We are IntechOpen,
the world's leading publisher of
Open Access books
Built by scientists, for scientists

6,900
Open access books available

186,000
International authors and editors

200M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

BOOK CITATION INDEX
CLARIVATE ANALYTICS
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

HIV Infection and Viral Hepatitis in Drug Abusers

Arantza Sanvisens, Ferran Bolao, Gabriel Vallecillo,
Marta Torrens, Daniel Fuster, Santiago Pérez-Hoyos,
Jordi Tor, Inmaculada Rivas and Robert Muga

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/53074

1. Introduction

The epidemiology of HIV infection and viral hepatitis among injection drug users (IDUs) is changing in western countries; reductions in the epidemic of blood-borne infections, such as HIV infection, and viral hepatitis among drug users are probably related to the generalization of harm-reduction interventions and to the treatment of both HIV/AIDS and substance abuse. Opioid substitution therapy for the treatment of patients with heroin dependence, needle exchange programmes, access to Highly Active Antiretroviral Therapy (HAART) and supervised injecting facilities, among other preventive interventions, have contributed to reduce the impact of the HIV epidemic among drug users.

Surveillance of HIV infection in Spain is available in 15 out of the country's 17 autonomous regions. According to the National AIDS Programme, 2,264 new HIV infections were diagnosed in 2009, which represents 79 cases per million of the population [1].

As previously reported [2], the beginning of the HIV epidemic in Spain was largely driven by IDUs and the initial decrease in the rates of infection were reported more than a decade ago [3]. In 2009, 77% of new HIV infections were reported as sexually transmitted and IDUs represented less than 8% of cases [1].

The HIV epidemic among IDUs continues to develop differently across different parts of Europe. In the European Union, the reported rates of newly diagnosed cases of HIV infection in IDUs are mostly stable or in decline [4]. Data on newly reported cases of HIV infection in IDUs for 2009 suggest that rates of infection are still declining in Europe, following a peak in 2002, which was due to outbreaks in eastern countries. Reductions in the rates of HIV infection in IDUs are partially the result of better preventive interventions and access to care

[5,6], however, Spain is one of the western European countries reporting high rates of newly diagnosed HIV infection among IDUs between 2004 and 2009 (Figure 1)[4].
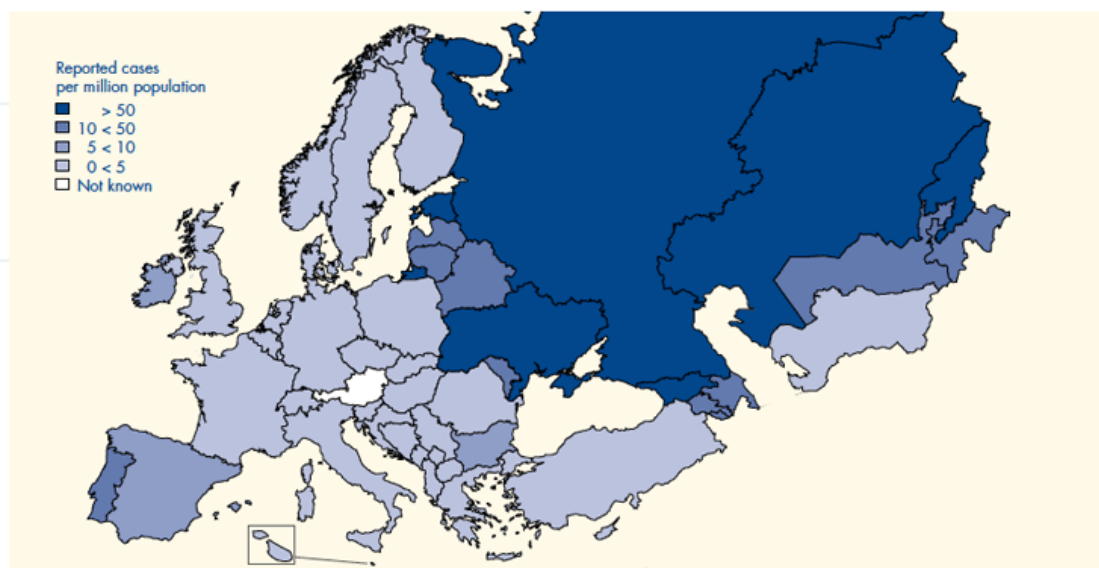

Figure 1. Newly diagnosed HIV infections among IDUs from Europe and central Asia in 2009. Source: *Annual Report 2011*, European Monitoring Centre for Drugs and Drug Addiction(4).

Several studies have shown that IDUs are at increased risk of sexually transmitted HIV infection [7,8] and other authors have shown higher rates of HIV infection among recent and younger IDUs [9,10].

Non-injecting drug users (non-IDUs) are not exposed to blood-borne infections, but remain at risk of sexually transmitted diseases including HIV. Some studies have found a relationship between non-IDU and the increased risk of HIV and other sexually transmitted diseases [11,12]. Moreover, there have been reports on the causal relationship between alcohol drinking and the risk of HIV infection [13-15].

1.1. Hepatitis B and C

About 80% of individuals exposed to hepatitis C virus (HCV) infection and 5% of adults exposed to hepatitis B virus (HBV) infection develop chronic liver disease. Cirrhosis and hepatocellular carcinoma are the most important sequelae of these infections [16].

It is well known that HCV infection is highly prevalent among drug users and that many IDUs contract the infection early in the course of injecting drugs; this implies that there may be only a small time window for initiating preventive interventions to reduce transmission of HCV infection.

About 10 million IDUs (range 6.0-15.2 million) worldwide were anti-HCV positive in 2010 and 1.2 million IDUs (range 0.3-2.7 million) were HBV infected (HBsAg positive). Geographical differences exist in the distribution of blood-borne infections among drug users and

eastern Europe, east Asia and southeast Asia have the largest populations of IDUs infected with viral hepatitis [4,17].

Two major risk factors for HBV infection include the IDU his/herself and unprotected sex [18-21]. Studies among drug users from the United States have shown that 70% of cases are infected within five years of initiating drug use [22] and that 38%-89% of IDUs from Europe and North America have markers of HBV infection in cross-sectional studies [23].

