Pre-Exposure Prophylaxis for HIV (it's easier than it sounds)

Anna K. Person

Jan 25, 2018

Special thanks to Dr. Sean Kelly

Vanderbilt Division of Infectious Diseases

Objectives

- Importance of PrEP in the Southeast
- Provider barriers for providing PrEP
- Becoming a PrEP provider
- Logistical considerations of a PrEP clinic
  - Visits
  - Labs
  - Truvada® access
  - Advertising

PrEP is primary prevention

It is intended to PREVENT the onset of a disease in those who are AT RISK

It is a concept, fulfilled by medication that has been FDA-approved for this purpose

But what is PrEP, really?

- Right now, PrEP is Truvada®

  - Fixed dose combination of tenofovir disoproxil fumarate (TDF) 300mg/emtricitabine (FTC) 200mg
  - Developed by Gilead
  - FDA-approved for use as PrEP on June 6, 2012
- Generic TDF/FTC approved 6/2017

Also approved in Australia, Canada, France, Norway, Belgium, Netherlands, Peru, Israel, Kenya, Botswana, Zimbabwe and South Africa

Coming soon in: Brazil, Nigeria, Zambia, Malawi, Uganda, India, Thailand, United Kingdom, Italy

This is different from PEP

- PrEP = Pre-Exposure Prophylaxis
  - HIV exposure has not yet occurred
    - Indefinite duration if HIV risk persists
- PEP = Post-Exposure Prophylaxis
  - HIV exposure HAS occurred
  - Goal is to reduce incidence of established infection
  - THREE drugs required: Truvada® (TDF/FTC) + dolutegravir
    - Limited duration of 28 days

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

How well does PrEP work?

iPrEX

The NEW ENGLAND JOURNAL of MEDICINE

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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

The NEW ENGLAND JOURNAL of MEDICINE

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., Aloysious Kakia, 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 Ngure, Ph.D., Cosmas Apaka, B.Sc., Harrison Tamooh, 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[c], 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)

IPERGAY

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

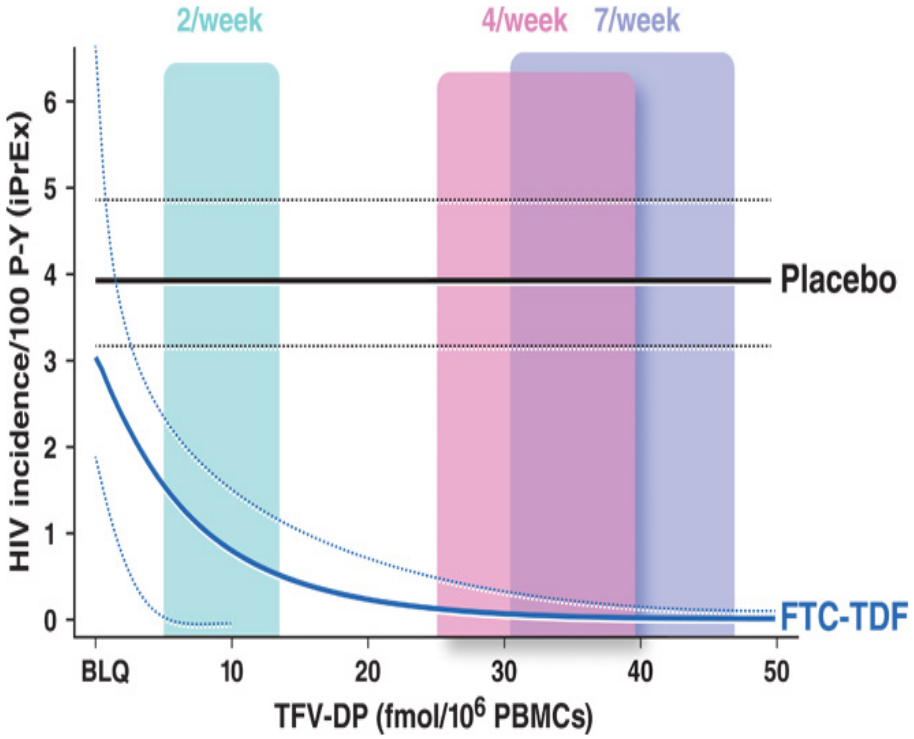
On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

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



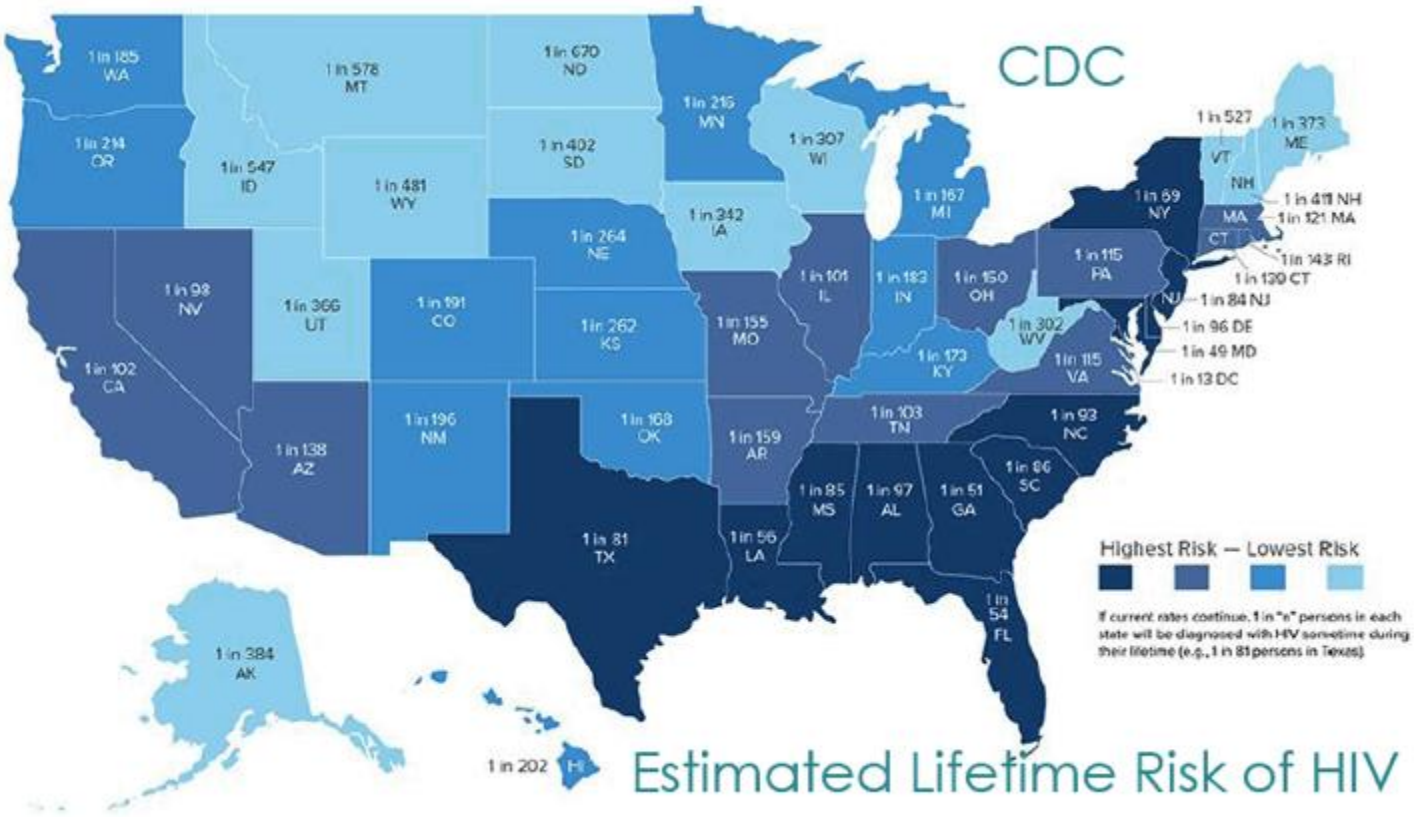
Using drug concentrations in iPrEX and STRAND, pharmacokinetic models predict **76%** risk reduction with 2 doses/week, **96%** with 4 doses/week, and **99%** with 7 doses/week.

