Opiates or cocaine: mortality from acute reactions in six major Spanish cities

José Sánchez, Begoña Rodríguez, Luis de la Fuente, Gregorio Barrio, Julián Vicente, Josep Roca, Luis Royuela, and the State Information System on Drug Abuse (SEIT) Working Group

Abstract

Study objective – To describe temporal and geographical variations in mortality from acute reactions to opiates or cocaine and the demographic and toxicological characteristics of persons who died from these in major Spanish cities between 1983 and 1991.

Design – Descriptive study. Data were obtained retrospectively from pathologists’ reports.

Setting – Cities of Madrid, Barcelona, Valencia, Seville, Zaragoza, and Bilbao.

Subjects – Deaths from acute reactions to opiates or cocaine were defined as those in which pathologists’ reports did not indicate any other cause of death and in which evidence was found of recent consumption of these drugs.

Main results – The mortality rate from acute reactions to opiate/cocaine per 100,000 population in the six cities as a whole rose from 1.2 in 1983 to 8.2 in 1991. Average annual rates for the whole period ranged from 1.7 in Seville to 4.9 in Barcelona. The male/female ratio was 5.9:1. The mean age of persons who died rose from 25-1 years in 1983 to 28 years in 1991. In more than 90% of the cases in whom toxicological tests were undertaken opiates were detected, and the proportion in which benzodiazepines or cocaine were detected increased during the period studied.

Conclusions – Between 1983 and 1991 mortality from acute reactions to opiates/cocaine rose dramatically in major Spanish cities and significant differences in mortality between cities were found. Deaths were concentrated among men and young people. Acute drug reactions became one of the leading causes of death in persons 15-39 years of age, representing 11-14% of mortality from all causes in 1988 for this age group. Future studies should examine the relationship between the temporal and geographical variations in this type of mortality and various personal, environmental and social factors.

Spain suffered a “drug crisis” during the 1980s that was mainly associated with injected heroin. At the end of that decade and the beginning of the 90s, however, other drugs (cocaine) and routes of administration (smoked or inhaled) were increasingly being used. One of the most dramatic consequences of this crisis has been premature death related to opiate or cocaine use, a phenomenon whose repeated presence in the mass media has caused considerable social alarm. Knowledge of the nature and evolution of these deaths is relevant for two reasons: firstly, because they are an important reflection of the social and health impact of opiate and cocaine consumption; and secondly, because they have been used, together with other indirect indicators, to monitor trends in the prevalence of opiate and cocaine use and, in some cases (before the application of multiplier and capture-recapture techniques), to estimate that prevalence. It is thus an important and necessary indicator in the design and evaluation of drug policies. In spite of their importance, however, these deaths are not adequately reflected in most countries’ official mortality statistics, based on the International Classification of Diseases, and on the usual certification procedure. Consequently, other sources, such as pathologists or the police, are necessary to study these deaths.

Since 1985 various feasibility studies have been undertaken in Spain to develop a routine information system to monitor trends in opiate and cocaine use and associated problems. Inspired by the US Drug Abuse Warning Network (DAWN) and the old Client Oriented Data Process (CODAP), three indicators were selected with relation to opiate and cocaine consumption: (1) outpatient treatment admissions for abuse/dependence (treatment indicator); (2) emergency department episodes related to use (emergency indicator), and (3) deaths from acute reaction after use (mortality indicator). The system began operating in 1987 under the name State Information System on Drug Abuse (SEIT). At first it included treatment and emergency indicators only, with the mortality indicator coming into regular use in 1990.

This report aims to describe temporal and geographical variations in mortality from acute reaction to opiates or cocaine in six major Spanish cities between 1983 and 1991, as well as the demographic and toxicological characteristics of those who died from such reactions during this period. Our analysis is based on regular data from the SEIT mortality indicator and data collected for feasibility studies, using the same methodology, which were carried out before this indicator was developed.
Mortality from opiates/cocaine in Spanish cities

Methods

GEOGRAPHICAL AREA
Six of the seven largest cities in Spain were studied (Madrid, Barcelona, Valencia, Seville, Zaragoza, and Bilbao). These cities have a total population of 7.2 million, and each of them has more than half a million inhabitants, except for Bilbao with a population of 375,054.21

The city of Málaga, with more than half a million inhabitants, was not included in the study because data were not available for the entire period covered.

