

The HIV continuum of care in European Union countries in 2013: data and challenges

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40 word summary: Definitions for a four-stage continuum of HIV care were standardised and applied to HIV surveillance and national cohort data in 11 European Union countries. These countries are nearing the UNAIDS 90-90-90 target, although reducing the proportion undiagnosed remains challenging.

Abstract

Background: UNAIDS has set a 90-90-90 target to curb the HIV epidemic by 2020, but methods used to assess whether countries have reached this target are not standardised, hindering comparisons.

Methods: Through a collaboration formed by the European Centre for Disease Prevention and Control (ECDC) with European HIV cohorts and surveillance agencies, we constructed a standardised, four-stage continuum of HIV care for 11 European Union (EU) countries for 2013. Stages were defined as: 1) number of people living with HIV (PLHIV) in the country by end of 2013; 2) proportion of stage 1 ever diagnosed; 3) proportion of stage 2 ever initiated ART; and 4) proportion of stage 3 who became virally-suppressed (≤ 200 copies/mL). Case surveillance data were used primarily to derive stages 1 (using back-calculation models) and 2, and cohort data for stages 3 and 4.

Results: In 2013, 674,500 people in the 11 countries were estimated to be living with HIV, ranging from 5,500 to 153,400 in each country. Overall HIV prevalence was 0.22% (range 0.09%-0.36%). Overall proportions, of each previous stage, were 84% diagnosed, 84% on ART, and 85% virally-suppressed (60% of PLHIV). Two countries achieved $\geq 90\%$ for all stages, and over half had reached $\geq 90\%$ for at least one stage.

Conclusions: EU countries are nearing the 90-90-90 target. Reducing the proportion undiagnosed remains the greatest barrier to achieving this target, suggesting further efforts are needed to improve HIV testing rates. Standardising methods to derive comparable continuums of care remains a challenge.

Introduction

The HIV continuum of care is a public health monitoring tool to conceptualise the care pathway that people living with HIV (PLHIV) progress through: diagnosis of HIV infection, linkage to and retention in HIV care, initiation of and adherence to antiretroviral therapy (ART), and suppression of viraemia [1]. This concept has increasingly been adopted to evaluate HIV programme performance. Four stages of the HIV continuum can also be used to monitor the UNAIDS '90-90-90' target (90% of PLHIV diagnosed, 90% of those diagnosed on ART, 90% of those on treatment virally-suppressed), which aims to curb the HIV epidemic by 2020 [2].

However, challenges with data quality, appropriate data sources and the absence of standardised definitions have hampered comparisons across countries. An initiative led by the European Centre for Disease Prevention and Control (ECDC) in 2014 to monitor the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia identified that many European countries lacked data for some, or all, continuum stages [3, 4]. This study, as well as a recent systematic review, concluded that, although many continuum estimates are being published, their comparability is limited by differences in data sources and methods used [3, 5].

Collaborations between public health surveillance and national clinical cohorts, where the latter exist, could help address gaps in data availability. The key advantage of using longitudinal clinical cohort data lies in their potential to enhance the internal consistency of care continuums by using the same group of individuals, defined as 'denominator-denominator linkage' [6], to analyse multiple stages. While the ideal continuum will maximise the number of stages with denominator-denominator linkage, additional data from HIV case surveillance systems are necessarily required to provide information on the diagnosed population, and as modelling inputs to estimate the total number of PLHIV.

We, therefore, aimed to construct a four-stage standardised continuum of HIV care for eleven European countries using HIV case surveillance and national clinical cohort data. We assess the utility of using cohort data and describe the challenges encountered.

Methods

Selection of countries and cohorts

HIV cohorts were drawn from EuroCoord (www.EuroCoord.net), a European Union (EU)-funded Network of Excellence that includes most European HIV cohorts [7, 8]. Only cohorts considered national, i.e. multi-centre and not restricted by risk group, were included. HIV cohorts and surveillance agencies in Austria, Belgium, Denmark, France, Germany, Greece, Italy, the Netherlands, Spain, Sweden and the United Kingdom (UK) took part (Supplement 1).

