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A Day of Promise, A Day of Reckoning

Making ARV-based prevention work for women

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STRIVE
Tackling the structural drivers of HIV

Recent Trials

Trial	Product	Population	Dosing	Effectiveness	Notes
Caprisa 004	Vaginal TDF gel	Heterosexual women in SA	Before & after sex	39% reduction (95% CI: 6-60%)	
iPrEx	Oral TDF/FTC pill	MSM	Daily	42% reduction (95% CI: 15 - 63)	70% among most adherent
Partners Prep	Oral TDF pill Oral TDF/FTC pill	Discordant couples	Daily	62% for TDF 73% for Truvada	More than 97% of dispensed doses taken
Treatment as Prevention (HPTN – 052)	HAART initiated at CD4 >350 <550 cells per µL	Discordant couples	Daily	96% (95% CI: 73-99)	28% of cases from non-index partner
Botswana TDF2 study	Oral TDF pill	Heterosexuals	Daily	63% (95% CI: 21-84)	Re-framed as safety study due to lack of endpoints
Fem-PREP	Oral TDF/FTC	High risk women	Daily	Trial stopped for futility	***CAUTION !***

In your packets…..

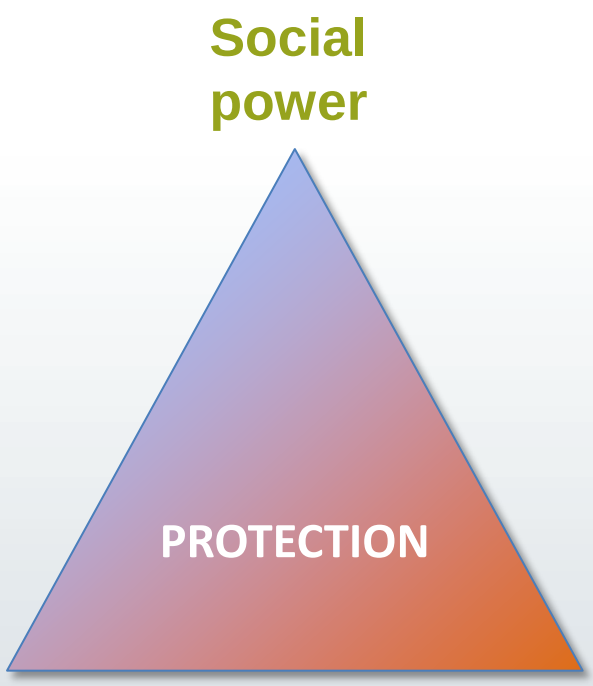
COMPARING ARV-BASED PREVENTION METHODS					
	Already in widespread use		Proof of concept established; Moving toward introduction and wider use		
	Vertical Prevention; Prevention of Mother-to-Child Transmission (pMTCT)	Post Exposure Prophylaxis (PEP)	ART Treatment as Prevention	Pre-Exposure Prophylaxis (PrEP)	Microbicides
Typical blood levels	Short-term equivalence with treatment levels	Equivalent with treatment levels	Depends on drug and dosing schedule	Equivalent with treatment levels	Each drug unique. PK studies of tenofovir gel shows levels in blood equivalent to 1/100th that seen with oral dosing
Present in genital tissue	Yes, with steady state levels of some drugs (AZT and 3TC) greater than that seen in blood	Yes, level depends on drug	Depends on drug and dosing schedule	Yes, level depends on drug	Yes. Genital tissue level generally higher with microbicides than with PrEP
Potential for Resistance	Resistance frequent with single dose nevirapine, but it has little impact on future treatment effectiveness if initiated at least 6 months after nevirapine use	Depends on PEP regimen and adherence and on whether source patient is treatment-experienced and has resistant virus.	Yes, level depends on drug (e.g., NNRTIs tend to have levels equivalent to that seen in blood, PIs vary from undetectable to equivalence)	Drug resistence will develop if individuals begin or stay on PrEP when already HIV+, hence the importance or routine testing	Unknown. Current and planned research examining potential.
Access issues	Only 33% of HIV positive pregnant women in low and middle income countries receive PMTCT services.	Available by prescription. Subsidized access depends on individual government policy.	Will develop in the setting of inadequate suppression of viral load	Where registered, it will be available immediately by prescription to those who can afford it. Subsidized programs will likely restrict access to highest risk groups TDF and (TDF + FTC) available as treatment in many countries, not yet registered in others. Generic costs $75 - $128 per person year in low income countries;higher in middle income countries; 5% royalty paid to Gilead;	No access until approved by regulators, country by country Will likely require prescription, at least until resistance questions are fully answered Cost reductions depend on moving away from platic prefille applicator to user-filled, cardboard applicator

