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Risk factors for mortality in patients admitted to a psychiatric acute ward: A prospective cohort study

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Abstract

Introduction: Associations between psychiatric disorders and mortality have been extensively studied, but limited evidence exists regarding influence of clinical characteristics on mortality risk, at the time of acute psychiatric hospitalization.

Methods: A prospective total-cohort study included all patients consecutively admitted to Haukeland University Hospital's psychiatric acute ward in Bergen, Norway between 2005 and 2014 ($n = 6125$). Clinical interviews were conducted at the first admission within the study period, and patients were subsequently followed for up to 15 years in the Norwegian Cause of Death Registry. Competing risks regression models were used to investigate associations between clinical characteristics at first admission and the risk of natural and unnatural death during follow-up.

Results: The mean age at first admission and at time of death was 42.5 and 62.8 years, respectively, and the proportion of women in the sample was 47.2%. A total of 1381 deaths were registered during follow-up, of which 65.5% had natural, 30.4% unnatural, and 4.1% unknown causes. Higher age, male sex, unemployment, cognitive deficits, and physical illness were associated with increased risk of natural death. Male sex, having no partner, physical illness, suicide attempts, and excessive use of alcohol and illicit substances were associated with increased risk of unnatural death.

Conclusion: Psychiatric symptoms, except suicide attempts, were unrelated to increased mortality risk. In the endeavor to reduce the increased mortality risk in people with mental disorders, focus should be on addressing modifiable risk factors linked to physical health and excessive use of alcohol and illicit substances.

KEYWORDS
indicated prevention, mental disorders, mortality, universal prevention

1 | INTRODUCTION

Mental disorders have a significant impact on mortality rates, with some studies showing shortened life expectancy by as much as 10–20 years in the most severe mental disorders.[1–4] A comprehensive review and meta-analysis by Walker et al.[3] found that mental disorders contribute to 14% of deaths globally, or about 8 million deaths annually. Despite a growing understanding of its underpinnings, the increased mortality risk remains high, and has even increased over the last decades.[4]

Physical illness is the leading cause of death in people with mental disorders, accounting for approximately 70%–80% of deaths,[3,4] which translates into a mortality risk two to three times higher than in the general population.[5] Several factors working in concert seem to underlie this increased risk.[6–9] People with severe mental illness (SMI) have an increased risk of cardiovascular disease and diabetes due to both a putative genetic vulnerability,[6,7] and a lifestyle with physical inactivity, unhealthy diet and higher prevalence of substance abuse and smoking.[8,10,11] SMI has also been linked to lower levels of physical health literacy,[8] and psychiatric symptoms, impaired cognition and problems with activities of daily living, have been associated with increased mortality.[12,13] Moreover, the follow-up care of physical illness offered to people with mental disorders is often inadequate.[14,15] Compared to the general population, people with severe mental disorders have lower utilization of specialist somatic health care, lower frequency of undergoing invasive cardiac procedures, fewer visits to a general practitioner and lower tendency of having prescribed somatic medication.[16,17] The use of psychotropic drugs, particularly antipsychotics, may also contribute to increased mortality risk, as these drugs have been linked to a higher risk of myocardial infarction, cerebrovascular events and sudden cardiac death.[9,18,19] However, non-adherence to antipsychotic drugs has been associated with increased risk of death in patients with schizophrenia,[20–22] suggesting that lifestyle factors and reduced capacity for health promoting behavior associated with both untreated and more prolonged psychotic diseases, may be of greater importance with regard to mortality risk than the long term- adverse effects of antipsychotic drugs.

Unnatural deaths, such as suicides, accidents, and overdoses, are significantly more common in people with mental disorders, compared to the general population. A large register study by Nordentoft et al.[5] found that the mortality rates from external causes were in the range from three to 77 times greater in this population, depending on gender, psychiatric diagnosis and the external cause of death. Substance use contributes significantly to unnatural deaths in patients with mental disorders.[5,23,24] Mental disorders and substance use often co-occur, and

Significant outcomes

- Psychiatric symptoms were generally not associated with increased mortality risk in patients admitted to a psychiatric acute ward.
- Many risk factors for mortality are modifiable, including physical illness and excessive use of alcohol and illicit substances.