Anderson PL, Glidden DV, Liu A, Buchbinder S, Lama JR, Guanira JV, et al. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. Sci Transl Med. 2012;4: 151ra125. doi: 10.1126/scitranslmed.3004006. pmid:22972843

Studies Summary

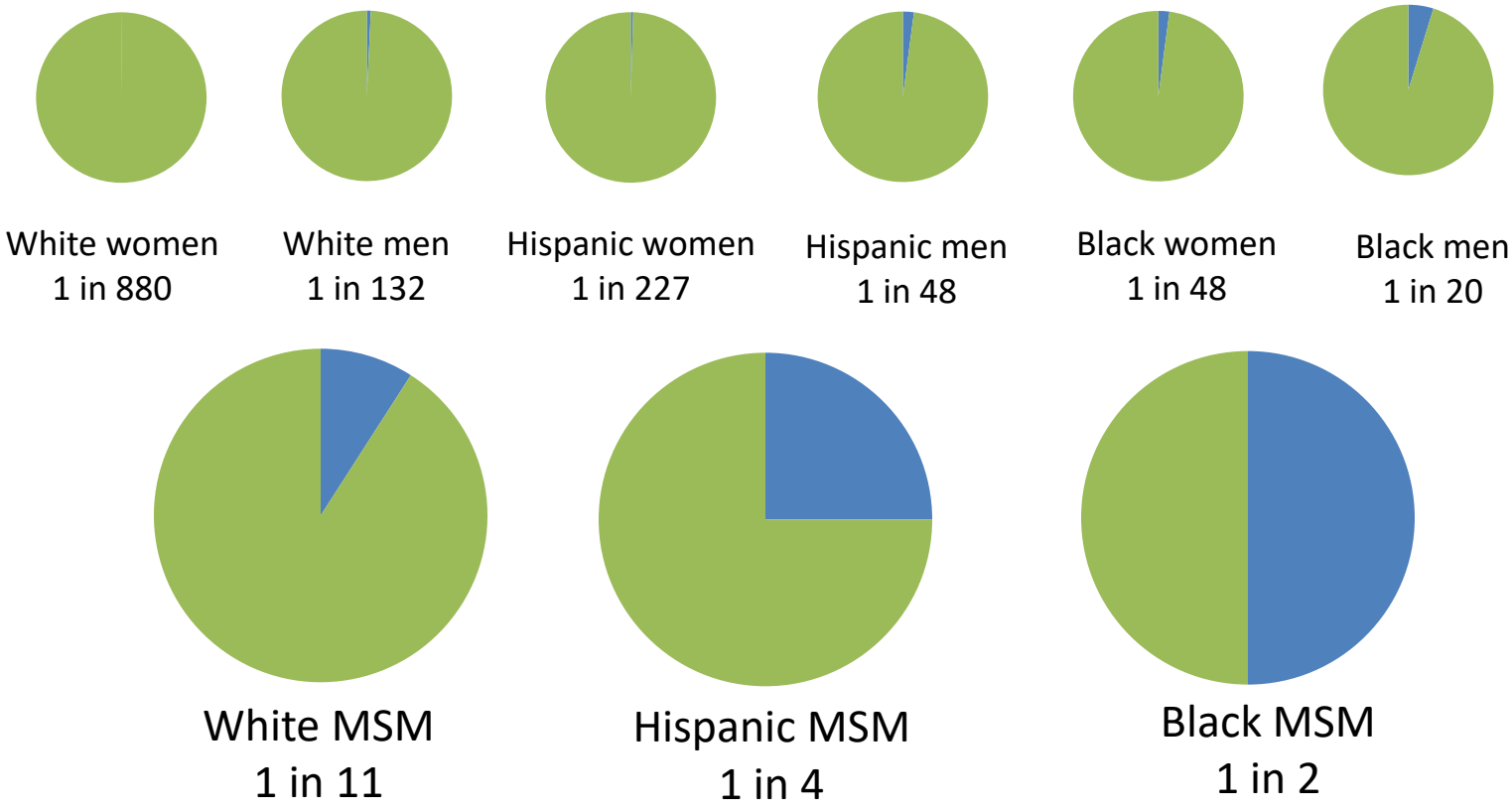
Study	Population	Dosing	Risk Reduction
iPrEX	MSM	Daily	44% (92% with ideal adherence)
TDF2	Heterosexual men and women	Daily	62.2%
Partners	Sero-discordant heterosexual couples	Daily	75% (90% with ideal adherence)
Bangkok Tenofovir Study Group	Intravenous drug users	Daily	48.9% (74% with ideal adherence)
IPERGAY	MSM	On-demand	86%

Why PrEP matters



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.

HIV Risk by Race/Ethnicity and MSM



CDC, 23 Feb 2016: http://www.cdc.gov/nchhstp/newsroom/2016/croi-press-release-risk.html

Who benefits from PrEP?

CDC Recommendations (for MSM)

- Adult man
- Without acute or established HIV infection
- Any male sex partners in past 6 months
- Not in a monogamous partnership with a recently tested, HIV-negative man

AND at least one of the following

- Any anal sex without condoms (receptive or insertive) in past 6 months
- Any STI diagnosed or reported in past 6 months
- Is in an ongoing sexual relationship with an HIV-positive male partner

https://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

CDC Recommendations (for heterosexual men and women)

- Adult person
- Without acute or established HIV infection
- Any sex with opposite sex partners in past 6 months
- Not in a monogamous partnership with a recently tested HIV-negative partner

AND at least one of the following

- Is a man who has sex with both women and men (behaviorally bisexual)
- Infrequently uses condoms during sex with 1 or more partners of unknown HIV status who are known to be at substantial risk of HIV infection (IDU or bisexual male partner)
- Is in an ongoing sexual relationship with an HIV-positive partner

https://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

CDC Recommendations (for IDU)

- Adult person
- Without acute or established HIV infection
- Any injection of drugs not prescribed by a clinician in past 6 months

AND at least one of the following

- Any sharing of injection or drug preparation equipment in past 6 months
- Been in a methadone, buprenorphine, or suboxone treatment program in past 6 months
- Risk of sexual acquisition

https://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

Who benefits from PrEP?

- Sero-discordant sexual activity (couples)
- Multiple sex partners (especially sex partners with unknown HIV status or at risk for HIV) with inconsistent or no condom use
- History of sexually transmitted infections
- Exchange of sex for money or commodities
- Injection drug use
- Study out of Chicago, 300 HIV neg MSM for 3 years, of those who contracted HIV only 49% met CDC criteria for PrEP
- Anyone who has sex in the South? Clinical judgement!

Who doesn’t benefit?

- HIV infection
- Those at risk for adverse effects due to pre-existing comorbid conditions (chronic kidney disease)
- Unwilling to take daily medication
- Not engaging in activity with increased HIV risk

HIV risk is behavioral

The only way to know is to ask (and listen)!

