Expansion and optimization of ART in Uzbekistan

February 2016

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Keywords
ANTIRETROVIRAL THERAPY
DRUG COSTS
DRUG USERS
HIV INFECTIONS
PREVENTION
ART SCALE-UP
UZBEKISTAN

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List of Abbreviations

3TC	Lamivudine
ABC	Abacavir
AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
ARV	Antiretroviral
CD4	T–lymphocyte cell bearing CD4 receptor
CSW	Commercial Sex Workers
d4T	Stavudine
ddI	Didanosine
d-list	Dispensary List
ECDC	European Centre for Disease Control
EFV	Efavirenz
ELISA	Enzyme-linked immunosorbent assay
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
FWS	Female sex workers
FTC	Emtricitabine
GF	Global Fund
HBV	Hepatitis B virus
HiE	HIV in Europe
HIV	Human immunodeficiency virus
HIVDR	HIV drug resistance
HTC	HIV testing and counselling
IBBS	Integrated Biological & Behavioural Surveillance
IDU	Intravenous Drug User
IFA	Indirect Immunofluorescence Assay
LTFU	Lost to follow up
MoH	Ministry of Health
MSF	Medecins Sans Frontieres
MSM	Men who have sex with men
MTCT	Mother-to-child transmission
NCPI	National Composite Policy Index
NGO	Non-governmental organization
NSP	Needle and syringe exchange programme
NVP	Nevirapine
OST	Opioid substitution therapy
PLHIV	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PWID	People who inject drugs
RAC	Republican AIDS Centre
RNA	Ribonucleic acid
STI	Sexually transmitted infections
SW	Sex worker
TB	Tuberculosis
TDF	Tenofovir
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNDP	United Nations Development Programme

UNDOC	United Nations office on Drugs and Crime
VL	Viral load
WHO	World Health Organization
ZDV	Zidovudine

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1. Executive Summary

Uzbekistan is a country with a concentrated HIV epidemic. Since the beginning of national reporting and through to the end of 2010, Uzbekistan has reported a cumulative total of 24 057 HIV cases, 651 AIDS cases and 323 deaths among AIDS cases to the WHO Regional Office for Europe and the European Centre for Disease Prevention and Control (ECDC). Since 2010, no official HIV/AIDS surveillance data have been available from the country. In 2015 the number of diagnosed PLHIV is 30 340, of these 26 989 are linked to care (having at least one visit in 2015 to the AIDS services), and 12 602 are on ART *(1)*.

The HIV response in Uzbekistan is heavily dependent on international sources, in particular from the Global Fund. The domestic spending was around 11 million US dollars in 2011 and has since increased by 20% annually *(1)*. For 2014 and 2015, the Government of Uzbekistan has allocated an additional 2 million US dollars as part of the cost-sharing agreement for ART scale-up that helped to cover enrolment of around 2000 new patients in 2014 and an additional 2015 patients in 2015 *(2)*. While international donor funding increased substantially from 7.3 million US dollars in 2011 to 13.5 million US dollars in 2012, it has since decreased. For 2014-2016 the largest donor, the Global Fund (GF), has allocated 27.7 million US dollars (approximately 9 million US dollars annually). In November 2015 the Global Fund approved a new grant of 13.8 million US dollars to finance the continued work on HIV prevention in 2016-2017. With around 60% of HIV prevention activities still depending on the GF (in 2015) the country urgently needs to ensure a continuation of essential services once this grant finishes at the end of 2017.

The mission observed a well-functioning reporting system of regional data from the 14 oblast AIDS centres to the Republican AIDS Centre (RAC) that is in charge of compiling the data. Surveillance, epidemiological and clinical data are, however, not easily combined and cross-analysed. A new database is in development and awaiting ministerial approval and this tool might enable the RAC to cross-analyse the data, follow trends in the epidemic, and improve strategic planning of key interventions. Data on late presentation should be monitored as reporting of late presentation (CD4 $\leq$350) is an important tool to evaluate the epidemic and efficiency of current HIV testing programmes.

Testing coverage is still low among key populations. The estimations made based on the Integrated Biological & Behavioural Surveillance (IBBS) surveys conducted among the most at risk groups found that only 23% of the MSM population, 28% of PWID, and 32% of SW have had an HIV test done in the last 12 months. Many tests are performed in the general population not at risk of HIV, such as blood donors, medical staff, newlyweds, and other people who are required to present HIV test results.

ART has been rapidly scaled up among PLHIV in Uzbekistan, and retention in ART is reported to be high. In 2015, 14 new national clinical protocols were adopted based on the 2012 WHO European protocols and incorporating elements from the WHO 2013 guidelines. A transition plan has been developed to fully implement the WHO 2013 guidelines over the coming years, and then by 2018 to implement the latest WHO 2015 recommendation to treat all diagnosed PLHIV.

In response to the Ministry of Health's determination to scale-up ART coverage over the coming years, the main focus of the WHO country mission was to provide input into an ART expansion and optimization plan.

Demands are increasing for higher domestic funding as a precondition for external support, and while the country is committed to ART scale-up, external funding is stagnating at current levels. Thus, to achieve the planned ART scale-up additional national funds are required.

With an adequate national investment in a successful rights-based HIV response with universal coverage of essential HIV services including ART, the HIV epidemic may be curved in Uzbekistan by 2030. Important advocacy work is necessary to keep HIV on the national political agenda and thus secure the future allocation of sufficient funds, and the MoH together with the RAC are the main actors in this field. This document is aimed to be a tool in this process.

The recommendations from the mission are as follows:

Scale up of antiretroviral therapy:

- Plan for universal access to antiretroviral therapy by the end of 2018. Uzbekistan has shown its ability to double the number of PLHIV on antiretroviral therapy in three years from 2012 to 2015. The goal will be achieved by another doubling of the number of PLHIV on antiretroviral therapy in the coming three years.
- Secure funding for the increased need of antiretroviral drugs.
- Streamline the distribution process of ARV from central to regional levels, and enlarge storage capacity.
- Use early warning indicator monitoring to identify the emergence of HIVDR and to decide on shifts from first to second line treatment regimens; only elaborate resistance tests after indication of failure of standard second line regimens.
- Use a one-tablet-a-day ART regimen (TDF+FTC+EFV) when starting ART for PLHIV who are naïve (new) to ART.
- Gradually shift patients on ABC-based regimens to the preferred TDF or ZDV-based regimens.
- Scale-up and secure funding for laboratory capacity for viral load (VL) measurement with larger sample trays and the acquisition of new high-output VL equipment.

Reaching the 90-90-90 targets:

- Consider the use of several models for data triangulation purposes in the estimation of the total number of PLHIV.
- Ensure HIV testing is free, voluntary and confidential, and increase testing coverage of the most at risk groups.
- Prioritize outreach activities, in particular HIV rapid testing at the community level and harm reduction services, targeting key populations
- Review the procedures around prevention of MTCT to prevent new HIV infections among children and implement WHO treatment Option B+.
- Make two care plans for PLHIV linked to care, one with more intensive follow up for the most vulnerable patients and one less intensive plan for motivated, compliant patients.
- Strengthen cross analysis of surveillance and clinical data to inform policy decisions on priorities within the national HIV programme.

- Reduce stigma related to HIV and key populations in all health care settings through targeted campaigns and education.

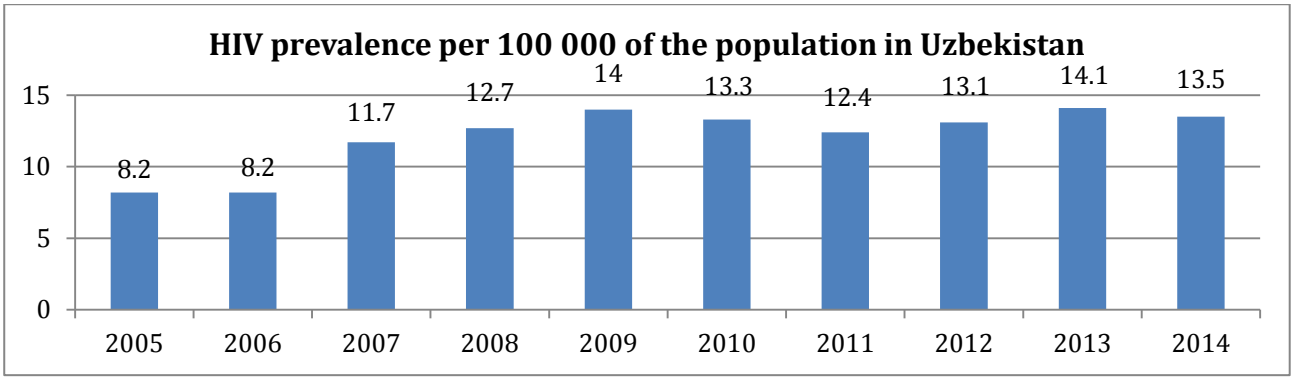
2. Introduction

2.1 The HIV epidemic in Uzbekistan: latest trends and figures

Uzbekistan is a post-Soviet Central Asian Republic (together with Kazakhstan, Kyrgyzstan, Tajikistan, and Turkmenistan), which gained independence from the collapsed Soviet Union in 1991. It is a lower-middle income country with an economy classified as a transitional, which has increased substantially in some areas.

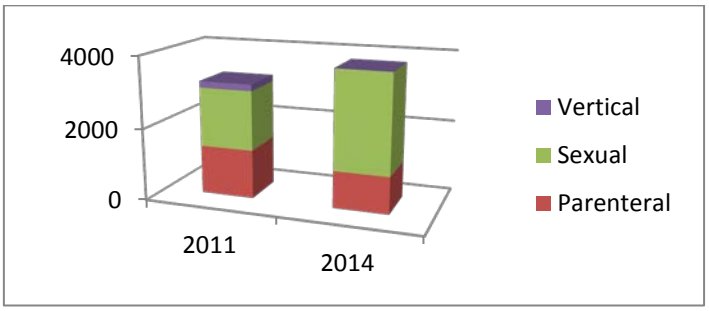
According to the Republican AIDS Centre, there were an estimated 37 712 PLHIV in 2012 and of these, 25 057 have been diagnosed *(2)*. By January 2015 the number of PLHIV that have been diagnosed was 30 340 *(1)*. After a tendency to increase from 2005-2009, the HIV prevalence in the population appears to have stabilized to just below 14 per 100 000 population (Fig. 1).

Fig. 1. Dynamics of HIV prevalence per 100 000 of the population in Uzbekistan *(3)*



From 2008 to 2014 the number of annual newly reported cases increased by 24%, reaching 4236 in 2014. Transmission routes for these new cases were parenterally (24.4%), sexually (64.7%) and mother-to-child (0.2%); 55.4% of the new HIV cases were male *(4)*. In 2011 the distribution of new HIV case transmission was 46% through sexually transmission and 38% through parenteral transmission (Fig. 2). Thus the country follows the tendency in Central Asia of recent increases in sexually transmitted HIV infections in a region where the HIV epidemic has, from the start, been closely related to injecting drug use.