Limitations

- The study lacked information about well-known risk factors for natural death, such as smoking habits, blood pressure, cholesterol, and body mass index.
- Psychiatric symptoms, function and addiction were assessed using crude measurements.

mental disorders are associated with increased risk of fatal opioid overdoses.[25] Furthermore, many mental disorders are well-known risk factors for suicide.[26] Self-harm has proved to be the most important predictor of suicide,[27,28] but psychiatric symptoms such as depression, hallucinations and delusions are also associated with increased risk of suicide.[26,29,30] Moreover, people with mental disorders are at increased risk of accidents and being victims of violent crime.[31,32] This may be due to increased impulsivity, disorganized thoughts, and poor problem-solving skills, which are common and can impair judgment and decision-making, but it may also be associated with socio-economic variables, increasing the likelihood of living in environments with increased risk of violence exposure.[31,33]

Taken together, the mortality risk in people with mental disorders remains high due to various factors.[1,3,4] It is therefore critical to identify modifiable risk factors associated with premature death in this population. Some psychiatric disorders, such as alcohol and drug abuse, dementia, and psychotic disorders, are known to be associated with a greater risk of death.[3,34] However, psychiatric diagnoses may not have sufficient precision alone to serve as reliable predictors of risk, as different combinations of symptoms may underlie any particular diagnosis, and many patients fulfill criteria for more than one diagnosis at the same time. A complimentary approach would be to also focus on the symptoms and functioning independently of diagnostic categories, and to investigate their associations to mortality risk. This might redirect focus from diagnoses alone to clinical phenomena in an attempt to increase the precision in risk reducing interventions. Accordingly, in this study, we aimed to

investigate the impact of psychiatric symptoms, physical illness, addiction, medication non-adherence, cognition and problems with relationships, housing and activities of daily living on the risk of natural and unnatural death in patients acutely admitted to a psychiatric ward.

2 | MATERIALS AND METHODS

2.1 | Sample and procedure

This study is based on the Suicidality in Psychiatric Emergency Admissions (SIPEA-II)-study.[35] A total of 7000 patients consecutively admitted to the psychiatric emergency ward at Haukeland University Hospital in Bergen, Norway between May 1st 2005 and June 15th 2014 were included in the study. The hospital serves approximately 95% of all patients requiring acute psychiatric hospitalization from a catchment area of around 400,000 people. All patients admitted to the psychiatric acute ward during the study period were included in the study. Patients were only excluded from the analyses if there was a chance that their possible death would not be recorded in the Norwegian death registry. This applied to individuals without a personal identification number ($n = 31$) and non-Norwegian citizens ($n = 844$) since deaths occurring abroad are not recorded in the Norwegian registry, and an unknown proportion of these patients left Norway after their hospitalization. Thus, the final sample included 6125 patients.

Clinical interviews were conducted at the first (index) admission during the study period, and at every following admission during the study period. However, only the assessments at index admission were the focus of the present study. The clinical interviews were carried out by healthcare professionals working in the psychiatric acute ward at the time of the patient admissions. To ensure accuracy and consistency of the clinicians' assessments, those involved received training in the rating scales used. After inclusion, patients were followed for up to 15 years in the Norwegian Cause of Death Registry. Data on deaths and causes of death were collected retrospectively from the Norwegian Cause of Death Registry for all deaths occurring before May 31st 2020.

2.2 | Measurements

The clinical interviews included recording of socio-demographic factors, such as age, sex, marital status, employment status, education level, and living arrangement. Furthermore, the clinical interviews included assessments of psychiatric symptoms, physical illness,

addiction, medication non-adherence, cognitive deficits and problems with relationships, housing, and activities of daily living.

The Health of the Nation Outcome Scales (HoNOS) was used in the assessment.[36] The HoNOS is a clinician-rated instrument that measures symptoms and function on a five-point scale from 'no problems' to 'severe to very severe problems'. HoNOS items 1, 4, 5, 6 and 7 assess overactive, aggressive, disruptive, and agitated behavior (item 1), cognitive problems (item 4), physical illness or disability problems (item 5), problems with hallucinations and delusions (item 6), and problems with depressed mood (item 7). HoNOS items 9–11 assess problems with relationships (item 9), problems with activities of daily living (item 10), and problems with living conditions (item 11). The scales for the items are presented in the Appendix S1 (supplementary item 4).

