The Office of HIV/AIDS Network Coordination (HANC) facilitates communication, coordination and harmonization across the National Institute of Allergy and Infectious Diseases HIV/AIDS Clinical Trial Networks. With the support of the National Institute of Mental Health (NIMH), HANC facilitates a trans-Institute, cross-network Behavioral Science Working Group (BSWG). The BSWG organized a meeting of over 30 behavioral and social scientists, NIH staff, and other content experts in Bethesda, MD on October 11, 2012. The focus of the meeting was to address key questions and recommendations related to electronic behavioral data capture technologies.

**EXECUTIVE SUMMARY**

**Context and Goals:**

- Provide recommendations for networks using (A)CASI and other electronic data capture technologies - particularly guidance on why, whether, and how trials might adopt these approaches.
- Identify key considerations for a cost/benefit analysis when protocols are considering new tools.
- Address the limits of “validation” given questions about transferability and challenges with self-report.
- Consider developing an electronic data capture technologies implementation costing tool applicable to a variety of clinical trial settings.

**Key Recommendations:**

- Create a vendor/technology table for researchers to reference as they consider adopting a tool.
- Identify funds to pilot novel technologies and cognitive testing of questions.
- Conduct a cost/benefit analysis and develop a budgeting tool and best practices guidance document modeled on the HANC “Recommendations for Standardizing Budgets for Clinical Trial Sites”.
- Create a cross-network “Technology and Measures Task Force” to develop standards and recommendations.

**DETAILED MEETING SUMMARY:**

The Network Leadership Group and the BSWG Data Capture Focus Group Steering Committee charged meeting participants with addressing ongoing research implementation challenges and evaluation of electronic data capture methodology and costs associated with the behavioral assessments. Discussants included representatives from the NIAID network behavioral/social scientists, network statistical and data management centers (SDMCs), NIMH, Division of AIDS, FDA, the Forum for Collaborative HIV Research, outside research partners, private industry developers, and protocol team leaders.

The meeting opened with a consideration of the key issues influencing the adoption of a behavior data capture technology. They include: international versus. domestic setting; age of population, language/dialect/accent; literacy/numeracy; type of study intervention; differing benefits depending on study question; sensitivity of behavioral questions; behavioral impact of monitoring and potentially real-time interventions; site capacity and training; and comparisons of face-to-face interview (FTFI)/paper questionnaires versus patient-entered electronic data capture.

The focus group participants went on to address a variety of concerns related to technologies: key questions about (audio) computer assisted self interviews (A)CASI; opportunities associated with new technological interventions; research and development needs; regulatory and ethical considerations and implications for real-time interventions. Details of the presentations and discussion follow.

**Key questions about (A)CASI** – Ariane van der Straten (Moderator)

Focus group participants discussed key question about (A)CASI, including what are the costs, advantages, and “value added” of (A)CASI. Jeff Schouten provided an (A)CASI literature review. The general consensus is that (A)CASI can be cost effective in certain settings and tends to lead
to increased reporting of socially undesirable behaviors and decreased reporting of socially desirable behaviors. There is little published research exploring the cost effectiveness of (A)CASI but costs decrease with increase study size. The SDMCs presented costing and logistical considerations and Ira Wilson discussed his experience comparing FTFT with technologically mediated interviews. He underscored the importance of cognitive testing to assure the participants understand the intent of the researcher’s question. Discrepancies in the data may be in part due to the framing of the question: no matter the methodology used to collect the data.

