

HIV Prevention in Resource Limited Settings

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Outline

- Current Epidemic and Targets for Prevention
- Diagnosis of HIV
- Individual Behavioral Approaches: Risk reduction, condoms, sexual violence and HIV
- Structural Interventions: Prevention of Mother to Child Transmission (PMTCT)
- New Biomedical Tools: Male circumcision, PrEP, ARVs as Prevention

Global HIV Epidemic, 2009

Number of people living with HIV

Total	33.3 million [31.4 million–35.3 million]
Adults	30.8 million [29.2 million–32.6 million]
Women	15.9 million [14.8 million–17.2 million]
Children (<15 years)	2.5 million [1.6 million–3.4 million]

People newly infected with HIV in 2009

Total	2.6 million [2.3 million–2.8 million]
Adults	2.2 million [2.0 million–2.4 million]
Children (<15 years)	370 000 [230 000–510 000]

AIDS deaths in 2009

Total	1.8 million [1.6 million–2.1 million]
Adults	1.6 million [1.4 million–1.8 million]
Children (<15 years)	260 000 [150 000–360 000]

Global prevention efforts: Positive results

- World-wide incidence has declined 19% between 1999 and 2009
- Incidence has declined >25% in 22 countries in sub-Saharan Africa
- Behavioral change is the most important factor accounting for these declines
- Drops in HIV incidence correlate with
 - increased condom usage
 - delayed sexual debut
 - reductions in multiple partnerships

ABCs of HIV Prevention



Botswana

HIV Prevention: UN AIDS 2010

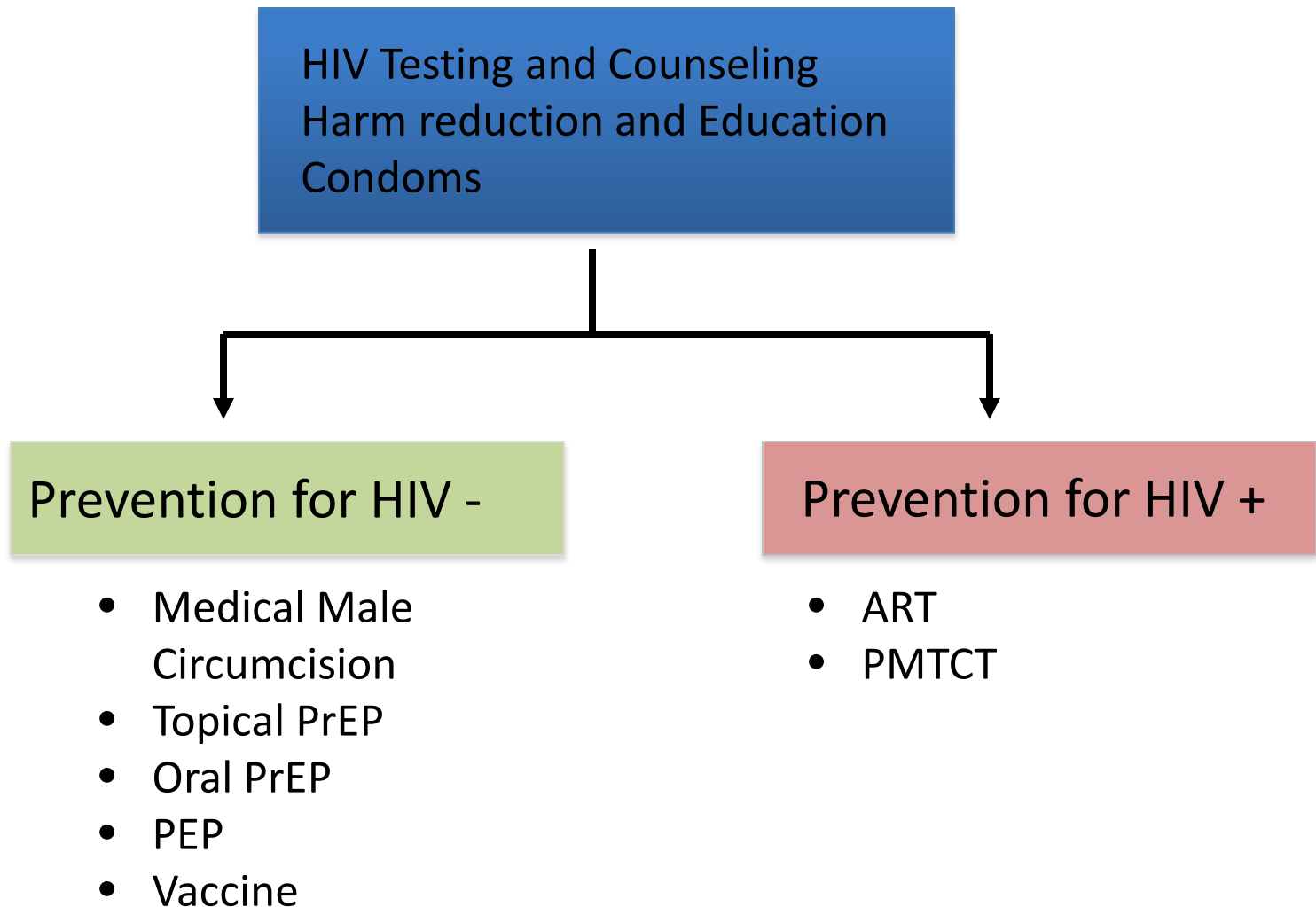
- Prevent sexual transmission
- Prevent maternal death and MTCT
- Provide access to ART
- Prevent people with HIV from dying with TB
- Empowerment and access to care for MSM, sex workers, TG people
- Meet the needs of women and girls, stop sexual and gender based violence
- Enhance social protection for people living with HIV
- Empower young people to protect themselves from HIV
- Remove punitive laws, practices, policies, stigma, and discrimination

