Drug induced mortality: a multiple cause approach on Italian causes of death Register

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ABSTRACT

BACKGROUND: Drug-related mortality is a complex phenomenon that has several health, social and economic effects. In this paper trends of drug-induced mortality in Italy are analysed. Two approaches have been followed: the traditional analysis of the underlying cause of death (UC) (data refers to theIstat mortality database from 1980 to 2011), and the multiple cause (MC)analysis, that is the analysis of all conditions reported on the death certificate (data for 2003-2011 period).
METHODS: Data presented in this paper are based on the Italian mortality register. The selection of Icd codes used for the analysis follows the definition of the European Monitoring Centre for Drugs and Drug Addiction. Using different indicators (crude and standardized rates, ratio multiple to underlying), the results obtained from the two approaches (UC and MC) have been compared. Moreover, as a measure of association between drug-related causes and specific conditions on the death certificate, an estimation of the age-standardized relative risk (RR) has been used.
RESULTS: In the years 2009-2011, the total number of certificates whit mention of drug use was 1,293, 60% higher than the number UC based. The groups of conditions more strongly associated with drug-related causes are the mental and behavioral disorders (especially alcohol consumption), viral hepatitis, cirrhosis and fibrosis of liver, AIDS and endocarditis.
CONCLUSIONS: The analysis based on multiple cause approach shows, for the first time, a more detailed picture of the drug related death; it allows to better describe the mortality profiles and to re-evaluate the con-tribution of a specific cause to death.

Key words: multiple causes, causes of death, drug-induced mortality

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INTRODUCTION

Drug-related mortality is a complex phenomenon that has several health, social and economic effects [1].

People who use drugs, especially by injection, are at higher risk of dying from both acute and chronic diseases, many of which are related to their drug use, than people who do not use these drugs. Fatal overdose and infection

with human immunodeficiency virus (HIV) and other blood-borne viruses transmitted through shared needles and syringes are the most common causes of death in this group [2-5]. Understanding causes of death is important when setting priorities for programs designed to reduce deaths from the use of drugs [6].

At European level two indicators are generally used to estimate the drug-related mortality: deaths directly caused by illegal drugs (drug-induced deaths) and mortality rates among problem drug users [7].

For Italy the drug related deaths figures are provided to the European Monitoring Centre for Drugs and Drug Addiction (Emcdda) by the Central Anti-Drug Services Department (Dcsa) – Ministerodell'Interno [8]. The Emcdda is one of the decentralized agencies of the European Union and has for its mandate the provision of sound, reliable, and comparable information on drugs and drug addictions and their consequences. Nevertheless an alternative source for drug-induced deaths indicators is the Italian Register of Causes of Death (CoD) held by the Italian National Institute of Statistics.

Concerning indicators of drug-related mortality, the estimation of mortality rates among drug users requires follow-up studies. Nevertheless, the improvement of data quality and availability of multiple cause of death data, allows to use CoD registers also to derive wider indicators than the traditional drug-induced mortality based only on the underlying cause of death [9-10]. By means of the study of multiple causes of death, it is possible, in fact, to provide a more comprehensive picture based also on deaths indirectly related to drug abuse.

Moreover, the multiple cause approach allows to estimate the statistical significance of the association between the cause of death "drug abuse" (reported as directly leading to death or indirectly related to it) and the other causes of death.

The aim of this study is to assess drug induced death indicators using the Italian mortality register and to describe the trends as well as geographical, gender and age differences of this indicators.

Moreover, using the multiple cause approach we aim to provide a supplementary indicator based on all causes of death mentioned in the death certificate and to evaluate the strength of associations between drug abuse and other conditions.

METHODS

Data

Data presented in this paper are based on the Italian mortality register that is a main source for epidemiological information for the Country. It is a population-based register including all deaths occurred in Italy independently from the country of residence of the deceased.

Data refer to individual death certificates (Istat forms D4 and D4bis) containing two parts: a medical certification of causes of death reported by a physician and a socio-demographic part filled in by local municipalities [11]. Socio-demographic information refer to sex, age, place of residence (municipality or foreign state), place of occurrence, education level and citizenship.

The cause of death certification includes the description of the sequence of conditions that directly lead to death and, where appropriate, other conditions that may have contributed to it but not directly linked to the final event. In the medical part of the death certificates, four conditions are reported on average (2011 data); nevertheless, the tabulated data refer to one single cause of death: the underlying cause which is defined as (a) the disease of injury which initiated the train of events leading directly to death, or (b) the circumstances of the accident or violence which produced the fatal injury. The classification of causes of death and the selection of the underlying cause is performed according to the rules and provisions of the International classification of diseases (Icd) provided and updated by the Who. Since reference data year 2003, Istat adopted the tenth revision of this classification (Icd-10) [12]. Since reference data year 1995, Istat implemented the automated coding system Micar-Acme, developed by the US National Centre for Health Statistics (Nchs). This software is considered the de facto standard for the selection of the underlying cause of death and allows to code automatically about 80% of all certificates. The remaining 20% (including all external causes) is manually coded by expert nosologists. The use of the automated coding system lowers the variability of data due to manual coding.

Besides the underlying cause database, since 2003, Istat disseminates also data referring to all conditions reported on the death certificates (multiple causes of death).

