

EVIDENCE BASED POLICY AND PRACTICE

Injecting and HIV prevalence among young heroin users in three Spanish cities and their association with the delayed implementation of harm reduction programmes

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Objectives: To evaluate changes in the prevalence of HIV infection among young heroin users in three Spanish cities, and their association with harm reduction programmes (HRPs).

Methods: Two cross sectional studies. The 1995 study included 596 users; half were street recruited and half were recruited at drug treatment centres. The 2001–03 study included 981 street recruited users. Face to face interviews were conducted using a structured questionnaire. Samples for HIV testing (saliva in 1995 and dried blood spot in 2001–03) were collected.

Results: The proportion who had ever injected (IDUs) decreased in all three cities. HIV prevalence in IDUs decreased by half in Barcelona (44.1% to 20.8%) and Seville (44.2% to 22.2%), but remained constant in Madrid (36.8% and 34.9%). This difference was attributable to a decrease in HIV prevalence in long term IDUs in Barcelona and Seville, but not in Madrid. The crude odds ratio for HIV prevalence in Madrid compared with Barcelona in long term IDUs was 2.3 (95%CI 1.4 to 3.7), increasing to 3.1 (95%CI 1.5 to 6.2) after adjusting for sociodemographic and risk factors. HIV prevalence in short term IDUs was similar in all cities. In 1992 Barcelona already had 20 heroin users in methadone maintenance programmes (MMPs) per 10 000 population aged 15–49 years; Seville reached this rate in 1994, and Madrid, not until 1998.

Conclusions: The prevalence of HIV infection did not decrease in long term injectors in Madrid. The delayed implementation of HRPs, especially MMPs, may be the most plausible hypothesis. This finding should shed light on decision making in countries in a similar epidemiological and sociological situation.

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In 1995 a cross sectional study of prevalence of heroin injection and HIV infection was carried out in Barcelona, Madrid, and Seville.¹ These cities were chosen because of their different geographical locations, prevalence of injection,² and preventive policies.

The efficacy of harm reduction programmes (HRPs) in HIV prevention has been well described.^{3–5} HRPs were implemented in Spain during the 1990s, later than in other European countries. From only 4000 users in methadone maintenance programmes (MMPs) in 1991, the number increased to 65 000 in 1998.⁶ However, there was wide variability among regions as to HRP start up, intensity, coverage, and organisational characteristics.⁷ This delay was attributable to the opposition of some sectors, arguing what is being said in some Eastern and Central European countries to avoid implementing these programmes: that HRPs may promote injection and send “the wrong message” by not making drug cessation the only objective.^{8,9}

In 2001, a cohort study (Itinere Project) was started in the same cities. The objective of this study is to compare the results of this cohort with those of 1995 to describe the evolution of injection, HIV infection and the main risk behaviours, and to explore their possible association with the development of HRPs during the 1990s.

METHODS

Design and study population

Two cross sectional studies. The first was carried out between March and December 1995, and the second between May 2001 and December 2003. A detailed methodological description has been published elsewhere.^{10–12}

Eligibility

Age 30 or younger, residence in the metropolitan area for most of the past 12 months, and current, regular heroin user (in 1995, lifetime use at least 12 times and at least once in the past month; in 2001–03, at least 12 times in the past 12 months and at least once in the past three months). Neither of the two samples included experimental users.

Recruitment procedures

The 1995 study

About half of the participants were recruited at admission in all the public drug treatment centres (hereinafter called “treatment users”). The other half were street recruited (“street users”) by chain referral procedures, combining targeted sampling¹³ with respondent driven sampling (RDS).¹⁴ Most participants (65%) were directly recruited by interviewers at drug scenes. Neither participants nor key informants received payment for recruitment or being interviewed, but they were invited for a drink or coffee.

