Київський міський центр профілактики
та боротьби зі СНІДом КМКЛ № 5

HIV Mother To Child Transmission: Highlights

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Київ, Україна, 05 – 06 липня 2019 року

In 2018, in Ukraine 49.4% HIV+ women were newly diagnosed during pregnancy, delivery or postpartum

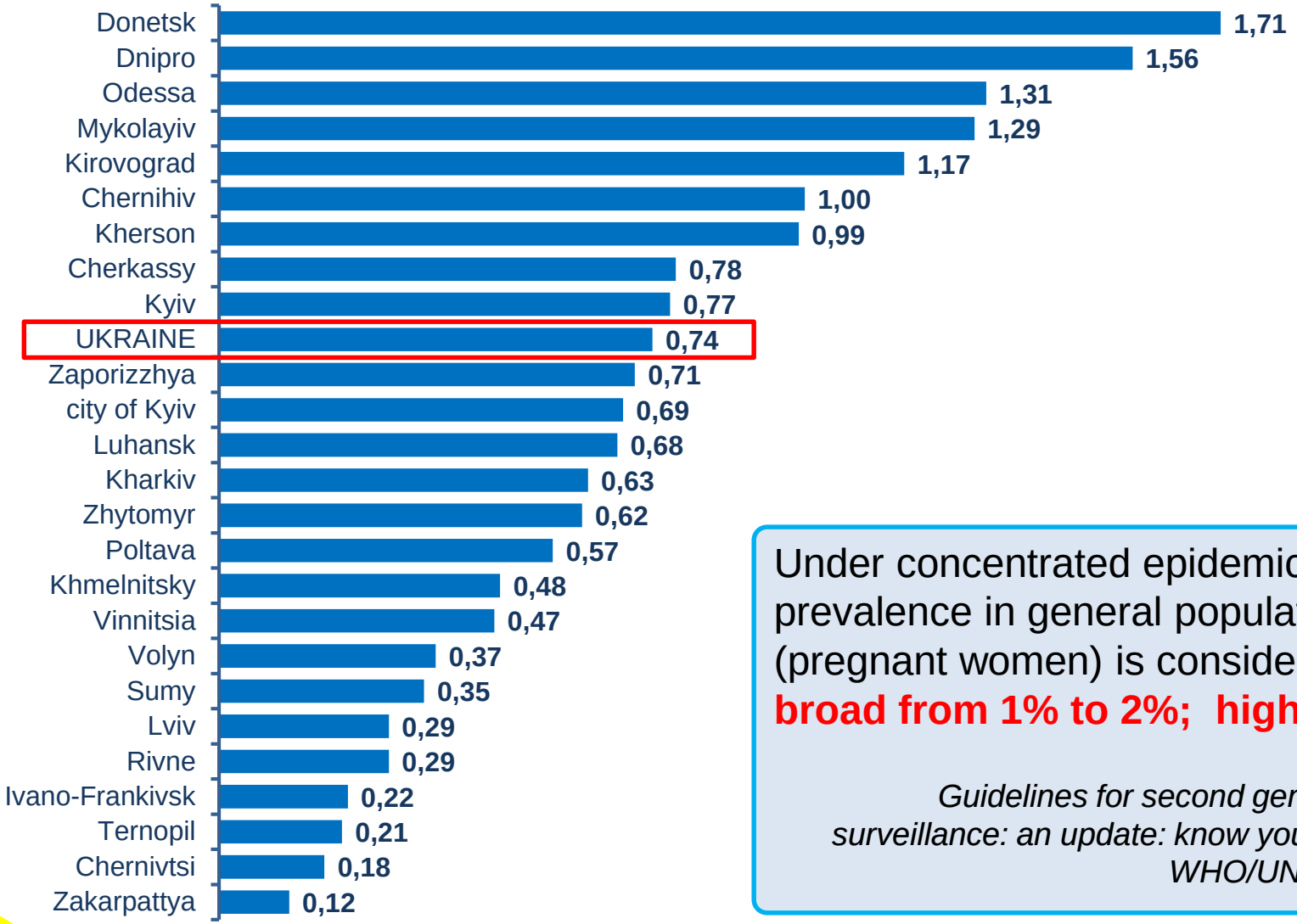
50.6% of pregnant women knew they were HIV+ before pregnancy. Percentage of these women increases each year

According to WHO, number of discordant married couples is 50% of all HIV+ patients

Percentage of pregnant women with HIV clinical stage III-IV of all newly diagnosed with HIV in pregnant women:

12.8% (2013) **16.9% (2015)** **21.7% (2017)**

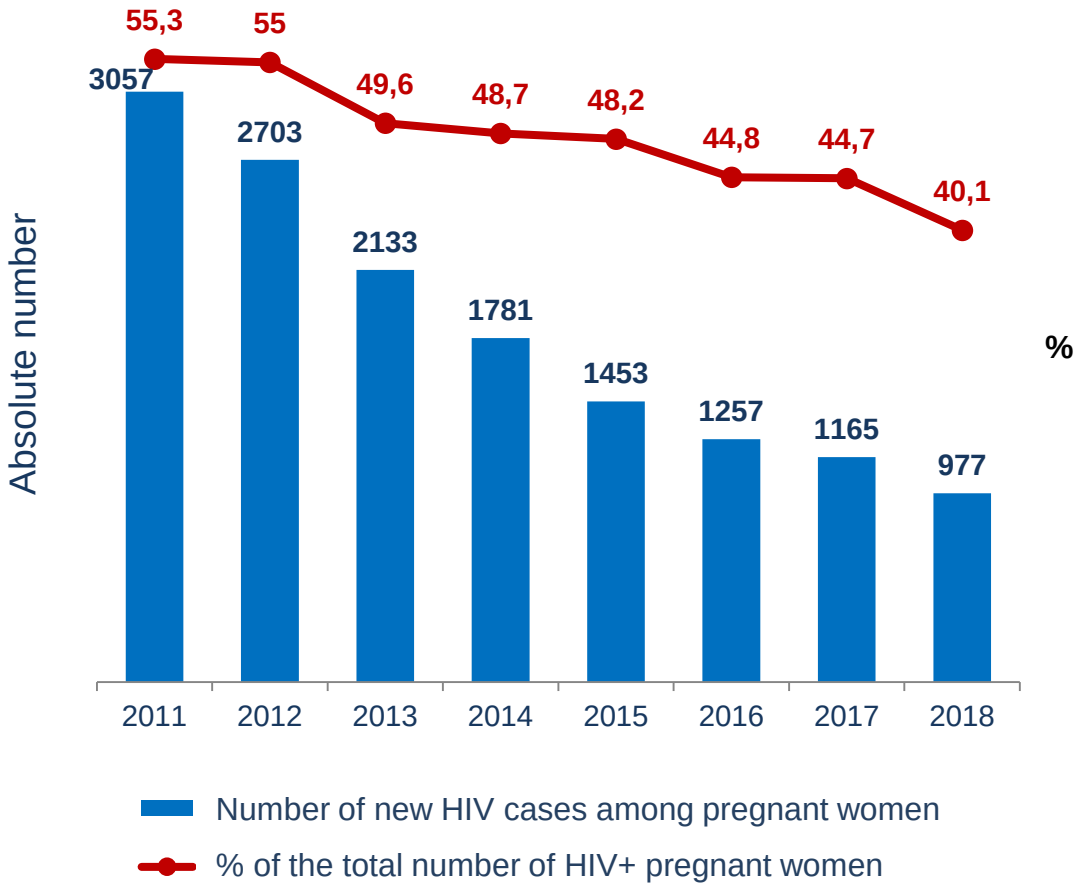
HIV Prevalence in Ukraine Among Pregnant Women, 2018

