

# THE ASSOCIATION BETWEEN INJECTING DRUG USE AND HIV OUTCOME MEASURES IN LATVIA

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# Background

- Thanks to the substantial developments in HIV treatment and care within the last 10-15 years:
  - Mortality rates among PLHIV decrease (including in EU in general). life expectancy increases<sup>1,2,3</sup>.
  - Mortality can even be as low as in the general population<sup>4</sup>.
  - Causes of death among PLHIV population tend to become similar to the causes existing in the respective age group of general population<sup>5</sup>.

1. The Data Collection on Adverse Events of Anti-HIV drugs (D:A:D) Study Group. Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D study // AIDS. 2010; 24: 1537-1548.
2. Lohse N., Hansen A. B. E., Pedersen G., et al. Survival of Persons with and without HIV Infection in Denmark, 1995-2005 // Annals of Internal Medicine. 2007; 146 (2): 87-96.
3. Hogg R., Lima V., Sterne J. A. C., et al. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies // The Lancet. 2008; 372: 293-299.
4. Lewden C., Bouteloup V., De Wit S., et al. All-cause mortality in treated HIV-infected adults with CD4  $\geq 500/\text{mm}^3$  compared with the general population: evidence from large European observational cohort collaboration // International Journal of Epidemiology. 2012; 41: 433-445.
5. McDavid Harrison K., Song R., Zhang X. Life Expectancy After HIV Diagnosis Based on National HIV Surveillance Data From 25 States, United States // Journal of Acquired Immune Deficiency Syndromes. 2010; 53 (1): 124-130.

**The purpose** of the study was:

- to establish whether the mortality trends among PLHIV in Latvia are similar to the above mentioned situation in EU,
- to clarify sociodemographic, health behaviour, health status and health care factors associated with the death mortality rates.

**Factors studied:**

- Gender
- Age at time of HIV diagnosis
- Ethnicity
- Place of residence
- Imprisonment at time of HIV diagnosis
- **Mode of transmission**
- Year of diagnosis
- Timeliness of diagnosis
- Viral load at time of HIV diagnosis
- Experience of ART and care
- HCV coinfection

# Methods

## ■ Data sources:

- National HIV/AIDS case registry (n=4888; 100%)
- Medical records of PLHIV at the HIV ambulatory department of the Infectology Centre of Latvia (n=3273; 98.9%)
- national Causes of Death database (n=690; 93.5%)
- data from the Central Statistical Bureau of the Republic of Latvia for calculating the age-standardized mortality

