



HIV 101: Pathogenesis and Treatment

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Disclosures

- Dr. Raffanti has no financial disclosures to make.

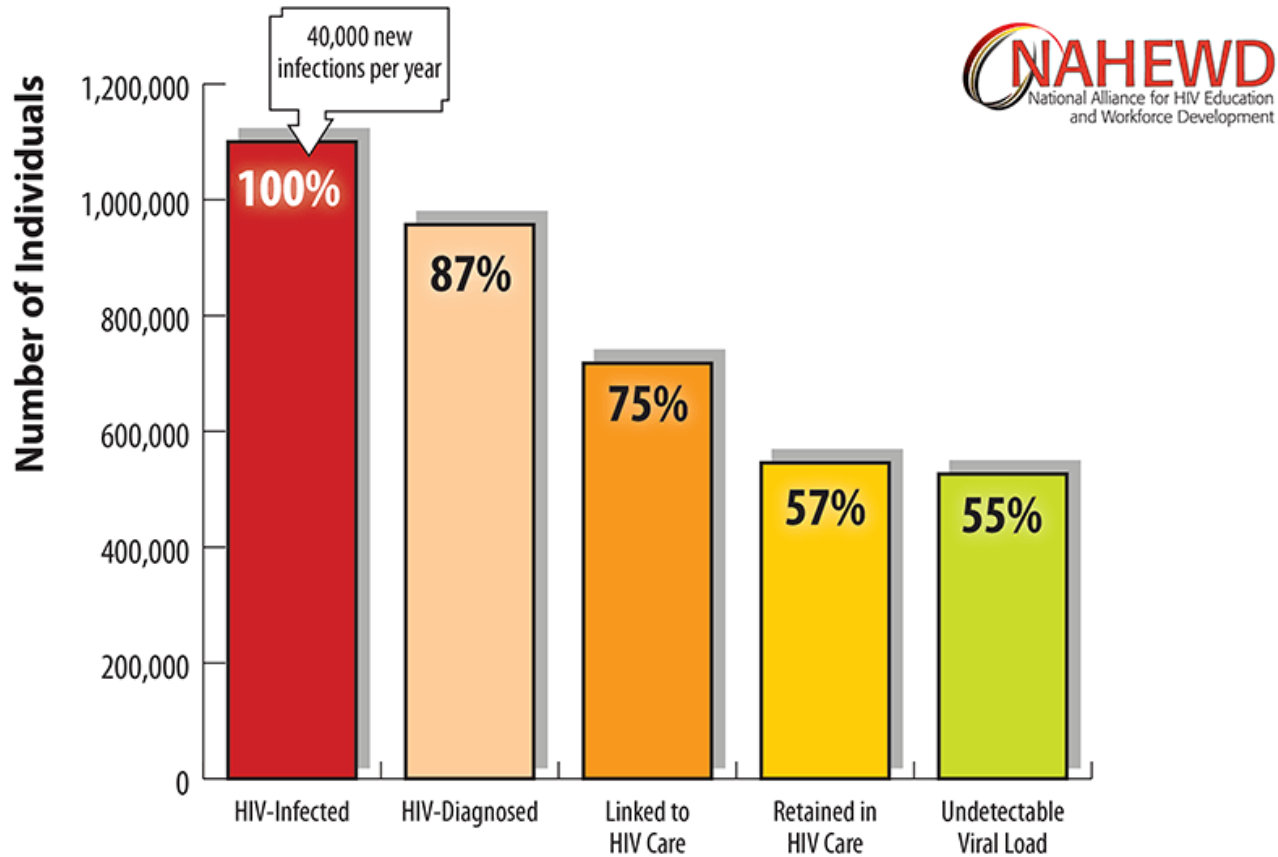


Objectives

- After this presentation the attendee should be able to:
 - Describe current issues in the epidemiology of the HIV epidemic.
 - Describe the life cycle of HIV;
 - Describe the way that HIV interacts with its host, producing disease.
 - Describe the principles of treatment.
 - Describe Acute HIV infection
 - Describe the initial evaluation of an HIV infected patient

