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HIV and Oral Health in the Era of Antiretroviral Therapy

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- The activity planners and speakers do not have any financial relationships with commercial entities to disclose.
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- This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation

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Objectives

- Identify the current demographics of HIV/AIDS and infections rates
- Understand the change in oral health needs in the Era of ART therapy
- Evaluate common oral manifestations related to HIV
- Discuss updates and current preferred ART for treatment of HIV
- Discuss common ART therapy's adverse effects
- Explain the role of the dental healthcare professional has in the continuum of HIV Care

HIV in the United States

In 2014, an estimated 44,073 people were diagnosed with HIV infection in the United States.

More than 1.2 million people in the US are living with HIV, and 1 in 8 of them don't know it.

Over the last decade, the annual number of new HIV diagnoses declined 19%.

Gay and bisexual men accounted for an estimated 83% (29,418) of HIV diagnoses among males and 67% of all diagnoses.

Black/African American gay and bisexual men accounted for the largest number of estimated HIV diagnoses (11,201), followed by white gay and bisexual men (9,008).

http://www.cdc.gov/hiv/statistics/overview/ataglance.html

HIV in the United States

Heterosexuals and people who inject drugs also continue to be affected by HIV.

Heterosexual contact accounted for 24% (10,527) of estimated HIV diagnoses.

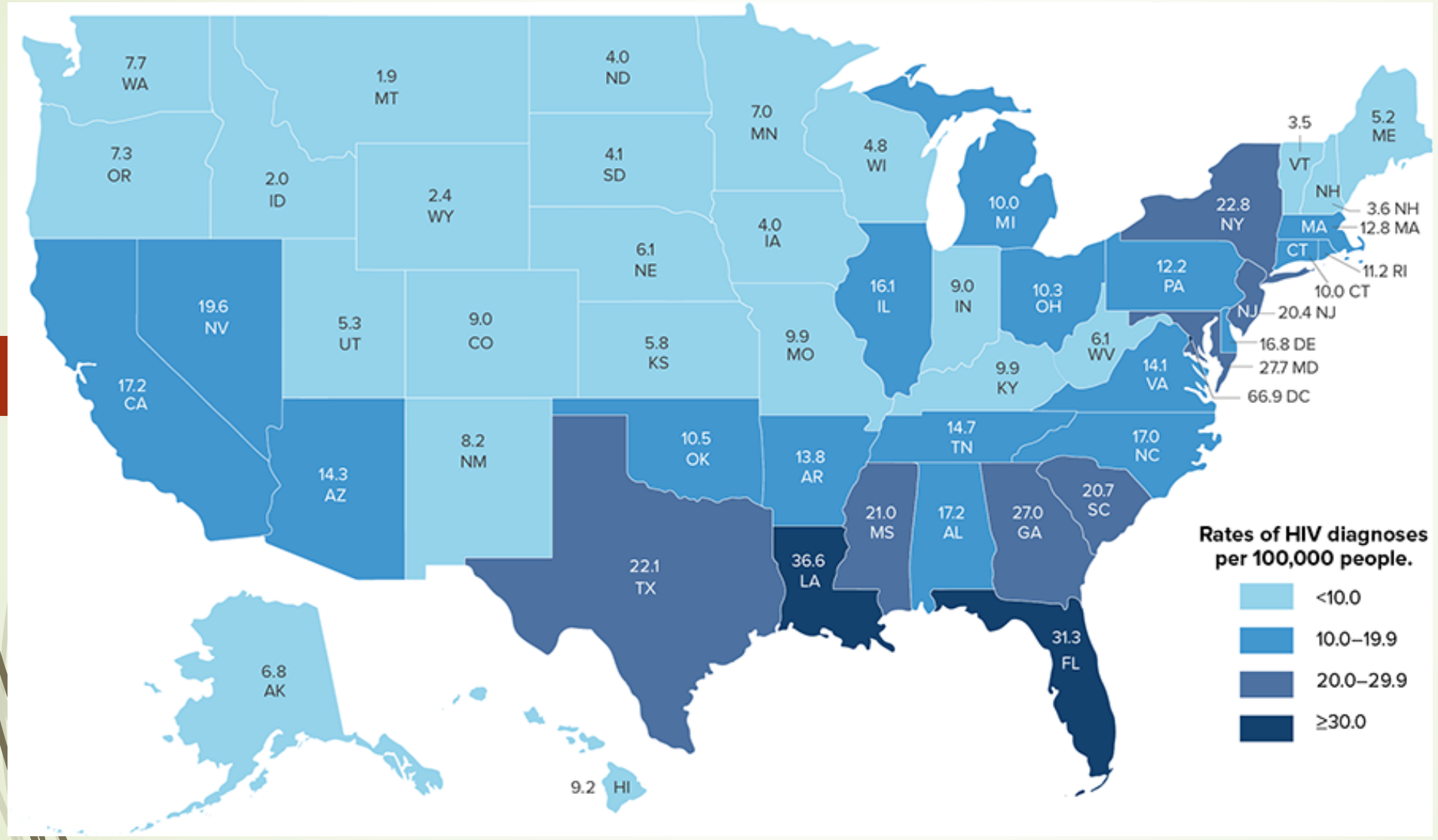
Women accounted for 19% (8,328) of estimated HIV diagnoses. Diagnoses among women are primarily attributed to heterosexual contact (87%, or 7,242) or injection drug use (13%, or 1,045).

An estimated 6% (2,635) of HIV diagnoses were attributed to injection drug use.

