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Mortality in mental health patients of the Emilia–Romagna region of Italy: A registry-based study

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ABSTRACT

Evidence from previous research demonstrated a gap in mortality between patients with mental disorders and the general population. However, a more exhaustive assessment is required to address this public health issue. The aim of this study was to provide comprehensive analysis of mortality examining all causes of death and all psychiatric diagnoses. We conducted a 10-year retrospective cohort study, including all in and out patients registered in the Mental Health Registry of Emilia-Romagna, Italy. Standardized mortality ratios (SMRs) were calculated. The cohort consisted of 137,351 patients 11,236 of whom died during the study period and the overall SMR was 1.99. 85.9 % of excess mortality was attributable to a broad range of natural causes. Diseases of circulatory and respiratory systems as well as neoplasms were the principal contributors to the mortality gap. All psychiatric conditions led to a higher risk of death. The greatest excess was due to neoplasms in depressed and neurotic patients and to cardiovascular diseases in patients with schizophrenia and personality disorders. Our results highlight the need for close collaboration between mental and primary health care services with the aim of reducing excess mortality as a result of medical diseases among all patients suffering from psychiatric condition.

1. Introduction

A wide mortality gap between patients with psychiatric disorders and the general population has been shown by a large number of studies from the '70s (Harris and Barraclough, 1998) up to the present day (Oakley et al., 2018). A recent meta-analysis (Walker et al., 2015) examining studies conducted worldwide in the last 50 years showed that the mortality risk for patients with psychiatric disorders is more than double (RR 2.22) that of the general population. The reason for this excess is attributable to suicide and other unnatural causes (Ko et al., 2018), but also to natural causes (Swaraj et al., 2019). However, the studies published are heterogeneous in their sample sources, varying from case registries (Grigoletti et al., 2009) to hospital records (Charrel et al., 2015), insurance databases (Bruckner et al., 2017) and random

samples from the general population (Lundin 2016). Most authors have ascertained mental disorders simply by using hospital discharge data, possibly selecting more severe cases and thus overestimating mortality (John et al., 2018). Moreover, the bulk of evidence focuses on patients with Serious Mental Illnesses, especially schizophrenia and psychoses (Lee et al., 2018; Oakley et al., 2018), that carry a higher mortality risk than Common Mental Disorders, like anxiety disorders and depression (Walker et al., 2015). Only a limited number of studies analysed the mortality gap in patients with anxiety and depression (Meier et al., 2016) even though their high prevalence makes them associated with the highest overall burden of mortality (Whiteford et al., 2013). Similarly, the evidence as to the mortality of patients with personality disorders, which are nowadays equally prevalent and possibly more challenging for mental health services (Flynn et al., 2019), is limited

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(Høve et al., 2013). As somestudies indicate a decrease in the mortality gap after the implementation of community mental health services (Wahlbeck et al., 2011) and others show an increase in the gap over the last two decades (Hayes et al., 2017; Lawrence et al., 2013) it is important to monitor excess mortality over time. Hence, it is necessary to better understand causes of mortality and how they impact on the different subgroups of patients with mental disorders, in order to develop evidence-based strategies aimed to implement and re-organize mental health services. This study aimed to explore the mortality gap between users of Mental Health Departments (MHD) in the Emilia-Romagna Region and the general population during a 10-year period (2008-2017). The regional Mental Health Registry permitted the recruitment of all patients referring to MHDs, irrespective of diagnosis, severity of illness or care setting. Changes in the mortality gap between the first and the second five-year period of the study have also been examined.

2. Methods

2.1. Study setting

This is a registry-based, retrospective cohort study carried out in Emilia-Romagna, a region in Italy with about 4.5 million inhabitants. The health system is tax funded and is a regional system with wide organizational autonomy that guarantees homogeneous services in the territory of the region. It covers all citizens through 8 Local Health Trusts. Each Local Health Trust has an MHD to deliver mental health care. Emilia-Romagna has a psychiatric community system that completed its transition from hospital-based psychiatry 30 years ago. MHDs are well established and their multi-professional teams ensure general psychiatric evaluation, comprehensive care and an assertive outreach for treatment and follow up.

