PrEP in Europe

Webinars on PrEP for women in Europe, 22 June and 13 July 2021

Final report

PrEP in Europe

PrEP in Europe has been a partnership of European NGOs aiming to improve knowledge of, provision of, and access to PrEP throughout the WHO European region.

Active since 2016, and initially conceived as a three-year project, it convened two pan-European summits in Amsterdam in February 2018 and Warsaw in October 2019, conducted webinars and wrote research briefs on PrEP for European populations.

In 2020 PrEP in Europe decided to concentrate on activities for specific key affected populations and about specific issues. Initially in-person small meetings were planned, but with COVID they became webinars.

They included webinars on PrEP and its effects on mental health; on PrEP and the trans community (preceded by a closed online meeting of community members); and PrEP and the new drug/formulation pipeline (organised in partnership with EATG, PrEPster and AVAC).

Evidence Briefings have been developed to accompany the subjects of the webinars and also on other topics such as PrEP and STIs and PrEP and drug resistance.

PrEP in Europe has now ended as a formal partnership but will continue as a clearing house for PrEP news and materials, and as a Facebook Group. See www.prepineurope.org and www.facebook.com/groups/PrEPinEurope.

All our webinars and conference presentations are on our YouTube channel here.

PrEP and women

PrEP in Europe had planned two webinars on PrEP for women in Europe from the outset. This is because, to borrow a title from the recent WAVE workshop at the 18th European AIDS Conference, women, especially cis women, form a “Special Majority” – individuals at risk of HIV are far more widely scattered than among key affected populations, but who may number just as many because of the size of the population.

The first webinar was on 22 June and the second on 13 July.

Presenters

22 June: First Webinar

Sylvain Chawki is an infectious disease physician at Hôpital Saint-Louis, Paris. Sylvain had presented at the Warsaw PrEP summit and is an expert on drug levels and absorption in different tissues and therefore in differences in PrEP efficacy between different populations.

Irene Ogeta, LEARN initiative, ATHENA Project, Kenya. The ATHENA Project co-ordinates work on HIV prevention and HIV vulnerability in young women in ten African countries. LEARN is a PrEP awareness and preparedness project that was conducted in anticipation of what is currently the world's largest programme providing PrEP to women.

Ana Silva Klug is an infectious diseases physician at Bellvitge Hospital near Barcelona in Spain. Bellvitge was one of the first clinics in Spain to start providing PrEP, in advance of national adoption, and Ana has particular expertise in interpreting and navigating guidelines.

13 July: second webinar

Kim Leverett is a nurse practitioner at The Royal London Hospital, run by Barts Health NHS Trust. The Royal London runs a dedicated clinic for female sex workers and recruited the largest number of women to the IMPACT PrEP demonstration study in England.

Olga Denisiuk is Head of Program Optimization and Research for the Alliance for Public Health in Ukraine, which is the co-ordinating NGO that has been implementing the piloting and expansion of PrEP in Ukraine.

Sophie Strachan is Director of the Sophia Forum, a UK-based advocacy organisation for women with or at risk of HIV. She was co-chair of the Women and Other Group of the IMPACT PrEP implementation trial in England.

Both webinars were introduced by **Gus Cairns**, the co-ordinator of PrEP in Europe. The panel discussions were facilitated by **Harriet Langanke**, director of GSSG, the Charitable Foundation for Sexuality and Health in Köln, Germany.

Panel discussants included **Yannis Mamaletzis**, infectious disease epidemiologist from WHO Ukraine (in the first webinar) and **Vanessa Apea**, HIV physician at Barts Health NHS Trust (in the second webinar). The second webinar was also joined by **Akiko** and **Glenda**, two women using PrEP in London.

The first webinar recording is at www.youtube.com/watch?v=m_X4ggo0bVw

The second webinar recording is at www.youtube.com/watch?v=0EqZSF9AkH4

Summaries of the presentations: first webinar

Owing to some invitation difficulties, this was only attended by about 35 participants.

