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Estimating the country-specific burden of late presentation to HIV care across Europe between 2010-2014

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Background

- Late presentation of HIV (LP) is associated with poorer health outcomes, increased healthcare costs and higher risk of onwards HIV-transmission [1–3].
- Despite increased attention and commitment to increase HIV testing, LP remains a significant problem across Europe[4].

Aims

- Linking cohort- and surveillance data, we aimed to
  - estimate the country-specific burden of LP in Europe *and*
  - assess the number of new clinical events within 1 year of HIV-diagnosis attributable to LP.

Methods

Participants and definitions

- People aged >16 years and diagnosed HIV-positive ≥ 1st January 2001 from EuroSIDA (Russia, Estonia, Poland) and ≥ 1st January 2010 from COHERE (all other countries) were included.
- People were included if they had ≥1 CD4 cell count within 6 months of diagnosis, and excluded if date of HIV diagnosis was missing or there was evidence of an earlier HIV diagnosis >1 month before first clinic visit
- A CD4 count <350/mm^3 at diagnosis or an AIDS-event within 6 months of HIV-diagnosis defined LP [4,5].
- A new AIDS-event was defined as an AIDS-event ≥1 month after HIV-diagnosis *or* a new AIDS-event subsequent to the AIDS-event used to classify a person as LP.
- Cohort-data from countries with >50 participants were categorised into regions according to ECDC classification[6]. [PANEL 1]

PANEL 1: Countries included in region estimates (as per ECDC classification)
West: Belgium, UK, Spain, Netherlands, Greece, Austria, France, Italy, Denmark, Switzerland, Sweden, Germany. **Central †:** Poland. Bulgaria included in regional estimates only. **East †:** Estonia, Russia. †Based on EuroSIDA data only.

Statistical analyses

- Assuming that the country-specific percentages of LP and the event rates observed in COHERE/EuroSIDA applied to all new HIV-diagnoses reported to ECDC [6], we estimated:
  - the number of LP in the whole population *and*
  - clinical events (AIDS/death) in the first year following HIV-diagnosis, attributable to LP (difference between LP and non-LP).
- Estimates from ECDC TESSy data were used to weight[7] our estimates of LP and clinical events to better reflect demographics (age, sex, HIV-transmission group) of the whole HIV population in each country/region.

Results

Baseline characteristics of participants

- We included 39,007 people from West (n=38,511 [98.7%]), Central (n=191 [0.5%]) and Eastern Europe (n=305 [0.8%]).
- Participants were predominantly MSM (51.4%), originated from Europe (65.7%), median age was 37 years (IQR 29-45), and median CD4 at diagnosis was 364 cells/mm^3 (IQR 186-552).

