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WEBINARS SUMMARY REPORTS

Developments in the HIV Biomedical Prevention Pipeline & PrEP Implementation Issues – An Update for Community Educators and Advocates

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EATG European AIDS Treatment Group

Contents

SCOPE partners

Background

This report summarises highlights from online-meetings on the HIV Biomedical Prevention Pipeline & PrEP Implementation Issues for Community Educators and Advocates on 24 May and 7 June 2023,[1] jointly organised by the European AIDS Treatment Group (EATG) together with AIDS Action Europe, AVAC and ECOM AIDS Action Europe, AIDES, AVAC (AIDS Vaccine Advocacy Coalition), Coalition PLUS, ECOM (Eurasian Coalition on Male Health), ESWA (European Sex Workers' Rights Alliance), FES (Foundation for Social Education), GS:SG (Gemeinnützige Stiftung Sexualität und Gesundheit), PrEPster/The Love Tank, TGEU (Transgender Europe). Thank you to EATG members Aisuluu Bolotbaeva, Harriet Langanke and Richard Stranz and SCOPE Community Expert Group Member Hirwa Carter Honorée Wolf for moderating the webinars!

Link to the recordings:

1. HIV Biomedical Prevention Pipeline: https://youtu.be/V9lQdvibqsA?feature=shared
2. PrEP Implementation Issues: https://youtu.be/pJ_7b4L0iLQ?feature=shared

1 The webinars were part of the SCOPE Project, which has been developed by the EATG and was made possible through a grant from ViiV Healthcare Europe Ltd. ViiV has not had any control or input into the structure or content of the events.

Executive Summary

This report summarises two webinars on HIV biomedical prevention research & PrEP implementation issues for community educators and advocates. It covers developments from the PREVENIR Cohort study, Long-Acting Intramuscular PrEP, DoxyPEP, vaccine and STI-PEP research. It reports on the uptake of PrEP among women and in particular migrant women from sub-Saharan Africa and trans people. The report examines the various challenges these communities face to access PrEP programmes. While challenges exist, continued research and advocacy efforts offer hope for more effective HIV prevention strategies in the future. Community advocacy plays a vital role in expanding access to these prevention tools, particularly in pressing for affordability pricing and equitable distribution of biomedical prevention tools as part of combination prevention.

What is in the pipeline and what are promising tools for prevention?

Jade Ghosn, Professor at Department of Infectious Diseases, Bichat University Hospital.

To access the slides (ENG/RUS) click here.

Pre-exposure prophylaxis (PrEP) with TDF/FTC in clinical trials achieved great levels of protection against HIV infection in clinical trials.

- Effectiveness and adherence: one of the issues with oral prep with TDF/FTC is adherence to the daily regimen. As of now, there is accumulated data showing that effectiveness improves with adherence to PrEP.
- On demand PrEP: having on demand PrEP instead of daily PrEP can improve adherence. This was demonstrated by the Ipergay trial, which was conducted in France and Canada. The study demonstrated that on demand PrEP with TDF/FTC was as effective as oral daily PrEP with TDF/FTC.
- WHO Europe recommendations: WHO Europe has endorsed the recommendation of PrEP 2-1-1 on an on-demand basis since 2019.

PrEP in real life setting, the ARNS PREVENIR Cohort Study

In 2017, French researchers have created the PREVENIR Cohort, which includes 30,000 participants, to collect data on PrEP in real-life settings rather than in a clinical trial. Participants can choose to take PrEP daily or on demand, as well as switch regimen during the study period. They are followed up according to French recommendation every three months with a fourth ELISA HIV test performed every three months in men who have sex with men (MSM), a renal function test, and a sexually transmitted infections (STIs) screening.

After a 2-year follow-up, results of the study show that half of the participants chose to take daily PrEP and the other half preferred PrEP on demand. The only characteristics that differ between both groups is the number of sexual partners in the last three months, which is higher in the daily group. This is not the result of randomisation; participants chose themselves the preferred way to take PrEP and can switch regimen depending on their sexual activity throughout the study period.

There have been 6 cases of HIV seroconversion, three in each group which yields a low HIV incidence rate of 0.11 for 100 participants. In all 6 cases, participants had stopped PrEP weeks before seroconversion while continuing to have highly at-risk sexual behaviour. There was no seroconversion in participants taking PrEP, meaning both regimens offer near to 100% protection in high-risk MSM, when they fully adhere to the PrEP regimen.

The barriers to PrEP implementation include forgetfulness, competing priorities, safety concerns, stigma, partners' negative feelings toward PrEP, and suboptimal uptake and coverage.

Long-Acting Intramuscular PrEP (LAI PrEP)

Currently, Cabotegravir offers robust data and is an integrase inhibitor that is given intramuscular every two months.

Successes:

- The HPTN 083 study performed in MSM showed that cabotegravir was superior to daily oral TDF/FTC with a reduction in HIV incidents above 70%, and to TDF/FTC on demand. The 084-study restricted to women shows the same results.
- There is a very low rate of failure with 18 seroconversions in the study HPTN 083 out of more than 2,200 participants.

