

13th Annual Conference of the
National HIV Nurses Association (NHVNA)



Dr Timothy Hallett

Imperial College London

16-17 June 2011, Arena and Convention Centre, Liverpool

The Future of HIV Prevention

Tim Hallett
Imperial College London

Contents

- Look at 'What works' in HIV prevention and the exciting findings from recent trials
- Discuss how to interpret those findings.
 - What could be achieved?
 - What will the next decisions need to be?

Focus on low/middle-income countries in southern Africa and Latin America – the epicentres of the HIV epidemic

What Works For HIV Prevention?

Intervention	Level	RCTs done	Number Showing Efficacy
Behaviour Change	Individual	2	0
	Cluster	5	0
Microbicides	Individual	6	0
STI Treatment	Individual	3	0
	Cluster	4	1
HIV Vaccines	Individual	4	0

Summer 2005

What Works For HIV Prevention?

Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial

Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial

Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial

Level

Individual

Cluster

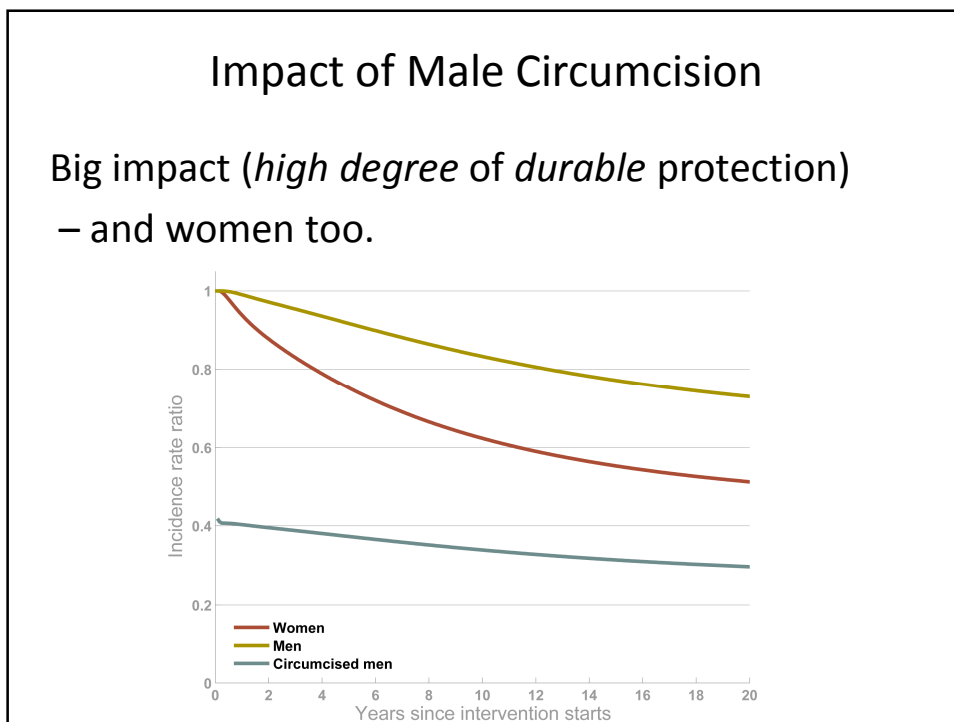
Individual

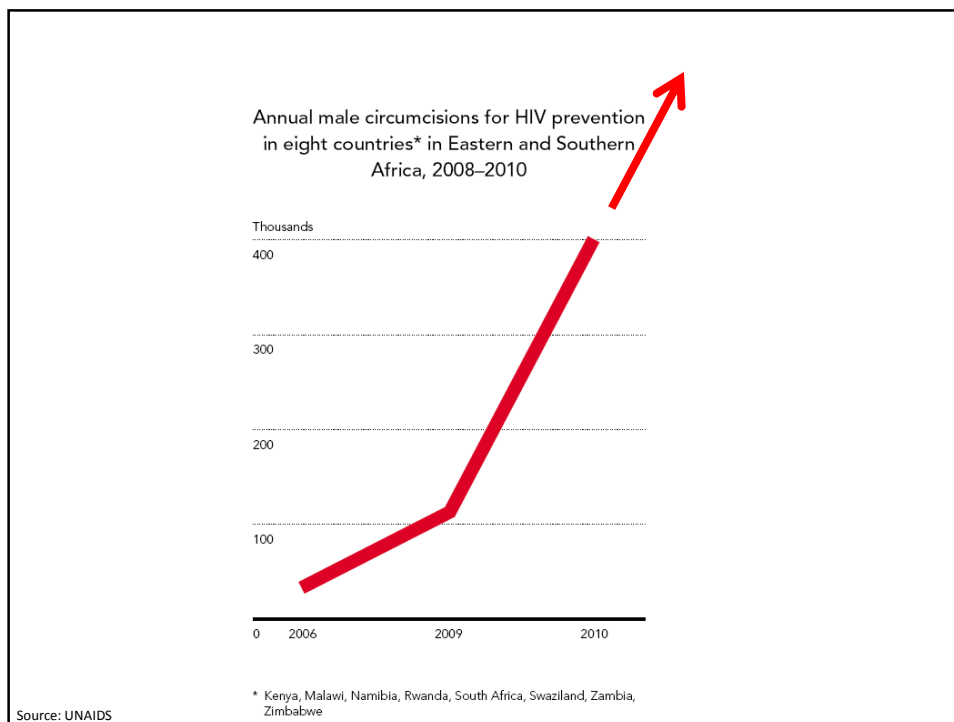
Individual

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Male Circumcision	Cluster	4	1
HIV Vaccines	Individual	4	0
Male Circumcision	Individual	3	3

Autumn 2005 + Spring 2007





Male Circumcision

Costs

- 36,000 men circumcised in Kenya.
- Cost per operation \$30.
- Total Cost = \$ 1,080,000

- Extra expected infections in that group if not circumcised: 5180
