



Improving People's Lives Through Innovations in Personalized Health Care

# An HIV Update - 2019

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The goal of this program is to provide a review and update of HIV care and to provide a forum for discussing the current local and national trends around the management of HIV.



In English, please!



# What does **HIV** stand for?

**H**uman

**I**mmunodeficiency

**V**irus

*Only humans can get this.*

Your immune system, which helps the body fight disease isn't working the way it should.

A tiny particle that causes infections by entering a cell and making copies of itself.

# What does **AIDS** stand for?

**Aquired**

You got this from someone else.

**Immuno-Deficiency**

Your immune system, which helps the body fight disease isn't working the way it should. It is deficient.

**Syndrome**

Cluster of signs and symptoms, may be specific to certain illnesses.

# Definitions

**CD4 Cells aka T-Helper Cells** – a subgroup of white blood cells that play role in maximizing capabilities of immune system

- Target of HIV

**Normal CD4 values between 500 and 1500**

- $> 500$  normal risk for infections
- $200 - 500$  increased risk for infections
- $< 200 =$  severe compromise (AIDS diagnosis), at risk for potentially fatal infections



# Definitions

## Viral Load

- Amount of virus in the body, copies/ml blood
- “High” vs “Low”

## ART – Antiretroviral Therapy

- HIV medications
- ARV – Antiretrovirals
- HAART vs ART



# HIV Transmission

- HIV infection occurs through contact with infected blood and body fluids via occupational and non-occupational exposures.

## YOU CAN GET HIV VIA...



Sex without  
a condom



Passed from  
mother to baby



Sharing injecting  
equipment



Contaminated blood  
transfusions &  
organ transplants



# HIV IS **NOT** TRANSMITTED BY...



Insect bites



Toilet seats



Kissing



Sharing cutlery



Touching

# HIV Transmission

- **Sexual Transmission**
  - Receptive anal intercourse is the highest risk
  - Vaginal sex less risky than anal sex
- **Injection Drug Use/Exposure to Contaminated Blood**
  - > 16 million injectors worldwide
  - US blood supply considered safe
  - Body piercing, acupuncture and tattooing via contaminated needles are rare causes
- **Mother to child, *including* through breastfeeding**
  - In utero, around delivery or after birth during breastfeeding
  - Prophylaxis or treatment with ART drastically reduced vertical transmission rate



# HIV Prevention

- Male circumcision reduced HIV infection by as much as 60% (female to male)
- Vaccine development has been disappointing
- Reduce risky behaviors
  - “Safer sex” practices should be encouraged
  - Condoms - Latex condoms protect against HIV and STDs (having an STD ↑ risk of acquiring and transmitting HIV)
  - PrEP (pre-exposure prophylaxis) programs
  - Needle exchange programs



# HIV Treatment as Prevention

- HIV-positive persons with an undetectable HIV VL > 6 months on ART are unlikely to transmit HIV to their sexual partners
- **HPTN 052**
  - Sero-discordant couples where one partner is positive and other is negative
  - 5 year HIV transmission rate was virtually nil if an undetectable HIV viral load was achieved

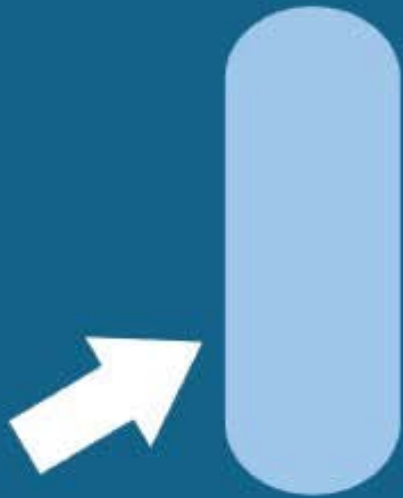


**#UequalsU**

**ScienceNotStigma**

# PrEVENTION

**in a pill.**



Taking a once-daily pill can reduce your risk of contracting HIV by more than 90%.

# Pre-exposure Prophylaxis (PrEP)



- **Approved since July 2012**
  - **MSM**
  - **Discordant adults**
  - **Injection drug users**
  - **Heterosexually active adults**
- **PrEP is most effective as part of a comprehensive prevention package including safer sex with condoms and behavior modification to reduce risky behavior.**

# The Global HIV/AIDS Epidemic



**36.7 MILLION**

people worldwide are currently living with HIV/AIDS.

**2.1 MILLION  
CHILDREN**

worldwide are living with HIV. Most of these children were infected by their HIV-positive mothers during pregnancy, childbirth or breastfeeding.





# The Global HIV/AIDS Epidemic

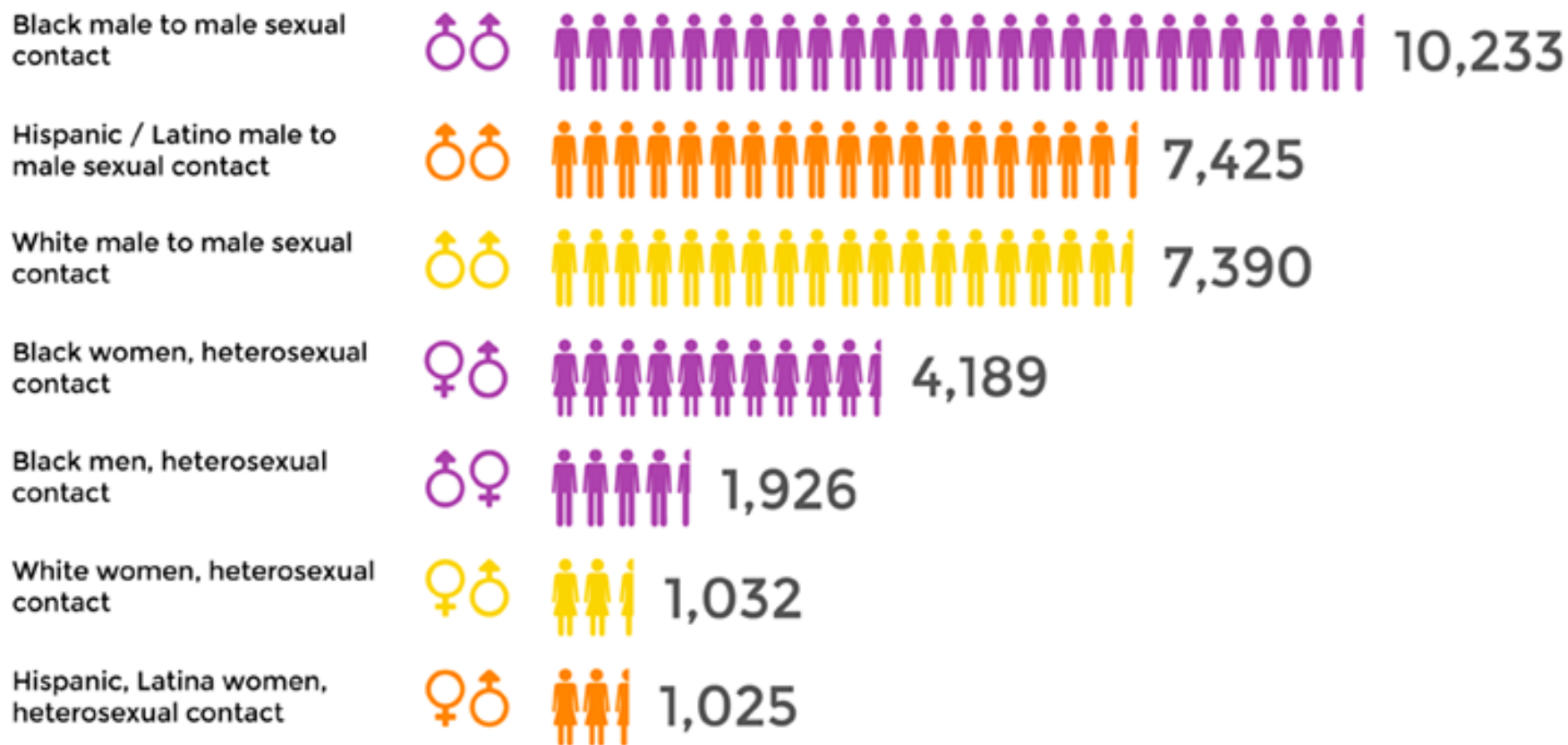
- 95% of new infections occurs in low- and middle-income countries, particularly sub-Saharan Africa
- Affects most productive years of life, half of new infections are in those under 25 years of age
- Most new infections are **heterosexually** transmitted
  - Varies by country - some countries most cases are by MSM or injection drug users
  - Women represent about **half of people living with HIV**