In the evaluation of suicidal ideation, suicide attempts, and non-suicidal self-harm, the clinical interview employed questions with binary (yes/no) answers. These inquired whether, prior to admission, patients had experienced any suicidal ideation or engaged in self-harm, distinguishing between acts with a clear intent to die (suicide attempt) and acts with no or low intent to die (non-suicidal self-harm).

In order to measure the patients' use of alcohol and drugs, the Alcohol Use Scale (AUS) and Drug Use Scale (DUS) were used.[37] The AUS and DUS are single-item clinician-rated screening tools of alcohol and drug use, measuring use of alcohol and illicit substances the last 6 months on a 5-point scale from no problems to extremely severe problems. The clinical interview also included retrospective questions regarding adherence to psychotropic medication 2 weeks prior to the admission. The adherence was classified as either "in accordance with the prescription," "partly in accordance with the prescription" or "not in accordance with the prescription."

Deaths were categorized as natural or unnatural based on the European Shortlist for Causes of Death.[38] Unnatural causes of death included suicide, accidents, accidental poisoning, and homicide, while natural deaths included all deaths caused by somatic diseases.

2.3 | Statistical analysis

Fine-Gray competing risks regression models[39] were used to analyze the associations between clinical characteristics at index admission and the risk of natural and unnatural death, which were defined as the competing endpoints of the study. Both multivariate and univariate analyses were conducted. The variables in the models included both clinical characteristics (physical illness or

TABLE 1 Baseline characteristics of the sample at index admission (n = 6125)

	N	Percent
Sex		
Male	3231	52.8%
Female	2894	47.2%
Education (n = 5565)		
Lower education	4552	81.8%
University or college	1013	18.2%
Employment status (n = 5936)		
Employed	1199	20.2%
Receiving social benefits	4737	79.8%
Living arrangements (n = 6077)		
House or apartment	4487	73.8%
Living in an institution	1590	26.2%
Marital status		
Married or partner	1633	26.7%
No partner	4492	73.3%
ICD-10 diagnoses at index discharge (more than 1 is possible)		
F00–F09 = Organic mental disorder	370	6.0%
F10.0–F19.9 = Substance use disorder	1151	18.8%
F20–F29 = Psychotic disorder	1110	18.1%
F30–F39 = Affective disorder	2568	41.9%
F40–F48 = Neurotic disorder	1266	20.7%
F60–F69 = Disorders of adult personality and behavior	379	6.2%
	Mean	**(Range)**	**SD**
Age at index admission	42.5	(16–101)	18.1

Note: If values are missing, the total *n* is presented.

Abbreviations: *N* = Number; SD = Standard deviation.

disability problems, cognitive problems, problems with hallucinations and delusions, problems with depressed mood, suicidal ideation, suicidal attempt, non-suicidal self-harm, overactive, aggressive, disruptive, and agitated behavior, problems with relationships, problems with activities of daily living, and problems with living conditions), as well as socio-demographic factors (age, sex, marital status, employment status, education level, and living arrangement). Sensitivity analyses which included psychiatric ICD-10 diagnoses[40] (organic mental disorder, substance use disorder, psychotic disorder, affective disorder, neurotic disorder, and disorder of adult personality and behavior) were also conducted. For the variables that had missing values, the missing portion of the total sample are listed in Table S1. Missing data were handled through multiple imputation, under the missing at random (MAR) assumption.[41] A total of 20 datasets were generated in the imputation model. Multicollinearity among the variables was explored.

The statistical software *R version 4.0.2* (https://www.r-project.org/) and the packages *survival* and *tidycmprsk* were used for the statistical analyses.

3 | RESULTS

The clinical and socio-demographic characteristics of the study sample are presented in Table 1. On average, patients were followed for a period of 9.5 years. During follow-up, 1381 (22.5%) patients died. Of these, 904 (65.5%) deaths were due to natural causes, 420 (30.4%) due to unnatural causes, and the causes of death were unknown for 57 (4.1%) patients. The number of natural and unnatural deaths per 100,000 patient years were 1551 and 721, respectively. Table 2 provides information on the causes of death and age at the time of death. The results of the competing risks models are presented in Tables 3 (Natural death) and 4 (Unnatural death).

