Prevalence of HIV infection among young adult injecting and non-injecting heroin users in Spain in the era of harm reduction programmes: gender differences and other related factors

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SUMMARY

The aims were to assess the prevalence of HIV infection among young adult heroin users, including injecting heroin users (IHUs) and non-injecting heroin users (NIHUs), and to explore the differences by gender and other factors. The design was a cross-sectional cohort study between April 2001 and December 2003, which included 961 current heroin users (HU), aged 18-30 years: 422 in Madrid, 351 in Barcelona and 188 in Seville; 621 were IHUs and 340 were NIHUs. All were street-recruited by chain referral methods. Face-to-face interviews were conducted using a structured questionnaire with computer-assisted personal interviewing (CAPI). Samples for HIV testing (dried blood spot) were collected and tested with ELISA and Western Blot. Bivariate, logistic regression, and classification and regression tree analyses were performed. The overall prevalence of HIV infection among IHUs was 25.8% (95% CI 22.3–29.3) [32.4%] (95% CI 26·6–38·1) in Madrid, 20·5% (95% CI 15·6–25·4) in Barcelona, and 20·6% (95% CI 9.8–31.4) in Seville, whereas in NIHUs it was 4.0% (95% CI 2.1–6.7), with no differences among cities. The prevalence was significantly higher in women than in men in NIHUs (10.9%, 95% CI 4·3–17·5 vs. 1·7 %, 95 % CI 0·5–4·2) and was non-significantly higher in IHUs (30·4 %, 95 % CI 23·0–37·8 vs. 24·1 %, 95 % CI 20·1–28·1). HIV prevalence in short-term IHUs was 12·9 % (CI 8·8–17·02), with no differences among cities. In the logistic analysis, the variables associated with infection in IHUs were ever having injected with used syringes (OR 3·4, 95 % CI 2·2–5·3), ever having been in prison (OR 2·6, 95 % CI 1·6-4·0), and heroin as the first drug injected at least weekly (OR 2·3, 95 % CI 1·1–4·5). Factors positively associated with HIV infection in NIHUs were female sex (OR 8·7, 95% CI 2·6–29·2) and age >25 years (OR 3·1, 95% CI 0·9–11·1), while primary educational level was inversely associated (OR 0·26, 95 % CI 0·1–0·9). Although there are important geographic differences, HIV prevalence in IHUs remains high, even in short-term IHUs, whereas it was almost six times lower in NIHUs. The prevalence in women is higher than in men, particularly among NIHUs. A wide range of preventive strategies should be developed, aimed primarily at empowering women to negotiate safe sex.

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INTRODUCTION

Cohort studies in young drug users make it possible to monitor trends in patterns of consumption, risk behaviours, and the prevalence and incidence of different health problems, among them, HIV, HCV and other viral infections. Including young people in such studies also allows a more complete analysis of the trajectory of risk exposure, a subject of considerable interest given that different studies have shown that the prevalence of risk behaviours and the prevalence and incidence of HIV and HCV injection is higher among younger people and in the first years after beginning to inject [1–7]. These studies have shown that, although HIV prevalence and incidence were initially higher in women than in men, in both injectors and non-injectors, the prevalence has tended to even out in most of the studies recently carried out in the United States, and in some studies it has even been higher in men [8]. In other places, like Vancouver [9] or Amsterdam [10], women continue to have a higher risk of infection. Furthermore, several studies carried out in the United States in recent years have shown that some sexual behaviours were the main determinants of the prevalence or incidence of infection among injectors, in both men and women [8, 11–13]. Practically all recent cohort studies with active periodic follow-up in young community-recruited drug users are being carried out in North America (the United States or Canada), whereas in Europe there has only been one study in Holland [10] and another in the United Kingdom [14]. Other existing cohorts are based in treatment centres, with follow-up only of those who voluntarily go back for monitoring, and generally a very limited amount of information on risk behaviours is collected [15]. Furthermore, most of these studies focus exclusively on drug injectors and not on those who use the same substances by other routes, despite the fact that these population groups share many of the same epidemiological characteristics.

For many years Spain has had the largest number of AIDS cases of any country in the European Union, as well as one of the highest prevalences of HIV infection [15, 16]. In addition, use of the injected route was found almost exclusively among heroin users, and was practically non-existent among persons who were not regular current or past users of this substance [17]. However, epidemiological phenomena of considerable importance began to take place in the mid-1980s, such as the progressive replacement of the injected

route by the diffusion of smoking as the main route of heroin use [18], together with the implementation of harm-reduction programmes [19]. These phenomena may have affected the level of HIV infection as well as its occurrence by gender and patterns of heroin consumption.

This study determines the prevalence of HIV infection, differences by gender, and the main factors associated with infection in young adult heroin users, including both users who had ever injected (injecting heroin users or IHUs) and those who had never injected (non-injecting heroin users or NIHUs), in three large Spanish cities: Barcelona, Madrid and Seville.

