Received: 17 December 2023 | Accepted: 31 January 2024

DOI: 10.1111/hiv.13620

ORIGINAL ARTICLE

SARS-CoV-2 testing, positivity, and factors associated with COVID-19 among people with HIV across Europe in the multinational EuroSIDA cohort

O. Fursa[1] | W. Bannister[1] | B. Neesgaard[1] | D. Podlekareva[1,2] | J. Kowalska[3] | T. Benfield[4] | J. Gerstoft[5] | J. Reekie[1] | L. D. Rasmussen[6] | I. Aho[7] | G. Guaraldi[8] | T. Staub[9] | J. M. Miro[10,11] | J. M. Laporte[12] | D. Elbirt[13] | T. Trofimova[14] | D. Sedlacek[15] | R. Matulionyte[16,17] | C. Oprea[18] | E. Bernasconi[19] | V. Hadžiosmanović[20] | A. Mocroft[1,21] | L. Peters[1] | EuroSIDA Study Group

Correspondence
O. Fursa and W. Bannister, Centre of Excellence for Health, Immunity and Infections, Rigshospitalet, Copenhagen DK-2100, Denmark.
Email: olga.fursa@regionh.dk and wendy.bannister@regionh.dk

Abstract

Background: Although people with HIV might be at risk of severe outcomes from infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; coronavirus 2019 [COVID-19]), regional and temporal differences in SARS-CoV-2 testing in people with HIV across Europe have not been previously described.

Methods: We described the proportions of testing, positive test results, and hospitalizations due to COVID-19 between 1 January 2020 and 31 December 2021 in the EuroSIDA cohort and the factors associated with being tested for SARS-CoV-2 and with ever testing positive.

Results: Of 9012 participants, 2270 (25.2%, 95% confidence interval [CI] 24.3–26.1) had a SARS-CoV-2 polymerase chain reaction test during the study period (range: 38.3% in Northern to 14.6% in Central-Eastern Europe). People from Northern Europe, women, those aged <40 years, those with CD4 cell count <350 cells/mm^3, and those with previous cardiovascular disease or malignancy were significantly more likely to have been tested, as were people with HIV in 2021 compared with those in 2020. Overall, 390 people with HIV (4.3%, 95% CI 3.9–4.8) tested positive (range: 2.6% in Northern to 7.1% in Southern Europe), and the odds of testing positive were higher in all regions than in Northern Europe and in 2021 than in 2020. In total, 64 people with HIV (0.7%, 95% CI 0.6–0.9) were hospitalized, of whom 12 died. Compared with 2020, the odds of positive testing decreased in all regions in 2021, and the associations with

Study members are listed in the appendix.

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cardiovascular disease, malignancy, and use of tenofovir disoproxil fumarate disappeared in 2021. Among study participants, 58.9% received a COVID-19 vaccine (range: 72.0% in Southern to 14.8% in Eastern Europe).

Conclusions: We observed large heterogeneity in SARS-CoV-2 testing and positivity and a low proportion of hospital admissions and deaths across the regions of Europe.

KEYWORDS

COVID-19, Europe, HIV, SARS-CoV-2 testing

INTRODUCTION

The infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) affected over 675 million people and caused almost 7 million deaths worldwide by 10 March 2023 [1]. Symptoms of coronavirus disease 2019 (COVID-19) ranged from mild or asymptomatic to severe and potentially lethal. As of 2020, and before vaccine rollout, the estimated case-fatality rate for COVID-19 ranged from 1% to 3% in different studies in the general population [2–4] but was higher in the presence of risk factors. In some studies, HIV was associated with increased susceptibility to SARS-CoV-2 infection [5], greater COVID-19 severity [6, 7], and death from COVID-19 [8–10], whereas others demonstrated no difference in susceptibility [11] or mortality compared with people without HIV [12]. As per the British HIV Association statement released in January 2021, people with HIV, especially those with advanced immunodeficiency and unsuppressed viral load, were at higher risk of severe COVID-19 [13]. Non-AIDS-related comorbidities, which are among the risk factors for COVID-19 severity and mortality, are also more prevalent in people with both HIV and COVID-19 infection than in people with HIV without COVID-19 [14]. Age, another factor contributing to COVID-19 severity in people with HIV [15], is increasing in this population, with western and central Europe and northern America having the highest estimated proportion of people with HIV aged >50 years [16]. Previous studies have shown that the risks of SARS-CoV-2 infection and severe COVID-19 vary across regions and countries [1, 4, 17–19].

Although some studies investigated the prevalence of SARS-CoV-2 in people with HIV in several national cohorts [20–23], regional and temporal differences in COVID-19 prevalence and outcomes in larger samples of people with HIV across European countries have not been described. We investigated SARS-CoV-2 testing, positivity, and hospital admissions in a large prospective cohort of people with HIV in Europe and looked at interregional differences in SARS-CoV-2 testing.

METHODS

Study population

Participants were enrolled from the EuroSIDA cohort, which collected prospective demographical and clinical data on over 24 000 adults with HIV from the WHO European region [24] and Argentina. Data collection in EuroSIDA before COVID-19 has been described elsewhere [25]. Starting from 2020, EuroSIDA also collected data on polymerase chain reaction (PCR) testing for SARS-CoV-2, hospital admissions due to COVID-19, and (from 2021) vaccination for COVID-19. We did not collect data on the type of clinical specimen used for SARS-CoV-2 testing or antigen testing data.

EuroSIDA participants from the countries of the WHO European region who were under prospective follow-up on 1 January 2020 (baseline) were included in the study. Participants enrolled in sites that did not collect any SARS-CoV-2 testing data were excluded from the analysis.

Outcome definitions

Of all eligible EuroSIDA participants, we calculated the proportion of people tested for SARS-CoV-2, the proportion who had a positive SARS-CoV-2 test result, and the proportion of those admitted to hospital due to COVID-19 from 1 January 2020 to 31 December 2021. We also looked at proportions during 2020 and 2021 separately, where eligible participants were included if they were under follow-up during that year.

Participants were considered tested for SARS-CoV-2, if they had at least one PCR test reported (positive or negative) during the study period and counted as testing positive if they had at least one positive test during the study period. Participants who had a completed COVID-19 admission form were considered hospitalized.

We also described the proportion of people vaccinated against SARS-CoV-2 (defined as at least one vaccination

during the study period) and the proportion of people who were vaccinated more than 14 days before the positive test result.

Statistical analysis

Descriptive statistics were summarized as frequencies and percentages for categorical variables. For continuous variables, data were presented as medians and interquartile ranges (IQRs).