2.2. Subjects

The study included all patients aged 18 years or over who had a diagnosis of mental disorder (ICD9-CM 290-319) during the period 1 January 2008 to 31 December 2017. The regional Mental Health

Registry was used to identify study participants and retrieve demographic data (age, gender, citizenship and residency), psychiatric diagnosis and date of first admittance. The Registry was implemented for administrative, clinical and epidemiological purposes in the '80s and contains information on ICD-9CM diagnosis (Table 1 in Supplementary Material), dates of visits and treatment (pharmaceutical, psychological, rehabilitative) of all in and outpatients who have accessed the MHDs in the region. Demographic features, as well as diagnoses, are routinely recorded at the first clinical evaluation and then constantly updated by clinicians; finally, all data are collected via an Information System at regional level. Residents outside the Emilia-Romagna Region, patients with an access to the MHD before 2008 and patients with intellectual disability, dementia, delirium or other mental disorders following organic brain damage (ICD9-CM 290, 293, 294, 299.0, 299.01, 310, 317, 318, 319) were excluded.

2.3. Procedures

To retrieve information on deaths (date and causes of death), we linked the Mental Health Registry with the regional Cause of Death Registry using a single anonymous identity code, which is given to all health records of residents by the regional authority. The regional Cause of Death Registry covers all the deaths in the region and contains anonymous information about sociodemographic characteristics, date, venue, circumstances and cause of death, according to the ICD9 and ICD10 (from 2009) (Table 2 in Supplementary Material). Both registries undergo regular systematic quality control. All the patients that went to live in another region were considered lost to follow-up because their life status could not be ascertained. The information about change of residence to another region was retrieved from the regional Registry Office. The period of exposure was calculated as the difference between the date of first admittance to a Mental Health Department and either 31 December 2017 or the date in which the patient left the region or died (where applicable). The study was approved by the local Ethical Committee (N. 341/2019). All the records in the Mental Health Register were anonymized.

Table 1Sociodemographic and clinical characteristics of the MHD population (all and subjects who died) on the first date of access to the MHD.

		MHD ^a popula Included	tion		Deaths	
		n.	Person-years	%	n.	%
Total		137,351	647,546	100.0	11,236	100.0
Gender	Men	53,935	244,665	39.3	5,375	47.8
	Women	83,416	402,881	60.7	5,861	52.2
Age group, year	18-24	12,644	58,681	9.2	61	0.5
	25-44	50,405	256,418	36.7	751	6.7
	45-64	46,643	219,813	34.90	2,769	24.6
	65-74	15,090	66,755	11.0	2,850	25.4
	75-84	10,417	39,808	7.6	3,535	31.5
	85+	2,152	6,071	1.6	1,270	11.3
Citizenship	Italian	123,132	585,661	89.7	11,028	98.2
	Non Italian	14,219	61,885	10.4	208	1.9
Residency	Urban	85,375	407,097	62.2	6,900	61.4
	Rural	51,976	240,449	37.8	4,336	38.6
Diagnostic group	Schizophrenia and other functional psychosis	7,940	39,813	5.8	745	6.6
	Mania and bipolar affective disorders	4,445	22,750	3.2	350	3.1
	Depression	56,489	260,939	41.1	5,484	48.8
	Neurotic disorders	44,998	209,075	32.8	2,688	23.9
	Personality and behaviour disorders	9,987	52,746	7.3	737	6.6
	Alcohol and substance use disorders	4,578	20,336	3.3	539	4.8
	other	8,914	41,888	6.5	693	6.2
Period at entry ^b	2008-2012	71,433	169,548	52.0	3,684	32.8
	2013-2017	65,918	161,155	48.0	2,976	26.5

^a MHD: Mental Health Department

^b Sum of deaths and person-years are less than the total because only deaths within this period and only the person-years of people included in this period were considered.

