

Current and future challenges and opportunities in HIV management in Ukraine

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HIV epidemiology in Ukraine as of 01.01.2019

Estimated population in Ukraine – 42 153 201 (as of 01.01.2019)¹

Estimated number of PLWHIV as of 01.01.2019² – 198 780 ** (~240 000 *)**

* Using UNAIDS/WHO software – Spectrum (version 5.756 beta 5)

** NOT including Crimea and uncontrolled territories of Lugansk and Donetsk regions

*** Including Crimea and uncontrolled territories of Lugansk and Donetsk regions



Registered in healthcare system ** as of 01.01.19²

- HIV-infected patients – **142 061 pts.**
 - ✓ Of them 113 106 received medical care at least once during previous 12 month – active group of medical care
 - ✓ Of them have AIDS– **46 380** (120,5 per 100 000 population)
 - ✓ Receive ART – **102 432** as of 01.01.2019, of them ~ 3 000 children
 - ✓ 48% of all PLWHIV registered in healthcare system are registered in 4 out of 25 Regions of Ukraine (Dnipro, Donetsk, Mykolaiv and Odessa)

1. Department for Population and Regional Statistics of the State Statistics Service of Ukraine

2. Data of Ukrainian Center for Public Health within MoH of Ukraine, 2019

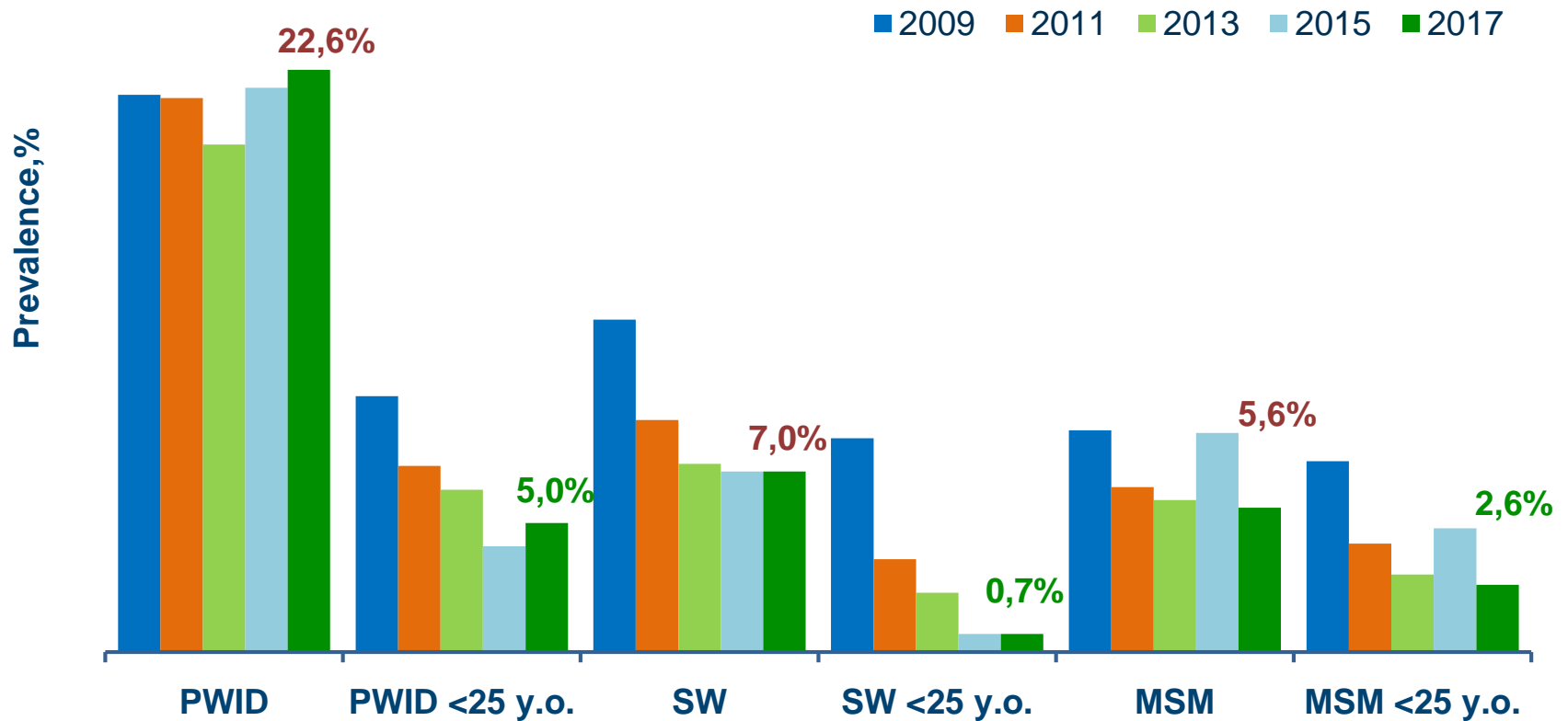
Key populations for HIV in Ukraine

Estimated number KPs in Ukraine, as of 01.01.2019:

- PWID – 350 300 persons (1,4% of population aged 15-49 years)
 - 58% of HIV+ PWIDs are aware of their HIV status
 - 38% of those PWIDs, who are aware of their HIV status, receive ART
- MSM – 179 400 persons (1,4% of men aged 15-49 years)
 - 59% of HIV+ MSM are aware of their HIV status
 - 46% of those MSM, who are aware of their HIV status, receive ART
- SW – 86 600 persons (0,7% of women aged 15-49 years)
 - 53% of HIV+ SWs are aware of their HIV status
 - 29% of those SW, who are aware of their HIV status, receive ART

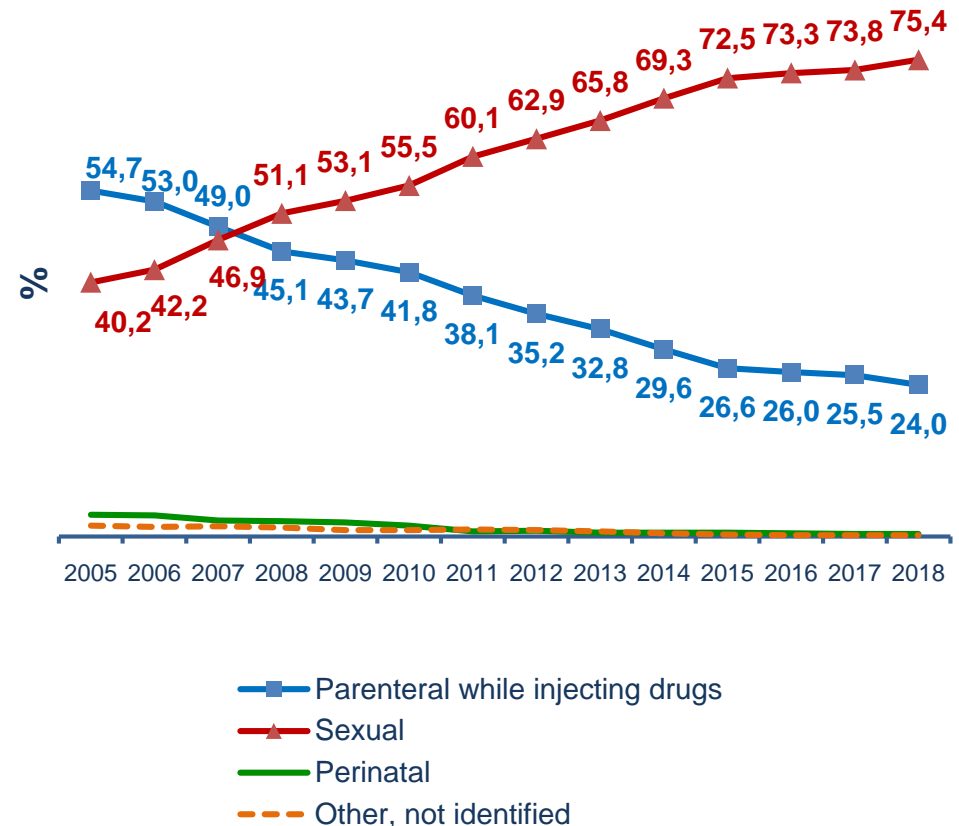
HIV prevalence among Key Populations aged <25 and older, Ukraine

