Qualitative Research: Best Practices Informed by Study Design, Data Collection, and Analysis

Subject Matter Expert Consultation Meeting Report

Sponsored and organized by the Office of HIV/AIDS Network Coordination’s Behavioral Science Working Group

Introduction:

This report describes the proceedings of a workshop organized by a planning committee convened by the Office of HIV/AIDS Network Coordination (HANC) entitled, “Qualitative Research: Best Practices Informed by Study Design, Data Collection, and Analysis”, which was held in Washington, DC on May 5, 2015. It was first noted in 2007 that a meeting dedicated to qualitative research was needed. This meeting was the first of its kind. The meeting was borne out of discussion within the HANC-facilitated Behavioral Science Working Group (BSWG) about studies that have collected a fair amount of qualitative data and used different methodologies to assess issues such as adherence, risk compensation and product acceptability.

The meeting objectives were to:

1) Identify and delineate the qualitative methods and tools utilized to assess adherence and product acceptability in ongoing and recently completed major HIV prevention trials
2) Develop best practices and/or recommendations for the most effective and efficient inclusion of qualitative data collection in future studies,
3) Identify potential datasets amenable to cross-protocol analyses from existing data.

The following is a summary of the invited presentations, discussion, lessons learned, and recommendations for the inclusion of qualitative data collection in future network trials and in the HIV prevention field. There were 32 meeting attendees, including researchers from the AIDS Clinical Trials Group (ACTG), HIV Prevention Trials Network (HPTN), HIV Vaccine Trials Network (HVTN), International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT), Microbicide Trials Network (MTN), Family Health International (FHI 360), Population Council, as well as representatives from the National Institutes of Health (NIH).

Session 1: Formative Studies to Inform Study Design and Feasibility, Barbara Friedland (Population Council) and Michele Peake Andrasik (HVTN), moderators

The session sought to address these questions:

- Where can qualitative research be most helpful in formative research?
- How can qualitative research be used to better inform and plan a trial?
- When is the best time to do qualitative work and how do we make the time to do the necessary work?

Barbara Friedland (Population Council): Carraguard Phase 3 trial

Purpose: The Council conducted formative research to test the lexicon for translation developed for Carraguard trials in South Africa. Carraguard was a first-generation topical microbicide tested first for safety in a Phase 2 trial, and ultimately in a Phase 3 efficacy trial. There was no pre-existing infrastructure so the Council established the sites, developed community advisory boards, and trained all of the staff for a phase II trial with 400 women.
Methods and Outcomes: In preparing for the trial, the Council worked with the sites to develop a lexicon for translations, focused primarily on the informed consent process. The draft consent forms were pre-tested in focus group discussions (FGDs) in the trial communities (Gugulethu, Cape Town and Ga-Rankuwa, near Pretoria) to find out how potential participants understood research terms and concepts. For example, participants misunderstood that the purpose of the study was to test Carraguard’s safety (versus efficacy). To address this, the form was revised to refer to the trial as a “safety study”. Participants also seemed to overstate risks, including saying using the gel could cause death. The Council added more background from Phase I trials to the consent form, and emphasized that likely risks were vaginal itching. The revised consent form also clarified the extent of care and increased compensation.

Capitalizing on a manufacturing delay, a 3-month feasibility study was conducted (with placebo gel), which enabled piloting the revised consent form before the actual Phase 2 trial. In-depth interviews were conducted with participants and it was discovered that women understood that the purpose of the study was “safety;” however, they equated the word “safety” with “keeping me safe from disease.” To address this, a Q&A was developed for study staff to use for assessing comprehension to make sure the participants understood key concepts before signing the consent form. The Council also created a study booklet with illustrations and analogies to help explain difficult concepts. For example, after the Phase 2 trial, the Council conducted focus group discussions (FGDs) and in depth interviews (IDIs) with a subset of participants. All of the women understood what was meant by safety and acceptability, and that the effectiveness of Carraguard was going to be studied at a later date. The participants said that they understood the importance of informed consent and that the one-on-one counseling was most helpful. The study booklet helped to explain the difficult concepts and helped explain the study to their male partners and other family members. The women didn’t like the cartoons in the booklet and recommended more realistic pictures or photographs and making a video to help explain things to future participants in the Phase 3 trial.

Lessons Learned:

- Pre-testing language is critical for ensuring comprehension and truly informed consent.
- Asking participants to explain their understanding of key concepts using their own words in the context of FGDs or IDIs uncovers potential misunderstandings and can help to develop translations/explanations using participants’ own words.
- Developing a lexicon for translation/language of consent is an iterative process, requiring resources (time and money). Asking community members/participants for their input and feedback is important for making information meaningful and understandable.

Michele Peake Andrasik (HVTN), Formative work to inform HVTN 505 and the upcoming HVTN 703/HPTN 081 joint collaboration protocol:

Purpose: Conduct formative research to enhance recruitment of MSM and transgender women for HVTN 505, a Phase 2b trial.