In 2004, 16% of acute viral hepatitis reported to the Center for Disease Control in the United States had recent use of injected drugs as a risk factor [24].

In any case, the epidemiology of hepatitis B virus infection in drug users and other subpopulations at risk may vary according to the extent of preventive immunization; in Spain, the first selective hepatitis B vaccination programme began in 1984 [25].

In this study among IDUs and non-IDUs seeking treatment of substance abuse in Barcelona, Spain, we aimed to analyse trends in the epidemiology of HIV, HCV and HBV infections.

2. Patients and methods

2.1. Setting and study population

Prospective study in a cohort of patients admitted to substance abuse treatment programmes in three teaching hospitals between January 1997 and December 2006. The treatment units are located in Barcelona (Hospital del Mar), Badalona (Hospital Universitari Germans Trias i Pujol) and L'Hospitalet de Llobregat (Hospital Universitari de Bellvitge).

Patients admitted to treatment were referred from primary care centres and the principal criterion for admission was the severity of addiction. Patients were required to be older than 18 years and the main objective of admission was to control signs and symptoms of withdrawal. Upon admission, we collected socio-demographic characteristics, the history of substance abuse (main drug, age at first drug use, route of administration, history of opioid substitution treatment) and blood samples to test for HIV infection, HCV infection and HBV (HBcAb) infection, as previously reported [26,27].

The blood samples were tested by Enzyme ImmunoAssay (EIA) for antibodies to HIV infection and the results were confirmed by Western blot.

At discharge, patients were referred to their primary care providers. Pharmacological treatment was recommended in the majority of cases and all patients were advised to continue with medical visits at the outpatient clinics.

For the purposes of this study, patients who were admitted more than once between 1997 and 2006 were analysed only with regard to the first admission. Similarly, data from two hospitals were controlled so that no duplicate patients existed.

All the participants gave their consent for the determination of HIV and hepatitis serology. The methods utilized to perform this study complied with ethical standards for medical research and with principles of good clinical practice.

2.2. Statistical analysis

Bivariate analyses were performed on the characteristics of patients according to the route of drug administration: 1) non-IDU patients were defined as those individuals without a history of injection drug use; 2) IDU patients were defined as those with current or past use of intravenous drug use. The bivariate analyses included the χ^2 Pearson test for categorical variables and Student's t test for continuous variables.

Prevalent cases correspond to patients that tested HIV, HCV or HBV-positive at admission.

Incident cases were defined as those HIV-seronegative patients at admission that subsequently became HIV-positive during follow-up.

We carried out a direct measurement of HIV incidence based on the follow-up of the initially HIV-seronegative patients. However, due to the relatively low percentage (44%) of patients that underwent new HIV tests, we used a sensitivity analysis in a scenario based on the absence of new infections among those not re-tested for HIV infection during follow-up. Sensitivity analysis is useful in predicting the outcome of a decision if a situation turns out to be different compared to that which was previously assumed. By creating a given set of scenarios, the method can determine how changes in one variable will impact on the results.

All incidence rates were calculated in person-years with the number of HIV infections (incident cases) in the numerator and the sum of follow-up times in the denominator.

Joinpoint regression models were fitted to analyse changes in trends of HIV and viral hepatitis over time. These models evaluate changes that are produced on a logarithmic scale with a binomial distribution for the prevalence of infection and a Poisson distribution for the incidence of infection.

Descriptive analyses of the data were performed with STATA, version 8.0 (Stata Corp., College Station, TX, USA). For the Joinpoint regression models, we used the US National Cancer Institute's Joinpoint Regression Program software [28].

P values less than 0.05 (p<0.05) were considered statistically significant.

3. Results

3.1. Characteristics of the study population

Between January 1997 and December 2006 there were 3,318 admissions corresponding to 2,488 patients, of which 2,432 were eligible. Median age at admission was 34 years (IQR: 29 - 40 years) and 78.7% were men. A total of 925 (38%) patients were non-IDUs and 1,507 (62%) were current or past IDUs.

The baseline characteristics of the patients according to the antecedent of IDU/non-IDU are presented in Table 1. The majority of non-IDUs cases were patients with alcohol use disorders.

The main drug of abuse in IDUs patients was opiates (57.8%) and the median duration of drug abuse was 12 years (IQR:5 – 17 years); 28.9% of them were receiving methadone at admission. Non-IDU patients were significantly older (37 years, IQR 30 – 45 years) than in IDU (32 years, IQR 28 – 37 years) (p<0.05). The non-IDU were admitted mostly (65.1%) during the 2002 – 2006 period, whereas IDUs were admitted mostly (63%) during the 1997 – 2001 period (p<0.05). As expected, the prevalence of HCV infection was significantly higher in IDUs (86.6%) than in non-IDUs (9.7%) (p< 0.05). In this sense, the prevalence of hepatitis B virus infection (HBcAb-positive) was significantly higher in IDUs (56.8%) than in non-IDUs (17.7%) (p<0.05) (Table 1).

	Non-IDU	IDU	
	N=925	N=1507	p-value
	N (%)	*n (%)*	
Male	726 (78.5)	1188 (78.8)	0.840
Age *median [IQR]*	37 [30-45]	32 [28-37]	<0.05
Year of admission *median [IQR]*	2003 [2000-2005]	2000 [1998-2003]	<0.05
Period of admission			
1997-2001	323 (34.9)	949 (63.0)	
2002-2006	602 (65.1)	558 (37.0)	<0.05
Duration of drug abuse, years			
(n=1888) *median [IQR]*	10 [5-18]	12 [5-17]	0.079
HIV positive	26 (2.8)	636 (42.2)	<0.05
HCV positive (n=2394)	88 (9.7)	1284 (86.6)	<0.05
HBcAb positive (n=1890)	136 (17.7)	636 (56.8)	<0.05
Main drug of abuse (n=2421)			
Opiates	231 (25.1)	867 (57.8)	
Alcohol	432 (46.9)	124 (8.3)	
Other	258 (28.0)	509 (33.9)	<0.05
Antecedent of imprisonment (n=2291)	168 (19.4)	716 (50.2)	<0.05
Methadone* (n=1499)	46 (7.7)	261 (28.9)	<0.05

* Available in two hospitals

Table 1. Characteristics of IDU and non-IDU patients admitted to substance abuse treatment programmes in the Barcelona area, Spain, 1997-2006.