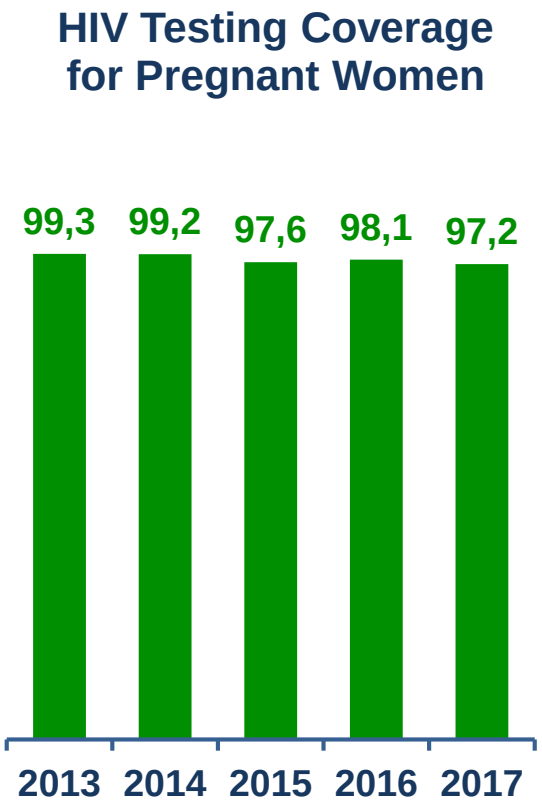


Under concentrated epidemic, HIV prevalence in general population (pregnant women) is considered to be **broad from 1% to 2%; high > 2%**

Guidelines for second generation HIV surveillance: an update: know your epidemic, WHO/UNAIDS, 2013

Number and Percentage of New HIV Cases Among Pregnant Women





Number of HIV+ Pregnant Women and Their Babies

Ukraine	2014	2015	2016	2017	2018
Number of HIV+ pregnant women	3 654	3 016	2 814	2 606	2 414
Number of deliveries in HIV+ pregnant women	3 573	2 962	2 710	2 544	2 317
Number of children born to HIV+ women (live births)	3 585	2 982	2 733	2 545	2 325

Global and National Elimination of Mother to Child HIV Transmission

National target for mother to child HIV transmission in Ukraine in 2018 – 1%

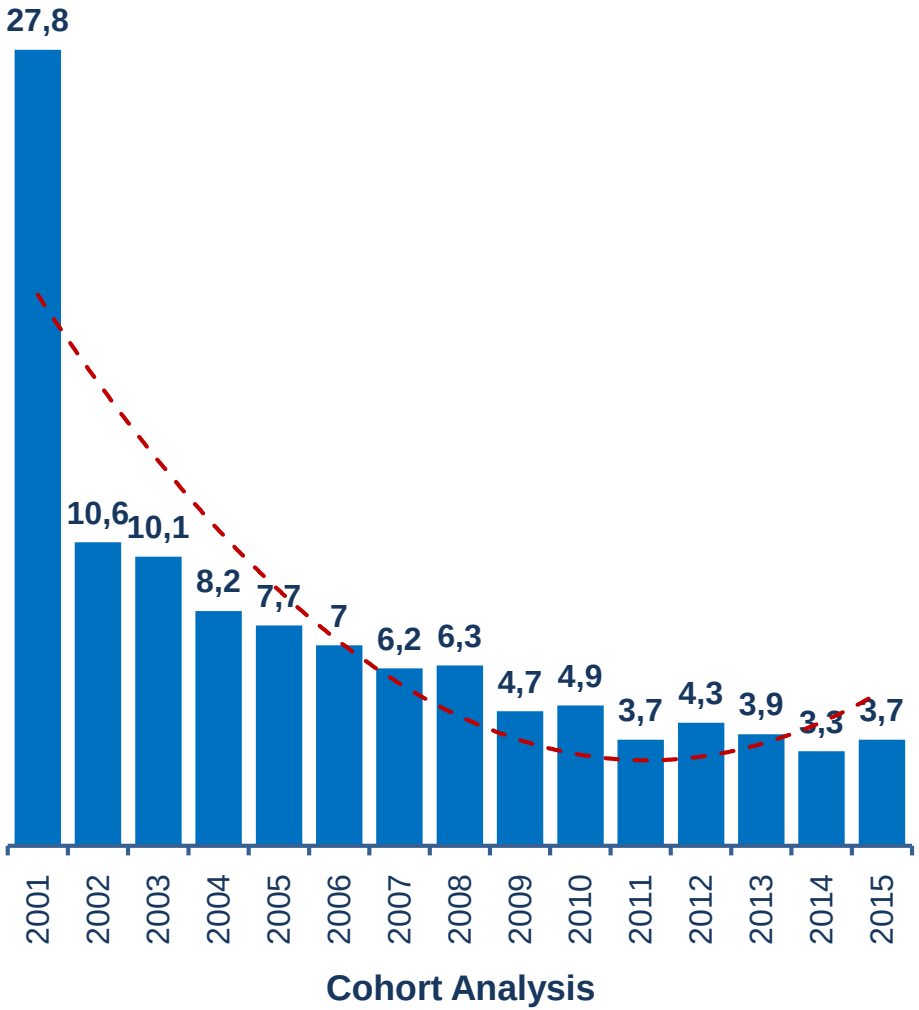
(under National Dedicated Social HIV/AIDS Response Program for 2014-2018)

WHO/UNAIDS Global Strategy till 2030:
Elimination of mother to child HIV transmissions and **decreasing MTCT rates to 0%**