# HIV in the United States

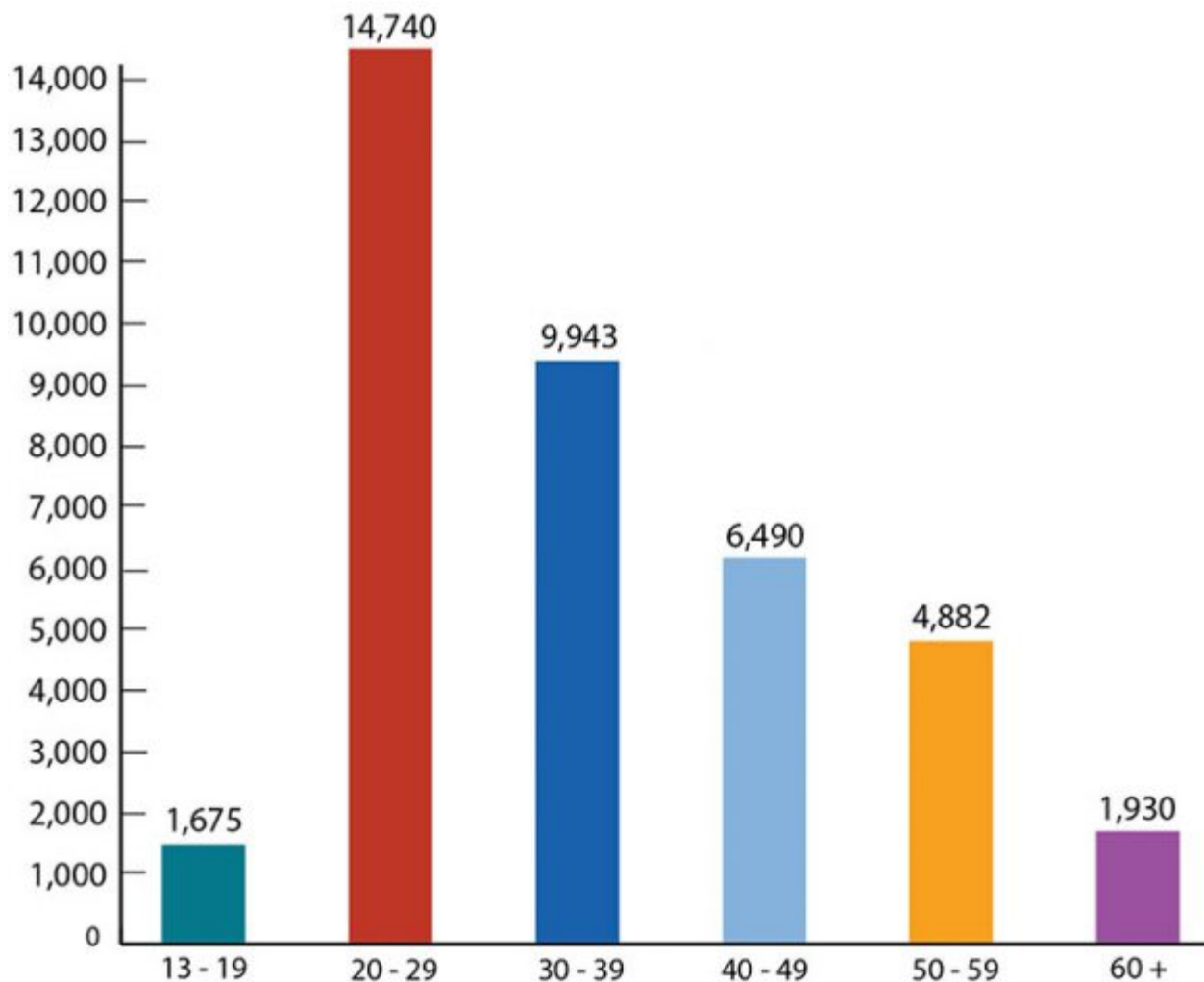


## New HIV diagnoses for the most-affected sub-populations, 2016

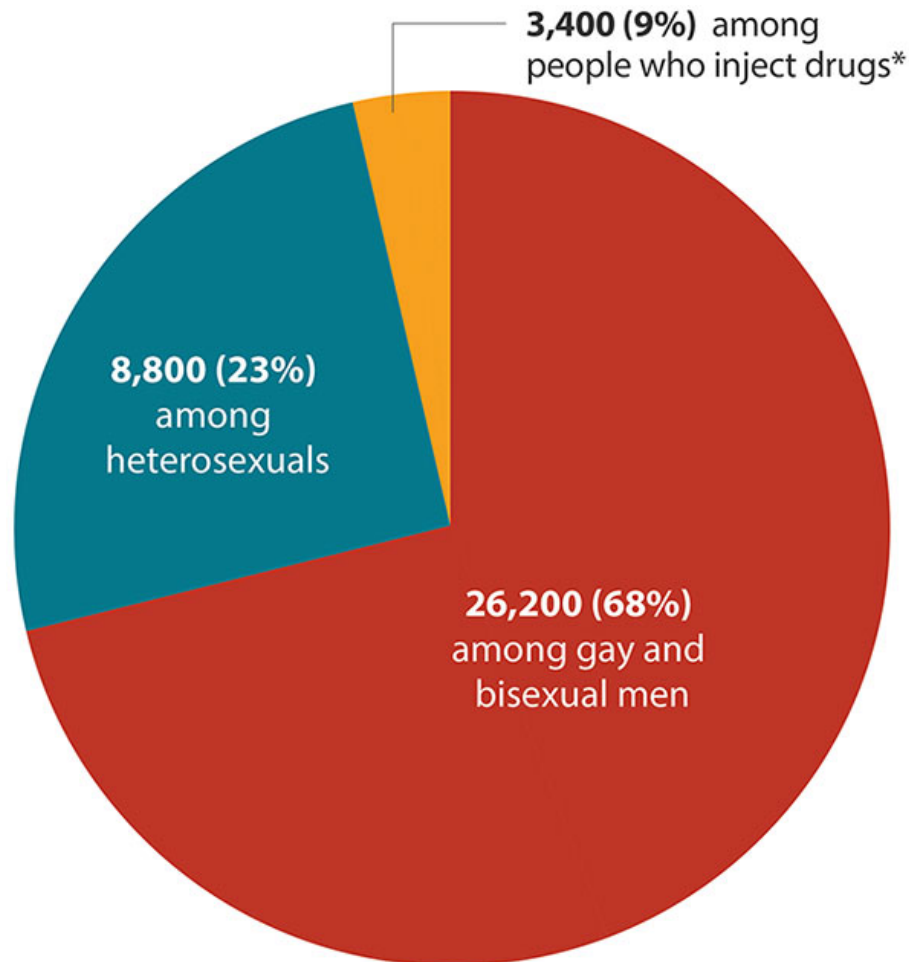


