The Botswana Combination Prevention Project (BCPP)

“The Next Phase of HIV Prevention in Botswana”

A collaboration between MoH CDC-Botswana, HSPH-BHP

Presenter: M.J. Makhema
NAC 4th September 2012
Interventions to Prevent Infection with HIV

A. Strategies based on individual’s action to reduce own risk:
   1. Education
   2. Behavior change
   3. Condoms
   4. Male circumcision
   5. Microbicides
   6. Post-exposure prophylaxis
   7. Pre-exposure prophylaxis
   8. Vaccines

B. Strategies based on action (ARV) to those already infected to reduce risk of new infections:
   1. Prevention of mother-to-child transmission
   2. Treatment of index case of discordant couples
   3. “Test and treat” to reduce community levels of HIV incidence
What’s Known……..

- MC reduces infection risk up to 60% (O. farm and Rakai)
- HTC influences behavior change positively (Tent/mobile/facility based/home-based)
- PMTCT can reduce infant infections to 1% (MmaBana)
- ABC strategy meant to reduce risk of infection (TEC: Failure Rates A=83%, B=33%, C=46%)
- HAART for treatment works (HPTN 052 = 96%)
- At the current rate of 2 new infections for every person put on ART it is not sustainable.

**WE MUST COME UP WITH EFFECTIVE, AFFORDABLE & SUSTAINABLE PREVENTION STRATEGY**
Clinical Trial Evidence of Efficacy for Prevention of Sexual transmission of HIV

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect size (CI)</th>
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<tbody>
<tr>
<td>ART in discordant couples (HPTN 052)</td>
<td>96% (73; 99)</td>
</tr>
<tr>
<td>PrEP in discordant heterosexual couples (Partners PrEP)</td>
<td>73% (49; 85)</td>
</tr>
<tr>
<td>PrEP for women (Botswana)</td>
<td>63% (21; 48)</td>
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<tr>
<td>Medical male circumcision (Orange Farm, Rakai, Kisumu)</td>
<td>54% (38; 66)</td>
</tr>
<tr>
<td>PrEP for MSMs (America's, Thailand, South Africa)</td>
<td>44% (15; 63)</td>
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<tr>
<td>Microbicide for women (CAPRISA 004 tenofovir gel)</td>
<td>39% (6; 60)</td>
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<tr>
<td>HIV Vaccine (Thai RV144)</td>
<td>31% (1; 51)</td>
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</table>
Extended high viremics: a substantial fraction of individuals maintain high plasma viral RNA levels after acute HIV-1 subtype C infection

Vladimir Novitsky\textsuperscript{a,b}, Thumbi Ndung’u\textsuperscript{c,d}, Rui Wang\textsuperscript{a}, Hermann Bussmann\textsuperscript{a,b}, Fundisiwe Chonco\textsuperscript{c}, Joseph Makhema\textsuperscript{a,b}, Victor De Gruttola\textsuperscript{a}, Bruce D. Walker\textsuperscript{d,e,f} and M. Essex\textsuperscript{ab}

\textit{AIDS} 2011, 25:1515–1522
HIV-1 RNA load in primary HIV-1C (pre-ART)

HIGH VIREMICS
Test and Treat for Prevention of HIV Transmission: Approaches

1) Identify and treat all HIV-positive individuals regardless of status of health or viremia.

2) Identify and treat all individuals who qualify based on AIDS-defining illness and CD4 reduction (test-linked care).

3) *Identify and treat all individuals who qualify based on high viral load (HVL) + those who fit criteria in (2).

*Strategy chosen for Mochudi Prevention Project.
**PEPFAR-Sponsored Combination Prevention Village-Randomized Trials in Africa**

<table>
<thead>
<tr>
<th>Study</th>
<th>LSTMH/PopART NIH – HPTN</th>
<th>HSPH/BHP CDC</th>
<th>JHU USAID</th>
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</thead>
<tbody>
<tr>
<td>Sites</td>
<td>Zambia/S Africa</td>
<td>Botswana</td>
<td>Tanzania</td>
</tr>
<tr>
<td>Trial Arms</td>
<td>1. SOC</td>
<td>1. SOC</td>
<td>1. SOC</td>
</tr>
<tr>
<td></td>
<td>2. Test and ARV for all positives, plus combination prevention package*</td>
<td>2. Test and ARV for all viral load above 10,000, plus combination prevention package*</td>
<td>2. Test-linked ARV for all CD4 &lt;350, plus combination prevention package*</td>
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<tr>
<td></td>
<td>3. Test-linked ARV for all CD4 &lt;350, plus combination prevention package*</td>
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<tr>
<td>Efficacy evaluation</td>
<td>24 villages (60,000)</td>
<td>30 villages (20,000)</td>
<td>24 clusters (12,000)</td>
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</table>

*Combined prevention package: highest possible HTC, MC, treatment for CD4 <350, PMTCT.
Hypothesis

Implementation of a combination of prevention interventions for HIV/AIDS – including treatment – at greater scale, quality, and intensity can greatly reduce incidence of HIV infection (i.e., by 50%?).

