Memorial Healthcare System

# An Update on the US HIV Epidemic and Recent Strides in HIV Care

Boca Raton Regional Hospital
Grand Rounds – 22/10/2019

Kenneth Poon MD FACP
*Division of Infectious Diseases*
*Memorial Physician Group*
*Memorial Health Systems*

# BACKGROUND

- Jackson Memorial Hospital and U of M 2004-08
  - Internal Medicine and Pediatrics Residency 2004-08
- Baylor College of Medicine 2008-10
  - Infectious Diseases Fellowship

- Broward Community and Family Health Centers 2011-14
  - HIV Ryan White Program Director
  - ID, HIV, and Primary Care Physician
  - Broward Regional HIV Health Planning Council
    - Medical Committee Member
- Vilmed, Inc. 2012-14
  - Group inpatient ID practice

# BACKGROUND

- FAU College of Medicine Internal Medicine Residency 2014-17
  - Associate Program Director
  - Assistant Professor of Clinical Biomedical Sciences
- Memorial Physician Group Division of Infectious Diseases 2017-present
  - Inpatient and outpatient general ID
    - Outpatient Ryan White Grant Part A funded clinic
  - Inpatient and outpatient solid organ and bone marrow transplant ID
  - Antibiotic Stewardship Committee
  - MHS Internal Medicine Residency ID Rotation Director

- I have no financial disclosures.

# OVERVIEW OF PRESENTATION

- Update on the epidemiology of HIV/AIDS in the US.
- Racial/Ethnic health disparities in HIV/AIDS epidemic.
- Update on the epidemiology of HIV/AIDS in Florida.
- Update on DHHS recommended anti-retroviral treatment.
- Dual Treatment
  - Carbotegravir
- Recent Agents
  - Ibaluzimab
- Novel Therapy
  - CRSPR
- UD=UT

# ABBREVIATIONS USED

- AIDS – Acquired Immunodeficiency Syndrome
- ART – Anti-Retroviral Treatment
- ARV – Anti-Retroviral Medications
- HIV – Human Immunodeficiency Virus
- InSTI – Integrase Strand Transfer Inhibitor
- NRTI – Nucleotide/side Reverse Transcriptase Inhibitor
- NNRTI – Non-nucleotide/side Reverse Transcriptase Inhibitor
- PLWHIV – People Living With HIV
- Antiretroviral medication nomenclature
  - Trade Name: *Tivicay*
  - Generic Name: Dolutegravir
  - Abbreviation: DTG

# EPIDEMIOLOGY

What is the current status of the HIV/AIDS epidemic in the US?
How has it changed over time?

# EPIDEMIOLOGY

What is the current status of the HIV/AIDS epidemic in the US?
How has it changed over time?


https://www.cdc.gov/hiv/statistics/overview/index.html

# DIAGNOSED HIV INFECTIONS IN US

What is the current status of the HIV/AIDS epidemic in the US?
How has it changed over time?

- In 2016, 1,008,929 people were living with diagnosed HIV infection.

https://www.cdc.gov/hiv/statistics/overview/index.html

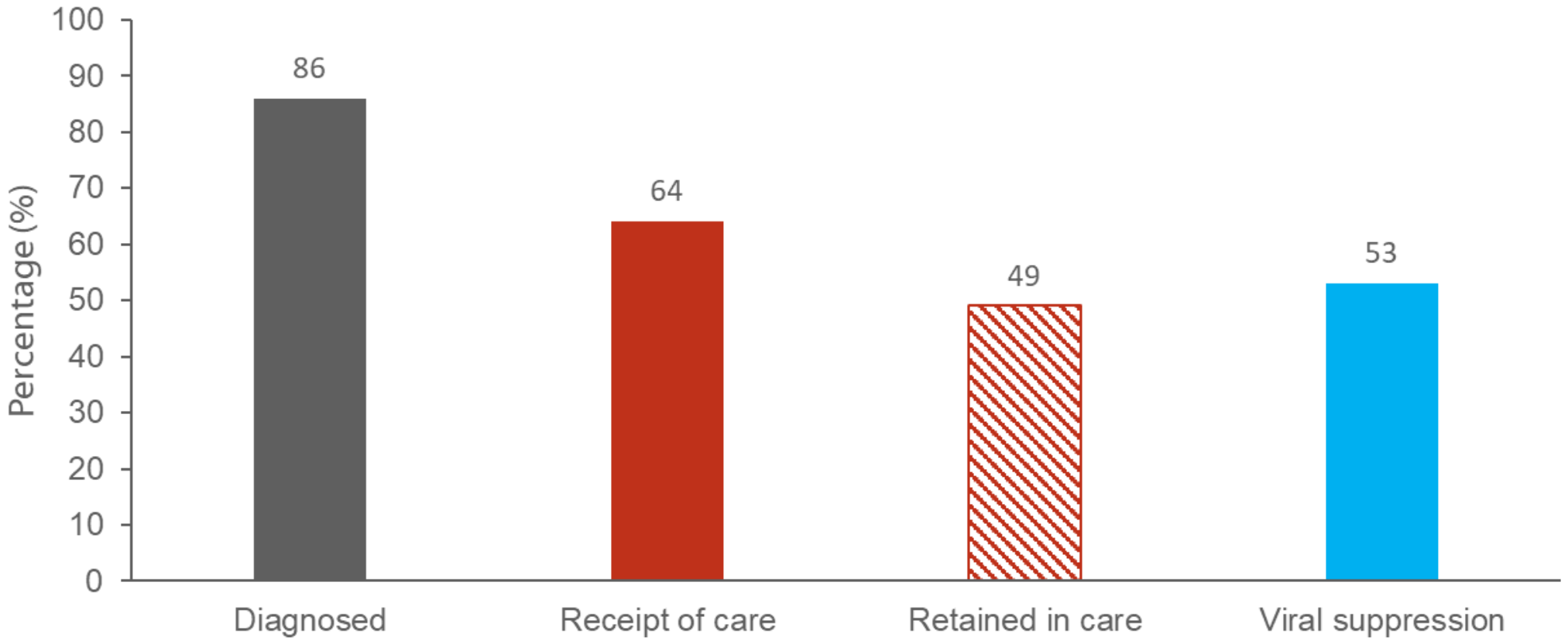
# DIAGNOSED HIV INFECTIONS IN US

What is the current status of the HIV/AIDS epidemic in the US?
How has it changed over time?

- In 2016, 1,008,929 people were living with diagnosed HIV infection.
- In 2017, 38,739 people received an HIV diagnosis in the US.
  - The annual number of new HIV diagnoses remained stable between 2012 and 2016.

https://www.cdc.gov/hiv/statistics/overview/index.html

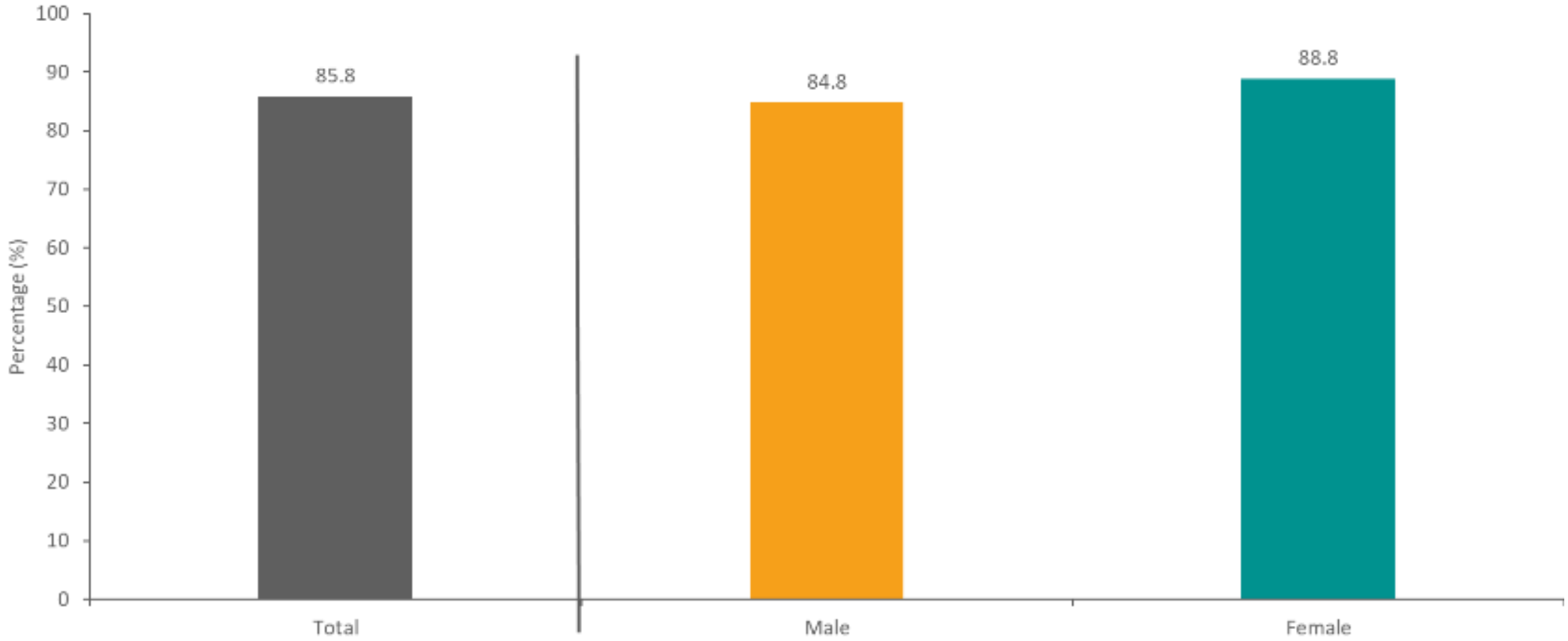
# Persons Living with Diagnosed or Undiagnosed HIV Infection
# HIV Care Continuum Outcomes, 2016 US




Note. Receipt of medical care was defined as ≥1 test (CD4 or VL) in 2016. Retained in continuous medical care was defined as ≥2 tests (CD4 or VL) ≥3 months apart in 2016. Viral suppression was defined as <200 copies/mL on the most recent VL test in 2016.

https://www.cdc.gov/hiv/statistics/overview/index.html

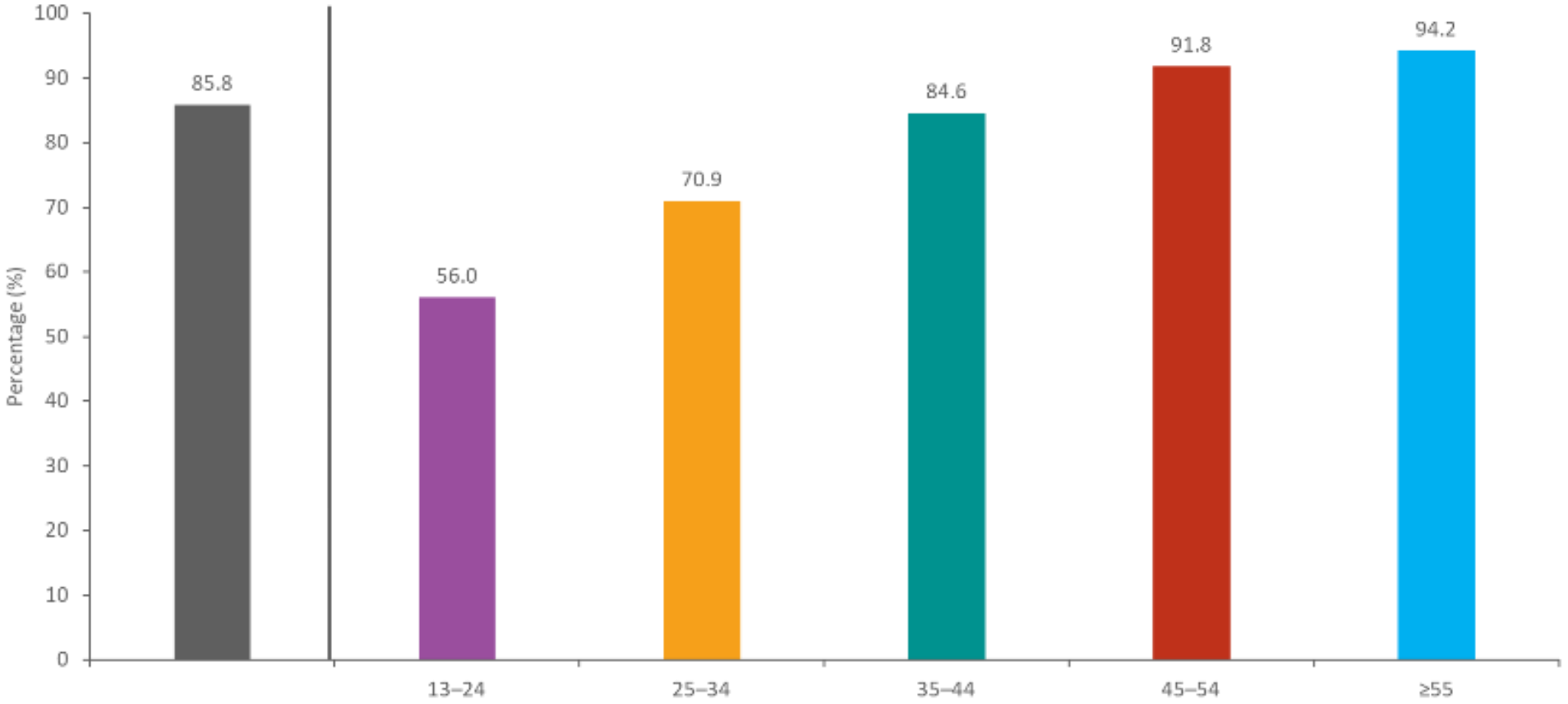
# Diagnosed Infection among Persons Aged ≥13 Years Living with Diagnosed or Undiagnosed HIV Infection, by Sex, 2016 US




Note. Estimates were derived from a CD4 depletion model using HIV surveillance data.

https://www.cdc.gov/hiv/statistics/overview/index.html

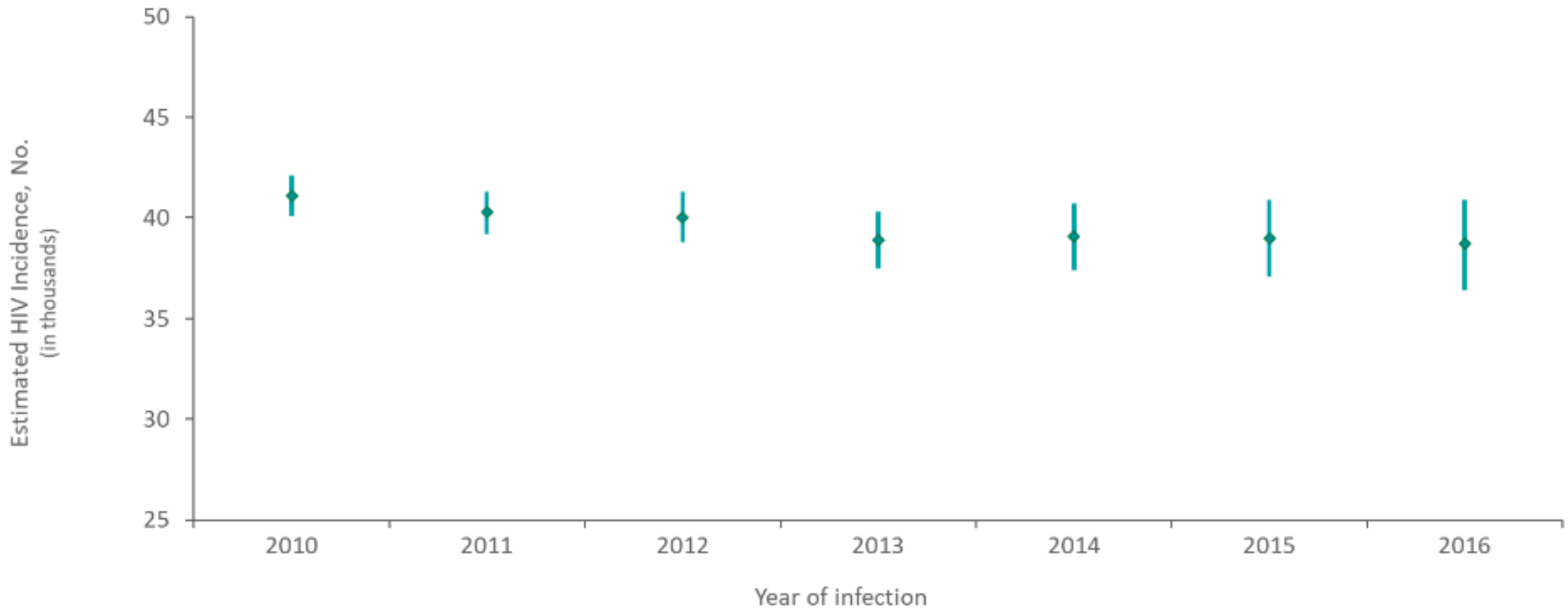
# Diagnosed Infection among Persons Aged ≥13 Years Living with Diagnosed or Undiagnosed HIV Infection, by Age, 2016 US




Note. Estimates were derived from a CD4 depletion model using HIV surveillance data.

https://www.cdc.gov/hiv/statistics/overview/index.html

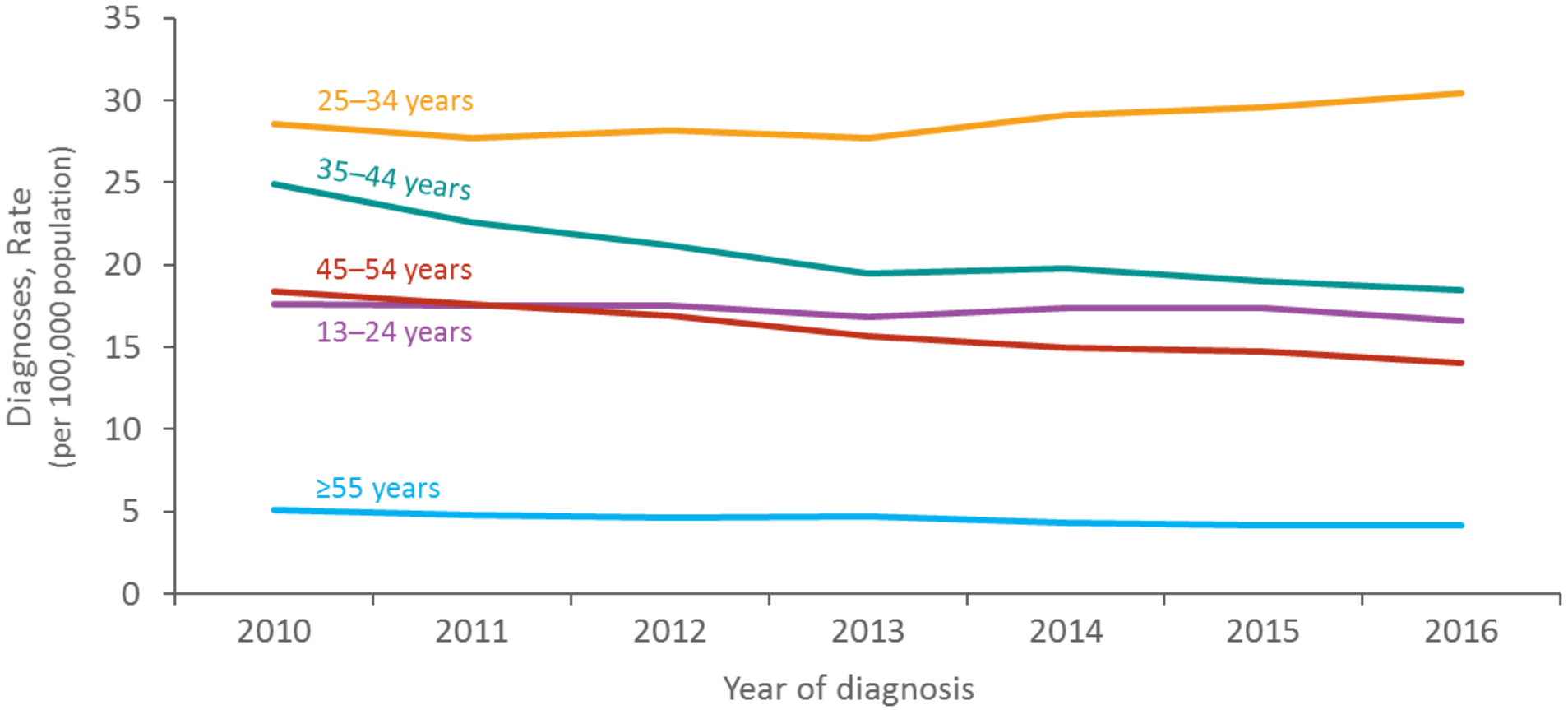
# Estimated HIV Incidence among Persons Aged ≥13 Years 2010–2016 US




Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Bars indicate the range of the lower and upper bounds of the 95% confidence intervals for the point estimate.

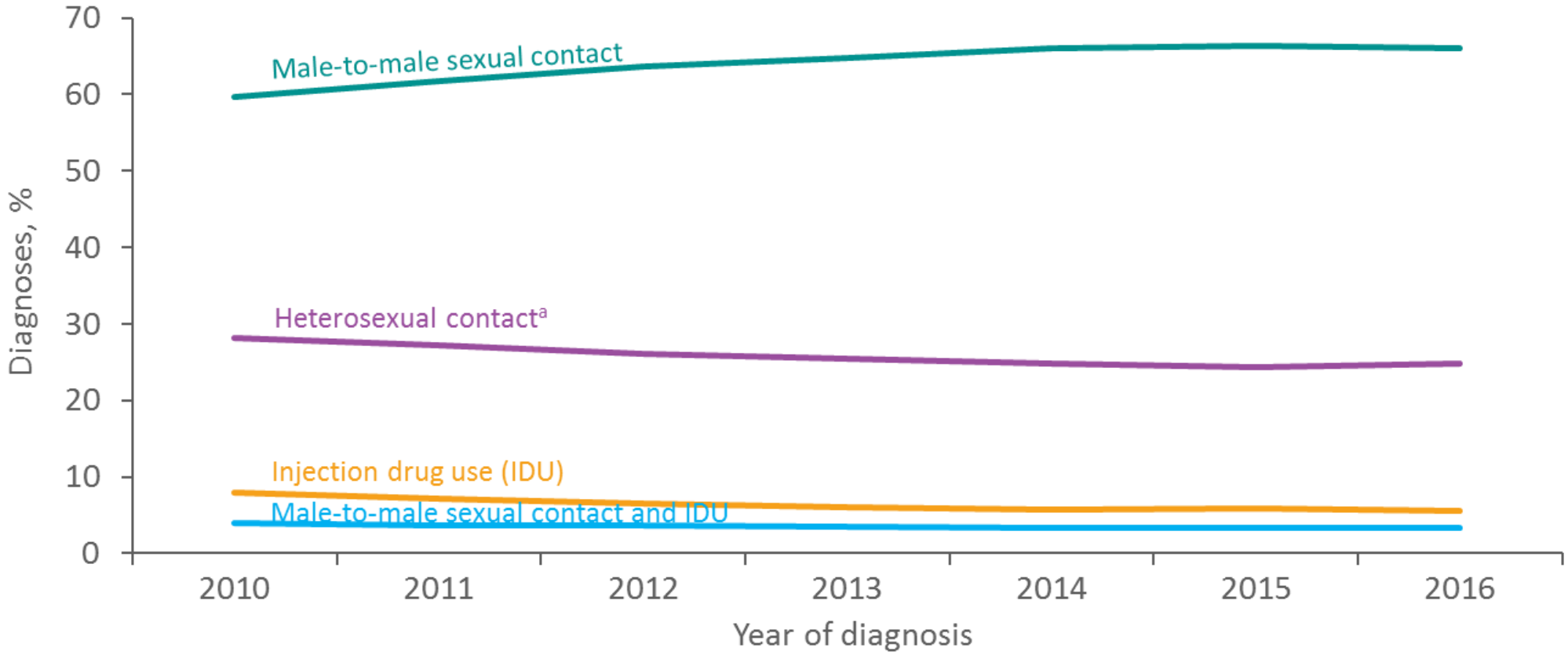
https://www.cdc.gov/hiv/statistics/overview/index.html

# Rates of Diagnoses of HIV Infection among Adults and Adolescents by Age at Diagnosis, 2010–2016 US




https://www.cdc.gov/hiv/statistics/overview/index.html

# Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2010–2016 US and 6 Dependent Areas

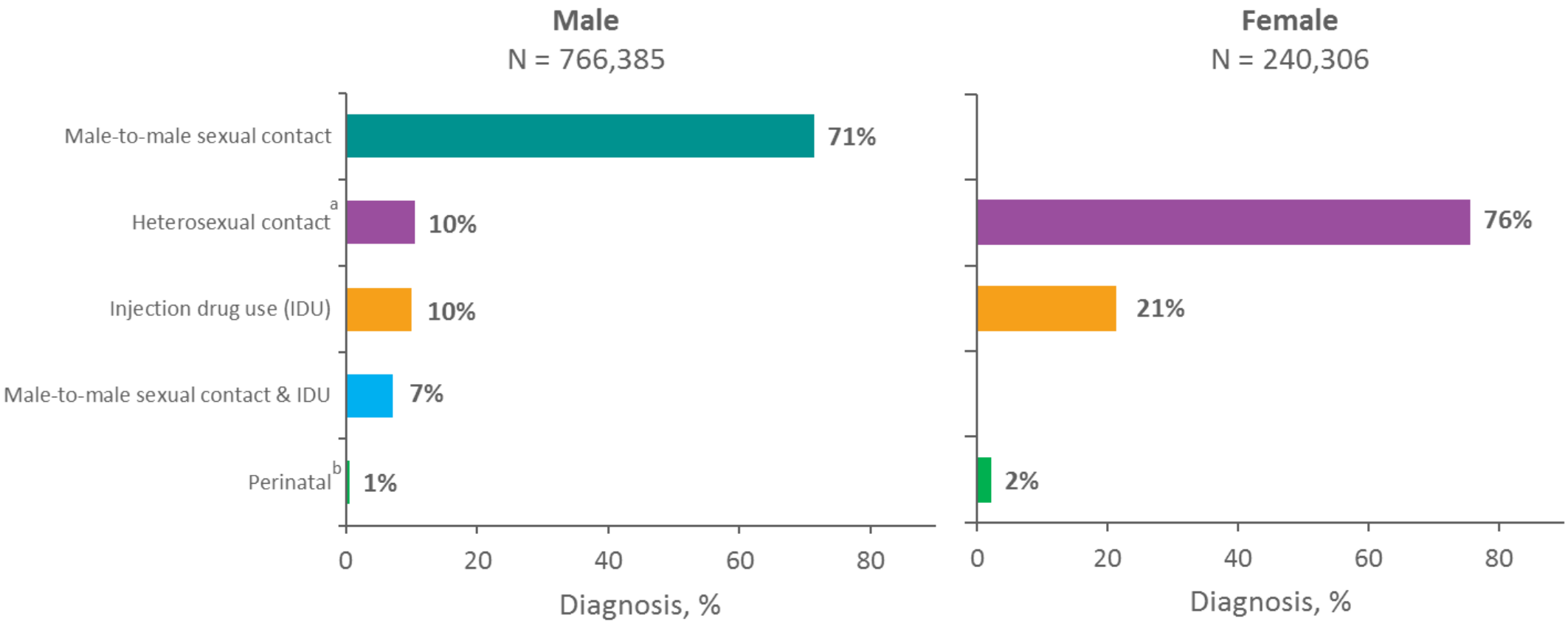



*Note*. Data have been statistically adjusted to account for missing transmission category. "Other" transmission category not displayed as it comprises less than 1% of cases.

