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ANALYSIS OF NATIONAL HIV PRE-EXPOSURE PROPHYLAXIS GUIDELINES IN SEVEN COUNTRIES OF EASTERN EUROPE AND CENTRAL ASIA

ARMENIA • GEORGIA • KAZAKHSTAN • KYRGYZSTAN

TAJIKISTAN • UKRAINE • UZBEKISTAN

ECOM
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РАСПРОСТРАНЯЕТСЯ БЕСПЛАТНО

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CONTENTS

LIST OF ABBREVIATIONS

ALT	Alanine transaminase
Anti HBc	Test for antibodies to hepatitis B core antigen
Anti HBs	Test for antibodies to hepatitis B surface antigen
CAB-LA	Long-acting injectable cabotegravir
DVR	Dapivirine vaginal ring
ED-PrEP	Event-driven pre-exposure prophylaxis for HIV
EECA	Eastern Europe and Central Asia
ELISA	Enzyme-linked immunosorbent assay
FTC	Emtricitabine
HBV	Hepatitis B virus
HBsAg	Test for hepatitis B surface antigen
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
MSM	Men who have sex with men
PEP	Post-exposure prophylaxis for HIV
PrEP	Pre-exposure prophylaxis for HIV
STI	Sexually transmitted infection
TAF	Tenofovir alafenamide
TDF	Tenofovir disoproxil fumarate
WHO	World Health Organization
3TC	Lamivudine

SUMMARY

In September 2015, the World Health Organization (WHO) recommended that oral pre-exposure prophylaxis (PrEP) containing tenofovir disoproxil fumarate (TDF) be offered as an additional prevention choice for people at substantial risk of human immunodeficiency virus (HIV) infection as part of combination HIV prevention approaches (1). In 2021, WHO recommended offering the dapivirine vaginal ring (DVR) as an additional HIV prevention option for cisgender women at substantial risk of HIV infection (2). Finally, in 2022, long-acting injectable cabotegravir (CAB-LA) was recommended as an additional method of HIV prevention for people at substantial risk of HIV infection (3).

In order to analyze the sustainability and institutionalization of successful examples of PrEP implementation in countries of the region, ECOM, in cooperation with the WHO Regional Office for Europe and a regional consultant, analyzed national guidelines on PrEP in seven selected countries: Armenia, Georgia, Kazakhstan, Kyrgyzstan, Tajikistan, Uzbekistan and Ukraine.

This is the first time that such an analysis has been carried out in the EECA region, and we hope that this report will serve as an exchange of experience and inspire countries to adopt successful practices that exist in the region, and to amend existing national guidelines for prescribing PrEP in accordance with WHO guidance.

This analysis and accompanying recommendations are focused on national guidelines and do not take into account additional activities currently underway in the countries included in the study. The purpose of this study is to attempt to assess the level of institutionalization and compliance of the adopted normative documents with current WHO recommendations on PrEP. The authors acknowledge that some of the recommended changes may have already been implemented outside of national PrEP programmes. We also recognize the significant contributions made by health care professionals, physicians, researchers, and key populations to expand access to and implement PrEP at the national level.

In this document PrEP is used to refer generally to TDF-based oral PrEP, unless stated otherwise.

PRIMARY RESULTS

National guidelines were updated relatively recently in all seven countries (in 2020 in Tajikistan, in 2021 in Uzbekistan, in 2023 in Kazakhstan, and in 2022 in the remaining countries). Georgia, Armenia, Uzbekistan and Tajikistan have separate national guidelines for PrEP, while PrEP services are part of national HIV guidelines in the other three countries.

In six countries, with the exception of Uzbekistan, PrEP is available both to members of key populations and to all individuals at substantial risk of HIV infection. PrEP may be prescribed at the request of the patient in four of the seven countries reviewed.

The most common PrEP regimen is TDF 300 mg/FTC 200 mg (used in all seven countries); the second most common PrEP regimen is monotherapy using TDF 300 mg. The largest number of PrEP regimens are available in Kazakhstan and Tajikistan, followed by Armenia, Georgia and Kyrgyzstan, then Uzbekistan, with the fewest regimens available in Ukraine. The national guidelines of Kazakhstan provide for the use of CAB-LA as PrEP. Only Armenia includes the use of DVR in its guidelines.

All seven countries provide HIV testing before starting PrEP and regular testing thereafter. Although self-testing and community-based testing services have already been introduced in a number of countries, the use of self-testing results to start or continue PrEP is only provided for in the national guidelines of Ukraine, where this is allowed in emergency situations. In Kyrgyzstan and Uzbekistan, national guidelines do not recognize the results of anonymous and community-based tests using oral fluid.

Oral event-driven pre-exposure prophylaxis (ED-PrEP) is mentioned in six of the countries, with the exception of Uzbekistan. In Kyrgyzstan and Ukraine, ED-PrEP is available to a wider range of people at increased risk of HIV infection. HBV infection may result in a denial of access to ED-PrEP in all countries of the region. Four of the seven countries describe the correct timing to start and stop ED-PrEP in their national guidelines. All six countries where ED-PrEP is approved use the FTC 300mg/FTC 200mg regimen, alternatively in Kyrgyzstan and Tajikistan, clients can receive TDF 300mg/3TC 300mg.

The need to integrate PrEP services with other health care services is not sufficiently discussed in any of the guidelines. This may be due to the existence of vertical systems for providing health care services, which rarely work closely with each other in the EECA countries. The national guidelines of Georgia, Kazakhstan, and Kyrgyzstan mention the need to refer PrEP clients to other medical and social services in certain specific situations.

GENERAL RECOMMENDATIONS FOR ALL COUNTRIES PARTICIPATING IN THE STUDY

DESIGN OF PREP PROGRAMMES

- Medical services should be accessible and acceptable for people from key populations based on the principles of medical ethics, avoidance of stigma, non-discrimination, and the right to health;
- Groups and organizations led by key populations should be key partners and leaders in designing, planning, implementing and evaluating PrEP services;
- Peer navigators should be employed to support people from key populations to access and navigate PrEP services, and to remain in care.

SIMPLIFIED MODELS FOR PREP DELIVERY

- Consider adopting decentralized and differentiated PrEP delivery models, including delivery through community-based services, in order to reduce barriers to access and increase coverage;
- Consider adopting same-day initiation of PrEP using rapid HIV tests as a standard procedure, resorting to laboratory tests in case the results of the rapid test are indeterminate and/or the client has symptoms or signs consistent with acute HIV infection; this should be done in accordance with the national testing algorithm to optimize resource and time management, and increase PrEP acceptance and uptake;
- When dispensing PrEP refills, it should be taken into account that users eligible for ED-PrEP often switch from a daily regimen to ED-PrEP; therefore, consider dispensing enough PrEP supply to cover the entire period until the next appointment, based on past usage data (e.g. for appointments every 3 months, dispense a 3-month supply the first time, then 1-month to 3-month supplies at subsequent appointments);
- Consider delivering online PrEP services as an additional option, in order to reduce barriers to access, while ensuring data security and privacy protection;
- Consider integrating HIV self-testing to create demand for initiating and continuing PrEP, in order to lower barriers to entry and reduce the number of visits required;
- Simplify laboratory test requirements for PrEP start and continuation by aligning national guidelines with the latest WHO guidance, especially in relation to kidney function and viral hepatitis.

