Eurosurveillance

Volume 14, Issue 48 - 3 December 2009

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EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Symptomatic primary HIV infection in a 49-year-old man who has sex with men: beware of the window phase

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This article was published on 9 December 2009.
Citation style for this article: van Oosten HE, Damen M, de Vries HJ. Symptomatic primary HIV infection in a 49-year-old man who has sex with men: beware of the window phase. Euro Surveill. 2009;14(48):pii=19424. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19424

A 49-year-old man with a history of receptive unprotected anal intercourse with multiple anonymous men presented with a symptomatic primary HIV infection. Upon his initial visit the rapid HIV antibody screening test was negative but a p24 antigen test suggested a highly infectious phase in the HIV infection. An immunoblot assay confirmed the HIV diagnosis only 14 days later. Recent infections are characterised by a highly infectious phase and, if gone unnoticed, can have a large contribution to the ongoing transmission of HIV. Healthcare providers should be aware of primary HIV infection and the pitfalls in its diagnosis.

Case report

A 49-year-old man visited the Amsterdam STI outpatient clinic in the fall of 2009 with fever, malaise, generalised rash, anal itching and rectal discharge after unprotected receptive anal and oral intercourse with an anonymous partner in a gay cinema one week before. In the last six months he had engaged in protected and unprotected receptive anal and oral intercourse with 15 different male partners. The last HIV test was performed one year ago and gave a negative test result. He was treated for a syphilis infection with unknown duration in 2004.

The patient presented with fever (39.2 degrees Celsius), generalised erythemato-squamous rash, generalised lymphadenopathy, erythematous pharyngeal mucosa and perianal ulceration. Anoscopy revealed erythematous rectal mucosa which bled easily upon manipulation.

Laboratory findings and follow up

The patient was routinely screened for syphilis, *Neisseria gonorrhoeae, Chlamydia trachomatis,* HIV and hepatitis B, according to the standard protocol described before [1]. Awaiting definite results of syphilis serology (*Treponema pallidum* particle agglutination assay, TPPA), secondary stage syphilis was excluded with a directly performed Rapid Plasma Reagin card test (RPR nosticon II, bioMerieux, France). The direct RPR card test was non reactive in both 1:1 and 1:32 serum dilutions. Also, a point of care rapid HIV ELISA antibody test (Determine HIV 1/2, Inverness Medical, United Kingdom) was negative. A Gram-stained smear obtained during anoscopy from the rectal mucosa showed more than 10 polymorphic nucleated leucocytes (PMNL) per high power field without intracellular diplococci, suggestive for a non-specific proctitis. Based on these preliminary results the patient was treated with doxycycline 100 mg twice a day and requested to return seven days later for additional results and follow-up.

From the rectal site a *N. gonorrhoeae* strain was cultivated which showed resistance to ciprofloxacin and tetracycline, intermediate resistance to penicillin and reduced susceptibility to cefotaxime (with a minimal inhibitory concentration [MIC] of 0.19 µg/ml). *C. trachomatis* infection was excluded with a nucleic acid amplification assay (Aptima combo, Tigris, Genprobe, United States) performed on a rectal swab and a first void urine sample. Syphilis serology was in concordance with a past, adequately treated, syphilis infection (TPPA 1:160, RPR negative, FTA-absorption positive, *Treponema pallidum* immunoblot positive). A polymerase chain reaction of the swab taken from the rectal ulcer was negative for *Treponema pallidum*, herpes simplex virus type 1 and 2 and varicella zoster virus [2,3]. Hepatitis B serology was indicative for a past recovered infection (hepatitis B core antibody positive, hepatitis B surface antigen negative). The rectal gonorrhoea infection was additionally treated with 500 mg ceftriaxone in one intra-muscular dose, while the doxycycline regimen was discontinued.

An HIV antigen/antibody (Ag/Ab) COMBO assay (AxSYM HIV Ag/Ab Combo, Abbott, United States) performed on the serum sample obtained during the initial visit showed a weak positive result (1.22 s/co). Since we suspected a primary symptomatic HIV infection, and according to routine laboratory procedures, the serum was further tested for the presence of HIV p24 antigen (VIDAS HIV P24, bioMérieux, France), and showed a positive result (31.2 pg/ml). The immunoblot analysis (INNO-LIA HIV I/II Score, Innogenetics, Belgium) was negative for all antigen bands. Based on these test results from the initial visit, the official criteria for an HIV diagnosis could not be met. Upon return seven days after the initial visit, the skin symptoms, proctitis complaints and fever had subsided. Again, the HIV Ag/Ab COMBO assay was weak positive (1.43 s/

co), the HIV p24 antigen load was 17.6 pg/ml and all bands in the immunoblot were negative. Only 14 days after the initial visit the HIV Ag/Ab COMBO assay turned positive (5.2 s/co), the HIV p24 antigen load was 64.6 pg/ml. Immunoblot analysis showed positive bands for anti-GP41 and anti-p24 which confirmed the HIV infection. The patient was referred to an HIV treatment centre for further monitoring and care.

Repeated serologic testing for syphilis 14 days after the initial visit showed the same results as before (TPPA 1:160, RPR negative) consistent with an adequately treated syphilis infection. The negative repeat TPPA may still miss an early syphilis infection but, given the negative polymerase chain reaction for *Treponema pallidum* of the swab taken from the rectal ulcer at the initial visit, an early syphilis infection was unlikely.

Discussion and conclusion

We report a 49-year-old male patient with marked exanthema, genital ulcer, and fever suspected for a primary HIV infection. A rapid HIV antibody test was negative at the initial visit. We could only establish the diagnosis 14 days after the initial visit, when the immunoblot turned positive for antibodies against HIV-1.

Primary HIV infections play a key role in the spread of HIV [4,5]. During this first phase, the viral load in blood plasma is high [6,7] and patients can shed high concentrations of HIV through semen, saliva and blood [8,9]. The Rakai study in Uganda showed that the average per-act transmission rate during primary infection equalled 0.03604 per sex encounter compared to 0.00084 per sex encounter for chronic HIV infections. In that same study, primary-phase transmission accounted for 89.1% of all transmission events in the first 20 months of follow-up [10,11]. It is possible that primary-phase transmission is even more frequent for MSM since anal intercourse contributes to transmission risk.

Patients with a primary HIV infection are often unaware of their (positive) HIV status and assuming they are uninfected they continue to engage in high-risk sexual behaviour [12]. Moreover, primary HIV infection can cause mucosal ulceration and, due to the disrupted mucosal barrier, HIV transmission risk is further increased. In our case the patient had peri-anal ulceration possibly due to the primary HIV infection (genital herpes and syphilis were all excluded by negative nucleic acid amplification test results for HSV-1 and 2 and *Treponema pallidum* on ulcer swabs). Both ulcerative and non-ulcerative STI further increase the risk of HIV transmission two- to five-fold [13,14]. Our patient also had a rectal co-infection with a multi-resistant *N. gonorrhoeae* strain with reduced susceptibility to third generation parenteral cephalosporins. We recently reported on a disquieting increase of *N. gonorrhoeae* strains with reduced susceptibility to cephalosporins among MSM [15]. Parenteral cephalosporins are recommended for *N. gonorrhoeae* in most countries nowadays. Further susceptibility reduction towards resistance for cephalosporins would set a serious limitation in available therapy options.

Primary HIV infections are often missed or misdiagnosed as common flu, since HIV viraemia can affect all organs and cause a wide variety of non-specific symptoms like fever, fatigue, exanthema and mucosal ulceration, diarrhoea and airway infection. Hence primary care physicians should be alert for a possible primary HIV infection in patients involved in high risk behaviour, especially if they have influenza-like symptoms.

Single antibody HIV tests in particular can be false negative in primary HIV infections, as it can take on average three to four weeks before HIV antibodies become detectable (the window-phase), as shown again in this case [16,17]. It is therefore generally advised to repeat serologic testing for both HIV and syphilis three months after the last high risk sexual contact. For the detection of a symptomatic primary HIV infection, antibody testing alone is insufficient. Combined HIV antigen/antibody assays reduce the diagnostic window period by circa six days compared to single antibody testing alone [18]. The addition of a Nucleic Acid Amplification Test (NAAT) for HIV RNA to an HIV screening algorithm increases the identification of infected cases with 3.9 percent compared to single antibody testing using enzyme linked assays (EIA) as shown by Pilcher *et al*. [19]. Data on cost-effectiveness are needed before implementation of HIV RNA NAAT assays in screening algorithms is effected. Apart from increased expenses of HIV screening, NAAT testing might add to the turnaround time for test results [20]. A combined HIV antigen/antibody assay as part of a screening algorithm is a good alternative which detects approximately 90% of the acute HIV infections compared to HIV RNA detection in a screening algorithm [21]. Presently we are introducing a rapid combined HIV antigen/antibody assay for screening purposes in our clinic. In cases suspected of symptomatic primary HIV infection with a negative combined HIV antigen/antibody combined assay result, HIV-RNA testing and/or repeated combined HIV testing is advisable.

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Recently acquired HIV infection in men who have sex with men (MSM) in France, 2003-2008

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This article was published on 9 December 2009.
Citation style for this article: Semaille C, Cazein F, Lot F, Pillonel J, Le Vu S, Le Strat Y, Bousquet V, Velter A, Barin F. Recently acquired HIV infection in men who have sex with men (MSM) in France, 2003-2008. Euro Surveill. 2009;14(48):pii=19425. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19425

An increase in the number of new HIV diagnoses among men who have sex with men (MSM) was observed in several countries in the early 2000s. In this article, we explore the trends among MSM in France between 2003 and 2008. To estimate the number of MSM newly diagnosed with HIV, we take into account the reporting delay, underreporting and missing data for HIV case notification. To identify recent infections (RI) (acquired an average of six months before diagnosis), we used an enzyme immunoassay for recent HIV-1 infections (EIA-RI) which has been performed routinely for new HIV diagnoses since 2003. Multivariate analysis was used to identify factors associated with RI. We estimate that between 1,900 and 2,400 MSM have been newly diagnosed with HIV every year: the proportion of MSM among all newly diagnosed with HIV cases has increased from 25.2% (95% confidence interval (CI): 23.3-27.1) in 2003 to 37.0% (95% CI: 35.2-38.7) in 2008 and was stable during the period 2006-2008. In 2008, the rate of newly diagnosed HIV cases per 10,000 MSM living in France was 72.5. The proportion of non-B subtypes of HIV-1 among cases diagnosed in MSM was 11.7% (2003-2008). The assessment of RI was performed for 4,819 MSM newly diagnosed with HIV in 2003-2008. Of these, 47.6% (95%CI = 46.2-49.0) (2,295 cases) were shown to have been recently infected. The risk of RI was greater for those of French nationality (adjusted odds ratio (aOR) =1.6 [95% CI: 1.4-1.9]), those with high economic status (aOR =1.4 [95% CI: 1.2-1.8]), those tested after a risk exposure (aOR =1.6[95% CI: 1.3-1.8]) or after presenting with clinical symptoms or abnormal biological markers (aOR =1.8 [95% CI: 1.5-2.0]), those who had tested for HIV three or more times during their lifetime (aOR =4.2 [95% CI: 3.4-5.2]) and those living in the Paris area (aOR =1.2 [95% CI: 1.0-1.3]). The risk of RI decreased with age. The HIV situation among MSM living in France is a cause of concern, despite the prevention campaigns dedicated to this highly educated sub-population.

Introduction

Men who have sex with men (MSM) were one of the largest groups of reported AIDS cases until 1999 in France. In the early 1990s, MSM in most countries adopted strategies for reducing the risk of HIV transmission. But since 1996, an increase in sexual risk practices has been observed in North America, Australia and most Western European countries [1-4]. An increase in frequency of unprotected anal intercourse (UAI) was observed for the first time in France in 2000, through the "Enquête Presse Gay" (EPG survey), a behavioural survey that has been conducted since 1985 among readers of the gay press in France (increase of UAI in the last 12 months with a casual partner from 19% to 26% between 1997 and 2000) [5]. The increase of sexual risk practices among MSM may have an impact on the incidence of sexually transmitted infections (STI), including HIV.

In this article, we analyse trends and characteristics of MSM newly diagnosed with HIV from 2003 to the end of 2008 in France and describe factors associated with recent infection (RI) defined as HIV transmission in the last six months preceding diagnosis [6].

Materials and methods

New HIV diagnoses

Case reporting of HIV infection became mandatory in France in early 2003 [7]. All laboratories must notify all new HIV diagnoses anonymously, and practitioners must provide clinical information. The following variables are collected and entered into the national database: sex, age, country of birth, current nationality, region of residence, mode of transmission, socio-professional category, clinical stage at the time of HIV diagnosis (primary infection, asymptomatic stage, symptomatic non-AIDS stage, AIDS stage), number of previous HIV tests and reasons for HIV screening (such as exposure to HIV, clinical symptoms or abnormal biological markers, routine testing). Information on 'primary infection' is reported by clinicians independently of the test result of recent infection. The data presented here are for diagnoses made between 1 January 2003 and 31 December 2008. The MSM category is compared with male heterosexuals when we describe characteristics in terms of age, clinical stage, socio-professional category, region of residence, reason for screening and testing frequency.

The estimated proportion of cases not reported per estimated total number of newly diagnosed HIV cases varied from 44% in 2003 to 29% in 2008, depending on the year of diagnosis. The methodology is described in details in previous published articles [8,9]. In this article, the underreporting rate and the reporting delay are taken into account when presenting the trends in MSM and the estimated numbers of new HIV diagnoses. Moreover, some crucial data (such as unknown mode of transmission or unknown current nationality) were missing for some cases. We used a multiple imputation method (ICE-STATA 9) to estimate missing data when we presented trends over time among MSM [10,11].

To estimate the rate of new HIV diagnoses per 10,000 MSM, we used an estimated number of MSM living in France in the denominator. This estimate is based on the results from a national survey on sexual practices conducted in 2005 (the definition used for MSM was "reported sexual intercourse with a man in the last 12 months")[12]. Based on this survey, the estimated number of MSM is 330,000 men, representing 1.6% of the male population in France.

Virological surveillance

Virological surveillance (VS) based on voluntary participation by both microbiologists and patients (the patient's consent is obtained by the reporting clinician through the HIV notification form) was implemented at the same time as the HIV case reporting system and described in detail in a previous publication [7]. For each case, the laboratories were asked to take a dried serum spot (DSS) from the stored serum sample and send it to the National Reference Center (NRC), to determine the type, group and subtype of HIV by serotyping and to perform a test for RI (EIA-RI) [6,13,14]. The RI assessment was done by an EIA-RI assay able to identify infections acquired less than six months before obtaining the sample. Similar to the various avidity assays, in the initial design of the EIA-RI, the cut-off for recently acquired infection was at 180 days and the biomarkers' threshold was estimated retrospectively [14]. Results from the NRC were linked to the epidemiological data in the HIV national database. Individuals diagnosed during the first half of 2003 were excluded because the virological surveillance was implemented progressively in early 2003.

Statistical analyses

Percentages were compared with the chi-squared test for raw data and by confidence interval for the data which have been corrected by multiple imputation. The threshold of significance was set at 5%. To identify factors associated with RI, we used multiple logistic regression (using backward procedure) including all variables that were significant in a univariate analysis; the Wald test was used for categorical variables. The goodness of fit of the resulting model was tested according to the Hosmer–Lemeshow test. SAS software version 9.1 was used for all analyses.

Results

Trends in newly diagnosed HIV cases among MSM

The proportion of new HIV diagnoses with missing information on mode of transmission was 31.2% for the study period 2003-2008. When the multiple imputation method is applied and underreporting is taken into account, MSM account for 32.0% and male heterosexuals for 28.3% of all new HIV diagnoses reported between 2003 and 2008. Sex between men was reported for more than 50% of male cases newly diagnosed with HIV every year and we estimate that between 1,900 and 2,400 MSM were diagnosed every year (1,858 in 2003; 2,059 in 2004; 2,288 in 2005; 2,409 in 2006; 2,340 in 2007 and 2,393 in 2008).

Sex between men represented the only risk category for which an increase was observed during the study period: the proportion of MSM among all newly diagnosed HIV cases has increased from 25.2% (95% CI: 23.3-27.1) in 2003 to 37.0% (95% CI: 35.2-38.7) in 2008, and the estimated number of MSM newly diagnosed with HIV increased from 1,858 (95% CI : 1604-2145) in 2003 to 2,409 (95% CI : 2175-2668) in 2006 and remained stable in 2007 and 2008 (Figure). The proportion of male heterosexuals was stable, at around 28%.

The estimated rate of new HIV diagnoses among MSM was 72.5 per 10,000 MSM population in 2008 (2,393 cases per estimated 330,000 MSM population living in France).

Characteristics of MSM newly diagnosed with HIV

Between 2003 and 2008, 6,213 cases of new HIV diagnoses in MSM were notified in France. The average age of MSM at diagnosis was 37 years and MSM aged under 30 years represented 24% of all cases. The majority of MSM (82%) were of French nationality, while 3.3 % were from the Americas, mainly Brazil and Peru, and 2.6% were from Western Europe, mainly from Italy and Portugal. Nearly one in five MSM (18.7%) discovered their infection at the time of primary infection ('PI' as reported by clinicians independently of the test result) whereas male heterosexuals rarely discovered their seropositivity at the PI stage (5.4%). Nevertheless, 11.5% of MSM were diagnosed at a very late stage of the disease (AIDS-defining illness) and this proportion was highest among MSM aged over 50 years (27.5%). However, the proportion of MSM presenting with an AIDS-defining illness at the time of diagnosis declined from 19.5% in 2003 to 8.8% in 2008. An exposure to HIV (whatever the type of exposure) was the reason for HIV testing for one in three MSM (31.5%) (compared to 18.5% for male heterosexuals). Among MSM aged below 40 years, the main reason for testing (37.4%) was a possible exposure to HIV, whereas among older MSM (> 40 years old) biological or clinical symptoms represented the principal reason for performing an HIV test (38.7%). Of the MSM newly diagnosed with HIV in 2003-2008, 42% had a high level of education, 24% were employees and 10.4% were blue collar workers.

Nearly one in three MSM newly diagnosed with HIV (29.8%) had been tested twice or more for HIV prior to their diagnosis (compared to 16% for male heterosexuals).

Recent infections among new HIV diagnoses

The results of the test for RI were available for 4,819 MSM (77.5% of MSM newly diagnosed with HIV). Nearly half of these patients (47.6%, 95% CI 46.2 to 49.0) had been recently infected.

The proportion of RI among all MSM newly diagnosed with HIV remained stable between 2003 and 2008. It was higher in young MSM (57% [CI 95% = 53.7-59.4] in the 15-29 age group) than among the oldest age group (30% [CI 95% = 26.3-34.2] in the > 50 age group) and higher in MSM with French nationality (49%, [CI 95% =47.6-50.7]) than in those with another nationality (40% [CI 95% = 37.2-43.8]). The proportion of RI varied according to socio-professional categories: RI was less frequent in blue-collar workers (37%) than in employees or other professions. The proportion of RI was also higher in the Paris area (51%) than in the rest of France (45%).

Results of the multivariate analysis

The year of diagnosis was not associated with recent infection in the univariate analysis and was not included in the multivariate analysis. MSM of French nationality (aOR=1.6), those who had undergone HIV testing because of clinical/biological manifestations (aOR=1.7), those who were tested after an exposure to HIV (aOR=1.6), those with high socio-economic status, residence in the Paris region, notification by a community physician and those who had undergone three or more tests were all independently associated with an increased risk of RI in multiple logistic regression analysis (Table). The risk of RI also decreased with age (>50 years

aOR= 1, <30 years, aOR=2.6). The risk of RI increased with the lifetime number of tests performed aOR=1 (one HIV test), aOR=2.0 (two HIV tests), aOR=4.2 (three or more tests).

HIV type, group and subtype

The results for the HIV type, group and subtype were available for 4,369 MSM newly diagnosed with HIV in 2003-2008. For the remaining individuals, the DSS was not sent by the biologist (811 cases) or the virus was not typeable by the serotyping method (710 cases). There were four cases of HIV-2 infection, one involving a French national, one from Peru, one from Colombia and one from the Ivory Coast. Most MSM were infected with HIV-1 subtype B (76.5%), non-B subtype was found in 11.7% and the M group HIV was detected in 11.8% of MSM.

