

PUBLIC ENGAGEMENT WEBINARS: RESPONSES TO DRAFT CLINICAL PRACTICE GUIDELINES FOR PREP IN THE US

Introduction: In March and April 2013, the Division of HIV/AIDS Prevention at the Centers for Disease Control and Prevention conducted three public webinars to present key recommendations from draft clinical practice guidelines for preexposure prophylaxis (PrEP) use in the United States. The purpose of the webinars was to obtain input from three groups of stakeholders: clinicians (April 2), community stakeholders (March 26), and public health leaders (March 29).

Below is a summary of the comments received during the webinars. These comments have also been provided to the panel of external peer reviewers now reviewing the draft guidelines (<http://www.cdc.gov/hiv/strategy/planning/pdf/PRP%20PrEP.2.pdf>).

Draft Recommendation 1A:

Daily oral PrEP with the fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg has been shown to be safe and effective in reducing the risk of sexual HIV acquisition in adults, therefore:

- PrEP is recommended as one prevention option for sexually-active adult MSM at very high risk of HIV acquisition
- PrEP is recommended as one prevention option for adult heterosexually active men and women who are at very high risk of HIV acquisition

Summary of Comments for Draft Recommendation 1A

➤ **Clinicians' Webinar:**

Given that this recommendation is based on clinical trial results and PrEP is for persons at very high risk, why is the strength of recommendation rating a B (moderately strong recommendation)?

➤ **Community Stakeholders' Webinar:**

Does the phrase "as one prevention option," mean that there should be multiple prevention option happening simultaneously, or are just that PrEP is a one prevention option?

➤ **Public Health Leaders' Webinar:**

It is challenging to define what is meant by "very high risk" and this term can be stigmatizing. Consider using "at risk" of HIV acquisition.

Draft Recommendation 1B:

PrEP should be discussed with heterosexually active women and men whose partners are known to have HIV infection (i.e. HIV discordant couples) as one of several options to protect the uninfected partner during conception and pregnancy so that an informed decision can be made in awareness of what is known and unknown about benefits and risks of PrEP for mother and fetus.

Summary of Comments for Draft Recommendation 1B

➤ **Clinicians' Webinar:**

No Comments

➤ **Community Stakeholders' Webinar:**

Health care providers will want additional information or documentation provided for having that conversation; making sure the discordant couples are well informed about the potential risks and benefits.

➤ **Public Health Leaders' Webinar:**

No Comments

Draft Recommendation 2:

There is currently insufficient data on the efficacy and safety of PrEP for these populations, therefore:

- PrEP is not a recommended option for persons exposed to HIV primarily through injection drug use.
- The risks and benefits of PrEP for non-adult adolescents should be carefully weighed in the context of local laws and regulations about autonomy for health care decision-making by minors.

Summary of Comments for Draft Recommendation 2

➤ **Clinicians' Webinar:**

Will recommendations about PrEP for injection drug users change once the results of the IDU trial is out?

Have any PrEP studies included non-adult adolescents? If not, should the language be more specific and say for adolescents under the age of 18 since there have been studies on 18 and older? Adolescence is such a long range of definitions of age, that maybe a little more clarity should be put into the statement.

➤ **Community Stakeholders' Webinar:**

For people who are sexually active and using drugs by injection it is difficult to know which is the primary risk. I would submit that anyone who is sexually active and using injection drugs may perhaps need information about PrEP, regardless of whether injection drugs are the primary risk or sexual activity is the primary risk. We have seen data from NYC and other places that among the population of people who inject drugs, the HIV transmission rate is similar to that of people who are non-injection drug users, such as cocaine snorters or crack smokers, suggesting that there is a substantial pool of sexual transmission, at least in areas with good coverage in prevention services for injection-mediated transmission. So, it would be helpful to clarify because a clinician

