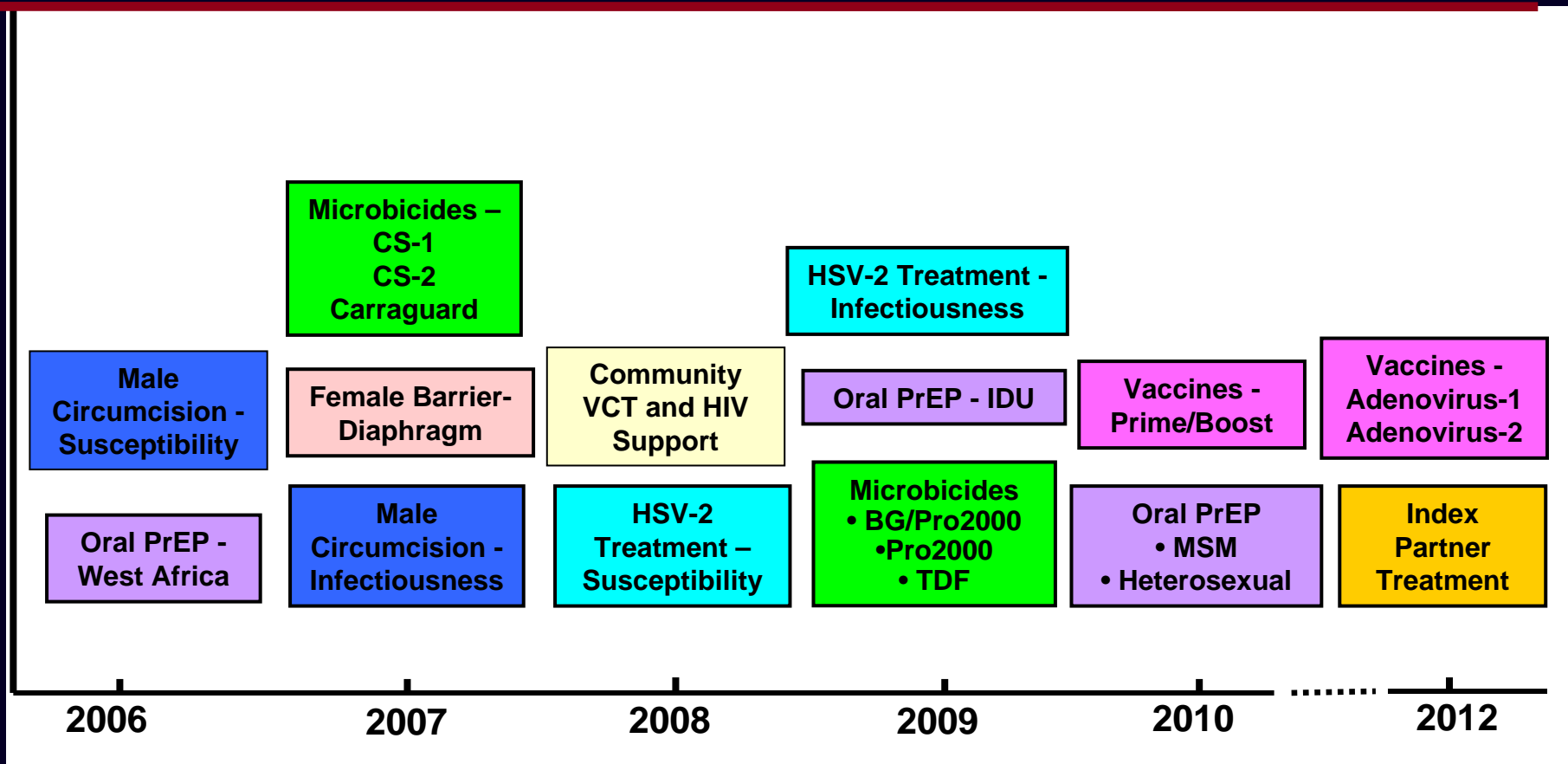


HIV Prevention Research: The Optimist's View

**Willard Cates, Jr., MD, MPH
Family Health International**

**IAS Meeting
Sydney, Australia
July 23, 2007**

July 2007 – Anticipated Trial Results



HIV Prevention Research – The Past Decade

- **Two new biomedical approaches**
 - **Nevirapine for PMTCT**
 - **Male Circumcision**
- **Ten valuable lessons learned**

Lessons Learned

- Adherence
- Pregnancy
- HIV Incidence
- Seroconverters
- Prevention Standards
- Comparison Groups
- Efficacy vs. Effectiveness
- Cost
- Community Engagement
- Communication Planning

Lessons Learned

- **Adherence**
- **Pregnancy**
- **HIV Incidence**
- **Seroconverters**
- **Prevention Standards**
- **Comparison Groups**
- **Efficacy vs. Effectiveness**
- **Cost**
- **Community Engagement**
- **Communication Planning**

