Pathways to High Adherence

An Adherence Support Manual for Vaginal Ring Trials

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Abbreviations

AIDS	acquired immune deficiency syndrome
ARV	antiretroviral
ASPIRE	A Study to Prevent Infection with a Ring for Extended Use (a Phase III safety and effectiveness trial of a vaginal ring containing the antiretroviral drug dapivirine)
CAB	community advisory board
CAPRISA	Centre for the Aids Programme of Research in South Africa
CLA	core literacy area
DiSC	personal assessment tool used to measure four behavioral traits: dominance, influence, steadiness, and conscientiousness
FEM-PrEP	not an abbreviation (a Phase III oral pre-exposure prophylaxis clinical trial of the antiretroviral drug tenofovir disoproxil fumarate and emtricitabine, or TDF–FTC)
FHI 360	not an abbreviation (a nonprofit human development organization formerly known as Family Health International and FHI)
HIV	human immunodeficiency virus
IPM	International Partnership for Microbicides
MTN	Microbicide Trials Network
PDCA	plan-do-check-act
PrEP	pre-exposure prophylaxis
SOP	standard operating procedure
SSP	study-specific procedure
USAID	U.S. Agency for International Development
VOICE	Vaginal and Oral Interventions to Control the Epidemic (a Phase IIb clinical trial of the antiretroviral drug tenofovir administered as gel and oral PrEP)

PATHWAYS TO HIGH ADHERENCE

About this Manual

Introduction

In HIV prevention trials for vaginal rings, as with trials for other HIV prevention products, **adherence** to the ring-use requirements is key to answering the research questions, such as whether the study product is safe and effective for HIV prevention.

In previous biomedical HIV prevention trials, approaches focusing on individual barriers and facilitators to participants' use of the study product, as well as on community engagement, have been used to promote adherence. However, participants of trials completed to date have had variable rates of product use. In some cases this resulted in **futility** — use-adherence rates so low as to make it impossible to determine if the product can prevent HIV infection. Exploratory research to understand what drives such variability in adherence has prompted new thinking about how to support adherence in the context of clinical prevention trials.

In this manual, we propose a holistic approach that begins with understanding that a participant's engagement in the study affects her initial and continued correct use of the vaginal ring. This **participant engagement** is influenced by the participant herself, her community, and the study (including the study product, clinic setting and culture, and study procedures), all of which continuously influence each other. As part of our approach, we recognize that a woman's engagement with the study may be less influential than her interactions with her community, which have been part of her life long before her study participation and will remain a constant in her life after

the study has ended. Thus, any proposed adherence strategies need to consider how the study (and clinic site) is viewed in the community. Using this framework, we map the **participant journey** through the trial and offer potential strategies to implement among participants, the study, and the community to create and support multiple pathways to high adherence. Some of these strategies may look familiar, and others may challenge study teams to think about adherence in a new way.

Although we developed this manual to address product-use adherence in the context of clinical trials of antiretroviral (ARV)-based vaginal rings, much of what we propose is also applicable to use-adherence issues related to other HIV prevention products, such as oral pre-exposure prophylaxis (PrEP), microbicide gels, and vaginal films. Study teams working on all of these types of trials will want to consider the utility of each proposed strategy for their particular study.

PURPOSE OF THE MANUAL

The purpose of this manual is to support research teams in assisting women with adherence to the use requirements of the vaginal ring. Our holistic approach involves strategies to implement before the trial begins, during the trial, and even after the trial ends. It is not a prescriptive manual outlining required steps to be taken; rather, it is intended as a tool to help research teams think through options for supporting participant adherence to the vaginal ring, by focusing on their engagement in the trial and on the interactions among the study, the participant, and the community. As teams consider the context of their site and particular trial, they can select strategies — or **"entry points" to the adherence pathways** — that align with this context, and then adapt or supplement the strategies as needed or appropriate. Doing this successfully will require the entire study team to work together in a way that recognizes each staff member's unique expertise and influence over the participant's experiences in the trial and, ultimately, her willingness and ability to use the study product.

Much of what we propose here can also be adapted for adherence issues with other HIV prevention products. Study teams should consider the utility of each proposed strategy for their particular study.

CHALLENGES ADDRESSED BY THE MANUAL

Despite much attention to adherence issues in HIV prevention trials, there has been variability in the levels of product-use adherence achieved across recent trials enrolling women and evaluating daily or peri-coital dosing regimens. The Partners PrEP trial (oral PrEP) and the TDF2 trial (oral PrEP) saw high adherence among

their participants, as did the Bangkok Tenofovir Study (oral PrEP), which offered directly observed therapy. CAPRISA 004 (gel) found moderate adherence, and the FEM-PrEP (oral PrEP) and VOICE (gel and oral PrEP) trials were plagued by low adherence despite extensive efforts to support sustained product use. In the trials testing oral PrEP with women, HIV risk perceptions and age played significant roles in use adherence (as older women were better product-use adherers than younger participants), as did stigma at multiple levels of women's communities.[1] With different adherence-support activities implemented in each trial, it is difficult to tell which activities had specific effects on adherence. Although we can speculate about which support activities contributed to particular adherence achievements, what is really needed is to understand the continuum of adherence and what leads women to different points along this continuum. In other words, adherence is not all or nothing — for instance, in the case of vaginal rings, some women may use the ring consistently all the time while others may remove the ring at different points and for different lengths of time during the month. We also need to understand that because women will all be starting the study with different beliefs and opinions about the trial and trial product, no two women will travel exactly the same pathway toward high adherence.

This tool is meant to address gaps in the two adherence approaches traditionally used in HIV prevention trials — an individual approach and one focusing on a participant's **community.** Individual approaches have used direct messaging to participants, including counseling them on the importance of adherence and attempting to increase their motivation and skills to adhere. Community engagement components have included outreach, forums, participatory events, and advisory boards to promote community knowledge and support of the research.

Because each woman will be starting the study with different beliefs and opinions about the trial and trial product, no two women will travel exactly the same pathway toward high adherence.

The two traditional approaches have not typically addressed how a participant's grounding in her community, such as her personal social network, influences her initial and ongoing engagement in the trial, including her decisions to try the study product and to continue using it as directed. These approaches may acknowledge the interactions among the participant, her community, and the study, but few have sought to address the influence of these interactions on her engagement in the trial and how she views and uses the study product. The approach used in this manual recognizes these multiple levels of influence on participant engagement and considers that there are also multiple pathways to adherence that take into account the interactions among the participant, the study, and the community.

1. Thomson KA, Baeten JM, Mugo NR, Bekker, L-G, Celum C, Heffron, R. Tenofovir-based oral PrEP prevents HIV infection among women. Curr Opin HIV AIDS. 2016;11(1): 18-26.

Objectives

- To present an integrated, holistic framework for understanding the conditions needed for optimal adherence to product use in research studies. This approach focuses on maximizing participant engagement by aligning the goals of the study, the participant, and the community. It also focuses on the participant's experience progressing through the trial from start to finish, and even post-trial.
- To offer concrete strategies, tools, and real-world examples that study teams can adapt to encourage participant and staff engagement with the trial in ways that support adherence to the study product.

USERS OF THE MANUAL

This *Pathways to High Adherence* manual has been developed for use by research teams working on studies testing the vaginal ring as a drug-delivery mechanism for HIV prevention. It is intended to be used by team members who are positioned to support adherence. Whereas previous adherence-support interventions in clinical trials have primarily focused on counselors, we advocate for the involvement of the full study team in efforts to achieve high adherence. Strategies and tools specifically designed for counselors are included, but creating alignment between participants, the study, and the community in a way that truly facilitates vaginal ring adherence requires involvement from all staff cadres.

HOW TO USE THIS MANUAL

We recommend that users of this manual first read each main section, in the order in which the sections appear, skipping the materials in the numbered subsections. This will enable you to get an overview of the approach being advocated here. Once you have gone through the main sections, go back to the subsections, starting in section B, to get an in-depth look and specific "how-to" information. A glossary with terms that appear in bold font at first use in the text is provided at the end of the manual.

B

PATHWAYS TO HIGH ADHERENCE

Preparing for the Journey

When preparing for any journey, gathering information will help ensure that the trip goes smoothly, without the travelers getting lost or tired along the way.

The purpose of the trip must be considered, the travelers identified, the destination chosen, maps gathered, potential routes explored, transport secured, and suitcases packed. In the journey toward high adherence in a clinical trial, researchers must also gather information and supplies in order to successfully reach our destination — a clinical trial in which participants' adherence to the study product is high enough to answer the research questions.

In this section, we define sources of influence that will affect participants' individual journeys through the trial — marked by the initiation of product use, persistence (or not) with the regimen, and eventual discontinuation, hopefully at the end of the study. We also set forth a framework for paths toward high adherence, and identify some of the supplies study teams will need for a successful journey.

WHO WILL INFLUENCE THE PARTICIPANT?

The approach used in this manual is based on the view that there are three main sources of influence affecting a participant's adherence. These are:

1. **The participant** herself, especially her beliefs, values, risk perceptions, evaluation of the study product, skills in using the study product, and perceptions of being supported in her participation in the trial. Equally important are her life circumstances: her home responsibilities; the physical environment where she lives, works, and plays; the activity patterns of her daily life and how they might vary by season; and her level of dependence on others for financial resources/ income, food, shelter, and transportation.

2. **The community,** including the current and historical social and political environment, local gender norms, economic (in)stability, and community members whose opinions and actions matter to and affect the participant. This may include partners, family members, and friends in the participant's intimate and social relationships.

3. **The study,** meaning the study staff, trial procedures and requirements, setting, and services and benefits offered to the participants. The study also includes the culture of the site, which establishes staff norms for interacting with participants and with other staff and the interactions between participants while at the site. In addition, the requirements specified in the study protocol, the staff's level of appreciation of participants' contributions, the extent to which staff and participant communities overlap in day-to-day life, and whether staff and participants share a vision for the trial's contributions also figure into the study as a source of influence, as do the product and regimen, and the extent to which training and supervision of the study team foster an open and collaborative atmosphere in which staff are professional and respectful.

The actual effectiveness of the product, because unknown, cannot influence the participant to be more adherent

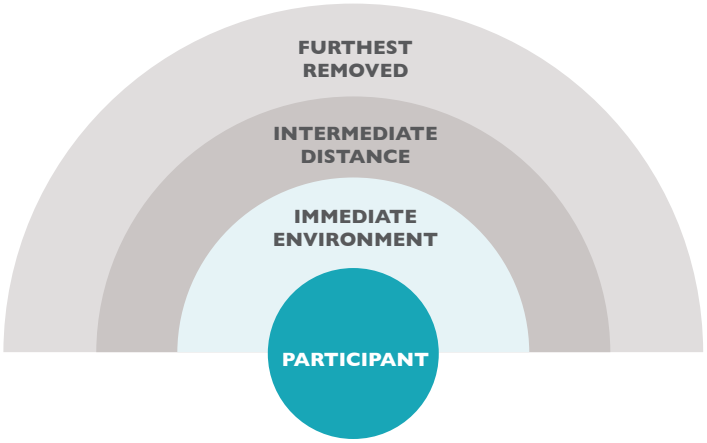
Product adherence is affected by how the participant maneuvers through the context of these three sources of influence, which are especially powerful in a trial situation in which the participant's use of an experimental study product does not guarantee her protection from HIV (and may even pose risks to her health). *The actual effectiveness of the product, because unknown, cannot influence the participant to be more adherent.*

Because there are multiple sources of influence that affect a participant's adherence, the burden of adherence rests not only on participants but also on the study and the community. This three-way responsibility for adherence exists because using the study product correctly at designated times is not something a participant executes in isolation, but rather is something that occurs within the contexts of the study itself and the participant's life in the community.

It is important to remember that each community is complex and made up of multiple groups and entities; there is not just one community. As shown in **Figure 1**, one way to think about community subgroups is by their proximity to the participant's life. For example, individuals in a woman's **immediate environment** might include her sexual partners, friends, and family members. Those at **intermediate distance** to the participant might include a religious congregation or leader, village elders, providers, and community groups. Those who are **furthest**

FIGURE 1

Subgroups of "the community" in the social environment of the participant, relative to their proximity to the participant's life



removed from the participant but still influential could include public health officials, political figures, or well-known spokespeople. The people in the community at various distances from the participant will be influential in the participant's adherence in different ways and to varying degrees. The relationships of family members and spouses, for instance, may include legal obligations and responsibilities that make these relationships qualitatively different from relationships with others in the community. Thus, it is important for study teams to intervene at various levels of the community, given that one approach may not be enough to influence the participant to engage fully in the trial and adhere to the ring. For example, strategies aimed at increasing research literacy or community support among one group, like public health stakeholders or religious leaders, may not translate into another group, such as a woman's sex partners, being in support of her using the ring.

With multiple participants in a clinical research study, there are also multiple overlapping communities. Each woman will have her network of near and far relationships. It is important to keep in mind that interventions that reach out to the broader community will be unlikely to address challenges that are specific to the near relationships of an individual participant. Similarly, interventions that target

a participant's more immediate environment may not effectively address challenges that originate in her more distant environment.

Examples:

1. If a woman's partner works as a laborer who is only home on alternate weekends, he may worry that her use of a vaginal ring would make her feel protected from HIV and "free" to have sex with other men when he is absent for work. In this case, broad community engagement with men or engagement with public officials may not reach her partner and address his specific concern. It may be more appropriate to explore ways to engage her partner directly or, if there are several participants whose partners are laborers, to engage these partners in a group setting where they can talk openly about their concerns.
2. Considering the same scenario, even if direct engagement with this participant's partner effectively addresses his concerns about her ring use, if he hears negative things about the study from government officials or the media, he may remain skeptical or not fully support her ring use. Interventions that target these more distant communities are also important for creating an environment supportive of ring adherence.

Both the study and the participant's community must support her by creating positive conditions for adherence. For this to happen, there must be a respectful, encouraging, collaborative atmosphere within the study. In addition, the community must have supportive views and actions regarding the study itself and the participant's role in the study — a stance encouraged in part by study staff working with communities to build trust about clinical research in general, and trust in the trial and the study product in particular. Without such trust, communities have the potential to discourage a participant's adherence and even derail the study. The study is responsible for fostering these dynamics through **staff engagement** (see Text Box 1 and Case Study 1).

In our model, the participant — also a source of influence — is not just a passive recipient of any support or opposition. She also has an impact on the study and her community through her own **participant engagement** (see Text Box 2), her expression of her beliefs about the trial and the study product, and her use or non-use of the study product.

WHAT IS STAFF ENGAGEMENT?

Staff engagement in the trial affects participant product-use adherence. Staff engagement involves:

1. Commitment to/belief in the trial: To create an environment in which participants feel motivated and supported to use the investigational product, staff members must value the work they are doing. They also need to understand how each interaction they have with a participant contributes to the overall study goals. Encouraging staff to explore their motivations for working on HIV prevention trials (beyond the paycheck they receive) can help them feel connected to the work they are doing and to the participants who enroll in the study.

2. Fidelity to study procedures: Support for product adherence is maximized when staff members demonstrate reliability and consistency in how study visits are conducted and a commitment to implementing study procedures as they have been trained to implement them. Trust is built when study staff are available to participants when they say they will be available and when procedures do not differ greatly from one staff member to the next. Fidelity to adherence-related study procedures, such as counseling methods and techniques, may be especially important.

3. Commitment to facilitating product use: This includes providing pro-active, positive support to participants (as opposed to haranguing and lecturing) for their contributions to the study in general, and more specifically for their attempts to use the product and share their experiences. A commitment to facilitating product use also includes staff members acknowledging the role they play in product adherence by ridding themselves of the notion that "bad participants" don't adhere. Instead, study staff should embrace the idea that it is their responsibility to create as supportive a context as possible — through counseling, community engagement, and implementation of trial procedures.

4. Commitment to open communication with participants and the community: This includes providing important study updates and being open with study successes as well as challenges or concerns, when appropriate. To build rapport and a sense of rallying around a common cause, staff members might also consider sharing more personal information, such as their motivations for doing HIV prevention research or their thoughts about the study product.

THE PARTICIPANT JOURNEY EXPLAINED

The **participant journey** is the participant's progress through the trial from start to finish, even extending beyond study participation. Tracking the participant journey and considering how the participant's movements back and forth between the study clinic and her community influence adherence can help provide a framework for developing successful adherence-support interventions.

Figure 2 (page 19) depicts the participant journey and the cycle of influence among the participant, the study, and the community. Imagine a potential participant traveling to the clinic for her first interaction at the study site. At the beginning of her journey, prior to joining the trial, she will have some preconceived beliefs and perceptions about the trial that have been influenced by her interactions with her community (e.g., the cultural context) and she may have already heard about the

STAFF ENGAGEMENT AND ADHERENCE SUPPORT IN MTN-020/ASPIRE

Within the ASPIRE study, it was critical to take advantage of the power of peer group dynamics to motivate study participants to adhere to product use. In the process, however, it became increasingly clear that "the messengers (staff) had to be convinced of the message they carried." What we communicate is more than the words we speak — it includes our body language, the way we deliver the message, and the passion we do or do not exhibit. In ASPIRE, we asked staff to reflect on how the HIV epidemic has affected their families and their own lives. Sharing these stories became an important part of the study's adherence intervention.

When staff shared their own stories of how they had been affected by the HIV epidemic, study participants identified with them and no longer saw the study product as "their product" (for staff), but instead as "our product." For example, at one of the sites in South Africa, a study member who was moderating a participant-adherence meeting shared how her own 12-year-old niece (orphaned to HIV) was raped, contracted HIV, and now lives on antiretroviral drugs. As the staff member shared her story, one of the study participants, who reported to have been previously non-adherent to product, was sobbing uncontrollably. She finally shared how the staff's story reminded her of her own 17-year-old daughter, who also contracted HIV when she was raped. She finished by saying, "I now do understand clearly why we should take collective responsibility in finding new HIV prevention tools. If we have fewer new infections, maybe our children will still be spared of HIV, even if they get raped." The study participants in this discussion were so touched by the stories shared at that meeting that they decided the successful demonstration of whether the dapivirine ring was effective or not was *their* fight, and not up to the study staff. They formed a ring-adherence group, elected a chairperson, and shared their new perspective on study participation with fellow participants, including making unscheduled visits to the study site (at no reimbursement cost) to talk to participants scheduled for each day.

Participant reactions to staff engagement and the sharing of stories like this were not unique to this site. At another site, after hearing about a staff member's brother who was failing a third-line antiretroviral treatment regimen and was likely to die soon, a participant revealed,

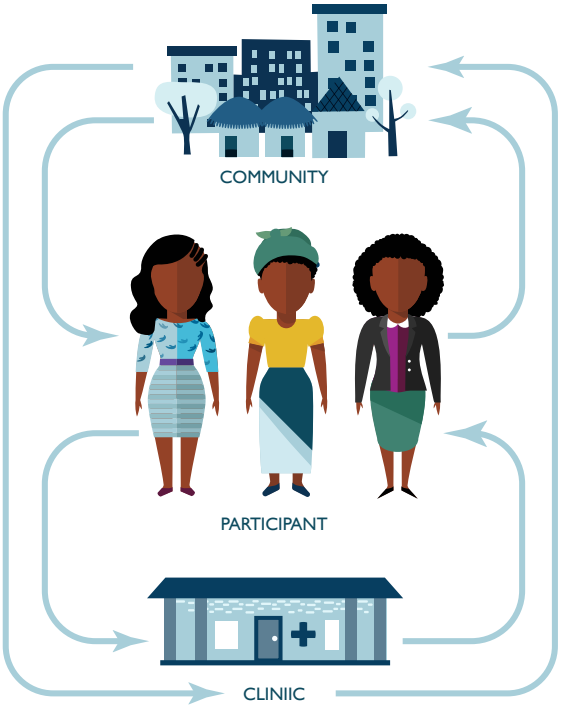
"I had been non-adherent to product largely because I never trusted study staff and thought they were above HIV. Now I understand you are just part of our community suffering similar fate. I shall start to abide by your instructions and fight to end the HIV epidemic."

- Patrick Ndase, MD, MPH, MTN regional physician

MTN-020/ASPIRE — A Study to Prevent Infection with a Ring for Extended Use — was a Phase III safety and effectiveness trial of a vaginal ring containing the antiretroviral drug dapivirine. ASPIRE enrolled HIV-negative women ages 18 to 45 at 15 clinical research sites in Malawi, South Africa, Uganda, and Zimbabwe. The study found that the dapivirine ring reduced the risk of HIV infection by 27 percent overall.

study (from her community, the media, or study outreach workers). She likely has some degree of openness about fully engaging in the study at this point, but she may also already have intentions to only partially engage (e.g., when motivated by study benefits she may not have access to otherwise, such as particular health care services or financial incentives). **Partial engagement** might include her intention to attend the study visits but not actually use the product. Such partial engagement may also happen not just in relation to her personal motivations for participating in the trial but also when trials are evaluating products that people in the community do not trust. As she begins to interact with the study, her preconceived beliefs and perceptions may shift positively or negatively, affecting her propensity toward adhering and engaging fully in the trial.

FIGURE 2
Cycle of influence among the participant, community, and study



The participant's experiences with the study will either reinforce or challenge her beliefs and perceptions. Study experiences might include her interactions with others in the clinic environment, her perceptions of the value added to her life by participation and the costs of participation, and the characteristics of the study product. If what she experiences in the study is different from her initial beliefs and expectations, she must then reconcile the discrepancy in her mind and through her actions as she returns home to the community. Alternatively, her experience may reinforce her beliefs and perceptions.

An inner adjustment takes place again as the participant attempts to use the product at home (in her community) and as she has new interactions with her partner(s), family, friends, and others in the community concerning the product and her trial participation.

This iterative process of adjustment and/or reinforcement (or its opposite, weakening) continues throughout the participant journey as the participant travels back and forth between the social spheres of her community and the research clinic, all the while detecting and reconciling differences or having her beliefs and those of the study and her community reinforced. Where there are discrepancies, the

WHAT IS PARTICIPANT ENGAGEMENT?

A participant's adherence to the study product is part of a larger process of her engagement in the study. We define engagement as it relates to adherence as the participant's:

1. Commitment to/belief in the trial: A participant's commitment to/belief in the trial may stem from her understanding of the goals of the research. For the participant to share the trial staff's understanding of the research, staff and participants will need to discuss these research goals. Participants need to feel free to ask questions and express their skepticism or support during these discussions. Staff can determine whether participants share their understanding of the research goals using tools developed for that purpose.

   Based on her understanding of the trial's goals, the participant's commitment to/belief in the trial influences her adherence by affecting her motivation to try the product and then continue using it. A participant who has doubts about the integrity of the trial and its ultimate, potential usefulness to herself or others in her community will likely lack the motivation to initiate or sustain use, expend the mental energy needed to overcome challenges related to use of the ring, or spend time for clinic visits.

2. Commitment to attending study visits: The participant needs to come to the study clinic during her visit window to obtain the product she will use and to inform the staff about her experiences with it. For this to happen, staff have to create a study environment in which the participant will be willing and able to come to the study clinic.

3. Commitment to using the product: This commitment is reflected in the participant trying the product, which is required for her to then adhere to the product. Again, staff play a prominent role here, for example by providing detailed and accessible instructions on how to use the product.

   We often assume that if a woman has enrolled in a study, then she has committed to try the product. Indeed, at enrollment she may have made this commitment. However, women may find that the demands of the study or of using the study product are greater than what they had anticipated. Or, for one reason or another, their desire to fully participate in the study or use the study product may change. The assumption that all participants at all times are highly committed to trying to use the product is likely inaccurate.

4. Commitment to being an active and open member of the study community: This commitment includes an ability to talk honestly about product use and experiences. Strong participant-participant and staff-participant relationships are central to helping participants feel a part of something larger than themselves, and to emphasizing how one person's actions influence overall awareness of the potential for participants to both positively and negatively influence each other (e.g., encouraging or discouraging each other from using the ring). Creating opportunities for staff and participants to gather as a group outside of regularly scheduled study visits, with activities that are both fun and educational, may also help foster a sense of community, encourage open dialogue, and create opportunities for positive peer influence.

participant is left to wrestle with what to do and how much to trust what she hears from and experiences with each source of influence. One way she can resolve these conflicts is by being more or less engaged in the study and, subsequently, more or less adherent to the study product.

