

# **Not Just a Handmaiden: The Critical Role of Social Science in Microbicides and Other Prevention Research**

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# Not Just a Handmaiden



# Integrating Social & Behavioral Research Into Microbicides Clinical Trials: Recent Reviews

- J. E. Mantell, et al. *Social Science & Medicine* 60 (2005): 319-330
- E. E. Tolley & L. J. Severy. *AJPH* 96 (2006):79-83
- K. M. Morrow & M. S. Ruiz *AIDS & Behavior* 12 (2008): 272-283

# Trial Results

PRODUCT(S) TESTED	STUDY SITE(S)	RESULT
<b>Nonoxynol-9</b> 52.5mg Vaginal gel, Surfactant	Benin, Cote d'Ivoire, South Africa, Thailand	N-9 could enhance HIV-1 infection
<b>Nonoxynol-9</b> 70 mg Vaginal Film, Surfactant	Cameroon	N-9 did not reduce HIV infection rates
<b>Savvy</b> Vaginal gel, Surfactant	Ghana	Stopped prematurely due to low HIV infection rates
<b>Savvy</b> Vaginal gel, Surfactant	Nigeria	Stopped prematurely due to fertility
<b>Carraguard/PC515</b> Vaginal gel; Entry inhibitors, anionic polymers	South Africa	Not effective in preventing HIV infection
<b>Cellulose Sulfate</b> 6% Vaginal gel; entry inhibitors, anionic polymers	South Africa, Uganda, Benin, India	May have increased risk of HIV acquisition Trial stopped prematurely
<b>Cellulose Sulfate</b> 6% Vaginal gel; entry inhibitors, anionic polymers	Nigeria	Stopped prematurely based on interim results of parallel trial
<b>HPTN 035 STUDY (2 products tested)</b> Carbopol 974P <b>Buffergel</b> Vaginal gel; vaginal milieu protectors, acidifying agents	Malawi, South Africa, Zambia, Zimbabwe, USA	PRO2000 0.5% had 30% lower HIV acquisition rate compared to placebo, but not statistically significant  Buffergel did not alter HIV infection risk
<b>PRO2000</b> 0.5% Vaginal gel; entry inhibitors, anionic polymers		
<b>PRO2000</b> 0.5% and 2% Vaginal gel; entry inhibitors, anionic polymers	South Africa, Zambia, Tanzania, Uganda	Not effective in preventing HIV infection

# Core Issues

- Acceptability
- Adherence
- Control
- Covert Use
- Pregnancy



# Acceptability Issues

- What is acceptability?
- What attributes of product matter?
- When to conduct acceptability research?
- Value of acceptability in absence of real products?
- Acceptable to whom?

# Acceptability: What Have We Learned?

- Acceptability:
  - *is variable*
  - *is not static over time*
  - *has different attributes, some which matter more than others*
  - *Is not a good predictor of actual use*

# Adherence Data Collection Modes

MEASURE	STRENGTHS	SOURCES OF BIAS
BIOMARKERS of product or effect	<ol style="list-style-type: none"> <li>1. Most direct adherence measure</li> <li>2. Collecting blood anyway</li> </ol>	<ol style="list-style-type: none"> <li>1. Only snapshot in time</li> <li>2. Affected by differences in absorption &amp; metabolism or drug potency</li> </ol>
DIRECTLY OBSERVED USE	<ol style="list-style-type: none"> <li>1. Direct measure of adherence</li> </ol>	<ol style="list-style-type: none"> <li>1. Error in computation likely</li> <li>2. Participant burden to return unused products</li> </ol>
SELF REPORTS	<ol style="list-style-type: none"> <li>1. Low cost</li> <li>2. Easy to Implement</li> <li>3. Moderate correlation with HIV outcomes</li> </ol>	<ol style="list-style-type: none"> <li>1. Subject to recall and social desirability bias</li> <li>2. Validity of measures may vary by site/culture</li> </ol>
SELF REPORT		
ACASI	<ol style="list-style-type: none"> <li>1. Increases Privacy</li> <li>2. Standardization</li> <li>3. Adaptable for low literacy</li> </ol>	<ol style="list-style-type: none"> <li>1. Technical Requirements</li> <li>2. Participants must be “trained” to use computer</li> <li>3. Data loss from electrical shortages or other technical problems</li> </ol>
STRUCTURED FTF INTERVIEW	<ol style="list-style-type: none"> <li>1. Easily administered</li> <li>2. Interviewer can help with complicated skip patterns, use of response scales or other clarifications</li> </ol>	<ol style="list-style-type: none"> <li>1. Decreased confidentiality may lead to under reporting</li> <li>2. Desire to please interviewer can lead to SDB</li> </ol>
IN-DEPTH FTF INTERVIEW	<ol style="list-style-type: none"> <li>1. Can identify subtle shifts in adherence</li> <li>2. Can check and reconcile contradictions</li> <li>3. Can tailor strategies to assist with recall</li> </ol>	<ol style="list-style-type: none"> <li>1. Intensive training of data collectors required</li> <li>2. Intensive data management and analysis issues</li> </ol>