Source: CDC, HIV Surveillance Report 2017

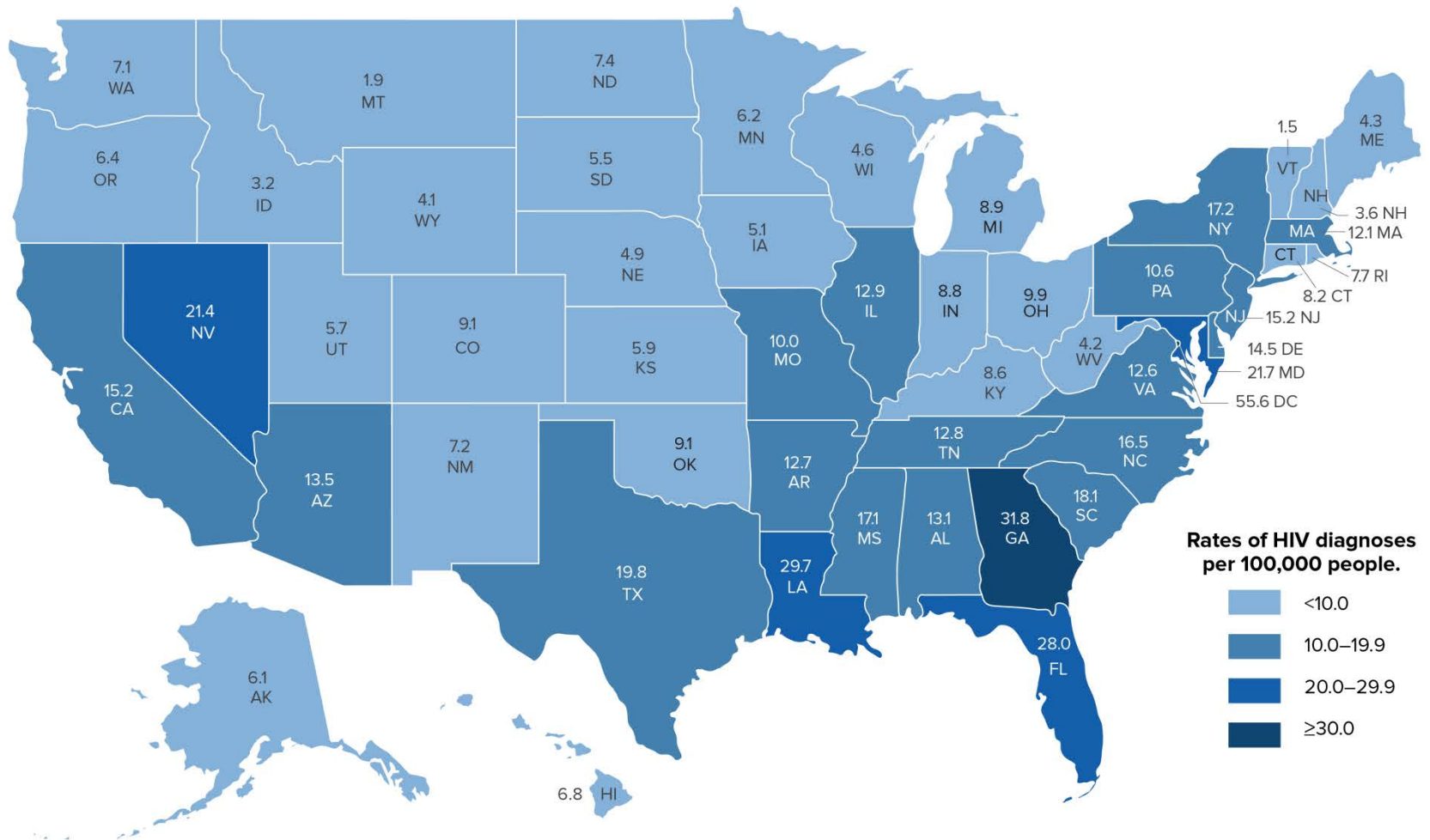
# New HIV Diagnoses in the United States by Age, 2016



