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Mortality Trends among Cocaine Users Treated between 1989 and 2013 in Northern Italy: Results of a Longitudinal Study

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ABSTRACT

A total of 852 participants attending 11 centers for addiction treatment in north Italy following problems due to cocaine abuse between 1989 and 2013 were recruited. Two typologies were created: cocaine users (never heroin) (CU) and heroin and cocaine users (HCU). During the 38-year follow-up period, 4.8% of the whole cohort died. Over the whole period, tumors were the main causes of death; starting in 2010, suicide deaths became the first cause of death. Among CUs, most deaths were due to road accidents and suicide; among HCUs, most of the deaths were from opiate overdose and from cardio-circulatory system diseases. The excess mortality observed for all causes in either sex was 6.24; higher in females (15.03) as compared in males (6.23), higher in HCUs (9.06) as compared in CUs (5.21). The directly age-sex standardized mortality rates were 5.31 per 100, higher for females, declining after 2009 for all patients and after 2004 for HCUs. Multivariate analysis confirms the decreasing trend in the risk of death and shows a higher mortality risk for participants in the under-25 age group. Among cocaine users, special attention should be paid to the prevention of suicide deaths.

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Cocaine; cohort study; mortality; overdose; public service dedicated to addictions; suicide

About 3.4 million (1%) of European Union citizens aged 15 to 64 have used cocaine over the past 12 months and 15.6 million (4.6%) in the course of their lifetime. In 2013, cocaine was the primary drug for 13% of clients entering specialized drug treatment in the EU and for 16% of those entering treatment for the first time (about 24,000 people in the EU, much less than the peak of 38,000 reached in 2008) (EMCDDA 2015a).

In Italy, among residents aged 18–64, the lifetime prevalence of cocaine use was 4.2%, while last year the prevalence was 0.6%. Among clients entering treatment, 14.7% reported cocaine as their primary drug (DPA 2015). Regular cocaine use is associated with a range of adverse consequences that potentially increase the risk of premature death, morbidity, and disability (Chen and Anthony 2004; Chen, Storr, and Anthony 2009; Devlin and Henry 2008; Ferri and Gossop 1999; Gossop et al. 1994; O'Brien and Anthony 2005; Pavarin et al. 2011; Riezzo et al. 2012; Wagner and Anthony 2002, 2007).

A review of mortality rates from cohort studies of cocaine users found that crude mortality rates (CMR) ranged from 5.3 to 61.6 per 1,000 person years. Standardized mortality rates (SMR) suggested that mortality was four to eight times higher among cocaine users than in their same age and sex peers in the general population (Degenhardt et al. 2011), and higher among participants with cocaine and heroin use (Barrio et al. 2012; De La Fuente et al. 2014; Pavarin 2013). As to temporal trends, Europe recorded a significant increase in cocaine-related deaths in the 2000s, followed by a decline in most countries (Giraudon et al. 2014). The decrease in the mortality risk for cocaine users has also been reported in cohort studies on primary cocaine abusers with heroin use, but it was not statistically significant (De La Fuente et al. 2014).

The aims of this study, which targeted residents in the metropolitan area of Bologna (northern Italy) who turned to a public treatment center for drug addiction (SERT) following problems due to primary cocaine use between 1989 to 2013, were to estimate mortality risk and to examine mortality trends for subjects who have never used heroin and for subjects who have used heroin.

Methods

Cohort study

We selected participants residing in the metropolitan area of Bologna (North Italy), aged between 18 and 64 years who, for the first time, had visited a public

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treatment center dedicated to drug addicts for problems caused by primary abuse of cocaine in the period from January 1, 1989 to December 31, 2013. The cases were selected from the IT systems of SERT (11 services). The information was collected at the first contact.

Data sources

At the SERTs, a digital regional folder is used to collect the data at first admission:, the personal data, health data, treatments undertaken, and substances of abuse. Admission involves the definition and the start-up of a therapeutic project agreed upon with the user in compliance with the diagnostic evaluation. Patients could receive more than one type of treatment at the same time and all treatments, except the residential Therapeutic Community, were offered in outpatient settings. Variables related to date of birth, gender, country of birth, residence, professional status, educational degree, substances of abuse, method of use, hepatitis C status, HIV status, and date of first and last contact with the SERT were used.

Follow-up

Person-years (PY) were calculated from the first documented episode to December 31, 2013, or to the date of death. Patients lost to follow-up were included in the person-years until the date they moved out of their last known stable place of residence. Personal identifiers were used following the rules of privacy regulation. Based on the ICD9 (until 2002) and ICD10 (from 2003) codes noted, mortality was verified at the registry offices of the municipality where the patients were living at the end of the study period (i.e., December 31, 2013) or at death.

In view of the fact that some participants receiving treatment for primary cocaine abuse had also used heroin in a period preceding the first access to a SERT or in subsequent periods, two user typologies were created: cocaine users (never heroin) (CU) and heroin and cocaine users (HCU).

The study design was approved by the local research ethics committee (Comitato Etico Interaziendale Bologna-Imola CE-BI) Cod. CE: 16082.

