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Clinician Attitudes Toward CDC Interim Pre-Exposure Prophylaxis (PrEP) Guidance and Operationalizing PrEP for Adolescents

Tanya L. Kowalczyk Mullins, MD, MS,[1,2] Michelle Lally, MD, MSc,[3,4] Gregory Zimet, PhD,[5] Jessica A. Kahn, MD, MPH,[1,2] and the Adolescent Medicine Trials Network for HIV/AIDS Interventions

Abstract

Prior to issuing formal HIV pre-exposure prophylaxis (PrEP) clinical practice guidelines in 2014, the US Centers for Disease Control and Prevention (CDC) had released interim guidance for oral PrEP use among adults. Because oral PrEP may be used off-label for youth and may soon be indicated for minor adolescents, we examined the potential adoption of the interim guidance among clinicians who care for HIV-infected and at-risk youth. Individual, semi-structured interviews were conducted with 15 US clinicians who were recruited through an adolescent HIV research network. The theory-driven interview guide, consisting primarily of open-ended questions, assessed demographics, familiarity with the guidance, attitudes toward the guidance, and attitudes toward the use of the guidance for adult and adolescent patients. Transcripts were analyzed using framework analysis. Most clinicians (11/15) reported that the guidance was compatible with their practice, although several reported that some aspects, particularly frequency of follow-up visits, needed to be tailored to meet their patients' needs. We found variability in clinician reported characteristics of appropriate PrEP candidates (e.g., youth with substance use and mental health issues were noted to be both suitable and unsuitable PrEP candidates) and PrEP use in serodiscordant couples (e.g., whether PrEP would be recommended to a patient whose HIV-infected partner is virally suppressed). Clinician reported steps for initiation, monitoring, and discontinuing PrEP were largely consistent with the guidance. The observed variability in clinician practice with regard to oral PrEP may be reduced through interventions to educate clinicians about the content and rationale for guideline recommendations.

Introduction

Globally, human immunodeficiency virus (HIV) infection remains a public health threat, with 2.3 million new infections occurring in 2012 alone.[1] Despite prevention efforts, US youth continue to be heavily impacted by HIV, with 26% of an estimated 47,500 new infections in 2010 occurring in people ages 13–24 years.[2] New prevention methods are being developed. One such method, oral pre-exposure prophylaxis (PrEP), is the use of anti-retroviral medications, specifically tenofovir–emtricitabine (TDF-FTC), by HIV-uninfected people in order to prevent HIV acquisition. Studies demonstrated a 44–75% decrease in HIV acquisition among sexually active adults taking oral PrEP, with relative effectiveness closely tied to daily adherence.[3–5] TDF-FTC (brand name Truvada®) was approved by the US Food and Drug Administration (FDA) in 2012 for PrEP in adults.[6,7] In order to guide clinician use of this new prevention intervention, the US Centers for Disease Control and Prevention (CDC) released interim guidance for oral PrEP use among men who have sex with men (MSM) in 2011,[8] heterosexual adults in 2012,[9] and injection drug users in 2013.[10] Each guidance contains information about steps in determining eligibility for PrEP, PrEP initiation, frequency and content of monitoring visits, and steps in the discontinuation of PrEP. More recently, in May 2014, the US Public Health Service released a new PrEP clinical practice guideline, ''Preexposure Prophylaxis for the Prevention of HIV

[1]Division of Adolescent and Transition Medicine, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.
[2]University of Cincinnati College of Medicine, Cincinnati, Ohio.
[3]Division of Infectious Diseases, Department of Medicine, Lifespan Hospital System/Alpert Medical School of Brown University, Providence, Rhode Island.
[4]Providence Veterans Affairs Medical Center, Providence, Rhode Island.
[5]Division of Adolescent Medicine, Indiana University, Indianapolis, Indiana.

Infection in the United States-2014'' that supersedes the CDC interim PrEP guidance.[11]

Although clinical guidelines are designed to support evidence-based practice, clinician adoption of clinical guidelines is a complex process. Even when guidelines are available, clinicians may not follow them. Physician adoption of and adherence to published guidelines for routine HIV testing,[12,13] STI testing,[14] and HPV vaccination[15] are low. In one study of general practitioners, characteristics of the guideline and practitioner-related factors (including attitudes and barriers) were drivers of guideline adoption. Practitioners preferred guidelines that could be adjusted to particular patients and/or practice circumstances and those that allowed for incorporation of the knowledge and expertise of the practitioner.[16] Although the CDC PrEP guidance targets oral PrEP use in adults, clinicians caring for high-risk youth under age 18 years may consider using Truvada® off-label for PrEP. Further, the results of ongoing studies of PrEP use among youth under the age of 18 years may lead to an indication for PrEP in younger adolescents in the near future.[17] Clinicians may adapt the guidance through application of their clinical expertise. However, whether, and in what ways, the guidance may be adapted for use in adolescents is unknown.

