

HIV Update: Epidemiology, Pathogenesis, Treatment and PrEp

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Objectives

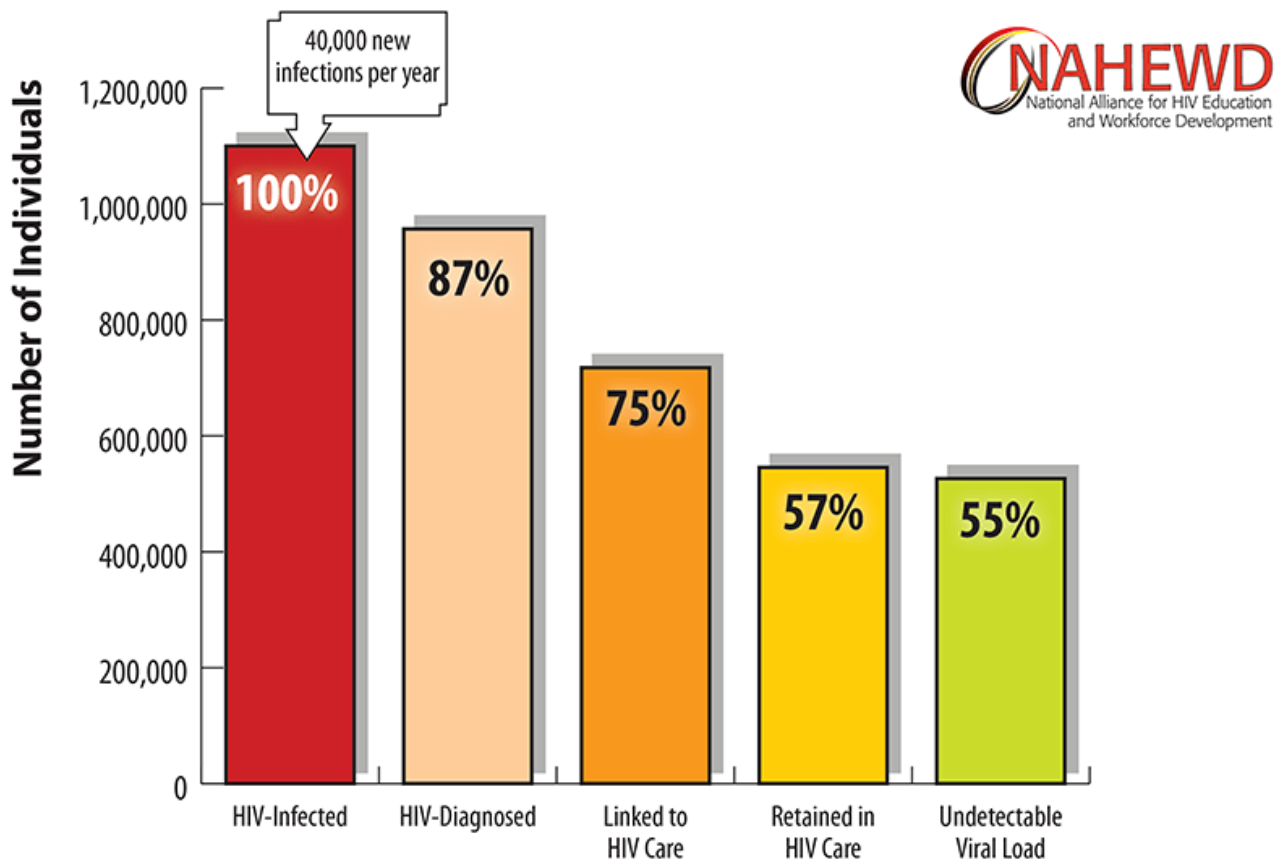
- After this presentation the attendee should be able to:
 - Describe current epidemiological trends in the HIV epidemic;
 - Describe key points in HIV pathogenesis;
 - Describe current treatment standards;
 - Describe PrEp

Objectives

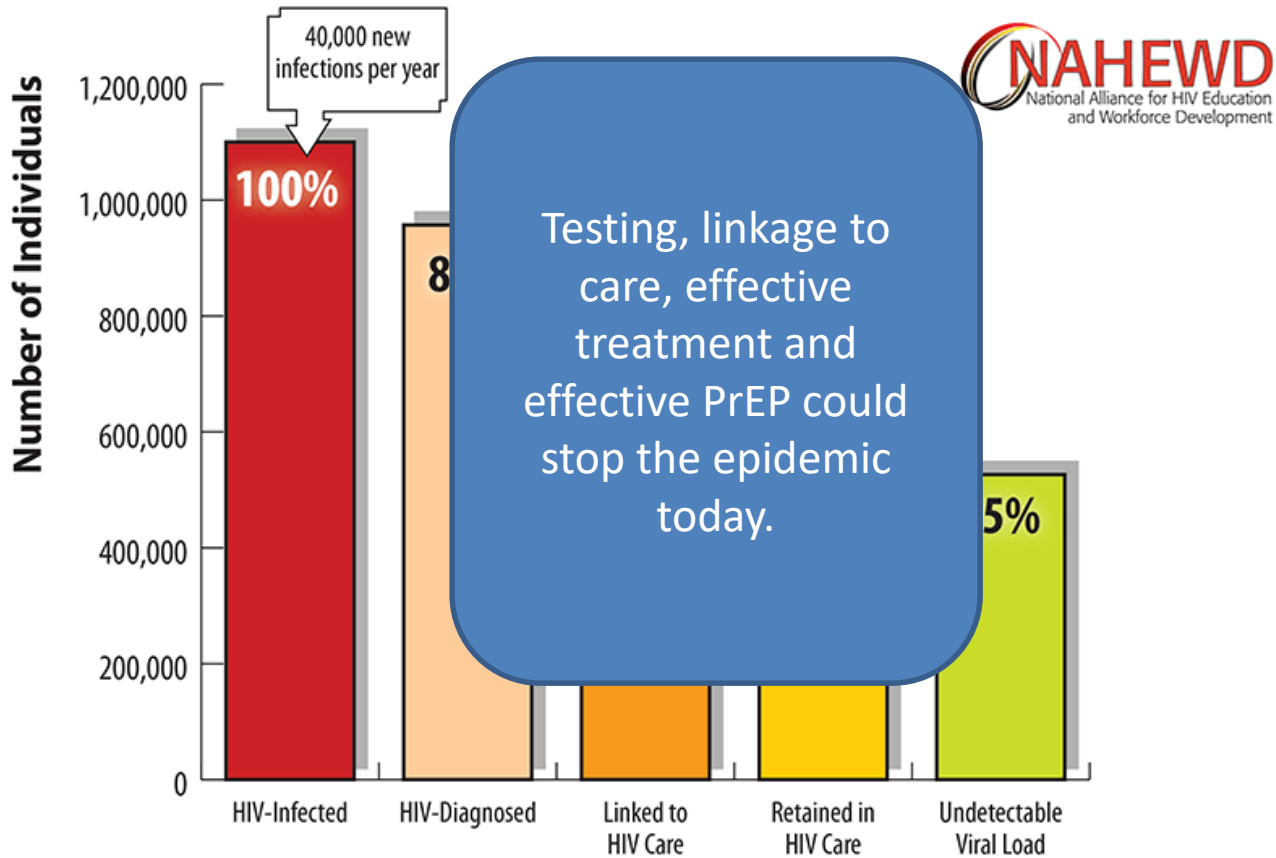
- After this presentation, the audience should be able to:
 - Describe the current status of the HIV epidemic;
 - Describe the impact of HIV on public health;
 - Describe the role of PrEP in HIV prevention;
 - Describe PrEP

Secret Objective: convince you to start screening, testing for HIV and prescribing PrEP as appropriate.

