MTN-003D:

An Exploratory Study of Potential Sources of Efficacy Dilution in the VOICE Trial

The Participant Perspective

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MTN
microbicide trials network

Aim of MTN-003D

- After early closure of oral & vaginal tenofovir arms of VOICE, **Stage 1** was designed to explore potential factors contributing to the dilution of efficacy using qualitative methods

- After release of VOICE results in March 2013 & availability of drug PK data, **Stage 2** has been designed to explore factors influencing adherence in greater depth, including HIV risk perception & motivation to join trial

Objectives of Stage 1

Primary Objectives

1. Explore contextual issues & specific aspects of VOICE trial that positively & negatively affected participants' actual & reported product use

2. Explore reasons, motivations and context of engaging in receptive anal intercourse (& rectal use of gel among VOICE participants in gel group)

Exploratory Qualitative Study designed to:

- Identify factors that may have affected participant adherence to study product in VOICE
- Describe context and norms around anal sex
- Describe how sexual behaviors, such as anal sex, may have had an effect on product efficacy

Stage 1 Methods

- 2-day Qualitative Training held in Durban in August 2012
  - In-depth interviewing skills & techniques for discussing sensitive topics such as product adherence & anal sex
  - Anal sex sensitisation & demystification
- In-depth interviews (IDIs) with former VOICE participants on product ≥ 3 months
- Data collection: December 2012 to March 2013

Total of **88** IDIs conducted across 4 CRS

1. UZ-UCSF, Harare, Zimbabwe: **26 IDIs**
2. MUJHU, Kampala, Uganda: **22 IDIs**
3. MRC Isipingo, Durban, South Africa: **20 IDIs**
4. MRC Overport, Durban, South Africa: **20 IDIs**

IDI Topic 1: Adherence

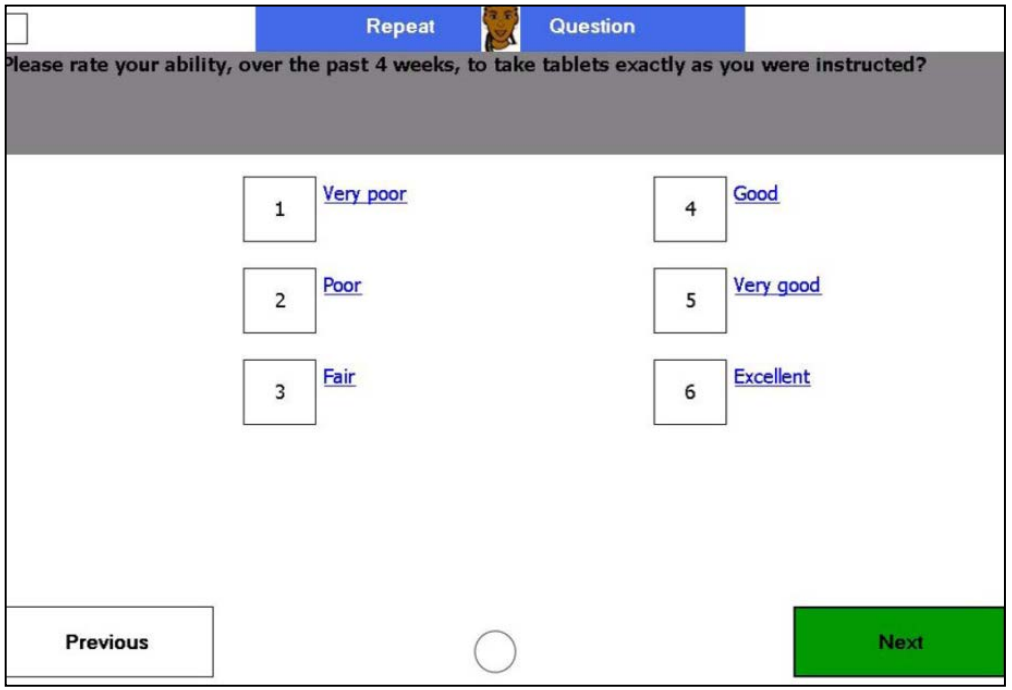
Motivations to join trials: Effect of motivation to use product and actual product use

Risk perception: Socio-cultural environmental factors contributing to risk perception & Influence of risk perceptions on product usage

