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Death from AIDS is preventable, so why are people still dying of AIDS in Europe?

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It is almost two decades since life-saving treatment for human immunodeficiency virus (HIV) became available. Life expectancy among people living with HIV, for whom optimal therapy is initiated timely, is now close to that of the general population [1]. Despite this, an estimated 1.6 million people died from acquired immunodeficiency syndrome (AIDS)-related illnesses globally in 2012, and the number who died within the World Health Organization (WHO) European Region reached almost 100,000 [2]. A large proportion of these deaths occur in the eastern part of the Region, and without changes in the HIV response, the death toll in this region is likely to continue to increase in the coming years [3]. Conversely, in the west, the risk of AIDS-related death continues to decline [3], reflecting some positive progress.

The majority of AIDS-related deaths would be preventable if available evidence were to be fully implemented. Research findings reported in this issue of *Eurosurveillance* exemplify the challenges we face as we enter the fourth decade of the epidemic. Better and more comprehensive testing strategies aimed at persons most at risk of contracting HIV are needed, linked to HIV care and treatment programs. Implementation research needs to be at the core of the HIV response.

Diagnosis at a late stage of HIV infection and subsequent delays in starting treatment with antiviral agents are the important factors for the high death toll in parts of Europe and certain subgroups. Pharris et al. in this issue present the latest trends in HIV diagnoses in the European Union/ European Economic Area [4] and show that, based on countries where information is available, about half of the 300,000 people diagnosed with HIV over the past decade had a CD4 cell count of 350 copies/mL or less at the time of diagnosis (defined as 'late diagnosis'). Consequently, their risk of death within the year of their diagnosis was more than 10 times higher than that of individuals diagnosed early and entering care promptly [5]; those diagnosed late aged 50 years and over carried an even greater risk [6]. This is of particular concern given the increase in the number of persons diagnosed at an older age in Europe

with almost two thirds diagnosed at a late stage of infection (personal communication Anastacia Pharris, November, 2014).

Encouraging signs of an overall decline in late diagnoses in western Europe in recent years should be interpreted with caution as this may be due to a modest decline in the number of new HIV diagnoses among migrants, the population with the highest proportion of late presenters, rather than improvements in earlier diagnosis [4]. Data on late diagnosis in the eastern part of the WHO European region are largely lacking and where available above rates reported in the west [3].

In addition to the increased risk of developing AIDS, early death and increased health costs associated with late presentation for HIV care, people living with HIV who remain unaware of their HIV positive status are more likely to pass on their infection to their sexual partners [7]. HIV treatment has public health benefits in reducing onward transmission and preventing new cases of HIV, as well as clinical benefits for the individual people living with HIV in restricting the progression of HIV [7,8]. Sadly, while there are indications that treatment uptake has improved over the past decade, there are few signs that HIV transmission is declining across Europe, and for some groups, namely men who have sex with men (MSM), the latest information points to increases in new infections [4]. This is despite the fact that the late presentation statistics for this population are among the most favourable with only around 30–40% presenting late for care across countries in the European Union and European Economic Area (EU/EEA) [4]. The situation in the eastern part of the WHO European region continues to deteriorate with increasing HIV incidence, mostly confined to injecting drug users and their sexual partners [3].

Routine information on HIV incidence among most at risk populations is crucial in informing the HIV response. Studies in this issue from Italy and Spain report high levels of HIV transmission among men who have sex with men, sex workers and persons who inject drugs (PWID) [9,10]. While it is reassuring that

a low incidence was found among prisoners in Estonia [11], imprisonment of people who inject drugs and prohibition of opioid substitution therapy further east has fuelled the epidemic [3].

So what are the implications from these findings? Has the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia [3] which set out a plan to combat HIV over the past 10 years failed? While some successes have been realised, clearly the analyses on late diagnosis presented here indicate that the challenges of diagnosing individuals at an early stage of HIV infection and ensuring linkage to HIV care have not been met across Europe. This is despite a growing body of scientific evidence on barriers to testing among most at-risk populations and effective ways of addressing them. For instance, awareness and education of healthcare staff can substantially increase the offer and acceptance of HIV testing in a wide range of settings in a non-discriminatory way and help normalise the testing process [12]. Novel methods to promote testing such as home sampling and testing kits are showing promise in reaching key populations [13]. Initiatives such as this week's *European HIV testing week* provide an opportunity to share and disseminate good practice and scale up testing efforts [14].

A core component of evaluating these novel testing approaches should include their ability to link and retain people living with HIV and in appropriate HIV treatment, care and support programmes. A proportion of people entering HIV care late are actually aware of their HIV-positive status, but failed to access care when first diagnosed. Whereas this is true for a relatively small fraction of late presenters in the western and central parts of Europe, [5] poor linkage and retention into care including adequate provision of HIV treatment and opioid substitution therapy are major shortcomings in the HIV response in the eastern part of the WHO European region [3].

UNAIDS has set ambitious targets for all countries: by 2020, governments will commit to ensuring that in any key population and any country in Europe, 90% of people living with HIV will know their HIV status, 90% of people with diagnosed HIV infection will receive sustained antiretroviral therapy, and 90% of people receiving antiretroviral therapy will have durable viral suppression [15]. These targets, while highly aspirational, provide a basis for concerted action. A first step is to require that countries have adequate and preferentially harmonised information systems to monitor progress in reaching these targets. However, data on CD4 count at diagnosis were only available from 14 EU/EEA countries to track late diagnosis, and even fewer countries have estimates of the number of persons living with diagnosed and undiagnosed HIV and receiving treatment [4]. Of particular concern is the lack of accurate information on the most at-risk and vulnerable populations.

Government leadership in partnership with civil society has been and should continue to be a critical component to the HIV response. Of paramount importance is the implementation of anti-discriminatory and protective laws and policies that ensure the human rights of all persons living with HIV and promotes their access to HIV testing and free (or affordable) healthcare regardless of sexuality, drug taking or residency status. Stigma and discrimination remain important barriers to timely HIV testing and access to healthcare in many parts of Europe. While test-and-treat policies are likely to be an essential component of the HIV response over the next decade, these should not be the only focus. Political and financial investment in a range of comprehensive HIV prevention strategies need to be tailored to meet the specific and nuanced needs of key populations most vulnerable to contracting HIV such as men who have sex with men, migrants, people in prison, sex workers, and people who inject drugs. Implementation research in each of these areas is essential to reducing onward transmission of HIV in Europe, enabling progress in the response to HIV, and continuing to steer the fourth decade of the response to HIV in Europe in the most effective direction.

Conflict of interest:

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Ten years after Dublin: principal trends in HIV surveillance in the EU/EEA, 2004 to 2013

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In 2004, the 31 countries of the European Union and European Economic Area (EU/EEA) adopted the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia. In 2013, 29,157 persons were diagnosed with HIV in 30 EU/EEA countries (adjusted rate: 6.2/100,000); new diagnoses have increased by 33% since 2004 among men who have sex with men and late diagnosis remains common. Evidence-based prevention measures and efforts towards earlier testing need to be expanded.

Newly diagnosed HIV infections

In 2004, countries in Europe and Central Asia adopted the Dublin Declaration on Partnership to Fight HIV/AIDS, making human immunodeficiency virus (HIV) an important political priority for countries in the European Union and European Economic Area (EU/EEA). Over the last decade, concerted efforts have been made to prevent and control HIV in the region and new effective tools have emerged to reduce HIV transmission [1]. However, since 2004, more than 300,000 people have been newly diagnosed with HIV in the EU/EEA [2] and a considerable proportion remain undiagnosed [3].

Enhanced HIV surveillance for the EU/EEA is coordinated by the European Centre for Disease Prevention and Control in collaboration with the World Health Organization (WHO) Regional Office for Europe. In 2013, 29,157 persons were diagnosed with HIV in 30 countries of the EU/EEA, a rate of 6.2 per 100,000 population and nearly 32,000 new diagnoses when adjusted for reporting delay [2,4]. The majority of those diagnosed were men (male-to-female ratio: 3.2). Transmission was mostly reported as sexual, with 12,228 new diagnoses attributed to sex between men (42%) and 9,449 to heterosexual sex (32%). Injecting drug use accounted for 1,455 cases (5%) and unknown transmission for 5,741 (20%), while mother-to-child, nosocomial and transfusion-related transmission accounted for less than 1% of new diagnoses.

Among cases with known information on region of origin or country of birth (88%, n = 25,568), 35% (n = 9,032) of people newly diagnosed with HIV in 2013 originated

from outside the country in which the diagnosis was made; 15% (n = 3,784) originated from a country with a generalised HIV epidemic.

Trends in newly diagnosed HIV infections

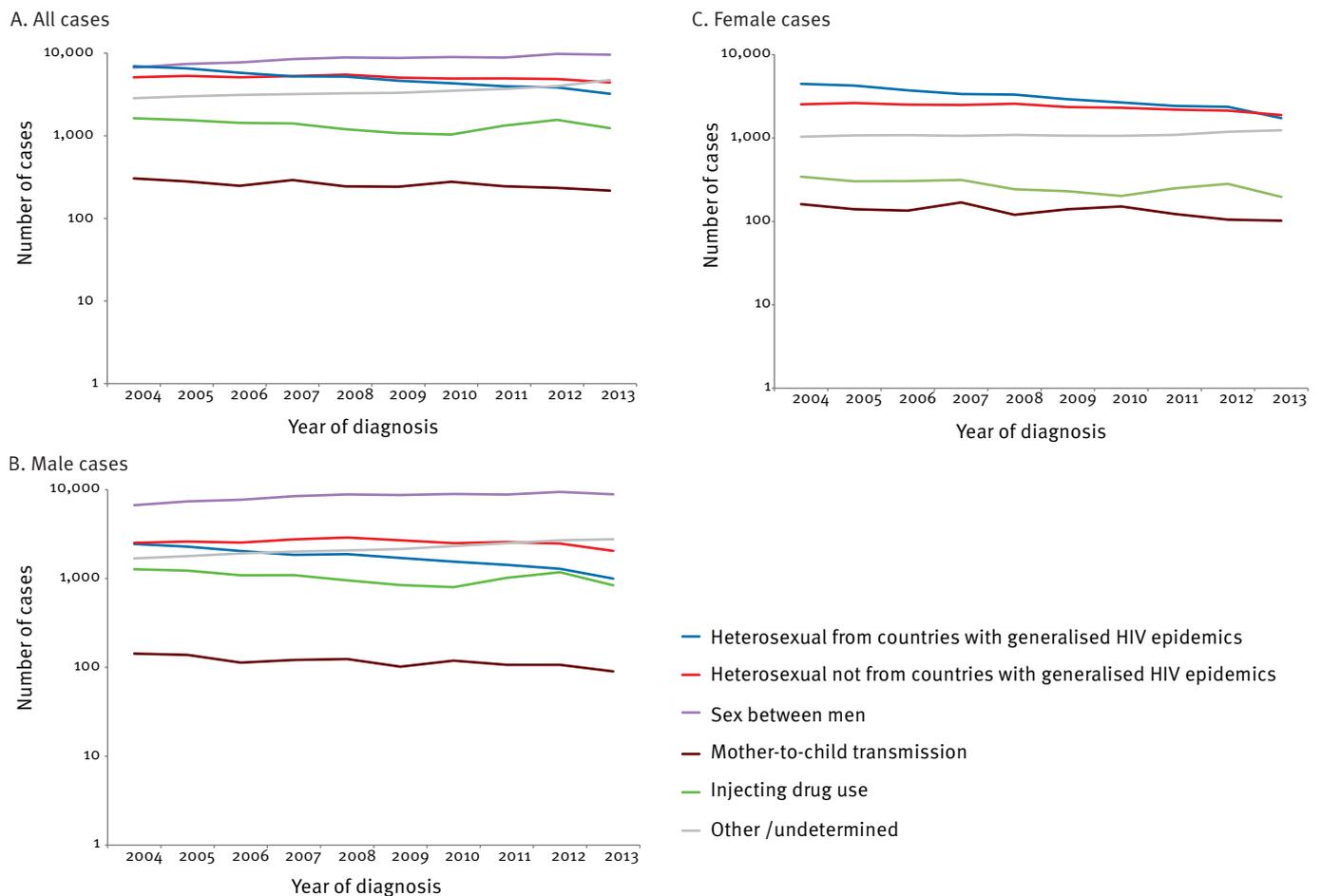
Overall, HIV diagnosis rates remained largely stable during the studied period, and ranged between 6.5 per 100,000 population in 2004 and 6.2 per 100,000 in 2013 when adjusted for reporting delay. To further understand trends by subgroup, we analysed data from 25 EU/EEA countries, all EU/EEA countries except Bulgaria, Estonia, Italy, Liechtenstein, Poland, and Spain which reported data on HIV transmission, sex and age group for more than 50% of their cases for the period 2004 to 2013 to The European Surveillance System (TESSy).

Among men, HIV diagnoses increased by 6% over the analysed period from 14,769 to 15,622, while HIV diagnoses among women decreased by 40% from 8,611 to 5,182 (Figure 1A-C). The increase in diagnoses among men is driven by the 33% increase among men who have sex with men (MSM) over the last decade, while diagnoses among male heterosexuals from countries with generalised epidemics and other male heterosexuals decreased by 60% and 19%, respectively (Figure 1B). Male cases attributed to injecting drug use declined by 34% from 1,273 to 840, although an increase was noted in 2011 and 2012 following localised outbreaks in Athens and Bucharest [5]. HIV diagnoses among women declined in all transmission categories, with the most notable decreases among heterosexuals from countries with generalised HIV epidemics (61%, from 4,465 to 1,733) and 43% fewer cases attributed to injecting drug use (from 344 to 197) (Figure 1C). These numbers are unadjusted and thus, a small part of the decreases observed may be due to reporting delay. For the same reason, increases observed over the period are likely to be underestimates.

Of all cases in all transmission categories notified between 2004 and 2013, 34% were aged 30 to 39 years (Figures 2A-C). The number of diagnoses among MSM increased annually in all age groups, with the largest

FIGURE 1

Trends in reported HIV diagnoses, by transmission mode and year of diagnosis, adjusted for reporting delay, EU/EEA, 2004–13



EU/EEA: European Union and European Economic Area; HIV: human immunodeficiency virus.

Case numbers are presented on a logarithmic scale. Excludes data from countries with changed coverage over the period (Bulgaria, Italy, Spain) and incomplete data on transmission mode (Estonia, Poland).

increases among men under 30 years of age, where cases nearly doubled (from 76 to 139 in 15 to 19 year-olds and from 1,585 to 2,728 in 20 to 29 year-olds) and among MSM older than 50 years, where diagnoses increased from 644 to 1,082 (Figure 2A). Among cases attributed to injecting drug use, there were decreases in all age groups except for those older than 50 years where diagnoses increased from 43 to 101 (Figure 2B). Among heterosexuals from countries with generalised HIV epidemics there were decreases in all age groups, most notably among those younger than 30 years where diagnoses declined to one quarter of the number diagnosed in 2004 (from 2,378 to 564) (Figure 2C).

