HHS Public Access

Author manuscript

Cogn Behav Pract. Author manuscript; available in PMC 2018 February 01.

Published in final edited form as:

Cogn Behav Pract. 2017 February ; 24(1): 38–49. doi:10.1016/j.cbpra.2016.02.004.

"Life-Steps" for PrEP Adherence: Demonstration of a CBT-Based Intervention to Increase Adherence to Preexposure Prophylaxis (PrEP) Medication Among Sexual-Minority Men at High Risk for HIV Acquisition

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Abstract

One dramatic advance in human immunodeficiency virus (HIV) prevention efforts has been the prescription of medications typically used for HIV treatment as prophylaxis against acquiring HIV. As a preventative agent, this practice is referred to as "preexposure prophylaxis" (PrEP). The U.S. Federal Drug Administration approved daily PrEP for adults at risk for HIV who do not consistently use condoms during sex with HIV-infected or unknown-status partners. In this paper, we describe a cognitive-behavioral therapy (CBT) PrEP adherence intervention developed for use

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Contains Video[1]

[1]Video patients/clients are portrayed by actors.

Please cite this article as: Taylor et al., "Life-Steps" for PrEP Adherence: Demonstration of a CBT-Based Intervention to Increase Adherence to Preexposure Prophylaxis (PrEP)..., *Cognitive and Behavioral Practice* (2016), http://dx.doi.org/10.1016/j.cbpra.2016.02.004

Disclosure Statement

The authors have no conflicts of interest to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.cbpra.2016.02.004.

in high-risk sexual-minority men in the United States, adapted from “Life-Steps,” an evidence-based CBT intervention to promote adherence to HIV treatment. Modules include creating a PrEP dosing schedule, adhering to daily PrEP, problem solving barriers to adherence, and sexual risk-reduction techniques. Supplemented with practical video vignettes, this novel intervention may help to enhance the clinical practice of health care providers in outpatient settings to increase PrEP adherence in sexual-minority men.

Keywords

CBT; HIV; MSM; medication adherence; PrEP

HUMAN immunodeficiency virus (HIV) continues to be a major global health problem, with approximately 35.3 million people living with HIV at the end of 2012, and more than 2 million new cases reported globally each year (UNAIDS, 2013). As of 2010, the Centers for Disease Control and Prevention (2012, 2014a) estimated that, of the 50,000 new HIV infections each year in the United States, approximately 30,000 (63%) occur in sexual-minority men (gay, bisexual, and other men who have sex with men [MSM]), and this rate of infection is at least 44 times greater than for heterosexual men in the United States. Condomless anal sex (Dodds, Mercey, Parry, & Johnson, 2004), underestimating personal HIV acquisition risk (MacKellar et al., 2007), low adherence to prevention strategies including consistent condom use (Centers for Disease Control and Prevention, 2014a), and the perception that HIV is no longer a serious health problem, are some of the factors that complicate HIV prevention efforts (Chen, 2013). Additionally, mental health, substance abuse, and other co-occurring health conditions may moderate the degree to which theory-based interventions to reduce HIV risk can be effective (Safren, Blashill & O'Cleirigh, 2011; Walkup et al., 2008). Accordingly, to curb the spread of HIV in the United States, it appears that, for MSM, promoting condom use alone has not been a successful strategy (see Crepaz et al., 2009; Herbst et al., 2005; Marks, Crepaz, Senterfitt, & Janssen, 2005; Pantalone, 2014; Safren, Reisner, Herrick, Mimiaga, & Stall, 2010).

Preexposure prophylaxis (PrEP) refers to the use of antiretroviral medications typically used to treat HIV infection instead to prevent HIV acquisition in individuals who are uninfected with the virus—analogous to the prophylactic use of antimalarial medication when individuals travel to endemic regions. In 2012, the U.S. Federal Drug Administration (FDA) approved the use of a co-formulated pill (emtricitabine and tenofovir disoproxil fumurate; commercially known as Truvada) as PrEP for use with HIV-negative sexual-minority men (Kashuba, Patterson, Dumond, & Cohen, 2012). In a multinational, randomized placebo-controlled trial of MSM and transgender women at high risk for HIV acquisition—known as the iPrEx Study—participants randomized to take the active medication daily were 44% less likely to become infected with HIV than those who were randomized to placebo (Grant et al., 2010). However, the PrEP efficacy was highly influenced by medication adherence. An expanded case-control study found that the chances of acquiring HIV were reduced by more than 90% for iPrEx participants who had detectable levels of the medication in their blood (Anderson et al., 2012). Although another study that enrolled young male and female heterosexuals in Botswana demonstrated the efficacy of tenofovir– emtrictabine as PrEP

(Thigpen et al., 2012), two other studies conducted in young women in southern Africa did not demonstrate PrEP efficacy, primarily because of suboptimal medication adherence (Marrazzo et al., 2013; Van Damme et al., 2012). In other existing PrEP trials, across different settings and populations, medication adherence has been the lynchpin of the demonstration of efficacy (Baeten, Haberer, Liu, & Sista, 2013).