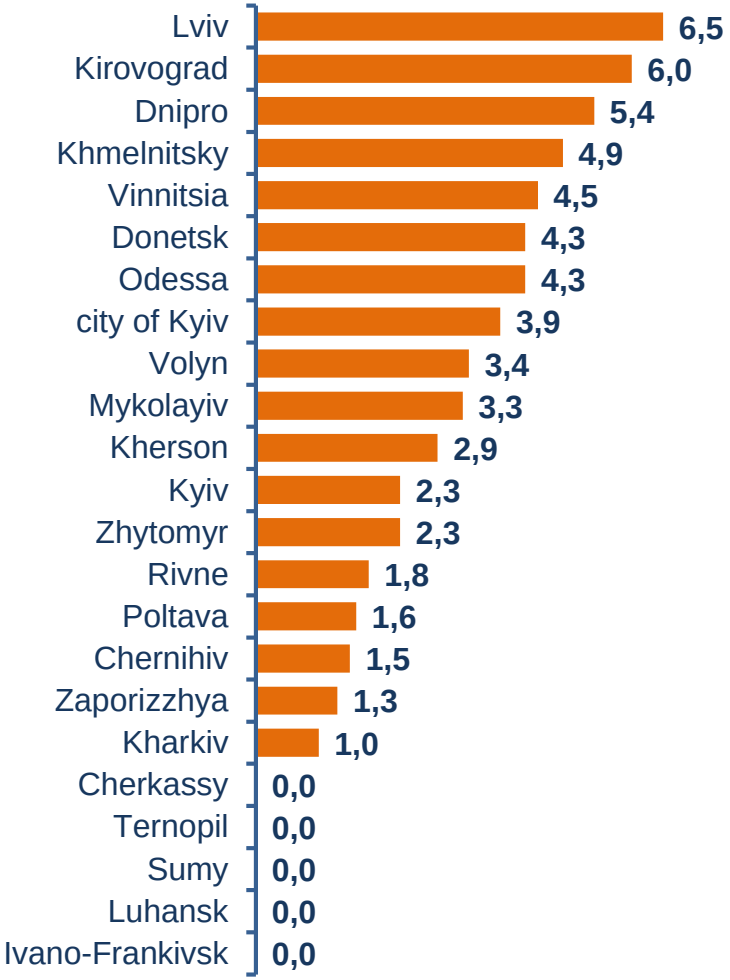
Global guidance on criteria and processes for validation: elimination of mother-to-child transmission (EMTCT) of HIV and syphilis, WHO (2014)

Mother to child HIV transmission rates	%
2016 pediatric cohort data (PCR +ELISA, Western blot)	3.6%
2016 cohort (PCR, coverage87%)	2.0%