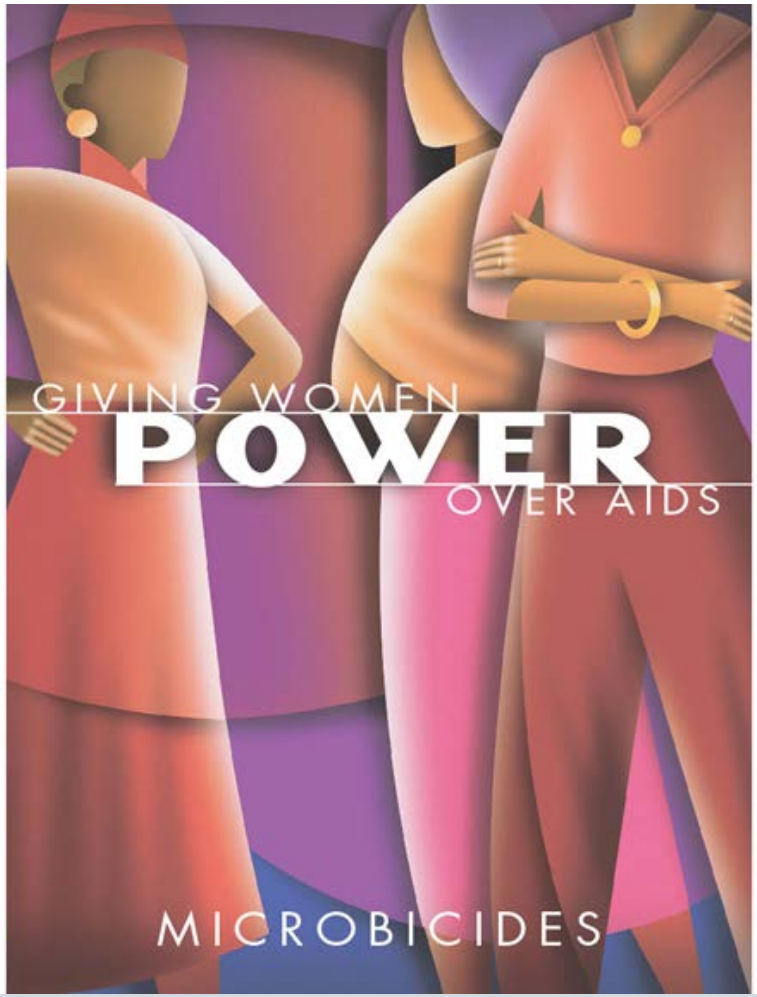
ARV-based prevention methods vary by:

- Which user groups and routes of exposure (e.g. IV drug use, rectal sex, vaginal sex) the method has been shown to work for…
- Level of systemic exposure and hence long term risk
- Potential for encouraging resistance
- Level of routine HIV testing likely to be required
- Dosing (daily; only when having sex, etc)
- Cost (lifetime vs. intermittent use; triple vs. single drug regimens; applicator costs)
- Political, ethical, and gender implications

Reclaiming the vision…

Girls' and women's protection strategies





Making ARV-based prevention work for women

1. Learn from the past . Don't underestimate the challenges of implementation
2. Demand that piloting and roll out of new prevention strategies investigate and address the economic, social, relationship, and rights-based barriers that women face in accessing and using such methods
3. Ensure that future implementation research includes a strong qualitative component that listens to women
4. Fight for continued investment into topical gels and other vaginally delivered prevention tools

1. Learn from the Past….

- Preventive behaviors are harder to adopt and sustain than those linked to symptoms
- Referral alone seldom increases access to care unless supplemented by accompaniment, counseling and subsidies for transport
- People have an abiding need to belong – hence the power of stigma and social norms to hamper protective behavior
- Men often hold the “purchasing power on prevention.” Hence, ARV-based prevention programs will need to address gender and power issues in relationships

Treatment as Prevention (TasP)

- Large and growing momentum for Treatment to be the central pillar of prevention programming
  - "Treatment *is* prevention. Let's go with it and you'll see how we can control HIV within this decade!" (Julio Montaner)
- The LANCET, May 21, 2011:
  - "Agencies such as PEPFAR and the Global Fund to Fight AIDS, Tuberculosis and Malaria need to reassess their prevention portfolios and consider *diverting funds* from prevention programmes with poor evidence (such as behavioural change communication) to treatment for prevention."

Can TasP deliver without rethinking our strategies…

- HIV testing is low: From 2005 to 2009 in sub-Saharan Africa a median of 17% of women and 14% of men had ever been tested for HIV infection and knew their results (Measure DHS)
- Early treatment will not prevent the roughly 40% of infections that appear to occur during acute infection (Cohen, et al NEJM; 364: 1943-54).
- Nor will it prevent the 27-33% of infections in discordant couples in East and Southern Africa who become infected from "outside partners." (Celum et al, NEJM; 362(5), 2010; Dunkel et al, 2010)

Protecting ourselves from uncomfortable truths…

- Not everyone wants to initiate treatment, even those who qualify medically
- Up to one-third of individuals eligible for ART in parts of Kenya and South Africa, actively resist starting treatment despite free access to drugs, regular CD4 testing, referrals to local treatment programmes, and counselling on the importance of ART (Guthrie, BL. *JAIDS*, 2011; Katz, It, et al. *AIDS, 2011)*

