

The emerging and re-emerging human immunodeficiency virus epidemics in Europe

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Abstract

We provide a summary of the current status of the human immunodeficiency virus (HIV) epidemic, including data on the transmission of drug-resistant virus in the European Region of the WHO. The review was conducted by searching the reports of the European Centre for Disease Prevention and Control and the United Nations General Assembly Special Session country reports to identify the number of HIV cases reported in 2002–2011, the number of HIV tests performed, and the results of the most recent HIV surveys in at-risk groups. In the West, a 5-year linear trend analysis suggests an increase in the number of reported HIV cases in Belgium, Greece, and Iceland, and a decline in The Netherlands, Ireland, Portugal, Switzerland, and the UK. In the Centre, the number of reported cases increased in Bulgaria and Turkey, and in the East, the number of reported cases increased in Armenia, Georgia, and Ukraine. Estonia and Latvia reported a significant downward trend. HIV transmission in men who have sex with men (MSM) and heterosexual transmission accounted for, respectively, 40% and 38% of newly reported HIV cases in the West in 2011, whereas the epidemic in the Centre is predominantly concentrated in MSM. Although injection drug use remains the key driving force of the epidemic in the East, there is increasing evidence of sexual transmission from the core groups of injection drug users, and increasing spread within MSM. The pattern of transmitted drug resistance (TDR) is heterogeneous across Europe; a significant number of clusters of TDR have been recently observed in several European countries.

Keywords: Epidemic, Europe, HIV, HIV tests, trend

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Introduction

Human immunodeficiency virus (HIV) infection is one of the major public health issues in Europe. According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), in 2011 900 000 (830 000–1 000 000) adults and children were living with HIV in the countries of western and central Europe, and 1 400 000 (1 100 000–1 800 000) in the countries of eastern Europe and Central Asia [1]. In 2011, an estimated 30 000 (21 000–40 000) new HIV infections occurred in western and central Europe, and 7000 (6100–7500) people died of AIDS. In the same year, it was estimated that there were 140 000 (91 000–210 000) new HIV infections in East and Central Asia, and 92 000 (63 000–120 000) deaths from AIDS.

According to the data of the European Centre for Disease Prevention and Control (ECDC), 53 974 HIV cases were reported in the European Region of the WHO (WHO EURO) (West—Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, The Netherlands, Portugal, Spain, Sweden, the UK, Iceland, Norway, Andorra, Israel, Monaco, San Marino, and Switzerland; East—Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan; Centre—Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Hungary, the Former Yugoslav Republic of Macedonia, Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia, Turkey) in 2011 [2]. Of these, 48.5% were reported

in the West, 45.9% in the East, and 5.6% in the Centre. In addition, 67 317 HIV cases were reported in the Russian Federation in 2011. In a decade (comparing the year 2011 with the year 2002), the absolute number of reported HIV cases increased by 89.4%, suggesting a changing pattern of the HIV epidemic across the Region [2,3].

The main modes of HIV transmission vary substantially across the Region. The dominant reported mode of transmission in the East in 2011 was heterosexual (56.7%), whereas, in the West and the Centre, transmission resulting from male-to-male sex predominated (40.1% and 27.3%, respectively) [2]. Notable differences exist across the Region with respect to the male-to-female ratio of the reported HIV cases; in 2011, the ratios were 1.3 : 1 in the East, 2.9 : 1 in the West, and 4.3 : 1 in the Centre.

There are also substantial regional differences in HIV-related morbidity: whereas the rates of reported AIDS cases were 1.0/100 000 and 0.4/100 000 in 2011 in the West and Centre, respectively, the rate was as high as 5.7/100 000 in the East [2].

The aim of this article is to present the recent changes in the HIV epidemics in Europe, with a particular focus on the countries where significant increases and/or a high number of new HIV diagnoses have been reported or where decreases in the reported HIV cases have been recorded since 2002. We also briefly review recent data on the transmission of drug-resistant HIV in Europe.

Methods

We reviewed the reports of the ECDC (for the period 2007–2011) and the reports of the European Centre for the Epidemiological Monitoring of AIDS (for the period 2002–2006) to identify the number of reported cases of HIV in the period 2002–2011 and the number of HIV tests performed per 1000 population. The data on HIV testing had to be sought for the years 2000 and 2001, as a number of countries did not report this data for the year 2002.

Linear regression was performed with STATA V.11.0 to calculate the trend in the reported new HIV diagnoses in a 10-year period (from 2002 to 2011) and in a 5-year period (2007–2011) [4]. The United Nations General Assembly Special Session (UNGASS) country reports on HIV and Global AIDS Response Country Progress reports were reviewed to find the most recent data on HIV prevalence from cross-sectional surveys. The literature review was also conducted with PubMed. The terms included were those relating to HIV infection, resistance to antiretrovirals, and the selected countries. The search included MESH terms and text words

to enhance the retrieval of relevant studies. The language was limited to English, and we searched for manuscripts published since the year 2007.

The summaries of the HIV epidemic are provided for the following countries according to the WHO EURO classification of the European Region: West—Belgium, Greece, Portugal, the UK, Switzerland, France, Spain, Italy, and Germany; Centre—Albania, Bulgaria, Cyprus, Czech Republic, Slovenia, and Turkey; East—Estonia, Latvia, Lithuania, Azerbaijan, Armenia, Georgia, Moldova, Russian Federation, and Ukraine. The countries of Central Asia were not included in the narrative review.

HIV Surveillance Data

Figs 1–3 show the number of newly reported HIV cases per 100 000 population in the period 2002–2011 by region. There was a significant increase in the number of reported HIV cases in the Centre in both the 5-year period (2007–2011) and the 10-year period (2002–2011). In the West, there was a declining trend in the past 5 years; in the East, there was a significant increase in the past 10 years.

