The continuum of care and late presentation – Implementing the consensus definition in HIV

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Late presentation for HIV
Where are we at?

- Late presentation for HIV: CD4 <350/mm^3 / AIDS diagnosis[1]
- LP is a significant problem across Europe leading to
  - poorer survival
  - increased healthcare costs
  - increased risks of onward HIV transmission
- Many European countries have published on LP using cohort studies
- Lack of common definitions used
- Scarce data from Eastern Europe, where surveillance of HIV infection may be more complex but HIV burden larger
- ECDC publishes an annual summary of HIV, including CoC and LP across Europe
  - may be more complete than data from an individual cohort
  - lacks information on outcomes after HIV diagnosis
  - issues with incomplete reporting, differences in data collection, gaps in information from some countries

[1]Antinori et al, 2011

Progress and challenges

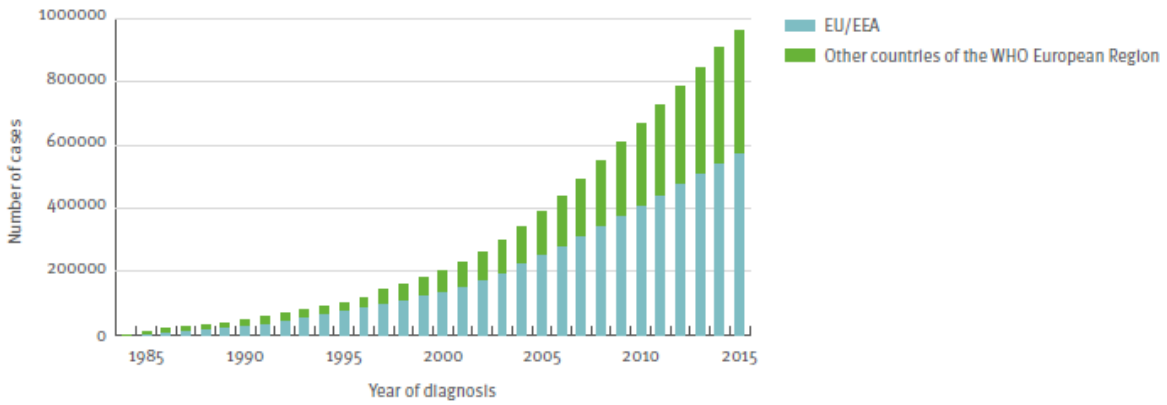
- ECDC reports recognition of strong political leadership on HIV in EU/EEA countries[1]
- **BUT**
  - low rates of testing and high rates of late diagnosis undermine the effectiveness of the HIV response
  - a significant proportion of people who are most at risk of infection have never been tested for HIV
  - almost half of the reported HIV cases are diagnosed late and are in need of treatment when they are diagnosed

[1]ECDC Special report. From Dublin to Rome: ten years of responding to HIV in Europe and Central Asia. Summary report

Response to challenges in HIV testing

In response to continuous challenges in HIV testing across Europe, ECDC commissioned report[1] giving guidance on increasing uptake and effectiveness of HIV testing in the European Union

Figure B: Cumulative number of new HIV diagnoses in the EU/EEA and other countries of the WHO European Region*, 1984–2015