- Cost per infection averted: ~\$200

- Cost of lifetime provision of ART per man: \$3000

- ***\$14.5 M saved***

Male Circumcision

- Even bigger effect for men?

Bailey et al, AIDS 2008; Kong et al., CROI 2011

- New devices for quicker, faster, cheaper deliver



- Direct effects on male-to-female transmission too?

What



1?

Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

Robert M. Grant, M.D., M.P.H., Javier S. Larra, M.D., M.P.H., Peter L. Anderson, Pharm.D., Vanessa Muthian, B.S., Albert Y. Liu, M.D., M.P.H., Ismael Vargas, Pedro Gutierrez, M.Sc., Martin Garcia, M.D., M.P.H., Juan Vicente Gaviria-Carranza, M.D., M.P.H., Maria E. Ramirez-Gardich, M.D., Orlando Montoya-Herrera, M.Sc., Tereza Fernandes, M.D., Valéria C. Veloso, M.D., Ph.D., Susan F. Buchbinder, M.D., Susan Charpentier, M.D., Ch.P.H., Mauro Schechter, M.D., Ph.D., Linda-Gail Bekker, M.B., Ch.B., Ph.D., Kenneth H. Mayer, M.D., Egon George Kibuka, M.D., Ph.D., K. Elizabeth Arora, Ph.D., Kathleen Mulligan, Ph.D., Lane S. Buchanan, B.Chem., Robert J. Hance, A.A., Camilla Gostha, M.D., Patricia Delchevalier, Ph.D., Brian Poitler, B.S., Fung Wang, M.D., J. Jeff McConville, M.A., Jia-Hua Zheng, Ph.D., James Lee, B.S., James F. Rooney, M.D., Howard S. Jaffe, M.D., Ana I. Martinez, R.Ph., David N. Burns, M.D., M.P.H., and David V. Glidden, Ph.D., for the IPDEC Study Team*

ABSTRACT

BACKGROUND: Antiretroviral chemoprophylaxis before exposure is a promising approach for the prevention of human immunodeficiency virus (HIV) acquisition.