Discussion

MSM account for more than 50% of new HIV diagnoses in men each year, while it is estimated that in 2005 they represented only 1.6% of the male population in France [15]. The rate of newly diagnosed HIV infection among MSM is therefore very high (72/10,000 MSM for the year 2008). Moreover, MSM are the only transmission group in which the number of new HIV diagnoses increased between 2003 and 2006 in France. Screening pattern trends in MSM can not fully explain this increase: in every year of the EPG survey, we observed a substantial and stable proportion of MSM who had never been tested for HIV (14.5% in 1997, 13.0% in 2000, 13.3% in 2004, p=0.16) [16].

The results of virological surveillance are worrying: 47.6% of MSM were infected within the six months preceding HIV diagnosis. This high proportion reflects, to a certain extent, the incidence of HIV infection in the MSM community. However, it also depends on other factors, particularly screening practices. We know that French MSM are more frequently tested for HIV than the rest of the population: 12% of MSM newly diagnosed with HIV reported more than three tests before their HIV diagnosis, compared with 2.5% of male heterosexuals. Moreover, among readers of the gay press based on a survey conducted regularly since 1985, 31% had had at least one test in the previous 12 months compared to 11% in the general male population [16,17]. A French study estimating the national incidence rate of HIV infection using the EIA-RI test and testing patterns will be published next year.

The probability of being diagnosed soon after the infection is also higher when the test is motivated by a high-risk event. This is confirmed by the high proportion of diagnoses made shortly after high-risk events of any type among MSM newly diagnosed with HIV (31.5%). However, this is not the case for MSM aged over 50 years, of whom nearly one in three discover their seropositivity at a late stage of the disease (AIDS-defining illness) and wait for clinical or biological manifestations to perform a HIV screening.

We also found that residence in Paris was independently associated with a diagnosis of RI and the Paris region was the area most affected by HIV (the Paris region accounted for 20% of all new HIV diagnoses between 2003 and 2008). Behavioural surveys showed no difference in risk behaviours between MSM living in Paris and other regions [18,19] . It therefore seems that the rate of HIV test per population is higher in the Paris area than in other regions [9]. In addition, seronegative and seropositive MSM may mix more frequently in Paris because of the many commercial gay-venues available in the city.

In addition to the test of RI, virological surveillance showed a high proportion of non-B subtype HIV-1 infection in France among MSM (12% in 2003-2008). In France, the HIV-1 epidemic has historically been dominated by strains of subtype B. The presence of non-B subtypes in MSM was detected as early as 1996-1998, but the proportion was only 2% [20]. The high proportion of non-B subtypes among MSM suggests an increasing genetic diversity of HIV strains that are transmitted within the homosexual community in France. In a pilot survey conducted in Berlin among 114 MSM newly diagnosed with HIV, the authors identified no strains of non-B subtypes [21]. The increase in non-B subtypes in France suggests also a closer interplay between the HIV epidemics in MSM and in the African population living in France.

The increase in the number of newly diagnosed HIV cases in MSM occurred in France during the same time period as the re-emergence of syphilis in the late 2000s [5,22], and the emergence of rectal lymphogranuloma venereum (LGV) in 2003 [23]. Half of MSM who had syphilis were HIV-seropositive and rectal LGV in France has been diagnosed exclusively in HIV positive MSM [24]. The recent outbreaks of syphilis in MSM have probably had a minor impact on HIV incidence because for many years now in France, most MSM with a new diagnosis of syphilis have already been infected by HIV and this is also true for some other countries [25].

The epidemiological situation regarding HIV and other STI in MSM in France is not very different from that in the neighbouring European countries. In the early 2000s, epidemics of syphilis and then of LGV occurred in all Western European countries, mainly among HIV-infected MSM [26-31]. The number of new HIV diagnoses among MSM and bisexual men increased by 86% between 2000 and 2006 in 23 European countries [32]. The rate of HIV notifications among MSM in eight countries with concentrated HIV epidemics (Australia, Canada, France, Germany, Netherlands, Spain, United Kingdom and the United States) increased by 3.3% per year from 2000 to 2005 and this increase is not wholly explained by changes in HIV patterns [33].

Prevention campaigns remain crucial, but they do not seem sufficient to contain sexual risk behaviours among MSM in France, despite the wide availability of screening, condoms and information and the fact that MSM represent a highly educated sub-population. Moreover, in view of the large proportion of HIV-seropositive MSM who are affected by STI, counselling of seropositive MSM during medical follow-up must be reinforced. Regarding the high proportion of MSM aged over 50 years who have been diagnosed with HIV at the AIDS stage and who have been screened for HIV only when they have presented with clinical manifestations, HIV screening should be encouraged among this specific sub-population of MSM. The HIV epidemic situation in MSM in France remains a serious issue and more research into the underlying causes may be necessary to adopt appropriate prevention and control measures.

Acknowledgements

We thank everyone who participates in HIV surveillance, in particular microbiologists, physicians and public health doctors. We also thank Marlène Leclerc, Lotfi Benyelles, Hélène Haguy, Sophie Couturier, Frédérique Biton, Sylvie Brunet, Damien Thierry, and Alain Moreau for their technical support.

Financial support

The InVS is funded by the French Ministry of Health. The National Reference Centres are funded by a grant from the InVS.

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HIV/STI co-infection among men who have sex with men in Spain

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This article was published on 9 December 2009.
Citation style for this article: Diaz A, Junquera ML, Esteban V, Martínez B, Pueyo I, Suárez J, Ureña JM, Varela JA, Vall M, del Romero J, Sanz I, Belda J, Boronat J, Gómez P, Gual F, Colomo C, López de Munain J, Balaguer J, Landa MC, Lezaun ME, Cámara MC, Fernández E, Bru FJ, Alastrue I, Ordoñana JR, de Armas C, Azpiri MA, Gomez L, Trullén J, Diez M, on behalf of STI Study Group and EPI-VIH Group. HIV/STI co-infection among men who have sex with men in Spain. Euro Surveill. 2009;14(48):pii=19426. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19426

In Spain, neither the HIV nor the STI national surveillance system collects information on HIV/STI co-infection. However, there are two networks based on HIV/STI clinics which gather this data. We describe HIV prevalence in men who have sex with men (MSM) diagnosed with infectious syphilis and/or gonorrhoea in 15 STI clinics; and concurrent diagnoses of STI in MSM newly diagnosed with HIV in 19 HIV/STI clinics. In total, 572 MSM were diagnosed with infectious syphilis and 580 with gonorrhoea during 2005-2007. HIV prevalence among syphilis and gonorrhoea cases was 29.8% and 15.2% respectively. In the multivariate analysis, HIV/syphilis co-infection was associated with being Latin American; having a history of STI; reporting exclusively anal intercourse; and having sex with casual or several types of partners. HIV and gonorrhoea co-infection was associated with age older than 45 years; having no education or only primary education completed; and having a history of STI. In total, 1,462 HIV infections were newly diagnosed among MSM during 2003-2007. Of these, 31.% were diagnosed with other STI at the same time. Factors associated with STI co-infection among new HIV cases in MSM were being Latin American; and having sex with casual partners or with both steady and casual partners. In Spain, a considerable proportion of MSM are co-infected with HIV and STI.

Introduction

HIV infection continues to disproportionately affect men who have sex with men (MSM) in the European Union [1], and many countries have reported an increase of the number of new HIV diagnoses in MSM since the early 2000s [2,3]. At the same time,

sexually transmitted infections (STI) have also re-emerged in this group [4] and the occurrence of several outbreaks mainly involving HIV-infected MSM [5], underlies the extent of HIV and other STI co-infections in this population. It is known that the presence of other STI may increase the likelihood of transmitting or contracting HIV [6].

While information on new HIV diagnoses is not yet available on a national basis in Spain, data collected in eight autonomous regions, covering 32% of the total Spanish population, show that the number of MSM newly diagnosed with HIV has been increasing among Spaniards as well as foreign-born population (Figure) [7]. Furthermore, nationwide surveillance data on gonorrhoea and syphilis show an increase in the number of reported cases of both diseases since 2002 [8], and syphilis outbreaks affecting MSM have been reported recently [9]. Unfortunately, at the moment, neither the HIV nor the STI national surveillance systems collect information on co-infection.

However, in addition to population surveillance systems, in Spain there are two networks that collect detailed data on new HIV, syphilis and gonorrhoea diagnoses, including information on HIV/STI co-infection. These networks are based on HIV/STI clinics which are very low-threshold public facilities, where barriers to access are minimised and medical consultation for HIV and STI is free of charge.

This report presents data coming from both networks and examines HIV/STI co-infection in MSM with the following aims:

a) To describe HIV prevalence and factors associated with HIV co-infection in MSM diagnosed with infectious syphilis and/or gonorrhoea in 15 STI clinics (STI Study Group)

b) To describe concurrent diagnoses of STI and factors associated with STI co-infection in MSM newly diagnosed with HIV in 19 HIV/STI clinics (EPI-VIH Group)

Methods

HIV prevalence among MSM with infectious syphilis and/or gonorrhoea

All infectious syphilis (primary, secondary and early latent) and/or gonorrhoea patients prospectively identified between July 2005 and December 2007 by the STI Study Group were included in this study. The Group is a network of 15 STI clinics located in 14 of the most populated Spanish cities: Madrid, Barcelona, Seville, Malaga, Bilbao (two clinics), Granada, Algeciras, Oviedo, Gijon, San Sebastian, Tarragona, Cartagena, Murcia and Alicante. Data from the Prison Health Service were incorporated since January 2007. These clinics have a long tradition of attending STI patients belonging to core at-risk populations (sex workers and their clients, migrants, MSM and heterosexuals with high-risk sexual behaviours). Participation is voluntary but, to our knowledge, all but one of this type of clinic in Spain belong to this network.

Cases included in this analysis were identified using the corresponding European case definitions [10].

Data on the patients´ socio-demographic (age, sex, country of birth, educational level) and clinical variables (HIV status, history of previous STI, transmission route), as well as information on the circumstances of infection, were collected in a standard questionnaire by the attending physicians, the majority of whom are STI specialists.

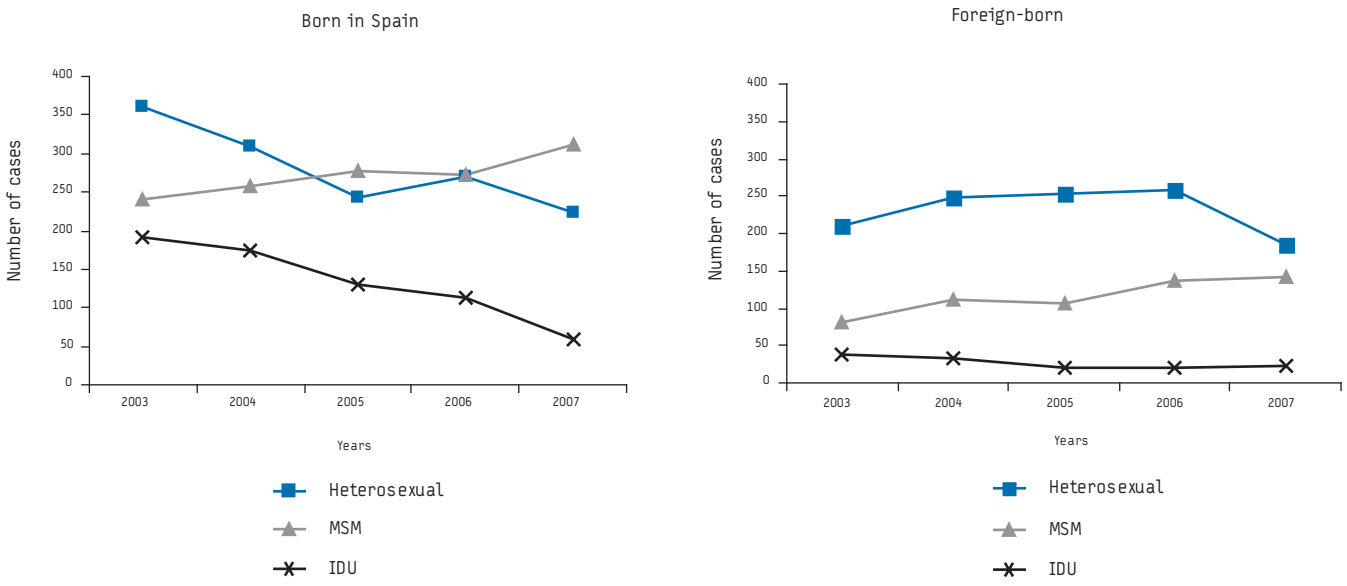
The study was performed according to the requirements of the Spanish legislation on data protection. No personal identifiers were collected.

Concurrent diagnosis of STI among HIV infections newly diagnosed in MSM

All MSM newly diagnosed with HIV between 2003 and 2007 by the EPI-VIH Group were prospectively identified and included in this study. The EPI-VIH Group is a network of HIV and STI clinics

Figure

Newly diagnosed HIV infections, by country of birth and transmission mode, Spain (eight autonomous regions), 2003-2007



MSM: Men who have sex with men; IDU: Intravenous drug user

located in 18 Spanish cities: Madrid (two clinics), Barcelona, Seville, Bilbao, Granada, Oviedo, Gijon, San Sebastian, Vitoria, Logroño, Pamplona, Cartagena, Murcia, Alicante, Castellón, Valencia, Santa Cruz de Tenerife, Santander. Ten of these clinics are also included in the STI Study Group; the rest are clinics specialised in HIV diagnosis that mostly serve HIV-vulnerable populations. Participation is voluntary, but more than 90% of the STI/HIV clinics in Spain belong to this network.

Table 1

HIV prevalence in syphilis and gonorrhoea cases in men who have sex with men (MSM), by different variables, Spain, 2005-2007

Variables	Syphilis cases			Gonorrhoea cases		
	Total number of cases	HIV prevalence n (%)	p*	Total number of cases	HIV prevalence n (%)	p*
Age groups (years)						
< 25	52	9 (17.3)		91	7 (7.7)	
25-34	210	56 (26.7)		207	28 (13.5)	
35-44	177	65 (36.7)	0.05	120	24 (20.0)	0.01
≥45	67	22 (32.8)		37	11 (29.7)	
Unknown	10	2 (20.0)		7	0 (0.0)	
Educational level						
Illiteracy/Primary education	115	29 (25.2)		68	16 (23.5)	
Secondary/University education	323	100 (31.0)	0.47	310	41 (13.2)	0.10
Unknown	78	25 (32.1)		84	13 (15.5)	
Region of birth						
Spain	399	110 (27.6)		377	52 (13.8)	
Western Europe	27	9 (33.3)		22	2 (9.1)	
Eastern Europe	3	0 (0.0)	0.09	3	0 (0.0)	0.05
Latin America	80	33 (41.2)		52	13 (25.0)	
North Africa	3	0 (0.0)		3	2 (66.7)	
Other/Unknown	4	2 (50.0)		5	1 (20.0)	
Previous STI						
Yes	178	68 (38.2)		212	42 (19.8)	
No	166	21 (12.6)	0.00	166	5 (3.0)	0.00
Unknown	172	65 (37.8)		84	23 (27.4)	
Sexual practices						
Only oral intercourse	106	35 (33.0)		125	20 (16.0)	
Only anal intercourse	21	10 (47.6)	0.00	44	6 (13.6)	0.01
Oral and anal intercourse	182	32 (17.6)		192	19 (9.9)	
Unknown	207	77 (37.2)		101	25 (24.7)	
Type of partners						
Sexual contact with a steady partner (solely)	33	2 (6.1)		59	3 (5.1)	
Sexual contact with a casual partner (solely)	189	55 (29.1)		230	30 (13.0)	
Sexual contact with a steady and casual partner	85	18 (21.2)		65	4 (6.1)	
Exchange of sex for drugs or money	14	3 (21.4)	0.01	11	5 (45.4)	0.00
Mixed**	26	11 (42.3)		24	8 (33.3)	
Unknown	169	65 (38.5)		73	20 (27.4)	
Number of sexual partners in the last 12 months						
1-2	61	12 (19.7)		74	6 (8.1)	
3-10	127	24 (18.9)		136	14 (10.3)	
≥11	126	36 (28.6)	0.00	141	22 (15.6)	0.00
Unknown	202	82 (40.6)		111	28 (25.2)	
TOTAL* **	**516**	**154 (29.8)**		**462**	**70 (15.2)**	

*Chi-squared or Fisher's test
**Mixed: sexual contact with different partners (casual, steady, exchange of sex for drugs or money)
***56 syphilis and 118 gonorrhoea cases were excluded from the table because their HIV status was unknown

Cases included in this analysis met the European case definition for new HIV diagnosis [10].

Epidemiological variables (age, sex, country of birth, educational level), clinical information (transmission route, history of previous and concomitant STI) and circumstances of the infection were collected by the attending physicians using a standardised questionnaire.

The study was performed according to the requirements of the Spanish legislation on data protection. No personal identifiers were collected.

Frequency distributions for each variable and prevalence of HIV/STI co-infection, global and stratified by different variables were calculated. To evaluate the association between qualitative variables, the chi-squared and Fisher's exact tests were used. Logistic regression models were fitted, following Hosmer and Lemeshow model-building strategies [11], to identify: a) factors associated with HIV co-infection among MSM with infectious syphilis or gonorrhoea; b) concomitant STI co-infection among newly HIV diagnosed MSM. Associations were measured using the odds ratio (OR) and its 95% confidence interval (95% CI). Data analyses were performed using the STATA statistical software package Version 10.0 [12].

Results

HIV prevalence among MSM with infectious syphilis and/or gonorrhoea

A total of 1,152 MSM with infectious syphilis and/or gonorrhoea were identified during the study period: 572 were diagnosed with

Table 2

Factors associated with HIV co-infection among men who have sex with men (MSM) diagnosed with syphilis or gonorrhoea, Spain, 2005-2007

Variables	HIV and syphilis co-infection		HIV and gonorrhoea co-infection	
	Adjusted OR	95% CI	Adjusted OR	95% CI
Age groups (25-34 years)				
< 25	0.8	(0.3-2.1)	0.6	(0.2-1.5)
35-44	1.6	(0.9-2.6)	1.4	(0.7-2.8)
≥45	1.5	(0.7-3.0)	3.4	(1.3-9.0)
Educational level (secondary/university education)				
Illiteracy/Primary education	0.8	(0.4-1.4)	3.4	(1.5-7.5)
Unknown	0.5	(0.2-1.1)	1.4	(0.5-3.6)
Region of birth (Spain)				
Western Europe	1.0	(0.4-2.5)	0.3	(0.1-1.5)
East Europe	-	-	-	-
Latin America	2.2	(1.2-4.0)	1.2	(0.4-3.0)
North Africa	-	-	4.3	(0.3-69.1)
Other/Unknown	4.1	(0.4-38.0)	0.8	(0.1-8.8)
Year of diagnosis (2006)				
2005	0.8	(0.4-1.4)	0.6	(0.3-1.5)
2007	1.8	(1.1-3.1)	1.2	(0.6-2.3)
Previous STI (No)				
Yes	4.3	(2.2-8.5)	6.0	(2.1-16.9)
Sexual practices (oral and anal intercourse)				
Only anal intercourse	5.5	(1.6-19.1)	1.5	(0.4-5.3)
Only oral intercourse	1.8	(0.9-3.5)	1.6	(0.7-3.6)
Type of partners (sexual contact with a steady partner only)				
Sexual contact with a casual partner (solely)	6.8	(1.3-36.0)	1.7	(0.4-7.4)
Sexual contact with a steady and casual partner	3.7	(0.7-21.1)	0.6	(0.1-3.4)
Exchange of sex for drugs or money	4.8	(0.4-62.2)	18.4	(0.9-363.7)
Mixed**	14.0	(2.1-91.7)	4.5	(0.8-25.6)
Unknown	6.8	(0.7-64.9)	8.4	(0.4-197.6)
Number of sexual partners in the last 12 months (1-2 partners)				
3-10	0.5	(0.2-1.2)	1.6	(0.4-5.9)
≥11	0.8	(0.3-2.0)	1.4	(0.4-4.9)
Unknown	2.1	(0.6-7.7)	2.3	(0.4-14.4)

*Reference categories in brackets; models adjusted by clinic of diagnosis
** Mixed: sexual contact with different partners (casual, steady, exchange of sex for drugs or money)
OR: odds ratio; CI: confidence interval

syphilis (215 primary, 265 secondary and 92 early latent) and 580 with gonorrhoea.

The mean age for syphilis patients was 35 years (SD: 9.2), (range 16-77 years), and the most affected age group was 25-34 years (40.7%). The majority (63.6%) had completed secondary/university education and almost a quarter (132 cases) were born outside Spain, mainly in Latin America and Western Europe.