INDICATIONS FOR PRESCRIBING PREP

- In order to reduce stigma and discrimination against people taking PrEP, it is recommended that belonging to a key population not be listed separately as an indication for PrEP. However, key populations should be the target of informational activities and activities aimed at creating demand.

ED-PREP

- Align contraindications for ED-PrEP in national guidelines with the latest WHO recommendations, which indicate that HBV infection should not be a barrier to use ED-PrEP (1);
- Align eligibility criteria for ED-PrEP with WHO recommendations, including that all males assigned at birth who have sexual contact and are not taking exogenous estradiol-based hormones are eligible for ED-PrEP.

PROCEDURES NECESSARY FOR INITIATING AND CONTINUING PREP

- Consider introducing rapid diagnostic tests for HIV, syphilis (as well as dual tests for HIV and syphilis), HBsAg, and HCV antibodies in order to simplify service delivery, and reduce the number of visits required and the costs of the PrEP programme;
- Align indications for kidney function measurement with WHO guidance regarding the frequency and individuals for whom such a procedure is recommended, and clarify that waiting for test results should not delay initiation or continuation of PrEP;
- Delay initiation of PrEP only for individuals with potential exposure to HIV- within the previous 72 hours (in this case offer PEP and then switch to PrEP if HIV-negative status is confirmed), and for individuals with signs or symptoms of acute HIV infection and potential recent exposure to HIV (postpone PrEP until HIV-negative status can be confirmed);
- Include in the national guidelines the procedure for resuming PrEP after a break, according to WHO guidance, this procedure consists of re-confirming that the client meets PrEP eligibility criteria and undergoes HIV testing before receiving a new prescription;
- Include in the national guidelines the procedure to be followed in case of seroconversion, in accordance with WHO recommendations, ART should be started as soon as possible after HIV infection is confirmed, without any gap between PrEP and ART.

USE OF HORMONAL CONTRACEPTIVES, PREGNANCY, AND BREASTFEEDING

- If DVR is included as PrEP, update provisions on the use of hormonal contraceptives in national guidelines with information that DVR is not recommended for use with vaginal contraceptive rings containing hormones.

VIRAL HEPATITIS

- HBsAg testing should be offered to all clients at or within three months from PrEP initiation. HCV antibody testing should be offered at or within three months from PrEP initiation, and every 12 months thereafter, in case of increased risk for HCV. Waiting for test results should not delay PrEP initiation or continuation (1).
- HBV infection is not a contraindication for daily PrEP or ED-PrEP (1).

MONITORING AND EVALUATION

- Consider introducing into existing national guidelines specific indicators for evaluating PrEP programmes. According to emerging consensus in the region, the following indicators are the most important:
  - % of people screened who are eligible for PrEP (14);
  - % of people continuing PEP at 3, 6 and 12 months after initiation (14);
  - % of people who stop treatment due to toxicity (14);
  - % of people who have seroconverted (14);
  - number of people who received oral pre-exposure prophylaxis at least once during the reporting period (14).

INTEGRATION OF PREP WITH OTHER MEDICAL AND SOCIAL SERVICES

- Consider gradually adding STI services to PrEP programmes using a phased approach, beginning with syndromic management, rapid diagnostic tests, laboratory immunoassays, point-of-care laboratory or molecular testing, etiological treatment, and vaccinations;
- When testing for chlamydia and gonorrhoea, self-collection of specimens, performing a NAAT test on urine rather than on a urethral swab and pooling samples for analysis should be considered in order to optimize resources and improve acceptability;
- If STI testing is included in PrEP programmes, also include etiological treatment and consider same-day treatment whenever possible, in accordance with WHO and national guidelines, in order to prevent loss of follow-up and improve outcomes;
- If STI services are not integrated into the PrEP programme, establish a referral mechanism to ensure timely linkage to care to the appropriate healthcare service and include it in the national guidelines;
- Consider establishing a mechanism to ensure linkage to care to the appropriate healthcare services on issues related to drug use and chemsex, mental health, reproductive health, and include it in the guidelines.

DRUGS USED FOR PREP

- In all countries (except Armenia and Kazakhstan), consider introducing PrEP using DVR and CAB-LA, which would also expand the possibility of prescribing PrEP to people with kidney disease and to those who have difficulty adhering to oral PrEP regimens. Women and girls may experience additional difficulties due to prevailing gender inequality and greater control exerted by their sexual partners and relatives. The option to use DVR would also greatly enhance the ability of women and girls to use PrEP.

INTRODUCTION

In September 2015, the World Health Organization (WHO) recommended that oral pre-exposure prophylaxis (PrEP) containing tenofovir disoproxil fumarate (TDF) be offered as an additional prevention choice for people at substantial risk of human immunodeficiency virus (HIV) infection as part of combination HIV prevention approaches (1). Oral PrEP has proven to be highly effective for HIV prevention when used as directed. In 2021, WHO recommended offering the dapivirine vaginal ring (DVR) as an additional prevention option for cisgender women at substantial risk of HIV infection (2), and in 2022, it recommended long-acting injectable cabotegravir (CAB-LA) as an additional prevention measure for those at substantial risk of HIV infection (3).

According to PrEPWatch, more than three million people worldwide were receiving PrEP by the end of 2022 (4). However, the number of PrEP users in the European region remains quite low. With a few exceptions, access to PrEP in Eastern Europe and Central Asia (EECA) lags significantly. According to the national cascades of HIV prevention and treatment services for the MSM population conducted by ECOM in 2022 in Armenia, Georgia, Kazakhstan, Kyrgyzstan and Ukraine, it was found that the number of people on PrEP in November 2022 in these countries was: Armenia — 23, Georgia — 742, Kazakhstan — 409, Kyrgyzstan — 133, and Ukraine — 7,264. There is no similar data for Tajikistan and Uzbekistan.

Therefore, this study aims to determine the availabilty of national PrEP guidelines in seven selected countries in the EECA region, and compare them with the latest WHO recommendations on PrEP services delivery. The following countries were included in this study: Armenia, Georgia, Kazakhstan, Kyrgyzstan, Tajikistan, Ukraine, and Uzbekistan. This is the first time such a comparative analysis of national PrEP guidelines in the countries of Eastern Europe and Central Asia is carried out.

