



QUESTIONS AND ANSWERS ON PrEP

Prepster

INTRODUCTION

This briefing paper is intended to answer some of the most common questions which frontline workers are asked about PrEP. It provides extra background information to help answer questions more accurately and completely. There are links in the online version to more detailed web pages and research studies.

The briefing paper has been produced following a number of training interventions undertaken by PrEPster with frontline outreach workers. In some instances, the briefing paper gives responses to more complex questions that are being asked by a small number of people, but to which outreach workers wanted to be able to give clear responses.

This first version (June 2018) addresses 39 questions, listed below. We'd welcome suggestions for other questions or amendments to existing responses, so that we can add them to updated versions of this briefing. These can be emailed to hello@prepster.info.

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A NOTE ON TERMINOLOGY

In this briefing, 'PrEP' refers to a pill containing tenofovir disoproxil fumarate and emtricitabine, unless otherwise specified.

'Men who have sex with men (MSM)' includes gay and bisexual men and other men who have sex with men. We include trans men who have sex with men in this term, unless otherwise stated.

'Trans' or 'transgender' refers to people whose gender identity is different from the one they were assigned at birth (for example an individual who was considered to be male as a child but now identifies as a woman). 'Cis' or 'cisgender' refers to people whose gender identity matches the one they were assigned at birth.

In general, statements about recommendations for 'women' are inclusive of cisgender and transgender women. Similarly, recommendations for 'men' are inclusive of cisgender and transgender men. However as most research studies almost exclusively recruited cisgender people, most statements about research data usually relate only to cisgender men or women, unless otherwise stated.

The term 'front hole', rather than 'vagina', is the preferred term for many trans men for their genitals, especially when they have not had lower surgery. In addition, the term 'frontal sex', rather than 'vaginal sex', is often preferred. Whenever the vagina and vaginal sex are mentioned in this briefing, this includes the front hole and frontal sex, unless otherwise stated.

1. WHAT IS PrEP?

Pre-exposure prophylaxis (PrEP) is an HIV prevention strategy that uses antiretroviral drugs to protect HIV-negative people from HIV infection. People take antiretrovirals (ARVs) when they are at risk of exposure to HIV, in order to lower their risk of infection.

PrEP is highly effective in preventing the sexual transmission of HIV, as long as the drugs are taken regularly, as directed. However, PrEP does not prevent other sexually transmitted infections or pregnancy.

PrEP is one of several ways in which antiretroviral drugs can be used to prevent HIV transmission:

- ARVs taken by an HIV-negative person before (and then after) possible exposure to HIV: Pre-Exposure Prophylaxis (PrEP).
- ARVs taken by an HIV-negative person *after* possible exposure to HIV: [Post-Exposure Prophylaxis \(PEP\)](#).
- ARVs taken by an HIV-positive person during pregnancy, childbirth and breastfeeding: [Prevention of Mother-to-Child Transmission \(PMCT\)](#).
- ARVs taken by an HIV-positive person: [Treatment as Prevention \(TasP\)](#), also referred to as Undetectable = Untransmittable (U=U).

2. WHAT DRUGS DOES PrEP CONTAIN?

Currently, people take PrEP as a pill which contains two drugs: tenofovir disoproxil fumarate and emtricitabine.

Several different companies produce this pill, under different brand names. The original, patented version is called *Truvada* and is manufactured by Gilead. Other brand names for PrEP include *Ricovir-EM* (produced by Mylan), *Tenvir-EM* (Cipla) and *Teno-EM* (GPO). These are generic medicines which are much cheaper than *Truvada* but contain exactly the same active ingredients.

In the future there will probably be other versions of PrEP, containing other antiretroviral drugs. As well as pills, PrEP might be available as a long-acting injection, a vaginal ring or a gel that is placed in the vagina or rectum (see question 39).

3. HOW DOES PrEP WORK IN THE BODY?

The principle of PrEP is similar to that of antimalarial tablets used to prevent malaria when travelling in tropical countries.

PrEP works in the following way. A person who does not have HIV takes enough antiretrovirals for there to be high levels of the drugs in their bloodstream, genital tract and rectum before any exposure to HIV. If exposure occurs, the ARVs stop the virus from entering cells and replicating. This prevents HIV from establishing itself and the person remains HIV negative.

The antiretrovirals which are currently used as PrEP were chosen because they have limited side-effects, have few problems with drug resistance, reach high levels in the genital tract and rectum, and remain in the body for a relatively long time.

4. WHAT ARE THE DIFFERENT WAYS OF TAKING PrEP?

For people whose HIV risk is through vaginal sex or injecting drug use, PrEP needs to be taken daily. For people whose risk is through anal sex, there are two additional options: four-days-a-week and on-demand dosing.

DAILY DOSING

This involves taking PrEP once a day, every day, on an ongoing basis. Most PrEP studies were based on daily dosing, so there is more scientific evidence for daily dosing than other approaches. Daily dosing has been tested in relation to anal sex, vaginal sex (with cisgender people) and injecting drug use. Many international guidelines recommend daily dosing as the only way to take PrEP.

FOUR DAYS A WEEK

Studies suggest that for people whose HIV risk is through anal sex, taking PrEP four days a week is highly effective (see question 19). This hasn't been tested in the most rigorous kind of study (a randomised controlled trial), but the experience so far suggests that this approach is effective.

Some people may decide to take just four doses a week, out of concern about cost or side-effects. In this case, it is best to take PrEP on alternate days, for example on Tuesdays, Thursdays, Saturdays and Sundays.

Due to differences in drug absorption in different parts of the body, this is unlikely to work when the HIV risk is through vaginal sex or injecting drug use.

ON-DEMAND DOSING

This approach, also known as 'event-driven' or 'event-based' dosing, involves taking PrEP just before and after having sex. The French IPERGAY study showed that on-demand dosing is very effective in preventing transmission through anal sex.

The on-demand IPERGAY regimen involves taking a double dose of PrEP (two pills) from 2-24 hours before anticipated sex, and then, if sex happens, additional pills 24 hours and 48 hours after the double dose. In the event of sex on several days in a row, one pill should be taken each day until 48 hours after the last sexual intercourse.

Most European guidelines support on-demand dosing for people whose HIV risk is through anal sex. There is more information on its effectiveness in question 13. The [UK guide to PrEP](#), published by HIV i-Base, gives practical examples of how this regimen can be used.

Due to differences in drug absorption in different parts of the body, on-demand dosing is not recommended for people whose HIV risk is through vaginal sex or injecting drug use. See question 14 for more information on this.

5. WHO IS PrEP RECOMMENDED FOR?

National and international guidelines generally recommend that PrEP users should be HIV-negative, with no suspicion of acute (recent) HIV infection, be at substantial risk of HIV infection, have no medical reasons why they should not take PrEP drugs (such as kidney problems) and be willing to use PrEP as prescribed, including regular HIV testing.

The question of who is considered to be at *sufficiently* substantial risk of HIV infection for public health agencies to recommend PrEP depends on the characteristics of the HIV epidemic in a particular place. The World Health Organization defines substantial risk of HIV in terms of an incidence of 3% or more. In other words, that in a particular group of people, at least 3 in 100 people would become HIV positive each year, if PrEP was not provided.

For example, in Europe, PrEP is generally recommended for men who have sex with men (MSM) and trans women who have sex with men who do not always use condoms with casual partners. This is because HIV prevalence is very high in these communities - there is a high probability that MSM and trans people will have partners who have HIV, including some whose HIV is undiagnosed and untreated.