Methods and outcomes: NIMH funding was utilized to conduct mixed methods research within these communities. HVTN developed a survey to find out answers to questions such as: what participants thought of the trial; what the barriers to participating in vaccine trials are; and what facilitated participation. The survey was distributed in six US cities including Atlanta, Boston, Houston, Los Angeles, New York, and Philadelphia. Two FGDs were conducted in each city. HVTN was proactive in the way they were recruiting for the survey and focus groups. It was known not all of the high risk populations that they sought to recruit would be online; 90% of their
recruitment was online and 10% was done in person. FGDs were all held in community settings and they discussed things such as perspectives and beliefs about HIV vaccine research. The surveys and interviews were all with MSM. HVTN went back to four of the cities that had sites with good ties to the transgender community and had good attendance by transgender women. HVTN went to the NAESM conference and held two FGDs at the meeting in 2011 asking the same questions of black MSM leaders. The following year, they took back their results to the NAESM conference as promised. All of the data was analyzed and a report with recommendations and strategies to engage the black MSM community and transgender community was written.

HVTN asked the site staff what HVNT core could do assist with retention with these populations in studies moving forward. The HVTN does not have qualitative expertise in the network that can assist with coding and data analysis. The amount of time that it takes to code and disseminate the information is long. It has taken five years. This has been a real challenge and one that HVTN has been discussing with SCHARP and trying to identify how they can build capacity within the network to get qualitative data analyzed in a timely manner. These efforts helped inform some of the strategies used moving forward with a new phase IIB studies in the US.

A phase IIB study called HVTN 703/HPTN 081 is a joint effort between HPTN and HVNT and it is being fast tracked and is set to open in November or December of 2015. The study is an HIV prevention trial using monoclonal antibody (VRC01) infusions. The study will take place in the US and South America where they will be recruiting 2,400 MSM and TG men and women. About 1500 high risk heterosexual women in South Africa will also be included. HVTN hasn’t been in the communities with an efficacy trial since the closure of HVTN 505 several years ago. They will be conducting formative work to look at acceptability and to think about community engagement. An acceptability questionnaire has been developed for phase I low risk populations, but phase II high risk populations are very different. They want to know about the acceptability of the procedure since they are asking people to receive infusions of the monoclonal antibody, along with what are people expecting from the visit and how can their experience be enhanced? There is a focus on participant burden since they are asking people to come in every two months for a total of 10 infusions. The capacity to do formative work is unclear. They also want to collect data that can contribute to the science of community engagement.

Lessons Learned: Building relationships with the community has been the most helpful method HVNT has used. Keeping the community informed is very important as is ensuring that there are ongoing and continuous efforts to give information to the community. When working with transgender populations, it is important to include posters with transgender women on them. Transgender women want to walk in a clinic and see their faces. Gender neutral bathrooms at sites are also important. All staff members need to be competent and create an environment that is welcoming and safe. One challenge is analyzing the qualitative data. It took five years for HVTN to analyze data from 505. There is not enough capacity at HVNT core to do the kind of ongoing qualitative work they would ideally like to do.

Paula Frew (ACTG, HPTN, HVTN), multiple studies:

Purpose: Predicting and retaining community participation in HIV biomedical studies

Methods and outcomes: A formative research agenda might include doing community consultation as done in HVNT 505, which excavates values, perceptions, and opinions. Behavioral research needs to be ‘packaged’ through persuasive communication. We also need to gauge the “market” position. In the urban South, they have learned that the more you engage the community, the community’s opinion of you will be better. This is similar to the idea of developing “brand loyalty”.

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The InvolveMENt study examined the Elaboration Likelihood Model (ELM) operant to inform study brand development and recruitment messages for “InvolveMENt”, “Brothers” (HPTN 061), and “LifeForward” (HVTN 505). They used FGDs. The intended audience, message, source, and communication channels are the four major components that are postulated by the ELM to induce more cognitive thinking. The major findings from “InvolveMENt” included recruitment messages would have greater persuasive potential if framed by highly relevant concerns (e.g. LGBT health disparities) for the intended audience; include key motivators (e.g. compensation) in your message, as well as include information about “what’s involved” and address challenges; use trusted and credible sources who are well informed about HIV research; and develop a strategy with highly targeted, dynamic approaches to reach MSM online (e.g., social media) and in person.

For example, LifeForward materials were diverse. A brand that will stick with individual messages that will appeal to different audiences needs to be created. This is important because of nuances in values, opinions, and perceptions. This helps develop message framing strategies. It can be enhanced by behavioral theory and framework testing. Develop a segmentation strategy based on typologies. This has resulted in consistent history of successful, rapid recruitment to NIAID network studies (HVTN, HPTN, ACTG, WIHS) and investigator-initiated studies.

Betsy Tolley (FHI 360), Sub-study of HPTN 059

Purpose: Formative research was conducted to develop scales for measuring acceptability in the context of HPTN 059.

Methods & Outcomes: The sub-study was conducted as an ancillary study, with separate funding and separate, but well-coordinated data collection activities. It was a multi-stage mixed method sub-study to assess the acceptability and sustained use of topical microbicides. The research was conducted in Pune, India between the years 2003-2007. The overall objectives of the study included determining what factors predict couples’ ability to use a microbicide gel consistently and long term, and to evaluate how the clinical trial context influences microbicide use behavior. The sub-study included women aged 18-50 and male partners; all female participants were HIV negative. Prior to implementing the research, they developed a conceptual framework based in part on the AIDS Risk Reduction Module (ARRM) and other behavioral theories, as well as social science research conducted in India, in order to guide the exploration of themes during the qualitative, in-depth interviewing and make explicit what the initial ideas about what factors would predict consistent microbicide use.