3.2. HIV infection

Table 2 shows the prevalence and incidence of HIV infection in non-IDUs according to the year of admission. Regarding HIV prevalence, 2.8% (95% CI: 1.8-4.1) of patients were HIV-positive at admission with the highest prevalence of infection observed in 1999 (8.3%).

Among the 899 non-IDU, HIV-negative patients, 364 (40.5%) were followed-up for a median of 2.3 years (IQR: 0.9 – 4.1 years; 1060 p-y); only five patients acquired HIV infection during follow-up (incidence rate 0.47 x 100 p-y; 95% CI: 0.2-1.1).

The prevalence of HIV in IDUs was 42.2% (636/1507). The highest prevalence was observed in 1997 (45.1%) and the lowest in 2006 (32.1%).

Among the 871 IDUs, HIV-negative patients, 47.1% were followed for a median of 2.7 years (IQR: 1.2 - 5.2 years, 1415.5 p-y) and 36 acquired HIV infection (incidence rate 2.54 x 100 p-y (95% CI: 1.8-3.5); the highest rate of infection was observed in 1999 (3.7 x 100p-y). Patients followed-up were similar to those not followed regarding the proportion of male/female, the main drug of abuse and the prevalence of HCV infection and HBV (HBcAb) infection.

	HIV PREVALENCE		HIV INCIDENCE				Incident rate	
			Patients at risk	Patients followed	P-Y	Incident cases		
	n (%)	95% CI		n (%)			x100 p-y	95% CI
1997	0 (0.0)	--	51	24 (47.1)	13.7	0	0.00	--
1998	2 (3.3)	(0.4-11.3)	59	30 (50.8)	37.8	1	2.65	(0.4-18.8)
1999	5 (8.3)	(2.8-18.4)	55	25 (45.5)	52.1	0	0.00	--
2000	2 (2.7)	(0.3-9.4)	72	24 (33.3)	71.1	0	0.00	--
2001	1 (1.3)	(0.03-7.0)	76	34 (44.7)	93.9	0	0.00	--
2002	4 (3.9)	(1.1-9.6)	99	44 (44.4)	112.8	0	0.00	--
2003	2 (1.7)	(0.2-6.0)	116	50 (43.1)	138.3	1	0.72	(0.1-5.1)
2004	3 (2.5)	(0.5-7.0)	119	50 (42.0)	170.1	1	0.59	(0.1-4.2)
2005	3 (2.5)	(0.5-7.0)	118	35 (29.7)	184.9	1	0.54	(0.1-3.8)
2006	4 (2.9)	(0.8-7.2)	134	48 (35.8)	185.3	1	0.54	(0.1-3.8)
1997-2006	26 (2.8)	(1.8-4.1)	899	364 (40.5)	1060	5	0.47	(0.2-1.1)

Table 2. HIV serial prevalence and HIV serial incidence among non-IDUs by year of admission to substance abuse treatment programmes in the Barcelona area, Spain, 1997-2006.

Table 3 shows the prevalence and incidence of HIV infection in IDUs according to the year of admission, ultimately showing values slightly lower than the rates registered since 1999.

Trends of HIV prevalence in non-IDUs is shown in the upper part of Figure 2 (Graphic A). Overall, changes in HIV prevalence were not statistically significant, in spite of the model indicating a decrease in prevalence over time (p=0.24).

In terms of HIV incidence (Figure 2, Graphic B), the model shows statistically significant differences over time (p=0.004).

The trend of HIV prevalence in IDUs showed a significant (p=0.01) decline between 1997 and 2006 (Figure 3, Graphic A). With respect to HIV incidence among IDUs, no changes in the trends of infection rate were detected after adjusting the regression model (p=0.944) (Figure 3, Graphic B).

	HIV PREVALENCE		Patients at risk	Patients followed	P-Y	Incident cases	Incident rate	
	n (%)	95% CI		n (%)			x100 p-y	95% CI
1997	124 (45.1)	(39.1-51.2)	151	84 (55.6)	45.3	1	2.21	(0.3-15.7)
1998	84 (43.5)	(36.4-50.8)	109	63 (57.8)	102.4	2	1.95	(0.5-7.8)
1999	83 (44.4)	(37.1-51.8)	104	52 (50.0)	133.3	5	3.75	(1.6-9.0)
2000	71 (41.8)	(34.3-59.6)	99	47 (47.5)	153.5	3	1.95	(0.6-6.1)
2001	53 (42.7)	(33.9-51.9)	71	29 (40.8)	163.3	4	2.45	(0.9-6.5)
2002	59 (38.6)	(30.8-46.8)	94	35 (37.2)	168.9	3	1.77	(0.6-5.5)
2003	50 (42.7)	(33.6-52.2)	67	31 (46.3)	174.0	6	3.45	(1.5-7.7)
2004	53 (42.7)	(33.9-51.9)	71	31 (43.7)	175.6	5	2.85	(1.2-6.8)
2005	34 (39.5)	(29.1-50.7)	52	21 (40.4)	160.4	4	2.49	(0.9-6.6)
2006	25 (32.1)	(21.9-43.6)	53	17 (32.1)	138.8	3	2.16	(0.7-6.7)
1997-2006	636 (42.2)	(39.7-44.7)	871	410 (47.1)	1415.5	36	2.54	(1.8-3.5)

Table 3. HIV serial prevalence and HIV serial incidence in IDUs by year of admission to substance abuse treatment programmes in the Barcelona area, Spain, 1997-2006.

In sensitivity analysis, the rate of HIV infection among non-IDUs was 0.19x100 p-y (95% CI: 0.07-0.45) and 1.08 x100p-y (95% CI: 0.5-1.5) among IDUs.