On the other hand, recommendations in relation to sex between cisgender men and women tend to be more nuanced. In most European countries, HIV prevalence is lower among cisgender heterosexual men and women. Therefore, even if an individual does not use a condom with a casual partner, it will be relatively unlikely that their partner would have HIV.

However the overall national picture may hide individuals, groups, communities and networks that are at greater risk of HIV infection. For example, people who have recently had a sexually transmitted infection or recently used post-exposure prophylaxis (PEP) may be more likely than some other people to have sexual behaviour that puts them at risk of HIV. People who buy or sell sex may also be at greater risk of HIV.

Furthermore, there may also be particular communities or neighbourhoods where the prevalence of HIV is unusually high.

The risk of acquiring HIV is higher for people who come from countries with a high prevalence of HIV (e.g. sub-Saharan Africa, south east Asia) and for their sexual partners. It is also higher for people travelling to those countries and having sex with people they meet there.

Guidelines therefore often refer to these kinds of factors to identify cisgender heterosexual men and women considered to be at substantial risk of HIV infection.

Nonetheless, individuals often have a clearer understanding of whether they need PrEP than their doctors. [The World Health Organization's PrEP implementation tool](#) suggests that if someone requests PrEP, this is an indication that they are likely to be at substantial risk of HIV. People asking for PrEP are likely to have made this choice based on a careful assessment of their personal circumstances, risk and desire for additional HIV prevention. Clinicians should consider any request for PrEP seriously, the World Health Organization says.

PrEP guidelines, driven by a public health concern with lowering HIV infections on a population basis, tend not to take into account the wide range of additional benefits that PrEP users report, in particular reducing fear and anxiety around sex. PrEP allows many people to have more enjoyable and satisfying sex, but this isn't usually included as a factor in PrEP guidelines.

See question 37 for more information on UK guidelines.

6. DOES PrEP WORK AS WELL FOR VAGINAL AS ANAL SEX?

Some of the strongest evidence for PrEP's efficacy has come from studies that enrolled MSM. Most participants' primary risks of HIV were from anal sex (receptive and/or insertive).

Strong evidence for PrEP efficacy has also come from [a large study conducted with cisgender heterosexual men and women in Uganda and Kenya](#). The primary risk of HIV for most participants was vaginal sex, but some participants may also have been exposed to HIV through anal sex. This showed a similarly efficacy to studies done with MSM, especially in participants who were able to take PrEP every day. Efficacy was also demonstrated in [a similar study from Botswana](#).

As a result of this evidence, national and international guidelines recommend PrEP for all people at risk of acquiring HIV through sex, whether the route is likely to be vaginal or anal sex.

Some other studies conducted with women in African countries have had [disappointing results](#). This was because many study participants [missed large numbers of doses, due to social barriers to taking PrEP](#).

So far, there haven't been any randomised studies done with cisgender heterosexual men and women in high-income countries. Moreover, there are no data to suggest that on-demand PrEP regimens are effective in relation to vaginal sex (see question 14).



7. WHAT EVIDENCE IS THERE THAT PrEP WORKS FOR TRANS PEOPLE?

There are data in relation to trans women, but no studies have been done on PrEP for trans men or non-binary people.

Concerning trans women, [data from the open-label extension of the iPrEx study](#) suggest that – as for other people – PrEP is highly effective when it is taken as prescribed. Among 151 trans women who have sex with men, nobody with drug levels equivalent to two to three pills a week or more acquired HIV. However three trans women with drug levels equivalent to less than two pills a week did acquire HIV.

Although trans women who have sex with men were eligible to join other randomised PrEP studies such as PROUD and IPERGAY, [trans recruitment to most studies was very limited](#), with no studies including enough trans women to be able to demonstrate efficacy. The iPrEx study did recruit 399 trans women, but adherence was low in this group. As a result the numbers of infections in the group receiving PrEP and the group receiving a placebo (dummy pill) were similar.

One factor leading to lower adherence in trans participants may be either a fear of, or lack of information about, drug-drug interactions between PrEP and gender-affirming hormone medications. [Many trans people will prioritise hormone use](#) over other health concerns, including HIV.

[Draft] [British HIV Association \(BHIVA\) guidelines](#) note that there are no known interactions between PrEP and feminising or masculinising hormones, except for ethinylestradiol (a hormone which is no longer recommended as part of gender affirming therapy). Trans people's concerns about drug – drug interactions should be explored and addressed, with reassurance provided to encourage PrEP use and good adherence.

Research is needed on each of the following points – currently, no data are available.

- PrEP effectiveness in trans men or non-binary people. However individuals whose only risk factor is anal sex could be expected to have similar levels of protection from PrEP as cisgender MSM, if achieving similar levels of adherence.
- PrEP effectiveness for frontal and vaginal sex in trans and non-binary people.
- On-demand dosing in trans people.

8. CAN ADOLESCENTS TAKE PrEP?

There are limited research data on the use of PrEP in adolescents. As a result, guidelines generally suggest that clinicians should carefully weigh up the risks and benefits of PrEP with an adolescent patient.

Key issues to consider include:

- A lack of data on safety and effectiveness of PrEP in adolescents.
- The potential impact of PrEP on bone mineral density during a period in which the bones are still growing and developing. This can be a side-effect of PrEP (see question 11). Although any loss of bone mineral density appears to be reversible after stopping PrEP, this is a key issue for clinicians to monitor.
- The adolescent's risk of acquiring HIV if PrEP is not prescribed.
- The provision of high quality adherence support. Adherence to medication is generally difficult for adolescents and [has been an issue in PrEP studies with adolescent MSM](#) in the United States.
- National laws and regulations about autonomy in health care decision-making by adolescents.

The American regulator has licensed PrEP for adolescents. For the moment, the European regulator has only licensed it for people *over* the age of 18. Nonetheless doctors can prescribe it 'off label' to younger people. 'Off label' means that the doctor is prescribing a medicine outside the terms of its license and has additional responsibilities to ensure that the prescription is safe and appropriate.

9. CAN PEOPLE WHO INJECT DRUGS TAKE PrEP?

People who use drugs may be exposed to HIV during sex and also through sharing equipment used to inject drugs. PrEP could have a different effectiveness in relation to the two transmission routes.

While there is no reason to think that PrEP does not prevent sexual transmission in people who inject drugs, its effectiveness when the risk is through sharing equipment is less clear.

Only [one randomised PrEP study has been done with people who inject drugs](#), in Thailand. It showed that tenofovir disoproxil fumarate (a single PrEP drug) was partially effective in preventing HIV infection in this population. Although the study aimed to assess the effectiveness of PrEP in preventing transmission through injecting drug use, it's possible that this level of effectiveness was [in part due to preventing sexual transmission](#).

Another difficulty with the study was that proven harm reduction interventions, including needle/syringe exchange, were not provided. The study's results are difficult to apply to settings where people who inject drugs have a much lower risk of acquiring HIV because harm reduction interventions are provided.

In terms of preventing HIV transmissions related to sharing injection equipment, [drug user activists argue that ensuring ongoing access](#) to sterile needles, syringes and other injecting equipment, as well providing opioid substitution therapy, is a greater priority than PrEP.

10. WHAT TESTS SHOULD SOMEONE HAVE WHEN STARTING AND USING PrEP?

These tests need to be done before starting PrEP, or around the same time. People who are buying generic PrEP can ask to have them done at an NHS sexual health clinic.

