

HIV prevention: Where is the evidence of interventions that work?



Presenter:

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Acknowledgements

- Most of this presentation is based on a presentation by Prof Geoffrey Setswe of the HSRC which he made to the HSRC Seminar Series on 23 November 2009
- A few additional slides are also based on Prof Geoffrey Setswe's presentation to the SBI Workshop which was in Durban on 31 March 2009 entitled *Is there evidence that social, behavioural and structural interventions work in reducing HIV/AIDS?*

In this presentation

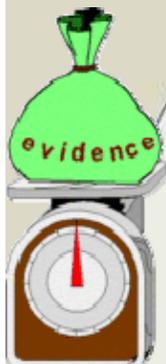
1. Introduction
2. What is evidence and levels of evidence in HIV prevention?
3. HIV prevention interventions
 - 3.1. Biomedical HIV prevention interventions
 - 3.2. Behavioural HIV prevention interventions
 - 3.3. Structural HIV prevention interventions
4. Summary of HIV prevention interventions that work
5. Conclusion

1. Introduction

- **Remarkable advances** in the molecular biology of HIV and major therapeutic discoveries in the past 28 years of the epidemic.
- Many interventions have been developed and implemented – some were tested for evidence of efficacy or effectiveness and some were not.
- In 2009, **we are not sure which interventions work!** We need to identify and use **best and good evidence** HIV prevention interventions that work.
- Policymakers, implementers, researchers, funders and the community - **all need evidence that an HIV prevention intervention works...**
- We present **evidence of HIV prevention interventions that work** and also present their **level of effectiveness or efficacy**.

2. What is evidence?

- Evidence refers to "*facts* or testimony in support of a conclusion, statement or belief" and "something serving as *proof*".
- Proof that something works.
- The Law uses witnesses and other forms of evidence to prove guilt beyond reasonable doubt.
- Epidemiology uses p-value to show level of significance e.g. $p \leq 0.05$ says we are 95% confident that the observed difference is not due to chance.



Social science that makes a difference

The Evidence Pyramid



Source: <http://library.downstate.edu/EBM2/2100.htm>

Social science that makes a difference

Proposed levels of evidence

Level of evidence	% Effectiveness or efficacy (in RCT)
	80% +
	60-79%
	30-59%
	0-29%

3.1. Biomedical HIV prevention interventions

3.1.1. Male circumcision (MC)

3.1.2. Highly Active Antiretroviral Therapy (HAART)

3.1.3. Prevention of mother to child transmission (PMTCT)

3.1.4. Condoms (Male and Female)

3.1.5. Treatment of Sexually Transmitted Infections (STI)

3.1.6. Microbicides and cervical barriers

3.1.7. HIV vaccine

Social science that makes a difference

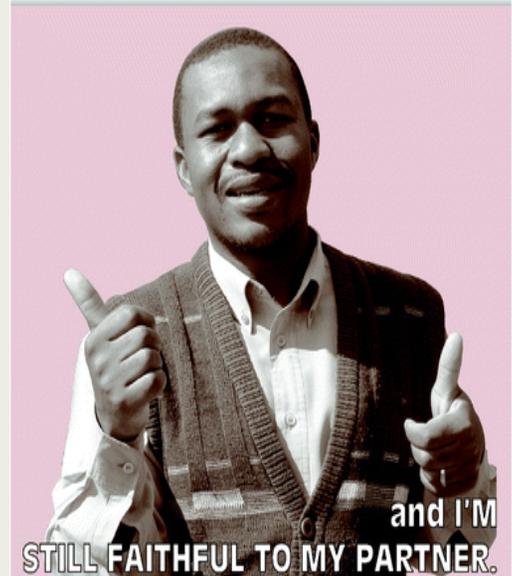
3.1.1. Male Circumcision (MC)

Good evidence

- RCTs on MC in South Africa, Uganda, and Kenya^[1] :
“There is compelling evidence that MC is 65% effective in reducing the risk of acquiring HIV in circumcised men...”
- A **Cochrane review** assessed data from trials in SA, Uganda, and Kenya between 2002 and 2006 that enrolled 11,054 males said that research on the effectiveness of MC for preventing HIV in heterosexual men is conclusive.

Reviewers concluded that **no further trials are required to establish that HIV infection rates are reduced in heterosexual men for at least the first two years after circumcision**^[2]

I'm Circumcised,
proud of it...



[1] Gray, H. et al. (2007). MC for HIV prevention in young men in Rakai: A RCT. *Lancet* 369:657-66.