The SDMC for HPTN, HVTN, and MTN, the Statistical Center for HIV Research and Prevention (SCHARP) presented its experience using DatStat Illume’s (A)CASI product. The web-based software with a Microsoft SQL backend server is a user-friendly package allowing lower-level staff to create fairly sophisticated surveys. SCHARP representative, Leslie Cottle noted it can be used by sites with existing hardware using familiar operating systems on touch screen or handheld devices. The SCHARP survey content has been developed by behavioral scientists and a subset of the protocol team. The majority of questions are behavioral (i.e., sexual activity, illicit drug use) and some adherence items are collected in studies where product is dispensed. Audio and text translations are done in Spanish, Portuguese, Thai, Bemba, Nyanja, and Xhosa. Participant completion times range from 10 minutes to over 2 hours depending on the visit and the study. Costs include license fees, site fees for local installation, high-level programming, less-complicated programming, translation, and testing. Factors that increase cost and effort involve length of survey, visual only or audio and visual, complexity of linkage between items (e.g., skip logic), number of translations needed, survey revisions that result in re-programming and custom programming.

Developers exploring the adoption of (A)CASI should consider:

- Survey size limits (number of questions, audio and image files). Some of the literature suggests that attention decreases significantly after 20 minutes.
- Minimum User System Requirements: Internet connection, hardware, software, web browsers, etc..
- Local administration options: Can the survey be administered locally (offline); how are audio and image files stored for local use?
- Audio and Image Files: What format(s), how stored, what add-ons/plug-ins required by users to access audio and image files?
- Software Features/Flexibility: Are survey elements customizable e.g., fonts, buttons, etc.; can you replay/pause audio?
- Programming: How are more complex features programmed?
- Documentation: How easy is it to produce a printed/PDF version of a survey and are all survey elements included in the printed survey? Does the software create a data dictionary for each survey?
- Translations: Does the software offer user-friendly translation process tools? Are all the fonts you need supported?
- Standardization: Can you create a library of common survey elements for use across multiple surveys?
- Product Technical Support (availability and cost)

Survey designers should be encouraged to adhere to established principles of effective survey design. It is critical to avoid re-work by finalizing text before survey programming starts to minimize costs. Site staff should confirm that translated text is correct and uses the local vernacular and is otherwise culturally competent. (Some challenges noted include translation when comparable words do not exist in the local language.) To minimize participant burden of answering long surveys and to increase the probability of meaningful/accurate data, developers should limit the number of questions and consistency checks. Participant literacy (text and computer) should be weighed when creating an (A)CASI survey. SCHARP noted in a study that more people completed the web (A)CASI at home than kept their appointments. So the tool can be used to enhance data collection and presumably adhere to study product.

The DMC for ACTG, IMPAACT, and PHACS, Frontier Science Technology and Research Foundation (FSTRF), has been using (A)CASI for six years. In FSTRF representatives Sue Siminski and Stephen Hart’s, experience, traditional case report forms (CRFs), may be suboptimal because skip logic has to be very simple or a participant may get confused; questions may be tedious and repetitive; the ability to complete the CRF depends on literacy; the question wording can’t vary depending on the participant’s gender, medications, sexual orientation, answers given at previous visits or to earlier questions; and there are no checks on whether answers are complete, consistent, or realistically plausible until data is keyed, sometimes many days later.

FSTRF is expanding their portfolio to include as many new technologies as possible. For example, PHACS has employed three behavioral (A)CASI surveys and experienced very good compliance. When exploring new technologies, FSTRF considers whether the tool will be easy to administer and complete; the variability of site technical capacities; participant literacy and cultural preferences. (A)CASI can assist with literacy challenges but it not as effective with longer/complex questions as it can be difficult to remember response options. Discomfort/unfamiliarity with computers can be a barrier for data collection.

When considering the use of a tool, FSTRF evaluates whether it:

- Allows use of many modes (audio/text, interview/self-administered, done locally or via the internet, etc.) and allows some data collection to be done in varying modes depending on the situation and on participant desires, without having to recreate the instrument.
- Allows creation of attractive, easy to navigate instruments that makes providing data enjoyable (for participants and staff) and makes it easy for respondents to do what the research requires.
- Provides good links to pre-existing data so it can readily make question dynamic and non-repetitive, reducing participant and staff burden.