[a] Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

https://www.cdc.gov/hiv/statistics/overview/index.html

# Adults and Adolescents Living with Diagnosed HIV Infection, by Sex and Transmission Category, Year-end 2016 US and 6 Dependent Areas



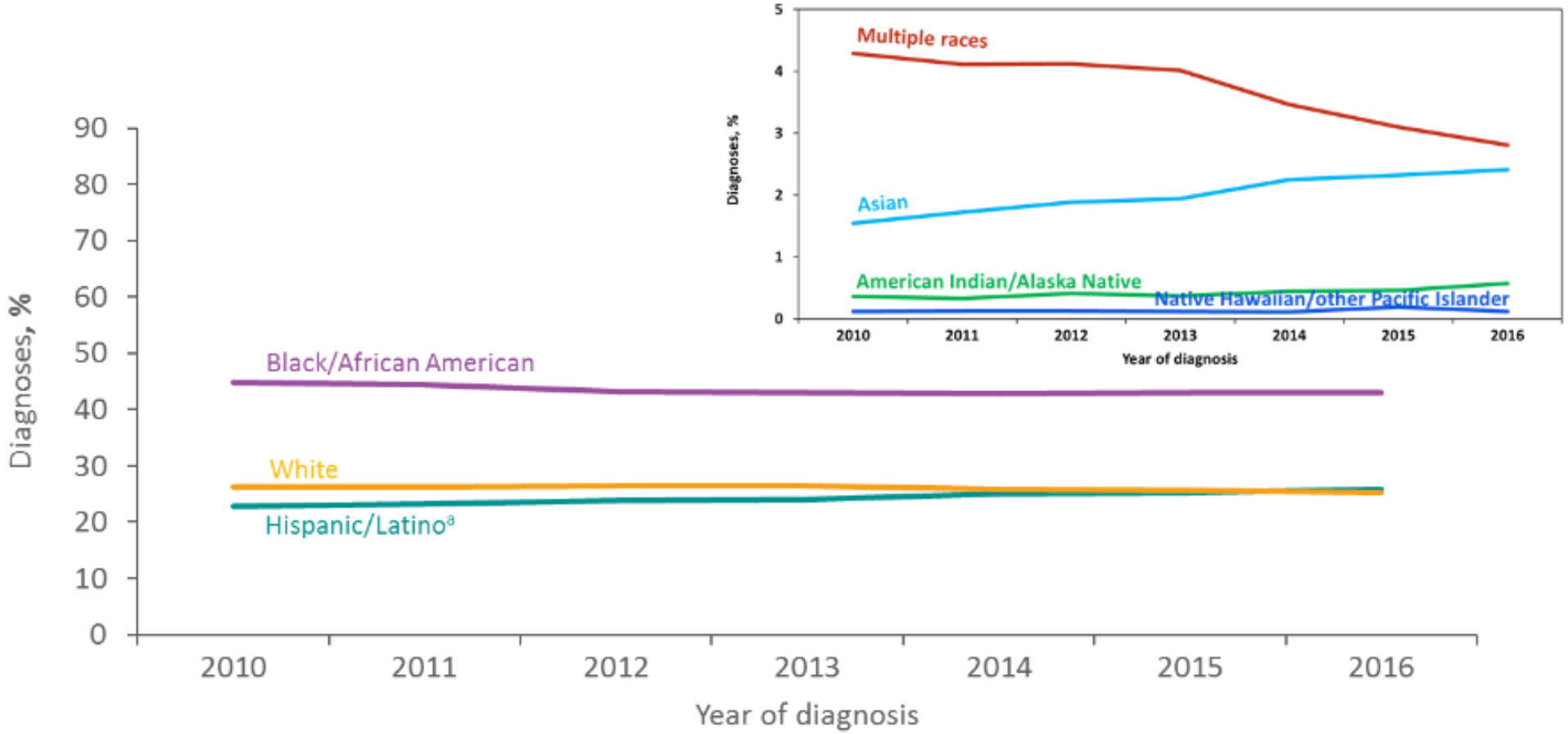

*Note.* Data have been statistically adjusted to account for missing transmission category. "Other" transmission category not displayed as it comprises 1% or less of cases.

[a] Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.

[b] Perinatal includes persons whose infections were attributed to perinatal transmission, but were aged 13 years and older at the end of 2016.

https://www.cdc.gov/hiv/statistics/overview/index.html

# Diagnoses of HIV Infection among Adults and Adolescents, by Race/Ethnicity 2010–2016—United States and 6 Dependent Areas




[a] Hispanics/Latinos can be of any race.

https://www.cdc.gov/hiv/statistics/overview/index.html

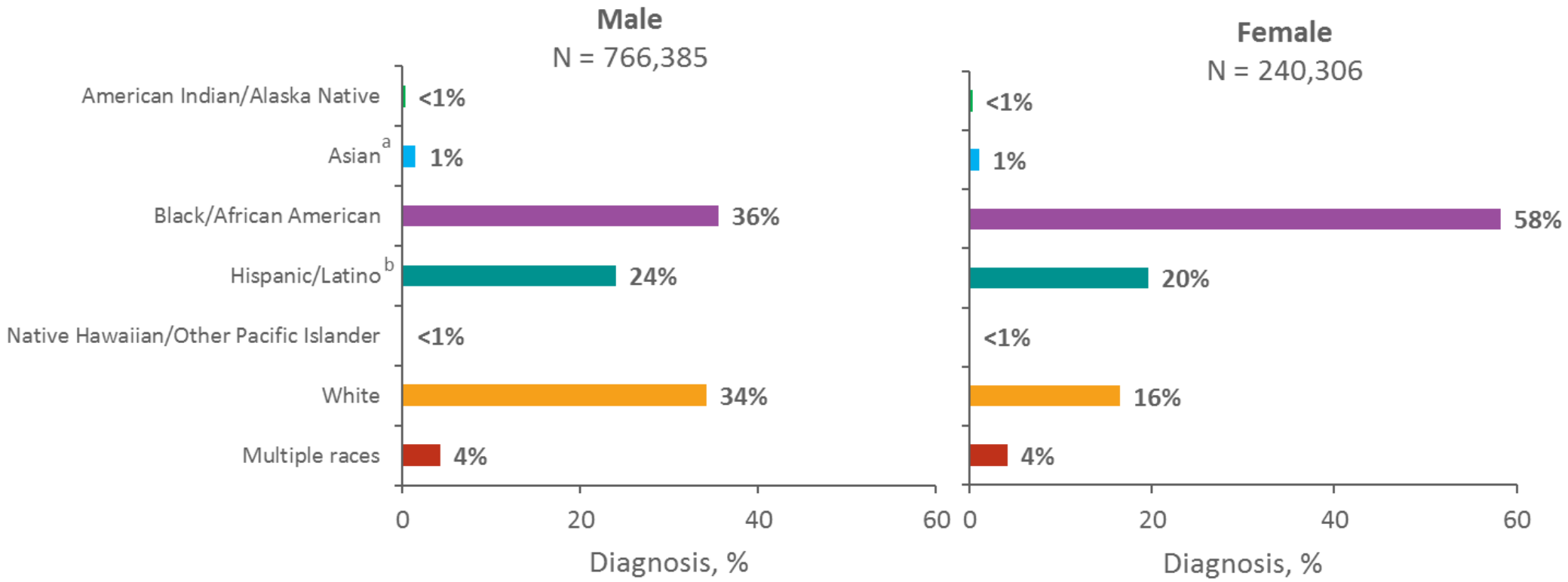
# Deaths of Persons with Diagnosed HIV Infection by Race/Ethnicity, 2016—United States

| Race/ethnicity | No. | Rate | % |
|---|---|---|---|
| American Indian/Alaska Native | 46 | 1.9 | 0.3 |
| Asian[a] | 95 | 0.5 | 0.6 |
| Black/African American | 6,795 | 16.9 | 44.0 |
| Hispanic/Latino[b] | 2,497 | 4.3 | 16.2 |
| Native Hawaiian/other Pacific Islander | 12 | 2.1 | <1 |
| White | 5,038 | 2.5 | 32.7 |
| Multiple races | 944 | 14.0 | 6.1 |
| **Total[c]** | **15,428** | **4.8** | **100** |

*Note.* Deaths of persons with diagnosed HIV infection may be due to any cause. Rates are per 100,000 population.
[a] Includes Asian/Pacific Islander legacy cases.
[b] Hispanics/Latinos can be of any race.
[c] Includes one person whose race/ethnicity is unknown.

https://www.cdc.gov/hiv/statistics/overview/index.html

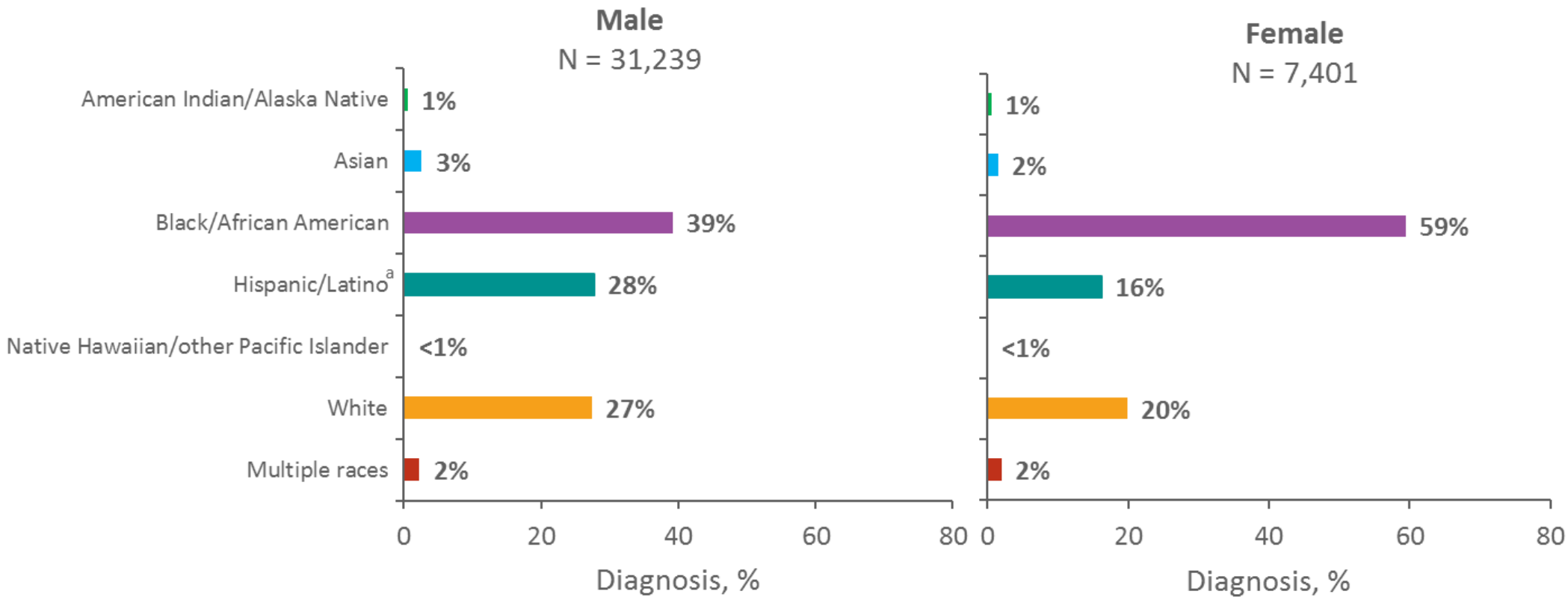
# Adults and Adolescents Living with Diagnosed HIV Infection, by Sex and Race/Ethnicity, Year-end 2016 US and 6 Dependent Areas




*Note*. Unknown race/ethnicity is not displayed because it comprises less than 1% of cases.
[a] Includes Asian/Pacific Islander legacy cases.
[b] Hispanics/Latinos can be of any race.

https://www.cdc.gov/hiv/statistics/overview/index.html

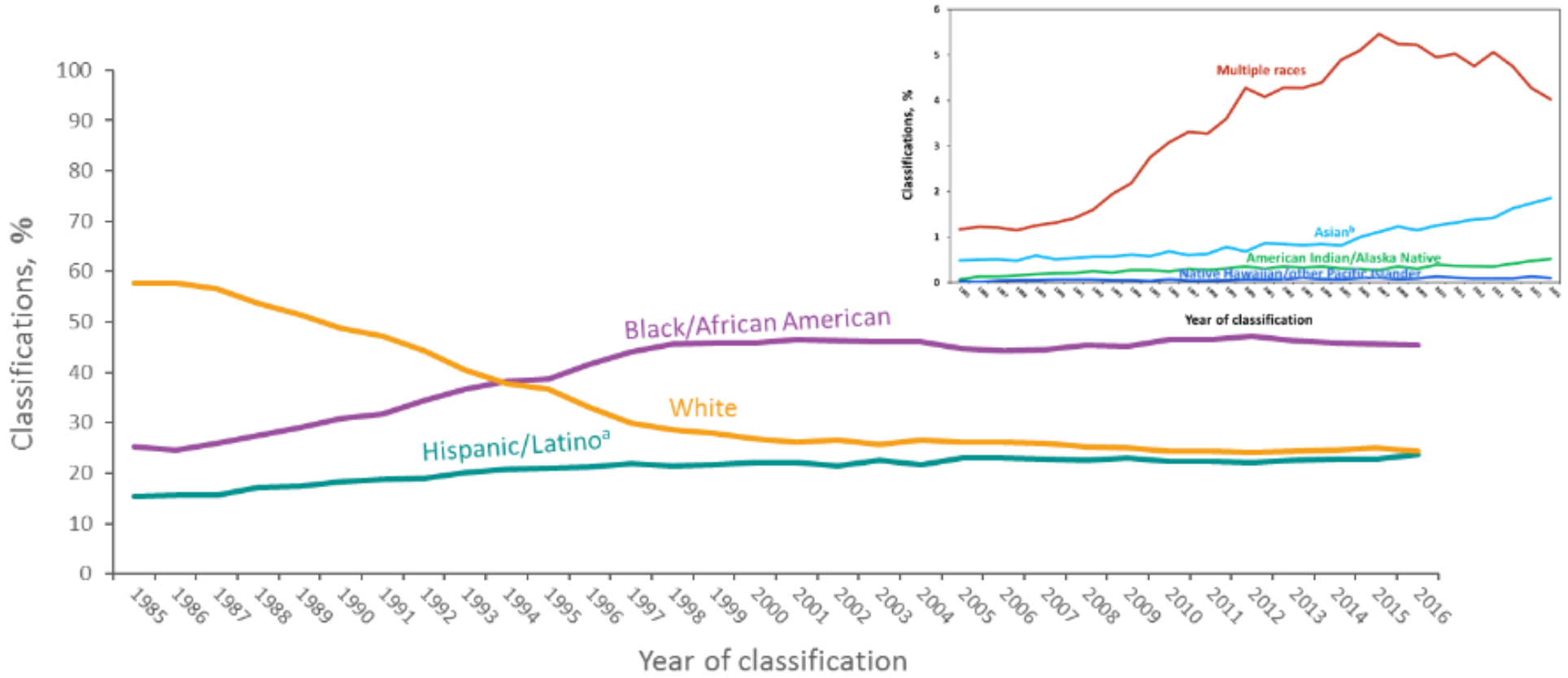
# Diagnoses of HIV Infection among Adults and Adolescents by Sex and Race/Ethnicity, 2017 US and 6 Dependent Areas




*Note*. Data for the year 2017 are considered preliminary and based on 6 months reporting delay.
[a] Hispanics/Latinos can be of any race.

https://www.cdc.gov/hiv/statistics/overview/index.html

# Percentages AIDS Classifications among Adults and Adolescents with Diagnosed HIV Infection (Race/Ethnicity, Year of Classification) 1985–2016 US and 6 Dependent Areas

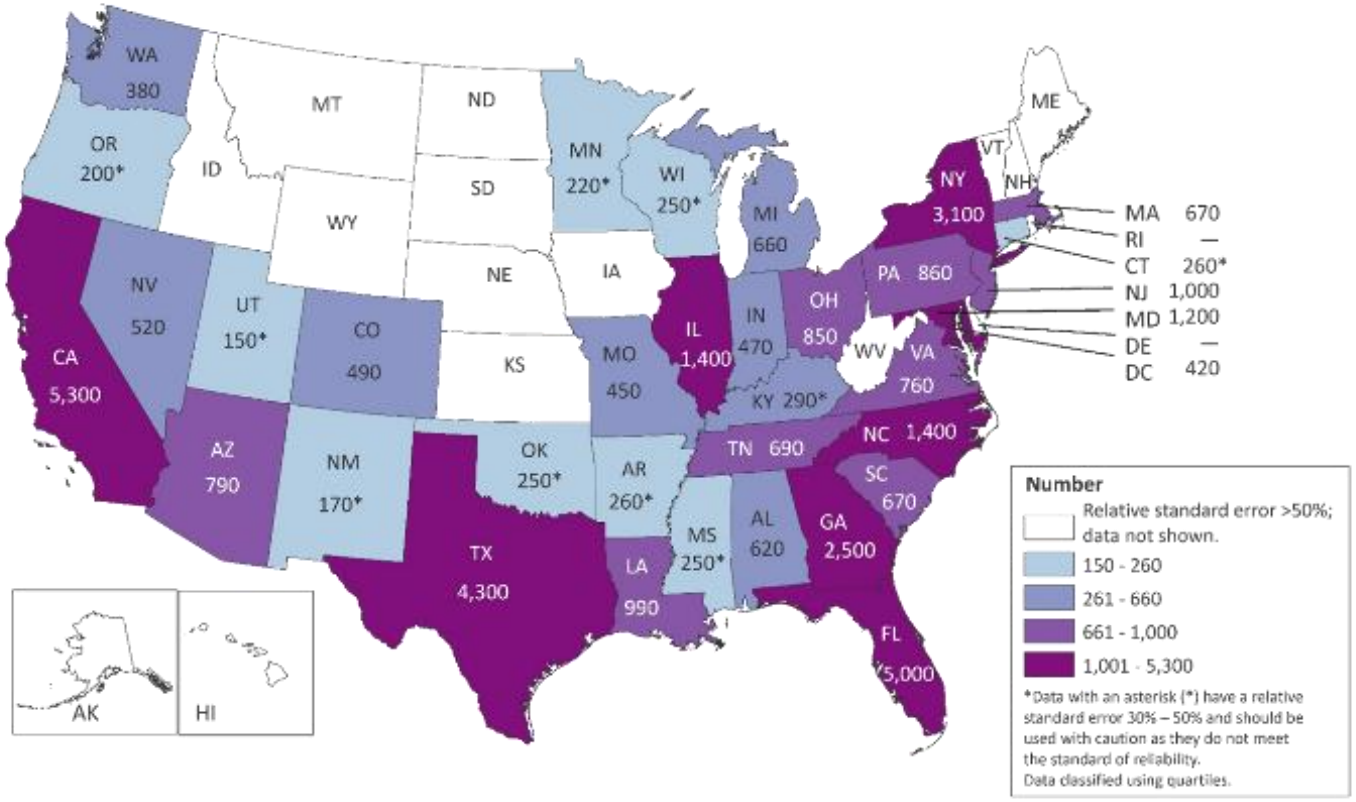



*Note*. Unknown race/ethnicity is not displayed because it comprises less than 1% of cases.
[a] Hispanics/Latinos can be of any race.
[b] Includes Asian/Pacific Islander legacy cases.

https://www.cdc.gov/hiv/statistics/overview/index.html

# Estimated HIV Incidence among Persons Aged ≥13 Years, by Area of Residence 2016 US

## Total = 38,700

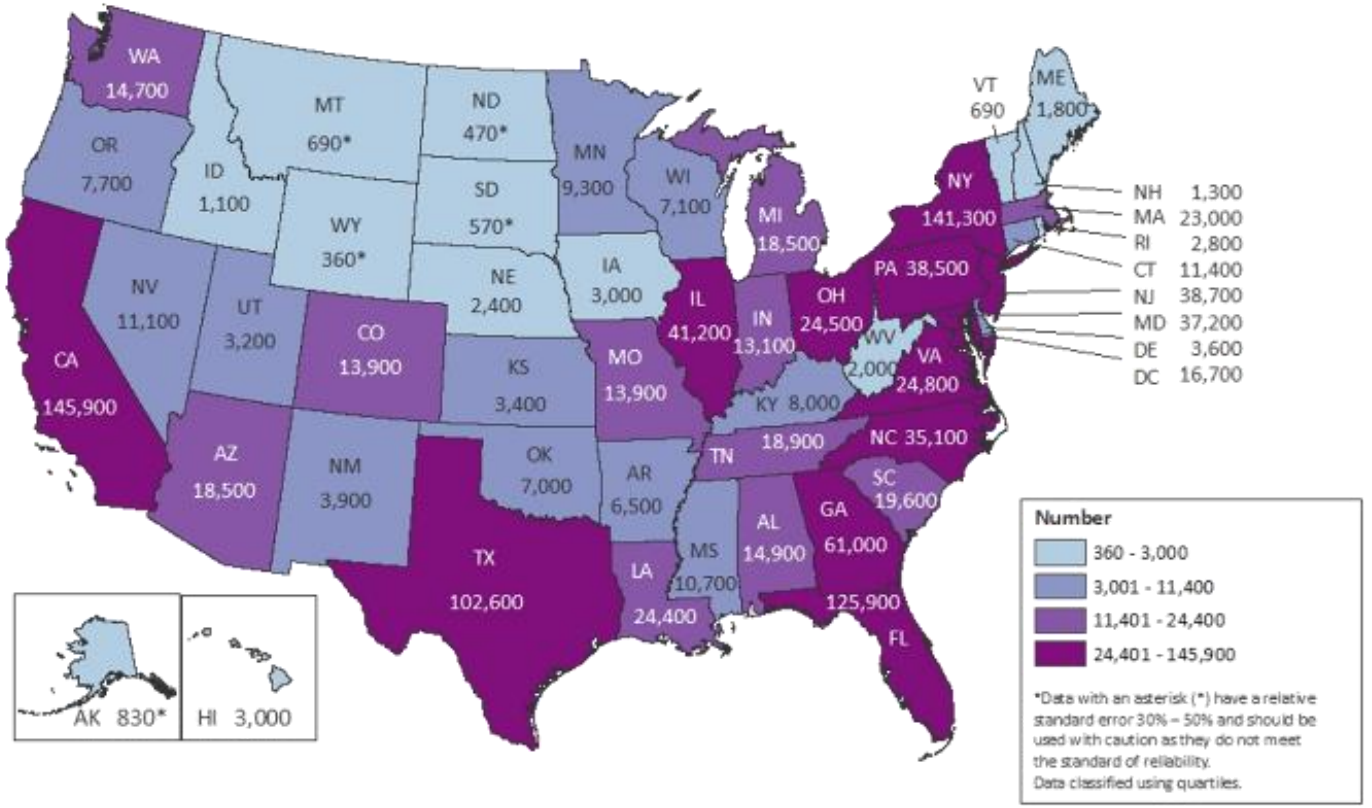



Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Estimates rounded to the nearest 100 for estimates >1,000 and to the nearest 10 for estimates ≤1,000 to reflect model uncertainty.

