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ORIGINAL ARTICLE

Mortality and cause of death among psychiatric patients: a 20-year case-register study in an area with a community-based system of care

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Background. Most mortality studies of psychiatric patients published to date have been conducted in hospital-based systems of care. This paper describes a study of the causes of death and associated risk factors among psychiatric patients who were followed up over a 20-year period in an area where psychiatric care is entirely provided by community-based psychiatric services.

Method. All subjects in contact with the South Verona Community-based Mental Health Service (CMHS) over a 20-year period with an ICD-10 psychiatric diagnosis were included. Of these 6956 patients, 938 died during the study period. Standardized mortality ratios (SMRs) and Poisson multiple regressions were used to assess the excess of mortality in the sample compared with the general population.

Results. The overall SMR of the psychiatric patients was 1.88. Mortality was significantly high among out-patients [SMR 1.71, 95% confidence interval (CI) 1.6–1.8], and higher still following the first admission (SMR 2.61, 95% CI 2.4–2.9). The SMR for infectious diseases was higher among younger patients and extremely high in patients with diagnoses of drug addiction (216.40, 95% CI 142.5–328.6) and personality disorders (20.87, 95% CI 5.2–83.4).

Conclusions. This study found that psychiatric patients in contact with a CMHS have an almost twofold higher mortality rate than the general population. These findings demonstrate that, since the closure of long-stay psychiatric hospitals, the physical health care of people with mental health problems is often neglected and clearly requires greater attention by health-care policymakers, services and professionals.

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Key words: Community-based system of care, mental health, mortality.

Introduction

Research on the causes of death of psychiatric patients is a worthwhile endeavour as it has long been recognized that death rates among patients with chronic mental illnesses are higher than among the general population (Farr, 1841; Malzberg, 1934; Babigian & Odoroff, 1969; Harris & Barraclough, 1998; Sims, 2001; Goff *et al*. 2005).

In a meta-analysis of 152 reports about the mortality of patients with mental disorders, Harris & Barraclough (1998) found that, although people with mental disorders have an increased risk of premature death, the highest risks from both natural and unnatural causes are from substance abuse and eating disorders. They also found that the risk of death from unnatural causes is especially high among people with schizophrenia and major depression whereas the risk of death from natural causes is markedly increased for organic mental disorders, mental retardation and epilepsy.

Regarding organic mental disorders, some studies have identified a high association between mortality and antipsychotic drugs in patients with dementia, although it is not clear whether this is due to a direct medication effect or to the pathophysiology underlying neuropsychiatric symptoms that prompt antipsychotic use (Schneider *et al*. 2005; Wang *et al*. 2005; Kales *et al*. 2007).

Most previous mortality studies have been conducted in areas where hospital-based systems of mental care are the norm. For example, a study by Craig & Lin (1981) suggested that, in the USA, deinstitutionalization, through a variety of mechanisms, may have had a beneficial effect on the mortality of elderly patients who remain hospitalized. Other studies have shown a decrease in the excess mortality of psychiatric patients

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after a reduction in the provision of long-stay psychiatric hospital care (Tsuang & Simpson, 1985; Allebeck & Wistedt, 1986; Casadebaig & Quemada, 1991). Deinstitutionalization, however, also seems to be associated with increased rates in deaths for causes considered 'behaviourally avoidable' (i.e. preventable with adequate health promotion policies), such as cardiovascular and unnatural causes for both genders (Hansen *et al*. 2001) and for suicide (Mortensen & Juel, 1993; Martiello *et al*. 2006).

Vreeland (2007) stated that the problem of increased morbidity and premature death in people with serious mental illness needed to be addressed with a transformation of the current mental health system and the integration of physical and mental health care, towards a system that uses a coordinated, multidisciplinary holistic approach. This should overcome some of the multiple barriers that make it difficult for individuals with serious mental illness to access quality health care.

Research and intervention studies for improving medical care for people with serious mental illness have spanned a continuum of interprofessional involvement, ranging from staff and patient training to on-site consultation by medical staff, multidisciplinary collaborative care approaches, and facilitated linkages between community and mental health and medical providers. Researchers suggest that it is important to develop and coordinate medical care in a community medical setting (Leucht & Fountoulakis, 2006; Druss & Newcomer, 2007). In addition, great attention should be paid to those patients who develop psychiatric symptoms as comorbidity of cardiovascular accident and stroke (Politi *et al*. 2006). This would contribute to diminish the mortality of people with a secondary psychiatric diagnosis.

However, there is still a need to explore mortality in different service settings, such as community services, because mortality is a useful indicator of the quality of a health-care system over time.

The aim of this paper was to study mortality, causes of death and associated risk factors among psychiatric patients followed up over a 20-year period in an area where psychiatric care is entirely provided by community-based psychiatric services and has been monitored by a case register since 1978 (Tansella *et al*. 2006). This research allowed us to repeat the mortality analyses published in a previous study by Amaddeo *et al*. (1995) conducted in South Verona for a time period of 10 years, on a sample followed up for a twofold longer period, also adding a detailed analysis of causes of death that was not possible to perform in our previous study because of the small sample size.

Method

Study setting

Data were drawn from the area of South Verona that includes part of Verona (a city of about 260 000 inhabitants in the Veneto region in northeast Italy) and two neighbouring small towns (Castel d'Azzano and Buttapietra). South Verona is a mainly urban area with a predominance of service and manufacturing industries. The total population is about 75 000 (population density 1073/km^2). The main agency providing psychiatric care for the adult population of this area is the South Verona Community-based Mental Health Service (CMHS), run by the Section of Psychiatry and Clinical Psychology of the University of Verona. This service provides a wide range of well-integrated hospital and community services, including a 15-bed inpatient acute ward at the University General Hospital, a Community Mental Health Centre (CMHC) that provides day care and rehabilitation, an out-patient department, scheduled domiciliary visits, an accident and emergency department, a 24-hour staffed hostel and sheltered apartments.