Adherence

- **Social desirability bias**
- **New approaches to improve accuracy**
 - **ACASI**
 - **Applicator testing**
 - **MEMS packets**
 - **Drug levels**
 - **PSA or Y chromosome**
 - **Directly observed adherence**
- **Reinforced counseling for specific circumstances**

Carraguard Study – Blue Dye Applicator Assay



Source: Wallace (2007)

Carraguard Assay – Validation Studies

- **Clinical setting – US**
 - 960 possible findings
 - Inserted – 97.5% accurate
 - Not-inserted – 96% accurate
- **Trial site setting – S. Africa**
 - 93% - 97% accuracy among the 3 sites
- **Applicator assay suitable for clinical trials**

Source: Wallace (2007)

HPTN 035 – Use of Gel When Condoms Are Not Used

	% Use with Condoms	% Use Without Condoms
Oct '05	84	47
Apr '06	82	57
Oct '06	83	64
March '07	83	71
May '07	83	78

Prevention “Standard of Care” – The Trial as an Intervention

- **Traditional components**
 - Reinforcing prevention counseling
 - Provision of male condoms
 - STI treatment
- **Female condoms – biologic plausibility**
- **Male circumcision – next ethical frontier**

Pre-Trial, During-Trial, and Post-Trial HIV Incidence

Trial	HIV Incidence/Per 100 p-y		
	Pre-Trial Estimate	During Trial	Post-Trial
Cameroon (1995-97)	14.0	6.7	3.7
Nairobi FSWs (2000-2002)	6.0	3.7	1.6

Source: Roddy (1998), Ngugi (2007)

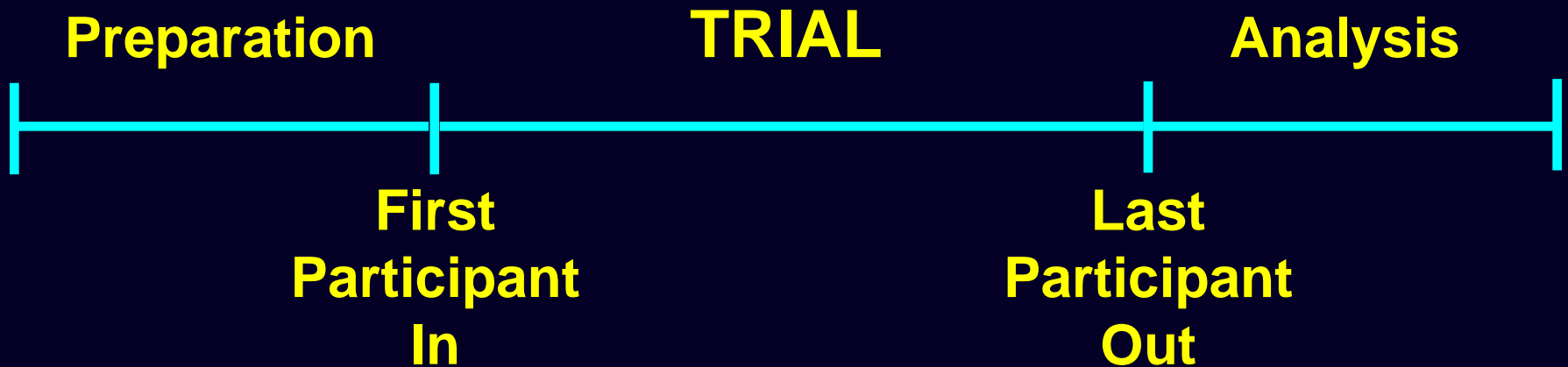
Male Circumcision - Ethics

- How do we counsel participants about the benefits and risks of MC?
- Must we offer MC to all participants (or their partners)?
- Require controls to be circumcised?
- Stratify enrollment by MC status?
- By how much will MC affect our power?