* Data from Russia not included

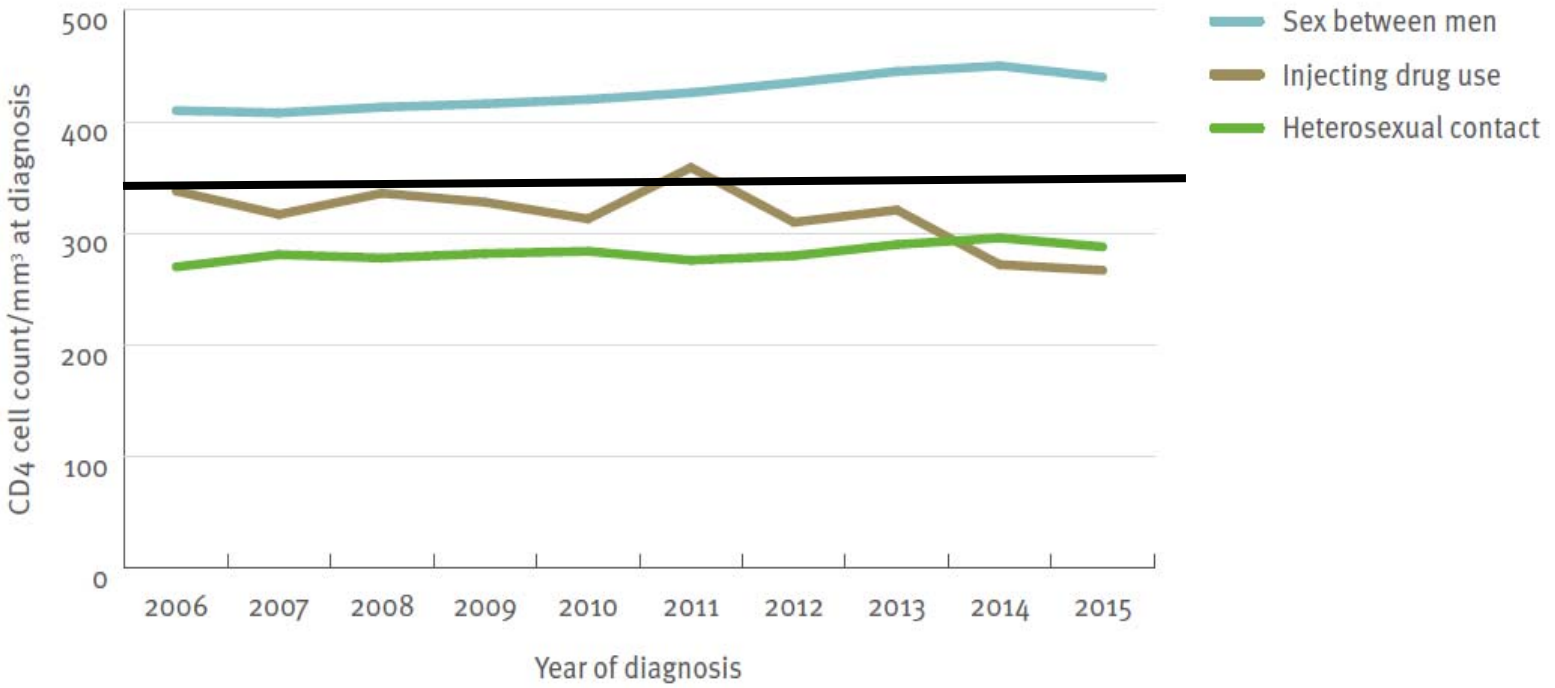
Table A: Characteristics of new HIV diagnoses reported in the WHO European Region, the EU/EEA, and West, Centre and East of the WHO European Region, 2015

	WHO European Region	West	Centre	East	EU/EEA
Reporting countries/Number of countries*	49/53 (50/53)	23/23	14/15	12/15 (13/15)	31/31
Number of new HIV diagnoses	55 230 (153 407)	27 022	5297	22 911 (121 088)	29747
Rate per 100 000 population**	7.6 (17.6)	6.3	2.8	20.6 (47.5)	6.3
Percentage age 15–24 years	9.8%	10.3%	14.6%	8.2%	10.8%
Male-to-female ratio	2.3	3.2	5.3	1.5	3.3
Transmission mode					
Sex between men	25.6%	43.4%	29.9%	3.6%	42.2%
Heterosexual	45.8%	33.0%	27.5%	65.2%	32.0%
Injecting drug use	13.0%	3.3%	4.4%	26.4%	4.2%
Mother to child transmission	0.9%	0.8%	1.0%	1.1%	0.8%
Unknown	14.5%	19.3%	36.9%	3.6%	20.2%

[1]European Centre for Disease Prevention and Control. HIV testing: increasing uptake and effectiveness in the European Union. ECDC Stockholm 2010. 2. Inserts taken from European Centre for Disease Control. HIV AIDS surveillance 2015.

CD4 cell count at HIV diagnosis

Figure 1.11: Median CD_4 cell count per mm^3 at HIV diagnosis, by transmission mode, EU/EEA, 2006–2015



Excludes countries with >60% incomplete data on CD_4 cell count during any year over the period (Belgium, Bulgaria, Croatia, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Latvia, Lithuania, Malta, Norway, Poland, Portugal, Slovakia, Sweden)

Figure from European Centre for Disease Control. HIV AIDS surveillance 2015.

