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ORIGINAL PAPER

Excess mortality in people with mental illness: findings from a Northern Italy psychiatric case register

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Abstract

Purpose People with mental disorders show mortality rates up to 22.2 times higher than that of the general population. In spite of progressive increase in life expectancy observed in the general population, the mortality gap of people suffering from mental health problems has gradually widened. The aim of this paper was to study mortality rates in people suffering from mental illness in a cohort of people (16,981 subjects) in the local mental health register of the province of Modena during the decade 2006–2015.

Methods Standardized Mortality Ratios (SMRs) were calculated to compare the mortality of people with mental disorders to the mortality of people living in the province of Modena and the excess of mortality was studied in relation to the following variables: gender, age group, diagnosis and causes of death. In addition, Poisson regression analysis was performed to study the association between patient characteristics and mortality.

Results An overall excess mortality of 80% was found in subjects under the care of mental health services as compared to the reference population (SMR = 1.8, 95% CI 1.7–1.9). Subjects in the 15–44 year group presented the highest SMR (9.2, 95% CI 6.9–11.4). The most prevalent cause of death was cancer (28.1% of deaths). At the Poisson regression, the diagnosis "Substance abuse and dependence" showed the highest relative risk (RR) (4.00). Moreover, being male, single, unemployed and with a lower qualification was associated with higher RRs.

Conclusions Our study confirms that subjects with mental illness have higher SMR. Noteworthy, the overall higher risk of mortality was observed in the younger age group.

Keywords Mental health · Mortality · Cause of death · Standardized mortality ratio

Introduction

People with mental disorders have mortality rates up to 22.2 times higher than that of the general population [1], both for natural (e.g., somatic diseases to chronic or acute nature) and "non-natural" (e.g., suicide, accidental traumas) causes [2–7].

The diagnosis of schizophrenia, for example, has been associated with a mean reduction in life expectancy of 18 years [8]. Up to 60% of this excess mortality is due to somatic diseases [9]. Several studies have also shown that the excess mortality rates are uniform across different diagnostic groups, including schizophrenia [10], depression [11], bipolar disorder [12, 13], and anorexia nervosa [14]; as well as across different geographic regions (Asia, Europe, America, Australia, Africa) [1]. In addition, mortality risk is increased in all mental health users and not just those who received in-patient treatment [15].

Factors leading to increased mortality rates in individuals suffering from mental illness are complex and not yet fully understood. Psychiatric conditions themselves are not a direct cause of these deaths. Rather, determinants of mortality are identified within a wide spectrum of contingent disorders (e.g., cardiovascular diseases, chronic diseases, infectious diseases) and behaviours (e.g., suicide). The presence of mental illness is also frequently associated with factors that can themselves increase mortality risk, including heritable risk factors, psychotropic treatment and unhealthy

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lifestyle characterized by poor diet, smoking, physical inactivity and substance abuse [16]. In addition, disparities in health care access and uptake for common conditions such as diabetes, obesity, respiratory and cardiovascular diseases contribute significantly to poorer physical health outcomes for persons with mental illness [17]. For example, individuals with mental illness may be less able to recognize, report and request the help necessary for their physical illnesses [18] and, due to the persistence of stigma and discrimination they may receive poorer medical care as compared to the general population [19]. Further, individuals with mental illness tend to be excluded from preventive medicine programmes, such as cancer screening, vaccinations, counselling for smoking cessation, etc. [18].

Finally, among people with mental illness suicide is the main cause of death, with rates from 8 to 14 times higher in persons suffering from major depression, schizophrenia or affective psychoses [20–22].

Since the excess mortality found in people suffering from mental illness is mainly associated with avoidable risk factors [23], it is paramount to study and better understand the relevance of these associations to formulate and implement more effective preventive strategies.

The objective of this study was to evaluate mortality rates in people suffering from mental illness within a defined geographical area, the province of Modena in Northern Italy, evaluating the phenomenon in residents who entered the local mental health register in the decade 2006–2015. Mortality rates were compared with those of the general population in the province of Modena.