Statistical analyses

Continuous and categorical variables were analyzed with Student's t- and chi-squared tests, respectively. Crude mortality rates (CMRs) per thousand PY and relative confidence intervals (CI) at 95% were calculated. Directly age-sex standardized mortality rates (DSMRs) per thousand PY and relative confidence intervals (CI) at 95% were calculated (Standard: Italia 2007) and year group (<2004, 2005/2009, 2010/2013) was entered into a Poisson model adjusted for age group (<25 years, 25/34 years, 35/44 years, >44 years) and sex to determine the significance of trends in standardized mortality over time.

To compare the mortality rates of cocaine users with those of the general population, we calculated the standardized mortality rates (SMRs), adjusted for age and calendar year (Standard: Emilia Romagna Region), and relative 95% CIs specifically for cause and gender. A Poisson regression analysis was performed to analyze the combined effect of gender, age, educational level, and year group on mortality (Clayton and Hills 1993; Selvin 2003). Data analyses were performed using the STATA 14.1 statistical software program.

Results

The cohort was made up of 852 participants, 12.2% female, 10.7% non-native, with an average age at first admission of 32.8 years. Follow-up continued until December 31, 2013 for 98.4% of the participants or until the date of death (14 were lost to follow-up); there were 6,454 at-risk person years (799 female, 5655 male) and 41 deaths, the first of which occurred in 1996. The average follow-up period was 7.6 years, the average period of contact with SERT was 3.3 years, and the average time spent from the last contact with the SERT to the end of the follow-up was 4.3 years.

Among participants who accessed the services, at least one in three had a high school degree and half had a regular income, 9.2% were hepatitis C positive and 1.9% were HIV positive. Modalities of cocaine use were known for 95.7% of participants (70.7% snorted,15.6% injected, 9.4% smoked). Almost one in five had injected a substance (Table 1).

CU participants (n = 678) had never used heroin (79.6%, follow-up completed for 99.3%, 4749 person years, 25 deaths), while HCU participants (n = 174) had used also heroin (20.4%, follow-up completed for 94.8%, 1705 person years, 16 deaths). A total of 66% of the CUs entered treatment after 2004, and 61% of the HCUs entered treatment before 2004. Over time, the quota of participants injecting any substance (44% period <2000, 2% period 2010/2013 < 0.0001), or injecting cocaine (24% period <2000, 2% period 2010/2013, p < 0.0001), or injecting heroin (38% period <2000, 1.5% period 2010/2013, p < 0.0001) decreased. In comparison with HCUs, CUs tended on average to be older, with a higher level of education, with a higher percentage of students,

Table 1. Public treatment centers of addiction in the metropolitan area of Bologna (Italy): 852 treated clients with cocaine use disorders, period 1989–2013.

	Total (852)	Cocaine not heroin (678)	Cocaine and heroin (174)	*p*
Period of first visit				<0.0001
<2000	11.7	7.7	27.6	
2000/2004	27.6	26.1	33.3	
2005/2009	37.6	38.9	32.2	
2010/2013	23.1	27.3	6.9	
Mean age	32.8	33.3	31.3	<0.0001
Sex (% Female)	12.2	11.2	16.1	0.079
Nationality (% Non-native)	10.7	10.6	10.9	0.909
Professional status				<0.0001
% Regular income	49.9	53.4	36.2	
% Unemployed	45.4	41.5	60.9	
% Student	2.1	2.5	0.6	
% Missing	2.6	2.7	2.3	
Educational level				0.070
% Primary/ Secondary school	64.4	62.4	72.4	
% High school diploma	29.3	30.7	24.1	
% University	3.5	3.8	2.3	
% Missing	2.7	3.1	1.2	
Method of cocaine use				<0.0001
% Injected	15.6	8.9	42.0	
% Sniffed	70.7	77.4	44.3	
% Smoked	9.4	9.6	8.6	
% Missing	4.3	4.1	5.2	
HCV status				<0.0001
% Positive	9.2	2.2	36.2	
% Missing	84.2	97.8	31.0	
HIV status				<0.0001
% Positive	1.9	0.9	5.8	
% Missing	85.5	99.1	32.2	
Method of substance use (% injected)	19.8	8.9	62.6	<0.0001
Other substances in the entire period				<0.0001
% Alcohol	14.3	12.2	22.4	<0.0001
% Hallucinogens	7.4	9.0	1.2	<0.0001
% Cannabis	6.2	2.2	21.8	0.006
% Benzodiazepines	2.0	1.3	4.6	<0.0001
% MDMA	1.9	0.9	5.8	

participants with regular income, cocaine sniffers, and hallucinogen abusers (Table 1).

Among HCU participants, there was a higher proportion of unemployed, of hepatitis C positive, of HIV positive, of injectors, of alcohol abuse, and of cannabis, MDMA, and benzodiazepines use. Modalities of heroin use were: 56.9% injected, 12.1% snorted, 12.6% smoked, 18.4% unknown ($p < 0.0001$).