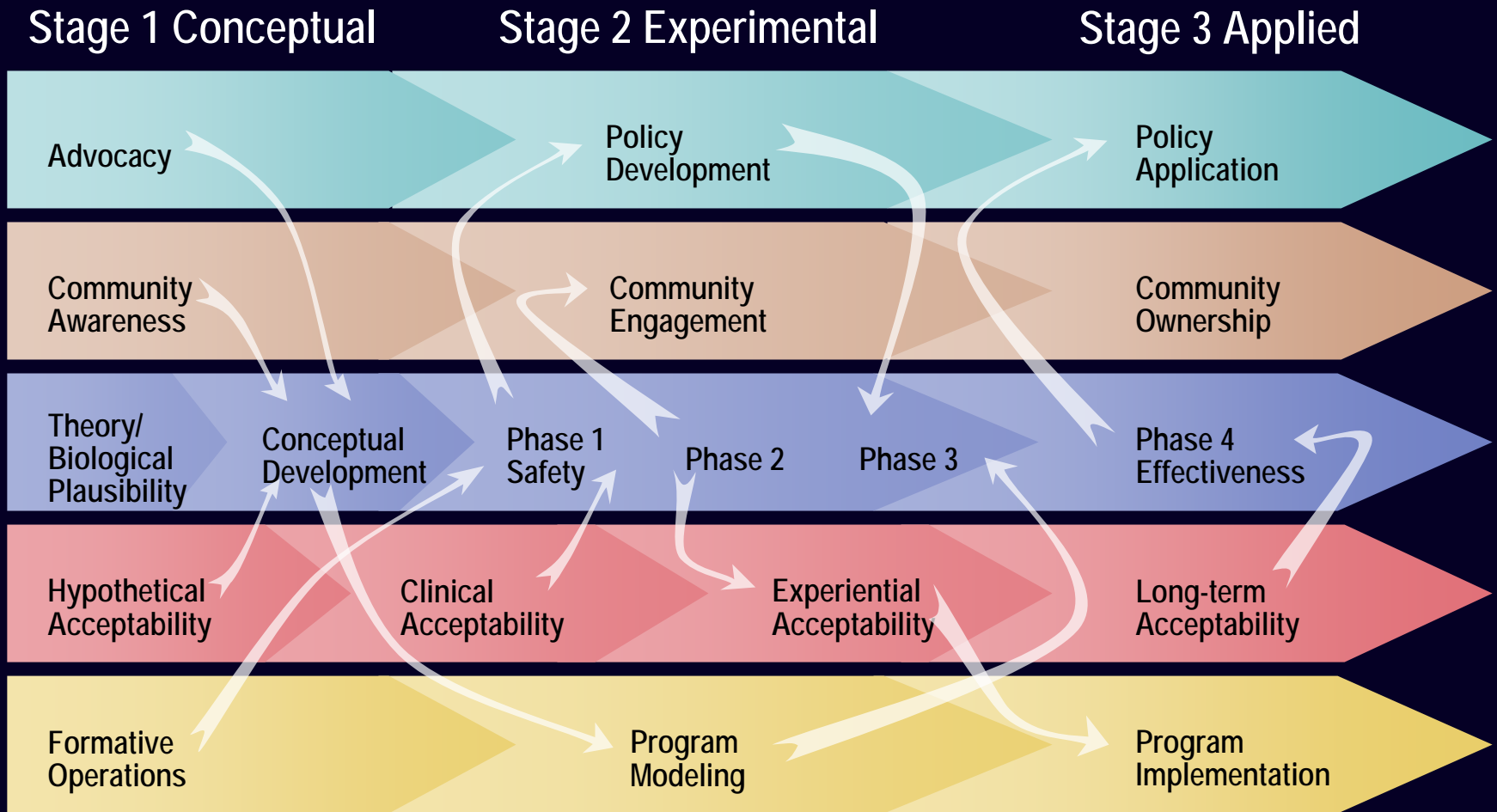
HIV Prevention Trials – Cost Considerations

- **Planned vs. Actual**
- **Trial Sequencing**
 - **Trial Preparation**
 - **Trial Operations**
 - **Trial Analyses**

HIV Prevention Trials – Operations Timeline



Components of the Prevention Research Continuum



HIV Prevention Trials – Cost Components

- **“Nested” Studies – preparatory, behavioral, laboratory surrogates, seroconverter followup**
- **Product Expenses**
- **Community Activities**
- **Communications Support**
- **Central vs. Field Costs**
- **Monitoring Visits**

Cost of HIV Prevention Trials, Phase 2b/3

Trials	Total Estimated Cost	No. Participants	No. HIV Endpoints	Cost per Participant	Cost per Endpoint
A	\$ 6.3 M	2142	17	\$2.9 K	\$ 371 K
B	\$ 8 M	2153	33	\$3.7 K	\$ 242 K
C	\$ 8.5 M	1644	21	\$ 5.2 K	\$ 405 K
D	\$ 17 M	1333	40	\$12.8 K	\$ 425 K
E	\$ 43 M	(6639) 6203	(194) 275	(\$ 6.5 K) \$ 6.9 K	(\$ 190 K) \$ 156 K
F	\$ 67 M	(3100)	(192)	\$21.6 K	\$ 349 K

 Microbicides

() = Planned

Cost of HIV Prevention Trials, Circumcision

Trials	Total Estimated Cost	No. Participants	No. HIV Endpoints	Cost per Participant	Cost per Endpoint
A	\$ 3.6 M	3,274	69	\$ 1.1 K	\$ 52 K
B	\$ 10.5 M	2,784	69	\$ 3.8 K	\$ 152 K
C	\$ 6 M	4,996	67	\$ 1.2 K	\$ 90 K