Sylvain Chawki

PrEP is potentially just as effective for cis women as for gay men and trans women. TDF/FTC oral PrEP was 75% effective in women in the TDF2 study and 66% effective in Partners PrEP (TDF alone was 71% effective).

However, two other randomised controlled studies, FEM-PrEP and VOICE, showed no efficacy. This appeared to be driven by low adherence and a deliberate choice by some participants not to take PrEP until its efficacy had been proven.

The importance of low adherence in cis women was underlined by the HPTN 084 study of injectable cabotegravir as PrEP, which showed 89% additional efficacy of injectable cabotegravir in cis women, over and above the efficacy of oral PrEP.

Trans women represented 12.4% of the study population in the HPTN 083 study. In this group, cabotegravir had 66% additional efficacy over oral PrEP, nearly as high as the 69% additional efficacy seen in the study overall.

One other alternative to oral PrEP for women has been licensed for Africa, the dapivirine vaginal ring. The efficacy of this in preventing HIV was only 39% in the HOPE open-label study, but there was advocacy in both webinars for it to be licensed in Europe too in order to increase the choices available to women.

TDF/FTC levels in the female genital tract are lower than in the rectum. Pharmacokinetic studies have shown that steady-state levels are not reached until the seventh daily dose, unlike in the rectum, which requires only two doses or one double dose. Therefore a seven-day lead is required before sexual contact for women. PrEP leaves vaginal tissues more quickly than rectal too, meaning that to ensure efficacy against HIV infection a longer period of dosing after exposure is recommended too. The World Health Organization still recommends 21 days but France decided to recommend seven days.

There is caution over the use of TAF/FTC (*Descovy*) as PrEP for women. Although TAF/FTC was 82% effective in animal studies, human efficacy studies have not yet been completed. In pharmacokinetic studies, levels in the female genital tract tissues were 100 times lower than in rectal tissues (1 picomol per gram steady state after five days compared with 100 picomols).

At the time of the webinar, the longer-lasting drugs islatravir (as an implant or long-lasting pill) and lenacapavir (as a subcutaneous injection) were looking promising as future options for women but trials of both have been halted, one due to unexpected CD4 declines being seen, the other due to formulation problems. In the longer term combinations of broadly neutralising or multispecific antibodies may hold out promise as longer-lasting PrEP for women.

Irene Ogeta

The ATHENA Network is a feminist organisation that works to address the factors that increase adolescent girls and young women's (AGYWs') vulnerability to HIV. It aims to advance the recognition, protection and fulfilment of women's and girls' human rights by supporting young women to conduct peer-to-peer advocacy to address young women's vulnerability to HIV, sexual violence and limited access to sexual health and reproductive services.

Through the #WhatGirlsWant project it has been amplifying the leadership of AGYW across ten countries in eastern and southern Africa.

In the LEARN (Lead, Evidence, Advocate, Research, Network) project launched in Kenya and Uganda in 2017, peer ambassadors explored the knowledge, views and preferences of adolescent girls and young women aged 15-24 about PrEP, in order to inform effective implementation and rollout, including assessing barriers and enablers.

LEARN also aimed to identify AGYW at the highest risk for contracting HIV, increasing HIV risk awareness among them, enhancing PrEP awareness, facilitating PrEP access and linking them to PrEP care.

What does pre-exposure prophylaxis mean for adolescent girls and young women? In qualitative research, 240 participants took part in ten dialogues.

Pre-dialogue questionnaires showed that 80% of the AGYW had heard of PrEP before taking part. But 43% of them thought it was PEP, i.e. a pill taken *after* unprotected sex to prevent HIV transmission, and only 33% knew it was a pill taken every day.

Dominant themes included:

Choice, agency, accurate information and understanding were important to AGYW thinking about whether they would take PrEP.

Trust was a dominant theme – trusting partners, knowing their HIV status and knowing if partners had other partners were all relevant to decision-making about PrEP.

