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## RESEARCH ARTICLE

# Mortality Risk for Individuals With Cocaine Use Disorders: Clients and Non-Clients of Public Treatment Centres for Drug Addiction

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## Abstract

**Background:** This study targeted individuals who turned for the first time to health services following problems caused by cocaine use (CUD). Our aim was to estimate mortality risk for individuals who were clients of PATS (public addiction treatment services) and never-PATS (those who were not).

**Method:** Follow-up study. People resident in Emilia Romagna Region (Northern Italy), aged 18 years and older who for the first time turned to a HOS (hospital ward), an ED (emergency department), a MHS (community mental health centre) or to a PATS for cocaine use disorder were selected. The reference period was between 01/01/2009 and 31/12/2019 and the territory was the metropolitan area of Bologna. CMR (Crude mortality rates) per 1000 PY (Person Years) and SMRs (standardized mortality ratios) were calculated.

**Results:** The cohort was made up of 3,196 subjects. CMR was 4.5 (95% CI 3.6-6.6) per thousand patient/years, SMRs were 4.3 (95% CI 3.5-5.4). The results highlight high CMRs (5.5, 95% CI 3.8-8.1) and SMRs (4.7, 95% CI 3.2-6.9) for individuals who never accessed PATS.

Higher and statistically significant incidence rate ratios were found from the multivariate analysis among females and natives, in patients never accessed to PATS, aged more than 35 years and reporting using alcohol or opioids at first admission.

**Conclusions:** Innovative strategies to facilitate the reduction of barriers to access and to facilitate taking charge in PATS for people with cocaine use disorders must be identified.

## 1. Introduction

It was estimated that roughly 22 million people worldwide, 0.4% of the adult population aged 15-64, had used cocaine in 2021 (UNODC, 2023), 1.2% in the European Union in 2021 (EMCDDA, 2022), and 1.1% in Italy in 2022 (DPA, 2023). Globally, the estimated age-standardised prevalence of cocaine dependence was 0.5 per 1,000 people (Peacock et al.,

2018). Despite substantial country-specific variation regarding cocaine prevalence and treatment demand, there has been, overall, a significant increase since 2015 in the share of cocaine-related treatment demand in western Europe (Antoine et al., 2021).

From reviews, elevated all-cause crude mortality rates (CMRs 12.4 per 1,000 person years [PYs]) and standardised mortality ratios (SMRs 6.3) among people with regular or problematic cocaine use has emerged. Drug-related, suicide, accidental injury, homicide, and AIDS-related mortality were all elevated compared with age and gender peers in the general population (Peacock et al., 2021). Mortality risk and excess mortality were significantly greater among those with cocaine and opiate use disorder in Pavarin et al. (2020) than among people with only cocaine and alcohol use disorder (CUD) (Colell et al., 2018). So, an element of distortion might be introduced by the over-representation of heroin users with concomitant use of cocaine in long-term historical cohorts, and their number is declining over time. Cocaine users are not a homogeneous population, and the concomitant use of cocaine with other drugs, primarily heroin, would establish differences among cocaine users in the prevalence of injected use, HIV, and other infectious diseases, as well as per an individual's socioeconomic background.

In Italy, there are at least an estimated 900,000 cocaine users; the expense of the total consumption of drugs within Italy's borders is estimated at 5.1 billion euros, and is steadily increasing over time (DPA, 2021). People with problems due to cocaine use can go to public facilities (PATS, hospitals, emergency departments, community mental health centres) for treatment. Access is voluntary and facilitated by a primary care physician, specialist, or another healthcare service provider, and there are no specific inclusion/exclusion criteria. PATS are facilities of the national health system and perform activities of prevention, cure, and rehabilitation from use/abuse disorders and intervene in addictions to psychoactive substances, both legal and illegal. In public facilities, the service is free to the patient.

The present study targeted individuals who turned for the first time to health services following problems caused by cocaine use between 2009 and 2019 in northern Italy. Our aim was to estimate the mortality risk for both individuals treated by PATS and those who were not (*never PATS*).

## 2. Materials and Methods

### 2.1. Study sample

People resident in Emilia Romagna Region (Northern Italy), aged 18 years and older who for the first time turned to a hospital ward (HOS), an emergency department (ED), a community mental health centre (MHS) or to a PATS for CUD (i.e. problematic use of or dependence on cocaine - Degenhardt et al., 2011) were selected. The reference period was between 01/01/2009 and 31/12/2019 and the territory was the metropolitan area of Bologna.

The information was collected at first contact. The cases were selected from the IT systems of PATS (10 services), HOS (10 facilities), EDs (16 facilities) and MHS (17 services). As an 'incident case', the subjects who had not been dismissed

to an HOS or who had not accessed an ED or who had not been admitted to a PATS or an MHS for CUD prior to 01/01/2009 were considered.

## 2.2. Study setting

At the PATS, a digital regional folder is used to collect the data at first admission, as well as personal data, health data, treatments undertaken and substances of use. Admission involves the definition and the start-up of a therapeutic project agreed upon with the patient in compliance with the diagnostic evaluation.

