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ARTICLE INFO

ABSTRACT

Objectives: The aim of this survey was to describe the current status of HIV care in the countries of Central and Eastern Europe and to investigate how close the region is to achieving the UNAIDS 2020 target of 90–90–90.
Methods: In 2014, data were collected from 24 Central and Eastern European countries using a 38-item questionnaire.

Results: All countries reported mandatory screening of blood and organ donors for HIV. Other groups subjected to targeted screening included people who inject drugs (PWID) (15/24, 62.5%), men who have sex with men (MSM) (14/24, 58.3%), and sex workers (12/24, 50.0%). Only 14 of the 24 countries (58.3%) screened pregnant women. The percentages of late presentation and advanced disease were 40.3% (range 14–80%) and 25.4% (range 9–50%), respectively. There was no difference between countries categorized by income or by region in terms of the percentages of persons presenting late or with advanced disease. The availability of newer antiretroviral drugs (rilpivirine, etravirine, darunavir, maraviroc, raltegravir, dolutegravir) tended to be significantly better with a higher country income status. Ten countries reported initiating antiretroviral therapy (ART) regardless of CD4+ T cell count (41.7%), five countries (20.8%) used the threshold of <500 cells/μl, and nine countries (37.5%) used the threshold of <350 cells/μl. Initiation of ART regardless of the CD4+ T cell count was significantly more common among high-income countries than among upper-middle-income and lower-middle-income countries (100% vs. 27.3% and 0%, respectively; $p = 0.001$). Drugs were provided free of charge in all countries and mostly provided by governments. There were significant discrepancies between countries regarding the follow-up of people living with HIV.
Conclusions: There are major disparities in the provision of HIV care among sub-regions in Europe, which should be addressed. More attention in terms of funding, knowledge and experience sharing, and capacity building is required for the resource-limited settings of Central and Eastern Europe. The exact needs should be defined and services scaled up in order to achieve a standard level of care and provide an adequate and sustainable response to the HIV epidemic in this region.

Introduction

The scaling up of HIV-related prevention programmes and wider availability of antiretroviral therapy (ART) have resulted in significant improvements in the global epidemiology of HIV infection. New HIV infections have fallen globally by 16% since 2010 and AIDS-related deaths by 48% since the peak in 2005 (UNAIDS Data, 2017). However, specific regions in the world continue to maintain an increasing trend. In 2016, a total of 160 453 new HIV diagnoses were reported from 50 out of 53 countries in the World Health Organization (WHO) European Region, corresponding to a rate of 18.2 per 100 000 population, continuing the increasing trend (European Centre for Disease Prevention and Control/WHO Regional Office for Europe, 2017). The contributions of Central and Western Europe were small (4% and 17%, respectively) compared to Eastern Europe, where the reported cases accounted for 80% of the total new HIV diagnoses in 2016 (European Centre for Disease Prevention and Control/WHO Regional Office for Europe, 2017). The incidence was highest in Eastern Europe (50.2 per 100 000 population), followed by Western (6.2 per 100 000) and Central (2.9 per 100 000) Europe (European Centre for Disease Prevention and Control/WHO Regional Office for Europe, 2017).

The Joint United Nations Programme on HIV/AIDS (UNAIDS) 90–90–90 target requires early diagnosis, timely linkage to care, early and uninterrupted access to treatment, strong health systems, and the mobilization of national resources by countries to fast-track the response to HIV infection (UNAIDS, 2014). However, reports indicate that the HIV epidemic in the European region is diverse, with substantial differences between Western European countries (which seem to have reached a high standard in HIV care) and Central and Eastern European countries, and that this region bears many challenges in terms of patient management and control of the epidemic (Mussini et al., 2016; Gökengin et al., 2016; Kowalska et al., 2016; Lazarus et al., 2016).

The aim of this article is to describe the current status of HIV care in the countries of Central and Eastern Europe, where accurate data are lacking, and to investigate how close the region is to achieving the UNAIDS 2020 target.

Methods

In 2014, a 38-item questionnaire on HIV care and patient management was developed by three of the authors (Deniz Gökengin, Cristiana Oprea, and Josip Begovac). The WHO definition of Central and Eastern Europe was used to select the countries for inclusion in the survey. The WHO HIV/AIDS surveillance definition includes 15 countries in Central Europe: Albania, Bosnia and Herzegovina, Bulgaria*, Croatia*, Cyprus*, the Czech Republic*, Hungary*, the former Yugoslav Republic (FYR) of Macedonia, Montenegro, Poland*, Romania*, Serbia, Slovak Republic*, Slovenia*, and Turkey; and includes 15 countries in Eastern Europe: Armenia, Azerbaijan, Belarus, Estonia*, Georgia, Kazakhstan, Kyrgyz Republic, Latvia*, Lithuania*, Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan (European Centre for Disease Prevention and Control and World Health Organization, 2009). This list includes European Union (EU) members (marked with an asterisk) and non-EU countries. Although not stated in the WHO definition, Kosovo was also included in the survey as an independent country.

For each country, one or two healthcare providers who care for HIV patients and/or national AIDS surveillance officers were contacted and were invited to join the survey in September 2014. Participants who accepted were asked to complete the questionnaire providing their national data, policies, and implementations on HIV care. In 2015, after the change in major antiretroviral treatment guidelines (European AIDS Clinical Society (EACS), Department of Helath and Human Sciences (DHHS) and WHO) to recommend the initiation of ART regardless of the patient's CD4+ T cell count, the survey respondents were asked to review and edit their data regarding the criteria for ART initiation in case they had changed. They were also asked to provide the latest list of antiretroviral drugs that were available in their countries in 2015.