Table 2Distribution of causes of death in the regional and MHD population, 2008-2017.

	Regional population	1	MHD ^a populatio	on
	n	%	n	%
Causes of death				
Natural	462,846	95.6	10,175	90.6
Certain infectious and parasitic diseases	14,054	2.9	430	3.8
Neoplasms	143,311	29.6	3,988	35.5
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	1,994	0.4	42	0.4
Endocrine, nutritional, and metabolic diseases	16,927	3.5	377	3.4
Mental and behavioural disorders	20,187	4.2	382	3.4
Diseases of the nervous system	17,152	3.5	391	3.5
Diseases of the circulatory system	175,725	36.3	2,821	25.1
Diseases of the respiratory system	37,366	7.7	873	7.8
Diseases of the digestive system	17,823	3.7	493	4.4
Diseases of the skin and subcutaneous tissue	799	0.2	22	0.2
Diseases of the musculoskeletal system and connective tissue	2,066	0.4	58	0.5
Diseases of the genitourinary system	9,594	2.0	212	1.9
Pregnancy, childbirth and the puerperium	8	0.0	0	0
Certain conditions originating in the perinatal period	3	0.0	0	0
Congenital malformations, deformations and chromosomal abnormalities	461	0.1	12	0.1
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	5,352	1.1	74	0.7
External causes of morbidity and mortality	21,256	4.4	1,061	9.4
Intentional self-harm	3,872	0.8	540	4.8
Total	484,102	100.0	11,236	100.0

^a MHD: Mental Health Department

2.3.1. Statistical analyses

The frequency distribution of causes of death was calculated for the whole population and by psychiatric diagnosis. Causes of death were plotted as natural and external, and grouped according to the main chapters of the ICD10; only suicide was analysed as a specific category. We grouped the ICD-9 CM codes of psychiatric diagnoses into 9 classes (Table 2 in Supplementary Material), as we had previously done in other papers (Berardi, 2018; Stivanello et al., 2020), following a similar method to that used by other authors (Lora et al., 2012). We used indirect standardization to calculate the Standardized Mortality Ratio (SMR), controlling for age (grouped in classes: 18-24, 25-44, 45-64, 65-74, 75-84, >84 years) and gender. We used the age, class and gender specific rates of the regional population as the standard (Table 3 in Supplementary Materials). SMRs with 95% Confidence intervals (CI) were calculated by gender (adjusting for age only), cause of death, diagnostic group and period of entry (2008-2012 and 2013-2017). SMRs by period of entry were calculated considering only the deaths occurred in this time-period. Person-years were used as the denominator. In addition to the SMR, which is a relative measure of the difference in mortality between the two populations, we also calculated the absolute difference between observed and expected deaths and the proportion of this absolute excess attributable to each characteristic (age, gender, cause of death and psychiatric diagnosis). We repeated the analyses by psychiatric diagnosis in order to study specific causes of death.

3. Results

During the period 2008-2017, 182,947 patients made their first visit to the MHDs. After applying the exclusion criteria described above, the final population comprised 137,351 patients with an average follow-up period of 4.7 years and 647,546 person-years, 3.0% became lost to follow-up.

The sociodemographic and clinical variables of the MHD population are summarized in Table 1. The mean age was 48.1 ± 17.5 years, there was a higher proportion of women (60.7%), most lived in urban areas (62.2%) and had Italian citizenship (89.7%) and 41.1% were suffering from depressive disorders. Of the 11,236 patients who died during the study period, almost half had a diagnosis of depression (48.8%).

Table 2 shows that 90.6% of the study population deaths were due to natural causes and less than 10% to external causes (accidental or intentional), whereas the latter represent less than 5% of the deaths in the general population of the region. The two most frequent causes of natural death were cancer and cardiovascular diseases both in the MHD population and in the general population.