# Estimated New HIV Infections in the United States by Transmission Category, 2015



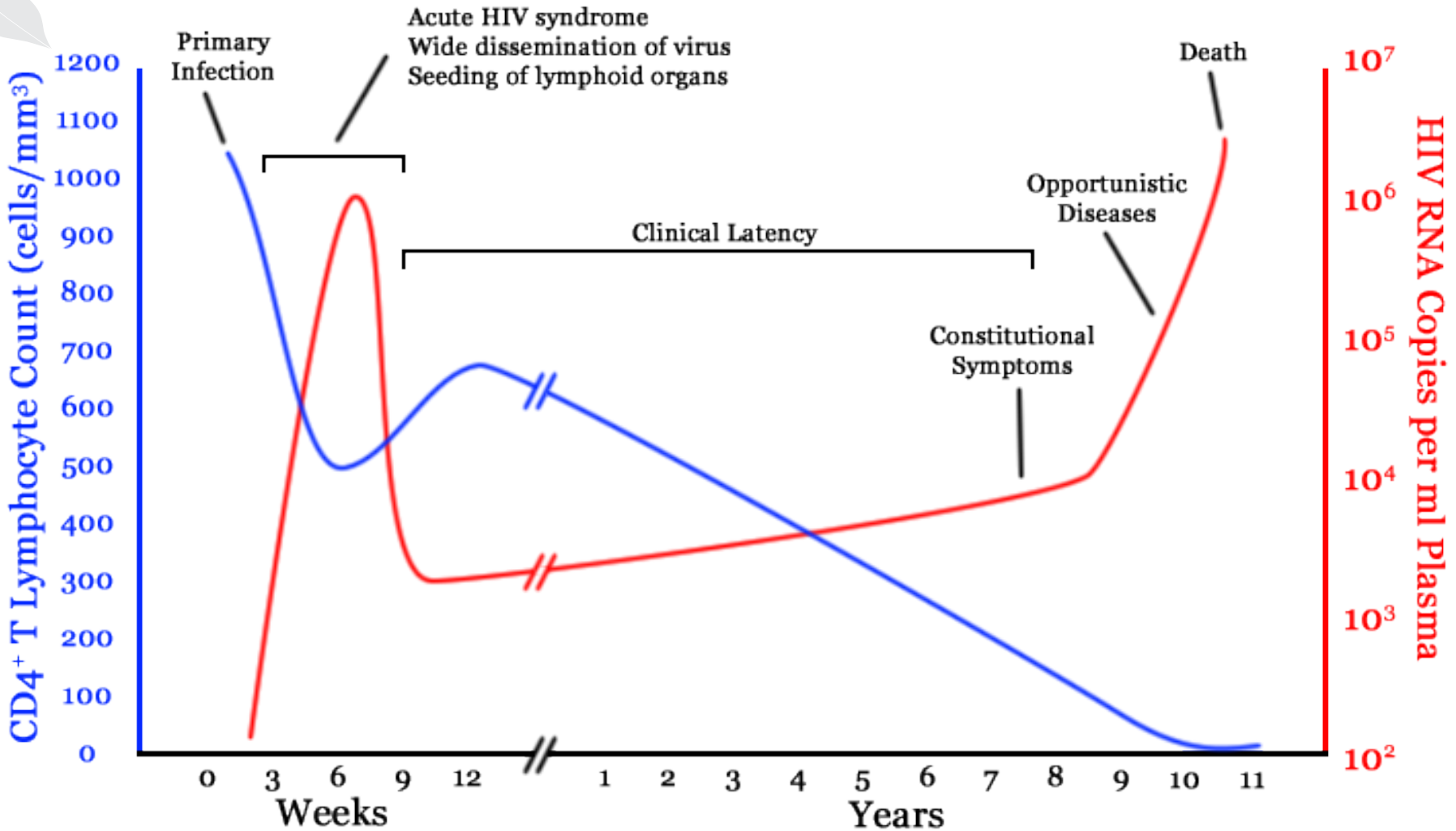
# Rates of HIV Diagnoses Among Adults and Adolescents in the US by State, 2016



# HIV Fast Facts

- ~ 1.2 million people in the US; 1 in 7 are unaware
- MSM, esp. young, black MSM, most affected by HIV
- African Americans face the most severe HIV burden
- The annual # of new HIV diagnoses has remained stable in recent years.
- If taking antiretroviral therapy (ART)
  - Survival is improved on ART
  - Life expectancy is still lower; accelerated aging?
  - HIV infection can be managed as chronic disease
- Pre-and post-exposure ART prophylaxis
  - Can reduce HIV transmission
  - False sense of security about becoming infected?

# Untreated HIV





# Treatment Goals

- Reduce HIV-related diseases; prolong duration and quality of survival
- Restore and/or preserve immunologic function (as indicated by CD4 count)
- Maximally and durably suppress HIV viral load
- Prevention of HIV transmission



## When to start ART?

- Based on **RESEARCH**, the recommendation is:
  - **ART for all HIV-1 infections regardless of CD4 cell count**

### **This will:**

- **Reduce morbidity and mortality associated with HIV**
  - **Prevent HIV transmission**
- 
- **Consider case-by-case deferral**
    - **Significant barriers to adherence**
    - **Co-morbidities that complicate or prohibit ART**
    - **“Elite controllers” and long-term non-progressors**