MATERIALS AND METHODS

Study design and population

The Itinere Project is a cohort study in young adult, regular current users of heroin in three Spanish cities: Barcelona, Madrid and Seville. These cities were chosen for two reasons: (1) Their geographic location: Madrid, in the centre of the country; Barcelona, 600 km to the northeast; and Seville, 600 km to the southeast, each city belonging to a different region. (2) They were thought to represent three very different epidemiological profiles with respect to the main route of heroin administration: Barcelona, where the intravenous route still predominated; Madrid, where smoking had been the most frequently employed route since the mid-1990s; and Seville, where smoking had predominated since the end of the 1980s [17].

Inclusion criteria for the study were age between 18 and 30 years, having used heroin at least 12 days in the last 12 months, and at least 1 day in the last 3 months, and residence in the metropolitan area of one of the study cities during most of the last 12 months.

Participants also had to have sufficient knowledge of Spanish to be able to answer the questionnaire easily, and to sign an informed consent document approved by the Ethics Committee of the Instituto de Salud Carlos III, acknowledging their voluntary participation in the study.

Recruitment

The entire sample was street recruited, using targeted sampling [20] and chain-referral methods; recruitment from socio-health services for the treatment of drug problems was avoided. The first links in the

chain were recruited directly by anthropologists and social workers belonging to the research team who worked at known points of drug purchases or meeting places of drug users, and by key persons who knew or worked in these settings. Many of these key persons or recruiters were ex-users or users who could not participate in the study because they did not meet the inclusion criteria – generally because they were older than 30 years. They were paid for each drug user contacted who participated in the study. The rest of the sample was recruited by respondent-driven sampling (RDS) [21, 20], consisting of an incentive-driven chain-referral procedure that combined incentives for recruiting other participants into the study and rewards for being interviewed.

Data collection

Users had a face-to-face, computer-assisted interview, using a structured, largely pre-coded questionnaire with some open questions. The section on sexual behaviour was administered by computer-assisted self interviewing (Audio-CASI) for all participants except those who even with this assistance did not have sufficient reading abilities to understand the questions properly. This allowed greater privacy in answering the section considered most sensitive. The questionnaire covered in considerable detail the aspects included in the present analysis: sociodemographic characteristics, social conflict, patterns of use of different psychoactive substances, initiation into injection, injection risk behaviours, sexual risk behaviours (differentiating the behaviours by gender and analysing homosexual behaviours in males), and knowledge of HIV status, including dates of testing and knowledge of seropositivity. It also included other sections related with the level of drug dependence, overdoses and other health problems - both physical and mental - related with drug use, health-related quality of life, and social support. In general, two basic reference periods were used: lifetime and last 12 months before the interview, although for some variables subjects were asked to indicate when the behaviour or event investigated had last occurred.

A dried blood sample was obtained from all participants, and it was explained that results were not for diagnostic purposes and would be used only for the study. At the same time, participants were informed of how to obtain free services at centres for the diagnosis and treatment of drug-related health problems. In many cases, such services were offered at the same

centres where the interviews took place, but at a different time. Participants were paid €18 at the end of the interview.

The interviews took place between April 2001 and December 2003 in health and social centres (medical or nursing consultations, social work departments, neighbourhood or district social centres, etc.), and in a very few cases in centres that could be identified directly with drug users (e.g. treatment centres). In the latter cases, it was clearly explained that the study was completely independent of the centre and that no information obtained in the interview would be conveyed to the treatment team.

Laboratory methods

Determination of HIV antibodies in the dried blood sample was made by commercial ELISAs (ELISA Genscreen HIV1/2 version 2 and New Lav Blot 1; Bio-Rad, Marnes-la-Coquette, France). Given that in the preliminary analysis of the results, the positive predictive value of the self-reports was over 99%, only positive samples from those who stated they were HIV negative or who had not had a previous test were confirmed by Western blot.

Statistical analysis

A descriptive analysis was made of the principal sociodemographic and injection characteristics of the sample. The prevalence of HIV infection and the 95 % confidence intervals (CI) were then calculated by city, sex, and by IHUs/NIHUs. All subsequent analyses were performed separately for IHUs and NIHUs. First, a bivariate analysis was performed to estimate the prevalence of HIV infection by different sociodemographic variables, and by variables related with patterns of drug use and injection, sexual behaviours, injection behaviours, and other risk behaviours. The Mantel-Haenzel odds ratio (OR) and the 95% CI were calculated to evaluate the magnitude of the association [22]. We then carried out a multivariate logistic regression analysis following the methodology proposed by Hosmer & Lemeshow [23]. Separate models were constructed for IHUs and NIHUs. Initially, the models included those variables whose significance in the bivariate analysis was <0.25, and the likelihood-ratio test was used to evaluate the contribution of each variable to the model. Finally, we evaluated the relevant firstdegree interactions. In IHUs, separate models were made for men and women in order to evaluate gender differences and to explore the effect of sexual relations between men. This analysis was not made for NIHUs, due to the small number of women in this subgroup.