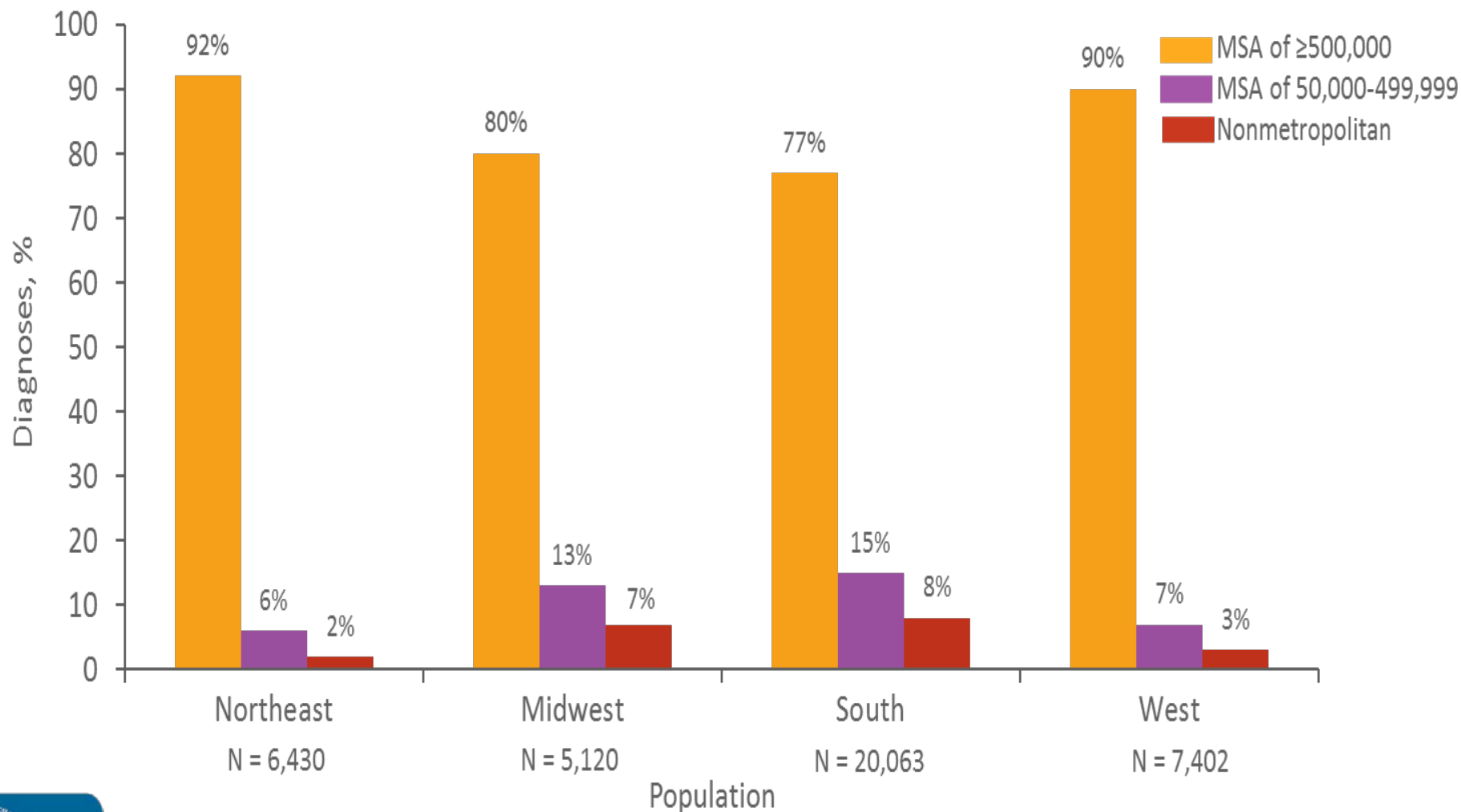
The U.S. HIV Care Continuum¹



The U.S. HIV Care Continuum¹



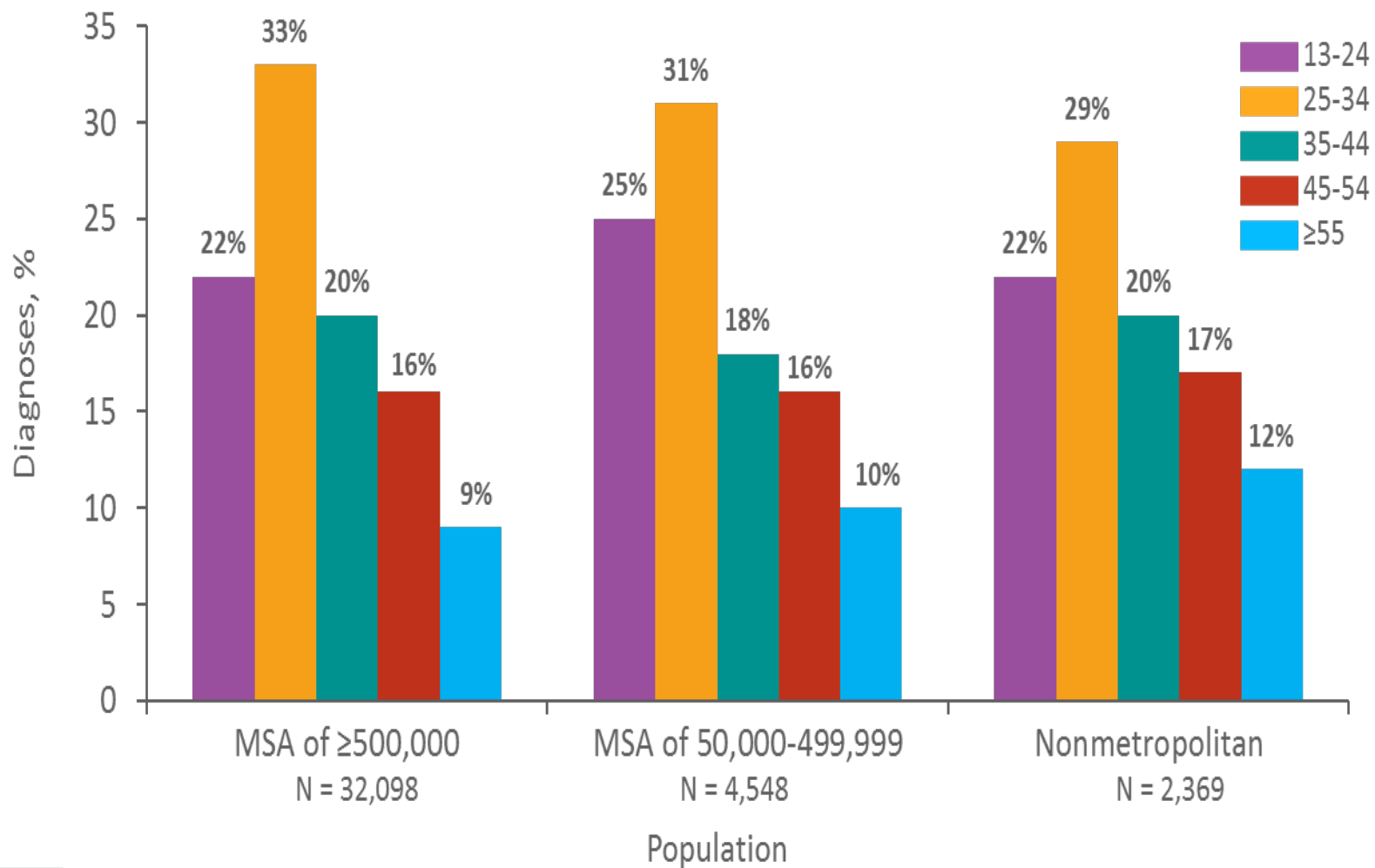
Percentages of Diagnoses of HIV Infection among Adults and Adolescents, by Region and Population of Area of Residence, 2015—United States



Note. 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.



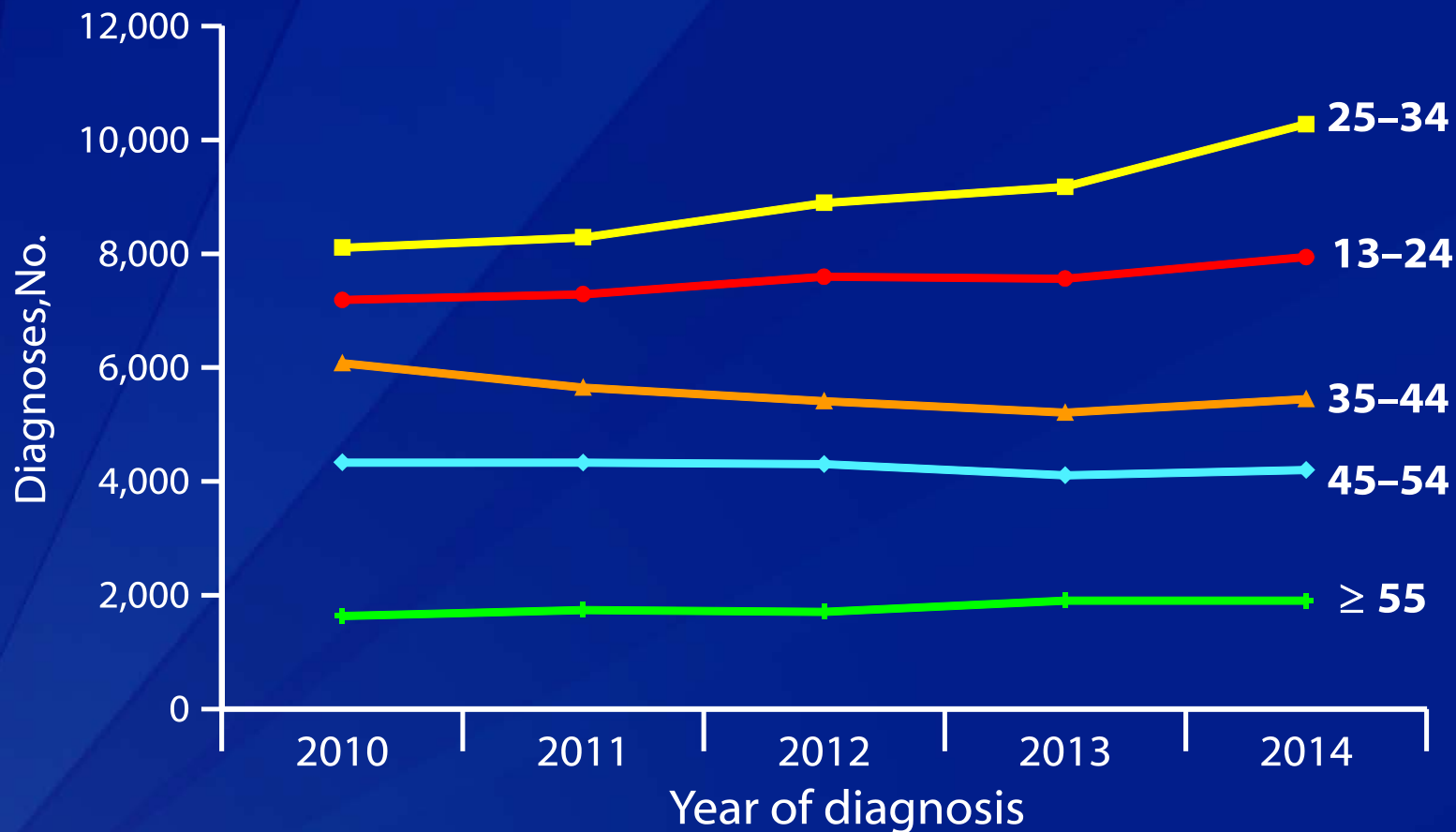
Percentages of Diagnoses of HIV Infection among Adults and Adolescents, by Population of Area of Residence and Age at Diagnosis, 2015—United States



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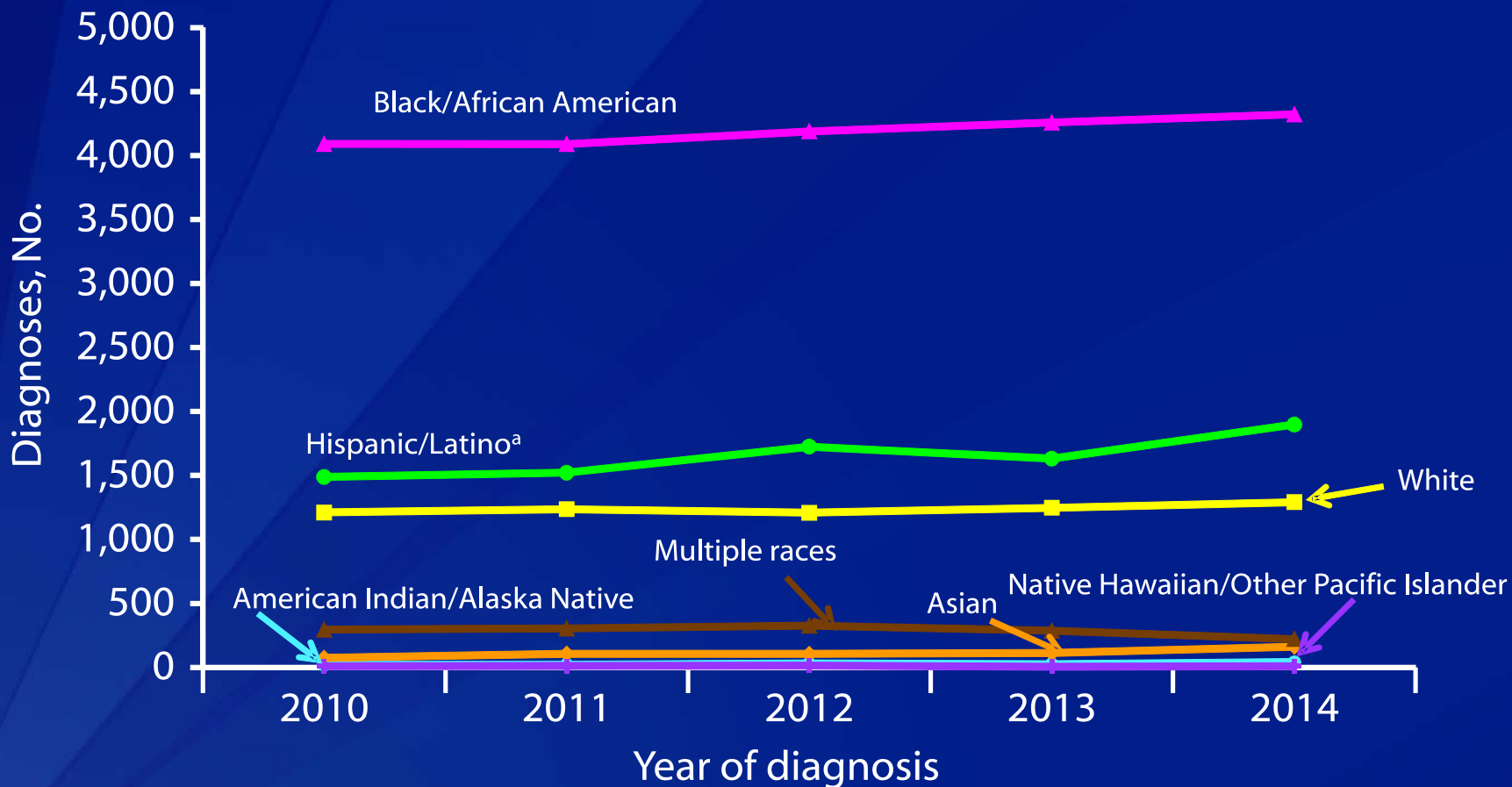
Diagnoses of HIV Infection among Men Who Have Sex with Men, by Age Group, 2010–2014—United States and 6 Dependent Areas



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 drug use.