In sensitivity analysis, trends of HIV incidence for non-IDU patients remained unchanged with respect to the direct method. However, HIV incidence for IDUs significantly decreased over time in the best scenario (no new infections among those lost to follow-up, p=0.04).

3.3. Viral hepatitis

The prevalence of HCV infection and HBV (HBcAb) infection in non-IDUs was 9.7%, and 17.7%, respectively. The prevalence of HCV in the years analysed oscillated between 6.8% and 15.6%, but differences were not statistically significant (p=0.589) (Figure 4, Graphic A). As expected, the prevalence of HCV infection in IDUs was high (86.6%) and changes over the years analysed were negligible (p=0.240) (Figure 5, Graphic A).

The prevalence of HBV (HBcAb) infection in non-IDUs oscillated between 8.3% and 22.9%, and changes over time were not statistically significant (p=0.696) (Figure 4, Graphic B). HBV (HBcAb) infection was observed in 56.8% of IDUs, which oscillated between 48.8% and 64.3% in the years analysed. Analysis of the trend did not show statistically significant differences during the period analysed (p=0.218) (Figure 5, Graphic B).
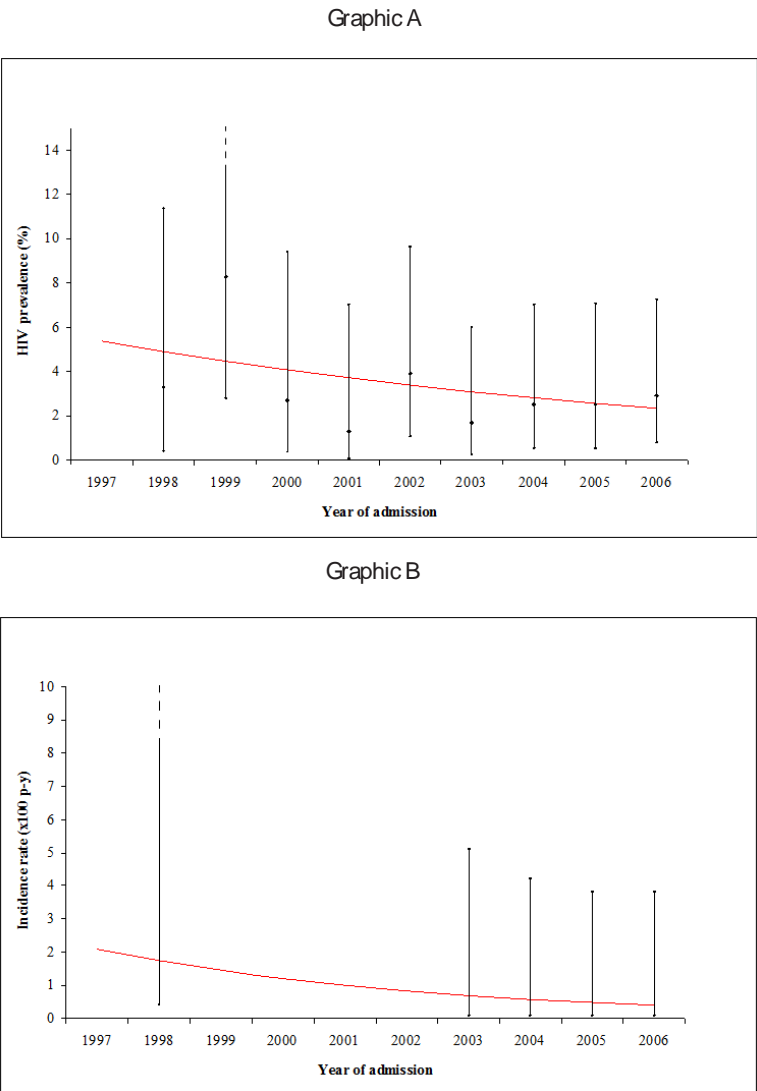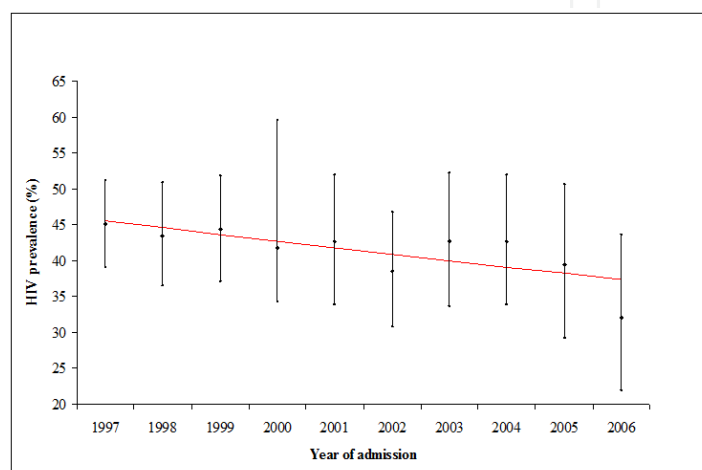
Graphic A

