AMERICAN ACADEMY OF HIV MEDICINE

In collaboration with

NHMA

National Hispanic Medical Association

HIV Next Steps

An Overview of the Current Epidemiology and Treatment of HIV

Wednesday, March 15, 2023 1:00– 2:00 PM Eastern

Target Audience

This activity has been designed to meet the educational needs of physicians. However, physician assistants, nurse practitioners, pharmacists, and registered nurses; other healthcare providers, such as nutritionists, social workers, and case managers are also encouraged to attend.

Statement of Need/Program Overview

Medical providers need access to a number of topics for accredited, continuing medical education that addresses the needs of their patients in real time. By using the Academy's provider network of dues paying members and credentialed providers to identify topics of needed medical education and rapidly develop live webinars that can be recorded for additional viewing, the National Hispanic Medical Association will meet CME needs from the community.

Accreditation Statement

In support of improving patient care, this activity has been planned and implemented by Amedco LLC and National Hispanic Medical Association. Amedco LLC is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

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Physician Continuing Medical Education

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Disclosure of Unlabeled Use

This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The planners of this activity do not recommend the use of any agent outside of the labeled indications.

The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

In this activity the faculty do discuss the use of investigational antiretroviral agents and treatment regimens that are not approved by treatment guidelines.

Disclaimer

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patient's conditions and possible contraindications on dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities.

Fee Information

There is no fee for this educational activity.

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Speaker Disclosure

- Speaker Bureau ViiV, Gilead, Janssen
- Research funding ViiV Gilead

Learning Objectives

- Appraise the current epidemiology and spread of HIV in the United States and factors affecting the spread of HIV
- Discuss when to initiate treatment for persons with HIV (PWA)
- Differentiate between PWA with detectable and undetectable viral loads and how this contribute to new infections
- Compare and contrast the recommended treatment regiments for PWA, especially newly the newly diagnosed
- Assess future treatment options for HIV
- Evaluate HIV-cure research

Agenda

- Epidemiology
- Treatment
  - When to treat
    - U=U
    - Rapid ART
  - What do we treat with
- Future treatment directions
- Cure research

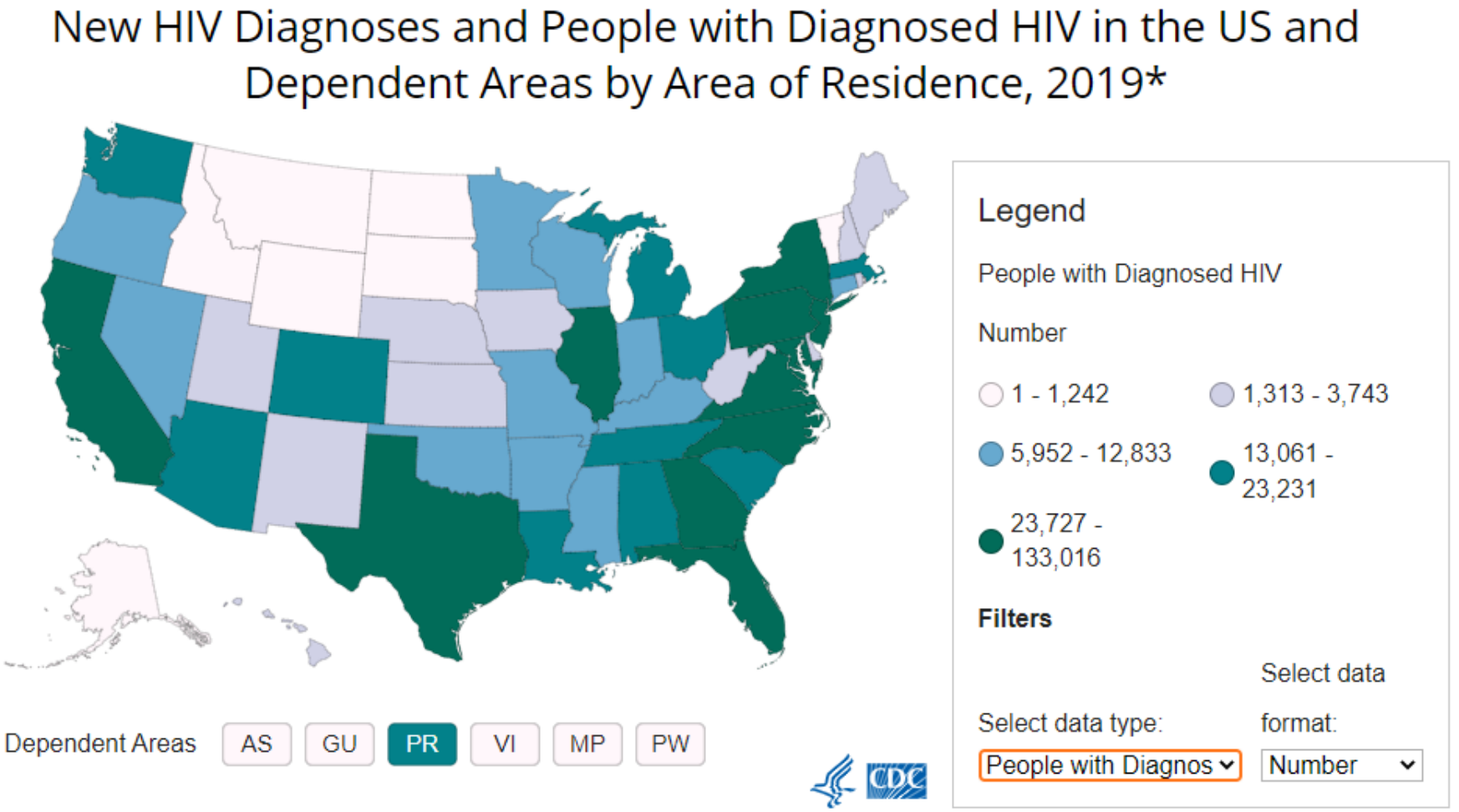
An introduction

- I do not have patients living with HIV and have not prescribed antiretroviral treatment and do not intend to
- I do not have patients with HIV and have not prescribed antiretroviral treatment but would like to
- I have a few patients living with HIV and have prescribed antiretrovirals a few times
- I have numerous patients with HIV and regularly prescribe antiretrovirals
- I am not in a position to treat patients living with HIV but have an interest in the state of HIV currently

Our case

- You are reviewing your daily schedule and your medical assistant advises you that you will be seeing a patient newly diagnosed with HIV. Since this is a last-minute add-on, you do not have further details on this patient yet.
- Take a moment, who may this patient be?
  - Are they younger, older?
  - Are they female, male, gender nonbinary?
  - What is their race/ ethnicity?

Epidemiology: HIV Prevalence



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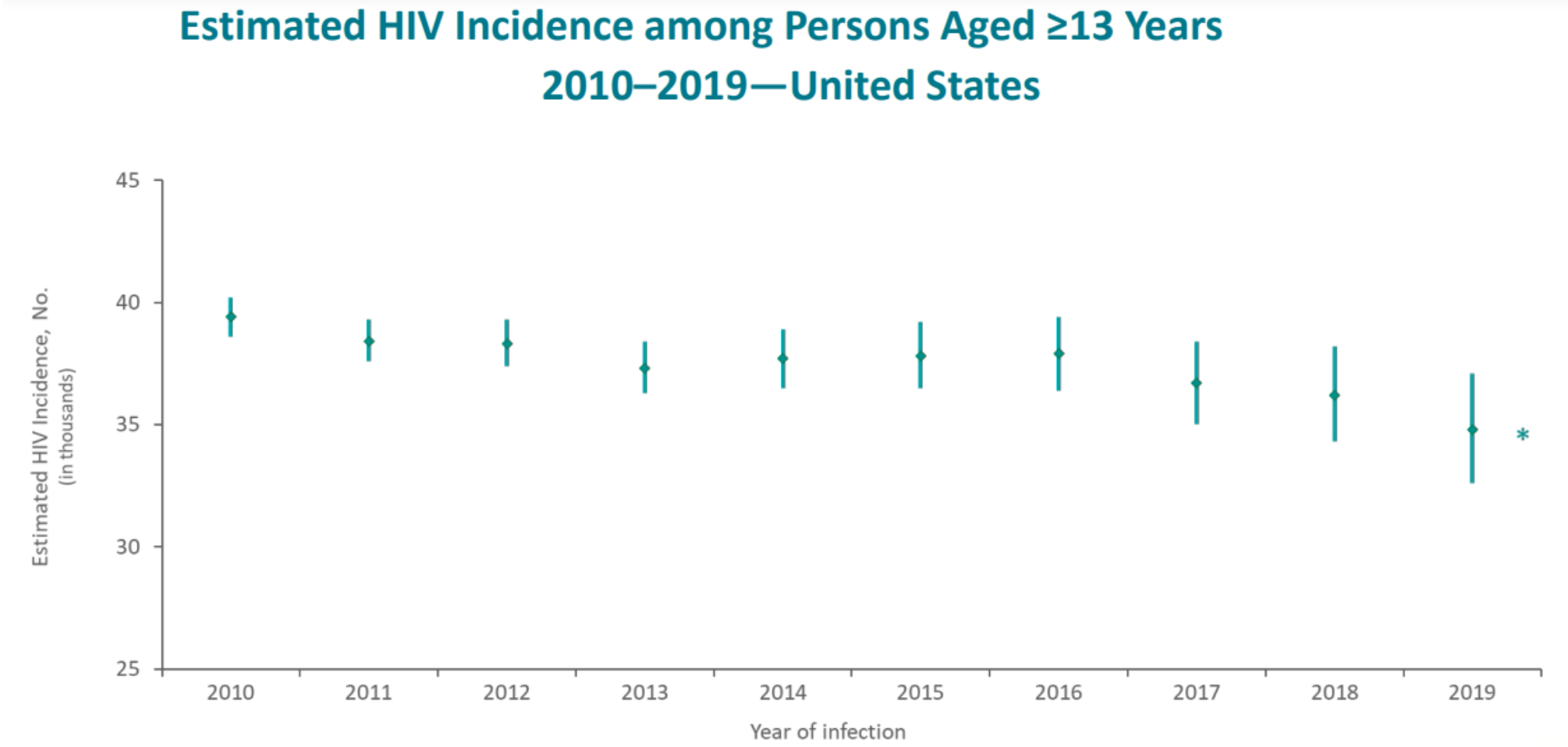
Epidemiology: HIV Incidence