Methods

The sample consisted of an open cohort of 16,981 subjects who entered the psychiatric case register of the province of Modena, followed up from 1 January 2006 to 31 December 2015. Those subjects who, during the above period, had only a single contact with a service ($n = 1177$) and those who turned out not to suffer from a mental disorder ($n = 258$) were excluded from the analyses. The province of Modena, in 2015, had a population of 702,481 people, with an average mortality rate of about 10 per 1000 residents during the second half of 2010.

Mortality and cause of death were verified through an electronic linkage with the local mortality register (REM: mortality register collection data) and the psychiatric case register (SISM: mental health information system). REM has been used since 1999 and collects information about mortality in the general population of Modena, whilst SISM has been available from 2005 and collects socio-demographics and clinical information of subjects under the care of community mental health services. Both registers were updated every 6 months. All deaths were identified via anonymised identification numbers.

Standardized mortality ratios (SMRs) were calculated, using the indirect method of standardisation, to compare the mortality of people with mental disorders (study population) with the mortality of people living in the province of Modena (reference population). The SMR were estimated by the ratio of observed vs expected numbers of deaths, summed across 5-year age strata. The expected number of deaths per stratum was estimated by applying the age-specific mortality rate in the reference population to the corresponding person-years at risk in the study population (e.g., the expected number of deaths per stratum in women was calculated by multiplying the mortality rate in the same stratum of the general women population by the corresponding person-years). Person-years were calculated as the time in years spent by each subject in the study period, that is before death or before being discharged by the mental health service. Mortality rates of the reference population were provided by the Epidemiology and Risk Management of Azienda Unità Sanitaria Locale (AUSL) of Modena (local public health provider). A SMR of 1 indicates that the mortality risk in the study population was equal to that in the reference (with SMR > 1 indicating an elevated risk and SMR < 1 a lower risk). Tests of the statistical significance of the SMR were established on the Poisson distribution (two-tailed), using 95% confidence intervals (CIs). If CIs do not overlap with unity are statistically significant [23].

The excess of mortality was studied in relation to the following variables: gender, age group, diagnosis and causes of death grouped in four categories (cardiovascular disease, cancer, injuries/poisoning and suicides). All causes of death were defined according to ICD-9-CM classification. Three age groups (15–44, 45–64 and 65+) were considered to assess the mortality risk at different ages. ICD-9 diagnoses were aggregated into seven diagnostic categories: Neuroses (ICD-9 codes 300.xx, 302.xx, 306.xx-316.xx); Bipolar disorders (ICD-9 codes 296.xx); Schizophrenia and other psychosis (ICD-9 codes 295.xx, 297.xx-299.xx); Personality disorders (ICD-9 codes 301.xx); Intellectual disabilities and Organic psychosis (ICD-9 codes 290.xx-294.xx, 317.xx-319.xx); Substance abuse and dependence (ICD-9 codes 303.xx-305.xx); Other diagnoses not yet classified (ICD-9 codes: V70.2 General psychiatric examination, other and unspecified; V71.0 Observation for suspected mental condition). Patients were grouped according to the following characteristics: Qualification (primary or no qualification vs higher qualification); Marital status (unmarried, divorced or widower vs married or in partnership); Occupation (unemployed, retired, disabled, student, housewife vs occupied); Housing status (live alone, residential accommodation, homeless vs subject living with family or partner).

A multivariable Poisson regression analysis was performed to analyse the combined effect of independent variables (gender, age, diagnoses, qualification, marital status, occupation and housing status) on mortality [24, 25].

The model was fit assuming a canonical log-link distribution. Using Poisson regression is possible to present the coefficients in terms of relative risk (RR). A 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. 95% CIs were also presented.

Analyses were performed using SAS Enterprise Guide, Version 5.1.

Availability of data and materials Data were gathered from the mental health case registered of Azienda Unità Sanitaria Locale (AUSL) of Modena (local health public provider), matched with the Mortality Register of the province of Modena (REM).

Results

Patients included in the analysis were 16,981 (10,138 women and 6843 men) for a total of 50,396.5 person-years (29,976.6 for women and 20,419.9 for men). During the study period a total of 1148 individuals died (549 women and 599 men). The mean age at the entry was 48 ± 17.4 years, the mean age at death was 72.1 ± 14.6 years.

An overall excess mortality of 80% was found in subjects under the care of mental health services compared to the reference population (SMR = 1.8; 95% CI 1.7–1.9).