Prevention interventions include:

1. Enhanced HIV testing/counseling (HTC ↑80%)
2. Enhanced rates of male circumcision (MC ↑80%)
3. Refined PMTCT
4. Improved linkage to care/treatment 
   and
5. New intervention to treat with ARV those with high viral load (i.e., >10,000) even when they do not qualify for ARV based on CD4 ≤50.
Study Objectives

• **Primary Objectives**

  • To determine whether implementation of a combination of prevention interventions can significantly reduce population-level, cumulative HIV incidence in 16-64 year old residents in Botswana. The combination prevention package consists of enhanced and accelerated scale-up of HTC, active linkage to HIV care and treatment according to local eligibility criteria, expanded ART among HIV-infected residents with high viral load (≥10,000 copies/mL), enhanced support for retention in care and ART adherence, and enhanced active linkage to expanded MC and PMTCT services.

  • To estimate population-level coverage of enhanced treatment and prevention services among eligible residents at baseline, and yearly thereafter, in intervention communities compared with standard-of-care communities.

  • To estimate the cost of the intervention per HIV infection averted in intervention communities compared with standard-of-care communities.
What is new about study beyond “scale-up” of current interventions according to government guidelines?

1. Targeting transmission with combination of new ARV criteria, CD4 >350 with high VL and rapid ARV for those who qualify based on CD4 ≤350.
   - Both should reduce number of transmitters and “transmission time.”

2. Evaluation of combination of available prevention interventions.
   - Complementarity? Synergism?

3. Cost effectiveness analysis for combination (and modeling of components) to determine:
   - Cost per infection averted.
RANDOMIZED COMMUNITIES:

**Standard of care (Arm A)**
- Standard ART (CD4≤350)
- Standard prevention services
- 20% of households

**Intervention (Arm B)**
- HIV testing
- Linkage to care & ART (CD4≤350)
- Expanded ART (CD4>350 & VL≥10K)
- Male circumcision
- PMTCT uptake
- 20% of households

Longitudinal Cohorts
- Initially HIV-neg
- ART-naive HIV-pos

**HIV Incidence Cohort**
**Closed Clinical Cohort**

Cost-effectiveness

Coverage & Safety Estimates:
- HIV Testing, Linkage to care and ART/pre-ART,
  Retention in care, Adherence support,
  PMTCT and MC

High Viral-Load Treatment Cohort (Arm B)
50 COMMUNITIES UNDER CONSIDERATION / 15 MATCHED PAIRS
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Brief Description</th>
<th>Target Coverage</th>
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</table>
| Enhanced HIV testing and counseling (HTC) | a) Mobile/Community HTC units  
b) Household-based HTC  
c) Facility-based HTC | Test ≥90% each year (who are either not documented to be HIV-infected or who have a negative HIV test in the past 1 year)  
a) >90% of newly diagnosed residents register at an HIV treatment clinic within 30 days after a positive HIV test |
| Active linkage to HIV care and antiretroviral treatment | a) Point-of-care CD4 testing  
b) Brief case management/active linkage by community health workers/expert clients (CHW)  
c) Transportation or cell phone compensation to facilitate linkage to HIV care clinic (20-30 pula) | >90% 12-month retention for the first ART year  
>95% annual retention from the second ART year onwards |
<p>| Enhanced support for retention in care | Active follow-up by CHW if missed visit |  |
| Expanded antiretroviral treatment for high viral load | Antiretroviral treatment for HIV-infected residents 16-64 years with viral load ≥10,000 cp/mL (in addition to ART for patients eligible by National Program criteria with CD4 ≤ 350 cells/mm³ or clinical criteria) | &gt;80% of those identified as eligible start ART |</p>
<table>
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<tr>
<th><strong>Enhanced ART adherence support</strong></th>
<th>At least monthly SMS text messages</th>
<th>≥90% with good adherence by self-report and timely pharmacy (ARV) refill</th>
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</table>
| **Enhanced linkage to expanded safe male circumcision services** | a) Targeted demand creation in communities  
  b) Active linkage/follow-up by CHW  
  c) Free transport to MC venue (where appropriate) | - |
| **PMTCT** | a) Support HCT at ANCs early in pregnancy  
  b) Support repeat HIV testing after 32 weeks gestation among women testing HIV-negative earlier in pregnancy  
  c) Actively link pregnant women to rapid ART initiation (as above)  
  c) POC CD4 | a) Test ≥97% women for HIV during pregnancy (unless known to be HIV-infected)  
  b) Retest ≥90% of HIV-negative pregnant women from 32 wks-delivery  
  c) Start ≥90% of HIV-infected women on ART by week 28 and ≥95% by delivery. |
Clustered PHIs

