

Pre-exposure Prophylaxis for HIV (PrEP)

Jennifer Hanrahan, D.O.

Division of Infectious Disease

MetroHealth Medical Center, Cleveland

Disclosures

- + Consultant for Astellas, Gilead, BMS
- + Was on Speaker's Bureau for Gilead and Astellas

Objectives

- + Participants will be able to describe current recommendations for PrEP
- + Participants will recognize the clinical presentation of Acute HIV and be able to test appropriately
- + Participants will be able to discuss the benefits and risks of PrEP for individuals at risk for HIV infection

Outline

- + HIV epidemiology
- + Current PrEP Guidelines
- + Follow-up for Individuals on PrEP

Case

- + A 42 y/o man presents to ED with a painless penile ulcer present for about a week. He denies any dysuria, penile discharge or any other problems. He had GC about 4 months ago, and was treated. He gets tested for HIV every 3-6 months. What would you counsel this patient to do?

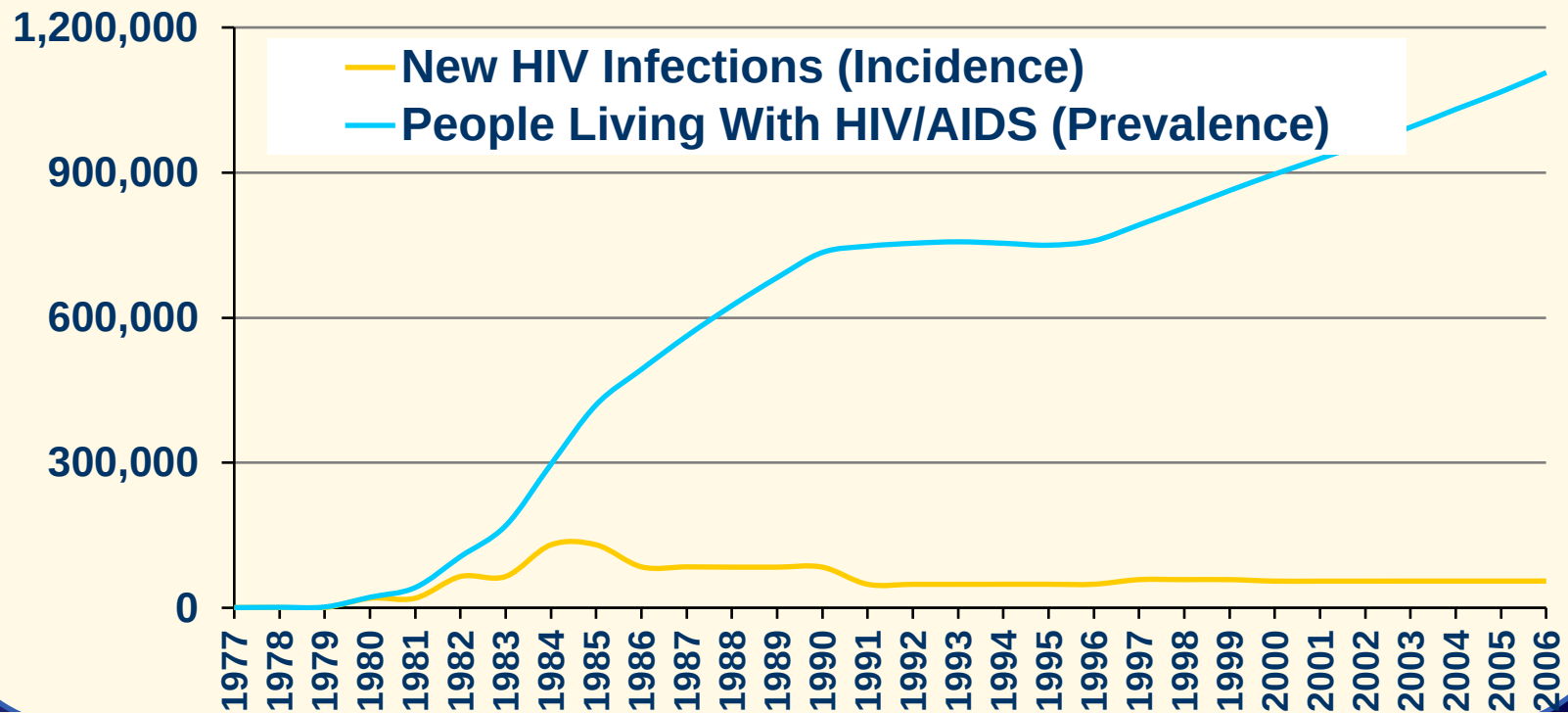
HIV: A Winnable Battle

- + About 1.2 million people in U.S. living with HIV
- + Approx 47,500 new infections every year
- + About 1 in 8 people infected with HIV do not know they are infected



Number of people living with HIV continues to increase sharply

HIV Incidence and Prevalence, United States, 1977–2006



Burden of HIV in the U.S.