Cost Summary

- **Many components of cost – Apples and Oranges...wide range of estimates**
- **Cost per participant necessary for budgeting**
- **Cost per endpoint most important for effectiveness**
- **HIV prevention “best buy” – male circumcision studies**

Community Engagement

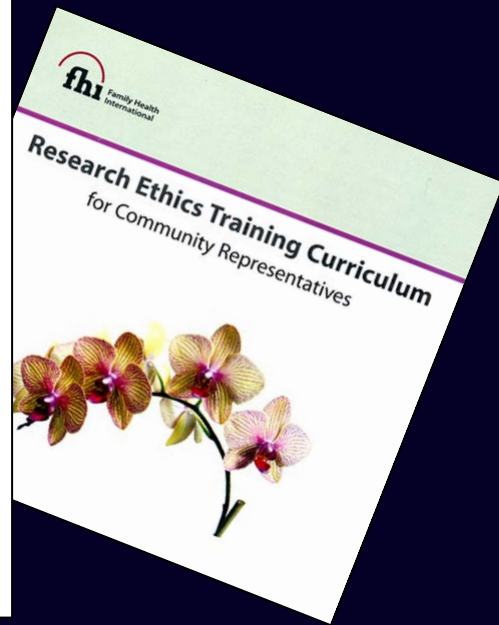
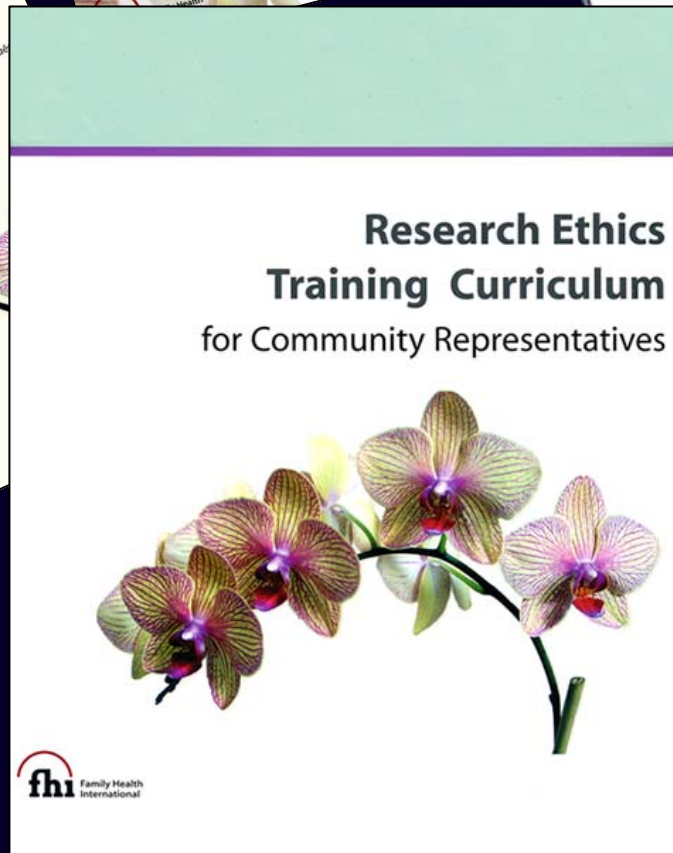
- **Multiple “communities”**
 - **Study participants**
 - **Advocates**
 - **Media**
 - **Academicians**
 - **Policy Makers, etc.**
- **“Research literacy” for community**
- **“Community literacy” for researchers**

Community – Lessons Learned

- **Must begin engagement early – when input makes a difference**
- **Requires resources and specialized skill set**
- **Must extend beyond local community**
- **Formative research necessary but not sufficient**

Research Literacy in the Community

- **Frequently Asked Questions (FAQs)**
 - **About the clinical trial process**
 - **About the intervention**
 - **About the specific study**
 - **About disparities in care...etc, etc**
- **Training that honors adult learning principles (relevance, immediacy, respect, safety, engagement, accountability)**



View the online version at:
<http://www.fhi.org/en/RH/Training/trainmat/ethicscurr/RETCCREn/index.htm>

Communications Planning

- **Power of communications**
- **Site/staff selection/preparation**
- **Communication plans in protocol**
- **Rapid response time**
 - **Global**
 - **National**
 - **Local**

Site/Staff Selection/Preparation

- **Sites with established relationships with local health authorities and opinion leaders**
- **Key personnel with proven ability to interact effectively with activists, media, public officials**
- **Prepare, prepare, prepare**

Media Training for Researchers



Conclusions

- **Iterative nature of research**
- **Complexities of HIV prevention science – disagreements common**
- **Current generation of HIV prevention trials on stronger methodologic and operational foundation**