Statistical analyses

The data were described using frequencies and percentages. Fisher's exact test was used to compare categorical variables between regions. The exact Chi-square test for trends was used to compare the different categorical variables of income levels (high-income, upper-middle-income, and lower-middle-income countries), and Fisher's exact test was used for the comparison of regions (Eastern and Central Europe). Percentages of late and advanced presentation to care were compared across regions and income levels with the exact Mann–Whitney test and exact Kruskal–Wallis test. Analyses were performed using SAS version

9.4 statistical software. A *p*-value of <0.05 was considered statistically significant.

Results

Twenty-four countries (Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Estonia, Georgia, Hungary, Kazakhstan, Kosovo, Kyrgyz Republic, FYR of Macedonia, Moldova, Montenegro, Poland, Romania, Russian Federation, Serbia, Slovak Republic, Slovenia, Turkey, and Uzbekistan) out of 31 (77.4%) responded to the invitation and were included in the survey. No contact person was available in Cyprus, Belarus, Latvia, Lithuania, Tajikistan, Turkmenistan, and Ukraine. The countries were classified as lower-middle-income (Armenia, Kosovo, Kyrgyz Republic, Moldova, and Uzbekistan), upper-middle-income (Albania, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Georgia, Kazakhstan, FYR of Macedonia, Montenegro, Romania, Serbia, and Turkey), and high-income (Croatia, Czech Republic, Estonia, Hungary, Poland, Russian Federation, Slovak Republic, and Slovenia) according to the World Bank definitions in 2014 (Countries and Economies, 2014)

The earliest date of the first reported case was 1985 for seven countries (Serbia, Romania, Czech Republic, Slovak Republic, Croatia, Poland, and Turkey) and the latest date was 1993 for Albania.

The cumulative number of reported HIV-positive cases as of December 2014 is shown in Table 1.

The major route of transmission was sex between men (41.7%, 10/24 countries), followed by heterosexual contact (37.5%, 9/24 countries) and injecting drug use (20.8%, 5/24 countries) (Table 2).

All countries reported mandatory screening of blood and organ donors for HIV. Other groups subjected to targeted screening included people who inject drugs (PWID) (15/24, 62.5%), men who have sex with men (MSM) (14/24, 58.3%), and sex workers (12/24, 50.0%). Other targeted HIV screening approaches were mandatory premarital screening (Turkey, Romania, and Azerbaijan), screening of patients with sexually transmitted infections (Russian

Federation and Romania), tuberculosis (Turkey, Albania, and Romania) and hepatitis B and C (Albania), HIV screening prior to major surgery (Turkey), and screening of immigrants (Kyrgyz Republic and Uzbekistan).

Pregnant women were screened in 14 of the 24 countries (58.3%), once or twice during pregnancy. Testing was not mandatory for pregnant women in Albania, Bosnia and Herzegovina, Croatia, Estonia, Hungary, FYR of Macedonia, Montenegro, Serbia, Slovenia, and Turkey.

There was no difference between countries in terms of screening strategies when compared according to income levels and regions (Supplementary material, Tables S1 and S2).

Eighteen countries (75.0%) provided data for the estimated percentage of cases with late HIV disease (CD4+ T cell count <350/μl or AIDS-defining illness regardless of CD4+ T cell count) and 19 countries (79.2%) for advanced HIV disease (CD4+ T cell count <200/μl or AIDS-defining illness regardless of CD4+ T cell count). The mean percentages of late and advanced HIV disease were 40.3% (range 14–80%) and 25.4% (range 9–50%), respectively (Figure 1). There was no difference between countries categorized by income or by region in terms of the percentages of persons presenting late or with advanced disease (Supplementary material, Tables S1 and S2).

Table 2
Main routes of HIV transmission by country.

Injecting drug use	Heterosexual contact	Sex between men
Azerbaijan	Albania	Czech Republic
Georgia	Armenia	Serbia
Kazakhstan	Bosnia and Herzegovina	Slovenia
Kyrgyz Republic	Kosovo	Hungary
Russian Federation	Estonia	Slovak Republic
	Moldova	FYR of Macedonia
	Romania	Bulgaria
	Turkey	Montenegro
	Uzbekistan	Croatia
		Poland

FYR, Former Yugoslav Republic.

Table 1
Cumulative number of reported HIV cases as of December 2014.

Country	Population[a]	Cumulative number of reported HIV cases[b]	Beneficiary of the Global Fund
Kosovo	1 812 771	100	Yes
Montenegro	621 810	175	Yes
FYR of Macedonia	2 075 625	217	Yes
Bosnia and Herzegovina	3 817 554	272	Yes
Slovenia	2 061 980	733	No
Slovak Republic	5 418 649	811	No
Albania	2 893 654	870	Yes
Croatia	4 238 389	1325	No
Armenia	3 006 154	1953	Yes
Bulgaria	7 223 938	2043	Yes
Serbia	7 130 576	2263	Yes
Hungary	9 866 468	2574	No
Czech Republic	10 525 347	2745	No
Georgia	3 727 000	4695	Yes
Azerbaijan	9 535 079	5439	No
Kyrgyz Republic	5 835 500	5760	Yes
Estonia	1 315 944	9260	No
Moldova	3 556 397	9389	Yes
Turkey	77 523 778	10 475	No
Poland	38 011 735	17 981	No
Romania	19 832 389	20 646	No
Kazakhstan	17 286 224	25 444	Yes
Uzbekistan	30 757 700	30 184	Yes
Russian Federation	143 819 569	913 035	No

FYR, Former Yugoslav Republic.
[a] World Bank report for 2014.
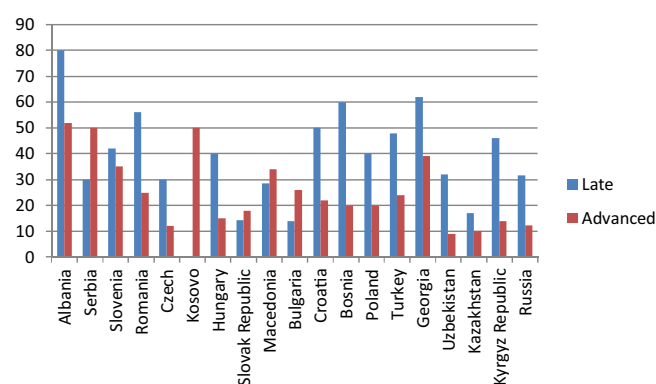[b] Cumulative number reported by the end of 2014.