TABLE 2 Causes and time of death.

		N	Percent
Died during follow-up period		1381	22.5[a]
Natural causes of death		904	65.5[b]
Neoplasms		185	13.4[b]
Cardiovascular disease		246	17.8[b]
Diseases of the respiratory system		126	9.1[b]
Dementia		136	9.8[b]
Other causes		211	15.3[b]
Unnatural causes of death		420	30.4[b]
Suicide		185	13.4[b]
Accidental poisoning		176	12.7[b]
Other accidents		56	4.1[b]
Homicide		3	0.2[b]
Unknown cause of death		57	4.1[b]

	Mean	(Range)	SD
Age at time of death			
Overall	62.8	(18.0–104.2)	20.0
F00–F09 = Organic mental disorder	79.7	(25.2–104.2)	10.9
F10.0–F19.9 = Substance use disorder	48.9	(18.0–89.9)	16.5
F20–F29 = Psychotic disorder	63.0	(19.3–100.3)	18.9
F30–F39 = Affective disorder	63.0	(18.7–96.9)	18.5
F40–F48 = Neurotic disorder	56.0	(19.5–96.9)	19.3
F60–F69 = Disorders of adult personality and behavior	48.5	(22.3–91.8)	17.6

[a]Percent of total ($n = 696$).
[b]Percent of deceased ($n = 68$).

Multicollinearity among the variables did not pose a significant issue, as no high levels of linear dependency between each variable and all other variables were found. The highest multivariate prediction explained approximately 30% of the variance.

3.1 | Natural death

Statistically significant positive associations were found in the multivariate analysis between age, cognitive problems and physical illness and the risk of natural death. For age, the mortality risk increased by 7% per year. Physical illness including disability problems was associated with 25% increased risk of natural death. Cognitive problems were linked to 14% greater risk of natural death. On the other hand, female sex and being employed were associated with 32%, and 48% lower risks of natural death, respectively. Moreover, problems with depressed mood, non-suicidal self-harm and suicide attempt prior to index admission

were associated with 10%, 36% and 32% lower risk of natural death, respectively.

No statistically significant associations were found between marital status, education level, living arrangement, problems with hallucinations and delusions, suicidal ideation, overactive, aggressive, disruptive, and agitated behavior, problems with relationships, problems with activities of daily living, problems with living conditions, excessive use of alcohol and illicit substances, or non-adherence to psychotropic medication use, and the risk of natural death.

The multivariate sensitivity analysis that included psychiatric ICD-10 diagnoses, showed the same results as the main analysis (Table S2). Neurotic disorder was associated with 27% lower risk of natural death in the multivariate sensitivity analysis. No statistically significant associations were found between organic mental disorder, substance use disorder, psychotic disorder, affective disorder, and disorder of adult personality and behavior, and the risk of natural death.

TABLE 3 Risk factors for natural deaths (N = 904).