TABLE 1

EMCDDA SELECTION B: SELECTION OF ICD CODES DE	
ICD-10: YEARS 2003, 2006-2011	
Mental and behavioural disorders due to psychoactive substance use	F11: Mental and behavioural disorders due to use of opioids; F12: Mental and behavioural disorders due to use of cannabinoids, F14: Mental and behavioural disorders due to use of cocaine; F15: Mental and behavioural disorders due to use of other stimulants, including caffeine; F16:Mental and behavioural disorders due to use of hallucinogens; F19: Mental and behavioural disorders due to multiple drug use and use of other psychoactive substances
Accidental poisoning	X421): Accidental poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified; X412): Accidental poisoning by and exposure to antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified
Intentional self-poisoning	X621): Intentional self-poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified; X612): Intentional self-poisoning by and exposure to antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified.
Poisoning undetermined intent	Y121): Poisoning by and exposure to narcotics and psychodysleptics [hallucinogens], not elsewhere classified, undetermined intent; Y112): Poisoning by and exposure to antiepileptic, sedative-hypnotic, antiparkinsonism and psychotropic drugs, not elsewhere classified, undetermined intent.

1) in combination with the T-codes: T40.0-9: Poisoning by narcotics and psychodysleptics [hallucinogens];

2) in combination with T code: T43.6 Poisoning by psychotropic drugs,Psychostimulants with abuse potential.

ICD-9: YEARS 1980-2002	
Drug psychoses	292
Drug dependence	304.0, 304.2-9
Nondependent drug abuse	305.2-3, 305.5-7, 305.9
Accidental drug poisoning	E850.0, E850.83), E854.1-2, E855.2, andE858.83)
Suicide and self-inflicted drug poisoning	E950.01) , E950.43)
Drug poisoning undetermined intent	E980.01), E980.43)

3) in combination with N-codes (N965.0, and/or N968.5, and/or N969.6, and/or N969.7)

This allows to analyse those causes that have had a role in causing death but which are not selected as underlying.

In the present analysis we refer to all deaths for which the certifying physician has reported drug dependence or drug poisoning in the death certificate. Two approaches have been followed:

1. the traditional analysis of the underlying cause of death;
2. the analysis of all conditions reported by the certifying physician (multiple cause approach with available data for 2003-2011 period).

Although the study of mortality trends is mostly based on the underlying cause of death, the use of multiple causes allows to better describe the mortality profiles and to re-evaluate the contribution of a specific cause to death [13]. This is particularly true for the conditions that are often reported as contributory causes and the role of which could be underestimated when only the underlying cause is considered.

The selection of Icd codes used for the analysis follows the definition of the Emcdda (selection B) [8]. It varies according to the year of death depending on the Icd revision used in the reference year. The list of selected codes is provided in table 1 allowing an extraction of cases with a consistent definition over time. In particular, according to the International classification of the diseases, drug-induced deaths can be classified in two main groups:

Group 1 :Mental and behavioral disorders due to psychoactive substance use (Icd-9: 304-305; Icd-10: F10-F19); this group mainly refers to drug dependence;

Group 2: Poisoning and exposure to noxious substances (Icd-9: E85, E85, E85, E85, E95, E98; Icd10: X42, X41, X62, X61, Y11, Y12); this group mainly refers to "overdose".

Due to major updates occurred in 2006, many cases that would have been classified in the first group before 2006, were classified in the second one from 2006 on [14]. This change does not allow a consistent analysis of trends for detailed causes (group 1 and 2 separately), but the trend remains well defined if all the subgroups of causes are pooled together as in the Emcdda selection B.

STATISTICAL ANALYSIS

The *underlying cause* approach has been used for analyzing the trends of drug-induced mortality and the differences of these by gender, geography and age. Data presented refer to years from 1980 to 2011. *Underlying cause* indicators used are the following:

- Absolute number of deaths is presented for the period 1980-2011 and refers to the present population (all deaths occurred in Italy)
- Standardized mortality rates are presented for the period 1992-2011 and refer to the Italian resident population. They are calculated with the direct method with age groups of five years, considering separately age 0 year and the last class 90 year and more (0, 1-5, 5-9,... , 90+); the standard population used refers to Italian census 2001. This indicator is used for gender and geographic comparisons.
- Age specific mortality rates for age groups 15-24, 25-44, 45-54 and 55-64.

These are calculated for the period 1992-2011 and refer to the Italian resident population

With the *Multiple cause* approach we consider as "drug related deaths" all those deaths certificates that contain one of the selected Icd-10 codes included in Emcdda selection B definition (table 1) both as the underlying and associated causes.

Data refer to the multiple cause data of the resident population aged from 15 to 64 years, pooled for years 2009-2011 and compared with similar data for years 2006-2008. For both periods the deaths occurred in the autonomous provinces of Bolzano-Bozen and Trento have been excluded due to the lack of multiple causes data.

For the study of mortality levels comparing the underlying and multiple cause approach the following indicators have been used (tables 2 and 3):

- Number of deaths obtained with the two methods
- Crude rates (age-specific and total)
- Standardized rates
- Ratio multiple to underlying cause defined as number of deaths obtained with multiple cause approach divided by number of deaths obtained with underlying cause approach (age-specific and total).

