

Study Report

Assessing Barriers for HIV/AIDS Treatment Coverage Expansion

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Introduction

The Joint United Nations Program on HIV/AIDS (UNAIDS) after analyzing the findings of many studies has recognized that the immediate administration of ARV therapy helps prevent millions of deaths and infections with the human immunodeficiency virus, and, therefore, lay the foundation for the victory over the epidemic. So, years of monitoring the dynamics of the epidemic under the impact of ARV therapy have caused the World Health Organization (WHO) to revise in 2015 the previous guidelines and to recommend that the antiretroviral therapy be administered to all HIV-positive patients as early as possible (from the date of the diagnosis). Such recommendations suggest an increase in the provision of ARV therapy, which poses for the healthcare community some complex and important tasks:

- to timely identify the patient's HIV infection
- to provide an incentive for treatment immediately after the diagnosis
- to ensure compliance to ARV therapy in patients.

However, the issue of compliance to the antiretroviral therapy around the world is still a serious problem. According to the UNAIDS, in 2009, one out of every five people (18%) who initiated the antiretroviral therapy in low- and middle-income countries discontinued the treatment after a year. Because of the gap in treatment and failed compliance, the resistance of the virus to the medicines administered under the regimen develops, and the therapy efficacy decreases. The elimination of the non-compliance consequences requires additional financial resources, time costs, and mobilization of efforts.

The maximum and persistent suppression of the human immunodeficiency virus (decrease in the virus RNA level), the restoration and preservation of the immune system functions cause preservation/improvement of the patient's quality of life and the reduction in mortality rate due to the disease. However, achievement of these objectives requires compliance with certain conditions:

- reasonable choice of a medical regimen considering the patient's lifestyle, medical history data (past diseases, information about the medicines earlier taken by the patient);
- choice of the initial regimen of antiretroviral therapy, considering the possibility of using a maximum number of options (combinations) of ARVs in the future in case of treatment failure (no cross-resistance);
- determination of drug resistance for the design of an optimal treatment regimen;
- the patients' maximum compliance to the treatment.

Taking ARVs does not fully destroy the virus in the patient's body. The medicines block viral enzymes, responsible for the introduction, replication, and further spread of the virus in the body. With the required concentration, they "preserve" the virus in the genome of the HIV-sensitive cells, so blocking further reproduction of the virus, its release into the blood, and destruction of new cells. By maintaining the required concentration of ARVs in the blood throughout the life, the patient can for many years maintain a stable medical status, characterized by:

- undetectable viral load, which causes his/her higher infectious safety for the others;
- content of intact CD4-lymphocytes within the norm which entails an adequate immune response of the body to any foreign and mutant invaders.

It is possible to ensure an optimal level of ARVs in the blood if the patient:

- uses an individually selected antiretroviral therapy regimen (ARVT),
- takes the medicines administered by the physician at the required intervals and in the prescribed dosage,
- complies with the diet recommended under the therapy regimen,
- takes into account the physician's recommendations on the compatibility of ARVs and other medicines, food additives, etc.,

- undergoes the laboratory control for viral load and immunological indicators with the recommended intervals,
- is aware of the possible side effects and the ways to overcome such effects and severity of consequences (for example, the actions in case of vomiting when taking the medicine to ensure the intake of a daily dose), etc.

Meeting all the required conditions of an effective treatment with maintenance of the health status requires from the patient certain efforts, discipline, and self-organization. The transition from denial of the need for treatment to consent to the therapy and the adaptation period for the medicines taking initiation are rather complex in terms of physical manifestations, emotional and psychological experiences. In this case, the success of the treatment is possible only subject to absolute compliance to ARVT and follow-up.

The patient's behavior in terms of compliance to treatment is influenced by effective cooperation between the patient and the healthcare professionals, confidence in the need for treatment and its positive long-term results, a steady motivation for the uninterrupted medicines administration.

When considering the aspects of the patients' compliance to treatment, it is worth mentioning such an important issue as the compliance of the healthcare professionals to the recommended approaches to dealing with the patients and the principles of treatment. The efforts aimed to create and maintain compliance to ARV therapy in patients, as well as any efforts aimed at behavior change, is a labor-intensive and energy-consuming process which requires from a healthcare professional competence, good communication skills, and a high level of tolerance.

The long-term behavior change and sustainable motivation for treatment require from the patient to be guided by his own decision, without coercion and intrusion of someone else's opinion.

Considering the significance and urgency of the above problem, it is required to study the issues of establishing compliance in HIV-positive patients to antiretroviral treatment and clinical follow-up considering their social, psychological, and other characteristics.

Rationale

In the Kyrgyz Republic (KR), as of January 01, 2017, 7,117 HIV infections were recorded, including 3,237 people who inject drugs (PWID). The estimated number of PLHIV in 2015 was 8,800 persons. ART was administered to 3,609 patients, of whom 2,668 PLHIV actually take ARVs.

In the Kyrgyz Republic, ARVT for PLHIV has been provided since March, 2005. The physicians who carry out clinical follow-up of the PLHIV, on a quarterly basis assess the PLHIV's compliance to ARV therapy. Currently, there is no data on the compliance assessment quality, but in accordance with the data of the e-monitoring system, the level of compliance across the country reaches 84.8%, with the lowest values in Talas (50%) and Chuya (59%) regions in 2015 (Table 1). In 2016, the same picture was observed across the country — 83.7%, with the highest value in the Issyk-Kul region, 100%.

Table 1. The level of compliance to ARV therapy in KR, the system of e-monitoring over HIV infections.

Region	Compliance	
	2015	2016
Naryn Region	100,0%	86,0%
Osh city	98,0%	89,0%
Osh region	97,0%	89,8%
Batken region	91,0%	84,3%
Bishkek	86,8%	80,9%
Jalal-Abad region	79,6%	93,5%
Issyk-Kul region	64,3%	100,0%
Chuya region	59,0%	70,5%
Talas region	50,0%	85,7%
KR	84,8%	83,7%

*source: reporting form 4 zdrav, AIDS Regional Center, the Ministry of Healthcare of the Kyrgyz Republic, 2015- 2016

It should be noted that the assessment of the compliance to treatment in the Kyrgyz Republic is based on the calculation of tablets. However, the draft findings of the recent studies on compliance to treatment in the Kyrgyz Republic raise doubts about the reliability of the above method of compliance determining. In this context, special attention should be paid to the PLHIV/PWID who occupy more than 50% in the structure of the people living with HIV and, due to their lifestyle characteristics, may least of all adhere to HIV treatment.

WHO notes that in the countries where the treatment coverage exceeded 60% of PLHIV, the dynamics of the epidemic has slowed down significantly. However, low compliance to antiretroviral treatment among the PLHIV poses a serious problem in the Kyrgyz Republic at the current stage of the epidemic's development.

Considering the importance and urgency of the above problem, the Partner Network Association has carried out a study on the barriers and problems preventing establishing compliance to antiretroviral treatment and clinical follow-up in HIV-positive PWID, taking into account their social, psychological, and other specific characteristics.

2. The Study goal:

2.1. Goals:

Studying the problems associated with PLHIV entry to ARV therapy and low compliance to ARV therapy among the PLHIV under treatment, in order to develop further recommendations for their elimination.

2.2. Objectives:

1. To study the factors being the barriers against initiating ARV therapy.
2. To study the factors influencing the compliance to the antiretroviral therapy in PLHIV, both associated and not associated with the underlying disease (demographic and social factors, the factors of injecting and sexual behavior, reasons for changing the regimen of ARV therapy, psychological specific features of PLHIV, etc.)
3. Development of recommendations and tools aimed to create conditions for expanded coverage with ARV and increase in compliance to treatment among PWID/PLHIV.
4. To promote the implementation of recommendations and tools aimed to expand coverage and increase PWID/PLHIV's compliance to HIV treatment at the national level.

3. Design of the Study:

The Partner Network Association has conducted the applied study according to the calendar schedule presented in Annex 1, using a combination of the qualitative and quantitative study methods, including:

- review of respective documents (please insert);
- in-depth interviews with the key stakeholders;
- in-depth interviews with the healthcare professionals;
- survey of PWID/PLHIV;
- in-depth interviews with the NGO representatives.

Such an integrated approach was used to collect the comparable data from various sources in order to obtain an exhaustive picture of the issues included into the Study for the sake of further development of a set of measures aimed to improve the quality and accessibility of the services in the sphere of the HIV control and prevention.

3.1. Study territory

For the assessment, the sites with the highest prevalence of the PWID/PLHIV group, registered with the healthcare organizations and administered with ARV therapy have been selected, please see Table 2.

Table 2. The number of the PLHIV and PLHIV-PWID at the pilot sites

No	Site studied	No of PLHIV as of 01.01.2017	of them PLHIV/PWID	PLHIV/PWID on ARVT
1	City AIDS Control & Prevention Center	1,055	560	192
2	Osh Regional AIDS Control & Prevention Center	2,272	937	107
3	Family Medical Center, Ysyk-Atin region	394	245	90
4	Family Medical Center, Zhaiyl region	367	249	43
5	Family Medical Center, Sokuluk region	550	384	59
		4,639	2,375	491

3.2. Assessment procedures

1. The documents analysis. The Study team has reviewed all available and related to the Study subject matter documents, protocols, reports, and standard operating procedures for HIV treatment and prevention at all levels, including:

- ✓ the national policy;
- ✓ the national clinical protocols;
- ✓ guidelines and reports;
- ✓ reports on official and unofficial assessments in the field of HIV treatment earlier conducted by local and international key persons;
- ✓ monitoring reports, such as data collection tools, registers, registration forms for HIV diagnostics and treatment services, data distribution reports, official statistical reports of the Ministry of Healthcare.
- ✓ electronic databases with data collection tools (electronic monitoring of HIV infections);
- ✓ ARVs release registers;

The purpose of review of the documents/databases was obtaining the information about the following aspects: the policy and legal framework, including their compliance with the national HIV policies and international recommendations (WHO, 2016); geographical availability of HIV services; information about the prevalence of HIV infection and the level of coverage with preventive programs; the existing problems and areas for improvement.

The analysis of the data of the HIV electronic monitoring system (EM system) allowed to study some issues related to timely linkage to care (regular medical check-ups) and initiation of ARV therapy, changes in the laboratory values due to ARVT, and so on.

2. In-depth interviews with the key stakeholders. The key stakeholders who have certain relevance to HIV treatment were interviewed in order to collect reliable information about the structure and components of the HIV services delivery system, the legislative environment, funding, opportunities for provision of more integrated services etc.

3. In-depth interviews with the healthcare professionals. The healthcare professionals who perform a wide range of roles and responsibilities in the HIV treatment and care system were interviewed in order to collect more detailed information about the PLHIV services delivery processes, HIV education

(including stigma and discrimination issues, compliance to treatment), monitoring, social support services, referral to other services, and existing difficulties.

4. PLHIV survey. The PLHIV linked to care were interviewed in order to collect information about their awareness of HIV infection, stigma and discrimination, availability and quality of services, the cost of services, access to ARV therapy, compliance to treatment and other factors which affect availability and quality of the services associated with HIV infection, as well as to explore the possible needs for additional services. These data will be used to assess the acceptability and satisfaction of the services being provided.

5. In-depth interviews with the representatives of the NGOs dealing with HIV infection. The NGOs representatives were interviewed in order to obtain more profound understanding of the problems faced by the PLHIV which affect ARVT coverage and compliance to treatment, and to explore possible needs for additional services.

3.3. Assessment objects

1. The documents analysis: the analysis includes the data from the regular medical check-up register of the HIV e-monitoring system.

2. In-depth interviews with the key stakeholders. The Study team has interviewed the key persons related to the problem of HIV infection. The key interviewed persons include the employees of the Ministry of Healthcare, the members of the Country's Coordination Committee, the Republic's AIDS Center, the Department of diseases prevention and the State sanitary and epidemiological surveillance, as well as the NGOs dealing with PLHIV, the UNDP/GFATM Project Implementation Unit, and other projects and programs in the sphere of HIV infection in the country.

3. In-depth interviews with the healthcare professionals.

Inclusion criteria:

- Physicians of the follow-up care departments of the AIDS Regional Centers, the City AIDS Control Center, and the Regional AIDS Control Centers;
- Primary healthcare physicians, namely at the level of the Family Medicine Center (FMC) (infectious disease doctor, family doctor) involved in the provision of services to PLHIV;
- Visiting nurses;
- Persons who gave a verbal informed consent for participation in the survey.

4. PLHIV survey. PLHIV were recruited based on the below criteria, compliance with which was determined by the researchers according to the medical records (registers in specialized institutions and offices). The fact of receiving ARV therapy was not a criterion for inclusion to or exclusion from the Study. PLHIV in correctional facilities of the Kyrgyz Republic and pregnant women/PLHIV were excluded from the Study, since their level of compliance significantly differs from the others (another medicine release system, administration control, specific features of the condition of pregnant women, etc.)

Inclusion criteria:

- The age of at least 18 years old.
- PLHIV linked to care in the medical establishments of the selected populated localities.
- Verbal informed consent to participate in the survey was given.

The exclusion criteria:

- The age of less than 18 years old.
- PLHIV in correctional facilities of the Kyrgyz Republic.
- Pregnant/PLHIV.
- Physical and mental limitations of the respondents which prevent them from participation in the study (failure to understand the interviewer's questions and inability to respond to them, inability to understand the instructions during the period of participation in the Study and to adequately respond to them).

- Refusal to participate in the Study.

5. Survey among the NGO representatives, dealing with PLHIV in the selected populated localities. The Study team has determined all NGOs dealing with PLHIV in the selected populated localities in order to select their representatives.

The inclusion criteria:

- The age of at least 18 years old.
- An NGO employee dealing with PLHIV in the selected populated localities.
- Verbal informed consent to participate in the survey was given.

The exclusion criteria:

- The age of less than 18 years old.
- Physical and mental limitations of the respondents which prevent them from participation in the study (failure to understand the interviewer's questions and inability to respond to them, inability to understand the instructions during the period of participation in the study and to adequately respond to them).
- Refusal to participate in the Study.

3.4. Sample size

1. The documents analysis: includes all data from the regular medical check-up register of the e-monitoring system for each populated locality within the Study.
2. In-depth interviews with the key stakeholders. Six key stakeholders were interviewed.
3. In-depth interviews with the healthcare professionals. 15 physicians and 6 visiting nurses were interviewed in five selected establishments.
4. Survey among PLHIV. Sample size was determined based on Tables 1 and 2 below. Sample size shown in the table provides a confidence interval of 95% for each item with an error of 7.6-8.99%, which is applicable separately to each establishment.

Table 3. Table for determining sample size.

The No of registered PLHIV	Sample size required to provide a confidence interval of 95%	The length of the 95% simple asymptotic confidence interval with a 50%-point estimate (with a finite population correction (FPC))	The No of registered PLHIV	Sample size required to provide a confidence interval of 95%	The length of the 95% simple asymptotic confidence interval with a 50%-point estimate (cFPC)
0-49	38	~ ± 7.6%	200-249	94	~ ± 8.0%
50-79	48	~ ± 8.9%	250-299	101	~ ± 7.9%
80-99	61	~ ± 7.8%	300-349	106	~ ± 7.9%
100-139	73	~ ± 7.9%	350-749	127	~ ± 7.9%
140-179	82	~ ± 8.0%	750-4.999	146	~ ± 8.0%
180-199	86	~ ± 8.0%	5.000 or more	150	~ ± 8.0%

Based on the national statistic data, as of 01.06.2017 743 PWID/PLHIV were registered with the medical establishments. The assumed sample size was 321 persons at all pilot sites and it allowed to analyze key findings with 95% confidence interval, 5% error and a design effect of 2.0. We did not expect significant data losses of more than 5%.

Table 4. Sample size in the sites studied

	Site studied	No of PLHIV as of 01.01.2017	Of them, PLHIV/PWID	PLHIV/PWID on ARVT	Sample size
1	City AIDS Control &	1,055	560	192	90

	Prevention Center				
2	Osh Regional AIDS Control & Prevention Center	2,272	937	107	77
3	Family Medical Center, Ysyk-Atin region	394	245	90	64
4	Family Medical Center, Zhaiyl region	367	249	43	40
5	Family Medical Center, Sokuluk region	550	384	59	50
		4,639	2,375	491	321

5. Survey among the NGO representatives, dealing with PLHIV. Ten NGO representatives, dealing with PLHIV were interviewed in the selected populated locality.

3.5. Data collection tools

1. The documents analysis. The checklist of the documents for analysis (Annex 2) was issued and used in order to clarify the availability of the documents and to obtain initial baseline information about the work associated with HIV treatment and prevention services at all levels.

Downloading the data from the medical regular check-ups register in Excel format allowed to analyze the required data.

2. In-depth interviews with the key stakeholders. In the interviews with the key stakeholders, an interviewing guide was used (Annex 3) in order to collect quality information. One interview took about 40 minutes.

3. In-depth interviews with the healthcare professionals. A guide on semi-structured interviews was used to interview the healthcare professionals (Annex 4). Each interview took about 60-80 minutes.

4. Survey among PLHIV. The Study team has interviewed the PLHIV, who participated in the Study, using structured questionnaires (Annex 5). Filling out the questionnaire took approximately 25-30 minutes.

5. Survey among the NGO representatives, dealing with PLHIV. A guide on semi-structured interviews was used to interview the NGO employees dealing with PLHIV (Annex 6).

3.6. Recruitment

1. The documents analysis. No

2. In-depth interviews with the key stakeholders. The Study team, after an advance invitation and agreeing on the date and time of the meeting via phone or e-mail, has interviewed the key persons.

3. In-depth interviews with the healthcare professionals. The healthcare professionals of the sites included into the Study were interviewed after an advance invitation and agreeing on the date and time of the meeting via phone or e-mail.

4. Survey among PLHIV. The researchers have compiled a list of PLHIV registered with each site for regular medical check-ups. An estimated number of the PLHIV invited by the physician to participate in the Study by phone using a set text was randomly selected from the list. All respondents who gave an informed consent to participate in the Study were advised of the tasks and objectives of the Study and were interviewed in the premises allocated by the directors of the Family Medicine Center or NGO.

5. In-depth interviews with the NGO representatives, dealing with PLHIV. The Study team, after an advance invitation and agreeing on the date and time of the meeting via phone or e-mail, has interviewed the employees of the selected NGOs.

4. Ethical considerations

4.1. Ethical Committee

This Study was conducted with the approval of the Ethics Committee of the Ministry of Healthcare of the Kyrgyz Republic.

4.2. Informed consent

Each informed consent form specified the objective of the Study, the risks and benefits of participating in the interview, alternative procedures, as well as the information about confidentiality and voluntary nature of participation. All respondents had the opportunity to ask clarifying questions. A copy of the form was kept by the respondents. The originals of the signed forms will be delivered to the Customer for further storage for three years. All groups of respondents were interviewed after receiving an informed consent:

1. Key stakeholders — the informed consent form as per Annex 7 was used.
2. In-depth interviews with the healthcare professionals — the informed consent form as per Annex 8 was used.
3. PLHIV survey by the employees — the informed consent form as per Annex 9 was used.
4. In-depth interviews with the NGO representatives, dealing with PLHIV – the informed consent form as per Annex 10 was used.

4.3. Benefits

The respondents from PLHIV who wished to participate in the survey received a remuneration of 200 Soms, an equivalent of 3 US dollars. Such a remuneration complies with the generally accepted compensation standards offered in similar studies, and it usually contributes to increasing the participants' motivation for interviewing. For key stakeholders, healthcare professionals, and NGO employees no remuneration was provided.

4.4. Confidentiality of data

Participation in the Study was voluntary. All its participants received an informed consent they could withdraw at any time. Possible risks for the participants included a violation of confidentiality and a slight psychological discomfort, which could be caused by the sensitive nature of some interview questions.

