

BOTSWANA COMBINATION PREVENTION PROJECT

(Tripartite Project: BHP, CDC & MoH)

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HYPOTHESIS

- Implementing multiple HIV treatment and prevention interventions with known efficacy at an enhanced scale, quality, and intensity compared with standard of care will impact the HIV/AIDS epidemic by **reducing the incidence** of HIV infection in a defined geographic area within 4 years and will be **cost-effective**.

Interventions to Prevent Infection with HIV

- A. Strategies to prevent exposure/infection based on action by targeted individuals at risk:

<u>Intervention</u>	<u>Efficacy</u>
1. Education/Behavior change	Variable
2. Condoms	Variable
3. Male circumcision	50–60%
4. Microbicides	Modest?
5. Pre-exposure prophylaxis(PrEP)	Moderate?
6. Vaccines	None yet

Interventions to Prevent Infection with HIV

- B.** Strategies to prevent exposure/infection based on actions targeted at potential transmitters to reduce virus release:

<u>Intervention</u>	<u>Efficacy</u>
1. PMTCT	Very high (>95%)
2. Index case of discordant couples	Very high (>95%)
3. “Test and treat” at community level	?

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 Botswana Combination Prevention Project.

PEPFAR-Sponsored Combination Prevention Village-Randomized Trials in Africa

Study	LSTMH/PopART Hayes/Ayles NIH – HPTN	HSPH/BHP Essex/DeGruttola CDC	JHU Celentano/Kerrigan USAID
Sites	Zambia/S Africa	Botswana	Tanzania
Trial Arms	<ol style="list-style-type: none"> SOC Test and ARV for all positives, plus combination prevention package* Test-linked ARV for all CD4 <350, plus combination prevention package* 	<ol style="list-style-type: none"> SOC Test and ARV for all viral load above 10,000, plus combination prevention package* 	<ol style="list-style-type: none"> SOC Test-linked ARV for all CD4 <350, plus combination prevention package*
Efficacy evaluation	24 villages (60,000)	30 villages (20,000)	24 clusters (12,000)

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

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 ($\geq 10,000$ 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.

Study Design

- Pair-matched cluster randomized trial

self-contained communities, N=30
Average 5800 inhabitants

15 pairs, each randomized

Control:
Standard of Care

Intervention:
Combination Prevention Package

- Methodology

- Primary objectives

- Longitudinal incidence cohort
 - Regular cross-sectional surveys to measure coverage

Intervention	Brief Description	Target Coverage
Enhanced HIV testing and counseling (HTC)	a) Mobile/Community HTC units b) Household-based HTC c) Facility-based HTC	Test $\geq 90\%$ each year (who are either not documented to be HIV-infected or who have a negative HIV test in the past 1 year)
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)	a) $>90\%$ of newly diagnosed residents register at an HIV treatment clinic within 30 days after a positive HIV test
Enhanced support for retention in care	Active follow-up by CHW if missed visit	$>90\%$ 12-month retention for the first ART year $>95\%$ annual retention from the second ART year onwards
Expanded antiretroviral treatment for high viral load	Antiretroviral treatment for HIV-infected residents 16-64 years with viral load $\geq 10,000$ cp/mL (in addition to ART for patients eligible by National Program criteria with $CD4 \leq 350$ cells/mm ³ or clinical criteria)	$\geq 80\%$ of those identified as eligible start ART

Enhanced ART adherence support	At least monthly SMS text messages	$\geq 90\%$ with good adherence by self-report and timely pharmacy (ARV) refill
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)	Circumcise $\geq 80\%$ of 16-49-year-old (and $\geq 60\%$ of 16-64-year old) males who are known to be HIV-uninfected, by the end of the second study year
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 $\geq 97\%$ women for HIV during pregnancy (unless known to be HIV-infected) b) Retest $\geq 90\%$ of HIV-negative pregnant women from 32 wks-delivery c) Start $\geq 90\%$ of HIV-infected women on ART by week 28 and $\geq 95\%$ by delivery.

Incidence cohorts

- To estimate HIV incidence over the study period, we will enroll and prospectively follow a random sample of all consenting HIV-negative adult members (16-64 years) of a random sample of 20% of households from all communities (Arms A and B). The incidence cohort participants will be followed through the entire study period with annual HIV testing and assessment of intervention uptake in a longitudinal cohort.
- End of Project Survey: At the end of study period as many adults as possible ($\geq 80\%$) in all communities will be surveyed to assess HIV prevalence, viral genetic linkage, and history of intervention uptake.

