

Anal Sex in Microbicide Trials - A Cause for Concern?

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Cape Town, South Africa

MTN Regional Meeting

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Overview

- Background information on anal intercourse (AI)
- How are we monitoring AI in MTN studies
- How might AI impact on the ability to conduct vaginal microbicide studies?
- Rectal use of vaginal products
- What else do we need to do?

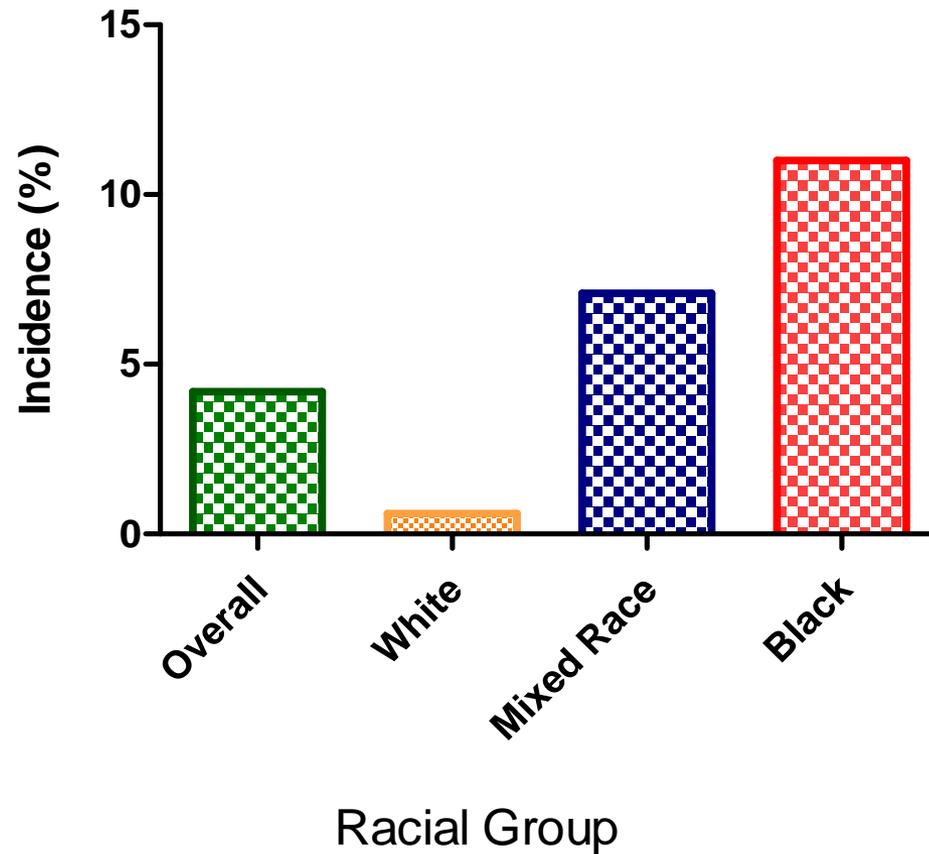
Background Information



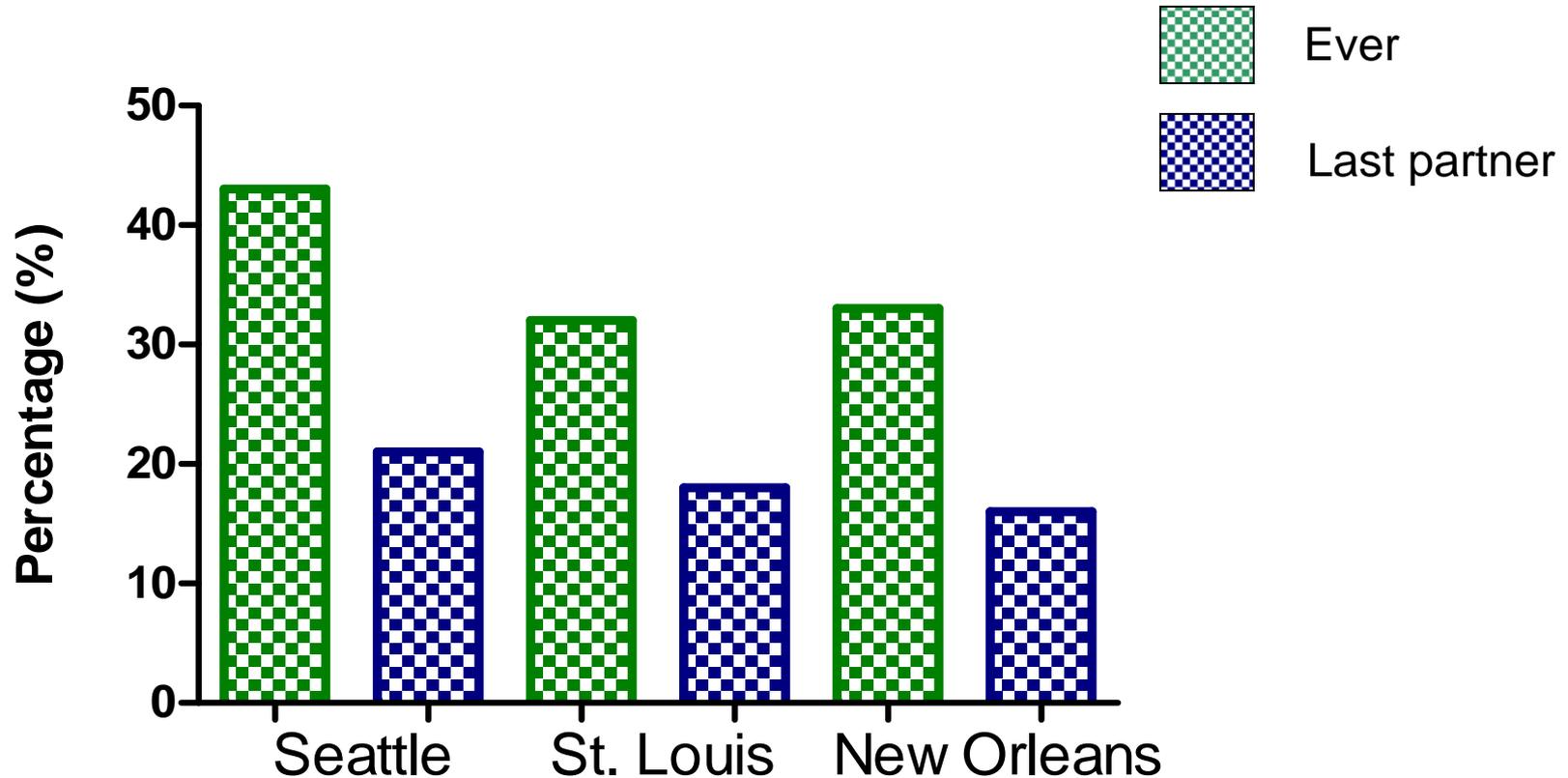
Anal Intercourse (AI)

- Common in MSM populations
- Increasingly recognized in heterosexual population
- AI practiced in developed and developing world populations
- Data collection suboptimal
 - Definitions
 - Frequency
 - Interview method