Taking a sexual history promotes comprehensive STI risk reduction counseling

Condom use
Knowing HIV status
Knowing partner's HIV status
PrEP

Stigma

A preventative measure against the consequences of sexual activity

… *condones* sexual activity

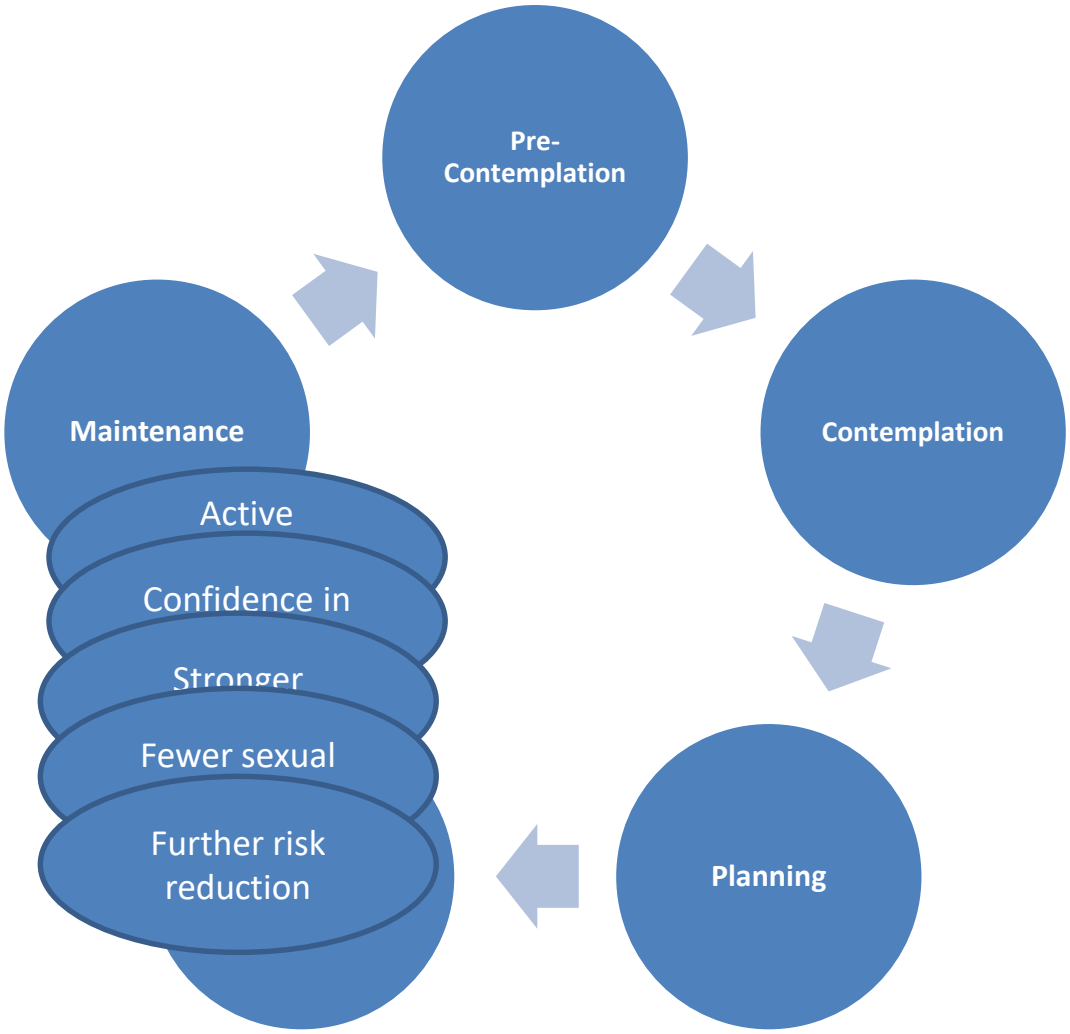
… *promotes* sexual activity

… *causes* sexual activity

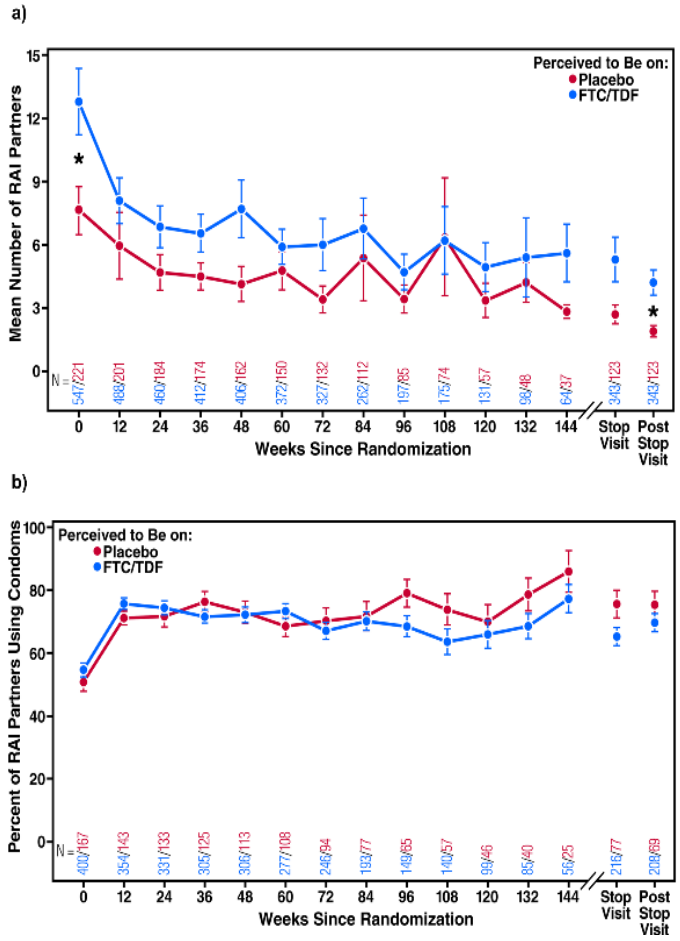
Stigma

- PrEP is a “party drug”
- PrEP promotes “bareback sex”
- PrEP users will stop using condoms
- PrEP users will acquire more STIs

But actually…



No evidence of sexual risk compensation in the iPrEx trial of daily oral PrEP

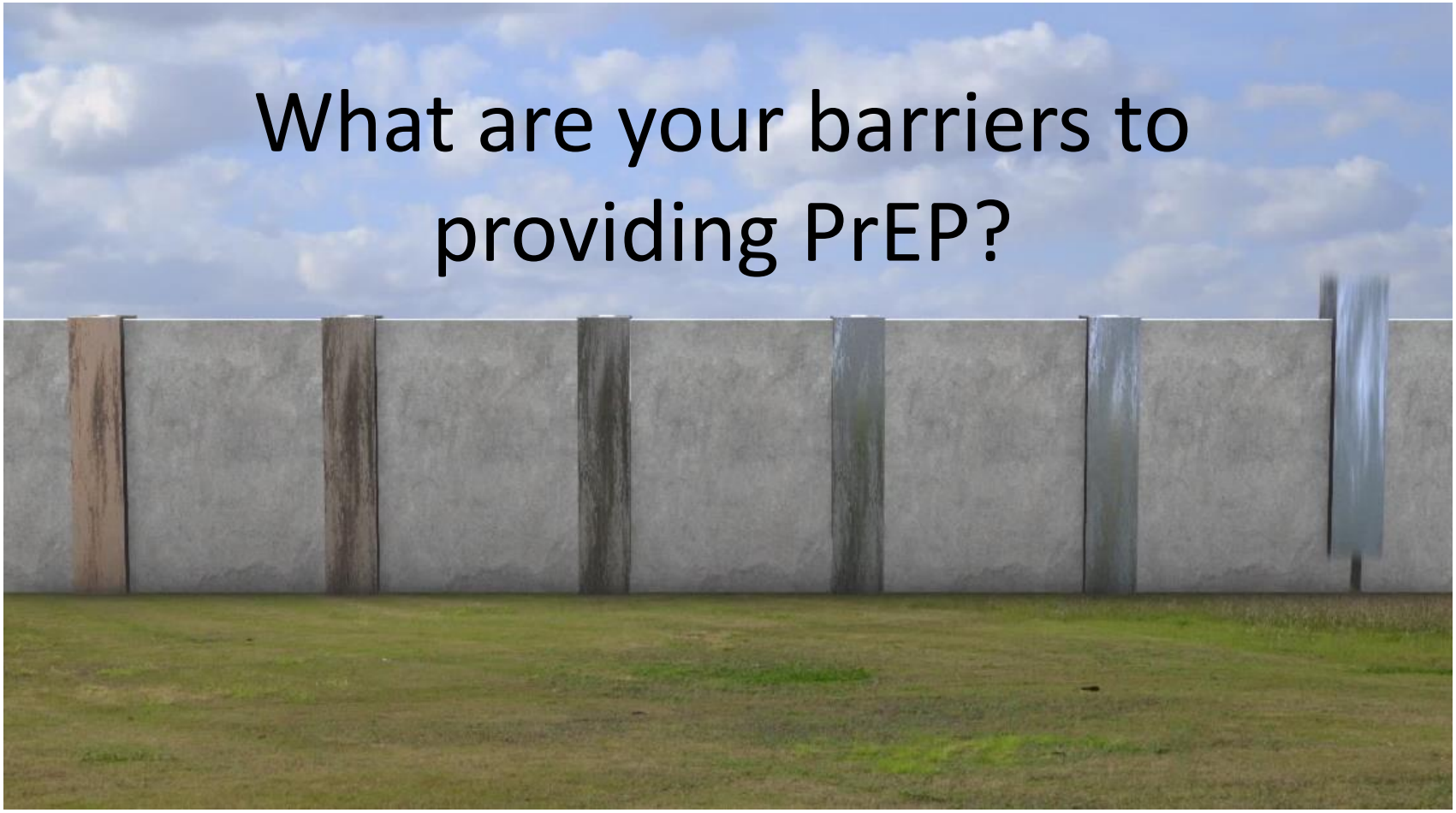


For patients believing they were on PrEP, the number of receptive anal intercourse partners decreased.