The aim of the first stage of research was to create and psychometrically validate scales that measured constructs related to HIV risk perception, couple harmony and sexual power/self-efficacy. Scales are multiple questions or statements that relate to an underlying unobservable latent construct. The scale development stage included three separate data collection activities. First, the item content for target scales was identified from two sources – an initial literature review and a qualitative study that included repeated, in-depth qualitative interviews with high- and low-risk women and their partners. Second, the team tested and revised the draft items by conducting cognitive interviews to understand how participants understood and responded to the draft items. Finally, in order to reduce the number of draft items, verify and assess construct validity of emergent scales, the sub-study team incorporated revised items into a survey that included other psychosocial and behavioral questions to assist validation. The survey was administered to 150 men and 300 women recruited through HPTN 059’s networks. Exploratory factor analysis of the draft scale items produced factors related to couple harmony, HIV risk perception and protection efficacy. The couple harmony scale had high internal reliability and included items
related to six dimensions. Several factors were produced that related to HIV risk perception. This gave a clear understanding of the dimensions underlying couple harmony, risk perception, as well as sexual power and control.

The scales produced in stage one of the HPTN -59 sub-study were then administered during a prospective study of enhanced acceptability, conducted in parallel to the HPTN 059 study to assess the safety and acceptability of tenofovir 1% vaginal gel. The parallel sub-study was conducted in the India site only and included 100 women participating in HPTN 150, 100 women from the same communities who were not participating in the clinical trial and 100 male partners drawn from across the two women’s groups.

**Lessons learned:** The formative qualitative study provided nuanced understandings of what might facilitate or inhibit couples’ use of microbicides. It enabled the development of quantitative measures that could be administered within a clinical trial. Structured surveys with clinical trials and non-clinical trial participants suggested that behaviors performed within a clinical trial took on different meanings from those undertaken outside a trial. The women that had more positive attitudes towards the gel were better gel users as well as higher condom users. Outside of the clinical trial in the non-clinical trial cohort, the women who had a more positive attitude about condoms were found to use condoms more frequently.

**Future directions:**

Funding: There are many challenges to conducting formative research. One of the larger challenges is funding. Fundraisers have been used to fund formative research. Outside funding has also been obtained. There are timing issues as well as site capacity issues. Some networks do not have the capacity to do ongoing qualitative research. There are language and cultural context issues that can also be challenging. Overcoming funding hurdles will be a challenge – need to incorporate funding for specific, critical formative research into trial budgets.

Rapid analytic approaches: Going forward, we need to think outside of the box to get rapid analytic approaches. There may be ways to formalize a more rapid approach. The methods of how we think about qualitative research are important. We need to look at other ways to analyze the data other than coding.

Share successful methods: For example, the Council and FHI360 developed a toolkit for creating lexicons for translation – this methodology can streamline the process of establishing translations. Database of clinical trial terms can be tapped into so that researchers don’t need to “start from scratch” with each new trial.

**Session II: Incorporation of Qualitative Research into Network Protocols: Challenges and Opportunities, Barbara Friedland (Population Council) and Elizabeth Montgomery (MTN), moderators**

Session discussion items:
- Models of incorporation: standalone ancillary vs. “qualitative component” of parent protocol vs. exit or post-trial research
- Data triangulation: How to optimize and reconcile qualitative data collected from multiple resources (mixed methods)
- Addressing tensions between traditional social science and clinical trials

**Elizabeth Montgomery (MTN): MTN trials**

MTN has a Behavioral Research Working Group (BRWG) and also assigns a behavioral scientist to each protocol. The BRWG helps design the research questions that are behavioral in nature and they help put together the modality of the data collection. This is not the case for most of the other networks.
VOICE C was a qualitative ancillary study to VOICE. VOICE had over 5000 women enrolled at 15 different sites throughout southern Africa. VOICE C was a stand-alone protocol, but was being conducted during VOICE. VOICE C was a joint effort between the community working group and the BRWG. They wanted to look at household factors that would influence product use in VOICE. The study was conducted at one site where 102 women enrolled. There were three other study groups, including male partners, CAB members, and community stakeholders. The methods used for qualitative data collection included IDIs and FGDs. They aimed to do ethnographic interviews, or rather, serial IDIs. The original intent was that the researchers would be going to the women’s houses, but it didn’t work out logistically to be able to do that.

Due to the results in VOICE, MTN turned to the qualitative researchers to try to explain what had happened. They went back into the field for VOICE D and tried to get more insight as to what had happened during the VOICE trial. They went to great strides to make it as neutral as possible in terms of interviewing women in locations separate from the VOICE trial setting and using interviewers not affiliated with the VOICE trial. VOICE D had two stages. First, they wanted to explore what contributed to the lack of effectiveness in VOICE. They looked at the lack of adherence and anal sex. Secondly, they looked at the PK results available from a subset of the sample. There were a very low percentage of women who had detectable drug levels in their results. They used the PK data to talk with the participant about what the drug level results showed about their actual use of product. This was an effective way to break down the barriers and to establish a greater openness in the interviews.

