Behavioral Research in the Microbicide Trials Network

HANC Behavioral Sciences Working Group Symposium
Miami June 8, 2014

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Senior Research Scientist, RTI International
Director, Women’s Global Health Imperative (WGHI)
Behavioral Research Working Group (BRWG) Scope of Work

- Serve on 25 of 28 protocol teams
- Assess product adherence and acceptability
  - Secondary objectives in phases I-III trials
  - Primary objectives in ancillary studies (035b, VOICE-C, VOICE-D)
- Assess feasibility
  - Primary or secondary objectives in pilot studies (Wisebag) or I-II trials (017)
  - Exploratory objective in OLE study (025)
- Describe ways in which participant behaviors affect trial outcomes
  - Sexual and other risk behaviors
  - Vaginal and rectal practices
- Test new methodologies to measure and understand sexual behavior and product adherence:
  - Pictorial ACASI (035b), Video interviewing (004; 024)
  - Integrated quantitative and qualitative methods (020, 017)
  - Electronic or drug monitoring, SMS, data convergence interviews
## BRWG Members

### 4 Core Members

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution/University</th>
<th>Title/Program</th>
<th>Year Joined</th>
<th>Chair Years</th>
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<tbody>
<tr>
<td>Alex Carballo-Diequez</td>
<td>Columbia University</td>
<td>PhD, Clinical Psychology</td>
<td>2006</td>
<td>2006-8</td>
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<tr>
<td>Pamina Gorbach</td>
<td>UCLA</td>
<td>DrPH, Public Health</td>
<td>2006</td>
<td>2006-8</td>
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<tr>
<td>Barbara Mensch</td>
<td>Population Council</td>
<td>PhD, Sociology &amp; Demography</td>
<td>2007</td>
<td>2007-11</td>
</tr>
<tr>
<td>Ariane van der Straten</td>
<td>RTI</td>
<td>PhD, MPH, Genetics, Public Health</td>
<td>2008</td>
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### Other Attendees at Meetings:

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<th>Name</th>
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<tbody>
<tr>
<td>Cynthia Grossman</td>
<td>NIMH, Division of AIDS Research</td>
<td>PhD, Clinical Psychology</td>
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<tr>
<td>Kristine Torjesen</td>
<td>MTN Operations, FHI/360</td>
<td>MD</td>
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<tr>
<td>Sharon Hillier</td>
<td>MTN Core, Univ. of Pittsburgh Medical School</td>
<td>PhD</td>
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### 2 New Members

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<tbody>
<tr>
<td>Kenneth Ngure</td>
<td>Jomo Kenyatta University</td>
<td>PhD, MPH, Public Health</td>
</tr>
<tr>
<td>Jose Bauermeister</td>
<td>University of Michigan</td>
<td>PhD, MPH, Public Health</td>
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Behavioral Protocols

- **035B (2008)** - New Approaches to Measuring Adherence of Microbicide Use: Assessing the Feasibility of ACASI in a Microbicide Clinical Trial (Gorbach PM, AIBE, 2013)

- **003C (2010-2012)** - Household and Community Level Factors Associated with Study Product Adherence in VOICE (van der Straten, PLOS ONE 2014)

- **003D (2012-2014)** - An Exploratory Study of Potential Sources of Efficacy Dilution in VOICE Trial (analysis ongoing)


CURRENT PROTOCOLS WITH SIGNIFICANT BEHAVIORAL COMPONENTS
MTN-020 (ASPIRE) Phase III trial of dapivirine ring

- 15 sites, randomized double-blind, placebo-controlled trial
- Malawi, RSA, Uganda, Zimbabwe
- N= 2520 enrolled as of 5/2014
- New ring inserted every 4 weeks
- ≥12 months of ring use
- Monitoring use: visual inspection of used rings & drug levels (blinded)
- Integrated qualitative component
- 3/2013: adherence workshop + start of participants engagement activities: site initiated & focused
Integrated Approach….

• Within sites
• Across sites
• At operations management & leadership levels
Ongoing BRWG Involvement in ASPIRE Trial Implementation

- Behavioral assessments (pictorial ACASI, CRFs)
- Monthly Adherence Working Group (AWG)
  - Review reports of frequency and reasons for ring removals and nonuse; qualitative findings/themes, etc.
- Participant engagement activities
- Qualitative component
- Added measures to study Exit CRF
  - Added social matrix questions based on evidence from VOICE re: importance of social influences, particularly fellow participants
  - Motivations for joining, intentions to join future ring studies
Qualitative Component

- 88/210 participants enrolled at 6 “qualitative” sites
- Multiple data collection methods:
  - Serial IDIs: Participants randomly selected at each site
    - Month 3, Month 12 and/or PUEV
  - Special cases purposively selected by site & approved
    by management team
  - Single IDIs: Premature product discontinuation (e.g.
    seroconversions, early terminations)
  - Exit FGDs (~2 groups per site)
- Integration with main trial/across sites
  - Debriefing reports circulated to management team
  - Themes discussed at: site clinic staff meetings; AWG
    calls; qualitative calls; protocol meetings
Participant Engagement