Proportions were compared across five regions, categorized in EuroSIDA as follows (countries that did not provide SARS-CoV-2 data were not included):

- Southern Europe: Greece, Israel, Italy, Portugal, and Spain
- Central-Western Europe: Austria, Belgium, France, Germany, Luxembourg, and Switzerland
- Northern Europe: Denmark, Finland, Iceland, Ireland, the Netherlands, Norway, Sweden, and the UK
- Central-Eastern Europe: Bosnia and Herzegovina, Croatia, Czech Republic, Hungary, North Macedonia, Poland, Romania, Serbia, and Slovenia
- Eastern Europe: Belarus, Estonia, Lithuania, and Russia.

The data are also presented at a country level for the countries with more than 50 participants under follow-up at baseline.

Sensitivity analyses were performed to check the influence of sites with the highest number of participants on regional estimates, excluding the three largest sites from each region, as well as the influence of sites with a low rate of SARS-CoV-2 testing, excluding those where the upper 95% confidence limit for the proportion of testing was below the median average of the full study population.

We used multivariable logistic regression with generalized estimating equations to adjust for within-person repeated assessments over time to determine factors from a prespecified set associated with being tested for SARS-CoV-2 (vs. untested) and with having at least one positive test result (vs. negative). Predictor variables included calendar year, European region, sex, age group, HIV transmission mode, body mass index category, CD4 cell count category, HIV viral load category, currently receiving a tenofovir disoproxil fumarate (TDF)-containing regimen, prior cardiovascular disease (CVD), prior malignancy, and diabetes. All predictor variables were included in the multivariable model, and we also adjusted for chronic kidney disease and liver fibrosis stage, defined as in the previous EuroSIDA studies [26, 27]. We further stratified the model by year to assess factors associated with SARS-CoV-2 testing reported between 1 January and 31 December 2020 and with that between 1 January and 31 December 2021.

Given the low number of participants who were vaccinated before the positive test result, and the direct correlation between vaccination and calendar year, we did not include vaccination as a variable in the regression model.

All analyses were performed using SAS 9.4 software (version 9.4; SAS Institute, Cary, NC, USA).

RESULTS

Of 24 297 people enrolled in EuroSIDA, 9488 were under follow-up on 1 January 2020; 476 of these were excluded because they were from sites that did not collect SARS-CoV-2 testing data. Of the 9012 participants included, 6562 (72.8%) were male, and 3510 (38.9%) were men who have sex with men (MSM, Table 1). Participants were enrolled in Southern (22.6%), Central-Western (22.0%), Northern (26.0%), Central-Eastern (16.8%), and Eastern (12.7%) Europe. The median age of participants was 54 years (IQR 46–60), and 33.6% of participants were aged ≥60 years.

During the study period (2020–2021), 2270 participants (25.2% of people with HIV under follow-up at baseline, 95% confidence interval [CI] 24.3–26.1) were tested for SARS-CoV-2, of whom 751 were tested more than once, and the median number of tests per person was 1 (IQR 1–2). Northern Europe had the largest proportion tested (38.3%, 95% CI 36.4–40.3), and Central-Eastern Europe had the lowest (14.6%, 95% CI 12.8–16.4). Overall, 390 people with HIV (4.3% of all study participants, 95% CI 3.9–4.8) had at least one positive test, ranging from 2.6% (95% CI 2.0–3.3) in Northern to 7.1% (95% CI 5.8–8.5) in Central-Eastern Europe.

During 2020–2021, 64 people were hospitalized due to COVID-19 (0.7% of the study population, 95% CI 0.6–0.9), and 12 of these people died. Compared with the overall cohort, the hospitalized group was slightly older (median age 58 years vs. 54 years in the overall cohort) and had a higher proportion of people with HIV from Eastern Europe (23.4% vs. 12.7%), with HIV RNA >200 copies/mL (9.4% vs. 2.5%), with latest CD4 cell count <350 cells/mm^3 (18.1% vs. 9.6%), with prior CVD (17.2% vs. 7.1%), and with diabetes (23.4% vs. 10.6%).

Sensitivity analyses excluding sites with the highest number of participants from each region and excluding sites with low SARS-CoV-2 testing showed results consistent with the main analysis. Sites with testing rates below the average in the study population were distributed evenly across all regions.

Overall, 5310 participants (58.9%, 95% CI 57.9–60.0) were ever vaccinated against SARS-CoV-2, ranging from 72.0% (95% CI 70.0–73.9) in Southern Europe to 14.8%

TABLE 1 Baseline characteristics of the study cohort in EuroSIDA according to availability of and results from a SARS-CoV-2 polymerase chain reaction test, and in those admitted to hospital due to SARS-CoV-2 over 2020–2021.

Variable, *N* (%)		Overall	Tested	Positive	Admitted
Number under follow-up at 1 January 2020		9012	2270	390	64
Sex	Male	6562 (72.8)	1609 (70.9)	261 (66.9)	47 (73.4)
European region	Southern	2035 (22.6)	502 (22.1)	76 (19.5)	11 (17.2)
	Central-Western	1981 (22.0)	423 (18.6)	77 (19.7)	19 (29.7)
	Northern	2340 (26.0)	897 (39.5)	61 (15.6)	10 (15.6)
	Central-Eastern	1512 (16.8)	220 (9.7)	107 (27.4)	9 (14.1)
	Eastern	1144 (12.7)	228 (10.0)	69 (17.7)	15 (23.4)
Mode of HIV transmission	MSM	3510 (38.9)	889 (39.2)	145 (37.2)	20 (31.3)
	Heterosexual	2566 (28.5)	692 (30.5)	132 (33.8)	25 (39.1)
	PWID	2347 (26.0)	530 (23.3)	87 (22.3)	13 (20.3)
	Other/unknown	589 (6.5)	159 (7.0)	26 (6.7)	6 (9.4)
BMI group, kg/m^2	<18.5	213 (2.4)	52 (2.3)	7 (1.8)	2 (3.1)
	18.5 to <25	2772 (30.8)	679 (29.9)	124 (31.8)	19 (29.7)
	25 to <30	1787 (19.8)	484 (21.3)	91 (23.3)	5 (7.8)
	≥30	633 (7.0)	194 (8.5)	36 (9.2)	7 (10.9)
	Unknown	3607 (40.0)	861 (37.9)	132 (33.8)	31 (48.4)
HIV RNA, copies/mL	<200	8244 (91.5)	2050 (90.3)	362 (92.8)	55 (85.9)
	≥200	311 (3.5)	66 (2.9)	15 (3.8)	6 (9.4)
	Unknown	457 (5.1)	154 (6.8)	13 (3.3)	3 (4.7)
CD4 count category, cells/mm^3	<350	867 (9.6)	246 (10.8)	46 (11.8)	12 (18.8)
	350–499	1190 (13.2)	301 (13.3)	54 (13.8)	8 (12.5)
	≥500	5119 (56.8)	1309 (57.7)	215 (55.1)	31 (48.4)
	Unknown	1836 (20.4)	414 (18.2)	75 (19.2)	13 (20.3)
Currently on ART		8873 (98.5)	2233 (98.4)	175 (99.4)	35 (94.6)
Currently on TDF-containing regimen		2310 (25.6)	645 (28.4)	104 (26.7)	16 (25.0)
Prior cardiovascular disease		639 (7.1)	188 (8.3)	23 (5.9)	11 (17.2)
Prior malignancy		1041 (11.6)	288 (12.7)	37 (9.5)	8 (12.5)
Diabetes		951 (10.6)	274 (12.1)	41 (10.5)	15 (23.4)
Chronic kidney disease[a]		881 (9.8)	251 (11.1)	29 (7.4)	6 (9.4)
Age (years), median (interquartile range)		54 (46–60)	55 (47–61)	51 (42–58)	58 (47–65)