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

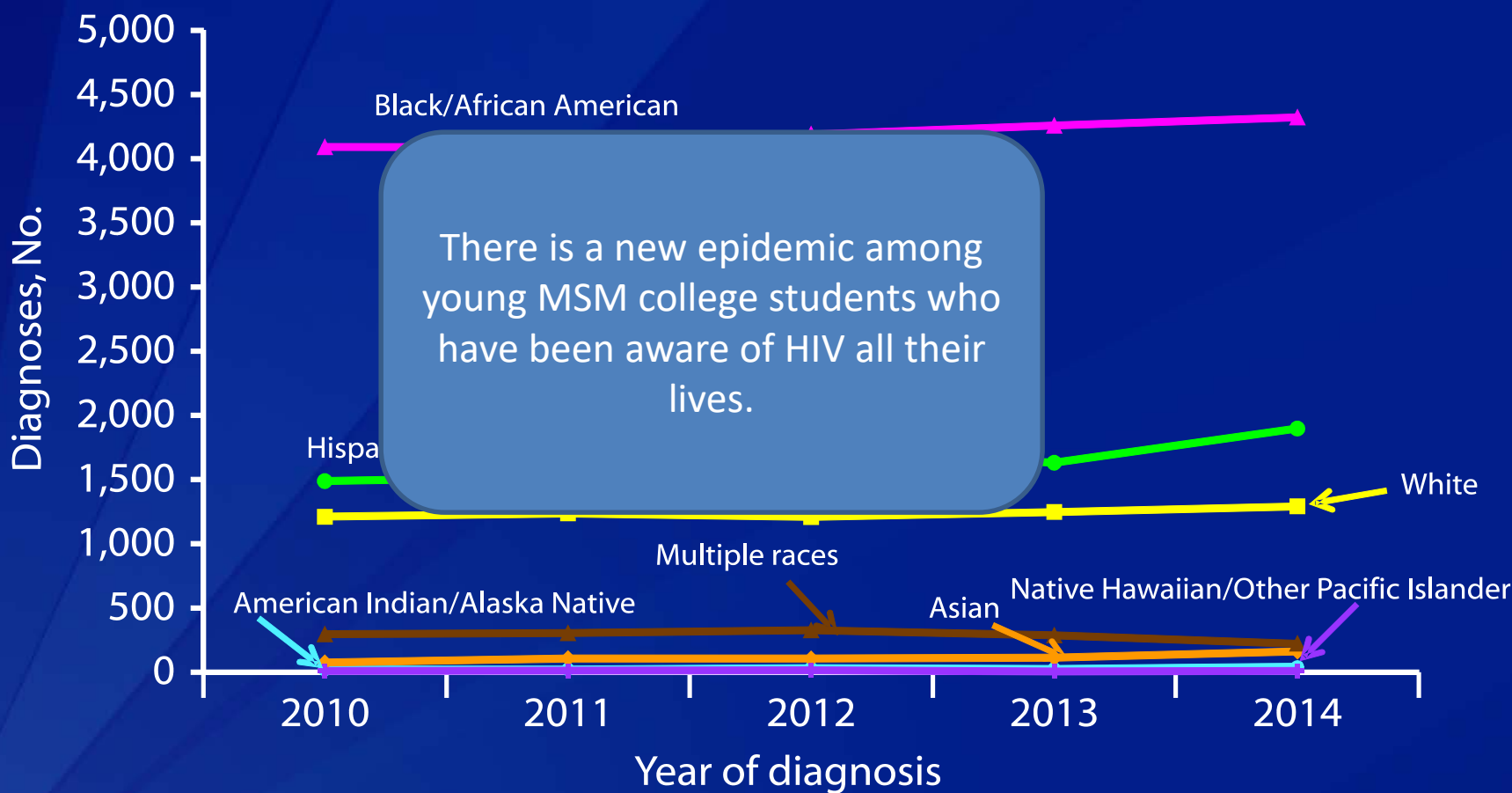


Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing transmission category, but not for incomplete reporting. Data on men who have sex with men do not include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

^a Hispanics/Latinos can be of any race.



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



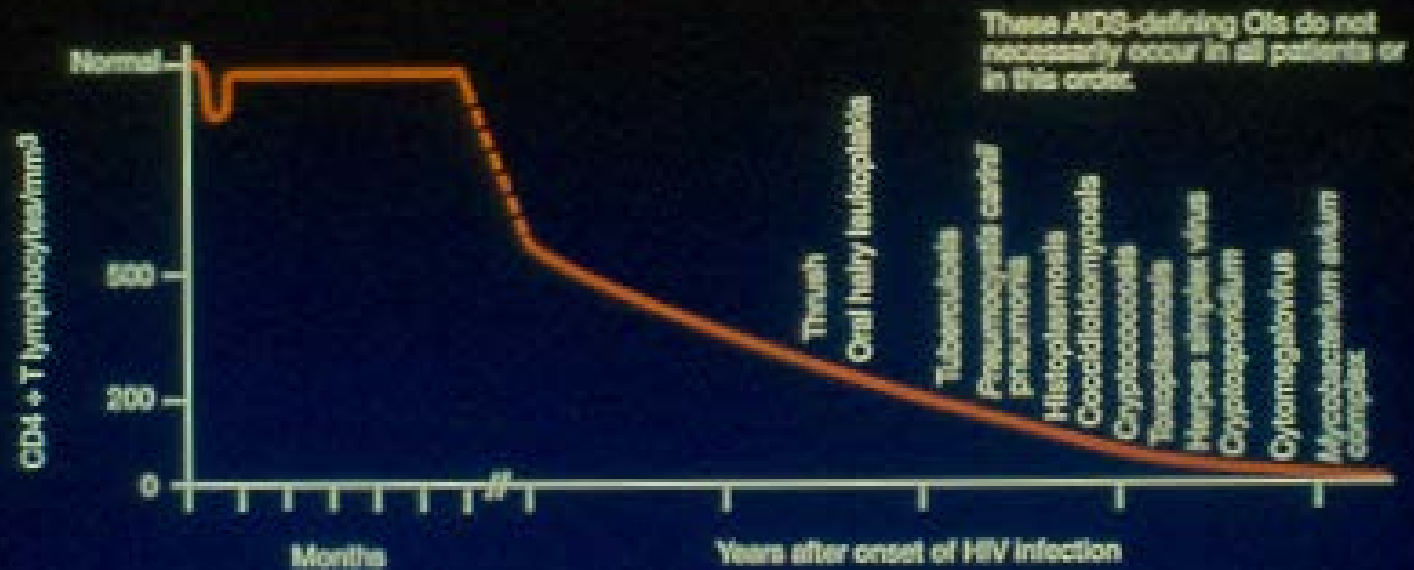
Note. Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing transmission category, but not for incomplete reporting. Data on men who have sex with men do not include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

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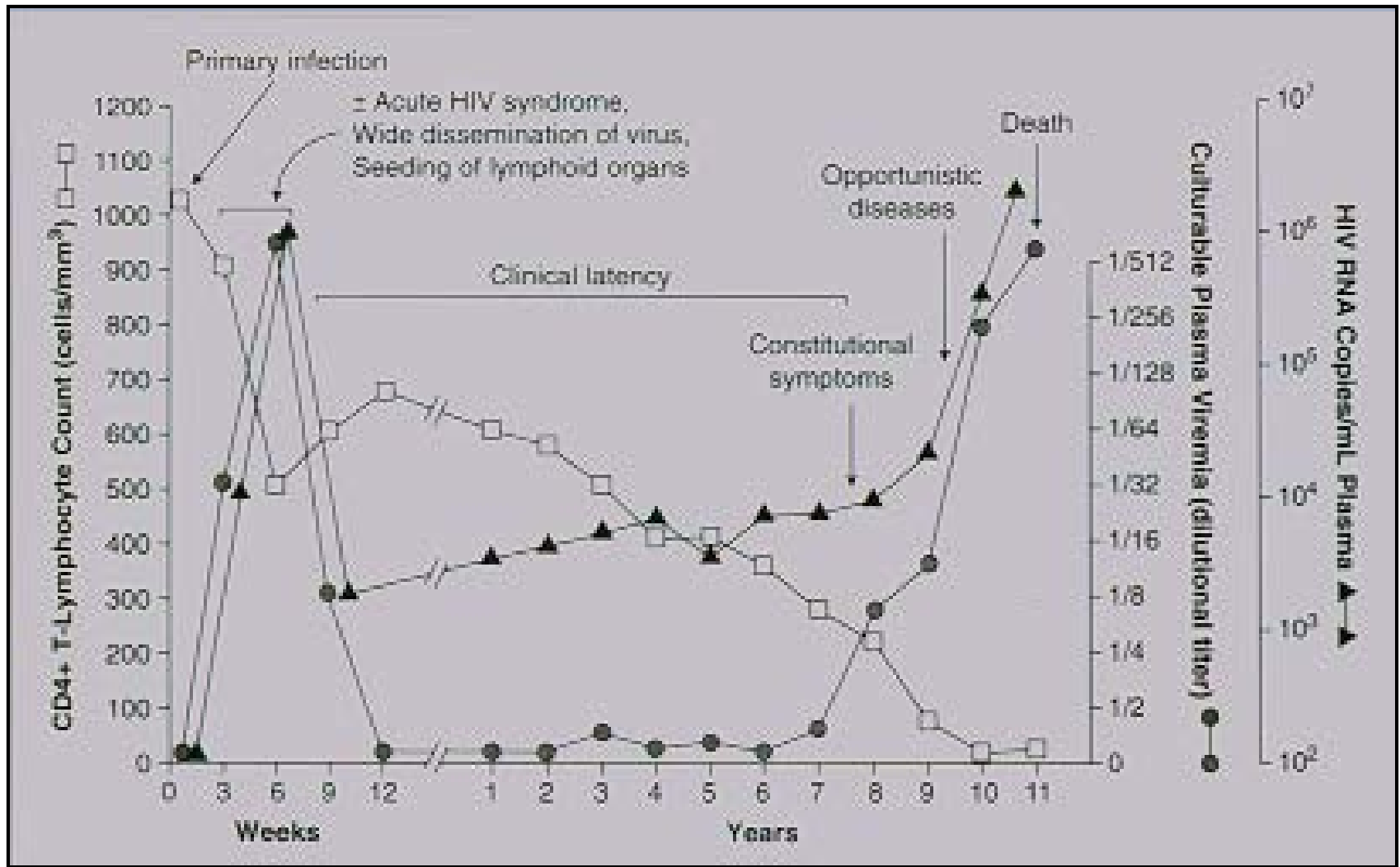


- HIV Pathogenesis

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.

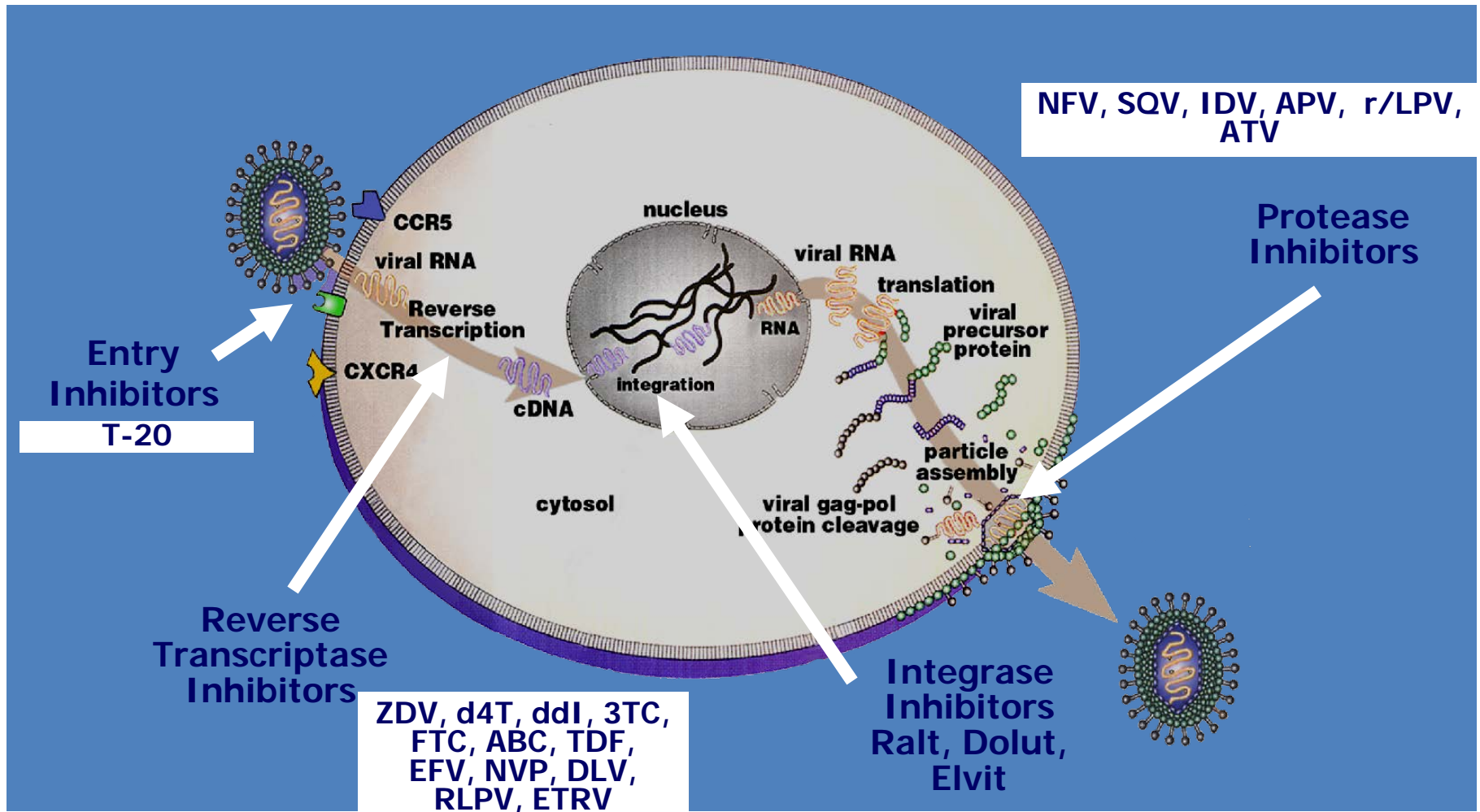
Treatment



Three Decades of Treatment Issues

- **1980's**: AIDS described, PCP kills 90% of pts., clinicians develop skills in diagnosing, preventing complications, treating and.
- **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, tipranavir, darunavir
- **Fusion I's:** enturvidine
- **CCR5 I's:** maraviroc
- **Integrase I's:** raltegravir, dolutegravir, elvitegravir, bictegravir

Current Available Medications

- **NRTI's:** zidovudine, didanosine, stavudine, lamivudine, abacavir, emtricitabine, tenofovir, TAF
- **NNRTI's:** efavirenz, rilpivirine
- **PI's:** darunavir, lopinavir, tipranavir,
- **Fusidic acid**
- **CCR5 I's:** maraviroc
- **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.