The ASPIRE trial is an ongoing large study testing a vaginal ring with dapivirine for the prevention of HIV in women. The qualitative component was built into the study from the beginning of the trial and included as part of the parent protocol. There are six out of 15 sites involved across four countries. There will be approximately 200 women enrolled and interviewed using a variety of interview mechanisms including serial IDIs, single IDIs, and FGDs. In ASPIRE, study interviewers complete a debriefing report within 24 hours of an interview, although it typically takes a week to receive. It’s a short (~two page) summary of the interviews. It’s used as a mechanism to keep closer tabs in near real time on what they are hearing from their participants and it’s been very useful. An additional benefit is being able to use the information to feed back into trial implementation. The interviewers are from the site and in most cases their primary responsibility is qualitative interviewing. The debriefing report includes open-ended questions following the key themes about motivation to join the trial, risk perception, adherence, and acceptability. At the end, MTN asks the interviewers if anything surprising came up during the interview. In the last series of serial IDIs, they built in categorical quantitative methods asking which preventive methods would they most likely use in the future and which ones would you least likely to use. A quick summation of the data will be completed summer 2015. Many of the participants consent as part of their main consent while some sites have a stand-alone consent process for the qualitative part of the trial. The consent informs the participants that their information won’t be shared outside of trial staff.

The sites that are part of the qualitative component reviewed a scope of the work and what it entailed. Sites had to complete an application process. One site that said they would need training to enhance their capacity. The qualitative data collected is complementing quantitative data. Having the qualitative component in place during the trial allows you to feed back the information you are getting from participants into trial conduct. There are most likely more cost efficiencies when qualitative components are built into the trial due to sharing of resources.

Ivan Balan (Columbia University): MTN 017

MTN 017 is a phase II rectal microbicide study. Conducting IDIs and ethnography was proposed. In the end, there were 40 IDIs in total (10 in each country), but no FGDs or ethnography was supported or conducted. All of
the interviews were conducted from New York. There was a Thai native to perform interviews with Thai speakers as well as a Xhosa speaker. A lot of adherence data was collected in these interviews.

In MTN 017 data triangulation was implemented. SMS data was collected as participants responded to text messages. The SMS reports allowed the researchers to create calendars to show when the participants reported use. The participants were asked to return unused product as another measure. There were also CASI interviews. The adherence counseling session was divided into two components: the data convergence interview and pK data interviews. The data convergence interview discussed the product use counts. The researchers also had blood draws. There were two usage numbers based on the SMS count and the product use count. The participants were asked which number was the most accurate number. Once the results from the blood work were received prior to the next monthly visit, they would compare the data with the participant’s calendars and pill counts.

In total, 1500 sessions have been recorded as no participant said no. MTN ensured the counselors were performing their job correctly. The goal was to make it easy for a participant to talk about not using the product.

The adherence counseling sessions had seven steps:

1. Welcome the participant.
2. Conduct data convergence interview.
3. Conduct PK convergence interview and refer to participant’s count calendar.
4. Explore what helped the participant use the product.
5. Assess motivation for the participant to continue using the product.
6. Identify and problem solve obstacles to adherence.
7. Close the session.

**Lessons learned:** During the study, there was “real-time” feedback on challenges and facilitators of product use. This action research was used to improve product use and counseling. They learned early on that the text messages the participants received helped with product use. The participants chose what time the text was received. Trial researchers took note of negative PKs.

**Mitzy Gafos (Microbicides Development Programme): MDP 301**

**Methods and Outcomes: MDP 301** was a phase III trial with over 9300 women participants. The MDP worked with six existing research centers in southern Africa from 2002-2009. Qualitative research was conducted the entire time. The benefits of having the qualitative data integrated into the trial included gaining buy in from the entire research trial team. The social science team was part of the main team. By being integrated, the research team could be flexible and make changes within the protocol. Robert Poole coordinated the social science work. He felt that the social science being integrated into the main trial does compromise independence. The overarching trial management group was very supportive.

The qualitative and quantitative research went hand in hand. Ten percent of participants were interviewed at two sites. There were 725 women interviewed three times through the course of the trial. The serial interviews were beneficial. The idea was there would be three interviews conducted by the same interviewers. There was at least six social science staff at each site. Most of the centers would have one person trained to a master’s level, but the vast majority of the team was trained locally. Couples data was gathered. FGDs were very valuable. There were focus groups with female trial participants and separate focus groups with male community members. Sensitive information came up during the focus groups. MDP also included invaluable ethnographic research as part of the trial protocol. The ethnographers were locally born and trained. They sat in waiting rooms and listened to
conversation. It was valuable to have all six centers involved in the qualitative research. They tried to integrate community engagement with social science research and this was found to be valuable. The staff was trained to do Nvivo coding locally. Each center recorded some sexual behavior questions. These proved to be useful. The IDI interviews gave women the best opportunity to be as accurate as they could. Overtime, the IDIs felt very representative.