As shown in Table 3, the risk of mortality in the study population was about twice (SMR 1.99, 95%CI 1.96-2.03) the risk in the regional population, with a difference of 5,594 between observed and expected deaths and with men showing a higher excess than women.

When considering the causes of death, external causes of mortality showed an SMR of 3.93, among theme, the risk of suicide in MHD users was more than 9 times as high as in the general population. Natural causes of death showed an SMR of 1.89 and infectious diseases had the highest ratio (SMR 2.59; 95%CI 2.35-2.89). All psychiatric diagnoses showed a significant excess mortality; the diagnostic groups with the highest SMR for all causes were alcoholism and substance abuse (5.16; 95%CI 4.7-5.6), followed by personality disorders (2.62; 95%CI 2.44-2.82). In absolute terms, natural causes accounted for 85.9% of the excess mortality. As far as the causes of death are concerned, the highest difference between observed and expected deaths was for cancer, which was responsible for 37% of the excess mortality, and for cardiovascular and respiratory diseases, responsible for 16.6% and 8.6% of excess mortality respectively (Table 3). With respect to psychiatric diagnosis, the greatest difference between observed and expected deaths was among patients with a diagnosis of depression, which accounts for 46.9% of the excess mortality, followed by neurotic disorders accounting for 19.7% (Table 3). From the separate examination of mortality, in the first and in the second time-periods, we found that there was a higher excess in the first five-years of the study, compared to the second, with an SMR of 2.62 and 2.38 respectively (Table 3). As Table 4 shows, the causes of excess mortality varied according to thepsychiatric diagnosis. Depressive and neurotic disorders had an SMR of 2.18 and 1.91 respectively for neoplasms that were responsible for more than 43% of the excess mortality among these diagnosis. An elevated proportion of the excess mortality among personality disorders (23.7%) was due to cardiovascular diseases, with an SMR of 2.22. Also a significant part of excess mortality among patients with schizophrenia and with mania and bipolar affective disorders was related to cardiovascular diseases, 21.3% and 26.1% respectively.

4. Discussion

The present registry based-study analyses a large cohort of patients in treatment at public mental health services in Emilia-Romagna, confirms the existence of a mortality gap between people affected by mental disorders and the general population. This consisted in an almost twofold higher mortality risk for the MHD population. Our results are broadly consistent with estimates from previous studies (Berardi et al., 2018; Grigoletti et al., 2009; Krupchanka et al., 2018; Starace et al., 2018).

The highest SMR was found for intentional self-harm, being 9.5 times more frequent among people with mental illnesses than in the general population. However, even if external causes of death had the highest SMR, the large majority of the mortality gap (85.9%) was due to natural causes. All causes of death related to general medical conditions were more frequent in the MHD population than in the general population. In particular, most excess mortality was a result of neoplasms and diseases of the circulatory and respiratory systems. This is coherent with recent studies based on different methodologies and carried out in other

Table 3SMR with 95% Confidence interval and excess mortality by sociodemographic and clinical characteristics.