Nearly one third of the cases (183, 32.0%) had a history of previous STI, and 97 (17.0%) had other STI concurrently diagnosed: 28 chlamydia, 24 genital warts, 22 gonorrhoea, 18 herpes simplex virus infection and five other STI.

Information on sexual practices considered to be the cause of the current syphilis episode was available for 321 (56.1%) cases. Of these, 108 (33.6%) reported exclusively oral sex, 24 (7.5%) had anal intercourse solely, whereas 189 (58.9%) recalled both. Regarding type of sexual partner thought to be the source of infection, data were available in 359 (62.7%) cases. Of these, 195 (54.3%) had sex with a casual partner solely; 36 (10.0%) with their steady partner only; 87 (24.2%) reported sex with both casual and steady partners; in nine cases (2.5%) the infection was attributed to being a sex worker; in five (1.4%) to being a client of a sex worker; and 27 patients reported a combination of the above categories.

Information on HIV status was available for a total of 516 (90.2%) syphilis cases. Of these, 154 (29.8%) were co-infected with HIV and the majority (125 cases) were aware of their infection. HIV co-infection was more likely in those with higher number of sexual partners in the last year; those with prior history of STI; those having sex with casual partners and those who reported anal intercourse as the most likely transmission mode for the syphilis episode (Table 1).

In the multivariate analysis, the probability of being co-infected with HIV and syphilis was higher among Latin Americans (OR: 2.2; 95% CI: 1.2-4.0), men with a history of previous STI (OR:4.3;

Table 3

STI co-infections in men who have sex with men (MSM) newly diagnosed with HIV, by different variables, Spain, 2003-2007

Variables	Total number of cases	STI and HIV co-infection	p*
	n	n, prevalence (%)	
Age groups (years)			
< 25	161	53 (32.9)	
25-34	712	222 (31.2)	0.54
35-44	407	121 (29.7)	
>=45	108	29 (26.8)	
Unknown	74	28 (37.8)	
Educational level			
Illiteracy/Primary education	228	76 (33.3)	
Secondary/University education	1078	325 (30.1)	0.51
Unknown	156	52 (33.3)	
Region of birth			
Spain	909	259 (28.5)	
Western Europe	55	20 (36.4)	
East Europe	19	7 (36.8)	0.04
Latin America	450	162 (36.0)	
Sub-Saharan Africa	6	1 (16.7)	
Other/Unknown	23	4 (17.4)	
Previous STI			
Yes	720	231 (32.1)	
No	658	196 (29.8)	0.65
Unknown	84	26 (31.0)	
Type of partners			
Sexual contact with a steady partner (solely)	175	42 (24.0)	
Sexual contact with a casual partner (solely)	695	223 (32.1)	
Sexual contact with a steady and casual partner	199	75 (37.7)	0.06
Exchange of sex for drugs or money	33	7 (21.2)	
Mixed**	309	91 (29.5)	
Unknown	51	15 (29.4)	
TOTAL	**1462**	**453 (31.0)**	

*Chi squared or Fisher's test
**Mixed: sexual contact with different partners (casual partner, steady partner, exchange of sex for drugs or money)

95% CI: 2.2-8.5), those reporting anal intercourse solely (OR: 5.5; 95% CI:1.6-19.1) and those having sex with casual (OR: 6.8; 95% CI:1.3-36.0) or several types of partners (OR:14.0; 95% CI:2.1-91.7) (Table 2).

In total, 580 MSM were diagnosed with gonorrhoea during the study period. Mean age at diagnosis was 32 years (SD: 8.3), (range 16-65) years, and the age group most affected was 25-34 years (44.1%). Almost 69% of the cases had completed secondary/university education and 121 (20.9%) were born in countries other than Spain, mostly in Latin America and Western Europe.

History of previous STI was very common (38.8% of the cases), and 132 (22.8%) gonorrhoea cases were concurrently diagnosed with other STI: 67 with chlamydia, 24 with genital warts, 22 with syphilis, 18 with herpes virus and 13 with other STI.

Gonorrhoea transmission was attributed to exclusively oral sex in 51 cases (12.8%), solely anal intercourse in 136 (34.1%) and to both oral sex and anal intercourse in 212 (53.1%); for 181 cases (31.2% of the total) this information was not available.

Regarding the category of sexual partner considered to be the possible source of infection, this information was available for 430 (74.1%) gonorrhoea cases. Of these, 256 (59.5%) attributed the infection to sex with casual partner only, 73 (17.0%) to sex with both casual and steady partners, 66 (15.3%) to sexual contact with their steady partner only, 10 (2.3%) to sexual contact with clients (sex work), and 25 (5.9%) to contact with several types of sexual partners.

Of the 462 (79.6%) gonorrhoea cases with data on HIV infection, 70 (15.2%) were co-infected and the majority of these (59 cases) had been aware of their HIV status. HIV prevalence increased with age and with number of sexual partners in the last 12 months; it was also higher in men with a history of previous STI, those recalling only oral sex as the practice most likely to be the cause of this gonorrhoea episode, and those who exchanged sex for drugs or money (Table 1).

In the multivariate analysis, HIV and gonorrhoea co-infection among MSM was associated with age older than 45 years (OR: 3.4; 95% CI: 1.3-9.0), having no education or only primary education

Table 4

Factors associated with STI co-infection in men who have sex with men (MSM) newly diagnosed with HIV, Spain, 2003-2007

Variables	STI and HIV co-infection	
	Adjusted OR	95% CI
Age groups (25-34 years)		
< 25	1.1	(0.7-1.6)
35-44	1.0	(0.7-1.3)
≥45	0.8	(0.5-1.3)
Educational level (Secondary/University education)		
Illiteracy/Primary education	1.2	(0.9-1.7)
Unknown	0.7	(0.5-1.1)
Region of birth (Spain)		
Western Europe	1.4	(0.8-2.5)
East Europe	2.2	(0.8-6.0)
Latin America	1.5	(1.2-2.0)
Sub-Saharan Africa	0.5	(0.1-4.7)
Other/Unknown	0.5	(0.2-1.7)
Year of diagnosis (2003)		
2004	1.3	(0.8-2.0)
2005	1.0	(0.6-1.5)
2006	1.5	(1.0-2.2)
2007	1.2	(0.8-1.7)
Previous STI (No)		
Yes	1.0	(0.7-1.2)
Type of partners (sexual contact with a steady partner only)		
Sexual contact with a casual partner (solely)	1.5	(1.0-2.3)
Sexual contact with a steady and casual partner	1.9	(1.2-3.2)
Exchange of sex for drugs or money	1.0	(0.4-2.7)
Mixed**	1.2	(0.8-1.9)
Unknown	1.2	(0.6-2.5)

*Reference categories in brackets; model adjusted by clinic of diagnosis
**Mixed: sexual contact with different partners (casual partner, steady partner, exchange of sex for drugs or money)
OR: odds ratio; CI: confidence interva

completed (OR: 3.4; 95% CI: 1.5-7.5), and having a history of STI (OR: 6.0; 95% CI: 2.1-16.9) (Table 2).

Concurrent diagnosis of STI among HIV infections newly diagnosed in MSM

In total, 1,462 HIV infections were newly diagnosed among MSM during the period 2003-2007. The majority (62.2%) were Spanish, mean age at diagnosis was 32.8 years (SD: 7.6) and almost two thirds (73.7%) had secondary/university education completed. Patients attributed their HIV infection to sexual contact with a casual partner in 695 (47.5%) cases, sex with their steady partner in 175 (12.0%), sexual contact with casual and steady partners in 199 (13.6%), exchanging sex for drugs or money in 33 (2.3%), and different combinations of the previous categories in 309 cases (21.1%). In 51 cases (3.5%) this information was not available.

History of previous STI was very common among the newly diagnosed HIV cases in MSM (49.2%). A total of 453 (31.0%) men were concurrently diagnosed with other STI at the time of HIV diagnosis. The most frequent infections diagnosed were: syphilis (223 cases), genital warts (92) and gonorrhoea (56). Concurrent STI and HIV co-infection was higher among those in the age-group 25-34 years and among Latin American men (Table 3).

In the multivariate analysis, factors associated with STI co-infection among newly diagnosed HIV cases in MSM were: being Latin American (OR: 1.5; 95% CI: 1.2-2.0), having sex with casual partners (OR: 1.5; 95%CI: 1.0-2.3) or with both steady and casual partners (OR: 1.9; 95%CI: 1.2-3.2) (Table 4).

Discussion

In this article data from Spain on HIV prevalence among MSM with syphilis and/or gonorrhoea, and concurrent STI diagnoses in MSM newly diagnosed with HIV are presented. Data were collected in clinics specialising in STI and/or HIV diagnosis. While results cannot be extrapolated to all MSM in the country, they provide valuable information on STI/HIV co-infections among MSM with risk behaviours for HIV and other STI resident in medium and big Spanish cities. This information is even more valuable because, to date, neither the HIV nor the STI national surveillance systems have collected information about HIV/STI co-infection.

HIV prevalence among MSM with syphilis in Spain is 29.8%. This figure is intermediate and within the range of 14%-59% found in different European countries [13]. Regarding HIV prevalence among MSM with gonorrhoea (15.2%), it is lower than the 32% reported in the United Kingdom in 2008 [2] or the 19% reported in New York City for 1990-1997 [14], but higher than the 11% found in a Stockholm STI clinic in 2004 [15].

Most of the syphilis and gonorrhoea cases co-infected with HIV were aware of their status. This finding, common to other studies [13,16,17], shows that some HIV-positive MSM continue to pursue risky behaviours even if they are aware of their HIV status, thus contributing to HIV transmission and putting themselves at risk of re-infection with HIV or infection with another STI.

Almost one third of MSM newly diagnosed with HIV during the period 2003-2007 were concurrently diagnosed with other STI, most commonly syphilis (15% prevalence). Similar results were found in a cohort of HIV-infected MSM in Sidney, where prevalence of syphilis among HIV-positive MSM was 19% (compared to 3.0% among HIV-negative MSM) [18]; whereas an even higher prevalence, 44.4%, was found among newly diagnosed HIV-infected MSM in a San Francisco STI clinic, in spite of the fact that only gonorrhoea and chlamydia infections were considered in this study [19].

Being born in Latin America was associated with both high HIV prevalence in syphilis and gonorrhoea patients and high STI prevalence in newly diagnosed HIV patients. This finding is consistent with what has been found in other studies in Spain [20] and shows that this MSM population is particularly vulnerable to HIV and other STI infections. Reasons for this are unclear. Latin Americans speak Spanish and, in theory, should have fewer problems to adapt to Spain. On the other hand, data from the EPI-VIH study show that a high percent of sex workers are Latin American [21,22]. Besides, it has been suggested that some HIV-positive Latin-American MSM might have migrated to Spain in search of a more socially-friendly environment.

Having sex with casual partners or having "mixed sexual contacts" (i.e. "casual partners + sex clients", "casual partners + contact with a sex worker" etc.) was also associated with HIV and syphilis co-infection. This result has been found also in other studies [17,23] and it is not surprising since in these situations people are less likely to know their partner's HIV status.

Although in this and in other studies [24,25] history of previous STI has been associated with higher HIV prevalence, both in syphilis and gonorrhoea cases, other factors associated with HIV and gonorrhoea co-infection differ clearly from those related to HIV and syphilis co-infection. Thus, among MSM with gonorrhoea, we found that HIV infection was more likely among men older than 45 years, those with low educational level and sex workers, variables that did not appear so relevant in MSM with HIV and syphilis co-infection. Further studies are needed to confirm these differences and provide insight into the possible reasons behind these differences.

Data presented in this paper show that there is a great degree of overlap among HIV and other STI among MSM in Spain. Implications of this finding are several: a) further studies are needed to better understand the epidemiology of HIV/STI co-infection in MSM; b) HIV-positive MSM should be a priority for HIV and STI prevention programmes; c) Latin American MSM should be a priority for prevention; d) in addition to HIV testing being included in the STI diagnostic process, the presence of other STI should be assessed in MSM newly diagnosed with HIV.

Financial support

This work was funded by two grants (36646/07; 36794/08) from the Foundation for Research and Prevention of AIDS in Spain (Fundación para la Investigación y la Prevención del SIDA en España–FIPSE).

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Lymphogranuloma venereum in Europe, 2003-2008

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This article was published on 9 December 2009.
Citation style for this article: Savage EJ, van de Laar MJ, Gallay A, van der Sande M, Hamouda O, Sasse A, Hoffmann S, Diez M, Borrego MJ, Lowndes CM, Ison C, on behalf on the European Surveillance of Sexually Transmitted Infections (ESSTI) network. Lymphogranuloma venereum in Europe, 2003-2008. Euro Surveill. 2009;14(48):pii=19428. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19428

Lymphogranuloma venereum, caused by the L serovars of *Chlamydia trachomatis*, emerged in Europe in 2003 and a series of outbreaks were reported in different countries. The infection presents as a severe proctitis in men who have sex with men, many of whom are co-infected with HIV and other sexually transmitted infections. This paper reviews the number of cases reported over a five year period, from 2003 to 2008, from countries that were part of the European Surveillance of Sexually Transmitted Infections (ESSTI) network. Reports were received from Belgium, Denmark, France, Germany, the Netherlands, Portugal, Spain, Sweden, and the United Kingdom. It appears that after five years the characteristics of the patients infected has overall remained unchanged, although the total number of cases has increased and more countries in Europe have now identified cases of LGV.

Introduction

After initial case reports in late 2003, an outbreak of lymphogranuloma venereum (LGV) among men who have sex with men (MSM) was described in the Netherlands in 2004 [1-3]. MSM with LGV have presented with severe proctitis, the majority were co-infected with HIV and other sexually transmitted infections (STI) such as Hepatitis C, and reported unprotected anal intercourse [2-5]. Prior to 2003, LGV had been unusual in Western Europe for many years with most cases being imported. Classically, LGV presents as genital ulceration with lymphadenopathy and a secondary anorectal syndrome in tropical and subtropical countries in Africa, Asia, Central and South America [6]. The causative agent of LGV is *Chlamydia trachomatis* belonging to the L serovars and the current outbreak in Europe has been almost exclusively attributed to L2 genotype.

LGV was not a notifiable disease in many countries but enhanced surveillance has been established since 2004 in the Netherlands (January) and the United Kingdom (UK, October), and sentinel surveillance was set up in Germany (May). France introduced sentinel surveillance in January 2005 while LGV reporting in Sweden was performed via the mandatory *Chlamydia* laboratory reporting system since 2004. Other EU Member States did not change their national STI notification systems and LGV cases were reported through routine clinical or laboratory observations. From June 2003, the European Surveillance of Sexually Transmitted Infections (ESSTI) network enabled epidemiologists and microbiologists to communicate, share information and raise alerts on emerging STI or outbreaks of STI via ESSTI_ALERT. This platform was also used to disseminate information about LGV. This report collates data collected through the ESSTI network and comments on the situation regarding LGV five years on from the apparent start of the outbreak in 2003.

Methods

In June 2008, the focal points of 24 countries participating in the ESSTI network were asked to provide information on LGV since 2003 for their respective countries (by short questionnaire). Countries were asked to provide available data on: monthly/quarterly number of cases, their sexual orientation, HIV status, age, sex, concurrent STI, travel abroad, clinical syndrome i.e. ano-rectal or inguinal, clinical symptoms, number of sexual partners in the last three months, and any other information available which they felt was relevant. Where no data or only incomplete data was available, information was compiled from reports of LGV submitted to ESSTI_ALERT during 2004 and 2008.

The ESSTI_ALERT system was developed as an informal system for epidemiologists and microbiologists to facilitate sharing and dissemination of early information on unusual events or outbreaks of STI across Europe. The system is based on a monthly active notification of unusual STI transmission events to the ESSTI coordinating centre meaning that notifications were requested actively each month from the coordination centre and were made using a standard reporting form.

Results

Nine countries (Belgium, Denmark, France, Germany, the Netherlands, Portugal, Spain, Sweden and the UK) provided data on LGV cases. For three additional countries: Ireland, Italy, and

Norway information was compiled using ESSTI alerts from 2007 and 2008.

Trends

From 2002 to 2007, the total number of cases reported was 1,693 (the UK 648 cases, France 556, the Netherlands 255, Germany 159, Belgium 45, Denmark 18, Portugal 8, Spain 4). LGV cases were already reported between 2002 and 2004 in Belgium, the UK, France, the Netherlands and Germany from where cases continued to be diagnosed. The highest number of cases was reported in the third quarter of 2005 with 96 cases diagnosed in the UK. The number of cases in the UK declined in 2006 but increased again in 2007 (Figure 1) and 2008 (191 cases) (data not shown). The Netherlands also saw an increase in the number of LGV cases reported starting towards the end of 2006. In France, the number of cases increased each year since 2002 until 2007 and seemed stable in 2008 with 170 and 174 cases respectively. Denmark, Portugal and Spain - countries that had not seen LGV cases early in the outbreak - started to report cases in 2006 and 2007 (Figure 2).

Characteristics

Characteristics of recent cases were similar to those in early outbreak reports. LGV cases were predominantly found among MSM with between 80-100% of cases in all countries reporting, except for Portugal (Table 1). In France, information on sexual orientation is not available; however, all French cases were male and C. trachomatis serovar L2 was identified from anorectal samples.

The majority of the European cases were co-infected with HIV, with the proportion of HIV-positives ranging from 40% in one sentinel site in Spain (Bilbao) to 100% in Sweden (Table 1).

Data on concurrent infections other than HIV was available from Belgium, Denmark, the Netherlands, Portugal, Spain (Bilbao), and the UK (Table 1). For gonorrhoea the proportion ranged from 0% in Portugal to 25% in the Netherlands and for syphilis co-infections the range was between 6% in the UK where a large number of LGV cases had been detected, to 40% in Portugal.

The clinical presentation was anorectal syndrome in the majority of cases: all cases in Netherlands, both cases in Portugal where the clinical syndrome was known, and 31 out of 36 cases in Denmark. Thirty-eight of 45 cases in Belgium had proctitis. In six cases, LGV was reported as inguinal manifestation (Denmark 5 cases, Spain 1 case).

LGV was mostly diagnosed in MSM aged above 25 years, with the exception of an outbreak in Catalonia where 25 of 28 cases of LGV were in MSM younger than 25 years (Table 1). High numbers of sexual partners were noted for cases in Spain, with more than 20 partners in the last six months reported for three of five cases; while more than five partners in the last six months were reported for eight of 15 cases in Belgium.

Only few male heterosexual cases were reported: two in Portugal, one in Spain (female partner also infected), and three in the UK. In Germany, cases were reported without additional information on sexual orientation.

Reports to ESSTI_ALERT

Reports to ESSTI-ALERT were received from Ireland; two LGV cases, both MSM, one HIV-positive; from Italy, three cases, all MSM, two of whom were HIV-positive; and from Norway, four cases, without additional information. These reports, however, do not necessarily represent the total number detected in each of these countries. Sweden described an LGV cluster of five cases with domestic transmission in a sexual network in Stockholm .

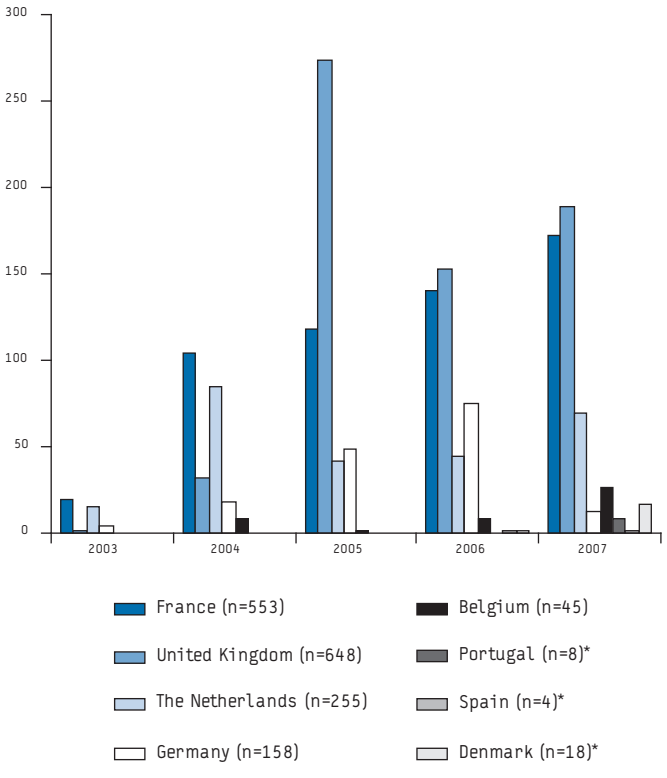
Discussion

From 2003 to 2008 the number of reported cases of LGV has increased in different countries in Europe, with the largest numbers reported in the UK, France, the Netherlands and Germany [7-10]. Moreover, since 2006 LGV has been reported in additional countries including Italy, Austria, Denmark, Portugal and Spain although often with a small total number of cases [11-15]. The profile of infected individuals, MSM with proctitis over 25 years of age and predominantly co-infected with HIV, has remained largely unchanged throughout the epidemic. Only some exceptions were reported, such as a small number of heterosexual cases detected by systematic screening in Portugal, with only few cases in total [14]. In the UK, where over 800 cases were detected, 13 presented with unusual clinical features: five cases of urethral LGV, three cases of LGV-associated inguinal buboes, one case of a solitary LGV penile ulcer and another case with a penile ulcer and bubonulus [16]. A case of bubonulus has also been reported from France [17].

