Pre-exposure prophylaxis (PrEP) is a daily course of antiretroviral drugs (ARVs) taken by HIV-negative people to protect themselves from infection.

Evidence shows that, when taken consistently and correctly, PrEP reduces the chances of HIV infection to near-zero.

PrEP is cost effective, and there is growing demand for it from people at higher risk of HIV infection, but the scale and coverage outside the USA currently remains extremely limited.

PrEP does not protect against other STIs so needs to be delivered as part of a comprehensive package of HIV/STI prevention services.

PrEP’s effectiveness decreases rapidly if not taken regularly as prescribed, so addressing the barriers preventing adherence is key to success.

Pre-exposure prophylaxis (PrEP) is a daily course of antiretroviral drugs (ARVs) that can protect HIV-negative people from HIV before potential exposure to the virus.

Trials have shown that, when taken consistently and correctly, PrEP is very effective and reduces the chances of HIV infection to near-zero.1 2 3 This has led some to describe PrEP as a ‘game changer’ for HIV prevention.4 5 6

While PrEP can provide very effective protection against HIV, it does not provide protection against other sexually transmitted infections (STIs) and blood-borne illnesses such as Hepatitis C, syphilis, and gonorrhoea. The effectiveness of PrEP is closely linked to adherence - if someone taking PrEP regularly misses daily doses, their risk of HIV infection will increase substantially. It is therefore
important that any programme offering PrEP provides it as part of a combination package of prevention initiatives, based on an individual's circumstances - with support and advice on the importance of PrEP adherence.

In 2015, recognising that PrEP has potential population-wide benefits, the World Health Organization (WHO) released new guidelines and a policy brief recommending that PrEP should be offered as a choice to people who are at substantial risk of HIV infection as part of a combination HIV prevention programme. Previous, PrEP was only recommended for certain key affected populations such as sex workers, men who have sex with men (sometimes referred to as MSM) and people who inject drugs (sometimes referred to as PWID). UNAIDS broadly defines priority populations for PrEP as groups with an HIV incidence of about 3 per 100 person-years or higher.

The United Nations General Assembly's 2016 Political Declaration on HIV and AIDS includes a commitment to providing three million people at higher risk of HIV infection with PrEP by 2020. However, as of October 2016, just 100,000 people were enrolled on it. The majority of people on PrEP live in the USA, although a significant number of people across the world are also thought to be accessing it through the internet.

Although the number and scope of PrEP activities is increasing globally, the scale and coverage of PrEP outside the USA currently remains extremely limited.

Truvada, a single pill that is a combination of ARVs tenofovir and emtricitabine, is currently the only drug approved for use as PrEP.

The case for PrEP

It works

The argument is over about PrEP. If you take the drug, it works, not only in a clinical trial but in the field.

- Anthony Fauci, Director, US National Institute of Allergy and Infectious Diseases (NIAID)

PrEP has been shown to reduce the risk of HIV infection from unprotected sex by over 90%, and from injecting drugs by more than 70%. These statistics include individuals with lower adherence levels, however, so the actual level of protection for those fully adhering is higher and near 100%.

For people facing limited options to protect themselves against HIV, PrEP allows them themselves to discreetly take control of their HIV risk.

A number of high profile trials have shown how PrEP can be an effective HIV prevention option in a number of different settings.

Started in 2007, the iPrEx study was the first to offer PrEP. PrEP was provided to 2,500 men who have sex with men at 11 sites in six countries on four continents. It found that the HIV infection rate in HIV-negative gay men who were given PrEP was reduced by 44% compared with men taking a placebo. However, importantly, among those who took PrEP seven days-a-week as prescribed, the risk of infection was reduced by 99%. Similarly, the IPERGAY study, which offered PrEP at six hospitals in France and Canada, reported an 86% reduction in the HIV infection rate compared to those taking a placebo.
The Partners PrEP trial recruited 4,758 heterosexual couples in which one partner was living with HIV across Kenya and Uganda. The risk of HIV infection was reduced by 62% among those who took tenofovir and 73% among those who received Truvada. Additionally, a number of trials have shown the effectiveness of PrEP in preventing HIV infection among women at a high risk of HIV.

