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Updates on Human Immunodeficiency Virus (HIV)

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Updates on Human Immunodeficiency Virus (HIV)

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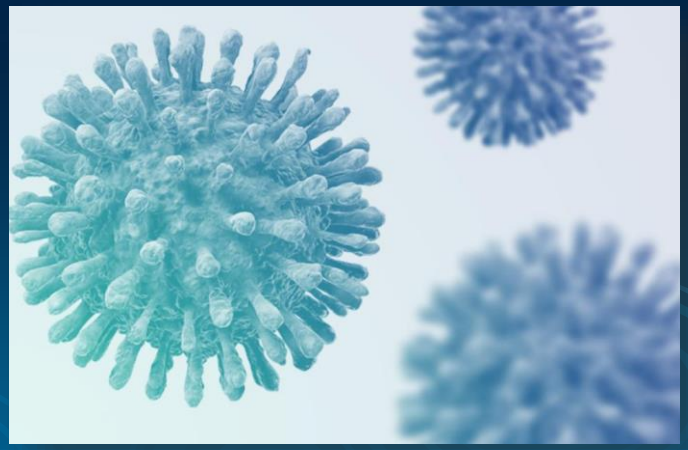


Baptist Health South Florida

Objectives

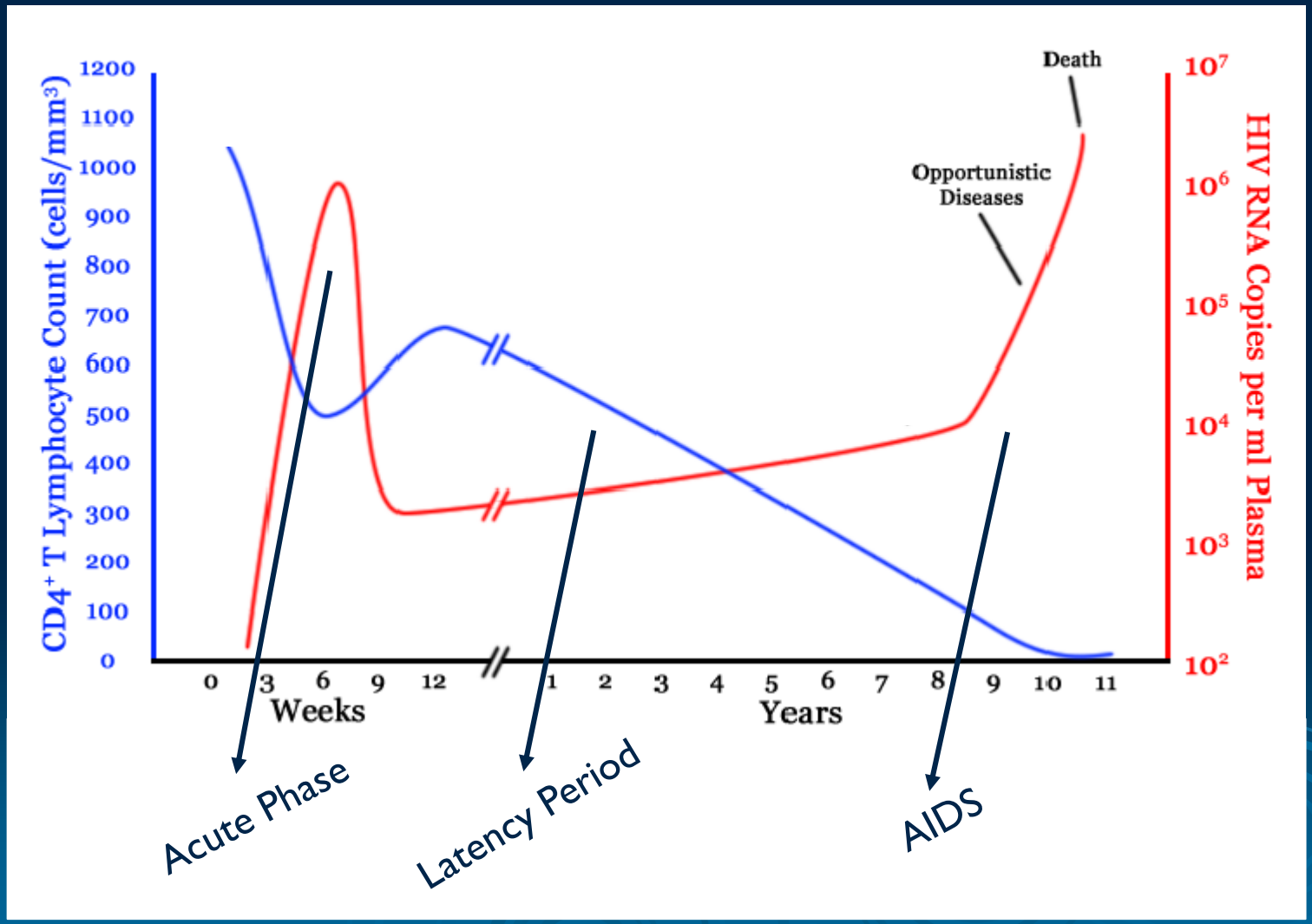
- Provide an overview on HIV
- Review the antiretroviral classes available for the management of HIV and their place in therapy
- Evaluate the new HIV treatment options
- Differentiate between pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP)
- Discuss the pharmacist role in the treatment of HIV

HIV Overview

- HIV attacks the body's immune system, particularly the CD4 cells which are used to fight off infections
- As the human body is unable to completely eradicate the virus, HIV is considered a life diagnosis and generally uncurable
- HIV can lead to acquired immunodeficiency syndrome (AIDS) if untreated
- With proper medical care, HIV can be controlled and patients are expected to have a similar life-expectancy to someone living without HIV
- Antiretroviral therapy (ART) are medications utilized in the treatment of HIV
- Patients are usually able to achieve an undetectable viral load by taking their ART as prescribed

Source: CDC- HIV Basics.

Stages of Untreated HIV



Source: Canadian Foundation for AIDS Research. Stages of Untreated HIV Infections.

HIV Stages

- **Stage 1: Acute Infection**
  - The virus invades the body's CD4 cells and starts to replicate
  - In the process of replication, the virus establishes reservoirs
  - During the acute phase, the individual's body tries to fight off the virus
  - Many people experience flu-like symptoms during this stage, which occurs around 2-4 weeks after initial exposure
  - Seroconversion occurs during this time

Source: Canadian Foundation for AIDS Research. Stages of Untreated HIV Infections.

HIV Stages

- **Stage 2: Latency Period**
  - Around 6 weeks following HIV infection, a stage with no signs or symptoms begins
  - This stage is characterized by a slow reduction in CD4 cell count and gradual increase in HIV viral load
  - Majority of patients remain in this disease stage for around 10 years (in the absence of treatment)

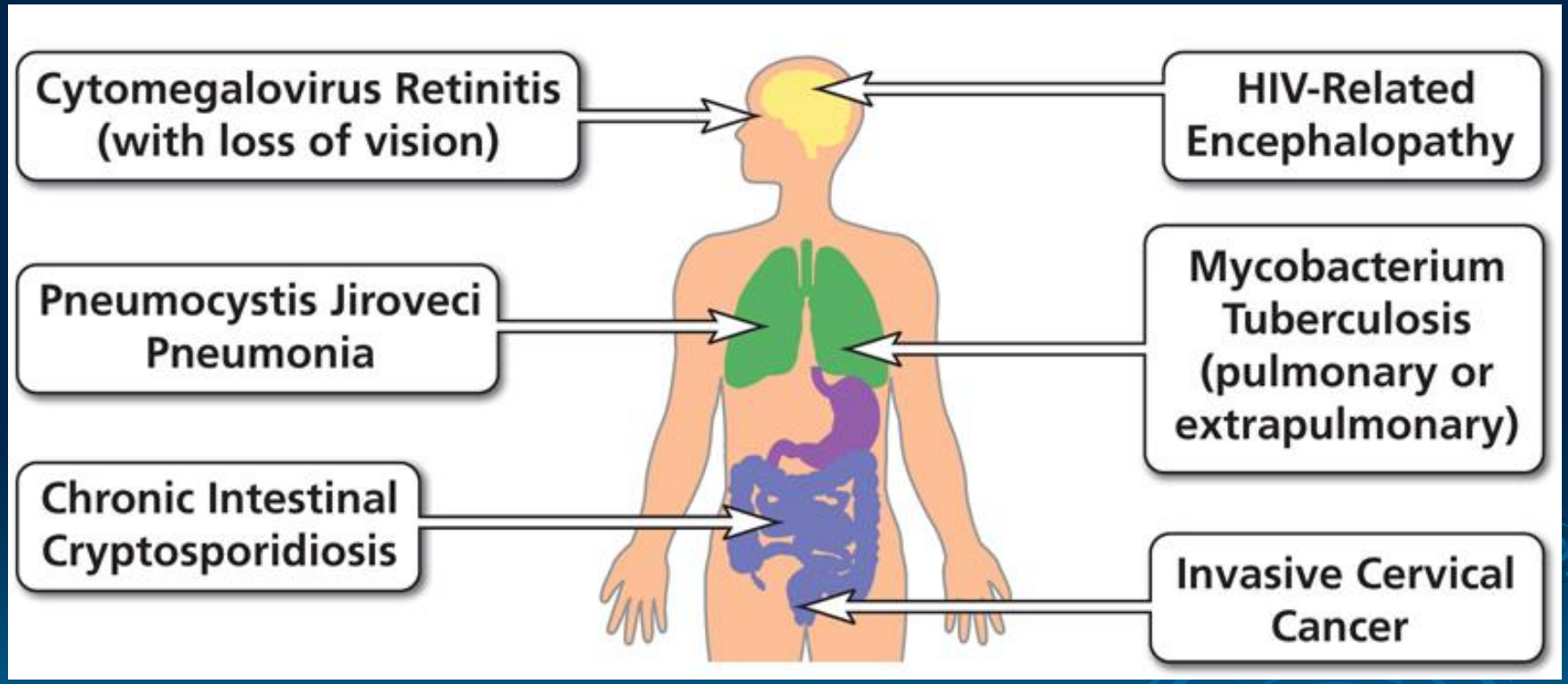
Source: Canadian Foundation for AIDS Research. Stages of Untreated HIV Infections.