The 2001–03 study

The whole sample was street recruited by targeted sampling and RDS. Workers visited all drug scenes to recruit the initial participants (17.1%); 1.7% answered advertisements, 34.1% were enrolled by key informants, and 47% were enrolled by participants themselves using RDS. A monetary incentive (€18) was offered for being interviewed or for recruiting others.

Abbreviations: HRP, harm reduction programme; MMP, methadone maintenance programme; RDS, respondent driven sampling; IDU, injecting drug user

Table 1 Sociodemographic characteristics, patterns of drug use, and sexual behaviours in two cross sectional studies carried out in Barcelona, Madrid, and Seville in 1995 and 2001–03 (%)

	Barcelona		Madrid		Seville		p Value†
	1995	2002	1995	2002	1995	2002	
	207	354	199	427	190	200	
Number	%	%	%	%	%	%	
Sociodemographic characteristics							
Mean age	26.1	24.9	26.4	26.3	26.7	25.6	
Age ≤25	35.3	53.1	27.6	32.8	26.8	41.5	***
Men	74.4	69.2	75.9	71.7	83.2	82.5	NS
Foreigners	3.9	18.1	1.5	7.0	0.5	3.5	***
Level of education higher than primary	21.7	65.5	28.1	59.0	14.2	23.5	**
Regular employment	21.7	30.8	26.4	32.3	20.5	31.5	***
Job as main source of income in past 12 months	18.8	33.8	24.6	37.9	17.4	28.5	***
Living mainly in a house or apartment in past 12 months	91.8	81.9	87.9	86.8	83.7	91.5	NS
Prison							NS
Never	56.8	60	63.8	60.2	48.1	55.4	
<1 year	18.9	19.7	16.1	19.4	20.6	19.5	
≥1 year	24.3	20.3	20.1	20.4	31.2	25.1	
Sexual behaviour (past 12 months)							
Two or more sexual partners	70.4	49.2	62.2	41.7	50.3	40.1	***
Sexual relation without condoms	66.7	62.1	66.0	49.4	66.5	52.0	***
Sexual relations for money	15.5	7.9	10.7	11.0	14.5	10.0	*
Patterns of drug use and injecting							
<18 years at first heroin use	51.2	53.4	48.2	63.5	47.9	66.5	***
Injecting as first main route of heroin administration	43.5	25.1	36.7	12.4	18.9	5.0	***
≤5 years since first heroin use	30.0	37.9	32.2	22.7	21.6	25.5	NS
Ever injected	87.9	80.2	70.4	65.1	53.2	33.0	**
Injected in the past 12 months	84.1	75.7	48.2	48.9	31.1	15.5	NS
Injected in the past 30 days	82.1	67.5	31.7	39.8	26.8	10.5	NS
Injecting as current main route of heroin administration (past 30 days)	80.7	64.1	20.3	19.7	20.5	0.0	***

†Comparison between 1995 and 2001–03 in the global sample. NS, not significant. * $p<0.05$; ** $p<0.01$; *** $p<0.001$.

Data collection: interviews

A structured questionnaire was administered, including sociodemographics, social conflict, patterns of substance use, injection risk behaviour, sexual risk behaviour, and knowledge of HIV status, including dates of testing.

The 1995 study

Face to face interviews were held with treatment users in treatment centres by workers who did not belong to the staff of these centres. HIV test results were obtained from clinical records. Saliva samples were not requested. Street users were interviewed by the same workers, and a saliva sample using Orasure-Epitope was requested.

The 2001–03 study

The face to face interviews were computer assisted. Participants were interviewed in health and social services centres that were not involved in drug dependence treatment. A dried blood spot was obtained. All participants signed an informed consent form.