Prevention: Key Populations

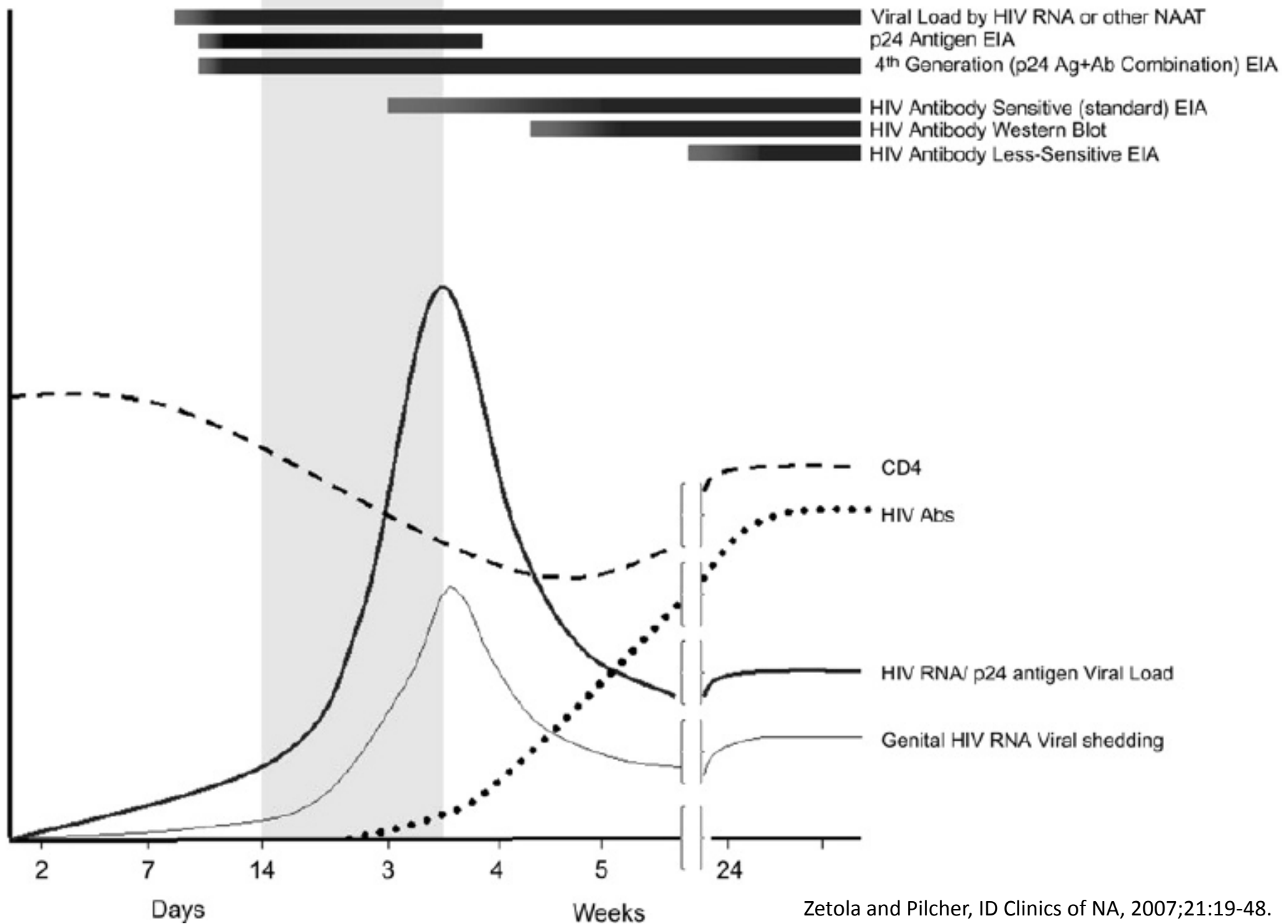
- Children and orphans
- Men who have sex with men
- Women and girls
- Indigenous people
- Migrant workers
- Prison settings
- People living with HIV
- Refugees and IDPs
- Rural communities
- Sex workers
- IV drug users
- Uniformed services
- Young people
- Educators and workforce