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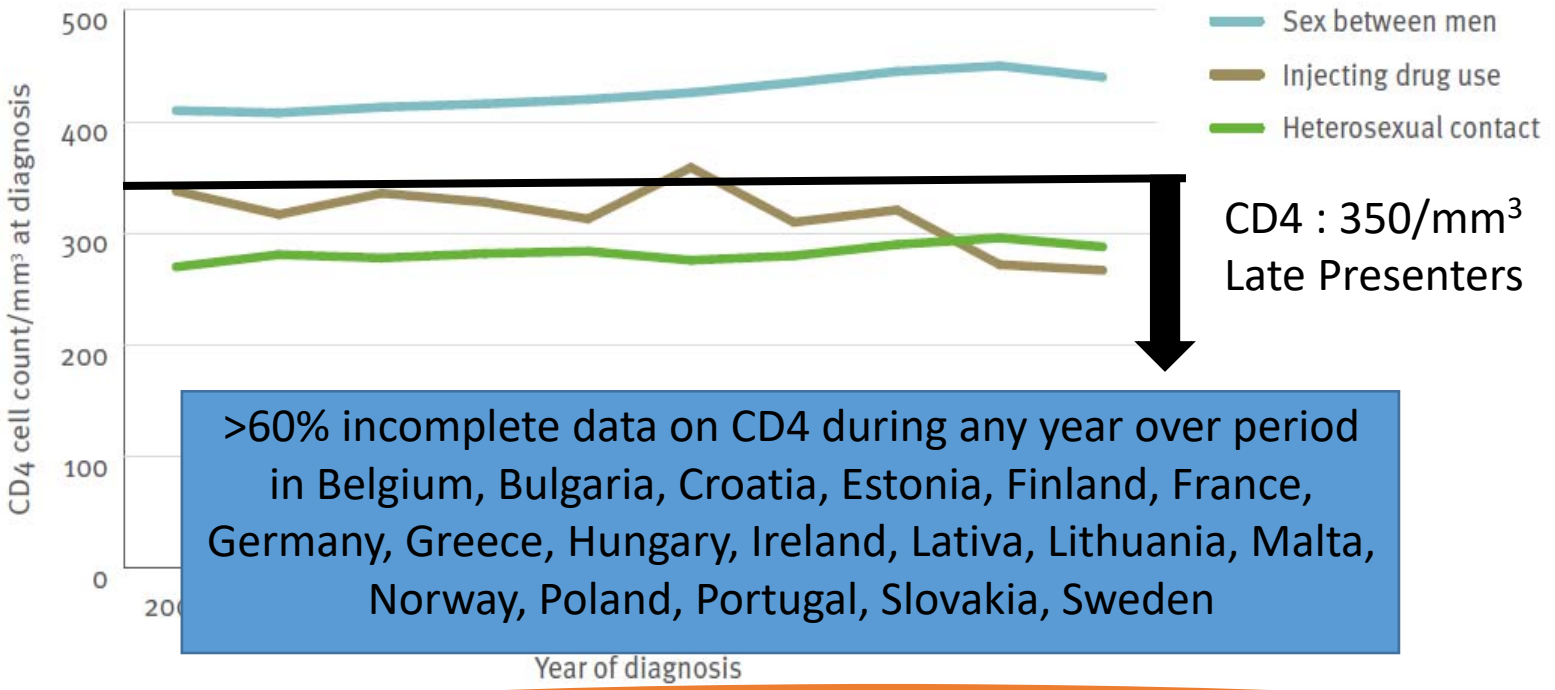

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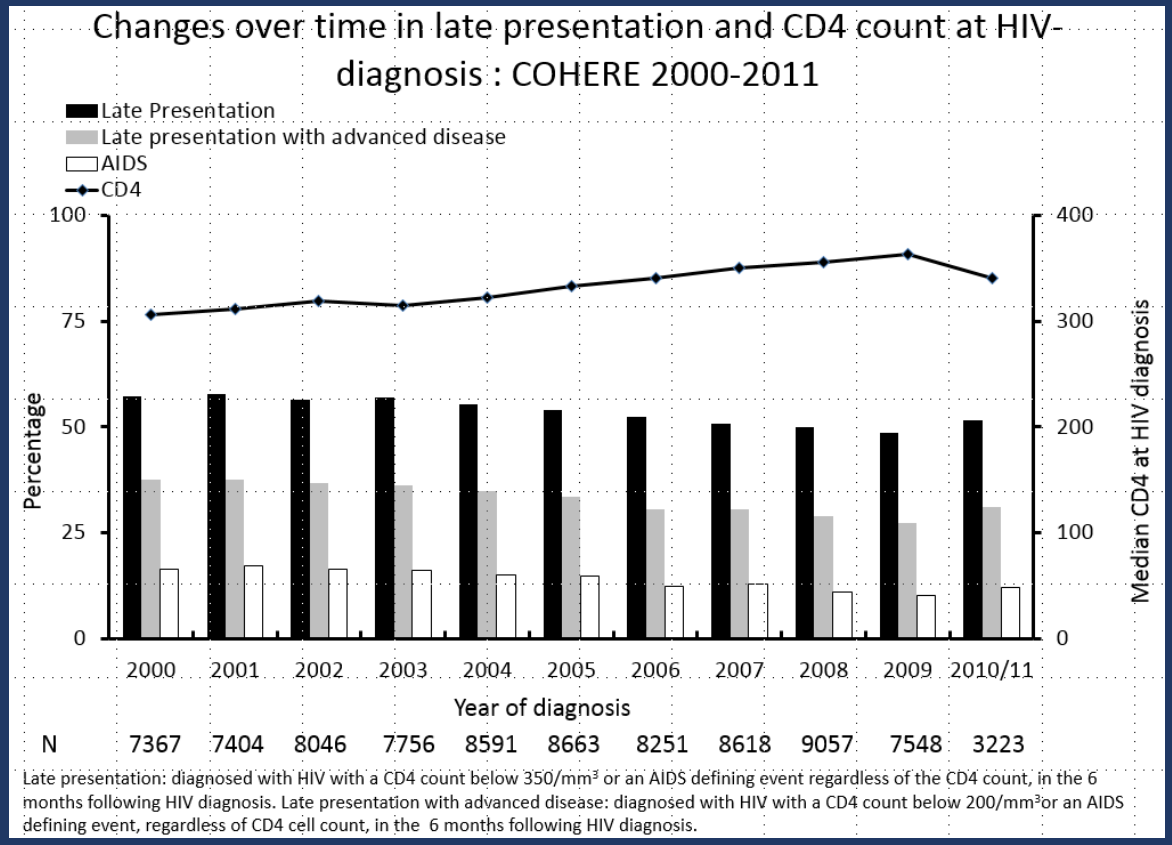
Figure from European Centre for Disease Control. HIV AIDS surveillance 2015.