PROVISIONS FOR THE JOURNEY

When a participant first comes into contact with the study, she is already equipped with a set of beliefs across five categories, which we see as the provisions she will use during her journey through the trial. As with any journey, the participant will draw from the provisions as needed, and she will replenish each type of provision with new and perhaps different contents as the landscape and her position in it change over time. The provisions required for a successful participant journey with high adherence to the study product fall into the following five main categories:

1. **Reasons for participation:** The participant's level of commitment to herself/her community to use the product and participate in the trial in order to contribute to the development of a personal or community solution for HIV prevention.

2. **Beliefs about the trial:** The degree to which a participant believes (or does not believe) that the trial promotes the interests and goals of the community, including being responsive, respectful, and ultimately responsible to the participants and the community. A participant's beliefs about the trial are closely linked to her level of understanding of the clinical trial and its procedures. (In other words, misconceptions and poor understanding have the potential to negatively affect her beliefs about the trial.)

3. **Beliefs about the study product:** The degree to which a participant believes (or does not believe) that:

   - The product will not harm her or those in her community.
   - The product could offer a solution to HIV prevention.
   - The product is "useable" in a practical sense (fits into her life and circumstances).
   - The value of the product outweighs the burden of actual use.
   - Side effects are tolerable.
   - The product is well matched to her needs or those of the community.
   - She is informed about the product and knows how to use it.

4. **Agency:** The degree to which a participant feels free to make her own choices about adherence and feels empowered to do so.

5. **Shared vision:** The degree to which a participant has (or does not have) a strong sense of a shared vision with or collaboration among herself, the other study participants, those of different sectors of the community, and the study.

SEEKING ALIGNMENT TO RESOLVE CONFLICT

When communities have some skepticism about the research or product — in this case the vaginal ring — it may be particularly challenging for participants to commit to trying to use the ring. Even though a woman may want to participate in the trial and use the ring, she may have to negotiate between messages from the study and what the study asks of her (e.g., those communicated in informed consent forms, informational pamphlets, and during conversations with staff); messages in her community and what the community asks of her; and her own beliefs, resources, and commitments with regard to study participation and ring use. When the messages from these sources of influence are similar, there is harmony. When they conflict, the participant can get pulled in many directions, creating tension that she will try to resolve.

One way a woman may try to resolve the tension is by adjusting her level of adherence to the study product. For example, she may keep trying to use the vaginal ring, even in the face of community pressure not to do so, because she believes in the ring, its safety, and the value of the study. Alternatively, she may abandon adherence efforts, even in the face of pressure from the study to adhere, because she does not fully believe in the ring's safety, its protection of her well-being, or the value of the study. She may also adjust her level of product use to protect important relationships (e.g., remove the ring during sex if she fears her partner's reaction to finding it).

The participant's five categories of provisions are affected by how she interacts with the three sources of influence (i.e., herself, her community, and the study) during her journey through the trial.

A SHARED VISION

The fifth category of provisions — shared vision — is worth a further look, given that how well a participant's beliefs about the study product and study align with the beliefs of researchers and people in her community can contribute importantly to adherence. In fact, we propose that positive **alignment** among all three sources of influence for at least a core set of shared beliefs and values is essential for high product-use adherence. In this manual, we focus on ways to achieve alignment when feasible, and how to work within a context when some beliefs are not aligned.

The first step in crafting a context for alignment is to create open dialogue among participants, communities, and staff to identify similarities and differences in beliefs. Where there is overlap, we have a core set of shared beliefs. Where there are differences, open dialogue is needed to understand differing agendas and to identify what each group can do to support the other groups' separate agendas, where appropriate and possible. Ways to do this include **community literacy** efforts, which are strategies research teams use to become "literate" in the community and within its cultural belief systems and norms, such as:

- Community mapping.
- Community advisory boards (CABs).
- Ethnographic approaches to learning.

We do not address community literacy efforts in this manual, as others have provided extensive guidance on how to go about this (See Resources at left).

What we do provide here are strategies for study teams to consider that touch on all three sources of influence — participants and community, but also study staff — and that have

the goal of creating alignment in a core of shared beliefs; these strategies are what we call the "entry points" to the multiple paths leading toward high adherence. We also equip study teams with a quality improvement process — the Plan-Do-Check-Act (PDCA) process — for continually evaluating whether their strategies are being effective and are proving to be entry points to the pathways toward high adherence.

FOLLOWING ROADMAPS: FIDELITY TO TRIAL PROTOCOLS AND PROCEDURES

When a clinical trial begins, several adherence-support activities will already be specified in what we might think of as the study's roadmaps: the study protocol, a study-specific procedure (SSP) manual, and site- or study-specific standard operating procedures (SOPs). Different studies may call these materials by different names, but all will have documents like these that help lay out the general roadmap for adherence support within the clinical trial context.

Study Protocol: The study protocol defines the research question(s), study design, participant population, and study procedures, including adherence-related procedures such as study product accountability requirements, objective measures of adherence (like residual drug analysis or pharmacokinetics testing), and the frequency of adherence counseling sessions.

SSP Manual: The SSP manual supplements the protocol by providing additional guidance on how to conduct protocol procedures, to ensure their standardization across sites and individual staff members. It provides more detail on how required protocol procedures are to be implemented. For instance, whereas a protocol might require that adherence counseling occur at every study visit, SSPs would likely include details about the general counseling approach for the study, the contents of each counseling session, and tools to assist with implementation.

Site- and Study-Specific SOPs: SOPs outline how study procedures in the protocol and SSP manual will be implemented in a specific location. SOPs should outline who is responsible for specific tasks at the site and any site-specific procedures. Like SSPs, SOPs are designed to reduce variability in the performance of study-related tasks from one staff member to the next.

RESOURCES

Stakeholder Engagement Toolkit for HIV Prevention Trials
https://www.fhi360.org/resource/stakeholder-engagement-tool-kit-hiv-prevention-trials

Adherence in HIV Prevention Research: A Primer for HIV Prevention Advocates
http://www.avac.org/sites/default/files/resource-files/Adherence%20Primer%20%28May%202011%29.pdf

Fidelity to these roadmaps — that is, staff members following the trial procedures related to product adherence as the trial planners intended — is essential to heading toward the destination of high adherence. Some of the strategies, or entry points, to the pathways leading toward high adherence that we suggest in subsection C3 will focus on fidelity. (Others will focus on adherence-support entry points that go beyond fidelity to existing procedures, focusing instead on site-specific challenges and context.)

TAILORING ADHERENCE SUPPORT TO TRIALS AND SITES THROUGH THE PDCA PROCESS

Each clinical trial site has a geographic setting with its own complex mix of:

- Political and cultural history.
- HIV history, including rates of and experiences with HIV.
- Experiences with clinical trials, including HIV prevention and treatment trials and trials related to other health issues.
- Health systems.
- Gender norms and dynamics.
- Ethnic and racial groups.
- Cultural traditions.

As a result, when it comes to providing adherence support, no one approach will be universally effective across sites — hence the flexibility afforded by research protocols to adapt adherence procedures to individual contexts in site-specific SOPs. Going beyond the issue of fidelity to study procedures as laid out in SOPs, we recommend that teams carry out mini assessments in the form of the PDCA cycle to determine whether an adjustment to an adherence procedure is improving that particular aspect of adherence. In this way, teams can figure out what works best at their site. These assessments should be performed in each site as needed over the course of the trial.

RECALCULATING YOUR ROUTE: PLAN-DO-CHECK-ACT

Once the journey is under way, there will inevitably be road hazards, construction, accidents, and detours slowing your progress and perhaps leading you toward a destination you do not wish to visit (e.g., low adherence). In addition, the contents of participants' provisions may not be exactly what the study or community would wish, meaning that the participants' core beliefs and values are not part of a shared vision that will likely lead to high adherence. In these instances, it is necessary to recalculate your route by modifying your **adherence-support strategies** or trying something different, always keeping in mind that the goal is to create alignment among the participant, community, and study.

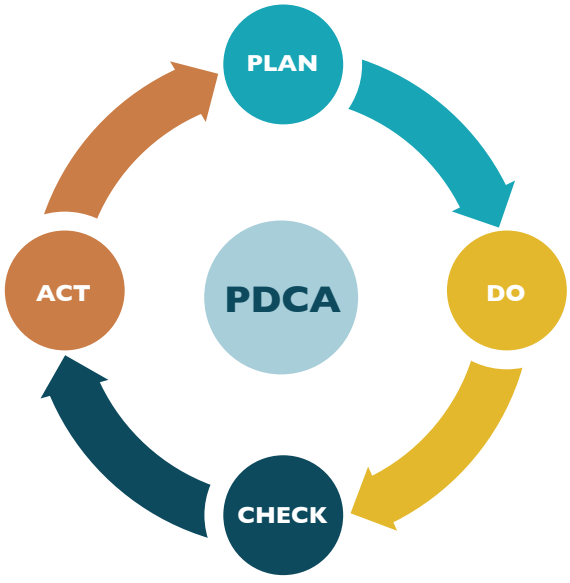
PDCA is a tool that site teams can use to improve the quality and effectiveness of the adherence support they offer within the general roadmap of the study protocol, SSPs, and study- or site-specific SOPs, which provide overall guidance for adherence support within a particular trial. Different site teams will likely implement different adherence-support strategies based on which procedures are required by the research protocol and on individual site-specific factors, such as where the trial is taking place and what population will be enrolled. However, even though the strategies will differ, the ***process*** each site team will use via the PDCA cycle (**Figure 3**) will be the same:

- ✓ **Plan:** Identify which current activity to adjust or new activity to initiate.
- ✓ **Do:** Implement the adjusted or new activity.
- ✓ **Check:** Evaluate the effects of the activity.
- ✓ **Act:** Modify or replace the activity until the desired effect is achieved.

The PDCA process provides a systematic way to think through how to address specific issues by tweaking or adding adherence-support strategies, quickly test promising approaches and measure their effects, and refine the general approach so that it is maximally effective at a particular site and for a particular trial. This process may look familiar, as it is based on the quality improvement cycle used in several industries and service programs to ensure that the efforts and resources expended are maximized and have the intended outcome.

See subsection B1 at the end of this section for more details about the tool and explicit instructions for using it. Subsection B2 provides an example of PDCA in use.

FIGURE 3
Plan-do-check-act cycle



FINAL CHECK BEFORE SETTING OUT ON THE JOURNEY

In section B, we have described who will influence the participant on her journey, the roles of participant and staff engagement in the journey, the participant journey itself, and the types of provisions the participant will have. We have also discussed the need for alignment, or a shared vision, related to some core beliefs about the study product and the study itself among participants, staff, and the community. Lastly, we have noted trial protocols, SSPs, and SOPs as the roadmaps and the PDCA process as a tool for recalculating the route, as needed. Before setting out on the journey and moving on to some practical aspects of adherence

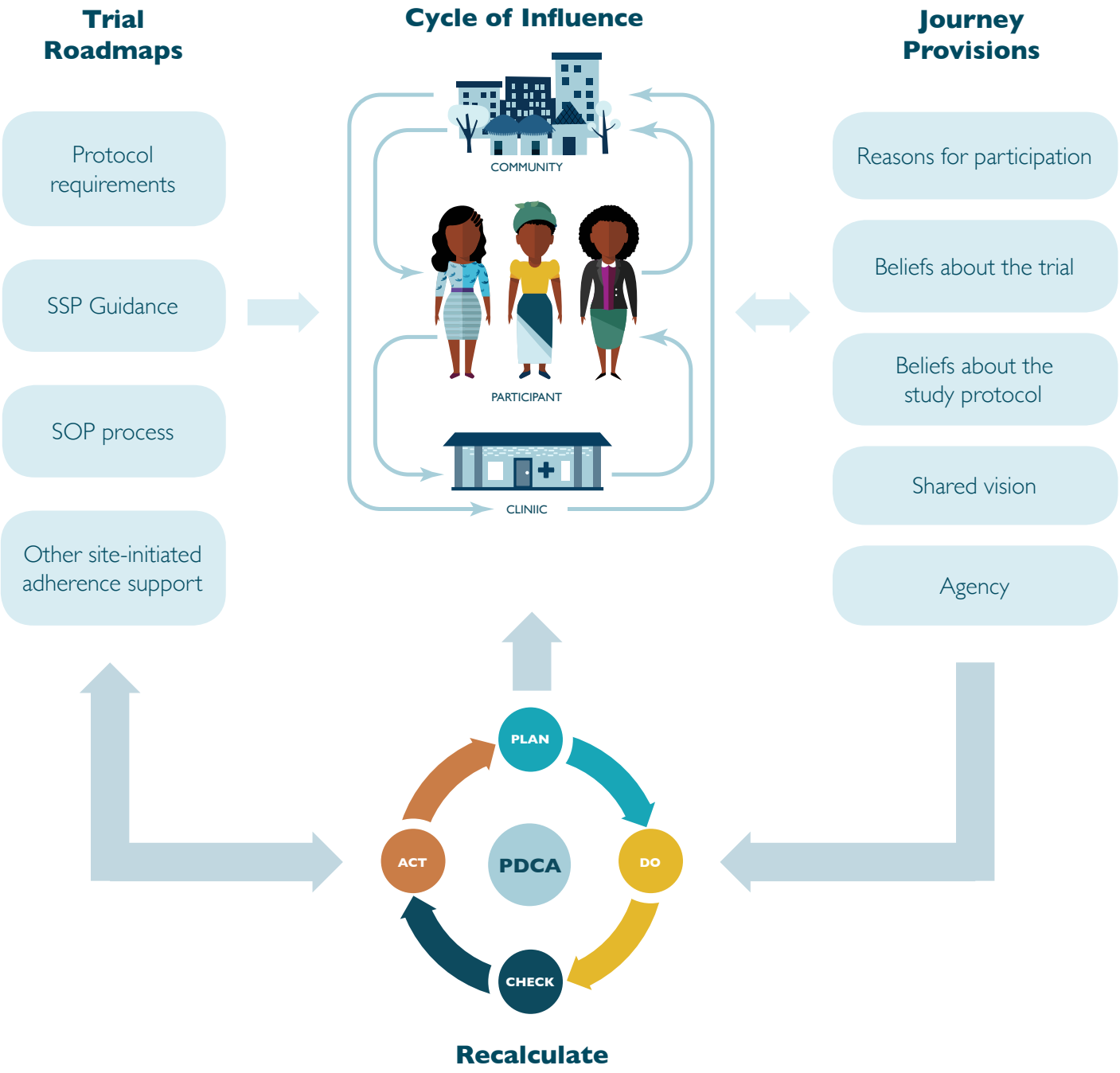
support, it may be helpful to consider how everything will come together on the journey. **Figure 4** shows the travel "package" that will comprise the overall trial journey. On the left side of the graphic, we start out with the prescriptive trial roadmaps that will direct the types of adherence support that staff will engage in, both in their direct interactions with participants and in working with the community. These activities will feed into the cycle of influence among the community, participant, and study as depicted in the center of the graphic. As the participant moves between the study and the community (or different levels of community as shown in Figure 1), she brings along her provisions, as listed on the right side of the graphic. These provisions (i.e., reasons for participation, beliefs about the trial, beliefs about the study product, agency, and shared vision) all affect her adherence-related behaviors and may change during the trial through the sway of the three sources of influence (i.e., participant, community, study).

When alignment of shared beliefs is off kilter, or activities don't have the desired effect, it is time to recalculate the route to high adherence using the PDCA quality improvement process.

When alignment of a core set of shared beliefs is off kilter, or when the activities outlined in the trial roadmaps are not having the desired effect of high adherence among the participants, it is time to recalculate the route by engaging in the PDCA quality improvement process, as shown in the bottom center of the graphic. The adjustments to trial activities that characterize the PDCA process then feed back into the adherence-support activities in the trial roadmaps by shifting the route, hopefully in the direction of high adherence. These adjustments also alter the cycle of influence among the participant, community, and study and how the cycle in turn shapes the contents of the participant's provisions for the journey.

Once you are engaging in the adherence-support activities and PDCA cycle, we recommend revisiting Figure 4 periodically to see how what you are doing fits in with the model.

FIGURE 4
The trial's overall travel package for the adherence journey



B1 • How to use the Plan-Do-Check-Act Process — Recalculating your Route Toward High Adherence

"I can't change the direction of the wind. But I can adjust my sails to always reach my destination."

— Jimmy Dean

WHAT YOU WILL FIND IN THIS SUBSECTION

In section B1, we describe each step of the PDCA process in detail. Despite the study staff's extensive planning for adherence support, their strict fidelity to the study- and site-specific roadmaps (i.e., protocol, SSPs, SOPs), and participants' potential desire to adhere to product use, there will sometimes — and perhaps frequently — be challenges preventing staff, participants, and the community from supporting and achieving high adherence. In this event, we urge study teams to use the PDCA process to improve their activities aimed at supporting adherence as soon as challenges become apparent. The PDCA process can first be used to adjust and tweak current activities; however, if these adjustments do not have the desired effect, PDCA can also be used to introduce new adherence-support activities as allowed by the protocol and ethics approvals.

STEP 1: PLAN

The Plan step of the PDCA process involves identifying which aspect of existing adherence support needs to be improved and creating a concrete plan for changing an activity, event, or intervention strategy that provides that support. Note that many activities, events, and intervention strategies will already be specified by the study protocol, SSPs, and SOPs, so the planning step for these activities consists of figuring out how to tweak them so you have some flexibility in how they are implemented. You may also be able to develop and implement additional site-specific adherence-support strategies that add value or reduce the burden of using the vaginal ring where existing or required interventions leave gaps. Note that in some cases, it will be necessary to gain the support of the overall study management team prior to implementing new site-specific activities.

Discuss Goals: Based on the stage of the study and the objectives of that stage, engage the full study team (or representatives from each staff cadre) to discuss goals for participant adherence. Be as specific as possible.

Assemble a Team: For each goal, assemble a team of staff members and, when appropriate or beneficial, members of the study community (including the participant population) who are knowledgeable about the topic and who may be able to contribute meaningfully to the planning process. Keep the team reasonably small (about three to five people) if possible and appropriate.

Develop a Plan: Once a team is assembled, members can think about the specific goals in more detail. Several elements are needed in the plan:

- A clear, concise statement of each goal.
- Activities or strategies already in place that contribute to the goals, or new strategies you would like to try.
- Resources needed for each activity or strategy (e.g., staff, money, time, materials, venues).
- Timeline.
- Monitoring and evaluation measures. These measures should be user-friendly and easy to administer, rather than a full-fledged monitoring and evaluation plan, as the PDCA cycle is intended to quickly assess specific activities that are or are not working well.

The following questions may help guide the planning process:

1. What have we done in the past or what are we doing to contribute to the adherence goals?
2. Given the resources we have at our disposal, how can we improve what is currently being done in a particular adherence strategy? Or, what new activity could we initiate that would contribute to the goals? Are there ineffective activities that should simply be dropped?
3. Who will be needed to implement the changes to this activity (including study staff and community members)?

4. What is our timeline for implementation?
5. How will we know if the activity or changes we implement are making a difference? How will we measure and monitor success? Site teams should consider quantitative and qualitative measures when thinking about ways to track improvements over time. (See Step 3: Check for ways to solicit feedback and measure improvements.)

ACTION PLAN TEMPLATE

In this action plan template, each overall goal or aim should get its own action plan and team. Then each team should think about the specific sub-activities that need to be implemented to achieve the stated goal and assign a point person or smaller team to work on each activity. Methods for monitoring and measuring each activity and its outcome should be included in the task list. You may choose to use this action plan template as is or modify it to be more useful for your specific site (e.g., you may choose to have one action plan per activity as opposed to per goal/aim)

ACTION PLAN TEMPLATE

ACTION PLAN							
Team Leader							
Team Members							
Goal/Aim							
Activity/Task	Person(s) Responsible	Trial Stage	Target Start Date	Target End Date	Resources Needed *(e.g., staff, money, space, materials)*	Measures	Notes

STEP 2: DO

In the Do step, teams implement the activities that were developed in the Plan step or that are specified by the protocol, SSPs, or SOPs. Be wary of implementing too many activities or modifications to activities at one time, as this will make it more difficult to determine which specific interventions are being effective and which are not. Instead, you may want to target one or two changes at a time. Prior to implementation, make sure you have clearly outlined how the effects of the specific activities will be measured and who is responsible for gathering this information. Collect the associated data during implementation to make evaluation possible.

STEP 3: CHECK

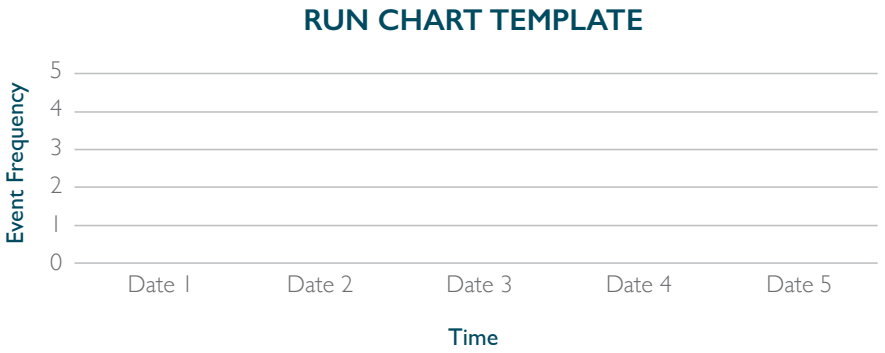
For the Check step, teams should use the measures agreed upon in the Plan (Step 1) to assess whether the modifications/activities implemented in the Do step resulted in improvements.

Examples of methods to solicit feedback and measure improvements:

- Round tables and/or community conversations.
- Tracking of media coverage of the study.
- Community surveys.
- Staff surveys and meetings to solicit feedback.
- Training evaluations.
- Feedback from standard participants or mystery participants.
- Pharmacokinetics monitoring.
- Counts for product returns.
- Participant self-reports of ring adherence or experiences using the ring (including problems or concerns related to ring use).

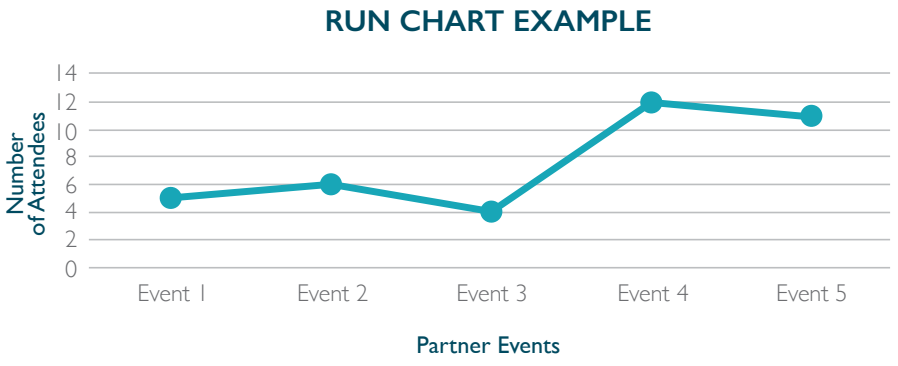
Some activities may have a distinct beginning and end, and others will be ongoing. The type of activity and time frame for each will help determine how and how often the activity should be monitored. Real-time data tracking or interim checkpoints for longer-term activities should be considered. Simple tools like run charts and check sheets, shown below, could assist with tracking changes. Keep the tracking process informative but as simple as possible. The staff burden should be minimal. Remember, the goal is to improve practices in the trial, not to conduct a comprehensive outcome evaluation.

Run Chart: A run chart is a line graph that tracks changes in an event or observation over time. Time is measured along the x-axis, and the event or observation being tracked is plotted along the y-axis.



To see how a run chart might be used, let's consider the following scenario: A vaginal ring study's SSP calls for the use of community-based events to engage men, including male partners, as a core component of adherence support for participants in the study. During implementation, the research team hosts events for partners of participants who have disclosed their ring use, but finds that few partners are attending events.

After holding three events with poor attendance, the study team wants to try a new approach. During the Plan step of the PDCA cycle, the members of the team decide that instead of relying on participants to tell their partners about events at the clinic, they will ask participants for permission to contact partners directly. The study team decides to do this before the next two planned events and to use a run chart to track attendance. Here's what the chart might look like:



By using this tool, it is easy to see that the intervention that was implemented between the third and fourth events successfully boosted attendance.

Check Sheet: A check sheet is a table that can be used to compile data, either in real time or from historical sources, like a retrospective chart review. On a typical check sheet, columns represent specific points in time and rows represent the challenges, events, and other occurrences that the team wishes to track. Using a check sheet, teams can tally how often certain events occur and can easily see patterns over time.