Figure 1. Estimated percentage of cases diagnosed with late* and advanced** disease in 2014. Montenegro, Estonia, Moldova, Armenia, and Azerbaijan had no data. Kosovo reported only cases with advanced disease.
*Late disease: CD4+ T cell count <350/μl or AIDS-defining illness regardless of CD4+ T cell count.
**Advanced disease: CD4+ T cell count <200/μl or AIDS-defining illness regardless of CD4+ T cell count.

Nineteen countries (79.2%) provided information on the most common AIDS-defining illness in 2014, which was tuberculosis (45.8%), followed by _Pneumocystis jirovecii_ pneumonia (36.0%).

Nineteen (79.2%) countries reported having national guidelines. The first country to develop national guidelines was the Russian Federation in 1994 and the latest country was Armenia in 2014. Eight countries (Albania, Bulgaria, Czech Republic, Georgia, Kyrgyz Republic, Romania, Uzbekistan, and Russian Federation) reported involving community and infectious diseases specialists in the development of their national guidelines. All countries except Slovenia and Montenegro, which did not provide data, reported that clinicians were totally adherent to recommendations in the guidelines. Countries reported updating their national guidelines annually (25.0%), every 2 years (25.0%), every 5 years (18.8%), every 4 years (6.5%), and as needed (0.04%); guidelines have not been updated in FYR of Macedonia or Turkey. Countries

without national guidelines reported using EACS (85.7%) and DHHS (14.3%) guidelines.

The Russian Federation and Turkey had the highest numbers of HIV clinics (90 and 35, respectively). Only Hungary, Czech Republic, and Poland had specific clinics for HIV-positive women. The availability of additional support for people living with HIV (PLWHIV), such as psychological, diet and nutrition, and peer support, showed variations among countries (Table 3).

Antiretroviral drug availability in Central and Eastern Europe in 2015 is shown in Table 4. The availability of many drugs, particularly the newer antiretroviral drugs (rilpivirine, etravirine, darunavir, maraviroc, raltegravir, and dolutegravir), tended to be significantly better in the countries with a higher income status (Table 4). All countries had at least one double fixed-dose combination. Armenia and Serbia had only one fixed-dose combination (tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) and zidovudine/lamivudine (ZDV/3TC), respectively). Three- or four-drug fixed-dose combinations were not available in any low-income country or in several upper-middle-income countries (Romania, Albania, and Serbia).

Ten countries out of 24 reported initiating ART regardless of CD4+ T cell count (41.7%). The ART initiation threshold was <500 cells/μl in five of the countries (5/24, 20.8%) and <350 cells/μl in nine of the countries (9/24, 37.5%) (Table 5). The initiation of ART regardless of the CD4+ T cell count was significantly more common among high-income countries than among upper-middle-income and lower-middle-income countries (100% vs. 27.3% and 0%, respectively; $p = 0.001$).

First-line therapies such as tenofovir + emtricitabine + rilpivirine, tenofovir + emtricitabine + darunavir/ritonavir, abacavir + emtricitabine + darunavir/ritonavir, and raltegravir-based initial ART tended to be more frequently given in countries with a higher income than in those with a lower income (Table 6). In contrast, countries with a lower income tended to use tenofovir + emtricitabine + efavirenz as first-line therapy more frequently than higher income countries (Table 6).

Drugs were provided free of charge in all countries. In the great majority of countries (17/24, 70.8%), they were provided by

Table 3
Number of HIV centres, availability of specific clinics for women, and additional support available for people living with HIV according to the country.

Country	Number of HIV centres	Specific clinics for women	Additional support		
			Psychological	Diet and nutrition	Peer counselling
Kosovo	1	No	Yes	Yes	Yes
Montenegro	1	No	Yes	No	Yes
FYR of Macedonia	1	No	Yes	No	Yes
Bosnia and Herzegovina	3	No	Yes	Yes	Yes
Slovenia	1	No	Yes	Yes	Yes
Slovak Republic	5	No	Yes	No	No
Albania	1	No	Yes	No	Yes
Croatia	1	No	Yes	Yes	Yes
Armenia	1	No	Yes	Yes	Yes
Bulgaria	5	No	Yes	Yes	Yes
Serbia	4	No	Yes	Yes	Yes
Hungary	4	Yes	Yes	Yes	Yes
Czech Republic	7	Yes	Yes	No	Yes
Georgia	5	No	Yes	No	Yes
Azerbaijan	2	No	Yes	Yes	Yes
Kyrgyz Republic	9	No	Yes	Yes	Yes
Estonia	5	No	Yes	Yes	Yes
Moldova	5	No	Yes	Yes	Yes
Turkey	35	No	Yes	No	Yes
Poland	14	Yes	Yes	Yes	Yes
Romania	9	No	Yes	Yes	Yes
Kazakhstan	22	No	Yes	Yes	Yes
Uzbekistan	15	No	Yes	Yes	Yes
Russian Federation	90	No	Yes	Yes	Yes

FYR, Former Yugoslav Republic.