## ■ Population:

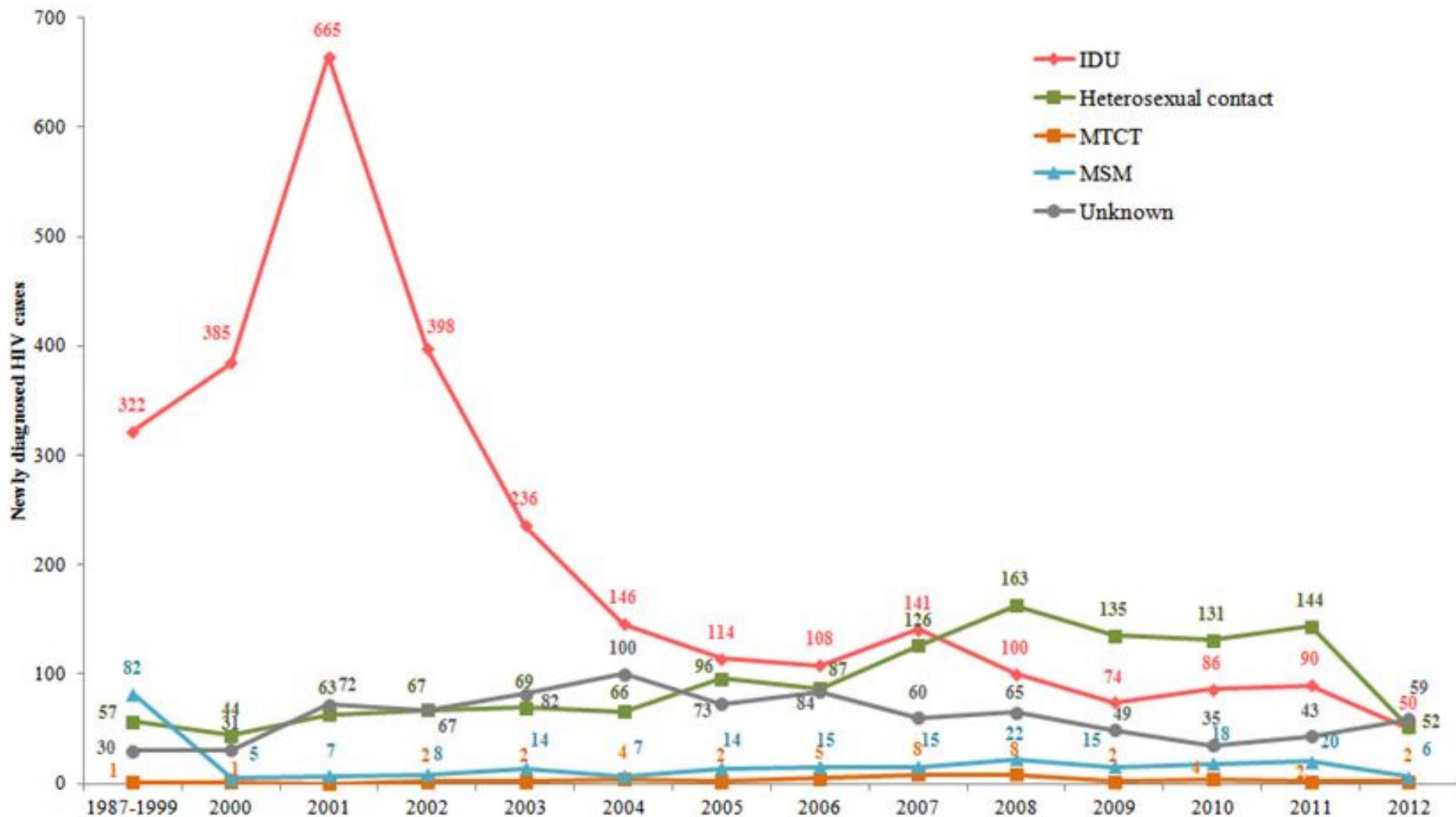
- individuals registered in the HIV/AIDS case registry within the period from 1987 (the first case of HIV in Latvia) to December 2010;
- **4888** PLHIV (incl. 738 *exitus letalis*);
- total time of follow-up: **31,192.6 py** (median – 6.8 py);
- when associated factors analyzed – persons under 14 years of age excluded.

# Methods (II)

## ■ Analysis:

- Indirect standardization (standard – age specific mortality rates of the general population)
- Time trends – log transformation and linear regression
- Survival analysis - Cox regression.
- Cause-specific MRR - Poisson regression
- MS Excel. SPSS 19.0