The average period of contact with SERT was 6.7 years for HCUs and 2.4 years for CUs ($P < 0.0001$). By the end of the follow-up, 32% of the HCUs had a therapeutic program in progress, 35% had previously completed the treatment, 29% had previously given up treatment; 18% of the CUs had a therapeutic program in progress, 44% had previously completed the treatment, 38% had previously interrupted treatment.

All SERT clients had previously received medical health check-ups and socio-educational support services. Half of the HCUs (51%) had undergone treatment with protracted integrated methadone, 57% had submitted to psychological interviews/assessment, 49% had been admitted to residential programs, 11% were undertaking psychotherapy. Similarly, about half of the CUs (48%) had submitted to psychological assessment, 31% had been treated with pharmacological therapies, 18% had been admitted to residential programs, 10% were undertaking psychotherapy.

Mortality

During the follow-up period, 41 participants (4.8% of the whole cohort) died. Thirty-six (4.8%) were males and five (4.8%) females. The mean age at death was 38.0 ± 8 years (males 37.4 ± 1 years, females 41.8 ± 4, CU 39.0 ± 2 years, HCU 36.3 ± 1 years). Table 2 reports deaths by heroin use and by gender; overall, there were seven unknown causes of mortality. Among men, 22% of the deaths were due to overdose, 17% from road accidents, 14% from circulatory diseases, 11% from suicide (three cases by hanging). Of the five deaths reported among women, one was due to AIDS, one to tumors, one to opiate overdose, one to homicide, and one to respiratory system diseases. Among CUs, 24% of the deaths were from road accidents and 16% from suicide. Of the deaths reported among HCUs, 44% were due to opiate overdose and 21% to diseases of the cardio-circulatory system. Among the five deaths for cardio-circulatory diseases, one participant had heroin as a secondary substance of abuse at the first admission and four participants in the period after the first admission. Three of these participants had ever injected heroin. The crude mortality rate was 6.35 per 1,000 person years (95% CI 4.68–8.63), similar for males (6.37, CI 4.59–8.83) and females (6.26, CI 2.60–15.03), higher but not statistically significant for HCUs (9.38, CI 5.75–15.31) than CUs (5.26, CI 3.56–7.79, $p = 0.067$).

Standardized mortality rates

Table 2, broken down according to substance of abuse and gender, reports standardized mortality ratios and 95% confidence intervals. Excess mortality was observed for all causes in both genders in the cohort as compared with the general population, where the SMR was at least five times higher among males and 15 times higher among females. The SMR was at least nine times higher among HCUs and five times higher among CUs.

Table 2. Standardized mortality rates for most common causes of death.

	Total				Males				Females				Cocaine no heroin				Cocaine and heroin			
	O	E	SMR	CI 95%	O	E	SMR	CI 95%	O	E	SMR	CI 95%	O	E	SMR	CI 95%	O	E	SMR	CI 95%
All causes	41	6.57	6.24	4.60–8.48	36	6.23	5.77	4.17–8.01	5	0.33	15.03	6.26–36.11	25	4.8	5.21	3.52–7.71	16	1.77	9.06	5.55–14.80
AIDS	2	0.3	6.57	1.64–26.26	1	0.29	3.44	0.49–24.44	1	0.01	71.18	10.03–505	1	0.2	4.98	0.70–35.34	1	0.10	9.65	1.36–68.49
All tumors	3	2.03	1.48	0.48–4.59	2	1.86	1.07	0.27–4.29	1	0.16	6.15	0.87–43.69	3	1.51	1.98	0.64–6.15			–	
Circulatory system	5	1.12	4.40	1.83–10.57	5	1.10	4.54	1.89–10.90			–				–		5	0.30	16.86	7.02–40.51
Respiratory system	2	0.11	17.88	4.47–71.49	1	0.11	9.40	1.32–66.70	1	0.10	183.94	25.91–1305	2	0.08	24.12	6.03–96.43			–	
External causes	21	2.20	9.53	6.22–14.62	19	2.13	8.93	5.70–14.00	2	0.07	26.70	6.68–106.7	14	1.60	8.73	5.17–14.74	7	0.60	11.70	5.58–24.54
Overdose	10	0.17	58.51	31.48–108.75	8	0.17	47.81	23.91–95.61	2	0.0	556.6	139.2–225.7	3	0.12	25.41	8.20–78.78	7	0.05	132.47	63.15–277.9
Road accidents	6	0.85	7.04	3.16–15.67	6	0.82	7.27	3.27–16.19					6	0.60	9.93	4.46–22.09				
Suicide	4	0.65	6.14	2.30–16.35	4	0.63	6.34	2.38–16.90					4	0.48	8.33	3.13–22.19				

O, observed death; E, expected death; SMR, standardized mortality ratio; CI, confidence interval.
Data adjusted for age and calendar year (standard: Emilia Romagna region).

The highest and most statistically significant SMRs for males were from overdoses, from cardio-circulatory system diseases, from road accidents, and from suicide. Among CUs, SMRs were higher for overdoses, diseases of the respiratory system, road accidents, and suicide. Among HCUs, SMRs were higher for diseases of the circulatory system and for overdoses.

