World Health Organization
REGIONAL OFFICE FOR Europe

chip Centre for Health & Infectious Disease Research

WHO Collaborating Centre on HIV and Viral Hepatitis

Optimization of ART in Ukraine: general principles of ART optimization from a public health perspective

Mission report
April 2016

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Abbreviations

3TC	lamivudine
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
ARV	antiretroviral
CD4	T–lymphocyte cell bearing CD4 receptor
ECDC	European Centre for Disease Prevention and Control
EECA	Eastern Europe and Central Asia
EFV	Efavirenz
FSW	female sex workers
FTC	Emtricitabine
HCV	Viral hepatitis C
HIV	human immunodeficiency virus
IDUs	injecting drug users
MDR	multi-drug resistant
MoH	Ministry of Health
MSM	men who have sex with men
MTCT	mother-to-child transmission
NVP	Nevirapine
OIs	opportunistic infections
OST	opioid substitution therapy
PITC	Provider initiated Testing and Counselling
PCR	polymerase chain reaction
PLHIV	people living with HIV
PMTCT	prevention of mother-to-child transmission
POC	point of care
PWID	people who inject drugs
STR	single table regimen
RNA	nucleic acid test
TB	tuberculosis
TDF	Tenofivir
TGF	The Global Fund
UCDC	Ukraine Centre for Disease Control
UNAIDS	Joint United Nations Programme on HIV/AIDS
STI	sexually transmitted infections
WHO	World Health Organization

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1. Introduction and background

Ukraine has a population of approximately 43 million people. The first cases of HIV were registered in 1987. Until the middle of the 2000s transmission was driven by injecting drug users (IDUs) but in recent years sexual transmission has grown and the epidemic has spread to partners of IDUs and other vulnerable groups. Antiretroviral therapy (ART) was introduced in Ukraine around the year 2000. In 2014 Ukraine experienced a devaluation of the national currency and a national financial, political and security crisis developed which has constrained the expansion of the HIV programme as intended.

Against this epidemiological challenge and the country's limited resources, discussions have begun in Ukraine on how best to invest the available resources to manage the epidemic. It is in this context that WHO was asked to provide technical support and make recommendations in relation to optimization and prioritization of care structures using a state-of-art scientifically evidenced-based approach, which Ukraine can use to rationalize its HIV programme.

As a premise for this technical support, it has been acknowledged by the national key stakeholders that WHO assumes that the governmental leadership in Ukraine recognizes the HIV situation as a public health emergency. Therefore, the financial surplus for the recommendations that the WHO makes in this report are intended to be invested into strengthening the national HIV programme. All key stakeholders involved with the mission acknowledged this premise.

2. Purpose and objectives

The objective of the mission was for an international consultant to support the development of a national ART protocol and optimization of ARV treatment in Ukraine; more specifically:

- to provide comments on the unresolved clinical key questions identified locally (e.g. selection of ART regimens given financial constrains in the country, balance between 1st-line and 2nd-line drugs, switching patients between regimens, use of generics and (fixed drug combinations (FDCs), etc.);
- to facilitate professional dialogue in Ukraine on the standardization/optimization of ART and development of the national protocol;
- to advocate for a public health approach in ART delivery; this approach is particularly appropriate for the current situation of limited resources in the country;
- based on the observations in the country, to provide WHO with an independent advice on the priority areas for technical support in Ukraine.

3. Methods

The report draws on a preparatory phase that included:

- a Skype conference on 11 March 2016
- review and analysis of available documents (WHO guidelines, national policy/strategy/plans, clinical guidelines, publications and reports),
- extensive electronic communication.

The WHO country mission took place from 5-7 April 2016. The international consultant participated in several face-to-face meetings, including a two day workshop on ART standardization/optimization in Kiev, with participation of national and international partners, health care professionals, decision- makers and PLHIV organizations.

4. Overall analysis of the situation in Ukraine and recommendations

This section of the report addresses the current challenges faced by Ukraine in its efforts to control the HIV epidemic, and it provides recommendations for how to use a public health approach to modify the national HIV programme towards a process of rationalization and prioritization of resources.