	Multivariate analysis			Univariate analyses		
	AHR	95% CI	p-Value	HR	95% CI	p-Value
Socio-demographic characteristics						
Age, per year	1.07	(1.07–1.08)	<0.01	1.09	(1.08–1.09)	<0.01
Female sex (male sex = 1)	0.68	(0.58–0.79)	<0.01	0.91	(0.80–1.04)	0.17
Marital status (no partner = 1)	1.02	(0.86–1.22)	0.79	1.48	(1.29–1.70)	<0.01
University/college education (no higher education = 1)	1.03	(0.83–1.23)	0.78	1.14	(0.95–1.35)	0.15
Employed (not employed = 1)	0.52	(0.37–0.72)	<0.01	0.18	(0.13–0.24)	<0.01
Living arrangement (no independent living in house or apartment = 1)	0.87	(0.70–1.09)	0.22	1.13	(0.97–1.32)	0.12
Symptoms and daily functioning						
Physical illness or disability problems (no problems = 1)	1.25	(1.17–1.34)	<0.01	1.80	(1.71–1.89)	<0.01
Cognitive problems (no problems = 1)	1.14	(1.06–1.22)	<0.01	1.87	(1.77–1.97)	<0.01
Problems with hallucinations and delusions (no problems = 1)	1.00	(0.94–1.07)	0.95	1.19	(1.13–1.25)	<0.01
Problems with depressed mood (no problems = 1)	0.90	(0.84–0.97)	<0.01	0.74	(0.70–0.79)	<0.01
Suicidal ideation (no suicidal ideation = 1)	0.89	(0.72–1.10)	0.29	0.61	(0.50–0.75)	<0.01
Suicide attempt (no suicide attempts = 1)	0.68	(0.47–0.99)	0.04	0.44	(0.30–0.63)	<0.01
Non-suicidal self-harm (no non-suicidal self-harm = 1)	0.64	(0.42–0.97)	0.03	0.36	(0.25–0.53)	<0.01
Overactive, aggressive, disruptive and agitated behavior (no problems = 1)	1.01	(0.94–1.09)	0.71	1.22	(1.15–1.29)	<0.01
Problems with relationships (no problems = 1)	1.00	(0.92–1.08)	0.93	1.11	(1.04–1.18)	<0.01
Problems with activities of daily living (no problems = 1)	1.08	(0.99–1.18)	0.06	1.46	(1.38–1.55)	<0.01
Problems with living conditions (no problems = 1)	0.96	(0.89–1.03)	0.27	1.04	(0.98–1.11)	0.16
Excessive use of alcohol (no = 1)	1.07	(0.98–1.16)	0.14	0.79	(0.72–0.87)	<0.01
Excessive use of illicit substances (no = 1)	0.89	(0.78–1.01)	0.07	0.60	(0.54–0.67)	<0.01
Non-adherence to psychotropic medications (no = 1)	1.08	(0.89–1.30)	0.44	1.00	(0.83–1.20)	0.97

Abbreviation: AHR, adjusted hazard ratio.

3.2 | Unnatural death

Suicide attempt prior to the index admission was associated with a 62% increased risk of unnatural death in the multivariate analysis. Furthermore, increasing use of alcohol and illicit substances was statistically significantly associated with increased risk of unnatural death. Specifically, excessive use of alcohol was associated with a 15% higher risk of unnatural death, while excessive use of illicit substances was associated with 47% increased risk. Moreover, problems with physical illness or disability were associated with 11% increased risk of unnatural death. On the other hand, female sex was associated with 30% lower risk of unnatural death, and having a partner was associated with a 35% lower risk, compared to not having a partner. Furthermore, compared to no problems, problems with living conditions and overactive, aggressive, disruptive, and agitated behavior, were

associated with 12% and 14% lower risk of unnatural death, respectively.

No statistically significant associations were found between age, education level, employment status, living arrangement, cognitive problems, problems with hallucinations and delusions, problems with depressed mood, suicidal ideation, non-suicidal self-harm, problems with relationships or activities of daily living, or non-adherence to psychotropic medication use, and the risk of unnatural death.

The multivariate sensitivity analysis that included psychiatric ICD-10 diagnoses (Table S3), showed the same results as the main analysis, except for physical illness that was not significantly associated with increased risk of unnatural death in the sensitivity analysis. Organic mental disorder was associated with 83% higher risk of unnatural death in the multivariate sensitivity analysis. No statistically significant associations were found between substance use

TABLE 4 Risk factors for unnatural death ($N = 420$).