CRITERIA FOR CASE SELECTION AND INFORMATION SOURCES
Deaths from acute reaction to opiates/cocaine were defined as deaths from acute adverse reaction after the recent consumption of products that contain opiates or cocaine, whether or not the users intended to commit suicide, that is, what are usually called ‘deaths from overdose’, even though it is not always clear whether they are due to a pharmacological overdose. In practice, to include a death as from an acute reaction to opiates/cocaine, we have required that two criteria be met, one negative and the other positive: (1) negative: lack of evidence of another cause of death, and (2) positive: existence of some indication or evidence of recent consumption of opiates or cocaine such as (a) evidence of consumption extracted from the clinical records or external examination (history of consumption mentioned by family or friends, presence of drugs or drug accessories at the place of death, existence of venopunctures); (b) positive post mortem toxicological test for opiates or cocaine; (c) presence of signs at necropsy compatible with death from an acute reaction to opiates/cocaine (generalised visceral congestion, acute pulmonary oedema, etc.)

We have excluded the following: suicides and acute reactions exclusively due to substances other than opiates or cocaine; deaths indirectly related to drug use (violence or unintentional accidents associated with drug abuse, infectious complications related to the mode of drug administration, etc.), even when the deceased had a positive toxicological test; and deaths from intrauterine exposure to drugs.

The only source of information was pathologists’ reports filed in each city’s institute of anatomy and pathology (IAF), the centre in which all judicially mandated necropsies in that city are carried out. The pathologist’s report can, in turn, contain information on toxicological tests carried out by other institutions, mainly the National Institute of Toxicology. We chose to review pathologists’ reports because validation studies before the SEIT mortality indicator,4 and for 1983–89 they were collected retrospectively within the framework of feasibility studies carried out before the indicator was developed. In both cases data collection involved a review of pathologists’ reports from each period.

DATA COLLECTION PROCEDURE
For the period 1990–91 data were collected annually within the framework of the SEIT mortality indicator,4 and for 1983–89 they were collected retrospectively within the framework of feasibility studies carried out before the indicator was developed. In both cases data collection involved a review of pathologists’ reports from each period.

ANALYSIS
We calculated annual mortality rates from acute reactions to opiates or cocaine (per 100,000 population) stratifying by age, sex, and city. The denominators for the rates were obtained by arithmetical interpolation based on the legal

Number of deaths from acute reaction to opiate or cocaine in six major Spanish cities, 1983–1991. The rest of the cities are: Bilbao, Seville, Valencia and Zaragoza.

sensitivity is that deaths from AROC are considered ‘non natural’ and, when they are suspected, both the health system and the police so inform the judge, who in turn orders the pathologist to carry out a complete medical investigation of the case with written results.

VARIABLES
For each death we compiled a record that included the following variables: date of death, age, sex, municipality of death, history of recent drug use, necropsy results and qualitative results of toxicological tests of biological material (blood, urine, or viscera). Whenever possible, age was recorded from the national identity document of the deceased, but in some cases it was obtained from family or friends of the deceased. The qualitative results of the toxicological tests of biological material were available only for a non-random sample of the deceased (sample fraction = 52.7%), for various reasons: either no tests were carried out, or the results went directly to the judge without going through the pathologist, or the test results were not filed in the IAF or were filed in other places that were difficult to access. However, no significant differences (p=0.05) were observed between the groups with and without test results with regard to mean age and distribution by sex.
Table 1  Number of deaths from acute reaction to opiates or cocaine in six major Spanish cities, by sex, year and city of death