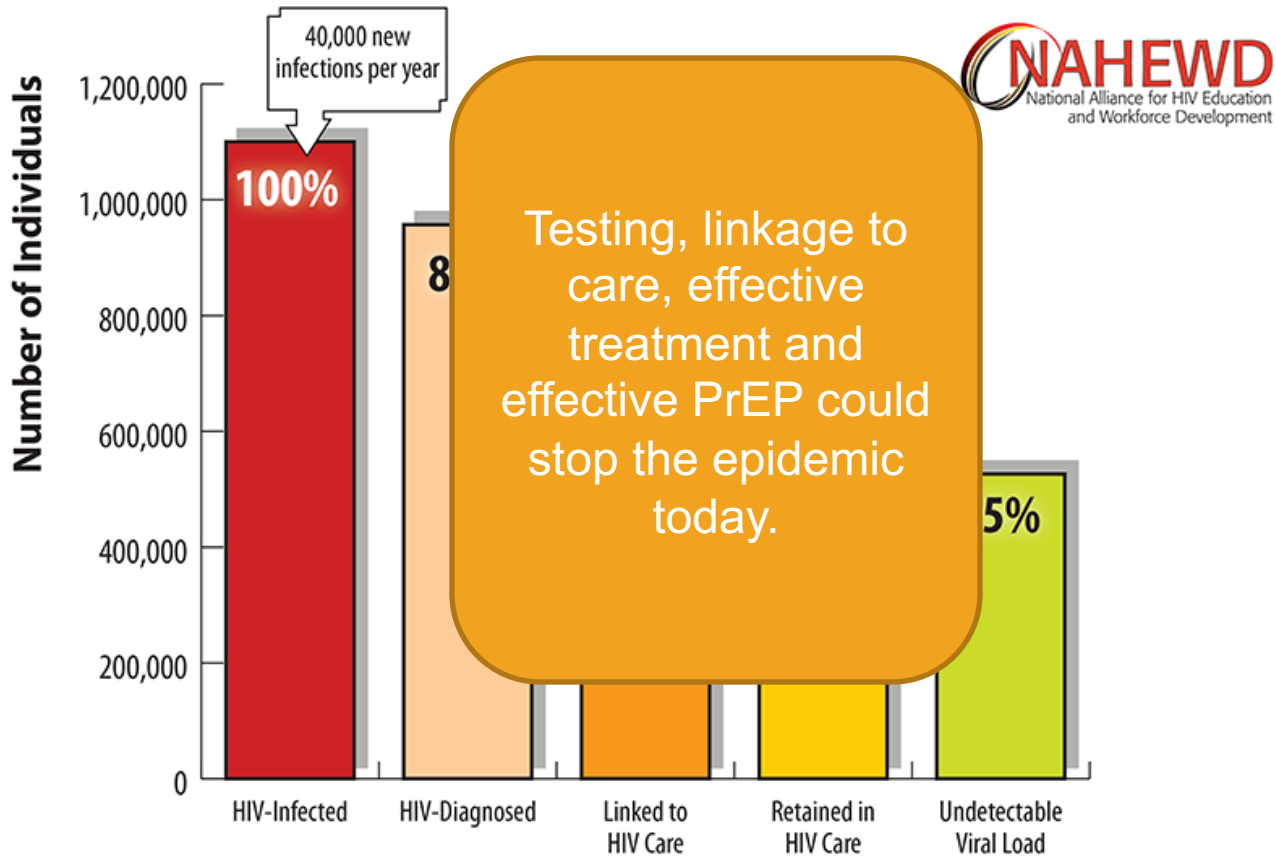


The U.S. HIV Care Continuum¹



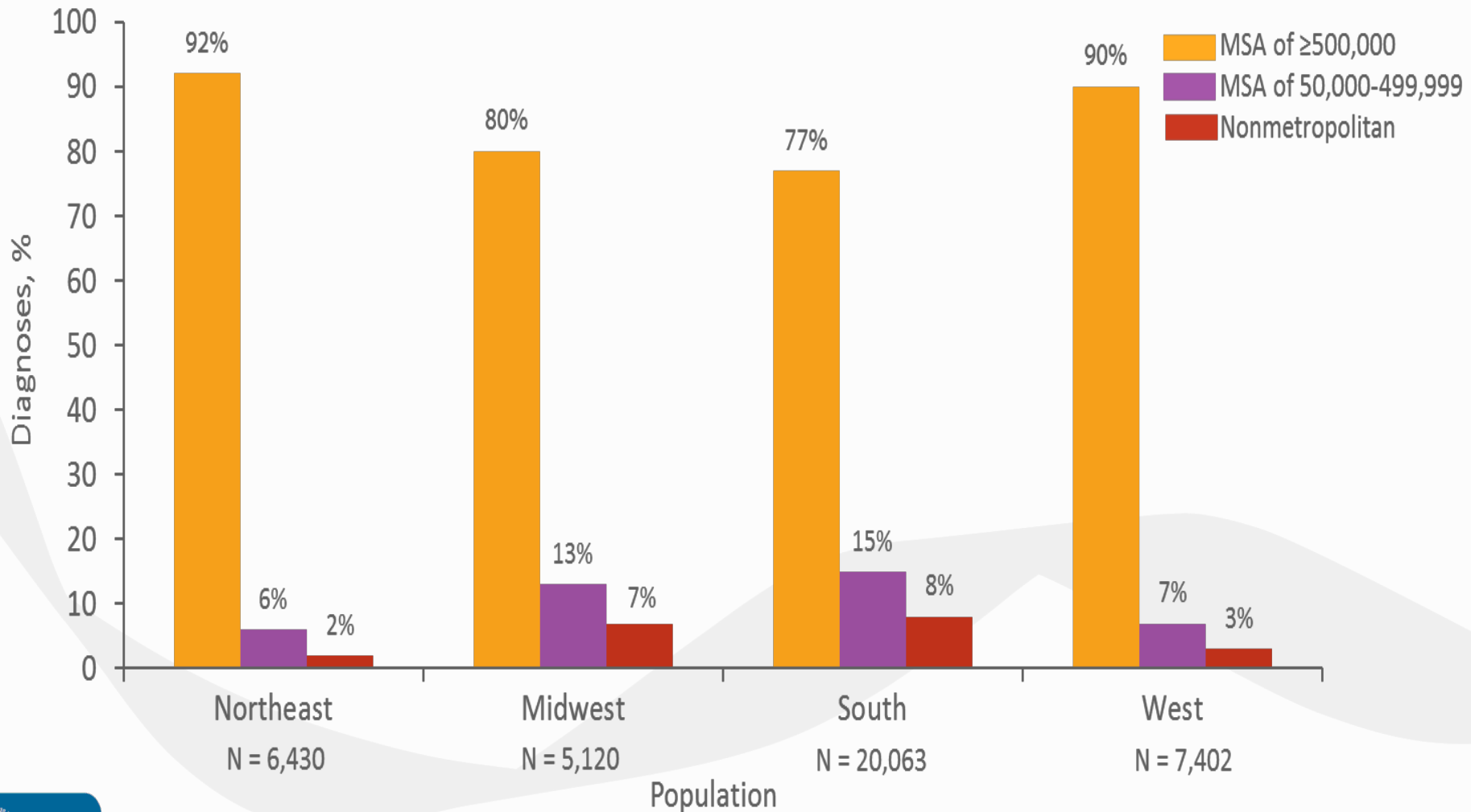


The U.S. HIV Care Continuum¹





Percentages of Diagnoses of HIV Infection among Adults and Adolescents, by Region and Population of Area of Residence, 2015—United States



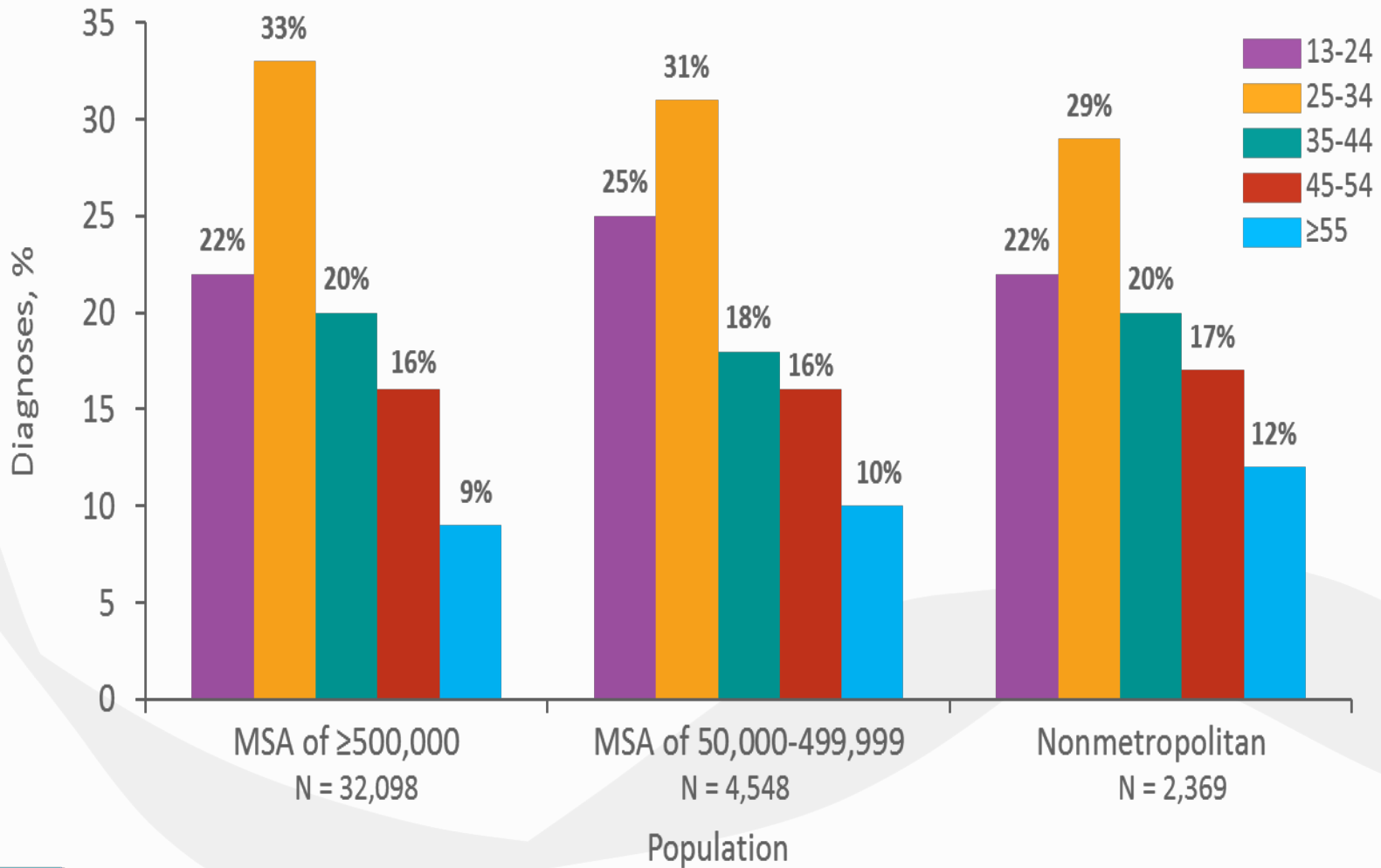
ETC
Southeast

AIDS Education &
Training Center Program

Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. Data for the year 2015 are preliminary and based on 6 months reporting delay. Data exclude persons whose county of residence is unknown.



Percentages of Diagnoses of HIV Infection among Adults and Adolescents, by Population of Area of Residence and Age at Diagnosis, 2015—United States



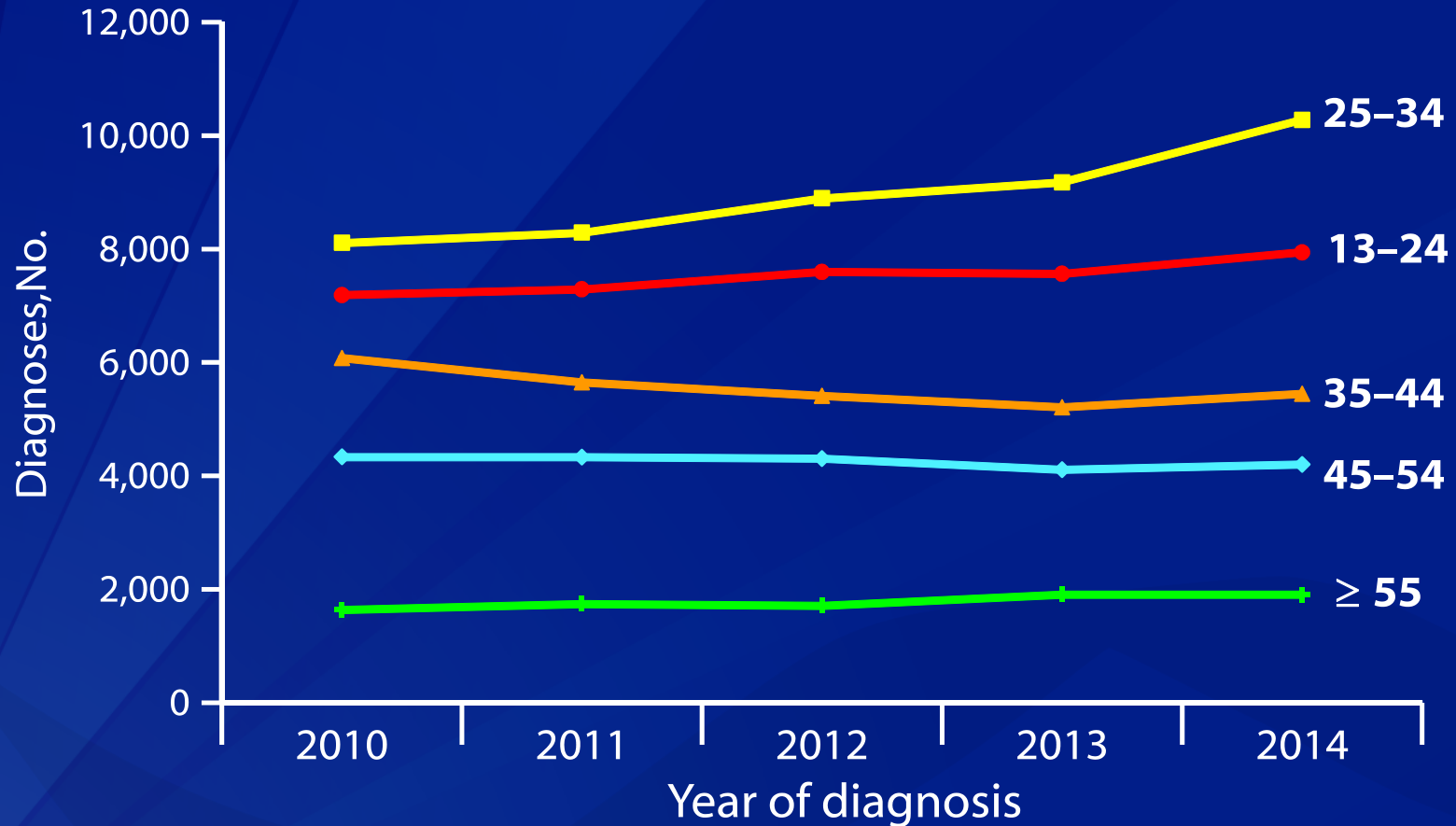
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ETC
Southeast