Moreover, there is no evidence that PrEP leads to a reduction in condom use and other safer sex behaviour. For example, the PROUD Study conducted in the United Kingdom (UK) reported no difference in condom usage or levels of sexually transmitted infections between the group given PrEP and the group that didn’t take the drug.

It is cost effective

PrEP drug costs are lower than HIV treatment costs, both per-dose and for the duration of use. Moreover, PrEP is prescribed to be taken consistently, but only when someone is at heightened risk of HIV, whereas, should someone acquire HIV, they will need to be on antiretroviral treatment (ART) for their entire life in order to stay healthy. With an estimated cost of less than 5% of an HIV programme’s total budget, PrEP is considered by UNAIDS to be a key component of a Fast-Track response.

Despite this, the cost of PrEP is an important concern, even in high-income countries. A survey of 31 western and eastern European countries conducted by the European Centre for Disease Prevention and Control found that 21 countries considered the cost of PrEP to be a highly important limiting factor against its implementation; the second most important limiting factor was the cost of service delivery.

Ultimately, the cost-effectiveness of PrEP will be determined by the cost of PrEP medication, how efficiently it can be delivered to the people in greatest need, and its impact.

There is a demand

Demand for PrEP is rising among people at substantial risk of HIV infection. A multi-country survey of people at higher risk of HIV found 61% of respondents would “definitely” use PrEP if it was available. Up to 92% of men who have sex with men surveyed in India said that they were likely to use PrEP.

In the UK, around half of men who have sex with men have shown an interest in taking PrEP. One study has predicted that providing PrEP with annual HIV testing alongside improved treatment services to just a quarter of men who have sex with men in the UK with a high risk of HIV infection, could prevent over 7,000 new HIV infections by 2020.

In Latin America, demonstration projects and qualitative research finds a high awareness and willingness to use PrEP among men who have sex with men, transgender women and sex workers, especially if PrEP is accessible in the public sector for free or at an affordable price. However, as of 2017 only Brazil had put in place plans to implement a public PrEP programme.

Case study: Accessing PrEP online

The National Health Service in England (NHS England) has only provided access to PrEP through small scale trials, which has led many people living in the UK to purchase generic versions on the internet. In a 2017 study, researchers offered drug monitoring to people purchasing PrEP online in order to verify whether internet-based drug concentrations were consistent with necessary clinical standards.
In their analysis, it was found that all concentrations of tenofovir (TFV) and emcitrabine (FTC) purchased over the internet were similar to, and in some cases slightly higher than, those measured in phase 1 studies of PrEP with the original formulation from Gilead (Truvada). Significantly, they also found that no new cases of HIV were seen among participants.

The results from this study are important in reassuring populations at risk of HIV, who cannot yet access PrEP on the NHS, that it is safe to purchase PrEP from recommended online websites. 29

PrEP pilot programmes

Demonstration projects, offering PrEP as a choice through user-friendly services, have shown its potential value in diverse settings, as well as strong demand and adherence among people at high risk of HIV infection, including

HIV-negative partners within mixed status couples, men who have sex with men, young women and female sex workers. 30

At least 27 countries have planned or ongoing demonstration projects, 31 a number of which are outlined below.

The San Francisco experience

San Francisco in the United States of America (USA) was one of the first places to implement PrEP, rolling out the service in 2012. 32 Between a quarter and one third of at risk men who have sex with men in San Francisco are now thought to be on PrEP.