- HIV. It's important to check that the person doesn't have HIV without realising it – if they did have HIV, taking PrEP could mean they develop resistance to drugs they may need for treatment. A '4th generation' blood test done in a clinic, with the sample sent to a laboratory for testing, is better at detecting recent infections than a rapid point-of-care test or a home test. People who have recently had flu-like symptoms or a rash should have them assessed by an HIV doctor, in case they could be related to a recent HIV infection (seroconversion).
- HIV viral load, for people who have possibly been exposed to HIV within the last four weeks (the window period of a 4th generation test). This could detect very recent HIV infections.
- Kidney function. One of the drugs used for PrEP (tenofovir disoproxil fumarate) can occasionally lower kidney function (see the next question), so monitoring the health of the kidneys is essential. A blood test for creatinine is used, with the result converted to a figure called eGFR. PrEP is not generally recommended if the eGFR is below 60.
- Hepatitis B. This is needed because PrEP drugs are active against hepatitis B. A person with hepatitis B can use PrEP, but would need additional clinical advice. Vaccination may be offered, depending on the results of the test.
- Full sexual health screen, including hepatitis C.

Every three months, it is recommended that the HIV and sexual health tests are repeated. Kidney function is monitored annually, but more frequently in people at risk of kidney disease.

Guidelines do not recommend routine monitoring of bone mineral density.

11. DOES PrEP HAVE ANY SIDE-EFFECTS?

Most people who take PrEP do not get side-effects. [When researchers pooled the data from ten different studies](#), there were no differences in the rates of side-effects between people taking PrEP and people taking a placebo.

Nonetheless, all medicines can have side-effects. We can consider PrEP side-effects under three headings: short-term side-effects; kidney function; and bone density.

SHORT-TERM SIDE-EFFECTS

Less than one-in-ten people report side-effects such as feeling sick, flatulence, abdominal pain, dizziness and headache in the first month of PrEP use. These side effects are usually mild and short-lived. Typically, they start in the first few days or weeks of PrEP use and last a few days, and almost always finish within a month.

Over-the-counter and prescription medications – such as painkillers and anti-sickness tablets – can help with these side-effects.

KIDNEY FUNCTION

One of the drugs used in PrEP, tenofovir disoproxil fumarate, is processed by the kidneys and can put additional strain on the kidneys in people who already have kidney problems. A blood test to check kidney function is required around the time of starting PrEP and at least once a year while on PrEP.

If a test shows a rise in creatinine levels, this could indicate a problem, but the test needs to be repeated. More often than not, results return to a normal level on the second test and it is safe to continue with PrEP.

A few people may be advised not to take PrEP, or to stop taking it, because they have reduced kidney function. After stopping PrEP, kidney function usually returns to its previous level, suggesting that PrEP does not cause any long-term harm.

People at greater risk of kidney problems are those over the age of 40, people who have high blood pressure or diabetes, and people taking other drugs which are processed by the kidneys.

BONE MINERAL DENSITY

A slight decrease in the hardness of bones has been seen in the first six months of taking PrEP. This reduction in bone density is small (0.5-1.5%) and will not make a difference to people with normal bone density prior to using PrEP. So far there have not been any reports of bone fractures related to PrEP use.

The loss of bone mineral density does not get worse with ongoing PrEP use. Importantly, bone mineral density returns to normal after stopping PrEP.

Doctors prescribing PrEP should make an assessment of whether a PrEP user has other risk factors for low bone mineral density (such as being over the age of 50, long-term use of some steroids, or having a low body weight). Personalised advice will be given to people at risk of bone problems. Lifestyle changes (such as weight-bearing exercise and stopping smoking) can be helpful.

12. HOW MIGHT SIDE-EFFECTS BE DIFFERENT FOR DIFFERENT GROUPS OF PEOPLE?

Our knowledge on side-effects is based both on the experience of the first generation of PrEP users (especially those taking part in clinical trials) and decades of experience of people taking the drugs in PrEP as part of their HIV treatment. However things could plausibly be a little different for some other people:

- Experience is almost all based on daily dosing. The kidney and bone side-effects might be lessened by use of event-based PrEP (as fewer tablets are taken), but this hasn't been formally studied.
- When a drug is used by larger numbers of people for longer periods of time, relatively uncommon side effects sometimes start to be noticed.
- Early adopters of PrEP tend to have been enthusiastic and motivated, and so could be more willing to put up with side-effects than some people who will be offered PrEP in the future.
- Similarly, people with HIV have been taking the drugs used in PrEP as part of treatment for a life-threatening condition. The balance of benefits and harms is different in people taking a preventative medicine, who may be less accepting of side-effects.

13. IS ON-DEMAND DOSING AS EFFECTIVE AS DAILY DOSING FOR PEOPLE WHOSE RISK IS THROUGH ANAL SEX?

Effectiveness results of the [French IPERGAY study](#), which tested on-demand dosing, were virtually identical to the [English PROUD study](#), which tested daily dosing. In both studies, no one who had been adherent to PrEP acquired HIV.

Since then, [on-demand PrEP has been rolled out in France](#), and also provided through implementation studies in other European countries. Again, there have been no reports of HIV infections in cisgender MSM who adhered to on-demand PrEP.

One issue with interpretation of IPERGAY results is that many study participants had sex very frequently and so took PrEP quite often. On average, participants took 15 pills a month and one-in-five participants took over 25 pills a month, i.e. the equivalent of almost daily dosing. This would mean that drug levels would not have time to drop far before another dose was taken.

Nonetheless, [an analysis of a subgroup of IPERGAY participants](#) who had less frequent condomless sex (on average, once a week) but followed the on-demand regimen as recommended, has shown that PrEP remained effective. There were no HIV infections in those taking PrEP, whereas infections did occur in the group taking the placebo (dummy pill).

As the on-demand regimen generally involves taking fewer doses than daily dosing, poor adherence and missed doses may make more of a difference to effectiveness. People taking daily PrEP, especially people whose risk is through anal sex, may still be protected even if they miss doses occasionally. This is less certain for the on-demand regimen.

Some international guidelines are cautious about the use of on-demand dosing. One reason for this is that only the IPERGAY study has evaluated its effectiveness – in general, it is preferable to have several studies with consistent results. Although it had very impressive results, IPERGAY was a relatively small study with a short period of follow-up.

14. WHY CAN'T ON-DEMAND DOSING BE USED BY PEOPLE EXPOSED TO HIV THROUGH VAGINAL SEX?

National and international guidelines are consistent in their recommendations on this point. On-demand dosing for people whose HIV risk is through vaginal sex is not recommended. Daily dosing is the only recommended regimen for vaginal sex.

The first reason is that on-demand dosing has only been tested with cisgender MSM, whose primary HIV risk is through anal sex.

The second reason is that [tenofovir \(one of the two drugs in PrEP\) takes much longer to reach protective levels in vaginal tissue than in rectal tissue](#). This means that on-demand dosing is much less likely to work. There is more information relevant to this in the next question and answer.

A trans man who has not had lower surgery may have both vaginal/frontal sex and anal sex. Also, a trans woman who has had lower surgery may have both vaginal/frontal and anal sex. While on-demand dosing may be assumed to be effective for a person whose only HIV risk is through anal sex, it is not expected to be effective in relation to frontal sex.