Limitations:

- 6 out of the 18 people who seroconverted did comply with the injection schedule. There is no explanation on why they seroconverted. There were no specific subtypes in these 6 failures. For the remaining, there were some delays in the injection schedule which might explain seroconversion.
- There is a delay in identifying HIV seroconversion while on Cabotegravir Long-Acting PrEP. The first HIV test that was detected on site after 40 weeks (about 9 months) since enrollment. Yet, retrospectively testing samples drawn before revealed that there was a 3 month delay before the identification of the seroconversion on site.
- The delay in detection yields to the selection of resistance in this individual to all the inhibitor class. This creates a risk for the virus to acquire major resistance mutations, which is a problem for future therapeutic options.

Overall, LAI PrEP provides very high rates of protection and low rates of seroconversion, but seroconversion might still happen in individuals fully complying with injection schedules and there may be a delay in the detection of HIV infection due to the long-acting antiretroviral exposure.

Today, there is also preliminary data on Lenacapavir, which is a capsid inhibitor given subcutaneously every six months and can be self-administrated. It differs from Cabotegravir because it is not intramuscular. Therefore, one does not need the healthcare worker to provide the injection.

Successes:

- High rates of protection in macaques after intra-rectal challenge with Simian-Human Immunodeficiency Virus (SHIV) with the highest dose of Lenacapavir given subcutaneously.
- 100% protection in female macaques after vaginal challenge with the highest dose of Lenacapavir given subcutaneously.

Next steps: Trials in humans are currently being conducted.

At CROI 2023, rectal insert of **TAF plus Elvitegravir (TAF/EVG)** is an integrase inhibitor was presented. This might be interesting because some people might be reluctant to take daily pills or undergo injections, and prefer a local device for PrEP, such as this rectal insert.

Successes:

- Pharmacokinetic data shows that one needs to have two rectal inserts inserted at the same time, and these two inserts might seal protection for 72 hours.

Next steps: the tolerance data is promising so far which might lead the rectal insert into development for further clinical trials.

Doxycycline as Post Exposure Prophylaxis (Doxy-PEP)

Doxy-PEP and STIs prevention

STIs are a growing issue in the MSM population globally, and especially in the PrEP user MSM population.

Below, the results of a Doxy-PEP study in MSM and trans women conducted in the US are shown:

- The trial was conducted in people living with HIV and in MSM or trans women using PrEP with Doxy-PEP, as post-exposure prophylaxis (PEP) which is two pills up to 72 hours after condomless sexual intercourse. There was a Doxy-PEP arm and a no PEP arm, and participants were screened every three months for STIs.
- 65% reduction in STIs incidence in the doxy PEP arm in comparison to the no-PEP arm. This was true in both the PrEP cohort and in people living with HIV.
- This was true for chlamydia, syphilis and gonococcal infections (gonorrhea), which was unexpected because of the high level of resistance of gonococcus to doxycycline.

Doxy-VAC trials in men living with HIV and men on PrEP, France:

- 80% reduction in chlamydia and syphilis with Doxy-PEP in men living with HIV and men on PrEP.
- 50% reduction in the incidence of gonococcal infection with Doxy-PEP in men living with HIV and men on PrEP.

Doxy-PEP study in women, Kenya:

- There was no demonstrated efficacy of the Doxy PEP to prevent chlamydia infection, which is in great contrast of what has been studied in male individuals.
- This failure could not be explained by the penetration of doxycycline in the vaginal tissues, as data suggests that there is higher concentration of doxycycline in the vagina than in the rectum.
- Another hypothesis is adherence issue in the context of women in Kenya.

Next steps: Further studies are needed to understand whether Doxy PEP works in women to prevent bacterial STIs.

Finally, there are efficacious levels of protection with antiretroviral with **Treatment as Prevention** (TasP) for people living with HIV and PrEP for HIV-negative individuals who are at risk of acquiring HIV.

To conclude, "whatever the next hottest, scientifically proven HIV treatment or prevention strategies are (PrEP or TasP), they will share a common denominator for implementation the HIV test. They all begin with learning one's HIV status", (Rochelle Walensky).

Summary of discussion and key take-aways for community advocacy

Moderator: Richard Stranz, Coalition PLUS

Today, there is a lot of data that allows us to be sure that PrEP will be as effective in heterosexual men that in MSM if it is given on demand.

WHO recommends that PrEP on demand should not be used by cisgender women. The fact that on demand PrEP with TDF/FTC cannot be recommended for cisgender women is mainly driven by the vaginal exposure, because you need a longer time to have protective concentration in the vagina than in the rectum. Even with the double dose, the 2+1+1, taken at least two hours before exposure does not allow for concentration to be protective in the vagina. Yet, it allows for protection to be effective in the rectum. Therefore, it is vaginal exposure that is preventing the use of TDF/FTC on an on-demand basis.