Procedures for HIV testing

The 1995 study

Saliva samples were analysed by ELISA (HIV 1+2 Ortho). These results were available for only 78.5%, with no significant differences by city. Given that the positive predictive value of self report for persons with both self reported and laboratory results was 94%, we accepted self reported serostatus for the 16% with no laboratory results.¹

The 2001–03 study

The dried blood samples were analysed by ELISA Genscreen HIV1/2 version 2 and New Lav Blot 1, Bio-Rad, Marnes La Coquette, France. As the self reports had a positive predictive value of 99%, only positive samples from subjects who stated they were HIV negative or had not previously been tested were confirmed by western blot.

Data on harm reduction programmes

Data on MMP patients and the number of NEPs were provided by the persons responsible for the regional drug information systems. Qualitative data were also obtained from a report on NEPs in southern Europe.¹⁵

Statistical analysis

A univariate analysis, stratified by city and cross sectional study, was performed. The analysis was then restricted to the 1051 users who had ever injected (IDUs). The significant differences between the two cross sectional studies were analysed using the χ^2 test, Student's *t* test, and Fisher's exact test.

Subsequent analyses focused on how the prevalence of HIV in IDUs had evolved in each city, stratifying by years since first injection (≤ 5 years, >5 years). Crude odds ratios with their 95% confidence intervals were calculated for each city in the four strata resulting from crossing the two studies (1995 and 2001) and the two categories of the variable "years since first injection". To determine if differences in the prevalence of infection by city in each of the four strata were attributable to differences in sample characteristics (arising from possible selection biases), the ORs were adjusted for sociodemographics and risk behaviours in four logistic regression models (one per stratum), in a model in a single step that included all the adjustment variables. The analysis was performed with SPSS (SPSS for Windows, version 12.0, 2003, Chicago) and Stata (Stata Statistical Software, release 8.0, 2003, College Station, TX).

RESULTS

Sociodemographic characteristics

A total of 596 participants were recruited in 1995 and 981 in 2001–03 (table 1). There were about three men for each woman. Subjects in the 2001–03 study were significantly younger (41.9% aged 25 or younger *v* 30%); had a higher

Table 2 Injecting behaviours of young heroin users who had ever injected in two cross sectional studies carried out in Barcelona, Madrid, and Seville in 1995 and 2001–03 (%)

Number	Barcelona		Madrid		Seville		p Value†
	1995	2001–03	1995	2001–03	1995	2001–03	
	182	284	140	278	101	66	
	%	%	%	%	%	%	
<18 at first injection	33.5	32.2	40.0	36.0	35.6	40.6	NS
Self injected at first injection	26.0	21.8	18.6	19.8	21.8	24.2	NS
≤ 5 years since first injection	36.8	51.9	35.7	40.8	24.8	35.9	***
First drug injected							***
Heroin	95.0	84.2	73.0	46.3	86.0	56.9	
cocaine, or cocaine+heroin mix	5.0	12.6	27.0	53.7	14.0	43.1	
Drugs most frequently injected‡							***
heroin	93.5	39.7	71.0	10.0	96.0	16.7	
cocaine, or cocaine+heroin mix	6.5	60.4	29.0	90.4	4.0	83.9	
Ever injected with a syringe used by someone else	72.0	41.6	60.7	39.6	62.7	38.2	***
Injected with a syringe used by someone else in past 12 months	33.0	23.2	20.0	15.1	18.8	6.6	**
Injected with a syringe used by someone else in past 30 days	7.1	10.9	7.9	7.0	12.9	3.3	

†Comparison between 1995 and 2001–03 in the global sample. NS, not significant. *p<0.05, **p<0.01, ***p<0.001. ‡Past 30 days in 1995, and past 12 months in 2001.

educational level, were more often foreigners (11% v 2%), more frequently had regular employment (31.5% v 23%), and more often derived their main source of income from work (34% v 20%). The two studies had about the same proportions of persons who were homeless most of the time or lived in institutions (<15%), or who had ever been in prison (40%).