In 2014, an estimated 20,896 people were diagnosed with AIDS. Since the epidemic began in the early 1980s, an estimated 1,210,835 people have been diagnosed with AIDS.

http://www.cdc.gov/hiv/statistics/overview/ataglance.html

HIV in the United States



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Oral Health and HIV

- 32-46 percent of PLWHA will have at least one major HIV-related oral health problem.
- 58-68 percent PLWHA do not receive regular health care.
- Barriers PLWHA face in receiving oral health care include lack of insurance, limited incomes, lack of providers, stigma, and limited awareness.
- Poor oral health can impede food intake and nutrition, leading to poor absorption of HIV medications and leaving PLWHA susceptible to progression of their disease.[4]
- HIV medications have side effects such as dry mouth, which predisposes PLWHA to dental decay, periodontal disease, and fungal infections.

http://hab.hrsa.gov/abouthab/files/oral_health_fact_sheet.pdf
Accessed March 28,2016

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Oral Health and HIV

- Bacterial infections (i.e., dental decay and periodontal disease) that begin in the mouth can escalate to systemic infections and harm the heart and other organs if not treated, particularly in PLWHA with severely compromised immune systems.

- A history of chronic periodontal disease can disrupt diabetic control and lead to a significant increase in the risk of delivering preterm low-birthweight babies.

- Poor oral health can adversely affect quality of life and limit career opportunities and social contact as result of facial appearance and odor.

http://hab.hrsa.gov/abouthab/files/oral_health_fact_sheet.pdf
Accessed March 28,2016

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Oral Manifestations of HIV

Significance of Oral Manifestations

- First sign of clinical disease
- Signify disease progression
- Signify possible ART failure
- Effects on medication adherence and nutrition

Oral Manifestations of HIV

In the Era of ART

Decreasing:

- Candidiasis
- Necrotizing Gingivitis
- Kaposi's Sarcoma
- Oral Hairy Leukoplakia

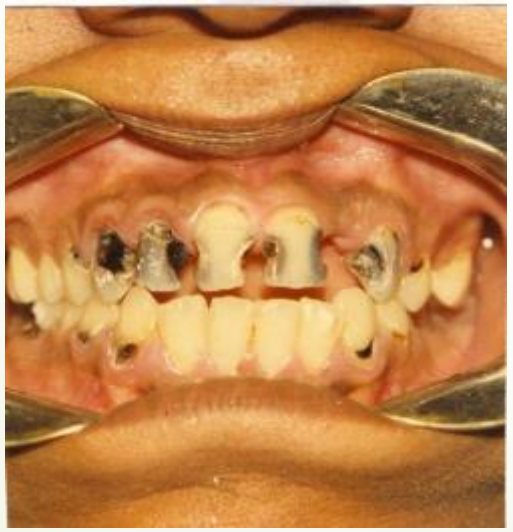
Increasing:

- Dental Decay/Periodontal Disease
- Oral HPV

Dental Decay

Factors that Increase Dental Decay

- Xerostomia
- Diet
- Substance Abuse
- Increased Life Expectancy



What can we do?

Refer to dental provider to remain compliant with HAB Oral Health Measures:

Once per year:

- Medical Dental History
- Treatment Plan
- Oral Health Education
- Periodontal Screening or Exam
- Phase I Treatment Plan Completed in 12 month

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What can we do?

An increase in caries can occur, so fluoride rinses (that can be bought over the counter) or prescription fluorides should be used daily, and visits to the dentist should occur two to three times per year.

OTC products (.05% NaF) ACT, Fluoroguard

Salivary stimulants such as sugarless gum or sugarless candies may provide relief.

Candies that are acidic should be avoided as frequent use may lead to loss of tooth enamel