Table 4
Antiretroviral drug availability in 24 countries in Central and Eastern Europe in 2015.

Variables	High income n = 8 (%)	Upper-middle income n = 11 (%)	Lower-middle income n = 5 (%)	Total n = 24 (%)[a]	p-Value
Zidovudine, yes	8 (100.0)	11 (100.0)	3 (60.0)	22 (91.7)	0.036
Lamivudine, yes	8 (100.0)	11 (100.0)	3 (60.0)	22 (91.7)	0.036
Stavudine, yes	4 (50.0)	3 (27.3)	0 (0.0)	7 (29.2)	0.071
Didanosine, yes	4 (50.0)	6 (54.5)	0 (0.0)	10 (41.7)	0.165
Abacavir, yes	8 (100.0)	10 (90.9)	4 (80.0)	22 (91.7)	0.337
Tenofovir, yes	6 (75.0)	10 (90.9)	4 (80.0)	20 (83.3)	>0.99
Emtricitabine, yes	5 (62.5)	7 (63.6)	4 (80.0)	16 (66.7)	0.772
Nevirapine, yes	6 (75.0)	11 (100.0)	4 (80.0)	21 (87.5)	0.701
Nevirapine extended release, yes	1 (12.5)	0 (0.0)	1 (20.0)	2 (8.3)	>0.99
Efavirenz, yes	7 (87.5)	11 (100.0)	4 (80.0)	22 (91.7)	>0.99
Rilpivirine, yes	6 (75.0)	2 (18.2)	0 (0.0)	8 (33.3)	0.005
Etravirine, yes	6 (75.0)	4 (36.4)	0 (0.0)	10 (41.7)	0.009
Atazanavir, yes	6 (75.0)	6 (54.5)	1 (20.0)	13 (54.2)	0.094
Fosamprenavir, yes	5 (62.5)	3 (27.3)	0 (0.0)	8 (33.3)	0.036
Lopinavir/ritonavir, yes	8 (100.0)	10 (90.9)	5 (100.0)	23 (95.8)	>0.99
Darunavir, yes	8 (100.0)	9 (81.8)	2 (40.0)	19 (79.2)	0.017
Darunavir/cobicistat, yes	4 (50.0)	0 (0.0)	0 (0.0)	4 (16.7)	0.017
Tipranavir, yes	3 (37.5)	1 (9.1)	0 (0.0)	4 (16.7)	0.135
Ritonavir, yes	7 (87.5)	10 (90.9)	2 (40.0)	19 (79.2)	0.094
Raltegravir, yes	8 (100.0)	9 (81.8)	0 (0.0)	17 (70.8)	<0.001
Dolutegravir, yes	7 (87.5)	4 (36.4)	1 (20.0)	12 (50.0)	0.023
Maraviroc, yes	7 (87.5)	3 (27.3)	0 (0.0)	10 (41.7)	0.001
Enfuvirtide	4 (50.0)	1 (9.1)	0 (0.0)	5 (20.8)	0.035
Zidovudine/lamivudine, yes	7 (87.5)	11 (100.0)	4 (80.0)	22 (91.7)	>0.99
Abacavir/lamivudine/zidovudine, yes	3 (37.5)	3 (27.3)	1 (20.0)	7 (29.2)	0.559
Tenofovir DF/emtricitabine, yes	8 (100.0)	9 (81.8)	5 (100.0)	22 (91.7)	>0.99
Abacavir/lamivudine, yes	7 (87.5)	7 (63.6)	2 (40.0)	16 (66.7)	0.141
Tenofovir DF/emtricitabine/efavirenz, yes	1 (12.5)	4 (36.4)	3 (60.0)	8 (33.3)	0.141
Tenofovir DF/emtricitabine/rilpivirine, yes	5 (62.5)	1 (10.0)[b]	0 (0.0)	6 (25.0)	0.008
Tenofovir DF/emtricitabine/cobicistat/elvitegravir, yes	3 (37.5)	0 (0.0)[b]	0 (0.0)[c]	5 (20.8)	0.039
Abacavir/lamivudine/dolutegravir, yes	4 (50.0)	1 (9.1)	0 (0.0)	5 (20.8)	0.039

Tenofovir DF = tenofovir disoproxil fumarate.
  [a] n = 23 for tenofovir DF/emtricitabine/rilpivirine and abacavir/lamivudine/dolutegravir, n = 22 for tenofovir DF/emtricitabine/cobicistat/elvitegravir. Azerbaijan did not provide data for the combinations of tenofovir DF/emtricitabine/rilpivirine, tenofovir DF/emtricitabine/cobicistat/elvitegravir, and abacavir/lamivudine/dolutegravir and Armenia did not provide data on tenofovir DF/emtricitabine/cobicistat/elvitegravir.
  [b] n = 10.
  [c] n = 4.

Table 5
Antiretroviral treatment initiation threshold for CD4+ T cell count according to country income (as of 2015, after the change in major guidelines).

Income	CD4+ T cells		
	<350/μl	<500/μl	Any
Lower-middle	Kosovo	Armenia	Georgia
	Uzbekistan	Kyrgyz Republic Moldova	
Upper-middle	Albania	Bosnia and Herzegovina	Turkey
	Azerbaijan Bulgaria FYR of Macedonia Montenegro Serbia	Kazakhstan	Romania
High	Russian Federation		Croatia Czech Republic Estonia Hungary Poland Slovak Republic Slovenia
Total	9/24 (37.5%)	5/24 (20.8%)	10/24 (41.7%)

FYR, Former Yugoslav Republic.

governments and health insurance systems, followed by international funds (4/24, 16.7%) and international funds and government (3/24, 12.5%). More than half of the countries (13/24, 54.2%) reported being a beneficiary of the Global Fund to Fight AIDS, Tuberculosis and Malaria. Significantly more lower-income countries (5/5, 100%) and upper-middle-income countries (8/11, 72.7%) were beneficiaries of the Global Fund compared to high-income countries (0/8, *p* < 0.001).