<table>
<thead>
<tr>
<th>Year</th>
<th>M</th>
<th>F</th>
<th>M</th>
<th>F</th>
<th>M</th>
<th>F</th>
<th>M</th>
<th>F</th>
<th>M</th>
<th>F</th>
<th>M</th>
<th>F</th>
<th>All cities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1983</td>
<td>15</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>44</td>
<td>8</td>
<td>2</td>
<td>0</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>71</td>
</tr>
<tr>
<td>1984</td>
<td>27</td>
<td>6</td>
<td>4</td>
<td>0</td>
<td>67</td>
<td>11</td>
<td>2</td>
<td>0</td>
<td>15</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>119</td>
</tr>
<tr>
<td>1985</td>
<td>36</td>
<td>7</td>
<td>9</td>
<td>0</td>
<td>58</td>
<td>14</td>
<td>3</td>
<td>0</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>116</td>
</tr>
<tr>
<td>1986</td>
<td>29</td>
<td>6</td>
<td>8</td>
<td>2</td>
<td>73</td>
<td>13</td>
<td>9</td>
<td>3</td>
<td>7</td>
<td>5</td>
<td>7</td>
<td>1</td>
<td>133</td>
</tr>
<tr>
<td>1987</td>
<td>33</td>
<td>18</td>
<td>6</td>
<td>5</td>
<td>107</td>
<td>25</td>
<td>7</td>
<td>1</td>
<td>19</td>
<td>3</td>
<td>9</td>
<td>1</td>
<td>181</td>
</tr>
<tr>
<td>1988</td>
<td>76</td>
<td>22</td>
<td>18</td>
<td>2</td>
<td>142</td>
<td>22</td>
<td>9</td>
<td>1</td>
<td>28</td>
<td>3</td>
<td>9</td>
<td>5</td>
<td>282</td>
</tr>
<tr>
<td>1989</td>
<td>134</td>
<td>33</td>
<td>16</td>
<td>1</td>
<td>167</td>
<td>24</td>
<td>16</td>
<td>3</td>
<td>38</td>
<td>11</td>
<td>1</td>
<td>1</td>
<td>382</td>
</tr>
<tr>
<td>1990</td>
<td>101</td>
<td>31</td>
<td>14</td>
<td>5</td>
<td>207</td>
<td>20</td>
<td>18</td>
<td>4</td>
<td>35</td>
<td>5</td>
<td>19</td>
<td>5</td>
<td>392</td>
</tr>
<tr>
<td>1991</td>
<td>124</td>
<td>35</td>
<td>23</td>
<td>2</td>
<td>260</td>
<td>25</td>
<td>25</td>
<td>1</td>
<td>46</td>
<td>4</td>
<td>30</td>
<td>4</td>
<td>508</td>
</tr>
</tbody>
</table>

All years: 575 | 164 | 100 | 17 | 1125 | 162 | 91 | 13 | 198 | 37 | 95 | 19 | 2184 | 412 |

M = male; F = female.

populations from official census data for 1981, 1986, and 1991. It is important to note that these are special rates because the numerators may not be completely contained in the denominators. In fact, the numerators refer to "deaths occurred in" the territory of a city, whether or not the persons reside in that territory, while the denominators refer to "persons resident" in that city, because information on the municipality of residence of the deceased was considered unreliable. This is because drug users change residence with some frequency, and there may be a high probability that the "actual" residence at the moment of death is not the same as the "nominal" residence on the identification documents or that which is eventually provided by family or friends. In order to calculate rates by sex and age group it was necessary to impute the unknown values of these variables, 27 (1 %) for sex and 61 (2-3 %) for age, in accordance with the distribution of cases with known values. Standardised age rates were not calculated because time and space variations in the age structure of the population were negligible. The difference in mortality between the strata of the variables has been expressed in both absolute (difference between rates) and relative (ratio of rates) terms.

For cases with available toxicological results, we calculated the proportion of deaths in which each drug or pharmacological group of drugs was detected. The statistical significance of the linear trend of these proportions was compared using the $\chi^2$ test for trends. Data processing and analysis was carried out using SPSS/PC+ version 4-0 and EPIINFO version 5-01.

Results

Based on pathologists’ reports, we identified 2596 cases who died from acute reactions to opiates or cocaine between 1983 and 1991 in the six large Spanish cities studied. Most of these deaths (78-0%) occurred in the two cities with the largest populations: Madrid (49-6%) and Barcelona (28-5%). In the following sections we describe the temporal and geographical variations and the demographic and toxicological characteristics of these deaths.