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; eGFR, estimated glomerular filtration rate; MSM, men who have sex with men; PWID, people who inject drugs; TDF, tenofovir disoproxil fumarate.

[a]Defined as confirmed (>3 months apart) eGFR <60 mL/min/1.73 m^2 for those with first eGFR >60 mL/min/1.73 m^2 and a confirmed (>3 months apart) 25% decline in eGFR for those with baseline eGFR ≤60 mL/min/1.73 m^2 or less.

(95% CI 12.7–16.8) in Eastern Europe (Table S1). The most frequent vaccines were Comirnaty (Pfizer/Biontech, 55.0% of all vaccinations overall), Vaxzevria (AstraZeneca, 13.3%) then Spikevax (Moderna, 12.9%), whereas, in Eastern Europe, 20.1% of all vaccinated people received the Sputnik V vaccine. Of the 218 participants with a positive test result in 2021, 67 (30.7%, 95% CI 24.6–36.9) received at least one vaccine >14 days before the positive test result, and the most frequent vaccine types in this group were similar to those received by the overall vaccinated population in EuroSIDA. Six people hospitalized because of COVID-19 received at least one vaccine >14 days before admission; five of these patients recovered.

Temporal changes and inter-regional differences in 2020 and 2021

The number of PCR tests per month was substantially higher in Northern Europe throughout the study period

(Figure 1a), whereas the curves for positive test results were less different across regions, and positive testing decreased in summer months in both years (Figure 1b).

Compared with in 2020, the overall proportion of people tested and the proportion of testing positive slightly increased in 2021 (Table S1). The largest increase in SARS-CoV-2 testing was reported in Eastern Europe (7.5% in 2020 vs. 16.4% in 2021), as was the largest increase in positive testing (1.8% vs. 4.9%). A high degree of heterogeneity in the proportions of positive test results, with the shift of increased positive testing to the East in 2021, was observed between European countries (Figure S1).

In total, 37 admissions due to COVID-19 (0.4% of the study population) were reported in 2020, and 29 (0.4% of those still under follow-up) were reported in 2021; two individuals were admitted in both years.

Factors associated with SARS-CoV-2 testing

Participants were more likely to be tested for SARS-CoV-2 in 2021 than in 2020 (adjusted odds ratio [aOR] 1.21 [95% CI 1.12–1.31], $p < 0.0001$, Figure 2a). Compared with Northern Europe, participants from other EuroSIDA regions had significantly lower odds of being tested. Women were more likely to be tested (aOR 1.25 [95% CI 1.10–1.42], $p = 0.0004$), as were people with prior CVD and malignancy. People aged <40 years were more likely to be tested than those aged ≥60 years, as were people with the latest CD4 cell count <350 cells/mm^3 compared with ≥500 cells/mm^3. Diabetes was associated with higher odds of being tested in the univariable model, whereas people who inject drugs were less likely to be tested than MSM, but neither of these associations persisted in the multivariable model.

In the analysis stratified by year, we observed a difference in the likelihood of being tested compared with Northern Europe for all other regions both in 2020 and in 2021 (Table 2). People with HIV aged <40 years were significantly more likely to be tested than were people with HIV aged >60 years in 2021 but not in 2020, as were people with CVD and malignancy. In a further comparison of years within regions we found a significantly higher likelihood of testing in 2021 versus 2020 in Eastern (aOR 2.47 [95% CI 1.87–3.27]) and Northern Europe (aOR 1.71 [95% CI 1.52–1.93]) and a lower likelihood in Central-Western Europe (aOR 0.77 [95% CI 0.64–0.93]).

Factors associated with ever testing positive for SARS-CoV-2

The adjusted odds of ever testing positive were significantly higher in Southern (aOR 2.64 [95% CI 1.73–4.03]), Central-Western (aOR 3.54 [95% CI 2.30–5.45]), Eastern (aOR 6.72 [95% CI 4.13–10.92]) and particularly Central-Eastern Europe (aOR 12.04 [95% CI 7.94–18.26]) compared with Northern Europe ($p < 0.0001$, Figure 2b). CD4 cell counts 350–499 cells/mm^3 and unknown CD4 cell count were associated with a higher likelihood of a positive test than a count ≥500 cells/mm^3.

In the stratified analysis, regional associations with a positive test result were significant in both 2020 and 2021. Although the odds of testing positive remained higher in Southern, Central-Eastern and Eastern versus Northern Europe, the magnitude of differences decreased in 2021 (Table 2). The negative association of TDF use with a positive test and the association of unknown CD4 cell count with testing positive were observed in 2020 but not 2021.

DISCUSSION

We investigated SARS-CoV-2 testing, positivity, and related hospitalizations in the EuroSIDA cohort in 2020 and 2021 to provide more information on SARS-CoV-2 testing coverage in people with HIV across Europe during the first 2 years of the COVID-19 pandemic. In our study, 25.2% of study participants were tested for SARS-CoV-2 during 2020–2021, and 4.3% of all study participants had a positive test, whereas hospitalization rates were low (0.7% during the 2 years). The odds of testing for SARS-CoV-2 and testing positive were both higher in 2021 than in 2020. The proportion of hospital admissions was similar in the 2 study years in the overall cohort but increased in Eastern Europe and decreased in Western Europe in 2021. The case-fatality ratio during the 2 study years was higher in our study than in the general population in the EU/European economic area (EEA): EuroSIDA 3.1%, EU/EEA 1.6% [28]. The percentage of deaths, albeit based on a small number of deaths, was somewhat lower than that in general population in the WHO European region (EuroSIDA: 0.13%, WHO Europe: 0.18% [1 706 727 COVID-19 deaths up to 31 December 2021 [29] per 927,3 million population [30]] and in the EU/EEA (0.2%: 908 731 deaths [28] per 446.7 million population [31]).