Standardised definitions and data sources

Continuums of HIV care were constructed for each country using national-level HIV case surveillance data and HIV clinical cohort data. Four stages of the continuum of HIV care were estimated for 2013, the most recent year of data available (Table 1).

Stage 1: Number of PLHIV

Stage 1 was defined as the estimated total number of PLHIV in each country by the end of 2013. Those who had died or out-migrated were excluded where possible. Several countries had no out-migration data or could only make assumptions about the proportion who out-migrated (Supplement 2).

Where feasible, back-calculation models that estimate HIV incidence and the undiagnosed fraction from routinely collected HIV case surveillance data were used. For consistency, PLHIV estimates

generated using a back-calculation modelling tool developed by the ECDC [9] were prioritised. Five countries used the ECDC Modelling Tool 'incidence method' [10]. If this was not appropriate, e.g. due to incomplete case surveillance data, similar back-calculation methods tailored to countries' own data were used (four countries), either to estimate the total number of PLHIV directly, or to estimate the undiagnosed population, combined with surveillance or survey-based estimates of the diagnosed population [11-13]. Otherwise, alternative approaches included multi-parameter evidence synthesis incorporating case surveillance and prevalence survey data (one country) [14], or surveillance/survey-based estimates (one country) (Supplement 2).

Where feasible, 95% confidence intervals were calculated using bootstrapping techniques. Adult prevalence was calculated using Eurostat population denominators for 2013 [15], excluding children <15 years.

Stage 2: Proportion diagnosed

Stage 2 was defined as the proportion of all PLHIV, estimated as above, ever diagnosed, excluding deaths and out-migrations (Supplement 2).

Ideally, the diagnosed population was derived from cumulative HIV case surveillance data to the end of 2013 (three countries). Where this was not feasible, e.g. surveillance systems that started recently or changed over time in geographic coverage, alternative approaches were used. These included: estimating the diagnosed fraction from the ECDC HIV Modelling Tool (two countries); combining estimates of the diagnosed population in care and not in care by triangulating data sources (one country) [16]; use of national cohort data, i.e. the number of patients diagnosed and in care, where linkage to care is expected to be extremely high (three countries); statistical modelling using recent HIV case surveillance data to estimate new HIV diagnoses for all years (one country); or infectious disease clinic survey-based estimates (one country) [17].

A range of uncertainty was calculated by dividing the number diagnosed by the lower/upper confidence limits for the number of PLHIV, to reflect the uncertainty in estimating stage 1.

Stage 3: Proportion on ART

Stage 3 was defined as the proportion of those diagnosed, as above, who have ever initiated ART, regardless of prevailing treatment guidelines, anti-retroviral regimens or number of drugs, treatment interruptions or discontinuations. This definition was applied to country-specific cohort datasets. Patients known to have died or out-migrated by the end of 2013 were excluded, as were patients with unknown year of diagnosis if it was unclear they were diagnosed before the end of 2013. Those with unknown ART status or unknown year of ART initiation were assumed to be untreated by the end of 2013.

Minimum and maximum estimates were calculated based on assumptions about patients lost to follow-up (LTFU) to the cohort and whether they were likely to be receiving care in non-cohort centres, or lost to care entirely and, therefore, likely not on ART and unsuppressed. For the maximum estimate, patients LTFU were excluded, and for the minimum estimate they were included and assumed to be untreated, unless their records indicated ART initiation. LTFU was defined as no clinic interaction 01/07/2012 - 31/12/2013 and, therefore, no ART or viral load (VL) data. Clinic interaction was based on any laboratory measurement, drug start date, or other evidence of an HIV clinic visit. The preferred estimate was the mid-point between the minimum and maximum estimate.

Stage 4: Proportion virally-suppressed

Stage 4 was defined as the proportion of those ever on ART, as above, with a VL measurement ≤ 200 HIV RNA copies/mL, or below the assay detection limit, at their last visit 01/07/12 - 31/12/13. This VL

threshold was chosen to allow for improvements over time in the lower limit of detection of the assay. Cohort data were used to calculate minimum and maximum estimates, and the mid-point between the two. Patients LTFU (i.e. no recent VL measurements) were excluded for the maximum estimate and included for the minimum estimate (assumed to be unsuppressed). Patients with no VL measurements 01/07/12 - 31/12/13, but classified as engaged in care based on other laboratory measurements, drug start dates or clinic visits, were assumed to be adherent to ART and suppressed.