Table 2  Mortality for acute reaction to opiates or cocaine in six major Spanish cities, by age group and year of death (per 100 000 population)

<table>
<thead>
<tr>
<th>Age group (%)</th>
<th>Year</th>
<th>&lt;15</th>
<th>15-19</th>
<th>20-24</th>
<th>25-29</th>
<th>30-34</th>
<th>35-39</th>
<th>40-44</th>
<th>&gt;44</th>
<th>All ages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1983</td>
<td></td>
<td>0.0</td>
<td>2.0</td>
<td>5.4</td>
<td>4.9</td>
<td>1.8</td>
<td>1.2</td>
<td>0.2</td>
<td>0.0</td>
<td>1.2</td>
</tr>
<tr>
<td>1984</td>
<td></td>
<td>0.0</td>
<td>2.0</td>
<td>9.0</td>
<td>8.2</td>
<td>5.3</td>
<td>0.9</td>
<td>0.7</td>
<td>0.0</td>
<td>1.9</td>
</tr>
<tr>
<td>1985</td>
<td></td>
<td>0.0</td>
<td>2.5</td>
<td>10.6</td>
<td>7.8</td>
<td>3.1</td>
<td>1.3</td>
<td>0.7</td>
<td>0.0</td>
<td>2.0</td>
</tr>
<tr>
<td>1986</td>
<td></td>
<td>0.0</td>
<td>2.2</td>
<td>10.1</td>
<td>11.0</td>
<td>4.5</td>
<td>2.2</td>
<td>0.0</td>
<td>0.0</td>
<td>2.3</td>
</tr>
<tr>
<td>1987</td>
<td></td>
<td>0.2</td>
<td>3.7</td>
<td>12.5</td>
<td>14.4</td>
<td>7.5</td>
<td>3.0</td>
<td>1.4</td>
<td>0.1</td>
<td>3.3</td>
</tr>
<tr>
<td>1988</td>
<td></td>
<td>0.0</td>
<td>3.1</td>
<td>17.0</td>
<td>23.1</td>
<td>13.8</td>
<td>3.7</td>
<td>0.9</td>
<td>0.1</td>
<td>4.8</td>
</tr>
<tr>
<td>1989</td>
<td></td>
<td>0.0</td>
<td>4.4</td>
<td>21.3</td>
<td>33.5</td>
<td>15.8</td>
<td>6.1</td>
<td>0.7</td>
<td>0.2</td>
<td>6.4</td>
</tr>
<tr>
<td>1990</td>
<td></td>
<td>0.0</td>
<td>2.8</td>
<td>18.1</td>
<td>33.4</td>
<td>20.3</td>
<td>7.5</td>
<td>1.9</td>
<td>0.1</td>
<td>6.5</td>
</tr>
<tr>
<td>1991</td>
<td></td>
<td>0.2</td>
<td>2.6</td>
<td>22.6</td>
<td>35.3</td>
<td>27.7</td>
<td>11.8</td>
<td>4.1</td>
<td>0.3</td>
<td>8.2</td>
</tr>
<tr>
<td>Average annual rate</td>
<td>0.0</td>
<td>2.8</td>
<td>14.1</td>
<td>19.6</td>
<td>11.5</td>
<td>4.2</td>
<td>1.2</td>
<td>0.1</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>Rates ratio 1991/83</td>
<td>2.6*</td>
<td>1.3</td>
<td>4.2</td>
<td>7.2</td>
<td>15.2</td>
<td>10.1</td>
<td>16.8</td>
<td>8.1</td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>Rates difference 1991-83</td>
<td>0.2</td>
<td>0.5</td>
<td>17.2</td>
<td>30.4</td>
<td>25.6</td>
<td>10.7</td>
<td>3.9</td>
<td>0.3</td>
<td>7.0</td>
<td></td>
</tr>
</tbody>
</table>

* Rates ratio 1991/1984, because the mortality rate in 1983 was 0.
Mortality from opiates/cocaine in Spanish cities

Table 3 Mortality for acute reaction to opiates or cocaine, by city and year of death (per 100 000 population)