It is critically important for an SDMC to evaluate how the device will improve the accuracy of the collected data, the overarching cost associated with a system, how flexible the tool is, whether it meets regulatory compliance requirements and how it can be integrated into a complex data management system.
Ira Wilson discussed the importance of considering the mechanisms involved in conducting (A)CASI and FTFI. These considerations include: components of the response process, how topics differ, how survey modes differ, and how topics and modes interact. The "cognitive burden" of an interview is impacted by the response process:

- Comprehension: question phrasing, instructions, and the question focus.
- Retrieval: generation of retrieval strategy and cues; specific versus generic memories; filling in missing details.
- Judgment: assess completeness and relevance of memories; draw inferences based on accessibility; integrate material retrieved; and make estimates based on partial retrieval.
- Response: map judgment onto response category and edit the response.

When designing questions, researchers should consider: frequency, salience, relevance, stigma, knowledge, "burdensomeness", emotion, cognitive effort, and identity issues. Wilson recommends developing items that make sense to all participants, rather than appealing to the lowest common denominator.

The method of administration can influence responses. Self-administration, as compared with interviewer administration, can increase underreporting of socially undesirable behaviors, decrease over reporting of socially desirable behaviors and decrease the effect of interviewer characteristics. (A)CASI helps if there are literacy problems, but is not as effective for longer or more complex questions. Comfort with computers can be barrier for some respondents and the programming does reflect social characteristics (e.g., phrasing, accent, etc.). (A)CASI cannot help with cognitive burden of the topic, but the problem of cognitive burden can be tractable if you write good items.

As an optimal approach, Wilson recommends qualitative research to understand confounding issues, develop items based on qualitative work, conduct iterative cognitive testing of items, test the mode of administration and pilot or field-testing. It is critical to engage experts in survey research. Mixed method approaches should also be considered.

Discussion: The scale and type of technology has an impact on cost. While there are inexpensive tools (e.g., Survey Monkey), the complexity of the data collected in the network trials is of a different magnitude. Regulations and structural limitations limit the adoption of lower cost options. The (A)CASI software must be transferrable to multiple browsers, Macs, and PCs. PopCouncil developed a customized solution that they could build into whatever requirements that the investigators needed and are developing a small pilot program using the internet across various platforms. They have been able to customize, build in graphics, moving graphics, and even graphics for sensitive questions such as a study in India and the color of a blanket that was used.

The group discussed their experience with providers such as DatStat Illume, ODS, CNIX, RedCAP, and Qualtrics. Pricing can vary by platform, package, and negotiations. Free open source software requires investment of developer time and offers very little trouble shooting assistance/training. Many of the RO1 grants have used less expensive options and their experiences should be shared with the networks and SDMCs. The behavior data collected in the CNIX network is done on open source software. However, it was also noted that "open source software is free like a free puppy." Some of these tools could be employed in smaller studies or pilot projects.

There have been very little cost effective assessments of (A)CASI completed to date and this is most needed to advance the field. There have been mixed experiences and challenges with multiple access platforms when using remote surveys. Customizable solutions are needed. Evaluating software requires a great deal of time and should be built into the protocol timeline. Most critically, researchers should be attuned to the fact that sensitive questions are not the same in every population. Researchers may consider hybrid studies which employ both (A)CASI and FTFI depending on the sensitivity of the topic. Moreover, what works in one study doesn’t necessarily translate to another study population or design. Cognitive testing of questions and the tool itself can help challenging areas before the study is rolled out to the field. Survey design should be completed before the (A)CASI is programmed to avoid unnecessary reviews and expense. When the SDMC is provided the survey instrument shortly before a study is ready to open costs increase significantly and this has not been an uncommon occurrence.

State of the Science - Exploring technologies - Pamina Gorbach (Moderator)

The “State of the Science” session considered select technologies from both the research and development perspectives. Participants discussed how to develop the pilot studies, support for the pilot studies, how are they implemented, how are these emerging technologies changing the science of adherence assessment and how the field could develop a systematic approach to selecting the best approach.

