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Drug-related mortality and its impact on adult mortality in eight European countries

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Objective: To estimate the mortality rates from drug-related deaths and other causes among problem drug users and population attributable risk of death due to opiate use in eight study sites in Europe. **Methods:** Opiate users were recruited from drug treatment centres during the period 1990–1998 and deaths followed up through national or local mortality registries. Gender-specific overall mortality rate, proportion of deaths by cause (drug-related, HIV, other), standardized mortality ratios (SMRs), and the attributable risk fraction (ARF) were estimated. **Results:** Crude mortality rates varied from 1 per 100 person-years in the Dublin and London cohorts to 3.8 per 100 person-years in Barcelona. The highest drug-related mortality rate was 10 per 1000 person-years in Barcelona; the rates were ~7 per 1000 person-years in Denmark, London, Rome, and Vienna, and <3.5 per 1000 person-years for the others cohorts. The mortality rate for AIDS was <2 per 1000 person-years in all the cohorts except Lisbon, Rome, and Barcelona, for which it was ~6 per 1000 person-years. The highest SMR among males was 21.1 in Barcelona, and among females the highest SMRs were 53.7 and 37.7 in Barcelona and Rome, respectively. In Denmark the ARF was 5%, whereas it was >10% in all other study sites and 24% in Barcelona. **Conclusion:** Cohort mortality studies, especially in combination with estimates of prevalence, provide useful insights into the impact of opiate use on mortality across European countries and emphasize how preventing overall and drug-related deaths among opiate users can significantly improve the health of the population.

Keywords: drug-related mortality, longitudinal studies, opiate addiction

The advantage of mortality statistics over most surveillance systems is that they are invariably complete;[1] information on cause of death can also be obtained, although only on the condition that one can identify the population one wants to be informed about. Although drug poisoning/overdose and drug dependence are key causes of death directly attributable to problem drug use, problem drug users can die from many other causes which are not readily visible in routine population mortality statistics because we cannot identify problem drug users in the register. Furthermore, any interpretation of drug-related deaths[2] over time has to distinguish between at least two potential explanations: changes in the prevalence of opiate use and in mortality risk. Mortality cohort studies which follow up samples of problem drug users identify all causes of death and measure both the overdose and all cause mortality rate. If successful, they offer the opportunity of a full picture of drug-related mortality and support the interpretation of mortality statistics.[3]

The occurrence of heroin use and the mortality associated with it vary between geographical areas.[4–10] In general, the opiate overdose mortality rate will be higher in populations with a higher prevalence of injecting drug use. However, other factors may govern the impact of opiate and injecting drug use on opiate poisoning and all cause mortality, notably HIV prevalence among injecting drug users (IDUs) and also the average age of the cohort and availability of substitution treatment. Many longitudinal studies show IDUs to have higher overall and cause-specific mortality rates than the general, gender- and age-matched, population,[7,11–13] with meta-analysis estimating that the risk of death among injectors was over 13 times higher and that the drug-related mortality rate was ~0.8% per annum.[14] In this study we estimate the excess of mortality among opiate users enrolled in eight European cohorts compared with the general population and the proportion of deaths in the general population that may be attributable to opiate use.

Methods

The study population included eight cohorts of opiate users collected by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) working group on cohort mortality studies among opiate addicts. All cohorts consisted of opiate users aged 15–69 years entering treatment during the period 1990–1999 and followed up using a comparable methodology. Deaths among the subjects were traced by linking the cohorts with national or municipal registers. A more detailed description of the different cohorts and the methodology has been published elsewhere.[15] Participant study sites were selected on

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the basis of the availability of basic information on patients entering treatment and access to population and/or mortality registries. Subjects contributed person-years at risk up to the age of 69 years, the end of the study period, or date of death, whichever came first. Causes of death where available were retrieved according to the following selection of ICD-IX and ICD-X codes:

Drug-related deaths: 292; 304.0–.9; 305.2–.9; 965.0–.9; 969.0–.9; E850–E858; E980.0-5; E980.9; E950.0-.5; E950.9; E962; F11–F16; F18–F19; X40–X44, X49; Y10–Y14, Y19; X60–X64; X85.

HIV-related deaths: 042.0–044.9; 279.1; 279.5; 279.8; B20–B24.