AVAILABILITY OF NATIONAL GUIDELINES

In 2021, nine EECA countries[1] reported having developed and adopted national guidelines on PrEP (4, 5). Four of the seven countries included in this analysis (Armenia, Georgia, Tajikistan and Uzbekistan) have separate national guidelines on PrEP while in Kazakhstan, Kyrgyzstan and Ukraine, PrEP is included in the clinical guidelines for HIV (6-11). The national guidelines for the introduction and implementation of pre-exposure prophylaxis for HIV infection in the Republic of Tajikistan were adopted in 2020. In Uzbekistan, the guidelines were introduced in 2022. The current national guidelines of Armenia, Georgia, Kyrgyzstan and Ukraine were adopted in 2022, and in 2023 in Kazakhstan.. The next revisions of national guidelines are planned in 2024 (Georgia) and 2025 (Ukraine), as new key evidence becomes available, in 2024 (Kyrgyzstan, Tajikistan), as new key evidence becomes available, or five years after the entry into force of the current guidelines (Armenia, Kazakhstan). Information about the next revision of the guidelines in Uzbekistan is not available and is not indicated in the current guidelines.

INDICATIONS FOR PRESCRIBING PREP

WHO recommends offering a differentiated, simplified, de-medicalized and comprehensive package of PrEP services to all HIV-negative people at substantial risk of HIV infection (1). HIV testing is strongly recommended at PrEP initiation, including through the expansion of HIV self-testing services (1). The main preconditions for starting PrEP are that the client is currently HIV-negative, has no signs or symptoms of acute HIV infection and is at substantial risk of HIV infection.

People living in geographic regions or from populations with high HIV prevalence may be more likely to be exposed (1). However, when prescribing PrEP, WHO recommends focusing on the characteristics and behaviors of individuals and their partners that may lead to HIV exposure (1). When prescribing PrEP, WHO also recommends prioritizing individuals who request PrEP, as they are most likely to be at substantial risk of HIV infection (1).

[1] Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Ukraine, and Uzbekistan.

Indications for prescribing PrEP in all seven of the national guidelines reviewed largely correspond to WHO recommendations. In six countries, PrEP can be prescribed both to key populations and to anyone else who is at «substantial risk» of HIV. However, in Uzbekistan, PrEP is only available to serodiscordant couples (where one of the partners is living with HIV).

The concept of «substantial risk of HIV infection» in the countries under review is approximately the same:

- ✔ Belonging to a key population;
- ✔ Anal or vaginal sex without the use of condoms with more than one partner;
- ✔ Having a sexual partner with one or more risk factor for HIV infection;
- ✔ Having an sexual partner living with HIV who is not taking ARV or who has not yet achieved a viral suppression, or if the partners living with HIV do not openly discuss their adherence to ARV treatment;
- ✔ Use of post-exposure prophylaxis (PEP);
- ✔ History of sexually transmitted infections (STIs).

It should be noted that belonging to key populations is mentioned in the guidelines of Armenia, Georgia and Ukraine. The national guidelines of Kazakhstan, Kyrgyzstan and Tajikistan only refer to substantial risk factors for HIV infection, thereby reducing the stigma associated with the use of PrEP. It should be noted that by restricting PrEP only to key populations, who often experience high levels of stigma and discrimination in EECA countries, national guidelines may inadvertently increase stigma against PrEP users.

A client's request for PrEP is an indication for prescribing PrEP in four out of the seven countries[2]. In the guidelines of Georgia and Armenia, this issue is not addressed when discussing the indications for prescribing PrEP.

[2] Kazakhstan, Kyrgyzstan, Tajikistan, and Ukraine.

CONTRAINDICATIONS FOR PRESCRIBING PREP

According to WHO, contraindications for prescribing PrEP include:

- HIV-positive status (1, 12);
- impaired kidney function, i.e. an estimated creatinine clearance of less than 60 mL/min (if known) is also a contraindication for PrEP regimens containing TDF (1);
- advanced liver disease, acute viral hepatitis, and confirmed hepatotoxicity are also contraindications for the use of CAB-LA as PrEP (3).

Contraindications for prescribing PrEP are clearly listed in a specific section in the national guidelines of Armenia, Kyrgyzstan, Tajikistan, Ukraine, and Uzbekistan. It should be noted that in Armenia, PrEP is not recommended for people at low risk of HIV infection. However, the meaning of «low risk of infection» is not explained and no examples are provided. In the national guidelines of Georgia and Kazakhstan, contraindications to the use of PrEP are described in other sections (when discussing screening tests, prescribing PrEP, or follow-up monitoring after initiation of PrEP), which makes the information slightly more difficult to understand. In all seven countries, HIV-positive status, symptoms of acute HIV infection, and impaired kidney function, i.e. estimated creatinine clearance of less than 60 mL/min (if known), are contraindications to PrEP. At the same time, Kazakhstan clarifies that «an increase in serum creatinine is not a reason to refuse prescription if the values remain above or equal to 60 mL/min for TDF/FTC and 30 mL/min for TAF/FTC». In addition, the national guidelines of Kazakhstan and Uzbekistan recommend additional counseling and referral to a nephrologist in case of a steady decrease in kidney function indicators while taking PrEP, even if the results remain above the indicators at which PrEP should be discontinued.

In addition, in Armenia, Kyrgyzstan, Tajikistan, Uzbekistan, and Ukraine contraindications for initiating PrEP include allergies or intolerance to PrEP drugs. Uzbekistan's guidelines notes that PrEP should not be prescribed to adolescents under 35 kg or under 15 years old, or to individuals with osteopenia, osteomalacia, or osteoporosis. According to these guidelines, PrEP should also not be prescribed to patients on therapy for multidrug-resistant tuberculosis (MDR TB). It should be noted that these limitations are not based on any evidence and are not included in existing WHO recommendations. According to the latest WHO recommendations from 2022, infection with viral hepatitis B is not a contraindication for either a daily PrEP regimen or for event-driven PrEP (ED-PrEP) (1). Nevertheless, infection with the hepatitis B virus (HBV) is mentioned as a contraindication for ED-PrEP in Armenia, Georgia, Kyrgyzstan, Kazakhstan and Tajikistan.

SUGGESTED PREP REGIMENS

In 2015, WHO recommended the use of oral PrEP containing TDF as an additional HIV prevention option and as part of combination HIV prevention approaches for people at substantial risk of HIV infection (strong recommendation, high certainty evidence) (1).

Monotherapy using TDF 300 mg as PrEP has shown comparative safety and efficacy in heterosexual men and women, and among people who inject drugs (1, 12).

In 2021, the recommended offering DVR as an additional HIV prevention option for cisgender women at substantial risk of HIV infection (conditional recommendation, moderate-certainty of evidence) (2).

In 2022, WHO recommended CAB-LA as an additional HIV prevention option for people at substantial risk of HIV infection (conditional recommendation, moderate-certainty of evidence) (3).

