Overview of ARV-based prevention trials

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Sex and Gender Differences in ARV-based Prevention Research, March 3, 2013, Atlanta
Overview of ARV-based prevention trials

- Place of ARV-based prevention in combination prevention
- Pre-exposure prophylaxis trials
- Early treatment for prevention:
  - HPTN 052
- Treatment as prevention: prevention benefits of scaling up treatment following national eligibility criteria
Combination Prevention: Basic Attributes

- Evidence-informed, human rights-based, and context-specific, tailored to local epidemics and needs
- Fully engages affected communities, promoting human rights and gender equality
- Operates synergistically on multiple levels—individual, family and society
- Invests in decentralized and community responses
  - Flexible—adapts to changing epidemic patterns and rapidly deploys innovations
  - Combines biomedical, behavioural and structural elements—to address immediate risks, underlying vulnerabilities, and pathways that link them
Antiretroviral Prevention Train
HIV prevention with ARVs (since 2010)

Topical pre-exposure prophylaxis (microbicides) for women
Abdool Karim Q, Science 2010

Oral pre-exposure prophylaxis
Grant R, NEJM 2010 (MSM)
Baeten J, NEJM 2012 (Couples)
Thigpen M, NEJM 2012 (Heterosexuals)

Treatment for prevention
Cohen M, NEJM 2011

HIV prevention (before 2010)

Male circumcision
Auvert B, PloS Med 2005
Gray R, Lancet 2007
Bailey R, Lancet 2007

Treatment of STIs
Grosskurth H, Lancet 2000

Female Condoms

Male Condoms

HIV Counselling & Testing
Coates T, Lancet 2000

Behavioural Intervention
- Abstinence
- Be Faithful

Note: PMTCT, Screening transfusions, Harm reduction, Universal precautions, Vaccines, etc. have not been included
Antiretroviral Drugs for Preventing Sexual HIV Transmission

Antiretroviral therapy for HIV+ persons

- **Reduces onward HIV transmission**
  - T4P: early *treatment for prevention* before CD4+ cells reach 350/uL
  - TasP: *treatment as prevention* i.e. population-level benefits of lower community viral load with ART scale-up following national eligibility criteria

Antiretroviral prophylaxis for HIV- persons

- **Reduces HIV acquisition**
  - **Pre-exposure prophylaxis** to prevent sexual transmission:  ♂ → ♀; ♂ → ♂; ♀ → ♂
Key requirements for effective PrEP

• Right drug (safe, effective, minimal resistance)
• Right place (sufficient concentrations at site of HIV exposure)
• Right time (short onset of activity and long half-life to optimize efficacy with variable adherence)
• Right population (at risk, motivated to use)
• Right timing (during periods of highest risk)
• Right delivery (cost-effective and efficient)
• Right decision-making (equity issues: prioritising key populations at highest risk of exposure – MSM, SW, PWID, young women while fully scaling up ART)
Pre-exposure prophylaxis strategies