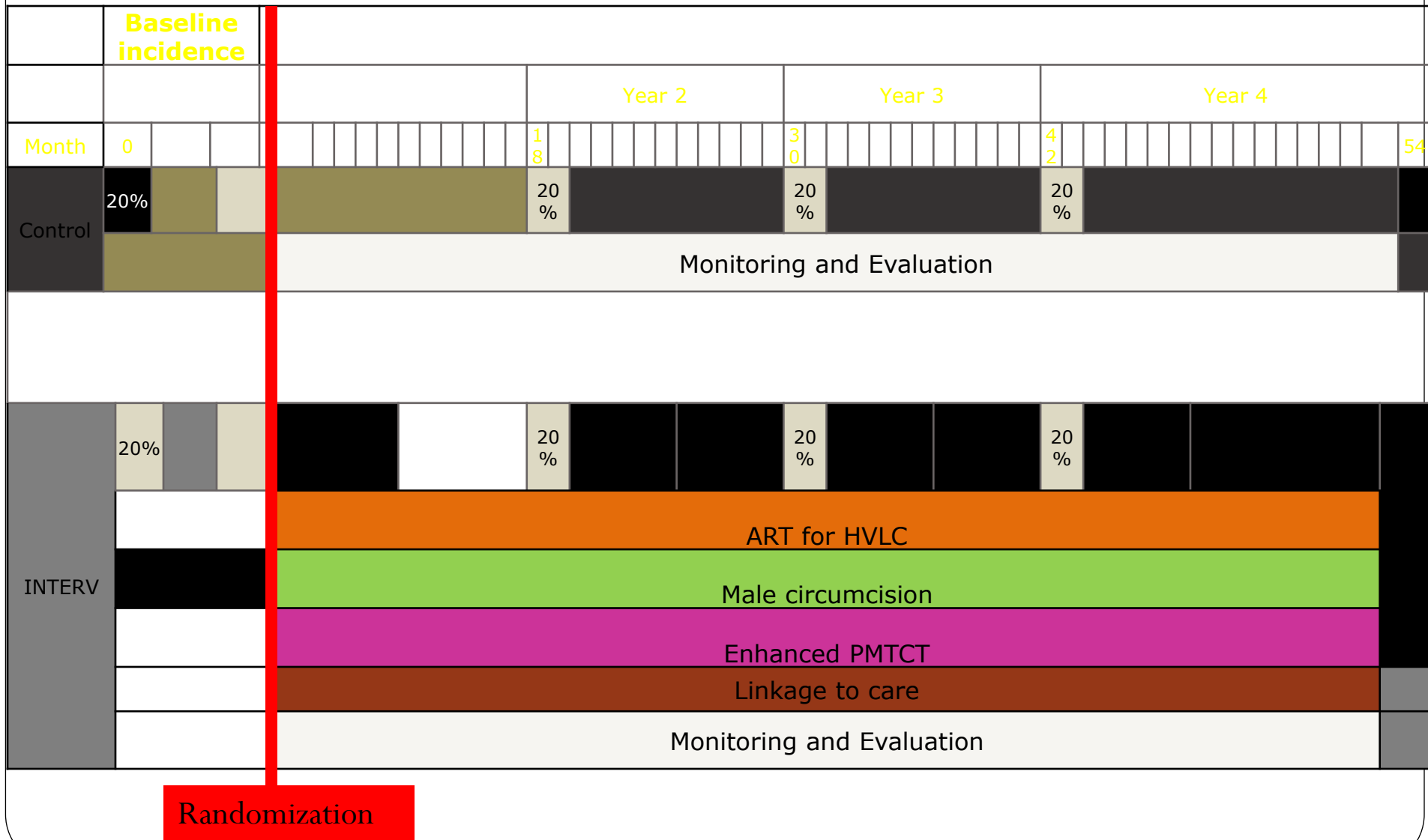
Clinical cohorts

- all consenting HIV-infected adults (16-64 years) identified in the 20% of households randomly selected for HIV incidence cohort who are not yet on treatment;
- These participants will be followed longitudinally for clinical and treatment outcomes over the course of the entire study period.

Service coverage data

- Implementation and outcomes of HTC, linkage to care, MC, PMTCT and ART will also be ascertained using active abstraction, extraction, and integration (at the individual patient level) of data from implementing partners and programs, throughout the course of the study.

Timeline



Value Adding Partnership



OUR VISSION: **HIV / AIDS FREE GENERATION BY 2016**