HIV Prevention 2011

Interventions by knowledge of HIV status



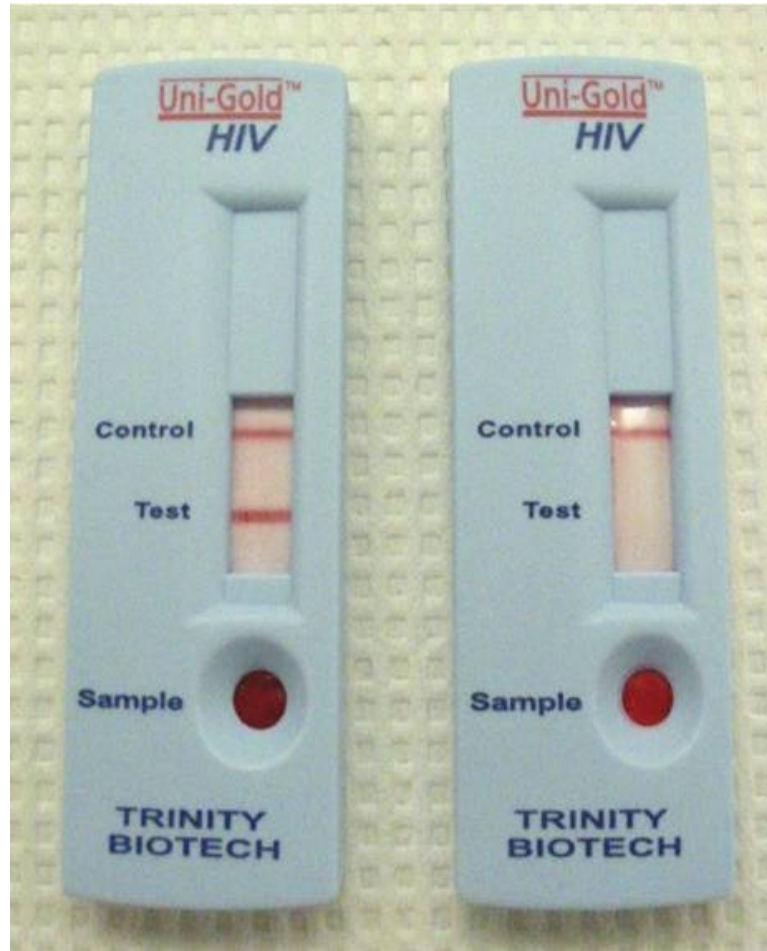
HIV Diagnosis



Rapid HIV 1/2 Antibody Tests



Insert device, test develops in 20 minutes



Read results in 10-12 minutes

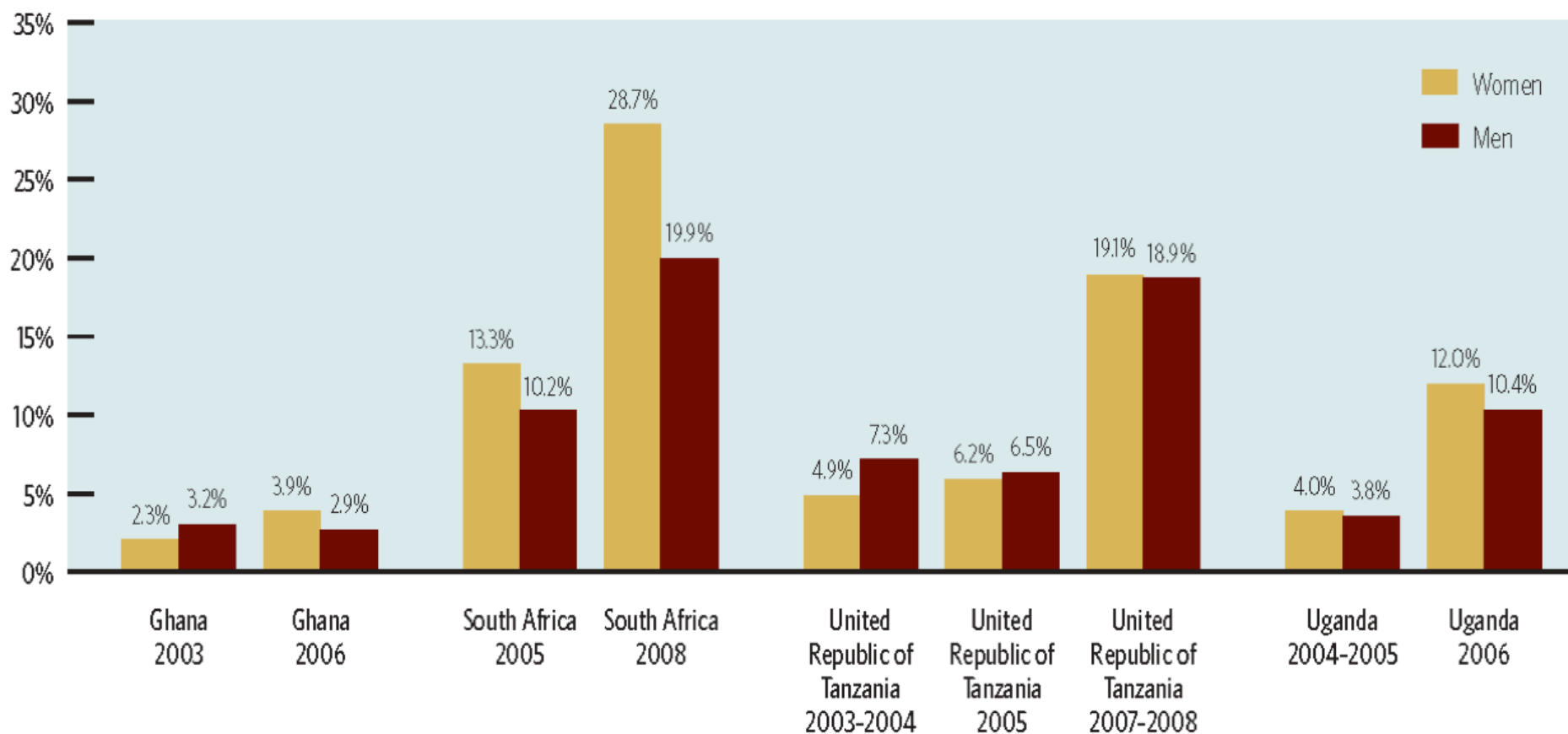
Rapid HIV Tests

	Sensitivity (95% C.I.)	Specificity (95% C.I.)
<hr/>		
OraQuick Advance		
- whole blood	99.6 (98.5 - 99.9)	100 (99.7-100)
- oral fluid	99.3 (98.4 - 99.7)	99.8 (99.6 – 99.9)
- plasma	99.6 (98.5 - 99.9)	99.9 (99.6 – 99.9)
Uni-Gold Recombigen		
- whole blood	100 (99.5 – 100)	99.7 (99.0 – 100)
- serum/plasma	100 (99.5 – 100)	99.8 (99.3 – 100)

Behavioral Strategies for Prevention

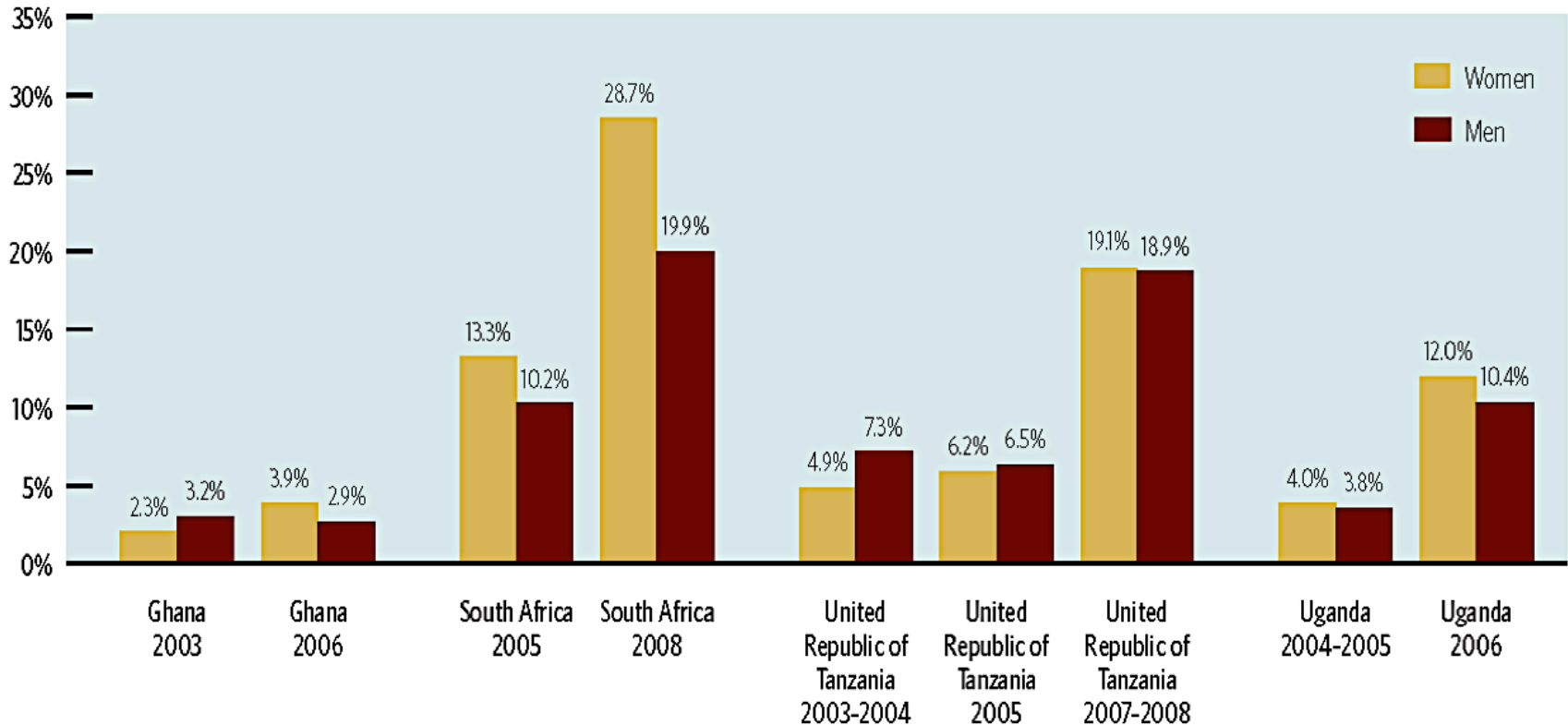
- Voluntary testing and counseling
- Risk Reduction
 - Condoms
 - Decreasing number of sexual partners
 - False security of “serial monogamy”
 - Dangers of concurrent partnerships
 - Occupational Hazards: sex workers, truck drivers, soldiers
 - Intimate partner violence: peer support
 - Harm reduction programs for IVDUs
 - Needle exchange, education, drug treatment