The number of LGV cases continued to increase in several European countries and the characteristics of the patients appear to have remained unchanged, despite a few exceptions. Countries have reported actively on the number of cases detected, however, the reporting is largely influenced by the existence of a national

Figure

Cases of lymphogranuloma venereum in selected European countries, 2002-2007



*Data for 2006 and 2007.

sentinel surveillance system for LGV and the active case finding practices in clinical care across and within countries. The LGV cases presented here are probably largely underestimated due to the fact that cases may not be recognised, remain undiagnosed or are not reportable to national surveillance systems. Furthermore, ESSTI_ALERTS have increased awareness throughout the network but did not involve clinicians in the participating countries. Another weakness in our data and in the literature is a lack of a consistent case definition across Europe and the lack of LGV genotyping in some countries particularly early in the outbreak. Nevertheless, the consistency in the characteristics of patients infected with LGV across Europe suggests that this is a distinct entity.

There is little evidence that the LGV outbreak in MSM has spread to a wider population since 2003. LGV still seems to occur amongst a core group of individuals infected with HIV and with high-risk sexual behaviour [18-20]. The low number of cases among HIV-negative and heterosexual men indicates little bridging between the core MSM and other sexual networks. Molecular typing studies have shown that, where the data is available, the infecting LGV strain belongs primarily to serovar L2b [21] and although variants have been found, these differ from the parent strain by only a few base pairs [22]. This seems to point towards transmission within a closed network but data needs to be interpreted with caution as the molecular typing methods are poorly discriminatory at present. Spaargaren et al. [21] compared strains from the current European outbreak with strains collected in the 1980s in the United States and found both belonging to serovar L2b. The conclusion from this might be that the outbreak has not emerged recently but may rather have gone undetected due to the lack of specific screening for LGV genotypes.

The reasons for the re-emergence of LGV in Europe over the last five to six years remain unclear and it has been suggested that it is the result of the increased availability of molecular diagnostic tests [23]. While there has certainly been considerable development [24-27] and increased use of molecular tests to directly detect C. trachomatis belonging to the L serovars [28], this appears to have been largely in response to a clinical need [29]. There do remain a number of elusive questions regarding the reservoir and mode of transmission that perpetuates the ongoing outbreak. Data regarding the existence of an asymptomatic reservoir are conflicting with only a small number of asymptomatic cases detected in the UK compared to a larger number in the Netherlands [28,30-32], although this may simply reflect variation in protocols for screening and testing of MSM patients across Europe. The inability to detect C. trachomatis serotypes causing LGV in the urethra points at possible transmission through inanimate objects such as sex toys, or the inability of the pathogen to colonise the urethra. High-risk behaviour is now well documented as a characteristic of individuals infected with LGV but the use of enemas and increased number of partners are the only risk factors currently identified [22]. There

Table

Risk factors of LGV cases in selected countries in Europe, 2004-2008

Country	Period	Number of male cases	No. MSM (%)	HIV positive (% of known status)	HIV unknown serostatus (% of total)	Concurrent STI (%)					Age Years
						Syphilis	Gonorrhoea	Hepatitis B	Hepatitis C	Chlamydia infection	
Belgium	2004-2008	43	42* (97.7)	41 (95.3)	0	6 (14)	5 (11.6)	-	-	-	Mean age 38 (range 20-58)
Denmark	2006-2008	43	42 (97)	15 (35)	6 (16.7)	3 (7)	2 (5)	NA	NA	NA	Mean age 38 (range 24-52)
France	2002-2008	725	NA	280 (90)	415 (57)	-	-	-	-	-	Median age 37 (range 20-58)
The Netherlands	2004-2007	225	224 (99.6)	117 (55)	14 (6.2)	27 (12)	56 (24.9)	3 (1.3)	-	-	Mean age 41
Portugal	2007–March 2008	5	3 (60)	3 (100)	2 (40)	2 (40)	-	-	-	3 (60)	Mean age 42 (range 29-52)
Spain: Bilbao	2006-June 2008	5	4* (80)	2 (40)	0	0	1 (20)	0	0	2 (40)	Mean age 35 (range 33-39)
Spain: Catalonia	2007-June 2008	17	17 (100)	16 (94)	0	-	-	-	-	-	Age group 15-24(n=25) 25-44 (n=3)
United Kingdom	2004-2008	848 (763 with further epidemiological data)	756 (99.1)	566 (74)	33 (4)	49 (6)	135(18)	1 (0.1)	112 (15)	-	Mean age 38 (range 19-67)
Sweden	2007-August 2008	9	9 (100)	9 (100)	0	-	-	-	-	-	NA

MSM: men who have sex with men; STI: sexually transmitted infections; NA: not available
*Includes 1 bisexual

is other epidemiological evidence that STI such as syphilis and resistant gonorrhoea are increasing in MSM in many countries, showing that STI infections can spread in sexual networks of MSM across Europe [33].

Sharing of information through the ESSTI has raised awareness for the problem of LGV in MSM. However, cases continue to be detected in many European countries, implying that control and prevention strategies which have so far concentrated on accurate diagnosis and treatment of cases and their sexual partners, have not been optimal. Activities also included raising awareness amongst healthcare professionals and the gay community in some countries. This is in contrast to the situation which occurred in the late 1990s when outbreaks of syphilis were first reported in Western Europe among MSM. A variety of control measures targeting MSM were introduced by countries such as health education and promotion, increased clinic capacity, syphilis screening at social venues and clinics and at HIV treatment centres, distribution of free condom packs, and contact tracing [34]. Despite all these efforts, syphilis rates have reached high levels almost equal to the pre-AIDS era in many countries. Although the numbers of LGV remain small in comparison to the number of syphilis cases reported, it is clear that LGV is becoming endemic in particular sexual networks and alternative approaches to the control of LGV should possibly be considered. Surveillance and monitoring of LGV is currently implemented at EU level by the European Centre for Disease Prevention and Control (ECDC) as part of the enhanced surveillance for STI as agreed with the Member States. Reporting to one European surveillance system shall contribute to the availability of more comparable data on LGV, and STI in general, in the future.

Members of the European Surveillance of Sexually Transmitted Infections, listed in alphabetical order by countries, are:

Austria: Angelika Stary, Outpatients' Centre for Diagnosis of Infectious Venero-Dermatological Diseases, Reinhild Strauss, FM for Health, Family and Youth; Belgium: Tania Crucitti, Institute of Tropical Medicine; Cyprus: Chrystalla Hadjianastassiou, Ministry of Health; Denmark: Susan Cowan, Statens Serum Institut; Estonia: Anneli Uusküla, Tartu University Clinics, Rutta Voiko, West Tallinn Central Hospital; Finland: Eija Hiltunen-Back, National Public Health Institute; France: Véronique Goulet, Institut de Veille Sanitaire, Patrice Sednaoui, Institut Alfred Fournier; Bertille de Barbevrac, National Reference Centre of Chlamydia Infection; Germany: Peter Kohl, Dept. of Dermatology and Venerology, Vívantes Klinikum Neukölln; Greece: Vasileia Konte, Hellenic Centre for Infectious Disease Control, Eva Tzelepi, National Reference Center for N.gonorrhoeae, Hellenic Pasteur Institute; Iceland: Guðrún Sigmundsdóttir, Centre for Infectious Disease Control, Directorate of Health, Guðrun Hauksdottir, Landspitali University Hospital; Ireland: Aidan O'Hora, Health Protection Surveillance Centre, Helen Barry, St. James Hospital; Italy: Paola Stefanelli, Barbara Suligoi, Istituto Superiore di Sanità; Latvia: Judite Pirsko, Elvira Lavrinovica, State Centre of Sexually Transmitted and Skin Diseases; Malta: Christopher Barbara, St Luke's Hospital, Jackie Maistre Melillo, Infectious Disease Prevention and Control Unit, Department of Health Promotion and Disease Prevention; Netherlands: Ineke Linde, GGD Amsterdam; Norway: Hilde Klovstad, Norwegian Institute of Public Health, Vegard Skogen, UNN Tromsø Universitetssykehuset; Portugal:Jacinta Azevedo, General Directorate of Health (DGS),; Slovak Republic; Jan Mikas, National Public Health Agency of the Slovak Republic; Slovenia: Irena Klavs, Centre for Communicable Diseases, Institute of Public Health of the Republic of Slovenia, Alenka Andlovic, Institute of Microbiology and Immunology, University of Ljubljana; Spain: Julio Vazquez, Instituto de Salud Carlos III; Sweden: Anders Blaxhult, Inga Velicko, Swedish Institute for Infectious Disease Control, Hans Fredlund, Swedish Reference Laboratory for Pathogenic Neisseria, Orebro University Hospital; Turkey: Peyman Altan, General Directorate of Primary Care Services, Ministry of Health; United Kingdom: Lesley Wallace, Health Protection Scotland, Hugh Young, Scottish Bacterial Sexually Transmitted Infections Reference Laboratory, Mike Catchpole, Michelle Cole, Health Protection Agency..

Acknowledgements

We would like to thank Sarah Alexander, Ian Simms and Cassandra Powers for data from the United Kingdom.

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HIV bio-behavioural survey among men who have sex with men in Barcelona, Bratislava, Bucharest, Ljubljana, Prague and Verona, 2008-2009

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This article was published on 9 December 2009.
Citation style for this article: Mirandola M, Folch Toda C, Krampac I, Nita I, Stanekova D, Stehlikova D, Toskin I, Gios L, Foschia JP, Breveglieri M, Furegato M, Castellani E, Bonavina MG, the SIALON network. HIV bio-behavioural survey among men who have sex with men in Barcelona, Bratislava, Bucharest, Ljubljana, Prague and Verona, 2008-2009. Euro Surveill. 2009;14(48):pii=19427. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19427

Data from 23 European countries show that the annual number of HIV diagnoses in men who have sex with men (MSM) increased by 86% between 2000 and 2006. This paper reports the main preliminary results of a bio-behavioural survey in MSM with a specific focus on HIV prevalence and use of United Nations General Assembly Special Session (UNGASS) indicators in six cities in Southern and Eastern Europe. Time-location sampling (TLS) was used. A total number of 2,356 questionnaires and 2,241 oral fluid samples were collected (invalid samples 4.1%). The data show different socio-demographic patterns across countries regarding age, level of education, living conditions, living area and self-identity. Southern European cities had the highest percentage of people who had tested for HIV and collected the result. More than 50% of respondents in the sample from Barcelona reported having used a condom last time they had anal sex (57.2%), whilst in all other cities this proportion was below 50%. The cities with the highest HIV prevalence in MSM were Barcelona (17.0%) and Verona (11.8%) whilst lower percentages were reported in Bratislava (6.1%), Bucharest (4.6%), Ljubljana (5.1%) and Prague (2.6%). The low prevalence in Eastern European cities is encouraging. However, with the level of high-risk sexual behaviour documented and the lower frequency of HIV test seeking behaviour, there is a clear risk of an increase in HIV transmission.

Introduction

HIV infection remains an important public health issue in Europe, with evidence of continuing transmission in many countries. Accounting for almost one third (7,693) of all reported newly diagnosed HIV infections reported in 2006 in European Union (EU) and European Free Trade Association (EFTA) countries, Men who have sex with men (MSM) continue to represent a population at high risk of HIV infection [1,2]. Data from 23 European countries show that the annual number of HIV diagnoses in MSM increased by 86% between 2000 and 2006 [2]. The results of some seroprevalence studies in gay community settings or healthcare services suggest levels of HIV prevalence between 10 and 20% among MSM, and available data suggest a possible hidden HIV epidemic in this population group [2,3].

In addition to the spread of HIV, an increase of high risk sexual behaviour among MSM is reported throughout Europe [1,2]. In this context, HIV testing has become a key surveillance activity for monitoring the HIV epidemic especially in hard-to-reach MSM. Since the introduction of highly active antiretroviral therapy (HAART), AIDS has become less indicative of the underlying trends in HIV infection. Another important factor linked to risk behaviour and risk of HIV transmission is the use of alcohol and other psychoactive drugs. According to the literature, alcohol and illicit drug consumption significantly increase the odds of having sex and have a significant positive association with the sexual risk.

Several studies, both in Europe and the United States (US), show a high percentage of MSM who use alcohol and drugs before and during sex and an association between these substances and sexual risk behaviour [4-6]. Additionally other studies suggest that even intermittent, recreational use of these drugs before or during sexual intercourse may lead to high-risk sexual behaviour (e.g. unprotected anal intercourse, UAI), especially with casual partners [7,8]. Recent studies of the sexual risk behaviour of MSM have also described a range of changes in sexual risk-taking behaviour in MSM in recent years, with an increased number of partners in some countries. The number of partners proved to be one of the strongest predictors of unsafe sex; according to the literature, the probability of having had unsafe sex ranged from 17% in men with one partner to 58% in men with more than 20 partners [9-11].

Despite these findings, few studies targeted MSM using outreach methods collecting behavioural and biological data in line with

Second Generation Surveillance System (SGSS) criteria [12,13] and United Nations General Assembly Special Session (UNGASS) indicators [3,14]. The Second Generation Surveillance System combines monitoring of newly diagnosed HIV cases and indicators of sexual behaviour among persons in groups at highest risk for infection.

Previous community-based surveys targeting MSM in Scotland, which included both questionnaires and anonymous oral fluid testing for HIV, found high levels of HIV prevalence and risk behaviour and low uptake of HIV testing [15]. The advantage of oral fluid collection for testing of infection is evident as it is a minimally invasive method for serological monitoring which is easy and safe. It has proven to be acceptable for various target audiences and it does not require trained staff [16,17]. Therefore, the use of oral fluid as a means for biological testing is of crucial importance in order to gather valid and reliable information about the spread of HIV among hard to reach populations such as MSM.

Taking these factors into account, the 2008-2009 study was designed to gather reliable information on HIV prevalence among MSM in Southern and Eastern Europe.

This paper reports preliminary results of the SIALON project Capacity building in HIV/Syphilis prevalence estimation using non-invasive methods among MSM in Southern and Eastern Europe, with a specific focus on HIV prevalence and use of UNGASS indicators.

Methods

Study design

The study was a descriptive multi-centre biological and behavioural cross-sectional survey and was carried out in seven cities of Southern and Eastern European countries: Athens, Greece; Barcelona, Spain; Bratislava, Slovakia; Bucharest, Romania; Ljubljana, Slovenia; Prague, Czech Republic; Verona, Italy. In this report Bratislava, Bucharest, Ljubljana and Prague were defined as Eastern European cities. The survey was designed to obtain an estimate of the prevalence of HIV in the study population, MSM attending gay venues.

Ethics Committee approval was obtained in each participating country and an informed consent form was collected for each respondent. The questionnaires and the oral fluid samples were collected anonymously. In order to make the test result available to interested individuals, a barcode was used to link the respondents to the test result via a card with the same barcode given to the respondents when oral fluid was collected. To comply with all ethical and legal aspects and minimise the risks of diagnostic mistakes, respondents interested in getting their test results were informed that the test result was not meant to be diagnostic and for this reason they should be tested again in line with international/

Figure 1

Age distribution of participants of an HIV bio-behavioural survey among men who have sex with men in Barcelona, Bratislava, Bucharest, Ljubljana, Prague and Verona, 2008-2009

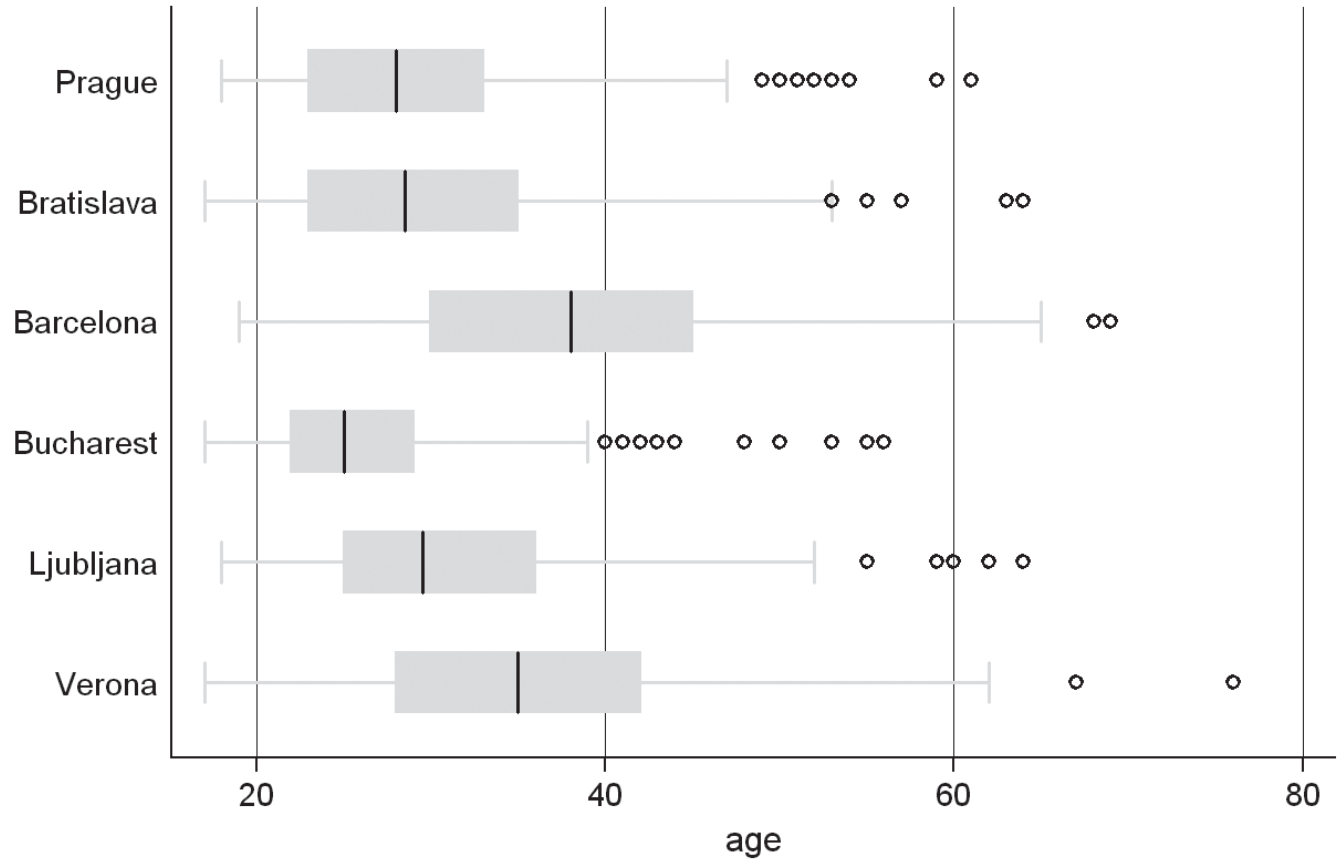


Figure 2

Percentage of men who have sex with men (MSM) who self-identified themselves as gay/homosexual, bisexual and heterosexual; HIV bio-behavioural survey among men who have sex with men in Barcelona, Bratislava, Bucharest, Ljubljana, Prague and Verona, 2008-2009

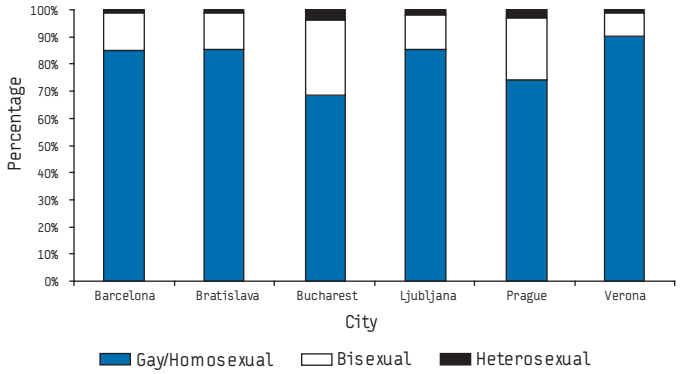


Table 1

United Nations General Assembly Special Session (UNGASS) indicators by city; HIV bio-behavioural survey among men who have sex with men in Barcelona, Bratislava, Bucharest, Ljubljana, Prague and Verona, 2008-2009

	UNGASS 8 HIV testing n=2,356	95%CI[a]	UNGASS 19 Condom use n=1,925	95%CI	UNGASS 23 HIV prevalence n=2,243	95%CI
Barcelona	56.2	±4.9	57.2	±5.1	17.0	±3.7
Bratislava	32.1	±4.9	30.8	±5.3	6.1	±2.5
Bucharest	43.2	±4.9	42.7	±5.3	4.6	±2.2
Ljubljana	38.2	±4.8	43.0	±5.6	5.1	±2.2
Prague	41.5	±4.8	29.8	±5.2	2.6	±1.6
Verona	53.0	±4.9	45.6	±5.2	11.8	±3.2

[a] Confidence interval

national guidelines. In case of a confirmed positive HIV test, the person was directed to the infectious disease department for further checks of their clinical situation and start antiretroviral treatment if needed.