For patients believing they were on PrEP, condom use increased.

Syphilis incidence also decreased in both study arms

Julia L. Marcus, David V. Glidden, Kenneth H. Mayer, Albert Y. Liu, Susan P. Buchbinder, K. Rivet Amico, Vanessa McMahan, Esper Georges Kallas, Orlando Montoya-Herrera, Jose Pilotto, Robert M. Grant. PLoS One. 2013 Dec 18;8(12):e81997


What are your barriers to providing PrEP?

Provider barriers

Knowledge

- Inexperience with Truvada/lack of knowledge (60%-77.5%)[3,6,8,10]
- Insufficient evidence of efficacy (22%-81%)[5,6,7,11]
- PrEP is cost-prohibitive (29%-92%)[4, 5, 6, 7, 10]
- Unfamiliarity with PrEP candidates (inability to assess high HIV risk) (61%)[6]

Provider barriers

Perception/Attitudes

- Sexual risk compensation (that use of PrEP will lead to increased high-risk behavior) (33%)[2,4]
- Discomfort using a drug with potential adverse effects in an otherwise healthy person (primary prevention vs. treatment) (67%)[5,7]
- Patients perceived as non-adherent, and risk HIV drug resistance selection (40%-77%)[4,5,7,11]
- PrEP is not a primary care activity ("not me") (34%)[4,5]
- Personal ideology[5]

Provider barriers

Behavior

- Low number of providers reported providing PrEP (9%-35%)[5,8]

Provider Barriers
Needs for practice transformation

- Nursing support (92%)[6]
- Social work support (90%)[6]
- CME (90%)[6]
- PrEP training event (OR 4.84, CI 1.77–13.21)[8]

As a society, we treat any HIV-related health care activities differently.

As healthcare providers, we need to accept our responsibility to protect our patients.

…Ready for it?

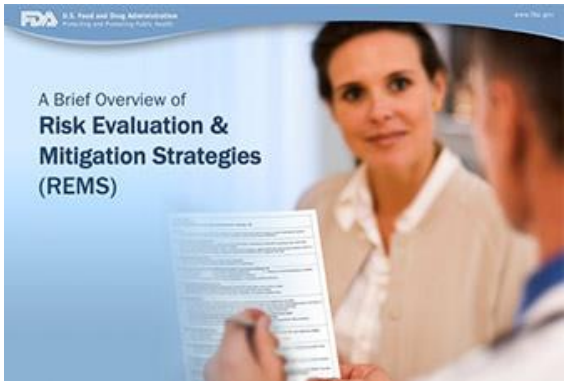
- Inquiring about a sexual history and sexual health counseling are part of primary care.
  - *You already do that!*
- The most important tool for assessing HIV risk is your clinical sense.
  - *You already have that!*
- Basic labs are required for Truvada prescriptions.
  - *You already do that!*
-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

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

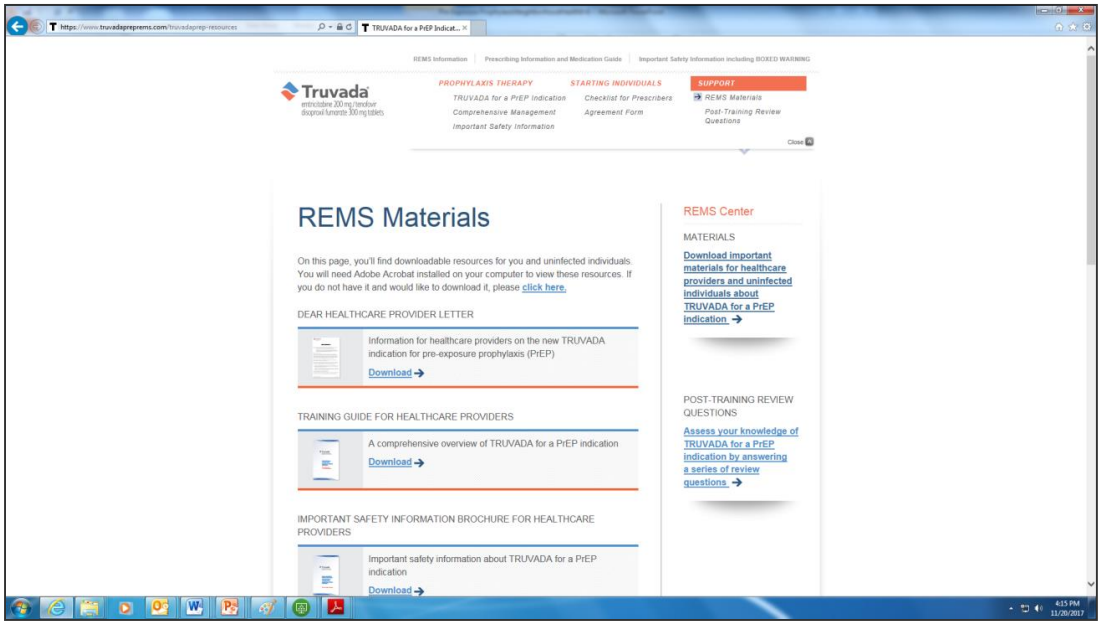
Before prescribing

- 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.



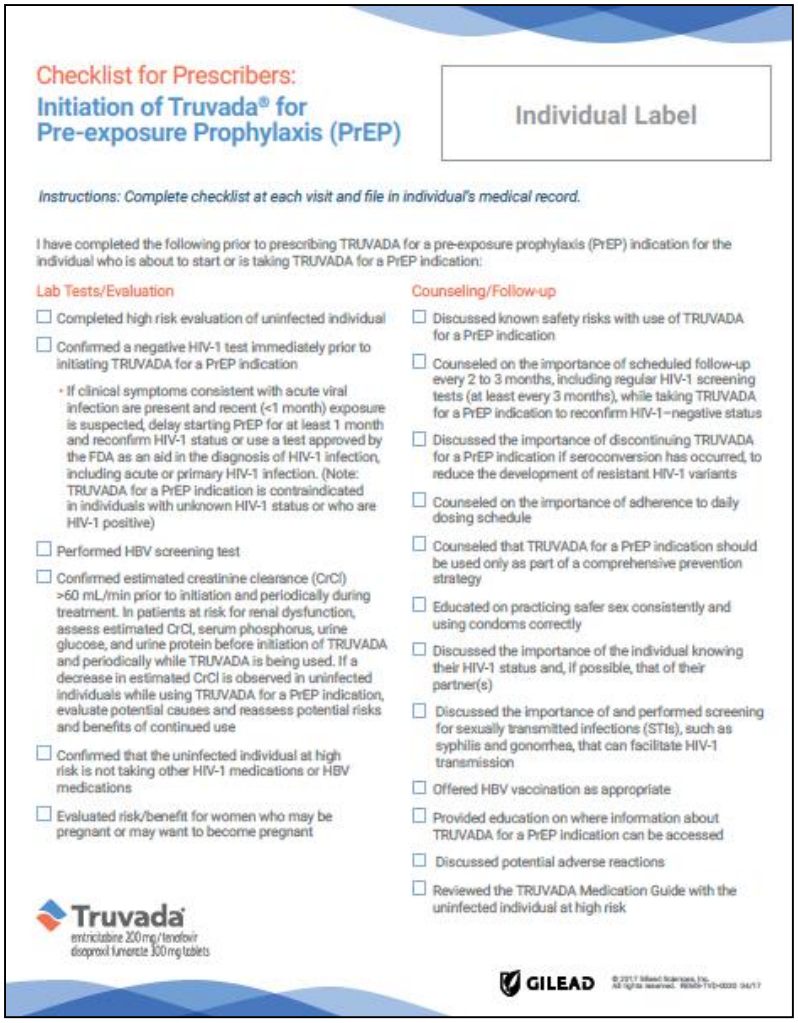
Before prescribing

- 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:

Lab Tests/Evaluation

- ☐ Completed high risk evaluation of uninfected individual
- ☐ Confirmed a negative HIV-1 test immediately prior to initiating TRUVADA for a PrEP indication
  - 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)
- ☐ Performed HBV screening test
- ☐ 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
- ☐ Confirmed that the uninfected individual at high risk is not taking other HIV-1 medications or HBV medications
- ☐ Evaluated risk/benefit for women who may be pregnant or may want to become pregnant

Counseling/Follow-up

- ☐ Discussed known safety risks with use of TRUVADA for a PrEP indication
- ☐ 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
- ☐ Discussed the importance of discontinuing TRUVADA for a PrEP indication if seroconversion has occurred, to reduce the development of resistant HIV-1 variants
- ☐ Counseled on the importance of adherence to daily dosing schedule
- ☐ Counseled that TRUVADA for a PrEP indication should be used only as part of a comprehensive prevention strategy
- ☐ Educated on practicing safer sex consistently and using condoms correctly
- ☐ Discussed the importance of the individual knowing their HIV-1 status and, if possible, that of their partner(s)
- ☐ Discussed the importance of and performed screening for sexually transmitted infections (STIs), such as syphilis and gonorrhea, that can facilitate HIV-1 transmission
- ☐ Offered HBV vaccination as appropriate
- ☐ Provided education on where information about TRUVADA for a PrEP indication can be accessed
- ☐ Discussed potential adverse reactions
- ☐ Reviewed the TRUVADA Medication Guide with the uninfected individual at high risk

Truvada
emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg tablets

GILEAD

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 if patient acquires bacterial STI

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
Nausea	20 (2)	22	9 (<1)	10	0.04
Unintentional weight loss (≥5%)	27 (2)	34	14 (1)	19	0.04
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.

iPrEX, 2010

Adverse Events

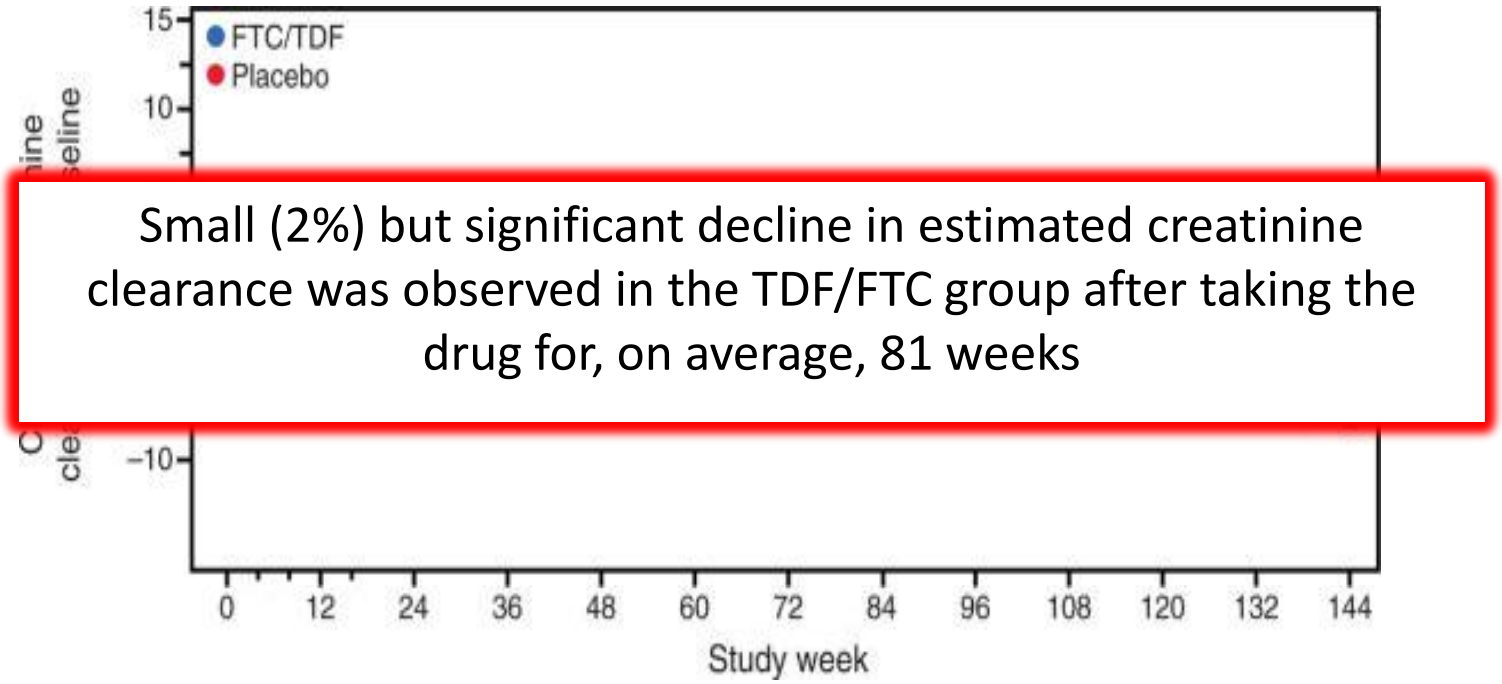
Table 2. Adverse Events, According to Treatment Group.*

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
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
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).

TDF2 Study Group, 2012

Adverse Events



Small (2%) but significant decline in estimated creatinine clearance was observed in the TDF/FTC group after taking the drug for, on average, 81 weeks

iPrEX, 2013

Adverse Events

Table 3. Bone Mineral Density Scores.*

Assessment	Forearm			Hip			Lumbar Spine		
	TDF–FTC (N=109)	Placebo (N=112)	P Value	TDF–FTC (N=109)	Placebo (N=112)	P Value	TDF–FTC (N=109)	Placebo (N=112)	P Value
T score			0.004			<0.001			<0.001
24 mo	−0.87	−0.13		0.20	0.76		−1.09	−0.28	

* In the TDF–FTC group, 58 participants completed bone mineral density testing at the 6-month visit, 45 at the 12-month visit, 36 at the 18-month visit, and 23 at the 24-month visit. In the placebo group, 66 participants completed bone mineral density testing at the 6-month visit, 44 at the 12-month visit, 33 at the 18-month visit, and 35 at the 24-month visit.

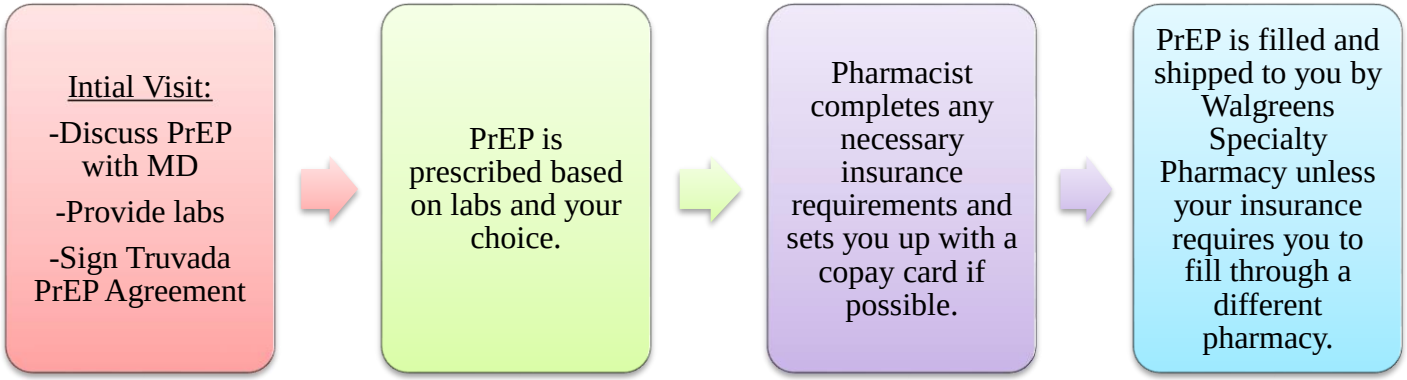
BUT THIS CAN RECOVER!

Bone mineral density recovered after 6 months of stopping TDF/FTC in both young and older adults.