One study conducted in East Africa that enrolled heterosexual HIV-serodiscordant (one partner HIV positive, the other partner HIV negative) couples—the Partners PrEP Study—found that overall PrEP efficacy was 75% for participants randomized to take tenfovir–emtricitabine, and reached almost 90% among individuals with detectable blood levels, a surrogate marker for medication adherence (Baeten et al., 2012). In an ancillary study to this trial, Haberer et al. (2013) found that, for participants whose patterns of pill box opening dropped to 80% or below, providing cognitive-behavioral therapy (CBT)-oriented counseling based on an intervention called Life-Steps for HIV treatment adherence (Psaros et al., 2014; Safren, Otto, & Worth, 1999; Safren et al., 2009), PrEP efficacy rose to 100% protection. Among participants who were not adherent, investigators found a temporal improvement in adherence after PrEP users received the intervention (Psaros et al., 2014).

Barriers to PrEP adherence are currently less well understood than barriers to HIV treatment adherence, which include depression and active substance abuse (Binford, Kahana, & Altice, 2012; Gonzalez, Batchelder, Psaros, & Safren, 2011; Gonzalez, Psaros, et al., 2011; Mellins et al., 2009), HIV-related stigma (Katz et al., 2013), perceived side effects, and forgetting, among others (Conway, 2007; Johnson, Dilworth, Taylor, & Neilands, 2011; Mills et al., 2006). Factors associated with PrEP nonadherence in the various PrEP trials include heavy alcohol use, stigma, missing clinic visits, changes in routine, side effects, social stigma, and stress (Gilmore et al., 2013; Haberer et al., 2013; Mack, Odhiambo, Wong, & Agot, 2014; Tangmunkongvorakul et al., 2013). Hence, interventions addressing PrEP adherence may benefit from assessing or addressing these potential factors.

Principles of CBT have been used to effectively increase adherence to antiretroviral therapy (ART) as treatment in HIV-positive individuals (e.g., Safren et al., 2009, 2012; Simoni et al., 2013). Safren et al. (1999) developed the Life-Steps adherence counseling intervention using principles of CBT, motivational interviewing (MI) techniques (Miller & Rollnick, 2012), and techniques from problem-solving therapy (D'Zurilla, 1986; Nezu & D'Zurilla, 1989) to identify and solve a variety of common adherence barriers. Life-Steps has been found to improve adherence in a study for individuals with adherence problems in the United States (Safren et al., 2001) and in China (Simoni et al., 2011), and also in combination with additional CBT skills for depression (Safren et al., 2009, 2012). Interventions designed to support ART as HIV treatment may help inform interventions designed to support PrEP adherence.

In sum, PrEP is a novel biomedical intervention with the promise to significantly alter the HIV prevention landscape. Adequate levels of adherence to the medication, however, are needed. Our study team developed a PrEP adherence intervention that draws on our prior work, using the Life-Steps intervention for treatment adherence and for HIV serodiscordant heterosexual couples as a point of departure. The goal of the present paper is to describe our

approach to increasing PrEP adherence using this intervention adapted for HIV-negative MSM in the United States, because HIV-negative sexual-minority men are, by virtue of their sexual behavior, at high risk for contracting HIV. The goal is to disseminate the approach for other health care professionals working with clients on PrEP in outpatient settings.

Process of Intervention Development

Our clinical research team followed a sequential approach to develop the PrEP adherence intervention. As a first step, we conducted four focus groups to help conceptualize PrEP adherence in sexual-minority men at risk for HIV (Taylor et al., 2014). Based on the interview guide and a within-case/across-case analysis, six descriptive thematic categories informed the preliminary content of the intervention: (a) motivations for PrEP use, (b) barriers to PrEP use, (c) facilitators to PrEP use, (d) sexual decision making in the context of PrEP, (e) potential PrEP education content, and (f) perceived effective characteristics of PrEP providers. Next, the study team used Life-Steps (Safren et al., 1999) and the Partners PrEP study intervention (Psaros et al., 2014) as a general platform to develop CBT-based education modules for a four-session, weekly intervention with two monthly booster sessions. The intervention is similar, but adapted for U.S. MSM versus serodiscordant heterosexual couples in Africa. Accordingly, the problem-solving steps include modules on sexual health as well as ways to help refer or begin to address co-occurring psychosocial problems, if they exist, such as mental health and substance use. To test for feasibility, acceptability, and the potential for efficacy, we openly piloted the resulting intervention with seven high-risk sexual-minority men. These men all reported regular engagement in the highest-risk sexual behaviors for HIV transmission (i.e., unprotected anal sex with HIV-infected or unknown-status partners at least once per month in the last 3 months; Psaros et al., 2013). After the pilot phase was completed, we conducted a pilot randomized controlled trial with 50 participants (Mayer et al., 2014).

