Common PrEP Questions: A Case-Based Discussion

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Financial Relationships With Commercial Entities

Dr Scott has no relevant financial affiliations to disclose. (Updated 11/18/19).

Learning Objectives

After attending this presentation, learners will be able to:

▪ Identify US populations at highest risk of HIV infection
▪ Counsel patients about how to take different Preexposure prophylaxis (PrEP) regimens
▪ Describe the impact of sexually transmitted infections (STIs) on PrEP and PrEP on STIs
▪ Explain U=U
Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2017—United States and 6 Dependent Areas

N = 38,640

- Male-to-male sexual contact: 67%
- Heterosexual contact—Female: 16%
- Heterosexual contact—Male: 7%
- Injection drug use (IDU)—Female: 3%
- Injection drug use (IDU)—Male: 4%
- Male-to-male sexual contact and IDU: 3%

Note: Data for the year 2017 are considered preliminary and based on 6 months reporting delay. Data have been statistically adjusted to account for missing transmission category. "Other" transmission category not displayed as it comprises less than 1% of cases.

Rates of Diagnoses of HIV Infection among Adults and Adolescents by Sex and Race/Ethnicity, 2017—United States

Note: Data for the year 2017 are considered preliminary and based on 6 months reporting delay. Hispanics/Latinos can be of any race.

Diagnoses of HIV Infection among Adults and Adolescents by Age at Diagnosis, 2017—United States

N = 38,182

- 25-34: 25%
- 25-44: 30%
- 45-54: 15%
- 55+: 18%

Note: Data for the year 2017 are considered preliminary and based on 6 months reporting delay.
Rates of Diagnoses of HIV Infection among Adults and Adolescents 2017—United States and 6 Dependent Areas

N = 38,640  Total Rate = 14.0

Note. Data for the year 2017 are considered preliminary and based on 6 months reporting delay.

ARS Question 1
Do you start PrEP on the same day, or wait for test results before prescribing PrEP?

A. Same day
B. Wait for lab results
C. Something else

Same day starts in NYC
**ARS Questions 2**

When you prescribe PrEP, how do you prescribe it?

A. 1 month of PrEP, require patient to return before giving refills  
B. 3 months of PrEP, require patient to return before giving refills  
C. 3 months of PrEP, with refills  
D. 12 months of PrEP  
E. Something else

**PrEP prescribing: The Goldilocks problem**

- Want to give enough PrEP to ensure coverage of risk, but not so much that PrEP users don’t come in for q 3 month HIV/STI testing  
- Analysis of data from San Francisco primary care clinics found that  
  prescriptions of <30 days were associated with higher rate of PrEP discontinuation (OR 1.5, 95% CI: 1.1-2.2)  
- However, only 2/3 of PrEP intervals had HIV/STI testing done, even when allowing for intervals of 4 months  
- Panel management associated with better adherence to follow-up HIV/STI testing  

Spinelli, CROI 2018 #1028  
Spinelli et al, OFID 2018

**ARS Question 3 – Case 1**

A 21 year old woman asks you to prescribe PrEP. She states that she always uses condoms with her multiple sexual partners but would like to stop using them.  

What do you recommend?  

A. You don’t offer PrEP because condoms have worked well for her up to this point, and you don’t want to risk STIs  
B. You don’t offer PrEP because it doesn’t work well in women  
C. You offer PrEP but tell her it works less well if she has bacterial vaginosis  
D. You offer PrEP and counsel that only condoms will prevent STIs, but leave the condom decision up to her
CDC Guidelines for PrEP among HTW

- It can be challenging to identify HIV risk among HT women.
- Risk assessment should also consider sexual networks and male partners' HIV risk.