> *"They are giving you something that could possibly save your life, so, on one hand why not take it and live with the side effects. On the other hand,...it's a reminder every day that you've got something…and maybe you don't necessarily want to do that."*

Vertical transmission (PMTCT) as an object lesson

- The proportion of pregnant women in low- and middle-income countries who received an HIV test was only 26% in 2010, up from 7% in 2005 (UNAIDS).
- According to a 4 country study in Africa, even where PMTCT services were available, less than 50% of women who delivered had antiretroviral drugs present in their cord blood. (Coetzee, et al. 2010; PEARL study)
- Overall in high burden countries, only 15-30% of mother-infant pairs complete the entire PMTCT "cascade." (Paintsil & Anderman, *Curr Opin Pediatr*, 21:2009)
- Community and health worker stigma is a major factor in this attrition

The STRIVE Consortium

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A final plea…

Keep the development of topical gels and other vaginal products on the agenda, including non ARV-based products!

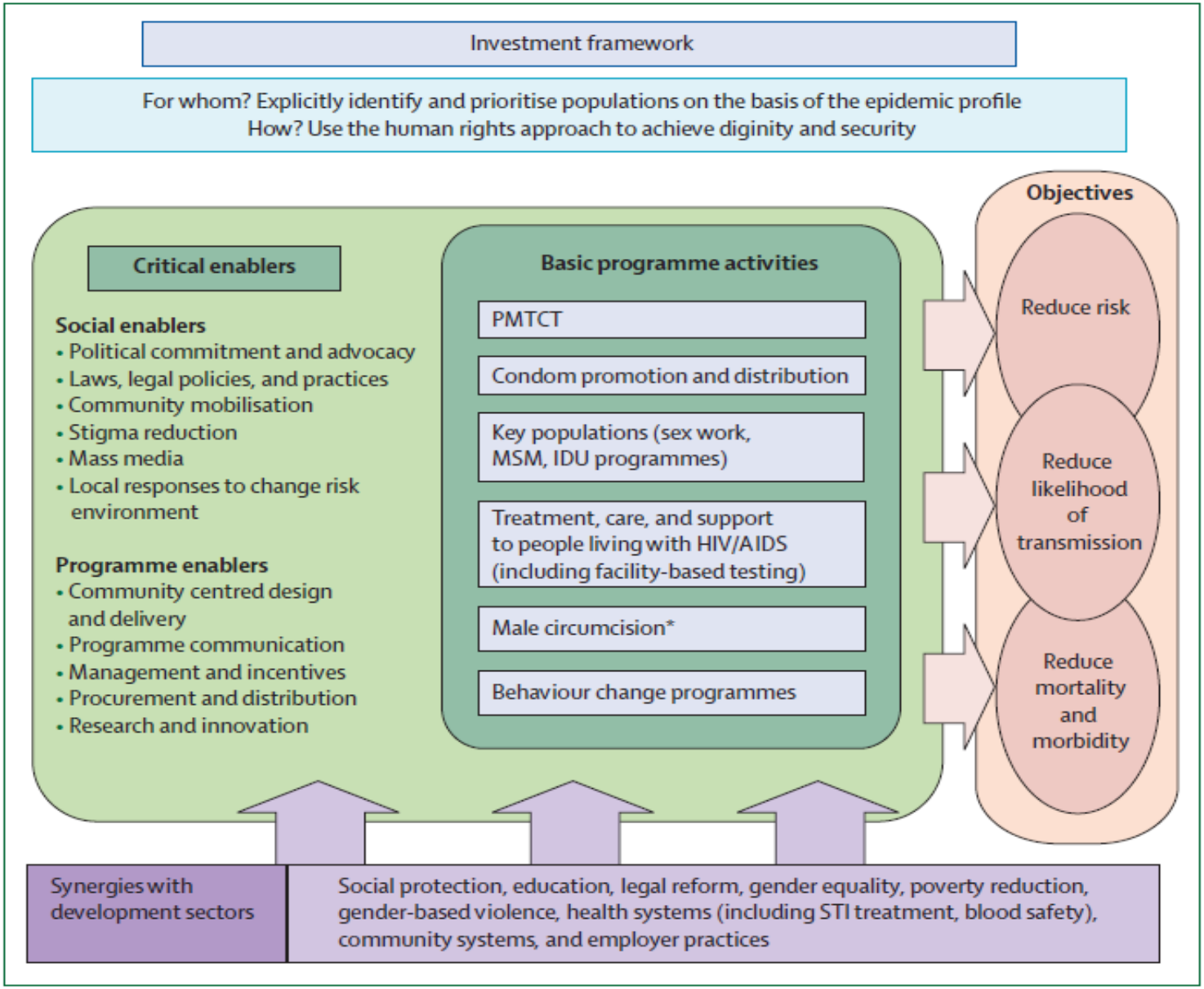

Figure 1: **Proposed framework for the new investment approach**

STRIVE Conceptual Framework