## Newly Diagnosed HIV Cases by Transmission Mode in Latvia, 1987-2012 (1 July)

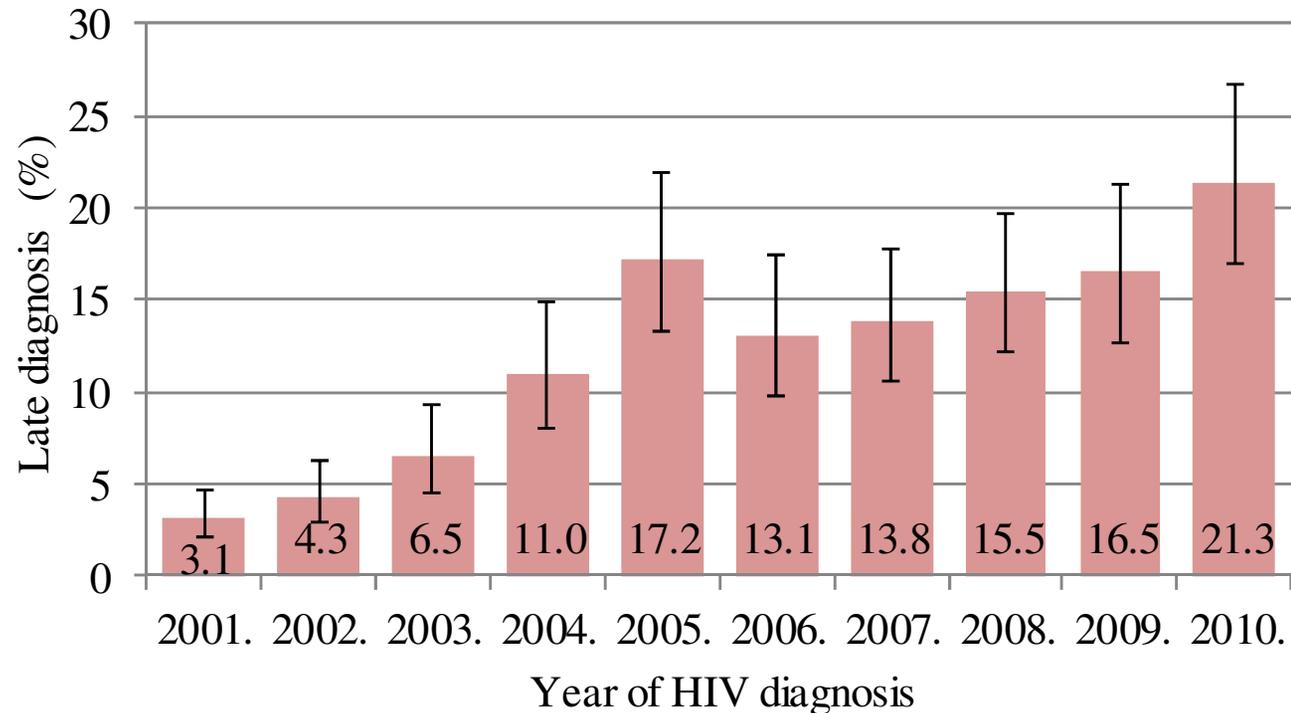


Prepared by NGO "Baltic HIV Association"

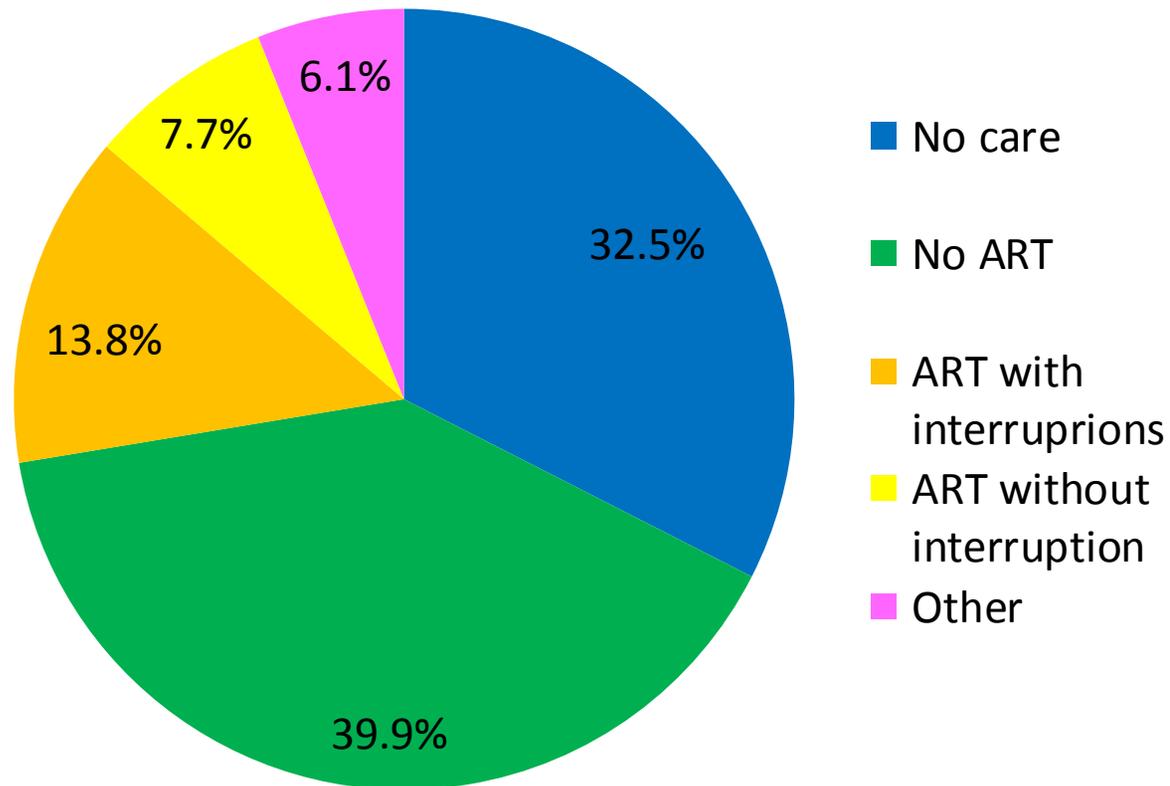
Sources: Centre for Disease Prevention and Control of Latvia