The remaining causes were classified as 'other'.

Standardized mortality ratios (SMRs) were calculated in order to estimate the overall mortality excess among opiate users compared with the general population of the same age and gender. SMRs were calculated separately for males and females, with the expected number of deaths in the cohort generated from the mortality rate of the individual country by 5-year age group (for the year in the middle of the follow-up period).[16] Two-sided 95% confidence intervals for SMRs were based on the Poisson distribution. The attributable risk fraction (ARF) was calculated as follows (for adults aged 15–49 years because prevalence estimates were available this age group):

$$\mathrm{ARF} = P_{\mathrm{opiate}}(\mathrm{SMR}-1)/\left(P_{\mathrm{opiate}}(\mathrm{SMR}-1)+1\right).^{17}$$

Estimates of the prevalence of opiate use were obtained from the literature and EMCDDA sponsored studies.[18–22] Credible estimates for Lisbon were not available, so the ARF was not calculated.

Results

The proportion of males in the cohorts ranged from 69% in Vienna to 82% in Rome, and the average age at recruitment was 25–29 years in six of the cohorts and >30 years in the Danish and Dutch cohorts. Table 1 shows the number of subjects in the cohort, the study period, and crude death rates overall and among males and females aged 15–69 years. The mortality rate varied from just over 1 per 100 person-years in Dublin and London to 2 per 100 person-years in Rome and 3.8 per 100 person-years in the Barcelona cohort (i.e. nearly 1 in 25 cohort subjects dying per year). Death rates for males and females were similar in the cohorts from Amsterdam, Denmark, Barcelona, Lisbon, and Rome, whereas in Dublin, Vienna, and London the death rate was 2–3-fold lower among females in the cohorts than among male opiate users (i.e. 0.5–0.8 per 100 person-years compared with 1.3–1.6 per 100 person-years).

Table 2 shows the mortality rates and proportion of deaths by cause. The proportion of drug-related deaths varies from ~7% in Lisbon to 60% in the London cohort. The highest mortality rate from fatal overdose was 13 per 1000 person-years in Barcelona, compared with ~7 per 1000 person-years in

Table 1 Number of subjects enrolled in the eight cohorts and crude death rates (per 1000 person-years)

Study site	Study period	Number of subjects	Person-years	Number of deaths	Crude death rate		
					Overall	Males	Females
Amsterdam	1996–2002	2575	10 576.31	174	16.45	16.72	15.39
Barcelona	1992–2001	5037	30 237.06	1137	37.60	38.94	33.38
Denmark	1996–2002	8808	40 317.80	701	17.39	18.33	14.78
Dublin	1994–1997	5285	10 345.27	114	11.02	13.17	5.30
Lisbon	1992–2003	3275	28 619.70	440	15.37	16.13	12.35
London	1997–2001	881	2850.39	35	12.28	13.82	7.97
Rome	1992–1997	5924	21 248.39	425	20.00	19.92	20.37
Vienna	1990–1998	4150	14 834.62	195	13.14	16.41	6.01

Age range 15–69 years for both calculation of person-years at risk and number of deaths

Table 2 Number and proportion of deaths, and mortality rate by cause, all ages (15–69 years), by cohort

Study site	Drug-related deaths			AIDS deaths			Other causes			Missing causes		
	n	%	Crude rate/ 1000	*n*	%	Crude rate/ 1000	*n*	%	Crude rate/ 1000	*n*	%	Crude rate/ 1000
Amsterdam[a]	—			—			—					
Barcelona	392	34.5	12.96	421	37.0	13.9	280	24.6	9.3	44	3.9	1.46
Denmark	285	40.7	7.07	17	2.4	0.42	169	24.1	4.19	230	32.8	5.70
Dublin	32	28.1	3.09	24	21.1	2.32	54	47.4	5.22	4	3.5	0.39
Lisbon	32	7.3	1.12	179	40.7	6.25	181	41.1	6.32	48	10.9	1.68
London	21	60.0	7.37	0	0.0	0.00	10	28.6	3.51	4	11.4	1.40
Rome	141	33.2	6.64	135	31.8	6.35	142	33.4	6.68	7	1.7	0.33
Vienna	98	50.3	6.61	37	19.0	2.49	60	30.8	4.04	0	0	0

a: No information on causes of death available

Denmark, London, Rome, and Vienna. No deaths from AIDS were found in the cohort recruited in London, while the proportion of AIDS deaths varied considerably across the other cohorts, from ~2% in Denmark to 41% in Lisbon, with similar death rates in Rome and Lisbon of ~6 per 1000. Several of the cohorts had substantial numbers of deaths with missing or unascertained causes, e.g. in Lisbon, London, and Denmark >10% were missing information on cause of death.