4.1 Epidemiology of HIV transmission

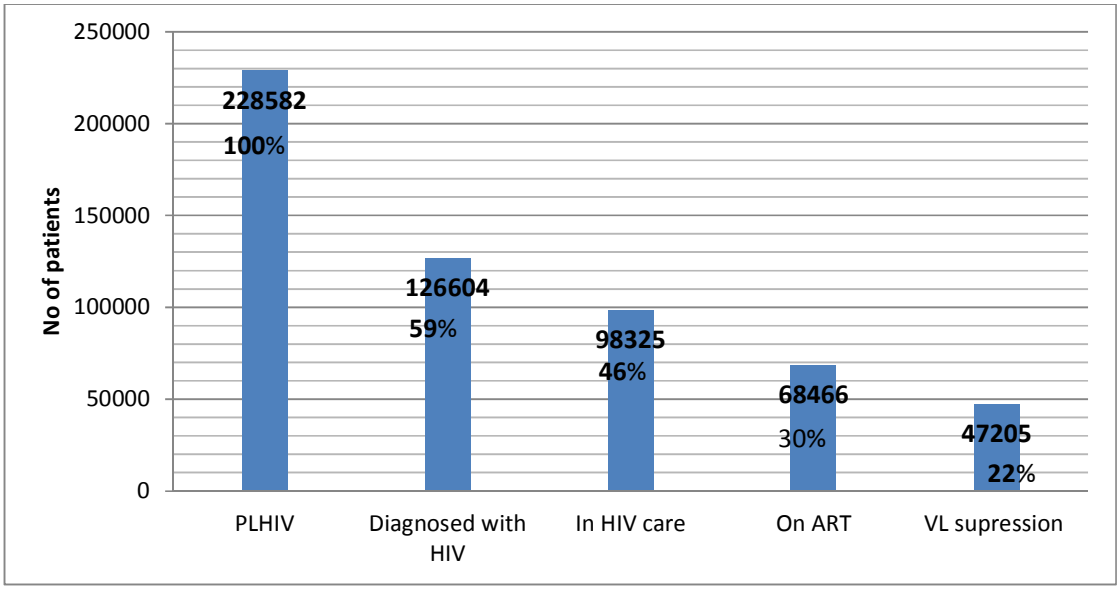
Ukraine has a population of approximately 43 million people. The first cases of HIV were registered in 1987. Until the middle of the 2000s transmission was driven by IDUs but the prevalence rate in this subpopulation has stabilized over time due to natural saturation. Harm reduction programmes (both needle exchange and OST) have been implemented since 2004, but their coverage has never reached optimal levels. In recent years the growing transmission is observed from the IDU subpopulation to partners of IDUs and other vulnerable groups. Current projections estimate that around 20-30% of new recent infections are due to IDU transmission and the remaining primarily due to sexual transmission. Approximately 70-80% of the IDU subpopulation are men, but the earlier male-driven HIV epidemic is now more gender-neutral. MSM transmission has emerged as an accompanying epidemic – probably hidden until recently – and most likely underreported due to stigma towards MSM.

It was outside the scope of this mission to evaluate the public response including campaigns and prevention interventions performed to limit population transmission risk other than the use of ART.

4.2 Continuum of care in Ukraine

The Ukrainian Center for Social Disease Control of the Ministry of Health of Ukraine (UCDC) has created a continuum of care estimate for the country (Fig. 1). It is estimated that a total of 230 000 people are living with HIV, of these 59% are diagnosed, 46% are in care, 28% are receiving ART, and 22% are virologically suppressed on ART.

Fig. 1. HIV cascade in Ukraine as of 01.01.2016



**On ART (GARPR data from 2015)*
***VL suppression - approximation based on the reporting of viral load (VL) testing (Source: UCDC)*

Recommendations:

- Consider supplementing the SPECTRUM modelling estimations of total size of infected population with estimations from other modelling tools. The SPECTRUM modelling tool is very dependent on specific information about populations most-at-risk to HIV (population size and HIV surveillance data). It can be considered to supplement with estimations from models using the profile of newly diagnosed persons, e.g. the London model *(1)* or the newly released ECDC HIV model *(2)*.

4.3 Testing strategies

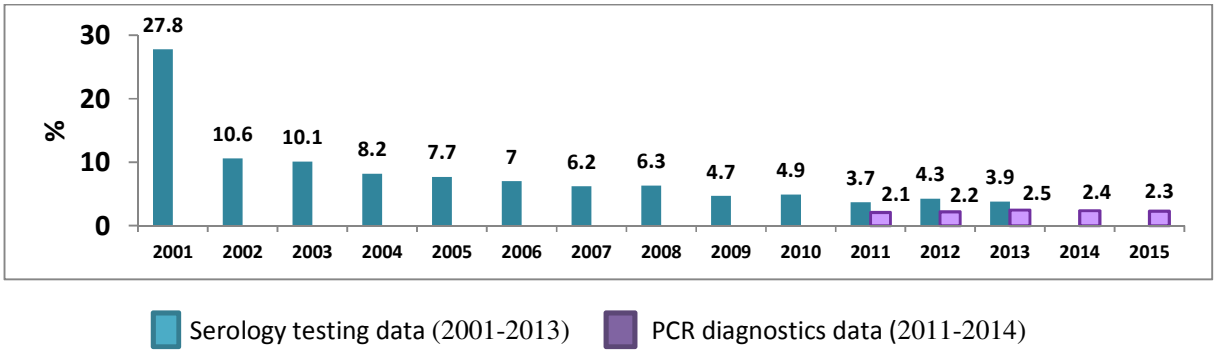
In 2014, approximately 50% of newly diagnosed persons had a CD4 count at presentation of < 350 cells/µL, and a similar percentage had WHO stage 3-4 clinical symptoms. Whereas the former percentage is seen throughout the European continent, the latter percentage is noteworthy. It was confirmed during the mission that many of these persons are IDUs and that TB is an important factor in advanced stage of HIV infection.

