

# **Reflections on the Role of Discordant Couples and the HIV Epidemic**

## **Implementation Science and Male Circumcision in Rakai**

Ron Gray & Maria Wawer  
Johns Hopkins University

# Discordant couples, why are they important?

- If most infections in a population occur in stable discordant couples, universal testing could identify couples at risk and promote:
  - Couples VCT (*Bunnell, Cherutich Lancet, 2008*)
  - Behavioral risk reduction (*Allen et al AIDS 2003*)
  - Use of PreP
  - Initiate ART to prevent transmission (*Dieffenbach, Fauci JAMA 2009, Granich et al Lancet 2009*)

# Premise for focus on discordant couples

*(Gray et al AIDS 2011)*

- A substantial proportion of all transmissions must occur within identifiable discordant dyads
- Can provide couples counseling and mutual disclosure
- Interventions for discordant couples must be efficacious and durable

# How Common are Discordant Couples in DHS surveys?

(Eyawa et al Lancet Infect Dis 2010)

	Discordant % of all couples
Burkina Faso	2.6
Cameroon	5.1
Ethiopia	1.7
Ghana	3.2
Guinea	1.5
Ivory Coast	3.5
Kenya	7.3
Lesotho	13.6
Malawi	9.7
Rwanda	2.2
Tanzania	7.9
Zimbabwe	12.9

Frequency of discordant couples varies from 1.5 to 13.6% of married couples

47% of discordant couples are female HIV+

## **Caveats:**

Only includes couples with both partners identified and tested

Excludes couples with absent partners

# Frequency of Discordant Couples in the Rakai Cohort *(Gray et al AIDS 2011)*

	Pre-ART (N=9434) %	After ART Available (N=13082) %
Not currently Married	36.6	39.4
<b>Currently Married</b>		
Concordant Negative	38.8	39.0
<b>Discordant</b>	<b>1.8</b>	<b>1.8</b>
Unknown partner status	22.8	19.8

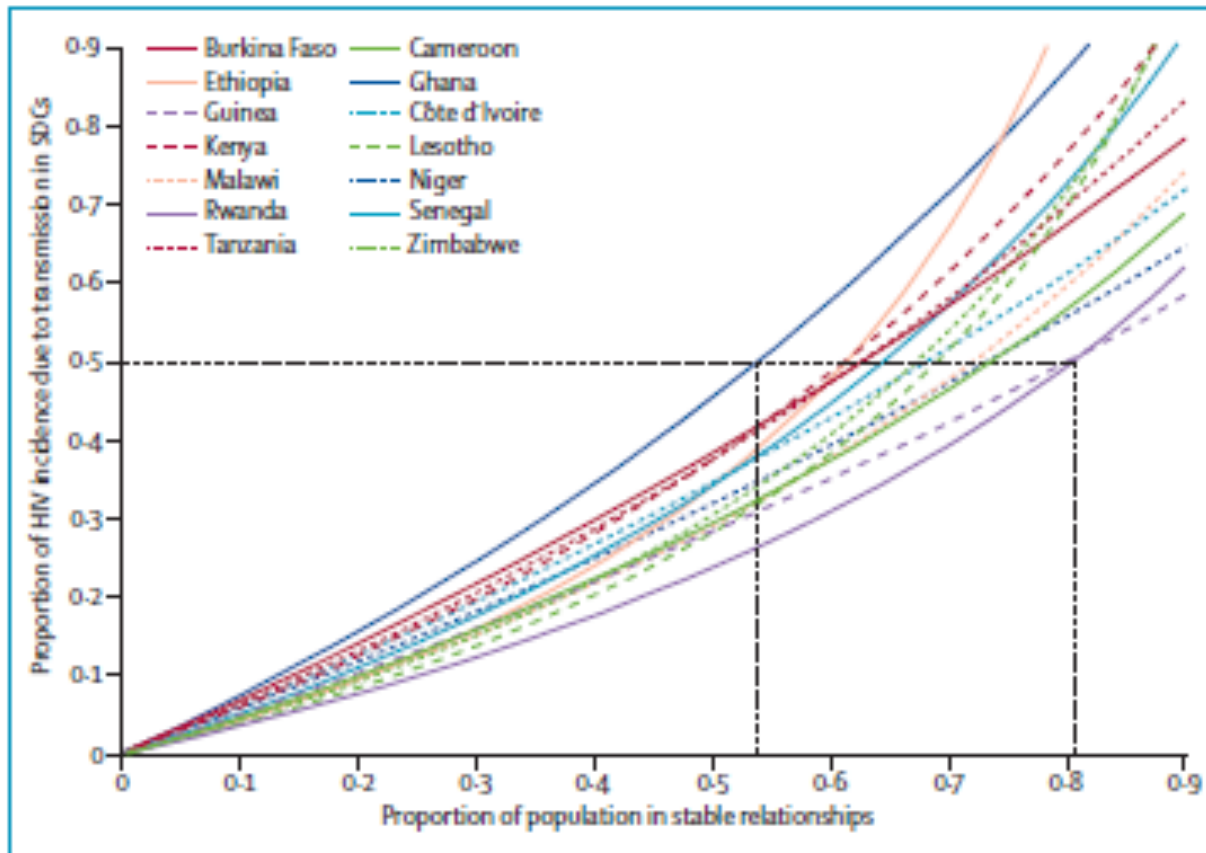
A high proportion of married persons do not have an identifiable partner at time of survey

# Modeling the Contribution of HIV Discordant Couples to the HIV Epidemic

- *Dunkle et al Lancet 2008*
  - Used DHS and VCT data from urban Zambia and Rwanda to model the contribution of stable HIV-discordant couples to the HIV epidemic.
  - Estimated 55-93% of new HIV infections occurred within HIV-discordant couples
- Numerous critiques
  - Overestimated transmission (20% per year)
  - Ignored introduction of infection into the dyad from external partners

# Modeling the Contribution of Discordant Couples to HIV Incidence

(Coburn et al, Lancet Infect Dis 2011)



Contribution of discordant couples to HIV incidence varies by proportion of stable relationships in the population and HIV prevalence