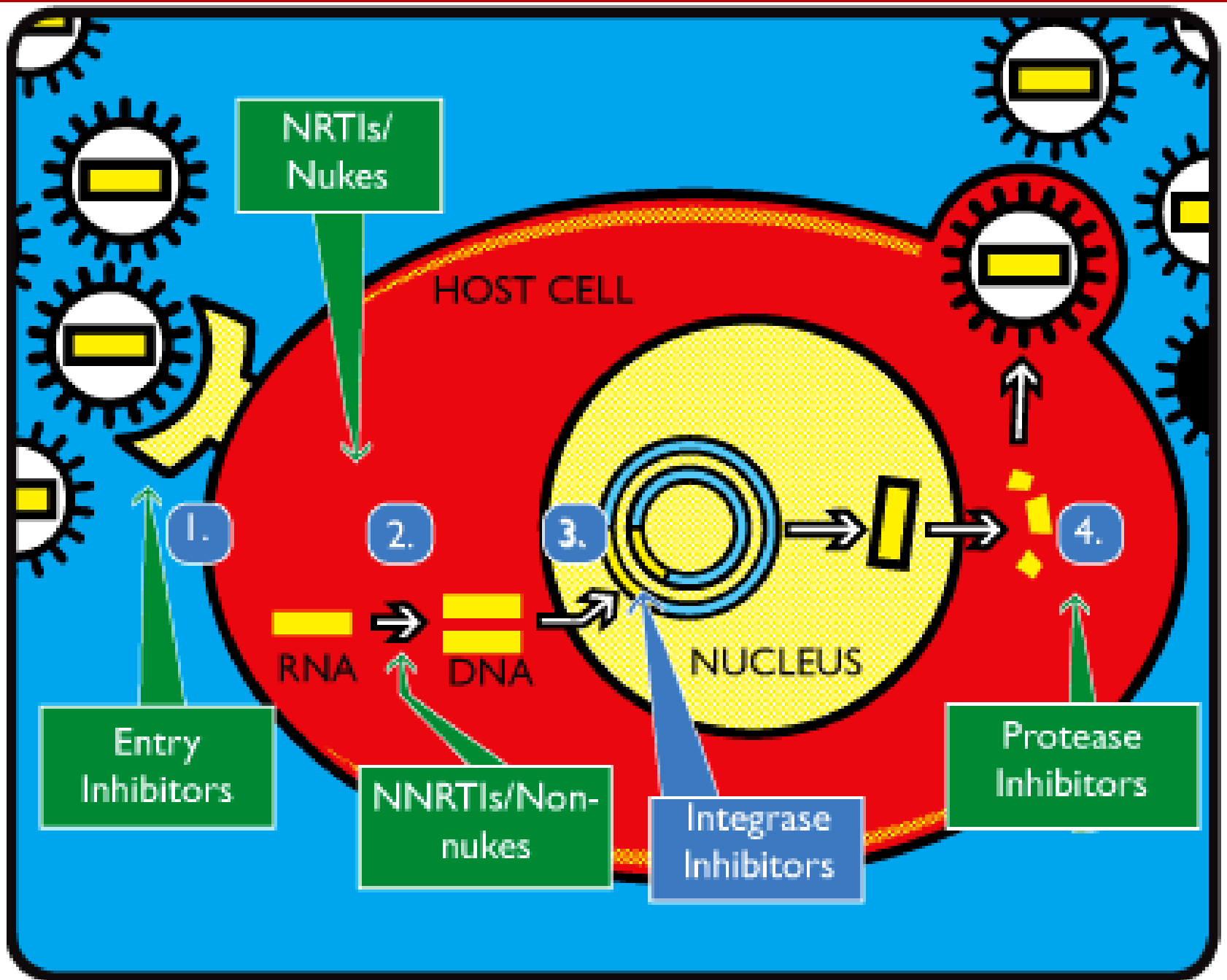


# Immediate ART upon HIV Diagnosis?

SAME  
DAY  
SERVICE

- Randomized trials in SA and Haiti
  - More likely to be suppressed at 10 mo than “standard of care”
  - Improvements in both proportion retained in care and in viral suppression at 1 year
  - Underlying HIV and TB epidemics limit generalizability of findings to US
- Same-day ART may be feasible and could potentially improve clinical outcomes
- Same day – **RESOURCE INTENSIVE**

*As these resources may not be available in all settings and the long-term clinical benefits of same-day ART initiation have yet to be proven in the United States, this approach remains investigational.*



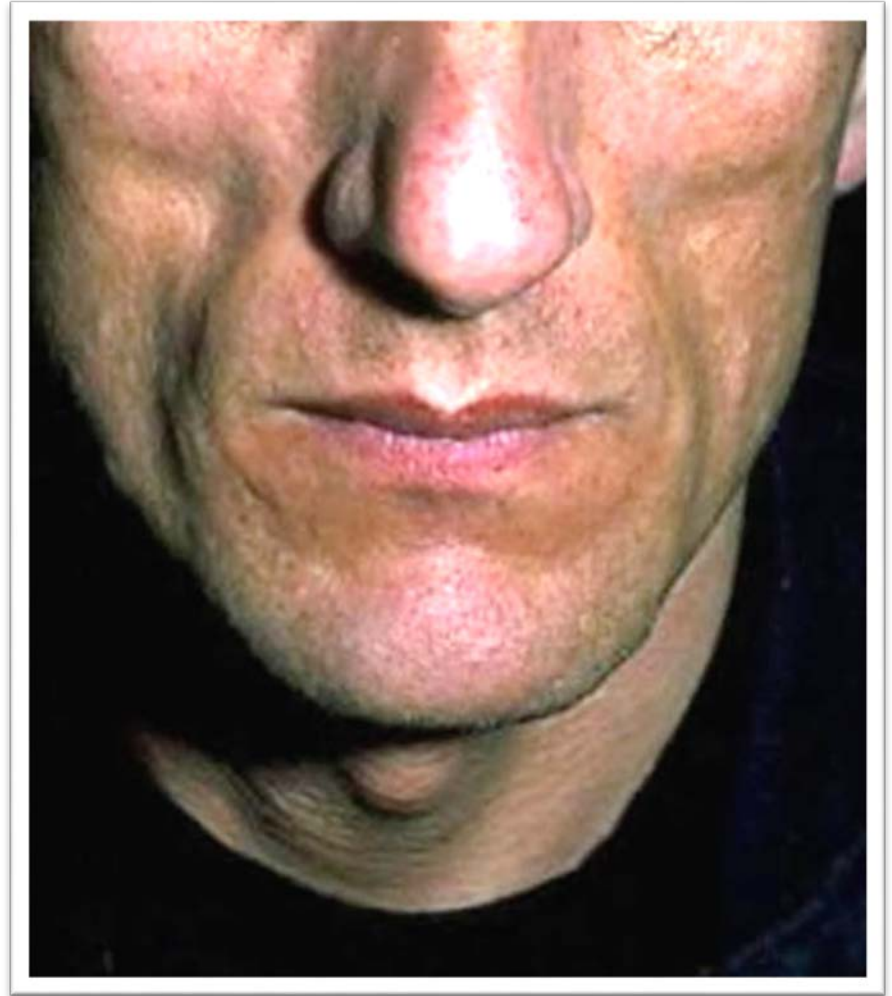
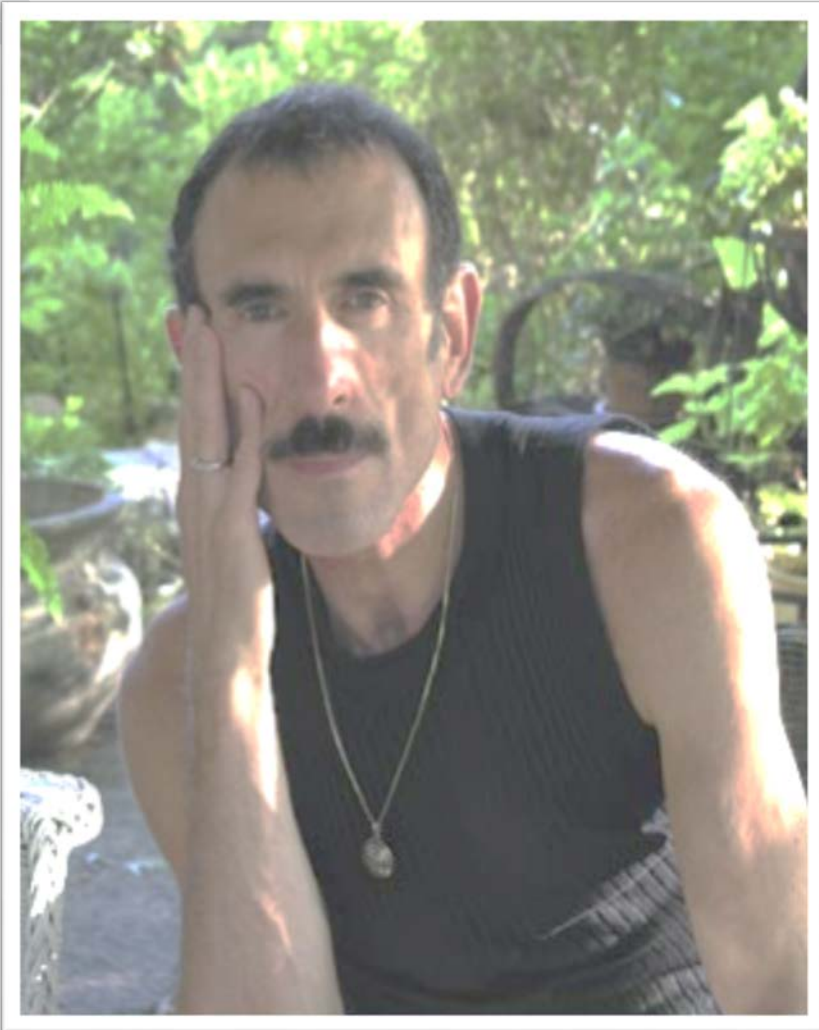