	Multivariate analysis			Univariate analyses		
	AHR	95% CI	p-Value	HR	95% CI	p-Value
Socio-demographic characteristics						
Age, per year	1.00	(0.99–1.01)	0.61	0.99	(0.99–0.99)	0.01
Female sex (male sex = 1)	0.70	(0.57–0.87)	<0.01	0.59	(0.48–0.72)	<0.01
Marital status (no partner = 1)	0.65	(0.49–0.85)	<0.01	0.56	(0.43–0.72)	<0.01
University/college education (no higher education = 1)	1.04	(0.78–1.40)	0.79	0.76	(0.57–1.01)	0.06
Employed (not employed = 1)	0.92	(0.69–1.22)	0.55	0.79	(0.69–1.02)	0.07
Living arrangement (no independent living in house or apartment = 1)	0.96	(0.76–1.22)	0.76	0.79	(0.64–0.97)	0.03
Symptoms and daily functioning						
Physical illness or disability problems (no problems = 1)	1.11	(1.01–1.24)	0.04	1.05	(0.95–1.16)	0.32
Cognitive problems (no problems = 1)	0.96	(0.85–1.09)	0.57	0.96	(0.87–1.06)	0.44
Problems with hallucinations and delusions (no problems = 1)	1.01	(0.93–1.10)	0.73	0.97	(0.90–1.04)	0.42
Problems with depressed mood (no problems = 1)	1.04	(0.95–1.15)	0.39	1.07	(0.99–1.16)	0.07
Suicidal ideation (no suicidal ideation = 1)	1.11	(0.85–1.45)	0.46	1.10	(0.86–1.40)	0.44
Suicide attempt (no suicide attempts = 1)	1.62	(1.15–2.28)	0.01	1.75	(1.29–2.37)	<0.01
Non-suicidal self-harm (no non-suicidal self-harm = 1)	1.26	(0.88–1.81)	0.21	1.24	(0.89–1.73)	0.20
Overactive, aggressive, disruptive and agitated behavior (no problems = 1)	0.86	(0.77–0.96)	0.01	0.92	(0.84–1.01)	0.07
Problems with relationships (no problems = 1)	1.05	(0.94–1.17)	0.39	1.08	(0.98–1.18)	0.11
Problems with activities of daily living (no problems = 1)	1.00	(0.89–1.12)	0.98	1.02	(0.93–1.13)	0.63
Problems with living conditions (no problems = 1)	0.88	(0.79–0.96)	0.01	1.04	(0.95–1.13)	0.38
Excessive use of alcohol (no = 1)	1.15	(1.06–1.26)	<0.01	1.35	(1.24–1.46)	<0.01
Excessive use of illicit substances (no = 1)	1.47	(1.36–1.59)	<0.01	1.50	(1.40–1.60)	<0.01
Non-adherence to psychotropic medications (no = 1)	1.10	(0.84–1.43)	0.50	1.16	(0.89–1.52)	0.26

Abbreviation: AHR, adjusted hazard ratio.

disorder, psychotic disorder, affective disorder, neurotic disorder, and disorder of adult personality and behavior, and the risk of unnatural death.

4 | DISCUSSION

In this cohort of 6125 patients consecutively admitted to an acute psychiatric ward, we identified risk factors associated with natural and unnatural death. We found that higher age, male sex, unemployment, cognitive deficits, and physical illness were associated with increased risk of natural death. Male sex, not having a partner, physical illness, suicide attempts, and excessive use of alcohol and illicit substances were associated with increased risk of unnatural death. Apart from suicide attempts, psychiatric symptoms were not associated with an increased risk of mortality in mental disorders.

The rates of natural and unnatural deaths per 100,000 patient years in our study were 1551 and 721, respectively. In comparison, a meta-analysis by Swaraj et al.[42] reported lower figures; 1128 deaths per 100,000 patient years for natural deaths and 479 deaths per 100,000 patient years for unnatural deaths. This discrepancy may arise from the fact that Swaraj et al. focused on in-patient psychiatric patients, whereas our study specifically examines acute psychiatric inpatients, who are anticipated to have higher morbidity and mortality rates. The mean age at the time of death in this population of patients acutely admitted to a psychiatric ward was merely 62.8 years, a figure notably below that of the general population. However, this number is expected to increase slightly when all included patients have died. This finding aligns with previous research on mortality in mental disorders, which has reported a shortened life expectancy by as much as 10–20 years in the most severe disorders.[1–4] This

study extends on previous studies by not only demonstrating a reduced mean age at the time of death, but also by identifying risk factors for both natural and unnatural deaths within this population.