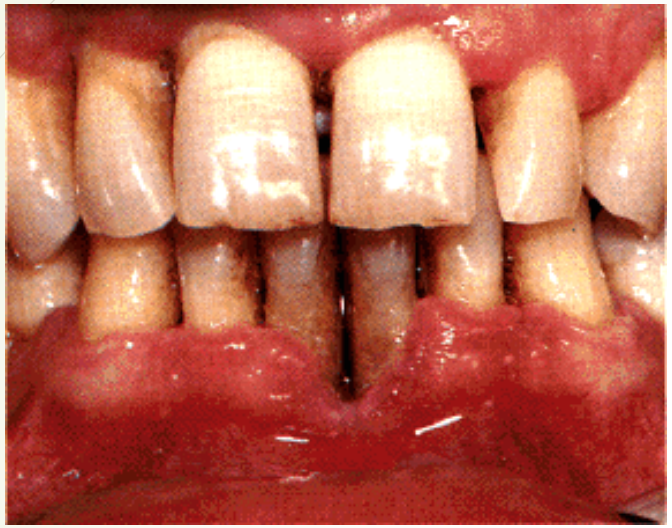
Increase intake of water

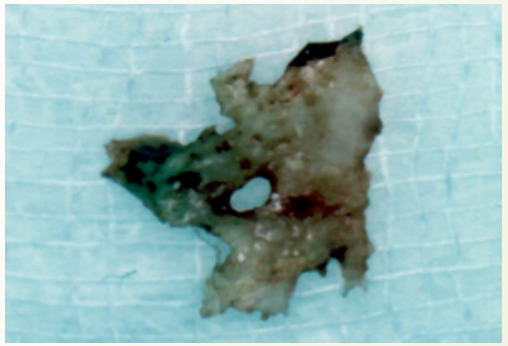
Home Care Instructions

Brush, Floss, Tongue Scraper

Work in Collaboration with Mental Health Professionals and Case Managers

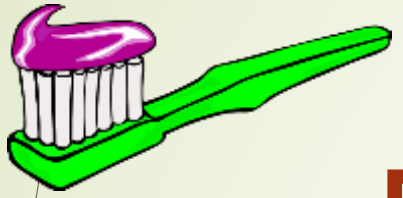
Periodontal Disease





Links between Periodontal Disease an other disease states

Mark Schweizer/2012



Periodontal Disease in the Era of ART

Shift of prevalence towards periodontal diseases. Lack of oral hygiene determined by plaque formation and reduced CD4-counts with pronounced periodontal inflammation can be seen as risk factors for periodontal disease. Overall high prevalence of manifestations underlines the importance of oral examination for the general practitioner and visits by oral specialists should become a routine procedure in HIV-patients care.

Kroidl A[1], Schaeben A, Oette M, Wettstein M, Herfordt A, Häussinger D. Eur J Med Res. 2005 Oct 18;10(10):448-53. Accessed December 12, 2015.

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Oral Manifestations of HIV

Human Papilloma Virus

- About 7% of Americans have oral HPV. That's far fewer than the number who have the genital version, which is the most common sexually transmitted disease in the U.S.
- Every day in the US, about 12,000 people ages 15 to 24 are infected with HPV. Approximately 26 million Americans on any given day have an oral HPV infection. Of those approximately 2600 are HPV16. The vast majority of individuals will clear the virus naturally through their own immune response, and never know that they were exposed or had it.

http://oralcancerfoundation.org/hpv/hpv-oral-cancer-facts.php

Human Papilloma Virus

More than 40 types of HPV can infect people, but only a few cause cancer. One of the types that causes most cervical cancers, called HPV16, is also linked with most HPV-related head and neck cancers.

Oral warts are caused by human papillomavirus (HPV) and may appear anywhere within the oral cavity or on the lips. They occur more frequently and more extensively in people with HIV infection than in those with normal immune function, especially in patients with advancing immune suppression (CD4 counts of <200-300 cells/µL).

Oral warts may be refractory to therapy.

The frequency of oral warts may increase, at least temporarily, in patients treated with antiretroviral therapy.

http://oralcancerfoundation.org/hpv/hpv-oral-cancer-facts.php

Human Papilloma Virus

- **Possible spread through Oral Sex and French Kissing**

http://saude-joni.blogspot.com/2012/02/hpv-oral.ht

Human Papilloma Virus

New England Journal of Medicine (NEJM), shows that men and women who reported having six or more oral-sex partners during their lifetime had a nearly nine-fold increased risk of developing cancer of the tonsils or at the base of the tongue

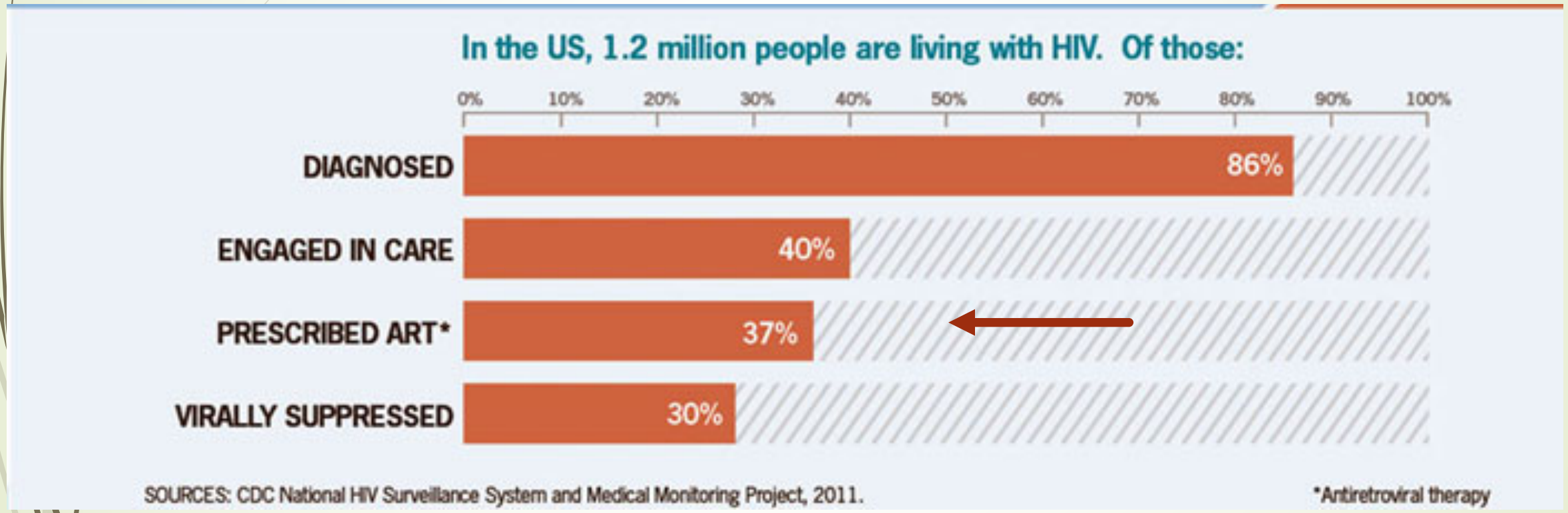
Gypsyamber D'Souza, Ph.D., Aimee R. Kreimer, Ph.D., Raphael Viscidi, M.D., Michael Pawlita, M.D., Carole Fakhry, M.D., M.P.H., Wayne M. Koch, M.D., William H. Westra, M.D., and Maura L. Gillison, M.D., Ph.D.
N Engl J Med 2007; 356:194-1956May 10, 2007DOI: 10.1056/NEJMoa065497Share:

Dental Recommendations for Treating HIV/AIDS Patients

- The magnitude of the viral load is not an indicator to withhold dental treatment for the patient. High viral loads may be present in a patient with early asymptomatic disease, while low viral loads can be seen in very advanced patients on suppressive antiviral therapy. Knowledge of these markers can tell the dentist the general health of the patient and the risk of progression

- The dentist can play an important part in reminding patients of the need for regular follow up and monitoring of these markers. It is recommended that the CD4 and viral load determinants be done every three-six months.

The HIV Care Continuum



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Current CDC Recommendations

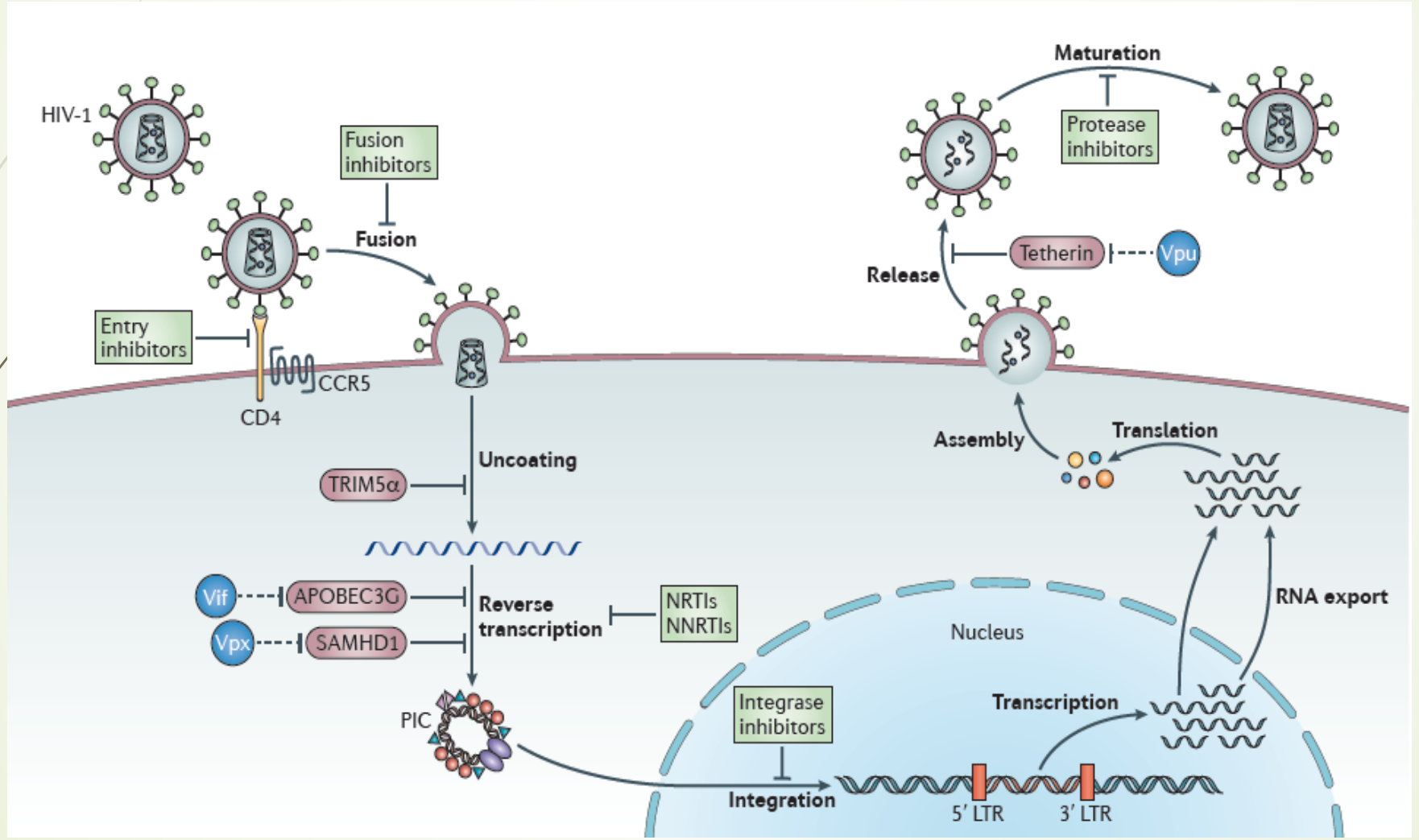
ART is recommended for all HIV-infected individuals, regardless of CD4 cell count, to reduce the morbidity and mortality associated with HIV infection (AI). ART is also recommended for HIV-infected individuals to prevent HIV transmission (AI).

When initiating ART, it is important to educate patients about the benefits of ART, and to address barriers to adherence and recommend strategies to optimize adherence. On a case-by-case basis.