According to the Italian psychiatric reform, inpatient care can only be provided in general hospital psychiatric wards or private psychiatric clinics. The Italian National Health Service (NHS) provides medical and psychiatric care, including admissions to some private clinics, free of charge. Further information on the research setting can be found elsewhere (Tansella *et al*. 1998).

The Psychiatric Case Register (PCR)

The South Verona Psychiatric Case Register (PCR) was started on 31 December 1978 and has been operating ever since (Tansella *et al*. 1998). The PCR collects the following information: at first contact with a psychiatric service, sociodemographic information, past psychiatric and medical history, and clinical data for each resident of South Verona aged $\geqslant$14 years. Diagnoses are made by a clinician according to ICD-10 and then coded into 12 standard diagnostic groups. The diagnoses of all new cases are routinely reviewed by the case-register administrator. All psychiatric services of South Verona and the larger province of Verona provide data to the PCR for South Verona residents. All contacts with the psychiatric staff (nurses, psychiatrists, psychologists, social workers, etc.) are recorded.

Study design and statistical analysis

The study design was approved by the Verona local research ethics committee of the University Hospital of Verona, Italy (Appr. Prot. No. 1098).

All subjects who had at least one contact with the South Verona CMHS during a 20-year period (from 1 January 1982 to 31 December 2001) and who at the first contact or later received an ICD-10 (ICD-9 until 1992, then converted to ICD-10 using World Health Organization conversion tables) psychiatric diagnosis were included in this study. Data were censored either on death date or date of emigration from the study area (19% of patients) or on 31 December 2001, whichever came first. Person-years were calculated for each patient. Four age groups were considered: 14–24, 25–44, 45–64, and $\geqslant$65 years. For the purposes of the present study, ICD diagnoses were collapsed into seven diagnostic groups: schizophrenia and related disorders (ICD-10 codes F20–F29, F84), affective disorders (ICD-10 codes F30–F33, F34.1, F34.8, F34.9, F38.00, F38.10, F38.8, F39, F41.2, F43.20–F43.22), neurotic, stress-related and somatoform disorders (F40, F41.0, F41.1, F41.3, F41.8, F41.9, F42, F44, F45, F48, F54), disorders of personality and behaviour of the adult (F34.0, F52, F60–F69), drug addiction (F11–F19.1, F19.2, F19.3, F55), alcohol addiction (F10.1–F10.3), and other diagnoses (including organic psychoses, eating disorders, mental retardation, dementia).

According to type of care received, person-years were classified as in-patient or out-patient. In-patient person-years refer to those that followed first admission to hospital. Out-patient person-years refer to the period preceding hospital admission and person-years of patients who had never been admitted to hospital.

Five time-intervals from registration in the PCR were considered: (1) first year after registration, (2) 1–2 years after registration, (3) 2–5 years after registration, (4) 5–10 years after registration and (5) >10 years after registration.

Mortality and cause of death were ascertained using different procedures and sources. Information about whether the patients were alive was provided by linkage to the Central Person Registry of the Municipalities of Verona, Castel d'Azzano and Buttapietra. For those not alive, causes of death were established through linkage to the database of the Local Health District of Verona. Consultation of the Registries of Deaths of the Municipalities of Verona, Castel d'Azzano and Buttapietra and of the Service of Forensic Medicine of the University of Verona provided missing information. The cause of death was established in 90% of cases. These agencies were also able to provide vital status and causes of death for people still registered in area of the municipality who had died outside the study area.

The causes of death were categorized as follows: (1) infectious diseases (including infectious complications of AIDS), (2) malignant neoplasms, (3) endocrine diseases, (4) blood diseases, (5) organic mental disorders, (6) nervous system diseases, (7) circulatory system diseases (including cardiovascular and cerebrovascular disorders), (8) respiratory system diseases, (9) digestive system diseases, (10) genital-urinary system diseases, (11) osteoarticular system diseases, (12) congenital disease, (13) diseases ill-defined and (14) traumatic episodes. All causes of death were defined according to ICD-9-CM classification (National Center for Health Statistics, 2006).

Standardized mortality ratios (SMRs) were used to assess the risk of premature mortality in the previously described groups. The SMR compares the observed number of deaths with the expected number for each cause. Person-years were calculated for each patient and were divided into five 4-year periods. The expected number of deaths was obtained by applying to the corresponding sex and age structure (person-years), for each of the five 4-year periods considered, the age- gender-, cause- and period-specific mortality rates of the general population in the Veneto region. These specific mortality rates were obtained from the Italian National Institute of Health.

Poisson regression analyses have been used previously to study the association between patient characteristics and mortality (Consul, 1989). In the current study, a multiple Poisson regression analysis was performed to analyse the combined effect of independent variables (gender, age, diagnoses and interval from registration) on mortality. To simplify the interpretation of the Poisson regression models, we present the coefficients in terms of mortality rate ratios (RRs) and their 95% confidence intervals (CIs). The estimated RR is equal to the log of the quotient between the expected number of events for each value of the predictor variable and the value used as referent, with the other variables held constant in the model. For example, a mortality RR <1 means that the expected number of deaths is lower for this particular value of the variables compared with the value used as referent (protective effect); and patients with a mortality RR >1 have an increased mortality rate.