Graphic B

Figure 2. Trends in HIV prevalence (Graphic A) and HIV incidence (Graphic B) in non-IDU patients admitted to substance abuse treatment programmes in the Barcelona area, Spain, 1997- 2006.
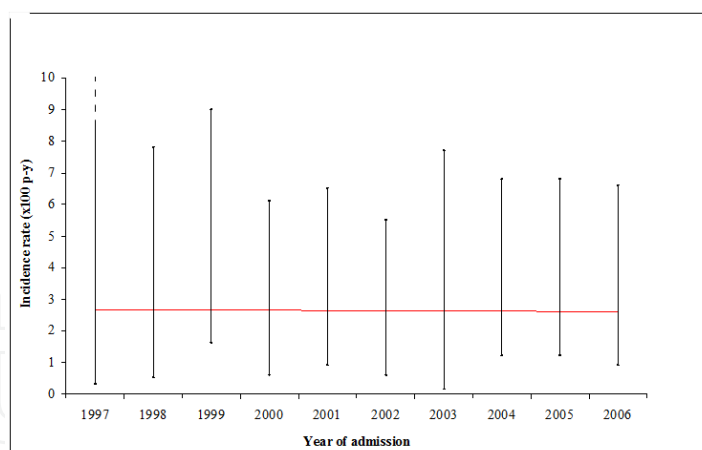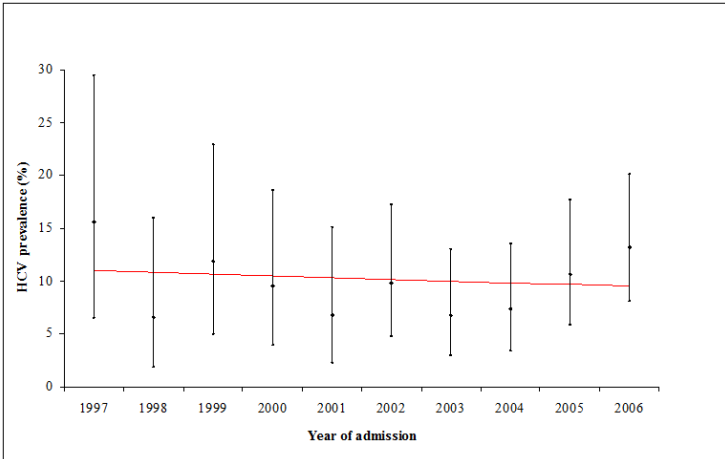
Graphic A

Graphic B

Figure 3. Trends in HIV prevalence (Graphic A) and HIV incidence (Graphic B) in IDUs admitted to substance abuse treatment programmes in the Barcelona area, Spain, 1997- 2006.

Graphic A

Graphic B

Figure 4. Prevalence of HCV infection (Graphic A) and HBV infection (Graphic B) in non-IDUs admitted to treatment programmes in the Barcelona area, Spain, 1997- 2006.

Graphic A

Graphic B

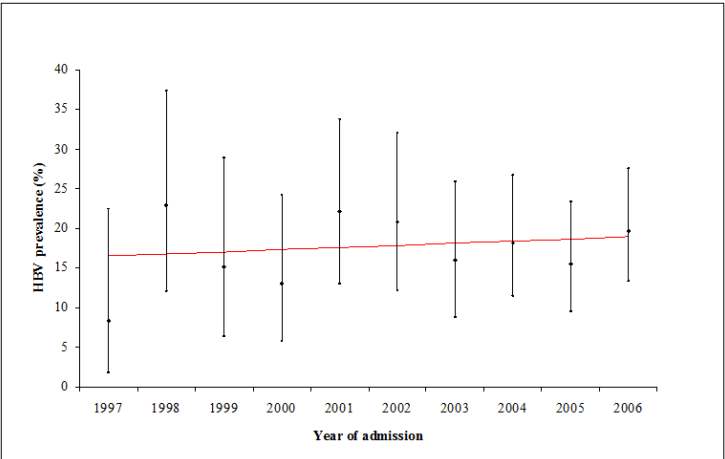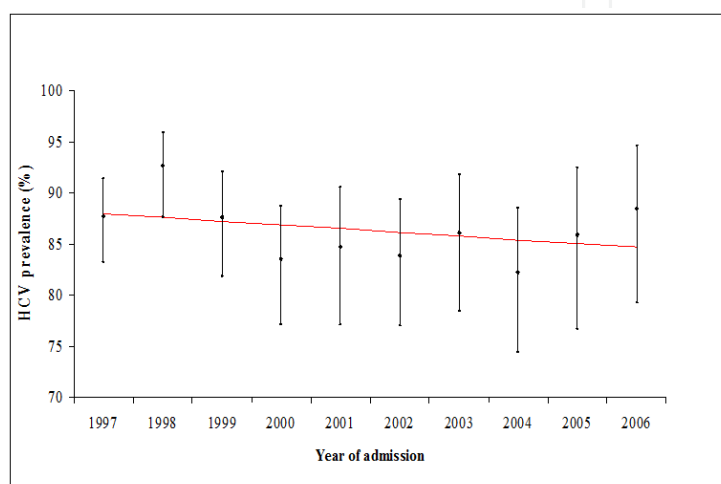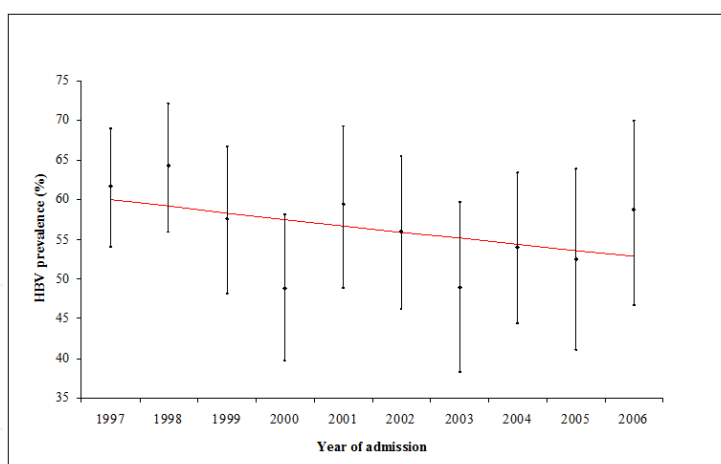**Figure 5.** Prevalence of HCV infection (Graphic A) and HBV infection (Graphic B) in IDUs admitted to treatment programmes in the Barcelona area, Spain, 1997- 2006.

4. Discussion

Results from this cohort of patients seeking substance abuse treatment indicate that drug users, irrespective of the main route of drug administration, are at increased risk of HIV infection and viral hepatitis. In fact, the prevalence of HIV infection and HCV infection in non-IDU patients is 2.8% and 9.7%, respectively. Several studies analysing risky sexual behaviour of drug and alcohol abusers suggest an association between cocaine, amphetamines or alcohol abuse and the sexual transmission of HIV [19-24], which could explain the relatively high prevalence of HIV infection among non-IDU patients from this study [29-34]. Despite the relatively high prevalence of HIV infection, there was a trend in the decline of HIV incidence among the non-IDUs. To some extent, the incidence of HIV infection was low (0.47 per 100 p-y) and the results shown here indicate that non-IDUs have a fivefold lower risk of HIV than the IDUs, as shown in a previous study [35].