IBBS data, 2009 – 2017



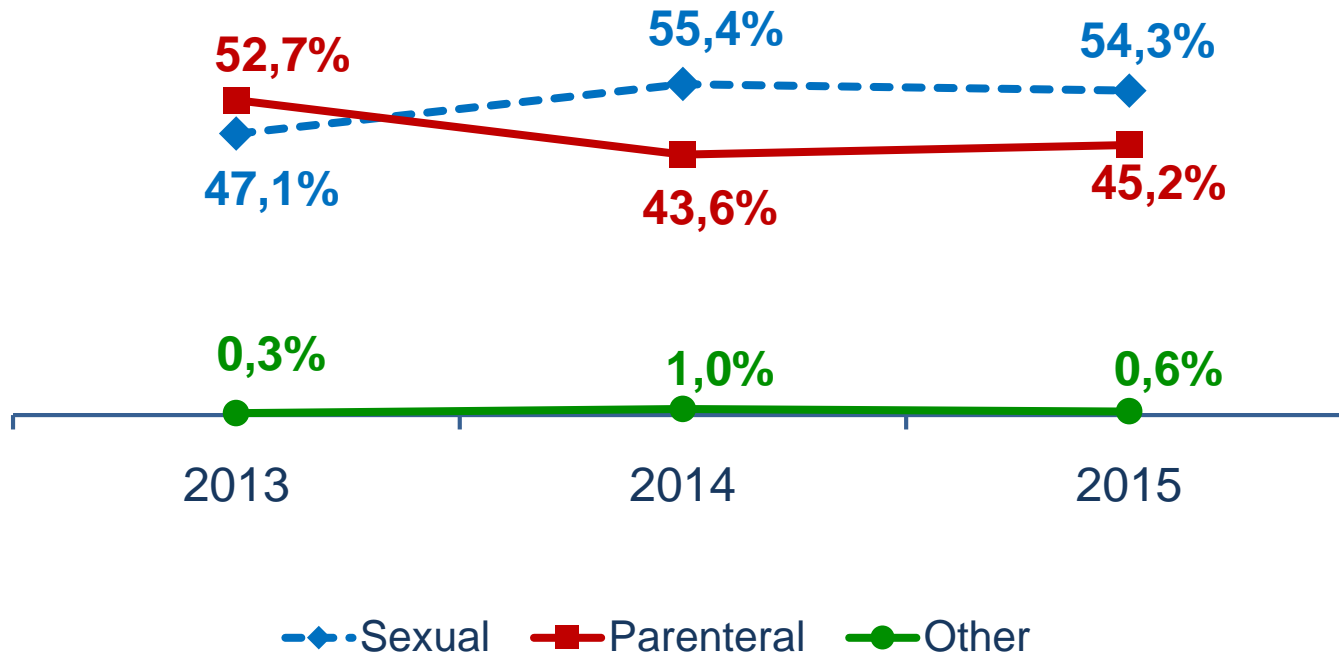
Structure of HIV transmission routes among newly registered cases, Ukraine

- HIV epidemic remains concentrated in key populations (PWID, MSM, SW) and geographically (south and east)
- Concentration in cities: 76.7% of new cases of HIV are registered among urban population
- The proportion of sexual transmission among new HIV cases continues to grow
- Annually, many newly diagnosed HIV-positive people are lost to medical follow up
- Proportion of late presenters is increasing