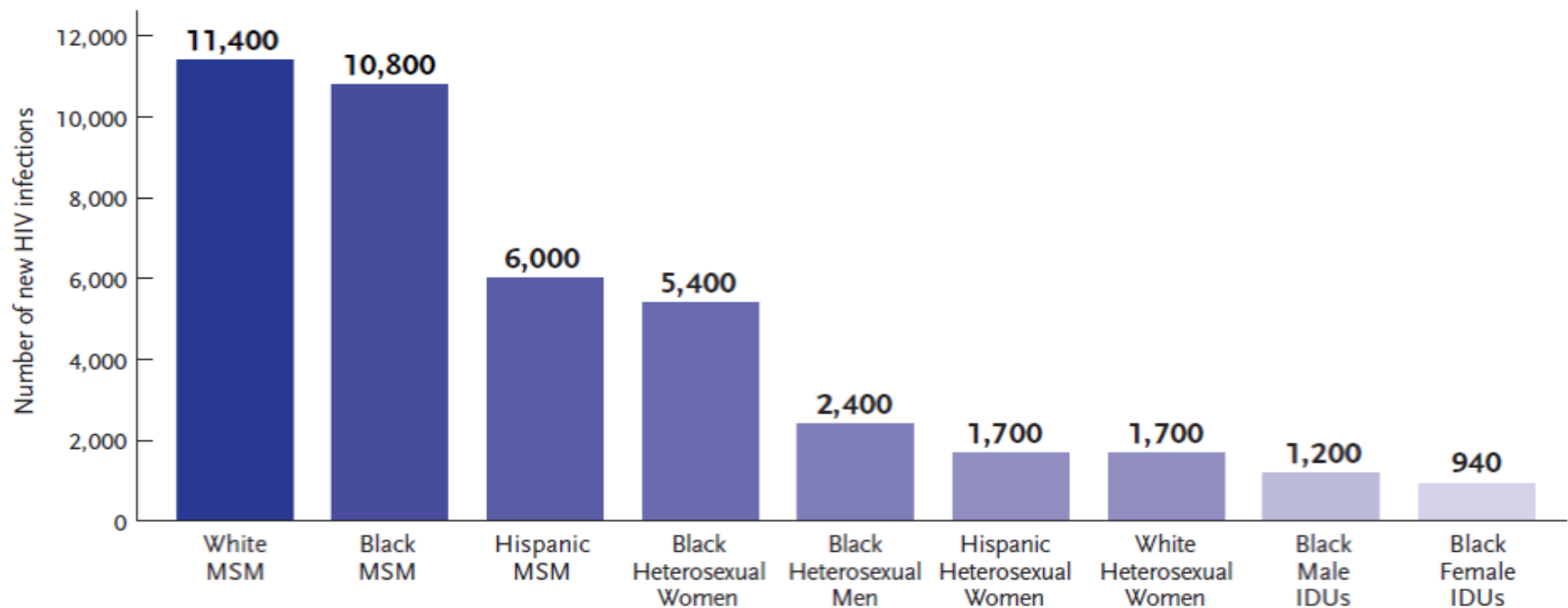
- ✦ Net increase of 40,000 people with HIV infections each year
- ✦ 56,000 new infections (2006)
- ✦ 16,000 deaths (2006)
- ✦ HIV infected people who start antiretroviral treatment (ART) are now expected to live at least an additional 35 years
- ✦ Lifetime treatment costs of ~\$400,000

Epidemiology



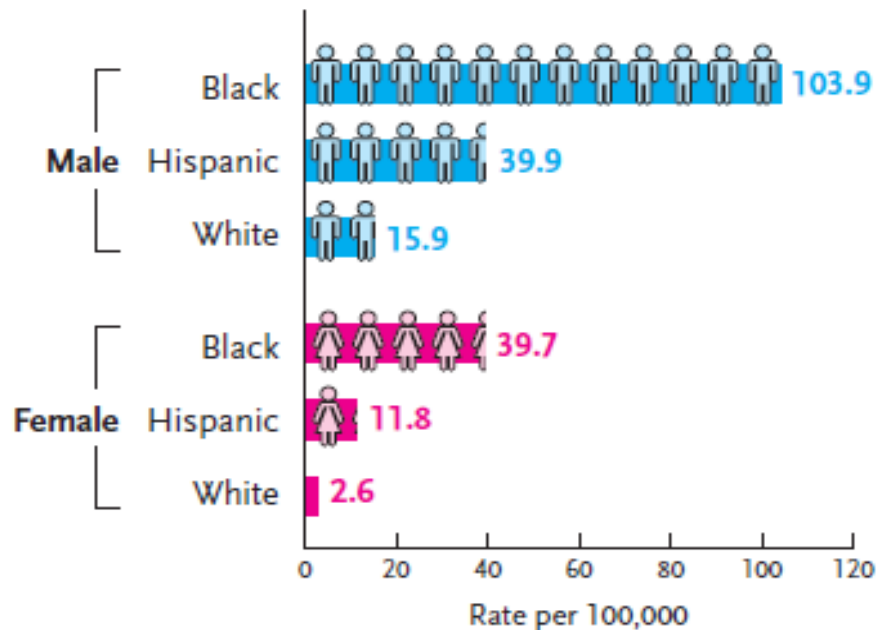
New HIV infections 2009

Figure 1: Estimated New HIV Infections in the U.S., 2009, for the Most-Affected Subpopulations

