



Temporal trends in the survival of drug and alcohol abusers according to the primary drug of admission to treatment in Spain



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ABSTRACT

Background: Mortality of alcohol and drug abusers is much higher than the general population. We aimed to characterize the role of the primary substance of abuse on the survival of patients admitted to treatment and to analyze changes in mortality over time.

Methods: Longitudinal study analyzing demographic, drug use, and biological data of 5023 patients admitted to three hospital-based treatment units in Barcelona, Spain, between 1985 and 2006. Vital status and causes of death were ascertained from clinical charts and the mortality register. Piecewise regression models were used to analyze changes in mortality.

Results: The primary substances of dependence were heroin, cocaine, and alcohol in 3388 (67.5%), 945 (18.8%), and 690 patients (13.7%), respectively. The median follow-up after admission to treatment was 11.6 years (IQR: 6.6–16.1), 6.5 years (IQR: 3.9–10.6), and 4.8 years (IQR: 3.1–7.8) for the heroin-, cocaine-, and alcohol-dependent patients, respectively. For heroin-dependent patients, mortality rate decreased from 7.3×100 person-years (p-y) in 1985 to 1.8×100 p-y in 2008. For cocaine-dependent patients, mortality rate decreased from 10.7×100 p-y in 1985 to $<2.5 \times 100$ p-y after 2004. The annual average decrease was 2% for alcohol-dependent patients, with the lowest mortality rate (3.3×100 p-y) in 2008.

Conclusions: Significant reductions in mortality of alcohol and drug dependent patients are observed in recent years in Spain. Preventive interventions, treatment of substance dependence and antiretroviral therapy may have contributed to improve survival in this population.

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1. Introduction

Individuals with alcohol and drug use disorders are at an increased risk of death compared to the general population (Bargagli et al., 2006; Degenhardt and Hall, 2012). This excess mortality is primarily due to the impact of well-known drug-related complications, such as overdose, other non-natural causes of death, and HIV/AIDS (Copeland et al., 2004; Wang et al., 2005; Degenhardt et al., 2006). According to the European Monitoring Center for Drugs and Drug Addiction (EMCDDA), more than 90% of deaths attributed

to illegal drugs in Europe are due to opiates (EMCDDA, 2011). In fact, heroin users represent the largest proportion of drug-use-related mortality in the European Union (EMCDDA, 2011). Regarding treatment of heroin addiction, the availability of opioid substitution therapy allows injection drug users (IDU) to reduce opiate consumption and improves social functioning. Furthermore, opiate substitution therapy has been associated with reductions in the incidence of HIV-infection and all-cause mortality (Vlahov et al., 2010; Torrens et al., 2013). Despite the many causes of death in this at-high risk population, the mortality of IDUs in Western Europe has decreased dramatically over the past decade (Muga et al., 2007; Huang et al., 2011).

Cocaine abuse is also associated with high mortality rates; according to a recent study, the mortality of cocaine-dependent patients is 4–8 times higher than that of the general population

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(Degenhardt et al., 2011a,b). Studies have found that most cocaine-related deaths occur in chronic drug users and are often the result of cardiovascular and neurological complications (European Monitoring Center for Drugs and Drug Addiction, 2009). In contrast to pharmacological treatment of heroin dependence, no substitution therapy is available for cocaine dependence; pharmacological treatment and risk-reduction approaches for cocaine-dependent patients have not been as effective (de Lima et al., 2002; Marsden et al., 2009; Martell et al., 2009) as reported for opiate addiction.

When physical harm and social consequences of addiction are analyzed together, alcohol is the most harmful substance of abuse (Nutt et al., 2010). To some extent, pharmacological and non-pharmacological interventions for the treatment of alcohol dependence have barely evolved over the last twenty years (Fiellin et al., 2000; Saitz, 2005). Longitudinal studies have shown that untreated alcohol-dependent patients have significantly high mortality with respect to the same age in the general population (Fudalej et al., 2010). Guitart et al. (2011) reported that the total excess mortality in 18–64-year-old individuals with alcohol-use disorders is 8 times higher than in the general population of Spain. The main causes of death among patients with alcohol use disorders are liver-related diseases, cancer, non-natural causes, and cardiomyopathy (Mann et al., 2005; Timko et al., 2006; Mattisson et al., 2011).

Addiction is a chronic disease; and to some extent, prognosis of disease as a function of the primary drug of abuse is not well characterized, partly because the frequent co-occurrence of multiple substance use. In terms of survival, the elapsing time between admission to drug treatment and the incidence of clinical outcomes may vary as a function of medical and psychiatric co-morbidities at baseline (Rivas et al., 2013). Trends in mortality may also differ among countries as a function of the continuous introduction of harm reduction interventions for each substance of abuse (Degenhardt et al., 2013). In this regard, mortality rates of alcohol and drug dependent patients have been reported in community-based studies from Spain. In the majority of cases studies have assessed the impact of heroin addiction in mortality; however, the association between survival of patients and addiction severity has received less attention.

The objective of the study was to characterize long-term mortality of patients with severe substance use disorders seeking drug treatment in Barcelona, Spain, according to the substance that motivates admissions to detoxification. In addition, we aimed to analyze changes in death rates and cause-specific mortality after 24 years of observation.