[2] Siegfried N, Muller M, Volmink J, Deeks JJ,. MC for prevention of heterosexual acquisition of HIV in men *Cochrane Database of Systematic Reviews*, Issue 4, 7 October 2009

3.1.2. Highly Active Antiretroviral Therapy (HAART)



Good evidence

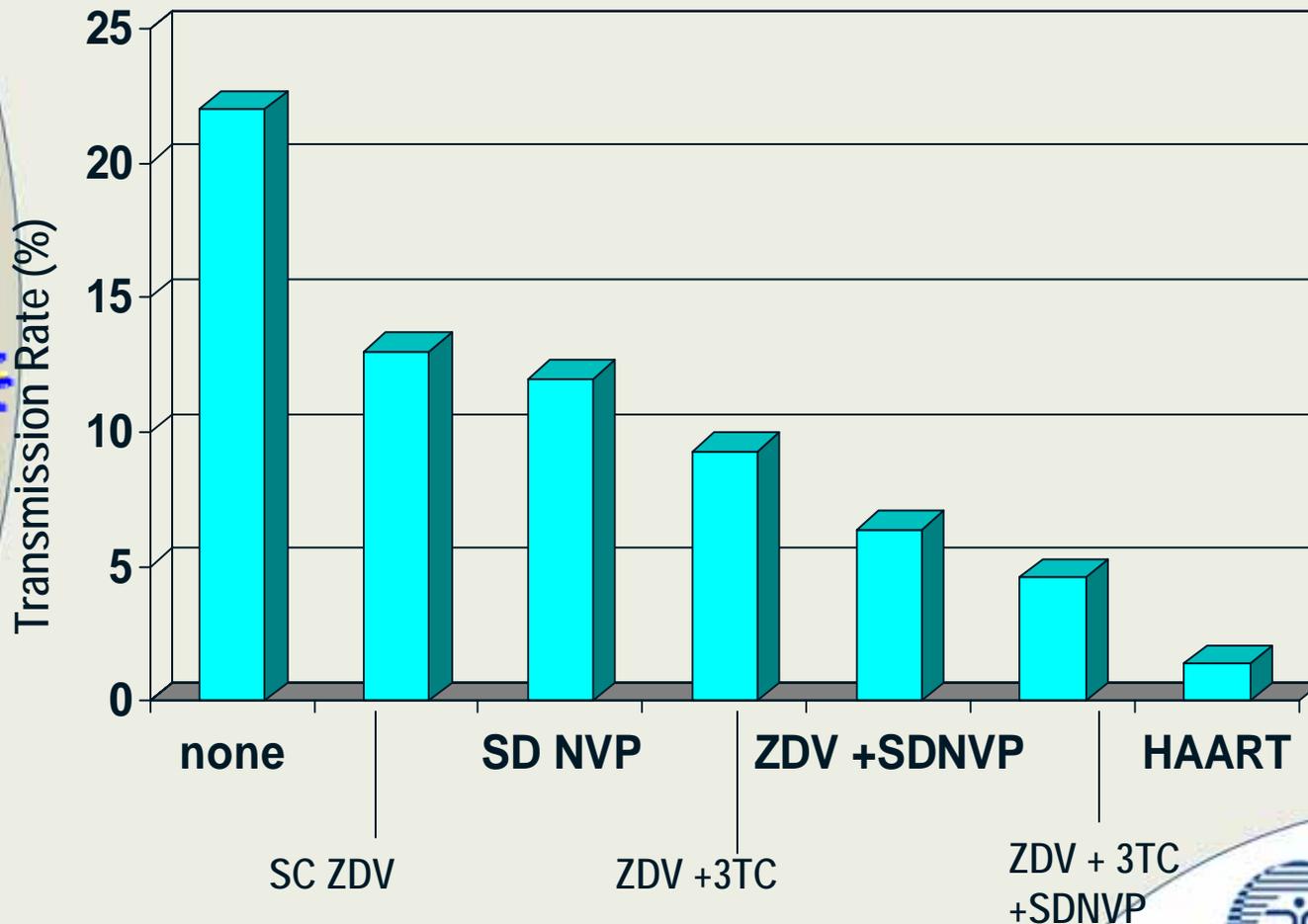
- RCTs on **HAART*** reported 60% to 80% reductions in new AIDS illnesses, hospitalizations and deaths
- A meta-analysis** of 54 antiretroviral clinical trials has demonstrated that:
 - Using one antiretroviral reduced progression to AIDS or death by 30% against placebo.
 - Using two antiretrovirals reduced progression to AIDS or death by 40% against one antiretroviral
 - Using three antiretrovirals reduced progression to AIDS or death by 40% against two antiretrovirals

*Jordan *et al.* (2002) *Systematic review and meta-analysis of evidence for increasing numbers of drugs in antiretroviral combination therapy*. *BMJ* 2002;324:757 <http://www.bmj.com/cgi/content/full/324/7340/757>

**Palella *et al.* (1998) *Declining morbidity and mortality among patients with advanced HIV infection*. *NEJM*. 338:853-860.