Fig. 2. Transmission routes for new HIV cases



Key populations

In Uzbekistan the main key populations at risk of HIV infection are PWID, CSW, and MSM, and recently there has been a focus on migrant workers as well. Estimations set the number of people in the key groups to be 8000 MSM, 21 000 CSW and 45 000 IDU *(3)*[1]. According to data from the Integrated Biological & Behavioural Surveillance (IBBS) surveys conducted nationally every second year, the key populations have a high prevalence of HIV, Hep C and Syphilis, which indicates risky behaviour (Table 1).

Table 1. Key populations' prevalence of HIV, Hep C and Syphilis *(3)*

	HIV	**Hep C**	**Syphilis**
PWID	7.3%	21.8%	3.2%
CSW	2.1%	4.8%	4.4%
MSM	3.3%	4.0%	1.3%

Significant subnational differences exist, however, for example with HIV prevalence above 5% for CSWs in five regions, and 24.5% among PWID in Tashkent *(3)*.

It is estimated that the use of shared injection equipment among PWID has caused approximately 33% of the cumulative registered HIV cases in Uzbekistan *(3)*. While the incidence of HIV infection among PWID has reportedly decreased from 6.6% in 2003 to 2.4% in 2010 *(5)*, PWID continue to be a key population group in a comprehensive HIV prevention and care system.

In 2012 the country adopted the WHO 2010 ART guidelines that recommend starting ART in HIV patients with CD4≤350 cells. This significantly increased the coverage of ART from 3853 patients at the end of 2011 to 6021 at the end of 2012. While more advanced recommendations have been issued by the WHO, in 2015 the country adopted, with UNAIDS Country Office support, new national clinical guidelines which maintain the recommendations to start ART in patients with CD4≤350 cells and incorporated elements of the WHO 2013 Consolidated ARV guidelines *(6)*. A transition plan has been developed to gradually fully adopt the WHO 2013 recommendation of ART initiation at CD4≤500 *(2)*.

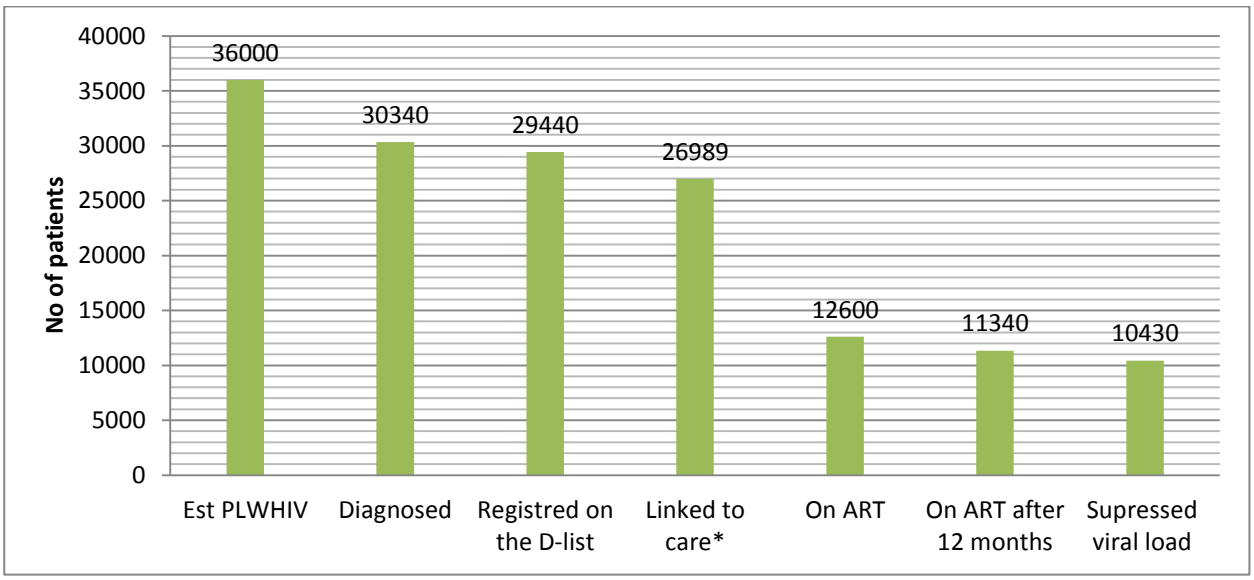
[1] Referenced estimated number of PWIDs and SWs were developed by the "Size Estimation Exercise" conducted in 2012 with UNAIDS support (Оценка численности группы потребителей инъекционных наркотиков (ПИН) и лиц, предоставляющие интимные услуги за вознаграждение (ЛПИУВ) в Республике Узбекистан, Министерства здравоохранения Республики Узбекистан, ЮНЭЙДС, 2013 год)

By October 2015, 12 602 HIV patients were on ART and the ART coverage has increased from an estimated 24% of PLHIV in 2013 to 37% in 2014, and to 39% in 2015 *(1)*. In 2014 the retention rate for HIV patients on ART was 89.4% after 12 months and 82.2% after 24 months *(4)*.

In terms of HIV testing, the number of tests have increased in recent years from 1 860 270 tests conducted in 2011 to 2 965 411 in 2014 *(3)*. For HIV testing, the national clinical guidelines recommend the use of IFA 3-4 generation tests and rapid tests with a sensitivity of at least 99% and specificity of 95-98%, and an immunoblot for the confirmatory tests *(6)*.

The continuum of care (shown below) for Uzbekistan was constructed by the mission team with numbers given by informants at the RAC and was discussed at the debriefing as an important tool to monitor the epidemic and its challenges in the country. The different steps of the continuum will be discussed throughout the report.

Fig. 3. Uzbekistan Treatment Cascade – November 2015



**Linked to care: Patients who visited the AIDS services at least once during 2015 for regular medical examinations (the total number of visits was 87 678 in 2015)*

2.2 ART scale up and transitional funding

Planning for ART scale-up

In October 2015, the WHO released a new *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV (7)* which recommends ART for everyone living with HIV at any CD4 cell count. These new evidence-based recommendations challenges Uzbekistan's capacity to provide ART for all who need it and requires strategic planning. A working group has been formed to develop a transitional ART plan considering the changed eligibility criteria for ART.

The MoH of Uzbekistan and the Global Fund signed an agreement in April 2015 on working towards providing ART to all PLHIV regardless of CD4 cell count by 2018 *(1)*. A scale-up plan has been developed which describes the gradual adaptation of the new eligibility criteria (Table 2).

Table 2. Projection of ARV therapy expansion *(1)*

	2015	2016	2017	2018
Eligibility criteria for ART in current national clinical guidelines (5) ART is always recommended to people living with HIV with CD4 cell counts below 350 cells/mm^3. For patients with a CD4 cell count above this level, the decision to start ART should be carefully considered based on individual need, especially if the patient requiring ART and ready to start treatment is experiencing any of the conditions listed above and/ or have any other personal problems that need to be taken into account. HIV-positive pregnant women on lifetime ART if CD4<500 or clinical stage III-IV; PLHIV co-infected with active TB or HBV with signs of chronic liver disease	All children aged 0-5 Children from 5-18 years at clinical stages I-II if CD4<500, and at Stages III-IV regardless of CD4 cell count	All children aged 0-18 All patients at clinical stage III-IV	All adults <30 years of age at clinical stages I-II and CD4<500 All patients at clinical stages III-IV	All diagnosed HIV patients regardless of CD4 cell count
ART Eligible (on ART)	12 676	16 340	20 340	
Adult eligible	8190	10 621	13 221	
Children eligible	4412	5719	7119	
Cost of ART (million US dollars)		1.9	2.8	

Funding of the HIV response

The Government of Uzbekistan has exercised leadership in financing substantial parts of its HIV response in recent years. International donor resources continue to play an important role, in particular the Global Fund, which has supported the country since 2003.

Since 2011, domestic spending on the national HIV response has remained stable at around 11 million US dollars annually. For 2014 and 2015, the Government of Uzbekistan has allocated an additional 2 million US dollars as part of the cost sharing agreement for ART scale-up, which helped to cover enrolment of around 2000 new patients in 2014 and an additional 2015 patients in 2015 *(2)*.

International donor funding increased substantially from 7.3 million US dollars in 2011 to 13.5 million US dollars in 2012, but has since decreased. For 2014-2016 the largest donor, the Global Fund, allocated 27.7 million US dollars (approximately 9 million US dollars annually) in donor funding. In November 2015 the Global Fund approved a new grant of 13.8 million US dollars to finance the continued work on HIV prevention in 2016-2017 *(8)*.

Uzbekistan is facing a situation where the prospects for continued stable international funding have diminished and the government needs to develop sustainability strategies for continuing the national HIV/AIDS response and in particular the planned ART scale-up.

3. Purpose, objectives and methods

Purpose & objectives

Uzbekistan's Ministry of Health has approached the WHO with a request for technical assistance and input into developing a National ART scale-up plan, considering recent internationally recommended criteria for starting ART and recommended ART regimens, with the ultimate goal to reach the UNAIDS 90-90-90 targets.

The country mission took place from 22-26 November 2015.

The document is intended to inform a scale-up ART plan and provide recommendations for its implementation. It begins with an evaluation of Uzbekistan's clinical recommendations and service delivery across the cascade of services, according to terms of reference for the WHO mission (Annex 1).

The program review includes 4 key components:

- Main barriers to HIV testing and linkage to HIV care services, and average time between the patient's HIV status confirmation and treatment initiation;
- Main reasons for lost to follow up within the cascade of HIV services (HIV testing, linkage to care, ART enrolment and retention, and monitoring of viral suppression);
- The National HIV treatment protocol, including criteria to start ART, ART regimens and recommendations on retention in HIV care; and
- Number of PLHIV receiving and planning to receive ART.

Methods

Readily available information had been drawn from secondary sources (publications, reports, etc.) during the preparation stage for desk review and analysis. During the country mission, WHO experts visited the Republican AIDS Centre (RAC), policy makers, and met international partners (see mission programme in Appendix). No visits to the Regional AIDS Centres and other regional HIV services were conducted.

If not indicated otherwise, all data and numbers included in this document were provided by the HIV experts at the Republican AIDS centre during the mission.

4. HIV treatment and care along the cascade of services

4.1 Shortcomings in the estimation of PLHIV

The starting point for the 90-90-90 targets is a correct estimation of the country's total PLHIV population. According to the Spectrum-based estimations for 2014, there are 36 000 PLHIV in Uzbekistan, and there is expected to be a slight decrease over the next few years to 31 300 in 2020 *(1)*. While the HIV epidemic may stabilize at the current level, it is questionable whether the projected fall in the total PLHIV population is realistic. In fact, a decrease in the total PLHIV population would only be possible due to deaths among PLHIV in the absence of ART.