For the period 2009-2011 an analysis of conditions associated to drug-related causes has been performed. For this analysis two groups of death certificates have been identified:

1. Certificates with mention of drug-related causes according the definition B of EMCDDA; this group will be referred as drug users deaths.
2. Certificates without mention of drug-related causes: non-drug users deaths.

As a measure of association between drug-related causes and specific conditions reported on the death certificate, an estimation of the age-standardized relative risk (RR) has been used. This estimation is defined as the ratio between the following proportions:

1. proportion of death certificates mentioning the specific morbid condition A among certificates of drug users (d)
2. proportion of death certificates with mention of the condition A among certificates of non-drug users ($\bar{d}$).

$$R = \frac{\hat{D}_{dA}}{D_d} \Big/ \frac{\hat{D}_{\bar{d}A}}{D_{\bar{d}}} = \frac{\hat{p}_{dA}}{\hat{p}_{\bar{d}A}}$$

where:

$\hat{D}_{dA}$ number of estimated deaths mentioning both: the cause A and drug-related cause d

D_d number of death certificates mentioning drug-related cause d

$\hat{D}_{\bar{d}A}$ number of estimated death certificates mentioning the cause A without mention of drug-related cause d

$D_{\bar{d}}$ number of death certificates without mention of drug-related cause d.

Deaths are estimated on the basis of the age distribution of deaths for the general population according to the following formulas:

$$\hat{D}_{\bar{d}A} = \sum_x {}_x\hat{D}_{dA} = \frac{{}_xD_{\bar{d}A}}{{}_xD_{\bar{d}}} \times \frac{{}_xD}{D} \times D_{\bar{d}}$$

estimate of deaths with drug-related cause and associated cause A

$$\hat{D}_{\bar{d}A} = \sum_x {}_x\hat{D}_{\bar{d}A} = \frac{{}_xD_{\bar{d}A}}{{}_xD_{\bar{d}}} \times \frac{{}_xD}{D} \times D_{\bar{d}}$$

estimate of deaths without drug-related cause and associated cause A.

The confidence intervals have been calculated using the log-normal distribution as:

$$CI_{95\%}(\ln RR) = \ln RR \pm 1,96 \quad ES(\ln RR) \quad \text{where} \quad ES(\ln RR) = \sqrt{\frac{(1 \quad \hat{p}_{dA})}{\hat{D}_{dA}} + \frac{(1 \quad \hat{p}_{\bar{d}A})}{\hat{D}_{\bar{d}A}}}$$

The relative risk can be seen as a measure of the strength of association of a certain cause with drug-related condition.

Finally, the percentages of mention of each condition both in drug users and non-drug users have been calculated. Both the percentage of mention and the age-standardized relative risk (RR) are shown in table 4.

RESULTS

Underlying cause approach

Figure 1 shows the trend of the absolute number of drug-induced deaths by year registered in Italy in the period 1980-2011. The number of deaths for this cause ranges between 156 cases registered in 1980 to 1,277 in 1991. After this peak there has been a decreasing trend lasted only two years. Successively a new maximum has been observed in 1996 (1,181 cases) with a significant decrease, reaching 254 cases in 2011, which is the last year of observation. Dotted line of figure 1 illustrates the trend of deaths obtained from Emcdda database [15] which refers to police reported data. Although trends are highly comparable in the two data sources, Istat data, using the underlying approach, show underreporting compared with Emcdda. In last years the distance between the two sources is closing in absolute terms.

The analysis of standardized mortality rates has been performed for the period 1992-2011 for resident population. It shows the same trend than the absolute numbers, with the highest value in 1996 (20.1 deaths per 1,000,000) and the lowest in 2011 (3.9) (data not shown).

In figure 2, standardized mortality rates per 1,000,000 resident inhabitants by sex are presented. Very different behaviour is observed with men showing higher risk of mortality for drug-induced causes. At the beginning of the observation period the risk of men was about 10 times compared to women (35.6 per 1,000,000 versus 3.7). Although this gap is reducing, in 2011 the risk in men is about 4 times higher than in women (6.3 versus 1.5).

Geography of mortality for drug-induced causes has changed in the last 20 years of observation (Figure 3). From 1992 to 2001 mortality was higher in Northern and Central Italy compared with Southern regions and Islands. Since 2002 values of North and South became more similar due to a more rapid decrease observed in Northern regions. In 2011 the mortality rates in these macro-areas range from 2.3 for the South to 4 of the North-West. On the other hand the Centre shows the highest value (6.6). The trend of this area was similar to the North until 2001. After this year the Centre experimented a slower decrease.