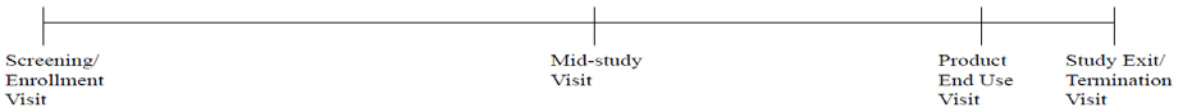
Adherence

- Understandings & interpretations of adherence questions & in relation to own experiences of product use
- Opinions on why differences existed between various adherence measures (e.g. self-reports, biological use)
- Discrepancies between actual & reported product use
- Social & cultural norms & effects of larger contextual issues, e.g. culture, community & social environment, as well as trial-specific context

ACASI rating scale show card



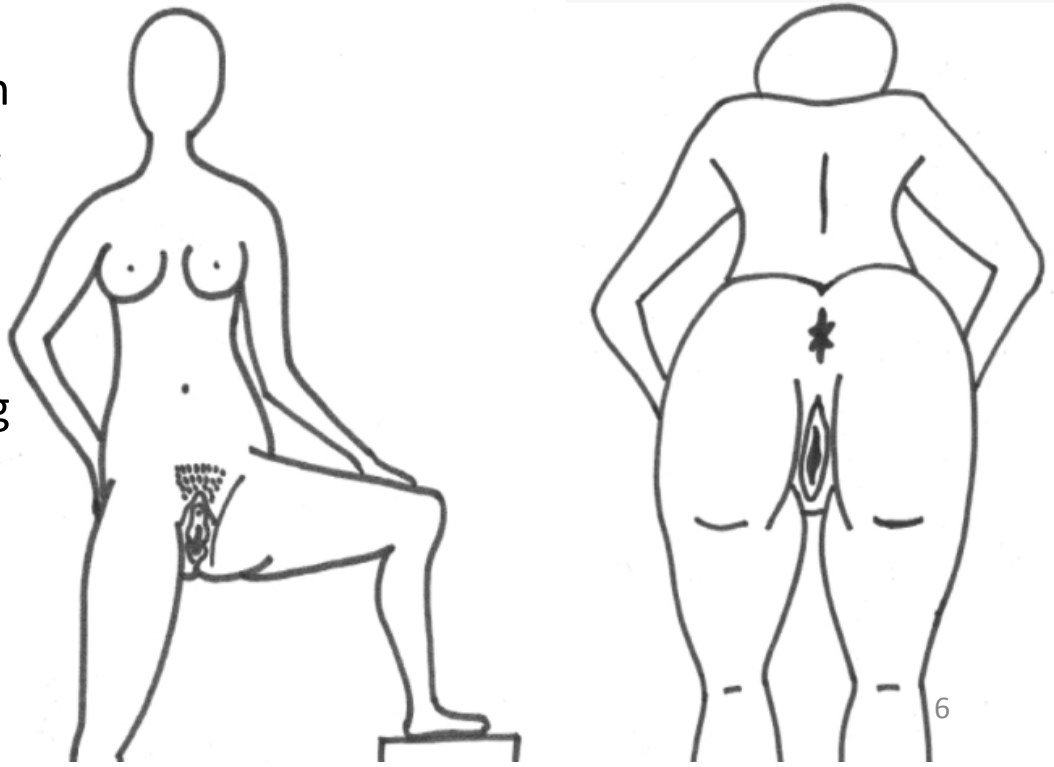
Visual VOICE study timeline



IDI Topic 2: Anal Sex (AI)

Study group:	Gel Users	Tablet Users	Total
Reported Anal Sex	18	17	35
Sero-converters	5	5	10
All other women	20	23	43
Total	43	45	88

- Body map template used to initiate discussion on sex & to clarify anatomical understanding, definition of “anal sex” to verify understanding of VOICE ACASI question
- Personal AI experiences discussed only if participant disclosed engaging in AI
- Rectal gel application among VOICE participants in vaginal gel group also investigated



Stage 1 Data management

- De-briefing reports filed by interviewers on same day as interviews conducted (real-time summary data)
- Audio files uploaded by sites onto FTP
- DTHF managed transcription/translation process:
  - 88 interview audio files transcribed into original language transcripts (Shona, Luganda & Zulu)
  - Original language transcripts reviewed by site interviewers before being translated into English
  - English transcripts reviewed by interviewers, before being QC'd by RTI
  - Once all queries addressed, transcripts declared final

Stage 1 data

- Qualitative data analysis codebook developed & tested
- ICR ≥ 80% among coding team members established
- Finalised English transcripts from Stage 1 currently being analysed using NVivo CAQDA programme
- Data from Stage 1 includes:
  - Interview transcripts
  - Annotated timeline tools
  - Annotated body map templates
  - Demographic data

