

# Effects of region of birth, educational level and age on late presentation among men who have sex with men newly diagnosed with HIV in a network of STI/HIV counselling and testing clinics in Spain

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This paper analyses late presentation (LP) of HIV infection, and its determinants, among men who have sex with men (MSM) in Spain, newly diagnosed with HIV (2003–2011) in 15 sexually transmitted infection/HIV counselling and testing clinics. LP was defined as <350 CD4 cells/μL or AIDS. In total, 3,081 MSM were included (2,499 having CD4/AIDS); overall LP was 25.3%. LP was higher in men older than 34 years, those not previously HIV-tested (adjusted odds ratio (aOR):3.1; 95% confidence intervals (CI):2.3–4.2), and those tested >12 months before diagnosis (12–24 months (aOR:1.4; 95% CI:1.0–2.0); >24 months (aOR:2.2; 95% CI:1.7–3.0)). LP was less likely in MSM reporting a known HIV-infected partner as infection source or symptoms compatible with acute retroviral syndrome. ‘Region of birth’ interacted with ‘educational level’ and ‘steady partner as infection source’: only African and Latin-American MSM with low educational level were more likely to present late; Latin-American men

attributing their infection to steady partner, but no other MSM, had LP more frequently. In Spain, HIV testing among MSM should be promoted, especially those > 34 years old and migrants with low educational level. The current recommendation that MSM be tested at least once a year is appropriate.

## Introduction

Delayed diagnosis and treatment of HIV infection is a huge problem worldwide, with important individual and public health consequences. People presenting with an impaired immune system at diagnosis have higher rates of morbidity and mortality than those diagnosed earlier [1,2], and treating them is more costly [3]. Moreover, HIV-infected people unaware of their status may inadvertently spread HIV [4].

Different definitions have been used for late presentation of new HIV diagnoses [5], most of them based

on different CD4 count levels at HIV diagnosis and/or simultaneous or recent diagnosis with acquired immunodeficiency syndrome (AIDS) [6–8]. To facilitate data comparisons, a consensus definition was proposed in Europe in 2010 and 2011 defining advanced disease (AD) as presenting a CD4 count below 200 cells/ $\mu$ L or AIDS at diagnosis, and late presentation (LP) as having less than 350/ $\mu$ L or AIDS [8,9].

In the European Union/European Economic Area (EU/EEA) countries, nearly half (49.3%) of new HIV diagnoses reported in 2012 were late presenters (defined as fewer than 350 CD4 cells/ $\mu$ L at diagnosis), with a range of 35–66% across countries [10]. The proportion of LP was higher among heterosexuals (59.1%) and people who inject drugs (PWID) (55.9%) than among men who have sex with men (MSM), (38.4%). In Spain, using the same definition, 48% of new HIV diagnoses reported to the national surveillance system that same year presented late; variations across exposure categories are similar, with MSM having the lowest proportion of LP in comparison to PWID and heterosexuals (39%, 59% and 65% respectively) [11].

In addition to the surveillance system, data on LP are available in Spain from the CoRIS cohort and the EPI-VIH Network. CoRIS is a Spanish cohort of treatment-naïve HIV patients which collects epidemiological/clinical data in a broad setting [12]; LP in this cohort was 48.6% in the period 2004–2006 [2]. The EPI-VIH Network includes all sexually transmitted infections (STI) and HIV counselling and testing (HCT) clinics operating in the main Spanish cities; these are low threshold public facilities attending all key populations at higher risk for HIV [13,14]. Between 2003 and 2010, the proportion of LP in new HIV diagnoses in this network was 27.6% [15], significantly lower than what was found in the comprehensive surveillance system [11].

Both in Spain (cohort and surveillance data) and elsewhere, several socio-demographic and epidemiological factors have been associated with LP, such as male sex, age, migration, low socio-economic status and HIV transmission mode [2,5,16–18]. Also, all the Spanish studies have showed that LP is less common in MSM than in other transmission categories, even after adjusting for other variables. However, little is known about factors affecting LP within this group. The objective of this paper is to analyse LP of HIV infection and its determinants among MSM newly diagnosed with HIV from 2003 to 2011 in the EPI-VIH Network.