- 36,801 people with an HIV diagnosis in 2019
  - 69% in gay and bisexual men
  - 23% in heterosexual men and women
  - 7% in people who inject drugs
- New diagnosis decreased 9% from 2015 to 2019

Incidence is decreasing over time



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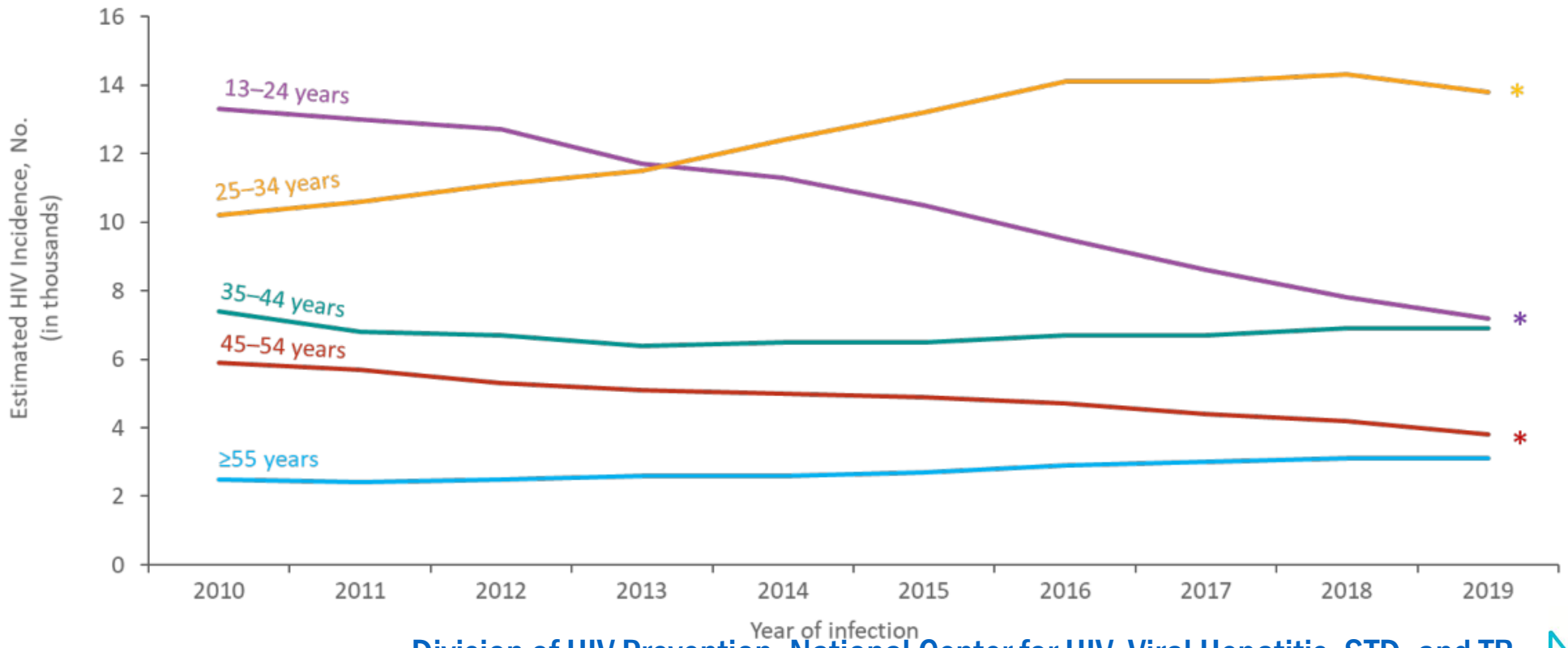
But not in all age groups

Estimated HIV Incidence among Persons Aged ≥13 Years, by Age 2010–2019—United States



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What is the lifetime risk of HIV for all people in the United States?