# Contributions of Discordant Couples to HIV Incidence in Rakai, Uganda *(Gray et al AIDS 2011)*

	Pre-ART Availability Proportion of HIV Incident Infection (%)	After ART Available Proportion of HIV Incident Infection (%)
Not married	29.3	42.7
Currently Married		
Concordant HIV-neg	23.2	26.0
<b>Discordant Couples</b>	<b>18.3</b>	<b>13.7</b>
Unknown partner status	29.3	17.6

Only a minority of incident HIV infections occur among identifiable discordant couples



## Conclusion

- Identification of HIV-discordant couples is important, but is unlikely to have a major effect on the epidemic because:
  - Discordancy is a transient state, infectivity is high during acute and recent HIV infection (*Wawer et al JID 2005*)
  - Many HIV+ persons have partners of unknown status
  - Discordant marriages have high rates of dissolution (*Porter et al Demography, 2004*)
  - Most infections occur in unmarried or concordant HIV-negative couples in Rakai
  - Models based on inferred infections may be misleading

# Implementation Science Research on Male Circumcision (MC)



The objective of implementation science is to promote the integration of research findings into policy and practice to improve the uptake, implementation and translation of evidence-based interventions (*Padian et al JAIDS 2011*)

# Implementation Science Research on Male Circumcision (MC)

- Training and achievement of competence
- Task sharing (MOVE)
- Task shifting: Physicians versus clinical officers
- Surgical procedures
  - Sleeve, dorsal slit forceps guided
  - Shang ring, PrePex device
  - Local anesthesia
- Impact:
  - Post-trial effectiveness and risk behaviors
  - Impact of MC on HIV incidence

# MC MOVE: Models for optimizing the volume and efficiency of MC services.

## Task Sharing Dino Rech PSI

- Assistant prepares site and provides local anesthesia
- Surgeon removes foreskin, secures hemostasis and inserts main mattress sutures
- Assistant inserts simple sutures and dressing

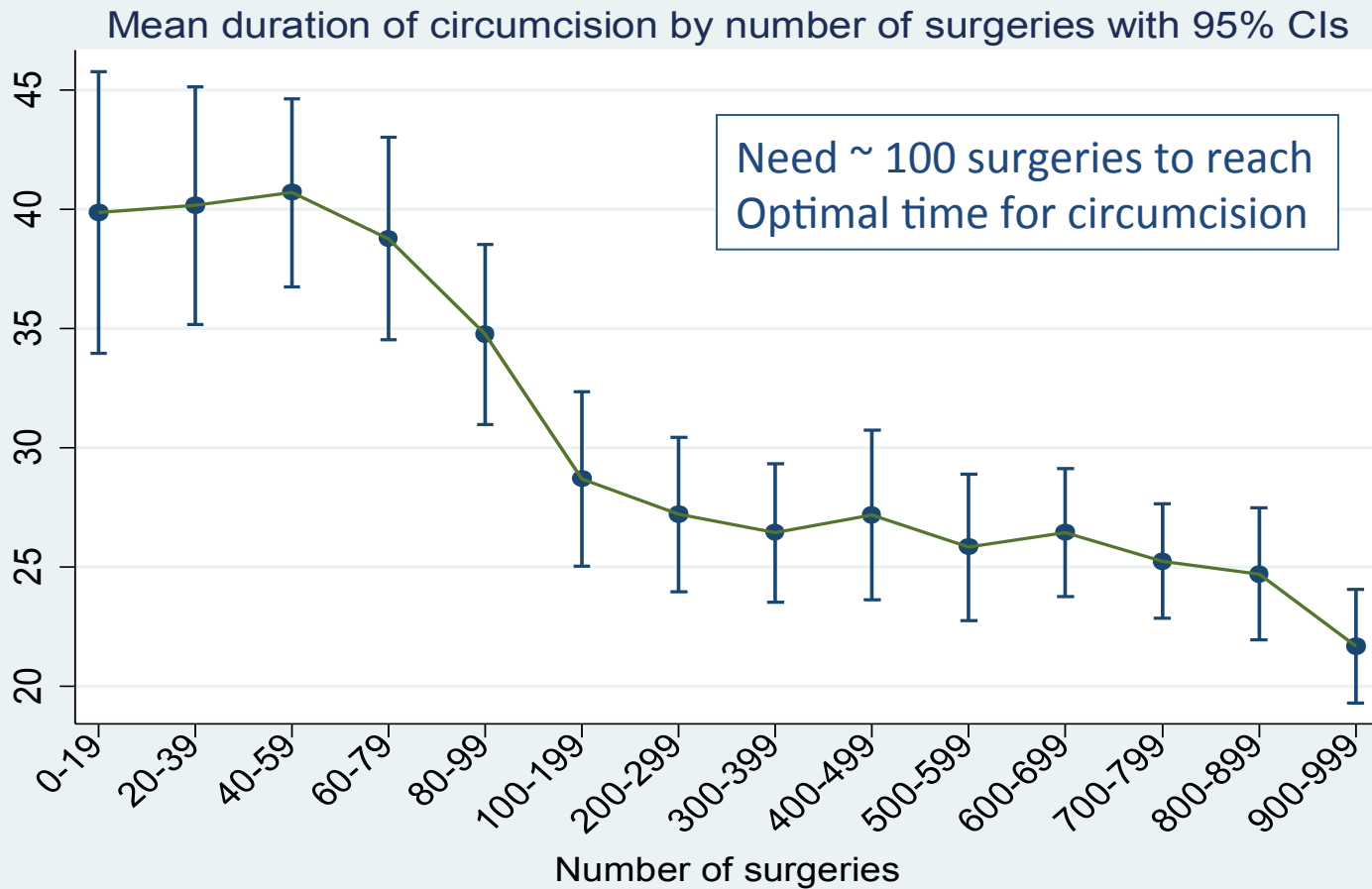
Indicator	Pre-MOVE	MOVE (Sleeve)	MOVE (Forceps Guided)
Doctor Operating Time (Minutes)	25-50 mins	10-20 mins	5-10 mins
# of Clients per hour	1-2/hour	3-5/hour	5-8/hour