2. Patients and methods

2.1. Design and study population

The study population included all patients admitted for hospital detoxification at three tertiary care facilities located in Barcelona, Spain and its metropolitan area between January, 1985 and December, 2006. These hospital units provide facilities for the treatment of substance use disorders and are located in Badalona (Hospital Universitari Germans Trias i Pujol), L'Hospitalet de Llobregat (Hospital Universitari de Bellvitge), and Barcelona (Hospital del Mar, Parc de Salut Mar).

Patients were referred to drug treatment by primary care physicians and specialists in addiction medicine at primary care clinics. The main criteria for the referrals to the drug treatment facilities were the severity of the disease according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R, DSM-VI, DSM-VI-TR), the risk of complicated withdrawal syndrome if detoxification was performed in an outpatient basis, and the severity of co-morbidity (American Psychiatric Association, 2000; Nocon et al., 2007). All patients were required to be older than 18 years of age, and the median duration of admission was 7 days.

Socio-demographic data, history of alcohol and/or drug-use characteristics (i.e., main substance of abuse, age at first consumption, route of administration), and blood samples for HIV infection, HBV infection (hepatitis B surface antigen, HBsAg), and hepatitis C infection were collected at admission. At discharge, the patients were asked to return for semiannual visits at the outpatient clinics. Additional admission

details were published previously (Muga et al., 2007; Rivas et al., 2010; Sanvisens et al., 2011).

For the purposes of the study, patients were classified into three categories according to the main substance of abuse at admission to drug treatment. Assessment of the main substance of abuse was based on history taking and clinical judgment and was established by the same physicians (MT, FB, RM) at each medical institution throughout the study period. Patients were categorized in (1) heroin-dependent, (2) cocaine-dependent, or (3) alcohol-dependent.

The methods of this study complied with ethical standards for medical research and the principles of good clinical practice in accordance with the World Medical Association's Declaration of Helsinki.

2.2. Follow-up, mortality rates, and causes of death

In all cases, vital status and cause of death were ascertained by reviewing clinical charts and cross-checks with the Catalan mortality register on December 31, 2008. Cause of death was established in accordance with the International Classification of Diseases, Version 9 (ICD-9) until 1998 (World Health Organization, 1979) and Version 10 (ICD-10; World Health Organization, 2007) between 1999 and 2008. Causes of death were later classified into eight categories:

- 1) Non-natural (including drug-related, alcohol-related, accidents, suicides, and traumas): ICD-9: 304, 305, E800–E999; ICD-10: F10–F19, X00–X99, V00–V99, W00–W99, Y00–Y36.
- 2) HIV/AIDS: ICD-9: 279.5, 795.8; ICD-10: B20–B24, R75.
- 3) Liver-related (including viral hepatitis, cirrhosis, decompensated liver disease, and hepatocarcinoma): ICD-9: 070, 155, 570–573; ICD-10: B15–B19, C22, K70–K77.
- 4) Neoplasia, excluding hepatocarcinoma: ICD-9: 140–154, 156–208, 273.3; ICD-10: C00–C21, C23–C97, D00–D09, D37–D48.
- 5) Cardiovascular: ICD-9: 390–460; ICD-10: I00–I99.
- 6) Other medical causes (including non-HIV/AIDS infectious diseases, respiratory or nervous system failures): all codes not specified in other categories.
- 7) Unknown or undefined causes: ICD-9: 799.8, 799.9; ICD-10: R09, R98, R99.

2.3. Statistical analysis

Prior to data analysis, the databases from the three participating hospitals were concatenated and checked for duplicates. Only the first admission of each patient was included in the descriptive analysis.

Mortality rates were calculated in person-years (p-y) by dividing the number of observed deaths during the study period by the sum of all individual follow-up times. The survival estimates were analyzed using the Kaplan–Meier method. Piecewise regression models were fitted to analyze changes in mortality and models were evaluated on a logarithmic scale with a Poisson distribution. Piecewise regression models allow the determination of changes in rates over time and the moment where that specific change(s) occur. Values of $p < 0.05$ were considered significant. The analyses were conducted using STATA Version 8.0 (Stata Corp., College Station, TX, USA). The US National Cancer Institute's Joinpoint Regression Program software was also used (US National Cancer Institute Software, 2010).

3. Results

A total of 5023 patients (78.2% men) were admitted. Median age at admission was 29 years (IQR: 25, 35 years). The main substance of abuse was heroin in 67.5% of cases, cocaine in 18.8%, and alcohol in 13.7%. Overall, 75.1% of the study population had antecedent of injection drug use.

Prevalence of HIV infection, HCV infection, and HBV (HBsAg) infection was 41.6%, 60%, and 5.5%, respectively. The socio-demographic and clinical characteristics of the patients are provided in Table 1.

3.1. Follow-up and outcomes

The median follow-up for the entire cohort was 9.3 years (IQR: 4.8, 14.6 years; 50,066 p-y), but the median follow-up was 11.6 years for heroin-dependent patients, 6.5 years for cocaine-dependent patients, and 4.8 years for alcohol-dependent patients. By December 31, 2008, 1525 patients had died (cumulated mortality 30.4%). The median age at death was 35.3 years (IQR: 30.4, 41.4 years).

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