For HOS and MHs, patients were selected on the grounds of ICD-9 primary or secondary diagnosis (304.2) Cocaine dependence and ICD-9 primary or secondary diagnosis (305.6) Cocaine abuse.

Records of ED visits for CUD were identified through cross-matching with the EHR of visits to EDs in the Metropolitan Area of Bologna. Records from each ED, including prehospital care reports, nursing notes and physician records, were verified using keywords from the International Classification of Diseases. The analysis of records was carried out by a multidisciplinary team comprising psychiatrists and epidemiologists (Pavarin et al., 2011). All information was obtained retrospectively, and data collection forms were abstracted for each case.

## 2.3. Outcome of interest

The results were separated into PATS and never-PATS clients.

Person-years (PY) were calculated from the first documented date of admission to 31 December 2020 or up to the date of death. Based on the ICD-10 codes, mortality was verified at the registry offices of the municipality where the patients were living at the end of the study period (i.e. 31 December 2020) or at death. Patients who were lost to follow-up were included in PY until the date they moved out of their last known stable place of residence. For people who accessed other health services before going to PATS, PY were calculated both for PATS and never-PATS period.

## 2.4. Variables

Variables related to age, gender, country of birth, residence, substance of use, contact sector and date of contact were used. Diagnoses of any other psychiatric disorders were identified by cross-matching with EHR registered by MHSs in the metropolitan area of Bologna in the entire considered period (ICD-9 codes at first contact).

## 2.5. Statistical analysis

Using the initial database - 3196 rows (one for each subject), categorical variables were analysed with the chi-squared test. Continuous variables were analysed with Student's t test; data distribution was tested using Shapiro–Wilk W test for normal data; equality of variance was tested using Levene's test.

CMRs per thousand PY and relative confidence intervals (CI) at 95% were calculated. To compare the mortality rates of

CUDs with those of the general population, we calculated the SMRs, adjusted for gender, age and calendar year (standard: Emilia-Romagna region) and relative 95% confidence intervals.

Poisson regression analysis was performed to assess the combined effect of gender, country of birth, age at first admission, main substances of use at first admission, any psychiatric diagnosis, service of first admission, and COVID-19 period (period up to and including 2019/the year 2020) on mortality risk. Data analyses were performed using Stata 15.1 statistical software.

The study protocol was approved by the local research ethics committee (Cod. CE: 20183).

### 3. Results

The cohort was comprised of 3,196 subjects, 14% female and 35% non-native, with an average age at first admission of 34 years; 77% were treated in a PATS. At first admission, in addition to CUD, 29% also reported the use of opioids, 20% alcohol, 16% cannabis, and 2% benzodiazepines; the services of first admission were PATS (66%), ED (25%), HOS (6%), and MHS (3%). Of the entire cohort, 6% (197 subjects) had received a diagnosis of at least one psychiatric disorder; the most common conditions were personality and behavioural disorders (4.2%) and depression (2%) (Table 1).

**Table 1.** Characteristics

		All cases (3196)	PATS (2457)	Never PATS (739)	P
		N (%)	N (%)	N (%)	
Sex	Males	2738 (85.7)	2134 (86.9)	604 (81.7)	<0.0001*
	Females	458 (14.3)	323 (13.2)	135 (18.3)	
Country of birth	Natives	2080 (65.1)	1580 (64.3)	500 (67.7)	0.094
	Non-natives	1116 (34.9)	877 (35.7)	239 (32.3)	
Age at first admission	Mean (± standard dev.)	34.0±9.5	33.9±9.2	34.2±10.3	0.7537
First admission	SERD	2096 (65.6)	2096 (85.3)	-	<0.0001*
	Emergency Department	813 (25.4)	222 (9.0)	591 (80.0)	
	Hospital	196 (6.1)	91 (3.7)	105 (14.2)	
	MHS	91 (2.9)	48 (2.0)	43 (5.8)	
Other substances at the first admission	Opioids	923 (28.9)	813 (33.1)	110 (14.9)	<0.0001*
	Alcohol	633 (19.8)	412 (16.8)	221 (29.9)	<0.0001*
	Cannabis	511 (16.0)	413 (16.8)	98 (13.3)	0.021*
	Benzodiazepines	55 (1.7)	32 (1.3)	23 (3.1)	0.001*
	Amphetamines	19 (0.6)	6 (0.2)	13 (1.8)	0.0001*
	Hallucinogens	15 (0.5)	7 (0.3)	8 (1.1)	0.005*
	MDMA	12 (0.4)	11 (0.5)	1 (0.1)	0.223
	Ketamine	9 (0.3)	4 (0.2)	5 (0.7)	0.021*
	Any Injecting	639 (20.0)	512 (20.8)	127 (17.2)	0.029*
Psychiatric diagnosis	Any	197 (6.2)	136 (5.5)	61 (8.3)	0.007*
	Personality and behavioural disorders	73 (4.2)	56 (4.2)	17 (4.1)	0.920
	Depression	34 (2.0)	20 (1.5)	14 (3.4)	0.016 *
	Neurotic and somatoform syndromes	27 (1.6)	17 (1.3)	10 (2.4)	0.103
	Schizophrenia and other functional psychoses	25 (1.4)	17 (1.3)	8 (1.9)	0.331
	Mania and bipolar affective disorders	15 (0.9)	9 (0.7)	6 (1.5)	0.138