Sexual behaviour

In all three cities there was a significant decrease in the proportion of persons who had had vaginal or anal relations with more than two persons of the opposite sex during the 12 months (from 61.3% to 44.1% overall) or who had had sexual relations in exchange for money (from 13.5% to 9.7%). In the latter case, the change was because of a major decrease among women, especially in Barcelona, as there was no significant change among men. There was also a significant reduction in the percentage of persons who had had sexual relations without condoms in the past 12 months (from 66.4% to 54.5%), which was mainly attributable to the decrease among men (from 66.5% to 48.5%) (table 1).

Patterns of drug use and prevalence of injecting

The percentage of those who began to use heroin before age 18 years and of users aged 25 years or younger was higher in

2001–03. However, whereas in Barcelona and Seville there was a significant decrease in all indicators of injecting prevalence, in Madrid the prevalence of injection in the past 30 days increased (from 31.7% to 39.8%) (table 1). In Seville, in 2001–03 no one stated that injecting was their current main route of administration.

Patterns of injecting and prevalence of injecting risk behaviour (table 2)

In ever injectors (423 in 1995 and 628 in 2001–03), there was no significant change in the proportion of those who injected for the first time before age 18 (36.2% and 34.7%), or in those who were injected for the first time by someone else (77.5% and 78.8%), but the proportion of those who had injected for five years or less changed significantly (33.6% and 45.3%). There was also a major change in the substances injected. Whereas in 1995 cocaine—alone or mixed with heroin—was the first drug injected for just 14.4%, and was the drug most frequently injected in the past 12 months for just 11%, the corresponding figures for 2001–03 were 35.4% and 73.7%, respectively. This change was notable in Seville, and even more so in Madrid. There was a significant decrease in the prevalence of those who had ever injected with borrowed needles or syringes (from 66.4% to 40.4%) or who had done

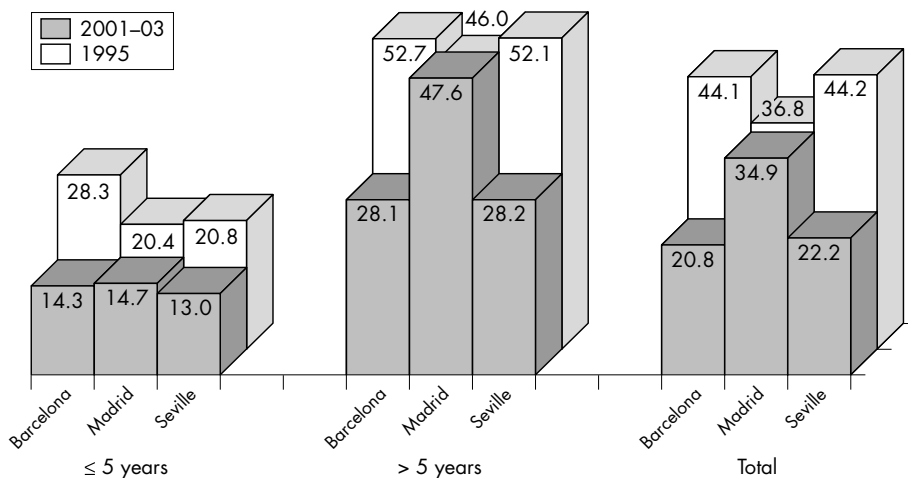


Figure 1 Prevalence of HIV infection among young injecting heroin users in two cross sectional studies carried out in Barcelona, Madrid, and Seville in 1995 and 2001–2003, by time since first injection.