	observed	expected	SMR ^a	% 95C	\mathbf{I}_{p}	Observed- expected	% of the excess
Total	11,236	5,641	1.99	1.96	2.03	5,595	100
Gender							
Men	5,375	2,365	2.27	2.21	2.33	3,010	53.8
Women	5,861	3,276	1.79	1.74	1.84	2,585	46.2
Causes							
Natural	10,175	5,371	1.89	1.86	1.93	4,804	85.9
Certain infectious and parasitic diseases	430	166	2.59	2.35	2.84	264	4.7
Neoplasms	3,988	1,880	2.12	2.06	2.19	2,108	37.7
Diseases of the blood and blood-forming organs certain disorders involving the immune mechanism (D50-89)	42	22	1.87	1.35	2.53	20	0.4
Endocrine, nutritional, and metabolic diseases	377	197	1.91	1.72	2.11	180	3.2
Mental and behavioural disorders	382	207	1.85	1.67	2.04	175	3.1
Diseases of the nervous system	391	204	1.92	1.74	2.12	187	3.4
Diseases of the circulatory system	2,821	1,892	1.49	1.44	1.55	929	16.6
Diseases of the respiratory system	873	392	2.23	2.08	2.38	481	8.6
Diseases of the digestive system	493	212	2.33	2.13	2.54	281	5.0
Diseases of the skin and subcutaneous tissue	22	9	2.50	1.57	3.78	13	0.2
Diseases of the musculoskeletal system and connective tissue (M00-99)	58	26	2.22	1.68	2.87	32	0.6
Diseases of the genitourinary system	212	101	2.09	1.82	2.39	111	2.0
Pregnancy, childbirth and the puerperium	0	0	0.00	0.00	21.00	0	0
Certain conditions originating in the perinatal period (P00-96)	0	0.	0.00	0.00	83.00	0	0
Congenital malformations, deformations and chromosomal abnormalities (Q00-99)	12	8	1.57	0.81	2.74	4	0.1
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00-99)	74	55	1.36	1.07	1.70	19	0.4
External causes of morbidity and mortality	1,061	270	3.93	3.7	4.18	791	14.
Intentional self-harm	540	56	9.56	8.77	10.00	484	8.7
Diagnostic group							
Schizophrenia and other functional psychosis	745	336	2.22	2.06	2.38	409	7.4
Mania and bipolar affective disorders	350	179	1.96	1.76	2.17	171	3.1
Depression	5,484	2,900	1.89	1.84	1.94	2,584	46.2
Neurotic disorders	2,688	1,587	1.69	1.63	1.76	1,101	19.7
Personality and behaviour disorders	737	281	2.62	2.44	2.82	457	8.2
Alcohol e substance use disorders	539	104	5.16	4.73	5.61	435	7.8
Other	693	253	2.74	2.53	2.95	440	7.9
Period ^c							• • •
2008-2012	3,684	1,409	2.62	2.53	2.70	2,275	40.7
2013-2017	2,976	1,249	2.38	2.30	2.48	1,727	30.9

^a SMR: Standardized Mortality Ratio

countries (Jayatilleke et al., 2017; Plana-Ripoll et al., 2019) that observed a reduction in life expectancy in people with mental illnesses largely due to natural deaths, particularly from cardiovascular and respiratory diseases as well as neoplasms.

We also observed that the gap in mortality related to all psychiatric diagnoses, with depressive disorders accounting for nearly half of the excess. This is consistent with the hypothesis that was suggested by a large meta-analysis according to which severe mental illnesses such as schizophrenia and bipolar disorders were shown to have a higher mortality ratio, while more prevalent but milder psychiatric conditions were demonstrated to be responsible for more deaths overall (Walker et al., 2015).

Various hypotheses have been made concerning the causes of the mortality gap between people affected by mental illness and the rest of the population. Unhealthy lifestyles such as a lack of good nutrition (Di Pasquale et al., 2013) and physical activity (Vancampfort et al., 2017), as well as being a smoker (Prochaska et al., 2017), are very prevalent among people with mental disorders and might partly explain the elevated risk of dying from cancer, cardiovascular and respiratory conditions. Chronic use of antipsychotic medication is also associated with metabolic and cardiovascular adverse effects (Fontaine et al., 2001) and may contribute to mortality due to diseases of the circulatory system. Moreover people affected by mental disorders are less likely to receive medical monitoring and specialized treatment for both cardiovascular diseases and neoplasms (Ayerbe et al., 2018; Kisely et al., 2013).