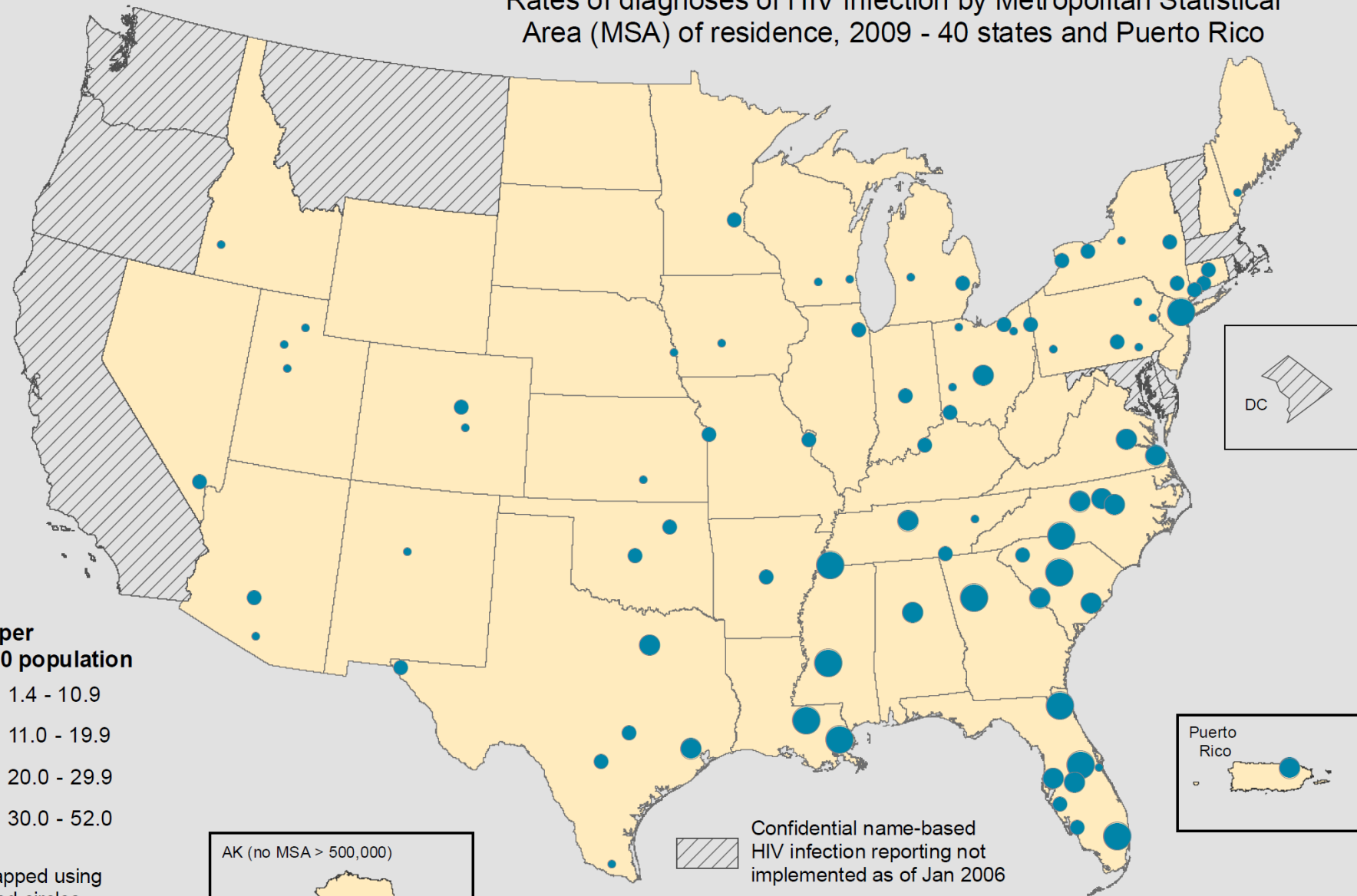


New HIV Infection By Gender and Race

Figure 7: Estimated Rate of New HIV Infections, 2009, by Gender and Race/Ethnicity



Rates of diagnoses of HIV infection by Metropolitan Statistical Area (MSA) of residence, 2009 - 40 states and Puerto Rico



Rates per 100,000 population

- 1.4 - 10.9
- 11.0 - 19.9
- 20.0 - 29.9
- 30.0 - 52.0

Data mapped using graduated circles, classed using natural breaks



Confidential name-based HIV infection reporting not implemented as of Jan 2006

Notes: Only MSAs with over 500,000 population included (where all parts of the MSA had confidential name-based HIV infection reporting implemented as of Jan 2006). Data include persons with a diagnosis of HIV infection regardless of the stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting. Data source: HIV Surveillance Report, 2009. Vol. 21, table 23. Inset maps not to scale.