SMR by gender, age and diagnostic groups are shown in Table 1.

SMR by gender and age group

The mortality risk was 2.1 times that expected in men (95% CI 1.9–2.3) and 1.7 times that expected in women (95% CI 1.6–1.8). SMR decreased with age in both sexes. Those in the 15–44-year group presented the highest risk of death compared to the general age matched population (SMR = 9.2; 95% CI 6.9–11.4).

SMR by diagnosis

SMRs were significantly higher across all the diagnostic groups (see Table 1). However, SMR was particularly high in those with a diagnosis of substance abuse (5.8 times greater than that of the general population). Considering diagnoses by gender, the greatest risk elevation for females was associated with a diagnosis of intellectual disabilities and organic psychiatric conditions (SMR = 2.9, 95% CI 2.4–3.4), and, for males, a diagnosis of substance abuse (SMR = 5.7, 95% CI

Table 1 Number of subjects, observed and expected deaths and SMRs in subjects in the local mental health register by gender, age groups and diagnoses (years 2006–2015)

	Number of subjects	Person-years	Obs	Exp	SMR	CI 95%
Gender						
Male	6843	20,419.9	549	259.4	2.1**	(1.9–2.3)
Female	10,138	29,976.6	599	348.7	1.7**	(1.6–1.8)
Age groups						
15–44	6163	16,206.0	65	7.1	9.2**	(6.9–11.4)
45–64	6540	20,480.6	242	71.2	3.4**	(3.0-3.8)
65+	4278	13,709.9	841	517.9	1.6**	(1.5–1.7)
Diagnoses						
Neuroses (300; 303–316)	8893	21,612.7	437	257.8	1.7**	(1.5–1.9)
Bipolar disorders (296)	2617	9130.5	174	140.6	1.2*	(1.1–1.4)
Schizophrenia and other psychoses (295, 297–299)	1444	7057.3	112	77.3	1.4**	(1.2–1.7)
Personality disorders (301)	1515	6039.4	98	36.8	2.7**	(2.1–3.2)
Intellectual disabilities and organic psych conditions (317–319; 290–294)	1062	3266.2	266	85.7	3.1**	(2.8–3.4)
Substance abuse and dependence (303–305)	227	795.2	23	4.0	5.8**	(3.4–8.1)
Other diagnoses not yet classified (V70.2; V71.0)	1223	2495.2	38	22.0	1.7**	(1.2–2.3)

Obs observed deaths, *Exp* expected deaths

**$P < 0.001$

*$P < 0.01$

3.2–8.3). Moreover, 21.7% of deaths of patients with substance abuse were found in the 15–44 age group.

SMR by causes of death

The most prevalent cause of death was cancer (28.1% of deaths), followed by cardiovascular diseases (25.3%) and injuries/poisoning (9.3%). The number of suicides registered during the decade of the study was 61 (5.3% of total deaths and 57% of deaths from injury and poisoning); 75.4% of suicides were completed by male subjects.

Among natural causes of death an excess mortality was found for cancer (SMR = 1.7; 95% CI 1.5–1.9); this was 1.8 (95% CI 1.5–2.1) in men and 1.7 (95% CI 1.4–2.0) in women. The SMR for cardiovascular diseases was 1.3 (95% CI 1.1–1.4).

In terms of external causes of death (i.e., non-natural) high SMR was observed with respect to suicide (SMR = 12.1, 95% CI 9.1–15.2).

Analysis by age group

The mortality rate was higher in the 15–44 age group for causes of death, psychiatric diagnosis and sex (see Tables 2, 3, 4). SMRs were: 6.4 for cardiovascular diseases, 5.1 for cancer and 25.3 for suicides. Regarding diagnoses, the highest SMR was found in subjects with a diagnosis of substance abuse (SMR = 37.2). Noteworthy, one in five deaths of patients with a diagnosis of substance abuse occurred in the 15–44 age group. Very high mortality excess rates were found also in subjects with intellectual disabilities and personality disorders.