Mother To Child HIV Transmission



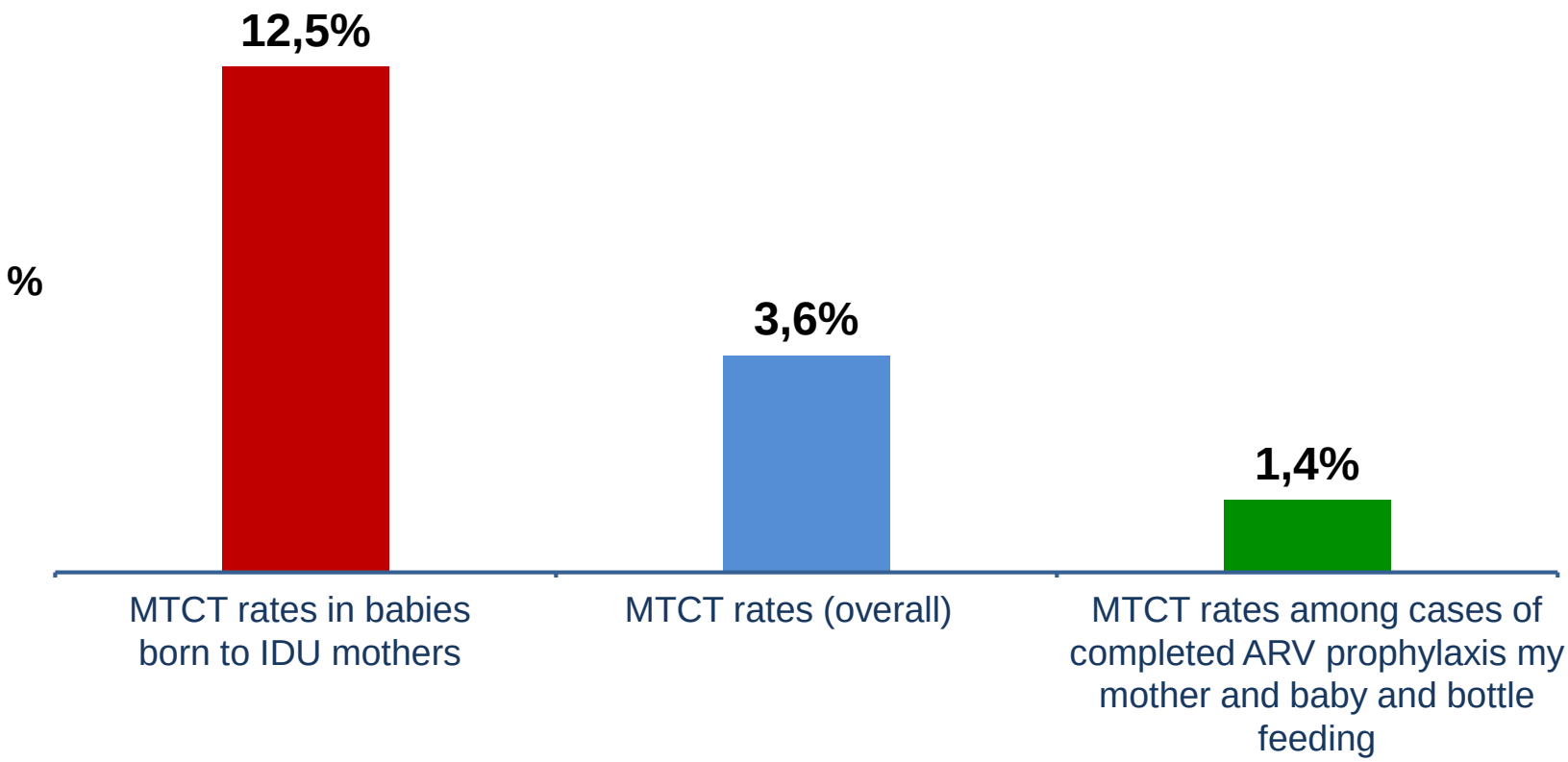
Cohort Analysis



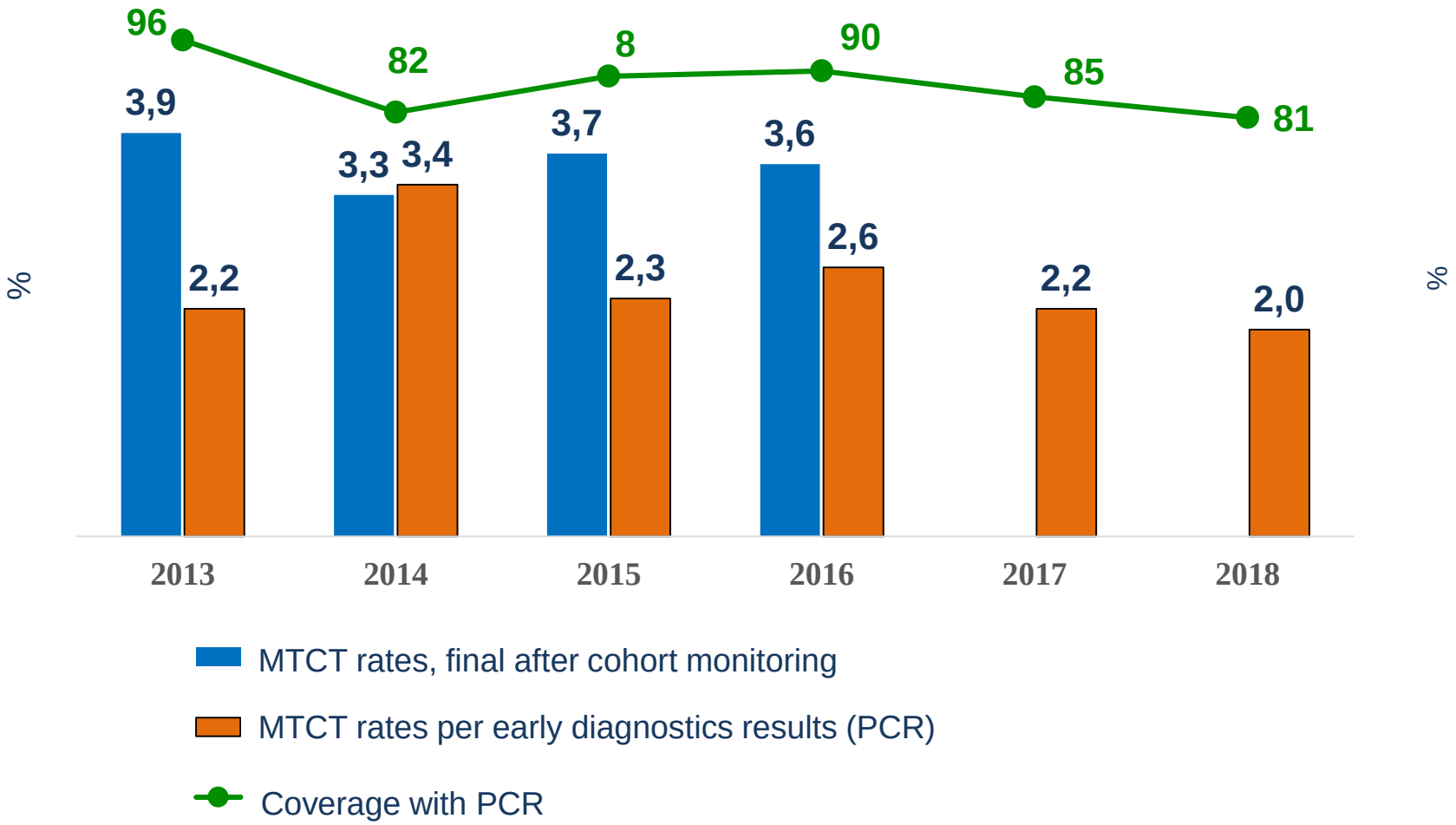
Public Health Center, MOH Ukraine

Mother To Child HIV Transmission Rates in Ukraine

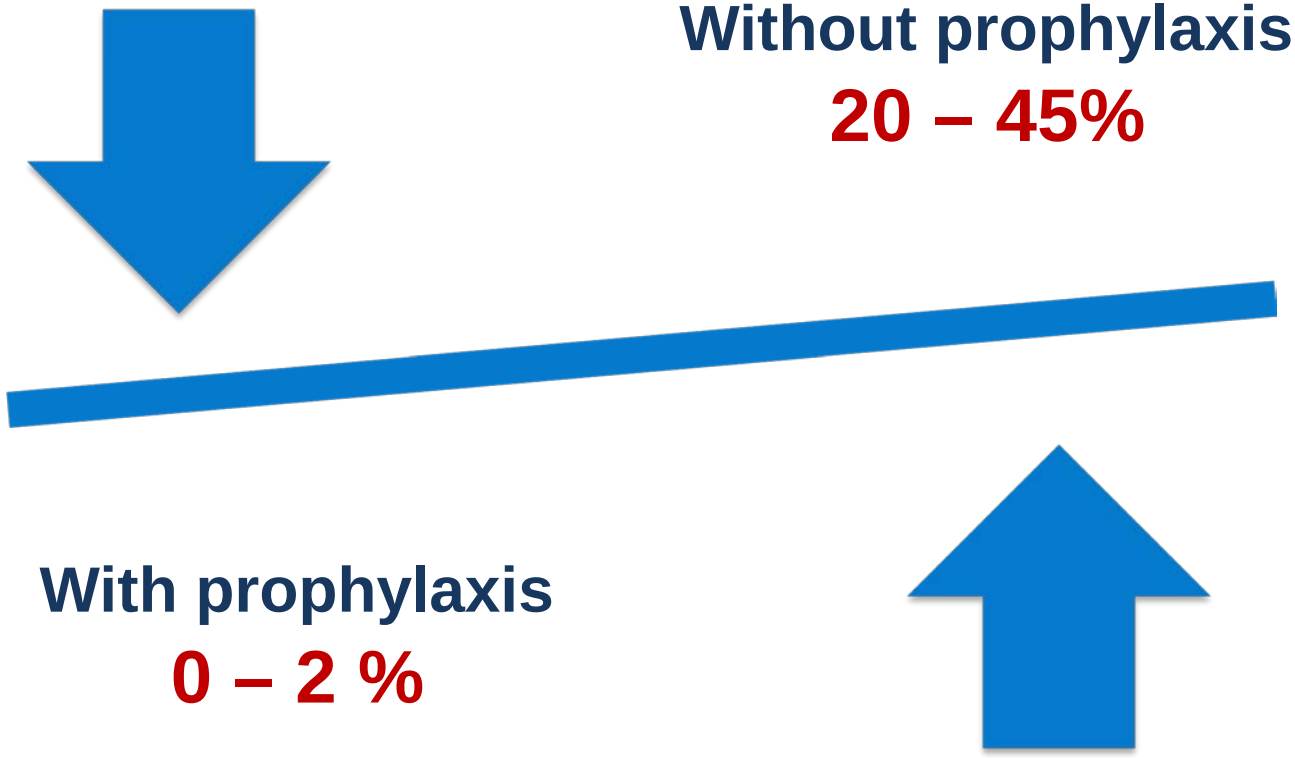
2016 Cohort



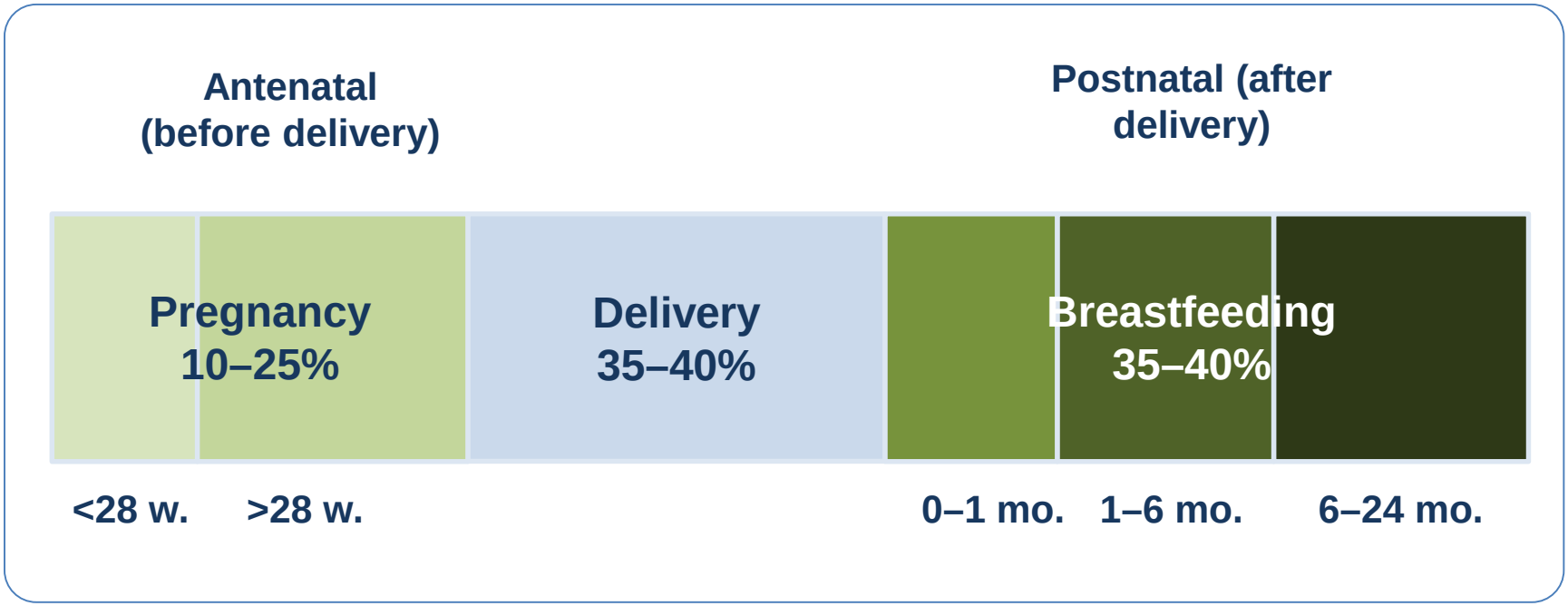
Mother To Child HIV Transmission Rates in Ukraine



Risk of Mother To Child HIV Transmission



VERTICAL HIV TRANSMISSION RATE

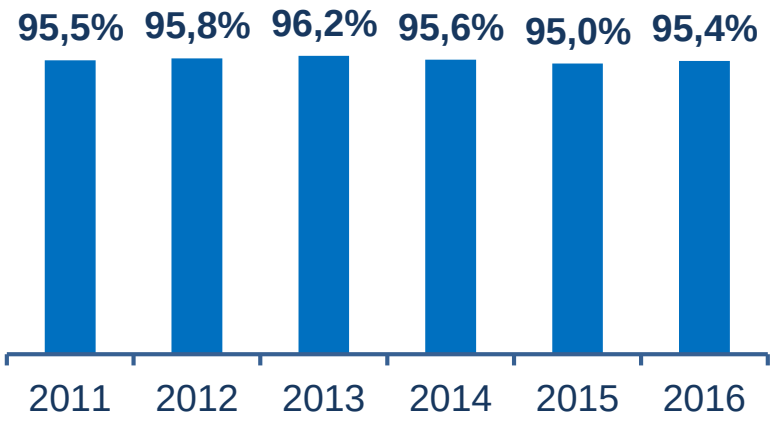


Anticipated mechanism of HIV transmission during delivery

- Direct contact between baby's skin and mucosa and maternal cervical-vaginal secretion and virus elimination from this secretion ***(during pregnancy HIV concentration in vaginal secretion is 4 times higher than in in blood***)
- Infected amniotic fluid
- Prolonged period after ROM

Antiretroviral Prophylaxis

Ukraine



Ukraine (2016)

Proportion of pregnant women who had ARV prophylaxis with three ARVs – 96%, of them:

- **because of health status – 46.8%**
- **continue ART after delivery - 74%**

Prescribed ARVP/ARV	MTCT Rate
ARV prophylaxis /ART because of health	**2.0 %**
ARV prophylaxis with three drugs	**2.5 %**
ARV prophylaxis with one drug	**16.0 %**
Did not have ARVP/ART	**23.8 %**

* without temporarily occupied AR Crimea, city of Sebastopol, from 2014 and part of the area of antiterrorist operations from 2015

Survey “Prioritizing Factors Influencing Mother To Child Transmission in Ukraine”

Risk factors for mother to child HIV transmission (p <0.001) (2016-2017)

1
- Late presentation to antenatal care
- HIV diagnosis during delivery or right after