Temporal trends

The DSMR was 5.31 (CI 2.96–7.67) per thousand patient/years, higher for females and for CUs, with a fluctuating trend over time, but declining for all causes after 2009 for both sexes, and after 2004 among males and among HCUs (Table 3). Over the whole period, cancer was the main cause of death, followed by suicide and overdose; starting from 2010, suicide deaths have been the main cause of death followed, in order of frequency, by overdoses and road accidents.

Poisson regression analysis

To analyze the combined effect of gender, injecting, age group, education level, and year (Barrio et al. 2012; Corkery 2012; De La Fuente et al. 2014; Giraudon et al. 2014; Hser et al. 2006; Pavarin 2008, 2013) on mortality, three separate regression analyses were performed using the Poisson method, distinctly for all cases, HCUs and CUs. The variables inserted in the model were gender, age group (<25 years, ≥25 years), calendar period (<2004, 2005/2009, 2010/2013), any substance injected in the period, educational level (primary/secondary school versus high school diploma/university degree), and use of heroin.

The multivariate analysis showed a higher mortality risk for younger participants and prior to 2005, with a progressive decrease in the following periods, statistically significant after 2009 for all cases and for participants who had used cocaine and heroin (Table 4). Among CUs, the risk of death was higher for participants aged less than 25 years.

Discussion

Study results, covering a period of 24 years, confirm what has been reported concerning the greater mortality risk connected to cocaine abuse (Arendt et al. 2011; Degenhardt et al. 2011; De La Fuente et al. 2014; Muhuri and Gfroerer 2011; Barrio et al. 2012; Pavarin 2008, 2013; Ribeiro et al. 2004, 2006; Tyndall et al. 2001; Van Haastrecht et al. 1996). Indeed, what emerges is an elevated mortality rate in the Italian cohort, akin to what has been reported by European studies, higher for

Table 3. Age and sex directly standardized mortality rates per 1000 person-years across time.

	Total		<2004		2005–09		2010–13		
	Rate	95% CI	Rate	95% CI	Rate	95% CI	Rate	95% CI	*p*
All participants	5.31	2.96–7.67	4.72	1.26–8.17	6.59	1.61–11.58	3.94	1.16–6.72	0.014
Males	4.85	2.73–6.97	5.31	1.45–9.17	4.71	1.70–7.71	3.88	1.0–6.76	0.016
Females	22.83	0–56.13	–		42.20	0–96.44	3.41	0–8.27	0.653
Cocaine no heroin	5.33	2.43–8.23	2.56	0–5.69	6.86	0.12–13.59	4.61	1.23–7.98	0.463
Cocaine and heroin	4.74	2.29–7.19	8.99	0.76–17.23	5.41	1.68–9.14	1.41	0–3.34	0.017
All tumors	1.10	0–2.56	–		3.20	0–7.84	0.18	0–0.53	0.372
Circulatory system	0.49	0.03–0.96	1.63	0–3.68	0.40	0–0.97	–		0.059
Suicide	0.97	0–2.32	0.37	0–1-10	0.38	0.1–12	1.27	0–3.49	0.471
Overdose	0.76	0.26–1.26	0.61	0–1.48	0.52	0–1.12	0.80	0.08–1.52	0.940
Road accidents	0.49	0–0.06–0.93	–		0.75	0–1.62	0.45	0–0.96	0.685

Rate, age, and sex directly standardized mortality rate; CI, confidence interval; P, Poisson test for time trend.

Data from Standard Italia (2007).

Table 4. Poisson multiple regression analysis.

	All cases			Cocaine and heroin			Cocaine not heroin		
	RR	95% CI	*P*	RR	95% CI	*P*	RR	95% CI	*P*
Sex									
Female	1	Referent		1	Referent		1	Referent	
Male	0.92	0.35–2.39	0.867	0.73	0.16–3.36	0.682	0.97	0.28–3.28	0.957
Age group									
≥25 years	1	Referent		1	Referent		1	Referent	
<25 years	3.03	1.04–8.82	0.042	1.68	0.21–13.49	0.628	4.38	1.25–15.37	0.021
Calendar period									
<2004	1	Referent		1	Referent		1	Referent	
2005/2009	0.71	0.31–1.60	0.402	0.63	0.22–1.82	0.390	0.93	0.25–3.46	0.910
2010/2013	0.39	0.16–0.91	0.029	0.11	0.02–0.56	0.008	0.78	0.22–2.85	0.711
Any substance injected									
No	1	Referent		1	Referent		1	Referent	
Yes	0.79	0.36–1.75	0.563	0.73	0.25–2.12	0.558	0.81	0.24–2.72	0.731
Educational level									
Primary/Secondary school	1	Referent		1	Referent		1	Referent	
High school diploma/University degree	1.17	0.58–2.37	0.656	2.63	0.59–11.77	0.205	0.84	0.37–1.93	0.689
Heroin									
No	1	Referent							
Yes	1.51	0.70–3.26	0.295						

females, with a fluctuating trend over time, but declining for all causes after 2009 for all patients and after 2004 for heroin and cocaine users.