An interesting outcome of our study was that the main causes of death changed according to the psychiatric diagnosis. Neoplasms were the most frequent cause of excess mortality in patients with depressive and neurotic disorders, which can be described under the term "common mental disorders". Patients with common mental disorders have an almost twofold risk of dying of cancer compared to the general population. In absolute terms, cancer accounted for 40% of excess mortality in common mental disorders and appears to be strongly associated with these psychiatric diagnoses. Other cohort studies also found elevated risk of death from neoplasms among patients with neurotic and depressive disorders (Das-Munshi et al., 2019; Plana-Ripoll et al., 2019). However it was not higher than for the other main causes of death, suggesting the association between common mental disorders and mortality is generic rather than cause-specific (Cuijpers et al., 2014). There are different possible explanations for this. Considering the elevated prevalence of depression and anxiety disorders following a diagnosis of cancer (Massie et al., 2004), our result could be due to the high proportion of oncology patients referring to the MHD via the primary care consultation-liaison services (Berardi et al., 2014). On the other hand, research has also suggested that depression is a risk factor in developing neoplasms (Laursen et al., 2016) because it may increase unhealthy lifestyle behaviours and reduce adherence to medical screening services (DiMatteo et al., 2000). Moreover, there may also be a common biological liability between depression and cancer induced by chronic inflammation, resulting in a bidirectional association (Sotelo et al., 2014). More research should be done on if and how this might

^b CI: Confidence Interval

^c Sum of deaths is less than total deaths because only deaths within this period were considered

SMR with 95% confidence interval and difference between observed and expected of most important causes of death by diagnostic group.

	SMR^a	SMR ^a 95% CI ^b	q1	O-Ec	yo %	SMR^a	95% CI	0	-0	Jo %	SMR^a	95% CI	$^{ m qL}$	$O-E^c$	Jo %	SMR^a	95% CI	ą.	-0	jo %
					excess				Еc	excess					excess				Еc	excess
	Natural causes	causes				Diseases	of the ci	Diseases of the circulatory system	system		Neoplasms	sms				Disease	Diseases of the respiratory system	espirator	y system	
Diagnostic group																				
Schizophrenia and other functional	2.04	1.89	2.21	333	81.5	1.75	1.52	2.01	87	21.3	1.49	1.27	1.74	25	12.7	3.14	2.47	3.95	50.5	12.4
psychosis																				
Mania and bipolar affective disorders	1.78	1.59	1.99	133	77.8	1.81	1.47	2.2	45	26.1	1.5	1.22	1.82	33	19.4	2.4	1.58	3.49	15.7	9.2
Depression	1.81	1.76	1.86	2249	87.0	1.42	1.34	1.49	414	16.0	2.18	2.09	2.28	1120	43.4	5.06	1.87	2.27	219	8.5
Neurotic disorders	1.66	1.6	1.7	994	90.3	1.32	1.22	1.4	169	15.3	1.91	1.79	2	485	44.1	1.88	1.63	2.2	96	8.7
Personality and behaviour disorders	2.29	2.11	2.48	339	74.4	2.22	1.92	2.55	108	23.7	1.8	1.55	2.09	79	17.3	2.92	2.19	3.82	35	7.6
Alcohol e substance use disorders	4.56	4.14	5.01	344	79.1	3.1	2.5	3.8	63	14.5	2.93	2.42	3.5	78	17.9	7.14	5.21	9.55	39	8.9
Other	2.72	2.51	2.94	412	93.8	1.53	1.28	1.83	44	10.0	3.99	3.58	4.43	261	59.3	2.53	1.83	3.41	569	5.9
Total	1.89	1.86	1.93	4,804	85.9	1.49	1.44	1.55	929	16.6	2.12	2.06	2.19	2,108	37.7	2.23	2.08	2.38	481	9.8

^a SMR: Standardized Mortality Ratio ^b CI: Confidence Interval ^c O-E: Observed-Expected affect the mortality of people with common mental disorders (Pinquart and Duberstein, 2010).