2
- Parity
- High viral load in pregnancy

3
- Low adherence of a pregnant woman to ART
- Presenting to care in labour

4
- No ART during pregnancy
- No ARV prophylaxis during delivery

5
- No ARV prophylaxis for a baby
- Mixed feeding

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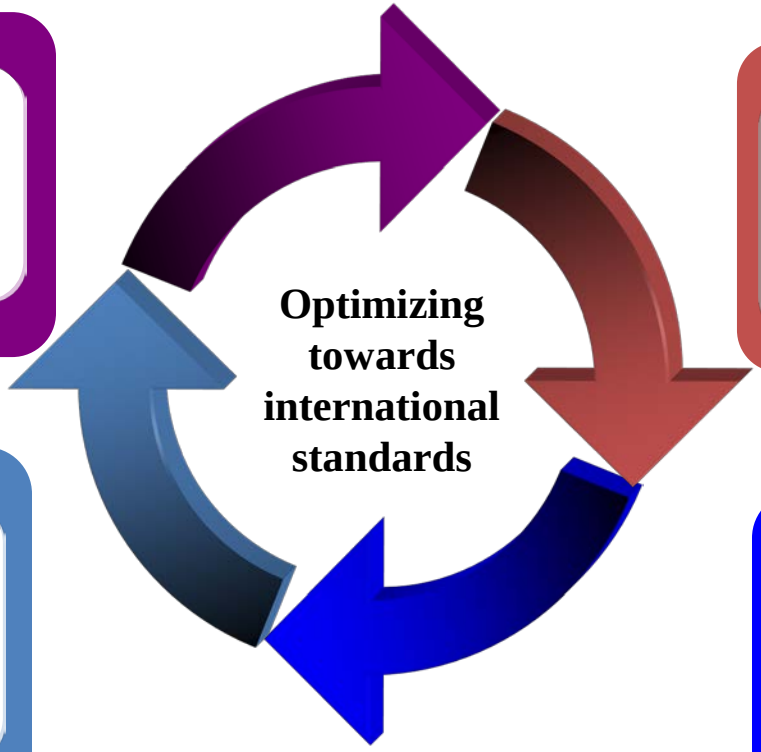
HIV with TB comorbidity

HIV+ woman never received ART

HIV+ woman received ART before pregnancy



Drug use in pregnancy of HIV+ women

Lost virologic suppression, low adherence, discontinuation of ART

HIV+ pregnant women with HCV/HBV coinfection

ART in Pregnancy

- **Recommended NRTI combinations in pregnant women:**

  TDF/FTC (tenofovir disoproxil 300 mg/emtricitabine 200 mg); instead of FTC (emtricitabine 200 mg) it's possible to use 3TC (lamivudine150 mg; ABC/3TC (abacavir 600 mg/lamivudine 300 mg); or AZT/3TC (zidovudine 300 mg/ lamivudine 150 mg)

- **Recommended protease inhibitor in pregnant women:**

  LPV/rtv (lopinavir 200 mg/ritonavir 50 mg); alternative – DRV, boosted rtv (darunavir 800 mg + ritonavir100 mg)

- **Recommended INSTI**: RAL (raltegravir 400 mg)

- **Recommended NNRTI**: EFV (efavirenz 600 mg), can be prescribed after 8 weeks of gestation

- **NVP – no longer recommended for vertical transmission prevention**

Case Scenario: HIV+ woman never received ART

1. Prescribe combination ART as soon as possible after HIV diagnosis
2. **Regardless of CD4 and VL**
   - ART is prescribed **for life and without interruptions** provided a patient gives his informed consent and is adherent to treatment
3. Recommended regimen TDF/FTC + LPV/rtv , ABC/3TC + LPV/rtv
4. Acceptable regimen TDF/FTC +RAL, TDF/FTC + EFV,
5. Alternative regimen
6. CD4 and VL testing and monitoring to ensure viral suppression;

1. Alternative, acceptable regimens and 2nd and 3rd line regimens are prescribed in case of intolerance or failure of the recommended one, considering teratogenic risk during pregnancy;

2. When choosing ART regimen for a pregnant woman, preference should be given to simplified fixed dose regimens and small pill burden;

Case Scenario: HIV+ woman received ART prior to pregnancy

- **Assess efficacy** of current ART regimen (BL testing) and consider regimen modification:
- In case of virologic success (VL< 50 copies/ml), continue on current ART regimen;
- In case of **virologic failure,** refer to adult ART specialist to assess the situation and **switch ART regimen**

Case Scenario: loss of virologic suppression in pregnancy, poor adherence

- **Assess current ART regimen** and previous ART prophylaxis and treatment regimens;
- **Assess adherence** to ART;
- Refer a pregnant woman to adult ART specialist to assess the situation and **switch ART regimen;**
- Refer a pregnant woman to **HIV drug resistance** testing if **VL > 2000** copies/ml (if possible);
- If **VL >50 copies/ml,** timely plan **elective C-section**

Case Scenario: HIV+ pregnant women with HBV/HCV coinfection

1. **Screen for Hepatitis B virus**, **vaccinate against Hep B**;
2. Screen for Hep A virus; vaccinate against Hep A;
3. Refer HIV+ pregnant woman with Hep B or C to **specialist in chronic Hepatitis for consultation;**
4. All pregnant women with HIV/HBV coinfection should receive cART per clinical protocol; **TDF/FTC + LPV/rtv)**
5. Assess **LFTs 2 weeks, 4 weeks** after ART prescription and every 4 weeks till the end of pregnancy;
6. Plan delivery in women with HIV/HCV coinfection with **elective Cesarean section;**
7. Within 12 hours of birth newborns should get **Hep B vaccination;**. evaluating babies according to standards

Case Scenario: drug use in HIV+ pregnancy

1. Consultation of **a substance abuse doctor**
2. If SMT with methadone, assess **interaction with ART**;
3. **Efavirenz should not be prescribed.**
4. ART per clinical protocol: **TDF/FTC + LPV/r,**
5. **A3T/3TC+ LPV/r, ABC/3TC + LPV/r**

consider teratogenic risk

Case Scenario: HIV and TB

1. Consultation of **a TB doctor**.
2. Assess **interaction** of TB drugs and **ART**;
3. ART per clinical protocol: **TDF/FTC + EFV, ABC/3TC + LPV/r, TDF/FTC + LPV/r .**

Management of Delivery

- **Elective Cesarean section** before labor at 38 weeks gestation:
- Up to 4 hours after rupture of membranes
- Woman with HCV, HBV coinfection
- VL > 50 c/ml before delivery
- Woman did hot receive ART or identified at maternity facility or before labor
- **Vaginal delivery** at VL < 50 c/ml
- **Emergency C-section necessitated by obstetrical or pediatric situation**

Cesarean Section Decreases HIV Transmission Risk by 80% at VL >400 copies/ml

Vaginal delivery
(10.2%) [1]

↓

Elective Cesarean section
(3.4%)