Donn Dennis of Xhale discussed the SMART Adherence System (Self-Monitoring and Reporting Therapeutics). This breath-based system can accurately verify that the study participant took the right dose of the right medication via the prescribed route at the right time. It enables improvement in medication adherence and persistence. SMART is a simple system and most of the development and design elements are completed. The system is easy to use at home and it can also remind the participant to take the study product or other medication. By providing a definitive measure of adherence, SMART can help identify and correct behavioral factors associated with poor adherence and clinical outcomes.
“SMART” can be used for any medication (e.g., oral, topical microbicide, or condom). In the instance of a pill, FDA “generally recognized as safe” (GRAS) food additives are incorporated into the capsule, as adherence-enabling markers (AEMs) to generate exhaled drug ingestion markers (EDIMs). While at home, the trial participant exhales into the SMART® device and biometric facial ID is used to identify the person. The device provides definitive breath analysis, establishes ingestion, and wirelessly reports adherence in real-time. The system can provide for monitored call-back within minutes to participants who miss doses. Dennis argues this leads to an increase in adherence, enhanced data quality/integrity, and more successful trial outcomes. The AEMs EDIMs can be designed to have a half-life appropriate to the study intervention dosing strategy. It has been validated in oral formulation, vaginal gels and condoms. Rectal microbicide use has not been tested as yet.

Ariane van der Straten shared her research using breath tests to assess vaginal products. Until recently, there was not a practical, validated method to monitor actual use of vaginal products in HIV prevention trials. Pill counts, self-report, directly observed insertion, electronic monitoring, and drug level tests have proved less than ideal. Her goal was to assess the feasibility of using a novel breath-test (SMART®) to detect women’s use of vaginal products (gel and condoms) tagged with GRAS flavorants in a clinical setting. She conducted three pilot studies. The first indicated that participants experienced mild adverse events (AEs) only, there was no detection of any taggants/metabolite after dermal application and that a “breath test” for adherence to microbicide gel application appears physiologically and technically feasible. The second study assessed the accuracy of the breath test to detect tagged versus untagged vaginal products (gel or condom), applied under direct observation. Again, participants report mild AEs and 100% accuracy in identifying placement of tagged (or untagged) gel and condom, confirmed by the presence (or absence) of taggants (and metabolites) in the breath. The third study considered the accuracy of the breath test to detect tagged vs. untagged vaginal products (gel or condom), applied concurrently under direct observation. Distinct and accurate breath signatures are created for vaginal use of gel and condom, used concurrently or at separate times, and tagged with two different esters. Results were similar in two-day and single-day cohorts: and argues for a breath test “proof of concept” demonstrated for vaginally applied products. Some participants experienced some abnormal taste associated with the exhaled volatile organic compounds. One major application of this technology would be the ability to assess adherence in placebo recipients in prevention trials.

William Brown offered considerations for implementing short message service (SMS) to monitor/aid adherence in biomedical research and moving from pilot phase to RCT. The open-source SMS system was found to be implementable for biomedical research and deemed scalable to national and international research. It collected and disseminated data effectively. At current scale, the open-source SMS system was also found to be cost-effective as compared to paper-based, interactive voice response, and other similar non-open-source data collection systems. His group was successful in improving reporting adherence through the use of automated SMS reminders and acceptability was high. They were able to develop a guide of lessons learned for future SMS HIV research. Further data analysis needs to be completed to compare the effectiveness of the SMS data collection and reporting system to that of a previously used phone reporting system, as well as to determine the feasibility of using SMS to improve the design of large national HIV studies. However, the preliminary review of the pilot data and of international implementation procedures is promising.