ART may be deferred because of clinical and/or psychosocial factors; however, therapy should be initiated as soon as possible. Patients should also understand that currently available ART does not cure HIV. To improve and maintain immunologic function and maintain viral suppression, ART should be continued indefinitely.

http://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

Overview of Drug Targets



Nat Rev Microbiol. 2013 Dec;11(12):877-83

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Six Classes of ART

- **Nucleoside or Nucleotide Reverse Transcriptase Inhibitors (NRTIs)**
- **Protease Inhibitors (PIs)**
- **Integrase Strand Transfer Inhibitor (INSTIs)**
- Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
- Fusion Inhibitors
- CCR5 antagonist

*Bold indicates part of a preferred therapy regimen

Treatment Backbone:

- Preferred HIV treatment regimens consist of a three-drug regimen :
  - Either a boosted PI, or an integrase strand transfer inhibitor
    - Used to include NNRTI, however this has been moved to alternative b/c CNS ADEs
  - Plus a 'backbone' consisting of two NRTIs
    - Lamivudine or emtricitabine forms part of the backbone of all currently recommended preferred antiretroviral regimens

OLD: Regimens in HIV-Infected Treatment Naïve Adults and Adolescents

~~Non-nucleoside Reverse Transcriptase-Base Regimen~~			
~~efavirenz~~	~~emtricitabine~~	~~tenofovir~~	
Protease-Inhibitor Based Regimen			
~~atazanivir~~	~~ritonavir (as booster)~~	~~tenofovir~~	~~emtricitabine~~
darunavir	ritonavir (as booster)	tenofovir	emtricitabine
Integrase Strand Transfer Inhibitor Based Regimen			
raltegravir	tenofovir	emtricitabine	
elvitegravir	cobicistat	tenofovir	emtricitabine
dolutegravir	tenofovir	emtricitabine	
dolutegravir	abacavir	lamivudine	

Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, the Panel recommendations on initial combination regimens for the antiretroviral therapy (ART)-naive. http://aidsinfo.nih.gov/contentfiles/upload/AdultARV_INSTIRecommendations.pdf. (Accessed on November 9, 2013).

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Preferred/Recommended ART (Antiretroviral therapy)

Protease-Inhibitor Based Regimen			
darunavir	ritonavir (as booster)	tenofovir	emtricitabine
Integrase Strand Transfer Inhibitor Based Regimen			
raltegravir	tenofovir	emtricitabine	
elvitegravir	cobicistat(as booster)	tenofovir *	emtricitabine
dolutegravir	tenofovir	emtricitabine	
dolutegravir	abacavir	lamivudine	

* Two different formulations, TDF for CrCl > 70 mL/min, and TAF for CrCL >30 mL/min

http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Accessed April 22nd, 2016.

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Brand Names for Preferred Regimens

Protease-Inhibitor Based Regimen		
PREZISTA®	**Ritonavir (**Norvir®)	**TRUVADA®**
Integrase Strand Transfer Inhibitor Based Regimen		
ISENTRESS®	**TRUVADA®**	
STRIBILD®		
GENVOYA®		
TIVCAY®	**TRUVADA®**	
TRIUMEQ®		

Key Points for Preferred ART

- Always have at least a 3 drug combination
- Always have a backbone of 2 NRTIs
  - Exceptions exist/uncommon (i.e.. HLA+ pt. with renal insufficiency)
- Many have 1 pill daily options

Caution: Drug-Drug Interactions and Medication Side Effects

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When prescribing any medications along with ART- Always Check!

- Ritonavir/Cobicistat Boosted Regimens
  - Example: INCREASES Clarithromycin concentrations/toxicities
- Tenofovir containing regimens
  - Added toxicities/concentrations with antivirals such as Acyclovir/Valganciclovir

Integrase Strand Transfer Inhibitors

INSTI	Adverse Effects	Comments
Raltegravir (Isentress®)	Rare Myalgias, severe rash, liver toxicity	Twice a day (adherence)
Elvitegravir (in Stribild®, and Genvoya®)	Drug Interactions, and renal toxicity (from TDF, not from TAF)	One pill, once a day with food (reduced pill burden)
Dolutegravir (Tivicay®)	Well tolerated	2nd Generation, with a higher barrier to resistance, once a day

Protease Inhibitors

Protease Inhibitor	Significant Adverse Effects
Lopinavir + Ritonavir (LPVr) Kaletra®	↑BG, fat maldistribution, N/V/D, ↑LFTs, hyperlipidemia
Ritonavir (RTV) Norvir®	CNS: paresthesias, asthenia GI: taste disturbances, hepatitis ↑ BG, fat maldistribution, N/V/D, ↑LFTs, hyperlipidemia
Atazanavir (ATV) Reyataz ®	CV: Arrhythmias GI: hyperbilirubinemia ↑ BG, fat maldistribution, N/V/D, rash
Darunavir (DRV) Prezista®	Derm: SJS GI:↑transaminase, hyperlipidemia ↑BG, fat maldistribution, N/V/D, rash

Non-Nucleoside Reverse Transcriptase Inhibitors: NNRTIs

NNRTI	Significant Adverse Effects/Comments
Efavirenz (EFV) Sustiva®	Rash CNS (insomnia, irritability, lethargy, vivid dreams)—CNS effects usually subside after 2 weeks of therapy Preferred NNRTI (Usually taken at night) Teratogenic (Contraindicated during pregnancy, neural tube defects esp from 1st trimester)
Nevirapine (NVP) Viramune®	Rash, SJS, Hepatitis & Hepatic necrosis more common than w/ other NNRTIs, Have to titrate up after 2 weeks
Etravirine (Intelence®)	rash and nausea K103N does not confer etravirine resistance
Rilpivirine (Edurant®)	depressive disorders, headache, insomnia and rash. K103N does not confer rilpivirine resistance