15. FOR HOW LONG DO PEOPLE NEED TO TAKE PrEP BEFORE IT STARTS TO WORK?

The research to answer this question comes from lab studies which show how long it takes for a maximum concentration or 'steady state' of drug to be reached in blood, vaginal tissues and rectal tissues. Drugs vary in how long they take to achieve this concentration in different parts of the body. For example, there are differences between the two drugs contained in PrEP, tenofovir and emtricitabine, although both are probably needed for PrEP to be effective.

The research is complex but incomplete (see the next question for more details). After reviewing it, the authors of [draft] [BHIVA guidelines](#) make the following recommendations for practical advice to give to PrEP users. There are different recommendations for people whose risk is through anal or vaginal sex.

For people whose risk of HIV is through anal sex, whatever dosing schedule they use:

- **Starting:** PrEP can be started with a double dose (two pills) taken 2–24 hours before sex.
- **Stopping:** PrEP should be continued daily until 48 hours after the last sexual risk.
- **Re-starting:** If PrEP has been stopped and it is less than 7 days since the last dose then PrEP can be restarted with a single dose. If it has been more than 7 days, take a double dose.

For people whose risk of HIV is through vaginal sex or frontal sex:

- **Starting:** PrEP should be started as a daily regimen of one pill a day, 7 days ahead of the likely sexual risk. If it is not possible to take PrEP for a full 7 days before a likely sexual risk, starting with a double dose (two pills) might provide some extra protection, but this is unproven. Condoms and other prevention strategies could also be used during the first few days of PrEP use.
- **Stopping:** PrEP should be continued daily until 7 days after the last sexual risk.
- **Re-starting:** The same guidance as for starting.

People who are at risk through injecting drug use (slamming) as well as sexual risk need to know that PrEP takes longer to achieve protective concentrations in the blood than in tissues. Taking PrEP for 7 days before and 7 days after is recommended.

16. WHAT ARE THE KEY CONCLUSIONS OF THE LAB STUDIES ON PrEP DRUG CONCENTRATIONS?

The key points of the research evidence used to develop guidance on starting and stopping PrEP (see previous question) are as follows:

- Very few studies have been done with trans men or women. The following data come from studies with cisgender men and women.
- The time to achieve a protective concentration in the body is determined by the drugs used, the dose, the frequency of dosing, and the body tissue.
- Of the two drugs contained in PrEP, tenofovir reaches far higher concentrations in rectal tissues than in vaginal tissues. In contrast, emtricitabine reaches higher concentrations in vaginal tissues than rectal tissues.
- In terms of time to protection, both drugs are absorbed more quickly in rectal tissues than in blood or vaginal tissues.
- Tenofovir takes longer to reach protective concentrations than emtricitabine, but then remains in the body for longer.
- The IPERGAY study, together with pharmacokinetic studies done in humans and animals, provide the key evidence for the recommendations on anal sex.
- Data are available on drug concentrations in rectal tissue (relevant for receptive anal sex), but there are virtually no data on drug concentrations in the foreskin or urethra. This is relevant for insertive anal sex or insertive vaginal sex. Nonetheless BHIVA's recommendations for anal sex are the same for the insertive and receptive partner; similarly, their recommendations for vaginal sex are the same for the insertive and receptive partner.

- The time to achieve a protective concentration for vaginal sex has been extrapolated from pharmacokinetic studies in humans. There is consensus that 7 days of dosing are needed before exposure to HIV, and 7 days after exposure.
- As drug levels in vaginal tissue drop quickly, high adherence to daily dosing is needed to maintain adequate levels in vaginal tissue.

17. WHY IS THERE CONTRADICTIONARY ADVICE ON WHEN TO START AND STOP PrEP?

International guidelines do not all provide the same advice on starting and stopping PrEP. As some PrEP users may have heard contradictory information, it can be helpful to be aware of what other guidelines say.

The discrepancy is partly due to different scientific interpretations of the limited evidence that is available.

It is also due to experts having different approaches to risk and harm reduction. In other words, should doctors recommend strategies that they are highly confident will be safe, even if they might be difficult for some people to put into practice? Or should they take a pragmatic approach that seeks to reduce risks rather than eliminate them entirely?

[The World Health Organization](#) advises that PrEP reaches a protective level, for either vaginal or anal sex, after 7 days of daily dosing. When stopping PrEP, WHO states it should be continued for 28 days after the last possible exposure to HIV.

[Guidance from the Centers for Disease Control and Prevention \(CDC\)](#) in the United States states that PrEP reaches maximum protection from HIV for receptive anal sex and receptive vaginal sex (in cisgender women) after 7 days and 20 days, respectively. These more cautious guidelines were published in 2014, before some of the relevant studies were done.

18. WHY DOES PrEP NEED TO BE TAKEN AFTER SEX, AS WELL AS BEFORE?

After a person has been exposed to HIV (for example, during sex), scientists believe that some HIV is likely to remain in body tissues for a number of days. By continuing to take PrEP for a few days after exposure, PrEP can continue to work to prevent HIV from entering cells and replicating. If PrEP is stopped immediately, it's possible that an HIV infection could take hold.

Pharmacokinetic studies (see question 16) show that, after a last PrEP dose has been taken, drug levels drop rapidly in cisgender women's vaginal tissue. In contrast, drug levels are maintained for longer in rectal tissues. This is why the recommendations on how long to continue taking PrEP after a sexual exposure are longer for vaginal than anal sex.

19. HOW ADHERENT DO PEOPLE NEED TO BE FOR PrEP TO BE EFFECTIVE?

By testing participants' blood for the presence of PrEP drugs, researchers have attempted to estimate the number of PrEP doses they have actually taken. They have then looked at the number of HIV infections in people with different levels of adherence.

The useful studies which have taken this approach have all been with MSM, where the HIV risk is through anal sex. Results for vaginal sex are likely to be different.

In the [iPrEX OLE study](#) of MSM and transgender women, most infections occurred in people taking less than two doses a week, with none occurring in individuals taking four or more doses. The researchers calculated the following levels of protection:

- Less than two doses a week: 44% fewer infections (credible range: -31 to 77%)
- Two or three doses a week: 84% fewer infections (credible range: 21 to 99%)
- Four or more doses a week: 100% fewer infections (credible range: 86 to 100%).

The 'credible range' shows the researchers' uncertainty about what the true level of protection is. For example, four doses a week is thought to provide protection of somewhere between 86% and 100%.

Nonetheless, for people whose risk is through anal sex, it may be reassuring to know that four or more doses a week appears to be highly effective.

Due to differences in drug absorption in different body tissues, it is thought that higher levels of adherence are required when the HIV risk is through vaginal sex – probably six or seven doses a week.