Trends in late diagnosis

Among 12 EU countries (Austria, Bulgaria, Czech Republic, Cyprus, Denmark, Spain, Luxembourg, Netherlands, Romania, Slovakia, Slovenia, and the United Kingdom) reporting data on CD4⁺ T-cell count at diagnosis for more than 50% of their cases for the period 2004 to 2013, the proportion of cases diagnosed late (CD4⁺ T-cell count < 350 cells/mm³) [6]

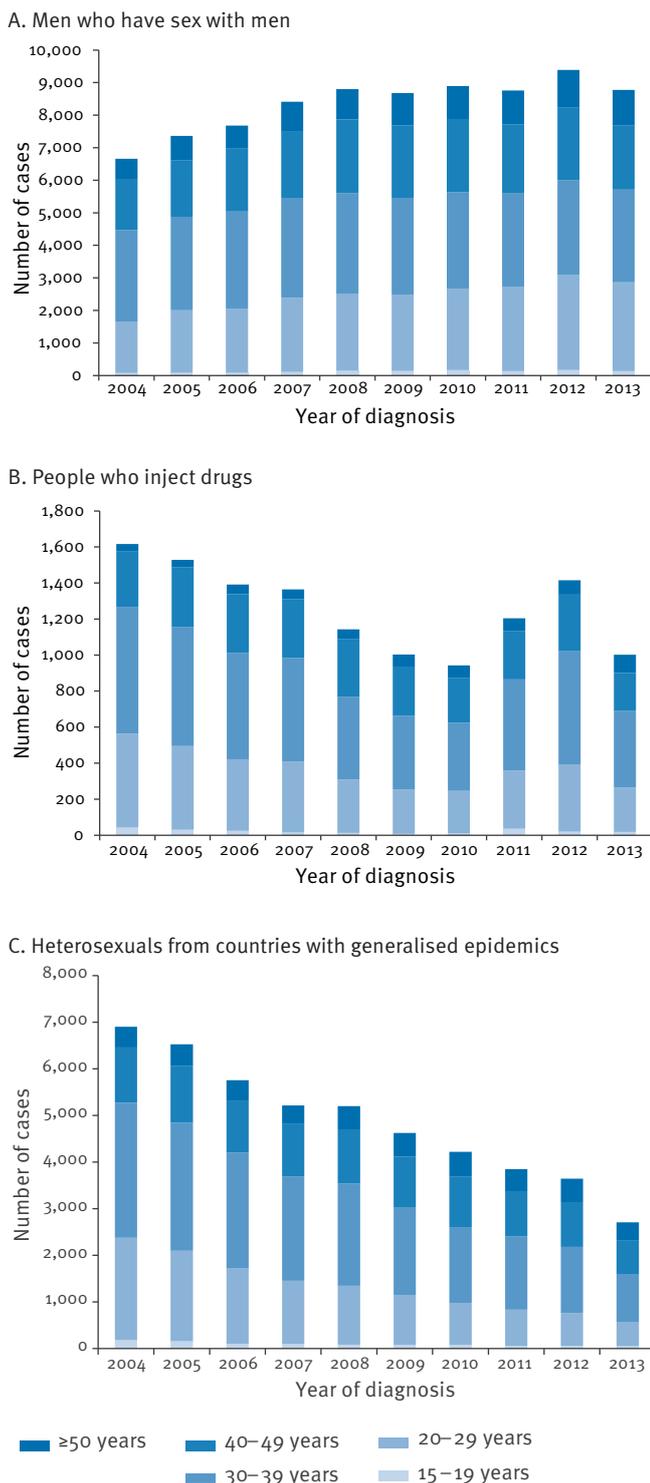
declined, from 55% of new diagnoses with CD4⁺ data available in 2004 to 44% in 2013 (Figure 3). During the same period, the median CD4⁺ T-cell count at diagnosis increased from 312 to 390 cells/mm³. Analysed by transmission group, there was a decline in late diagnosis among MSM (from 43% to 34%) as well as among heterosexuals from countries with generalised epidemics (from 66% to 60%). Late diagnosis among heterosexuals not originating from countries with generalised HIV epidemics was 54% in 2004 and 53% in 2013. Late diagnosis attributed to injecting drug use increased slightly, from 50% to 53%.

Discussion and conclusion

Although the rates of HIV diagnoses in the EU/EEA have remained largely stable since 2004, the year the Dublin Declaration was adopted, the epidemiology of HIV in the region has changed substantially. New HIV diagnoses among MSM have increased considerably and presently account for more than 40% of all diagnosed cases in the EU/EEA. The observed increases among younger MSM are of particular concern, as these are likely to

FIGURE 2

Trends in reported HIV diagnoses, by age group, year of diagnosis and transmission category, EU/EEA, 2004–13



EU/EEA: European Union and European Economic Area; HIV: human immunodeficiency virus.

Excludes data from countries with changed coverage over the period (Bulgaria, Italy, Spain) and incomplete data on transmission mode (Estonia, Poland).

have been infected more recently and suggest that current prevention efforts may not be having the impact necessary to reduce transmission. Increased HIV incidence and high proportions of undiagnosed infections among MSM have been reported in various settings in the EU/EEA [7-9] and to counter this, evidence-based, comprehensive prevention and testing programmes must urgently be scaled up in many EU/EEA countries.

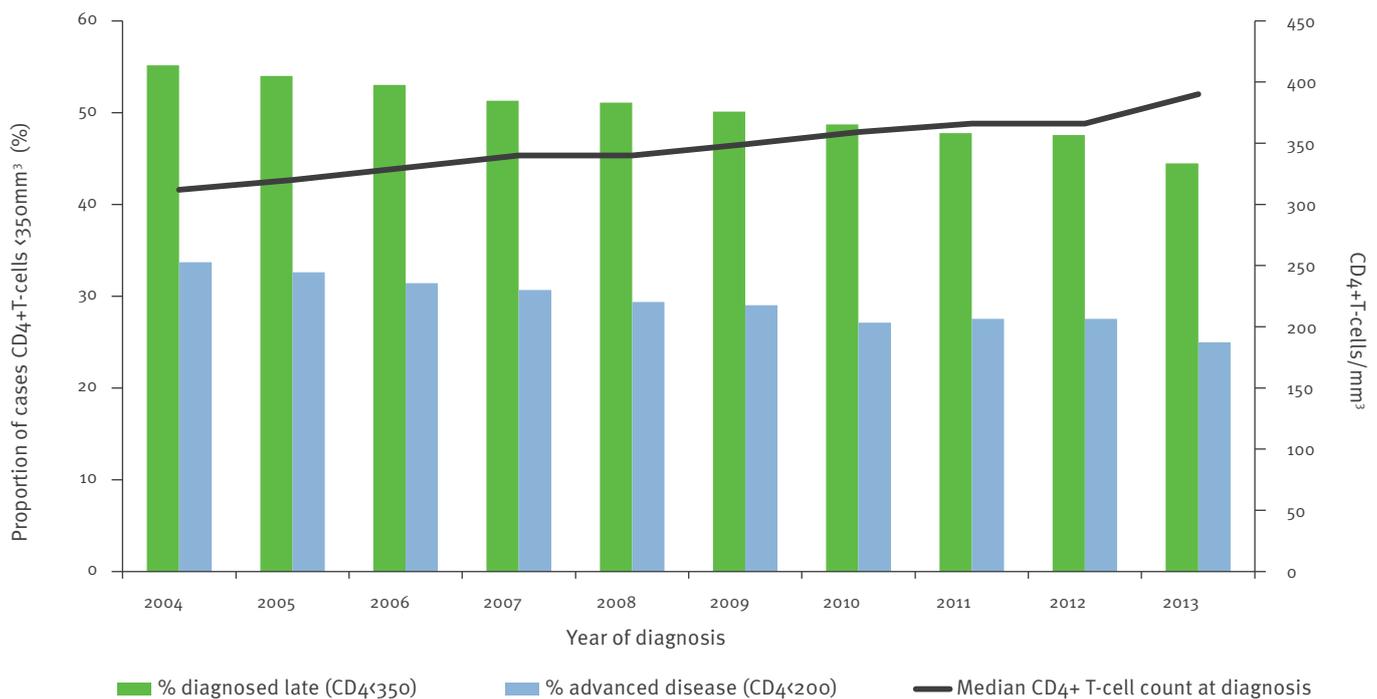
Our analysis indicates that 35% of new HIV diagnoses in Europe occurred in people born outside of the country in which the diagnosis was made. Although HIV diagnoses among migrants from countries with generalised HIV epidemics have decreased significantly over the last decade, they still constitute 15% of all HIV diagnoses in the region. Prevention programmes targeting migrants have not increased in most EU/EEA countries during the period [10], however, the observed decline may partially reflect the documented declining incidence of HIV in many countries with generalised HIV epidemics [11], changes in migration flows to and/or from EU/EEA countries or a combination of these and other factors. Considering that post-migration HIV acquisition can account for a significant proportion of infections, it is becoming more and more crucial that HIV prevention and testing are promoted and delivered in a manner that is acceptable to migrant populations, along with policies to ensure linkage and access to HIV care [12,13].

Late HIV diagnosis is a critical public health challenge in EU/EEA countries. Late diagnosis is associated with nearly 10-fold higher mortality in the year following diagnosis, higher morbidity and healthcare costs, and increased duration of possible HIV transmission before being diagnosed and treated [14-16]. While HIV surveillance data indicate that the proportion of people diagnosed late has decreased slightly over the last decade, late diagnosis remains prevalent in all subgroups and constitutes a major obstacle to the success of HIV prevention and control in the EU/EEA. Some subgroups, such as people from countries with generalised HIV epidemics and people who inject drugs, were persistently diagnosed later than others, potentially indicating poorer access to HIV testing and inadequate linkage to care [17]. Scaled-up and innovative approaches to routine HIV testing offered in community and clinical settings, including indicator-guided testing can help reach people that are at higher risk and reduce rates of late diagnosis in Europe [18].

There are several limitations to this analysis. Firstly, data quality for some variables (transmission mode, CD₄⁺ T-cell count) was low or changed over the period for some countries. This was addressed by limiting the analysis to countries with more than 50% completeness on these variables for all years during the period. Secondly, data on transmission mode in particular, contained a significant proportion of unknowns (overall ca 20% in 2013); for MSM in particular, numbers are likely to be underestimated. Finally, surveillance

FIGURE 3

Proportion of new HIV diagnoses with CD4+ T-cell count $<350/\text{mm}^3$ and $<200/\text{mm}^3$ and median CD4+ T-cell count at diagnosis, 12 EU/EEA countries, 2004–13 (n = 112,764)



EU/EEA: European Union and European Economic Area; HIV: human immunodeficiency virus.

Countries included: Austria, Bulgaria, Czech Republic, Cyprus, Denmark, Spain, Luxembourg, the Netherlands, Romania, Slovakia, Slovenia and the United Kingdom.

data are subject to reporting delay, and this was only partially taken into account in the analyses presented here. This could mean that reported decreases are likely to be overestimated while reported increases are likely to be underestimates.

Over the past decade, HIV has been high on the political agenda in the EU/EEA. This is reflected in a number of high-level events hosted by the European Council and the adoption of two EU Commission Communications and Action Plans on HIV/AIDS [19,20]. In November 2014, the Italian Presidency of the Council of the European Union will host a ministerial conference in Rome to reflect on achievements made since the adoption of the Dublin Declaration in 2004 and to focus attention on aspects of the response that need to be strengthened. Based on an analysis of the epidemiology of HIV in the EU/EEA, in order to have a measurable impact on reducing the HIV epidemic in EU/EEA countries in the next decade, the following key priorities should be considered: (i) scaling up of evidence-based and comprehensive HIV prevention programmes targeted towards MSM; (ii) developing and scaling up migrant-sensitive prevention programmes targeted towards foreign-born nationals; and (iii) addressing the critical issue of late HIV diagnosis in the region.

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Conflict of interest

None declared.

Authors' contributions

AP developed the concept of the manuscript, analysed the data, wrote the first draft and responded to reviewers' comments. GS, TN and AJAG contributed to the concept of the manuscript and analysis and revised the article to ensure important intellectual content. All authors have read and approved the final manuscript.

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Continuous increase in HIV-1 incidence after the year 2000 among men who have sex with men in Rome: insights from a 25-year retrospective cohort study

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To assess trends in HIV-1 incidence and risk factors for seroconversion among men who have sex with men (MSM) resident in Rome, Italy, a retrospective longitudinal cohort study was conducted over 25 years. Incidence rates and trends were modelled using Poisson regression and risk factors were assessed by multivariate Cox models. Of 1,862 HIV-1-negative individuals, 347 seroconverted during follow-up. HIV-1 incidence rates increased from 5.2/100 persons/year (p/y) in 1986 (95% confidence interval (CI): 2.3–11.5) to 9.2/100 p/y in 1992 (95% CI: 6.4–13.0), decreased to 1.3/100 p/y in 2001 and increased until 2009 (11.7/100 p/y; 95% CI: 7.4–18.6). The risk of HIV-1 seroconversion increased during the study period in younger MSM (incidence rate ratio (IRR)=17.18; 95% CI: 9.74–30.32 in 16–32 year-olds and IRR=5.09; 95% CI: 2.92–8.87 in 33–41 year-olds) and in those who acquired syphilis (IRR=7.71; 95% CI: 5.00–11.88). In contrast, the risk of seroconversion decreased among highly educated MSM (IRR=0.54; 95% CI: 0.35–0.82) and those without Italian citizenship (IRR=0.45; 95% CI: 0.28–0.71). The HIV epidemic in MSM living in Rome continues to expand. Targeted prevention programmes against sexually transmitted infections to enhance knowledge transfer and behavioural skills are urgently required.

Introduction

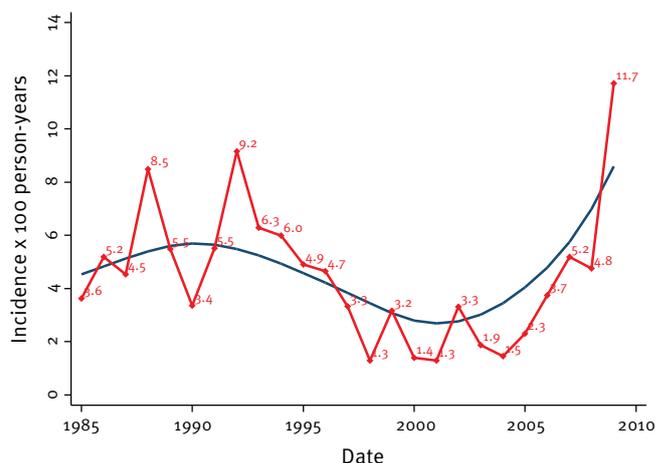
In Europe, human immunodeficiency virus (HIV) incidence declined among men who have sex with men (MSM) after the first phase of the epidemic because of a decrease in risky sexual practices [1]. This decline continued until the mid-1990s when the introduction of combination antiretroviral therapy (cART) dramatically changed the quality of life and survival of infected individuals and boosted the re-emergence of sexual risk behaviour which exposed MSM to sexually transmitted infections (STI) in general and HIV-1 in particular [2-5]. National surveillance systems and observational

studies suggest that since the early 2000s, HIV-1 incidence among MSM has been increasing in high-income countries, including many European countries, Australia, and the United States (US), thus causing the epidemic to re-emerge [6]. In developed countries, incidence rates of HIV-1 infection are therefore disproportionately higher among MSM than in other sexually active adult populations, despite decades of public health efforts and the benefits, after 1996, of cART on the transmission risk of HIV-1 [7-9].

In Italy, ca 1,200–1,300 MSM acquire HIV infection every year, and in 2011, nearly 40% of the newly diagnosed HIV cases were MSM. Moreover, the proportion of HIV infections attributable to sex with a same-sex male partner almost doubled from 2000 to 2011 [10,11].

FIGURE 1

Fitted HIV-1 incidence trend in men who have sex with men repeatedly tested in Rome, Italy, 1985–2009 (n=1,862)



Although rates of HIV infection among MSM decreased until the late 1990s, data for the period after 2000 indicate an increase in the occurrence of HIV infection in this population, which is consistent with the re-emergence of ulcerative STIs in the same period [4,12].

To assess HIV-1 incidence trends and risk factors among MSM living in Rome, a cohort of individuals repeatedly tested for HIV antibodies was identified among a large population of men attending a structured HIV screening programme in the largest STI clinic of the city. The following study contains data from a 25-year follow-up period.

Methods

Site recruitment and study population

Of the MSM attending the STI clinic of the San Gallicano Dermatological Institute in Rome, Italy between April 1984 and December 2010 who were tested for HIV-1 antibodies at least twice and were negative in the first test, we included opportunistically in the study all those who had never used drugs intravenously. The site of enrolment represents an important counselling and testing service for at-risk groups such as STI patients, MSM and migrants, who voluntarily access an ongoing HIV-1 screening programme. The centre's activity is directed at an urban population of more than 2.5 million inhabitants and its catchment population comprises also patients from other regions in Italy and from abroad (ca 20%).