\* Statistically significant

As for mean age at first admission, using Levene's test, variances were different (P 0.0004), so a two-sample t-test with unequal variances was calculated. Compared to PATS, among the never-PATS patients, there was a higher percentage of females, of people with a psychiatric diagnosis, and people with alcohol and benzodiazepine use; otherwise, a lower percentage of people injecting substances, with cannabis and opioid use, was observed. We noted that 80% of never-PATS individuals first accessed an ED.

### 3.1. PATS

Among the PATS clients, the average period of contact with the service was 2.6 years; 1 in 4 had a high school diploma; 25% had a regular income; 9% were hepatitis C-positive; and 2% were HIV-positive. Modalities of cocaine use were known for 71% of the subjects (of the total sample, 44% snorted, 7% injected, and 20% smoked cocaine).

The PATS clients had all submitted to medical health check-ups and had received various forms of socio-educational support. Patients could receive more than one type of treatment concurrently, and all treatments (medical health check-ups, socio-educational support services, psychological interviews/assessments, psychotherapy, and pharmacological therapies), except residential therapeutic community interventions, were offered in outpatient settings. By the end of follow-up, 47% had completed a therapeutic programme and were dismissed; 20% continued in a therapeutic programme; 32% had already left treatment; and 1% died during the treatment programme.

### 3.2. *Proportional mortality*

Follow-up continued until 31 December 2020, or until the date of death for 95% of the subjects. The average follow-up period was 6.1 years, including 6.2 years for PATS patients and 5.8 years for never-PATS patients. There were 18,575 at-risk PYs (2,628 female, 15,947 male) and 84 deaths (62 males, 22 females), the first of which occurred in 2009. There were 13,698 PYs (57 deaths) among patient who accessed PATS and 4,877 PYs (27 deaths) among those who had never accessed PATS. The mean age at death was  $44.1 \pm 12$  years: men –  $46.2 \pm 13$  years; women –  $38.2 \pm 9$  years; never-PATS –  $45.3 \pm 15$  years; and PATS –  $43.6 \pm 11$  years.

Three deaths were of ill-defined or unknown causes. The main causes of death were opiate overdose (22 cases, 26%); suicide (11 cases, 13%); tumours (10 cases, 12%); road accidents (eight cases, 10%); diseases of the circulatory system (six cases, 7%); and diseases of the respiratory system (five cases, 6%). Among suicides, we noted the large number of suicides by hanging (seven cases).

### 3.3. *Crude mortality rates*

The CMR was 4.5 (95% CI [3.7-5.6]) per thousand PYs; it was higher for the women (CMR 8.4, 95% CI [5.5-12.7]) than the men (CMR 3.9, 95% CI [3.0-5.0]) and for never-PATS clients (CMR 5.5, 95% CI [3.8-8.1]) compared to PATS clients (CMR 4.2, 95% CI [3.2-5.4]) (Table 2). The CMRs were higher for patients of first admission to HOS (CMR 12.3, 95% CI [10.2-25.8]) versus those admitted to MHS (CMR 8.7, 95% CI [3.6-20.8]), ED (CMR 4.3, 95% CI [2.8-6.6]), or PATS (CMR 3.3, 95% CI [2.4-4.5]).

Regarding the causes of death, the CMR was higher for overdose, followed by suicide and all tumours. The CMRs were higher, but not statistically significant, for the never-PATS patients than for the PATS patients for overdose, suicide, transport accidents, respiratory system diseases, and circulatory system diseases. Among the PATS clients, the CMRs were higher than among the never-PATS, but not statistically significant, for infectious diseases.

Of note, 361 people accessed other health services before going to PATS, and their mortality rates were higher than those of patients who first accessed PATS and those who never accessed PATS. As for COVID-19, the CMRs were lower

in the year 2020 than during the 2009/2019 period (Table 3).