Construction of combined regional estimates

Country-level results were compiled and combined, and weighted averages calculated for each stage to construct a summary continuum for the region based on all 11 countries (Supplement 3). Percentages were calculated using the previous stage as the denominator, as well as using a single denominator of PLHIV.

Ethics approvals

All participating clinical cohorts obtained ethics approvals from local ethics committees, national data agencies or institutional review boards. Informed consent of patients was sought in accordance with national regulations. Surveillance data are collected under the authority of the public health agencies that abide with strict confidentiality and privacy data protection laws.

Results

Continuum of HIV care estimates by country

National estimates for the total number of PLHIV by the end of 2013 ranged from 5,500 in Denmark to 153,400 in France, corresponding to a prevalence of 0.12% and 0.29%, respectively (Table 2). Prevalence was lowest in Austria and Sweden (both 0.09%), and highest in Spain (0.36%).

There was variation across the countries in the proportions estimated for each stage. In 2013, of all PLHIV, the proportions diagnosed ranged from 78% in Greece to 91% in Denmark, with two other countries (Italy and Sweden) also reaching $\geq 90\%$, and Austria just below this threshold at 88%. Of those diagnosed, the proportions on ART range from 76% in Spain to 96% in Belgium. Five other countries (Austria, Denmark, France, the Netherlands and Sweden) achieved $\geq 90\%$ on ART. There was less variation between countries in the proportions virally-suppressed. Of those on ART, the proportions virally-suppressed were $\geq 81\%$ in all countries, with the highest proportion estimated at 93% in both Denmark and Sweden. France and the Netherlands also achieved $\geq 90\%$ virally-suppressed. Only two countries, Denmark and Sweden, achieved $\geq 90\%$ for each of the three continuum stages using our standardised definitions. Of the total PLHIV, Denmark and Sweden reached $\geq 73\%$ virally-suppressed, with France and the Netherlands nearing this target, at 72% and 70% respectively.

Combined estimates for the European region (11 EU countries)

Overall, 674,500 people were estimated to be living with HIV in the eleven EU countries by the end of 2013 (prevalence 0.22%). Overall, the proportions at each stage were: 84% of PLHIV diagnosed (79%-90%); 84% of those diagnosed on ART (81%-87%); and 85% of those on ART with viral suppression (76%-91%) (Figure 1). Of the total PLHIV, 60% were estimated to be virally-suppressed. The greatest drop between successive stages of the continuum was observed between the number of PLHIV and the number diagnosed with 16% of undiagnosed individuals falling out of the continuum.

Discussion

Main findings

The eleven EU countries included in this study, constituting roughly three quarters of the EU population and three quarters of HIV diagnoses in the EU in 2005-2014 [18], are nearing the UNAIDS 90-90-90 target, well ahead of 2020. Although few countries achieved $\geq 90\%$ for each stage, based on our standardised definitions, over half had reached, or were close to, the target for at least one stage. Further improvements are also expected to have occurred since 2013, following recent changes in treatment guidelines [19]. However, reducing the undiagnosed proportion remains the biggest barrier to achieving this goal, with the largest drop between successive stages of the continuum observed at this first stage. To our knowledge, this is the first attempt to standardise definitions and derive continuum of care estimates for the EU. Our estimates may differ from previously published results and official national statistics due to differences in data sources, definitions and time-periods, although these differences are relatively minor [20-25].

UNAIDS estimates for the number of PLHIV in 2013, derived using Spectrum/EPP software with HIV prevalence data and most suitable for countries with generalised epidemics [26], were only reported for four of the countries in our study [27]. Our estimates, based primarily on back-calculation modelling and routinely-collected HIV case surveillance data, strengthen data availability for this stage and provide valuable information for HIV programme monitoring and planning. We observed the highest HIV burden in France, Spain, Italy and the UK, accounting for the majority of PLHIV in this region, concurring with earlier reports [27].