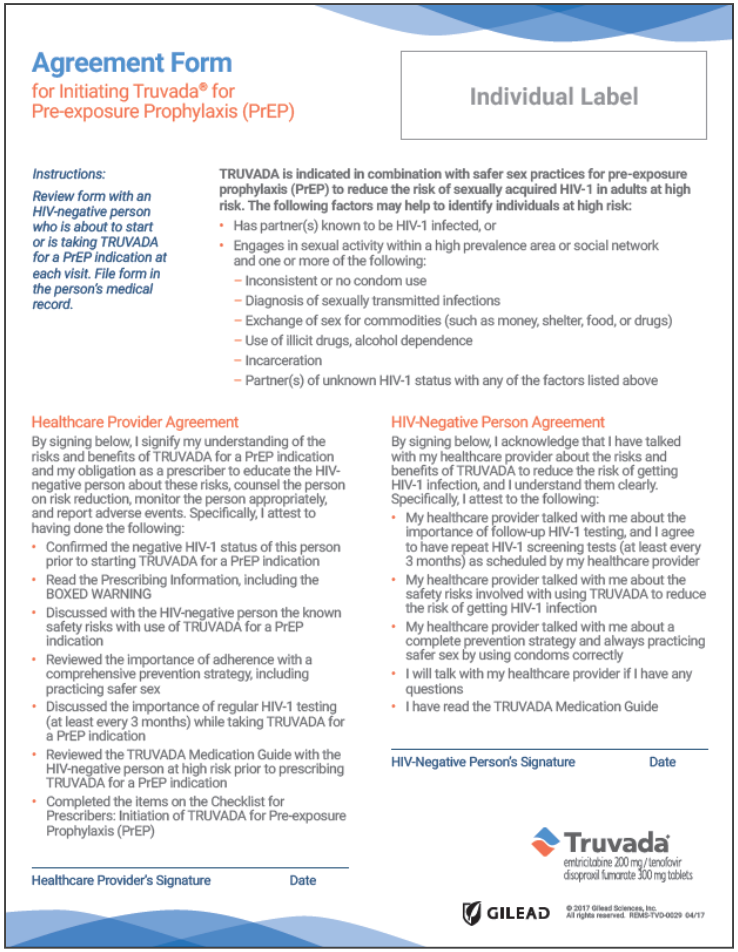
TDF2 Study Group, 2012

Grant RM, et al. Recovery of bone mineral density after stopping oral HIV pre-exposure prophylaxis. CROI 2016 Feb 20-24 Boston

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)

Healthcare Provider's Signature Date

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

HIV-Negative Person's Signature Date

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

GILEAD

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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

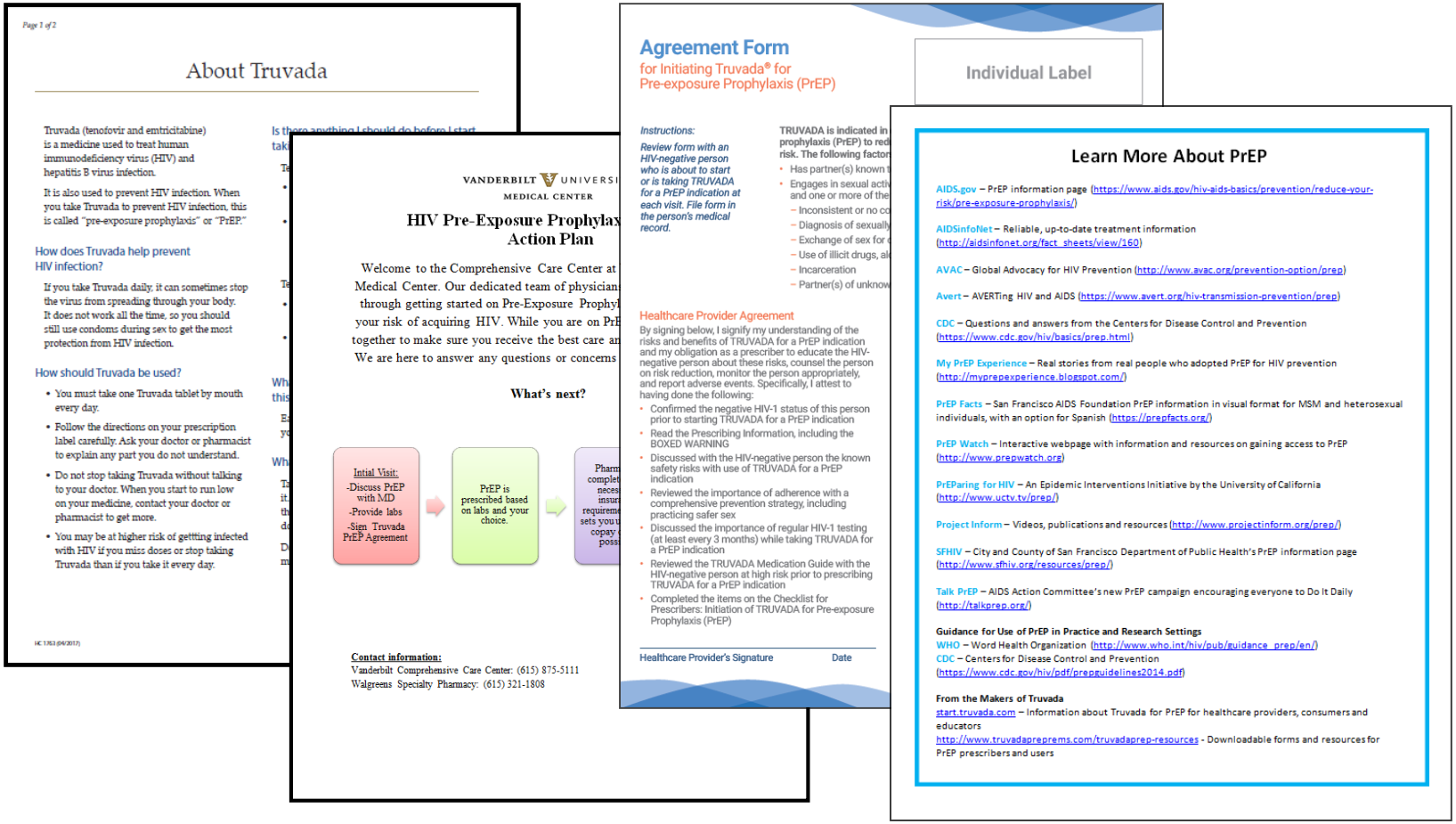
The First Visit

- 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

PrEP resources for patients

- PrEP welcome packet
    1. Truvada® medication guide
    2. CDC PrEP medication information sheet for patients
    3. Patient/Provider Agreement
    4. PrEP Action Plan and Next Steps
    5. Walgreens Specialty Pharmacy contact information
    6. Additional PrEP resources

PrEP resources for patients



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 gettting infected with HIV if you miss doses or stop taking Truvada than if you take it every day.

VANDERBILT UNIVERSITY MEDICAL CENTER

HIV Pre-Exposure Prophylax Action Plan

Welcome to the Comprehensive Care Center at Medical Center. Our dedicated team of physician through getting started on Pre-Exposure Prophyl your risk of acquiring HIV. While you are on PrE together to make sure you receive the best care ar We are here to answer any questions or concerns

What's next?

Intial Visit: -Discuss PrEP with MD -Provide labs -Sign Truvada PrEP Agreement

PrEP is prescribed based on labs and your choice.