COHERE : 2000-2010/11



LP decreased from 57.3% in 2000 to 51.7% in 2010/2011 (adjusted OR 0.96; 95% CI 0.95–0.97)

LP decreasing in

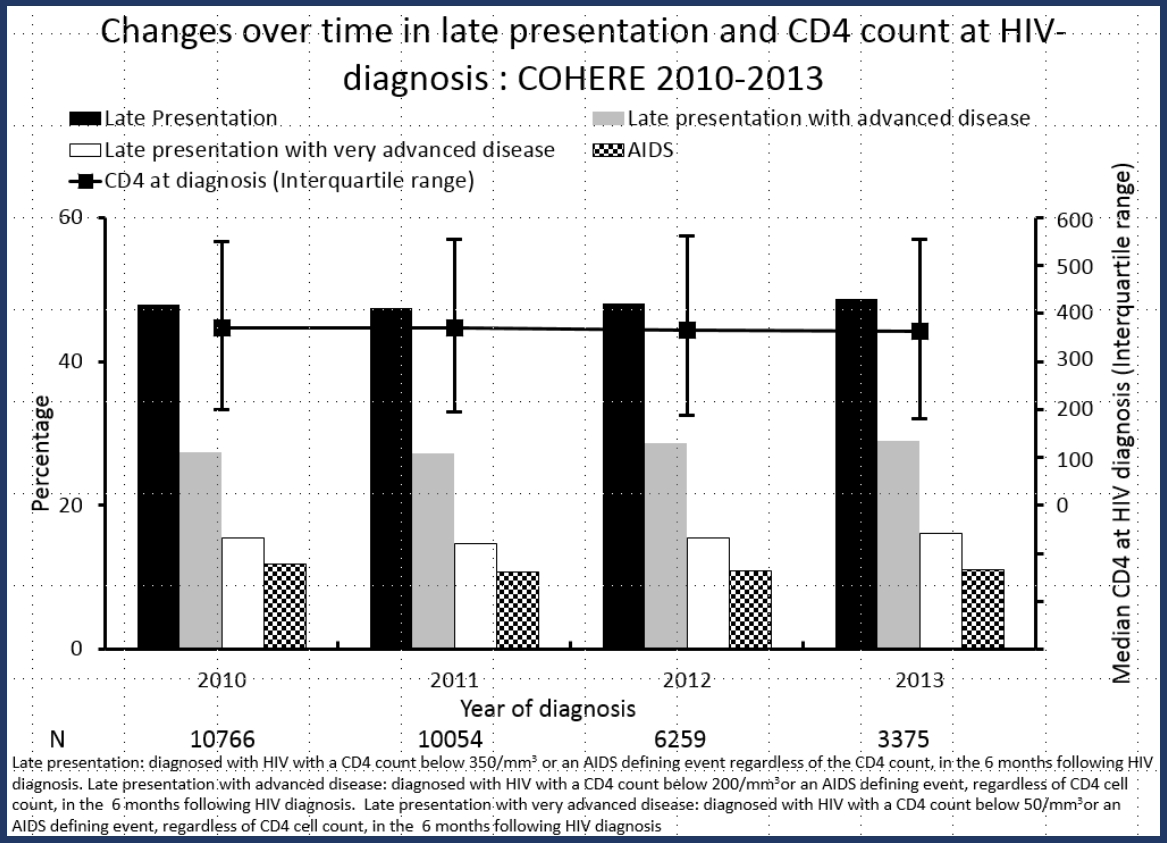
MSM in Central and Northern Europe
Male and female heterosexuals in Central and Northern Europe

LP increasing in

Male IDUs from Southern Europe
Male and Female IDUs from Eastern Europe
Female heterosexuals Southern Europe

Mocroft et al, 2013

COHERE : 2010-2013



47.5% were LP in 2010, compared to 48.7% in 2013 or later. After adjustment, the proportion of people with LP, advanced disease, very advanced disease, or AIDS did not change significantly over time (all p>0.05).