Stock-outs were reported by nine of 23 countries (39.1%); Azerbaijan did not provide any data for stock-outs. Three countries had stock-outs once a year and one country had stock-outs twice a year. Five countries experienced stock-outs very rarely.

The frequencies of testing for HIV RNA, CD4+ T cell count, and biochemical parameters are shown in Table 7.

Thirteen countries (Slovenia, Romania, Czech Republic, Bulgaria, Croatia, Bosnia and Herzegovina, Georgia, Estonia, Moldova, Uzbekistan, Kazakhstan, Russian Federation, and Armenia) reported data for the HIV continuum of care analysis for 2014. There were significant variations between countries in terms of the methodologies used for calculations of the elements of continuum of care. Therefore the results given here are not comparable with each other. Nine countries (Armenia, Czech Republic, Estonia, Georgia, Moldova, Kazakhstan, Romania, Russian Federation, and Uzbekistan) used the UNAIDS tool 'Spectrum' as an estimation method (Anon, 2016a). Slovenia made a rough estimation. Croatia used the European Centres for Disease Prevention and Control (ECDC) tool (Anon, 2015) and Bosnia and Herzegovina used the total reported number of PLWHIV. Estonia and Moldova did not report the definition of undetectable HIV RNA. The cut-off for undetectable viral load was <20 copies/ml for Slovenia and Czech Republic, <40 copies/ml for Bulgaria and Bosnia and Herzegovina, <50 copies/ml for Kazakhstan, Serbia, Romania, and the Russian Federation, <250 copies/ml for Armenia, <400 copies/ml for Croatia, <500 copies/ml for Uzbekistan, and

Table 6
First-line combinations in 22 countries of Eastern and Central Europe, 2014.

First-line combination	High income countries n = 8 (%)	Upper-middle income countries n = 10 (%)	Lower-middle income countries n = 4 (%)	Total n = 22 (%)	p-Value
Non-nucleoside analogue combinations					
Tenofovir + emtricitabine + efavirenz	2 (25.0)	9 (81.8)[a]	4 (100.0)	15 (68.2)	0.004
Abacavir + lamivudine + efavirenz	3 (37.5)	2 (20.0)	0 (0.0)	5 (22.7)	0.182
Zidovudine + lamivudine + efavirenz	0 (0.0)	4 (40.0)	2 (50.0)	6 (27.3)	0.053
Tenofovir + emtricitabine + rilpivirine	5 (62.5)	0 (0.0)	0 (0.0)	5 (22.7)	0.003
Abacavir + lamivudine + rilpivirine	4 (50.0)	0 (0.0)	0 (0.0)	4 (18.2)	0.015
Tenofovir + emtricitabine + nevirapine	1 (12.5)	1 (10.0)	2 (50.0)	4 (18.2)	0.264
Abacavir + lamivudine + nevirapine	1 (12.5)	0 (0.0)	0 (0.0)	1 (4.5)	0.546
Zidovudine + lamivudine + nevirapine	0 (0.0)	1 (10.0)	2 (50.0)	3 (13.6)	0.042
Protease inhibitor combinations					
Tenofovir + emtricitabine + darunavir/r	6 (75.0)	2 (20.0)	0 (0.0)	8 (36.4)	0.005
Abacavir + lamivudine + darunavir/r	6 (75.0)	2 (20.0)	0 (0.0)	8 (36.4)	0.005
Tenofovir + emtricitabine + lopinavir/r	2 (25.0)	2 (20.0)	0 (0.0)	4 (18.2)	0.467
Abacavir + lamivudine + lopinavir/r	2 (25.0)	2 (20.0)	0 (0.0)	4 (18.2)	0.467
Tenofovir + emtricitabine + atazanavir/r	2 (25.0)	1 (10.0)	0 (0.0)	3 (13.6)	0.408
Abacavir + lamivudine + atazanavir/r	2 (25.0)	1 (10.0)	0 (0.0)	3 (13.6)	0.408
Zidovudine + lamivudine + atazanavir/r	1 (12.5)	0 (0.0)	0 (0.0)	1 (4.5)	0.546
Integrase inhibitor combinations					
Tenofovir + emtricitabine + raltegravir	4 (50.0)	1 (10.0)	0 (0.0)	5 (22.7)	0.036
Abacavir + lamivudine + raltegravir	4 (50.0)	1 (10.0)	0 (0.0)	5 (22.7)	0.036
Tenofovir + emtricitabine + dolutegravir	3 (37.5)	1 (10.0)	0 (0.0)	4 (18.2)	0.133
Abacavir + lamivudine + dolutegravir	3 (37.5)	1 (10.0)	0 (0.0)	4 (18.2)	0.133
Tenofovir + emtricitabine + cobicistat + elvitegravir	3 (37.5)	0 (0.0)	0 (0.0)	3 (13.6)	0.078

[a] For tenofovir/emtricitabine/efavirenz the number of responding countries is 23. Armenia did not provide data for this table.

Table 7
HIV RNA and CD4+ T cell testing frequency and routine follow-up testing.