Study participants were men who stated they had had anal sex with at least one male partner during the six months before the first HIV-1 antibody test. Two thirds of them perceived themselves to be at risk because of their sexual behaviour and therefore repeatedly self-referred to our STI centre for HIV testing. Other participants were individuals to whom HIV testing was offered because of their self-reported risky behaviour or a diagnosis of an STI. During the study period, recruitment was promoted according to the methodology of 'snowball' sampling, also in collaboration with non-governmental associations for human and health rights of MSM. At local level, brochures and leaflets were used to advertise the screening programme and to sustain the peer-to-peer recruiting. The 'snowball' procedure was used during the whole duration of the study. At each visit, participants were also visited and managed for the risk of other STIs according to the European guidelines for STI diagnosis and treatment [13]. In this context, participants were screened for *Treponema pallidum* infection and for rectal and pharyngeal *Neisseria gonorrhoeae* infection. Blood samples for serological tests and biological samples were collected from all participants.

Ethics statement

The study was approved by the San Gallicano Dermatological Institute Ethics Committee and performed in compliance with the Helsinki Declaration.

Informed consent was obtained from all participants according to Italian law concerning strategies for HIV-1 counselling and testing.

Data collection

During each consultation, a standardised questionnaire, administered face-to-face by an interviewer, was used to collect information on demographics, medical history, lifestyle (i.e. alcohol and/or intravenous drug use) and sexual behaviour (i.e. sexual practices, total number of partners ever, number of partners in the previous six months, characteristics of sexual partnership etc.). For all participants, additional clinical data were also retrieved from individual medical records available in the electronic clinical archive of the STI clinic.

Laboratory testing

Blood samples were tested for HIV-1 antibodies using consecutive generations of commercially available screening assays (Abbott Laboratories, Illinois, US; Abbott Park, Illinois, US; bioMérieux, France). All seroreactive samples were confirmed by Western blot (Genelabs Diagnostics, Singapore). Participants were screened for *T. pallidum* infection by serological assays (Rapid Protein Reagin (RPR), Treponema Pallidum Haemagglutination Assay (TPHA), IgG and IgM) and for rectal and pharyngeal *N. gonorrhoeae* infection by culturing samples from anal and throat swabs.

Statistical analysis

Incidence rates were calculated using the person-years (p/y) approach for MSM who were HIV-negative at enrolment and who underwent at least one additional HIV test during the study period. Time at risk was defined as the difference between the date of the first (entry into the study) and the last blood test (exit from the study). Because the exact time of seroconversion was not known, we assumed that HIV seroconverters were at risk for half the interval between the last negative and the first positive HIV test. HIV incidence was computed from 1985 to 2009. To minimise potential biases in the rates estimated at the two extremes of the study period, the first (1984) and the last (2010) year were excluded from the analysis of the HIV-1 trend owing to the potential incompleteness of

TABLE 1

Modelling of HIV-1 incidence rate curves in men who have sex with men in three calendar periods using Poisson regression, Rome, Italy, 1985–2009 (n=1,862)

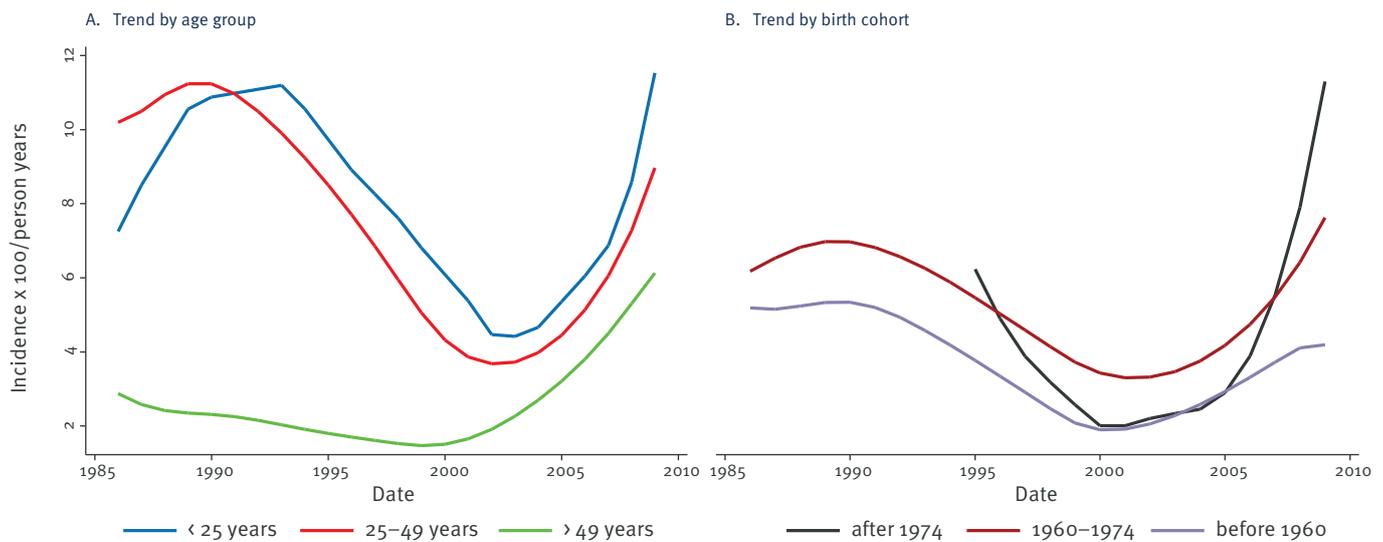
Calendar period	IRR _{adjusted}	95% CI	p value
1985–1992	1.07	1.00–1.16	0.059
1993–2000	0.72	0.65–0.81	<0.001
2001–2009	1.56	1.40–1.75	<0.001

CI: confidence interval; IRR: incidence rate ratio.

IRR per year within the selected period was adjusted by age at the time of diagnosis.

FIGURE 2

Fitted HIV-1 incidence trend in men who have sex with men, by age group (A) and selected birth cohorts (B), Rome, Italy, 1985–2009 (n=1,862)



follow-up data. Because incidence estimates varied greatly from year to year, the incidence trend over time was obtained using the locally weighted scatterplot smoothing (Lowess) technique. In addition, the incidence trend was modelled using Poisson regression with the calendar year as a continuous variable and allowing smoothing of varying trends via linear splines. The model was adjusted according to age at HIV seroconversion, included in the regression as a continuous covariate and modelled using linear splines.

Specific incidence rate ratios (IRR) for HIV-1 seroconversion were calculated for participants who were free of syphilis or gonorrhoea (any sites) at the beginning of the study and who acquired either syphilis or gonorrhoea during the study period. The date of diagnosis was used to estimate the time at risk for each participant. The follow-up of a given individual who became infected with syphilis was split into an exposed and an unexposed period. In the same way, the follow-up for gonorrhoea was split into an exposed and an unexposed period. Potentially predictive variables for HIV seroconversion identified in univariate analyses were included in a multivariate Cox proportional hazards model and adjusted IRR were calculated. All statistical analyses were conducted using STATA statistical package 11 (Stata Corporation 2009, Stata Statistical Software Release #11, College Station, TX: StataCorp LP).

Results

From April 1984 to December 2010, 4,352 MSM attended the HIV screening programme of the STI clinic of the San Gallicano Dermatological Institute in Rome, Italy. Among them, 1,862 HIV-seronegative MSM were tested more than once and qualified for inclusion in the longitudinal study. The total time at risk for the participant population was 8,638.4 years. The median number of

HIV tests received over time by the study participants was 3.0 (interquartile range (IQR): 2–6) and the median follow-up time was 2.76 years (IQR: 0.92–5.50). No change in the median number of tests per individual was observed during the study period. A total of 347 HIV-1 incident infections were observed, with an overall seroincidence rate (IR) of 4.0 (95% confidence interval (CI): 3.6–4.5) per 100 p/y.

HIV-1 incidence trend analysis

The annual incidence rates showed relevant changes during the 25-year study period. At the beginning, HIV incidence increased from 5.2 per 100 p/y (95% CI: 2.3–11.5) in 1986 to 9.2 per 100 p/y (95% CI: 6.4–13.0) in 1992. After 1992, the incidence decreased progressively to 1.3 per 100 p/y in 2001. After 2001, the incidence showed a progressive increase and reached a peak in 2009 at 11.7 per 100 p/y (95% CI: 7.4–18.6). The decennial fitted HIV-1 incidence curve, obtained after smoothing correction, made it possible to define a trend with an initial mild increase until 1992, followed by a decrease until 2001 and a noticeable increase in incidence until 2009 (Figure 1).

The Poisson regression analysis adjusted according to age at HIV seroconversion showed a slight increase in the HIV-1 incidence rate from 1985 to 1992 (the IRR was 1.07 per calendar year; 95% CI: 1.00–1.16; $p=0.05$) and a significant decrease from 1993 to 2000 (IRR=0.72; 95% CI: 0.65–0.81; $p<0.001$). From 2001 onwards, the HIV-1 incidence rate increased significantly until 2009 (IRR=1.56; 95% CI: 1.40–1.75; $p<0.001$) (Table 1). No significant difference in the median time at risk per individual was calculated in the three different calendar periods of analysis (1985–1992: 2.81 years (2.50–3.16); 1993–2000: 3.08 years (2.87–3.29); 2001–2009: 2.90 years (2.71–3.09)).

TABLE 2

Characteristics of men who have sex with men repeatedly tested for HIV-1 antibodies, by HIV status at the end of the study period, Rome, Italy, 1985–2009 (n=1,862)

	Non HIV-seroconverters (n=1,515)	HIV seroconverters (n=347)	IRR	(95% CI)	p value
Age at diagnosis in years ^{a,b} : median (range)	36 (29–44)	34 (29–40)	0.94	0.93–0.95	< 0.001
Age at diagnosis ^a , tertiles: n (%)					
>41 years	505 (33)	81 (23)	1	-	-
33–41 years	502 (33)	140 (40)	2.33	1.58–3.44	< 0.001
16–32 years	508 (33)	126 (36)	4.99	3.46–7.19	< 0.001
Educational level ^c : n (%)					
Low	253 (20)	83 (30)	1	-	-
Medium	652 (52)	147 (53)	0.89	0.66–1.20	0.454
High	360 (28)	45 (16)	0.46	0.31–0.68	< 0.001
Nationality: n (%)					
Italian	1,196 (79)	299 (86)	1	-	-
Non-Italian	319 (21)	48 (14)	0.49	0.34–0.70	< 0.001
Age at first intercourse in years ^b : median (range)	18 (16–25)	17 (16–22)	0.96	0.94–0.97	< 0.001
History of selected STI ^d : n (%)					
No	1,457 (96)	323 (93)	1	-	-
Yes	58 (4)	24 (7)	0.96	0.60–1.52	0.873
History of gonorrhoea (any sites): n (%)					
No	1,499 (99)	340 (98)	1	-	-
Yes	16 (1)	7 (2)	1.22	0.52–2.86	0.660
History of syphilis: n (%)					
No	1,469 (97)	327 (94)	1	-	-
Yes	46 (3)	20 (6)	0.93	0.57–1.53	0.786
Occurrence of syphilis ^e : n (%)					
No	1,048 (69)	241 (69)	1	-	-
Yes	467 (31)	106 (31)	1.69	1.31–2.19	< 0.001
Occurrence of gonorrhoea ^e : n (%)					
No	1,270 (84)	290 (84)	1	-	-
Yes	245 (16)	57 (16)	1.79	1.29–2.47	< 0.001

CI: confidence interval; IRR: incidence rate ratio; STI: sexually transmitted infections. Subtotals differ depending on how the number of individuals for whom the information was known.

^a For non-seroconverted individuals, the age at last HIV-negative test is shown.

^b Age at diagnosis/first intercourse was used as continuous variable.

^c Information missing for 72 HIV-infected and 250 HIV-uninfected individuals.

^d At enrolment. The STIs investigated includes: syphilis, gonorrhoea (any sites), genital herpes, genital warts, non-gonococcal genital infections and chlamydia.

^e During follow-up period.

Using the smoothing curve, the analysis adjusted according to age at HIV seroconversion showed that the increase in incidence from 1985 to 1992 was mainly sustained by individuals who were younger than 25 years and by those aged 25 to 49 years (Figure 2A). For the young MSM, a peak in incidence was reached in 1993 (incidence rate (IR)=11.3; 95% CI: 7.0–35.1). In contrast, in MSM aged 25 to 49 years, the peak was reached already in 1989 (IR=11.6; 95% CI: 4.9–18.5). MSM older than 49 years did not contribute to the observed increase in incidence; the annual incidence rate in this age group decreased constantly from 1985

to 2000 (Figure 2A). After 1992, HIV incidence among MSM up to 49 years of age decreased progressively until 2001; thereafter, incidences in all age groups showed a dramatic increase until 2009. Surprisingly, after 2000, for the first time since 1985, the oldest age group also showed an increase in HIV incidence from ca 0.5 per 100 p/y (95% CI: 0.15–3.5) in 2001 to 6.1 per 100 p/y (95% CI: 1.3–20.5) in 2009, which is consistent with the level of increase found for the other age groups.

The trend analysis by birth cohort was consistent with the findings observed when stratifying the data according to age group and showed that all the three selected birth cohorts contributed to the increase in the HIV-1 incidence after 2001. This increase was mostly due to MSM born after 1975 who were tested for the first time after 1995 (Figure 2B). HIV-1 incidence curves for the birth cohorts of MSM born before 1960 and between 1960 and 1974 were almost parallel and consistent with the overall trend (Figure 1). In contrast, the HIV-1 trend for the birth cohort born after 1974 showed a rapid decrease from 1995 to 2000, followed by a rapid increase until 2009.

Risk factor analysis

No difference in the median number of HIV tests performed was observed between seroconverters and non-seroconverters (3.0 vs 3.0, OR=1.01; 95% CI: 0.98–1.03). For seroconverters, the median time of infection was 1.72 years (IQR: 0.47–3.93) following enrolment. No difference in median age between HIV seroconverters and non-seroconverters (35.4 years vs 35.2 years) was observed. In addition, no statistically significant difference in the number of sexual partners (both lifetime and in the six months preceding the HIV tests), in the proportion of condom use per sexual act, and in the characteristics of partnership were observed between HIV seroconverters and non-seroconverters (data not shown).

Other demographic characteristics and risky sexual behaviour of the participants by HIV status at the end of the study are presented in Table 2. The risk of HIV infection increased inversely with the age at diagnosis. Compared with MSM older than 41 years, the incidence rate was more than doubled (IRR=2.33) for those aged 33 to 41 years and five times higher (IRR=4.99) for those aged 16 to 32 years. Moreover, the risk of HIV-1 seroconversion was reduced by half in individuals with a high educational level (IRR=0.46) and in those who were not Italian citizens (IRR=0.49). No significant difference in the risk of seroconversion was observed between individuals with a history of STIs at enrolment compared with those with no history of STIs. However, a significant increase in the risk of HIV-1 infection was found among MSM who became infected with syphilis (IRR=1.69; 95%CI: 1.31–2.19) or gonorrhoea (IRR=1.79; 95% CI: 1.29–2.47) during the study period.

Potential confounders for HIV-1 seroconversion were included in the multivariate Cox model. Independent risk factors for HIV-1 seroconversion in MSM living in Rome included: young age, low educational level, Italian nationality and occurrence of syphilis and/or gonorrhoea during the year preceding HIV-1 seroconversion (Table 3).

More specifically, our data confirmed that the risk of becoming HIV-infected increased inversely with the age at the diagnosis. The incidence rate was 17 times higher in MSM younger than 33 years and five times

TABLE 3

Multivariate analysis of risk factors for HIV infection among men who have sex with men with no history of injecting drugs, Rome, Italy, 1985–2009 (n=1,540^a)

	IRR _{adjusted}	95% CI	p value
Age at diagnosis in years (tertiles)			
>41	1	-	-
33–41	5.09	2.92–8.87	<0.001
16–32	17.18	9.74–30.32	<0.001
Educational level			
Low	1	-	-
Medium	0.92	0.68–1.25	0.593
High	0.54	0.35–0.82	0.004
Nationality			
Italian	1	-	-
Non-Italian	0.45	0.28–0.71	0.001
Occurrence of gonorrhoea^b (any sites)			
No	1	-	-
During the year preceding SC	1.66	1.01–2.71	0.045
More than one year before SC	1.63	1.06–2.49	0.025
Occurrence of syphilis^b			
No	1	-	-
During the year preceding SC	7.71	5.00–11.88	<0.001
More than one year before SC	1.16	0.83–1.62	0.376
Birth cohort			
After 1974	1	-	-
1960–1974	0.33	0.22–0.50	<0.001
Before 1960	0.14	0.07–0.25	<0.001

CI: confidence interval; IRR: incidence rate ratio; SC: HIV-1 seroconversion.

