HIV pre-exposure prophylaxis (PrEP)

Annex 2 **to the Recommended Practice for HIV-Infected Adults and Post-Exposure Prophylaxis HIV infection** (Society of Infectious Medicine of the Czech Medical Association of J. E. Purkyně)

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Introduction

Based on the World Health Organization (WHO) recommendations of September 2015, "Oral pre-exposure prophylaxis (PrEP) should be offered as an additional preventive option for people at significant risk of HIV infection as part of a combined approach to HIV prevention". Subsequently, WHO developed a series of modules designed to support the implementation of PrEP, with stakeholders in the planning, implementation and delivery of PrEP to use those recommendations that are appropriate to local conditions and needs. On this basis, the Workflow for Providing Pre-Exposure Prophylaxis of HIV Infection was created, according to which PrEP has been applied in the Czech Republic since 2017.

PrEP should not replace or compete with effective and well-established HIV prevention practices. These include, in particular, the general provision of condoms to sex workers and men who have sex with men, and harm-reduction strategies for people who inject drugs. Many of the people who could benefit most from PrEP belong to population groups that may face legal and social barriers to accessing health services. These factors need to be taken into account when developing and increasing the availability of PrEP-related services. Although public health based on current WHO guidelines is intended to support people at risk of HIV infection in the use of PrEP, the decision to use PrEP should always be made voluntarily by the individual concerned.

Theoretical introduction for healthcare professionals

HIV prevention strategies have been based for many years on promoting safer sex (in particular condom use) and injecting drug programmes (in particular exchange of injecting material and substitution programmes). Nevertheless, the WHO registers a large number of new cases of HIV infection every year. Therefore, the administration of antiretroviral drugs to HIV-negative persons as pre-exposure prophylaxis (PrEP) is a useful additional preventive activity. It is based on experience with post-exposure prophylaxis (PEP) in healthcare professionals, with non-occupational PEP (nPEP) and prevention of mother to child transmission (PMTCT).

Clinical studies have shown the effectiveness of PrEP in various target groups at high risk of HIV infection. The most important of them are:

- **The iPrEx study (**CO-US-104-0288) evaluated tenofovir emtricitabine (TDF-FTC) compared to placebo in 2499 men who were not HIV infected, had sex with men and were at high risk of HIV infection. Their average age was 27 years. Sexual risk factors: an average of 18 partners in the last 12 weeks, 60% reported unprotected intercourse in the last 12 weeks, and 80% reported unprotected intercourse with an HIV-infected partner or unknown condition in the last 6 months. In the placebo group, 83 out of 1217 people were infected, while in the TDF-FTC group, 48 out of 1224 people became infected – a relative risk reduction of 42%. In the group of men who reported unprotected receptive intercourse in the 12 weeks prior to enrolment, the relative reduction in

the risk of infection was 52%. Efficacy was strongly related to adherence to treatment: in those receiving TDF-FTC who became infected with HIV, the drug was detected in the blood in only 8% of them, while in 92% of those infected, the drug was not found in the blood.

- **The Partners PrEP STUDY** (CO-US-104-0380) followed 4758 non-HIV-infected individuals from Kenya and Uganda who lived in serodiscordant heterosexual couples. Tenofovir with emtricitabine resulted in a relative reduction in the risk of HIV infection by 75%, and in the adherence support and monitoring subgroup by 100%.
- **The IPERGAY study** followed 400 men having unprotected sex with men: 199 took tenofovir with emtricitabine and 201 took placebo "on-demand", i.e. 2 tablets 2-24 hours before sexual activity, a third tablet 24 hours after the first drug was taken, and a fourth tablet 24 hours later. Participants consumed an average of 15 tablets per month. On average, they were followed for 9.3 months – the study was terminated prematurely and participants in the placebo group were offered effective PrEP. In the TDF-FTC group, there were 2 HIV infections (those infected did not have a proven drug in their blood and returned 58 and 60 tablets out of 60 dispensed, respectively), and 14 people in the placebo group. The relative risk reduction was thus 86%.
- **The PROUD study** followed 544 men having sex with men who had intercourse without a condom in the past 90 days. They were divided into two groups: one received tenofovir with emtricitabine immediately, the other with a delay of one year. In the first group there were 3 HIV infections, in the deferred group 20 people were infected. The relative risk reduction was 86%. Due to the proven effectiveness, the study was terminated prematurely and PrEP was offered to people with an initially delayed start. The study suggests that in a similar population, 13 men would need to be given PrEP for one year to prevent one new HIV infection.
- **The Bangkok Tenofovir Study (BTS) Open-Label Extension (OLE) Study** followed 1315 injecting drug users, of whom 798 received PrEP. Of these, due to low adherence, 339 patients completed the year-long follow-up, with one HIV infection detected in a patient who had not taken PrEP properly. The relative risk reduction was 95%.