https://www.cdc.gov/hiv/statistics/overview/index.html

# Estimated HIV Prevalence among Persons Aged ≥13 Years, by Area of Residence 2016 US

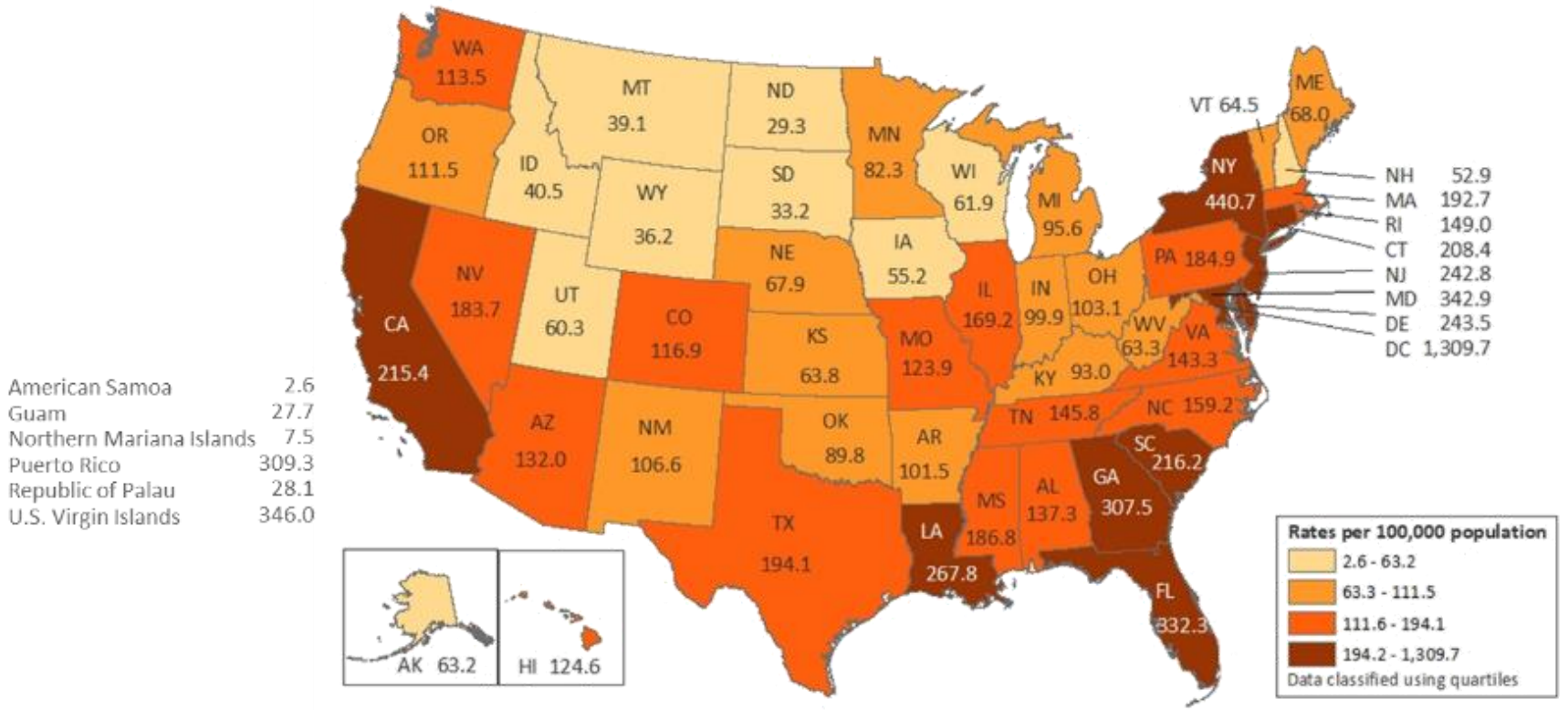
## Total = 1,140,400




Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Estimates rounded to the nearest 100 for estimates >1,000 and to the nearest 10 for estimates ≤1,000 to reflect model uncertainty.

https://www.cdc.gov/hiv/statistics/overview/index.html

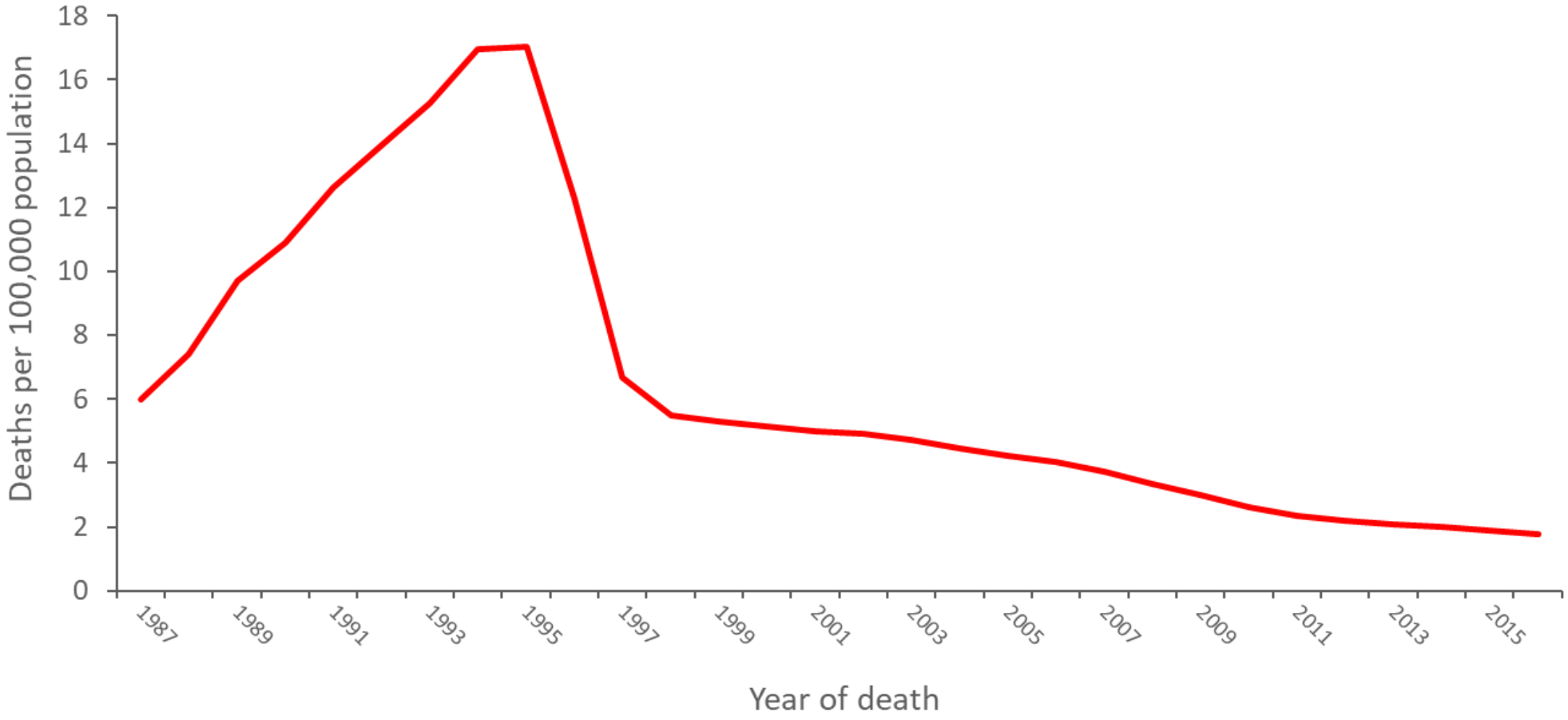
# Rates of Adults and Adolescents Living with Diagnosed HIV Infection Ever Classified as Stage 3 (AIDS), Year-end 2016
## US and 6 Dependent Areas
## N = 534,515  Total Rate = 195.2




*Note.* Data are based on address of residence as of December 31, 2016 (i.e., most recent known address).

https://www.cdc.gov/hiv/statistics/overview/index.html

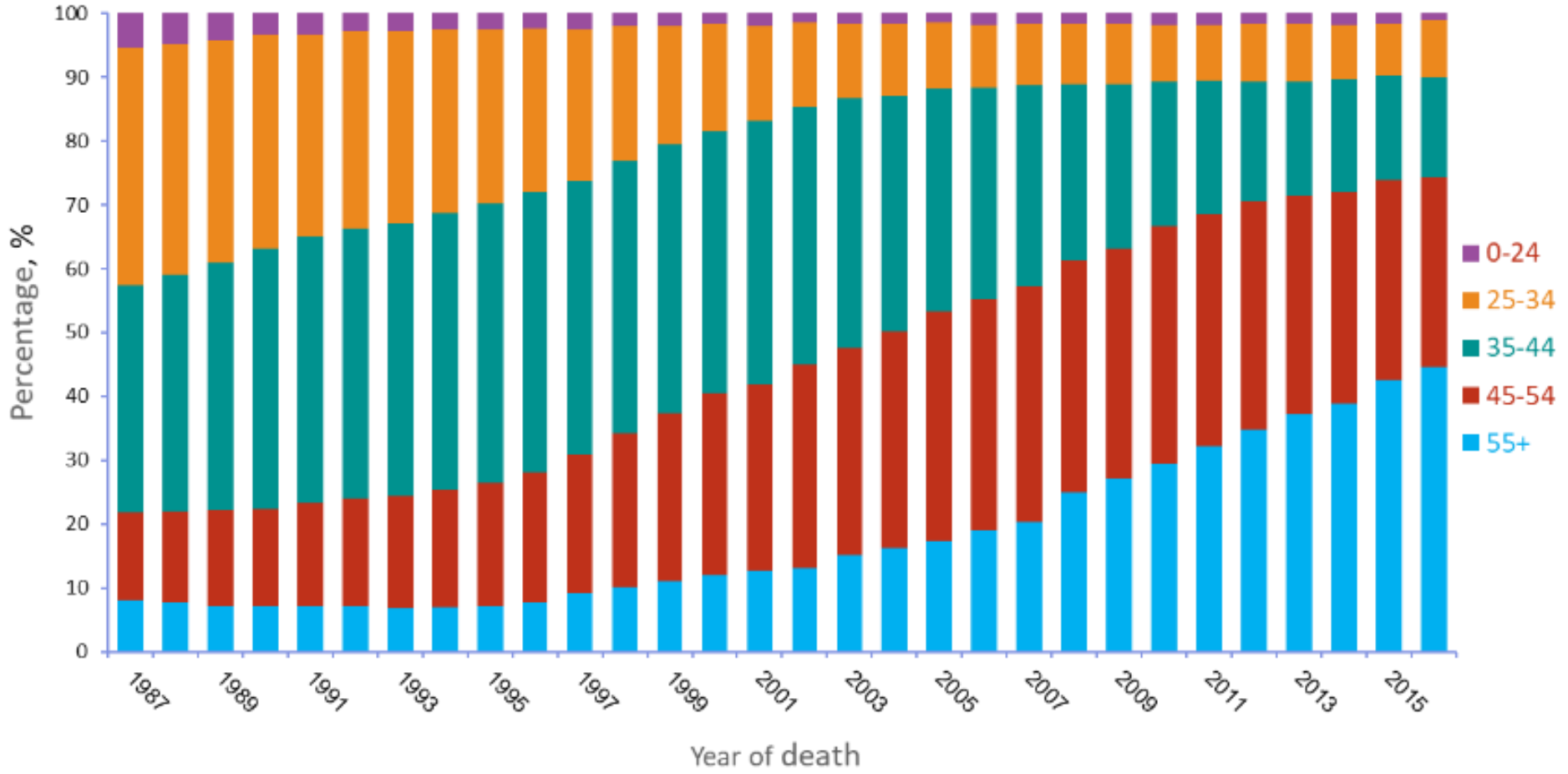
# Trends in Annual Age-Adjusted* Rates of Death Due to HIV Infection 1987–2016 — United States




*Note.* For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for *ICD-10* rules instead of *ICD-9* rules.
*Standard: age distribution of 2000 US population.

https://www.cdc.gov/hiv/statistics/overview/index.html

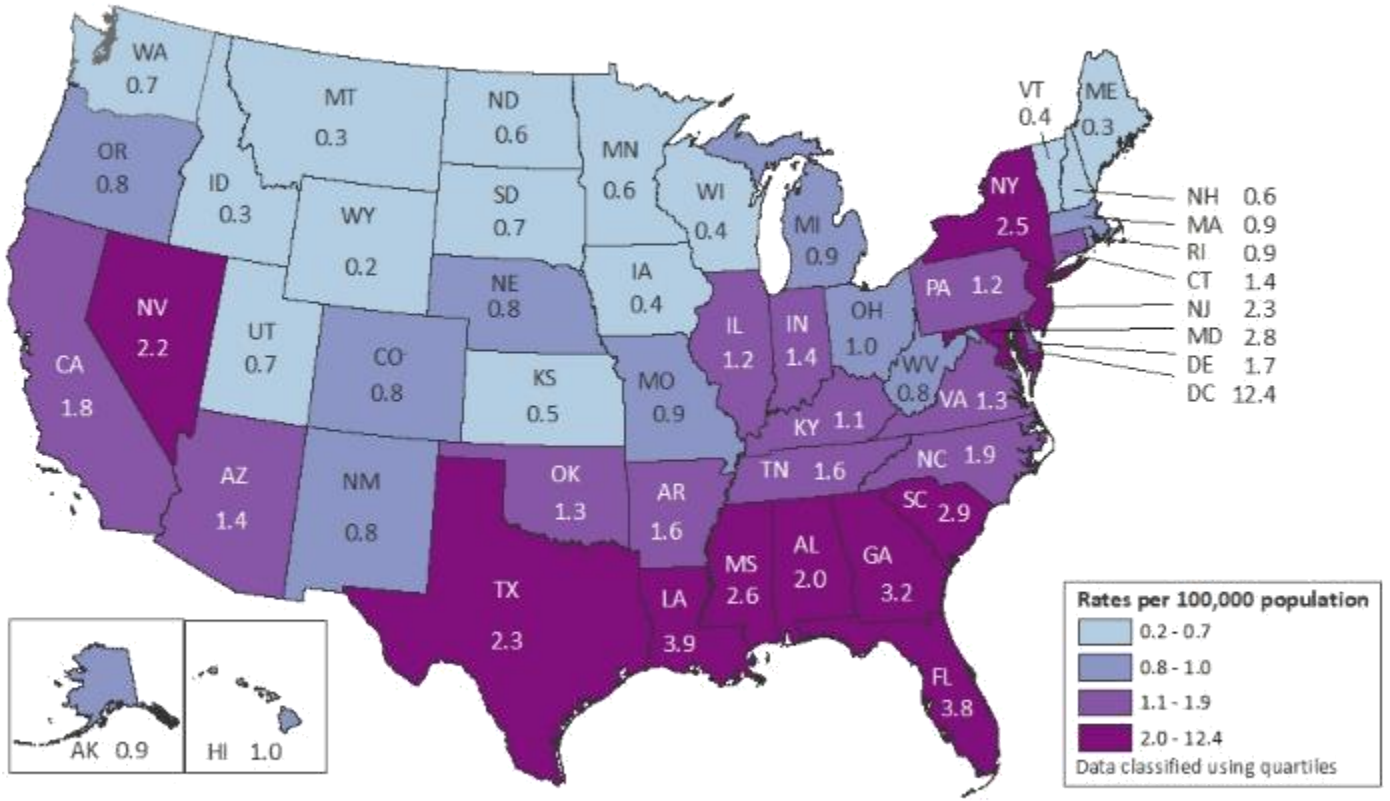
# Trends in the Percentage Distribution of Deaths due to HIV Infection by Age Group 1987–2016 — United States




*Note*. For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for *ICD-10* 10rules instead of *ICD-9* rules.

https://www.cdc.gov/hiv/statistics/overview/index.html

# Age-Adjusted* Rates† of Death due to HIV Infection in the General Population, by State, 2016 US

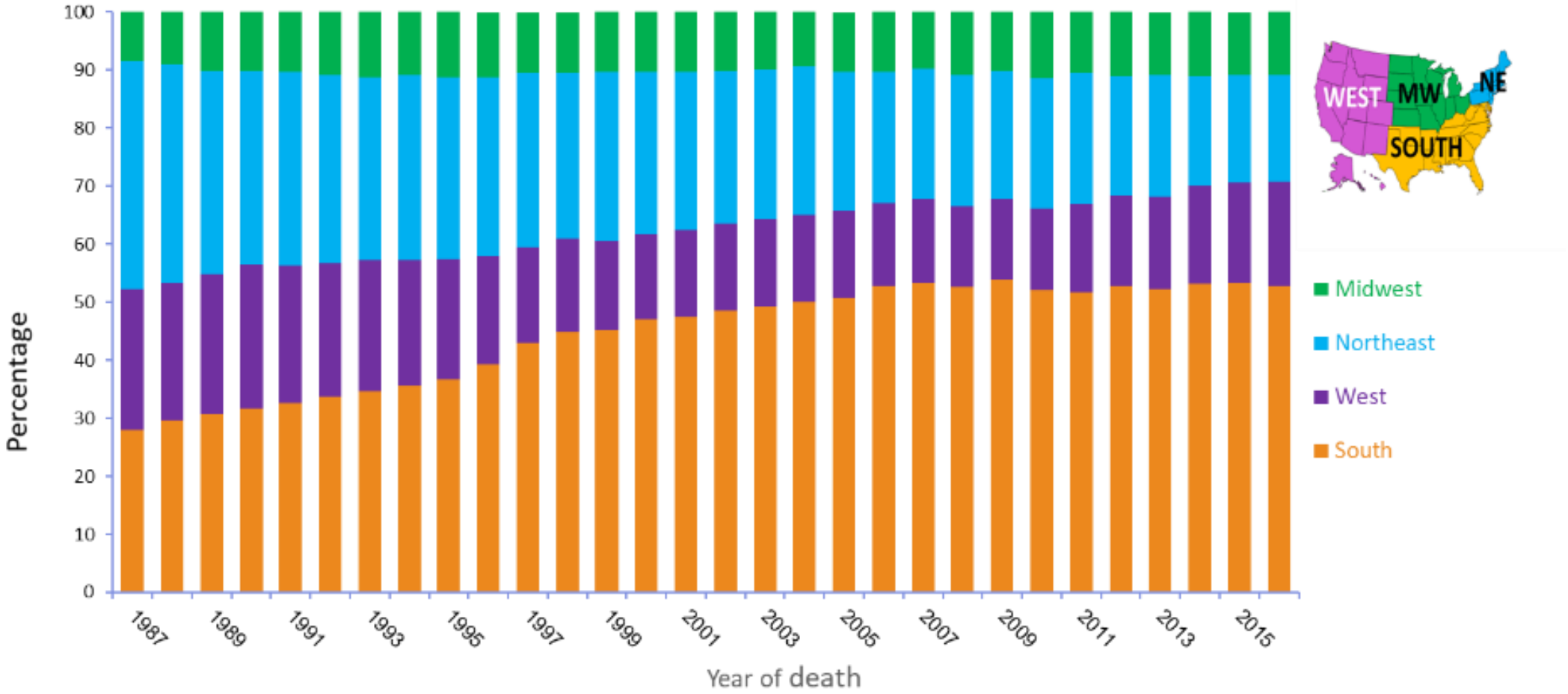



Standard: age distribution of 2000 US population.

†Per 100,000 population.

https://www.cdc.gov/hiv/statistics/overview/index.html

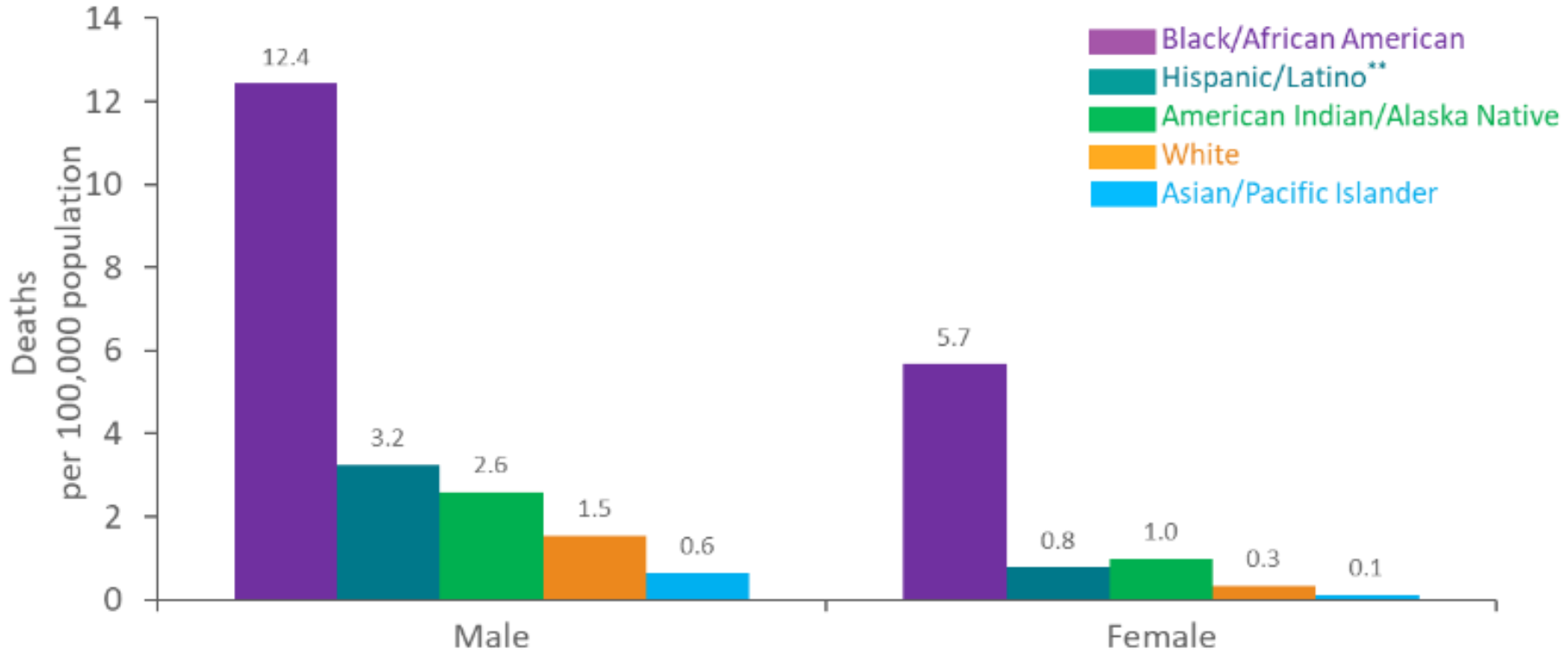
# Trends in the Percentage Distribution of Deaths due to HIV Infection, by Geographic Region, 1987–2016 — United States




*Note*. For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for *ICD-10* 10rules instead of *ICD-9* rules.

https://www.cdc.gov/hiv/statistics/overview/index.html

# Age-Adjusted* Average Rates of Death due to HIV Infection by Sex and Race/Ethnicity, 2012–2016 — United States




*Standard age distribution of 2000 US population
**Hispanics/Latinos can be of any race.

https://www.cdc.gov/hiv/statistics/overview/index.html

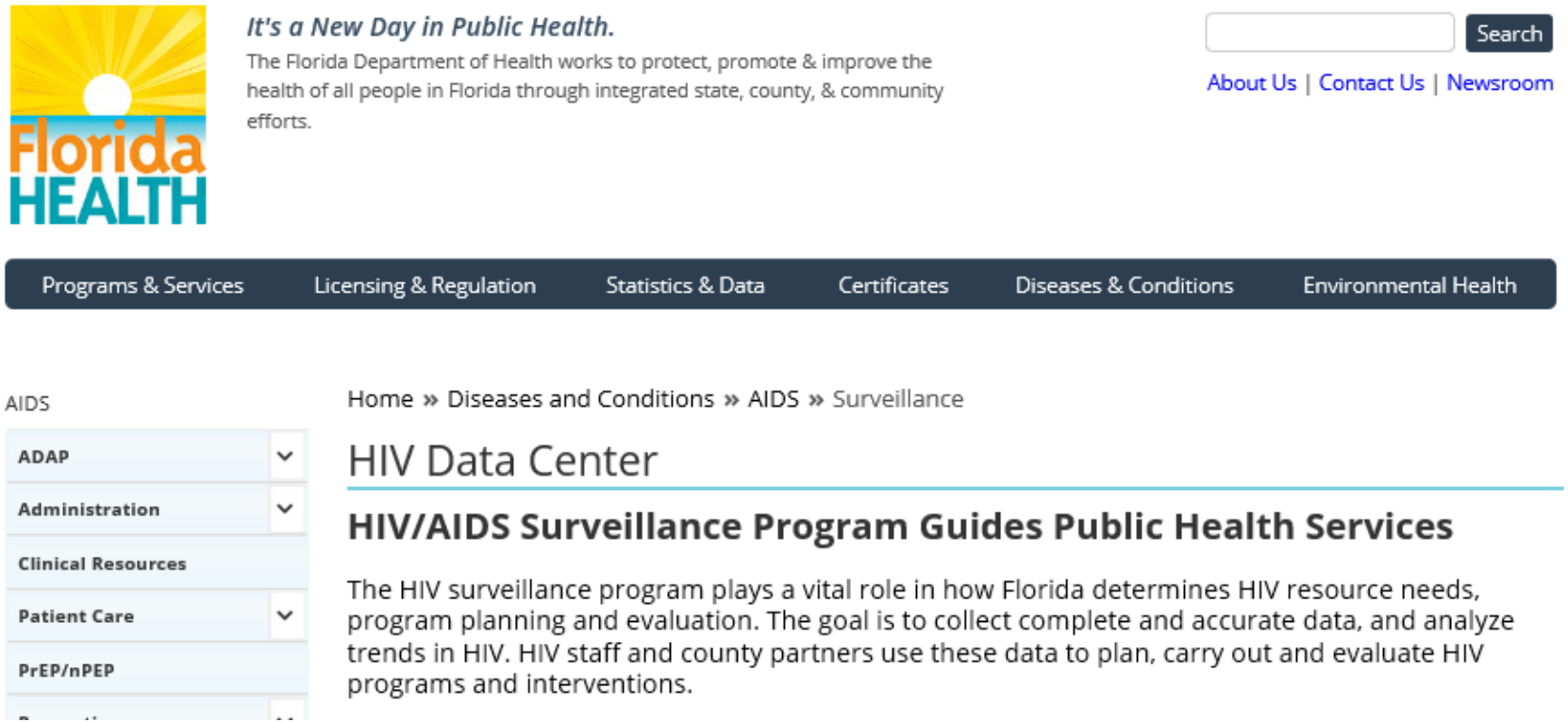
# EPIDEMIOLOGY

- What is the current status of the HIV/AIDS epidemic in the state of Florida?
- How has it changed over time?