Because the estimation of the total PLHIV population is so crucial for assessing the 90-90-90 targets, it is suggested to utilize several models in addition to the major Spectrum model promoted by UNAIDS in order to be able to triangulate the results. It is widely acknowledged that Spectrum modelling works best where the HIV surveillance system is based on sentinel surveys in key populations rather than based on HIV case reporting systems (the latter is the case in Uzbekistan). Therefore other existing models should be considered for use, such as the recently released ECDC model *(9)* and the "London method 1" *(10)*. It is recommended to consider the use of several models for data triangulation purposes in the estimation of the total number of PLHIV.

4.2 Shortcomings in HIV Testing

Testing coverage

The number of HIV tests conducted has almost doubled in recent years, from 1 860 270 tests in 2011 to 2 965 411 in 2014 (Table 3). However, the increased number of HIV tests performed does not necessarily equal an increased coverage of HIV testing. It is a shortcoming of the available data that the testing coverage is not calculated annually. Moreover, the number of HIV-positive cases identified with this expanded testing has remained almost stable. This can either indicate that the epidemic has stagnated or that inappropriate groups are being tested. It is a shortcoming that testing in key populations has not increased proportionally to the increase in overall number of HIV tests. Prevalence rates calculated for key populations based on HIV tests conducted are lower than the ones presented in Table 1, based on IBBS surveys. This might indicate that the HIV testing being conducted is not adequately reaching key populations (Table 3).

Table 3. HIV Testing 2011 & 2014 *(1)*

	2011	**2014**	**Positive cases in 2014**	**Prevalence among the tested in 2014**
The overall number of HIV tests	1 860 270	2 965 411	4236	
The overall number of HIV tests per 100 000 people	7013	-	-	
The number of HIV tests among key vulnerable groups				
PWID	7222	6738	47	0.7%
CSW	3379	2695	24	0.9%
MSM	12	50	0	-
Partners of HIV positive persons	2359	3332	380	11.4%
Patients with STI	-	17 248	30	0.17%
Clinical indications (Viral Hepatitis, Oncology, TB)	221 185	375 958	1597	0.4%
Other	112 485	187 292	753	0.4%
Anonymous tests	16 610	23 001	*	*
Routine testing				
Pregnant women	626 825	739 351	281	0.04%
Migrants	161 003	606 051	621	0.15%
Medical staff	118 552	232 472	35	0.02%
Blood donors	119 702	150 206	69	0.05%
Newly weeds	409 233	572 722	261	0.04%

**People that test positive as anonymous tests are referred for confirmatory testing, and in the case of a positive confirmatory test are included under other categories*

It is important that HIV testing is focused on main risk groups. One example is the group labelled 'partners of HIV-positive persons'. The testing data from 2014 show that HIV prevalence was 11.4% in this group, which is alarmingly high; another is the one labelled 'other' which had an HIV prevalence of 0.4% (Table 3).

The epidemiologists at the RAC explained that the group categorized as 'other' probably includes persons reluctant to disclose sexual or other risk behaviours. When the epidemiologists at the AIDS centres analyse the mode of transmission among new positive HIV cases, cases originally labelled as 'other' are re-classified as either sexual or parenteral transmission. For example, among new HIV cases in 2014, parenteral transmission accounted for 24.4%, a number which includes both self-reported IDU (6.6%) and assessed IDU from the group that was registered as 'other' at testing (13.3%) as well as nosocomial transmission (4.4%). The category 'unknown transmission mode' is not used which may cause the placement of cases into erratic groups.

For surveillance purposes, it is important to break down the numbers of tests per year into age, gender and place of testing. This also applies to the anonymous testing sites, where the number of positive cases found should be reported. For the anonymous testing, the UNICODE system could be applied so that it will be possible to track whether the HIV positive persons are getting a confirmative HIV test and are eventually linked to care.

It is recommended to:

- Calculate the testing coverage annually to monitor developments in coverage of HIV testing;
- Break down the numbers of tests per year into age, gender and place of testing, including for the anonymous testing; and
- Use the existing UNICODE system to track whether anonymously tested HIV positive persons get a confirmative HIV test and are eventually linked to care.

Testing key populations

Increased testing of key populations is central. Behavioural surveillance surveys have been conducted regularly, and the one in 2013 found that 23% of MSM had an HIV test conducted in the previous 12 months and knew their results; for PWID it was 28.4% and for CSW it was 31.9% *(3)*. The WHO recommends that people in the most at risk groups get tested at least once per year; there is room for improvement of testing coverage in the most at risk groups. PWID is by far the largest population group and it has the highest HIV prevalence (Table 4). It is estimated that the proportion of PWID among the officially registered PLHIV was 12.5% in 2013 *(3)*.

Table 4. HIV prevalence among key populations *(3)*

	PWID	**CSW**	**MSM**
2013	7.3% (n=5600)	2.1% (n=3360)	3.3% (n=150)
2011	8.4% (n=5600)	2.2% (n=3379)	0.7% (n=150)
2009	11.0% (n=4098)	1.9% (n=2493)	6.8% (n=118)

One way to scale up HIV testing is through Trust Points and Friendly Cabinets, which are service points for key population groups. At the Trust Points, medical staff provide education, counselling, needle and syringe exchange, and distribution of free condoms as the main preventive activities, and, if necessary, provide referrals to specialists and/or HIV testing. At the Friendly Cabinets, medical staff provide education and anonymous counselling on STI symptoms. Some Friendly Cabinets have outreach workers, employed by local NGOs, in order to locate the target groups on the streets and bring them to the Friendly Cabinet for counselling. By the end of 2014, 23 277 PWID, 1475 MSM, and 11 602 female SW had been covered by basic HIV preventions services at the 139 204 Trust Points and 30 Friendly Cabinets operating across the country *(11)*. There are, however, regional variations as some local authorities have not approved a number of NGOs as sub-recipients of the Global Fund grant as outreach workers. This has limited the access to services such as counselling on HIV transmission, psycho-social support for HIV-positive patients, anti-stigma training, and distribution of condoms and syringes in 10 regions for female SW and three regions for MSM *(21)*.

In 2015, within the framework of the Regional Cooperation Programme, funded by the Russian Federation, the UNAIDS Country office provided the Republican AIDS Centre with a high number of express test systems for multiple markers (HBc/HIV/HCV and TP/HIV). As a result, Trust Points began to offer rapid diagnostic tests for HIV. This service is still very new and no data are available

on number of tests conducted or the number of positive cases. It is recommended to gather and analyse this information in order to assess the efficiency of this testing strategy.

When the Global Fund scales down it donor support, it is crucial that the government takes on the responsibility to procure and distribute rapid tests to the Trust Points. The current national guidelines do not mention saliva tests, which may be considered. Saliva tests are adequate for outreach purposes and are done easily in non-medical settings, for example in an ambulance, in soup kitchens or other venues where vulnerable groups can be found. Saliva tests are user friendly, for example for PWID for whom it may be difficult to find a vein for traditional blood tests and for children and others who would prefer not to have a blood sample taken.

Because STIs are one of the strongest indicators for HIV infection, it is recommended to begin offering clients with STI symptoms at confidential rooms a rapid diagnostic HIV test immediately onsite (blood or saliva test).

It is recommended to:

- Focus HIV testing strategically on the populations most at risk for HIV, including hard to reach populations such as PWID and MSM;
- Secure continuation of harm reduction and preventive activities in Trust Points and Friendly Cabinets (needle and syringe exchange, distribution of free condoms, and education and information);
- Secure supplies of rapid HIV blood tests, and if possible, rapid test systems for multiple markers (HBsAg/HIV/HCV and TP/HIV) for Trust Points and expand this service to Friendly Cabinets. There should also be consideration for other community-based outreach testing;
- Develop comprehensive reporting on results of rapid HIV tests by collecting and analysing data from Trust Points, Friendly Cabinets and other testing services on the number of rapid blood tests conducted, positive cases identified, as well as confirmative testing and linkage to care; and
- Allow lay persons to conduct rapid blood testing and/or saliva tests in order to scale-up outreach testing targeting hard to reach populations such as PWID and MSM (this will require a revision of clinical protocols).

Co-infections & indicator conditions-based HIV testing

TB and Hepatitis C are the most common co-infection among HIV patients. The national clinical protocols recommend routine HIV testing for patients with viral hepatitis or TB and vice versa *(5)*. It seems that with regards to TB this is implemented successfully, but there is no routine analysis of new HIV patients for co-infections of Hepatitis B and C *(1)*. In 2016 the National Institute of Virology and MSF will begin a project to treat approximately 100 HIV/Hepatitis C co-infected patients with Interferon *(12)*.

The national testing data report on testing conducted on patients with ‘clinical indications’, which includes TB, viral hepatitis, oncology and others (Table 3). The HIV prevalence in this patient group was 0.4% in 2014. It is important to separate the number of tests conducted according to the specific clinical indications, to be able to, for example, identify the number of viral hepatitis patients tested for HIV.

One efficient way to scale-up testing and identify more undiagnosed PLHIV is by applying indicator conditions-based HIV testing *(13)*. The challenge is to get all relevant specialists and general doctors to recommend HIV testing to all patients with indicator conditions. The strategy is most efficient when the test can be done immediately. If the patients need to go to another clinic or site to get an HIV test there is a greater risk that people will be lost between health care settings and will never make it to the HIV testing site.

It is recommended to:

- Implement the use of rapid test systems for multiple markers (e.g. HBc/HIV/HCV, TP/HIV);
- Gather data and perform routine analysis on the number of new HIV patients tested for co-infections with Hepatitis B and C (and vice versa);
- Report testing data for HIV tests based on clinical indications separately for viral hepatitis, TB and the other clinical indications; and
- Inform and train all relevant specialists and general doctors to recommend HIV testing to all patients presenting with indicator conditions.

Late presentation

The efficiency of applied testing strategies can be assessed based on the level of late presentation among new HIV cases. Uzbekistan's national clinical guidelines define four clinical stages of HIV infection in accordance with the WHO guidelines *(6)*. According to the RAC, in 2014, 75% of newly detected HIV cases were in clinical stages I and II, and 27% were in stage III and IV (Table 5).

Table 5. Clinical stages of newly detected HIV cases *(1)*

1st clinical stage	2nd clinical stage	3rd clinical stage	4th clinical stage
41%	34%	19%	8%

The internationally agreed definition of late presentation is: "persons presenting for care with a CD4 count $\leq$350 cells/mm^3 or presenting with an AIDS-defining event, regardless of the CD4 cell count." *(14)*. Thus for Uzbekistan, the current level of late presentation among newly diagnosed HIV cases is around 27%.

It is recommended to:

- Monitor the CD4 cell count of people presenting for care and disaggregate the information to identify regional differences.

4.3 Shortcomings in prevention of HIV transmission

PMTCT

Among the 29 022 PLHIV registered in November 2015 on the dispensary list (d-list), 5905 (20%) are children below the age of 15 years *(1)*. This is a very high percentage, and it remains an open question as to why there are so many HIV infected children in Uzbekistan.