HIV among African Americans

- + While blacks represent approximately 12% of the U.S. population, they account for almost half (46%) of people living with HIV in the US, as well as nearly half (45%) of new infections each year.
- + At some point in their life, approximately one in 16 black men will be diagnosed with HIV, as will one in 30 black women.

HIV among MSM

- + MSM account for more than half (53%) of all new HIV infections in the U.S. each year, as well as nearly half (48%) of people living with HIV.
- + MSM account for just 4% of the US male population aged 13 and older, but the rate of new HIV diagnoses among MSM in the US is more than 44 times that of other men and more than 40 times that of women.
- + MSM is the only risk group in the U.S. in which new HIV infections have been increasing since the early 1990s.

HIV and AIDS Diagnoses and Death

- + A CDC study found that in 2008 19% MSM in 21 major US cities were infected with HIV
- + 44% were unaware of their infection.

Prevention Challenges

- + Alcohol and illicit drug use contributes to increased risky behavior and thus increased risk of HIV and other STD's
- + Many MSM are unaware of HIV status
 - ✂ Study in urban MSM in 21 cities in 2008 demonstrated that 55% hadn't been tested in prior 12 months
 - ✂ Young MSM and MSM of color less likely to know status
- + CDC recommends all MSM get tested once a year, or more if at high risk
 - ✂ Multiple partners or use drugs during sex

Other Barriers

- + Racism, poverty, lack of access to healthcare are barriers to HIV prevention services, especially for MSM from racial or ethnic minorities
- + There is a correlation between education and awareness of HIV status- higher education linked to greater likelihood of knowing HIV status

Barriers

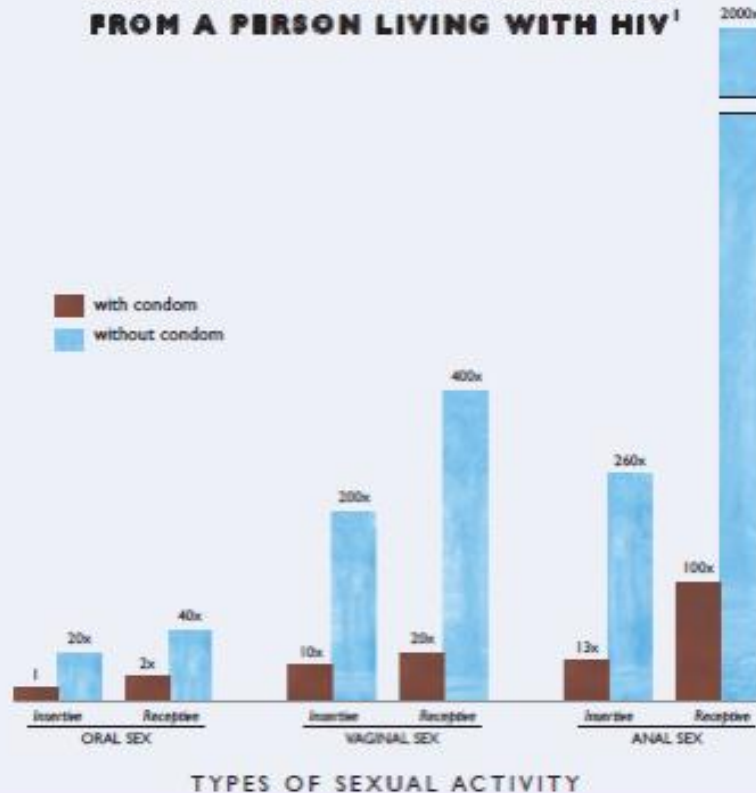
- + Stigma and homophobia have an impact on mental and sexual health services for MSM
- + Untreated depression can also prevent access to adequate healthcare services
- + Internalized homophobia can impact an individual's decision to seek healthcare and can lead to substance abuse
- ✂ Some patients think they “deserve” HIV

Other HIV prevention strategies

- ✦ Antiretroviral drugs (ARVs):
 - To prevent perinatal transmission
 - To reduce infectiousness
 - To prevent new infections (as Pre-Exposure Prophylaxis [PrEP])
- ✦ Male circumcision
 - To reduce risk of HIV infection through penile-vaginal sex



RELATIVE RISK FOR TRANSMISSION FROM A PERSON LIVING WITH HIV¹



Decisions about sexual activity and condom use have a major effect on the risk for HIV transmission.

PrEP

Why consider PrEP?