The personal data of the respondents were recorded neither in the questionnaires nor in the Study report. Each respondent from PLHIV was assigned a unique identification code (UIC). The UIC consists of the first two letters of the respondent's mother's name, the first two letters of his/her father's name, a code indicating the gender (1 — male, 2 — female), and the last two digits of the year of birth. The findings of all interviews, surveys, and discussions are presented in a summarized form.

All forms and data related to the Study will be stored under double locks. Access to the Study information will be provided in advance only to the authorized persons.

4.5. Personal data protection

Protection of the personal data and confidentiality was ensured at all stages of the Study, the data analysis and distribution. The interviews were conducted in the physicians' offices with restricted access for everybody except for the persons directly involved in the assessment. The personal data will not be used; only summarized information about all participants is presented in the reports. All forms of consent and the data obtained during the interviews with the respondents will be kept locked up in the Contractor's office. The aggregated data was used in the analysis and reports. Access to the answers to questions and records made during the interview was provided only for the members of the Study team. All data in electronic form will be stored in a computer protected with a password accessible only by the members of the Study team. All investigators involved in the assessment have signed confidentiality agreements (Annex 1).

4.6. Possible risks

Participation in the Study usually involves a risk of breach of confidentiality, also in cases when a person can be seen at the interview site, but every site has taken the required measures in order to minimize

such a risk (an interview in private environment, in the absence of unauthorized persons). Measures have also been taken to ensure respect for the personality and the dignity of everyone involved in the Study; the employees were advised of the need to maintain confidentiality and avoid stigmatization. All information was analyzed and presented in reports in a summarized form. The answers in the final report are not associated with the names or belonging to any category.

4.7. Adverse events and protocol deviations

All adverse events identified as “any unforeseen problems posing a threat to the persons surveyed and other persons” had to be reported to the supervisory Ethics Committee within two business days of their occurrence.

Protocol deviations not classified as adverse events had to be reported to the supervisory Ethics Committee within ten business days of their occurrence.

During the Study, no adverse events or protocol deviations were observed.

5. Data handling

The Contractor shall bear all liability for the data handling, including development, implementation, and support of the electronic data systems of the Study, development and implementation of a complete data management plan.

5.1. Data collection and entry

The survey data were transferred from paper forms into a database in EPI-INFO 3.5.4 program developed by the Centers for Disease Control (CDC).

5.2. Data storage and archiving

All collected data will be stored in a database on a password-protected computer in the Contractor's office. The Contractor shall be liable for ensuring the operation of the computer. The computer is physically protected from the environmental impact, network threats, and provided with uninterrupted power supply. The database will be backed up. After the data scrubbing and processing, their final set will be stored, maintained, and archived on the Researcher's computer for five years; afterwards, all data will be deleted.

5.3. Data accuracy

In order to minimize possible errors, the data collection tool for the PLHIV survey was supplemented with the validation tools, including restrictions by the type of the data to be entered, predefined values (code sets) for categorical data, range constraints for numerical data, and logical control. In order to sift non-relevant data, as well as to ensure proper documentation of the survey, skips were used.

Before the start of the Study, the interviewers were trained in the content of the data collection tools and the use of the tools for interviewing. The data collection process was supervised.

5.4. Data scrubbing and processing

The data scrubbing included such processes as the data verification for duplication and repeated survey, for errors in decoding and measuring, for the internal sequence, for observing the range, for invalid values and outlying values.

6. Data analysis

The information about all the issues studied was collected from different sources using a combination of methods. The information collected was triangulated in order to assess and compare the availability, coverage, quality, possible outcome/impact of the HIV treatment services.

The data obtained from the interviews with the key informants, healthcare professionals, and NGO employees were grouped according to the main regularities through substantial and thematic analysis. Within the thematic analysis, the data were grouped into topics appeared during the interview.

Descriptive statistics were prepared, and a stratified analysis was carried out across the entire sample of the PLHIV/PWID respondents (by the types of the institutions providing ARV therapy services).

The data obtained from the PLHIV/PWID survey was used to triangulate the interviews with the key individuals, healthcare professionals, and NGO representatives. Analysis of the statistical data has been carried out in EPI-INFO 3.5.4. program.

The analysis of the data of the system of e-monitoring over HIV infections included clinical and laboratory data.

7. Data distribution and amendments planning

The Study team will prepare a complete written summary report. The findings communication process will include discussion of the findings and recommendations with the national and international stakeholders involved in HIV prevention activities in the Kyrgyz Republic, as well as presentations at national and international conferences, and publications in peer reviewed scientific journals.

The Study team will present the report data to all entities concerned in the Kyrgyz Republic. In order to further discuss the findings and recommendations following the assessment within this applied Study, the Partner Network Association will hold a national round table to be attended by the representatives of governmental and non-governmental organizations involved in implementing HIV prevention activities.

During this meeting, the partners will develop a comprehensive plan for improving the quality of treatment, care, and support services for PWID/PLHIV, which will describe the specific responsibilities of various stakeholders. Afterwards, this plan will be submitted to the Ministry of Healthcare, as well as to the GFATM and PEPFAR for funding. The implementation of the recommendations will be monitored and regularly discussed at the respective meetings of the partners and the meetings of the Country Coordinating Mechanism for proper consolidation of the findings. The selected sites, which most of all need support, will be included into the technical assistance programs funded by PEPFAR.

Furthermore, a work group will be established under the Ministry of Healthcare with the aim to develop the Regulation determining the mechanisms for ensuring compliance to ARVT among PWID/PLHIV, including expanding the ARVT coverage of PWID/PLHIV.

8. Study findings

Legislation

The legislation and policies governing access to treatment and support for compliance have a direct impact on establishing compliance to ARV treatment. For example, the barriers associated with the possibility of receiving ARVs, depending on the presence of a "propiska", i.e. a person's registration at a particular place of residence.

Ensuring the availability of HIV treatment in the Kyrgyz Republic is regulated by some legal acts. The basic document is the Law on HIV/AIDS in the Kyrgyz Republic, which guarantees access to all types of healthcare and medicines for people living with HIV/AIDS in healthcare institutions free of charge and on preferential terms in accordance with the State Healthcare Guarantees Program (SHGP). The State Healthcare Guarantees Program ensures the exercise of the rights of the Kyrgyz Republic nationals to

receive healthcare in healthcare institutions regardless of the form of incorporation, which participate in this program. In accordance with this program, people living with HIV are included into the List of the residents' categories eligible for free healthcare under the State Healthcare Guarantees Program across all types of medical care provided for in the State Healthcare Guarantees Program, including antiretroviral therapy and treatment of opportunistic infections.

Along with that, the measures to overcome the HIV epidemic have been included into the national healthcare programs. For example, the Den Sooluk ("Health") National Health Reform Program for 2012-2016, defines HIV as one of the key priorities. State programs aimed at overcoming the HIV epidemic are being implemented on an ongoing basis, which key areas are ensuring easy access to treatment. For example, the HIV Epidemic Control Government Program for 2017-2021 provides as one of its underlying principles to "treat all people living with HIV", and the strategic areas are based on the universal coverage with HIV treatment of everybody who needs it.

Strategic area 1.

Item 1.3. Provision of PLHIV treatment, care, and support services in accordance with the national protocols. Antiretroviral therapy will have been provided to at least 90% of the identified men, women, and children living with HIV by 2021. It will be made available in the correctional facilities and healthcare institutions in the civil sector.

Strategic area 2.

Item 2.3. Uninterrupted supplies of medicines, reagents, and equipment for diagnostics and treatment of HIV infection, as well as opportunistic infections will be ensured; algorithms of storage, transportation, and distribution of medicines will be improved.

The above legal acts provide for the measures that should increase PLHIV's compliance to HIV treatment. For example, PLHIV will be offered free treatment of opportunistic infections and their prevention. With the physician's referral, PLHIV will obtain free of charge most of the general tests, including basic laboratory and diagnostic tests, a general blood analysis, an electrocardiogram, etc. Furthermore, the national legislation provides for social support for PLHIV in the form of monthly benefits and disability pensions, including for the children born to mothers with HIV, up to 18 months, and children with HIV+ status — until they reach legal age. Parents and other legitimate representatives of minor PLHIV are eligible for joint stay with children under 14 in an inpatient medical institution with payment of a temporary disability allowance at the expense of the republican and local budgets; breast milk substitute until the infant's age of one year to be provided by the family medicine centers at the place of permanent residence. Furthermore, the children living with HIV/AIDS when in clinics, rehabilitation centers or for health reasons staying at home, are eligible to study under special programs of the general education school and primary vocational education, approved by the Government of the Kyrgyz Republic.

Furthermore, the State program provides for a number of measures aimed to ensure availability of ARVs, including development of new clinical protocols, the expansion of the list of available ARVs, improvement of the procurement procedures.

The State Healthcare Guarantees Program provides for supply of the medicines primarily from the Essential Drugs List (EDL), which includes ARVs specified in the national clinical protocols. Along with that, the national clinical protocols are regularly updated based on the WHO recommendations. In 2017, a clinical protocol was approved which includes treatment regimens with the ARVs which were earlier not administered but recommended by WHO, such as dolutegravir, rilpivirin, and darunavir. These changes provide an opportunity to receive treatment with more modern medicines, which will reduce the extent of the medicines side effects and, accordingly, affect the increase in compliance to treatment.

8.1. The findings of the survey of the key informants and NGOs (directors of governmental and public entities, representatives of international organizations).

Activities of the organizations which representatives participated in the survey are anyhow related to the issues of treatment, prevention, and follow-up of PLHIV, as well as the issues determining strategic development and coordination in the field of HIV infection. Six persons were interviewed within the Study.

The HIV situation in the region and description of the HIV transmission pathways

In comparison with other regions, the Osh region is the leader after the Chuya region: about 100 new cases a year are identified; currently, the injection pathway dominates, but among the newly identified cases, the sexual transmission pathway prevails. In comparison with 2010, the share of the sexual pathway of HIV transmission increased, while the share of the parenteral pathway comparatively with other transmission pathways is decreasing. The same trend is observed all over the world, as well as the increase in the share of an unidentified transmission pathway, while the vertical transmission from mother to child is decreasing. In comparison with the past years, there has been an increase in the share of female PLHIV and a decrease in the share of male PLHIV.

The main groups of risk in terms of HIV infection, according to all respondents, included representatives of the key population groups, CP, PWID, MSM, prisoners, as well as sexual partners of PWID and PLHIV.

Access to ARV therapy in the region/town, compliance to ARVT

ARV therapy can be obtained in the AIDS centers, both regional and town, as well as at the primary level, in the Family Medicine Centers at the place of permanent residence. Sufficient medicines quantity is available for everyone administered with ARVT who wants to commence therapy. Currently, the process of integration of the services for PLHIV at the primary healthcare level is underway, i.e. the medical services are as close as possible to the patient's place of residence. Right now, the ARVs are purchased at the expense of the donated funds, and the Government HIV/AIDS Control Program for 2017-2021 includes the plan of transition to funding from the national budget and, starting from 2018, the share of funding from the national budget should gradually increase.

The vast majority of the respondents said that equality in obtaining ARVs is respected, all PLHIV who wish can receive ARV therapy for free. Access to this service is available to all those who wish, but not always, due to the behavioral characteristics of the key populations, stigma, and discrimination. An important role in respecting the rights of PLHIV as well as in the equality of access to treatment is played by the civil sector representing the interests of the PLHIV community.

The main problems identified by the majority of the respondents are stigma, self-stigmatization, PLHIV's low awareness of ARV therapy, the severity of the therapy side effects, the existing myths about ART among the key populations (KP), the use of alcohol and psychoactive substances (PAS), and the workload on the physicians who observe PLHIV.

The majority of the respondents noted that the overall compliance across the country is not at the desired level. As of 01.11.2017, ARVT was administered for 4,050 PLHIV, 3,075 actually receive the therapy, i.e. 76%; however, of the patients who receive therapy just 60% are marked as compliant, according to the viral load tests.

Specific features of dealing with PWID/PLHIV

The vast majority of the respondents said that PWID/PLHIV is a complex category of patients who depend on PAS, alcohol, have other diseases (tuberculosis, hepatitis C, etc.), many of whom are in a difficult life situation without permanent income, housing, etc. Besides that, PWID/PLHIV remain a hard-to-reach category, many of them refuse to accept ARV therapy or interrupt treatment. This category of patients is characterized by low compliance to ARV therapy.

Dealing with PLHIV/PWID, who receive opioid substitution therapy with methadone (OST) and/or tuberculosis treatment, also has its own specific characteristics. The doctor who observes such patients needs to select the medicines dose, in particular, taking into account the methadone intake, if the patient receives OST. Furthermore, if a patient receives both OST and tuberculosis treatment, then the patient has to take a large number of medicines every day, many of which have side effects, which also significantly affects the compliance to therapy.

The measures aimed to increase the compliance

The vast majority of the respondents said that a lot of efforts aimed to increase compliance among the key populations are made in the country, including outreach education both among the employees of the NGOs and in public medical institutions. The NGOs effect payments of incentive packages and payments to the therapy compliants, provide peer-to-peer counseling, and training activities. Also, there is certain cooperation with the law enforcement agencies in terms of advising of specifics of dealing with the key populations, covering the issues of HIV prevention, and collaboration with the NGOs.

Most of the respondents said that just an integrated approach to addressing the problem of compliance to treatment would solve this problem. It is required to involve both the governmental organizations and the civil society, to increase the quality of services, to collaborate with the law enforcement agencies, families, and other agencies. It is also required to increase the physicians' incentive in the form of adequate wages, to seek sustainability of the projects based on the NGOs.

Assistance to the PWID/PLHIV patients who receive OST also requires an integrated approach, providing a "single window" system, where in one place, at the OST facility, the patients may also receive ARVs, it is required to collaborate with the law enforcement agencies. Furthermore, among other answers, the respondents noted that the OST program is currently unattractive for PWID, there are no outreach activities and reimbursement of transportation costs, which had been provided earlier. Also, according to the respondents, it is required to increase the competence of the program staff.

All respondents noted that the role of the healthcare professionals in maintaining the compliance is of a key nature, because these are the healthcare professionals who provide post-test counseling, motivational enhancement, administer therapy. Whether PLHIV commences taking ARV therapy, whether he/she adheres to it, all these depend on the quality of the services. Furthermore, everyone was absolutely unanimous that the main factor on which compliance depends is knowledge, skill, and competence of the healthcare professional. The respondents also noted that a physician can take very little time to PLHIV patient due to his/her excessive workload. The wages remain low, which directly affects the healthcare professionals' incentives, prompting them to perform their functional duties, as well as the quality of the services and, as a consequence, the patient's compliance as a whole.

All respondents said about the importance of the NGO sector participation in maintaining PLHIV compliance to ARV therapy, because they are that link between the key populations and the government institutions. Furthermore, incentive payments and social packages are provided to the patients who adhere to the ARV therapy via NGOs under various projects.

The vast majority of the respondents pointed out that close interaction between the state structures and the NGO sector is required for more efficient work with the key populations, and the partnership should be equal and permanent. Also, it is required to jointly carry out the activities aimed at improving the quality of the services and the competence of the employees of both NGOs and the government agencies.

8.2. The deliverables of the survey among PWID/PLHIV

8.2.1. General

When making the efforts aimed to establish a patient's compliance to antiretroviral therapy and regular medical check-ups, an expert should consider multiple factors which can both help in developing new behaviors and become a serious barrier against achievement of sustainable motivation to take the medicines. The impact factors may be associated with various aspects of the life of a HIV-positive patient, with his/her personal characteristics, the environmental conditions, etc. Not all impact factors can be eliminated or neutralized, but it is required to ascertain their existence and to take them into account.

The factors which may potentially affect a patient's compliance to ARV therapy and regular medical check-ups are usually classified according to the nature of their occurrence into socioeconomic/socio-demographic, organizational, psychological/individual, medical, and others.

8.2.2. The data analysis findings

Socio-demographic characteristics of PWID/PLHIV

The socio-demographic and socio-economic factors have an impact on establishing compliance. These factors should be considered when assisting to PLHIV

The Study area

The Study included the areas with the highest prevalence of drug use and a high level of HIV infection. 321 PLHIV-PWID were surveyed, registered with the healthcare establishments in five populated localities: Bishkek, Osh, Kant, Kara-Balta, and Sokuluk.

According to the HIV infection e-monitoring system, in five localities studied a half of the registered PLHIV are PWID.

Table 5. The share of PWID among PLHIV in the sites studied.

Place of residence	PWID		NON-PWID		Total
Osh	156	50%	158	50%	314
Bishkek	206	46%	241	54%	447
Zhaiyl district	75	50%	76	50%	151
Sokuluk district	127	54%	110	46%	237
Ysyk-Ata district	110	49%	116	51%	226
Total	674	49%	701	51%	1,375

Gender

Female patients often have multiple obligations to their children, spouses, etc. The patient's additional obligations cause impossibility of concentrating on one's own needs as a priority and entail "forgetfulness" and "lack of time" for compliance to the medicines regimen and compliance with the medicines and food compatibility guidelines. In this regard, the physicians must take into account the specific features of female patients during follow-up. In the PWID group, both in sample and in the EM system, in the sites studied the majority are men (85-89%). In the mixed group (PWID and non-PWID) from the EM system in the sites studied the share of female PLHIV is close to the men's share.

Table 6. PLHIV breakdown by gender in E-monitoring system and sample.

	Women	Men
Common group (EM system)	41,2%	58,8%
Among PWID (EM system)	11,0%	89,0%
Among PWID (sample)	15,3%	84,7%

Age

The patients' age may influence their compliance to treatment. For example, the studies have revealed that men over 65 and under 35 have lower compliance to treatment¹. HIV in elderly patients has its own specifics, which include higher rates of complications, side effects, and concurrent diseases, and some of these complications may aggravate or accelerate because of prolonged intake of certain ARVs. Consequently, in elderly patients with HIV, the risk of development of low compliance to treatment may increase². At a young age under 35, low compliance can be affected by poor awareness of HIV and treatment, a greater number of unmarried people, lack of responsibility for one's health, etc. Half of the

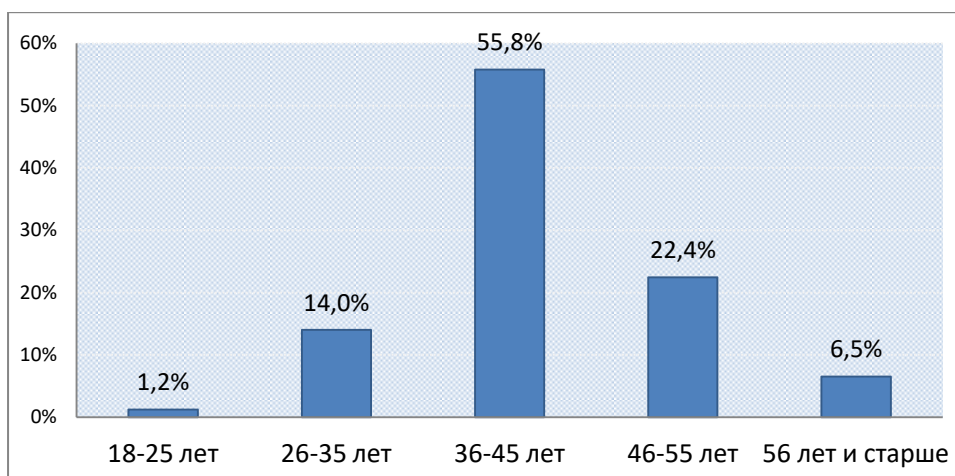
¹ G. E. Gafurov "Factors which influence adherence to antiretroviral therapy in PLHIV"

<http://rep.bsmu.by/bitstream/handle/BSMU/9299/2.pdf?sequence=1&isAllowed=y>

² Antiretroviral therapy for elderly PLHIV: Review. <http://hivmedinfo.org/global/nportal/view/19>

respondents (55,8%) are from 36 to 45 years of age. The average age is 42,5 years, the median age is 42 years, the maximum age is 68 years, and the mode is 41 year.

Fig. 1. PLHIV breakdown by age groups in sample.