## Proportion of late diagnosis among annually registered HIV cases, 2001-2010

- Mean time from HIV dg till first count of CD4 cells – **5.1 months** (SD 13.0);
- 59.8% - within one month;
- 68 PLHIV (2.2%) - 5 years or more



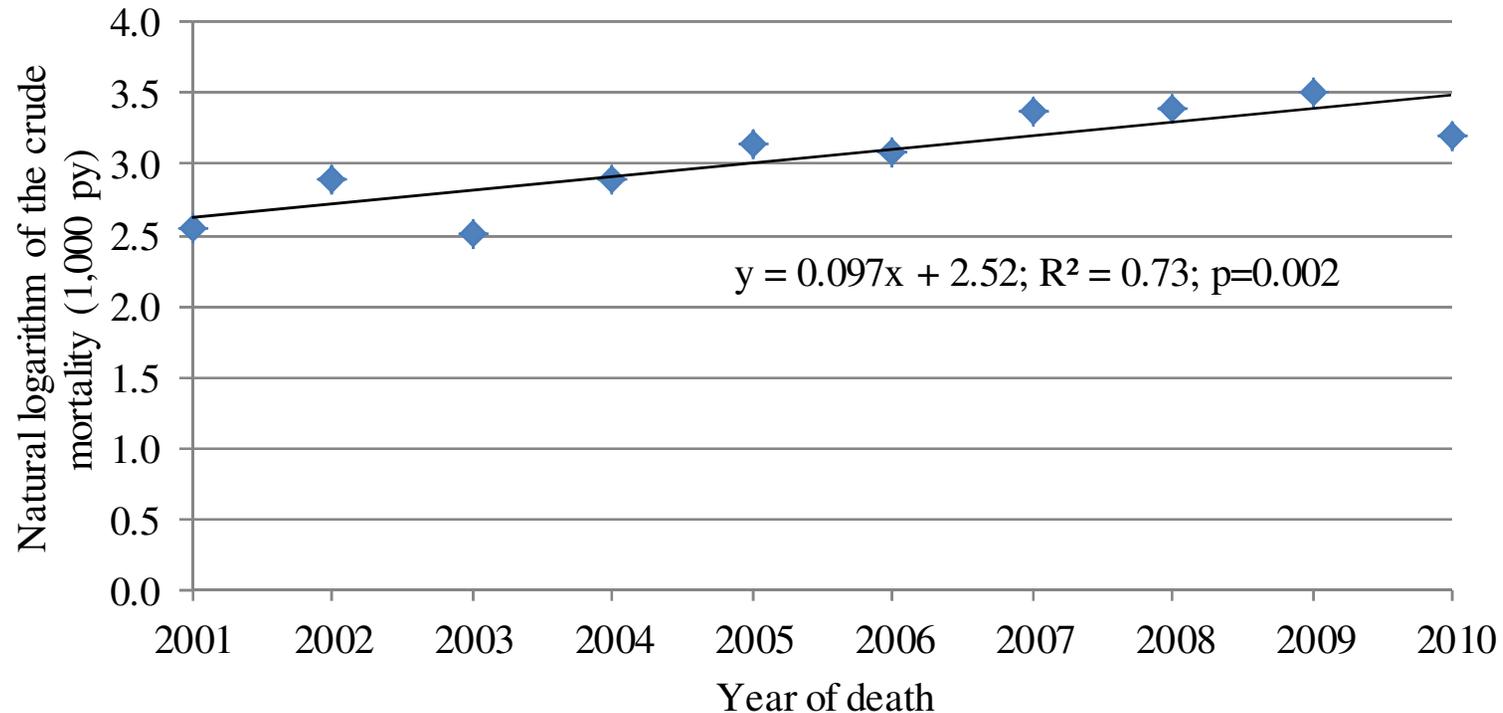
## ART and care experience



- Average time from HIV dg till ART – **33.8 months** (0-153 months) (median – 19.9 months);
- **80%** of persons with ART interruptions – adherence issues