Results

In this study, 6956 patients (3135 males and 3821 females) for a total of 59 139 person-years (26 922 males and 32 217 females) were included. About 8% of the patients had a diagnosis of schizophrenia, 29% affective disorders, 14% drug or alcohol addiction, 22% neurotic and somatoform disorders, 6% personality disorders and 21% other diagnoses. Of the whole sample, 938 (527 males and 411 females) died during the study period.

Table 1. *Mortality in psychiatric patients by patient characteristics and time interval from registration*

	PY	O	E	SMR	95% CI	*p*
All patients (age group, years)	59 139	938	499.33	1.88	1.8–2.0	**
14–24	7334	27	5.25	5.15	3.5–7.5	**
25–44	23 755	154	24.51	6.28	5.4–7.4	**
45–64	18 775	236	107.49	2.19	1.9–2.5	**
⩾65	9275	521	362.08	1.44	1.3–1.6	**
Males (age group, years)	26 922	527	249.66	2.11	1.9–2.3	**
14–24	4121	18	4.22	4.26	2.7–6.8	**
25–44	12 356	118	17.01	6.93	5.8–8.3	**
45–64	7509	149	65.95	2.26	1.9–2.6	**
⩾65	2936	242	162.48	1.49	1.3–1.7	**
Females (age group, years)	32 217	411	249.67	1.65	1.5–1.8	**
14–24	3213	9	1.02	8.81	4.6–16.9	**
25–44	11 399	36	7.50	4.80	3.5–6.7	**
45–64	11 266	87	41.55	2.09	1.7–2.6	**
⩾65	6339	279	199.61	1.40	1.2–1.6	**
In-patients	15 007	368	140.97	2.61	2.4–2.9	**
Out-patients	44 153	613	358.38	1.71	1.6–1.8	**
Diagnosis						
Schizophrenia	4613	69	32.13	2.15	1.7–2.7	**
Affective disorders	17 180	293	189.14	1.55	1.4–1.7	**
Neurosis and somatoform disorders	12 956	114	96.83	1.18	0.9–1.4	
Personality disorders	3627	41	14.95	2.74	2.0–3.7	**
Drug addiction	5266	77	12.45	6.19	4.9–7.7	**
Alcoholism	2986	93	29.47	3.16	2.6–3.9	**
Other diagnoses	12 511	251	124.37	2.02	1.8–2.3	**
Interval from registration (years)						
⩽1	6710	193	56.09	3.44	3.0–4.0	**
1–2	6086	126	48.21	2.61	2.2–3.1	**
2–5	15 338	214	118.40	1.81	1.6–2.1	**
5–10	17 144	209	137.33	1.52	1.3–1.7	**
>10	13 861	196	139.31	1.41	1.2–1.6	**

PY, Person-years; O, observed death; E, expected death; SMR, standardized mortality ratio; CI, confidence interval.
** $p < 0.01$.

The total SMR of our psychiatric population was 1.88 (95% CI 1.8–2.0), representing an increase of 88% in mortality compared with the general population. The SMR was slightly higher among males than females (2.11, 95% CI 1.9–2.3, *v.* 1.65, 95% CI 1.5–1.8). The data presented in Table 1 reveal that the younger the patient, the higher the SMR. This inverse correlation seems to be more evident among females than males; female SMRs decrease from 8.81 (95% CI 4.6–16.9) in younger patients to 1.40 (95% CI 1.2–1.6) in the older patients, whereas in males SMRs vary from only 4.26 (95% CI 2.7–6.8) to 1.49 (95% CI 1.3–1.7) and the highest excess in mortality rate is attributable to the young-adult group (age 25–44 years, SMR 6.93, 95% CI 5.8–8.3).

Mortality was significantly high for out-patients (SMR 1.70, 95% CI 1.6–1.8) and, as expected, it was higher after the first admission (SMR 2.61, 95% CI 2.4–2.9).

Time interval since registration had a negative correlation with the SMR, which was higher during the first year after registration (SMR 3.44, 95% CI 3.0–4.0), remained fairly high between the first and the second year after registration (SMR 2.61, 95% CI 2.2–3.1), and then decreased to 1.80 after 2 years, 1.52 after 5 years, and 1.40 after 10 years.

All psychiatric diagnoses showed a significant excess mortality ($p < 0.01$). The diagnostic group with the highest SMR for all causes (Table 1) was drug addiction (SMR 6.19, 95% CI 4.9–7.7), followed by alcoholism (SMR 3.16, 95% CI 2.6–3.9) and personality disorders (SMR 2.74, 95% CI 2.0–3.7).

With regard to the single causes of death, our data reveal 27 observed death for infectious diseases, out of