# **Reverse Transcriptase Inhibitors**

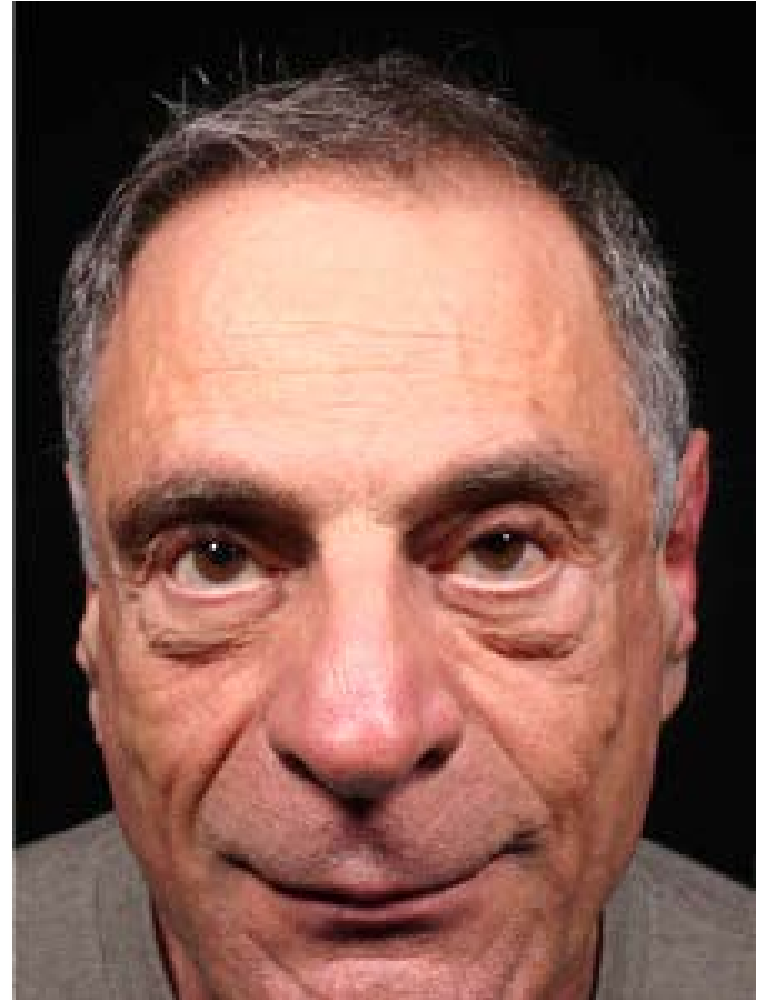
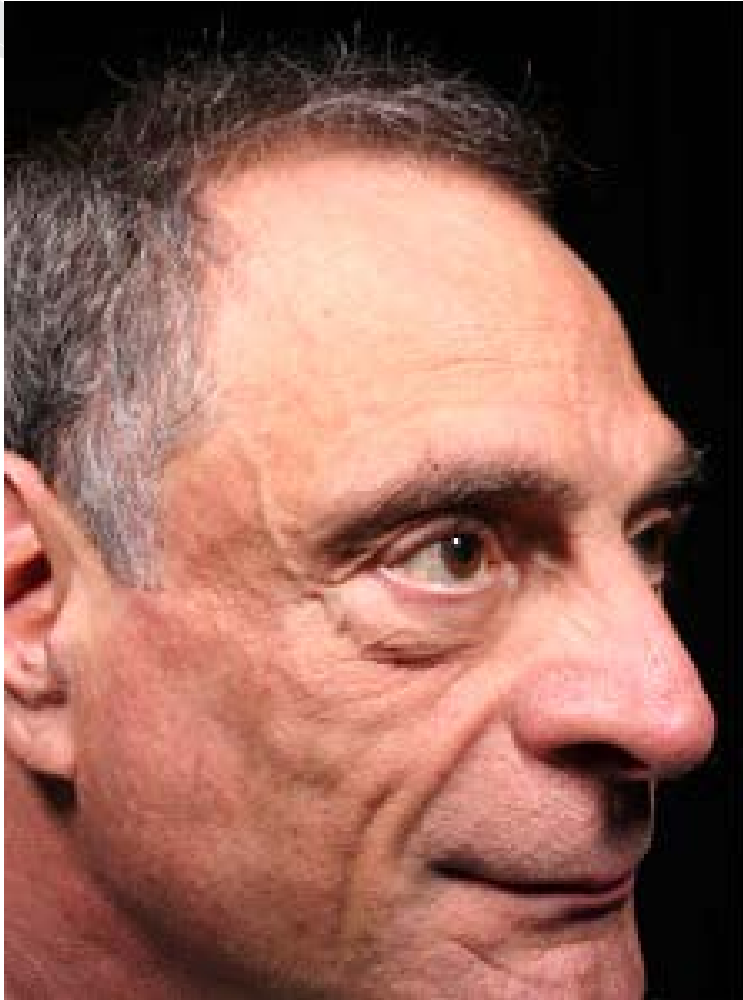
**(Includes AZT, Truvada,  
Descovy and Epzicom)**



# HIV-Associated Lipoatrophy



# HIV-Associated Lipoatrophy



# NRTIs

## Combinations Frequently used

**Epzicom (abacavir/lamivudine)**

**Truvada (tenofovir DF/emtricitabine)**

**Descovy (tenofovir AF/emtricitabine)**





# Non-Nucleoside Reverse Transcriptase Inhibitors




# Non-Nucleosides

**1 NNRTI + 2 NRTIs  
are a Complete HIV  
regimen**

**Atripla<sup>®</sup>  
Complera<sup>®</sup>  
Odefsey<sup>®</sup>  
Delstrigo<sup>®</sup>**

1. Nevirapine (*Viramune<sup>®</sup>*)
2. Efavirenz (*Sustiva<sup>®</sup>*, also in ***Atripla***)
3. Delavirdine (*Rescriptor<sup>®</sup>*)
4. Rilpivirine (*Edurant<sup>®</sup>*, also in ***Complera*** and ***Odefsey***)
5. Etravirine (*Intelence<sup>®</sup>*)
6. Doravirine (*Pifeltro<sup>®</sup>*)
  - **NEW for 2018**
  - In combination with Truvada as **Delstrigo**