The PrEP regimens offered vary by country (see Table 1 below). The most common PrEP regimen is a fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and emtricitabine (FTC) 200 mg, which is available in all seven countries reviewed. This is the only PrEP regimen offered by the national guidelines of Ukraine. The next most common regimen is TDF monotherapy (300 mg), which is not recommended as PrEP for men who have sex with men (MSM) in Georgia, Kyrgyzstan, and Tajikistan. The national guidelines of Kazakhstan do not mention restrictions on the use of TDF monotherapy (300 mg) among MSM. In Armenia, Tajikistan, Kyrgyzstan, and Uzbekistan, a fixed-dose combination of tenofovir disoproxil fumarate (TDF) 300 mg and lamivudine (3TC) 300 mg is available as an alternative PrEP option. A fixed-dose combination of tenofovir alafenamide (TAF) 25 mg and FTC 200 mg is recommended as PrEP in Kazakhstan and Tajikistan. In Tajikistan, this combination is recommended only for adult MSM and transgender women. The national guidelines of Kazakhstan do not specify which key population this combination is suitable for, but recommends not to use this combination as ED-PrEP.

All countries, with the exception of Uzbekistan, recommend using the TDF 300 mg/FTC 200 mg fixed-dose combination for ED-PrEP. In Kyrgyzstan and Tajikistan, the TDF 300 mg/300 mg 3TC fixed-dose combination may also be used for ED-PrEP.

The national guidelines of Armenia and Kazakhstan also provide for the use of long-acting injectable cabotegravir (CAB-LA) as PrEP. The Kazakh guidelines details exactly which muscles should be injected with CAB-LA, what tests are required before initiating CAB-LA PrEP, and which tests should be performed and how often during follow-up, in accordance with WHO recommendations. It also mentions how to correctly transition a client from CAB-LA to oral PrEP if they wish so. The national guidelines do not recommend prescribing CAB-LA together with other antiretroviral drugs. At the same time, the guidelines in Armenia briefly describes the main results of research conducted, and emphasizes the safety and effectiveness of this method, including for trans women. However, there is no description of the practical application of this PrEP regimen in the guidelines in Armenia.

Of all the countries reviewed in this study, only the guidelines of Armenia suggest the use of a dapivirine vaginal ring (DVR) as PrEP for women. However, as in the case of CAB-LA, this section of the guidelines is a summary of the effectiveness of this regimen, and does not include any recommendations for its use and implementation in practice.

RECOMMENDED PREP REGIMENS

	ARMENIA	GEORGIA	KAZAKHSTAN	KYRGYZSTAN	TAJIKISTAN	UZBEKISTAN	UKRAINE
TDF 300 mg/FTC 200 mg	+	+	+	+	+	+	+
TDF 300 mg	–	+	+	+	+	–	–
TDF 300 mg/3TC 300 mg	–	–	–	+	+	+	–
TAF 25/ FTC 200 mg	–	–	+	–	+	–	–
DVR	+	–	–	–	–	–	–
CAB-LA	+	–	+	–	–	–	-

RECOMMENDED SERVICE PACKAGE FOR PREP INITIATION

HIV TESTING

According to the latest WHO recommendations, the main test for initiating PrEP should be HIV testing, using national testing algorithms. WHO also recommends introducing HIV self-testing along with existing HIV testing services to support differentiated delivery of PrEP (1). Reducing the need to visit medical institutions to start or continue PrEP can help increase PrEP coverage, its effective use, and HIV testing.

All seven countries require HIV testing before starting PrEP, as well as screening for symptoms of acute HIV infection. Symptoms of acute HIV infection or if a client reports a recent risk of HIV infection may cause the initiation of PrEP to be postponed in Kazakhstan (the duration of such postponement is not discussed) and Tajikistan (4 weeks). In Armenia, if acute HIV infection is suspected, it is recommended to conduct an additional molecular blood test in order to detect the virus. In other countries, national guidelines do not specify what to do when a client has symptoms of acute HIV infection, but such symptoms are a contraindication for initiating PrEP in all seven countries.

Although self-testing is already available in a number of countries, initiating PrEP based on self-testing results is only mentioned in Ukraine's national guidelines, which allows the use of self-testing results in emergency situations. In Georgia, Kazakhstan, Kyrgyzstan and Tajikistan, national guidelines stipulate that HIV testing can be carried out using a rapid test. However, for Kazakhstan it is not specified whether it can be used for PrEP. At the same time, in Tajikistan, it is recommended that rapid tests are carried out preferably at the place where PrEP services are provided. The national guidelines of Kyrgyzstan clarify that when testing for HIV, an enzyme-linked immunosorbent assay (ELISA) or a rapid test using capillary blood should be used. The results of anonymous testing or of rapid tests using oral fluid (which are available for self-testing and through non-governmental organizations) are not taken into account. The guidelines of Armenia do not specify what type of testing should be offered to clients who express a desire and/or qualify for inclusion in the programme. These guidelines only mention that the absence of HIV infection must be documented by providing a negative result before initiating PrEP. The guidelines of Uzbekistan state that a 4th generation HIV test is required, and that oral fluid testing is not recommended.

The introduction of rapid testing could allow same-day initiation of PrEP, and reduce the number of visits required and potential barriers to accessing PrEP.

VIRAL HEPATITIS TESTING

Prior to or within the first three months of starting PrEP, WHO also recommends testing for hepatitis C virus (HCV) antibodies and HBV surface antigen (HBsAg) where appropriate (1). It notes that waiting for test results should not be a barrier to initiating PrEP (1).

In Kyrgyzstan, screening for HCV is provided subject to availability prior to initiation of PrEP. In case of a positive result, the client is referred for additional tests to confirm the diagnosis according to the national testing algorithm, and to receive appropriate treatment. It is also recommended to test for HBV before initiating PrEP, if possible. If the test result is negative, the client is referred for HBV vaccination; if the result is positive, additional tests are carried out according to the national testing algorithm, and treatment for HBV is prescribed. Waiting for viral hepatitis test results is not a barrier to initiating PrEP.

In Kazakhstan, the need for testing for viral hepatitis is mentioned, but the guidelines do not specify which tests should be taken. At the same time, the national guidelines allow clients to start taking PrEP without waiting for the results of tests for viral hepatitis.

In Armenia and Georgia, clients must also be tested for HCV (antibodies for HCV) and HBV (HBsAg, anti-HBs, anti-HBc) before starting PrEP. Georgia's national guidelines provide a table for interpreting HBV test results, and describes further steps depending on the tests results (vaccination for negative HBV tests, documentation for past HBV immunity or vaccination, monitoring and evaluation for treatment of acute HBV, assessment for treatment of chronic HBV, and an individualized approach for uncertain HBV status). Recommendations for vaccination in case of negative HBsAg and anti-HBc are also included in the guidelines of Armenia.

Tajikistan's national guidelines does not mention screening for HCV, but suggests testing patients for HBV (HBsAg) before initiating PrEP. Furthermore, depending on the results of the analysis, the client may be offered a PrEP regimen containing TDF and vaccination against HBV.

In Ukraine, testing for HBV is mandatory before or during the first 3 months after initiation of PrEP. In the event of a negative result, the client will be offered the HBV vaccine. If the test results are positive, daily oral PrEP is recommended. Screening for HCV in Ukraine is desirable but not mandatory. If the result is positive, the client may be referred for appropriate treatment. The guidelines also make it clear that waiting for viral hepatitis test results should not be an obstacle to initiating PrEP.