Access was critical too – PrEP being free, in accessible clinics and with no stock-outs.

PrEP being short-term, rather than lifelong antiretroviral therapy (ART), was seen as a major reason to consider it.

Perceived advantages included:

Ability to stay in school for sexually active school-going AGYW.

Opportunity to conceive without risk of HIV acquisition.

Able to have sexual relationships without worry about HIV – some participants talked specifically about sex work, transactional sex or multiple partners.

More opportunities for partners and relationships.

Reduced stress and worry about contracting HIV.

Reduced discrimination among discordant couples.

Reduced gender-based violence among the AGYW where men tend to have control.

Perceived disadvantages included:

Many participants said they disliked taking pills – some might consider injectables.

Side effects were a big concern. Many participants cited side effects they had heard of. Impact on appetite, nausea/vomiting, stomach ache, headache, 'morning flu', and long-term damage to health could plausibly be acute or chronic PrEP side effects. But others, like weight gain, nightmares, hallucinations, dizziness, weakness and blood pressure problems are either associated with other antiretrovirals (e.g. efavirenz) or not at all.

Impact of PrEP on behaviour was also cited, with some AGYW talking about immoral behaviour and promiscuity if PrEP was made available.

Managing multiple pills if using oral contraception as well was a big issue. AGYW cited need for integration of HIV prevention and family planning.

Challenges

PrEP stigma – people making judgements about you or assumptions about your behaviours based on PrEP use.

HIV stigma – pills and packaging are the same as for ART, so people may think you have HIV.

Relationships – trust issues, judgement, multiple partners, conflict.

The lessons learned from the LEARN project influenced the Ministry of Health in Kenya to strengthen the PrEP Technical Working Group whose mandate was to provide strategic

direction and oversight for the implementation of PrEP in Kenya in line with health sector policies and the Kenya AIDS Strategic Framework.

Ana Silva Klug

Why has the introduction of PrEP been so slow in Europe, compared to the US?

The European Medicines Agency (EMA) approved TDF/FTC in 2016, four years after the US Food and Drug Agency. The EMA only specified that PrEP should be offered to people "at high risk".

GESIDA, the Spanish AIDS Study Group, issued guidelines the same year that said PrEP should be offered to gay and bisexual men and transgender women who had had condomless sex in the previous six months *and* one of the following:

- More than two sexual partners
- Diagnosis of at least one STI
- Use of post-exposure prophylaxis (PEP)
- Chemsex.

They added that PrEP could also be offered to other people "who may be at high risk or for whom there is some evidence of benefit", for instance sex workers, injecting drug users who share needles, people with HIV-positive partners with unsuppressed HIV or "people in situations of social vulnerability exposed to condomless sex with partners at high risk of HIV infection."

However when Spain issued its *coverage* criteria in 2018, in anticipation of making PrEP available through its national health service (which finally happened in November 2019), the only cis women to be included were "HIV-negative female sex workers who report condomless sex". Other cis women were excluded and there was no concessionary language about "evidence of benefit" or "social vulnerability".

This puts women in a difficult position if seeking PrEP. Even if women actually are sex workers, they often find it difficult to talk about their situation for different reasons: being in a situation of extreme vulnerability; social stigma; or fear, since practicing prostitution is not completely decriminalised in Spain.

When a ciswoman meets guideline criteria but not coverage criteria, it is difficult for them to get PrEP. The Bellvitge clinic has been prescribing PrEP since June 2018 and currently only has five female recipients out of 250 PrEP users – three transgender and two cisgender women.

Ana said that there needed to be a two-pronged strategy to increase PrEP access to women: first, to adapt the coverage criteria so they align with the clinical guidelines. Secondly to raise awareness of PrEP as an option among the professionals women go to for sexual and reproductive health: gynaecologists, midwives, GPs etc.