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

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 prophylaxis (PrEP) to red risk. The following factor

- Has partner(s) known t
- Engages in sexual activ and one or more of the
  - Inconsistent or no co
  - Diagnosis of sexually
  - Exchange of sex for
  - Use of illicit drugs, al
  - Incarceration
  - Partner(s) of unknow

Healthcare Provider Agreement

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- 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

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/)

SFHIV – City and County of San Francisco Department of Public Health's PrEP information page (http://www.sfhiv.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 – Word 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.truvadaprepreams.com/truvadaprep-resources - Downloadable forms and resources for PrEP prescribers and users

Prescribing process
Specialty Pharmacy

- Specialty Pharmacy may complete all prior authorization and copay assistance requirements and connect with the patient
- May also send the prescription and prior authorizations to another pharmacy if the patient requests this

Prescribing process

Specialty Pharmacy

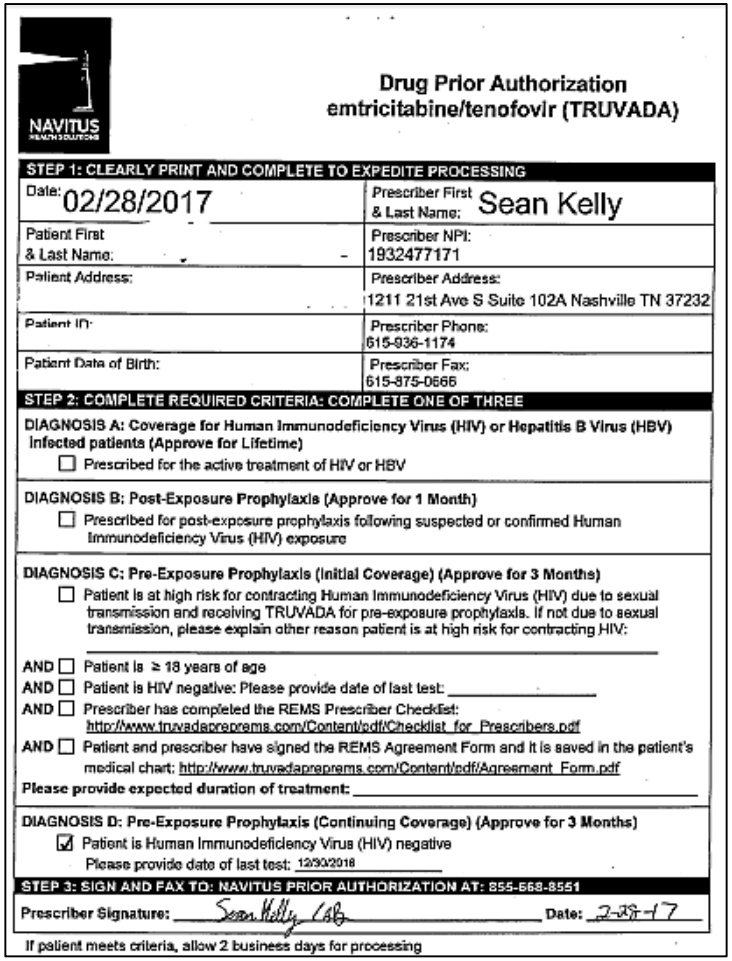
- Send prescription electronically to Specialty Pharmacy
  - 30 tabs, 2 refills (total 90-day supply)
- When HIV Ag/Ab and serum creatinine are available, send message to clinic RN to fax lab results to pharmacy
- Pharmacy contacts patient for further counseling and to arrange PrEP delivery
- Pharmacy contacts patient intermittently over 6 months to assess tolerability and adherence

Prescribing Process

No Specialty Pharmacy

- Send prescription to pharmacy
- Fax HIV Ag/Ab, serum creatinine when available
- Complete PA if required
  - Information requested: last date of screening and sometimes PrEP Agreement form
- Copay card
  - Gilead copay card: $3600/year benefit
  - https://www.gileadadvancingaccess.com/copay-coupon-card
  - Federal beneficiaries not eligible

Prior Authorization



NAVITUS HEALTH SOLUTIONS

Drug Prior Authorization
emtricitabine/tenofovir (TRUVADA)

STEP 1: CLEARLY PRINT AND COMPLETE TO EXPEDITE PROCESSING

Date: 02/28/2017	Prescriber First & Last Name: Sean Kelly
Patient First & Last Name:	Prescriber NPI: 1932477171
Patient Address:	Prescriber Address: 1211 21st Ave S Suite 102A Nashville TN 37232
Patient ID:	Prescriber Phone: 615-936-1174
Patient Date of Birth:	Prescriber Fax: 615-875-0666

STEP 2: COMPLETE REQUIRED CRITERIA: COMPLETE ONE OF THREE

DIAGNOSIS A: Coverage for Human Immunodeficiency Virus (HIV) or Hepatitis B Virus (HBV) Infected patients (Approve for Lifetime)

☐ Prescribed for the active treatment of HIV or HBV

DIAGNOSIS B: Post-Exposure Prophylaxis (Approve for 1 Month)

☐ Prescribed for post-exposure prophylaxis following suspected or confirmed Human Immunodeficiency Virus (HIV) exposure

DIAGNOSIS C: Pre-Exposure Prophylaxis (Initial Coverage) (Approve for 3 Months)

☐ Patient is at high risk for contracting Human Immunodeficiency Virus (HIV) due to sexual transmission and receiving TRUVADA for pre-exposure prophylaxis. If not due to sexual transmission, please explain other reason patient is at high risk for contracting HIV: _____

AND ☐ Patient is ≥ 18 years of age

AND ☐ Patient is HIV negative: Please provide date of last test: _____

AND ☐ Prescriber has completed the REMS Prescriber Checklist: http://www.truvadapreprems.com/Content/pdf/Checklist_for_Prescribers.pdf

AND ☐ Patient and prescriber have signed the REMS Agreement Form and it is saved in the patient's medical chart: http://www.truvadapreprems.com/Content/pdf/Agreement_Form.pdf

Please provide expected duration of treatment: _____

DIAGNOSIS D: Pre-Exposure Prophylaxis (Continuing Coverage) (Approve for 3 Months)

☑ Patient is Human Immunodeficiency Virus (HIV) negative

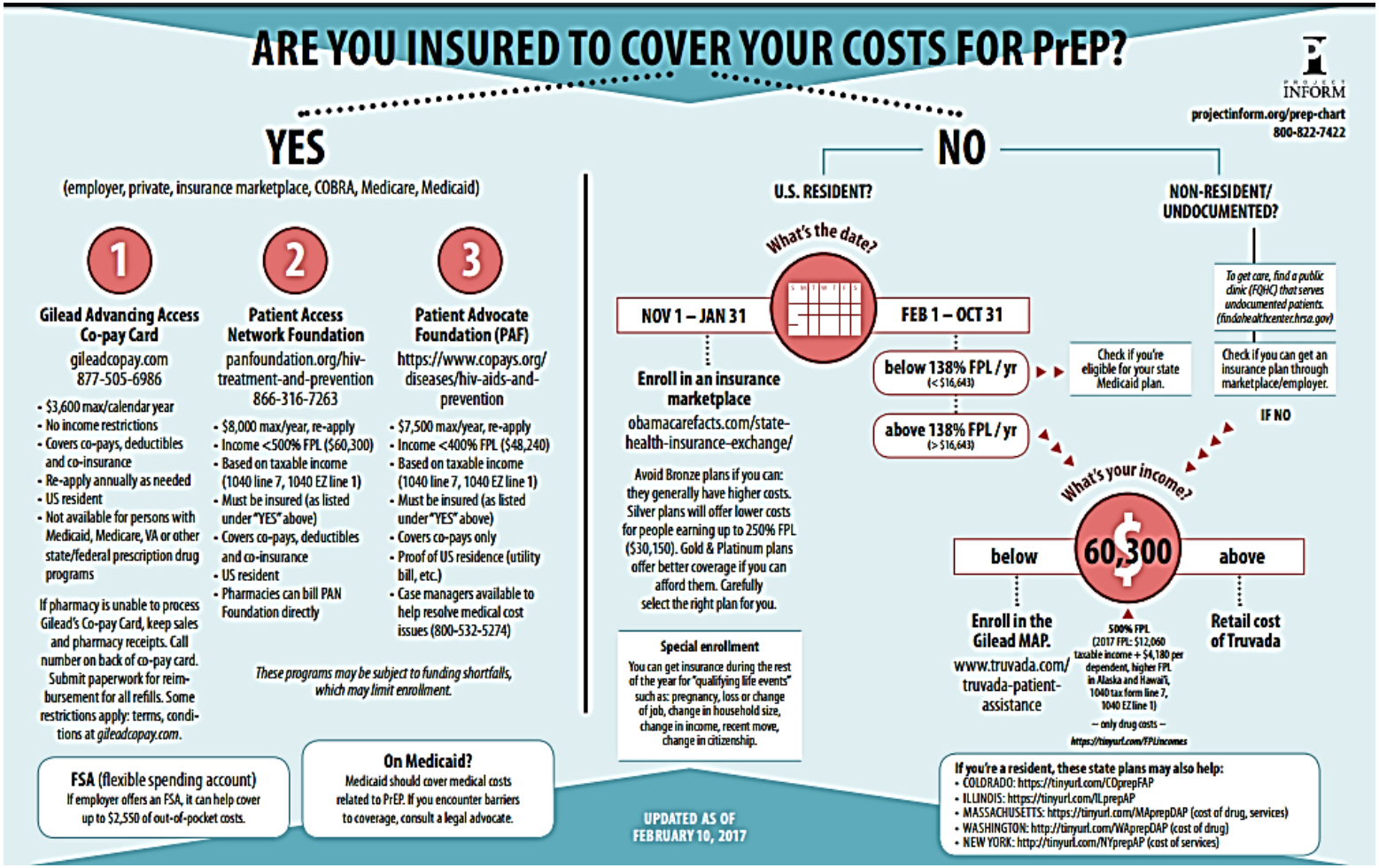
Please provide date of last test: 12/30/2016