Table 2 Observed and expected deaths and SMRs in subjects in the local mental health register by age groups and cause of death (years 2006–2015)

	Obs	Exp	SMR	CI 95%
Cardiovascular diseases				
15–44	5	0.8	6.4**	(0.8–12.0)
45–64	29	13.7	2.1**	(1.1–2.4)
65+	256	201.9	1.3**	(1.1–1.4)
Cancer				
15–44	10	2.0	5.1**	(1.9–8.3)
45–64	90	39.0	2.3**	(1.8–2.8)
65+	223	151.6	1.5**	(1.3–1.7)
Injuries and poisoning				
15–44	26	2.6	10.1**	(6.2–14.0)
45–64	37	4.8	7.6**	(5.2–10.1)
65+	44	13.8	3.2**	(2.2–4.1)
Suicides				
15–44	20	0.8	25.3**	(14.2–36.4)
45–64	24	1.9	12.8**	(7.7–18.0)
65+	14	2.2	6.3**	(3.0-9.6)

Obs observed deaths, *Exp* expected deaths

**$P < 0.001$

Table 3 Observed and expected deaths and SMRs in subjects in the local mental health register by age groups and diagnoses (years 2006–2015)

	Obs	Exp	SMR	CI 95%
Neuroses				
15–44	20	3.0	6.8**	(3.8–9.7)
45–64	100	31.8	3.1**	(2.5–3.8)
65+	317	215.4	1.5**	(1.3–1.6)
Bipolar disorders				
15–44	6	0.8	7.2**	(5.0-13.2)
45–64	27	13.4	2.0**	(1.3–2.8)
65+	141	127.0	1.1	(0.9–1.3)
Schizophrenia and other psychoses				
15–44	11	1.2	9.0**	(3.7–14.3)
45–64	29	8.8	3.3**	(2.1–4.5)
65+	72	65.5	1.1	(0.8–1.4)
Personality disorders				
15–44	14	1.1	13.0**	(6.2–19.8)
45–64	33	9.3	3.5**	(2.3–4.8)
65+	51	34.0	1.5*	(1.1–1.9)
Intellectual disabilities and organic psych conditions				
15–44	5	0.4	11.6**	(1.4–21.7)
45–64	27	2.9	9.2**	(5.7–12.7)
65+	266	54.1	4.3**	(3.8–4.9)
Substance abuse and dependence				
15–44	5	0.1	37.2**	(4.6–69.8)
45–64	15	1.4	10.4**	(5.1–15.7)
65+	3	2.8	1.1	(0.1–2.3)

**$P < 0.001$

*$P < 0.01$

Multivariate analysis

All factors entered in the Poisson regression showed significant RRs except for "housing situation", namely "living alone, in residential accommodation, homeless" which showed a lower RR as compared to the reference category (i.e., subjects "living with family or partner"). Taking as a reference the category "other non-psychiatric diagnoses", the RRs was significantly higher with respect to all the diagnoses considered: "substance abuse" (RR 4.00), "personality disorders" (RR 2.75), "intellectual disabilities"(RR 2.74), "neuroses" (RR 1.52), "bipolar disorders" (RR 1.65) and "schizophrenia and other psychoses" (RR 2.29). Other factors associated with significantly greater risk of mortality (Table 5) included: male gender (RR 1.55), unemployment

Table 4 Observed and expected deaths and SMRs in subjects in the local mental health register by age groups, gender and diagnoses (years 2006–2015)

	Obs	Exp	SMR	CI 95%
Male				
15–44	43	4.2	10.3**	(7.2–13.4)
45–64	138	37.1	3.7**	(3.1–4.3)
65+	368	223.4	1.6**	(1.5–1.8)
Female				
15–44	22	2.6	8.3**	(4.8–11.8)
45–64	104	30.8	3.4**	(2.7-4.0)
65+	473	283.0	1.7**	(1.5–1.8)
Male				
Neuroses	211	104.1	2.0**	(1.8–2.3)
Bipolar disorders	60	58.5	1.0	(0.8–1.3)
Schizophrenia and other psychoses	48	25.3	1.9**	(1.4–2.4)
Personality disorders	54	18.6	2.9**	(2.1–3.7)
Intellectual disabilities and organic psych conditions	134	40.3	3.3**	(2.8–3.9)
Substance abuse and dependence	19	3.3	5.7**	(3.2–8.3)
Other diagnoses not yet classified	23	9.3	2.5**	(1.5–3.5)
Female				
Neuroses	226	144.9	1.6**	(1.4–1.8)
Bipolar disorders	114	77.8	1.5**	(1.2–1.7)
Schizophrenia and other psychoses	64	48.7	1.3	(1.0-1.6)
Personality disorders	44	17.8	2.5**	(1.7–3.2)
Intellectual disabilities and organic psych conditions	132	46.2	2.9**	(2.4–3.4)
Substance abuse and dependence	4	1.1	3.7	(0.1–7.3)
Other diagnoses not yet classified	15	12.3	1.2	(0.6–1.8)