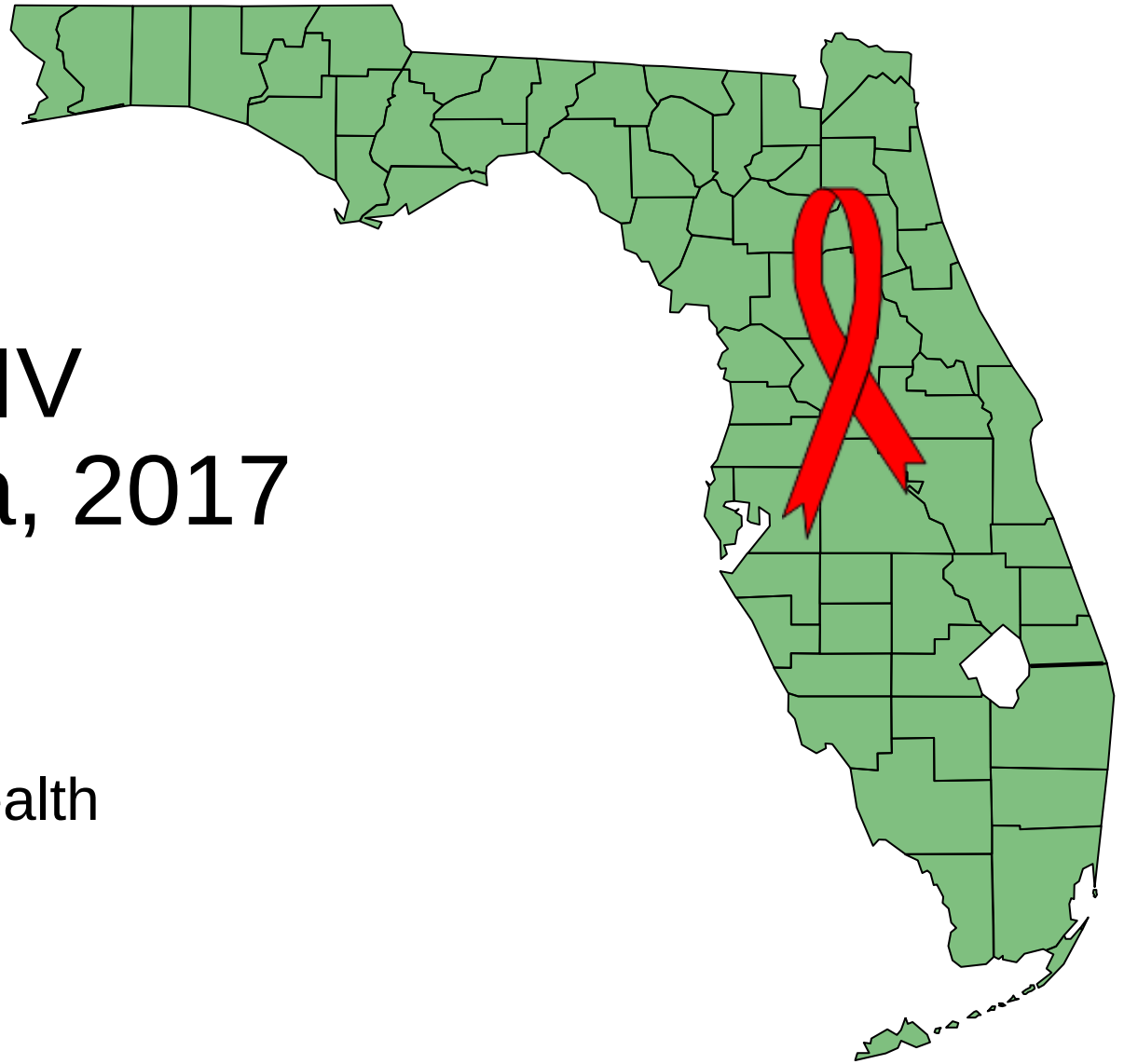
http://www.floridahealth.gov/diseases-and-conditions/aids/surveillance/epi-slide-sets.html

# EPIDEMIOLOGY

- What is the current status of the HIV/AIDS epidemic in the state of Florida?
- How has it changed over time?




http://www.floridahealth.gov/diseases-and-conditions/aids/surveillance/index.html
http://www.floridahealth.gov/diseases-and-conditions/aids/surveillance/epi-slide-sets.html



# State of the HIV Epidemic in Florida, 2017

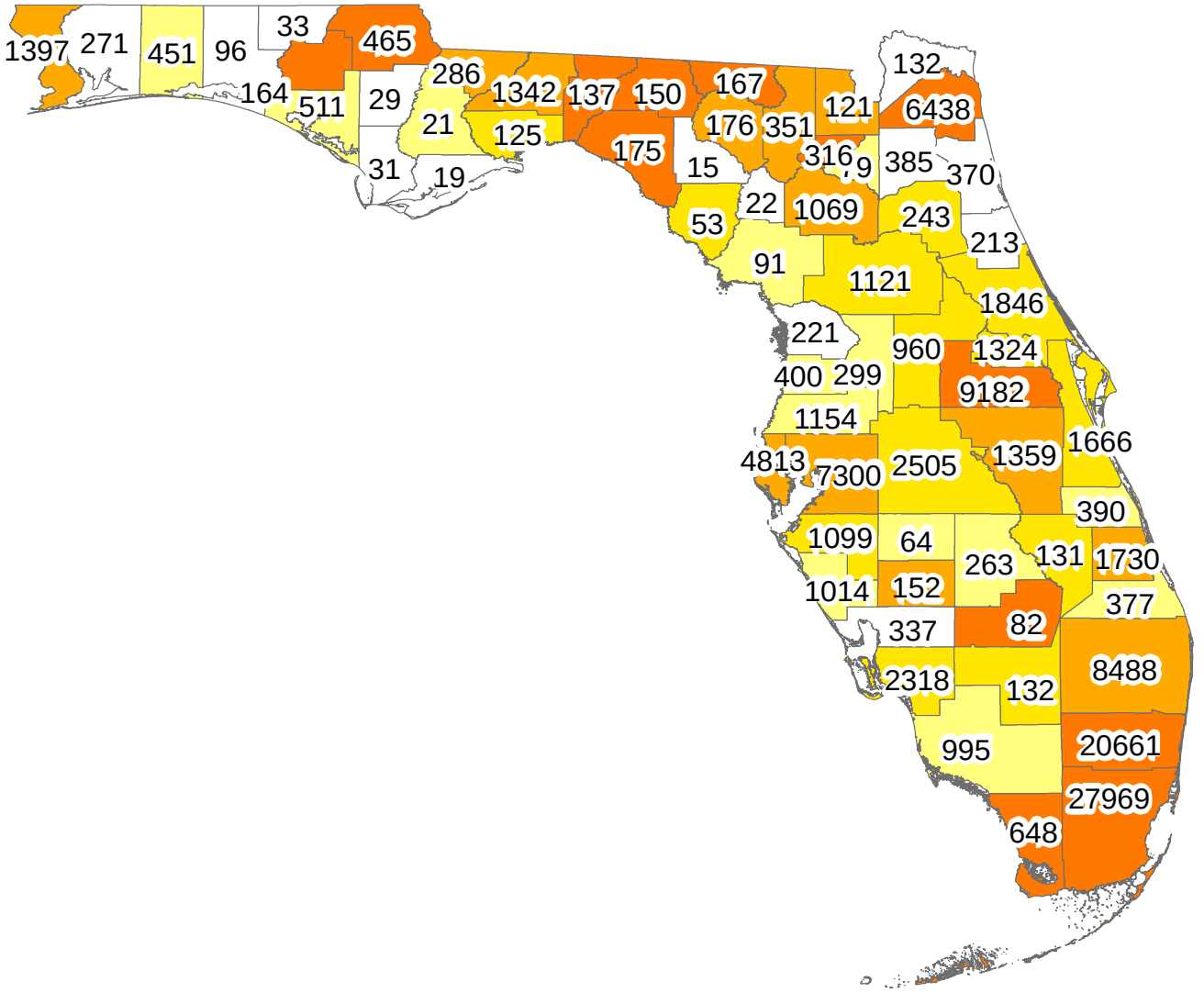
Florida Department of Health
HIV/AIDS Section
Data as of 6/30/2018

# Persons Living with HIV (PLWH) Rates[1] by County of Residence[2] Diagnosed in 2017, Florida

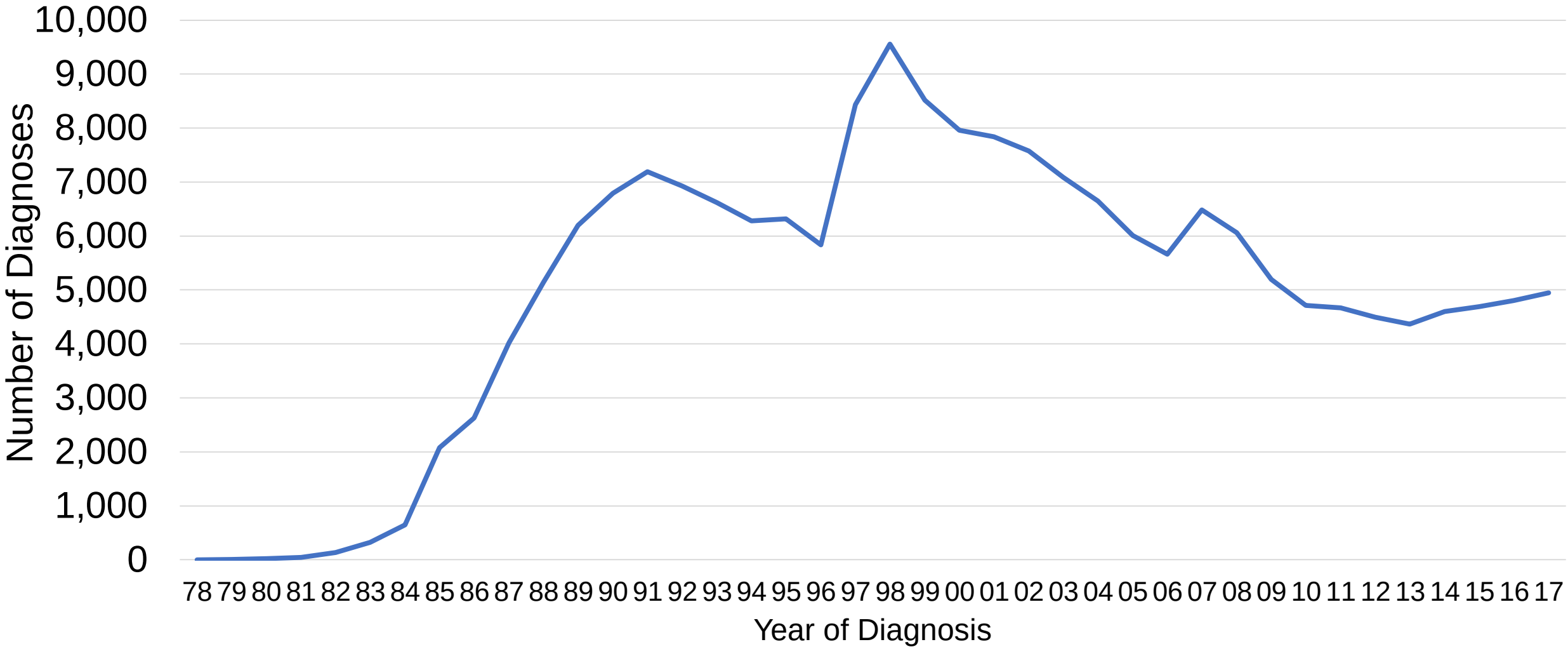
PLWH Rate
per 100,000 population
State Rate=569

- 130 - 201
- 202 - 286
- 287 - 389
- 390 - 602
- 603 - 1988

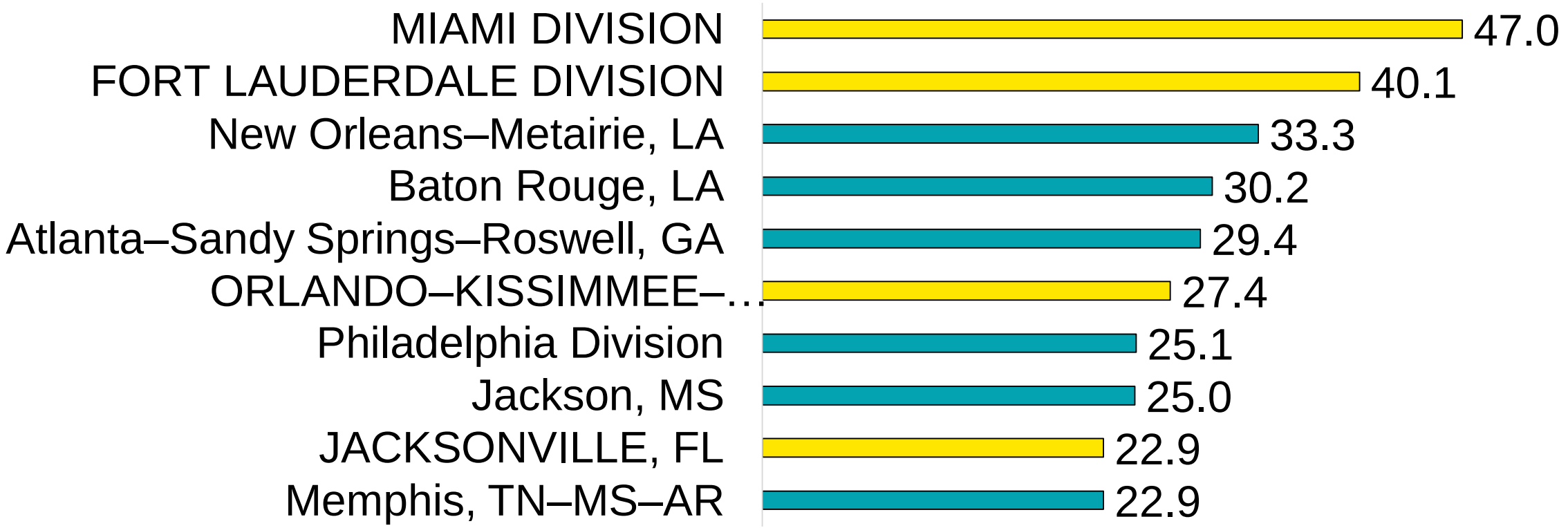
Numbers on map are number of PLWH
State Total N=116,944



# HIV Diagnoses by Year of Diagnosis, 1978–2017, Florida



# Rankings of HIV Case Rates (all ages) by MSA[1] Diagnosed in 2016, United States




Rate per 100,000 population



[1] Source: US data: HIV Surveillance Report, 2016 (most recent available) Vol. 28, Table 24 (HIV data for all 50 states)
http://www.cdc.gov/hiv/topics/surveillance/resources/reports/index.htm

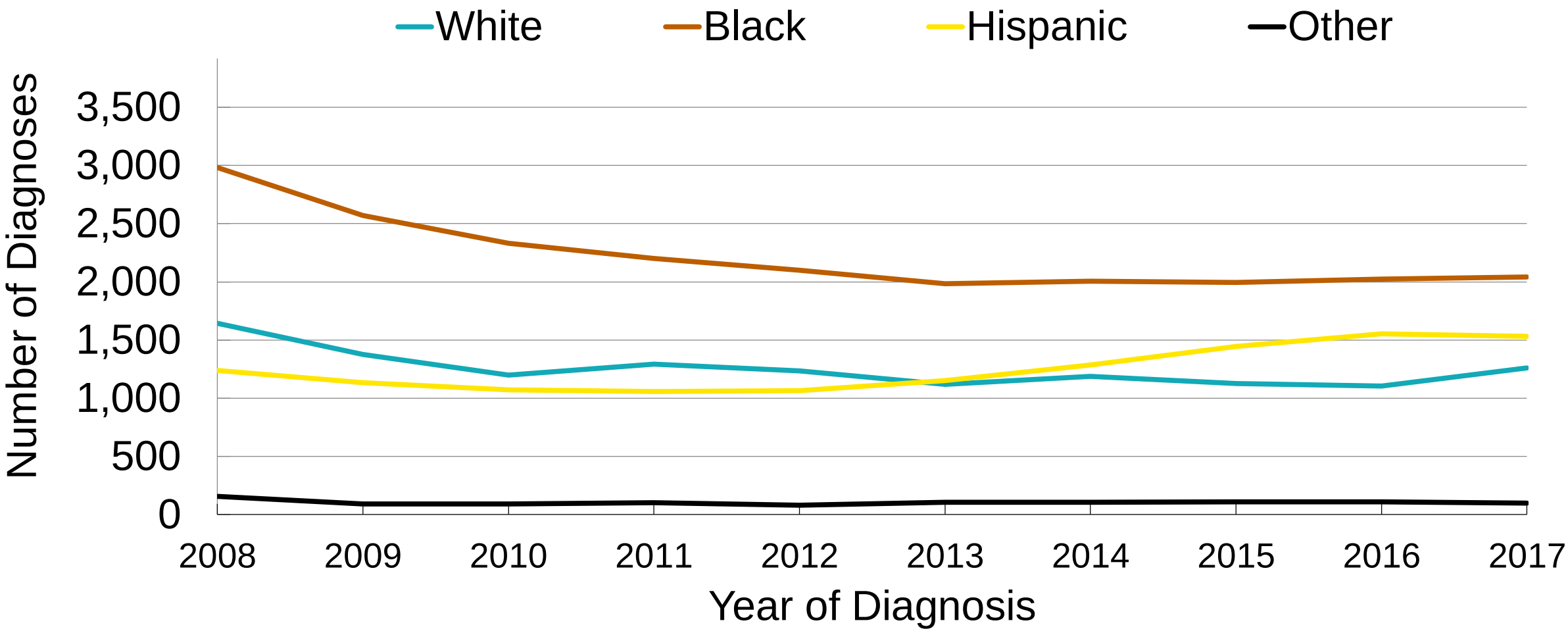
# Adults (Age 13+) Living with HIV Year-end 2017, Florida, N=116,782

| Race/Ethnicity | Males | | Females | |
|---|---|---|---|---|
| | No. | Percent | No. | Percent |
| White | 29,050 | 34% | 4,898 | 15% |
| Black | 31,719 | 37% | 21,488 | 67% |
| Hispanic | 22,245 | 26% | 4,990 | 16% |
| Other | 1,740 | 2% | 652 | 2% |
| **Age Group** | | | | |
| 13–19 | 331 | 0% | 225 | 1% |
| 20–29 | 7,783 | 9% | 2,120 | 7% |
| 30–39 | 13,235 | 16% | 5,568 | 17% |
| 40–49 | 18,264 | 22% | 8,368 | 26% |
| 50+ | 45,141 | 53% | 15,747 | 49% |
| **Mode of Exposure** | | | | |
| MSM | 58,756 | 69% | --- | --- |
| IDU | 5,169 | 6% | 3,875 | 12% |
| MSM/IDU | 4,344 | 5% | --- | --- |
| Heterosexual | 15,713 | 19% | 27,277 | 85% |
| Other Risk | 773 | 1% | 876 | 3% |
| TOTAL | 84,754 | 100% | 32,028 | 100% |

# Adults (Age 13+) Living with HIV Year-end 2017, Florida, N=116,782

| Race/Ethnicity | Males | | Females | |
|---|---|---|---|---|
| | No. | Percent | No. | Percent |
| White | 29,050 | 34% | 4,898 | 15% |
| Black | 31,719 | 37% | 21,488 | 67% |
| Hispanic | 22,245 | 26% | 4,990 | 16% |
| Other | 1,740 | 2% | 652 | 2% |
| **Age Group** | | | | |
| 13–19 | 331 | 0% | 225 | 1% |
| 20–29 | 7,783 | 9% | 2,120 | 7% |
| 30–39 | 13,235 | 16% | 5,568 | 17% |
| 40–49 | 18,264 | 22% | 8,368 | 26% |
| 50+ | 45,141 | 53% | 15,747 | 49% |
| **Mode of Exposure** | | | | |
| MSM | 58,756 | 69% | --- | --- |
| IDU | 5,169 | 6% | 3,875 | 12% |
| MSM/IDU | 4,344 | 5% | --- | --- |
| Heterosexual | 15,713 | 19% | 27,277 | 85% |
| Other Risk | 773 | 1% | 876 | 3% |
| TOTAL | 84,754 | 100% | 32,028 | 100% |

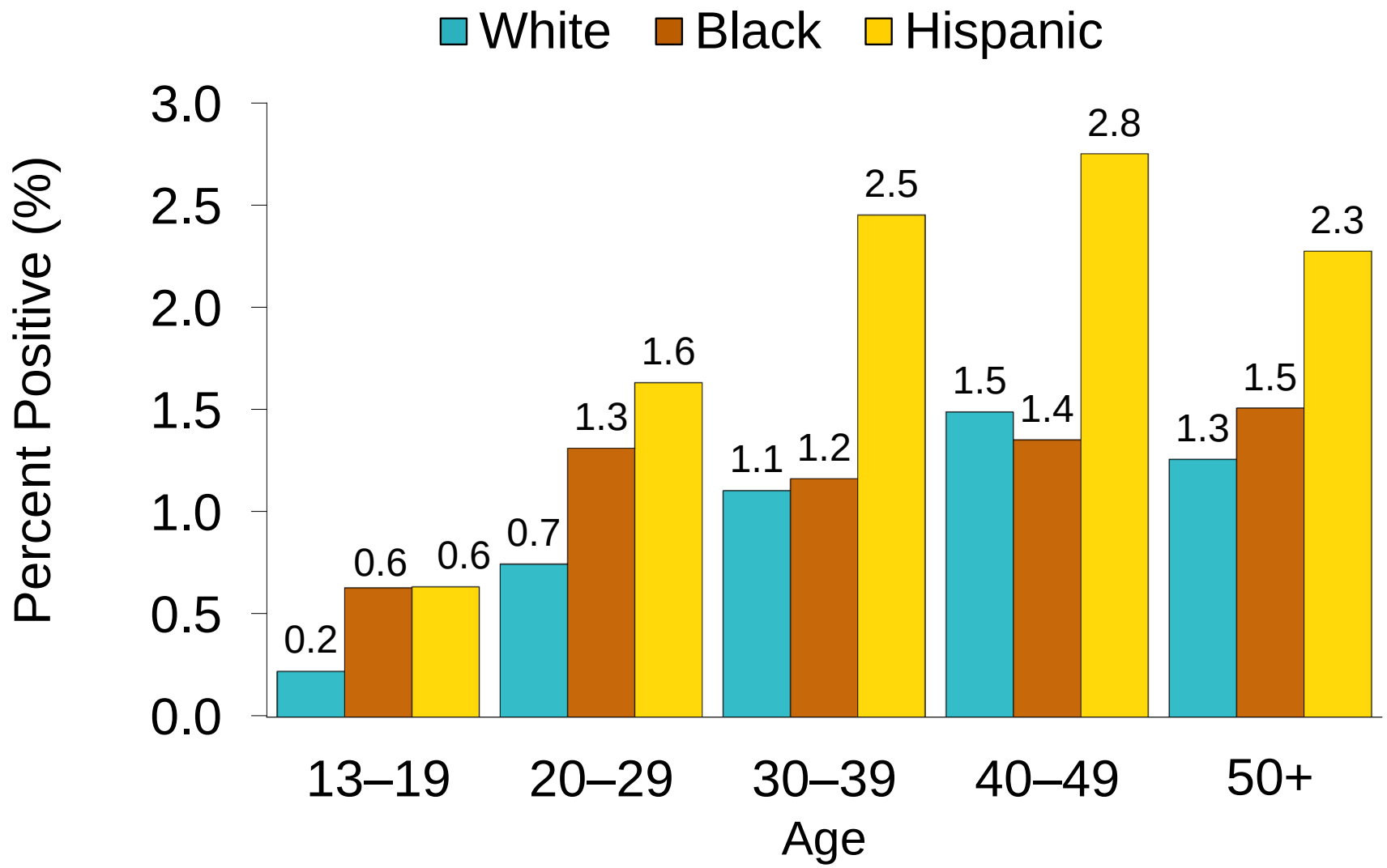
# Adult (Age 13+) HIV Diagnoses, by Race/Ethnicity and Year of Diagnosis, 2008–2017, Florida






Other includes American Indian/Alaska Native, Asian/Pacific Islander, and multi-racial.

