ABSTRACT

Aims To estimate the annual incidence of heroin use in Spain. Participants and design Data on individuals’ year of first heroin use (from 1971 to 2005), year of first heroin treatment between 1991 and 2005 and most frequent route of heroin administration when presenting to treatment were obtained from the Spanish Drug Observatory Register and used to calculate the delay between onset and treatment. By using a log-linear model approach it was possible to correct for missing observations (heroin users who presented for treatment before 1991 and those who had still not presented by the end of 2005) and to estimate heroin incidence over time. Findings The estimated incidence of problematic heroin use in the population aged 15–44 peaked at 190 per 100 000 in 1980—after rising rapidly from less than 40 per 100 000 in 1971—and fell subsequently to about 8 per 100 000 in 2005. On average, incidence was five times higher in men. Injecting heroin incidence peaked and declined rapidly from 1980; as heroin smoking did not decline as rapidly, from 1985 onwards its estimated incidence has remained above that of heroin injecting. The delay between starting heroin use and entering treatment had a median of 3 years. Conclusions We demonstrate the utility of a method to estimate heroin incidence from analysis of observed trends in presentations at specialist drug treatment facilities. The estimates suggest that incidence of heroin use, especially injecting, has fallen since 1980 and is now lower than in the early 1970s.

Keywords Epidemiology, heroin, incidence, latency period, log-linear model, route of administration.
so, if not corrected, they result in an underestimated incidence caused by delay in reaching information systems, which in the case of drug use is due to the existence of users who had still not been admitted into treatment at the time of observation. As Hickman [7] discussed, the length of time during which treatment admissions are observed is very important. If this interval is long enough, the incidence estimated through RDA may approach population values, relative to individuals who have entered treatment at some point. However, in treatment admission registers the length of time available is often too short, so heroin users who take longer to be admitted escape the analysis because the maximum LP in RDA is equal to the length of the period observed [7]. Allowing the year of first heroin use to be earlier than the beginning of the period actually observed by the treatment admission register, something for which the RDA method provides no solution, means that a longer LP can be contemplated and that far more subjects can be included in the analysis.

Brookmeyer et al. [8] had already suggested that Poisson regression might be an alternative method to RDA. In fact, it provides the same LP distribution when data are conditioned to the same individuals [9], therefore it is easy to demonstrate that incidence results are identical. However, they recognized that the large number of parameters to be estimated could pose a problem, and also that the database used should be large enough. They considered that RDA seemed easier to work with. However, in contrast to RDA, Poisson regression does not restrict estimates to years within the observed period nor the length of the LP [10].

To develop this methodology further, the aim of the present analysis was to estimate the annual incidence of problematic heroin use in Spain between 1971 and 2005 by using log-linear models as a generalization of the Poisson regression method.

**MATERIAL AND METHODS**

**The data**

As in any country with universal health coverage, the Spanish drug treatment system is mainly public or publicly funded, and most patients entering treatment for drug dependence are screened in specialized out-patient treatment centres before being assigned a treatment modality, which may include in-patient treatment. Each autonomous community (Region) has its own treatment system organization. The SDO collects information about drugs from all the Spanish Regions, its basic function being to evaluate the situation of drug problems in the country. Data on drug treatment admissions, an indirect indicator of drug use, come from all public and publicly funded out-patient centres (initially 250, now some 500) in the whole country since 1987, and is available in a large database which includes socio-demographic information and drug profile. Double-counting is avoided at regional level with a confidential personal code. The quality of this indirect indicator of drug use was assessed in 1988 [11] and has been providing relevant information since then [12,13].

From that indicator, we selected for this study treatment admissions between 1991 and 2005, as prior to 1991 the registry did not collect, with a specific item, whether or not a treatment admission was reported by the patient as the first treatment ever. We were only interested in first ever treatment admissions. We obtained subjects from this database who were aged 10–44 years when they began heroin use, and 15–54 years when admitted for their first heroin treatment ever. These age restrictions, in order to avoid misleading values, occasioned a loss of 1.3% from the total. Year of onset of heroin use was restricted to the period from 1971 to 2005. There were isolated cases in years before 1971 (<0.5%) that were removed to ensure stability in the statistical modelling. In total, 167753 individuals were analysed.

The most important variable was the reported year of heroin use onset. LP length was defined as the delay from this first heroin use to the treatment admission date reported as first. Other variables used in the analysis were gender and most frequent route of heroin administration in the last 30 days before that treatment admission.