CHECK SHEET TEMPLATE

CHALLENGE	TIME					TOTAL
	Time 1	Time 2	Time 3	Time 4	Time 5	
Challenge 1						
Challenge 2						
Challenge 3						
Challenge 4						
Total						

To see how a check sheet might be used, see PDCA Example 1 in subsection B2. In addition to assessing whether the activities resulted in improvements, study teams should be encouraged to consider whether the activities are sustainable, what challenges or problems were encountered, and if there were any unexpected consequences or side effects (positive or negative). Your team should also document problems, unexpected effects, and general observations.

STEP 4: ACT

The Act step in the PDCA process involves using the measurements and conclusions drawn during the Check step to decide on actions and activities moving forward. For instance, if the activity that was implemented was successful, the team might decide to standardize how the activity is carried out and continue to use it throughout a particular stage of the study. However, if the team concludes that an intervention was not successful or that it could be more successful if modified, the PCDA cycle would begin again with a new Plan step.

B.2 • Plan, Do, Check, Act Examples

WHAT YOU WILL FIND IN THIS SUBSECTION

In this section, we provide two examples of how to use PDCA to improve adherence support. The first example is based on a hypothetical scenario and does not reflect data from an actual clinical trial. The second example is a real-life example from a clinical trial.

PDCA Example 1

Scenario: In the early stages of trial implementation, a study team realizes that some participants are returning for study visits without their rings in place.

PLAN

During its weekly meeting, the study team discusses this issue and decides on a goal to increase the number of participants returning to the clinic with their vaginal rings in place. The team designates staff from several cadres to form a smaller team tasked with working on this issue. This smaller group decides to create a check sheet to document the reasons why participants are returning without their rings in place. The check sheet looks like this:

CHECK SHEET EXAMPLE 1

REASON	MONTH					TOTAL
	June	July				
Removed for sex and not reinserted	II	I				
Fell out while using the toilet	III	II				
Removed for menses and not reinserted		I				
Partner objected to ring use	IIII	IIII				
TOTAL	9	8				

From the check sheet, the team sees that "Partner objected to ring use" and "Fell out while using the toilet" are the most common reasons rings are not in place when participants come to the clinic for their visits. The team decides to focus their action plan on addressing these issues and comes up with a new activity/task to address each reason:

ACTION PLAN EXAMPLE

ACTION PLAN							
Team Leader	Study Coordinator						
Team Members	Counselor 1, Counselor 2, Research Nurse 1, Community Educator 1						
Goal/Aim	Increase the number of participants returning for study visits with their rings in place						
Activity/Task	Person(s) Responsible	Trial Stage	Target Start Date	Target End Date	Resources Needed *(e.g., staff, money, space, materials)*	Measures	Notes
Organize an educational event for male partners at the clinic	Community Educator 1, supported by full team	Trial	Sept 15, 2016	Sept 15, 2016	$50 for food, meeting space at clinic, educational pamphlets, and props	Number of rings removed and not reinserted because of partner objection	
Review proper ring insertion/placement by demonstrating with sample ring and pelvic model	Research Nurse 1 to lead all research nurses	Trial	August 1, 2016	August 31, 2016	Sample ring and pelvic model	Number of rings not returned because fell out in toilet	

DO

Once the team has outlined a clear plan for addressing the identified challenges, each team member begins implementing the activity he/she is responsible for, with the agreement to reconvene in three months to see what progress has been made.

CHECK

Since the site already has a log for tracking ring returns, this is used as the main indicator of whether the strategies have been successful. At the beginning of November, the check sheet looks like this:

CHECK SHEET EXAMPLE 2

REASON	MONTH					TOTAL
	June	July	Aug	Sept	Oct	
Removed for sex and not reinserted	II	I	I		I	5
Fell out while using the toilet	III	II	II	I	II	10
Removed for menses and not reinserted		I	I			2
Partner objected to ring use	IIII	IIII	III	II		13
TOTAL	9	8	7	3	3	30

By looking at the bottom row of the check sheet, the study team easily sees overall improvements over time. When they look in more detail, however, they realize that while fewer women are having challenges with their partners, the number of women who report their rings falling out while using the bathroom has not changed much. During a full staff meeting, feedback solicited from counselors and research nurses echo these results.

ACT

After completing the Check step, the team concludes that their efforts to lessen partner opposition to ring use has been successful. Moving forward, the study staff decides to make male partner events a regular, quarterly activity. Counselors are also encouraged to continue periodic check-ins with participants about their ring-use experiences with their partners. Since the site did not see a reduction in the number of participants whose rings were expelled while using the bathroom, the team decides to return to the planning stage to develop new interventions that might more effectively address this challenge.

PDCA Example 2

During MTN-020/ASPIRE implementation, site staff in Zimbabwe become aware of community rumors claiming that blood samples collected at the clinic are being used in the practice of Satanism and that site staff are profiting from the sale of blood.

Challenge: Participant education about the purpose of collecting blood samples is in conflict with messages participants may hear in the community.

Issue and Provision Targeted

- **Issue:** Rumors and/or misconceptions related to HIV and/or the study.
- **Provision:** Participant beliefs about the trial. Without intervention, participants must reconcile different messages about clinical trial conduct and procedures on their own. Beliefs about the trial may be eroded, and participants may become distrusting of the study and of using the study product.

Site staff meet to discuss this problem and agree that simply educating participants about blood draws, protocol testing, and sample storage has not been effective in combatting community rumors about blood sales and satanism. They hypothesize that showing participants and CAB members what happens with blood samples may be more impactful.

One CAB member and two participants from each of three study sites are invited to attend a laboratory tour. During the day, tour participants take notes and ask questions as laboratory technicians demonstrate specimen management and testing processes. The CAB representative is encouraged to share information in the community, and participant representatives are invited back to share their experiences with groups of participants from that study site.

Tour participants are asked to provide feedback immediately after the tour to study staff. The reaction to the lab tour is overwhelmingly positive; participant representatives and the CAB members feel honored to have participated, and they have learned a lot. As lab

tour participants share their experiences during group sessions at the clinics, staff keep a list of participant attendees. These participants are encouraged to talk about the lab tours and their impact during individual study visits and at group events. After hearing about lab procedures from their peers, study participants report greater confidence in the clinic's handling of blood samples and say they feel empowered to approach their communities with the correct information.

ACT

Site staff, participants, and CAB members have made several suggestions for improving this intervention. Many study participants have recommended making lab tours available to all participants and starting these tours earlier during the trial. The site staff are also considering extending lab tour invitations to community leaders to create a more ideal platform for current and future study implementation.

— MTN-020/ASPIRE UZ-UCSF clinical research sites, Harare, Zimbabwe

PATHWAYS TO HIGH ADHERENCE

The Journey is Under Way: Pathways Toward Adherence

"There is not ONE path. There is not even the RIGHT path. There is only YOUR path — and you know it's yours by how it feels to you."

– Sue Krebs

Now that we have laid out the rationale and process this manual advocates for supporting adherence, we move on to forging the actual pathways toward adherence traveled during the participant journey. Each path launches from an **entry point**, from which the implementation of a specific adherence-support strategy points someone in the direction of high adherence. The strategies presented in this section include ideas to implement or adapt during different stages of the study.

The journey starts in the pre-trial stage, before screening and enrollment begin. The study team may already have an idea about what one route to high adherence will look like for the study and its participants. However, along the way, it will become clear that there are many pathways leading toward the same place. The entry points to these paths may be strategies introduced by the study management team, the site team, participants, or members at different levels of the community — each having the ability to affect travel toward high adherence.

Site teams use the PDCA cycle throughout the stages of the study to continually improve the various adherence-support strategies they are implementing. In this way, the teams can assess which entry points have steered participants down the wrong path and can also determine how each new strategy will forge a new path. The paths to high adherence are not single, straight roads; they may also have many bumps and potholes. Nonetheless, traveling these paths together — as staff, community, and participants — and with determination can make the journey both successful and rewarding.

OBJECTIVES OF EACH TRIAL STAGE

Understanding the adherence-related objectives of each stage of the trial will help study teams decide on the strategies that are appropriate to adjust, or on the new strategies that should be implemented, during each stage.

WORKING IN COMMUNITIES PRE-TRIAL

In the pre-trial phase, many or even most sites will have community engagement activities or formative research under way to help prepare for recruitment and retention efforts, identify community attitudes and concerns, and otherwise explore how to best integrate the trial into the community and vice versa. Any work associated with establishing a positive context for adherence needs to be integrated into these community engagement and research activities in order for staff working across these efforts to represent the trial in a seamless way. For this to happen, all staff involved in activities with community stakeholders will need to be aware of and understand what other staff members are doing. Using one voice, they will need to articulate the goals of the formative and planned clinical research, and the mission of their engagement activities, clearly and consistently.

Pre-Trial Stage

The pre-trial stage of the study lays the groundwork for a successful trial, including all that must be done before the first participant can be recruited, screened, and enrolled. This stage involves hiring staff, seeking regulatory approvals, and gathering the materials necessary for study implementation. It is also a crucial time for sites to think about how to positively position the research within the community, recruit participants, and design the clinic environment in such a way that product adherence is fully supported and facilitated. Study sites will have only one opportunity to lay this foundation, and a successful trial with high adherence depends on how well this is done.

Where adherence is concerned, the primary pre-trial objective is for study staff to promote alignment between the goals and views of the researchers and those of the community prior to the trial stage. This translates into study staff not only encouraging community understanding, acceptance, and support for the trial but also coming to understand community perspectives and concerns. Both aspects have the potential to positively affect adherence later, during the trial stage. This is because when there is some degree of alignment between the research site and the community at the time of participant screening and enrollment, participants who are open to trying the vaginal ring and adhering to the product regimen may feel supported to do so — since, as the participant travels back and forth between the research site and her community, her feelings of conflict will be minimal.

RESOURCES

Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials
http://www.avac.org/sites/default/files/resource-files/Good%20Participatory%20Practice%20guidelines_June_2011.pdf

Recommendations for Community Engagement in HIV/AIDS Research version 2.0
https://www.hanc.info/cp/resources/Pages/recommendationsInvolvement.aspx

Stakeholder Engagement Toolkit for HIV Prevention Trials:
https://www.fhi360.org/resource/stakeholder-engagement-toolkit-hiv-prevention-trials

Trial Stage

The trial stage begins with participant screening and enrollment and continues through participant follow-up. Adding to the pre-trial objective of striving for alignment between the study and the community, the trial stage also seeks to achieve alignment with each individual participant, such that there is the core of shared beliefs among all three entities. Strategies to achieve this three-way alignment include ensuring staff members'

fidelity to trial procedures as specified in the roadmaps; using the PDCA quality improvement process to make adjustments to adherence-related activities that are not good entry points to adherence pathways; and finding new ways, as needed, to support participants in using the ring.

Post-Trial Stage

Pathways to high adherence do not dead end at the participant's final clinic visit. On the contrary, the actions of a study team during the post-trial stage have great implications for continuing to foster community trust in research, and for investing in product adherence during future clinical trials, both within and outside of the immediate community. This may include implications for open-label follow-on studies, as well as for post-trial product use should the vaginal ring become available on the open market.

One of the main goals for study staff in the post-trial stage, then, is to maintain alignment of a shared core among the study, participants, and community by fulfilling the study's obligation to disseminate and explain trial results to participants and the community. The dissemination process should include ways for the research staff to hear and learn from participants, community members, and other stakeholders about their experiences with the trial and the meaning of the trial's outcomes. As in the pre-trial stage, this may include formative research to gain deeper understanding about the trial's outcomes or how to transition from a randomized controlled trial to an open-label extension of the randomized controlled trial. In this way, the team can perpetuate the supportive environment they worked so hard to create during the pre-trial and trial stages of the study.

C1 • Overcoming Roadblocks

WHAT YOU WILL FIND IN THIS SUBSECTION

In this section, we describe several adherence-related issues to consider in each stage of the trial that, if not properly assessed and addressed, could become roadblocks on the pathways to high adherence. The list of issues below is not intended to be comprehensive, and your study team may also find that not all of the issues present a challenge for your site. As your study team convenes during the pre-trial stage to think about ways to maximize adherence throughout

all stages of the study, it will be important to identify which issues specific to your local context may facilitate or hinder high adherence once the trial begins. Research clinics must make difficult decisions about how to spend their limited time and resources, keeping in mind that the quick and inexpensive fix may not always be the most effective. Research teams will need to prioritize which of the issues below might be most important to work on. Subsection C2 is a tool study teams can use to prioritize the issues at their site. Subsection C3 presents potential strategies — the entry points to the pathways toward high adherence — for addressing the issues.

ISSUES TO CONSIDER

- **Community's experience with previous research studies**

  Significance for adherence: Many communities where the vaginal ring is being studied are not naïve to research. Because the process for establishing a clinical research site is long and rigorous, the number of places where clinical research can take place is limited. This is especially true in resource-limited settings where clinics that have been approved as research sites tend to implement many studies within the same community. If the community has had positive experiences interacting with the study site or with clinical research in the past, there may already be high levels of trust and understanding, both of which will support high adherence in the current trial. If, however, a community has had negative experiences with past clinical trials, adherence in the current trial may be undermined unless or until the past negative experiences are dealt with. Issues that may be especially important to address include:

  - Previous trials that were ended early or had null results.
  - Rumors or misinformation never addressed during past trials.
  - Perceived lack of benefits to the community from previous trials.
  - Perceptions that previous research efforts caused harm to participants or the community

RESOURCE

Communications Handbook for Clinical Trials: Strategies, Tips, and Tools to Manage Controversy, Convey Your Message, and Disseminate Results

https://www.fhi360.org/resource/communications-handbook-clinical-trials-strategies-tips-and-tools-manage-controversy-convey

- **Community's beliefs about the benefits of biomedical research and the concept of reciprocity**
  Significance for adherence: Regardless of whether a particular community has experience with clinical trials, it is important to understand if and how a community believes it will benefit from the research being proposed and what the community perceives to be the costs of supporting the study. High adherence will likely be easiest to achieve in communities where perceived costs of supporting the research are low and perceived benefits are high. Emphasizing and ensuring **reciprocity** within the community is necessary for creating an environment in which study participants feel free to engage fully in the trial, including being willing to try and to continue using the vaginal ring. Reciprocity alone is not sufficient for ensuring high adherence, but in communities where perceived costs are high, or perceived benefits are low, participants will likely face substantial barriers to study product use.

  It is important to remember that perceived costs and benefits will differ throughout the community and across stakeholders. Costs and benefits may be personal, political, financial, or social in nature, and the study team will need to consider what benefits are likely to be of value to each stakeholder or community group. One benefit that is often highlighted and discussed in preparations for a new trial is access to the product if it proves safe and effective. However, such access requires approvals, licensing, production, cost agreements, and programming support — all of which may take years to complete. In communities that are unlikely to gain access to an effective product for a long time, it will be especially important for study teams to ensure that other benefits to the community are highlighted.

- **Media coverage of biomedical research in general, the current research study, and HIV**
  Significance for adherence: Media coverage can help increase research literacy and knowledge of HIV in a way that supports product adherence. Media reports can also lend legitimacy

to the study and reinforce messages coming from staff so that communities will have trust and participants will have confidence in using the study product. Conversely, media misrepresentations of biomedical research and HIV may jeopardize adherence by breeding mistrust or spreading misinformation.

- **Rumors/misconceptions related to HIV and/or the study**
  Significance for adherence: Rumors and misconceptions related to HIV and/or the study (including the research site, the staff, the vaginal ring, and the study procedures) can spread quickly, if not thoughtfully addressed early on. When rumors and misconceptions come from the community or important others in a participant's life, they can carry as much, if not more, weight and importance than messages coming from the study clinic. Left to reconcile these competing messages on her own, a participant may become hesitant to try or continue using the study product. If a participant finds she has to continually defend her choice to use the product, she can quickly become discouraged and stressed by the competing demands placed on her.

- **Resource availability in the community**
  Significance for adherence: By joining a clinical trial, participants gain access to resources including medical care, financial compensation, and HIV prevention services and supplies. If the trial operates in a community where these resources are otherwise scarce, women are often motivated to participate in the trial for reasons other than to help test a new HIV prevention product. Instead of denying that these motivations exist or denouncing participants who join the trial primarily to gain access to these benefits, study staff may benefit from embracing the concept of mutuality and working to achieve it. Mutuality is the idea that participants and the study are dependent on one another and that if both parties honor their commitments to one another, both will benefit. The trial should provide an environment in which participants and study staff can feel free to express their motivations for participation in a way that also helps both parties understand how the actions of one affect the other. The hope is that participants would agree to use the study product for the benefit of the study and that the study would reciprocate by providing the medical care, reimbursement, and other benefits as outlined by the research protocol.

RESOURCE

Communications Handbook for Clinical Trials: Strategies, Tips, and Tools to Manage Controversy, Convey Your Message, and Disseminate Results
https://www.fhi360.org/resource/communications-handbook-clinical-trials-strategies-tips-and-tools-manage-controversy-convey

A Media Handbook for HIV Vaccine Trials for Africa
http://www.unaids.org/en/resources/documents/2001/20010307_jc475-mediahandb_en.pdf

Handling the Media: A toolkit
http://www.unicef.org/magic/resources/civicus_handling_the_media.pdf

Stakeholder Engagement Toolkit for HIV Prevention Trials
https://www.fhi360.org/resource/stakeholder-engagement-toolkit-hiv-prevention-trials

RESOURCE

Appendix D: Mutuality Framework (in this manual)

- **Relationships with stakeholders and community gatekeepers**[2]

  Significance for adherence: A stakeholder is a critical ally in any HIV prevention research endeavor. By definition, a stakeholder is someone at the local, national, or international level who can affect or be affected by the researc — potentially a large group of people who are deeply interested in the results of your trial. A stakeholder's perception of the research is important not only for the success of your trial but also for the support of future research. Effective stakeholder engagement is built on trusting relationships and building common goals. Developing someone's trust takes time, and trust grows as one demonstrates appropriate and reliable behavior. Identifying potential conflicts in research goals or procedures and the goals, values, or beliefs of groups or members of the community can direct efforts to better align the research in the community. Prior to and during the study, teams can reach out to groups that may be indirectly affected by the research, such as parents and partners, traditional healers, or religious and tribal leaders, to discuss goals and procedures. At all points, self-assessment of transparency is critical. Do you do what you say you will do? How do you handle mistakes and misunderstandings? Are you open, honest, and transparent? Do you consider the concerns of others when you make a decision? Successful stakeholder engagement with community gatekeepers — including male members — is essential to building and sustaining an environment of trust and support for trial participants (see Case Study 2). It decreases the likelihood that a participant will need to defend her product use with others in the community.

RESOURCE

Stakeholder Engagement Toolkit for HIV Prevention Trials
https://www.fhi360.org/resource/stakeholder-engagement-toolkit-hiv-prevention-trials

- **Cultural and religious beliefs and customs**

  Significance for adherence: Religious and cultural beliefs and customs are important to understand, especially if participating in the clinical trial or using the vaginal ring would be challenging within the context of these beliefs. When previous clinical studies have failed to address these issues, rumors and fears have been quick to form in the community, negatively affecting participants' trust of the research site and their willingness to use the study product. Some of these rumors and fears include:

  - Misconception that the study clinic is selling blood or other biological samples collected during study visits.

2. Source: Adapted from the *Stakeholder Engagement Toolkit for HIV Prevention Trials*

SOCCER TOURNAMENT TO ENGAGE WITH COMMUNITY MEMBERS IN IPM 027/THE RING STUDY

The importance of support from the community, and specifically men from the community, is a critical factor for success in conducting microbicide trials. However, many obstacles such as women's non-disclosure to male partners of their participation in microbicide trials make it challenging to engage with men. During The Ring Study, the sponsor worked closely with research centers' community engagement teams to develop a strategy whereby men in the community could be engaged and informed about the study. With the difficulty of bringing men together for a meeting or workshop, one strategy was to approach local soccer/football clubs or associations within the research center's catchment area for support in hosting a soccer tournament.

Research centers identified and liaised with their local soccer clubs/associations to explain the rationale behind the tournament and the need for their involvement. As far as possible, events were hosted in partnership with local stakeholders and partners, including the municipal/provincial Departments of Health, that offered health education and health tests at these tournaments. In some cases, walks were arranged through the community with banners of messages from men and local organizations in support of the event.

Each research center managed its own event planning and had the freedom to add activities it felt would have high impact in the community. Some examples were combining the events with other activities, such as traditional dancing and music, and at one center arranging a netball tournament (for women) alongside the male event. One research center preferred to host six teams in the tournament on one day, while another preferred to host four tournaments over a 12-month period. The highest recorded male attendance at a single event was more than 750 men. In total, nine soccer tournaments were hosted, with more than 1,200 men in attendance.

During these events, The Ring Study was discussed and time was allowed for questions and answers. During the sessions, men asked many diverse questions related to research and sexual and reproductive health. Questions allowed an opportunity to identify areas of misconception and/or lack of knowledge around sexual and reproductive health as well as The Ring Study.

In general, these events were very successful, as demonstrated by the comments below:

"Can't we have this event annually even if the study is completed, as we want to have more information on latest HIV developments? What is there for men besides the condom?"

"We are happy to be involved in such an important initiative, hoping you will always remember us as men."

At one research center, the local soccer club managers and team captains signed a pledge of support for the study and for the women in the study. Male engagement and support for clinical trials through sport proved to be a good platform for sharing information, as men are not easily drawn into meetings or workshops. Men were, however, comfortable participating in the more informal setting of these events.

- IPM 027/The Ring Study team

IPM 027/The Ring Study is a Phase III safety and effectiveness trial of a vaginal ring containing the antiretroviral drug dapivirine. The study enrolled HIV-negative women ages 18 to 45 at six clinical research sites in Uganda and South Africa. Data collected through October 16, 2015, showed that the dapivirine ring reduced the risk of HIV infection by 31 percent overall.

- Rumors about study staff and/or participants practicing witchcraft or satanism.
- Fear of dying with the ring inserted, due to religious beliefs that bodies should not be buried with any foreign objects in place (see Case Study 3).

- **Gender dynamics within the community**
  Significance for adherence: Gender dynamics and gender norms in the community may also affect adherence and influence how communities view the research (e.g., communities may not be supportive of the female autonomy provided by the ring or may think the study is encouraging promiscuity by promoting an HIV prevention method for women). Similarly, gender norms will influence an individual participant's comfort with using the ring and possibly disclosing ring use to her sexual partner(s). For vaginal ring trials, it is critically important to achieve a balance between positive male engagement in support of product use by trial participants, and support of women's right to choose whether they will inform a partner about their trial participation and product use (see Case Study 4).

- **Staff training on participant-centered care**
  Significance for adherence: Staff training on participant-centered counseling techniques (See Appendix B) and clinical care is essential because it gives staff the tools they need to support and build rapport with participants. Support and rapport, in turn, will influence the willingness of women to participate and be engaged fully with the trial. Training staff in these methods of care will help them address the specific needs of each participant related to trying and continuing to use the ring, as well as to being comfortable in openly and honestly reporting experiences using the ring.

SUPPORTING WOMEN IN DECISIONS ABOUT DISCLOSURE OF THE RING

Although most women's adherence will benefit from disclosure of vaginal ring use to their partners, some women may find that disclosure results in a partner actively undermining their ability to use the product or even placing them at risk of physical harm. A nuanced understanding of the range of partnership experiences and how these may evolve over time is important for appropriately and effectively supporting adherence. It is important to remember that disclosure is not necessarily an all-or-nothing affair: women may elect to disclose their use of the vaginal ring at different points during the study, and they may elect to disclose initially or eventually to some partner types (e.g., stable partners such as husbands or cohabitating boyfriends) and not others (e.g., casual partners). Supporting women in their decisions about disclosure will involve counseling that supports women's decision making around disclosure to different partner types, as well as a focus on approaches women might use when/if they do decide to tell a partner about the ring and their trial participation.

RESOURCE

Manual for Conducting a Gender Analysis for Microbicide Introduction.
http://www.fhi360.org/sites/default/files/media/documents/GenderAnalysisGuidance_WithHyperlinks_0805.pdf

A SANAC Pocket Guide to Thinking about Gender and Vaginal Microbicides.
http://www.fhi360.org/sites/default/files/media/documents/pta-gender-south%20africa-pocket%20card-print%20ready%203.pdf

Appendix B: Follow-up Adherence Counseling — Collaborative Discussions to Promote Product Uptake and Use (in this manual)

CASE STUDY 3

CULTURAL BELIEFS IN MTN-020/ASPIRE

During participation in MTN-020/ASPIRE, one participant raised concerns about what would happen if she died while using the vaginal ring and was buried with a foreign object in place. She relayed a true story from her past — that her family saw her mother removing an eye prosthesis from their father when he passed away since, according to their family's beliefs, a person should not be buried with a foreign object in the body.