US HIV Incidence in MSM

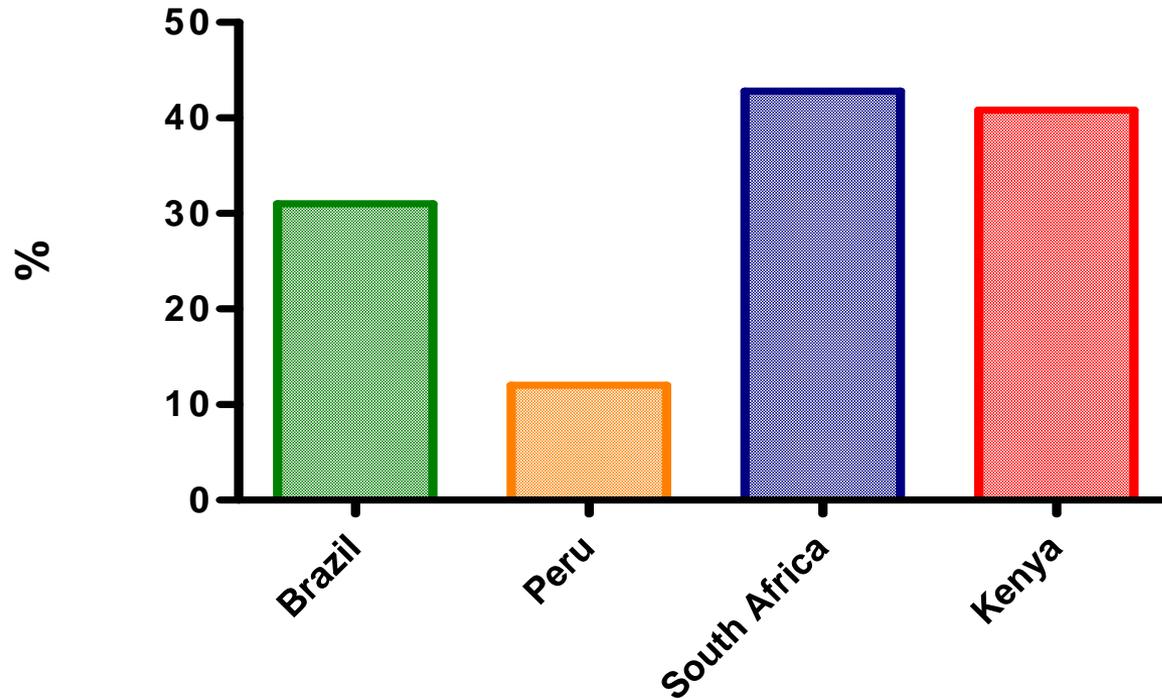


Prevalence of AI in US Women



Gorbach PM et al. Sex Transm Dis, 2009 36(4):193-198.

EX-US Prevalence of Female AI



Brazil: Guimares MD et al. 1995,
Peru: Caceres C et al. 1997,

South Africa: Karim SS and Ramjee G 1998
Kenya: Schwandt M et al. 2006

HIV Among MSM in West Africa

Country	Sample Size	MSM Prevalence (95% CI)	Reproductive Age Male HIV Prevalence
Senegal	943	21.6 (19.0-24.3)	0.7%
Ghana	N/A	25.0%	1.4%
Nigeria	1961	13.5 (12.0-15.0)	2.4%
Mauritania	21	19.0% (2.0-36.0)	1.2%
Cote D'Ivoire	54	18.5%	2.9%

Baral, S. et al. A Systematic Review of HIV epidemiology and risk factors among MSM in Sub-Saharan Africa 2000-2008. International AIDS Conference, Mexico City, 2008



HIV Among MSM in Southern Africa

Country	Sample Size	MSM Prevalence (95% CI)	Reproductive Age Male HIV Prevalence
South Africa	574	15.3 (12.4-18.3)	15.89%
Zambia	641	32.9 (29.3-36.6)	15.72%
Malawi	201	21.4 (15.7-27.1)	11.46%
Namibia	218	12.4% (9.0-17.0)	10.8%
Botswana	117	19.7% (14.0-28.0)	18.1%



HIV Incidence Rates

- African HIV incidence data is available only from Mombasa, Kenya
- Among MSM who report:
 - Insertive sex only
 - 8.8 %/person-year
 - Receptive sex only
 - 12.9 % per person-year
 - Both receptive and insertive sex it is
 - 20.4 % per person years



Data Capture Issues

- Asking the right questions
- Capturing time frame of sexual behavior
 - Any history of AI
 - Last episode of AI
- Optimal interview technique
 - Face-to-face interviews
 - ACASI