One obvious transmission route is mother-to-child transmission (MTCT). There is a national plan for the elimination of MTCT and the country has achieved important progress in reaching this. In 2013 the testing coverage of pregnant women reached 98.4% *(4)*. Rapid diagnostic tests should be available and offered to women about to give birth who have not been previously tested for HIV during their pregnancy. To prevent transmission to the child it is crucial that *all* pregnant women tested and found to be HIV-positive are offered life-long ARV treatment immediately regardless of CD4 cell count, as recommended by the WHO (Option B+).
In 2011, 593 children were born to HIV-infected mothers, and 88.7% of these children received antiretroviral prophylaxis. This coverage needs to be raised so that *all children* born to HIV-positive women receive prophylaxis. Early infant diagnosis should be sustained and consistently applied. All children living with HIV must be offered ARV treatment irrespective of CD4 cell count.

The WHO recommends the provision of free formula milk to HIV-infected mothers in order to prevent MTCT. In Uzbekistan's National Composite Policy Index (NCPI) report for 2013, providing formula milk to all HIV-infected mothers was described as a challenge *(15)*. The review team has not seen any new data on whether this has been overcome. The RAC explained that regional health authorities in the 14 regions are providing formula milk in collaboration with the Global Fund, but that disruptions in the provision still occur. In 2014, part of the Global Fund grant was set aside to procure infant formula to children born in 2014 and partially in 2015 *(1)*.

It is recommended that the country implements WHO Option B+ and treat both mother and child with ARVs; this would eliminate the risk of HIV transmission and enable mothers to safely breastfeed infants.

It is recommended to:

- Offer rapid diagnostic tests to women about to give birth who have not been previously tested for HIV during their pregnancy;
- Implement WHO Option B+ and ensure that *all* pregnant women tested and found to be HIV-positive are immediately offered (life-long) ARV treatment;
- Sustain and consistently apply early infant diagnosis, and supply prophylaxis to *all children* born to HIV-positive women; and
- *All* children living with HIV must be offered ARV treatment regardless of CD4 cell count.

Nosocomial transmission
HIV transmission in health care settings is another possible mode of transmission for HIV-infected children. All new cases of children with HIV without HIV-positive parents should receive a thorough epidemiological investigation to clarify the transmission route as soon as possible. Appropriate follow up after the results of the epidemiological investigation should be initiated immediately. It would be important to separate the number of children infected vertically and parenterally to get an overview of, and to address, the situation.

It is recommended to:

- Conduct a thorough epidemiological investigation all new cases of children with HIV without HIV-positive parents to clarify the transmission route; and
- Separate the numbers of children infected vertically and parenterally to get an overview of, and to address, the situation.

4.4 Shortcoming in enrollment and retention in care

Enrolment into care

In Uzbekistan, HIV care is managed by the Republican AIDS Centre and the 14 regional AIDS centres. Anonymous and regular HIV testing is conducted at diagnostic laboratories in the 14 regional AIDS centres and at 59 inter-laboratory facilities across the country. After a positive ELISA test, the blood sample is sent to one of the three laboratories conducting confirmatory immunoblot testing. Generally, the results are available to the regional AIDS centre within one week and within a few days thereafter the centre will notify the patients. This implies that in principle, a person testing positive could be enrolled in care within 2-4 weeks from the first positive test result *(1)*.

After a confirmed positive HIV diagnosis, patients are registered on the d-list and called in to the AIDS centres to have their CD4 cell count and viral load measured. By 1 January 2015, 30 340 persons had been identified as HIV positive, and of these 29 123 were registered on the d-list. Then patients are offered medical check-ups at the AIDS centres' policlinics (outpatient clinics) every six months to assess eligibility for ART, and to be seen by the associated medical specialists as required (paediatricians, derma-venerologists, etc). During 2015, 26 989 patients visited an AIDS centre at least once and the total number of visits was 87 678 in 2015. Thus 2451 PLHIV patients were not linked to care in 2015. For 2015 the RAC reported the number of visits to an AIDS centre per patient on the d-list and the numbers of CD4 cell count measures taken (Table 6).

Table 6. PLHIV on dispensary list: Visits to AIDS Centre and measures of CD4 cell count *(1)*

	Visit to AIDS Centre in 2015	Measures of CD4 in 2015
4 times	67%	45%
3 times	15%	33%
≤2 times	18%	22%

The regional AIDS centres can remit severe patients to the specialized 60 beds hospital for HIV patients in Tashkent. The hospital has on average 50 occupied beds and the patients typically have opportunistic infections, such as candida/fungi, or are suffer from chronic illnesses or ARV side-effects *(1)*.

Depending on the progression of the HIV infection, the patients maybe on the d-list and enrolled in care for several years while their CD4 cell count slowly decreases. In 2014, there were 1534 PLHIV on the d-list that died (1). The causes of death for these patients are reported annually to the MoH. The review team have not seen these data, but these deaths may indicate there is low access to ART even for those with CD4≤350.

By 1 January 2015, the number of diagnosed PLHIV not linked to care was 1217 or approximately 4% of the total number of diagnosed PLHIV. This group may include people who need time to accept the diagnosis or for other reasons do not wish to enrol in care. It is important to address these patients and try to link them to care. A recent study from the United States has suggested that PLHIV who drop out of HIV care after their HIV diagnosis may contribute to the majority of HIV

transmission *(16).* The review team did not see data on the number of PLHIV registered on the d-list that have dropped out of care and are lost-to-follow-up.

It is recommended to:

- Make a concerted effort to link all PLHIV that have been diagnosed to care; and
- Minimize lost-to-follow up of patients on the d-list and attempt to track patients not showing up for regular medical checks.

TB-HIV co-infections

According to data reported to the WHO, as many as 98% of TB patients (22 347 cases) were screened for HIV in 2014. 780 TB patients were found to be HIV positive. Of the TB/HIV co-infected patients 79% (615 patients) received co-trimoxazole preventive therapy and 45% (354 patients) were started on ART *(17)*.

According to the national clinical protocols, all new HIV patients should be tested for TB (and the negative cases receive treatment with isoniazid) *(6).* For the positive cases, the country's national protocols follows the WHO recommendation to first start the patients on TB treatment and after 2-12 weeks, when good tolerability of TB treatment is secured, start the patient on ART (1). In the country there are separate treatment protocols for TB; the republican DOTH centre is using the WHO recommended DOTS methodology (supported by the Global Fund) and the National Institute for Physiatry and Pulmonology uses a non-DOTS approach to treatment *(18).*

In 2014 it was reported to the WHO that 780 HIV-positive people were screened for TB and that 2439 HIV-positive people were provided with IPT *(17)*. The former does not correspond with the national clinical guidelines' recommendation to screen *all* new HIV cases for TB nor with information provided by the RAC to the review team that all new HIV cases are screened for TB.

In 2014, out of 4236 new HIV cases, 780 were co-infected with TB (18%) and of these, 112 died during the year *(1).* As only 45% (354 patients) of the co-infected patients were started on ART in 2014 there might be a relation between these deaths and lack of TB and ART treatment. The RAC could not present data on the cause of death as only the MoH can provide this information, which suggests limited data sharing between HIV and TB programmes.

It is recommended to:

- Ensure that the clinical protocol guidelines to screen *all* new HIV positive patients for TB is implemented;
- Provide ART to *all* TB/HIV co-infected patients regardless of CD4-count; and
- Analyse the causes of death of patients co-infected with TB to see if the correct treatment was effectuated.

4.5 National guidelines on ART for adults and children

National clinical guidelines

In January 2015, the country adopted 14 new clinical protocols *(6)*. They follow the WHO 2012 European protocols and incorporate elements from the WHO 2013 guidelines. With regards to ART eligibility criteria it is stated that:

"ART is always recommended to people living with HIV CD4 cell counts below 350 cells/mm^3. For patients with a CD4 cell count above this level, the decision to start ART should be carefully considered based on individual need, especially if the patient requiring ART and ready to start treatment is experiencing any of the conditions listed above and/ or have any other personal problems that need to be taken into account."

In line with the WHO "Option B", as of 2015 lifelong ARV therapy is recommended to all pregnant HIV-positive women with a CD4 cell count ≤500. National guidelines also recommend ART for all HIV-positive patients with active TB or hepatitis B severe liver disease, and ART for the HIV-positive partner in serodiscordant couples *(6)*.

The national clinical guidelines recommend assessing the patients' motivation and ability for compliance prior to initiation of ARV. During the mission, the review team was not able to observe how this is done in practice and which criteria are used.

As mentioned, an ART scale-up plan has been developed by the country (Table 2), which will implement the 2013 WHO recommendation start ART at CD4≤500 stepwise over the next few years. This implies a 1.5-2.0 fold increase in the ART patient population, and the goal is to apply the 'treat-all' strategy by the end of 2018.

It is recommended to:

- Update the national clinical protocols in accordance with the country's ART scale-up plan.

4.6 ART Coverage

ARV treatment

In recent years, ART coverage for PLHIV has been expanded and improved considerably. In 2006 only 278 patients were on ART, and by the end of 2012 it had risen to 6021 patients. A 2-fold growth in the ART coverage was observed from 2011 to 2012 when the country moved from the eligibility criteria of CD4 cell count ≤200 to CD4≤350. By October 2015 there were 12 602 PLHIV on ART, equaling an increase in ART coverage from 24% of PLHIV in 2013 to 37% 2014, and to 39% in 2015. In 2014 the retention rate for HIV patients on ART was 89.4% after 12 months and 82.2% after 24 months *(4)*.

ARV treatment is free for eligible PLHIV. As already mentioned, patients eligible for ART are enrolled quite fast, if the patient is ready and willing to start treatment, and there is no waiting list or shortage of ARV. From 2011-2013 the percentage of new HIV cases with a CD4 cell count ≤350 has decreased, and the average CD4 cell count at treatment start increased (Table 7).

Table 7. Average CD4 cell count at treatment initiation *(1)*

	2011	**2012**	**2013**
% of new HIV cases with a CD4 cell count below 350 at time of diagnosis	42%	38%	36%
HIV patients' average CD4 cell count at ART-initiation	CD4<278	CD4<310	CD4<330

In 2014 around 50% of the new HIV cases were started on ARV immediately after diagnosis *(1)*. This does not correspond with the numbers in the table above, and may indicate that late presentation is common. No information was provided to the review team on ARV drug shortages or on waiting lists to start ART.

The 14 Regional AIDS Centres have between 200 and 3000 HIV patients linked to care. For adult patients, the percentage on ART varies from 19% as the lowest to 61% as the highest coverage (Table 8), and for children <15 years of age there is a variation between 63% as the lowest and 96-100% as the highest coverage. The difference in ART coverage reflects, according to RAC, the eligibility and needs of the patients determined by the 'age' of the local epidemic *(1)*. In September 2015 of the total 12 602 PLHIV on ART, 85 discontinued the treatment and of these, 36 (3%) died and 49 were LTFU (4%).