LP decreasing in

Northern Europe
aOR 0.89 (0.85 – 0.94)

LP increasing in

male and female IDUs
aOR 1.16 (1.02 – 1.32)

Mocroft et al, 2015

Strengths and weaknesses of cohort approach

Strengths

- Access to data from large number of countries
- Data from countries without national registries
- Access to complete data on ART-coverage
- Standardized data collection allows direct comparison between countries
- Possibility of comparing temporal trends
- Outcome data

Weaknesses

- COHERE not necessarily representative of all HIV+ in the whole country
- Maybe more or less complete than surveillance data

Where are the gaps in knowledge?

- Data from Eastern European countries poorly represented in Cohort studies or surveillance data
- Given the excess morbidity and mortality seen in LP, especially in the first 12 months following HIV diagnosis, the burden of clinical events potentially attributable to LP
- The representativeness of cohorts compared to surveillance data
  - Can be assessed using ECDC TESSy data as 'gold standard' representing number of persons diagnosed with HIV and using stabilised weights[1]

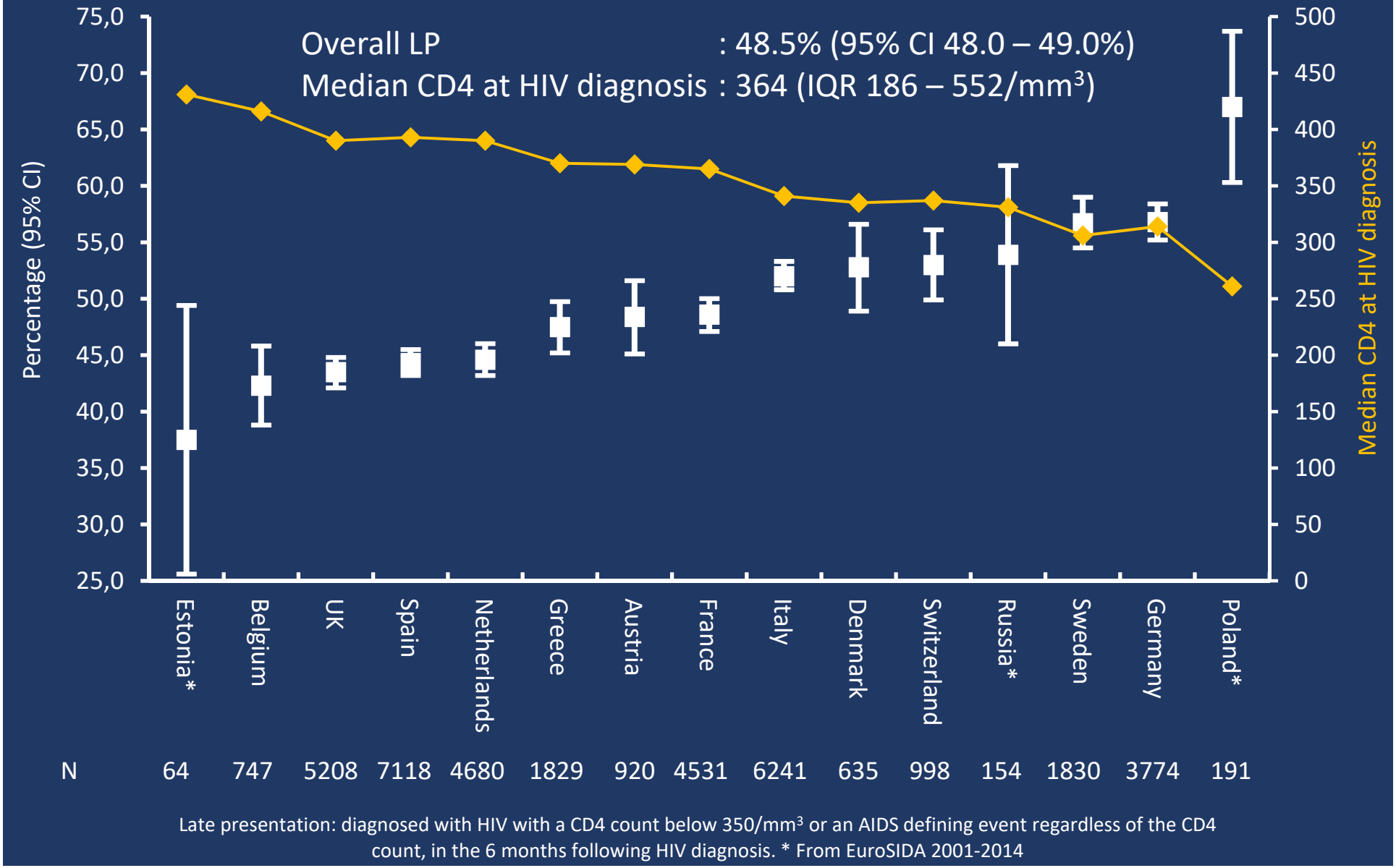
[1]Vourli et al, The value of the weights are interpreted as the copies of himself/herself cohort participants should contribute to produce a population representative of the corresponding group of diagnosed individuals that have the same gender, mode of infection and age at diagnosis. A weight < 1 indicates that person is under represented in those cohort compared to TESSy data and >1 over represented