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.
- Treating people with AIDS greatly improves CD4 count (CD4 count > 50 CD4).
- Treating people with AIDS greatly improves immune function (may decrease the risk of opportunistic infections).
- 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.

PrEP: What about never getting infected in the first place?



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 male presents to ED with cough, fever, and malaise.
 - Slight weight loss
 - No other symptoms
- Back in school, had fever, severe malaise and myalgias.
 - HIV serology indeterminate, HIV-1 RNA 2,466,303 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.

Primary Prevention

HIV

Myocardial infarction or Stroke

Assess risk	Take a sexual history	Take a past medical, family, social history, check cholesterol and screen for diabetes, calculate 10-year ASCVD risk by 2013 ACC/AHA guidelines
Laboratory evaluation	Serum creatinine, HIV screen	Comprehensive metabolic panel, cholesterol profile, hemoglobin a1c
Further risk reduction	Condom use, sexual health and substance use counseling, STI screening	Lifestyle and diet modification counseling, treat comorbid conditions (hypertension, diabetes), smoking cessation
Medication options	Truvada®	Atorvastatin Rosuvastatin Pravastatin Pitavastatin Simvastatin Fluvastatin Aspirin

Primary Prevention

	HIV	Myocardial Infarction or Stroke
Assess risk	Take a sexual history	Family, social history, cholesterol and blood pressure, calculate 10-year ASCVD risk by 2013 ACC/AHA guidelines
Laboratory evaluation	Serum creatinine	Comprehensive metabolic panel, cholesterol profile, hemoglobin a1c
Further risk reduction	Counseling on condom use, STI testing	Lifestyle and diet modification counseling, treat comorbid conditions (hypertension, diabetes), smoking cessation
Medication options		Atorvastatin Rosuvastatin Pravastatin Pitavastatin Simvastatin Fluvastatin Aspirin

PREP IS EASY

Who benefits from PrEP

Who benefits from PrEP

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:	<ul style="list-style-type: none"> Sexual partner with HIV Recent bacterial STD High number of sex partners History of inconsistent or no condom use Commercial sex work 	<ul style="list-style-type: none"> 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 	<ul style="list-style-type: none"> HIV-positive injecting partner Sharing injection equipment Recent drug treatment (but currently injecting)
Clinically eligible:	<ul style="list-style-type: none"> 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 		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90 day supply		
Other services:	<ul style="list-style-type: none"> Follow-up visits at least every 3 months to provide: 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 		
	<ul style="list-style-type: none"> Do oral/rectal STD testing 	<ul style="list-style-type: none"> Assess pregnancy intent Pregnancy test every 3 months 	<ul style="list-style-type: none"> Access to clean needles/syringes and drug treatment services

Source: US Public Health Service. Preexposure prophylaxis for the prevention of HIV infection in the United States—2014: a clinical practice guideline.

Who benefits from PrEP

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:	<ul style="list-style-type: none"> Sexual partner Recent bacter High number partners History of inco no condom us Commercial se 	HIRI-MSM Risk Index*	
		1 How old are you today (yrs)?	<ul style="list-style-type: none"> <18 years score 0 18–28 years score 8 29–40 years score 5 41–48 years score 2 ≥49 years score 0
		2 How many men have you had sex with in the last 6 months?	<ul style="list-style-type: none"> >10 male partners score 7 6–10 male partners score 4 0–5 male partners score 0
Clinically eligible:	<ul style="list-style-type: none"> Docume No signs Normal r Docume 	3 In the last 6 months, how many times did you have receptive anal sex (you were the bottom) with a man?	<ul style="list-style-type: none"> 1 or more times score 10 0 times score 0
Prescription	Da		
Other services:	<ul style="list-style-type: none"> Follow-u HIV test, side effe At 3 mor Every 6 r 	4 How many of your male sex partners were HIV positive?	<ul style="list-style-type: none"> >1 positive partner score 8 1 positive partner score 4 <1 positive partner score 0
	<ul style="list-style-type: none"> Do oral/rectal S 	5 In the last 6 months, how many times did you have insertive anal sex (you were the top) with a man who was HIV positive?	<ul style="list-style-type: none"> 5 or more times score 6 0 times score 0
		6 In the last 6 months, have you used methamphetamines such as crystal or speed?	<ul style="list-style-type: none"> Yes score 5 No score 0
		7 In the last 6 months, have you used poppers (amyl nitrate)?	<ul style="list-style-type: none"> Yes score 3 No score 0
			Add down entries in right column to calculate total score Total score†
<p>*To identify sexually active MSM in their practice, we recommend clinicians ask all their male patients a routine question: "In the past (time) have you had sex? (if yes), with men, women, or both?"</p> <p>†If score is 10 or greater, evaluate for PrEP or other intensive HIV prevention services; If score is 9 or less, provide indicated standard HIV prevention services.</p>			

Source: US Public Health Service. Preexposure prophylaxis

Who benefits from PrEP

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Source: US Public Health Service. Preexposure prophylaxis

*To identify sexually active MSM their male patients a routine question: men, women, or both?"

†If score is 10 or greater, evalu services; If score is 9 or less, provide

Medication Guide
TRUVADA® (tru-VAH-dah)
(emtricitabine and tenofovir disoproxil fumarate)
tablets

Read this Medication Guide before you start taking TRUVADA and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

This Medication Guide provides information about two different ways that TRUVADA may be used (see the Medication Guide section "What is TRUVADA?" for important information about how TRUVADA may be used):

- to treat Human Immunodeficiency Virus-1 (HIV-1) infection, and
- to reduce the risk of getting HIV-1 infection in adults who are HIV-negative

HIV is the virus that causes AIDS (Acquired Immune Deficiency Syndrome).

What is the most important information I should know about TRUVADA?
If you also have hepatitis B virus (HBV) infection and take TRUVADA, your hepatitis B may become worse if you stop taking TRUVADA.

- Do not stop taking TRUVADA without first talking to your healthcare provider.
- Do not run out of TRUVADA. Refill your prescription or talk to your healthcare provider before your TRUVADA is all gone.
- If your healthcare provider stops TRUVADA, your healthcare provider will need to watch you closely for several months to check your hepatitis B infection, or give you a medication to treat hepatitis B.

Tell your healthcare provider about any new or unusual symptoms you may have after you stop taking TRUVADA. For more information about side effects, see the section "What are the possible side effects of TRUVADA?" in this Medication Guide.

Other important information for people who take TRUVADA to help reduce their risk of getting HIV-1 infection:
Before taking TRUVADA to reduce your risk of getting HIV-1 infection:

- You must be HIV-negative to start TRUVADA. You must get tested to make sure that you do not already have HIV-1 infection.**
- Do not take TRUVADA to reduce the risk of getting HIV-1 unless you are confirmed to be HIV-negative.**
- Many HIV-1 tests can miss HIV-1 infection in a person who has recently become infected. If you have flu-like symptoms, you could have recently become infected with HIV-1. Tell your healthcare provider if you had a flu-like illness within the last month before starting TRUVADA or at any time while taking TRUVADA. Symptoms of new HIV-1 infection include:
 - tiredness
 - fever
 - joint or muscle aches
 - sore throat
 - vomiting or diarrhea
 - rash

Who benefits from PrEP

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Anyone with high risk for HIV acquisition, as determined by the patient's and/or provider's assessment, in which the risk of Truvada[®] does not outweigh the benefit.

*To identify sexually active MSM their male patients a routine question: men, women, or both?"
 †If score is 10 or greater, evaluate services; If score is 9 or less, provide

Medication Guide:
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How well does PrEP work?

iPrEX



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FOR AUTHORS ▾

CME >

ORIGINAL ARTICLE

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier R. Lama, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa McMahan, B.S., Albert Y. Liu, M.D., M.P.H., Lorena Vargas, Pedro Goicochea, M.Sc., Martín Casapía, M.D., M.P.H., Juan Vicente Guanira-Carranza, M.D., M.P.H., Maria E. Ramirez-Cardich, M.D., Orlando Montoya-Herrera, M.Sc., Telmo Fernández, M.D., Valdilea G. Veloso, M.D., Ph.D., Susan P. Buchbinder, M.D., Suwat Chariyalertsak, M.D., Dr.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Esper Georges Kallás, M.D., Ph.D., K. Rivet Amico, Ph.D., Kathleen Mulligan, Ph.D., Lane R. Bushman, B.Chem., Robert J. Hance, A.A., Carmela Ganoza, M.D., Patricia Defechereux, Ph.D., Brian Postle, B.S., Furong Wang, M.D., J. Jeff McConnell, M.A., Jia-Hua Zheng, Ph.D., Jeanny Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the iPrEx Study Team*

N Engl J Med 2010; 363:2587-2599 | [December 30, 2010](#) | DOI: 10.1056/NEJMoa1011205

44% HIV risk reduction, but 92% risk reduction when taken consistently among MSM and transgender women

TDF2 Study Group



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ORIGINAL ARTICLE

Antiretroviral Preexposure Prophylaxis for Heterosexual HIV Transmission in Botswana

Michael C. Thigpen, M.D., Poloko M. Kebaabetswe, Ph.D., M.P.H., Lynn A. Paxton, M.D., M.P.H., Dawn K. Smith, M.D., M.P.H., Charles E. Rose, Ph.D., Tebogo M. Segolodi, M.Sc., Faith L. Henderson, M.P.H., Sonal R. Pathak, M.P.H., Fatma A. Soud, Ph.D., Kata L. Chillag, Ph.D., Rodreck Mutanhaurwa, M.B., Ch.B., Lovemore Ian Chirwa, M.B., Ch.B., M.Phil., Michael Kasonde, M.B., Ch.B., Daniel Abebe, M.D., Evans Buliva, M.B., Ch.B., Roman J. Gvetadze, M.D., M.S.P.H., Sandra Johnson, M.A., Thom Sukalac, Vasavi T. Thomas, M.P.H., R.Ph., Clyde Hart, Ph.D., Jeffrey A. Johnson, Ph.D., C. Kevin Malotte, Dr.P.H., Craig W. Hendrix, M.D., and John T. Brooks, M.D., for the TDF2 Study Group*

N Engl J Med 2012; 367:423-434 | [August 2, 2012](#) | DOI: 10.1056/NEJMoa1110711