Panel discussion

Sylvain: Discussing PrEP in terms of gender could be an obstacle to assessing risk. Cis women have anal sex too; we know little about neovaginal transmissibility of HIV in transitioned women and the same of vaginal atrophy in trans men. People's clinical need for PrEP does not necessarily align with their gender identity and maybe it is 'acts' we need to cover, not people.

This has direct clinical significance in terms of what we say to PrEP seekers about how long they should take PrEP for before/after possible exposure.

Yannis: Guidelines created with European-born populations in mind can discriminate against migrants. A woman from a high-prevalence country may be at more risk of HIV in her host country than her home country, as migrants tend to socialise and find partners within their own community, which will be smaller and more closely connected than at home. In addition, migrants are often faced with poverty, violence, housing insecurity, unemployment and many other stresses that may exacerbate HIV vulnerability, via everything from depression to transactional sex. Mobilising knowledge and demand in minority-ethnic communities is very important. One thing guidelines are very bad at is dealing with people *entering* "seasons of risk" – which could be a young gay man moving to university, or a young migrant entering a new country.

Gus: There should be less regulation of supply and more emphasis on mobilising demand in PrEP anyway. It is important to raise people's knowledge and awareness of PrEP to start with, but beyond a certain knowledge level, if parallels with the gay male community can be drawn, people seem to have a good idea of when they are at risk and seek PrEP accordingly. "The indication for PrEP is that the person asks for it" (Bob Grant).

Yannis: This is also fundamentally an issue of *choice,* which is why I think the dapivirine vaginal ring should be licensed in Europe, even if it is only moderately effective.

Irene: The first two challenges to overcome with PrEP are availability and effectiveness. In Kenya, we have availability and are working to improve adherence to raise its effectiveness. Effectiveness is impeded by misconceptions (about side effects, etc) and the stigma that prevents people coming forward for it. That can be self-stigma, but I hear a lot about a stigmatised image of PrEP: "Oh, that's the thing that gay men take in New York."

Yannis: Kenya and South Africa are the biggest PrEP providers in the world and their strategies are very different. South Africa started with programmes for key populations – sex workers, then gay men – and have only recently moved into programmes for young heterosexual men and women. Kenya promoted PrEP for the general population from the start, and as a measure to take control over one's health. I think Kenya's strategy was better.

Sylvain: Educating other healthcare workers about PrEP is very important. In France, allowing GPs to prescribe PrEP, even if not many are doing so yet, has two possible benefits. Firstly, you have to educate GPs about PrEP. Secondly, they will see a much broader range of patients than sexual health clinics and can start educating their patients about it.

Ana: It is also a generational thing. Doctors tend to hang onto the principles they were taught at medical school, so including PrEP in medical teaching curricula is important. Young medics are also often motivated to improve services towards their own community if that community is underserved, whether that's minority ethnic populations or women. Very important to educate workers in NGOs who have hitherto not dealt much with HIV or are too busy helping their clients with other things, e.g. sex worker organisations. PrEP should also be available in retail pharmacies especially as now 30 TDF/FTC can sometimes cost less than 30 condoms.

Yannis: Greece doesn't really have a functioning GP service, but women do see gynaecologists and midwives and go to family planning services. These trusted providers are the people to reach. Even workers who cannot themselves prescribe can recommend.

Summaries of the presentations: second webinar

This was attended by about 80 participants.

Kim Leverett

We had the advantage of already running a twice-weekly sexual health clinic for female sex workers in London, with a small group of five consistent and trusted staff.

Our service users are around 80% migrants: especially from Brazil, Romania, Poland. Ages 18-62. Mainly cis women, a few trans women. At least a quarter of the 333 cis women in the IMPACT trial came from the Barts clinic.

We use the NETREACH communication and support model, with bookings and consultations via phone, usually with WhatsApp. Translation (live, Google translate) has to be widely used.

No cis service users had heard of PrEP before we introduced it. Once the IMPACT trial started, all who'd had condomless sex in last three months were offered PrEP and most started it.