Given the limited number of outcomes and the potential interacting correlates, the analysis of associated factors in NIHUs was also performed by classification and regression tree analysis (C&RT). This is a non-parametric statistical procedure that identifies mutually exclusive subgroups whose members share common characteristics that influence the dependent variable (in this case, HIV prevalence). The C&RT procedure examines all possible independent or splitting variables and selects the one that results in binary groups that are most highly differentiated with respect to the dependent variable, according to a predetermined splitting criterion (in our case, the Gini index). This method appears to have affinity with the way clinicians make decisions [24, 25]. The procedure was performed with the SPSS module Answer Tree 2.0 [26].

RESULTS

Sociodemographic characteristics of the global sample

The cross-sectional cohort study of the Itinere Project recruited 991 heroin users, however, the present analysis includes only the 961 for whom a HIV result was available from the dried-blood sample: 351 in Barcelona, 422 in Madrid and 188 in Seville. The mean age of those recruited was 25.7 years and the median was 26.0 years; 72.7% were men, 10.3% were 'non-Spanish nationals', and 45.5% had primary educational level or less (maximum of 5 years of elementary school – until age 11). During the last 12 months, 31.5% had worked most of the time, and 14% had lived in an institution or were homeless. In total, 41.8% had been in prison at some time; 64.6% (621) had injected at some time (IHUs), and 35.4% (340) had never injected (NIHUs).

HIV prevalence

A total of $80\cdot2\%$ (95% CI $78\cdot0-83\cdot1$) knew their serological status, a percentage that was significantly higher among injectors than among non-injectors (88·4%, 95% CI 86·3–91·4 vs. 66·6%, 95% CI 60·3–70·7).

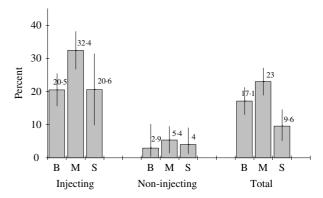


Fig. 1. Prevalence of HIV infection in young adult heroin users in Barcelona (B), Madrid (M), and Seville (S). The Itinere Project, 2001–2003.

HIV prevalence in the whole group of users was 18·2% (95% CI 15·7–20·7) with significant differences by city (Fig. 1): Seville (9·6%, 95% CI 5·1–14·0), Barcelona (17·1%, 95% CI 13·0–21·2) and Madrid (23·0%, 95% CI 18·9–27·1). These overall prevalences are basically determined by the percentage of IHUs in each city: only 33% in Seville, 65% in Madrid, and 80% in Barcelona. The prevalence of HIV infection in IHUs was 25·8% (95% CI 22·3–29·3); the percentage was similar in Barcelona (20·5%, 95% CI 15·6–25·4) and Seville (20·6%, 95% CI 9·8–31·4), and higher in Madrid (32·4%, 95% CI 26·6–38·1). The prevalence in NIHUs was 4·0% (95% CI 2·1–6·7), with no significant differences among cities.

HIV prevalence was higher in women (22.9%, 95%) CI 17.6-28.2) than in men (16.4%, 95%) CI 13.6-19.3) (P=0.02), mainly due to the significant difference in the prevalence among NIHUs: 10.9% (95% CI 4.3-17.5) in women vs. just 1.7% (95% CI 0.5-4.2) in men. Although difference in the prevalence between male and female IHUs was of considerable magnitude (30.4%, 95% CI 23.0-37.8 vs. 24.1%, 95% CI 20.1-28.1 respectively), it was not statistically significant (Fig. 2). In short-term injectors (those who had injected for no more than 5 years), the prevalence was 12.9% (95% CI 8.8-17.02).

Correlates of HIV infection in IHUs

Crude analysis

The following factors were significantly associated with higher HIV prevalence: (a) sociodemographic factors: age >25 years, Spanish nationality, residence in the city of Madrid, and ever having been in prison;

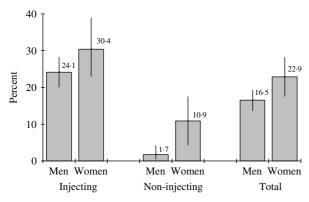


Fig. 2. Prevalence of HIV infection by sex in young adult heroin users. Barcelona, Madrid, and Seville. The Itinere Project, 2001–2003.

(b) patterns of drug use: cocaine binges, mainly by the injected route in the last 12 months; having ever sniffed or having sniffed in the last 12 months with used tubes or other devices; (c) sexual behaviours: having traded sex ever or in the last 12 months, having had a steady partner in the last 12 months who had ever injected drugs or traded sex, and having none or no more than two occasional partners in the last 12 months; (d) other risk behaviours: having received tattoos or piercings (Table 1); (e) patterns of injecting and injecting risk behaviours: injecting as the first main route of heroin administration, age <18 years at first injection, >5 years since first injection, having injected powdered cocaine weekly in the last 12 months, and ever having injected with a used syringe (Table 2).