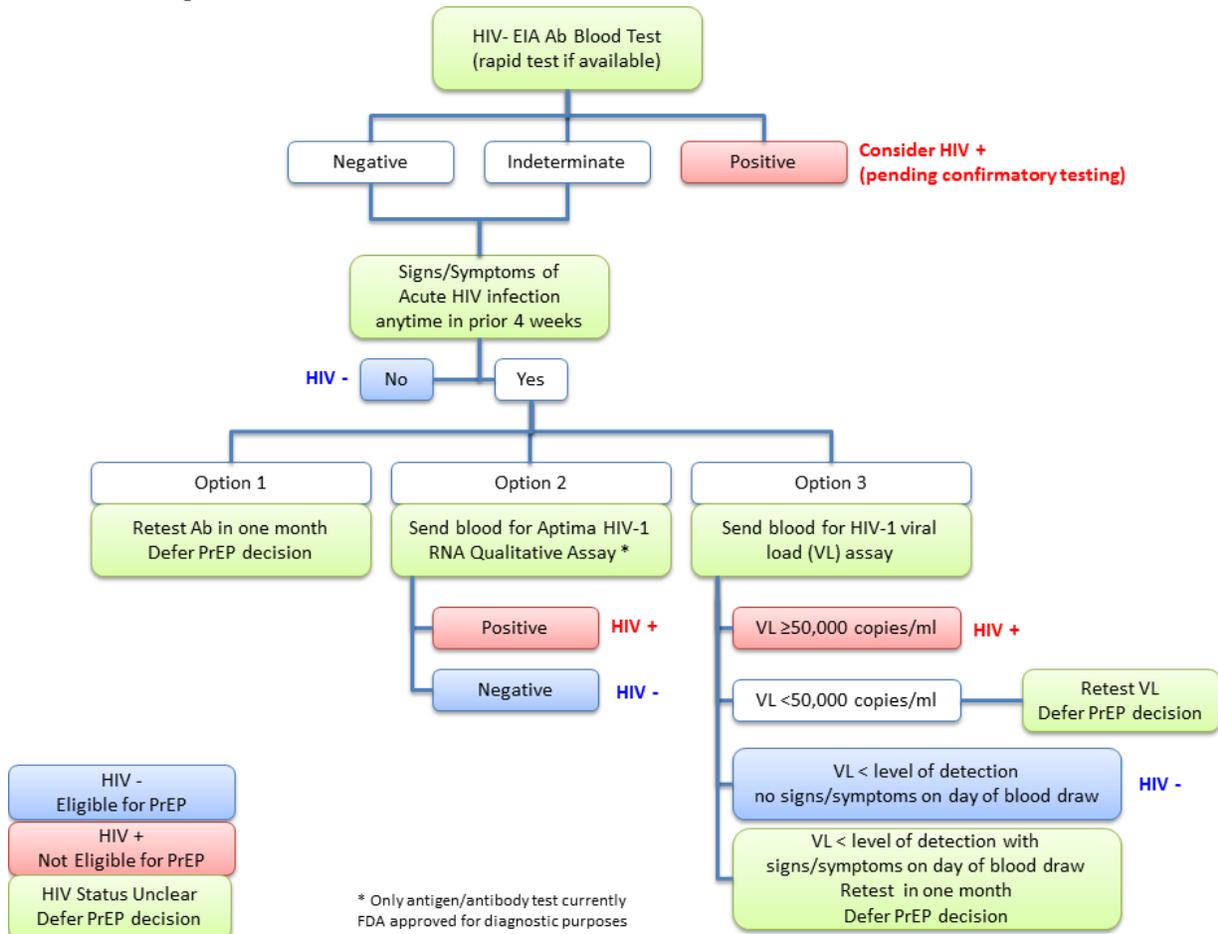
might simply see one risk behavior in front of them if they are seeing them primarily as an injection drug user, the language here might discourage them from appropriately addressing sexual risk of transmission.

➤ **Public Health Leaders' Webinar:**

No Comments

Draft Recommendation 3:

Acute and chronic HIV infection must be excluded by symptom history and HIV testing immediately before PrEP is prescribed.



Summary of Comments for Draft Recommendation 3

➤ **Clinicians' Webinar:**

This algorithm makes sense for screening for acute HIV infection, but the cost associated with actually doing either qualitative or quantitative testing and the accessibility of those tests to some providers is concerning. Waiting a month to institute PrEP is also concerning because if someone

is in a high risk for transmission category, that's a month of potential exposure to HIV when they could become infected. You want to be sure that people are not prescribing PrEP who unable to rule out acute infection but that would limit the number of providers.

Consider amending the box to say not only people with minor symptoms, but risk of potential exposure in the prior four weeks to rule out acute infection.

➤ **Community Stakeholders' Webinar:**

More precise testing protocols and algorithms should be provided to ensure that assessment of acute and chronic HIV infection is clearly determined before PrEP is prescribed.

➤ **Public Health Leaders' Webinar:**

No Comments

The guidelines are clear as they are written and simplicity and clarity in the HIV testing algorithm is important. However, offering PrEP to a population who is at risk for HIV infection makes it likely to be starting someone on PrEP who has acute HIV infection. A symptom screen alone may not be adequate to pick up acute HIV infection. Consider recommending in the guidelines that if available, a HIV test that is more sensitive for early indicating HIV infection be used (e.g. a fourth generation HIV antigen/antibody assay). If that is not available, then repeat an HIV four weeks after PrEP is initiated, rather than waiting for three months for the first repeat HIV test. This would, detect a person started on PrEP during acute infection sooner rather than later, and decrease the number of resistance mutations that may develop.