Overview of Life-Steps for PrEP Adherence Intervention

The goal of the intervention is to provide interventionists with optimal content to improve PrEP adherence in sexual-minority men who are at high risk for HIV acquisition, and who have been prescribed PrEP by a medical provider. As shown in Table 1, the intervention consists of four weekly sessions and two booster sessions, which are offered 2 and 3 months after PrEP initiation. All sessions give therapists ideas for what content to cover but allow for the intervention content to be flexibly determined based on the unique situation of the client. The first weekly session includes a psychosocial assessment (to develop rapport and to understand the social context in which PrEP use will occur), provision of PrEP education, guiding the client through some techniques of brief MI, and the establishment of a dosing schedule. Session 2 may focus on understanding the clients' experiences taking PrEP so far, continuing brief MI techniques, or engaging in problem solving required to address any barriers to adherence.

Session 3 begins with an adherence "check-in" and introduces sexual risk behavior education, which builds on knowledge about HIV transmission, high-risk activities for HIV acquisition, factors that increase and decrease risk for HIV infection and other sexually

transmitted infections (STIs), understanding HIV viral load, and ways to reduce risk of becoming HIV infected in the context of taking PrEP. The core components of the intervention focus on understanding and enhancing adherence to the medication, and problem solving barriers to adherence and to reducing sexual risk behavior overall. Subsequent session content (for the remainder of weekly Session 3 and Session 4) is designed to be flexible, such that modules may be selected based on a client's adherence needs. In the final weekly session, the interventionist revisits PrEP adherence goals and prior session content, as well as plans for continued PrEP taking in the future, upon intervention completion.

Offered at Months 2 and 3, booster sessions may provide an opportunity for the interventionist to assess PrEP adherence in the absence of weekly support. Interventionists can use booster sessions to review PrEP adherence over a longer time span and address any remaining or novel barriers to adherence using problem-solving skills learned during the earlier sessions. For clients who have no identified challenges to adherence, the interventionist can use the booster session to review and ensure that the existing adherence plan is working, and help the client identify potential future barriers to adherence that have yet to present themselves (e.g., travel, changes in work schedule).

Session 1: Introduction, Assessment, Education, and Dosing Scheduling

Session 1 provides the foundation for the subsequent intervention content, and begins with the interventionist working to establish an alliance with the client. Qualitative data from the individuals who took PrEP in the context of an efficacy trial suggested that a strong, positive relationship with the adherence interventionist was key to successful adherence counseling (Taylor et al., 2014). Because it can be challenging to balance the need for the client to express his concerns about safer sex, with the interventionist's need to gather background information and cover the required intervention content, we suggest setting the tone of the session as follows:

> I am happy to be working with you as your adherence counselor for PrEP. I have a lot to learn about you, so that I can be as helpful to you as possible during our work together. I would like to begin by telling you a little about the counseling. I will then ask you some questions about yourself, so that I can begin to get to know you better and learn about what your life is like these days. We have a lot to cover today, so we are going to do our best to limit that part of our visit to about 15 minutes. Does this sound okay? [wait for response] What questions do you have so far?

After providing an overview of the adherence intervention, the interventionist conducts a brief psychosocial assessment (e.g., living situation, health status, substance use, sexual partnerships) to determine potential facilitators of and barriers to daily PrEP adherence. Next, the interventionist introduces the client to the PrEP education that provides the client with a foundation of knowledge about PrEP. This component allows the client to learn more about PrEP and to clarify questions or misconceptions that he might have about PrEP use. Based on Centers for Disease Control (2011, 2014b) guidelines for PrEP use in sexual-minority men, educational topics include the importance and rationale of daily dosing, long-

term safety and tolerability, common side effects and side-effect management, substance using behaviors that can impact adherence to PrEP, and the importance of not sharing PrEP medication with others.

To introduce clients to taking PrEP on a daily basis, we provide a “Starting PrEP” introductory video that addresses motivation for taking PrEP, understanding PrEP effectiveness, and what to expect in terms of side effects. “Brett” is a 23-year-old gay man who has been taking PrEP for 8 months (see Video Clip 1). He describes his motivation to take PrEP, some mild side effects, and his own strategy to eliminate these side effects. Brett takes PrEP because it makes him feel safer when he has sex with his partner who is HIV positive. For him, PrEP is added protection to condoms and lubricant, particularly if a condom falls off or breaks, or if he decides not to use condoms during sex.

Deciding to take a daily medication to help prevent HIV is a significant commitment that may require ongoing motivation. One component of the intervention is the use of some MI techniques that are designed to help clients identify their motivations to adhere to PrEP on a daily basis. For the purposes of this intervention, motivation to adhere to PrEP should be viewed as fluid. Motivation may change over time in response to a variety of events (e.g., medication side effects, the end of a partnered relationship, introduction of new partners, or an increase or decrease in overall sexual activity). To facilitate this discussion, the interventionist introduces a “Pros and Cons” worksheet to better understand clients’ possible reasons to maintain high PrEP adherence versus not adhering regularly to PrEP. This can be a basis for different problem-solving approaches to take later in the intervention. Sometimes clients have a difficult time identifying their own pros and cons, so the interventionist may need to help guide this discussion based on his or her experience working with other PrEP users. Table 2 shows an example of a completed worksheet.