62.2% HIV risk reduction among
heterosexual men and women

Partners PrEP Study Team



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ORIGINAL ARTICLE

Antiretroviral Prophylaxis for HIV Prevention in Heterosexual Men and Women

Jared M. Baeten, M.D., Ph.D., Deborah Donnell, Ph.D., Patrick Ndase, M.B., Ch.B., M.P.H., Nelly R. Mugo, M.B., Ch.B., M.P.H., James D. Campbell, M.D., Jonathan Wangisi, M.B., Ch.B., Jordan W. Tappero, M.D., M.P.H., Elizabeth A. Bukusi, M.B., Ch.B., Ph.D., Craig R. Cohen, M.D., M.P.H., Elly Katabira, M.B., Ch.B., Allan Ronald, M.D., Elioda Tumwesigye, M.B., Ch.B., Edwin Were, M.B., Ch.B., M.P.H., Kenneth H. Fife, M.D., Ph.D., James Kiarie, M.B., Ch.B., M.P.H., Carey Farquhar, M.D., M.P.H., Grace John-Stewart, M.D., Ph.D., Aloysius Kania, M.B., Ch.B., Josephine Odoyo, M.P.H., Akasiima Mucunguzi, M.B., Ch.B., Edith Nakku-Joloba, M.B., Ch.B., Ph.D., Rogers Twesigye, M.B., Ch.B., M.P.H., Kenneth Ngunjiri, Ph.D., Cosmas Apaka, B.Sc., Harrison Tamoo, M.B., Ch.B., Fridah Gabona, M.B., Ch.B., Andrew Mujugira, M.B., Ch.B., Dana Panteleeff, B.S., Katherine K. Thomas, M.S., Lara Kidoguchi, M.P.H., Meighan Krows, B.A., Jennifer Revall, B.A., Susan Morrison, M.D., M.P.H., Harald Haugen, M.S., Mira Emmanuel-Ogier, B.A., Lisa Ondrejcek, M.A., Robert W. Coombs, M.D., Ph.D., Lisa Frenkel, M.D., Craig Hendrix, M.D., Namandjé N. Bumpus, Ph.D., David Bangsberg, M.D., M.P.H., Jessica E. Haberer, M.D., M.P.H., Wendy S. Stevens, M.D., F.C.Path., Jairam R. Lingappa, M.D., Ph.D., and Connie Celum, M.D., M.P.H., for the Partners PrEP Study Team*

N Engl J Med 2012; 367:399-410 | August 2, 2012 | DOI: 10.1056/NEJMoa1108524

75% HIV risk reduction among heterosexual sero-discordant couples, 90% among those with detectable drug levels

Bangkok Tenofovir Study Group



THE LANCET

Volume 381, Issue 9883, 15–21 June 2013, Pages 2083–2090



Articles

Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial

Kachit Choopanya, MD^a, Dr Michael Martin, MD^{b, c},  , Pravan Suntharasamai, MD^a, Udomsak Sangkum, MD^a, Philip A Mock, MAppStats^b, Manoj Leethochawalit, MD^d, Sithisat Chiamwongpaet, MD^d, Praphan Kitisin, MD^d, Pitinan Natrujirote, MD^d, Somyot Kittimunkong, MD^e, Rutt Chuachoowong, MD^b, Roman J Gvetadze, MD^e, Janet M McNicholl, MD^{b, c}, Lynn A Paxton, MD^c, Marcel E Curlin, MD^{b, c}, Craig W Hendrix, MD^f, Suphak Vanichseni, MD^a, for the Bangkok Tenofovir Study Group

48.9% risk reduction, but 74% HIV risk reduction when taken consistently, among IDUs (TDF only)

I PERGAY



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ORIGINAL ARTICLE

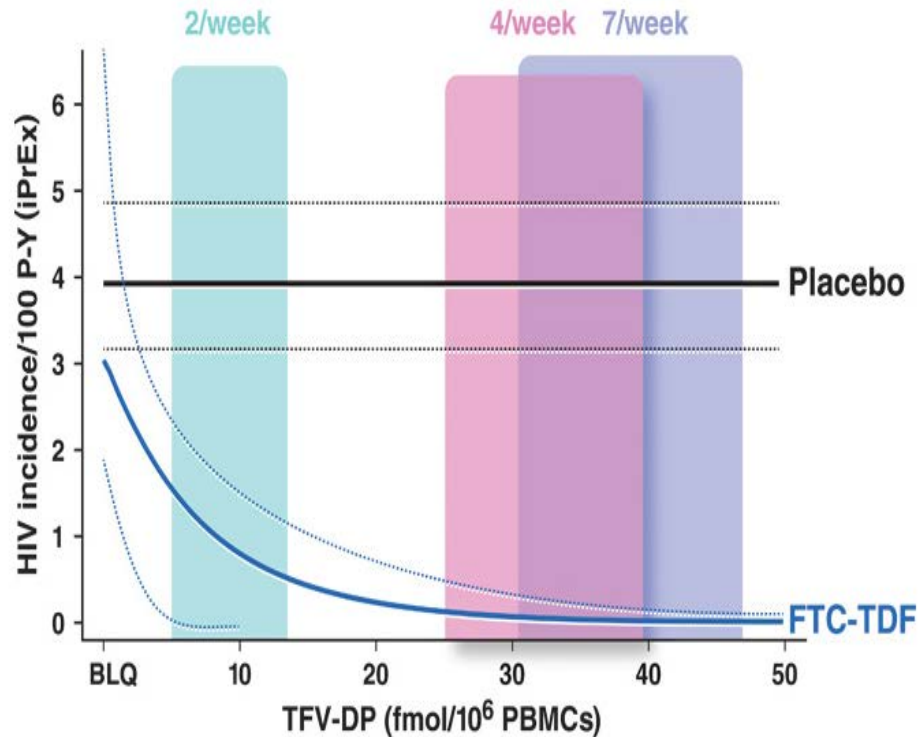
On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

Jean-Michel Molina, M.D., Catherine Capitant, M.D., Bruno Spire, M.D., Ph.D., Gilles Pialoux, M.D., Laurent Cotte, M.D., Isabelle Charreau, M.D., Cecile Tremblay, M.D., Jean-Marie Le Gall, Ph.D., Eric Cua, M.D., Armelle Pasquet, M.D., François Raffi, M.D., Claire Pintado, M.D., Christian Chidiac, M.D., Julie Chas, M.D., Pierre Charbonneau, M.D., Constance Delaugerre, Pharm.D., Ph.D., Marie Suzan-Monti, Ph.D., Benedicte Loze, B.S., Julien Fonsart, Pharm.D., Gilles Peytavin, Pharm.D., Antoine Cheret, M.D., Ph.D., Julie Timsit, M.D., Gabriel Girard, Ph.D., Nicolas Lorente, Ph.D., Marie Préau, Ph.D., James F. Rooney, M.D., Mark A. Wainberg, Ph.D., David Thompson, B.C.L., LL.B., Willy Rozenbaum, M.D., Veronique Doré, Ph.D., Lucie Marchand, B.S., Marie-Christine Simon, B.S., Nicolas Etien, B.S., Jean-Pierre Aboulker, M.D., Laurence Meyer, M.D., Ph.D., and Jean-François Delfraissy, M.D., for the ANRS IPERGAY Study Group*

N Engl J Med 2015; 373:2237-2246 | [December 3, 2015](#) | DOI: 10.1056/NEJMoa1506273

86% HIV risk reduction in MSM using on-demand PrEP

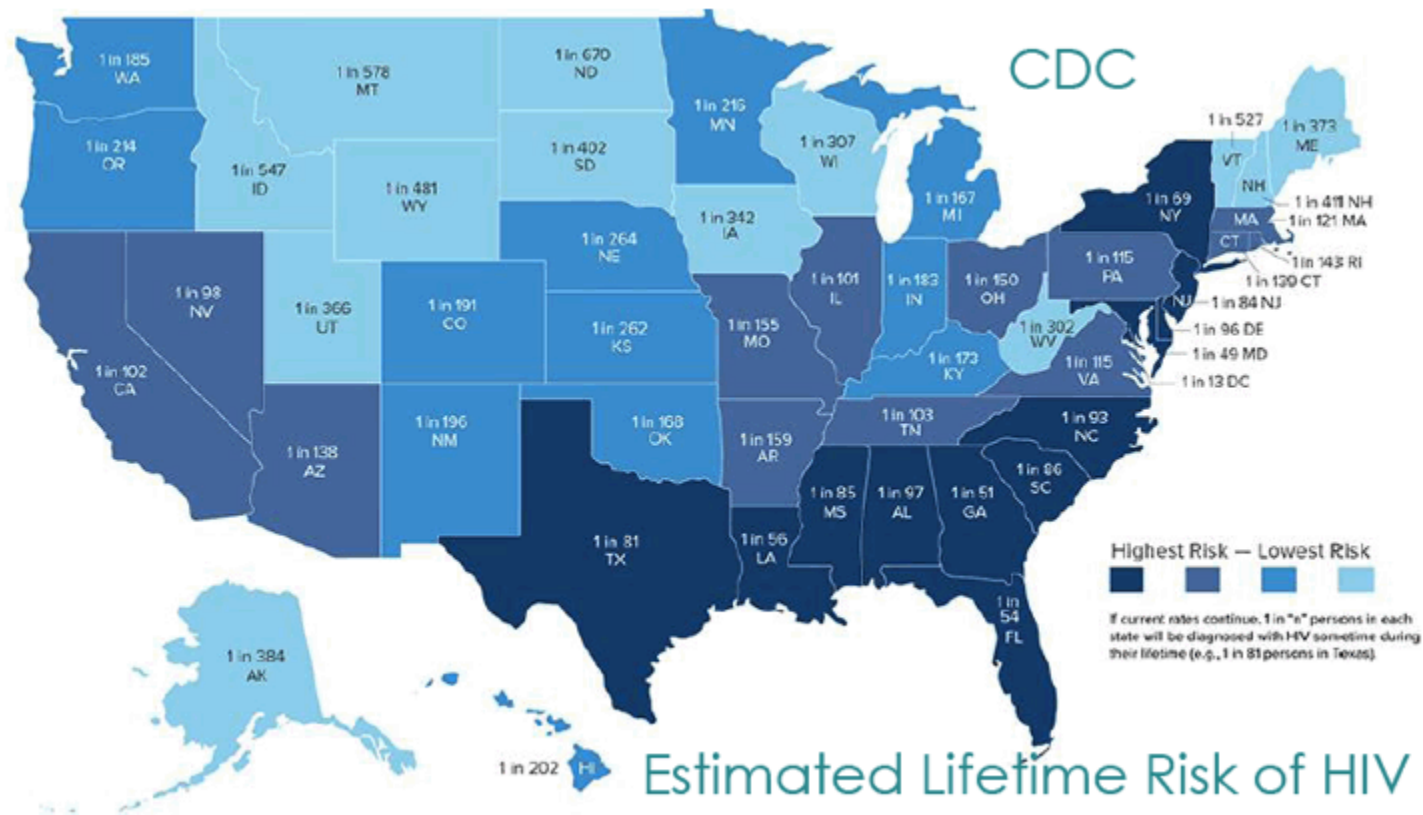
Dosing matters



Using drug concentrations in iPrEx and STRAND, pharmacokinetic models predict **76%** risk reduction with 2 doses/week, **96%** with 4 doses/week, and **99%** with 7 doses/week.