## Methods

All new HIV diagnoses among MSM testing for HIV between 2003 and 2011 in the EPI-VIH Network were included. The network in this period comprises 21 clinics located in the main Spanish cities: Alicante, Barcelona, Bilbao, Cartagena, Castellón, Gijón, Granada, Logroño, Madrid (two clinics), Málaga, Murcia, Oviedo, Palma de Mallorca, Pamplona, San Sebastián, Santander, Seville, Tenerife, Valencia and Vitoria. Fifteen of these

clinics (excluding Castellon, Gijón, Granada, Malaga, Seville and Vitoria) systematically collect data on CD4 count after diagnosis. The clinics are public low-threshold facilities, operating on a free basis, where every effort is made to maximise accessibility for key populations at higher risk. Participation in the EPI-VIH group is voluntary but, to our knowledge, all specialised STI/HCT clinics in Spain belong to this network.

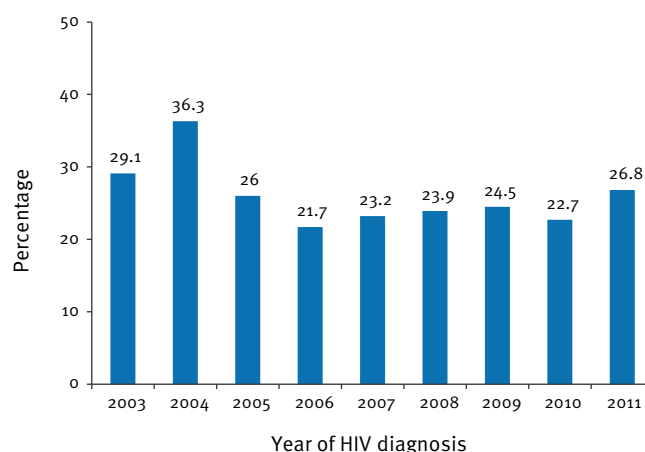
Cases included in this analysis met the European case definition for new HIV diagnosis [19].

Epidemiological variables (age, sex, country of birth, educational level, date of HIV diagnosis, type of sexual partner reported as probable source of infection (casual partner, steady partner, known HIV-infected partner (steady/casual), commercial partner (sex worker/client)), existence of a previous HIV test, date of previous HIV test, and clinical information (CD4 count, AIDS diagnoses, symptoms compatible with an acute retroviral syndrome, availability of health insurance card) were collected by the attending physicians using a standardised questionnaire.

LP was defined as having a CD4 count below 350 cells/ $\mu$ L in the first determination after HIV diagnosis and/or AIDS at diagnosis, following recent European recommendations [8,9]. The analyses were dealt with at the level of ‘country/region of birth’; to assign ‘region of birth’, the World Health Organization Regional Office for Europe’s classification was used. Frequency distributions for each variable and prevalence of LP, overall and stratified by different variables, were calculated. To evaluate the association between categorical variables, chi-squared tests were used; the associations between LP and individual explanatory variables were considered statistically significant at a p value < 0.05. Trends in LP over time were analysed using a joinpoint regression model. To identify factors associated with

**FIGURE 1**

Prevalence of late presentation among men who have sex with men newly diagnosed with HIV, by year of diagnosis, EPI-VIH Network, Spain, 2003–2011 (n=2,499)



**TABLE 1**

Characteristics of men who have sex with men newly diagnosed with HIV, and prevalence of late and not late presentation in different subgroups, EPI-VIH Network, Spain, 2003–2011 (n=2,499)