Multivariate analysis

The variables most strongly and positively associated with HIV infection were: ever having injected with used syringes (OR 3.4, 95% CI 2.2–5.3), ever having been in prison (OR 2.6, 95% CI 1.6-4.0), female sex (OR 1.9, 95% CI 1.2–3.1), and heroin as the first drug injected weekly (OR 2·3, 95% CI 1·1-4·5). Having injected for >5 years in Madrid (interaction between length of injection and city) almost reached significance (OR 2·3, 95% CI 0·9-6·1). Having sniffed drugs with used devices (OR 0.5, 95% CI 0.3–0.8) and having had piercings (OR 0.6, 95% CI 0.4-1.0) were inversely associated with being HIV positive (Table 3). The models by gender did not show any important differences. Nor were homosexual relations between men found to be associated with HIV prevalence in a model restricted to men who had injected for ≤ 5 years.

Correlates of HIV infection in NIHUs

Crude analysis

Only female sex, ever having traded sex or having done so in the last 12 months, and having had a stable partner in the last 12 months who had ever injected were significantly associated with higher HIV prevalence. Age >25 years almost reached statistical significance (Table 1).

Multivariate analysis

The only variable significantly associated with infection was female sex (OR 8·7, 95% CI 2·6–29·2). Age >25 years (OR 3·1, 95% CI 0·9–11·1) was close to reaching significance. Conversely, primary or lower educational level was associated with a lower risk of infection (OR 0·3, 95% CI 0·1–0·9) (Table 3).

Tree analysis

Gender was also the strongest predictive variable in the tree analysis. In women, this process then chose age and subsequently the variable city in persons aged ≤ 25 years, and having been in prison in those >25 years. This led to three final groups with different prevalences: Group I, with a high prevalence (33%): women >25 years who had been in prison. Group II, with a medium prevalence (8–12%): women >25 years who had not been in prison, and women <25 years in Madrid or Seville; and Group III, with a low prevalence (<2%): women <25 years from Barcelona, and all the men (Fig. 3).

DISCUSSION

This study offers important findings about HIV infection in young, community-recruited heroin users in Spain. These results may well represent the HIV situation in young adult heroin users throughout the country [17]. In fact, during the last two decades in Spain, 'injectors' was synonymous with 'heroin users', given that drug injection occurred almost exclusively among users of this drug. Data from some studies of injectors [27] and all the ethnographic work carried out for the recruitment process in our 2001–2003 study confirmed that there were virtually no injectors of other substances (especially cocaine) who did not use heroin often enough to meet the inclusion criteria required in our study.

The first important finding is confirmation that the prevalence of HIV infection in IHUs remains high.

Table 1. Demograhics, patterns of drug use, sexual and other behaviours associated with HIV prevalence among injecting and non-injecting heroin users from Barcelona, Madrid, and Seville [Itinere Project, 2001–2003 (crude analysis)]

	Injecting heroin users			Non	Non-injecting heroin users			
	n	HIV+ (%)	OR	95% CI	n	HIV+ (%)	OR	95 % CI
				Socioden	nogranhi			
City				500100011	.rogrup.ii			
Barcelona	283	20.5	1		68	2.9	1	
Madrid	275	32.4	1.9	$(1\cdot 3-2\cdot 7)$	147	5.4	1.9	(0.4-9.3)
Seville	63	20.6	1	(0.5-2.0)	125	4	1.4	(0.3-7.3)
Sex								
Male	460	24.1	1		239	1.7	1	
Female	161	30.4	1.4	(0.9-2.0)	101	10.9	7.2	$(2\cdot 2-23\cdot 8)$
Age group (yr)								
≤25	228	14.9	1		174	2.3	1	
>25	393	32.1	2.7	(1.8-4.1)	166	6.6	3	(0.9 - 9.7)
Nationality								
Foreign	79	12.7	1		20	5	1	
Spanish	542	27.7	2.6	$(1\cdot 3-5\cdot 3)$	320	4.4	0.9	(0.1-7.0)
Educational level								
Primary level or less	266	26.3	1	(0.7-1.5)	171	2.3	0.3	$(0 \cdot 1 - 1 \cdot 1)$
Any higher level	354	25.4	1		169	6.5	1	
Labour status								
Regular employment	187	25.1	1		116	4.3	1	
Other	434	26	1	(0.7-1.5)	224	4.5	1	(0.3-3.2)
Type of accommodation								
House or apartment	509	25.3	1		318	4.7	_	
Homeless/Institution	112	27.7	1.1	(0.7-1.8)	22	0		
Ever in prison								
No	320	15.6	1		238	3.8	1	
Yes	300	36.7	3.1	$(2 \cdot 1 - 4 \cdot 6)$	102	5.9	1.6	(0.6-6.6)
				Patterns of	of drug u	ise		
Cocaine binges in last 12 months								
No	280	19.3	1		144	5.6	1	
Yes, but not mainly by intravenous route	191	28.3	1.6	$(1 \cdot 1 - 2 \cdot 6)$	185	3.2	0.6	(0.2-1.7)
Yes, mainly by intravenous route	142	35.2	2.3	(1.4-3.6)				
Ever sniffed with used tubes								
No	93	39.8	1		89	4.5	1	
Yes	524	23.1	0.5	(0.3-0.7)	251	4.4	1	(0.3-3.1)
Sniffed with used tubes in last 12 months								
No	307	30.9	1		166	6	1	
Yes	309	20.7	0.6	(0.4-0.8)	173	2.9	0.5	(0.2-1.4)
				Sexual b	ehaviour	·s		
Ever traded sex				Serial C	· ciia vio ai	.5		
No	509	24.6	1		304	3.6	1	
Yes	111	31.5	1.4	(0.9-2.2)	34	11.8	3.6	$(1 \cdot 1 - 11 \cdot 7)$
Traded sex in last 12 months								, ,
No	555	24.1	1		313	3.5	1	
Yes	66	39.4	1.9	(0.8-4.6)	27	14.8	4.8	$(1\cdot 4-16\cdot 2)$
Steady partner in last 12 months who ever injected				,				` ,
No	428	24.5	1		285	3.5	1	
Yes	190	28.4	1.1	(0.7-1.7)	50	10	2.4	(0.6-9.0)