лет	years
56 лет и старше	56 years old and older

Education

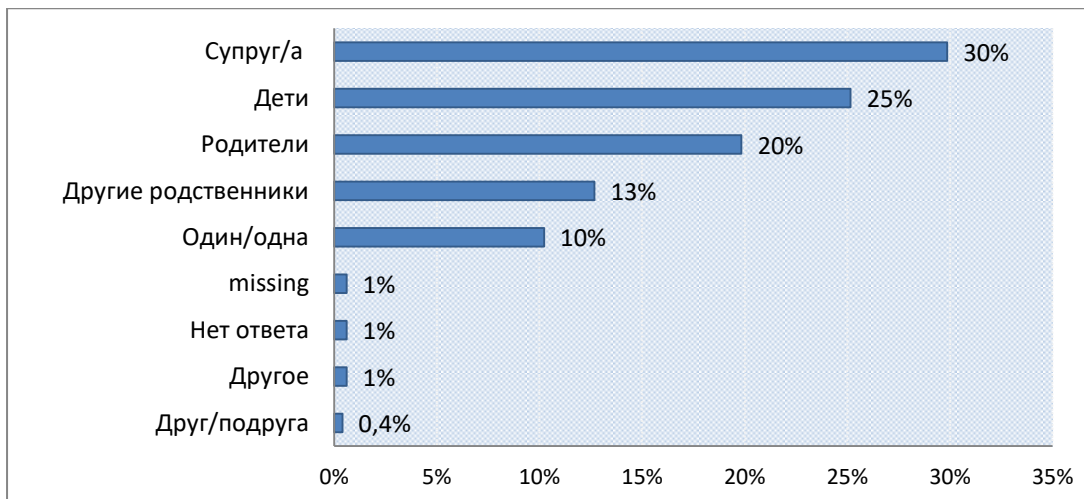
Undereducation may cause difficulties in establishment of compliance. Among PWID/PLHIV, 18% of the respondents either do not have any education or have just primary or partial secondary education; the majority of the respondents received secondary or vocational secondary education (75%). There is also a small percentage of respondents with higher or incomplete higher education (7%).

Marital status, friends and relatives

Stable relationship in the family, with friends or even with employees can have a positive impact on the success of compliance to treatment. On the other hand, PLHIV do not usually want to disclose their HIV status and, therefore, usually do not take medicines in the presence of the other people. The presence of at least one person trusted by PLHIV can help decide to initiate the therapy, remind to timely take a dose of medicine and provide emotional support.

The studied group of PWID/PLHIV includes both married people (49%) and single people (50%), but, despite the high prevalence of single/unmarried people, nevertheless, the vast majority of the respondents (90%) live together with their relatives and close people (spouses, parents, children, and other relatives).

Fig. 2. Close relatives of PLHIV.



Супруг/а	Spouse
Дети	Children
Родители	Parents
Другие родственники	Other relatives
Один/одна	Single
Нет ответа	No answer
Другое	Other
Друг/подруга	Single

Income level

During the administration of ARVs, it is quite important to adhere to the regimen, the diet recommendations, and to observe compatibility of various substances with the medicines; otherwise, the medicine's absorbability can significantly reduce, and its concentration may become insufficient to achieve a virologic effect. Lack of cash may influence PLHIV's ability to follow dietary guidelines, undergo various examinations, purchase additional medicines, travel to a physician's office from remote settlements, etc.

Many PWID/PLHIV in the studied sites have no employment (40%), that's why 30% of the respondents have no income, and 19% earn only up to 5,000 Kyrgyz Som (75 USD) per month, possibly as casual earnings. The other 60% of PWID/PLHIV have employment (of them, 1% both work and study), while the income of a third of the respondents (28%) is relatively low, from 6,000 to 10,000 Som. Also, sample features a category of the respondents with higher income: from 11,000 (158 USD) to 20,000 Som (286 USD) in 17%, and from 21,000 (300 USD) to 50,000 Som (715 USD) in 7% of PWID/PLHIV.

Place of residence

Set up housekeeping, availability of a place of residence and stay facilitate formation of behavior which cause regular medicines intake. Quite the opposite, problems with housing, when PLHIV have to share it with other people or often stay in different places can adversely affect the integrity of the stock of medicines and the regularity of their intake. Most PWIDs have their own housing: a private house (62%) or an apartment (16%), but the other 22% of the respondents live in a rented housing (dormitory, shared apartment).

Time of linkage to care, administration of ARV therapy and initiation of ARV therapy

Efficient treatment along with the clinical benefits, when the patient himself is satisfied with the treatment progress, facilitates good compliance to ARV therapy. In turn, the treatment efficiency depends on timely linkage to care and early initiation of ARV therapy. When studying in the EM system a period elapsed from the time of validation of the HIV infection diagnosis until the time of linkage to

care, as well as establishment of clinical indications for ARVT and the initiation of ARVT, there is a difference between these indicators in the PWID/PLHIV and PLHIV-non-PWID groups. In order to compare data in two groups, the median was taken due to extreme values in the data set, since the median in such cases most adequately estimates the average trend in comparison with the arithmetic mean.

So, in the PWID/PLHIV group, the median in the periods studied is several-fold more than that in the PLHIV-non-PWID group. For example, **in the PWID/PLHIV group, it may take 1.5 years both until establishment of the clinical indications for ARVT and until initiation of ARVT, whereas in the PLHIV-non-PWID group, the median period until establishment of the clinical indications for ARVT is 18 days**, and the median period until the initiation of ARVT is 84 days, i.e. it can be assumed that there are problems with timely linkage to care, as well as with the initiation of ARV therapy among PWID/PLHIV.

Table 7. Period from communicable disease (CD) until first linkage to care; until establishment of the clinical indications for ARVT; until initiation of ARVT.

MEDIAN	PWID	NON-PWID	TOTAL
Period from communicable disease (CD) until first linkage to care, years	55 days	10 days	15 days
Period from CD until establishment of the clinical indications for ARVT, years	1.5 years	18 days	55 days
Period from CD until initiation of ARVT, years	2.4 years	84 days	9 months

The Study revealed the fact of the epidemiological investigation after validation of the HIV test, during which the epidemiologists had to carry out post-test counseling and refer PLHIV to the respective specialist for further medical check-up, specify the exact address of the medical institution.

According to most of the respondents (257 persons, 80%) they were briefed concerning the HIV infection risk factors by someone other than a doctor who provides ARV therapy, but only 50% could specify whether this person was an epidemiologist or an assistant epidemiologist. Especially doubtful are the results in Sokuluk and Ysyk-Ata districts, where only 5% to 9% of PLHIV could report that they had a conversation with an epidemiologist or an assistant epidemiologist.

Table 8. Carrying out epidemiological investigation after revealing HIV-infection.

	N	Epidemiological investigation performed		Physician's/epidemiologist assistant's name specified	
		No.	%	No.	%
City AIDS Control & Prevention Center	90	76	84%	58	76%
Osh AIDS Control & Prevention Center	77	59	77%	53	90%
Family Medical Center, Sokuluk region	50	39	78%	2	5%
Family Medical Center, Zhaiyl region	40	27	68%	11	41%
Family Medical Center, Ysyk-Atin region	63	55	87%	5	9%
TOTAL	320	257	80%	129	50%

Of all the respondents, slightly more than a half of the PWID/PLHIV (61%) during the epidemiological investigation were assigned codes of the surveyed populations related to the persons who injected drugs; the rest of the PWID/PLHIV were assigned other codes, i.e. the fact of injecting drug use is

established later by the follow-up physicians. This fact evidences the problems with performance of a qualitative epidemiological investigation at the first contact of the epidemiologists with PWID/PLHIV.

Table 5. Codes of the populations assigned to PWID/PLHIV following the epidemiological investigation upon revealing HIV infection.

Code	Population	%
102	PWID	41.4%
112.1	Prisoners, including PWID	19.0%
113	Examined for clinical indications, adults	8.1%
113.1	Including diagnosed with tuberculosis	8.1%
112	Persons in special institutions	5.0%
101.1	Persons who were in contact with PLHIV, including sexual contact	4.4%
120	Others	3.1%
104	Patients with STDs	2.2%
108	Donors	1.9%
202	Foreign nationals, including PWID	1.2%
113.2	Examined for clinical indications, adults, including newly revealed patients diagnosed with tuberculosis	0.9%
101.2	Persons who were in contact with PLHIV, including collective drugs injection	0.6%
106	Persons travelling abroad	0.6%
220	Foreign nationals, other	0.6%
101.3	Persons who were in contact with PLHIV, including household contact (skin penetration)	0.3%
109	Pregnant women	0.3%
114	Surveyed anonymously	0.3%
116	Sexual partners of pregnant women	0.3%
118	Healthcare professionals	0.3%
204		0.3%
212	Foreign nationals, including persons in special institutions of the Ministry of Internal Affairs	0.3%
213		0.3%
215.1		0.3%

The reasons for initiation of ARV therapy

Prior to administration of ARV therapy, 61.1% of the patients had been consulted by a psychologist and 63.8% by a "peer" consultant.

In the respondents' answers, the most common factors which influenced the decision to initiate ARV therapy were a medical condition (74%), a doctor's counseling (65%), fear of one's life (52%), fear of infecting others (43%) and his/her sexual partner (34%), as well as counseling by an NGO employee (39%). Less commonly mentioned were such reasons as the example of another PLHIV, information obtained from friends or colleagues, as well as information from the Internet.

Fig. 3. The reasons for making a decision to initiate ARV therapy.



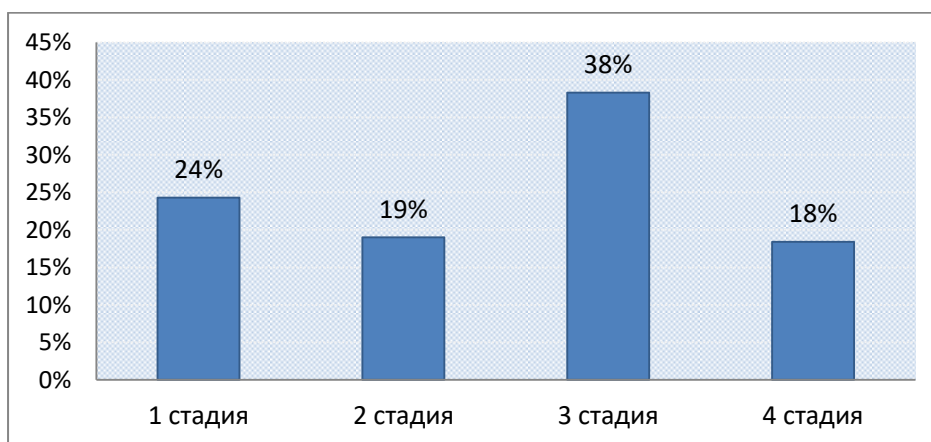
Состояние здоровья	Health status
Консультация врача	Physician's advice
Страх за свою жизнь	Fear for one's life
Боязнь заразить окружающих	Fear of infecting others
Консультация сотрудника НПО	Advice of an NGO employee
Боязнь заразить полового партнера	Fear of infecting a sexual partner
Пример другого ЛЖВ	Example of another PLHIV
Полученная информация от друзей/коллег	Information obtained from friends/colleagues
Другое	Other
Нет ответа	No answer

The stage of the disease, opportunistic infections

The clinical picture and the patient's condition can influence development of compliance. The presence of severe opportunistic infections, concurrent mental disorders, including sadness, anxiety, depression, aggravate the patient's condition. Treatment of the patients with a coinfection, such as HIV infection and tuberculosis, may cause a significant increase in the medicinal burden, an increased risk of adverse events, the condition deterioration in the process of taking medicines and a decrease in motivation for treatment.

In this Study, more than a half of the respondents were at stages 3 and 4 of the HIV infection (182 persons, 57%) with a predominance of patients at stage of the disease in the sample (38%).

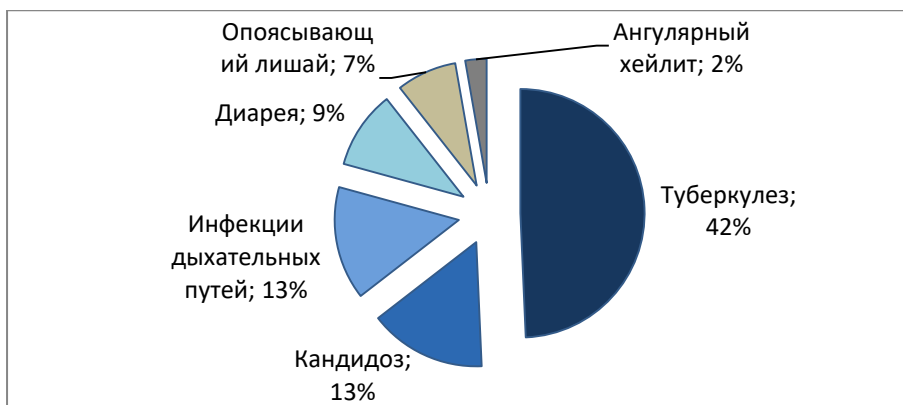
Fig. 4. PLHIV breakdown by the HIV infection stage.



Стадия	Stage
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According to the e-monitoring system, the vast majority of PWID/PLHIV from the sample (n = 253, 79%) have opportunistic infections, mostly tuberculosis (n = 107, 42%). However, only 150 respondents (46.7%) reported opportunistic infections at the interview.

Fig. 5. Opportunistic infections in PLHIV.



Опоясывающий лишай	Shingles
Диарея	Diarrhea
Инфекции дыхательных путей	Respiratory tract infections
Кандидоз	Candidiasis
Ангулярный хейлит	Angular cheilosis
Туберкулез	Tuberculosis

Treatment status, treatment gaps, and change in the treatment regimen in the past medical history

The treatment status has been studied based on three sources:

- PLHIV survey,
- data from the HIV infection e-monitoring system
- analysis of the records in the ARVs release registers at the sites

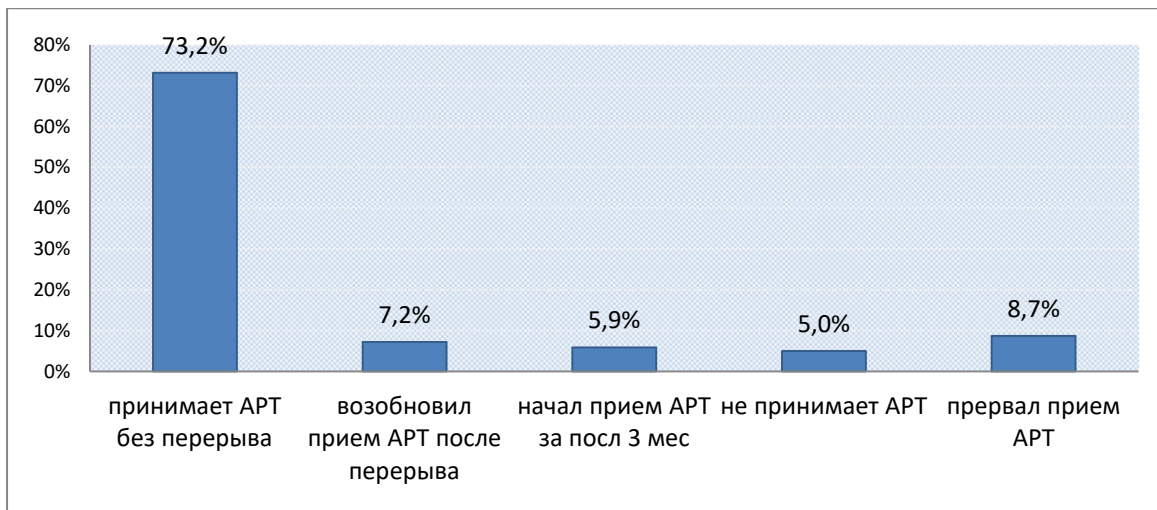
The treatment status according to the findings of the PLHIV survey

According to the findings of the analysis of the respondents' answers, the average duration of ARV therapy is 3.6 years, the median is 4.8 years, the minimum period is 37 days, and the maximum period of ARV therapy is 17.8 years. The question about taking ARVs was affirmatively answered by 301 (94%) patients. 67 patients (22.3%) reported changes in the treatment regimen, and 76 respondents (25.2%) reported that they ceased taking ARVs on their own initiative. 27 respondents (8.9%) simultaneously ceased treatment and changed their treatment regimen. 116 (38.5%) PWID/PLHIV either ceased taking medicines or changed their treatment regimen.

The treatment status according to the findings of the analysis of the records in the ARVs release registers at the sites

The treatment status was assessed based on the frequency of the medicines release and the number of the days of the released medicines administration. At the time of the Study, 277 (86.3%) of the respondents received treatment, including those who did not cease ARV therapy — 235 (73.2%) (which means not treatment compliance, but rather a failure to complete the treatment); 23 respondents (7.2%) resumed treatment after a break, and 19 respondents (5.9%) started ARVT in the last three months. The other 28 (8.7%) patients either discontinued treatment or did not start treatment at all — 16 (5%).

Fig.6. The ARV therapy status according to the findings of the analysis of the records in the ARVs release registers at the sites



Принимает АРТ без перерыва	Takes ARV without gaps
Возобновил прием АРТ после перерыва	Resumed ARV intake after interruption
Начал прием АРТ за посл 3 мес	Commenced ARV intake in recent 3 months
Не принимает АРТ	Does not take ARV
Прервал прием АРТ	Interrupted ARV intake

The treatment status according to the data from the HIV infection e-monitoring system

When assessing the status of ARV therapy according to the data from the HIV infection e-monitoring system cited in the respondents questionnaires, continuation of ARV therapy without changing the treatment regimen at the time of the survey was noted in 253 patients (84%); 36 (12%) changed their treatment regimen, and 11 (3.7%) ceased the treatment, i.e. according to the e-monitoring system, 289 (96%) of the patients continue their ARV therapy.

Information about the change in the treatment regimen was studied based on two sources:

- PLHIV survey
- the data from the HIV infection e-monitoring system

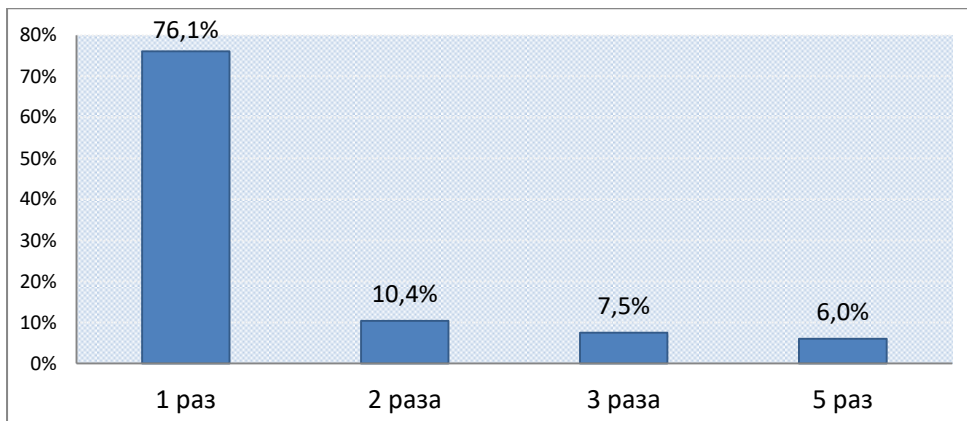
Change in the treatment regimen according to the findings of PLHIV survey

Replacement of one treatment regimen with another one in the absence of objective reasons to change the medicines, associated with the patient's insufficient motivation to take ARVs, can significantly increase the risk of the treatment interruption.

During the survey, 22.3% of PLHIV (67 persons) said that in the past they had changed the treatment regimen. For most respondents (76.1%), the treatment regimen was changed only once, while for the other PWID/PLHIV (23.9%) the treatment regimen was changed two to five times. Furthermore, 65.7% of the patients showed significant changes in their state of health after the medicines change.

No questions were asked concerning the reasons for changes in the treatment regimen during the Study.

Fig. 7. The number of changes in the patient's treatment regimen.