In 2015, Ukraine tested a total of 2.3 million persons for HIV, diagnosed 23 200 and 15 800 were registered as new cases of HIV. Almost half of the HIV tests were performed in blood donors and pregnant women (45%); it is current practice to test most women at least twice during pregnancy. According to official statistics in 2015 the number of pregnant women tested once was 442 766, 1 482 (0.33%) of whom tested positive for HIV. The number of women tested a second time for HIV during pregnancy (code 109.2) was 366 226, 29 (0.008%) of whom tested positive for HIV.

The percentage of MTCT has decreased over time from 28% in 2001 to 3.9% in 2013 (Fig. 2). In 2015 a national study with 71.5% coverage by PCR the transmission rate was 2.3%. Most of the

transmissions occur in women linked with the IDU community who are not accessing prenatal screening programmes.

Fig. 2. Incidence of mother-to-child HIV transmission in Ukraine *(Source: UCDC)*



Since 2015 in particular Ukraine has scaled up its testing efforts among IDUs (estimated to 250 000-310 000 persons)[1]. In 2015 130 000 IDUs were tested and approximately 3 000 new cases were diagnosed (2.3%). It is possible that the subpopulation of IDUs at continued risk of HIV transmission is becoming smaller, because younger persons tend to use synthetic drugs, which are not injected, and thus may not be considered as part of the IDU population and hence not at increased risk of HIV infection.

Recommendations:

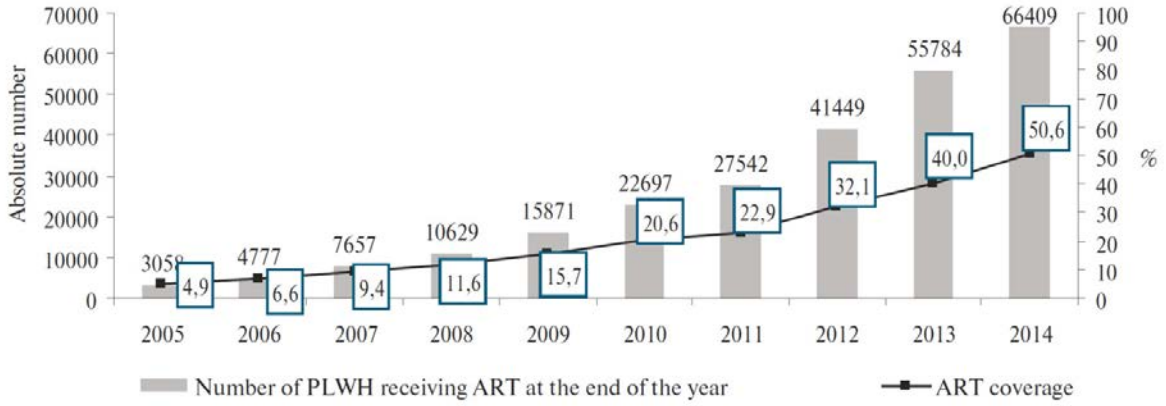
- Maintain focus of HIV testing in most-at-risk populations and consider further scale-up of testing in these populations
- Allow non-medical personnel at community clinics to offer testing
- Use more rapid tests for screening purposes
- Clarify procedures for active linkage to HIV care facilities for all testing locations
- Strengthen surveillance data on the reasons for testing
- Evaluate the coverage of most-at-risk groups and changes over time
- Evaluate the benefit of the second test made during pregnancy and consider removing it.

4.4 Scale up of ART and financial coverage

The number of PLHIV on ART in Ukraine has increased markedly, particularly over the last five years (Fig. 3). At the same time it is acknowledged that improving the ART coverage rates is required. Using UNAIDS fast track estimations, the number of persons on ART should increase three-fold over the next four years (from 60 000 to 180 000). Such a rapid scale-up seems unfeasible. The country aims to have 85 000 PLHIV on ART by the end of 2016.

[1] One reference on OST in Ukraine assesses the estimated amount of IDUs consuming opioids to around 250,000 – based on this the total IDU population would more like be around 300,000 (see Figure 5)

Fig. 3. ART scale-up in Ukraine *(3)*



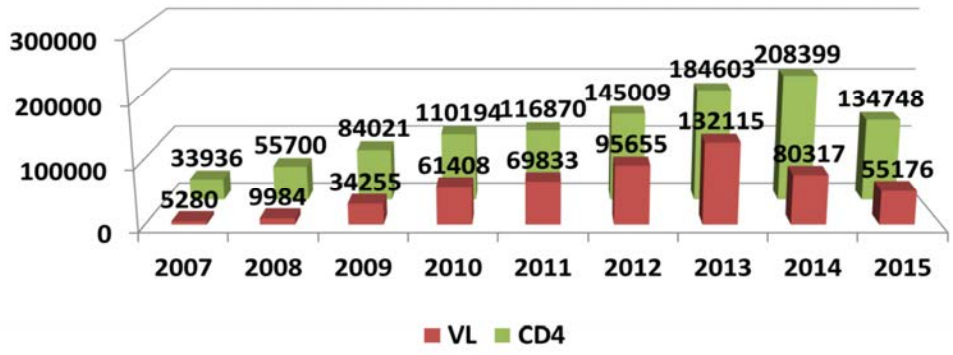
**: defined as total diagnosed with CD4 count ≤ 350 cells/µL.*

In total 235 clinics across the country are able to distribute ART and this number seems to be sufficient to ensure scale-up. During the mission it was however not possible to assess the proximity of these clinics relative to the persons that will be accessing care.