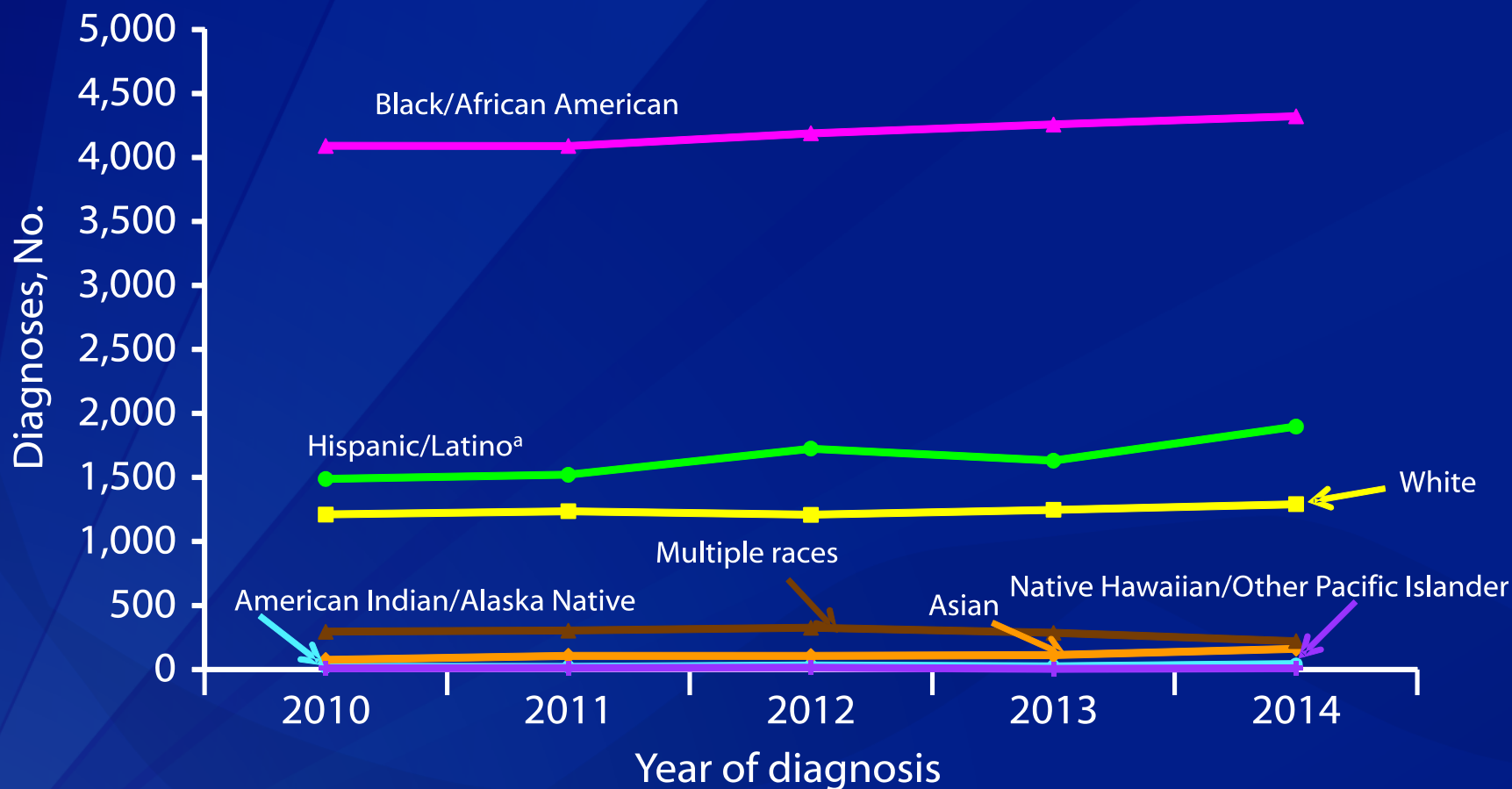


Diagnoses of HIV Infection among Men Who Have Sex with Men, by Age Group, 2010–2014—United States and 6 Dependent Areas



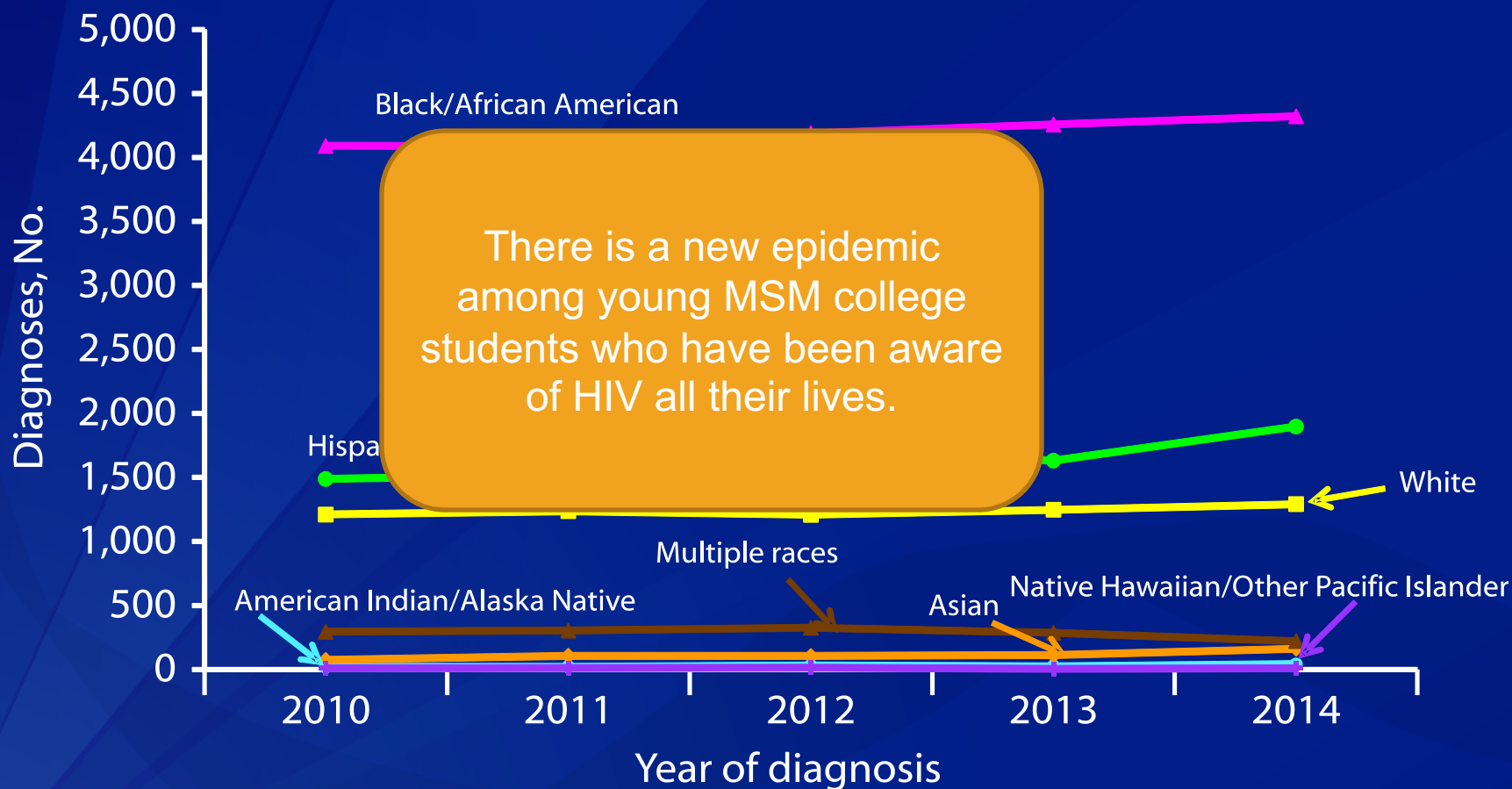
Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing transmission category, but not for incomplete reporting. Data on men who have sex with men do not include men with HIV infection attributed to male-to-male sexual contact and injection

Diagnoses of HIV Infection among Men Who Have Sex with Men Aged 13–24 Years, by Race/Ethnicity, 2010–2014 United States and 6 Dependent Areas



Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing transmission category, but not for incomplete reporting. Data on men who have sex with men do not include men with HIV infection attributed to male-to-male sexual contact and injection drug use.