The objective of the current study was to describe the potential adoption of the CDC PrEP interim guidance by a sample of clinicians who provide care to HIV-infected adolescents. Many of these clinicians also care for youth at-risk for HIV. This study sample was chosen because their attitudes and practices regarding oral PrEP are particularly important to define. These clinicians are likely to be early adopters of prescribing PrEP, as they have expertise with the PrEP medication and also may interact with adolescents who are at high risk of acquiring HIV, including sexual partners of HIV-infected patients. In addition, they are thought leaders with regard to PrEP, serving as content experts for other clinicians and likely influencing their prescribing practices. This study specifically examined adoption of the CDC interim guidance for the use of oral PrEP in adult MSM and heterosexual adults; the guidance for injection drug users had not been released at the time of the study. The aims of this analysis are to describe how these clinicians interpreted and adapted the CDC PrEP interim guidance for their clinical practice, in order to learn general lessons about how guidelines may be used in clinical practice and to provide insight into how such guidelines might be improved for use in clinical practice. Therefore, the findings from this study are relevant despite the recent release of new PrEP guidelines. Although this study focuses on US guidelines, lessons learned about clinician responses to national guidelines will be applicable to clinicians in other regions of the world. Because the guidance documents for MSM and heterosexual adults are very similar, these are collectively referred to as ''the guidance'' throughout this report.

Methods

The current analysis is part of a mixed-methods study designed to assess clinician attitudes and practices toward PrEP. The study, consisting of qualitative interviews followed by development and administration of a survey, was conducted through the NIH-funded Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN). The ATN supports research at 14 different sites in the US Eligible participants included clinicians (physicians, nurse practitioners, and physician assistants) who were affiliated with an ATN clinical site and who spoke English; personal experience prescribing PrEP was not required. Contact information for eligible clinicians was obtained from the ATN and from each of the site leaders. A recruitment email was sent to all eligible clinicians, and we attempted to maximize the geographic diversity and diversity of types of clinicians. The study was reviewed and approved by the institutional review board of Cincinnati Children's Hospital Medical Center, and the requirement for written informed consent was waived.

Interviews were conducted between October 2, 2012 and April 23, 2013, after the US FDA approval of Truvada® for oral PrEP in July 2012 and prior to the release of the new US Public Health Service guidelines in May 2014. Participants completed one individual semi-structured interview. All interviews were conducted in a private location and by the same trained interviewer (TKM). Interviews were conducted face-to-face at the twice-yearly network meeting or by phone at the preference of the participant. The Theory of Planned Behavior (TPB) and Diffusion of Innovations Theory (DOI) provided the theoretical framework for the interviews. The TPB states that attitudes, subjective norms, and perceived control predict intention to perform a behavior, such as prescribe PrEP.[18] The DOI proposes that characteristics of an innovation (such as relative advantage, compatibility, and complexity), individual characteristics of adopters of the innovation, and characteristics of the setting are associated with adoption of an innovation.[19] Interview guides, composed primarily of open-ended questions, were designed to explore personal and practice demographics, level of familiarity with PrEP guidance, attitudes toward the guidance (i.e., ''How well does this guidance fit with your practice?'' ''What factors would help or facilitate use of the guidance in your practice?''), and clinician use of the guidance, both for adults and for adolescents younger than age 18 (i.e., characteristics of potential PrEP candidates, monitoring while on PrEP, and conditions to stop PrEP). A copy of the interim guidance for PrEP use in MSM and heterosexual adults was provided for clinicians to review and comment upon. Interviews lasted about 1 h on average. Participants received a $50 gift card in compensation for their time. Interviews were digitally audio-recorded and transcribed by an independent transcription agency. All transcripts were cleaned by the interviewer through review of the transcript and the original audio-recording. Field notes taken during interviews were added to transcripts prior to analysis. Data were analyzed using a five-step framework analysis approach (familiarization, identification of thematic frameworks, indexing, charting, mapping/interpretation)[20,21] and employing NVivo (version 10). Following familiarization with the data, the first author generated preliminary themes. A team of researchers (GZ, JK, ML) who were blinded to participant identities independently reviewed themes and thematic coding to develop consensus.

Results

Participant characteristics

Fifteen participants completed the interviews: 13 physicians and 2 nurse practitioners. Physician specialties included

adolescent medicine, immunology, infectious diseases, and pediatrics. Participant characteristics are shown in Table 1. Overall, 6 participants (40%) had prescribed PrEP in the past.