HIV Stages

- **Stage 3: AIDS**
  - Usually occurs when CD4 cell count decreases to <200 cells/mm^3 or the patient develops an AIDS-defining condition
  - Opportunistic infections and cancers start to emerge due to depletion of the immune system
  - Viral load once again begins to rapidly increase
  - ART prevents patients from reaching this stage
  - For patients that have been untreated and reach this stage, ART can still improve CD4 cell count and decrease viral load

Source: Canadian Foundation for AIDS Research. Stages of Untreated HIV Infections.

AIDS-Defining Conditions



Source: NIH. HIV/AIDS Glossary: AIDS Case Definition.

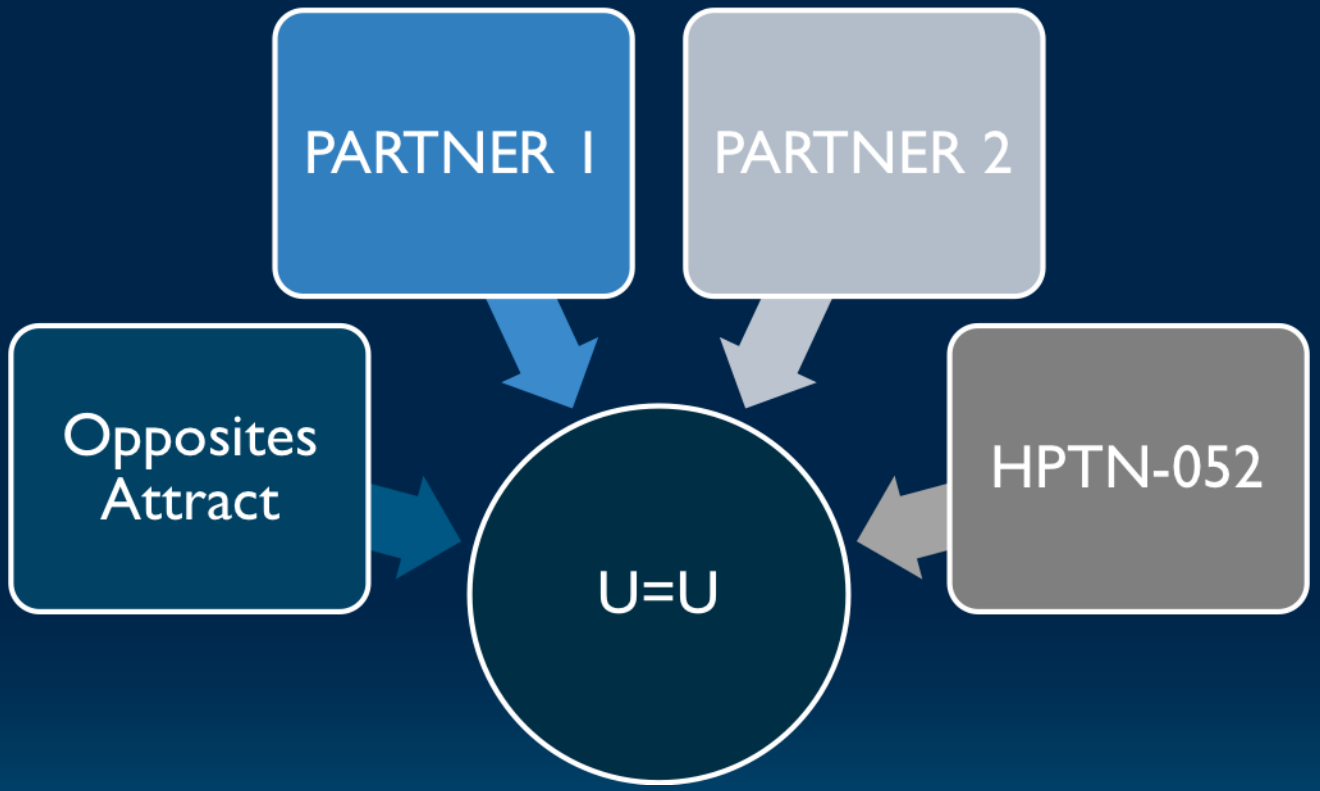
HIV Transmission Myths

Source: Myths About HIV and AIDS. Avert.

HIV Transmission

Source: Myths About HIV and AIDS. Avert.

HIV Transmission Studies

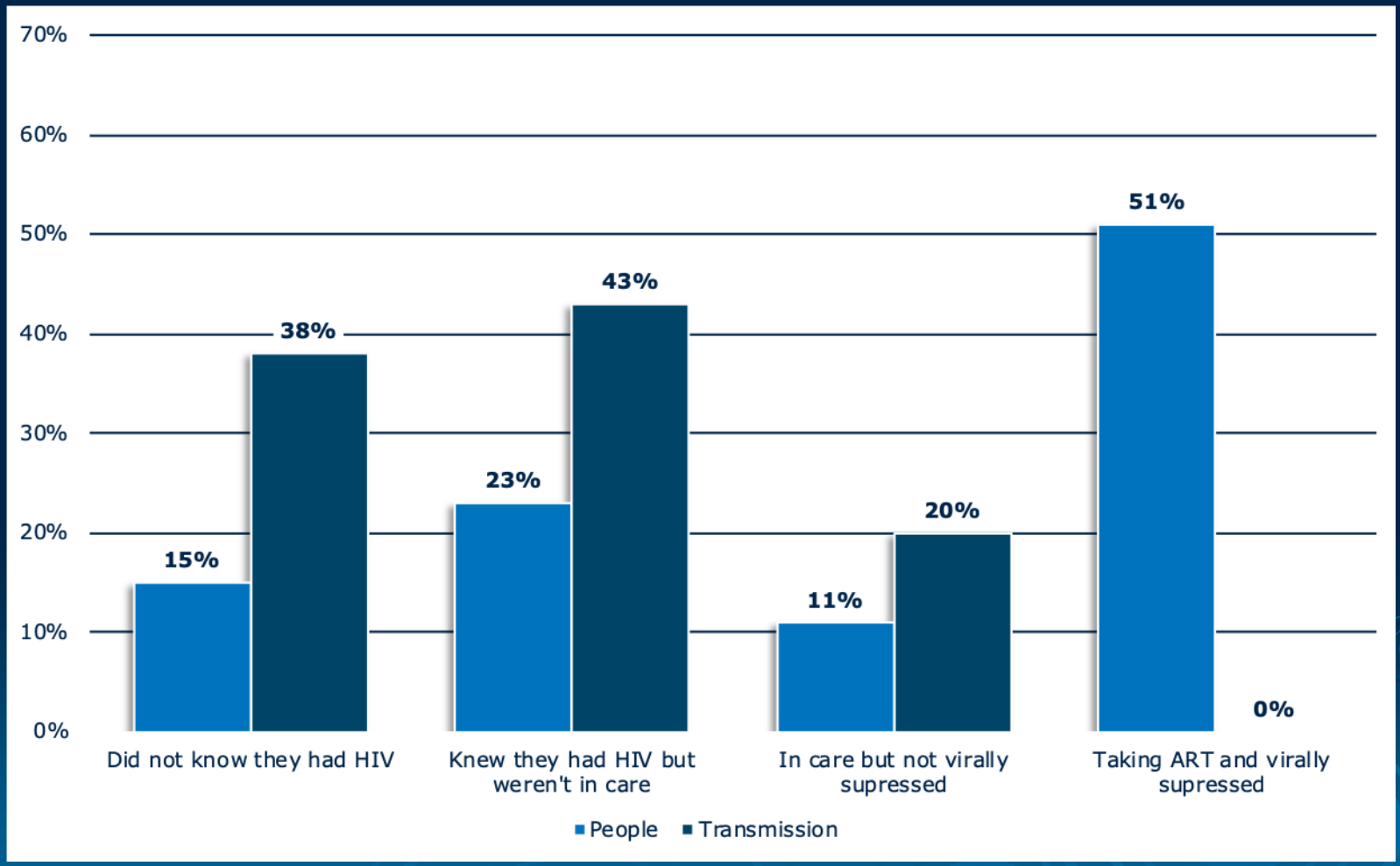


Undetectable = Untransmittable

These four studies included more than a 100,000 sex acts without condom use; yet there were ZERO cases of HIV transmission in partners of undetectable patients