Table 8. Geographical distribution of PLHIV Retention in ART (August/September 2015) *(1)*

15 regional health care institutions providing ART	Registered PLHIV (adults > 15 years)	Registered PLHIV (children <15 years)	On ART (adults >15 years)	On ART (children <15 years)	Discont. ART (adults >15 years)	Discont. ART (children <15 years)	Deaths among those on ART (adults > 15 years)	Deaths among those on ART (child. <15 years)
1. Андижанский обл. ЦСПИД (Andijan region. TSSPID)	2933	2000	958 (33%)	1420 (71%)	18	3	4	2
2. Бухарский обл. ЦСПИД (Bukhara region. TSSPID)	723	65	222 (47%)	59 (91%)	2	0	4	0
3. Джизакский обл. ЦСПИД (Jizzakh region. TSSPID)	257	50	120 (47%)	44 (88%)	0	0	0	0
4. Кашкадарьинский обл. ЦСПИД (Kashkadarya region. TSSPID)	615	182	212 (43%)	138 (76%)	1	0	1	0
5. Навоийский обл. ЦСПИД (Navoi region. TSSPID)	189	26	**116 (61%)**	**25 (96%)**	3	0	0	0
6. Наманганский обл. ЦСПИД (Namangan region. TSSPID)	771	413	280 (36%)	**259 (63%)**	3	0	1	0
7. ЦСПИД РК (RK AIDS. TSSPID)	264	5	152 (58%)	**5 (100%)**	2	0	0	0
8. Самаркандский обл. ЦСПИД (Samarkand province.TSSPID)	2174	321	426 (20%)	228 (71%)	0	0	2	0
9. Сурхандарьинский обл. ЦСПИД	1313	129	**252 (19%)**	96 (74%)	4	0	0	0

(Surkhandarya region. TSSPID)								
10. Сырдарьин7+0ский обл. ЦСПИД (Syrdarya region. TSSPID)	876	218	394 (45%)	198 (91%)	3	0	4	0
11. Ташкентский 0+0обл. ЦСПИД (Tashkent region.TSSPID)	4138	805	1168 (28%)	583 (73%)	7	0	7	0
12. Ташкентский гор. ЦСПИД (Tashkent Mountains. TSSPID)	6183	839	1971 (32%)	582 (69%)	22	4	8	0
13. Ферганский обл. ЦСПИД (Ferghana region. TSSPID)	1644	763	698 (42%)	596 (78%)	6	1	3	0
14. Хорезмский обл. ЦСПИД (Khorezm region. TSSPID)	640	49	174 (27%)	48 (98%)	1	0	0	0
15. РЦ СПИД МЗ РУз (Ministry of Health of the Republic of Uzbekistan RAC)	186	40	181 (97%)	40 (100%)	0	0	0	0
16. ГУИН* (GUIN*) (Penitentiary system)	211	0	211 (100%)	0	6	0	0	0
17. ВБГ (VBG) (MSF)			645	91				
Total	23 117	5905	8190 (35%)	4412 (75%)	77	8	34	2
Total	29 022		12 602 (43%)		85		36	

**Status September 2015*

During the mission, the review team was informed that until now, information on ART coverage has not been disaggregated by main key populations, but that the RAC is currently working on providing this aggregated data. The RAC reported that by the end of 2015, the patients on ART included this percentage of key populations: PWID 17% and SW 26%. There are no data on MSM. Continued work to improve disaggregation of data on ART coverage by main key populations is important to be able to assess the impact of the ART scale-up and to adjust the interventions. Among HIV-positive patients eligible for ART there is a large group suffering from co-infections with TB, viral hepatitis and/or STIs, which may also suffer from other co-morbidities. To address the special needs of these HIV patients, integrated approaches to clinical management are recommended.

At the Tashkent city AIDS centre, MSF runs a project that introduces eligible PLHIV into ARV care with a case-management approach that facilitates co-infected people's way into the health care system, for example by accompanying people to appointments at different clinics *(12)*. When they are stable on ART the management of patients is 'handed over' to the Tashkent city AIDS centre.

The experiences from this project can be used in the other AIDS centres to address the need for enhanced integration of care.

It is recommended to:

- Analyze the regional data on CD4 cell count at diagnosis and at treatment start to identify and address regional differences;
- Analyze the regional data on LTFU and deaths to identify and address regional differences;
- Disaggregate data on ART coverage by main key populations to be able to assess the impact of the scale-up; and
- Apply integrated approaches to clinical management that address the special needs of HIV-infected patients on ART with co-infections or co-morbidities.

Antiretroviral regimens

In the past few years the ARV drug regimens used in the country have been simplified according to WHO recommendations, and further simplification is planned for 2016. This process of simplification and/or optimization of ART has been supported by UNAIDS consultants and others.[2] The objective of this simplification process is to optimize ART in the country in accordance with the WHO recommended public health approach for selecting ART regimens.

Currently, the number of ART regimens in the first line is seven, including paediatric regimens. This is a considerable reduction compared to 2011 where 24 regimens were used. The recommended first line regimen is TDF/3TC(FTC)/EFV, which is in accordance with WHO 2013 guidelines. In addition, for patients who have been taking a drug combination with AZT (ZDV) for a long time, it is recommended to gradually shift them to schemes with tenofovir. A one-pill-a-day combination is the preferred mode of delivery. The proportion of PLHIV on first line ART is currently 86.5% and there are 13.5% on second line ART. The most common third agent in the regimens is efavirenz (64.9%) followed by nevirapine (21.5%) and lopinavir/ritonavir (13.5%). Only 0.1% of patients receive triple nucleoside therapy. The distribution of third agents in ART regimens follows very well with WHO recommendations.

The most common nucleoside combination in the ART regimens is AZT+3TC (46.7%), followed by TDF+3TC/FTC (31.9%) and ABC+3TC (21.4%). Stavudine (d4T) and didanosine (ddI) are no longer used in Uzbekistan.

There are no third line regimens currently available, but there are plans to introduce some in 2016. For patients on standard first line treatment, the WHO recommends that national ART programmes monitor early warning indicators for HIV drug resistance (HIVDR) via routine available data (CD4 cell count, viral load, etc.) and base decisions to shift patients to standard second line regimens hereon *(19)*. Only after indications of failure of standard second line regimens is it recommended to elaborate individual HIVDR testing.

[2] Under the Regional Cooperation Programme, in 2015 the UNAIDS Country Office supported a national training workshop on the "Implementation of new Guidelines from MoH # 81 on ARV treatment" with participation of three international consultants that formulated recommendations on optimization of ART in Uzbekistan

The use of d4T and ddI has been stopped which greatly reduces adverse effects of ART. The proportion of PLHIV receiving AZT+3TC is still quite large in Uzbekistan. The use of AZT-containing nucleoside backbone poses a risk to cause lipoatrophy over the years *(20)*. ABC possesses a possibility for hypersensitivity reactions. The ethnic background of the population in Uzbekistan is mixed, which carries a possibility of PLHIV having the genetic propensity (HLA-B57*01) for this reaction.

To facilitate the planned ART scale-up and manage the greatly expanded number of PLHIV receiving ART, initiation of ART should take place in the simplest manner. Therefore, the one-tablet-a-day ART regimen TDF+FTC+EFV should be preferred in starting ART for PLHIV who are naïve (new) to ART. A one tablet ART regimen will simplify the logistics in dispensing medications and will eliminate the possibility of PLHIV having incomplete regimens *(21)*. In addition, patients already on ABC-based regimens should gradually be switched to the preferred TDF or ZDV-based regimens.

It is recommended to:

- Continue the work on simplifying the used ARV drug regimens;
- Use early warning indicator monitoring to identify the emergence of HIVDR and to decide on shifts from first to second line treatment regimens; only elaborate resistance tests after an indication of failure of standard second line regimens;
- Use one tablet ART regimens to simplify the logistics in dispensing and to eliminate the possibility of PLHIV having incomplete regimens; and
- Gradually shift patients on ABC-based regimens to the preferred TDF or ZDV-based regimens.

4.7 CD4 and Viral load

Point-of-care CD4 technology is implemented in Uzbekistan and national clinical guidelines recommend viral load monitoring before the start of ART, three months after the initiation of ART, and then every 12 months *(6)*.

Retention in care

The last of the three 90-90-90 targets is to have 90% of PLHIV on ART with undetectable viral loads. Retention to ART is crucial for reaching this target and for curbing the HIV epidemic by 2030. Available data on the current ART programs suggest that their quality is good, with 89.4% retention after 12 months and 82.2% after 24 months. In 2012, 92% of patients on treatment had suppressed viral load, and in 2015 the percentage of patients on ART with an undetectable viral load was 87.1% *(1)*.

As mentioned previously, around 3% of patients ever started on ART have died and 4% were LTFU (Table 4). The latter group are typically people migrating abroad for work. In case of the deaths, the regional AIDS centres are notified by the respective responsible authorities, and the RAC reviews these data annually and sends a report to the MoH.

The majority of HIV patients are motivated to take their medicines and continue normal lives, but when the 'treat-all' policy is in place there will eventually be more vulnerable people among the patients who will need special attention to remain in care. Rather than treating all patients equally the AIDS centres should consider establishing two treatment plans: 1) one for compliant patients with annual medical check-ups and supply of ARV drugs for periods of 6-12 months (this is already in practice with some patients that live far away from the AIDS centres or that are going abroad for migrant work); and 2) an intensive care plan for the more vulnerable patients who need support to comply with ARV treatment. For this group, pill boxes, calendars, SMS and other reminder tools are important facilitators to ensure ART adherence.

It is recommended to:

- Gather and analyse data on the patients' viral load and use this to assess the treatment quality at the regional levels;
- Implement a care plan for compliant patients with annual medical check-ups and supply of ARV drugs for longer time periods for the convenience of the patients and for the reduction of human resources in AIDS centres; and
- Implement an intensive care plan for vulnerable patients who need extra support to comply with ARV treatment.

5. ART scale-up plan 2016-2020

In 2015 an estimated 39% of PLHIV in Uzbekistan were on ART and to be able to treat 90% of diagnosed PLHIV requires an important scale-up of ART.

5.1 Three possible scenarios

During the mission the review team did not have access to data on the costs of HIV care, except for ART, and this is why this section draws on data from the report *Modelling an Optimized Investment Approach for Uzbekistan* by the MoH/RAC and UNDP published in November 2015 (2). The report models three different scenarios for achieving ART therapy expansion with different ART starting thresholds, and calculates the number of new infections, DALYs averted (when compared to no intervention) and the estimated size of PLHIV population in the country.

- **Scenario 1: CD4≤350 as a criteria to start ART (current national guidelines)**

The current ART eligibility criteria (CD4≤350) is maintained and the HIV programmes proceed with current (2012 level) investment allocations and budget level. Testing rates are not increased.