4.1 | Natural death

In accordance with what we would expect in the general population, the results showed that higher age, physical illness, and cognitive problems were associated with increased risk of natural death. Older individuals with physical illness or cognitive impairment may have difficulties with activities of daily living such as preparing meals, managing medications, seeking medical care, or maintaining personal hygiene, which may increase the risk of somatic illness and death.[12,43,44] Furthermore, we found an association between male sex and increased risk of natural death, which is in accordance with previous studies reporting higher mortality risk, and in particular higher cardiovascular mortality risk in men than in women with mental disorders.[23,45] An association between being employed and reduced risk of natural death was also found. This is not surprising, as having a job is often an indicator of good health, and previous studies have indicated that unemployment is associated with increased risk of death.[46,47]

A high number of previous studies have described how excessive use of alcohol and illicit substances are associated with increased risk of somatic diseases and death.[10,48–52] In contrast to these studies, we did not find associations between excessive use of alcohol or illicit substances and increased risk of natural death. However, it is important to keep in mind that we adjust for both physical disease and use of alcohol and illicit substances in the multivariate analysis. Accordingly, a correct interpretation of our results could be that when the use of alcohol or illicit substances increases in patients with otherwise similar risk factors, including similar level of physical disease, the increased use of alcohol or illicit substances is not associated with increased risk of natural death. Thus, our results suggest that the level of physical disease is a better predictor for natural death than excessive use of alcohol and illicit substances.

While depression is often associated with increased risk of death,[53] we found that depressed mood, suicidal attempts, and non-suicidal self-harm were associated with lower risk of natural death in the analysis. The multivariate sensitivity analysis that included diagnoses, also showed that neurotic disorder was associated with lower risk of natural death. Similar findings have been reported in a study by Hayes et al.,[54] where depression was associated with lower mortality in patients with schizoaffective disorders. This could indicate that, when studying a group of patients acutely admitted to a psychiatric ward, depression and neurotic disorder may actually be markers of less severe illness, as they represent the least severe forms of mental illness that could result in an acute psychiatric admission. Another hypothesis could be that individuals with depression or neurotic disorder may be more likely to seek medical attention and engage in healthy behaviors, as health concerns are common in these groups.[55]

As expected, the results in the univariate analyses were quite different from those in the multivariate analysis. Age and physical illness are important risk factors for natural death, and results of analyses that do not adjust for these factors must be cautiously interpreted. For instance, having a partner, which tends to be more prevalent among older individuals, are associated with increased risks of natural death in the univariate analyses, but not in the multivariate analysis that adjust for age and other risk factors.

4.2 | Unnatural death

We found that male sex was associated with increased risk of unnatural death. This is in line with previous studies reporting that men with mental disorders are at higher risk of death caused by suicide, accidents, and overdoses, compared to women.[23] Moreover, an association was found between suicide attempts prior to index admission and increased risk of unnatural death. This finding aligns with previous research linking suicide attempts to an increased risk of suicide.[27,28,56,57] Consistent with other studies that have identified physical illness as a key risk factor for suicide,[28,54,56,58] we found that problems with physical illness or disability were associated with a higher risk of unnatural death. Previous studies have also highlighted the protective effect of having a partner.[59,60] A meta-analysis by Kyung-Sook et al.[61] showed that the suicide risk is higher in non-married individuals. Our results are in line with this study, as we found an association between having a partner and reduced risk of unnatural death.

It is well documented that excessive use of alcohol or illicit substances is linked to an increased risk of unnatural death,[10,52] as these substances can lead to fatal overdoses, which are common causes of unnatural death in individuals with mental disorders.[23] Additionally, the use of alcohol or illicit substances has been linked to an increased risk of accidents and suicide.[50,52] Our results replicate these findings, as we found that excessive use of alcohol and illicit substances was associated with an increased risk of unnatural death.

As opposed to previous studies that have highlighted aggression as an important risk factor for suicide,[62] we found that aggressive behavior was associated with a lower risk of unnatural death. Interestingly, we also found that problems with living conditions were associated with reduced risk of unnatural death. Potential explanations could include that homeless patients may stay longer in the hospital before being discharged, and patients with aggressive behavior may tend to receive longer inpatient treatment to prevent harmful actions. Hence, it is possible that longer inpatient treatment may have a protective effect on the risk of unnatural death.

The multivariate sensitivity analysis that adjusted for diagnoses showed that organic mental disorder was associated with increased risk of unnatural death. While the exact mechanism remains uncertain, a plausible explanation is that individuals with organic mental disorders, including dementia, frequently experience cognitive impairment and diminished self-care capabilities. This, in turn, may render them more vulnerable to accidents, thereby increasing their risk of unnatural death.