West: Continuing High HIV Transmission in Men Who Have Sex with Men (MSM)

Western European countries are considered to have a long-lasting, mature HIV epidemic; however, there has been little overall evidence of a reversal of the epidemic. In 2002, the rate of newly reported infections in the West was 6.5 per 100 000 inhabitants, whereas 10 years later the rate was the same (Fig. 1). Of 26 204 new infections reported in 2011, 74.4% were in males [2]. In 2011, 3905 AIDS cases and 955 deaths from AIDS were reported (Table 1). The most common AIDS indicator disease in 2011 was *Pneumocystis pneumonia* (diagnosed in 27.2% of AIDS cases), followed by oesophageal candidiasis and Kaposi's sarcoma.

The overall average rate of HIV infection in the West in 2011 was 4.1 times higher than that in the Centre [2]. As in other regions, there was considerable variation in the rates of HIV infection between countries and within countries. Sexual transmission was the main mode of transmission: sex between men accounted for 40.1% and sex between men and women for 37.9% of new infections in 2011 [2]. Several countries had a rate of reported infections in 2011 that was considerably higher than the average for the region (per 100 000 inhabitants: Belgium, 10.7; UK, 10.0, Portugal, 8.5; and Spain, 8.4). A formal 5-year and 10-year linear trend analysis of the rate of

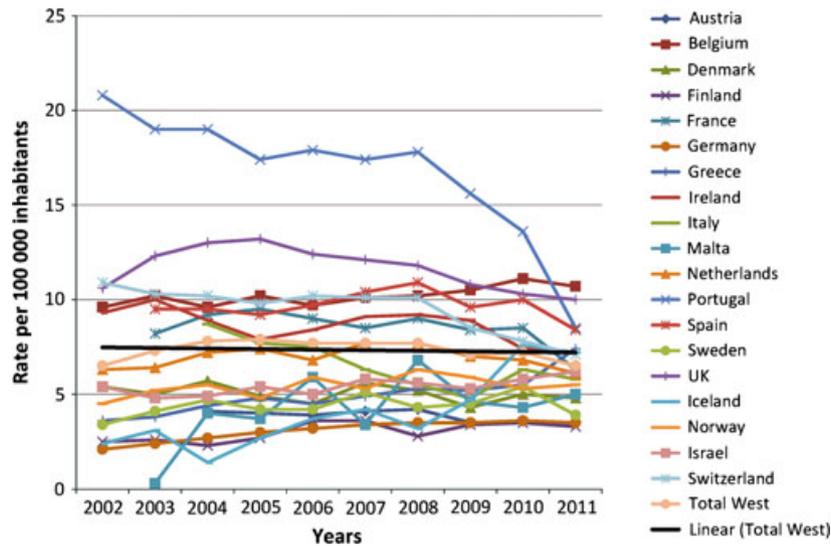


FIG. 1. Annual rates of reported HIV infections per 100 000 inhabitants in 19 countries of the WHO region of Western Europe (West) for the period 2002 to 2011. The black line represents a linear trend line for the region. Data source: ECDC/WHO Regional Office for Europe. HIV/AIDS surveillance in Europe 2011. Stockholm: ECDC; 2012.

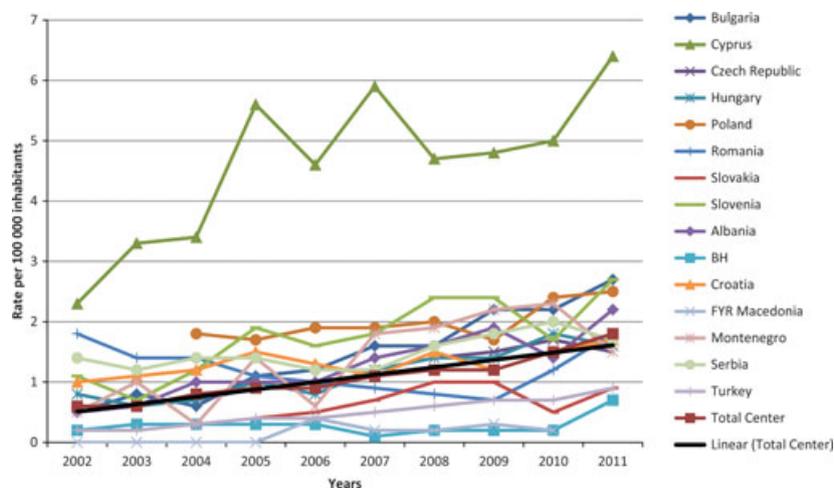


FIG. 2. Annual rates of reported HIV infections per 100 000 inhabitants in 15 countries of the WHO region of central Europe (Centre) for the period 2002 to 2011. The black line represents a linear trend line for the region. BH, Bosnia and Herzegovina. Data source: ECDC/WHO Regional Office for Europe. HIV/AIDS surveillance in Europe 2011. Stockholm: ECDC; 2012.

reported cases suggests an increasing trend in Belgium, Greece, and Iceland, a declining trend in The Netherlands, Ireland, Portugal, Switzerland, and the UK, and no change in Denmark, Finland, Germany, Israel, Malta, Norway, and Sweden. It is challenging to assess the 5-year or 10-year trend of reported HIV infections in Italy and Spain, as HIV case reporting in these two countries does not have national coverage [2].

In the West, a significant proportion of heterosexually acquired cases originated from persons from countries with a generalized HIV epidemic. For example, in 2011, >61.9% of

heterosexually acquired cases in Belgium were reported in persons originating from countries with a generalized epidemic [2]. However, the increasing number of newly reported infections in Belgium is mostly attributable to an increasing epidemic among MSM, whereas a decline in infections acquired through sex between men and women has been observed [2,5]. A recent venue-based cross-sectional study using time–location sampling found that the HIV prevalence in MSM who attended different types of venue ranged from 1.4% at younger MSM venues, to 4.9% at more general gay venues, to a high of 14.5% at cruising venues [6].