Proportion of HIV transmission routs among women in Ukraine, study results

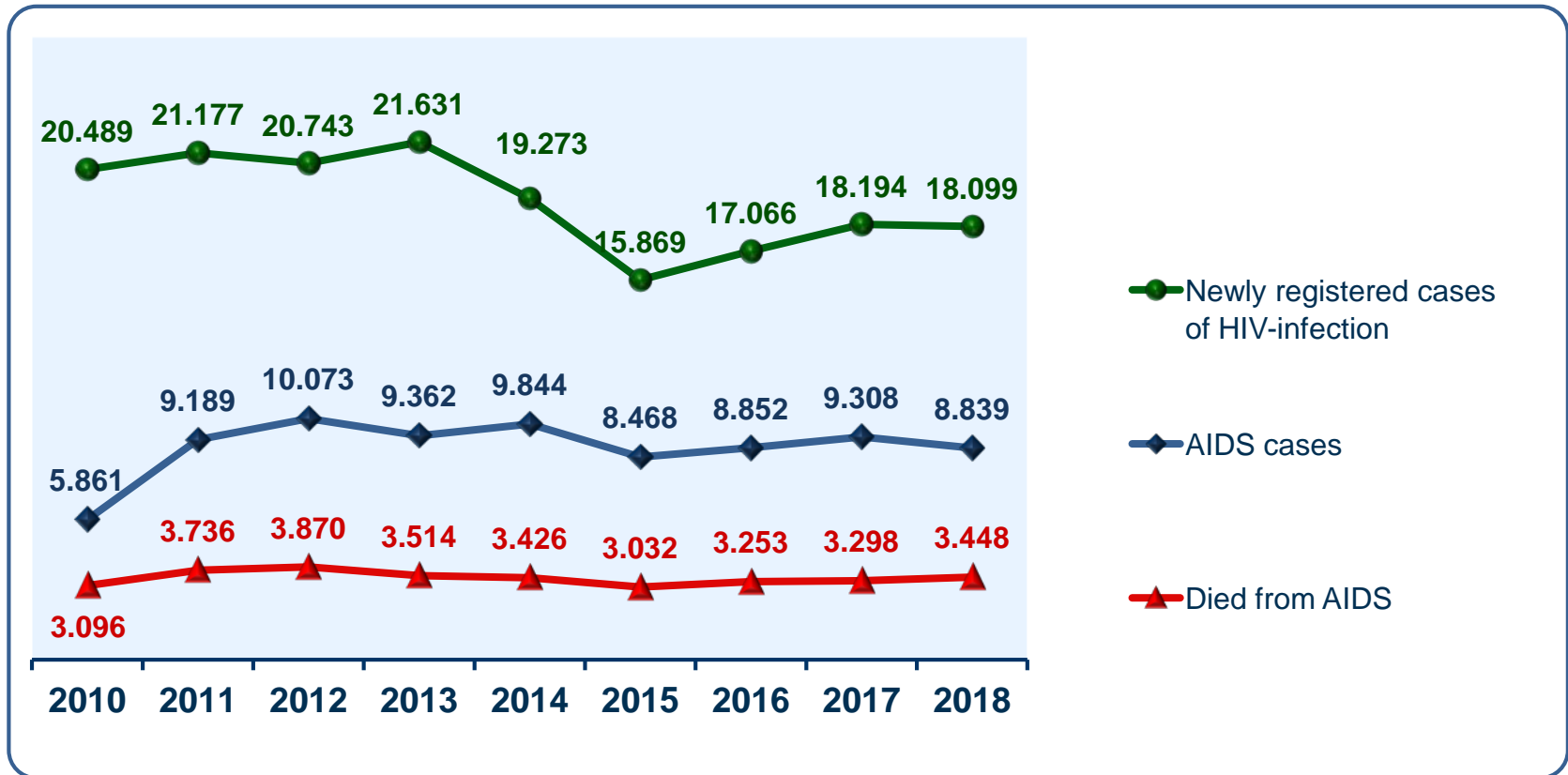
**p-value for trend <0.05



Project «M&E-related Technical Assistance and Improved Data Application in HIV» (**METIDA**), Study Assessment of reported mode of transmission (MOT), 2016-2017

Dynamics of newly registered cases of HIV infection, AIDS cases, deaths from AIDS in Ukraine, 2010 – 2018*

(annually, official registration data *)

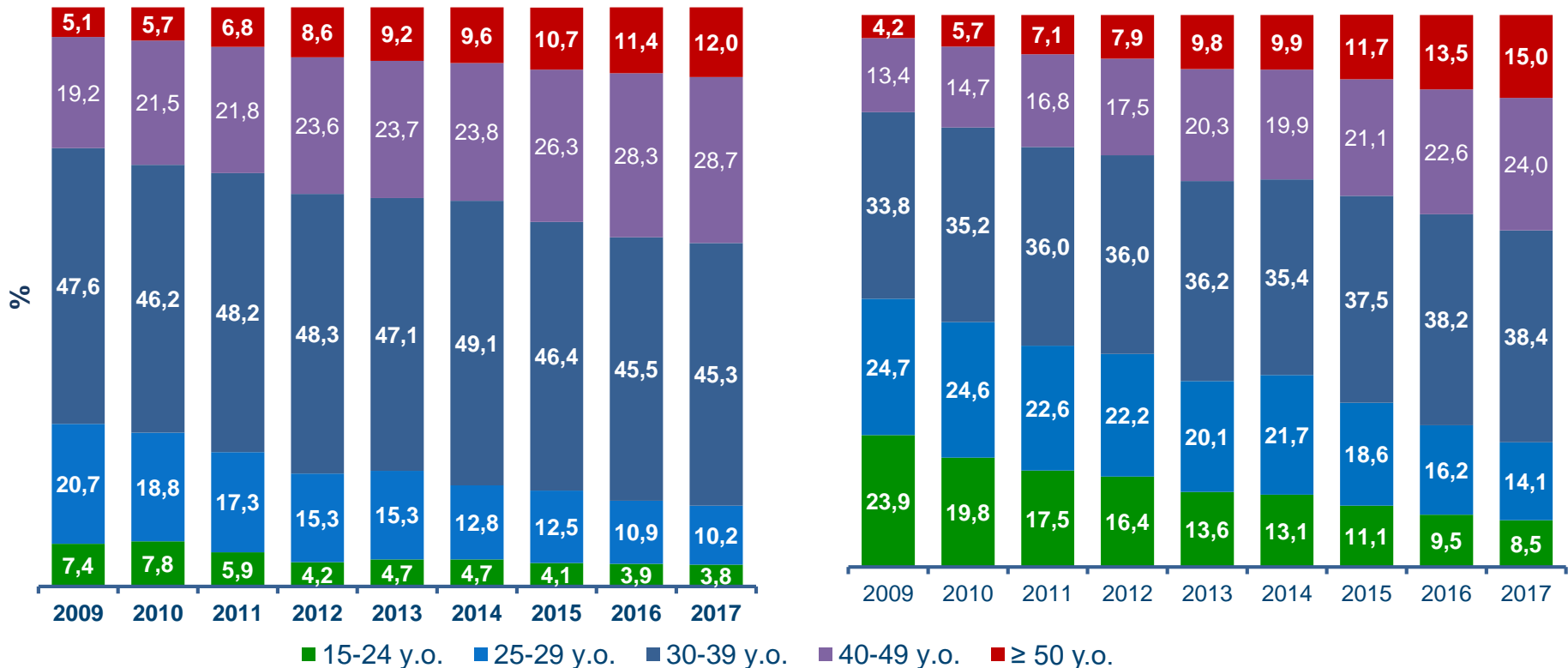


- 2014-2018 – excluding Crimea, and uncontrolled territories of Lugansk and Donetsk regions (2015-2018)
- TB was diagnosed in 4 830 (54,6%) patients with newly diagnosed AIDS cases in 2018

Increase the proportion of older people among newly registered PLHIV in Ukraine (2009-2018*)