During her conversation with study staff, the participant was reminded about using the ring daily and the purpose of the study. She was counseled about risk of HIV infection. Once it was confirmed that she knew and understood the purpose of the study, the conversation returned to her concern about the ring, and her challenge was acknowledged. It came out that she had not disclosed study participation or product use to any of her family or friends, which was contributing to her worry that no one would know she had a vaginal ring in place if she passed away. Study staff discussed the option of study disclosure with the participant and she agreed that it would be good to disclose to somebody who is close to her. That person would be able to inform her relatives about the ring if it happens that she passes on while she is in the study and still using the ring. The participant was reassured and was informed that study staff would give the family support and assistance should she pass on and the ring need to be removed. The participant felt at ease after this counseling session, and chose to continue on the product.

- MTN-020/ASPIRE CAPRISA eThekwini clinical research site, Durban, South Africa

MTN-020/ASPIRE — A Study to Prevent Infection with a Ring for Extended Use — was a Phase III safety and effectiveness trial of a vaginal ring containing the antiretroviral drug dapivirine. ASPIRE enrolled HIV-negative women ages 18 to 45 at 15 clinical research sites in Malawi, South Africa, Uganda, and Zimbabwe. The study found that the dapivirine ring reduced the risk of HIV infection by 27 percent overall.

The basic idea of participant-centered care is to provide care in a way that is as responsive as possible to each participant's specific needs. Although the mechanical properties of the vaginal ring (e.g., size, stiffness), the drug(s) it contains, and its use requirements cannot be changed during a trial, some aspects of the clinical trial experience could be adjusted by staff to better meet the needs of individual participants. Creating a participant-centered environment is necessary but not sufficient to support adherence (just as any other single adherence-support strategy would not be effective on its own). Within a participant-centered environment, the other strategies identified to promote open discourse, explore decision making around ring-use, and gather frank feedback on experiences have great chance of being effective.

- **Study team plan for supporting participant engagement and autonomy**
  Significance for adherence: Having a clear plan to support **participant engagement** in the ongoing conduct and monitoring of the trial is an

CASE STUDY 4

GENDER DYNAMICS AND PARTNER DISCLOSURE IN MTN-020/ASPIRE

At one of her MTN-020/ASPIRE visits, a participant reported that her partner, who was not aware of her study participation or ring use, developed a pimple on his penis a day after having sexual intercourse with her. Her partner stated, "Something is wrong with you," and wanted her to go to a traditional healer. Afraid that the healer would discover her use of the vaginal ring, the participant disclosed her study participation to her partner. He was angry, threw the ring in the toilet, and blamed his symptom on the ring. The participant further explained the study to her partner, and he appeared to understand, although he still took her to the traditional healer for a consultation.

At the participant's study visit, staff asked her if she needed help or assistance in any other way and she said no. Telephonic and face-to-face counseling were offered for her partner, but she declined. She was not worried about the possibility of her partner finding the ring again, as her partner had never felt the ring before. The participant stated that she would continue with ring use and did not wish to disclose her continued use to her partner. Study staff asked the participant to inform the clinic of further problems and if she would agree to be followed up telephonically, but also expressed support for her decision on how to handle this issue, acknowledging that she understood her partner best. Staff reassured the participant that the ring had not been shown to adversely affect partners in this way and that it was especially unlikely that the ring had caused her partner's symptom, as she had used the ring for a long time with no problems

- MTN-020/ASPIRE CAPRISA eThekwini clinical research site, Durban, South Africa

MTN-020/ASPIRE — A Study to Prevent Infection with a Ring for Extended Use — was a Phase III safety and effectiveness trial of a vaginal ring containing the antiretroviral drug dapivirine. ASPIRE enrolled HIV-negative women ages 18 to 45 at 15 clinical research sites in Malawi, South Africa, Uganda, and Zimbabwe. The study found that the dapivirine ring reduced the risk of HIV infection by 27 percent overall.

important part of building a cohesive team that makes participants feel valued and heard. Numerous methods for facilitating participant engagement, outlined later in this manual, may help participants feel a sense of ownership over the trial and investment in its success. Successful participant engagement fosters strong participant-participant and staff-participant relationships, helping participants feel a part of something larger than themselves and emphasizing how the actions of one person influence the whole. However, because ring use and persistence with use is a behavior executed predominantly outside of the research clinic/site, **participant autonomy** must also be discussed and encouraged. Overt discussions between staff and participants about adherence as a choice is recommended. One-way messaging, advice, lecturing, or "telling" participants to engage with the product is not envisioned to promote adherence; talking with participants about their decisions to use or not use the product, and about the factors influencing those decisions, is likely to be more productive.

C2 • Tool for Identifying and Prioritizing Roadblocks

WHAT YOU WILL FIND IN THIS SUBSECTION

In this section, you will find a tool for identifying issues that may require special attention in adherence-support activities in the community during the pre-trial stage. The tool includes nine questions referring to issues that may be potential roadblocks for your site, and a key for determining whether they should be a priority for your site to address. The tool is intended for use during the Plan step of the PDCA, in the pre-trial stage when each site team should take time to examine the structure and dynamics of the study site, as well as the characteristics of the community in which the research will take place. However, if you find the tool useful, you can also use it during later stages of the trial, either with the same questions included or with a modified list of questions that are more appropriate for the particular stage of the trial (e.g., questions during the trial stage would likely need to include questions about the participants, in addition to questions about study staff and the community).

Once you have identified high-priority issues using the tool, the next part of the Plan step involves honing in on distinct strategies that might be able to be improved, and/or identifying new strategies that can be implemented to strengthen adherence support. See subsection C3 for potential strategies.

TOOL FOR PRIORITIZING ISSUES RELATED TO ADHERENCE

Instructions: For each question, choose the option (i.e., yes, no, mixed, unsure) that best fits your current community and research environment. Once you have decided on an answer for each question, look at the key provided to help you determine which topics should be a high priority for addressing in adherence-support activities, which should be a lower priority, and which might require more information gathering before they are assigned a priority level.

	Yes	No	Mixed	Unsure
1. Has the community had a positive experience with past research trials? Note: If the community has not had any previous experience with research trials, mark "Unsure."				
2. Does the community believe that biomedical research offers benefits to them and some form of reciprocity?				
3. Does the media accurately cover issues related to biomedical research and HIV?				
4. Is the community free of rumors and/or misconceptions related to HIV, the research site, and the study (including study procedures and the investigational product)?				
5. Are the resources that are provided by joining the study (e.g., medical care, financial compensation, HIV prevention services) otherwise readily available to women in the community?				
6. Does the study site have strong relationships established with stakeholders and community gatekeepers?				
7. Do the study protocol and investigational product fit within/support the existing cultural and religious beliefs and gender dynamics in the community?				
8. Are study staff well-trained in providing participant-centered care?				
9. Does the study team have a clear plan for supporting participant autonomy and engagement in the conduct and ongoing monitoring of the trial?				

KEY

OPTIONS	INTERPRETATION	ACTION
Yes	This area is strong and supportive of product adherence during the trial.	Lower priority for site team to work on. "Do" activities should be focused on maintaining strength in this area, rather than implementing big changes.
No	This area is weak or represents an area in which the study and community are not aligned. This has the potential to undermine/negatively affect product adherence in the trial, if not addressed by the study team.	This is a high priority area. "Do" activities should be focused on creating change and strengthening this area.
Mixed	This area is neither strong nor weak, but there is an opportunity for improvement.	This is a medium priority area. "Do" activities should focus on exploring this area in more depth to identify where specific strengths and weaknesses exist so that actions can be targeted appropriately.
Unsure	This area needs more research in order to determine whether current conditions are supportive of or detrimental to adherence in the study.	"Do" activities should focus on researching this topic and gathering more information so that this area can accurately be assigned a priority level.

C3 • Entry Points to Adherence Pathways

WHAT YOU WILL FIND IN THIS SUBSECTION

In this section, we present a list of potential **adherence-support strategies**, which we call entry points, organized by trial stage and by whether they pertain to **fidelity** to the study procedures or other types of adherence-related efforts, which we call shared learning entry points. These strategies are the entry points to the **pathways** to adherence. It is up to each site study team to add to this list of potential strategies and then decide which ones are most relevant for each priority area. Remember to work with your site's community engagement, outreach, and communications team members on all of these activities, as many of them are likely already under way for the current study or have been implemented in some form in previous studies. The goal should be to thoughtfully supplement other ongoing community engagement activities to address any adherence-related concerns.

HOW TO DECIDE WHICH ENTRY POINTS TO USE

For each high-priority area you have identified using the tool in subsection C2, consider the following questions to help you prepare for assisting participants to adhere to ring-use procedures:

- Does your site have established mechanisms for addressing the issue? If yes, is there anything about the planned trial that suggests that those mechanisms need to be adjusted? Have there been recent local events or changes that may require doing things differently?
- If your site does not have established mechanisms for addressing the issue, is there guidance from the trial sponsor or funder that needs to inform your approach?

As you decide on strategies to implement or adjust, remember that each one should move you closer to the goal of creating alignment among the study, the participant, and the community, and as a result promote high adherence. Whether these entry points focus on the study staff, the community, or the participant herself, they are also your opportunity to affect the content of the participant's provisions for the journey and, as a result, alignment among all three sources of influence. In addition to identifying adherence-related priority issues to address, it may be useful to think about the potential for each strategy to influence

TIP

When choosing a strategy to implement, make sure to invlove representatives from each staff cadre. Involving staff members with different sets of skills and expertise will help the team come up with a comprehensive list of pros and cons for each strategy.

an individual participant's provisions or the provisions of your participants as a whole. One way to do this is to create a table of existing or potential strategies and the provisions each is likely to affect. **Table 1** illustrates how you might do this, using a few example strategies for the trial stage and the provisions each one might influence. Your table will look a little different from this one, since strategies will be tailored to your site, your participants, and the local community. (Note: Strategies related to fidelity likely do not fit within a table like this since they are more about making certain that study procedures are being implemented as intended than about directly influencing participant provisions.)

TABLE 1

Potential pathways and their relationships to provisions for the journey

ENTRY POINT STRATEGIES	PROVISIONS FOR THE JOURNEY				
	Reasons for participation	Beliefs about trial	Beliefs about product	Shared vision	Agency
Psychometric screening of potential participants	x			x	
Counseling at screen out		x	x	x	
Research literacy education		x	x	x	
Adherence clubs			x	x	x

PRE-TRIAL STAGE

Fidelity Entry Points

- **Staff training**

  Use training to make sure study staff are well-versed in the study goals and protocol procedures, as well as know how to implement the procedures in a way that is flexible (when possible), non-judgmental, and participant-centered. Remember that poor staff comprehension of clinical trials will result in poor comprehension among community members and participants, which very often results in poor adherence to the investigational product during study follow-up. Remember, too, that even staff members who are well-trained in their respective fields (e.g., nurse, counselor) will need to undergo sometimes extensive *retraining* to make sure their service-delivery techniques are in line with the approaches called for by the protocol and other study guidance documents. For instance, someone classified as a counselor who may have been trained to be directive and authoritarian with clients may need to adapt their previous counseling style to be in line with the approach adopted by the study (see Case Study 5).

- **Staff practice sessions with standard participants**

  A standard participant is someone very similar to a trial participant who is trained to go through the trial procedures and observe how the staff treat and respond to her. The standard participant then debriefs with the staff she interacted with and gives input on how well they adhered to procedures and supported her throughout her visit. The staff know that the standard participant is not a real trial participant. This technique may be especially useful to improve adherence-counseling practices and to make sure that assessments of ring use are done in a non-judgmental way. It is derived from the standard patient model used in medical schools to improve the clinical skills of medical students and residents.

Shared Learning Entry Points

- **Team-building exercises**

  Team-building exercises can help promote cohesion among study staff members, which is essential if cohesion among the study, community, and participants is going to be achieved (see Case Study 6).

RESOURCE

Standardization Patients (SP) Tip Sheet
https://www.womenshealth.gov/files/assets/docs/heart-truth/sptips.pdf

Association of Standardized Patient Educators
http://www.aspeducators.org/

TIP

In addition to conducting team-building exercises with study staff, think about ways to apply the concepts of team building in the community and eventually with participants to create one cohesive study team. The purpose of team building is to help a group of people come together around a common goal by sharing experiences and improving communication and trust. This is exactly what needs to happen among the study staff, comminuty, and participants in order for adherence in a clinical trial to be high. Some team-building exercises are educational, while others are purely for fun.

INDIVIDUAL EFFECTIVENESS WORKSHOP WITH RESEARCH CENTER STAFF TO IMPROVE ADHERENCE AND RETENTION OF STUDY PARTICIPANTS IN IPM 027/THE RING STUDY

The ability of research center staff to make a personal connection with study participants has been shown to hugely improve retention and adherence in a clinical trial. To improve this connection, the starting point has to be with the individuals working at the research center. Therefore, IPM decided to embark on a series of workshops at all of its research centers, with the key objective of improving the research center employees' level of self-awareness.

The workshops also had additional goals, which followed increasing an individual's level of self-awareness:

- Increase understanding of colleagues' work styles and preferences.
- Improve communication among team members.
- Improve teamwork and productivity.

To achieve these goals, the DiSC® tool was used. DiSC is the leading personal assessment tool used by more than 40 million people worldwide. It is a non-judgmental tool that required each research center employee to complete a series of questions that produced a detailed report about his or her personal style and behavior.

During the workshops, each workshop participant received this report, which described the participants' own personal style, workplace priorities, motivators, stressors; how they are likely to react to people with styles different from their own; and suggestions to improve their workplace effectiveness.

The IPM facilitators took the workshop participants through a series of exercises over two days to work through the above topics. This helped research center staff fully understand their own styles and behaviors, thus greatly increasing their level of self-awareness. The feedback was overwhelmingly positive, ranging from people now feeling more sure of themselves when interacting with study participants, to one research center staff member stating that "I finally understand why I interact so well with certain study participants, and why I struggle with others. Just knowing this already improves my attitude towards the ones I struggle with."

During the workshop, the additional objective of improved teamwork naturally emerged. For example, two employees were having major workplace conflicts, and after understanding how their styles were very different, one comment was:

"Thank you, you have saved our working relationship. We now understand why we don't get along. This is the first step to overcome our differences."

It was clear throughout the workshop that a focus on purely protocol-related training will not be sufficient for obtaining required retention and adherence results in long-term clinical studies. The research center staff's personal development is critical in enabling them to improve their connection with study participants. Without this connection, retention and adherence will be difficult to achieve.

-IPM 027/The Ring Study team

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STUDY TEAM EFFECTIVENESS WORKSHOP WITH RESEARCH CENTER STAFF TO IMPROVE ADHERENCE AND RETENTION OF STUDY PARTICIPANTS IN IPM 027/THE RING STUDY

As a follow-up to the DiSC training (see Case Study 5), IPM along with an external service provider embarked on a series of team effectiveness workshops for research center staff conducting The Ring Study. Working as effective teams was identified as a key issue affecting retention and adherence. In addition, a key aspect was the incorporation of customer service (treatment of participants by research center staff).

Remarkable growth was seen in these sessions, as teams learned about themselves, their team members, and how to apply the tools to which they were introduced. The following is an extract from one of the leaders who attended the workshop: "Thank you so much for the team building you did at our research center. The lessons we learned were very valuable. I think a lot of the methods and the feedback tools must get practiced, but I believe we will get there eventually. I do believe we will be able to grow in our relationships and in our working methodologies so we can be more effective and more able to deal honestly and openly with each other."

A key highlight of the workshop centered around a "Presence and Impact" session. The customer (study participants) received varied levels of service depending on whom they interacted with during their engagement with a research center. This could be due to different levels of understanding of who the customer actually is and how their treatment affects retention and adherence. Some questions were therefore asked:

- How do I "show up" when I engage with the participant?
- What is my attitude toward them?
- Do I acknowledge them, and how do I address them?

To answer the above questions, the attendees were introduced to the **"8 commandments of customer care"** and were recommended to display them in the various centers to heighten awareness and serve as a reminder of their attitudes toward those they were serving:

1. The client (study participant) is the most important person in my business.
2. The client (study participant) is not dependent on me; I am dependent on the client.
3. The client (study participant) is not an interruption of my work, but the purpose of it.
4. The client (study participant) does me an honor when calling on me; I am not doing them a favor by serving them.
5. The client (study participant) is not a number, but flesh and blood, a human being with emotions like my own.
6. The client (study participant) is not an outsider, but my guest.
7. The client (study participant) brings me his or her needs; it's my job to meet and exceed them.
8. The client (study participant) is not someone to argue or compete with; the client deserves my best attention and attitude.

Participants viewed these sessions as very powerful and practical in helping them work with both their external clients/participants and their internal team members.

- IPM 027/The Ring Study team

IPM 027/The Ring Study is a Phase III safety and effectiveness trial of a vaginal ring containing the antiretroviral drug dapivirine. The study enrolled HIV-negative women ages 18 to 45 at six clinical research sites in Uganda and South Africa. Data collected through October 16, 2015, showed that the dapivirine ring reduced the risk of HIV infection by 31 percent overall.

- **General community meetings, forums, or round-table discussions**
  This strategy may be one of the most important and most common in the pre-trial stage, since it could be used to address a wide variety of priority areas. When planning a meeting with community members, you may want to consider some of the following issues:

  - *Audience:* Who should the meeting be with (e.g., men or women, particular neighborhoods, existing community groups, religious congregations)? Is a small audience or a large audience most appropriate for the goals of this particular activity?
  - *Venue:* Should the meeting take place in the community or at the research site? What requirements will the space need to meet in order for the discussion to be successful?
  - *Format:* What will the agenda look like? Will this be a formal presentation, an informal discussion, or a hands-on activity? How will the site team ensure give-and-take between the research staff and the community?
  - *Visual Aids, Props, etc.:* Could the meeting be enhanced by the use of pictures, diagrams, videos, props (e.g., sample rings), or other creative aids?

- **Meetings, forums, or round table discussions with stakeholders, gatekeepers, media representatives, and/or religious leaders**
  In addition to conversations with the general community, conversations with higher-level leaders who may be particularly influential in the community can be held through meetings, forums, and round tables.

- **Male engagement**
  During the pre-trial stage, you have the opportunity to lay a foundation for men to support women who choose to join the trial and use the vaginal ring (see Case Study 7). This will require a more targeted outreach than the general community meetings, because you want to reach men who regularly interact — as partners, siblings, parents, and friends — with the women your site will be recruiting for the trial. Male engagement needs to be done thoughtfully and with sufficient time for men to talk through the many questions and concerns they are likely to have, and if necessary to work with the research team to find ways to resolve or alleviate persistent concerns. The activities used to engage men need to be appropriate for the local context, and they need to be delivered by staff that men will be comfortable with. You may want to partner

TIP

Don't feel constrained just because something is called a meeting — be creative and think outside the box! A "meeting" could actually be a community theater performance about clinical research. It could be a staff-moderated debate where community members have a chance to argue the pros and cons of trial participation. Think about ways to get the meeting audience out of their roles as passive recipient of information an into the role of active participant.

CASE STUDY 7

MALE ENGAGEMENT IN FEM-PREP

Extensive community engagement activities involving men were conducted as part of the FEM-PrEP oral PrEP clinical trial. At the site in Bondo, Kenya, it was recognized early on — during the pre-trial formative research phase and then continuing throughout the trial — that limited partner support could impede participants' willingness to adhere to the study pill and/or attend their clinic visits. During the trial, some men expressed concern about not having been informed at the beginning about their partner's participation in the trial, while others voiced suspicions of infidelity related to trial participation. The Bondo team built relationships with the men in the community and conducted extensive outreach focusing on men, with activities ranging from holding meetings with men in the community in general, to responding to specific participants' requests for research staff to meet with their partners. This resulted in more positive feedback from men and from participants regarding their partners' views of their trial participation. However, while important, support from men was shown to be only one piece of the complex adherence puzzle. Ultimately, FEM-PrEP was unable to demonstrate effectiveness of the study pill due to low adherence. During follow-up interviews with trial participants to learn the reasons for low adherence, numerous participants described having been discouraged from taking the study pill by their sexual partners (and also from members of their community and other participants), although the main reasons described were concerns about taking an investigational drug and the potential side effects of the drug.

- Natasha Mack and Amy Corneli, on behalf of the FEM-PrEP social, behavioral, and community team

FEM-PrEP was a Phase III safety and effectiveness study of the antiretroviral drug Truvada among women at high risk of HIV exposure in Kenya, South Africa, and Tanzania. Despite targeted counseling and other adherence-support measures for participants, Truvada use was low and Fem-PrEP was unable to demonstrate whether Truvada was able to reduce the risk of HIV infection.

with community gatekeepers in developing and delivering male engagement activities. Just be certain that the gatekeepers understand and are respected by the particular men you are trying to reach. Carefully consider how religion, politics, social status, and cultural affiliations may come into play, especially if you will be recruiting a diverse group of participants.

- **Potential participant engagement**

  During the pre-trial stage, it is important to think about whom the potential participants in your trial are and how to engage them in conversations about the study and in preparatory trial activities. The study protocol will define the basic eligibility criteria for your participants, but your study site may want to target other participant characteristics for inclusion as well. Think about what might make a participant a good fit for the study and study product and what

recruitment locations and methods might be appropriate. Once you have given this some thought, you can use your conclusions to target your outreach efforts. The more you engage potential participants, the more you can learn about what facilitators of and barriers to ring adherence might exist in their lives.

- **Media and social media campaigns**

  Media campaigns can be useful when the study site wants to provide standard information to a large group of people all at once. Because media messages go out to a wide audience, the information communicated must be accurate; if someone other than a staff member will be developing the media message(s), it will be essential to establish a strong relationship with this person. Some examples of ways to utilize media include:

  - Newspaper or magazine articles.
  - Advertisements for the study site and/or clinical trial in various media outlets (e.g., print, television, radio).
  - Radio appearances.
  - Establishing a website and/or utilizing social media.

TIP

Be wary of falling into the trap of thinking that media can only be used to provide information *from* the research site *to* the community. Think of ways you can also use media to *exchange* information with the community. For instance, ask if a radio spot can include a call-in session or have a way for visitors to submit comments and questions to a study website.

- **Clinic tours and meet and greets with clinic staff**

  Inviting members of the community to tour the clinic and chat with research staff could be an effective way to remove some of the mystery surrounding the study clinic and what goes on there. Community members can see the site firsthand and talk to study staff about what happens there, rather than speculate about these things. Inviting community members into the research clinic may also help establish it as part of the community and prevent some of the "us versus them" mentality that generates mistrust and can undermine adherence.

TRIAL STAGE — SCREENING AND ENROLLMENT

When entering the trial stage, the first step should be to use the PDCA cycle to determine which strategies from the pre-trial stage you should continue, tweak, or discontinue during the trial stage. Once this is complete, the next step is to think about new strategies to implement that are specific to the trial stage, like the ones outlined below. Strategies for encouraging and supporting adherence during the trial stage are split into two sections based on when they may be most relevant — during screening and enrollment or during study follow-up.

Strategies during screening and enrollment that support vaginal ring adherence involve enrolling participants who are likely to adhere, providing targeted counseling for participants who screen out of the study, and making sure that enrolled participants have the knowledge they need to feel confident to try the study product (including skills building, by allowing participants to practice inserting and removing the ring). Make sure that you anticipate potential problems that the participant may encounter and consider if/how the participant's provision(s) (i.e., her reasons for participation, beliefs about the trial and study product, agency, shared vision) may be affected by the actions you take as well (see Table 1).

Fidelity Entry Points

- **Mystery participants and debriefs**

  Similar to a standard participant (see pre-trial pathways list), a mystery participant is someone very similar to a trial participant who is trained to go through trial procedures and observe how the staff treat and respond to her. However, in the mystery participant approach, the counselors do not know when the person being counseled is not a "real" trial participant. The mystery participant reports back on how well staff adhered to procedures and counseling approaches.

