Schizophrenia

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Increased mortality risk in people with schizophrenia in Lithuania 2001–2020

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The aim of this study was to assess mortality risk in people with schizophrenia in Lithuania from 2001 and 2020. Cause-specific and all-cause mortality risk among patients with schizophrenia was assessed using a retrospective cohort study design. The cohort identified all patients with schizophrenia diagnosis (ICD-10 code F20) who were admitted to the Vilnius Republican Psychiatric Hospital from 1 January, 2001 to December 31, 2020. Dates of death and emigration were obtained from the Central Population Register. The standardized mortality ratios (SMRs) were calculated by dividing the observed number of deaths among patients with schizophrenia by the expected number of deaths, calculated using the national rates. The final cohort included 7883 patients, with 2458 observed deaths. An increased all-cause mortality risk was found for both sexes (SMR = 1.96; 95% CI 1.88–2.04) compared to the general population. The most common cause-specific mortality risk was found for diseases of the circulatory system (SMR = 2.17; 95% CI 2.05–2.30). Other significant increases in cause-specific mortality risk were observed for infectious diseases, mental and behavioural disorders, diseases of the nervous system and respiratory system, diseases of the genitourinary system, as well as external causes. Patients with schizophrenia do not benefit from the health strategies that have led to reduced mortality in the general population. To close the mortality gap, smoking and alcohol cessation interventions, cardiovascular and cancer screening and monitoring, early diagnosis, and interventions for identified physical diseases should be regarded as imperative.

Schizophrenia (2025)11:7 ; https://doi.org/10.1038/s41537-024-00549-y

INTRODUCTION

Schizophrenia is a severe and chronic psychiatric disorder with often poor long-term outcomes[1]. People with schizophrenia are reported to have an elevated risk of premature mortality and a 10 to 20-year shorter life expectancy compared to the general population[2,3]. A previous meta-analysis showed that schizophrenia was associated with an average of 14.5 years of potential life loss, with higher numbers for males (15.9 years) than for females (13.6 years)[4]. Despite progress in treatment, recent analysis indicate that the mortality gap is increasing over time, suggesting that people with schizophrenia are not benefiting from medical advances as much as the general population[2,5,6].

A recent systematic review and meta-analysis showed significantly higher all-cause mortality among patients with schizophrenia compared to the general population (Risk ratio (RR) = 2.94; 95% CI 2.75–3.13). Higher mortality risk from cardiovascular diseases (RR = 2.09; 95% CI 1.76–2.47), infectious diseases (RR = 3.84; 95% CI 2.10–7.01), respiratory diseases (RR = 3.75; 95% CI 2.99–4.70), and endocrine diseases (RR = 3.80; 95% CI 1.75–8.26) was also observed[7].

The World Health Organization has identified lifestyle and health factors that contribute to earlier mortality, including heavy smoking, physical inactivity, obesity, hyperglycaemia, high cholesterol levels, and hypertension[8]. Together, these risk factors are responsible for increasing global mortality by 42.1%, and patients with schizophrenia have a higher incidence of these factors[9]. Despite major concerns regarding suicide in patients with schizophrenia, the majority of deaths associated with psychotic disorders are primarily attributed to natural causes, such as cardiovascular disease, cancer, and respiratory diseases[10,11]. Only a few studies present data on the influence of specific risk factors on mortality. Beary et al. concluded that while there is limited data in this field, interventions targeting modifiable risk factors such as hypertension, physical activity, and smoking could potentially improve the lifespan of individuals with schizophrenia[12]. Health inequalities in people with schizophrenia are a serious public health problem that warrants urgent attention to optimise healthcare services and reduce preventable deaths in this population[13]. To close the mortality gap between people with schizophrenia and the general population, certain interventions are needed, such as monitoring and screening for cardiovascular diseases, promoting healthy lifestyle education, and providing early interventions for diagnosed physical illnesses[7].

Conducted studies report a high heterogeneity of mortality risk among patients with schizophrenia. To contribute to the existing literature and to explore the patterns of mortality risk, we conducted a single-centre, retrospective study to assess mortality risk in people with schizophrenia compared to the general population during the study period from 2001 to 2020.

MATERIALS AND METHODS

Study design and data source

Cause-specific and all-cause mortality risk among patients with schizophrenia in Lithuania were assessed using retrospective cohort study design. The cohort included all male and female patients diagnosed with schizophrenia (ICD-10 code F20) admitted to the Vilnius Republican Psychiatric Hospital.