Scenario 1:	2020 (estimated)
Estimated number of total PLHIV population	35 000
Number of patients eligible for ART	19 200
ART coverage	11 000
ART coverage for PLHIV eligible for ART	57%
Diagnosed and eligible without ART	5100
Undiagnosed	14 200 (40% of all PLHIV)
Total programme cost (2014-2020 not counting inflation)	167.1 million US dollars
Annual cost of HIV/AIDS response	23.9 million US dollars
Return on investment	Avoid 12 500 new HIV infections and 49 000 DALYS by 2020

- **Scenario 2: CD4≤500 as a criteria to start ART (WHO 2013 guidelines)**

The WHO 2013 ART eligibility criteria (CD4≤500) is adopted, and the HIV programmes proceed with current (2012 level) investment allocations and budget level, adding 1 million US dollars annually from the government of Uzbekistan to contribute to ART scale-up. Testing rates are not increased.

Scenario 2:	2020 (estimated)
Estimated number of total PLHIV population	36 000
Number of patients eligible for ART	24 000
ART coverage	10 500 (8300 on first-line and 2200 on second-line)
ART coverage for PLHIV eligible for ART	44%
Diagnosed and eligible without ART	7.500
Undiagnosed	14 200 (39% of all PLHIV)
Total programme cost (2014-2020 not counting inflation)	174.1 million USD
Annual cost of HIV/AIDS response	24.9 million USD
Return on investment	Avoid 13 000 new HIV infections and 74 000 DALYS by 2020

- **Scenario 3: Scaling up to universal coverage by 2020**

Using the same model structure as above and starting with the 2012 service coverage, budget and investments, scenario 3 models a scale-up to reach WHO's 'treat-all' recommendation and universal coverage by 2020.

Scenario 3:	2020 (estimated)
Estimated number of total PLHIV population	33 799
Diagnosed PLHIV (90%)	30 420
ART coverage (90%)	27 378
Undiagnosed	3380
Total programme cost (2014-2020 not counting inflation)	248.8 million US dollars
Annual cost of HIV/AIDS response	35.5 million US dollars
Return on investment	Avoid 26 818 new HIV infections and 232 061 DALYS by 2030

According to the ART scale-up plan provided by the RAC (Table 2) Uzbekistan is working towards fully implementing universal coverage by 2018, which would be close to scenario 3.

5.2 2030: Modelling the long-term outcomes of ART scale-up

The modelling exercise calculates the long-term outcomes of the three scenarios, and the 'treat-all' strategy is the only one that can effectively secure a decrease in the number of HIV infected people and end the epidemic by 2030 *(2)*.

If the 'treat-all' strategy scenario 3 is applied successfully, prevention of new infections will lead to an important decrease in new HIV cases, and thus the size of PLHIV population will decrease by 30-40% in 2030, which will markedly reduce the burden of HIV to the Uzbekistan health system (Table 9, Scenario 3, Option C).

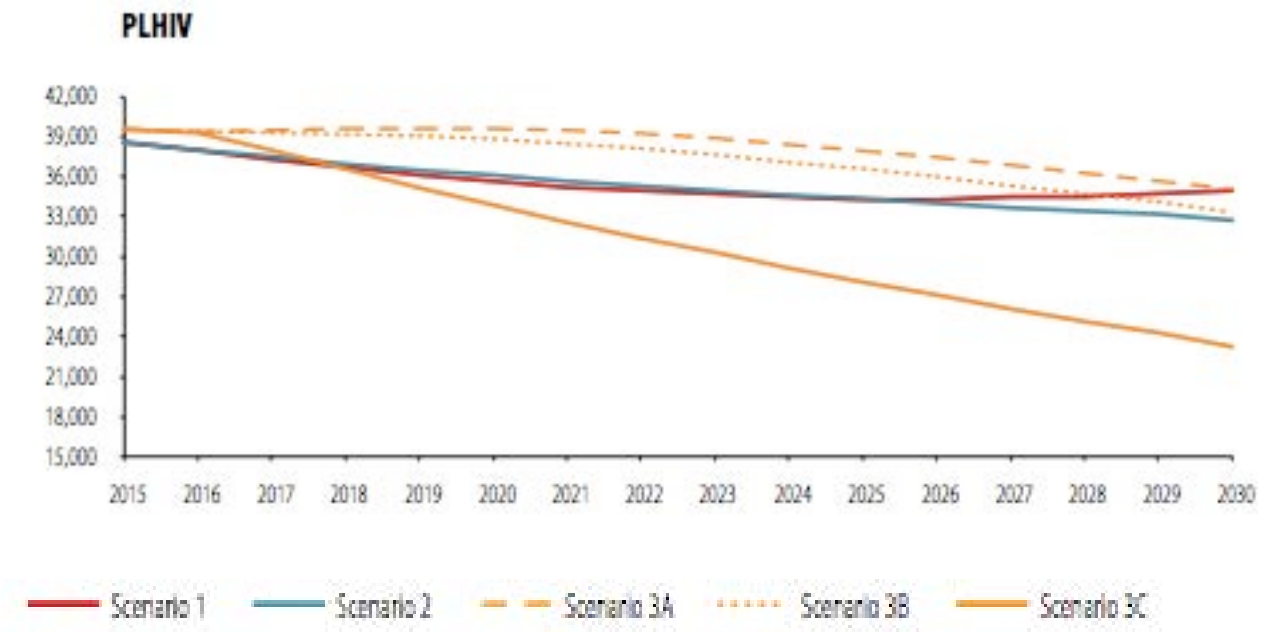
Table 9. Long term comparisons (2015-2030) of the epidemiological impact of scenario 1, 2 and 3 A, B, C *(2)*

	Scenario 1	Scenario 2	Scenario 3 Option A*	Scenario 3 Option B*	Scenario 3 Option C*
New HIV infections averted	12,869	13,151	20,270	21,150	26,818
DALYs averted	49,218	74,110	222,622	229,149	232,061
Total programme costs	$ 167.1 million	$ 174.1 million	$ 210.6 million	$ 228.1 million	$ 248.8 million

* Option A: 95% of diagnosed AND eligible PLHIV by 2020, 2012 national guideline; option B: 95% of diagnosed AND eligible PLHIV by 2020, WHO 2013 guidelines; option C: 95% of all diagnosed PLHIV by 2020 ("test and treat").

Note: Scenario 1: 'Maintaining the 2012 investment allocations and budget level', Scenario 2: 'Optimizing the investment allocations under 2012 budget level', Scenario 3: 'Scaling up to universal coverage by 2020' (2)

Fig. 4. Cumulative new HIV infections averted, cumulative DALYs averted and total programme costs under the three different scenarios (2014-2020) *(2)*



Thus a successful implementation of the 'treat-all' strategy would, by 2030, lead to a decrease in the number of new HIV cases in Uzbekistan and in the estimated PLHIV population from the current 39 000 to around 24 000. It would imply an aversion of more than 26 000 new HIV infections and save 232 061 DALYs when compared to no intervention.

5.3 Inclusion of key populations

The planned ART scale-up cannot be implemented, nor the set goals reached, without including key populations in the ART coverage including, in particular, PWID, which is the largest of the key populations.

In Uzbekistan the national strategic program to counter HIV infections sets a task to ensure coverage of not less than 60% of PWID with HIV prevention services. One modelling exercise based on data from Dushanbe, Tajikistan, which has low HIV prevalence among PWID similar to in Uzbekistan, found that with 20-60% coverage of NSP + ART among PWID it is possible to achieve a 30-50% relative decease in HIV incidence or prevalence over 10 years. For a decrease in HIV incidence to less than 1% or decrease in HIV prevalence to less than 10% over 20 years, it would require coverage levels of about 40-65% and 27-42% of any pair of interventions (NSP+ART+OST); however, if all three are combined the required coverage levels is much lower (23-34%) *(22)*.

Thus, substantial reduction in HIV prevalence and incidence among PWID can best be achieved by continued and expanded NSP coverage, providing ART for the infected PWID, and possibly combining with OST treatment for opioid users. OST is one of nine interventions in a comprehensive package recommended by the WHO for HIV-related services for drug users *(23)*. Currently, OST is not available in Uzbekistan, except for through a planned pilot project. Studies in other countries have found that PWID can be encouraged to maintain a high ART retention rate

when the drugs are distributed, for example, every day or once a week depending on the persons' needs in conjunction with OST and others services. As OST is not available it could be considered to link ARV distribution to other services that may attract PWID, for example food coupons, in connection to the NSP service.

6. Human resources, legislation, and finance: availability and needs

6.1 Human resources

Expanding ART coverage to treat all PLHIV would mean starting ART for about 18 000 additional PLHIV over the coming years. Uzbekistan's Republican AIDS Centre already has plans to increase the number of PLHIV on ART to 20 340 by the end of 2017, which will mean an increase in the number of PLHIV on ART by 8000 (Table 2). Thus a further expansion of 10 000 additional PLHIV should be started in 2018-2020 with ART. If it is presumed that starting ART would require three additional visits to an infectiologist, the expansion to treat all PLHIV would require an additional 40 000 visits to infectiologists during 2016-2020.

However, the net increase in the demand of physicians providing HIV care will not be great as currently PLHIV on the d-list without ART already have to visit a physician twice a year, which is the same as PLHIVs on ART. However, if the goal is to treat all, there will be a transient period for some years when ART is started to catch up for the new equilibrium.

Required human resources:

- Physicians: In 2015, 29 123 people were on the d-list, 26 989 visited the AIDS centres at least once (the total number of visits were 87 678), and according to scenario 3, in 2020 30 420 PLHIV will be diagnosed so the net increase in the demand of physicians providing HIV care is minimal.
- Infectiologist: If an additional 10 000 PLHIV are started on ART in 2018-2020 this would require an additional 40 000 visits during 2016-2020.

6.2 Legislation and stigma

The WHO defines critical enablers as "elements outside of health sector interventions that allow interventions and services to be provided effectively and safely" *(24)*. Examples range from tolerance in the broader society towards key population to human rights-based legal and regulatory frameworks.

The Government of Uzbekistan is aware of the need to improve legislation in order to further a tolerant attitude towards PLHIV, and this is one main objective in the National Strategic Programme *(6)*. As a part of this process, national legislation criminalizing certain people and behaviours should also be revised, because it is contrary to an environment enabling people to learn their HIV status. Also such legislation may negatively affect the possibilities for NGOs to work with key populations, which would hamper important preventive work.

Reduction of stigma related to HIV and key populations in all health care settings, commitment to preserve confidentiality, and adequate pre- and post-test counselling are also critical elements for an enabling environment. Health service providers working with PLHIV in Uzbekistan must receive adequate guidance on these issues through targeted campaigns and education.

Required legal changes:

- Improve national legislation in order to further a tolerant attitude towards PLHIV in all settings including workplaces.
- Revise national legislation criminalizing certain people and behaviours which may be contrary to an environment enabling people to learn their HIV status.
- Reduce stigma related to HIV and key populations in all health care settings.