**Table 2.** Crude Mortality Rates and Standardized Mortality Ratios\*

	All cases (PY 18575)					PATS (PY 13698)					Never PATS (PY 4877)				
	O/E	CMR	95% CI	SMR	95% CI	O/E	CMR	95% CI	SMR	95% CI	O/E	CMR	95% CI	SMR	95% CI
<b>Total</b>	84/19.4	4.5	3.6-5.6	4.33	3.50-5.37	57/13.7	4.2	3.2-5.4	4.17	3.22-5.41	27/5.7	5.5	3.8-8.1	4.72	3.24-6.88
<b>Males</b>	62/17.9	3.9	3.0-5.0	3.46	2.70-4.44	40/12.8	3.3	2.4-4.5	3.12	2.29-4.25	22/5.1	5.6	3.7-8.5	4.32	2.85-6.57
<b>Females</b>	22/1.5	8.4	5.5-12.7	15.06	9.92-22.88	17/0.83	10.0	6.2-16.1	20.46	12.72-32.92	5/0.6	5.4	2.2-12.9	7.94	3.30-19.07
<b>Infectious diseases</b>	8/0.6	0.4	0.2-0.9	13.73	6.69-26.74	7/0.4	0.5	0.2-1.1	16.68	7.95-34.98	1/0.2	0.2	0.0-1.5	5.60	0.79-39.79
<b>AIDS</b>	3/0.2	0.2	0.1-0.5	13.14	4.24-40.74	3/0.2	0.2	0.1-0.7	17.91	5.78-55.41	0/0.01	-	-	-	-
<b>All tumors</b>	10/6.8	0.5	0.3-1.0	1.48	0.80-2.75	7/4.7	0.5	0.2-1.1	1.49	0.71-3.12	3/2.1	0.6	0.2-1.9	1.46	0.47-4.53
<b>Circulatory system</b>	6/3.6	0.3	0.1-0.7	1.66	0.75-3.69	3/2.5	0.2	0.0-0.7	1.21	0.39-3.75	3/1.1	0.6	0.2-1.9	2.64	0.85-8.18
<b>Respiratory system</b>	5/1.0	0.3	0.1-0.6	5.20	2.16-12.49	2/0.7	0.1	0.0-0.6	3.09	0.77-12.37	3/0.3	0.6	0.2-1.9	9.51	3.07-29.49
<b>Digestive system</b>	2/0.8	0.1	0.0-0.4	2.56	0.64-10.23	1/0.7	0.1	0.0-0.5	1.78	0.25-12.64	1/0.2	0.2	0.0-1.5	4.54	0.64-32.21
<b>External causes</b>															
<b>Overdose</b>	22/0.3	1.2	0.8-1.8	81.90	53.93-124.38	15/0.2	1.1	0.7-1.8	73.62	44.38-122.11	7/0.1	1.4	0.7-3.0	107.91	51.45-226.36
<b>Suicide</b>	11/1.6	0.6	0.3-1.1	6.78	3.76-12.24	7/1.2	0.5	0.2-1.1	5.78	2.76-12.12	4/0.4	0.8	0.3-2.2	9.73	3.65-25.92
<b>Transport accidents</b>	8/1.6	0.4	0.2-0.9	4.94	2.47-9.87	5/1.2	0.4	0.2-0.9	4.14	1.72-9.95	3/0.4	0.6	0.2-1.9	7.26	2.34-22.52

\* Adjusted for age and calendar year (Standard: Emilia Romagna Region)

**O**, observed death; **E**, expected death; **CMR**, crude mortality rate per 1000 PY; **SMR**, standardized mortality ratios; **CI**, confidence interval

SMRs were higher for the never-PATS than the PATS for respiratory system diseases, overdose, suicide and transport accidents; SMRs were higher for the PATS than for the never-PATS from infectious diseases.

**Table 3.** Risk profile - Poisson multiple regression analyses

		Death	PY	CMR	95% CI	RR	95% CI	P
Country of birth	Natives	79	12427	6.4	5.1-7.9	1	REFERENCE	
	Non-natives	5	6148	0.8	0.3-2.0	0.18	0.07-0.44	<0.0001
Age at first admission	<35 years	28	10610	2.6	1.8-3.8	1	REFERENCE	
	>=35 years	56	7966	7.0	5.4-9.1	2.12	1.34-3.36	0.001
Substance at first admission	Cocaine	32	9508	3.4	2.4-4.8	1	REFERENCE	
	Opioids	30	5597	5.4	3.7-7.7	1.80	1.09-3.00	0.022
	Alcohol not opioids	22	3471	6.3	4.2-9.6	1.62	0.94-2.80	0.084
Calendar period	<=2019	74	15634	4.7	3.8-5.9	1	REFERENCE	
	Year 2020	10	2941	3.4	1.8-6.3	0.49	0.25-0.94	0.033
Psychiatric diagnosis	Not	71	17361	4.1	3.2-5.2	1	REFERENCE	
	Any	13	1214	10.7	6.2-18.4	1.68	0.92-3.09	0.089
First admission	PATS	40	12007	3.3	2.4-4.5	1	REFERENCE	
	First other services, than PATS	17	2375	7.2	4.4-11.5	1.63	0.90-2.95	0.106
	Other services, never PATS	27	4193	6.5	4.4-9.4	1.89	1.15-3.12	0.012

**PY**, Person Year; **CMR**, crude mortality rate per 1000 PY; **95% CI**, 95% confidence interval; **IRR**, Incidence Rate Ratio