Table 2. *Mortality by causes of death and gender*

	Male (PY 26922)				Female (PY 32217)				Total (PY 59139)			
	O	E	SMR	95% CI	O	E	SMR	95% CI	O	E	SMR	95% CI
Infectious disease	22	1.29	17.09**	11.2–26.0	5	1.36	3.66**	1.5–8.8	27	2.65	10.18**	6.9–14.8
Neoplasm	113	88.54	1.28**	1.1–1.5	92	75.99	1.21	0.9–1.5	205	164.53	1.25**	1.1–1.4
Endocrine disease	5	4.22	1.18	0.5–2.8	10	8.02	1.25	0.7–2.3	15	12.24	1.22	0.7–2.0
Blood disease	2	0.56	3.56	0.9–14.2	2	0.64	3.11	0.8–12.4	4	1.20	3.32*	1.2–8.8
Organic mental disorder	8	2.48	3.22**	1.6–6.4	7	4.20	1.67	0.8–3.5	15	6.68	2.24**	1.3–3.7
Nervous system	8	4.18	1.91	0.9–3.8	12	5.87	2.04*	1.2–3.6	20	10.05	1.99**	1.3–3.1
Circulatory system	113	88.06	1.28**	1.1–1.5	114	106.84	1.07	0.9–1.3	227	194.90	1.65*	1.0–1.3
Respiratory system	39	15.73	2.48**	1.8–3.4	24	12.92	1.86**	1.2–2.8	63	28.65	2.20**	1.7–2.8
Digestive system	35	14.75	2.37**	1.7–3.3	23	13.73	1.68*	1.1–2.5	58	28.48	2.04**	1.6–2.6
Genital-urinary system	9	2.84	3.16**	1.6–6.1	6	3.01	1.99	0.9–4.4	15	5.85	2.56**	1.5–4.2
Osteoarticular system	4	0.55	7.30**	2.7–19.5	2	1.37	1.46	0.4–5.8	6	1.91	3.13**	1.4–7.0
Congenital disease	3	0.47	6.33**	2.0–19.6	0	0.46	0.00	–	3	0.94	3.20*	1.0–9.9
Ill defined	37	2.50	14.79**	10.7–20.4	34	3.24	10.48**	7.5–14.7	71	5.75	12.36**	9.8–15.6
Traumatic episodes	90	20.42	4.41**	3.6–5.4	48	10.61	4.52**	3.4–6.0	138	31.03	4.45**	3.8–5.2

PY, Person-years; O, observed death; E, expected death; SMR, standardized mortality ratio; CI, confidence interval.
* $p<0.05$, ** $p<0.01$.

2.65 expected, with an SMR of 10.18 (95% CI 6.9–14.8, $p<0.01$), the highest after the 'ill-defined' cause of death group (Table 2). Males seem to be at a higher risk of infectious diseases with an SMR of 17 (95% CI 11.2–26) compared with 3.66 (95% CI 1.5–8.8) among females.

SMRs for infectious diseases are higher among younger patients, as death from such causes are very rare at a young age in the general population (low expected deaths). Mortality for endocrine disease was significantly high only in the 25–44 years age group (Table 3).

Mortality for all causes became similar to that of the general population in patients older than 65 years except for causes related to respiratory, osteoarticular, congenital diseases, traumatic and ill-defined causes.

Table 4 shows the effect of psychiatric diagnoses on each cause of death. SMRs for infectious diseases are extremely high in patients with drug addiction (SMR 216.40, 95% CI 142.5–328.6) and personality disorders (SMR 20.87, 95% CI 5.2–83.4); those for blood diseases and the genital-urinary system are significant only in patients with schizophrenia; and for ill-defined causes of death and for traumatic episodes, SMRs are significant in all psychiatric diagnoses. The risk of dying from neoplasm is higher when compared with the general population, but only for patients diagnosed with alcoholism.

Poisson regression results

Gender, age, diagnosis and interval from registration were all significantly associated with mortality in a univariate Poisson regression analysis. For all causes of death, the likelihood ratio test result was 42.76 ($p<0.001$) for gender, 925.67 ($p<0.001$) for age, 103.27 ($p<0.001$) for diagnosis, and 87.01 ($p<0.001$) for interval from registration. Similar results were obtained when analysing separately in-patients, out-patients and mortality for neoplasms, cardiovascular diseases, infectious diseases and traumatic episodes, but not for age, which was shown to be not significantly associated with mortality for traumatic episodes.

The combined effect of these variables on mortality, for all causes of death and separately for neoplasms, cardiovascular diseases, infectious diseases and traumatic episodes, was obtained from a multiple Poisson regression analysis (Table 5). Gender and age were always significantly associated with mortality, females had a lower RR in all groups, an RR that significantly increased for every 5 years of age, except for infectious diseases. Drug addiction was significantly associated with mortality for traumatic episodes (RR 0.48, 95% CI 0.26–0.89) and not associated with all causes, neoplasms infectious and cardiovascular diseases; alcoholism was significantly associated with mortality for all causes (RR 1.44, 95% CI 1.05–1.97) and for neoplasms (RR 2.51, 95% CI 1.27–4.97). The interval from registration showed a significant association with mortality in the four groups, except infectious diseases.

Discussion

Compared to the previous mortality study by Amaddeo *et al*. (1995), the current study followed up