Obs observed deaths, *Exp* expected deaths

**$P < 0.001$

(i.e., "unemployed, retired, disabled, student or housewife") (RR 1.67), low education (i.e., "primary or no qualification") (RR 1.31) and civil status (i.e., "unmarried, divorced, widower") (RR 1.31).

Discussion and conclusions

Despite progressive increases in life expectancy in the general population, the mortality gap of people suffering from mental illness has gradually widened: this is true for a large number of psychopathological conditions [1]. Even in countries with a comprehensive, accessible welfare system, with an overall high quality of public health services, the risk of mortality from cardiovascular disease in people with severe mental illness has risen by five times for men and three times for women during the last decades as compared to general population [24]. The increase in mortality risk for people with mental illness is even larger when looking at younger age groups.

Our study confirms these data: people with mental disorders have higher SMR than other members of the general population. A major concern is that the overall higher risk of mortality was observed in the younger age group: the 15–44 age group showed the highest SMR: 9.2 (versus 2.9 of 45–64 group, and 1.4 of 65+ group). Suicide rates found in younger patients were extremely elevated compared to their peers (SMR: 25.3). Increased mortality in the younger population was more pronounced in individuals with substance use disorders, personality disorders and intellectual disabilities. These findings confirm that young people suffering from mental illness present highest relative risk of mortality [1].

In terms of SMR by cause of death our sample showed a smaller increase of risk for cardiovascular diseases (SMR: 1.3) as compared with previous studies: [6, 25]. However, cardiovascular risk found in our sample was particularly high in younger subjects (SMR: 6.4). This is consistent with Osborn et al. [26] and Foley et al. [27]. The lower SMR found in our sample might be explained, at least in part, by the relatively high prevalence of patients with diagnosis of neuroses (52.4% of the sample), a diagnostic group whose lifestyle is generally less pervasively affected by unhealthy behaviours and less exposed to antipsychotic medications iatrogenic effects.

There is broad consensus regarding increased mortality for cancer in the population suffering from mental illness,

Table 5 Relative risk (RR) by gender, diagnoses, qualification, marital status, occupation and housing status—Poisson regression analyses

Variables	RR	95% CL RR	Pr > χ^2
Age at entry in the cohort	1.06	(1.05; 1.07)	< 0.0001
Gender			
Male	1.55	(1.38; 1.75)	< 0.0001
Female (ref)	1.00	–	–
Diagnoses			
Substance abuse and dependence	4.00	(2.38; 6.73)	< 0.0001
Personality disorders	2.75	(1.89; 4.00)	< 0.0001
Neurosis	1.52	(1.09; 2.12)	0.0137
Intellectual disabilities	2.74	(1.94; 3.86)	< 0.0001
Schizophrenia and other psychoses	2.29	(1.58; 3.31)	< 0.0001
Bipolar disorders	1.65	(1.16; 2.34)	0.0049
Other diagnoses not yet classified (ref)	1.00	–	–
Qualification			
Primary or no qualification	1.31	(1.14; 1.51)	0.0002
Higher qualification (ref)	1.00	–	–
Marital status			
Unmarried, divorced or widower	1.31	(1.14; 1.50)	< 0.0001
Married or in partnership (ref)	1.00	–	–
Occupation			
Unemployed, retired, disabled, student, housewife	1.67	(1.35; 2.07)	< 0.0001
Occupied (ref)	1.00	–	–
Housing status			
Live alone, residential accommodation, homeless	0.90	(0.78; 1.04)	0.1326
Subjects living with family or partner (ref)	1.00	–	–