Men, older 15 years, by age groups

Women, older 15 years, by age groups

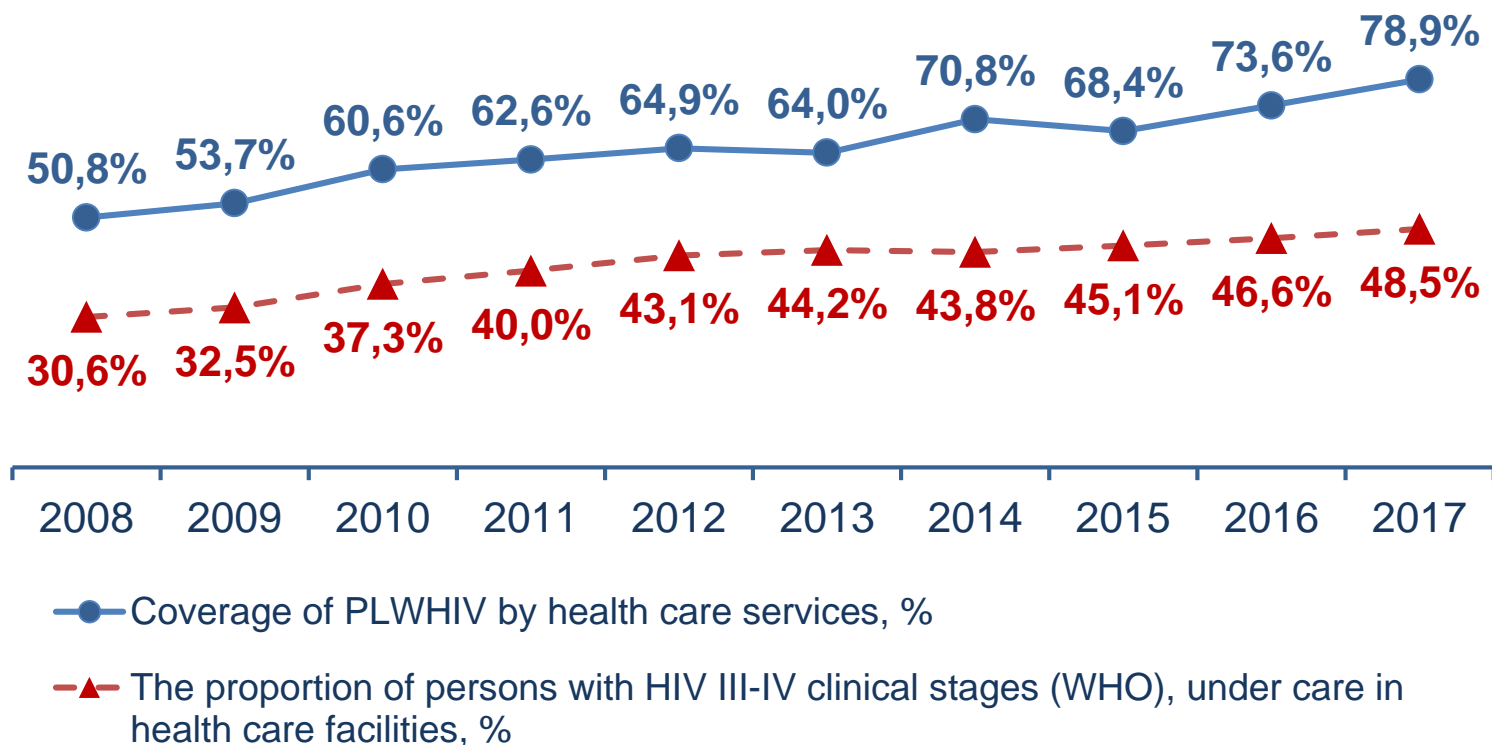


2018: among newly registered HIV cases 61% were men; 39% – women

2018: 84,7% of newly registered HIV cases were in age group 25-49 y.o. (among ≥50 y.o. – 14,8%)

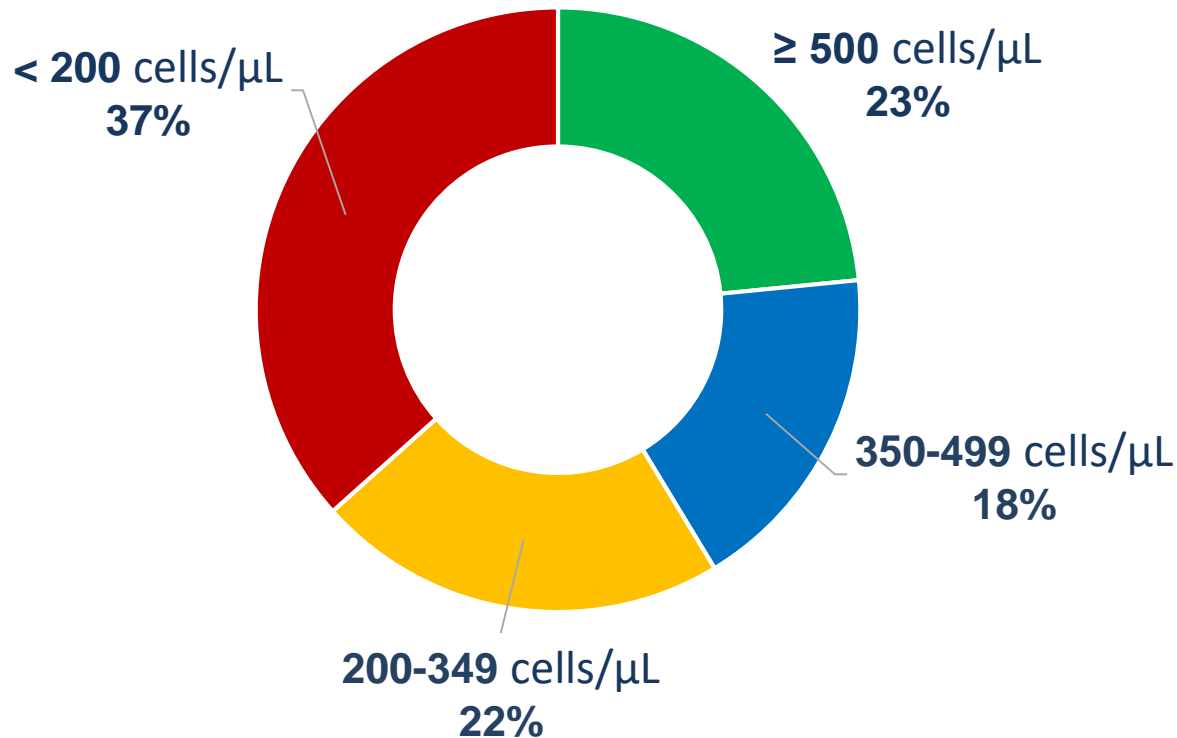
Data of Ukrainian Center for Public Health within Ministry of Health of Ukraine, 2017, 2019
 * NOT including Crimea and uncontrolled territories of Lugansk and Donetsk regions starting 2015

Medical care coverage and the proportion of patients in the WHO HIV III-IV clinical stages among the newly registered cases of HIV infection in Ukraine



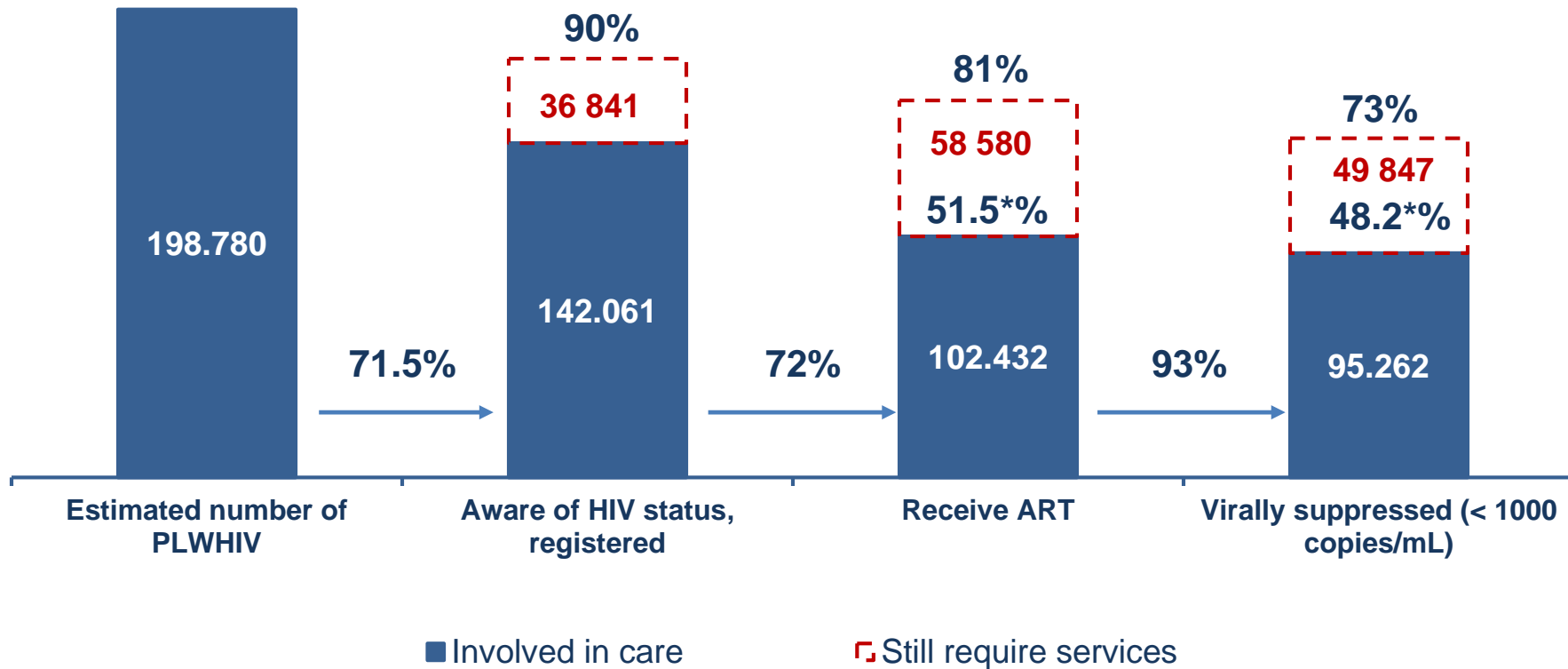
Annually, many newly diagnosed HIV-positive people are lost to medical follow up