3.1.3. Preventing Mother-To-Child Transmission (PMTCT) of HIV

ARV and Perinatal Transmission in Africa, 1995-2006



Transmission rates are as high as 35% when there is no intervention and below 5% when antiretroviral treatment and appropriate care are available

Best Evidence

3.1.4. Condoms

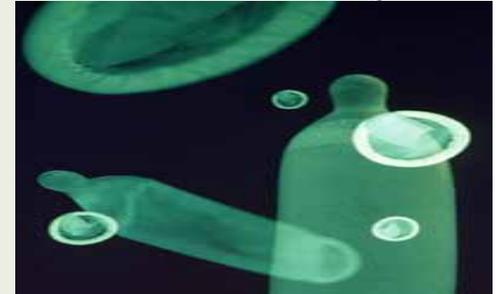


- A meta-analysis commissioned by UNAIDS* = male condom use is 90% effective in preventing HIV transmission.
- “Evidence from Family Planning programs over many years makes it abundantly clear that the condom is a safe and relatively effective method...”



- Based on laboratory and clinical evidence, the US FDA approved the **female condom** as 94-97% effective in reducing the risk of HIV infection, if used correctly and consistently**.

Weapons of mass protection!



*Hearst N and Chen S, *Condom promotion for AIDS prevention in the developing world: is it working?* Studies in Family Planning, 2004, 35(1):39-47. <http://www.usp.br/nepaids/condom.pdf>

**AVERT, "The Female Condom" fact sheet, available online at <http://www.avert.org/femcond.htm>

3.5. STI treatment

Promising
evidence

- Evidence from a **cluster RCT in Mwanza, Tanzania**, suggests that improved STI treatment services were shown to reduce HIV transmission by about 40%.

NO
evidence

- Two trials (Mwanza & Rakai) indicate no evidence for substantial benefit from STI treatment of all community members.

Promising
evidence

- Cochrane Reviewers concluded that limited evidence from RCTs indicates that STI control serves as an effective HIV prevention strategy.

Schulze KF (2004) Population-based interventions for reducing sexually transmitted infections, including HIV infection. *The WHO Reproductive Health Library*, Geneva

Wilkinson D, Rutherford G. Population-based interventions for reducing sexually transmitted infections, including HIV infection. *The Cochrane Library*, Issue 1 2003.

3.1.6. Microbicides and cervical barriers

NO
evidence

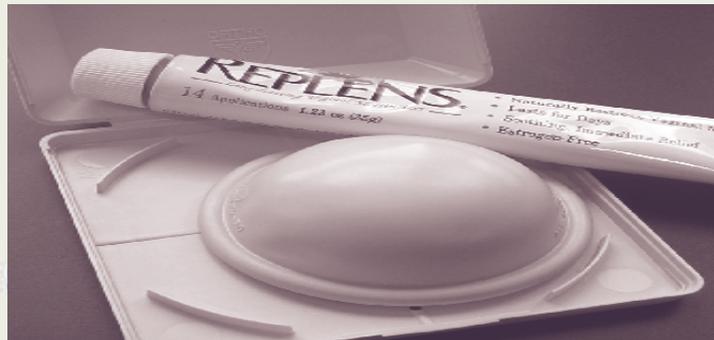
- Studies of **early-generation microbicides** have failed to detect a prevention benefit, and disappointing results were reported on the HIV prevention potential of female diaphragms.

Promising
evidence

- **HPTN 035**: A multi-centre clinical trial conducted at 7 sites (6 in Africa) evaluated the safety and effectiveness of two candidate microbicides, BufferGel and PRO 2000 with 3,099 participants. **PRO 2000** was 30% effective compared with no gel but BufferGel had no detectable effect on preventing HIV infection.

NO
evidence

- **Topical microbicides** have not performed well in human HIV prevention studies, with 10 trials of surfactant and polyanionic compounds yielding negative results.



3.1.7. HIV vaccine



Promising
evidence

- The Thai Phase III HIV vaccine clinical trial (RV 144), tested the “prime-boost” combination of two vaccines: ALVAC[®] HIV vaccine (the prime), and AIDSVAX[®] B/E vaccine (the boost). The vaccine combination was based on HIV strains that commonly circulate in Thailand. The trial demonstrated that the vaccine regimen was safe and modestly effective in preventing HIV infection. The results show that the prime-boost combination lowered the rate of HIV infection by 31.2%*

NO
evidence

HIV Vaccine Trials Network (HVTN) launched the first large-scale study to evaluate a candidate clade B HIV HIV vaccine. The phase IIb or “test of concept” efficacy trial involved 3,000 participants at 5 sites in South Africa. Unfortunately, the trials were halted in September 2007 owing to the vaccine’s lack of efficacy