<table>
<thead>
<tr>
<th>Table 1: Summary of Guidance for PrEP Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Directing substantial risk of acquiring HIV infection:</td>
</tr>
<tr>
<td>HIV-positive sexual partner</td>
</tr>
<tr>
<td>Recent heterosexual sex</td>
</tr>
<tr>
<td>History of transaction or use of Commercial sex work</td>
</tr>
<tr>
<td>HIV-positive sexual partner</td>
</tr>
<tr>
<td>Recent heterosexual sex</td>
</tr>
<tr>
<td>History of transaction or use of Commercial sex work</td>
</tr>
<tr>
<td>HIV-positive injecting partner</td>
</tr>
<tr>
<td>Sharing injection equipment</td>
</tr>
</tbody>
</table>

CDC. 2017 PrEP Clinical Guideline update

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PrEP Works if You Take It — Effectiveness and Adherence in Trials of Oral and Topical Tenofovir-Based Prevention

- Tenofovir concentrates at 10-100 fold higher in rectal than vaginal tissue
- Tenofovir also cleared more rapidly from vaginal than rectal tissue
- PK suggests women need to take daily TDF/FTC 6-7 days/week to maximize effectiveness

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Does TDF/FTC for PrEP work for cis women?

Yes, if they take it regularly

BUT:
- Tenofovir concentrates at 10-100 fold higher in rectal than vaginal tissue
- Tenofovir also cleared more rapidly from vaginal than rectal tissue
- PK suggests women need to take daily TDF/FTC 6-7 days/week to maximize effectiveness
ARS Question 4 – Case 2

A 34 year-old MSM has sex with new partners approximately twice per month. He doesn’t want to take a daily pill because his sexual exposures are relatively infrequent, but he doesn’t always use condoms.

What would you do?

A. Encourage him to use condoms
B. His exposure is relatively low, so don’t worry about PrEP
C. Encourage him to take daily PrEP
D. Have him start PrEP 7 days before sexual episodes
E. Prescribe “on-demand” or “2-1-1” PrEP, even though this is not FDA approved

Ipergay: Event-Driven iPrEP

- 2 tablets (TDF/FTC or placebo) 2-24 hours before sex
- 1 tablet (TDF/FTC or placebo) 24 hours later
- 1 tablet (TDF/FTC or placebo) 48 hours after first intake

“2-1-1”

Ipergay: Event-Driven iPrEP

- 2 tablets (TDF/FTC or placebo) 2-24 hours before sex
- 1 tablet (TDF/FTC or placebo) 24 hours later
- 1 tablet (TDF/FTC or placebo) 48 hours after first intake
- Daily pills until 48 hour after last dose
- If last pill within 7 days, take single pill to start

“2-1-1-1…”
Ipergay Results

HIV Incidence (mITT Analysis)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Follow-up Pts-years</th>
<th>HIV Incidence per 100 Pts-years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (double-blind)</td>
<td>212</td>
<td>6.60 (3.60-11.1)</td>
</tr>
<tr>
<td>TDF/FTC (double-blind)</td>
<td>210</td>
<td>0.89 (0.11-3.20)</td>
</tr>
<tr>
<td>TDF/FTC (open-label)</td>
<td>515</td>
<td>0.19 (0.01-1.56)</td>
</tr>
</tbody>
</table>

Median Follow-up in Open-Label Phase: 18.4 months (IQR: 17.5-19.1)

97% relative reduction vs. placebo

Molina et al, Lancet HIV 2017;4:e402-10

What about less frequent sex?

• An analysis of IPERGAY study evaluating 269 patients (134 person-years) who took on-demand TDF/FTC PrEP less frequently (<15 pills/month) AND reported using PrEP systematically or often during sexual intercourse

<table>
<thead>
<tr>
<th>PERSIERGAY RCT</th>
<th>2017 Subanalysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median # sex acts/month</td>
<td>10</td>
</tr>
<tr>
<td>Median # pills taken/month</td>
<td>9.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Person years</th>
<th># HIV infections</th>
<th>HIV incidence rate/100 py (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>64.8</td>
<td>6</td>
<td>9.3 (3.4-20.1)</td>
</tr>
<tr>
<td>TDF/FTC</td>
<td>68.9</td>
<td>0</td>
<td>0.0 (0.0-5.4)</td>
</tr>
</tbody>
</table>

Antoni et al, AIDS 2017

Recommendations for 2-1-1 TDF/FTC PrEP

• CDC continues to recommend daily TDF/FTC PrEP only
  ◦ only licensed indication by FDA