Table 3 Crude and adjusted odds ratios and confidence limits of association between HIV prevalence, and city by year of cross sectional study and years since first injection. Young heroin users who had ever injected in two cross sectional studies carried out in Barcelona, Madrid and Seville in 1995 and 2001–03

Years since first injection	City	1995		2001–03	
		Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
≤5	Barcelona	1	1	1	1
	Madrid	0.6 (0.2 to 2.0)	0.9 (0.1 to 6.5)	1.0 (0.5 to 2.0)	1.3 (0.5 to 3.5)
	Seville	0.7 (0.3 to 1.6)	0.2 (0.0 to 1.2)	0.9 (0.2 to 3.2)	0.7 (0.1 to 4.3)
>5	Barcelona	1	1	1	1
	Madrid	0.8 (0.4 to 1.3)	1.2 (0.5 to 2.8)	2.3 (1.4 to 3.7)	3.1 (1.5 to 6.2)
	Seville	1 (0.5 to 1.8)	1.3 (0.6 to 2.3)	1.0 (0.5 to 2.3)	1.5 (0.5 to 4.8)

Adjusted for the following variables (included and retained in the model): sex, employment status, educational level, prison, first drug injected, drug most frequently injected, sexual relation without condoms, sexual relations for money, injected in past 30 days, ever borrowed, and borrowed in past 30 days.

so in the past 12 months (from 25.3% to 17.9%), whereas the proportion of those who had done so in the past 30 days remained stable.

Prevalence of HIV in injection drug users (fig 1)

The percentage of HIV infected IDUs decreased by about half in Barcelona (from 44.1% to 20.8%; $p < 0.001$) and Seville (from 44.2% to 22.2%; $p < 0.01$), whereas it remained practically the same in Madrid (36.8% and 34.9%). After stratifying by years since first injection, this differential trend was seen to be attributable to a change in those who had injected for more than five years (long term injectors). The prevalence in this group decreased in Barcelona (52.7% in 1995 and 28.1% in 2001–03; $p < 0.001$) and Seville (52.1% and 28.2%; $p < 0.01$), but not in Madrid (46.0% and 47.6%) (fig 1). In contrast, the prevalence of infection among those who had injected for five or fewer years decreased in all three cities, although the difference did not reach statistical significance in Seville because of the small sample size. In Madrid, 55% of long term injectors had been diagnosed as HIV positive before 1998, and in another 12% of cases it is reasonable to assume that they were infected before that year (considering various parameters: date of first injection and date and result of their tests). An analysis of the crude odds ratios of prevalence by city and of the logistic regression models shows that adjusting for sociodemographic variables and risk behaviours does not change the findings of the stratified analysis; significant differences among cities were found only in long term injectors in Madrid in 2001–03, whereas the odds ratio

What is already known about the topic

The efficacy of harm reduction programmes (methadone maintenance and needle exchange) to prevent HIV infection has been recognised since the end of the 1980s.

in comparison with Barcelona increased after adjustment, from 2.3 (CI:1.4 to 3.7) to 3.1 (CI:1.5 to 6.2) (table 3).

Development of harm reduction programmes

NEPs in all three cities began in 1991. In 1996 the rate of syringes per 10 000 population aged 15–49 years was 181 in Madrid region and 297 in Barcelona. In 1998 both areas had similar rates (around 500). However, whereas there were only 55 syringe exchange points in Madrid region, there were

What this paper adds

- The main finding of this study is the differential trend in HIV prevalence in long term injectors in Madrid compared with those in Barcelona or Seville.
- The delayed implementation of harm reduction programmes probably meant a lost opportunity to prevent HIV dissemination in Madrid.

