Feasibility of Implementing Biomedical Prevention Program in Africa: The case study of Nigeria

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Outline

• The need Biomedical Prevention Technologies
• Reason for long wait for studies on use of ART to prevention HIV transmission in the general population
• Who needs Biomedical Prevention?
• Nigeria: the case for PrEP and TasP
• Conclusions
The need for Biomedical Prevention Technologies

- Decline in new infections much slower in adults compared to children.
- Decline in new infections in many SSA countries but recent increase in Mozambique and Tanzania and prediction that new cases may rise in Nigeria from rapid population growth.
- To keep pace with current spending, globally, $30 billion required by 2031. Where is that money going to come from?
Nigeria: situation Analysis

Nationwide prevalence stabilized around 4%, but 12 + 1 states carry higher burden

Nigeria is behind target in several important indicators:

- Only 1 out of 3 people in need treated (target 80% by 2015)
- Only 19.7% of HIV positive pregnant women receive prophylaxis against mother child transmission (target 90%)
- Only 0.3% States’ contribution to HIV spending

With 3.4 million people living with HIV, Nigeria carries the 2nd largest HIV burden globally

Nigeria: situation Analysis

- 58.0% of PLHIV population are women
- An estimated 388,864 became newly infected by HIV in 2011
- An estimated 217,148 people died from AIDS related causes in 2011
- External donor funds accounted for 75% of the expenditure in 2011
- Decreasing domestic and external funding for the national response: total funding for HIV treatment, care and support reduced by 28.5% in 2010 ($132,870,029) from $185,911,643 in 2008
What Will It Take to Substantially Reduce HIV Transmission in an Entire Population

Answer: Treatment AND Prevention

Why did we wait so long before researching whether ART can stop transmission in the gen population?

• Treatment – Prevention divide
• Early studies ended up in controversies
• Cost and availability of ARVs
• ARV side effects
• Fear of ARV resistance
Using Antiretroviral Medications for HIV-1 Prevention

PrEP

Prior to exposure

Advantages
- Demonstrated efficacy

Challenges
- Adherence
- Delivery
- Cost-effectiveness
- Resistance

PEP

Time of transmission

Advantages
- Shorter course than PrEP

Challenges
- Limited data
- Recognition of risk
- Initiation < 48 hrs
- Adherence
- Public health impact

ART

After infection

Advantages
- Clinical benefits and reduced infectiousness

Challenges
- Scale up; resources
- Long-term adherence
- Long term toxicity
- Resistance
Efficacy of HIV Prevention Strategies From Randomized Clinical Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect Size, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART for prevention; HPTN 052, Africa, Asia, Americas</td>
<td>96 (73-99)</td>
</tr>
<tr>
<td>PrEP for discordant couples; Partners PrEP, Uganda, Kenya</td>
<td>73 (49-85)</td>
</tr>
<tr>
<td>PrEP for heterosexual men and women; TDF2, Botswana</td>
<td>63 (21-84)</td>
</tr>
<tr>
<td>Medical male circumcision; Orange Farm, Rakai, Kisumu</td>
<td>54 (38-66)</td>
</tr>
<tr>
<td>PrEP for MSMs; iPrEX, Americas, Thailand, South Africa</td>
<td>44 (15-63)</td>
</tr>
<tr>
<td>Sexually transmitted diseases treatment; Mwanza, Tanzania</td>
<td>42 (21-58)</td>
</tr>
<tr>
<td>Microbicide; CAPRISA 004, South Africa</td>
<td>39 (6-60)</td>
</tr>
<tr>
<td>HIV vaccine; RV144, Thailand</td>
<td>31 (1-51)</td>
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</tbody>
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Benefit of PrEP in Heterosexual Men and Women in Botswana: TDF2 Study

- **Design:** Placebo-controlled, trial of daily TDF/FTC
- **Population**
  - 1,200 followed for seroconversion
  - 33% did not complete study
  - 45% women
  - 94% married
- **Results**
  - 33 seroconverters
    - 21 women (7 on TDF/FTC and 14 PLC)
    - 12 men (2 on TDF/FTC and 10 PLC)
- **Conclusions**
  - PrEP beneficial in this population
  - Protection in women in contrast with results of FEM-PrEP trial

iThgpen MC, et al. 6th IAS; Rome, Italy; July 17-20, 2011. Abst. WELBC01.