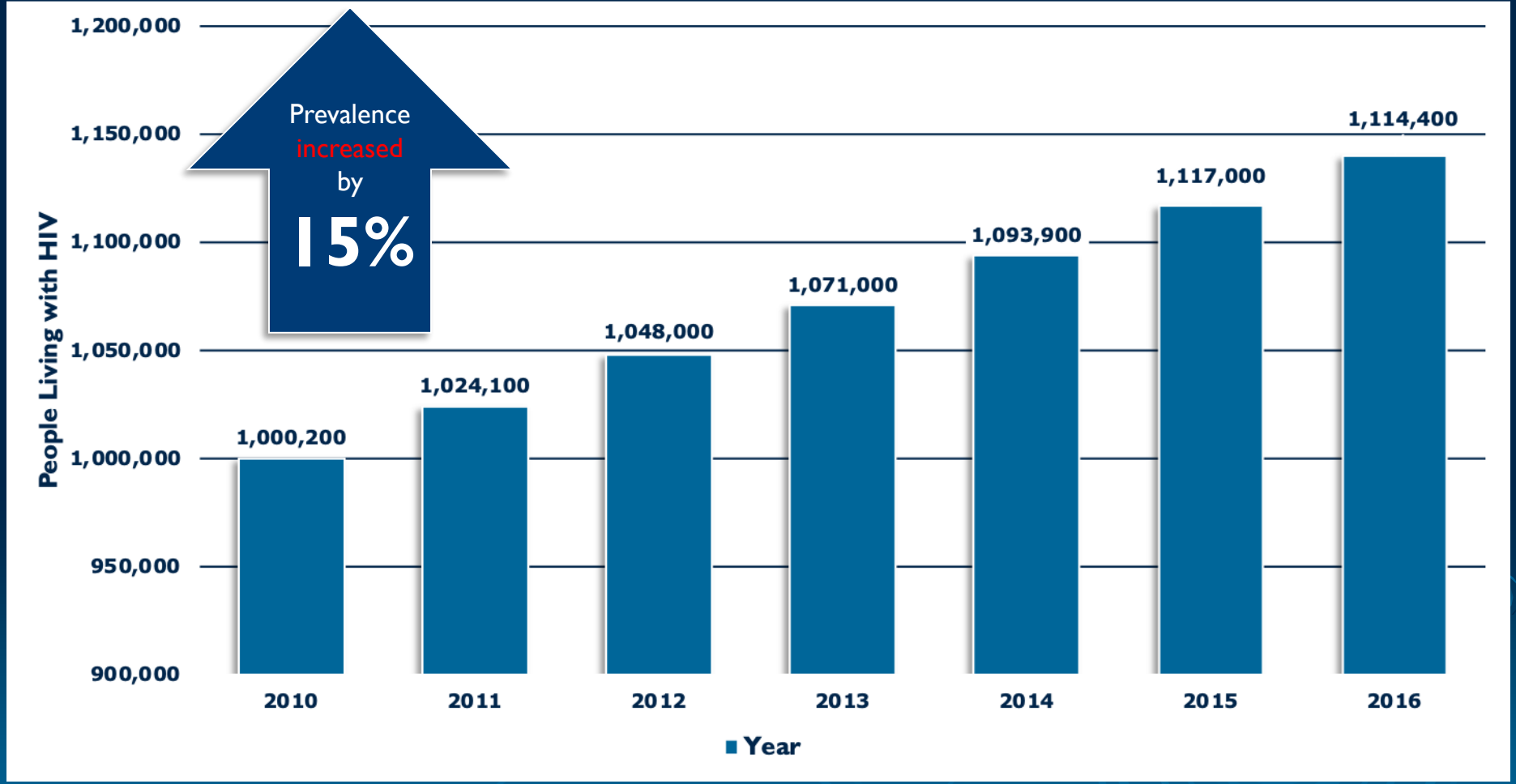
Source: Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.

HIV Transmission



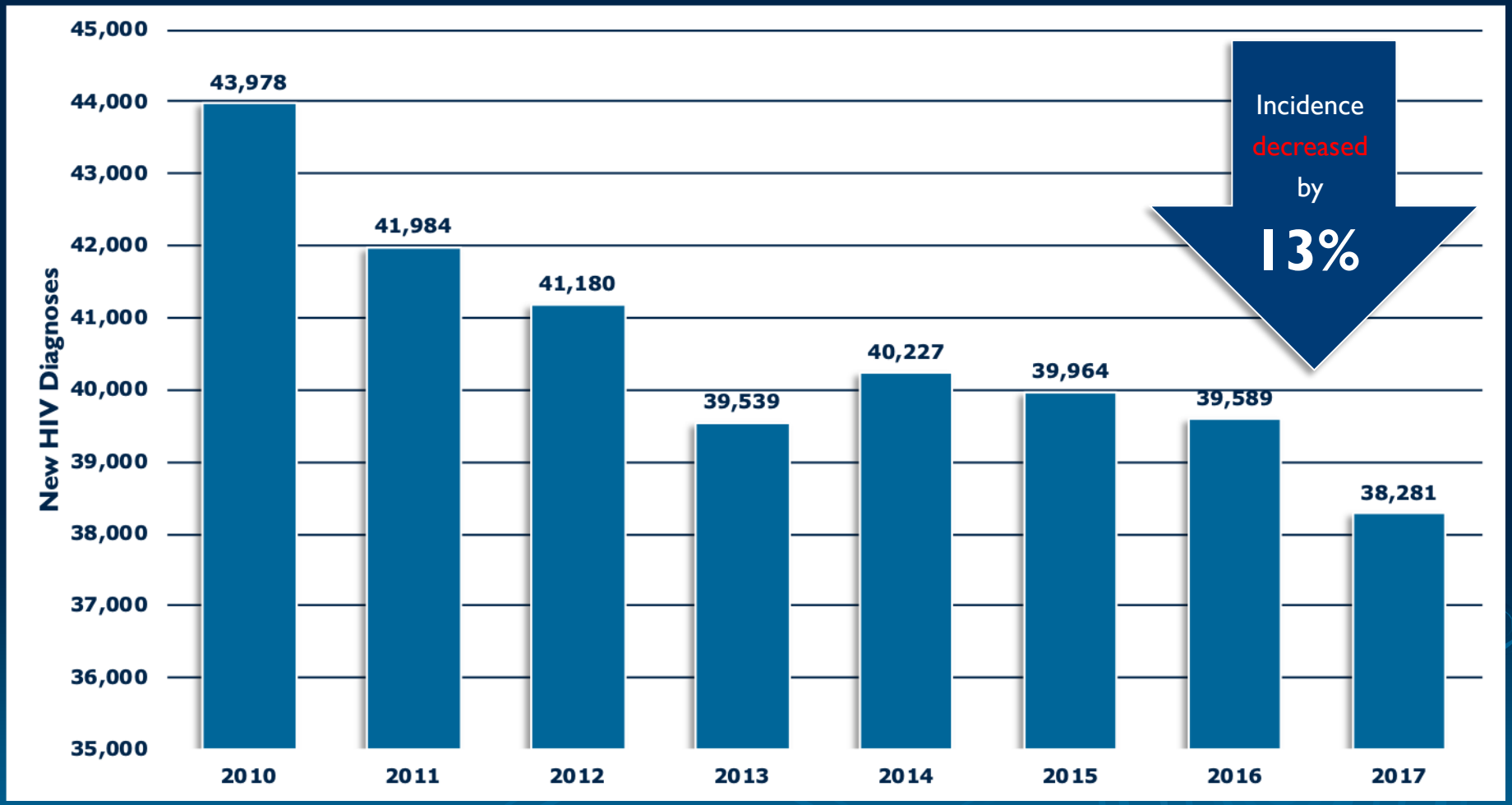
Source: CDC- Vital Signs: HIV Transmission Along the Continuum of Care — United States, 2016.