Variables	Characteristics of MSM newly diagnosed with HIV		Prevalence of late presentation		Prevalence of not-late presentation		p value
	No	%	No	%	No	%	
<b>Age group (years)</b>							
<25	363	14.5	74	20.4	289	79.6	0.00
25–34	1,232	49.3	285	23.1	947	76.9	
35–44	668	26.7	192	28.7	476	71.3	
≥45	208	8.3	75	36.1	133	63.9	
Unknown	28	1.1	5	17.9	23	82.1	
<b>Educational level</b>							
Illiterate/primary education	375	15.0	107	28.5	268	71.5	0.13
Secondary education	1,023	40.9	257	25.1	766	74.9	
University education	912	36.5	212	23.2	700	76.8	
Unknown	189	7.6	55	29.1	134	70.9	
<b>Region of birth</b>							
Spain	1,617	64.7	384	23.7	1,233	76.3	0.02
Western Europe	78	3.1	20	25.6	58	74.4	
Central/Eastern Europe	42	1.7	10	23.8	32	76.2	
Latin America	713	28.5	205	28.8	508	71.2	
Africa	17	0.7	8	47.1	9	52.9	
Unknown	32	1.3	4	12.5	28	87.5	
<b>Source of infection: steady partner</b>							
Yes	938	37.5	243	25.9	695	74.1	0.56
No	1,561	62.5	388	24.9	1,173	75.1	
<b>Source of infection: casual partner</b>							
Yes	1,978	79.2	506	25.6	1,472	74.4	0.46
No	521	20.8	125	24.0	396	76.0	
<b>Source of infection: commercial sexual contact</b>							
Yes	153	6.1	40	26.1	113	73.9	0.79
No	2,346	93.9	591	25.2	1,755	74.8	
<b>Source of infection: known HIV- infected partner</b>							
Yes	263	10.5	50	19.0	213	81.0	0.01
No	2,236	89.5	581	26.0	1,655	74.0	
<b>Acute retroviral syndrome</b>							
Yes	361	14.4	55	15.2	306	84.8	0.00
No	735	29.4	220	29.9	515	70.1	
Unknown	1,403	56.1	356	25.4	1,047	74.6	
<b>Previous HIV-negative test</b>							
No	532	21.3	192	36.1	340	63.9	0.00
Yes, <12 months before HIV diagnosis	611	24.5	87	14.2	524	85.8	
Yes, 12–24 months before HIV diagnosis	557	22.3	114	20.5	443	79.5	
Yes, >24 months before HIV diagnosis	779	31.2	236	30.3	543	69.7	
Yes, but date unknown	20	0.8	2	10.0	18	90.0	
<b>Health insurance card</b>							
Yes	2,271	90.9	568	25.0	1,703	75.0	0.27
No	103	4.1	24	23.3	79	76.7	
Unknown	125	5.0	39	31.2	86	68.8	
<b>Total</b>	<b>2,499</b>	<b>100</b>	<b>631</b>	<b>25.3</b>	<b>1,868</b>	<b>74.7</b>	

MSM: men who have sex with men.

**TABLE 2**

Factors associated with late presentation among men who have sex with men newly diagnosed with HIV, univariate/multivariate analysis, EPI-VIH Network, Spain, 2003–2011 (n=2,499)

Variables	Univariate analysis		Multivariate analysis		
	OR	95% CI	aOR	95% CI	p value
Age group (years)					
<25	0.8	0.6–1.1	0.8	0.6–1.0	0.08
35–44	1.3	1.1–1.7	1.3	1.0–1.7	0.02
≥45	1.8	1.4–2.6	1.8	1.3–2.5	0.00
Educational level (university education) <sup>a</sup>					
Illiterate/primary education	1.3	1.0–1.7	n.a.	n.a.	n.a.
Secondary education	1.1	0.9–1.4	n.a.	n.a.	n.a.
Unknown	1.4	0.9–1.9	n.a.	n.a.	n.a.
Region of birth (Spain) <sup>a</sup>					
Western Europe	1.1	0.7–1.9	n.a.	n.a.	n.a.
Central/eastern Europe	1.0	0.5–2.1	n.a.	n.a.	n.a.
Latin America	1.3	1.1–1.6	n.a.	n.a.	n.a.
Africa	2.9	1.1–7.5	n.a.	n.a.	n.a.
Source of infection: steady partner (No) <sup>a</sup>					
Yes	1.1	0.9–1.3	n.a.	n.a.	n.a.
Source of infection: casual partner (No)					
Yes	1.1	0.9–1.4	1.0	0.7–1.3	0.74
Source of infection: commercial sexual contact (No)					
Yes	1.1	0.7–1.5	0.8	0.5–1.2	0.22
Source of infection: known HIV-infected partner (No)					
Yes	0.7	0.5–0.9	0.7	0.5–0.9	0.02
Acute retroviral syndrome (No)					
Yes	0.4	0.3–0.6	0.5	0.4–0.7	0.00
Previous HIV-negative test (Yes, <12 months before HIV diagnosis)					
No	3.4	2.6–4.5	3.1	2.3–4.2	0.00
Yes, 12–24 months before HIV diagnosis	1.6	1.1–2.1	1.4	1.0–2.0	0.03
Yes, >24 months before HIV diagnosis	2.6	2.0–3.4	2.2	1.7–3.0	0.00
Yes, but date unknown	0.7	0.2–3.0	0.6	0.1–3.0	0.54
Health insurance card (No)					
Yes	1.1	0.7–1.8	1.2	0.7–2.1	0.47
Unknown	1.5	0.8–2.7	1.3	0.6–2.5	0.51

aOR: adjusted odds ratio; CI: confidence interval; MSM: men who have sex with men; n.a.: not applicable; OR: odds ratio. Reference categories in brackets. Model adjusted by clinic of diagnosis.