Assessing motivation frequently can assist the interventionist and client to identify periods in which lowered motivation may result in decreased adherence to PrEP and, thus, increased risk for HIV acquisition. The following video shows how the interventionist assesses “Cody's” motivation to take PrEP as part of his HIV risk-reduction strategy. In this case, the interventionist wonders if Cody, a 20-year-old gay man, understands the degree to which taking a daily medication to help prevent HIV may require a bit of a commitment, and he is interested in understanding what is guiding or motivating Cody to begin this change in his life.

In Video Clip 2, after Cody generated pros and cons, the interventionist assessed his motivation to take PrEP every day by introducing a numerical scale from 0 (*not at all motivated*) to 10 (*highly motivated*). Cody rated his motivation as a 7, which is moderate-high on the motivation scale. Then, the interventionist inquired about why Cody chose a 7, noting that motivation changes over time. Last, the interventionist summarized the discussion and noted how, over the course of the intervention, they will continue to discuss Cody's motivation. Because motivation naturally changes over time, an interventionist should assess the client's motivation at the start of every session and explicitly discuss steps to increase motivation when necessary.

While it may be possible in the future that PrEP will not need to be taken daily, current FDA guidelines call for daily dosing (Centers for Disease Control, 2014b). Upon completion of the educational component and introductory video, the interventionist and client work together to establish a daily dosing time, based on the client's preferences, and discuss when and how PrEP dosing can be linked to an already established, daily-occurring behavior. The goal of this conversation is to obtain a sense of when the client would like to take his PrEP medication, and how he spends his time on a weekly basis—to see if there might be any problems with the preferred dosing time. Questions and comments to consider could be:

- "You may already have a time of day in mind, but before we talk about that time, please tell me a little about a typical day for you."
- "Does this schedule vary at all, for example, were you thinking about a weekday or a weekend?"
- "What are some activities that you do every single day, no matter what else is going on, no matter where you are?"
- "What are you thinking would be the ideal time to take your PrEP? Why then and not earlier or later?"

Next, the interventionist guides the client to plan ahead to develop reminder strategies, as a backup plan for his established dosing time. Reminders could include cell phone reminders, calendar reminders, watch alarms, reminder stickers placed in visible locations, and friend/partner reminders. If possible, the interventionist works with the client to set the reminder during the session (e.g., setting an alarm on a watch or smartphone). For clients who are unable to set a reminder while in the session, the interventionist works with the client to develop a concrete plan of when and how he will set the reminder after the session is over.

Although many people who take PrEP do not experience any short-term side effects, it is important to create a plan if side effects do occur. The most common side effects with PrEP are gastrointestinal in nature (e.g., increased gas, diarrhea, changes in bowel habits, or nausea). The interventionist can explain that each of these side effects is relatively uncommon (Centers for Disease Control, 2011) and tend to be limited in duration to the early period of adjustment to the medication, and typically resolve within days to weeks of medication initiation without the need for additional intervention. If any of those side effects occur, the interventionist and client develop a plan to overcome those side effects. Examples of side-effect managing solutions include eating multiple small meals instead of fewer larger meals, using over-the-counter medication for symptom relief, or calling a trained medical professional if the symptoms persist for multiple days. The interventionist then gives the client an opportunity to ask questions, summarizes the content of the session, reviews the adherence plan for the week, reviews the plan of what to do if side effects occur, and informs the client about what will be covered at the next session.

Session 2: Focus on PrEP Adherence and Ongoing PrEP Education

The purpose of this session is to understand the client's experiences taking PrEP since the last visit with the interventionist, identify any side effects, monitor any missed doses through self-report, engage in problem solving barriers to adherence, and provide further

psychoeducation when needed. If the client has experienced any side effects, the interventionist should review the plan (established in Session 1) to make sure that the client feels confident about managing those side effects before moving forward with the Session 2 content. The interventionist may review PrEP education for an explanation of ways to manage common side effects such as using over-the-counter medications, adjusting dietary habits, or changing the dosing time. The client should consult a provider if there is concern about side effects or if there might be serious medication interactions; the interventionist and client can work as a team to develop a plan for this consultation if it arises.

It may be difficult for clients to talk to interventionists about missed doses as a result of social desirability bias, or even the clients' forgetting that they missed a dose. Because talking about missed doses is integral to effective adherence counseling, the interventionist should normalize nonadherence, and adopt a nonjudgmental attitude. For example, the interventionist could say:

- "It's been a week since we last met and I'm curious to hear about how the past week has gone. Taking PrEP can be difficult and I don't expect things to have gone perfectly this week. That is why we are here together!"
- "I want you to feel open about sharing your experiences this week with PrEP, even if things did not go perfectly. In fact, sharing that information will give us specific things to work on and make our time together most effective."
- "How many doses did you miss? What got in the way? Tell me about any times where you almost missed a dose."