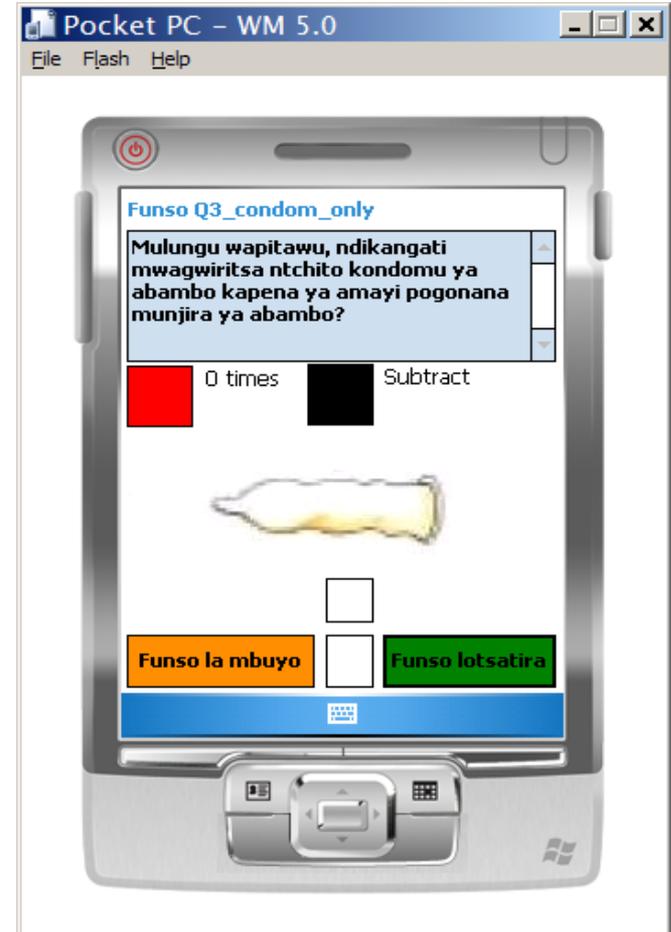
Asking the Right Question

- Males - “In the past 12 months, with how many males have you had anal or oral sex?”
- and “With how many of these males have you had only oral sex? ”
- “In the past 12 months, about how many times have you had vaginal or anal sex?”
- “In the past 12 months, about how often have you had vaginal or anal sex without using a condom?”

Time Frame for Reported AI

	Last Anal Sex	Last Week (7 days)	Past 2 weeks	Past Month (30 days)	Past 3 months (90 days)	Since last visit	Ever AI
Carraguard				X	X	X	
IPM			X				
Cellulose Sulfate		X		X			
MTN-004					X		
HPTN-059	X	X		X			X
HPTN-035	X	X			X		X
MTN-003					X		

Interview Techniques



Data on AI: FTFI versus ACASI

	PC Study (Enrollment/Month1)			HPTN 035B		
	FTFI (%)	ACASI (%)	Sig.	FTFI (%)	ACASI (%)	Sig.
> 1 partner	1.7 <i>(last month)</i>	14.0	***	0.0 <i>(last 3 months)</i>	1.0	*
Anal sex	1.9 <i>(last month)</i>	7.8	***	0.2 <i>(last 3 months)</i>	4.8	***