The tuberculosis situation in Ukraine was superficially discussed during the mission. It was recognized that a substantial percentage of TB cases are MDR, that TB progresses quickly to symptomatic infection in immunodeficient person. It was also acknowledged that the provision of ART to all diagnosed with HIV people is highly effective in preventing the development of symptomatic TB (including MDR) infections. This argument is hence important in the further discussions on how to secure funding for ART scale-up in Ukraine.

The devaluation of the national currency in 2013 and the current national financial, political and security crisis, combined with decisions from The Global Fund to scale down support to middle income countries have strained the ability to expand the HIV programme as intended. For example, the number of HIV RNA tests conducted for monitoring peaked in 2013 and has since then declined due to budget cuts (Fig. 4).

Fig. 4. Laboratory monitoring of ART



Source: UCDC

The US based Centre for Disease Control and Prevention (CDC) is present in Ukraine and is considering investing in the national HIV programme but decisions are limited to annual forecasting. The Global Fund contribution is guaranteed until 2018 only. The financial sustainability of the Ukrainian HIV programme is therefore uncertain.

Recommendations:

- Develop transmission models that can be used to estimate impact on transmission risk depending on different approaches to future scale up of ART[2]. Incorporate the benefits from reducing clinical impact from TB (incl. MDR) and slowing the progression of organ disease (incl. liver disease in particular in those co-infected with HCV - most prevalent viral hepatitis co-infection).
- Continue to ensure national political support by emphasising the financial burden if the scale-up of the HIV programme is not achieved.
- Consider optimizing the HIV programme in order for international donors to continue to consider supporting the programme in future years.

4.5 When to start ART

In December 2015 Ukraine adopted the current WHO guidelines to treat all HIV positive persons irrespective of their CD4 count *(4)*; a recommendation that is based on results from the large randomized study START *(5)*. The country is however unable to fully implement this decision due to financial constraints and hence is focusing on prioritizing initiation in persons presenting with opportunistic disease and in asymptomatic persons with CD4 count < 500 cells/µL. As such, the country will continue to use the CD4 count as a treatment initiation indicator before initiating ART in asymptomatic patients.

[2] For examples of mathematical transmission models see http://www.hivmodelling.org/countries/gb

Recommendations

- The national clinical protocols' recommendations for initiation of ART are consistent with current WHO recommendations and should be maintained although full implementation is not feasible at present.

4.6 What to start with

According to the national clinical protocols, and supported by all stakeholders present at the 6-7 April meeting, WHO's current recommendations to utilize one preferred 1st line regimen *(6)* is largely adopted in the country.

4.7 Optimization of choices of ART in those already on 1st line ART

It is estimated that approx. 55 000 persons are currently on 1st line ART (Table 1). Approximately 1 in 3 are currently receiving the WHO's preferred 1st line regimen (TDF/FTC+EFV).

Table 1. ART composition at 1 March 2016 among adult PLHIV on 1st line treatment

1st line (naïve and changed due to side effects)	57.894	
Adults (>18 years old)	55.546	
Out of them receiving ART regimens:		
TDF/FTC+EFV (WHO preferred 1st line regimen)	12 174	21,9
AZT+3TC+EFV	10 790	19,4
AZT+3TC+LPV/r	9 287	16,7
TDF+3TC+EFV	5 957	10,7
TDF/FTC+LPV/r	4 614	8,3
TDF+3TC+LPV/r	3 438	6,2
ABC+3TC+LPV/r	3 110	5,6
ABC+3TC+EFV	2 704	4,9
AZT+3TC+NVP	1 611	2,9
TDF+3TC+NVP	591	1,1
TDF/FTC+NVP	443	0,8
ABC+3TC+NVP	329	0,6
AZT+3TC+ABC	250	0,5
AZT+3TC+TDF	103	0,2

Extensive discussion took place during the mission to consider whether it would be medically safe to switch the composition of ART for the remaining 2/3 of patients in order for more patients to receive the preferred regimen. Based on the distribution of combinations used, three strategies for switching were identified during the mission (Table 2).

Table 2. Drug switched considered as part of optimisation of 1st line ART

• **AZT to TDF**
• **ABC to TDF**
• **LPV*/r to either ATV/r, EFV or NVP**

**Reasons why 40% of 1st line patients receive LPV/r are diverse: Teratogenic concerns with use of EFV; Prior treatment-limiting toxicity to EFV; Patient choice; Physician choice; Prior limited access to EFV*

It was not possible to fully evaluate the extent to which these switches are feasible, although it was agreed that it would be possible for many patients (likely 60-90%) and this would result in substantial cost savings.