Table 1 (cont.)

	Injecting heroin users				Non	Non-injecting heroin users			
	n	HIV+ (%)	OR	95% CI	n	HIV+ (%)	OR	95% CI	
Steady partner in last 12 months who ever traded sex									
No	565	25.1	1		319	4.4	1		
Yes	37	35.1	1.6	(0.8-3.6)	13	7.7	1.8	(0.2-15.0)	
Occasional partners in last 12 months									
0	339	29.5	1		192	5.7	1		
1–2	104	28.8	1	(0.6-1.6)	52	1.9	0.3	(0.0-2.6)	
>2	171	17	0.5	(0.3-0.8)	88	3.4	0.6	(0.2-2.1)	
				Other risk	behavio	urs			
Ever been tattooed									
No	183	20.2	1		178	3.4	1		
Yes	438	28.1	1.5	(1.0-2.3)	159	5.7	1.7	(0.6-5.0)	
Ever been pierced									
No	242	29.3	1		146	4.8	1		
Yes	379	23.5	0.7	(0.5-1.0)	191	4.2	0.9	(0.3-2.5)	

Nevertheless, in comparison with another study made in 1995 in these same cities [28, 29], the prevalence is half of what it was in Barcelona and Seville, although it remains about the same in Madrid. The prevalence in NIHUs, on the other hand, is almost six times lower than in injectors.

The second finding is that for both IHUs and especially NIHUs, the prevalence is higher in women, and these differences are even larger after adjusting for the sociodemographic and behavioural factors. The combined analysis of these findings reflects a situation in sharp contrast to what Strathdee and colleagues describe in a reanalysis of various studies in North America [8, 11, 30, 31], which shows that the differences in HIV prevalence and incidence between IDUs and NIDUs, and between men and women, are not as high as in Spain. Furthermore, in studies restricted to IDUs, certain sexual behaviours (prostitution, having injecting partners, men who have sex with men, etc.) [8, 13] practically always emerge as significant correlates of HIV prevalence in the logistic analyses, indicating the important role that sexual behaviours may be playing in HIV transmission among IDUs.

In the present study, however, the considerable difference in HIV prevalence between women and men in IHUs, and especially in NIHUs, together with the low prevalence of infection found among male NIHUs, leads us to believe that sexual behaviours are

an important determinant of prevalence only in women, both in IHUs and NIHUs. In fact, no sexual behaviour was found to be associated with infection in the logistic analysis, not even homosexual relations between men when the analysis was restricted to injecting males with no more than 5 years of injection.

Nevertheless, it should be noted that this study has certain limitations in its ability to detect specific sexual behaviours that act as significant predictors: some behaviours refer only to the 12-month period before the interview, and among the NIHUs there were only 15 persons who were HIV positive, and only 101 women. It is possible that some of the persons classified as NIHUs in Madrid or Seville were in fact previous injectors, because injection has not been the predominant route for a number of years. It does not seem reasonable to suppose that this hypothetical misclassification would occur more in women than in men, since the differences in prevalence were also seen in Barcelona where injection is the predominant route. The differences between our results and those in the United States, may lie in the percentage of men in the present study who had sex with men (9.1% in IHUs and 4.6% in NIHUs), and especially in the number of men who had traded sex with other men (4.7% in IHUs and 1.6% in NIHUs), as well as the percentage who had had an injecting partner (19% in IHUs and 4.6% in NIHUs), all of which are much lower than what was found in the United States.