## Time trends of crude mortality rate among PLHIV, 2001-2010



- Increase – **10.1%** per year;
- Among females – **12.0%** per year. males – **10.2%** per year

## Number of deaths. crude mortality and standardized mortality ratio in PLHIV population, 2001-2010

Year of the case of death	Number of deaths	Total person-time at risk (person-years)	Crude mortality (per 1000 person-years)	95% confidence interval	Standardized mortality ratio	95% confidence interval
2001	17	1.334.6	12.7	7.4-20.4	5.4	3.1-8.6
2002	36	2.000.9	18.0	12.6-24.9	8.0	5.6-11.1
2003	30	2.421.3	12.4	8.4-17.7	5.8	3.9-8.3
2004	49	2.743.6	17.9	13.2-23.6	8.1	6.0-10.7
2005	70	2.985.6	23.4	18.3-29.6	9.2	7.2-11.6
2006	70	3.208.7	21.8	17.0-27.6	8.1	6.3-10.2
2007	100	3.457.7	28.9	23.5-35.2	9.9	8.0-12.0
2008	110	3.705.3	29.7	24.4-35.8	11.0	9.0-13.2
2009	130	3.897.2	33.4	27.9-39.6	12.6	10.5-14.9
2010	99	4.057.3	24.4	19.8-29.7	8.6	7.0-10.5

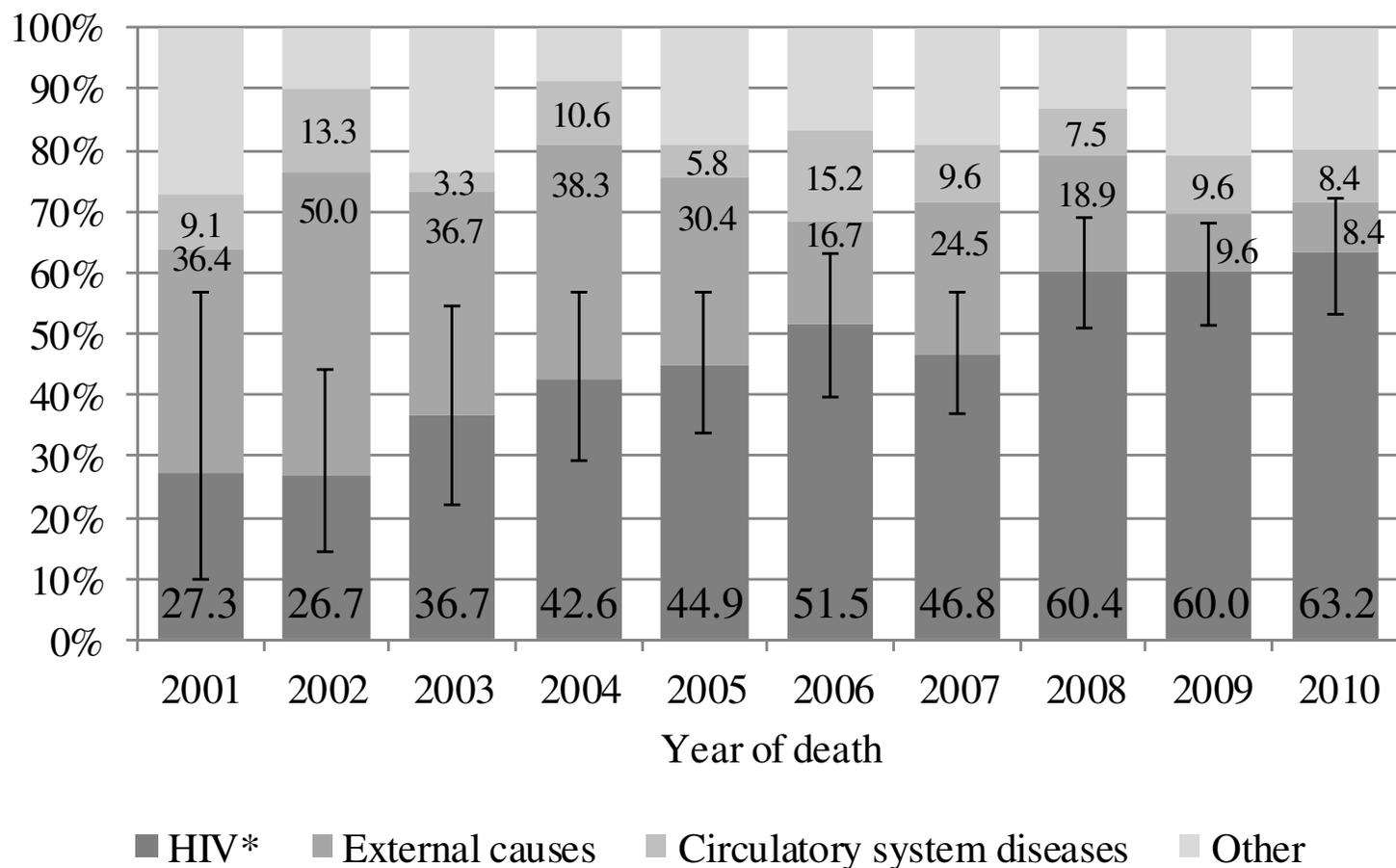
## Number of deaths and proportional mortality among PLHIV according to underlying cause of death, 1991-2010