In November 2014, roughly 600 men who have sex with men enrolled on PrEP at the Magnet sexual health clinic in the Castro neighbourhood of San Francisco. After one year, there were no new HIV infections among the group. Adherence remained high over time - 95% after one month, and 94% in the seventh month reported that they had missed fewer than three doses during the past week. 33

Steve Gibson, Director of the Magnet clinic, said:

The bottom line is that there were no new HIV infections. We've found that the combination of clinical services combined with benefits navigation is what helps ensure that people can start taking the medication the same day, often costing the client nothing. 34

A website has been launched that sends SMS reminders to new clients to help them adhere to their medication and links them to health professionals and peers via an online social network if they have any questions. They are also supported to select health insurance plans that cover at least a portion of their PrEP costs. 35
CASE STUDY: The PrEP Brazil Study

The PrEP Brazil Study focuses on men who have sex with men and transgender women. It uses a number of innovative ways to increase PrEP adherence, including SMS reminders and engagement through social media.36

Preliminary results of the study are promising with uptake of PrEP over 50%, and notable increases in awareness of the service and knowledge of high-risk sexual behaviour among participants.37

Growing awareness and demand for PrEP is expected to increase its rollout. In 2011, only 22% of men who have sex with men in Brazil had heard about PrEP.38 By 2015, PrEP awareness among this group was 60% in Sao Paulo and Rio de Janeiro, and nearly 95% said that they would like to use PrEP to prevent HIV.39

Following the success of this study, Brazil is currently preparing to start offering PrEP free of charge to those in need of it via its national Unified Health System.40

CASE STUDY: The SAPPH-IRe project, Zimbabwe

In 2009, the Sister with a Voice programme was launched to strengthen Zimbabwe’s HIV response among sex workers. Within this programme, the SAPPH-Ire project is trialling offering antiretroviral treatment (ART) to women who test positive for HIV and PrEP to women who test negative for HIV.41

Offered at 14 locations, community-based adherence support is provided to both groups where each woman in the programme selects a 'sister', another woman in the programme with whom she attends monthly peer group sessions.42

Their HIV status is kept confidential unless they choose to disclose it, and the programme sisters support each other with medication adherence. SMS reminders are used to encourage women to attend both clinic and medication refill appointments.43

Another key component of the programme is legal advice provided to participants by peer educators. The peer educators inform sex workers of their basic rights and how they can legally protect themselves against violations of those rights.44

CASE STUDY: Scale up of PrEP in Kenya

Kenya and South Africa are the first African countries to begin implementing a PrEP strategy, and to date, have employed small-scale pilot projects to start introducing PrEP. The Bridge to Scale project has now been established in Kenya to scale-up PrEP for HIV prevention.

Awarded US$ 22.3 million in funding in September 2016, the project aims to reach 20,000
people who are at high risk of HIV, including adolescent girls and young women. The project will examine barriers to accessing PrEP and other HIV prevention services for those at highest risk of HIV and aims to find the most effective strategies for implementing PrEP so that it reaches these groups.45

Challenges of PrEP

Access

The availability of PrEP is currently extremely limited, with less than 5% of people at substantial risk of HIV infection having access to it.46

National regulatory approval for PrEP, which legalises the use of medicines, is limited to a small but growing number of countries. The United States approved the use of PrEP in 2012 and clinical guidelines were issued in 2014. In January 2016, France began offering PrEP within its national healthcare system and by mid-2016, 60 clinics were offering the service but only 437 people had started taking it.47

In December 2015, South Africa became the first country in sub-Saharan Africa to issue full regulatory approval of PrEP and to include PrEP in its national HIV programme. It was followed swiftly by Kenya. Other national regulatory authorities have also approved PrEP including Australia, Canada, Belgium, Portugal and Brazil among others.48 The European Medicines Agency has also granted market authorisation for PrEP to be marketed across the European Union’s 28 countries. 49 The European Medicines Agency has also granted market authorisation for PrEP so it can be marketed across the European Union’s 28 member states.50