						Non-late presenters	Late presenters	Difference LP versus non-LP
Country	Percentage LP observed in COHERE/ EuroSIDA	Total number diagnosed HIV-positive 2010-2015§	Estimated number of LP in the whole country	Mean follow-up in COHERE/EuroSIDA in the first year following HIV-diagnosis	Number included from COHERE/ EuroSIDA	1-year incidence of clinical disease observed in COHERE/EuroSIDA*	1-year incidence of clinical disease observed in COHERE/EuroSIDA*	Ratio of 1-year incidence of clinical disease between LP and non-LP	Estimated excess clinical events attributable to LP (difference LP – non-LP)**
	% (95%CI)	n	n (lower-upper bound)	mean PYFU	n	Rate/100 PYFU (95%CI)	Rate/100 PYFU (95%CI)	Incidence rate ratio (95%CI)	n (lower-upper bound)
Estonia†	37.5 (25.6-49.4)	1669	626 (427-824)	0.95	64	0.00 (0.00-9.32)	4.37 (0.11-24.37)	n/a	26 (1-53)
Belgium	42.3 (38.8-45.8)	5754	2434 (2230-2638)	0.84	747	0.28 (0.01-1.54)	7.94 (4.54-11.33)	28.77 (3.87-213.88)	155 (93-189)
UK	43.5 (42.1-44.8)	31418	13664 (13241-14087)	0.75	5208	0.54 (0.27-0.97)	3.76 (2.84-4.69)	6.95 (3.67-13.19)	314 (255-351)
Spain	44.3 (43.2-45.5)	15520	6881 (6702-7060)	0.77	7118	0.19 (0.07-0.42)	5.29 (4.38-6.20)	27.32 (12.05-61.94)	267 (227-301)
Netherlands	44.6 (43.2-46.0)	4770	2127 (2059-2196)	0.84	4680	0.54 (0.28-0.95)	6.98 (5.74-8.22)	12.81 (7.08-23.18)	113 (96-126)
Greece	47.5 (45.2-49.7)	3948	1874 (1783-1964)	0.80	1829	0.50 (0.14-1.28)	4.30 (2.76-5.84)	8.62 (3.04-24.47)	56 (39-66)
Austria	48.4 (45.1-51.6)	1368	661 (617-706)	0.89	920	0.47 (0.06-1.70)	6.33 (3.85-8.81)	13.46 (3.19-56.82)	34 (22-41)
France	48.6 (47.1-50.0)	31608	15347 (15172-15551)	0.68	4531	0.25 (0.07-0.65)	5.98 (4.74-7.22)	23.66 8.69-64.42)	596 (487-682)
Italy	52.0 (50.8-53.3)	17546	9126 (8908-9343)	0.80	6241	0.50 (0.26-0.88)	4.48 (3.67-5.30)	8.88 (4.90-16.09)	293 (250-327)
Denmark	52.8 (48.9-56.6)	1231	649 (602-697)	0.82	635	0.79 (0.10-2.85)	6.18 (3.60-9.89)	7.82 (1.81-33.85)	29 (19-39)
Switzerland	53.0 (49.9-56.1)	2903	1539 (1449-1629)	0.83	998	0.53 (0.06-1.93)	2.50 (1.25-4.46)	4.67 (1.03-21.06)	26 (15-35)
Russia†	53.9 (46.0-61.8)	370586	199731 (170470-229022)	0.96	154	0.00 (0.00-5.35)	3.75 (0.77-10.97)	n/a	7196 (1485-12256)
Sweden	56.7 (54.5-59.0)	1919	1088 (1046-1132)	0.82	1830	0.79 (0.26-1.85)	3.27 (2.06-4.48)	4.13 (1.60-10.71)	24 (17-27)
Germany	56.8 (55.2-58.4)	15546	8832 (8586-9077)	0.82	3774	0.44 (0.16-0.96)	5.86 (4.73-6.99)	13.26 (5.82-30.19)	400 (333-453)
Poland†	67.0 (60.3-73.7)	5128	3437 (3092-3779)	0.97	191	0.00 (0.00-5.91)	5.65 (2.27-11.63)	n/a	188 (76-291)

Table 1: Estimated burden of late presentation and clinical events in the first year after HIV-diagnosis by country. §As reported by ECDC. *****Estimated number of events among LP or non-LP was estimated by applying event rates from COHERE/EuroSIDA to the total number diagnosed HIV-positive in the whole country (incidence rate (PYFU) x mean follow-up (PYFU) x number of LP or non-LP in the whole country). ******Excess events were estimated as clinical events in LP compared to non-LP. CI = confidence interval. PYFU = person years of follow-up. LP = late presentation.

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TABLE 1: Country-specific burden of LP and excess clinical events

- Almost half of the participants in COHERE/EuroSIDA (48.5%; 95% CI 48.0–49.0) presented late, but the proportion of LP varied widely by country from 37.5% (Estonia) to 67.0% (Poland).
- Within EuroSIDA/COHERE, LP had a 12-fold (incidence rate ratio 12.09 [95% CI 9.42-15.52]) higher incidence of clinical events in the first year after diagnosis, compared to non-LP, but between-country variation was substantial.
- Estimates of excess clinical events attributable to LP varied accordingly, when extrapolated to the whole HIV-positive population.