- **Tenofovir (TDF)**
- **Tenofovir/emtricitabine TDF/FTC**

- **Partners PrEP**
- **Topical PrEP: 1% tenofovir gel**

- **Injectable PrEP: subcutaneous or intramuscular (Phase 1 trials)**

- **Intermittent PrEP trials**

- **iPrEx**
- **Partners PrEP**
- **TDF2**

- **CAPRISA 004**

- **ASPIRE and IPM trials**
<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>N</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CAPRISA 004</strong>&lt;br/&gt;<em>South Africa</em></td>
<td>Women</td>
<td>889</td>
<td>39% [CI = 6-60] efficacy coitally-dependent vaginal TFV gel</td>
</tr>
<tr>
<td><strong>iPrEx</strong>&lt;br/&gt;<em>Brazil, Ecuador, Peru, South Africa, Thailand, US</em></td>
<td>Gay men, other MSM, transgender women</td>
<td>2499</td>
<td>42% [CI = 18-60] efficacy daily oral FTC/TDF</td>
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<tr>
<td><strong>TDF2 Study</strong>&lt;br/&gt;<em>Botswana</em></td>
<td>Men and women</td>
<td>1200</td>
<td>62% [CI = 22-83] efficacy daily oral FTC/TDF</td>
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<tr>
<td><strong>Partners PrEP Study</strong>&lt;br/&gt;<em>Kenya, Uganda</em></td>
<td>Serodiscordant couples</td>
<td>4758</td>
<td>67% [CI = 44-81] efficacy daily oral TDF&lt;br/&gt;75% [CI = 55-87] efficacy daily oral FTC/TDF</td>
</tr>
<tr>
<td><strong>FEM-PrEP</strong>&lt;br/&gt;<em>Kenya, S Africa, Tanzania</em></td>
<td>Women</td>
<td>1950</td>
<td>Futility of daily oral FTC/TDF&lt;br/&gt;6% [CI = -52-41]</td>
</tr>
<tr>
<td><strong>VOICE</strong>&lt;br/&gt;<em>South Africa, Uganda, Zimbabwe</em></td>
<td>Women</td>
<td>5029</td>
<td>Futility of daily oral TDF&lt;br/&gt;Futility of daily vaginal TFV gel&lt;br/&gt;Daily oral FTC/TDF ongoing&lt;br/&gt;Results expected at CROI, March 2013</td>
</tr>
<tr>
<td><strong>Bangkok Tenofovir Study</strong>&lt;br/&gt;<em>Thailand</em></td>
<td>IDUs</td>
<td>2400</td>
<td>Daily oral TDF ongoing&lt;br/&gt;Results expected by June 2013</td>
</tr>
<tr>
<td><strong>FACTS 001</strong>&lt;br/&gt;<em>South Africa</em></td>
<td>Women</td>
<td>2900</td>
<td>Coitally-dependent vaginal TFV gel enrolling&lt;br/&gt;Results expected in 2015</td>
</tr>
<tr>
<td>Trial</td>
<td>Country</td>
<td>1% Tenofovir vaginal gel</td>
<td>Oral TDF (tenofovir) daily tablets</td>
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</tr>
<tr>
<td>CAPRISA 004</td>
<td>South Africa</td>
<td>✓</td>
<td>-</td>
</tr>
<tr>
<td>VOICE gel [daily]</td>
<td>Uganda, South Africa, Zimbabwe</td>
<td>X</td>
<td>-</td>
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<tr>
<td>FACTS 001</td>
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<td>?</td>
<td>-</td>
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<tr>
<td>Fem PrEP</td>
<td>Ken, SA, Tanz</td>
<td>-</td>
<td>-</td>
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<tr>
<td>VOICE oral</td>
<td>Uga, SA, Zim</td>
<td>-</td>
<td>X</td>
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<tr>
<td>Partners PrEP</td>
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<td>✓</td>
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<tr>
<td>TDF-2</td>
<td>Botswana</td>
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Research and Development Pipeline: 
*New Trials*

**MSM populations:**
- Intermittent PrEP ([IPERGAY, France](#)): TDF/FTC versus placebo [controversy post FDA announcement]
- ADAPT (HPTN 067): daily versus intermittent TDF/FTC [no point in testing unpopular regimens]
- NEXT-PREP (HPTN 069): TDF/FTC +/- maraviroc [CCR5 blocker not used much in treatment]
- PROUD: UK immediate vs deferred TDF/FTC

**Women:**
- Ring study (IPM) & ASPIRE (MTN) phase III dapivirine ring

**Safety and acceptability**
- Follow-up to Phase I trials of long-acting injectables: NNRTI rilpivirine (TMC 278) and integrase inhibitor S/GSK1265744
HPTN 052: HIV-1 Transmission
(Cohen et al NEJM 2011)

Total HIV-1 Transmission Events: 39

Linked Transmissions: 28

Unlinked or TBD Transmissions: 11

96% reduction

1763 stable, healthy, serodiscordant, sexually active couples in 9 countries [CD4 count: 350 to 550 cells/mm$^3$] randomised for the HIV+ partner to:

- start ART immediately or
- wait until CD4 250

Immediate Arm: 1

Delayed Arm: 27

p < 0.001
HIV-infected:
Individual, geo-located, HIV + adults identified through population-based HIV surveillance (2004-2011)

Patients on ART:
Individual, geo-located adult patients actively on ART in June (2004-2011)

ART coverage:
% all HIV-infected population receiving ART

At 30-40% ART coverage, HIV acquisition hazard reduced by 38% (1.4% for 1% ART increase)
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With thanks for ideas and slides to:

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Thank you for your attention!