# Seropositivity[1] among Males by Age Group and Race/Ethnicity from HIV Tests Conducted in Florida 2017

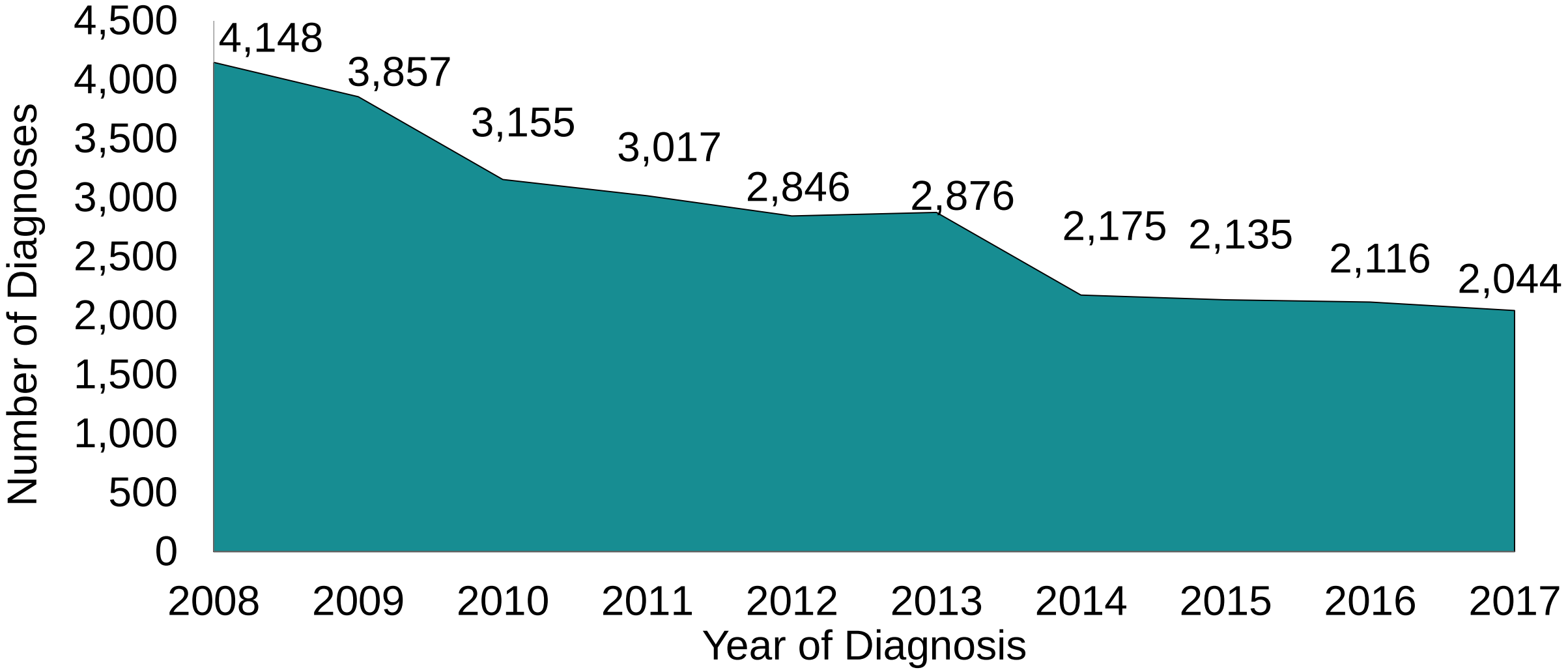




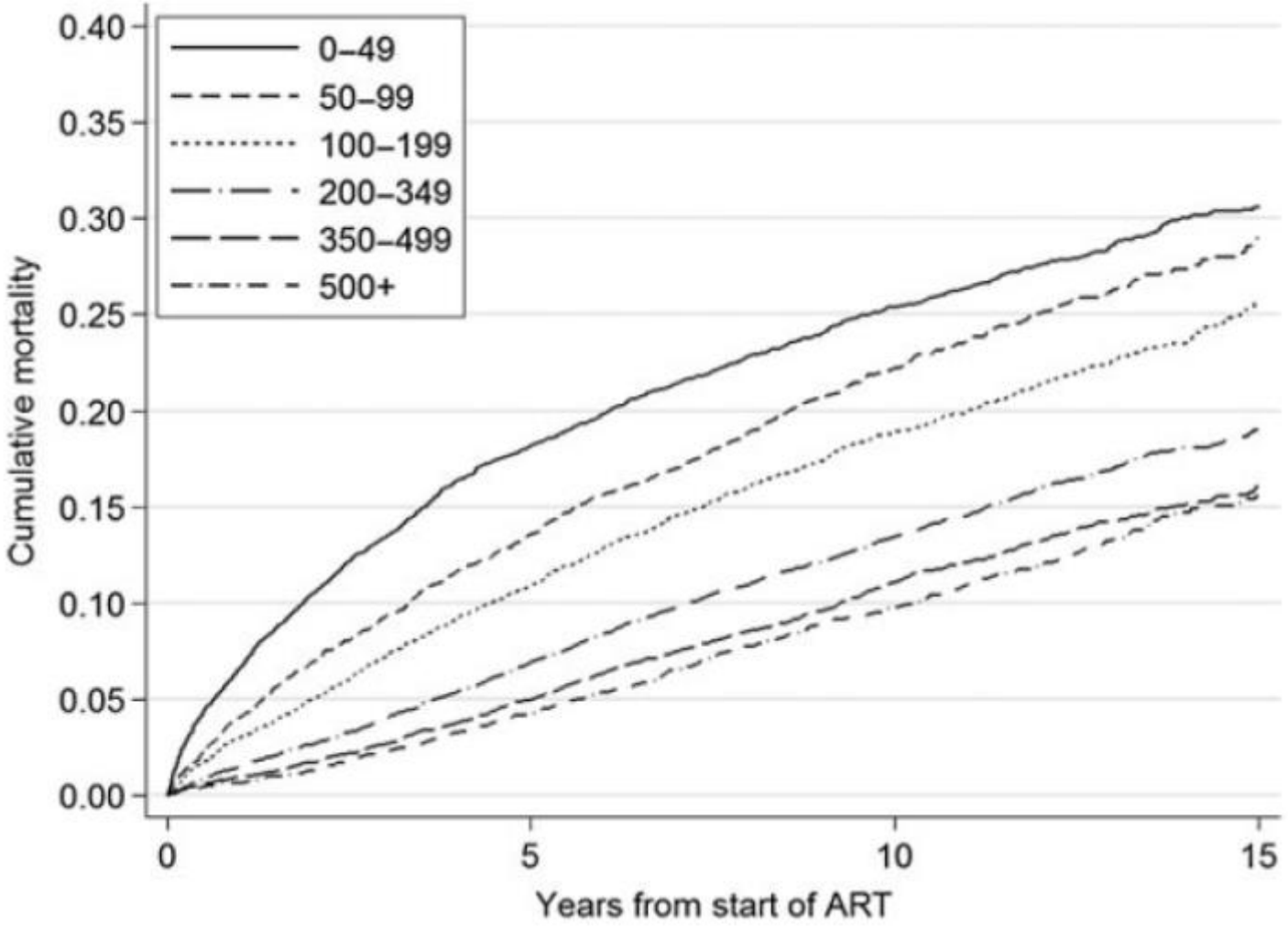

[1]Seropositivity is defined as the percent of positive over the number of tests conducted each year. HIV Counseling and Testing data as of 6/30/2018.

# AIDS Diagnoses by Year of Diagnosis, 2008–2017, Florida

## 10 year % change (2008–2017) = 51% decrease

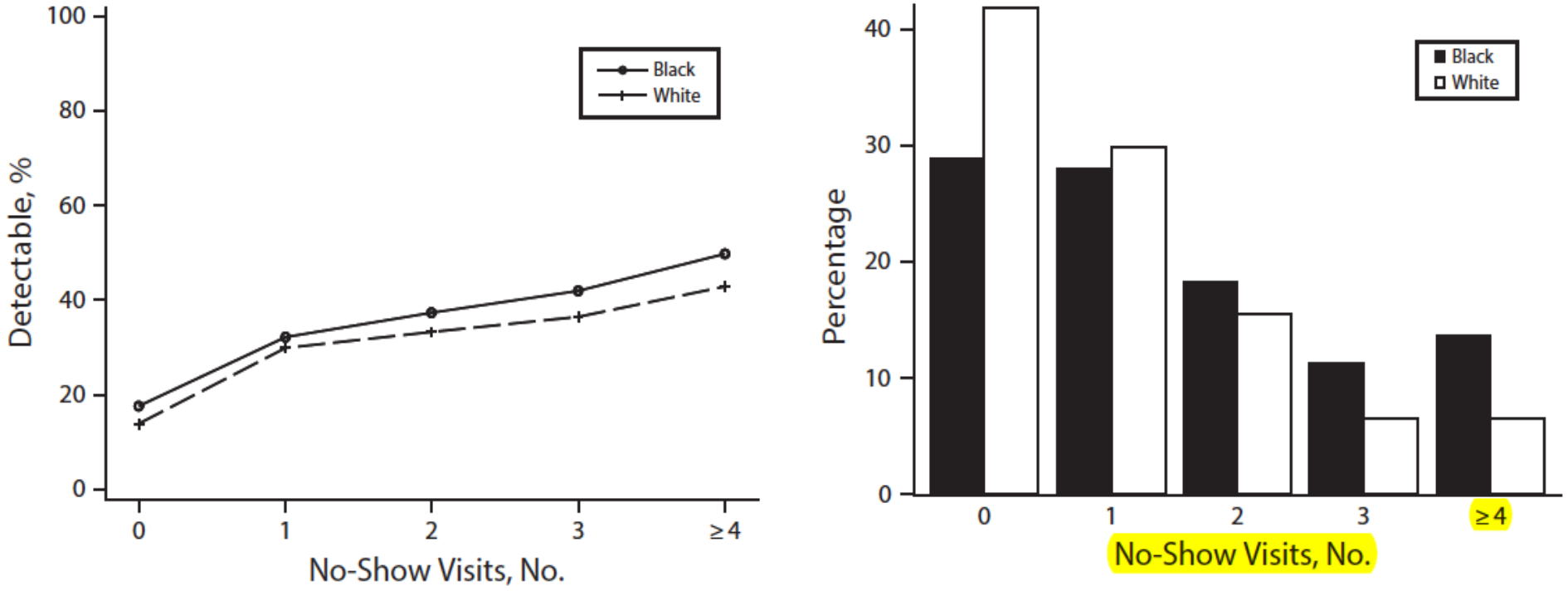


# HOW DOES LATE ENTRY INTO CARE AFFECT OUTCOMES?




May, **Clin Inf Dis,** 2016.

# RACIAL/ETHNIC DISPARITIES DRIVE MISSED CLINIC VISITS AND HIV VIRAL LOAD




*Note*. The metropolitan areas surveyed were in Baltimore, MD; Birmingham, AL; Boston, MA; Brooklyn, NY; Houston, TX; and Miami, FL.

**FIGURE 1—Percentage of (a) virological failure by race stratified by frequency of no-show visits and (b) no-show visits by race: Centers for Disease Control and Prevention and Health Resources and Services Administration Retention in Care preintervention, 6 US metropolitan areas, May 2008 to April 2009.**

Zinski A, **Am J Public Health,** 2015.

# RACIAL/ETHNIC DISPARITIES DRIVE MISSED CLINIC VISITS AND HIV VIRAL LOAD

**TABLE 2—Odds of Virological Failure in Multivariable Analyses for Characteristics With Patient Variables and No-Show Visit Count: Centers for Disease Control and Prevention and Health Resources and Services Administration Retention in Care Preintervention, 6 US Metropolitan Areas, May 2008–April 2009**

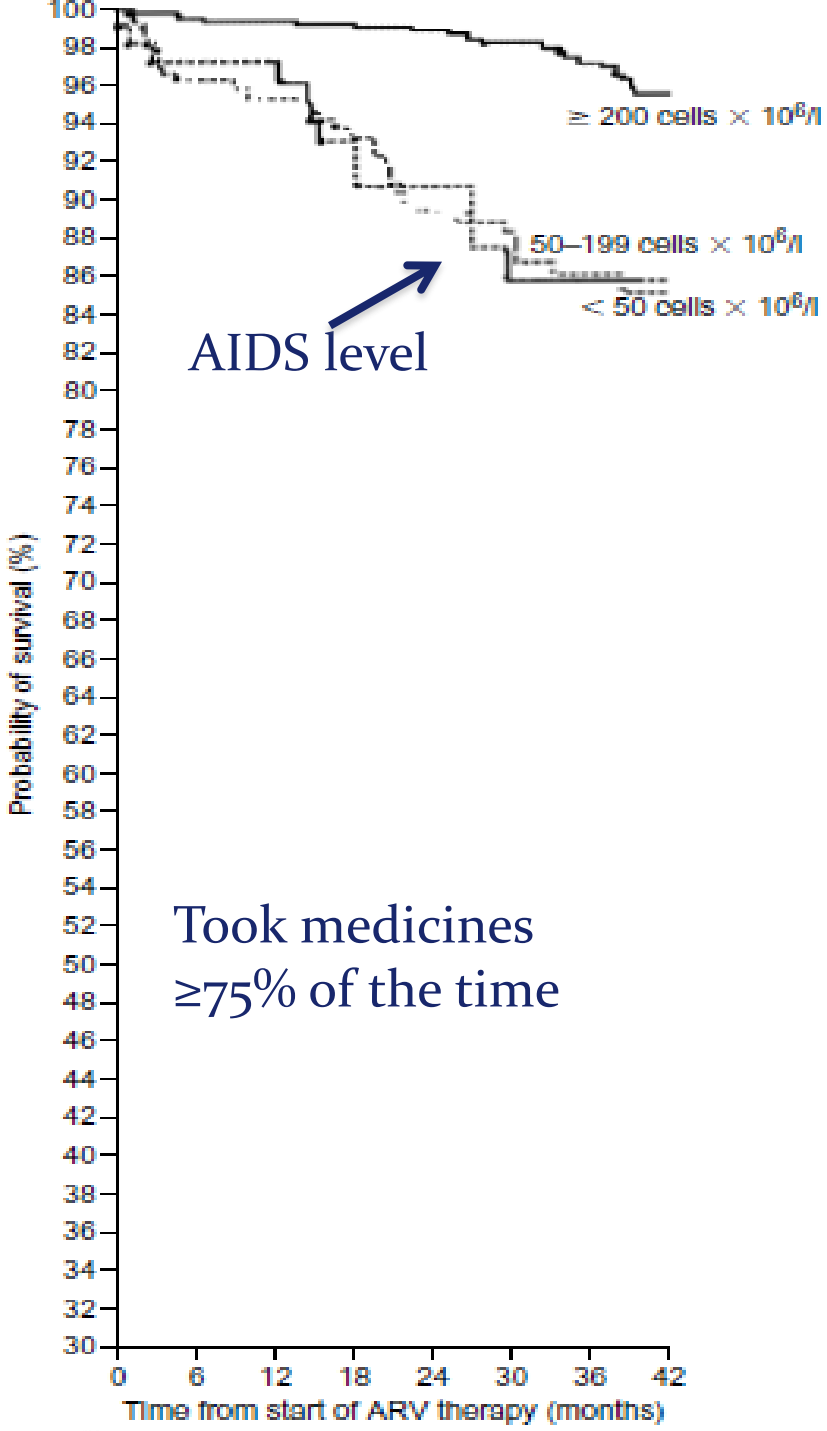
| Characteristic | Odds of VF, Patient Variables Only | | Odds of VF, With No-Show Count | |
|---|---|---|---|---|
| | OR (95% CI) | *P* | OR (95% CI) | *P* |
| Gender: male vs female | 1.05 (0.91, 1.21) | .526 | 1.07 (0.92, 1.23) | .371 |
| Ethnicity: Hispanic vs non-Hispanic | 0.81 (0.67, 0.98) | .03 | 0.79 (0.65, 0.96) | .015 |
| Race | | | | |
| Black vs White | 1.19 (1.01, 1.40) | .039 | 1.11 (0.94, 1.32) | .202 |
| Other vs White | 1.24 (0.89, 1.73) | .198 | 1.20 (0.85, 1.68) | .283 |

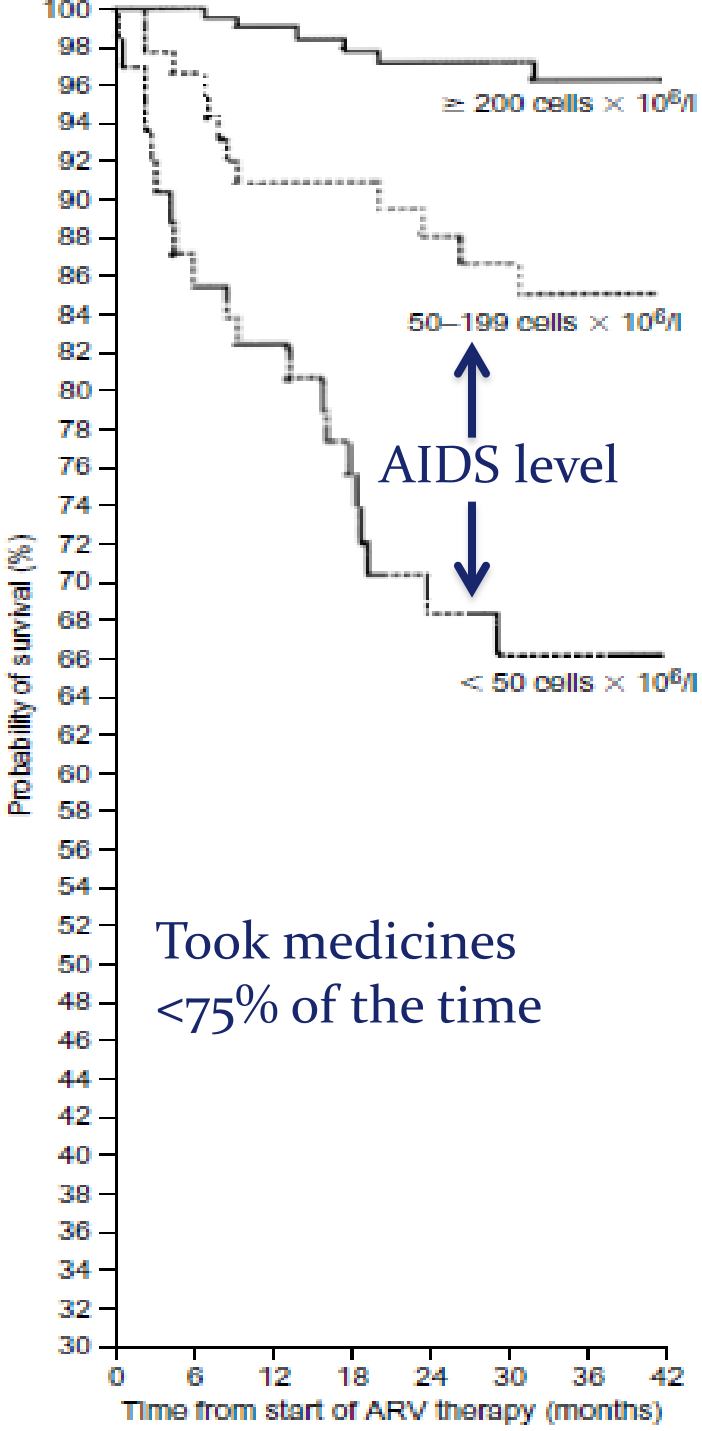
Zinski A, **Am J Public Health**, 2015.

# CARE ENGAGEMENT: DO MISSED VISITS MATTER?

| Variable | Adjusted hazard ratio (95% CI) | *P* |
|---|---|---|
| No. of quarters with visit[a] | | |
| 1 | 1.94 (1.36–2.76) | <.001 |
| 2 | 1.68 (1.24–2.26) | <.001 |
| 3 | 1.41 (1.10–1.82) | <.01 |
| 4 | 1.00 | |
| Baseline $CD4^+$ cell count | | |
| ≤200 × $10^6$ cells/L | 2.35 (1.82–3.05) | <.001 |
| 201–350 × $10^6$ cells/L | 1.36 (0.99–1.87) | .06 |
| >350 × $10^6$ cells/L | 1.00 | |

Giordano T, **Clin Infect Dis**, 2007.




Giordano T, **Clin Infect Dis,** 2007.

# ANTIRETROVIRAL AGENTS

What are the current antiretroviral agents approved for treatment of HIV?

# ANTIRETROVIRAL AGENTS

What are the current antiretroviral agents approved for treatment of HIV?

- There are a lot of them. A lot.

MEMORIAL HEALTHCARE SYSTEM

# POZ™ 2019 HIV DRUG CHART

HEALTH, LIFE & HIV

Antiretroviral (ARV) options abound for both those who are new to HIV treatment and those who are experienced. This quick-reference chart compares medication options, including adult dosing and dietary restrictions.

## Single-Tablet Regimens

### ATRIPLA
**(efavirenz + tenofovir disoproxil fumarate + emtricitabine)**
One tablet once a day. Each tablet contains 600 mg efavirenz + 300 mg tenofovir disoproxil fumarate + 200 mg emtricitabine. Take on an empty stomach. Dose should be taken at bedtime to minimize dizziness, drowsiness and impaired concentration.

### BIKTARVY
**(bictegravir + tenofovir alafenamide + emtricitabine)**
One tablet once a day. Each tablet contains 50 mg bictegravir + 25 mg tenofovir alafenamide + 200 mg emtricitabine. Take with or without food.

### COMPLERA
**(rilpivirine + tenofovir disoproxil fumarate + emtricitabine)**
One tablet once a day. Each tablet contains 25 mg rilpivirine + 300 mg tenofovir disoproxil fumarate + 200 mg emtricitabine. Take with a meal.

### DELSTRIGO
**(doravirine + tenofovir disoproxil fumarate + lamivudine)**
One tablet once a day. Each tablet contains 100 mg doravirine + 300 mg tenofovir disoproxil fumarate + 300 mg lamivudine. Take with or without food.

### DOVATO
**(dolutegravir + lamivudine)**
One tablet once a day. Each tablet contains 50 mg dolutegravir + 300 mg lamivudine. Take with or without food.

### GENVOYA
**(elvitegravir + cobicistat + tenofovir alafenamide + emtricitabine)**
One tablet once a day. Each tablet contains 150 mg elvitegravir + 150 mg cobicistat + 10 mg tenofovir alafenamide + 200 mg emtricitabine. Take with food.

### JULUCA
**(dolutegravir + rilpivirine)**
One tablet once a day. Each tablet contains 50 mg dolutegravir + 25 mg rilpivirine. Take with a meal.

## Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs, or nukes)

### CIMDUO
**(tenofovir disoproxil fumarate + lamivudine)**
One tablet once a day. Each tablet contains 300 mg tenofovir disoproxil fumarate + 300 mg lamivudine. Take with or without food.



### COMBIVIR *
**(zidovudine + lamivudine)**
One tablet twice a day. Each tablet contains 300 mg zidovudine + 150 mg lamivudine. Take with or without food.

### DESCOVY
**(tenofovir alafenamide + emtricitabine)**
One tablet once a day. Each tablet contains 25 mg tenofovir alafenamide + 200 mg emtricitabine. Take with or without food.

### EMTRIVA
**(emtricitabine; FTC)**
One 200 mg capsule once a day. Take with or without food.

### EPIVIR *
**(lamivudine; 3TC)**
One 300 mg tablet once a day, or one 150 mg tablet twice a day. Take with or without food. Also approved for the treatment of hepatitis B virus (HBV) but at a lower dose. People living with both viruses should use the HIV dose.

### EPZICOM *
**(abacavir + lamivudine)**
One tablet once a day. Each tablet contains 600 mg abacavir + 300 mg lamivudine. Take with or without food. Should be used only by individuals who are HLA-B*5701 negative.

### RETROVIR *
**(zidovudine; AZT)**
One 300 mg tablet twice a day. Take with or without food.

### TRIZIVIR *
**(abacavir + zidovudine + lamivudine)**
One tablet twice a day. Each tablet contains 300 mg abacavir + 300 mg zidovudine + 150 mg lamivudine. Take with or without food. Should be used only by individuals who are HLA-B*5701 negative.

## Protease Inhibitors

### APTIVUS
**(tipranavir)**
Two 250 mg capsules plus two 100 mg Norvir tablets twice a day. Aptivus plus Norvir should be taken with food.

### CRIXIVAN
**(indinavir)**
Two 400 mg capsules every eight hours, or two 400 mg capsules with either one or two 100 mg Norvir tablets twice a day. Drink at least 48 ounces of water daily to prevent kidney stones. Without Norvir: Take on an empty stomach (no food two hours before or one hour after dosing) or with a low-fat snack. With Norvir: Take with or without food.

### EVOTAZ
**(atazanavir + cobicistat)**
One tablet once a day. Each tablet contains 300 mg atazanavir + 150 mg cobicistat. Take with food.