  Mystery participants may be especially useful during enrollment and early follow-up of HIV prevention trials, to monitor the initial adherence-counseling sessions, identify potential problems early in the trial, and adjust procedures as needed. Because using mystery participants involves an aspect of secrecy, it may be important to gauge the acceptability of this approach with study staff members at your site. Although the timing and identity of the mystery participant(s) should remain unknown, it is acceptable for staff to know in general that the mystery participant strategy is one that the study will use.

  The benefit of using mystery participants is that they will experience what real participants experience during screening and enrollment. They can help identify places where research staff may not be aware of a problem. For example, a counselor might think she is appropriately asking participants if they understand what to do if the ring is expelled when she says, "Now if that is all clear to you we can move on. OK?" But the participants may interpret this to mean,

"OK, I'm done explaining all that, so we can move on," and the "OK" is confirmation to move on (not confirmation that there are no questions). Identifying these kinds of nuances requires direct observation. Mystery participants may also be informative about what goes on in the waiting area during the usually lengthy enrollment process, whether staff are maintaining confidentiality in a busy clinic setting (e.g., if they realize they can be overheard from certain locations where participants may be present but not seen), and whether the information provided to participants is consistent and clear.

Another variant of the mystery participant strategy is to identify one or two participants per month who are willing to collect information during their visit and provide their recommendations to the clinic. Each month, new individuals could comment on time efficiencies and inefficiencies, the degree to which the visit was experienced as participant-centered, and other concerns and recommendations. This may increase the sense of involvement and engagement among participants and lead to identification of areas for improvement.

Shared Learning Entry Points

- **Psychometric screening**

  When a potential participant is first screened, it may be useful to assess how well clinical trial participation fits with their personal motivations, understanding, and capabilities. For example, women who believe they will get *personal and health benefits* from participating in the trial are more likely to be motivated to aattend visits and use the product than women who are primarily motivated by the money but see few other benefits from participation. Similarly, women who feel able to ***disclose*** trial participation to their partner, who trust trial researchers, and feel sure that the product is safe are more likely to be adherent than those who distrust the clinical trial enterprise or worry about the safety of the trial product. Finally, some individuals are just more committed overall to attending appointments and following doctor's advice than others.

PSYCHOMETRIC SCREENING TOOL

We have developed and validated a tool that can be used at screening to identify – in advance – these aspects of the potential participant's personality or her attitudes and motivations towards trial participation. Trial staff can use the tool to address issues concerning trust, partner disclosure, or other life circumstances that appear *incompatible* with good adherence. Sections of this tool could also be administered over the course of trial participation to determine whether motivations, understanding, or capabilities have shifted. A second tool has been developed to identify potential barriers to vaginal ring adherence during the trial. These tools will be made available as an appendix to the electronic version of this manual at a later date.

RESOURCE

Psychometric Screening Tool

Please check the fhi360.org website for a link to this tool.

- **Counseling for participants who screen out**

  Participants who enroll in the trial interact with the study and their community and can act as a conduit of information and influence between the two. The education and counseling that happens with participants at the study clinic helps ensure that information being passed by the participant to the community about the study is accurate. Additionally, it is possible that those who have screened out may pass along information about the screening process that would make it possible for others to give the "correct" answers regarding eligibility criteria they do not meet and regarding motivations for participation.

  It is important to remember that participants who screen out of the study also return to their communities to have conversations about the research, and that these conversations often center on why the participant did not enroll. Equipping participants with language to use when talking about why they did not join the study can help prevent the creation of rumors and the spreading of misinformation. Some participants may not feel comfortable divulging the true reason they did not enroll (e.g., testing HIV-positive). In this case, a counselor could help a participant think about what aspects of the study would have been challenging if she had been eligible (e.g., trial duration, length of individual visits, tests or other clinical procedures). The participant could select a reason she can elaborate on, and that resonates with her, when asked why she didn't enroll. In this way, the participant is armed with a response to provide to the community that she is comfortable with and that does not spread misinformation about the study.

Participants who screen out of the study will talk to people in their communities about the research. Counseling them on how to talk about why they did not join the study can help prevent rumors and misinformation.

- **Optimizing study and trial literacy**

  Ensuring that women have a solid understanding of the product and procedures is essential, but making sure that people actually believe the information they are provided is also important. One way to achieve this is by holding facilitated workshops where potential, novice, and experienced users can talk together, and where the more experienced users can share their knowledge and experiences with the new users. Additional strategies and key components of research literacy are outlined in Appendix A, Supporting Adherence through Research Literacy. Given the central role that enhancing research literacy has in the trial and for research more generally, and given the need to educate participants in a manner that encourages trust in the accuracy of the information shared, Appendix A has been formatted in such a way that study teams could use it as a separate "supplement" to the current document, as a stand-alone tool. Teams

RESOURCE

Appendix A: Supporting Adherence through Research Literacy (in this manual)

can use and revise this tool to operationalize their approach to this critical component of study participation. The tool includes suggested strategies to foster high levels of literacy and critical thinking around trial participation.

TRIAL STAGE — FOLLOW-UP

In the follow-up portion of the trial stage, emphasis should be on preventing product discontinuation and on finding strategies to help participants maintain high adherence for the duration of their study participation. Continue to use the PDCA cycle to improve on strategies you have already implemented. Develop new strategies as needed. Revisit the strategies outlined above for the pre-trial stage and for screening and enrollment. Even if you chose not to implement a strategy during those times, you may find one useful now. The PDCA Example 2 in subsection B2 gives one example of how a team used a strategy we introduced for the pre-trial stage — clinic tours — to address a challenge they encountered during study follow-up.

During the trial stage, continue to use the PDCA cycle to improve on strategies you already began implementing pre-trial. Also revisit the pre-trial strategies you did not implement, as you may find some of them useful now.

Fidelity Entry Points

- **Formal and informal supervision**

  In addition to benefitting from observations, study staff members may benefit from regular **"case conferences"** in which a counselor presents a specific case and the counseling team provides insights and feedback on the case. These can take place every other week, or as needed; they tend to be particularly helpful as staff members implement a new approach. This allows for supervisors and fellow staff to help adapt and refine the counseling approach.

- **Staff debrief meetings**

  Debrief meetings provide staff members a chance to meet with supervisors to talk about their experiences implementing adherence-counseling protocols and other adherence-related study procedures, to report on any challenges they encountered, and to share solutions for addressing challenges. Notes from the debrief meetings can be monitored or reviewed to see if study staff are following procedures and how problems are being addressed.

- **Checklists for assessing counseling**

  Checklists are often used to assess fidelity to protocols and procedures. In this approach, a checklist of the key messages and techniques to be used

during adherence counseling would be provided. Although lists can be helpful, particularly at the beginning of the trial as counselors are learning new skills, we DO NOT recommend using checklists in counseling sessions. Rather, the counselor can use the checklist after a session to track areas covered and left unaddressed. Checklists tend to distract from the conversation and reduce the counselor's ability to be genuine with or responsive to a participant. The checklists can be monitored or reviewed to identify areas that may have seemed important to include during preparation for the trial, but turn out to be seldom discussed. They should be used to highlight areas of the counseling session that could be improved or topics that may be helpful to discuss during conversations with participants.

- **Observation of randomly selected counseling sessions or other adherence-related study procedures**

  In this strategy, a supervisor or trained monitor randomly selects counseling sessions or other adherence-related study procedures to observe, in order to assess overall fidelity to the counseling approach and to provide feedback and support to staff (see Case Study 8). The supervisor or monitor would be physically present in the room, which has the potential to affect how the staff member performs; however, randomly selecting procedures for observation will help lessen the chance that the counselor or other staff member has specially prepared for the assessment. Trial participants would need to give permission to be observed. Less intrusive alternatives include audio-taping or videotaping (if deemed acceptable by participants and site staff).

- **Motivational interviewing with counselors/other staff to improve adherence support**

  Motivational Interviewing is a conversational counseling approach used to strengthen a person's motivation and commitment to change. As this manual also promotes, it is often used as an adherence-counseling approach with participants in HIV prevention trials. But motivational interviewing could be used to motivate adherence counselors and other study staff to improve their skills as counselors and providers of participant-centered care. For example, a supervisor or mentor could use motivational interviewing techniques by asking staff, "What kinds of barriers make it hard for you to deliver the best adherence-support counseling to participants in this trial? How could you do it better?" Staff members then write their own prescriptions about how to improve the counseling they provide to participants.

ASSESSING FIDELITY TO ADHERENCE COUNSELING IN MTN-017

OVERVIEW

Adherence-counseling sessions in MTN-017 followed a standardized manual that provided an outline of each session's tasks as well as examples of how each task was to be conducted. All adherence-counseling sessions were audio-recorded and uploaded onto a secure server. To prevent substantial divergence from the counseling manual, fidelity ratings were conducted throughout the study.

ASSESSING FIDELITY

Fidelity to the counseling intervention was assessed across two components: 1) how well each session task was completed and 2) client centeredness of the participant-counselor interaction. Each session task was rated on a scale from 0 (poor/not done) to 7 (excellent) based on how well it was completed. The client-centeredness component consisted of five sub-components, each of which was rated on a scale ranging from 0 (low) to 5 (high). Fidelity to the session was met if the mean rating for the session tasks was 5 or higher and the mean rating for client centeredness was 4 or higher.

Following initial training, each counselor had to conduct two mock sessions with a peer, at least one of which had to meet fidelity criteria in order for the counselor to begin seeing study participants. If neither session met criteria, feedback and coaching were provided, and the counselor had to submit mock sessions until one session met fidelity criteria. Once in the study, each counselor's sessions were reviewed as follows: each of the first 10 sessions, then one of every five sessions, then one of every 10 sessions.

USE OF RECORDINGS FOR COACHING COUNSELORS

After being reviewed, sessions in which a counselor did particularly well, overcame challenges, or really struggled were selected for review during monthly group coaching sessions held via Skype or telephone. Audio recordings of sessions were played and stopped periodically to discuss what was going well with the sessions and, if necessary, ways of overcoming challenges encountered.

REACTIONS & LESSONS LEARNED

Concerns about recording sessions were unrealized, as approval was granted from all institutional review boards involved in the study and none of the participants refused to be audio-recorded. Some counselors initially expressed some apprehension about being audio-recorded. However, this diminished after experiencing that the coaching sessions were conducted in a supportive manner. As the study progressed, some counselors specifically asked that their "bad" sessions be reviewed during the coaching calls in order to get feedback and improve their skills. In general, counselors appreciated the use of the recordings as a learning tool.

This trial was not designed to assess the impact of this counseling intervention on adherence to product use, but close fidelity monitoring did allow us to verify that in the great majority of cases, counselors worked with participants to help them maintain or improve their adherence. Some counselors did struggle with conducting the counseling as intended, though; fidelity monitoring clearly demonstrated drift in the counselors' ability to deliver the intervention consistently, with only about half of the counselors being able to deliver the intervention consistently throughout the study. Additionally, there were a few counselors whose sessions consistently failed to meet fidelity criteria. By monitoring fidelity, we could identify when drifting was occurring so that it could be quickly addressed.

Two specific recommendations emerge in regards to fidelity monitoring:

1. To better assess consistency across sessions, require more "passing" sessions before beginning to see study participants.
2. Establish a priori decisions on what to do with counselors who consistently fail to meet fidelity criteria.

- Ivan C. Balan, PhD, on behalf of the MTN-017 team

MTN-017 was a Phase II open label crossover study of daily oral Truvada and tenofovir 1% gel used rectally either daily or before and after receptive anal intercourse (or at least twice weekly, if no receptive anal intercourse occurred). The study enrolled HIV-uninfected males and transgender females who were 18 or older in the United States, Puerto Rico, Peru, and Thailand. Adherence was lowest during the daily gel regimen and similar for the other two product regimens. Rectal application of the tenofovir gel was safe for both men and transgender females.

RESOURCE

Appendix C: Counselor Self-Assessment Tool (in this manual)

Appendix B: Follow-up Adherence Counseling — Collaborative Discussions to Promote Product Uptake and Use (in this manual)

- **Self-assessment tools**

  Several studies have developed self-assessment tools that counselors can use to refine their skills and reiterate key aspects of counseling discussions. An example of a self-assessment tool is included in Appendix C.

Shared Learning Entry Points

- **Partner engagement**

  Research has shown that male partners play a critical role in many women's willingness and ability to use "female-initiated" HIV prevention products. As a result, many researchers have called for increased strategies for involving partners in trials for these products (e.g., couples counseling), along with evaluation of these strategies.[3] One study showed that male partner support stemmed from the men's understanding of the purpose of the study, the biological properties of the product, and the biological effects of the product, as well as from being agreeable to women's participation in the study and use of the product.[4] Thus, it may be beneficial for the content of partner engagement strategies to focus on these areas.

  Engaging men shows them that the study team recognizes and respects their role within the community and within their relationship with their enrolled partner. However, not all women elect to disclose to their partners, at least not right away. Some research has suggested that women in less stable, non-cohabitating partnerships with men may be less likely to disclose product use to their partners.[5] On the other hand, women who do wish to disclose need to be supported in that decision, such as by counseling to help them decide whether to disclose to partners and, if so, how.[6]

3. Montgomery ET, van der Straten A, Chidanyika A, Chipato T, Jaffar S, Padian N. The importance of male partner involvement for women's acceptability and adherence to female-initiated HIV prevention methods in Zimbabwe. AIDS Behav. 2011;15(5): 959-69.
4. Montgomery ET1, van der Straten A, Stadler J, Hartmann M, Magazi B, Mathebula F, Laborde N, Soto-Torres L. Male partner influence on women's HIV prevention trial participation and use of pre-exposure prophylaxis: the importance of "understanding." AIDS Behav. 2015;19(5):784-93.
5. Mngadi KT, Maarschalk S, Grobler AC, Mansoor LE, Frohlich JA, Madlala B, et al. Disclosure of microbicide gel use to sexual partners: influence on adherence in the CAPRISA 004 trial. AIDS Behav.2014;18(5): 849-54.
6. Lanham L,Wilcher R, Montgomery ET, Pool R, Schuler S , Lenzi R, et al. Engaging male partners in women's microbicide use: evidence from clinical trials and implications for future research and microbicide introduction J Int AIDS Soc. 2014; 17(3 Suppl 2): 19159.

Taking these points into consideration, partner engagement activities should be designed not to force women to disclose to partners if they do not wish to do so, but rather to help partners who have been informed about the study, the study product, and what it means for women to use the product. Keep in mind that the goal of partner engagement is not to obtain the partners' permission for women to participate in the trial and use the product, but to gain their support for women who decide to do so. This will require open dialog about situations in which a woman might choose not to disclose participation or product use to her partner. Finally, it is important to recognize that sometimes a partner may not have a woman's best interest at heart or that a woman in a new relationship may need to negotiate her way to disclosure and support over several months.

The goal of partner engagement is not to obtain the partners' permission for women to participate in the trial and use the product, but to gain their support for women who choose to do so.

- **Participant quality improvement and quality improvement teams**

  Participants can be engaged in the quality improvement evaluation directly. Individual participants or groups of participants can be approached and asked to provide specific feedback about their experiences with counselors and other team members regarding their use of the vaginal ring for a given visit or set of visits. Their feedback can be collected and used in the "Check" process to identify areas in need of modification or strengths to carry forward. Where possible, allowing for anonymous feedback or feedback to a study team member who does not interact with participants during study visits is ideal. Performance based on participant evaluators can be shared with other participants, as can steps toward correction. The idea is to not only engage participants in the quality improvement process but also overtly and clearly identify how their input has led to concrete changes.

- **Participatory study team meetings**

  Creating opportunities for staff to work collaboratively on specific cases or issues can build team morale and refine the team's skills in working together seamlessly. For study teams adopting a mystery participant process or engaging participants in a formal quality improvement review, full team meetings where feedback is provided from these data sources and where strengths and gaps are identified can lead to innovative approaches. These approaches should not be punitive or focused on a single individual. Rather, they should be creative and allow for cross-disciplinary discussion and bridging of gaps (see

Creating opportunities for staff to work collaboratively on specific cases or issues can build team morale and refine the team's skills working together.

Case Study 9). Engaging each team (i.e., clinical, recruitment, scheduling, nursing, pharmacy, counseling) to present a challenging case in a case-conference format can also help to solidify teams. Resources allocated toward building collaborative teams are not only recommended but also tend to be well worth the commitment, as participants experience the study through the team.

- **Adherence clubs**

  Adherence clubs are meetings for participants that typically take place outside of their regularly scheduled study visits. It is important for clubs to be facilitated by a member of the study team, but also for them to provide a more casual environment in which to share experiences with the study and, more specifically, with the vaginal ring. Adherence clubs should be flexible and responsive to specific participant needs and interests at various points throughout the trial. Clubs should incorporate other activities (e.g., team-building activities) and topics (e.g., HIV experiences in the community) to keep the clubs interesting and relevant to participants' lives both within and outside of the study. Some sites may choose to recognize milestones (e.g., completing a certain number of follow-up visits) during these meetings. When establishing an adherence club at your site, the following questions should be considered:

ADHERENCE AND RETENTION WORKSHOP FOR RESEARCH CENTER RECRUITERS, COMMUNITY LIAISON OFFICERS, AND COUNSELORS IN IPM 027/THE RING STUDY

IPM approached an external contractor to facilitate a one-day learning experience for research center recruiters, community liaison officers, and counselors. The overall purpose of the workshop was to unpack the challenges experienced with the retention and adherence approach. Both retention and adherence were core to the success of The Ring Study, and as such needed to be unpacked and tested for alignment to drive the appropriate behaviors associated with them. The workshop provided an interactive platform for open and frank conversation around these issues, with an opportunity for each research center to identify specific actions and solutions.

The workshop participants had a range of educational skills, and therefore an environment needed to be provided where everyone could equally participate. From previous educational interventions, a more interactive/"ask" facilitated style, rather than the usual "tell" approach, was required.

The process used to gather the information was Participlan™ — a visual mapping tool that encourages participation from all attendees. Key aspects to be addressed were the following:

- How are retention and adherence defined?
- What outcomes were desired for these two areas?
- What was working and what not?
- What do ideal adherence and retention look like?
- What changes and messaging did the study team want?
- Which tools could be used for the above-mentioned purposes?

Important questions that were asked to guide the conversations:

- When you think of adherence and retention, what attitudes and feelings does it invoke within you?
- What lessons have you learned about adherence and retention that you can share?
- Based on current operations, in terms of adherence and retention, what is working well and what is not?

At the end of a brainstorming session, different themes were summarized, and the following broad definition of adherence and retention was presented by the facilitator: "Adherence is about the daily correct use of the ring, according to the provided guidelines distributed with the appropriate level of support from counselors, motivation of participants, level of customer care, compassion, communication, and the committed documented monitoring to ensure retention of participants for a successful study."

Three of the main challenges with regards to adherence and retention were identified and ranked from greatest to least:

1. Relocation of participants for work or change of school.
2. Fatigue of participants and staff.
3. Scheduling and work load — booking lots of participants per day.

The workshop attendees identified solutions for these and other challenges. The workshop ended with great excitement and enthusiasm, and with a commitment from each research center that it would apply its energy and ability to ensure that the center-specific action plans arrived at during the workshop would be implemented.

-IPM 027/The Ring Study team

IPM 027/The Ring Study is a Phase III safety and effectiveness trial of a vaginal ring containing the antiretroviral drug dapivirine. The study enrolled HIV-negative women ages 18 to 45 at six clinical research sites in Uganda and South Africa. Data collected through October 16, 2015, showed that the dapivirine ring reduced the risk of HIV infection by 31 percent overall.

- How often should the clubs occur?
- How many participants should attend each event?
- Who should facilitate the club?
- Which participants should be invited to each event (e.g., a mix of high and low adherers, new and more experienced participants)?
- What topics and activities should be incorporated into each event?

Although many of the topics addressed in adherence clubs are the same as those discussed in individual adherence-counseling sessions, different information and themes may emerge from peer-to-peer sharing than from staff-participant interactions. Additionally, adherence clubs create opportunities to nurture a shared vision about the trial and a sense of belonging to a group that is working toward a common goal.

- **Biomarker feedback**

  Depending on the study product and trial design, it may be possible to provide periodic feedback to participants on biomarkers of adherence, such as drug levels in the blood. This may need to be at a site level to protect blinding, and to also reinforce the idea that individual actions influence how well the team as a whole does. Biomarkers can be useful because they provide an objective, respondent-independent measure of product use. Tracking biomarkers over time may allow you to demonstrate declines or improvements in study-product adherence that can be incorporated into direct conversations with participants and/or used in the Check step of a PDCA cycle to evaluate the effectiveness of other adherence-support activities. If you are considering using biomarker feedback as one of your adherence-support strategies, you will need to evaluate how accurate the biomarker you plan to use is and recognize that, although biomarkers are objective, these measures also have weaknesses. For instance, if you plan to measure drug levels in the blood, you may be able to tell whether a participant used her ring for the day or two before her clinic visit, but you may not be able to tell if she wore her ring consistently for the entire month as instructed.

- **Study-participant team building**

  Creating opportunities for study team members and participants to exchange ideas, views, and experiences can build trust between participants and the staff team (see Case Study 10). These activities are not intended to make participants "like" team members (as liking the team is not necessarily related to trust in

STUDY-PARTICIPANT TEAM-BUILDING ACTIVITIES AT NDLOVU RESEARCH CENTER IN IPM 027/THE RING STUDY

During each participant's monthly visit to the research center, emphasis is placed on consistent product adherence. However, adherence messaging can become repetitive and tedious for participants to hear month after month. Adherence events were scheduled to enhance the monthly individual adherence counseling. Novel ideas were implemented to keep participants interested in attending the events, such as discussing other health-related topics and messaging adherence in innovative ways. It was clear that adherence events should be interactive, and they usually included question-and-answer sessions, group discussions, "girl talk" (whereby participant brought up topics related to women and the female body), and agree/disagree statement games. One of the creative activities implemented by the Ndlovu Research Centre included a craft activity in which participants created loop bracelets. The activity was linked to The Ring Study in a variety of ways, including explanations that:

- Each part of the bracelet is important, as each and every participant is important in the success of the study.
- If participants don't adhere to the pattern of the loop bracelet, it will break. Linking that to the study meant that if participants were non-adherent, the opportunity to prove whether the ring is effective was "broken."
- Community is important and people should support each other. The loop bracelets were sold to support a project within the community to drive home this message.

These fun-filled adherence events helped create a secure and comfortable environment for adherence discussions. Furthermore, it helped spread awareness of and support for the study within the community, which is critical to conducting microbicide trials.

-IPM 027/The Ring Study team

IPM 027/The Ring Study is a Phase III safety and effectiveness trial of a vaginal ring containing the antiretroviral drug dapivirine. The study enrolled HIV-negative women ages 18 to 45 at six clinical research sites in Uganda and South Africa. Data collected through October 16, 2015, showed that the dapivirine ring reduced the risk of HIV infection by 31 percent overall.

the product or study), but rather to model and help them engage in critical thinking around an issue. Examples can be "games" in which a nurse, doctor, counselor, pharmacist, lab person, data entry staff, or receptionist engages in a problem-solving activity with women in the waiting area. The following are some examples of study-participant team building activities, but we encourage teams to develop their own strategies during a PDCA cycle aimed at enhancing participant-study team relationships:

Creating opportunities for study team members and participants to exchange ideas, views, and experiences can build trust between participants and the staff team.

TIP

Where possible, ask participants to share games that they are familiar with in a suggestion box/sheet and use or modify these for use.

Debates: Two participants or participant groups in the waiting area can be asked to debate a relevant topic, such as a known negative belief in the community (e.g., the ring gives you HIV). Each of the two teams represents one side (viewpoints should be assigned, not chosen), and the others in the waiting area distribute points to each side depending on whom they think has the most convincing arguments. The staff can either join sides or moderate the discussion. Be sure to close the activity with resources people can use to get accurate information and to continue discussions in their communities once they leave the study clinic.

Decision Making: It can be very useful to have activities focused on decision making around topics not necessarily overtly linked to the study. These activities can highlight steps in decision making and how people know when to check and revise their beliefs and decisions. Staff sharing their own experiences with some decision can build trust and highlight that decisions change over time. This can also show that being skeptical and exploring are key parts to making a good decision.

- **Sharing of study progress**

  As detailed in , sharing formal progress markers with participants is recommended. This could include detailing the study's progress toward completing enrollment, where the enrolled participants are in terms of nearing study completion, data on retention, data on drug levels/exposure among the enrolled participants, recent challenges and changes, and any new data that would be relevant to participants. Providing an executive summary is recommended to help participants feel involved with the full study and to foster ownership, knowledge, and a collaborative spirit.