The newest WHO recommendations recommend daily prep for people that might be exposed to HIV due to injective practices.

An existing **PrEP implant programme** was put on hold because of potential toxicity on CD4 and lymphocytes. As of now, there are no developments of **Islatravir** on PrEP but there are other options with implants that might come into clinical trials. Implants that would be biodegradable, or that could be refilled or changed once a year might also be a very good option.

Food for thought for the community, PrEP, STI PEP and Vaccines

Cindra Feuer, AIDS Vaccine Advocacy Coalition (AVAC)

To access the slides (ENG/RUS) click here.

Overview of the HIV prevention product pipeline

A short summary of the HIV prevention pipeline and what community should know about research for PrEP, DoxyPEP and vaccines to better understand where these new interventions fit in. The existing prevention tools include:

- **Condoms;**
- **VMMC** (voluntary male circumcision) recommended in heterosexuals only, and especially in the African context where heterosexual men are the most at risk;
- **Daily oral TDF/FTC PrEP;**
- **Daily oral TAF/FTC** which is currently under review;
- **Dapivirine vaginal ring** which has been recommended by WHO, and EMA approved for Africa, but not for Europe.

Promising prevention tools in efficacy studies:

- **Dual prevention pill:** it combines PrEP with contraception - looking very promising and might soon be available on the market.
- **Broadly neutralising antibodies (BNAb):** no overall efficacy but proof concept is moving ahead.

Prevention tools recently failed trials:

- **Ad26 vaccine:** it was the last large scale vaccine trial that was ongoing, but in January 2023 it was proven to be ineffective.
- **Islatravir implants:** this study was looking at a monthly pill instead of a daily one was shown to deplete T-cells leading the study to be discontinued.

HIV prevention research is conducted by combining active drugs, antiretrovirals and others, some of which are experimental and others that are already used for treatment. It explores different modes of delivery including diaphragms, injections, implants, patches, mucosal inserts, oral pills, vaginal film, vaginal gels, and vaginal rings.

Researchers also seek to develop **multi-purpose technologies,** which could, for instance, prevent STIs, HIV and pregnancy.

Communities need to follow these developments as some of these products will soon come out. If they do come out, communities need to be prepared on how to respond to the results, how and whether they want to move forward with implementation and how they want to communicate it to their communities.

PrEP research

Daily oral FTC/TAF (F/TAF) is another version of existing oral TDF/FTC PrEP. It has been proven to work in cisgender men, but it has not been proven to be superior to standard PrEP, except for people with kidney and bone issues. Moreover, it causes a significant increase in blood fat levels and weight gain. There is an ongoing study testing its efficacy in cisgender women as it was not originally studied on this group. This study in cisgender women runs alongside the Long-Acting Injectable Lenacapavir study as Gilead is testing both. The results are expected in 2024. Importantly, for Europe, F/TAF is not available in generic form and will probably not be for the coming 20 years.

Islatavir monthly oral PrEP efficacy trials have been discontinued because it was shown to deplete T cells.

Dual prevention pill combines TDF/FTC oral PrEP with oral contraceptive pill. A very promising tool that could soon be on the market. This would represent a revolutionary multi prevention technology that prevents pregnancy and HIV simultaneously.

Lenacapavir is a six monthly injectable that people would only have to get a shot twice a year to prevent HIV. Results are very promising, and the product could enter the market in the next couple of years. It is currently being studied in South Africa, Uganda, Brazil, Peru and the US.

Cabotegravir Intramuscular Long-Injectable PrEP Results: As mentioned above, there were 6 seroconversions in people who complied with their regimens as the standard test was unable to detect seroconversion. Therefore, stronger viral load testing may be required, which would be extremely costly and not realistic to be rolling it out for all HIV prevention for every test. Cabotegravir could also lead to resistance to HIV treatments in case of seroconversion and there are also still questions about pregnancy and breastfeeding. In addition, there is general scepticism about how to get people to adhere to six clinic visits a year and that this would not hold up in implementation.

Cabotegravir access and advocacy: There are currently implementation projects rolling out throughout several African countries, the US and Australia. In different geographies and populations that were not studied in the actual clinical trials, we still need to understand the best way to roll it out. There is no information about how it could be resourced, which is an important problem in Europe. As advocates, we are recommending that ViiV Healthcare (ViiV), the manufacturer of Cabotegravir, engages with the community, especially around fair pricing and equitable access. Until now, in Europe, it is unclear whether communities will be able to get a fair price that is realistic to roll out when compared to oral PrEP. ViiV is currently experiencing a stock problem and their manufacturing capacity cannot keep up with demand. WHO, UNAIDS, National Health Ministries and AIDS programmes need to have clear plans, milestones and funding to move forward, and communities need to make sure that they are part of that planning and its monitoring. Given that this drug works, how best to get it to the people should be answered as it is rolling it out. Otherwise, it may delay its implementation by several years, as was the case in the oral PrEP impact trials (i.e. IMPACT trial in London).