The interventionist should identify and discuss *each* missed dose—rather than talking about them in general, which typically would result in not having the kind of detailed information that would be most helpful for the interventionist to use for CBT-consistent problem solving. Then they can work together to identify real or potential adherence barriers, and implement a problem-solving plan to overcome those barriers. Some common barriers clients may face when taking PrEP consist of forgetting, unexpected travel or overnight travel, staying at someone else's (could be a sex partner) place, experiencing side effects, mental health concerns, substance use, or actual or perceived stigma (e.g., that the client is sexually promiscuous).

In the following video, we return to Cody whose self-reported adherence indicated he did not miss a daily dose the first week. However, in Week 4, he reports missing a weekend dose and we provide a video example of how to problem solve and address his nonadherence. At this point in their work, Cody and his interventionist did not need to problem solve any barriers to adherence (although his adherence changes in Session 4). For clients who have 100% adherence, and who cannot articulate any barriers that may arise over the next week, reinforce their use of any of the strategies for maintaining adequate adherence, review their adherence plan as developed in Session 1, then flexibly move to another module that might meet the client's needs. However, after reviewing adherence and discussing in-depth the importance of daily dosing, Cody presented two questions commonly asked by PrEP users that focus on daily adherence (see Video Clip 3). While the first question broaches the importance of daily PrEP use to prevent HIV infection and resistance, the second question

relates to the risk of HIV infection from a partner who is HIV positive with a suppressed viral load.

During discussions of adherence to PrEP, some clients might state a common misconception that the body can build up a “tolerance” to the medications used in PrEP. This may be due to all the information about resistance to antiretrovirals, which can happen as a result of low adherence in the context of treatment. Thus, clients might believe that Truvada may not work to treat HIV should they become infected in the future. Clients should be provided with the correct information that the body does not build up tolerance to these medications. “Resistance” can only occur if as person has HIV, and there is the opportunity for the virus to mutate to a version that is resistant to one's medications. However, if a person does not have HIV, then there is no virus in the bloodstream, and it cannot therefore mutate to be resistant to PrEP.

Session 3: Follow-Up on Adherence and Focus on Sexual Risk Behavior

For clients who are experiencing little difficulty adhering to daily dosing, the sexual risk-reduction component is usually introduced at the third weekly visit. It is important to recognize that consistent condom use may not be a goal that clients have and, irrespective of their intentions, may not be attainable for all individuals at all times and in all contexts. In fact, this may be what drives some individuals to seek out PrEP. Thus, the goal of this module is to help individuals recognize any areas of vulnerability for HIV risk, as well as to minimize their risk of acquiring other STIs, and to help formulate a plan for behavior change, should the client wish to change any of the behaviors that may place him at risk.

The aim of this session is to help clients make informed decisions about sex and sexual risk, and involves a detailed review of sexual behavior (e.g., condomless sex), including a discussion about how individuals may still be vulnerable to HIV exposure and/or other STIs. To facilitate this discussion, the following questions may be helpful when completing the worksheet:

- “When it comes to sex, what do you do that is okay and what is not okay for you?”
- “How happy are you with your current sexual behaviors? What, if any, changes are you considering?”
- “What factors (e.g., your mood, where you have sex, partner type) make you step outside of your sexual comfort zone?”
- “Everyone who is sexually active with other people is at some risk of acquiring HIV or other STIs. Given your sexual comfort zone, and what you know about HIV transmission, which behaviors put yourself, or others, at risk for HIV and STIs?”

Upon completing the Sexual Comfort Zone exercise, the interventionist introduces the client to HIV knowledge and transmission risk behaviors. Topics in this educational component include understanding the highest risk activities for HIV acquisition (e.g., receptive anal sex without condoms), factors that increase risk of HIV infection (e.g., having a concurrent STI),

understanding the HIV viral load of HIV-infected partners, identifying the lowest risk activities (e.g., oral sex), and noting ways to reduce the risk of acquiring HIV and STIs. Next, the interventionist assesses what, if anything, the client wants to change, then asks if there are behaviors he is considering moving inside or outside of the comfort zone. If so, problem solving and MI may be used to change and formulate a plan for behavioral change in sexual behavior; if not, then the interventionist and client may move on to another module or end the session. An overarching framework is that the interventionist is not guiding the depiction of the sexual risk limits, nor having a preconceived judgment about risky behaviors, but instead is helping the client generate his own goals.

