

INTRODUCTION TO

HIV & **AIDS**

Helena Kwawa, MD, MPH
Director, HIV Clinical Services
Philadelphia Department of Public Health

CE Objectives

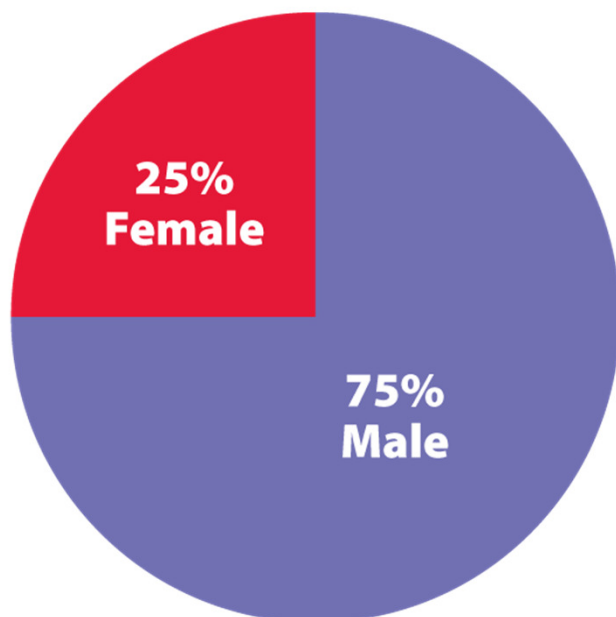
- Review epidemiology
- Discuss transmission
 - Course of HIV infection
- Review HIV life cycle and treatment options
- Highlight recent developments
 - Treatment guidelines
 - Treatment trends
 - HIV prevention



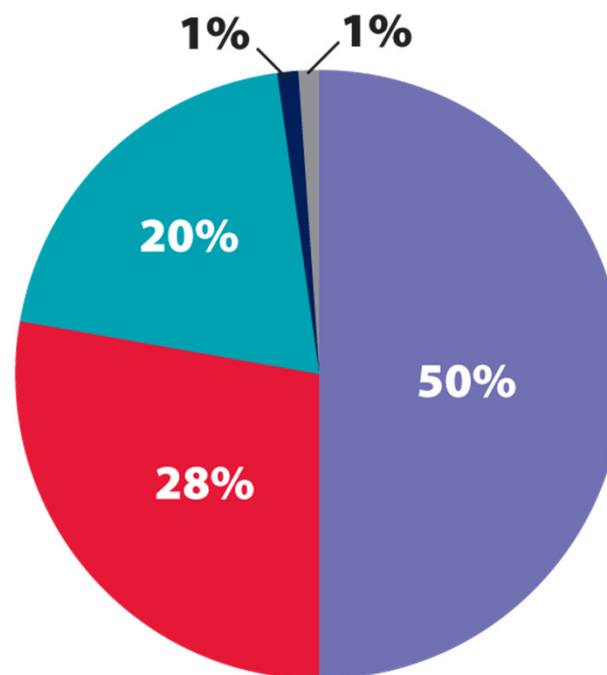
**Epidemiology in the US:
New Infections**

New HIV Diagnoses in the US by Gender and Race/Ethnicity, 2010*

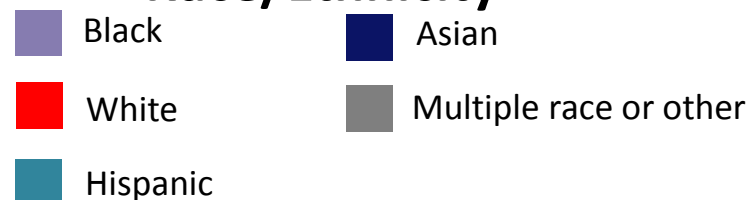
In 2010, there were an estimated 48,079 new HIV diagnoses in the US



Gender

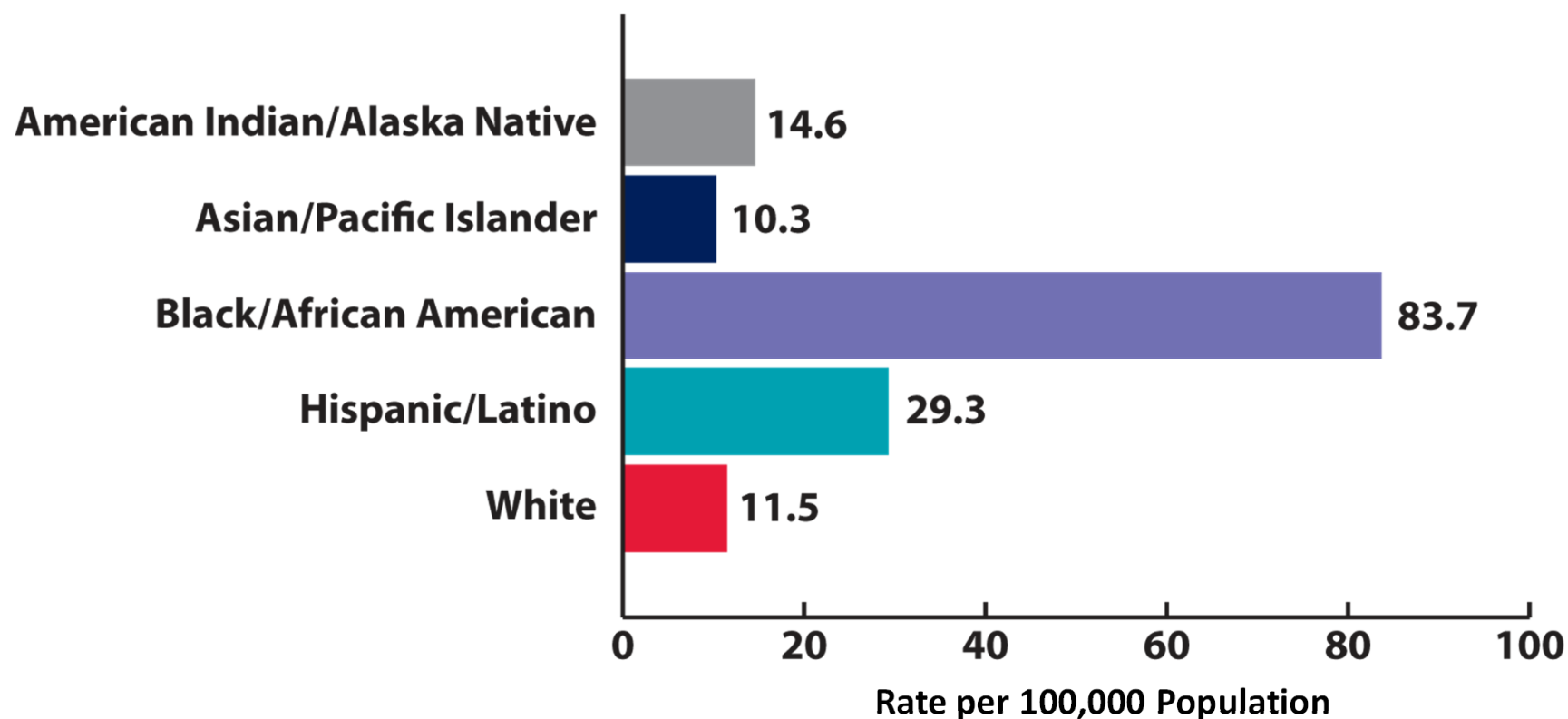


Race/Ethnicity



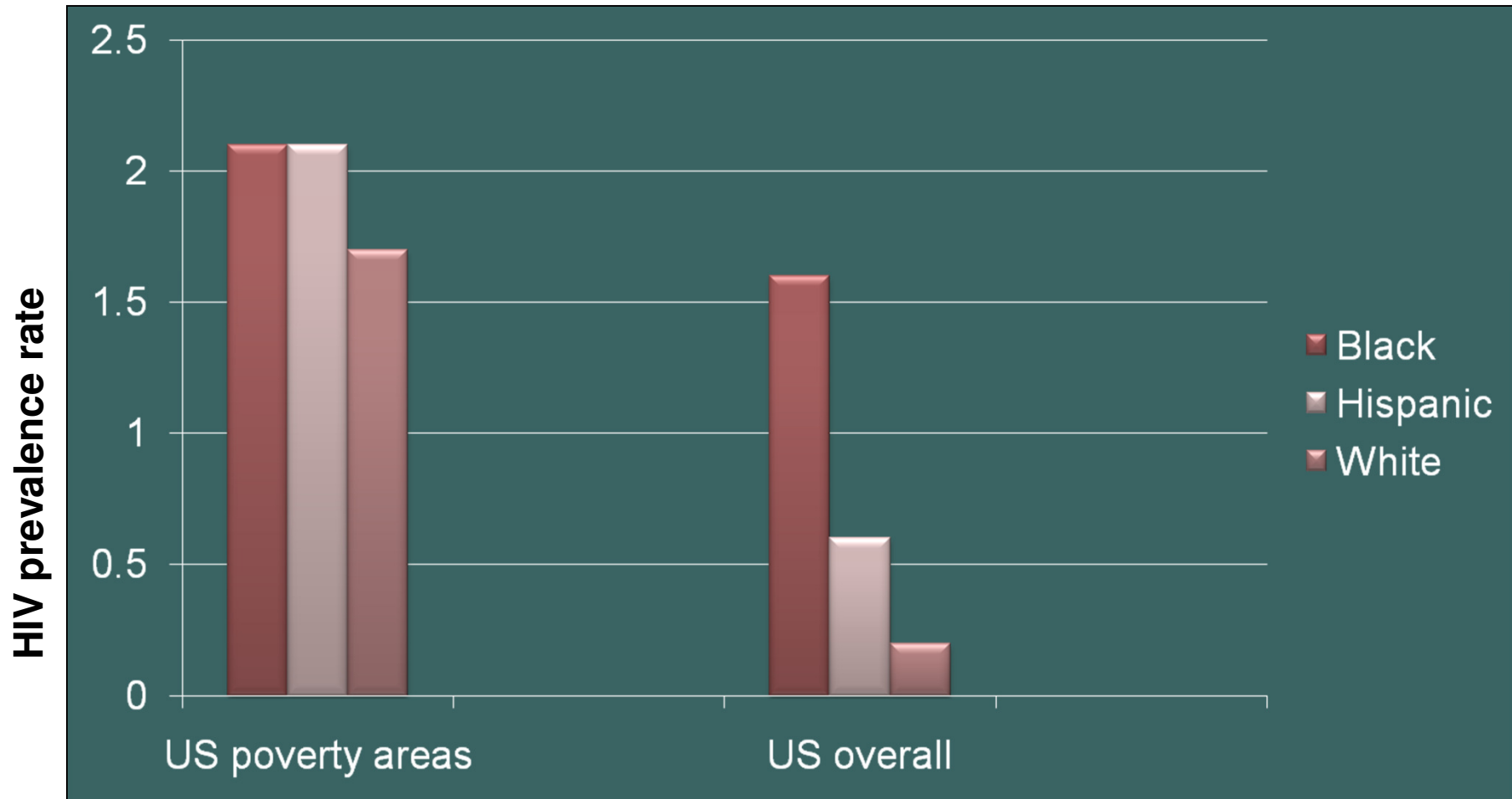
*Adults and adolescents; data from 46 states and 5 US dependent areas

Estimated Rates of New HIV Diagnoses in the US by Race/Ethnicity, 2010

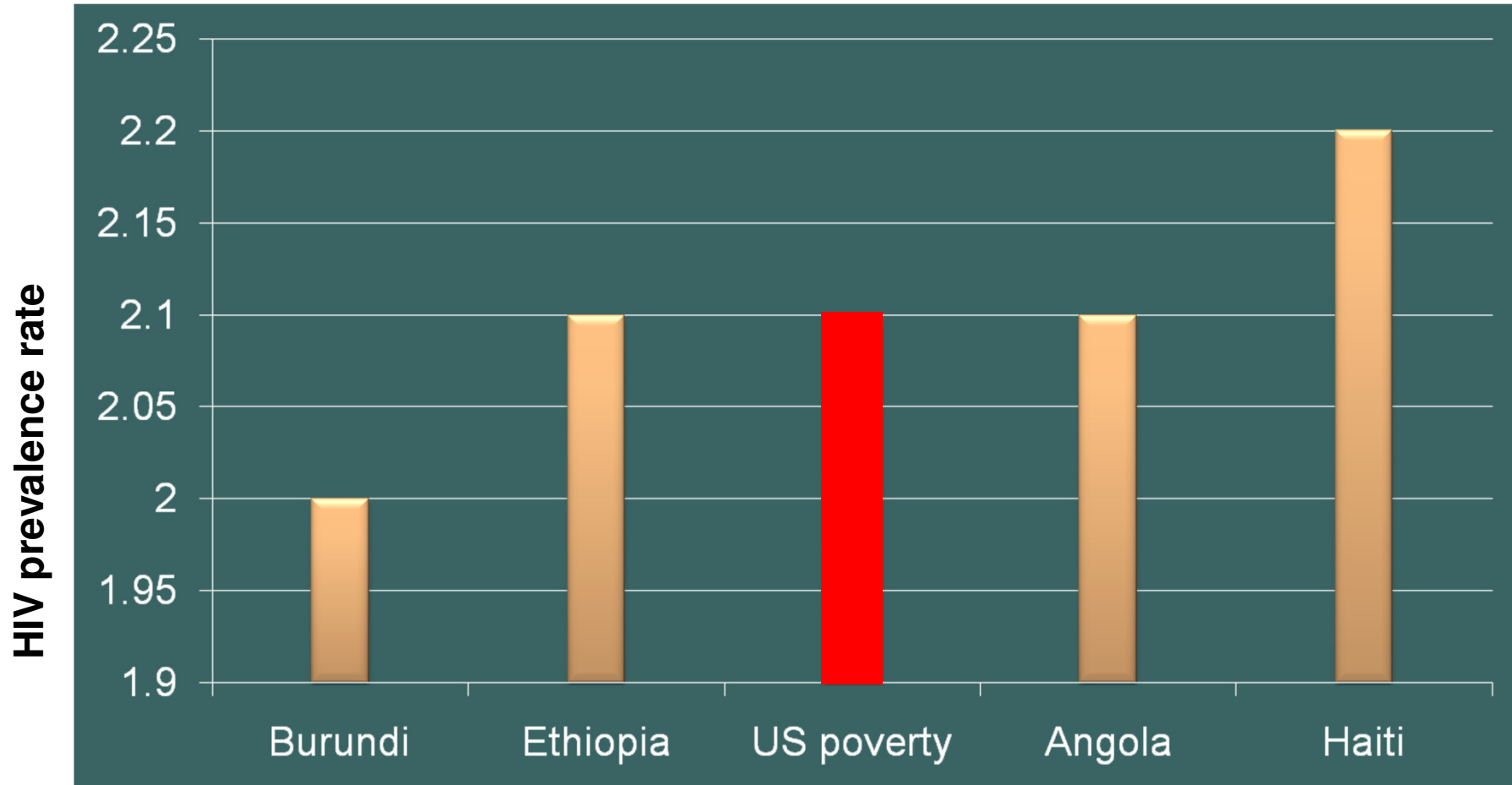


Data have been adjusted for reporting delay.