^a Missing values on educational level for 322 individuals.

^b During follow-up period.

higher in those aged 33 to 41 years compared with the oldest age group. Similarly, MSM born after 1974 and those born between 1960 and 1974 showed a seven and three times higher risk of seroconversion compared with those born before 1960.

Furthermore, the risk of becoming HIV-1-infected was twice as high for MSM with a low educational level and for Italian citizens than for MSM with a high educational level (IRR_{adjusted}=0.54) and those with other citizenship (IRR_{adjusted}=0.45).

The multivariate analysis confirmed a dramatic increase in the risk of becoming infected with HIV after acquiring syphilis. In particular, the risk increased ca eight-fold for the first year (IRR_{adjusted}=7.71) and ca 13-fold (IRR_{adjusted}=13.5, data not listed in the Tables) for the first six months since diagnosis of syphilis, but decreased after the first year, matching the risk for syphilis-free MSM (IRR_{adjusted}=1.16). A smaller but statistically significant increase in the risk of HIV-1 seroconversion was also observed for subjects who had

contracted gonorrhoea during the year before HIV-1 seroconversion ($IRR_{\text{adjusted}} = 1.66$).

Discussion

Our longitudinal study on MSM living in Rome has provided valuable insights about the dynamics and the characteristics of the HIV epidemic in this urban population over the last 25 years. Preliminary data from this cohort about HIV-1 trends until 2003 have already been published previously [12].

Between 1985 and 1992, the first period of virus circulation in Italy, we observed a slight increase in HIV-1 incidence year by year. This is consistent with other studies which suggest that the HIV epidemic among MSM in southern Europe started later than in northern Europe and the US. In particular, our findings differ from those of the Dutch cohort of MSM in Amsterdam, where the incidence rates were higher in the first half of the 1980s and decreased between 1985 and 1992 [14].

The fast and progressive decline in HIV-1 incidence rates in our cohort between 1992 and 2001 was also described in other Western countries and can be attributed to important behavioural changes in MSM populations who adopted stable safe sexual practices in the 1990s, a fact reported in several large studies [2,15-17]. Finally, we observed a dramatic increase in HIV-1 incidence after 2001 and until 2009, consistent with our previous findings collected in the same population until 2003 [12].

This increase in incidence observed in MSM in Italy is in accordance with observations from other European studies despite different methodological approaches [9,18]. The trend was larger and accelerated among younger MSM, although it was observed for all the age groups, including those 50 years and older, who did not contribute to the increase in HIV-incidence at the beginning of the study period (from 1985 to 1992).

The dramatic increase in incidence measured since 2001 coincided with the re-emergence of bacterial STIs, such as syphilis and gonorrhoea observed among MSM living in Rome from 2000 to 2007 [4, and data not shown]. Similar findings apply to other European countries during the same period [19,20]. We observed that the risk of acquiring HIV-1 infection was higher among MSM who contracted syphilis during follow-up than for those remaining syphilis-free until the end of the study. The presence of these genital ulcerative lesions and the increased number of inflammatory cells, which enhance the potential for HIV transmission in MSM who contracted syphilis, may explain the higher HIV rates that we and other authors found for these subjects [5,21]. Besides the biological synergism between syphilis and HIV, the high number of Italian MSM who contracted HIV-1 infection within six months of being diagnosed with syphilis may also be due to the fact that both infections share a common

route of transmission and pattern of risk factors, and that social networks of persons with syphilis or at risk for syphilis are also at higher risk for HIV infection, a fact also reported in a 12-month prospective study in Chinese MSM from 2006 to 2007 [22]. Another obvious explanation may be heightened perception of being at risk for HIV-1 and/or other sexually transmitted infections among individuals already diagnosed with syphilis, which would lead at first to a larger number of MSM being tested and consequently to an earlier diagnosis of HIV, and later to a change in sexual behaviour. The adoption of safer sexual practices as a response to educational programmes to which MSM were enrolled after the diagnosis of primary or secondary syphilis may also explain why the risk of becoming infected with HIV-1 dramatically declined within the first year since diagnosis of syphilis.

The association between the occurrence of gonorrhoea and the risk of HIV-1 seroconversion is consistent with data from the Amsterdam Cohort Study, although Dutch MSM who had contracted gonorrhoea in the six months before seroconversion had a much higher risk than that observed in our study [14]. The risk of HIV-1 seroconversion increased after the diagnosis of gonorrhoea and remained stable for MSM who had contracted gonorrhoea in the year before seroconversion, suggesting that gonorrhoea may be considered as a proxy for risky sexual practices but, in contrast to syphilis, did not increase the biological susceptibility of seronegative individuals for HIV.

Other relevant predictors of HIV-1 seroconversion in our cohort were young age, low educational level and Italian nationality. After 2000, association of young age with a higher risk of HIV-1 infection was reported in several incidence studies in Europe [14,23] and in the US [24], perhaps due to a lower ratio of condom use per sexual act in the young population [14,25], the way young individuals select partners (i.e. Internet-based recruitment of partners) [26,27] or their specific psychosocial attitudes (i.e. involvement in the homosexual community, importance of gay identity, self-homophobia) [28]. To the same extent, a low educational level was found to increase the risk of HIV-1 seroconversion in other European studies [14].

Our study may have suffered from some limitations and biases. Firstly, the repeatedly tested MSM in our longitudinal cohort study may not be representative of the whole MSM population living in Rome. In fact, our data probably describe the circulation of HIV-1 in a subpopulation of MSM with an increased risk of sexually transmitted infections. Nor can we exclude that attending an HIV-1 monitoring programme which offers counselling activities aimed at the reduction of sexual risk behaviour may reduce the risk of HIV-1 infection so that our population may have been at a lower risk than the general MSM population in Rome. Secondly, the individual data collection form, defined more than two decades ago, may have failed to evidence the role of

certain risk factors for HIV-1 infection, especially those relevant among the homosexual communities in recent years (i.e. non-injection recreational drugs use, choosing sexual partners using the Internet or serosorting practice).

Despite these limitations, our findings suggest that, in accordance with the re-emergence of syphilis and gonorrhoea observed in Rome after 2000, particularly among young Italian MSM with a low educational level, HIV-1 infection continues to be contracted disproportionately more frequently by the homosexual community in Rome. These findings highlight the need for improved monitoring systems for HIV-1 risk in urban communities of MSM and more effective interventions targeted at limiting the circulation of other STIs in this population and to prevent waning of the benefits of ART on the HIV-1 transmission rate at community level.

We have started in mid-2011 a programme with multiple approaches based on opt-out strategies for HIV testing, outreach testing by a rapid saliva-based assay and the reduction of barriers to accessibility for MSM to our STI clinic (also supported by local non-governmental organisations for homosexuals) to decrease the fraction of MSM unaware of their HIV infection, to increase the number of individuals tested for the first time, and to reduce the span between last negative and first positive HIV-1 antibody tests among those tested more than once. In addition, continuing behavioural interventions are needed to improve basic information and attitudes to promote persistent condom use in the homosexual community in Rome, particularly among the young and those with low educational level as well as among HIV-1 infected MSM.

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Conflict of interest

None declared.

Authors' contributions

MG and GR conceived and designed the study, MG and MFV performed the data analysis and interpreted the results, MG, MFV and GR prepared the manuscript for publication, MG, AL, GP and ADC consulted patients and collected clinical and behavioural data after 2000, FP and FE carried out the laboratory work and performed the serological and microbiological

analyses, MGD, FS and FC contributed to data input and management. All authors have read and approved the final version of the manuscript.

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Trends in HIV testing, prevalence among first-time testers, and incidence in most-at-risk populations in Spain: the EPI-VIH Study, 2000 to 2009

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During 2000 to 2009, data on people undergoing HIV testing and on those newly diagnosed with HIV were collected in a network of 20 Spanish clinics specialising in sexually transmitted infections and/or HIV testing and counselling. The number of tests performed, overall and disaggregated by different variables, was obtained. HIV prevalence among first-time testers and HIV incidence among repeat testers were calculated. To evaluate trends, joinpoint regression models were fitted. In total, 236,939 HIV tests were performed for 165,745 individuals. Overall HIV prevalence among persons seeking HIV testing was 2.5% (95% CI: 2.4 to 2.6). Prevalence was highest in male sex workers who had sex with other men (19.0% (95% CI: 16.7 to 21.4)) and was lowest in female sex workers (0.8% (95% CI: 0.7 to 0.9)). Significant trends in prevalence were observed in men who have sex with men (MSM) (increasing) and heterosexual individuals (decreasing). The incidence analysis included 30,679 persons, 64,104 person-years (py) of follow-up and 642

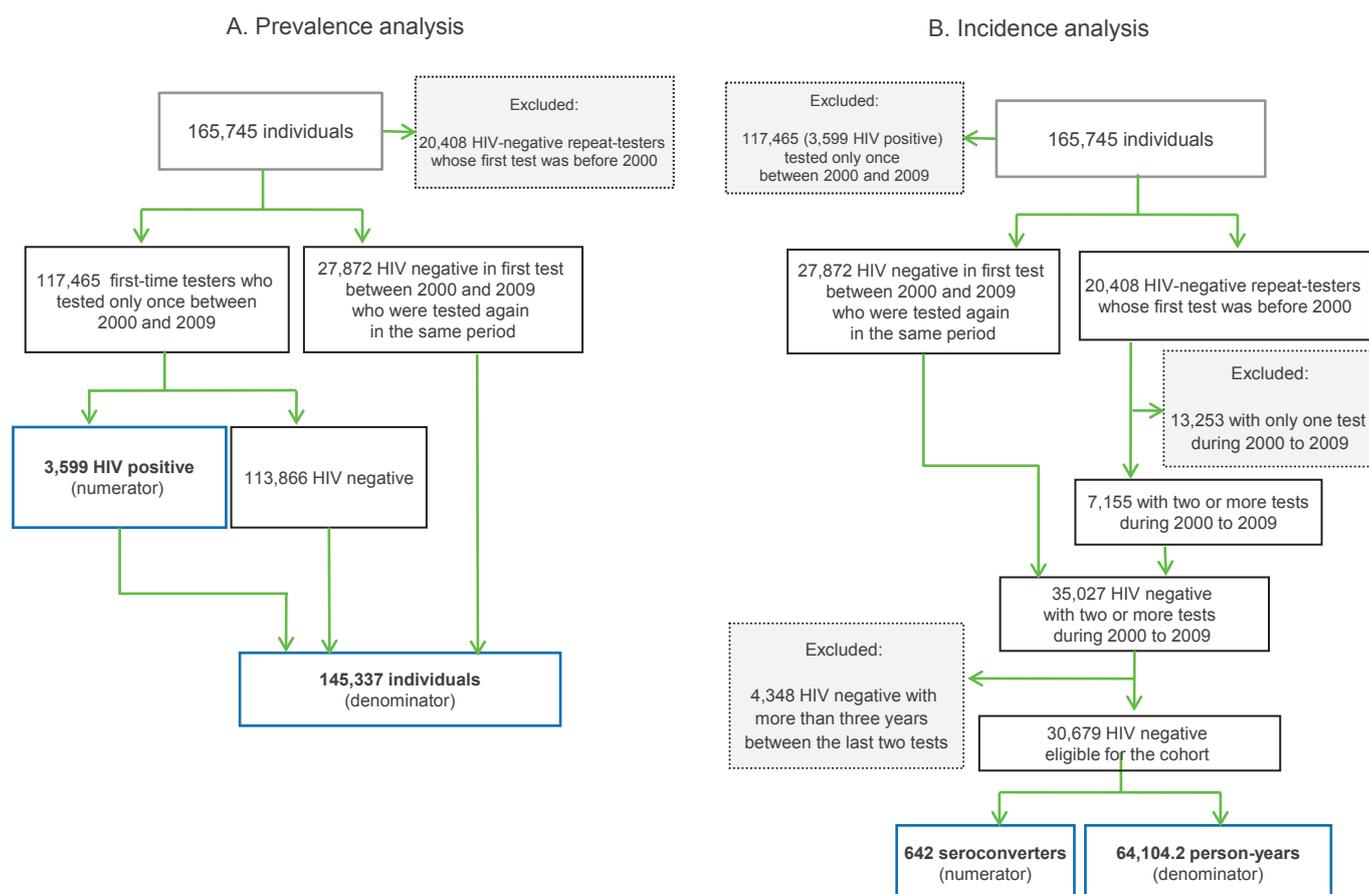
seroconversions. The overall incidence rate (IR) was 1.0/100 py (95% CI: 0.9/100 to 1.1/100). Incidence was significantly higher in men and transgender females than in women (1.8/100 py (95% CI: 1.6 to 1.9), 1.2/100 py (95% CI: 0.5 to 2.8) and 0.1/100 py (95% CI: 0.09 to 0.2) respectively) and increased with age until 35–39 years. IRs in MSM and people who inject drugs were significantly greater than in heterosexual individuals (2.5/100 py (95% CI: 2.3 to 2.7), 1.6/100 py (95% CI: 1.1 to 2.2) and 0.1/100 py (95% CI: 0.09 to 0.2) respectively), and an upward trend was observed in MSM. Our results call for HIV prevention to be reinforced in MSM and transgender women in Spain.

Introduction

During the 1980s and 90s, Spain had the highest AIDS incidence in western Europe (with a peak of 184 cases per million population in 1994), and HIV transmission was attributed in most cases to the use of contaminated material (injection equipment and substance injected)

FIGURE 1

Flowchart of inclusion of persons undergoing HIV testing in prevalence and incidence analyses, EPI-VIH Study, Spain, 2000–09



by people who inject drugs (PWID) [1]. Widespread dissemination of highly active antiretroviral therapy (HAART) in 1996 produced a sharp decrease in AIDS incidence and mortality [2,3], while harm reduction and other public health programmes resulted in less drug injection [4-6]. As a result, the number of new HIV diagnoses in PWID decreased, and sexual transmission emerged as the most common transmission category in the country, in particular among men who have sex with men (MSM). Meanwhile, people born abroad, whose presence was barely registered in the Spanish HIV epidemic before 2000, came to play an important part in it [7], as a consequence of the influx of foreign-born persons, whose proportion in the Spanish population increased from 2.9% in 1998 to 14.3% in 2012 [8]. Of all foreigners living in Spain in 2012, 40.8% had been born in other European countries, 36.4% in Latin America, 12.6% in northern Africa and 3.7% in Sub-Saharan Africa [8].

As the benefits of HAART became obvious, early diagnosis and treatment of HIV infection became a priority in Spain, reflected in the national multi-annual strategic plans on HIV/AIDS [9]. Anyone can be tested for HIV free of charge in primary care centres and other public facilities, and private laboratories also perform the

test; free-of-charge antenatal care, including HIV testing, is offered to all pregnant women. Nevertheless, actions aiming at reducing late presentation have increased, especially since 2005: these include information campaigns, opening of HIV counselling and testing (HCT) community centres, and the introduction of rapid tests in community programmes, health centres and pharmacies.

In the framework of second generation surveillance for HIV [10], the systematic collection of prevalence data in key populations is recommended for countries with concentrated epidemics, such as Spain. To this end, in 1999, the so-called EPI-VIH Study was initiated in 10 clinics (EPI-VIH Network) specialising in sexually transmitted infections (STI) or HCT. What distinguish these clinics from other public health facilities offering testing is that they are low-threshold, highly accessible centres that traditionally have attended most-at-risk populations for HIV and other STI. Analysis of retrospective and prospective data collected in the network documented a decrease in HIV prevalence from 1992 to 2002 in all most-at-risk populations, including PWID, MSM, female sex workers (FSW) and high-risk heterosexual individuals (i.e. those with a history of risk behaviours for HIV infection) [11,12].