- 1 in 56
- 1 in 120
- 1 in 245
- 1 in 500

Lifetime HIV Risk

- Based on 2017-2019 US data, the lifetime risk of a HIV diagnosis was

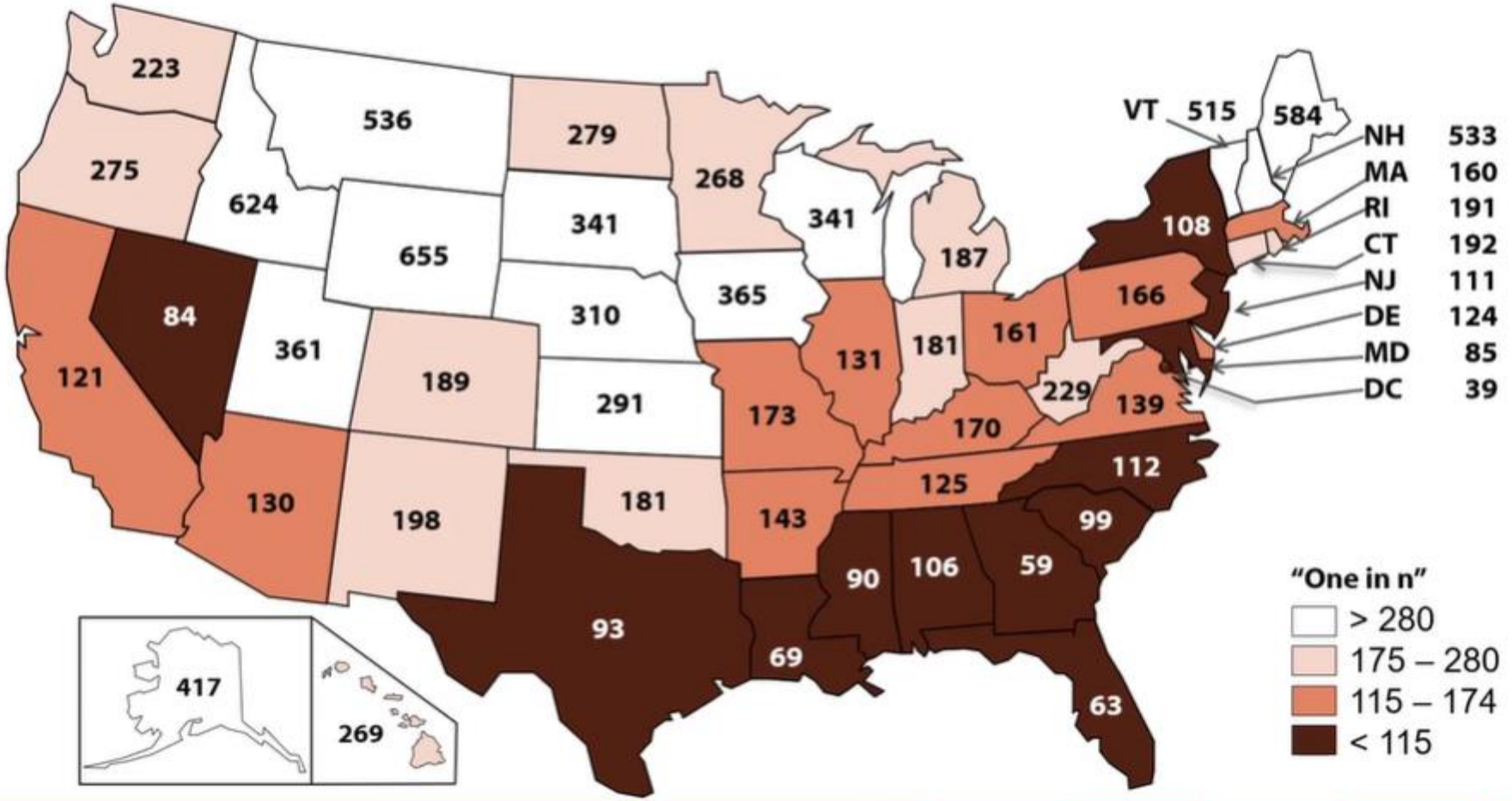
1 in 120

  - 1 in 76 for males
  - 1 in 309 for females

Singh, Abstract 43, CROI, 2022

Lifetime Risk of an HIV Diagnosis by State

- **Overall: 1 in 120**



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Epidemiology: Disparities

Black Mothers Keep Dying After Giving Birth. Shalon Irving's Story Explains Why

December 7, 2017 · 7:51 PM ET
Heard on All Things Considered

NINA MARTIN, PROPUBLICA

RENEE MONTAGNE

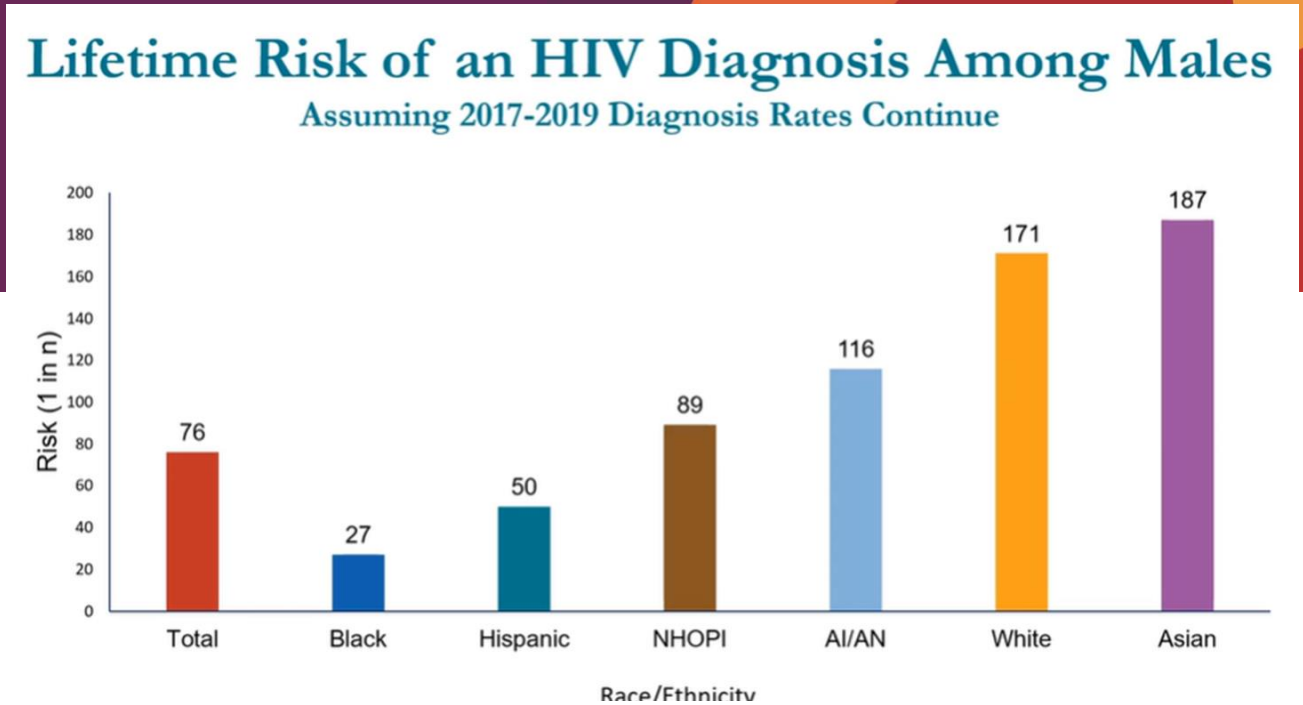
12-Minute Listen

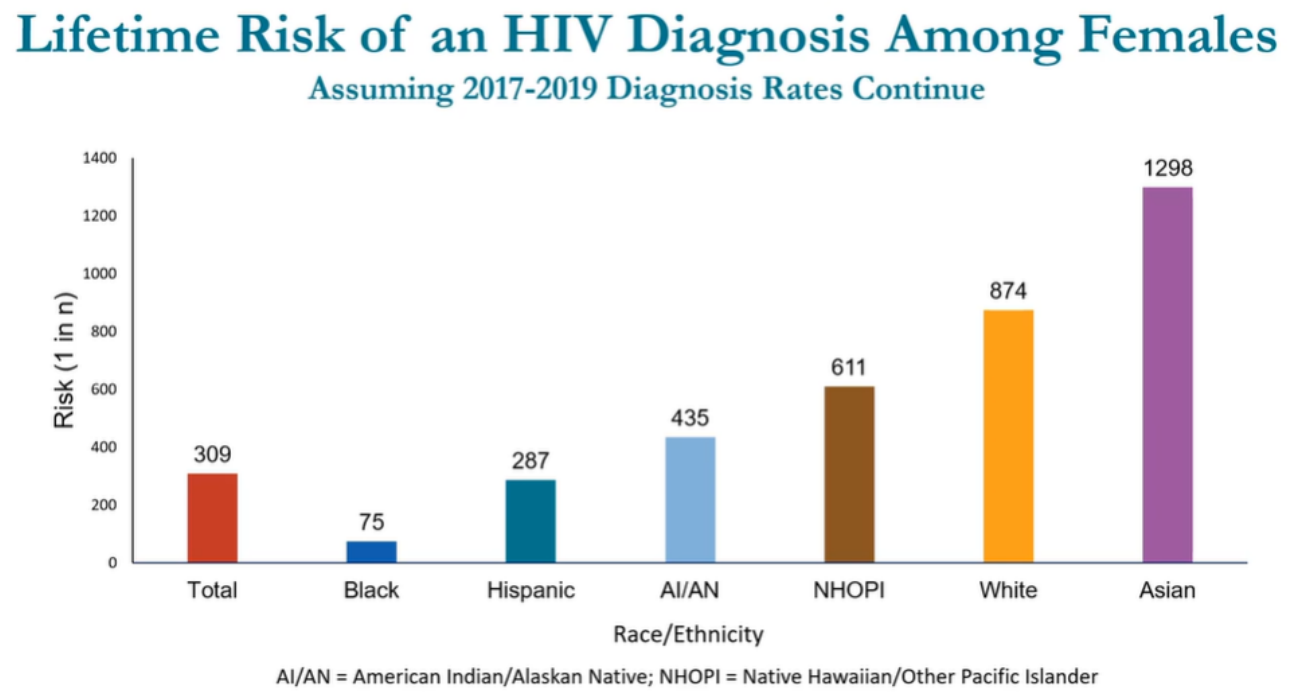
What are the 3 groups are at highest risk for HIV in the United States?

- Black males, Latino males, Hawaiian/PI males
- Black males, Latino males, White males
- Black males, Latino males, Black women
- Black males, Latino males, Asian males

Risk by Race / Ethnicity

- The 3 groups at highest risk for HIV are Black men, Latino men and Black women
- Risk per group:
  - 1 in 20 Black males
  - 1 in 50 Latino males
  - 1 in 75 Black women