• IAS-USA guidelines recommend 2-1-1 TDF/FTC PrEP as alternative to daily PrEP for MSM
  ◦ Use if can plan ahead for pre-dose, can take post-doses, use with all partners
  ◦ Does not avoid adverse events

• Daily TDF/FTC PrEP is the only recommended option for cis- and transgender women and PWID
Considerations of 2-1-1 vs Daily TDF/FTC PrEP

<table>
<thead>
<tr>
<th>2-1-1 PrEP</th>
<th>Daily PrEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Who can use it?</td>
<td>Only studied in MSM</td>
</tr>
<tr>
<td>Chronic HBV</td>
<td>Can trigger a flare</td>
</tr>
<tr>
<td>Planning</td>
<td>Need to plan sex at least 2hrs in advance</td>
</tr>
<tr>
<td>“Forgiveness”</td>
<td>Not forgiving of missed doses</td>
</tr>
</tbody>
</table>

ARS Question 5 – Case 3

A 48 year-old MSM with hypertension comes in requesting PrEP. He has multiple partners, frequent sex, and frequent STIs. His creatinine is 1.7, creatinine clearance is 61 ml/min.

What would you do?

A. Prescribe daily TDF/FTC
B. Prescribe daily TAF/FTC
C. Prescribe every other day TDF/FTC
D. Prescribe 2-1-1 TDF/FTC
E. Tell him he should use condoms. PrEP won’t work well because of multiple STIs.

Modest TDF/FTC renal effects in older persons

- In iPrEx OLE and SF Kaiser (Marcus JAIDS 2016), risk of eGFR<70 if:
  - Baseline eGFR<90
  - >40-50 years old
- In Partners PrEP and Partners Demo (Mugwanya, JAIDS 2016)
  - Same as above or weight < 55kg
  - >75% of creatinine increases unconfirmed on repeat test
  - No difference in picking up true renal effects if q 3 vs 6 month testing
- In Thai IDU study (Martin, CID 2014)
  - No effect of recent IDU on creatinine
  - More likely to have renal effects with increased age
- All studies
  - Creatinine reverts to near baseline after trial
  - Re-challenge has been used successfully
In IPERGAY, fewer pills had less renal effect

<table>
<thead>
<tr>
<th>Estimation of the effect on eGFR (ml/min/1.73m²)</th>
<th>PT 1</th>
<th>Uncorrected analysis</th>
<th>Adjusted analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pills per month in the last two months¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 pills (n=1341)</td>
<td>250</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>30 pills (n=2279)</td>
<td>370</td>
<td>-1.30 (±0.30)</td>
<td>-0.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Luminol plasma concentration at the time of eGFR assessment²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2 mg/mL (n=1745)</td>
<td>225</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>2.2 mg/mL, (n=5744)</td>
<td>90</td>
<td>-1.27 (±0.30)</td>
<td>-0.04 (±0.49)</td>
</tr>
<tr>
<td>10 mg/mL, (n=512)</td>
<td>88</td>
<td>-1.42 (±0.42)</td>
<td>-1.36 (±0.42)</td>
</tr>
<tr>
<td>40 mg/mL, (n=2232)</td>
<td>354</td>
<td>2.06 (±0.30)</td>
<td>1.82 (±0.30)</td>
</tr>
</tbody>
</table>

¹ Fewer points in the lower trend line indicate fewer pills taken over the last two months.
² Plasma concentrations were measured at the time of eGFR assessment.

Renal Safety at Week 48

Hare, CROI 2019, Abstract 104H

DISCOVER Primary Endpoint Analysis: HIV Incidence

Hare, LHUJ 2019, Abstract 104H
4 Doses/Week has Similar Efficacy to Daily TDF/FTC for MSM


Do STIs modulate the efficacy of PrEP?