20. DOES PrEP INTERACT WITH ANY OTHER MEDICATION?

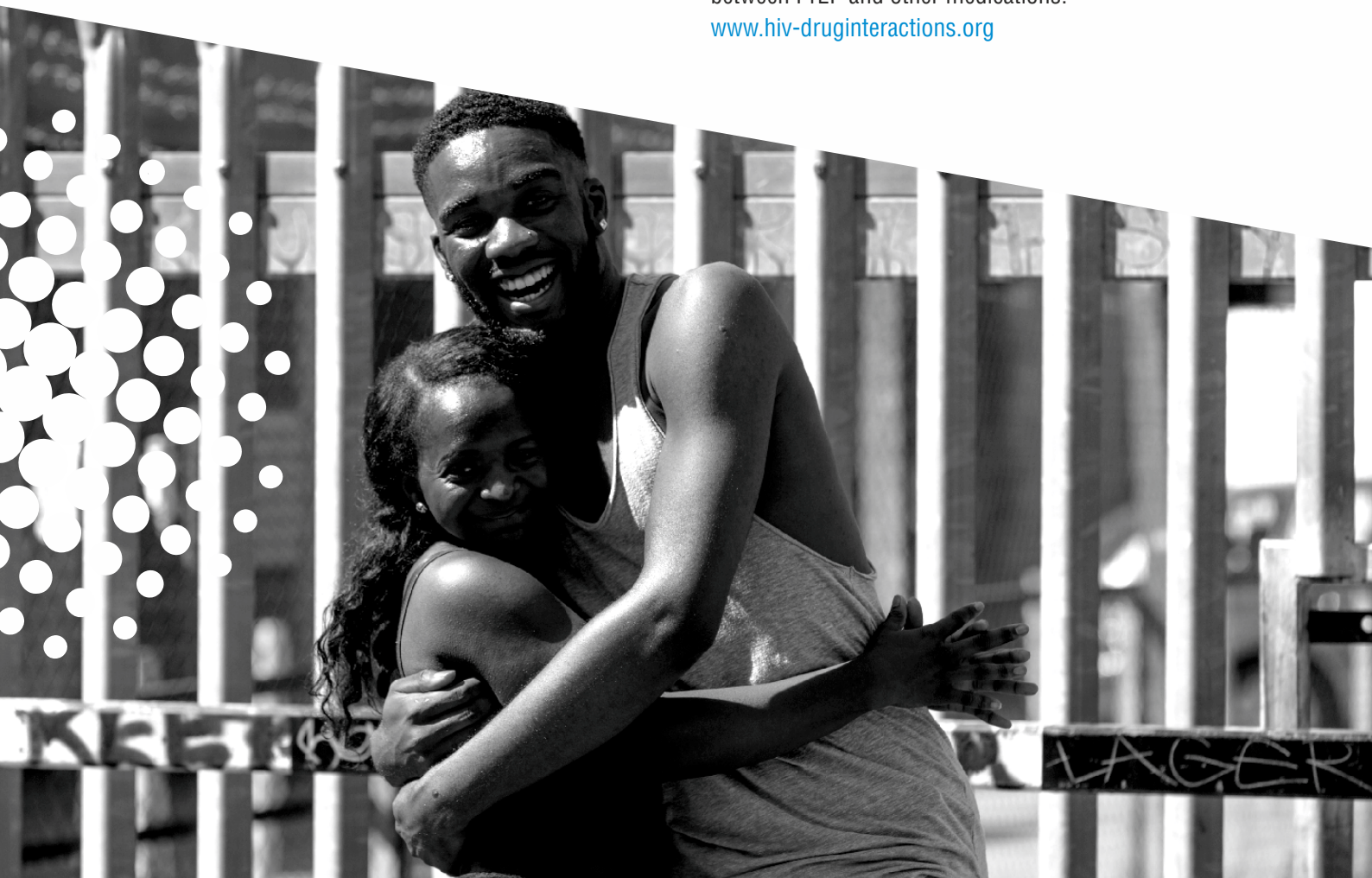
PrEP does not interact with most other medicines.

PrEP can be taken when drinking alcohol or using recreational drugs. PrEP can be taken by people who are taking hormonal contraceptives and most over-the-counter medications. PrEP is safe for trans people taking gender-affirming hormone medications.

However, tenofovir disoproxil fumarate (one of the drugs in PrEP) may interact with other medicines which are also associated with kidney problems. These include some non-steroidal anti-inflammatory drugs (NSAIDs), especially diclofenac; aminoglycosides, used to treat certain bacterial infections; and acyclovir and valaciclovir, used to treat herpes.

When PrEP users are prescribed other medicines, it is strongly advised that they tell the doctor or pharmacist about taking PrEP and ask them to check for drug interactions. A useful website from Liverpool University allows anyone to look up information on interactions between PrEP and other medications:

www.hiv-druginteractions.org



21. IS IT SAFE TO TAKE PrEP DURING CONCEPTION, PREGNANCY AND BREASTFEEDING?

The research data on the safety of PrEP drugs during conception, pregnancy and breastfeeding are incomplete, but generally reassuring. National and international guidelines say that PrEP can be used by people who wish to conceive, who are pregnant and who are breastfeeding.

No problems have been seen in the people who became pregnant while taking PrEP in research studies. The medicines used as PrEP have been thoroughly studied among pregnant women living with HIV and hepatitis B and there is no known increased chance of birth defects, growth problems, or complications during pregnancy, including preterm birth and miscarriage.

Only tiny amounts of PrEP drugs are present in breast milk, meaning that daily PrEP can be taken safely during breastfeeding.

An HIV-negative person who has HIV-positive partners may be interested in using PrEP while trying for a baby. In this situation, it's important to check that there is an accurate understanding of transmission risks - people with an undetectable viral load do not pass HIV on. Nonetheless, someone trying to become pregnant may still decide to use PrEP, for extra reassurance, or because their partner's viral load is detectable.

It's also worth noting that [the risk of HIV infection increases during pregnancy](#), as does the risk of onward transmission to the baby. Access to effective HIV prevention, including PrEP, is important during pregnancy.

22. WHAT SHOULD SOMEONE DO IF THEY MISS A DOSE OF PrEP?

People who take PrEP and occasionally miss a dose will still have high levels of protection. PrEP users can be advised to simply take another dose when they remember and then continue with their usual dosing schedule. It is safe to occasionally take two tablets in one day.

23. ARE PEOPLE EXPECTED TO TAKE PrEP FOR LIFE?

A person's risk of HIV infection is not constant. It is likely to vary over time as circumstances change. For example, moving to a new city or the break-up of a stable relationship may start a period of higher risk. These are sometimes called "seasons of risk".

People may decide to stop using PrEP for a variety of reasons. For example, they may have changed their sexual behaviour, their HIV-positive partner may have achieved an undetectable viral load, or a relationship may have become stable and mutually monogamous. Support for PrEP users should include recognition of situations that may involve exposure to HIV and education on safe stops and restarts of PrEP.

When stopping PrEP, doses still need to be taken for a few days after the last possible HIV exposure.

See questions 15 and 17 for more information on starting and stopping PrEP.

24. DOES PrEP CREATE PROBLEMS IN RELATION TO DRUG RESISTANCE?

Some anxiety has been expressed about PrEP and drug resistance, with people's concerns not always being clearly thought through. [It's worth separating out the potential issues](#):

- PrEP users acquiring HIV and developing drug resistance.
- Drug resistance becoming more of a problem due to the widespread use of PrEP.
- PrEP not working because of drug resistance.

PrEP USERS ACQUIRING HIV AND DEVELOPING DRUG RESISTANCE

The concern is that if someone either already has HIV and then starts to take PrEP or acquires HIV despite taking PrEP and stays on PrEP, the PrEP they are taking will amount to a sub-optimal HIV treatment. The two anti-HIV drugs in PrEP are not enough to treat HIV infection (three anti-HIV drugs are usually used for treatment). In these conditions, the person's HIV will replicate and could become resistant to those anti-HIV drugs, potentially limiting their future HIV treatment options.

Data shows that this happens occasionally. [In clinical trials HIV drug resistance was found in less than 1 in 50 people](#) who were offered PrEP and who seroconverted to HIV.