Non-B Subtypes
Cost Effectiveness
Cost of ART over Time Including Extra 25% Treated for Prevention

National ART Program scenario
stable 1% incidence

Mochudi Project scenario
incidence reduction 0.3% per year

Initial difference in costs between two scenarios
Initial extra costs

Crossover time

Time
“A key challenge to optimizing biomedical interventions is addressing the social realities and socio economic co-morbidities of people and communities at risk and living with HIV”
“Optimizing the impact of biomedical interventions requires us to complement them with behavioural interventions”
Behavioural & Social Science Endpoints to Optimize HIV Biomedical Interventions

- Reduce HIV stigma
- Reduce risk compensation
- Enhance access to & retention in care
- Enhance BMI treatment awareness
- Enhance BMI treatment adherence
- Enhance HIV counselling, testing & referral (CTR)
- Enhance program sustainability
- Enhance acceptability and initial adoption
BCPP Systems Overview

MoH
M & E Data Warehouse
API access

BCPP ANALYSIS
Receive De-identified datasets per agreed monitoring schedule

BCPP DMC
Send transactions for Community RDS
- Created or updated Patient Records
- Patient Transfer Confirmation
- Response to data queries

RDS (MASTER)
Intermittent connectivity between community and RDS Master

Lab
Send transactions for Community RDS
- Created or updated Patient Transfer Records (minimal)
- Full patient record if requested
- Data queries from BCPP QA Team

DISALAB and/or PMS

RDS (Community)

Query RDS with details of new patient and/or for fully updated record when available

PIMS
BHP Survey EDC
HTC and Survey
Manual and Other...

Community

- API: Application Programmer’s interface
- EDC: Electronic Data Collection, database application for the household survey (Patient Demographics, HTC, PCC Labs, Samples, Behavioral).
- PIMS: Patient Information Management System, MoH system that captures data on clinic-based services (Patient Demographics, Lab Results, ART, PMTCT, SMC, HTC).
- RDS: Reference Data System, database application that updates its master and is a reference data system of patient records from all 30 communities. For known patients, the record may be complete or just that found on the patient transfer.

- Each source system in the community updates the RDS with new information by interacting with the RDS’s API.
- Community RDS updates the Master RDS with all data inserts, updates and deletes generated locally.
- Based on programmed data reporting requirements, RDS updates local source systems, via their APIs, with information it received from the other local source systems and from remote source systems via the Master RDS.
## Timeline

<table>
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<tr>
<th>Baseline incidence</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
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<tbody>
<tr>
<td><strong>Month</strong></td>
<td>0</td>
<td>18</td>
<td>30</td>
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<tr>
<td>Control</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
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<tr>
<td>Monitoring and Evaluation</td>
<td></td>
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<tr>
<td>INTERV</td>
<td>20%</td>
<td>20%</td>
<td>20%</td>
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<tr>
<td>enhanced HTC</td>
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<td>ART for HVLC</td>
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<tr>
<td>Male circumcision</td>
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<tr>
<td>Enhanced PMTCT</td>
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<td>Linkage to care</td>
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<tr>
<td>Monitoring and Evaluation</td>
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**Randomization**
Conclusions

1. Opportunity to Evaluate Optimized Combination Strategies

   **Hypothesis:** Combination strategies shall reduce HIV-1C incidence

2. About 25–30% of new HIV-1C infections in Botswana and South Africa maintain high VL (50,000–100,000) for 200–400 days as HVL carriers.

   **Hypothesis:** “Treatment for Prevention” of HVLs can lower incidence as cost-effective intervention.

3. Viral genome linkage analysis of prevalent and incident infections can increase sensitivity of efficacy measurements for prevention interventions such as “test and treat.”

   **Hypothesis:** Correlates of viral linkage at community level can validate efficacy for reduction of incidence targeting HVL carriers.
What’s Next after BCPP......

OUR VISSION: HIV/AIDS FREE GENERATION BY 2016