Study population

Participants were recruited according to the following four inclusion criteria: having had sex (any kind of sex: oral and anal, penetrative or not) at least once with another man during the last 12 months before the study; having signed a written informed consent form; having agreed to answer the study questionnaire; having accepted to donate an oral fluid sample. Three exclusion criteria were adopted: age below 18 years; currently active injecting drug use (IDU) and having already participated in the study.

Sampling

Time-location (or time-space) sampling (TLS) was used to recruit representative samples of men visiting the gay scene in each city. The method used was consistent with the approach adopted in previous studies [15-21]. In the TLS, spaces (or locations) are venues attended by the target population; times refer to specific days and time periods when the target population congregates in each space. This method allows a sample with known properties to be identified and enables statistical inferences to be made to the larger population of venue visitors. Formative research was conducted in each collection location in order to identify the list of potential TLS units, the attendance time frame, opening days and hours of each venue. Bars, discos, saunas, cruising venues, sex-shops, sex-clubs were identified in all cities. All venues were mapped and visited when information on attendance patterns was not sufficient to prepare a TLS units list. The spaces and their associated days were divided into standardised time segments (four-hour periods). Subjects were enrolled over the entire TLS unit time period. Information on the number of refusals per TLS unit was collected. Furthermore, settings or special gay events that did not occur frequently were identified. A "special events" category was created and included in the sampling list because such occasions may attract members of the target population. The list of TLS units obtained with this process for each collection site included the primary sampling units (PSU). PSU were randomly selected from complete list of eligible TLS list in each city. The sample size estimation for a prevalence study was calculated on

Table 2

Percentage of respondents who consistently used a condom in the last six months with steady and casual partners, separately for anal and oral sex; HIV bio-behavioural survey among men who have sex with men in Barcelona, Bratislava, Bucharest, Ljubljana, Prague and Verona, 2008-2009

	Condom use during anal sex with steady partner		Condom use during anal sex with casual partner		Condom use during oral sex with steady partner		Condom use during oral sex with casual partner	
Total	N=1,402		N=1,383		N=1,517		N=1,567	
	%	95%CI[a]	%	95%CI	%	95%CI	%	95%CI
Barcelona	43,0	±7,0	65,4	±5,5	9,3	±4,0	13,1	±3,8
Bratislava	19,9	±5,2	41,7	±6,9	1,2	±1,4	6,2	±3,1
Bucharest	43,1	±6,0	51,8	±6,2	8,6	±3,3	15,1	±4,3
Ljubljana	36,6	±6,1	58,8	±7,2	5,5	±2,7	10,4	±4,0
Prague	25,6	±5,4	36,3	±6,8	5,8	±2,8	9,6	±3,7
Verona	40,2	±6,4	56,1	±5,9	5,8	±3,0	8,1	±3,0

[a]Confidence interval

the basis of previous prevalence estimation studies when available [22]. A total of 2,800 persons (400 per city) were included in the planned survey.

Data collection

Questionnaire

A self-administered pen-and-paper questionnaire was used to obtain information on the social/cultural/environmental context of respondents, access and barriers to voluntary counseling and testing (VCT), behavioural data on sex practices, risk-reducing strategies, condom use), STI history, self-reported/perceived serostatus and type of partner. A steady partner was defined in the questionnaire as "a person who you are committed to and have sex with, not meaning that, you are exclusively monogamous"; casual partner as "person you have sex with, occasionally without a steady partnership". In addition, UNGASS indicators were taken into account when designing the questionnaire [3,14]. The preliminary version of the questionnaire was piloted among MSM attending gay venues to check on the time needed to complete it and to ensure the questions were not ambiguous or confusing. The English version of the questionnaire was translated into the languages of the participating countries and then translated back into English.

A questionnaire manual and a training module were developed in order to guarantee uniform data collection. Specific training of data collectors was held in each country in a one day session by a data collection coordinator. The same coordinator was in charge of monitoring the local data collection and coaching the data collectors during the task. An ongoing evaluation process was organised through regular meetings with data collectors.

Oral Fluid sampling and testing

To collect oral fluids, Oracol oral fluid collection kits (Malvern Medical Developments, Worcester, UK) were used. The main advantages for replacing serum with oral fluid were easy access and non-invasive collection. After collection, oral fluid samples were kept refrigerated and sent to the national reference laboratory for HIV/AIDS in the respective countries no more than 72 hours after collection.

Laboratory testing

The oral fluid samples were sent for the analysis by each national reference laboratory to the Teaching Hospital-University of Verona, Immunology Unit, Verona, Italy. EIA testing GENSCREEN HIV 1/2 version 2, BIO-RAD on oral fluid sample was performed according to the manufacture's instructions [23]. All positive samples were confirmed with a Western Blot test. As quality control, for each oral fluid sample, a total IgG antibodies ELISA test was performed in order to assess the sample suitability for testing. Samples below 3.5 titre (cut-off) were excluded from the study as invalid. A validation study of Bio-Rad OF testing comparing serological testing involving 37 HIV positive patients and 35 controls per country was carried out according to commission decision of 7 May 2002 on common technical specifications for in vitro medical devices. Validation, with 504 paired oral fluid and serum samples, yielded a 99% sensibility and 99% specificity, which gives PPV of 94.6% and NPV of 99.8% for a prevalence of 15%. For a prevalence of 5% these figures are 83.9% and 99.9% respectively.

Enrolment

According to the data collection calendar, trained field workers from gay associations distributed anonymous self-complete questionnaires and Oracol oral fluid collection kits. Both self-complete questionnaire (behavioural data) and oral fluid samples (biological data) were collected for each subject. A barcode was used to link behavioural and biological information. The enrolment period varied between cities. The data collection calendar varied from two months in Barcelona and Verona to nine months Bratislava and Bucharest.

Table 3

Number of steady and casual partners in the last six months; HIV bio-behavioural survey among men who have sex with men in Barcelona, Bratislava, Bucharest, Ljubljana, Prague and Verona, 2008-2009

		Barcelona	Bratislava	Bucharest	Ljubljana	Prague	Verona
Steady partner		n=161	n=238	n=256	n=258	n=242	n=221
	Mean	1,6	2,0	3,3	2,1	2,7	2,6
	SD[a]	1,7	2,2	4,5	2,5	3,6	3,6
	P25	1	1	1	1	1	1
	Median	1	1	2	1	1	1
	P75[b]	1	2	3	2	3	3
	IQR[c]	0	1	2	1	2	2
Casual partner		n=269	n=232	n=249	n=219	n=205	n=293
	Mean	16,3	6,1	7,1	5,7	7,5	12,0
	SD	20,5	8,6	9,4	8,9	10,5	16,1
	P25	4	2	2	2	2	3
	Median	10	3	3	3	4	6
	P75	20	6	7	6	10	12
	IQR	16	4	5	4	8	9

[a]SD: standard deviation
[b]P: percentile
[c]IQR: inter-quartile range

Statistical Analysis

As the focus of the study was descriptive, mean, median, standard deviation, quartiles and inter-quartiles were used and proportions with 95% confidence intervals (CI) were calculated for all variables and indicators. STATA 11 survey commands suite was used.

Results

A total of 2,362 questionnaires and 2,365 oral fluid samples were collected in six of the seven cities. The total number of valid questionnaires was 2,356 (99.7%) whilst for the valid oral fluid samples it was 2,241 (94.8%) The proportion of valid oral fluid samples over valid questionnaires by city was respectively: Barcelona 97% (388/400), Bratislava 98% (342/349), Bucharest 86.7% (345/398), Ljubljana 97.7% (389/398), Prague 95.1% (387/407), Verona 96.5% (390/404). Athens, Greece was not included in the analysis as data was not available at the time of this paper.

The time of questionnaire completion ranged from 10 to 20 minutes. The time length was related to age and the type of venues.

Study population

The median age and 1st and 3rd quartile by city are presented in Figure 1. Respondents in Barcelona and Verona had a similar age distribution and were older, (38 and 35 years respectively) than those in the Eastern European cities; in Bucharest the median age of respondents was 25 years, followed by Prague and Bratislava (28 years). In Ljubljana the median age was 29.5 years.

As regards education level, MSM in Barcelona had the highest proportion of university degrees (53.6%) and MSM in Prague the lowest (27.4%).

In most of the cities the largest group of respondents lived alone (living conditions): 41.8% in Prague, 40.8% in Verona, 37.4% in Barcelona and 36.9% in Ljubljana. Exceptions were Bucharest and Bratislava, where respondents lived mostly with their parents (34.1% and 30.2% respectively). In Verona, a high proportion of MSM lived with their parents (30.1%), although a larger number lived alone. Barcelona had the highest proportion of respondents living with friends (22.9%), while the highest proportion living with male partners were in Prague (27.5%) and Bratislava (27.6%) followed by Ljubljana (23.4%). The percentage of respondents living with a heterosexual family (female partner and/or offspring) was generally lower than 8%, ranging from 4.9% in Bratislava to 7.7% in Verona.

In almost all cities the majority of respondents lived in areas with more than 100,000 inhabitants, ranging from 61.4% in Bratislava to 82.9% in Bucharest, with the only exception of Verona, where the majority of respondents lived in a village with less than 10,000 inhabitants (32.7%) or in a small town with 10,000 to 100,000 inhabitants (25.3%).

The data for self-identified sexual orientation are presented in Figure 2. More than 80% of the respondents self-identified themselves as homosexual in Barcelona, Bratislava, Ljubljana and Verona. The highest proportion of bisexuals and heterosexuals was found in Bucharest (27.6% and 3.9% respectively) and in Prague (22.6% and 3% respectively), while the lowest was in Verona (8.7% and 1% respectively). In the remaining cities the percentage of bisexuals was similar, ranging from 12.7% in Ljubljana to 14.4% in Bratislava.

HIV prevalence and testing

Table 1 presents the prevalence of HIV infection among MSM based on the oral fluid tests. The cities with the highest HIV prevalence were Barcelona (17.0%) and Verona (11.8%); lower percentages were reported in Bratislava (6.1%), Bucharest (4.6%) and Ljubljana (5.1%). Prague had the lowest HIV prevalence (2.6%).

In order to monitor HIV testing uptake, UNGASS indicator number eight was used. This indicator comprises the percentage of MSM tested for HIV over the last 12 months who also collected the result. Table 1 presents the UNGASS 8 estimate by city.

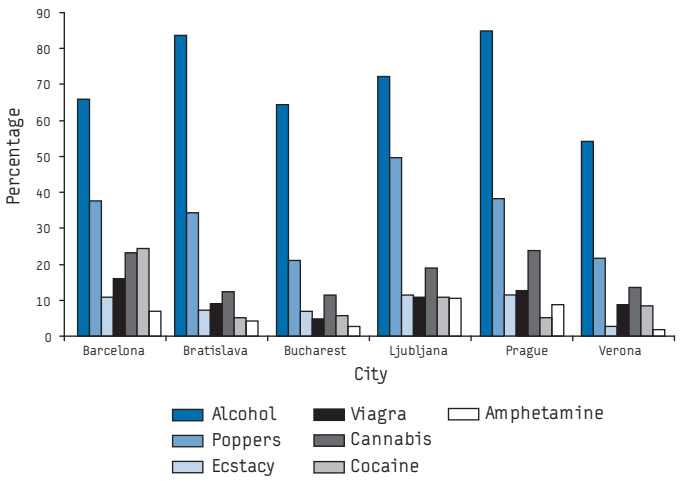
Southern European cities had the highest percentage of tested people who received their HIV test result (56.2% in Barcelona and 53% in Verona), while the Eastern European cities had the lowest percentages, ranging from 32.1% in Bratislava to 43.2% in Bucharest. Among the respondents who had taken an HIV test over the last 12 months, the percentage of subjects who decided to collect the test result was over 90% in Verona and Barcelona (93.9% and 92.6% respectively) while in Prague it was 85.9%, in Bratislava 83.6% and 78.3% in Ljubljana. The lowest percentage was in Bucharest (74.9%).

Condom use

In order to estimate the risk reduction strategies of MSM during the most at-risk sexual behaviour, namely anal sex, UNGASS indicator number 19 was used. This indicator describes the percentage of men reporting the use of a condom during their last anal sex episode with a male partner in the previous six months. Table 1 presents the UNGASS 19 estimate by city. More than 50% of respondents in the sample from Barcelona reported using a condom the last time they had anal sex (57.2%), while in all other cities this percentage was below 50%. In three cities percentages were above 40% (Verona: 45.6%, Ljubljana: 43%, Bucharest:

Figure 3

Percentage of respondents reporting use of alcohol, poppers, ecstacy, Viagra, cannabis, cocaine and amphetamine before or during sex over the last six months; HIV bio-behavioural survey among men who have sex with men in Barcelona, Bratislava, Bucharest, Ljubljana, Prague and Verona, 2008-2009



42.7%), while percentages were lowest in Prague (29.8 %) and Bratislava (30,8%).

Consistent condom use

Respondents were asked to indicate the frequency of protected anal and oral sex both with a steady and a casual partner over the last six months. Consistent condom use is defined as the use of a condom (often or always) in the last six months during sexual intercourse, both receptive and insertive. Sexual behaviour was analysed separately for anal sex and oral sex. Table 2 shows the percentage of consistent condom use by type of partner and city. As far as anal sex is concerned, condom use with a steady partner was declared by 43.1% of respondents in Bucharest and 43% in Barcelona, followed by Verona (40.2%) and Ljubljana (36.6%), while the lowest condom use was reported in Prague (25.6%) and Bratislava (19.9%). Condom use with a casual partner for anal sex is in general more likely to be reported than with a steady partner. The highest level of consistent condom use with a casual partner was reported by MSM in Barcelona (65.4%), whilst the lowest was in Prague (36.3%). In Ljubljana consistent condom use was reported by 58.8% of respondents who had anal sex with a casual partner, followed by MSM in Verona (56.1%), in Bucharest (51.8%) and in Bratislava (41.7%).

As far as consistent condom use in oral sex over the last six months is concerned, the level was dramatically lower compared with anal sex. In Barcelona, 9.3% of respondents reported condom use with a steady partner followed by Bucharest (8.6%); a virtually identical level was reported in Prague (5.8%), Verona (5.8%) and Ljubljana (5.5%). The lowest level of condom use in oral sex with a steady partner was reported in Bratislava (1.2%). For casual partners, consistent condom use in oral sex was reported by 15.1% of respondents in Bucharest, 13.1% in Barcelona and 10.4% in Ljubljana, whilst the lowest proportion was found in Verona (9.1%) and Bratislava (6.2%).

Number of partners

The highest average number of steady partners over the last six months reported by respondents was in Bucharest (3.3) and the lowest in Barcelona (1.6), although the medians show a more similar distribution between the cities, with two partners in Bucharest and one partner elsewhere (Table 2). For casual partners, the highest mean and median were reported in Barcelona (mean 16.3, median 10), followed by Verona (mean 12, median 6) and Eastern European cities (mean ranging from 5.7 to 7.5 and median from 3 to 4).

Psychoactive and recreational drug use over the last six months

Substance use before or during sex over the last six months is demonstrated in Figure 4. As expected, alcohol proved the substance with the highest rate of consumption in each city. The highest percentages were reported in Prague and Bratislava (85% and 83.7% respectively), whilst the lowest level was in Verona (54.2%).Poppers are one of the most popular substances in the gay scene and some authors refer to it as a gay drug [4]. The highest rate of poppers use was found in Ljubljana (49.8%) whilst lower use was reported in Prague, Bucharest and Barcelona (38.1%, 34.2% and 37.6% respectively). The lowest percentages were reported in Verona (21.6%) and Bucharest (21%). For ecstacy, the percentages of consumption were 11.4% in Prague, 11.3% in Ljubljana and 10.9% in Barcelona. Sixteen per cent MSM in Barcelona reported use of viagra, 12.7% in Prague. Lower levels of consumption were reported in Bucharest (4.7%), Verona (8.6%) and Bratislava (9.1%).High levels of Cannabis use were reported in Prague, Barcelona and Ljubljana (23.8%, 23.2% and 19.1% respectively), while lower rates were reported in Verona (13.4%), Bratislava (12.5%) and Bucharest (11.5%). A high consumption of Cocaine was found in Barcelona (24.5%). Similar levels of consumption were found in the MSM samples in Prague (5.1%), Bratislava (5.2%), Bucharest (5.8%) and Verona (8.3%). The rate of amphetamine use ranged between 1.9% in Verona and 10.4% in Ljubljana.

Discussion and conclusion

Valid and comparable data on HIV prevalence related to HIV risk behaviour in a hard to reach population are lacking. However, such information is important for development of effective prevention strategies. In order to respond to this limitation, the SIALON project, used three key elements of behavioural and prevalence studies among MSM for improving data comparability: time and location sampling (TLS) method, oral fluid testing in outreach settings and UNGASS indicators.

The use of TLS as a sampling method proved to be feasible and efficient in cities with highly developed gay scenes as well as in cities with less developed scenes. As previous studies among MSM have shown, TLS increases the possibility of involving a variety of participants, producing more valid results [15]. A generalisation of the estimates obtained with this method to the wider population of MSM attending sampled venues is also possible. TLS can be adopted on a larger scale and the method is easily applicable in cities with a considerable number of eligible gay venues. It is more difficult to implement in cities where the gay community is poorly organised and where there are few specific and easily accessible venues. Few venues means that the venues available are over-visited by data collectors, thus reducing the acceptance of the data collection process both to owners of venues and attendees. This aspect may impact the representativeness of the MSM sample of the whole MSM population and therefore reduce the efficiency of TLS. In addition, the TLS method does not take into account other ways of recruiting, such as the internet, gay magazines, chat room etc. However, as one of the main focuses of our study was to estimate HIV prevalence through the collection of biological samples, these alternative sources of recruitment were excluded.

For surveillance and epidemiological purposes, oral fluid testing has clear advantages over venopuncture in community settings and is an alternative screening tool in outreach settings among high-risk populations. Oral fluid testing simplifies the diagnostic process in specific populations in which drawing blood is difficult and dangerous. As previously demonstrated in other studies, the number of oral fluid collections in all sites confirmed the general acceptability of the study by MSM in outreach settings [16,24]. In our study, an info-pack containing a condom, a lubricant and information about STD prevention and screening centres available in the area was given to respondents in order to facilitate the enrolment and to promote safer sex and testing practice, during the data collection.

The introduction of UNGASS indicators is a key measure for the basic monitoring of HIV across countries with comparable indicators. According to UNAIDS, data from multiple countries collected following UNGASS procedures can supply critical information and comparative insights at the regional and the global level. Data can provide a snapshot as well as trend analysis of the epidemiology of HIV over time [3,14]. As far as our study results are concerned, the data shows a variety of socio-demographic patterns among the cities in relation to age, education, living conditions,

living area and self-identity. At this stage, the results presented in this paper are mainly descriptive and this is of course a limitation of the study. A multilevel, multivariate analysis will be carried out in the future to better understand the relationship between HIV prevalence and other factors.

