Pre-Exposure Prophylaxis (PrEP)

*Daily medication to reduce HIV*

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Disclosures

- None declared
Agenda

- What is PrEP?
- How effective is it?
- Why do we need it?
- Who benefits from PrEP?
- What are drawbacks?
- Who can prescribe?
- How to prescribe?
- The future of PrEP
But first, a case

62-year-old man presents to discuss primary prevention to reduce his risk of MI and stroke. He has a 30-pack-year smoking history (quit 2 years ago), is moderately overweight, and has well-controlled hypertension on HCTZ. What do you do?
Case 1

A: Encourage weight loss only
B: Recommend daily aspirin 81mg
C: Congratulate him on his smoking cessation
D: Refer him to a cardiologist

(you can only do only do one thing)
Case 12.0

22-year-old man presents to discuss primary prevention to reduce his risk of HIV infection. He has 20 lifetime sexual partners (uses condoms), practices anal receptive sex, has a history of treated chlamydia. What do you do?

62-year-old man presents to discuss primary prevention to reduce his risk of MI and stroke. He has a 20-pack-year smoking history (quit 2 years ago), is moderately overweight, and has well-controlled hypertension on HCTZ. What do you do?
Case 2.0

A: Encourage weight loss only

B: Recommend daily aspirin 81mg

C: Congratulate him on his smoking cessation

D: Refer him to a cardiologist

A: Encourage abstinence only

B: Recommend daily Truvada PrEP

C: Congratulate him on his condom use

D: Refer him to an Infectious Disease specialist
What is PrEP?
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/emtracitabine (FTC) 200mg
  - Developed by Gilead
  - FDA-approved for use as PrEP on June 6, 2012

Also approved in Australia, Canada, France, Peru, Israel, Kenya, and South Africa
This is different from PEP

- **PrEP** = Pre-Exposure Prophylaxis
  - HIV exposure has not yet occurred
- **PEP** = Post-Exposure Prophylaxis
  - HIV exposure HAS occurred
  - Goal is to reduce incidence of established infection
  - THREE drugs required: Truvada (TDF/FTC) + raltegravir
How well does PrEP work?
44% HIV risk reduction, but 92% risk reduction when taken consistently among MSM and transgender women
62.2% HIV risk reduction among heterosexual men and women
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 9863, 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, Dr Michael Martin, MD, Pravan Suntharasmart, MD, Udomsak Sangkum, MD, Philip A Mock, MAPStats, Manoj Leelochawali, MD, Sitisat Chiamwongpaet, MD, Praphan Kitisin, MD, Phitnan Natrujote, MD, Somyot Kittimunkong, MD, Ruth Chuachoowong, MD, Roman J Gvetadze, MD, Janet M McNicholl, MD, Lynn A Paxton, MD, Marcel E Curnin, MD, Craig W Hendrix, MD, Suphak Vanichseni, MD, for the Bangkok Tenofovir Study Group

48.9% risk reduction, but 74% HIV risk reduction when taken consistently, among IDUs (TDF only)
86% HIV risk reduction in MSM using on-demand PrEP
IPERGAY

- Study was discontinued early, all offered on-demand PrEP in open-label phase and more enrolled.
- Mean pill use: 18 pills/month
- 97% reduction in relative risk of HIV in this extended arm versus the discontinued placebo arm
On-Demand Dosing

24 hours

TDF/F
TC

TDF/F
TC

24 hours

TDF/F
TC

24 hours

TDF/F
TC

24 hours

TDF/F
TC

24 hours

TDF/F
TC

24 hours

TDF/F
TC

24 hours

TDF/F
TC

24 hours

TDF/F
TC

24 hours

TDF/F
TC

24 hours
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

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Dosing</th>
<th>Risk Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>iPrEX</td>
<td>MSM</td>
<td>Daily</td>
<td>44% (92% with ideal adherence)</td>
</tr>
<tr>
<td>TDF2</td>
<td>Heterosexual men and women</td>
<td>Daily</td>
<td>62.2%</td>
</tr>
<tr>
<td>Partners</td>
<td>Sero-discordant heterosexual couples</td>
<td>Daily</td>
<td>75% (90% with ideal adherence)</td>
</tr>
<tr>
<td>Bangkok Tenofovir Study Group</td>
<td>Intravenous drug users</td>
<td>Daily</td>
<td>48.9% (74% with ideal adherence)</td>
</tr>
<tr>
<td>IPERGAY</td>
<td>MSM</td>
<td>On-demand</td>
<td>86%</td>
</tr>
</tbody>
</table>
Why PrEP matters
Joint United Nations Program on HIV/AIDS (UNAIDS) goal to have 90% of those living with HIV to know their status, 90% of those to be on ART, and 90% of those on ART to be virologically suppressed by 2020.
As of 2015, 60% of those living with HIV know their status, 46% of those are on ART, and 38% of those on ART are virologically suppressed.