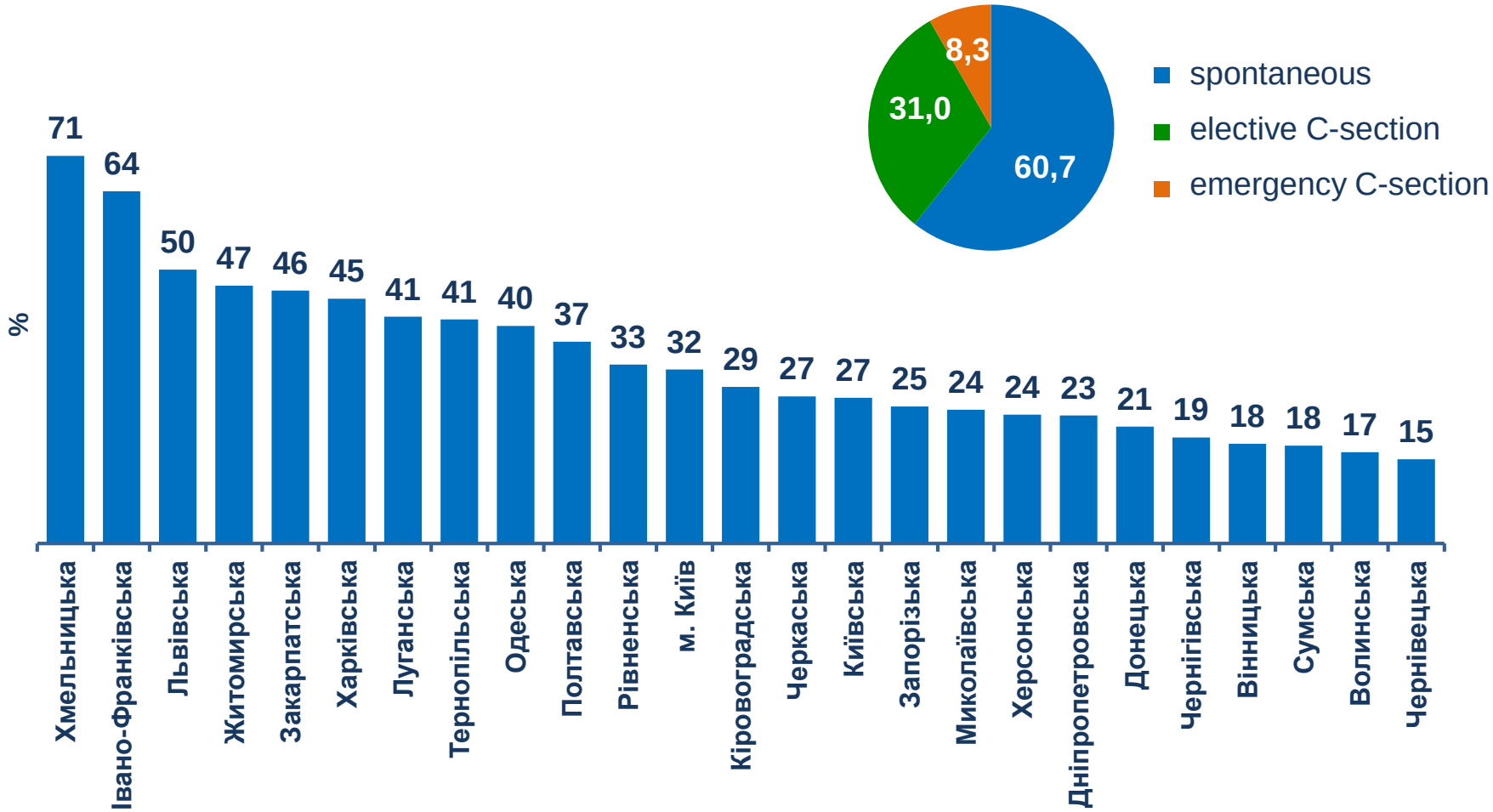
Vaginal delivery + ART
(6.6%) [2]

↓

Elective Cesarean Section + ART
(0.8%)

1. European Mode of Delivery Collaboration Lancet 1999;353:1035–1039;
2. Mandelbrot L et al. JAMA 2008;280:55–60.

Ukraine:
Elective Cesarean Section in 2018 – 31%



Since 1987, 48 387 babies born to HIV+ Women in Ukraine

95.2% babies born to HIV+ mothers

4.8% infected through other routes

(drug use, blood and blood products transfusion, unprotected sex, victims of violence)

As of 01.01.2019 in Ukraine:

- 3,251 HIV+ babies born to HIV+ mothers registered;
- **4,885** babies were still awaiting their confirmatory HIV test
- On ART – **2,920 children**

Public Health Center, MOH Ukraine

Standard Approaches ARV Prophylaxis for Perinatal HIV Transmission

Three steps-based principle:

1. **Antenatal phase** – during pregnancy if diagnosed with HIV - from 14 weeks of gestation start ART, after delivery – continue ART
2. **Intranatal phase** – mother and baby during delivery
3. **Postnatal phase** – baby after birth

VL < 50 copies/ml - vaginal delivery

AZT to baby - 4 weeks

VL > 50 copies/ml - elective C-section

baby – AZT+ 3TC - 4 w

NVP - 2 w

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Term pregnancy or pre-term delivery at 34-37 weeks on ART

VL < 50 copies/ml HIV RNA

AZT- 4 mg/kg; during 4 weeks every 12 hours

If baby can not take medications orally:

- AZT monoprophylaxis IV

1.5 mg/kg every 12 hours

VL >50 copies/ml HIV RNA

AZT 4 weeks every 12 hours:

≥ 35 weeks gestation - 4 mg/kg;

30-34 weeks gestation – first 2 weeks 2 mg/kg, last 2 weeks - 3 mg/kg;

up to 30 weeks gestation : 2 mg/kg;

3TC- 2 mg/kg- 4 weeks PO every 12 hours;

- NVP 2 weeks PO every 24 hours: first week 2 mg/kg, second week 4 mg/kg;

Virologic Methods of HIV Diagnosis in Babies in Ukraine, since 2005

HIV DNA PCR – highly sensitive method of identifying genetic material of the virus inside cells (provirus phase)

Test sensitivity:

- **29-46% - 48** after birth
- **93%** - second week of life
- **96-98%** - at **28-30** days
- **99-100%** - at **3-5** months