Data on SARS-CoV-2 testing in people with HIV in Europe are scarce and mostly cover the first months of the pandemic. Three studies investigated COVID-19 in people with HIV in European countries for a longer period: in the Dutch ATHENA cohort study, 2301 SARS-CoV-2 infections were registered among 21 289 people with HIV between February 2020 and 31 December 2021 [20]; the Danish national registry study found that 13.5% of people with HIV tested positive for COVID-19 in 2020–2021 [32]; and in the PISCIS cohort in Catalonia (Spain), 5.7% of people with HIV were diagnosed with

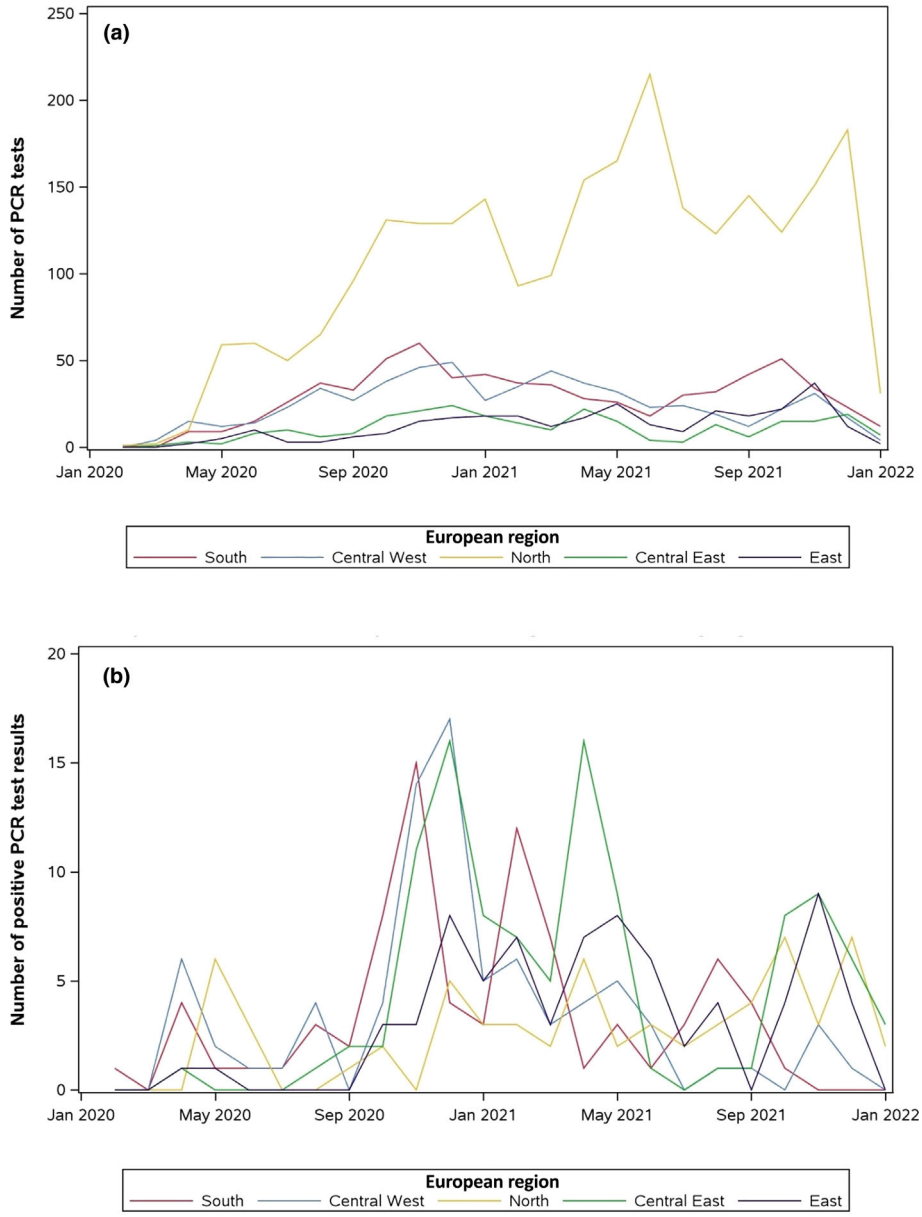

FIGURE 1 Number of polymerase chain reaction (PCR) tests per month during 2020 and 2021 by region of EuroSIDA.

COVID-19 during 2020 [21]. The Dutch study utilized infections, and not participants who were ever diagnosed, as an outcome definition, which meant we could not compare results with those from the EuroSIDA participants enrolled in the Netherlands. The cumulative incidence of positive COVID-19 testing in the Danish study was substantially higher than in our study; the most prominent increase was observed starting from the end of 2021, whereas, due to the EuroSIDA data collection schedule, we could not capture all data from the last weeks of 2021. The estimates in the PISCIS study were higher than in our study, where 2.2% of people with HIV followed up in Spain tested positive in 2020, but this might be partially explained by the wider range of tests used for the outcome definition in PISCIS (PCR, antigen, and antibody detection). Large interregional differences in testing and positivity rates across Europe were likely driven by differences in COVID-19 prevalence and in testing policies. In the early stage of the pandemic, Southern Europe was disproportionally affected by COVID-19 [33, 34], and we observed the highest proportion of positive tests in Southern Europe in the earlier results of our study covering 2020 [35]. Combined with the 2021 data and data on outcomes that occurred in 2020 but were reported after the first analysis, the largest proportions of positive testing were in Central-Eastern and Eastern Europe, where a surge of COVID-19 cases started closer to the end of 2020 [36]. In the Northern European region,