Patients not on ART	CD4+ T cells
	Twice a year 50.0%
	Every 3 months 25.0%
	Every 4 months 20.8%
	Once a year 4.2% (Albania)
	HIV RNA
	Twice a year 45.8%
	Every 3 months 20.8%
	Every 4 months 20.8%
	Once a year 12.5% (Russian Federation, Uzbekistan, Albania)
Patients who have recently initiated ART	CD4+ T cells
	First month, then every 3 months 45.8%
	Twice a year 20.8%
	Every 3 months 20.8%
	Every 4 months 12.5%
	HIV RNA
	First month, then every 3 months 37.5%
	Twice a year 20.8%
	Every 4 months 20.8%
	Every 3 months 16.7%
	Once a year 4.2% (Albania)
Patients stable on ART	CD4+ T cells
	Twice a year 60.9%
	Every 4 months 17.4%
	Once a year 13.0%
	Every 3 months 8.7%
	HIV RNA
	Twice a year 73.9%
	Once a year 13.0%
	Every 4 months 8.7%
	Every 3 months 4.3%
Routine follow-up testing	
Test	Countries that run the test/calculation (%)
eGFR	47.8
Framingham score	43.5
Liver function tests	100.0
Renal function tests	95.8[a]
Glucose	100.0
Vitamin D	30.4

ART, antiretroviral therapy; eGFR, estimated glomerular filtration rate.
[a] Montenegro reported no regular testing for renal function.

Table 8
Data reported from Central and Eastern European countries on the continuum of care for HIV for 2014.[a,b]

	Armenia	Georgia	Moldova	Uzbekistan	Kazakhstan	Estonia	Russia	Bulgaria	Romania	Bosnia and Herzegovina	Slovenia	Croatia	Czech Republic
PLWHIV	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Diagnosed	39%	56%	38%	52%	85%	85%	78%	64%	98%	77%	58%	76%	51%
Linked to care	33%	41%	17%		25%	51%	58%	31%	88%	74%	53%	66%	31%
On ART	19%	34%		23%	25%	32%	19%	23%	87%	53%	50%	62%	31%
Undetectable	16%	29%			13%		16%	20%	51%	50%	48%	54%	24%

PLWHIV, people living with HIV; ART, antiretroviral therapy.

[a] The data are not directly comparable across countries because there were methodological differences between countries regarding the method of estimation for the number of PLWHIV, the number of PLWHIV on ART, and the viral load cut-off definition for being undetectable.

[b] For the definitions and methodology used for each element of the continuum, please refer to the Methods section.

<1000 copies/ml for Georgia. Ten countries reported the percentage of undetectable HIV viral load among all PLWHIV. Of the five EU countries, three reported having an undetectable rate close to or above 50%, whereas among the five non-EU countries, only one reported this percentage at 50%. Table 8 shows the elements of the continuum for the 13 countries that provided data for the continuum.

Seventeen countries had data for hepatitis B virus surface antigen (HBsAg) prevalence and 18 countries for antibody to hepatitis C virus (anti-HCV) prevalence in the HIV-infected population. HBsAg positivity rates were lowest in Kosovo (0%) and the Kyrgyz Republic (0.02%) and highest in Kazakhstan (30%) and Bosnia and Herzegovina (20%), with a mean rate of 10.3% for the whole region. Anti-HCV rates were lowest in Kosovo (0%) and the FYR of Macedonia (1%) and highest in Azerbaijan (51.7%), Kazakhstan (50%), the Russian Federation (48%), and Georgia (39%), with a mean rate of 23.4% for the whole region. Estonia reported 22% prevalence for HBsAg and 71% for anti-HCV, with a note that the data were extracted from research and did not represent national data.

Table 9 shows the availability of drugs for hepatitis B and C in the countries of Central and Eastern Europe. Several of the new drugs for hepatitis C were reported to be available in Bulgaria, Czech Republic, Georgia, Russian Federation, Slovak Republic, Slovenia, Poland, and Turkey. Direct-acting antivirals (DAAs) were not available in seven countries (Albania, Serbia, Kosovo, FYR of Macedonia, Montenegro, Bosnia and Herzegovina, and Kazakhstan).

Discussion

This appears to be the largest report on HIV care in Central and Eastern Europe to date: the survey included approximately 80% of the countries in the WHO defined regions. The results of this study show that there are significant variations between countries regarding the epidemiology of HIV infection and HIV care and that many countries in the region and especially in Eastern Europe are far from reaching the UNAIDS 2020 goal of 90–90–90.

The data presented in the report suggest that despite efforts to scale up testing, late diagnosis and late presentation of HIV cases are still major problems in the region, with late presentation rates as high as 60–80% in Bosnia and Herzegovina, Georgia, and Albania. Furthermore, no significant difference between regions and income levels was found regarding late presentation rates. Progression to AIDS and death is significantly high among late presenters, especially within the first year of diagnosis (Mocroft et al., 2013; Chadborn et al., 2006). Achieving and maintaining undetectable viremia with ART is associated with a good prognosis in late presenters, regardless of the CD4+ T cell count (Jevtović et al., 2009), underlining the importance of early diagnosis and treatment. Almost 50% of PLWHIV in Europe were reported to be late presenters between 2010 and 2013, ranging from >60% of heterosexual men or people of African origin to almost 39% of MSM and female PWID (The late presenters working group in COHERE in EuroCoord, 2015). Even in well-established indicator conditions, the testing rates across Europe were found to be low, with many missed opportunities for early diagnosis (Raben et al., 2015), and the overall late presentation rates across Europe between 2010 and 2013 did not change significantly over time (The late presenters working group in COHERE in EuroCoord, 2015). In addition, late presentation rates increased between 2000 and 2011 among female heterosexuals and male PWID in Southern Europe and in male and female PWID in Eastern Europe (Mocroft et al., 2013). While the ECDC reported a 58% increase in the overall number of tests performed in the region between 2007 and 2016, the rates for late presentation (51%) and advanced disease (30%) still remained high in 2016 (European Centre for Disease Prevention and Control/ WHO Regional Office for Europe, 2017).