Attitudes toward CDC interim PrEP guidance

Overall, clinicians rated themselves as somewhat or very familiar with the guidance for PrEP use in heterosexual adults (9/15) and adult MSM (13/15). Most clinicians (11/15) reported that the guidance was compatible or ''fit'' with their practice, providing a useful reference tool and validating the clinician's use of PrEP. Among the 4 clinicians who reported that the guidance was not compatible with their practices, the recommended frequency of visits (i.e., every 3 months) was the most remarked upon part of the guidance. Clinicians described a need to individually tailor the frequency of visits and suggested that adolescents may require more frequent follow-up. Following review of the guidance during interviews, clinicians reported several barriers to adoption. Highlighted was the complexity of the guidance and lack of compatibility with physician practice, including: (1) cautions against using PrEP in women of childbearing age while Truvada® is used for HIV treatment in this group of women; (2) lack of clarity about how to define ''substantial ongoing risk'' (''Just sort of the details you'd like to know aren't completely delineated…'Substantial ongoing high risk' is a little vague, so it leaves room for judgment, that's all.''); and (3) concern that suggested limits on provision of refills may negatively impact the harm reduction intent of PrEP. Facilitating factors for guidance adoption included adequate access to PrEP and inclusion of the recommendations into a template in an electronic medical record. Clinicians offered suggestions to improve the compatibility of the guidance with practice, specifically through the inclusion of additional recommendations for (1) counseling about potential development of HIV resistance with intermittent use of PrEP, (2) counseling pregnant women about PrEP, (3) use of PrEP in serodiscordant couples who are trying to conceive, and (4) the benefits of PrEP in youth.

Table 1. Clinician Characteristics

Characteristic	*Number (percent)*	*Mean (SD) [range]*
Training background		
Physician	13 (87)	
Nurse practitioner	2 (13)	
Female	9 (60)	
Age (years)		47.1 (8.9) [34–61]
Region of the United States in which participant practices		
Northeast	5 (33)	
Southeast	4 (27)	
Midwest	3 (20)	
Southwest	1 (7)	
West	2 (13)	
Medical practice setting		
Urban/academic	15 (100)	
Years worked with at-risk youth		16 (9) [3–30]
Number of HIV-infected adolescents (age less than 18 years) seen per week		9.6 (12.9) [0–50]
Experience prescribing PrEP	6 (40)	

Adaptation of PrEP guidance

Determining eligibility for PrEP. According to the CDC guidance, potential PrEP candidates include patients who are ''at ongoing, high risk for acquiring HIV infection,''[8,9] have a calculated creatinine clearance of ≥ 60 mL per min, and are not breastfeeding.[8,9] Although the guidance recommends treating active hepatitis B, it does not cite hepatitis B infection as a contraindication to PrEP.[8,9] The guidance advises cautioning women that the effects of PrEP on infants are unknown, but PrEP is not contraindicated in pregnant women or women of childbearing age.[9]

Clinicians who were interviewed provided detailed descriptions of the characteristics of people who would and would not be appropriate PrEP candidates (Table 2). Interestingly, presence of mental health diagnoses or substance abuse issues were reported to be characteristics both of appropriate and unsuitable candidates for PrEP. Some clinicians reported that presence of either of these issues was an indicator of a person potentially engaging in higher risk sexual behavior, while other providers suggested that mental health diagnoses and substance abuse may negatively impact adherence to PrEP. One-third of clinicians reported that decisions about who would not be a suitable PrEP candidate needed to be individualized for each potential PrEP user. A few providers noted that those who would be most successful at adhering to PrEP would likely be able to use other HIV prevention measures, while those patients who would most benefit from PrEP would have the greatest challenges for adherence: ''You want to use it with the highest risk people, but those are the kids—and adults too—who are least likely to follow through.''

Tremendous variability in clinician approaches to the use of PrEP in serodiscordant couples was noted. Use of PrEP was thought to be appropriate for serodiscordant couples who were attempting pregnancy. Viral load and ART status were important factors in decision making about PrEP in serodiscordant couples, but there was not consensus on how these factors would influence clinician decisions. Some clinicians ($n=5$) would recommend PrEP even if the HIV-infected partner was on ART and virally suppressed, while other clinicians ($n=4$) would not recommend PrEP in that scenario. Other clinicians described using PrEP as a bridge prevention method until the HIV-infected partner was virally suppressed and using the viral load to help tailor their counseling of patients about the risks and benefits of PrEP in their particular situation.

Initiating PrEP. When initiating PrEP, the CDC guidance recommends documenting that a patient is HIV-uninfected via antibody testing; testing for acute HIV infection in the presence of symptoms; confirming that the patient is at risk of HIV infection; testing for creatinine levels, hepatitis B infection, and other STIs; and providing ''risk-reduction and PrEP medication–adherence counseling and condoms.''[8,9] The guidance also recommends prescribing once daily TDF-FTC, discussing the patient's plans for pregnancy, and