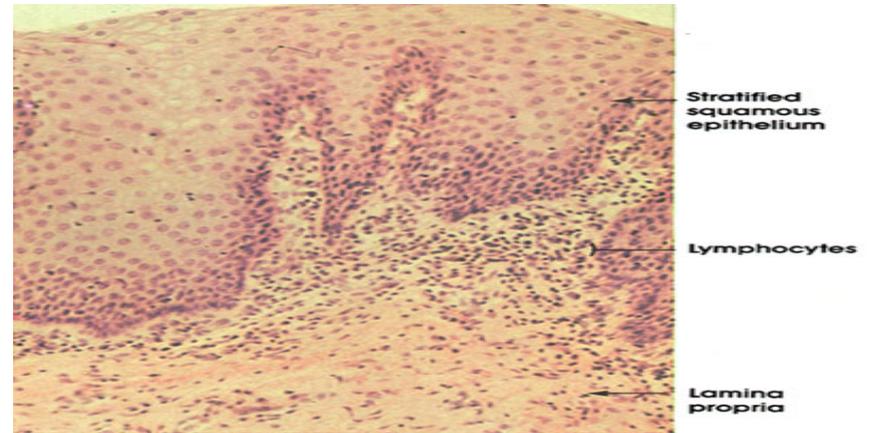
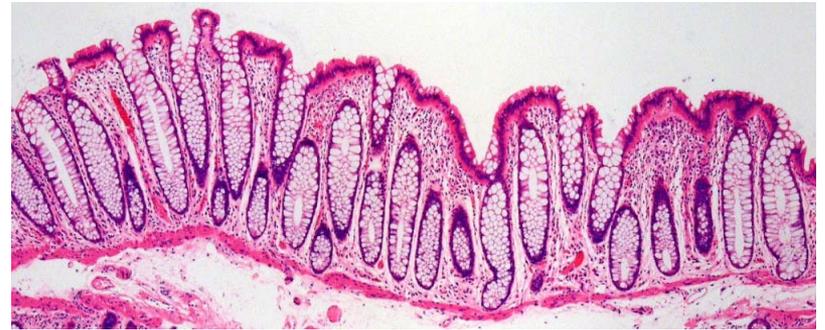
*** p<.001; * p<.05;

Rectal Use of Vaginal Products

Rectal and Vaginal Mucosa

- Histology
- Immunology
- Microbiology

- Differential susceptibility to candidate microbicides



Impact of AI on the Ability to Conduct Vaginal Microbicide Studies?



AI in Vaginal Microbicide Trials

- Vaginal microbicide trials are designed to test the hypothesis that use of a vaginal product would result in reduced HIV acquisition in a “high risk” population.
- This assumes that HIV infection is acquired vaginally
- But what if.....



Alternative Routes of HIV Acquisition

- Anal intercourse
 - Increasing epidemiological evidence that both men and women practice RAI in developed and developing world settings
 - RAI is 20-80 times more efficient than vaginal intercourse in acquiring HIV infection
- Intravenous drug use
 - Not a major problem in Sub Saharan Africa but might be an issue in Eastern Europe