### 3.4. Standardised mortality ratios

The SMRs were 4.33 for the total sample, including 4.17 among the PATS and 4.72 among the never-PATS clients; they were 3 times higher among men and 15 times higher among women (Table 2). The highest and most statistically significant SMRs for the PATS patients were from overdose, AIDS, suicide, and transport accidents. Among the never-PATS, the SMRs were higher from overdose, diseases of the respiratory system, suicide, and road accidents. We noted that there was no statistically significant difference between PATS and never-PATS for the various causes of death, excluding AIDS (three deaths, only PTC clients). Moreover, the SMRs were lower in the initial phases of COVID-19 for all cases (period 2009/2019: SMR 4.71, 95% CI [3.75-5.91]; year 2020: SMR 2.73, 95% CI [1.47-5.08]) and for PATS clients (period 2009/2019: SMR 4.54, 95% CI [3.44-6.0]; year 2020: SMR 2.63, 95% CI [1.26-5.52]), while for the never-PATS clients, they were lower but not statistically significant in 2020 (period 2009/2019: SMR 5.09, 95% CI [3.41-7.59]; year 2020: SMR 2.99, 95% CI [0.96-9.27]).

### 3.5. Multivariate analysis

From our multivariate analysis, lower and statistically significant incidence rate ratios (RRs) were found in the initial phases of the COVID-19 pandemic (RR 0.49, 95% CI [0.25-0.95]), and among non-natives (RR 0.18, 95% CI [0.07-0.44]), while higher statistically significant incidence RRs were found among females (RR 1.83, 95% CI [1.11-3.01]), in people aged more than 35 years first-accessing health services following problems caused by cocaine use (RR 2.12, 95% CI [1.34-3.36]), and in those reporting using opioids at first admission (RR 1.80, 95% CI [1.09-3.0]). We noted those patients with first admission to HOS, MHS, or ED, and never-PATS clients (RR 1.89, 95% CI [1.15-3.12]) had higher and

statistically significant incidence RRs than the PATS clients (Table 3).

## 4. Discussion

This study targeted a cohort of people who accessed health services following problems caused by cocaine use and confirmed what had been reported in the literature concerning the greater mortality risk connected to cocaine abuse. The results highlight high CMRs and SMRs both for individuals with CUD who had accessed PATS and those who had never accessed PATS. As reported by other studies of hospital detoxification (Accurso et al., 2015; Savinsens et al., 2014), the mortality risk was higher for those first accessing a hospital.

The mortality risk and excess mortality rate with respect to the general population was relatively higher for females and in the period before COVID-19. Indeed, higher and statistically significant incidence RRs were found from the multivariate analysis in the period before the COVID-19 pandemic, among females and natives, in patients who never accessed PATS, and in those aged more than 35 years at first admission and reporting using opioids at first admission.

Overdose was the main cause of death, followed by suicide and all tumours. Among suicides, we noted a large number of suicides by hanging (Corkery et al., 2017; Sheehan et al., 2015), but this was based on a small number of cases. We also noted that AIDS deaths were found only among PTC patients.

The mortality rate and the excess mortality rate observed for all causes in either typology was lower in our cohort than those reported by recent reviews (Peacock et al., 2021), perhaps partly due to the relatively recent enrolment period (2009/2019) that reduced the over-representation of heroin users with the concomitant use of cocaine, and partly to the composition of the cohort itself, which was based on people with varying levels of substance impairment, risk perception, mental health problems, and services accessed. According to other studies (e.g., Colell et al., 2018), mortality risk was significantly greater among those with cocaine and opiate use disorder than among people with only CUD. The higher SMRs for females in our study probably reflected the lower risk of death for women in the general Italian population. The lifetime cumulative probability of transition from use to dependence indicated that 1 in 5 cocaine users would become dependent at some point in their life (Lopez-Quintero et al., 2011), and females were seen to advance faster than males from recreational cocaine use to CUD in Vsevolozhskaya et al. (2016). Indeed, the research has shown higher substance use, more severe clinical presentation (Sanvicente-Vieira et al., 2019), and more severe adverse outcomes in females with CUD (Lejuez et al., 2007).

Excluding gender, age, nationality, and substances used, we did not have enough information to compare the characteristics between the PATS and never-PATS patients. While we observed no age difference at first admission, among the never-PATS we observed a higher percentage of females, of patients with a psychiatric diagnosis and with alcohol use, and a lower percentage of people with opioid use and injecting substances compared to the PATS population.

In this study, many people with problems caused by cocaine use who accessed PATS accessed other health services too,

and vice versa. We can therefore hypothesize that this population can access any source of treatment based on severity, risk perception, circumstances, choices, or other reasons. Most likely, those who applied directly to PATS could have specific characteristics (males, opioid use, and injecting substances) and, above all, different motivations for accessing treatment compared to those who have or had applied only to other health services.

Many never-PATS clients with CUD did not turn to PATS because they did not perceive their cocaine use as problematic, because they did not think they needed it, because of various barriers that hindered access (e.g., times, geographical location), or to avoid situations of stigma/labelling. The choice to enter treatment at PATS guarantees a change of lifestyle, a modification of the relationship with the substances abused, and greater attention to one's health. Overall, treatment retention in PATS was shown to be effective in reducing mortality in cohorts of subjects with opioid use disorders (Santo et al., 2021).