Table 2. Clinician Reported Factors for Determining Eligibility for PrEP

Clinician reported factors for determining eligibility for PrEP	*N (%)*	*Illustrative quotations*
Characteristics of good candidates for PrEP		
Populations at high risk of HIV		
Long-term partners of HIV-infected patients	12 (80)	''And then I also would consider prescribing PrEP in anybody who's negative who…is in a serodiscordant relationship, whether the patient is male or female.''
Sex workers/transactional sex participants	9 (60)	''We see a fair number of YMSM [young MSM] and transwomen who are engaged in sex work, and they're often not in as good a place in terms of negotiating condom use but often a little bit more willing to regularly engage in taking medication, that that wouldn't affect their economics.''
Men who have sex with men	7 (47)	''I would consider using PrEP in young men who have sex with men who report history of risky behavior, meaning that they have receptive anal intercourse or that they have inconsistent use with condoms.''
People with unsafe sexual behaviors	7 (47)	''If they had a history or they had ongoing like statement that they were unwilling to use condoms.''
High risk heterosexual people	5 (33)	''Basically for heterosexual, what their risk is for acquiring HIV. Are they high-risk, meaning, do they have a known partner who's positive, are they having multiple partners, are they engaged in sex work or sex trade?''
People who have sexual contact with known HIV-infected partners (not in an ongoing relationship)	4 (27)	''If somebody said, you know, kind of gave me a compelling reason to say 'I really have a hard time regularly using condoms. I come in contact with [HIV-infected] people.'''
Transgender women	3 (20)	''…Essentially any patient who…male patient or transgender female who identifies any sex with other men…will trigger an automatic sort of assessment [for PrEP].''
People with problem-level alcohol or substance abuse	3 (20)	''If they told me that they were doing a lot of injection drugs or club-type drugs and going to a lot of those kinds of parties or social gatherings where they were basically incapacitated to make good decisions, especially in the MSM population that we take care of here…''
People with history of multiple STIs	1 (7)	''If you have someone who's had multiple recent STIs, then that's another good proxy for being at risk for HIV infection.''
Anyone who asks for PrEP and is willing to take it	4 (37)	''…Someone who asked for it, I'd be much more likely to prescribe it because I think that that's sort of a conscious decision of them actually wanting it and a sign that they may be more adherent to it.''
Ability to adhere to PrEP regimen	3 (20)	''Now, I would want to make sure that they know that they would have to, first of all, use it every day for it to be effective.''
Ability to adhere to necessary ongoing monitoring for PrEP	3 (20)	''I'd have to have at least some assurance from the patient that I'd be able to see them regularly.''
Ability to access PrEP	2 (13)	''So if they [PrEP candidates] did happen to have insurance then I could prescribe, but…I can't prescribe Truvada® to someone who doesn't have insurance…And then if they do have insurance, I'm sure that I'm going to get a hard time from insurance companies, so that it may not be practical for them [those patients] either.''
Older age (over age 18 years)	1 (7)	''I would be more willing [to prescribe PrEP] with someone who is 18 [years old] or older.''
Other methods of risk reduction have been exhausted	1 (7)	''I think that I would also seriously consider it in someone who has the means to access it who we may have exhausted all other tools at that point and we want to reduce risk.''

(*continued*)

TABLE 2. (CONTINUED)

Clinician reported factors for determining eligibility for PrEP	*N (%)*	*Illustrative quotations*
Inability to control risk, such as due to relationship factors	1 (7)	''I think I would look at the patient's level of risk, their ability to control that level of risk, and then perhaps other markers such as frequency of having had other STIs that they've not been able to control well themselves.''
Characteristics of unsuitable candidates for PrEP		
Inability to adhere to PrEP	9 (60)	
Unwilling or unable to adhere	6 (40)	''If they were unwilling to take a pill, I guess that would sort of exclude the idea [of PrEP].''
Substance abuse	4 (27)	''If they're a drug user, probably not a good candidate [for PrEP].''
Mental health diagnoses	2 (13)	''Issues with substance abuse and unfortunately mental health that is not necessarily addressed. It definitely plays a role as well [in determining who is a candidate for PrEP].''
Unstable housing	1 (7)	''It would be patients that you could not see them for long term follow-up, so I will not be comfortable, again, prescribing PrEP if the patient doesn't have a stable situation or is homeless, or doesn't have kind of a way to contact them. Again, because there are risks and that medication needs to be followed up, you know, as HIV medications are as well.''
Not at risk or low risk for HIV infection	8 (53)	
Lack of risk factors or low risk for transmission	6 (40)	''If they are using condoms and talk about sort of the either long-term relationship or series of serial monogamy, if they don't have a history of STDs, if they are fairly consistent in terms of their preventive care and that sort of thing, then I would think of them as probably being a group way down on the totem pole in terms of the sort of things that would make me want to bring up PrEP with them.''
Heterosexual people not in a serodiscordant relationship	4 (27)	''I think in heterosexuals that the risk of seeing somebody casually coming into contact with someone HIV positive is too low to really say that this is a viable alternative or viable option.''
Uninfected partners of HIV-infected patients who are on ART with undetectable viral load	1 (7)	''If their partner, you know, is my patient and on antiretroviral therapy and has an undetectable viral load, then I would not recommend it [PrEP].''
Presence of a co-existing medical illness	8 (53)	
Renal disease	6 (40)	''Someone with renal disease would not be a candidate [for PrEP].''
Hepatitis B	3 (20)	''If they have hepatitis B infection, I would be uninclined to use it because of the fear of making the hepatitis worse.''
Liver disease	2 (13)	''I mean, I guess someone who obviously had medical reasons not to [take PrEP], right?…Had kidney problems or other fulminant liver disease or other major medical problems.''
Low bone mineral density	2 (13)	''Bone mineral density issues.''
Presence of allergic reaction, toxicity, or side effects to medication	3 (20)	''I guess only if they had somehow a sensitivity to the ingredients, but I don't know that we would know that.''
Inability to access PrEP medication (e.g., lack of insurance)	2 (13)	''The only other people I guess who wouldn't be a candidate is who I couldn't get it for. Completely uninsured and couldn't pay for it…''
Pregnant or breastfeeding	2 (13)	''I would probably…be reluctant to prescribe anything in pregnant women that isn't, you know, hasn't been clearly approved for them and it [Truvada®]'s not clearly approved for women who are pregnant and don't have HIV.''
Unlikely to reduce risk behaviors	1 (7)	''I think that I'm not sure if I will necessarily prescribe [PrEP] if I see that I cannot necessarily change the high risk behavior…PrEP should be used as kind of a bridge to overcome a high risk scenario, but with the goal that at some point, you know, it can be discontinued.''