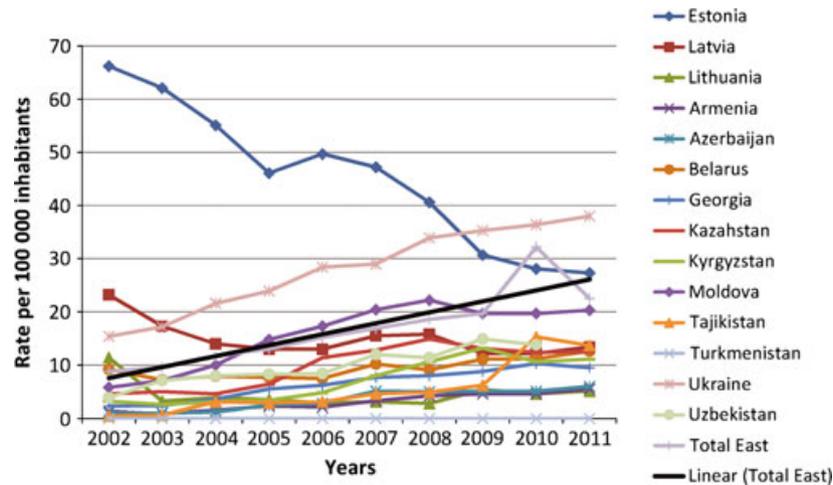


FIG. 3. Annual rates of reported HIV infections per 100 000 inhabitants in 14 countries of the WHO region of Eastern Europe and central Asia (East) for the period 2002 to 2011. The black line represents a linear trend line for the region. Data source: ECDC/WHO Regional Office for Europe. HIV/AIDS surveillance in Europe 2011. Stockholm: ECDC; 2012.

In Greece, the rate of new infections was 7.4/100 000 in 2011 [2]. An outbreak among injection drug users (IDUs) occurred in 2011, and was the main reason for a 35.7% increase in reported HIV cases in 2011 as compared with 2010 [2,7]. Of all cases reported to the ECDC ($n = 837$) in 2011, 84.9% were males, and MSM accounted for 34.1% of cases. The HIV prevalence among MSM was estimated to be 6.5% [8].

The declining trend in reported HIV infections in Portugal in recent years is mainly attributable to fewer infections among individuals acquiring HIV through heterosexual contact and injection drug use. However, Portugal is still a country with a relatively high annual rate of reported infections (8.5/100 000 in 2011); in 2011, 63.9% of 902 cases were reported as resulting from heterosexual contact, 27.0% in MSM, and 6.9% in IDUs [2]. There seems to be a discrepancy between the relatively low number of cases reported in MSM and the results of a survey based on snowball and Internet sampling that found an HIV prevalence of 11.0% [8].

There is a declining trend in reported HIV infections in the UK; however, the annual rate in 2011 (10/100 000) was still among the highest in the West [2]. This decreasing trend is explained mainly by fewer numbers of reported infections among those born outside of the UK. The highest rates were reported in MSM (47/1000) and the black African community (37/1000) [9]. Of 6280 new infections reported in 2011, 71.1% were in males, and the main transmission modes were sex between men (48%) and heterosexual contact (48%) [9]. However, the annual number of new HIV infections among MSM has been increasing since 2007, and reached 3010 cases in 2011. In a CD4-staged back-calculation model of HIV incidence, no evidence of a decline in incidence among MSM

was observed over the period 2001–2010, with between 2300 and 2500 new infections per year [10]. The estimated model-based calculations suggest a 5.3% prevalence of HIV infection in MSM [8].

Switzerland has had a decreasing annual rate of newly reported infections over the past 5 years, and the rate was 7.1/100 000 in 2011 [2]. There are, however, different dynamics between risk groups and time-spans, so the number of new HIV diagnoses among MSM rose until 2008 and has been declining since 2009. In persons with heterosexually acquired HIV infection, particularly among women, a decline in newly reported HIV infections has been observed since 2004. As in other European countries, the proportion of non-Swiss nationals among persons acquiring HIV through heterosexual contact was high (68%) as compared with the MSM group (40%) [11].

In France, the number of reported HIV infections in 2011 was 6.3/100 000 [2]. The epidemic is mainly driven by new infections among MSM. A population-based HIV-1 incidence modelling analysis for the period 2003–2008 showed a persistent and high incidence of HIV in MSM. In all other vulnerable populations, the HIV incidence declined [12].

The rate of new HIV infections in Spain in 2011 (8.4/100 000) was considerably higher than the average for the West [2]. In 2011, 2759 new HIV diagnoses were notified, mostly in men (83.4%), and the major mode of transmission was sex between men (53.7%). The prevalence of HIV among MSM was relatively high in both serosurveys (17.0%) and in an Internet-based survey (14.9%) [8].

Although the rate of newly reported infections in Italy has declined recently, the absolute number of notified cases is

TABLE 1. Summary of the human immunodeficiency virus (HIV)/AIDS epidemic in Europe

Characteristic	Region			
	West	Centre	East	All Europe
Estimated number of people living with HIV/AIDS in 2011 ^a	900 000 (range: 830 000–1 000 000) ^b		1.4 million (range: 1.1–1.8 million)	2.3 million
Total number of new diagnoses in 2011 and proportional contribution by regions ^c	48.5%	5.6%	45.9%	53 974
Rate of newly reported HIV cases in 2011 ^c	6.5/100 000	1.6/100 000	22.4/100 000	7.6/100 000
Trend in new diagnoses in the last 10 years ^c	Stable (no evidence of a decrease)	Increasing	Increasing	–
Proportion of male/female reported HIV cases	74/26	81/19	57/43	67/33
Major mode of transmission in 2011 ^c	Sex between men: 40.1% Heterosexual: 37.9% (>1/3 of heterosexually acquired infections are from migrants from countries with generalized HV epidemics) ^d	Sex between men: 27.3% ^d Heterosexual: 25.7%	Intravenous drug use: 37.6% Heterosexual: 56.7%	–
Number of reported AIDS cases in 2011	3905 ^f	736	6282 ^g	–
Trend in AIDS diagnosis	Considerable decline	Heterogeneous ^h	Increasing	–
Number of AIDS deaths	955	362	1359	–
Most common AIDS indicator diseases in 2011	<i>Pneumocystis pneumonia</i> (27.2%) Oesophageal candidiasis (14.1%) Kaposi's sarcoma (9.1%)	Wasting syndrome (28.4%) Pulmonary tuberculosis (19.4%) <i>Pneumocystis pneumonia</i> (14.6%)	Pulmonary tuberculosis (36.1%) Wasting syndrome (25.4%) Oesophageal candidiasis (22.6%)	–
Late presentation to care ⁱ	–	–	–	28.8% ^{k,l} ; 37.7% ^{k,l}
HIV infection among patients with tuberculosis in 2011 ^m	0–16.7% ⁿ	0–0.3% ^o	1.2–18.5% ^p	48.9% ^l ; 61.7% ^{k,l}

EU/EEA, European Union and European Economic Area countries.

