RESEARCH REPORT

A 10-year follow-up study on the health status of heroin addicts based on official registers

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Abstract

Aims. To determine the health status of a cohort of heroin addicts. Design. Longitudinal follow-up study of a cohort for 10.5 years (March/July 1985–December 1995) based on official registers. Setting. Catalonia, Spain. Participants. One hundred and thirty-five heroin addicts who started treatment in four specialized drug addiction services in Catalonia in 1985. Measurements. (a) Total and annual numbers of AIDS and tuberculosis diagnoses and admissions to drug treatment; (b) annual morbidity rate; (c) average annual morbidity rate; and (d) standardized morbidity ratio. Kaplan–Meier (log rank test) was used to assess predictive factors. Findings. During the follow-up period, 34 heroin addicts were diagnosed with AIDS (25%), the average annual morbidity rate was 2.7% and the standardized morbidity ratio was 82. The most frequent diseases indicative of AIDS were Pneumocystis carinii pneumonia (11 cases) and tuberculosis (seven cases of disseminated or extrapulmonary tuberculosis and two cases of pulmonary tuberculosis). Twenty addicts were diagnosed with tuberculosis and 15 were co-infected with AIDS and tuberculosis. Seventy-six addicts were readmitted to treatment and generated 124 drug treatment episodes, 94 of whom were drug-free and 30 on methadone maintenance. Conclusions. Follow-up through registers is a novel, low-cost technique that may provide important and comparable information on the long-term evolution of drug addicts in different European regions. The measures of disease frequency and association obtained allow us to describe and compare the distribution of patterns of infectious complications (AIDS and tuberculosis) and relapses in such a pervasive disorder as heroin addiction. Other advantages of follow-up based on official registers are efficiency, reliability, sensibility and comparability.

Introduction

Despite the scope of heroin use and the resources devoted to its treatment (Plan Nacional sobre Drogas, 1999), the course of heroin addiction in Spain is still unknown. The Estudio Multicentrico de Evaluación de Tratamientos Y Seguimiento de Toxicoomanos (EMETYST Project) has been the only long-term attempt. Personal and telephone interviews were used to describe the course of the addiction during the first 2 years and its relationship with treatment and demographic characteristics (Sánchez-Carbonell, Cami & Brigos, 1988; Sánchez-Carbonell, Brigos & Cami, 1989). In the Catalonia subcohort, the mortality rates and the immediate causes of death 10 years after appli-

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cation for treatment have been reported recently (Sánchez-Carbonell & Seus, 2000). In summary, 30% of heroin addicts died and their risk of dying was 29 times higher than that of a person of the general population. The most frequent causes of death fell in ICD-9 chapter III (which includes AIDS) and in chapter XVII (which includes overdose). In comparison with other countries in Europe, the authors observed that the average annual mortality rate in Catalonia was almost twice that among cohorts in Great Britain and similar to that in Scandinavian countries. The survival rate, in comparison to the general population, was lower than that of their peers in other European countries.

Catalonia is a region in the Northeast of Spain with a well-developed state health-care network and epidemiological surveillance, which allows the study of the course of drug addicts through social and health care indicators, such as mortality, AIDS, tuberculosis and treatments for drug abuse. In Spain, as in Italy and Portugal, HIV and AIDS has had a large effect on intravenous drug users. Forty to 80% of them are HIV-infected (Rebagliato et al., 1995; Egea et al., 1996) and AIDS is a frequent cause of death (Muga et al., 1999). In fact, intravenous drug users represent more than 60% of total cases. The consequence among the general population is that the Spanish rate of cumulative incidence of 176.2 AIDS cases per million inhabitants in 1995, was the highest in Europe (Ministry of Health and Consumption, 1997).