Draft Recommendation 4:

The only medication regimen approved by the FDA and recommended for PrEP in this guideline is daily tenofovir disoproxil fumarate (TDF) 300 mg with emtricitabine (FTC) 200 mg (Truvada®).

- It is not recommended to use other antiretroviral medications for PrEP, either in place of TDF/FTC, or in addition to it
- It is not recommended to prescribe PrEP for intermittent, coitally-determined, or other noncontinuous daily use.

Summary of Comments for Draft Recommendation 4

➤ **Clinicians' Webinar:**

Absolutely agree that “not recommended for intermittent, coitally determined”. Consider different wording that allows clinicians to recognize that there may be different phases of life where they may be using PrEP and then they may not (e.g., for three months while trying to get pregnant).

There is concern about the wording about the intermittent use related to timing of intercourse. When you say it's not recommended, that opens the door for insurance companies not to pay for

it. There's no data yet to support it which may be the same as saying it's not recommended. But phrasing it that way limits its use in situations where it is likely to be helpful.

➤ **Community Stakeholders' Webinar:**

Consider adding language in the recommendations about preventing people from using PrEP on their own intermittently and a coitally-dependent way, as opposed to taking it daily. Are there any instructions to physician or testing that can be used to detect intermittent or coitally dependent use and possibly discourage it until we have more information.

People who are having sporadic sex or have partners in another city and they see them once a month, are not taking PrEP every day. They are taking it before they go and while they are there, a few days after, but not at other times. It might be helpful to flesh out how something like that could potentially work for folks who are not having sex on a regular basis, but they know when their sex is going to be because it is all planned.

Consider adding a recommendation on how many days after daily PrEP is started you can consider yourself protected. So do you have to take it for five days before you're protected? Do you have to take it for three days? A recommendation like that might address issue of the once a month person and intermittent use is defined.

➤ **Public Health Leaders' Webinar:**

No Comments

Draft Recommendation 5:

HIV infection should be assessed at least every 3 months while patients are taking PrEP so that those with incident infection do not continue taking it.

Summary of Comments for Draft Recommendation 5

➤ **Clinicians' Webinar:**

This recommendation makes it sound like people who take Truvada[®] for PrEP will not be able to take it for treatment if they become infected with HIV.

➤ **Community Stakeholders' Webinar:**

Include here also that the testing for incident infection is going to be the same as the baseline testing.

It should be tied to a prescription. So, before the physician makes another prescription for another three months' worth of Truvada, they must have another HIV test.

The recommendation should have some type of reference towards someone who might be seroconverting or has seroconverted in the last three months. There is an assumption made that they will be discontinuing, and a reference to the next steps might be beneficial.

It is important to strongly recommend an adherence assessment to make sure they are typically taking the medications properly.

➤ **Public Health Leaders' Webinar:**

No Comments

Draft Recommendation 6:

Renal function should be monitored while patients are taking PrEP so that those in whom renal failure is developing do not continue to take it.

Summary of Comments for Draft Recommendation 6

➤ **Clinicians' Webinar:**

Six months is pretty liberal and if at any time we are seeing any trending, we would like to do it every three or four months with our patients. We think six months is a little too long to go.

I think though that the most recent versions of the treatment guidelines recommends it every six months. So that would make it that people on PrEP would have to get it more often than people on treatment?

➤ **Community Stakeholders' Webinar:**

No Comments

It is also very important to have a baseline renal function as a way to identify people who really find benefit, and not have renal functioning risk in long term use of the medication.

➤ **Public Health Leaders' Webinar:**

No Comments

Draft Recommendation 7:

When PrEP is prescribed, clinicians should provide access, directly or by facilitated referral, to other proven effective risk reduction services.

Because high medication adherence is critical to PrEP efficacy but was not uniformly achieved in trial participants, patients should be encouraged and enabled to use PrEP in combination with other effective prevention methods.

Summary of Comments for Draft Recommendation 7

➤ **Clinicians' Webinar:**

No Comments

➤ **Community Stakeholders' Webinar:**

List or describe some of those proven effective risk reduction services or prevention methods.

Include services to avert or prevent homelessness are risk reduction, gender based violence (same thing), and for young women dropping out of school (same thing) in addition to condom use and clean injection equipment. Address them in much more depth in the part of the guidance that tells the provider what to do and also include training for providers. Training needs to be more than how to provide PrEP and how to administer PrEP, there also needs to be training on other factors that put people at very high risk for HIV and how a risk reduction response to those factors can be organized.

Be careful in the guidance in how it discusses condom use and recognizes that for people who are already using condoms pretty consistently and correctly, PrEP really isn't a thing that they necessarily need or should want. But someone who doesn't use condoms, PrEP is protection where there currently is none. If someone is interested in PrEP, they shouldn't be hit over the head hard with the strong, "use a condom every time" method in the face of the fact that they are not already using condoms and that they are not going to start using condoms every time and take a pill. The guideline should use the harm reduction method.