- No evidence STIs lower PrEP efficacy in RCTs
  - IP/EX: Syphilis incidence of 7/100 py; no interaction with PrEP efficacy (Solomon, CD 2014)
  - Partners PrEP: No difference in PrEP efficacy among those with STIs (Murnane, AIDS 2013)

- No evidence in open label studies
  - PROUD in UK: 73% with baseline STI & 86% effectiveness of PrEP (McCormack, Lancet 2015)
  - Partners PrEP: No difference in PrEP efficacy among those with STIs (Murnane, AIDS 2013)

- No evidence in open label studies
  - PROUD in UK: 73% with baseline STI & 86% effectiveness of PrEP (McCormack, Lancet 2015)
  - US MSM PrEP Demo study: 90/100 p-yr STI incidence & 0.43/100 p-yr HIV incidence (Lu, JAMA Int Med 2015)

Effect of PrEP on STIs

- Rates of bacterial STIs increasing over time; however, rises pre-PrEP use
- High rates of STIs in many studies of PrEP users
- Mixed results about whether PrEP increases rate of STIs and interpretation complicated by association of PrEP use with high-risk sexual practices
- PrEP users should be screened every 3 months for STIs

Traeger et al, CID 2018
ARS Question 6 – Case 4

A 29 year old MSM in a serodifferent relationship with an HIV positive partner comes in requesting PrEP. When you ask him, he explains that his partner is fully virally suppressed and has been for over a year, but he would feel more comfortable being on PrEP.

What do you do?
A. Prescribe PrEP
B. Prescribe PrEP for now, with the hope of eliminating PrEP in the future if his partner remains suppressed
C. Tell the patient that he doesn’t need PrEP because U=U
D. What’s U=U??

HPTN 052: Immediate vs. Delayed ART

1763 sexually active serodiscordant couples, HIV positive partner CD4+ 350-550 cells/mm³

Randomized to
• Immediate ART vs.
  • Delayed ART (CD4+ ≤ 250 cells/mm³ or AIDS defining illness)

Cohen et al, NEJM 2016
Efficacy 93%

Observational Data: 3 couples studies

<table>
<thead>
<tr>
<th>Number of couples</th>
<th>Partner 1</th>
<th>Partner 2</th>
<th>Opposites Attract</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>888</td>
<td>793</td>
<td>343</td>
</tr>
<tr>
<td>Risk</td>
<td>Heterosexual, MSM, MSM</td>
<td>MSM</td>
<td>MSM</td>
</tr>
<tr>
<td># Condomless sex acts</td>
<td>58,000</td>
<td>77,000</td>
<td>17,000</td>
</tr>
<tr>
<td># Unlinked infections</td>
<td>11</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td># Linked infections</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Rodger et al, JAMA 2016;316:171-181
Bavinton et al, Lancet HIV 2018; 5(8) e438-e447
Rodger et al, AIDS 2018; 32:450-462

Policy statements on U=U

On September 27, 2017, the US CDC sent out a “Dear Colleague” letter stating:

“…. people who take ART daily as prescribed and achieve and maintain an undetectable viral load have effectively no risk of sexually transmitting the virus to an HIV-negative partner.”

Condom Effectiveness

**Heterosexuals** (Giannou et al, Expert Rev Pharmacoecon Outcomes Res 2016)
- Meta-analysis of 25 studies, >10,000 couples
- Overall effectiveness: 71-77%

**MSM** (Smith et al, JAIDS 2015;68:337-344)
- Data from 2 large cohorts
- 70% effective

Underutilization of PrEP in Partners of HIV positive MSM

10% of MSM HIV patients with HIV-negative partners reported having a partner taking PrEP

Among all reported HIV-negative partners...

- 6% taking PrEP
- 67% not taking PrEP and patient not virally suppressed
- 27% not taking PrEP and patient not virally suppressed

Beer et al. CROI 2018, #1052
Self-reported vs. actual VL among men stating VL undetectable

Teran, CROI 2018, #997

ARS Question 7 – Case 5

A 28 year old HIV negative woman is in a serodifferent relationship with an HIV positive man. He is newly diagnosed, and not yet stably virally suppressed. The couple wants to have a baby.

What do you recommend?