^aUNAIDS Report on the Global AIDS Epidemic, 2012.

^bEstimate includes West and Centre.

^cEuropean Centre for Disease Prevention and Control report (data not available from Monaco, Russian Federation, Uzbekistan, and Liechtenstein).

^dSex between men probably under-reported.

^eFrom countries with generalized epidemics.

^fNo data from Sweden and Monaco.

^gNo data from Russia and Uzbekistan.

^hIncrease in Bulgaria, Hungary, Albania, and Turkey; decrease in Poland, Serbia, and Romania.

ⁱData from EU/EEA countries.

^jFewer than 200 CD4 cells per microlitre.

^kData from non-EU/EEA countries.

^lFewer than 350 CD4 cells per microlitre.

^mTuberculosis surveillance and monitoring in Europe 2013. Stockholm, European Centre for Disease Prevention and Control, 2013 (<http://www.euro.who.int/tuberculosis-surveillance-and-monitoring-2013>). Only countries with both reported percentage and with >50% of tuberculosis cases tested for HIV are included.

ⁿBelgium, Iceland, Israel, Malta, and Spain.

^oBulgaria, Montenegro, Slovakia, and Slovenia.

^pArmenia, Azerbaijan, Belarus, Estonia, Kazakhstan, Latvia, Moldova, Tajikistan, Ukraine, and Uzbekistan.

Countries of the West (n = 23): Andorra, Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, The Netherlands, Norway, Portugal, San Marino, Spain, Sweden, Switzerland, the UK.

Countries of the Centre (n = 15): Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Hungary, the former Yugoslav Republic of Macedonia, Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia, and Turkey.

Countries of the East (n = 15): Armenia, Azerbaijan, Belarus, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Tajikistan, Turkmenistan, Ukraine, and Uzbekistan.

higher because of the greater coverage of the surveillance system. There were 3461 cases notified in 2011, whereas in 2007 and 2002, 2227 and 1472 cases were reported, respectively. The epidemic in Italy has changed over time; there is a declining trend in reported infections in IDUs and an increasing number of sexually acquired HIV infections (via both heterosexual sex and sex between men) [13].

Germany has a relatively low annual rate of new infections (3.5/100 000) [2]. According to a report of the Robert Koch Institute, the modelled estimated annual number of new HIV infections increased from approximately 2000 in 2001 to approximately 3400 in 2007, and then declined to 2700 in 2011 [14]. New infections continue to be mostly associated with MSM. Data modelling suggests that the HIV incidence among MSM started to decline as of 2007 [14]. The HIV prevalence in MSM is estimated to be between 5.0% and 7.5% [14].

Centre: Low-level HIV Epidemics but Evidence of Increases in Transmission

In 2011, the rate of newly reported infections in the Centre was 1.6 per 100 000 inhabitants as compared with 0.6 in 2002 (Fig. 2). Of 2997 new infections reported in 2011, 79.1% were in males [2]. Linear 10-year trend analysis suggested significant increases in the numbers of reported cases in all countries of the Centre except for Romania and Bosnia and Herzegovina, and a 5-year trend analysis showed significant increases in Bulgaria and Turkey.

In 2011, there were 736 newly reported cases of AIDS and 362 cases of deaths from AIDS (Table 1). The most common AIDS indicator disease in 2011 was wasting syndrome (diagnosed in 28.4% of AIDS cases), followed by pulmonary tuberculosis and *Pneumocystis pneumonia*.

In 2011, the highest number of reported HIV cases in the Centre was in Cyprus (6.4/100 000), followed by Bulgaria and Slovenia (2.7/100 000) [2]. In 2011, the male-to-female ratio in newly reported HIV cases ranged from 2.4 : 1 in Romania to 15.3 : 1 in Slovakia.

HIV prevalence data in the UNGASS country reports for 2010–2011 were not available for Albania, Cyprus, and Turkey.

In Albania, 2.2 cases of HIV were reported per 100 000 population in 2011, which is a steady increase from the 0.7 cases reported in 2002 [2,3]. The most commonly reported mode of transmission in newly reported cases in 2011 was heterosexual transmission (83.1%), and the male-to-female ratio in newly reported cases was 2.7 : 1. A study using convenience sampling conducted in 2008 in Tirana in 90 female sex workers (FSWs) found an HIV prevalence of 1.1% [15]. In the same year, respondent-driven sampling (RDS) surveys found no HIV cases among IDUs, whereas the HIV prevalence among MSM was 1.8% [16].

The most common modes of transmission in newly reported HIV cases in Bulgaria in 2011 were heterosexual transmission (44.3%) and injection drug use (31.3%) [2]. The highest measured HIV prevalence in surveys conducted in 2009 was in IDUs (7.1%), followed by MSM (0.6%) [17]. This might imply an increase in the HIV prevalence in IDUs, as a survey conducted in 2003 in 773 IDUs in Sofia using convenience sampling found that 0.5% of IDUs were infected [18].

The rate of new HIV infections in Cyprus in 2011 (6.4/100 000) was considerably higher than in 2002 (2.3/100 000) [2,3]. MSM contributed most of the newly reported HIV cases (50.0%), followed by heterosexuals (40.7%).