1 paz	Once
2 paza	Twice
3 paza	3 times
5 paz	5 times

Change in the treatment regimen according to the data from the HIV infection e-monitoring system

In total, according to the data from the e-monitoring system, the treatment regimen was changed for 19% of the patients, while in the PWID group the regimen was changed for 17% patients and for 21% of non-PWID patients.

The reasons for the change in the treatment regimen according to the data from the HIV infection e-monitoring system

When analyzing the reasons for switching to another treatment regimen in the e-monitoring system, the following main reasons can be identified: availability of new medicines (Atripla, 64%), other reasons (7%) (not detailed in the system), 15% had toxic side effects, and 4% showed resistance to the ARVs administered.

Table 10. The reasons for changes in ARV treatment regimen, source: HIV infection e-monitoring system, Kyrgyz Republic AIDS Control Center.

The reason for the last change in ART	Medicine change		
	PWID	NON-PWID	TOTAL
Pregnancy		2	2
Planned pregnancy		1	1
Virological inefficiency	5	12	17
Availability of new medicines	86	124	210
✓ Availability of new medicines, %	65%	63%	64%
Other	11	13	24
✓ Other, %	8%	7%	7%
Immunological inefficiency		1	1
Clinical inefficiency	2	1	3
A new case of tuberculosis	2	2	4
Lack of medicines	4	1	5
Resistance to medicines	6	8	14
✓ Resistance to medicines %	5%	4%	4%
Toxic/side effects	16	33	49
✓ Toxic/side effects %	12%	17%	15%
Total	132	198	330
Those changed ARVT regimen, total	17%	21%	19%
TOTAL in PWID and non-PWID groups	775	962	1737

The treatment interruption was studied based on three sources:

- PLHIV survey;
- the data from the HIV infection e-monitoring system;
- analysis of the records in the ARVs release registers at the sites.

Interruption of the ARVs taking according to the respondents

25.2% (76) of the respondents reported that they ceased taking medicines for a long period at their own initiative. However, 44.7% noted significant differences in their health with a repeated administration.

The reasons for interruption of the ARV therapy according to the respondents

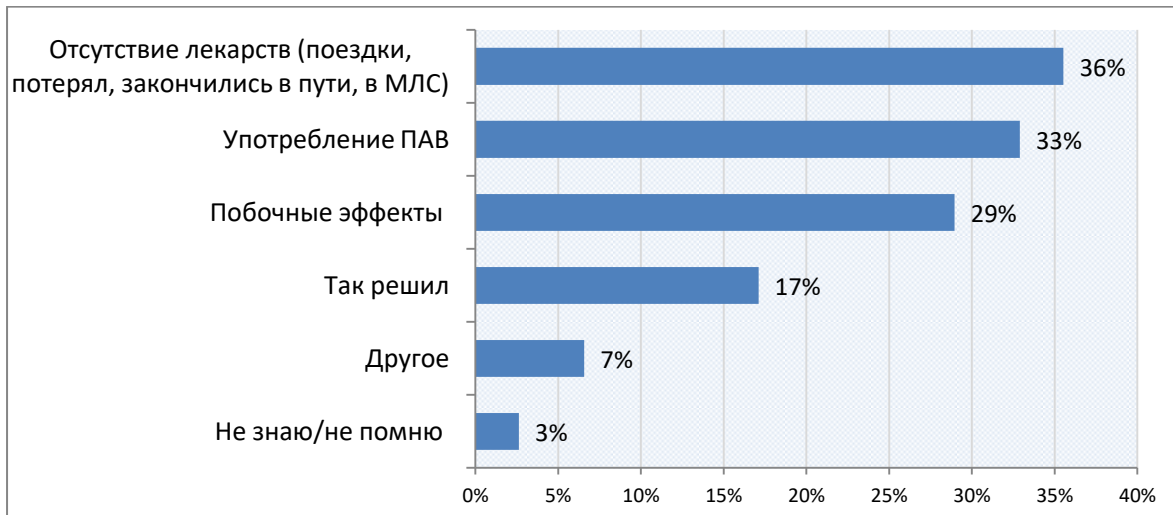
Low responsibility for one's health, the patients' carelessness in the medicines storage when travelling, lack of advice and information from the healthcare professionals, the patients' unawareness of the danger of the therapy interruption may result in a situation where the patients don't have enough ARVs when outside their permanent place of residence. Absence of medicines during journeys for any reasons whatsoever (forgot, lost, not enough) was the most common reason for self-interruption of ARV therapy (36%).

When analyzing the reasons for the treatment interruption during the Study, the second highest prevalence was consumption of PAS 33% (alcohol or narcotics).

During the Study, 29% of the respondents reported side effects which influenced their self-interruption of ARV therapy, such as nausea (11%), depression (8%), impaired coordination (7%), sleep disturbances and vomiting (7%), i.e. 29% of the patients could continue their treatment in the event of timely medical assistance.

The patient's decision is also one of the most common reasons for the interruption of ARV therapy (17%), specified by the respondents without any explanation. This factor may evidence a lack of responsibility for one's own health and a low compliance to treatment.

Fig. 8. The reasons for interruption of the ARVs therapy according to the respondents.



Отсутствие лекарств (поездки, потерял, закончились в пути, в МЛС)	Lack of medicines (journeys, lost, ran out of stock during journey or in prison)
Употребление ПАВ	Consuming PAS
Побочные эффекты	Side effects
Так решил	Own decision
Другое	Other
Не знаю/не помню	Do not know/do not remember

The reasons for interruption of the ARV therapy according to the data from the HIV infection e-monitoring system

According to the analysis of the data from the HIV infection e-monitoring system, 18% of the patients interrupted their ARVT, while PWID/PLHIV interrupted their treatment 1,5 times more often (22%) vs. the PLHIV-non-PWID group (15%).

The main reason for interrupting the treatment according to the e-monitoring system is the so-called "patient's decision" (60.1%), which, in fact, means that the patient ceased to visit the site in order to receive administered ARVs without explaining the reasons. Most likely, this is due to low compliance to treatment, although low compliance as a reason for ceasing treatment is specified in a separate line of the e-monitoring system and is just 3.9%.

25.7% of the respondents have interrupted their treatment for other reasons not mentioned in the system, which can be specified only through studying the outpatient medical records of the PLHIV patients.

It is widely known that side effects are one of the common reasons for interruption of ARV therapy. At the sites studied, 7% of the patients stopped taking ARVs because of toxic side effects, which may indirectly evidence a lack of timely medical care. Moreover, side effects significantly more frequently influenced the patient's decision to stop taking ARVs in the PLHIV-non-PWID group (14%) than among PWID/PLHIV (1%).

Table 11. The reasons for interrupting ARV therapy, source: HIV infection e-monitoring system, Kyrgyz Republic AIDS Control Center.

The reasons for ARVT interruption	PWID	NON-PWID	TOTAL
Imprisoned	2	1	3
Low compliance to treatment	8	4	12
✓ Low compliance to treatment, %	5%	3%	4%
Lack of medicines	2		2
According to the patient's decision	101	86	187
✓ According to the patient's decision %	60%	60%	60%
Interruption for other reasons	49	31	80
✓ Interruption for other reasons %	29%	22%	26%
Toxic/side effects	2	20	22
✓ Toxic/side effects %	1%	14%	7%
Severe clinical condition not associated with HIV and ARVT	2		2
Died	2	1	3
Total	168	143	311
✓ Patients interrupted ARVT, total, %	22%	15%	18%
TOTAL in PWID and non-PWID group	775	962	1737

Compliance to treatment

Common criteria for assessing compliance

The patient's compliance can be determined with such criteria as:

- the proportion of the patient's correct taking of the ARVs doses vs. all doses administered by the physician,
- the number of single doses missed by the patient per month,
- count of daily medicines takings per month,
- compliance with the time of taking the medicines with the doctor's recommendations,
- fluctuations in the time of taking the medicines,
- compliance with the specified diet when taking the medicines,
- self-missed medicines takings, not authorized by the physician, without good reason,
- mental attitude towards compliance.

The rate of compliance to antiretroviral therapy can be quantified by calculating the ratio of the taken medicines to the quantity administered, expressed as a percentage. So, depending on the number of the doses taken, compliance can be expressed as a percentage from zero (no doses taken) to 100% or more, when the patient takes more doses than administered by the physician, and is determined with the following formula (Shalansky SJ, Levy AR, Ignaszewski AP, 2004):

Compliance rate = $B/A \cdot 100\%$, where *A* is the number of the doses to be taken within a certain period, usually a month, and *B* is the number of the doses actually taken during this period

Ideally, the patient should have a 100% compliance, but in real life, when treating a long-term chronic disease, it is almost impossible to achieve such a rate. Usually it is believed that reaching 80% rate is already a good compliance, but this approach is unacceptable for HIV infection. According to the findings of the studies, efficient treatment for HIV infection means taking at least 95% of the medicine doses³. It is this threshold which ensures the best virologic response to treatment.

WHO proposes the following scale to describe the rate of compliance to ARVT in PLHIV:

- good compliance rate – $\geq 95\%$;
- medium compliance rate – 85–94%;
- low compliance rate – $\leq 85\%$.

In practice, this scale means that a patient with a recommended compliance rate cannot miss more than one day of the medicine taking or three single doses per month (Table 12).

Table 12. Criteria for compliance assessment by various methods.

Compliance criteria	High compliance	Medium compliance	Low compliance
The proportion of intake of the doses administered by the physician	95% and more	80-94%	79% and less
The No of missed single doses per months in case of 2 intakes per day	Less than 3 or 1 day	3-10 doses or 1,5 — 5 days	More than 10 doses or 5,5 days and more
Daily medicine intakes per month	29 days and more	25-28,5 days	24,5 days and less
Timely intake with the following deviations	Max. 30 minutes	Max. 2 hours	More than 2 hours
Compliance with the dietary recommendations	Always	Sometimes	Mostly not
Self missing without good reason	no	some	frequent
Mental attitude towards compliance	yes	Does not take an active position, but agrees with the physician	no

It should be considered that a physician always overestimates the rate of compliance to treatment by his/her patients. The real ratio of compliant and non-compliant patients in the population taking ARVs has been demonstrated by the Study findings: the proportion of highly compliant patients is about 70% and non-compliant — about 10%⁴, and based on the findings of the studies using the cluster analysis, highly compliant patients' proportion is 64%, moderately compliant – 24,6%, and non-compliant — 11,4%.

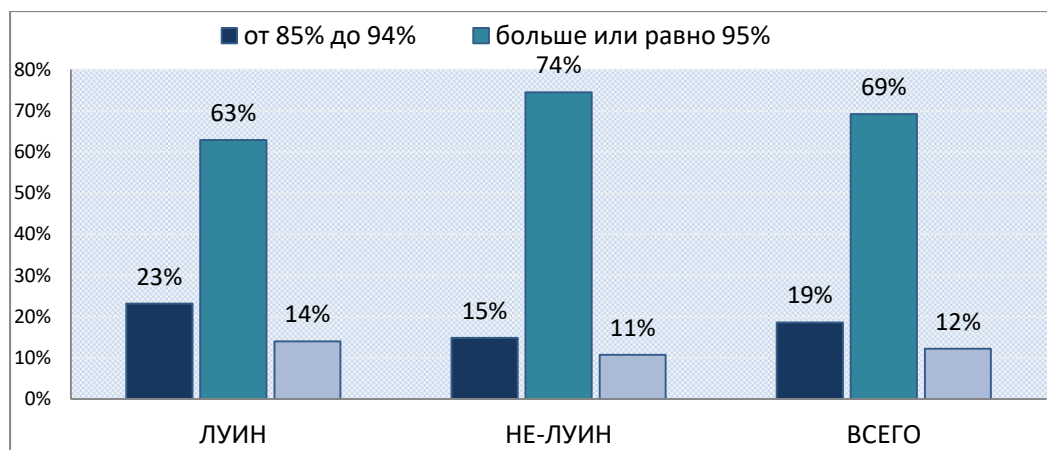
Assessment of the compliance by the ARV therapy providers (in the e-monitoring system)

According to the analysis of the data from the HIV infection e-monitoring system, in the Kyrgyz Republic in Q4 2016, at the sites studied the compliance rate "95% and more" was registered among 63% of PWID/PLHIV, 74% among PLHIV-non-PWID, and 69% in PLHIV common group.

³ Paterson DL, Swindells S, Mohr J et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med.* 2000; 133(1):21-30.

⁴ T.K. Tangisheva, 2006; J.Z. Li, S. Gallien, H. Ribaudo et al., 2013.

Fig. 9. Compliance to ARV treatment, source: HIV infection e-monitoring system, Kyrgyz Republic.



От 85% до 95%	85% — 95%
Больше или равно 95%	95% or more
ЛУИН	PWID
НЕ-ЛУИН	NON-PWID
ВСЕГО	TOTAL

Assessment of the compliance by the estimates of the ARVs release

In order to get a real picture, it is not enough to ask the patient general questions about the therapy. A detailed review of the situation and an accurate picture of the patient's compliance to therapy can be made using various methods. In this Study, compliance to ART was assessed over the past six months, to which end the dates of release of ARVs and the number of the days for which these medicines were released for the period from March 01, 2017 until August 31, 2017 were recorded at all the sites studied (from the ARVs release registers).

In the sample, the patients have been categorized as follows:

1. The patients taking ARVs during the Study period, without formal completion of treatment — 235, 73,2%;
2. The patients who interrupted treatment — 28; 8,7% (i.e. the patients who failed to take medicines for more than 90 days)
3. The patients who resumed treatment after a break — 23; 7,2%;
4. The patients who commenced ARVT in the last three months — 19; 5,9%;
5. The patients who failed to commence ARVT — 16; 5%

In order to assess the compliance, of the entire list of the patients those have been excluded who started taking ARVs in the last three months (No 4), as it is too early to draw conclusions about development of compliance, as well as those who did not start ART (No 5). Compliance was assessed among the patients in items 1, 2, and 3, n = 286. The missings were calculated by adding the tablets released and comparing them with the number of the days of ARVT based on the following formula:

$$\text{Calculation of missings} = \frac{\text{No. of days of taking} - \text{No. of the tablets dispensed}}{\text{No. of days of taking}/30}$$

In the above calculations, the tablets remaining from the previous medicine dispensing were counted. If this was the case, such tablets were added to the number of the tablets dispensed during the next month. Compliance was assessed for each month of ARVT. A satisfactory compliance rate was considered 95% or more, i.e. maximum one failure to take the medicine per month. The respondents who ever started ARV therapy and interrupted it, were from the very beginning assigned to patients with low compliance.

Compliance of 95% and more was determined in 22% of the patients, from 12% to 30%, broken down by populated localities.

Table 6. The rate of compliance among PWID/PLHIV broken down by populated localities.

	Share of compliants	Patients total
City AIDS control & prevention center	30%	82
Osh regional AIDS control & prevention center	27%	70
Family Medical Center, Ysyk-Atin region	14%	42
Family Medical Center, Zhaiyl region	15%	33
Family Medical Center, Sokuluk region	12%	59
Total	22%	286

Among those 235 patients who did not complete the treatment, the duration of ARV therapy at the time of the analysis averaged 11.8 months, median 11 months, minimum 3 months, maximum 28 months, mode 13 months.

Assessment of the strength of association of various factors with low compliance to ARV therapy

Initially, 38 factors were tested by the method of univariable analysis, of which 12 factors with P-value ≤ 0.1 were selected for testing in the logistic regression model to exclude confounding factors.

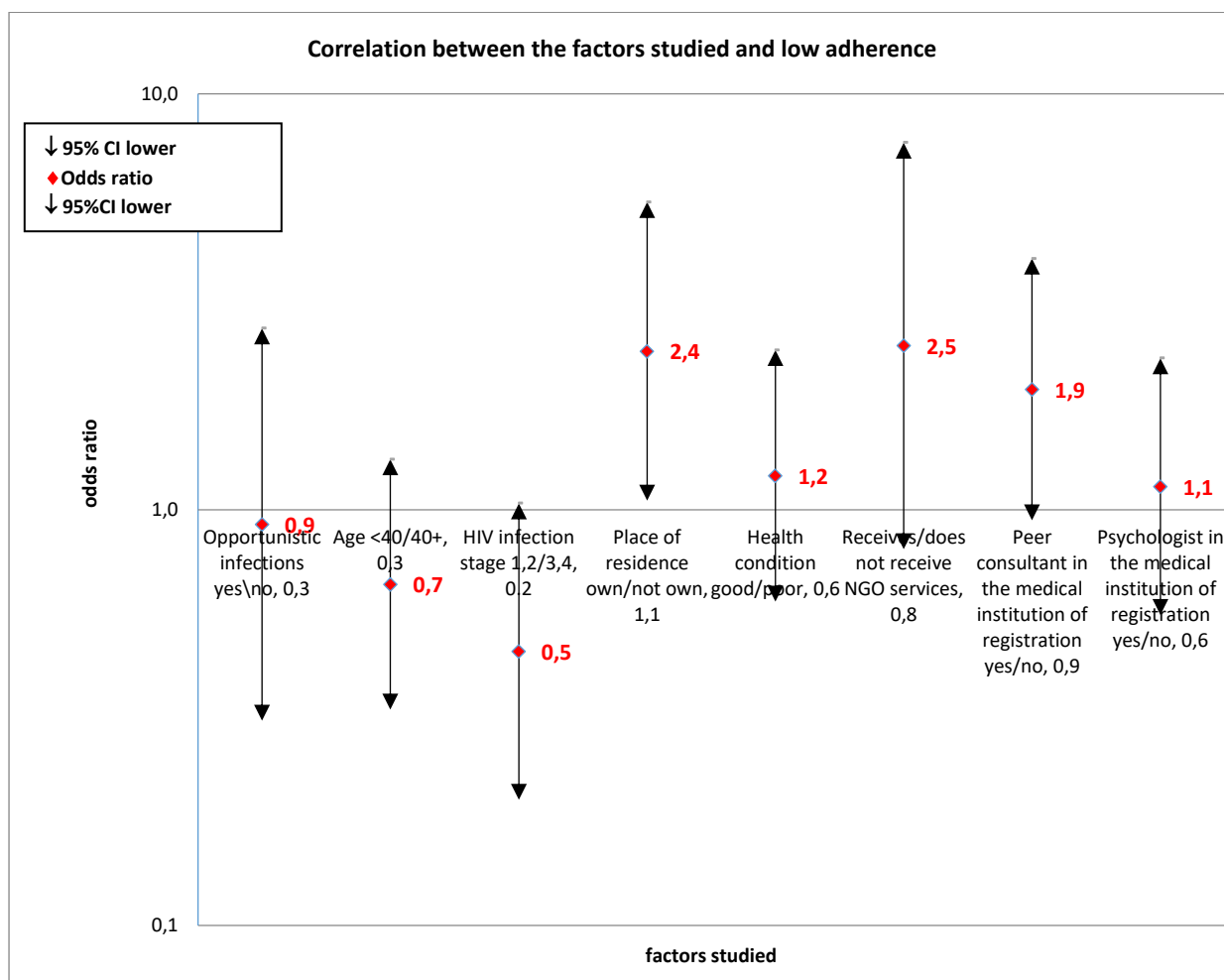
Table 7. The list of the factors included into the logistic regression model, P-value ≤ 0.1

No	Risk factors	%	Odds assessment (OA)	95% CI (confidence interval)		P-value
				low	upper	
1	age under 40	85%	0,53	0,27	1,01	0,054
2	without opportunistic infections	87%	0,49	0,22	1,10	0,082
3	resides not in his/her own housing	86%	1,94	0,90	4,19	0,092
4	stage 1-2 of HIV infection	86%	0,44	0,24	0,82	0,010
5	1 tablet in a dose	82%	0,35	0,18	0,69	0,002
6	2 doses per day	83%	0,35	0,18	0,69	0,002
7	no queue to the follow-up physician	83%	0,59	0,32	1,07	0,084
8	no peer consultant in the organization providing linkage to care	84%	2,18	1,23	3,89	0,008
9	no psychologist in organization of the linkage to care	82%	1,62	0,92	2,86	0,098
10	poor (depression, fatigue, fear, etc.) condition for the last 6 months	83%	1,68	0,92	3,07	0,091
11	did not receive NGO services	91%	3,21	1,10	9,35	0,032
12	were not imprisoned	83%	0,60	0,33	1,09	0,093

According to the findings of the logistic regression analysis, the chance of low compliance (<95%) was higher among those living with relatives or renting housing (OR = 2.4, 95% CI 1.1-5.5) and among those PWIDs who reported the lack of a peer consultant in the medical institution with which they are registered.