The observed decline in the prevalence of HIV infection among IDUs is likely the result of some preventive interventions introduced in Spain at the beginning of 1990s. Harm-reduction interventions to reduce the impact of the HIV epidemic associated with heroin dependence included the access to opioid substitution therapy with methadone and the needle exchange programmes, among other interventions. Our findings indicate that HIV infection among IDUs from metropolitan Barcelona has stabilized and that rates of new infections are moderate with respect to reports from other cities [36-38]. In addition, our results agree with those reported nationally, indicating that sexual transmission now represents 80% of new HIV infections in Spain [39]. Further, our results show that the proportion of IDUs being admitted for substance abuse treatment is declining, suggesting a decrease in the number of IDUs in Spain [40].

Data from European countries show tendencies toward a low rate of HIV infection in drug users. For example, Poland, Finland and Germany have considerably reduced the rates of infection to two cases per million inhabitants in 2007 [41]. In this study, we determined an overall rate of infection of 2.54 per 100 p-y between 1997 and 2006, which is similar to that observed in other studies [6].

In contrast, the decline in the prevalence of HIV infection is not accompanied by a decline in HCV prevalence [42,43]. This observation suggests that IDUs still maintain non-sterile injection practices. The HIV and hepatitis C virus are transmitted primarily by large or repeated direct percutaneous exposures to contaminated blood. In Spain, IDU is a factor in 28% of all contemporary AIDS cases and it accounts for more than 60% of new hepatitis C infections in Europe and the USA [1,44].

It is well known that the majority of IDUs become infected with hepatitis C during their first year of injecting and that because of its infectivity HCV spreads more rapidly than HIV [45,46,47].

In this study, the prevalence of HBV is high. A recent systematic review suggests that worldwide around 1.2 million IDUs are chronic carriers of HBV infection and that the pat-

tern of infection shows clear geographical differences [17]. In fact, rates of HBcAb-positive varied widely between countries from 4.2% in Slovenia to 85.0% in Mexico [17].

Because of the high rate of both HCV and HBV infection, the probability of coinfection in IDUs is high. In this sense, vaccination against HBV must be prioritized for all susceptible drug users.

There are several limitations to this study that need to be mentioned. First of all, a proportion of patients, HIV-seronegative, were not re-tested for HIV infection during follow-up despite the fact that many of them were regularly visited in their primary care centres; in this sense, assessment of risk behaviour and awareness of drug use disorders by health care professionals are key components for developing preventive interventions. Second, in this study assessment of HBV infection was limited to one marker of infection; in other words, more accurate estimation of chronic carriers of HBV infection, susceptibility to infection or immunization due to HBV vaccination was not available. For the HCV pattern of infection we only analysed antibodies against HCV and RNA-HCV was not available; it is well known that a minority (10-15%) of the individuals infected with HCV clear the virus during the natural history of the disease. Third, in this study we did not analyse the impact of sexual transmission of HIV and viral hepatitis on the results shown here. In this sense, drug-addicted women have been reported to have a higher risk of HIV infection than drug-addicted men [48].

In contrast, the strength of this cross-sectional and longitudinal study is based on data collected at three centres that provide clinical care and treatment for the majority of severe drug addicts in Barcelona and its metropolitan area. Having data from the three hospitals adds external validity to the results and may reflect changes in the epidemiology of HIV and viral hepatitis in young adults seeking treatment for substance abuse in an urban area.

In summary, since 1997 we observed a significant decline in the prevalence of HIV infection in IDUs, however, background prevalence of HIV and viral hepatitis is still high thus suggesting that prevention efforts and treatment of substance abuse are necessary to further reduce transmission of blood-borne infections in this population.

Nomenclature

HIV= Human Immunodeficiency Virus.

IDU= Injecting Drug User.

AIDS= Acquired Immunodeficiency Syndrome.

HAART= Highly Active Antiretroviral Therapy.

HCV= Hepatitis C virus.

HBV= Hepatitis B virus.

HBsAg= Surface Antigen of Hepatitis B Virus.

HBcAb= Hepatitis B core Antibody.

EIA= Enzyme Immunoassay.

IQR= Interquartile Range.

CI= Confidence Interval.

RNA= Ribonucleic Acid

Acknowledgments

Author details

Arantza Sanvisens[1], Ferran Bolao[2], Gabriel Vallecillo[3], Marta Torrens[4], Daniel Fuster[5,8], Santiago Pérez-Hoyos[6], Jordi Tor[5], Inmaculada Rivas[7] and Robert Muga[1*]

*Address all correspondence to: rmuga.germanstrias@gencat.cat

1 Department of Internal Medicine and AIDS Vaccine Research Project – HIVACAT. Hospital Universitari Germans Trias i Pujol, Badalona, Universitat Autònoma Barcelona, Spain

2 Department of Internal Medicine. Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, Universitat de Barcelona, Spain

3 Department of Internal Medicine and Institute of Neuropsychiatry & Addictions. Parc de Salut Mar, Barcelona, Universitat Autònoma Barcelona, Spain

4 Institute of Neuropsychiatry & Addictions. Parc de Salut Mar, Barcelona, Universitat Autònoma Barcelona, Spain

5 Department of Internal Medicine. Hospital Universitari Germans Trias i Pujol, Badalona, Universitat Autònoma Barcelona, Spain

6 Department of Preventive Medicine and Public Health. Vall d'Hebrón Institut de Recerca. Universitat Autònoma Barcelona, Spain

7 Municipal Centre for Substance Abuse Treatment (Centro Delta). IMSP Badalona, Spain

8 Section of General Internal Medicine. Boston Medical Center, Boston University School of Medicine; Boston (MA), U.S.A.

References

[1] Vigilancia epidemiológica del VIH en España. Nuevos diagnósticos de VIH en España. Periodo 2003-2009. Ministerio de Sanidad, Política Social e Igualdad, Ministerio de Ciencia e Innovación; 2010.