CD4 counts (testing coverage ~40%) when taking HIV + under medical care, Ukraine, 2018



Proportion of late presenters is increasing

HIV care Cascade in Ukraine as of 01.01.2019



*of estimated number of PLWHIV

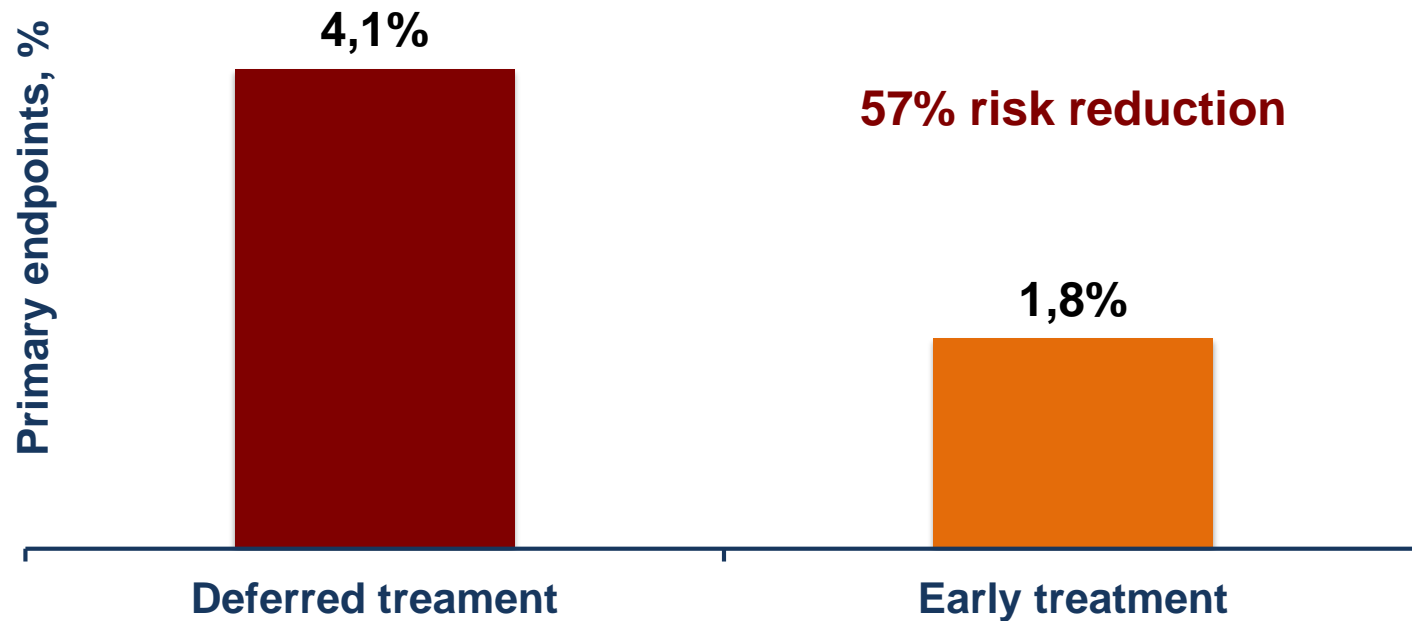
Information about healthcare facilities, providing ART to PLWHIV in Ukraine, as of 01.01.2019 (MoH data)

- Regional AIDS Centers – 25
- City AIDS Centers – 12
- ART sites at Regional Hospitals, City Hospitals and Polyclinics – 313
- ART sites at TB Hospitals – 24
- ART sites at STI Clinics – 3
- ART sites at Psychiatric/Narcology Clinics – 8
- National Level Clinics – 2
 - Clinic of the Gromashevsky Institute of epidemiology and Infectious diseases (Adults)
 - Centre «Clinic for treating children with HIV/AIDS» within «OHMATDET» Clinic (Children)

TOTAL: 387 ART sites

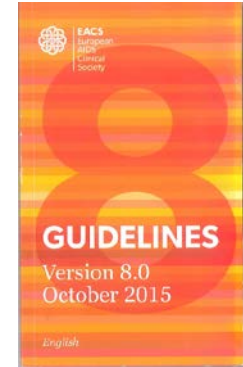
START: primary results

Risk of AIDS progression,
serious non-AIDS conditions or death



“Combined antiretroviral therapy (ART) should be recommended to all HIV-positive people, regardless of the number of CD4.”

Руководство EACS 2015



- Во время 15 Европейской Конференции по СПИД (21-24.10.2015: Барселона) была представлена новая 8.0 версия Европейского руководства по лечению ВИЧ-инфекции:

- The EACS panel, in charge of updating the Guidelines, recommends starting treatment for all HIV-positive persons, irrespectively of CD4 cell count

«...рекомендует начинать лечение всех ВИЧ-позитивных, независимо от уровня CD4 лимфоцитов»

«Руководство настоятельно рекомендует лечение в случае, если уровень CD4 менее 350 кл/мм³»



Пресс-релиз от
22.10.2015

Update of the National HIV Guidelines, Ukraine, 2015: When to start ART

- **ART is recommended to all HIV-infected patients to reduce risk of disease progression and prophylactics of HIV transmission, at any CD4 counts**

1. Ukrainian National clinical guidelines on antiretroviral treatment of HIV-infection in adults and adolescents (third edition, recycled and supplemented), approved by the Order of the Ministry of Health of Ukraine of 12.07.10 № 551

2. Update of Ukrainian National clinical guidelines on antiretroviral treatment of HIV-infection in adults and adolescents , approved by the Order of the Ministry of Health of Ukraine of 22.12.2015 № 887.