Vaccine research

Late phases: Since 2020, three trials have failed and there are no large-scale HIV vaccines in late-stage phases of the pipeline.

Ad26 vaccine was the last large scale vaccine trial that was ongoing, but it was recently proven to be ineffective.

"Upstream" or early phases: There are multiple studies in early stages (either in pre-clinical or phase 1), but it will be years before they could provide potential vaccines to take to the market. It is not known whether, or when, a safe, effective, affordable and acceptable HIV vaccine will ever be achieved but communities need to keep pushing the funding and interest for HIV vaccine research as this would be the best method of preventing and eventually controlling the HIV epidemic.

Messenger mRNA vaccines use the same technology as the mRNA COVID vaccine. These deliver a genetic material that instructs the body to create a protein fragment of HIV. Subsequently, the body sees that protein and responds by creating its own antibody. Currently, there are three ongoing trials in phases zero and phase 1.

Vaccines using **Cytomeglavirus Vectors (CMV)**, like in the herpes virus, were able to control and then clear the virus in all infected monkeys. It would work to elicit T cells but not antibodies, trials for these vaccines are entering phase one.

Broadly neutralizing antibody (bNAb) infusions (VRC 01 bNAb infusion) are not vaccines; rather, they correspond to what vaccines prompt the body to create. People who have been living with HIV for years make these bNAbs because it is the natural response of the body against foreign invaders like the virus. Researchers have thus cloned these bNAbs and infused them in HIV negative people.

BNAbs infusions got proof of concept because it was shown to work when a patient had a strain that responded to that specific antibody. There are currently several ongoing phases which combine antiretrovirals with multiple bNABs that work against different strains. This process is still in the early stages because they are unsure of which antibodies to test.

Vaccine advocacy: Finding an HIV vaccine has been the biggest scientific challenge yet if found, HIV vaccine would be inexpensive (if ideally one single dose), acceptable (few side-effects), durable (last forever), more equitable and provide a choice in the most efficient way of preventing HIV.

The funding of vaccine research has gone down globally by 5.5%. However, European funding decreased by 31% in just one year. In Europe, between 6,300 EUR to 15,000 EUR is spent per year per person living with HIV. There is a need to keep advocating for vaccine research in Europe. Healthcare systems need to be strengthened to ensure that when the vaccine comes out, there is effective and equal distribution.

STI-PEP research

DoxyPEP[2] combines PEP with doxycycline. Doxycycline is a tetracycline, an antibiotic used to treat bacterial infections, including chlamydia and syphilis. Uptake corresponds to a dose of 200 milligrams within 24 hours of condomless sex and no later than 72 hours. It has been proven to reduce chlamydia, gonorrhoea and syphilis in MSM. However, studies on the reduction of gonorrhoea have been mixed because of gonorrhoea resistance, especially in Europe. Three large scale studies showed that it works, and people are now taking it off-label (especially MSM). It has not been recommended nor approved, and national regulatory bodies have yet to provide normative guidance. Importantly, there are concerns regarding possible microbial resistance. In addition, it did not work for women in Kenya (see p. 5).

→ **Next steps for DoxyPEP research:**

1. Potential negative impact on microbiomes
2. Understand whether and how much DoxyPEP drives antimicrobial resistance
   a. More studies to determine if DoxyPEP drive antibiotic resistance
   b. Need population-based long-term follow-up
3. Understand why it did not work in women: whether it was anatomy or adherence
4. Need for international and national guidance because people are already using DoxyPEP without recommendations

DoxyVac is a meningococcal vaccine (4cMenB) that was studied recently alongside DoxyPEP. Meningitis is similar enough to gonorrhoea that the vaccine reduces the rate of gonorrhoea. This is important because gonorrhoea does not respond as well to DoxyPEP. The objective is to combine DoxyPEP with the 4cMenB vaccine to reduce chlamydia, syphilis and gonorrhoea simultaneously. However, the ANRs, the French study that showed that the vaccine worked, is currently undergoing an independent audit because there may have been some data confusion. This vaccine trial also did not work for women in Kenya. Outstanding questions still remain as this is a new area of study, but it is very promising.

→ **Next steps for DoxyVac research:**

1. Monitor the outcomes of DoxyVac independent audit of the final analysis.
2. Confirm whether the gonorrhea vaccine worked in other studies underway in Australia and the United States.
3. Confirm the duration of protection and whether it needs a booster.
4. Research on whether a more specific gonorrhea vaccine be developed.
5. Consider whether it is cost effective.

2 For up-to-date information from CROI 2024, please read here: https://avac.org/blog/croi-round-up-highlights-from-monday/.

Summary of discussion and key take-aways for community advocacy

Moderator: Richard Stranz, EATG & Coalition PLUS

Although oral PrEP is very efficient, it is doing less well at the implementation level. The 2020 goal to have 3 million people starting oral PrEP was not reach; 3.9 million was only reached in 2023. In parallel, there is a real retention problem on oral PrEP – drop-off rates are high within 3 months, people cannot or do not want to take a daily oral pill. Ultimately, this is why we continue looking for diverse prevention tools such as injectables, and why a vaccine is the best option.