Percentage of women and men receiving an HIV test and results in the 12 months preceding the survey in countries with repeat population surveys, 2003–2008



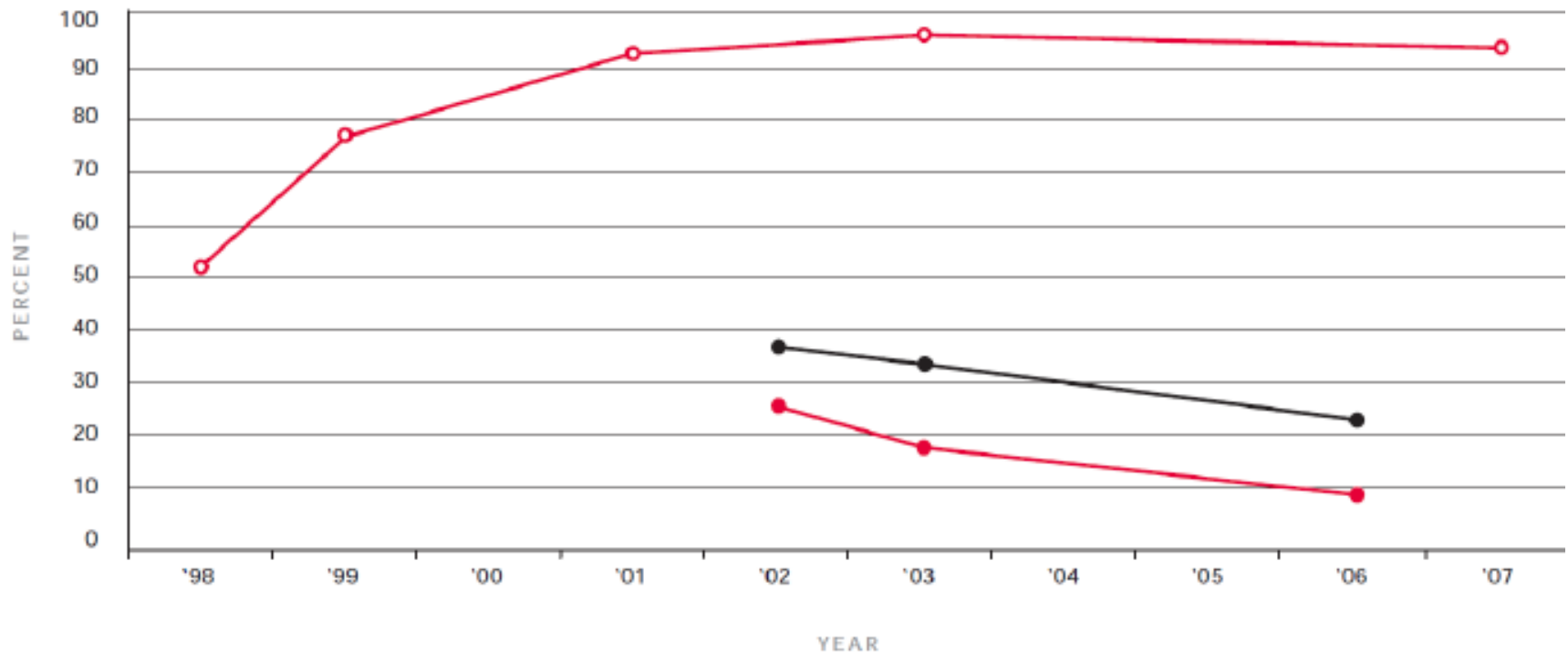
Source: Demographic and Health Surveys.