- **Technologies**

  Where possible, cell phones can be programmed to remind participants about appointments or even about occasionally checking the ring position, which can help participants remain aware of the ring without overwhelming them. Texting content that does not include HIV, the study name, or the site name, but rather a simple check-in from the site that could be replied to with a request for follow-up may be helpful. Research on adherence to antiretroviral therapy for

HIV has found weekly text-delivered outreach (e.g., Doing OK?) to promote adherence. For ring use in a study, the text could be explained to be a check-in on any side effects, social harms, or concerns, or for any other reason. This may promote engagement and create a research approach that is highly responsive to the needs of participants in near-real time.

Research on adherence to antiretroviral therapy for HIV has found that simple weekly text messages (e.g., Doing OK?) help promote adherence.

POST-TRIAL STAGE

Shared Learning Entry Points

As you review the ideas below, remember that although the strategies implemented during the post-trial stage may seem somewhat removed from study-product adherence, the actions of a study team during this time can actually have substantial implications for product adherence during future clinical trials and for post-trial product use, should the vaginal ring become available on the open market. Maintaining alignment among the study, participants, and the community by fulfilling the study's obligation to disseminate and explain trial results is an expression of reciprocity. It also offers opportunities for the study staff to listen to the groups and incorporate their feedback into future studies or service delivery.

Fulfilling the study's obligation to disseminate and explain trial results is an expression of reciprocity and creates opportunities for the study staff to hear and incorporate feedback into future work.

- **Dissemination of trial results**

  By the time a study closes, the communications planning should be well under way and a detailed strategy should be in place to ensure that study results, when available, are communicated to the appropriate parties. Think carefully about who needs to be informed of study results, how you will communicate to each audience, and what methods you will use to solicit reactions and feedback on the outcome of the trial. The list of stakeholders will probably be very long by the time your study is over! At the very least, results should be provided to staff members, study participants, community advisory boards, key community stakeholders, ethics committees, media representatives, government officials (including ministries of health), and the scientific community (through conference presentations and journal articles). The method for providing results, as well as the timing, will vary depending on who is being targeted. Research participants, for instance, should receive the results in person, but there may be others for whom a written summary of results would be sufficient. In addition to providing results to participants and key stakeholders in the community, think about participatory ways to involve them in the actual sharing of study results.

CASE STUDY 11

YOUTH ADHERENCE SUPPORT STRATEGIES IN MTN-023

At our site, we were impressed by the commitment the young women in our cohort demonstrated both to the study protocol and to the use of the dapivirine ring itself. We had a diverse cohort of young women from different backgrounds and with varying levels of knowledge about their anatomy, sexual health, and HIV. Something each of the young women shared was the desire to be able to speak openly with study clinicians and to be treated with respect and autonomy when discussing their sexual health.

Instilling a feeling of empowerment was key to adherence for each of our participants, regardless of their individual backgrounds. We understood that if this new prevention strategy was going to be successful, the young women at our site would need to feel ownership of the ring instead of feeling like the ring belonged to us (study staff). Young women who were nervous to put it in for the first time were still encouraged to hold it and bend it, and were taught where the ring was placed inside their bodies and why its location was so important.

After three months of participating, one young woman reported being sexually active with two young men. She carefully explained to study staff why she had made the decision to talk extensively with one partner about her study participation and the ring, while never mentioning any of it to her second partner. It was clear that she had taken complete ownership of the ring and didn't feel obligated to share information with anyone unless she had made the decision to do so. She emphasized that if her partner felt the ring, she was equipped to explain what it was but that unless that happened, she was going to keep her use of the ring to herself. This participant was empowered and excited about this potentially groundbreaking new prevention technique. As a result of participation, she had for the first time become the sole decision maker of her own body and sexual health.

- Julian Dormitzer, RN, BSN, MTN-023 project manager at The Fenway Institute

MTN-023 is a Phase IIa study of the safety and acceptability of the dapivirine vaginal ring among adolescents 15 to 17 years old in the United States. At the time of publication of this manual, MTN-023 follow-up was ongoing.

- **Participation in advocacy groups**
  Although many people (e.g., staff, community members, participants) participate in or support research in the hope of one day making an effective vaginal ring available in their community, the reality is that some trials may not find a successful product, and even if they do, the ring may not be available for a very long time in the settings where it was researched. This can be incredibly frustrating, even heartbreaking, for those who have contributed to the research. It can also erode the trust in and support of the study team that was built

PATHWAYS TO HIGH ADHERENCE FOR YOUNG WOMEN

Young women are at the highest risk for HIV infection in several regions around the world. We still have a lot to learn about ring use in young women, and the evidence base for adherence support in youth in general is sparse. However, because of the high incidence of HIV infection among young women, they are clearly an important population to include in prevention trials. When it comes to HIV prevention technologies, the vaginal ring may be more ideal for young women than a method that requires daily or coitally-dependent dosing, since neurocognitive development is not as advanced in younger women, who tend to have less impulse control, prospective planning, and regulation of thought and emotions. Young women may struggle more with using the vaginal ring than older women and have a host of unique challenges that should be considered when mapping their journey through a clinical trial. When compared with older women, young women may have fewer resources at their disposal, less autonomy, and different and more variable daily or seasonal schedules. Young women may also have different motivations for joining a clinical trial, different things or people that influence them, and different ways of communicating. Young women may still be learning about their bodies and may have less stable sexual relationships, making inserting the vaginal ring or keeping the ring in during menses or sex more difficult. It is important to remain open to and aware of the unique experiences of young women. In addition to developing pathways based on consultations with targeted participant community members, it may be important to:

- Make the clinic space more youth-friendly.
- Allow for flexibility when scheduling appointments and offer additional support getting to the clinic (e.g., provide transportation).
- Spend extra time on familiarizing a young participant with her anatomy.
- Assist young women in gaining comfort in inserting the ring.
- Emphasize that all questions are smart questions and that study staff are eager to answer them.
- Encourage young women to insert the ring themselves at their second or third clinic visit, if they had asked a clinician to do it the first time.
- Use study staff to role play a conversation with sexual partners about ring use.
- Offer clear instructions for what to do if experiencing discomfort or re-inserting the ring if expelled.
- Clearly depict the ring and its safety during menses.
- Help develop strategies for retaining the ring during sex and/or if partner feels the ring.
- Offer added support for reminders for study visits.
- Leverage technologies commonly used (e.g., cell phone apps, texting).
- Identify peer mentors and leverage peer-to-peer support for young women.

RESOURCE

Communications Handbook for Clinical Trials: Strategies, Tips, and Tools to Manage Controversy, Convey Your Message, and Disseminate Results
https://www.fhi360.org/resource/communications-handbook-clinical-trials-strategies-tips-and-tools-manage-controversy-convey

AVAC
http://www.avac.org/

among the participants and community during trial implementation, which is essential to ensure the success of any future studies at the same research site. To address these issues, consider establishing or contributing to existing advocacy groups (like AVAC) that can offer motivated parties information and strategies to influence important decision makers and policy experts at the local, national, and international levels.

PATHWAYS TO HIGH ADHERENCE

Glossary and Key References

GLOSSARY

Adherence: The degree to which a person takes or uses a drug or product as instructed

Adherence support strategies: Activities with participants, in the community, and with study staff aimed at supporting participants to take pathways leading to high adherence

Alignment: How well a participant's beliefs about the study product and study match up, or align, with the beliefs of researchers/the study and people in her community

Autonomy: An ethical principle referring to the degree to which a person has the ability to make her own decisions

Community: In the context of a clinical trial, the multiple groups and entities in varying proximities to the participant's life, including her partner, family, and friends; includes the historical and current social and political environment, local gender norms, economic (in)stability, and community members whose opinions and actions matter to and affect the participant

Entry points: The strategies serving as ways to access the pathways participants, community members, and staff might take that lead toward high adherence

Fidelity: Staff members following trial procedures as trial planners intended them to be implemented

Futility: When adherence in a trial is so low as to make it impossible to determine if the product is effective

Mutuality: The idea that participants and the study are dependent on one another and that if both parties honor their commitments to one another, both will benefit

Mystery participant: Someone very similar to a trial participant, who is trained to go through trial procedures and observe how the staff treat and respond to her; in the mystery participant approach, the counselors would not know when the person being counseled is not a "real" trial participant; the mystery participant would report back on how well staff adhered to procedures and counseling approaches

Partial engagement: When a participant does not fully commit herself to participation in the trial (e.g., has an intention to attend the study visits to get access to health care benefits but not an intention to actually use the product)

Participant engagement: The participant's commitment to/belief in the trial; compliance with study visits; commitment to using the product; ability to talk openly with staff regarding her product use and experiences

Participant journey: The participant's path progressing through the trial from start to finish, and even extending beyond study participation post-trial, as well as her movements back and forth between the study clinic and her community

Participant-centered care: A method of care that recognizes each person as an individual and advocates training staff to help them address the specific needs of each participant

PDCA: The Plan-Do-Check-Act process for quality improvement

Provisions for the journey: A set of beliefs across five categories that the participant will take with her on the journey, namely her reasons for participation, beliefs about the trial, beliefs about the study product, agency, and shared vision, all of which affect her adherence actions and may change during the trial through the sway of the three sources of influence (i.e., participant, community, study)

Reciprocity: An exchange between the community and the research study that is mutually beneficial

Run chart: A line graph that tracks changes in an event or observation over time; time is measured along the x-axis and the event or observation being tracked is plotted along the y-axis

Sources of influence: In our framework, the three entities that have the potential to affect a participant's adherence, namely, the participant herself, the community, and the study

Staff engagement: Staff members' commitment to/belief in the trial; fidelity to study procedures; commitment to facilitating product use; commitment to open communication with participants and the community

Standard participant: Someone very similar to a trial participant, who is trained to go through the trial procedures and observe how the staff treat and respond to her; the standard participant would then debrief the staff she interacted with to give input on how well they adhered to study procedures and supported her throughout her visit; the staff know that the standard participant is not a real trial participant

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APPENDIX

A

PATHWAYS TO HIGH ADHERENCE

Supporting Adherence Through Research Literacy

WHAT YOU WILL FIND IN THIS APPENDIX

Appendix A contains guidance on conducting individual and group education and discussions to promote product use and research literacy. Study teams can help create an environment that supports full participant engagement and high adherence by providing education to community members and participants about clinical trials and by encouraging high levels of research literacy among these groups. Although improving research literacy requires that a certain amount of information be provided by study staff to participants and community members, it is important to remember that there is as much, if not more, to learn from participants and the community during educational conversations. Staff-facilitated education discussions are one step in building a supportive environment in which participants can share their ***experiences***, both with the investigational vaginal ring and with the study as a whole. Education sessions for individuals and groups that focus on core concepts used in research can create transparency and facilitate buy-in from participants and community stakeholders, both of whom are central to participant engagement in the trial. They can also help study staff understand where myths and misperceptions exist and where participants and community members may have concerns about trial conduct. High levels of research literacy will assist participants in their efforts to adhere to the study product by increasing their understanding of the study and heightening their trust in the trial when skepticism or concerns might otherwise limit women's full participation in the trial and use of the study vaginal ring.

WHO SHOULD USE IT

Community outreach workers and any staff who will lead educational discussions with participants in the clinic.

HOW TO USE IT

In the pages that follow, we outline several key educational topic areas that will help study teams increase research literacy among participants and relevant segments of their communities, and in turn support adherence. We refer to these as **core literacy areas (CLAs)**. Regardless of whether educational messages are delivered to participants or communities, individually or in groups, and within or outside of the study clinic, the CLAs described below should be a high priority early in the trial process and should also be supported throughout implementation of the study. Without high levels of research literacy, participants and communities are likely to

Core literacy areas (CLAs) are key topic areas for increasing research literacy among participants and their communities.

TIP

In communities where there is ongoing skepticism about the integrity of the study, the intentions of researchers, and/or the safety of the study vaginal ring, efforts to increase research literacy will also need to focus on building trust by increasing the transparency of study activities. For example, in addition to talking about study procedures, it may be necessary to invite community representatives to the clinic to see how and where the procedures are performed.

have high levels of distrust, uncertainty, or ambivalence about the trial, which may undermine efforts to maximize adherence.

Study teams are encouraged to use the Plan-Do-Check-Act process described earlier in this manual to determine which messages are most important for their particular population of potential participants, enrolled participants, and relevant community members. During this process, teams should also focus on identifying the methods for addressing the CLAs that are likely to be most effective at their particular research site for promoting trial engagement and ultimately supporting high adherence among participants. Creative strategies, such as those using multi-media and multiple learning channels (e.g., discussion, debate, role-playing, demonstration) are strongly encouraged. Study teams are reminded that the list of CLAs included in this manual is not comprehensive and that individual participants and different segments of the community require different types of educational support from the study clinic.

CORE LITERACY AREAS

CLA #1: Information about Clinical Research, the Study, and Study Procedures

Why is this a core literacy area for adherence?

An understanding of clinical research in general, as well as the details of a specific research study, is vital for community support and full participant engagement in the trial. If communities and participants do not understand why the research is being done, the purpose of the study procedures, what the ultimate goals are, and how adherence to the ring affects study results, their support for ring adherence and participants' motivation to adhere will be low.

What are the key educational components of this core literacy area?

- Explain what clinical research is, why it is important, and how previous research studies have informed or led to the current trial.
- Describe available HIV prevention methods, the goal of this study, and how the results might affect the community.
- Educate on the basics of the trial design and research concepts that may be difficult to understand, like randomization, placebo, and blinding.
- Summarize the key trial procedures and why each one is necessary.
- Identify what the study endpoints are and why (including information about *how* study endpoints will be achieved when HIV risk-reduction counseling and condom provision are included as study procedures).

- Outline participant rights and researchers' responsibilities, including:
  - » Duty of researchers to not harm participants, to track and treat adverse events, and to provide new information about HIV prevention if/when it becomes available.
- Encourage open conversation by reviewing/addressing the concerns and benefits identified by participant(s) and communities. It may also be important to clarify what will happen if/when participants report challenges with ring use or non-adherence (e.g., "If you have any challenges with ring use, we want to know what those are so we can work with you to overcome them. The staff will be happy with you for openly reporting your challenges, and you will not be dropped from the study just because you do not use the ring perfectly.")

What are some tools and resources to help educate about this core literacy area?

- ✓ Stakeholder Engagement Toolkit for HIV Prevention Trials. *https://www.fhi360.org/resource/stakeholder-engagement-toolkit-hiv-prevention-trials*
- ✓ Site-designed educational booklets or information sheets.
- ✓ Props to help explain research concepts (e.g., coin flip to demonstrate randomization).
- ✓ How Research Happens: AVAC resource materials. *http://www.avac.org/how-research-happens*

CLA #2: Information about the Vaginal Ring and the Drug in the Ring

Why is this a core literacy area for adherence?

Understanding the study device and study drug will help increase participants' confidence in using the investigational vaginal ring. Myths and misconceptions about using antiretroviral drugs for HIV prevention can be addressed in these educational activities. Talking about and showing the ring can make it less mysterious to women and communities who may be unfamiliar with vaginal rings or only be familiar with contraceptive rings.

What are the key educational components of this core literacy area?

- Explain what a vaginal ring is and why it was chosen as the study product.
- Define the difference between a placebo and an active ring, if applicable.
- Describe the drug that is in the device, how it works, and how it gets from the ring into the body.
- Demonstrate how to insert the ring, show where it tends to be located inside the vagina following insertion, and demonstrate that a ring inserted too low in the vagina may be more likely to be expelled.

- Discuss why it is important to wear the ring all the time and how ring adherence affects the overall goals of the study.
- Encourage conversation about benefits and drawbacks of the device and the drug.
- Address any known myths or misconceptions about the ring (e.g., it will get lost, dissolve, stretch the vagina, cause cervical cancer).
- Address questions about ring use and male partners (e.g., ring use during sex, whether male partners will feel the ring, and if the ring will harm male partners).
- Review "What to do" instructions for participants about how to handle possible scenarios they might experience when using the ring (e.g., the ring falling out).

What are some tools and resources to help educate about this core literacy area?

- ✓ Site-designed educational booklets or information sheets (e.g., see IPM 027 Ring Use Instructions in Appendix F).
- ✓ Pelvic model and sample ring.
- ✓ Diagrams, photos, videos, and/or illustrations.

CLA #3: Information about the Body

Why is this a core literacy area for adherence?

A basic understanding of human anatomy and physiology is essential for high adherence because it helps research participants understand their bodies and how the ring interacts with it. Study teams can address common myths and misconceptions about the ring's effects on the body (e.g., that the ring causes cancer or affects menses) by helping participants learn more about their own biology.

What are the key educational components of this core literacy area?

- Teach about the basic anatomy of the female body, with a focus on the sexual and reproductive organs and where a properly inserted ring sits.
- Review basic physiology of the female body, including information about menses and pregnancy.
- Provide information about possible side effects of the study drug and other common pharmaceuticals participants might use during study participation (especially contraceptives, as these often have side effects that are falsely attributed to the ring).
- Educate about infectious and non-infectious diseases, especially those that participants and/or community members fear might be associated with ring use (e.g., cervical cancer) or that cause genital symptoms (e.g., sexually transmitted infections).

- Discuss harmful vaginal practices that may be pervasive in the community and explain what effect these activities have on the body and the study and why they are discouraged.

What are some tools and resources to help educate about this core literacy area?

- ✓ Site-designed educational booklets or information sheets.
- ✓ Pelvic models, diagrams, videos.
- ✓ Examples of locally relevant products that should not be used vaginally with the ring.

CLA #4: Information about the Use of Research Data

Why is this a core literacy area for adherence?

Helping participants and communities understand the "big picture," what is involved in demonstrating efficacy, and what is involved in bringing an investigational drug to the open market increases transparency and supports adherence by allowing participants to understand how their actions influence these long-term goals. Explaining how research data get used in this process also builds trust and helps study teams emphasize the importance of open conversation about adherence and women's general study experiences.

What are the key educational components of this core literacy area?

- Explain what happens to research data after they are collected, including a discussion linking adherence data to the ability or inability to answer the research question.
- Describe the possible study outcomes and what each result means.
- Outline the process for making an effective product available to study participants and, ultimately, the community at large.

What are some tools and resources to help educate about this core literacy area?

- ✓ Communications Handbook for Clinical Trials. *https://www.fhi360.org/resource/communications-handbook-clinical-trials-strategies-tips-and-tools-manage-controversy-convey*
- ✓ Site-designed educational pamphlets and information sheets.
- ✓ Diagrams showing steps of data collection and reporting and/or drug regulatory approval process.

CLA #5: Information about the Roles of Participant, Community, and Study Teams

Why is this a core literacy area for adherence?

Study staff can build a sense of teamwork by emphasizing the unique roles that the participant, the community, and the study team each have to play in reaching a common goal — preventing HIV. By explaining how trial participation, engagement, and successful results are mutually beneficial and rely on all three groups (participants, the community, and the study team) working in harmony, study staff can help create an environment in which participants feel motivated and supported to use the study product.

What are the key educational components of this core literacy area?

- Explain the main components of staff engagement (See "What is Staff Engagement?" text box on p. 17 of this manual) and participant engagement (see "What is Participant Engagement?" text box on p. 20 of this manual).
- Emphasize the concept that participants, the community, and the study staff are partners in the research.
- Identify the responsibilities and obligations each party must fulfill in order for the trial to be a success. Discuss what happens in and after the study when obligations are met, and when they are not.
- Note processes that the study team has in place to monitor study implementation, solicit and react to feedback from participants and the community, and provide updates on study progress.

What are some tools and resources to help educate about this core literacy area?

- ✓ Stakeholder Engagement Toolkit for HIV Prevention Trials. *https://www.fhi360.org/resource/stakeholder-engagement-toolkit-hiv-prevention-trials*
- ✓ Communications Handbook for Clinical Trials. *https://www.fhi360.org/resource/communications-handbook-clinical-trials-strategies-tips-and-tools-manage-controversy-convey*
- ✓ Improve Research Conduct (AVAC resources). *http://www.avac.org/improve-research-conduct*

APPENDIX

B

PATHWAYS TO HIGH ADHERENCE

Follow-up Adherence Counseling — Collaborative Discussions to Promote Product Uptake and Use


DKNY

WHAT YOU WILL FIND IN THIS APPENDIX

Appendix B contains guidance on a collaborative approach to providing adherence counseling.

WHO SHOULD USE IT

Adherence counselors.

HOW TO USE IT

Several counseling approaches have been used in previous clinical trials to support the use of study-provided drugs. Most of these approaches emphasize participant identification of factors that either help or hinder product use, and then encourage brainstorming potential solutions to identified problems and setting adherence-related goals for the upcoming month. Because clinical trials require a certain level of standardization of procedures, the counseling approach often involves standard steps for counselors to follow with varying levels of adaptation and flexibility allowed. Some studies may require all steps or messages, while others allow counselors to tailor content as needed.

The approach presented here is a **process approach**, meaning that a general manner of discussing experiences with product use, and in the trial more generally, is recommended. Although the approach is presented as steps, counselors should focus on learning the general approach, rather than memorizing specific content or messages to deliver. We believe this will optimize opportunities for staff to engage in genuine, highly tailored, and targeted discussion with participants. We prioritize genuine discussions (specifically characterized by following participant concerns and guiding the participant toward optimized engagement) over message delivery or pre-determined content because we believe it affords greater opportunity to foster collaboration, engagement, and commitment toward trying to use the ring. It also allows counselors to remain more neutral and natural in discussions. Moreover, several emerging frameworks (such as the mutuality framework in Appendix D, as well as community-based participatory principles more generally) suggest that specific product-related messages, as well as the process of identifying and addressing adherence barriers, may be appropriate for some but not all participants

in a research trial. The process approach we advocate aims to initiate discourse with participants and engage them "where they are" with their approach to study-provided ring use.

A COUNSELING PROCESS TO DISCUSS EXPERIENCES[7]

Several adherence-support approaches have been developed and implemented in the context of adherence to pre-exposure prophylaxis, and to ring use more specifically. For the counseling aspect of discussions with participants, we recommend seven general steps to structuring discussions involving the participant and one designated team member (often a counselor) at each study visit, modeled most closely around the MTN-020/ASPIRE approach. Other approaches, however, can and should be considered given the specific needs of the study and populations engaged in it. The steps we suggest here are part of a continuous discussion with an identified trained team member as a check-in that occurs as part of the clinic visit. When possible, the discussions should occur *early in the visit, but after the collection of any self-reported adherence data*; avoid having these discussions during the last part of a participant's study visit. Teams can determine whether it is more beneficial to develop tools or procedures that would flag struggles with adherence for other team members' attention or whether these discussions should remain largely private.

7. The suggested team-initiated discussion approach draws from the ASPIRE Counseling and Education (ACE) Manual, the VOICE Adherence Strengthening Program, the iPrEx Next Step Counseling (NSC) approach, and the HPTN067/ADAPT study's mutuality framework (see Appendix D).

GOALS

To acknowledge the participant as a true partner in the research by providing important study updates and then using active-listening skills and an individualized approach, to create a comfortable environment for participants to talk about their experiences.

CLIMATE

Supportive, non-judgmental, neutral, reinforcing of open discussion/efforts, avoidance of "fixing," recognition of limited role, and emphasis on participant as a whole person.

METHOD

Exploration of context (experiences, thoughts, beliefs, feelings, skills) to identify what would need to happen or continue happening for the behavior to be most manageable or "easier."

IMPLICIT ASSUMPTION

Participants choose whether or not to do something based on feeling well informed, motivated, and skilled. We cannot make a participant adopt a behavior, but we can provide opportunities to develop information, motivation, and skills relevant to her in her life.

STEPS IN COUNSELING DISCUSSION

1 ENGAGE

Provide study update. Discuss study visit and product satisfaction. Identify ways the study can improve and contributions participants can make.

2 FRAME

Explain purpose of discussion.

3 EXPLORE

Explore participant experiences with study with attention to facilitators/challenges to engagement: 1) trust in study, 2) retention, 3) degree of continuation, and 4) adherence.

4 IDENTIFY NEEDS

Ask what would need to happen for area identified in Step 3 to improve, be less stressful, be easier, or be maintained.

6 STRATEGIZE

Explore new strategies or how maintenance of established ones can be accomplished to address needs identified

6 GOAL

Identify a strategy discussed for the team, the participant, or another active party to try/consider.