## Training and achievement of competence

- All trainees perform 15-20 supervised MCs before certification
- Assessed time required for surgery and moderate/severe adverse events (AEs) by number of surgeries

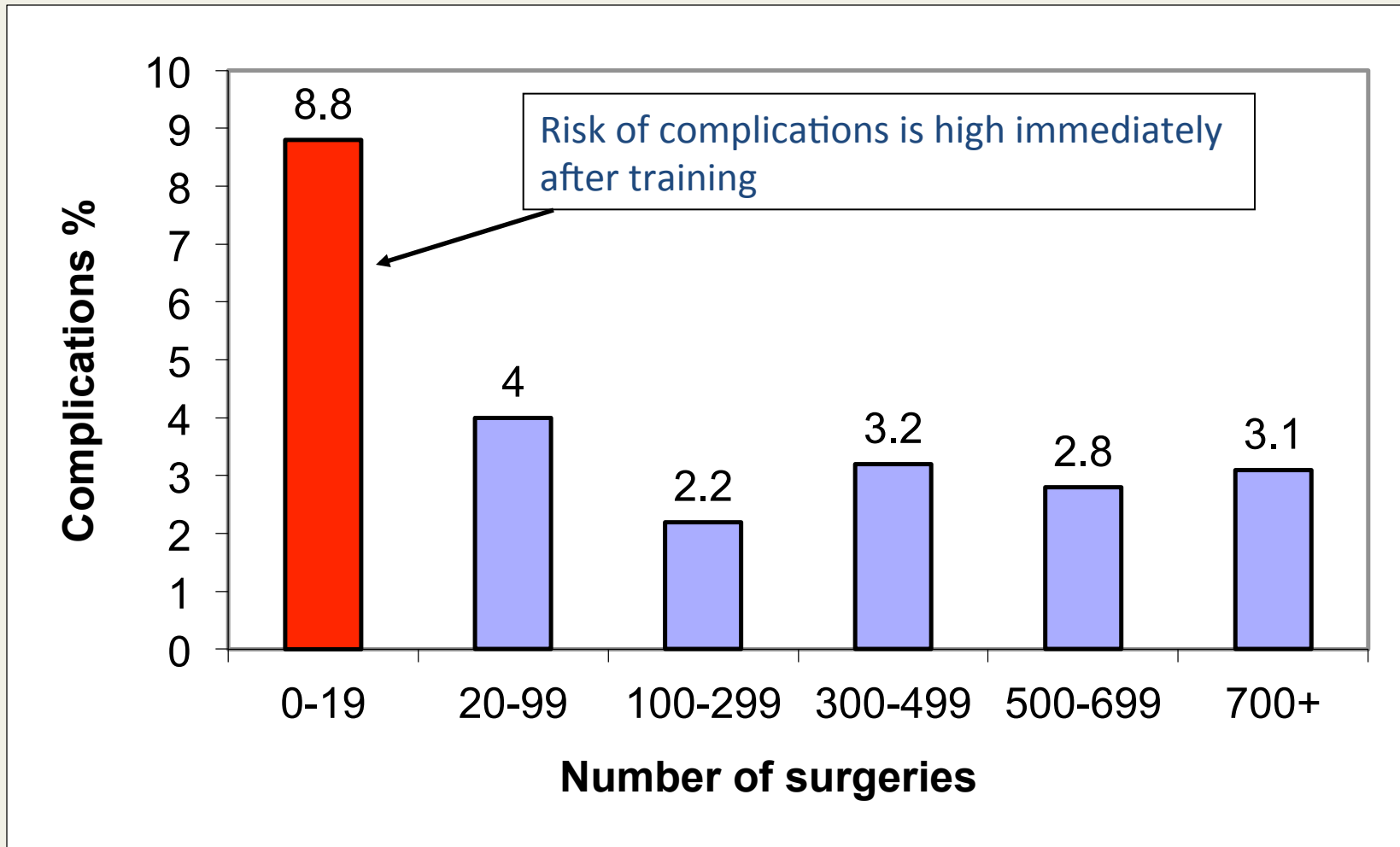
# Duration of surgery by number of procedures performed

(Kigundu BJU 2009)



# Complications by number of surgeries performed after training

(Kigundu BJU 2009)



## Complication rates and duration of surgery with two procedures and two types of providers (Buwembo, Br J Urol 2011)

	Sleeve Circumcision (n=1050)	Dorsal Slit Circumcision (N=971)	Physicians (n=564)	Clinical Officers (n=1457)
Complications	0.9%	0.6%	0.9%	0.7%
Duration of surgery	28.5 min	24.5 min	24.3 min	29.9 min

Dorsal slit is faster and as safe as sleeve circumcision  
Clinical officers were slower, but as safe as physicians



# Randomized trial of Local anesthesia

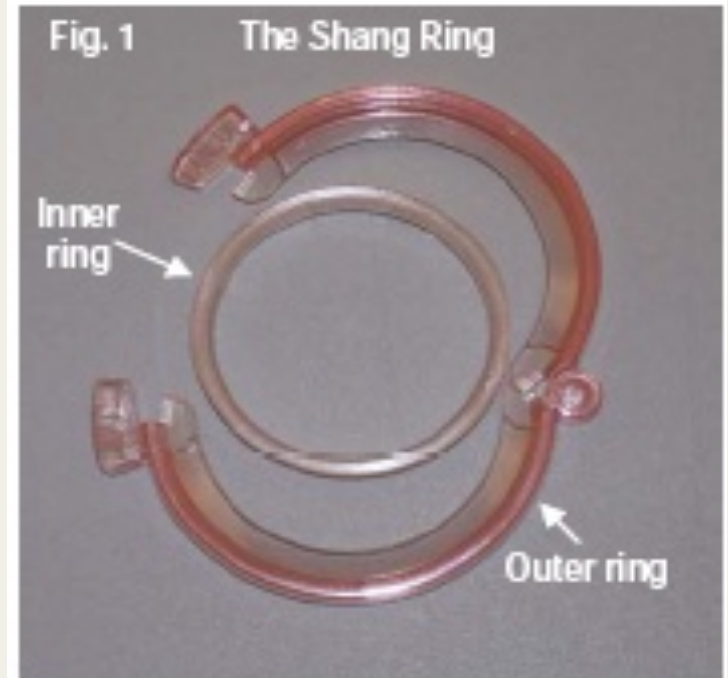
*(Kigozi et al BJU 2011)*

Lignocaine alone (N=179) vs mixture of lignocaine and Bupivacaine (N=181)