In countries with regulatory approval for PrEP, the availability of the drug may still be restricted by several factors. People may only be able to access PrEP through a demonstration/implementation project; it may be legal, but because it’s difficult to get a prescription people would need to buy it online; where there are no national clinical guidelines or policies on PrEP, despite it being legal, doctors may feel unable to prescribe PrEP. Even in places where everything is currently in place, the drug may still not be made available for free under a national health system.51

A study, which charted primary care clinicians’ knowledge of, and attitudes towards, PrEP in the USA between 2009 and 2015, found their awareness of PrEP increased from 24% in 2009 to 66% in 2015. Overall, 91% of clinicians indicated a willingness to prescribe PrEP to at least one group at high risk of HIV, with 63% indicating support for public funding of PrEP by the end of the study period.52

To increase access to PrEP in California USA, a company called Nurx is allowing people to get a prescription for PrEP via a mobile app without having to see a doctor. The information put into this app is reviewed by a doctor remotely who decides whether the treatment is suitable for the person. Before they can receive their prescription, they must also have blood and urine tests.53

Though there has been significant progress in rolling out PrEP for certain groups such as men who have sex with men, young people and adolescents in high prevalence settings are being left behind.54

Attempts to address this include two pilot programmes called Pluspills and UChoose in Cape Town, South Africa. Pluspills is looking into the acceptability and use of PrEP among girls and boys between 15 and 19 years of age, while UChoose is examining PrEP delivery through different contraceptive options among girls aged 16 to 17 years.55
Working in Kenya, Lesotho, Malawi, Mozambique, South Africa, eSwatini, Tanzania, Uganda, Zambia and Zimbabwe, PEPFAR’s DREAMS initiative is also supporting adolescent girls and young women who are at high risk of HIV to access PrEP. By the end of 2017, DREAMS aims to reach 10,500 adolescent girls and young women with initiation and adherence services for the intervention.56

Awareness

Where knowledge of PrEP is high, demand is also high. However, many people who could benefit from PrEP are still unaware of the service.

One study surveying awareness and acceptability of PrEP among men who have sex with men in Scotland, Wales, Northern Ireland and the Republic of Ireland, found that only one third (34.5%) were aware of PrEP. Men who tested for HIV every six months were most likely to be aware of PrEP.57

Likewise, research from the USA among young men who have sex with men aged 18 to 24, found that only 27% of the sample had heard about PrEP. They were more likely to have heard about PrEP if they were older, better educated, had no permanent residence, had health insurance, or reported having at least one sexually transmitted infection (STI) in their lifetime.58

A further US-based study among young black men who have sex with men, one of the most vulnerable groups for HIV in the USA, found awareness and uptake of PrEP to be low, echoing the treatment disparities that this group experienced earlier in the HIV response. This suggests that real-world PrEP use by those facing high HIV incidence rates will bring with it major implementation challenges, which require purposeful and sustained engagement with the communities they are there to serve.59

Crucially, advocacy and awareness-raising for PrEP targeted at key populations must be led by those groups in order to effectively respond to the stigma they face, as well as structural barriers such as criminalisation and gender based violence.60

PrEP needs to be offered as part of a package of HIV/STI prevention services

Because PrEP is only fully effective when it is adhered to exactly as prescribed - and also does not protect against other STIs - it needs to be delivered as part of a comprehensive package of HIV/STI prevention services, based on an individual's circumstances. These might include condoms and lubricant, safer sex counselling, frequent STI check-ups and treatment, and regular HIV testing.61

A range of models for delivering PrEP have been proposed, including STI clinics, primary care clinics, and community-based organisations with links to clinics.62 63 64 However, each of these options presents challenges.