### INVIRASE
**(saquinavir)**
Two 500 mg tablets plus one 100 mg Norvir tablet twice a day. Take with food or within two hours after a meal.

### KALETRA
**(lopinavir + ritonavir)**
Two tablets twice a day, or four tablets once a day, depending on HIV drug resistance. Each tablet contains 200 mg lopinavir + 50 mg ritonavir. Take with or without food.

### LEXIVA
**(fosamprenavir)**
Two 700 mg tablets twice a day, or two 700 mg tablets plus one or two Norvir tablets once a day, or one 700 mg tablet plus one Norvir tablet twice a day (recommended for individuals who have used other PIs in the past). Take with or without food.

### PREZCOBIX
**(darunavir + cobicistat)**
One tablet once a day. Each tablet contains 800 mg darunavir + 150 mg cobicistat. Take with food.

## Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs, or non-nukes)



### EDURANT
**(rilpivirine)**
One 25 mg tablet once a day. Take with food.

### INTELENCE
**(etravirine)**
One 200 mg tablet twice a day. Take with food.

### PIFELTRO
**(doravirine)**
One 100 mg tablet once a day. Take with or without food.

### RESCRIPTOR†
**(delavirdine)**
Two 200 mg tablets three times a day, or four 100 mg tablets three times a day. Take with or without food. Discontinued by manufacturer; phaseout to be completed by 2020.

### SUSTIVA *
**(efavirenz)**
One 600 mg tablet once a day, or three 200 mg capsules once a day. Take on an empty stomach or with a low-fat snack. Dose should be taken at bedtime to minimize dizziness, drowsiness and impaired concentration.

### VIRAMUNE *
**(nevirapine)**
One 200 mg Viramune immediate release (IR) tablet once a day for the first 14 days, then one 400 mg Viramune extended release (XR) tablet once a day. Take with or without food.

## Entry Inhibitors

### FUZEON
**(enfuvirtide)**
One 90 mg (1 ml solution) subcutaneous injection twice a day. Take with or without food. Fuzeon comes as a white powder that must be mixed with sterile water in a vial each day.

## Single-Tablet Regimens

### ODEFSEY
**(rilpivirine + tenofovir alafenamide + emtricitabine)**
One tablet once a day. Each tablet contains 25 mg rilpivirine + 25 mg tenofovir alafenamide + 200 mg emtricitabine. Take with a meal.

### STRIBILD
**(elvitegravir + cobicistat + tenofovir disoproxil fumarate + emtricitabine)**
One tablet once a day. Each tablet contains 150 mg elvitegravir + 150 mg cobicistat + 300 mg tenofovir disoproxil fumarate + 200 mg emtricitabine. Take with food.

### SYMFI AND SYMFI LO
**(efavirenz + tenofovir disoproxil fumarate + lamivudine)**
One tablet of either Symfi or Symfi Lo (above) once a day. Each tablet of Symfi contains 600 mg efavirenz + 300 mg tenofovir disoproxil fumarate + 300 mg lamivudine. Each tablet of Symfi Lo contains 400 mg efavirenz + 300 mg tenofovir disoproxil fumarate + 300 mg lamivudine. Take on an empty stomach. Dose should be taken at bedtime to minimize dizziness, drowsiness and impaired concentration.

### SYMTUZA
**(darunavir + cobicistat + tenofovir alafenamide + emtricitabine)**
One tablet once a day. Each tablet contains 800 mg darunavir + 150 mg cobicistat + 10 mg tenofovir alafenamide + 200 mg emtricitabine. Take with food.

### TRIUMEQ
**(dolutegravir + abacavir + lamivudine)**
One tablet once a day. Each tablet contains 50 mg dolutegravir + 600 mg abacavir + 300 mg lamivudine. Take with or without food. Should be used only by individuals who are HLA-B*5701 negative.

## Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTIs, or nukes)

### TRUVADA
**(tenofovir disoproxil fumarate + emtricitabine)**
One tablet once a day. Each tablet contains 300 mg tenofovir disoproxil fumarate + 200 mg emtricitabine. Take with or without food.

### VIDEX EC * †
**(didanosine, ddI)**
One 400 mg capsule once a day. (One 250 mg capsule once a day for those weighing less than 133 lbs.) Take on an empty stomach (two hours after or one hour before a meal). Brand-name product discontinued; phaseout to be completed by 2020.

### VIREAD *
**(tenofovir disoproxil fumarate)**
One 300 mg tablet once a day. Take with or without food.

### ZERIT * †
**(stavudine; d4T)**
One 40 mg capsule twice a day. (One 30 mg capsule twice a day for those weighing less than 133 lbs.) Take with or without food. Brand-name product discontinued; phaseout to be completed by 2020.

### ZIAGEN *
**(abacavir)**
One 300 mg tablet twice a day, or two 300 mg tablets once a day. Take with or without food. Should be used only by individuals who are HLA-B*5701 negative.

## Protease Inhibitors

### PREZISTA
**(darunavir)**
One 800 mg tablet (or two 400 mg tablets) plus one 100 mg Norvir tablet, or one 150 mg Tybost tablet once a day, or one 600 mg tablet plus one 100 mg Norvir tablet twice a day, depending on drug resistance. Take with food.



### REYATAZ *
**(atazanavir)**
Two 200 mg capsules once a day, or one 300 mg capsule plus one 100 mg Norvir tablet, or one 150 mg Tybost tablet once a day. Take with food.



### VIRACEPT
**(nelfinavir)**
Two 625 mg tablets twice a day, or five 250 mg tablets twice a day, or three 250 mg tablets three times a day. Take with food.

## PK Boosters



### NORVIR *
**(ritonavir)**
Six 100 mg tablets twice a day. The full dose of Norvir is rarely used. It is most often used at lower doses to boost the levels of other ARVs in the blood. Take with food.



### TYBOST
**(cobicistat)**
One 150 mg tablet once a day in combination with ARVs that require boosting. Used only to boost other drugs. Take with food.

## Entry Inhibitors



### SELZENTRY
**(maraviroc)**
One 150 mg, 300 mg or 600 mg tablet twice a day, depending on other meds used. Take with or without food.



### TROGARZO
**(ibalizumab)**
Administered intravenously as a single loading (or initial) dose of 2,000 mg followed by a maintenance dose of 800 mg every two weeks.

## Integrase Inhibitors

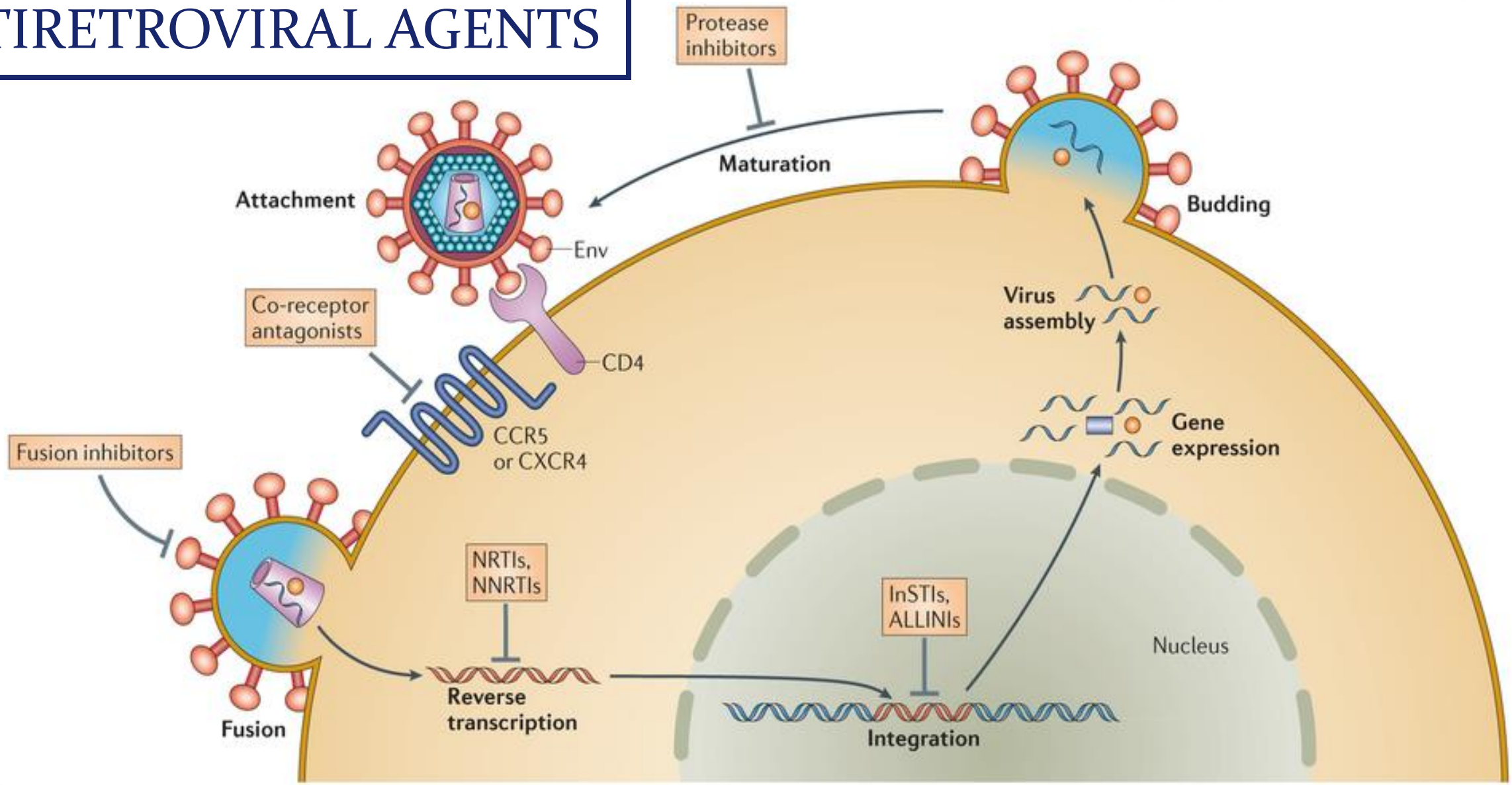


### ISENTRESS
**(raltegravir)**
Two 600 mg Isentress HD tablets (above) once a day for those who are treatment naive or whose virus has been suppressed on an initial regimen. One 400 mg Isentress tablet twice daily for people with HIV treatment experience. Take with or without food.



### TIVICAY
**(dolutegravir)**
One 50 mg tablet once a day for those first starting ARV therapy or for those who have not used an integrase inhibitor in the past. One 50 mg tablet twice a day for treatment-experienced individuals who have HIV that is resistant to other integrase inhibitors and when taken with certain ARVs. Take with or without food.

# ANTIRETROVIRAL AGENTS




Nature Reviews | Microbiology

# ANTIRETROVIRAL AGENTS

- Antiretroviral Therapy (ART) AKA "*cART*" AKA "*HAART*"
  - Backbone = 2 Nucleoside Reverse Transcriptase Inhibitors (NRTI)

+

  - Anchor = 1 of the options below

# ANTIRETROVIRAL AGENTS

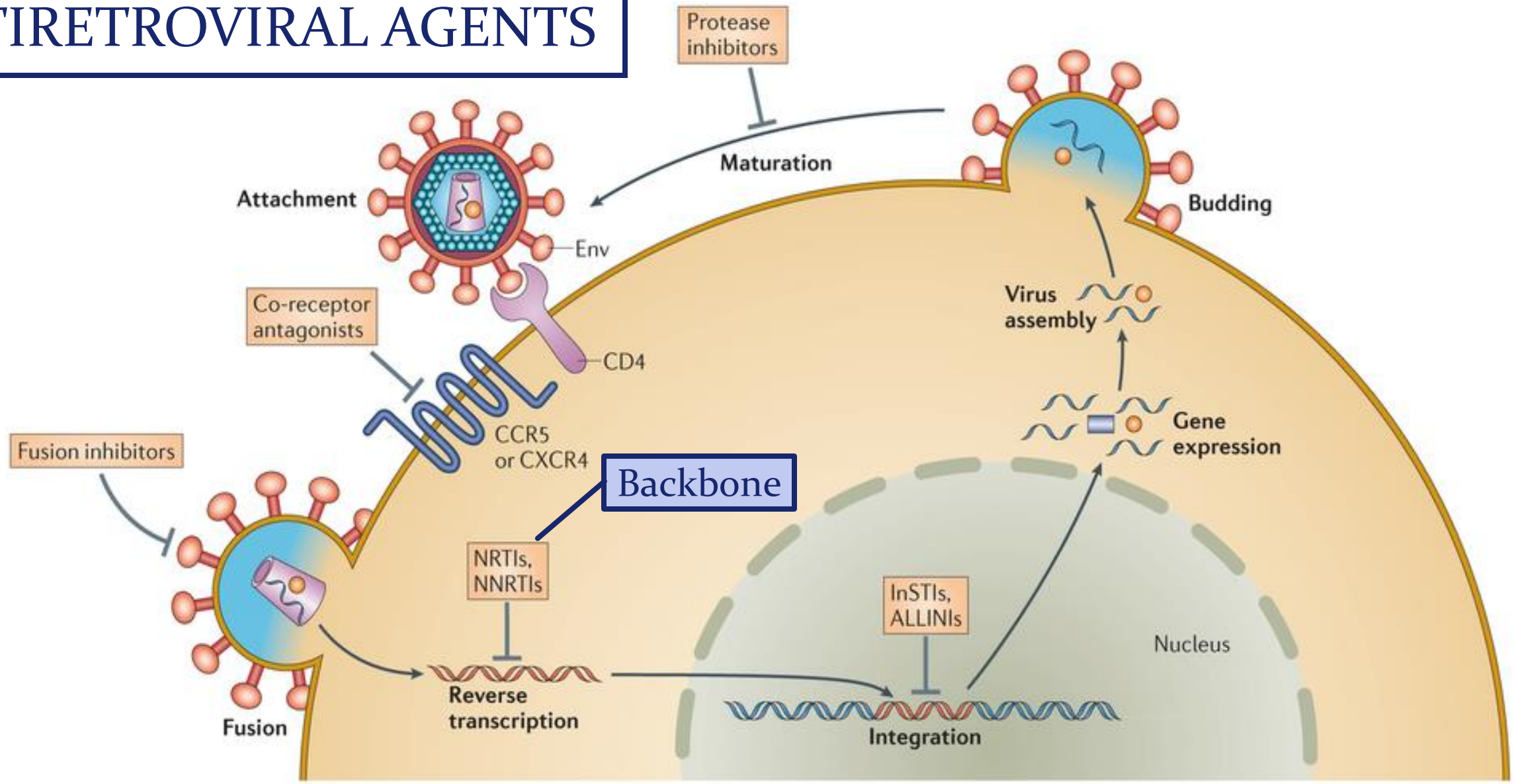
- Antiretroviral Therapy (ART) AKA *(cART) (HAART)*
  - Backbone = 2 Nucleoside Reverse Transcriptase Inhibitors (NRTI)

| | |
|---|---|
| Recommended | ABC, FTC, 3TC, TAF, TDF |
| Salvage | ddI, d4T, ZDV |

+

  - Anchor = 1 of the options below

# ANTIRETROVIRAL AGENTS



# ANTIRETROVIRAL AGENTS

- Antiretroviral Therapy (ART) AKA *(cART) (HAART)*
  - Backbone = 2 Nucleoside Reverse Transcriptase Inhibitors (NRTI)

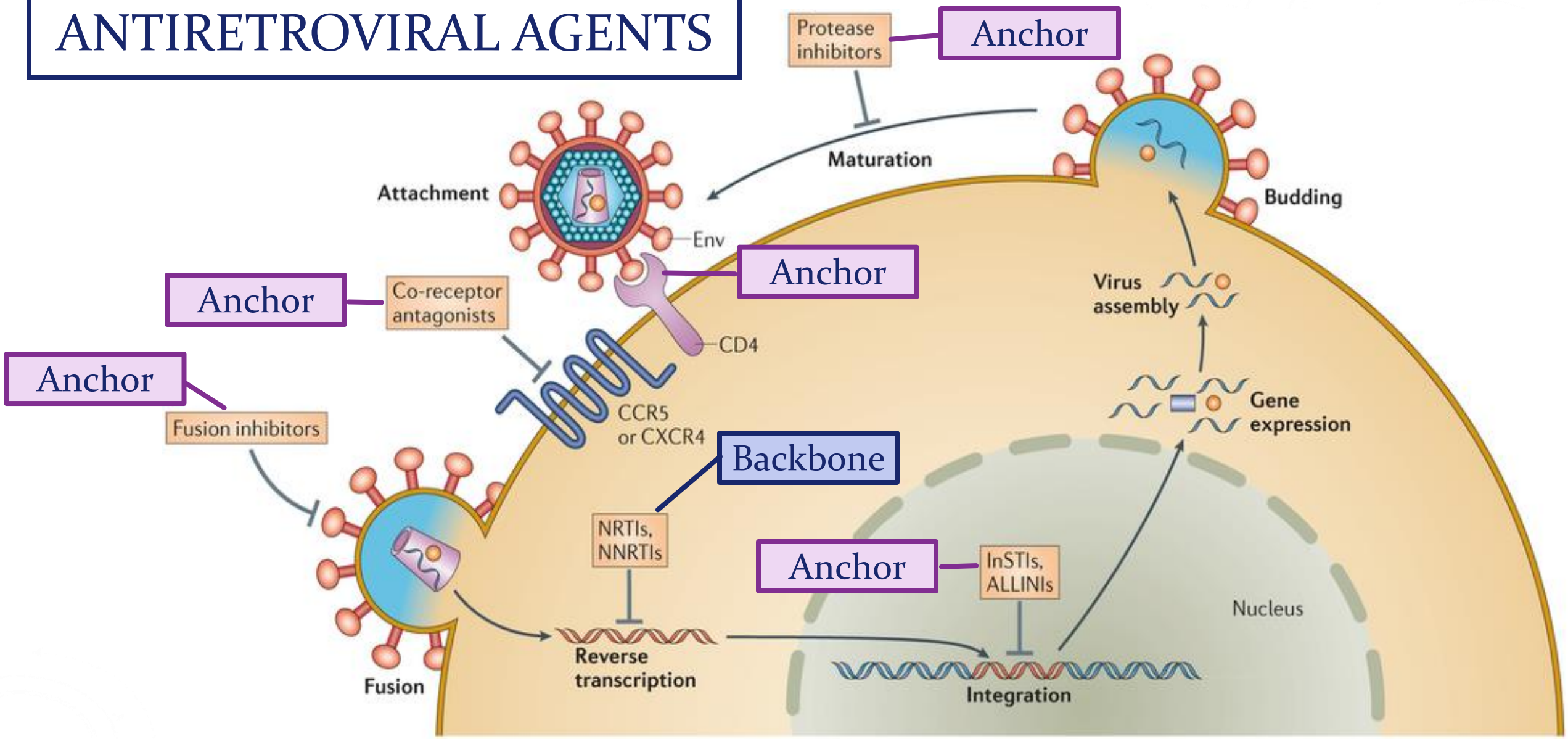
| | |
|---|---|
| Recommended | ABC, FTC, 3TC, TAF, TDF |
| Salvage | ddI, d4T, ZDV |

+

  - Anchor = 1 of the options below

| | |
|---|---|
| InSTI | DTG, EVG, RAL |
| NNRTI | DLV, DOR, EFV, ETR, NVP, RPV |
| PI | ATV, DRV, FPV, IDV, LPV, NFV, TPV, SQV |
| Entry/Fusion Inh | ENF, IBA, MVC |

# ANTIRETROVIRAL AGENTS




Nature Reviews | Microbiology

# ANTIRETROVIRAL AGENTS
# DHHS RECOMMENDATIONS

First line recommended agents for treatment naïve individuals:

- TAF/FTC/BIC (*Biktarvy*)
- ABC/3TC/DTG (*Triumeq*)
- TDF/FTC or TAF/FTC (*Truvada* or *Descovy*) + DTG (Dolutegravir)
- TDF/FTC or TAF/FTC (*Truvada* or *Descovy*) + RAL (Raltegravir)

DHHS, Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV, 2019.

# ANTIRETROVIRAL AGENTS
# DHHS RECOMMENDATIONS

Shift away from agents using Cobicistat (booster):

- TDF/FTC/EVG/c (*Stribild*) and TAF/FTC/EVG/c (*Genvoya*) are **no** longer 1st line agents for naïve individuals.
  - Cobicistat (c) causes more Cytochrome 3A4 associated drug interactions.
  - Elvitegravir (EVG) has a lower barrier to resistance than Dolutegravir (DTG) and Bictegravir (BIC).

DHHS, Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV, 2019.

# ANTIRETROVIRAL AGENTS
# DHHS RECOMMENDATIONS

Recommended options when Tenofovir or Abacavir cannot be used

-and-

HIV RNA Qnt<100,000 copies/mL and $CD_4$ cell count is >200/$mm^3$:

- DTG (Dolutegravir) + 3TC (Lamivudine)
- DRV/r (boosted Darunavir) + RAL (Raltegravir)
- DRV/r (boosted Darunavir) + 3TC (Lamivudine)

DHHS, Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV, 2019.

# ANTIRETROVIRAL AGENTS
# DHHS RECOMMENDATIONS

Recommended options when Tenofovir or Abacavir cannot be used

-and-

HIV RNA Qnt<100,000 copies/mL and $CD_4$ cell count is >200/$mm^3$:

- DTG (Dolutegravir) + 3TC (Lamivudine)
- DRV/r (boosted Darunavir) + RAL (Raltegravir)
- DRV/r (boosted Darunavir) + 3TC (Lamivudine)

  - DTG + 3TC is <u>noninferior</u> to TDF/FTC + DTG
    - Virological failure
    - Development of resistance

DHHS, Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV, 2019.

# OLD CONCEPT RENEWED
# DUAL THERAPY

DHHS Guideline 2 Drug Options

- Dolutegravir (INSTI)
  +
  Rilpivirine (NNRTI)

- Boosted Protease Inhibitor (PI)
  +
  Lamivudine or Emtricitabine (NRTI)
  - ATV/r + 3TC or FTC
  - DRV/r + 3TC or FTC
  - LPV/r + 3TC or FTC

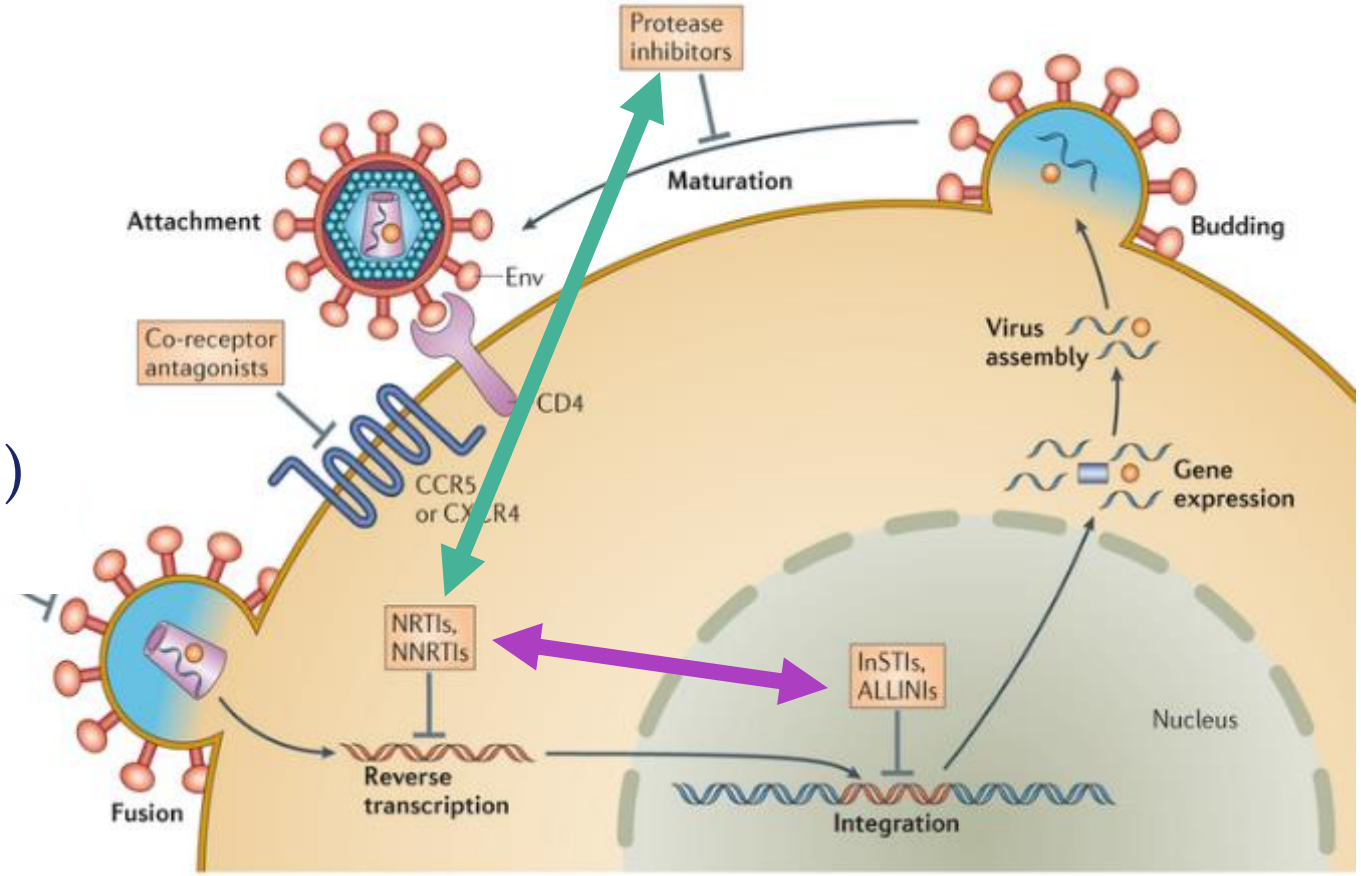
DHHS, Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV, 2019.

