



Does Provision of Incentives Conditional on Use Increase Product Adherence?

**MTN 031 Open-label incentive study of the Dapivirine
Vaginal Ring: Reflections on potential designs**

MTN Annual Meeting, March 16, 2015

Barbara S. Mensch, Ph.D.

Population Council

Why conduct an incentive study within the MTN & where might we conduct it?

Why?

- Rationale: Low level of adherence in VOICE, FACTS and other PrEP and microbicide trials
- Research Priority for MTN 2.0: design and implement a behavioral protocol with active product and objectively measured adherence as outcome to assess strategies to increase levels of product use in microbicide trials
- Large literature in psychology, preventive medicine and behavioral economics demonstrating effectiveness of incentives to improve health and other outcomes

Where?

Selected ASPIRE sites in sub-Saharan Africa

Primary and secondary objectives

- Primary objective:
 - To determine if a financial incentive — provided via a fishbowl lottery and conditional on the prior month's product use — promotes adherence to the IVR when inserted once every 4 weeks
- Secondary objectives:
 - To determine whether the effect of a financial incentive on adherence remains after the incentive is withdrawn
 - To determine whether the effect of a financial incentive varies depending on the time of offer
 - To investigate the acceptability of a conditional financial incentive tied to product use

Primary and secondary endpoints

- Primary endpoint:
 - Adherence based on drug concentrations in plasma; (residual drug in IVR under consideration)
- Secondary endpoint:
 - Participant report of acceptability of fishbowl lottery and incentive system based on a structured exit interview questionnaire and in-depth interviews conducted with a subset of participants

Proposed design #1

- Participants randomized to one of 3 groups
- No “pure” control arm to ensure that each group has opportunity to obtain incentive
- Each participant on product for 6 months (plus 1 month run-in)

Group	Financial incentive offered during this period	
	Months 1-3	Months 4-6
1	Yes	No
2	Yes	Yes
3	No	Yes

Design #1 can address 4 questions

1. What is the effect of an incentive on early adherence?
 - Do incentives promote adoption of product and adherence during the first 3 months of the study?
 - **Comparison:** Group 1 and Group 2 vs. Group 3: 1-3 months
2. What is the effect of any incentive on adherence?
 - Does an incentive promote adherence regardless of whether offered only during the first 3 months, offered only during the second 3 months, or offered throughout the 6 month study period?
 - **Comparison:** Group 1 (1-3 months) and Group 2 (1-6 months) and Group 3 (4-6 months) versus Group 1 (4-6 months) and Group 3 (1-3 months)

Design #1 can address 4 questions (cont'd)

3. What is the durability of the incentive effect?
 - Do participants need to be incentivized throughout the study period or do those consistently incentivized and those incentivized early have the same level of adherence?
 - **Comparison:** Group 1 (4-6 months) versus Group 2 (4-6 months)
4. Does the timing of the incentive affect longer term adherence?
 - Is adherence at 6 months unrelated to the timing of the incentive? Who is more adherent, participants incentivized:
 - in the first 3 months,
 - throughout the 6 months,
 - in the last 3 months?
 - **Comparison:** Group 1 (4-6 months) versus Group 3 (4-6 months) versus Group 2 (4-6 months)

Design #1 sample size

- Powered to detect an increase of 15% in adherence from a baseline level of 60% (90% power and $\alpha = 0.05$)
- Hypothesis test corresponding to Q1: requires sample size of 124 participants per arm
Total N = 372 participants
- With N=372, 80% power, $\alpha = 0.05$ to address Q2

Proposed design #2

- Participants randomized to one of two groups
- No “pure” control arm to ensure that each group has opportunity to obtain incentive
- Each participant on product for 12 months (plus 1 month run-in)

Financial incentive offered during this period		
Group	Months 1-6	Months 7-12
1	Yes	No
2	No	Yes

Design #2 can address 3 questions

1. What is the effect of an incentive on early adherence?
 - Do incentives promote adoption of product and adherence during the first 6 months of the study?
 - **Comparison:** Group 1 and Group 2 @ months 1-6
2. What is the effect of any incentive on adherence?
 - Does an incentive promote adherence regardless of when it is offered?
 - **Comparison:** Group 1 (1-6 months) and Group 2 (7-12 months) versus Group 1 (7-12 months) and Group 2 (1-6 months)
3. Does the timing of the incentive affect longer term adherence?
 - Is adherence at 12 months unrelated to the timing of the incentive?
Who is more adherent, participants incentivized:
 - in the first 6 months,
 - in the last 6 months?
 - **Comparison:** Group 1 (1-12 months) versus Group 2 (1-12 months)