The Vilnius Republican Psychiatric Hospital, situated in the capital of the Vilnius region, is the largest specialised psychiatric hospital in the country, with approximately 5000 hospital admissions each year. The hospital database contains a wide

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Published in partnership with the Schizophrenia International Research Society

range of information, including demographics, personal identification numbers, dates of admission and discharge, principal diagnoses, and any coexisting medical conditions.

A cohort of patients with schizophrenia was established for analysing different aspects of their health conditions. A total of 8985 patients were admitted to the Vilnius Psychiatric Hospital during the period from January 1, 1992, until December 31, 2017.

The study population was followed for dates of emigration and dates of death from the date of hospitalisation to December 31, 2020. Dates of death and emigration were obtained from the Central Population Register. Underlying causes of death were obtained from death certificates. For mortality risk analysis we selected only patients, who were alive at January 1, 2001. This restriction relates to the availability of the causes of death from the Causes of Death Register.

The final cohort included 7883 patients.

Statistical analysis

To assess cause-specific mortality risk in the study cohort, common causes of death were classified into 15 broad categories according to the ICD-10.

The standardised mortality ratios (SMRs) were calculated by dividing the observed number of deaths among patients with schizophrenia by the expected number of deaths, calculated using national rates. The expected number of deaths was calculated by multiplying the exact person-years under observation in the cohort by sex, calendar year, and 5-year age-group specific national mortality rate. The person-time of observation was computed from January 1, 2001, or the date of the first hospitalisation with a schizophrenia diagnosis until the cohort exit date. Exact 95% confidence intervals (CIs) for standardised mortality ratios (SMRs) are calculated directly from the Poisson distribution using the R statistical package (R Core Team. 2024. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria).

All statistical analyses were carried out using STATA 15 statistical software (StataCorp. 2020. Stata Statistical Software: Release 15.1. College Station, TX, USA).

The study was conducted in accordance with the Declaration of Helsinki, and the Vilnius Regional Biomedical Research Ethics Committee (No. 2022/6-1449-915) approved the protocol.

RESULTS

The study population's baseline characteristics are described in Table 1. The number of males and females in the study group was similar, comprising 50.5% and 49.5%, respectively. Additionally, 18.9% of males and 34.5% of females were first hospitalised at the age of 50 years or more.

In total, 2458 deaths were observed in our study: 50.8% in the male group and 49.2% in the female group. An increased all-cause mortality risk was found for both male (SMR = 1.66; 95% CI 1.57–1.75) and female (SMR = 2.40; 95% CI 2.27–2.54) patients with schizophrenia combined (SMR = 1.96; 95% CI 1.88–2.04) compared to the general population.

The observed and expected numbers and the SMRs for the specific cause of death by sex are shown in Table 2. The absolute majority of death cases were due to natural causes. The most significant increase in natural cause-specific mortality risk was observed in both sexes for circulatory system diseases (47.7% of all cases with SMR = 2.17; 95% CI 2.05–2.30). Further subdivision of circulatory system diseases showed that deaths from ischaemic heart disease and cerebrovascular disease were significant in both sexes separately and combined. Statistically significant results for increased cause-specific mortality risk were observed in several diseases. These include infectious diseases (SMR = 2.34; 95% CI 1.81–2.98), mental and behavioural disorders (SMR = 10.72; 95% CI 7.76–14.44), diseases of the nervous system (SMR = 1.75; 95% CI 1.22–2.43), diseases of the respiratory system (SMR = 2.01; 95% CI 1.61–2.48), and disease of the genitourinary system (SMR = 2.46; 95% CI 1.52–3.76). Increased mortality risk due to cancer (SMR = 1.25; 95% CI 1.06–1.46), endocrine and metabolic diseases (SMR = 2.35; 95% CI 1.37–3.76), and digestive system diseases (SMR = 1.39; 95% CI 1.01–1.87) was observed only in female patients with schizophrenia, but not in males. In terms of unnatural causes of death, our results show that both genders died statistically significantly more (SMR = 2.70; 95% CI 2.47–2.95) than the general population.

Table 1. Characteristics of the study population.