4.3 | Strengths and limitations

One of the strengths of our study is the large sample size of over 6000 patients with up to 15 years of follow-up. As a total-cohort study, patients were included regardless of their ability to consent. Accordingly, even severely ill patients without the capacity to consent and cooperate, were included. The sample is therefore highly representative of patients discharged from hospital after an acute psychiatric admission. Additionally, the long follow-up period with an average of 9.5 years allows for comprehensive analyses of risk factors for natural and unnatural death. In contrast to registry-based studies, we had available and took into account many and well-described clinically relevant variables in the models. Hence, our findings provide valuable insights into the risk factors for death in patients admitted to a psychiatric acute ward. We are not aware of similar studies conducted in a consecutively included total-cohort with corresponding sample size and length of follow-up.

We did not have sufficient information on several other potential risk factors for natural death, such as smoking habits, blood pressure, cholesterol, body mass index, somatic diseases, the patients' use of health care services or prescription of psychotropic drugs. However, we did include "Physical illness or disability problems" (HoNOS item 5) as a variable in our analyses. This variable includes illness or disability from any cause that limits or prevents movement, or impairs sight or hearing, or otherwise interferes with personal functioning.[36]

Nevertheless, residual confounding will always be a potential limitation in studies like this. In our statistical models, we analyzed values of the HoNOS items, AUS and DUS, measured at index admission, and accordingly, we did not analyze how change over time in these clinical characteristics affects the mortality risk. The HoNOS, AUS, and DUS are crude measurements, and their accuracy may be further compromised when assessed solely during an acute admission when not all relevant information is readily available. Regarding the clinical interviews, precise data on the number of clinicians involved and the interrater reliability is not available. Furthermore, we had to exclude non-Norwegian patients, and our study is therefore representative for Norwegian patients acutely admitted to hospital only, but not for patients with a non-Norwegian background.

4.4 | Clinical implications

Psychiatric symptoms, with the exception of suicide attempts, were not associated with an elevated risk of mortality. Although indirect relationships cannot be ruled out, these findings suggest that psychiatric symptoms cannot serve as reliable predictors of death when analyzed at an admission. When a risk factor is prevalent and includes most members of the population, as in this case, it loses its ability to predict an outcome. Accordingly, our results indicate that, in a population with a very high symptom complexity and level, psychiatric symptoms and functioning should be evaluated within the framework of psychiatric diagnoses, and not independently of diagnostic categories.

Numerous studies have previously reported that certain psychiatric disorders, in particular substance use disorder and psychotic disorders, entail a higher mortality risk compared to others.[3,34] This observation is also strongly suggested in the present material, as the age at time of death exhibits significant variations across distinct psychiatric diagnoses (see Table 2). However, this pattern is not mirrored in the multivariate sensitivity analysis adjusted for psychiatric diagnosis. This discrepancy can be attributed to the adjustments made for a comprehensive set of factors, including symptoms, substance use, functional status, and sociodemographic characteristics. This theory is further strengthened by the significant associations observed between several diagnoses and the risk of natural and unnatural death in the univariate models.

Physical illness and excessive use of alcohol and illicit substances were associated with increased risk of both natural and unnatural death. Given the modifiable nature of these risk factors, the findings suggest potential

for prevention. However, it is important to underline that this study cannot conclude on any causal relations; it solely reports on associations between clinical characteristics and the risk of natural and unnatural death.

With a large and comprehensive sample, and up to 15 years of follow-up, the study is unique in an international context. The study identifies risk factors, some modifiable, associated with natural and unnatural death in patients admitted to a psychiatric acute ward. Notably, psychiatric symptoms, except for suicide attempts, were unrelated to increased mortality risk. Thus, in the endeavor to reduce the increased mortality risk in mental disorders, focus should be on addressing modifiable risk factors linked to physical health and excessive use of alcohol and illicit substances.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/acps.13657.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the Norwegian Social Science Data Service, the Norwegian Directorate of Health, and the Regional Committee for Medical Research Ethics (approval number REK 46004). Use of patient information without informed consent was authorized by the abovementioned instances.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.