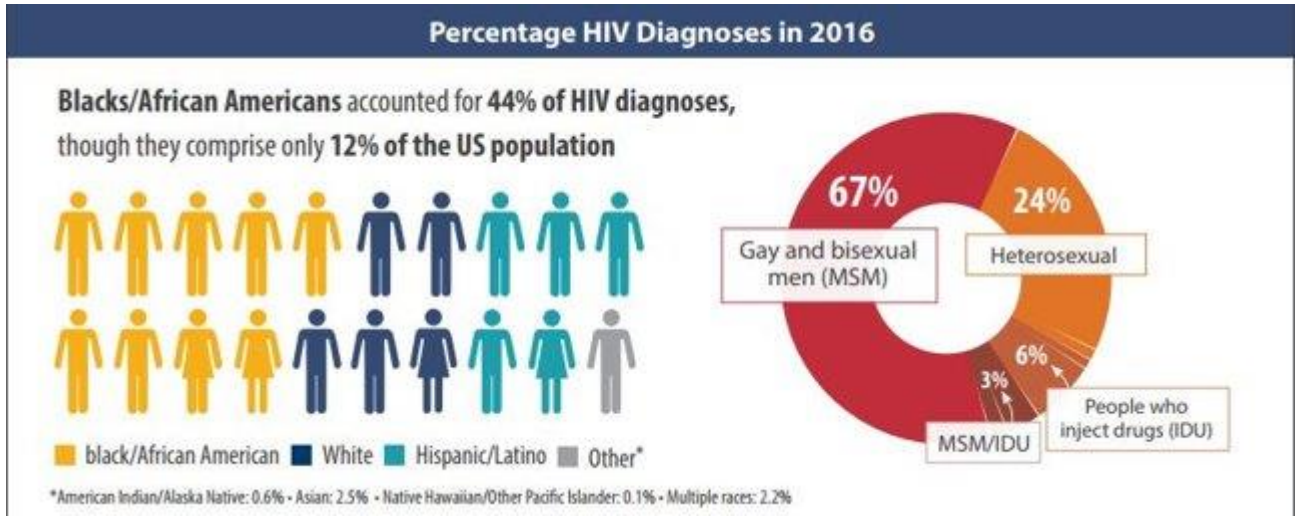




Singh, Abstract 43, CROI, 2022

Disparities

- Black/African American people are 14% of the total US population, made up 46% of new diagnosis of HIV in 2019
- Latinx/Hispanic are 18% of the US population but 29% of new HIV diagnosis



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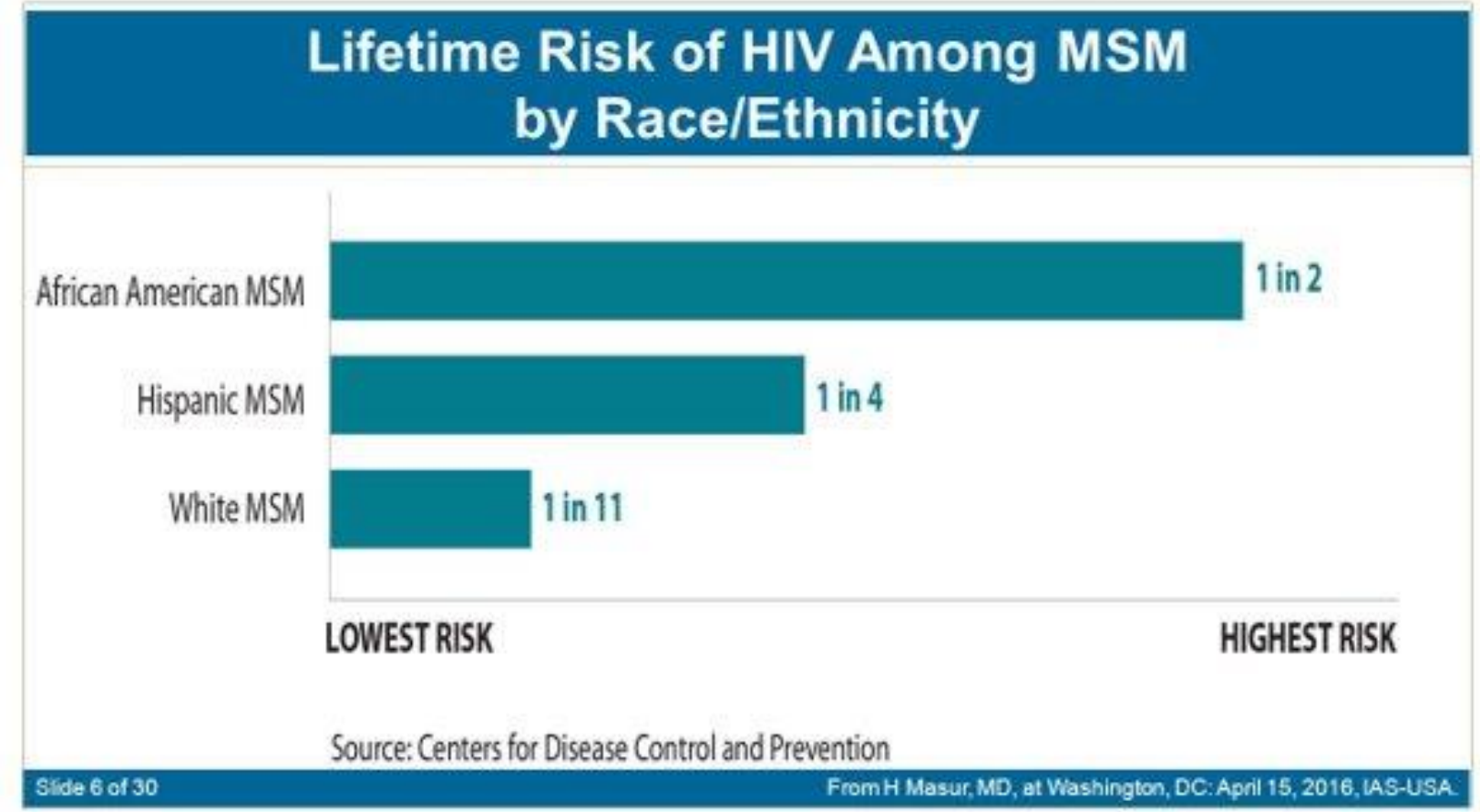
Disparities



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Questions/ Clarifications?

Our case continued

- Your patient, Antonio, is a 25-year-old cisgender Latinx male who has sex with men. He tested positive for HIV 2 weeks ago. He has been getting every 3–6-month STD screening and had last tested negative for HIV 6 months ago. He wants to know what the next steps are and if he can start treatment right away.

Our case continued

What do you do next?

- Order baseline labs and recommend treatment start when you have results
- Order labs and recommend treatment start when CD4 count is <500
- Order labs and start treatment today
- Order labs and refer to an HIV specialist for treatment start

When to Start ART?

What's the Data?

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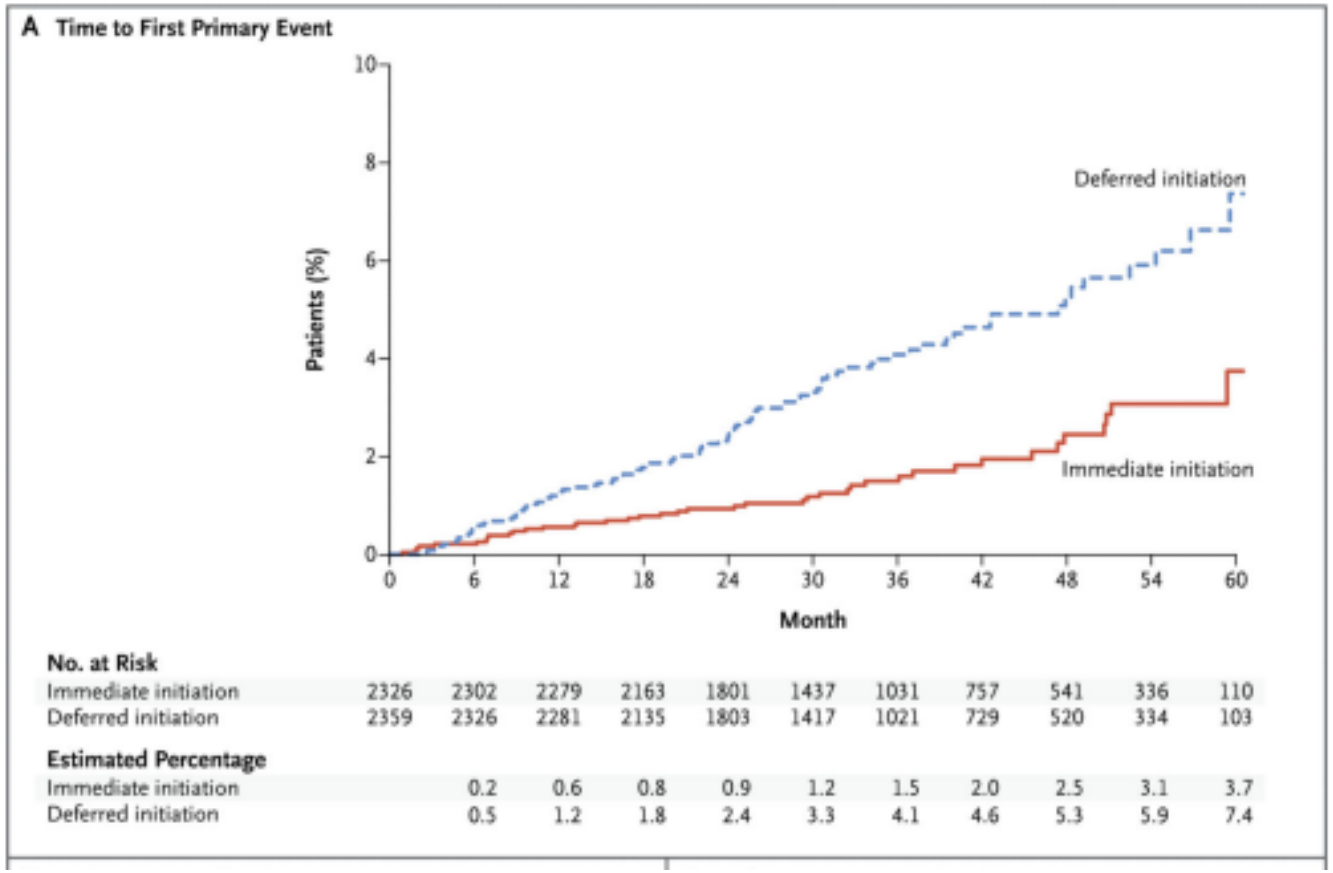
Initiation of ART in Early Asymptomatic HIV Infection