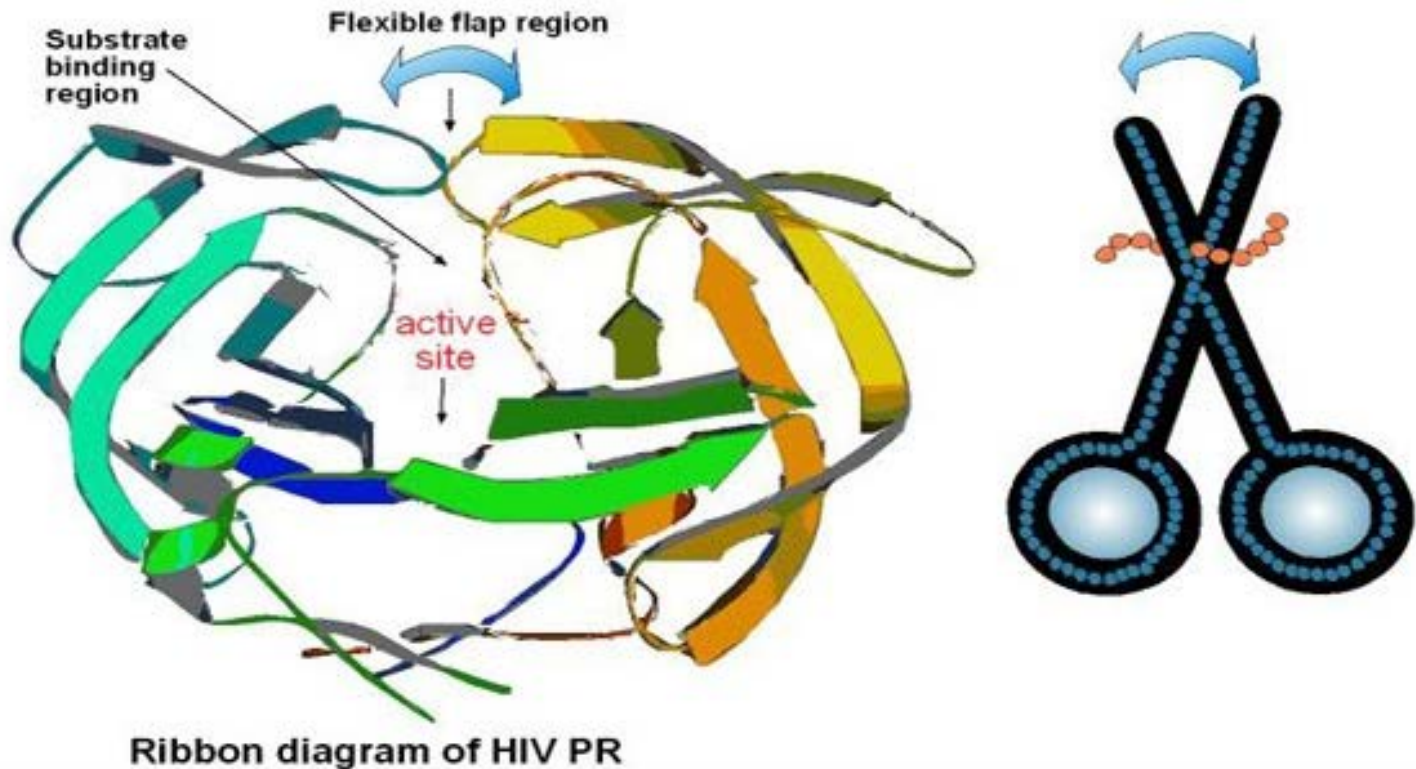


**Not all drugs are equally as effective or easy to use.**

**Rilpiverine (Edurant, Stribild and Genvoya) is contraindicated with proton pump inhibitors (Prilosec, Nexium, Prevacid).**

**Caution in initial therapy for patients with high viral loads and low CD4 counts.**

# Protease Enzyme and Inhibitors

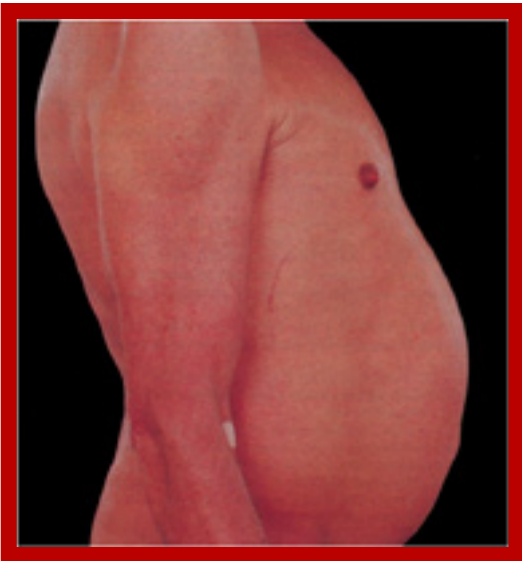


# Protease Inhibitors Fast Facts

- Credited with making HIV a “**chronic**” disease rather than a “fatal” disease.
- Most must be boosted with a second agent to achieve effective drug levels.
  - Ritonavir
  - Cobicistat
- PIs are **generally** associated with ***inhibition of CYP*** enzyme system causing multiple drug interactions



# HIV-Associated Lipodystrophy



## Meet the PIs

**Co-formulated  
with a booster:  
Kaletra (with  
ritonavir)  
and Prezcofix  
and Evotaz (with  
cobicistat)**

1. Saquinavir (Invirase<sup>®</sup>, Fortovase<sup>®</sup>)
2. Ritonavir (Norvir<sup>®</sup>)
3. Indinavir (Crixivan<sup>®</sup>)
4. Nelfinavir (Viracept<sup>®</sup>)
5. Amprenavir (Agenerase<sup>®</sup>)
6. Fosamprenavir (Lexiva<sup>®</sup>)
7. Atazanavir (Reyataz<sup>®</sup>, Evotaz<sup>®</sup>)
8. Darunavir (Prezista, Prezcofix<sup>®</sup>)
9. Lopinavir/rtv (Kaletra<sup>®</sup>)
10. Tipranavir (Aptivus<sup>®</sup>)



**Darunavir is better tolerated; but atazanavir can be given unboosted in some cases.**

Most commonly used Protease Inhibitors are atazanavir (Reyataz) and darunavir (Prezista).