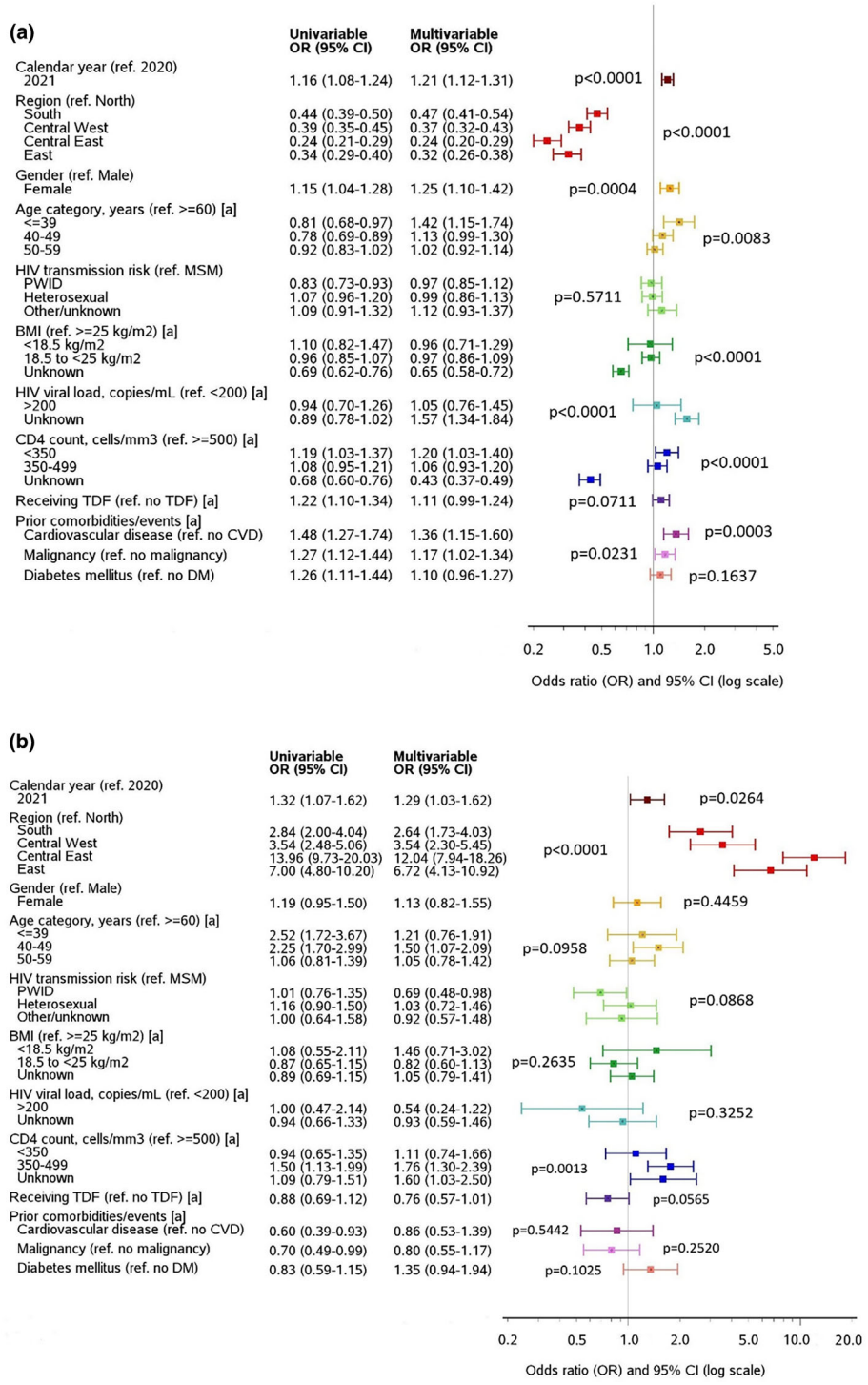

FIGURE 2 Number of positive polymerase chain reaction (PCR) tests per month during 2020 and 2021 by region of EuroSIDA.

the higher proportion of tested and the lower proportion of positive test results were likely driven by the earlier launch of wide testing strategies in Denmark and the UK [37], and, in Denmark, the availability of electronic SARS-CoV-2 testing data for physicians, who were then able to report it to EuroSIDA [38, 39]. Testing policies varied greatly across Europe in 2020: for example, in Denmark, testing was available for free for the general population from May 2020 [40], whereas development of testing infrastructure in Poland took several months and then testing decreased in September 2020 due to a lack of resources [41].

We found that younger age, female sex, and prior CVD or malignancy were associated with being tested for

TABLE 2 Factors associated with ever being tested for SARS-CoV-2 and with ever testing positive in 2020 and 2021, multivariable models.

	Associations with ever being tested (vs. untested)				Association with ever testing positive (vs. negative)			
	2020		2021		2020		2021	
Variables	**aOR (95% CI)**	***p*-value**	**aOR (95% CI)**	***p*-value**	**aOR (95% CI)**	***p*-value**	**aOR (95% CI)**	***p*-value**
Region (ref. North)								
South	**0.59 (0.49–0.70)**	<0.0001	**0.39 (0.32–0.47)**	<0.0001	**5.66 (2.86–11.22)**	<0.0001	**1.67 (0.95–2.95)**	<0.0001
Central-West	**0.48 (0.40–0.57)**		**0.29 (0.24–0.36)**		**7.05 (3.58–13.91)**		**1.85 (1.01–3.41)**	
Central-East	**0.27 (0.22–0.35)**		**0.22 (0.17–0.27)**		**14.97 (7.45–30.08)**		**12.57 (7.23–21.86)**	
East	**0.25 (0.19–0.33)**		**0.38 (0.29–0.49)**		**10.13 (4.21–24.34)**		**5.60 (3.03–10.37)**	
Sex (ref. male)								
Female	**1.36 (1.15–1.60)**	0.0003	1.15 (0.98–1.36)	0.0872	1.38 (0.85–2.23)	0.1952	0.99 (0.65–1.51)	0.9667
Age category (ref. ≥60 years)[a]								
≤39	1.23 (0.93–1.62)	0.4689	**1.83 (1.39–2.40)**	<0.0001	1.85 (0.91–3.75)	0.2114	0.83 (0.44–1.55)	0.2046
40–49	1.11 (0.92–1.34)		1.16 (0.96–1.40)		1.60 (0.96–2.66)		1.40 (0.90–2.17)	
50–59	1.06 (0.92–1.22)		0.98 (0.84–1.14)		1.16 (0.74–1.80)		0.93 (0.62–1.42)	
HIV viral load (ref. ≤200 copies/mL)[a]								
>200	0.94 (0.58–1.52)	<0.0001	1.16 (0.75–1.78)	0.0794	0.29 (0.06–1.27)	0.1168	0.75 (0.27–2.07)	0.6024
Unknown	**1.80 (1.50–2.16)**		**1.41 (1.03–1.92)**		1.50 (0.79–2.84)		0.71 (0.33–1.55)	
CD4 count (ref: ≥500 cells/mm^3)[a]								
<350	**1.30 (1.06–1.59)**	<0.0001	1.12 (0.90–1.38)	<0.0001	1.53 (0.89–2.61)	0.0271	0.78 (0.41–1.47)	0.0578
350–499	1.09 (0.92–1.30)		1.03 (0.86–1.23)		**1.79 (1.12–2.87)**		**1.67 (1.09–2.53)**	
Unknown	**0.42 (0.34–0.51)**		**0.40 (0.32–0.50)**		**1.98 (1.03–3.81)**		1.23 (0.64–2.39)	
Receiving TDF-containing regimen (ref. no TDF)[a]	1.13 (0.98–1.31)	0.0943	1.06 (0.91–1.23)	0.4812	**0.49 (0.30–0.81)**	0.0053	1.03 (0.71–1.49)	0.8796
Prior comorbidities (ref. none)[a]								
Cardiovascular disease	**1.53 (1.25–1.87)**	<0.0001	1.13 (0.89–1.44)	0.309	0.81 (0.41–1.59)	0.5382	0.99 (0.50–1.93)	0.9684
Malignancy	**1.34 (1.13–1.59)**	0.0006	0.96 (0.79–1.16)	0.6645	0.77 (0.48–1.25)	0.2956	0.85 (0.47–1.53)	0.5887

Note: Significant associations shown in bold. Variables with no significant associations in any of the multivariable models were not included in the table.