<sup>a</sup> For convenience, adjusted odds ratio for interactions between these variables are shown in Figure 2.

LP, logistic regression models were fitted using a backward elimination procedure. Associations were measured using the odds ratio (OR) and its 95% confidence interval (CI). Data analyses were performed using the STATA statistical software package Version 13 (Stata Corporation, College Station, TX, US).

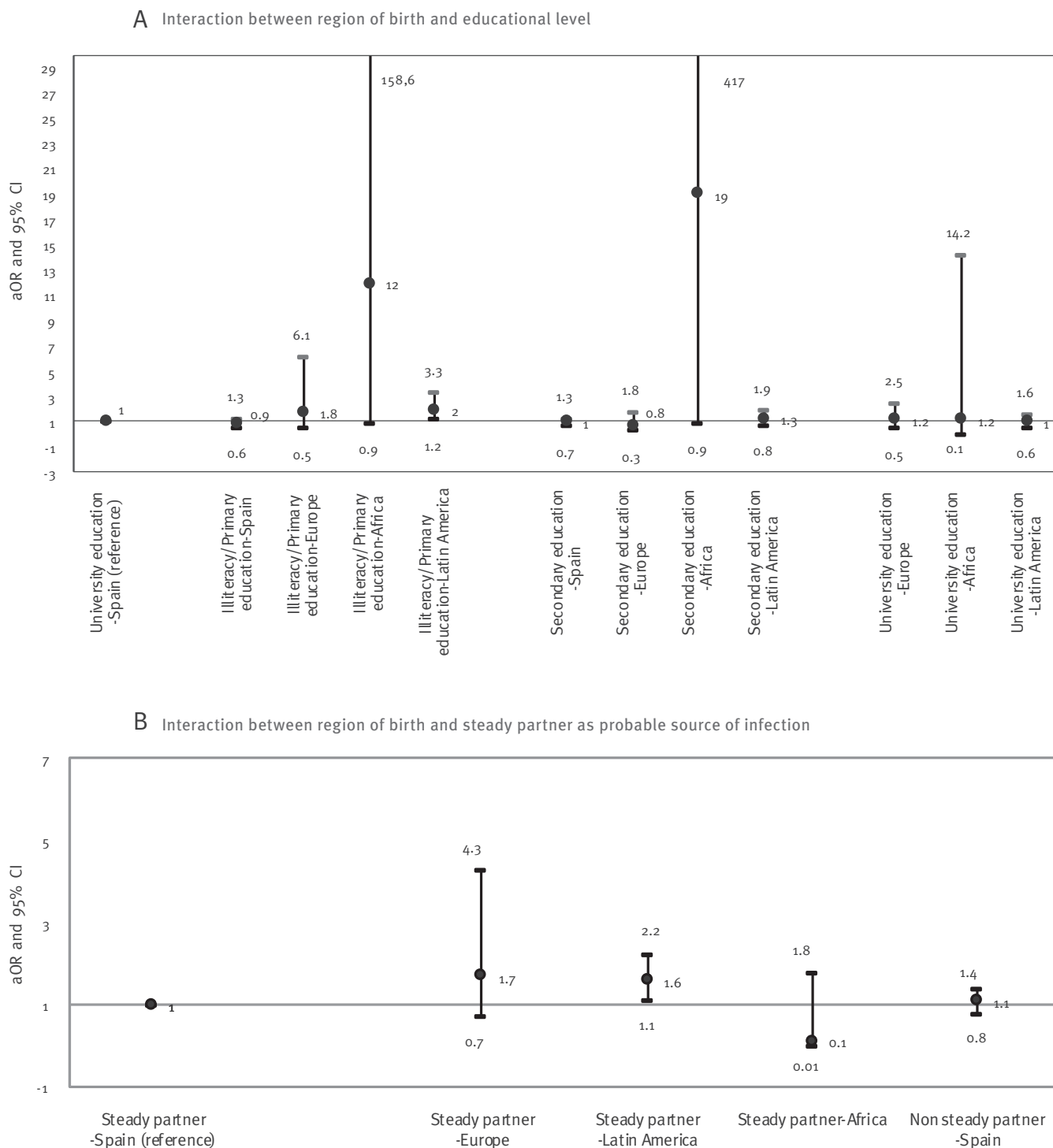
The EPI-VIH Network is an HIV sentinel surveillance system, and the database was registered in the Spanish Data Protection Agency (registry number 2080910068). No personal identifiers were collected.