Table 2. Patterns of injecting and injecting risk behaviours associated with HIV prevalence among injecting heroin users from Barcelona, Madrid, and Seville [Itinere Project, 2001–2003 (crude analysis)]

		HIV+		
	n	(%)	OR	95 % CI
First main route of				
administration				
Not injecting	471	21.9	1	(1.5.0.5)
Injecting	150	38.0	2.2	(1.5-3.7)
Current main route of				
administration	200	250		
Not injecting	309	25.9	1	(0.7.1.4)
Injecting	312	25.6	1	(0.7-1.4)
Injected in last				
12 months	117	21.4	1	
No Yes	117 504	21·4 26·8	1 1·3	(0.8–2.2)
	JU T	20 0	1 3	(0 0-2 2)
Injected in last 30 days				
No.	188	23.9	1	
Yes	428	26.2	1.1	(0.8-1.7)
Aga at first injection				(* * - /)
Age at first injection <18 yr	211	39.3	2.8	(2.6-4.2)
≥18 yr	401	18.2	1	(20.2)
First drug injected				
Heroin	392	27.8	1	
Cocaine	151	19.9	0.6	(0.4-1.0)
Speed-ball	65	29.2	1.1	(0.6–1.9)
First drug injected at				
least weekly				
Heroin	352	30.7	2.9	(1.6-5.4)
Cocaine	98	21.4	1.8	(0.9-3.8)
Heroin + cocaine	51	31.4	3.0	(1·3–6·9)
Never injected weekly	115	13.0	1	
Self-injected at first				
injection	490	27.4	1	
No Yes	489 132	27·4 19·7	1 0·6	(0.4–1.0)
	132	191	0.0	(0.4–1.0)
Frequency of injecting	164	28.7	1.5	(0.9.2.6)
Every day 1–6 times a week	201	25.4	1.3	(0.8-2.6) (0.7-2.1)
Less than weekly	130	27.7	1.4	(0.8-2.5)
None	117	21.4	1	(0020)
Years since first injection				
≤5 yr of injection	279	12.9	1	
>5 yr of injection	334	35.9	3.8	(2.5-5.8)
Frequency of heroin				Í
injection in last				
12 months				
Never injected	205	25.9	1	
≤1 day/week	165	26.7	1	(0.7-1.7)
>1 day/week	251	25.1	0.9	(0.6-1.5)

Table 2 (cont.)

	(%)	OR	95 % CI
238			
238			
238			
238			
	23.1	1	
		1.2	(0.7-1.9)
236	28.4	1.3	(0.9-2.0)
205	18.5	1	
.58	27.2	1.6	(1.0-2.7)
258	30.6	1.9	$(1\cdot 2-3\cdot 0)$
243	40.7	3.6	$(2\cdot 4-5\cdot 4)$
355	16.1	1	
13	31.0	1.5	(0.9-2.3)
179	23.6	1	
49	26.5	1	(0.6-2.1)
543	24.9	1	
18	28.8	1.2	(0.8-1.9)
503	25.0	1	. ,
	236 205 58 258 243 255 13 179	28·4 28·4 28·4 28·5 28·4 28·5 28·4 28·5 28·6 28·6 28·6 28·6 28·6 28·6 28·6 28·6	28.4 1.3 28.4 1.3 28.5 1 58 27.2 1.6 58 30.6 1.9 243 40.7 3.6 555 16.1 1 13 31.0 1.5 179 23.6 1 49 26.5 1 443 24.9 1

However, the percentage of Spanish women who had had an IHU partner in the last 12 months (63.8% in IHUs and 22.7% in NIHUs) or who had ever traded sex (31.7% in IHUs and 17.7% in NIHUs) is much higher than in men (13.1% and 6.7%).

The third important finding is that, even after adjusting for the variables included in the model, IHUs who had been in prison had a 2.6 times greater risk of being infected than those who had never been in prison. This fact had been described in studies carried out in the early years of the epidemic [32]. It is noteworthy that this situation is still found in young injectors, even after adjusting for years since first injection (or in the model restricted to young injectors). Part of this effect could be due to imprisonment acting as a proxy for other variables that we cannot control but that would define a risk behaviour profile in all areas of behaviour. It may also indicate that there continues to be an increased risk of

Table 3. Risk correlates of HIV infection among young injecting heroin users and non-injecting heroin users from Barcelona, Madrid, and Seville [Itinere Project, 2001–2003 (multivariate analysis)]

	Injecting heroin users		Non-injecting heroin users		
	OR	95% CI	OR	95% CI	
City Barcelona Madrid Seville	1 1·9 1	(0·6–2·9) (0·3–4·0)	1 2·1 2·7	1 (0·4–10·9) (0·4–18·3)	
Sex Male Female	1 1·9	(1·2–3·1)	1 8·7	(2·6–29·2)	
Age group (yr) ≤25 >25			1 3·2	(0.9–11.1)	
Educational level Primary level or less Any higher level			0·3 1	(0.1-0.9)	
Ever in prison No Yes	1 2·6	(1·6–4·0)			
Ever sniffed with used tubes No Yes	1 0·5	(0·3–0·8)			
Ever been tattooed No Yes			1 2·6	(0.8–8.0)	
Ever been pierced No Yes	1 0·6	(0.4–1.0)		(* * * *)	
First drug injected at least weekly Heroin Cocaine Heroin+cocaine	2·3 1·1 2	$(1 \cdot 1 - 4 \cdot 5)$ $(0 \cdot 5 - 2 \cdot 6)$ $(0 \cdot 8 - 5 \cdot 1)$			
Never injected weekly Years since first injection ≤5 yr of injection	1	,			
>5 yr of injection >5 yr of injection × Madrid (interaction)	1·6 2·3	(0.8-3.1) (0.9-6.1)			
Ever injected with used syringe Yes No	3·4 1	(2·2–5·3)			
Backloaded in last 12 months Yes No	0·8 1	(0.4–1.3)			