<table>
<thead>
<tr>
<th>Year</th>
<th>Barcelona</th>
<th>Bilbao</th>
<th>Madrid</th>
<th>Sevilla</th>
<th>Valencia</th>
<th>Zaragoza</th>
<th>All cities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1983</td>
<td>1.1</td>
<td>0.5</td>
<td>1.7</td>
<td>0.3</td>
<td>0.8</td>
<td>0.5</td>
<td>1.2</td>
</tr>
<tr>
<td>1984</td>
<td>1.9</td>
<td>1.0</td>
<td>2.5</td>
<td>0.3</td>
<td>2.3</td>
<td>0.9</td>
<td>1.9</td>
</tr>
<tr>
<td>1985</td>
<td>2.6</td>
<td>2.3</td>
<td>2.3</td>
<td>0.5</td>
<td>1.4</td>
<td>0.7</td>
<td>2.0</td>
</tr>
<tr>
<td>1996</td>
<td>2.1</td>
<td>2.6</td>
<td>2.8</td>
<td>1.9</td>
<td>1.6</td>
<td>1.4</td>
<td>2.3</td>
</tr>
<tr>
<td>1987</td>
<td>3.0</td>
<td>2.9</td>
<td>4.3</td>
<td>1.2</td>
<td>3.0</td>
<td>1.7</td>
<td>3.3</td>
</tr>
<tr>
<td>1988</td>
<td>5.8</td>
<td>5.3</td>
<td>5.4</td>
<td>1.5</td>
<td>4.2</td>
<td>2.4</td>
<td>4.8</td>
</tr>
<tr>
<td>1989</td>
<td>10.0</td>
<td>4.5</td>
<td>6.3</td>
<td>2.8</td>
<td>6.6</td>
<td>2.0</td>
<td>6.4</td>
</tr>
<tr>
<td>1990</td>
<td>8.0</td>
<td>5.1</td>
<td>7.5</td>
<td>3.3</td>
<td>5.1</td>
<td>4.1</td>
<td>6.5</td>
</tr>
<tr>
<td>1991</td>
<td>9.7</td>
<td>9.5</td>
<td>9.5</td>
<td>3.9</td>
<td>6.6</td>
<td>5.7</td>
<td>8.2</td>
</tr>
<tr>
<td>Average annual rate</td>
<td>4.9</td>
<td>3.4</td>
<td>4.7</td>
<td>1.7</td>
<td>3.5</td>
<td>2.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Rates ratio 1991/83</td>
<td>8.8</td>
<td>13.0</td>
<td>5.7</td>
<td>12.3</td>
<td>8.2</td>
<td>10.9</td>
<td>7.1</td>
</tr>
<tr>
<td>Rate difference 1991–83</td>
<td>8.6</td>
<td>6.3</td>
<td>7.8</td>
<td>3.5</td>
<td>5.8</td>
<td>5.2</td>
<td>7.0</td>
</tr>
<tr>
<td>Inter-city ratio*</td>
<td>2.8</td>
<td>1.9</td>
<td>2.7</td>
<td>1.0</td>
<td>2.0</td>
<td>1.2</td>
<td></td>
</tr>
</tbody>
</table>

* Ratio for the period 1983–91 between the average rate of each city and the average rate of Sevilla (taken as reference).

Table 4 Qualitative results of toxicological tests of biological material from a sample of deaths from acute opiate/cocaine reactions, 1983–91

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>% of deaths in which selected drugs detected†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opiates</td>
<td>93.3</td>
<td>95.8</td>
<td>92.4</td>
<td>93.0</td>
<td>NS</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>35.7</td>
<td>23.0</td>
<td>30.9</td>
<td>42.0</td>
<td>**</td>
</tr>
<tr>
<td>Cocaine</td>
<td>20.1</td>
<td>9.4</td>
<td>16.7</td>
<td>25.0</td>
<td>***</td>
</tr>
<tr>
<td>Alcohol</td>
<td>138.1</td>
<td>94.9</td>
<td>181.1</td>
<td>138.9</td>
<td>NS</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>4.1</td>
<td>3.8</td>
<td>7.4</td>
<td>2.4</td>
<td>*</td>
</tr>
<tr>
<td>Non-opiate analogs</td>
<td>2.8</td>
<td>2.8</td>
<td>3.2</td>
<td>2.7</td>
<td>NS</td>
</tr>
<tr>
<td>Anxiolytics</td>
<td>0.9</td>
<td>0.9</td>
<td>1.0</td>
<td>0.8</td>
<td>NS</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Other drugs</td>
<td>13.3</td>
<td>11.7</td>
<td>9.6</td>
<td>15.8</td>
<td>*</td>
</tr>
<tr>
<td>No of deaths with toxicological tests</td>
<td>1369</td>
<td>213</td>
<td>408</td>
<td>748</td>
<td></td>
</tr>
<tr>
<td>% of deaths with toxicological tests over the</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>total number of deaths</td>
<td>52.7</td>
<td>58.2</td>
<td>55.6</td>
<td>50.0</td>
<td></td>
</tr>
</tbody>
</table>