*Rerks-Ngarm R, Pitisuttithum P, Nitayaphan S, Kaewkungwal J, Chiu J et al. Vaccination with ALVAC and AIDSVAX to Prevent HIV-1 Infection in Thailand. *NEJM* 20 October 2009

Summary: Evidence of Biomedical HIV prevention interventions

Level of evidence	Interventions	% Effectiveness or efficacy
 Best Evidence	Male Condoms Female Condoms PMTCT [Dual & triple therapy]	80-95% [Natural experiment] 94-97% [Natural experiment] 92-98% [RCTs]
 Good evidence	HAART Male Circumcision	60-80% [RCTs] 65% [3 RCTs]
 Promising evidence	HPTN 035 (PRO 2000) STI treatment RV 144 Thai vaccine trial	30% [1 RCT] 40% [1 RCT] 31.2% [1 RCT]
 NO evidence	HIV Vaccine Trials Network (HVTN) Early-generation microbicides & topical microbicides	No efficacy [RCT] Failed [RCTs] and negative results [10 RCTs]

Prevention of the Sexual Transmission of HIV-1: Results from RCTs

Intervention	RCTs Completed	RCTs Effective
Behavior change	9	0
Circumcision	4	3
Diaphragms	1	0
Microbicides	9.5	0
PrEP	1	0
STD Treatment	7	1
Vaccines	2	0

- 1) *RCT results are one measure of success*
- 2) *15 RCTs in progress: new results each year*

Social science *Wasserheit, WHO, 2007*

3.2. Behavioural HIV prevention interventions

3.2.1. Abstinence-only and ABC interventions

3.2.2. Voluntary Counselling & Testing (VCT)

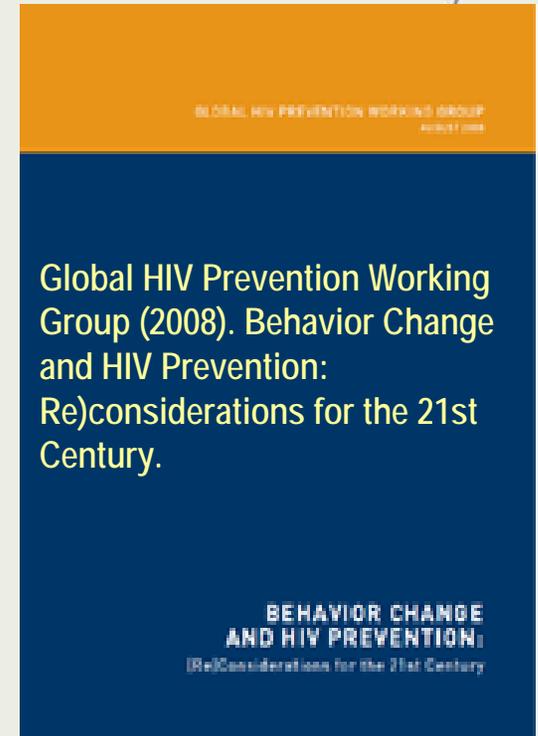
3.2.3. Stepping Stones counselling intervention

3.2.4. Concurrent sexual partnerships

“Behavioral HIV prevention works. Some have been pessimistic that it’s possible to reduce HIV risk behaviors on a large scale, but this concern is misplaced”

Dr. Helene Gayle, co-chair of the Working Group

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3.2.1. Abstinence-only and ABC interventions

NO
evidence

A Cochrane review of 13 RCTs comparing abstinence-only programs to various control groups in the US concluded that ...abstinence-only programs do not appear to reduce or exacerbate HIV risk among participants in high-income countries, although this evidence might not apply beyond US youth. Of the 13 trials, 7 trials reported incidence of vaginal sex.



NO
Evidence?

“It is time to scrap the ABCs and elevate the debate on HIV prevention beyond the incessant controversies over individual interventions. Small scale, isolated HIV prevention programs, however effective, will not bring the AIDS epidemic under control...Policy makers, donors and advocates need to demand national prevention efforts...ABC infantilizes prevention, oversimplifying what should be an ongoing, strategic approach to reducing incidence.”

Collins et al, *AIDS*, 2008

Underhill K, Operario D, Montgomery P. Abstinence-only programs for HIV infection prevention in high-income countries. *Cochrane Database of Systematic Reviews* 2007, Issue 4.

3.2.2. HIV Counseling and Testing (HCT)



Good evidence

- Meta-analysis of 11 studies of the impact of counseling and testing for PLWH/A*
 - 68% reduction in high risk sexual behaviors with partners not already HIV+ (95% CI: 59% - 76%)
 - Very similar findings for men and women

NO evidence

- Examining pool of 27 studies, a meta-analysis** found no significant impact of “counseling *and* testing” bundle on behavior relative to the untested

*Marks G et al. *JAIDS* 2005;39:446-453.