HIV prevalence rate, by race/ethnicity

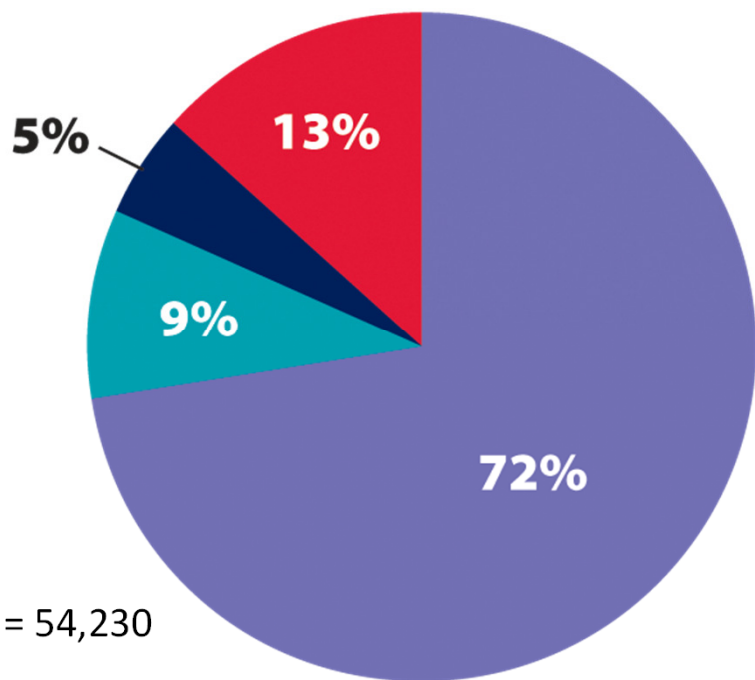


HIV prevalence among US poor comparable to developing world



New HIV Diagnoses in the US by Gender and Transmission Category, 2010

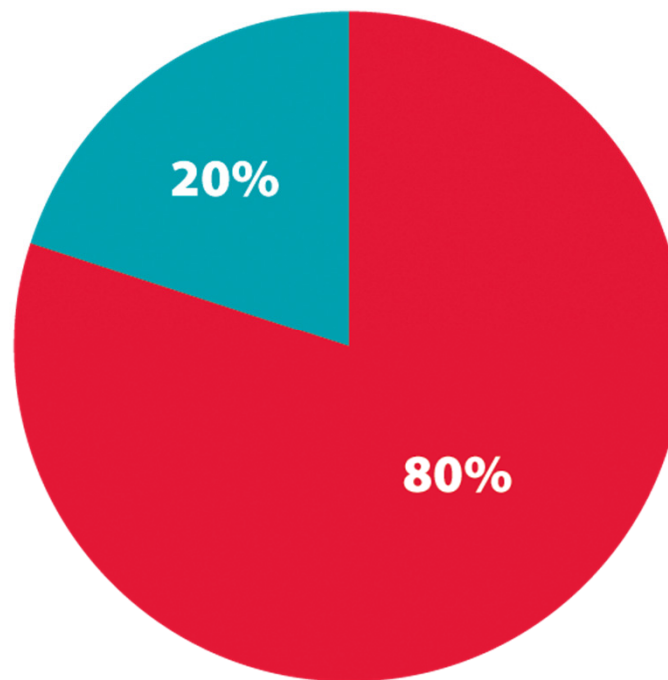
Male



N = 54,230

- Male-to-male sexual contact
- Injection drug use (IDU)
- Male-to-male sexual contact and IDU
- Heterosexual contact*

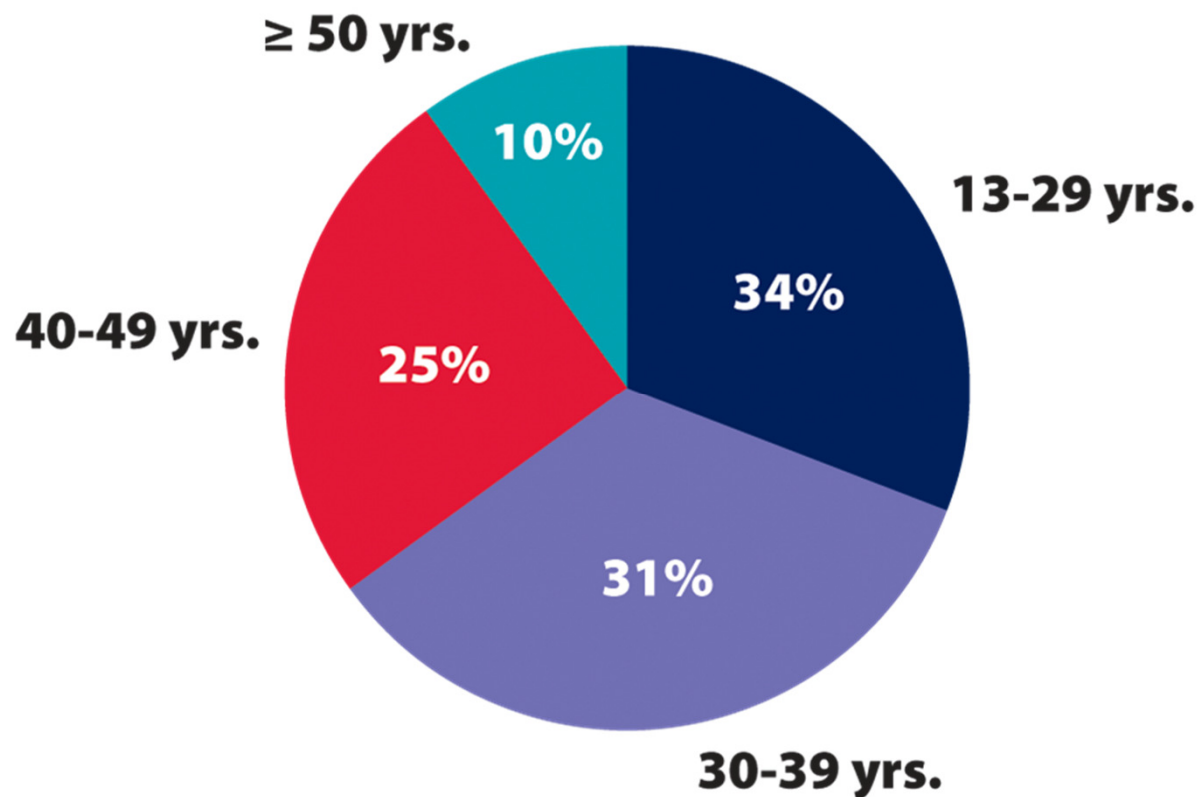
Female



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

Data have been adjusted for reporting delay and cases without risk factor information were proportionately redistributed.

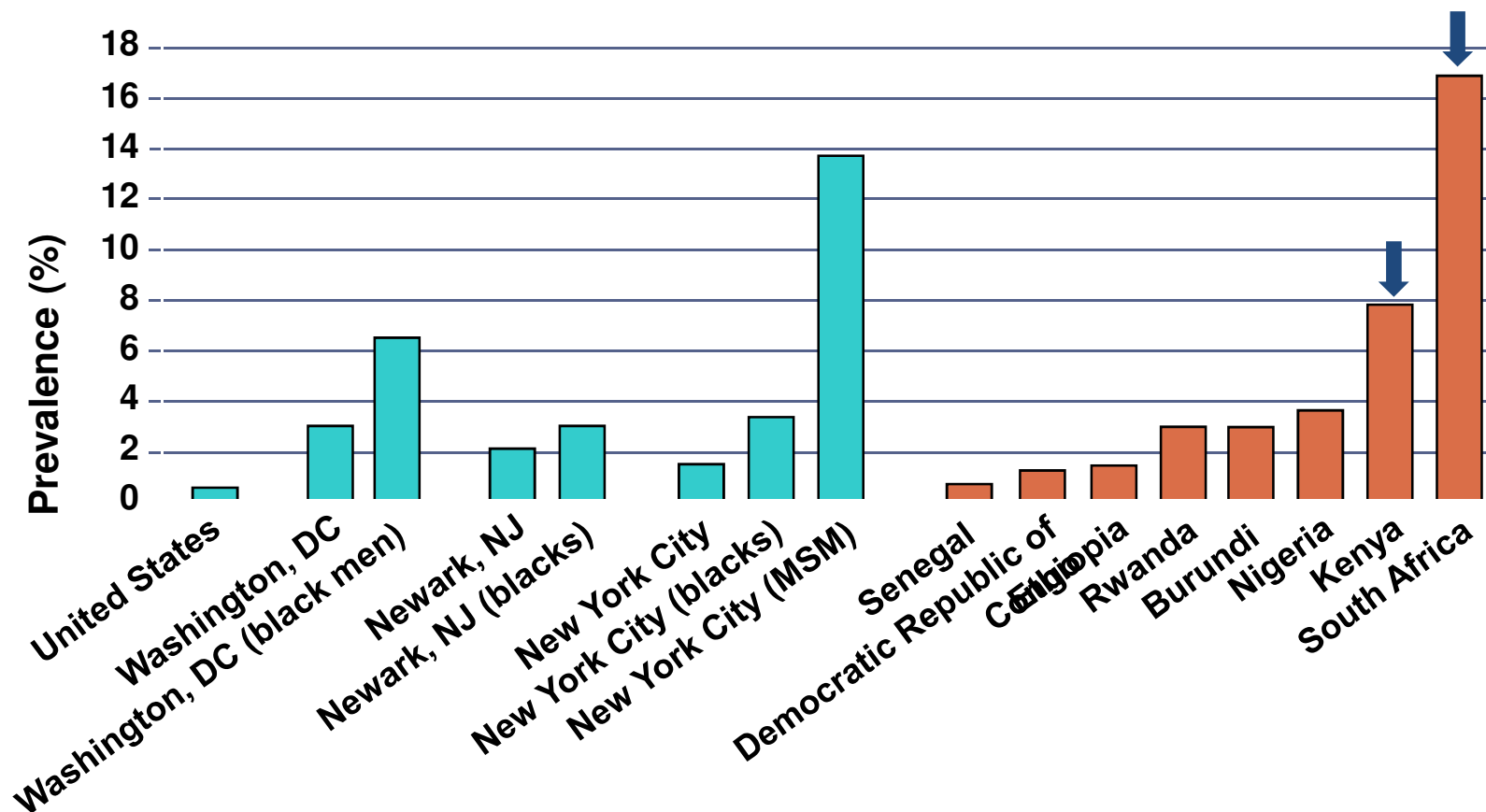
New HIV Diagnoses in the US by Age, 2010



Data have been adjusted for reporting delay.