Similar to what has happened in other periods of economic crisis, when some studies observed a decrease in cocaine use (Zuccato et al., 2011) because individuals experienced reduced incomes and purchasing power (Epele, 2011), the effects of reduced mortality risk in our cohort during the first phases of COVID-19 might be due both to a change in consumption behaviours and to the disruption of drug markets and the reduced supply of illicit drugs (EMCDDA, 2020), although it is necessary to verify this trend over time with targeted studies. The data available from online surveys suggest an overall decline in cocaine use in the general population during the initial phases of the COVID-19 pandemic in Europe, mostly resulting from the implementation of confinement and social-distancing measures (EMCDDA, 2020; Palamar et al., 2021; Winstock et al., 2021). In Italy, both analysis of wastewater and the number of PATS clients revealed a decrease in the use of cocaine in 2020 (DPA, 2021).

#### 4.1. *Limitations*

This study had some limitations that reduce the generalisability of the results, and thus further research is required with specifically targeted studies. The data used were those available from first admission, so much information was missing. Also, the variables related to modalities of cocaine use, professional status, educational degree, hepatitis C status, and HIV status were regularly collected only for the PATS patients. Furthermore, it was impossible to consider data concerning age at first use, average consumption, variations over time, or the use of other substances because they were not assessed uniformly by the different service providers. Conversely, the strengths of this study were the cross-matching of EHR of different NHS services, and the specific “cohort study” design, which permitted us to calculate mortality and mortality excess rates in respect to the general population and to identify patients at higher risk.

## 5. Conclusion

The results of this study show that even those who turned to a health service following problematic cocaine consumption but did not seek treatment at PATS had a high mortality risk. Innovative strategies to overcome barriers to access and facilitate taking charge in addiction services for people with CUD must be identified. Further studies to analyse the effects

of the COVID-19 pandemic on the problematic consumption of cocaine and on the risk of death are also warranted.

## References

- Accurso, A. J., Rastegar, D. A., Ghazarian, S. R., & Fingerhood, M. I. 2015. Impact of hepatitis C status on 20-year mortality of patients with substance use disorders. *Addiction science & clinical practice*, 10, 20. <https://doi.org/10.1186/s13722-015-0041-6>
- Aharonovich, E., Scodes, J., Wall, M. M., & Hasin, D. S. 2021. The relationship of frequency of cocaine use to substance and psychiatric disorders in the U.S. general population. *Drug and alcohol dependence*, 227, 108933. <https://doi.org/10.1016/j.drugalcdep.2021.108933>
- Antoine, J., Berndt, N., Astudillo, M., Cairns, D., Jahr, S., Jones, A., Kuijpers, W., Llorens, N., Lyons, S., Maffli, E., Magliocchetti, N., Molina Olivas, M., Palle, C., Schwarzkopf, L., Wisselink, J., and Montanari, L. 2021. Cocaine treatment demands in 10 western European countries: observed trends between 2011 and 2018. *Addiction (Abingdon, England)*. 116(5), 1131–1143. <https://doi.org/10.1111/add.15237>
- Arendt, M., Munk-Jørgensen, P., Sher, L., and Jensen, S. O. 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), 134–139. <https://doi.org/10.1016/j.drugalcdep.2010.09.013>
- Colell, E., Domingo-Salvany, A., Espelt, A., Parés-Badell, O., and Brugal, M. T. 2018. Differences in mortality in a cohort of cocaine use disorder patients with concurrent alcohol or opiates disorder. *Addiction (Abingdon, England)*, 113(6), 1045–1055. <https://doi.org/10.1111/add.14165>
- Corkery, J. M., Claridge, H., Goodair, C., and Schifano, F. 2017. An exploratory study of information sources and key findings on UK cocaine-related deaths. *Journal of psychopharmacology (Oxford, England)*, 31(8), 996–1014. <https://doi.org/10.1177/0269881117711923>
- Degenhardt, L., Singleton, J., Calabria, B., McLaren, J., Kerr, T., Mehta S, Kirk, G., and Hall W. D. Mortality among cocaine users: a systematic review of cohort studies. 2011. *Drug and Alcohol Dependence*, 113(2-3): 88–95.
- JessicaSingletona, BiancaCalabriaa, JenniferMcLarena, Thomas Kerrb, ShrutiMehtac, GregoryKirkc, WayneD.Halld
- de la Fuente, L., Molist, G., Espelt, A., Barrio, G., Guitart, A., Bravo, M. J., Brugal, M. T., and Spanish Working Group for the Study of Mortality among Drug Users. 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), 219–226. <https://doi.org/10.1016/j.jsat.2013.07.001>
- DPA. 2019. Relazione annuale al Parlamento sullo stato delle tossicodipendenze in Italia. <https://www.politicheantidroga.gov.it/it/attivita/relazioni-annuali-al-parlamento/relazione-annuale-al-parlamento-sul-fenomeno-delle-tossicodipendenze-in-italia-anno-2019-dati-2018/> (accessed 30 November 2023)
- DPA. 2021. Relazione annuale al Parlamento sullo stato delle tossicodipendenze in Italia. <https://www.politicheantidroga.gov.it/it/attivita/relazioni-annuali-al-parlamento/relazione-annuale-al-parlamento-sul-fenomeno-delle-tossicodipendenze-in-italia-anno-2021-dati-2020/> (accessed 30 November 2023)
- EMCDDA. 2020. EU drug markets: impact of COVID-19.