Pharmacokinetic bases of PrEP

PrEP drugs must meet the following requirements: efficacy, safety and good tolerability, simple dosing, minimal drug interaction, independence from food intake, low risk of developing HIV resistance, non-seriousness of missing a dose, and cost-effectiveness.

The effect of both tenofovir and emtricitabine is determined by phosphorylation in cells with the participation of host enzymes. Both drugs accumulate in cells and are present there significantly longer than in plasma: the intracellular half-life of tenofovir is about 150 hours (6.25 days) and emtricitabine about 39 hours (1.6 days). Therefore, missing a dose does not reduce the efficacy of PrEP.

Efficiency is affected by the achievement of steady state in cells. This is achieved in a time corresponding to four halves of the drug, i.e. about 25 days for tenofovir and about 6 days for emtricitabine. Protection against HIV infection is provided by the TDF-FTC already at a concentration that is reached in 1-2 weeks of daily use. For at least this period, the client should follow other procedures to reduce the risk of acquiring HIV.

The potential toxicity of tenofovir is due to inhibition of host cell mitochondrial DNA polymerase with subsequent mitochondrial dysfunction. Accumulation of tenofovir in renal proximal tubular cells may lead to renal impairment and renal insufficiency. A decrease in phosphate reabsorption in the kidneys leads to a decrease in bone density.

At different stages of development, other preparations are applicable to PrEP. A combination of emtricitabine **with tenofovir alafenamide (TAF-FTC) is available** that achieves the same efficacy as the currently used combination with tenofovir disoproxil (TDF-FTC); the advantage is less effect on renal function and bone density and a smaller tablet, the disadvantage is a slight increase in weight, changes in lipids and especially the high price. Use in the Czech Republic is only possible off label and would be considered for older clients with documented renal or bone risk. While TDF-FTC is not administered at creatinine clearance (ClCr) < 60 ml/min, TAF/FTC can be used at ClCr < 30 ml/min.

Study HPTN 083 examined the efficacy of long-acting injectable **cabotegravir given** once every 8 weeks in a set of 4566 MSM and transgender women and demonstrated 69% greater efficacy compared to a control group taking oral TDF-FTC (12 vs 39 new HIV infections). In a similar study of HPTN 084, 3223 women were enrolled and the risk of heterosex HIV acquisition was 89% lower compared to the TDF-FTC group (4 vs 36 newly infected). Adverse reactions were uncommon and consisted mainly of a local application site reaction.

Risk groups – indications for PrEP

An HIV-negative person is indicated for PrEP who:

- **has a sexual partner with HIV infection, in whom viral suppression is not achieved, or viral load is unknown; it includes family planning cases in serodiscorate couples OR**
- **is sexually active and comes from a population with a high HIV incidence/prevalence * OR**
- **had a sexually transmitted infection (proven laboratory, anamnestic or with its symptoms) OR**
- **has been recently indicated or repeatedly indicated for post-exposure HIV prophylaxis (nPEP) OR**
- **o PrEP actively applies ****

Contraidation of PrEP is:

- **HIV infection / positivity**
- **creatinine clearance below 60ml/min**
- **symptoms of acute HIV infection, recent HIV exposure**
- **allergy or other contraindication to the use of tenofovir or emtricitabine**

To start PrEP, the client decides to take the medication and attends regular visits including blood tests.