AIDS in America: “Forgotten But Not Gone”

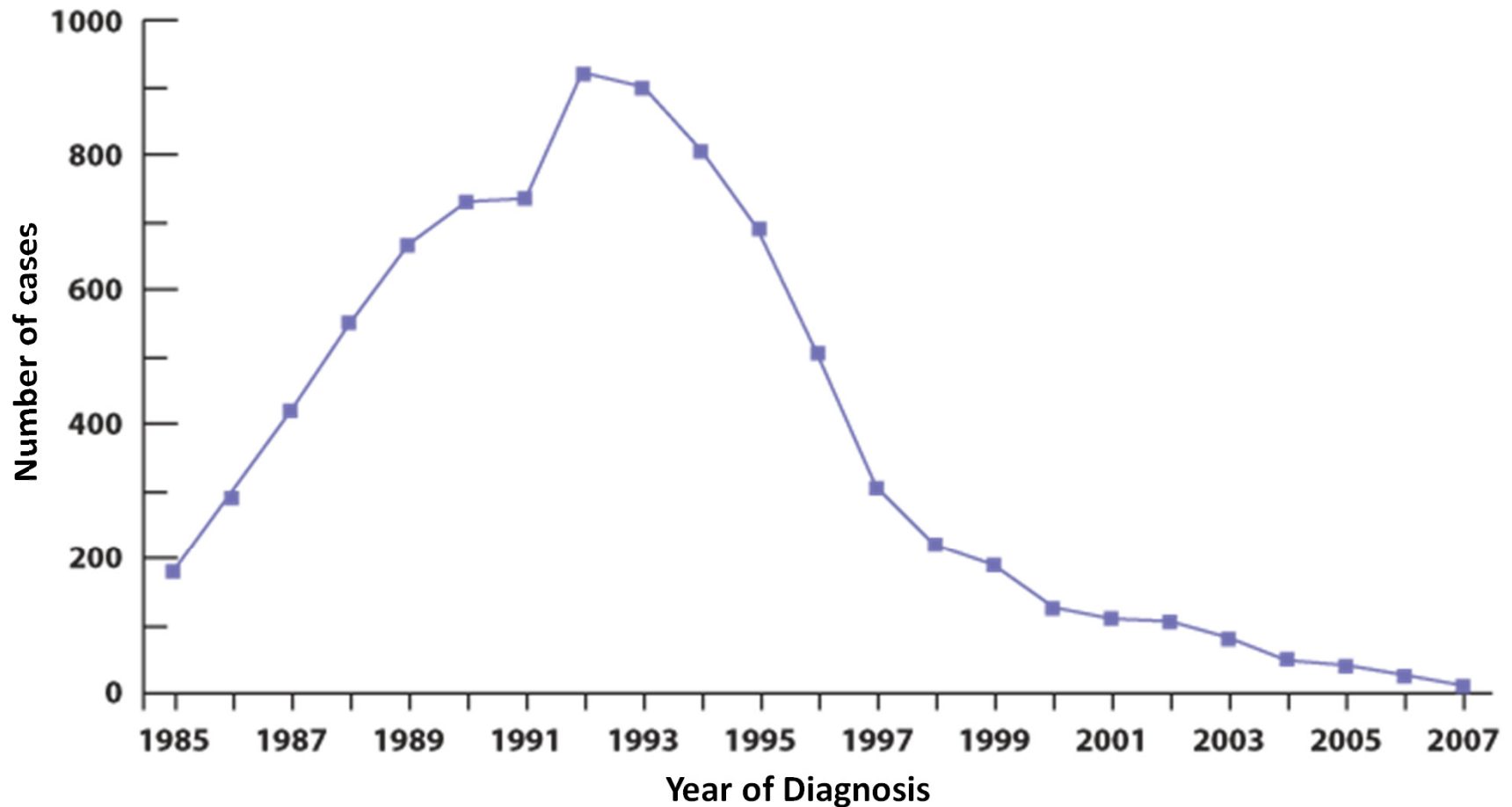
Prevalence of HIV infection (key US cities vs. sub-Saharan African countries)



MSM=men who have sex with men.

Reprinted with permission from El-Sadr WM, et al. *N Engl J Med.* 2010;362:968-970.

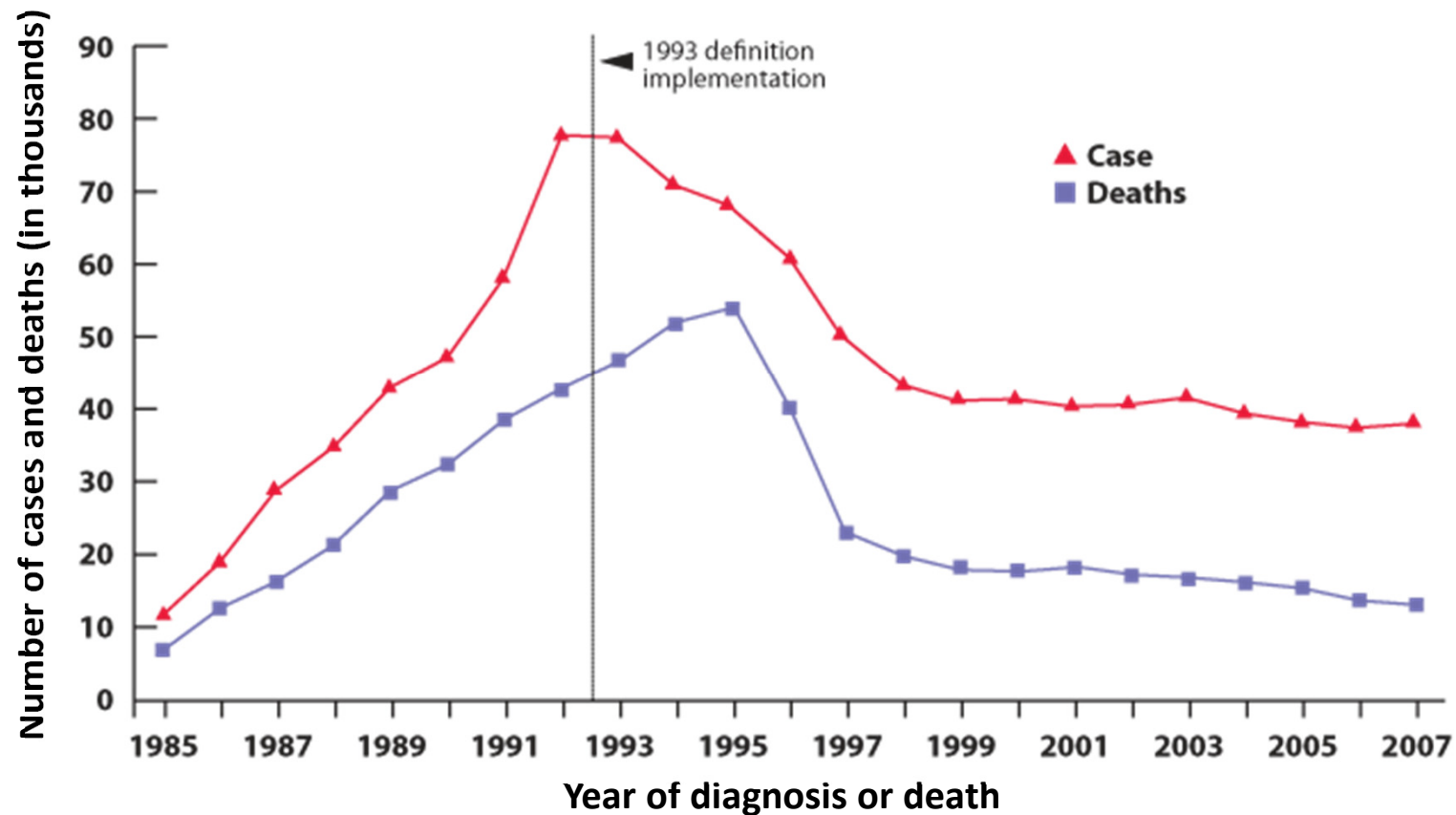
Perinatally-Acquired AIDS Cases in the US, by Year of Diagnosis





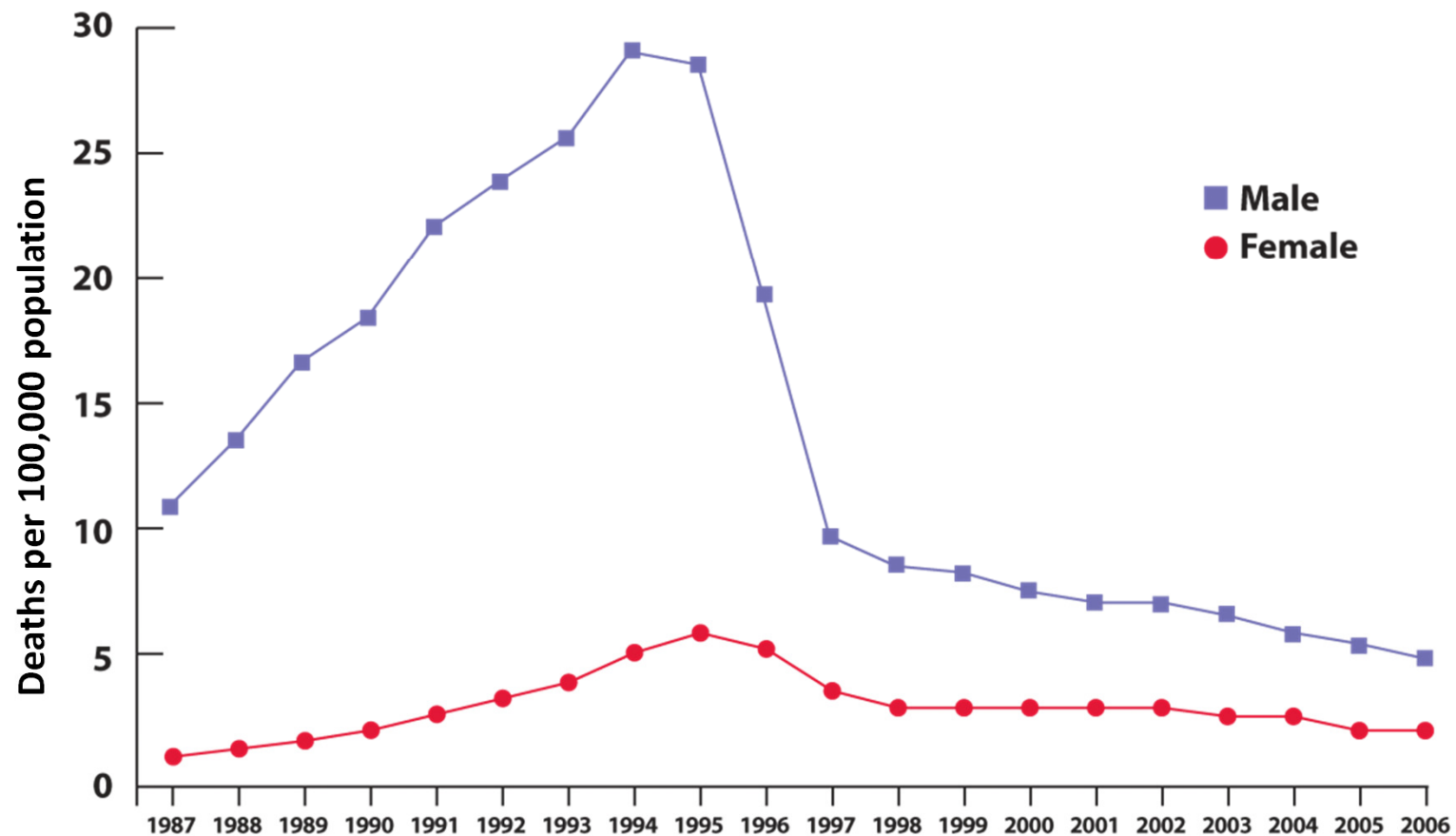
Epidemiology in the US: Mortality

AIDS Cases and Deaths Among Adults and Adolescents in the US



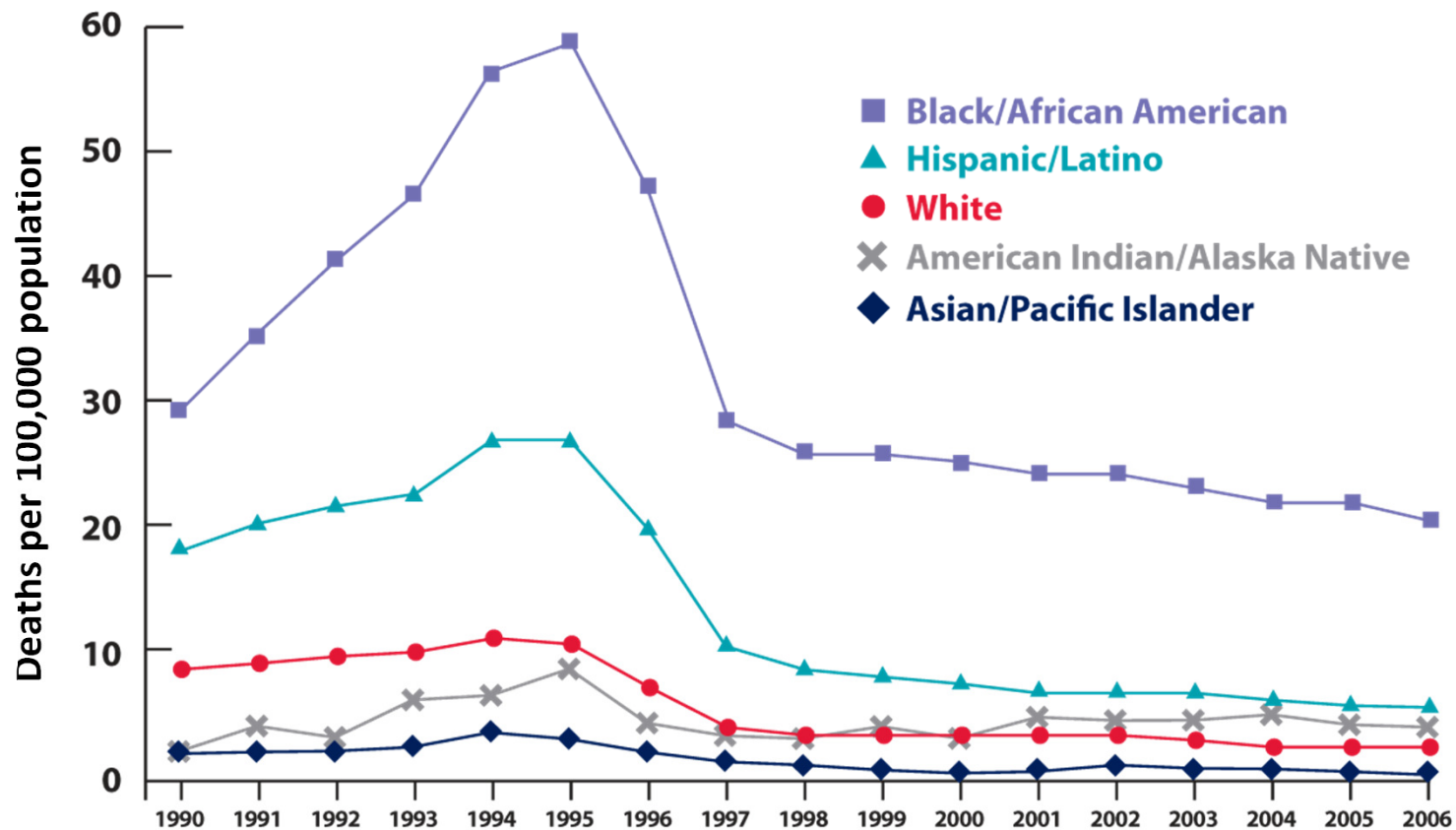
Data have been adjusted for reporting delay.