Abbreviation: aOR, adjusted odds ratio; CI, confidence interval; TDF, tenofovir disoproxil fumarate.

[a]Included as time-updated factors assessed at the last visit/CD4/HIV viral load assessment in each year if available, else at the midpoint of the year.

SARS-CoV-2 but not with a positive test result. Although reasons for testing differ and can include symptoms, contact with a person who tested positive, lockdown policies, or travel requirements, which we were unable to account for, our findings were in line with those of other studies that showed no evidence of an association between age and positive test results in people with HIV [42], as well as no sex-based difference in positive testing [21, 42, 43]. We also found no association with HIV transmission mode, suggesting no substantial impact of possible behavioural differences or stigma on SARS-CoV-2 testing in our study population. Higher odds of being tested in people with lower CD4 cell count could be driven by lower CD4 count being a risk factor of severe COVID-19, which might result in better testing coverage in this group. On the other hand, people with missing CD4 cell count had lower odds of testing and higher odds of positive results.

TDF use was not significantly associated with testing or with a positive test result during the whole study period; however, we found a lower risk of testing positive for the year 2020. Some of the previous studies observed a protective effect of TDF against severe infection in 2020 [11, 44–47], whereas other studies did not confirm this association [14, 48]. One of the suggested explanations was channelling bias due to differences in background characteristics between people who were prescribed TDF and those who were not [49]. However, in our study, 26.3% of people receiving TDF were from Eastern Europe, where TDF is prescribed because tenofovir alafenamide is less available, and not depending on baseline factors [50]. After adjustment for comorbidities and for chronic kidney disease, the association with TDF persisted in 2020. The disappearance of this association in 2021, along with the decrease in regional differences in testing positive compared with 2020, might be attributed to the strong protective effect of vaccination modifying the effect of the other factors in the model.

In our study population, 58.9% of all participants were ever vaccinated against COVID-19, and only 14.8% of people with HIV were vaccinated in Eastern Europe. These results are in line with those from other studies demonstrating a high variability in vaccination rollout and vaccine coverage across Europe [51–53]. This difference could not be fully explained by the later vaccination start, given that the difference between the median dates of vaccination in the best-performing region (Southern Europe) and Eastern Europe was 2 weeks in our study. A survey performed by the Euroguidelines group showed that people with HIV from Eastern European countries were not prioritized for vaccination as of 19 March 2021 [54]. As of January 2022, in the general population, Eastern and Central-Eastern European countries had lower proportions of people vaccinated against SARS-CoV-2 than did the EU [53] and higher rates of vaccine hesitancy [53, 55].

To our knowledge, this study is the first to describe SARS-CoV-2 testing in a large cohort of people with HIV from different European countries, data from most of which have not previously reported in other studies. In particular, EuroSIDA collected SARS-CoV-2 data from Eastern Europe, where the population prevalence of HIV is high and testing and diagnosis of COVID-19 in people with HIV has not been previously described. EuroSIDA participants are followed prospectively, so changes in SARS-CoV-2 testing and outcomes could be assessed and compared across 2 years of the pandemic, and the common system of data collection allowed for inter-regional comparisons.

The main limitation of this study is differences in the availability of SARS-CoV-2 testing data across EuroSIDA sites. Although many countries implemented testing and contact tracing systems during the pandemic, HIV clinics in several EuroSIDA countries unfortunately did not have direct access to national SARS-CoV-2 testing data or information from other healthcare/testing providers (personal communication with the EuroSIDA investigators). This affected reporting of negative PCR test results more than positive results, whereas the proportions of hospitalizations and deaths were reported more accurately, since the designated COVID-19 form and cause of death form required detailed information and were centrally validated. To limit the impact of information bias, we excluded clinical sites that did not report any COVID-19 data, while also ensuring that the size of the included population allowed for assessment of the outcomes of interest. EuroSIDA collected data from a limited number of clinical sites, mostly located in larger cities, so the results cannot be generalized to an overall population of people with HIV. Further, since EuroSIDA collects data once annually between October and December, a potential time lag in reporting data might reach up to 3 months, which, in our study period, applies to the end of 2021, when the omicron surge started in Europe. Therefore, our study only covers the pre-omicron period of the pandemic. The low number of hospital admissions reported during the study period meant we could not perform a granular analysis in this group. We also could not assess any association with ongoing drug use and were only able to use the reported transmission mode, since less than 2% of the cohort had a record of ongoing drug use during the study period. Finally, residual confounding by factors not collected and known to have an impact on SARS-CoV-2 testing and outcomes, such as socioeconomic status, migration history, and mental disorders, cannot be excluded.

CONCLUSIONS

Our study demonstrated a high variability in SARS-CoV-2 testing and positive test results in people with HIV across regions of Europe, whereas the proportion of severe COVID-19 was consistent across regions and the proportion of deaths was lower than that in the general population. The EuroSIDA region was the strongest factor associated with SARS-CoV-2 testing, suggesting the need to address the large inter-regional disparity in testing in a population that remains vulnerable to COVID-19. In 2021, the proportion of positive testing increased most substantially in Eastern Europe and decreased in Central-Western Europe, following the later surge of SARS-COV-2 infections in Eastern European countries and wider vaccination coverage in the Western European countries. Female sex, younger age, and prior CVD and malignancy were associated with a higher likelihood of being tested, whereas TDF use was negatively associated with testing positive in 2020 but not in 2021. The changes in these associations in 2021, along with the decline in the proportion of admissions due to COVID-19 in the regions with better vaccine coverage, highlight the importance of SARS-CoV-2 vaccine provision to protect people at risk.

AUTHOR CONTRIBUTIONS

OF and WB are co-first authors of this manuscript. OF, WB, and LP contributed to the study design and developing the analysis plan, and the analysis and interpretation of data. OF wrote the first draft of the manuscript and subsequent drafts after revisions. WB carried out the main analysis. WB, BN, JR, AM, DP, and LP reviewed all versions of the manuscript and provided critical suggestions. JK, TB, JG, LDR, IA, GG, TS, JMM, JML, DE, TT, DS, RM, CO, EB, and VH substantially contributed to acquisition of data for the submitted work. All authors reviewed and approved the final version of the manuscript.