- [https://www.emcdda.europa.eu/system/files/publications/13097/EU-Drug-Markets\\_Covid19-impact\\_final.pdf](https://www.emcdda.europa.eu/system/files/publications/13097/EU-Drug-Markets_Covid19-impact_final.pdf) (accessed 30 March 2022)
- EMCDDA. 2022. European Drug Report 2022: Trends and Developments. [https://www.emcdda.europa.eu/publications/edr/trends-developments/2022\\_en](https://www.emcdda.europa.eu/publications/edr/trends-developments/2022_en) (accessed 20 February 2024)
- Epele M. E. 2011. New toxics, new poverty: a social understanding of the freebase cocaine/Paco in Buenos Aires, Argentina. *Substance use & misuse*, 46(12), 1468–1476. <https://doi.org/10.3109/10826084.2011.576745>
- Gilmore, D., Zorland, J., Akin, J., Johnson, J. A., Emshoff, J. G., & Kuperminc, G. P. 2018. Mortality risk in a sample of emergency department patients who use cocaine with alcohol and/or cannabis. *Substance abuse*, 39(3), 266–270. <https://doi.org/10.1080/08897077.2017.1389799>
- Lejuez, C. W., Bornovalova, M. A., Reynolds, E. K., Daughters, S. B., & Curtin, J. J. 2007. Risk factors in the relationship between gender and crack/cocaine. *Experimental and clinical psychopharmacology*, 15(2), 165–175. <https://doi.org/10.1037/1064-1297.15.2.165>
- Leri, F., Bruneau, J., & Stewart, J. 2003. Understanding polydrug use: review of heroin and cocaine co-use. *Addiction (Abingdon, England)*, 98(1), 7–22. <https://doi.org/10.1046/j.1360-0443.2003.00236.x>
- Lopez-Quintero, C., Pérez de los Cobos, J., Hasin, D. S., Okuda, M., Wang, S., Grant, B. F., & Blanco, C. 2011. Probability and predictors of transition from first use to dependence on nicotine, alcohol, cannabis, and cocaine: results of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). *Drug and alcohol dependence*, 115(1-2), 120–130.
- <https://doi.org/10.1016/j.drugalcdep.2010.11.004>
- Mena, G., Giraudon, I., Álvarez, E., Corkery, J. M., Matias, J., Grasaasen, K., Llorens, N., Griffiths, P., & Vicente, J. 2013. 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. <https://doi.org/10.1159/000341719>
- Miró, Ò., Dargan, P. I., Wood, D. M., Dines, A. M., Yates, C., Heyerdahl, F., Hovda, K. E., Giraudon, I., Euro-DEN Plus Research Group, & Galicia, M. 2019. Epidemiology, clinical features and management of patients presenting to European emergency departments with acute cocaine toxicity: comparison between powder cocaine and crack cocaine cases. *Clinical toxicology (Philadelphia, Pa.)*, 57(8), 718–726. <https://doi.org/10.1080/15563650.2018.1549735>
- Palamar, J. J., Le, A., & Acosta, P. 2021. Shifts in Drug Use Behavior Among Electronic Dance Music Partygoers in New York During COVID-19 Social Distancing. *Substance use & misuse*, 56(2), 238–244.
- <https://doi.org/10.1080/10826084.2020.1857408>
- Pavarin, R., Lugoboni, F., Mathewson, S., Ferrari, A. M., Guizzardi, G., & Quaglio, G. 2011. Cocaine-related medical and trauma problems: a consecutive series of 743 patients from a multicentre study in Italy. *European journal of emergency medicine: official journal of the European Society for Emergency Medicine*, 18(4), 208–214. <https://doi.org/10.1097/MEJ.0b013e3283440f25>
- Pavarin, R. M., Sanchini, S., Marani, S., Turino, E., Tadonio, L., & Cantarelli, B. 2020. Mortality Risk among Cocaine Users before and after the Economic Recession: Results of a Longitudinal Study. *European addiction research*, 26(1), 10–19. <https://doi.org/10.1159/000503343>
- Peacock, A., Leung, J., Larney, S., Colledge, S., Hickman, M., Rehm, J., Giovino, G. A., West, R., Hall, W., Griffiths, P.,