# Adherence Rates

CLINICAL TRIAL	TREATMENT	PLACEBO
<b>Nonoxynol-9</b> 52.5mg Vaginal gel, Surfactant	79%	81%
<b>Nonoxynol-9</b> 70 mg Vaginal Film, Surfactant	89%	87%
<b>Savvy</b> Vaginal gel, Surfactant	75%	77%
<b>Savvy</b> Vaginal gel, Surfactant	78%	79%
<b>Carraguard/PC515</b> Vaginal gel; Entry inhibitors, anionic polymers	41%	43%
<b>Cellulose Sulfate</b> 6% Vaginal gel; entry inhibitors, anionic polymers	87%	87%
<b>Cellulose Sulfate</b> 6% Vaginal gel; entry inhibitors, anionic polymers	81% Overall	
Carbopol 974P <b>Buffergel</b> Vaginal gel; vaginal milieu protectors, acidifying agents	81% across study arms	
<b>PRO2000</b> 0.5% Vaginal gel; entry inhibitors, anionic polymers		
<b>PRO2000</b> 0.5% and 2% Vaginal gel; entry inhibitors, anionic polymers	92% Overall	

# Adherence: What Have We Learned?

- Adherence:
  - *Rates are variable*
  - *Is measured differently in different studies*
  - *Is reported inconsistently by study participants*
  - *Is patterned*
  - *Varies within trials by site, partnership type, sex act, context of trial*
  - *Depends on participants' understanding of product use*

# Adherence: What Have We Learned?

- Adherence:
  - *Is affected by participants' beliefs about efficacy of product*
  - *Is affected by sexual, vaginal, and rectal practices*
  - *Is affected by gender and relationship dynamics*

# Control & Covert Use: What Have We Learned?

- Control and Covert Use:
  - *are important to some women, but not to others*
  - *importance varies by population, site, relationship type*
  - *“control” is an alien concept or has nuanced meanings*
  - *covert use is undesirable to many women & men*

# Pregnancy Rates

CLINICAL TRIAL	PREGNANCY OUTCOMES
<b>Savvy</b> Vaginal gel, Surfactant	Kaplan Meier pregnancy probability at 12mos: 75% on Savvy, 77% on Placebo
<b>Savvy</b> Vaginal gel, Surfactant	Proportion of participants who became pregnant at least once during follow-up: 25% on Savvy, 26% on placebo
<b>Carraguard/PC515</b> Vaginal gel; Entry inhibitors, anionic polymers	11% in both arms became pregnant during follow-up
<b>Cellulose Sulfate 6%</b> Vaginal gel; entry inhibitors, anionic polymers	Incidence of pregnancy during follow-up: 22% on CS, 23% on placebo  68% of women interrupted product use due to a positive pregnancy test
<b>Cellulose Sulfate 6%</b> Vaginal gel; entry inhibitors, anionic polymers	Incidence of pregnancy during trial: 29% on CS, 28% on placebo  Proportion of time off product due to pregnancy: 5.1% on CS, 4.5% on placebo
<b>Carbopol 974P Buffergel</b> Vaginal gel; vaginal milieu protectors, acidifying agents	610 pregnancies during trial (n=3099)  Pregnancy Incidence Rate during trial: 11.3%
<b>PRO2000 0.5%</b> Vaginal gel; entry inhibitors, anionic polymers	5.9% of person-time off product during follow-up in gel arms

# Pregnancy: What Have We Learned?

- *Not much behavioral and social research*
- *Notion of “intention” may not be meaningful*
- *Expectations & desires about fertility & parenthood are deeply rooted and normative and usually override concerns about disease prevention*
- *Triple or quadruple “protection” required in trials may be unreasonable and unrealistic*

# Social Science Contributions: What Have We Learned?

- Practices are more relevant than behaviors
- Practices are imbued with meanings, values, beliefs
- HIV is relational; and relationships are dynamics
- Interventions (trials) are part of and not separate from “real life”
- Practices, meanings, relationships, and environments are variable and not static

# “Critical” Social Science Contributions

- Medical research is socially embedded and it produces social relations.
- Trials and technologies affect people and communities and vice-versa.
  - *Interrogate how technology is incorporated by people in local contexts*
  - *Elucidate contextually-specific ways in which research and participants are intertwined*

# Conclusion

- Biomedical research on HIV prevention tools and technologies must be complemented and informed by social science within and outside the context of clinical trials.
- A more meaningful investment by funders in social research—theoretical, qualitative, quantitative—is needed to answer core questions related to the potential and real effectiveness of new technologies and tools for stemming HIV epidemics.

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