**Statistical methodology**

Year of heroin use onset was cross-tabulated against LP length (in years); see Fig. 1. Attention is drawn to the two subsets of empty cells, resulting from truncations: left truncation, affecting people admitted to their first treatment prior to 1991, the first year observed; and right truncation, affecting people still not admitted into treatment by 2005. Because of these empty cells the row totals of the observed table, which provide the observed incidence, are not reflecting the real incidence correctly: we would need the full frequency table. Therefore, the proposal is to estimate the full table by means of an extension of a log-linear quasi-independence model (see equation 3 below) adjusted to the observed data. The row totals of the resulting table will constitute the estimated incidence (see equation 5 below).

Let $T$ be the full table of frequencies $f_{ij}$, where $i = 1, \ldots , I$ and $j = 1, \ldots , J$, resulting from cross-tabulation of onset years and the years of LP, and let $S \subseteq T$ be the observed (incomplete) table. Equation 1 gives the cumulative sums of each $i$th row of the observed table, while equation 2 gives the cumulative sums of each $j$th column.
where $m_{ij}$ was the expected value of the cell $(i,j)$, $\mu$ the mean of the model, $\alpha_i$ the parameter representing row $i$ and $\beta_j$ the parameter representing column $j$. In equation 3 independence is assumed only for cells from $S \subset T$. Such models are called quasi-independence models [14,15].

The software used for the statistical analysis was R version 2.7.1 [16]. Three models were assessed: Poisson, negative binomial and quasi-Poisson model, all with log-link and treatment contrast with baseline in the first level. We found that the Poisson distribution fitted better than the negative binomial ($\chi^2$ Poisson: 6543; $\chi^2$ negative binomial: 8437). In order to adjust for overdispersion we used the quasi-Poisson model (dispersion parameter: 18.6), whose parameter estimates coincided with those of the Poisson model.

The iteratively reweighted least squares technique (IRLS) was used to estimate the parameters of the model and, once performed, the expected value of each cell of the table was calculated as:

$$\hat{m}_{ij} = \exp(\hat{\mu} + \hat{\alpha}_i + \hat{\beta}_j), \hspace{1cm} \forall (i,j) \in T.$$  

Note that the estimation method allows us to extrapolate for unobserved cells. The resulting table is algebraically equivalent to an independence one for the general population, while in fact it has been obtained by fitting a quasi-independence model for the incomplete table actually observed. Lacking a more sophisticated alternative, this implicit assumption of independence seems reasonable.

The estimated incidence values were calculated as:

$$\hat{X}_i = \sum_{(i,j)\in T} \hat{m}_{ij}.$$  

The variance of the estimated parameters $\mu$, $\alpha_i$ and $\beta_j$ and that of the estimated incidence values were computed through the Delta method, a standard procedure for estimating variances of parametric functions [15]. Simultaneously, the distribution of LP was calculated in an analogous way:

$$\hat{F}(j) = \sum_{(i,j)\in T} \hat{m}_{ij} / \hat{M}, \hspace{1cm} \text{where} \hspace{1cm} \hat{M} = \sum_{(i,j)\in T} \hat{m}_{ij}.$$  

The standard errors of $\hat{F}(j)$ were also calculated with the Delta method. The distribution of LP (equation 6) offers the cumulative probabilities of delay between onset of heroin use and the first treatment episode. Therefore, it represents the percentage of people who started their first treatment before $j$ years.

The observed and estimated incidences were converted to population rates for ages ranging from 10 to 44 years, based on yearly population census estimates extracted from the website of the Spanish National Statistics Institute [17]. The rates were smoothed with cubic splines to present the graphics as continuous curves.

In order to compare incidences between different categories of gender and route of administration, we stratified the data and analysed each category separately in the same manner.

**RESULTS**

Table 1 presents a descriptive analysis of the available variables. The mean age of onset was 21 years, and that
of first treatment was 28. In terms of gender, males predominated (84%), sex differences in age of onset and first treatment being significant. Smoking was the most frequent route of heroin administration in the 30 days before admission to treatment (60.5%), followed by injection (29.1%) and snorting (6.2%). In women, snorting was more frequent (9.7%) than in men (5.5%).

Figure 2 shows the observed and estimated incidence curves, all smoothed and converted to rates for ages 10–44 years. The observed incidence rates from available treatment data increased slowly until 1990, when the rate was approximately 70 per 100 000 inhabitants, dropping gradually afterwards. Based on these observed data, the estimated incidence rates of problematic heroin use increased rapidly during the 1970s, from less than 40 new users per 100 000 inhabitants in 1971, until 1980 when 190 new problematic heroin users per 100 000 inhabitants per year were estimated. After that, incidence decreased steeply until the mid-1990s, 30 new users per 100 000 inhabitants being estimated for 1995, then more slowly until 2002, having remained practically stable since then at approximately eight per 100 000 inhabitants.