**Darunavir (DRV, Prezista<sup>®</sup>, Prezcofix<sup>®</sup>)**

- Less food effect, OK with PPIs
- Requires boosting always
- Useful for PI-resistant viruses (*dosed BID*)
- *Caution* if **severe** sulfa allergy



# **Integrase Inhibitors (INSTIs)**

**HIV integrase enzyme has no equivalent in the host cell.**

**Integrase inhibitors are considered safe because they do not interfere with normal cellular processes.**

**Provide rapid drop in viral load.**

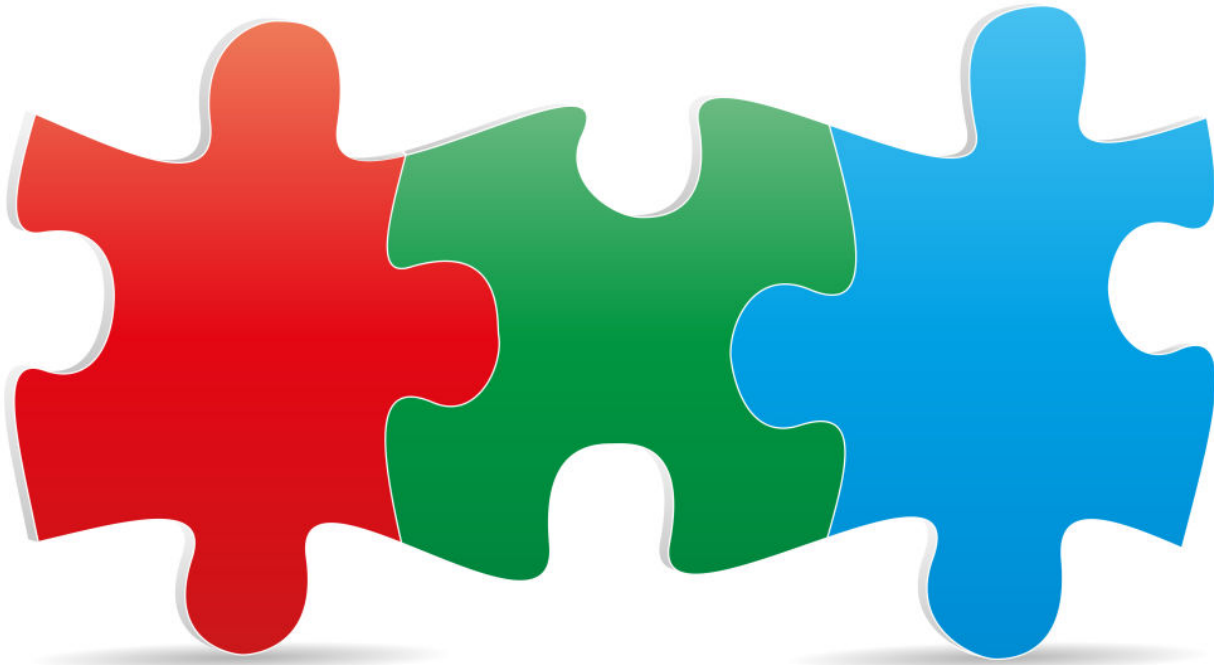


1 INSTI + 2 NRTIs =  
Complete HIV  
regimen

Triumeq<sup>®</sup>  
Stribild<sup>®</sup>  
Genvoya<sup>®</sup>  
Biktarvy<sup>®</sup>

1. Raltegravir (Isentress<sup>®</sup>)
2. Dolutegravir (Tivicay<sup>®</sup>,  
also in *Triumeq*)
3. Elvitegravir (in *Stribild*  
and *Genvoya*)
4. Bictegravir (in *Biktarvy*)





# There's help!



- Treatment guidelines available to provide information about recommended regimens ([aidsinfo.nih.gov](http://aidsinfo.nih.gov))
- **Individualize for the patient**



**Putting  
it all  
together  
for an  
effective  
regimen**

- **Initial** antiretroviral therapy **generally** consists of **two NRTIs** (*termed a nucleoside backbone*) plus **one** active drug from another class:
  - **Integrase Inhibitor**
  - **Protease Inhibitor**
  - **Non-NRTI**
  - **CCR5 antagonist (entry inhibitor)**
- Regimens for **experienced** patients is complex, **expert advise** is critical.
  - Consider past regimens
  - Consider resistance



# Recommended Initial Regimens for *Most* People with HIV

- Bictegravir/tenofovir alafenamide/emtricitabine
  - **Biktarvy**
- Dolutegravir/abacavir/lamivudine (only for patients who are HLA-B\*5701-negative)
  - **Triumeq**
- Dolutegravir plus tenofovir/emtricitabine
  - **Tivicay plus Truvada** or **Tivicay plus Descovy**
- Raltegravir plus tenofovir/emtricitabine
  - **Isentress plus Truvada** or **Isentress plus Descovy**
- **NOTICE THESE ARE ALL INTEGRASE BASED REGIMENS** (with a 2-NRTI backbone)



# Recommended Initial Regimens *In Certain Clinical Situations*

## INSTI + 2 NRTIs:

- EVG/c tenofovir/emtricitabine (**Stribild** or **Genvoya**)
- RAL + abacavir/lamivudine (if **HIV RNA < 100,000 copies/mL**)

## Boosted PI + 2 NRTIs:

- DRV/c or DRV/r + tenofovir/emtricitabine
- ATV/c or ATV/r + tenofovir/emtricitabine
- DRV/c or DRV/r + abacavir/lamivudine

## NNRTI + 2 NRTIs:

- EFV + tenofovir/emtricitabine (**Atripla**)
- RPV + tenofovir/emtricitabine (if **HIV RNA <100,000 copies/mL** and **CD4 >200 cells/mm**) (**Complera**)
- **DOR + tenofovir/emtricitabine or tenofovir/lamivudine**





# Treatment-Experienced Patients

- In clinical studies of ART, most patients maintained virologic suppression for at least 3-7 years
  - Appropriate initial ARV regimens should suppress HIV **indefinitely**, assuming **adequate adherence**
- In patients with **undetectable** viral load:
  - Assess adherence frequently
  - Simplify ARV regimen as much as possible
    - **Reduce pill burden**
      - Are there combination tablets now available? Would this reduce co-pays?
    - **Reduce dosing frequency**
      - Are there now once daily regimens that would be appropriate?
    - **Enhance tolerability**
      - Ask about side effects
    - **Decrease food and fluid requirements**
      - Review specific food requirements



# Treatment-Experienced- Failing Patients

- Assess and address aggressively
  - This is complex – expert advice is critical
  - Drug resistance testing should be done - expert review
  - New regimens should include at least 2 and preferably three fully active agents
  - In **some** patients with multidrug resistant HIV, being undetectable may not be possible
    - **ART should be continued** with regimens designed to minimize toxicity, preserve CD4 count and delay clinical progression



"There were some complications. It looked way easier on YouTube."

**If you have any questions, write to me...**

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