Table 3 shows the SMR comparing the mortality rate in the cohort with the general population. In four of the eight sites the mortality rate was 10 times higher than in the general population. In Barcelona the SMR was 21.1 in males and 53.7 in females; in Rome female opiate users were nearly 40 times more likely to die than females in the general population. In Lisbon the SMR among males was just over 6 times higher than in the general population, and in Vienna the SMR among females was just over 10 times higher. Given that death rates in the adult population are higher in males than in females, the largest differences in SMR between males and females were observed for those cohorts where the mortality rate of opiate users by gender was similar (see table 1), whereas cohorts with higher death rates among male opiate users reported similar SMRs for males and females.

Table 4 shows estimates of the ARF (i.e. the proportion of deaths in the general population that may be attributable to opiate use if the total surplus of deaths in the cohort were causally related to opiate use). Denmark is the only country-level cohort; it has a low prevalence of opiate use and therefore <5% of adult mortality at ages 15–49 attributable to opiate use. In contrast almost one in four adult deaths in Barcelona could be a consequence of opiate use. In the other study sites the ARF ranged from 10 to 17%.

Discussion

This descriptive study emphasizes the public health importance of drug-related mortality, the scale of risk experienced by opiate users (mostly heroin injectors), and the potential impact of opiate use on the health of the adult population, especially in cities in Europe. The evidence is clear: if we manage to prevent opiate use, transmission of HIV among IDUs, and fatal overdose we will improve significantly the overall health of the population. The findings also underline the value of mortality cohort studies. Further, the difference between the sites suggests that there is unlikely to be any standard or inherent drug mortality rate or SMR among problem drug users. Nevertheless, most of the cohort estimates suggested a higher mortality rate and SMR than an earlier meta-analysis[14]—i.e. that the annual mortality rate of opiate users is >1 in 100 and could be as high as 3.7 per 100, with an SMR ranging from 6 to 54 and 10–20% of adult mortality at ages 15–49 years attributable to opiate use. In Barcelona nearly one in four deaths among young adults are potentially due to opiate use. The drug-related mortality rate across the sites was more consistent, ranging from 0.7 to 1% in five of the sites. However, the lower rate, represented in Lisbon, may reflect problems with the coding/certification of deaths. Part of the variation in overall mortality between the cohorts reflects the uneven distribution of HIV infection in Europe, with high death rates and SMRs found in Southern European countries where the prevalence of HIV also is higher.[3]

Although they illustrate the scale of the problem, the study estimates need to be treated cautiously, and our analyses were limited by a lack of information on the generalizability of the cohorts to all opiate users and IDUs in the respective sites. There are several potential biases that could lead to an

Table 3 All causes standardized mortality ratios (SMRs) and 95% confidence intervals (95% CI), all ages (15–69 years), by cohort, 1990–2000

Study site	Observed		Expected		SMR 15–69 (95% CI)	
	Males	Females	Males	Females	Males	Females
Amsterdam	141	33	19.7	2.7	7.2 (6.1–8.4)	12.2 (8.7–17.2)
Barcelona	894	243	42.4	4.5	21.1 (19.8–22.5)	53.7 (47.4–60.9)
Denmark	543	158	68.4	15.2	7.9 (7.3–8.6)	10.4 (8.9–12.1)
Dublin	99	15	9.2	1.3	10.7 (8.8–13.1)	11.4 (6.9–18.9)
Lisbon	369	71	58.3	4.3	6.3 (5.7–7.0)	16.7 (13.2–21.0)
London	29	6	2.4	0.4	12.2 (8.5–17.6)	15.8 (7.1–35.1)
Rome	347	78	25.5	2.1	13.6 (12.2–15.1)	37.7 (30.2–47.1)
Vienna	167	28	16.8	2.7	9.9 (8.5–11.6)	10.2 (7.1–14.8)