	Lignocaine (%)	Mixture (%)	RR (95% CI)
Pain during surgery	17.3	1.7	11.6 (3.5-37.9)
Additional anesthesia required	6.7	1.7	4.8 (1.4-17.1)
Post-operative pain	68.2	19.3	3.4 (2.3-5.0)

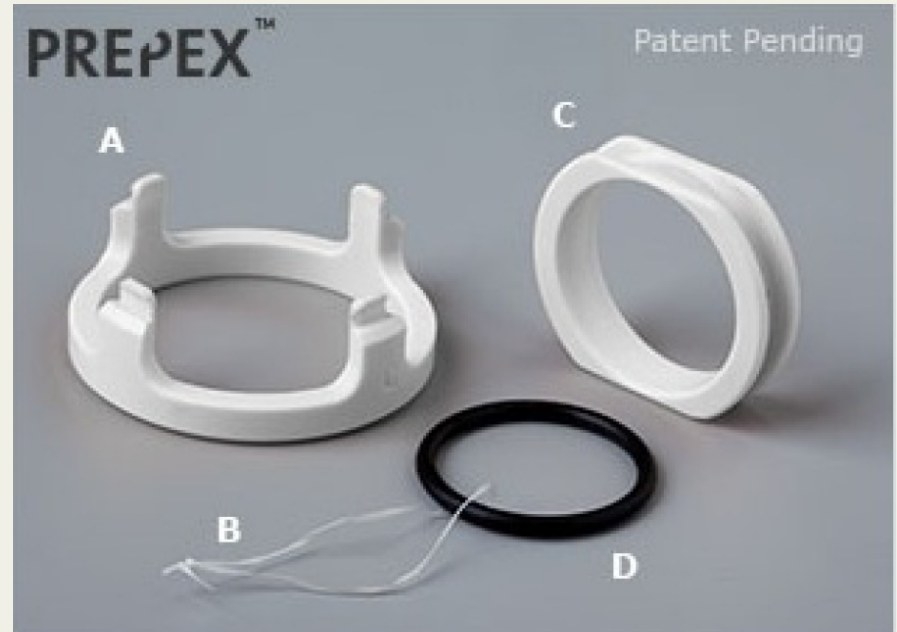
# Minimally invasive circumcision: Shang Ring

- **Developed in China**
- **Surgical time ~ 5 minutes**
- **Removed after 7-9 days**
- **Low complication rates reported to date**
- **Frees up theater time**
- **Study of safety and acceptability in Rakai: how will this work in rural Africa?**



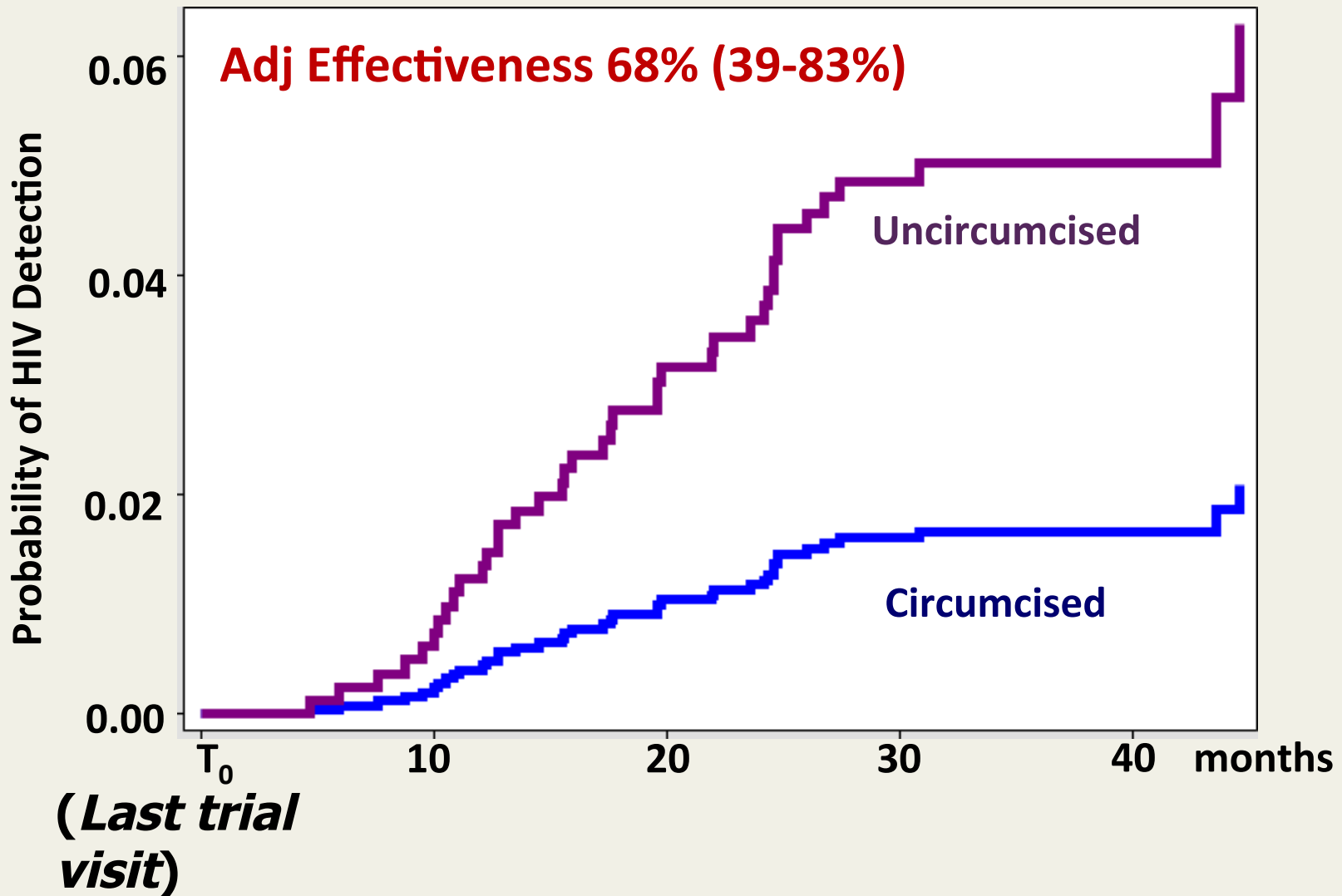
# PrePex Device

- No local anesthesia
- Minimal surgical facilities
- No bleeding: foreskin crushed and becomes necrotic
- Removed 7-9 days
- Minimal safety data (42 cases)