HIV testing (UNGASS 8) is an important indicator of the healthcare system's ability to reach MSM and to efficiently provide access to screening. Verona and Barcelona had the highest percentages of tested people who collected the HIV test result. This finding reflects not only the lower access to HIV testing in Eastern European cities, but also how VCT is organised and might be an indicator of health practitioners' attitudes on health seeking behaviour. The high percentage of MSM seeking the test result in Verona and Barcelona seems to indicate better VCT practice. Differences in stigma, health service organisation and country specific barriers to accessing VCT could explain the gap between Southern and Eastern European cities. Data on condom use (UNGASS 19) seem to suggest that protected sex is more frequently performed in Southern European cities, particularly in Barcelona. Interestingly, HIV prevalence was highest in Barcelona and Verona, where condom use was also highest. This may reflect a different distribution of HIV prevention programmes. In more detail, data about the type of sexual partner, sexual intercourse and condom use confirm the findings of other studies. It is evident that the differentiation between steady and casual partners leads to different distribution of sexual practice. According to the literature, in some countries the number of sexual partners seems to have increased in recent years [25,26]. This may be a good proxy variable for unsafe sex [9]. As expected, throughout our sample, the number of casual partners was higher than the number of steady partners, although in some countries this difference was far more marked than in others. When considering different sexual behaviour (anal and oral sex) related to different types of sexual partners in the last six months, similar patterns occur. As already well-established by other studies, the rates of condom use differ in relation to the kind of partners and sexual practices: protected sex with casual partners is more frequent than with a steady partner, and protected anal sex is more frequent than protected oral sex [27].

As far as substance use is concerned, alcohol consumption is broadly reported in all cities, with the highest levels in Prague and Bratislava. These findings may be related to the younger age of respondents but also to some contextual variables in Eastern European cities. According to the international literature, poppers seems to be the main substance used in the MSM population [4]. Our findings confirm the high levels of poppers consumption, especially in Ljubljana, Prague and Barcelona. As far as the use of other illicit drugs is concerned, cannabis is widely used, but there are large differences between cities. With regard to cocaine consumption, in Barcelona, 24.5% of respondents reported they had used it sometimes or often during the last six months, before or during sex. Even though an overestimation of substance use could not be excluded, it seems that drug use was frequent in our sample. Taking into account the fact that even an intermittent recreational use of drugs before or during sexual intercourse may lead to high-risk sexual behaviour, the data seem to be relevant and suggest a need for prevention programmes targeting MSM, with particular attention to alcohol, poppers and drug use.

Despite possible biases in this prevalence study in some countries, the data emerging from the survey show varying levels of HIV infection among the recruited MSM. The highest prevalence was in Barcelona and Verona, while the prevalence in Eastern European countries was lower. Previous studies carried out in some of the cities participating in this study, came to different prevalence estimates. In Barcelona HIV prevalence found in a last previous study carried out in MSM venues (using a convenience sample) was slightly higher than the prevalence found in this study [28]. The lower figures found in Ljubljana and Bratislava in previous studies, may be partly related to a different sampling method and lower number of samples collected [29,30].

The low prevalence found in the four Eastern European cities is encouraging. However, with the level of unprotected anal sex in some of these cities, even with casual partners, and a generally low frequency of HIV test- seeking behaviour, the potential for further HIV transmission in Eastern European cities is evident.

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Ivo Procházka, Czech AIDS Help Society (ČSAP), Czech Republic; Alex Horký, Czech Youth Queer Organization,Czech Republic; Zeno Menegazzi, Arcigay Italia; Alin Robert Zoltan, ACCEPT Romania, Romania; Jaro Gyurik, Združenie Prevencie AIDS (ZPA), Slovakia; Miran Šolinc, ŠKUC Magnus, Slovenia; Rafa Muñoz, Stop Sida,Spain.

Financial support:

The Capacity building in HIV/Syphilis prevalence estimation using non-invasive methods among MSM in Southern and Eastern Europe - SIALON project was funded by the European Commission under the European Commission Public Health Programme 2003-2008.

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HIV risk behaviour knowledge, substance use and unprotected sex in men who have sex with men in Tallinn, Estonia

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This article was published on 9 December 2009.
Citation style for this article: Tripathi A, Rüütel K, Parker RD. HIV risk behaviour knowledge, substance use and unprotected sex in men who have sex with men in Tallinn, Estonia. Euro Surveill. 2009;14(48):pii=19429. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19429

This study examines HIV risk behaviour knowledge, substance use and unprotected sex in a sample of 79 men who have sex with men (MSM) in Tallinn, Estonia. Median age of the study population was 30 years (range 18-62 years); 35 were bisexual; 56 answered correctly to at least 10 out of 13 questions about HIV risk behaviors; 23 consumed more than seven alcoholic drinks in the week before the survey; nearly half (n=34) of the participants reported some illicit drug use in the past 12 months; 40 did not use a condom regularly in the 12 months preceding the survey, and 41 did not use a condom during their last sexual intercourse. Alcohol consumption in the week before the survey was negatively associated with condom use during last intercourse (RR 0.48; 95% CI 0.41-0.56). Use of illicit drugs varied significantly by ethnicity (p-value = 0.02). Multivariable analysis showed that higher consumption of alcohol in the week before the survey could be predicted by education, age group and sexual orientation. In conclusion, socio-demographic factors such as education, age, ethnicity and sexual orientation may affect HIV risk behavior knowledge, sexual behavior and substance use among MSM in Estonia, and need to be taken into consideration for targeted HIV prevention.

Introduction

Since 2001, HIV prevalence has increased rapidly in Russia and Eastern Europe. Between 2001 and 2007, countries in Eastern Europe experienced a 150% increase in newly diagnosed HIV infections, a much larger increase than other European regions [1]. Of the former Soviet republics, Estonia has experienced the largest increase in the estimated HIV prevalence [2]. In 2008, Estonia had the highest number of newly diagnosed cases of HIV per million population (406/ million) among 28 out of 30 European Union (EU) and European Economic Area (EEA) countries [3]; and in 2007, the second highest estimated HIV prevalence, with over 1% of the adult population infected [4]. In Estonia, the HIV epidemic is mainly attributed to needle sharing among injecting drug users (IDU) and consequently, over the past decade, most research and HIV prevention has targeted IDU [5, 6].

In Eastern Europe the HIV epidemic is mainly concentrated among IDU and commercial sex workers and their respective sexual partners, whereas overall in EU/EEA, unprotected sex between men continues to remain the predominant mode of HIV transmission [3,7]. In recent years, newly diagnosed HIV cases among men who have sex with men (MSM) have increased in several Western European countries [3, 8, 9]. In Central Europe, the predominant mode of transmission is heterosexual contact, although reported HIV cases among MSM have increased rapidly over the past few years [10]. According to the European Center for Disease Prevention and Control (ECDC) and World Health Organization's (WHO) report on HIV/AIDS surveillance in Europe for 2007, more than half of the newly diagnosed cases of HIV infection were reported among MSM in Central European countries such as the Czech Republic, Slovenia, Slovakia, Croatia and Montenegro [2]. MSM are at risk of exposure to HIV for various reasons which may be facilitated by stigmatization [11,12]. In Eastern Europe, gay communities are newly established compared with their Western counterparts, which may be an impediment for peer-driven prevention strategies [13]. Limited research has been published on HIV risk behavior among MSM in Estonia [6]. To facilitate preventive policies towards maintaining lower HIV prevalence among MSM, there is a need to understand risk behavior in relation to socio-demographic and behavioural characteristics. Our study aims to explore the relationship of socio-demographic and behavioral characteristics with HIV risk behaviour knowledge, substance use and unprotected sex among MSM in Tallinn, Estonia.

Methods

Our study uses data collected from a larger project aimed to pilot HIV rapid testing in Tallinn, Estonia in 2008. The Tallinn Medical Research Ethics Committee approved this project. Data were collected by a self-administered 47-item study questionnaire, that was based on validated and widely used surveys of Family Health International (FHI), WHO and the United States Centers for Disease Control and Prevention (US CDC) for specific risk behaviour populations [6, 14-16]. The questionnaire was designed to collect data on three distinct domains: demographics, HIV risk behaviour knowledge and behavioral characteristics such as sexual orientation, substance use and condom use. Additionally, HIV rapid tests were conducted by study staff paid by the Estonian National Institute for Health Development. Anonymous results of the rapid HIV tests were linked to the questionnaire data using a unique identifier.

MSM were identified as men who self-identified their sexual orientation as either homosexual or bisexual. The study population of 79 MSM was recruited in Tallinn, Estonia, from AIDS counseling centers (n=13), a low threshold needle exchange center (n=5), a gay and lesbian information center (n=8), a gay sauna (n=22), and a gay bar (n=31). The use of a convenience sample was in consensus with other recently published studies [17,18]. HIV risk behaviour knowledge was assessed through 13 questions about

transmission, social perception and treatment (see Table 2). One point was awarded for each correct answer and the total knowledge score was calculated summing up the correct answers. Alcohol consumption was assessed by number of cans, bottles, glasses and shots of standard alcoholic drinks such as beer, cider, wine and strong alcoholic drinks, consumed by the participant in seven days prior to the survey. Participants also reported consumption of alcohol during four weeks preceding the survey, using the following categories: everyday, more than once per week, once per week or never. Characteristics of drug use were assessed by questions asking

Table 1

Characteristics of study participants, Tallinn, Estonia, 2008 (n = 79) [a, b]

	Data by age group			All
	18-25 years n (%)	26-35 years n (%)	> 35 years n (%)	
Ethnicity				
Estonian	16 (76)	18 (58)	19 (83)	53 (71)
Russian	5 (24)	9 (29)	2 (9)	16 (21)
Others	0	4 (13)	2 (9)	6 (8)
Level of education				
Less than secondary	4 (19)	2 (7)	3 (14)	9 (13)
Secondary	7 (33)	3 (10)	3 (14)	13 (18)
Vocational	3 (14)	7 (24)	3 (14)	13 (18)
Post-secondary	7 (33)	17 (59)	12 (57)	36 (51)
Income*				
≤ 7,500 EEK per year	13 (68)	6 (21)	4 (20)	23 (34)
> 7,501 EEK per year	6 (14)	23 (79)	16 (80)	45 (66)
Sexual orientation				
Homosexual	13 (62)	17 (55)	11 (48)	41 (55)
Bisexual	8 (38)	14 (45)	12 (52)	34 (45)
HIV knowledge score				
(13 points max.)	10.5 (±1.5)[c]	10.48 (±1.8)[c]	10.0 (±1.7)[c]	10.4 (±1.7)[c]
Standard alcohol drinks in last week				
	5.8 (±6.3)[c]	8.0 (±8.2)[c]	5.6 (±3.8)[c]	7.1 (±6.8)[c]
Alcoholic drinks in last month				
None	0	3 (10)	1 (4)	4 (6)
1 or less per week	11 (55)	13 (45)	11 (48)	35 (49)
> 1 per week	8 (40)	13 (45)	9 (39)	30 (42)
Everyday	1 (5)	0	2 (4)	3 (4)
Illicit drug use*				
No	9 (43)	15 (50)	18 (78)	42 (57)
Not regular	11 (52)	11 (37)	5 (22)	27 (37)
Frequent/regular	1 (5)	4 (13)	0	5 (7)
Condom used in last intercourse				
Yes	12 (57)	14 (48)	14 (64)	40 (56)
No	9 (43)	15 (52)	8 (36)	32 (44)
Condom use in last 12 months				
Regular	9 (47)	14 (45)	12 (63)	35 (51)
Sometimes	5 (26)	13 (42)	4 (21)	22 (32)
Never	5 (26)	4 (13)	3 (16)	12 (17)
Previous HIV test*				
No	13 (62)	5 (16)	6 (29)	24 (33)
Yes	8 (38)	26 (84)	15 (71)	49 (67)

EEK: Estonian Kroons; SD: standard deviation
[a] chi-squared test for categorical variables and Mann-Whitney test for continuous variable. Fisher's exact test was used if any individual cell in cross-tabulation had less than five observations
[b] numbers do not always add up to 79 due to missing values, only available data reported; percentages may not add up to 100% due to rounding
[c] mean (±SD)
* Indicate significant differences (p<0.05) among age groups

about the mode of drug use (pills, injecting, inhaling, smoking, mixed in food/drink), type of drugs used (amphetamine, heroin, cocaine, marijuana, ecstasy, China White and others), and frequency of drug use (every day, frequently, occasionally). Participants were asked about history of sexually transmitted infections (STI) in the past 12 months before the survey and whether they were previously tested for HIV and result from it. Demographic data were collected, such as age, sex, level of education, ethnicity and monthly income (Table 1).

Statistical Analyses

Descriptive and exploratory analyses were done by chi-squared test for categorical variables and Mann-Whitney test for continuous variables. Fisher's exact test was used if any individual cell in cross-tabulations had less than five observations. Preliminary data analysis detected one outlier: a respondent reporting consumption of 140 drinks in seven days prior to the survey, whereas rest of the data ranged between 0-33 drinks. This observation was removed in further analyses for alcohol consumption. Univariate analysis of alcohol consumption in seven days prior to the survey indicated significant association with various socio-demographic and behavioral characteristics. Therefore, we further explored these relationships with a multivariable Poisson regression model, where total number of drinks consumed in seven days prior to the survey (count data with satisfactory normal distribution) was the response variable and socio-demographic and behavioural characteristics such as sexual orientation were predictor variables. In order to control for potential bias due to site of recruitment, this variable was included in the Poisson regression equation. Goodness-of-fit indicated a significant model with a statistically good fit ($\chi 2$ = 240.7; $p < 0.001$). Statistical significance was set at $\alpha \leq 0.05$ and a two-sided p value or 95% confidence intervals (CI) are reported for the corresponding analysis. Stata 10.0 was used for statistical analyses (StataCorp LP. College Station, TX).

Results

Characteristics of participants

The mean age of the participants was 32 years (SD ±11), with most participants between 25 and 35 years of age (median age, 30, range 18-62). More than a quarter of the sample was of non-Estonian ethnicity: 16 (20%) were Russian and 7 (9%) were other (not defined). More than half of the participants (n=38) reported a higher than secondary level education and 48 (67%) reported a monthly income of more than 7,500 Estonian kroons (EEK). In Tallinn, according to the national statistics, 2008, the net average monthly wage was about 11,800 EEK (668 Euros) and median monthly income was about 7,500 EEK (480 Euros) [19]. Less than half of the men (n=35; 44%) reported bisexual orientation. There were no significant differences in sexual orientation by age group, ethnicity, level of education and monthly income. The mean age of anal or vaginal sexual debut in the sample was 17.6 (SD ±3.7) years. Mean age at sexual debut was statistically higher in homosexual men compared to bisexual men (18.4 vs. 16.3 years; p-value = 0.04). Table 1 presents participant characteristics by age group.

More than two-thirds of the participants (n= 52; 68%) were tested previously for HIV. Of these, eight men were aged 18-25 years, compared with 26 aged 26-35 years and 15 aged > 35 years (p-value < 0.01). Uptake of previous HIV testing did not show statistically significant differences by ethnicity, level of education, monthly income and sexual orientation. Of the 25 participants who were not tested previously, 12 reported not considering getting tested, seven reported not having had an opportunity, and seven stated that they had had no time for taking the test. Of the two men who tested HIV-positive from the rapid test, one was detected during the study rapid testing and the other was tested before our study. Six participants reported having had STI in the previous 12 months.

HIV risk behavior knowledge and socio-demographic characteristics

The median score for HIV related knowledge was 11 points. Only six men answered all 13 questions correctly. The total number of correct answers did not differ significantly by socio-demographic characteristics. The participant responses to HIV risk behavior questions are presented in Table 2. Least correctly answered statements were: "Does washing the genitals after sex protect from

Table 2

Assessment of HIV risk behavior knowledge, Tallinn, Estonia, 2008 (n=79)[a]

	Questions	Correct n (%)	Wrong n (%)	Not sure n (%)
1	Can using a condom correctly prevent HIV?	68 (88)	5 (7)	4 (5)
2	Can a person get HIV from mosquitoes?	64 (81)	7 (9)	8 (10)
3	Can a person get HIV from sharing a meal with someone with HIV?	75 (95)	2 (3)	2 (3)
4	Can a person get HIV from sharing a needle or works from someone with HIV?	78 (99)	1 (1)	0
5	Can you tell if a person has HIV by looking at them?	64 (81)	3 (4)	12 (16)
6	Do birth control pills protect from HIV?	68 (88)	1 (1)	8 (10)
7	Getting a tattoo/piercing by a non-licensed person increases the risk of contracting HIV.	67 (85)	11 (14)	1 (1)
8	Can a pregnant woman with HIV transmit HIV to her child?	64 (81)	4 (5)	11 (14)
9	Can breastfeeding children get HIV from an HIV infected mother?	38 (51)	11 (15)	26 (35)
10	Does washing the genitals after sex protect from HIV?	51 (66)	10 (13)	16 (21)
11	Does pulling out interrupted intercourse before orgasm protect against HIV?	55 (71)	11 (14)	11 (14)
12	If you are HIV positive, can you get treatment?	49 (65)	7(9)	20 (26)
13	Do HIV medications improve the quality of life for people with HIV?	53 (68)	10 (13)	15 (19)

a numbers do not always add up to 79 due to missing values, only available data are reported

HIV?"; "Does pulling out interrupted intercourse before orgasm protect against HIV?"; "Can breastfeeding children get HIV from an HIV infected mother?"; "If you are HIV positive, can you get treatment?" and "Do HIV medications improve the quality of life for people with HIV?".

We further assessed the association of socio-demographic and behavioral characteristics with the range of knowledge about HIV risk behavior by the Fisher's exact test. With regards to ethnicity, the misconception that pulling out before orgasm protects against HIV was statistically significant higher among ethnic Russians than ethnic Estonians or other ethnicities (p-value = 0.03). Statistically significant differences were observed in the HIV/AIDS knowledge by level of education. Less than secondary school education was associated with higher proportion of wrong or 'not sure' answers. For example, two out of 10 men with less than secondary education reported 'not sure' about HIV transmission through sharing meals compared to none among those with higher than secondary education (p-value <0.01). No significant differences were observed in HIV knowledge with regards to income, age categories, sexual orientation and site of recruitment.

Substance use

Nearly all participants (n=72) reported having consumed alcohol in the four weeks prior to the survey, 32 had consumed more than one drink per week and five reported having consumed daily. Reported patterns of monthly consumption did not differ statistically significant by characteristics of participants. We also assessed the number of standard alcoholic drinks consumed in the week before the survey. Mean consumption was 7.1 drinks (SD ±6.8; median = 5). Poisson regression analyses explored the association of the number of drinks consumed with socio-demographic and behavioral characteristics. After adjusting for other variables in the multivariable model, results showed a significant independent association of the rate of mean number of drinks consumed in seven days before the survey with education, age group, illicit drug use and sexual orientation. The rate of consumption was significantly lower in those with a higher education - vocational education (RR 0.26; 95% CI 0.16-0.42) or post-secondary education (RR 0.48; 95% CI 0.33-0.69) compared to less than secondary education. Whereas, the rate was significantly higher in 26-35 years old men (RR 1.92; 95% CI 1.35-2.73) as compared to youngest age group (18-25 years); in those who reported 'not frequent' use of drugs (RR 1.73; 95% CI 1.38-2.16) and 'regular use' of drugs (RR 2.02; 95% CI 1.12-3.62) as compared to those who reported 'no use ever'; and in those who reported homosexual orientation (RR 1.61; 95% CI 1.27-2.06) as compared to bisexual orientation.

Thirty-four of the 79 men (46%) in our study reported some illicit drug use, the majority (n=29) 'not frequent' users. More than half (12 out of 21) in the 18-25 years age group reported drug use compared to five out 23 participants older than 35 years (p-value = 0.05). Fisher's exact test showed significant differences (p-value = 0.02) in drug use by ethnicity: 11 of the 16 Russian ethnic participants used illicit drugs compared with 20 out of 54 Estonians. No significant differences were observed with regards to level of education, monthly income and sexual orientation. Among the 34 participants who used illicit drugs, most commonly used drugs (some participants used more than one drugs), were amphetamines (11 cases), marijuana (11 cases), cocaine (6 cases), China White or White Persian (3 cases), ecstasy (8 cases), and eight cases for other or unknown drugs. Injecting drug use was reported by five men in our sample.

Unprotected sex

About half (n=37) of the men did not use condoms regularly over last 12 months, of which 13 men reported never using condoms. A higher proportion of men with less than secondary education reported never using condoms (4 out of 7) compared to those with higher than secondary levels of education (3 out of 38). Differences however, fell little short of statistical significance (p-value = 0.08). No significant differences were observed by ethnicity, monthly income, age group category, sexual orientation and substance use.