counseling pregnant women about the unknown effects of PrEP on the fetus.[9]

Interviewed clinicians described three primary steps in initiating PrEP that largely paralleled the steps in the CDC guidance: counseling at the time of prescription (including discussing risks and benefits of PrEP), performance of screening laboratory testing (including HIV testing), and actual prescription of the medication (Table 3). HIV testing was reported to be critical in ensuring that the patient is uninfected, but there was lack of consensus about the optimal testing method. Clinicians voiced concerns that negative HIV antibody tests might be obtained while a patient is in the window period of infection and suggested that two sequential negative tests might be required prior to starting PrEP. Other clinicians suggested that viral load testing might be an optimal method to establish that a patient is HIV-uninfected or could be used for testing someone with symptoms concerning for acute HIV infection.

Clinicians were asked about the potential role of behavioral interventions in the delivery of PrEP, such as interventions to promote safer sexual behaviors or adherence. Consistent with the guidance, most clinicians (11/15) reported that behavioral interventions should be a necessary part of PrEP delivery: ''I think in order to maximize the benefit of PrEP, PrEP needs to come with other non-biomedical interventions or prevention methods, and that includes behavioral interventions and condom promotion and the avoidance of multiple sex partners and STDs. The main thing about PrEP is adherence, so I think the intervention to improve adherence has to be there.'' Suggested topics for interventions included: condom use/safer sexual behaviors, education about the risks/benefits of PrEP, adherence to PrEP, avoidance of substance use, and building self-esteem. Clinicians described various strategies to enhance patient adherence to PrEP, including educating about the potential side effects of PrEP and the need for adherence, encouraging patients to ''practice'' using a placebo pillbox before starting PrEP, discussing the use of social support networks, promoting use of reminder systems, and scheduling frequent follow-up visits. Clinicians suggested that such interventions could be delivered by a team, the clinician, or as part of a formal program. In contrast to the guidance, three clinicians reported that such interventions would not be necessary: ''I don't think it [a behavioral intervention] has to be [required]. I think it depends on the person's risk.''

Monitoring and follow-up after PrEP initiation. The CDC guidance recommends follow-up visits every 2–3 months, consisting of assessment of adherence, assessment of risk behaviors, and testing for HIV, pregnancy, STIs, and serum creatinine.[8,9] Consistent with the guidance, clinicians noted that regular monitoring and follow-up visits were an important aspect of providing PrEP (Table 4). However, there was variation in the suggested frequency of follow-up visits. Most clinicians recommended that the first follow-up visit occur within 2–4 weeks of PrEP initiation, with subsequent visits at intervals varying from monthly to every 6 months. Several clinicians noted a need for flexibility (such as having phone follow-up) and sensitivity to each patient's situation: ''Because I'm dealing with adolescents, it would depend a little bit on the situation and on the person and how reliable I think they were to talk to me on the phone or come in or whatever.'' One clinician noted that intensive follow-up and monitoring may interfere with the harm reduction goals of PrEP: ''So we have to pretty much come up with some understanding that's going to take into account the reality of the behavior in their lives at the same time that we don't create a situation that may be causing them sort of significant physical harm from Truvada® side effects.''