Most of these cases involved individuals who started taking PrEP when they were already in the very early stages of HIV infection. Although an HIV test before beginning PrEP is standard practice, a test may miss recent infection due to each test's 'window period'. This situation could also occur if someone took a break from PrEP, acquired HIV during that time, and then restarted PrEP without taking another HIV test.

These cases underline the importance of using a '4th generation' blood test done in a clinic, with the sample sent to a laboratory for testing when starting or restarting PrEP (rapid point of care tests and home tests are less able to detect recent infections). They also highlight the importance of clinical assessment if someone who wants to start PrEP has symptoms that could be related to HIV seroconversion (such as fever or rash).

Resistance could also develop if someone missed too many PrEP doses, resulting in drug levels being too low to prevent HIV infection and hence the person acquiring HIV.

Resistance has most often developed to emtricitabine, rather than to tenofovir. If someone develops drug resistance while on PrEP, there are several other HIV drugs that they can use for treatment.

DRUG RESISTANCE BECOMING MORE OF A PROBLEM DUE TO THE WIDESPREAD USE OF PrEP

If the scale-up of PrEP resulted in a large number of the cases described above, then drug resistant strains of HIV might spread more widely and become more prevalent. This would have an impact on the effectiveness of both PrEP and HIV treatment in the community.

The experience so far does not suggest that this is happening. Nonetheless, the situation could evolve as PrEP is rolled out with less frequent clinical monitoring than during clinical trials. There could also be more cases of resistance if future PrEP users have lower adherence than 'early adopters' of PrEP.

In considering this, the risk of drug resistance needs to be weighed against the number of HIV infections that PrEP prevents. [For example, in one research study](#) five individuals developed drug resistance, but PrEP also prevented around 120 HIV infections. Drug resistance is a concern, but HIV infection is a much more serious threat to health.

PrEP NOT WORKING BECAUSE OF DRUG RESISTANCE

The concern is that if a PrEP user has sex with an HIV-positive person whose virus is resistant to PrEP drugs, then PrEP might not be able to prevent infection. As it is rare for people with HIV to have resistance to both emtricitabine and tenofovir, the drugs used in PrEP, this is expected to be a rare event. Resistance to other drugs that are not used as PrEP is more common.

So far across the world, only four cases have been reported at scientific conferences of people who became HIV positive even though they appear to have been taking PrEP correctly. [Two of the cases](#) involved exposure to virus that was resistant to PrEP drugs. [A third case](#) may also have done so, but not enough information is available for researchers to be certain.

[In a fourth case](#), transmission occurred with a strain of HIV with no drug resistance, despite high adherence to PrEP. It is not clear what conclusions can be drawn from this unusual case, other than that PrEP failure is extremely rare but not impossible.

25. CAN SOMEONE BECOME RESISTANT TO PrEP?

It is viruses that develop resistance, not people. So a person can't be resistant to the drugs in PrEP. Also, as an HIV-negative person does not have HIV, they can't have drug-resistant HIV.

26. IF SOMEONE USES PrEP AND IS EXPOSED TO HIV, WILL AN HIV TEST COME BACK AS POSITIVE?

HIV tests detect signs of HIV infection – for example, antibodies that are produced by the body in response to an HIV infection that has taken hold. HIV tests do not detect signs of just being exposed to HIV. If someone was exposed to HIV but PrEP prevented an infection from occurring, the test will not come back as positive.

27. IF SOMEONE ACQUIRES HIV DESPITE USING PrEP, WILL AN HIV TEST COME BACK AS POSITIVE?

Occasionally, some PrEP users may acquire HIV, because they did not have good enough adherence to PrEP or for the reasons discussed in question 24. This may mean that they may be taking PrEP during the early stages of infection, before a diagnosis is made.

In this case it is possible that the window period (the period when HIV testing cannot detect HIV infection) may be a little longer than usual. In some cases, tests may not detect signs of infection in the first few weeks or months after infection, especially when rapid point-of-care tests are used. (Fourth generation laboratory tests are more sensitive).

The explanation for this appears to be that having some antiretroviral drugs in the body during the first stages of infection (acute HIV infection) slows down replication of HIV. This in turn decreases or delays the development of an immune response to HIV, including the production of antibodies. This has been observed in [some](#) but [not all](#) PrEP studies.



28. DOES PrEP PROTECT AGAINST ANYTHING OTHER THAN HIV?

PrEP has only been proven to be effective in preventing HIV infection. While some research suggests that PrEP may have some impact in preventing new [herpes simplex virus type 2](#) and [hepatitis B](#) infections, this is uncertain.

In contrast, when used correctly and consistently, condoms protect against HIV, gonorrhoea, chlamydia, syphilis, hepatitis C, and numerous other infections.

In addition, PrEP does not protect against pregnancy. Some PrEP users may need advice on contraception, including reassurance that PrEP does not interfere with any contraceptive method.

29. HOW DOES PrEP WORK AS PART OF A COMBINATION PREVENTION APPROACH?

People often argue for and against different HIV prevention methods, pitting one method against another.

This is unhelpful. The media may report an innovation (such as PrEP) as if it is a silver bullet, a simple solution that on its own will end the HIV epidemic. Debates about condoms and PrEP can become heated, with people enthusiastically promoting one method and denigrating the other. This has the implication that what works for one person will be (or should be) the same approach that will work for everyone else.

Instead, public health research and policy supports the idea of combination prevention, in other words the co-ordinated use of complementary strategies. The strategies should include behavioural interventions (e.g. education), biomedical interventions (e.g. testing) and structural interventions (e.g. legal equality for affected populations).

Regular testing, condoms, PrEP and an undetectable viral load can be promoted together as part of combination prevention.

This reflects synergies between the methods – they have a greater impact when used together than if they were employed separately. [The dramatic fall in HIV diagnoses at some London clinics](#) is explained by a combination of increased testing, treatment initiation and PrEP. Importantly, this happened in a context of continued condom use by many people – a dramatic reduction in condom use could reverse these gains.

Synergies can work in a number of ways, for example:

- If individuals test frequently at clinics where HIV treatment can be started immediately after diagnosis, those who are diagnosed will only be infectious for a short period of time.
- Using condoms and PrEP together provides protection against HIV and many other sexually transmitted infections (STIs). Preventing the spread of STIs is relevant to HIV prevention, as a number of STIs make HIV transmission more likely when prevention methods (condoms, PrEP or an undetectable viral load) are not in place.
- People need to engage with sexual health care in order to be prescribed PrEP, facilitating regular testing for HIV and STIs, as well as access to behavioural support.
- For couples in which one person has HIV and the other does not, PrEP and treatment as prevention may both be used as prevention strategies, at different points in time. If the HIV-positive partner is not yet taking treatment or has only recently started, then PrEP can be provided to the HIV-negative partner. Once the positive partner is stable on treatment, with an undetectable viral load for at least six months, then the couple can be confident that 'Undetectable = Untransmittable'. At this point, PrEP would no longer be needed, unless the HIV-negative partner needs PrEP for protection with additional partners outside this relationship.
- The combination of PrEP availability and a greater understanding of 'Undetectable = Untransmittable' are reducing stigma towards people living with HIV, especially in sexual contexts.

30. WHAT DOES RESEARCH SAY ABOUT PrEP USE AND OTHER STIs?

People who use PrEP, especially MSM, tend to have higher rates of gonorrhoea, chlamydia, syphilis and other sexually transmitted infections (STIs) than other people. These high rates of STIs exist both before they use PrEP and while they are taking it.