In Spain and Catalonia, tuberculosis is an endemic disease that is not completely controlled. Although some estimates estimate the rate in the range from 40 to 60 cases per 100,000 inhabitants (Collaborative Group for the Study of Tuberculosis in Spain, 1995), in Catalonia the declared incidence rate was 37.03 cases per 100,000 inhabitants in 1997 (Tuberculosis Prevention and Control Programme, 1999). Tuberculosis is a chronic infectious disease with a key role in the diagnosis and development of AIDS. Being a mandatory notification disease subjected to active epidemiological surveillance, it is possible to study its effects on population groups such as drug addicts. Drug use and the social rejection implied may have given rise to a resurgence of tuberculosis, the prevalence of which had been in decline until the 1980s (Caylà et al., 1996, 1998).

In spite of the fact that mortality registers are used widely in follow-up studies of drug addicts (Engstrom et al., 1991; Perucci et al., 1991; Oppenheimer et al., 1994; Orti et al., 1996; Frischer et al., 1997; Fugelstad et al., 1997) the use of other official registers is limited. Personal or telephone interviews are preferred, with official registers being used only as an aid in locating the cohort or to check reliability. However, personal follow-up presents some problems, such as high cost, failure to contact, use of different independent variables, reliability of self-report and problems of comparability. Wille (1981) was the first to analyse, using official registers, clinic attendance, abstinence and mortality in a sample of 128 London heroin addicts 10 years after applying for treatment. The wide availability of record linkage (Allgulander, 1989; Newman & Bland, 1991; Nienhuis, Goldacre & Seagroatt, 1992) allows reconsideration of the strategies for drug addicts follow-up.

This phase of the EMETYST Project aims to describe the health status of a cohort of heroin addicts followed-up through official registers of AIDS, tuberculosis and drug treatments.

Method

Subjects
The study involved 135 heroin addicts (96 men and 39 women) who applied for treatment for the first time in four outpatient drug-free services in Catalonia, between 1 March and 30 July 1985. At the start of treatment they had an average age of 23.6 years. In the last year before admission to treatment, 70% had worked at least 1 day, 22% had been in prison at least 1 day and 73% lived with their parents (for further details about subjects, see Sánchez-Carbonell & Seus, 2000).

Data sources
We consulted and linked registers from the Department of Health and Social Security of Catalonia: “Register of AIDS”, “Register of Tuberculosis” and “Register of Individualized Notification of New Cases of Drug Treatment”. The “Register of AIDS” centralizes epidemiological information on AIDS in Catalonia. This register was used to identify cases of AIDS and disease indicative of AIDS, and to identify cases of tuberculosis as a disease indicative of AIDS not provided by other registers. The 48 countries
of the WHO European Region participating in the surveillance of AIDS use a uniform AIDS case definition (European Centre for the Epidemiological Monitoring of AIDS, 1993), that differs from the definition used in the United States only in that it does not include CD4 lymphocyte count criteria. From the Barcelona City Council we used the “Register of the Tuberculosis Prevention and Control Programme in Barcelona” and the “System of Information on Drug Addictions in Barcelona”.

The Service of Information and Studies of the Department of Health and Social Security provided census information for the general population in Catalonia by sex and 5-year age groups from 1985 until 1995. The Centre d’Estudis Epidemiològics sobre la Sida a Catalunya (CEESCAT) provided statistics on AIDS to calculate the excess morbidity rate of the disease.

**Data analysis and procedure**

This was a longitudinal study of a cohort through linkage of official registers. Unclear cases were checked individually. The study was started in May 1985 and the date of censure was fixed at 31 December 1995, so the follow-up period was 10.5 years.

The operational definitions of the dependent variables were as follows. AIDS is diagnosed when an individual appears in the “Register of AIDS”; tuberculosis is diagnosed when they appear in one of the three registers: “Register of Tuberculosis”, “Register of the Tuberculosis Prevention and Control Programme in Barcelona” or “Register of AIDS”, with tuberculosis diagnosis as the disease indicative of AIDS. A person is considered readmitted to drug treatment when he/she appears in the “Register of Individualised Notification of New Cases” or in the “System of Information on Drug Addictions” subsequently to the episode that motivates the inclusion in the cohort. Although one person could present more than one episode of tuberculosis and of treatment, only the first episode of each has been taken into account in calculating survival.