A rough estimate sets present average cost per patient for one year of treatment to 360 US$ and this can possibly be reduced to 120-140 US$ per patient per year if optimization as described in table 2 is implemented. The financial surplus could be channelled towards providing ART to more PLHIV and possibly attract additional international support as such optimization is a prerequisite for many international donors including The Global Fund.

In case Ukraine decides to implement a switching strategy a proposal has been outlined for how to switch patients to other agents as part of process to optimize the ART programme in Ukraine, how patients can be instructed and the recommended HIV RNA monitoring around the time of the switch (see Table 3).

Table 3. Proposal for how to switch patients using Zidovudine, abacavir, and LPV/r-based regimens as part of 1st line ART to other regimens

Other drug: reason for being on this	Proposed drug to switch to	Need for HIV RNA monitoring post-switch (pre-switch relevant)	Comments
ZDV: preferred choice at the time	TDF	Not necessary but can be done	TDF is a safer drug than ZDV (less risk of anaemia and lipoatrophy)
ZDV: current severe kidney impairment	Stay on ZDV or switch to ABC	Not necessary but can be done	TDF may further impair kidney function
ABC: preferred choice at the time	TDF	Not necessary but can be done	TDF is a cheaper and probably more effective and safer drug than ABC
ABC: current severe kidney impairment	Stay on ABC or switch to ZDV	Not necessary but can be done	TDF may further impair kidney function
LPV/r: Teratogenic concerns with use of EFV	EFV*	Yes (prioritised if earlier use of EFV or NVP)	Current evidence does not suggest that this concern is relevant to humans
LPV/r: Prior treatment-limiting toxicity to EFV	NVP**, ATV/r*** or EFV*	Yes if switching to either one of the two NNRTI's (prioritised if earlier use of EFV)	Choice of drug to switch to depends on circumstances when original switch was done (if well documented, EFV should be avoided; if not EFV may be considered); drug to possible switch to depends on which drugs national programme is focusing on
LPV/r: Prior limited access to EFV	EFV*	Yes (prioritised if earlier use of EFV or NVP)	Reason no longer relevant
LPV/r: prior switch from nelfinavir (the preferred PI/r at the time)	EFV*	Yes (prioritised if earlier use of EFV or NVP)	Switching from one drug class to another with lower genetic barrier is safe if patient remains adherent and has no archived drug resistance mutation
LPV/r: Currently having accepted contraindications to using EFV	NVP** or ATV/r***		Recognised contraindications to EFVs; drug to possible switch to depends on which drugs national programme is focusing on mutation
LPV/r: current using methadone	EFV*	Yes (prioritised if earlier use of EFV or NVP)	EFV and methadone can be safely co-administrated
LPV/r: Patient choice (other than above)	EFV*	Yes (prioritised if earlier use of EFV)	Patients are to be reassured by their health care professionals that EFV is a safe drug
LPV/r: Physician choice (other than above)	EFV*		Health care professionals are to be reassured that EFV is a safe drug when prescribed under the correct medical conditions*

*: Patients should be informed prior to the switch about possible adverse drug reactions of EFV and that these usually diminish within days or a few weeks; if the patient experiences these adverse effects he or she should continue to take the drug until instructed otherwise in consultation with ART centre.

**: Patients should be informed to contact ART centre in case of rash and liver toxicity; these toxicities are reduced for persons with higher CD4 counts if HIV RNA is suppressed at time of switch.

***: Patients should be informed to contact ART centre if icteric sclerae is cosmetically debilitating; this manifestation is not health threatening.

Recommendations

- Develop a strategy that will result in switches to the WHO recommended 1st line ART for a substantial percentage of patients currently on other 1st line ART combinations. This strategy should have at least three components:
    - institute post-graduate training of health care professionals to ensure that this community is supporting the strategy;
    - make a decision on which drugs in addition to WHO preferred 1st line ART Ukraine will be prioritised for procurement – this depends in part on price of the drug;
    - follow recommendations as outlined in table 3.
- Consider asking WHO to review strategy document prior to implementation.

4.8 Laboratory monitoring of ART

Ukraine has adopted WHO recommendations on monitoring of patients on ART. However, they have not adopted recommendation to monitor ART efficacy using viral load monitoring (and thereby cease using CD4 cell count as an indicator) because there is limited access to VL testing products in the country..

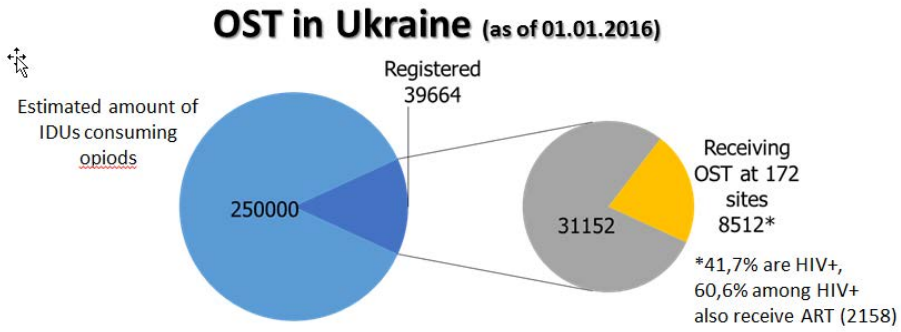
Recommendation

- VL monitoring should be prioritized so that all newly initiated people receive one measurement after approximately six months of therapy.