HAART alone is not the only key

HIV Awareness and Testing

- HIV-
- HIV+

Risk Assessment/Counseling

- PrEP

Address socioeconomic, mental health, substance use barriers to care

Linkage to care

Enroll in Care

HAART initiation

Adherence

Virologic suppression

Decrease in HIV transmission

FIVE PREVENTION PILLARS

1. Young women and adolescent girls and their male partners
2. Key populations
3. Condoms
4. Voluntary medical male circumcision
5. Pre-exposure prophylaxis

United Nations General Assembly prevention targets

Ensure that **90%** of people at risk of HIV infection access comprehensive prevention services, including harm reduction, by 2020.

Reduce **below 100,000** per year the number of adolescent girls and young women aged 15–24 years newly infected with HIV globally by 2020.

Ensure that **90%** of people at risk of HIV infection access comprehensive prevention services, including harm reduction by 2020.

Make **20 billion** condoms annually available in low- and middle-income countries by 2020.

Reach **25 million** additional young men in high HIV incidence areas with voluntary medical male circumcision by 2020.

Reach **3 million** people at higher risk of HIV infection with pre-exposure prophylaxis by 2020.

COUNTRIES THAT HAVE DEMONSTRATION PROJECTS OR HAVE APPROVED TENOFOVIR DISOPROXYL FUMARATE/EMTRICITABINE FOR PRE-EXPOSURE PROPHYLAXIS, AS OF JUNE 2016

*These countries also have completed, ongoing and/or planned demonstration projects.

** These projects investigate different aspects of PrEP provision and impact including acceptability, safety, adherence, effect, appropriate service delivery, integration in combination prevention services, costing and associated behavioural aspects. Their aim is to increase access to PrEP for those people who could benefit most from it, especially in situations of stigma, marginalization and criminalization.
How are we doing?

- By the end of 2015, 79,684 individuals had prescriptions for PrEP (TDF/FTC) in the US
  - Out of an estimated 415,000 eligible
  - 19.2% of those eligible

Estimated annual HIV infections in the U.S. declined 18%.

Between 2008 - 2014 infections fell from 45,700 to 37,600.

- 56% decline among people who inject drugs.
- 36% decline among heterosexuals.
- 26% decline among gay and bisexual men aged 35-44 years.
- 18% decline among gay and bisexual men aged 13-24 years.

Gay and bisexual men remain most affected.

- 37,600 New HIV Infections in 2014.
- Gay and bisexual men: 26,200 infections (70%).
- People who inject drugs: 1,700 infections (5%).
- Gay and bisexual men who inject drugs: 1,100 infections (3%).

Heterosexuals: 8,600 infections (23%).

Diagnoses of HIV Infection among Men Who Have Sex with Men, by Region of Residence and Race/Ethnicity 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. Hispanics/Latinos can be of any race.
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.
HIV Risk by State

Estimated Lifetime Risk of HIV
HIV Risk by Race/Ethnicity and MSM

White women: 1 in 880
White men: 1 in 132
Hispanic women: 1 in 227
Hispanic men: 1 in 48
Black women: 1 in 48
Black men: 1 in 20

White MSM: 1 in 11
Hispanic MSM: 1 in 4
Black MSM: 1 in 2

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

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

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

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
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
Taking a sexual history

- Survey of 85 HIV-infected MSM
  - 77 of MSM had a sexual history documented
  - 75 of those who were sexually active had STI screens offered, and 68 of those accepted screening
  - Of these, **16 had an STI**
  - 63 had a recreational drug use history taken
  - 17 of these reported active drug use, 3 used drugs for sex ("chemsex")

Taking a sexual history promotes comprehensive STI risk reduction counseling

Condom use
Knowing HIV status
Knowing partner’s HIV status
PrEP
Sexual history and comprehension of PrEP

- Counseling on PrEP after a sexual history discussion significantly increases comprehension of HIV-prevention strategies.
- Engagement in a sexual history discussion may heighten the self-relevance of information, increasing memory and cognitive processing during PrEP education.

STI Epidemic

- Between 2014 and 2015
  - Chlamydia cases increased 5.9% (to 1.5 million cases)
  - Gonorrhea cases increased 12.8% (to 400,000 cases)
  - Syphilis cases increased 19% (to 24,000 cases)
  - Adolescents/young adults age 15-24 account for half of these

- Screening in MSM
  - Syphilis, chlamydia, gonorrhea, and HIV screen annually if sexually active
  - More frequent (every 3 or 6 months) if multiple or anonymous partners

- Screening in women
  - Gonorrhea, chlamydia annually if ≤25 years, or annually if >25 and multiple partners
  - Syphilis, HIV, chlamydia, gonorrhea, and HBV in all pregnant women

Chemsex

- Use of recreational substances to augment the sexual experience
- Among MSM, associated with:
  - Having HIV or HCV-infected partners
  - Higher risk-taking behaviors (i.e. condomless sex, multiple partners)
  - Acute bacterial STIs
  - Rectal STIs
  - Hepatitis C incidence
  - HIV incidence

How often do you discuss sexual behavior with your patients?