6.3 Finance

According to the country's own scale-up plan, scenario 2 will be implemented stepwise during 2016 and 2017 (Table 2), and this will require a 2.6 million US dollar increase in domestic spending (Table 10). The goal is to implement the 'treat-all' strategy in 2018, and this would require an increase of 20.1 million US dollars in domestic spending. Yet, as described above, the strategy to 'treat-all' is the only strategy that will significantly reduce the number of PLHIV in Uzbekistan by 2030 *(2)* and thus resources will be saved in the long run.

Table 10. Funding of the HIV/AIDS response (in million US dollars)

	Scenario 1 – CD4 ≤ 350				**Scenario 2 – CD4 ≤500**		**Scenario 3 – 'treat-all'**		
	2012	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**
Total investment	23.9	22.4	24.4	24.4	24.9	24.9	35.5	35.5	35.5
Domestic spending	10.3	11	12	12	**14.6**	**14.6**	**32.1**	**32.1**	**32.1**
International spending* (The Global Fund in parenthesis)	13.5 (10.1)	12.4 (9)	12.4 (9)	12.4 (9)	10.3 (6.9)	10.3 (6.9)	3.4	3.4	3.4

*Assuming that the Global Fund phases out its support after 2017 and that other international donor spending remain at 3.4 million US dollars per year

UNDP announced in November 2015 that it has achieved further price reductions and now can purchase the most widely used first-line one pill combination of three HIV medicines (known as TLE) for less than 100 US dollars per year per patient (a fall from 150 US dollars). If Uzbekistan is able to take advantage of these price reductions on ARV the financial burden of the 'treat-all' strategy will be eased substantially.

Required financial commitment:

- The ART scale-up plan is only feasible with a substantial rise in national spending on HIV care by 2018 (a more than 100% increase from 2017 to 2018).

6.4 Supply management

The MoH plans the purchase of ARV with a buffer stock that covers six months use of ARV. The drugs are distributed to the regional AIDS centres, which distribute to patients on a monthly basis. The RAC reported that there have been no recent central stock-outs *(1).* A recent Global Fund audit of TB and HIV implementing entities found gaps in storage conditions in nine out of 20 visited storage facilities and periodic stock-outs of up to one to two months for main TB and HIV drugs were identified in five out of 10 visited treatment facilities. Stock-outs were mainly caused by a lack of automated drug management systems in the country coupled with the absence of buffer stocks in the regions *(17)*.

UNDP has worked on strengthening the supply chain management and distribution system, including the facilities for adequate storage of drugs at the regional AIDS centres. To meet future requirements, further streamlining of procurement and distribution is needed, and the regional storage capacity has to be assessed and likely enhanced with an additional fridge in every storage room.

Required logistics:

- A further streamlining of procurement and distribution is needed through implementation of automated drug management systems.
- Regional storage conditions and capacity have to be assessed and likely enhanced with an additional fridge in every storage facility.

6.5 Laboratory capacity

Currently a count of blood CD4 positive lymphocytes (CD4 cell count) is used to determine whether a PLHIV is eligible for ART. The national clinical guidelines recommend measuring CD4 cell count every six to 12 months for those on the d-list who are not yet eligible for ART *(6).* During 2015, 78% of patients on the d-list had 3-4 CD4 measures taken (Table 6). When implementing the 'treat-all' strategy, the need for CD4 cell count determination will decrease because the need to monitor CD4 prior to being eligible for ART will no longer be required.

The equipment used for CD4 cell count is the German Partech that has functioned in general well, but occasionally there have been problems obtaining spare parts.

HIV viral load (VL) is essential to monitor adherence to treatment and monitor the effect of ART. VL's are measured with Australian Roto-Gene equipment with Russian kits. The standard detection level for VL is 500 copies per millilitre, but it can be "pressed" to 50 copies per millilitre. In addition to Tashkent there are two other cities where VL measurements take place. The closest service point for VL equipment is in Kazakhstan, which has created problems. Furthermore, the provision of laboratory standardization samples has been lacking.

Current development plans include improving the current equipment by using an advanced version of sample trays that would allow for the analysis of 72 (or even 100) samples with one run. Participation in external quality assurance rounds is planned to start in 2016. Acquisition of automated VL equipment (e.g. Roche Ampliprep Taqman) is planned. The acquisition of another VL detection system would allow for within country quality controls.

The plans for scaling up laboratory capacity for the expanded demand of VL measurements (the RAC estimates this to 39 000 in 2017) created by starting ART at CD4 $\leq$500 seem realistic. The acquisition of high output VL equipment (e.g. Roche Ampliprep Taqman) should be included in the budget at the latest for 2017.

Requited laboratory capacity:

- Secure the supply of spare parts for the German Partech equipment used for CD4 cell counts.
- Develop national capacity to service the VL equipment.
- Secure the provision of laboratory standardization samples to conduct internal quality controls.
- Acquire sample trays allowing the analysis of 72 (or even 100) samples with one run.
- Implement planned acquisition of automated VL equipment (e.g. Roche Ampliprep Taqman).

7. Recommendations

7.1 Main recommendations

Scale up of antiretroviral therapy:

- Plan for universal access to antiretroviral therapy by the end of 2018. Uzbekistan has shown its ability to double the number of PLHIV on antiretroviral therapy in three years from 2012 to 2015. The goal will be achieved by another doubling of the number of PLHIV on antiretroviral therapy in three years.
- Secure funding for the increased need of antiretroviral drugs.
- Streamline the distribution process of ARV from central to regional levels, and enlarge storage capacity.
- Use a one-tablet-a-day ART regimen (TDF+FTC+EFV) when starting ART for PLHIV who are naïve (new) to ART.
- Scale-up and secure funding for laboratory capacity for viral load (VL) measurement with larger sample trays and the acquisition of new high-output VL equipment.

Reaching the 90-90-90 targets:

- Use more than one model to estimate the total number of PLHIV.
- Ensure HIV testing is free, voluntary and confidential, and increase testing coverage of the most at risk groups.
- Prioritize outreach activities, in particular HIV rapid testing at the community level and harm reduction services, targeting key populations.

- Review the procedures around prevention of MTCT to prevent new HIV infections among children and implement WHO treatment Option B+.
- Make two care plans for PLHIV linking to care; one with more intensive follow up for the most vulnerable patients and one less intensive plan for motivated, compliant patients.
- Strengthen cross analysis of surveillance and clinical data to inform policy decisions on priorities within the national HIV programme.
- Reduce stigma related to HIV and key populations in all health care settings through targeted campaigns and education.

7.2 Specific recommendations

Estimation of PLHIV

- Consider the use of several models for data triangulation purposes in the estimation of the total number of PLHIV.

Optimizing HIV Testing

- Calculate the testing coverage annually to monitor developments in coverage of HIV testing in key populations.
- Break down the numbers of tests per year into age, gender and place of testing, and include this for anonymous testing.
- Use the existing UNICODE system to track whether anonymously tested HIV-positive persons get a confirmative HIV test and are eventually linked to care.
- Focus HIV testing strategically on the populations most at risk for HIV, including hard-to-reach populations such as PWID and MSM.
- Secure continuation of harm reduction and preventive activities in Trust Points and Friendly Cabinets across the country (needle and syringe exchange, distribution of free condoms, and education and information).
- Secure a supply of rapid HIV blood tests, and if possible, express test systems for multiple markers (HBsAg/HIV/HCV and TP/HIV) for the Trust Points, expand this service to Friendly Cabinets and consider community based outreach testing.
- Develop comprehensive reporting on results of rapid HIV tests by collecting and analysing data from Trust Points, Friendly Cabinets and other testing services on the number of rapid blood tests conducted, positive cases identified, as well as confirmative testing and linkage to care.
- Allow lay persons to conduct rapid blood testing and/or saliva tests in order to scale-up outreach testing targeting hard-to-reach populations such as PWID and MSM (will require a revision of clinical protocols).
- Gather data and perform routine analysis of the number of new HIV patients tested for co-infections with Hepatitis B and C (and vice versa).
- Report testing data for HIV tests based on clinical indications separately for viral hepatitis, TB and the other clinical indications.
- Inform and train all relevant specialists and general doctors to recommend HIV testing to all patients presenting with indicator conditions.
- Monitor CD4 cell count of people presenting for care and disaggregate the information to identify regional differences.

Prevention of HIV transmission

- Offer rapid diagnostic tests to women about to give birth who have not been previously tested for HIV during their pregnancy.
- Implement WHO Option B+ and ensure that *all* pregnant women tested and found to be HIV-positive are immediately are offered (life-long) ARV treatment.
- Sustain and consistently apply early infant diagnosis, and ensure a supply of prophylaxis to *all* children born to HIV-positive women.
- All children living with HIV must be offered ARV treatment regardless of CD4 cell count.
- Conduct a thorough epidemiological investigation of all new cases of children with HIV without HIV-positive parents to clarify the transmission route.
- Separate the numbers of children infected vertically and parenterally to get an overview of, and to address, the situation.

Enrollment and retention in care

- Make a concerted effort to link all PLHIV that have been diagnosed to care.
- Minimize lost-to-follow up of patients on the d-list and attempt to track patients not showing up for regular medical checks.
- Ensure that the clinical protocol guidelines to screen *all* new HIV-positive patients for TB are implemented.
- Provided ART to all TB/HIV co-infected patients regardless of CD4 cell count.
- Analyse the causes of death of patients co-infected with TB to see if the correct treatment was effectuated.

National guidelines on ART for adults and children

- Update the national clinical protocols in accordance with the country's ART scale-up plan.

ART Coverage

- Analyse the regional data on CD4 cell count at diagnosis and at treatment initiation to identify and address regional differences.
- Analyse the regional data on LTFU and deaths to identify and address regional differences.
- Disaggregate data on ART coverage by main key populations to be able to assess the impact of the scale-up.
- Apply integrated approaches to clinical management that address the special needs of HIV-infected patients on ART with co-infections or co-morbidities.
- Continue working on simplifying ARV drug regimens.
- Use early warning indicator monitoring to identify the emergence of HIVDR and decide on shifts from first to second line treatment regimens; only elaborate resistance tests after an indication of failure of standard second line regimens.
- Use one tablet ART regimens to simplify the logistics in dispensing and to eliminate the possibility of PLHIV taking an incomplete regimen.
- Gradually shift patients on ABC-based regimens to the preferred TDF or ZDV-based regimens.

CD4 and Viral load

- Gather and analyse data on the patients' viral load and use this to assess the treatment quality at the regional levels.
- Implement a care plan for compliant patients with annual medical check-ups and supply of ARV drugs for longer time periods for the convenience of the patients and for the reduction of human resources in AIDS centres.
- Implement an intensive care plan for vulnerable patients who need extra support to comply with ARV treatment.

7.3 Resources needed for ART scale-up

Human resources

- Physicians: In 2015 29 123 people were on the d-list, 26 989 visited the AIDS centres at least once (the total number of visits were 87 678), and according to scenario 3, in 2020, 30 420 PLHIV will be diagnosed; the net increase in the demand of physicians providing HIV care is minimal.
- Infectiologist: If an additional 10 000 PLHIV are started on ART in 2018-2020 this would require an additional 40 000 visits during 2016-2020.