Comprehensive knowledge of HIV (2007-2008) Women and men age 15-49



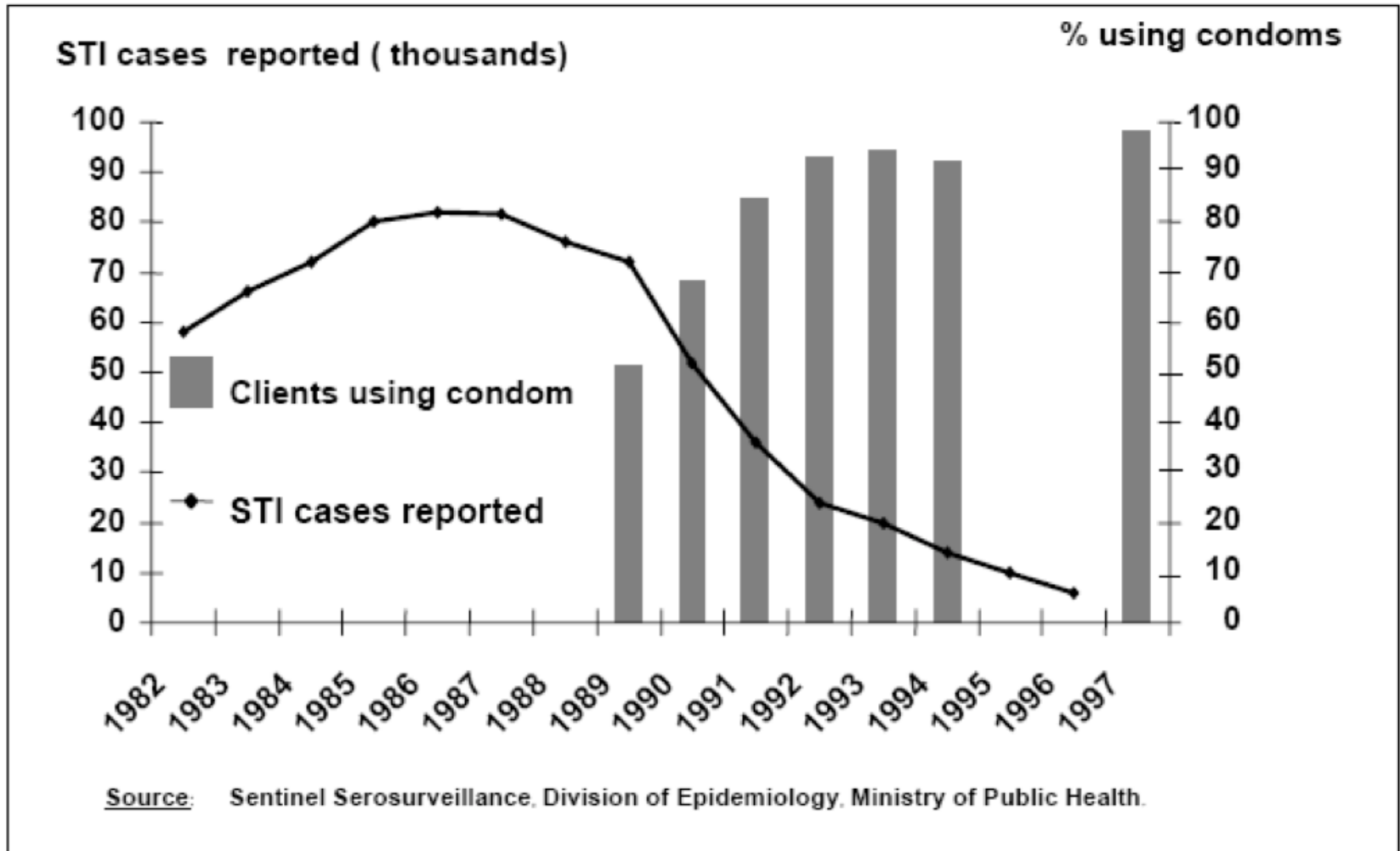
Source: Demographic and Health Surveys.

Condom usage and HIV prevalence: Sex workers in Cambodia



- HIV prevalence among women working less than 1 year at brothel
- HIV prevalence among women working less than 2 years at brothel
- Percent of sex workers reporting condom use at last sex

Success in Thailand



Concomitant with decreased STIs, HIV prevalence declined in high risk groups and pregnant women


PMTCT: Perinatal HIV in the US

- Prior to 1994: transmission rates 20-25%
- Current transmission rates: <2%
- 6,000-7,000 HIV+ women deliver/year
 - Status of most are known by delivery
 - HAART recommended for all regardless of CD4
 - Elective cesarian section if VL>1000
 - 10-12% receive little or no prenatal care
- < 100 infants infected in 2009

PMTCT: Resource-Limited Settings

- Worldwide 2.2 million HIV+ women deliver/year
- 370,000 new infections in children each year
 - Most due to mother-to-child transmission
 - Transmission rates 25-40% without ARVs
 - With ARVs peri-partum transmission 8-10%
 - Transmission rates at 18-24 months 15-25%
 - Breastfeeding accounts for $\frac{1}{3}$ to $\frac{2}{3}$ transmissions

Studies Shown to Prevent MTCT

	<u>AP</u>	<u>IP</u>	<u>PP</u> (baby, mother or both)	HIV+ rate
	14 ↓ wks	28 ↓ wks	36 ↓ wks	3d to ↓ 1 wk
				6 ↓ wks
				6 wks+
PACTG 076				8.3%
Thai (Harvard)				6.5%
Thai (Harvard)				4.7%
Thai (Harvard)				8.6%
IvC (ANRS), PETRA				15.1%, 5.7%
Thai (CDC), IvC (CDC)				8.3%, 16.5%
PETRA, 012, SAINT				8.9%, 11.9%, 9.3%
NVAZ				15.3%

Regimens:

AZT; AZT+3TC; single dose (SD) NVP; AZT + SD NVP

Post-partum HIV infection

- Increased morbidity and mortality with mixed feeding (formula or cow's milk)
- Exclusive breast milk recommended for 1st 6 months
- Post-natal infection occurs in 16% of all breastfeeding infants by 24 months
- PEPI trial, Malawi
 - Extended infant prophylaxis 14 weeks post-partum
 - Advantage lost by 9-15 months

WHO Guidelines: PMTCT

- Women who meet criteria for treatment
 - start ART irrespective of gestation age and continue through delivery: life-long therapy
 - CD4 <350 cells/ μ L
 - CD4 > 350 cells, symptomatic (WHO stage 3 or 4)
- Women who do not meet criteria for HAART
 - Antepartum AZT + single dose NVP
 - AZT + 3TC x 1 week
- ARV prophylaxis either to mother or infant while breastfeeding

PMTCT transmission coverage in low and middle income countries, December 2008

Geographical region	Reported number of pregnant women living with HIV receiving ARVs for PMTCT	Estimated number of pregnant women living with HIV needing ARVs for PMTCT	Prevention of mother-to-child transmission coverage
Sub-Saharan Africa	576 800	1 280 000	45%
Latin America and the Caribbean	17 100	32 000	54%
East, South and South-East Asia	21 700	85 000	25%
Europe and Central Asia	12 600	13 400	94%
North Africa and the Middle East	<200	13 400	1%
Total	628 400	1 400 000 [1.1–1.7 million]	45% [37–57%]

Prevention of HIV in Women

- Sub-Saharan Africa: 57% of people living with HIV are women
 - Population study in Uganda:
 - Women > men risk of incident HIV infection
 - Men > women with sexual partners outside marriage
 - Risk of marriage: 2.0 infections per 100 person years
 - Never married individuals: 0.7 infections per 100 person years

