

# HIV Prevention

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New Investigators Workshop, CROI  
February 8, 2009

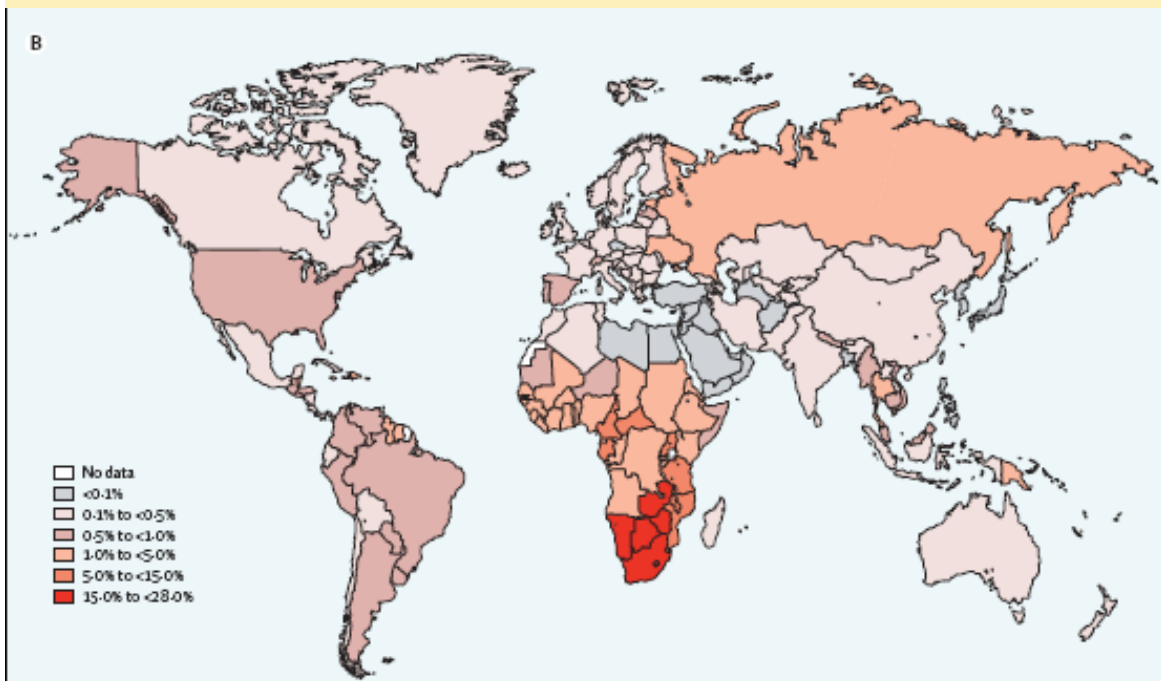
## Questions

1. Who is becoming HIV infected? Why?
2. What can we learn from "negative" trials?
3. How do we build on successes?

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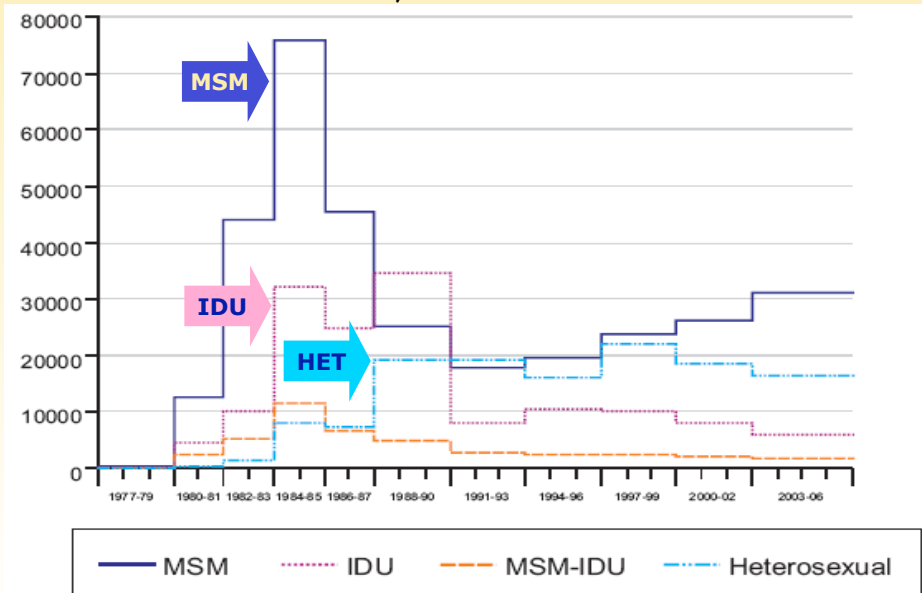
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## "Know Your Epidemic, Know Your Response"