This indicates that PrEP is being used by people who are likely to benefit from it. They are people who were already having condomless sex and were vulnerable to STIs before they began to take PrEP.

But PrEP could have an impact on rates of STIs in other ways.

The protection provided by PrEP might encourage people to use condoms less than before, or to have more sexual partners. This is sometimes called 'risk compensation'. It could facilitate the spread of STIs. It might be a particular concern in groups where the prevalence of STIs is already high, such as among MSM.

PrEP may also have an impact by facilitating engagement with sexual health care. Screening for STIs every three months is recommended for PrEP users, resulting in infections being diagnosed promptly. In the short term, reported rates of STIs in PrEP users will be high, in part because more testing will result in more diagnoses.

But more importantly, prompt diagnosis will mean that STIs are treated before the individual has the chance to pass them on to multiple other partners. As a result of PrEP users having more engagement with sexual health care, chains of transmission may be cut.

The research evidence on this is conflicting. The most valuable studies to look at are open-label studies, demonstration projects and cohort studies. They are difficult to interpret but more closely resemble 'real world' conditions than placebo-controlled, randomised studies.

Data collected include PrEP users' self-reports about their use of condoms and their number of sexual partners. As people do not always report their behaviour fully or consistently, researchers put more weight on actual diagnoses of STIs, considered a more objective reflection of people's behaviour.

Nonetheless there can be several possible explanations for a rise in STIs in a group of PrEP users:

- 'Risk compensation'.
- STIs are on the rise in the wider community anyway, regardless of PrEP.
- PrEP users are being tested more often.
- Clinics are using more sensitive tests, which detect more infections than older tests.



This table below summarises the available evidence, which is contradictory and inconclusive. A number of studies have recorded statistically significant increases in STIs or condomless sex, while others have not.

All the studies, except the first one mentioned, relate primarily to cisgender MSM.

Study	Analysis	Findings that do not suggest “risk compensation”	Findings that suggest “risk compensation”
Demonstration project following Partners PrEP, for serodiscordant cisgender heterosexual couples in Kenya and Uganda.	Comparison with the earlier phase of the study, when PrEP's efficacy was unclear.	No change in condomless sex with main partner. No change in STIs. No change in pregnancy.	Slight increase in condomless sex outside the main partnership.
PROUD study, MSM in England.	Comparison of MSM given PrEP immediately and MSM who had not yet received it.	No difference in overall partner numbers. No difference in STIs.	More PrEP users had condomless sex with 10 or more partners.
Open label phase of IPERGAY study, MSM in France.	Analysis of changes during 18 months of PrEP use.		More condomless sex.
Open label extension of iPrEx study, with MSM and trans women, multiple countries.	Analysis of changes during 72 weeks of PrEP use.	Fewer sexual partners. Less condomless sex. Comparing PrEP users and non users, no difference in STIs.	
US demonstration project, with MSM and trans women.	Analysis of changes during first year on PrEP.	No change in partner numbers. No change in condomless sex. No change in STIs.	
STRUT clinic, San Francisco, MSM and trans men.	Analysis of changes during first 16 months on PrEP.	No increase in STIs.	More condomless sex.
Victoria, Australia demonstration project.	Analysis of changes during first year on PrEP.		More condomless sex. More STIs.
Kaiser Permanente cohort in San Francisco.	Analysis of changes during first year on PrEP.		More gonorrhoea and chlamydia.
Seattle cohort of MSM.	Comparisons between baseline and first year on PrEP.		More condomless sex. More STIs.
Cohorts of MSM in Chicago and New York.	Comparison of periods of time using PrEP with periods when PrEP was not used.		More condomless sex when PrEP used.

31. SHOULD A PrEP USER STILL USE CONDOMS?

The reason many people want to use PrEP is because they want to avoid HIV infection but find it difficult to consistently use condoms.

In supporting PrEP users, it's important to check that they are aware of the benefits to using condoms in combination with PrEP, in particular preventing other sexually transmitted infections. It's also worth checking that the difficulties they have with condoms can't be remedied with information and education. This could be the case if someone has problems with fit or breakages, for example.

Nonetheless, it is to be expected that many PrEP users will not always use condoms. It would be illogical to deny PrEP to people who feel unable to use condoms all the time – they are precisely the people who need it.

PrEP users tend to be highly motivated to avoid infection with HIV. Some PrEP users may be more prepared to live with the possibility of acquiring other STIs, most of which are easier to treat and cure, as well as being less stigmatised. PrEP users may manage their STI risks through frequent check-ups which will allow any STIs to be diagnosed and treated.

Moreover an individual may consider, for example, that managing erectile dysfunction or building intimacy with partners are higher priorities for their sexual health than avoiding all possible infections. Support for people in relation to PrEP and condom use needs to take account of each individual's sexual health needs and personal priorities.

32. WHY IS PrEP UPTAKE SOMETIMES LOWER IN SOME GROUPS OF PEOPLE WHO COULD BENEFIT FROM IT?

There are social inequalities in health in all countries, with people who are socially disadvantaged by income, employment status, education or place of residence having poorer health and shorter lives than other people.

Moreover, those who most need health services are least likely to receive them, while those with less need of healthcare tend to use health services more often and get more out of them.

This pattern has already been seen in the [roll-out of PrEP in the United States](#), with ethnic minorities, younger people and economically marginalised individuals being less likely to access PrEP than other groups. This does not align with need - for example, young black MSM in the US are at exceptionally high risk of HIV.

In most western countries, awareness and uptake of PrEP is much higher in some networks of MSM than in other social groups. This stems in part from a long history of engagement with HIV issues and awareness of personal vulnerability to HIV in gay communities, as well as more recent community activism around PrEP. In other groups, many people may be less aware that they are at risk of being exposed to HIV and might not know that PrEP exists. This includes people who have limited information about HIV risks, or do not believe or understand that the sex they are having might expose them to HIV.

There may be specific reasons why awareness and uptake of PrEP is low in some specific groups. For example, MSM born outside the UK face economic, cultural and language barriers to accessing sexual health services. Many African women in the UK prefer to visit GPs (family doctors) for sexual health issues, rather than the sexual health clinics where PrEP is currently being provided.

[Some actions which could diversify access to PrEP](#) include ensuring that communication and engagement activities over-serve sub-groups of people who might most benefit from PrEP but who might be least knowledgeable about it. There should be liaison with organisations which do not usually do sexual health work but which could reach people who could benefit from PrEP, such as women's advocacy organisations, asylum organisations and drug services. Work needs to be done with GPs and gender identity clinics to raise awareness and understanding of PrEP. Information about PrEP should be available in non-written formats and in languages other than English.

33. HOW MUCH DOES PrEP COST?

The listed price charged to the NHS for branded *Truvada* is £361 a month. Other versions of the same PrEP medications (generic drugs) are sold for a fraction of the cost by online pharmacies or the 56 Dean Street clinic in London.

In practice, large health organisations (such as the NHS) negotiate lower prices when they buy medicines in bulk. This happens whether they are buying branded or generic drugs.

As well as the cost of the drug, clinical services providing PrEP also have costs in relation to staff, facilities and laboratory services.

34. WHEN DOES GILEAD'S PATENT ON TRUVADA EXPIRE?

The cost of PrEP has been an important factor in policy debates about PrEP and in decisions on PrEP availability. The expiry of the patent protection for *Truvada* will make it easier for health services to use cheaper, generic versions of PrEP. When this happens, PrEP will probably be much more widely available.