HIV Prevalence



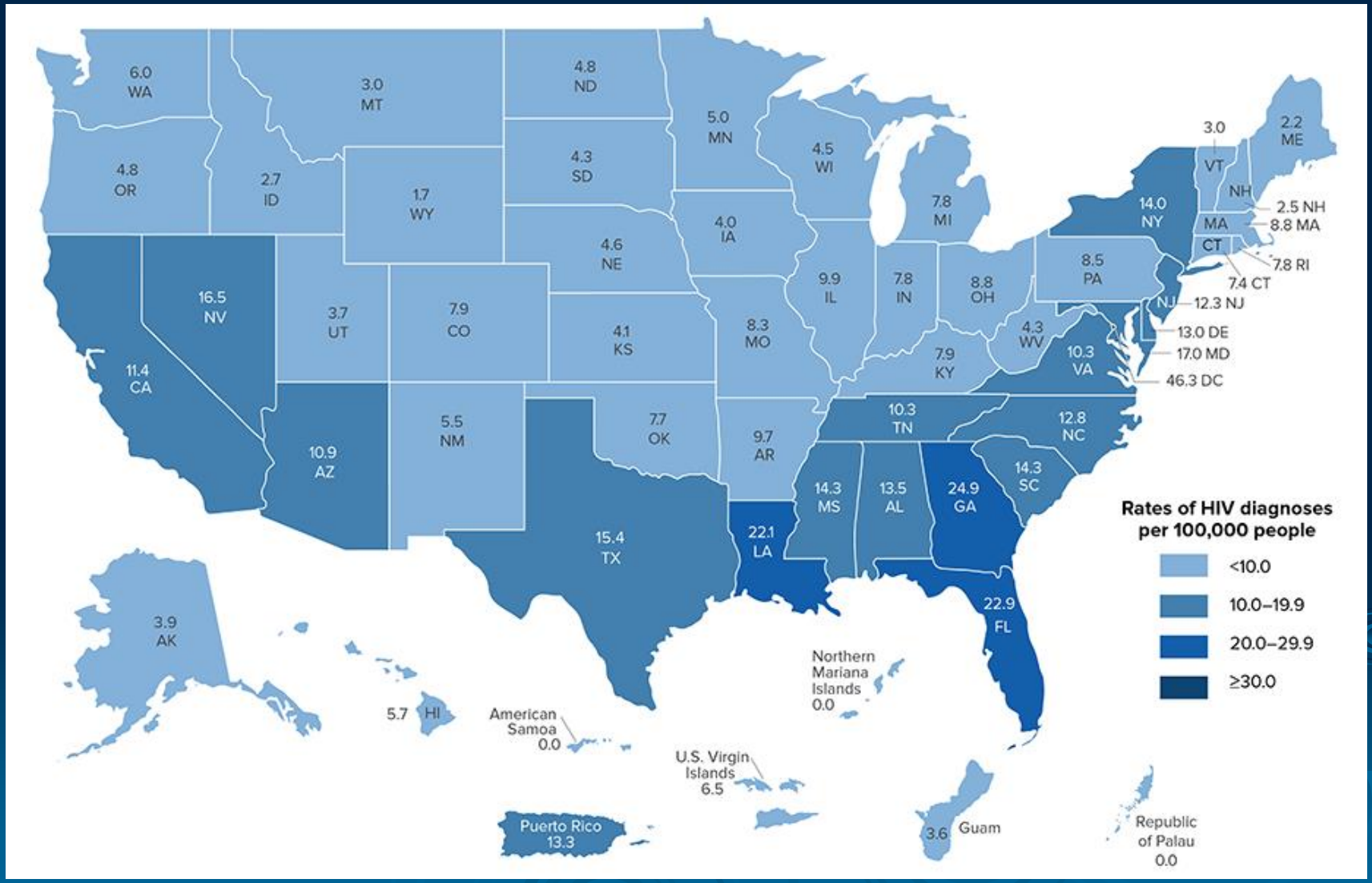
Source: Epidemiology of HIV. National HIV Curriculum.

HIV Incidence



Source: Epidemiology of HIV. National HIV Curriculum.

HIV Rates in the U.S.



Source: CDC- HIV in the United States by Region. 2017.

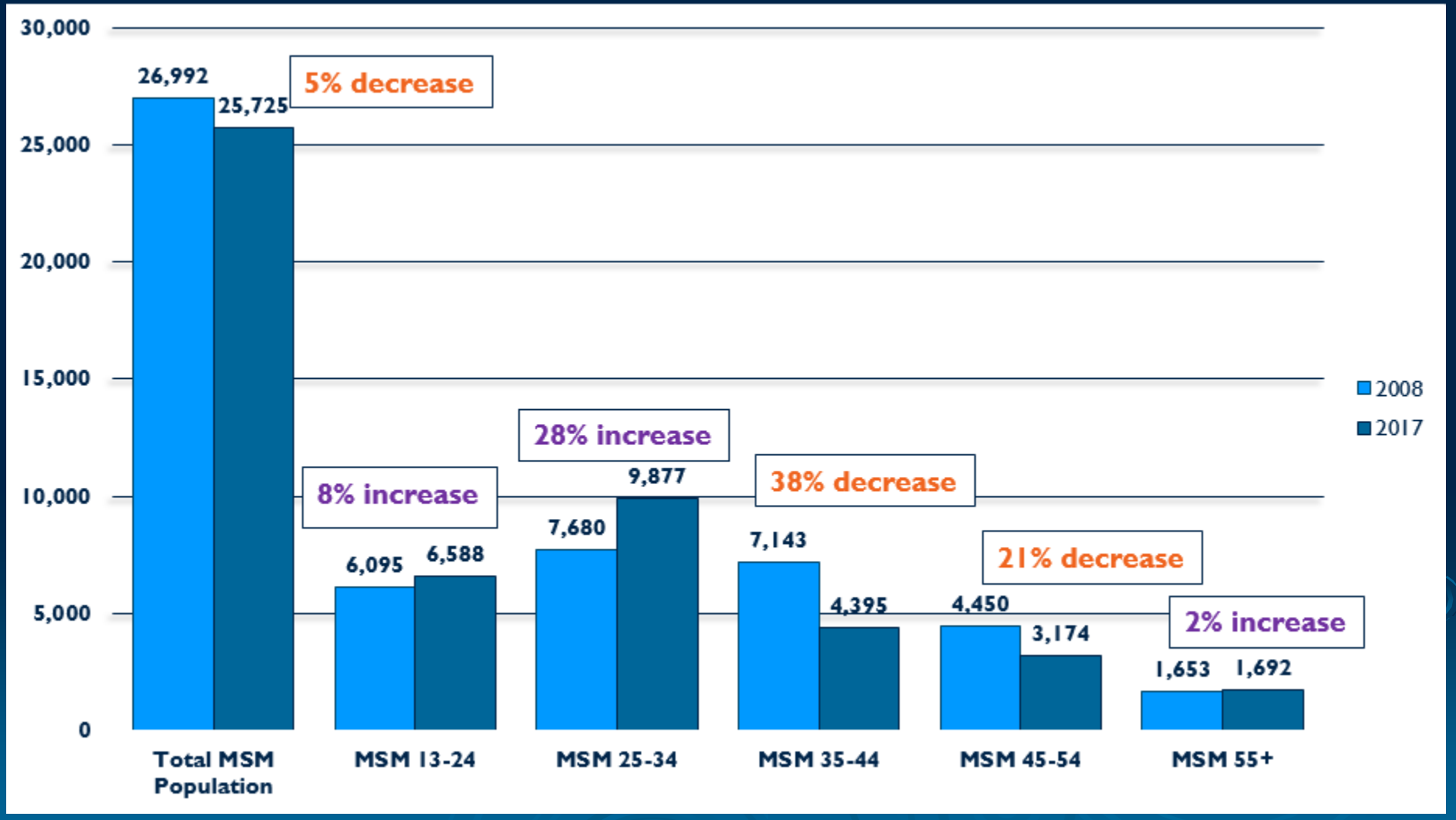
New Diagnosis of HIV in the U.S.