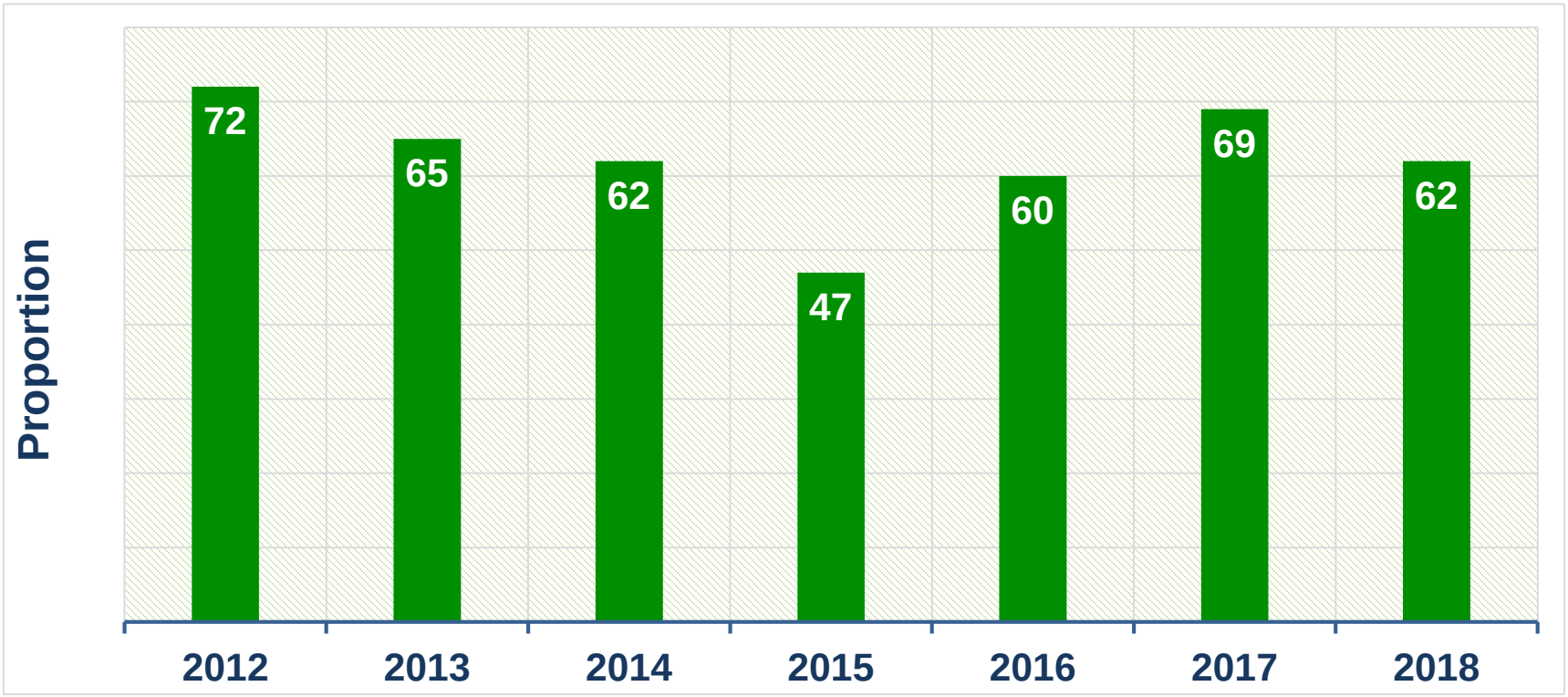
HIV RNA PCR – ensures quantitative an qualitative identification of virus in plasma

Viral load – number of HIV RNA copies in 1 ml of plasma

Important for monitoring and control of antiretroviral therapy

Diagnosing Babies Early

Proportion of babies born to HIV+ mothers who undergo virologic HIV testing in the first 2 months of life



Feeding Babies Born to HIV+ Mothers:

According to WHO criteria, all babies born to HIV+ mothers should be recommended exclusively formula feeding from birth

Consult HIV+ mother on issues of safe feeding of her baby and monitor safety and correct use of formula feeding

Inform HIV+ mother about free-of-charge provision of her baby with adapted formula per procedure established in the region

Control receipt by family and intended use of adapted formula for feeding babies

PCP Prophylaxis

Cotrimoxazole (TMP/SMX) to all babies from 4–6 weeks until 2 negative virologic test results are obtained віку

I DNA PCR – after **1 month** of age

II DNA PCR – after **3 months** of age

provided the baby was not breastfed for at least 6 weeks before the first negative result and there are no clinical signs of HIV infection

Рекомендована доза для прийому 1 раз на добу з урахуванням віку та маси тіла	Суспензія або сироп (в 5 мл 40/200 мг)	Дитяча таблетка (20/100 мг)	Звичайна таблетка для дорослих (80/400 мг)	Подвійна таблетка для дорослих (160/800 мг)
До 6 міс (до 5 кг) 20/100 мг	**2,5 мл**	**1 таблетка**	**¼ таблетки, можна змішувати з їжею**	**-**
6 міс. – 5 років (5–15 кг) 40/200 мг	**5 мл**	**2 таблетки**	**½ таблетки**	**-**

Vaccination of Babies Born to HIV+ Mothers

Scheduled vaccination is done per Immunization Calendar approved by the Order of MOH Ukraine of 11.08.2014 # 551 “About Improving Prophylactic Vaccination Practices in Ukraine” registered with the Ministry of Justice Ukraine of 13.10.2014 #1237/26014.

Order of MOH Ukraine as of 18.05.2018 # 947 “About Changes to Immunization Calendar in Ukraine”

Algorithm of Monitoring of Babies Born To HIV+ Women

Baby born to HIV+ mother (code per ICD-10 Z-20.6)		
Age of baby	**Prescribe**	**Discontinue**
1 day	• AZT or AZT + 3TC + NVP; • CBC (per clinical indications); • Vaccination according to current Vaccination Calendar	
2–3 day	• **HIV DNA PCR*** to identify antenatal HIV infection (if possible) DBS	
14 day		NVP (if prescribed)
28 day	• CBC (per clinical indications) • Cotrimoxazole (TMP /SMX) for PCP prophylaxis	AZT or AZT + 3TC
4–6 weeks	- **HIV DNA PCR***	
3–4 months	- **HIV DNA PCR***	
Baby likely not HIV infected, if 2 DNA PCR (-) - 1 test not earlier than 2 weeks after ARV prophylactic course completed, 2 test – after 3 months of age (code per ICD-10 Z20.6) and the baby is on formula feeding for more than 6 weeks before 1st negative PCR result obtained, provided there is no clinical or laboratory signs of HIV infection.		
	• Vaccination per current Vaccination Calendar	TMP/SMX
18 months	• ELISA to identify anti-HIV	-
Baby not infected with HIV, if: ELISA (-), baby on bottle feeding for more than 6 months before getting negative ELISA test results, provided there is no clinical or laboratory signs of HIV infection.		
	-	Preliminary diagnosis ruled out (Z 20.6 deassigned)

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RELATIONSHIP: doctor - patient

Right of a child to be healthy

If necessary, including when mother (parents) refuse from their baby undergoing post-exposure ARV prophylaxis or in case of their poor adherence the following get involved:

- social worker,
- Service on Children, local government bodies;
- law enforcement

Right of a doctor to provide PMTCT

In case mother (parents) refuse from care and treatment of their HIV+ baby who needs it, or in case of poor adherence of parents to treatment and care of their HIV+ baby, **consider it violent behavior in the form of medical neglect**.

If all possibilities of health care workers have been exhausted without success, a health care facility should approach local Service on Children and Prosecution Office to ensure baby's right to health and life granted by the Constitution.

Thank you for your attention

Questions