Table 3. *Mortality by causes of death and age group*

	14–24 years (PY 7334)				25–44 years (PY 23755)				45–64 years (PY 18775)				>65 years (PY 9275)			
	O	E	SMR	95% CI	O	E	SMR	95% CI	O	E	SMR	95% CI	O	E	SMR	95% CI
Infectious disease	1	0.05	18.95**	2.7–134.5	23	0.32	72.26**	48.0–108.7	1	0.59	1.69	0.2–12.0	2	1.69	1.18	0.3–4.7
Neoplasm	1	0.44	0.28	0.3–16.2	13	6.51	2.00*	1.1–3.4	73	54.52	1.34*	1.1–1.7	118	103.06	1.14	0.9–1.4
Endocrine disease	0	0.04	0.00		2	0.24	8.38**	2.1–33.5	3	1.74	1.72	0.5–5.3	10	10.23	0.98	0.5–1.8
Blood disease	0	0.07	0.00		2	0.15	13.15**	3.3–52.6	1	0.17	6.02	0.8–42.7	1	0.81	1.23	0.2–8.7
Organic mental disorder	0	0.02	0.00		2	0.30	6.61**	1.6–26.4	3	0.60	4.96**	1.6–15.4	10	5.76	1.74	0.9–3.2
Nervous system	0	0.14	0.00		1	0.49	2.06	0.3–14.6	6	1.81	3.32**	1.5–7.4	13	7.63	1.70	0.9–2.9
Circulatory system	0	0.31	0.00		11	3.27	3.36**	1.9–6.1	43	26.27	1.64**	1.2–2.2	173	165.05	1.05	0.9–1.2
Respiratory system	1	0.11	8.70*	1.2–61.8	2	0.48	4.14*	1.0–16.5	11	2.66	4.14**	2.3–7.5	49	25.39	1.93**	1.4–2.5
Digestive system	1	0.08	11.94*	1.7–84.7	12	1.84	6.53**	3.7–11.5	20	8.69	2.30**	1.5–3.6	25	17.87	1.40	0.9–2.1
Genital-urinary system	0	0.04	0.00		2	0.23	8.58**	2.1–34.3	4	0.81	4.91**	1.8–13.1	9	4.77	1.89	0.9–3.6
Osteoarticular system	0	0.02	0.00		0	0.09	0.00		1	0.40	2.50	0.3–17.7	5	1.40	3.56**	1.5–8.5
Congenital disease	1	0.09	11.30*	1.6–80.2	0	0.23	0.00		0	0.33	0.00		2	0.29	6.93**	1.7–28.0
Ill defined	2	0.12	16.75**	4.2–67.0	9	0.38	23.47**	12.2–45.1	26	0.78	33.31**	22.7–48.9	34	4.46	7.62**	5.4–10.7
Traumatic episodes	18	3.77	4.78**	3.0–7.6	60	8.07	7.44**	5.8–9.6	28	7.86	3.56**	2.5–5.1	32	11.33	2.82**	1.9–4.0

PY, Person-years; O, observed death; E, expected death; SMR, standardized mortality ratio; CI, confidence interval.
* $p<0.05$, ** $p<0.01$.

Table 4. *Mortality by causes of death and psychiatric diagnosis*

	Schizophrenia (PY 4613)		Affective disorders (PY 17180)		Neurosis (PY 12956)		Personality disorders (PY 3627)		Drug addiction (PY 5266)		Alcoholism (PY 2986)		Other diagnosis (PY 12511)	
	SMR	95% CI	SMR	95% CI	SMR	95% CI	SMR	95% CI	SMR	95% CI	SMR	95% CI	SMR	95% CI
Infectious disease	5.53	0.8–39.2	1.01	0.1–7.1	0.00		20.87**	5.2–83.4	216.40**	142.5–328.6	0.00		1.64	5.2–83.4
Neoplasm	1.07	0.6–1.9	1.22	0.9–1.5	0.94	0.6–1.3	1.26	0.6–2.6	0.49	0.1–3.5	2.28**	1.6–3.3	1.28	0.9–1.7
Endocrine disease	0.00		1.23	0.5–2.7	0.40	0.1–2.8	0.00		0.00		0.00		2.57**	1.3–5.1
Blood disease	12.85*	1.8–91.2	0.00		0.00		0.00		0.00		0.00		9.3**	3.0–28.9
Organic mental disorder	0.00		0.78	0.2–3.1	0.00		0.00		0.00		13.32**	4.3–41.3	5.26**	2.8–9.8
Nervous system	1.52	0.2–10.8	2.28*	1.2–4.4	0.51	0.1–3.6	3.52	0.5–25.0	0.00		4.11*	1.0–16.4	2.4*	1.1–5.3
Circulatory system	1.27	0.8–2.1	1.01	0.8–1.3	0.95	0.7–1.3	1.54	0.7–3.2	0.49	0.1–1.9	2.07**	1.3–3.2	1.36**	1.1–1.7
Respiratory system	0.64	0.1–4.5	1.62*	1.0–2.6	1.50	0.7–3.0	6.05**	2.3–16.1	1.11	0.1–7.9	3.83**	1.6–9.2	3.21**	2.2–4.7
Digestive system	3.04**	1.4–6.8	1.29	0.8–2.2	1.41	0.7–2.8	3.17*	1.0–9.8	9.57**	3.9–23.0	5.68**	3.2–10.0	1.6	0.8–2.9
Genital-urinary system	8.65**	2.8–26.8	2.76*	1.2–6.1	0.00		0.00		5.22	0.7–37.0	0.00		3.14*	1.3–7.5
Osteoarticular system	0.00		5.21**	1.9–13.9	2.52	0.3–17.9	0.00		0.00		0.00		2.16	0.3–15.3
Congenital disease	0.00		3.33	0.5–23.6	0.00		0.00		0.00		0.00		10.1**	2.5–40.4
Ill defined	24.21**	12.1–48.4	11.48**	7.5–17.6	6.73**	3.4–13.5	14.44**	3.6–57.7	18.76**	7.8–45.1	41.48**	21.6–79.7	10.14**	6.4–16.1
Traumatic episodes	7.91**	4.9–12.5	4.03**	2.9–5.6	1.5	0.8–2.9	6.40**	3.5–11.5	11.03**	7.8–15.5	3.62**	1.7–7.6	3.32**	2.2–4.9

PY, Person-years; SMR, standardized mortality ratio; CI, confidence interval.
* $p<0.05$, ** $p<0.01$.