A PrEP discussion check box was added to our health check proforma. We had a follow-up call two weeks after starting PrEP, then a month, then three-monthly.

We encouraged peer-to-peer communication; many service users chat to each other between clients.

We educated and communicated with the wider staff group at the hospital to clarify issues and challenge mindsets. We have disseminated our work in sex worker conferences and support groups. But what we need above all are more female PrEP users to be 'PrEP champions', to both promote and deliver care to their peers and to ensure ongoing continuity when PrEP for women is expanded.

Olga Denisiuk

Eastern Europe and central Asia is one of the only two global regions with a growing HIV epidemic (the other being the Middle East and North Africa): diagnoses rose 72% between 2010 and 2019.

There is a big 'PrEP gap' in Europe between people who say they are interested in PrEP and people who use it. There is a lack of funding and lack of awareness. We lack realistic and usable guidelines, and detailed understanding of dosing and efficacy.

In women, there is a strong association between HIV risk and violence/coercion. Relationship risk should be added to sexual health and behavioural risks as PrEP indicators. Women who experience violence often blame themselves for HIV/risk rather than partners.

Other risk factors include disability, being a refugee or internally displaced person (many of these in Ukraine owing to the Ukraine/Russian conflict); being under 30 or over 40, performing unpaid work (e.g. in a family business), and having children at home.

Between April 2020 and March 2021, 1440 people started PrEP in Ukraine, of whom 216 were non-MSM, including 114 women (8%). In total (including women already on PrEP and women re-starting it) 252 women were on PrEP during this period. They were predominantly partners of people living with HIV or sex workers, with a small number from other groups.

The Alliance for Public Health, the main NGO charged with co-ordinating PrEP outreach, operates a mixed referral model: PrEP seekers can be assessed directly at a clinic, but can also be assessed for PrEP indirectly at an NGO before referral to clinic. This is particularly useful for vulnerable minorities such as sex workers, people who inject drugs and their partners.

We aim to expand assessment and referral services to GPs, obstetric and gynaecology services, women's refuges, drug services and services for women in conflict zones.

Beyond that, women's need for PrEP should not always be framed in terms of vulnerability. There is a significant population of young women and men, not in key populations, who are unreached: the club-kids and social media generation. There is a need for social media messaging that "PrEP is about freedom of choice, equity and self-confidence", not just about sex.

Sophie Strachan

As co-chair of the non-MSM group in the IMPACT trial, we held initial discussions about "preparing women for PrEP".

We talked a lot about the indicators for PrEP that Olga mentioned and especially the association between HIV risk and gender-based violence. However we also felt that limiting the discussion only to vulnerability risks disempowerment and the idea that female PrEP users are vulnerable/victims.

We collaborated with i-Base to develop resources and knowledge for cis and trans women about PrEP: see www.womenandprep.org.uk for videos, posters, discussion groups and www.youtube.com/channel/UCtcrwliT4Dhsdyv-CpSI0YQ for more videos.

Staged model of adoption: PrEP literacy -> PrEP candidacy -> PrEP uptake. It is an issue that criteria for assessing need for PrEP is more complex in women than in gay and bisexual men, with no clear indicators set out in guidelines; this is why the central step of 'PrEP candidacy' is so important. This means allowing women the information but also the space to reflect on their own degree and pattern of risk, their need for PrEP, and whether it is the right lifestyle choice for them.

A questionnaire developed for the IMPACT trial for all female STI clinic users increased recruitment during the last month of the trial. The eventual total of non-MSM in the IMPACT trial was 1038 out of 24,255 = 4.3%. Of these, 359 were trans women and 333 cis women.

The lack of offer was as much the cause of low uptake as lack of demand: a low HIV risk perception was shared by clinicians and service users, especially outside London.

Two UK PrEP users – in their own words

Akiko

I heard about PrEP from my clinic and Sophie, but had already heard about it through friends.

I am Filipina and come from a conservative religious country where open discussion of sexual risk just doesn't happen.