DESIGN: We randomly assigned 2489 HIV-seronegative men or transgender women who have sex with men to receive a combination of two oral antiretroviral drugs, emtricitabine and tenofovir disoproxil fumarate (FTC-TDF) or placebo once daily. All subjects received HIV testing, risk-reduction counseling, condoms, and management of sexually transmitted infections.

RESULTS: The study effects were followed for 3284 person-years (median, 1.2 years maximum; 28 months). Of these subjects, 10 were found to have been infected with HIV at enrollment, and 300 became infected during follow-up (56 in the FTC-TDF group and 64 in the placebo group), indicating a 49% reduction in the incidence of HIV (95% confidence interval, 3% to 61%; $P=0.005$). In the FTC-TDF group, the most drug was detected in 22 of 48 of seronegative subjects (46%) and in 5 of 24 HIV-infected subjects (21%) ($P<0.001$). Urines were reported more frequently during the first 4 weeks in the FTC-TDF group than in the placebo group ($P<0.001$). The two groups had similar rates of serious adverse events ($P=0.57$).

CONCLUSIONS: Oral FTC-TDF provided protection against the acquisition of HIV infection among the subjects. Detectable blood levels strongly correlated with the prophylactic effect (funded by the National Institutes of Health and the Bill and Melinda Gates Foundation; ClinicalTrials.gov number, NCT00861813).

Number Showing Efficacy

0
0
0
0
1
0
3

Intervention
Behaviour Change
Microbicides
STI Treatment
HIV Vaccines
Male Circumcision
Oral PrEP for MSM

Individual	1	1
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December 2010

Oral PrEP for MSM

- *But it's still expensive!*

If you want to reduce new infections by 1/3 over ten years

	What to do	Cost
Option 1	Scale-up over 2 years; Highly prioritise to most at risk; Use 434,000 PY of PrEP.	\$370-540 M
Option 2	Scale-up over 5 years; Do not prioritise; Use 630,000 PY of PrEP.	\$540-790 M
Approved HIV Grants to Peru from Global Fund		\$85 M

What Works For H

Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis

Summary
Background: High plasma HIV-1 RNA concentrations are associated with increased risk of HIV-1 transmission. Initiation of antiretroviral therapy (ART) reduces plasma HIV-1 concentrations. We aimed to assess the effect of ART on HIV-1 transmission in heterosexual partners.

Methods: 100 couples were eligible for analysis. All HIV-1 positive partners initiated ART during the study. The mean CD4 cell count at ART initiation was 320 cells per mm³. High plasma HIV-1 RNA concentrations were associated with increased risk of HIV-1 transmission. ART initiation during the study was associated with a 96% reduction in HIV-1 transmission. The greatest reduction was observed in HIV-1 transmission when ART was initiated within 2 weeks of HIV-1 infection.

FOR IMMEDIATE RELEASE:
Thursday, 12 May 2011, 11 am EST

Initiation of Antiretroviral Treatment Protects Uninfected Sexual Partners from HIV Infection (HPTN Study 052)

96% reduction in HIV transmission, according to study conducted by HIV Prevention Trials Network

Washington, DC - Men and women infected with HIV reduced the risk of transmitting the virus to their sexual partners through initiation of oral antiretroviral therapy (ART), according to findings from a large multinational clinical study conducted by the HIV Prevention Trials Network (HPTN), a global partnership dedicated to reducing the transmission of HIV through cutting-edge biomedical, behavioral, and structural interventions.