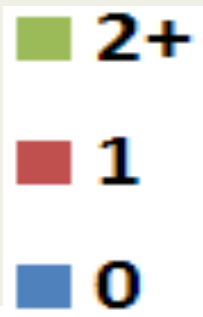


Will conduct a stepwise safety and acceptability study in Rakai

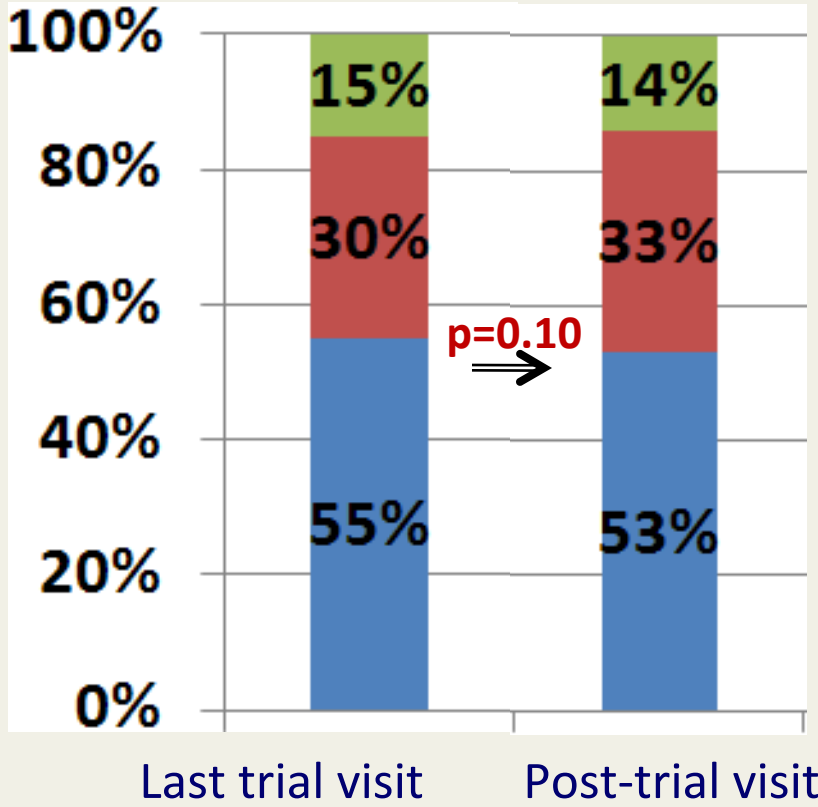
# MC effectiveness for HIV prevention: Control arm participants post-trial (Kong et al CROI 2011)



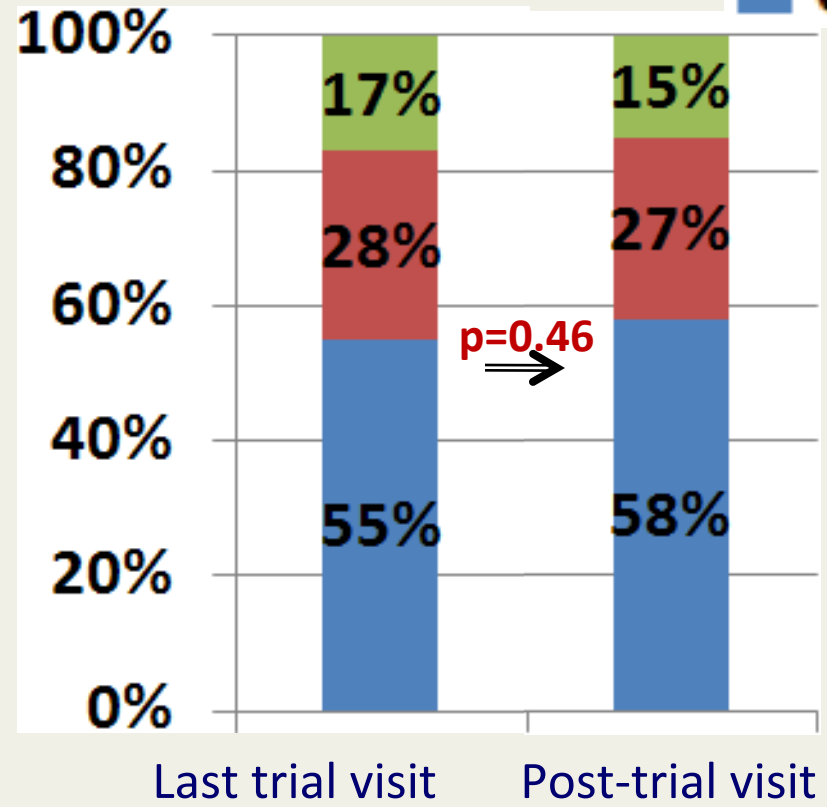
# Non-marital sex partners control arm men by MC adoption post-trial