Sexual health advisors should work on reassuring individuals that PrEP is OK and can discuss it in our social circles. Social media is all very well, but there is nothing like word of mouth.

Eventually this could develop into "PrEP influencers".

I have been taking PrEP since the IMPACT trial and use it on-demand, when I get ready for a sexual partner. It definitely puts me at ease.

Glenda

I heard about PrEP from the Dean St clinic but had also already heard about it through friends, including Akiko.

This made talking to a sexual health advisor and admitting I was quite "active" (or used to be) easier.

I also use it on-demand, have been doing it about a year.

Panel discussion

The dapivirine ring should be available in Europe. Women should have choice, everywhere in the world.

Undocumented people, including sex workers face big problem in many other European countries, unlike in the UK, where sexual health services are available regardless of immigration status.

Should the COVID epidemic have provided us with more options re digital health – e.g. 'tele-PrEP', with contact, assessment and drug delivery?

We need to 'normalise' PrEP for our broader communication outside of HIV specialists and activists, including within the medical community. PrEP should be just another 'no-brainer' option for any person who is sexually active, like condoms and lubricants. We should take PrEP awareness and offers to women where they access services: drugs services, GPs, contraception/menopause support, abortion clinics. We should not expect them to be proactive and at the same levels of PrEP literacy that we know took years for gay men to acquire.

There is considerable interest in hearing more about women who use drugs, including sex workers who use drugs. Also regarding services in prisons, as many drug users and sex workers end up in prison. There has not been much discussion on people who inject drugs in the UK and similar European countries, though more in Scotland which saw a recent epidemic in drug users.

In Ukraine, the Alliance Global NGO is now planning to launch a national information and advertising campaign to other categories of the population at increased risk of HIV infection (including people who inject drugs, sex workers, discordant couples and others) – with the support of the Public Health Centre of the Ministry of Health of Ukraine.

In eastern Europe, where infection via needle sharing is common, there is a need for more information on and provision of PrEP for people who inject drugs. In the Ukraine programme, some people who inject drugs, were covered as well: among women starting,

restarting or using PrEP, 49% were drug users, though people who inject drugs only formed 3% of PrEP starters in 2020-21 as so many were gay men.

In Ukraine, it should not be so hard to add PrEP to its large harm reduction service serving over 200,000 people a year. We have also started a social network strategy to approach partners of people who inject drugs who may not be so aware of their risk. What is the thought behind not giving it to drug-using women? Intravenous drug-using people are prioritised for hepatitis C treatment, after all.

The lack of specific provision for people who inject drugs in western Europe may be due to only having one rather flawed randomised study that showed PrEP worked for drug users. In addition, in some western European countries harm reduction has meant that the proportion of people who inject drugs who have HIV is quite low (unlike hepatitis C).

We are now seeing new infections among gay men who inject drugs during chemsex and ironically this may lead the way to a new awareness of the need to address people who inject drugs. Many sex workers and trans women also use drugs.

We need to understand that women may have different attitudes to and understanding of their risks of HIV than gay men, and place them in a different context: move away from medical criteria assessments towards empowering self-assessment for HIV risk and one's need for PrEP – What would need to change? The language of PrEP, among other things.

Funding and time is a reality too; many services for vulnerable women are already overstretched. We can help by assisting them in applying for funding for a PrEP service.

Summing up: four main points from two webinars

One theme heard is the need to move more towards awareness-raising and demand-side work – PrEP candidacy – and see initiating PrEP as a *dialogue* between provider and seeker.

The second follows on: women may think and talk about their HIV and sexual health risk in quite different ways from gay men and in a broader context. We need to meet them where they are.

The third is that PrEP for people who inject drugs and their partners and providing it through harm reduction services will be an important issue in many countries in Europe, more so than in other global regions.

The fourth is that we need to enable PrEP provision in the services women use for sexual and reproductive health, and train, fund and raise awareness and skills in professionals.