Discontinuing PrEP. According to the CDC guidance, PrEP may be discontinued at the request of the patient, if the patient becomes HIV infected, or for safety issues.[8,9] In contrast, most interviewed clinicians (14/15) identified lack of adherence to PrEP or missed monitoring visits as a reason to stop PrEP (Table 5). A few clinicians (3/15) reported that they would tolerate some degree of nonadherence without discontinuing PrEP: ''…Because I don't really know whether intermittent PrEP works and if they say, 'I can't remember to take it every day, but I always take it before I go out on the weekends and afterwards,' then I'd maybe leave them on it.'' Over half of clinicians reported that they would be willing to restart PrEP if the patient wanted to restart it, although some clinicians reported that they would need to be convinced that the patient's adherence would be better. Clinicians voiced a number of concerns about continuing to prescribe PrEP in the face of inconsistent adherence, including concerns about development of viral resistance, misuse of resources, lack of protection against HIV infection, and patients feeling protected from HIV when they are not.

Discussion

In this study, we describe how clinicians who provide clinical care to HIV-infected adolescents and at-risk youth interpreted and adapted or planned to adapt the CDC PrEP interim guidance for their clinical practice. This is the first study to our knowledge that examines attitudes about and use of this guidance among clinicians. The clinicians included in this study are likely to be among the earliest adopters of PrEP in adolescents due to their experience with the medication and their contact with the sexual partners of HIV-infected adolescents, persons likely to be among the first target groups for PrEP.

Although clinicians overall were familiar with the guidance, there were areas in which clinician practice diverged from the guidance. Similar to findings in other studies,[22–27] we found variability in clinician reports of PrEP target populations. Clinicians were explicit in reporting which patients would be eligible for PrEP, including patients who are members of specific populations who are at high risk of HIV infection, as well as those able to access and adhere to PrEP and PrEP monitoring. This explicitness may be related to clinicians attempting to construct an operational definition for PrEP candidates who would be seen in their clinical settings, particularly as clinicians reported feeling that the guidance is vague in terms of determining exactly who would be an appropriate candidate. Clinicians also varied in their approaches to using PrEP in serodiscordant couples. These differing approaches may be driven by evidence that treatment of the HIV-infected partner in a serodiscordant relationship significantly decreases the risk of HIV transmission.[28,29] Variability was also noted in frequency of follow up-visits: clinicians often preferred more frequent follow-up than is

Table 3. Clinician Reported Steps in Initiating PrEP

Clinician steps in initiating PrEP	*N (%)*	*Illustrative quotations*
Counseling at the time of prescription		
Discuss risks and benefits of PrEP	7 (47)	''And then I think the second part is really an educational piece about the risks and benefits, the potential efficacy, the potential downsides of PrEP, and then write a prescription and hope they take it.''
Ensure that patient is at risk for HIV infection	4 (27)	''Well, first off, recognizing risk in your patients. So, you know, you have to be able to ask the questions to understand whether or not there is potential risk [of acquiring HIV] there.''
Counseling about the efficacy of PrEP	3 (20)	''And talking about the data to support that it's [PrEP is] helpful—or it's effective [for preventing HIV infection].''
Counseling about PrEP as part of a comprehensive prevention package, which includes condoms and other safer sex behaviors	3 (20)	''The first important thing is to make sure, number one, that the person who you're prescribing for understands what PrEP is, that it's not 100% protection against getting HIV, and that we do recommend using it as part of a comprehensive HIV prevention strategy if they're using condoms and STI testing, partner communication, all the things that we're already doing and using PrEP as an added component to that.''
Counseling about need for adherence to PrEP medication	3 (20)	''The main thing about PrEP is adherence, so I think the intervention to improve adherence has to be there.''
Assessment of substance abuse and mental health issues	1 (7)	''We'll include conversations or assessments about substance abuse and mental health, basically those other referrals that we can do.''
Assessment of patient willingness to take long-term medications	1 (7)	''Typically, it [a PrEP candidate] will be a patient that is HIV negative that is involved in high risk sexual activity and is willing to take a long term therapy.''
Performance of screening laboratory testing		
HIV testing to ensure that patient is HIV-uninfected	4 (27)	''Second thing would be making sure that the person who you're going to prescribe PrEP to is HIV uninfected. ''
Hepatitis B serology	3 (20)	''I think obviously it's also important to know what the person's Hep[atitis] B status or risk factors would be because Truvada® is treatment for Hep B, which would be great if they have it but if you're not even assessing if they have it, or whether they're immune to it or providing immunizations…''
Creatinine testing	1 (7)	''If they're [HIV] uninfected at baseline, you would do baseline creatinine screening…''
Liver function testing	1 (7)	''Basically we'll do serological testing for…liver function.''
Testing for other sexually transmitted infections (STIs)	1 (7)	''If they're uninfected at baseline, you would do…baseline sexually transmitted infection testing.''
Actual prescription of PrEP medication		
Oral tenofovir/Truvada®	11 (73)	''Well, definitely the recommendation is for the one medication – Truvada®…I know from my adult [medicine] colleagues, mostly the accepted PrEP has just been Truvada®.''
Prescribe for daily use	7 (47)	''Well, the way that I would prescribe it would be probably Truvada® and then I would say one pill once a day every day for somebody who I assessed to be at high risk [of acquiring HIV infection].''
Potentially add a protease inhibitor to tenofovir regimen	1 (7)	''Well, definitely the recommendation is for the one medication—Truvada®—and some [patients], if they're able to, should actually get the PI [protease inhibitor] also.''
Topical tenofovir	1 (7)	''There are the topical tenofovir that's—I think it's commercially available.''