Annual Age-Adjusted* Rate of Death Due to HIV in the US by Gender



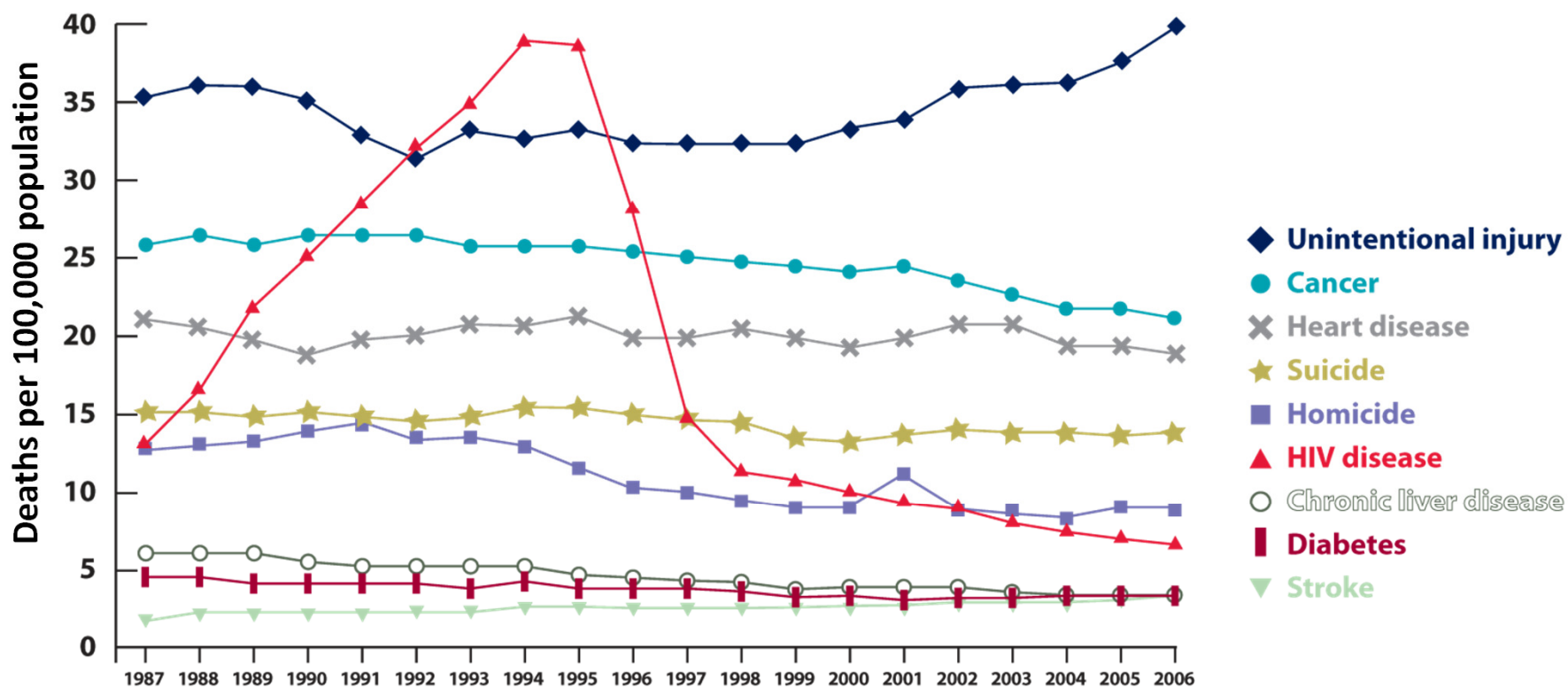
*Standard age distribution of 2000 US population

Age-Adjusted* Rate of Death Due to HIV in the US, by Race/Ethnicity



*Standard age distribution of 2000 US population

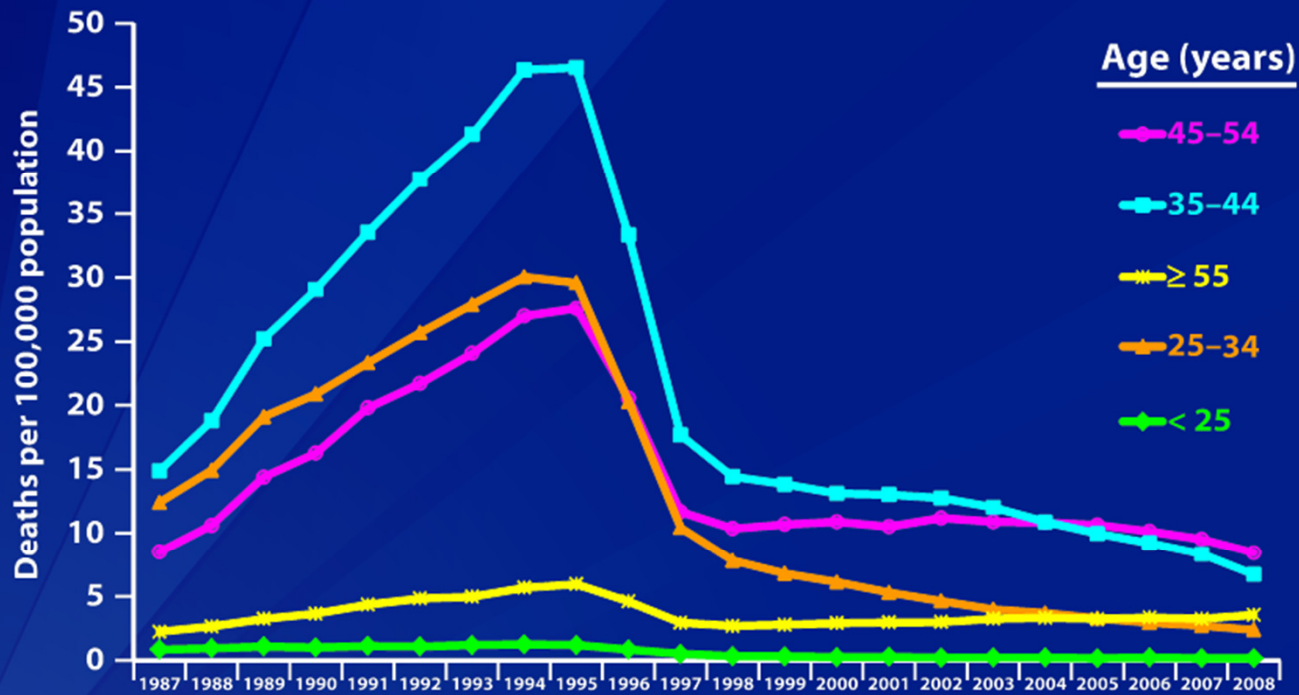
Leading Causes of Death in the US among People 25 to 44 Years Old



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.

Highest death rates due to HIV disease is now among 45-54yr age group

Trends in Annual Rates of Death due to HIV Disease by Age Group, United States, 1987–2008



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.



Transmission of HIV

HIV Transmission

- HIV is transmitted through contact with contaminated body fluids, such as:
 - Blood and blood products
 - Semen
 - Vaginal secretion
- HIV is not transmitted through other body fluids such as saliva, tears, or sweat
- HIV is not transmitted via air, water, or insects (including mosquitoes)

Modes of Transmission for HIV: Part 1

- Unprotected sexual contact is one of the most common methods of transmitting HIV
 - Unprotected anal intercourse has a higher risk of HIV transmission than unprotected vaginal intercourse
 - Unprotected receptive anal intercourse has a higher risk of HIV transmission than unprotected insertive anal intercourse
 - Unprotected oral intercourse has a much lower risk of HIV transmission than anal or vaginal intercourse
- Risk of HIV transmission from sexual contact may also increase with:
 - Multiple sex partners
 - Presence of other sexually transmitted diseases (STDs)

Modes of Transmission for HIV: Part 2

- HIV can be transmitted by shared needles
 - In addition to needles, sharing syringes, rinse water, or other equipment used to prepare intravenous drugs can also increase the risk of HIV infection
- Mothers can transmit HIV to their babies during pregnancy, birth, or breast-feeding
- Receiving blood transfusions, blood products, or organ/tissue transplants contaminated with HIV
 - While originally an important mode of transmission, this risk is now extremely low in the US due to rigorous testing of the blood supply and donated organs/tissue

Modes of Transmission for HIV: Part 3

- Less common modes of HIV transmission include:
 - Occupational exposures such as accidental needle sticks
 - Tattooing or body piercing with unsterile instruments
 - Contact between broken skin, wounds, or mucous membranes and HIV-infected blood or blood-contaminated body fluids, such as in a health care setting
- Though unlikely, transmission can also occur in the following situations if blood is present in the mouth of the person infected with HIV (eg, bleeding gums)
 - Person with HIV bites someone else and breaks the skin
 - Open-mouth kissing
 - Person with HIV chews food and then transfers it to someone else (usually a child)

HIV Prevention

- Health care professionals can counsel patients on ways to prevent transmission of HIV, including:
 - Abstaining from sexual activity or being in a long-term mutually monogamous relationship with an uninfected partner
 - Using latex condoms correctly and consistently
 - Considering male circumcision, which has been shown to reduce the risk of transmission during vaginal sex
 - Not injecting drugs. If the patient is unable to stop injecting drugs, encourage the use of clean needles when injecting

Post and Pre exposure Prophylaxis

- When started within 48-72 hours after exposure to HIV and continued for 28 days, antiretroviral therapy has been shown to decrease the risk of HIV transmission
- Exposures can be occupational (eg, health care providers) or behavioral (eg, unprotected sex)
- The risk of infection from exposure to HIV should be considered and weighed against the possible toxicities associated with different regimens
- There are some data to support efficacy of pre-exposure prophylaxis – data are very preliminary

HIV Testing

Purpose of Routine HIV Screening

- HIV infection is consistent with all generally accepted CDC criteria that justify routine screening
 - HIV infection is a serious health condition that can be diagnosed before symptoms develop
 - HIV can be detected by reliable, inexpensive, and noninvasive screening tests
 - The costs of screening are reasonable in relation to the anticipated benefits
 - Infected patients have years of life to gain if treatment is initiated early, before symptoms develop

CDC Recommendations for Routine HIV Screening in the US: Details

- Routine screening for HIV infection is recommended in people aged 13–64 years in all health care settings*
- Screening should be voluntary and undertaken only with the patient's knowledge and understanding of the testing planned
- All patients initiating treatment for tuberculosis (TB) should be screened routinely for HIV infection
- All patients seeking treatment for STDs should be screened routinely for HIV during each visit for a new complaint, regardless of whether the patient is known or suspected to have specific behavior risks for HIV infection

*Screening should not be disregarded unless health care providers have documented a prevalence of undiagnosed HIV in <0.1% in their patient population

CDC Recommendations for Repeat HIV Screening in the US: Details

- Health-care providers should test all persons likely to be at high risk for HIV at least annually
 - Persons likely to be at high risk include:
 - Injection-drug users and their sex partners
 - Persons who exchange sex for money or drugs
 - Sex partners of HIV-infected persons
 - MSM or heterosexual persons who themselves or whose sex partners have had more than one sex partner since their most recent HIV test
- Repeat screening of persons not likely to be at high risk for HIV should be performed on the basis of clinical judgment

CDC Recommendations for HIV Screening in Pregnant Women in the US: Details

- CDC recommends that all pregnant women in the United States should be screened for HIV infection as early as possible during each pregnancy
- Screening should occur after a woman is notified that HIV screening is recommended for all pregnant patients and that she will receive an HIV test as part of the routine panel of prenatal tests unless she declines (opt-out screening)

CDC Recommendations for Diagnostic Testing for HIV in the US: Details

- In addition to routine screening, all patients with signs or symptoms consistent with HIV infection or an opportunistic illness characteristic of AIDS should be tested for HIV
- Clinicians should maintain a high level of suspicion for acute HIV infection in all patients who have a compatible clinical syndrome and who report recent high-risk behavior

Types of HIV Tests

- The most common type of HIV screening test uses an enzyme immunoassay [enzyme immunoassay (EIA) or enzyme linked immunosorbant assay (ELISA)] to look for antibodies to HIV
 - Test can use blood, oral fluid, or urine
 - Rapid testing is available, with results in about 20 minutes
 - To make a diagnosis, a positive enzyme immunoassay must be confirmed with Western blot or immunofluorescent assay
- An RNA (or pro-viral DNA) test detect viral genetic material
 - This test can be used for detecting acute HIV infection and can detect HIV before antibodies are made
 - This test can be used to screen the blood supply
- P24 antigen/HIV antibody combination testing is approved for detection of acute HIV infection

HIV Impact on Health

HIV Targets the Immune System

- HIV targets the immune system by specifically infecting CD4 cells
- Over time, HIV depletes the body of CD4 cells, causing an immune deficiency
- This immune deficiency leads to increased risk of infections that those with normal immune function would not be susceptible

CD4 Cell Count (cells/mm³) and Risk for Specific Infections

Some examples of OIs seen with specific CD4 cell counts*:

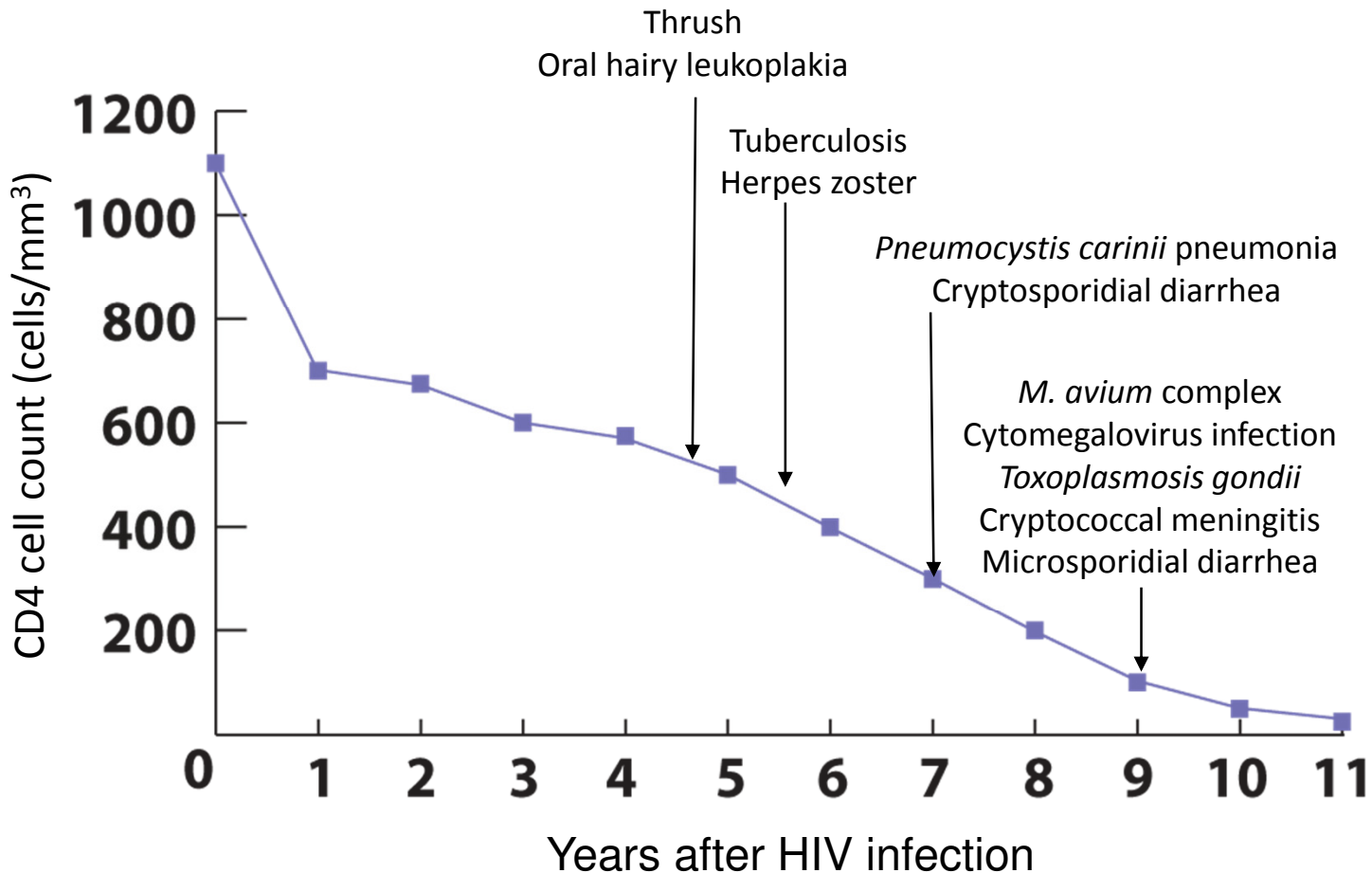


PCP = *Pneumocystis pneumonia*; MAC = *Mycobacterium avium* complex; CMV = Cytomegalovirus

*This is not a complete list of all OIs associated with the CD4 cell counts listed.

MMWR. 2009;58(Early Release):1-198.

Risk for Development of Opportunistic Infections Based on CD4 Cell Count Over Time



AIDS-defining Conditions

- **AIDS-related malignancies**
 - Kaposi's sarcoma
 - Lymphoma
 - Cervical cancer (invasive)
- **Other conditions**
 - HIV related encephalopathy
 - Wasting syndrome attributed to HIV
- **Opportunistic infections***
 - Candidiasis of esophagus
 - Cryptococcosis, extrapulmonary
 - Cytomegalovirus disease
 - Herpes simplex: chronic ulcers or esophagitis
 - Histoplasmosis, disseminated or extrapulmonary
 - *Mycobacterium avium* complex
 - *Mycobacterium tuberculosis* of any site
 - *Pneumocystis jirovecii* pneumonia
 - Progressive multifocal leukoencephalopathy
 - Toxoplasmosis of brain

*Examples only; not an exhaustive list

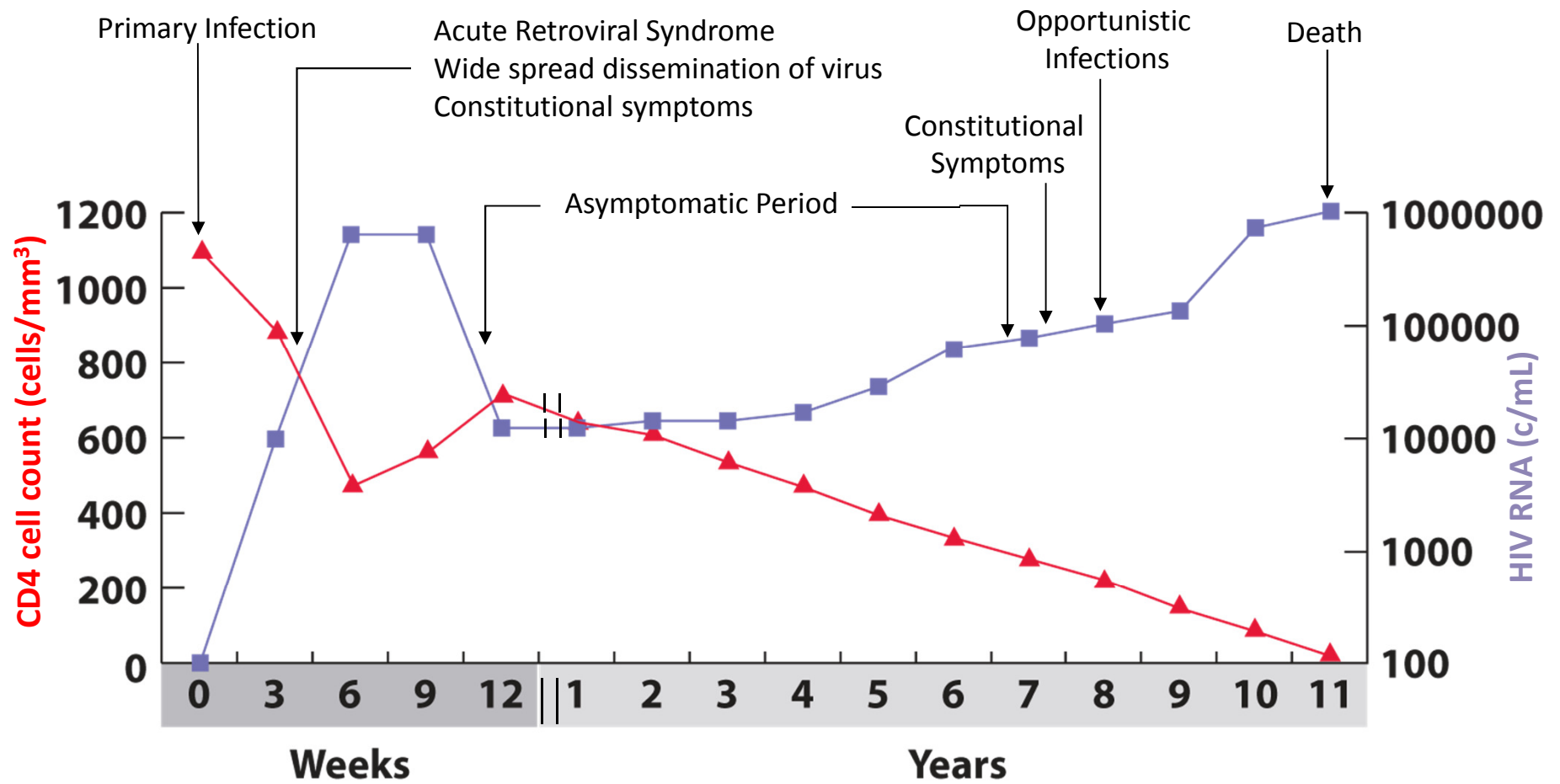
HIV and Organ Damage

- Although immune deficiency from HIV infection can cause significant morbidity and mortality, the direct effects of the virus itself as well as inflammation associated with HIV can also lead to end-organ damage
- Conditions associated with organ damage due to HIV
 - HIV-associated nephropathy (HIVAN)
 - Co-infection with hepatitis B or C
 - Cardiovascular disease
 - Non-AIDS associated malignancies
 - Neurocognitive decline

Monitoring HIV Infection Using Surrogate Markers

- Two surrogate markers are used routinely to assess patients with HIV infection
 - CD4+ cell count: indicator of immune function
 - HIV-1 RNA or viral load: measure of viremia and treatment response
- CD4 cell count is the strongest predictor of subsequent disease progression and survival
- Lower viral loads are associated with improved clinical outcomes