infection in Spanish prisons, either because there is more injection with used syringes, or because the probability that the syringe has been used by an infected person is very high (given the high prevalence of infection among injectors in prison). If this is true, it suggests that, even in recent years, infections have occurred that were clearly preventable if exchange programmes had been implemented more efficiently

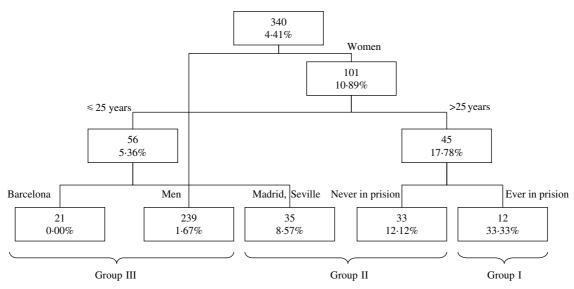


Fig. 3. Classification tree analysis for binary outcome of HIV prevalence among young adult non-injecting heroin users from Barcelona, Madrid, and Seville. The Itinere Project, 2001–2003.

and rapidly. Access to sterile syringes is legal in all Spanish prisons. However, an analysis of how this process has been implemented and the number of syringes exchanged [33] leads to the suspicion that it has developed very slowly, that the number of potential injectors may be much higher than that of real users, and that its development has an enormous symbolic value, but a very limited capacity for prevention if the current parameters of use are maintained.

The explanation for the fact that the adjusted model in IHUs shows that having sniffed with used tubes or devices or having had piercings are inversely associated with infection could perhaps be that these variables are merely indicators of a lower frequency of injection or sexual risk behaviours which have not been adequately collected in the variables introduced in the model.

This study has limitations inherent in the nature of a study of this type: a cross-sectional study in a population difficult to access, lacking a clear sampling framework, and in which most of the information is derived from self-reports. In all such studies it is very difficult to evaluate how representative the sample is. Even though intensive efforts were made to reach all possible drug use sites, the more sporadic and 'normalized' users are under-represented. Although this type of bias may have a large impact on epidemics in expansion, the evidence gathered in our field work, together with that derived from a combined analysis of various information sources, all of which show a very low incidence of new users in the heroin epidemic

in Spain [18] suggests that this was a minimal problem in the present study. The social desirability bias may have led to under-reporting of risk in injection behaviours, while the use of Audio-CASI may have helped to minimize under-reporting of sexual risk behaviours. The fact that interviews were held outside the drug social services setting may also have helped to reduce this bias.

CONCLUSIONS

This investigation has shown that, despite important geographic differences, the prevalence of HIV in IHUs continues to be high in young adult drug injectors in Spain, even in short-term IHUs. In NIHUs, on the other hand, the prevalence is almost six times lower. In both IHUs and NIHUs, women had higher prevalences than men, but this difference was especially notable in NIHUs. In fact, one could almost say that the problem of HIV infection in non-injecting users in Spain is primarily a problem for women, given the very high percentage who have a stable injecting partner. Consequently, a wide range of strategies targeting both men and women should be developed to raise their awareness of the risk of sexual relations and specifically aimed at empowering women to negotiate safe sex.

APPENDIX. The Project Itinere Group

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DECLARATION OF INTEREST

None.

REFERENCES

- 1. Nicolosi A, et al. Parenteral and sexual transmission of human immunodeficiency virus in intravenous drug users: a study of seroconversion. The Northern Italian Seronegative Drug Addicts (NISDA) Study. American Journal of Epidemiology 1992; 135: 225-233.
- 2. Thorpe LE, et al. Injection-related risk behaviors in young urban and suburban injection drug users in Chicago (1997-1999). Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology 2001; **27**: 71–78.
- 3. van Ameijden EJ, et al. A longitudinal study on the incidence and transmission patterns of HIV, HBV and HCV infection among drug users in Amsterdam. European Journal of Epidemiology 1993; 9: 255–262.