From 2000, 10 more clinics joined the EPI-VIH Network and the EPI-VIH Study was expanded. The aim of the new project was to prospectively collect and analyse data on the following: (i) the number of HIV tests carried out in the EPI-VIH Network and characteristics of people requesting testing; (ii) HIV prevalence in most-at-risk populations attending the network clinics; and (iii) HIV incidence among all people attending the network clinics. Yearly publications describing both people tested and prevalence results [13], as well as some preliminary incidence analyses from the network [14], have provided useful insight into the HIV situation in Spain and have been used to define health policy.

The objective of this paper is to describe trends in HIV testing, HIV prevalence among first-time testers, and HIV incidence in most-at-risk populations attending the EPI-VIH Network clinics in a 10-year period, from 2000 to 2009.

Methods

The EPI-VIH Network

From 2000 to 2009, the EPI-VIH Network comprised 20 STI/HCT clinics located in Spain's most populated cities: Madrid (two clinics), Barcelona, Seville, Bilbao, Granada, Oviedo, Gijón, San Sebastián, Vitoria, Logroño, Pamplona, Cartagena, Murcia, Málaga, Alicante, Castellón, Valencia, Santa Cruz de Tenerife and Santander. These are public, low-threshold facilities, operating free of charge, where every effort is made to maximise accessibility for most-at-risk populations. Of the 20 clinics, 13 are regular STI clinics, which offer HCT, while the remaining seven specialise in HCT. All clinics work on demand (i.e. people attending the clinic do not need to be referred by healthcare staff), no incentives are offered, and there are no differences between STI and HCT clinics regarding the provision of HIV-related services or the referral of newly diagnosed patients; nevertheless, HCT clinics were created specifically to perform HIV testing and tend to receive clients at higher risk for HIV.

Participation in the EPI-VIH Study is voluntary but, to our knowledge, all specialised STI/HCT clinics in Spain are included in the EPI-VIH Network.

HIV testing practices

All HIV tests performed in the EPI-VIH Network during the study period were analysed. The testing included pre- and post-test counselling and was performed using an enzyme-linked immunosorbent assay (ELISA) followed by a western blot to confirm positive results. For each test, people undergoing testing were classified according to whether this was the first time they had ever been tested in one of the network's clinics (first-time tester) or whether they had previously been tested in the same clinic (repeat tester). Anamnestic information about previous tests was not collected because for the incidence analysis (described below), the exact date of all tests performed had to be

documented. Linkage between tests performed in different clinics was not feasible. Epidemiological information (age, sex, country of birth, date of testing, test result, status as first-time/repeat tester, and probable HIV transmission category) of the person being tested was collected through use of a questionnaire by the attending physician.

Data were collected in the context of HIV sentinel surveillance and the database was registered in the Spanish Data Protection Agency (Registry number 2080910068). No personal identifiers were collected.

Study population

All participants meeting the definition of first-time testers during the study period were included in the prevalence analysis (Figure 1A).

To estimate HIV incidence, an open cohort of people tested two or more times for HIV at one of the clinics belonging to the EPI-VIH Network between 1 January 2000 and 31 December 2009 was identified. People were eligible to enter the cohort if they met the following three criteria: (i) a documented negative result in the first HIV test performed during the study period at one of the network's clinics; (ii) at least one additional documented HIV test in the same clinic; and (iii) less than three years between their last two documented HIV tests (Figure 1B). The three-year time frame was chosen to identify true incident cases and to improve the estimates' precision.

New HIV diagnosis was defined according to the European case definition [15]. All FSW in our study had sex only with men whereas male sex workers fell into two categories: those who had sex with men (MSM sex workers) and those who had intercourse only with women. Since the latter were very few ($n=242$) and their HIV prevalence did not differ from that of other heterosexual men, it was decided to classify them as heterosexual men for all analyses.

Statistical analyses

We calculated the number of tests performed for first-time and repeat testers each year, stratified by type of most-at-risk populations, as well as the distribution of study participants by the variables of interest. Chi-squared tests were used to compare categorical variables.

HIV prevalence and its 95% confidence interval (CI) was calculated overall and stratified by different variables. A new HIV diagnosis for the prevalence analysis was classified as HIV prevalent when the person tested met the definition of first-time tester.

Only patients meeting the criteria for inclusion in the above-mentioned open cohort were included in the incidence analysis. Incidence rates (IR) and their 95% CIs were calculated overall and stratified by different variables, assuming a Poisson distribution. Although

TABLE 1

Characteristics of people undergoing HIV testing, by category of transmission, EPI-VIH Study, Spain, 2000–09 (n=165,745)

Variable	Transmission category						Total Number (%)
	PWID	MSM	Heterosexual men and women	Female sex workers	MSM sex workers	Unknown	
	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	Number (%)	
Sex							
Male	3,378 (76.2)	29,528 (99.6)	53,548 (55.9)	NA	954 (72.5)	3,624 (56.8)	91,032 (54.9)
Female	1,051 (23.7)	NA	42,196 (44.1)	28,210 (100.0)	NA	2,702 (42.4)	74,159 (44.7)
Transgender women	2 (0.0)	113 (0.4)	1 (0.0)	0 (0.0)	362 (27.5)	51 (0.8)	529 (0.3)
Unknown	2 (0.0)	3 (0.0)	9 (0.0)	8 (0.0)	0 (0.0)	3 (0.0)	25 (0.0)
Age group (years)							
<20	68 (1.5)	1,283 (4.3)	4,460 (4.7)	1,280 (4.5)	56 (4.3)	570 (8.9)	7,717 (4.7)
20–24	478 (10.8)	5,969 (20.1)	21,347 (22.3)	8,164 (28.9)	411 (31.2)	1,181 (18.5)	37,550 (22.7)
25–29	936 (21.1)	7,170 (24.2)	25,245 (26.4)	7,959 (28.2)	391 (29.7)	1,492 (23.4)	43,193 (26.1)
30–34	1,130 (25.5)	6,012 (20.3)	17,948 (18.7)	5,236 (18.6)	222 (16.9)	1,145 (17.9)	31,693 (19.1)
35–39	987 (22.3)	4,320 (14.6)	10,935 (11.4)	3,097 (11.0)	123 (9.3)	848 (13.3)	20,310 (12.3)
40–44	592 (13.4)	2,413 (8.1)	6,718 (7.0)	1,612 (5.7)	68 (5.2)	506 (7.9)	11,909 (7.2)
45–49	183 (4.1)	1,164 (3.9)	4,132 (4.3)	590 (2.1)	24 (1.8)	278 (4.4)	6,371 (3.8)
≥50	59 (1.3)	1,313 (4.4)	4,969 (5.2)	280 (1.0)	21 (1.6)	360 (5.6)	7,002 (4.2)
Region of birth							
Spain	3,331 (75.1)	23,612 (79.7)	70,351 (73.5)	2,147 (7.6)	258 (19.6)	4,486 (70.3)	104,185 (62.9)
Western ^a /eastern Europe	465 (10.5)	1,417 (4.8)	6,847 (7.2)	3,189 (11.3)	100 (7.6)	355 (5.6)	12,373 (7.5)
Latin America	128 (2.9)	3,440 (11.6)	11,310 (11.8)	19,589 (69.4)	910 (69.1)	559 (8.8)	35,936 (21.7)
Sub-Saharan/North Africa	60 (1.4)	145 (0.5)	4,046 (4.2)	2,427 (8.6)	19 (1.4)	408 (6.4)	7,105 (4.3)
Other	16 (0.4)	326 (1.1)	1,080 (1.1)	160 (0.6)	6 (0.5)	46 (0.7)	1,634 (1.0)
Unknown	433 (9.8)	704 (2.4)	2,120 (2.2)	706 (2.5)	23 (1.7)	526 (8.2)	4,512 (2.7)
Year							
2000	1,078 (24.3)	2,924 (9.9)	7,418 (7.7)	3,662 (13.0)	101 (7.7)	765 (12.0)	15,948 (9.6)
2001	711 (16.0)	2,547 (8.6)	7,947 (8.3)	3,239 (11.5)	89 (6.8)	631 (9.9)	15,164 (9.1)
2002	564 (12.7)	2,458 (8.3)	8,512 (8.9)	3,537 (12.5)	122 (9.3)	597 (9.4)	15,790 (9.5)
2003	495 (11.2)	2,603 (8.8)	8,769 (9.2)	3,050 (10.8)	133 (10.1)	454 (7.1)	15,504 (9.4)
2004	419 (9.5)	2,916 (9.8)	9,607 (10.0)	2,944 (10.4)	142 (10.8)	577 (9.0)	16,605 (10.0)
2005	333 (7.5)	2,834 (9.6)	9,802 (10.2)	2,586 (9.2)	151 (11.5)	618 (9.7)	16,324 (9.8)
2006	253 (5.7)	3,202 (10.8)	10,090 (10.5)	2,559 (9.1)	123 (9.3)	702 (11.0)	16,929 (10.2)
2007	215 (4.8)	3,365 (11.4)	10,646 (11.1)	2,587 (9.2)	148 (11.2)	673 (10.5)	17,634 (10.6)
2008	207 (4.7)	3,578 (12.1)	11,650 (12.2)	2,269 (8.0)	187 (14.2)	697 (10.9)	18,588 (11.2)
2009	158 (3.6)	3,217 (10.9)	11,313 (11.8)	1,785 (6.3)	120 (9.1)	666 (10.4)	17,259 (10.4)
HCT/STI clinic location^b							
Northern Spain	520 (11.7)	3,576 (12.1)	21,435 (22.4)	8,147 (28.9)	166 (12.6)	808 (12.7)	34,652 (20.9)
Southern Spain	223 (5.0)	4,494 (15.2)	20,125 (21.0)	2,948 (10.4)	91 (6.9)	1,103 (17.3)	28,984 (17.5)
Eastern Spain	2,799 (63.1)	8,992 (30.3)	29,586 (30.9)	6,757 (23.9)	550 (41.8)	3,151 (49.4)	51,835 (31.3)
Central Spain	686 (15.5)	11,288 (38.1)	19,078 (19.9)	9,375 (33.2)	456 (34.7)	767 (12.0)	41,650 (25.1)
Canary Islands	205 (4.6)	1,294 (4.4)	5,530 (5.8)	991 (3.5)	53 (4.0)	551 (8.6)	8,624 (5.2)
Total	4,433 (100)	29,644 (100)	95,754 (100)	28,218 (100)	1,316 (100)	6,380 (100)	165,745 (100)

HCT: HIV counselling and testing; MSM: men who have sex with men; NA: not applicable; PWID: people who inject drugs; STI: sexually transmitted infections.

^a Excluding Spain.

^b Northern Spain: Oviedo, Gijón, Santander, Navarre, Vitoria, Bilbao, Guipuzcoa and La Rioja. Southern Spain: Granada, Málaga and Seville. Eastern Spain: Castellón, Alicante, Valencia, Barcelona, Murcia and Cartagena. Central Spain: Madrid-Sandoval and Madrid-Ayuntamiento. Canary Islands: Tenerife.

personal identifiers were not used in the study, linkage of different tests performed for the same person in the same clinic was possible through the use of a unique identifying number: this allowed the identification of seroconverters and the calculation of person-years (py) of exposure in the incidence analysis. A new HIV diagnosis for the incidence analysis was classified as HIV incident (seroconverter) if the person tested was eligible to enter the open cohort and their HIV test changed from negative to positive, i.e. they were positive in their last visit to one of the network's clinics having been HIV negative in their previous visit to the same clinic. Seroconversion was assumed to have taken place at the midpoint between the first HIV-positive visit and the last previous HIV-negative visit. To calculate py of exposure, non-seroconverters contributed the time elapsing between their first and last HIV tests during the study period, while seroconverters contributed the time elapsing between their first HIV test and the estimated date of seroconversion. For annual estimates of HIV incidence, we allocated each person's py to the years that they contributed.

To evaluate trends in the number of tests, HIV prevalence and incidence, joinpoint regression models were fitted [16]. Statistical significance was considered at a p-value <0.05. All statistical analyses were performed using Stata statistical software (release 11.1, College Station, TX, United States, 2009).

Results

From 2000 to 2009, a total of 236,939 HIV tests were carried out in the EPI-VIH Network for 165,745 individuals (Table 1). Of these, 117,465 were tested for the first time ever in one of the network's clinics during the study period (3,599 with a positive result) and never came back, i.e. they were tested only once; 27,872 were first-time testers at some time between 2000 and 2009: the result of the first test was negative and later they underwent testing again, thus becoming repeat testers; and 20,408 were tested for the first time before the study period with a negative result and were retested again during the study period (these persons were always considered repeat testers). People who were tested once were eligible only for the prevalence analysis; those tested before 2000 were eligible for the incidence analysis if they met the criteria to enter the open cohort. The remaining 27,872 were included in the HIV prevalence analysis the first time they were tested during the study period, and also in the HIV incidence analysis if, later on, they met the criteria to enter the open cohort (Figure 1A and 1B).

In total, 145,337 individuals met the definition of first-time tester during the study period and were eligible for the prevalence analysis, of whom 3,599 tested positive (Figure 1A).

There were initially 48,280 HIV-negative repeat-testers potentially eligible to enter the open cohort: the 27,872 and 20,408 mentioned above. Of the latter, 13,253 had

only one HIV test during the study period and therefore were excluded from the open cohort. Of the remaining 35,027 HIV-negative individuals with two or more HIV tests during the study period, 4,348 were excluded because more than three years had passed between their last two tests, leaving 30,679 HIV-negative subjects eligible for the cohort. Over the study period, they totalled 64,104.2 py of follow-up and 642 seroconverters were identified among them (Figure 1B).

HIV tests

The 236,939 tests took place in the following years: 17,402 (7.3%) in 2000, 19,436 (8.2%) in 2001, 22,244 (9.4%) in 2002, 22,389 (9.4%) in 2003, 24,395 (10.3%) in 2004, 24,639 (10.4%) in 2005, 25,723 (10.9%) in 2006, 26,502 (11.2%) in 2007, 27,797 (11.7%) in 2008 and 26,412 (11.1%) in 2009.

Of the total tests, 145,337 (61.3%) were carried out in first-time testers and 91,596 (38.7%) in repeat testers; in six instances, no information was available. Over the study period, the annual number of tests increased significantly ($p < 0.05$) among both first-time and repeat testers: in first-time testers, the increase was 44.7%, from 11,084 tests performed in 2000 to 16,035 in 2009; in repeat-testers, the increase was 64.2%, from 6,318 in 2000 to 10,377 in 2009.

First-time testers differed from repeat testers most notably by transmission category. The majority, 87,120 (59.9%), of first-time testers were heterosexual individuals (men and women), 24,600 (16.9%) were FSW, 24,099 (16.6%) MSM, 3,182 (2.2%) PWID, 1,222 (0.8%) MSM sex workers and 5,114 (3.5%) unknown. Among repeat testers, 28,792 (31.4%) were FSW, 26,817 (29.3%) MSM, 27,129 (29.6%) heterosexual individuals, 3,369 (3.7%) PWID, 1,258 (1.4%) MSM sex workers and 4,231 (4.6%) unknown.

The number of tests significantly increased from 2000 to 2009 in first-time and repeat testers in all most-at-risk populations except PWID and FSW. In first-time testers, the number of tests increased in MSM from 1,483 to 2,943 ($p < 0.05$), in heterosexual individuals from 5,848 to 10,723 ($p < 0.05$) and in MSM sex workers from 63 to 113 ($p < 0.05$). In PWID, it decreased from 630 to 130 ($p < 0.05$) and from 2,432 to 1,592 ($p < 0.05$) in FSW. In repeat testers, the number of tests increased in MSM from 1,760 to 3,555 ($p < 0.05$), in heterosexual individuals from 1,927 to 3,425 ($p < 0.05$) and in MSM sex workers from 71 to 151 ($p < 0.05$). The number decreased in PWID from 561 to 225 ($p < 0.05$). Among FSW, the number of tests increased from 1,811 to 3,394 ($p < 0.05$) from 2000 to 2005 and decreased afterwards, to 2,319 in 2009 ($p < 0.05$).