Over the whole period, cancer was the main cause of death, followed by suicide and overdose; starting from 2010, suicide deaths have been the first cause of death followed, in order of frequency, by overdose and road accidents. Multivariate analysis confirms the decreasing trend in the risk of death and shows a higher mortality risk for participants aged less than 25 years. As compared with the general population, the excess mortality observed for all causes in either sex (at least six times higher) is similar to that reported by other studies (Arendt et al. 2011; Barrio et al. 2012; Pavarin 2008). The highest excess mortality rate was for females and for HCUs. We also report high SMRs for overdose deaths, diseases of the respiratory system deaths, transport accidents deaths, AIDS-related deaths, suicide deaths, and deaths due to circulatory system diseases.

Another finding from the study concerns the change in the characteristics of the primary cocaine abusers who turn to the SERT for treatment, and the results highlight two separate populations with different socio-economic characteristics, different consumption styles, and different causes of death: participants who have never used heroin, and participants who have used heroin in periods before or after the first access to the treatment.

In the literature, drug users entering treatment for problems related to cocaine have been divided into two groups: powder cocaine users and poly-drug users, including use of powder cocaine and heroin (EMCDDA 2007). The former group is represented by participants who take cocaine (either snorted or smoked) alone or in combination with other psychoactive substances. This group is reported to be socially integrated, with stable living conditions and in regular employment (Decorte 2001; Gossop et al. 1994; Leri, Bruneau, and Stewart 2001; Pavarin, Berardi, and Consonni 2013; Prinzleve et al. 2004; Van Der Poel et al. 2009; Pavarin 2011). The latter group (socially marginalized users) includes either

former heroin users receiving substitution treatment and now experiencing problems related to primary cocaine use, or current heroin users, combining heroin with cocaine consumption (Davoli et al. 2007; Pavarin 2013; Siliquini et al. 2005). Compared to cocaine users who do not use heroin, those who consume cocaine and heroin are more likely to inject, and are likely to inject with a great frequency because of cocaine's short half-life. Consequently, there is an increase in the health risks related to injecting, such as contracting HIV, HCV, and other blood-borne infectious diseases (Leri et al. 2003).

In our cohort, HCUs were one in five, but over time, both the quota of heroin users and that of participants injecting have decreased. CUs came later to drug services, enjoyed a better social integration, had a regular income and a high level of education. In contrast, HCUs seem to be associated with particular socio-economic problems (i.e., unemployment) and higher-risk consumption styles (e.g., alcohol abuse, injecting), with a higher proportion of unemployed people, of hepatitis C positive and HIV positive participants. The differences between the two typologies are evident also after analyzing proportional mortality: among CUs, most deaths were from road accidents and suicides, while among HCUs most deaths were from opiate overdose and from cardio-circulatory system diseases. The cardiovascular effects of cocaine are amplified when it is co-administered with opioids (Polettini 2005). As regards AIDS deaths, it should be considered that regular cocaine use, independent of the administration route, is associated with the transmission of infectious diseases via unprotected sex (Brugal et al. 2009).

Numerous studies have documented the association between overdose, excessive drug consumption (Bennet and Higgins 1999), dose and frequency of injection (Kerr et al. 2006), previous overdose experiences (Stoové, Dietze, and Jolley 2009), longer duration of injecting (Bartu et al. 2004), and intermittent injecting (Oliver and Keen 2003), but it is difficult to ascertain whether a death was primarily due to cocaine poisoning, a combination of substances, or the result of a pre-existing health condition exacerbated by cocaine use (Corkery 2012).

Regarding suicides, we found a high mortality rate, concentrated among CUs, and increasing in the last period, and most of the cases were caused by hanging. From a study conducted in New York, in one of every five cases of death by suicide, the person who committed suicide had used cocaine within days of his or her death (Marzuk and Tardiff 1992). Furthermore, from a recent study which examined the autopsy presence of drugs among suicide victims in Colorado from 2004 to 2009, it emerged that the participants deceased with a high school education, and those who tested positive for cocaine, were more likely to opt for hanging than firearms (Sheehan, Rogers, and Boardman 2015).

In contrast to what was reported by cohort studies on heroin users, we did not find liver-related deaths among HCUs (Degenhardt et al. 2014; EMCDDA 2015b; Gibson, Randall, and Degenhardt 2011; Pavarin 2015). This could arise from the different recruitment criteria, but it might also mean that people with primary cocaine abuse who use heroin may have a different mortality from patients with primary heroin abuse. Further, SMRs in our study are similar for cocaine users alone (SMR 5.9), but lower for cocaine and heroin users (SMR 9.1), to what has been reported by some recent European studies among primary cocaine abusers (Arendt et al. 2011; De La Fuente et al. 2014; Pavarin 2013).

As to temporal trend, in Europe during the 2000s there has generally been an increasingly upward trend in cocaine-related deaths, followed by a decline in most countries (Giraudon et al. 2014). For some authors, part of the decline in cocaine-related deaths may be related to a decline in cocaine purity and/or shift to using alternative stimulants, including "legal highs" (Corkery 2012; Mena et al. 2012). Our study raises different hypotheses, as we found a statistically significant decrease from 2004 only among patients with heroin use. The decrease in drug-related deaths for HCUs has also been reported in a recent study on primary cocaine abusers with heroin use, the results of which were not statistically significant (De La Fuente et al. 2014).

