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## Mortality trends among heroin users treated between 1975 and 2013 in Northern Italy: Results of a longitudinal study

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#### ABSTRACT

*Background:* The aim of this study was to examine heroin mortality trends and changes in causes of death, across time and age, in a cohort of the heroin population of treated.

Methods: 5899 subjects attending twelve centers for addiction treatment (SERT) in north Italy following problems due to heroin abuse between 1975 and 2013 were recruited.

*Results*: This study documented elevated mortality among subjects with primary heroin abuse, with an elevated death risk in all the classes of age, declining until 2009 ad increasing starting from 2010. AIDS was the first cause of death, followed by overdose and liver-related diseases.

In the course of time mortality for AIDS and for drug-related deaths has declined, whereas liver mortality and all tumors mortality have risen over time, becoming the most common causes of death by the end of the follow up. As compared with the general population, the excess mortality (SMR) observed for all causes in either sex was 13.2, higher in females (SMR = 21.5) as compared with males (SMR = 12.1). Higher SMRs were found in 25/34 age-group patients, with a progressive decrease in subjects with age > 34 years.

Conclusions: In the course of time, among heroin users, mortality and the causes of death have changed; for SERT clients special attention should be paid to the prevention and treatment of liver-related diseases.

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#### 1. Introduction

The use of heroin accounts for the majority of deaths related to illicit drug use. Crude mortality rates (CMR) and the risks of death among heroin users are substantially higher than in the general population worldwide, with a pooled CMR of 20.9 for 1000 person years (PY) and an excess mortality at least 14 times higher as compared with that of the general population (Degenhardt et al., 2011).

The risk of death is increased by older age, long-term use of drugs, poly-drug use, injecting administration, somatic and psychiatric comorbidity, and not being enrolled in any drug treatment (Davoli et al., 2007; Clausen, Anchersen & Waal, 2008; Cornish, Macleod, Strang, Vickerman & Hickman, 2010; Degenhardt et al., 2009; Mathers et al., 2013). Causes of death vary across studies, but AIDS and overdose were the most common (Best et al., 2000; Darke, Degenhardt & Mattick, 2006; Degenhardt et al., 2011; Giraudon, Vicente, Matias, Mounteney & Griffiths, 2012; EMCDDA, 2015a).

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Drug-related deaths declined over time, SMRs declined with follow-up, and the highest excess mortality rate was in the youngest age group (Nambiar et al., 2015), even if opioid users' excess mortality persists into old age (Pierce, Bird, Hickman & Millar, 2015). Accidental opioid overdose, suicide, transport accidents, and violent causes declined with age; death from cardiovascular disease, liver disease, and cancer increased (Degenhardt, Larney, Randall, Burns & Hall, 2014).

In the past few years, the characteristics of the subjects referring to public services for problems of addiction due to heroin use have also changed. Indeed, while their number is declining, their average age is rising and their levels of injecting are decreasing (Han et al., 2015; EMCDDA, 2015b).

Mortality in the population of heroin users in Italy is characterised by a fair amount of local variability, as results from the analysis of several cohorts of drug addicts referring to the public treatment centres for drug addiction (SERT), and the specific studies reporting an SMR for all causes for males from 8.2 to 21.3 and from 10.3 to 42.8 for females (Ciccolallo, Morandi, Pavarin, Sorio & Buiatti, 2000; Sabbatani, Di Crescenzo, Giorni & Giordano, 1996; Pavarin & Prata, 2001; Antolini, Pirani, Morandi & Sorio, 2006; Gruppo Esedra, 1997; Cipriani et al., 1998; Bargagli, Sperati, Davoli, Forestiere & Peducci, 2001; Galli, Musicco & COMCAT Study group, 1994; Mezzelani et al., 1998; Quaglio et al., 2001; Rocchi, Miotto

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## & Preti, 2003; Preti, Miotto & De Coppi, 2000; Goedert et al., 1995; Zaccarelli et al., 1994; Pavarin, 2008; Pavarin, 2015; Ferri et al., 2007).

The main causes of death are AIDS and overdose, but a mortality excess is also described in respect of the general population for cirrhosis, tumours, infections, road accidents, homicides, and suicides. The overall mortality rate has tended to fall since 1997 thanks to the substantial drop in the mortality rate for AIDS and for overdose. The differences between the various studies reflect different access criteria to the services, and the testing of different therapeutic treatments, the introduction of different models of intervention to the territory, the temporal geographical variability of the drugs market, different time ranges for recruitment and follow-up, differences in genders between the various cohorts.

Differences between the mortality rates are also noticeable at the European level, where, in a multicentre study conducted in eight countries from 1990 to 1998, the correlated drug mortality rates varied from 3.5 per thousand PY to 10 per thousand in the various cohorts (Bargagli et al., 2006). In the cohort studies of the overall mortality among opioid drug users enrolled in treatment during the period 1995–2011 in nine European countries, the mortality was roughly 10 to 20 times that of the general population of the same age and gender, with an overall rate of 14 deaths per 1000 PY followed up, but varied geographically from 3.5 to 22.7. The causes of death vary across studies, but AIDS and overdose were the most common (EMCDDA, 2015a). Excess mortality risk is usually higher in females than in males, largely due to lower mortality rates among women in the general population. In addition, the excess mortality risk is usually higher in younger drug users than in older ones, again largely due to lower mortality rates among their peers in the general population.