For age comparison (Figure 4), age-specific mortality rates have been used, focusing on the population aged 15-64 years. Higher mortality rates are observed in age group 25-44 years in the all period of study (1992-2011). This age group shows the most relevant decrease in the mortality compared to all the others groups considered. As a consequence, in 2011 drug-induced mortality level at 25-44 years narrows to the value of other age groups. A similar continuous decrease in the whole

FIGURE 1

NUMBER OF DRUG-INDUCED DEATHS IN ITALY REGISTERED IN ISTAT CAUSES OF DEATH DATABASE (PRESENT POPULATION). YEARS 1980-2011*
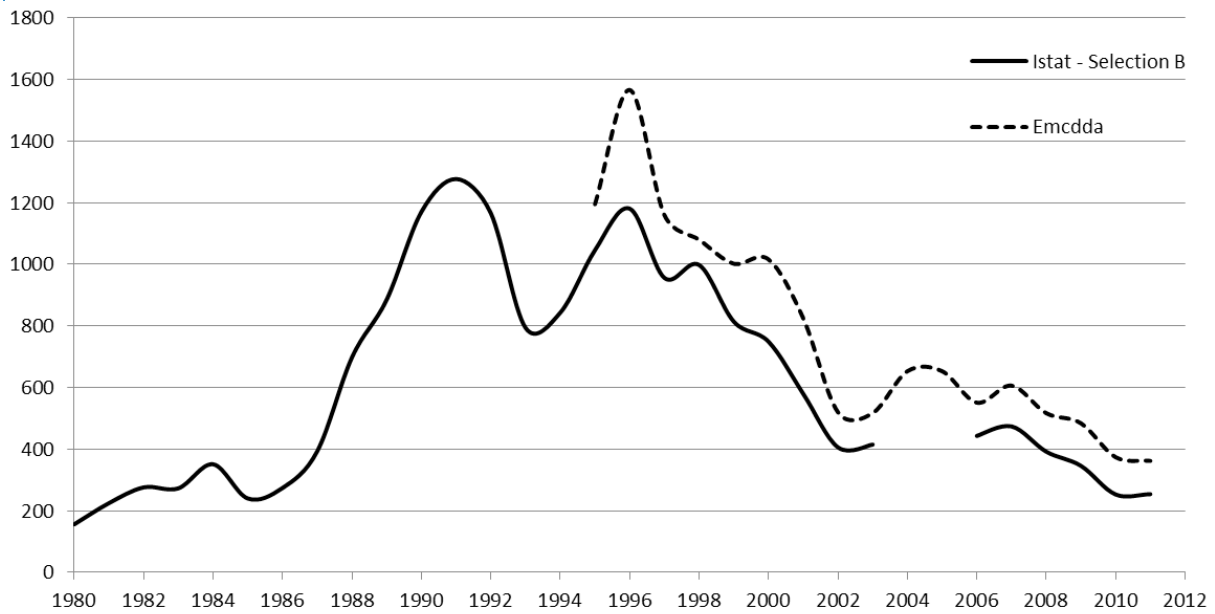
*Data for years 2004 and 2005 have been estimated as they are not available.
Sources: Istat, Causes of death Register [14]

FIGURE 2

TRENDS IN DRUG-INDUCED MORTALITY BY SEX AND YEAR OF DEATHS. POPULATION RESIDENT IN ITALY. YEARS 1992-2011*. STANDARDIZED MORTALITY RATES PER 1.000.000 INHABITANTS

*Data for years 2004 and 2005 have been estimated as they are not available.
Sources: Istat,Causes of death Register [14]