A. Wait for the male partner to become fully virally suppressed for at least 6 months before attempting pregnancy
B. Use PrEP – it’s safe peri-conception and in pregnancy
C. Don’t use PrEP – its safety is unknown. Use sperm washing instead
D. Something else

HIV risk increases during pregnancy

- 2,751 HIV-uninfected females in African HIV serodiscordant couples followed for ≤48 mos in 2 HIV prevention studies between 2004-2012
- Frequent HIV and pregnancy testing
- Genetic linking of HIV infections
PrEP safety in pregnancy

- Study of 30 women who became pregnant while on PrEP (compared with 96 women not exposed to PrEP)
  - No difference in miscarriage, congenital anomalies, or growth through 1 year of infancy
  - Slightly lower z-scores for length (-1.73 v. -0.79, p=0.05) and head circumference (0.24 v 1.07, p=0.04) at 1 month, but NS at 1 year.

Heffron et al AIDS 2018

ARS Question 8 – Case 6

A 35 year old MSM in a serodifferent relationship comes in seeking PrEP. He states that his partner has been unsuppressed, and is just starting a new treatment regimen. The partner had to change his regimen because of antiretroviral resistance, and he’s pretty sure his partner mentioned M184V. He doesn’t like using condoms.

What do you recommend?

A. They should continue to use condoms until the partner has been fully virally suppressed for at least 6 months.
B. You prescribe TDF/FTC or TAF/FTC
C. You prescribe 3-drug PEP
D. Something else

Breakthrough infections

- PrEP Breakthrough infections despite documented high adherence

<table>
<thead>
<tr>
<th>Location</th>
<th>Duration on PrEP before HIV diagnosis</th>
<th>Resistance Mutations</th>
<th>Adherence Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohen et al</td>
<td>US</td>
<td>13 months</td>
<td>M184V, L74V</td>
</tr>
<tr>
<td>Knox et al</td>
<td>Canada</td>
<td>24 months</td>
<td>M41L, D67G, T69D, K70R, M184V, Y115E</td>
</tr>
<tr>
<td>Markowitz et al</td>
<td>US</td>
<td>6 months</td>
<td>K65R, M184V</td>
</tr>
<tr>
<td>Hoornenborg et al</td>
<td>Amsterdam</td>
<td>8 months</td>
<td>No major resistance</td>
</tr>
<tr>
<td>Thaden et al</td>
<td>US</td>
<td>14 months</td>
<td>M184V, K70T, K65R</td>
</tr>
<tr>
<td>Colby et al</td>
<td>Thailand</td>
<td>8 weeks</td>
<td>M184V</td>
</tr>
</tbody>
</table>

DBS = Dried Blood Spot
Cohen et al Lancet HIV 2018
ARS Question 9 – Case 7

A 29 year old woman in a serodifferent relationship would like to stop using condoms. Her partner is not virally suppressed. She wants to know how long she has to take daily PrEP before she is protected. What do you tell her?

A. 3 days
B. 7 days
C. 21 days
D. 28 days
E. I have no idea

How long do you need to take PrEP before protected?

In blood (PBMCs)
• 89% achieve EC90 after 7 doses
• 98% by 13th dose

Recommended for MSM:
• Start TDF/FTC PrEP 7 days before
• Continue 28 days after (based on animal data)

Recommend for Women
• CDC recommends 21 days before, but growing consensus that 7 days may be adequate
• Women need 6-7 doses/week while men only need 4-7 doses for maximal protection

Proportion achieving EC90 of tenofovir in PBMCs

ARS Question 10 – Case 8

A 35 year old transgender woman reports that she has infrequent condomless sex and is reluctant to start PrEP because she believes PrEP will interfere with her gender-affirming hormones. How do you counsel her?