Losses from the continuum occurred between all stages, but were greatest between stages 1 and 2. Overall, 16% of PLHIV were undiagnosed, indicating further efforts are required to improve HIV testing rates, particularly among most at-risk populations. Late presentation remains a major concern in Europe, with around half of new diagnoses presenting with $CD4 < 350$ cells/mm³ [18, 28]. A systematic review published in 2011 suggested that rapid testing and counselling in community settings, community-based peer counselling campaigns, and expanding opt-out testing policies may

be effective interventions to improve HIV testing rates in men who have sex with men in high-income countries [29]. Provision of rapid HIV tests in pharmacies [30], and provider-initiated HIV-testing in general practice or individuals presenting with indicator conditions [31, 32], may offer further opportunities to increase testing uptake. Widening legislation for and increasing access to self-testing and self-sampling are likely to increase testing, but must be coupled with channels for linkage to care [21].

The lowest proportions of diagnosed individuals on ART were estimated in Spain, Italy, Greece, and the UK. National treatment guidelines are likely to play a key role here. For example, in 2013, treatment guidelines in Greece, Spain and the UK recommended ART initiation in patients with CD4 counts of ≤ 350 cells/mm³. The proportion on ART is expected to improve once the recent changes in guidelines [19] are implemented. Lack of, or delayed, linkage to care following HIV diagnosis is a possible explanation. Although patients in high-income countries are usually linked to care within three months of diagnosis, delays among specific sub-groups have been reported [16, 33]. Failure to achieve viral suppression after starting ART may reflect poor adherence, treatment interruptions or discontinuations, or insufficient time to achieve suppression for those recently initiating ART [16].

Increasing awareness of the continuum of care, e.g. through national treatment and/or service delivery guidelines, and providing evidence-based recommendations to improve the testing and care environment, may also improve the care continuum [34].

Key challenges

These results must be interpreted in light of several key methodological challenges encountered. Use of the HIV Modelling Tool [9] facilitated the standardisation of estimates for PLHIV, but applying the same approach to countries with different HIV surveillance systems was not always possible due to insufficient historical case surveillance data availability in some countries. Triangulation of data

sources provides one possible solution, for example, summing estimates of the undiagnosed population with cohort or survey-based estimates of the diagnosed population in care/ not in care [12].

Difficulties capturing out-migration, or linking surveillance or cohort datasets to population migration and death registries were additional challenges. Misclassification of vital status or out-migration will potentially over-estimate the number still alive and living in a country. Few countries in our study had access to reliable out-migration data (Supplement 2), with linkage to population registries usually precluded by the lack of unique identifiers. Where possible, adjustments were made using estimated levels of out-migration. In the long-term, efforts to improve the recording of vital status and out-migration in surveillance databases, as well as linkage to registries via unique identifiers, are needed. In some cases, lack of reliable in-migration data also complicated modelling of HIV incidence and the separating of earlier infections from new infections occurring after arrival within the country.

Estimating proportions using cohorts that are not representative of the diagnosed population nationally may introduce bias, so efforts are required to understand and correct for this. The cohorts in our study were large, including national cohorts with near complete coverage of the diagnosed population, and were fairly representative (Supplement 1) [35]. Nevertheless, estimates from cohorts with low coverage should be interpreted with caution. Ideally, estimates derived using cohort data would be adjusted by calculating and applying weights based on the distribution of demographic variables in cohort and surveillance datasets [35].

Patients LTFU in cohort data present another challenge, namely the assumptions that are made about whether they are still in care, taking ART and virally-suppressed, or truly lost from care and unsuppressed. Assuming all have been lost from care entirely would underestimate retention in care

and the proportion suppressed, as suggested by a clinical audit in the UK [36]. Ideally cohorts would collect and update data on patients who transfer to other clinics, although this is challenging in practice. In the absence of reliable patient transfer data, plausible limits should be calculated based on varying assumptions, as we have done, with the true value likely to lie between these limits.