Although the data in this report do not provide any insight into the factors related to late presentation, they have been described in

Table 9
Available drugs for hepatitis B and hepatitis C treatment in 23 Central and Eastern European countries for 2014.[a]

Drugs for hepatitis B	Number	Drugs for hepatitis C	Number
Interferon alpha	11	Interferon alpha	11
Peg-interferon alpha	17	Peg-interferon alpha	22
Lamivudine	20	Ribavirin	22
Emtricitabine	11	Boceprevir	11
Telbivudine	7	Simeprevir	9
Adefovir	6	Telaprevir	10
Tenofovir disoproxil fumarate	17	Sofosbuvir	9
Entecavir	11	Daclatasvir	7
		Ombitasvir/paritaprevir/ritonavir	8
		Sofosbuvir/ledipasvir	6
		Ombitasvir/paritaprevir/ritonavir + dasabuvir	8

[a] Azerbaijan reported no data for hepatitis B and hepatitis C drugs.

other reports as a low level of testing due to obstacles such as fear of stigma, reduced accessibility of tests, lack of focused screening programmes for key populations, and low perception of risk (Network of Low Prevalence Countries in Central and Southeast Europe (NELP), 2014). The ECDC has reported that testing rates among key populations are very low and only a few countries report testing data for these populations (Network of Low Prevalence Countries in Central and Southeast Europe (NELP), 2014). The lower than expected rates of targeted screening among key populations in Central and Eastern European countries in the present study, especially MSM and sex workers, suggests a need for a more focused and novel approach for specific groups with a high risk of acquiring HIV infection to remove obstacles to testing. HIV testing is reported to be cost-effective if HIV prevalence exceeds 0.1% (Paltiel et al., 2005; Sanders et al., 2005); thus, screening of the general population, such as premarital testing, rather than screening of key populations in low-prevalence countries such as Turkey and Azerbaijan, may be an unwise use of resources. Although the rising number of new HIV diagnoses in the region may be attributed in part to the increasing number of annual HIV tests, a targeted screening strategy rather than screening of low-risk populations may be a more favourable and effective approach for achieving the UNAIDS targets.

While overall the main mode of HIV transmission seemed to be sex between men, the major variations by geographical area is an indicator of the diversity in the epidemiology of HIV in Europe. All countries reporting injecting drug use as the major route of HIV transmission were in Eastern Europe, all with high rates of hepatitis C virus co-infection. The ECDC reported that the most common mode of transmission was sexual transmission between men in the EU/European Economic Area (EEA) and heterosexual contact and injecting drug use in the Eastern European countries (European Centre for Disease Prevention and Control/WHO Regional Office for Europe, 2017). Recent reports have suggested an increasing trend in transmission through sex between men in the region (European Centre for Disease Prevention and Control/WHO Regional Office for Europe, 2017; Gökengin et al., 2016; Pharris et al., 2015), and the numbers for transmission through sex between men may be underestimations due to the high stigma as well as laws and sanctions against gay people in some countries in the region (Eurasian Coalition, 2015; Santos et al., 2017; Takacs et al., 2013).

Almost all countries had developed national guidelines, and those without guidelines reported the use of the two major guidelines (EACS and DHHS). However, despite the change in the recommendations of major guidelines following the publication of the results of the START study (INSIGHT START Study Group et al., 2015), i.e., to start ART in all people diagnosed with HIV regardless of CD4+ T cell count, more than half of the countries were not able to act fast enough to comply with this recommendation (Anon, 2017; Panel on Antiretroviral Guidelines for Adults and Adolescents, 2017; Anon, 2016b). About one third of the countries still required the patient to have a CD4+ T cell count under 350 cells/μl before initiating ART, regardless of the recommendation in EACS, DHHS, and WHO guidelines. All but one of these countries was a beneficiary of the Global Fund, which had already ended in 2014 or 2015 or would be over by 2018. Although the scene has started to change in Europe recently, with the number of countries initiating treatment regardless of the CD4+ T cell count increasing from four in 2014 to 30 in 2016, only two countries (Montenegro and Serbia) included in the present study had changed their ART initiation policy in agreement with the guidelines in 2016 and two other countries (Bulgaria and Uzbekistan) increased their CD4+ T cell threshold from <350 to <500 cells/μl (EDC Special Report, 2017; personal communication with Teymur Noori of the ECDC). Even in the EU/EEA, one out of six people were still not on treatment in 2016 (ECDC Special Report, 2016).

Although ART was reported to be offered free of charge in all countries, the unavailability of newer first-line drugs with better tolerability and lower short- and long-term toxicity, as well as the lack of single-tablet regimens, which are associated with better adherence in many countries, seems to be another major obstacle for early and effective treatment of HIV infection. This was reflected in the choice of treatment regimens, with high-income countries significantly more often choosing the regimens including newer drugs compared to low- and middle-income countries. Besides, although the study did not provide information on the use of toxic drugs such as didanosine (ddI) and stavudine (d4T), their continuing availability is alarming. It is well-established that a simpler, less toxic treatment, with fewer drug–drug interactions, is the key to greater uptake and better adherence, which ultimately results in higher rates of viral suppression (Gulick, 2014; Cihlar and Fordys, 2016).

The high prevalence of hepatitis C in Eastern European countries correlates well with the major transmission route and high screening rates reported by Lazarus et al. for that region (Lazarus et al., 2016). Unfortunately, similar to the findings of Lazarus et al., the availability of new hepatitis C drugs is low in these countries, with few of them having access to DAAs.

