Understanding PrEP Effectiveness

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Outline

• Prevention Modalities for HIV
• PrEP
• Efficacy vs Effectiveness
• Effectiveness of TDF/FTC as PrEP
• Factors contributing to Effectiveness
1.8 Million New Infections in 2016

New HIV Infections (2014)
- 13,000 [9,600 – 17,000]
- 22,000 [13,000 – 33,000]
- 85,000 [48,000 – 130,000]
- 87,000 [70,000 – 100,000]
- 140,000 [110,000 – 160,000]
- 340,000 [240,000 – 480,000]
- 1.4 million [1.2 – 1.5 million]

New HIV Infections (2016)
- 18,000 [11,000 – 39,000]
- 73,000 [68,000 – 78,000]
- 370,000 [270,000 – 490,000]
- 97,000 [79,000 – 120,000]
- 190,000 [160,000 – 220,000]
- 270,000 [190,000 – 370,000]
- 790,000 [710,000-870,000]

Middle East and North Africa
Western & Central Europe & North America
Western & Central Africa
Latin America
Eastern Europe and Central Asia
Asia and the Pacific
Eastern & Southern Africa

HIV Prevention

- There are various “tools” that can prevent HIV acquisition
- New “tools” to prevent getting HIV are urgently needed
Prevention Modalities

- Condoms
- PEP
- Voluntary Male Circumcision
- Needle Exchange
- Vaccine
- Abstinence
- HIV Treatment
- Microbicides
- HIV & STI Testing
- STI Treatment
- Harm Reduction
What is PrEP?

• Taking drugs before exposure to an infectious agent is called Pre-Exposure Prophylaxis
• It is a concept. A drug or combination of drugs can be used for PrEP but concept of PrEP not limited to a drug.
• Not a new concept, for example Malaria prophylaxis common for travelers is also PrEP for Malaria
Why Antiretroviral Drugs for HIV PrEP?

• Data suggesting that ARV prophylaxis may be effective
  – ARVs for PMTCT
  – Post-exposure prophylaxis for HIV (PEP)
  – Monkey models for SHIV transmission

• Available ARVs appear safe
• In 2012 the FDA approved Truvada® to be used as PrEP in the US for HIV prevention
• Used as part of a HIV prevention package (risk reduction counseling and condoms)
Other Candidates for PrEP

• Other drugs are being evaluated as PrEP agents: e.g. Injectable Cabotegravir, Dapivirine rings etc.

• SO Truvada is one option for PrEP, and we hope not the only option.

• SO we have to start understanding that PrEP and Truvada are not interchangeable. PrEP is a concept, Truvada is one type of PrEP

• Similar to Xerox is not the only photocopier OR Fedex is not the only courier
Efficacy and Effectiveness

- Efficacy is the effect in perfect conditions: maximum possible effect of drug

- Effectiveness is the effect in the real world: A useful clinical effect

**Example**

**Efficacy:** Antibiotics kill bacteria and are efficacious in curing infections.

**Effectiveness:** If you do not take the pills as prescribed, infection may not get cured, and may lead to a ‘rebound’ of those strains not killed (resistant microbes).
**Efficacy of Daily/iPrEP with Oral Truvada**

-72h/+2h (n=6); HR=14.5; \( p=0.01 \)
-22h/+2h (n=6); HR=15.9; \( p=0.007 \)
-2h/+22h (n=6); HR=3.9; \( p=0.03 \)
+2h/+26h (n=6); HR=3.8; \( p=0.03 \)

Garcia-Lerma, G and Heneine W
CDC, Division of HIV/AIDS Prevention, Laboratory Branch
Effectiveness of Daily TDF/FTC in Clinical Trials

| Study | TDF/FTC | CI: 58-96 | Effectiveness of Daily TDF/FTC in Clinical Trials
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>PROUD</td>
<td>(TDF/FTC)</td>
<td>86%</td>
</tr>
<tr>
<td>iPrEx</td>
<td>(TDF/FTC)</td>
<td>49%</td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td>(TDF/FTC)</td>
<td>80%</td>
</tr>
<tr>
<td>TDF2</td>
<td>(TDF/FTC)</td>
<td>CI: -52-41</td>
</tr>
<tr>
<td>VOICE</td>
<td>(TDF/FTC)</td>
<td>CI: 15-63</td>
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Relationship Between Effectiveness and Adherence in Microbicide & PrEP Trials

Pearson correlation = 0.86, p=0.003

Percentage of Participants’ Samples with detectable drug levels

SS Abdool Karim, personal communication
Adherence and HIV Protection: Oral PrEP

<table>
<thead>
<tr>
<th>Program</th>
<th>% of blood samples with tenofovir detected</th>
<th>HIV protection efficacy in randomized comparison</th>
<th>HIV protection estimate with high adherence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partners PrEP</td>
<td>81%</td>
<td>75%</td>
<td>90% (tenofovir in blood)</td>
</tr>
<tr>
<td>TDF/FTC arm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDF2</td>
<td>79%</td>
<td>62%</td>
<td>78% (prescription refill)</td>
</tr>
<tr>
<td>BTS (PWID)</td>
<td>67%</td>
<td>49%</td>
<td>70% - 84% (tenofovir in blood / pill count)</td>
</tr>
<tr>
<td>iPrEx</td>
<td>51%</td>
<td>44%</td>
<td>92% (tenofovir in blood)</td>
</tr>
<tr>
<td>FEM-PrEP &amp; VOICE</td>
<td>&lt;30%</td>
<td>No HIV protection</td>
<td>N/A</td>
</tr>
</tbody>
</table>

When adherence was high, HIV protection is consistent and high.

Achieving Steady State in Rectal vs FGT.

Cottrell et al J Infect Dis. 2016 Jul 1;214(1):55
Slide courtesy: Angela Kashuba

Emtricitabine Tenofovir-DF Truvada

Achieving Steady State in Rectal vs FGT.

iPrEx OLE = ↓ HIV incidence by 90%
with 2 Truvada doses per week

Partners PrEP = ↓ HIV incidence by 90%
with 7 Truvada doses per week


TDF/FTC PrEP for Women: Adherence

Maximizing the Potential Effectiveness

TDF/FTC (7x/week)
CI: 96 - 99
99%

Some adherence forgiveness with retained protection

TDF/FTC (~1x/24°)
CI: -17 - 100
94%

6-7 doses per week likely required
Cottrell ML et al, JID, 2016.
**Summary**

- Prevention of HIV is an urgent priority - PREP is one tool
- Truvada is the only approved agent for HIV PREP
- Oral Truvada works as PrEP if taken daily
- Variability in Effectiveness in women may be due to factors like adherence, drug concentration in female genital tract

**CDC recommendation:**
When taken every day, Truvada as PrEP is safe and highly effective in preventing HIV infection.
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Questions?
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