In the Cabotegravir trials, women who missed their 2-months shot were still protected when receiving a shot every 3-months. If further studies are conclusive, it would mean that cabotegravir and contraception schedules align, and women would only have to go to the clinic every three month to receive both shots.

When it comes to advocacy, it is important to **push for the largest choice possible.** As observed in the pregnancy prevention field, as more protective methods are introduced, the number of protected people globally will also increase. As activists we do not know what people want, so rather than act as gatekeepers, it is helpful to push to give communities a choice. For example, Cabotegravir may be too expensive for already overburdened clinics, but it could constitute a viable alternative for communities.

Pricing should be discussed early in the development, because if a drug shows efficacy in PrEP and the price is very expensive, it will not be reimbursed, especially in Europe. The European Commission had joint procurement mechanisms for COVID and Mpox, but there is no such discussion for PrEP. For this to happen, national authorities need to ask the European Health Emergency authorities to prepare a joint procurement plan. This would require advocacy to strongly pressure national Ministries of Health. In the past, the EU has considered HIV as a health emergency, advocates could bring this up again as well as demonstrate how it can constitute a cross-border threat.

Cabotegravir has licensed three generic manufacturers to make it available in low- and middle-income countries. This means that it will probably lead to voluntary licensing in wealthier European countries. Communities need to scale up their advocacy if they want cabotegravir to be affordable in Europe because otherwise it will not be available, given that oral PrEP is cheaper and already in circulation.

There is voluntary licensing where the community and the government should discuss it with ViiV and ask to receive a license to roll it out. There is also compulsory licensing where they can declare a health emergency and they would be allowed under WTO laws to import or manufacture any drug without the permission of the drug company. However, it is very unlikely that it would happen for Cabotegravir. It may be more feasible when it comes to Hepatitis C.

ViiV will apply for a license in any country where it finds a ground for demand from national governments and communities. Community advocates can work at rendering that demand explicit. The price negotiations will begin when they submit their file for review to the national regulatory authorities. It is important to know whether ViiV is open to volume price agreements or some kind of price reduction because this could in turn drive demand.

PrEP access: Is a steady, ongoing increase enough to deliver us from danger?

Cindra Feuer, AVAC

To access the slides (ENG/RUS) click here.

Global Overview

The trend in infection rates has been consistently declining. Yet, achieving the target of reducing new infections to 370,000 annually by 2025 appears challenging. This assessment is based on the data from 2021, which recorded 1.5 million new infections. To effectively reach this goal, the expansion and implementation of PrEP is crucial.

Oral PrEP

Daily oral PrEP FTC/TDF, also known as Truvada, is being rolled out in many countries in Europe. Oral PrEP was proven effective 13 years ago through studies. The United States was the first to approve this medication 11 years ago, and in 2015, the World Health Organisation (WHO) released guidelines for its use.

Daily oral PrEP TAF is not being rolled out at the same scale. TAF is specifically intended for individuals who engage in vaginal receptive sex, but its high cost limits the accessibility.

On-demand PrEP, also known as the 2-1-1 method, involves taking the medication orally two times before sexual activity and once afterward.

Uptake of PrEP worldwide

The goal set for 2020 was to have 3 million individuals at high risk of HIV seroconversion start taking PrEP. This milestone was reached only in 2023, with 3.8 million people initiating PrEP. Looking ahead, the objective has been revised to aim for 10 million PrEP initiations by 2025. Notably, there has been a significant increase in PrEP initiation rates, with the number nearly doubling between 2021 and 2022. However, studies have shown that **retention rates among people who initiate PrEP are low, with about 20% discontinuing PrEP within the first month and less than 5% maintaining their regimen after six months.** This highlights the need for in-depth research to understand the reasons behind these high dropout rates and to develop strategies to address them. Additionally, exploring and offering new alternatives for PrEP could be crucial in improving long-term adherence and effectiveness.

Having clear PrEP guidelines are essential to roll out the medication. Currently, 30 countries where PrEP is available have guidelines, 15 still lack these guidelines. In 23 out of 55 countries, PrEP costs are covered, yet migrants and people who use drugs are often ineligible or struggle to access these programmes. There are 17 countries where PrEP has not been formally implemented yet. Barriers to PrEP implementation include the high price of the drug, dropout rates, and the reluctance of the healthcare sector to prescribe and promote PrEP due to a concern that sexually transmitted infections may increase because of lower condom use. Finally, there are 15 countries where generic PrEP is available in healthcare settings. The European Centre for Disease Prevention and Control (ECDC) has published operational guidelines that can be adopted and adapted by each country. Generic PrEP is very important for access in Europe.