Design #2 sample size

- Powered to detect an increase of 15% in adherence from a baseline level of 60% (90% power, $\alpha = 0.05$)
- Hypothesis test corresponding to Q1: requires sample size of 165 participants per arm
Total N = 330 participants

Proposed design #3

- Participants randomized to one of two groups
- Pure control arm
- Each participant on product for 12 months (plus 1 month run-in)

Financial incentive offered during this period		
Group	Months 1-6	Months 7-12
1	Yes	Yes
2	No	No

Proposed design #4

- No randomization
- Delayed enrollment in experimental arm so that inclusion of pure control arm is potentially less problematic
- Each participant on product for 6 months (plus 1 month run-in)
- Assumes no temporal effects in either participant characteristics or behavior

Financial incentive offered during this period

Group	Months 1-3	Months 4-6	Months 7-9	Months 10-12
1	No	No	Off product	Off product
2	Not yet enrolled	Not yet enrolled	Yes	Yes

Study design questions

- Is it feasible to include a “pure” control arm (Design #3)?
- Will there be anticipatory effects for study designs including arms with delayed incentive (Designs #1 and #2)?
- Will a complex design confuse participants (Design #1)?
- Is delayed enrollment scientifically defensible (Design #4)?
- Informed consent process: how do we explain the study to participants?

Study design considerations

- Month 1 run-in to assess adherence for incentive
- Amount of incentive
- Use of score algorithm to recruit high-risk (presumably low-adherent) participants
- Withdraw payment if not adherent (capitalize on loss aversion) or incentivize if adherent (reward behavior)
- Provide drug level to participants not being incentivized, to assess the effect of incentive over and above feedback
- 3-4 sites in Africa, preferably South Africa due to proximity to Parexel Lab
- Why fishbowl? Experimental research indicates uncertain reward more motivating even if it has a lower expected value (Shen, Fishback, and Hsee 2015)

Preliminary feasibility and acceptability assessment after 2nd month

- Since:
 1. incentives have not been used in prior MTN trials,
 2. conditional cash payments may be perceived as coercive, and
 3. social harms may result from participation in a study where a considerable amount of money will be provided

... a preliminary assessment will be made after 25 women have been enrolled for 2 months
- If > 8 women report social harms, the protocol will be discontinued

Implementation of MTN-031 contingent on . . .

- ASPIRE demonstrating that the Dapivirine ring is effective in preventing HIV
- Individual level adherence in ASPIRE indicating sufficient variability
- Ability to reliably measure adherence at the individual level

Acknowledgements

MTN:

Jen Balkus, Jose Bauermeister, Elizabeth Brown, Bob Bucklew, Alex Carballo-Diequez, Charlene Dezzutti, Luis Duran, Beth Galaska, Pamina Gorbach, Sharon Hillier, Milly Katana, Ian McGowan, Kenneth Ngure, Kristine Torjesen, Ariane van der Straten, Rhonda White, CWG and CRWG

NIMH:

Cyndi Grossman

Economists:

Omar Galarraga, Sebastian Linnemayr

HANC Behavioral Sciences Consultative Group:

Michele Andrasik, Rivet Amico, Carlos Del Rio, Chris Gordon, Jessica Haberer, Sybil Hosek, Mallory Johnson, Steve Safren, Jeff Schouten, Jane Simoni, Ira Wilson

The Microbicide Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UM1AI068633, UM1AI068615, UM1AI106707), with co-funding from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health.

END

Extra Slide follows

Fishbowl lottery varying amounts of incentive

- Behavioral experiment: 87 University of Chicago college students asked to drink a large amount of water in two minutes
 - Randomized to two groups: one group told they would receive \$2 for completing task, second group told they would receive either \$1 or \$2
 - More people in the uncertain group finished the water (70%) than in certain group (43%) ($p=0.012$)
- Researchers noted that the concept that uncertainty can be more motivating than certainty is “counterintuitive”
- **“Findings useful for marketers, policymakers, managers and [those] who design incentives to motivate people.”**

See: Shen, Fishback and Hsee (2015) The motivating-uncertainty effect: Uncertainty increases resource investment in the process of reward pursuit, *Journal of Consumer Research*