Extending previous work of COHERE with additional EuroSIDA and TESSy data

- Data were combined from COHERE (2010-2014) and Central Eastern/Eastern European countries from EuroSIDA[1] (2001-2014) with > 50 participants
- Estimates of number of new HIV diagnoses 2010-2014 from whole region were obtained from ECDC[2]
- Observed rates of LP from cohort applied to the total population for each country[3] with 95% CI used to provide an upper/lower bound for LP
- The clinical event rate[4] in COHERE/EuroSIDA in the first 12 months after HIV diagnosis in each country was calculated for those with/without LP and applied to the country specific population diagnosed with HIV from ECDC to estimate number of deaths attributable to LP within each country

[1]where HIV-1 test was within 12 months of enrolment to EuroSIDA. [2] http://ecdc.europa.eu/en/healthtopics/aids/surveillance-reports/Pages/surveillance-reports.aspx. [3]There was no evidence of a change over time in LP in either COHERE 2010-2014 or EuroSIDA 2001-2014. [4]New AIDS defining event occurring > 30 days after HIV diagnosis or death

Late presentation by country of care in COHERE / EuroSIDA



Late presentation: diagnosed with HIV with a CD4 count below 350/mm³ or an AIDS defining event regardless of the CD4 count, in the 6 months following HIV diagnosis. * From EuroSIDA 2001-2014

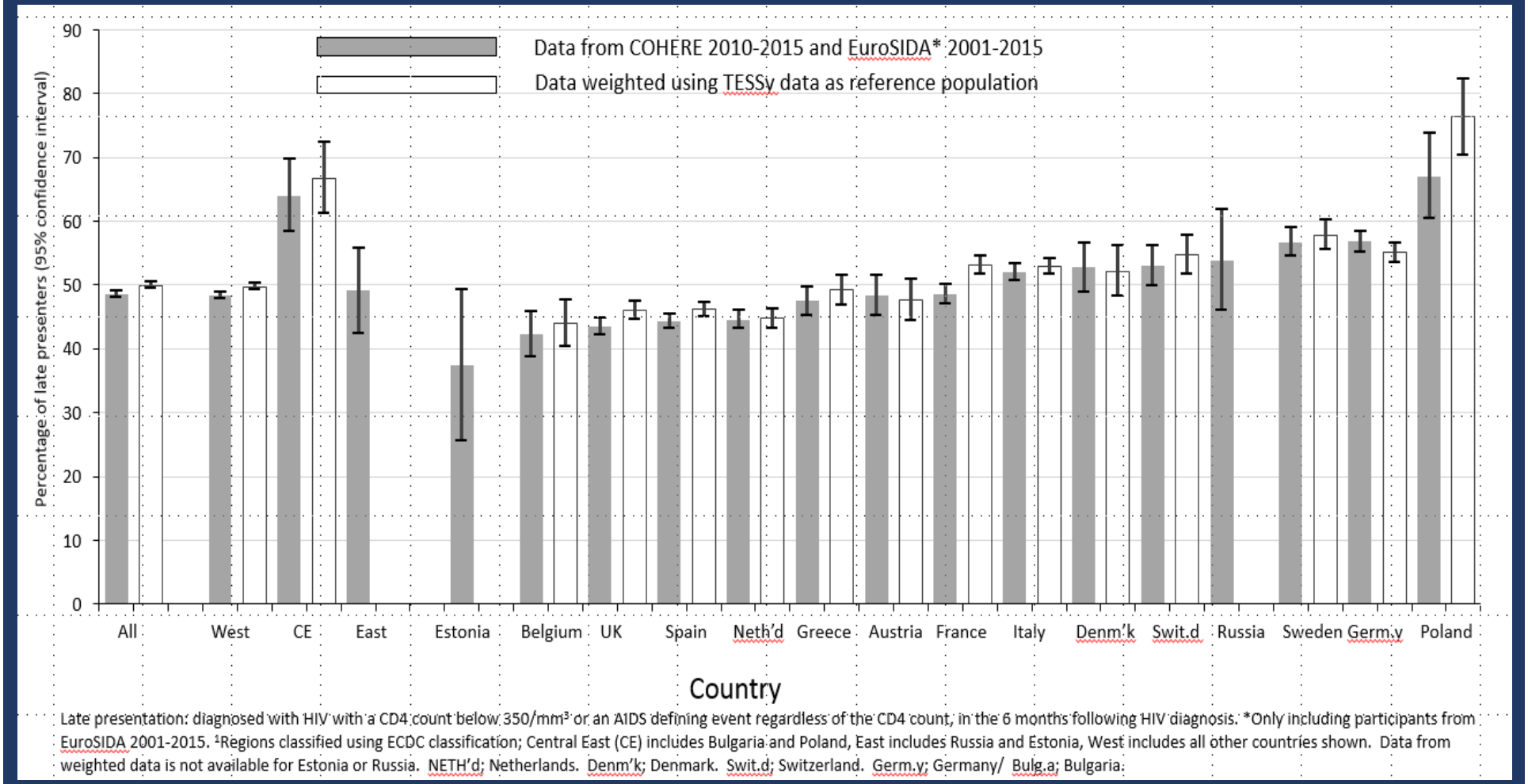
Extending previous work of COHERE with additional EuroSIDA and TESSy data