4.9 Strengthening medical management of opioid dependency

Less than 10 000 of the estimated 250 000-300 000 persons consuming opioids are enrolled in substitution maintenance therapy – receiving either buprenorphine or methadone (<3%) (Fig. 5).

Fig. 5. OST in Ukraine (as of 01.01.2016)



(Source: UCDC)

It was outside the scope of the mission to further analyse the medical handling of IDUs. It was however stressed during the mission that scale up of OST would be required as part of further scale-up of ART coverage in the country.

Recommendation

- Important consideration should be given to the initiation of ART distribution at community clinics where IDUs on substitution treatment are receiving opioid substitution therapy.

4.10 Technical capabilities within Ukraine

Ukraine has a technically very advanced team at the Ukrainian Center for Social Disease Control of the Ministry of Health of Ukraine (UCDC) which should be supported by the medical professional speciality in order to continue progressing in the approach to treating HIV according to the WHO recommendations and by continued building capacity through cross-country dialogue and interactions with European institutions and post-graduate training opportunities. Moreover, the dissemination of information regarding approach to HIV response in the Ukraine should be presented in the peer-reviewed international medical publications

Recommendations

- Support continued professional dialogue with the surveillance institutions, like ECDC.
- Ensure that the medical community receives comprehensive and continued post-graduate training. The recently launched e-learning course by EACS and WHO Regional office for Europe is recommended as it can be understood by a Russian speaking audience. This course will be updated regularly as new evidence develops and feedback from participants is received.
- Create professional pathways for future generations of HIV professionals in Ukraine and use international networks to further leader's academic careers.
- Create a plan to publish research findings around Ukraine's HIV programme design and function in international journals. Consider consulting and collaborating with existing academic groups interested in this field of research.

5. Conclusions and key recommendations

Ukraine faces a HIV epidemic that requires urgent attention. Responsible national stakeholders need to operationally attempt to control HIV transmission and reduce HIV-related deaths. A major reason for the current epidemiological situation is a lack of clarity around the drivers of the HIV epidemic, particularly in the IDU population. As long as this remains unaddressed it will continue to fuel the HIV epidemic.

Ukraine is experiencing financial challenges and the resources available for handling the epidemic are limited. Due to this situation it is of upmost importance that available resources are used and invested most effectively, and that the HIV programme is rationalised and optimized based on state-of-art scientific evidence. For WHO it is a premise for this technical support that any the financial surplus generated by these proposed recommendations is reinvested into the national HIV programme.

Key recommendations:

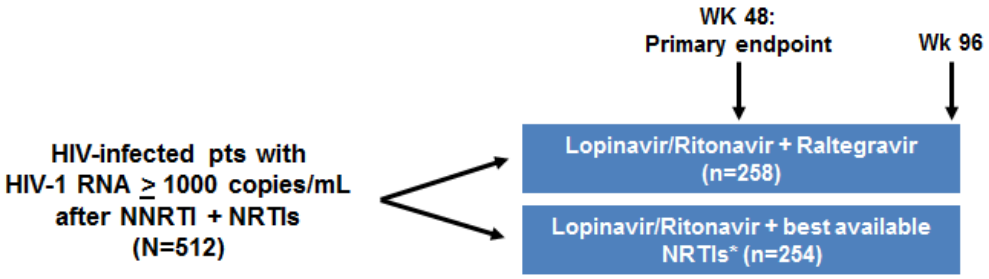
- Develop transmission models to estimate impact of transmission risk depending on different approaches to future scale up of ART. Incorporate benefits from reducing clinical impact from TB (incl. MDR) and reducing the progression of organ disease (in particular liver disease in those co-infected with HCV - most prevalent viral hepatitis co-infection).
- Continue to ensure national political support by stressing the greater financial burden if scale-up of HIV programme response is not undertaken.
- Consider optimizing the HIV programme so international donors will consider supporting the national programme in the future.
- Consider supplementing the SPECTRUM modelling estimations of total size of infected population with estimations from other modelling tools, e.g. the London model or the newly released ECDC HIV model.
- Focus and scale-up HIV testing in most-at-risk populations, expand the use of rapid tests for screening purposes and allow non-medical personnel in community clinics to offer HIV testing.
- Optimize the ART programme by switching a substantial proportion of patients currently on other 1st line ART combinations to the WHO recommended 1st line ART regimen.
- Scale-up HIV RNA monitoring so that all newly persons who initiated ART are tested at least once after approximately six months of therapy.
- Consider distributing ART at community clinics where IDUs on substitution treatment are receiving methadone.