* **Key populations at increased risk of infection** are considered to be injecting drug users, men who have sex with men, transgender people, sex workers, foreigners from countries with concentrated HIV/AIDS epidemics, prisoners, persons reporting risky sexual behaviour (in particular or vaginal intercourse without a condom with more than one partner or with a sexual partner with one or more risk factors for HIV infection) and persons, in whom another sexually transmitted infection has been detected – syphilis, gonorrhea, infection caused by *Chlamydia trachomatis.*

** Clinical studies have shown that **active PrEP applicants (based on their own risk assessment) are at significantly higher risk of HIV infection than other people in the same population group and are significantly more likely to become infected** without PrEP. After starting PrEP, they also achieved significantly higher adherence – they took the medication better and stayed in the program longer.

Practical procedure for providing PrEP

Initial examination

- **interview** with a question about
  - sexual behavior, condom use
  - history of sexually transmitted diseases (hereinafter STDs)
  - current signs and symptoms of early HIV infection or STDs
  - previous use of PrEP and PEP
  - alcohol and recreational drug use
  - vaccinations completed (including compulsory hepatitis B vaccination for persons born in 1989 and later)
  - pregnancy, breastfeeding
- **physical examination** focused mainly on the manifestations of possible HIV infection and STDs

- **4th generation HIV test** (combined detection of p24 antigen and antibody)
- serum creatinine examination **with estimation of creatinine clearance or urine chemically**
- hepatitis serology examination **(HBsAg,** anti-HCV, **facultative anti-HAV total, anti-HBs and anti-HBc total)**
- Examination for **sexually transmitted diseases**
    - syphilis screening serologically by a combination of one nontreponemal and one treponemal test (e.g. RRR + TPPA)
    - PCR Chlamydia trachomatis and Neisseria gonorrheae in rectum, throat and urethra swabs or from the first morning urine sample, swabs from all three sites can be performed with three swabs into one PCR collection tube
- **advice**, instruction
    - with special emphasis on adherence
    - on possible side effects
    - Maximum protection against HIV is achieved only after a steady concentration of the drug in the cells is reached, i.e. after 7-21 days of use
    - on other practices to prevent HIV infection and other STDs (use of condoms and lubricating gel, not sharing injection material, etc.)
- agreement on the method of **communicating the results of the initial examinations** and the resulting recommendations
    - for vaccination against hepatitis A and B
    - for the treatment of eventual STDs
- **Prescription**

An HIV **test before starting** (or restarting) PrEP is necessary to detect the presence of HIV infection because

- PrEP is not sufficient to treat HIV infection
- the use of PrEP in a person with HIV infection may lead to the development of resistance to drugs used for PrEP

The initial visit should be divided into two sessions, with medication being dispensed after HIV negativity is verified along with the results being communicated. During the initial visit, it is also possible to use the results from the previous HIV collection if it was performed no later than a week ago and the IV generation test was used.

In the presence **of symptoms of an acute viral disease**, when acute HIV infection cannot be excluded (especially in the case of recent HIV exposure), it is advisable to postpone the start of PrEP for a month and perform a control test for HIV in 4 weeks.

During pregnancy and lactation , PreP can be both initiated and continued in case of continuing risk of HIV infection.

Clients who have not had **hepatitis B** should be offered vaccination. If they have not had hepatitis B or A, it is preferable to vaccinate against both hepatitis with a combined vaccine. If **HBsAg is positive**, the indication for treatment shall be assessed in accordance with the guidelines:

- if treatment of hepatitis B with an antiviral drug is indicated, a TDF-FTC combination that also serves as PrEP can preferably be used
- If treatment is not indicated, the risk of flare-up of virus infection should be discussed with the client hepatitis B, if the termination of PrEP occurs.