A. Every single encounter
B. Initial encounter only
C. Occasionally
D. Very seldom
E. Almost Never
What are your barriers to the discussion?
*Wordcloud*
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…

- Pre-Contemplation
- Contemplation
- Planning
- Action
- Further risk reduction
- Stronger relationships
- Fewer sexual partners
- Confidence in sexual health
- Active commitment to health
- Confidence in sexual health
No evidence of sexual risk compensation in the iPrEx trial of daily oral HIV preexposure prophylaxis.

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.

Real questions, real barriers

- Cost
- Judgment from providers
- Judgment from partners
- Partner could find out about sex outside of the relationship
- Partner would misinterpret taking PrEP as having HIV

…and Missed Opportunities

- PrEP is experimental
- PrEP is too expensive
- PrEP is not a primary care activity
- Recommending condom use is enough
- Uncomfortable prescribing PrEP
- Unaware of PrEP

The drawbacks of PrEP
Cost

- $13,000 for one year in USA
- Covered by most private insurance companies
  - Variable co-pays, deductibles, etc.
- Medicaid coverage varies by state
- Co-pay and cost assistance available
  - Up to $3,600/year in co-pay assistance
  - Medication assistance if <500% federal poverty level
Adverse Events

Table 2. Adverse Events.*

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>FTC-TDF (N = 1251)</th>
<th>Placebo (N = 1248)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of patients (%)</td>
<td>no. of events</td>
<td>no. of patients (%)</td>
</tr>
<tr>
<td>Any adverse event</td>
<td>867 (69)</td>
<td>2630</td>
<td>877 (70)</td>
</tr>
<tr>
<td>Any serious adverse event</td>
<td>60 (5)</td>
<td>76</td>
<td>67 (5)</td>
</tr>
<tr>
<td>Any grade 3 or 4 event</td>
<td>151 (12)</td>
<td>248</td>
<td>164 (13)</td>
</tr>
<tr>
<td>Grade 3 event</td>
<td>110 (9)</td>
<td>197</td>
<td>117 (9)</td>
</tr>
<tr>
<td>Grade 4 event</td>
<td>41 (3)</td>
<td>51</td>
<td>47 (4)</td>
</tr>
<tr>
<td>Elevated creatinine level</td>
<td>25 (2)</td>
<td>28</td>
<td>14 (1)</td>
</tr>
<tr>
<td>Headache</td>
<td>56 (4)</td>
<td>66</td>
<td>41 (3)</td>
</tr>
<tr>
<td>Nausea</td>
<td>20 (2)</td>
<td>22</td>
<td>9 (&lt;1)</td>
</tr>
<tr>
<td>Unintentional weight loss (≥5%)</td>
<td>27 (2)</td>
<td>34</td>
<td>14 (1)</td>
</tr>
<tr>
<td>Death</td>
<td>1 (&lt;1)‡</td>
<td>1</td>
<td>4 (&lt;1)</td>
</tr>
<tr>
<td>Discontinuation of study drug</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Permanently</td>
<td>25 (2)</td>
<td>26</td>
<td>27 (2)</td>
</tr>
<tr>
<td>Permanently or temporarily</td>
<td>79 (6)</td>
<td>99</td>
<td>72 (6)</td>
</tr>
</tbody>
</table>

* 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.
# Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>TDF–FTC (N=611)</th>
<th>Placebo (N=608)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>557 (91.2)</td>
<td>536 (88.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Any serious</td>
<td>63 (10.3)</td>
<td>66 (10.9)</td>
<td>0.90</td>
</tr>
<tr>
<td>Grade 3 or 4 only</td>
<td>19 (3.1)</td>
<td>29 (4.8)</td>
<td>0.17</td>
</tr>
<tr>
<td>At least possibly related to study drug</td>
<td>20 (3.3)</td>
<td>27 (4.4)</td>
<td>0.35</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>231 (37.8)</td>
<td>241 (39.6)</td>
<td>0.84</td>
</tr>
<tr>
<td>Headache</td>
<td>227 (37.2)</td>
<td>226 (37.2)</td>
<td>0.73</td>
</tr>
<tr>
<td>Nausea</td>
<td>113 (18.3)</td>
<td>43 (7.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dizziness</td>
<td>92 (15.1)</td>
<td>67 (11.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Vomiting</td>
<td>69 (11.3)</td>
<td>43 (7.1)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

*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).
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.
Adverse Events

Table 3. Bone Mineral Density Scores.