6. Key studies supporting current WHO recommendations

A) Current Role of New ARV Options in 2015 WHO Guidelines *(4)*

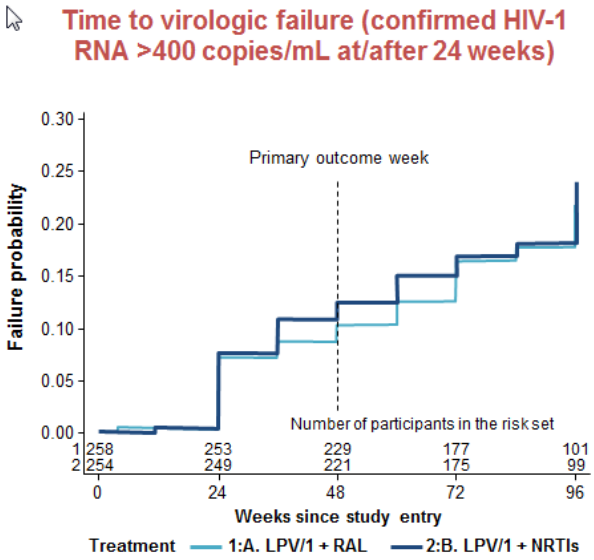
ARV	Population	1st line	2nd line	3rd line	Comments
EFV_{400}	Adult/Adol	✓			• No dose reduction studies in children is needed
DTG	Adult/Adol	✓		✓	• Not approved in children less than 12 years old . • Twice daily dose probably needed in TB patients using RMP
	Children			✓	
RAL	Adult/Adol		✓	✓	• Currently preferred as 3rd line option in adults and as 2nd line option in children • Limited use as alternative 2nd line option in adults. (RAL+ LPV/r)
	Children		✓	✓	
DRV/r	Adult/Adol		✓	✓	• Currently preferred as 3rd line option
	Children			✓	

B) The randomized trial of 2nd-line ART called ACTG A5273 (SELECT), which was a phase III, open-label, randomized, non-inferiority study *(7)*

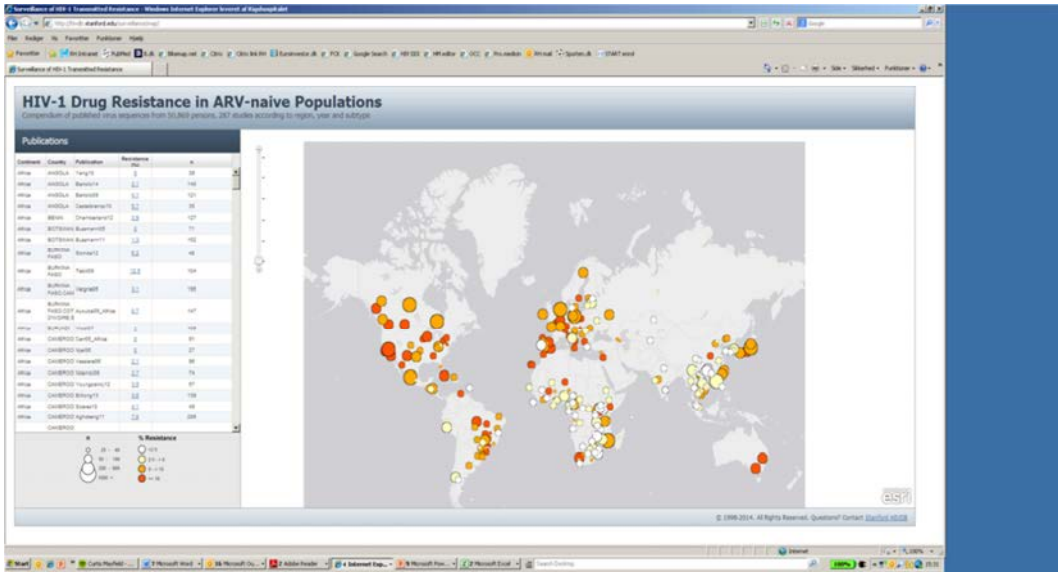


- Study objective: to determine noninferiority of raltegravir arm vs NRTI arm at Week 48
- Study powered to detect noninferiority at 10% margin
- Primary endpoint: time to virologic failure, defined as confirmed HIV-1 RNA >400 copies/mL after ≥ 24 weeks of 1st-line ART

*NRTIs selected according to algorithm, including substitution of zidovudine for tenofovir DF and vice versa



C) Meta-analysis of studies on HIV-1 Drug Resistance in ARV-naïve populations *(8)*
287 studies: N=50,870 persons from 111 countries