Recommended first line ART regimens in Ukraine, 2010-2019

Recommended regimens:

NNRTI + 2 NRTI

PI/rtv + 2 NRTI

EFV + TDF/FTC or

LPV/rtv + TDF/FTC

EFV + TDF + 3TC

Alternative regimens:

NNRTI: NVP + 2 NRTI

PI/rtv:

ATV/rtv + 2 NRTI

NRTI backbone:

**+ AZT/3TC or
+ ABC/3TC**

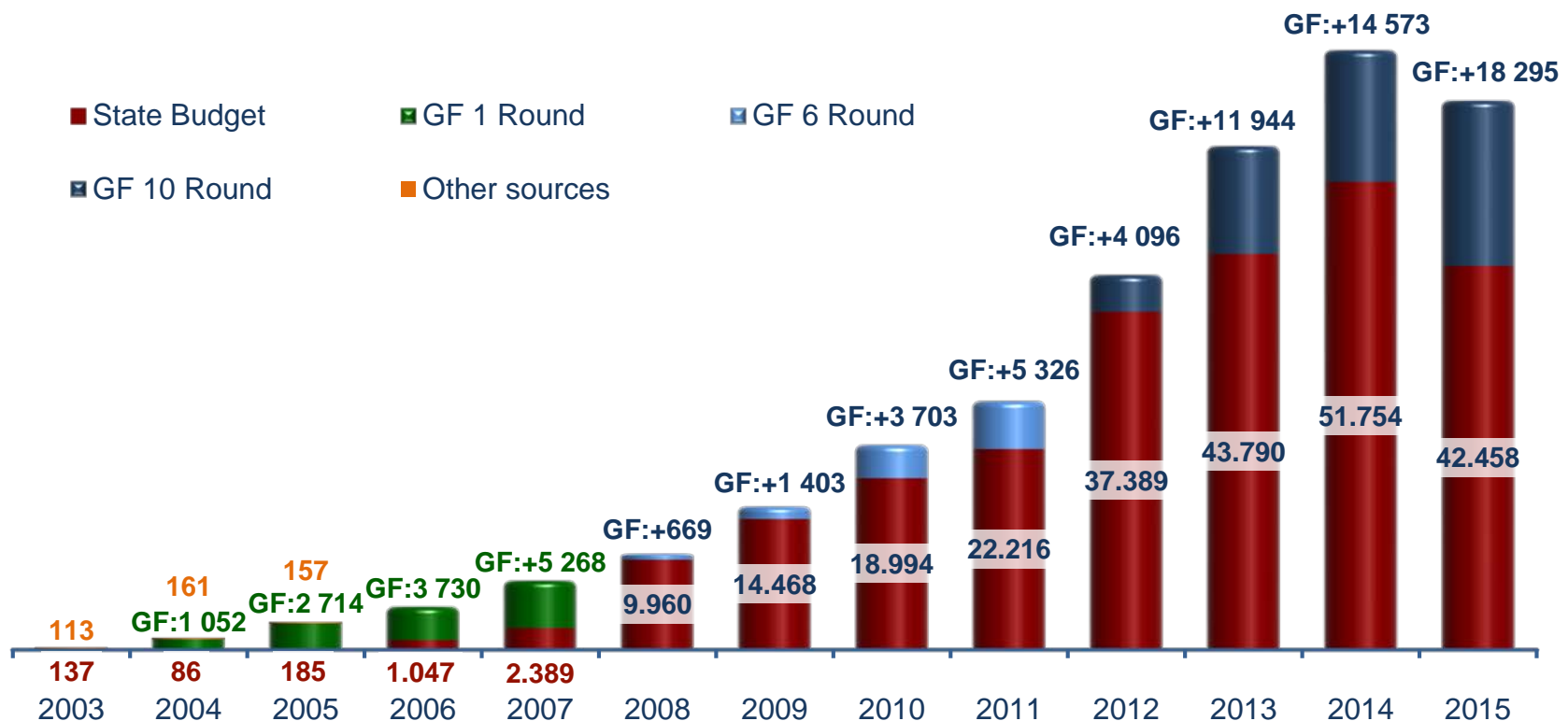
NRTI backbone:

**+ AZT/3TC or
+ ABC/3TC**

History of expanding access to ART in Ukraine

(the number of patients, cumulative data, continue ART, year)

Year	2014	2015	2016	2017	2018
Plan/indicator	65 898	85 898	105 748	115 940	118 240



Data of the Ukrainian Centre for socially significant diseases control of MoH of Ukraine, 2016

History: ART in Ukraine was introduced in 2000

History: First-line ART regimens recommended in Ukraine (2006)

Recommended regimens:

NNRTI based

**EFV + (AZT/3TC
or TDF*/FTC* or TDF*+3TC)**

PI based (by indications)

**LPV/rvt + (AZT/3TC or TDF*/FTC* or
TDF*+3TC)**

* Registration in Ukraine is required

Alternative regimens:

NNRTI based

NVP + AZT (or d4T) + 3TC

PI based

NFV + AZT (or d4T) + 3TC

Ukrainian National clinical guidelines on antiretroviral treatment of HIV-infection in adults and adolescents, 2006.

Order of the Ministry of Health № 658 of 04.10.2006

Recommended initial ART regimens for most of the naïve patients in Ukraine

(Project of the new Clinical Guidelines, 2017)

Recommended ART regimens for most patients, starting treatment for the first time in life

2 NRTI

- TDF^b/FTC^a or
- TDF^b + 3TC

+ third component: 1 INSTI

INSTI

- **Dolutegravir**

^a 3TC can be changed to FTC and vice versa

^b For patients with eGFR > 60 mL/minute (TDF)

Alternative ART regimens for naïve patients in Ukraine (Project of the new Clinical Guidelines, 2017)

ART regimens for patients, starting treatment for the first time in life, in special clinical situation

2 NRTI

- ABC/3TC (if HLA-B*5701 negative)

Third component

INSTI

- RAL
- EVG/cobi/TAF/FTC (registered, never procured)

NNRTI

- EFV
- RPV (registered, never procured)

PI/boosted

- ATV/r
- LPV/r

ART regimens for patients, starting treatment for the first time in life, in special clinical situation (Project of the new Clinical Guidelines, 2017)

Режим	Лекарственная форма	Ограничения приема пищи	Предостережения
НИОТ-щадящие схемы			
ЗТС + LPV/r	ЗТС 300 мг, 1 таб. 1р/сут. + LPV/RTV 200/50 мг, 2 таб. 2р/сут.	Во время еды	
RAL + DRV/r	RAL 400 мг, 1 таб. 2р/сут. + DRV 800 мг, 1 таб. 1р/сут. + RTV 100 мг 1 таб. 1р/сут.	Во время еды	Только если количество CD4 > 200 кл/мкл и ВН ВИЧ < 100 000 копий/мл. Не рекомендовано назначение совместно с антацидами, содержащими Al или Mg.

- Если ЗТС 300 мг, 1 таб. недоступен, альтернативой может быть применение ЗТС 150 мг, 2 таб./сут.