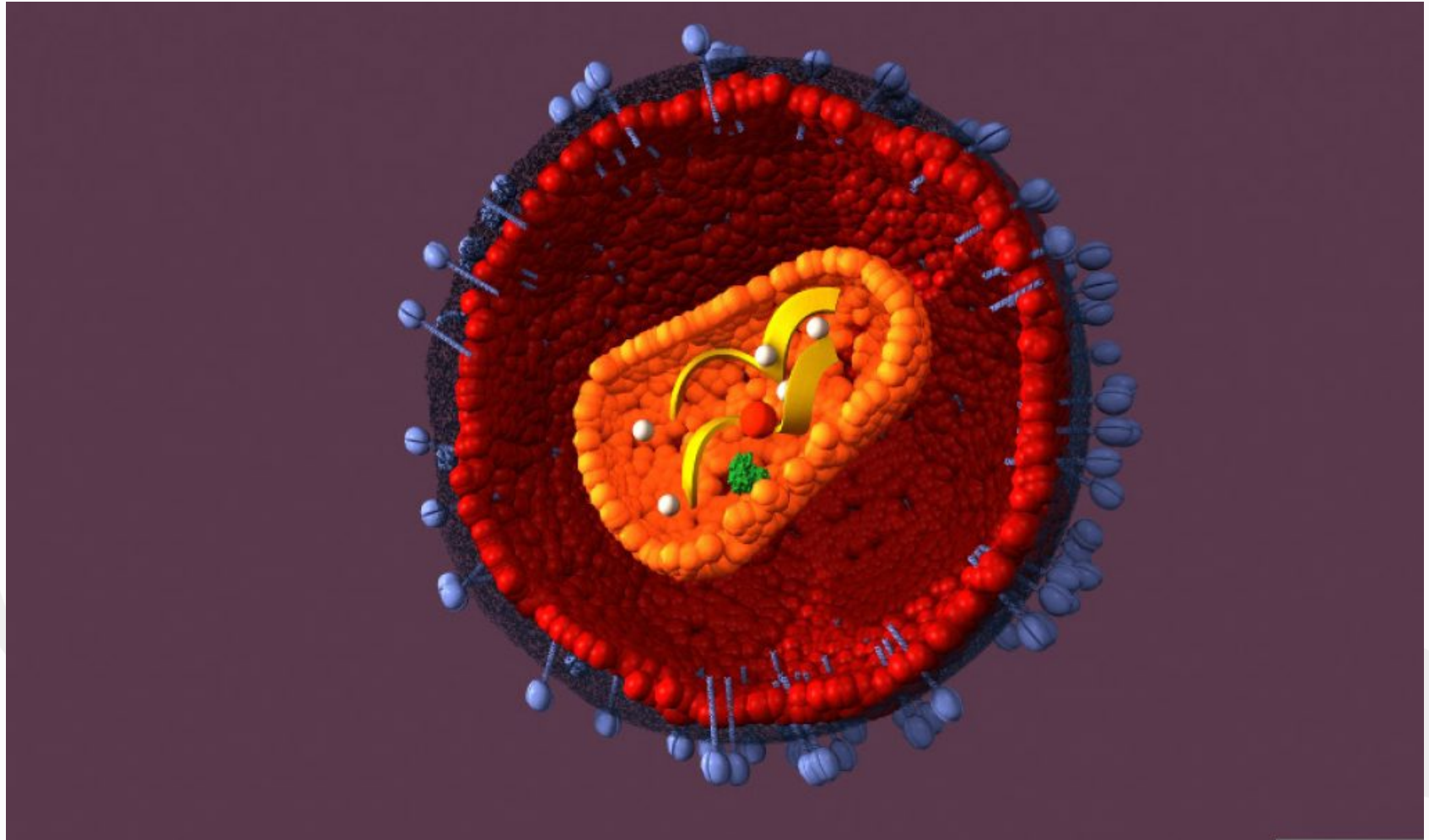
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The Virus





Retroviruses

- **Subfamily Orthoretrovirinae:**
 - Genus Alpharetrovirus; type species: Avian leukosis virus; others include Rous sarcoma virus
 - Genus Betaretrovirus; type species: Mouse mammary tumour virus
 - Genus Gammaretrovirus; type species: Murine leukemia virus; others include Feline leukemia virus
 - Genus Deltaretrovirus; type species: Bovine leukemia virus; others include the cancer-causing **Human T-lymphotropic virus**
 - Genus Epsilonretrovirus; type species: Walleye dermal sarcoma virus
 - Genus Lentivirus; type species: **Human immunodeficiency virus 1**; others include Simian, Feline immunodeficiency viruses
- **Subfamily Spumaretrovirinae:**
 - Genus Bovispumavirus
 - Genus Equispumavirus
 - Genus Felispumavirus
 - Genus Prosimiispumavirus; type species: Brown greater galago prosimian foamy virus
 - Genus Simiispumavirus; type species: Eastern chimpanzee simian foamy virus



Unique Qualities of HIV Infection

- It is a disease caused by a retrovirus:
 - Ubiquitous organisms in nature;
 - Rare cause of human illness;
 - Integration of the proviral genome into the host genome;
- HIV has an unusual relationship with host:
 - Once integrated, latent reservoirs guarantee persistence of infection;
 - Recruits immune cells that are essential for replication;
 - Enormous diversity in host response to HIV infection

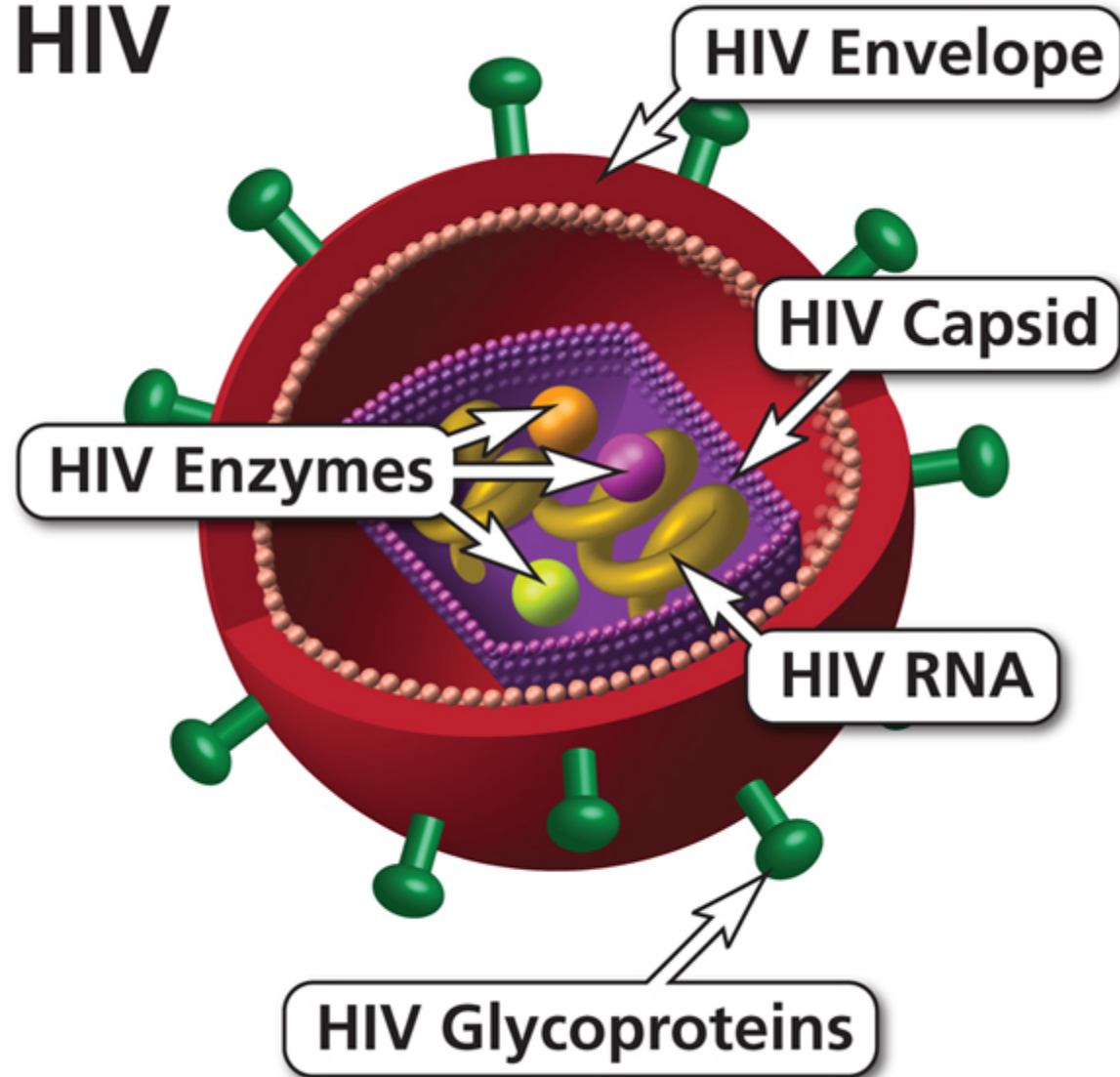


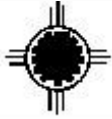
Unique Qualities of HIV Infection

- HIV is a small, fragile and error prone virus:
 - Not especially infectious as a communicable disease;
 - Every mutation in the viral genome can and will occur in the setting of drug pressure.
 - Swarms will occur over time and strains will be archived.
 - It is very sensitive to available antiviral agents.