Code. International Statistical Classification of Diseases and Related Health Problems 10th Revision	Number of deaths	Proportional mortality rates (%)	95% confidence interval
B20-B24 (Human immunodeficiency virus [HIV] disease). including:	355	51.4	47.7-55.2
B20.0 (HIV disease resulting in mycobacterial infection)	110		
B23.2 (HIV disease resulting in hematological and immunological abnormalities. not elsewhere classified)	64		
B24 (Unspecified human immunodeficiency virus [HIV] disease)	34		
V.W.X.Y (External causes of morbidity and mortality). including:	150	21.7	18.8-25.0
X40-X49 (Accidental poisoning by and exposure to noxious substances)	50		
X60-X84 (Intentional self-harm)	29		
X85-Y09 (Assault)	19		
I00-I99 (Diseases of the circulatory system). including:	65	9.4	7.5-11.8
I30-I52 (Other forms of heart disease)	42		
I20-I25 (Ischemic heart diseases)	16		
I60-I69 (Cerebrovascular diseases)	6		

## Number of deaths and proportional mortality among PLHIV according to underlying cause of death, 1991-2010 (II)

Code. International Statistical Classification of Diseases and Related Health Problems 10th Revision	Number of deaths	Proportional mortality rates (%)	95% confidence interval
K00-K93 (Diseases of the digestive system)	50	7.2	5.5-9.4
C00-D48 (Neoplasms)	18	2.6	1.7-4.1
A00-B99 (Certain infectious and parasitic diseases)	17	2.5	1.5-3.9
F00-F99 (Mental and behavioral disorders)	9	1.3	0.7-2.5
G00-G99 (Diseases of the nervous system)	7	1.0	0.5-2.1
J00-J99 (Diseases of the respiratory system)	6	0.9	0.4-1.9
R00-R99 (Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified)	4	0.6	0.2-1.5
L00-L99 (Diseases of the skin and subcutaneous tissue)	3	0.4	0.1-1.3
Q00-Q99 (Congenital malformations, deformations and chromosomal abnormalities)	2	0.3	0.1-1.1
D50-D89 (Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism)	1	0.1	-
M00-M99 (Diseases of the musculoskeletal system and connective tissue)	1	0.1	-
N00-N99 (Diseases of the genitourinary system)	1	0.1	-
E00-E90 (Endocrine, nutritional and metabolic diseases)	1	0.1	-
Total	690	100	
Cause of death unknown	48		