We have used different measures of disease frequency and association (Hennekens & Buring, 1987). The first was the total and annual number of events. The second measure used was the annual cumulative incidence rate (number of annual cases divided by the total population at risk; population at risk was obtained by subtracting from 135 those deceased in previous years and those previously diagnosed). In the case of AIDS we were also able to calculate the standardised morbidity ratios with regard to the general population of Catalonia, controlled by sex and period. Mortality data were obtained from a previous study in this cohort (Sánchez-Carbonell & Seus, 2000).

Survival analysis (Kaplan–Meier: log-rank test) was used to assess the predictive factors: (a) sex; (b) age at admission to treatment (15–24 and 25–34 years); (c) living circumstances (family of origin and other situations); (d) legal status (with and without criminal record); (e) in prison in the last year (yes and no); (f) work in the last year (yes and no); (g) age at first consumption of heroin (10–19 and 20–29 years); (h) route of administration (injected and others); and (i) previous addiction treatments (yes and no). The period of survival of each person was calculated between the date of entry into this study and the date of death or date of censure if still alive. Although statistical significance was initially set at $p < 0.05$, we applied the Bonferroni correction and established $p$ at 0.002. We also analysed the relationship among AIDS diagnosis, tuberculosis diagnosis and readmission to treatment.

**Results**

**AIDS**

From the start of the study in March 1985 until December 1995, 34 addicts (25.2%) were diagnosed with AIDS. In 1985, 1986 and 1987 no cases of AIDS were diagnosed. The first case of AIDS in a woman of the cohort was diagnosed in 1991. The years when more cases were diagnosed were 1994 (seven cases), and 1990 and 1992 (six cases). The year with the highest diagnostic rate was 1994 (8.53%) (Table 1). Table 2 shows the disease indicative of AIDS in the 34 cases diagnosed. The most frequent disease indicative of AIDS was Pneumocystis carinii pneumonia (11 cases), followed by tuberculosis (seven cases of disseminated or extrapulmonary tuberculosis and two cases of pulmonary tuberculosis). Thirty-four cases of AIDS were diagnosed as opposed to the 0.416 expected in the general population, so the standard morbidity ratio was 81.81. That is, a heroin addict of the cohort had a risk of being diagnosed with AIDS 82 times higher than that of a person from
Table 1. Evolution of AIDS, tuberculosis and readmission to treatment in a cohort of 135 heroin addicts (1985–95) in Catalonia, Spain

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<td>2</td>
<td>0</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>8</td>
<td>8</td>
<td>5</td>
<td>8</td>
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<tr>
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<td>0</td>
<td>1</td>
<td>3</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>6</td>
<td>2</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
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<td>135</td>
<td>134</td>
<td>132</td>
<td>131</td>
<td>127</td>
<td>116</td>
<td>108</td>
<td>94</td>
<td>82</td>
<td>50</td>
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<td>for AIDS diagnosis(^1)</td>
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<td>0</td>
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<td>Addicts at risk</td>
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<td>134</td>
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<td>129</td>
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<td>118</td>
<td>112</td>
<td>100</td>
<td>89</td>
<td>82</td>
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<tr>
<td>Readmission to treatment</td>
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<tr>
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<td>2</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^1\)Addicts at risk are obtained by subtracting from 135 those deceased in previous years and those previously diagnosed.  
\(^2\)Annual cumulative incidence rate.

Table 2. Disease indicative of AIDS, by sex, in a cohort of 135 heroin addicts (1985–95) in Catalonia, Spain

<table>
<thead>
<tr>
<th>Disease indicative of AIDS</th>
<th>Men</th>
<th>Women</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptosporidiosis</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary tuberculosis</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Toxoplasmosis of brain</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Extrapulmonary tuberculosis</td>
<td>7</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Toxoplasmosis of brain</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mucocutaneous Herpes simplex</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Extrapulmonary cryptococcosis</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Pneumocystis carinii pneumonia</td>
<td>9</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Burkitt's lymphoma</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>HIV-related encephalitis</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Wasting syndrome due to HIV</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>8</td>
<td>34</td>
</tr>
</tbody>
</table>

Up to 31 December 1995, 23 people (68%) of the 34 diagnosed with AIDS had died (although the underlying cause of death may not necessarily have been AIDS) (Fig. 1).