A condom was not used during last sexual intercourse by 35 of the 79 men (46%) in our study group. We assessed the association between condom use during last intercourse and number of alcoholic drinks in the week before the survey. Higher alcohol consumption was negatively associated with use of condom during the last intercourse (RR 0.48; 95% CI 0.41-0.56). No other significant differences were observed with regards to socio-demographic characteristics, sexual orientation and illicit drug use.

Discussion and conclusion

Our results show that about half of the 79 men participating in our study answered correctly for more than 10 out of 13 questions/statements about HIV transmission and risk behavior. Similar findings were reported in an internet based survey conducted in spring 2004 and autumn 2005, by the Estonian Gay League and the National Institute of Health and Development (NIHD) [16, 20]. However, we found significant differences in the range of HIV risk behavior knowledge. Whereas, the majority of the men knew about prevention of HIV by correct use of condom or that HIV could be transmitted through sharing needles, a lower proportion of men could answer correctly about the fact that pulling out before orgasm or washing genitals after sex does not prevent HIV, that HIV could be transmitted to babies through breast-feeding, and that HIV treatment is available to all in Estonia, and it may improve quality of life. Our results indicated that HIV risk behavior knowledge may vary by socio-demographic factors such as education and ethnicity. Other studies in the geographical region have shown similar differences in HIV knowledge [21]. In a study by Kelly *et al.*, on MSM in St. Petersburg, Russia, only 4% bisexual male participants were able to answer correctly to all the questions on HIV risk behavior knowledge; and 54% of the participants believed that washing carefully after sex protects against HIV [22].

We found that lower education, belonging to age group 25-35 years, using illicit drugs and homosexual orientation were significantly associated with higher rate of consumption of alcohol over past seven days. About half of the men used illicit drugs, although most where non-frequent users. Moreover, illicit drug use was found to be higher among Russian men and the youngest age group (18-25 years). Higher level alcohol consumption among MSM has been indicated in other regional studies [17, 23]. In a study based in Zagreb, Croatia, Stulhofer *et al.* reported that more than third of the MSM participants used illicit drugs before having sex in the 12 months before the survey and more than half consumed alcohol before sex over the same period. Higher alcohol and substance use has been shown to increase overall risk of HIV transmission [24, 25]; therefore it is important to consider the socio-demographic differences in substance use among MSM in Estonia for directing HIV public health interventions.

In our study, about half of the men did not use condoms regularly in the 12 months before the survey and a similar proportion reported not using condoms during the last sexual intercourse.

Lower education and high rates of alcohol consumption were found to be negatively associated with condom use. However, since we did not know whether the last intercourse was with a regular or a casual partner and the number of concurrent partners, interpretation of these results warrant caution. Nevertheless, other regional studies have indicated that having casual partners is very common in MSM social networks [17, 21]. Overall, studies investigating the correlation of unprotected sex between men with socio-demographic and behavioral characteristics have given mixed results. In a recent study by Amirkhanian *et al.*, results showed that more than half (56%) of MSM participants, from Hungary and Russia, had the most recent unprotected anal sex with a casual partner and that condom use significantly depended on psychosocial factors [26]. A large study based in Denmark, by Cowan and Haff, concluded that in recent years there has been an increase in the frequency of unprotected sex in MSM despite high level knowledge about HIV [27]. Stulhofer *et al*. however, found no relation between alcohol and drug use before sex and condom use over the last 12 months or during last anal sex [18]. Further investigation is warranted to understand the reasons for these mixed findings.

Our research has several limitations. We used a convenience sample, which limits the ability to represent the population, and could potentially bias some behavioral characteristics, such as alcohol use in men recruited from gay bars. Information about sexual partners of the participants, regular or casual, as well as the number of concurrent sexual partners, was not available, and therefore the results could not be adjusted for number of (casual) sex partners. The sample size was small and moreover, data presented in these analyses are self-reported, which resulted in missing data on some questions.

Despite these limitations we conclude that, socio-demographic and behavioral characteristics affect knowledge of HIV transmission, sexual risk behavior and substance use among MSM in Estonia and need to be taken into account for targeted intervention towards HIV prevention. Further research is needed to understand the complex association of HIV risk taking behavior and substance use among MSM.

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The effectiveness of behavioural and psychosocial HIV/STI prevention interventions for MSM in Europe: A systematic review

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This article was published on 9 December 2009.
Citation style for this article: Berg R. The effectiveness of behavioural and psychosocial HIV/STI prevention interventions for MSM in Europe: A systematic review. Euro Surveill. 2009;14(48):pii=19430. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19430

Given the need of programme planners and policy makers for descriptions of specific interventions and quantitative estimates of intervention effects to make informed decisions concerning prevention funding and research, there is a need for a systematic review that updates the current knowledge base about HIV/STI preventive interventions targeted at men who have sex with men (MSM) in Europe. The aim was to summarise and assess the effectiveness of HIV/STI prevention interventions for MSM living in Europe, and to identify intervention characteristics associated with effectiveness as well as potential gaps in the evidence base. A systematic search for relevant literature in eight international databases and in reference lists of relevant reviews and included studies was performed. Studies were selected according to pre-specified criteria and appraised for risk of bias. We summarised results using tables and calculated effect estimates for sexual behaviour outcomes. Results from six controlled studies, involving a total of 4,111 participants at entry from four different European countries were summarised. The results showed that there was 'high' or 'unclear' risk of bias in one or more of the assessed domains in all studies. The pooled effect estimate of the four interventions for which data were available suggested that MSM who participate in HIV/STI prevention initiatives may be somewhat less likely to report unprotected anal intercourse (UAI). The evidence base was insufficient to examine characteristics of interventions most closely associated with magnitude of effect and to draw solid conclusions about unique gaps in the evaluation literature. Despite the maturity of the HIV epidemic, rigorous outcome evaluations of any form of behavioural HIV/STI intervention for MSM in Europe are scarce. The results point to possible short term effects of interventions in terms of reductions in the proportion of MSM who engage in UAI, but the paucity of controlled studies demonstrates the need for research in this area. There is an overall deficit in outcome evaluations of interventions aimed at reducing HIV/STI risk behaviour among MSM in Europe. Designing behavioural HIV/STI preventive strategies to avert new infections, and the evaluation of such prevention programmes for MSM is an important component of a comprehensive HIV/STI containment strategy across the continuum of prevention and care.

Introduction

Across Europe, the HIV/AIDS epidemic has caused tremendous human suffering and financial loss as the number of new diagnoses of HIV infections has continued to increase: from 2000 to 2007, the annual rate of reported HIV infection increased from 39 to 75 per million [1]. In Europe, men who have sex with men (MSM) continue to be the population most affected by HIV, and the rate of infections is increasing faster among MSM than among other populations [2,3]. In high-income European countries, MSM remain the group at highest risk for HIV [1], and unprotected sex remains the most frequent mode of transmission. There has been an increase in the rate of MSM who report unprotected anal intercourse (UAI). For example, in London, between 1998 and 2002 there was a doubling in the percentage of MSM reporting UAI with a casual partner of unknown or discordant HIV status, increasing from 7% to 16% [4]. Recent outbreaks of syphilis and gonorrhoea in several major European cities suggest a trend for increased sexual risk taking among MSM [5,6,7].

In the absence of an effective and affordable vaccine and non-curative abilities of current antiretroviral therapies, behavioural and psychosocial prevention with the goal of limiting sexual risk behaviours remains central to the efforts to decrease sexual HIV/STI transmissions among MSM [8]. Further, while antiretroviral therapy treatments have tremendous life-saving potential, they are expensive and carry debilitating side-effects for some people [9]. Behavioural and psychosocial HIV/STI risk reduction interventions to reduce unprotected sex among MSM range from individual-level interventions and group level-programmes, to community-level interventions [10,11]. Such interventions will continue to be vital in the battle against HIV/STI, and therefore it is important to find out whether they help, harm or are ineffective.

The effectiveness of HIV/STI preventive interventions targeted at MSM has been assessed in various publications. Most recently, in 2008 Johnson *et al*. systematic Cochrane review evaluated the effects of behavioural interventions to reduce risk for sexual transmission of HIV among MSM [12]. The review included 58 randomised controlled trials (RCT), of which almost three quarters were from the United States (US). The review concluded that behavioural interventions reduced UAI by 27% compared to minimal or no HIV preventive intervention. A few other reviews have been published about the effectiveness of HIV prevention interventions, but most of these are not specific to MSM. When the target population has comprised MSM, MSM in Europe have not been the focus. Further, the majority of reviews have neither utilised a comprehensive search strategy nor clear inclusion criteria, and many of the reviews are out of date, having been published before or shortly after the year 2000. Therefore, there is a need for a systematic review that incorporates explicit inclusion criteria and that updates the current knowledge base about HIV/STI preventive

interventions targeted at MSM in Europe. The objectives of the systematic review were to

1. Identify and describe outcome studies evaluating the effectiveness of HIV/STI prevention interventions on UAI for MSM living in Europe.
2. Summarise the effectiveness of HIV/STI prevention interventions for MSM in reducing unprotected anal sex, and, if available and possible, HIV/STI infections.
3. Identify intervention characteristics associated with effectiveness.
4. Identify gaps in a) subpopulations targeted, b) intervention characteristics incorporated, c) outcomes evaluated, d) methodological matters.

Methods

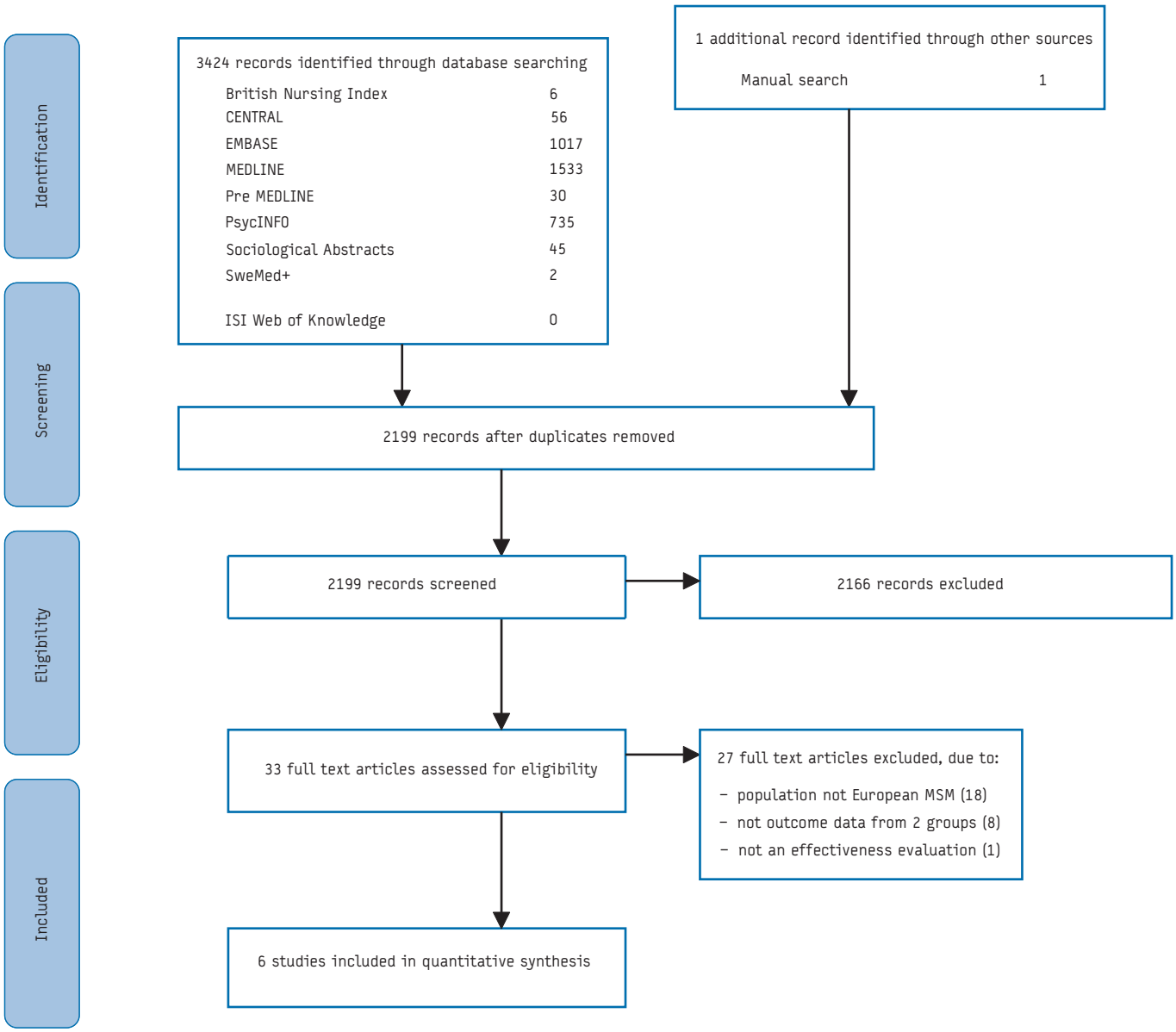
The completion of the systematic literature review was in accordance with the Cochrane Collaboration standards [13].

Search methods for identification of studies

The primary method of study identification was electronic searches. Under the guidance of the author, a research librarian designed and executed the electronic database search. References

Figure 1

PRISMA flow diagram of the literature reviewing process. Literature review on the effectiveness of behavioural and psychosocial HIV/STI prevention interventions for men who have sex with men in Europe. Berg R, 2009



Source: Effectiveness of behavioural and psychosocial HIV/STI prevention interventions for MSM in Europe, 2009. European Centre for Disease Prevention and Control.

in obtained reviews and included primary studies were scanned to identify new leads and included studies were looked up in ISI Web of Knowledge in order to identify further studies.

We applied the population, intervention, comparison, outcome (PICO) model described by Sackett *et al*. with respect to criteria for considering studies [14]. Concerning population, the intervention had to be received by MSM, who resided in the European region. We introduced the regional specification to ensure the included studies were clearly relevant for European-based research and intervention activities. We enforced no other limitations on participant characteristics. All forms of behavioural and psychosocial interventions designed to promote safer sexual risk behaviours among MSM were eligible for inclusion. There were no restrictions in level or mode of delivery. Regarding types of comparisons, we accepted no intervention, minimal intervention, placebo psychotherapy, standard treatment, or other active HIV/STI preventive intervention condition. We viewed studies in scope if they included measurement of sexual behavioural or biological outcome indicative of HIV/STI transmission risk.

With respect to study design, eligible studies were RCT, controlled clinical trials (CCT), and controlled before-and-after (CBA) studies. Lastly, only publications written in English, German, or one of the Scandinavian (Danish, Norwegian, Swedish) languages were included. To ensure that all research included was relatively new, we included only publications that were published in or after the year 2000.

The screening of literature was carried out in a three-stage procedure (screening of title, abstract, full text) whereby each level consisted of increasing scrutiny of the studies based on the inclusion and exclusion criteria of the review, as described above.

Table 1

Description of included studies (n=6). Literature review on the effectiveness of behavioural and psychosocial HIV/STI prevention interventions for men who have sex with men in Europe. Berg R, 2009

Author, year (data collected) (follow up)	Population characteristics				Intervention	Comparison	Outcome
	n	Residency	Age	HIV status			
RCTs							
Amirkhanian, 2005 (2003–2004) (3 months, 12 months follow-up)	276	Russia (St. Petersburg), Bulgaria (Sofia)	Mean 22.5	Not reported	Standard individual HIV risk-reduction educational counselling (20 min) + HIV prevention advice, by trained network leaders. Participants reported mean of 6.1 conversations about AIDS and 8 about safer sex	Wait list control usual care	UAI; UAI with multiple partners
Harding, 2004 (~2000) (2 months, 5 months follow-up)	50	England	Mean 41.5	22% HIV+, 57% HIV-, 20% untested	Course about SM sex. Four group sessions of 7h (total 28h), by volunteers at community-based, volunteer-led organisation	Wait list control	UAI
Imrie, 2001 (1995–1997) (6 months, 12 months follow-up)	343	England (London)	Median 29	Not reported	Standard 20 min sexual risk behaviour counselling + one day cognitive behavioural (group) workshop, by trained counsellors from STI clinic	Standard treatment (20 min counselling)	UAI; new STI
van Kesteren, 2007 (2004–2005) (3 months follow-up)	162	Netherlands	Mean 43.2	100% HIV+	Self-help booklet + motivational interview (face-to-face) + motivational interview (telephone), by HIV specialist nurses	Wait list control usual care	UAI with casual partner; UAI with steady partner
CBAs							
Elford, 2001 (1997–1999) (6 months, 12 months, 18 months follow-up)	1 004	England (London)	Mean 33.0	~15.5% HIV+	Gym-based HIV risk reduction education, by trained popular opinion leaders. 46 peers engaged on average 10 conversations each	No intervention	Status unknown UAI
Flowers, 2002 (1996–1999) (7 months follow-up)	2 276	Scotland (Glasgow, Edinburgh)	Mean 31.7	Not reported	Gay specific GUM services + sexual health info hotline + bar-based sexual health promotion, by trained peers. 42 peer educators interacted with 1 484 men, ~10 min each	No intervention	UAI with casual partner

RCT: Randomised Controlled Trials; CBA: Controlled before-and-after; UAI: Unprotected Anal Intercourse

Source: Effectiveness of behavioural and psychosocial HIV/STI prevention interventions for MSM in Europe, 2009. European Centre for Disease Prevention and Control.

Data extraction and analysis

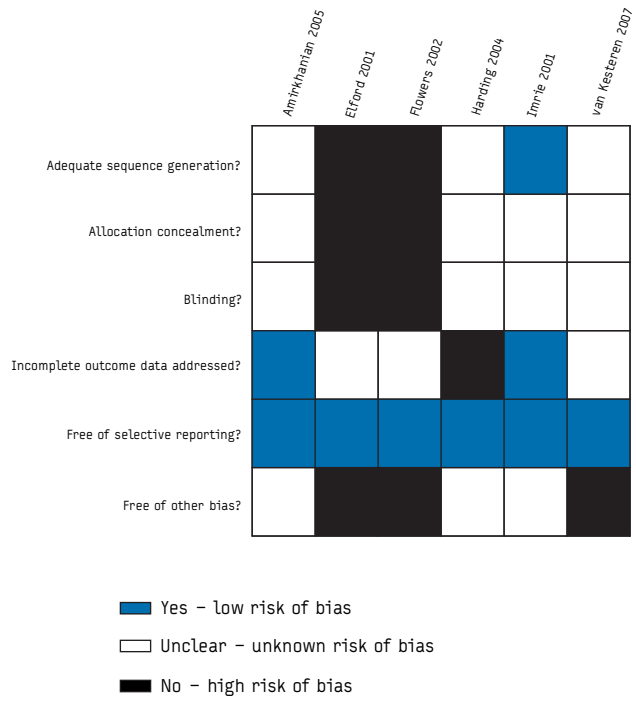
Data from each included study were extracted using a pre-designed data extraction form. All data were entered twice and the accuracy of all data extracted by the main reviewer was checked, including data in tables, before analyses were initiated. With respect to quality of the evidence, we used the Cochrane Collaboration's tool for assessing risk of bias [13]. Two reviewers discussed and agreed about the adequacy of risk of bias for six domains by assigning a judgement of 'yes' indicating low risk of bias, 'no' indicating high risk of bias, and 'unclear' indicating unclear or unknown risk of bias. Criteria set by the Cochrane handbook and adapted to the health promotion field were used to make these judgements. We estimated effects of interventions in two ways for binary outcome measures. One, by the adjusted absolute risk difference (ARD) in which the pre-post change score (in percentage points) in the control group was subtracted from the pre-post change score in the intervention group, and two, by the risk ratio (RR) and 95% confidence interval (CI) (95%CI) based on the post intervention data. We also decided, *a priori*, to perform meta-analyses to estimate intervention effect. We used Mantel-Haenszel random effects meta-analyses because it was assumed that the intervention effects would vary across studies. All analyses were conducted using RevMan5 [15]. Where there were several follow up times, we analysed them separately.

Results

The literature search resulted in 2,199 potentially relevant records (Figure 1).

FIGURE 2

Result of risk of bias assessment. Literature review on the effectiveness of behavioural and psychosocial HIV/STI prevention interventions for men who have sex with men in Europe. Berg R, 2009



Source: Effectiveness of behavioural and psychosocial HIV/STI prevention interventions for MSM in Europe, 2009. European Centre for Disease Prevention and Control.