### Opted for MC



### No MC

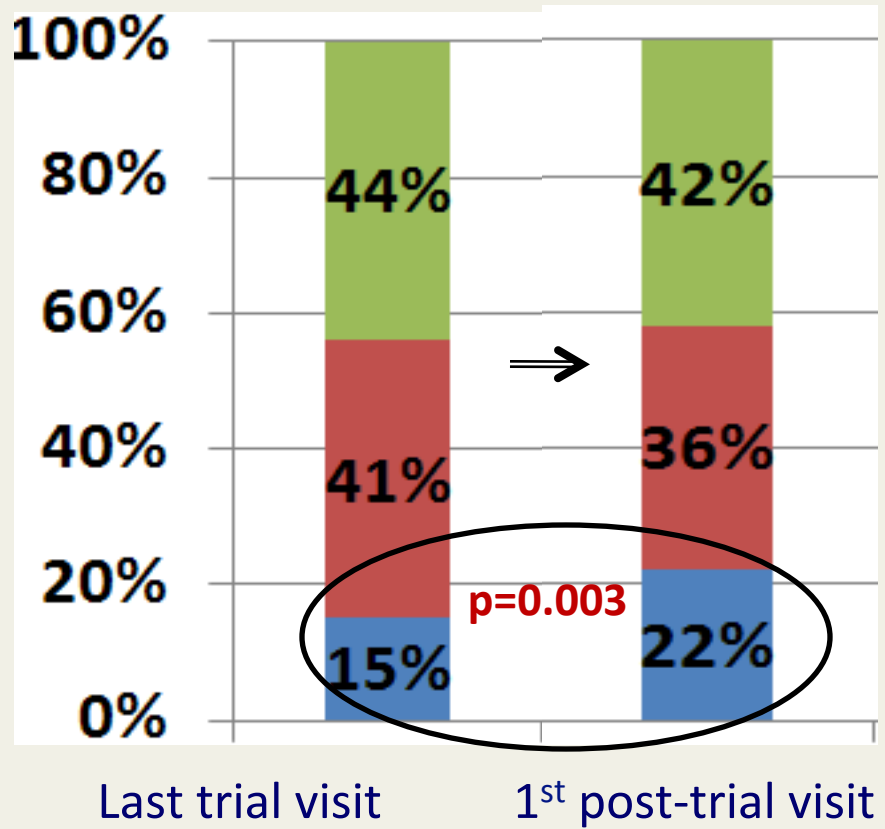


No difference in behaviors

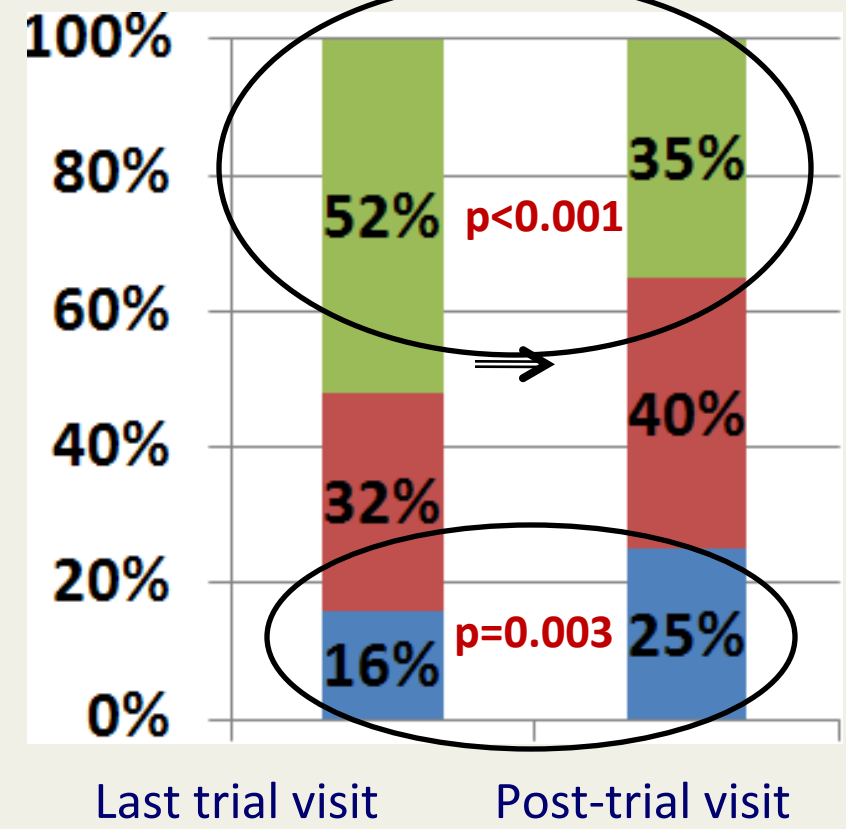
# Condom use with non-marital partners by control arm men post-trial