Table 5. *Rate ratios for all causes of death, neoplasms and cardiovascular disease* (*Poisson multiple regression analyses*)

	All causes		Neoplasms		Cardiovascular diseases		Infectious disease		Traumatic episodes	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Gender										
Male	1	Referent	1	Referent	1	Referent	1	Referent	1	Referent
Female	0.53	0.47–0.61	0.48	0.36–0.65	0.54	0.41–0.71	0.75	0.26–2.12	0.53	0.36–0.77
Age										
Every 5 years	1.07	1.06–1.07	1.07	1.06–1.08	1.10	1.09–1.11	1.03	1.00–1.06	1.02	1.01–1.03
Diagnosis										
Schizophrenia	1	Referent	1	Referent	1	Referent	1	Referent	1	Referent
Affective disorders	0.75	0.58–0.98	1.16	0.63–2.13	0.80	0.46–1.40	0.23	0.01–3.77	0.48	0.27–0.85
Neurosis and somatoform disorders	0.59	0.44–0.80	0.89	0.45–1.73	0.82	0.45–1.49	3.87	0–0	0.19	0.08–0.42
Personality disorders	1.04	0.71–1.54	1.05	0.41–2.66	0.99	0.40–2.43	2.92	0.26–32.73	0.79	0.37–1.67
Drug addiction	1.09	0.83–1.42	1.07	0.56–2.04	1.22	0.70–2.15	0.39	0.02–6.32	0.48	0.26–0.89
Alcoholism	1.44	1.05–1.97	2.51	1.27–4.97	1.46	0.73–2.91	2.94	0–0	0.46	0.19–1.11
Other diagnoses	2.80	1.99–3.93	0.22	0.03–1.74	0.45	0.10–1.99	28.25	3.35–238.52	1.79	0.97–3.31
Interval from registration (years)										
⩽1	1	Referent	1	Referent	1	Referent	1	Referent	1	Referent
1–2	0.75	0.60–0.94	0.71	0.43–1.18	0.95	0.61–1.49	0.70	0.12–4.21	1.05	0.60–1.85
2–5	0.51	0.42–0.62	0.61	0.41–0.92	0.44	0.28–0.68	0.25	0.04–1.49	0.58	0.35–0.97
5–10	0.40	0.33–0.49	0.40	0.26–0.62	0.45	0.30–0.68	1.08	0.30–3.87	0.44	0.26–0.74
>10	0.36	0.29–0.44	0.39	0.26–0.61	0.54	0.36–0.80	0.69	0.17–2.72	0.37	0.21–0.66

RR, Rate ratio; CI, confidence interval.

psychiatric patients over a 20-year period, allowing for a more detailed exploration of the causes of death; the results of the earlier study have been widely confirmed.

Our data show that psychiatric patients have an almost twofold higher mortality rate than the general population. This value is lower than that of previous studies. For example, a meta-analysis conducted by Harris & Barraclough (1998) revealed an SMR ranging from 0.96 to 20.73. Other studies confirm that there is a decrease in mortality on moving from hospital-based to community-based psychiatric care (Casadebaig & Quemada, 1991; Sohlman & Lehtinen, 1999), and this could be the reason for the lower SMR in our population, which was served by a community-based system of care.

The majority of studies investigating mortality among psychiatric patients analysed cohorts of long-stay in-patients (Licht *et al*. 1993; Rasanen *et al*. 2002) or patients who had had at least one admission to a psychiatric ward (Haugland *et al*. 1983; Allebeck & Wistedt, 1986; Zilber *et al*. 1989; Mortensen & Juel, 1993), even if studies were conducted in deinstitutionalized service systems (Hansen *et al*. 2001). A recent Italian study (Meloni *et al*. 2006) found an SMR of 3.0 in a cohort of psychiatric in-patients in Florence followed up for 16 years after hospital discharge. Few studies have calculate the SMR of both in-patients and out-patients. Of note, one of these studies (Hassall *et al*. 1988) found an SMR of 1.8, very similar to the SMR of 1.88 of our population, with a clear difference between in-patients (2.2) and out-patients (1.4), a difference that is also confirmed in our sample (2.6 *v*. 1.7). Harris & Barraclough (1998) report a similar difference between patients treated in community-based systems of care (1.98) compared to patients admitted to hospitals (2.79). This may be due to the more severe physical and/or psychiatric status of patients after their admission to hospital.

Our study demonstrated that both male and female psychiatric patients are at a higher risk of premature death, but males have an overall SMR that is more than twofold higher than the general population, whereas females have a mortality rate that is about 65% higher than the general population. Similar results are presented by Politi *et al*. (2002) and Kisely *et al*. (2005). Even though, for the both genders, the SMR is statistically significant in each age group, younger females (aged 14–24 years) having the highest SMR. This is probably referable to the high incidence of drug addiction and alcoholism diagnosis found in this group. Women with a diagnosis of alcohol addiction were also reported to have a higher mortality risk in the meta-analysis of Harris & Barraclough (1998).

Other studies confirm the higher risk of death for younger patients and for patients with substance abuse (Malzberg, 1934; Babigian & Odoroff, 1969; Zilber *et al*. 1989; Amaddeo *et al*. 1995; Harris & Barraclough, 1998; Rosen *et al*. 2008). Our finding of high SMRs for infectious diseases among younger patients (18.95 for the 14–24 years age group and 72.26 for the 25–44 years age group) is probably due to the fact that deaths from these causes are very rare at a young age in the general population (low expected deaths). As regards SMR for specific causes of death, in an Italian study conducted in Florence among discharged patients, the SMR for violent cause was 13.0, much higher than our value of 4.45 (Meloni *et al*. 2006).