# OLD CONCEPT RENEWED
# DUAL THERAPY

DHHS Guideline 2 Drug Options

- Dolutegravir (INSTI)
  +
  Rilpivirine (NNRTI)

- Boosted Protease Inhibitor (PI)
  +
  Lamivudine or Emtricitabine (NRTI)
  - ATV/r + 3TC or FTC
  - DRV/r + 3TC or FTC
  - LPV/r + 3TC or FTC

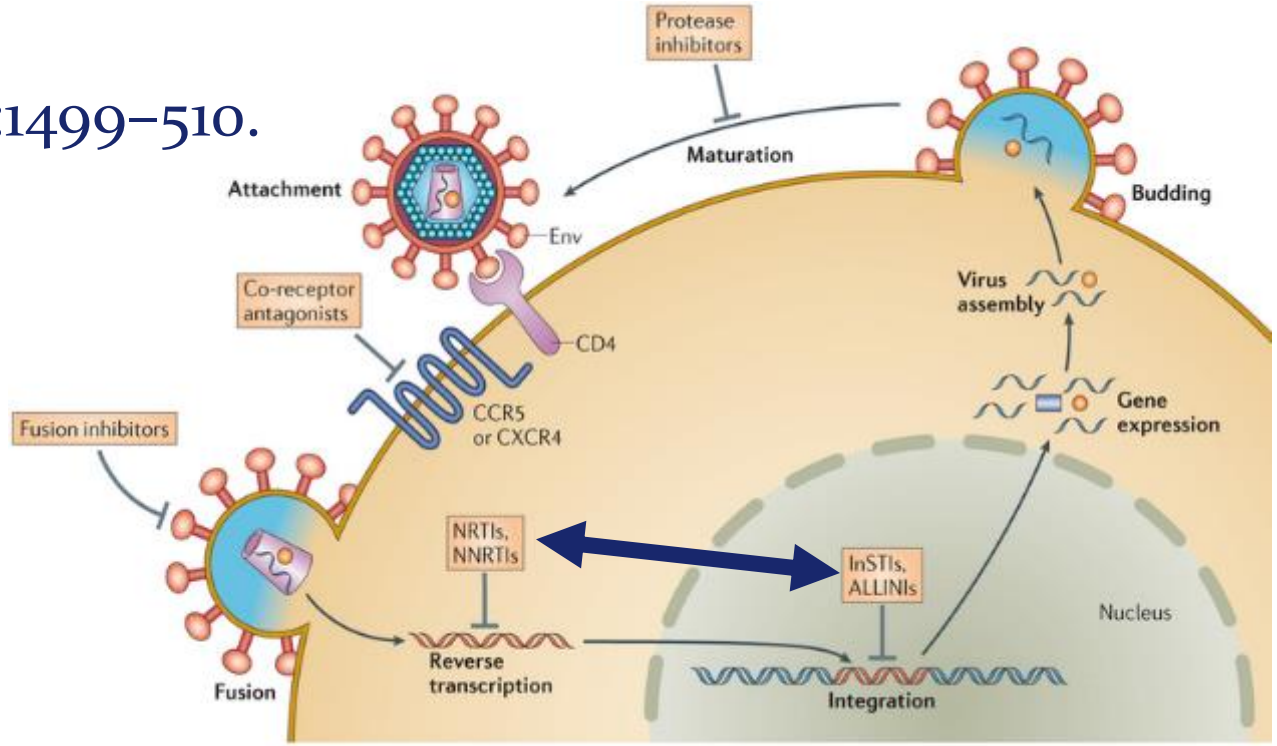



DHHS, Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV, 2019.

# OLD CONCEPT RENEWED
# DUAL THERAPY - CARBOTEGRAVIR

"Long-acting intramuscular Carbotegravir and Rilpivirine in adults with HIV-1 infection (LATTE-2): 96-week results of a randomized, open-label, phase 2b, non-inferiority trial"

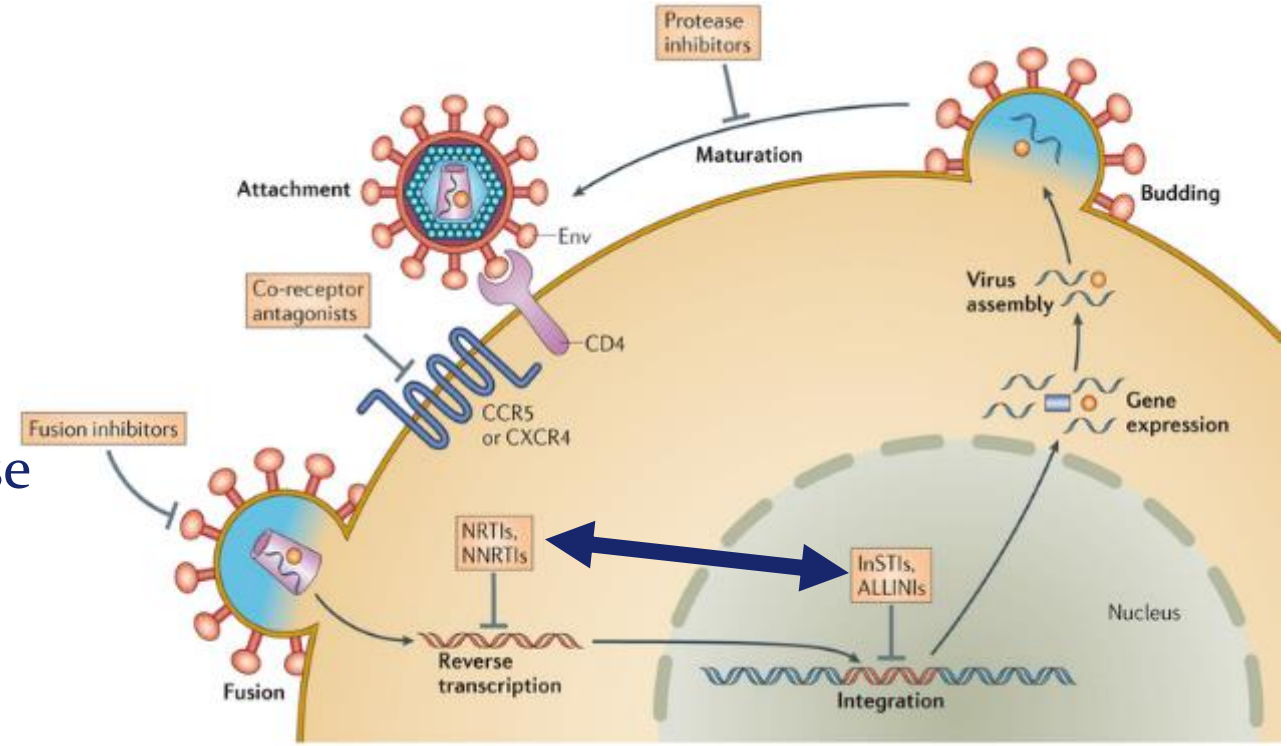
Margolis DA, et al. *Lancet*. 2017;390:1499–510.



# OLD CONCEPT RENEWED
# DUAL THERAPY - CARBOTEGRAVIR

"LATTE-2: 96-week results, phase-2b non-inferiority trial"
Margolis DA, et al. *Lancet*. 2017;390:1499–510.

- Carbotegravir
  - Integrase Strand Inhibitor (InSTI).
  - Analogue of Dolutegravir.
  - QMonth IM long-acting nanosuspension.
- Rilpivirine
  - Non-Nucleoside Reverse Transcriptase Inhibtor (NNRTI)



# OLD CONCEPT RENEWED
# DUAL THERAPY - CARBOTEGRAVIR

"LATTE-2: 96-week results, phase-2b non-inferiority trial"
Margolis DA, et al. *Lancet*. 2017;390:1499–510.

| 96 Week Data | Carbotegravir IM + Rilpivirine IM Q4Weeks (n=115) | Carbotegravir IM + Rilpivirine IM Q8Weeks (n=115) | Carbotegravir PO + Abacavir/Lamivudine PO QDaily (n=56) |
|---|---|---|---|
| Virological Response (VL<50) | 87% | 94% | 84% |
| Virological Non-Response | 0 | 4% | 2% |

# OLD CONCEPT RENEWED
# DUAL THERAPY - CARBOTEGRAVIR

"LATTE-2: 96-week results, phase-2b non-inferiority trial"
Margolis DA, et al. *Lancet*. 2017;390:1499–510.

| 96 Week Data | Carbotegravir IM + Rilpivirine IM Q4Weeks (n=115) | Carbotegravir IM + Rilpivirine IM Q8Weeks (n=115) | Carbotegravir PO + Abacavir/Lamivudine PO QDaily (n=56) |
|---|---|---|---|
| Virological Response (VL<50) | 87% | 94% | 84% |
| Virological Non-Response | 0 | 4% | 2% |

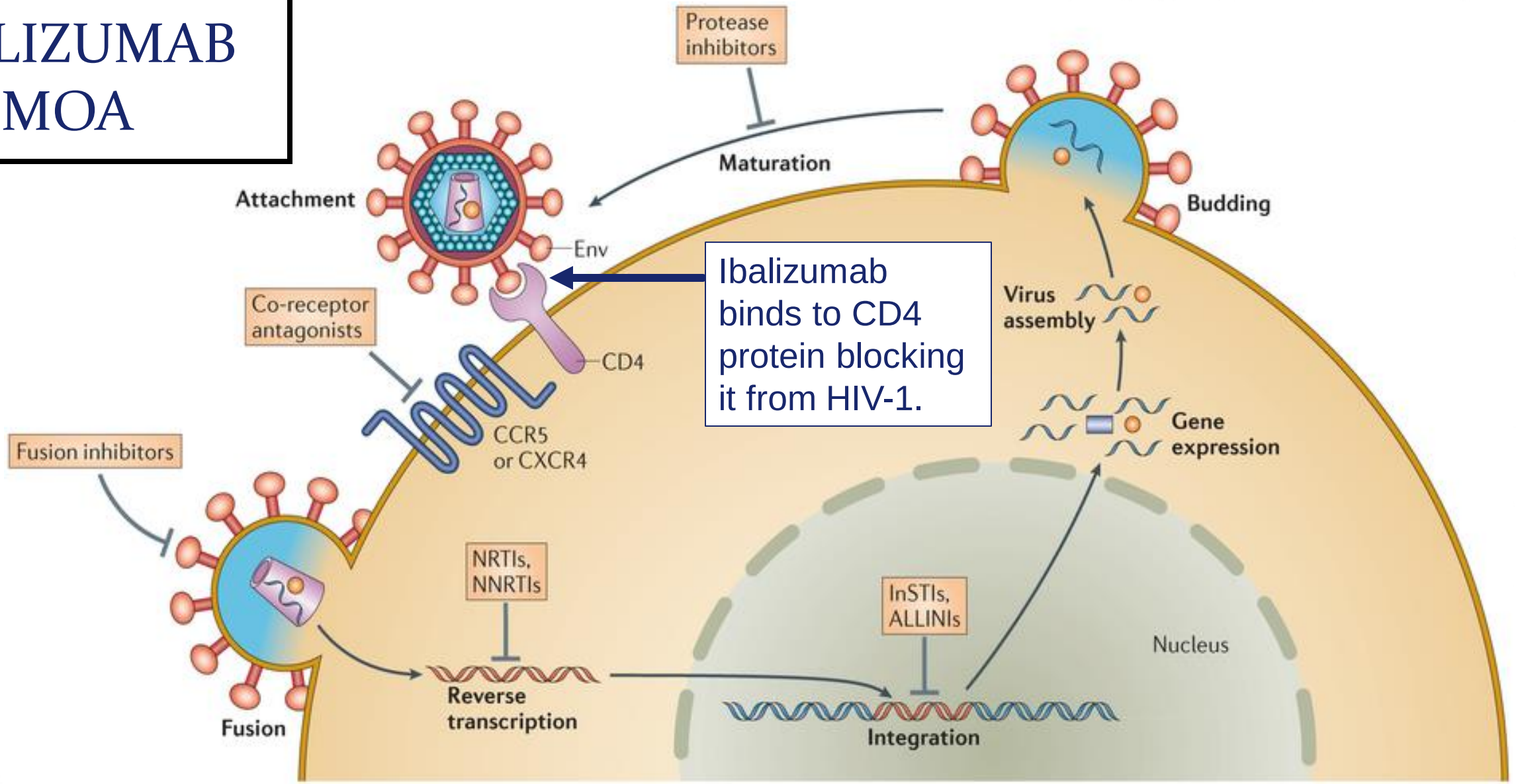
- ATLAS-2M: Phase 3 study pending.

# NOVEL TREATMENT
# IBALIZUMAB

"Phase 3 Study of Ibalizumab for Multidrug Resitant HIV-1"
Emu B, et al. *N Engl J Med*. 2018;379:645-654.

- Ibalizumab
  - Humanized IgG4 monoclonal antibody. (1st agent of its class)
  - Blocks the entry of HIV-1 by noncompetitive binding to CD4 surface protein on lymphocytes.
  - "Trogarzo" Q2 week IV infusions.
  - Indications: Multi-drug class resistant HIV-1 failing their current regimen.

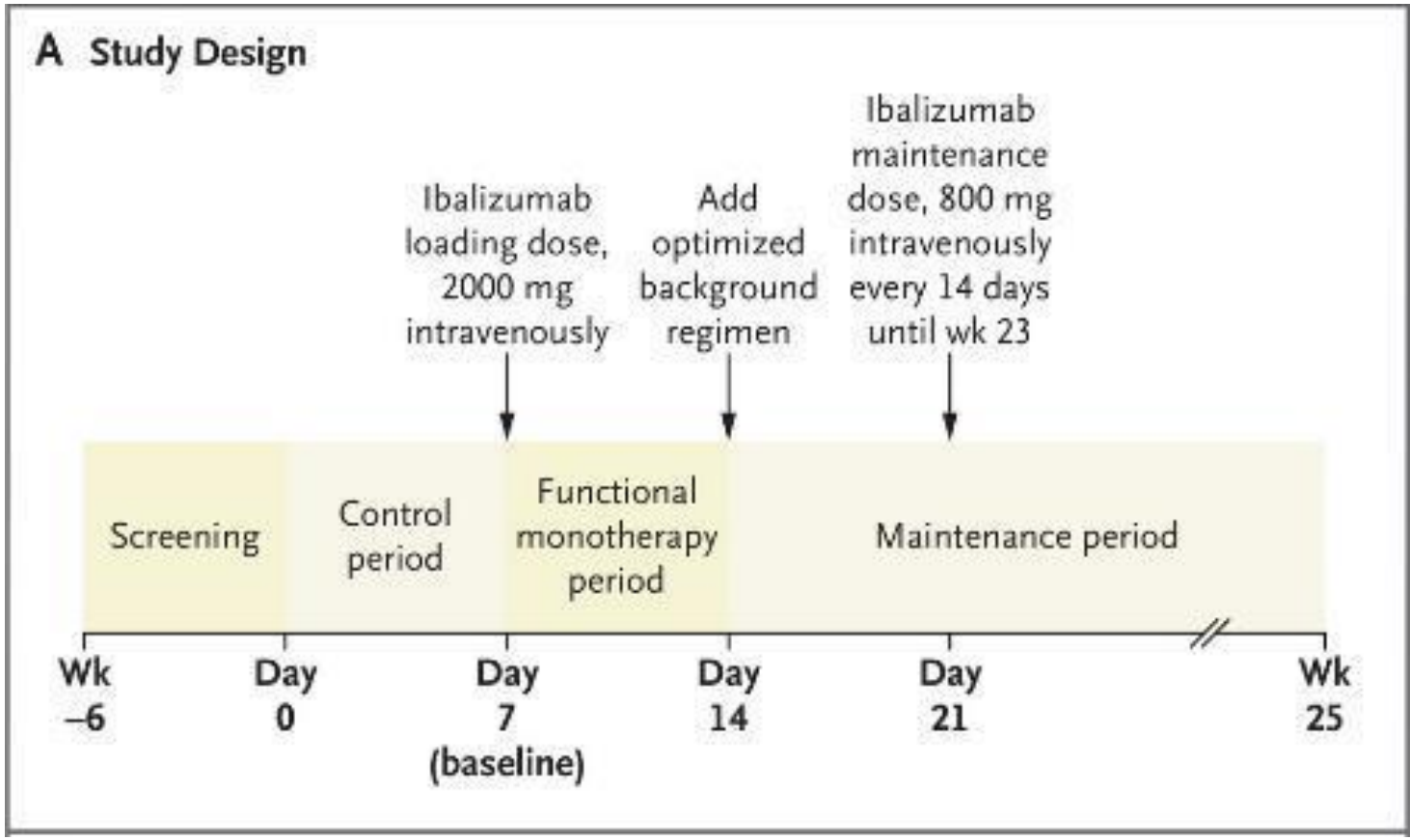
# IBALIZUMAB MOA



# NOVEL TREATMENT
# IBALIZUMAB

Emu B, et al. *N Engl J Med*. 2018;379:645-654.

- Open label, phase 3 study.
- Single-group (n=40)
- Adults with multidrug-resistant HIV-1 and multi-regimen failure.
  - Intervention: Ibalizumab monotherapy, then combined therapy.
  - Primary endpoint: Percentage of patients who decrease viral load by ≥ 0.5 $\log_{10}$



# NOVEL TREATMENT
# IBALIZUMAB

Emu B, et al. N Engl J Med. 2018;379:645-654.

**Table 2. Virologic Response before and after Loading Dose of Ibalizumab and at 25 Weeks in the 40 Study Patients.***

| Response | Before and after Loading Dose | | | Week 25 |
|---|---|---|---|---|
| | Control Period | Functional Monotherapy Period | P Value | |
| Decrease in viral load of ≥0.5 $\log_{10}$ copies/ml — no. (%) | 1 (3)† | 33 (83) | <0.001 | 25 (63) |
| Decrease in viral load of ≥1.0 $\log_{10}$ copies/ml — no. (%) | 0 | 24 (60) | NA | 22 (55) |
| Mean change in viral load from baseline — $\log_{10}$ copies/ml | 0.0±0.2 | −1.1±0.6 | <0.001 | −1.6±1.5 |

# NOVEL TREATMENT
# CRISPR-EDITED STEM CELLS

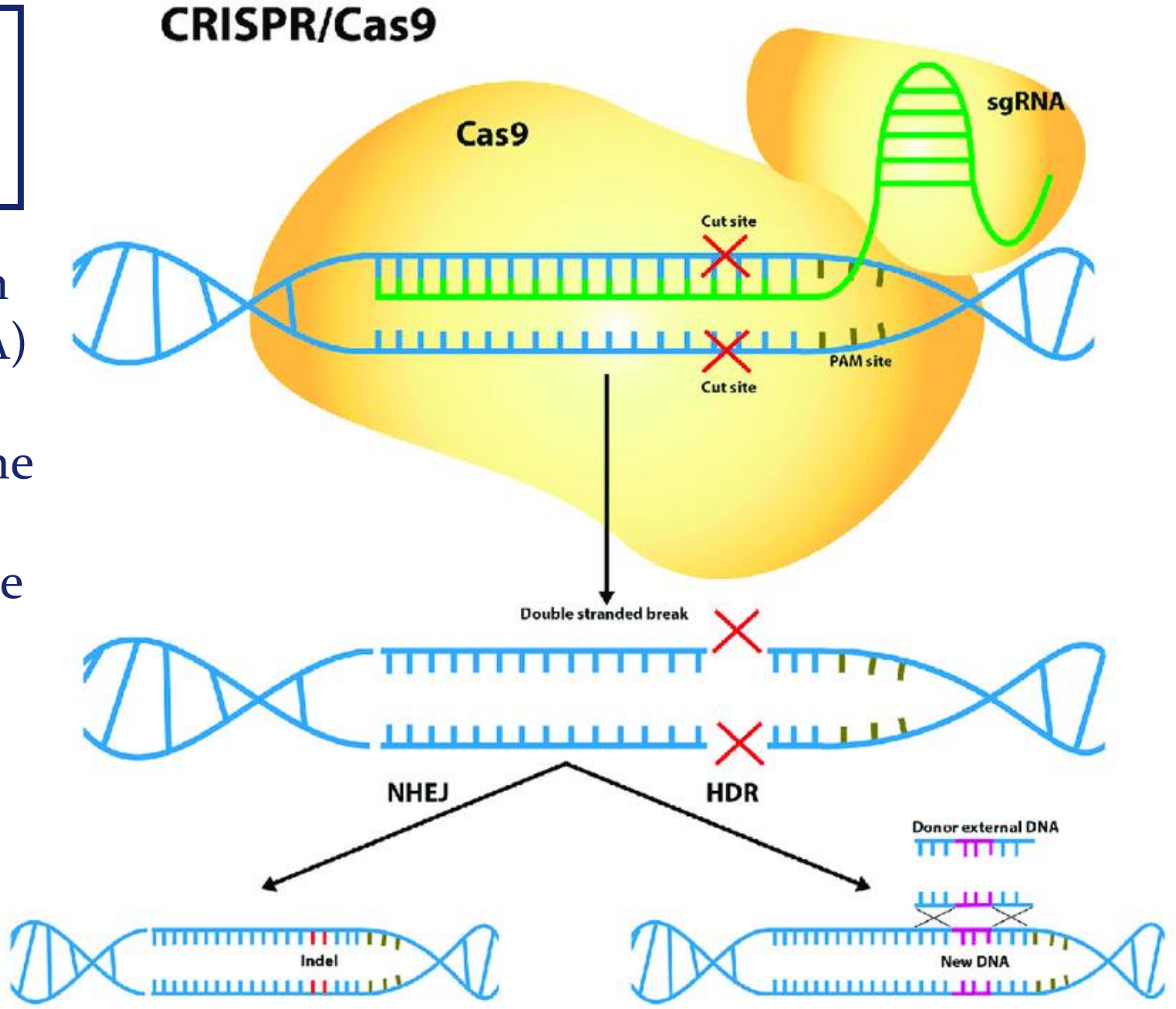
"CRISPR-Edited Stem Cells in a Patient with HIV and Acute Lymphocytic Leukemia"

Xu L, et al. *N Engl J Med*. 2019;381:1240-1247.

- "CRISPR" Gene Editing
  - **C**lustered **R**egularly **I**nterspaced **S**hort **P**alindromic **R**epeats
    - OK, is that supposed to mean something to me?
  - Create artificially disrupted CCR5 Hematopietic Stem Cells.
- CCR5
  - One of two cell membrane coreceptors necessary for HIV entry into lymphocytes.
  - People without normal CCR5 are resistant to CCR5 "tropic" HIV strains.

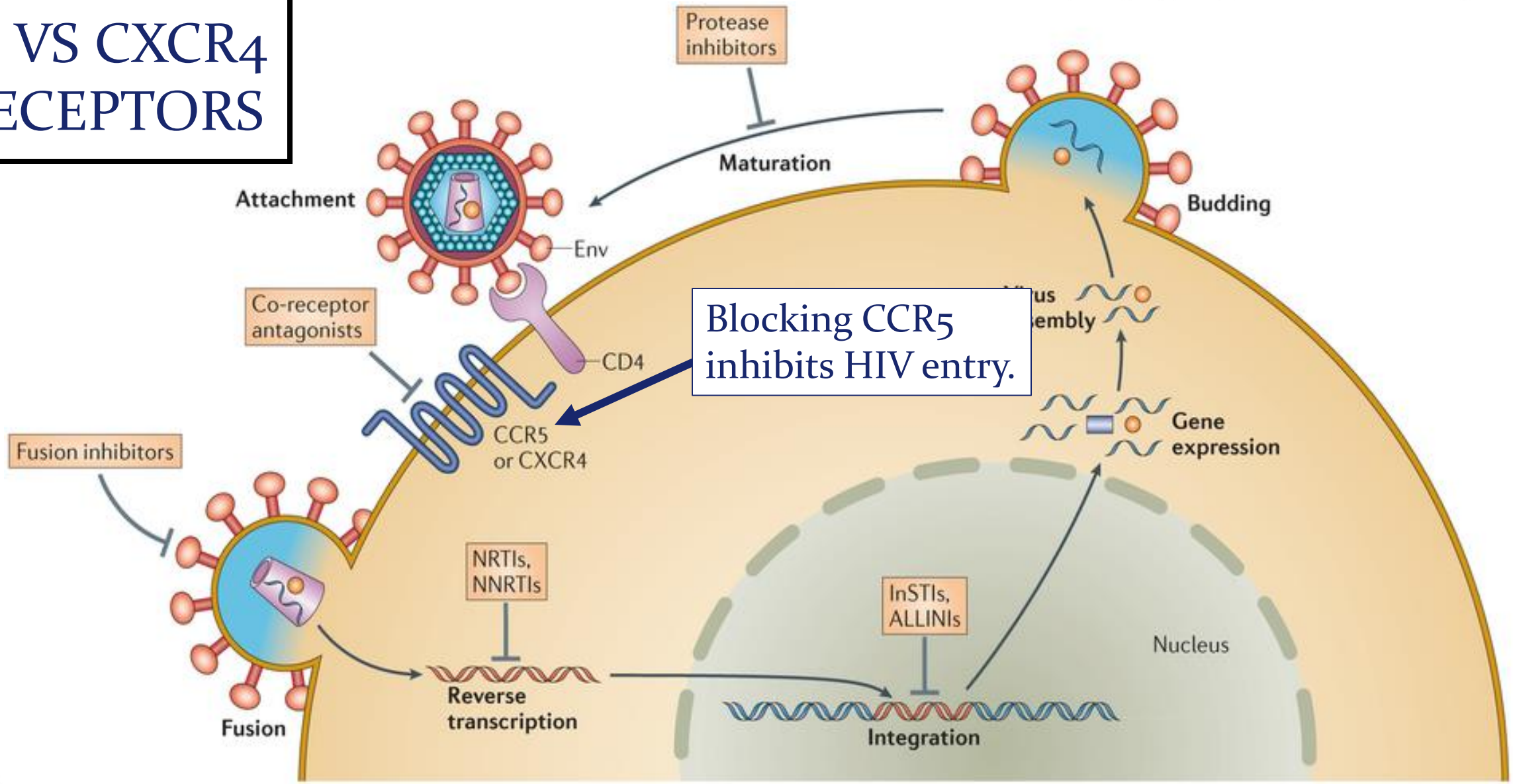
# CRISPR-CAS9

- Cas9 nuclease complexed with a synthetic guide RNA (sgRNA) cuts the cell's genome at a desired location targeted by the PAM.
- This allows existing genes to be removed and/or new ones added.