The study, known as HPTN052, was designed to evaluate whether immediate versus delayed use of ART by HIV-infected individuals would reduce transmission of HIV to their HIV-uninfected partners and potentially benefit the HIV-infected individual as well. Findings from the study were reviewed by an independent Data and Safety Monitoring Board (DSMB). The DSMB recommended that the results be released as soon as possible and that the findings be shared with study participants and investigators. The DSMB concluded that initiation of ART by HIV-infected individuals substantially protected their HIV-uninfected sexual partners from acquiring HIV infection, with a 96 percent reduction in risk of HIV transmission. HPTN 052 is the first randomized clinical trial to show that treating an HIV-infected individual with ART can reduce the risk of sexual transmission of HIV to an uninfected partner.

"This is excellent news," said Dr. Myron Cohen, HPTN 052 Principal Investigator and Associate Vice Chancellor for Global Health and Director of the Institute of Global Health and Infectious Diseases at the University of North Carolina at Chapel Hill. "The study was designed to evaluate the benefits to the sexual partner as well as the benefits to the HIV-infected person. This is the first randomized clinical trial to definitively indicate that an HIV-infected individual can reduce sexual transmission of HIV to an uninfected partner by beginning antiretroviral therapy sooner. HPTN recognizes the significant contribution that this study's participants have made to furthering the progress in HIV treatment and prevention. We are very grateful for their participation."

Oral PrEP for MSM

ART

Individual

Individual


1

1

Spring 2010+ last month!



The Economist: June 4-10th, 2011



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This is a landmark finding, said Dr. Mary-Celise, HPTN 052 Principal Investigator and Associate Vice-Chancellor for Global Health and Director of the Institute of Global Health and Infectious Diseases at the University of North Carolina at Chapel Hill. "The study was designed to evaluate the benefit to the sexual partner as well as the benefit to the HIV-infected person. This is the first randomized clinical trial to definitively indicate that an HIV-infected individual can reduce sexual transmission of HIV to an uninfected partner by initiating antiretroviral therapy sooner. HPTN 052 represents the significant contribution that this study's participants have made to furthering the progress in HIV treatment and prevention. We are very grateful for their participation."

CD4 250-550

+



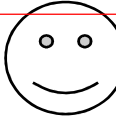
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27 transmissions

CD4 250-550

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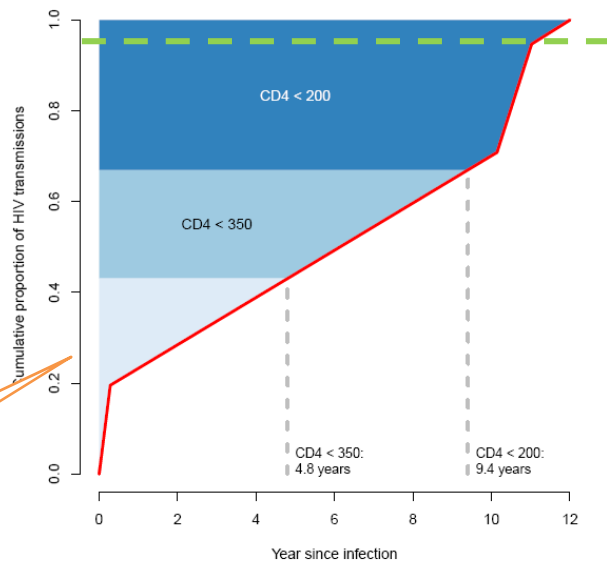


1 transmission

96% Reduction in transmission

96% reduction in risk transmission in couples over 2 years may not translate into a 96% reduction in population level HIV incidence.

Is this above or below $R_0=1$?



Treatment for prevention

The questions will be all about:

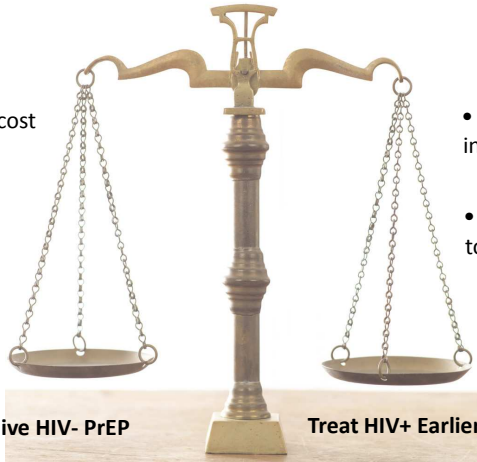
- Feasibility and acceptability
- Effectiveness study
(Design challenges to that)

But.... would it ever be better to protect the HIV-uninfected individual?