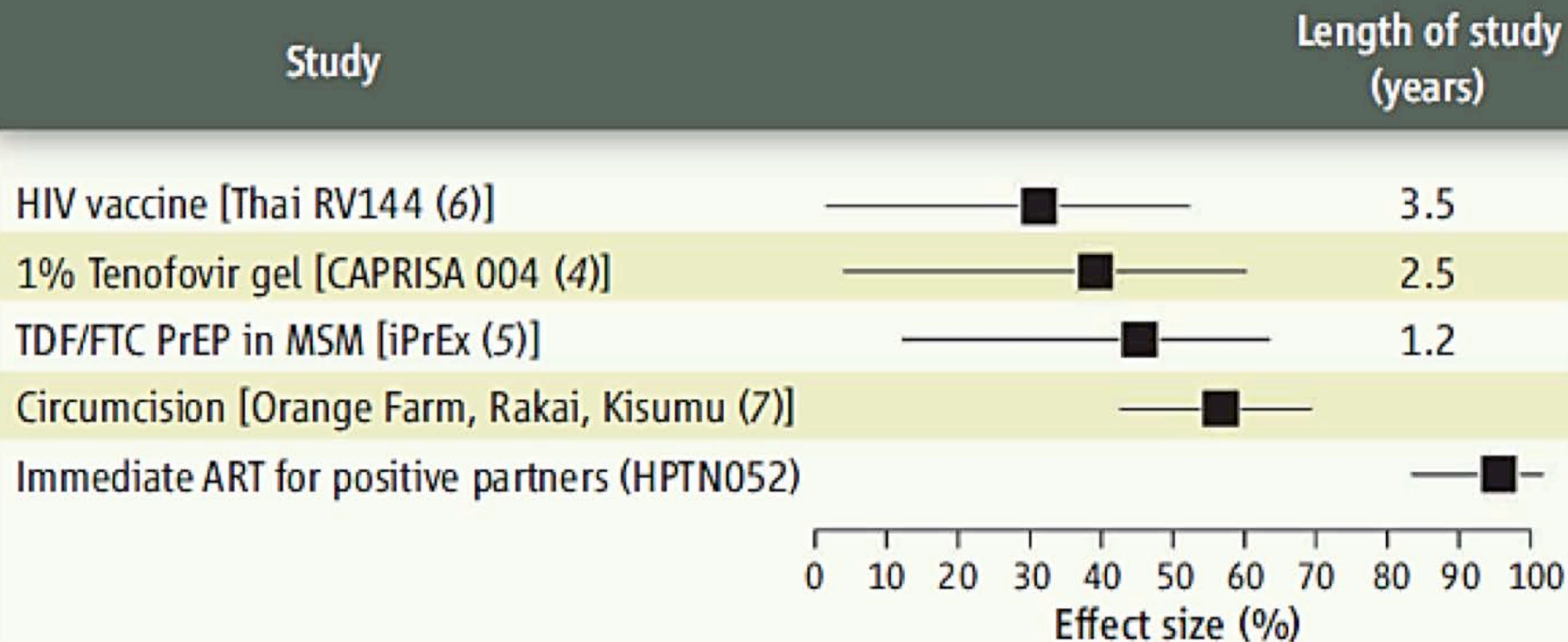
Special Considerations: Trauma and Sexual Violence

- 6-46% of women experienced attempted or completed forced sex by an intimate partner
- Rwanda:
 - HIV+ pregnant women risk of IPV 2x that of HIV-
 - Risk for IPV in pregnancy associated with sexual abuse prior to 14 yrs of age
 - 150-200K women infected with HIV as a result of rape in 1994 genocide

Victims of trauma, sexual violence

- Prophylactic treatment for STIs (syphilis, gonorrhea, chlamydia, chancroid, trichomonas)
- Consider post-exposure prophylaxis for HIV
 - No conclusive evidence regarding efficacy
 - PEP not widely available
 - Treatment with 2-3 ARVs for 28 days
- Hepatitis B vaccine within 14 days if possible
- Tetanus vaccination if tears, abrasions

Biomedical Prevention of HIV



Male Circumcision (MC) as HIV Prevention

- Meta-analysis in SSA: aRR 0.42 (CI 0.34-0.54) for heterosexual acquisition of HIV in circumcised males
- No prevention of transmission from men to women
- Unclear if benefit in MSM
- Increased risk of transmission during healing

2006: Potential Impact of MC on HIV in Sub-Saharan Africa

- Modeling: over the next ten years in SSA, MC could avert:
 - 2.0 (1.1-3.8) million new HIV infections (men and women)
 - 0.3 (0.2-0.5) million deaths (men and women)
- In the ten years after, MC could avert:
 - 3.7 (1.9-7.5) million new HIV infections
 - 2.7 (1.5-5.3) million deaths
- 2006: Cost effectiveness in South Africa
 - Cost per HIV infection averted: \$181
 - 3 circumcisions → 1 averted HIV infection

Roll out of MC in 9 countries

	Number circumcised	Time period	Number of sites established
BOTSWANA	6 180	April 2009 – March 2010	35
KENYA	91 300 (90 000 in Nyanza alone)	2009 – June 2010	
NAMIBIA	350	September 2009 – June 2010	3
RWANDA	542	October 2009 – April 2010	9
SWAZILAND	10 000	2008 – June 2010	
UGANDA	5 340	October 2008 – March 2010	
UNITED REPUBLIC OF TANZANIA	4 700	September 2009 – May 2010	3
ZAMBIA	9 906 10 000 9 179	January – June 2010 2009 2007 – 2008	56
ZIMBABWE	6 070	May 2009 – April 2010	5