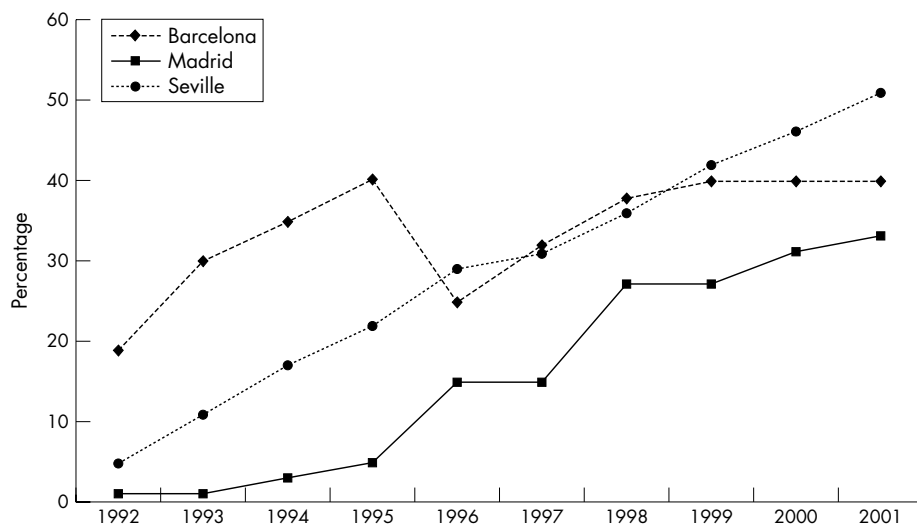


Figure 2 Rate of persons in methadone treatment per 10 000 population aged 15–49 years in Madrid, Barcelona, and Seville, 1992–2001.

more than 150 in Barcelona. This was largely because of the participation of pharmacies, which represented 90% or more of syringe exchange points. In Seville, these programmes were much less well developed as the number of persons who injected as the main route had decreased, although no good data are available on the number of syringes distributed. With respect to MMPs, whereas in Barcelona 20 persons per 10 000 population aged 15–49 were already being treated with methadone in 1992, and in Seville this rate was exceeded in 1995, this rate was not reached in Madrid until 1998 (fig 2).

DISCUSSION

The main finding of this study is the differential trend in the prevalence of HIV in IDUs in Madrid in comparison with those in Barcelona or Seville. In 1995, all three cities had an extremely high HIV prevalence. Six or seven years later the prevalence had decreased by half in Seville and Barcelona, whereas it remained practically the same in Madrid, because HIV prevalence in Madrid did not decrease among those injecting for longer than five years.

What could explain this differential trend? Firstly, it could simply be attributable to selection biases in recruitment. However, this hypothesis, although impossible to rule out, is unlikely. In 1995, there were no significant differences in HIV prevalence between treatment IDUs and street IDUs. In 2001–03, the main recruitment method was RDS, followed by recruitment by users over 30 or former users. Over 80% of the participants in the three cities were recruited using these two methods. RDS strongly reduces the most important biases that could be introduced by targeted sampling.¹⁴ Other indicators of uniform recruitment methods among cities in 2001–03 were the similar proportions of people who had been in treatment in the past 12 months (60% in Barcelona and Madrid and 66% in Seville), and of those who had obtained at least half of their syringes through NEPS (over 85%). Finally, the crude odds ratio for HIV prevalence among long term injectors in Madrid in comparison with Barcelona in 2001–03 was 2.3 (95% CI 1.4 to 3.7), and rose to 3.1 (95% CI 1.5 to 6.2) after adjusting for sociodemographic characteristics or risk behaviours, which suggests that the difference is not explained by a differential recruitment bias for these characteristics.

A second explanation could be differences in the strategy of laboratory analysis. These differences are unlikely to introduce major bias, given that we are dealing with injectors with a high prevalence of infection, and because the biases that might be produced by the different types of samples (lower sensitivity in saliva) and by not carrying out a confirmation test (not ruling out some false positives) would tend to cancel each other out.

Thirdly, the differential trend could be attributable to different rates of mortality or migration. However, there is no evidence of lower mortality in Madrid; if anything, the reverse may be true: 48.9% of those infected in Barcelona had been in antiretroviral treatment, compared with 38% in Madrid and 35% in Seville. No information is available to evaluate migration, but a restricted analysis of those who had

lived over five years in each city did not change the trends in HIV prevalence.

Fourthly, the differential trend might be attributable to the different availability among cities of treatments with a high capacity for retention (as is the case of methadone). However, considering the time when these programmes were implemented in each city, it is logical to think that the differential trend found in Madrid should actually be much larger.