Tuberculosis

From the start of the study in March 1985 until December 1995, the research team had evidence that 20 addicts (15%) had tuberculosis diagnosed. No cases were diagnosed in 1985, 1986, 1987 and 1995. The year 1992 presented the highest diagnostic rate (3.57%) (Table 1). When registers of AIDS and tuberculosis were linked, we observed that 15 people were co-infected with AIDS and tuberculosis (Fig. 1).
Figure 1. Interaction among AIDS, tuberculosis and drug-treatment, between themselves and in relation to death. The numbers in brackets show the number of deceased for each group. Of the 39 people who received no diagnosis, six had died.

Table 3. Evolution of the 124 treatment episodes produced by 76 heroin addicts (1985–95) in centres recognized by the Register of Individualised Notification of New Cases

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</thead>
<tbody>
<tr>
<td>Drug-free programs</td>
<td>8</td>
<td>20</td>
<td>11</td>
<td>13</td>
<td>15</td>
<td>17</td>
<td>8</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Methadone maintenance</td>
<td>9</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>20</td>
<td>11</td>
<td>13</td>
<td>15</td>
<td>26</td>
<td>15</td>
<td>7</td>
<td>9</td>
</tr>
</tbody>
</table>

Readmission to drug treatment
Until 31 December 1995, 53 men and 23 women (56% in total) restarted drug treatment, and at the end of this 10.5-year period only 26.5% of living addicts had not been readmitted to drug treatment at some time during follow-up. The highest rates of readmission to treatment occurred in 1988, 1990 and 1991 (Table 1). Relapse in drug use, as opposed to death or AIDS diagnosis, is a multi-episodic phenomenon. In total, the 76 addicts produced 124 treatment episodes, 94 (75.8%) of which were drug-free and 30 methadone maintenance (Table 3). Many addicts (57 of 76) had requested a second treatment without AIDS or tuberculosis diagnosis.

Predictive factors
No demographic or heroin use characteristics at admission reached statistical significance to predict AIDS, tuberculosis or readmission to treat-
The 34 addicts diagnosed with AIDS had a greater risk of readmission to treatment (log-rank test: 10.36; \( p = 0.0013 \)) and of dying (log-rank test: 32.38; \( p < 0.0001 \)) and of being diagnosed with tuberculosis (log-rank test: 39.82; \( p < 0.0001 \)) than those not diagnosed. The 20 cases of tuberculosis had a greater risk of being diagnosed with AIDS (log-rank test: 42.56; \( p < 0.0001 \)) and of dying (log-rank test: 13.23; \( p = 0.0003 \)), but not of restarting drug treatment.

Discussion

To analyse the relationship between AIDS and drug use two variables have been used in the literature. Commonly, AIDS registers provide the percentage of people diagnosed with AIDS who were or had been intravenous drug users, whereas treatment centres provide the percentage of drug addicts who at admission to treatment were HIV seropositive. However, in this study, we have obtained a more direct measure: the number of cohort members diagnosed with AIDS. AIDS has a decisive and dramatic influence on the health status and is the leading cause of death among heroin addicts who started treatment in the 1980s. This effect is pointed out for three measures in the EMETYST cohort. First, 25% of them were diagnosed with AIDS between 1985 and 1995. Secondly, a member of the cohort has a risk of contracting the disease 82 times higher than that of a person from the general population. Besides that, mortality among AIDS cases (68%) is higher than mortality of the EMETYST cohort (30%) and of the total cases of AIDS in Catalonia (63%) (CEESCAT, 1999).