## Estimated number of new HIV infections U.S., 1977-2006

Hall, JAMA 2008



## Attributable risk

- Combines information on:
  - Increment in risk
  - Prevalence of exposure
- Estimates potential proportion of new infections hypothetically avoided by eliminating that exposure in given population
- Helpful in understanding factors that contribute most heavily and should be targeted for interventions

**Predictors of HIV seroconversion in MSM**  
**Explore: 4295 MSM in 6 US cities, 1999-2003**

Variable	PAR	OR <sub>adj</sub>	95% CI
4-9 male sex partners	32.3%	1.6	1.1-2.4
≥ 10 male sex partners		1.8	1.2-2.7
Use of alcohol or drugs before sex	29.0%	1.6	1.1-2.3
Unprot receptive anal sex w/ unknown sero	28.4%	2.9	2.1-3.8
Unprot receptive anal sex w/ HIV negative	21.6%	1.9	1.4-2.7
Unprot receptive anal sex w/ HIV positive	18.3%	3.4	2.2-5.1
Depression	16.7%	1.5	1.1-1.9
Amphetamines	16.3%	2.0	1.4-2.6
Unprot insertive anal sex w/ HIV positive	8.6%	1.6	1.0-2.4
Heavy alcohol use	6.1%	2.0	1.2-2.8
Self-reported gonorrhea	4.3%	2.5	1.5-4.2

Koblin, AIDS 2006

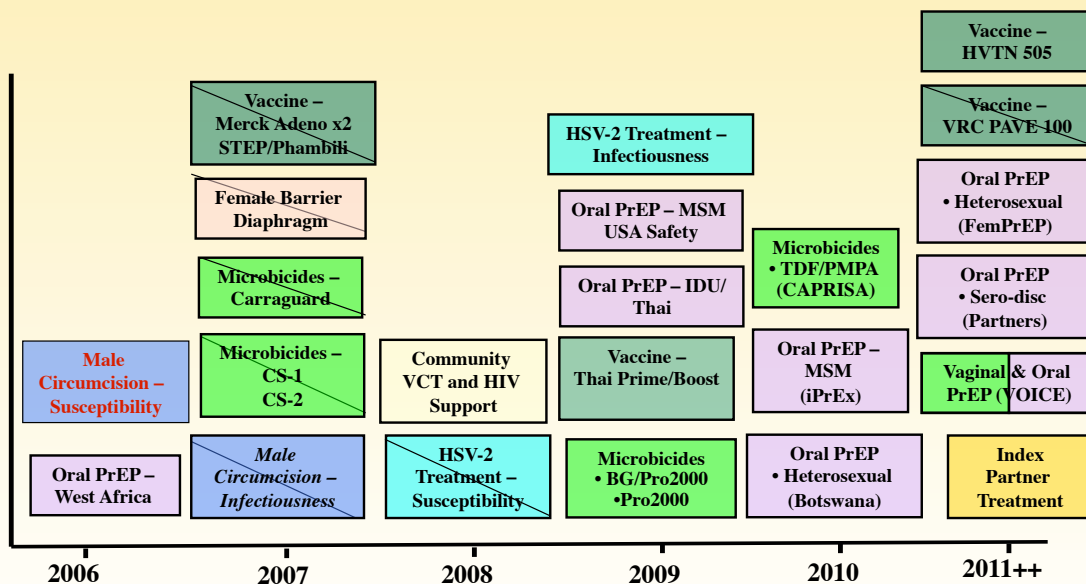
**"Seroadaptation" in San Francisco**  
**Stall, IAS 2008**

Sex Practice	HIV neg	HIV pos
No sex partners	14%	15%
No anal sex	13%	12%
100% condom use	29%	18%
Unprotected anal sex w/ partners of same HIV status	42%	43%
Seropositioning	<1%	<1%
No discernable strategy	<2%	11%

# Questions

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## Snapshot of Research in Biomedical Prevention



See also <http://www.avac.org/timeline-website/index.htm>

The important thing in science is not so much to obtain new facts as to discover new ways of thinking about them.