suggested by the guidance. Our findings are consistent with a prior study of HIV healthcare providers which found departure from the CDC guidance recommendations in testing for HIV infection, confirming high risk for acquiring HIV infection, screening/treatment for STIs, and screening for Hepatitis B.[27] Variability in approaches to PrEP may be due to lack of familiarity with the guidance or adaptation of the guidance to fit a clinician's practice. Such variability may be reduced through inclusion of more specific recommendations for determining eligibility for PrEP and development of resources for clinicians to use when evaluating patients. The new 2014 PrEP clinical guideline contains more concrete recommendations for determining eligibility for PrEP and counseling about PrEP, and if used in combination with the clinical providers' supplement to the guideline, may reduce the variability that we found in the current study.[11,30]

When considering how these clinicians adapted the guidance, several general lessons emerged. In general, clinicians

Table 4. Clinician Reported Content of Follow-Up Visits Following PrEP Initiation

Clinician reported content of follow-up visits	*N (%)*	*Illustrative quotations*
Assess risk behavior	4 (27)	''We would want to see them relatively often in order to…continue to assess their risk behavior…''
Assess adherence to PrEP	1 (7)	''You would need to follow…adherence.''
Assess for side effects	1 (7)	''I think there would be the need to have early contact about side effects and to know if there's tolerability of the medications…''
Laboratory monitoring		
HIV testing	11 (73)	''Follow up HIV testing of course would always be necessary to see if there was actually some kind of conversion during the subsequent activities and use of PrEP.''
Hepatitis B testing	3 (20)	''You also want to talk about hepatitis B risk and do hepatitis B testing.''
Monitoring for PrEP toxicity		
Renal function testing	10 (67)	''And then, because [of] the medication that is used, also renal function.''
Liver function testing	2 (13)	''We've got the regular sort of follow-up on the liver function and kidney function and that sort of stuff.''
Complete blood count	1 (7)	''…We need to also monitor for toxicities from the PrEP itself…probably a CBC…I think it would be hard to have someone on an antiviral or antibiotic or anything in the antimicrobial realm, anti-infective, and not check blood counts…''
STI testing	7 (47)	''Obviously testing for other STIs, because it doesn't do much good if you're getting syphilis or gonorrhea or chlamydia or whatever.''
Pregnancy testing	1 (7)	''For young women, young natal females, their pregnancy status.''
Any other testing recommended in most recent iteration of the guidance	3 (20)	''I would go with I guess what the latest recommendations would be.''

found the guidance to be compatible with their practices, demonstrating that the guidance is compatible overall with the needs of this group of clinicians. Lack of a clear definition of which patients would be considered ''at substantial ongoing risk of HIV infection''[8,9] negatively impacted the ease of use of the guidance. Additionally, many clinicians adjusted the recommendations in the guidance based on their own clinical experience, including in determining PrEP eligibility and frequency of follow-up visits. Prior studies of clinicians also demonstrated that clinician adoption of guidelines is influenced by their expertise and to meet the needs of their patients.[16,31] Further, the PrEP guidance is clearly labeled ''interim guidance,'' which may be perceived differently by clinicians than other formal guidelines. Clinicians may perceive that there is less evidence supporting an ''interim guidance'' and thus may be more likely to adapt the guidelines to their own clinical practice. In addition, the guidance is designed for adults over age 18 years, which is the age group for which PrEP is FDA-approved. Because the clinicians in this study have experience caring for HIV-infected adolescents who face great psychosocial challenges,[32] these clinicians may perceive that adolescents receiving PrEP need more intensive support and monitoring.

Clinicians offered suggestions that may be important in the design of future guidance. First, clinicians suggested including more specificity about who would be a candidate for PrEP. Clinicians also voiced confusion about the inclusion of a caution against using PrEP in women of childbearing age because these clinicians use Truvada® for HIV treatment in this group. In considering their use of the guidelines, clinicians reported a need for additional guidance on counseling about development of HIV resistance with intermittent use of PrEP, counseling pregnant women about PrEP, use of PrEP in discordant couples who are trying to conceive, and data supporting benefits of PrEP in youth. The newly released 2014 PrEP clinical guidelines address some of these areas, including providing more specificity about PrEP candidates, removing the caution about PrEP use in women of childbearing age, and providing information about PrEP use during conception, pregnancy, and breastfeeding.[11,30] These guidelines also provide clinicians with the information needed to counsel patients about many of the concerns that patients themselves may have about PrEP, including short and long term health effects, the use of PrEP as part of a combination prevention package, and cost.[11,33–35] Including additional topics, such as intermittent use of PrEP and use of PrEP in youth, in future iterations of the guidance may help meet the needs of clinicians who are prescribing PrEP.