Pulmonary or extrapulmonary tuberculosis is the disease indicative of AIDS that is most commonly diagnosed, especially in drug addicts, followed by *Pneumocystis carinii* pneumonia (Ministry of Health and Consumption, 1997; CEESCAT, 1999). In our cohort the order is reversed, pneumonia being the most frequent disease indicative of AIDS, followed by tuberculosis, a situation similar to that observed by Caylà et al. (1993) until 1991 in the city of Barcelona. In the EMETYST cohort all cases of AIDS, whose disease indicative of AIDS is tuberculosis, are men; a tendency shared by the other transmission categories. As morbidity, mortality and number of cases of AIDS has decreased due to new antiretroviral treatments it may be convenient to improve the AIDS indicator by introducing an epidemiological surveillance system for HIV infection (Center For Disease Control and Prevention, 1999).

The impact of tuberculosis in our cohort was dramatic and, if our data were extrapolated to the general population, there would be 12,000 cases per 100,000 inhabitants. Moreover we must consider that, although there are both preventive and therapeutic treatments, they are difficult to follow, especially by non-controlled heroin addicts in a marginalized social situation. The third aggravating factor of this problem is that imprisonment, so common in drug addicts, increases the risk for having tuberculosis and for being co-infected (Bellin, Fletcher & Safyer, 1993; Martin et al., 1995). The association between AIDS and tuberculosis in the collective of drug addicts in Catalonia defines a situation that reduces their survival and quality of life, and moreover has repercussions on public health that require urgent control measures. A limitation of the indicator tuberculosis is that it was under-notified in the first years of follow-up because it was not possible to link the EMETYST cohort with the register until its computerization (1987 in the city of Barcelona; 1991 in the rest of Catalonia).

Relapse is a common and expected phenomenon in the recovery of drug addicts. In Spain in 1997, of the 52,440 people admitted to psychoactive substance use treatment, 32,568 (62.10%) had followed previous treatments (Observatorio Español sobre Drogas, 1999). Among others Hubbard & Marsden (1986), Oppenheimer, Sheeman & Taylor (1990), Simpson, Joe & Bracy (1982) and Wille (1981) had also observed high rates of ‘treatment during the follow-up period’ and ‘in treatment at follow-up’ but these studies are not comparable due to the variety of operational definitions and duration of follow-up period. Starting a new treatment is the consequence of a continued drug use, represents a poor health status and implies behavioural changes to overcome the problem. Although the risk for relapse decreases as the duration of abstinence increases, admissions to treatment take place throughout the whole period. Drug addiction must be viewed as a disease with a high risk for becoming chronic (O’Brien & McLe llan, 1996). The indicator treatment has two major limitations and two conceptual problems. First,
data on treatment readmissions are not available between 1985 and 1987. Secondly, there is a high risk of under-notification, either because an addict may begin treatment in a non-officially recognized centre (a religious therapeutic community, for instance) or a person may use drugs repeatedly and never apply for treatment. The first conceptual problem of the indicator treatment is that relapse is not a permanent status; it is possible to restart drug use, but it is also possible to overcome relapse. Our analysis gives priority to the cumulative aspect, but it does not allow ascertainment, for instance, of how many addicts were abstinent at the end of the follow-up. The second conceptual problem is that we have used readmission as a marker of treatment failure and in some cases a heroin addict who returns to treatment will have a better outcome, and a lower chance of death, than one who continues to use drugs and remains untreated.

The predictive power of demographic or heroin use characteristics at admission seems very weak. It should also be noted that when we used these variables to predict mortality among this same group (Sánchez-Carbonell & Seus, 2000), no variable reached statistical significance. Social variables and addictive behaviour at admission to treatment in 10-year or longer follow-up studies are not strong predictors, due to changes in behavioural, psychological and social aspects over such an extended period. The statistical significance of most predictor variables diminishes as outcome measures become more temporally distant (Simpson & Marsh, 1986) or explain only a small fraction of the outcome variable. Although it is extremely difficult to establish causal relationships among variables, we can observe in Fig. 1 a strong association between AIDS and death, tuberculosis and death and between AIDS and tuberculosis. These connections would underline the extraordinary importance that the prophylaxis of tuberculosis should have in the collective of heroin addicts. Infectious complications, probably related to the limitation of the therapeutic use of agonists (Villalbi & Brugal, 1999; Sánchez-Carbonell & Seus, 2000) and to the use of the intravenous route (De la Fuente et al., 1999) seem to be related more with death than relapse in heroin consumption.