Mortality risk from respiratory diseases was about three times higher in patients suffering from severe mental illnesses and personality disorders than in the general population, which is probably due to the high prevalence of smoking in this group (Sharma et al., 2016). Nevertheless, the bulk of excess mortality related to those diagnoses was attributable to diseases of the circulatory system, particularly among patients with personality disorders, who had more than twice the risk of death. Few other studies have investigated the cardiovascular mortality of people affected by personality disorders. A study conducted in Sweden (Bjorkenstam et al., 2015) reported the same SMR that we found in males and even higher in women, whereas an Italian study on this issue (Grigoletti et al., 2009) found a lower excess mortality, though in this sample patients with personality disorders were underrepresented. Evidence for an elevated risk of dying from cardiovascular diseases can also be found in some cross-sectional studies on the subject, showing the high prevalence of cardiometabolic conditions among patients affected by personality disorders (Dokucu and Cloninger, 2019). The elevated frequency of impulsive or dysfunctional behaviour such as smoking, alcohol and drug misuse (Frankenburg and Zanarini, 2004), as well as the common off-label prescription of antipsychotic medications (Aguglia et al., 2019), may underlie the elevated cardiovascular risk in those patients.

When comparing the two time periods of the study, the mortality gap narrowed in the last five years of the study, in comparison with the first five years. However, most recently published studies found an increase in mortality excess over the years (Lawrence et al., 2013; Westman et al., 2018) especially those conducted only on severe mental illness (Laursen et al., 2018; Lee et al., 2018; Staudt Hansen et al., 2019). These inconsistent findings could be explained by a different case selection or a different follow-up duration. But it could be also hypothesized that public health policies, such as collaboration with primary care and other community general health services (Berardi et al., 1999, 2014) could have contributed to the reduction of the mortality excess. Thus further research is needed in order to understand the trend over time of the mortality gap and ascertain the effectiveness of public intervention plans.

The results of our study should be considered in the context of its various limitations. Our cohort was entirely composed of people officially resident in the Emilia-Romagna region. People who were not officially resident in the region and homeless people might be exposed to conditions of social disadvantage and hence prone to higher mortality (Mackenbach et al., 2003). This could theoretically have caused an underestimation of mortality in our cohort. However the proportion of people excluded due to their not being resident was low (about 1% of the caseload). Patients treated solely by drug addiction services could not be included and this could have led to an under-representation of these patients in our sample. It is well known that patients with alcohol and drug use disorders have high mortality for both natural and unnatural causes of death (Pavarin et al., 2017, 2020) and this might lead to the cohort mortality being underestimated. Finally, the results of our study concern patients with mental illnesses that accessed the services of the MHD and cannot be extended to the entire regional population of people affected by psychiatric disorders. Some of them may only refer to general practitioners or to private psychiatrists or, especially among patients with common mental disorders, remain undiagnosed and untreated.

In conclusion, the present study found a mortality gap between mental health users and the general population that was mainly due to natural causes, above all cardiovascular and respiratory diseases and neoplasms. All patients affected by mental disorders should be considered as being at a higher risk of death from medical illness, even those affected by milder conditions. Therefore mental health services should enhance their collaboration with primary care services and protect physical well-being through interventions aimed at lifestyle

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improvement, such as smoking cessation and medical comorbidity monitoring. Adherence to screening activities and accessibility to specialized medical treatment should also be promoted. In addition, our study suggests that in order to develop more effective prevention strategies, further research is needed to explore the relationship between common mental disorders and death from neoplasms, as well as between personality disorders and cardiovascular mortality.

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Authors' contribution

All authors contributed to the study conception and design. Data collection was performed by Alessio Saponaro and data analysis was performed by Elisa Stivanello and Muriel Assunta Musti. The first draft of the manuscript was written by Domenico Berardi, Federico Chierzi and Elisa Stivanello and all authors commented on previous versions of the manuscript. All authors red and approved the final manuscript.

Availability of data and material: Data of the study will be shared on reasonable request.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.psychres.2020.113702.

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