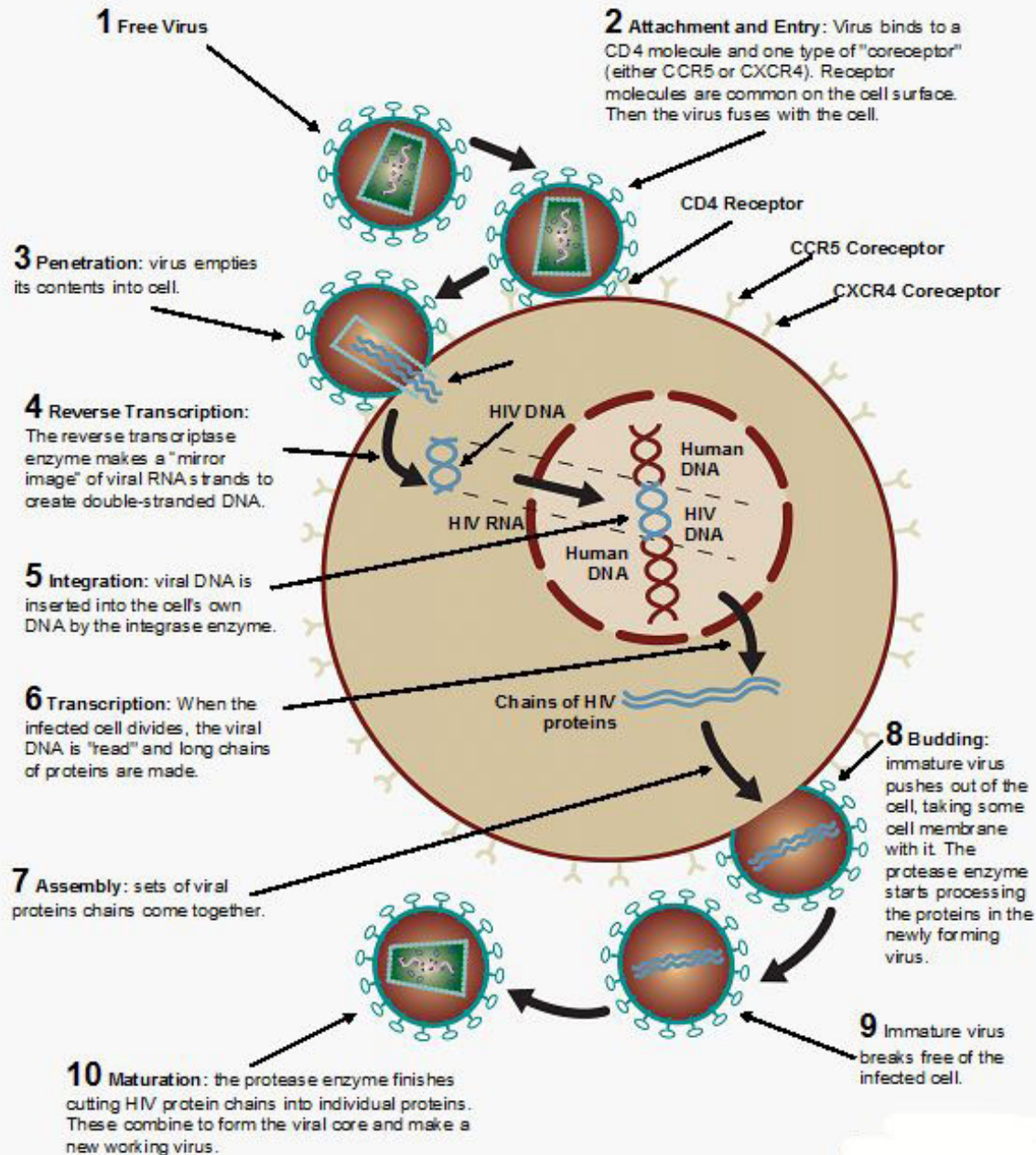


HIV



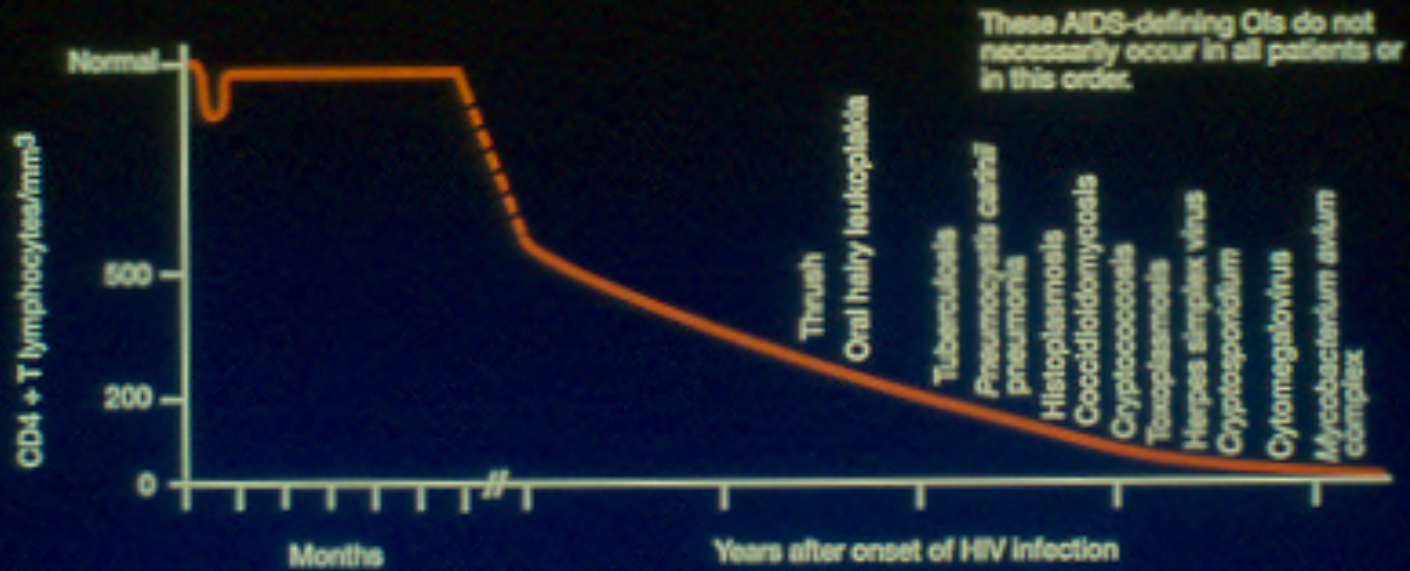


HIV LIFE CYCLE

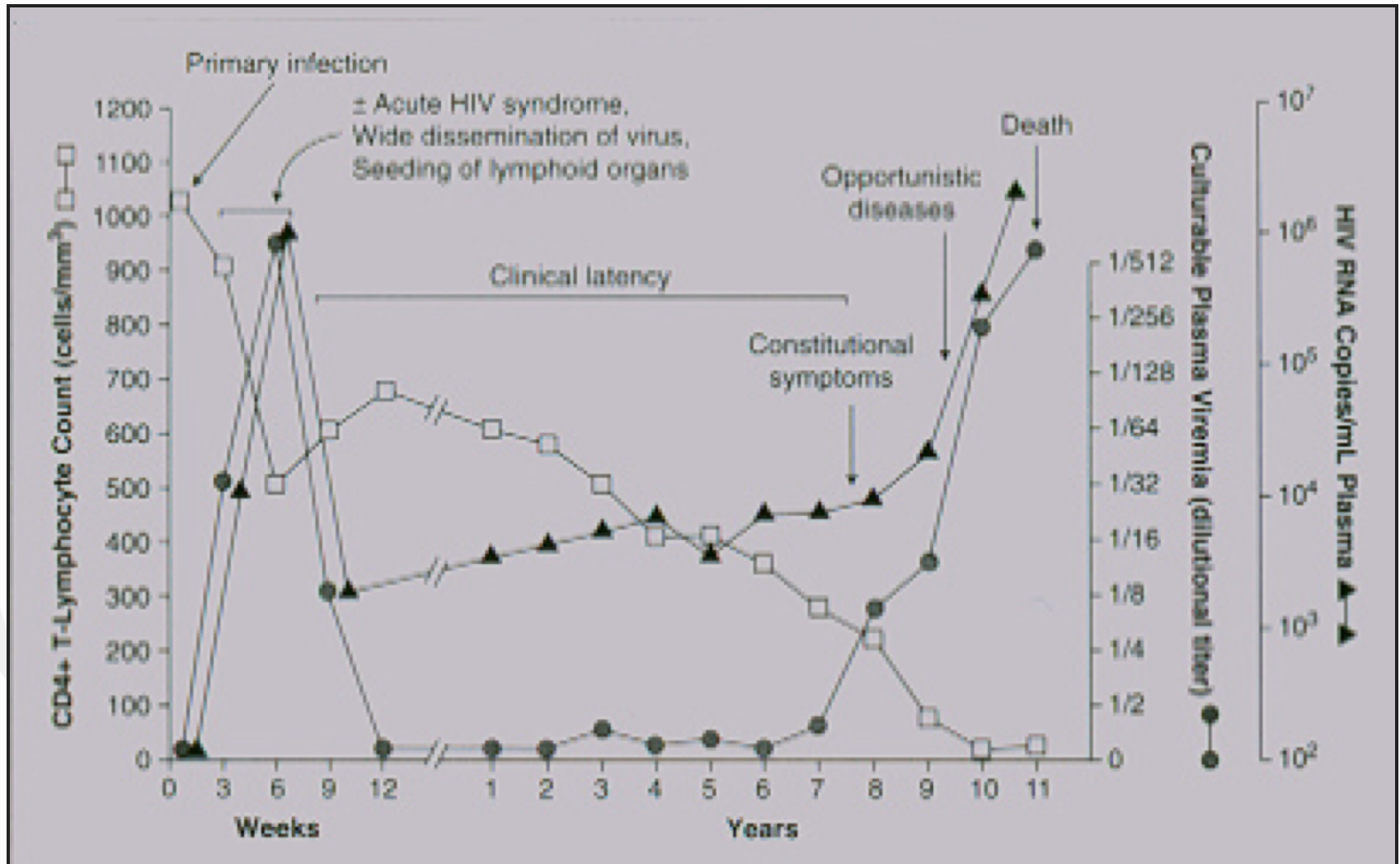


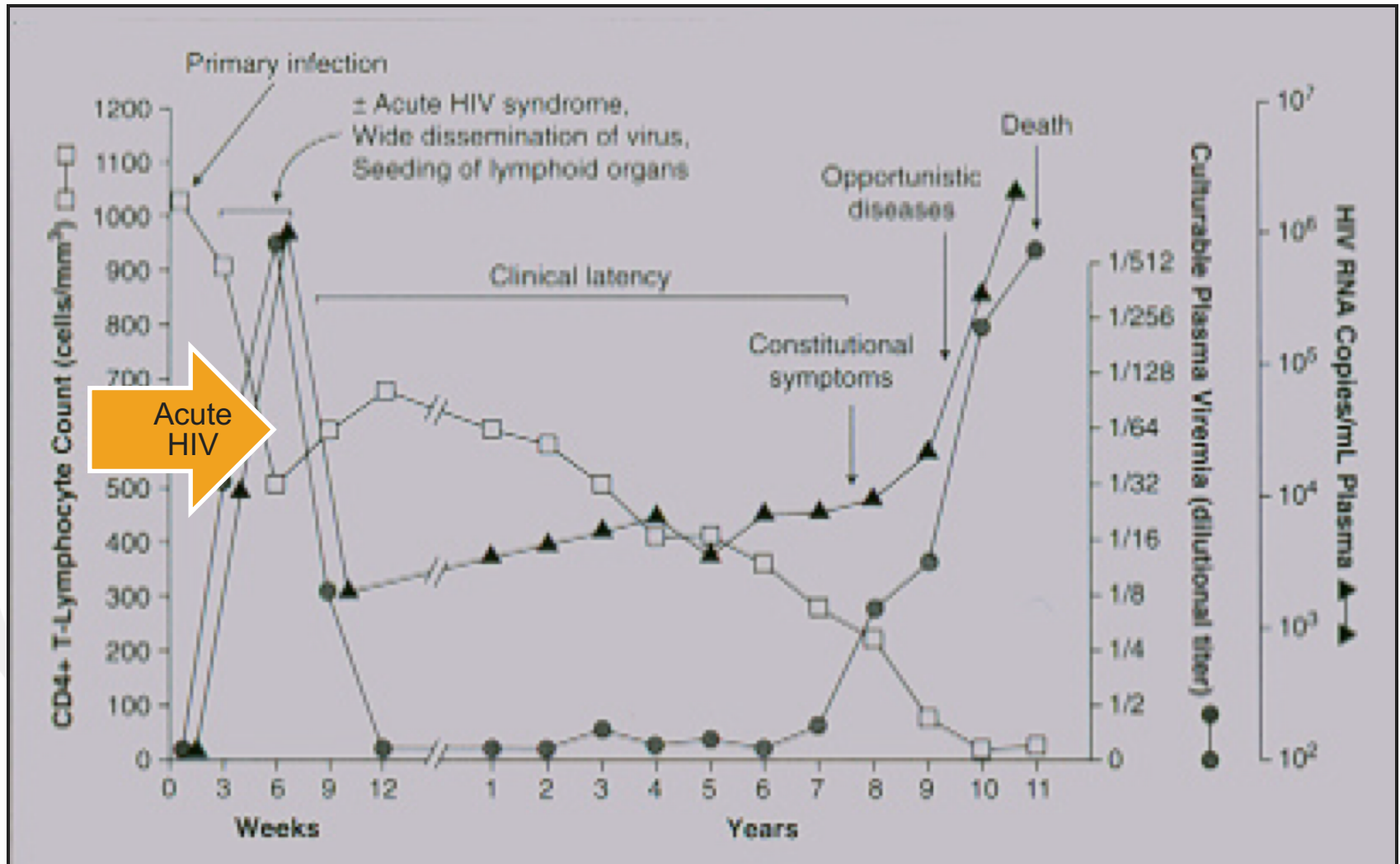