The technique which has been used most widely for collecting information in studies involving follow-up of drug addicts and evaluation of treatment is the interview, either face-to-face or by telephone. Our view is that the use of linkage of official registers offers a series of advantages over the interview.

1. It is more efficient. In an era of limited resources the cost of evaluation is important when trying to obtain funds. The methodology employed in North American studies such as DARP and TOPS implies an investment which is difficult to sustain. Follow-up through registers is cheaper, and consequently more likely to obtain public funding.

2. Information in official registers is reliable. Official registers have been used to verify reliability and validity of responses obtained through personal and telephone interviews.

3. Information in official registers is sensitive. Although the information may be obtained more quickly by interview, in the long term official registers also detect relevant health aspects. For example, the interview would detect a recognized relapse in drug consumption sooner, but if the individual continues to consume drugs he will eventually seek treatment, and thus be identified by the register. Interviews and self-reports are more suitable for short periods of follow-up as occur in evaluation of psychotherapy techniques.

4. The information is comparable between registers and with that of other diseases. Follow-up and treatment evaluation studies use different independent variables. The use of official registers allows status and trends in the population to be analysed using recognized measures of incidence and data analysis techniques (for example, average annual mortality rate, standard morbidity ratio, survival analysis).

5. Participation of the whole cohort is assured, without losses due to refusals, failures to attend, unable to locate, etc. The problem of experimental mortality is overcome by follow-up through registers.

6. Their use can be extended to social variables such as employment status and criminal registers.

Follow-up studies of this type, however, require certain minimum conditions, apart from the existence of the register itself and its quality:

1. A very important point is the potential ethi-
cal barrier to conduct research in this area. Some official registers could be very sensitive about releasing information and studies such this could be difficult to conduct in some countries. This type of research is only possible if there is collaboration between various institutions. One strategy to obtain permission is to get institutional funding, or to undertake research under the auspices of a public health institution.

(2) The register should provide coverage of a region that has ecological significance in the life-style of the addict. State or regional coverage is preferable to municipal coverage alone.

(3) Measures must be taken to ensure confidentiality, given that the information being manipulated is very delicate. With appropriate precautions, the use of registers can be considered to have the advantage of being less intrusive than personal contact, which runs the risk of evoking unpleasant personal memories and increasing the risk of relapse.

(4) Due to the large number of life events, which cannot be controlled in 10 years of an addict’s life, information from official registers cannot be used to establish causal relationships between variables.

(5) Attention must be paid to the danger of underreporting of cases. For example, a death may not be registered due to difficulties of corpse identification. Also a subject may leave the area or the country and not be included in the register. There is also a potential for exclusion of certain treatment services (religious therapeutic communities, as an example) from specific data collections.

Conclusions
Follow-up through registers is a novel, low-cost technique that may provide valuable and comparable information on the long-term health and social evolution of drug addicts in different European regions. The measures of disease frequency and association obtained allow us to describe and compare the distribution of patterns of infectious complications (AIDS and tuberculosis) and relapses in such a pervasive disorder as heroin addiction. Among others, the advantages of follow-up based on official registers are efficiency, reliability, sensibility and comparability. It should be pointed out, however, that this kind of approach has some limitations. It is necessary to assure confidentiality and avoid under-reporting of cases. This study corroborates the poor health status of heroin addicts in Catalonia, the high AIDS, tuberculosis and relapse rates, and that their health is worse than that of the general population. The demographic characteristics and those of drug use at admission to treatment have little predictive value in the long term.

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