--Sir William Bragg  
Nobel Prize, 1915

## Operational insights

- Impact of risk reduction counseling
- Importance of measurement
- Interactions with treatment arm

Diaphragm trial  
Padian, Lancet 2007

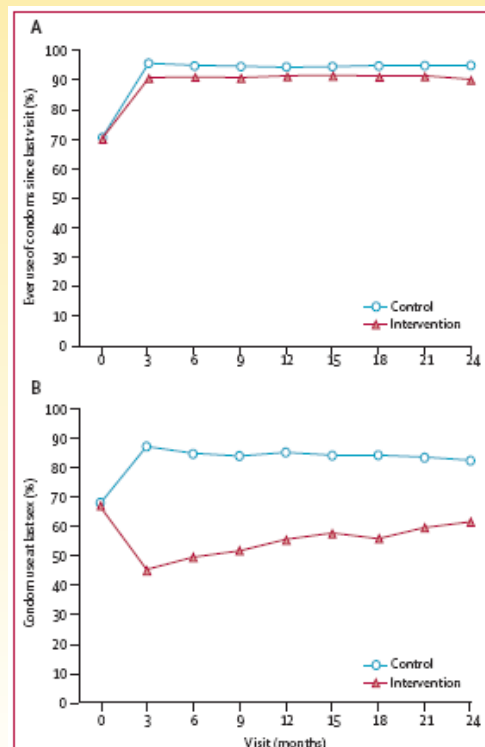
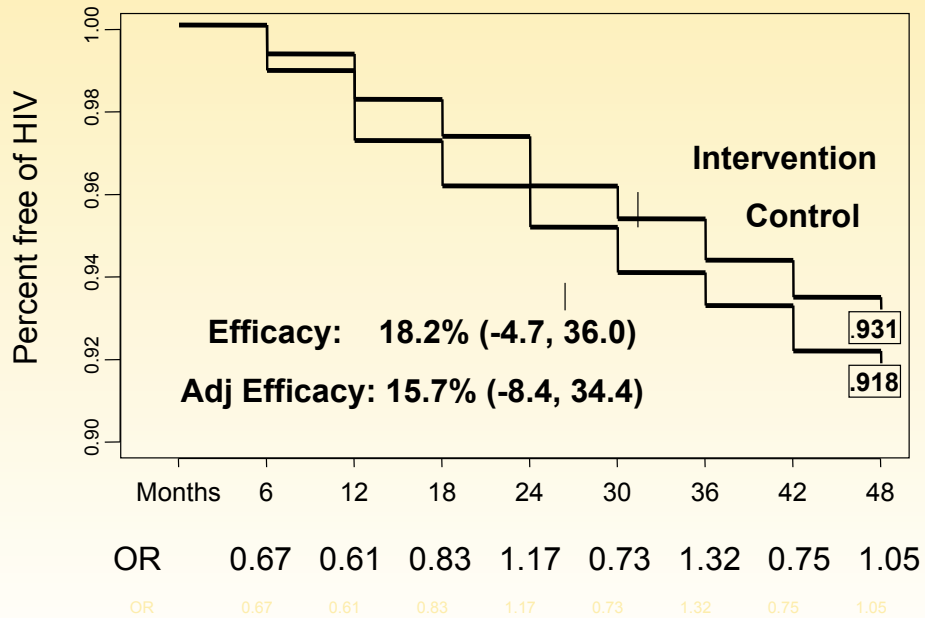


Figure 3: Proportions of women reporting (A) ever using condoms since last visit and (B) condom use at last sex, by visit

## EXPLORE Behavioral Trial



## Estimated Relative Risk of HIV Infection Step Vaccine : Placebo (95% CI)

MODEL	Circumcised		Uncircumcised	
	Ad5 ≤18 N=578	Ad5 >18 N=421	Ad5 ≤18 N=168	Ad5 >18 N=620
Univariate	0.7 (0.3, 1.4)	1.6 (0.7, 3.8)	3.3 (0.7, 16)	3.9 (1.3, 11)
<b>Multivariate</b>				
Model 1	0.8 (0.4, 1.6)	1.4 (0.6, 3.2)	2.5 (0.8, 8.0)	4.3 (1.7, 11.0)
Model 2	0.8 (0.4, 1.7)	1.7 (0.7, 3.8)	2.4 (0.8, 7.3)	4.8 (1.8, 12.6)
Model 3	0.6 (0.3, 1.2)	1.3 (0.6, 3.0)	2.0 (0.6, 6.3)	4.6 (1.8, 12)
Model 4	0.6 (0.3, 1.2)	1.4 (0.6, 3.1)	2.1 (0.7, 6.6)	4.2 (1.6, 11.1)

Men with unknown circumcision status (49, 2.7%) were excluded from analyses. All analyses are based on the Cox proportional hazards regression model for time-to-event data.