In Uzbekistan, testing for HbsAg before initiating PrEP is mandatory, and further actions are determined by the national algorithm, including offering HBV vaccination if the test is negative. HCV testing is recommended but not required.

KIDNEY FUNCTION MEASUREMENT

Kidney function testing before starting PrEP is recommended by WHO only for certain groups of people (1). This test may be considered optional for individuals younger than 50 years of age without kidney-related comorbidities (1). For individuals aged 50 years or older, those who have kidney-related comorbidities, and those who have previously shown at least a mild decrease in kidney function (creatinine clearance less than 90 mL/min) on a previous kidney function test, it is recommended to conduct a kidney function test before the initiation of PrEP or during the first three months after starting PrEP. At the same time, it is noted that waiting for the results of this test should not be a barrier to starting PrEP (1).

All seven countries provide serum creatinine testing. At the same time, the national guidelines of Kazakhstan, Kyrgyzstan, Tajikistan and Ukraine note that the absence of creatinine clearance results should not be a barrier to initiating PrEP. In Kyrgyzstan, assessment of kidney function is not mandatory for patients under 30 years of age and without comorbidities or risk factors for kidney disease.

In Georgia, PrEP can be prescribed the same day, if the results of all necessary tests are available. In case the tests results are not ready, it is noted that PrEP must be provided within the next 7 days. Other national guidelines do not discuss the maximum number of days to wait for test results before starting PrEP. The guidelines of Armenia lack a clearly defined algorithm of action for cases where there are no current creatinine clearance tests, and does not mention that this test is optional and not mandatory for starting PrEP.

OTHER PROCEDURES

In addition to the procedures mentioned above, depending on the country, clients may need to undergo additional tests and procedures to obtain PrEP. Georgia has the longest list of tests required for starting PrEP: before starting PrEP, in addition to the procedures discussed above, it is necessary to have a complete blood panel, an alanine aminotransferase test (ALT), a serological test for syphilis, and a molecular test for gonorrhoea and chlamydia. Women will also be asked to take a pregnancy test. A serological test for syphilis is also mentioned in the national guidelines of Kyrgyzstan, and it is offered only if resources are available. Screening for other STIs is also provided in Kyrgyzstan and Ukraine. At the same time, in Kyrgyzstan, screening is mandatory, but testing for STIs (syphilis, chlamydia, trichomoniasis, and gonorrhoea) is only carried out if resources are available. In Ukraine and Armenia, screening for STIs is not mandatory, but recommended. The national guidelines of Ukraine recommend prescribing PrEP to clients testing positive for STIs, and referring them for necessary treatment.

The national guidelines of Tajikistan do not mention the need for screening for STIs before initiating PrEP. In Uzbekistan, in addition to the creatinine clearance test, it is necessary to take a urine test to assess kidney function, and it is also recommended to take a serological test for syphilis. Waiting for STI test results or having an STI is not a barrier to initiating PrEP in Armenia, Kazakhstan, Kyrgyzstan and Ukraine.

Five out of seven countries offer pregnancy tests: Armenia, Georgia, Kyrgyzstan, Kazakhstan, and Uzbekistan. In other countries, pregnancy tests are not mentioned.

According to the latest WHO recommendations on simplified PrEP delivery, there should be no mandatory testing other than for HIV before initiating PrEP. This will also reduce the cost of testing needed to start PrEP, and such funds can be reinvested in additional services that may be useful to PrEP users (for example STI testing).

RECCOMMENDED SERVICE PACKAGE FOR PREP FOLLOW-UP

HIV TESTING

WHO recommends offering regular HIV testing to PrEP users, the first time being within 1 to 3 months of PrEP initiation, and no more frequently than every 3 months thereafter; HIV testing is also strongly recommended before restarting PrEP (1, 3, 12). National guidelines in all countries require an HIV test within one month and then every 3 months after starting PrEP.

VIRAL HEPATITIS TESTING

WHO recommends HCV testing every 12 months after starting PrEP in settings where PrEP services are available to populations at higher risk of HCV infection (1). In Kazakhstan and Tajikistan, the need for monitoring tests for viral hepatitis after starting PrEP is not mentioned. In Kyrgyzstan, it is suggested that HBV and HCV testing be repeated 3 and 12 months after starting PrEP, if possible. In Armenia and Ukraine, PrEP clients will be asked to take an HCV test every 12 months. In Georgia and Uzbekistan, all PrEP clients are encouraged to be tested for HCV (HCV antibodies) and HBV (HBsAg, anti-HBs, anti-HBc) every 6 months.

KIDNEY FUNCTION MONITORING

WHO recommends conducting monitoring assessments of kidney function every 6-12 months for PrEP clients over 50 years of age with potential comorbidities that may affect kidney function, and for those whose test results have previously indicated at least a mild decrease in kidney function (1). This recommendation is followed by Kazakhstan and Ukraine, in the other countries more frequent assessment of kidney function is suggested. Georgia recommends that kidney function be assessed before starting PrEP, one month after starting PrEP, and every 3 months thereafter for all people. Tajikistan suggests assessing the kidney function of all clients every 3 months in the first year after starting PrEP, and then once a year. Armenia and Kyrgyzstan suggest assessing kidney function every 3–6 months. At the same time, unlike in Armenia, in Kyrgyzstan, regular monitoring is not mandatory for clients under the age of 30 and without concomitant kidney diseases. In Uzbekistan, monitoring of kidney function is required at 3 and 6 months after starting PrEP and then every 6 months.

OTHER PROCEDURES

In addition to the procedures mentioned above, in Georgia, Kazakhstan, Kyrgyzstan and Ukraine, PrEP clients undergo additional tests after starting PrEP. For example, in Georgia, after the start of PrEP, clients should have a complete blood panel (within one month and then every 3 months), an ALT test, tests for syphilis, gonorrhoea and chlamydia (every 6 months), and tests for viral hepatitis (every 6 months if necessary).

Kazakhstan, Kyrgyzstan and Ukraine also provide for screening and testing for STIs every 3 months after starting PrEP. At the same time, in Kyrgyzstan, testing for STIs (syphilis, chlamydia, trichomoniasis, and gonorrhoea) is carried out only if funding is available. In Ukraine, only screening for STIs is carried out. The need for further STI screening after starting PrEP is not mentioned in the guidelines of Tajikistan. In Armenia, STI screening is recommended every 3–6 months. In Uzbekistan, testing for syphilis is recommended every 6 months.

In Kazakhstan, a pregnancy test is also carried out every 3 months for all women of reproductive age, while in Armenia this interval is not specified. Additionally, in Kazakhstan, triglycerides, cholesterol and weight are to be monitored in clients using TAF/FTC, at least once every 6 months. In Kazakhstan, clients receiving CAB-LA have more frequent monitoring tests that coincide with their appointments for follow-up injections. For example, women should have a pregnancy test every 2 months, and STI screening should be carried out for MSM and transgender women every 4 months, and for heterosexual men and women every 6 months.

In Kyrgyzstan and Uzbekistan, women of reproductive age are offered a test every 3 months after starting PrEP. This test is not required if the client is taking oral contraceptives.