The incidences estimated for men were higher than for women (for example, rates per 100 000 inhabitants in 1980 were: males, 316; females, 55), although showing similar trends (data not shown). Regarding route of administration (Fig. 3), estimated incidence for injection reached a peak of approximately 150 per 100 000 inhabitants in 1980 and then decreased rapidly, whereas that for smoking did not show such a prominent peak, but maintained its higher level throughout the 1980s at approximately 60 per 100 000 inhabitants. Although in the final years injection seems to have disappeared, the decrease of smoking is less and appears to be stable from

Table 1 Descriptive analysis of people admitted to treatment for heroin as the main drug for the first time in their life in treatment centres in Spain between 1991 and 2005.

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th></th>
<th>Male</th>
<th></th>
<th>Missing</th>
<th></th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
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<td>%</td>
</tr>
<tr>
<td>Total admitted to treatment</td>
<td>26 571</td>
<td>15.9%</td>
<td>140 788</td>
<td>83.9%</td>
<td>394</td>
<td>0.2%</td>
<td>167 753</td>
<td>100%</td>
</tr>
<tr>
<td>Route of administration</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Injecting</td>
<td>7 264</td>
<td>27.3%</td>
<td>41 468</td>
<td>29.5%</td>
<td>143</td>
<td>36.3%</td>
<td>48 875</td>
<td>29.1%</td>
</tr>
<tr>
<td>Smoking</td>
<td>15 584</td>
<td>58.7%</td>
<td>85 673</td>
<td>60.8%</td>
<td>189</td>
<td>48%</td>
<td>101 446</td>
<td>60.5%</td>
</tr>
<tr>
<td>Snorting</td>
<td>2 588</td>
<td>9.7%</td>
<td>7 738</td>
<td>5.5%</td>
<td>38</td>
<td>9.6%</td>
<td>10 364</td>
<td>6.2%</td>
</tr>
<tr>
<td>Other/missing</td>
<td>1 135</td>
<td>4.3%</td>
<td>5 909</td>
<td>4.2%</td>
<td>24</td>
<td>6.1%</td>
<td>7 068</td>
<td>4.2%</td>
</tr>
<tr>
<td>Age of first use (mean ± SD)</td>
<td></td>
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<td></td>
<td>21.4 (5.78)</td>
<td>21.2 (5.57)</td>
<td>20.7 (5.48)</td>
<td>21.2 (5.61)</td>
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<tr>
<td>Age of first treatment (mean ± SD)</td>
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<tr>
<td></td>
<td>27.6 (6.43)</td>
<td>28.5 (6.54)</td>
<td>29.2 (5.96)</td>
<td>28.3 (6.53)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Excluding cases with gender missing. SD: standard deviation.

Figure 2 Observed and estimated problematic heroin use incidence rates* in Spain with 95% confidence interval. *Estimated incidences are relative to ever entering treatment.
2003 to 2005, about six new users per 100 000 inhabitants.

Table 2 shows the distributions of LP globally and by route of administration. Note that the three distributions by route of administration were truncated at 32 years of LP length to allow direct comparison (with stratified data there were null counts if larger LP periods were used). Overall, 50% of people delayed less than 3 years before entering treatment for the first time. Subjects already injecting at their first visit had a slightly higher probability of starting treatment earlier than the others (at 3 years of heroin use 56% of them had done so, whereas the corresponding figures for smoking and snorting were 50% and 48%, respectively).

**DISCUSSION**

We estimated that the incidence of problematic heroin use peaked in 1980 following a rapid increase from the early 1970s and declined rapidly until 2000, when a levelling-off was observed. This curve was similar by gender, although five times higher in men, and differed by route of administration; injecting heroin incidence peaked in 1980 then declined rapidly, whereas heroin smoking did not decline until 1990.

The method used develops Brookmeyer’s approach [8], as suggested, by adopting log-linear modelling. As a consequence, a longer LP could be considered and more subjects contributed to the analysis. The approach used
has permitted estimating incidence for practically the complete heroin epidemic in Spain, avoiding the limitation inherent in previous analyses that could only estimate incidence from the year the register started [7], and has provided an idea of the different relative importance of the two routes of administration during the epidemic. The large number of observations provided reasonable precision for the model estimates even after subdividing the database.