Engagement events strive to:
- decrease social distance between participants and staff
- build motivation for adherence and retention
- reduce trial fatigue for both participants and staff
- create sense of commitment and ownership over the trial

Event types:
- small group discussions with participants
- social
- male partner meetings
- couples
- milestone (retention)
- holiday

Events conducted and documented:
- 199 events conducted across 15 sites: 3/2013 to 4/2014
- summaries and participant attendance logs collected from all sites quarterly
MTN 003D – An exploratory qualitative study of potential sources of efficacy dilution in the VOICE trial

- **Stage 1** (10/12-03/13) – to explore potential factors contributing to efficacy dilution after early closure of oral and vaginal tenofovir arms in VOICE (N=88)

- **Stage 2** (11/13-04/14) – to explore factors influencing adherence in greater depth, including HIV risk perception & motivation – includes disclosure of drug PK results to participants (N=131)

See poster presentation #267
MTN 017- Phase II Randomized Expanded Safety & Acceptability Study of Rectally-Applied Reduced-Glycerin (RG) Formulation Tenofovir 1% Gel and Oral Truvada

- Multisite: USA, Thailand, South Africa and Peru
- Randomized open label six-sequence, crossover study: three 8-week periods
- Three regimens:
  1. Daily oral Truvada
  2. Daily Tenofovir RG1% gel
  3. RAI-associated Tenofovir RG 1% gel
- Sexually active HIV(-) males or transgender females, ≥18 years w/ history of receptive anal intercourse (RAI) in prior 3 months
- Study regimens compared for safety, acceptability, systemic and local absorption and adherence
MTN 017 Behavioral Objectives and Measures

- **Acceptability**
  - Investigate associations between # of tablets and applicators used during 8-week cycles and acceptability, demographic, and background factors
  - Acceptability = participant self-report of ease of use, liking product, likelihood of use if shown effective; *(baseline and follow-up behavioral questionnaires [CASI], in-depth phone interview)*

- **Adherence**
  - Identify factors associated with product adherence and whether they differ by product used or regimen
  - Adherence = percentage of doses taken orally or administered rectally in an 8-week period; *(follow-up behavioral questionnaire, SMS question, applicator and pill counts, PK test results, data convergence interview, in depth phone interview)*
MTN 017 Data Convergence

- Adherence data collected via:
  - Product return counts
  - Daily SMS
  - PK test results (provided 5 times)

- Discrepancies between measures may occur

- Data convergence and PK data interviews allow for clarification of discrepancies and confirmation of correct number of doses taken

- Behavioral team will review each data convergence interview and PK data convergence CRF and estimate adherence to product use
US-based Ring Trials: 013, 023, 024

- 013: 4-weeks ring use among sexually abstinent women – PK/safety
  first multidrug ring trial (Dapivirine, Maraviroc), CASI, CRFs and exit semi-structured interviews

- 024: 3-months ring use in menopausal women – CASI, CRFs, exit Video interviewing (IDI)
Phase 2a Safety Study of Vaginal Ring in Adolescent Females (MTN-023)

- Cross-network collaboration
- Done in collaboration with ATN – behavioral investigator (Greg Zimet) member of team and 3 of 4 sites are ATN sites
- Baseline & quarterly visit – ACASI Behavioral Questionnaires
- SMS Check-in
  - Adherence assessment
  - Support
- Qualitative Interviews at exit
This is a check-in. Is it in or out…?

Step 1

Step 2

Step 3

Step 4

Participant reply forwarded…

In/Out

Participant reply received
Qualitative Interviews – MTN 023

- Measure and explore factors that affect adherence
  - Social/partner networks
  - Intercourse experience
  - Partner response to ring use
  - Removal timing
  - Expulsion occurrence
  - Vaginal hygiene
  - Condom use behavior
  - Menstruation issues and practices

- Examine Study SMS & ACASI Survey issues
  - Privacy concerns, ease of use, adherence support, feasibility

- Video interviewing Conducted by GoToMeeting
MTN 015 Behavioral Assessments

- Behavioral Objectives
  To describe post-conversion changes in sexual behaviors and partnership status of women who seroconvert during participation in microbicide trials

- Behavioral Evaluations
  - Baseline behavioral questionnaire
  - Follow-up behavioral questionnaire
    - 3, 12, 24 months post-conversion or post-initiation ART
  - Antiretroviral therapy adherence
  - Social Harms Assessment
  - Disclosure of HIV status
  - Depression
Depression Analyses

1. Evaluate the utility of a depression scale to assess the presence of depression among recently infected women in five African countries

2. Describe the prevalence of depression symptoms among recently infected women

3. Identify factors associated with depression among recently infected women
MTN-015: Depression

- Depression and anxiety were modeled off of the Hopkins Symptom Checklist (HSCL-25)
  - 10-item index of anxiety and a 15-item index for depression

- Validation studies of HSCL-25 conducted by Kaaya et al. determined that a subset of 8 of the questions, along with adjusting the “caseness” cutoff score to 1.06 or greater, yielded highly sensitive and specific results in identifying anxiety and depression

- Thus, MTN-015 used the 8-item index to identify anxiety and depression
Acknowledgements

BRWG team members

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