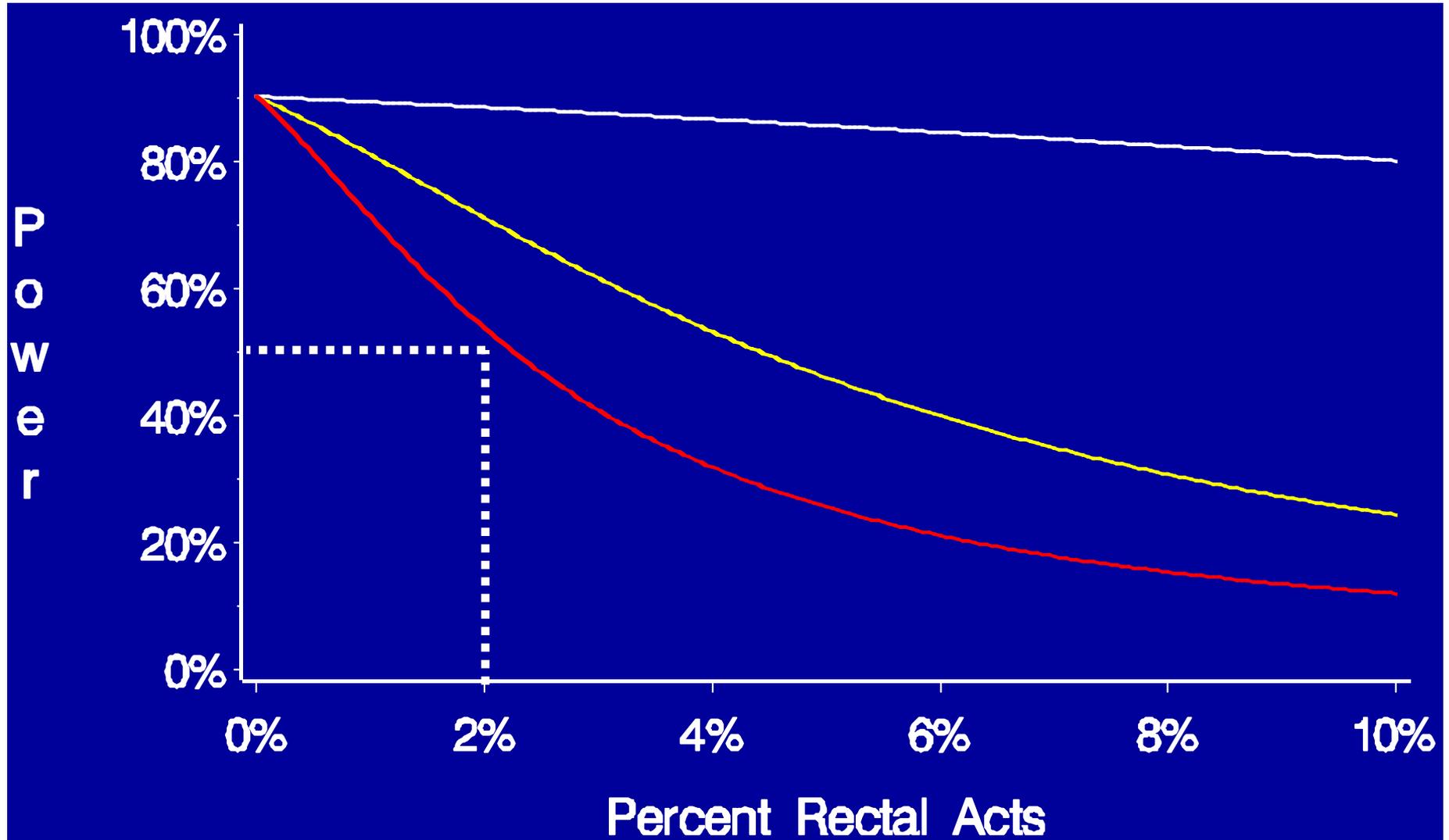
Anal Intercourse in VM Trials

- COL 1492
 - Prior history of anal intercourse was reported to range from 41% among sex workers in Durban, South Africa to less than 5% in Thailand
- HPTN-035
 - Ever had anal sex: 5%
 - Anal sex in the last week: 1%
- CAPRISA 004
 - Baseline rate: 0.4%

Modeling Impact of AI in VM Studies

- Mathematical model looking at the impact of RAI in vaginal microbicide trials
- Definitions
 - Transmission probability of vaginal sex (T_V)
 - Transmission probability of rectal sex (T_R)
 - Apparent effectiveness of vaginal microbicide (E_A)

$$E_A = 1 - \frac{(1 - \text{efficacy} \times U_M) T_V P_V + T_R (1 - P_V)}{T_V P_V + T_R (1 - P_V)} = 1 - \frac{(1 - E_V) P_V + (T_R / T_V) (1 - P_V)}{P_V + (T_R / T_V) (1 - P_V)}.$$