**Weinhardt LS et al. *Am J Public Health*. 1999;89:1397-1405.

3.2.3. Stepping Stones counseling intervention: Impact on HIV-1, HSV-2 & Behaviour

Promising
evidence

- *Stepping Stones*, a 50-hour “participatory learning” counseling program, lowered the risk of herpes simplex virus type 2 (HSV-2) infection by 34.9 per 1000 people exposed in a community RCT of 70 E.Cape villages. Compared with a shorter program, Stepping Stones did not lower incidence of HIV-1 infection and had variable impacts on risk behavior in the young adults studied.

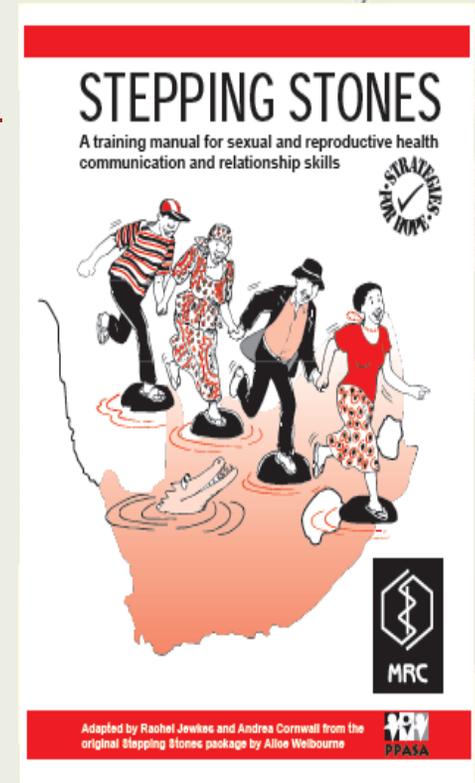
NO
evidence

Promising
evidence

Men who completed the *Stepping Stones* program reported less intimate partner violence (IPV) over 2 years, less transactional sex over 12 months, and less problem drinking over 12 months.

NO
evidence

But Stepping Stones women reported more transactional sex than women in the control program.



Jewkes, Nduna, Levin, Jama, Dunkle, Puren, Duvvury. Impact of Stepping Stones on incidence of HIV and HSV-2 and sexual behaviour in rural South Africa: Cluster randomised controlled trial. *BMJ*. 2008;337:a506

3.2.4. Concurrent Sexual Partnerships

- Taken together, the evidence that concurrency is driving the Africa AIDS epidemics is limited. There is as yet no conclusive evidence that concurrency:
 - (1) is associated with HIV prevalence;
 - (2) increases the size of an HIV epidemic;
 - (3) increases the speed of HIV transmission;
 - (4) increases the persistence of HIV in a population; or
 - (5) that this relationship has a large magnitude of effect.
- Current data on MCP comes from cross-sectional and ecological studies only; no RCTs or observational studies.

NO
evidence

Lurie M and Rosenthal S (2009) Concurrent Partnerships as a Driver of the HIV Epidemic in Sub-Saharan Africa? **The Evidence is Limited**. AIDS and Behavior

Mah T. L. and Halperin D. T. (2008). Concurrent sexual partnerships and the HIV epidemics in Africa: Evidence to move forward. AIDS and Behavior

3.3. Structural HIV prevention interventions

IMAGE study on micro-finance

Promising
evidence

- Intervention with Microfinance for AIDS and Gender Equity (IMAGE) RCT in rural Limpopo assessed a structural intervention that combined a microfinance programme with a gender and HIV training curriculum. They study found that experience of intimate-partner violence (IPV) was reduced by 55%.
- The intervention did not affect the rate of unprotected sex with a non-spousal partner (aRR 1.02, 0.85–1.23), and there was no effect on the rate of unprotected sex at last occurrence with a non-spousal partner (0.89, 0.66–1.19) or HIV incidence (1.06, 0.66–1.69) in Cohort 3

NO
evidence

Pronyk P, Hargreaves J, Kim J, et al. (2006) Effect of a structural intervention for the prevention of intimate-partner violence and HIV in rural South Africa: a cluster randomised trial. *Lancet* Vol 368: 1973-83

