROUD Study

- **Purpose:** Assess effect of risk compensation in PrEP users
- **Design:** Open-label RCT
 - MSM randomized 1:1 to daily TDF/FTC immediately (n = 275) vs deferred by 1 year (n = 269).
- **Results:**
 - Immediate vs Deferred group: 3 HIV infections (1.2/100 person-years) vs 20 (9/100 person-yr)
 - No difference in acquisition of STIs between groups
 - NNT: 13 men with PrEP x 1 year to prevent 1 infection
- **Conclusion:** Refutes concerns that effectiveness would be lower in real-world setting

PrEP Algorithm

- Multiple sexual partners or HIV+partner
- Inconsistent condoms
- Recent (6 mo) history STI
 - Sex Worker
- Sharing needles/IV drugs

PrEP not indicated

NO

Patient at substantial risk for HIV acquisition?

YES

- Documented **negative HIV test**
- No signs/symptoms of acute HIV
- Normal renal function (CrCl >60)
- Documented HBV infection & vaccination status

NOT oral rapid test!

NO

Not eligible

Prescribe ≤ 90 days daily Truvada (TDF/FTC)

Q3 mo HIV test

At 3 mo and then q6mo: renal function

Q6 mo test for other STIs

Q3 mo pregnancy tests

Q 3 mo assess for access to clean needles

Adapted from CDC PrEP Guidelines, Table 1

Who would qualify for PrEP in US?

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Transmission Risk Group	% with PrEP indication	Estimated Number	(95% CI)
MSM (ages 18-59)	24.7	492,000	(212,000-772,000)
IVDA (≥ age 18)	18.5	115,000	(45,000-185,000)
Heterosexually active adults (ages 18-59)	0.4	624,000	(404,000-846,000)
Men	0.2	157,000	(62,000-252,000)
Women	0.6	468,000	(274,000-662,000)
TOTAL	---	1,232,000	(661,000-1,803,000)