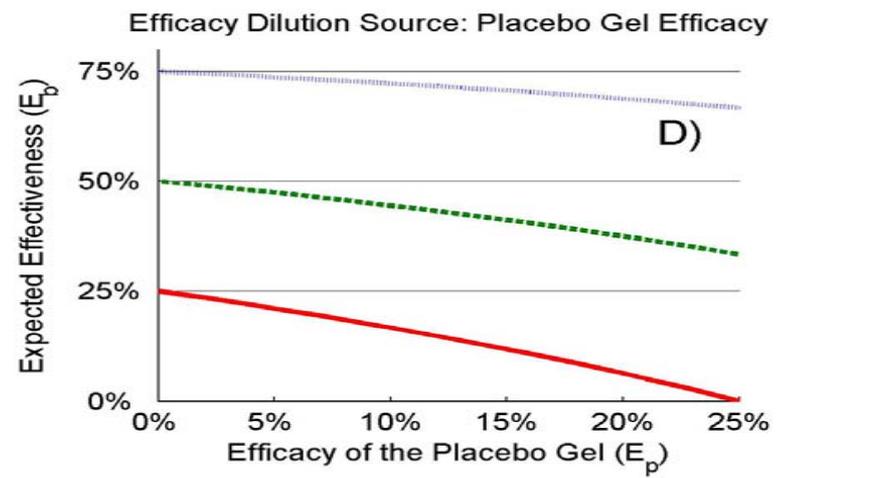
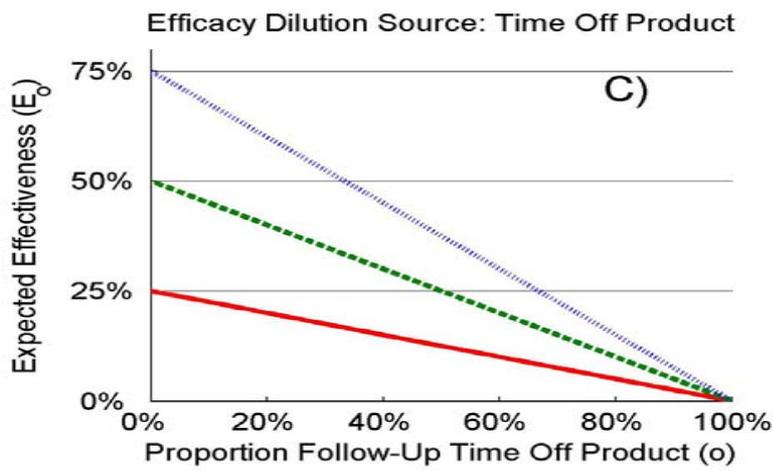
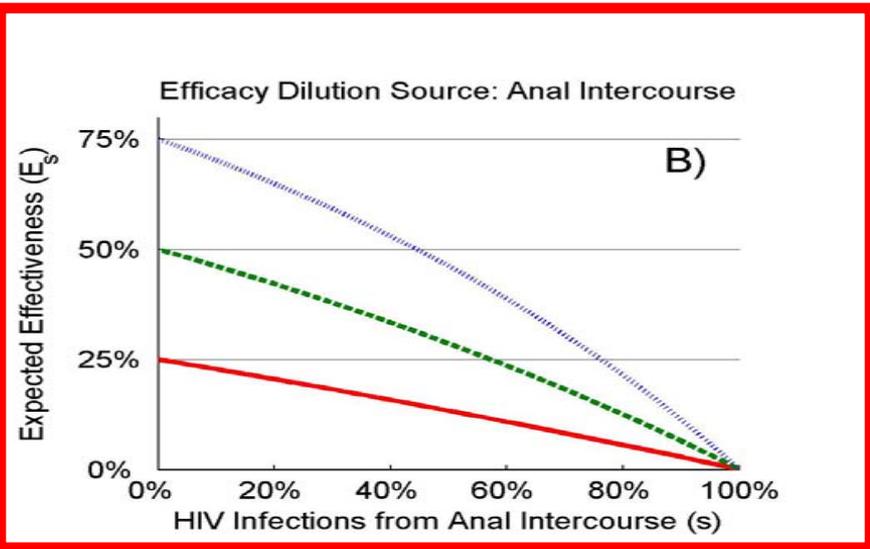
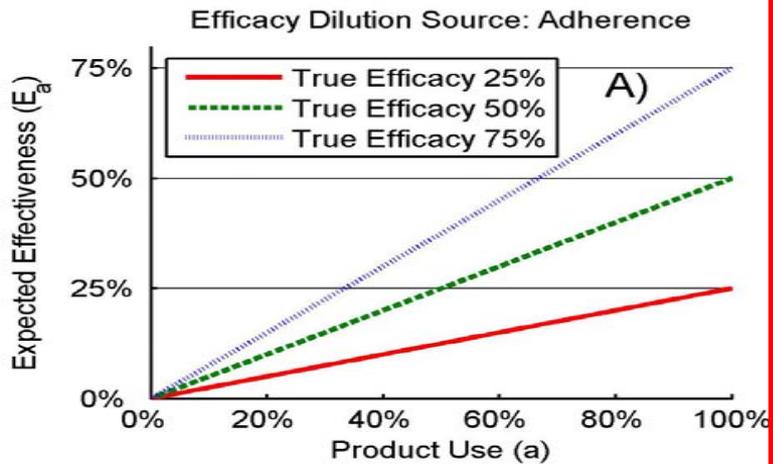