Dimagi principal, Neal Lesh, described his group’s activities using phone-based data collection in low-income countries. He shared advantage and challenges associated with phone-based data collection compared to paper, discussed how to secure electronic data on phones, what interventions work for lower-literacy users and advantages of phone over paper forms. In Dimagi’s SMS adherence study, they explored fatigue, content, and frequency associated with text interventions. The pilot study’s goals were to improve the safety, quality, and protocol compliance in a dengue vaccine trial. SMS allowed for appointment reminders and confirmation, broadcast messaging, staff group messaging, “call me back” service and AE reporting. Challenges with phone-based interventions include: privacy, data security, phones getting lost/stolen, charging phones, and airtime. Advantages include the additional functionality of taking pictures, playing audio and visual content, GPS, location bar codes, and real-time feedback to identify anomalous patterns at sites and with individual participants. Dimagi builds open source, cloud-based systems. Their main focus is working in low-income countries. Dimagi focuses most on intervention. They use a variety of platforms including SMS, “feature” phone apps, and smart phone apps. The group is also working with smart pill boxes similar to the Wisepill device.
Lesh noted the importance of engaging with gateway SMS providers early in the study design to minimize delays and logistical challenges once the study rolls out to the field.

As a complement to the discussion of technological interventions, Craig Hendrix provided a pharmacokinetic (PK) assessment of PrEP adherence. Based on the data from intensive PrEP studies (e.g., CAPRISA 004, VOICE, iPrEx, HPTN 066, etc.) which indicated that concentration differences among sub-groups were due to adherence, not pharmacokinetics; he argues we can infer that the variation in the oral PrEP studies is due largely to adherence-driven concentration differences.

Hendrix discussed the potential uses of PK-based adherence assessment implemented during a study. The HIV prevention research field recognizes the need for a quantitative adherence assessment intervention. Post-study PK and behavioral analyses do not provide the opportunity to intervene with a particular individual. Moreover, it is difficult to identify the failure source; i.e., the drug, PK in the individual, and/or adherence. PK measures cannot effectively be identified for the individual given these variables but population level concentration targets can be helpful.

The following model reflects the variables influencing HIV infection:

![Image of model showing variables influencing HIV infection](Figure 2: Graphic provided by Craig Hendrix)

Beyond information about relative concentrations in various anatomic compartments, drug concentrations can provide information on adherence to a prescribed drug regimen. The challenge is to differentiate the variable of adherence from pharmacokinetics. This model shows the interrelationship of adherence and pharmacokinetics. In all prior studies discussed, except the observed single dose studies, adherence is unknown.

The objectives associated with using PK measures involve:

- Identifying the population effect
- Explaining RCT outcomes post hoc
- Identifying crude targets for future studies
- Comparing population adherence vs. individual adherence
- Informing design changes (e.g., adherence, regimen)
- Targeting adherence intervention real time
- Understanding exposure-response and covariates
- Enabling clinical trial simulation
- Can be logistically simple to test (e.g., hair, dried blood spots)
- Matrices are insensitive to adherence gaps ("holidays") and subject to the "white coat" effect
- Only provide average (but longer look-back)
- Expense of individual measurements

Hendrix noted that one must use caution when extrapolating results across study populations (e.g., serodiscordant heterosexual couples and MSM). He noted that prevention groups should keep in mind that seroconverter adherence wanes with time and may be predictive of preventative interventions. Furthermore, target concentration needs more work especially since drug concentration cannot explain all risk. By and large, quantitative, objective adherence assessments are lacking. Adherence has a major impact on drug exposure and outcomes: it is...
critical to ascertain drug concentration insofar as it is an adherence measure. Individual levels cannot be extrapolated into population expectations due to individual variability but aggregate assessments of exposure drug can be most useful.