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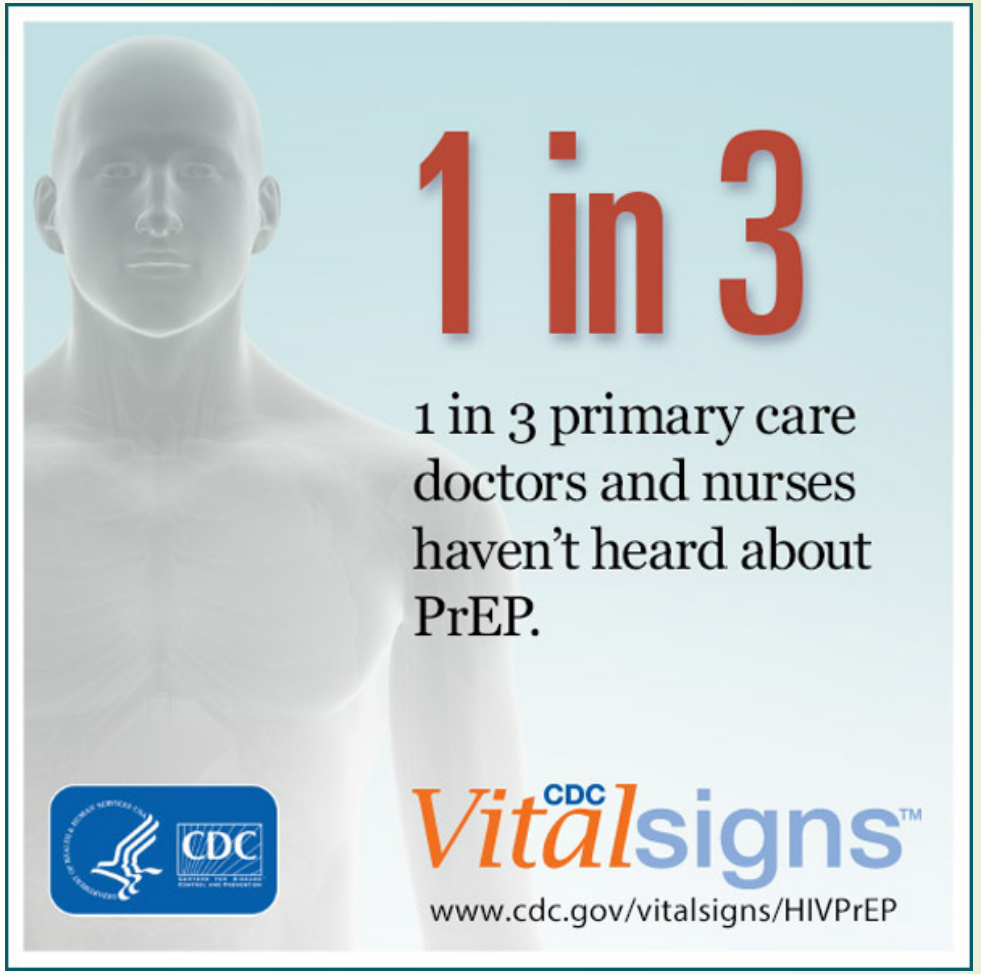
Nuceloside Reverse Transcriptase Inhibitors

NRTI	Significant Adverse Effects
Abacavir (ABC)	Fatal hypersensitivity Rxn: SJS, genetic screening to predict, May ↑ risk of MI
Lamivudine (3TC), Epivir®	Minimal
Emtricitabine (FTC), Emtriva®	Minimal
Tenofovir (TDF), Viread®	Asthenia, HA N/V/D, flatulence Renal insufficiency
Zidovudine (AZT, ZDV) Retovir®	Bone marrow suppression, macrocytic anemia GI intolerance HA, insomnia, asthenia



Pre-Exposure Prophylaxis (PrEP) for HIV Prevention

http://www.cdc.gov/media/dpk/2015/dpk-vs-hiv-prep.html

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Pre-Exposure Prophylaxis (PrEP) for HIV Prevention

- Use of antiretroviral meds by *uninfected* patients to prevent HIV infection
- Used before and during periods of risk
- Truvada® (tenofovir/emtricitabine) is the only ARV FDA approved for PrEP
  - PrEP efficacy more than 90% for sexually acquired
  - PrEP efficacy more than 70% in IVDU
- Drug assistance program:
  - https://start.truvada.com/paying-for-truvada

CDC, USPHS. Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014: A clinical practice guideline. Available at: http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf.

How do patients take PrEP?

- **Must be taken DAILY**
- PrEP reaches maximum protection from HIV for **receptive anal sex** at about **7 days** of daily use.
- For **all other activities**, including insertive anal sex, vaginal sex, and injection drug use, PrEP reaches maximum protection at about **20 days** of daily use.

http://www.cdc.gov/hiv/basics/prep.html. Accessed April 22, 2016.