- 4. Levine OS, et al. Differences in the incidence of hepatitis B and human immunodeficiency virus infections among injecting drug users. Journal of Infectious Diseases 1996; **173**: 579–583.
- 5. Garfein RS, et al. Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. American Journal of Public Health 1996; 86: 655-661.
- 6. Diaz T, et al. Factors associated with prevalent hepatitis C: differences among young adult injection drug users in lower and upper Manhattan, New York City. American Journal of Public Health 2001; 91: 23–30.
- 7. Hahn JA, et al. Hepatitis C virus infection and needle exchange use among young injection drug users in San Francisco. *Hepatology* 2001; **34**: 180–187.
- 8. Strathdee SA, Sherman SG. The role of sexual transmission of HIV infection among injection and noninjection drug users. Journal of Urban Health 2003; 80 (Suppl. 3): 7–14.
- 9. Spittal PM, et al. Risk factors for elevated HIV incidence rates among female injection drug users in Vancouver. Canadian Medical Association Journal 2002; 166: 894-899.
- 10. Welp EA, et al. HIV prevalence and risk behaviour in young drug users in Amsterdam. AIDS 2002; 16: 1279-1284.
- 11. Shafer KP, et al. Prevalence and correlates of HIV infection among young injection drug users in San Francisco. Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology 2002; 31: 422-431.
- 12. Kral AH, et al. Trends in human immunodeficiency virus seroincidence among street-recruited injection drug users in San Francisco, 1987-1998. American Journal of Epidemiology 2003; 157: 915-922.
- 13. Doherty MC, et al. Correlates of HIV infection among young adult short-term injection drug users. AIDS 2000; 14: 717-726.
- 14. Judd A, et al. Incidence of hepatitis C virus and HIV among new injecting drug users in London: prospective cohort study. British Medical Journal 2005; 330: 24-25.
- 15. European Monitoring Center for Drugs and Drug Addiction (EMCDDA). Annual report 2004: the state of the drugs problem in the European Union and Norway. Lisbon: EMCDDA, 2004.
- 16. EuroHIV. HIV/AIDS Surveillance in Europe. End-year report 2003. No. 70. Saint Maurice: Institut de Veille Sanitaire, 2004.
- 17. de la Fuente L, et al. The transition from injecting to smoking heroin in three Spanish cities. The Spanish Group for the Study of the Route of Heroin Administration. Addiction 1997; 92: 1749-1763.
- 18. State Office for the National Plan on Drugs. Spanish Monitoring Centre for Drugs. Report No. 6. Madrid: Ministry of the Interior, 2003.
- 19. de la Fuente L, et al. Lessons from the history of the human immunodeficiency virus/acquired immunodeficiency syndrome epidemic among Spanish drug

- injectors. Clinical Infectious Diseases 2003; 37 (Suppl. 5): S410–S415.
- Watters JBP. Targeted sampling: options for the study of hidden populations. *Social Problems* 1989; 36: 416–430.
- 21. **Heckathorn DD.** Respondent-driven sampling: a new approach to the study of hidden populations. *Social Problems* 1997: **44**: 174–179.
- Breslow N, Day NE. Statistical Methods in Cancer Research. Vol 1: The analysis of case-control studies. Lyon: International Agency for Research on Cancer, 1980.
- Hosmer DW, Lemeshow S. Applied Logistic Regression, 2nd edn. New York: John Wiley & Sons Inc., 2000.
- Lemon SC, et al. Classification and regression tree analysis in public health: methodological review and comparison with logistic regression. Annals of Behavioral Medicine 2003; 26: 172–181.
- 25. **Marshall RJ.** The use of classification and regression trees in clinical epidemiology. *Journal of Clinical Epidemiolology* 2001; **54**: 603–609.
- 26. SPSS Inc. Answer Tree 2.0. Chicago: SPSS Inc., 1998.
- Bravo MJ, et al. Prevalence of indirect sharing of druginjecting paraphernalia in Galicia, Madrid, Seville and Valencia, Spain [in Spanish]. Gaceta Sanitaria 2004; 18: 472–478.

- 28. **de la Fuente L,** *et al.* The prevalence of human immunodeficiency virus infection and the risk behaviors in the heroin addicts of Barcelona, Madrid and Seville: an example of the advantages of centering studies on addicts and not just on intravenous users [in Spanish]. *Medicina Clinica (Barcelona)* 1999; **113**: 646–651.
- 29. de la Fuente L, et al. Injecting and HIV prevalence among young heroin users in three Spanish cities and their association with the delayed implementation of harm reduction programmes. Journal of Epidemiology and Community Health 2006; 60: 537–542.
- Kral AH, et al. Sexual transmission of HIV-1 among injection drug users in San Francisco, USA: risk-factor analysis. Lancet 2001; 357: 1397–1401.
- Gyarmathy VA, et al. Risk correlates of prevalent HIV, hepatitis B virus, and hepatitis C virus infections among noninjecting heroin users. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 2002; 30: 448–456.
- Zunzunegui MV, Rodríguez MA, Sarasqueta C. Intravenous drug addiction and the risk of HIV infection in Madrid in 1990 [in Spanish]. *Gaceta Sanitaria* 1993; 7: 2–11.
- Lines R, et al. Prison Needle Exchange: Lessons from a comprehensive review of international evidence and experience. Canada: Canadian HIV/AIDS Legal Network, 2004.