Adapted from Smith, MMWR 2015

CROI 2016: Reported PrEP Use in Last 12 Months Among MSM in the US

**3 nationwide cross-sectional internet surveys of MSM in U.S
2012-2015**

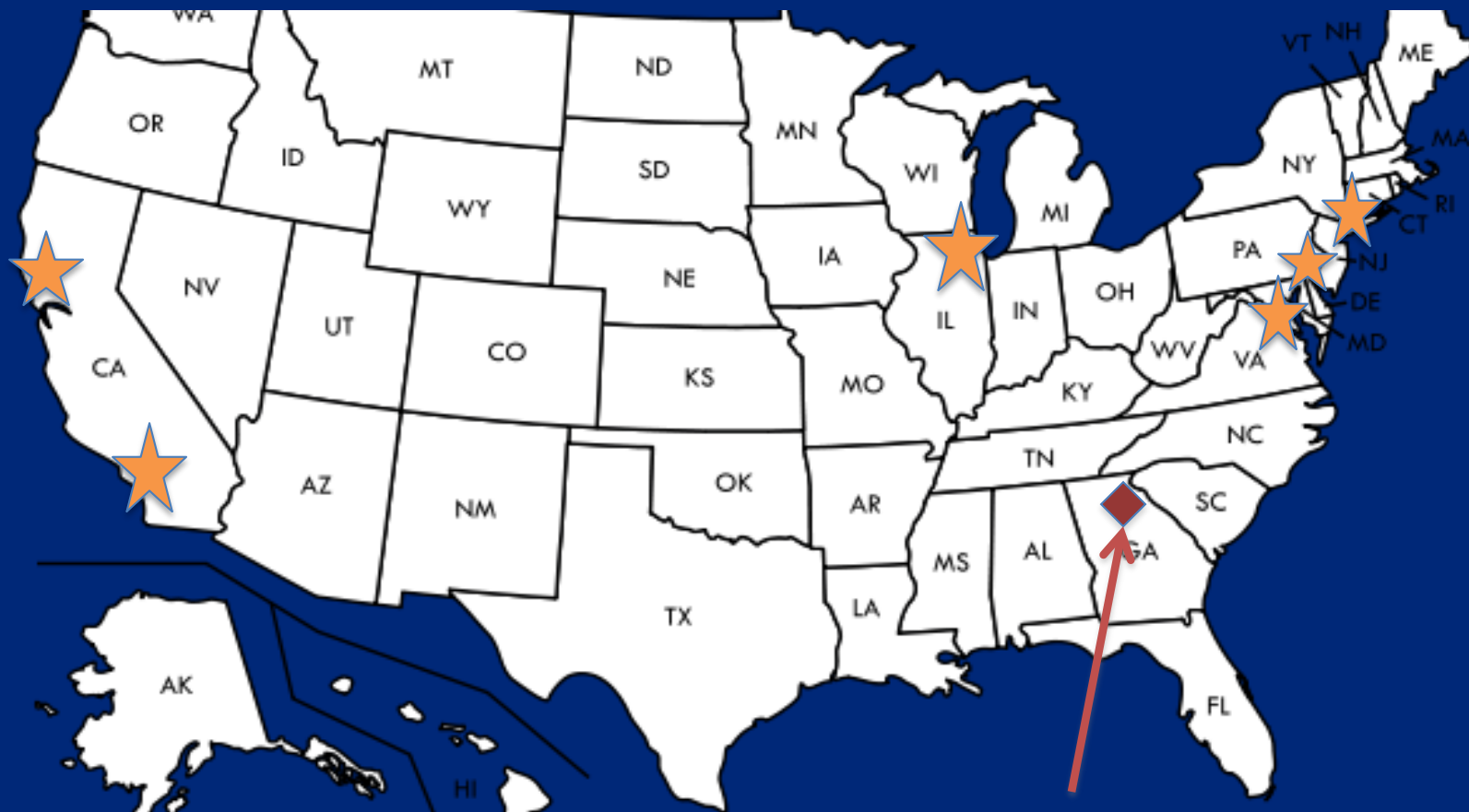


RESULTS

- **Increased Awareness:** 44.7% → 68.7%
- **Increased Use:** Greatest in MSM with h/o STI in last 12 months (~10%)
- Race, income, education associated with awareness but not with PrEP Use
- Surveys under-represented black MSM



CROI 2016: US Cities with significant increase in PrEP use 2012-2015



Out of 9 US Cities, Atlanta had lowest reported PrEP Use by 2015!



Local PrEP Infrastructure

Fulton County Health Department PrEP CLINIC



Dr. David Holland,
Chief Clinical Officer,
Fulton County Department of Health
and Wellness

- Started October 1, 2015
- As of February 26, 2016:
 - 39 referrals
 - 8 PrEP starts
 - 7 follow-up visits
- Backlog of patients waiting for initiation visit: numbers expected to double in next couple of weeks!



PrEP Take Home Points

- Daily PrEP is safe and effective in reducing the risk of HIV acquisition in adults.
- HIV negative MSM, heterosexual men and women and IV drug users at increased risk of HIV acquisition should be evaluated for PrEP.
- Uptake of PrEP nationally and especially locally has been slow but is starting to build



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What's new in HIV diagnostics?

Older HIV Diagnostics

Old algorithm:

Immunoassay HIV Antibodies → HIV Western Blot

- Fails to identify acute HIV infections
 - Higher risk of HIV transmission during early infection
 - ART Initiation in early HIV infection can benefit patients and reduce transmission
- Immunoassays can detect HIV infection earlier now, leading to false negatives on Western Blots
- Western Blots misclassify HIV-2 infections



4th gen

3rd gen

Rapid testing

b



Aptima (-26)

-25



Architect (-20)

-20



Advia (-14)

-15

Vitros (-13)

GS + O (-12)

-10



Reveal
Multispot (-7)

Statpak/Complete (-5)

Reveal G2 & G3 (-6)

-5

Unigold (-2)

Oraguid (-1)