- + Need more than condoms and counseling
- + Effective microbicides and vaccines still years away
- + Not coitally-dependent
- + Will be used with, and can enhance, existing prevention modalities
- + Significantly reduces HIV acquisition for both women and men
 - ✂ Women get HIV infection from male partners
 - ✂ Men get HIV infection from female partners
 - ✂ All HIV transmission occurs in discordant partnerships (however brief)

PrEP: Benefits and risks (so far)

+ Primary care benefits

✂ hepatitis vaccination,
reproductive health care

+ Cost-effective

✂ Yes, if targeted to those
with high incidence

+ Resistance

✂ Uncommon if screening
for acute infection

+ Toxicities/side
effects

✂ Few, mild, and
transient

+ Adherence

✂ Poor in some trials,
high in others

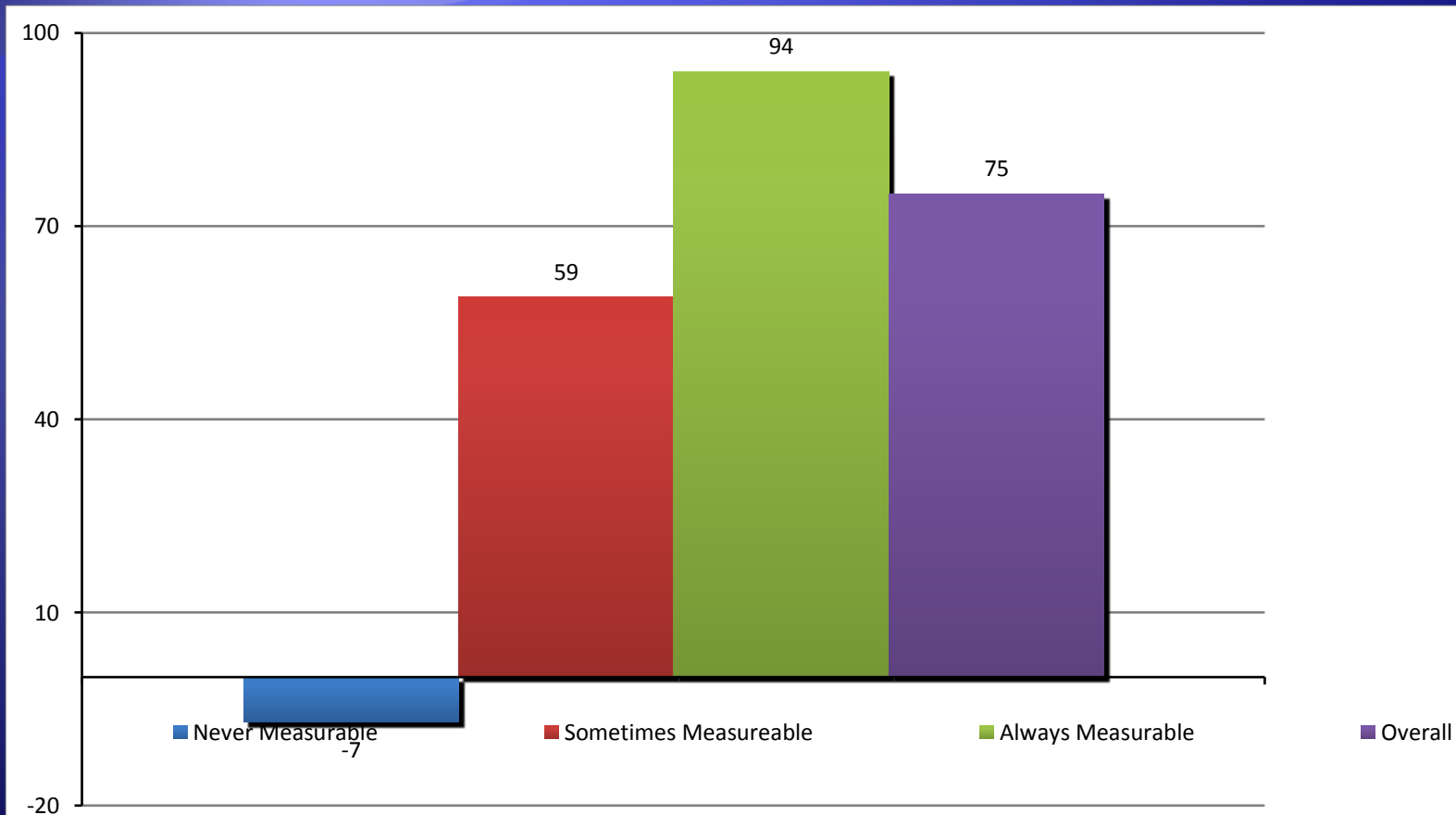
+ Risk compensation

✂ Not seen (yet), models
suggest unlikely to
exceed benefit

Key Concerns for the Safe and Effective Use of PrEP

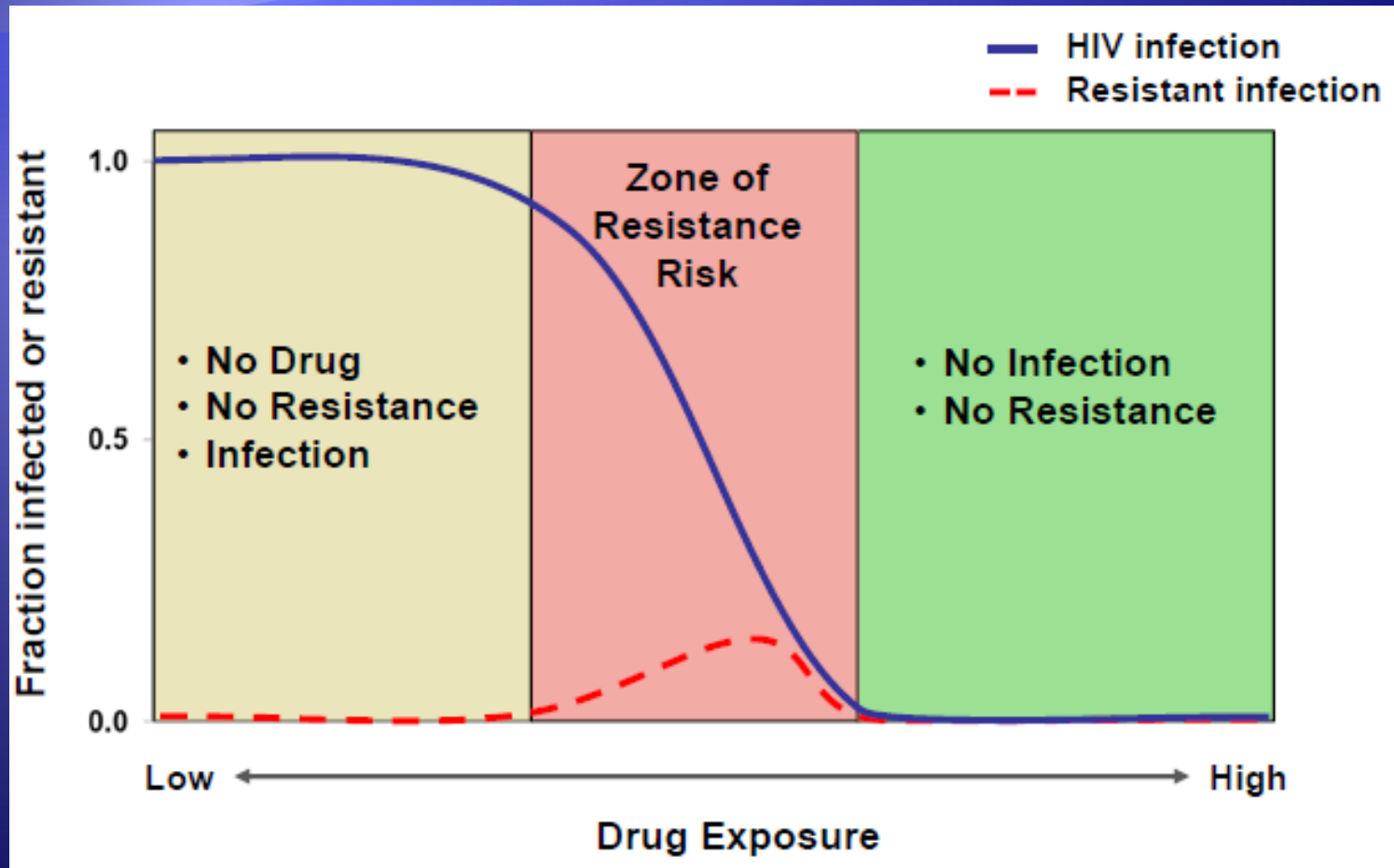
- + Risk Compensation
 - ✂ Condom substitution
 - ✂ Increased risk behaviors
- + Medication Adherence
 - ✂ Daily dosing
- + Viral Resistance
 - ✂ Exclusion of acute HIV infection
 - ✂ Repeated HIV testing

Relative risk reduction in acquiring HIV infection* based on plasma TFV concentrations (Partners PrEP)



*compared with placebo

Adherence and Resistance



PrEP

- + Pre-exposure prophylaxis, or PrEP, is a way to help prevent HIV by taking a pill every day.
- + People who are at substantial risk for HIV should talk to their doctor about PrEP.
- + PrEP must be taken every day to be most effective.

Who should consider PrEP?

- + Anyone who is in an ongoing relationship with an HIV-positive partner
- + Anyone who is not in a mutually monogamous relationship with a partner who recently tested HIV-negative
- + Anyone man who has sex with men, who has had anal sex without a condom or been diagnosed with an STI in the past 6 months
- + heterosexual man or woman who does not regularly use condoms during sex with partners of unknown HIV status who are at substantial risk of HIV infection (e.g., people who inject drugs or have bisexual male partners).