HIV Disease Course Without Treatment



HIV Lifecycle

Organization of the HIV-1 Virion

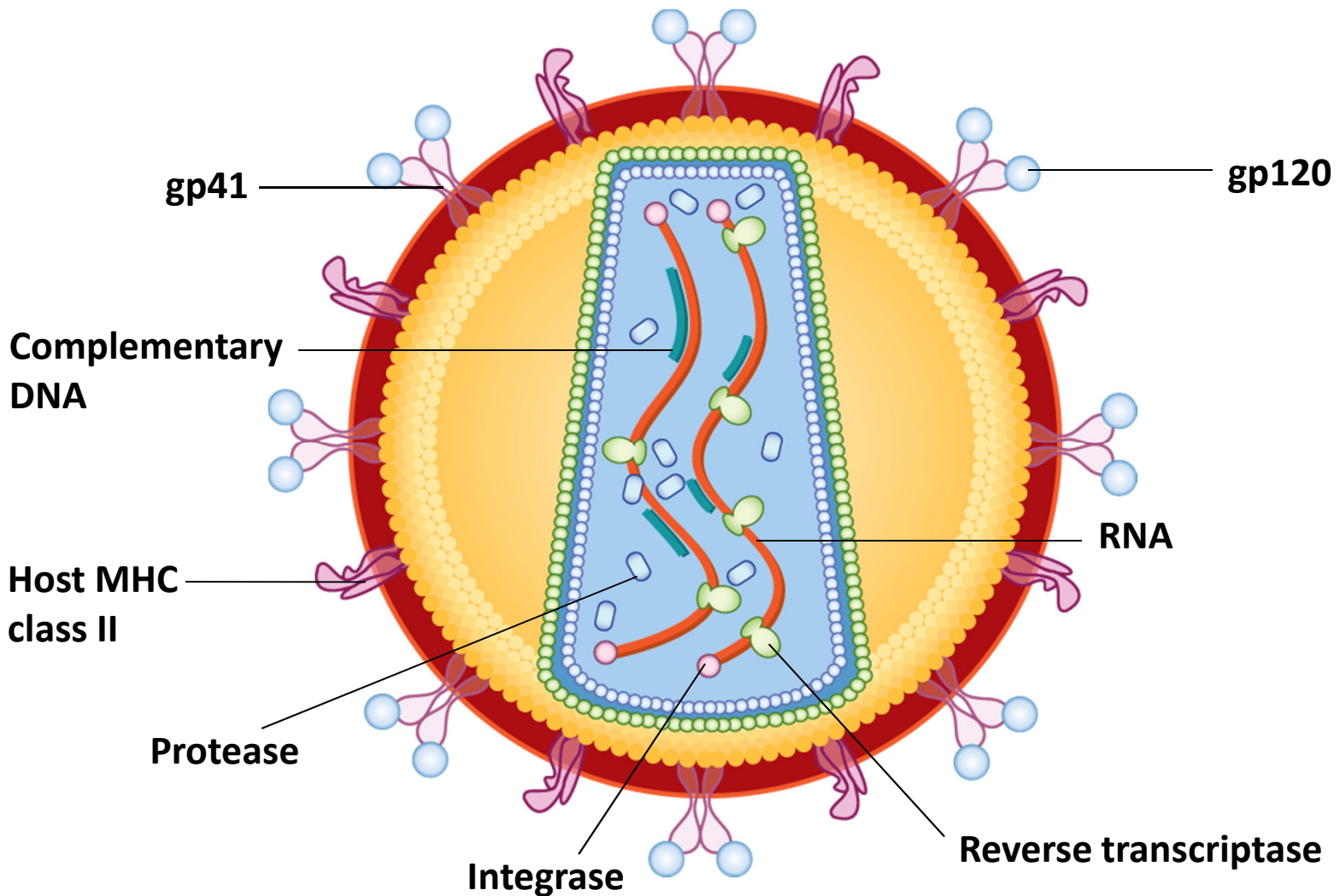
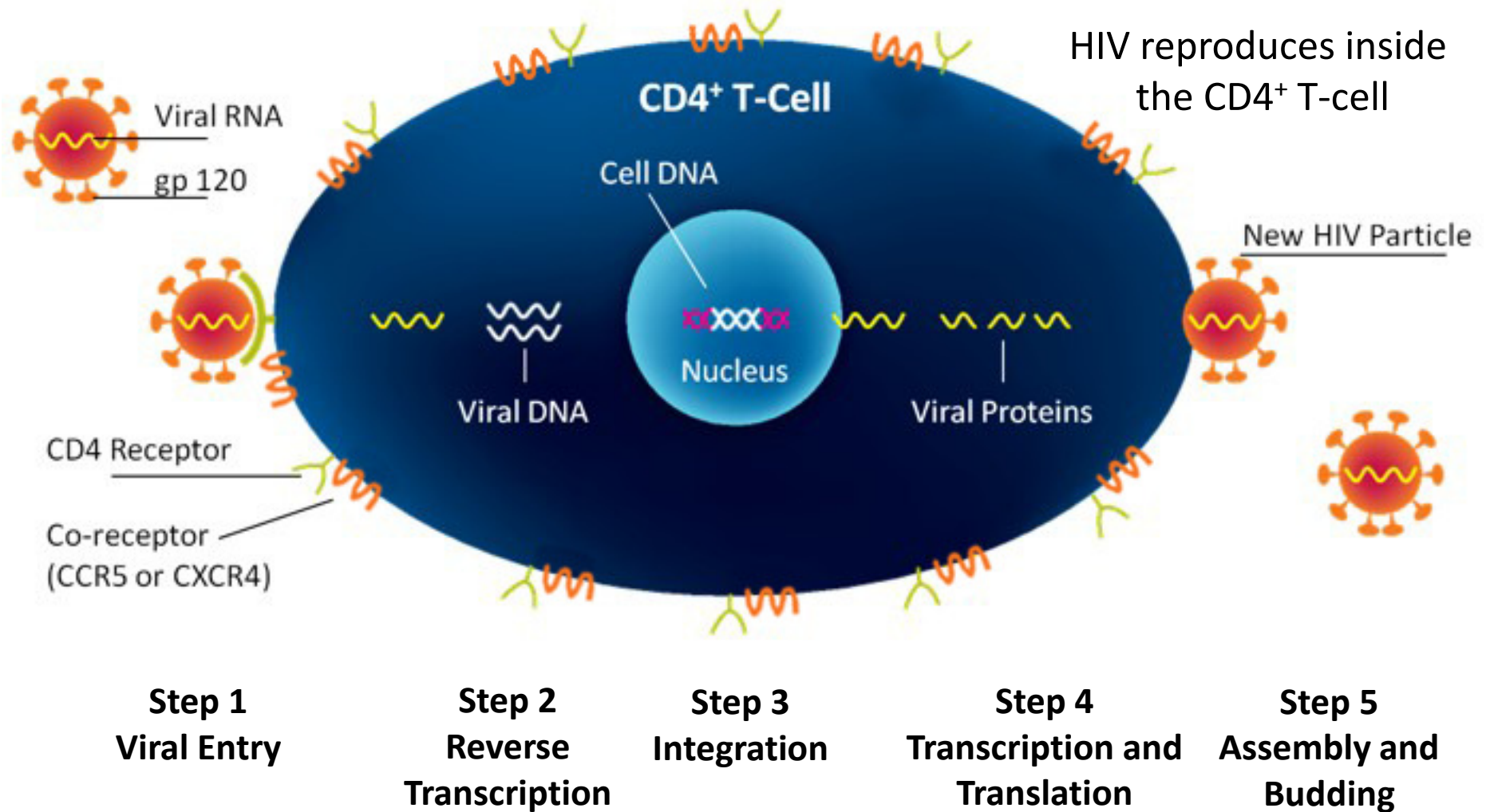
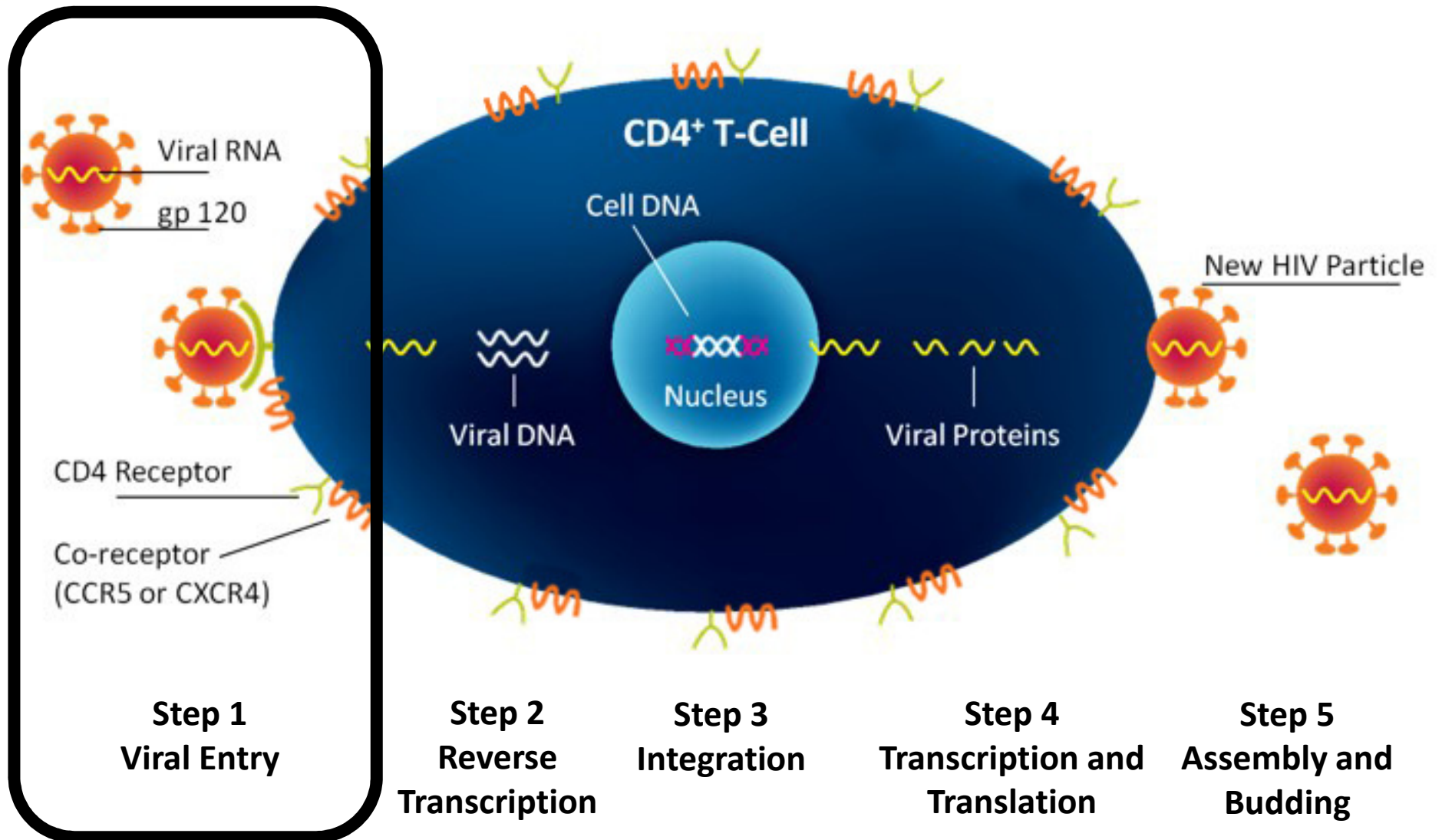


Image adapted from *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*, 6th Edition.