## Results

A total of 3,081 MSM newly diagnosed with HIV were identified during the study period. Of these 2,499 (81.1%) had data on CD4 and/or AIDS diagnosis. The majority were born in Spain (64.7%), were in the 25–34 year age group (49.3%), and had secondary/university education (77.4%). Almost one in six reported symptoms compatible with an acute retroviral syndrome, and 78.7% had been tested for HIV previously (Table 1). Median CD4 at presentation was 497 (interquartile range: 349–690). Overall, 631 MSM (25.3%) met

**FIGURE 2**

Interactions of 'region of birth' with 'educational level' (A) and with 'steady partner as probable source of infection' (B), multivariate analysis, EPI-VIH Network, Spain, 2003-2011 (n=2,499)



aOR: adjusted odds ratio; CI: confidence interval.

Bars represent 95% confidence intervals.

Model adjusted by all variables shown in Table 2 plus clinic of diagnosis.

the definition of LP (593 cases had fewer than 350 CD4 cells/ $\mu$ L, 5 presented AIDS at diagnosis and 33 had both). The proportion of LP increased with age, and was higher in men with a low educational level (28.5%), in MSM born in Africa (47.1%) or Latin America (countries of the American continent where Spanish or Portuguese is the main national language) (28.8%), and among those without a previous HIV-negative test (36.1%). Conversely, the prevalence of LP was lower in men attributing their infection to intercourse with a known HIV-infected partner (19%) and those reporting an acute retroviral syndrome (15.2%) (Table 1). No trend was found in the prevalence of LP during the study period (Figure 1).

In the multivariate analysis, factors associated with LP were age over 34 years ((35–44 years: adjusted odds ratio (aOR): 1.3; 95% CI: 1.0–1.7;  $p=0.02$ ) (>44 years: aOR: 1.8; 95% CI: 1.3–2.5)), having no history of previous tests (aOR: 3.1; 95% CI: 2.3–4.2) or having been tested more than 12 months before the diagnostic test ((12–24 months: aOR: 1.4; 95% CI: 1.0–2.0) (>24 months: aOR: 2.2; 95% CI: 1.7–3.0)). Factors inversely associated with LP were reporting sexual contact with a known HIV-infected partner as the source of infection (aOR: 0.7; 95% CI: 0.5–0.9) or symptoms compatible with an acute retroviral syndrome (aOR: 0.5; 95% CI: 0.4–0.7). Region of birth presented interactions with ‘educational level’ and with ‘probable source of infection: steady partner’: MSM born in Africa or Latin America, with low educational level (but not those with high educational level) had higher odds of presenting late, although, for Africans, results were on the edge of significance and confidence intervals were very wide due to the small sample size. Latin-American MSM attributing their infection to their steady partner (but not any other subgroup) were also more likely to present late (Table 2, Figure 2).

## Discussion

This paper presents data on LP among MSM newly diagnosed with HIV in the EPI-VIH Network in Spain. Among MSM diagnosed in this network, LP is less common than in those diagnosed elsewhere, but presenting late is not evenly distributed, and the effect of region of birth on LP varies depending on the levels of two other variables.

Reducing diagnostic delay is a policy priority in Spain [20], and HIV testing is free of charge in all public facilities. Since 2009, HIV testing at least once a year has been recommended for MSM, and HIV testing guidelines that reinforce the importance of timely testing in this population have been issued recently [21]. In order to increase HIV testing availability and to facilitate anonymous testing, several regions have implemented testing in pharmacies [22] and others have made available rapid HIV tests in STI clinics and primary health care centres [23,24]. Testing programmes implemented by nongovernmental organisations are also playing an important role [25,26].

The proportion of LP among MSM found in this study (25.3%) is lower than what has been reported in this group in other Spanish settings: in a study performed in Barcelona from 2001 to 2009 the proportion was 47.7% [17], and in another analysis of data from 11 autonomous regions during the period 2007–2011, the figure was 39.1% [18], although in this case the definition of LP did not include AIDS. The prevalence in our study was also lower than the 34% reported in the United Kingdom in 2012 [27]. This finding is not surprising since the main purpose of the clinics belonging to the EPI-VIH Network is to be highly accessible to people with a high perceived risk for HIV, irrespective of their circumstances [15]. Also, MSM attending these clinics are probably very much aware of the importance of frequent testing: almost 80% of the participants in this study reported previous testing, while in the Spanish sample of the European MSM Internet Survey (EMIS-Spain) the proportion of men ever tested was 74% [28]; furthermore, our clinics are located in the main cities, and EMIS-Spain showed that MSM living in big cities were more likely to have been tested for HIV [28].