Strengths and limitations

Collaborations formed between cohort investigators and surveillance agencies facilitated the construction of HIV continuums from PLHIV to viral suppression. We attempted to standardise methods to enhance comparability between countries, and to generate summary estimates for the region. However, complete standardisation was not possible, given the different limitations in data availability and quality in each country, as well as inherent differences in cohort inclusion criteria. For example, the Italian and Spanish cohorts require participants to be ART-naïve at baseline (Supplement 1). Although the use of cohort data improved the internal consistency of the estimates, we were unable to link surveillance and cohort datasets in most countries to maximise internal consistency. For some countries we were unable to distinguish between those diagnosed and those linked to care, i.e. enrolled in a cohort, although linkage to care is expected to be very high.

Additionally, our cross-sectional definitions do not address the timeliness of reaching each stage, or time spent at each stage, for example time since starting ART [16]. Using a single VL measurement may also over-estimate durable viral suppression [37]. However, they provide a snapshot of the continuum in 2013 which is simple to interpret and communicate to policy-makers. Treatment discontinuations or interruptions were not accounted for, which may result in over-estimating the proportion 'on ART'. However, a sensitivity analysis conducted for a few countries, restricting the definition of 'on ART' to a record of ART between 01/07/12 and 30/12/13, made little difference to the overall proportions of PLHIV that were virally-suppressed.

Finally, our study omitted 17 EU countries, mainly from Eastern and Central Europe as national cohort data were lacking and, as such, estimates for the whole EU region may be lower than those presented here.

Conclusions

The 11 EU countries in our study are nearing the UNAIDS 90-90-90 target, with over half having achieved $\geq 90\%$ for one or more stage of the continuum. The main barrier to achieving this goal appears to be reducing the proportion undiagnosed. These data provide useful comparisons to governments and healthcare planners, but must be interpreted in context of the limitations and key challenges above, as well as cohort and country differences. Challenges remain in constructing and standardising the continuum of care for all stages. Enhancements to data sources and methods are required to derive accurate estimates for national-level continuums of care, to facilitate comparisons between countries and to generate regional and global estimates.

NOTES

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Figure 1. Continuum of HIV care in 11 EU countries[^] for 2013

[^] Austria, Belgium, Denmark, France, Germany, Greece, Italy, The Netherlands, Spain, Sweden and the United Kingdom

* Percentages out of the previous stage

**Percentages out of all PLHIV by end 2013

Weighted averages, accounting for the number of HIV-positive individuals at each stage in each country, were taken across all countries for each stage.

Table 1. Standardised definitions used to estimate the continuum of care

<i>Stage</i>	<i>Definition</i>	<i>Data source</i>	<i>Analysis and estimation approaches</i>
i) PLHIV	Number of people living with HIV (diagnosed and undiagnosed) in each country by end 2013	HIV case surveillance data if available, or cohort data otherwise	Back-calculation models to estimate HIV incidence and the undiagnosed fraction (ECDC HIV Modelling Tool [9], 5 countries ^a ; other models, 4 countries ^b), otherwise Multi-Parameter Evidence Synthesis (United Kingdom), or other surveillance/survey-based estimates (Sweden).
ii) Diagnosed	Proportion of (i) ever diagnosed	HIV case surveillance data if available, or cohort data otherwise	Cumulative number of diagnosed by end of 2013, excluding out-migrations and deaths before the end of 2013 if feasible (3 countries ^c using surveillance data, 3 countries ^d using national cohort data). Otherwise, the diagnosed population was estimated using: ECDC HIV Modelling Tool (Austria, Belgium), statistical modelling (Spain), combining estimates of the population in care/ not in care (France), or clinic-based surveys (Italy).
iii) ART	Proportion of (ii) who ever initiated ART (regardless of treatment guidelines, antiretroviral drug regimens or number of drugs, treatment interruptions or discontinuations)	Country-specific HIV cohorts	Descriptive statistics. Patients lost to follow-up to the cohort (ART/viral load status unknown) were excluded to give a high estimate, and included (assumed never on ART, where ART status unknown) in the low estimate. The preferred estimate was taken as the mid-point.
iv) Virally-suppressed	Proportion of (iii) who were virally-suppressed (≤ 200 copies/mL or below the level of detection of the assay) at last visit (01/07/12 - 31/12/13) ^e	Country-specific HIV cohorts	As above. Patients lost to follow-up to the cohort with no recent viral load measurements were assumed to be unsuppressed in the low estimate.