- Assigned HIV positive adults with CD4 >500 to immediate treatment initiation versus delayed initiation once CD4<350
- End points serious AIDS related event, serious non-AIDS related event, death from any cause



Insight Start Study Group: Initiation of Antiretroviral Therapy in Early Asymptomatic Infection

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Initiation of ART in Early Asymptomatic HIV Infection

Immediate treatment start prevents morbidity and mortality

Transmission in serodifferent couples

- HPTN 052:
  - HIV serodifferent couples randomized to early/immediate treatment versus treatment when CD4 fell below standard of care
  - >1,600 heterosexual couples over 10 years
  - 8 of HIV transmission within couples after HIV-infected partner was given ART
    - Four of these eight cases were diagnosed soon after ART initiation and transmission]
    - 4 HIV-infected partner had detectable levels of virus in the blood despite being on ART (i.e., treatment failure).
  - **no HIV transmission observed when partner was fully virally suppressed**

Transmission in serodifferent couples

- PARTNERS
  - All serodifferent couples (1166 couples heterosexual and gay)
  - 58,000 sex acts without condoms
- PARTNER2
  - 800 gay couples, 77,000 sex acts without condoms
- Opposites Attract
  - 358 gay male couples
  - 16,800 acts of anal sex without condoms

ALL SHOWED NO LINKED TRANSMISSIONS

Undetectable = Untransmittable

Media Advisory Thursday, January 10, 2019

The science is clear: with HIV, undetectable equals untransmittable

NIH officials discuss scientific evidence and principles underlying the U=U concept.

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Undetectable = Untransmittable

There is no risk of transmission of HIV from an HIV+ partner to a HIV- partner if the HIV+ partner's viral load is undetectable ≥ 6 months

CAVEATS:

- Applies only to sexual transmission
  - No data on IDU as mode of transmission
  - Does not apply to perinatal transmission

What is defined as “undetectable” when saying undetectable = untransmittable?

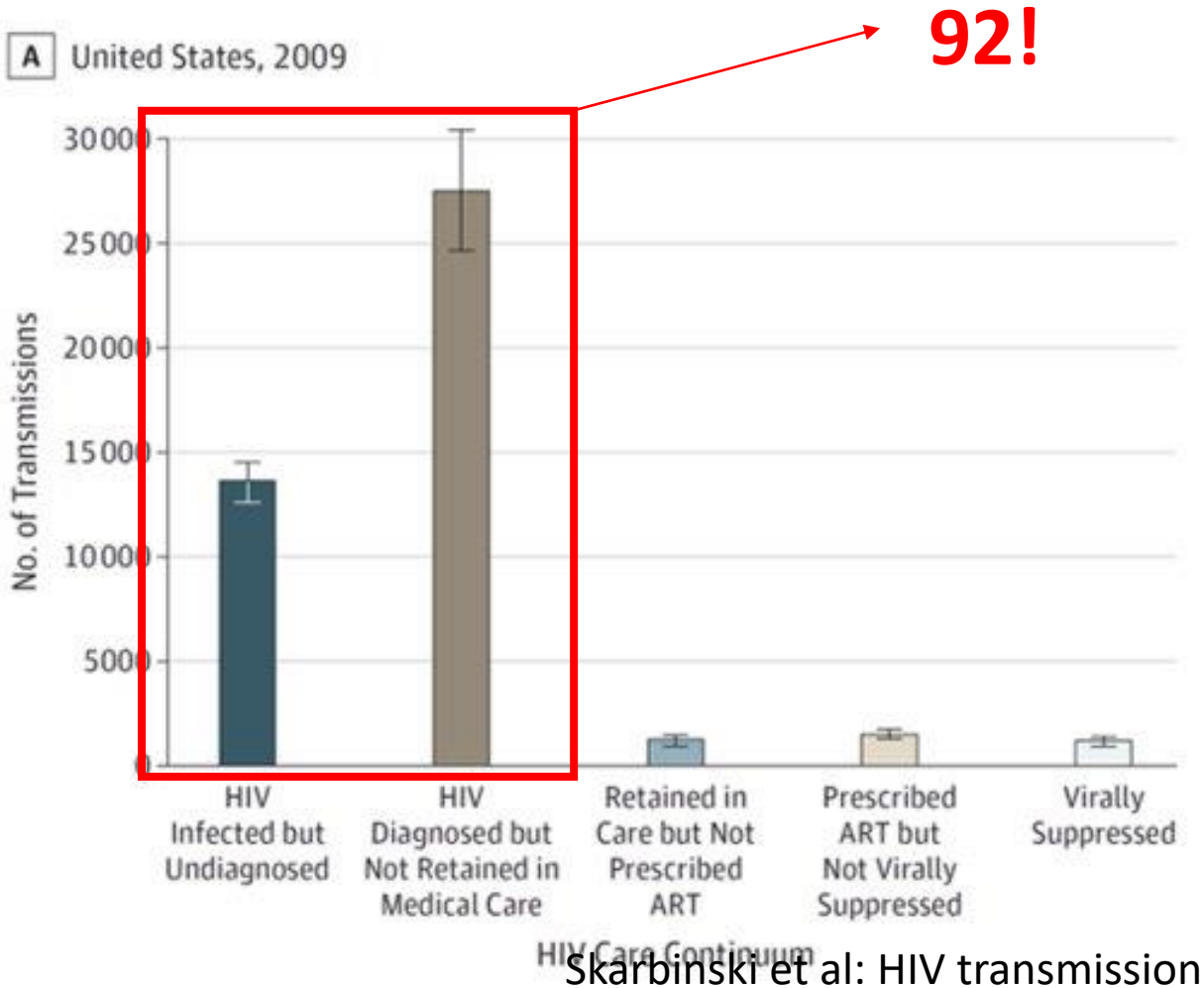
- Less than 20 copies/mL
- Less than 40 copies/mL
- Less than 100 copies/mL
- Less than 200 copies/mL
- Less than 500 copies/mL

What is defined as “undetectable” when saying undetectable = untransmittable?

Less than 200 copies

- Sometimes referred to as viral suppression
- Suppressed = untransmittable

HIV Transmission at Each Step of the Care Continuum



Skarbinski et al: HIV transmission at each step of the care continuum in the United States

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Treatment As Prevention

Given the efficacy of antiretroviral treatment in eliminating sexual transmission of HIV, starting treatment early is a way to prevent new HIV transmissions

Rapid Start: SF Data

- In 2013-14 SF piloted the Rapid ART Program Initiative for New Diagnosis (RAPID)
- Goal: Linkage to care within 5 days of HIV diagnosis and ART initiation within 1 day of the first care visit
- Persons with a rapid ART start were **more likely to be virologically suppressed within 12 months of diagnosis** than those with a non-rapid start (RR, 1.17; 95% CI, 1.10–1.24).

Bacon et al. Clinical Infectious Diseases. 2021

Rapid Start: SF Data

Starting treatment early increases likelihood of remaining virologically suppressed over time

When to start treatment?

DHHS Guidelines:

The Panel of Antiretroviral Guidelines for Adults and Adolescents recommends **initiating ART immediately (or as soon as possible) after HIV diagnosis** in order to:

- Increase the uptake of ART and linkage to care
- Decrease the time to viral suppression for individual patients
- Improve the rate of virologic suppression among person with HIV

DHHS Guidelines FOR THE Use of Antiretroviral Agents in Adults and Adolescents with HIV

Questions/ Clarifications?

What to Start?

What are the guidelines?