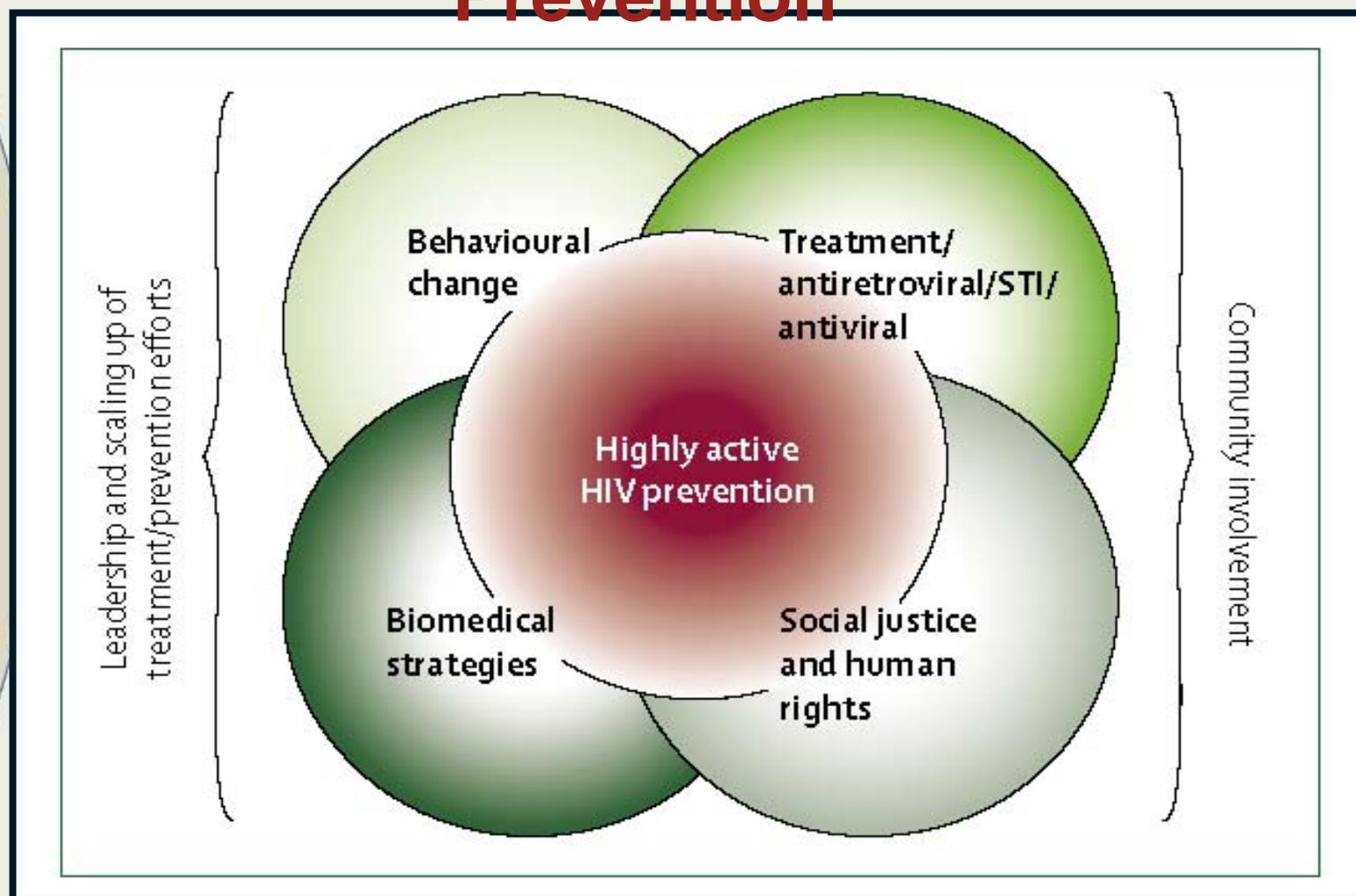


Research Council

Summary: Behavioural and Structural HIV prevention interventions that work

Level of evidence	Interventions	% Effectiveness or efficacy
		
	HCT for PLWHA	68% reduction in high risk sexual behaviors [1 comm RCT]
	Stepping Stones IMAGE study	Lowered the risk of HSV-2 by 34.9 per 1000 people exposed; less IPV and less transactional sex [comm RCT] IPV was reduced by 55% [comm RCT].
	Abstinence-only interv's HCT on untested Stepping Stones IMAGE Concurrency	7/13 reported sex [SR] no impact of C&T on behavior of untested did not lower incidence of HIV-1 No effect on HIV incidence [comm RCT] No conclusive evidence

Highly Active (combination) HIV Prevention



HIV social and behavioural prevention interventions



- The goal of social and behavioural interventions is to reduce the risk of HIV-related behaviours.
- Specifically, interventions seek to:
 - delay the onset of sexual intercourse,
 - reduce the number of sexual partners a person has,
 - reduce the incidence of unprotected sex by increasing condom use, or
 - reduce or eliminate the incidence of substance (alcohol and drug) use

Levels of evidence and criteria for social and behavioural prevention interventions

- **Best-evidence HIV behavioural interventions** include interventions that have been **rigorously evaluated** and have shown significant effects in eliminating or reducing risk behaviours, reducing the rate of new HIV/STD infections, or increasing HIV-protective behaviours.