Based on the interpretation of the values of the confidence interval in the logistic regression, all factors with a value above 0 have a protective effect. So, availability of one's own housing and a "peer? consultant in the PWID/PLHIV medical institution contribute to increasing compliance to ARVT.

Fig.10. Testing the correlation between the factors and low level of compliance by logistic regression method.



The laboratory values at the time of the therapy administration and their changes under the ARVT impact

Analysis of the laboratory data from the HIV infection e-monitoring system showed no significant difference in a decrease in the viral load and an increase in the number of CD4 cells between the patients compliant and not compliant to ARV therapy, which may indirectly evidence that those who timely receive ARVs in a medical institution, in fact, do not take all such medicines.

Table 15. Decrease in the viral load broken down by the compliance rate, source: HIV infection e-monitoring system, Kyrgyz Republic AIDS Control Center.

Viral load	Compliant	Non-compliant
decrease two-fold and more	41 (66%)	113 (50%)
no decrease	15 (24%)	71 (32%)
N/A	6 (10%)	40 (18%)
	62	224

Table 16. Increase in the number of CD4 cells broken down by the compliance rate, source: HIV infection e-monitoring system, Kyrgyz Republic AIDS Control Center.

CD4	Compliant	Non-compliant
increase two-fold and more	16 (26%)	47 (21%)
no increase	45 (73%)	176 (79%)
N/A	1 (2%)	1 (0,4%)
	62	224

ARV therapy administration regimen

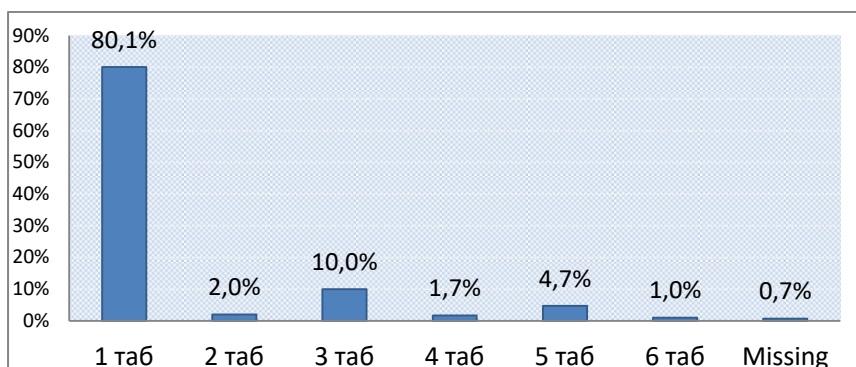
Before starting ARV therapy, the patient must realize that he will have to take ARVs regularly throughout his life, and since each person's lifestyle is individual, the decision to start the therapy should be made on an individual basis, considering personal situation, such as a work schedule or other activities. Furthermore, assigning the therapy, doctor shall take into account the needs and preferences of the patient regarding the frequency of the medicines intake, probability of side effects, and possible interactions with other medicines.

The number of the tablets, frequency of intake, and certain dietary requirements can also complicate the intake of the medicines. For example, if a person is in a public place, he is unlikely to be able to take the medicine unnoticed by the others. Compliance to the regimen of the medicines combinations intake which must be taken three or more times a day is more difficult than taking medicines with a fixed combined dose with a lower intake frequency. Currently, there is already a therapeutical opportunity to take medicines once a day.

Under this Study, the majority of the patients (82.4%) were switched to a single dose of ARV therapy per day, but, nevertheless, the other 23.9% of PWID/PLHIV continue to take their medicines 2 or 3 times a day.

As far as the number of tablets is concerned, as expected, 80.1% of the patients take one tablet a day (Atripla), while the rest of the respondents take two to six tablets per day (19,4%).

Fig. 11. The number of the tablets taken among PWID/PLHIV.



таб	tablet(s)
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Of all PWID/PLHIV receiving ARVs, 98.7% of the patients received a doctor's advice on how and when to take ARVs, so that it would have as little effect on the everyday routine activities.

The vast patients majority (94%) said that they can always rely on the assistance and support when asking for them in all aspects of ARV therapy from the attending physician.

ARV medicines release management

As already reported, the absence of medicines during journeys for any reasons whatsoever (forgot, lost, not enough) was the most common reason for self-interruption of ARV therapy (36%) in the past medical history.

When investigating into the possible reasons for the lack of the medicines, 50.5% of the patients reported that no one else can receive the ARVs on their behalf if required, and 4.3% did not know what to answer. Also, 67.4% of the patients reported that they cannot receive ARVs in other institutions of their city or region, and 11.9% did not answer the question. Of the other respondents who are aware of the possibility of receiving ARVs by their relatives or for a longer period, 64.4% reported that they can arrange this with their attending physician, and 20.5% reported the possibility of filing an application to the director of the AIDS Control Center. In fact, many medical institutions which provide assistance to

PLHIV, are authorized to release ARVs to relatives, or release the medicines for more than 30 days upon application to the head physician of the institution, or by agreement with the doctor, but the respondents either do not know about these opportunities, or do not take advantage of them for unknown reasons.

Fig. 12. The conditions for release of ARVs to relatives of PWID/PLHIV.



Договоренность с врачом	Arrangement with a physician
Заявление на имя директора Центра СПИД/ЦСМ	Application to the director of the AIDS Center/FMC
Доверенность от руки (без нотариуса)	Handwritten power of attorney (not notarized)
Не знаю/не помню	Do not know/do not remember
Нотариальная доверенность	Notarized power of attorney
Нет ответа	No answer
Никакие, не дают	Nothing, not given

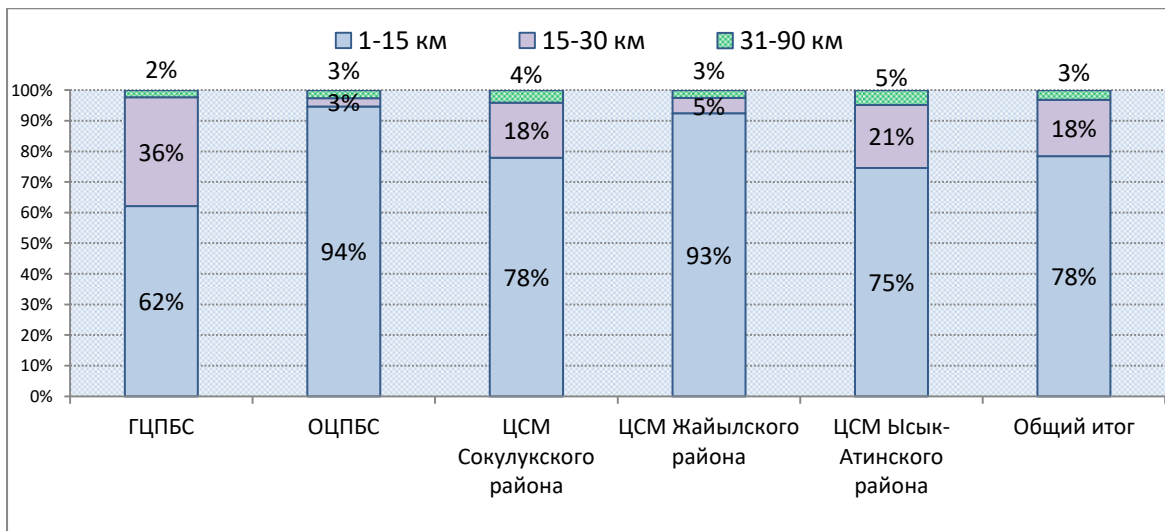
Medical services accessibility

Poor accessibility and inconvenience of the services, such as remote location of the special services, inconvenient visiting hours, and queues represent a huge barrier against getting assistance, especially for PWID patients.

The place of residence remoteness from the medical institution

As it turned out, most of the PWID/PLHIV respondents (78%) live not far from a medical institution (1-15 km), but in three settlements from 18% to 36% of the respondents live at a distance of 15 to 30 km from their institution, and from 2% to 5% of the respondents live at a distance of 31 to 90 km.

Fig. 13. The distance between the medical institution and the place of residence of PWID/PLHIV.

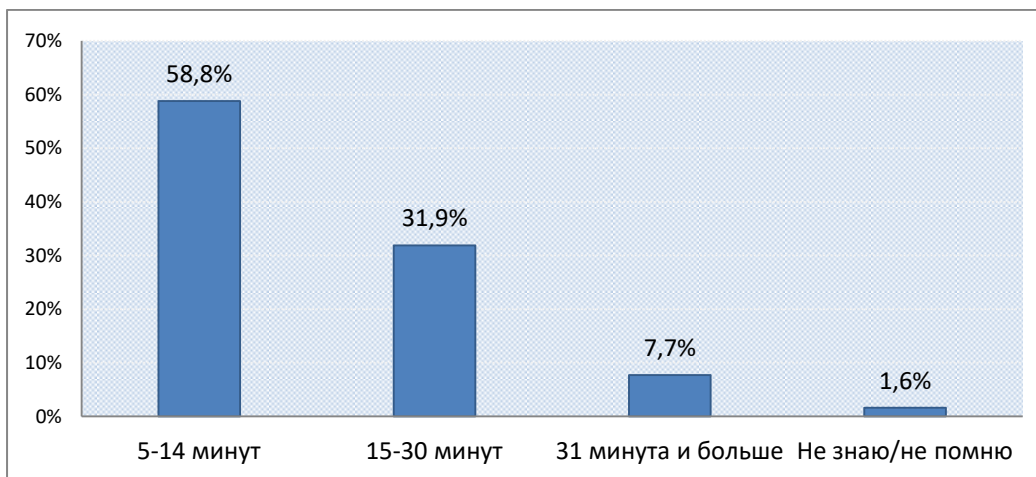


ГЦПБС	City AIDS Control & Prevention Center
ОЦПБС	Regional AIDS Control & Prevention Center
ЦСМ Сокулукского района	Family Medical Center, Sokuluk region
ЦСМ Жайылского района	Family Medical Center, Zhaiyl region
ЦСМ Ысык-Атинского района	Family Medical Center, Ysyk-Atin region
Общий итог	Grand total

The waiting time in queue during visits to a doctor who provides ARV therapy

59,7% of PWID/PLHIV reported that during the visits to the doctor of the follow-up department of the AIDS Control Centers or to the infectious diseases physician in the Family Medicine Center, sometimes there are queues in which half of the respondents wait from 5 to 14 minutes, 32% of the respondents wait from 15 to 30 minutes, and 8% wait for more than half an hour.

Fig. 14. The waiting time in queue during visits to a doctor who provides ARV therapy.



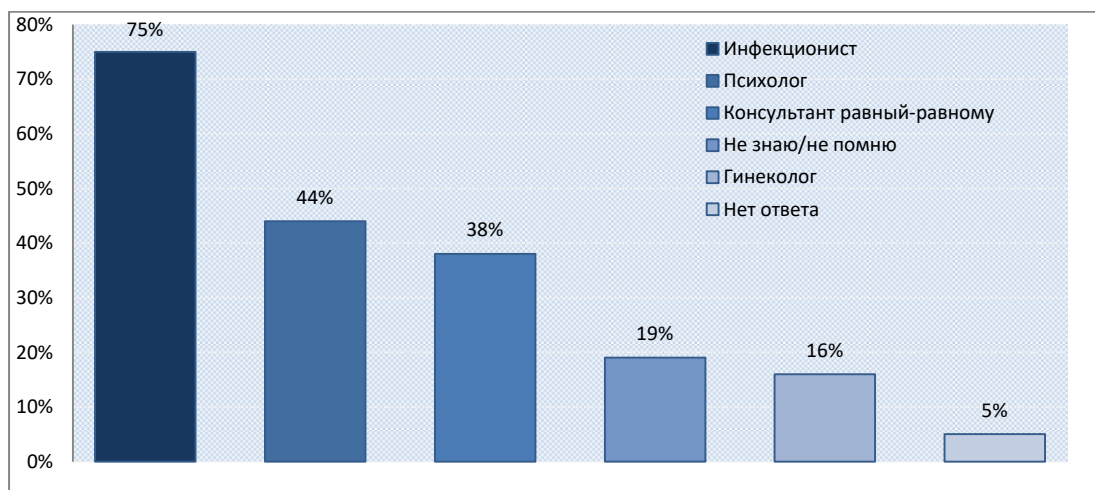
5-14 минут	5-14 minutes
15-30 минут	15-30 minutes
31 минута и больше	31 minutes and longer
Не знаю/не помню	Do not know/do not remember

Integrated services

Coordinated performance of medical and non-medical services (for example, providers of medical services and that providing psychological, social, and legal assistance), facilitates the organization of integrated PLHIV support programs that motivate the patients to stay healthy. Consistency in providing medical/social/psychological/legal assistance through their integration into multidisciplinary teams provides the opportunity for cross-referral of the patients between the specialists and for integrated resolution of the problems which prevent compliance.

According to the survey findings, the institutions with which the respondents are registered, employ the "peer" consultants, psychologists, gynecologists, and infectious diseases specialists.

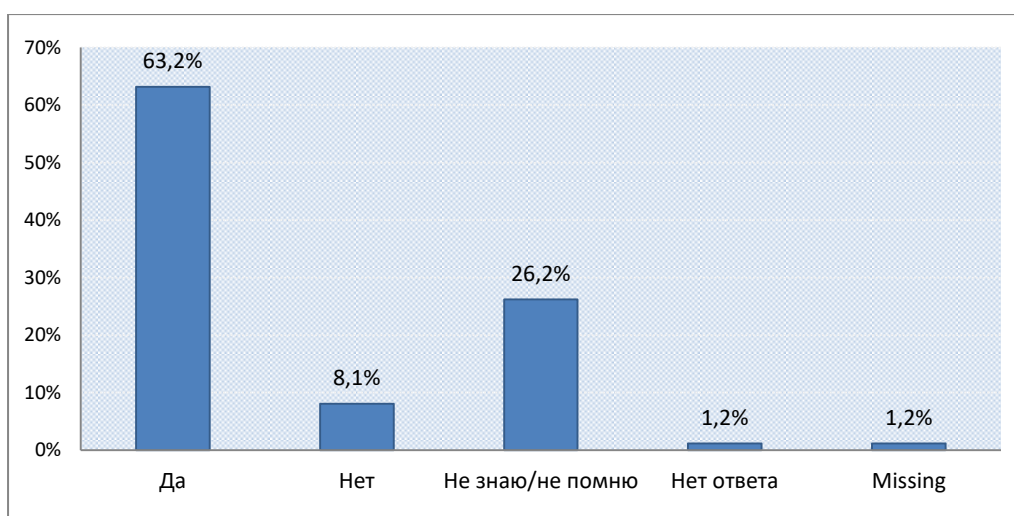
Fig. 1. Possibility to obtain integrated services at the site of ARV therapy provision.



Инфекционист	Infectious disease specialist
Психолог	Psychologist
Консультант равный-равному	Peer consultant
Не знаю/не помню	Do not know/do not remember
Гинеколог	Gynecologist
Нет ответа	No answer

63,2% of PWID/PLHIV believe that during one visit they can also see other specialists as well, while 26% are not aware of this possibility.

Fig. 2. The share of PWID/PLHIV who are aware of the possibility to see other specialists during the visit to their attending physician.



Да	Yes
Нет	No

Не знаю/не помню	Do not know/do not remember
Нет ответа	No answer

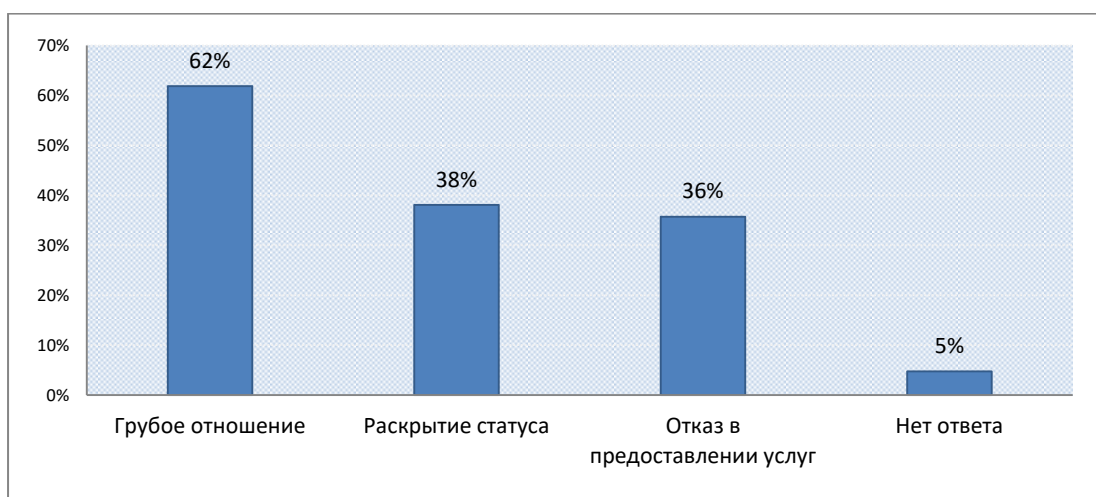
The healthcare providers attitude towards PLHIV

For development of compliance in PLHIV, it is extremely important to take into account the attitude to them in the governmental institutions. Stigmatizing attitude of the doctors, discrimination, refusal to provide special care — dental, surgical, etc. have negative consequences for PLHIV. The quality of the services provided (negative impression of medical care) causes unwillingness to apply for care again.

The vast majority of the respondents (94.4%) say that the healthcare professionals of the medical institution they're registered with are friendly towards them, in the opinion of 3.1% of the respondents their attitude is neutral, and the other 4 persons experienced either rude or indifferent attitude.

13% (42) of the patients reported difficulties when applying to other specialists due to their HIV status (Family medicine centers, hospitals, etc.) Of them, 62% further reported that they experienced rude attitude, 38% complained about the disclosure of their status, and 36% were refused services.

Fig. 3. The healthcare providers attitude towards PLHIV.



Грубое отношение	Rood attitude
Раскрытие статуса	Status disclosing
Отказ в предоставлении услуг	Refuse to provide services
Нет ответа	No answer

Visiting nurces

In the medical institutions included into the Study where the PLHIV are registered, the visiting nurces jobs were provided, whose functions include: efforts to develop the patients' compliance to ARV therapy, including their friends and relatives, general patient care, performance of administrations, search for PLHIV, who have not visited their medical facility for a long time, etc. The visiting nurces may visit the patients at home only with a written consent of the patient at each site. According to the interview with the key person, most PWID/PLHIV refuse the visits of the visiting nurces.

In total, 12 visiting nurces work at the sites under study, with the following breakdown by the sites:

- City AIDS control & prevention center — 4
- Osh regional AIDS control & prevention center — 3
- Family Medical Center, Zhaiyl district — 1
- Family Medical Center, Ysyk-Ata district — 2
- Family Medical Center, Sokuluk district — 2

The visiting nurses services cover 30 (9.3%) patients with the biggest coverage at two sites: Osh city (18%) and Zhaiyl district (15%).

Fig. 4. PWID/PLHIV visited by visiting nurses.

Medical establishment	visited by visiting nurse		Sample size
	Number	%	
City AIDS control & prevention center	3	3%	90
Osh AIDS control & prevention center	14	18%	77
Family Medical Center, Sokuluk district	3	6%	50
Family Medical Center, Zhaiyl region	6	15%	40
Family Medical Center, Ysyk-Ata district	4	6%	64
Total	30	9.3%	321

The respondents listed all the services and types of care provided by the visiting nurses during their visits. The most frequently provided service is advice on ARV therapy (70%).