There should be more language that supports adherence as a part of the last sentence. Patients should be informed of tools that we know increase adherence.

➤ **Public Health Leaders' Webinar:**

No Comments

Recommended Eligibility Criteria for MSM

Box A1: Male Risk Behavior Assessment (for MSM)

In the past 6 six months:

- Have you had sex with men, women, or both?
 - *(if men or both sexes)* How many men have you had sex with?
 - How many times did you have receptive anal sex (you were the bottom) with a man without a condom?
 - How many of your male sex partners were HIV positive?
 - *(if any positive)* With these HIV positive male partners, how many times did you have insertive anal sex (you were the top) without a condom?
 - Have you used methamphetamines (such as crystal or speed)?
-

Summary of Comments for Draft Recommended Eligibility Criteria for MSM

➤ **Clinicians' Webinar:**

One issue that is not specifically addressed is that the person (MSM) is having sex with somebody who is on antiretroviral therapy and is suppressed. So it becomes a little unclear about the magnitude of risk, and/or the type of sexual activity they are having (i.e. oral sex with a suppressed patient).

In the context of HIV treatment, when ART is being recommended, there is a caveat in the guidelines that the patient must be interested and willing to participate and be assessed and be likely to adhere. There is nothing here that is that addresses a commitment from the participant or the patient.

➤ **Community Stakeholders' Webinar:**

No Comments

➤ **Public Health Leaders' Webinar:**

No Comments

Recommended Eligibility Criteria for Heterosexually Active Men and Women

Box A2: Risk Behavior Assessment (for heterosexual men and women)

In the past six months:

- Have you had sex with men, women, or both?
- *(if opposite sex or both sexes)* How many men/women have you had sex with?
- How many times did you have vaginal sex with a partner without a condom?
- How many of your sex partners were HIV positive?
- *(if any positive)* With these HIV positive partners, how many times did you have vaginal sex without a condom?

Summary of Comments for Draft Recommended Eligibility Criteria for Heterosexually Active Men and Women

➤ **Clinicians' Webinar:**

For box A2 and A1 as well, what about a person who is in a monogamous partnership with a person of unknown HIV status?

Think about taking out “not in a monogamous partnership” in both boxes. Men and women may think they are in a monogamous relationships but not be.

➤ **Community Stakeholders' Webinar:**

Consider some social factors and social determinants of health that might be also appreciating the potential for high risk, rather than just the behavioral definition.

There could be some recognition of where the HIV epidemic is geographically. Having unprotected sex in Laramie, Wyoming is a lot different than in Atlanta, Raleigh, or New York.

In the last bullet in the first section, that “monogamous partnership” and “recently tested” are usually mutually exclusive. People who believe they are in monogamous partnerships are unlikely to have been recently HIV tested. Consider deleting “recently tested”.

The last bullet about “infrequently uses condoms in an ongoing sexual relationship with a partner of unknown HIV status” doesn’t take into account some people, like sex workers, who may be infrequently using condoms with partners of unknown status, but not in the context of an ongoing relationship. Consider deleting “in an ongoing sexual relationship”.

This may be addressing male sexual risk and risk patterns pretty well. Women in particular, not only are not aware of their partner’s status, but they are also not aware that they are at high risk for HIV infection. Consider defining risk screening criteria separately for heterosexually active men and women.

➤ **Public Health Leaders' Webinar:**

No Comments

The last bullet point under the AND says, “Infrequently uses condoms in an ongoing sexual relationship,” which I think is rather specific. Some heterosexuals, who are at risk for HIV infection who might not be in an ongoing sexual relationship with a partner who is at high risk of HIV infection, but may have multiple casual partners who are at risk, particularly people who may be commercial sex workers or otherwise exchanging sex for money or drugs. That criteria may be too narrow.

General Comments:

Summary of Comments

➤ **Clinicians' Webinar:**

Concise guidelines are appreciated. Patient education materials for provider use will also be needed. Is CDC working on that?

The guidelines should include strong wording urging public insurers and private insurers to pay for patients’ PrEP.

➤ **Community Stakeholders' Webinar:**

How were ideas generated by the external working groups that CDC convened a couple years ago incorporated into these guidelines? Several of the issues that came up today were raised in those

working group consultations and do not appear to have made it into this stage of the guidelines. It might be important to bring more social science into the mix when making recommendations like this, even when they are recommendations directed to clinical staff, because clinical providers need to become more broadly educated on what contributes to harm and what their role is on connecting people with harm reduction more broadly.

➤ **Public Health Leaders' Webinar:**

No Comments