Another important feature of the sexual risk-reduction component, however, may be the assessment of the client's pros and cons of relying solely on PrEP for HIV prevention, versus using PrEP in combination with additional methods such as condoms or other behavioral risk-reduction practices like serosorting (choosing partners of the same serostatus), strategic positioning (choosing sexual positions that are less likely to acquire HIV), or withdrawal without ejaculation (Parsons et al., 2005). For clients who choose to rely solely on PrEP, interventionists may use MI techniques, nonjudgmentally as always in MI, to identify the pros and cons of this strategy, and can make sure that clients have a realistic understanding of the health risks to condomless sex. To introduce clients to incorporating safer-sex practices, we provide them with a video of a PrEP user named “Brett,” who describes how he uses condoms and discusses HIV status and PrEP use with his sexual partners (see Video Clip 4).

Many clients may view PrEP as part of a “sexual risk-reduction package” to be used in addition to condoms, testing, and other risk-reduction strategies. For these clients, problem solving and MI techniques may further create plans for developing and maintaining ongoing safer-sex practices. Booster sessions (see below) offer opportunities to reassess the comfort zone and evaluate any changes the client may be interested in making as his motivation to take PrEP changes.

Session 4: Follow-Up on Adherence and Problem Solving Barriers to PrEP Adherence

When the interventionist and client have identified barriers or potential barriers to PrEP adherence, they work together using a problem-solving approach (D'Zurilla, 1986; Nezu & D'Zurilla, 1989; Psaros et al., 2014; Safren et al., 1999) to generate a plan and a backup plan to overcome those barriers. This involves listing all (or potential) barriers to adherence, such as forgetting, unexpected travel (e.g., overnight), side effects, change in sexual risk activity, mental health concerns, substance use, or actual or perceived stigma associated with taking PrEP (e.g., stigma from partner or from another health care or non-health care professional). Next, the interventionist and client generate as many solutions to each problem as possible, via brainstorming. Then, the interventionist helps the client evaluate the pros and cons of each potential solution, with the goal of assigning each potential solution a rating from 1 (*least desirable*) to 10 (*most desirable*; rankings are not mutually exclusive). The best solution, and one potential backup solution, should be identified based on participant acceptability, likelihood of success, and ease of implementation. Some barriers may require

the merging of two solutions (e.g., for forgetting, a participant may wish to store his medication in an obvious place as well as to set a cell phone reminder).

We now return to Cody, who during Session 2 reported not missing any daily doses of PrEP, but for the past couple of weeks a pattern had emerged in which he has missed doses on Friday and Saturday nights. The client identified the potential barrier of forgetting, but the interventionist probed deeper and an assessment revealed that Cody's alcohol use was the precipitating barrier to adherence. Identifying the correct barrier is essential for the success of problem solving. Video Clip 5 provides an example of problem solving barriers to adherence. Problem solving involves identifying the problem (listing barriers to adherence), generating as many possible solutions to that problem as possible (i.e., brainstorming), and then picking one or two solutions and a backup plan for that problem.

After identifying the barrier, Cody and his interventionist brainstorm several potential solutions (see Video Clip 5). Brainstorming should occur without judgment. Even an idea that seems pretty outrageous at first, upon reflection, may be the key to an idea that works. During this time, it is important to be creative and to focus on quantity over quality of potential solutions. Next, the interventionist and client evaluate each of them by weighing the pros and cons of each potential solution, and scoring the potential solutions (with 1 = *least desirable* and 10 = *most desirable*; rankings are not mutually exclusive). Based on the rating, the interventionist and client work together to create a plan to ensure or enhance adherence. While the interventionist may offer potential solutions, it is important to remain nonjudgmental and allow the client to score each solution. Cody decided that taking his PrEP dose before he goes out with friends on Friday and Saturday nights, when drinking alcohol might later lead to forgetting to take a dose, would be the best possible solution. Finally, Cody developed a plan for implementation, identified when and how it will be implemented, and set up an alarm on his cell phone to remind him to take his medication. It is important to note that *problem solving* is a process that continues over time. If the plan or the backup plan does not work, then the client and interventionist can try again over the next week. If new problems arise, the interventionist and client can address those too, but treat each barrier as an individual problem to be solved.

Optional Mini-Modules: Mental Health and Substance Use Barriers

Because gay and bisexual men in the United States are, due to sexual-minority stress, at greater risk of mental health problems (e.g., depression and anxiety) and substance abuse (Cochran & Mays, 2008), and these problems can affect ART adherence in HIV-positive sexual-minority men (Blashill, Perry, & Safren, 2011; Magidson, Blashill, Safren, & Wagner, 2015; Mellins et al., 2009; Tucker et al., 2004), the intervention has additional optional, short-term modules to identify the impact of both mental health symptoms and substance use on PrEP adherence. These modules may be reviewed at the request of a participant, or when it becomes clear that a mental health concern (e.g., depression or anxiety— substance abuse will be addressed separately) is serving as a barrier to PrEP adherence. The goal is to focus on motivating individuals to seek outside treatment for those issues and problem solving ways to minimize the impact of such symptoms on PrEP adherence, assuming that not all persons delivering this intervention will be qualified to treat

mental health or substance use disorders, and that the duration of the intervention (four sessions today) would not be adequate to deliver an intervention to address substantial mental health symptoms.