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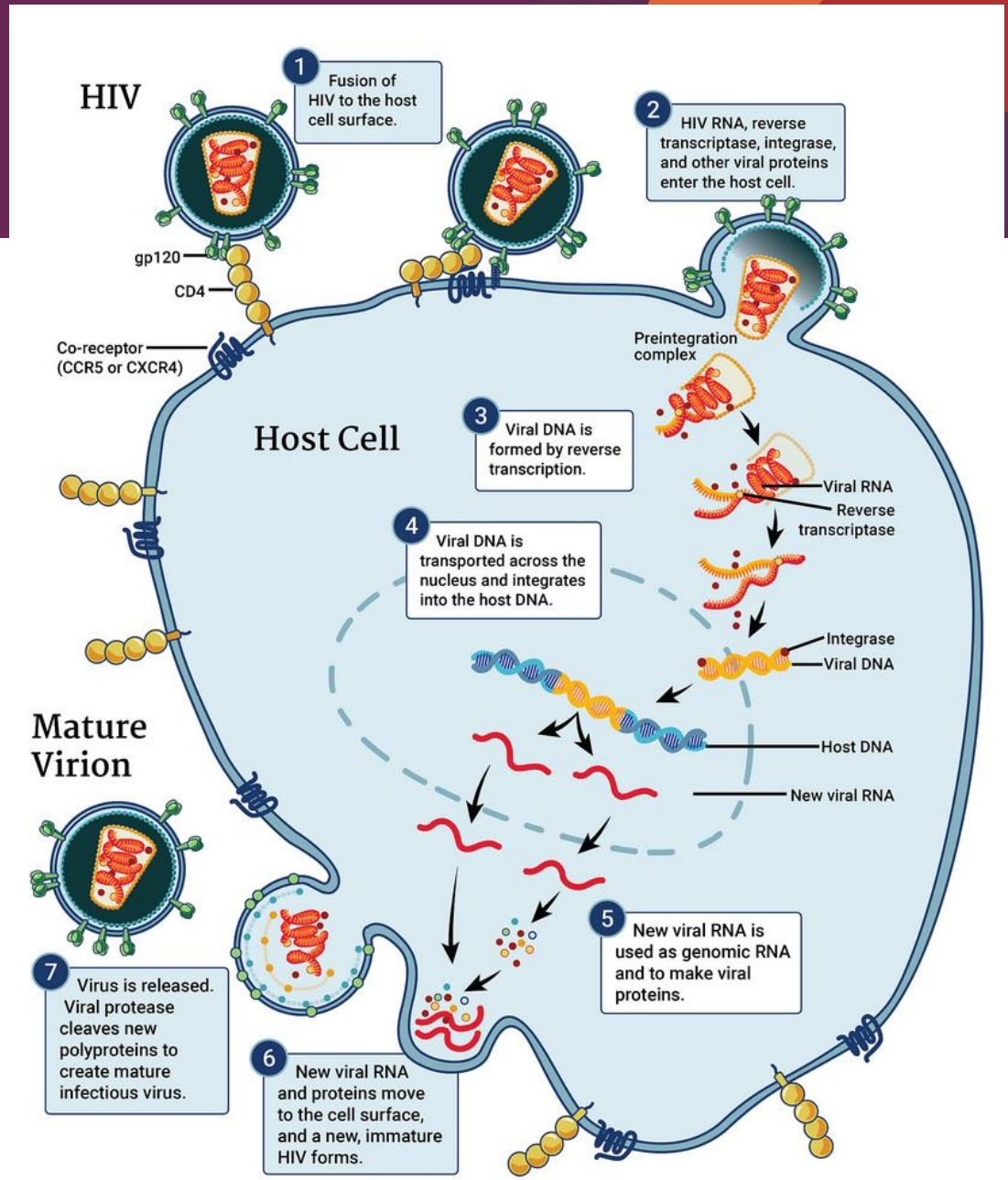
The HIV Replication Process



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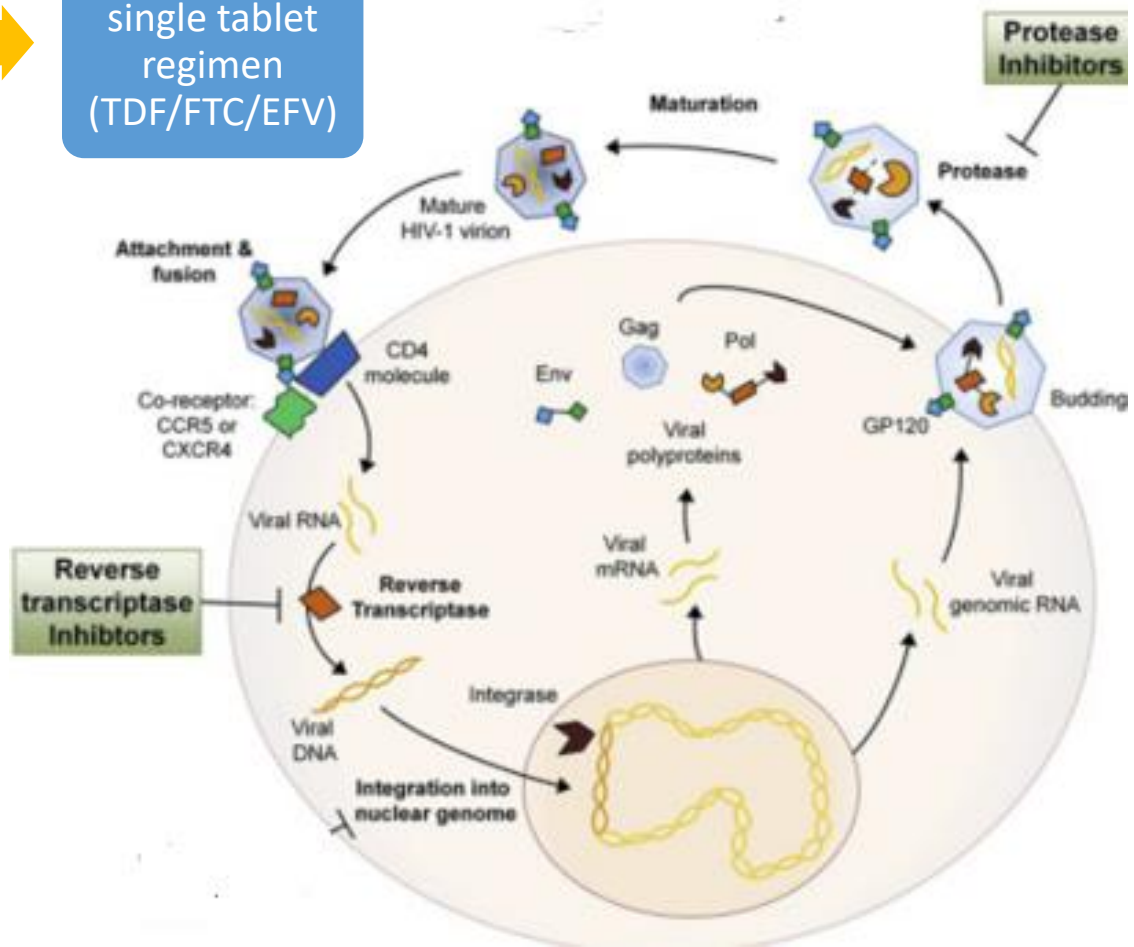
HIV Treatment Targets 1980's - 2007

1987: AZT approved → 1995: first PI approved → 1996: cART → 2006: first single tablet regimen (TDF/FTC/EFV)