New Clinical Guidelines, ART, Ukraine

- *«The guidelines that are selected for approval as new clinical protocols should be: developed by national and / or professional medical associations of the member states of the European Union (membership as of January 1, 2017), the United States of America, Canada and the Australian Union; developed by existing methods and based on evidence-based medicine; written in English and/or Ukrainian».*
- ✓ From the Order of MoH of Ukraine of **29.12.2016** № 1422, registered with the Ministry of Justice of Ukraine 24.04.2017 № 530/30398 «On Amendments to the Order of the Ministry of Health of Ukraine dated September 28, 2012 No. 751» (**Order of MoH of Ukraine of 29.12.2016 № 1422, acting**)
- *The Ministry of Health recommends to use the translated into Ukrainian "Consolidated guidelines on the use of antiretroviral drugs for the treatment and prevention of HIV infection: Recommendations for the Public Health Approach – 2nd Edition, 2016», developed by the WHO, as a "New Clinical Protocol" in the aspect of a public health approach.*
- ✓ From the Order of MoH of Ukraine of **05.06.2019** N 1292 «On approval of the new Clinical Protocol on the use of antiretroviral drugs for the treatment and prevention of HIV infection» (**Order of MoH of Ukraine of 05.06.2019 № 1292, acting**)

2016: «New» WHO recommendations on HIV treatment in adults

forward to the future (DLG)

DHHS, 2016 ¹		EACS, 2016 ²		IAS-USA, 2016 ³		WHO, 2016 ⁴		WHO, 2016 ⁴ (альтернатива)	
ABC/3TC	DTG	ABC/3TC/DTG		ABC/3TC	DTG	TDF + 3TC (или FTC)	EFV	TDF + 3TC (или FTC)	DTG
TDF (TAF)/FTC	DTG EVG/c RAL	TDF/FTC	DTG EVG/c RAL	TAF/FTC*	DTG EVG/c RAL			TDF + 3TC (или FTC)	EFV или NVP
	DRV/r	TDF/FTC	DRV/r DRV/c	альтернативные					
		TDF/FTC	DRV/r	TDF(TAF)/FTC	DRV/r				
		TDF/FTC	RPV**	ABC/3TC	DRV/r				
				TDF(TAF)/FTC	RPV**				
			TDF/FTC	EFV	AZT + 3TC				

- НИОТ
- ННИОТ
- ИП
- ИНИ

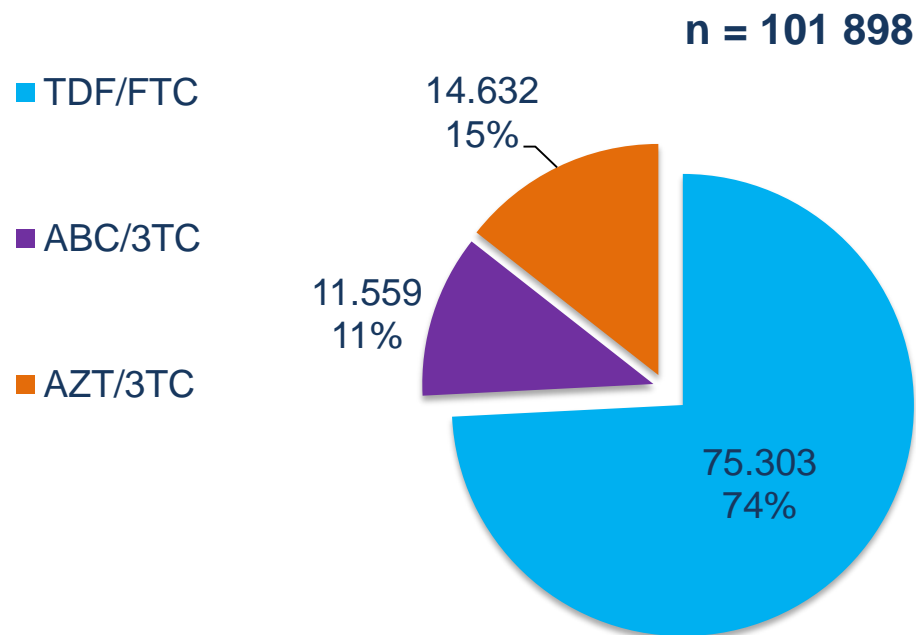
* Если TAF/FTC недоступен, то возможна замена на TDF + FTC или 3TC

** Только при вирусной нагрузке <100 000 коп/мл

1. DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents, January 2016
2. EACS Guidelines Version 8.1, October 2016
3. Günthard HF, et al. JAMA. 2016;316(2):191-210
4. WHO HIV Guidelines. Second Edition. Updated 2016

Proportion of NRTIs in Ukraine as of 01.04.2019 (adults, abs.; %)

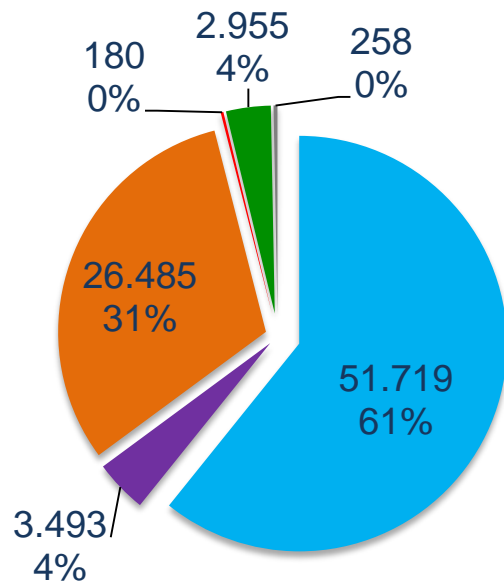
01.04.2019



Proportion of NNRTIs, PIs and INSTIs in ART regimens as of 01.01.2018 compared to 01.04.2019 (adults, abs.; %)

01.01.2018

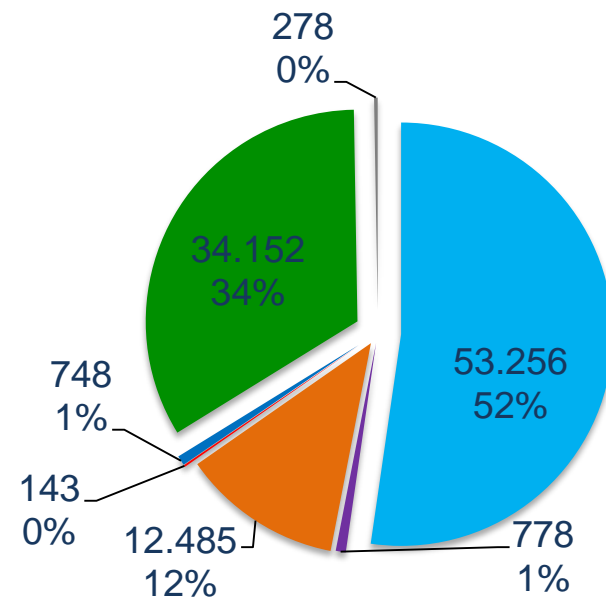
n = 85 327*



- EFV
- NVP
- LPV/rtv
- DRV/rtv
- ATV/rtv
- DTG
- RAL

01.04.2019

n = 101 898**



* 216 pts. – 3 NRTI regimen,
258 pts. – RAL-based regimen

** 41 pts. – 3 NRTI regimen,
278 pts. – RAL-based regimen

The risk rates when switching patients who are on suppressive ART

HIGH

- Replacing a boosted PI with another 3rd component, especially if there is a history of failure and/or resistance

MODERATE

- Switching from 2 p / day to 1 p / day after registering such a regimen
- Replacing the 3rd component with a drug of a new class (INSTI), if there is no failure and/or resistance in history