Pre-Exposure Prophylaxis (PrEP)

Oral

Topical



The image shows a balance scale with two pans. The left pan is labeled 'Give HIV- PrEP' and the right pan is labeled 'Treat HIV+ Earlier'. The scale is balanced, indicating a comparison of costs and benefits between the two strategies.

- Cheaper drug cost
- Protects from infection from any source

- 96% reduction in transmission!
- Clinical benefit to HIV+

Unless PrEP is highly effective (>60%) and very cheap (<40% annual cost of ART) then it would be more cost-effective to initiate ART at CD4 500 cells/ μ L.

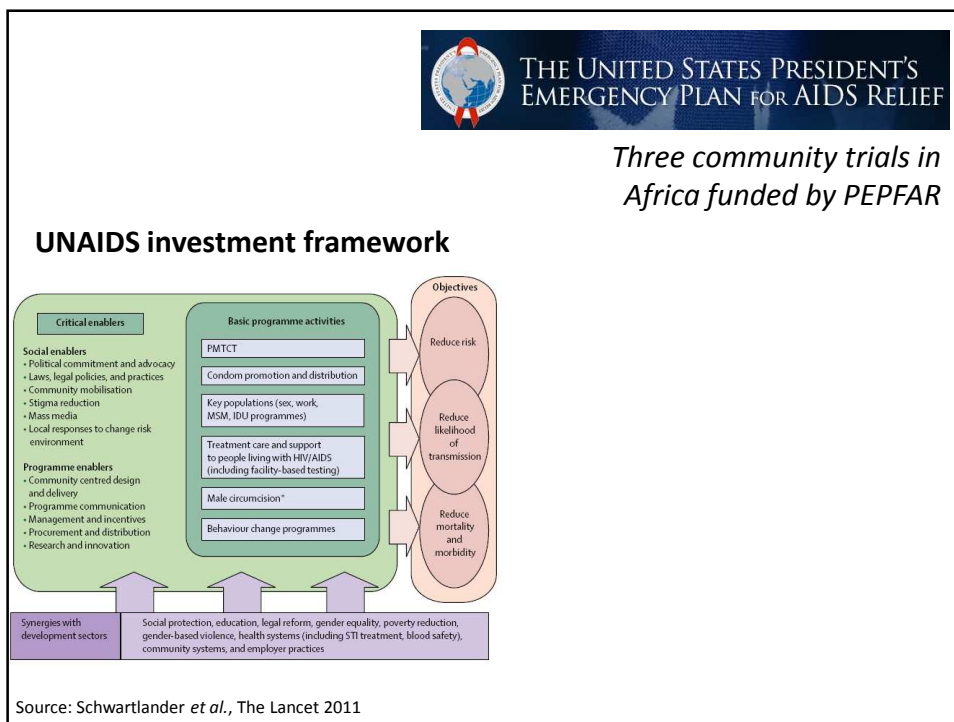
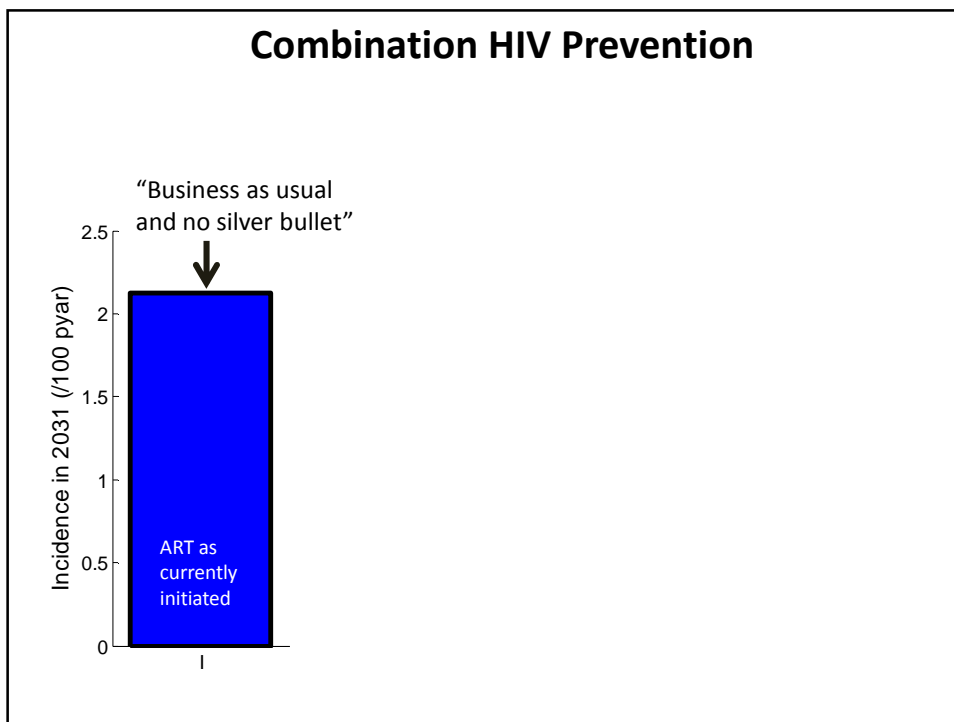
What Works For HIV Prevention?