7 CLOSE THE SESSION

Review and summarize session. Remind participant of the check-in that will occur during the next visit. Thank the participant. Document session.

Engage

Provide study update. Discuss study visit and product satisfaction. Identify ways the study can improve and contributions participants can make.

GOAL

Engage participant in the study process and procedures, and in identifying successes and areas for improvement.

CRITICAL COMPONENTS

- Provide an executive summary of where the study stands (# enrolled, longest enrollment of a participant (e.g., "We have someone all the way in week 52"), community events and how well the community received those events, concerns emerging from the community and the trial's responses to them, feedback from any reviews of quality of study implementation (e.g., for studies using mystery participants, engagement of participants in quality-improvement feedback, other procedures to evaluate study implementation), any data on drug levels or other objective measures of adherence at the site, and any new data or science related to the study.
- Create a team approach in which information is shared with the participant, and the participant's response/reactions are sought.
- Enhance the participant's literacy by flagging issues or concepts that have appeared confusing to others and offer explanations of them.

Example of Engage Step

At each visit, we give an update on the study. Here is where we are now… We also wanted to let you know that the community event we had last week was well attended. People seemed most concerned with whether or not study results will matter to people in this community. The study team and community board talked about it and here is where that stands… There were also concerns about long-term effects of the medication being tested. The science team looked into this and came up with this material. Let's take a quick look. What are your thoughts on that? Any ideas you might have about what we missed or how to better work with people? One thing I worry about is how trustworthy people will find data that come from the very place they think may be lying to them. We are asking all participants to think about that more and give us suggestions for how to give people information that is trustworthy…

STEP 1

IS intended to be …

- ✓ A review of the study
- ✓ A report back to participants on what is being done in the community
- ✓ An opportunity for the participant to advise the study
- ✓ A conversation with data and milestones

IS NOT intended to be …

- × Overly long
- × Read from a sheet
- × A one-way presentation
- × Punitive
- × Boring

STEP
2

Frame

Explain purpose of discussion.

GOAL

Introduce or remind participant of the purpose of the discussion and reinforce that she is the one who decides her level of involvement in the trial and in the discussion. Clearly explain the purpose of the discussion and establish trust. Specifically ask if the participant is okay with talking with you.

CRITICAL COMPONENTS

- Specifically recognize and appreciate the participant having shown up today. Note her number of weeks of participation and the weeks remaining. Do not assume that her attendance or length of participation in the trial means that she is invested in or committed to taking the product. Allow step 1 to advise on which parts of this to emphasize (e.g., parts of the discussion about the study and study progress that seemed most interesting or contentious).
- Explain that you talk with all participants at each visit in order to learn valuable information about how the study is going; what it is like right now to participate in the study given any burdens related to the study, community, or adherence; and what the study can be doing to support participants.
- Explain the scope and limitations of confidentiality in your discussion (e.g., what will you keep private and what will you have to discuss with other team members?).
- Give the participant permission to be honest and open and get her permission to proceed.

Examples of Frame Step

Thanks for your advice. This is your first week in the study, so you have another 10 months in the study. We'll get the chance to talk a lot, and the things that are most concerning for you will probably change a lot over the course of the study, too. I would like to spend a few minutes talking with you about the ring and your experiences with the study. Is that OK?

Can we spend a few minutes talking about how things are going for you personally with being in this study? A lot of people struggle with really trusting the ring or other parts of the study, like the samples we collect. That is normal and understandable, especially when people feel side effects or hear concerning things from other people. Can we spend a few minutes today talking openly about that?

STEP 2

IS intended to be …	IS NOT intended to be …
✓ A sincere invitation	× A long explanation
✓ An opening to a frank conversation	× Read from a sheet
✓ An opportunity for the participant to exercise choice	× Non-responsive or non-participatory
✓ Genuine	

STEP
3

Explore

Explore participant experiences with study with attention to facilitators/challenges to engagement: 1) trust in study, 2) retention, 3) willingness to try and continue using product (persistence), and (4) adherence.

GOAL

Ask about factors that may influence trust; retention; willingness and commitment to try and continue using the ring (persistence); and/or adherence. Emphasize that the study product is being developed for women like her/us and that her thoughts and opinions about the ring will help researchers and the makers of the ring better understand the experiences women have using it, including any problems and issues they have with the ring.

For return visits, first check in with the participant about any goals set at the last visit and provide support for efforts made. Then transition to a focus on how the participant has experienced ring use over the past month.

CRITICAL COMPONENTS

- Ask about her greatest concerns right now: Is she feeling skeptical about the ring or things she has to do as part of the study (e.g., allow collection of blood, have regular pelvic exams), feeling confident in the study and product but struggling to use the ring as instructed, and/or feeling that the community and people

important to her need to better understand the study and its results.

- Based on the discussion, identify the focus of the remainder of the conversation. Would it be most helpful in terms of engaging this participant if you focused on 1) building trust and confidence in the study and/or ring, 2) coming regularly to study visits, 3) ring persistence (i.e., willingness to try and continue using the ring), or 4) adherence (i.e., she is committed to trying to use it, but may struggle with doing so according to instructions).

  - » You may decide some combination of these is needed.
  - » You may decide that this participant is "beyond" these topics and is more in a dynamic of **"mutuality"** where she is a champion for the study and ring in her community and among other participants. In this case, it would be preferable to engage her to discuss her advocacy and check in on how you can support her (See Appendix D).

- For whatever aspect of participation that is prioritized, ask about **facilitators**: What would help? What does help?
- Then transition to asking about **challenges**: What does not help or what makes things harder?
- The critical aspect of this conversation is to let the participant know that study staff recognize that ring use is a key part of participation but is only possible when people trust the study and the product —and, even then, that ring use can be difficult. Study staff also recognize that ring use 1) is a choice, 2) is a behavior that is influenced by many things, and 3) needs to be as easy and manageable as possible. Counselors must convey that the context of the participant's life is what is important first and foremost, and that ring use is a behavior that exists in relation to other things going on in her life.

Examples of Explore Step:

Last time you were here, you said your partner had some concerns about your ring use because he didn't know very much about the study product and was worried it would be harmful to you or to him. You were going to try to talk to him about the ring and show him some of your study materials. How did that go?… Thank you for sharing that. What would you say your overall experience with the ring was like this past month? Thinking specifically about how things have been since you tried to have that conversation, what would you say helped with using the ring recently?… What are the times, situations, or

things that have made using the ring feel more difficult or less easy to manage?

You mentioned last visit that you felt that using the ring was not challenging for you, and you wished there was a way for you to share your experiences — and some of your techniques for making ring use easy — with other participants who might be having more challenges. Can you tell me how things have been going since then and if you were able to talk with any other participants?… If you had to identify what it is that really

STEP 3

IS intended to …

- ✓ Briefly check in on goals from last visit to provide continuity
- ✓ Explore experiences
- ✓ Identify where the participant "is" in her approach to using the ring
- ✓ Begin to narrow the conversation by focusing on one or some aspects of engagement that is/are most relevant to this participant at this time

IS NOT intended to …

- × Have previous goals set the content for the current conversation
- × Find and "fix" barriers
- × Identify times when the participant removed the study ring
- × Require or suggest movement to action
- × Push beyond what the participant is comfortable sharing

STEP 4

Identify Needs

Ask what would need to happen for area identified in Step 3 to improve, be less stressful, be easier, or be maintained.

makes this easy for you, what would it be?

GOAL

Based on what was determined to be most relevant for this participant in Step 3, work with her to identify what she would need in order for this issue to improve, be easier, or be maintained.

CRITICAL COMPONENTS

- Help the participant to identify what she would need to facilitate, support, or develop high commitment, motivation, and skills for using the ring by focusing on what would make it as easy/manageable as possible for this participant.
  - » This may be things that the study can do, her community can do, her partner can do, or that she can do. Do not focus only on what she can or needs to do.
- Empower problem-solving: Emphasize that having personal needs or conditions for the ring to be feasible for her are normal and understandable. For example, in response to a participant's report of what would need to be in place for things to feel easier, the counselor may say, "That is completely understandable," or, "That sounds very reasonable," or, "Other participants have shared the same concerns". If a participant can identify **what** she needs for ring use to feel manageable and believes that this is a reasonable need, her motivation and efficacy in actual use of the ring can be enhanced. Here, we target facilitating the

feasibility of her using the ring and not specifically her ring use or non-use.

Examples of Identify Needs Step

What do you think you would need for ring use to feel just a little more manageable in your life? What would need to change or be different?

What would need to be different for you to feel more confident that the information you get here is actually true?

What would you need to keep feeling like an advocate for this study in your community?

STEP 4

IS intended to …	IS NOT intended to …
✓ Let the participant identify what she needs	× Tell the participant what her needs are
✓ Focus on needs, desires, and options before moving to concrete strategies	× Fix barriers or address needs

Examples of adherence-related needs

I would need to have my partner's support
I would need to feel that the ring was really ok to use during menses
I would need to know that it is inserted right
I would need to have my partner/family understand more about it
I would need to feel that it is not hurting or is not dangerous to my partner
I would need to feel comfortable getting it back in if it comes out
I would need to better understand why I have to leave the ring inserted, even on days when I don't have sex
I would need to be able to do this on my own, without telling anyone
I would need to be able to get to my clinic visits

Examples of counseling when ring use is reported as easy

Counselor: *What would need to happen for you to keep feeling that it's easy for you?*

Participant: *Nothing, it's already easy for me, I don't really notice it.*

Maintenance

Counselor: *Is there anything you could foresee happening in the next month that would change that for you?*

Counselor: *Other participants I meet with express some difficulty with the ring, like when they have sex or during menses. Can you share with me what has made it so manageable for you? It would be very helpful to me and others. Since you are not having challenges, perhaps we could talk about what you might need to become a participant advocate or peer educator.*

Confirm that you understand and identify strategies that are in place and the need(s) they satisfy

Counselor: *It sounds like you have talked with your partner [strategy] to get his support [need] and that has really made ring use possible for you…even easy. Is that correct?*

STEP
5

Strategize

Explore new strategies or how maintenance of established ones can be accomplished to address needs identified.

GOAL

Work with participants to have them identify possible new strategies or to continue the use of current strategies to address the needs they discussed in Step 4.

CRITICAL COMPONENTS

- Empower problem-solving: First ask the participant to identify and explore strategies that may meet the need(s) identified in Step 4. Offer suggestions as needed.
- Address unmet needs: Identify several strategies that the participant could use or already uses to address needs.
- Support met needs: If a participant has shared that she has strategies in place that have lasting benefits (e.g., enlisting partner support), strategizing will focus on her continued use of a strategy or access to support already established. In this case, counselors may simply check in to see if the participant feels confident in using an existing strategy or having access to established support through the next month.

Examples of Strategize Step

Addressing unmet needs

You mentioned that something that would make it easier is having your partner's support. How could you see that happening?

One of the things that would make it feel more manageable for you to get to visits is to feel like it would not be a waste of your whole day. Can you see any scenario for that in which it would not feel like a waste?

Supporting met needs

You mentioned that you feel this is pretty easy for you because you have your partner's support. I was wondering how you feel about having his support over the next month. Do you see any changes to it? Any concerns with maintaining that support?

You're feeling that this is easy for you because neither you nor your partner notices the ring. Over the next month, do you see any challenges to this? How are you feeling about the next month with the ring? Any concerns?

STEP 5

IS intended to …	IS NOT intended to …
✓ Encourage the participant to draw from her own resources to identify potential strategies to address her needs	× Identify new strategies if there are current ones in place that are perceived to be effective
✓ Offer several possibilities for the participant to consider as ways to address needs	× Push the participant toward "your" strategies

STEP 6

Goal

Identify a strategy discussed for the team, the participant, or another active party to try/consider.

GOAL

Create a "goal" by working with the participant to help her choose a strategy (or strategies) from the ideas generated in the previous step that she is willing to try or to continue with between now and the next time you meet.

CRITICAL COMPONENTS

- Support the selection of a goal that is achievable and realistic. It is critical that the participant feels progress and success, which may involve the selection of a "small" step.
- The goal may relate to supporting her confidence in or maintenance of things she already has in place that she believes help her with ring use (e.g., maintaining partner support or confidence in her ability to re-insert the ring as needed).
- The goal may simply be to come back to talk with you, to remain open to discussing experiences, or to just observe her experiences over the next few weeks. These are all very good goals for participants who are unsure about challenges, needs, or strategies. It is better to respect and work with a participant's uncertainty than to suggest product-use strategies that may be a poor fit with where she is. By focusing instead on her engagement in the discussion, commitment toward exploring adherence, or ownership of this aspect of her participation in the study, overall engagement is fostered.

Examples of Goal Step

Of the things we just discussed, are there one or two that you'd be willing to try between now and the next time we meet?

Would you be willing to continue with the strategies you identified [summarize her needs and current strategies] between now and the next time we meet?

Sounds like you feel really confident in being able to manage using the ring, and you don't foresee any challenges to your partner's support or comfort with the ring in the next month. Can you keep going with your current strategies until we meet again? It sounds like they have worked well in helping you to feel that this is feasible and easy for you.

Given that you're not sure what might make ring use easier for you, maybe just trying to be aware of what using the ring is like for you would be most useful right now. Is that something you'd be willing to do between now and the next time we meet?

STEP 6

IS intended to …

- ✓ Identify a concrete, realistic, accomplishable goal
- ✓ Provide participants with the opportunity to experience progress and success around experiences with product use
- ✓ Focus on strategies that increase the participant's comfort, ease, and confidence about product use

IS NOT intended to …

- × Assign tasks or strategies that are not reflective of the participant's context, needs, or engagement
- × Identify strategies related to actual use of product or to the rate of adherence

STEP 7

Close the Session

Review and summarize session. Remind participant of the check-in that will occur during the next visit. Thank the participant. Document session.

GOAL

Provide a summary of what was discussed and how it influences ring use. Express appreciation for the participant's engagement in this conversation as an important contribution to the study. After the participant leaves, document or finalize documentation of the session.

CRITICAL COMPONENTS

- Model, empower, and celebrate problem-solving around product use by providing a summary of the discussion and thanking the participant.
- A thorough summary will include brief comments on 1) the **context** surrounding the participant's use of the ring; 2) her **needs** for fitting use of the ring most easily into her life; 3) the new or current **strategies**, focused on increasing or sustaining ease of use of the ring, that were discussed; and 4) a **goal** to implement, try, or continue to use a strategy (or strategies) between now and the next visit.

- Document the session so that the next counseling visit can reflect on the strategy/strategies the participant said she would consider. This will provide continuity for the participant, even if she meets with another counselor. Subsequent sessions may be shorter, especially if a participant mentions that the context has not really changed, or that previous strategies continue to "work" well. Each step is still briefly touched upon, but a sense of history can ease the discussion (e.g., by the counselors having documented previous sessions and reviewed them before the participant visit). Participants should always have some goal from the previous visit and this must be well documented in order for the next visit to appropriately reflect on potential progress toward that goal.

Example of Close the Session Step

We've talked about a few different things today. Thank you for that. You mentioned that you feel confident in your partner's continued support, at least for the next month, and that that is key to the ring being easy for you to use. You're feeling that this will continue; I'll check in with you next time to see how things go. We also talked about coming to clinic and how that has been difficult for you. One thing that seemed really important was making sure you had child care, and we talked about it being OK to bring your son with you if needed. You also identified being able to call the clinic to reschedule if needed, or seeing if your sister could help. Those are great ideas and I will be eager to find out at your next visit if any of them seem to help ease the burden of coming to the site. Does that sound all right to you?... Thank you very much for all you are doing.

MAIN PRINCIPLES IN COUNSELING DISCUSSIONS

Client-centered

The participant is the expert on her life and behaviors.

Comprehensive (multi-targeted)

Providing accurate information is necessary but insufficient to produce behavior change or promote participant engagement in discussions about product use. Motivation (personal and social) and skills are also critical to help produce change.

Context-driven

The counseling session explores the context in which one negotiates product use. It is not focused on the assessment of ring adherence. The focus is on the aspects of engagement in the study that facilitate or challenge uptake and use of the ring.

Counselor-guided

The counselor guides the discussion through questioning, but does not do most of the talking. The participant should have the majority of "talk time" in any given session.

Genuine

The counselor maintains a genuine interest in the participant and reflects that interest through exploration of the participant's experiences. Counselors seek to remain engaged and authentic (real, honest, present, and attentive) throughout the conversation.

Individualized

Counseling for product use is individually tailored to the levels of engagement and product-use behaviors of a given participant at a given point in time.

Neutral stance

The counselor maintains a supportive but neutral stance throughout the session to convey acceptance of both the participant and her disclosures of positive and negative aspects of product use.

Recognizes limited role

The counselor recognizes that her impact is in the immediate session and that she cannot "make" a participant do anything. The counselor can, however, ensure that a safe environment is consistently provided for the participant to openly discuss product use.

COUNSELOR SKILLS

Active listening

Active listening (or attending) refers to the counselor's ability to communicate listening through frequent and varied eye contact, facial expressions, and other forms of non-verbal communication. This includes sitting in a relaxed posture, leaning forward occasionally, using natural hand and arm movements that are responsive and encouraging, and being aware of the patient's demeanor.

Elicit-Provide-Elicit

Elicit-Provide-Elicit is a strategy from motivational interviewing that involves asking the participant to explore some aspect of a feeling, experience, or behavior (eliciting information from the participant); providing the participant with relevant information about what she has shared (the counselor shares knowledge or expertise he or she has on the issue in a supportive manner); and then again asking the participant to share what she makes of the information (given what the counselor has shared, what the participant makes of that information, how it fits or does not fit with the participant's sense of things). This is a marked difference from simply giving the participant information and then moving on to some other topic area. The Elicit-Provide-Elicit approach offers greater opportunity to build consensus and keep the session participant-centered. An example of Elicit-Provide-Elicit would be to ask about experiences, provide information to correct misinformation, and then elicit reactions. The counselor may ask about experiences with the study product [Elicit] and hear in the participant's response that the participant believes that if her ring gets out of place, she should take it out entirely until the next visit. The counselor can provide information about re-positioning the ring [Provide], and then ask the participant how she feels about that new information [Elicit].

Open-ended questions

Open-ended questions are those questions that are not easily answered with a one-word response ("yes" or "no") and do not assert the counselor's values or

objectives. Counselors should use them when they are seeking information about the context in which product use occurs or when exploring attitudinal, cultural, economic, and/or social factors that may play a role in product use. Open-ended questions invite further disclosure by the participant and help to build rapport and trust. What the counselor asks and how it is asked can also demonstrate positive regard for the participant and a genuine interest in knowing how the participant feels. An example of a closed-ended question (with a "yes" or "no" answer) would be: "Is it easy to leave your ring inserted?" An open-ended approach would be: "What is your experience with the ring? What makes it easier? What makes it more challenging?"

Pausing

Pausing provides opportunities for participants and counselors to digest material and to make room for feelings or thoughts to emerge. Giving the participant time to "experience the

moment" by allowing silence to happen is a sign of respect for the power of the participant's thoughts and feelings. Sometimes a counselor's discomfort with silence can interrupt the participant's process. Remember: Silence is also a form of communication.

Paraphrasing

Paraphrasing refers to rewording the content of what the participant has said in similar but fewer words. This can help the counselor clarify the basic message expressed in the verbal content of the participant's communication. Paraphrasing neither expands nor builds on the topic, but is a way to help the participant feel heard and to build rapport. A participant may say that her brother-in-law is visiting and he's shifted much of the routine of the family. After her detailed explanation of how this occurs, the counselor paraphrases with a short sentence. "Since he has moved in, things that were predictable each day are not predictable anymore." Note that paraphrasing does not try to reflect back the participant's exact words or expressions (explained below); it is more like summarizing (also explained below), but on a smaller scale. It is a good practice when paraphrasing or summarizing to either pause for several seconds to allow for a reaction from the participant, or elicit (ask) the participant specifically if the paraphrase feels accurate: "Am I understanding correctly?"

Process comments

Process comments are observations a counselor shares about what is going on in the session itself. This could be something the counselor has observed about the exchange, discussion, or process of communication between the counselor and the participant; it is typically (but not necessarily) followed with a question (elicitation) about the observation. If, for example, the participant was suddenly looking at her watch, a good process comment could be: "I see you're looking at your watch . . . do you have concerns about how long our session is taking?" If the participant suddenly crosses her arms and looks away, you could say, "Your body looks tense right now. I'd like to take a moment and check in with you. . . How are you feeling right now?" When a discussion feels "stuck," consider whether or not there is a process comment that might help to move the discussion forward.

Reflective listening statements

Reflective listening statements refer to listening carefully to what a participant is sharing or expressing and then "reflecting" back to them something they said that feels important. These statements do not offer an interpretation of what was shared, nor are they just "repeating back" everything the participant says. Rather, they are short statements that reflect some important aspect of what was said using the same language that the participant used. Using the participant's own words or expressions conveys that you are actively listening; also, hearing the reflection can help participants clarify their feelings and thoughts. Counselors often use reflective statements in situations in which they hear something meaningful in what the participant says, but the participant doesn't appear to have fully appreciated it. For example, a participant explains that her days consist of taking care of everyone else in the family and has said this in a very casual way, moving quickly to another topic. The counselor may simply reflect back, "Every day it's the same, taking care of others," and follow this with silence to allow the participant to process the observation and respond.

Reframing

Reframing refers to offering an alternative way of looking at something that the participant has just said — usually one that is more constructive and positive. For example, when a participant might say, "I get so frustrated with myself because I take a long while to get my ring back in if it comes out," a counselor may reframe this toward a productive strengths-based discussion by saying, "Which also means that you are really committed to getting it back in. Right?"

Summarizing

Summarizing refers to the technique of highlighting for the participant the most important aspects of the session that have been discussed. For this study, summarizing the context, needs, strategies, and goals will be a critical part of modeling and empowering problem-solving.

Third-personing

Third-personing refers to a counselor noting what "others" have done, experienced, or found helpful. The counselor refers to someone outside the session (e.g., another participant she has worked with) as a way to normalize the participant's experiences. For example, a counselor might say, "Many other participants have shared similar concerns with me," or suggest alternative ways of thinking about or doing things based on the shared experiences of others (e.g., "I have worked with a few participants struggling with this, and they have found some interesting approaches to deal with it. Obviously, everyone is different, but would you be interested in hearing about what worked for them?")

Ventilation and validation

Ventilation (venting) refers to "getting something off your chest." When someone has complaints about something or someone, it can be helpful at times to "vent" or verbalize feelings and frustration, when used constructively. Validation is when the participant's frustration is recognized by the counselor as valid, understandable, and within reason. By allowing the frustration to be legitimate and a reasonable, understandable response, the pressure and discomfort in experiencing the frustration can be reduced. In this regard, it is most important for the counselor to validate feelings and not the content or specifics of the events attributed to causing the frustration. For example, a counselor may reply to venting about wait times for the visit by saying, "It is perfectly reasonable to feel frustrated about waiting so long" or, "That does sound really taxing." Note that the counselor is not trying to reduce the frustration by saying it is inappropriate or by providing excuses for the event (the long wait time). Instead, the counselor simply recognizes that the feelings are legitimate without placing or necessarily taking on blame for the feelings.

NOTES:

PATHWAYS TO HIGH ADHERENCE

Counselor Self-Assessment Tool

WHAT YOU WILL FIND IN THIS APPENDIX

Appendix C contains a self-assessment tool that can be used by counselors, supervisors, or any team member seeking to align their interactions with participants toward a patient- or participant-centered communication style.

WHO SHOULD USE IT

All team members.

HOW TO USE IT

If teams record their counseling visits or interviews, the audio (or video) can be reviewed using the tool to capture areas of competence and areas in need of improvement.

Given that many people will not record their interactions with participants, the tool can also be used immediately following a participant interaction (e.g., a counseling session, an education meeting, an interview) where the counselor, educator, or interviewer rates herself to identify where she would like to focus improvement. It could also be used with recorded role-plays or supervisors may like to use it as a way to structure feedback.

This tool can also be used with role-plays.

The tool should NOT be used punitively.

COUNSELOR SELF-ASSESSMENT TOOL

Tools that counselors can use to monitor their skills and identify areas that need additional refining can be very helpful. As an example, we provide a self-assessment tool developed for implementation of integrated Next-Step Counseling adapted to the counseling approach recommended in this *Pathways to High Adherence* manual that could be further adapted to any approach using the same principles. Counselors can complete this tool after a session, or if audio recording is used, they can complete the tool while listening to a session tape.