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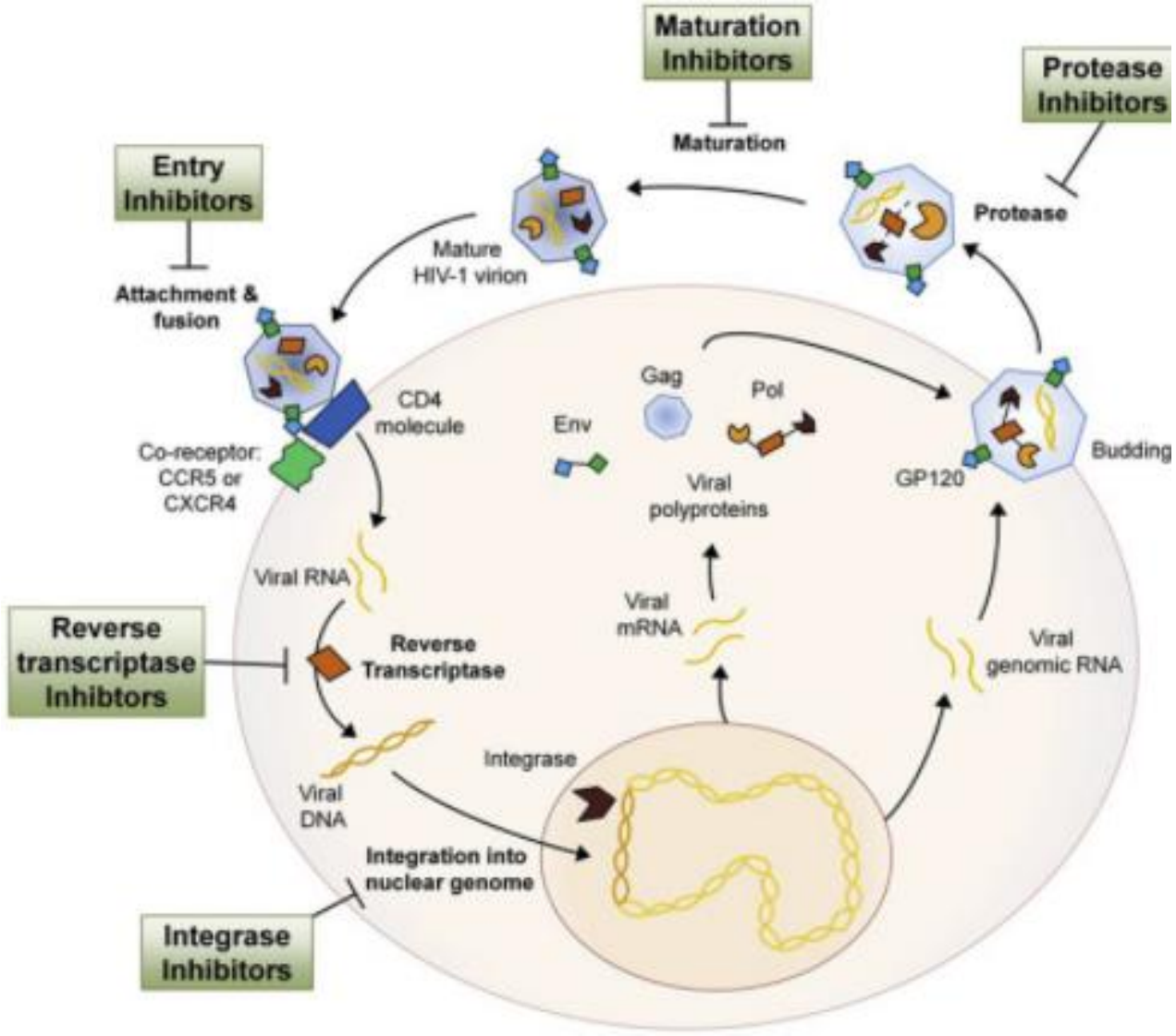
HIV Treatment Targets: 2022



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2022 Treatment Options

Generic name	Trade name	Formulation	Standard adult dose	Pills/day
Single-tablet regimens				
Bictegravir/ emtricitabine/tenofovir alafenamide	*Biktarvy*	Tablet comprising 50mg bictegravir, 200mg emtricitabine, 25mg tenofovir alafenamide	One tablet once a day	1
Darunavir/cobicistat/ emtricitabine/tenofovir alafenamide	*Symtuza*	Tablet comprising 800mg darunavir, 150mg cobicistat, 200mg emtricitabine, 10mg tenofovir alafenamide	One tablet once a day	1
Dolutegravir/abacavir/ lamivudine	*Triumeq*	Tablet comprising 50mg dolutegravir, 600mg abacavir, 300mg lamivudine	One tablet once a day	1
Dolutegravir/rilpivirine	*Juluca*	Tablet comprising 50mg dolutegravir and 25mg rilpivirine	One tablet once a day	1
Doravirine/lamivudine/ tenofovir disoproxil	*Delstrigo*	Tablet comprising 100mg doravirine, 300mg lamivudine, 245mg tenofovir disoproxil	One tablet once a day	1
Efavirenz/emtricitabine/ tenofovir disoproxil *Generic product, appearance will vary*	generic	Tablet comprising 600mg efavirenz, 200mg emtricitabine, 245mg tenofovir disoproxil	One tablet once a day	1
Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide	*Genvoya*	Tablet comprising 150mg elvitegravir, 150mg cobicistat, 200mg emtricitabine, 10mg tenofovir alafenamide	One tablet once a day	1
Elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil	*Stribild*	Tablet comprising 150mg elvitegravir 150mg cobicistat 200mg emtricitabine 245mg tenofovir disoproxil	One tablet once a day	1
Rilpivirine/ emtricitabine/tenofovir alafenamide	*Odefsey*	Tablet comprising 25mg rilpivirine, 200mg emtricitabine, 25mg tenofovir alafenamide	One tablet once a day	1
Rilpivirine/ emtricitabine/tenofovir disoproxil	*Eviplera*	Tablet comprising 25mg rilpivirine, 200mg emtricitabine, 245mg tenofovir disoproxil	One tablet once a day	1
Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs)				
Emtricitabine	*Emtriva*	200mg capsule	200mg once a day	1
Lamivudine *Generic product, appearance will vary*	generic	150 and 300mg tablets	150mg twice a day **or** 300mg once a day	2 1
Tenofovir disoproxil *Generic product, appearance will vary*	generic	245mg tablet	245mg once a day	1
Zidovudine *Generic product, appearance will vary*	generic	250mg capsule	250mg twice a day	2
NRTI fixed-dose combinations				
Abacavir/lamivudine *Generic product, appearance will vary*	generic	Tablet comprising 600mg abacavir and 300mg lamivudine	One tablet once a day	1
Emtricitabine/tenofovir alafenamide	*Descovy*	Tablet comprising 200mg emtricitabine and 10mg or 25mg* tenofovir alafenamide	One tablet once a day. The 10mg version is recommended for use in combination with some boosted protease inhibitors	1
Emtricitabine/tenofovir disoproxil *Generic product, appearance will vary*	generic	Tablet comprising 200mg emtricitabine and 245mg tenofovir disoproxil	One tablet once a day	1
Lamivudine/zidovudine *Generic product, appearance will vary*	generic	Tablet comprising 150mg lamivudine and 300mg zidovudine	One tablet twice a day	2
Integrase inhibitors				
Dolutegravir	*Tivicay*	50mg tablet	50mg once a day **or** 50mg twice a day if taken with efavirenz, nevirapine or tipranavir, or for HIV known to be resistant to integrase inhibitors	1 or 2
Raltegravir	*Isentress*	400* and 600mg tablets	400mg twice a day **or** two 600mg tablets once a day	2
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)				
Doravirine	*Pifeltro*	100mg doravirine	100mg once a day	1
Efavirenz *Generic product, appearance will vary*	generic	600mg tablet and 200mg capsule	600mg once a day	1 or 3
Etravirine	*Intelence*	100 and 200mg* tablets	200mg twice daily	2 or 4
Nevirapine *Generic product, appearance will vary*	generic	200mg and 400mg (extended-release) tablets	200mg once a day for two weeks then 200mg twice a day **or** 200mg once a day for two weeks then 400mg once a day	2 or 1
Rilpivirine	*Edurant*	25mg tablet	25mg once a day	1
Protease inhibitors				
Atazanavir *Generic product, appearance will vary*	generic	150, 200 and 300mg capsules	300mg with 100mg ritonavir once a day	2 or 3 §
Atazanavir/ cobicistat	*Evotaz*	Tablet comprising 300mg atazanavir and 150mg cobicistat	One tablet once a day	1
Darunavir *Generic product, appearance will vary*	generic	600 and 800mg tablets	800mg with 100mg ritonavir once a day **or** 600mg with 100mg ritonavir twice a day	2 to 4 §
Darunavir/ cobicistat	*Rezolsta*	Tablet comprising 800mg darunavir and 150mg cobicistat	One tablet once a day	1
Lopinavir/ ritonavir	*Kaletra*	Tablet comprising 200mg lopinavir and 50mg ritonavir	Two tablets twice a day **or** four tablets once a day	4
CCR5 inhibitor				
Maraviroc	*Celsentri*	150* and 300mg tablets	300mg twice a day **or** 150mg twice a day with ritonavir-boosted PI except tipranavir and fosamprenavir **or** 600mg twice a day with efavirenz or etravirine without a ritonavir-boosted PI	2 to 4

More than **30** antiretroviral drugs available including >10 single tablet regimens!

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DHHS Recommended Initial Regimens

- **Bictegravir**/tenofovir alafenamide/emtricitabine
- **Dolutegravir**/abacavir/lamivudine*
  - only for HLA-B*5701 negative and without chronic hepatitis B virus
- **Dolutegravir** plus (emtricitabine or lamivudine) plus (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF])
- **Dolutegravir**/lamivudine*
  - except for HIV RNA >500,000 copies/mL, HBV coinfection, or unknown genotype and/or HBV serologies

DHHS Recommended Initial Regimens

All 4 first line recommended treatment regimens are integrase inhibitors based!

- Well-tolerated
- Few drug-drug interactions
- High barrier to resistance

What about transmitted resistance?