In about four of 10 tests, the person tested was born outside Spain (52,358/145,337 (36.0%) of tests in first-time testers vs 36,380/91,596 (39.7%) in repeat testers). In first-time testers, the proportion of foreigners increased during 2000 to 2002, from 2,993/8,594

TABLE 2

HIV prevalence in people undergoing HIV testing, by different variables, EPI-VIH Study, Spain, 2000–09 (n=145,337)

Variables	Prevalence (%) by year of diagnosis										Total n=145,337 % (95% CI)
	2000 n=11,084	2001 n=12,466	2002 n=13,559	2003 n=13,647	2004 n=14,937	2005 n=14,895	2006 n=15,366	2007 n=16,160	2008 n=17,188	2009 n=16,035	
Sex											
Male	4.5	3.4	3.4	3.4	3.2	4.0	3.3	3.1	3.8	3.8	3.6 (3.4 to 3.7)
Female	1.5	1.5	0.9	1.2	1.2	0.9	0.8	0.8	0.9	0.6	1.0 (1.0 to 1.1)
Transgender women	0.0	18.8	33.3	20.0	20.5	29.7	25.0	26.6	26.5	22.0	24.5 (20.4 to 29.0)
Age group (years)											
<20	0.8	0.8	0.7	1.0	1.5	0.5	0.6	1.6	1.6	0.8	1.0 (0.8 to 1.3)
20–24	1.7	1.5	1.2	1.4	1.5	1.9	1.2	1.4	2.1	1.9	1.6 (1.5 to 1.7)
25–29	2.6	1.5	2.0	2.4	1.8	1.9	2.4	2.5	2.7	2.7	2.2 (2.1 to 2.4)
30–34	4.3	3.4	3.4	3.0	2.6	3.9	2.2	2.4	2.8	2.9	3.0 (2.8 to 3.2)
35–39	5.9	4.7	3.4	4.8	4.0	3.7	3.8	2.7	2.6	3.0	3.7 (3.5 to 4.0)
40–44	3.6	4.7	3.6	2.7	4.1	4.1	3.8	2.9	3.6	3.5	3.7 (3.3 to 4.0)
45–49	2.9	2.2	1.6	2.6	2.8	3.0	3.1	2.5	4.6	4.4	3.1 (2.7 to 3.6)
≥50	4.2	4.1	1.6	1.0	2.1	2.6	2.0	2.4	3.4	2.2	2.5 (2.1 to 2.9)
Region of birth											
Spain	3.0	2.6	2.0	2.2	2.1	2.3	1.8	1.9	2.3	2.4	2.2 (2.1 to 2.3)
Western Europe ^a	3.4	3.4	1.7	3.0	2.5	3.2	2.1	1.3	2.1	1.9	2.3 (2.0 to 2.8)
Eastern Europe	1.1	1.5	3.0	1.6	1.1	1.7	2.0	1.5	2.5	1.6	1.8 (1.4 to 2.1)
Latin America	1.5	2.0	2.1	2.2	2.5	3.5	3.4	3.2	3.9	3.3	2.8 (2.6 to 3.0)
Sub-Saharan Africa	5.4	5.4	5.8	6.8	6.9	6.9	3.0	4.9	3.8	4.7	5.3 (4.7 to 6.0)
North Africa	0.9	2.3	3.6	3.8	2.6	3.1	3.0	1.8	0.9	2.7	2.5 (1.9 to 3.3)
Type of clinic											
HCT	5.4	3.7	3.0	2.9	3.0	2.7	2.8	3.4	2.8	3.2	3.2 (3.0 to 3.5)
STI	2.5	2.2	2.1	2.3	2.2	2.6	2.1	2.0	2.7	2.5	2.3 (2.2 to 2.4)
Total	3.0	2.5	2.2	2.4	2.3	2.7	2.2	2.2	2.7	2.6	2.5 (2.4 to 2.6)

CI: confidence interval; HCT: HIV counselling and testing; STI: sexually transmitted infections.

^a Excluding Spain.

(34.8%) to 5,612/13,558 (41.4%), decreasing thereafter to 5,420/16,035 (33.8%) in 2009 (statistically significant trend with a turning point in 2002, $p < 0.05$). The proportion of foreigners among people testing several times followed a similar pattern, but the trend was not statistically significant. Latin America was the most common region of birth among foreigners (60,526 (25.5%) of the total number of tests), followed by eastern Europe (9,430 (4%)).

HIV prevalence

In total, 145,337 persons, of whom 3,599 were HIV-positive, were tested for the first time ever in one of the network's clinics during the study period (Figure 1A). Of the 3,599 found to be positive, 1,484 (41.2%) were born outside Spain, with the proportion ranging from 15.6% (84/540) among PWID to 90.7% (195/215) among MSM sex workers.

The overall HIV prevalence during the study period in these first-time testers was 2.5% (95% CI: 2.4–2.6) and

was higher in HCT than in STI clinics (3.2% (95% CI: 3.0 to 3.5) vs 2.3% (95% CI: 2.2 to 2.4)). HIV prevalence was highest in transgender women (24.5% (95% CI: 20.4 to 29.0)), and increased with age until it reached a peak of 3.7% (95% CI: 3.5 to 4.0) in the age group 35–39 years (Table 2). These differences in prevalence were statistically significant.

Very high HIV prevalence estimates throughout the study period were found among MSM sex workers (19.0%; range: 10.5–24.5) and PWID (17.0%; range: 13.3–21.2), although in both groups, yearly estimates were rather unstable because the number of MSM sex workers was small and the number of PWID decreased over the study period. Among MSM, HIV prevalence during the study was 7.6%, ranging from 6.4% in 2001 to 9.4% in 2009. Prevalence was much lower in heterosexual individuals (0.9%; range: 0.7–1.1) and FSW (0.8%; range: 0.5–1.2). There were no differences by sex in HIV prevalence among heterosexual individuals, therefore combined estimates are presented. Joinpoint

models fit to evaluate trends in HIV prevalence by transmission category showed a decreasing trend in heterosexual individuals and an increasing trend in MSM (Figure 2).

Foreign-born participants had a higher HIV prevalence during the study period than did those who were Spanish born (2.9% (95% CI: 2.7 to 3.0) vs 2.2% (95% CI: 2.1 to 2.3), $p < 0.05$) and the same was true for each region of birth except eastern Europe. An increasing trend in HIV prevalence was observed among Latin American-born participants ($p < 0.05$) (Table 2).

HIV incidence

In all, 30,679 individuals entered the open cohort, totalling 64,104.2 py of follow-up and 642 seroconverters. The majority of eligible persons 17,288 (56.3%), tested only twice during the study period, 6,068 (19.8%) tested three times and 7,323 (23.9%) tested more than three times; the corresponding figures among seroconverters were 289 (45.0%), 136 (21.2%) and 217 (33.8%). The median time between tests was 9.3 months (interquartile range: 5.9–15.7) for the overall cohort and 10.6 months for seroconverters (interquartile range: 6.3–17.6).

The overall HIV IR for the study period was 1.0 seroconversions/100 py (95% CI: 0.9/100 to 1.1/100), with no statistically significant differences by type of clinic. The IR was highest in the country's biggest cities, Madrid, Barcelona, Valencia and Seville (1.5/100 py (95% CI: 1.4 to 1.7), 1.1/100py (95% CI: 0.8 to 1.5), 1.2/100py (95% CI: 0.9 to 1.4) and 1.0/100 py (95% CI: 0.8 to 1.3) respectively), although Bilbao, which has about the same population as Valencia or Seville, had a much lower IR (0.4/100 py (95% CI: 0.3 to 0.7)). In general, centres located in northern Spain had lower seroconversion rates than those located in the eastern and southern parts of the country. Men and transgender females had higher IR than women (1.8/100 py (95% CI: 1.6 to 1.9), 1.2/100 py (95% CI: 0.5 to 2.8) and 0.1/100 py (95% CI: 0.09 to 0.2) respectively). With respect to age, the peak IR was found in people younger than 20 years, but the sample size was small, with a wide 95% CI. The next highest IR was in the 35–39 year age group (1.2/100 py; 95% CI: 1.0 to 1.5). Spanish-born participants as well as those born elsewhere in Europe had higher seroconversion rates than people born outside Europe (Table 3).

Results by transmission category showed that the highest IR was among MSM sex workers (3.0/100 py), although the 95% CI was quite wide (2.2 to 4.1), followed by MSM who were not sex workers and PWID (2.5/100 py (95% CI: 2.3 to 2.7) and 1.6/100 py (95% CI: 1.1 to 2.2) respectively). Since there were no differences in HIV incidence between male and female heterosexual individuals, combined estimates are presented (Table 3).

Joinpoint models fit to evaluate trends in incidence showed a statistically significant increase in overall HIV incidence over the study period, but stratification by transmission category showed that the increasing trend was present only among MSM (Figure 3).

Discussion

During the study period, the number of HIV tests increased in MSM, heterosexuals and MSM sex workers but not among PWID and FSW. HIV prevalence decreased in heterosexual individuals and increased in MSM, remaining stable in the other transmission categories. HIV incidence was highest among MSM sex workers and showed an increasing trend in MSM. The study provides seroconversion estimates among migrants after their arrival in Spain.

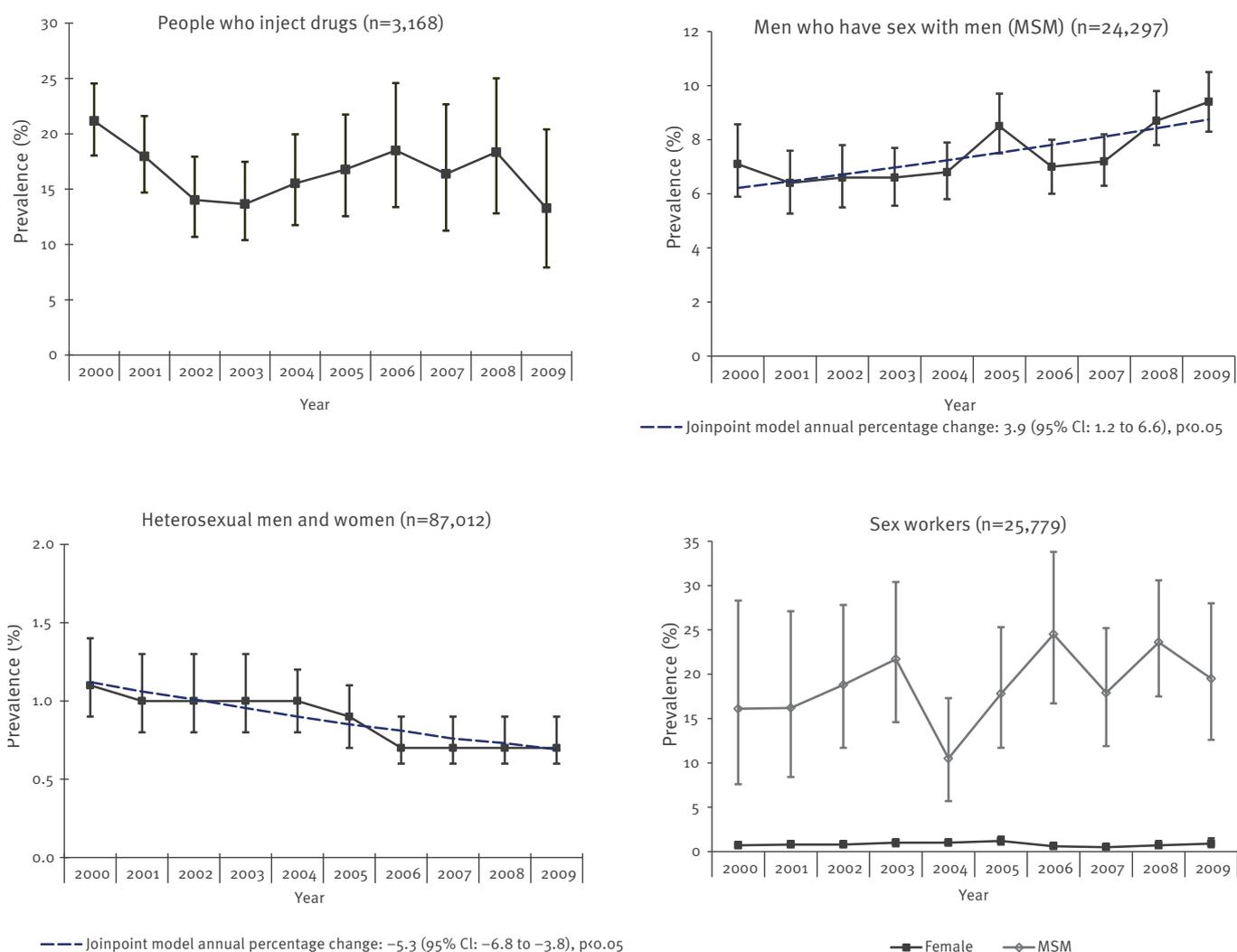
Early HIV diagnosis and treatment is a policy priority in Spain [9] and the total number of HIV tests performed increased from 24.8 per 1,000 inhabitants in 2002 to 38.2 per 1,000 in 2009 [17]. Our results suggest that the increase in testing is not uniform across most-at-risk populations and that testing might actually be decreasing in some groups. The reduced number of tests among PWID seems logical because the PWID population is rapidly decreasing [6], but the decrease observed among FSW warrants further investigation. There are some data on the size of the FSW population in Spain [18] but none on its trend, although a decrease in the number of FSW that might explain the decrease in testing in this group seems unlikely. A change in the testing facilities preferred by FSW seems equally unlikely, because the clinics in the network are free of charge, highly accessible and have a long tradition of caring for this population. A more likely explanation is worsening access to these clinics in the network due to the increased proportion of foreign FSW – from 46% in 1998 [19] to 93% in 2009 (our study) – and the shift in the working environment from outdoors to indoors (i.e. apartments or clubs), a tendency noted throughout Europe, which makes sex workers less accessible to intervention measures [20]. The lack of HIV prevalence data among FSW working only indoors in Spain warrants further investigation.

Decreasing trends in HIV prevalence among all most-at-risk populations were reported from 1992 to 2001 in the 10 centres that initially comprised the network [11,12]. Data from the expanded network show that from 2000 to 2009, HIV prevalence remained stable among PWID and male and female sex workers, and increased in MSM, whereas it continued to decrease only in heterosexual individuals. This last group has increased the most in size; thus, declining HIV prevalence could also be a result of testing more people at lower risk.

HIV prevalence in transgender women was higher than that found previously in other Spanish studies [21,22]. In comparison with other countries, our figure (24.5%) is higher than the 21.7% reported in the United States and the same as the 24.5% found in Italy according to

FIGURE 2

HIV prevalence by year of diagnosis and transmission category, EPI-VIH Study, Spain, 2000–09 (n=145,337)



Bars represent 95% confidence intervals (CIs).

a meta-analysis of studies published from 2000 to 2011 [23]. The situation of MSM sex workers is of particular concern since they present the highest HIV prevalence and incidence estimates, in clear contrast to the situation in FSW. As there is a dearth of recent studies on MSM sex workers in Spain [21,24], more information is needed on the reasons explaining this situation. The high proportion of foreigners, use of illegal drugs and the particular stigma associated with male sex work could all be important factors, together with the high background HIV prevalence in MSM.

HIV prevalence among MSM attending clinics in the network (7.6%) was higher than that found in MSM in a community centre in Barcelona (5.4%) between 2007 and 2012 [25] but lower than figures for MSM reported in studies carried out in Barcelona in 2002 (18.3%), Bangkok, Thailand, in 2007 (30.8%) or 21 cities in the United States in 2008 (19%) [26-28]; nevertheless the downward trend previously observed in MSM in Spain

[12] has been reversed, which is not surprising given our findings that HIV incidence is also on the rise in MSM. The overall IR for MSM in our study (2.5/100 py) was lower than that found among American or Italian MSM in the 1990s (2.8/100 py and 4.6/100 py respectively) [29,30] or that estimated in Bangkok during 2003 to 2007 (from 4.1 to 7.7%) [27], but higher than figures reported in London, England, in 1997 to 1998 (1.8/100 py) or Catalonia, Spain, during 1995 to 2001 (1.92/100 py) [31,32].