Studies Summary

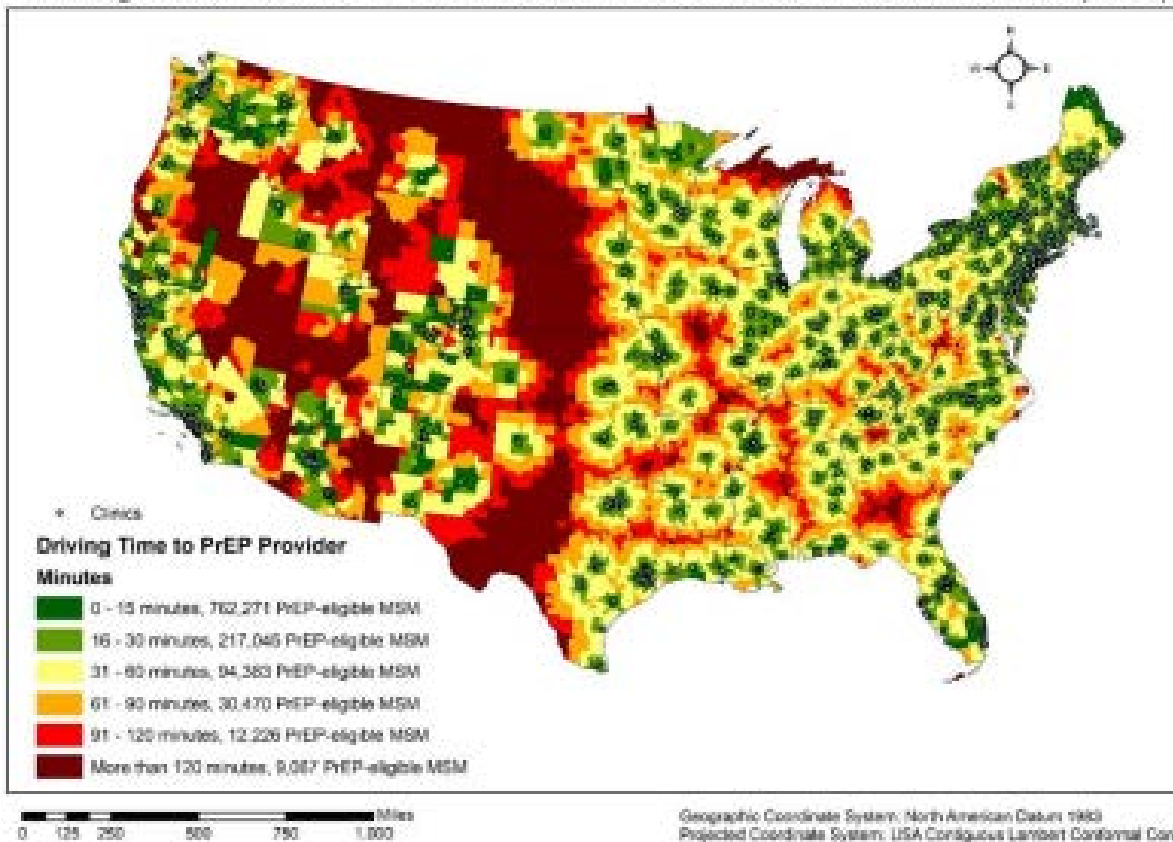
Study	Population	Dosing	Risk Reduction
iPrEX	MSM (2499)	Daily	44% (92% with ideal adherence)
TDF2	Heterosexual men and women (1219)	Daily	62.2% (100% in open-label extension with regular follow-up)
Partners	Sero-discordant heterosexual couples (4758 couples)	Daily	75% (90% with ideal adherence)
Bangkok Tenofovir Study Group	Intravenous drug users (2413)	Daily	48.9% (74% with ideal adherence)
IPIRGAY	MSM (400)	On-demand	86%



The Southeast remains the region with the highest HIV incidence, which can be markedly reduced with widespread use of pre-exposure prophylaxis (PrEP) among high-risk individuals.

PrEP Deserts

Driving Time to Nearest PrEP Provider for men who have sex with men (MSM)



- Most MSM with reduced geographic access to PrEP providers (“PrEP deserts”) reside in the South.
- Over 50% of MSM in the South must drive >60 minutes to a PrEP provider.
- PrEP deserts are generally non-urban areas.

Low PrEP Uptake

- Based on the most recent CDC estimates, only 27% of providers **who care for HIV+ AND HIV-patients** have ever prescribed PrEP.
- Among other recent national surveys, low numbers of primary healthcare providers reported providing PrEP (9%-35%).

Provider Barriers to PrEP

- Insufficient evidence;
- Inexperience;
- Cost Prohibitive;
- Not a primary care activity;
- Sexual history taking issues;
- Fear of non-adherence, resistance and sexual risk compensation.

...Ready for it?

- Inquiring about a sexual history and sexual health counseling are part of primary care.
 - *You already do that!*
- The most important tool for assessing HIV risk is your clinical sense.
 - *You already have that!*
- Basic labs are required for Truvada[®] prescriptions.
 - *You already do that!*
- Most common medications, like Truvada[®], require follow-up and monitoring.
 - *You already do that!*

Ready, set, PrEP!

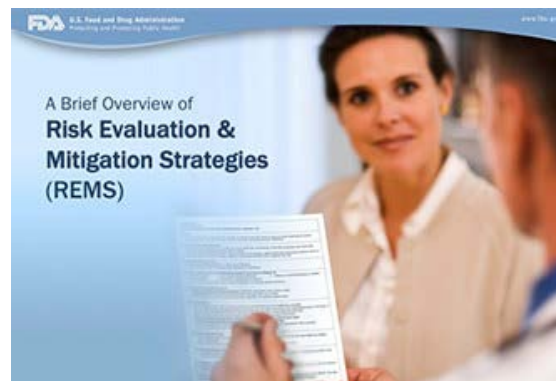


PrEP Clinic Needs

- Provider
- Nursing
 - Assistance in communicating with patient
 - Providing labs and other documents to pharmacy
 - Assisting in completing prior authorization
- Pharmacy
 - Specialty pharmacy partnership highly recommended
- Phlebotomy, blood draws
- Ability to provide treatment and counseling for STIs

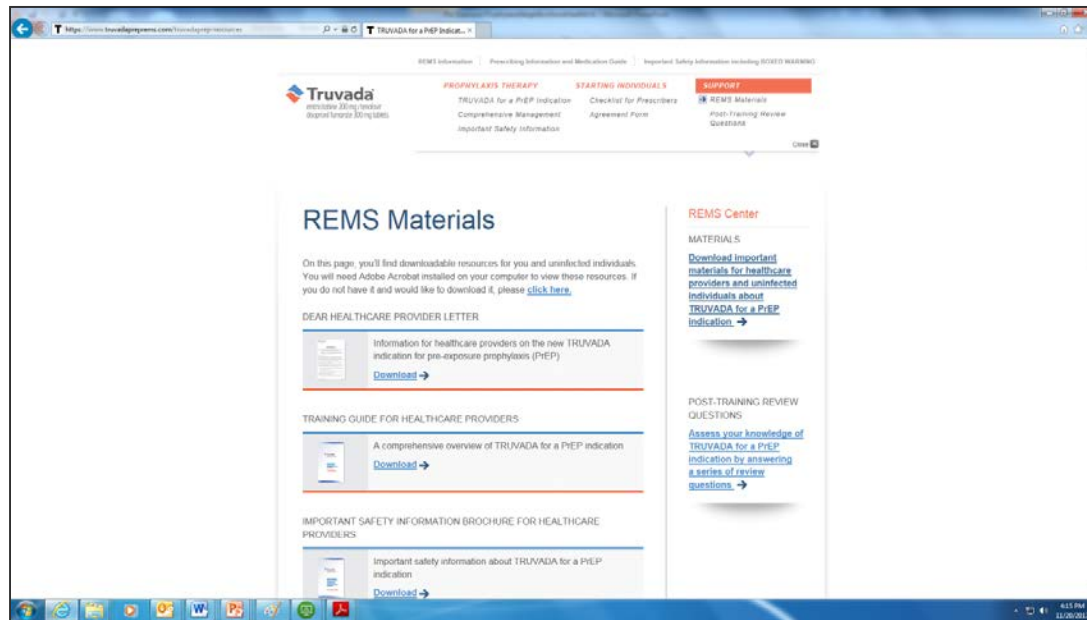
Before prescribing

- Risk Evaluation and Mitigation Strategies (REMS)
 - REMS is a safety strategy to manage risks associated with a drug and to enable continued access to the drug by managing its safe use.
 - REMS is a safety measure beyond the professional labeling to ensure the drug's benefits outweigh its risks.
 - REMS requirements are different for different drugs.



Before prescribing

- Risk Evaluation and Mitigation Strategies (REMS)



<https://www.truvadapreprems.com/truvadaprep-resources>

Before prescribing


Checklist for Prescribers: Initiation of Truvada® for Pre-exposure Prophylaxis (PrEP)

Individual Label


Instructions: Complete checklist at each visit and file in individual's medical record.

I have completed the following prior to prescribing TRUVADA for a pre-exposure prophylaxis (PrEP) indication for the individual who is about to start or is taking TRUVADA for a PrEP indication:

<p>Lab Tests/Evaluation</p> <ul style="list-style-type: none"><input type="checkbox"/> Completed high risk evaluation of uninfected individual<input type="checkbox"/> Confirmed a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication<ul style="list-style-type: none">- If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposure is suspected, delay starting PrEP for at least 1 month and reconfirm HIV-1 status or use a test approved by the FDA as an aid in the diagnosis of HIV-1 infection, including acute or primary HIV-1 infection. (Note: TRUVADA for a PrEP indication is contraindicated in individuals with unknown HIV-1 status or who are HIV-1 positive)<input type="checkbox"/> Performed HBV screening test<input type="checkbox"/> Confirmed estimated creatinine clearance (CrCl) >60 mL/min prior to initiation and periodically during treatment. In patients at risk for renal dysfunction, assess estimated CrCl, serum phosphorus, urine glucose, and urine protein before initiation of TRUVADA and periodically while TRUVADA is being used. If a decrease in estimated CrCl is observed in uninfected individuals while using TRUVADA for a PrEP indication, evaluate potential causes and reassess potential risks and benefits of continued use<input type="checkbox"/> Confirmed that the uninfected individual at high risk is not taking other HIV-1 medications or HBV medications<input type="checkbox"/> Evaluated risk/benefit for women who may be pregnant or may want to become pregnant	<p>Counseling/Follow-up</p> <ul style="list-style-type: none"><input type="checkbox"/> Discussed known safety risks with use of TRUVADA for a PrEP indication<input type="checkbox"/> Counseled on the importance of scheduled follow-up every 2 to 3 months, including regular HIV-1 screening tests (at least every 3 months), while taking TRUVADA for a PrEP indication to reconfirm HIV-1-negative status<input type="checkbox"/> Discussed the importance of discontinuing TRUVADA for a PrEP indication if seroconversion has occurred, to reduce the development of resistant HIV-1 variants<input type="checkbox"/> Counseled on the importance of adherence to daily dosing schedule<input type="checkbox"/> Counseled that TRUVADA for a PrEP indication should be used only as part of a comprehensive prevention strategy<input type="checkbox"/> Educated on practicing safer sex consistently and using condoms correctly<input type="checkbox"/> Discussed the importance of the individual knowing their HIV-1 status and, if possible, that of their partner(s)<input type="checkbox"/> Discussed the importance of and performed screening for sexually transmitted infections (STIs), such as syphilis and gonorrhea, that can facilitate HIV-1 transmission<input type="checkbox"/> Offered HBV vaccination as appropriate<input type="checkbox"/> Provided education on where information about TRUVADA for a PrEP indication can be accessed<input type="checkbox"/> Discussed potential adverse reactions<input type="checkbox"/> Reviewed the TRUVADA Medication Guide with the uninfected individual at high risk
--	---



Truvada
emtricitabine 200 mg / tenofovir
disoproxil fumarate 300 mg tablets



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<https://www.truvadapreprems.com/truvadaprep-resources>

Patient Intake

- Most new PrEP patients will seek out PrEP
- Since many have no PCP, allow self-referrals
- Consider patient insurance status
 - Cost of medication
 - Cost of quarterly visits
 - Cost of labs
 - Cost of vaccination, parenteral antibiotics and their administrations

The First Visit

- Assess patient's knowledge and attitudes about PrEP
- Assess patient's HIV risk
- Medication counseling

PrEP Medication Counseling

- Dosing
 - One tab daily, with or without food
- Adherence, and its relationship to efficacy
- Time to effectiveness
 - 7-10 days for men, 21 days for women
 - Barrier protection especially needed during that time
- Adverse effects
 - Nausea, vomiting, diarrhea, loss of appetite, weight loss
 - Fatigue, headache
- Requirements for monitoring
- Refill process
 - “Call when you have 7-10 days left”

Adverse Events

Table 2. Adverse Events.*

Adverse Event	FTC–TDF (N = 1251)		Placebo (N = 1248)		P Value†
	no. of patients (%)	no. of events	no. of patients (%)	no. of events	
Any adverse event	867 (69)	2630	877 (70)	2611	0.50
Any serious adverse event	60 (5)	76	67 (5)	87	0.57
Any grade 3 or 4 event	151 (12)	248	164 (13)	285	0.51
Grade 3 event	110 (9)	197	117 (9)	225	0.65
Grade 4 event	41 (3)	51	47 (4)	60	0.57
Elevated creatinine level	25 (2)	28	14 (1)	15	0.08
Headache	56 (4)	66	41 (3)	55	0.10
Depression	43 (3)	46	62 (5)	63	0.07
Nausea	20 (2)	22	9 (<1)	10	0.04
Unintentional weight loss (≥5%)	27 (2)	34	14 (1)	19	0.04
Diarrhea	46 (4)	49	56 (4)	61	0.36
Bone fracture	15 (1)	16	11 (<1)	12	0.41
Death	1 (<1)‡	1	4 (<1)	4	0.18
Discontinuation of study drug					
Permanently	25 (2)	26	27 (2)	33	0.82
Permanently or temporarily	79 (6)	99	72 (6)	92	0.49

* A listing of all laboratory abnormalities and clinical adverse events of grade 2 or higher that were reported in 25 or more subjects (1%) is provided in Tables S9 and S10 in the Supplementary Appendix. FTC–TDF denotes emtricitabine and tenofovir disoproxil fumarate.