The vast majority of newly diagnosed HIV cases in the Czech Republic in 2011 were MSM (73.9%) [2]. The most recent surveys, performed in 2010, found HIV prevalence rates of 0.2% in IDUs, 4.8% in MSM, and 0.1% in FSWs [19]. Earlier studies performed in the mid-2000s in several cities using convenience sampling in 585 FSWs and 462 IDUs found HIV prevalence rates of 0.7% and 0.2%, respectively [20].

Sex between men was the most common HIV transmission category (63.6%) in 2011 in Slovenia, followed by heterosexual transmission (14.5%). [2]. The HIV prevalence among MSM was 2.2% according to sentinel surveillance and 5.1% in a survey using time–location sampling, both conducted in 2009 [21,22].

The reported rate of HIV infection in Turkey in 2011 was 0.9/100 000. The vast majority of cases in 2011 had an unknown mode of transmission reported (60.4%), followed by heterosexual contact (38.3%). Although no case of HIV in MSM was reported in 2011, the male-to-female ratio in newly reported cases was 2.9 : 1.

East: Transmission from IDUs Sustains the Heterosexual Epidemic

In 2011, the rate of newly reported infections in the East was 22.4/100 000, which was markedly higher than a decade previously (8.8/100 000 in 2002) (Fig. 3). Of 24 773 HIV infections reported in 2011, 57.4% were in men [2]. All countries of the East registered a significant increase in newly diagnosed HIV cases in the past 10 years, with the exception of Estonia and Latvia, which had a significant downward trend (no significant difference was found for Lithuania). Similarly, a significant 5-year decline was found in Estonia and Latvia, and increases were found in Armenia, Georgia, and Ukraine. In 2011, the highest number of newly diagnosed HIV cases reported to the ECDC from the East was in Ukraine (38.0/100 000), followed by Estonia (27.3/100 000) [2]. The Russian Federation reported 67 317 new HIV cases in 2011. The male-to-female ratio ranged from 1.1 in Belarus and Moldova to 4.1 in Lithuania. The most common transmission mode was heterosexual transmission (56.7%), followed by injection drug use (37.6%).

In the year 2011, 6282 AIDS cases and 1359 deaths from AIDS were reported (Table 1). The most common AIDS indicator disease in 2011 was pulmonary tuberculosis (diagnosed in 36.1% of AIDS cases), followed by wasting syndrome and oesophageal candidiasis.

In the Baltic, the number of reported HIV cases in Estonia dropped from the high level of 66.0/100 000 in 2002 to 27.3/100 000 in 2011 [2,3]. In 2011, 65.3% of cases had an unknown mode of transmission and/or transmission mode other than injection drug use, sex between men, heterosexual transmission, or mother-to-child transmission, and 18.9% of cases were reported as in IDUs [2]. RDS surveys conducted in IDUs in Tallinn from 2005 found an HIV prevalence of slightly over 50% (54% in 2005, 55% in 2007, and 51% in 2009). However, the HIV prevalence declined among new injectors (34% in 2005, and 16% in 2009), reflecting the implementation of an expanded needle and syringe exchange programme [23]. An HIV data triangulation project also found evidence for a decline in HIV transmission since mid-2000 [24].

Latvia reported 13.4 HIV cases per 100 000 population in 2011, the most frequent mode of transmission being heterosexual transmission (48.2%), followed by injection drug use (30.1%) [2]. Nonetheless, a study based on modelling and phylogenetic analyses revealed that more than half of the cases of heterosexual transmission in Latvia were caused by IDUs [25]. The highest measured HIV prevalence in 2011 was in FSWs (22.2%); the prevalence rates among IDUs and MSM were 11.2% and 7.8% [26].

In Ukraine, heterosexual transmission predominated among reported HIV cases in 2011 (59.1%), followed by injection drug use (38.0%) [2]. The highest HIV prevalence assessed in surveys in 2011 was in IDUs (21.5%, 2.5–43.8% per city), followed by FSWs (9.0%, 0–38.2% per city) and MSM (6.4%, 0–20.0% per city) [27]. In 2011, the HIV prevalence in pregnant women was 0.47%, although there were substantial regional variations, from 0.02% in the Zakarpattya region to 1.08% in Dnipropetrovsk. In spite of increases in the numbers of reported HIV cases in Ukraine in the past 10 years, the recently conducted HIV data triangulation study found evidence for a declining HIV incidence among IDUs and the potential for HIV spread among MSM, owing to low prevention coverage [28]. Additionally, it was found that male IDUs and MSM may be misclassified as heterosexual men in the case reporting system.

According to the Federal Statistics Agency of the Russian Federation, and as reported by the ECDC, 67 317 new HIV cases were registered in the Russian Federation in 2011 [2]. This is an increase as compared with the 62 581 cases reported to the ECDC for 2010 [2]. According to the latest available UNGASS report, in 2008–2009 the leading mode of transmission was injection drug use (62%).

In 2008–2009, the HIV prevalence rates were 2.6–61.1% in IDUs, 4.5–19.6% in FSWs, and 4.6–8.3% in MSM [29]. The HIV prevalence in pregnant women in Russia in 2009 was 0.5% [29].

In 2011 in Moldova, the rate of reported HIV cases was 20.3/100 000, with a male-to-female ratio of 1.1 : 1 [2]. The major reported mode of HIV transmission was heterosexual (85.0%), followed by injection drug use (8.5%). The HIV prevalence rates in IDUs in RDS surveys conducted in 2009 in Chisinau and Balti were 12.6% and 39.0%, respectively, whereas in the same cities they were 0.2% and 1.7% in MSM [30]. RDS surveys performed in 2009–2010 in FSWs found HIV prevalence rates of 6.9% in Chisinau and 24.7% in Balti [31]. In spite of a high number of HIV cases being reported as resulting from heterosexual transmission, a recently conducted HIV data triangulation found that two-thirds of recent HIV infections in 2010 resulted from transmission within and from the most at-risk groups [32].