**Discussion:** When using SMS, one must adjust for the size of characters when conducting a survey. For example, Thai characters take more space than English. Some studies have shown that there is missing data with SMS interventions. Text reminders have mixed results but more research should be conducted to assess their efficacy. There seems to be a lot of participant dropout in studies using text interventions. Increased frequency of texting seems to correlate with dropout rate. There is a difference for active (e.g., “please respond”) and passive (e.g., “take your medicine”) reminders. Security is a challenge with SMS and mobile apps but passcodes and generic reminders can alleviate some of the concerns. At scale, (A)CASI becomes less expensive per user while SMS is more costly at volume since each text incurs a charge. Open source programs almost always entail additional expense for customization.

**Guiding Principles for R&D - Development process, pilot studies, identifying a vendor, and scale-up - Michael Stirratt (Moderator)**

The moderated discussion considered the following framing questions:

- What are the facilitators and obstacles involved in the development of new tools for use in clinical research?
- What novel capabilities might they provide? Do they offer the promise of increasing the validity of these kinds of assessments?
- How do we develop the evidence base? Does one of the technologies allow for more accurate reporting than another?
- How transferable is the tool in the “context of use”?
- How do we engage with industry around research needs?

Discussants agreed there is a great need to be creative and innovative when engaging emerging technologies. New tools should have the advantages of minimizing participant burden, improving the accuracy of collected data, be logistically easy to implement and be cost effective. The question of “validity” still poses problems. Even with a tool as widely used as (A)CASI, the evidence of utility is mixed. Participants adapt to technology quickly but enduring acceptability and improved outcomes are ongoing challenges. Moreover, successful adoption or rejection of a tool does not necessarily transfer across settings and studies. For example, in the United States, participants are inundated with technology so they ignore the texts and get bored with (A)CASI while in many low-tech literacy populations, tools such as (A)CASI are often very popular. Although some of the literature notes a challenge in low-tech populations with older participants.

Technology fatigue can settle in as novel interventions become routine or older media fail to match user interface expectations established by popularly available devices. Researchers should learn from tools being adopted in the general population, engage industry partners, in the development process, harness international expertise and share lessons learned.

There is a great need for pilot studies to assess these issues before a technology is incorporated in larger trials. Such targeted studies can be challenging to conduct because of limited funding, regulatory approvals, and tight timelines associated with the parent protocol development. Current examples of this research can be found in the variety of supplements that are available for existing research (e.g., the SBIR grant). MTN has also discussed doing run-in/run-out phases in selected studies. Often the study team relies on informal site input to test the instruments prior to implementation, rather than focus groups and pilot studies. Pilot research arenas include transferability, acceptability, biomarkers to validate self-reported data, and training. Similarly, clinical trialists should not conflate “content” (measured behavior) and delivery system (technology). Pilot testing should consider each element separately and together. The networks could also learn from investigators such as Ron Kessler and their work exploring question validation. Developing a mini-RFA funding mechanism would greatly facilitate this research, benefit all of the networks, and leverage existing network infrastructure.

Focus Group participants agreed it would be valuable to consider creating a “Technology and Measures Task Force” to assess emerging technologies, review behavioral questions, provide input on validation and study participant experience. The group could be composed of behavioral/social scientists, SDMC representatives, community members, regulatory partners, developers in industry and principal investigators. In addition to the issues noted above, the group could consider stigma, social desirability effect, risk assessment and adherence measure standardization. The research community needs to harmonize validations and define the validation process. An “(A)CASI Validity Focus Group”, exploring vendor pricing, module design, site experience/training needs may also be beneficial.

**Regulatory and ethical considerations – Michael Arnold & Veronica Miller (Moderators)**

The moderated discussion considered the following framing questions:

- What are the limits of “validation” given the questions around transferability across social settings?
- What are the primary regulatory considerations when applying novel technologies?
- How will participants relate to these technologies and how might it impact the accuracy of responses?
- From the regulatory perspective, how does the adherence self-report data relate to PK/PD data?
- How do we compare the technologies that are participant (behaviorally) dependent, such as answering questions, following prompts, etc. vs. those that are more objective?
Discussants considered FDA patient-report outcomes (PRO) guidance addressing the use of computerized data. The document is designed to help researchers negotiate this complicated landscape of developing technologies. It would be helpful to include additional behavioral data in FDA applications. For example, in iPrEx, the behavioral adherence data apparently did not match up well with the PK data. This discrepancy cast a pall over all the self-report data, but it should be noted that risk compensation self-reported behavior did correlate with STI data.