HIV prevalence among PWID in this study was a third to a half of what it was in the 1980s and 90s in Spain [11,33], although the overall prevalence was very high (17%), only lower than that found among MSM sex workers. During the study period, these figures remained stable. Compared with other studies, the HIV prevalence was lower than the 26.9% self-reported HIV infection among PWID entering drug treatment in 2009 in Spain [34] and similar to the 17.2% found in

TABLE 3

HIV incidence rate in people undergoing HIV testing, by different variables, EPI-VIH Study, Spain, 2000–09 (n=30,679)

Variable	Number of persons tested	Number of seroconversions	Person-years	Incidence rate ^a (95% CI)
Sex				
Male	15,672	601	34,086.2	1.8 (1.6 to 1.9)
Female	14,840	36	29,588.1	0.1 (0.09 to 0.2)
Transgender women	167	5	429.8	1.2 (0.5 to 2.8)
Age group (years)				
<20	1,193	14	1,051.2	1.3 (0.8 to 2.3)
20–24	6,899	88	9,595.1	0.9 (0.7 to 1.1)
25–29	8,071	163	15,886.3	1.0 (0.9 to 1.2)
30–34	6,304	163	14,737.5	1.1 (1.0 to 1.3)
35–39	4,065	132	10,826.6	1.2 (1.0 to 1.5)
40–44	2,126	50	6,178.0	0.8 (0.6 to 1.1)
45–49	1,015	19	2,974.2	0.6 (0.4 to 1.0)
≥50	1,006	13	2,855.2	0.5 (0.3 to 0.8)
Region of birth				
Spain	15,970	423	33,340.2	1.3 (1.2 to 1.4)
Western ^b /Eastern Europe	1,912	29	3,224.5	0.9 (0.6 to 1.3)
Latin America	9,796	121	19,999.2	0.6 (0.5 to 0.7)
Sub-Saharan/ North Africa	1,132	8	1,901.6	0.4 (0.2 to 0.8)
Other	167	6	250.4	2.4 (1.1 to 5.3)
HIV transmission category				
PWID or ex-PWID	884	32	2,016.1	1.6 (1.1 to 2.2)
MSM	8,492	529	21,181.0	2.5 (2.3 to 2.7)
Heterosexual men and women	10,500	23	17,914.2	0.1 (0.09 to 0.2)
Female sex worker	9,808	16	21,027.9	0.1 (0.05 to 0.1)
MSM sex worker	549	39	1,311.0	3.0 (2.2 to 4.1)
Year				
2000	4,294	20	2,161.9	0.9 (0.6 to 1.4)
2001	3,337	28	4,825.2	0.6 (0.4 to 0.8)
2002	3,566	37	6,378.7	0.6 (0.4 to 0.8)
2003	3,330	55	7,445.2	0.7 (0.6 to 1.0)
2004	3,407	77	8,203.6	0.9 (0.8 to 1.2)
2005	3,133	70	8,510.6	0.8 (0.7 to 1.0)
2006	3,181	87	8,483.1	1.0 (0.8 to 1.3)
2007	3,134	105	8,152.6	1.3 (1.1 to 1.6)
2008	2,410	110	6,848.3	1.6 (1.3 to 1.9)
2009	887	53	3,095.0	1.7 (1.3 to 2.2)
HIV/STI clinic location^c				
Northern Spain	6,341	36	11,819.5	0.3 (0.2 to 0.4)
Southern Spain	3,828	83	8,426.8	1.0 (0.8 to 1.2)
Eastern Spain	9,809	195	20,482.2	0.9 (0.8 to 1.1)
Central Spain	9,321	301	20,787.5	1.4 (1.3 to 1.6)
Canary Islands	1,380	27	2,588.2	1.0 (0.7 to 1.5)
Type of clinic				
HCT	5,056	106	10,764.2	0.9 (0.8 to 1.2)
STI	25,623	536	53,340.0	1.0 (0.9 to 1.1)
Total	30,679	642	64,104.2	1.0 (0.9 to 1.1)

HCT: HIV counselling and testing; MSM: men who have sex with men; PWID: people who inject drugs; STI: sexually transmitted infections.

^a Number of seroconversions per 100 person-years.^b Excluding Spain.^c Northern Spain: Oviedo, Gijón, Santander, Navarre, Vitoria, Bilbao, Guipuzcoa and La Rioja.

Southern Spain: Granada, Málaga and Seville.

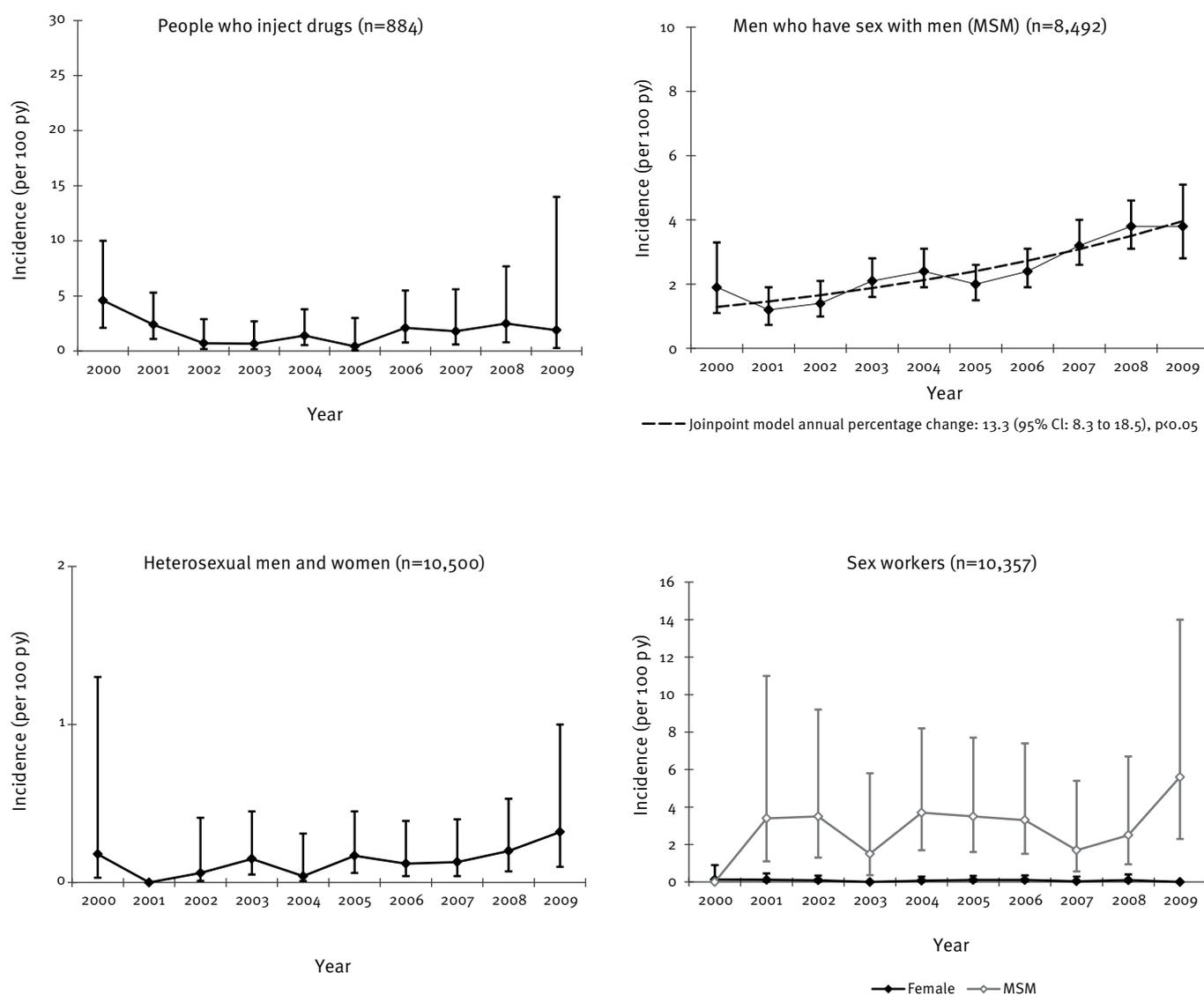
Eastern Spain: Castellón, Alicante, Valencia, Barcelona, Murcia and Cartagena.

Central Spain: Madrid-Sandoval and Madrid-Ayuntamiento.

Canary Islands: Tenerife.

FIGURE 3

HIV incidence rate^a by year of diagnosis and transmission category, EPI-VIH Study, Spain, 2000–09 (n=30,679)



Bars represent 95% confidence intervals (CIs).

^a Number of seroconversions per 100 person-years (p-y).

Portugal in the same setting in 2009, but this was to be expected since PWID attending clinics in the EPI-VIH network are likely to have better social conditions than other PWID in Spain; in any case, these prevalence figures indicate that Spanish PWID are still among the most HIV-infected PWID in the European Union [35]. Surveillance data show that new HIV diagnoses in PWID in Spain have decreased sharply since 2004 [36], as a result of the decrease in the size of the PWID population and decreased HIV transmission after implementation of harm reduction programmes [4,6]; however, our findings show that seroconversion among current injectors, though much less frequent than in the past [37,38], is still very common.

Latin-American migrants have always been present in Spain, but their numbers increased greatly since the mid-1990s, and since 2000 people from other areas have also been attracted to the country [8]. Migration into Spain is therefore a relatively recent phenomenon, so the generally higher HIV prevalence among foreign-born people in our study probably reflects the HIV prevalence in their country of origin, as well as differences in the distribution of HIV transmission categories between those who were Spanish-born and the other groups. However, the diagnostic delay among those newly diagnosed with HIV in Spain is greater among people who are foreign-born [39], in spite of them

being entitled to HIV testing and care free of charge; thus, it is possible that they are experiencing difficulties in accessing HIV testing and care due to discrimination or other barriers.

Our HIV incidence estimates in MSM (2.5/100 py) are fairly similar to those found in MSM in California, United States, from 1997 to 2006 (2.0/100 py in 1997, increased to 2.4/100 py in 2003 and then decreased to 1.9/100 py in 2006) [40], but whereas researchers in California report a decreasing trend there since 2003, the opposite is occurring in our setting. The rising trend in incidence among MSM in our study is consistent with findings from surveillance data in Spain showing an increase in the number of new HIV diagnoses in this group, but not in heterosexual individuals or PWID since 2004 [36]. While part of this increase could be the result of more frequent testing, other sub-populations in our study have a similar trend in testing but not in new HIV diagnoses. Furthermore, other studies in Spain have documented an over-representation of MSM among syphilis and gonorrhoea cases in 2006 [41] as well as outbreaks of lymphogranuloma venereum and hepatitis A in MSM since 2007 [42-45]. Behavioural monitoring in this group has found an increase in risk behaviours [46].

This study has some limitations. People attending the clinics in the EPI-VIH Network are by no means representative of the general Spanish population and the reasons for seeking care in the network are not independent of HIV infection: thus the results cannot be extrapolated to other settings. However, while the estimates presented probably reflect only the experience of the population at greater risk of HIV infection in each transmission category, the clinics have been operating on the same basis for many years, so if selection biases are present, they are unlikely to affect the results on trends. A change in the populations attending the clinics could influence trends, thus multivariate analyses need to be performed to have a better insight into the results. The questionnaires were administered by many individuals, making it difficult to control reproducibility. Testing patterns in the different most-at-risk populations might have evolved over the years in a different way. Finally, for some groups, e.g. transgender individuals, the numbers were very small.

The information obtained with this study shows the changing face of HIV epidemiology in Spain, is of great public health relevance and very useful for adjusting HIV policy to the real needs. In contrast with the 1980s and 90s, when most HIV infections occurred among PWID, MSM have emerged as the population at greatest risk for HIV in Spain and should be given priority in preventive efforts. Nevertheless, although injection of drugs is becoming rare, PWID should not be forgotten since HIV prevalence and incidence in this group remains very high and shows no signs of decreasing.

HIV infection remains a huge problem in transgender women and MSM sex workers that warrants further research in preventive interventions in these groups. With regard to FSW, efforts should be made to guarantee access to HIV testing and prevention, in particular for those working in places not easy to reach. Investigation of the situation of those who are hard to reach is also a priority. In addition, this study illustrates the increasing impact of migrants on the HIV epidemic in Spain; interventions tailored to their needs should therefore be urgently promoted.

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Conflict of interest

None declared.

Authors' contributions

MD was the main study researcher. She supervised field work and data collection, wrote the statistical analysis plan and the first version of the manuscript. MJB performed data collection and management, quality control and statistical analysis, and reviewed all the manuscript drafts. AD prepared the figures and most of the tables and made important contributions to successive versions of the manuscript. JAV, JRO, MAA, MV, CS, LJV, CA, JMU, JT, IP, BM, TP, MV, IS, MLJ, MCL, EM, MMC, JB, FJB and EPI-VIH Study Group: were the clinicians responsible for patient recruitment and follow-up in the participating centres. They all participated in development of the study protocol, collection of epidemiological and clinical data, and critical review of all versions of the manuscript

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HIV testing and counselling in Estonian prisons, 2012 to 2013: aims, processes and impacts

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We present data from an observational cohort study on human immunodeficiency virus (HIV) prevention and control measures in prisons in Estonia to assess the potential for HIV transmission in this setting. HIV testing and retesting data from the Estonian prison health department were used to estimate HIV prevalence and incidence in prison. Since 2002, voluntary HIV counselling and testing has routinely been offered to all prisoners and has been part of the new prisoners health check. At the end of 2012, there were 3,289 prisoners in Estonia, including 170 women: 28.5% were drug users and 15.6% were infected with HIV. Of the HIV-positive inmates, 8.3% were newly diagnosed on prison entry. In 2012, 4,387 HIV tests (including retests) were performed in Estonian prisons. Among 1,756 initially HIV-negative prisoners who were in prison for more than one year and therefore tested for HIV twice within 12 months (at entry and annual testing), one new HIV infection was detected, an incidence of 0.067 per 100 person-years (95% confidence interval (CI): 0.025–5.572). This analysis indicates low risk of HIV transmission in Estonian prisons. Implementation of HIV management interventions could impact positively on the health of prisoners and the communities to which they return.

Introduction

In most countries, the rates of human immunodeficiency virus (HIV) infection, tuberculosis (TB) and hepatitis B and C among prisoners are higher than those in the general population [1] owing to risk behaviour before and during incarceration. These risks include injection drug use [2,3], exchange of sex for money or drugs [4], multiple sex partners [5], and low socioeconomic status (homeless people). [6–8] Many people who inject drugs (PWID) engage in low-level criminal activity to support their drug use and many experience incarceration at least once in their lifetime [9]. Research has shown that HIV-infected people are frequently incarcerated during the course of their disease, with an estimated 17% of people living with HIV/AIDS in the United States (US) and incarcerated at some point in a given year [10]. In addition, female prisoners

who have been involved with sex work, which is frequently associated with injection drug use and contact with HIV-infected sexual partners, are at additional risk of HIV being infected when entering prison. [11] The high prevalence of HIV infection and drug dependence among prisoners, combined with the sharing of injecting drug equipment, make prisons a high-risk environment for the transmission of HIV. Therefore, the World Health Organization (WHO) has recommended that HIV testing in prison settings should be prioritised [12].

A review by Dolan et al. suggests that prisons are a particular focus of the HIV epidemic in several countries in Europe, and that HIV infection rates are substantially higher among prisoners than among the general population in some countries in eastern Europe, e.g. above 10% nationally in Estonia, Romania, and Slovakia, and in a single prison or region in Lithuania and Ukraine [13]. Less is known about the implementation and effectiveness of HIV prevention and harm reduction programmes introduced in prisons in these countries.

This article assesses the prevalence of HIV infection among prisoners, and describes prison policies and practices on voluntary HIV testing and counselling (VCT) and retesting in Estonian prisons between January 2012 and March 2013.

Situation in Estonia

Estonia is a small country in north-eastern Europe with a population of ca 1.3 million [14]. In 2009, the estimated HIV prevalence among 15–49 years-olds in Estonia was 1.2% compared with 1.0% in Russia and 1.1% in Ukraine. In 2011, Estonia had the third highest rates of HIV diagnosis in Europe (27.3/100,000), after Russia (44.1/100,000 in 2010) and Ukraine (38.0/100,000) [15]. Estonia has one of the highest prevalences of PWID among people aged 15–64 years (1.5% in 2007) coupled with a 40–90% HIV prevalence among PWID [16,17].