- Ali, R., Gowing, L., Marsden, J., Ferrari, A. J., Grebely, J., Farrell, M., & Degenhardt, L. 2018. Global statistics on alcohol, tobacco and illicit drug use: 2017 status report. *Addiction* (Abingdon, England), 113(10), 1905–1926. <https://doi.org/10.1111/add.14234>
- Peacock, A., Tran, L. T., Larney, S., Stockings, E., Santo, T., Jr, Jones, H., Santomauro, D., & Degenhardt, L. 2021. All-cause and cause-specific mortality among people with regular or problematic cocaine use: a systematic review and meta-analysis. *Addiction* (Abingdon, England), 116(4), 725–742. <https://doi.org/10.1111/add.15239>
  - Prinzleve, M., Haasen, C., Zurhold, H., Matali, J. L., Bruguera, E., Gerevich, J., Bácskai, E., Ryder, N., Butler, S., Manning, V., Gossop, M., Pezous, A. M., Verster, A., Camposeragna, A., Andersson, P., Olsson, B., Primorac, A., Fischer, G., Güttinger, F., Rehm, J., Krausz, M. 2004. Cocaine use in Europe - a multi-centre study: patterns of use in different groups. *European addiction research*, 10(4), 147–155. <https://doi.org/10.1159/000079835>
  - Sami, F., Chan, W. C., Acharya, P., Sethi, P., Cannon, C., Hockstad, E. S., Tadros, P. N., Wiley, M. A., & Gupta, K. 2022. Outcomes in patients with history of cocaine use presenting with chest pain to the emergency department: Insights from the Nationwide Emergency Department Sample 2016-2018. *Journal of the American College of Emergency Physicians open*, 3(1), e12618. <https://doi.org/10.1002/emp2.12618>
  - Santo, T., Jr, Clark, B., Hickman, M., Grebely, J., Campbell, G., Sordo, L., Chen, A., Tran, L. T., Bharat, C., Padmanathan, P., Cousins, G., Dupouy, J., Keltly, E., Muga, R., Nosyk, B., Min, J., Pavarin, R., Farrell, M., & Degenhardt, L. 2021. Association of Opioid Agonist Treatment With All-Cause Mortality and Specific Causes of Death Among People With Opioid Dependence: A Systematic Review and Meta-analysis. *JAMA psychiatry*, 78(9), 979–993. <https://doi.org/10.1001/jamapsychiatry.2021.0976>
  - Sanvicente-Vieira, B., Rovaris, D. L., Ornell, F., Sordi, A., Rothmann, L. M., Niederauer, J. P. O., Schuch, J. B., von Diemen, L., Kessler, F. H. P., & Grassi-Oliveira, R. 2019. Sex-based differences in multidimensional clinical assessments of early-abstinence crack cocaine users. *PloS one*, 14(6), e0218334. <https://doi.org/10.1371/journal.pone.0218334>
  - Sanvisens, A., Vallecillo, G., Bolao, F., Rivas, I., Fonseca, F., Fuster, D., Torrens, M., Pérez-Hoyos, S., Pujol, R., Tor, J., & Muga, R. 2014. Temporal trends in the survival of drug and alcohol abusers according to the primary drug of admission to treatment in Spain. *Drug and alcohol dependence*, 136, 115–120. <https://doi.org/10.1016/j.drugalcdep.2013.12.022>
  - Sheehan, C. M., Rogers, R. G., & Boardman, J. D. 2015. Postmortem Presence of Drugs and Method of Violent Suicide. *Journal of drug issues*, 45(3), 249–262. <https://doi.org/10.1177/0022042615580988>
  - UNODC, World Drug Report 2023 (United Nations publication, 2023).
  - <https://www.unodc.org/unodc/en/data-and-analysis/world-drug-report-2023.html> (accessed 20 February 2024)
  - Winstock AR, Davies EL, Gilchrist G, Zhuparris A, Ferris JA, Maier LJ, Barratt MJ. Global Drug Survey special edition on COVID-19 global interim report. 2021. [https://www.globaldrugsurvey.com/wp-content/themes/globaldrugsurvey/assets/GDS\\_COVID-19-GLOBAL\\_Interim\\_Report-2020.pdf](https://www.globaldrugsurvey.com/wp-content/themes/globaldrugsurvey/assets/GDS_COVID-19-GLOBAL_Interim_Report-2020.pdf) (accessed 30 November 2023)
  - Vsevolozhskaya, O. A., & Anthony, J. C. 2016. Transitioning from First Drug Use to Dependence Onset: Illustration of a Multiparametric Approach for Comparative Epidemiology. *Neuropsychopharmacology: official publication of the*

American College of Neuropsychopharmacology, 41(3), 869–876. <https://doi.org/10.1038/npp.2015.213>

- Zuccato, E., Castiglioni, S., Tettamanti, M., Olandese, R., Bagnati, R., Melis, M., & Fanelli, R. 2011. Changes in illicit drug consumption patterns in 2009 detected by wastewater analysis. *Drug and alcohol dependence*, 118(2-3), 464–469. <https://doi.org/10.1016/j.drugalcdep.2011.05.007>