This study had several limitations. First, participants were recruited through a single research network. However, clinicians practiced at different clinical sites with varied patient populations; thus we would expect these clinicians to represent a range of views of clinicians who treat HIV-infected and high risk adolescents. Second, this is a relatively small sample of clinicians. However, our purpose in using qualitative research was to generate in-depth understanding of

Table 5. Clinician Reported Reasons to Discontinue PrEP

Clinician reported reasons to discontinue PrEP	*N (%)*	*Illustrative quotations*
Lack of adherence		
Failure to adhere to follow-up monitoring visits	14 (93)	''If someone is really not coming in for monitoring, I wouldn't re-prescribe it.''
Poor adherence to PrEP medication	7 (47)	''I think if somebody was having such poor adherence that it seemed like it might not be effective, then I might say, 'Maybe this isn't the best strategy for you, and we can work on other prevention strategies.'''
Patient is selling or sharing PrEP medication	3 (20)	''If they were using it very inappropriately, you know, if they were giving it to friends…sharing it.''
Presence of a mental health or substance abuse issue that interferes with adherence	1 (7)	''…Mental health or substance abuse. I think that any of those scenarios would be included to decide on discontinuing PrEP.''
Patient self-discontinues PrEP	1 (7)	''I think probably what would happen is they would just stop coming to clinic to get it and that would be where it would end.''
Decreased risk of patient acquiring HIV		
Patient in a serodiscordant relationship in which the HIV- infected partner has started ART/virologically suppressed	4 (27)	''If they're in a stable relationship and the positive partner is now having good virologic control, then I might stop PrEP in the negative person.''
Patient has skills/power to negotiate safer sexual behavior	3 (20)	''If the person had enough skills that he or she could negotiate safer sex techniques and be in more control over partner selection…''
Patient is now in a monogamous relationship	2 (13)	''And then if someone felt that their risk level was decreased, so if it was someone who had had multiple partners before who is now in a mutually monogamous relationship.''
Patient has matured developmentally	1 (7)	''One part would be the positive aspect where the developmental shift has occurred in an individual. They're more empowered, able to manage and negotiate barrier use, and in a sense then the benefit of Truvada® is outweighed by the risks of Truvada®.''
Safety reasons		
Development of abnormal laboratory testing or toxicity (i.e. decreased bone mineral density, renal dysfunction)	7 (47)	''And of course if there are side effects, you know, changes in bone density, or renal, or if they have any adverse effects, I'd stop prescribing it.''
HIV seroconversion	5 (33)	''Obviously if somebody were to seroconvert and become HIV positive, I would stop PrEP.''
Allergic reaction to drug	2 (13)	''You've had an allergic reaction then I'd clearly have to stop it and not re-prescribe it.''
Newly acquired hepatitis infection	2 (13)	''If they acquired a hepatitis infection.''
Development of new medical contraindications	1 (7)	''Other medical diagnoses come into play that was not there initially that, you know, we have to be aware of or would be like a relative contraindication…to continue prescribing it.''
Pregnancy	1 (7)	''Become pregnant…. I think that it's not approved in pregnancy.''
Psychosis	1 (7)	''Someone who is floridly psychotic, I wouldn't feel comfortable to prescribe [PrEP].''
Severe side effects	1 (7)	''If someone was having side effects or adverse effects from PrEP that were so severe that they weren't able to tolerate taking the medications and the interventions that we had recommended to decrease that [side effects].''
Other		
Patient wants to stop PrEP	1 (7)	''First of all, if the patient wants to stop, I would stop. I can't go on without their consent.''
Availability of better biomedical prevention method	1 (7)	''If something better comes out, like a vaginal or anal instilled product.''

clinician attitudes, intentions, and practices, not to necessarily produce widely generalizable results. Third, this sample of clinicians included both clinicians who had experience prescribing PrEP and those who had not prescribed PrEP; the specific attitudes of these subsets of clinicians may be different. However, our objective was to describe the full range of attitudes toward the guidance.

In conclusion, this is the first study to our knowledge to examine clinician attitudes toward, and adaptation of, the CDC PrEP guidance. Overall, we found that clinician practice diverged from the guidance in several areas. Variability in clinician adoption of guidelines may be reduced by developing educational interventions targeting clinicians. Our findings suggest that providing education to clinicians about the content of guidelines and the rationale for guideline recommendations should be included in such interventions. Guideline authors should recognize that clinicians adapt guidelines to fit the needs of their patients and practices and consider identifying where such flexibility would be acceptable while still meeting the guideline recommendations.

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Address correspondence to:
Tanya L. Kowalczyk Mullins, MD, MS
Division of Adolescent
and Transition Medicine, MLC 4000
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue
Cincinnati, OH 45229

E-mail: tanya.mullins@cchmc.org