† P values were calculated by the log-rank test.

‡ This death was due to a motorcycle accident.

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Adverse Events

Table 2. Adverse Events, According to Treatment Group.*

Adverse Event	TDF-FTC (N=611)		Placebo (N=608)		P Value†
	no. of participants (%)	no. of events	no. of participants (%)	no. of events	
Any	557 (91.2)	4357	536 (88.2)	4390	0.003
Any serious	63 (10.3)	68	66 (10.9)	79	0.90
Grade 3 or 4 only	19 (3.1)	21	29 (4.8)	32	0.17
At least possibly related to study drug	20 (3.3)	21	27 (4.4)	29	0.35
Upper respiratory tract infection	231 (37.8)	385	241 (39.6)	439	0.84
Headache	227 (37.2)	390	226 (37.2)	411	0.73
Dizziness	92 (15.1)	109	67 (11.0)	82	0.03
Abdominal pain	155 (25.4)	215	156 (25.7)	217	0.78
Nausea	113 (18.5)	132	43 (7.1)	48	<0.001
Vomiting	69 (11.3)	87	43 (7.1)	47	0.008
Diarrhea	76 (12.4)	93	65 (10.7)	76	0.22
≥5% Weight loss	75 (12.3)	113	61 (10.0)	72	0.13
Back pain	57 (9.3)	72	68 (11.2)	90	0.37
Rash	39 (6.4)	44	42 (6.9)	48	0.81
Fracture	7 (1.1)	7	6 (1.0)	8	0.74
Elevated creatinine	1 (0.2)	1	0	0	1.00
Hypophosphatemia	142 (23.2)	219	159 (26.2)	245	0.65
Hyperamylasemia	315 (51.6)	997	302 (49.7)	1017	0.45
Elevated AST	36 (5.9)	43	38 (6.2)	42	0.90
Elevated ALT	38 (6.2)	48	43 (7.1)	66	0.57
Death‡	2 (0.3)	2	4 (0.7)	4	0.45

* ALT denotes alanine aminotransferase, and AST aspartate aminotransferase.

† All P values were calculated with the use of a time-to-first-event analysis (regression analysis of survival data on the basis of the Cox proportional-hazards model), with the exception of the P values for weight loss of 5% or more and death, which were calculated with the use of Fisher's exact test.

‡ The causes of death in the TDF-FTC group were motor vehicle accident (one participant) and suicide (one); the causes of death in the placebo group were motor vehicle accident (two), homicide (one), and cerebrovascular accident (one).

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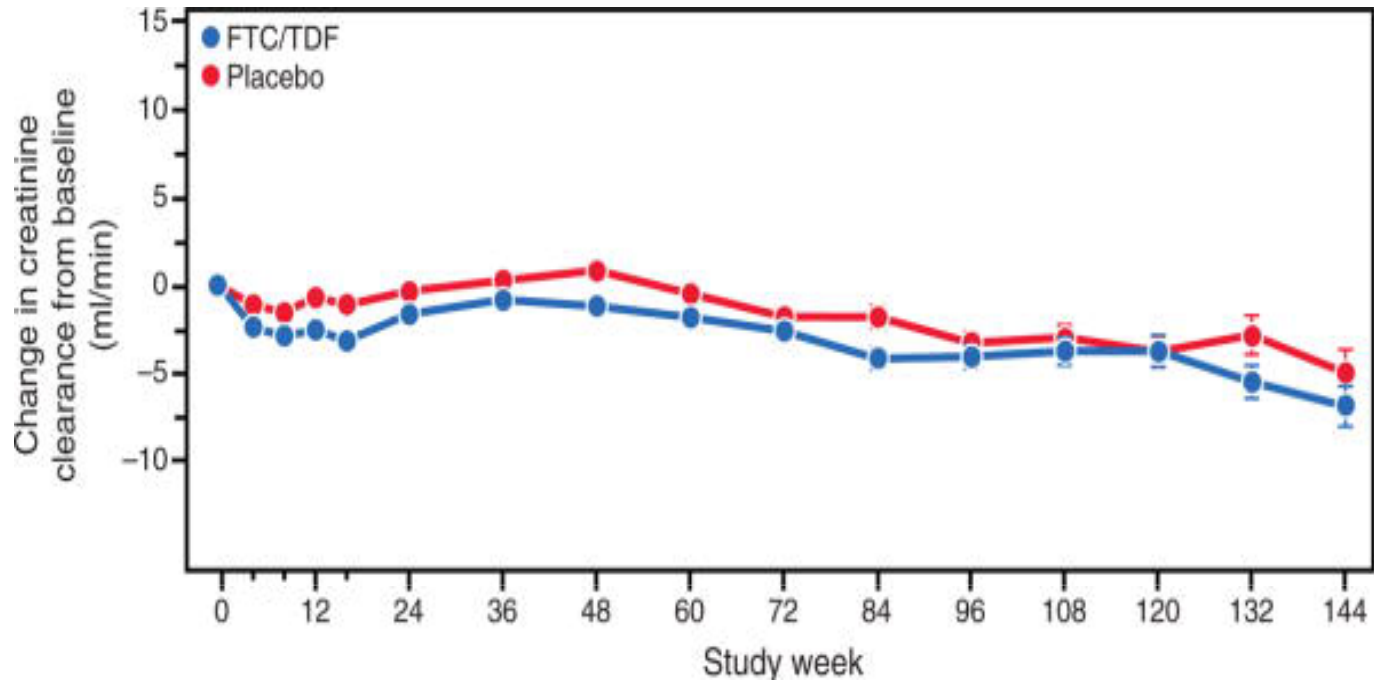
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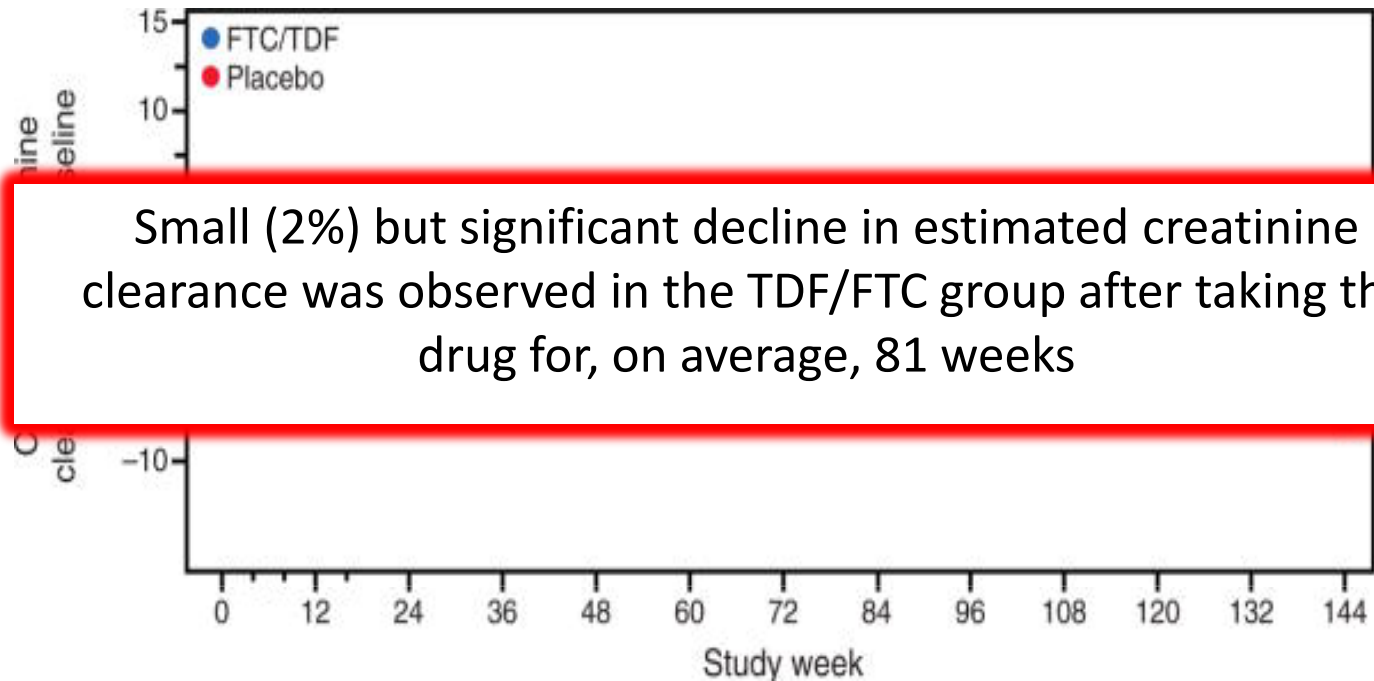
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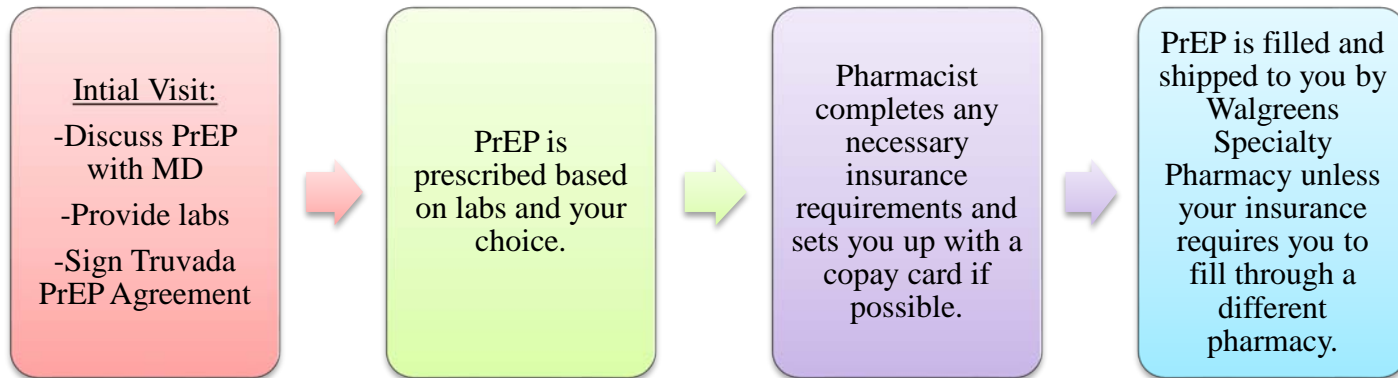
Adverse Events



Adverse Events



The First Visit



The First Visit

Agreement Form

for Initiating Truvada® for
Pre-exposure Prophylaxis (PrEP)

Individual Label

Instructions:

Review form with an HIV-negative person who is about to start or is taking TRUVADA for a PrEP indication at each visit. File form in the person's medical record.