* Statistical significance of χ² test for trend: NS = not significant, * p<0.05, ** p<0.001.
† Each case may have positive results for different drugs.
‡ Results for the period 1990–91.

The mean annual rates in Madrid and Barcelona for the whole period were 2.7 and 2.8 times greater respectively than those for Seville (table 3).

DEMOGRAPHIC CHARACTERISTICS
Most of those who died were male (table 1): the male/female rates ratio for all cases studied was 5.9/1, and ranged from 3.9/1 in Barcelona to 8.1/1 in Seville. The ratio decreased between 1983 and 1987 for the six cities as a whole, going from 6.0/1 to 3.8/1. The ratio then increased up to 7.9/1 in 1991.

Some 97.1% of cases were between 15 and 39 years of age. Between 1983 and 1991 the mean age of those who died increased progressively, going from 25.1 to 28.0 years.

TOXICOCOLOGICAL CHARACTERISTICS
Table 4 shows the qualitative results of the toxicological tests in the mentioned sample of the deceased. It can be observed that opiates or their metabolic derivatives (principally heroin/morphine) were found in almost all cases in which toxicological tests were available, and cocaine in about one fifth of such cases. Overall, 94.8% of the cases were positive for opiates or cocaine. These drugs were not found in the remaining 5.2% of cases, but all these cases fulfilled at least one of the other two positive criteria for inclusion: signs at necropsy or recent history of opiate or cocaine consumption.

Derivatives of more than one type of psychoactive substance were found in 61.2% of the cases, with the most frequent association being opiates/benzodiazepines. Opiates as a single drug were found in 34.3% of cases, while cocaine was almost always detected in conjunction with opiates; cocaine alone was isolated in only 0.7% of cases. The ratio between tests positive for opiates and negative for cocaine, and tests negative for opiates and positive for cocaine, was 49.

During the period 1983–91 there was an increase in the proportion of deaths in which cocaine and benzodiazepines were detected.

Discussion
Various conclusions can be drawn from the data on mortality from acute reactions to opiates of cocaine in the major Spanish cities.

LARGE INCREASE IN MORTALITY
In the period 1983–91 there was a very large increase in mortality from this cause (also confirmed by police data[36]). The factors that might explain this increase are not clear but, in accordance with other authors,[1425-29] various can be suggested.

Increase in the number of heroin and cocaine users.
Increases in the indirect indicators available – the SEIT treatment and emergency indicators...
and drug seizures\textsuperscript{1,2} – suggest that the number of users has increased during this period, although the latency period between drug consumption and resulting problems may mean that the value of the indicators continues to increase even when the level of consumption is stabilising or decreasing.

Accumulation of health problems attributable to increasing years of use (length of use) of opiate or cocaine users

The increase in length of use has been verified by the SEIT treatment indicator\textsuperscript{3} and by other studies.\textsuperscript{30}

Spread of HIV infection in this population

HIV infected drug users may have a higher risk of death by accidental or suicidal overdose than those who are not infected. If this hypothesis is correct, this factor has quite probably contributed in some degree to the increasing mortality from acute opiate/cocaine reactions in Spain, because the prevalence of HIV infection among opiate or cocaine users is very high (in 1989 it was estimated at 40\%-75\%\textsuperscript{31}) and it will inevitably have increased over the period 1983–91. However, this factor may be closely linked to the previous one, because some studies have found a positive association between the prevalence of HIV infection and length of drug use.\textsuperscript{32}

Changes in drug availability and purity

These changes are unknown, but they are unlikely to have been of sufficient magnitude to explain such a major increase in mortality.