Criteria: Prospective study design; at least a 3-month post-intervention follow-up assessment for *each* study arm; at least a 70% retention rate at a single follow-up assessment for *each* study arm.

- **Promising-evidence HIV behavioural interventions** include interventions that have been **sufficiently evaluated** and have shown significant effects in eliminating or reducing risk behaviours, reducing the rate of new HIV/STD infections, or increasing HIV-protective behaviours.

Criteria: Prospective study design; at least a 1-month post-intervention follow-up assessment for *each* study arm; at least a 60% retention rate at a single follow-up for *each* study arm; positive and statistically significant ($p \leq .05$) intervention effect for ≥ 1 relevant outcome measure; no evidence that any additional limitation was a fatal flaw

Other examples of evidence-based social and behavioural prevention interventions from South Africa

- Apart from IMAGE and Stepping Stones, there are several other social and behavioural prevention interventions from South Africa and other resource-limited settings.
- One useful source is the Global Health Literature Digest produced on a biweekly basis by UCSF Global Health Sciences (GHS) on <http://hivinsite.ucsf.edu/InSite?page=jl-00-00> Part 1.
- These studies of behavioral, policy, and prevention interventions have one or more of the following aims:
 - to reduce sexual or drug-related risk behaviors,
 - to decrease primary or secondary transmission,
 - to improve health service delivery and quality of life,
 - and to improve HIV treatment and treatment adherence.

Other examples of evidence-based social and behavioural prevention interventions from South Africa (contd)

Intervention	Type & Target group	Site(s)	Behaviour(s) targeted for change	Theory/ Model	Evaluated? Evidence?
Phaphama STI	Clinic intervention STI clinic attendees	Spencer Road Clinic, CT	↑Knowledge of HIV ↑Motivation for safer sex	IMB	Yes in USA and SA Large RCT in 3 PHC clinics Effectiveness in 13 clinics in Mpumalanga
Phaphama Alcohol	Community intervention Patrons of shebeens	Delft, CT	↓Alcohol as risk factor for HIV	IMB & social networking	Yes
Phaphama Men	Community Men :	Gugulethu, CT Nyanga, CT	GBV HIV risk Alcohol use HIV HIV risk	Social constructionism & social networking	Both interventions demonstrated positive effects on some of the outcomes

Other examples of evidence-based social and behavioural prevention interventions from South Africa (contd)

Intervention	Type & Target group	Site(s)	Behaviour(s) targeted for change	Theory/ Model	Evaluated? Evidence?
Phaphama Community Alcohol	Community intervention Patrons of shebeens	Gugulethu, Nyanga, Crossroads, Phillipi	↓Alcohol as risk factor for HIV	IMB, Social cognitive & social networking	Large efficacy RCT in 12 communities currently underway No effectiveness
Men as Partners	Community (men & women)	National	↓gender-based violence, ↑ attitudes toward women, and ↓ HIV and STI risk	Social cognitive & social networking	No effectiveness evaluation ?Evidence

Other examples of social and behavioural prevention interventions from South Africa (contd)

Intervention	Type & Target group	Site(s)	Behaviour(s) targeted for change	Theory/ Model	Evaluated? Evidence?
Phaphama Male circumcision	Men undergoing medical or traditional male circumcision	Witbank, Mpumalanga	↓ HIV risk behaviour	IMB & social networking	Feasible & acceptable; Efficacy currently underway No effectiveness evaluation
Project Accept	Community RCT; Standard v.s Intervention community Rural community (Adults & young people)	Sweetwaters KZN Mobile vans in rural community	↑ HIV testing ↑ HIV disclosure & discussion ↓ Stigma & discrimination ↓ HIV risk behaviour	Diffusion of Innovations; Tipping point theory Social action theory	↑ Diffusion of VCT ↑ Uptake of VCT by men, women, youth ↑ Mobilization of youth Combination prevention
NIDA Standard Intervention/ Woman-Focused Intervention	CSWs	Pretoria	↑ condom use and ↓ alcohol and crack cocaine use ↓ GBV		Efficacious

Other examples of evidence-based social and behavioural prevention interventions from South Africa (contd)

Intervention	Type & Target group	Site(s)	Behaviour(s) targeted for change	Theory/ Model	Evaluated? Evidence?
Positive Prevention 1 - Healthy Relationships	Community intervention PLWHA in support groups	KSD district in EC	↑ Disclosure ↓ Primary HIV infection ↓ Secondary HIV infection	Social cognitive theory	Yes efficacy in USA; Feasibility and acceptability in pilot in Botswana and SA Currently being evaluated
Positive Prevention 2 - Options for Health	Individual PLWHA in clinical care	Durban Hospital PMB	↓ Primary HIV infection ↓ Secondary HIV infection	IMB	Yes efficacy in USA and also in a pilot study in Durban RCT in PMB currently underway; also effectiveness in Mpumalanga