However, the treatment registry data employed can provide information only on heroin users who have been admitted into treatment in public or publicly funded centres during the observed interval. Heroin use incidence curves are thus limited to heroin users who might have been or will be admitted to heroin treatment in these centres: i.e. the incidence is conditional on ever starting a treatment. In this analysis we are not able to take into account those not observed because either their use was non-problematic, they were treated in private centres (of which there are very few in Spain) or they died or ceased use before ever requesting treatment. However, even with an underestimation of the magnitude of the problem, the incidence trend is an appropriate indicator to determine whether drug use is spreading (or diminishing), and if we assume that the proportion of non-observed users is constant from year to year the estimated trend will be similar to the real trend in incidence.

Our log-linear model approach implicitly entails independence: that is, the distribution of LP is the same for every year of onset. We assessed this by estimating LP distributions for three different treatment admission intervals: (A) 1991–1995, (B) 1996–2000 and (C) 2001–2005. The three distributions were truncated at 24 years of length in order to make them comparable. As observed in Fig. 4, people from (A) delayed longer before being admitted into treatment than people from (B) or (C). This could be explained because methadone mainte-

Figure 4 Latency period distributions of heroin use by three time-periods of treatment admission, Spain (latency period: years between first use and first treatment)
peak of the HIV epidemic in Spain (where at that point injecting drugs was the predominant risk factor) was estimated to be between 1984 and 1987 [21], just 4–7 years after the estimated peak of heroin use incidence. This fact underscores the importance of the huge heroin epidemic in Spain and the importance of the decrease in heroin injection for the evolution of the human immunodeficiency virus (HIV), and probably hepatitis C virus, epidemics.

However, it is difficult to ascertain the reasons for such trends, and in fact problematic heroin incidence seems to have decreased even before there was any social or public concern about the existence of a ‘heroin problem’. Socio-economic conditions prevailing at the end of Franco’s dictatorship and over the years which followed may have favoured its spread among young people [20]. Heroin market changes might help to explain why injecting was substituted by smoking [22,23] but are unlikely to have contributed to the large decrease of new users. The emergence of other substances considered less risky than heroin, such as cocaine or ecstasy, might have contributed to a shift of main drug of abuse, particularly in light of the severe consequences of the HIV epidemic in Spain [2]. Nevertheless, we consider it important to point out that the decrease of heroin incidence, particularly by injecting, has coexisted for several years with extensive development of harm reduction programmes, which can constitute evidence against the hypothesis that such programmes could contribute to spreading heroin use [24].

Using log-linear models we have been able to observe that the increase and later decrease in problematic heroin use incidence appeared much earlier than was thought from overall analysis of SDO indirect indicators [3], and that the decrease was related primarily to the fall of injecting. According to these indicators, a decrease of injecting as the main route of heroin administration occurred in some Regions in the late 1980s [12,13], but could not be observed in the context of a national incidence decrease until later on. Data from the present study allow us to see the actions taken to overcome the serious heroin epidemic in Spain in a new light: public health interventions clearly arrived late in various fields. In fact, it was not until 5 years after the heroin incidence peak (1980) that the National Plan on Drugs (an institution devoted mainly to ‘solve’ heroin problems) was created (1985); the information system with indirect indicators to monitor the problem was not available until 7 years had passed (1987); and 11 years had passed by the time the National Plan on Drugs (an institution devoted mainly to ‘solve’ heroin problems) was created (1980) that the National Plan on Drugs (an institution devoted mainly to ‘solve’ heroin problems) was created (1980); the information system with indirect indicators to monitor the problem was not available until 7 years had passed (1987); and 11 years had passed by the time the National Plan on Drugs (an institution devoted mainly to ‘solve’ heroin problems) was created (1980). Also, from the treatment viewpoint, methadone prescription, which began in the early 1980s at the individual physician’s discretion, was restricted in 1985 to public treatment centres of recent establishment, and it was not until 1990 that methadone treatment was legis- lated with a wider scope [25]. It took several years to be implemented fully, needing an important change in physician practice from an abstinence-orientated philosophy to one of risk reduction. In some Regions it was not until 1995 that methadone maintenance programmes were accepted widely: this was 15 years after the epidemic peak, when probably a large proportion of those who had started use around 1980 had already died or were infected with, and possibly suffering the consequence of, HIV or hepatitis C virus [26].

Overall, our analysis provides further support for both the feasibility and relevance of estimating the incidence of problematic drug use with treatment data. Some methodological handicaps still exist which need to be solved, such as the problem of heterogeneity in the distribution of LP over the years.

Declarations of interest

None.

Acknowledgements

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