A. You tell her we have data that PrEP does not affect hormone levels and encourage PrEP use
B. You tell her we don’t know if PrEP affects hormone levels but encourage PrEP use
C. You tell her we don’t know if PrEP affects hormone levels, nor do we know if it works for trans women and encourage condoms
D. You recommend 2-1-1 PrEP so that she has less PrEP exposure
Pharmokinetic study of men and trans women

- Design: Open label, one way (estrogen on TFV/FTC) study
- Subjects: 8 cis men, 8 trans women (HIV-Neg; 18-65 years)
- Inclusion: Screening estradiol > 100 pg/mL (TGW only)
- Creatinine Clearance (CrCl) > 70 mL/min
- No contraindication to TDF/FTC

Findings: Lower intracellular TFV-DP and FTC-TP among TGW, but NS

<table>
<thead>
<tr>
<th>TFV-DP</th>
<th>FTC-TP</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBMC</td>
<td>Colon Cell</td>
</tr>
<tr>
<td>C_{ini} AUC</td>
<td>C_{ini}</td>
</tr>
<tr>
<td>% Reduction (TGW/CGM)</td>
<td>16%</td>
</tr>
<tr>
<td>p value</td>
<td>0.30</td>
</tr>
</tbody>
</table>

Shieh et al. HIVR4P 2018

Does PrEP work for trans women?

In iPrEx, 339 participants were identified as trans women
- No infections in women with detectable tenofovir in blood, but only 18% had detectable levels

Trans women express concern about interaction of TDF/FTC with hormones
- In iPrEx, women on hormones less likely to take PrEP

Studies planned or underway to evaluate interaction of TDF/FTC on hormones
- Several studies suggest small reductions in TDF levels

Bottom line: limited data, TDF/FTC likely works in trans women but more data needed

Deutsch et al. Lancet HIV 2015; Anderson et al. JAIDS 2016

ARS Question 11 – Case 9

Your 31 year old patient on PrEP comes in for his routine quarterly lab tests. His 4th generation antibody test comes back positive, but the confirmatory test and viral load come back negative.

What do you do?

A. Repeat the tests but continue PrEP, as you assume the 4th gen test is a false positive
B. Repeat the tests and stop PrEP, but start ART for acute HIV infection
C. Repeat the tests and stop PrEP until you can determine what the infection status is
D. Something else
How to manage ambiguous HIV Test Results

Quarterly PrEP Screening

Ambiguous or Discrepant HIV Tests
1. Confirm the presence or absence of infection - Repeat serologic or RNA tests (DNA tests not validated) - Use a test from another manufacturer
2. Manage antiretroviral drugs
   - Stop PrEP, reassess HIV Status
   - Continue PrEP if adherent
   - Start ART if not adherent to PrEP

Maintains Protection
Risk of Resistance
Facilitates Diagnosis
Risk of Infection
Drug Related AEs
Confirm Diagnosis

More experience needed to manage ambiguous test results

For false-positive results:
Repeat HIV testing, discuss with clinicians and virologists. Seek expert opinion and potentially additional research testing (ultrasensitive HIV VL testing).

PrEPLine: 855-448-7737 (11am-6pm PST)
ARS Question 12
What is most exciting to you in the future of PrEP?
A. Long-acting injectable cabotegravir
B. Long-acting injectable rilpivirine
C. Oral EtdA (MK-8591)
D. Broadly neutralizing antibodies
E. Vaginal rings
F. Maraviroc

What's happening with topical PrEP?
Dapivirine ring studies
- Early efficacy: ~30%
- Open label extension: 54%
- Undergoing regulatory review

Multipurpose technology
- Possibility of combining with contraception or anti-STD interventions
- Rectal douches also under development

Systemic approaches
- Long-acting ARVs
  - Cabotegravir (INSTI) being evaluated
  - Challenges: oral lead-in, long pharmacologic tail needs coverage
  - Other agents, other methods of delivery (e.g., implants)
- Active vaccination
  - 2 efficacy trials in sub-Saharan Africa; 1 planned in the Americas/Europe
  - Use viral vectors with protein sub-unit boost
- Passive vaccination
  - 1 efficacy trial in SSA, 1 in North/South America
  - Use broadly neutralizing antibody infused or injected
Implantable devices

Drug must be extremely potent, as total mass dose to be loaded is small:
- e.g., estradiol implant 80mg/day

Formulation PK profiles compared

Question-and-Answer Period