WB POSITIVE

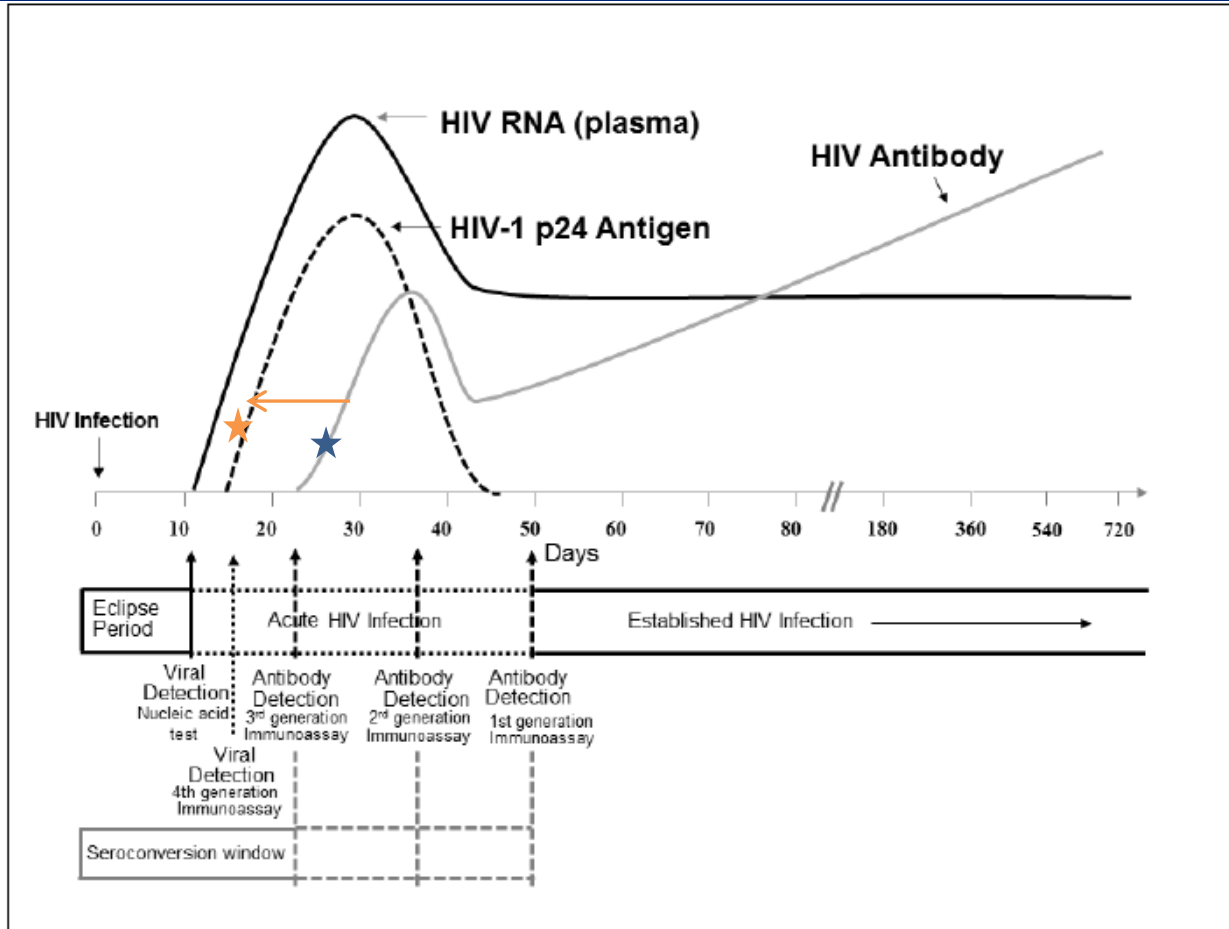
0

Days before Western blot positive



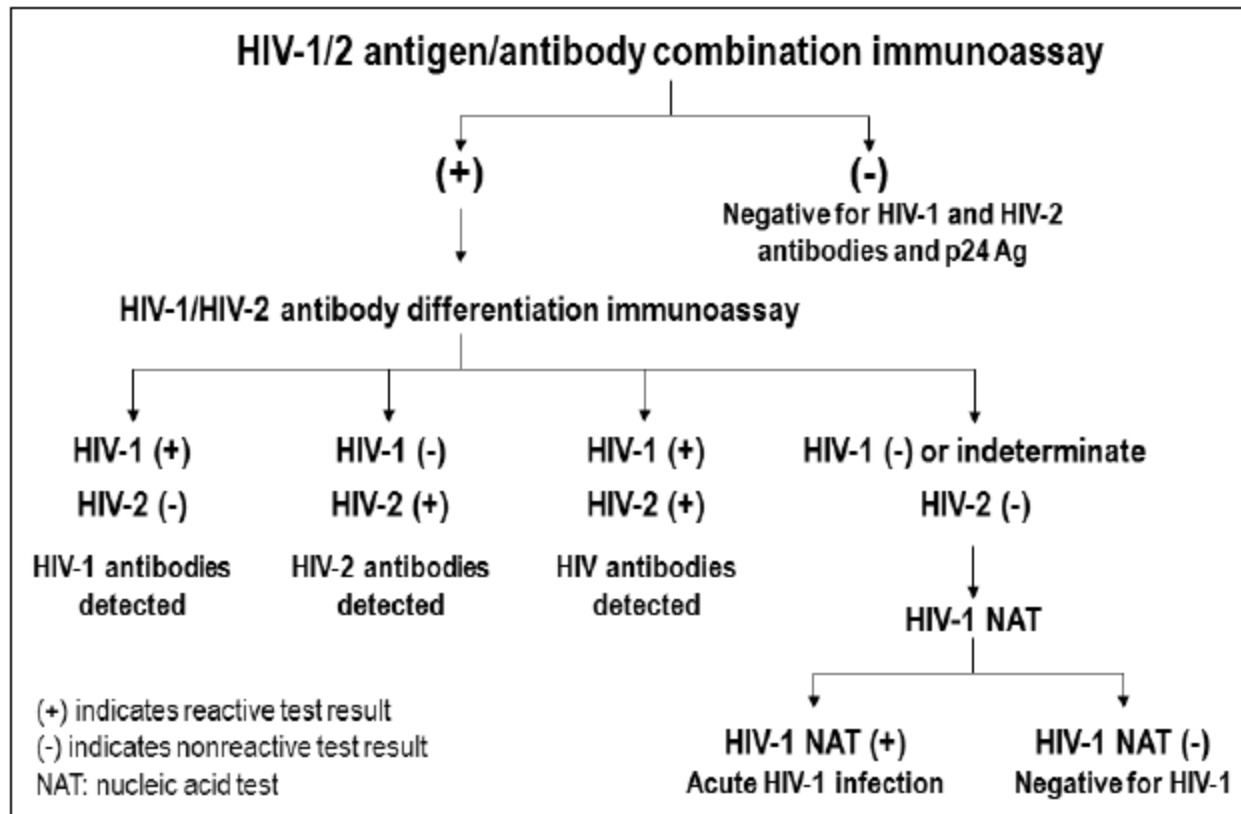


New HIV diagnostics: 4th generation Ag/Ab combination tests



Adapted from 2014 CDC Laboratory Testing for the Diagnosis of HIV Infection, Figure 1.

CDC recommended New Testing Algorithm



Adapted from 2014 CDC Laboratory Testing for the Diagnosis of HIV Infection, Box 1.

Take Home Points: HIV Testing

- HIV Western Blots have been removed from newer HIV testing algorithms
- 4th generation Ag/Ab tests:
 - Detect HIV infection before seroconversion
 - Lower false + and false - rates than 3rd generation
 - Do not distinguish between acute and chronic HIV
 - Will NOT capture all acute HIV infections



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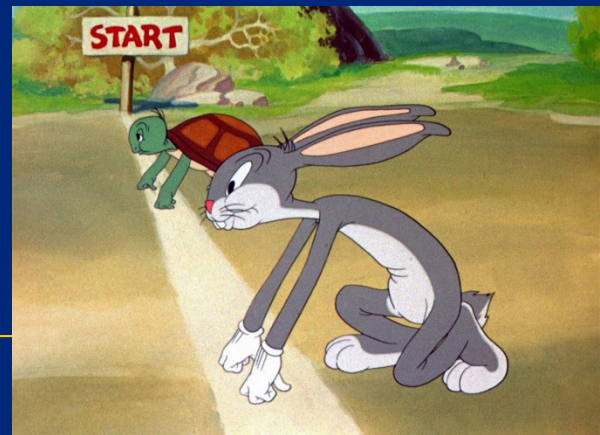
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What's new in HIV treatment?





When to start ARVs?



Short answer: NOW!!!!!!