The aim of this retrospective cohort study, which targeted residents of the Emilia-Romagna region (North Italy) who turned to a SERT following problems due to heroin abuse between 1975 and 2013, was to examine mortality trends and changes in causes of death, across time and age in Italy. Our aims were to estimate overall mortality rates and excess mortality by age, gender, calendar period, and time of the first visit.

The analyses were performed for all the causes, and separately for the most common causes, of death (e.g., drug-related, liver-related, AIDS, injury) and for all alcohol-related deaths (Randall, Roxburgh, Gibson & Degenhardt, 2009).

#### 2. Material and methods

#### 2.1. Participants

Subjects resident in the metropolitan area of Bologna and in the territory of the Local Health Unit of Forlì (Emilia Romagna region – North Italy), aged between 14 and 64 years who, for the first time, turned to a drug abuse treatment service run by the National Health Service for problems caused primarily by heroin abuse, were selected. The reference period spans between 1975 and 2013.

The information was collected at the first contact. The cases were selected from the IT systems of SERTs (in 12 health services).

At the SERTs, a digital regional folder is used to collect the data at the 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.

The variables used were related to date of contact, age, gender, country of birth, residence, professional status, educational degree, substance of abuse, method of use, hepatitis C status, HIV status.

In the Emilia Romagna region the public addictions service performs an activity of prevention, cure and rehabilitation from use/ abuse disorders, addiction to psychoactive substances, both legal and illegal. Within the SERT there is a multidisciplinary team, made up of professionals possessing diverse skills (physicians, psychologists, social assistants, professional educators, nurses, health workers) to guarantee a global and integrated assistance valorising the centrality of the person. The pathway of observation and diagnosis, enforced in the initial phase, is finalised by putting forward therapeutic-rehabilitation treatments that are personalised, integrated and flexible. The SERT deals with all the issues correlated to the treatment of the pathological addictions, by means of multidisciplinary strategies of rehabilitation and assistance, both from the health point of view and the educational, social, and psychological ones, implementing measures safeguarding health and reinsertion into the social fabric. Special attention is addressed to the prevention of infectious diseases, to chronic pathologies correlated to substance abuse, to quality of life, and to the person's social integration.

**Table 1**How the characteristics of the subjects with heroin use disorders are changing. Period 1975–2013.

		<1995 (2040)	1995–1999 (1366)	2000–2004 (1020)	2005–2009 (1029)	2010-2013 (444)	Total (5899)	P
Age at time of admission	Mean age	26.5	29.6	30.2	30.5	31.2	29.1	< 0.0001
Sex	% Female	22.2	20.1	18.5	25.6	25.2	21.9	< 0.0001
Nationality	% Non-native	2.2	3.6	8.8	13.0	16.0	6.6	< 0.0001
Professional status at time of admission	% Regular income	62.0	70.8	67.6	61.8	57.0	64.6	< 0.0001
	% Unemployed	16.2	25.3	28.9	32.5	33.3	24.6	< 0.0001
	% Student	1.2	1.8	2.7	4.6	5.9	2.5	< 0.0001
	% Missing	20.7	2.1	0.7	1.2	3.8	8.3	< 0.0001
Educational level at time of admission	% Primary/secondary school	36.9	54.1	50.3	42.8	38.7	44.3	< 0.0001
	% High school diploma	36.3	39.4	44.9	49.6	51.8	42.0	< 0.0001
	% University	1.3	1.8	3.2	6.9	7.4	3.2	< 0.0001
	% Missing	25.5	4.8	1.6	0.8	2.0	10.5	< 0.0001
Method of heroin use at time of admission	% Injected	93.5	87.1	62.1	42.8	35.4	73.4	< 0.0001
	% Smoked	0.2	2.0	9.7	37.5	46.6	12.3	< 0.0001
	% Sniffed	0.4	6.0	23.3	16.6	12.8	9.4	< 0.0001
	% Missing	5.9	4.9	4.9	3.1	5.2	4.9	< 0.0001
HIV status in the whole period	% Positive	23.1	11.4	7.0	2.4	3.4	12.5	< 0.0001
	% Missing	31.2	15.8	29.6	31.6	27.9	27.2	< 0.0001
HCV status in the whole period	% Positive	49.7	59.1	40.1	31.2	22.3	44.9	< 0.0001
	% Missing	37.2	18.1	30.0	29.2	27.5	29.4	< 0.0001
Other substances in the whole period	% Benzodiazepines	10.4	9.9	6.2	2.9	1.1	7.5	< 0.0001
	% Alcohol	15.0	16.0	15.6	10.7	6.1	13.9	< 0.0001
	% Cannabis	26.3	37.7	32.5	26.7	19.1	29.5	< 0.0001
	% Cocaine	24.4	39.2	53.5	41.0	19.6	35.4	<0.0001

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