Fig. 5. The visiting nurses services.

Services and assistance	Number	%
Advice on ARVT issues	21	70%
No care provided	10	33%
Training the family members in right care for PLHIV	9	30%
Reminder to daily take the medicines	9	30%
Training in the proper performance of the medicinal administrations	8	27%
Assessment of compliance to ART	7	23%
Reminder of the necessity to collect the medicines	7	23%
Performance of the physician's instructions	7	23%
Assessment of the needs in terms of ARVT	6	20%
Control over the medicines intake	6	20%
General care for PLHIV	3	10%
No answer	5	17%
TOTAL	30	100%

PWID/PLHIV also reported other services of the visiting nurses: blood sampling, advice on medical services and other diseases, reminder of the medical tests delivery, referral to medical specialists, referrals to the examinations, an invitation to visit the Family medicine center, delivery of ARVs, delivery of syringes and condoms, collection of the documents copies.

Side effects during intake of ARVs and assistance provided by the healthcare professionals

Side effects

The occurrence of side effects is a well-known cause of decreased compliance to treatment. Toxicity (hepatotoxicity) and side effects of ARVs, their interaction with other medicines or substances can aggravate the patients' health condition. Some side effects become quite a serious problem right after the start of treatment, but later on, as a rule, after a short period of time, they disappear. These side effects may manifest as headache, indigestion, poor health, restless sleep, or altered states of mind. It is important for the patient to know in advance about possible side effects, how to cope with them, and where to seek urgent advice.

In the Study, among the patients who self-interrupted their ARV treatment, 29% reported that in their past medical history they had interrupted treatment because of side effects. Currently, 67 patients

(22.3%) reported side effects associated with ARVs administration, the most common being nausea, impaired coordination, and sleep disorder.

Fig. 6. The reasons for the treatment interruption by PWID/PLHIV treatment (among the Study participants)



Тошнота	Nausea
Нарушение координации	Impaired coordination
Нарушение сна	Sleep disorder
Депрессия	Depression
Боли в области печени, сухость во рту, понос,...	Pain in liver, dry mouth, diarrhea, ...
Плохое самочувствие, интоксикация, слабость	Feeling sick, intoxication, weakness
Рвота	Vomiting
Головокружение	Dizziness
Головная боль	Headache

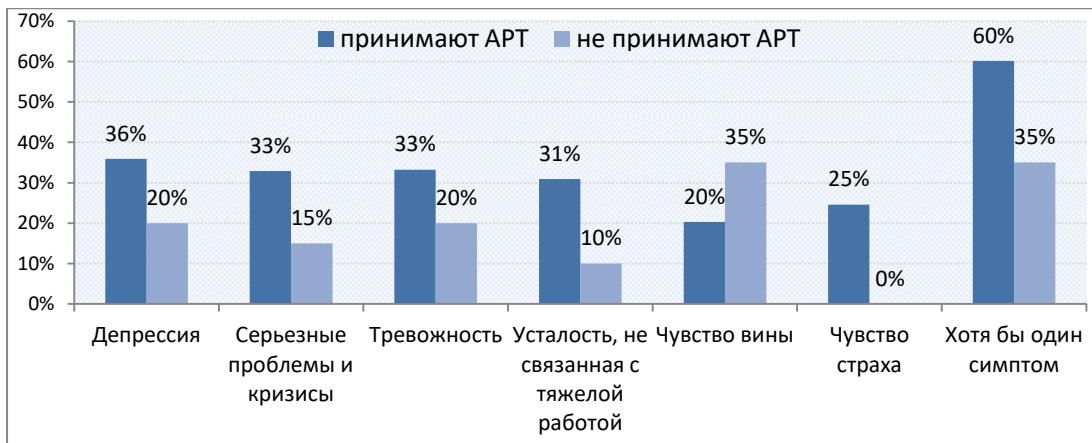
Assistance provided by the healthcare professionals in the event of side effects

Of 67 patients who experienced side effects, 53 (79.1%) said that the attending physician help them treat such effects, while 16.4% of the respondents do not obtain such care, and 3% could not answer thus question.

Depression and psychological problems

Problems with mental health, severe problems and crises, as well as depressed states affect compliance. A high level of anxiety, according to the studies data, directly correlates with the level of non-compliance to ARV therapy. Fatigue from prolonged intake of medicines, from the need for uninterrupted self-control cause failure or disruption of the therapy regimen. Sometimes it is even better to undergo treatment for depression before starting ARV therapy. Also, the patients who take ARVs sometimes have a depressed state or irritability. Analysis of the data showed that depression, severe problems and crises, anxiety, fatigue, not associated with hard work, sense of guilt, and feelings of fear are much more common among those who take ARV therapy. At least one of these manifestations is observed twice as often among patients on ARV therapy (60%) compared to the group of patients who do not receive treatment (35%).

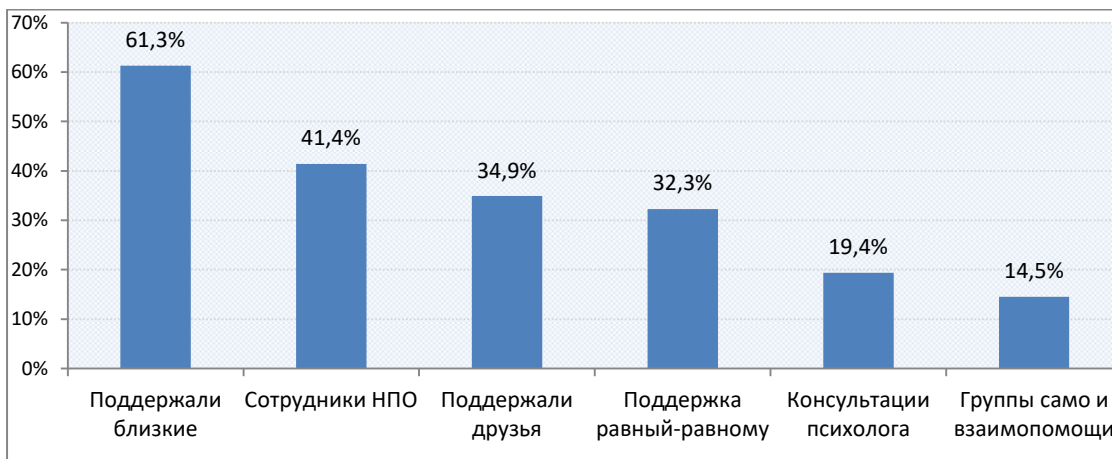
Fig. 7. Psychological problems in PWID/PLHIV



Депрессия	Depression
Серьезные проблемы и кризисы	Serious problems and crises
Тревожность	Anxiety
Усталость, не связанная с тяжелой работой	Fatigue, not associated with hard work
Чувство вины	Sense of guilt
Чувство страха	Feelings of fear
Хотя бы один симптом	At least one symptom

If the above problems occur, 82.1% of the patients receiving ARVs receive assistance from different sources, which major share is their relatives (61%). It's also worth mentioning the assistance and support from the NGO staff (41.4%), peer consultants, specialists, and friends.

Fig. 8. Sources of assistance and support of PWID/PLHIV in case of problems.

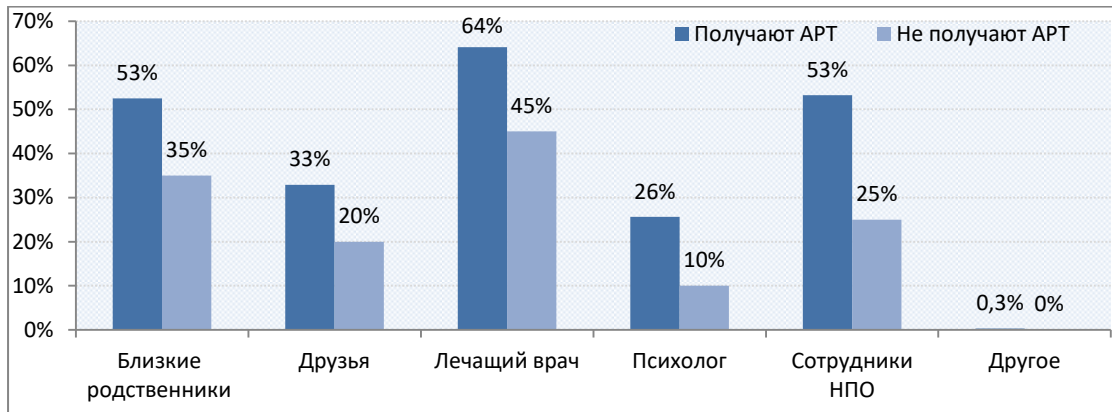


Поддержали близкие	Supported by family members
Сотрудники НПО	NGO employees
Поддержали друзья	Supported by friends
Поддержка равный-равному	Peer-to-peer support
Консультации психолога	Psychologist's consultations
Группы само и взаимопомощи	Self-care groups, peer support groups

Obtaining assistance and support from the family members, NGO employees and healthcare professionals

The majority of PWID/PLHIV (85%) say that in their environment there are people who are aware of their HIV status and provide them with all kinds of support. The patients on ARV therapy receive help more frequently (86%) than the PWID/PLHIV group not receiving ARVT.

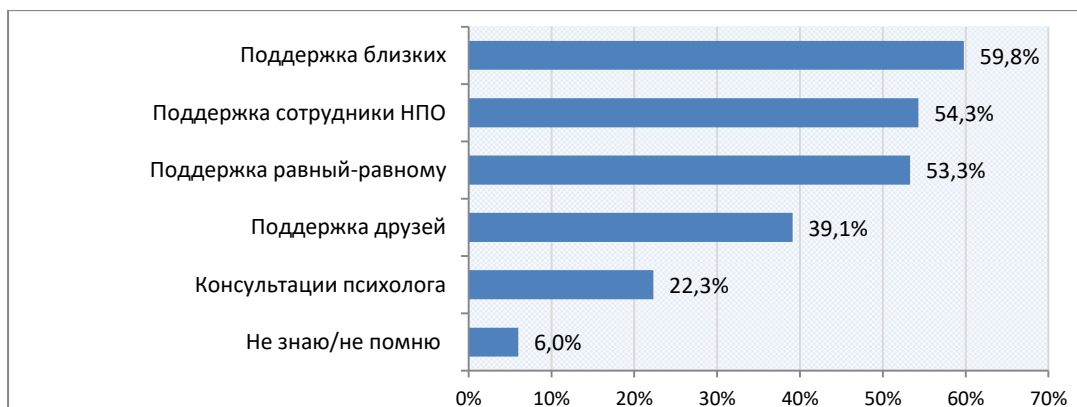
Fig. 9. Obtaining assistance depending on the ARV therapy administration status.



Получают АРТ	Take ARVT
Не получают АРТ	Do not take ARVT
Близкие родственники	Close relatives
Друзья	Friends
Лечащий врач	Attending physician
Психолог	Psychologist
Сотрудники НПО	NGO employees
Другое	Other

In the environment of 57% of the respondents there are PLHIV compliant to ARV treatment, supported in their compliance by such factors as: support of relatives (59.8%), NGO employees (54.3%), peer consultants (53.3%), friends (39.1%), and psychologist's advice (22.3%).

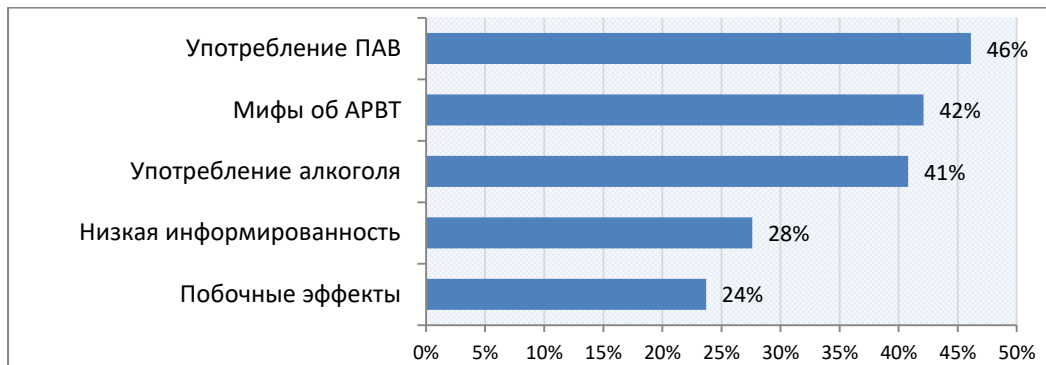
Fig. 10. The factors for maintaining compliance to ARV therapy (according to PWID/PLHIV).



Поддержка близких	Supported by family members
Поддержка сотрудники НПО	Supported by NGO employees
Поддержка равный-равному	Peer-to-peer support
Поддержали друзья	Supported by friends
Консультации психолога	Psychologist's consultations
Не знаю/не помню	Do not know/do not remember

Along with the compliant PLHIV, among friends and relatives of 78 respondents (24.3%) there are also PLHIV, who are not compliant to ARV therapy, who, in opinion of the respondents, refuse ARV therapy due to drug use (46%), belief in the myths about ARVT (42%), alcohol consumption (41%), low awareness (28%), and side effects (24%).

Fig. 11. The factors decreasing compliance to ARV therapy (according to PWID/PLHIV).

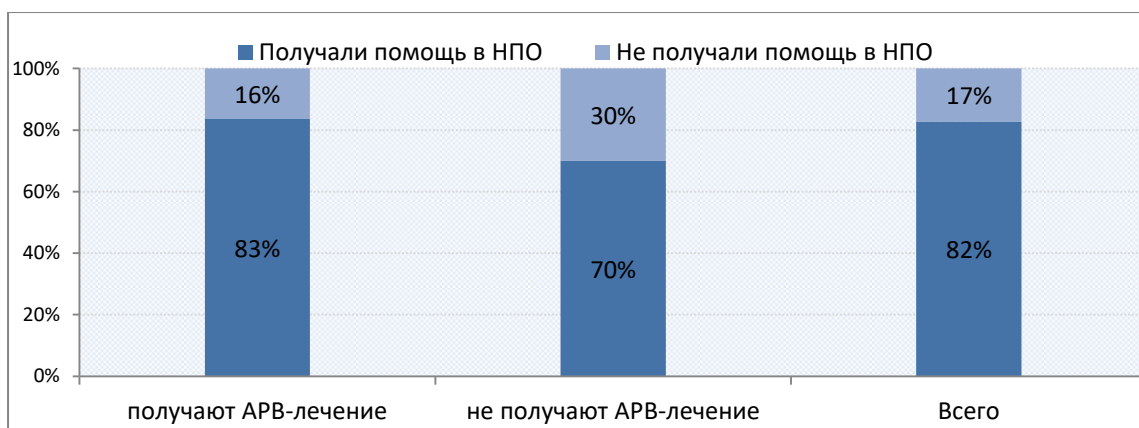


Употребление ПАВ	PAS consumption
Мифы об АРВТ	Myths about ARVT
Употребления алкоголя	Alcohol consumption
Низкая информированность	Low awareness
Побочные эффекты	Side effects

Public support (AIDS service organizations providing comprehensive care for PLHIV) creates more favorable conditions for individual client-focused performance and motivation for treatment, etc.

ARV-receiving patients are to a greater extent covered by NGO services.

Fig. 12. Coverage with NGOs services depending on the status of ARV therapy.



Получали помощь в НПО	Received assistance from NGO
Не получали помощь в НПО	Received no assistance from NGO
получают АРВ-лечение	receive ARV therapy
не получают АРВ-лечение	receive no ARV therapy
Всего	Total

When studying the range of the services received at NGOs, it was observed that those PLHIV-PWID who take ARV treatment are more active in receiving the NGOs services.

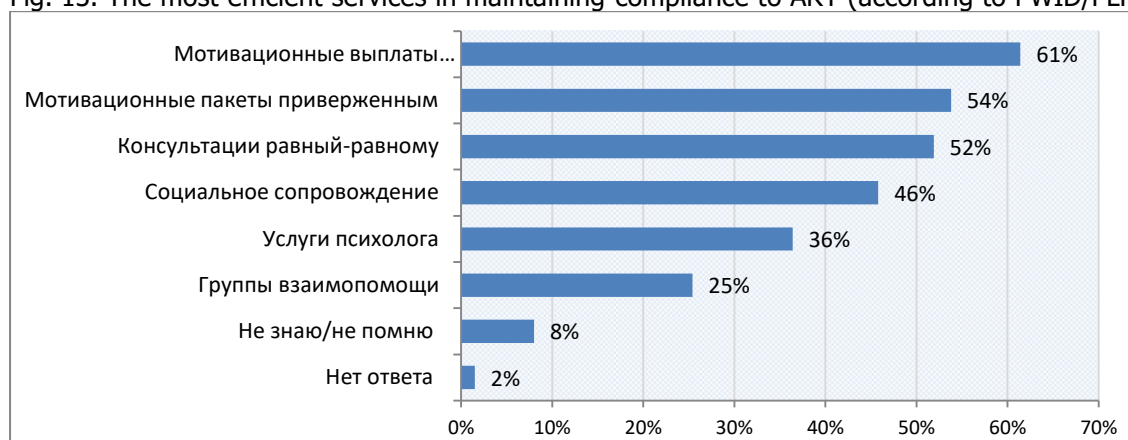
Table 8. Access to services depending on the status of ARV therapy.

	receive ARV therapy		receive no ARV therapy	
HIV testing	50	20%	4	29%

Peer support groups	84	34%	1	7%
Peer-to-peer counseling	140	56%	8	57%
Incentive payments to compliants	151	60%	0	0%
Incentive packages to compliants	187	75%	0	0%
Psychologist's services	86	34%	2	14%
Social support	124	50%	6	43%
Received syringes	10	4%	11	79%
Do not know/do not remember	1	0%	0	0%
no answer	0	0%	0	0%
total	264		14	

According to the respondents, the NGOs most efficient services in maintaining compliance to ART are the services of tangible nature: incentive payments, incentive packages, and peer-to-peer counseling, but they did not exclude such services as social support, psychologist's services, and peer support groups.

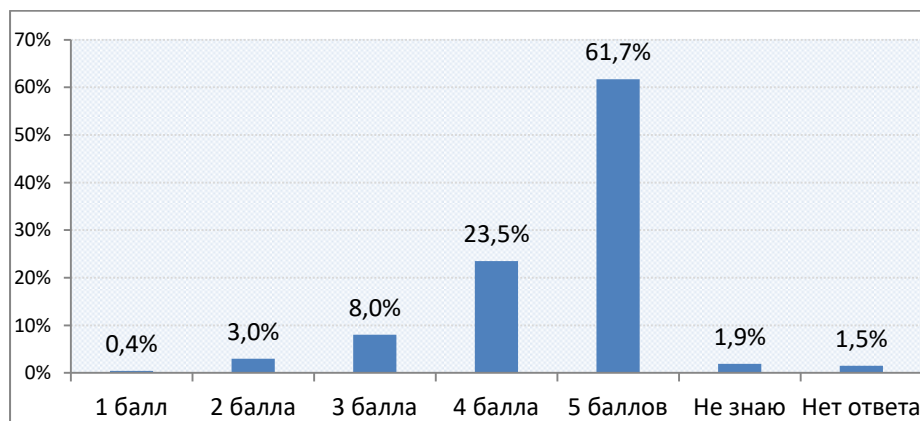
Fig. 13. The most efficient services in maintaining compliance to ART (according to PWID/PLHIV).



Мотивационные выплаты	Incentive payments
Мотивационные пакеты приверженным	Incentive packages for compliants
Консультации равный-равному	Peer-to-peer consultations
Социальное сопровождение	Social support
Услуги психолога	Psychologist's services
Группы взаимопомощи	Peer support groups
Не знаю/не помню	Do not know/do not remember
Нет ответа	No answer

Most of the PWID/PLHIV (85,2%) assessed NGO services 4 and 5 points.