FIGURE 3

TRENDS IN DRUG-INDUCED MORTALITY BY GEOGRAPHICAL AREA AND YEAR OF DEATH. POPULATION RESIDENT IN ITALY. YEARS 1992-2011*. STANDARDIZED MORTALITY RATES PER 1.000.000 INHABITANTS
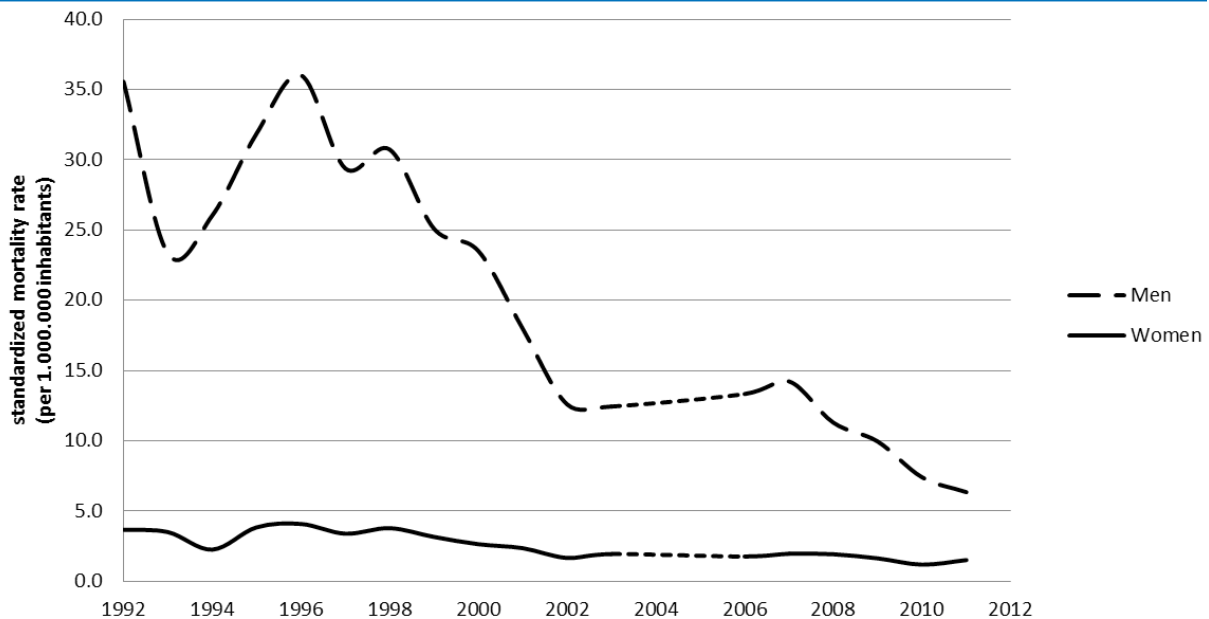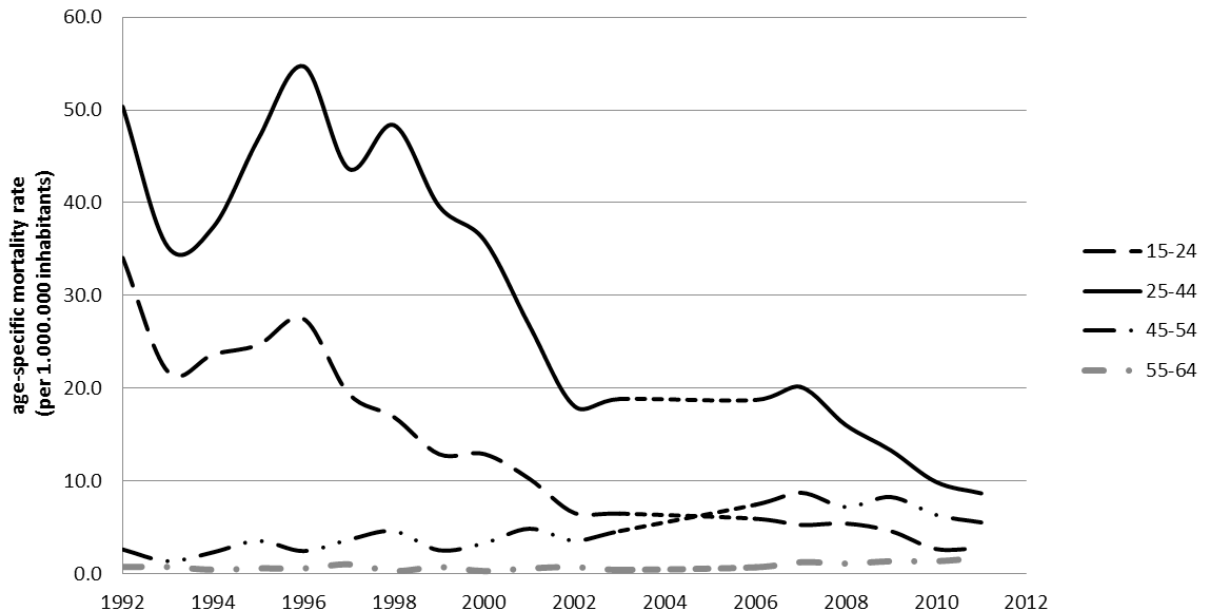

*Data for years 2004 and 2005 have been estimated as they are not available.
Sources: Istat,Causes of death Register [14]

FIGURE 4

TRENDS IN DRUG-INDUCED MORTALITY BY AGE AND YEAR OF DEATH. POPULATION RESIDENT IN ITALY. YEARS 1992-2011*. AGE-SPECIFIC MORTALITY RATES PER 1.000.000 INHABITANTS
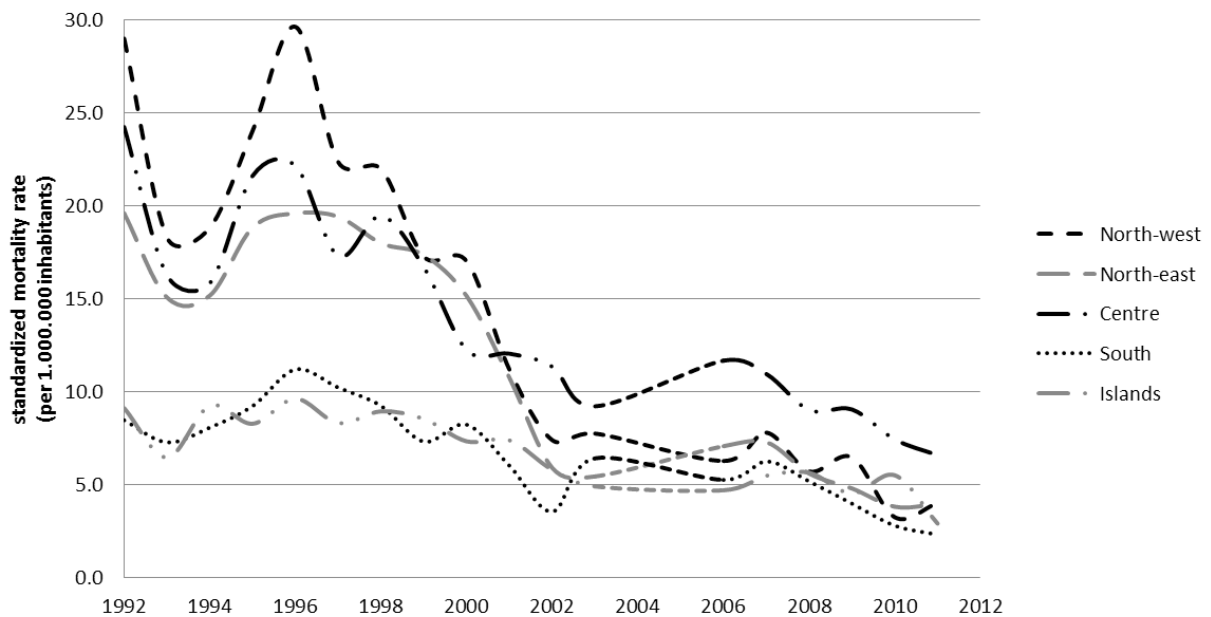