The patents for the two components in PrEP, emtricitabine and tenofovir disoproxil fumarate, expire in 2016 and 2018 respectively. There is also a Supplementary Protection Certificate (SPC) which extends the protection for the pill which combines these two drugs (*Truvada*) until February 2020.

The validity of the SPC has been challenged by generic manufacturers. Courts in several European countries have examined cases between Gilead and generic manufacturers, with varying results. Whereas Spanish and German courts judged in favour of Gilead, the French court rejected the validity of the SPC and a generic combination pill is now available in French pharmacies.

In December 2016, an English court referred a case in which generic manufacturers challenge Gilead's SPC to the European Court of Justice. This was because the judge sought clarification on European case law. The European hearing took place in February 2018; a preliminary legal opinion prepared by a court official in April 2018 supported the generic manufacturers' challenge. However it is likely to be several more months before the European court makes its final decision and the case returns to the English court.

This means that Gilead's patent – giving it the exclusive right to manufacture and sell a pill combining emtricitabine and tenofovir disoproxil fumarate – is still in force in England and Wales.

Nonetheless there are some exceptions and ambiguities in the law, which creative and committed people have used to widen access to PrEP. This has allowed people to import generic PrEP for personal use, for research studies like IMPACT to use generic PrEP and for the 56 Dean Street to sell generic PrEP.

35. IS PrEP COST-EFFECTIVE?

Especially as PrEP is more expensive than some other HIV prevention interventions, health policy makers need to know that the benefits of providing PrEP are likely to be greater than the benefits of other healthcare interventions that may no longer be provided if resources are committed to PrEP. Health economists calculate the benefits of PrEP in terms of people having additional years lived in good health and lower spending on HIV treatment, because people have avoided HIV infection.

A recent analysis found that a PrEP programme for MSM in the UK would not only be cost-effective, but actually cost-saving (in other words, both improving health and lowering NHS spending) in a number of different scenarios.

The researchers based their calculations on PrEP being offered to all MSM who have recently had condomless anal sex, but only a proportion of those men actually taking PrEP. In terms of drug costs, PrEP was expected to cost around £4000 per person per year and HIV treatment around £6000 per person per year. The rate of new HIV infections in men eligible for PrEP but not taking it was calculated at 2% per year, similar to the rate seen in repeat testers in sexual health clinics.

Although PrEP would save the NHS money, the savings would not come immediately. Spending on PrEP would be high for the first 20 years, with the financial savings coming later. As a person who acquires HIV may need HIV treatment and care for several decades, PrEP is more cost-effective when this is assessed over a long time scale.

PrEP is less likely to be cost-effective if it used by people who would probably not acquire HIV anyway or if PrEP is less effective because of low adherence.

36. IS PrEP FREELY AVAILABLE IN THE UK?

Decisions on health policy are made separately in England, Wales, Scotland and Northern Ireland. The NHS in each country has taken a different approach to PrEP.

People living in England who meet the eligibility criteria can access PrEP from some sexual health clinics by taking part in the IMPACT trial. The trial is providing PrEP to 10,000 people over three years. Each participating sexual health clinic is allocated a limited number of places, some of which are reserved for women, heterosexual men and trans people (i.e. everyone except MSM).

In **Wales** and **Scotland**, PrEP is available at sexual health clinics.

In Northern Ireland, there is no NHS provision of PrEP.

Additionally, some people are taking part in a study called **DISCOVER**, comparing two versions of PrEP drugs. This study is already fully enrolled.

Many people also pay for PrEP:

- By importing generic PrEP medications from overseas, using online pharmacies.
- By purchasing generic PrEP medications through the 56 Dean Street clinic in London. The drugs need to be paid for but the tests and monitoring are provided for free by the NHS.
- By purchasing branded Truvada, with a prescription from a private healthcare clinic.

See question 38 for more information on using generics.

37. WHAT ARE THE ELIGIBILITY CRITERIA FOR PrEP IN THE UK?

In terms of assessing risk of HIV infection, [draft] **BHIVA guidelines** recommend that PrEP should be recommended to people in the following circumstances:

- HIV-negative men who have sex with men and trans women who report condomless anal sex in the previous 3-6 months and on-going condomless anal sex.
- HIV-negative individuals having condomless sex with partners who are HIV positive, unless the partner has been on antiretroviral therapy for at least 6 months and their viral load is less than 200 copies/ml.

PrEP can also be offered on a case-by-case basis to people considered to be at increased risk of HIV acquisition. This relies on an assessment by a clinician, considering the sexual history and personal circumstances of the person. It is crucial for permitting access to PrEP to a wider range of people, particularly heterosexual men and women.

BHIVA's [draft] guidelines suggest a wide range of potential risk factors in table 4.1.1, including condomless sex with multiple partners, having sexual partners from a population group with a higher HIV prevalence, being a recent migrant to the UK, being a transgender woman, and coercive power dynamics within a relationship.

38. IS IT SAFE AND LEGAL TO BUY PrEP ONLINE?

Several online pharmacies based overseas sell generic PrEP medications. It is legal to buy and import PrEP to the UK, as long as it is for personal use. In order to show that the drugs are only for personal use, individuals are advised to buy no more than three months' worth (usually up to 3 bottles of 30 pills) at once.

The website iwantprepnnow.co.uk lists a number of online pharmacies that have been checked and verified. Checks have been made to ensure that the sites are reliable and that the PrEP they are selling is genuine. [Over 200 people who bought PrEP from the websites featured on iwantprepnnow had drug levels in their blood measured.](#) There were comparable levels to people using branded Truvada, with no evidence of counterfeit drugs. In addition, PrEPster has not received any reports of people being 'ripped off' from the pharmacies reviewed on iwantprepnnow.co.uk.

People who buy their own PrEP drugs are strongly recommended to get clinical advice and support, for example from an NHS sexual health clinic, in order to take PrEP safely. This is supported by [draft] [BHIVA guidelines](#). People buying PrEP drugs need the same tests as other PrEP users – regular screening for HIV, sexually transmitted infections and kidney function. See question 10 for more information on these tests.

39. WHAT OTHER FORMULATIONS OF PrEP ARE IN DEVELOPMENT?

A study called [DISCOVER](#) is ongoing (including in the UK), in order to research the effectiveness of a slightly different PrEP pill. In this form, tenofovir disoproxil fumarate (TDF) is replaced by tenofovir alafenamide (TAF), a newer version of the same drug which may have less impact on the kidneys and bones. The study is expected to complete in late 2020.

Studies are also investigating the effectiveness of [an injection](#), containing the antiretroviral cabotegravir-LA. The drug is processed quite slowly in the body, so this might work as a long-acting form of PrEP that only needs to be taken every eight weeks. These studies may continue until 2021 or 2022.

[The vaginal ring](#) is the alternative formulation of PrEP that is furthest advanced in research. It could be made available in some countries in 2019. It looks like a contraceptive ring, but releases the antiretroviral drug dapivirine. It is long-acting (the ring only needs to be replaced once a month) but user-controlled (the woman can remove the ring herself). In this form of PrEP, the drug remains concentrated in the genital tract, rather than spreading throughout the body, therefore only protecting against vaginal exposure to HIV. All vaginal ring research has been done with cisgender women.

Research on other forms of PrEP is progressing more slowly. Researchers would like to develop a combination vaginal ring that could provide both PrEP and a contraceptive. A microbicide gel for anal sex might be a product that looks and feels like a lubricant but also contains an anti-HIV drug.



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