START trial

HIV + with
CD4 > 500

1:1
Randomization

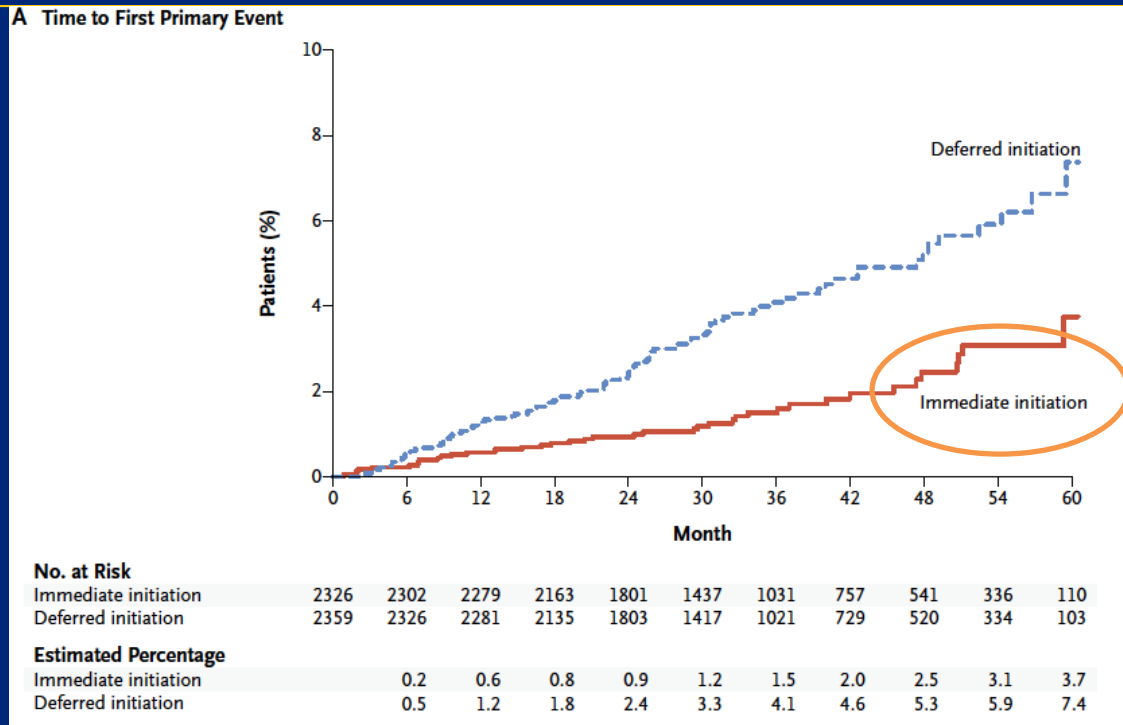
Immediate
ART
n = 2326

Deferred ART
(CD4 < 350 or
AIDS event)
n = 2359

Composite primary endpoint: any serious AIDS-related event, serious non-AIDS event, death from any cause.



START Trial Results



Immediate vs Deferred ART group had:

- 57% decrease in composite primary endpoint
- 72% decrease in AIDS-related events
- 39% decrease in non-AIDS related events

HIV First-Line Regimens: Easier on Patients and Providers!

First-Line Regimens

- 4 integrase-inhibitor based
 - High efficacy
 - Well tolerated
 - 2 are one pill once daily options
- 1 protease-inhibitor based
- NNRTI-based regimens (e.g Atripla) no longer recommended 1st line
 - Toxicity
 - Poorly tolerated

One Pill Once a Day Options

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Medications	Brand	Year approved	Pill
TDF/FTC/Efavirenz	ATRIPLA	2006	
TDF/FTC/Rilpivirine	COMPLERA	2011	
TDF/FTC/Elvitegravir/co bicistat	STRIBILD	2012	
Abacavir/lamivudine/do lutegravir	TRIUMEQ	2014	
TAF/FTC/Elvitegravir/co bicistat	GENVOYA	2015	
TAF/FTC/Rilpivirine	ODEFSEY	2016	

What's on the horizon?

- Long-acting injectables
 - LATTE 2 Study: Cabotegravir + Rilpivirine
 - Phase IIb study
- Drugs with less toxicity
 - TAF (tenofovir alafenamide): easier on kidneys and bone
- New classes of ARVs
 - Maturation inhibitors





Treatment take home points

- All HIV-infected persons should be started on combination ART, regardless of CD4 count
- Integrase inhibitor-based regimens have moved to forefront due to potency and tolerability
- Development of new treatment options is focused on non-oral formulations and minimizing long-term toxicity

Acknowledgements

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THANK YOU!!





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Extra Slides