Fig. 14. NGO services assessment by PWID/PLHIV.



балл	point
балла	points
Не знаю	Do not know
Нет ответа	No answer

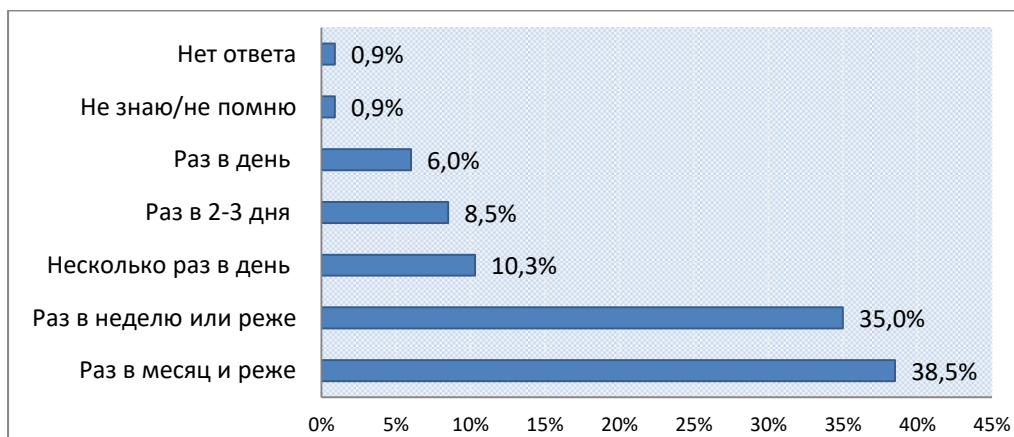
Consumption of psychoactive substances (PAS)

As known, alcohol and psychoactive substances have a toxic effect on the body. Also, with the use of these substances, the antiretroviral therapy efficiency decreases, compliance to treatment decreases due to development of depressive states, and various side effects develop (primarily associated with the combination of the antiretroviral medicines and alcohol toxic effects on the liver) that require additional examination and administration of additional medicines. Most of all, hepatotoxicity is possible in case of treatment of patients with HIV and hepatitis C co-infection⁵ [1,2,3,4,5].

Furthermore, compliance to treatment can be complicated for the persons who have an unstable lifestyle due to consuming PAS, because under the influence of narcotics and alcohol the probability of missing a dose increases.

Almost all respondents overuse alcohol, of which 59.8% drank alcohol from once a week to several times a day.

Fig. 15. Frequency of drinking alcohol by PWID/PLHIV for the last 30 days.



Нет ответа	No answer
Не знаю/не помню	Do not know/do not remember
Раз в день	Once a day
Раз в 2-3 дня	Once every 2-3 days
Несколько раз в день	Several times a day
Раз в неделю или реже	Once a week or less often
Раз в месяц и реже	Once a month and less often

24 PWID/PLHIV (7,5%) used injection drugs in the last 30 days.

1. AIDS. 2008. – № 2: 109-128.

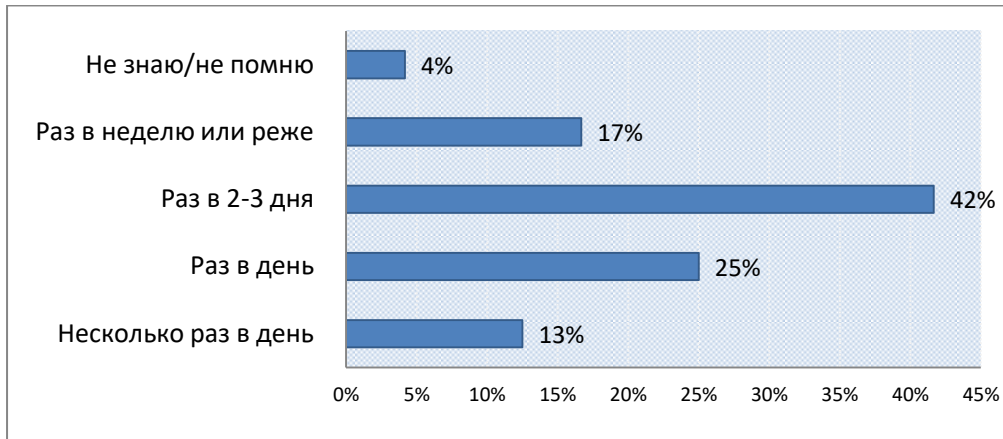
2. **Nuñez MJ, Martín-Carbonero I, Moreno V, Valencia E, García-Samaniego J, Gonzales-Castillo J, et al.** Impact of antiretroviral treatment-related toxicities on hospital admissions in HIV infected patients. *AIDS Res Hum Retroviruses* 2006; 22: 825-829.

3. **Patella F, Baker R, Moorman A, Chmiel J, Wood K, Brooks J, et al.** Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. *J Acquir Immune Defic Syndr.* 2006; 43:27-43.

4. **Tuldra A et al.** Prospective randomized two-arm controlled study to determine the efficacy of a specific intervention to improve long-term adherence to highly active antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes*, 2000, 25(3):221–228.

5. **Walsh JC et al.** Reasons for nonadherence to antiretroviral therapy: patients' perspectives provide evidence of multiple causes. *AIDS Care*, 2001, 13(6):709–720.

Fig. 16. Frequency of injecting drugs by PWID/PLHIV in the last 30 days.



Не знаю/не помню	Do not know/do not remember
Раз в неделю или реже	Once a week or less often
Раз в 2-3 дня	Once every 2-3 days
Раз в день	Once a day
Несколько раз в день	Several times a day

64 PWID/PLHIV (54,7%), who receive ARV treatment, earlier were imprisoned.

PWID/PLHIV sexual partners

The number of non-regular sexual partners in the last 12 months: 64 respondents (19.9%) confirmed having non-regular sexual partners with whom they had sex once or several times (including sex for money). The average number of sexual partners is 4.8, median 3, minimum 2, maximum 20.

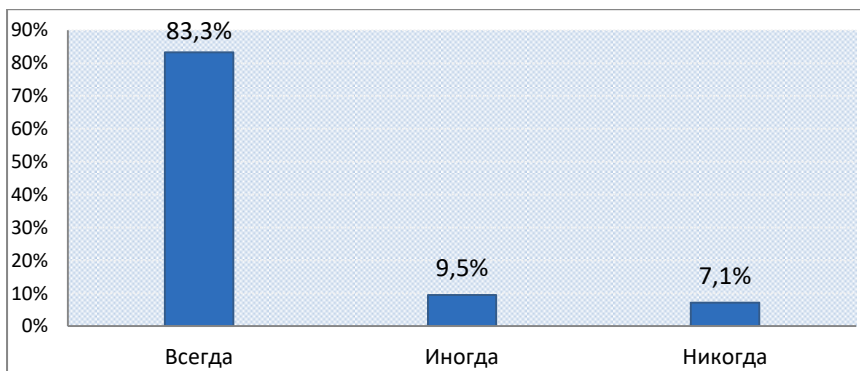
The number of spouses/partners in the last 12 months

When asked about the marital status at the beginning of the survey, 49% answered that they had either a legal or a civil spouse. When asked about having a legal or a civil spouse, 51.4% of the respondents answered affirmatively, of them 98% had one spouse, three had two spouses (2%), and one PLHIV had three spouses/partners.

Using condoms with sexual partners

Among those who had sex with non-regular sexual partners in the last 12 months, 16.6% of the respondents practiced dangerous sexual behavior (did not use a condom at all or used it occasionally).

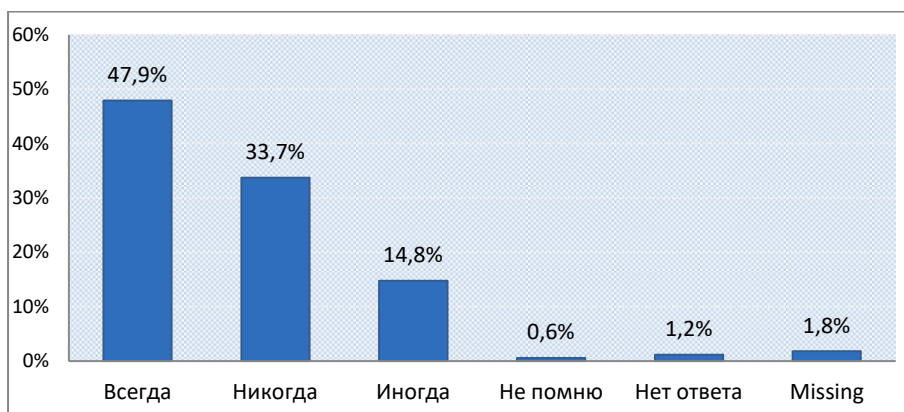
Fig. 17. Using condoms with non-regular sexual partners.



Всегда	Always
Иногда	Sometimes
Никогда	Never

Among the respondents who had spouses/partners in the last 12 months, 48,5% of the respondents practiced dangerous sexual behavior (did not use a condom at all or used it occasionally).

Fig. 18. Using condoms with regular sexual partners.

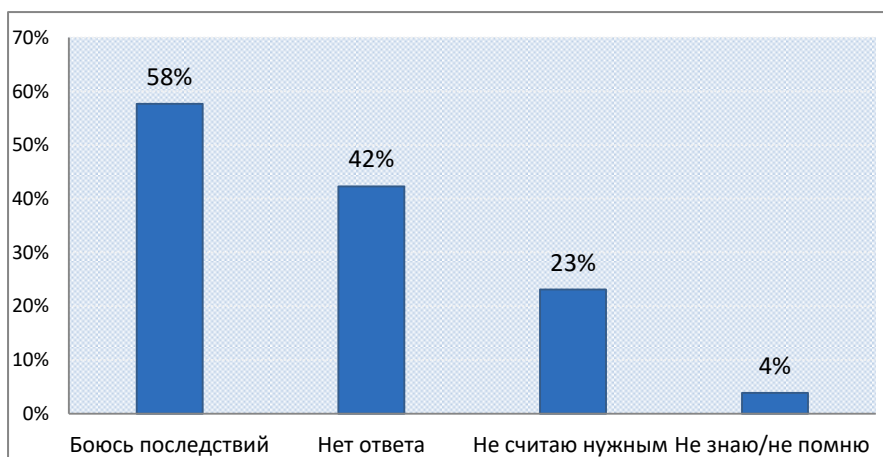


Всегда	Always
Иногда	Sometimes
Никогда	Never
Не помню	Do not remember
Нет ответа	No answer

Disclosing the status to a legal spouse/partner

Few respondents (15.4%) did not disclose their HIV status to their spouse/partner mainly because of the fear of consequences, 23% do not consider it necessary, the rest did not answer this question.

Fig. 19. The reasons preventing disclosing HIV status to a regular sexual partner.



Боюсь последствий	Afraid of consequences
Нет ответа	No answer
Не считаю нужным	Do not consider it necessary
Не знаю/не помню	Do not know/do not remember

When asked what may help them disclose their HIV status to their spouse/partner, 38% of the respondents found it difficult to answer this question, 19% they said they were not ready to disclose or were not going to disclose, the rest listed the physician's assistance (23%), the psychologist's assistance (15%), and a peer consultant's assistance (15%), 8% did not answer this question.

143 respondents (84.6%) know the status of their legal spouse/partner, i.e. 15.4% are not aware of the status of their partner.

Of 143 PLHIV, 54 have partners with HIV-positive status (37.8%), 86 have partners with HIV-negative status (60.1%), two have partners with unknown HIV status (1.4%).

Of 86 HIV-negative spouses/partners, 78 respondents were tested for HIV (90.7%), i.e. 5% of the spouses/partners are still not tested, 4.6% do not know the test findings.

Since the last HIV-test of a spouse/partner, as of November 01, 2017, an average of 10.7 months elapsed, a median of 5 months, a minimum of 1 month, and a maximum of 3.9 years.

Of 169 PWID/PLHIV who have a spouse/partner, 11.8% have the partners who inject drugs.

The reasons for refusal ARV therapy

Of 20 PWID/PLHIV who answered that they did not receive ARV treatment, 14 respondents were recommended ARV therapy and they refused treatment mainly due to the sense of well-being (7 persons), do not want to be an "experimental rabbit" (3), others doubted the treatment efficiency (2), feared side effects (2), feared that the medicine stock might come to an end and feared the respective consequences (2), indifference to their own health (1), doubt in their own ability to correctly take ARVs (1), someone became sick (1), and one PLHIV was preparing for the initiation of ARV treatment.

When asked about what could help them initiate ARV treatment, the respondents listed the following factors:

- Information about the benefits of therapy — 3
- Employment — 4
- Positive attitude and support of other people — 2
- Own housing — 1
- Positive own attitude towards therapy — 2
- Stable psychoemotional condition — 3
- Desire to live — 4
- Availability of psychological assistance — 1

8.3. The deliverables of the survey among healthcare professionals (physicians, visiting nurses)

The healthcare professionals who perform a wide range of roles and responsibilities in the HIV treatment and care system were interviewed in order to collect more detailed information about PLHIV services delivery routine processes, HIV education (including the issues of stigma and discrimination, compliance to treatment), monitoring, social support services, referral to other services and the existing difficulties. 15 physicians who provide regular medical check-ups, treatment, and follow-up of PLHIV, and 6 visiting nurses available at the time of the data collection were surveyed.

According to the clinical protocol dated 16.10.2017, the functional duties of the infectious disease doctor responsible for HIV, include:

1. Post-test advice in case of detection of HIV infection and regular medical check-ups.
2. Provision of treatment and preventive care.
3. PLHIV (clinical and laboratory monitoring of PLHIV) along with coordination of the primary healthcare providers (family doctors, paramedics of rural health posts, Joint Practice/Family Medicine Centers).
4. Providing PLHIV with supportive counseling in terms of development of compliance to regular medical check-ups and monitoring the PLHIV scheduled visits to healthcare establishments.
5. Counseling PLHIV on the healthy lifestyle issues.
6. Coordination of the efforts of the primary healthcare providers (family doctors, paramedics of rural health posts, Joint Practice/Family Medicine Centers) in provision of PLHIV with antiretroviral therapy

(preparation, administration, release, assessment of compliance to treatment, monitoring of its efficiency, timely identification and arresting of side effects), participation in counseling.

7. Assistance in PLHIV hospital admission if required.

8. Proper management of the medical records, its filling in and storage in compliance with the principles of confidentiality.

9. Ensuring interaction with the healthcare specialists of various specialties (dermatovenerology, narcology, phthysiology, etc.) in order to address medical problems, as well as with the social development agencies to provide social assistance to PLHIV and the children born to mothers with HIV, as well as with NGOs.

10. Provision of palliative care for those PLHIV who need it.

11. Maintaining the database through collecting and filling out clinical data from the patient's outpatient card into the health cards and entering into the e-monitoring system according to the standards of the HIV e-monitoring system for the region, issuance and submitting HIV reports in accordance with the approved forms.

12. Monitoring and assessment of the performance of the therapeutic and preventive work on a regular basis.

13. Use in practice of the new methods for the prevention, diagnosis, and treatment of HIV infection.

14. Providing information about HIV infection to general and specific population groups.

Furthermore, according to the new clinical protocol, adults and adolescents living with HIV should be clinically screened for TB symptoms at each healthcare facility visit.

The medical examination for active tuberculosis shall be carried out in case of the following four symptoms:

- current cough;
- body heat;
- body weight loss;
- night sweat.

All PLHIV, if suspected of tuberculosis, should be screened in accordance with the diagnostic algorithm, in order to confirm or exclude tuberculosis.

During the survey, the healthcare professionals specified their functional responsibilities: referral for testing for CD4 and determining the viral load; determining the stage of HIV infection; conducting discussions on HIV prevention with discordant couples of PLHIV; outpatient examination of PLHIV; screening for TB symptoms; control over ARVT intake; screening, diagnosis, and treatment of STD; briefings for PLHIV, counseling before and after the test, referral to other specialists, diagnosis of HIV infection.

Within their job responsibilities, the visiting nurses provide care and support to PLHIV patients, including: advising PLHIV on treatment, assessing the needs and requirements of the patients for treatment, monitoring compliance to the treatment regimen and assessing compliance to ARV therapy. Furthermore, most of the interviewed nurses noted that they educate the patients at home to properly take the medicines administered, to provide general care for the patient and to perform the medical prescriptions. Among other responses, the respondents mentioned palliative care and carrying out various medical procedures (blood pressure measurement, injections).

Diagnostic tests performed at an outpatient facility prior to initiation of ARVT according to the HIV infection clinical protocol

- general blood analysis (hemoglobin, platelet and erythrocyte count, leukocyte formula, ESR);
- common urine analysis;
- biochemical parameters of liver function (ALT, AST, bilirubin);
- cholesterol, HDL, LDL;
- ELISA test for hepatitis C (anti-HCV) and hepatitis B (HBsAg);
- ELISA test for syphilis (for medical reasons);
- pregnancy test (for women of reproductive age);
- serum creatinine and estimated glomerular filtration rate (eGFR);
- chest X-ray (for medical reasons);

- ECG (for medical reasons);
- ultrasound of the abdominal cavity (for medical reasons);
- GeneXpert (according to the TB diagnostic algorithm), sputum smear microscopic evaluation.

Of the tests to be performed prior to ARV therapy administration, most of the physicians who monitor PLHIV mention the following: viral load tests, CD4 count, general blood test, biochemical blood test, urine analysis, and fluorography. Besides, it was noted that, whenever required, ultrasound of internal organs, liver tests, and ECG are administered. The physicians did not specify such tests as cholesterol, hepatitis ELISA tests, a pregnancy test (in women of reproductive age), serum creatinine.

It is required to be consulted by a specialist in case of a clinical indication. The specialists' counseling shall not be provided on a mandatory basis.

Indications for the specialists' counseling based on the Clinical Protocol

- The experts of the regional AIDS Control and Prevention Center or district AIDS Control Center: signs of/suspected ARVT inefficiency, change of ARVT;
- Infectious diseases specialist: signs of/suspected opportunistic infections, viral hepatitis;
- Phthisiatrician: signs of/suspected tuberculosis, MAC complex;
- Neuropathologist: signs of/suspected cryptococcal meningitis, HIV-encephalopathy, toxoplasmosis of the CNS, PML, brain lymphoma, peripheral polyneuropathy;
- Psychiatrist: signs of/suspected mental disorder, depression, HIV-encephalopathy/dementia;
- Psychotherapist (psychologist): in case of psychological problems;
- Ophthalmologist: signs of/suspected retinitis (examination of the fundus, especially with a low number of CD4 lymphocytes < 100 cells/μl);
- Cardiologist: signs of/suspected cardiomyopathy;
- Oncologist: signs of/suspected malignant neoplasm;
- Gynecologist: signs of/suspected cervical cancer;
- Other specialists — for medical reasons.

According to the survey findings, about a third of the respondents said that advice from a phthisiatrician and a psychologist is required before ARVT administration. PLHIV are referred to other specialists, such as a neurologist, a narcologist, a cardiologist, a psychiatrist, a gynecologist, etc. for advice whenever required, i.e. in case of complaints or clinical indications.

Difficulties and obstacles on the way to ARVT

The main obstacles to receiving ARV therapy were reported the lack of PLHIV willingness for treatment and active drug use. Few respondents mentioned the other reasons which prevent administration of ARV therapy: the lack of citizenship and registration, legal proceedings against patients, because this has little effect on the physician's decision to initiate ARV therapy. Inter alia, the problems with administration of ARV therapy are caused by discrimination on the part of relatives and friends or inability to take the medicines because of relatives' unawareness of the patient's status.

In the opinion of all the professionals surveyed, during the current year there were no problems in administering and/or releasing ARVs, such as inadequate medicines supply, unavailability of one or several medicines due to supply failures, problems within the supply chains, or rise in the medicines price.