Security and user authentication are key when using remote technologies. Some tools employ GPS locators which allow for follow-up/retrieval, but this could present privacy concerns if not disclosed. Working with communities to establish acceptability is essential. In South Africa, the use of a fingerprint reader is very common to reduce multiple trial enrollment by some participants. Studies employing hair as an objective measure of adherence have experienced resistance do to cultural beliefs.

In primary medical care email and SMS are generally not considered as private or confidential modes of communication; the content is protected as far as the local law allows it. MTN is planning on using coded messages via SMS. This requires training participants to know what the coded language means. Mobile health apps are more secure in that a user can create a personalized password and the data is encrypted.

Triangulation of data across multiple tools can provide insight into behavior and the utility of any intervention. It is unlikely that the data will be entirely congruent but will represent overlapping perspectives. However, as noted above consistency checks increase the length of the assessment tool and may be counterproductive. Ideally, to ensure the highest quality data, researchers should pilot tools and study questions within a community before employing a tool.

It was emphasized that researchers have an ethical obligation to provide study participants explicit details about what information will be captured, how it will be captured and stored and the risks of inadvertent disclosure. Examples of this challenge include: sharing of phones, phone data taken from cell towers, lost phones featuring personal details and third parties collecting usage data (e.g., email service providers, governmental agencies, Facebook, Google, etc.). Researchers should frequently review corporate privacy policies as terms of agreement can change without prior approval or notification.

**Implications for real-time interventions** – Chris Gordon (Moderator)

The moderated discussion considered the following framing questions:

- How is might a study be impacted if you are conducting real-time interventions based on real-time measures?
- What is the relationship between adherence and risk behavior? For example, if real-time adherence interventions are implemented, might that mean the low-adherent participants would be contacted with greater frequency, what is the possible interaction with adherence and risk behavior and how might this influence study results?

Since the goal of a Phase III trial is to demonstrate efficacy, product exposure is generally maximized. Various interventions to improve adherence may be more appropriately examined in Phase IV implementation or dosing-strategy trials. Regardless, researchers are still faced with understanding the effect of participant monitoring and exploring whether it is advisable to have different subset interventions within trial design. It is unclear how intervening with a clinical trial subpopulation of low-adherers may impact on the overall outcomes.

There is an imminent need to develop a measure of sexual exposure-related events to better understand the effects of a biomedical intervention. Much of the existing real-time intervention research relates to blinded PrEP studies. For instance, the HPTN 052 team is just starting to look at self-report adherence data and correlates with HIV RNA plasma levels. The research community is in need of generalizable measures and combination approaches to assess imperfect adherence. At present, there is still a great deal to be learned about what behavior represents a “covered act”. If the field could develop a method to measure events and compare to PK data, then it would be possible to establish drug exposure. With that information, the review could be reversed, i.e., drug exposure data would indicate risk. If researchers could understand the adequately participant exposure rate, they could more effectively design trial sample sizes.

There is a need to monitor cyclical and intermittent use in all clinical trials. In some instances, participants with poor adherence to study medication maintained almost undetectable HIV RNA plasma levels. This may be due to individual PK or sporadic non-adherence. Modest non-adherence is understood to be possible in some people with current regimens in regard to plasma HIV RNA but HIV DNA levels still can be shown to increase. So accurate assessments of adherence remain critical in both prevention and therapeutic trials.