Follow-up visits

Follow-up visits are usually planned at intervals of 3 months. Individually, it is useful to schedule the first follow-up visit after a month to evaluate side effects and especially to promote adherence. Visits include:

- **interview** with a question about

- sexual behavior, condom use; assessment of the need to continue PrEP
- adherence

    - Side effects
    - the difficulties and symptoms of early HIV infection or sexually precise disease (STD)
    - Newly used drugs and important changes in medical history
- **HIV test** every 3 months with a 4th generation test; in case of reactivity, the requisition form must be
  confirmatory examination clearly indicate that the patient is taking PrEP due to a significant effect on the development of the antibody response. It is also always necessary to critically consider the possibility of breaking the prophylaxis and in case of suspicion of the possibility of HIV infection, an HIV PCR test should be performed. Delivery
  PrEP significantly lengthens the immunological window and delays seroconversion (both in EIA assays and, even more significantly, in western blot/immunoblot assays)
- serum creatinine examination **with estimated creatinine clearance (possibly urine chemically + sediment) after the first 3 months and every 6 months thereafter**
- examination for **sexually transmitted diseases** at least every 6 months, optimal is every 3 months
    - syphilis screening serologically by a combination of one nontreponemal and one treponemal test (e.g. RRR + TPPA)
    - PCR Chlamydia trachomatis and Neisseria gonorrheae in rectum, throat and urethra swabs or from the first morning urine sample, swabs from all three sites can be performed with three swabs into one PCR collection tube
- testing for **hepatitis** in seronegative subjects once a year (HBsAg, anti-HCV)
- In some cases, it is appropriate to supplement **the bone density test**
- **consultancy** with a special emphasis on adherence
- **physical examination** with a focus on the manifestations of possible HIV infection and STDs
- **Prescription**

The minimum length of visits therefore includes an interview asking about the duration of the need for PrEP, adherence, and symptoms of acute HIV or other sexually transmitted infection. HIV testing every 3 months, creatinine and STD screening once every 6 months, anti-HCV and HBsAg testing for seronegative persons once a year are also mandatory. The services provided must be properly documented. It is possible to use uniform forms and check-lists, or patient questionnaires.

PrEP is provided by a physician experienced in the diagnosis and treatment of HIV infection and sexually transmitted diseases and in working with people with risky behaviors. In addition to nurses, it is advantageous to include other workers capable of providing counselling in the team. Close cooperation with collection centers (check points) and counseling centers is ideal.

Termination of PrEP

The reasons for stopping PrEP can be different – reducing the risk due to lifestyle changes, subjective or objective side effects, frequent forgetting of medication, etc. Termination of PrEP or change of regimen should always be consulted with the doctor who prescribes PrEP. It is advisable to document the date of last risk, recent medication and HIV status at the end of PrEP and recommend the use of PrEP for 7 days after the last risk of infection (on a daily regimen).

Forms of PrEP

The daily regimen is based on most of the above studies, WHO recommendations and the marketing authorisation of Truvada and its generic variants. Characteristics of this method of use:

- respects the pharmacokinetic properties of TDF-FTC; The accumulation of the drug in the cells guarantees the effectiveness of even
  in case of occasional omission (prophylactic effect is ensured when taking five or more tablets per week)
- allows regular stereotypical use
- It is suitable for people with more frequent sexual activities
- protects during unplanned sexual activities

- is associated with potentially higher mitochondrial and renal toxicity with effects on bone density
- after the start of use, some time is needed to achieve a protective level of the drug in the blood and tissues; therefore
  clients should use additional preventive measures against HIV infection (safer sexual practices,

condom). This is at least the first 7 days in the case of MSM for receptive intercourse, but up to 21 days in the case of receptive vaginal intercourse. There is not enough data for insertive vaginal or sex.

- PrEP is taken daily for as long as the risk of HIV infection persists; In the period when the risk is low or non-existent, use may be interrupted or terminated 7 days after the last risk. An example might be the moment when a person stops providing sexual services for money, when he travels to an area with low
  occurrence of HIV, establishing a monogamous relationship, etc. Restarting PrEP is appropriate in a situation where
  the client is again exposed to a significant risk of HIV infection. At least for the first 7 to 21 days should use additional preventive measures against HIV infection.