	MALE		FEMALE		OVERALL	
	No.	%	No.	%	No.	%
Total	3973	50.5	3910	49.5	7883	100.0
Period of admission						
1992–1996	1165	29.3	1152	29.5	2317	29.4
1997–2001	975	24.5	991	25.3	1966	24.9
2002–2006	749	18.9	736	18.8	1485	18.8
2007–2011	524	13.2	493	12.6	1017	12.9
2012–2017	560	14.1	538	13.8	1098	13.9
Age at first admission						
0–19	319	8.0	203	5.2	522	6.6
20–29	1202	30.3	615	15.7	1817	23.0
30–39	985	24.8	855	21.9	1840	23.3
40–49	715	18.0	888	22.7	1603	20.3
50–59	477	12.0	772	19.7	1249	15.8
60–69	223	5.6	397	10.2	620	7.9
70+	52	1.3	180	4.6	232	2.9

DISCUSSION

As mortality is considered one of the most important measures in medicine to monitor the quality of psychiatric and somatic healthcare[14], we performed, to our knowledge, the first and largest study on all-cause and disease-specific mortality in people with schizophrenia in Lithuania. These results confirm previous findings that people with schizophrenia have a higher mortality rate than the general population, and the increase in mortality risk is due to almost all the diseases that are the leading causes of death in the general population.

The most recent meta-analysis, which included 135 studies comparing 4.5 million patients with schizophrenia, reported significantly increased all-cause mortality in people with schizophrenia compared to the general population (RR = 2.94, 95% CI 2.75–3.13)[7]. In terms of sex analysis, British and Norwegian studies found that males were characterised by higher mortality than females compared to the general population[15,16]. In our study, we also found increased all-cause mortality in people with schizophrenia combined compared to the general population (SMR = 1.96; 95% CI 1.88–2.04); however, females with schizophrenia had a higher SMR = 2.40 (95% CI 2.27–2.54) than males with schizophrenia (SMR = 1.66; 95% CI 1.57–1.75).

Most deaths in patients with schizophrenia are attributable to natural causes. A previous meta-analysis found that 67.3% of deaths among people with mental disorders were due to natural causes[17]. As mentioned before, higher mortality from cardiovascular diseases (RR = 2.09; 95% CI 1.76–2.47), infectious diseases (RR = 3.84; 95% CI 2.10–7.01), respiratory diseases (RR = 3.75; 95% CI 2.99–4.70) and endocrine diseases (RR = 3.80; 95% CI 1.75–8.26) was observed[7]. We observed the most significant increase in

Table 2. Standardised mortality ratios (SMR) for causes of death in patients with schizophrenia according to sex.

	MALE					FEMALE				OVERALL			
Diagnosis	ICD–10	Obs	SMR	95% CI		Obs	SMR	95% CI		Obs	SMR	95% CI	
All causes	A00–Y98	1249	**1.66**	1.57	1.75	1209	**2.40**	2.27	2.54	2458	**1.96**	1.88	2.04
Certain infectious and parasitic diseases	A00–B99	41	**2.12**	1.52	2.88	25	**2.82**	1.82	4.16	66	**2.34**	1.81	2.98
Tuberculosis	A15–A19	18	**1.81**	1.07	2.86	2	**1.02**	0.12	3.68	20	**1.68**	1.03	2.59
Sepsis	A40–A41	8	**1.98**	0.85	3.90	9	**2.50**	1.14	4.75	17	**2.22**	1.29	3.55
Viral hepatitis	B15–B19	6	**8.44**	3.10	18.37	1	**2.97**	0.08	16.55	7	**6.68**	2.69	13.76
Malignant neoplasms	C00–C96	135	**0.84**	0.70	0.99	159	**1.25**	1.06	1.46	294	**1.02**	0.91	1.14
Endocrine, nutritional and metabolic diseases	E00–E89	5	**0.79**	0.26	1.84	17	**2.35**	1.37	3.76	22	**1.62**	1.02	2.45
Diabetes mellitus	E10-E14	3	**0.53**	0.11	1.55	14	**2.14**	1.17	3.59	17	**1.39**	0.81	2.23
Mental and behavioural disorders	F00–F99	23	**10.04**	6.36	15.06	20	**11.64**	7.11	17.98	43	**10.72**	7.76	14.44
Diseases of the nervous system	G00–G99	20	**1.77**	1.08	2.73	15	**1.72**	0.96	2.84	35	**1.75**	1.22	2.43
Diseases of the circulatory system	I00–I99	526	**1.83**	1.68	1.99	647	**2.56**	2.37	2.77	1173	**2.17**	2.05	2.30
Hypertensive diseases	I10–I15	15	**1.48**	0.83	2.44	36	**3.70**	2.59	5.12	51	**2.56**	1.91	3.37
Ischaemic heart diseases	I20–I25	346	**1.96**	1.76	2.18	386	**2.64**	2.38	2.92	732	**2.27**	2.11	2.44
Acute myocardial infarction	I21	25	**1.16**	0.75	1.71	20	**1.53**	0.93	2.36	45	**1.30**	0.95	1.74
Cerebrovascular diseases	I60–I69	72	**1.34**	1.05	1.69	152	**2.16**	1.83	2.53	224	**1.80**	1.57	2.05
Diseases of the respiratory system	J00–J99	57	**1.80**	1.36	2.33	30	**2.60**	1.75	3.71	87	**2.01**	1.61	2.48
Pneumonia	J12–J18	30	**2.11**	1.42	3.01	19	**3.67**	2.21	5.73	49	**2.53**	1.87	3.34
Diseases of the digestive system	K00–K93	67	**1.23**	0.95	1.56	44	**1.39**	1.01	1.87	111	**1.29**	1.06	1.55
Gastroduodenal ulcer	K25–K27	12	**2.22**	1.15	3.88	10	**3.00**	1.44	5.52	22	**2.51**	1.57	3.80
Diseases of liver	K70–K77	34	**0.96**	0.66	1.34	13	**0.74**	0.39	1.27	47	**0.88**	0.65	1.17
Diseases of the genitourinary system	N00–N99	9	**2.23**	1.02	4.23	12	**2.67**	1.38	4.66	21	**2.46**	1.52	3.76
Findings, not elsewhere classified	R00–R99	50	**2.69**	2.00	3.55	34	**5.68**	3.93	7.94	84	**3.42**	2.73	4.23
External causes	V00–Y89	308	**2.07**	1.85	2.31	191	**5.35**	4.62	6.16	499	**2.70**	2.47	2.95
Suicides	X60-X84	122	**2.95**	2.45	3.52	67	**9.06**	7.02	11.51	189	**3.88**	3.35	4.47
Transport accidents	V00-V99	15	**0.92**	0.51	1.52	11	**2.57**	1.28	4.60	26	**1.27**	0.83	1.86