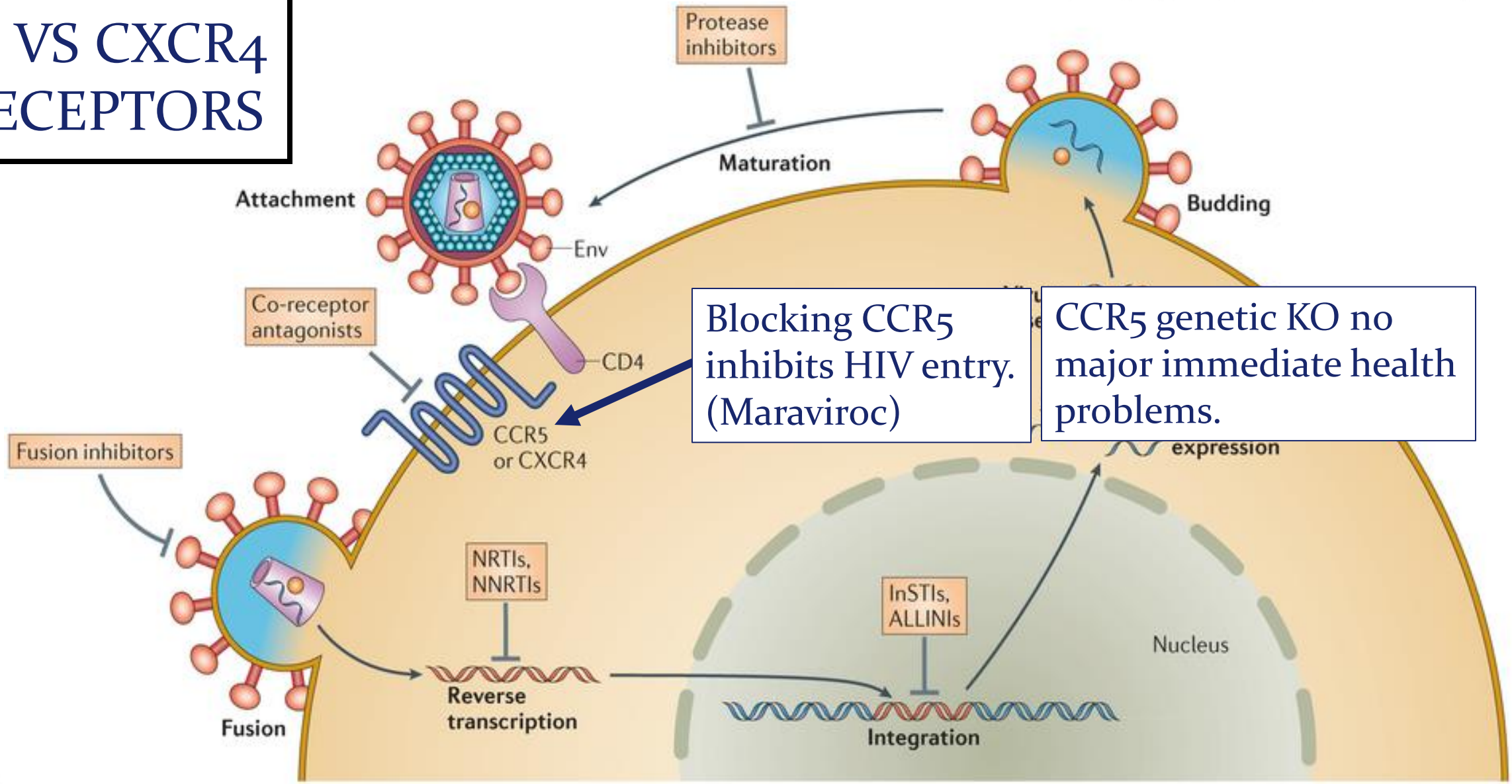



Cribbs A, et al. *Yale J Biol Med*. 2017;90:625-34.

# CCR5 VS CXCR4 CORECEPTORS



# CCR5 VS CXCR4 CORECEPTORS

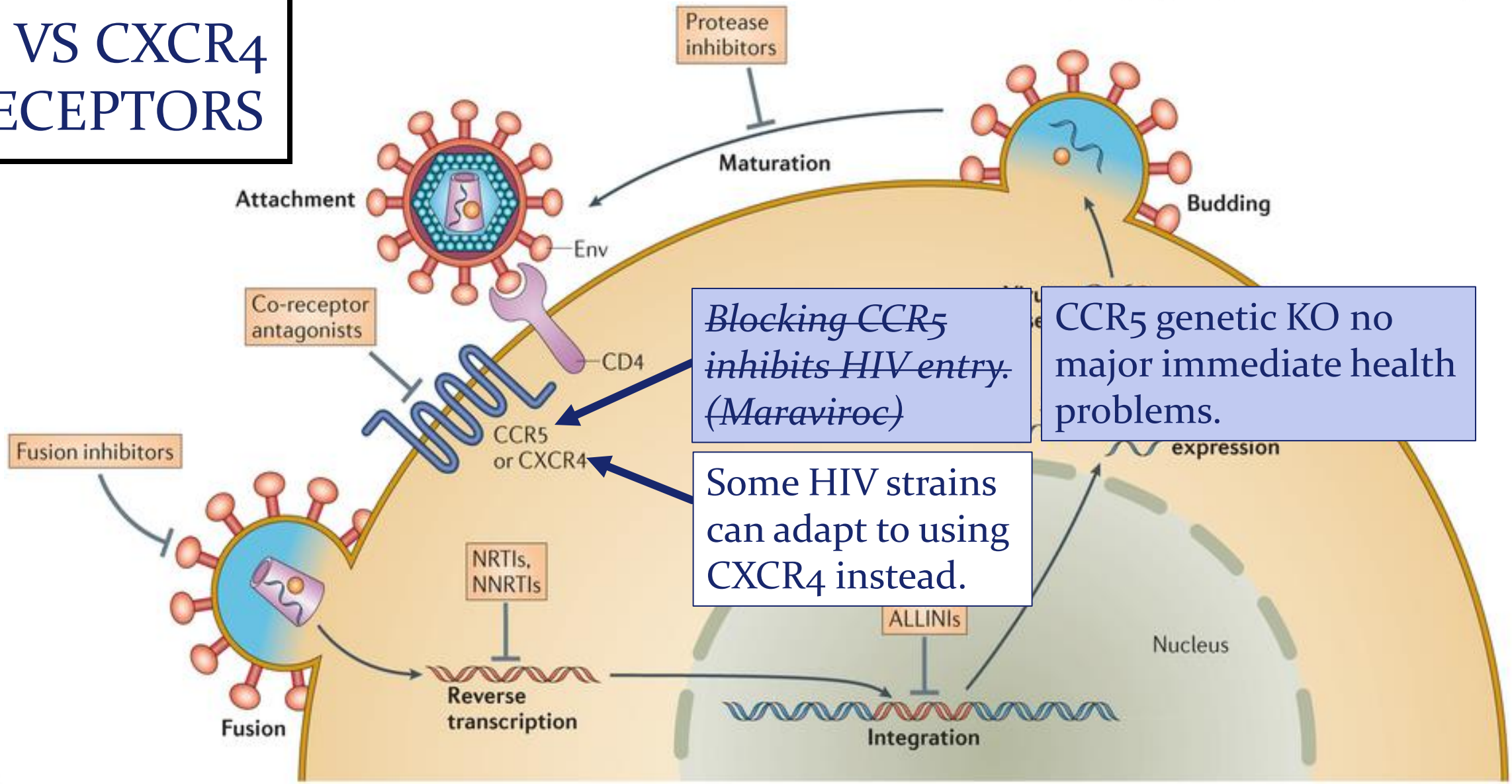



Blocking CCR5 inhibits HIV entry. (Maraviroc)

CCR5 genetic KO no major immediate health problems.

Nature Reviews | Microbiology

# CCR5 VS CXCR4 CORECEPTORS



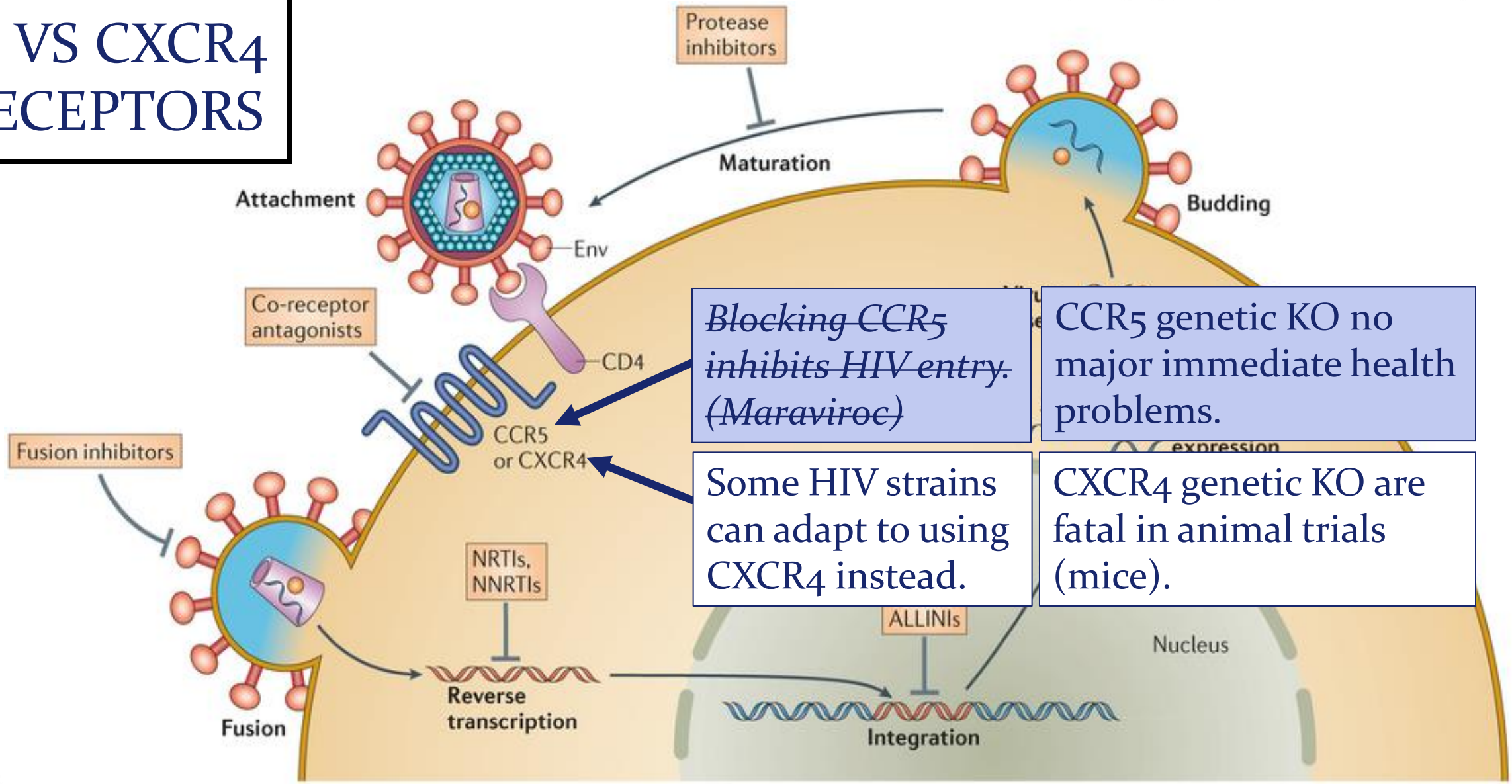

~~*Blocking CCR5 inhibits HIV entry. (Maraviroc)*~~

CCR5 genetic KO no major immediate health problems.

Some HIV strains can adapt to using CXCR4 instead.

Nature Reviews | Microbiology

# CCR5 VS CXCR4 CORECEPTORS




~~*Blocking CCR5 inhibits HIV entry. (Maraviroc)*~~

CCR5 genetic KO no major immediate health problems.

Some HIV strains can adapt to using CXCR4 instead.

CXCR4 genetic KO are fatal in animal trials (mice).

Nature Reviews | Microbiology

# NOVEL TREATMENT
# CRISPR-EDITED STEM CELLS

"CRISPR-Edited Stem Cells in pt w/ HIV and ALL"
Xu L, et al. *N Engl J Med*. 2019;381:1240-1247.

- TR Brown, "The Berlin Patient", was given HSCT from a matched donor with natural CCR5 deletion and remains undetectable from his pre-transplant HIV infection despite being off of ART.
  - Only approximately 1% of humans naturally have CCR5 deletion.

# NOVEL TREATMENT
# CRISPR-EDITED STEM CELLS

"CRISPR-Edited Stem Cells in pt w/ HIV and ALL"
Xu L, et al. *N Engl J Med*. 2019;381:1240-1247.

- TR Brown, "The Berlin Patient", was given HSCT from a matched donor with natural CCR5 deletion and remains undetectable from his pre-transplant HIV infection despite being off of ART.
  - Only approximately 1% of humans naturally have CCR5 deletion.
- CRISPR-Cas9 edited CCR5 deletion was performed on mice models of HIV showing some response.
  - Has not been done in humans yet.

# NOVEL TREATMENT
# CRISPR-EDITED STEM CELLS

"CRISPR-Edited Stem Cells in pt w/ HIV and ALL"
Xu L, et al. *N Engl J Med*. 2019;381:1240-1247.

- 27y gentleman living w/ HIV/AIDS and Acute Lymphoblastic Anemia
  - CD4=528, VL=UD
  - ART=TDF, 3TC, LPV/r
  - CCR5 tropic

  - Receives chemotherapy and HSCT w/ edited CCR5 cells.
  - Stays on antiretroviral therapy the entire time.

# NOVEL TREATMENT
# CRISPR-EDITED STEM CELLS

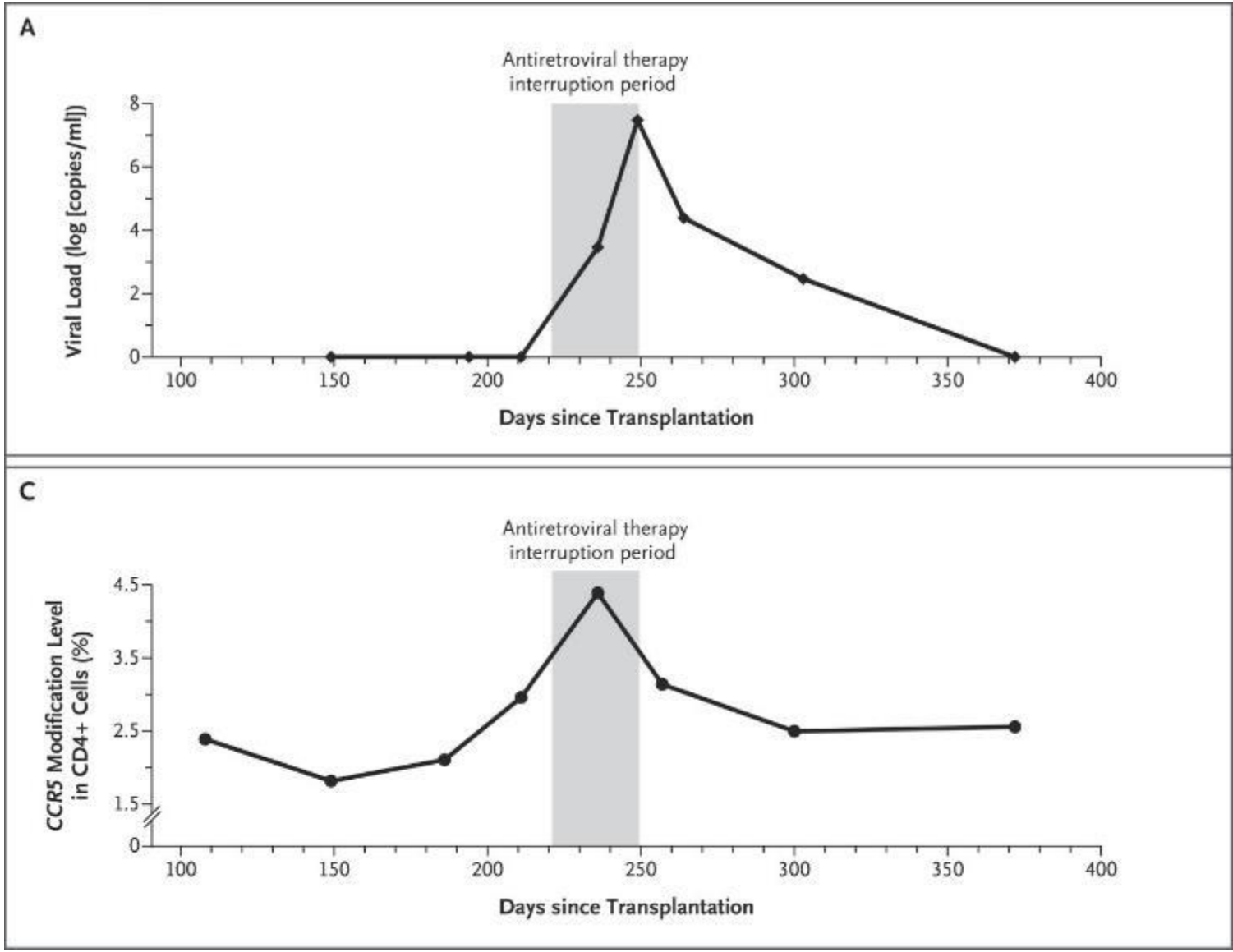
"CRISPR-Edited Stem Cells in pt w/ HIV and ALL"
Xu L, et al. *N Engl J Med*. 2019;381:1240-1247.

- Receives 6 cycles of standard chemotherapy achieving remission.
- Receives HSCT (mix of CRISPR CCR5 edited CD34 and wt CD34 donor cells).
  - CD4=201, VL=UD at time of transplant
  - Myeloablative conditioning (Cyclophosphamide, total body XRT)
  - GVHD prophylaxis (Cyclosporine, MTX, Basiliximab, MMF)
- Antiretroviral medications are held on Day + 220 to Day +250.

# CRISPR-EDITED STEM CELLS

Xu L, et al. *N Engl J Med*. 2019.

- Full donor chimerism occurs on Day +28.
  - In bone marrow, CCR5 ablation ranged 5.20% to 8.28%.
  - In CD4 lymphocytes, CCR5 peaked at 4.39%.




Xu L, N Engl J Med 2019

# UNDETECTABLE=UNTRANSMITTABLE
# U=U

- Started with the HIV treatment as prevention movement.
- To date, longitudinal studies demonstrate no effective risk of sexual transmission from an undetectable person living with HIV.
  - HPTN 052 Clinical Trial
  - PARTNER Study
  - PARTNER 2 Study
  - Opposites Attract Study

Xu L, N Engl J Med 2019

# UNDETECTABLE=UNTRANSMITTABLE
# U=U

- Started with the HIV treatment as prevention movement.
- To date, longitudinal studies demonstrate no effective risk of sexual transmission from an undetectable person living with HIV.
  - HPTN 052 Clinical Trial (2005-2015)
    - 1763 serodiscordant partners,
    - No phylogenetically linked HIV transmissions occurred in HIV suppressed individuals.
  - PARTNER 1 Study
  - PARTNER 2 Study
  - Opposites Attract Study

Cohen MS, New Engl J Med, 2016.

# UNDETECTABLE=UNTRANSMITTABLE
# U=U

- Started with the HIV treatment as prevention movement.
- To date, longitudinal studies demonstrate no effective risk of sexual transmission from an undetectable person living with HIV.
  - HPTN 052 Clinical Trial
  - PARTNER 1 Study (2010-2017)
    - 782 gay and heterosexual serodiscordant couples
    - HIV+=UD. HIV-=PrEP+/-.
    - No phylogenetically linked HIV transmission occurred.
  - PARTNER 2 Study (2010-2017)
  - Opposites Attract Study

Rodger AJ, *Lancet,* 2019.

# UNDETECTABLE=UNTRANSMITTABLE
# U=U

- Started with the HIV treatment as prevention movement.
- To date, longitudinal studies demonstrate no effective risk of sexual transmission from an undetectable person living with HIV.
  - HPTN 052 Clinical Trial
  - PARTNER 1 Study
  - PARTNER 2 Study (2010-2017)
    - 972 gay serodiscordant couples.
    - HIV+=UD. HIV-=PrEP+/-.
    - No phylogenetically linked HIV transmission occurred.
  - Opposites Attract Study

Rodger AJ, *Lancet,* 2019.

# UNDETECTABLE=UNTRANSMITTABLE
# U=U

- Started with the HIV treatment as prevention movement.
- To date, longitudinal studies demonstrate no effective risk of sexual transmission from an undetectable person living with HIV.
  - HPTN 052 Clinical Trial
  - PARTNER 1 Study
  - PARTNER 2 Study
  - Opposites Attract Study (2012-2016)
    - 972 gay serodiscordant couples.
    - HIV+=UD. HIV-=Many were on PrEP.
    - No phylogenetically linked HIV transmission occurred.

Bavington BR, *Lancet,* 2018.

# SUMMARY

- The incidence of HIV/AIDS is decreasing, but the population of HIV-1 infected people continues to grow.
- Racial/ethnic minorities over-represent the HIV infected population and remain at risk for health care disparities.
- Late entry into care and poor adherence to care is strongly associated with increased mortality.
- Dual antiretroviral regimens are safe in specific populations w/ HIV RNA Qnt<100,000 c/mL.
- Ibaluzimab is a monoclonal antibody novel class entry inhibitor approved for treatment experienced patients with multiple class resistance.
- CRISPR-Cas9 gene editing may be a promising avenue for an HIV “cure”.
- Multiple longitudinal studies support UD=UT.

# REFERENCES


- Bavington BR, et al. Viral suppression and HIV transmission in serodiscordant male couples: an international, prospective, observational, cohort study. *Lancet HIV*. 2018;5(8):PE438-E447.
- Center for Disease Control and Prevention. HIV Statistics Center. Available at https://www.cdc.gov/hiv/statistics/overview/index.html. Accessed 2019/10/11.
- Cohen MS, et al. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. *N Engl J Med*. 2016; 375:830-839.
- Emu B, et al. Phase 3 Study of Ibalizumab for Multidrug-Resistant HIV-1. **N Engl J Med.** 2018;379:645-54.
- Florida Department of Health: Division of Disease Control and Health Protection, Bureau of Communicable Diseases, HIV/AIDS Section. Slide Set: State of the HIV Epidemic in Florida, 2017. Available at http://www.floridahealth.gov/diseases-and-conditions/aids/surveillance/epi-slide-sets.html. Accessed 11/10/2019.
- Giordano TP, et al. Retention in Care: A Challenge to Survival with HIV Infection. *Clin Infect Dis*. 2007; 44:1493–9.
- May MT, et al. Mortality According to CD4 Count at Start of Combination Antiretroviral Therapy Among HIV-infected Patients Followed for up to 15 Years After Start of Treatment: Collaborative Cohort Study. *Clin Infect Dis*. 2016. DOI: 10.1093/cid/ciw183. Advanced Access online: Accessed 18 May 2016.
- Margolis DA, et al. Long-acting intramuscular cabotegravir and rilpivirine in adults with HIV-1 infection (LATTE-2): 96-week results of a randomised, open-label, phase 2b, non-inferiority trial. *Lancet*. 2017;390: 1499–510.
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Accessed 11/10/2019.

# REFERENCES


- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Accessed 2019/10/11.
- Rodger AJ, et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. *Lancet*. 2019;393: 2428–38.
- Xu L, et al. CRISPR-Edited Stem Cells in a Patient with HIV and Acute Lymphocytic Leukemia. *N Engl J Med*. 2019;381:1240-1247.
- Zinski A, et al. The Contribution of Missed Clinic Visits to Disparities in HIV Viral Load Outcomes. *Am J Public Health*. 2015;105:2068–2075.