**Lessons learned:** Having the ethnographers in the waiting rooms proved to be very useful. Serial interviewing was excellent for capturing changes, but in practice it did not capitalize on the serial nature. The interview content ended up being the same. There were interpretation problems. Nearly 50% of the interviews had some inconsistency. There was a lot of coding training. The step they struggled with was moving to the interpretation part. They discussed options of post-interview briefing, site staff translating transcripts directly versus translations from transcripts. There is a lot of incomplete data needing review and analysis currently. The team collected a huge volume of qualitative data in an effort to overcompensate for prior ‘failed’ trials that did not incorporate any qualitative data. Moving forward and based on the experiences of the qualitative researchers in the MDP 301, deriving a more reasonable sample sizes and having sufficient experts available to analyze and write up the qualitative research are recommended.

**Cynthia Woodsong (International Partnerships for Microbicides):**

Researchers need to start with the goals of their research in mind. Qualitative research needs to be used in an applied ongoing manner. The design needs to allow one to have access to the data. Most IPM trials have qualitative research components. HPTN 035 took a while to develop. Whenever there was a delay, that time was used to develop more tools such as the informed consent booklet that was created. Formative research was conducted. HPTN 035A was an ancillary study done at two sites. There was separate staff that had a background in social science and/or behavioral science counseling. They conducted a round of key informant interviews, IDIs, FGDs, and then more IDIs. They did rounds of interviews with stakeholders, community leaders, policy stakeholders, etc. Staff had debriefing forms they completed after the IDIs. They were locally transcribed and coded. They were only allowed to schedule two interviews in one day. The next day, they had to work on the transcription. The analysis was going on throughout. They were able to respond to challenges and questions emerging in the study in real time. A preliminary analysis report was completed and was able to provide value to the sites if they were having problems. There was a lot of sharing of information. Lessons learned are being applied in the ongoing RING study based on value shown in prior studies. It is critical to have the support of the protocol team leadership.

**Summary:** There are many different models used to incorporate qualitative research into network protocols. VOICE C was a qualitative ancillary study that was being conducted during the parent study VOICE. VOICE D, another qualitative VOICE study, was conducted to try to gain more insight retrospectively as to what happened during VOICE. The qualitative component of ASPIRE was built into the study from the beginning stages of the protocol. MTN collected qualitative data in MTN 017 for data triangulation so that the information could be used to improve the trial in real time. MDP 301 collected qualitative data for the entirety of the trial. With it being integrated into the trial, the protocol team was able to be flexible and make changes to the protocol as necessary. HPTN 035A was an ancillary study to HPTN 035 and was conducted with completely separate site staff. Lessons learned from HPTN 035A are being applied to other IPM studies.

There are several challenges with incorporating qualitative research into protocols. Qualitative research methods may seem foreign in biomedical studies. Also, qualitative research requires lots of advocacy on
communicating about the relevant contribution that can be made in biomedical trial research. Moving forward, qualitative researchers need to challenge each other to make qualitative research invaluable in these studies. Qualitative researchers also need to think beyond traditional approaches to gathering and analyzing qualitative data.

Session 3: Methodology and Data Collection, Betsy Tolley (FHI 360) and Kim Koester (UCSF), moderators

Session discussion items:
- QRM best practices (design issues, data collection and management, data analysis)
- Case studies (data triangulation, rapid analysis and feedback, joint analysis)

Kate MacQueen (FHI 360): CAPRISA trials

CAPRISA 104/004 included a qualitative analysis of disclosure of study participation. The primary objectives were to statistically model the odds of HIV infection for women in the tenofovir (TDF) gel group compared to those in the placebo group, while controlling for reported gel use, and to qualitatively evaluate patterns of gel use behavior among participants. They identified the cases as participants with a positive or discordant HIV test. If the test was positive, the researchers would ask for consent to do an interview on the spot or to do one a bit later. Women that were not positive were also interviewed. The controls were unmatched. There were five target dates for recruitment each month at the two sites. Five participants were randomly chosen for an interview. Previously interviewed women were excluded from the list. The interviewers were not told the HIV status of the participants, although several women self-disclosed as some of them had just found out they are were HIV infected. Time-line follow-back was used to collect detailed 3-month recall data on sexual events and gel use. An interview guide that had guidance for the interviewer to figure out the timing of the sex act and the insertion of the gel was developed. This was used to help walk women through the previous three months. There was a thematic analysis of qualitative interview data. They looked at the participants’ general feelings about trial participation, gel and condom use patterns and challenges, communication with others about the trial, community perceptions about the trial, as well as beliefs about the gel.

In CAPRISA 106/008, there was an attempt to qualitatively drill down into the disclosure process to gain perspectives on how this differed in a blinded vs. open-label trial. Women that were enrolled in CAPRISA 004 could participate. Analysis objectives included the influence of gender dynamics on TDF gel use disclosure, adherence, and continuation. They also wanted to find out about women’s motivations to join, continue to partake, and adhere to study product in the blinded versus open-label trials. They held IDIs and FGDs with participants at an urban and rural site. There were 13 male partners of women who fully disclosed trial participation and gel use. There were four FGDs (two at each site) with community men who were not partners of the participants. The qualitative data analysis combined structural coding to identify text associated with specific topics of inquiry covered in the interview and focus group guides, thematic analysis to identify broad emergent themes, and constant comparison to drill down specific topics and themes for a detailed analysis. The study team was blinded to adherence grouping used to select participants. There was high, medium, and low adherence of participants and they were categorized by their adherence levels. There was a staff member that spent a lot of times at the sites. She’s a trained anthropologist and was a huge help.