11 years of Oral PrEP: Lessons learned from implementation

Investing in and increasing efforts to create demand for PrEP through awareness and knowledge sharing is crucial. In Africa, this approach involved making PrEP more known and accepted among the general population. This strategy was aimed at ensuring that those at risk would learn about PrEP and seek it from service providers. However, in Europe, particularly in Western Europe, where HIV is not widespread in the general population, there is a question about the best approach. It is unclear whether advertising PrEP to everyone or focusing specifically on key groups at higher risk of HIV is more effective.

There are innovative methods that have shown great success in making PrEP more accessible by taking it directly to the communities instead of just offering it in traditional medical clinics. These methods include health services via mobile phones, providing medications for multiple months at a time (like three or six months), combining PrEP with other sexual and reproductive health services, linking it with HIV self-testing, and supporting services led by the community to ensure everyone is treated fairly. More funding for prevention efforts would help develop these systems further, creating a stronger foundation for future preventive healthcare strategies.

Long-Acting PrEP

Existing products:

Dapivirine Vaginal Ring is a silicone ring that a user can insert into the vagina once a month, where it stays in place for the entire month. It is designed to be undetectable by a sexual partner and does not affect sexual activity. This ring works locally, meaning it does not enter the bloodstream. Instead, it slowly releases an antiretroviral drug over the month, concentrating its effect in the vaginal area. It is the first ever long-acting HIV prevention product.

Implementation: It has been approved in several African countries where implementation projects are now underway. Although the European Medicines Agency (EMA) has approved the device in 2020 and provided guidelines in 2021, there is no regulatory approval in Europe. There is still the question of whether there is enough demand for it.

Cabotegravir long acting injectables involve receiving a shot of an ARV drug shot in the buttocks every two months, totalling six times a year. However, there are ongoing concerns about the potential for this drug to lead to resistance against HIV treatments, as discussed above.

Implementation of Cabotegravir long acting injectables: In 2022, the World Health Organization (WHO) issued the guidelines that has been approved in the United States, Australia, Zimbabwe, South Africa, Malawi, and Botswana. ViiV, the only drug's manufacturer, is also seeking approval in Europe through the EMA and in Ukraine. As the drug is being introduced, studies are ongoing to assess the risk of developing resistance to it. Major efforts by PEPFAR and the Global Fund are underway to make the drug available in low- and middle-income countries. In addition, ViiV has limited stock due to its current manufacturing capacity. Addressing this, ViiV has granted sublicenses to the Medicines Patent Pool, allowing three other manufacturers to produce a generic version of cabotegravir injectables. These manufacturers will need time to develop their production capabilities, meaning it could take several years before there are sufficient stocks for a full-scale rollout.

In Europe, implementation projects are planned in France, Belgium and Ukraine. However, these studies do not involve people who use drugs, and only three of these studies include gender non-conforming people, and five of them trans men.

Advocacy: To widen the access to cabotegravir, it's important activists to advocate for the availability of generic cabotegravir and for lower prices. Additionally, there is a need to provide training to service providers on how to effectively administer these new medical treatments.

Advocacy: The Coalition for access to long-acting PrEP, of which Global Health Advocacy, Access and Equity (AVAC) serving as the secretariat, convened a collaborative effort with Unitaid, WHO, UNAIDS and Global Fund PEPFAR. Its focus is on intellectual property matters related to the development of generics and voluntary licensing, implementation strategies that engage civil society. The coalition collaborates with ViiV, donors and civil society organisation to ensure access to all existing and upcoming long-acting PrEP medications. Currently no European representation in the coalition, interested parties are welcomed to reach out to AVAC.

Results from the FemiPrEP Project: The construction of Pre-Exposure Prophylaxix (PrEP) by prevention actors as a tool, or not, for African migrant women

Sarah Demart and Grâce Ntunzwenimana, Plateforme Prévention Sida

To access the slides (ENG/RUS) click here.

Research: The research's aimed to better understand what facilitates or hinders the uptake of PrEP among women and in particular migrant women from sub-Saharan Africa. It was a yearlong project conducted during the pandemic. The data was collected among prevention professionals and the results therefore speak to their perspective.

Context: While HIV prevention organisations have increased attention to migrant women from sub-Saharan Africa, these women are by large excluded by the way in which PrEP is delivered. In Belgium, the situation with PrEP is complex. While it is promoted as a universal solution to the epidemic, undocumented individuals face significant challenges in accessing it. As they lack insurance and only have access to urgent medical assistance, it is uncertain whether they can get reimbursement for PrEP.

Results of the study:

Insufficient knowledge and education about PrEP: this key population is made absent because **many are** not **informed** about PrEP nor receive information about it. The limited outreach regarding PrEP is partly due to healthcare professionals and prevention experts believing that this group might struggle with the daily with the daily management of PrEP. This **belief arises from the assumptions about their prior understanding of sexual and reproductive health and the challenges posed by cultural taboos around sexuality.** Furthermore, there's a concern that promoting PrEP to this group could increase the risk of transmitting other sexually transmitted infections (STIs).