Stage 1 Study Population Demographic Characteristics

Characteristics	South Africa (N=40)	Zimbabwe (N=26)	Uganda (N=22)	Overall (N=88)
Mean Age (median)	26.7 (25)	29.5 (30)	31 (31)	28.6 (27)
Currently married	-	22 (85%)	13 (59%)	35 (40%)
Has current primary sex partner or married	38 (95%)	24 (92%)	22 (100%)	84 (95%)
Same partner as during VOICE *	27 (71%)	22 (92%)	19 (86%)	68 (81%)
Currently living with primary sex partner *	5 (13%)	22 (92%)	10 (45%)	37 (44%)
Partner provides financial support *	32 (84%)	22 (92%)	20 (91%)	74 (88%)
Vaginal sex in past 3 months with primary sex partner *	37 (97%)	24 (100%)	22 (100%)	83 (98%)
Mean # of other partners in the past 3 months (median) *	0.1 (0)	0 (0)	16 (1)	4.1 (0.4)
Mean Total partners in lifetime (median)	3.3 (2)	2.1 (1)	31.2 (5)	9.9 (2)

* those with primary sex partner or married

Stage 1 participant PK data

- Biological use (detectable plasma drug PK): 24%
  - based on subset of 76 among the 88 participants from Stage 1 who were on active product

  This represents the average of the proportion of visits with detectable drug for women in Stage 1 003D at all sites with available PK results (and across all active products)

Preliminary findings on AI

- Discussion by several participants that they understood AI question in ACASI to mean ‘vaginal sex from behind’
- Participants in South Africa spoke of AI more openly – associated with youth and casual sex partners (in heterosexual relations)
- Ugandan participants associate AI with sex workers, many of the participants disclosed sex work
- Zimbabwean ppts least open to talk about AI – strong association of AI with homosexual men
- AI generally described as male-initiated
- Generally not spoken about openly amongst friends or in community
- Poor knowledge of condom & lubricant use for AI

Rationale for Stage 2

Preliminary findings from Stage 1:

- Participants largely did not admit to personal non-adherence but spoke widely of 'other women' not adhering
- Participants suggested that presenting women with blood test results would encourage honesty in reporting product use level
- Participants suggested presenting blood test results as way of ensuring accurate reporting of adherence & disclosure of non-use
- Participants demonstrated poor understanding of adherence questions, rating scale and response categories

Stage 2 Background

Statement 1: Presenting women with drug PK results data may generate more candid discussions around product use during VOICE participation

- When presented with biological use data will participants be forthcoming about personal experience with products, including motivations/reasons for non-use & use?
- Why didn't participants use products & what was importance of various reasons?
- How do participants explain high study retention but low product use despite high incidence/high risk?
- How do participants explain motivations for adherence reporting- (i.e. continued access to services, personal relationships or social contract)?

Statement 2: Presentation of PK results data may help identify unique characteristics of positive deviants contributing to consistent use (e.g. attitude or characteristics of participants, successful strategies, or broader social/structural circumstances)

- Narratives of consistent use with participants classified as adherents based on biological use data

Stage 2 Design

Preparation: 1-day Qualitative research training held in Durban in October 2013

- Reflection on successes/challenges faced in Stage 1 data collection
- In-depth interviewing skills re-cap
- FGD facilitation skills
- Using research tools: Life Events Timeline, PK illustrative tools

Design:

- Approximately 108-144 participants in Stage 2 taking part in IDIs and FGDs
- Participants systematically selected from former VOICE participants at participating VOICE sites (same sites as Stage 1: UZ-UCSF, MUJHU and MRC Durban)
- Participants with PK drug results available considered eligible
- Assignment to either FGD or IDI or both is dependent upon participants' level of product adherence

Study Team and Key Roles

Core/US

- **Protocol Chair**: Ariane van der Straten
- **Co-chairs**: Liz Montgomery, Barbara Mensch
- **Operations (FHI 360)**: Lisa Levy, Kristy Alston
- **Data coordination (RTI/WGHI)**: Miriam Hartmann
- **MTN Core**: Beth Galaska Burzuk, Sonia Gor
- **NIH/DAIDS:** Jeanna Piper, Roberta Black, Cynthia Grossman, Dianne Rausch

Site Teams

- **UZ-UCSF**: Nyaradzo Mgodi, Petina Musara, Imelda Mahaka, Otilia Munaiwa
- **MU-JHU**: Clemensia Nakabiito, Juliane Etima, Teopista Tibaijuka, Josephine Nabukerra
- **MRC**: Sarita Naidoo, Kubashni Woeber, Funeka Mthembu, Nozipho Vilakazi

Behavioral Consultants

- **DTHF:** Zoe Duby, Thola Bennie

Thank you

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