Change in patterns of drug consumption

An increase in polyconsumption throughout the period would probably have acted to increase the risk of death of users (the increase in the proportion of those who die from acute reactions to opiates or cocaine in whom cocaine and benzodiazepines are detected; table 4), and the increase in the prevalence of cocaine use among heroin addicts admitted to treatment\textsuperscript{1} suggests that there has been some increase in polyconsumption. The recent observation of a decrease in the prevalence of the parenteral route and a simultaneous increase in the pulmonary route, however,\textsuperscript{31} would probably act to decrease mortality.

In summary, we believe that, in keeping with the foregoing comments, the factors with the greatest explanatory value for the increase in mortality would be the first three. On the other hand, the increase detected in Spain is not an isolated phenomenon in the context of western countries. During the 80s similar increases have also been detected in many areas of the United States\textsuperscript{15,16} and Europe,\textsuperscript{14,16,37} although not in other areas such as Inner London, Amsterdam, Copenhagen, or Stockholm.\textsuperscript{14}

**GEографical differences in mortality**

We observed major differences in mortality between the cities studied. These can be explained by differences in the factors mentioned with regard to the temporal changes, by differences in the phenomenon of attraction of users to large cities that will be discussed below, and by other factors such as differences in the prevalence of use of the parenteral route among opiate or cocaine users. For example, Seville has the lowest mortality from acute reactions to opiates/cocaine of the six cities, the lowest prevalence of use of the parenteral route,\textsuperscript{4} and probably also the lowest prevalence of HIV infection among opiate or cocaine users.\textsuperscript{38}

The available data suggest that mortality from an acute reaction to opiates/cocaine in large Spanish cities is not very different from that of other European cities.\textsuperscript{14} It should be pointed out, however, that in Europe the comparison of drug-related mortality among different geographical areas is very problematical because of differences in definitions, sources, and data collection procedures.\textsuperscript{14,39} For example, the definition used in Spain seems to be more restrictive than that used in some other countries.

**ACute drug reactions – a major cause of death in young adults**

This has become a major cause of death among young adults, principally young men. Combining our data with general mortality statistics,\textsuperscript{30} it is calculated that in 1988, the last year with available statistics, deaths from acute reactions to opiates/cocaine accounted for 11\%-1% of deaths from all causes in those aged 15–39 years of age and 16\%-7% of deaths in those aged 20–29 years in the six Spanish cities studied. Bearing in mind the trends detected, it is possible that in 1991 these proportions will be 1-7 times larger. Some studies have indicated that in Barcelona, at the end of the 80s, acute opiate/cocaine reaction was the main cause of death from toxic origin in the general population,\textsuperscript{41} and the second cause of potential years of life lost in the 15–39 year age group, after traffic accidents.\textsuperscript{22}

**INCREASE IN AGE OF THOSE DYING FROM ACUTE OPIATE/COCaine reaction**

In recent years the age of persons dying from acute opiate/cocaine reaction has been on the increase. Between 1987 and 1991 the mean age of those who died has been higher than that of users included in the SEIT treatment and emergency indicators, and the mean age for all three indicators has increased.\textsuperscript{4} This increase in the age of people dying has also been detected in other European countries\textsuperscript{13,14,36,42} and in the US,\textsuperscript{32} but it still seems that those who die from acute opiate/cocaine reactions in Spain are younger than those in other western countries.\textsuperscript{13,43,44}

**Male preponderance**

Most people who die from acute opiate/cocaine reactions are male. The proportion of males is higher among users detected by the mortality...
indicator than among those detected by the other two SEIT indicators or by population surveys, which could suggest the existence of lethality factors associated with the condition of being a male user. In recent years the proportion of deaths in women had decreased, which has coincided with a simultaneous decrease in the SEIT treatment indicator. On the other hand, it seems that in Spain the proportion of drug associated deaths in women is lower than in other western countries.13,45

**TYPES OF DRUGS USED**

The drugs most frequently found in the biological samples of the deceased are those derived from heroin/morphine; often, more than one drug is found, with the most frequent association being heroin/morphine + benzodiazepines, which is considered high risk.46 Heroin/morphine derivatives are also the most frequently detected drugs in other European studies,42,47,48 while in the US cocaine is the most frequently cited drug.15 The fact that this study found that opiates in the absence of cocaine were detected 49 times more often among people dying from acute reactions to opiates/cocaine than cocaine in the absence of opiates could suggest that cocaine use has not been a major contributing factor in deaths from acute opiate/cocaine reactions in Spain (in spite of the fact that the prevalence of cocaine consumption is higher than that of heroin). A similar suggestion has been made in Milan,50 but additional studies are needed to clarify this question, because it is possible that pathologists are less likely to detect cocaine deaths than deaths from opiates.