ECDC, European Centre for Disease Prevention and Control

^a Austria, Belgium, Denmark, Greece, the Netherlands

^b France, Germany, Italy, Spain

^c Germany, Greece, United Kingdom

^d Denmark, the Netherlands, Sweden

^e Six months of 2012 were included to allow for delays in updating cohort records.

Table 2. Estimates for four stages of the continuum of HIV care for 2013, by country

Country	i) PLHIV [95% CI]	HIV Prevalence ^a	ii) % Diagnosed [estimated range] ^b	iii) % Ever on ART [min, max estimate]	iv) % Suppressed [min, max estimate]	% Suppressed of all PLHIV
Austria	6500 [6300-6700] ^c	0.09%	88% [86%,91%]	90% [85%,94%]	84% [76%,91%]	66%
Belgium	18,000 [17,700-18,300]	0.19%	84% [83%,85%]	96% [96%,96%]	82% [77%,87%]	66%
Denmark	5,500 [5,000-6,000] ^d	0.12%	91% [83%,100%]	94% [93%,94%]	93% [93%,93%]	80%
France	153,400 [150,600-155,900]	0.29%	84% [82%,85%]	93% ^e	92% ^e	72%
Germany	80,000 [69,000-91,000]	0.11%	83% [73%,96%]	87% [83%,90%]	81% [69%,92%]	58%
Greece	14,200 [13,700-14,600]	0.15%	78% [76%,81%]	82% [79%,84%]	81% [72%,89%]	52%
Italy	128,100 [122,400-133,500] ^f	0.25%	90% [86%,94%]	80% [75%,85%]	82% [74%,90%]	59%
The Netherlands	22,000 [21,400-22,800]	0.16%	85% [82%,88%]	91% [90%,92%]	91% [88%,94%]	70%
Spain	140,700 [128,200-155,200]	0.36%	82% [78%,86%] ^g	76% [73%,78%]	81% [72%,89%]	50%
Sweden	7,000 ^h	0.09%	90% ^h	92% [92%,92%]	93% [93%,93%]	77%
United Kingdom	99,100 [93,000-107,400]	0.19%	81% [75%,87%] ⁱ	82% [76%,88%]	82% [70%,94%]	54%

CI confidence interval; PLHIV people living with HIV

Percentages shown for stages ii) iii) and iv) are out of the previous stage. Percentages in the final column are calculated out of the total PLHIV (i).

Estimates were constructed using standardised methods and may differ from previously published results and official national statistics due to differences in data sources, definitions and time-periods. [20-24]

^a Adult HIV prevalence was estimated by dividing the number of PLHIV by Eurostat population denominators for adults aged ≥15 years in 2013.

^b Estimated ranges for the % diagnosed were calculated by dividing the number diagnosed by the upper and lower confidence limits for stage 1 (PLHIV), to reflect the uncertainty in the estimate for stage 1, unless otherwise indicated.

^c Estimate for PLHIV generated using Austrian cohort data which covers approx. 76% of people living with HIV in Austria.

^d Estimated range (CI not available), informed by the ECDC Modelling Tool and triangulation with other estimates.

^e Minimum estimates are not applicable due to the methodology and data sources used to derive the population in care in France. Upper estimates were used to substitute the (missing) minimum estimates when calculating the combined estimates for the proportion on ART and proportion virally-suppressed in the 11 EU countries.

^f Range for PLHIV in Italy calculated using the 95% CI for the undiagnosed estimate and, separately, a range of uncertainty for the number diagnosed and lost from care.

^g 95% CI, reflecting the uncertainty in estimating the diagnosed population nationally in Spain, using a statistical model.

^h Surveillance and survey-based estimate for PLHIV; confidence intervals were therefore not available for the estimate of PLHIV, nor was a range available for the diagnosed estimate. However, in Sweden, the number diagnosed is reliably estimated from the national cohort and surveillance data, for which there is no under or delayed reporting. Point estimate of 7,000 PLHIV used to substitute the (missing) upper and lower limit when calculating the overall range for the % diagnosed in the 11 EU countries combined.

ⁱ Absolute number diagnosed in the UK is reliably derived from national surveillance data. The range presented reflects the uncertainty in the estimate for stage 1.

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Figure 1