The "on-demand" regime is based on the results of the IPERGAY study, its use in the Czech Republic is so-called "off label" (it is not listed in the marketing authorization documentation of Truvada and its generic variants approved by the State Institute for Drug Control). The advantage can be:

- lower economic demands (on average half the consumption of tablets) – an important factor where the user pays for the medication himself
- it is useless to take prophylactic antiretroviral drugs in the period without possible exposure to HIV
- Potentially higher adherence in relation to sexual activity
- Potentially lower toxicity

The effectiveness of on demand is not sufficiently understood in women, heterosexual men, transgender people and injecting drug users, so it is not recommended in these groups.

Method of use:
** taking 2 tablets 2-24 hours before the planned sexual activity, taking the third tablet 24 hours after the first drug and the fourth tablet 24 hours later,
** if the risky sexual activity continues for other days, 1 tablet per day is taken until the last day Contact. Then the post-exposure tablet continues at 24 and 48 hours
** Subsequent sexual activity: if it occurs after more than a week, 2 tablets should be taken 2-24 hours before intercourse. If less than a week has passed since the last use of the drug, then 1 tablet is taken 2-24 hours before intercourse. In both cases, the post-exposure tablet is continued at 24 and 48 hours.

Adherence

Clinical and observational studies have shown that when used correctly, PrEP provides a high degree of protection against HIV – a risk reduction of more than 90%. Adherence, i.e. taking PrEP in accordance with the recommendation, is crucial to the effectiveness of this procedure. For example, in the iPrex study, the risk reduction in HIV infection was 42% in the entire population, but the subgroup with the detectable drug in the blood achieved a risk reduction of 92%. Continuous support for adherence is therefore essential. In real conditions, PrEP users achieve adherence of 80 – 90%, retention (keeping the client in the PrEP program) is up to 50 – 80%.

As part of the advice, the PrEP applicant should receive information on **procedures that will increase the likelihood of regular daily use of PrEP:**

- take the tablets at the same time every day
- in relation to regular daily activity (e.g. brushing teeth, always after dinner, at the beginning of the TV news)
- with regular alarm settings in your mobile phone
- using a drug dispenser
- simultaneously with other drugs taken
- carry sufficient reserves of medicines during planned overnight stays away from home and when travelling

Support to meet the date of planned visits (e.g. SMS reminders) and the availability of services (office hours, threshold-free) are also suitable.

PreP toxicity, adverse reactions

U one in ten PreP users will experience mild complaints of several days at the beginning that do not require interruption of PrEP and almost always resolve within a month:

- **gastrointestinal problems**: nausea, vomiting, diarrhoea, cramping abdominal pain, flatulence, decreased appetite
- **dizziness, headache, joint pain**

One in 200 PrEP users experience

- **elevation of serum creatinine**; If **cretinin clearance decreases** below 60 ml/min, discontinuation of the drug should be considered. Normalization of renal function usually occurs in 1-3 months. After
  When the value rises above 60 ml/min, PrEP can be restarted. Particular caution should be exercised
  in the event that
- The creatinine value rises to more than 1.5 times the upper limit of the norm
- renal function does not return to normal after three months of interruption of PrEP or even deteriorates further
- the applicant for PrEP has diabetes mellitus, uncontrolled arterial hypertension, chronic hepatitis C, liver failure from another cause, pre-eclampsia during pregnancy, older age

Distorted results of renal function tests tend to occur in sporting people with large muscle mass, Especially if they take some dietary supplements.

V On average, when taking PrEP,

- 1% **decrease in bone density**; normalization occurs after discontinuation of PrEP. There was no increased incidence of bone fractures in the studies.

Interaction of PrEP with drugs, food, alcohol and drugs

PrEP tablets can be taken at any time of the day and regardless of the meal (i.e. on an empty stomach, during or after a meal).