Intervention	Level	RCTs done	Number Showing Efficacy
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	Cluster	5	0

The table is filling-up...

... But does not look as though any single intervention is likely to bring the epidemic under control by itself.

Male Circumcision	Individual	1	1
Oral PrEP for MSM	Individual	1	1
ART	Individual	1	1



Other things I didn't have time to talk about:

- **NIMH Project Accept:**
 - Randomized Controlled Trial of *Community Mobilization, Mobile Testing, Same-Day Results, and Post-Test Support* for HIV in Sub-Saharan Africa and Thailand
 - Results due: mid 2012.
- **Schooling, Income and HIV Risk (SIHR) trial:**
 - School girls whose families receive monthly cash transfer were much less likely to become infected (Zomba, Malawi).
 - Due to changes in own behaviour and in sexual contact patterns – mostly because “income shock” reduces transactional sex. Longer-term impact?
- **RV144 Vaccine:**
 - Four priming injections of a recombinant canarypox vector vaccine (ALVAC-HIV [vCP1521]) plus two booster injections of a recombinant glycoprotein 120 subunit vaccine (AIDSVAX B/E).
 - Result: 30% protective effect.

Conclusions

- Increasing number of things that “work” (show efficacy in trials).
- Questions will now about their impact in limiting transmission at population level.
- No clear silver bullet...
 - ... but plenty of difficult trade-offs ...
 - ... And complicated findings to try to interpret.

In the next few years we could see some real achievements in HIV prevention --- but will development in science be matched by further financial commitments?

Thanks to...

Imperial College London

Geoff Garnett,

Simon Gregson

Ide Cremin,

Annick Bourquez,

Gabriela Gomez,

Jeff Eaton,

Pete Dodd,

John Williams,

Christophe Fraser

UNAID & WHO

Bernhard Schwartzlander

Peter Ghys

Kevin O'Reilly

University of Washington

Connie Celum,

Ramzi Alsallaq,

Jared Baeten,

Jim Hughes,

Weill-Cornell

Laith Abu-Raddad

Hiam Chemaitelly

LSHTM

Peter Piot

Georgetown

Mark Dybul

Funded by: The Wellcome Trust, Bill & Melinda Gates Foundation, NIH