STEP 3: SIGN AND FAX TO: NAVITUS PRIOR AUTHORIZATION AT: 855-668-8551

Prescriber Signature: Sean Kelly CMA **Date:** 2-28-17

If patient meets criteria, allow 2 business days for processing

Other Cost Options



https://www.projectinform.org/pdf/PrEP_Flow_Chart.pdf

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

- N[illegible] sugg[illegible]
  - Z72.52 – High [illegible]osexual behavior

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	• Screen for HIV • Confirm HBV and HCV status • Check serum creatinine • Screen for STIs • Counseling • Prescribe
Month 3	• Screen for HIV • Check serum creatinine • Counseling • Prescribe
Month 6	• Screen for HIV • Screen for STIs • Counseling • Prescribe
Month 9	• Screen for HIV • Check serum creatinine • Counseling • Prescribe
Month 12	• Screen for HIV • Screen for STIs • Counseling • Prescribe

Labs:

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

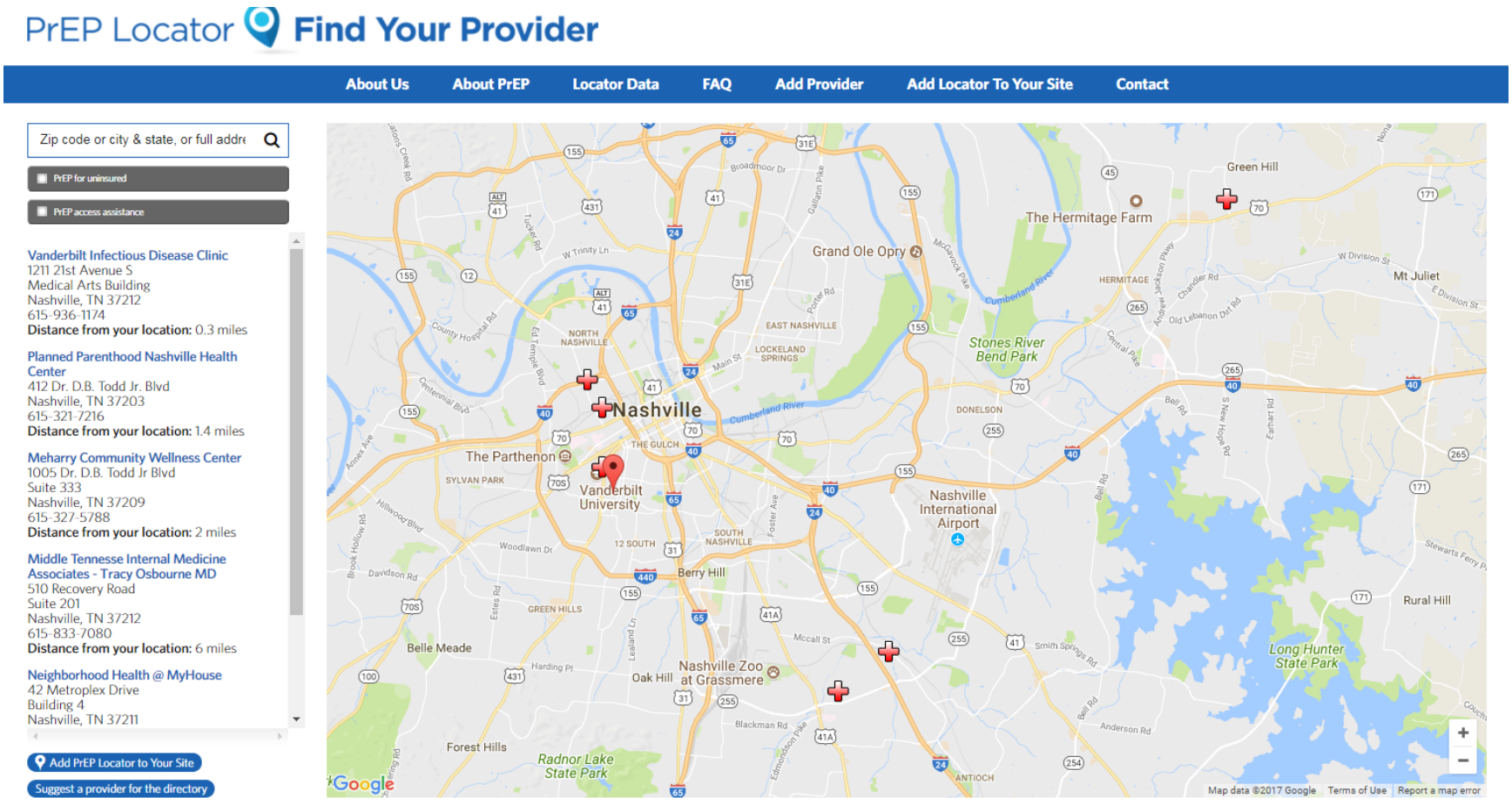
Prescriptions/Refill authorizations: 5

Discussions: 5+

Advertise!

Pre-Exposure Prophylaxis (PrEP) at the Vanderbilt Comprehensive Care Center
If you have a partner who is not HIV-infected, the Vanderbilt Comprehensive Care Center now offers pre-exposure prophylaxis (PrEP) to reduce his or her risk of HIV infection.
PrEP is an HIV-prevention strategy. It is a pill, taken once daily
containing some of the sar
taken by an HIV-uninfected
HIV, PrEP may reduce tha
If your partner is interested
an appointment with a Var
PrEP provider b
VANDERBI
MED
PROTECT YOURSELF WITH PREP
PATIO315
Love is sweet
PATIO 315 WELCOMES NASHVILLE PRIDE! STOP BY FOR FOOD AND DRINK SPECIALS
HAPPY PRIDE MONTH, NASHVILLE!
bam
REPORTER
SEARCH
FOR MEDIA
Combination therapy PrEP offers effective way to prevent HIV infection
by Bill Snyder | Thursday, Sep. 7, 2017, 9:44 AM
Vanderbilt Comprehensive Care Clinic
Infectious disease experts Katie White, M.D., Ph.D., and Sean Kelly, M.D., are working to raise awareness of effective w
to prevent HIV infection, including the combination drug therapy called pre-exposure prophylaxis, or PrEP. (photo by Daniel Dubois)
Rates of new HIV infections in the United States are declining — except among men who have
sex with men. Rates are particularly high among African-American and Hispanic men and
especially in the South.

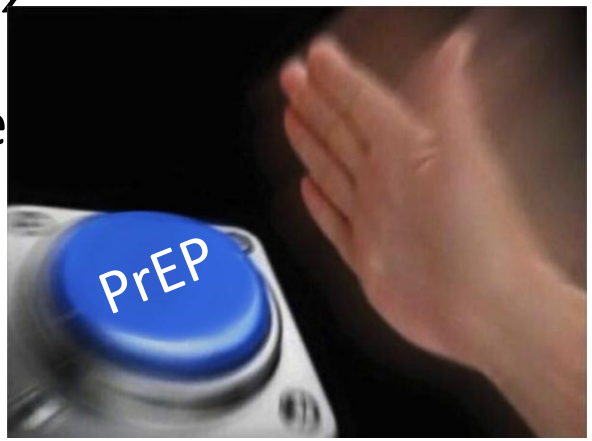
PrEP Locator



https://preplocator.org

Conclusion

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



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