It is important to note that the role of the interventionist in the context of a focused, short-term intervention like this is not characterized as that of a mental health provider for any/ all issues that arise in the context of the sessions. The interventionist could identify and reflect on mental health symptoms and their impact on adherence—or on the client's functioning more broadly—as a problem to be solved, or teach some straightforward intervention strategies like diaphragmatic breathing to decrease autonomic arousal, for example, as a coping skill consistent with a CBT approach. However, as we have noted, the present intervention is too brief and there is too much adherence-related material to cover for mental health symptoms to be a primary focus. Thus, we decided that the best way to address significant or interfering mental health symptoms was through supportive referral.

If substance use appears to be impacting PrEP adherence, the interventionist may want to introduce harm-reduction messages to clients who might not want to refrain from all substance use entirely, but who are interested in making some reductions to increase PrEP adherence or to improve other aspects of their lives. Before engaging in any change planning, the therapist should elicit from the participant an affirmation that substance use is, in fact, a problem for him, and that he is open to receiving information about changing his behavior, knowing that the decision to change rests firmly with the client. Given that the present intervention is too brief, and has its major focus elsewhere, addressing substance use cannot be a primary focus. Thus, the goals for the optional substance use mini-module are to help the client (a) identify his own patterns of substance use and the impact on adherence and/or sexual risk behavior, (b) determine that some aspect of his use or the consequences of that use are problematic, (c) assess/ ensure that the client is motivated to alter his substance use, and (d) give the participant referral resources for accessing the necessary level of treatment.

Follow-Up Booster Sessions

The goal of the booster sessions is to evaluate the success of the adherence plan developed in previous sessions and to identify and correct any new or potential barriers to adherence. That will, necessarily, look different depending on the client. Optional mini-modules may also be reviewed during these sessions, whether or not they were explored during the first four sessions. The interventionist may check in with the client, review previous or last session notes, review adherence over the time period since the last visit (e.g., past month), assess motivation to change behaviors for missed doses, identify strategies that require modification, and assess for any anticipated barriers to adherence. At a final visit, the interventionist can summarize the scope of work completed with the client since the beginning of their time together (e.g., challenges to adherence motivation, adherence skills, other sexual risk-reduction strategies). The interventionist may generate these study termination messages by asking:

- “Given all of our conversations over the past few months, what are your ‘take-home messages’ from this therapy?”

- "What are the things that you are really going to remember about PrEP and PrEP adherence?"
- "What are the things that you are really going to remember about sexual risk and protecting yourself against HIV?"

Conclusions

Based on Life-Steps for HIV treatment adherence (Safren et al., 1999) and the adapted Life-Steps for PrEP use in the context of serodiscordant couples in the Partners PrEP study (Psaros et al., 2014), our team constructed a CBT-based intervention to meet the adherence needs of PrEP using sexual-minority men in the United States. PrEP use, to prevent HIV acquisition in MSM, is an effective biomedical intervention strategy that requires adequate adherence for optimal protection (Anderson et al., 2012; Grant et al., 2010; Kashuba et al., 2012). In this manuscript—including a description of the intervention, case illustrations, and video role-play examples—we provide an overview of a CBT-based intervention for sexual-minority men who are at high risk of acquiring HIV, and who elect to take PrEP.

The video clips provide some useful examples of topics that interventionists might use during the course of the sessions that focus on improving PrEP adherence for sexual-minority men, as well as CBT-based clinical skills to address those topics. The video examples, which were designed to capture the "best-case" scenario for the sake of illustrating the techniques, might not be representative of this population as a whole. Participants in this study were highly motivated to take PrEP, though some sexual-minority men may not be highly motivated or may have comorbid conditions (e.g., mental health and substance use concerns) that limit their motivation and/or ability to adequately adhere to PrEP. A client seeking PrEP in the "real world" likely has some baseline motivation to receive and then adhere to PrEP. However, motivation may change over time based on changes in sexual behavior and HIV risk, adherence "fatigue," or a number of other factors. The intervention is designed so that interventionists gain a nuanced understanding of why an individual would like to use PrEP as an HIV prevention strategy at this time. Interventionists then help the client think through the pros and cons of using PrEP as an HIV prevention strategy, also at this particular time in his life. Often through these conversations, any ambivalence about PrEP use is resolved, either in favor of using PrEP or not, based on an individual's current circumstances.

Other psychosocial problems may be present for clients who are seeking PrEP (e.g., homelessness). The problem-solving module in this intervention could easily be adapted to deal with these problems by changing the target of the problem-solving exercise. Depending on the qualifications of the interventionist, the best "solution" may be to identify another provider who is better trained to directly manage the issue (e.g., referral to a case manager with access to housing information). The intervention could also be integrated into other cognitive behavioral-based interventions, such as CBT for depression, by understanding how depressive symptoms may impact PrEP adherence, or how depressive symptoms may contribute to another barrier to adherence, such as substance abuse. Lack of these complex

examples is a limitation to the current manuscript. However, therapists who have not worked with this population may find them useful to enhance their clinical practice.