The standards of HIV care require regular and close follow-up of HIV patients. Follow-up includes both markers of HIV, such as CD4 + T cell count and HIV RNA testing, as well as tests for comorbidities and co-infections that may complicate HIV infection and vice-versa. All guidelines have clear definitions for standards of HIV care and have similar recommendations for follow-up of PLWHIV (Anon, 2017; Panel on Antiretroviral Guidelines for Adults and Adolescents, 2017 Although most countries reported having national guidelines or using major guidelines, marked discrepancies were noted between countries regarding the follow-up of HIV patients.

Antiretroviral resistance testing is not a common approach in the Eastern European region due to the unavailability of the procedure or high costs (Kowalska et al., 2016; Lazarus et al., 2016). Thus, the reported low frequency of HIV RNA testing in some countries may prevent early intervention in the case of virological failure, resulting in the development of resistant virus. In addition, the lack of regular testing/calculations for markers of comorbidities may hamper efforts for the prevention or early treatment of major comorbidities that may occur due to the aging population of PLWHIV or adverse effects of drugs or drug–drug interactions.

Although it is difficult to comment on the continuum of care graphics due to considerable methodological differences between countries, the most common breakpoint in the continuum of care seems to be between the estimated number of PLWHIV and those who are diagnosed. While it has been rather easy to reach the 'third 90', which is having an undetectable viral load (even in resource-limited settings), the major obstacle is to achieve the 'first and second 90', which are diagnosis and the initiation of ART (Jevtović et al., 2014). Also, 12 out of 24 countries could not provide any data for the continuum of care. According to UNAIDS, out of an estimated 1.5 million PLWHIV in Eastern Europe and Central Asia, 67% know their HIV status, 21% are on ART, and 19% are virally suppressed (UNAIDS, 2016). Drew et al. (Drew et al., 2017) reported that among 16 EU and non-EU countries, 77% and 45% (overall 76%) of PLWHIV had been diagnosed, 62% and 21% (overall 60%) of those diagnosed were on treatment, and 55% and 14% (overall 53%) of those on treatment were virally suppressed, respectively, which corresponds well with the present study results. The data from the present study support the conclusions of the 2017 ECDC report on the continuum of HIV care (Monitoring implementation of the Dublin Declaration on Partnership to fight HIV/AIDS in Europe and Central Asia: 2017 progress report), which also stressed the high proportion of people with HIV who did not know their status or

who were diagnosed late. Similar to the present study findings, non-EU countries had lower viral suppression rates among all people estimated to be living with HIV compared to EU countries (EDC Special Report, 2017).

A modelling study looking at the potential impact on HIV incidence and prevalence of needle and syringe programmes (NSP), opioid substitution therapy (OST), and ART in the Russian Federation, Estonia, and Tajikistan, reported that even if all three interventions were combined, reducing HIV incidence to less than 1% and prevalence to less than 20% would be very difficult (Vickerman et al., 2014).

UNAIDS announced that the pace of decline in new HIV infections was far too slow to reach the Fast-Track Target agreed upon by the United Nations General Assembly in 2016, which was to reduce the number of new infections to fewer than 500 000 per year by 2020 (UNAIDS Data, 2017). The low levels of ART coverage, low viral suppression rates, and improper testing strategies, combined with the low availability of NSP and OST in Eastern European countries (Lazarus et al., 2016), imply that we are still a long way off the set targets.

This study has some limitations, as outlined below.

(1) The questionnaire did not include all aspects of HIV care.
(2) The respondents of the survey were not randomly selected; the responses may be biased.
(3) Only one or two HIV specialists from each country were included in the survey, and although the questions were intended to assess country-specific approaches to HIV care, there may have been respondent-specific interpretations and the data may not necessarily reflect the actual HIV care approach of the country.
(4) Some data were extracted from the personal records of the respondents or from various surveys and may not represent national data.
(5) The comparison of small numbers may have hampered the accuracy of statistical analyses.
(6) The time to find contacts in each country, to start and continue correspondence, and to collect data was very long, and some data might have changed between the time the questionnaire was completed and the time the manuscript was published.

Conclusions and the way forward

Many countries in this region, especially those with a low income, are highly dependent on donor funding. However, this support has started to fade out and national governments will have to mobilize their local resources to compensate for this. The right of access to affordable, tolerable, durable, and sustainable ART regimens, as well as to prevention, diagnosis, and treatment of comorbidities and co-infections, is the key element for the right to health and to control the HIV epidemic. Unfortunately, many of those elements seem to be lacking in low-income and several middle-income countries in the region.

There was a clear correlation between the World Bank gross national income classification of countries and several elements of HIV care. Countries with a higher income had a tendency to initiate ART earlier, had better access to novel drugs, and tended to prefer new fixed-dose formulations and new drug classes as first-line treatment more commonly than lower income countries. Although all countries provided drugs free of charge, the high level of donor dependency of lower-income and several upper-middle-income countries may be one of the major reasons for the unavailability of newer drug classes and drug formulations and the discrepancies between countries regarding the regular follow-up and care of HIV

patients. Even if longer term funding is secured, many people, mostly those in key populations, will continue to face many obstacles to accessing HIV care and prevention, which also needs to be addressed.

There are major disparities in the provision of HIV care among sub-regions in Europe, which should be addressed. More attention in terms of funding, knowledge and experience sharing, and capacity building is required for the resource-limited settings of Central and Eastern Europe. The exact needs should be defined and services scaled up in order to achieve a standard level of care and provide an adequate and sustainable response to the HIV epidemic in this region.

Conflict of interest

The authors of the manuscript declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.ijid.2018.03.007.

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