Rank	Area	Rate*
1	Miami – Fort Lauderdale – West Palm Beach, Florida	34.4
2	Atlanta – Sandy Springs – Roswell, Georgia	28.5
3	Memphis, Tennessee	27.8
4	Baton Rouge, Louisiana	27.5
5	Orlando – Kissimmee – Sanford, Florida	27.3
6	New Orleans – Metairie, Louisiana	24.6
7	Jackson, Mississippi	23.6
8	Augusta – Richmond County, Georgia	23.5
9	Jacksonville, Florida	21.2
10	Houston – The Woodlands – Sugar Land, Texas	20.6

*Rates are per 100,000 people

Source: CDC- HIV Surveillance Supplemental Report Vol. 30. 2018.

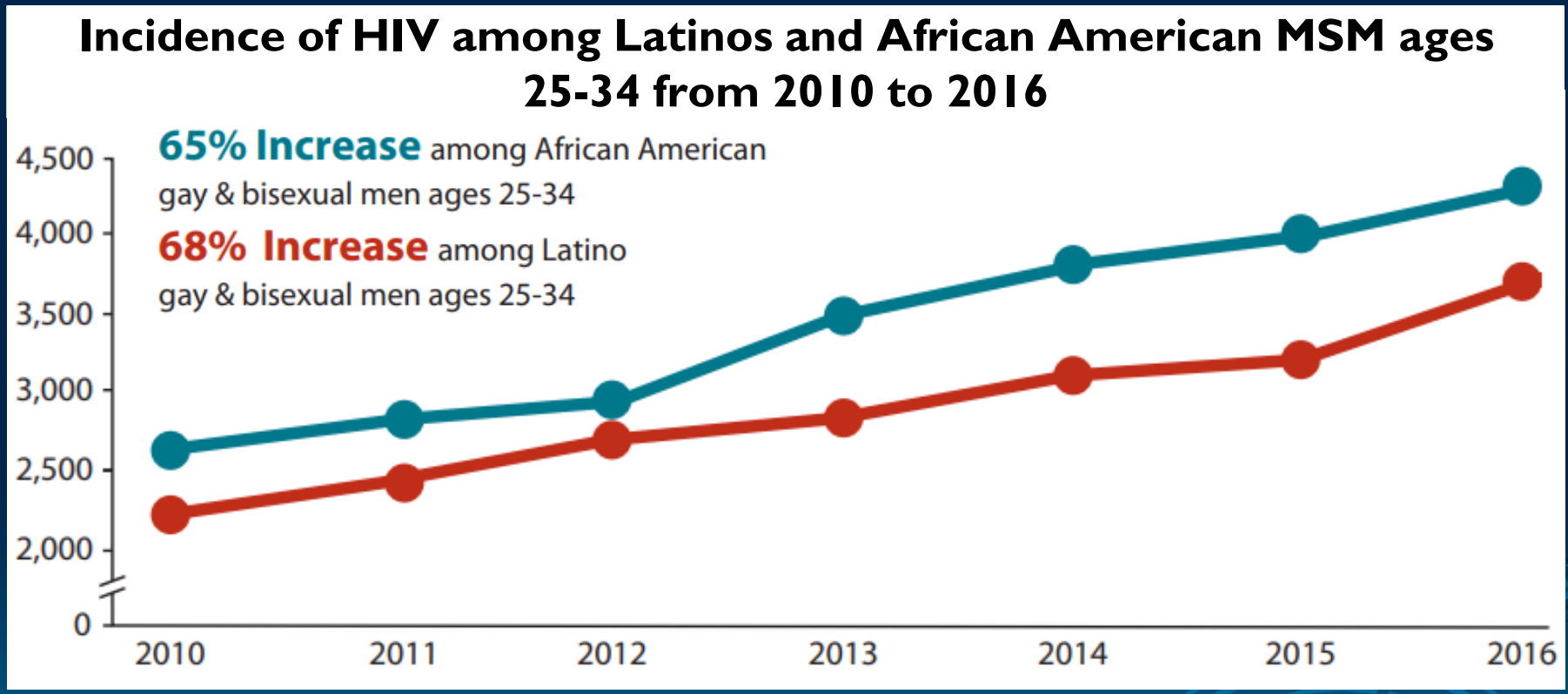
New HIV Diagnosis among MSM



MSM: Men who have sex with men

Source: Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.

New HIV Diagnosis among MSM



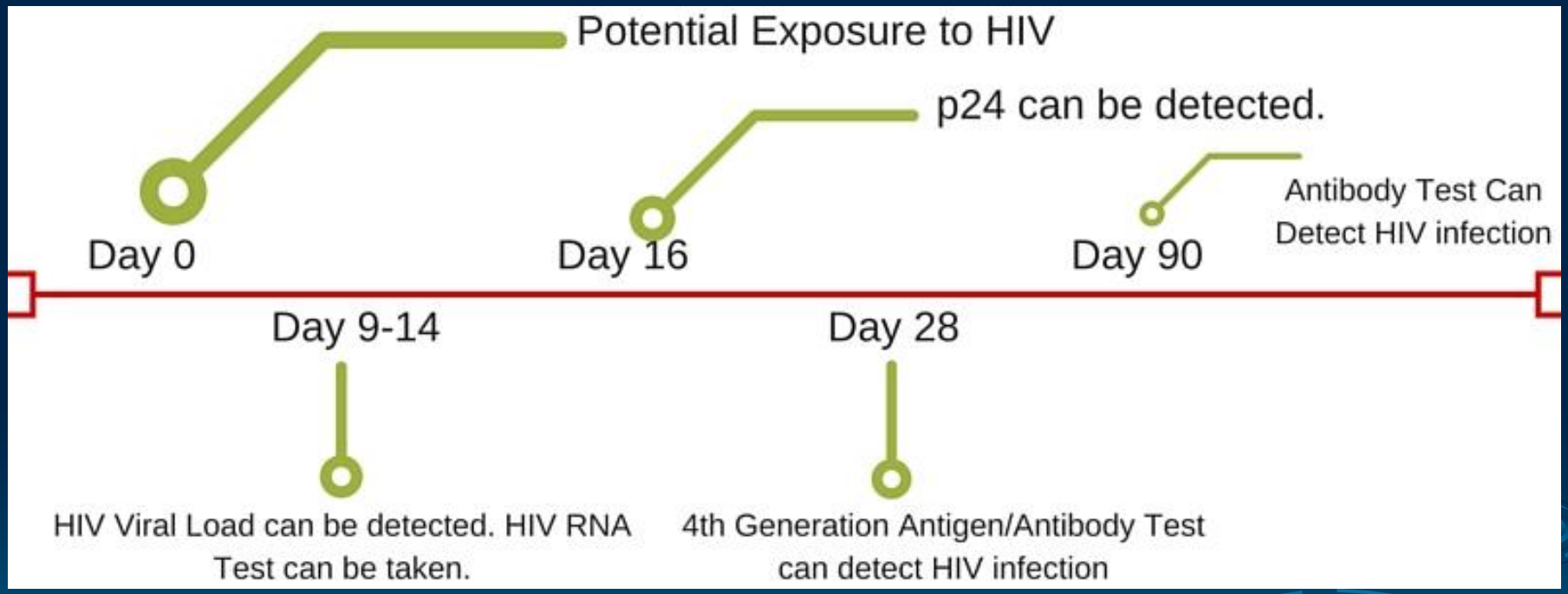
Source: CDC- HIV Incidence: Estimated Annual Infections in the U.S., 2010-2016.

Types of HIV Tests

Type of Test	What does the test detect?		
	RNA/DNA	Antigen	Antibody
PCR/viral load	X		
p24 test		X	
4th generation test		X	X
1st/2nd/3rd generation tests			X
Rapid test: finger prick and oral swab (ex: OraQuick)			X
Western blot tests			X

Source: HIV i-Base. Different Types of HIV tests.