## Picking through the data....



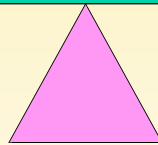
- NHP studies use high-dose challenge
- Macaques are not a natural host for Ad5
- Models have not evaluated foreskin or insertive role

## What does "back to basics" mean?

Discovery

Development

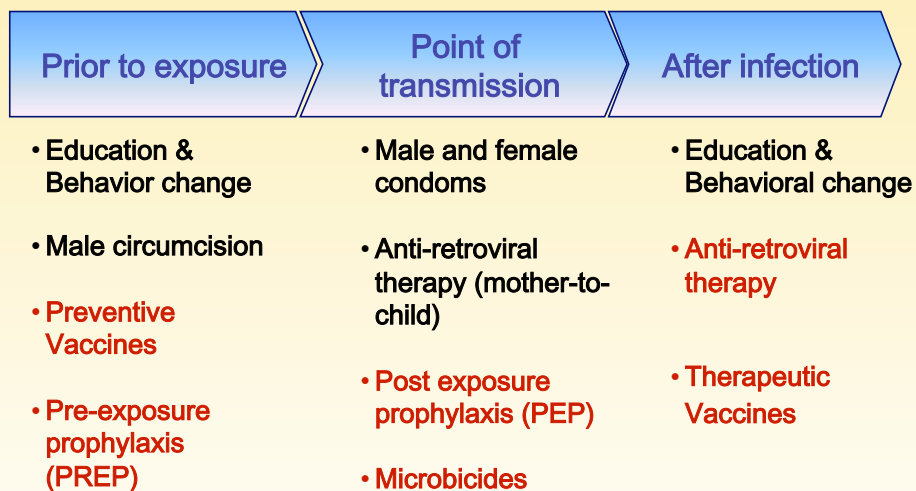
1. Basic
2. Preclinical
3. Clinical



## Questions

1. Where are new infections occurring?
2. What can we learn from "negative" trials?
3. How do we build on successes?

## Behavioral and Biomedical HIV Prevention Strategies



## Male circumcision reduces male HIV risk by >50%

Open access, freely available online PLOS MEDICINE

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

Bertran Auvert<sup>1,2,3,4\*</sup>, Dirk Taljaard<sup>5</sup>, Emmanuel Lagarde<sup>2,4</sup>, Joëlle Sobngwi-Tambekou<sup>2</sup>, Rémi Sitta<sup>2,4</sup>, Adrian Puren<sup>6</sup>

1 Hôpital Ambroise-Paré, Assistance Publique—Hôpitaux de Paris, Boulogne, France, 2 INSERM U 687, Saint-Maurice, France, 3 University Versailles Saint-Quentin, Versailles, France, 4 IFR 69, Villejuif, France, 5 Progressus, Johannesburg, South Africa, 6 National Institute for Communicable Disease, Johannesburg, South Africa

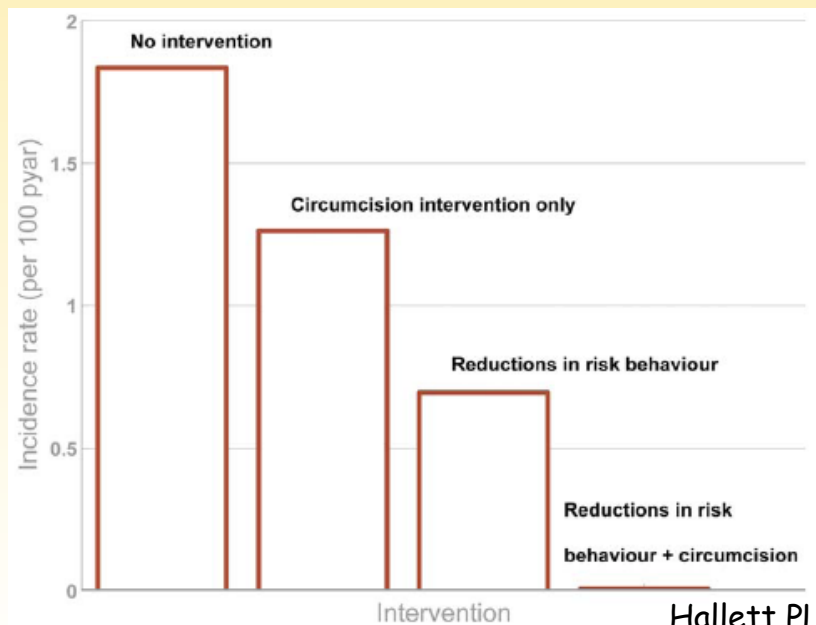
### Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial

Ronald H Gray, Godfrey Kigozi, David Serwadda, Frederick Makiyimbizi, Stephen Watya, Fred Nalugoda, Noah Kiwanuka, Lawrence H Moulton, Mohammad A Chaudhary, Michael Z Chen, Nelson K Sewankambo, Fred Wabwire-Mangen, Melanie C Bacon, Carolyn F M Williams, Plus Opendi, Steven J Reynolds, Oliver Laeyendecker, Thomas C Quinn, Maria J Wawer

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

Robert C Bailey, Stephen Moses, Corette B Parker, Kawango Agot, Ian Mudean, John N Krieger, Carolyn F M Williams, Richard T Campbell, Jeckoniah O Ndinya-Achola

## Effect of 90% circumcision +/- 30% risk reduction



Hallett PLOS One, 2008

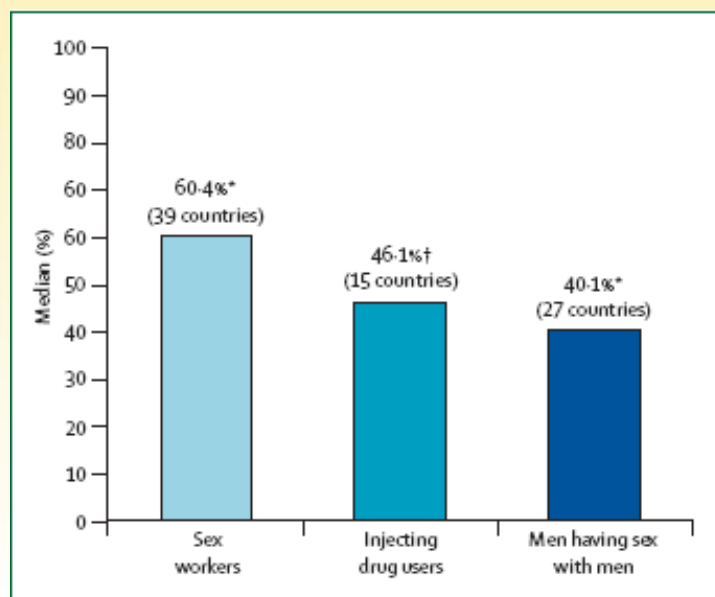
"If we really want to advance the effectiveness of HIV prevention, we have to disabuse ourselves of the notion that the epidemic can be conquered by a single best intervention."

-Michael Merson and colleagues  
Lancet, 2008

## Pre-Exposure Prophylaxis (PrEP): The way forward

- Compelling NHP data, 6 efficacy trials launched and/or planned
- Challenges:
  - Coordinating trials/data to maximize understanding
  - Maximizing, measuring adherence
  - Minimizing "risk compensation", resistance
  - Next generation studies: new drugs, new dosing schedules
  - Impact on other trials
  - Access

## Proportion of high-risk populations reached with HIV prevention programs



UNAIDS, 2008

## Roadmap of Prevention Sessions

- **Sunday**
  - The Global Epidemic (2-4pm)
  - N'Galy-Mann Lecture (4-6pm)
- **Monday**
  - HIV Transmission (10am -12pm)
  - A Tale of 4 Cities (4-6 pm)
- **Tuesday**
  - PrEP Plenary (8:30 am)
  - HIV Vaccines (10am -12pm)
  - Learning from Negative Trials (4-6pm)
- **Wednesday**
  - HIV Transmission (4-6pm)
  - HIV Vaccines (4-6pm)