- Always
- Sometimes
- No use

**Opted for MC**



**No MC**

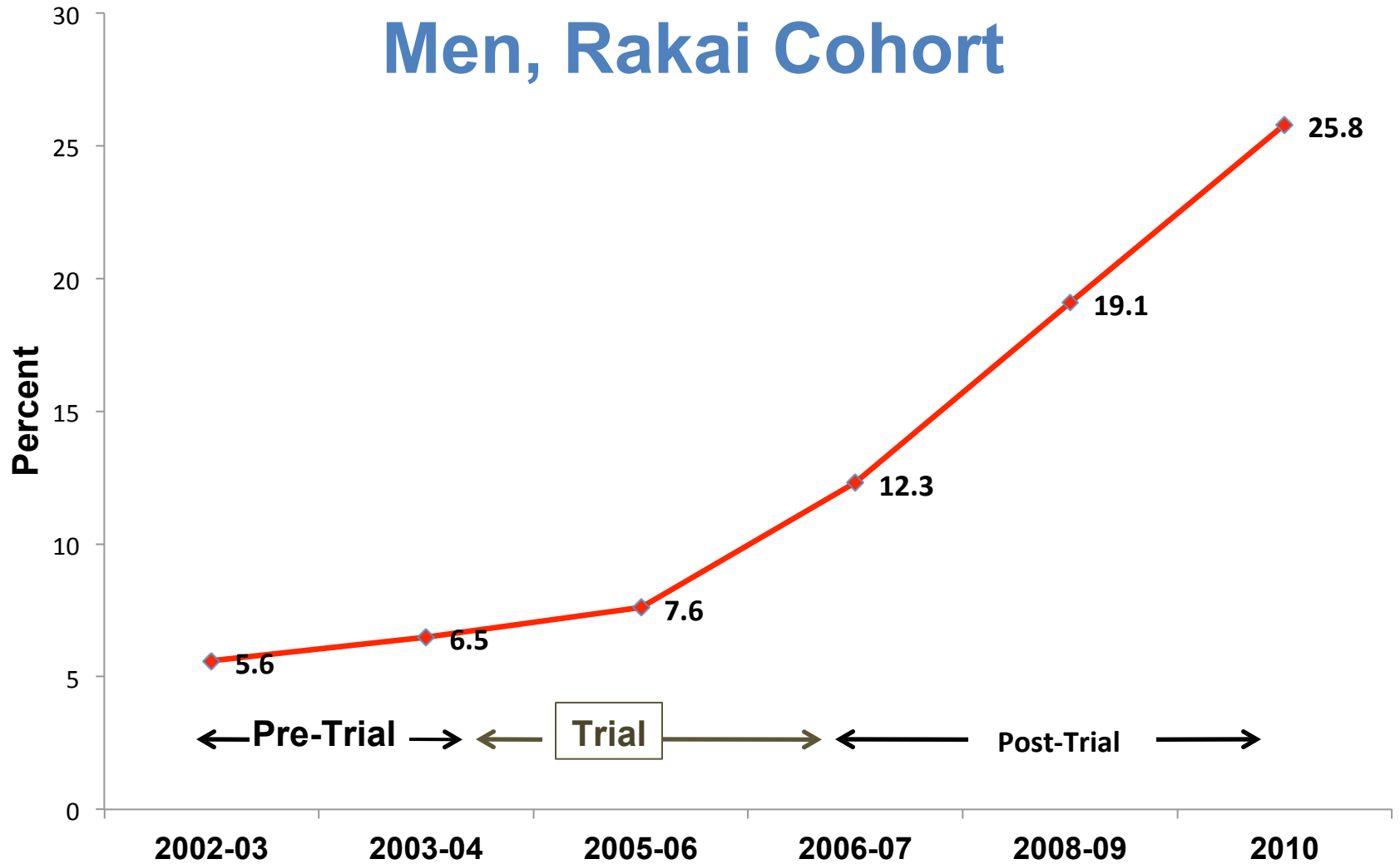


**Non-use increased in both groups**  
**Consistent use decreased in uncircumcised men**

# Population impact of MC, Rakai

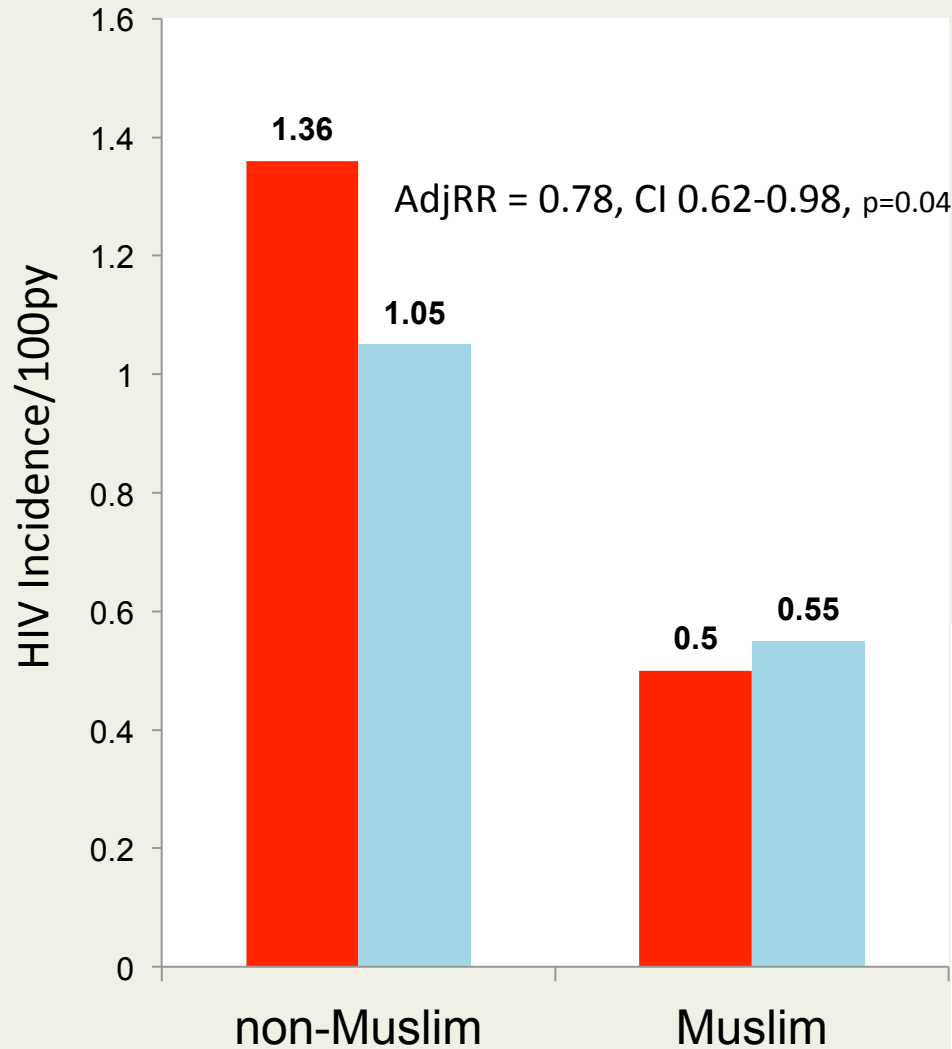
- **Rakai Community Cohort Study (RCCS)**
- ~14,000 persons 15-49, in 50 communities
- Approximately annual surveillance since 1994
- Interview and sample collection (blood, genital swabs)