In the countries of the southern Caucasus (Armenia, Azerbaijan, and Georgia), the rate of reported HIV cases was four to six times larger in 2011 (per 100 000 population: 5.5, 6.0, and 9.5, respectively) than in 2002 [2,3]. The principal mode of transmission in the region seems to be changing, as the epidemic was initially concentrated in IDUs, whereas in 2011 the most common mode of HIV transmission was heterosexual transmission in Armenia and Georgia (69.6% and 47.6%, respectively, of all HIV cases reported) and injection drug use in Azerbaijan (57.6%). Consequently, the male-to-

female ratio in 2011 ranged from 1.7 : 1 in Armenia to 2.9 : 1 in Azerbaijan.

Surveys conducted among IDUs found prevalence rates of HIV infection of 2–16.7% per site in 2011 in Azerbaijan and 10.7% in Armenia in 2010–2011 [33,34]. In RDS surveys conducted in 2011 in IDUs in five cities in Georgia, the HIV prevalence ranged from 1.5% to 4.4%. A higher HIV prevalence of 6.4% was found in a survey in MSM in 2010 in Tbilisi (Chikovani *et al.*, Sixth IAS Conference on HIV Pathogenesis, Treatment, and Prevention, 2011, Abstract TUPE480). Surveys conducted among MSM in 2010 using RDS found a prevalence of HIV infection in Azerbaijan of 0.4% (Suleymanova, FEMP 2011, Abstract TUPE480; http://www.smittskyddsinstitutet.se/upload/femp/097_Multiple_Suleymanova_Javahir.pdf). The finding from Georgia and the male-to-female ratio raise concerns that MSM behaviour is under-reported.

Transmitted Drug Resistance (TDR) in Europe

Transmission of antiretroviral drug-resistant HIV strains from treated individuals experiencing suboptimal suppression of viral replication or virological failure to treatment-naïve individuals has been reported in the majority of European countries.

The prevalence of TDR at a European level has been systematically monitored since 2002 by the Strategy to Control the Spread of HIV-1 (SPREAD) surveillance programme, which is based on a representative cohort of newly diagnosed individuals sampled within 6 months of diagnosis. A SPREAD study that included 2793 individuals diagnosed with HIV infection from 20 European countries and Israel estimated the overall prevalence of TDR at 8.4% [35]. No time trend in the prevalence of TDR and nucleoside reverse transcriptase inhibitor (NRTI) resistance was observed during the study period, whereas the prevalence of TDR to protease inhibitors (PIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs) significantly decreased. Infection with subtype B was the strongest predictor for transmission of resistance in SPREAD participants [35]. Recently, Frenzt *et al.* [36] reviewed 215 studies published up to 2009 on the epidemiology of HIV-1 TDR that included 43 170 patients from different continents and showed the following prevalence rates: North America, 12.9%; Europe, 10.9%; Latin America, 6.3%; Africa, 4.7%; and Asia, 4.2%. An analysis of European studies ($n = 82$, 25 446 patients, 75 studies from western Europe) showed a 7.4% prevalence of TDR to NRTIs, a 3.4% prevalence of TDR to NNRTIs, and a 2.9% prevalence of TDR to PIs. Time trend analysis showed a decrease in the

prevalence of TDR over time in Europe (11.5% in 2003, decreasing to 7.7% after that year), which can be attributed to the decline in resistance to NRTIs (from 8.0% to 4.3%) and PIs (from 3.3% to 1.4%). In contrast, the prevalence of TDR to NNRTIs showed little change in the same period of time (from 2.9% to 3.2%) [36,37].

However, more recent data on the prevalence of TDR in Europe are available in a number of national and regional studies (Table 2) [35,38–62]. Analysis of TDR prevalence according to drug classes shows that the majority of surveillance drug resistance mutations observed in newly diagnosed individuals are associated with NRTI resistance [35,38–62]. Nevertheless, the prevalence of TDR to NRTIs is below 10% in the majority of European national studies (Table 2). TDR to PIs and multiclass TDR have been rarely observed in Europe in recent years. However, one should be cautious in comparing different studies, because of many methodological issues, including variations in how mutations were defined [63,64].

The reported prevalence of TDR in Europe in individuals diagnosed with HIV infection since 2005 ranges between 0% and 25%. An important contribution of transmission clusters to the spread of resistant virus (particularly among MSM carrying T215 revertants, and Y181C and M41L mutations) has been described in several countries and regions within countries (Sweden, Denmark, Greenland, Italy, Croatia, northern Greece, the Basque Country in Spain, and Geneva) [38–40,44,47,49,61]. Although subtype B infection was a significant predictor of TDR in the SPREAD study and several more recent national studies (Croatia and Italy), other studies have found a comparable risk of TDR in subtype B and non-subtype B infections (France) [42,53,61].

Comment

Notable changes are occurring in HIV epidemics across Europe. In the West, the trends in reported HIV cases vary. Whereas declines since 2007 have been noted in The Netherlands, Ireland, Portugal, Switzerland, and the UK, increases have been observed in Belgium, Greece, and Iceland. Nonetheless, HIV case reporting data cannot be reliably used to interpret the trends in recent HIV infections, as they depend on patterns of HIV testing and reporting practices. Thus, the study in the UK found no decrease in the HIV incidence in MSM in the period 2001–2010, whereas incidence-based surveillance suggests that 16% of people newly diagnosed with HIV in 2011 had been infected recently (in the previous 4–6 months) [9,10]. In Paris, France, the first community-based survey on recent HIV infections in MSM

found a high HIV incidence of 3.8% person-years in spite of a high uptake of HIV testing, whereas the HIV prevalence was 17.7% [65,66]. Another study conducted in France estimated that the time between HIV infection and diagnosis ranged from 37.0 months for MSM to 53.0 months for heterosexual men, implying the need to scale up HIV testing [67].

In the countries where estimates of recent infections are not available, the changes in the reported cases have to be interpreted in the context of the changes in the number of HIV tests performed, although such data are rarely available for the countries of the West in the ECDC reports. Of note is a low and decreasing number of HIV tests performed in Greece since 2007 (in 2011, the testing rate was 1.1/1000), whereas in Austria, Belgium and Ireland the numbers of tests have increased since 2007 [2].