Amy Corneli (FHI 360): FemPrEP

FemPrEP was a phase III, placebo-controlled trial to assess the effectiveness and safety of Truvada (FTC/TDF) as PrEP for HIV prevention in women. It was conducted from June 2009 to April 2011. There were four sites with
2,120 women enrolled. There were 33 infections in the FTC/TDF arm and 35 in the placebo. There was behavioral research embedded within the clinical protocol. There were several rapid analysis topics. They wanted to look at adherence. There was a vitamin run-in period to get participants used to taking a daily pill. Informed consent as well as recruitment was looked at. There were two CRFs related to adherence: the vitamin adherence that was collected once at enrollment to identify challenges and the study pill adherence, which was collected at every visit and reflected the past four weeks to identify challenges and brainstorm solutions. The analysis of the CRFs was conducted through descriptive statistics and frequency tables were created. They would be able to identify potential problem areas such as low self-reported adherence and reasons study pills were skipped.

Reports were provided monthly for the first 4-5 months, then quarterly. Each report included a disclaimer on what the report was intended to do and what it was not intended to do. The report listed the response frequencies from the CRF questions. They would highlight the frequency tables for the potential areas of concern. They would describe possible trends over time. They provided commentary on the frequency table and recommendations. For barriers frequently mentioned, counselors were encouraged to proactively ask participants about these barriers in subsequent adherence counseling sessions and help the participant consider strategies to overcome these barriers as their monthly adherence goal. They commented on the potential for socially desirable responses and asked counselors to encourage participants to be as open as possible about pill use. Telephone conferences or email discussions followed the sessions with the point person at the site.

FemPrEP used qualitative, semi-structured interviews. The interviewers were trained social scientists that received two weeks of additional training before starting any work. Interviews would happen every 3-4 months after site initiation. They interviewed 5% of HIV-negative participants via random sample. The objectives of the interviews were to monitor self-reported adherence, participants’ trial experiences and to gather supporting data related to the secondary FEM-PrEP objectives on adherence and sexual behavior. The interviews were designed to be an hour, but many were shorter. At the conclusion of the interview, the interviewers completed the transcription.

A rapid analysis was conducted in Microsoft Excel. Adherence-related data that was examined included:

- Any reported difficulties or challenges with daily pill taking
- Things that made taking pills easier
- Positive statements about adherence
- Ever missed or never missed a pill
- Suggestions to improve adherence counseling
- Any effect of her pill guess (Truvada vs. placebo) on pill taking
- Any discussion of how she normally took the pill and where it was kept
- Any discussion of sharing or selling the pill, including other trial participants’ behaviors, and
- Any discussion of reporting on pill taking by the respondent or by other trial participants.

The rapid analysis logistics was conducted every 3-4 months following the SSI period. It was initiated after the first transcript was completed. One was completed roughly one month after the last SSI was conducted. Up to three analysts conducted the analyses and drafted the report. The data was presented in tables for each section for easy review. Each section ended up with a summary, recommendation, and discussion questions.

**Lessons learned:** The staff appreciated the reports. There was a lot of emphasis placed on ensuring that the counselors did not feel like they were being evaluated. The approach can only be as useful as the data provided. It
is important to focus on the fewer accounts of non-adherence when making recommendations. The fidelity of following through with recommendations is difficult to track. Well-trained interviewers are very important. You cannot train everyone to be an interviewer.

Session 4: Overcoming Qualitative Data Analytic Challenges across the Networks, Michele Andrasik (HVTN) and Deborah Kacanek (Harvard School of Public Health), moderators

The session sought to address these questions:

- How do we overcome qualitative data analytic challenges such as coding and software issues across the networks?
- How do you validate your qualitative data for IND studies?
- When do you draft your manuscripts?
- Can it be streamlined?
- To what extent are the CABs involved in receiving/interpreting any of the data as well as the participants?

Norma Ware (Harvard Medical School), Partners PrEP

Purpose: The goal of the qualitative research was to characterize influences on PrEP adherence by HIV-uninfected partners in serodiscordant couples participating in the Partners PrEP study and the ancillary adherence study. This would help inform the high rates of adherence observed in the ancillary adherence study.

Partners PrEP study was a phase III, double-blinded, three-arm randomized, placebo controlled trial evaluating safety and effectiveness of once-daily oral TDF and co-formulated TDF/FTC PrEP for preventing HIV acquisition by uninfected partners in 4,758 serodiscordant couples in Kenya and Uganda. The qualitative study was a study within a study that was within a study. There was the Partners PrEP Study, the ancillary adherence study, and then the qualitative study.

Methods and Outcomes: There were 60 participants, 45 HIV-uninfected partners taking PrEP and 15 HIV-infected ‘index’ partners. The data was collected through single, in-depth, open-ended interviews focusing on adherence. The analytic steps included:

1. Repeated reading of transcripts for content on adherence influences
2. Data reduction:
   a. Write case summaries, aka adherence stories
   b. Derive categories from the summaries representing “types of adherence influences”
3. Matrix building:
   a. Enter “types of influence” categories into a matrix
   b. Enter content (examples) corresponding to “types of influence” categories into matrix
4. Thematic analysis of matrix data to arrive at final categories
5. Assemble final categories into an “explanatory logic” or “story”. This is the main explanatory part.