# MC Prevalence in non-Muslim Men, Rakai Cohort





# HIV incidence in men before (2000-mid 2004) and after availability of MC



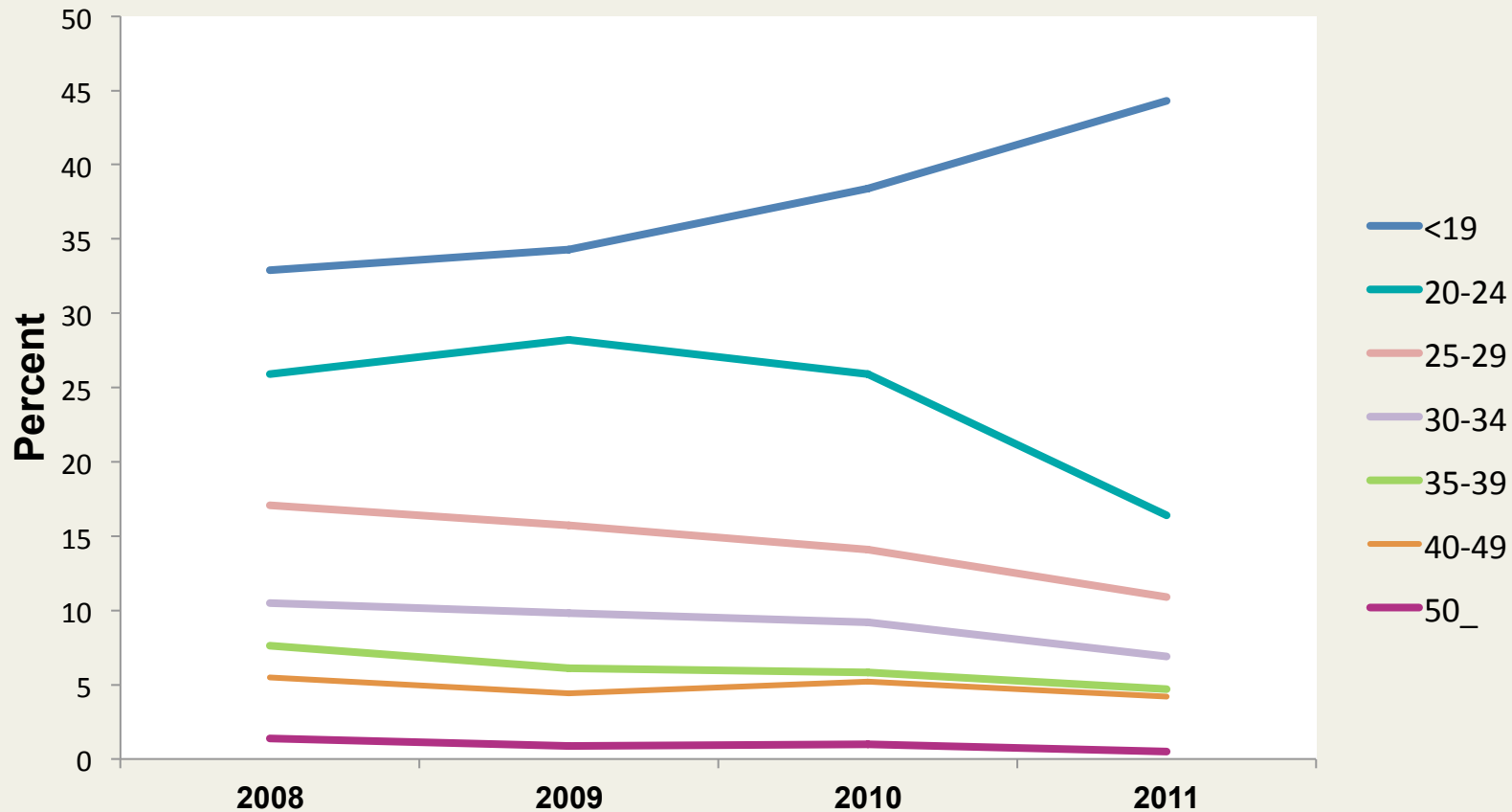
■ Pre-MC  
■ Post-MC

Preliminary evidence of a population-level reduction of HIV incidence in non-Muslim men  
Average MC coverage 18.5%

## MC Services in Rakai

- >18,000 MCs since 2007
- Mainly by clinical officers using dorsal slit
- 1 central facility with 5 operating rooms
- 4 satellite facilities in rural health centers
- Maximum efficiency with dedicated MC teams

# Age Distribution of Clients for Service Circumcision Rakai 2008-2011



Increased uptake by adolescents

Decrease in older men (Also seen in Kisumu and Orange Farms)

# Implementation Science RFA

2012-15

- Aim 1. To increase uptake of MC, particularly among higher risk men in a rural setting by:
  - Improved messaging/outreach
  - Increased mobile services
  - Task sharing and task shifting
- Aim 2. To conduct an acceptability/safety study of Early Infant Male Circumcision (EIMC) by non-physicians.
  - Randomized trial of NMWs vs Clinical Officers
- Aim 3. To assess the population prevalence of MC, estimate the impact of MC on HIV incidence, number of MCs per infection averted and cost per infection averted, using Rakai cohort data.

# Preliminary qualitative studies and messaging

(NICHD 1R01 HD070769-01; Gates Foundation 22006.03)

- Focus group discussions (FGD) and in-depth interviews (IDIs) on barriers to and facilitators of MC
- Male MC acceptors and non-acceptors, women and community leaders/gatekeepers
- Preferred messages and methods of MC information and service delivery (e.g., outreach in venues where men congregate in bars, markets, transport hubs), use of static or mobile clinics
- Messages disseminated through village opinion leaders, general community meetings, drama/music groups, radio talk shows and a film/video van

# Mobile MC Camps

- Travel time and time off work barriers to MC (Herman-Roloff et al Plos One 2011)
- Static services can “saturate” catchment populations
- Need to bring services to the communities
- Pilot camps
  - >900 MCs in 15 working days
  - Low Aes
- Major new program of mobile MC services

# Early Infant MC (EIMC)

- Simpler, cheaper and safer than adolescent/adult MC
- Delayed impact on HIV
- Need task shifting to nurse-midwives (NMWs) who have contact with mothers during and after pregnancy