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Forearm</th>
<th>Hip</th>
<th>Lumbar Spine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TDF–FTC (N=109)</td>
<td>Placebo (N=112)</td>
<td>P Value</td>
</tr>
<tr>
<td>T score</td>
<td>0.004</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

BUT THIS CAN RECOVER!

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

* 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.
How to provide PrEP

- Complete Risk Evaluation and Mitigation Strategies (REMS) training and registration
- Identify patient who will benefit (they may not ask)
- Engage in discussion
  - If unable or unwilling to offer, refer
- Advise patient to contact their insurance
  - May need co-pay assistance, prior-authorization
How to provide PrEP

- Follow CDC Guidelines
  - Make sure the patient is HIV-negative!
    - Screen for HIV prior to starting PrEP
    - Assess for symptoms of acute HIV
    - Document HIV-negative status
  - Make sure they have normal renal function
    - Check serum creatinine
  - Obtain and document hepatitis B and C status
    - Check HBV serologies to evaluate immunity or infection
    - Check HCV screen
  - Screen for other STIs
  - Assess pregnancy intention
How to provide PrEP

- Prescribe PrEP
  - No more than 3 months at a time
- At 3 months
  - 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
How to provide 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
How to provide PrEP

- Every 6 months
  - Screen for other STIs
  - Repeat serum creatinine
How to provide PrEP

- At any time, stop PrEP if:
  - 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
## How to provide PrEP

<table>
<thead>
<tr>
<th>Encounter</th>
<th>To do</th>
</tr>
</thead>
</table>
| 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+
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 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 repeated 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
Trademarks of Gilead Sciences, Inc. 18/0217-0079

Gilead Sciences, Inc.
Special considerations

- Pregnant or breastfeeding women
  - Pregnancy Category B (No known risk)
  - Minimally secreted in breastmilk, not contraindicated in breastfeeding

- Chronic HBV
  - TDF and FTC are active against HBV
  - If TDF/FTC no longer used for PrEP, consider continuing with chronic HBV as the indication

- Chronic Renal Failure (eGFR <60ml/min)
  - Don’t use TDF/FTC; safety has not been adequately determined

- Adolescent Minors
  - Careful consideration, no subjects <18 years were included in trials
Adolescent Trials Network for HIV/AIDS Interventions (ATN) study

- 78 HIV-negative MSM, ages 15-17, who reported HIV risk behavior during the previous 6 months received daily PrEP
- Follow-up monthly for 12 weeks, then quarterly for the remainder of 48-week study
- Adherence was high during monthly follow-up, then dropped dramatically (by more than half)
- 32 discontinued before the end of the study
- HIV acquisition rate: 6.4%
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.

http://www.truvadapreprems.com
REMS for TDF/FTC

- Required for TDF/FTC for use in PrEP because
  - The benefit is different than for its use in HIV infection
  - The risk/benefit scale changes, depending on patient behavior
Future of PrEP
Tenfovir Alafenamide (TAF)

- More potent than TDF
- No known side effects of bone loss or reduced renal function
- Formulation as subdermal implant in development

Cabotegravir

- Integrase inhibitor with long half-life
- Long acting, depot-controlled nanosuspension has an even longer half-life (25-54 days)
- Use as PrEP in phase 2 trials:
  - Oral lead-in
  - Will likely need every 2 months (6 injections/year)
  - Injection site reactions common
  - Most patients still preferred this over daily oral PrEP

Rilpiverine

- Non-nucleoside reverse-transcriptase inhibitor
- Long-acting, depot-controlled nanosuspension has a long half life (44-62 days)
- Use in PrEP remains undetermined
Maraviroc

- CCR5-antagonist currently used in some ART regimens
- A recent phase 2 trial demonstrated it’s as safe and well-tolerated as TDF/FTC
- Efficacy remains under investigation

Rectal tenofovir gel

- On-demand use, vs. every day dosing
- Integrated into lubricant
- In a recent phase 2 study, there was no difference in adherence, or preference, compared to daily oral PrEP
- Efficacy remains under investigation
- A tenofovir vaginal film and gel is also under investigation

Cranston R, et al. MTN-017: Rectal Phase 2 Extended Safety and Acceptability Study of 1% Tenofovir Gel. Presented at: CROI, February 22–25, 2016, Boston, Massachusetts
Dapivirine vaginal ring

- Non-nucleoside reverse-transcriptase inhibitor
- Empowering women in HIV-endemic countries
- A recent phase III trial demonstrated disappointing HIV risk reduction (only up to 37%)
Where to start, learn more

- Review prescribing guidelines
- Start asking your patients
- Use reliable sources:
  - www.cdc.gov/hiv/prep
  - www.truvada.com
Thank you!

Questions?