This study presents some limitations that reduce the generalizability of the results and it requires further research with specifically targeted studies. The data used are those available from first admission and so data are lacking. Furthermore, it has not been possible to consider data concerning the age at the first use, average consumption variations over time, and the use of other substances, since they were not retrieved uniformly by the operators. In particular, a significant amount of clinical data relating to hepatitis C and HIV screening was missing.

Conclusion

In this sample, mortality and the causes of death for patients with primary cocaine disorders have changed over the last 30 years. Since 2010, suicide has become the main cause of death in this population. There was also a significant change in the social and clinical characteristics of the population with this disorder accessing public addiction treatment services. Socially integrated cocaine consumers (mostly with no heroin use) are

increasing and socially marginalized users are decreasing. Pure cocaine users (CUs) and cocaine users who use also heroin (HCUs) have different causes and risks of death. Among CUs, most deaths were due to road accidents and suicide, and the risk of death was higher for participants aged less than 25 years. Among HCUs, most deaths were from opiate overdose and from cardio-circulatory system diseases, but the risk of death has been declining since 2004. This study calls for specific activities aimed at preventing suicide among cocaine users attending public treatment services.

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References

Arendt, M., P. Munk-Jørgensen, L. Sher, and S. O. Jensen. 2011. Mortality among individuals with cannabis, cocaine, amphetamine, MDMA, and opioid use disorders: A nationwide follow-up study of Danish substance users in treatment. *Drug and Alcohol Dependence* 114 (2–3):134–39.

Barrio, G., G. Molist, L. La Fuente, F. Fernández, A. Guitart, M. J. Bravo, and M. T. Brugal. 2012. Mortality in a cohort of young primary cocaine users: Controlling the effect of the riskiest drug-use behaviours. *Addictive Behaviors* 38 (3):1601–04. doi:10.1016/j.addbeh.2012.10.007.

Bartu, A., N. C. Freeman, G. S. Gawthorne, J. P. Codde, and C. D. J. Holman. 2004. Mortality in a cohort of opiate and amphetamine users in Perth, Western Australia. *Addiction* 99 (1):53–60. doi:10.1111/j.1360-0443.2004.00602.x.

Bennet, G. A., and D. S. Higgins. 1999. Accidental overdose among injecting drug users in Dorset, UK. *Addiction* 94 (8):1179–89. doi:10.1046/j.1360-0443.1999.94811798.x.

Brugal, M. T., J. Pulido, C. Toro, L. De La Fuente, M. J. Bravo, R. Ballesta, V. Soriano, G. Barrio, F. Vallejo, A. Domingo-Salvany, and Y. Castellano. 2009. Injecting, sexual risk behaviors and HIV infection in young cocaine and heroin users in Spain. *European Addiction Research* 15 (3):171–78. doi:10.1159/000220345.

Chen, C. Y., and J. C. Anthony. 2004. Epidemiological estimates of risk in the process of becoming dependent upon cocaine hydrochloride power versus crack cocaine. *Psychopharmacology* 172 (1):78–86. doi:10.1007/s00213-003-1624-6.

Chen, C. Y., C. L. Storr, and J. C. Anthony. 2009. Early-onset drug use and risk for drug dependence problems. *Addictive Behaviors* 34 (3):319–22. doi:10.1016/j.addbeh.2008.10.021.

Clayton, D., and M. Hills. 1993. *Statistical models in epidemiology*. New York, NY: Oxford University Press.

Corkery, J. M. 2012. Analysis of the data sources, numbers and characteristics of cocaine-related DRD cases reported in special mortality registries, or eventually in general mortality registries (GMR) when necessary. EMCDDA, Lisbon and University of Hertfordshire, Hatfield. http://www.emcdda.europa.eu/attachements.cfm/att_191876_EN_Cocaine_deaths_DRD_final-1.pdf

Davoli, M., F. Pasqualini, V. Belleudi, A. M. Bargagli, and C. A. Peducci. 2007. Changing pattern of drug abuse among patients entering treatment in Lazio, Italy, between 1996 and 2003: Transition from heroin to cocaine use. *European Addiction Research* 13 (4):185–91. doi:10.1159/000104880.

De La Fuente, L., G. Molist, A. Espelt, G. Barrio, A. Guitart, M. J. Bravo, and M. T. Brugal. 2014. Mortality risk factors and excess mortality in a cohort of cocaine users admitted to drug treatment in Spain. *Journal of Substance Abuse Treatment* 46 (2):219–26. doi: 10.1016/j.jsat.2013.07.001.

Decorte, T. 2001. Quality control by cocaine users: Underdeveloped harm reduction strategies. *European Addiction Research* 7 (4):161–75. doi:10.1159/000050737.