LOW

- Switching from separate tablets to a combined form, eg, replacement:

TDF+FTC+ EFV to

TDF/FTC/EFV in one pill, FDC

TDF/FTC+ DTG to

TDF/3TC/DTG in one pill, FDC

ART, women and pregnancy: what to use Ukrainian Guidelines, 2016

(Order of MoH of Ukraine №449 of 16.05.2016, acting)

- **HIV+ pregnant woman, never received ART**
 - Start AHN as fast, as possible, regardless of VL and CD4 count
 - NRTI: TDF + FTC (TDF + 3TC), ABC + 3TC, AZT + 3TC
 - 3-rd drug:
 - PI based: LPV/rvt; (DRV/rvt – alternative)
 - NNRTI based: EFV (after 8 weeks of pregnancy),
 - INSTI based: RAL
 - 1-st line: TDF/FTC+LPV/rvt, TDF/FTC+RAL, TDF/FTC+EFV (3TC may be used instead of FTC)
- **HIV+ pregnant woman on stable ART before pregnancy**
 - Continue current ART regimen, if it is effective and well tolerated
 - In case of virologic failure (VL > 1000 copies/mL) consider resistance testing; **start 2 line ART**

Recommendations on DTG use in women

Receiving DTG at the moment?	Pregnancy status	DTG recommendations		
		DHHS ^[1]	BHIVA ^[2]	WHO ^[3]
No	Early pregnancy stage *	Red	Red	Red
	Late pregnancy stage †	Yellow	Red	Green
	Childbearing potential, no contraception	Red	Red	Red
	Childbearing potential, effective contraception	Green	Green	Green
Yes	Early pregnancy stage *	Yellow	Red	Red
	Late pregnancy stage †	Green	Green	Green
	Childbearing potential, no contraception	Red	Red	Red
	Childbearing potential, effective contraception	Green	Green	Green

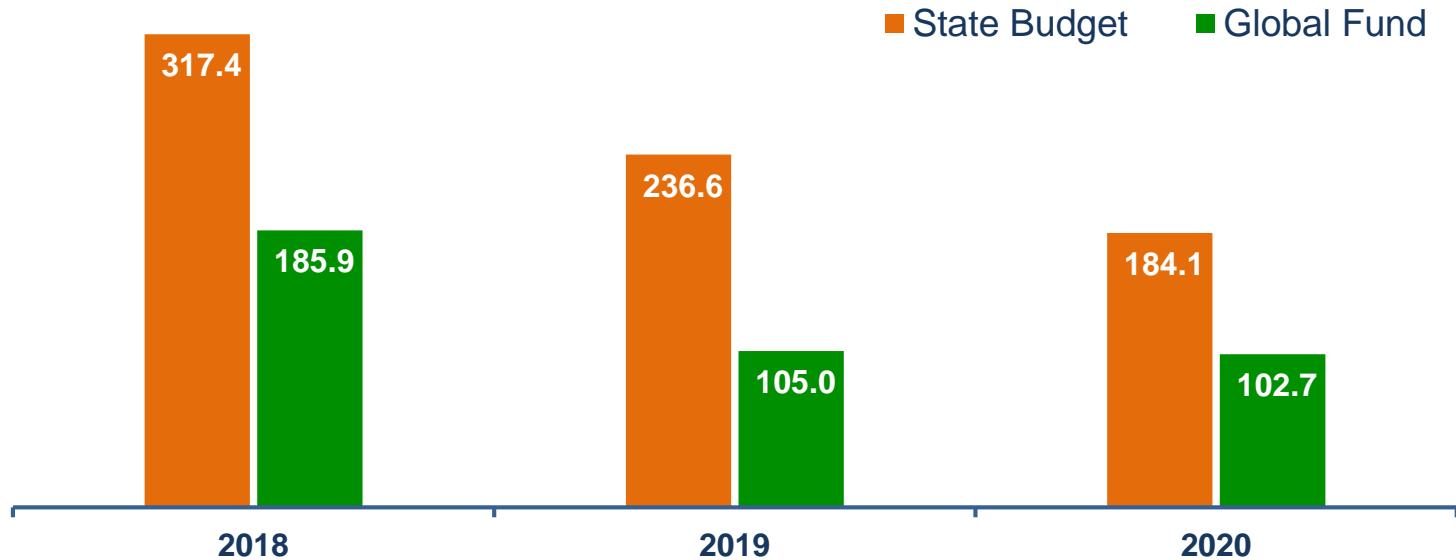
* DHHS: < 8 weeks after last period; BHIVA и WHO: first trimester.

† DHHS: ≥ 8 weeks after last period; BHIVA и WHO: second and third trimester.

ART «optimization» plan, 2017-2020

	2017		2018		2019		2020	
	Number of pts.	%	Number of pts.	%	Number of pts.	%	Number of pts.	%
AZT	24 063	30%	20 750	16%	10 179	7%	5 272	3%
ABC	8 834	11%	11 163	9%	12 577	8%	8 960	5%
TDF	42 142	53%	93 299	73%	123 970	83%	161 935	90%
EFV	45 386	57%	64 867	50%	52 285	35%	51 725	29%
LPV/r	26 267	33%	18 933	15%	11 521	8%	5 272	3%
DTG			39 912	31%	78 920	53%	111 170	62%
ATV/r			4 958	4%	7 458	5%	11 458	6%
TOTAL, without NGCA			128 670		150 184		179 625	
NGCA (UNICEF)			16 000		16 000		16 000	
TOTAL			144 670		166 184		195 625	

Change in treatment regimen cost per year (weighted average) in Ukraine due to optimization, USD



The desire to reduce prices "at any cost" now, for unrealistic goals that are not achieved now ... Is very hard to understand...

Challenges and Questions

- Ukraine today fails to achieve proper success in achieving «90-90-90» targets.
- According to national estimates supported by WHO and UNAIDS, both in Ukraine and in other countries of the Eastern European Region of WHO, we see a huge “gap” between the estimated number of PLHIV, the number of PLHIV with known HIV+ status and the number of people who are actually under medical care.
- Why is the proportion of undiagnosed HIV infection so high?
- Why HIV testing effectiveness in real life does not correspond to data of our IBBS?

Challenges and Questions

- Are HIV testing strategies appropriate? Whom to test for HIV? When to test? Where? How? Coverage of the entire population and/or key and vulnerable groups? Combined testing and innovation strategies for detecting HIV?
- Why such a low proportion of people with positive HIV test results, compared to estimates and our expectations, end up in the health care system?
 - Do they actually know about their HIV status? Are they still alive? Are they still in the country? Because we haven't seen them for years after the test...
 - We can't initiate ART in patients whom we don't know...
- Proportion of late presenters is increasing

Challenges and Questions

- ART regimens, optimal for women with childbearing potential?
- Virological failure – inability to achieve or maintain suppression of HIV replication at the level of HIV VL reduction < 200 copies/mL (2018) and ??? < 1000 copies/mL (2019)
- Patients with ART experience and history of failure. Is it safe to switch stable patients receiving ART so “massively” and quickly: more than 10 thousand switched from PI/boosted in a single year
- How to ensure harmonious cooperation between epidemiologists, M&E and health care system?

Questions?



THANK YOU!