Legal barriers in access to PrEP: prevention experts might refrain from promoting PrEP use among migrant women, particularly those who are undocumented and uninsured, due to the limited access options for them, this reluctance stems from not wanting to generate a demand for a service that cannot be adequately provided.

Medicalisation of PrEP: in Belgium cisgender women, including migrant African cisgender women, can only receive PrEP in hospital settings, unlike for MSM and trans women. Since PrEP prescriptions come from the hospital's HIV service, this raises concerns about stigma and discrimination. Additionally, institutional barriers such as long waiting times and questionnaires on sexuality designed primarily for white MSM populations further deter the key population from reaching out to these services. There have been instances where clients reported having been denied access to PrEP.

Privation of rights: while access to PrEP for these women is currently a challenge, they deserve to be informed about PrEP. The increased knowledge about this prevention tool would empower them to advocate a broadening of access to PrEP access. An example of this can be seen in France, where advocacy efforts have led to PrEP to be made available to all people, including undocumented migrants.

Priority for actions: Plateforme Prévention Sida seeks to empower and enable women to make informed decisions about their health through community awareness-raising campaigns. Plateforme Prévention Sida produces educational materials, such as flyers, posters and videos in the native languages of key populations, using easily understandable images. The organisation engages with professionals to educate them on PrEP, guiding them to adopt a positive approach to sexual health to support women in making informed choices about their sexual health. The organisation has initiated a women-led project where community members are trained to disseminate knowledge about PrEP in their own communities. The programme reached about 100 people in one year. Currently, the community is advocating decentralised access to PrEP via general practitioners (GPs) and community organisations. A prevention project proposal has been submitted to the national authorities.

Community access challenges to PrEP

Amanita Calderón-Cifuentes, Transgender Europe (TGEU)

To access the slides (ENG/RUS) click here.

The speaker presented research on trans populations' access to PrEP, conducted in partnership with the THRiVE Consortium. The study focused on Trans asylum seekers and undocumented migrants, trans sex workers, trans people in prison, trans people of colour who inject drugs, including Black and indigenous people. To understand the challenges trans people face in accessing PrEP, we have to understand the various overlapping issues and obstacles they encounter.

According to data from the **European Centre for Disease Control PrEP**: Out of 55 countries in Europe and Central Asia, 20 reported that they have developed and are implementing PrEP guidelines. However, these guidelines frequently overlook undocumented migrants.

Regarding trans individuals' eligibility for PrEP, 22 out of 30 countries that responded to this query confirmed their eligibility *(please refer to the presentation slides for additional information).*

Despite this, only a handful of countries reported offering PrEP to undocumented migrants, and an even smaller number provide it free of charge.

Stigma and discrimination within healthcare settings are major issues. They often lead to reduced empathy among healthcare professionals and a lack of gender-specific services. This environment can make trans people feel uncomfortable accessing HIV-related services.

Many countries still have harsh laws that target trans individuals. These laws can criminalise a range of behaviours, from cross-dressing to same-sex relations. As a result, many trans people end up in prison not just for crimes, but also because of their gender identity or sexuality. This puts trans people, even in Europe, at a high risk of incarceration and criminalisation. Data provided by the United Nations Office on Drugs and Crime (UNODC) reveals that the rate of HIV is significantly higher among trans people in prison compared to cisgender people. Furthermore, trans prisoners people are estimated to be up to 13 times more likely to be sexually assaulted than cisgender people.

The absence of gender affirming care and legal recognition of gender identity within prisons, combined with the high risk of drug use due to environment-induced mental health issues, greatly trans people. The ease with which transgender or gender-diverse people can be incarcerated because of their gender identity, sexual orientation, or involvement in sex work – which remains criminalised in many parts of the world, including Europe – adds to their vulnerability. Moreover, being 13 times more likely to experience sexual assault, and often being denied access to PrEP and other forms of prevention, significantly increases the risk of contracting HIV.

Access to PrEP

Transphobia in HIV related services constitutes a real barrier to access to PrEP.

There is a general lack of understanding about HIV, its risks, and how PrEP works, mainly due to insufficient state-led education and prevention programmes. Peer-workers are well-positioned to bridge these knowledge gaps.

PrEP is only available in 30 countries via medical doctors. Yet, when these doctors do not acknowledge non-binary or non-trans women individuals as key groups, it creates access barriers. The medical professionals' lack of gender sensitivity and specialised services can discourage trans individuals from seeking or continuing with prevention services.

Additionally, structural inequalities often put trans people in financially unstable situations, making it difficult for them to afford PrEP, which costs around 434 EUR a month.

Summary of discussion and key take-aways for community advocacy

Moderated by Aisuluu Bolotbaeva, EATG Combination Prevention Committee Member

Resistance to cabotegravir long-acting PrEP: Resistance is a common problem in messaging.