In the Centre, the number of cases reported since 2007 increased significantly in Bulgaria and Turkey. In some of the countries in the Centre, the numbers of HIV tests increased markedly. For example, in Albania, 1.6/1000 tests were performed in 2000, as compared with 30.5/1000 in 2011 [2,68]. In Bulgaria, the testing rate almost doubled from 2000 to 2011 (from 12.8/1000 to 24.0/1000), and in Turkey it increased from 14.1/1000 in 2002 to 25.7/1000 in 2006 [2,68,69]. Cyprus had a relatively high HIV testing rate according to the most recent available data (53.6/1000 in 2008), but there are no HIV prevalence data for groups at higher risk [70]. According to the available data, although they are often of insufficient quality, the HIV prevalence continues to be relatively low in all key vulnerable groups in the examined countries of the Centre, with the exception of IDUs in Bulgaria [15,17,21,22,71–73].

In the East, Armenia, Georgia and Ukraine recorded a significant rise in the number of HIV cases since 2007, whereas the rate declined in Estonia and Latvia. Georgia and Latvia are the only countries in the East where HIV testing decreased from 2011 to 2002. The increase in HIV testing was high in Armenia (1.3/1000 in 2001 and 21.0/1000 in 2011), Azerbaijan (13.0/1000 in 2002 and 40.1/1000 in 2011), Belarus (37.1/1000 in 2002 and 99.0/1000 in 2011), and Moldova (14.1/1000 in 2002 and 51.6/1000 in 2006) [2,69,74,75]. In Estonia, it increased from 42.6/1000 in 2002 to 63.4/1000 in 2011 [2,69]. However, it is not known to what extent the increase in testing rate reflects the increase in testing in the groups most at risk of HIV, and this applies to all of the countries included in this review [2].

In all countries of the East described in this review (with the exception of Georgia), the HIV burden is high in IDUs and fuels heterosexual HIV transmission. Although there is no evidence of generalized HIV transmission in the East, the significance of sexual HIV transmission is substantial.

TABLE 2. The prevalence of transmitted drug resistance (TDR) in human immunodeficiency virus (HIV)-infected individuals from Europe (selected national studies including patients who were sampled after 2004)

Country or region	Number of participants and year of sampling	Overall prevalence of TDR	Resistance by ARV class	Comment	Reference
SPREAD study 20 European countries and Israel	N = 2793 (2002–2005)	8.4%	NRTI: 4.7% NNRTI: 2.3% PI: 2.9%	No time trend in the prevalence of TDR and RTI resistance	Vercauteren et al. [35]
National studies from western Europe Denmark	N = 1405 (2001–2009)	6.1%	NRTI: 2.9% NNRTI: 1.3% PI: 2.6% Dual class TDR: 14% of patients with TDR	Resistant viruses carrying T215 revertant SDRMs in transmission chains	Audelin et al. [44]
Greenland	N = 60 (1999–2007)	25%	NRTI: 23% PI: 10% Dual class TDR: 6/15 patients with TDR	Contribution of transmission strains to the spread of resistant viruses	Madsen et al. [38]
France	N = 466 (2006–2007)	10.6%	NRTI: 5.8% NNRTI: 2.8% PI: 4.7%	42% of non-B subtype infections Comparable TDR in B and non-B subtypes	Descamps et al. [42]
Germany	N = 2078 (2001–2009)	9.2%	NRTI: 5.8% NNRTI: 2.8% PI: 2.7%	A study focusing on chronically infected patients Declining prevalence of TDR in 2008 and 2009	Oette et al. [55]
Ireland	N = 856 (2004–2008)	6.3%	Single class resistance: 5.7% Dual class resistance: 0.5% Triple class resistance: 0.1% 69/856 patients with SDRM in RT region 12/756 patients with SDRM in PI region	The majority of TDR was in Irish-born individuals with subtype B infection	De Gascun et al. [58]
Northern Greece	N = 369 (2000–2007)	12.5%	NRTI: 7.6% NNRTI: 5.4% PI: 3.3% Dual class resistance: 3.8%	Infection with subtype A was a predictor of TDR Transmission clusters of patients infected with a T215 revertant HIV strain with Y181C mutations	Skoura et al. [47]
Italy	N = 169 (1998–2009)	15.4%	NRTI: 11.8% NNRTI: 6.5% PI: 7.1%	A study limited to individuals infected with the F1 subtype	Franzetti et al. [54]
Italy	3163 (2000–2010)	12%	Non-acute non-recent infection (n = 2937): NRTI: 7.4% NNRTI: 5% PI: 9.9%. Acute or recent infection (n = 226): NRTI: 7% NNRTI: 7% PI: 3%	Subtype C vs. subtype B infection predicted lower odds of TDR TDR declined overall and for the single drug classes	Colafigli et al. [53]
Sicily	N = 108 (2004–2008)	15.7%	NRTI: 10.2% PI: 2.8%	K103N was the most frequently found SDRM	Bonura et al. [52]
Spain	N = 1864 (2007–2010)	8.6%	NRTI: 3.9% NNRTI: 3.9% PI: 2.3%	15.9% of non-B subtypes	Monge et al. [50]
Basque Country, Spain	N = 261 (2004–2007)	11.1%	NRTI: 7.6% NNRTI: 2.3% PI: 0.4% PI + NNRTI: 0.4%	84.3% of subtype B infections Transmission cluster of individuals carrying T215D revertant SDRM, mostly MSM	Cuevas et al. [40]
Sweden	N = 1463 (2003–2010)	5.6%	NRTI + NNRTI: 0.4% 68% of TDR patients had single class resistance Five patients had multiclass resistance	TDR significantly associated with MSM group and subtype B infection A cluster of MSM carrying M41L SDRM from Stockholm TDR concentrated among MSM, clustering of TDR strains	Karlsson et al. [49]
UK	N = 14 584 (2002–2009)	11.3%	2007: NRTI 5.4%, PI 1.5% 2009: NRTI 6.6%, PI 2.1%	A study focusing on subtype B infections that were probably acquired in the UK) T215 revertants were the most frequent mutations associated with NRTI TDR	UK Collaborative Group on HIV Drug Resistance [51]
Geneva, Switzerland	N = 637 (2000–2008)	8.5%	NRTI: 6.3% NNRTI: 3.5% PI: 1.9%	Transmission clusters were more frequent in individuals with TDR than in those with sensitive strains	Yerly et al. [39]