**Time to Event Analysis of Seroconverter Data**

- 9 HIV-infected in TDF-FTC group and 24 HIV-infected in placebo group
- Overall protective efficacy 62.6% (95% CI 21.5 to 83.4, P=0.0133)
Partners PrEP: Both PrEP Strategies Significantly Reduce HIV Acquisition

- No difference in efficacy of TDF vs TDF/FTC in reducing HIV acquisition ($P = .18$)
- Both PrEP strategies associated with significant reduction in HIV transmission vs placebo in both men and women
  - TDF efficacy: 68% in women, 55% in men
  - TDF/FTC efficacy: 62% in women, 83% in men

<table>
<thead>
<tr>
<th>Primary Efficacy Outcome, mITT* Analysis</th>
<th>TDF (n = 1584)</th>
<th>TDF/FTC (n = 1579)</th>
<th>Placebo (n = 1584)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV acquisitions, n</td>
<td>18</td>
<td>13</td>
<td>47</td>
</tr>
<tr>
<td>HIV incidence/100 PY</td>
<td>0.74</td>
<td>0.53</td>
<td>1.92</td>
</tr>
<tr>
<td><strong>Efficacy vs placebo, % (95% CI)</strong></td>
<td><strong>62 (34-78)</strong></td>
<td><strong>73 (49-85)</strong></td>
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</tr>
<tr>
<td>*P value</td>
<td>&lt; .0003</td>
<td>&lt; .0001</td>
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*mITT analysis includes HIV acquisitions not detected at enrollment.

**HPTN 052: Immediate vs Delayed ART in Serodiscordant Couples**

- Immediate ART
  - Initiate ART at CD4+ cell count 350-550 cells/mm$^3$
  - ($n = 886$ couples)

- Delayed ART
  - Initiate ART at CD4+ cell count ≤ 250 cells/mm$^3$*
  - ($n = 877$ couples)

*Based on 2 consecutive values ≤ 250 cells/mm$^3$.

- Primary efficacy endpoint: virologically linked HIV transmission
- Primary clinical endpoints: WHO stage 4 events, pulmonary TB, severe bacterial infection and/or death
- Couples received intensive counseling on risk reduction and use of condoms

HPTN 052: HIV Transmission Reduced by 96% in Serodiscordant Couples

Total HIV-1 Transmission Events: 39
(4 in immediate arm and 35 in delayed arm; \( P < .0001 \))

Linked Transmissions: 28

Delayed Arm: 27

Immediate Arm: 1

Unlinked or TBD Transmissions: 11

Single transmission in patient in immediate ART arm believed to have occurred close to time therapy began and prior to HIV-1 RNA suppression

Opportunities for PrEP in Nigeria

- Nigeria’s epidemic is generalized with high rates of transmission in geographical locations and among key populations.
- In addition, other analysis suggest a large variation in HIV prevalence among serodiscordant couples.
- Expansion of combination prevention programs in Nigeria offer a unique opportunity to introduce PrEP and/or T as P for needy populations (serodiscordant couples, sex workers, MSM, vulnerable populations).
The Nigeria PreP Agenda
The National PreP study

- The Modelling study
- The feasibility study
- The Demonstration project
Potential participants for the PrEP feasibility study

• Serodiscordant couples
• Most at Risk Populations
Challenges with serodiscordancy

- High risk of sero-conversion (1.2 per 100 person-years in even highly controlled clinical trials).
- Difficulty to use condoms for many couples.
- Extra spousal relationships occur with seroconversion from external spouse in about 20% of cases.
Importance of the study

- High prevalence of sero-discordancy
- Implications for PMTCT and ART

- PEPFAR/GF programming to promote PrEP and TasP prioritisation and assess

- National emphasis on HIV prevention
- National interest in combination prevention
RESULTS OF MODEL STUDY
Kate Mitchell, Fern Terris-Prestholt, Peter Vickerman (LSTHM)
More than 40% of impact due to **baseline scenario** – giving ART when CD4<350

Highest **impact** from **TasP + long-term PrEP + condom promotion**

Impact & cost-effectiveness: infections averted
(compared with current ART coverage levels)
Most cost-effective intervention: condom promotion (with ART at CD4<350)
As more resources become available, after giving ART to HIV positives with CD4<350, suggest:

- Condom promotion
- Additionally give short-term PrEP to HIV negatives
- Switch from short-term to long-term PrEP strategy
Conclusions

• These results suggest that the best first intervention strategy for discordant couples in Nigeria would be to ensure that all HIV positives are offered ART at current national guidelines.
Conclusions

• Additional reduction in new infections could be achieved by promoting condom use amongst discordant couples, offering PrEP to HIV negatives until their partner initiates ART or giving HIV positive partners TasP.
Conclusions

• Additional survival gains could be achieved through condom promotion for couples and TasP for HIV positive partners, which would both be incrementally highly cost-effective; addition of PrEP to the mix is not predicted to be cost-effective.
Thank You and Questions