TDF-FTC has no significant drug interactions, they can be verified in one of the databases: http://www.hiv-druginteractions.org/checker##table-view-wrap (University of Liverpool) http://hivinsite.ucsf.edu/interactions (University of California)
The TDF-FTC has no interaction with hormonal contraceptives or other hormone treatments (used for gender reassignment, pre-artificial insemination, etc.). Therefore, PrEP does not reduce the effectiveness of contraceptives, hormonal contraceptives do not reduce the effect of PrEP.

PrEP can be taken with alcohol. However, excessive alcohol use may be associated with more risky sexual behaviour and the client forgetting to take a PrEP tablet. Use of recreational drugs, including methamphetamine, heroin, or other opioids or cocaine, does not reduce the effectiveness of PrEP.

Pregnancy and lactation

PrEP does not protect against pregnancy. PrEP can be safely combined with all methods of preventing pregnancy. PrEP may be an appropriate strategy for safe conception in serodiscordant couples.

PrEP can be used during pregnancy and during breastfeeding if there is a significant risk of HIV infection during this time. PrEP users showed no variation during pregnancy, in newborn weight, or in the incidence of congenital malformations. TDF and FTC are excreted in breast milk in very low concentrations.

Information about the drug and how to treat it

PrEP uses a combination of two antiviral medicines pressed into one tablet; this contains 300mg tenofovir disoproxil fumarate (TDF) and 200mg emtricitabine (FTC). Sometimes the TDF content is

given as a tablet of 245mg, which is the weight of tenofovir disoproxil alone, excluding weight

contained fumarate salts (tenofovir disoproxil fumarate). The container contains 30 tablets and Desiccant. Storage is recommended at temperatures between 15 and 30 °C.

Users should be instructed that

- They should not leave medication in an environment that is too hot (e.g. in a car) or too cold (e.g. in a car).
  in the refrigerator), in direct sunlight and in places with excessive humidity
- should leave medicines in a container with a desiccant; In the drug dispenser they can prepare tablets for
  7 days
- Tablets can be taken with food, after or without a meal
- If you forget to take a tablet, take it as soon as you remember
- If you do not know if you have taken a tablet, taking two tablets occasionally is safe. Never take more than two tablets per day
- If you remember the next day, there is no need to take two tablets on that day – take one, as usual.

In case of vomiting: if the tablet is visibly vomited, wait at least one hour after the vomiting has resolved and take a new tablet. If vomiting occurs more than an hour after taking the tablet and you do not see it vomiting, take another tablet the next day as usual.

It is recommended to provide the user with an extra pack for one month at the beginning – it is advantageous if the client has a reserve of medicines in case he comes for a check-up later for various reasons.

HIV resistance

PrEP reduces the risk of HIV infection. A person who has not contracted HIV cannot develop HIV resistance to drugs. Unlike patients with HIV infection, who receive antiretroviral therapy in the presence of the virus in the body, there is no selection pressure in people taking PrEP.

Clinical studies have investigated whether HIV infection in people taking PrEP is due to resistance Virus. Only 3% of PrEP users who became infected with HIV were resistant to TDF or FTC.

Resistance at the time of PrEP use was rare in clinical trials, on average in one in 1,000 PrEP users. This is almost exclusively among people who started TDF-FTC at the time of early HIV infection — who were still HIV negative at baseline and seroconversion occurred in the first month of PrEP. Conducting an HIV test before starting PrEP and at follow-up is an essential measure, which prevent the development of drug resistance.

Acute HIV infection

Acute HIV infection is often symptomatic: fever, sore throat, headache, muscle and joint pain, enlarged nodes, mouth ulcers or rash. The symptoms are not specific, and most patients with signs of acute viral disease have an infection other than HIV. Conversely, a person who reports sex without a condom in the last 14 days should always consider the possibility of acute HIV infection. Initiation of PrEP at the time of acute HIV infection is associated with the risk of developing resistance to PrEP components. In such a situation, it is advisable to postpone the start of PrEP and repeat the HIV test in 4 weeks.

If an applicant for PrEP arrives within 72 hours of a high-risk contact, it is advisable to first post-exposure prophylaxis (PEP).