Time to HIV Antigen and Antibody Detection

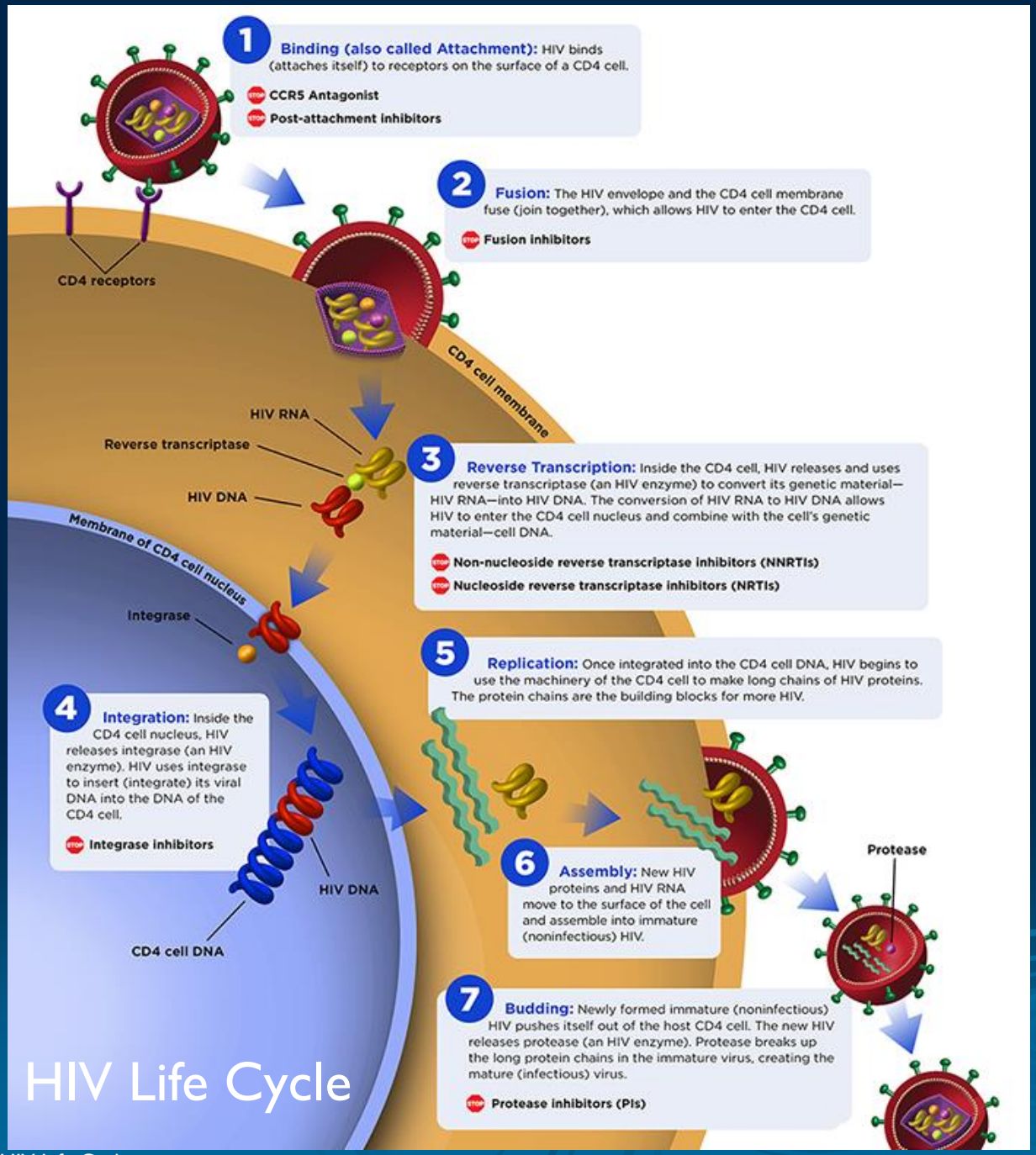


Source: HIV RNA Test. HIV RNA Test for HIV Early Detection.

Rapid ART Initiation

- ART should be initiated as soon as possible
- Immediate ART treatment has been shown to reduce both AIDS and non-AIDS related events
- There is no increase in adverse events with immediate versus delayed ART

Source: Rapid ART Initiation. Clinical Guidelines Program. New York State Department of Health AIDS Institute.



HIV Life Cycle

Source: NIH: AIDSinfo – The HIV Life Cycle.

HIV Treatment

- An ART regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a 3rd active drug from one of the following classes:
  - Integrase strand transfer inhibitors (INSTI)
  - Non-nucleoside reverse transcriptase inhibitors (NNRTI)
  - Protease inhibitors (PI)
- Currently, the Department of Health and Human Services (DHHS) guidelines recommend INSTI-based regimens for most ART-naive patients

Source: US DHHS. Guidelines for Use of Antiretroviral Agents in Adults and Adolescents with HIV. 2019.

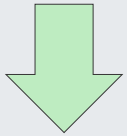
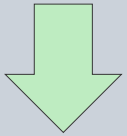
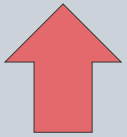
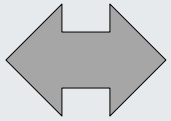
First-Line Treatment

Brand	Recommended Initial Regimen
Biktarvy®	Bictegravir/tenofovir alafenamide/emtricitabine
Dovato®	Dolutegravir/lamivudine (Except for patients with HIV RNA >500,000 copies/mL or with hepatitis B co-infection)
Triumeq®	Dolutegravir/abacavir/lamivudine (Except for patients who are HLA-B*5701 positive or with hepatitis B co-infection)
Tivicay® and Truvada® or Descovy®	Dolutegravir plus tenofovir*/emtricitabine
Isentress® and Truvada® or Descovy®	Raltegravir plus tenofovir*/emtricitabine

*Tenofovir formulation can be either tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF)

Source: US DHHS. Guidelines for Use of Antiretroviral Agents in Adults and Adolescents with HIV. 2019.

TAF versus TDF

	TAF	TDF
Efficacy	Comparable	Comparable
Renal toxicity risk		
Bone density decrease risk		
Weight gain		

Source: The Lancet. 2015; 385(9987): 2606-2615.

INSTI-Based Regimen Selection

Factors that influence the choice of INSTI regimen in treatment-naive patients:

Agent	Advantages	Disadvantages
Dolutegravir	• Few drug interactions • Single-tablet formulation • Higher barrier to resistance • Preferred ARV in pregnancy • Can be used for rapid ART start	• Co-formulated with abacavir and lamivudine
Bictegravir	• Few drug interactions • Single-tablet formulation • Higher barrier to resistance • Can be used for rapid ART start	• Lack of data in pregnancy
Raltegravir	• Few drug interactions • Available as daily dosing • Preferred ARV in pregnancy	• Not available as a single-tablet formulation • Lower barrier to resistance • Twice daily option
Elvitegravir	• Single-tablet formulation • Can be used for rapid ART start	• Lower barrier to resistance • Avoid in pregnancy due to inadequate drug concentrations in the 2nd/3rd trimesters

Sources: US DHHS. Guidelines for Use of Antiretroviral Agents in HIV-1–Infected Adults and Adolescents. 2019.
Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.

Abacavir Hypersensitivity Reaction

- **Black box warning:** 2-9% incidence of hypersensitivity reaction
  - Caucasian > African American > Latino > Asian
- HLA-B*5701 testing should precede the use of abacavir
  - Record positive result as a true allergy
- Patients should be counseled on signs and symptoms of abacavir hypersensitivity, which include:
  - Fever, rash, nausea/vomiting, flu-like symptoms
  - Onset is 4-6 weeks with a median of 9 days

Source: Clinical Infectious Diseases. 2002; 34(8): 1137–1142.

True/False Question

- The initial antiretroviral regimen recommended for most treatment-naive patients consists of two NRTIs and a boosted PI

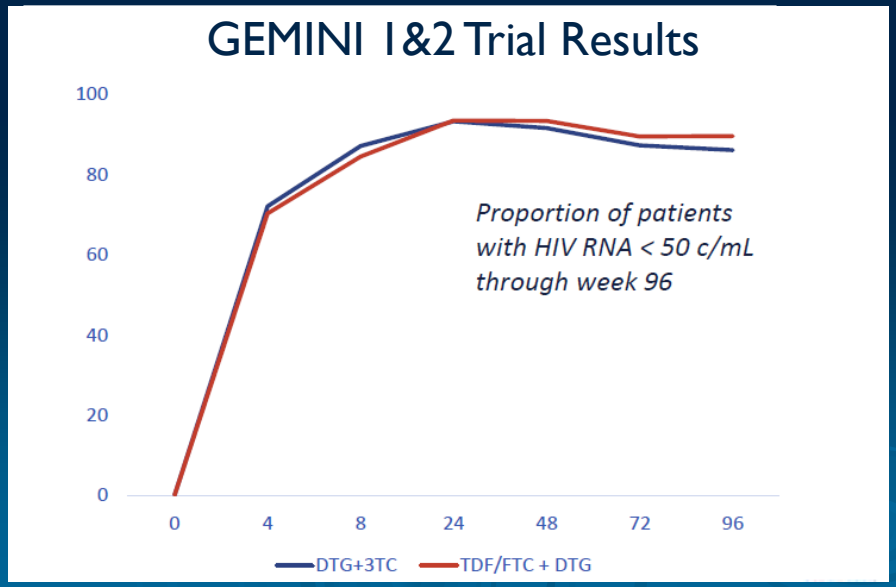
True/False Question

Answer

- The initial antiretroviral regimen recommended for most treatment-naive patients consists of two NRTIs and a boosted PI –False!
  - The initial antiretroviral regimen for a treatment-naive patient usually consists of two NRTIs plus an INSTI

Complete Two-Drug ART

- Dovato® is now recommended for treatment-naive patients first-line
- There are considerations as to whom should be taking this medication
  - Still not recommended for certain patient populations
  - Adherence is extremely important
  - Good for patients that cannot use abacavir, TDF, or TAF



Source: Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.