Legislation and stigma

- Improve national legislations in order to further a tolerant attitude towards PLHIV.
- Revise national legislation criminalizing certain people and behaviours which may be contrary to an environment enabling people to learn their HIV status.
- Reduce stigma related to HIV and key populations in all health care settings.

Finance

- The ART scale-up plan is only feasible with a substantial rise in national spending on HIV care by 2018 (a more than 100% increase from 2017 to 2018).

Supply management

- A further streamlining of procurement and distribution is needed through the implementation of automated drug management systems.
- Regional storage conditions and capacity have to be assessed and likely enhanced with an additional fridge in every storage facility.

Laboratory capacity

- Secure the supply of spare parts for the German Partech equipment used for CD4 cell count.
- Develop national capacity to service the VL equipment.
- Secure the provision of laboratory standardization samples to conduct internal quality controls.
- Acquire sample trays allowing for analysing of 72 (or even 100) samples with one run.
- Implement planned acquisition of automated VL equipment (e.g. Roche Ampliprep Taqman).

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Annex 1. Timeline for key steps towards ART scale-up

The implementation strategy to scale up ART coverage will be initiated in 2016 (short-term) and the vast majority of the key steps are expected to be completed by 2017 (mid-term); however, a few activities are expected to take longer to implement and will continue through to 2018-2020 (long term).

Table 11. Timeline for key steps in the ART scale up plan in Uzbekistan

Key steps	**2016** **Immediate tasks**				**2017** **Mid-term tasks**				**2018-2020** **Long-term tasks**			
	Target 1: 90% of the PLHIV in Uzbekistan are tested											
1. The MoH allows the RAC to use various models to estimate total PLHIV population	Undertaken	Report available										
2. The RAC assesses cost-effectiveness of actual testing strategies				X								
3. The relevant ministry approves the new database and it is put to use by the RAC	Approval	Implementation started		Implementation completed								
4. The RAC systematically monitors data on late presentation		Database is approved and in use		Implementation completed								
5. Testing of key populations is increased through layperson outreach HIV testing		Application to allow laypersons to test		Pilots on outreach testing started		Results of outreach testing viewed						
6. The MoH introduces indicator condition-based HIV testing across specialities	Strategy planned	Begin educating other specialities			Education of other specialities completed							

	Target 2: 90% of diagnosed PLHIV in Uzbekistan are on ART											
7. The RAC should trace diagnosed PLHIV not linked to HIV care	Planning actions e.g. outreach projects			Starting actions								
8. Simplified antiretroviral regimens				Target: One-pill-a-day is used for 65% of PLHIV starting ART		Target: One-pill-a-day is used for 85% of PLHIV starting ART						
9. ARV procurement and dispensing				MoH has taken over 100%								
10. Scale-up of laboratory capacity	Apply for high output Rotor gene trays	Start to apply for automated VL equipment in 2017 budget	QA rounds started	High output rotor gene trays in use		Automated VL in use in RAC						
12. Human resources						More outreach workers are gained						
	Target 3: 90% of PLHIV on ART have undetectable viral load											
13. Retention in care	Start planning for “2 tracks" for care			“Two tracks” for care started		“Two tracks” evaluated				“Two tracks” evaluated		
14. Key populations		OST pilot project is started		OST pilot project is evaluated		Opioid users/ PWID on ART are offered OST				PWID retention in care is evaluated		

Annex 2. ToR for the mission

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR EUROPE

WELTGESUNDHEITSORGANISATION
REGIONALBÜRO FÜR EUROPA

ORGANISATION MONDIALE DE LA SANTÉ
BUREAU RÉGIONAL DE L'EUROPE

ВСЕМИРНАЯ ОРГАНИЗАЦИЯ ЗДРАВООХРАНЕНИЯ
ЕВРОПЕЙСКОЕ РЕГИОНАЛЬНОЕ БЮРО

Development of a plan on expansion and optimization of ART in Uzbekistan

23-26 November 2015

1. Background

Since the beginning of national reporting and through to the end of 2010, Uzbekistan had reported a cumulative total of 24 057 HIV cases, 651 AIDS cases and 323 deaths among AIDS cases, to the WHO Regional Office for Europe and the European Centre for Disease Prevention and Control (ECDC). Since 2010, no official HIV/AIDS surveillance data have been available from the country.

Of the newly diagnosed HIV infections with information about transmission mode in 2010 (73% of cases), 67% were transmitted through injecting drug use, 31% through heterosexual contact and there were no cases through sex between men. 54% of the new HIV cases were male. Uzbekistan has reported a cumulative total of 363 children infected through mother-to-child transmission, including 73 in 2010.

Between 2004 and 2010 the rate of newly diagnosed HIV infections increased by 71%, from 8.0 per 100 000 population (2055 cases) in 2004 to 13.7 per 100 000 population (3795 cases) in 2013. The increase is of concern and indicative of some weaknesses in HIV prevention for key populations.

Also of concern is the eight-fold increase in the rate of newly diagnosed AIDS cases, from 0.1 per 100 000 population (11 cases) in 2004 to 0.8 (220 cases) in 2010, indicative of late diagnoses and insufficient ART coverage.

Taking undiagnosed infections into account, the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the WHO estimate that 35 000 (27 000-48 000) people were living with HIV in Uzbekistan at the end of 2013, that 1100 people became newly infected, and that 2700 people died from AIDS-related causes during 2013. HIV prevalence in the adult population was estimated to be 0.2% (0.1-0.3%).

The number of people receiving antiretroviral therapy (ART) increased from 259 in 2006, to 2479 in 2010 to 8291 in 2013. The number of people enrolled in medical HIV care increased from 4400 in 2006, to 14 167 in 2010 to 28 250 in 2013. Among the total estimated number of adults living with HIV in the country, an estimated 24% were receiving ART at the end of the year.

Adaptation of the WHO 2013 Guidelines on the use of ARVs for the Prevention and Treatment of HIV infection within national guidelines remains ongoing, with a target set for 12 325 of those requiring ART receiving the necessary treatment by 2015, 14 340 by 2016 and 16 340 by 2017. For

adults and adolescents, the recommended CD4 threshold for initiating ART is <350 cells/mm^3. For children, the protocol suggests initiation of ART in all children under the age of one year irrespective of symptoms. The recommended first line regimen is TDF/3TC(FTC)/EFV in accordance with WHO guidelines. For the prevention of mother-to-child transmission (MTCT) of HIV, a national plan for the elimination of MTCT is in place, and the current nationally recommended PMTCT "Option B" was adopted in 2008. National guidelines also recommend ART for all HIV-positive patients with active TB or hepatitis B severe liver disease, however do not recommend ART for the HIV-positive partner in serodiscordant couples. Routine viral load monitoring is recommended at three months following ART initiation and then subsequently every six to nine months. Point-of-care CD4 technology is implemented and the country does have a national HIV drug resistance strategy in place.

In terms of HIV testing and counselling (HTC), the national policy addresses all population groups, key populations and pregnant women included, and recommends provider-initiated testing and counselling in all patient encounters. The policy also supports rapid testing with same day results, however does not support HTC provided by community services, or point-of-care rapid testing done by lay or community workers.

Uzbekistan is a country implementing a Global Fund grant on HIV. In 2014 it reprogrammed grant implementation in order to address the priority issues for interventions. One of the key issues is access to ART and ART coverage, and the Government of Uzbekistan has committed to increasing financing of ART in 2016-2017 using domestic funds. The Global Fund has made a decision to extend the current grant for half a year in 2016, considering that a transitional plan on financing of ART with increasing proportion of governmental input will be developed and as well as the consideration of the increasing demand for ART.

In October 2015 the WHO released a new *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV*[3], recommending ART to everyone living with HIV at any CD4 cell count. New evidence-based recommendations challenge the country capacity to provide ART for all who need it and requires strategic planning.

A working group has been formed to develop a transitional ART plan considering changes to the eligibility criteria for ART. The Ministry of Health has approached the WHO with a request for technical assistance for the working group in developing an ART scale-up plan.

2. Objective and tasks

The objective is to develop a National ART scale-up plan, considering new internationally recommended criteria for starting ART and recommended ART regimens, with ultimate goal to reach the UNAIDS' 90-90-90 targets.

Evaluation of the country's clinical recommendations and service delivery across the cascade of services should inform the ART plan and recommendations for its implementation. In particular, the following should be addressed:

- Main barriers to HIV testing and linkage to HIV care services;

[3] http://www.who.int/hiv/pub/guidelines/earlyrelease-arv/en/

- Main reasons for lost to follow up within the cascade of HIV services (HIV testing, linkage to care, ART enrolment and retention, and monitoring of viral suppression) and an average time between the patient's HIV status confirmation and treatment initiation;
- National HIV treatment protocols, including criteria to start ART, ART regimens and recommendations on retention in HIV care; and
- Number of PLHIV receiving and planned for ART.

3. Methodology

The preparation phase will include a desk review and analysis of available country documents, including: the National Strategic Plan on HIV, including plans on ART; National clinical recommendations on ART; National HIV testing guidelines, estimates of PLHIV, cost of ART regimens, etc.

During the country mission WHO experts will visit relevant institutions, discuss issues with key informants and will work closely with the working group members on developing the ART expansion plan.

4. Participants

Two external WHO experts:

- ✓ Matti Antero Ristola, clinical expert, head of HIV services, Helsinki University Hospital Finland
- ✓ Stine Finne Jakobsen, public health expert, WHO CC on HIV and viral hepatitis, Denmark

External consultants will be supported by the WHO country staff member, Dr Ogtay Gozalov.

5. Time, duration and geographical sites of the mission

The mission is planned for 23-26 November 2015. Additional days will be added for desk review and analysis of national background documents and the developing ART Plan.

Public health expert: 14 days of preparation for the mission and reporting, including a desk review of the country documents and developing ART plan and a 4 day country mission (18 days).

Clinical expert: 8 days of preparation for the mission and reporting, including a desk review of the country documents and developing ART plan and a 4 day country mission (12 days).

Translation services and logistic support will be provided by the WHO CO in Uzbekistan.

6. Deliverables

A National ART scale up plan with clear strategy for the proposed rapid ART expansion, including:

1) a clear explanation of the reasons for lost-to-follow-up rates under the current program;
2) an outline of key strategies to address these issues;
3) a description of key steps towards formulating an implementation plan; and

4) an indication of the cost implication of moving criteria for ART initiation from CD4<350 to all PLHIV regardless of CD4 cell count.

The deliverables should be submitted to the WHO Regional Office for Europe and WHO Country Office by **15 December 2015.**

Annex 3. List of informants

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Other RAC staff:	Epidemiologist Spectrum Expert Head Nurse Paediatrician Dermatologist	Republican centre to fight AIDS	
Medical Staff:	Doctor Doctor	Trust Point Friendly Cabinet	
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