A strong association between drug addiction and infectious diseases was found (SMR 216.40, 95% CI 142.5–328.6), and this could be related to the fact that, among patients with drug addiction, there is a high prevalence of organic diseases and infectious diseases that are highly contagious, such as hepatitis or HIV (Carra *et al*. 2008). High values of SMRs for infectious diseases were observed in the whole cohort (10.18), and this suggests that deinstitutionalization has not adequately improved the detection and treatment of physical diseases, which should be avoidable with access to a well-resourced health-care system or appropriate health policies (Amaddeo *et al*. 2007).

The diagnosis of alcohol addiction showed an SMR of 3.16, but the higher risk is especially related to particular causes of death, such as organic mental disorder (SMR 13.32, 95% CI 4.3–41.3), digestive system disease (SMR 5.68, 95% CI 3.2–10.0), nervous system disease (SMR 4.11, 95% CI 1.0–16.4) and respiratory system diseases (SMR 3.83, 95% CI 1.6–9.2). This result concurs with the meta-analysis of Harris & Barraclough (1998), where the highest correlations with alcoholism are for organic mental disorder (SMR 13.69), cirrhosis (SMR 8.86) and digestive system disease.

The association between alcoholism and damage to the central and peripheral nervous system is well known and the consequent alterations in the functioning of the nervous system could be responsible for the greater number of traumatic episodes, which in our population have an SMR of 3.62 (95% CI 1.7–7.6), similar to the findings of Harris & Barraclough (1998) with an SMR of 3.89.

Regarding the mortality risk for neoplasm, there was no difference found between schizophrenic patients and the general population (SMR 1.07, 95% CI 0.6–1.9); our data confirm the findings of Goldacre *et al*. (2005), that there is no evidence that schizophrenia provides protection against cancer.

Regression analyses confirmed other findings that women have a lower mortality rate, that there is an

increase in mortality for every 5 years of age, and that the diagnoses have different associations with various causes of death. The negative trend in relationship between the mortality rate and the time interval since registration, found in our previous study (Amaddeo *et al*. 1995), was confirmed and the time extension of our study to 20 years has made the results more robust.

In this study we found an SMR for psychiatric patients lower than the rate found in other studies. It could be the case that a community-based service is conducive to reducing mortality. However, it is also clear that a psychiatric disorder acts as a chronic disease in influencing a patient's life expectancy.

The strengths of this study are the reliability of the SMR as a good and widely used indicator for mortality comparisons and the fact that this is, to our knowledge, the largest register-based study on mortality conducted in an area totally served by a CMHS.

One limitation of this study is that it was not possible to obtain information about physical activity, smoking and drinking habits of patients with a different diagnosis from alcoholism. These lifestyle factors could be important measures of how such behaviours influence mortality, especially in a community setting, and could help in constructing hypotheses with regard to how the implementation of health promotion and preventive programmes, targeted to psychiatric patients, could reduce mortality.

Other possible limitations of this study are the amount of missing data on causes of death (approximately 10% of the whole sample). The sample size was too small to reach statistical significance in the analyses of some, more rare, causes of death when the sample was divided by diagnoses. Because of the missing data on causes of death, caution is required in the interpretation of the SMRs, which could be underestimated. Nevertheless, having explored several sources to obtain causes of death information (including Forensic Registries), we assume that the missing data are equally distributed between all the causes.

From our results we can conclude that it is important for mental health services to improve their capacity to manage more effectively the physical health problems of patients, with multidisciplinary collaborative care approaches, or facilitating linkages between mental health services and medical primary care providers.

Further research, which is ongoing in our setting, is needed to investigate the relationship between mortality in psychiatric patients and neoplasms.

It could be useful to analyse the mortality of patients treated in community-based mental health services, where a better integration between mental health care and primary and secondary medical care exists, in order to confirm if this kind of integration leads to a reduction in mortality and if a multidisciplinary holistic approach could reduce the risk of premature mortality in psychiatric patients.

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Declaration of Interest

None.

References

Allebeck P, Wistedt B (1986). Mortality in schizophrenia. A ten-year follow-up based on the Stockholm County inpatient register. *Archive of General Psychiatry* **43**, 650–653.

Amaddeo F, Barbui C, Perini G, Biggeri A, Tansella M (2007). Avoidable mortality of psychiatric patients in an area with a community-based system of mental health care. *Acta Psychiatrica Scandinavica* **115**, 320–325.

Amaddeo F, Bisoffi G, Bonizzato P, Micciolo R, Tansella M (1995). Mortality among patients with psychiatric illness. A ten-year case register study in an area with a community-based system of care. *British Journal of Psychiatry* **166**, 783–788.

Babigian HM, Odoroff CL (1969). The mortality experience of a population. *American Journal of Psychiatry* **126**, 470–480.

Carra G, Montomoli C, Monti MC, Clerici M (2008). Does HIV serostatus affect outcomes of dually diagnosed opiate dependents in residential treatment? *Epidemiologia e Psichiatria Sociale* **17**, 77–81.

Casadebaig F, Quemada N (1991). Changes in mortality among psychiatric inpatients, 1968–1982. *Social Psychiatry and Psychiatric Epidemiology* **26**, 78–82.

Consul PC (1989). *Generalized Poisson Distributions*. Marcel Dekker Inc.: New York and Basel.

Craig TJ, Lin SP (1981). Death and deinstitutionalization. *American Journal of Psychiatry* **138**, 224–227.

Druss BG, Newcomer JW (2007). Challenges and solutions to integrating mental and physical health care. *Journal of Clinical Psychiatry* **68**, e09.