AREAS INCLUDED IN THE SELF-ASSESSMENT TOOL (ALPHABETICAL ORDER)

AREAS		Basic definition
Advise (AD)	With permission (ADP)	Asking before providing advice/recommendation
	Without permission (ADW)	Giving advice unsolicited or without permission (note: may be appropriate depending on context)
Affirm (AF)	Appreciation, expressed confidence, reinforcement for specific behavior/ thought	Reinforcing client comments/reflections on positive things/insights (note: does not include general praise or positive comments)
Confront (CO)	Challenge ideas, confrontation	Expressing opposing ideas or overt debating with client (note: may be appropriate depending on context)
Contingencies (CT)	Praise, punishment, disapproval, moralizing in response to client discourse	Using praise, disappointment, or concern to motivate adoption of change resulting in direct or implied contingencies for client to "earn" counselor respect or positive regard (note: typically inappropriate in most situations)
Emphasize Control (EC)	Emphasis on client personal control, choice, and responsibility	Reflections or comments that reinforce or introduce client choice and power in discourse or in general
Evocation (EV)	Question, reflection, or strategy to foster alternative viewpoints/change talk	Introducing or steering conversation toward alternatives or inconsistencies in views or behaviors (note: distinct from confrontation by counselor's use of reflection and questions that target change talk)
Facilitate (FA)	Verbiage that supports exploration or unfolding issue more	Questions, reflections, and non-verbal cues that move client toward continued or deeper exploration of an issue
Filler (FI)	Chit chat/rapport building	Generic conversation, often promoting a sense of history between client and counselor, or promoting commonality or courtesy
Follow Change Talk (FC)	Counselor focus/reflection on change talk (FC)	Counselor notes and explores client verbiage that reflects desire, ability, reasons for change, need for change, commitment toward change, action, or taking of steps
	Missed opportunities to explore change talk (MO)	Client expresses desire, ability, reasons, need, commitment, action, or taking of steps and counselor does not reflect or explore
Giving Information (GI)	General information (GI)	Provision of general information
	Protocol-specific information (PI)	Information about sexual risk, risk management, adherence, or vaginal ring (or other material related to protocol/study)
Question (QU)	Closed question (QUC)	Questions with answers that resemble response options or yes/no
	Open question (QUO)	Questions that cannot be answered with a simple option or reply; choices for response not provided or implied
Raise Concern (RC)	With permission (RCP)	Asking to share a concern, worry, or fear, typically in relation to what the client just shared
	Without permission (RCW)	Stating a concern, worry, or fear about something the client shared without asking/permission (note: may be appropriate depending on context)

AREAS		Basic definition
Redirection (RD)	Focusing/refocusing conversation intentionally (RDI)	Changing topics or shifting conversation to different content intentionally (e.g., to close a topic, refocus an unproductive discussion, or manage conversation length)
	Changing topic unintentionally or producing missed opportunity (RDU)	Topic shifts or changes are introduced that were not intentional; questions that redirect conversation from one area to a different one for unclear reasons
Reflect (RE)	Simple (RES)	Reflecting back client statements or experiences in a way that maintains client's content or level of insight (e.g., echo, repeat, rephrase, reword)
	Complex (REC)	Statements that paraphrase to emphasize connections, emphasize new insights, or offer potential for deeper understanding/meaning or feeling
Reframe (RF)	Providing alternative explanations/ viewpoints	Offering an alternative and typically more functional or empowering way of looking at something the client has shared
Righting (RT)	Advocating for prevention/health rather than joining in ambivalence	Statements or questions that emphasize what the client should think or do that are pro-health or pro-self-care
Roll with Resistance (RR)	Joining client in reflecting on/feeling negatively about pro-health/pro-self-care options	Statements, questions, reflections that join client's negative feelings/ thoughts about adopting/maintaining a health behavior; specific avoidance of touting the "should do" point of view
Silence (SI)	Strategic use of silence (versus filling silence or unintentional interruption of it)	Allowing for silence in an appropriate manner; productive silences; using silence to learn about client
Other:		
Other:		
Other:		

GLOBAL RATINGS	BASIC DEFINITION
Acceptance	Counselor demonstrates openness to client and, during conversation, is willing to discuss difficulties without judging or correcting them.
Empathy/Understanding	Counselor demonstrates ability to "sit with" difficult content, positions client experiences within the context of his/her life, and genuinely engages with client.
Spirit	Overall presence of counselor promotes a supportive environment. Counselor appears engaged in conversation and mixes his or her own expressions and affect to create a positive, productive working alliance with client.

SELF-ASSESSMENT TOOL

Participant ID: _____

Visit: _____

Counselor: _____

Date: _____

SPECIFIC AREAS		TO WORK ON… (GOAL FOR BUILDING SKILLS)						
		1	2	3	4	5	6	7
		Increase			No change			Decrease
Advise (AD)	With permission (ADP)	1	2	3	4	5	6	7
	Without permission (ADW)	1	2	3	4	5	6	7
Affirm (AF)	Appreciation, expressed confidence, reinforcement for specific behavior/thought	1	2	3	4	5	6	7
Confront (CO)	Challenge ideas, confrontation	1	2	3	4	5	6	7
Contingencies (CT)	Praise, punishment, disapproval, moralizing in response to client discourse	1	2	3	4	5	6	7
Emphasize Control (EC)	Emphasis on client personal control, choice, and responsibility	1	2	3	4	5	6	7
Evocation (EV)	Question, reflection, or strategy to foster alternative viewpoints/ change talk	1	2	3	4	5	6	7
Facilitate (FA)	Verbiage that supports exploration or unfolding issue more	1	2	3	4	5	6	7
Filler (FI)	Chit chat/rapport building	1	2	3	4	5	6	7
Follow Change Talk (FC)	Counselor focus/reflection on change talk (FC)	1	2	3	4	5	6	7
	Missed opportunities to explore change talk (MO)	1	2	3	4	5	6	7
Giving Information (GI)	General information (GI)	1	2	3	4	5	6	7
	Protocol-specific information (PI)	1	2	3	4	5	6	7
Question (QU)	Closed question (QUC)	1	2	3	4	5	6	7
	Open question (QUO)	1	2	3	4	5	6	7
Raise Concern (RC)	With permission (RCP)	1	2	3	4	5	6	7
	Without permission (RCW)	1	2	3	4	5	6	7

SPECIFIC AREAS		TO WORK ON… (GOAL FOR BUILDING SKILLS)						
		1	2	3	4	5	6	7
		Increase			No change			Decrease
Redirection (RD)	Focusing/refocusing conversation intentionally (RDI)	1	2	3	4	5	6	7
	Changing topic unintentionally or producing missed opportunity (RDU)	1	2	3	4	5	6	7
Reflect (RE)	Simple (RES)	1	2	3	4	5	6	7
	Complex (REC)	1	2	3	4	5	6	7
Reframe (RF)	Providing alternative explanations/viewpoints	1	2	3	4	5	6	7
Righting (RT)	Advocating for prevention/health rather than joining in ambivalence	1	2	3	4	5	6	7
Roll with Resistance (RR)	Joining client in reflecting on/ feeling negatively about pro-health/pro-self-care options	1	2	3	4	5	6	7
Silence (SI)	Strategic use of silence (versus filling silence or unintentional interruption of it)	1	2	3	4	5	6	7
Support (SU)	General support for efforts	1	2	3	4	5	6	7
Other:		1	2	3	4	5	6	7
Other:		1	2	3	4	5	6	7
Other:		1	2	3	4	5	6	7

GLOBAL RATINGS	LOW						HIGH
Acceptance	1	2	3	4	5	6	7
Empathy/Understanding	1	2	3	4	5	6	7
Spirit	1	2	3	4	5	6	7

FIDELITY (example from Next Step Counseling protocol)

ENTER STEPS FOR PROTOCOL	WHAT DID YOU DO WELL?	WHAT WOULD YOU LIKE TO WORK ON?
1. ENGAGE Provide study update. Discuss study visit and product satisfaction. Identify ways the study can improve and contributions participants can make.		
2. FRAME Explain purpose of discussion. Seek permission to continue discussion.		
3. EXPLORE Explore participant experiences with study with attention to facilitators/ challenges to engagement: 1) trust in study, 2) retention, 3) persistence, and 4) adherence.		
*******WHAT WAS IDENTIFIED AS RELEVANT AREA(S)?*******	❑ Trust ❑ Retention ❑ Persistence ❑ Adherence ❑ Advocacy ❑ Other	
4. IDENTIFY NEEDS Ask what would need to happen for area identified above to improve, be less stressful, be easier, or be maintained.		
5. STRATEGIZE Explore how improvement/ maintenance can be accomplished.		
6. GOAL Identify a strategy discussed for the team, the participant, or another active party to try/consider.		
7. CLOSE Review and summarize session. Remind participant of the check-in that will occur next visit. Thank the participant. Document session.		

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APPENDIX

D

PATHWAYS TO HIGH ADHERENCE

Mutuality Framework

WHAT YOU WILL FIND IN THIS APPENDIX

Appendix D contains the mutuality framework that helped inform the collaborative counseling approach. Here we adapt the model to how it would apply to ring adherence.

WHO SHOULD USE IT

Using the mutuality framework can be helpful for project planners, community liaisons, and intervention developers and implementers as a way to think about how a participant may approach using a study-provided ring. The main contribution of this framework is to call attention to the possibility that even though someone may willingly engage in a study that provides rings, she may have reservations or concerns that limit her use of the ring in practice. Thinking about how communities map onto the four dimensions identified by the framework can also direct community mobilization efforts to help position the ring, agencies providing the ring, and procedures needed for monitoring ring-use safety as legitimate and trustworthy. The framework has particular relevance in communities where trust in the ring, the drugs in the ring, the research institution, or biomedical research and products in general is tentative, making people skeptical or cautious about engaging in the prevention strategy. Communities with histories of discrimination or real or perceived questionable research practices may be wary of the ring and its safety but eager to participate in a trial or demonstration project to access resources/services provided as part of participation.

HOW TO USE IT

Here we provide information about the framework. This is intended to be educational for providers, researchers, and community representatives. Different groups may use the framework in different ways. We suggest starting with a map of where participants in a given community are likely to fall among the four dynamics described below, which will help to plan for culturally relevant mobilization and engagement strategies.

MUTUALITY FRAMEWORK

The mutuality framework (Figure 5) was developed from qualitative interviews with young women in Cape Town, South Africa, who had participated in an open-label oral pre-exposure prophylaxis (PrEP) trial looking at adherence to different kinds of non-daily, as well as daily, regimens.[8] In that work, a narrative emerged that helped explain why some people would avoid using PrEP entirely, while others would champion PrEP in their community. Specifically, four approaches to PrEP were identified: actively avoiding PrEP, being uncertain about using PrEP, being committed to trying to use PrEP, and being highly invested in PrEP.

Each of these approaches is explained by the different dynamics playing out among participants, the community, and the study. As indicated in the figure below, four dynamics are identified: distrust, uncertainty, alignment, and mutuality. Each dynamic is detailed in terms of tensions and synergies among the participant, community, and study; the resulting approach to PrEP; and implications for where and how to engage participants.

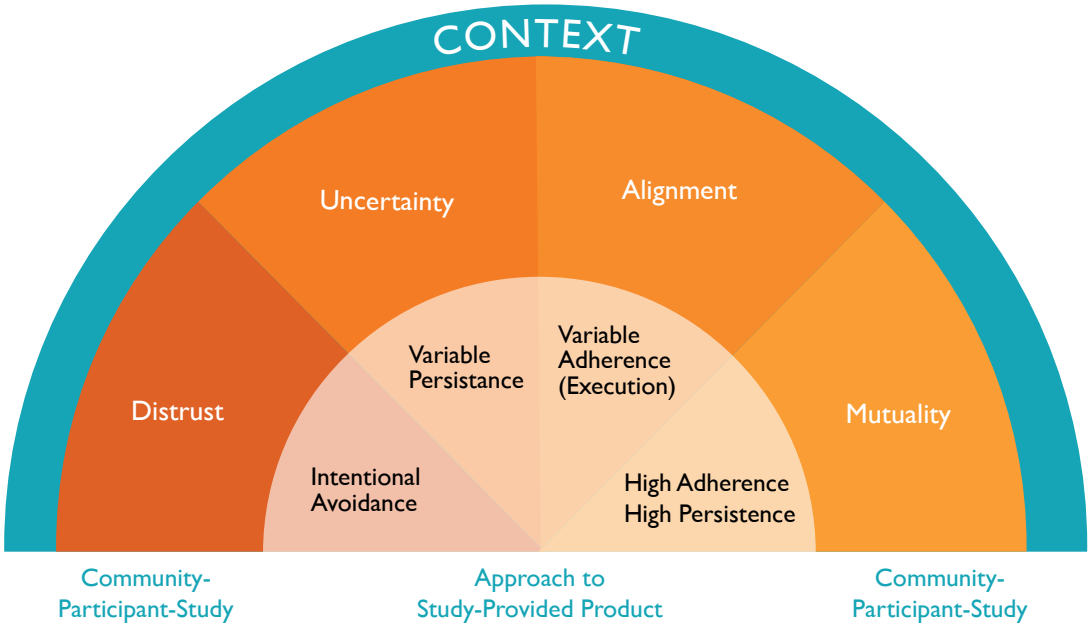
Any dynamic, regardless of what it is, is influenced by:

- Social and personal resources, whether tangible or intangible.
- Social-political history with research and site (skepticism).
- Identity attributes (e.g., self, important others, research, community) as participant or product "user."
- World view regarding where self and community intersect. (In the case of South African women, we identified *Ubuntu*, meaning where there is a priority of one's own contributions having real benefit to one's community.)
- Product attributes, regimen burden, ease of use, and match to context.

8. See Amico KR. PrEP experiences among South African women in the HPTN067 (ADAPT) study: Healthy paranoia (skepticism), Ubuntu, champions and challenges to resolving PrEP dissonance. 8th IAS Conference on HIV Pathogenesis, Treatment and Prevention. 20 July 2015. Vancouver, Canada. Presentation available at: https://www.youtube.com/watch?v=1nFO2r2sO88

FIGURE 5

Mutuality Framework: Four dynamics that describe study product use by characterizing intersections among the participant, community, and study.



DYNAMICS

Distrust:

- **Dynamic:** Rejection of integrity of stated goals of study or its benefits to community.
- **Approach to Product:** Active avoidance of study-provided product.
- **Engagement Challenge:** Avoidance of disclosure of concerns to study; may manage tension by dissuading others.
- **Intervention Implications:** Build trust and try to move toward ambivalence (e.g., through staged debates, normalization/invitation of skepticism, transparency, community and participant engagement strategies).

Uncertainty (skepticism):

- **Dynamic:** Skeptical kind of exploration; is the study and/or the study products good for self or community?
- **Approach to Product:** Variable persistence (e.g., on again/off again engagement with regimen).
- **Engagement Challenge:** Discomfort while weighing options; may not disclose concerns to study.
- **Intervention Implications:** Support exploration process; move skepticism from private to public. For example, through use of staged debates, normalization/invitation of skepticism, transparency, peer-to-peer interventions, reinforcement of efficacy (when possible), on-demand use designs, engagement of participant(s) in quality improvement procedures and evaluation of the study and study procedures (e.g., "secret shoppers or mystery clients") to build ownership.

Alignment

- **Dynamic:** Provisional acceptance that the study and product do benefit self and community in ways that are relevant and meaningful.
- **Approach to Product:** Variable execution (e.g., high persistence, variable success with adherence).
- **Engagement Challenge:** Maintaining alignment with study while improving execution.
- **Intervention Implications:** Support of alignment; building of adherence motivation and skills (e.g., through peer support, barriers/strengths-based approaches, low-burden regimen, high-value regimen).

Mutuality

- **Dynamic:** Alignment of study goals and vision are seen as mutual; the vision is shared, and a kind of ownership of the work and advocacy in the community takes place.
- **Approach to Product:** Good persistence/good execution of adherence.
- **Engagement Challenge:** Maintaining high sense of ownership.
- **Intervention Implications:** Support of alignment; create opportunities to lead and advocate (e.g., through peer supporters, community liaisons, participant advisory panel, post-trial advocates).

APPLICATION TO RING USE

The mutuality framework can help explain the interactions women have with the vaginal ring, their social surroundings, and the agency, clinic, or site providing the rings. The dynamics described in the framework are fluid, and women may move between dynamics over time and in response to accumulated experiences with the product, her community, and providers of the ring. Consistent with the overall approach of promoting engagement throughout a woman's journey toward high levels of use, the framework also emphasizes reasons for participation, beliefs about the product and those providing it, and sense of agency, as well as the perceived congruence between what one believes about the ring and those providing it, and what one's own desires and core values are. The goal is to have women in the alignment and mutuality dynamics, and for the strategies that support movement toward those dynamics to be prioritized and to move beyond individual one-on-one discussion-based counseling with a research, clinic, or agency member. The *Pathways to High Adherence* manual offers diverse strategies — aimed to optimize overall engagement with the ring as a prevention method — that are well aligned with the mutuality framework.

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APPENDIX

E

PATHWAYS TO HIGH ADHERENCE

Adherence Support Templates

WHAT YOU WILL FIND IN THIS APPENDIX

Appendix E contains the blank templates that are provided throughout this manual as adherence support tools.

WHO SHOULD USE IT

Study coordinators, investigators, counselors, and other team members involved in adherence support activities at research clinics.

HOW TO USE IT

Templates should be modified for use, as needed, based on site- and study-specific adherence support needs and strategies.

ACTION PLAN TEMPLATE

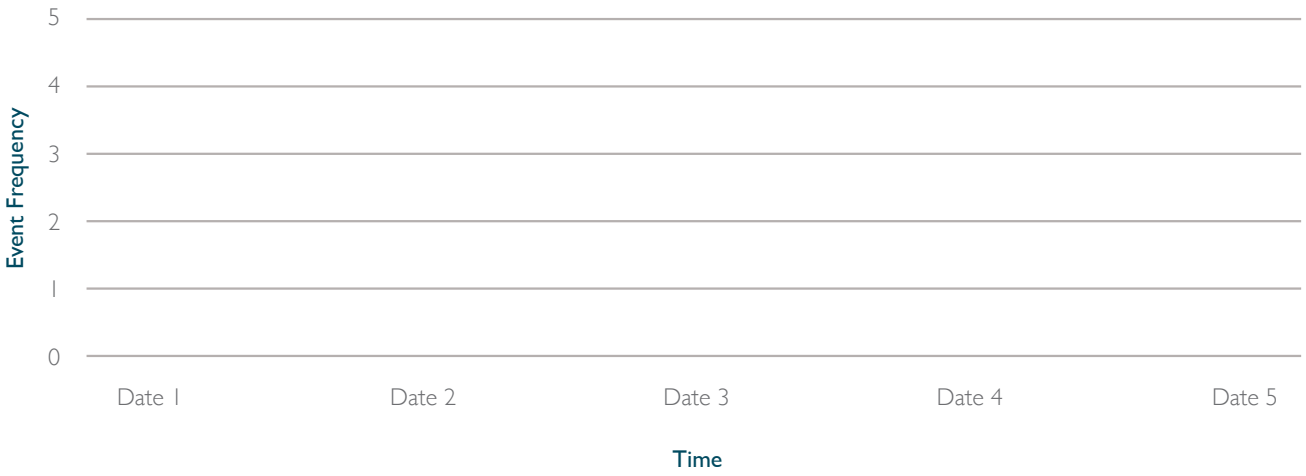
In this action plan template, each overall goal or aim should get its own action plan and team. Then each team should think about the specific sub-activities that need to be implemented to achieve the stated goal and assign a point person or smaller team to work on each activity. Methods for monitoring and measuring each activity and its outcome should be included in the task list. You may choose to use this action plan template as is or modify it to be more useful for your specific site (e.g., you may choose to have one action plan per activity as opposed to per goal/aim)

ACTION PLAN							
Team Leader							
Team Members							
Goal/Aim							
Activity/Task	Person(s) Responsible	Trial Stage	Target Start Date	Target End Date	Resources Needed *(e.g., staff, money, space, materials)*	Measures	Notes

RUN CHART TEMPLATE

A run chart is a line graph that tracks changes in an event or observation over time. Time is measured along the x-axis, and the event or observation being tracked is plotted along the y-axis.

See page 32 for a run chart example.



CHECK SHEET TEMPLATE

A check sheet is a table that can be used to compile data, either in real time or from historical sources, like a retrospective chart review. On a typical check sheet, columns represent specific points in time and rows represent the challenges, events, and other occurrences that the team wishes to track. Using a check sheet, teams can tally how often certain events occur and can easily see patterns over time.

CHALLENGE	TIME					TOTAL
	Time 1	Time 2	Time 3	Time 4	Time 5	
Challenge 1						
Challenge 2						
Challenge 3						
Challenge 4						
Total						

TEMPLATE TOOL FOR PRIORITIZING ISSUES RELATED TO ADHERENCE

For each question, choose the option (i.e., yes, no, mixed, unsure) that best fits your current community and research environment. Once you have decided on an answer for each question, look at the key provided to help you determine which topics should be a high priority for addressing in adherence-support activities, which should be a lower priority, and which might require more information gathering before they are assigned a priority level.

	Yes	No	Mixed	Unsure
1. Has the community had a positive experience with past research trials? Note: If the community has not had any previous experience with research trials, mark "Unsure."				
2. Does the community believe that biomedical research offers benefits to them and some form of reciprocity?				
3. Does the media accurately cover issues related to biomedical research and HIV?				
4. Is the community free of rumors and/or misconceptions related to HIV, the research site, and the study (including study procedures and the investigational product)?				
5. Are the resources that are provided by joining the study (e.g., medical care, financial compensation, HIV prevention services) otherwise readily available to women in the community?				
6. Does the study site have strong relationships established with stakeholders and community gatekeepers?				
7. Do the study protocol and investigational product fit within/support the existing cultural and religious beliefs and gender dynamics in the community?				
8. Are study staff well-trained in providing participant-centered care?				
9. Does the study team have a clear plan for supporting participant autonomy and engagement in the conduct and ongoing monitoring of the trial?				

KEY

OPTIONS	INTERPRETATION	ACTION
Yes	This area is strong and supportive of product adherence during the trial.	Lower priority for site team to work on. "Do" activities should be focused on maintaining strength in this area, rather than implementing big changes.
No	This area is weak or represents an area in which the study and community are not aligned. This has the potential to undermine/negatively affect product adherence in the trial, if not addressed by the study team.	This is a high priority area. "Do" activities should be focused on creating change and strengthening this area.
Mixed	This area is neither strong nor weak, but there is an opportunity for improvement.	This is a medium priority area. "Do" activities should focus on exploring this area in more depth to identify where specific strengths and weaknesses exist so that actions can be targeted appropriately.
Unsure	This area needs more research in order to determine whether current conditions are supportive of or detrimental to adherence in the study.	"Do" activities should focus on researching this topic and gathering more information so that this area can accurately be assigned a priority level.

NOTES:

APPENDIX

F

PATHWAYS TO HIGH ADHERENCE

Supplementary Materials

WHAT YOU WILL FIND IN THIS APPENDIX

Appendix F contains an instructional sheet provided to IPM-027/The Ring Study participants to help them know how to insert the ring and what to do if a ring came out of the vagina between visits.

WHO SHOULD USE IT

Study team members, especially counselors, who will be working one-on-one with participants to help them learn about how to properly insert the ring and manage removals or expulsions.

HOW TO USE IT

Provide this sheet as a handout for participants to refer to between study visits.

Vaginal Ring • Ring Use Instructions

Vaginal ring should be worn all day and all night

What to do if the ring comes out

If the ring comes out in a place that is NOT DIRTY, such as the bed, or in your clothes, you may wash it and put it back into your vagina

If the ring comes out and touches something that is DIRTY, such as the toilet or the ground you should not put it back into your vagina. You must put it in the bag and bring in to the research centre

Prepare to insert the ring

How to insert the ring

Use your thumb and index finger to press the sides of the ring together. It may be easier to insert the ring if you twist it into the shape of the number 8

Use your other hand and hold open the folds of skin around your vagina

Place the tip of the ring in the vagina opening and then use your index finger to gently push the folded ring into your vagina

Push the ring up towards your lower back as far as you can. If the ring feels uncomfortable, you probably did not push it into your vagina far enough. Use you finger to puch the ring as far as you can into your vagina

The ring should now be in your upper vagina. Wash your hands when you are done

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