TRUVADA is indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk. The following factors may help to identify individuals at high risk:

- Has partner(s) known to be HIV-1 infected, or
- Engages in sexual activity within a high prevalence area or social network and one or more of the following:
 - Inconsistent or no condom use
 - Diagnosis of sexually transmitted infections
 - Exchange of sex for commodities (such as money, shelter, food, or drugs)
 - Use of illicit drugs, alcohol dependence
 - Incarceration
 - Partner(s) of unknown HIV-1 status with any of the factors listed above

Healthcare Provider Agreement

By signing below, I signify my understanding of the risks and benefits of TRUVADA for a PrEP indication and my obligation as a prescriber to educate the HIV-negative person about these risks, counsel the person on risk reduction, monitor the person appropriately, and report adverse events. Specifically, I attest to having done the following:

- Confirmed the negative HIV-1 status of this person prior to starting TRUVADA for a PrEP indication
- Read the Prescribing Information, including the BOXED WARNING
- Discussed with the HIV-negative person the known safety risks with use of TRUVADA for a PrEP indication
- Reviewed the importance of adherence with a comprehensive prevention strategy, including practicing safer sex
- Discussed the importance of regular HIV-1 testing (at least every 3 months) while taking TRUVADA for a PrEP indication
- Reviewed the TRUVADA Medication Guide with the HIV-negative person at high risk prior to prescribing TRUVADA for a PrEP indication
- Completed the items on the Checklist for Prescribers: Initiation of TRUVADA for Pre-exposure Prophylaxis (PrEP)

HIV-Negative Person Agreement

By signing below, I acknowledge that I have talked with my healthcare provider about the risks and benefits of TRUVADA to reduce the risk of getting HIV-1 infection, and I understand them clearly. Specifically, I attest to the following:

- My healthcare provider talked with me about the importance of follow-up HIV-1 testing, and I agree to have repeat HIV-1 screening tests (at least every 3 months) as scheduled by my healthcare provider
- My healthcare provider talked with me about the safety risks involved with using TRUVADA to reduce the risk of getting HIV-1 infection
- My healthcare provider talked with me about a complete prevention strategy and always practicing safer sex by using condoms correctly
- I will talk with my healthcare provider if I have any questions
- I have read the TRUVADA Medication Guide

Healthcare Provider's Signature

Date

HIV-Negative Person's Signature

Date

 **Truvada**
emtricitabine 200 mg / tenofovir
disoproxil fumarate 300 mg tablets

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<https://www.truvadapreprems.com/truvadaprep-agreement-form#>

The First Visit

- Labs:
 - HIV Ag/Ab
 - Basic Metabolic Panel
 - Hepatitis B sAg, sAb
 - Hepatitis C Ab
 - Treponemal IgG
 - Gonorrhea/chlamydia PCR
 - (with the recent hepatitis A outbreak, consider hepatitis A IgM/IgG)

The First Visit

- Tips

- If a specialty pharmacy will be used, make sure to document the patient's preferred pharmacy
 - Provides more efficient prescription for azithromycin if +chlamydia!
- Get contact information!
- Taking a sexual history is an excellent opportunity to discuss substance use
- High risk behavior often occurs during travel, so ASK!
- Use patient-friendly terms

The Second Visit

- Repeat HIV screen, repeat serum creatinine
- Assess adherence
- Reassess eligibility
- Assess for side effects
- Provide behavioral risk reduction support
- Assess pregnancy intention (test if could be pregnant)
- If HIV-negative and eligible, refill PrEP

Every 3 months

- HIV screen
- Assess adherence
- Reassess eligibility
- Assess for side effects
- Provide behavioral risk reduction support
- Assess pregnancy intention (test if could be pregnant)
- If HIV-negative and eligible, refill PrEP

Every 6 months

- Screen for other STIs
- Repeat serum creatinine

STOP PrEP

- The patient doesn't want it
- Behavior or life situations have changed that lower risk for HIV infection
- Intolerable adverse events/toxicities
- Nonadherence despite attempted interventions to improve
- HIV-infection



A year of PrEP

Encounter	To do
Month 0	<ul style="list-style-type: none">• Screen for HIV• Confirm HBV and HCV status• Check serum creatinine• Screen for STIs• Counseling• Prescribe
Month 3	<ul style="list-style-type: none">• Screen for HIV• Check serum creatinine• Counseling• Prescribe
Month 6	<ul style="list-style-type: none">• Screen for HIV• Screen for STIs• Counseling• Prescribe
Month 9	<ul style="list-style-type: none">• Screen for HIV• Check serum creatinine• Counseling• Prescribe
Month 12	<ul style="list-style-type: none">• Screen for HIV• Screen for STIs• Counseling• Prescribe

Labs:

- HIV screen: 5
- Serum creatinine: 3
- STI screen: 3

Prescriptions/Refill authorizations: 5

Discussions: 5+

PrEP resources for patients

PrEP resources for patients

Page 1 of 2

About Truvada

Truvada (tenofovir and emtricitabine) is a medicine used to treat human immunodeficiency virus (HIV) and hepatitis B virus infection.

It is also used to prevent HIV infection. When you take Truvada to prevent HIV infection, this is called "pre-exposure prophylaxis" or "PrEP."

How does Truvada help prevent HIV infection?

If you take Truvada daily, it can sometimes stop the virus from spreading through your body. It does not work all the time, so you should still use condoms during sex to get the most protection from HIV infection.

How should Truvada be used?

- You must take one Truvada tablet by mouth every day.
- Follow the directions on your prescription label carefully. Ask your doctor or pharmacist to explain any part you do not understand.
- Do not stop taking Truvada without talking to your doctor. When you start to run low on your medicine, contact your doctor or pharmacist to get more.
- You may be at higher risk of getting infected with HIV if you miss doses or stop taking Truvada than if you take it every day.

Is there anything I should do before I start taking Truvada?

Tell your doctor and pharmacist:

- if you are allergic to tenofovir, emtricitabine, or any other medicines
- about all prescription and over-the-counter medicines you take, including vitamins, nutritional supplements, and herbal products.

Tell your doctor:

- if you have (or ever had) kidney or liver disease
- if you become pregnant or you are breastfeeding.

What should I eat while taking this medicine?

Eat your normal diet unless your doctor tells you something else.

What should I do if I forget a dose?

Take the missed dose as soon as you remember it. If it is almost time for the next dose, skip the missed dose and keep to your normal dosing schedule.

Do not take a double dose to make up for a missed one.

(continued)

PrEP resources for patients

Page 1 of 2

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HC 1383 (04/2017)

Is there anything I should do before I start taking...

VANDERBILT UNIVERSITY
MEDICAL CENTER

HIV Pre-Exposure Prophylaxis (PrEP) Action Plan

Welcome to the Comprehensive Care Center at Vanderbilt University Medical Center. Our dedicated team of physicians are here to guide you through getting started on Pre-Exposure Prophylaxis (PrEP) to reduce your risk of acquiring HIV. While you are on PrEP, we will be working together to make sure you receive the best care and access to medication. We are here to answer any questions or concerns during your treatment.

What's next?

```
graph LR; A["Initial Visit:  
-Discuss PrEP with MD  
-Provide labs  
-Sign Truvada PrEP Agreement"] --> B["PrEP is prescribed based on labs and your choice."]; B --> C["Pharmacist completes any necessary insurance requirements and sets you up with a copy card if possible."]; C --> D["PrEP is filled and shipped to you by Walgreens Specialty Pharmacy unless your insurance requires you to fill through a different pharmacy."];
```

Contact information:
Vanderbilt Comprehensive Care Center: (615) 875-5111
Walgreens Specialty Pharmacy: (615) 321-1808

PrEP resources for patients

Page 1 of 2

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HC 131 (04/2017)

VANDERBILT UNIVERSITY
MEDICAL CENTER

HIV Pre-Exposure Prophylaxis Action Plan

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-Provide labs
-Sign Truvada PrEP Agreement

PrEP is prescribed based on labs and your choice.

Pharmacist completes insurance requirements and sets up your copy process.

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Agreement Form for Initiating Truvada® for Pre-exposure Prophylaxis (PrEP)

Instructions:
Review form with an HIV-negative person who is about to start or is taking TRUVADA for a PrEP indication at each visit. File form in the person's medical record.

TRUVADA is indicated in prophylaxis (PrEP) to reduce risk. The following factors:

- Has partner(s) known to be HIV-negative
- Engages in sexual activity and one or more of the following:
 - Inconsistent or no condom use
 - Diagnosis of sexually transmitted infection
 - Exchange of sex for money, drugs, or other favors
 - Incarceration
 - Partner(s) of unknown HIV status

Healthcare Provider Agreement
By signing below, I signify my understanding of the risks and benefits of TRUVADA for a PrEP indication and my obligation as a prescriber to educate the HIV-negative person about these risks, counsel the person on risk reduction, monitor the person appropriately, and report adverse events. Specifically, I attest to having done the following:

- Confirmed the negative HIV-1 status of this person prior to starting TRUVADA for a PrEP indication
- Read the Prescribing Information, including the BOXED WARNING
- Discussed with the HIV-negative person the known safety risks with use of TRUVADA for a PrEP indication
- Reviewed the importance of adherence with a comprehensive prevention strategy, including practicing safer sex
- Discussed the importance of regular HIV-1 testing (at least every 3 months) while taking TRUVADA for a PrEP indication
- Reviewed the TRUVADA Medication Guide with the HIV-negative person at high risk prior to prescribing TRUVADA for a PrEP indication
- Completed the items on the Checklist for Prescribers: Initiation of TRUVADA for Pre-exposure Prophylaxis (PrEP)

Healthcare Provider's Signature _____ Date _____

Individual Label

Learn More About PrEP

AIDS.gov – PrEP information page (<https://www.aids.gov/hiv-aids-basics/prevention/reduce-your-risk/pre-exposure-prophylaxis/>)

AIDSinfoNet – Reliable, up-to-date treatment information (http://aidsinfonet.org/fact_sheets/view/160)

AVAC – Global Advocacy for HIV Prevention (<http://www.avac.org/prevention-option/prep>)

Avert – AVERTing HIV and AIDS (<https://www.avert.org/hiv-transmission-prevention/prep>)

CDC – Questions and answers from the Centers for Disease Control and Prevention (<https://www.cdc.gov/hiv/basics/prep.html>)

My PrEP Experience – Real stories from real people who adopted PrEP for HIV prevention (<http://myprepexperience.blogspot.com/>)

PrEP Facts – San Francisco AIDS Foundation PrEP information in visual format for MSM and heterosexual individuals, with an option for Spanish (<https://prepfacts.org/>)

PrEP Watch – Interactive webpage with information and resources on gaining access to PrEP (<http://www.prepwatch.org/>)

PrEParing for HIV – An Epidemic Interventions Initiative by the University of California (<http://www.uctv.tv/prep/>)


Project Inform – Videos, publications and resources (<http://www.projectinform.org/prep/>)

SFHV – City and County of San Francisco Department of Public Health's PrEP information page (<http://www.sfhv.org/resources/prep/>)

Talk PrEP – AIDS Action Committee's new PrEP campaign encouraging everyone to Do It Daily (<http://talkprep.org/>)

Guidance for Use of PrEP in Practice and Research Settings
WHO – World Health Organization (http://www.who.int/hiv/pub/guidance_prep/en/)
CDC – Centers for Disease Control and Prevention (<https://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf>)

From the Makers of Truvada
start.truvada.com – Information about Truvada for PrEP for healthcare providers, consumers and educators
<http://www.truvadaprep.com/truvadaprep-resources> - Downloadable forms and resources for PrEP prescribers and users



Billing/coding

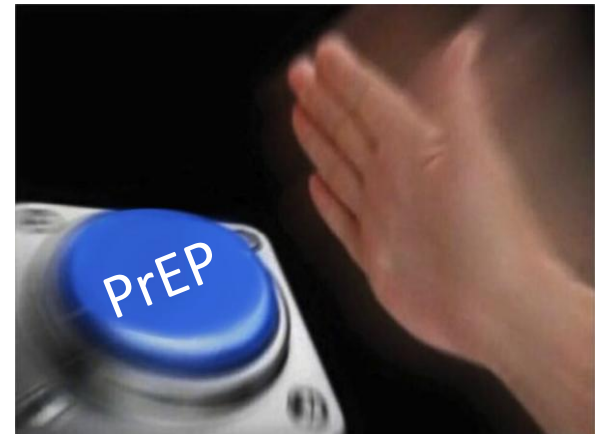
- While ICD-10 does not provide specific codes for PrEP, the following codes have been discussed with billing and used for PrEP visits:
 - Z20.6 “Contact with and (suspected) exposure to HIV ”
 - Z17.1 “Human immunodeficiency virus [HIV] counseling”
 - Z11.3 “Encounter for screening for infection with a predominantly sexual mode of transmission”
 - Z79.2 “Long-term (current) use of antibiotics”
- Note: Can also bill by time, >25 minutes = level 4
- Not suggested
 - Z72.52 – High risk homosexual behavior

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- Not suggested for Z72.52 “High risk homosexual behavior”

PrEP Conclusions

- PrEP is an extremely effective preventive strategy
- Many PrEP barriers exist, but can *easily* be overcome
- Understand PrEP prescribing guidelines
- Evaluate individual clinic needs
- Identify individual beliefs and perceptions
- Ask for help!
sean.g.kelly@vanderbilt.edu
- steve.raffanti@vanderbilt.edu



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

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If Pablo were to present with his HIV infection today, he would have labs drawn, be started on a pill to treat HIV and his wife would be started on PrEP. He would raise his kids and live out his life.

DWS

memo

e bx

Useful HIV Websites

www.seatc.com

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.ucsf.edu/medical

www.virology.net

Questions?