Extending to incorporate TESSy data

- Cohorts participating in COHERE or persons in EuroSIDA likely not generalisable to all those diagnosed with HIV
- Use country specific estimates from the TESSy data (where available[1]) provided by the ECDC to weight estimates of LP and clinical event rates to better reflect the complete population with HIV in each country
- Compared the proportion of our study population with key characteristics (gender, HIV exposure group, and age) to that reported to ECDC and assigned weights to either increase or decrease different demographic groups in our study[2]

[1]Data not available for Russia or Estonia,. [2] unpublished ECDC report, Vourli and Touloumi

Proportion of LP in COHERE/EuroSIDA and using ECDC as a reference population



Late presentation: diagnosed with HIV with a CD4 count below 350/mm³ or an AIDS defining event regardless of the CD4 count, in the 6 months following HIV diagnosis. *Only including participants from EuroSIDA 2001-2015. [1]Regions classified using ECDC classification; Central East (CE) includes Bulgaria and Poland, East includes Russia and Estonia, West includes all other countries shown. Data from weighted data is not available for Estonia or Russia. NETH'd; Netherlands. Denm'k; Denmark. Swit.d; Switzerland. Germ.y; Germany/ Bulg.a; Bulgaria.

Burden of LP and clinical events in the first 12 months after HIV diagnosis in Europe 2010-2014

		West	Central East	East
N HIV+ 2010-2014[1]		134250	18306	497603
LP; % (95% CI)	EuroSIDA/COHERE	48.4 (47.9 – 48.9)	64.0 (58.4 – 69.7)	49.1 (42.4 – 55.7)
	With TESSy weights	49.8 (49.4 – 50.4)	66.7 (61.2 – 72.3)	n/a
Estimated N LP (lower – upper bound)	EuroSIDA/COHERE	64,941 (64,271 – 65,611)	11,721 (10,688 – 12,754)	244,236 (211,214 – 277,259)
	With TESSy weights	66,834 (66,163 – 67,504)	12,216 (11,202 – 13,230)	n/a
Clinical event rate/100 PYFU in first 12 months following HIV diagnosis In EuroSIDA/COHERE	Non-LP (95% CI)	0.43 (0.33 – 0.54)	0 (0 – 3.73)	0 (0 – 3.40)
	LP (95% CI)	5.15 (4.79 – 5.52)	6.38 (3.19 - 11.42)	3.89 (1.06 – 9.96)
Excess N events (lower – upper bound)	EuroSIDA/COHERE	2,407 (2,275 – 2,539)	710 (355 – 1,038)	8,933 (2,434 – 14,771)
	With TESSy weights	2,491 (2,352 – 2,630)	740 (370 – 1,109)	n/a