## Proportional mortality for 3 most prevailing underlying causes of death among PLHIV, 2001-2010



\* Line segments show 95% confidence interval of HIV proportional mortality

## Factors associated with death hazard

Factor studied	aHR	95% CI	p
Age at dg per year increase	<b>1.06</b>	<b>1.05-1.06</b>	<b>&lt;0.001</b>
Mode of transmission PWID vs. MSM	<b>2.07</b>	<b>1.29-3.33</b>	<b>0.003</b>
heterosexual vs. MSM	1.30	0.82-2.07	0.27
unknown vs. MSM	2.37	1.40-4.03	0.001
Year of HIV dg 1987-1999 vs. 2008-2010	<b>0.69</b>	<b>0.48-0.99</b>	<b>0.04</b>
2000-2007 vs. 2008-2010	0.77	0.49-0.89	0.09
Timeliness of the diagnosis late vs. not late/not known	<b>3.81</b>	<b>3.14-4.88</b>	<b>&lt;0.001</b>
Viral load (log <sub>10</sub> RNS copies/ml) ≥5 vs. <4	<b>2.02</b>	<b>1.56-2.63</b>	<b>&lt;0.001</b>
4-5 vs. <4	<b>1.30</b>	<b>1.00-1.68</b>	<b>0.049</b>
unknown vs. <4	1.94	1.52-2.47	<0.001

## Factors associated with external causes specific mortality

Factor studied	aMRR	95% CI	p
Gender			
male vs. female	<b>1.58</b>	<b>1.001-2.51</b>	<b>0.049</b>
Age at dg			
per year increase	<b>1.04</b>	<b>1.02-1.06</b>	<b>&lt;0.001</b>
Mode of transmission			
PWID vs. MSM	<b>5.96</b>	<b>1.31-27.14</b>	<b>0.02</b>
heterosexual vs. MSM	2.21	0.47-10.33	0.32
unknown vs. MSM	3.91	0.74-20.61	0.11
ART and care experience			
ART without interruption vs. with interruptions	0.47	0.16-1.39	0.17
no ART experience vs. with interruptions	<b>2.38</b>	<b>1.43-3.96</b>	<b>0.001</b>
no care vs. with interruptions	0.55	0.14-2.18	0.40
other vs. with interruptions	1.06	0.33-3.36	0.93

## Factors associated with HIV cause specific mortality

Factor studied	aMRR	95% CI	p
Age at dg per year increase	<b>1.04</b>	<b>1.03-1.05</b>	<b>&lt;0.001</b>
Mode of transmission			
PWID vs. MSM	<b>2.28</b>	<b>1.16-4.49</b>	<b>0.02</b>
heterosexual vs. MSM	1.63	0.84-3.15	0.15
unknown vs. MSM	<b>2.95</b>	<b>1.37-6.38</b>	<b>0.006</b>
Year of HIV dg			
1987-1999 vs. 2008-2010	<b>0.37</b>	<b>0.23-0.59</b>	<b>&lt;0.001</b>
2000-2007 vs. 2008-2010	<b>0.47</b>	<b>0.33-0.66</b>	<b>&lt;0.001</b>
Timeliness of the diagnosis			
late vs. not late/not known	<b>4.78</b>	<b>3.54-6.45</b>	<b>&lt;0.001</b>
Viral load (log <sub>10</sub> RNS copies/ml)			
≥5 vs. <4	<b>3.24</b>	<b>2.12-4.93</b>	<b>&lt;0.001</b>
4-5 vs. <4	<b>1.57</b>	<b>1.01-2.45</b>	<b>0.046</b>
unknown vs. <4	<b>3.82</b>	<b>2.54-5.73</b>	<b>&lt;0.001</b>
ART and care experience			
ART without interruption vs. with interruptions	0.89	0.61-1.30	0.55
no ART experience vs. with interruptions	1.28	0.97-1.70	0.09
no care vs. with interruptions	<b>0.15</b>	<b>0.06-0.35</b>	<b>&lt;0.001</b>
other vs. with interruptions	0.74	0.38-1.42	0.36

## Limitations

- Underestimation - registered cases is not all cases (UNAIDS estimates twice as more PLHIV in Latvia);
- Registered cases is not all diagnosed cases – but preventive measures carried out;
- Problems with «no late diagnosis» (if AIDS is not registered, it does not mean that a person don't have the stage);
- ART interruptions – definition not precise although used in literature;
- ART duration, drug combinations etc. not taken into account.

# Conclusions

- in contrast to the situation in EU mortality rates among PLHIV in Latvia increase annually;
- mortality rates are remaining considerably higher than those among general population;
- HIV has been established as the underlying cause of death for half of the PLHIV; HIV specific proportional mortality also tends to increase annually;
- PLHIV who became HIV infected via drug injection have two times higher death hazard (vs. MSM), two times higher HIV specific mortality and six times higher mortality from external causes of death.

**Paldies!**

**Thank you!**



Average Joe, 1994 «One World. One Hope» (Canada)