The discovery was that serodiscordance destabilizes couples. A “discordance dilemma” ensues for HIV-uninfected partner, the desire to avoid acquiring HIV and the advantages of preserving the relationship become competing priorities. PrEP is seen as a solution to the “discordance dilemma”. It is a means of safeguarding health without ending the relationship. To maximize the benefits of this resource and resolve a major life problem (threatened loss of spouse), PrEP users work to adhere well.¹
Challenges of conducting qualitative behavioral research on HIV include the qualitative analysis needs to be flexible, even individualized, whereas reviewers lean towards a “checklist” approach to evaluation, word limits in major journals impede optimal presentation of qualitative research, and qualitative research is underrepresented in major HIV conferences. To deal with the word limit issue, it was noted that certain journals are more open to being lobbied for longer word counts for articles on qualitative data. Quotes can be put into tables which do not count against the word limit or in the supplemental data section available to online readers. You can also publish the full qualitative paper in a qualitative journal with longer word limits and then write a short commentary for one of the more clinical type journals and refer back to the full paper.

Demonstration of the value of qualitative research leads to the inclusion in the future. It is very important for local involvement. Some sites have capacity and others do not. Training requires a major investment. How to keep people who were trained engaged in studies in the future is also a major challenge; some people cannot retain the social and behavioral researchers because they get hired elsewhere. Rural sites also have a difficult time keeping people. Desmond Tutu has had challenges retaining trained social/behavioral scientists. There is a need for qualitative research training in South Africa. There is a major need for longitudinal qualitative data collection and analysis. How to deal with couples-based qualitative data and analysis is challenging.

Amy shared her technique of the one step translation/transcribing process and having interviewers prioritizing that before moving on to more interviews. You get the data more quickly and you have the benefit of the person there for the interview translating it. Norma made a great point about not limiting ourselves to very specific means for coding.

There was a discussion of different sampling approaches – random or purposive – which is more appropriate for your research question and stratifying your sample among different levels? If you’re stratifying, you need think about your analysis approach and blinding yourself and the analysts to minimize the bias in the analysis process. We’ve heard of innovative interview processes such as MTN 017’s telephone interviewing. Video interviewing has been done. It is important to rapidly turn around findings and methods to do that. We discussed a few examples and techniques. How can we think outside of the box to develop more techniques for rapidly getting back results? There are techniques to get real time PK results and to use those. It is a new method of enhancing discussions and encourages greater depth and honesty in your discussions with the participants.

Session 5: Opportunities for Cross-Protocol Analyses of Qualitative Datasets, Betsy Tolley (FHI 360) and Elizabeth Montgomery (RTI), moderators

Due to time constraints, session five was very brief. PopCouncil has created a Lexicon database. This utility can be shared across networks and institutions. This is one outcome of a value of the initial investment. The group thought that post-meeting discussions should continue on this topic area.

Two examples of combining qualitative data sets were included in the workshop packets. In the first example FHI 360 set to explore best practices for engaging male partners in microbicide roll out. There was an in-person meeting to discuss key themes and issues. They came up with a series of key questions that they wanted to get input from selected studies. They didn’t take raw data sets, but rather had the researchers respond and then the responses were synthesized. The group reconvened and discussed on what the key messages were. The second was an example of a meta-ethnography where the authors did a desk review of published papers to explore their research questions. A third approach to doing cross-protocol analyses would be to combine raw datasets. This would involve many issues such as re-coding, consent, etc.
Session 6: Recommendations, Next Steps, and Conclusions, Betsy Tolley (FHI 360) and Elizabeth Montgomery, (RTI), moderators

The last session of the meeting was reflecting on the discussion throughout the meeting. The discussion was broad (benefits of qualitative research, challenges, questions to consider, best practices, and possible next steps) and engaging. The OBSSR put out a paper on best practices on mixed method design. There have been two qualitative meta-analysis of ART adherence, intervention for studies.\(^1\),\(^2\). A list of recommendations was an objective of this meeting.

**Benefits of qualitative research:**

1. Qualitative research can provide explanatory framework.
2. Qualitative research has proven to be effective when championed by leadership; it seems that many of the contributions of qualitative research are being disregarded outside of adherence information.
3. Informed consent is a critical part of the trial regardless of trial outcome. If conducting qualitative research can advance the trial population to help them understand what they are participating in, then it has intrinsic valuable.
4. To help justify qualitative research, we can focus on the areas of inquiry that qualitative research is best at, such as uncovering new information that is presently unknown and not measured in other ways or behaviors and attitudes that are moving quickly and dynamically. Where will qualitative research get you further than quantitative research would?
5. Qualitative data improves the implementation of trials, but it can also help interpret the findings from the trial. That is an important contribution, even if it does not inform the conduct of the trial while it is ongoing.
6. Qualitative research that is formative and iterative can help inform study design. There are many opportunities to gather more information pre-enrollment during study design. In defining eligibility requirements, informed consent, is all qualitative.