AFFILIATIONS

[1]Centre of Excellence for Health, Immunity and Infections, Rigshospitalet, Copenhagen, Denmark
[2]Department of Respiratory and Infectious Diseases, Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark
[3]Department of Adults' Infectious Diseases, Medical University of Warsaw, Warsaw, Poland
[4]Department of Infectious Diseases, Copenhagen University Hospital-Amager and Hvidovre, Hvidovre, Denmark
[5]Department of Infectious Diseases, Rigshospitalet, Copenhagen, Denmark
[6]Department of Infectious Diseases, Odense University Hospital, Odense, Denmark
[7]Division of Infectious Diseases, Helsinki University Hospital, Helsinki, Finland
[8]Modena HIV Cohort, Università degli Studi di Modena, Modena, Italy
[9]Centre Hospitalier de Luxembourg, Service des Maladies Infectieuses, Luxembourg City, Luxembourg
[10]Infectious Diseases Service, Hospital Clínic-IDIBAPS, University of Barcelona, Barcelona, Spain
[11]CIBERINFEC, Instituto de Salud Carlos III, Madrid, Spain
[12]Hospital Universitario de Alava, Vitoria-Gasteiz, Spain
[13]Allergy, Immunology and HIV Unit, Kaplan Medical Center, Rehovot, Israel
[14]Novgorod Centre for AIDS prevention and control, Veliky Novgorod, Russian Federation
[15]Department of Infectious Diseases and Travel Medicine, Medical Faculty and Teaching Hospital Plzen, Charles University Prague, Plzen, Czech Republic
[16]Department of Infectious Diseases and Dermatovenerology, Faculty of Medicine, Vilnius University, Vilnius, Lithuania
[17]Vilnius University Hospital, Vilnius, Lithuania
[18]Victor Babes Clinical Hospital for Infectious and Tropical Diseases, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[19]Division of Infectious Diseases, Ente Ospedaliero Cantonale Lugano, University of Geneva and University of Southern Switzerland, Lugano, Switzerland
[20]Infectious Diseases Clinic, Clinical Center University of Sarajevo, Sarajevo, Bosnia and Herzegovina
[21]UCL Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), London, UK

FUNDING INFORMATION

EuroSIDA was supported by the European Union's Seventh Framework Programme for research, technological development, and demonstration under EuroCoord grant agreement no. 260694. Current support includes unrestricted grants by ViiV Healthcare LLC, GlaxoSmithKline R&D Limited, Janssen Scientific Affairs, Janssen R&D, Bristol-Myers Squibb Company, Merck Sharp & Dohme Corp, and Gilead Sciences. The participation of centres from Switzerland was supported by The Swiss National Science Foundation (grant 148522). The study is also supported by a grant (grant number DNRF126) from the Danish National Research Foundation and by the International Cohort Consortium of Infectious Disease (RESPOND). JMM received a personal 80:20 research grant from Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain, during 2017–24.

CONFLICT OF INTEREST STATEMENT

JMM received a personal 80:20 research grant from Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain, during 2017–24. JMM has also received consulting honoraria and/or research grants from AbbVie, Angelini, Contrafect, Cubist, Genentech, Gilead Sciences, Jansen, Medtronic, MSD, Novartis, Pfizer, and ViiV Healthcare outside the submitted work. IA has received honoraria/research grants from Gilead, GSK, and MSD outside the submitted work. AM has received honoraria, travel support, and lecture fees from ViiV and Gilead, and consultancy fees from Eiland and Bonnin, outside the submitted work. All other authors report no conflicts of interest.

ORCID

O. Fursa https://orcid.org/0000-0002-1596-9880
W. Bannister https://orcid.org/0000-0003-4780-3364
D. Podlekareva https://orcid.org/0000-0003-3187-0597
J. Kowalska https://orcid.org/0000-0003-1166-4462
J. Reekie https://orcid.org/0000-0001-8529-3559
G. Guaraldi https://orcid.org/0000-0002-5724-3914

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Fursa O, Bannister W, Neesgaard B, et al. SARS-CoV-2 testing, positivity, and factors associated with COVID-19 among people with HIV across Europe in the multinational EuroSIDA cohort. *HIV Med*. 2024; 25(6):711-724. doi:10.1111/hiv.13620

APPENDIX A

The multicentre study group, EuroSIDA (national coordinators in parenthesis)