Table 4 Attributable risk fraction (ARF) of all cause mortality by opiate use, ages 15–49 years, by cohort

Study site	Population	Estimated number of opiate users	Prevalence of opiate use (%)	Standardized mortality ratio (15–49 years)	ARF (%)	Study period
Amsterdam	369 000	5000	1.4	10.1	10.9	1996–2002
Barcelona	746 318	9176	1.2	25.6	22.8	1992–2001
Denmark	2 553 000	14 000	0.5	9.2	4.3	1996–2002
Dublin	588 000	12 250	2.1	10.9	17.0	1994–1997
London	3 919 000	62 000	1.6	13.6	16.6	1997–2001
Rome	1 317 000	14 500	1.1	15.4	13.7	1992–1997
Vienna	786 000	10 200	1.3	9.8	10.3	1990–1998

under- or overestimate of the different mortality measures. First, the mortality rates observed among the cohorts may not be representative of the rates of the total population of opiate users. The study populations were recruited through treatment centres, which under-represent recent opiate users. Moreover, different criteria to enter treatment may result in differential selection across countries. Cohort mortality may be higher if treatment attracts those drug users with the most serious morbidity or it may be lower (immediately after recruitment) because of the protective effect of treatment.

Second, prevalence estimates and thus ARF are based on the official population. Larger cities, however, may attract drug users who do not belong to the registered population of that city.

Third, not all excess mortality is likely to be caused by opiate use: strong risk factors for mortality such as deprivation, smoking, drinking, and other risky behaviour are strongly associated with opiate use; controlled for these might reduce the SMR.

Fourth, the SMR underestimates the risk ratio based on the general population rather than a non-opiate using cohort. However, it must be considered that because we use national reference rates rather than local ones this effect will be small.

In addition to potential methodological issues, the information about the cohorts is too limited to draw conclusions concerning drug policy. Data on injecting status and drug profile were not collected from enough of the subjects in the cohorts to test whether these could explain differences in the mortality rate between the cohorts. Moreover, although all subjects were selected from treatment sites they also differ across sites in terms of age distribution, years of follow-up, and length of time in contact with treatment services, all of which can have an impact on the risk of death.[23–26] Thus, any differences in the distribution of these factors between subjects in the cohort and the underlying population would add bias to the findings.

Ideally the ARF would be estimated separately for males and females; however, the prevalence estimates were not sufficiently robust and we did not want to compound the uncertainty. In general, the ARF would be larger for males than for females, given that it is likely that about three-quarters of opiate users would be male. Finally, the current cohorts include too many unknowns to permit a comparative assessment of the risk of death among countries. For instance, do the sites with higher mortality rates indicate inequalities in provision of specialist drug treatment or other harm reduction/prevention initiatives and/or greater environmental risk?

Joint evaluation of the mortality rates, SMRs, and prevalence of opiate use, however, could provide useful insights into the impact of opiate use on mortality across European countries and should be a goal of future surveillance of drug-related deaths. Our data corroborate reports that in many European countries drug users have a high mortality risk of death from infectious diseases, AIDS, drug-related deaths, and violence.[27–30] In conclusion, our results suggest that public health interventions targeted towards opiate users/IDUs, though a comparatively small proportion of the population, may produce a major effect on the health of the general population overall, especially in cities. Moreover, we urge investment in standardized mortality cohorts of opiate users across Europe and reliable estimates of the prevalence of opiate use. These instruments will enable a clearer comparison among countries of the scale of different causes of death among problem drug users in order both to monitor this important public health problem and to identify sites which have reduced the risk of death and improved the health of the population.

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Key points

- The study estimates mortality rates of opiate users in Amsterdam, Barcelona, Denmark, Dublin, Lisbon, London, Rome, and Vienna.
- Mortality rates range from 1 per 100 person-years in Dublin and London to 3.8 per 100 in Barcelona and are 6–54 times higher than expected in the general population.
- 10–20% of adult mortality at ages 15–49 years is attributable to opiate use.
- Public health interventions targeted towards opiate users/IDUs may produce a major effect on the health of the general population overall.
- Investment in mortality cohort studies among drug users is required to monitor temporal and geographical trends in overall and cause-specific mortality.

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