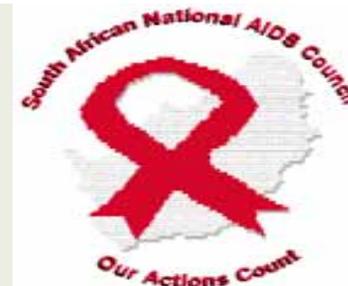
Other examples of evidence-based social and behavioural prevention interventions from South Africa (contd)

Intervention	Type & Target group	Site(s)	Behaviour(s) targeted for change	Theory/ Model	Evaluated? Evidence?
19 AIDS communication programmes e.g., Soul City; Siyayinqoba Beat It, loveLife, TshaTsha, Takalani Sesame Street.	All age groups	National	<ul style="list-style-type: none"> ↑ Condom usage, ↑ self efficacy in condom usage; ↑ discussion of HIV testing and testing and knowledge of ARVs and ↑ helping someone sick with AIDS 	Multiple theories	<p>No effectiveness evaluation</p> <p>Indirect evidence of impact on outcomes (based on modelling)</p>
LoveLife	Communication campaign Young people 15 – 29 yrs	760 sites. Media, Cellphones, Billboards,	<ul style="list-style-type: none"> ↑ Opportunities in life for youth ↑ Communication among youth 	“Eclectic model” 10 Commitments (ARRM)	<p>No effectiveness evaluation</p> <p>?Evidence</p>
Scrutinize	Communication campaign Young people 18-32 years	SABC TV audiences	<ul style="list-style-type: none"> ↓ MCP ↑ Condom use ↓ HIV risk ↓ Transactional sex ↓ Alcohol and sex 	Social ecology model	<p>No effectiveness evaluation</p> <p>?Evidence</p>

Other examples of social and behavioural prevention interventions from South Africa (contd)

Intervention	Type & Target group	Site(s)	Behaviour(s) targeted for change	Theory/ Model	Evaluated? Evidence?
Soul City	<p>Communication campaign</p> <p>Young people 15 – 26 yrs</p>	Multimedia	<p>↓MCP</p> <p>↓GBV</p> <p>↓Alcohol</p>	Social Ecology Model	<p>No effectiveness evaluation yet.</p> <p>?Evidence</p>
One Love	<p>Communication campaign</p> <p>Young people and adults 8 -14 years; 16 - 45 years</p>	<p>SABC TV audiences</p> <p>LSM 1-10</p>	<p>↓MCP</p> <p>↑Talk, respect & protect</p>	Social Networking Theory	<p>No effectiveness evaluation yet.</p> <p>?Evidence</p>

Evidence-based HIV behavioural interventions in the US



- CDC's AIDS Prevention Research Synthesis (PRS) project identified 18 best evidence, theory-based behavioural interventions demonstrating "**best evidence**" of efficacy for reducing HIV risk. They were targeted at heterosexual men and women, MSM, Youth, PLWHA and low income populations, etc.

"The...PRS efficacy review process has identified 49 evidence-based HIV behavioral interventions (as of November 2007)."

- The compendium of HIV prevention interventions... contains about 24 "**other evidence-based interventions**", while "**promising-evidence**" HIV behavioural interventions are being evaluated.

Case study: How to diffuse effective behavioural interventions that work

- **The Diffusion of Effective Behavioural Interventions (DEBI) project** was designed to bring science-based, community, group, and individual-level HIV prevention interventions to community-based service providers and state and local health departments.
- The goal is to enhance the capacity to implement effective interventions at the state and local levels, to reduce the spread of HIV and STDs, and to promote healthy behaviors.

The Big Challenge NOW

Great HIV treatment success...

- **22 antiretroviral agents available**
- **More than 2 million people receiving ART**

But 2.5 million new HIV infections/yr

HIV prevention lags behind and has not married treatment *except for MTCT!*

HIV prevention MUST marry treatment NOW: With the community...a unified strategy

5. Conclusion

No “Magic Bullet” for HIV

“It is critical to note that there is no “magic bullet” for HIV prevention. None of the new prevention methods currently being tested is likely to be 100 percent effective, and all will need to be used in combination with existing prevention approaches if they are to reduce the global burden of *HIV/AIDS*.”

Source: Global HIV Prevention Working Group (2008)

The AIDS epidemic has taught us to be innovative and to invent, test and implement new interventions.
We now have evidence of HIV prevention strategies that work!



Picture source: Naidoo D (2007). Science, Technological and Innovation – A Strategic Imperative for South Africa

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However, despite our innovation, inventiveness and compelling evidence of effective strategies, the “killer virus” is still chasing and killing us!



Picture source: Naidoo D (2007). Science, Technological and Innovation – A Strategic Imperative for South Africa



THANK YOU

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