In addition, the national guidelines of Armenia, Kazakhstan, Kyrgyzstan and Uzbekistan discuss the need to address patients' side effects after starting PrEP at each of their follow-up appointments. At the same time, the national guidelines of Kazakhstan describe exactly how to address some of the most common side effects, such as headache, nausea, abdominal discomfort, diarrhoea, and rashes. The guidelines of Uzbekistan notes that describing potential side effects at the start of PrEP can improve adherence to treatment. The national guidelines of Tajikistan and Ukraine mention the need to address side effects, but do not mention how often side effects should be discussed with clients and how clients who experience side effects can be supported. In Tajikistan, the guidelines only list the most common side effects of PrEP, and advise that clients wait for them to disappear over time. The need for counseling on side effects is mentioned only before starting PrEP. The Armenian guidelines clarify the importance and need of counseling, and suggests informing clients prior to starting PrEP about potential side effects and addressing this topic at every visit. Side effects are not mentioned in any way in the national guidelines of Georgia.

INDICATIONS FOR DISCONTINUING PREP

According to the latest WHO recommendations, impaired kidney function (estimated creatinine clearance of less than 60 mL/min) is an indication for discontinuing PrEP containing TDF (1). WHO does not recommend the use of CAB-LA as PrEP for patients with advanced liver disease or acute viral hepatitis, and recommends discontinuing CAB-LA PrEP when hepatotoxicity is confirmed (3). Indications for discontinuing PrEP are found in all seven national guidelines, but they vary. In Georgia, Kazakhstan and Kyrgyzstan, PrEP may be terminated due to:

- client's choice;
- changes to or cessation of factors for substantial risk of HIV infection;
- a positive HIV test result;
- intolerance to PrEP drugs (only in Georgia and Kazakhstan);
- chronic problems with adherence to PrEP (Georgia and Kazakhstan only. However, in both countries additional interventions and support for adherence will be offered before PrEP is discontinued due to adherence problems);
- decrease in kidney function below 60 mL/min (only in Kyrgyzstan).

At the same time, the national guidelines of Kazakhstan states that if a client is diagnosed with HIV during routine testing after the start of PrEP, he should be referred for additional tests to confirm the diagnosis in accordance with the national HIV testing algorithm. While waiting for the result of the confirmation test, the client can be offered one of 3 options:

1. continue taking PrEP;
2. add a third drug to the PrEP regimen for 28 days;
3. stop taking PrEP for 1-2 weeks.

In the national guidelines of Tajikistan and Ukraine, the only indication for discontinuing PrEP is the cessation of the factors fo substantial risk of HIV risk, while in Uzbekistan, creatinine clearance below 60 mL/min is also mentioned.

The timing for discontinuing PrEP is clearly defined in the national guidelines of Georgia, Kyrgyzstan, and Ukraine in accordance with WHO recommendations. In Tajikistan and Uzbekistan, national guidelines recommend continuing to PrEP for an additional 28 days after the last potential exposure to HIV, well beyond the WHO recommended 2 days for those who are eligible for ED-PrEP and 7 days for those who are not. Kazakhstan's national guidelines does not clearly indicate how to discontinue PrEP, but mentions that protection against HIV will decline after 7–10 days after stopping daily PrEP.

EVENT-DRIVEN PRE-EXPOSURE PROPHYLAXIS (ED-PREP)

According to WHO recommendations, all cisgender men, as well as trans and gender diverse people who were assigned male at birth, who have sexual exposure and are not taking exogenous estradiol-based hormones, are eligible for ED-PrEP (1). HBV infection is not a contraindication for ED-PrEP (1). The possibility of choosing ED-PrEP is indicated in six national guidelines. At the same time, the national guidelines of Armenia, Georgia, Kazakhstan and Tajikistan provide for the prescription of ED-PrEP only to MSM; while according to the national guidelines of Kyrgyzstan and Ukraine, ED-PrEP can be prescribed for all cisgender men, transgender women and non-binary people who are assigned male at birth, and who are not taking hormonal drugs for gender-affirming therapy.

The national guidelines of Armenia, Georgia, Kazakhstan, Kyrgyzstan and Ukraine clearly describe the exact schedule for using ED-PrEP in accordance with WHO recommendations. According to the algorithm for using ED-PrEP in the national guidelines of Tajikistan, ED-PrEP clients are encouraged to continue taking 1 tablet per day for 48 hours after taking the first two PrEP tablets, regardless of whether sexual activities continue or not. The recommended ED-PrEP regimen in all six countries is a fixed-dose combination of TDF 300 mg/FTC 200 mg. In Kyrgyzstan and Tajikistan, national guidelines also provide for an alternative ED-PrEP regimen using a fixed-dose combination of TDF 300 mg/300 mg 3TC. In all 6 countries, HBV infection is a contraindication for prescribing ED-PrEP.

SPECIAL SITUATIONS

Five of the seven countries discuss in their national guidelines special situations that may occur while taking PrEP. For example, the national guidelines of Ukraine mentions that PrEP can be taken regardless of food intake, and that the drugs do not result in any unwanted interactions with alcohol and other substances.

HORMONAL CONTRACEPTIVES

The guidelines of Tajikistan, Uzbekistan and Ukraine note that PrEP is safe and effective even when using hormonal contraceptives (1,11,12). In the remaining four countries, national guidelines do not mention the use of hormonal contraceptives while on PrEP.

PREGNANCY AND BREASTFEEDING

The national guidelines of four countries (Armenia, Tajikistan, Uzbekistan and Ukraine) address the safety and effectiveness of PrEP use during pregnancy and breastfeeding (1, 7, 10, 13). Kazakhstan mentions pregnancy and having an partner living with HIV as an indication for starting PrEP, but the guidelines does not discuss the safety or efficacy of PrEP in pregnant women. In the remaining countries, national guidelines do not discuss the use of PrEP during pregnancy and breastfeeding. At the same time, in Georgia and Kazakhstan, pregnancy tests are provided for women before the start of PrEP. In Kazakhstan, a pregnancy test is also carried out every 2-3 months after starting PrEP.

HEPATITIS B

Specific considerations regarding the preferred PrEP regimen for clients with HBV are discussed in the guidelines of three countries: Georgia, Tajikistan and Ukraine. All three countries suggest prescribing a PrEP regimen containing TDF if a client has HBV. In Georgia and Ukraine, further monitoring of an HBV-positive PrEP client is suggested after discontinuing PrEP containing TDF, as this may reactivate HBV and cause irreversible liver damage. The required testing and next steps for monitoring HBV in prospective and current PrEP clients are described in the most detail in the national guidelines of Georgia. HBV infection is a contraindication for prescribing ED-PrEP in all countries.

KIDNEY DISEASE

Since no renal toxicity is expected when DVR and CAB-LA are used as PrEP (1-3), they may be a good alternative regimen for clients whose test results have previously indicated at least a slight decrease in kidney function. However, PrEP using CAB-LA is mentioned in the guidelines of Kazakhstan and Armenia, while the use of DVR is mentioned in only one of the seven national guidelines (Armenia). In Kazakhstan, the national guidelines emphasizes that the use of CAB-LA injections «may be particularly suitable for patients with kidney disease and those who have difficulty adhering to oral PrEP».