Fifthly, the trend could be attributable to a phenomenon that constitutes another important finding of this study: that cocaine or heroin-cocaine mixtures are replacing heroin as the most frequently injected substance in the three cities. This change has also been described,¹⁶ and is of concern, because the risk of HIV infection is much higher among cocaine injectors.¹⁷ Although this does not seem to be the main reason why HIV prevalence has not decreased in Madrid (the variable was included in the adjusted model), it suggests we may need to rethink the role of HRP. Another hypothesis is whether this differential trend could be related with the implementation of HRP. The data on harm reduction programmes show that 20 persons per 10 000 population aged 15–45 years were in MMPs in Barcelona in 1992 and in Seville in 1995, whereas in Madrid this rate was not reached until 1998, despite ample knowledge of the preventive capacity of MMPs.^{3,4} In the mid-90s, this difference between Madrid and Barcelona had already been noted,⁷ a difference that was even more important given the estimated number of users in each city—higher in Madrid than in Barcelona.^{18,19} In fact, among HIV positive IDUs in Madrid who had injected for over five years, more than two of three became infected before 1998, before MMPs could have benefited a large number of users.

Few data are available to evaluate the association between the trend in HIV infection and syringe exchange programmes. The programmes in all three cities began in 1991. However, in Seville the percentage of frequent injectors was already very low, so that the demand for syringes was, logically, lower. Thus, it is difficult to compare the data from Seville with Madrid and even more so with Barcelona.²

Although an aetiological association cannot be established between the late development of HRP, especially MMPs, in Madrid and the continued high prevalence of HIV in long term IDUs, we know of no more plausible hypothesis that can better explain the differential evolution in these cities. It would be useful to have data on the use of preventive services during the years in which the differential HIV incidence among cities seems to have occurred. Such information could have helped strengthen the hypothesis about the effect of methadone availability. Unfortunately, however, our data on the use of services refer to lifetime use or to the past 12 months. However, HRP obviously not only have a direct effect on those who use them, but also have an indirect effect on the community at large.²⁰ What is more, Seville and Barcelona started with a disadvantage, as they had higher prevalences in the mid-90s. Furthermore, the trend in young injectors, who were able to benefit more consistently in each city, has been similar in all three cities, and preliminary data on HIV incidence in Barcelona and Madrid in the 2001–03 study show a similar incidence among IDUs in both cities.²¹

Furthermore, indicators of injecting in 2001–03 confirmed the trend described in 1995.¹¹ This downward trend began in the early 1980s. At least in the early stages there must have been other decisive factors in addition to the catalysing effect that HIV prevention policies may have had in producing the changes that occurred in all areas.^{11,22}

In all three cities the percentage of those who had ever injected with used syringes also decreased. Some authors have suggested that the concomitant existence of different

Policy implications

To curtail an HIV epidemic, harm reduction programmes must be developed on time and on a scale proportional to the damage observed. The Spanish experience may facilitate decision making in other countries with similar social and epidemiological conditions.

prevalences of HIV infection and similar prevalences of risk behaviours among geographical areas could partly be explained by the type of heroin in each area.²³ As brown heroin must be heated before it can be dissolved, it is thought this could inactivate the virus and decrease transmission.²⁴ In our study, however, this does not seem to be a plausible explanation. By the mid-1990s, brown heroin was already practically the only type that existed in Madrid and Seville, whereas white heroin continues to exist in Barcelona.

Although it is difficult to confirm definitively, all the evidence suggests that Madrid lost an opportunity to prevent the dissemination of HIV among injectors during the first half of the 1990s by not rapidly implementing MMPs while other cities were doing so. A similar situation may currently be taking place in other areas which already have high prevalences of infection,²⁵ but which in some cases even prohibit MMPs. The description of what has happened in Spain may facilitate decision making in a context of public debate on the effectiveness of certain measures.

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