Before beginning any PrEP regimen, a person must be HIV negative. Yet, cabotegravir is so strong that it lowered the viral load of people who were seroconverting while they were starting treatment, making them undetectable. In parallel, there were some breakthrough infections which were not detected for several months. In both cases, the delay in diagnosis combined with uptake of cabotegravir as monotherapy led to some patients developing a resistance to the drug. Addressing late diagnosis would require using more sensitive NAP tests, which are more costly. This creates a challenge in rolling out the LAI cabotegravir for PrEP. Each country will tailor its approach based on its guidelines and resources.

Involvement of migrant women in research: In the Plateforme Prévention Sida research, the researchers chose not to directly interview migrant women from Sub-Saharan Africa. They felt it was unethical to demand time and energy from women in precarious situations, particularly those facing homelessness, without compensating them for participating in focus groups. Additionally, the women expressed the wish to have men involved also in focus groups highlighting that the responsibility for HIV prevention should not be theirs alone. Another challenge was the discomfort among women in discussing their sexual health and practices. Consequently, the study shifted its focus to examining healthcare providers' experiences with structural barriers to access. However, some women showed interested in becoming community relays for the research, which again brought up the issue of fair payment.

Access to the dapivirine vaginal ring: EMA approved the vaginal ring under the article 52, a decision intended primary for African countries since Africa lacks a unified regulatory body to gain approval in Europe, the product would need undergo a completely new application process. International Partnership for Microbicides (IPM), the non-profit organisation which owns and manufactures the ring, decided not to pursue EMA approval. This decision was due to the high costs involved and the rings' lower efficacy compared to oral PrEP, as it reduces the risk by 50%. While this rate is considered beneficial widespread epidemics, it is viewed as less effective in Europe. However, IPM is no longer operational, and the Population Council has taken over ownership of the ring. They would need encouragement to apply for regulatory approval in Europe.

Trans men and long-acting PrEP: Records show that trans men did not take part in the trials for the dapivirine vaginal ring. While trans men were included in the cabotegravir trials, their numbers were too small to yield statistically significant results. However, research on this is still ongoing.

Access to information and Advocacy: Key populations, especially those not proficient in English, which is often the case in many countries where English is not the primary language, usually lack access to information on latest drug developments. Therefore, it is crucial to spread this information effectively so these communities can voice their needs and interest. This in turn, informs manufacturers and policy makers about the level of demand.

Making the case for prevention: in challenging financial times and during conflicts, how can

we effectively advocate for prevention? It is essential to unite across sectors - key populations and their advocates need to collaborate and seek support outside the HIV sector.

Demand for the dapavirine vaginal ring: Data shows that people struggling with adherence and may also find bi-monthly injections challenging. Access to the vaginal ring is vital as it provides another option. The more choices available, the higher the likelihood of people staying protected, even with a 50% risk reduction. It is important that people have these options and that advocates don't restrict choices. Initial findings from Africa suggest that women who opt for the ring over oral PrEP tend to use it more consistently and therefore stay protected longer. This insight shifts the focus from efficacy to actual usage and protection. The ring is particularly appealing for marginalised women, who might face resistance from male partners regarding their choice of protection. There's also a stigma associated with oral PrEP and challenges in accessing injectables due to hospital visits required by national laws. Meanwhile, in Europe, women at risk often perceive PrEP as a treatment solely for men and LGBTQIA+ individuals, which might deter them from considering it. Offering the ring could extend protection to those who might not otherwise use PrEP or condoms.

HIV prevention and LBGTQIA+ rights: Working together across different key populations is crucial. For instance, TGEU has created an HIV research and advocacy officer position working on research, advocacy, and capacity-building. The capacity building aspect is particularly aimed at keeping local members across Europe and Central Asia up to date with latest developments in the field. However, in some countries, especially in Central Asia, these activities face legal challenges due to the association between LBGTQIA+ and HIV advocacy. In these regions, funding for HIV services and advocacy are being cut. These practices are happening all over the world, not only Central Asia but also Eastern Europe, the United States and Africa. Therefore, non-profits organisations and activists must support each other. Additionally, researchers, policy-makers and legislator should engage with these groups and strive to reach the people affected.

PrEP and genital cutting: PrEP works regardless of the status of genital cutting.

On demand PrEP for people with vaginas and people who have sex with people with vaginas: on demand PrEP is generally not recommended for them because the drug's absorption and concentration are faster and higher in the anus compared to the vagina. While experts previously believed that cisgender women couldn't afford to miss even one dose a week, definitely study results on on-demand PrEP for cisgender women are still pending. Additionally, a comparative study involving transgender men is important, considering the effects of hormonal differences.

European
AIDS Treatment
Group

About the European AIDS Treatment Group:

The European AIDS Treatment Group (EATG) is a patient-led NGO that advocates for the rights and interests of people living with or affected by HIV/AIDS and related co-infections within the WHO Europe region. Founded in 1992, the EATG is a network of more than 150 members from 45 countries in Europe. Our members are people living with HIV and representatives of different communities affected by HIV/AIDS and co-infections. EATG represents the diversity of more than 2.3 million people living with HIV (PLHIV) in Europe as well as those affected by HIV/AIDS and co-infections.

For more information, please visit www.eatg.org