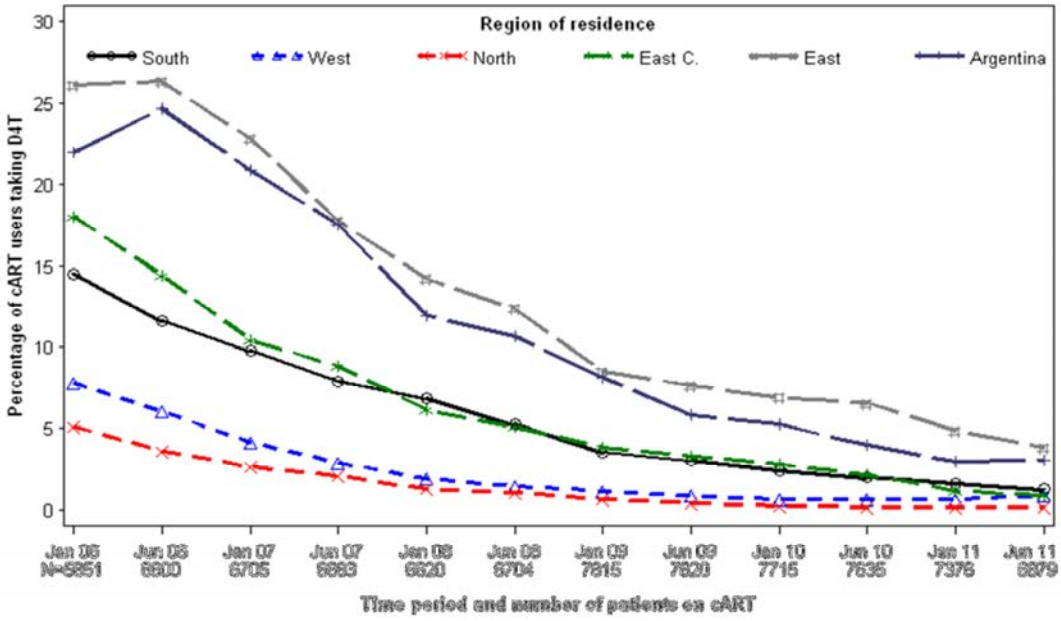
*N=50,870 persons from 111 countries

D) Studies on ART simplification strategies

Study	Intervention	Major outcomes	N	Country	Expected Completion
DREAM	Maintenance with LPV/r monotherapy or TDF/FTC/EFV	Efficacy, and tolerability (Phase II/III)	420	France	2014
SALT	Maintenance with ATV/r + 3TC OD	Efficacy/non-inferiority (Phase III)	325	Spain	2014
PROTEA	Maintenance with DRV/r (800/100 OD) monotherapy	Safety, tolerability and efficacy (Phase IIIb)	274	Multicountry (13)	2015
MOBIDIP	Maintenance with mono or bi-therapy with bPIs (±3TC)	Efficacy (Phase III)	264	Burkina Faso, Cameroon, Senegal	2017

*Dream *(9)*; Salt *(10)*; PROTEA *(11)*; MOBIDIP *(12)*

E) Decreasing prevalence of D4T use across Europe & Argentina *(13)*

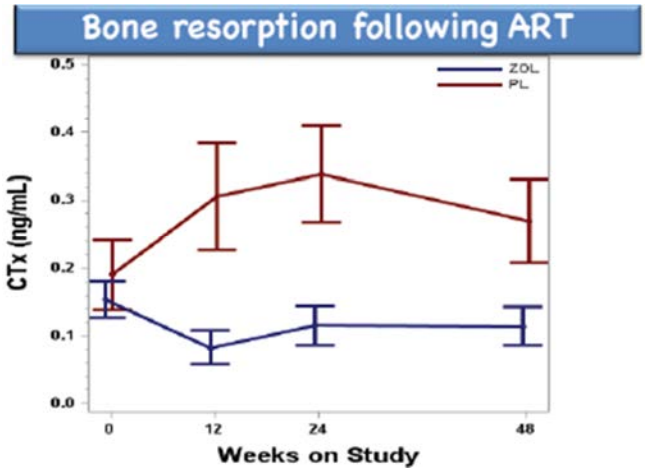


F) Association between abacavir usage and myocardial infarction risk - absolute risk difference only if elevated underlying risk* *(14)*

	Pre-March 2008	Post-March 2008
Events	672	269
PYRS	210,250	157,309
Rate	0.32 (0.30, 0.34)	0.17 (0.15, 0.19)
Recent exposure	1.97 (1.68, 2.33)	1.97 (1.43, 2.72)

*See also refs: *15,16,17*

G) A Single Dose Zoledronic Acid Prevents Antiretroviral-Induced Bone Loss *(18)*



- Phase 2, double-blind randomized, placebo controlled trial
- 63 non-osteoporotic treatment naïve HIV+ subjects were randomized to receive ART (ATV/r + TDF/FTC) and 1 dose ZOL (5 mg IV) or placebo
- Treatment with ZOL associated with a 73% and a 65% reduction in bone resorption relative to PL at 12 and 24 weeks, respectively, an effect that lasted through 48 weeks

7. References

1. HIV in hiding: methods and data requirements for the estimation of the number of people living with undiagnosed HIV ("London method 1"). By Working Group on Estimation of HIV Prevalence in Europe. AIDS 2011, 25:1017-1023.
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