The events of changes/adjustments to the therapy regimen

According to the answers of the healthcare professionals, adjustments or changes to the treatment regimen in most cases are made in the absence of the effect from the previous treatment regimen, or in the event of severe side effects, as well as the medicine intolerance by the patient. Only a little more than one third of the respondents reported the lack of the required medicines; apparently, the reason is that recently the problems have become irrelevant, because the medicines are being purchased by the Global Fund at its own expense. Furthermore, it was noted that each situation requires an individual approach; also, the regimen should be adjusted if the viral load remains high for a year after commencement of the ARVs intake.

Administration of ARV therapy to PWID/PLHIV, PWID/PLHIV who receive OST and/or TB therapy

The most important key point is assessment of the PLHIV willingness to start and continue ARVT. From awareness of the problem before starting ART, the patient goes through the way consisting of five stages. Understanding the stage of the patient's willingness is determined by the physician with special methods.

The respondents say that the following factors shall be considered during assessment of the patient's willingness:

- duration of the medicines intake;
- ability to comply with the treatment regimen (dosage, frequency of intake, time of intake);
- the dose of heroin if the patient consumes drugs,
- depression in a patient which prevalence among PLHIV is much higher (20-40%) than among the general population (7%). Development of depression significantly reduces the patient's capacity and weakens the treatment efficiency. Screening for depression should be done every 1-2 years;
- participation in the OST program, which, according to the experts, can have effect on compliance to treatment;
- an OST participant's methadone dose;
- affective disorders;
- PWID remission stage;
- duration of remission;
- housing conditions.

According to the 2017 Clinicap protocol, all PLHIV with diagnosed tuberculosis need treatment for both TB and HIV infection, regardless of the number of CD4 cells. As a rule, TB treatment in PLHIV should be considered a priority and begin as soon as possible after the TB diagnosis, without waiting for the results of determining the biological agents drug resistance. The treatment of tuberculosis rapidly reduces the tuberculosis-related mortality, and stops the transmission of TB.

9 of 15 respondents said that they had refused ARV therapy. The reasons for the refusal of therapy in most cases were the use of alcohol and drugs, denial of the "HIV infection" diagnosis, development of side effects, as well as the depression and the patient's age (elderly patients are more likely to refuse).

The factors which influence compliance

The factors which could potentially affect the patient's compliance to ARV therapy and follow-up are classified according to the nature of their occurrence into socio-economic/socio-demographic, organizational, psychological/individual, medical, etc.

So, among all these factors within the survey, the respondents listed the grade of tolerance of the friends, relatives, and physicians to PLHIV; comfortable family life and available housing; and, finally, availability of the medicines, reliable information about HIV infection, and public support. Furthermore, an important factor which influences the compliance is the PLHIV marital status.

The respondents said that an important aspect in supporting compliance to ARVT is the coordinated performance of medical and non-medical services. Also, the vast majority of the respondents mentioned the consistency in the provision of services and the level of their quality.

Among the individual, psychological factors which affect compliance, all the respondents noted consumption of drugs or alcohol, and most of them mentioned such factors as the patient's state of health/condition, additional family obligations of the patient (minors, night work, etc.), severity of side effects, the patient's psychological state, awareness of the need for therapy, incentive, and self-assessment of the patient.

Among the medical factors which affect compliance to therapy, the vast majority of the respondents noted opportunistic infections, right selection of the treatment regimen, the medicines' hepatotoxicity.

NGO services

The healthcare professionals have listed the following range of services provided by NGOs: peer support groups, peer-to-peer counseling, incentive payments to compliants, incentive packages for the compliants, and psychologist's services. Among other services, they listed information sessions and information as a whole, social support for referring PLHIV to other service organizations.

Drug addiction treatment

More than half of the respondents mentioned that drug addiction treatment is provided, about a quarter said that treatment is not provided, and some respondents could not answer this question. Among the drug addiction services for PWID/PLHIV before initiating ART, most of the respondents listed methadone maintenance treatment, peer counseling, self-care groups, and peer support groups.

Just a third of the respondents knew about detoxification therapy with methadone, less than a quarter of the respondents knew about rehabilitation, and the same number of the respondents knew about classical detoxification therapy (medical arrest of the abstinence syndrome). The drug addiction rehabilitation service in the required scope is currently virtually unavailable in the country, because this is a costly service and the international donors do not fund this activity.

Just few respondents knew that in the event of administration of ARVs to active PWID/PLHIV, the prevention of relapse of drug addiction is provided. The interviewed specialists could not specify the medicines used to prevent relapses.

Patients with hepatitis C co-infection

Making decision to initiate treatment for hepatitis C by PLHIV is more complex than in patients with hepatitis C single infection, because the response rate to treatment is lower, the risk of possible toxic effects is higher, the treatment is complicated by high medical burden, cross-toxicity, and interaction of the medicines used to treat hepatitis C and HIV.

The vast majority of the respondents mentioned high prevalence of HCV among PWID/PLHIV. Only one third of the interviewed specialists are treating HCV simultaneously with ARVT. According to the respondents, the main clinical indicators to be considered by a physician in administration of treatment for hepatitis C for PLHIV patients, is hepatic cirrhosis and viral load. Some respondents in administration of HCV treatment consider the patient's financial capacity (until recently, there was no free HCV treatment in Kyrgyzstan, and only from 2018 this service will be provided for PLHIV free of charge), hepatotoxicity of the medicines, liver tests values, and hepatologist's recommendations.

Assessment of compliance

Most respondents said that the assessment of compliance is carried out by calculating the ratio of the number of the tablets administered to the number actually taken, and just few respondents said about a survey based on Morisky-Green questionnaire.

For the purpose of development and maintenance of the patients compliance, the visiting nurces daily ring up the patients in order to remind them to take their medicines, as well as advise them of the importance of compliance to ARVT regimen (time, dosage, intervals). Also, the visiting nurces observe a positive effect of the successful treatment cases on other PLHIV, who motivate the patients to make a decision to initiate therapy and maintain compliance. Almost all respondents said that they mainly deliver ARVs, and few added that they also deliver anti-tuberculosis and other medicines for the prevention of tuberculosis and other opportunistic infections.

Half of the interviewed visiting nurces said that they release ARVs once a month. More than half of the patients personally come to pick up their medicines, and for the rest of the PLHIV the medicines are delivered to the place of address. If PLHIV do not come to pick up their medicines on the established day, the visiting nurces ring up such patients or deliver the medicines to the place of address and inform the attending physician thereof. Some nurses practice early phone calls (two days in advance) to remind the patients of the need to come to pick up their ARVs.

Half of the interviewed nurses conduct a weekly survey on compliance to the ARVs regimen.

All visiting nurses perform monthly screening for tuberculosis (asking a standard set of questions about weight loss, temperature, weakness, and cough) and (1 nurse could not answer the question about the frequency of TB screening).

9. Conclusions and assumptions.

9.1. Entry of PWID/PLHIV to antiretroviral therapy

As known, timely linkage to care and early initiation of ARV therapy affect the HIV treatment efficiency in general. When studying in the E-monitoring system a period of time that elapses from confirmation of the diagnosis of HIV infection until linkage to care, the establishment of indications for ARVT and the initiation of ARVT, it has been revealed that in the PWID/PLHIV group it can take 1,5 year both before establishing the indications for ARVT and before the initiation of ARVT, which is much higher than in the PLHIV-non-PWID group, and it evidences the problems with timely linkage to care, as well as with initiation of ARV therapy among PWID/PLHIV. Furthermore, it should be noted that more than half of those who applied for treatment were at HIV stages 3 and 4, which may also evidence late application for treatment. The survey found that problems with timely linkage to care may be caused by certain specifics in PWID behavior associated with PAS consumption, poor post-test counseling, and low awareness of the risks of delaying ARV treatment.

Furthermore, the important point in linkage of the identified PLHIV to care is the epidemiological investigation, which identifies the risk factors of HIV transmission, includes post-test counseling with the mandatory referral of PLHIV to a respective expert for further medical examination. The findings of the survey have demonstrated existence of problems both in terms of insufficient coverage of the identified cases of HIV infection with the epidemiological investigation, and with its quality.

The respondents themselves have determined the following key reasons which have influenced the initiation of ARV therapy: deterioration of the health status, getting a doctor's advice, fear for one's life, fear of infecting others and his/her sexual partner, as well as advice given by an NGO employee.

9.2. Compliance to antiretroviral therapy

The officially estimated compliance to ARV therapy at the national level according to the HIV cases e-monitoring system is 83.7%, ranging from 70.5% in the Chuya region to 100% in the Issyk-Kul region, which considerably differs from the assessment of compliance at five studied sites in the Chuya region and Osh city, which was calculated by adding the given tablets and comparing with the number of ARVT days based on the following formula:

$$\text{Calculation of missings} = \frac{\text{No. of days of taking} - \text{No. of the tablets assigned}}{\text{No. of days of taking}/30}$$

So, the **compliance of 95% or higher was determined in 22% of the patients**, ranging from 12% to 30% broken down by populated localities.

However, studying the dynamics of changes in the level of the viral load and SD-4 count in the HIV infection E-monitoring system among PWID/PLHIV compliant and non-compliant to ARV treatment demonstrated no significant difference between these groups, which may indirectly evidence that so-called compliant patients even if timely receive ARVs, in fact do not take them.

While the proportion of the patients with low compliance based on the calculation results was 78%, during the survey only 25.2% of the respondents reported self-interruption of the medicines intake for a long period. Based on the analysis of the data in the HIV infection E-monitoring system, in total 18% of the patients interrupted ARVT, with PWID/PLHIV interrupting their treatment 1.5 times more often (22%) compared to the PLHIV-non-PWID group (15%).

Furthermore, an analysis of the reasons for the treatment interruption according to the survey data, as well as the information obtained from the Kyrgyz Republic HIV infection E-monitoring system, allowed to conditionally divide them into the following groups:

1. Reasons caused by the experts' poor performance.
2. The patients' state of health.
3. Social factors.
4. Behavioral factors.

The groups of low compliance caused by the experts' poor performance.

- 1) Lack of advice and information from the healthcare professionals, the patients' unawareness of the danger of the therapy interruption.
- 2) Absence of medicines during journeys for any reasons whatsoever (forgot, lost, not enough) was the most common reason for self-interruption of ARV therapy (36%). When investigating into the possible reasons for the lack of the medicines, 50.5% of the patients reported that no one else can receive the ARVs on their behalf if required. Also, 67.4% of the patients reported that they cannot receive ARVs in other institutions of their city or region, and 11.9% did not answer the question.
- 3) Inconvenient visiting hours, and queues represent a huge barrier against getting assistance, especially for PWID patients. For example, during the visits to the doctor of the follow-up department of the AIDS Control Centers or to the infectious diseases physician in the Family Medicine Center, sometimes there are queues in which 32% of the respondents wait from 15 to 30 minutes, and 8% wait for more than half an hour. 26% are not aware of the possibility to see other specialists during the same visit. 13% (42) of the patients reported difficulties when applying to other specialists due to their HIV status (Family medicine centers, hospitals, etc.), including rude attitude, disclosure of their status, refusal to provide services.
- 4) For development and maintenance of compliance in the healthcare facilities where PLHIV are registered, the visiting nurces were employed, but unfortunately the PWID/PLHIV group is extremely poorly covered by this service (9.3%), which is provided only with a written consent of the patient. Perhaps, the low coverage with the visiting nurces services is caused by the lack of access to this group, the lack of experience of the epidemiologists and the medical staff of the AIDS Control Centers/Family Medicine Centers dealing with PWID, as well as the specifics in the behavior of PWID.
- 5) Public support (AIDS service organizations providing comprehensive care for PLHIV) creates more favorable conditions for individual client-focused performance and motivation for treatment. According to the findings of the logistic regression analysis, the chance of low compliance (<95%) was higher among those PWIDs who reported the lack of a peer consultant in the medical institution with which they are registered (OR=1,9, 95% CI 0,94-4,0). Also, it is important to highlight that according to respondents' answers, in case of problems they receive support mainly from their family members, NGO employees (including peer consultants), friends, psychologists, self-care groups, and peer support groups.
- 6) Among the factors which influence compliance, the healthcare professionals and the NGO employees mentioned the need for coordinated efforts of the healthcare professionals, tolerant attitude towards the patients in public institutions, and the quality of the services provided. Also, the specialists understand that it is required to ensure availability and convenience of the services (location, work hours, queues, etc.) for PLHIV.
- 7) Furthermore, it should be noted that the Kyrgyz Republic legislation on accessibility of the treatment in general is favorable for timely therapy, the law "On HIV/AIDS" and the state guarantees program provide guarantees for free ARVT and the treatment of opportunistic infections, the clinical protocols are updated in a timely manner, the required medicines are included into the Essential Drugs List. However, given the importance of the social factors in developing compliance to HIV treatment, such as employment, a permanent place of residence, the legislation in these terms requires improvement.

The patients' health status

- 1) In the Study, among the patients who self-interrupted their ARV treatment (25%), 29% reported that in their past medical history they had interrupted treatment because of side effects. Currently, 67 patients (22.3%) reported side effects associated with ARVs administration, the most common being nausea, impaired coordination, and sleep disorder.
- 2) Problems with mental health, severe problems and crises, as well as depressed states affect compliance. A high level of anxiety, according to the studies data, directly correlates with the level of non-compliance to ARV therapy. Fatigue from prolonged intake of medicines, from the need for uninterrupted self-control cause failure or disruption of the therapy regimen. Analysis of the data showed that depression, severe problems and crises, anxiety, fatigue, not associated with hard work, sense of guilt, and feelings of fear are much more common among those who take ARV therapy. At least one of these manifestations is observed among patients on ARV therapy (60%).

Social factors

- 1) Set up housekeeping, availability of a place of residence and stay facilitate formation of behavior which cause regular medicines intake. Quite the opposite, problems with housing, when PLHIV have to share it with other people or often stay in different places can adversely affect the integrity of the stock of medicines and the regularity of their intake. According to the findings of the logistic regression analysis, the chance of low compliance (<95%) was higher among those living with relatives or renting housing (OR = 2.4, 95% CI 1.1-5.5). Probably, non-disclosure of the HIV status has become the reason for low compliance.
- 2) Also, 20% to 41% of the respondents live at a distance of more than 15 km from the healthcare facility where they receive ARV therapy.
- 3) Among PWID/PLHIV under 40 years of age, the number of non-compliers to therapy is statistically significantly higher. The lack of opportunistic infections also correlates with low compliance. Probably, these two factors are interrelated, as, in fact, among the patients under 40 years of age, 26.5% reported no opportunistic infections, while among the patients over 40 years of age, just 18% had no opportunistic infections. Also, among PLHIV at clinical stages 1 and 2, there are significantly more non-compliers to therapy. Perhaps, the mild course of HIV infection and the absence of complaints about the symptoms of secondary infections have caused irregular visits to the physician.

Behavioral factors

- 1) Compliance to treatment can be complicated for the persons who have an unstable lifestyle due to consuming PAS, because under the influence of narcotics and alcohol the probability of missing a dose increases. According to the respondents, more than half of them overuse alcohol (60%). Moreover, during the analysis of the reasons for the treatment interruption according to the respondents' answers, the second highest prevalence was consumption of psychoactive substances (alcohol or narcotics).
- 2) The so-called patient's decision is also one of the most common reasons for the interruption of ARV therapy (17%), specified by the respondents without any explanation, which may evidence a lack of responsibility for one's own health, and a low compliance to treatment.
- 3) No information about imprisonment in the past medical history in terms of P-value is associated with low compliance as, probably, correctional facilities exercise strict control over PLHIV therapy.

9.3. PWID/PLHIV sexual partners

Development of the recommendations for the prevention of sexual transmission of HIV infection requires awareness of the sexual behavior of PWID/PLHIV. Based on the results of the collected data analysis, 49% of PWID/PLHIV have regular sexual partners, and 20% of PWID/PLHIV have sex with non-regular sexual partners.

Most PWID/PLHIV (85%) are aware of the HIV status of their regular partner, 38% of whom are HIV-positive. PWID/PLHIV practice dangerous sexual behavior with both types of sexual partners (49% of PWID/PLHIV do not use condoms with regular sexual partners and 17% do not use condoms with non-regular sexual partners). The other PWID/PLHIV did not tell their regular partner about their status.

Most PWID/PLHIV (84.6%) are aware of the status of their legal spouse/partner, of whom 37.8% are PLHIV. Of the 86 HIV-negative spouses/partners, the vast majority are tested for HIV (90.7%), while 5% of the spouses/partner are not. Of 169 PWID/PLHIV who have a spouse/partner, 11.8% have partners who inject drugs.

Since the last HIV-test of a spouse/partner, as of November 01, 2017, an average of 10.7 months elapsed, a median of 5 months, a minimum of 1 month, and a maximum of 3.9 years

10. Recommendations

Taking into account the above conclusions, first of all, the measures shall be developed at the national level to improve compliance to HIV treatment, including:

1. Enhancing the competence of the healthcare professionals who provide assistance to and are in contact with PLHIV in terms of post-test counseling, the regulations on the provision of ARVs, other types of medical and social assistance for PLHIV;
2. Introduction of the indicators which allow to assess the quality of post-test counseling by the healthcare professionals;
3. Timing of the workload of the healthcare professionals who provide PLHIV with counseling for the purpose of subsequent determination of the adequate workload on the healthcare professionals, which will allow to provide high quality counseling. If required, considering the allocation of individual staff positions of infectious disease doctors in primary healthcare facilities in order to address socially significant infections;
4. Strengthening the integration of the field healthcare services with non-governmental organizations supporting PLHIV. Enhancing the involvement of peer consultants in the provision of counseling and support services for PLHIV, including with state social order procedures.
5. Ensuring control over timely provision of the medicines for the treatment of opportunistic infections, inclusion of the medicines for side effects into the statutory guaranteed set of medicines.
6. Partial delegation of PLHIV care liaison functions to the employees of non-governmental organizations which have broader access to PLHIV/PWID groups.
7. Strengthening PLHIV social support programs by non-governmental organizations, especially in regions with a high PLHIV concentration.
8. Extending and improving the quality of routine voluntary testing of PWID with mandatory counseling before and after testing.
9. Development and approval of the algorithm for assessing the PWID/PLHIV willingness for entry to ARV therapy.
10. Development and approval of the algorithm for maintaining compliance to ARV therapy in the first weeks of treatment.
11. Modification of the existing algorithm for assessment of PLHIV compliance to ARV therapy (counting methods + change in the viral load level) in order to increase the assessment reliability.
12. Ongoing monitoring of compliance to ARV therapy according to the developed algorithm.
13. Introduction of the bonus system for physicians for maintaining high compliance to ARV therapy (via Compulsory Medical Insurance Fund).
14. Including PLHIV/PWID sexual partners into the PLHIV social support programs (identification, anonymous notification, counseling, testing, linkage to ARV therapy, efforts towards compliance).
15. Extending activities aimed to change the sexual behavior of PLHIV-PWIDs in the course of counseling in the healthcare facilities and NGO services.

16. Introduction of the tools for monitoring the reliability and quality of the epidemiological investigation in the event of detecting HIV infection, including monitoring the quality of pre-test counseling by the epidemiologists of the AIDS Regional State Center/Mental Health Center and the State Sanitary and Epidemiological Supervision.
17. The OST program is currently not attractive for PWID, there are no outreach activities, reimbursement of transportation costs for the program participants, the competence of the program staff is inadequate. An integrated approach is required, including introduction of a single window for release of methadone and ARVs.
18. Energizing the measures aimed to reduce stigma and discrimination, increasing the efficiency of the outreach activities among the healthcare professionals and the general population.
19. Assistance in resolving social issues (accommodation, meals) for PWID/PLHIV, and PWID/PLHIV on OST.
20. In order to increase compliance to therapy, it is required to introduce the recommended methods (WHO): peer counseling among PLHIV, reminders in the form of messages, calendars, etc., and trainings.
21. Based on the Study findings, it is recommended to involve psychologists in the PLHIV treatment efforts and to strengthen counseling on ARVT issues among PLHIV who consume psychoactive substances.