We excluded 2,166 records at title or abstract level which were clearly outside the scope of this systematic review (e.g. descriptive studies), leaving 33 potentially relevant records which were read in full text. We included six studies presented in seven publications for our evaluation [16-22]. One study is unpublished but results were made available [23].

Description of studies

Four of the included studies employed a randomised controlled design, including two cluster RCT, and the remaining two included studies were CBA studies [16,21-23]; [16,23]; [17,19] (Table 1).

The included studies involved a total of 4,111 participants at entry (range 50-2,276) from four different European countries: Russia and Bulgaria, the Netherlands, and the United Kingdom [16];[23];[17,19,21,22].

The studies targeted gay and bisexual men of various ages (one study also included 55 women) [16]. One study specifically targeted young MSM, another aimed to promote sexual health in HIV-positive MSM [16];[23]. In the four studies that reported information about ethnic background, the populations were predominantly white (about 90%) [17,21,22,23].

The self-help and motivational enhancement intervention of van Kesteren *et al*. was individual-based and consisted of a self-help guide, a face-to-face motivational interview, and a motivational interviewing telephone call [23]. Two interventions consisted of group sessions; one covered various aspects about sadomasochistic sex [21], while the other was a cognitive behavioural workshop [22]. The remaining three studies were community-based and modelled after the popular opinion leader interventions developed by Kelly *et al*. and Kegeles *et al*. [24,25];[26,27]. In sum, not two interventions were identical, but the three peer-led, social behavioural interventions were similarly modelled and all but one of the interventions were theory-based [16,17,19];[21]. With respect to intensity and duration (dose) of the interventions, this was not clearly ascertained from the texts, but the programmes appeared to have 'intervened' from one peer conversation of about ten minutes duration to about 28 hours of education. Primary mode of delivery was in person, generally one-on-one.

Only one category of comparison was used in the six included studies: Minimal to no intervention. Imrie *et al*. used standard treatment at an STI clinic as comparison [22]. Three studies placed the comparison group on a waiting list to receive the intervention after the study [16,21,23].

With respect to outcome measures, all the included studies had collected self-report data about UAI with men. One study included a biological measure of new sexually transmitted infection [22]. Follow up ranged from two months post intervention to 18 months [21];[17]. Several studies incorporated multiple follow ups [16,17,21,22].

Risk of bias in included studies

The risk of bias assessment comprised six domains and we judged that there was 'high' or 'unclear' risk of bias in one or more of the assessed domains in all studies (Figure 2).

Briefly, with respect to sequence generation, there was insufficient information in all studies, except one, to judge whether it was adequate [22]. The situation was similar for allocation concealment and blinding. The issue of incomplete outcome data

was adequately addressed in two studies [16,22] and unclear or insufficiently addressed in the remaining four studies. All studies were judged to be free of selective reporting. Lastly, we judged other risk of bias, including intervention exposure, which varied greatly among the studies. It was lowest in the gym-based study – 3% of the participants reported having spoken to a peer educator during the intervention [17].

Effects of HIV/STI prevention interventions for MSM

A priori we decided to focus our effectiveness analyses on UAI because it is the most epidemiologically pertinent behaviour for MSM in an HIV risk context, and likely to be included in most studies [28]. UAI was reported as a dichotomous outcome, thus, we calculated ARD and RR with 95% CI based on the post intervention data. Two texts did not provide data in sufficient detail for us to include them in analyses (requested data from the authors were not received in time for inclusion in the analysis) and we reproduced the results of their significance tests [21,23]. With respect to sexual risks, we could calculate effect estimates for six outcomes (multiple assessment points) across four studies (Table 2).

At study level, four of the six included studies reported null effect. While all ARD results indicated that the interventions had positive effect, inspection of the effect estimates show that three quarters of the outcomes failed to reach significance.

We used Mantel-Haenszel random effects meta-analyses to estimate the intervention effect of the four interventions for which we obtained data. Collectively, the four interventions that were measured against minimal to no HIV prevention intervention appeared to reduce the probability of gay-or bisexual identified men engaging in UAI (Figure 3).

The pooled effect estimate of the four interventions suggested that MSM who participated in HIV/STI prevention initiatives were 10% less likely to report UAI (RR 0.90, 95%CI 0.83-0.96). The total MSM sample in these four interventions was 3,777. One study included 2,380 MSM, and consequently, the study contributed disproportional weight (84.9%) to the pooled effect estimate [19]. In subgroup analyses the pooled effect estimate showed that the result of the two interventions with design of highest internal

Table 2

Sexual risk behaviour outcomes at baseline and follow up, and effect estimates for included studies.). Literature review on the effectiveness of behavioural and psychosocial HIV/STI prevention interventions for men who have sex with men in Europe. Berg R, 2009

Author, year	Outcomes (follow-up)	Intervention		Control		Adjusted ARD	RR	95% CI for RR
		Pre (%)	Post (%)	Pre (%)	Post (%)			
RCTs								
Amirkhanian, 2005[a]	UAI (3 months)	57.3	35.5	54.5	57.7	25.0	0.62	0.47–0.81
	UAI with multiple partners (3 months)	22.6	9.7	17.4	16.2	11.7	0.60	0.31–1.17
	UAI (12 months)	57.3	39.5	54.5	50	13.3	0.79	0.59–1.05
	UAI with multiple partners (12 months)	22.6	7.6	17.4	16.1	13.7	0.47	0.22–0.99
Harding, 2004	UAI	Not stated		Not stated		_	No significant differences[b]	
Imrie, 2001	UAI (6 months)	37	24	30	32	15	0.74	0.50–1.10
	UAI (12 months)	37	27	30	32	12	0.86	0.58–1.29
	New STI (12 months)		31		21		1.66	1.00–2.74[c]
van Kesteren, 2007	UAI with casual partner	Not stated		Not stated		_	No significant differences[b]	
CBA studies								
Elford, 2001	Status unknown UAI (6 months)	13	11	15	14	1	0.79	0.57–1.10
	Status unknown UAI (12 months)	13	14	17	16	-2	0.88	0.63–1.23
	Status unknown UAI (18 months)	14	12	15	15	2	0.81	0.49–1.33
Flowers, 2002	UAI with casual partner (7 months)	38.9	35.4	36.3	37.4	4.6	0.95	0.78–1.11

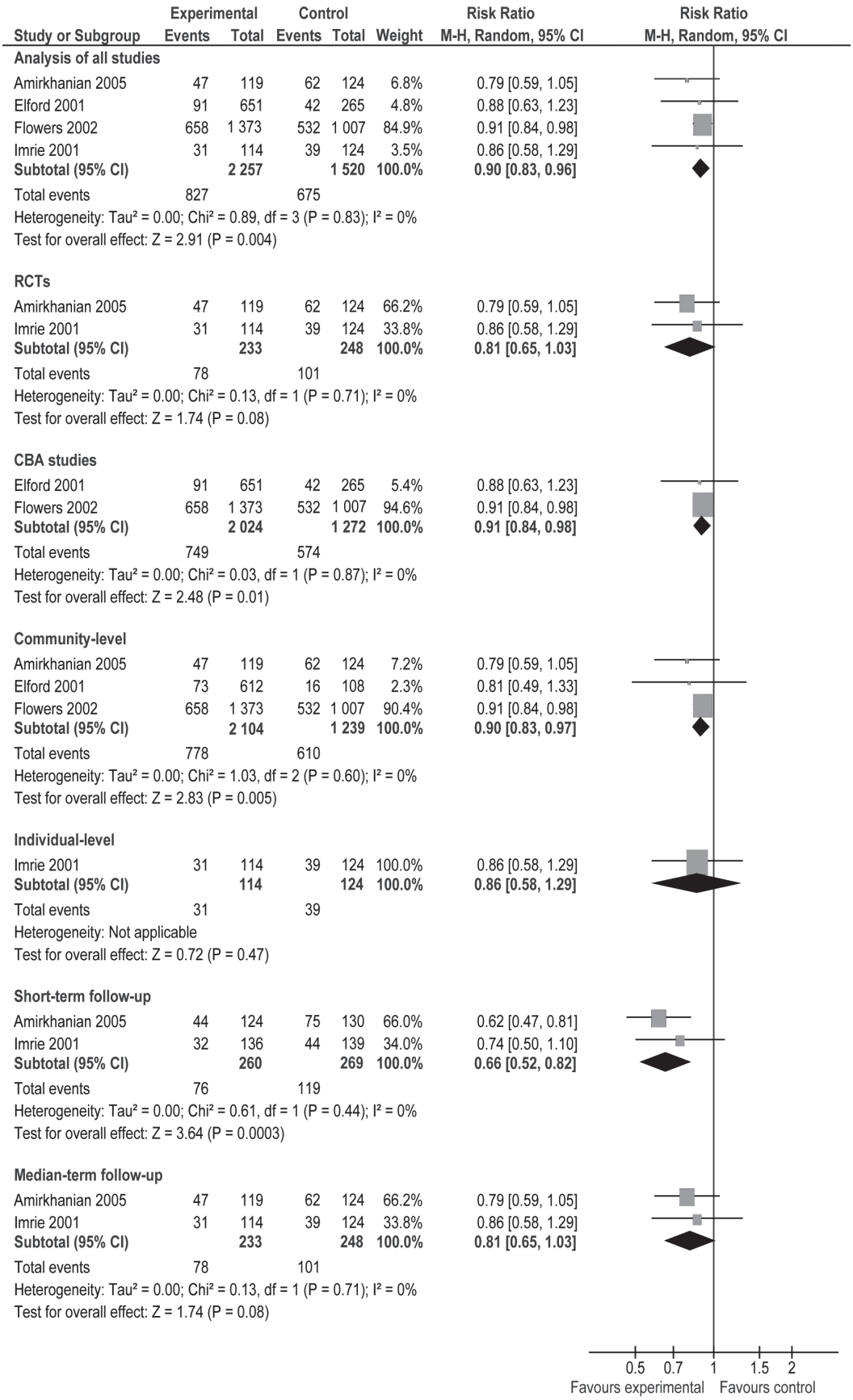
RCT: Randomised Controlled Trials; CBA: Controlled before-and-after

Note: Pre- and post scores are reproduced from the study publication. We calculated change scores in percentage points, adjusted absolute risk difference (ARD) and relative risk (RR) with 95% confidence interval (CI).
Legend:
[a] n for various groups and outcomes were not given in Amirkhanian (2005) table1, therefore n is assumed as stated in text: at baseline, n=133 for intervention group and n=143 for comparison group; at three-month follow-up, n=124 for intervention group and n=130 for comparison group; at 12-month follow-up, n=119 in intervention group and n=124 for comparison group;
[b] stated in study publication;
[c] adjusted odds ratio reproduced from publication.

Source: Effectiveness of behavioural and psychosocial HIV/STI prevention interventions for MSM in Europe, 2009. European Centre for Disease Prevention and Control.

FIGURE 3

Forest plot of effect sizes, main effect and subgroup analyses for unprotected anal intercourse (UAI). Literature review on the effectiveness of behavioural and psychosocial HIV/STI prevention interventions for men who have sex with men in Europe. Berg R, 2009



Source: Effectiveness of behavioural and psychosocial HIV/STI prevention interventions for MSM in Europe, 2009. European Centre for Disease Prevention and Control.

validity (RCT) became non-significant (RR 0.81, 95%CI 0.65-1.03), while the result of the CBA studies was significant (RR 0.91, 95%CI 0.84-0.98), with one study contributing disproportional weight (94.6%) to the pooled effect estimate. Similarly, the pooled effect estimate of the three community-level interventions reached significance (RR 0.90, 95%CI 0.83-0.97), with one study contributing disproportionate weight (90.4%).

In subgroup analyses, the pooled effect estimate for the short-term effects (three-six months) of the two RCT with least risk of bias suggested that MSM participating in HIV/STI interventions were 34% less likely to report engaging in UAI (RR 0.66, 95%CI 0.52-0.82). The effect was not significant at medium-term follow up (12 months) (RR 0.81, 95%CI 0.65-1.03).

The evidence base was insufficient to examine characteristics of interventions most closely associated with magnitude of effect and to draw solid conclusions about unique gaps in the evaluation literature on HIV/STI interventions for MSM in Europe.

Discussion

This is the first systematic review to summarise and assess the effectiveness of HIV/STI prevention interventions for MSM living in Europe. The main finding of the review is the dearth of HIV/STI prevention interventions for European MSM which have been evaluated in such a way as to enable reliable conclusions about effectiveness. Among the six studies identified and included the proportion of information from studies at high risk of bias was sufficient to affect the interpretation of results.

Effectiveness of HIV/STI prevention interventions for MSM

The meta-analysis results of four studies showed that one pooled effect size is most valid. The subgroup analysis for the short-term effects of the interventions by Amirkhanian *et al*. and Imrie *et al*. suggested that MSM participating in HIV/STI interventions were significantly less likely to report engaging in UAI than MSM in the control groups at short-term follow up [16]; [22]. An effect size associated with significant reduction in UAI was not found at 12 months follow up. The findings mirror other high-quality reviews showing that effects of non-US interventions are limited and become attenuated over time [18,12,29]. In stratified analyses of rate ratios for small group and individual-level interventions, a recent Cochrane review found that while studies performed in the US yielded a net reduction of 22% in unprotected sex, studies performed elsewhere in the world showed a much smaller net reduction that was not statistically significant [12]. Nonetheless, the findings in the current systematic review give cause for guarded optimism. The controlled studies included in this systematic review demonstrate that it is possible to successfully conduct rigorous HIV/STI prevention trials for MSM in Europe, and there may be some effect of interventions aimed at reducing HIV/STI risk behaviour among this population.

Gaps

It is not presently possible to know which unique gaps in the evaluation literature on HIV/STI interventions for MSM in Europe exist. However, it should be noted that all but one of the six included studies are from Western Europe; four of them were set in the United Kingdom. Further, the samples included mainly white MSM. Non-white MSM appear to be underserved. Only one study included a biological outcome measure.

Implications for future behavioural HIV/STI interventions for MSM

Almost thirty years into the HIV epidemic, it is disheartening to find so few behavioural HIV/STI prevention interventions that have been rigorously evaluated for MSM in Europe. The paucity of controlled studies demonstrates the need for research in this area: more and better outcome evaluations of HIV/STI prevention interventions for MSM living in Europe are warranted. While there is no other reliable substitute for evaluating the effect of interventions than controlled trials, other designs such as interrupted time series designs can also be used [30,13,31]. Researchers who are concerned about the ethics of allocation to experimental groups can use waiting list controls whereby the control group receives the potential beneficial intervention post data collection. The drawback is the difficulty of establishing long-term effectiveness of the intervention [32]. It also remains important to integrate process assessment into the evaluation design in order to learn about feasibility, acceptability, practical constraints, and related issues. Implementation and adherence are typically difficult to measure in multi-component intervention programmes, but provide critical information [33]. For example, Elford *et al*. process evaluation helped explain the likely reasons for lack of programme effectiveness [34]. Researchers and journal editors should strive to disseminate also null findings and related issues in intervention research [35].

As far as possible, prevention professionals should incorporate clinical HIV/STI outcomes, and not just rely on self-reported changes in cognitions and behaviours. Cognitive processes are not necessarily pre-requisites for behaviours and as self-reported behavioural outcomes, tend to overestimate intervention benefits [31,36]. Further, because risk assessment for HIV transmission by self-report covers a wide range of behaviours it would be important to specify UAI according to partner type and partners' serostatus, as done by two of the included studies [17,19]. One alternative suggested by Newman *et al*. is to use new technology, such as computer assisted self-assessment, to improve the truthfulness of self-reported sexual behaviours [37]. Biological outcomes reliably assess potential harms as well as benefits. Of the six included studies in this systematic review, only one included clinical outcomes and it found that incidence of STI significantly increased in the intervention group compared to the control group. Imrie *et al*. state that screening of asymptomatic infection was not part of the original study protocol because they believed it would affect recruitment, but the return of specimens by post worked well [22]. Lastly, multiple follow up assessments allow for an evaluation of the longevity of effectiveness and should be attempted. Several of the included studies in this systematic review did, but the longest follow up was 18 months. Ideally, since incidence of HIV/STI infections is the most important and reliable outcome and changes cannot be reliably measured in a short time period, long-term follow up of several years is desirable.

Strengths and limitations of this review

This systematic literature review was conducted according to the Cochrane Collaboration standards [13]. A further strength is that controlled studies were evaluated, i.e. studies that can reliably say something about effects of interventions. Additionally, meta-analyses were conducted to synthesise independent and diverse studies to derive an overall estimate of effectiveness of interventions, allowing also for an exploration of differences across studies. However, findings must be viewed within the context of the limitations of the systematic review. The reviewer was not at any screening level blinded to the authors or other information about the publication when assessing the studies. Only recent publications

in five languages were included in the literature search because of resource limitations. While it is possible that the resulting search may have excluded relevant studies, this does not seems likely because the reviewer inspected 14 related literature reviews, which had no publication year- or language restrictions (see literature list) and no other behavioural HIV/STI outcome evaluations for MSM in Europe were identified.

Conclusion

The main finding of this systematic review is that despite 30 years into the HIV epidemic, rigorous outcome evaluations of any form of behavioural HIV/STI intervention for MSM in Europe are scarce. Evaluating the effectiveness of interventions poses significant challenges to the scientific community, but if one were to have evidence-based policies and practices to prevent HIV/STIs among MSM in the future, additional behavioural interventions with accompanying outcome evaluations should be implemented. Interventions should target both individuals, groups, and communities, strive for biological outcomes alongside behavioural measures, and include multiple follow up assessments. Evidence from this systematic review demonstrates that it is possible to successfully conduct rigorous HIV/STI prevention studies for MSM in Europe which meet these criteria, they indicate sexual risk behaviour change, and such studies should to a greater extent become part of a comprehensive continuum of behavioural and biomedical HIV/STI prevention and care.

Acknowledgements

The study author is grateful to Dr van Kestern and her colleagues for making their study available for this systematic review. The author gratefully acknowledges the expert contributions provided by information search specialist Sari Ormstad, statistician Jan Odgaard-Jensen, and senior researcher Geir Smedslund at the Norwegian Knowledge Centre for the Health Services in the preparation of this systematic review. The systematic review would not be possible without the support of Dr Ronny Tikkanen..

Financial support

The project was funded by the European Centre for Disease Prevention and Control, publication reference: OJ/2009/06/03-PROC/2009/022. No financial or other conflict of interest is reported by the author.

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Health Protection Agency publishes Annual Evidence Update focussing on HIV in children and adolescents

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This article was published on 9 December 2009.
Citation style for this article: Hansraj F. Health Protection Agency publishes Annual Evidence Update focussing on HIV in children and adolescents. Euro Surveill. 2009;14(48):pii=19431. Available online: http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19431

The United Kingdom NHS Evidence-infections have produced an Annual Evidence Update (AEU) on HIV in children and adolescents to coincide with World AIDS day on 1 December. This update which contains evidence that has emerged in the last year is accompanied by commentaries from experts in the field.

Worldwide, there are an estimated 33 million people living with HIV, with children making up over two million of the total. The United Nations Joint Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO) estimate that 2.9 million lives have been saved by the availability of antiretroviral therapy (ART), with better access leading to a decline in HIV related deaths by around 10% in the last 5 years [1].

Despite this, there were still 2.7 million new infections of HIV worldwide, with over half of these in young people aged 15-24. Of these new HIV infections, 420,000 are in children, with 1,200 children globally acquiring HIV every day and the majority of these being acquired by mother to child transmission (MTCT). Approximately half of all the children infected by MTCT would die by the age of two without access to ART [1].

New figures from the Health Protection Agency show that the very low MTCT transmission in the UK of around 1% overall is the result of the very high uptake of HIV screening (95%) in the antenatal setting [2,3]. At least 90% of women with HIV are diagnosed prior to delivery, and an estimated 200,000 new infections in children have been prevented since 2001 resulting from HIV positive mothers using ART to avoid transmitting the virus to their children. Consequently, the average age of perinatally infected children is now over 10, meaning that many of these children in the UK are now entering adolescence and transitioning from paediatric to adult services, which brings with it added clinical and psychosocial complexities [4].

One comment to the report stresses that HIV testing needs to be accepted as part of routine screening in order to prevent MTCT and address the one third of 7,298 people diagnosed in 2008 who presented late in the course of their illness, and contributed to half of all the deaths in HIV infected individuals last year [2].

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