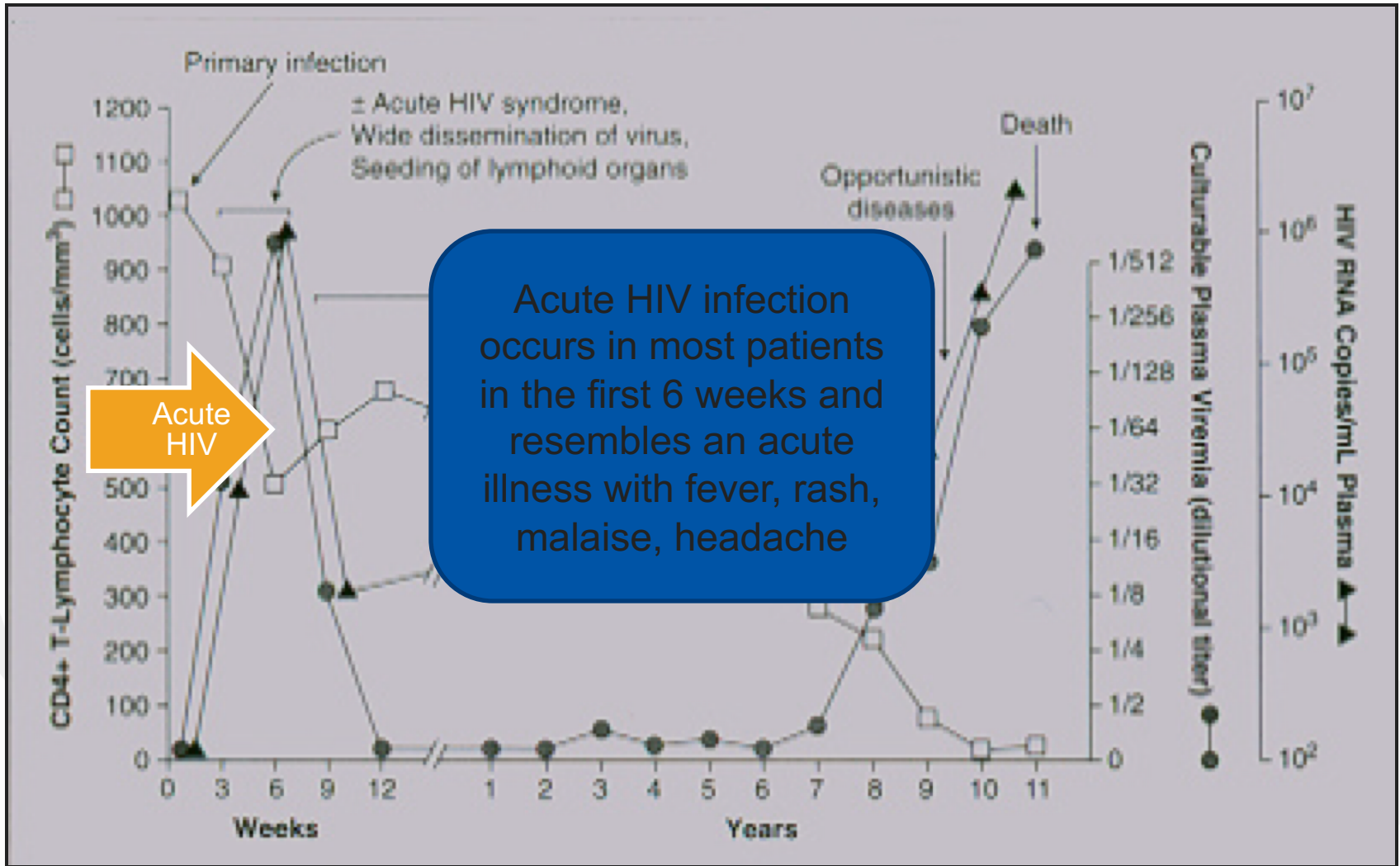
Opportunistic Infections in HIV Disease



This graph is idealized. Specific OIs can occur earlier/later and at higher/lower CD4 cell counts.