although with some variability with respect to type and site of cancer [28, 29]. Several factors have been associated with the risk for developing malignancies and receiving late diagnosis: unhealthy lifestyle (e.g., smoking, substance/alcohol abuse), underestimation of somatic morbidity, such as blood-borne viral infections (e.g., hepatitis B or C) [30] and interpreting physical complaints as "psychosomatic" by health professionals. As a matter of fact, a comparative meta-analysis showed significant disparity, with regards to rates of mammography screening, in women with mental disorders compared to the general population [31]. Not least, physical problems may be underreported by individuals with mental illness [32]. Cancer SMRs in our sample, were consistent with available data, representing the most frequent natural cause of death (28.1%); interestingly, the analysis showed highest SMR for cancer in younger subjects.

A diagnosis of substance abuse disorder showed the highest SMR among all diagnostic groups; SMRs were higher both in the whole sample and in each age group with the only exception of the 65+ subjects. Non-accidental poisoning, traffic related-accidents and suicide are highly represented in people with drug abuse, despite they may be under-estimated (e.g., drug intoxications might be reported as "overdose" and therefore may not appear as suicide attempts in the statistics) [33]. People suffering from substance abuse are 10 times more likely to commit suicide in case of alcohol abuse and 14 times higher in case of intravenous drug use compared to the general population [34]. Up to 40% of patients requesting access to drug abuse services have been reported as having a history of suicide attempts.

Our results make the case that attention and prevention efforts should deal with the high mortality rate observed in the 15–44 age group with personality disorders as well as intellectual disabilities/organic disorders. Large population studies, recently provided evidence of substantially increased SMRs across all clusters of personality disorders [35] along with sub-optimal assessment of physical health [36]. Less information is available regarding the health status of people with intellectual disabilities [37, 38]. This requires more systematic investigation, as this group shows a trend toward premature and avoidable deaths [39].

Relative risk of mortality was significantly elevated in subjects outside the labour market, who were unmarried, divorced, or widowed and with low levels of education. These findings could be interpreted as the negative additional effect exerted by social determinants of mental health on mortality risk. However, it is not possible to rule out a reversal causality, i.e., the conditions considered (marital status, unemployment, low education) being an effect, rather than a consequence, of mental illness.

There are some limitations of this study. Our sample was represented by subjects in the register of general psychiatric services and did not include individuals whose conditions were managed solely by general practitioners or by drug and alcohol services. This is likely to have resulted in underestimating the scale of the problem. Second, the use of medication was not included in the analysis. Controversy is ongoing regarding the impact of psychotropic medication on mortality in people with mental illness, especially concerning antipsychotic medication. While there is increasing evidence suggesting a protective effect of antipsychotic and antidepressants on mortality in people suffering from severe mental illness [40], for schizophrenia in particular [41, 42], it is widely acknowledged that several psychotropic treatments, with particular reference to antipsychotic drugs, increase the incidence of metabolic disturbances linked to the risk of cardiovascular complications [43, 44].

The mortality gap between people suffering from mental illness and the general population, as found in the current study, reinforces the notion of inequitable access to physical care for users of mental health services [45]. If the goal is indeed to reduce the mortality gap, equity of access to all levels of care and intervention (acute and long-term care, preventive medicine and health promotion) should be guaranteed. The available evidence, instead, suggests that interventions such as smoking cessation, which are effective also in people suffering from severe mental illness are not given the appropriate priority and resources in clinical practice [46, 47].

Our findings confirm the importance of overcoming institutional barriers to equitable access, particularly in younger subjects, who are at very substantial higher risk of mortality compared to their peers. In addition, the very high mortality excess found in people with substance use disorders, demands the rethinking of policies addressing the way the health system (and, possibly, society as a whole) interact with this vulnerable group.

At policy level, to arrest the excess mortality of people suffering from mental illness, it seems necessary to broaden the availability of preventive medicine and achieve a better integration between mental health and primary care services. These interventions must be universal and include individuals with high mortality risk. In our opinion, this is the only way to overturn the ongoing disparities faced by people with mental illness.

Compliance with ethical standards

Conflict of interest The authors declare that there is no conflict of interest regarding the publication of this paper.

Ethics statement Ethical approval was not required as this study was performed as secondary data analysis on anonymous datasets.

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