Effectiveness studies attempting to improve adherence should minimize informed consent barriers as well as blind participants to monitoring above the standard of care. The latter approach will minimize the potential of influencing behavior and can provide a more accurate assessment of what adherence might be outside of a clinical trial framework. Measures in blinded RCTs may be quite different than open label trials where the study product has been proved efficacious. Efficacy established in a RCT is not synonymous with “real world” effectiveness. Early adopters of an intervention like PrEP may be more adherent than the broader class of individuals that might use the intervention when widely commercially available. Furthermore, the confounding influence of risk perception is still undetermined. It was also noted that we lack any ability to assess an individual risk of HIV acquisition based on exposure. Like the most useful PK data, this data is derived from population estimates.
Conclusions and possible next steps – Jeff Schouten & Amy Ragsdale (Moderators)

The BSWG Data Capture Technologies Focus Group considered various software programs, the pros and cons of the software, and associated costs. It was noted that (A)CASI programming is the primary cost but per person costs decrease as the study size increase. SMS is priced per text and therefore more expensive at scale. The (A)CASI literature does not specifically address the cost effectiveness of (A)CASI versus FTFI.

Focus Group participants reviewed select newer technologies and learned more about the suite of products that developers Dimagi and Xhale offer to both monitor and improve adherence to study products. Regulatory and ethical concerns frame the adoption of all technological interventions. Recommendations and suggested research opportunities follow:

- **Data Capture Technologies Costing Tool**: Using the model of the “Recommendations for Standardizing Budgets for Clinical Trial Sites” document and associated costing tool, network researchers and the SDMCs could provide guidance for protocol team members in evaluating the costs of alternative data capture options. The tool could address expenses associated with programming, pilot testing, site costs, data and statistical analysis, integration into existing SDMC systems, per unit cost of device, server space, training, licenses, technical support, upversioning, etc.

- **Engage Developers and Vendors**: Discussants considered what would be necessary to engage industry partners around the research needs. Utilization of a product is appealing for developers. HANC might be able to work with SDMCs and networks to negotiate pricing with vendors.

- **Leveraging Network/SDMC Experiences**: In order to understand what tools are being employed at present, HANC will create a listing of vendors, tools, research context, network contacts, pricing, etc.

- **Data Capture Technologies Best Practices**: There is a need for a validation best practices or guidance document for research teams considering the use of data capture devices. Focus Group participants recognize that while the concept of validation is enticing, it will be a challenge to create a detailed manual addressing all research settings. Issues such as cultural context, population, age, and language influence acceptability. Usefulness of a tool may not transfer across settings. HANC will develop a matrix of essential components to be considered when adopting a tool. The project could build on a MTN pilot testing manual and the networks’ IT Best Practices document. The document could dovetail with the ongoing HANC-facilitated SDMC Work Group electronic data capture (EDC) discussions.

- **Pilot Study Funding**: The group urges funders to support validation pilot studies through existing or novel funding mechanisms. Individual technologies and even the concept of “validation” itself call for additional research. Similarly, protocol teams should engage focus groups to test acceptability of the measures and devices before use in the field. Cognitive testing of questions and biomarker research are of critical importance as well. The discussants suggested a NIH and/or network driven “mini-RFA” program to address these research needs.

- **Cross-network Tools and Measures Task Force**: Discussants agreed that a cross-network and SDMC task force charged with developing best practices, exploring new technologies, reviewing measures, and establishing validation parameters could be most helpful. A task force of this kind could assist in a cost-benefit analysis of (A)CASI and would also be charged with pursuing the recommendations noted above.

Questions about HANC, the BSWG, and other HANC-facilitated behavioral science activities can be directed to: [www.hanc.info/about/Pages/contactHANC.aspx](http://www.hanc.info/about/Pages/contactHANC.aspx)
Behavioral Science Working Group Data Capture Technologies Focus Group

Key Questions and Recommendations for DAIDS Networks’ Behavioral Research Agenda

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