cause-specific mortality risk associated with circulatory system diseases (SMR = 2.17; 95% CI 2.05–2.30). Further subdivision of circulatory system diseases showed that deaths from ischaemic heart disease and cerebrovascular disease were significant in both sexes, separately and combined. According to a large meta-analysis that processed data from over 3 million patients, those with severe mental illness had a 53% higher risk of suffering from cardiovascular disease, a 78% higher risk of developing cardiovascular disease, and an 85% higher risk of dying from cardiovascular disease compared to the general population[18]. In Sweden, male and female patients with schizophrenia died from ischemic heart disease 14.5 and 12.7 years earlier than individuals in the general population[19]. Moreover, people with schizophrenia who died from myocardial infarction were less often diagnosed with ischemic heart disease compared to people who died from the same cause in the general population[19]. Interestingly, mortality due to cardiovascular disease in patients with schizophrenia did not decrease over the past few years, despite the fact that decreasing mortality rates from cardiovascular disease have been reported worldwide[20].

The second most common cause of mortality in our study is due to cancer-related deaths. We found a statistically significant increase in mortality risk for female patients with schizophrenia (SMR = 1.25; 95% CI 1.06–1.46). In contrast, male patients showed no significant increase in mortality risk (SMR = 0.84; 95% CI 0.70–0.99), and the results for both genders do not show a statistically significant difference compared to the general population. In our previous study, we found a higher breast cancer mortality risk among female patients (SMR = 1.90; 95% CI 1.44–2.51), which could partially explain the higher overall cancer-related mortality risk among females with schizophrenia. Moreover, in the same study, we did not find any statistically significant differences in lung and colorectal cancer mortality in both males and females[21]. However, research findings on the relationship between schizophrenia and cancer mortality risk are very diverse. The latest meta-analysis on cancer mortality showed that the SMR for cancer mortality in patients with schizophrenia compared to the general population was 1.40 (95% CI 1.29–1.52), with statistically significant results in both female and male subgroups[22]. Stigmatisation of schizophrenia diagnosis, present among healthcare specialists, may limit patients' access to healthcare[10]. Interestingly, the aforementioned Swedish study reported that malignant neoplasms were less often diagnosed in schizophrenia patients dying from cancer compared to those dying from the same cause in the general population[19].