*Data for years 2004 and 2005 have been estimated as they are not available.
Sources: Istat,Causes of death Register [14]

period considered, is observed for the group of age 15-24years (the number of registered cases ranges from 295 in 1992 to 17 in 2011); the stability of rates between 2010 and 2011 suggests to monitor the mortality levels for these causes in the young population in next years for a confirmation of this trend.In contrast to the behavior of other age groups, in the period 1992-2011 people aged 45-54 years have experimented an increase in drug-induced mortality with a little decline only in the last two years. The observed changes in mortality levels resulted in a reduction of differences by age.

Multiple cause approach

Table 2 shows that in the period 2009-2011 the total number of certificates whit mention of drug use or poisoning is 1,293; this is 60% higher than the number based on the only underlying cause of death (813 cases). The rate multiple to underlying cause differs according to the age and shows higher values for older age

groups (1.3 for 15-44 years and about 2.4 for 45 years and more). As observed for the underlying causes of death also the mentions of the drug-related causes differ by gender and they are about 6 times higher in men (standardized death rate is 1.8 per 1,000,000 inhabitants) than in women (0.3 per 1,000,000 inhabitants) with not relevant differences in the rate multiple to underlying cause (1.6 and 1.5 respectively).

Comparing the rates for drug-related deaths in the two periods 2006-2008 (table 3) and 2009-2011, we observe a decrease in both underlying and multiple causes indicators with a greater reduction for the underlying standardized rate: -50% compared to -28% observed for the multiple standardized rate. This reduction is observed in both sexes although with greater rapidity in men.

For the underlying cause of death a small increase in the levels of mortality is observed only in the older age group (55-64 years), while the others ages show a decrease. In multiple cause indicators by age, instead, an increase is observed also for deaths in 45-54 year group.

TABLE 2

DRUG-RELATED DEATHS IN SELECTED AGE GROUPS AS UNDERLYING AND MULTIPLE CAUSE. ABSOLUTE NUMBER, CRUDE AND STANDARDIZED RATES (PER 1.000.000). RESIDENTS IN ITALY (A). YEARS 2009-2011

AGE	UNDERLYING CAUSE OF DEATH			MULTIPLE CAUSE OF DEATH			RATIO MULTIPLE/ UNDERLYING
	DEATHS	CRUDE RATE	STANDARDIZED RATE	DEATHS	CRUDE RATE	STANDARDIZED RATE	
MALES							
15-44	517	1.48		705	2.02		1.4
45-54	153	1.19		346	2.70		2.3
55-64	22	0.21		64	0.60		2.9
Tot (15-64)	692	1.19	1.17	1,115	1.91	1.84	1.6
FEMALES							
15-44	88	0.26		111	0.32		1.3
45-54	22	0.17		52	0.40		2.4
55-64	11	0.10		15	0.13		1.4
Tot (15-64)	121	0.21	0.20	178	0.30	0.29	1.5
TOTAL							
15-44	605	0.87		816	1.18		1.3
45-54	175	0.67		398	1.53		2.3
55-64	33	0.15		79	0.36		2.4
Tot (15-64)	813	0.69	0.69	1,293	1.10	1.07	1.6

(a) Deceased in Trentino-Alto Adige have been excluded as the multiple cause data are not available for this autonomous region
Sources: Istat, Cause of death register [14]

Using the multiple cause approach it is possible to analyze the pathological pattern of drug-users deaths. This group of the population is generally characterized by a complex morbid framework. In fact, for the total population, the average number of conditions reported on the death certificate is about 4, while for drug-users group this value is about 5 (2011 data).

In table 4, the results of analysis of conditions associated to drug-related causes are presented. The group of conditions more strongly associated with drug related causes is the mental and behavioral disorders (F01-F99) and in particular the RR for mental and behavioral disorders due to use of alcohol is very high with a value of 17.5 and the prevalence among drug users of 9.6%.

A relevant association is also found for the group of infectious and parasitic diseases (A00-B99; RR=3.4). Among these the higher relative risk is observed for viral hepatitis (B15-B19 and B94.2; RR=10.7). This conditions are also very frequent in this group of deaths (18.2%). The association with hepatitis is confirmed also

analyzing this condition when it is classified in the group of diseases of the digestive system (K00-K92). This is when the physician reports the "chronic hepatitis" without specifying the viral origin (K73). In fact, the relative risk for this condition is 19.5 although with a low prevalence among drug-users. Actually, besides the hepatitis, some other chronic liver diseases are significantly associated with drug-related causes. In fact, within the group of diseases of the digestive system the cirrhosis and fibrosis of liver (K74) have a relative risk of 3.3 with a very high prevalence among drug-users (14.3%) and alcoholic liver diseases (K70) shows a RR 2.7 and a prevalence 3.3%.