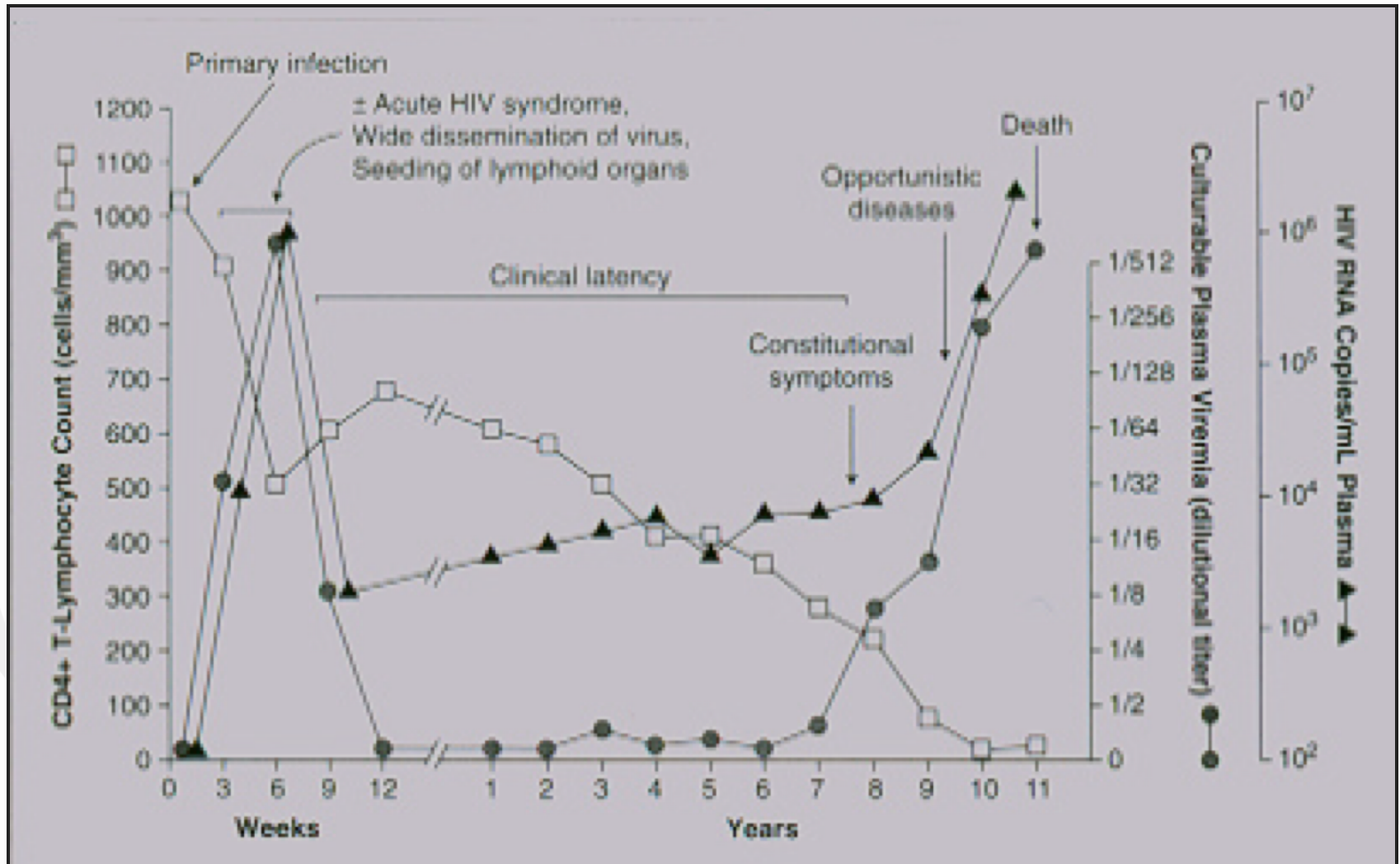


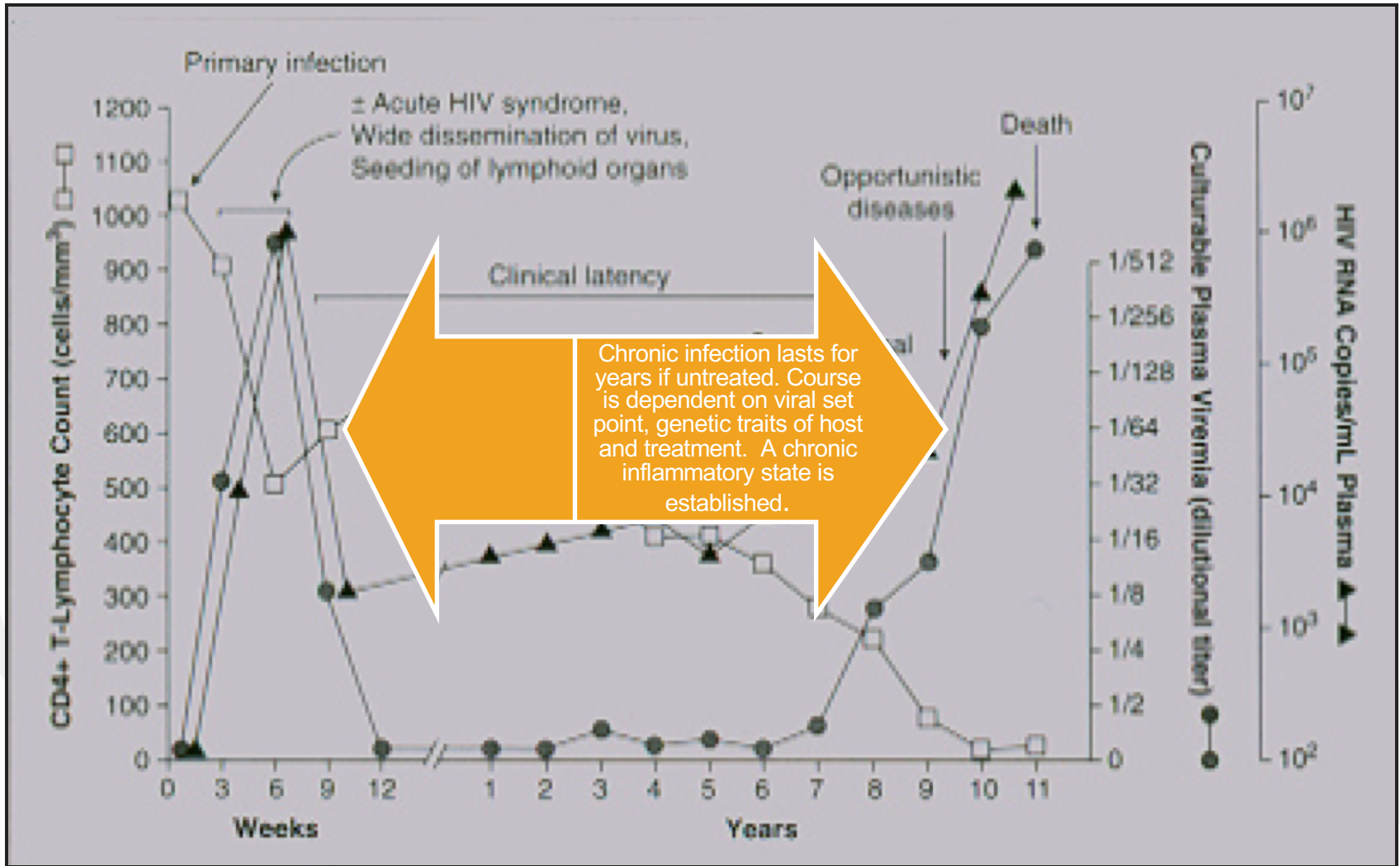




HIV Pathogenesis

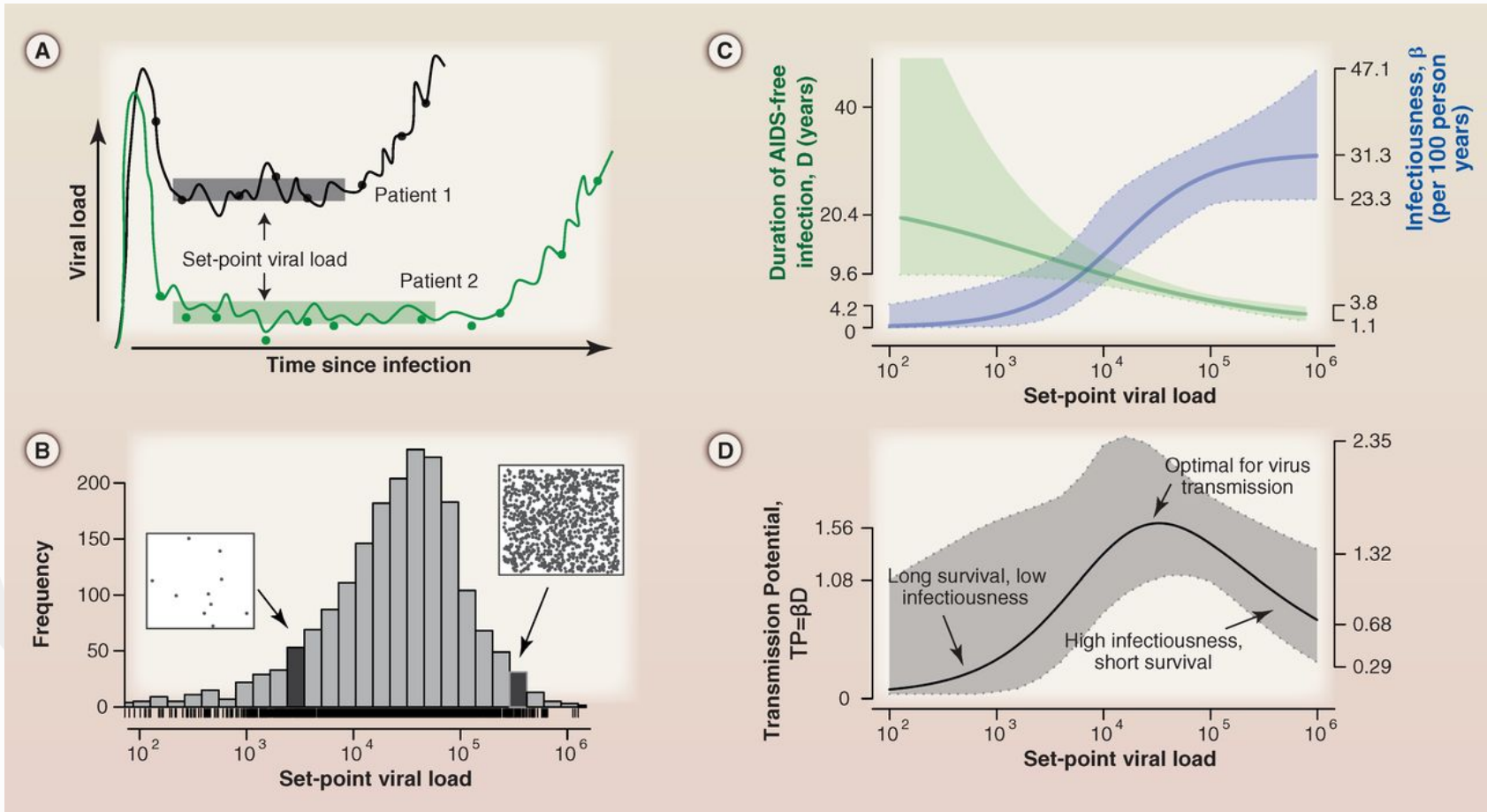
- HIV infection disseminates quickly in the host and causes disease in almost all patients, if left untreated.
- Although thought of as an “Immune Deficiency “ disease, other critical factors are involved in generating poor outcomes for patients.
- Effective treatment of HIV ameliorates much of the damage done by the virus.