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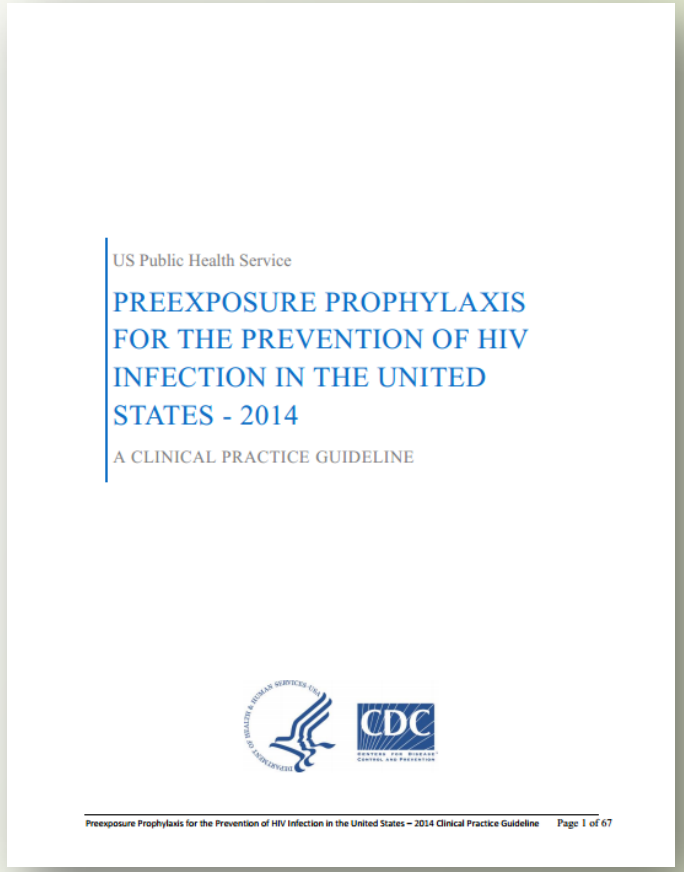
Indications for PrEP – CDC Guidelines

Adults at substantial risk of HIV acquisition:

- Sexually-active MSM
- Heterosexually active men & women
  - HIV-discordant couples
  - Multiple partners OR partners whose HIV status is unknown
    - AND Do not always use a condom for sex with
      - people who inject drugs
      - bisexual men
- Injection drug users



CDC, USPHS. Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014: A clinical practice guideline. Available at: http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf.

PrEP Side Effects

- Headache, nausea, flatulence
  - Use OTC meds
- Side effects uncommon in PrEP trials
  - Often resolved in first month
- Counsel patients about symptoms indicating need for urgent evaluation
  - Acute renal injury, acute HIV infection

CDC, USPHS. Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014: A clinical practice guideline. Available at: http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf.

PrEP Clinical Monitoring

- Every 3 months
  - Repeat HIV test (RX refill for no more than 90 days (until next HIV test)
  - Pregnancy test for child-bearing women
  - Assess side effects, adherence, risk behaviors
- Every 6 months
  - Monitor CrCl (Patients with CrCl < 60 ml/min should not be prescribed PrEP)
  - STI tests (syphilis, gonorrhea, chlamydia)
- Every 12 months
  - Evaluate need to continue PrEP

CDC, USPHS. Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014: A clinical practice guideline. Available at: http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf.

Interprofessional Practice (IPP)

Interprofessional Practice (IPP) is a collaborative practice which occurs when healthcare providers work with people from within their own profession, with people outside their profession and with patients and their families.