Farr W (1841). Report upon the mortality of lunatics. *Journal of the Statistical Society* **4**, 17–33.

Goff DC, Cather C, Evins AE, Henderson DC, Freudenreich O, Copeland PM, Bierer M, Duckworth K, Sacks FM (2005). Medical morbidity and mortality in

schizophrenia: guidelines for psychiatrists. *Journal of Clinical Psychiatry* **66**, 183–194.

Goldacre MJ, Kurina LM, Wotton CJ, Yeates D, Seagroat V (2005). Schizophrenia and cancer: an epidemiological study. *British Journal of Psychiatry* **187**, 334–338.

Hansen V, Jacobsen BK, Arnesen E (2001). Cause-specific mortality in psychiatric patients after deinstitutionalisation. *British Journal of Psychiatry* **179**, 438–443.

Harris EC, Barraclough B (1998). Excess mortality of mental disorder. *British Journal of Psychiatry* **173**, 11–53.

Hassall C, Prior P, Cross KW (1988). A preliminary study of excess mortality using a psychiatric case register. *Journal of Epidemiology and Community Health* **42**, 286–289.

Haugland G, Craig TJ, Goodman AB, Siegel C (1983). Mortality in the era of deinstitutionalization. *American Journal of Psychiatry* **140**, 848–852.

Kales HC, Valenstein M, Kim HM, McCarthy JF, Ganoczy D, Cunningham F, Blow FC (2007). Mortality risk in patients with dementia treated with antipsychotics versus other psychiatric medications. *American Journal of Psychiatry* **164**, 1568–1576.

Kisely S, Smith M, Lawrence D, Maaten S (2005). Mortality in individuals who have had psychiatric treatment: population-based study in Nova Scotia. *British Journal of Psychiatry* **187**, 552–558.

Leucht S, Fountoulakis K (2006). Improvement of the physical health of people with mental illness. *Current Opinion in Psychiatry* **19**, 411–412.

Licht RW, Mortensen PB, Gouliaev G, Lund J (1993). Mortality in Danish psychiatric long-stay patients, 1972–1982. *Acta Psychiatrica Scandinavica* **87**, 336–341.

Malzberg B (1934). *Mortality Among Patients with Mental Disease*. State Hospital Press: New York.

Martiello MA, Cipriani F, Voller F, Buiatti E, Giacchi M (2006). The descriptive epidemiology of suicide in Tuscany, 1988–2002. *Epidemiologia e Psichiatria Sociale* **15**, 202–210.

Meloni D, Miccinesi G, Bencini A, Conte M, Crocetti E, Zappa M, Ferrara M (2006). Mortality among discharged psychiatric patients in Florence, Italy. *Psychiatric Services* **57**, 1474–1481.

Mortensen PB, Juel K (1993). Mortality and causes of death in first admitted schizophrenic patients. *British Journal of Psychiatry* **163**, 183–189.

National Center for Health Statistics (2006). *ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification, Sixth Edition*. Practice Management Information Corporation (PMIC): Los Angeles, CA.

Politi P, Piccinelli M, Klersy C, Madini S, Segagni LG, Fratti C, Barale F (2002). Mortality in psychiatric patients 5 to 21 years after hospital admission in Italy. *Psychological Medicine* **32**, 227–237.

Politi P, Sciarini P, Lusignani GS, Micieli G (2006). Depression and stroke: an up-to-date review. *Epidemiologia e Psichiatria Sociale* **15**, 284–294.

Rasanen P, Hakko H, Jokelainen J, Tiihonen J (2002). Seasonal variation in specific methods of suicide: a national register study of 20,234 Finnish people. *Journal of Affective Disorders* **71**, 51–59.

Rosen CS, Kuhn E, Greenbaum MA, Drescher KD (2008). Substance abuse-related mortality among middle-aged male VA psychiatric patients. *Psychiatric Services* **59**, 290–296.

Schneider LS, Dagerman KS, Insel P (2005). Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *Journal of the American Medical Association* **294**, 1934–1943.

Sims AC (2001). Mortality statistics in psychiatry. *British Journal of Psychiatry* **179**, 477–478.

Sohlman B, Lehtinen V (1999). Mortality among discharged psychiatric patients in Finland. *Acta Psychiatrica Scandinavica* **99**, 102–109.

Tansella M, Amaddeo F, Burti L, Garzotto N, Ruggeri M (1998). Community-based mental health care in Verona, Italy. In *Mental Health in Our Future Cities* (ed. D. Goldberg and G. Thornicroft), pp. 239–262. Psychological Press: Hove.

Tansella M, Amaddeo F, Burti L, Lasalvia A, Ruggeri M (2006). Evaluating a community-based mental health service focusing on severe mental illness. The Verona experience. *Acta Psychiatrica Scandinavica* (Suppl.) **429**, 90–94.

Tsuang MT, Simpson JC (1985). Mortality studies in psychiatry. Should they stop or proceed? *Archive of General Psychiatry* **42**, 98–103.

Vreeland B (2007). Bridging the gap between mental and physical health: a multidisciplinary approach. *Journal of Clinical Psychiatry* **68** (Suppl. 4), 26–33.

Wang PS, Schneeweiss S, Avorn J, Fischer MA, Mogun H, Solomon DH, Brookhart MA (2005). Risk of death in elderly users of conventional vs. atypical antipsychotic medications. *New England Journal of Medicine* **353**, 2335–2341.

Zilber N, Schufman N, Lerner Y (1989). Mortality among psychiatric patients – the groups at risk. *Acta Psychiatrica Scandinavica* **79**, 248–256.