Degenhardt, L., S. Larney, D. Randall, L. Burns, and W. Hall. 2014. Causes of death in a cohort treated for opioid dependence between 1985 and 2005. *Addiction* 109 (1):90–99. doi:10.1111/add.2014.109.issue-1.

Degenhardt, L., J. Singleton, B. Calabria, J. McLaren, T. Kerr, S. Mehta, G. Kirk, and W. D. Hall. 2011. Mortality among cocaine users: A systematic review of cohort studies. *Drug and Alcohol Dependence* 113 (2–3):88–95. doi:10.1016/j.drugalcdep.2010.07.026.

Devlin, R. J., and J. A. Henry. 2008. Clinical review: Major consequences of illicit drug consumption. *Critical Care* 12 (1):202. doi:10.1186/cc6166.

DPA (Dipartimento Politiche Antidroga), Presidenza Consiglio dei Ministri. 2015. *Relazione annuale al Parlamento 2015 sullo stato delle tossicodipendenze in Italia*. http://www.politicheantidroga.gov.it/attivita/pubblicazioni/relazioni-al-parlamento/relazione-annuale-2015/presentazione.aspx

EMCDDA. 2007. *Cocaine and crack cocaine: A growing public health issue*. http://www.emcdda.europa.eu/publications/selected-issues/cocaine

EMCDDA. 2015a. European drug report 2015: Trends and developments. EMCDDA Lisbon.

EMCDDA. 2015b. *Mortality among drug users in Europe: New and old challenges for public health*. Lisbon, Portugal: EMCDDA.

Ferri, C. P., and M. Gossop. 1999. Route of cocaine administration: Patterns of use and problems among a Brazilian sample. *Addictive Behaviors* 24 (6):815–21. doi:10.1016/S0306-4603(99)00036-2.

Gibson, A., D. Randall, and L. Degenhardt. 2011. The increasing mortality burden of liver disease among opioid

dependent people: Cohort study. *Addiction* 106 (12):2186–92. doi:10.1111/add.2011.106.issue-12.

Giraudon, I., G. Mena, M. João, and V. Julian 2014. Emergency health consequences of cocaine use in Europe: A review of the monitoring of drug-related acute emergencies in 30 European countries. EMCDDA. http://www.emcdda.europa.eu/system/files/publications/778/Cocaine_emergencies_report_final_467089.pdf

Gossop, M., P. Griffiths, B. Powis, and J. Strang. 1994. Cocaine: Patterns of use, route of administration and severity of dependence. *The British Journal of Psychiatry* 164 (5):660–64. doi:10.1192/bjp.164.5.660.

Hser, Y. I., M. E. Stark, A. Paredes, D. Huang, M. D. Anglin, and R. Rawson. 2006. A 12-year follow-up of a treated cocaine-dependent sample. *Journal of Substance Abuse Treatment* 30 (3):219–26. doi:10.1016/j.jsat.2005.12.007.

ISTAT. 2007. *National Institute of Statistics Demografia in cifre*. http://demo.istat.it/. Accessed June 1, 2017.

Kerr, T., M. W. Tyndall, C. Lai, J. S. G. Montaner, and E. Wood. 2006. Drug-related overdoses within a medically supervised safer injection facility. *The International Journal on Drug Policy* 17 (5):436–41. doi:10.1016/j.drugpo.2006.05.008.

Leri, F., J. Bruneau, and J. Stewart. 2001. Understanding polydrug use: Review of heroin and cocaine co-use. *Neuropsychopharmacology* 25 (1):104–17.

Leri, F., J. Flores, H. Rajabi, and J. Stewart. 2003. Effects of cocaine in rats exposed to heroin. *Neuropsychopharmacology* 28 (12):2102–16.

Marzuk, P. M., and K. Tardiff. 1992. Prevalence of cocaine use among residents of New York City who committed suicide during a one-year period. *The American Journal of Psychiatry* 149 (3):371–75. doi:10.1176/ajp.149.3.371.

Mena, G., I. Giraudon, E. Álvarez, J. M. Corkery, J. Matias, K. Grasaasen, N. Llorens, P. Griffiths, and J. Vicente. 2012. Cocaine-related health emergencies in Europe: A review of sources of information, trends and implications for service development. *European Addiction Research* 19 (2):74–81. doi:10.1159/000341719.

Muhuri, P. K., and J. C. Gfroerer. 2011. Mortality associated with illegal drug use among adults in the United States. *The American Journal of Drug and Alcohol Abuse* 37 (3):155–64. doi:10.3109/00952990.2011.553977.

O'Brien, M. S., and J. C. Anthony. 2005. Risk of becoming cocaine dependent: Epidemiological estimates for the United States, 2000–2001. *Neuropsychopharmacology* 30 (5):1006–18. doi:10.1038/sj.npp.1300681.

Oliver, P., and J. Keen. 2003. Concomitant drugs of misuse and drug using behaviours associated with fatal opiate related poisonings in Sheffield, UK, 1997–2000. *Addiction* 98 (2):191–97. doi:10.1046/j.1360-0443.2003.00303.x.