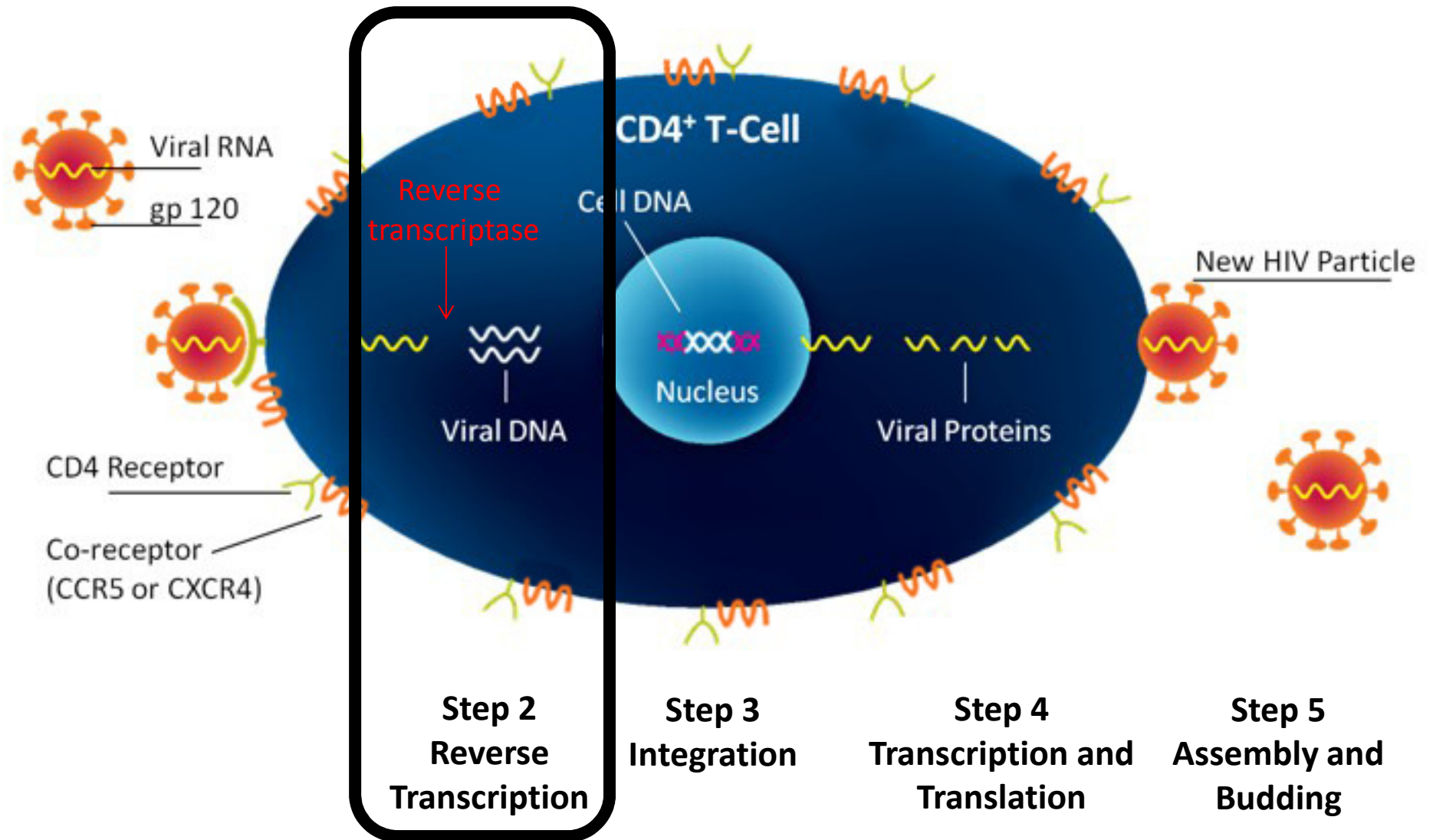
The HIV Life Cycle



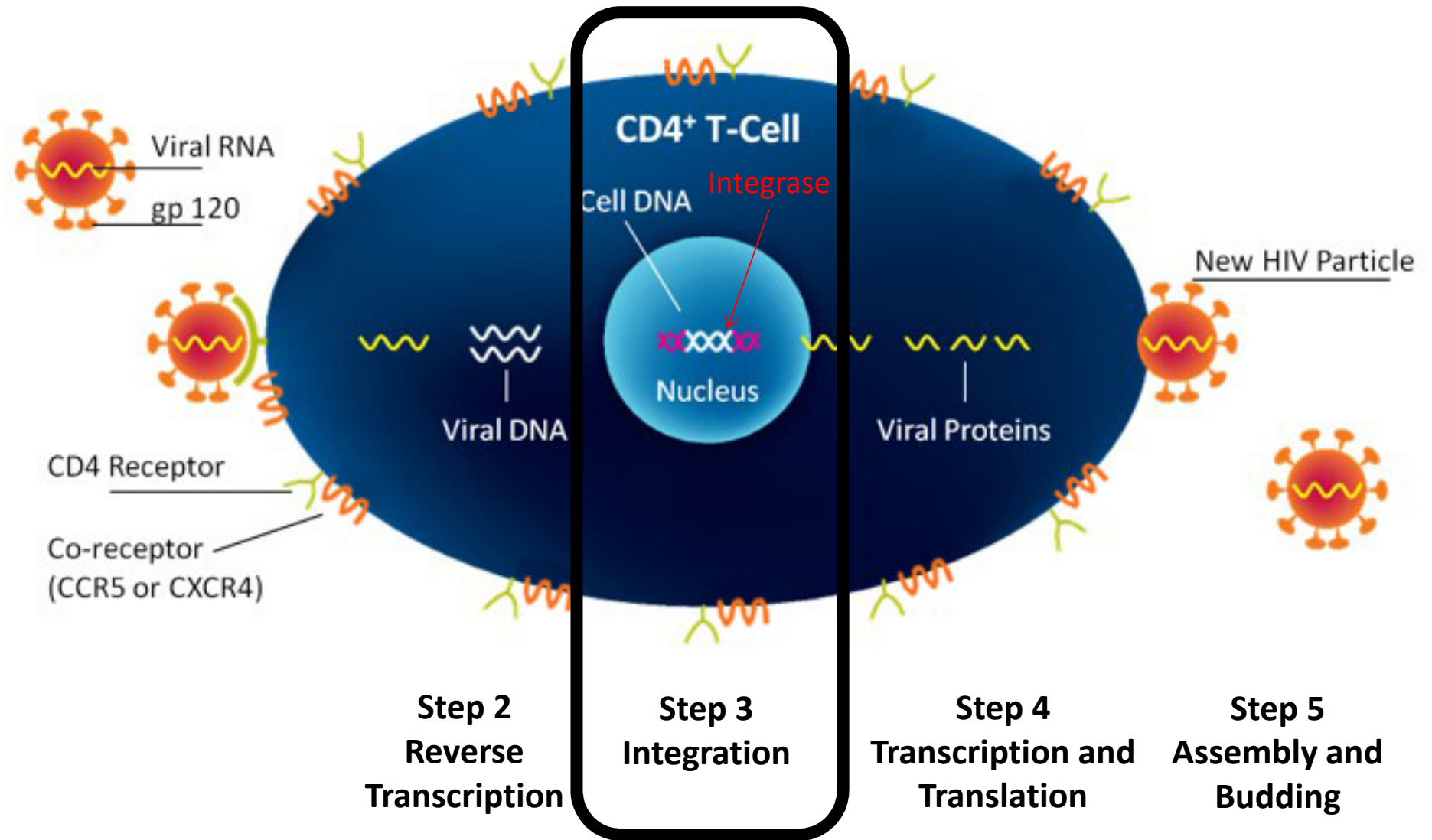
The HIV Life Cycle



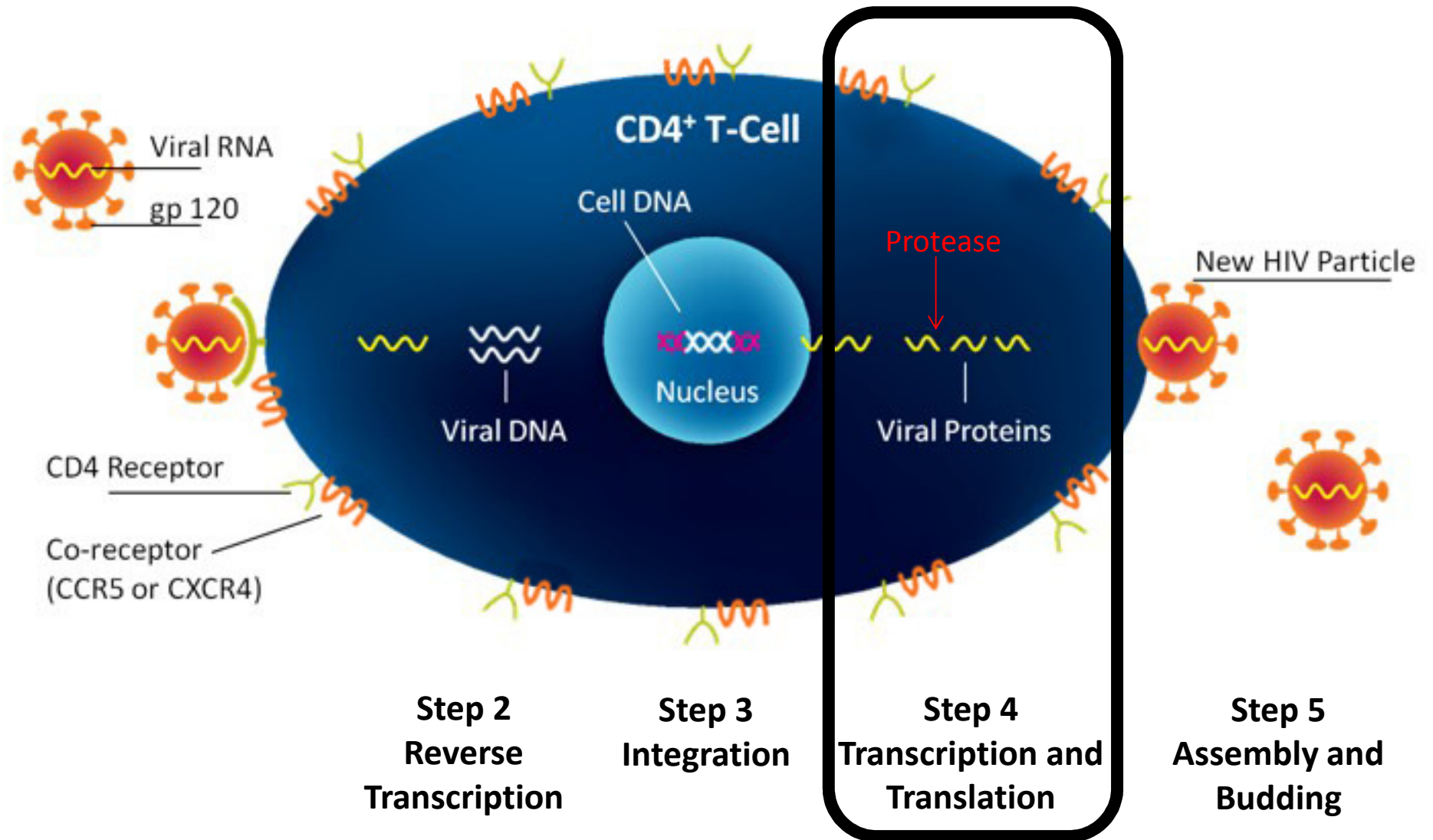
The HIV Life Cycle



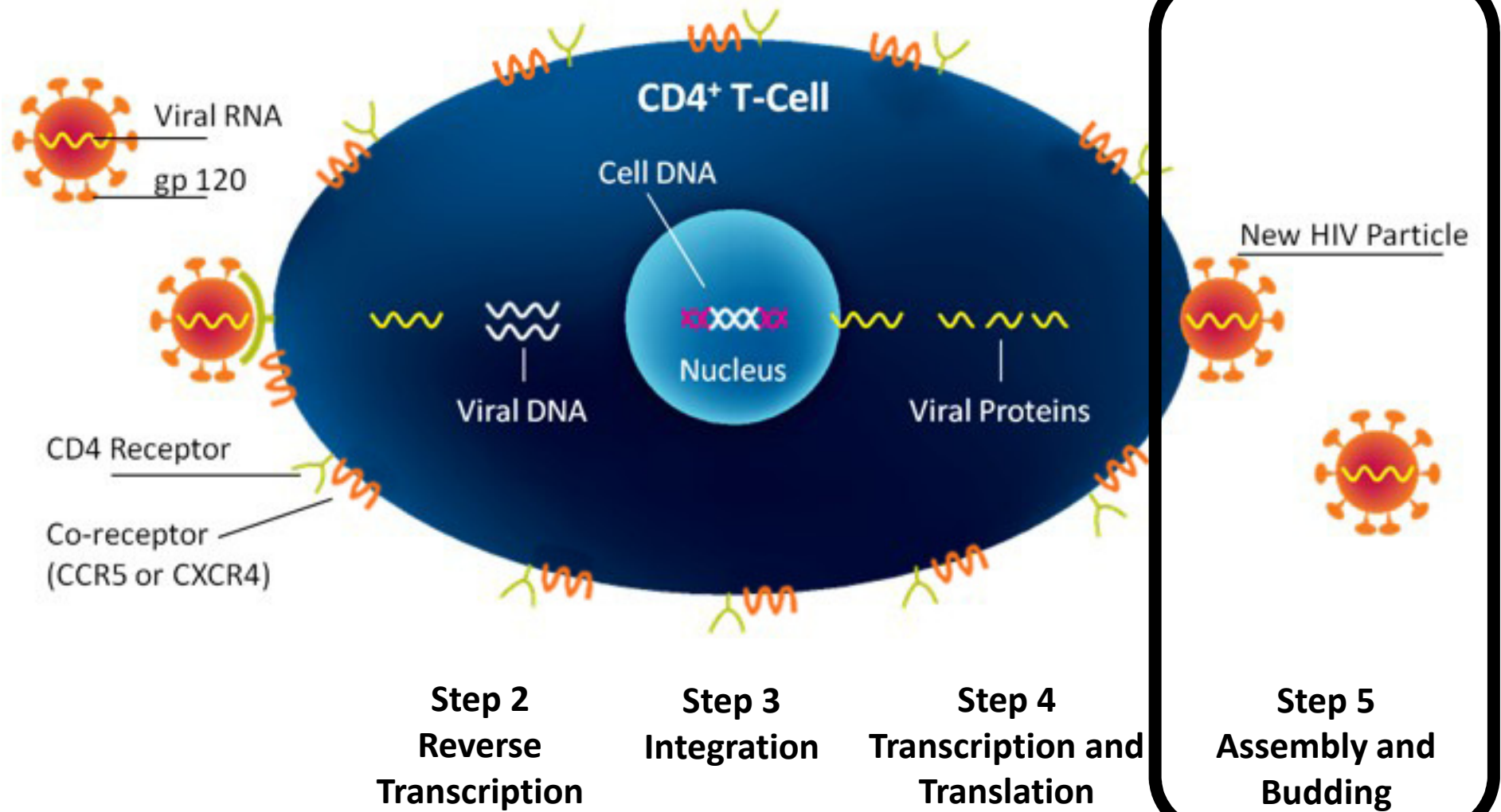
The HIV Life Cycle



The HIV Life Cycle



The HIV Life Cycle

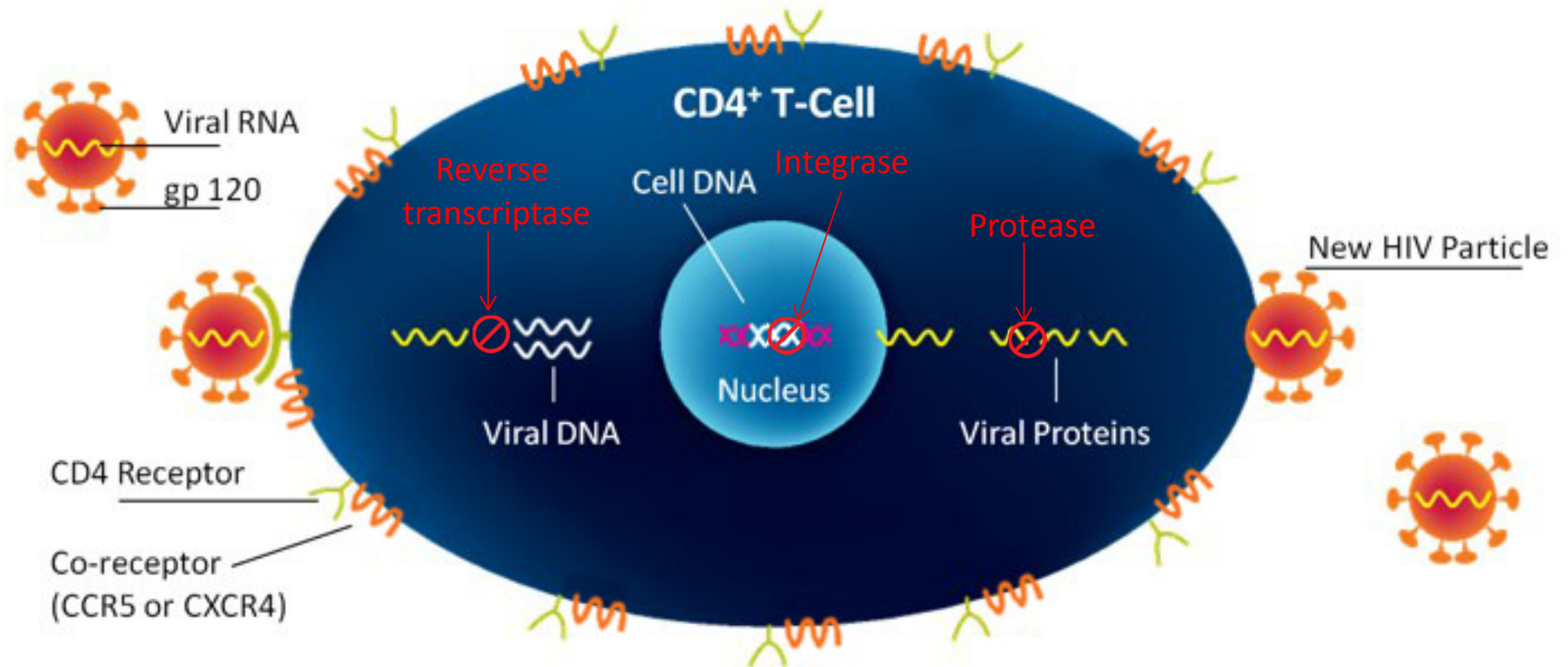


Treating HIV

FDA Approved Classes of Antiretroviral Drugs

- Entry inhibitors:
 - CCR5 antagonists
 - Fusion inhibitors
- Reverse transcriptase inhibitors:
 - Nucleoside reverse transcriptase inhibitors (NRTI), including nucleotides
 - Non-nucleoside reverse transcriptase inhibitors (NNRTI)
- Integrase inhibitors
- Protease inhibitors (PI)