For example, while STI clinics serve a population at risk of HIV infection, most operate on a drop-in or urgent care basis and do not provide ongoing care and monitoring. Conversely, primary care clinics are experienced with ongoing care, but need to be able to identify people eligible for PrEP and offer risk reduction and adherence counselling.65

A study of 2,120 women from Kenya, Tanzania, and South Africa found that, despite all participants having been identified as being of heightened HIV risk, around half of those enrolled in the study thought they had “no chance” of acquiring HIV in the next 12 weeks. This meant they were unlikely to initiate or adhere to PrEP despite being given access to it. To combat this, the study suggested integrating HIV risk assessment and PrEP dispensation into established sexual and reproductive health services, including HIV/STI testing and counselling, antenatal care, and contraceptive
counselling, which women access routinely.66

Adherence

Understanding the rates at which people are able to adhere to PrEP, and addressing the barriers preventing adherence, will be crucial to the long-term success of this intervention.67

One study of three cities in the USA reported very different levels of PrEP adherence among men who have sex with men. In San Francisco, 52% of participants took PrEP daily compared to 35% in Washington DC and just 13.5% in Miami.68

A further 27% of those from Miami, 18% from Washington and 4% from San Francisco only took two doses a week - offering about 70% protection (compared to over 90% if taken daily). Moreover, 11%, 2% and 4% respectively took just one dose a week, offering very little protection; and 4.5%, 2% and 0% of participants had no detectable tenofovir in their blood.69

A number of factors were attributed to this difference in adherence levels including knowledge and awareness of PrEP, its availability and the participants’ lifestyle.70

Another factor which can affect adherence is exposure to abuse and violence within a relationship. A study carried out among mixed status couples across Africa found that women who had experienced verbal, physical, or economic abuse from a partner were more likely to have low PrEP adherence. The reasons given included stress and forgetting, leaving home without pills, and partners throwing pills away.71

To address PrEP adherence among high-risk men who have sex with men, an approach that uses cognitive-behavioural therapy (CBT) has been developed in the USA. The ‘Life Steps’ intervention consists of a number of CBT modules such as creating a PrEP dosing schedule, adhering to daily PrEP, problem-solving barriers to adherence, and sexual risk-reduction techniques. An assessment of Life Steps found that, when supplemented with short videos on PrEP, it had the potential to increase PrEP adherence for this key population.72

Another approach is to address the issue of daily pill-taking by investigating the use of long-acting injectable ARVs. Two trials on this intervention, ECLAIR and HPTN 077, began in 2016 and 2017.7374

Stigma and discrimination

As with other HIV services, stigma and discrimination have a negative effect on uptake and adherence to PrEP.

In some settings, PrEP is associated with high-risk sexual activity. It also has the stigma of being related to HIV (which may also relate to other stigmas, such as homosexuality, sex work, and/or drug use) and the stigma of PrEP being an alternative to condoms (as condom use is often associated with responsible sexual activity).75

PrEP-related stigma has been reported by trial participants at a range of sites among different key affected populations spanning several countries. Authorities may also persecute sex workers for the possession of PrEP pills as evidence of sex work.76

A study of around 240 US-based, HIV-negative, men who have sex with men identified a number of barriers to PrEP. Crucially, it found that participants who recently engaged in transactional sex were more likely to report that anticipated stigma from primary and casual partners would deter them from using PrEP, suggesting that those who face multiple stigmas may need more focused interventions to enable them to access PrEP.77
Of 440 respondents consulted by the Global Network of Sex Work Projects in 40 countries, only a few staff or volunteers had heard of PrEP. They also held suspicions and scepticism about the treatment, including concerns that it might reduce condom use, be forced on sex workers or facilitate mandatory HIV testing.

The research showed that non-governmental organisations and sex work groups are concerned about a range of issues surrounding PrEP, including cost and discrimination.

**Photo by Jason/ CC BY-NC-ND 2.0**

Tools and resources:

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• 30. UNAIDS (2016) 'Prevention Gap Report' [pdf]

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41. AVAC ‘Sisters Antiretroviral therapy Programme for Prevention of HIV –an Integrated Response (SAPPH-Ire)’ [accessed February 2016]

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