Pavarin, R. M. 2008. Cocaine consumption and death risk: A follow-up study on 347 cocaine addicts in the metropolitan area of Bologna. *Annali dell'Istituto Superiore di Sanità* 44 (1):91–98.

Pavarin, R. M. 2013. Mortality risk for cocaine abusers in relation to heroin use: A follow-up study. *Substance Use & Misuse* 48 (9):702–10. doi:10.3109/10826084.2013.786731.

Pavarin, R. M. 2015. Mortality risk among heroin abusers: Clients and non-clients of public treatment centers for drug addiction. *Substance Use & Misuse* 50 (13):1690–96. doi:10.3109/10826084.2015.1027932.

Pavarin, R. M., D. Berardi, and D. Consonni. 2013. Determinants of seeking treatment for cocaine abuse: A case-control study. *European Addiction Research* 19 (2):61–67. doi:10.1159/000339837.

Polettini, A., V. Poloni, A. Groppi, C. Stramesi, C. Vignali, L. Politi, and M. Montagna. 2005. The role of cocaine in heroin-related deaths: Hypothesis on the interaction between heroin and cocaine. *Forensic Science International* 153 (1):23–28. doi:10.1016/j.forsciint.2005.04.017.

Prinzleve, M., C. Haasen, H. Zurhold, J. L. Matali, E. Bruguera, J. Gerevich, E. Bácskai, N. Ryder, S. Butler, V. Manning, M. Gossop, A. M. Pezous, A. Verster, A. Camposeragna, P. Andersson, B. Olsson, A. Primorac, G. Fischer, F. Güttinger, J. Rehm, and M. Krausz. 2004. Cocaine use in Europe: A multi-centre study: Patterns of use in different groups. *European Addiction Research* 10 (4):147–55. doi:10.1159/000079835.

Ribeiro, M., J. Dunn, R. Sesso, A. C. Dias, and R. Laranjeira. 2006. Causes of death among crack cocaine users [Causa mortis em usuários de crack]. *Revista Brasileira de Psiquiatria* 28 (3):196–2. doi:10.1590/S1516-44462006000300010.

Ribeiro, M., Y. Dunn, R. Laranjeira, and R. Sesso. 2004. High mortality among young crack cocaine users in Brazil: A 5-year follow-up study. *Addiction* 99:1133–35. doi:10.1111/j.1360-0443.2004.00804.x.

Riezzo, I., C. Fiore, D. De Carlo, N. Pascale, M. Neri, E. Turillazzi, and V. Fineschi. 2012. Side effects of cocaine abuse: Multiorgan toxicity and pathological consequences. *Current Medicinal Chemistry* 19 (33):5624–46. doi:10.2174/092986712803988893.

Selvin, S. 2003. *Statistical analysis of epidemiologic data*. New York, NY: Oxford University Press.

Sheehan, C. M., R. G. Rogers, and J. D. Boardman. 2015. Postmortem presence of drugs and method of violent suicide. *Journal of Drug Issues* 45 (3):249–62. doi:10.1177/0022042615580988.

Siliquini, R., A. Morra, E. Versino, and G. Renga. 2005. Recreational drug consumers: Who seeks treatment? *European Journal of Public Health* 15 (6):580–86. doi:10.1093/eurpub/cki031.

Stoové, M. A., P. M. Dietze, and D. Jolley. 2009. Overdose deaths following previous non-fatal heroin overdose: Record linkage of ambulance attendance and death registry data. *Drug and Alcohol Review* 28 (4):347–52. doi:10.1111/j.1465-3362.2009.00057.x.

Tyndall, M. W., K. J. Craib, S. Currie, K. Li, M. V. O'Shaughnessy, and M. T. Schechter. 2001. Impact of HIV infection on mortality in a cohort of injection drug users. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 28 (4):351–57. doi:10.1097/00126334-200112010-00008.

Van Der Poel, A., G. Rodenburg, M. Dijkstra, M. Stoele, and D. van de Mheen. 2009. Trends, motivations and settings of recreational cocaine use by adolescents and young adults in the Netherlands. *The International Journal on Drug Policy* 20 (2):143–51. doi:10.1016/j.drugpo.2008.02.005.

Van Haastrecht, H. J. A., E. J. C. Van Ameijden, J. A. R. Van Den Hoek, G. H. C. Mientjes, J. S. Bax, and R. A. Coutinho. 1996. Predictors of mortality in the Amsterdam cohort of human

immunodeficiency virus (HIV)-positive and HIV-negative drug users. *American Journal of Epidemiology* 143 (4):380–91. doi:10.1093/oxfordjournals.aje.a008752.

Wagner, F. A., and J. C. Anthony. 2002. From first drug use to drug dependence: Developmental periods of risk for dependence upon marijuana, cocaine and alcohol. *Neuropsychopharmacology* 26 (4):479–88. doi:10.1016/S0893-133X(01)00367-0.

Wagner, F. A., and J. C. Anthony. 2007. Male-female differences in the risk of progression from first use to dependence upon cannabis, cocaine and alcohol. *Drug and Alcohol Dependence* 86 (2–3):191–98. doi:10.1016/j.drugalcdep.2006.06.003.