HIV Pathogenesis





Treatment



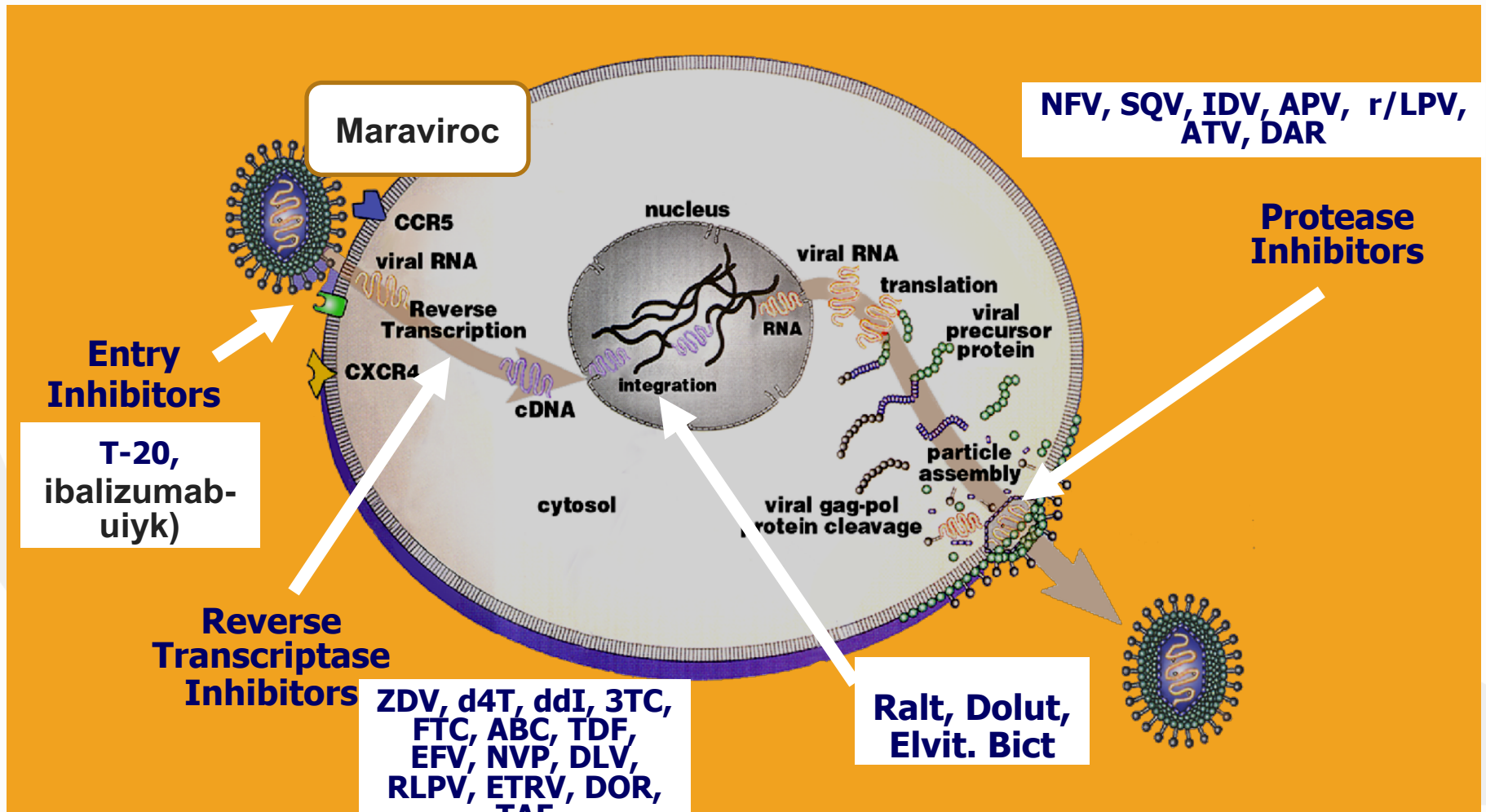


Three Decades of Treatment Issues

- **1980's**: AIDS described, PCP kills 90% of pts., clinicians develop skills in diagnosing, treating and preventing complications.
- **1990's**: First effective treatments, patients respond, death rates drop.
- **2000's**: New toxicities arise, resistance is critical, adherence issues emerge, limitations of therapy become apparent.
- **2007**: Second round of effective antiretroviral agents-integrase and CCR5 inhibitors.
- **2013**: Serious talk of “cure”.
- **2015**: PrEP



Targets for HIV Inhibition





Current Available Medications

- **NRTI's**: zidovudine, didanosine, stavudine, lamivudine, abacavir, emtricitabine, tenofovir, TAF
- **NNRTI's**: efavirenz, nevirapine, delavirdine; etravirine, rilpivirine, doravirine
- **PI's**: indinavir, ritonavir, saquinavir, nelfinavir, fosamprenavir, lopinavir, atazanavir, tipranavir, darunavir
- **Fusion I's**: enturvidine,
- **CD4 Binding**: ibalizumab-uiyk
- **CCR5 I's**: maraviroc
- **Integrase I's**: raltegravir, dolutegravir, elvitegravir, bictegravir



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- **NNRTI's:** efavirenz, rilpivirine
- **PI's:** indinavir, zalcitabine, tipranavir, darunavir, atazanavir, lopinavir, nelfinavir
- **Fusion Inhibitors:** maraviroc
- **CCR5 Inhibitors:** vicriviroc
- **Integrase I's:** raltegravir, dolutegravir, elvitegravir, bictegravir

Currently most patients can be treated with one or two pills a day. New treatment modalities may include long acting injectables and immune enhanced therapies.



- Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents
 - <https://aidsinfo.nih.gov/guidelines>



Guidelines for HAART

- Updated regularly by group of experienced HIV treaters, researchers and virologists.
- Recommendations are graded based on quality of evidence.
- New medications or new critical findings are quickly incorporated into guidelines.
- Room is left for individual interpretation.
- Available as easy to use app's.



Treatment Principles

- Most treatment regimens try to utilize three active agents.
- Most HAART regimens are one or two pills a day.
- Overlapping toxicities and potential resistance should be avoided.
- Drug interactions are a significant concern.
- Response to treatment is measured by drop in HIV 1 RNA (viral load) and ultimately increase in CD4+ cell numbers.



Benefits of Treatment

- Treating people with AIDS greatly improves survival and quality of life.
- Treating people with advanced HIV (200-350 CD4 count) **may** delay disease progression and improve quality of life.
- Treating people with early HIV (>350 CD4 count) **may** delay progression of disease and preserve immune function.
- Treating HIV may have important benefits independent of immune function preservation.



Benefits of Treatment

- Treating people with AIDS greatly improves survival and quality of life.
- Treatment may improve quality of life.
- Treatment may delay the progression of immune function.
- Treating HIV may have important benefits independent of immune function preservation.

Why Treat all patients?

- 1) Medications are much less toxic.
- 2) Treating HIV slows the inflammatory process.
- 3) Treating HIV decreases the risk of transmission.



James

- 19 year old college freshman, presents to ED with fever, slight headache, some rash and cough.
 - Slightly elevated LFT's, CXR clear.
 - Sent home with OTC recs for fluids and antipyretics.
- Back to the ED 48 hours later, continued fever, severe malaise and myalgias.
 - HIV serology indeterminate, HIV-1 RNA 2,466,303 copies/ml



James

- 19 year old college freshman, presents to ED with fever, slight headache, some rash and cough
 - Slightly elevated liver enzymes
 - Sent home with acetaminophen and NSAIDs for fever, severe malaise and cough
- HIV serology positive, viral load 466,303 copies/ml

James grew up in a small town in East TN. His family PCP knew him well but when James asked him to consider prescribing PrEP, he declined, saying he did not feel comfortable prescribing it.



James

- Intake labs:
 - CBC, CMP, UA, wnl;
 - Treponemal, Toxoplasma serology negative;
 - HAV serology shows positive IgG, negative IgM;
 - HBV serology shows positive IgG, >20;
 - Urine screen for GC/Chlamydia negative;
 - CD4 count 443/22%;
 - HLA B2701: negative;
 - HIV 1 Genotype shows wild type.
- Physical exam:
 - No abnormal findings, some anxiety regarding diagnosis.
- Other:
 - No co-morbidities, on no meds. No known medication allergies. Family is supportive.



James

- Intake labs:

- CBC, CMP, UA, wnl;

- T

- Provider provides detailed discussion of HIV pathogenesis, treatment and ongoing healthcare issues.

- Living with HIV is discussed.

- Transmission risks and strategies to decrease transmission risk as well as sexual health issues are reviewed.

- STI screening for oral and anal exposure is obtained.

- **Patient feels he is ready for treatment of his HIV infection.**

- Options discussed include TAF/FTC/Bictegravir (Biktarvy);

- abacavir/lamivudine/dolutegravir (trumeq);

- TAF/FTC/elvitegravir/cobicistat (Genvoya)

- Physical exam:

- No abnormal findings, some anxiety regarding diagnosis



James

- Intake labs:

- CBC, CMP, UA, wnl;

- T

Provider provides detailed discussion of HIV pathogenesis, treatment and ongoing healthcare issues.

Lifestyle discussed.

Transmission risk well reviewed.

STI screen is obtained.

Patient feels he is not an issue with his HIV infection.

Options discussed include Bictegravir (Biktarvy);

abacavir/lamivudine/dolutegravir (trumeq);

TAF/FTC/elvitegravir/cobicistat (Genvoya)

- Physical exam:

- No abnormal findings, some anxiety regarding diagnosis



James

- James agrees to starting TAF/FTC/bictegravir, one pill per day.
 - He meets with the RN CPS Case Manager who reviews treatment goals, potential side effects, adherence issues and how to contact us in case of issues with the medication.
 - The prescription is sent to the pharmacy of the patient's choice and the CPS RN calls to make sure there are no issues getting the medication filled.
- James is scheduled back in 4 weeks.
 - He has repeat CMP, and HIV 1 RNA done. Repeat STI screenings were negative.
 - HIV 1 RNA is now 942 copies/ml.
 - He will return in 8 weeks for follow up labs and then on follow up will be directed by his response to therapy and will ultimately be seen twice a year.



AIDS 1985- One Patient's Experience

- 322 IV insertions
- 14 hospital admissions
- 11 months of hospital stay
- 60 phlebotomies
- 32 chest x-rays
- 5 CT scans of head
- 3 abdominal ct scans
- 6 bronchoscopies
- 8 intubations
- 4 lumbar punctures
- 3 bone marrows
- 5 cycles of chemo
- 2 lymph node bx



AIDS 1985- One Patient's Experience

- 322 IV infections
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- 11 months in hospital
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- 6 bronchoscopies
- 2 lymph node bx
- 2 bone marrow punctures
- 2 bone marrow biopsies
- 2 cycles of chemotherapy

Pablo never received a medicine to treat his HIV or prevent any of the complications of AIDS.



Useful HIV Websites

www.vanderbilthealth.com/vccc

www.aidsinfonet.org

www.aidsetc.org

www.hivatis.org (DHHS, USPHS/IDSA Guidelines)

www.cdc.gov/nchstp/hiv_aids.htm

www.hiv-web.lanl.gov (Resistance mutations)

www.niaid.nih.gov

www.AIDS.medscape.com

www.hopkins-aids.edu

www.iapac.org

www.igm.gov

www.centerwatch.com

www.ucsf.edu/medical

www.virology.net



Useful HIV Websites

www.vanderbilthealth.com/vccc

www.aidsinfonet.org

www.aidsetc.com

www.hivatis.com

www.cdc.gov

www.hiv-we.com

www.niaid.nih.gov

www.AIDS.gov

www.hopkins.edu

www.iapac.org

www.igm.gov

www.centerwatch.com

www.ucsf.edu/medical

www.virology.net

WWW.SEAETC.COM



Questions?