Within the above mentioned group of infectious diseases, a significant association is found also for AIDS (B20-B24) with a relative risk of 5.9 and a prevalence of 7.1% among drug-users. Besides AIDS, also the positivity to HIV (R75), classified among the group of symptoms and signs (R00-R99), shows a significantly high relative risk (9.1).

Finally, although the diseases of circulatory

TABLE 3

DRUG-RELATED DEATHS IN SELECTED AGE GROUPS AS UNDERLYING AND MULTIPLE CAUSE. ABSOLUTE NUMBER, CRUDE AND STANDARDIZED RATES (PER 1.000.000). RESIDENTS IN ITALY (A). YEARS 2006-2008

AGE	UNDERLYING CAUSE OF DEATH			MULTIPLE CAUSE OF DEATH			RATIO MULTIPLE/ UNDERLYING
	DEATHS	CRUDE RATE	STANDARDIZED RATE	DEATHS	CRUDE RATE	STANDARDIZED RATE	
MALES							
15-44	876	2.46		1,081	3.03		1.2
45-54	158	1.33		299	2.52		1.9
55-64	15	0.15		29	0.28		1.9
Tot (15-64)	1,049	1.82	1.79	1,409	2.44	2.38	1.3
FEMALES							
15-44	117	0.34		154	0.44		1.3
45-54	23	0.19		38	0.31		1.7
55-64	4	0.04		5	0.05		1.3
Tot (15-64)	144	0.25	0.25	197	0.34	0.34	1.4
TOTAL							
15-44	993	1.41		1,235	1.75		1.2
45-54	181	0.76		337	1.41		1.9
55-64	19	0.09		34	0.16		1.8
Tot (15-64)	1,193	1.03	1.03	1,606	1.39	1.36	1.3

(a) Deceased in Trentino-Alto Adige have been excluded as the multiple cause data are not available for this autonomous region
Sources: Istat, Cause of death register [14]

TABLE 4

MEASURES OF ASSOCIATION OF CONDITIONS WITH DRUG-RELATED CAUSES (DEFINED AS MCDDA SELECTION B) MENTIONED ON THE DEATH CERTIFICATES. AGE GROUP 15-64 YEARS. YEARS 2009-2011. (A)

ICD10	CONDITION	PREVALENCE IN DRUG USERS DEATHS	PREVALENCE IN NON-DRUG USERS DEATHS	AGE-STANDARDIZED RR	INF95	SUP95	CERTIFICATES MENTIONING THE CONDITION AMONG DRUG USERS DEATHS	CERTIFICATES MENTIONING THE CONDITION AMONG NON-DRUG USERS DEATHS
A00-B99	Infectious and parasitic diseases	23.8	9.4	3.4	3.2	3.7	308	20,104
A41	Other septicemia	6.0	5.7	1.3	1.1	1.6	78	12,205
B20-B24	AIDS	7.1	1.2	5.9	4.8	7.2	92	2,626
B20	Human immunodeficiency virus [HIV] disease resulting in infectious and parasitic diseases	2.6	0.4	5.2	3.5	7.7	33	832
B22	Human immunodeficiency virus [HIV] disease resulting in other specified diseases	1.6	0.3	6.3	4.4	9.2	21	725
B24	Unspecified human immunodeficiency virus [HIV] disease	6.5	1.2	5.6	4.5	6.9	84	2,499
B15-B19. B94.2	Viral hepatitis	18.2	2.5	10.7	9.7	11.8	235	5,271
B16	Acute hepatitis B	1.2	0.3	3.6	2.1	6.4	15	558
B18	Chronic viral hepatitis	17.6	2.2	11.3	10.2	12.5	227	4,647
F01-F99	Mental and behavioural disorders (excluded those included in EMCDDA)	14.2	4.0	6.8	6.2	7.5	184	8,497
F10	Mental and behavioural disorders due to use of alcohol	9.6	0.9	17.5	15.4	20.0	124	1,988
F17	Mental and behavioural disorders due to use of tobacco	1.2	0.5	6.2	4.5	8.5	15	1,018
F32	Depressive episode	1.7	0.9	3.9	2.9	5.3	22	1,827
I00-I99	Diseases of the circulatory system	40.4	48.0	1.1	1.0	1.2	522	102,872
I10	Essential (primary) hypertension	2.1	6.9	1.2	1.0	1.5	27	14,782
I33	Acute and subacute endocarditis	0.9	0.1	7.0	3.9	12.6	11	270
I38	Endocarditis. valve unspecified	1.2	0.3	2.0	1.0	3.9	15	709
I51	Complications and ill-defined descriptions of heart disease	7.2	6.3	1.2	1.0	1.5	93	13,452
I85	Oesophageal varices	2.1	0.8	2.3	1.5	3.5	27	1,659
I99	Other and unspecified disorders of circulatory system	1.7	0.9	2.8	2.0	4.0	22	1,925
I60-I69	Cerebrovascular diseases	3.4	6.8	1.6	1.3	1.8	44	14,580
I61	Intracerebral haemorrhage	1.8	2.7	2.3	1.8	2.8	23	5,736