[2] Hernandez-Aguado I, Avino MJ, Perez-Hoyos S, Gonzalez-Aracil J, Ruiz-Perez I, Torrella A, et al. Human immunodeficiency virus (HIV) infection in parenteral drug users: evolution of the epidemic over 10 years. Valencian Epidemiology and Prevention of HIV Disease Study Group. Int J Epidemiol 1999;28(2):335-340.

[3] Castilla J, Lorenzo JM, Izquierdo A, Lezaun ME, Lopez I, Moreno-Iribas C, et al. Characteristics and trends of newly diagnosed HIV-infections, 2000-2004. Gac Sanit 2006;20(6):442-448.

[4] European Monitoring Centre for Drugs and Drug Addiction. Annual report 2011: The state of the drug problems in Europe. EMCDDA, Lisbon, November 2011. http://www.emcdda.europa.eu/attachements.cfm/att_143743_EN_EMCD-DA_AR2011_EN.pdf (accessed 30 July 2012)

[5] Muga R, Sanvisens A, Bolao F, Tor J, Santesmases J, Pujol R, et al. Significant reductions of HIV prevalence but not of hepatitis C virus infections in injection drug users from metropolitan Barcelona: 1987-2001. Drug Alcohol Depend 2006;82 Suppl 1:S29-33.

[6] Hurtado I, Alastrue I, Ferreros I, del Amo J, Santos C, Tasa T, et al. Trends in HIV testing, serial HIV prevalence and HIV incidence among people attending a Center for AIDS Prevention from 1988 to 2003. Sex Transm Infect 2007;83(1):23-28. DOI: 10.1136/sti.2005.019299.

[7] Celentano DD, Latimore AD, Mehta SH. Variations in sexual risks in drug users: emerging themes in a behavioral context. Curr HIV/AIDS Rep 2008;5(4):212-218.

[8] Nelson KE, Galai N, Safaeian M, Strathdee SA, Celentano DD, Vlahov D. Temporal trends in the incidence of human immunodeficiency virus infection and risk behavior among injection drug users in Baltimore, Maryland, 1988-1998. Am J Epidemiol 2002;156(7):641-653.

[9] Chitwood DD, Comerford M, Sanchez J. Prevalence and risk factors for HIV among sniffers, short-term injectors, and long-term injectors of heroin. J Psychoactive Drugs 2003;35(4):445-453.

[10] Miller CL, Wood E, Spittal PM, Li K, Frankish JC, Braitstein P, et al. The future face of coinfection: prevalence and incidence of HIV and hepatitis C virus coinfection among young injection drug users. J Acquir Immune Defic Syndr 2004;36(2):743-749.

[11] Jenness SM, Neaigus A, Hagan H, Murrill CS, Wendel T. Heterosexual HIV and sexual partnerships between injection drug users and noninjection drug users. AIDS Patient Care STDS 2010;24(3):175-181. DOI:10.1089/apc.2009.0227.

[12] Strathdee SA, Sherman SG. The role of sexual transmission of HIV infection among injection and non-injection drug users. J Urban Health 2003;80(4 Suppl 3):iii7-14.

[13] Howe CJ, Cole SR, Ostrow DG, Mehta SH, Kirk GD. A prospective study of alcohol consumption and HIV acquisition among injection drug users. AIDS 2011;25(2): 221-228. DOI:10.1097/QAD.0b013e328340fee2.

[14] Zakhari S, Li TK. Determinants of alcohol use and abuse: Impact of quantity and frequency patterns on liver disease. Hepatology 2007;46(6):2032-2039. DOI:10.1002/hep. 22010.

[15] Shuper PA, Neuman M, Kanteres F, Baliunas D, Joharchi N, Rehm J. Causal considerations on alcohol and HIV/AIDS--a systematic review. Alcohol Alcohol 2010;45(2): 159-166. DOI:10.1093/alcalc/agp091.

[16] Te HS, Jensen DM. Epidemiology of hepatitis B and C viruses: a global overview. Clin Liver Dis 2010;14(1):1-21, vii. DOI:10.1016/j.cld.2009.11.009.

[17] Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. Lancet 2011;378(9791):571-583. DOI:10.1016/S0140-6736(11)61097-0.

[18] Mast EE, Weinbaum CM, Fiore AE, Alter MJ, Bell BP, Finelli L, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. MMWR Recomm Rep 2006;55(RR-16):1-33; quiz CE1-4.

[19] Kuo I, Sherman SG, Thomas DL, Strathdee SA. Hepatitis B virus infection and vaccination among young injection and non-injection drug users: missed opportunities to prevent infection. Drug Alcohol Depend 2004;73(1):69-78.

[20] Alter MJ. Epidemiology and prevention of hepatitis B. Semin Liver Dis 2003;23(1): 39-46. DOI:10.1055/s-2003-37583.

[21] Goldstein ST, Alter MJ, Williams IT, Moyer LA, Judson FN, Mottram K, et al. Incidence and risk factors for acute hepatitis B in the United States, 1982-1998: implications for vaccination programs. J Infect Dis 2002;185(6):713-719. DOI:10.1086/339192.

[22] Garfein RS, Vlahov D, Galai N, Doherty MC, Nelson KE. Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. Am J Public Health 1996;86(5): 655-661.

[23] Levine OS, Vlahov D, Koehler J, Cohn S, Spronk AM, Nelson KE. Seroepidemiology of hepatitis B virus in a population of injecting drug users. Association with drug injection patterns. Am J Epidemiol 1995;142(3):331-341.

[24] Burt RD, Hagan H, Garfein RS, Sabin K, Weinbaum C, Thiede H. Trends in hepatitis B virus, hepatitis C virus, and human immunodeficiency virus prevalence, risk be-

haviors, and preventive measures among Seattle injection drug users aged 18-30 years, 1994-2004. J Urban Health 2007;84(3):436-454. DOI:10.1007/s11524-007-9178-2.