There are four prisons in Estonia: Tartu, Tallinn, Viru, and Harku and Murru. Data from the Estonian Ministry

of Justice show that the prison population was ca 3,300 in January 2013 [18], translating into an imprisonment rate of 246 per 100,000 population. According to the Health Services Organisation Act, healthcare in prisons is part of the national healthcare system [19]. Prisoners' treatment costs are covered through the Ministry of Justice from the state budget [20].

HIV/AIDS prevention in prisons is based on the national HIV/AIDS Strategy 2006–2015. The main objective is to block HIV transmission inside prison. Antiretroviral therapy (ART) is available in all prisons and is administered according to the national guidelines, which require that ART should be initiated at a CD4 T cell count < 350 cells/mm³. Condoms are distributed free of charge in long-term visiting rooms. Drug prevention in the prison system was commenced in 1998. Until 2003 the focus was primarily on reducing the supply by inspection, but recently more attention has been paid to reducing the demand by treatment and rehabilitation of drug addicts [21]. Two types of drug dependency treatment are offered in Estonian prisons. Abstinence-based treatment is the most common and is available in all prisons. The only form of opiate substitution is methadone maintenance treatment and coverage is increasing every year. No prisons in Estonia offer needle exchange programmes.

On entry, all detained persons undergo an initial health check and VCT is a component of every new prisoner health check [20]. VCT is carried out by medical personnel and performed with the informed consent of the prisoner. Retesting for those who were HIV-negative at previous/initial testing is offered once a year or more often if necessary, i.e. if a prisoner can identify a specific incident of HIV exposure. Exposure incidents are tattooing, fighting, self-harm with dirty razors, unprotected sexual intercourse or injecting.

All HIV tests are performed in regional HIV screening laboratories (in Jõhvi, Tartu and Tallinn) using fourth-generation HIV screening tests (i.e. Vironostika HIV Uniform II Ag/Ab, BioMerieux method). Confirmatory HIV testing (for those testing positive in a screening test) is done at the national HIV/AIDS reference laboratory in Tallinn (using the INNO LIA HIV I/II Score Western blot algorithm) [22]. According to the Communicable Diseases Prevention and Control Act [23] new cases of HIV are reported to the Estonian Health Board, an institution responsible for infectious disease surveillance in Estonia.

Methods

This work was based on the analysis of administrative data. The term 'prisoner' is used for all those, including adults and juveniles, detained during the investigation of a crime, while awaiting trial, after conviction, before sentencing, and after sentencing.

Data and data sources

Prison health reports

Data on the occurrence of drug dependence among inmates were obtained from the quarterly health reports from prisons summarised in the Estonian Ministry of Justice Drug Monitoring Report 2012 [24] which compiles all prison data on drug use, treatment and other preventive activities for the period from 1 January to 31 December 2012. Defining drug addiction status was based on ICD 10 diagnosis codes F11–F16 and F18–F19 [25].

These data were used to describe the prison population in Estonia in 2012, including HIV prevalence and ART coverage among those with HIV.

Prison goals database

The prison goals database is an electronic database containing aggregated information about HIV infection, HIV testing and retesting. Since the introduction of mandatory reporting of HIV testing in 2011, the database has been updated monthly by all prison medical departments. Data on HIV testing between 1 January and 31 December 2012 was extracted from the prison goals database. These data were used to describe HIV testing and retesting conducted in prisons in 2012.

Prison electronic patient database

The prison electronic patient database is an information system containing information from the electronic health records designed for prison healthcare. Individualised HIV testing and retesting results for the period from 1 January to 31 March 2013 were collected from the electronic prison patient database. Analysis was limited to prisoners who had been in prison for more than one year and had previously had a negative HIV test, i.e. those who were eligible for retesting. This information was used to explore the occurrence of newly acquired HIV infections (HIV incidence) among the prison population.

The data sources used for this study cover all the prisons in Estonia. Data on HIV/hepatitis C virus (HCV) testing and results, history of injection drug use, and condom use during conjugal visits (from the case management interview held following HIV diagnosis) on inmate newly infected in prison were also collected from the prison electronic patient database.

Statistical analysis

Descriptive statistics (proportions with 95% confidence intervals (CIs)) were calculated using Microsoft Excel 2010. HIV incidence and 95% CIs were calculated using Poisson distribution.

The study complied with local data protection regulations. Data characteristics of the prison population, HIV testing and retesting in the year 2012 contained only non-identifiable (aggregated) data. The analysis of HIV testing and retesting results for the period 1 January

TABLE 1

Selected characteristics of prisoners in Estonia, 1 January–31 December 2012 (n=3,289)

	Viru	Tartu	Tallinn	Harku /Murru	All
Number of prisoners on 31 December 2012	950	920	1,157	262	3,289
Number of female prisoners	9 (0.9%)	5 (0.5%)	46 (4.0%)	110 (42.0)	170 (5.2)
HIV-infected prisoners (n, % of all)	162 (17.1%)	78 (8.5%)	236 (20.4%)	43 (16.4%)	519 (15.8%)
Number of female HIV-infected prisoners	3 (33.3%)	1 (20.0%)	19 (41.3%)	42 (38.2%)	65 (38.2%)
Prisoners on ART (n, % of those infected)	86 (53.1%)	57 (73%)	112 (47.5%)	26 (60.4%)	281 (54.1%)

ART: antiretroviral therapy; HIV: human immunodeficiency virus.

to 31 March 2013 was based on identifiable individual human data, analysed by authorised personnel (author KK), and considered eligible for exemption by the ethics review board as the research was conducted by the head of a governmental agency (author KK is the Prison Department medical adviser) authorised to evaluate public programmes.

Results

The prison population in Estonia consisted of 3,289 people at the end of 2012. Of these, 5% were women, 32% were 30–39 years-old, 1.2% were juveniles (under 18 years) and 1% were over 60 years-old [21].

At the end of 2012, 15.6% of the 3,289 prisoners were infected with HIV (Table 1). The HIV prevalence was 38.2% among female and 14.5% among male prisoners in Estonian prisons. One third (28.5%; n=906) of the total prison population were diagnosed with drug addiction (diagnosis codes F11-16, F18-19) [25]: 50% of them were opiate users, 25% users of multiple drugs, 19% stimulant users, 4% cannabis users and 2% other (solvent).

A total of 4,387 HIV tests (including retests) were performed across Estonian prisons in 2012 (Table 2). Of those, 2,425 were tests of people when entering prison, a testing uptake rate of 97.3%. Of the tests on admission, 1.8% (43/2,425 resulted in a new HIV diagnosis. These 43 individuals diagnosed on prison entry correspond to 8.3% of the total of 519 HIV-positive inmates in 2012. In addition, 23 prisoners self-reported being

HIV-negative (or not sure of their HIV status) but were found to have had a previous HIV-positive test result recorded at the national HIV/AIDS reference laboratory. Two prisoners who self-reported being HIV-positive, had negative results when tested.

To estimate the HIV incidence in prison, data on HIV retesting conducted from 1 January 2013 to 31 March 2013 were used. The following analysis is limited to the 1,756 prisoners who had been in prison more than one year and who therefore had an opportunity for HIV retesting during the indicated period (the total prison population in Estonia (including persons under pre-trial) was 3,294 as of 31 March 2013 [9]).

On admission to prison, 220 prisoners (12.5% of the 1,756; 95% CI: 11.5–13.6%) were already infected with HIV (Table 3). Of those who were HIV-negative at prison entry: 97% (1,489/1,536; 95% CI: 96.4–97.6%) were retested and found to be negative at the retest a year later. One prisoner was HIV-positive at the retest (translating into an HIV incidence of 0.067 per 100 person years; 95% CI: 0.025–5.572), while 3% (46/1,536; 95% CI: 2.4–3.6%) did not agree to repeat testing.

Data from prison health medical records (previous HIV/HCV testing and results, history of injection drug use and case management interview held following HIV diagnosis) on the newly infected inmate indicated that this prisoner may have become infected during conjugal visits from an HIV-positive partner. The inmate has been in prison for more than five years and their

TABLE 2

HIV testing and retesting in Estonian prisons, 1 January–31 December 2012 (n=4,387)

	Viru	Tartu	Tallinn	Harku /Murru	All
Total number of HIV tests done	992	1,172	1,987	236	4,387
Number of retests done	596	693	437	236	1,962
Number of those tested on admission to prison	396	479	1,550	0	2,425
Number of previously undiagnosed infections among those tested on admission to prison (new infections detected)	16	2	25	0	43
Number of HIV-positive prisoners	162	78	236	43	519

HIV: human immunodeficiency virus.

TABLE 3

HIV retesting in prisons, Estonia, 1 January–31 March 2013 (n=1,756)

	Viru	Tartu	Tallinn	Harku /Murru	All
In prison for more than one year	569	581	412	194	1,756
Prisoners HIV-positive on entry to prison	67	58	57	38	220
Prisoners HIV-negative at annual retest	490	513	341	154	1,489
Prisoners HIV-positive at annual retest	0	0	0	1	1
Prisoners refusing annual HIV retesting	12	10	24	0	46

previous HIV tests were negative. Moreover, the inmate also tested negative for HCV in 2012, an indication that the inmate probably did not inject drugs in prison as the HCV prevalence in PWID in Estonia has been documented very high (>90%) [26]. There was no information in the medical records that would suggest a history of drug injection of the newly infected prisoner. During the year 2012, the inmate had several conjugal visits from their partner. The inmate indicated that they did not use condoms. Therefore, the infection was probably acquired sexually during a one of those visits.

Discussion

To our knowledge, this is the first article providing data on HIV in prisons from one of the European countries witnessing HIV epidemics related to injection drugs since the early 2000s. Our results document an HIV prevalence of 15.6% in prisons in Estonia. Based on the high prevalence of drug addiction among inmates and of drug-related crimes as a reason for imprisonment, we suggest that the high HIV prevalence observed among prisoners is probably related to injection drug use. Prisoners should not leave prison in a worse health condition than when they entered [27]. HIV transmission does occur in custody; however, many experts conclude from the available data that most HIV-infected inmates are probably infected before entering prison [10,28]. Nevertheless, collecting data on risk behaviours in prison is important because the absence of such data can be used to justify inaction [29].

In a systematic review on HIV prevalence in prisons in low and middle income countries in 2003-2004, information was presented for 75 countries. The HIV prevalence in prisons was more than 10% in 20 countries [13]. In 2001, Rotily et al. published results of a multicentre pilot study estimating the HIV prevalence in prisons in several European countries (including 4.1% in France, 3.1% in the Netherlands, 2.7% in Sweden, 1.2% in Italy, 0.9% in Germany, 0.7% in Scotland) [30]. However, it has recently been reported that the HIV prevalence was significantly higher among prisoners in those European countries that witnessed HIV epidemics driven mainly by injection drug use, e.g. 6.0% in Portugal [31], 10% among female prisoners in Portugal [32], 10.8% in Spain [33], and 19.8% in individuals released from prison within the last six months in Ukraine [34]. In most industrialised countries in western Europe and

North America, many prison entrants have a history of injecting drug use and thus already have a high HIV prevalence, higher than those in the respective general populations. Furthermore, the lack of or insufficient supply in most prisons of preventive measures such as clean needles and syringes or condoms, combined with stressful social conditions, create further opportunities for HIV transmission [35]. Several studies, including from Estonia, report that drug injecting occurs among prisoners [36]. However, few studies have documented the epidemic spread of HIV within prisons [37].

According to our data, the risk of HIV transmission was low in Estonian prisons in 2012 and 2013 (0.067 per 100 person-years). Low levels of transmission have previously been identified in prison, with an incidence of zero to four per 1,000 person-years [28]. A systematic review conducted on the basis of studies from the US reporting HIV incidence in the prison population provides a pooled HIV incidence of 0.08 per 100 person-years (95% CI: 0.0–0.24) among continuously incarcerated populations with a similar incidence estimation method to that used in our report [38].

Our results have several implications: they show (i) a need to provide comprehensive HIV prevention within prisons and (ii) a need to provide comprehensive HIV care to those infected, including substance abuse management.

In Estonia, 10–28% of all new HIV infections during the period from 2000 to 2009 were diagnosed in prisons [39]. Our findings also indicate that, close to one 10th (8.3%) of HIV infected inmates were newly diagnosed on prison entry. We argue that there is a strong case for routine testing on entry into the Estonian prison system as newly diagnosed cases are identified and previously known cases can be referred for treatment. Early diagnosis of HIV infection provides an opportunity to improve patient health outcomes and will also improve public health. At the end of 2012, 54% of HIV-seropositive prisoners in Estonia were receiving ART in prison [24], compared with ca 40% coverage of PWID in the community (data not shown).

Our analysis indicated a low risk of HIV transmission in Estonian prisons. However, it is important to retest those who tested negative but are at ongoing risk for

acquiring HIV through high-risk behaviours and those who may be in the early stages of infection but have not yet developed a sufficient antibody level to be detected by serological testing, i.e. during the 'window period' [40].

Our finding that the HIV prevalence in female inmates is substantially higher than in male inmates is in agreement with other published reports [41-45].

Our study has several limitations. It is possible that we have underestimated the risk of HIV transmission in the prison setting if the small proportion of inmates who refused retesting had a different risk profile (higher HIV incidence) from those who were retested. In the unlikely scenario of all of those declining retesting (n=46) being infected with HIV within those 12 months, our HIV incidence estimate would have been higher (3.06 per 100 person-years). Furthermore, the HIV risk could be different among those in prison for periods shorter than 12 months. However, we believe that our results are representative of the prison population in Estonia given that the databases used cover all prisons in Estonia and are considered to be complete.

The state is responsible for adequately securing a prisoner's health by providing the required medical assistance [46]. Prisons continue to be effective targets for public health interventions [10]. HIV testing and linkage to care, both within prisons and in the community, comprise an important component of the 'seek and treat' strategy to prevent further HIV infections. Prison-based screening of infectious diseases, especially but not limited to HIV, in conjunction with treatment and linkage to community care is an important component of HIV prevention among high-risk communities. Significantly, for drug users at high risk of parenteral as well as sexual transmission, combined prevention strategies to reduce both transmission paths should not be overlooked.

Conclusions

Estonia is one of the European countries witnessing injection drug-related HIV epidemics since the early 2000s. Data on HIV prevalence of prison populations in the region of central and eastern Europe is very limited. The study was launched in 2013 and, at the time, no data on HIV transmission in Estonian prisons had been published. To our knowledge, this is one of few detailed descriptions and analyses of HIV testing designed to assess in-prison transmission of HIV infection in a country with high HIV prevalence in both the general population and the prison population. The aim of this article was to describe the HIV prevention and control measures used in Estonian prisons and to assess the potential for HIV transmission in this setting. Further we provide an estimate of HIV incidence inside prison (based on HIV testing and retesting results). This analysis indicates a low risk of HIV transmission in Estonian prisons. Outbreaks of HIV infection have occurred in prisons in several countries,

demonstrating how rapidly HIV can spread in such settings. Retesting can ensure that if an outbreak occurs, control measures can effectively be implemented in the event of an outbreak [47]. HIV testing and counselling in prisons should not be limited to promoting prisoners' access to HIV testing and counselling, but must at the same time aim to mitigate the stigma and discrimination related to HIV [48].

Prison staff, in partnership with public health officials, should assess the adequacy of existing programmes and services for incarcerated populations and develop strategies to reduce HIV infection, both in prisons and in the community [49,50]. Implementation of the HIV management interventions described in this article could have public health benefits including a positive impact on the health of prisoners and the communities to which they return. These findings provide a basis for prison and public health authorities to consider whether HIV testing, counselling and other preventive measures should be part of an HIV prevention package in prisons. The implementation of routine testing policies in prison offers opportunities to reach high risk individuals and engage them in HIV prevention and treatment.

Conflict of interest

KK is employed by the Estonian Ministry of Justice. The Estonian Ministry of Justice did not provide any financial support or place any restrictions on this research or publication.

Authors' contributions

All authors were involved in the design of the study. KK did the database research and was responsible for data management. All authors contributed to the writing of the paper and approved the final version.

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