- 50,747 persons in the analysis
- 9,616 (18.9%) had ≥1 transmitted drug resistance mutation
  - **0.8% for integrase strand transfer inhibitors (INSTIs)**
  - 4.2% for protease inhibitors
  - 6.9% for nucleoside reverse transcriptase inhibitors (NRTIs)
  - 12.0% for non-NRTIs.

McClung et al Clinical Infectious Diseases 2021

DHHS Recommended Initial Regimens: Rapid Start

- **Bictegravir**/tenofovir alafenamide/emtricitabine
- **Dolutegravir**/abacavir/lamivudine*
  - only for HLA-B*5701 negative and without chronic hepatitis B virus
- **Dolutegravir** plus (emtricitabine or lamivudine) plus (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF])
- **Dolutegravir**/lamivudine*
  - except for HIV RNA >500,000 copies/mL, HBV coinfection, or unknown genotype and/or HBV serologies

Case 2

- Monique is a 46 yo transwoman who was diagnosed with HIV in the 1990's. She has been on various treatment regimens and she cannot recall them all. She has been off treatment for the past 5 years, a period when she was dealing with opiate dependence. She is now in remission and is motivated to improve her health so she would love to start treatment as soon as possible. On ROS, she complains of headaches and you note that her vitals show a fever of 101.

Case 2

Patient with established HIV, off treatment, coming in with headache and fever, would you start treatment today?

- Yes
- No

When should we pause when considering rapid treatment?

- Highly treatment experienced patients
- CKD with GFR <30
- Some opportunistic infections
  - Cryptococcal meningitis
  - TB meningitis

DHHS Recommended Initial Regimens

Treatment	GFR
Bictegravir/tenofovir alafenamide/emtricitabine	GFR>30
Dolutegravir/ abacavir/ lamivudine	GFR>30
Dolutegravir plus (emtricitabine or lamivudine) plus (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF])	GFR>30 if using tenofovir alafenamide GFR>60 if using tenofovir disoproxil
Dolutegravir/lamivudine*	GFR> 30 (and close monitoring for GFR 30-50)

OI's and treatment start

- Immune Reconstitution Inflammatory Syndrome (IRIS)
  - Paradoxical worsening of pre-existing infection/ neoplasm following ARV start

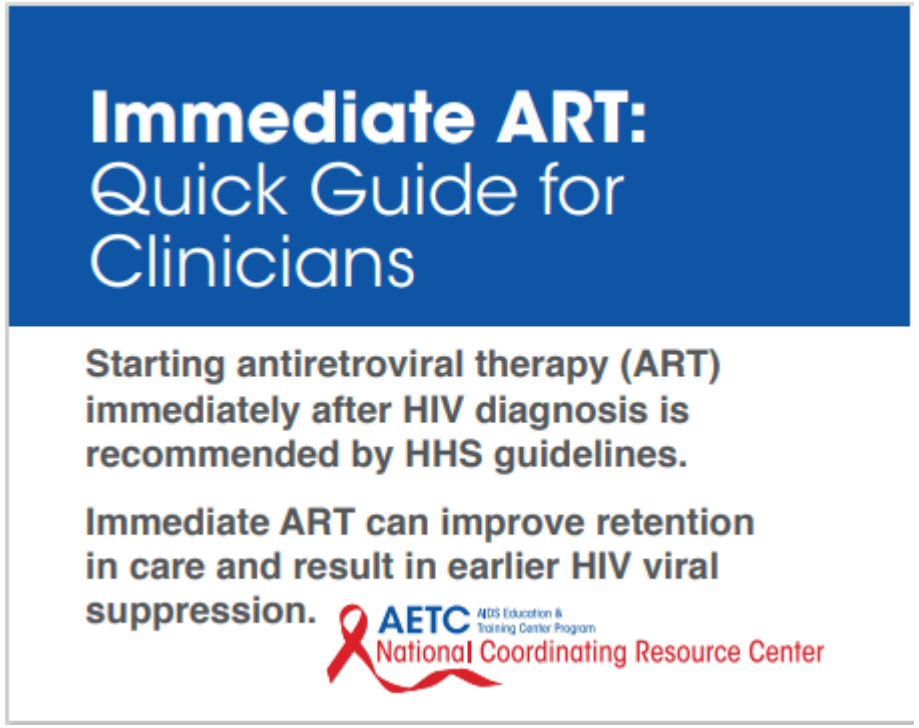
- Only 2 OI's should cause treatment delay due to increased mortality related to IRIS
  - Cryptococcal meningitis
  - TB Meningitis

Who you gonna call?

HIV Warm Line 1-800-933-3413

NATIONAL CLINICIAN CONSULTATION CENTER

Translating science into care



ncrc-rapid-art-pocket-guide-2-14-20.pdf (aidsetc.org)

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Questions/ Clarifications?

Back to case 1

Antonio comes back to discuss his labs and treatment. He has been taking bictegravir/ tenofovir alafenamide/ emtricitabine. His labs show he has no transmitted treatment mutations. He is immune to Hepatitis B due to childhood vaccination. He has no other medical conditions aside from his newly diagnosed HIV.

He is tolerating his regimen well but he admits that he finds it exceedingly hard to take his medication regularly due to his work schedule, which varies from day to day.

Case 1 continued

What options does Antonio have that may help with his adherence?

- Use a blister-packs
- Use his phone alarm
- Set his medication next to his toothbrush
- Transition to an injectable antiretroviral regimen

Future Directions: 2 drug regimens

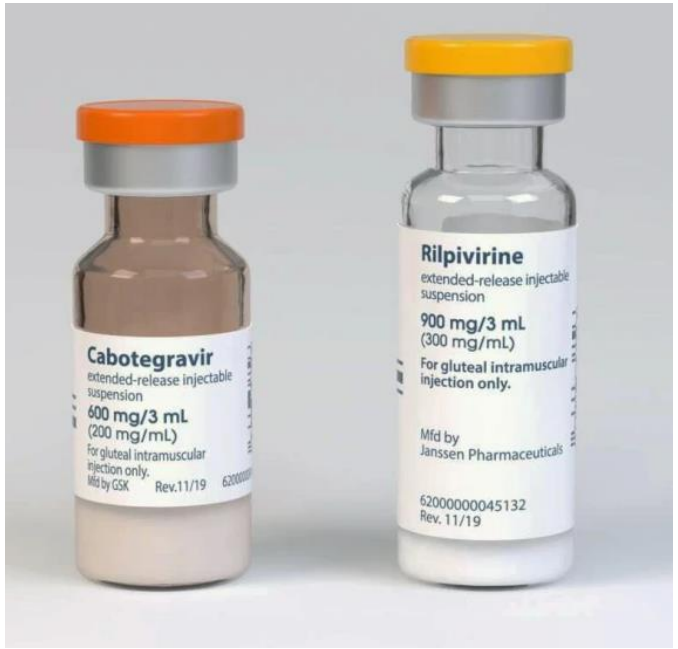
- Currently 3 available options (and more in development)
  - 3TC/DTG
  - DTG/RPV
  - CAB/RPV

- Typically studied in treatment naïve or virally suppressed patients without known resistance
- Cannot be used for people who are HBV co-infected

Future Directions: Long-acting regimens

CAB-RPV

- FDA approved
- IM injectable regimen given every 4 or 8 weeks
- Requires in office visit
- Most common adverse effect is injection site reaction



Future Directions: Long-Acting Regimens

Lenacapavir

- Capsid inhibitor
- Twice yearly injections

Islatravir

- Oral, injection, implant
- For treatment once weekly oral treatment
- Development halted

What About Cure?

- Research is looking at
  - Sustained ART-Free remission
  - Viral Eradication

Sustained ART-Free Remission

- Broadly neutralizing antibodies (bNAbs)
  - Block HIV strains from infecting human cells and facilitate killing of infected cells
- Botswana proof-of-concept study:
  - 28 children who had received ART from <7 days and had HIV VL<40
  - Entered study at >96 weeks
  - bNAb started and ART held after 8 weeks overlap
  - ART restarted if VL>400
  - 3 early viral rebound, 14 rebounded at 4 weeks, 11 children maintained VL<40 x 24 weeks,

Shapiro et al, CROI 2022, Abstract 32

HIV Eradication

- Shock and kill
  - Induce latently infected cells to express HIV proteins that therapeutic agents could kill
  - Latency reversing agents are under investigation

- Gene editing therapies
  - CCR5: remove immune cells, edit CCR5 gene and transfuse back
  - Removal of viral genes from latently infected cells

Conclusions

- Epidemiology
  - HIV Incidence is decreasing except in 25- to 44-year-olds
  - There are ongoing disparities in the populations affected with HIV
- Treatment
  - Guidelines recommend starting treatment early when possible
  - Integrase based regimens are first line
- Newer areas of treatment development include long-acting regimens and 2-drug treatment options
- Cure research continues and is focused on both remission and eradication

Questions/ Clarifications?