Sites of Action for Antiretroviral Therapy



Step 1
Block Viral Entry:
CCR5 antagonists
Fusion inhibitors

Step 2
Stop Reverse Transcription:
Reverse transcriptase inhibitors

Step 3
Prevent Integration:
Integrase inhibitors

Step 4
Stop Transcription and Translation:
Protease Inhibitors

Step 5
Assembly and Budding

Highly Active Antiretroviral Therapy—HAART

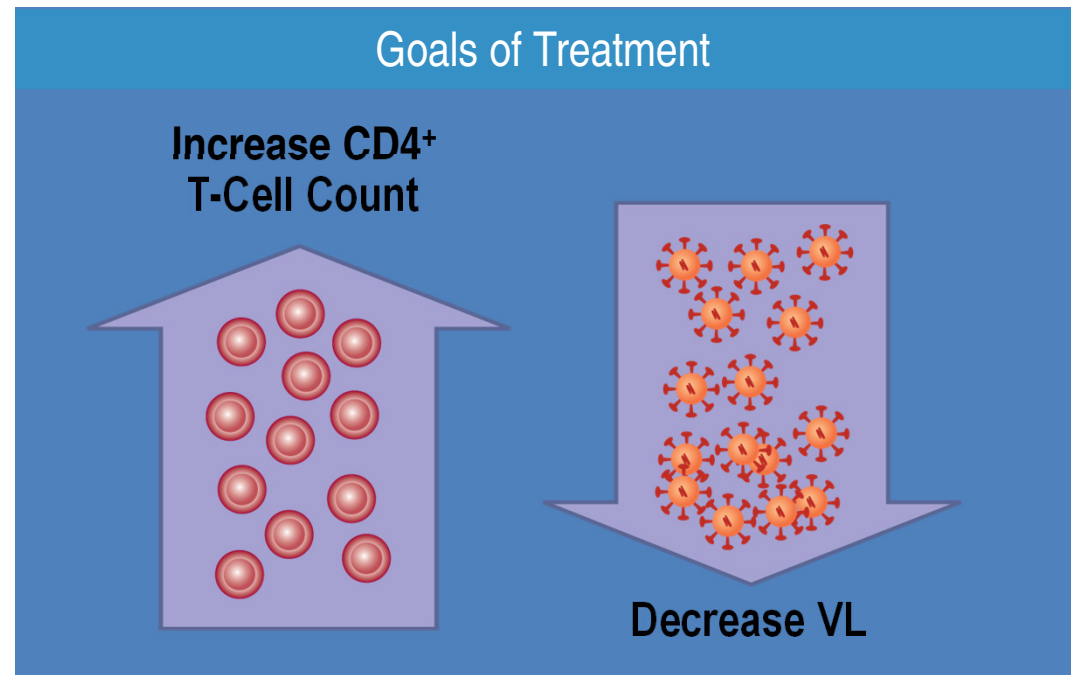
- HAART usually consists of at least three drugs to decrease viral replication
 - There are more than 20 approved antiretroviral agents available in 6 mechanistic classes
- With lower rates of viral replication, fewer CD4 cells are destroyed and immune function can improve
- A key goal of therapy is suppression of viral load to "undetectable," meaning, it is below the limit of detection of commercially-available HIV assays (usually 50 copies/mL)
 - A person with "undetectable" viral load may still have low levels of ongoing viral replication, and therefore can still transmit HIV to others

Can HIV Be Eradicated?

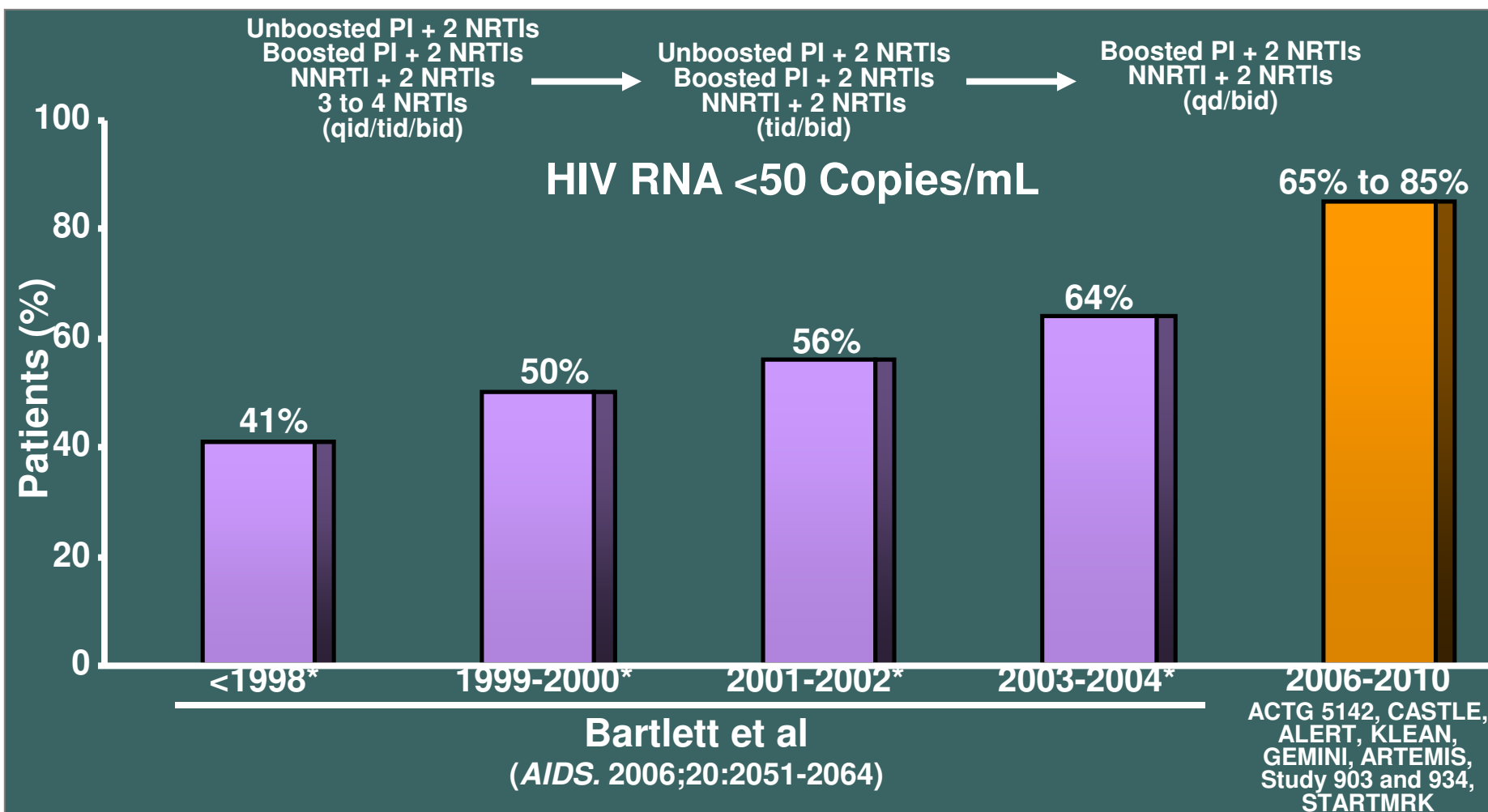
- With currently-available therapy, it is not possible to eradicate HIV from the body
- It is believed that pools of HIV-infected but dormant CD4 cells (reservoirs) are established in the earliest stages of HIV infection and can persist with a long half-life, even with prolonged suppression of viral replication
- Approaches targeting these viral reservoirs may be an option for treatment of HIV

Goals of Antiretroviral Therapy

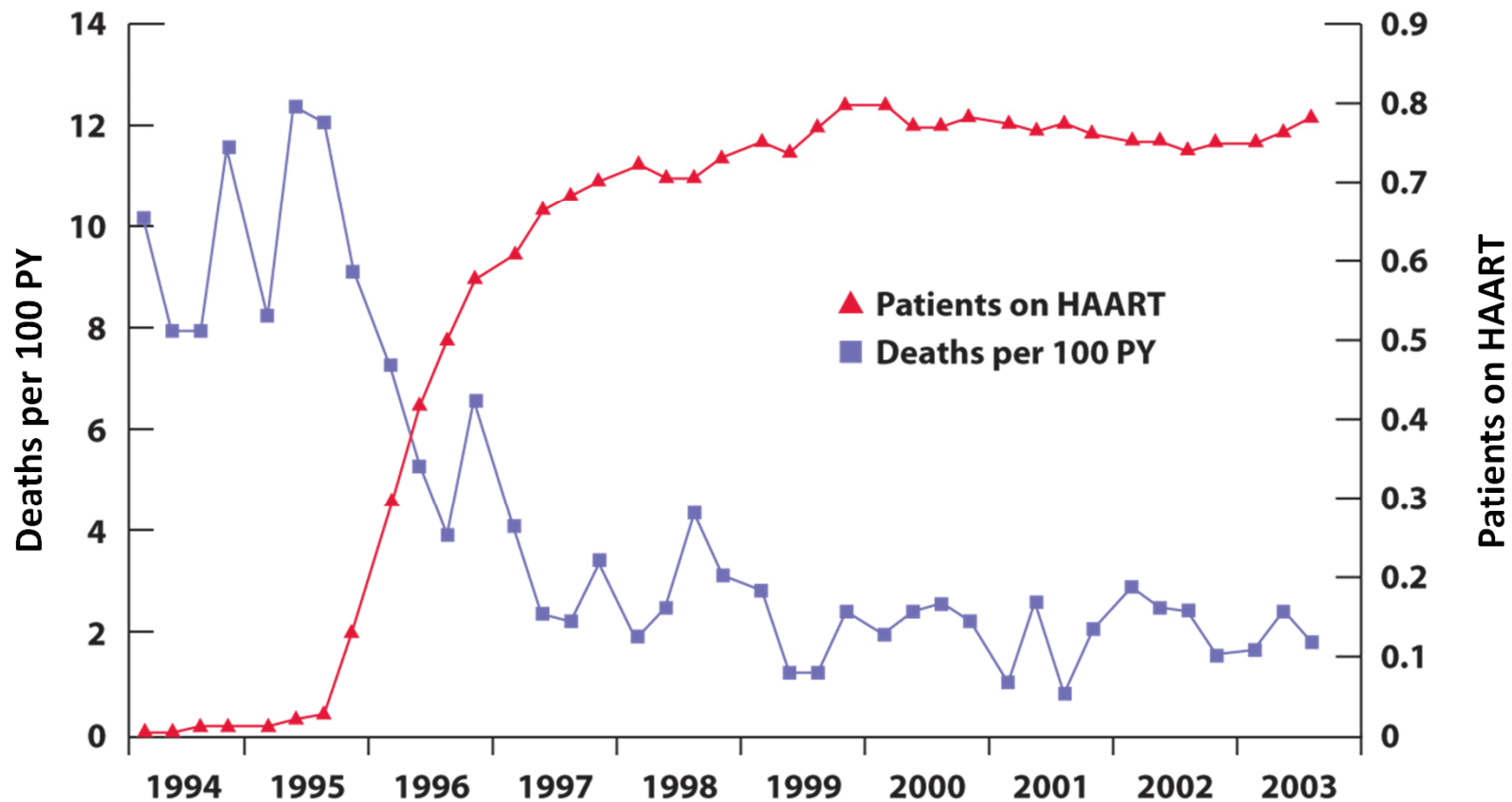
- Maximally and durably suppress viral load
- Reduce HIV associated morbidity and mortality and prolong survival
- Restore and preserve immune function
- Prevent HIV transmission
- Improve quality of life



Improving Efficacy of Initial HAART Regimens



Treatment and Mortality Trends: Data from the HIV Outpatient Study (HOPS)



HAART = highly-active antiretroviral therapy

DHHS Guidelines, 2012: When to Start

- ART recommended for all HIV-infected patients; *strength* of recommendation varies according to CD4+ cell count

CD4+ Cell Count	Recommendation
▪ < 350 cells/mm ³	▪ Start ART (AI)
▪ 350-500 cells/mm ³	▪ Start ART (All)
▪ > 500 cells/mm ³	▪ Start ART (BIII)
Clinical Conditions Favoring Initiation of Therapy Regardless of CD4+ Cell Count	
<ul style="list-style-type: none"> ▪ History of AIDS-defining illness (AI) ▪ Pregnancy (AI) ▪ HIV-associated nephropathy (All) ▪ HBV coinfection (All) ▪ Patients at risk of transmitting HIV to sexual partners (AI, heterosexuals; All, others) ▪ HCV coinfection* (BII) ▪ Patients > 50 years of age (BIII) 	

* Patients with cirrhosis. Some pts with CD4+ counts > 500 cells/mm³ may elect to defer ART until after HCV therapy is completed.

DHHS Guidelines for Antiretroviral Therapy in Adults and Adolescents. March 27, 2012.

Current trends in antiretroviral therapy

- Early initiation
- Convenience
- Tolerability and safety
- Individualization
 - Long-term safety and monitoring
 - Data accrued on current agents/regimens
 - Genetic testing (Resistance, viral subtypes, HLA B-5701, viral tropism)

Factors Associated with Poor Adherence to Antiretrovirals

- Low levels of literacy
- Certain age-related challenges (e.g., vision loss, cognitive impairment)
- Psychosocial issues (e.g., depression, homelessness, lower social support, stressful life events, dementia, or psychosis)
- Active (but not history of) substance abuse, particularly for patients who have experienced recent relapse
- Stigma
- Difficulty with medication taking (e.g., trouble swallowing pills, daily schedule issues)
- Complex regimens (e.g., pill burden, dosing frequency, food requirements)
- Adverse drug effects
- Treatment fatigue

Summary

- The increasing number of people living with HIV despite the decreasing rates of new HIV infections reflects the impact of antiretroviral therapy
- Earlier diagnosis of HIV and continued prevention efforts may:
 - Prevent HIV transmission
 - Prevent loss of immune function
 - Decrease morbidity and mortality from HIV
- The availability of potent antiretroviral therapy has helped to reduce HIV-related morbidity and mortality