Other natural causes that have been shown to have an increased mortality risk in research studies of patients with schizophrenia are diabetes and infectious diseases. Brown et al. demonstrated a statistically significant higher SMR for diabetes in schizophrenia patients[14]. Our results on diabetes show an increased mortality risk for females (SMR = 2.14; 95% CI 1.17–3.59); however, this risk was not observed for males. A recent observational longitudinal study, which aimed to analyse mortality risk in people with schizophrenia with comorbid illness (type II diabetes), revealed that mortality was three times higher in the subgroup of patients with schizophrenia with type II diabetes compared to those who did not have any of the studied diseases. After adjustment for age, the risk of death in those with type II diabetes and schizophrenia increased to a 27-fold greater risk compared to those without either condition[23]. A recent meta-analysis found that patients with schizophrenia had approximately a 3-fold increased risk of hepatitis C and B compared to the

general population, and authors discussed that this could be explained by certain behavioural factors: substance use and extreme sexual behaviours[24]. Our results indicate that, although the observed number of cases of viral hepatitis is low (overall 7), there is an increased overall mortality risk for both genders (SMR = 6.68).

In our study, increased mortality risk from mental and behavioural disorders was observed (SMR = 10.72). Similar to our study, Italian researchers reported a higher risk of deaths from psychiatric disorders (ICD-10 F00–F99) in both males (SMR = 13.2; 95% CI 10.5–16.2) and females (SMR = 6.8; 95% CI 5.3–8.6)[25].

An increasing number of studies emphasise the importance of modifiable risk factors in reducing mortality risk, such as poor lifestyle behaviours, comorbid illnesses, and irregular use of antipsychotic drugs[2]. Patients are encouraged to monitor their weight, diet, exercise programs, and use of antipsychotics[26]. One study showed reduced cardiorespiratory fitness in people with schizophrenia compared to the general population, and the authors concluded that promoting physical activity might reduce overall and cardiovascular-associated mortality[27]. In addition, there is a shortage of advice on lifestyle changes, such as smoking cessation, which is particularly important, given that there is an 70–162% increased risk of chronic obstructive pulmonary disease, asthma, and pneumonia in patients with schizophrenia[28]. The association of schizophrenia and smoking has long been recognised[29]. Brown et al. analysed smoking habits in patients with schizophrenia and found that not only were there more smokers among people with schizophrenia (73%) than in the general population (35%), but the SMR was also significantly higher in smokers (SMR = 2.79) than in non-smokers (SMR = 1.94)[14].

Although antipsychotics are associated with adverse cardiometabolic effects that can increase the risk of cardiovascular death[30], it has been observed that there is a protective role of antipsychotic use in people with schizophrenia treatment compared to non-use[31]. Taipale et al. reported that antipsychotic medication use was not associated with an increased risk of hospitalisation due to cardiovascular disorders; in fact, they found a significantly decreased risk of dying from cardiovascular illness in people with schizophrenia who regularly used antipsychotics (HR = 0.62, 95% CI 0.57–0.67)[31]. Additionally, patients who used antipsychotics less often discontinued antidiabetic medication (HR = 0.56, 95% CI: 0.47–0.66) and antihypertensives (HR = 0.63, 95% CI: 0.56–0.71)[32].

Unnatural deaths, which comprises suicide, homicide, and accidents, account for 20–25% of the total number of deaths in patients with schizophrenia[33]. In our study, we found that the percentage of unnatural deaths stands at 20.30% of all death cases with the majority of deaths due to suicides. Studies report that antipsychotic use has a significant protective effect against suicide-related mortality[34].

Disparities between people with schizophrenia and the general population have been repeatedly reported in terms of lack of medical care and screening procedures for cancer and cardiovascular diseases[35,36]. Various findings from the aforementioned studies indicate that patients with psychiatric disorders are receiving suboptimal care. To date, there is evidence that people with schizophrenia may encounter stigma. One research study reported that a large proportion of health service staff held negative attitudes toward patients with mental illness, which may hamper the provision of care[37].

Our study is subject to certain limitations. Firstly, it is important to note that this is a single-centre study, which means it may not represent the entire population of Lithuania. Our results should be interpreted with caution, as the data was collected from just one source. However, this source is the largest hospital database in Lithuania, encompassing the most hospitalisations per year. There is a significant possibility that our study may overestimate mortality rates, and the actual situation for all individuals with schizophrenia could be more favourable. Nevertheless, it remains the only and most comprehensive study with the longest follow-up period ever conducted in Lithuania to date. Secondly, as the number of autopsies are low and continuously decreasing (in 2022, 12.2% of all deceased in Lithuania underwent an autopsy compared to 14.9% in 2018[38]) the accuracy of cause of death data can be highly influenced by the quality of the medical records and documentation. In some cases, the cause of death may not be definitively established, because some diseases or conditions may be closely related, complicating the assignment of a single cause of death. This can result in variation in data accuracy. Thirdly, in this study, we were unfortunately unable to investigate lifestyle factors, which could improve the interpretation of the results.