TABLE 4 (CONTINUED)

MEASURES OF ASSOCIATION OF CONDITIONS WITH DRUG-RELATED CAUSES (DEFINED AS MCDDA SELECTION B) MENTIONED ON THE DEATH CERTIFICATES. AGE GROUP 15-64 YEARS. YEARS 2009-2011. (A)

ICD10	CONDITION	PREVALENCE IN DRUG USERS DEATHS	PREVALENCE IN NON-DRUG USERS DEATHS	AGE-STANDARDIZED RR	INF95	SUP95	CERTIFICATES MENTIONING THE CONDITION AMONG DRUG USERS DEATHS	CERTIFICATES MENTIONING THE CONDITION AMONG NON-DRUG USERS DEATHS
J00-J99	Diseases of the respiratory system	32.6	24.6	1.2	1.1	1.3	422	52,759
J80	Adult respiratory distress syndrome	1.0	0.4	2.2	1.3	3.9	13	896
J81	Pulmonary oedema	16.4	4.4	1.8	1.5	2.2	212	9,544
J12-J18	Pneumonia	4.8	4.1	1.4	1.1	1.8	62	8,692
J40-J47	Chronic lower respiratory diseases	2.5	3.5	2.7	2.3	3.2	32	7,464
J44	Other chronic obstructive pulmonary disease	1.7	2.4	3.4	2.9	4.1	22	5,179
K00-K92	Diseases of the digestive system	22.1	16.1	1.8	1.6	1.9	286	34,557
K76	Other diseases of liver	5.1	2.8	1.3	1.0	1.8	66	5,957
K70. K73-K74	Cirrhosis. fibrosis and chronic hepatitis	16.2	6.2	3.6	3.2	4.0	209	13,213
K70	Alcoholic liver disease	3.3	1.3	2.7	2.0	3.6	43	2,765
K73	Chronic hepatitis. not elsewhere classified	1.1	0.2	19.5	14.3	26.7	14	362
K74	Fibrosis and cirrhosis of liver	14.3	5.2	3.3	2.9	3.7	185	11,108
L00-L99	Diseases of the skin ans subcutaneous tissue	1.2	0.7	3.8	2.7	5.2	16	1,595
N17	Acute renal failure	1.9	2.1	1.4	1.0	1.9	25	4,573
R00-R99	Symptoms signs and ill-defined causes	38.6	33.6	1.1	1.1	1.2	499	71,997
R09	Other symptoms and signs involving the circulatory and respiratory systems	14.2	5.1	2.9	2.6	3.4	184	10,900
R18	Ascites	1.7	1.5	2.6	1.9	3.3	22	3,323
R40	Somnolence. stupor and coma	4.6	4.2	1.5	1.2	1.8	59	9,054
R68	Other general symptoms and signs	6.5	2.8	1.4	1.0	1.8	84	6,009
R75	Laboratory evidence of human immunodeficiency virus [HIV]	1.3	0.1	9.1	5.4	15.2	17	271
V00-Y99	External causes of death (excluded those included in EMCDDA)	52.6	14.0	2.4	2.2	2.6	680	30,113
Total deaths							1,293	214,501

Conditions reported only if with a significantly positive RR and with robust values defined as a prevalence in drug user deaths group >=1%.

system (I00-I99), taken as a whole, show a very low positive RR, within this group the acute and sub-acute endocarditis (I33) is present 7 times more frequently in the drug-users compared to the non–drug users.

DISCUSSION

The quality and the informative content of the Italian mortality register has been improving during the last years. The increasing convergence,in absolute terms, between the deaths reported by Emcdda and those described in depth by the Istat mortality register is an helpful result.

The victims of drug poisoning or abuse sharply decreased during the last decades, reaching 254 cases in 2011.Observing the trends of the last twenty years, those who died for drug-induced causes continue to be predominantly male.Moreover, while the largest proportionof deaths continued to be among those aged25-44 year, the percentage of individuals aged 45-54 increased, with a little decline only in the last two years (2010, 2011).

The analysis based on multiple cause approach shows, for the first time, a more detailed picture of the drug related deaths. In the years 2009-2011, the total number of certificates with mention of drug use was 60% higher than the number based only on the underlying cause of death. Comparing with the period 2006-2008, the increase of death rates in 45-54 year group is also confirmed by multiple death rates. This finding could reflect the fact that the age structure of the population of drug users might be changing.It seems to suggest the hypothesis that the older drug users are those who survived the drug epidemics of the80s and the 90s. After this period the survival of this population increased due to treatment availability, harm reduction interventions and anti-retroviral therapy. Therefore the impact of this ageing cohort of individuals using drugs could be an issue in the future to be assessed interms ofgrowing service provision, costs and resource planning.

The analysis of conditions associated to drug-related causes presented the pathological pattern of drug-users deaths; the groups of conditions more strongly associated with drug related causes are the mental and behavioral disorders, especially those linked to alcohol consumption; higher relative risks are also observed for viral hepatitis, cirrhosis and fibrosis of liver, AIDS and endocarditis.

Developing data linkages to collect further data on hospital admissionsis an area for potential developments. This enhancement may be used to explore co-morbidities in more detail.

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