INTEGRATION OF PREP WITH OTHER HEALTH CARE SERVICES

WHO CAN PRESCRIBE PREP?

The integration of PrEP services with existing health care services is not sufficiently discussed in any of the seven national guidelines. Most likely, in all seven countries it is assumed that only qualified infectious disease doctors who can prescribe ARV drugs can prescribe PrEP. For instance, the guidelines of Armenia mentions that only an infectious disease doctor with "experience in the use of ARV drugs" can prescribe PrEP. In Uzbekistan, the use of PrEP must be supervised by an infectious disease physician, or by a gynaecologist with experience in reproductive and sexual health and with experience in the use of ART, if possible as part of joint patient monitoring. Other national guidelines do not discuss who can prescribe PrEP and ED-PrEP.

The only exception is Georgia's national guidelines, which provides for facility-based and community-based PrEP services. The description of material and human resources at the community level mentions the need for resources for storing medicines (desirable), and an infectious disease specialist (desirable), which can be interpreted as allowing for PrEP to be prescribed at the community level by other medical specialists as well.

INTEGRATION OF PREP AND STI SERVICES

Although the national guidelines of Armenia, Georgia, Kazakhstan, Kyrgyzstan, Ukraine, and Uzbekistan mention the need for STI screening and testing before and during PrEP, the national guidelines often do not discuss where exactly clients will receive these services. This may be due to the fact that all countries have separate guidelines for the diagnosis and treatment of STIs, which discuss in more detail the delivery of services related to the prevention, diagnosis and treatment of STIs.

Still, it should be noted that the national guidelines of Kyrgyzstan mention that screening for STIs should be carried out by an employee of the medical institution prescribing PrEP. If a client has symptoms of an STI, they are referred to an STI specialist. It is also mentioned that the client may be referred to another organization for STI testing.

INTEGRATION OF PREP WITH OTHER SERVICES

The national guidelines of Georgia and Armenia discuss the need to provide additional services, depending on the needs of the PrEP client, such as substance abuse problems, depression, housing problems, other social problems and factors that may have a negative effect on the patient's adherence to PrEP. Both national guidelines recommend taking these issues into account, providing appropriate services, or referring clients to existing services.

MONITORING AND EVALUATION

Indicators for monitoring and evaluating the performance of PrEP programmes are described only in the national guidelines of Armenia, Tajikistan and Ukraine. In Armenia and Tajikistan, it is recommended to collect data on the number of people who received antiretroviral drugs for PrEP for the first time, disaggregated by sex, administrative division, key population, and vulnerable group. The recommended frequency for data collection is every 12 months.

In Ukraine, it is recommended to collect data on the number of people who started PrEP. The recommended frequency of data collection is every quarter, and cumulatively throughout the year.

Separately, the guidelines of Armenia mention the importance of recording side effects that occur in people taking PrEP, and recording all "failures" (infections that occurred while the client was on PrEP). The guidelines also propose to collect data on all those who refused to take PrEP, with a detailed description of their reasons for not participating in the programme.

RECOMMENDATIONS BY COUNTRY

ARMENIA

INDICATIONS AND CONTRAINDICATIONS FOR PRESCRIBING PREP

- Consider providing PrEP upon request to all individuals at substantial risk of HIV infection, regardless of the degree of risk. Individuals who request PrEP are likely to be at substantial risk of HIV infection (1).

DISCONTINUING PREP

- Consider aligning the timing for discontinuing PrEP with WHO recommendations, namely: reducing the timing for discontinuing daily PrEP from 28 to 7 days after the last risk of HIV exposure. Also indicate that ED-PrEP can be discontinued 48 hours after the last potential HIV exposure.

SIMPLIFIED MODELS FOR PRESCRIBING PREP

- Consider amending provisions regarding the centralization of the PrEP programme in the country, and allow PrEP to be prescribed in all major administrative centers.

GEORGIA

INDICATIONS AND CONTRAINDICATIONS FOR PRESCRIBING PREP

- Consider providing PrEP upon request to all individuals at substantial risk of HIV infection, regardless of the degree of risk. Individuals who request PrEP are likely to be at substantial risk of HIV infection (1);

- Consider listing all contraindications for prescribing PrEP and ED-PrEP in a specific section of the national guidelines.

NECESSARY PROCEDURES FOR INITIATING AND CONTINUING PREP

- Consider not requiring pregnancy testing for women before and after initiating PrEP, given that DVR and PrEP regimens containing TDF are safe for use during pregnancy and breastfeeding (1, 2). Retain this option for when clients request it;
- Consider eliminating additional testing requirements for initiating and continuing PrEP (complete blood panel, ALT, calcium);
- Consider conducting a full HBV serology test only once at the start of PrEP, and then only offer HbsAg testing to unvaccinated clients.

USE OF HORMONAL CONTRACEPTIVES, PREGNANCY, AND BREASTFEEDING

- Supplement national guidelines with information on the safety and effectiveness of using PrEP with hormonal contraceptives;
- Clarify that pregnant and breastfeeding women are eligible to receive PrEP because it is safe to use during pregnancy and breastfeeding.

KYRGYZSTAN

USE OF HORMONAL CONTRACEPTIVES, PREGNANCY, AND BREASTFEEDING

- Supplement national guidelines with information on the safety and effectiveness of using PrEP with hormonal contraceptives;
- Clarify that pregnant and breastfeeding women are eligible to receive PrEP because it is safe to use during pregnancy and breastfeeding.

INTEGRATION OF PREP WITH OTHER MEDICAL AND SOCIAL SERVICES

- Consider extending the existing vaccination policy for PLHIV to PrEP users (HAV and HPV vaccinations).

KAZAKHSTAN

NECESSARY PROCEDURES FOR INITIATING AND CONTINUING PREP

- Consider offering HCV testing before or within the first three months after starting PrEP, then routine HCV testing should be offered every 12 months for key populations at increased risk of infection;
- Consider not requiring pregnancy testing for women before and after initiating PrEP, given that DVR and PrEP regimens containing TDF are safe for use during pregnancy and breastfeeding (1, 2). Retain this option for when clients request it;
- Consider listing all contraindications for prescribing PrEP and ED-PrEP in a specific section of national guidelines.

DISCONTINUING PREP

- Consider making the national guidelines more explicit about how to discontinue PrEP for those who are not eligible for ED-PrEP, starting 7 days before the first potential exposure and stopping 7 days after the last potential exposure.

USE OF HORMONAL CONTRACEPTIVES, PREGNANCY, AND BREASTFEEDING

- Supplement national guidelines with information on the effectiveness and safety of using PrEP with hormonal contraceptives;
- Clarify that breastfeeding women are eligible to receive PrEP because it is safe to use during pregnancy and breastfeeding.