Additional Considerations for PrEP

- + For people who inject drugs, this includes those who have injected illicit drugs in past 6 months and who have shared injection equipment or been in drug treatment for injection drug use in the past 6 months.
- + Also consider for discordant couples who are trying to conceive

Summary of Guidance for PrEP Use

	Men Who Have Sex With Men	Heterosexual Women and Men	Injection Drug Users
Detecting substantial risk of acquiring HIV infection:	• Sexual partner with HIV • Recent bacterial STD • High number of sex partners • History of inconsistent or no condom use • Commercial sex work	• Sexual partner with HIV • Recent bacterial STD • High number of sex partners • History of inconsistent or no condom use • Commercial sex work • Lives in high-prevalence area or network	• HIV-positive injecting partner • Sharing injection equipment • Recent drug treatment (but currently injecting)

PrEP Eligibility

- + Documented negative HIV test before prescribing PrEP
- + No signs/symptoms of acute HIV infection
- + Normal renal function, no contraindicated medications
- + Documented hepatitis B virus infection and vaccination status

PrEP Follow-Up

- + Follow-up visits at least every 3 months to provide prescription; don't prescribe more than 90D at a time to improve f/u
- + Every 3 months, obtain HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STD symptom assessment
- + At 3 months and every 6 months after, assess renal function
- + Every 6 months test for bacterial STDs

PrEP

- + The only antiretroviral medication currently approved for PrEP is Truvada
- + This is a fixed dose combination of emtricitabine and tenofovir
- + Cannot be used in patients with CKD; while label does not require dose reduction for Creat Cl > 50, PrEP not recommended for individuals with GFR < 60
- + Immediate side effects include nausea, flatulence, HA, "start-up syndrome"
- + Long term side effects include loss of bone mineral density and renal impairment

PrEP Follow-Up

- + For women assess for pregnancy at follow-up visits every 3 months
- + For IDU's assess clean needle use, refer for treatment services
- + For MSM's obtain oral, rectal and urine tests to check for STI's

Other Risk Reduction Behaviors

- + Encourage using condoms consistently and correctly
- + Getting HIV testing with partners
- + Choosing less risky sexual behaviors, such as oral sex
- + For people who inject drugs, getting into drug treatment programs and using sterile equipment

Acute HIV

Acquisition of HIV infection

- + Infection often occurs across mucosal barriers
- + Virus first encounters epidermal dendritic cells (DC)
- + Dendritic cells facilitate spread of HIV to CD₄ cells
- + DC-SIGN, and HIV-specific DC receptor binds HIV-1 at its gp-120 domain without requiring direct infection of cell and transports HIV-1 to lymphoid tissue where it replicates over days to weeks

HIV Pathogenesis

- + HIV-1 entry into host cells requires binding at 2 sites: the CD4 T-cell receptor and the CCR5 coreceptor
- + Genetic mutations in the CCR5 receptor give relative protection to both heterozygous and homozygous individuals: individuals can be highly exposed and not infected, or can be long-term nonprogressors

Pathogenesis

- + Once entry into host cell occurs, virus integrates into host genetic material and replicates
- + Dissemination into anatomic reservoirs such as CNS occurs early
- + Time to initial viremia is 4-11 days, but clinically detectable viremia may be longer

Pathogenesis

- + Host immune response attempts to control dissemination during initial period of rapid replication
- + Activation of HIV-1 specific cytotoxic T lymphocytes is a critical immune response and coincides with a decrease in viral load
- + Development of clinical symptoms coincides with high-level viremia and host immune response

Seroconversion

- + Cause of clinical syndrome of seroconversion is not clear, may be direct cytopathic effects or host immune response
- + Classic mononucleosis-like syndrome typically lasts days to weeks
- + Development of HIV-1 specific antibodies mark the end of seroconversion
 - ✂ Usually 3-12 weeks, rarely up to 6-12 months
- + The viral load set point which occurs after seroconversion is prognostic for disease progression

Differential Diagnosis

- + Viral infection:

- ✂ EBV, CMV, primary HSV, parvovirus B19, rubella, influenza, WNV

- + Bacterial infection:

- ✂ Streptococcal disease, secondary syphilis, lyme disease, rickettsial disease, disseminated GC

- + Acute toxoplasmosis

- + Other: Adult Still disease, SLE, Drug reaction, systemic vasculitides

Clinical Presentation

- + About 40-90% of patients will have symptoms of acute HIV infection
- + Symptoms usually occur 2-6 weeks after exposure
- + Typical symptoms: fever, LAD, sore throat, weight loss, nightsweats, fatigue, rash, myalgia, HA, N/V and diarrhea
- + Cytopenia and transaminitis may be present