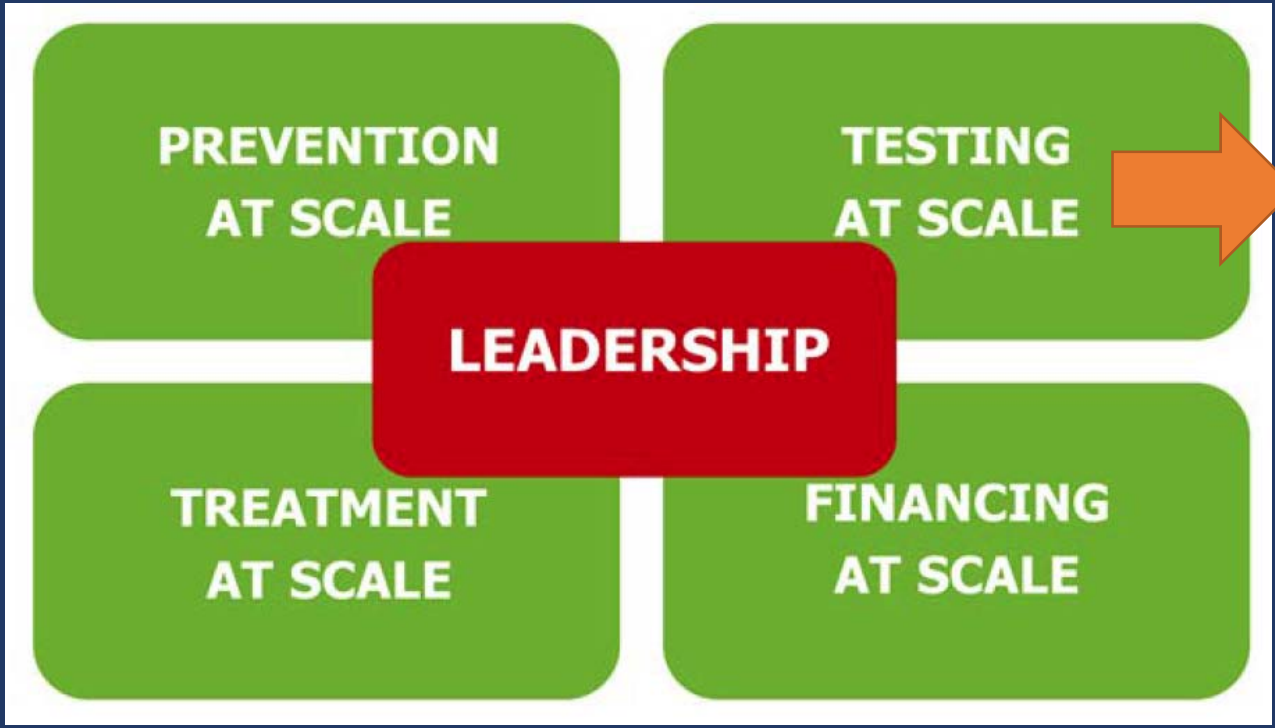
Regions were classified using ECDC classification; Central East includes Bulgaria and Poland, East includes Russia and Estonia, West includes all other countries. [1]From ECDC Surveillance data. n/a could not be estimated in Eastern Europe due to small numbers in COHERE/EuroSIDA and/or data not available in ECDC TESSy data

Perspectives

- Despite using 2 large cohorts, data only available for 3 countries from outside Western Europe
- Cohort data extrapolated to whole region
- Efforts to include more persons from Central Eastern or Eastern Europe important in both cohorts and surveillance data
- Remains important to explore data from the Eastern region of Europe, where the burden from HIV and late presentation is highest
- All estimates of LP and burden of clinical disease were increased after taking country representativeness into account
- First step to quantifying public health burden from LP

How to get more people tested for HIV and into care, reducing LP?

Essential priorities for action[1]



- address low rates of HIV testing/high rates of LP in key populations
- increase uptake of HIV testing among key populations
- Promote earlier diagnosis

[1]ECDC Special report. From Dublin to Rome: ten years of responding to HIV in Europe and Central Asia. Summary report

How are we doing?

Evaluation of impact of ECDC guidance on HIV testing[1]

- ECDC 2010 HIV testing guidelines widely referenced and used to develop policies, guidelines and/or programmes/strategies in the EU/EEA
- Guidelines have contributed to changes in HIV testing strategies across EU/EEA countries
- Reached a wider audience than intended and used for advocacy

Table 20. Topics to include in an updated ECDC testing guidance

Testing approaches
New technologies and innovative testing approaches (e.g. IC guided testing, community testing, self-testing/sampling)
Diversification and complementarity of testing approaches
Economic appraisal elements
Testing approaches for high risk groups and other vulnerable groups (e.g. minorities, higher risk MSM, PrEP users)
Diagnostic window and testing strategies
Frequency of testing
Comprehensive testing approaches (e.g. STI, HBV, HCV)
Partner notification
Regulatory issues
Testing among youth (under 18 years)
Confidentiality and anonymity of testing
De-medicalisation of testing and task-shifting
Monitoring and evaluation
Monitoring and evaluation of HIV testing interventions

Table from ECDC Technical Report. HIV testing in Europe. Evaluation of the impact of the ECDC guidance on HIV testing: increasing uptake and effectiveness in the European Union

Conclusions

- Remains a significant burden of LP across Europe, with an excess morbidity and mortality for the individual, as well as the risk of onward HIV transmission
- Greatest burden in Eastern Europe
- Substantial efforts from different stakeholders to increase testing (and reduce LP)
  - Indicator disease guided testing
  - More testing
  - Increasing access to testing
  - Community based approach to testing
  - Targeted testing
- Continued monitoring, more data, increased surveillance to determine best ways of increasing testing and how this translates, over time, to reducing LP

Acknowledgements

- The entire EuroSIDA study group; details at http://www.cphiv.dk/Studies/EuroSIDA/Study-group
- The Late Presenters Working Group in COHERE and the COHERE study, details at http://www.cphiv.dk/cohere_org/
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- Georgia Vourli and Giota Touloumi, University of Athens