Complete Two-Drug ART

- Juluca® (dolutegravir/rilpivirine) is FDA-approved for HIV treatment in select patients
- Considerations for this medication include:
  - Not recommended for treatment-naive patients
  - Approved for use in patients that are virologically suppressed ≥ 6 months on a stable regimen with no treatment failure and no resistance mutations
  - Adherence is very important
  - Rilpivirine requires food for optimal absorption
  - Patients should not use proton pump inhibitors

Source: Lancet HIV. 2019; 6(9): e576-e587.

True/False Question

- Dovato® is the first FDA-approved complete two-drug regimen for treatment-naive HIV-infected patients

True/False Question

Answer

- Dovato® is the first FDA-approved complete two-drug regimen for treatment-naive HIV-infected patients–True!
  - Dovato® components include dolutegravir and lamivudine

HIV Comorbidities

- Evaluate the patient as a whole when initiating ART treatment
- Most common comorbidities in people living with HIV include:
  - Hypertension: 25-65%
  - Hyperlipidemia: 22-48%
  - Diabetes: 9-31%
  - Renal impairment: 5-20%
  - Cardiovascular (CV) events: 3-16%

Source: Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.
The Journal of Infectious Diseases. 2017; 216(12): 1481–1483.

HIV Treatment

ART to avoid in patients with select comorbidities:

Condition	Consider Avoiding	Rationale
Chronic Kidney Disease (CrCl ≤ 59 mL/min)	TDF Exception: ESRD	Risk of nephrotoxicity
Osteoporosis	TDF	Risk of decreasing bone mineral density
Severe Liver Disease	Abacavir, nevirapine, atazanavir, darunavir, elvitegravir	Risk of increasing liver enzymes
Psychiatric Disorders	Efavirenz, rilpivirine	Risk of exacerbating psychiatric behaviors and/or increasing suicide risk
Cardiovascular Risk	Abacavir, lopinavir/ritonavir	Increased CV risk observed in studies
Dyslipidemia	Boosted protease inhibitors, efavirenz, elvitegravir/cobicistat, TDF	Risk of hyperlipidemia

CrCl: Creatinine clearance

Source: Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.

Opportunistic Infection Prophylaxis

	Pneumocystis jiroveci Pneumonia (PJP)
Indication for initiation	1. CD4 count < 200 cells/mm^3 *or* 2. CD4 percentage < 14% *or* 3. CD4 count 200-250 cells/mm^3 with delayed initiation of ART and frequent CD4 count monitoring not possible
Prophylaxis	**Preferred therapy:** • TMP/SMX DS or SS daily **Alternative therapy:** • TMP/SMX DS three times per week • Dapsone 100 mg daily or dapsone 50 mg twice daily • Atovaquone 1,500 mg daily • Aerosolized pentamidine 300 mg (nebulizer) every month
Indication for discontinuation	• CD4 count ≥ 200 cells/mm^3 for ≥ 3 months in response to ART • CD4 count between 100-200 cells/mm^3 and HIV RNA undetectable for ≥ 3 months

TMP/SMX: Sulfamethoxazole/ Trimethoprim
DS: Double strength; SS: Single strength

Source: US DHHS. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. 2019.

Opportunistic Infection Prophylaxis

	Toxoplasma gondii Encephalitis
Indication for initiation	1. CD4 count < 100 cells/mm^3 and Toxoplasma IgG positive
Prophylaxis	**Preferred therapy:** • TMP/SMX DS daily **Alternative therapy:** • TMP/SMX DS three times per week • TMP/SMX SS daily • Atovaquone 1,500 mg daily
Indication for discontinuation	• CD4 count ≥ 200 cells/mm^3 for ≥ 3 months in response to ART • CD4 count between 100-200 cells/mm^3 and HIV RNA undetectable for ≥ 3 months

Source: US DHHS. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. 2019.

Opportunistic Infection Prophylaxis

	Mycobacterium avium complex (MAC)
Indication for initiation	Primary prophylaxis **<u>is not recommended</u>** for adults and adolescents who immediately initiate ART 1. CD4 count < 50 cells/mm^3 not on fully suppressive ART
Prophylaxis	**Preferred therapy:** • Azithromycin 1,200 mg once weekly • Azithromycin 600 mg twice weekly • Clarithromycin 500 mg twice daily **Alternative therapy:** • Rifabutin 300 mg daily
Indication for discontinuation	• Initiation on effective ART

Source: US DHHS. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. 2019.

PrEP versus PEP

- PrEP and PEP are methods for preventing HIV infection that involve taking HIV medications
- PreP and PEP are for people who do not have HIV but are at risk of acquiring it

	PrEP	PEP
When is it taken?	Before HIV exposure	After HIV exposure, should be taken within 72 hours after possible exposure
Who is it for?	For people that are HIV-negative and: • Have sex with an HIV-positive partner • Have multiple partners or partner(s) with unknown HIV status • Share injection drug equipment	For people that are HIV-negative but may have been exposed through: • Sexual intercourse • Needle-stick injury • Sharing injection drug equipment • Sexual assault
How effective is it?	If used as directed, can reduce HIV risk from: • Sexual intercourse by 99% • Injection drug use by at least 74%	PEP effectiveness decreases as time passes after exposure, but if started soon after exposure, it can reduce HIV risk by more than 80%

Source: NIH: AIDSinfo – PrEP vs PEP and World Health Organization: Post-exposure prophylaxis to prevent HIV infection. 2014.

PrEP

ESTIMATED NUMBER OF ADULTS WHO COULD POTENTIALLY BENEFIT FROM PREP, UNITED STATES, 2015

	Gay, bisexual, or other men who have sex with men	Heterosexually active adults	Persons who inject drugs	Total by race/ethnicity
Black/African American, non-Hispanic	309,190	164,660	26,490	500,340
Hispanic/Latino	220,760	46,580	14,920	282,260
White, non-Hispanic	238,670	36,540	28,020	303,230
Total who could potentially benefit from PrEP	**813,970**	**258,080**	**72,510**	**1,144,550**

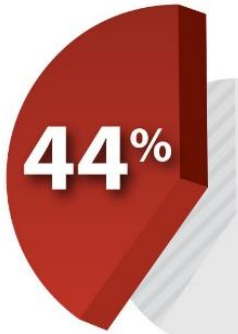
Notes: PrEP=pre-exposure prophylaxis; data for "other race/ethnicity" are not shown

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Only 90,000 PrEP prescriptions were filled in 2015

Source: CDC – HIV Prevention Pill Not Reaching Most Americans Who Could Benefit.

PrEP



of people who could potentially benefit from PrEP are **African American – approximately 500,000 people**…

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

of people who could potentially benefit from PrEP are **Latino – nearly 300,000 people**…