INTEGRATION OF PREP WITH OTHER MEDICAL AND SOCIAL SERVICES

- Consider offering HBV vaccination services to clients who test negative for HBsAg;
- Consider extending the existing vaccination policy for PLHIV to PrEP users (HAV and HPV vaccinations).

UKRAINE

PREP DRUGS

- Specify the exact dosing of drugs used for PrEP and ED-PrEP in national guidelines. Indicating exact doses can be especially helpful in settings where PrEP or ED-PrEP is administered by someone who is not an infectious disease specialist;
- Clarify that the time needed for protection for people who are not eligible for ED-PrEP is 7 days before the first potential exposure;
- Clarify the suggested STI testing procedures and their frequency.

TAJIKISTAN

PREP DRUGS

- Specify the exact dosing of drugs used for PrEP and ED-PrEP in national guidelines. Indicating exact doses can be especially helpful in settings where PrEP or ED-PrEP is administered by someone who is not an infectious disease specialist.

NECESSARY PROCEDURES FOR INITIATING AND CONTINUING PREP

- Consider testing for HCV before or within the first three months after starting PrEP, then routine HCV testing should be offered every 12 months for key populations at increased risk of infection;
- Consider removing requirements to test for HbsAg prior to starting PrEP;
- Consider testing for syphilis every 3-6 months. Consider introducing testing for chlamydia and gonorrhoea if resources are available.

DISCONTINUING PREP

- Consider aligning the timing for discontinuing PrEP with WHO recommendations, namely: reducing the timing for discontinuing daily PrEP from 28 to 7 days after the last risk of HIV infection for people who are not eligible for ED-PrEP;
- Clarify that in a serodiscordant couple, if the partner living with HIV does not have a detectable viral load, there is no risk of HIV transmission and that the HIV-negative partner can stop taking PrEP;
- Clarify that it is not necessary to perform a complete blood panel, urine analysis, biochemical blood tests (glucose, bilirubin and its fractions, ALT, AST, alkaline phosphatase, urea, creatinine), or ECG in order to prescribe PrEP, as these tests are not required to start or continue PrEP.

UZBEKISTAN

INDICATIONS AND CONTRAINDICATIONS FOR PRESCRIBING PREP

- Consider providing PrEP, also upon request, to all individuals at substantial risk of HIV infection. Individuals who request PrEP are most likely to be at substantial risk of HIV infection (1);

NECESSARY PROCEDURES FOR INITIATING AND CONTINUING PREP

- Consider offering testing for HCV every 12 months to individuals at increased risk for this infection;
- Consider removing the requirement to test for HbsAg prior to starting PrEP;
- Consider allowing the prescription of PrEP without waiting for all test results, apart from HIV.

DISCONTINUING PREP

- Consider aligning the timing for discontinuing PrEP with WHO recommendations, namely: reducing the timing for discontinuing PrEP from 28 to 7 days after the last risk of HIV infection for those not eligible for ED-PrEP.

СДКП

- Introduce ED-PrEP as an additional option for all cisgender men, transgender women and non-binary people who are assigned male at birth and not taking exogenous estradiol-based hormones.

INTEGRATION OF PREP WITH OTHER MEDICAL AND SOCIAL SERVICES

- Consider introducing testing for chlamydia and gonorrhoea if resources are available.

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ANNEX 1. COMPARATIVE ANALYSIS OF NATIONAL PREP PROTOCOLS

Table 1. Core indicators — key features and possible barriers to access

	ARM	GEO	KAZ	KGZ	TJK	UKR	UZB
PrEP available to key populations[3]	+	+	+	+	+	+	–
PrEP available to all individuals at substantial risk of HIV upon request	–	–	+	+	+	+	–
All individuals assigned male at birth who have sexual exposure and are not taking exogenous estradiol-based hormones are eligible for event-driven PrEP	–	–	–	+	–	+	–
Persons with HBV infection are eligible for event-driven PrEP	–	–	–	–	–	N/S	–
Pregnant and breastfeeding women are eligible to receive PrEP	+	N/S	~[4]	N/S	+	+	+
Community-based PrEP delivery is possible	–	+	–	–	–	–	–
HIV testing is required for PrEP start	+	+	+	+	+	+	+
Regular HIV testing is required for PrEP continuation	+	+	+	+	+	+	+
Creatinine clearance testing is not required for PrEP start	–	–	+	+	+	+	–
Creatinine clearance testing is not required for PrEP continuation	–	–	+	+	+	+	–
Creatinine clearance testing is offered based on age group and comorbidities	~[5]	–	~[c]	+	–	~[c]	–
HBsAg testing is not required for PrEP start	–	–	+	+	+	+	–

[3] Men who have sex with men, sex workers, people who inject drugs and transgender people.
[4] Not specified for breastfeeding women.
[5] Only for follow-up.

Table 2. Secondary indicators — additional recommended services and features

	ARM	GEO	KAZ	KGZ	TJK	UKR	UZB
HBsAg testing is offered at PrEP start	+	+	+	+	+	+	+
HBV vaccination is offered	+	+	–	+	+	+	+
HCV Ab testing is offered at PrEP start	+	+	+	+	–	+	+
HCV Ab testing is offered at follow-up	+	+	+	+	–	+	+
T. pallidum Ab testing is offered at PrEP start	+	+	+	+	–	+[6]	+
T. pallidum Ab testing is offered at follow-up	+	+	+	+	–	+[d]	+
C. trachomatis and N. gonorrhoeae NAAT testing is offered at PrEP start	+	+	+	+	–	+[d]	–
C. trachomatis and N. gonorrhoeae NAAT testing is offered at follow-up	+	+	+	+	–	+[d]	–
STI syndromic management	N/S	+	+	–	–	+	N/S
Referral for STIs treatment	N/S	+	N/S	+	–	+	N/S
HAV vaccination is offered	–	–	–	–	–	–	–
HPV vaccination is offered	–	–	–	–	–	–	–
Counselling is offered at PrEP start	+	+	+	+	+	+	+
Counselling is offered at follow-up	+	+	+	+	+	+	+
Pregnancy tests are offered	+	+	+	+	–	–	+
Involvement of peer workers	–	+	–	–	+	–	–
Use of telehealth solutions	–	–	–	–	–	–	–
Use of RDTs	–	+	N/S	+	+	–	–
Use of HIV self-test	–	–	–	–	–	+	–
Referral available for drug use and chemsex issues	N/S	N/S	+	N/S	N/S	+	–
Referral available for mental health issues	N/S	–	–	–	–	+	–
Referral available for reproductive health issues	–	–	–	+	–	+	–
Specific indications for CAB-LA as PrEP	+	–	+	–	–	–	–
Specific indications for DPV vaginal ring as PrEP	+	–	–	–	–	–	–

Table 3. Legend

+	Item in the national PrEP protocol aligned to WHO recommendations
~	Item in the national PrEP protocol partially aligned to WHO recommendations
–	Item in the national PrEP protocol not aligned to WHO recommendations
N/S	Item not specified in the national PrEP protocol