**Challenges:**

1. There are challenges with getting data from networks for cross-protocol meta-analysis.
2. Resources. There is a need for adequate resources to support the qualitative research, both at the site level, the investigator level, and the analytic level. The networks SDMCs do not have in-house expertise and resources for qualitative data analysis.
3. A challenge we face moving forward is that social and behavioral science is there to serve the clinical trial. There is limited support for social and behavioral research in some networks. The success and failures of a clinical trial do not solely depend on social and behavioral science.
4. There’s a commitment to continue doing this work and to continue getting our work out there and to share the value of qualitative research both through trying to publish and demonstrate what we think are the best practices and efficiencies (cost and scientific wise).

**Questions to consider:**

1. How can we position ourselves to address very specific questions? Start with the end goal in mind and work backwards. Think about the audience you want to reach. We need to think about the topics that the publications are discussing.
2. Is coding too much of a short cut, in some ways, if you’re taking transcripts and immediately placing codes on them? It is just one of multiple approaches and the approaches you select should be well justified. The parallel is with the quantitative analysis. There is often no interpretation with the coding. Ultimately, you want to tell a story at the end.

3. How do we better engage our local, in-country collaborators in analysis??

4. How do we interpret the different adherence measures? Using the value and tools that you have in qualitative research to answer very relevant questions would be very useful. Qualitative work could make a significant impact in locating “truth” in the wake of all of the different results in the PrEP trials.

5. How do qualitative methods enhance implementation of the trial? What kind of methodologies could inform a trial?

6. How do you use qualitative research to enhance trials? HVTN 505 had significant formative work to assess where people were in terms of the trial (e.g. in Rochester, NY).

7. What is the commitment of sponsors to fund qualitative work?

8. How do we rapidly turn around findings so that we can inform a trial?

9. How would a cross-protocol analyses guide of network procedures be validated?

10. How do you operationalize iterative trial design based on qualitative research? It is being done in a few trials such as the IPM RING and ASPIRE study where data is provided back to sites on adherence challenges. Weekly updates to site staff are provided while preserving the blind. ASPIRE has a dedicated Adherence Working Group that meets monthly. Qualitative research is a data collection tool just like quantitative research.

11. What are the key reasons of gathering the qualitative data? It is not necessarily about optimizing qualitative work broadly; it’s about improving optimization of qualitative work in the context of HIV prevention trials.

12. What makes qualitative research most attractive to HIV prevention trialists and funders is optimizing the chances of trial success. There have been some great examples of qualitative methods and examples explaining trial successes and failures.

13. How do we iteratively use data during the trial to optimize the chance of trial success? Do we have best practices that address this? If the research only explains things after the fact, it may not be as helpful. Maybe best practices aren’t there yet but we could significantly inform that discussion.

**Best Practices discussed during the meeting:**

1. There needs to be social and behavioral expertise (including qualitative) at the beginning of the protocol development. This is the way it is done for other areas of protocol development such as laboratory, pharmacology, immunology, clinical, etc. At every phase of a trial, we heard great examples of the importance of the qualitative research component. The cognitive testing scales, fidelity tests, clear informed consent, new ways to market products, etc. Qualitative research adds a lot of value to these critical research areas.

2. Simultaneous translation and transcription – interviewers do their own transcribing ASAP after each interview.

3. Involve local study staff in data interpretation and analysis as much as possible – resources are critical for training to have qualitative researchers on staff.
Possible next steps:

1. Conduct a literature review. It would be valuable to get a sense of the qualitative research on HIV prevention trials. HANC has started putting together a qualitative research library on the Behavioral Science Interest Group Resources Page on the HANC portal.

2. Write an advocacy paper highlighting the value of qualitative research with specific examples of how qualitative research led to specific results. This could help get more qualitative research incorporated into more network trials. It would be less about the cross-cutting data analysis, but more about what has worked. A paper summarizing qualitative research in HIV prevention research would be a significant contribution.

3. Put together a supplement to highlight the work presented at the SMEC. If we could get 6-8 papers covering these topics, it could be very helpful to reach the audience we want to reach.

4. There is a keen interest in sharing amongst this group (resources, ideas, instruments, etc.).

5. Map the pathway/history of how one study has had an impact on the next one. Think more broadly.

6. Have additional conversations about when qualitative research has been useful and what the elements were. Results of qualitative research need to be reported back to network leaders who need to understand the importance.

7. Sharing IRB approved language that allows for an ethnographer in the waiting room with participants would be very useful. There are parts of recommendations of how people have incorporated it in the past. What is the language used in the consent form that discusses ethnographic research? Similar requests have not been favorably received by some protocol teams and regulatory bodies for other studies.

8. Identify the themes in studies that use rapid assessment and look at and see if they corroborate with other methodologies. Any kind of costing analysis assuming dollars saved would be a positive.

As noted at the start of the day, this type of meeting has been long overdue. The concerted focus on qualitative research in the content of the HIV/AIDS Clinical Trials Networks and some other large HIV prevention studies led to a very rich discussion with many opportunities for productive ongoing collaborations as noted above. These recommendations will be discussed with the planning committee for this subject matter expert consultation and the HANC Behavioral Sciences Work Group as well as the participating NIH Institutes.
References:


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Behavioral Science Working Group Qualitative Research SMEC
Qualitative Research: Best Practices Informed by Study Design, Data Collection, and Analysis
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Qualitative Research: Best Practices Informed by Study Design, Data Collection, and Analysis

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