Clinical Presentation

- + Aseptic meningitis may occur in 10-24%
- + OI may also be a presenting sign
- + AKI and myopericarditis have been reported
- + Illness usually lasts 10-14 days, may be more than 2 months
- + Illness is non-specific and few patients initially diagnosed correctly although most seek medical attention

Case

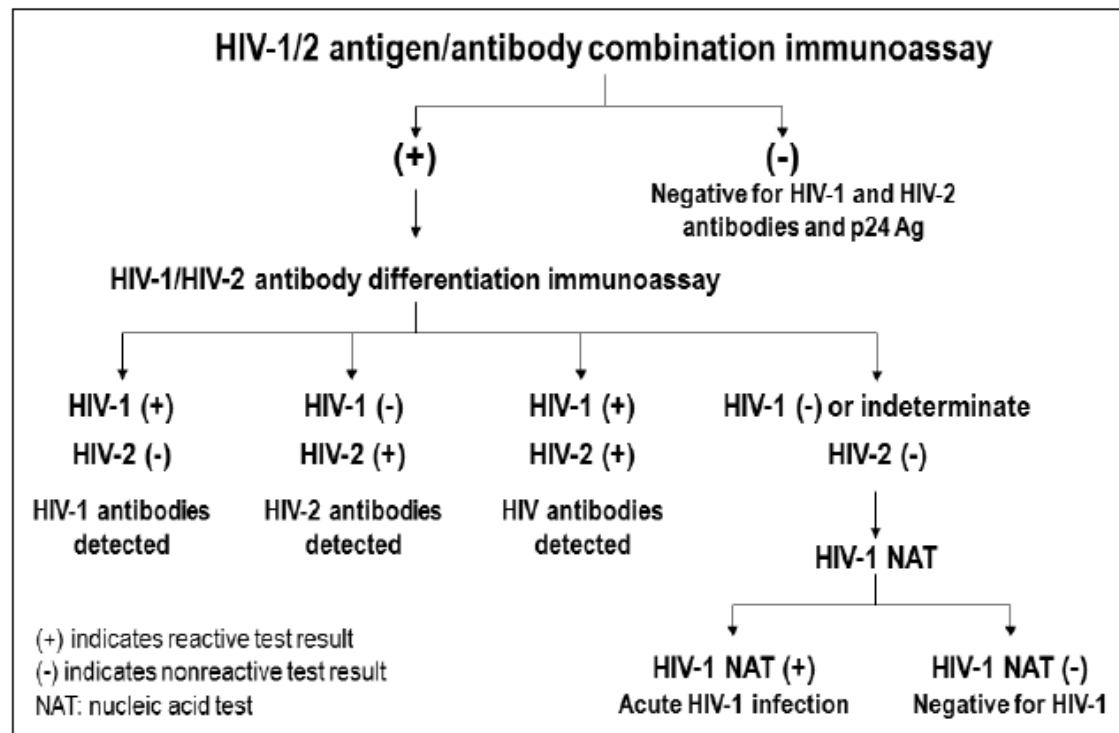
- + 32 y/o man, monogamous with male partner for 15 years, presented with fever 104° , violaceous macular rash on trunk, LAD, transaminitis, pancytopenia and pleural effusion. He had been camping about 3 weeks earlier with his partner in the woods in July.
- + Differential?
- + What would you do?

Case

- + The patient later revealed that he and his partner had had a third partner while camping, and because they were both present, he still considered this to be monogamous.
- + Symptoms persisted more than a month, and he was started on ARV.

Diagnosis

Box 1. Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens



From: Laboratory Testing for the Diagnosis of HIV infection: Updated Recommendations from CDC, December 2014

Aptima HIV-1 Qualitative Assay

- + In vitro nucleic acid assay system for the detection of human immunodeficiency virus (HIV-1) in human plasma and serum.
- + The only commercial FDA-approved nucleic acid amplified test (NAAT) for detection of HIV-1 RNA.
 - ✂ Supports the most recent (June, 2014) CDC HIV testing guidelines¹ and may help prevent the spread of HIV
- + Presence of HIV-1 RNA in the plasma or serum of patients without antibodies to HIV-1 is indicative of acute or primary HIV-1 infection.
- + RNA NAAT detects the presence of HIV-1 up to 7-10 days earlier than the latest 4th generation immunoassays and 26 days before Western Blot

How long after exposure should testing occur?

- + “Window period” (time between exposure and detectable HIV antibody): average is 25 days
- + Most will have antibodies within 2-8 weeks
- + 97% will seroconvert by 3 months
- + Some individuals may take up to 3 months to seroconvert, and rarely up to 6-12 months
- + For high-risk exposures, consider repeat testing > 3 months after exposure

Caveats about VL

- + VL is generally very high during acute infection
- + False positive tests can occasionally occur
- + A threshold of $>10,000$ copies should be used when considering acute infection

Conclusions

- + HIV prevalence is increasing
- + MSM are highest risk group for HIV infection
- + HIV is preventable
- + PrEP should be considered for any high risk individuals