Transmission Probability

1X

10X

20X





What Else do We Need to
Do?



Next Steps

- Exclude participants from Phase 2B/3 vaginal microbicide trials with a history of RAI?
- Counsel participants not to practice RAI in vaginal microbicide trials
- Conduct Phase 1 rectal safety trials of vaginal microbicides

Rectal Safety of Vaginal Microbicides

Product	Status	Timeline	Sponsor
UC-781	Completed		DAIDS
RMP-02 /MTN-006	Enrolling	Q3 2009	DAIDS
MTN-007	Planned	Q1 2010	DAIDS
VivaGel	Planned	Q3 2010	NICHD
PRO-2000	Planned	Q1 2010	MRC-UK
Dapivirine	Planned	?	IPM



U.S. Department of Health and Human Services

NIH News

National Institutes of Health

“For this reason, NIAID places a priority on developing HIV prevention tools that women can implement independently. One such method under study is a microbicide—a gel, cream or foam intended to prevent the sexual transmission of HIV when applied topically inside the vagina or **rectum**.

Statement of Anthony S. Fauci, M.D.

Director, National Institute of Allergy and Infectious Diseases

National Institutes of Health on National Women and Girls HIV/AIDS

Awareness Day

March 10, 2009



Microbicide Safety in Young Men

- NICHD R01
 - Pittsburgh, Boston, Puerto Rico
- Phase 1 safety and acceptability of VivaGel™
 - Ethnically diverse MSM (18-30)
 - Consensual RAI in last month
 - Unprotected RAI in last year



Rectal Specific Products

- CHARM Program
 - Combination HIV Antiretroviral Rectal Microbicide Program
 - DAIDS IPCP Program
 - Consortium
 - University of Pittsburgh
 - UCLA
 - Johns Hopkins
 - UNC
 - CONRAD



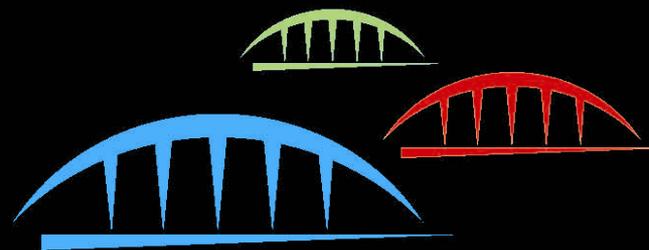
Summary

- RAI occurs in non-MSM populations and in vaginal microbicide trials
- RAI might impact the potential to identify a safe and effective vaginal microbicide
- Participants in Phase 2B/3 vaginal microbicide trials need to be counseled about RAI
- We need to continue to screen the rectal safety of vaginal microbicides
- We need to move towards development of rectal specific and rectal/vaginal combination products

SAVE THE DATE!

May 22-25, 2010
Pittsburgh, Pennsylvania, USA

www.microbicides2010.org



M2010

MICROBICIDES:
Building Bridges
in HIV Prevention



Acknowledgements

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Thank You