Sexually transmitted diseases

PrEP does not provide protection against sexually transmitted infections other than HIV, so it does not protect against syphilis, gonorrhea, chlamydial infection, trichomoniasis or genital herpes. Consistent

condom use should therefore also be recommended for PrEP users. Because PrEP is preferentially prescribed to people at increased risk of HIV infection and other sexually transmitted infections, regular testing for STDs (once every 3-6 months) is beneficial for both the tested person and public health protection.

Groups of people at increased risk

The main group at high risk of acquiring HIV infection in the Czech Republic consists of **men having sex with men.** However, the risk varies significantly from person to person. Some protect themselves by using a condom consistently (with each partner and at every penetrative intercourse), always using a water- or silicone-based lubricant. Others are in a mutually monogamous relationship with a partner who is HIV negative or HIV positive with undetectable viremia for more than 6 months with effective antiretroviral therapy. Non-penetrative sex, including joint / mutual masturbation, is safe.

Increased HIV exposure can be episodic – people taking PrEP may alternate between periods of increased risk and periods of low risk when PrEP is not needed. Clients and counselling people should be able to recognise situations where the risk of HIV infection is increased and the use of effective prevention, including PrEP, is therefore appropriate. They should also learn when and how to safely start, interrupt, resume, and end PrEP. A suitable situation to start or restart PrEP can be: sex without a condom (planned or unexpected) diagnosis of STDs in the client or partner, periods with a higher number of sexual partners, use of alcohol or recreational drugs before sex visits to a gay club, sauna, darkroom or party Ending a long-term relationship leaving school or home Moving to a city with a high incidence of HIV Provision of sexual services for payment, relationship with an HIV-positive person who has not achieved full suppression of the virus using ART.

Condoms remain an essential preventative measure for **sex workers**. PrEP is an additional preventative tool — it can't replace a condom because it doesn't protect against sexually transmitted infections other than HIV. PrEP users in this group should be recommended regular monitoring by a venereologist and STD tests at intervals of 2-4 weeks.

For **IDUs,** access to clean injection material through exchange programmes and substitution treatment remain the basis of prevention. The provision of these services is a priority because they significantly reduce the risk of HIV transmission and also protect against the transmission of other infections through the blood (hepatitis C, B). Non-injecting drug users may be at increased risk of HIV transmission sexually, especially if they use amphetamine-type stimulants that promote risky sexual behaviour. In these cases, PrEP can be a useful additional preventive activity.

PrEP Cost-Effectiveness

The implementation of PrEP requires resources for salaries, training, medications, and lab tests. Nevertheless, it is a cost-effective procedure because

- Treatment of HIV infection is expensive: it is lifelong, it often uses original products with a higher price, more laboratory examinations are performed, complications of HIV infection and treatment are more expensive. Cheaper generic drugs are available for PrEP, they are used for a shorter period of time – during periods of significant risk of HIV infection,
- A side benefit of PrEP is that it motivates people at increased risk to get tested for HIV. Earlier diagnosis and treatment of HIV infection prevents complications and the spread of infection in the population,
- continuous screening and treatment of other sexually transmitted diseases reduces the individual risk of HIV infection and limits the spread of STDs in the population,
- other health and social problems can be addressed in the provision of PrEP, support is provided for safer sexual practices and condom use, as well as participation in harm reduction programmes (exchange of injection material, substitution treatment);
- cost-effectiveness in the Czech Republic was confirmed in a pharmacoeconomic model published in 2020 (Skoupá J, et al.).

PrEP Prescription Monitoring

A healthcare provider who has prescribed pre-exposure prophylaxis of HIV infection reports electronically cumulative data on its administration once a year (as of 31.1. of the following year) to the National Reference Laboratory for HIV/AIDS in the range:

a. Number of all subjects who received pre-exposure prophylaxis at least once in a given year
b. the number of all subjects who received pre-exposure prophylaxis for the first time in a given year

Data are presented by gender (men, women, transgender people), key population affiliation (men having sex with men, intravenous drug users, commercial sex workers, prisoners, permanent partner of the HIV+ patient, others) and dosing regimen (regular, occasional).

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