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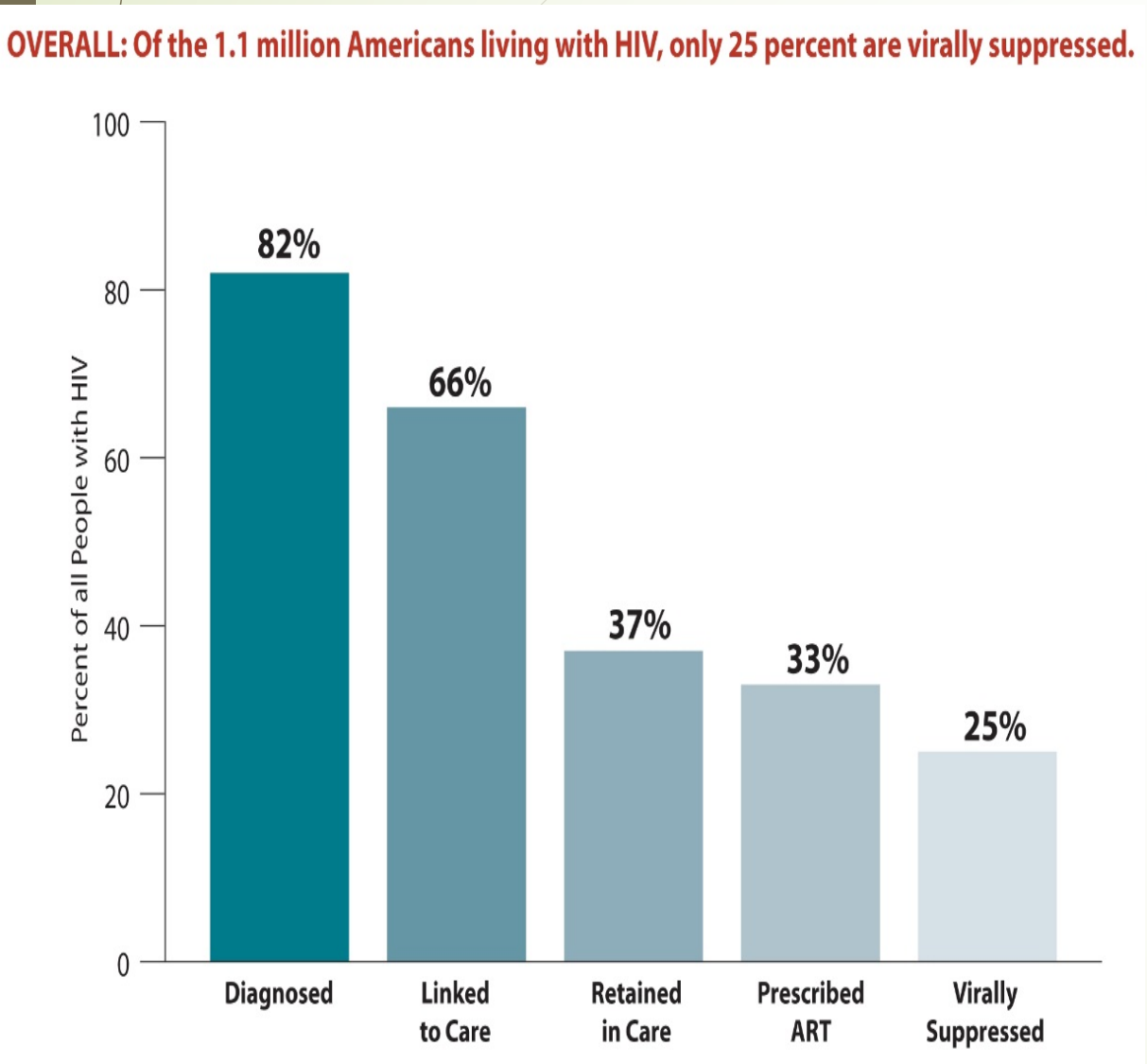
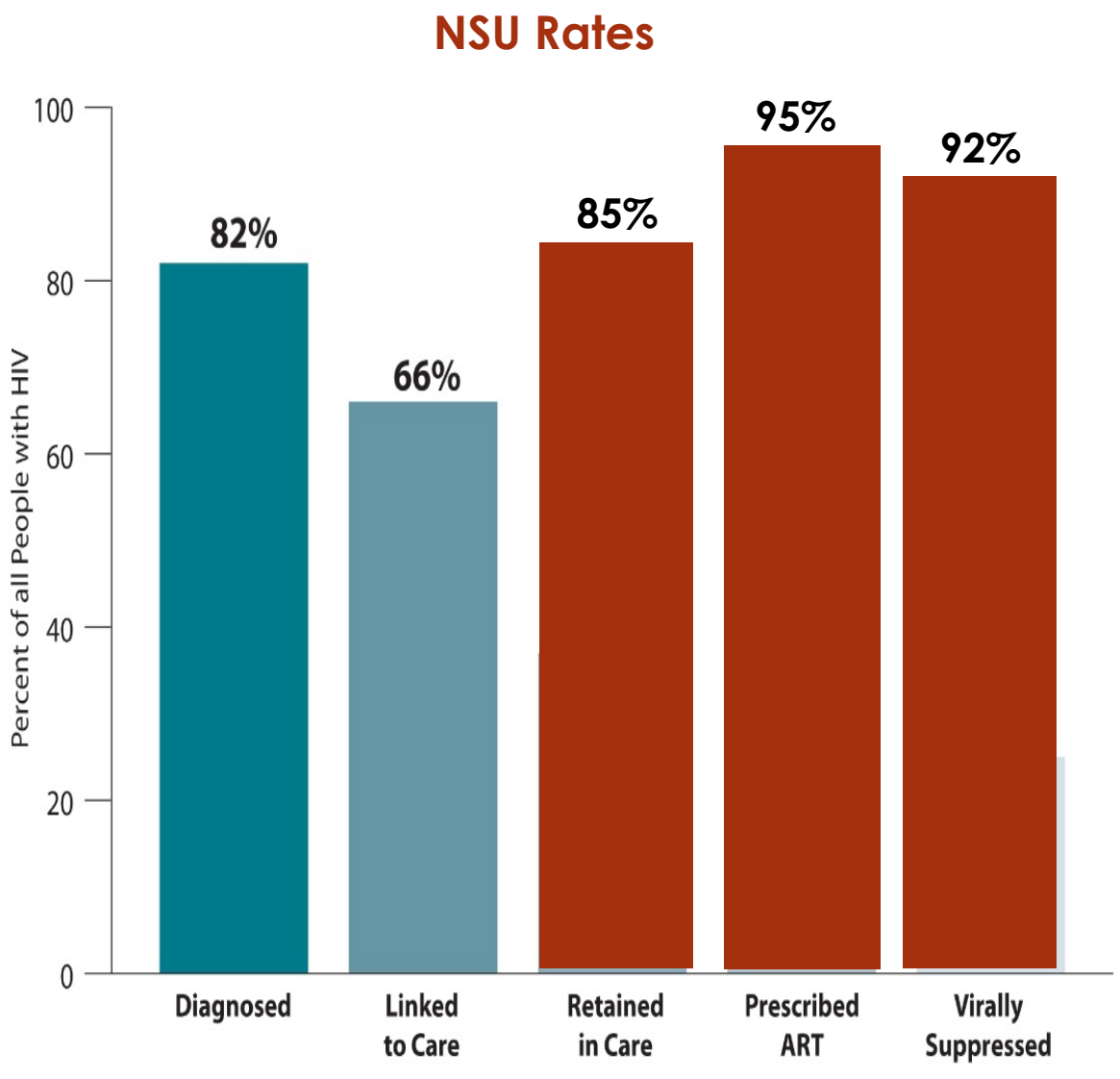
National vs. NSU Interprofessional Program





We are available for clinical consultations and trainings

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