Participants older than 34 years were found to be more likely to have LP, and the risk increased with increasing age. This finding is frequent in studies analysing LP [16,18,29], and is consistent with results from a study conducted in England, Wales, and Northern Ireland in 2007, where MSM over 50 years of age were almost three times more likely to have a CD4 count of less than 350 cells/ $\mu$ L at HIV diagnosis [30].

Low educational level [2] and migrant status [17,18] have been described as predictors of LP in Spain, and poor education and little knowledge about HIV were also associated with being untested in an online Norwegian sample of MSM [31]. In our study, there was an interaction between education and migrant status, so that Latin-American and African MSM with low educational level (but not those from the same regions with high educational level or men from other regions) were more likely to present late. These results might reflect factors, such as lack of knowledge about HIV infection, lack of access to HIV diagnostics in their country of birth or lack of knowledge about HIV testing policies/facilities in Spain, operating mainly in less educated migrants. In EMIS-Spain, MSM with low to middle educational level or lesser knowledge about HIV/STI, and those who were not confident about accessing HIV testing were more likely never to have been tested for HIV although, surprisingly, Spaniards were less likely than migrants to have been tested [28]; the likely explanation for this finding is that, in this particular study, most participating migrants were Latin-American with better educational level than their Spanish counterparts.

The fact that Latin-American MSM who attribute their HIV infection to their steady partners are at greater risk of LP warrants further investigation and suggests that emotional factors have to be considered

when analysing LP. In any case, Latin-American MSM living in Spain appear to be highly vulnerable to HIV. They are over-represented in new HIV diagnoses [11] and showed higher levels of risky behaviours in EMIS-Spain, despite being highly educated and very knowledgeable about HIV [32].

It seems logical that men experiencing symptoms compatible with an acute retroviral syndrome and those reporting a known HIV-infected partner as their probable source of infection would have sought HIV testing quickly and therefore be less likely to present late. It is less obvious why not having a health card had no effect on LP, but this is not so surprising in our setting because this card is not required to be tested for HIV. LP was inversely associated with repeat HIV testing, a finding also reported in Danish MSM [33]. Our results even show an upward gradient of risk for LP as the time lag between the previous negative HIV test and the diagnostic test increased, underlining the importance for MSM to follow the recommendation of testing at least yearly.

This study has some limitations. Most importantly, MSM attending the EPI-VIH Network are not representative of the Spanish MSM population, thus our results cannot be extrapolated to all MSM in the country; unfortunately, educational level and probable source of infection are not collected in the regular surveillance system, thus preventing replication of the same analysis with these data. Furthermore, many persons were involved in data collection, thus increasing the probability of introducing mistakes; nevertheless, the EPI-VIH Network has been operating for many years, participating clinicians are very experienced, and a standard questionnaire is used to collect data. Finally, some degree of misclassification might exist if someone newly infected with HIV and presenting a low CD4 count was classified as late presenter.

On the other hand, we believe that results from this study are important to define effective interventions to increase HIV testing in the MSM subgroup that is probably at highest risk of infection. The need to test for HIV at least yearly should be further disseminated among the MSM community, and efforts should be made to increase awareness about symptoms suggestive of an acute antiretroviral syndrome. In addition, measures aiming at improving early diagnosis in poorly educated Latin- American and African migrants are a priority; in these MSM subgroups better knowledge about their situation is also needed to determine the best way to assist them.

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#### Conflict of interest

The authors declare that they have no conflicts of interest.

#### Authors' contributions

MD was the main study researcher. She supervised field work and data collection, wrote the statistical analysis plan and the final version of the manuscript. AD performed data collection and management, quality control and statistical analysis, and wrote the first version of the manuscript. JdR, CR, IA JB, FJB, MMC, MLJ, IS, LJV, LG, EM, FG, MCL, IP, JMU, BM, JAV, JT, MAA, and EPI-VIH Study Group: were the clinicians responsible for patient recruitment and follow-up in the participating centres. They all participated in development of the study protocol, collection of epidemiological and clinical data, and critical review of all versions of the manuscript. All authors have seen and approved the final manuscript.

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