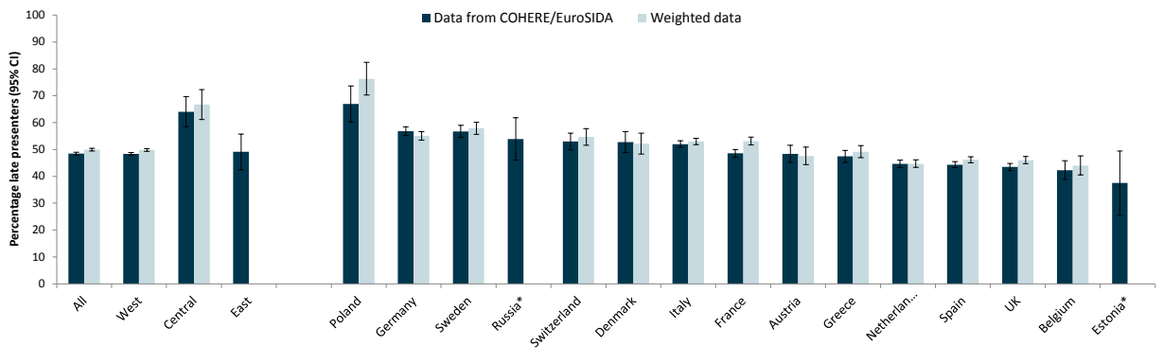

Figure 1: Weighted estimates of LP using TESSy data as reference population. Demographic characteristics of COHERE/EuroSIDA participants (age, sex, HIV transmission group) were increased or decreased to better reflect the population of people diagnosed HIV positive in the whole country. * Could not calculate weighted estimated due to small numbers in cohorts and/or data not available in ECDC TESSy data

FIGURE 1: Weighted estimates of LP

- We assigned weights to each cohort participant to reproduce the demographic characteristics of the TESSy reference population in each country. Overall females, people infected by IDU and people aged >50 years were underrepresented in COHERE/EuroSIDA.
- When applying weights to adjust for country representativeness, country-specific estimates of LP tended to increase.
- The effect of applying weights differed by country and region.

		West	Central	East
Total diagnosed HIV-positive 2010-2015*		134250	18306	497603
Clinical event rate/100 PYFU**	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)
Using COHERE/EuroSIDA data only	LP (95% CI)	48.4 (47.9 – 48.9)	64.0 (58.4 – 69.7)	49.1 (42.4 – 55.7)
	Estimated number LP (lower-upper bound)	64941 (64271 – 65611)	11721 (10688 – 12754)	244236 (211214 – 277259)
	Estimated excess event rate (lower-upper bound)	2407 (2275 – 2539)	710 (355 – 1038)	8933 (2434 – 14771)
Using COHERE/EuroSIDA data with weightings from TESSy data	LP (95% CI)	49.8 (49.4 – 50.4)	66.7 (61.2 – 72.3)	n/a†
	Estimated number LP (lower-upper bound)	66834 (66163 – 67504)	12216 (11202 – 13230)	n/a†
	Estimated excess event rate (lower-upper bound)	2491 (2352 – 2630)	740 (370 – 1109)	n/a†

Table 2: Regional burden of LP and excess clinical events attributable to LP. Region-specific percentages observed in COHERE/EuroSIDA were applied to the number diagnosed HIV-positive in the whole region as reported by ECDC and numbers are not summations of those estimated for each country. *As reported by ECDC. **Using region-specific event rate observed in COHERE/EuroSIDA. † Could not be estimated due to small numbers in cohorts and/or data not available in ECDC TESSy data.

TABLE 2: Regional burden of LP and excess clinical events

- The estimated burden of LP was highest in the Eastern European region (n =244,236 [lower-upper bound 211,214-277,259]).
- Assuming that LP were diagnosed and treated similarly to non-LP, an estimated 2,407 (2,275-2,539), 710 (355-1,038) and 8,933 (2,434-14,771) AIDS/deaths could be potentially avoided in West, Central and Eastern Europe, respectively.

Conclusions

- Across regions of Europe, we estimated that more than 320,000 LP and more than 12,050 new AIDS/deaths could potentially have been avoided through earlier testing and treatment over a five year period 2010-2015
- Patterns of LP varied across countries and regions, and the highest estimated burden of LP was in Eastern Europe.
- We were able to present country-specific estimates of the burden of LP from 15 countries across Europe, but despite using two large cohorts, data on LP were only available for 3 countries outside Western Europe.
- There is a sparsity of data on status at HIV presentation in Eastern Europe and more data are urgently needed in this important area.
- Improvements in current testing strategies should translate into lower numbers of LP and potentially avoidable clinical events.

References: [1]Fleishman et al, Med care 2010, [2]Lanoy et al Antivir Ther 2007, [3]Quinn N Engl J Med 2000, [4]Mocroft et al Eurosurveillance 2015, [5]Antinori et al HIV Med 2011, [6]https://ecdc.europa.eu/en/infectious-diseases-public-health/hiv-infection-and-aids/surveillance-and-disease-data/annual [7]Vourli et al HepHIV 2017 PS3/01

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