MC: Attitudes and Behaviors

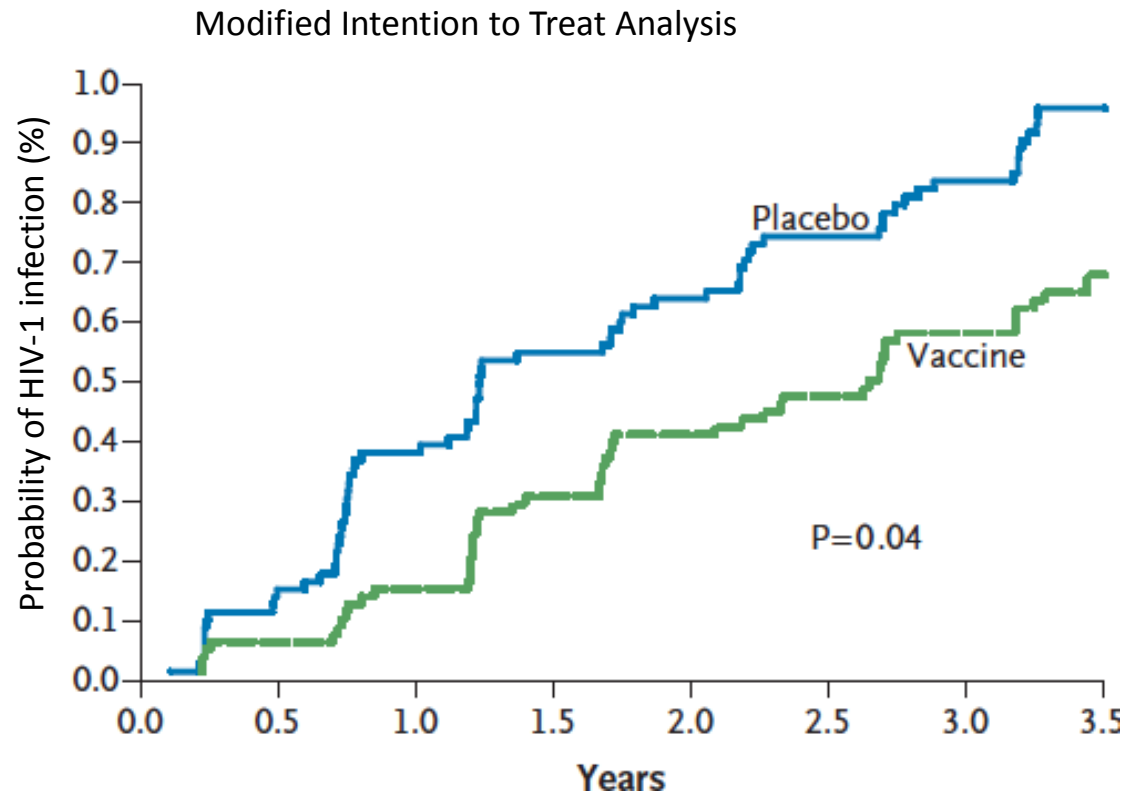
- 2008: Botswana, Namibia, Swaziland
 - Nearly half of men planned MC
 - 2/3 of men and women planned to have male children circumcised
 - Inaccurate beliefs/perceptions of MC
 - 9-15%: circumcised male fully protected from HIV
 - 20-26%: no HIV test needed before MC
 - 14-26%: circumcised HIV+ men cannot transmit HIV
 - 8-34%: OK for circumcised male to expect sex w/o condom

Behavioral Change and Risk after MC

- Multi-site qualitative study, Swaziland
- Positive behaviors following MC
 - More responsible attitudes towards safe sex
 - Reducing number of sexual partners
 - Easier condom usage
- Risky behaviors following MC
 - Expressed in a minority of interviews
 - Period of sexual experimentation
- HIV counseling through MC critical to views

Thai HIV Vaccine Trial: ALVAC and AIDSVAX

- MITT: **31.2% efficacy**
- Low-moderate risk population
- Duration of effect?
- Insight into host immune response
- Correlates of protection?



Microbicides: female controlled chemical barrier

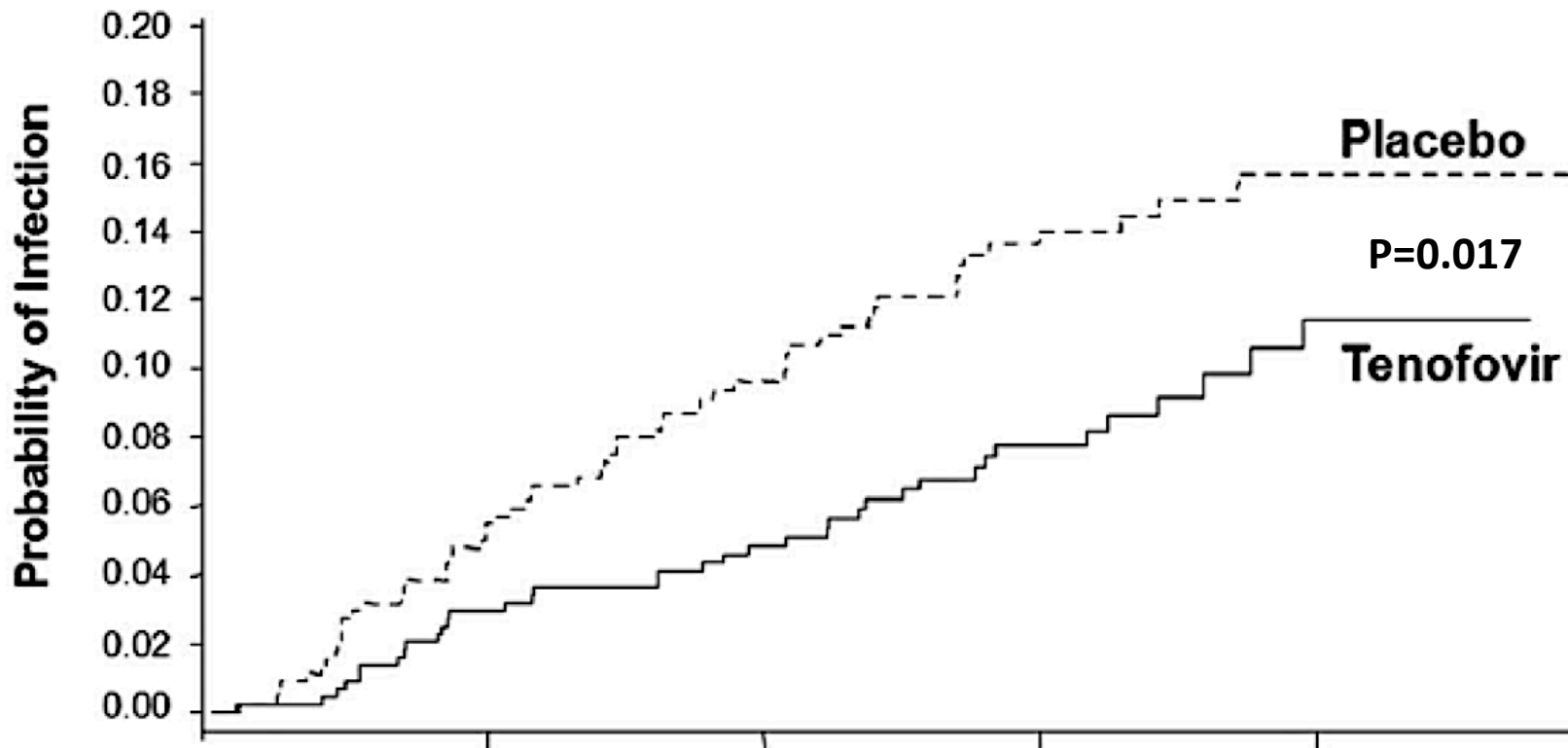
- Nonoxynol-9
 - HIV incidence: N-9 16% vs Placebo 12%
 - 3+ uses of N-9 per day **increased HIV 1.8x**
- Cellulose sulfate: S. Africa, Benin, Uganda, India
 - 1425 enrolled, stopped early 2007: HR 2.02 (p=0.05)
 - Final analysis: **cellulose sulfate HR 1.61 (p=0.13)**
- Carraguard Phase III trial, South Africa
 - HIV incidence 3.3 per 100 woman years in Carraguard group vs. 3.8 per 100 woman-years in placebo
 - **No statistical difference**