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

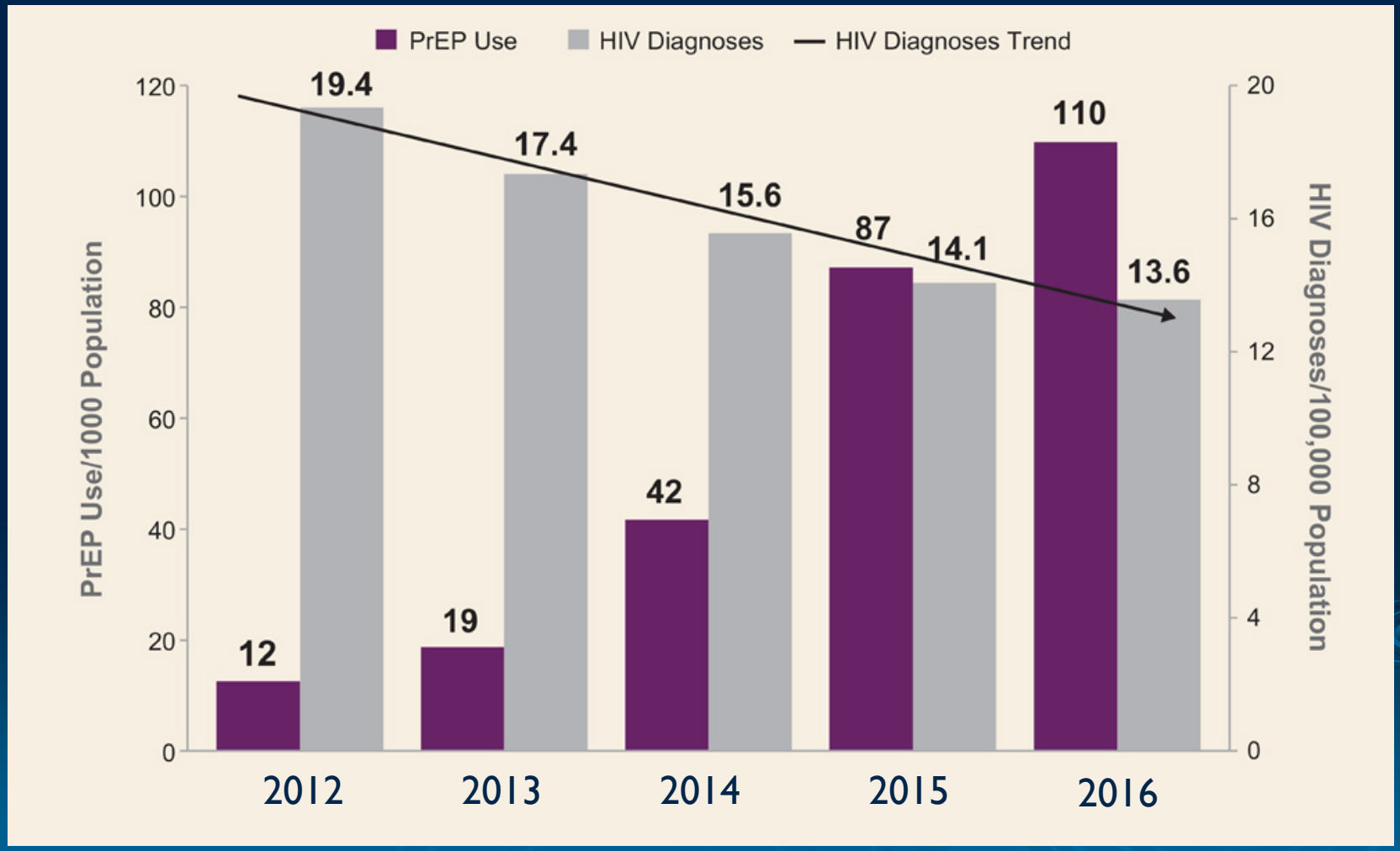
Source: CDC – 2018 Conference on Retroviruses and Opportunistic Infections.

PrEP

- As of December 2019, there are two FDA-approved medications that can be utilized for PrEP
  - Truvada® (TDF plus emtricitabine)
  - Descovy® (TAF plus emtricitabine)
- There are other options currently being tested for PrEP
  - Long acting injectable (late phase development)
  - Long acting implantable (early phase development)
  - Topical/local approach (early phase development)

Source: Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.

Why is PrEP important?



Source: 22nd International AIDS Conference. Amsterdam, Netherlands. 2018.

True/False Question

- PrEP is 99% effective in reducing the risk of acquiring HIV through sexual contact

True/False Question

Answer

- PrEP is 99% effective in reducing the risk of acquiring HIV through sexual contact –True!

PEP

Age Group	Preferred/ Alternative	Medication
Adults, adolescents ≥ 13 years of age, or pregnant women with normal renal function (CrCl ≥ 60 mL/min)	Preferred	Emtricitabine/tenofovir once daily *with either*: • Raltegravir 400 mg twice daily *or* dolutegravir 50 mg once daily
	Alternative	Emtricitabine/tenofovir once daily *with both*: • Darunavir 800 mg once daily *and* ritonavir 100 mg once daily
Adults, adolescents ≥ 13 years of age, or pregnant women with renal dysfunction (CrCl ≤ 59 mL/min)	Preferred	Lamivudine/zidovudine once daily (renally adjusted) *with either*: • Raltegravir 400 mg twice daily *or* dolutegravir 50 mg once daily
	Alternative	Lamivudine/zidovudine once daily (renally adjusted) *with both*: • Darunavir 800 mg once daily *and* ritonavir 100 mg once daily

Duration: Taken for 28 days

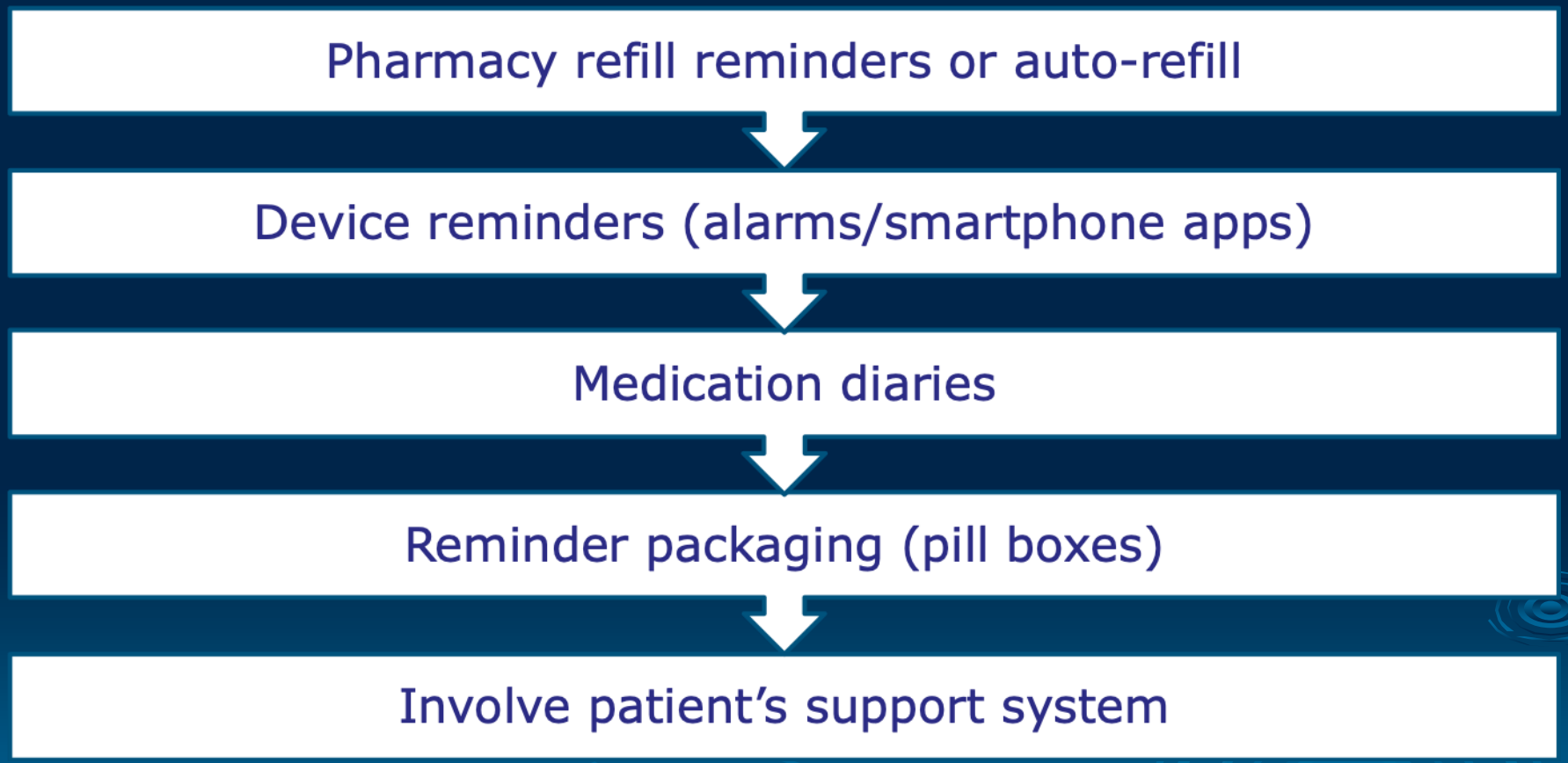
Source: Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV. 2016.

Pharmacist Role

- Counseling
  - Adherence
  - Common and severe side effects
  - Time to undetectable viral load
- Supportive treatment
  - Serve as a liaison to provide the most appropriate treatment to patients
- Therapy recommendation
  - Support the patients and encourage them to advocate for themselves
  - Contact prescribers and inform them about possible side effects

Source: Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.
Journal of Acquired Immune Deficiency Syndrome. 2011; 58(2): 181-187.

Tools to Assist with Adherence



Source: Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.

Conclusion

- New and groundbreaking ART options keep emerging
- Populations such as MSM are still at risk
- Novel and simpler therapies are being integrated into the guidelines
- Pharmacists can have a significant impact on HIV treatment
  - Linkage to care
  - Counseling
  - Selection and optimization of ART
  - Management of concurrent disease states

Source: Insights and Developments in HIV Treatment Strategies. Presentation. Las Vegas, NV. 2019.

Questions?

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