Table 2 (Continued)

Country or region	Number of participants and year of sampling	Overall prevalence of TDR	Resistance by ARV class	Comment	Reference
Israel	N = 148 (2002–2009)	15.5%	NRTI: 6.7% NNRTI: 6% PI: 4.7%	A study focusing on HIV-infected MSM	Levy <i>et al.</i> [59]
National studies from eastern Europe					
Estonia	N = 145 (2008)	5.5%	NRTI: 2.8% NNRTI: 2.1% PI: 2.8%	85% of infections with CRF06_cpx	Avi <i>et al.</i> [48]
Georgia	N = 126 (2006–2008)	3.9%	Dual class TDR: 2% NRTI: 2.4% PI: 1.6%	90.2% of subtype A infections clustered with Former Soviet Union A subtype	Dvali <i>et al.</i> [56]
Latvia	N = 117 (2005–2006)	3.4%	NRTI: 0.8% NNRTI: 0.8% PI: 1.6%	20% of national coverage in the two selected years	Balode <i>et al.</i> [41]
National studies from central Europe					
Croatia	N = 118 (2006–2008)	22.0%	NRTI: 19.5% NNRTI: 2.5%	Transmission cluster of subtype B individuals carrying T215S mutation (mostly MSM)	Grgic <i>et al.</i> [61]
Cyprus	N = 53 (2007–2009)	No resistance	No resistance	48.6% of subtype B, 18.9% of subtype A	Kousiappa <i>et al.</i> [45]
Slovenia	N = 150 (2005–2010)	4.7%	NRTI: 2% NNRTI: 2% PI: 0.7%	89% of subtype B TDR limited to MSM	Lunar <i>et al.</i> [62]
Romania	N = 61 (1997–2011)	14.8%	NRTI: 13.1%	Declining TDR trend in the period 2005–2011	Temereanca <i>et al.</i> [60]
Poland	N = 95 (2008)	5.3%	NNRTI: 1.1% PI: 4.2%	TDR limited to single classes of antiretroviral drugs	Stanczak <i>et al.</i> [43]
Hungary	N = 30 (2008–2010)	16.6%	NRTI: 10% NNRTI: 6.6%	29 of 30 subtype B infections	Mezei <i>et al.</i> [46]
Istanbul (Turkey)	N = 20	4 patients	Mutations causing resistance to NRTIs, NNRTIs and PIs were detected	HIV subtype diversity (B, A1, C, CRF02_AG, CRF03_AB, CRF06_cpx)	Alpsar <i>et al.</i> [57]

ARV, antiretrovirals; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitors; RT, reverse transcriptase; SDRM, surveillance drug resistance mutation; SPREAD, Strategy to Control the Spread of HIV-1.

It is encouraging that several countries in the East with a high burden of HIV (Estonia, Moldova, and Ukraine) carried out HIV data triangulation and synthesis, which enabled better characterization of the epidemic. Such projects are particularly important in the East and the Centre, where HIV incidence-based surveillance has not been established and where HIV case reporting data provide biased information about modes of transmission. In such circumstances, population-based HIV bio-behavioural surveys in the groups most at risk provide more valid data on the burden of infection and the need for various HIV interventions.

Because of the availability and early introduction of antiretroviral therapy, there has been a marked decline in new AIDS cases and HIV-related mortality in the West. However, the number of AIDS cases and the associated mortality in the East is still increasing, mainly because of low treatment coverage [1,2]. Tuberculosis is a prevalent disease in HIV-infected people in the East, and is still a major cause of mortality among people living with HIV/AIDS [1,2]. Many of the WHO high-priority countries for tuberculosis control (Armenia, Azerbaijan, Belarus, Bulgaria, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Republic of Moldova, Romania, Russian Federation, Tajikistan, Turkey, Turkmenistan, Ukraine, and Uzbekistan) are in the eastern part of the

European Region, and many of those countries also have an increasing HIV epidemic or already have a high burden of HIV cases. HIV testing coverage of tuberculosis patients in the whole European Region is still inadequate; it is estimated to be 60% [76]. Hence, tuberculosis is still an important public health issue in Europe, and tuberculosis–HIV co-infection requires good coordination within the healthcare system and prompt provision of both HIV and tuberculosis care and treatment. Late presentation to care occurs in the whole European Region; an expansion of testing and the introduction of different testing strategies are urgently needed. One of the limitations in comparing the number of newly reported HIV cases across the European Region lies in the fact that the validity of these data strongly depends on the patterns of HIV testing, the accessibility of HIV testing for the groups most at risk of HIV, and the reporting of HIV cases.

The fact that sex between men is stigmatized in many European countries not only affects testing rates, access to early HIV diagnosis, and the overall wellbeing of MSM, but may also result in under-reporting of such behaviour in the surveillance system [71,72]. We suspect that, in countries with a high male-to-female ratio and a large number of heterosexual or unknown HIV transmissions, sex between men was mainly not disclosed.

In terms of TDR, literature data suggest high heterogeneity in the prevalence of TDR in Europe at the regional level, particularly in the context of the local HIV molecular diversity and the contribution of transmission clusters to the spread of resistant viruses in closed populations.

In conclusion, effective and repeated surveillance in IDUs, MSM and FSWs and bridging groups needs strengthening in all regions of Europe, particularly in the countries where there is evidence for increases in the numbers of diagnosed HIV cases and where population-based HIV data are lacking. There are encouraging signs that HIV prevention interventions are making an impact on HIV transmission in several countries. However, the HIV epidemic continues to grow in most parts of Europe, driven by high levels of risky behaviour and insufficient provision of and access to HIV prevention and treatment services.

Transparency Declaration

The authors declare no conflicts of interest.

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