Table 1 provides an outline of each session, the components and goals of each session, and worksheet topics for interventionists to consider when helping clients take PrEP regularly. This intervention manual was designed to be flexible, so that interventionists may introduce the components that are most important to the client's needs at different time points. In addition, the intervention might be most effective if it is introduced to the client during the first few weeks on PrEP and/or when reinitiating PrEP after discontinuation. Last, not everyone will need intensive adherence counseling or extended visits to complete all intervention components, so fewer sessions may be tailored as needed.

As noted earlier, sexual-minority men in the United States are at greater risk of mental health problems (e.g., depression and anxiety) and substance use behaviors (Cochran & Mays, 2008), and interventionists should be aware of these specific concerns when working with this population. Further, we understand that HIV transmission risk behavior co-occurs with multiple psychosocial conditions (Safren, Blashill, et al., 2011; Safren, O'Cleirigh, et al., 2011; Stall et al., 2003), and interventionists may need to augment their therapeutic approach to address these comorbidities. Therefore, future PrEP adherence interventions for patients with significant mental health symptoms could integrate mental health and substance use topics more thoroughly into a longer intervention, as described above. The Life-Steps intervention, as developed for treatment adherence, is a key component of CBT adherence, which integrates CBT for depression with Life-Steps for adherence. A similar approach could occur if mental health clinicians seek to integrate adherence counseling into their work with clients who use PrEP and need assistance with adequate protection from HIV via adherence to this agent. Another option would be that, for therapists who are treating male sexual-minority clients who begin PrEP, they might introduce components of the current intervention either formally or informally as part of their ongoing work (noting that there is not efficacy data on that approach).

Although high adherence of PrEP has demonstrated efficacy in decreasing acquiring HIV, a number of implementation questions still remain. Baeten et al. (2013) outline priority topics and questions to consider with an overarching unknown: Will HIV protection efficacy from PrEP use translate into substantive effectiveness in real-world practice? Additional important questions might be How might PrEP use increase sexual benefits and satisfaction (e.g., connection with others, pleasure and intimacy)? and How might these benefits increase PrEP adherence? Further research might include these considerations when implementing sexual risk-reduction strategies. This clinical manuscript may serve as a practical guide for interventionists, nurses, or other professionals involved with clients on PrEP in an outpatient setting to help sexual minority men adhere to PrEP directly as prescribed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This publication was made possible with the help from NIMH grant R34MH095584 awarded to Drs. Kenneth H. Mayer and Steven A. Safren. Some additional author time and support is from 5K23MH096651 (Dr. Christina Psaros). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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Table 1

Overview of Intervention Sessions

Sessions	Time point	Components	Main goals	Worksheet(s)
Session 1	Week 1	Introduction, assessment, education, and dosing scheduling	Build rapport, provide key PrEP information, set client's dosing schedule.	Pros and Cons of Adherence vs. Nonadherence
Session 2	Week 2	Focus on adherence and motivational interviewing techniques	Identify motivation around adherence, problem solving barriers to adherence.	Problem-Solving Worksheet
Session 3	Week 3	Follow up on adherence and focus on sexual risk behavior	Assess client's sexual risk behavior and build knowledge around sexual safety.	Sexual Comfort Zone and Pros/Cons to Condoms added to PrEP vs. PrEP alone worksheets
Session 4	Week 4	Follow up on adherence and optional mini-module (as needed)	Review previous topics, conduct an optional module.	See Optional Modules
Optional Module 1	Week 4	Mental health and breathing retraining (if needed)	Identify links between mental health symptoms and health behaviors.	Problem-Solving Worksheet
Optional Module 2	Week 4	Substance abuse counseling messages	Increase motivation to alter substance use patterns, harm reduction.	Substance Use Worksheet
Booster Sessions	Months 2 and 3	Follow up on adherence and content review	Specific content revisited is tailored to each client.	Previous worksheet(s) as needed

Table 2

Possible Pros and Cons to Taking PrEP

Topic	Pros	Cons
Maintaining high PrEP adherence	PrEP may afford me additional protection from HIV Allows me to achieve a greater sense of intimacy while feeling safer Counseling sessions may be helpful in supporting high adherence and making healthier lifestyle choices more generally	Possibility of side effects Have to take a pill every day Taking a pill every day reminds me that I am risky Not sexually active every day, so I wonder if I really need to take a pill every day May not get anything out of the counseling sessions
Not adhering to PrEP	Would be easier to take PrEP in a way that was consistent with sexual activity rather than every day It is easier not to take PrEP or attend study visits No medications mean no side effects Fewer reminders of my HIV risk	I remain at risk/high risk for acquiring HIV Not taking PrEP as prescribed may make me vulnerable to HIV I may need the support of the counseling sessions, at least in the beginning, to make sure I am taking PrEP properly