This study covers only part of the Spanish population (18%), all of them residents in the largest cities. Thus, the conclusions obtained are not applicable to the whole of the Spanish population. SEIT data4 suggest that mortality from acute opiates/cocaine reaction is considerably less in mid-size cities and in rural areas than in the largest cities.

**SOURCES OF ERROR**

The mortality measurements in this study can be affected by two sources of error that could limit the interpretation of the results.

**Errors in the identification of cases**

(a) Some drug related deaths (especially from cocaine) may be labelled as “natural” and consequently do not come to the attention of the pathologist. This can occur because the clinical physician who establishes the cause of death does not suspect the association with drugs or because he or she deliberately hides such an association to avoid legal implications for the family of the deceased. However, in spite of underestimating to some degree the real number of deaths all studies in Spain,22,23 as in the US,49 show that pathologists are a more appropriate and complete source of information on deaths from acute opiate/cocaine reaction than general mortality statistics. (b)

There may be “unnatural” deaths not resolved by the pathologists or errors at the time of classifying a death as from an acute drug reaction. These sources of error have not been evaluated but it has been suggested that their influence is negligible.22 Even though among users of multiple drugs it is sometimes difficult to identify the cause of death or attribute the death to a specific drug,50 the pathologist has available more tools to do this job (testimony, necropsy, toxicological and serological tests) than clinical physicians and, of course, than the police. Toxicological test results can to some extent validate the other criteria used to include a death as an acute drug reaction, such as external evidence of use or positive necropsy results. The fact that, of the cases for whom toxicological test results are available, only 5-2% are negative for opiates or cocaine is a guarantee of the validity of the information collected.

**The atypical nature of the rates calculated**

The numerator refers to deaths that occur within a territory and the denominator to residents of that territory which can, in some cases, affect the temporal and geographical comparisons of mortality data. There is a constant flux of users between the large cities and their surrounding areas. If the net result of this flux at the time of death varies much between cities and between periods, the comparisons can be distorted. Furthermore, as the probable end result is a net attraction of users to the large cities, it is possible that the mortality rates are somewhat overestimated in these areas at the expense of the rest of the territory. This phenomenon has not been precisely quantified, but two recent studies indicate that approximately 25% of people who died from acute opiates/cocaine reactions in Madrid and Barcelona had their formal residence outside those cities, principally in their metropolitan areas.22,23 Unfortunately, the inverse phenomenon (residents in these cities who die outside of them) has not been quantified, though it is thought to be less important.

The net result of the three sources of error cited could be a slight overestimation of the mortality in the large cities. For this to distort the comparisons, however, there would have to be major temporal and geographical differences in the overestimation in time and space, and there is no evidence to indicate that such differences have been produced.

We agree with other authors51 that more complete studies are necessary to clarify the nature of the temporal and geographical variations in mortality from acute reactions to opiates/cocaine as well as their relation with public policy on drugs and other environmental and social factors.

The SEIT Working Group for this study comprised the following, in alphabetical order: José M Abenda (Instituto Anatómico-Forense (IAF) Madrild), José Alameda (Consejería de Asuntos Sociales, Sevilla), Rafael Alcaraz (IAF, Bilbao), Josep M Abreu (Instituto Municipal de Investigación Médica de Barcelona (IMIM), Barcelona), José Asua (Departamento de Sanidad y Consumo, Vitoria), Elena Balanza (IAF, Sevilla), Andrés Bedate (IAF, Madrid), Teresa Brugal (IMS, Barcelona), Berta Candia (DGPNRD), María Castellano (Facultad de Medicina de