Van Damme, Lancet 2002

Van Damme, NEJM 2008

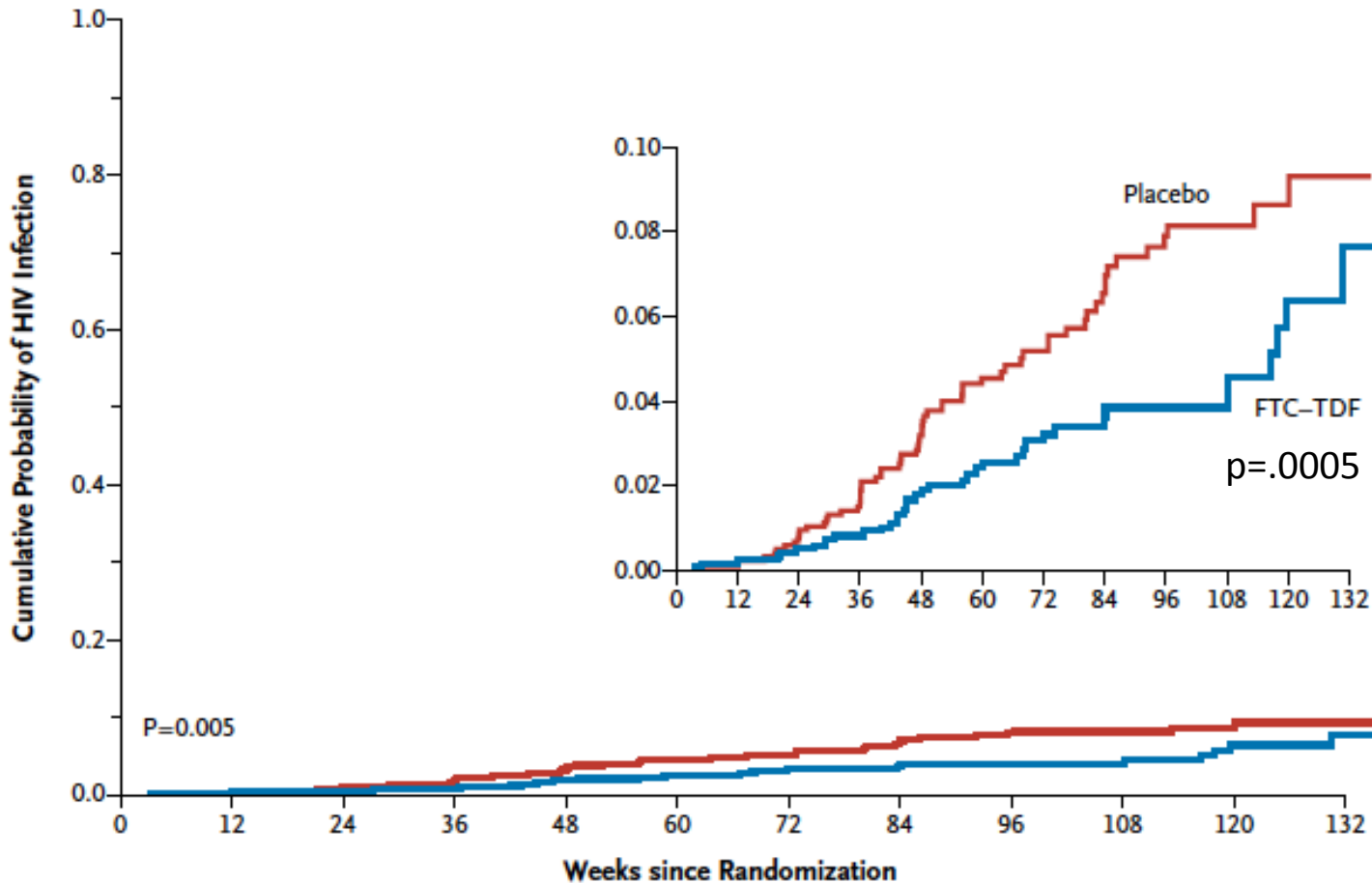
Skoler-Karpoff, Lancet 2008

CAPRISA: Topical 1% Tenofovir gel



- **39% reduction** in HIV acquisition
- No increased adverse events
- No TDF resistance in seroconverters

iPrEx: Tenofovir-Emtricitabine (TDF-FTC) pre-exposure prophylaxis in HIV-neg MSM



44% reduction in incidence of HIV infection

Fem-PrEP: TDF-FTC in women

- Tenofovir-emtricitabine vs. placebo in Kenya, South Africa, Tanzania
- 1951 women enrolled, 95% adherence reported
- Study stopped early (Feb 2011)
- Equal number of new HIV infections in TDF-FTC and placebo groups
- Data analysis ongoing
 - Adherence?
 - Giving away/selling pills?
 - Differences in tissue levels of drug?

HPTN052: Early vs delayed ART for HIV-1 infection prevention

- HIV- infected individuals in stable serodiscordant couples randomized to early ART (CD4+ 350-550 cells/ μ L) vs delayed (CD4+ <250 cells/ μ L)
- Couples attended visits together, received risk reduction counseling, condoms
- Early ART: **relative reduction 96%** in linked HIV-1 transmissions

Challenges

- Resistance to ARVs used in PMTCT/PrEP
- How to supply PrEP when 50% of those with HIV infection and indication for treatment are not receiving treatment
- Long-term toxicities from PrEP
- Adherence to PrEP
- Vaccine development
- Evaluation of combination approaches
- Hormonal Contraception and HIV prevention
- Behavioral compensation?

Summary

- HIV testing is feasible in resource limited settings and is integral to prevention
- PMTCT is essential
- Circumcision is a viable method that should become an accepted part of prevention programs

Summary

- Condoms, education, and risk reduction are integral parts of HIV prevention programs
 - Oversimplified “ABCs” may not adequately address needs of community
 - Identify peer education and support groups
 - Victims of sexual violence, marginalized populations: structural interventions
- Successful HIV prevention: Behavioral, Structural, and Biomedical Interventions

Acknowledgements

- Michelle Haas, MD
- David Cohn, MD