Albania: (A Harxhi), University Hospital Center of Tirana, Tirana. **Argentina**: (M Losso), M Kundro, Hospital JM Ramos Mejia, Buenos Aires. **Austria**: (B Schmied), Klinik Penzing, Vienna; R Zangerle, Medical University Innsbruck, Innsbruck. **Belarus**: (I Karpov), A Vassilenko, Belarusian State Medical University, Minsk; VM Mitsura, Gomel State Medical University, Gomel; D Paduto, Regional AIDS Centre, Svetlogorsk. **Belgium**: S De Wit, M Delforge, Saint-Pierre Hospital, Brussels; E Florence, Institute of Tropical Medicine, Antwerp; L Vandekerckhove, University Ziekenhuis-Gent, Gent. **Bosnia-Herzegovina**: (V Hadziosmanovic), Klinicki Centar Univerziteta Sarajevo, Sarajevo. **Croatia**: (J Begovac), University Hospital of Infectious Diseases, Zagreb. **Czech Republic**: (L Machala), D Jilich, Faculty Hospital Bulovka, Prague; D Sedlacek, Charles University Hospital, Plzen. **Denmark**: T Benfield, Hvidovre Hospital, Copenhagen; J Gerstoft, O Kirk, Rigshospitalet, Copenhagen; C Pedersen, IS Johansen, Odense University Hospital, Odense; L Ostergaard, Skejby Hospital, Aarhus, L Wiese, Sjællands Universitetshospital, Roskilde; L N Nielsen, Hillerod Hospital, Hillerod. **Estonia**: (K Zilmer), West-Tallinn Central Hospital, Tallinn; Jelena Smidt, Nakkusosakond Siseklinik, Kohtla-Järve. **Finland**: (I Aho), Helsinki University Hospital, Helsinki. **France**: (J-P Viard), Hôtel-Dieu, Paris; K Lacombe, Hospital Saint-Antoine, Paris; C Pradier, E Fontas, Hôpitalde l'Archet, Nice; C Duvivier, Hôpital Necker-Enfants Malades, Paris. **Germany**: (J Rockstroh), Universitäts Klinik Bonn; O Degen, University Medical Center Hamburg-Eppendorf, Infectious Diseases Unit, Hamburg; C Hoffmann, HJ Stellbrink, ICH Study Center GmbH & Co. KG, Hamburg; C Stefan, JW Goethe University Hospital, Frankfurt; J Bogner, Medizinische Poliklinik, Munich; G. Fätkenheuer, Universität Köln, Cologne. **Georgia**: (N Chkhartishvili) Infectious Diseases, AIDS & Clinical Immunology Research Center, Tbilisi. **Greece**: (H Sambatakou), Ippokration General Hospital, Athens; G Adamis, N Paissios, Athens General Hospital 'G Gennimatas', Athens. **Hungary**: (J Szlávik), South-Pest Hospital Centre –National Institute for Infectology and Haematology, Budapest. **Iceland**: (M Gottfredsson), Landspitali University Hospital, Reykjavik. **Ireland**: (E Devitt), St. James's Hospital, Dublin. **Israel**: (L Tau), D Turner, M Burke, Ichilov Hospital, Tel Aviv; E Shahar, LM Wattad, Rambam Health Care Campus, Haifa; H Elinav, M Haouzi, Hadassah University Hospital, Jerusalem; D Elbirt, AIDS Center (Neve Or), Rehovot. **Italy**: (A D'Arminio Monforte), Istituto Di Clinica Malattie Infettive e Tropicale, Milan; G Guaraldi, R Esposito, I Mazeu, C Mussini, Università Modena, Modena; F Mazzotta, A Gabbuti, Ospedale S Maria Annunziata, Firenze; A Lazzarin, A Castagna, N Gianotti, Ospedale San Raffaele, Milan; M Galli, A Ridolfo, Ospedale L. Sacco, Milan. **Lithuania**: (R Matulionyte) Vilnius University Hospital Santaros Klinikos, Vilnius; R Matulionyte, Vilnius University, Faculty of Medicine, Department of Infectious Diseases and Dermatovenerology, Vilnius. **Luxembourg**: (T Staub), R Hemmer, Centre Hospitalier, Luxembourg. **Netherlands**: (Marc v d Valk), Academisch Medisch Centrum bijde Universiteit van Amsterdam, Amsterdam. **North Macedonia**: (J Trajanovska), University Clinic for Infectious Diseases & Febrile Conditions, Mother Teresa 17, Skopje. **Norway**: (DH Reikvam), A Maeland, J Bruun, Oslo University Hospital, Ullevaal. **Poland**: (B Knysz), B Szetela, M Inglot, Medical University, Wroclaw; E Bakowska, Centrum Diagnostyki i Terapii AIDS, Warsaw; R Flisiak, A Grzeszczuk, Medical University, Bialystok; M Parczewski, K Maciejewska, B Aksak-Was, Medical University, Szczecin; M Beniowski, E Mularska, Osrodek Diagnostyki i Terapii AIDS, Chorzow; E Jablonowska, J Kamerys, K Wojcik, Wojewodzki Szpital Specjalistyczny, Lodz; I Mozer-Lisewska, B Rozplochowski, Poznan University of Medical Sciences, Poznan. **Portugal**: (A Zagalo), Hospital Santa Maria, Lisbon; K Mansinho, Hospital de Egas Moniz, Lisbon; F Maltez, Hospital Curry Cabral, Lisbon. **Romania**: (R Radoi), C Oprea, Carol Davila University of Medicine and Pharmacy Bucharest, Victor Babes Clinical Hospital for Infectious and Tropical Diseases, Bucharest. **Russia**: D Gusev, Medical Academy Botkin Hospital, St Petersburg; T Trofimova, Novgorod Centre for AIDS, Novgorod, I Khromova, Centre for HIV/AIDS & and Infectious Diseases, Kaliningrad; E Kuzovatova, Academician n.a. I.N. Blokhina Nizhny Novgorod Scientific Research Institute of Epidemiology and Microbiology, Nizhny Novgorod; E Borodulina, E Vdoushkina, Samara State Medical University, Samara. **Serbia**: (J Ranin), The Institute for Infectious and Tropical Diseases, Belgrade. **Slovenia**: (J Tomazic), University Clinical Centre Ljubljana, Ljubljana. **Spain**: (JM Miro), JM Miró, M. Laguno, E. Martinez, F. Garcia, JL Blanco, M. Martinez-Rebollar, J. Mallolas, P Callau, J Rojas, A Inciarte, Hospital Clinic –IDIBAPS University of Barcelona, Barcelona; S Moreno, S. del Campo, Hospital Ramon y Cajal, Madrid; B Clotet, A Jou, R Paredes, J Puig, JM Llibre, JR Santos, Infectious Diseases Unit & IrsiCaixa AIDS Research Institute, Hospital Germans Trias I Pujol, Badalona; P Domingo, M Gutierrez, G Mateo, MA Sambeat, Hospital Sant Pau, Barcelona; JM Laporte, Hospital Universitariode Alava, Vitoria-Gasteiz. **Sweden**: (P Novak), A Thalme, A Sönnerborg, Karolinska University Hospital, Stockholm; J Brännström, Venhälsan-

Sodersjukhuset, Stockholm; L Flamholc, Malmö University Hospital, Malmö. **Switzerland**: (K Kusejko), D Braun, University Hospital Zurich; M Cavassini, University Hospital Lausanne; A Calmy, University Hospital Geneva; H Furrer, University Hospital Bern; M Battegay, University Hospital Basel; P Schmid, Cantonal Hospital St. Gallen. **Ukraine**: A Kuznetsova, Kharkiv State Medical University, Kharkiv. **United Kingdom**: A Milinkovic, St. Stephen's Clinic, Chelsea and Westminster Hospital, London; AM Johnson, S Edwards, Mortimer Market Centre, London; A Phillips, MA Johnson, A Mocroft, Royal Free and University College Medical School, London (Royal Free Campus); C Orkin, Royal London Hospital, London; A Winston, Imperial College School of Medicine at St. Mary's, London; A Clarke, Royal Sussex County Hospital, Brighton; C. Mackintosh, C Leen, Western General Hospital, Edinburgh. **EuroSIDA Steering Committee**: I Karpov, M Losso, J Lundgren, J Rockstroh, I Aho, LD Rasmussen, P Novak, G Wandeler, C Pradier, N Chkhartishvili, R Matulionyte, C Oprea, JD Kowalska, J Begovac, JM Miró, G Guaraldi, R Paredes. **Chair**: G Wandeler. **Co-chair**: R Paredes. **Study lead**: L Peters. **Coordinating centre staff**: L Peters, JF Larsen, M Gardizi, O Fursa, N Jaschinski, B Neesgaard, D Raben, AH Fischer, TW Elsing. **Statistical staff**: A Mocroft, J Reekie, W Bannister, A Roen, ES Tusch, A Pelchen-Matthews, A Cozzi-Lepri.