[25] Salleras L, Bruguera M, Taberner JL, Dominguez A, Batalla J, Buti M, et al. Effectiveness of the mass antihepatitis B program in preadolescents in Catalonia. Med Clin (Barc) 2003;121 Suppl 1:79-82.

[26] Muga R, Roca J, Egea JM, Tor J, Sirera G, Rey-Joly C, et al. Mortality of HIV-positive and HIV-negative heroin abusers as a function of duration of injecting drug use. J Acquir Immune Defic Syndr 2000;23(4):332-338.

[27] Rivas I, Martinez E, Sanvisens A, Bolao F, Tor J, Torrens M, et al. Hepatitis B virus serum profiles in injection drug users and rates of immunization over time in Barcelona: 1987-2006. Drug Alcohol Depend 2010;110(3):234-9. DOI:10.1016/j.drugalcdep.2010.03.005.

[28] US National Cancer Institute Software. Jointpoint Regression Program. 2010;3.4.3.

[29] Wang B, Li X, Stanton B, Zhang L, Fang X. Alcohol Use, Unprotected Sex, and Sexually Transmitted Infections Among Female Sex Workers in China. Sex Transm Dis 2010;37(10):629-36. DOI:10.1097/OLQ.0b013e3181e2118a.

[30] Baliunas D, Rehm J, Irving H, Shuper P. Alcohol consumption and risk of incident human immunodeficiency virus infection: a meta-analysis. Int J Public Health 2010;55(3):159-166. DOI:10.1007/s00038-009-0095-x.

[31] Booth RE, Kwiatkowski CF, Chitwood DD. Sex related HIV risk behaviors: differential risks among injection drug users, crack smokers, and injection drug users who smoke crack. Drug Alcohol Depend 2000;58(3):219-226.

[32] de Azevedo RC, Botega NJ, Guimaraes LA. Crack users, sexual behavior and risk of HIV infection. Rev Bras Psiquiatr 2007;29(1):26-30.

[33] Colfax G, Santos GM, Chu P, Vittinghoff E, Pluddemann A, Kumar S, et al. Amphetamine-group substances and HIV. Lancet 2010;376(9739):458-474. DOI:10.1016/S0140-6736(10)60753-2.

[34] Van Tieu H, Koblin BA. HIV, alcohol, and noninjection drug use. Curr Opin HIV AIDS 2009;4(4):314-318. DOI:10.1097/COH.0b013e32832aa902.

[35] Kellogg TA, McFarland W, Perlman JL, Weinstock H, Bock S, Katz MH, et al. HIV incidence among repeat HIV testers at a county hospital, San Francisco, California, USA. J Acquir Immune Defic Syndr 2001;28(1):59-64.

[36] Kozlov AP, Shaboltas AV, Toussova OV, Verevochkin SV, Masse BR, Perdue T, et al. HIV incidence and factors associated with HIV acquisition among injection drug users in St Petersburg, Russia. AIDS 2006;20(6):901-906. DOI:10.1097/01.aids.0000218555.36661.9c.

[37] Duan S, Xiang LF, Yang YC, Ye RH, Jia MH, Luo HB, et al. Incidence and risk factors on HIV infection among injection drug users in Dehong prefecture area of Yunnan province. Zhonghua Liu Xing Bing Xue Za Zhi 2009;30(12):1226-1229.

[38] Hurtado Navarro I, Alastrue I, Del Amo J, Santos C, Ferreros I, Tasa T, et al. Differences between women and men in serial HIV prevalence and incidence trends. Eur J Epidemiol 2008;23(6):435-440. DOI:10.1007/s10654-008-9246-2.

[39] Valoración de los nuevos diagnósticos de VIH en España a partir de los sistemas de notificación de casos de las CCAA. Periodo 2003-2008. Ministerio de Sanidad y Política Social, Ministerio de Ciencia e Innovación;2009. http://www.isciii.es/htdocs/pdf/nuevos_diagnosticos_ccaa.pdf. (accessed 30 july 2012)

[40] Sanchez-Niubo A, Domingo-Salvany A, Melis GG, Brugal MT, Scalia-Tomba G. Two methods to analyze trends in the incidence of heroin and cocaine use in Barcelona [Spain]. Gac Sanit 2007;21(5):397-403.

[41] European Monitoring centre for Drugs and Drug Addiction. Drug-related infectious diseases and drug-related deaths. http://www.emcdda.europa.eu/situation/diseases-and-deaths/1 (accessed 30 july 2012).

[42] Somaini B, Wang J, Perozo M, Kuhn F, Meili D, Grob P, et al. A continuing concern: HIV and hepatitis testing and prevalence among drug users in substitution programmes in Zurich, Switzerland. AIDS Care 2000;12(4):449-460. DOI: 10.1080/09540120050123855.

[43] van Beek I, Dwyer R, Dore GJ, Luo K, Kaldor JM. Infection with HIV and hepatitis C virus among injecting drug users in a prevention setting: retrospective cohort study. BMJ 1998;317(7156):433-437.

[44] Centers for Disease Control and Prevention (CDC). HIV Infection Among Injection-Drug Users --- 34 States, 2004--2007. MMWR 2009;58:1291-1295.

[45] Thorpe LE, Ouellet LJ, Levy JR, Williams IT, Monterroso ER. Hepatitis C virus infection: prevalence, risk factors, and prevention opportunities among young injection drug users in Chicago, 1997-1999. J Infect Dis 2000;182(6):1588-1594. DOI: 10.1086/317607.

[46] Garfein RS, Vlahov D, Galai N, Doherty MC, Nelson KE. Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphotropic viruses. Am J Public Health 1996;86(5):655-661.

[47] Hagan H, Des Jarlais DC. HIV and HCV infection among injecting drug users. Mt Sinai J Med 2000;67(5-6):423-428.

[48] Evans JL, Hahn JA, Page-Shafer K, Lum PJ, Stein ES, Davidson PJ, et al. Gender differences in sexual and injection risk behavior among active young injection drug users in San Francisco (the UFO Study). J Urban Health 2003;80(1):137-146. DOI: 10.1093/jurban/jtg137.