CONCLUSIONS

Despite the increasing public health interventions and improvements in the management of chronic diseases, it is well recognised that patients with schizophrenia do not fully benefit from the health strategies that have led to reduced mortality in the general population. To close the mortality gap, smoking and alcohol cessation interventions, cardiovascular and cancer screening and monitoring, early diagnosis, and interventions for detected physical diseases should be regarded as imperative. We believe that a larger number of studies on causative mortality risk factors with schizophrenia are necessary to improve the devastating mortality results.

DATA AVAILABILITY

Data is available upon reasonable request.

CODE AVAILABILITY

Code is available upon reasonable request.

Received: 8 October 2024; Accepted: 23 December 2024;
Published online: 16 January 2025

REFERENCES

1. Volavka, J. & Vevera, J. Very long-term outcome of schizophrenia. *Int. J. Clin. Pract.* **72**, e13094 (2018).
2. Saha, S., Chant, D. & McGrath, J. A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time? *Arch. Gen. Psychiatry* **64**, 1123–1131 (2007).
3. Chesney, E., Goodwin, G. M. & Fazel, S. Risks of all-cause and suicide mortality in mental disorders: a meta-review. *World Psychiatry* **13**, 153–160 (2014).
4. Hjorthøj, C., Stürup, A. E., McGrath, J. J. & Nordentoft, M. Years of potential life lost and life expectancy in schizophrenia: a systematic review and meta-analysis. *Lancet Psychiatry* **4**, 295–301 (2017).
5. Lee, E. E. et al. A widening longevity gap between people with schizophrenia and general population: a literature review and call for action. *Schizophr. Res.* **196**, 9–13 (2018).
6. Hodgson, R., Wildgust, H. J. & Bushe, C. J. Cancer and schizophrenia: is there a paradox? *J. Psychopharmacol.* **24**, 51–60 (2010).
7. Correll, C. U. et al. Mortality in people with schizophrenia: a systematic review and meta-analysis of relative risk and aggravating or attenuating factors. *World Psychiatry* **21**, 248–271 (2022).
8. Global health risks: mortality and burden of disease attributable to selected major risks [Internet]. Available from: https://www.who.int/publications-detail-redirect/9789241563871. (2023).
9. Wildgust, H. J., Hodgson, R. & Beary, M. The paradox of premature mortality in schizophrenia: new research questions. *J. Psychopharmacol.* **24**, 9–15 (2010).
10. Piotrowski, P. et al. Causes of mortality in schizophrenia: an updated review of European studies. *Psychiatr. Danub* **29**, 108–120 (2017).
11. John, A. et al. Premature mortality among people with severe mental illness - New evidence from linked primary care data. *Schizophr. Res.* **199**, 154–162 (2018).

12. Beary, M., Hodgson, R. & Wildgust, H. J. A critical review of major mortality risk factors for all-cause mortality in first-episode schizophrenia: clinical and research implications. *J. Psychopharmacol.* **26**, 52–61 (2012).
13. Yung, N. C. L., Wong, C. S. M., Chan, J. K. N., Chen, E. Y. H. & Chang, W. C. Excess mortality and life-years lost in people with schizophrenia and other non-affective psychoses: an 11-year population-based cohort study. *Schizophr. Bull.* **47**, 474–484 (2021).
14. Brown, S., Kim, M., Mitchell, C. & Inskip, H. Twenty-five year mortality of a community cohort with schizophrenia. *Br. J. Psychiatry* **196**, 116–121 (2010).
15. Chang, C. K. et al. All-cause mortality among people with serious mental illness (SMI), substance use disorders, and depressive disorders in southeast London: a cohort study. *BMC Psychiatry* **10**, 77 (2010).
16. Høye, A., Jacobsen, B. K. & Hansen, V. Increasing mortality in schizophrenia: are women at particular risk? A follow-up of 1111 patients admitted during 1980-2006 in Northern Norway. *Schizophr. Res.* **132**, 228–232 (2011).
17. Walker, E. R., McGee, R. E. & Druss, B. G. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. *JAMA Psychiatry* **72**, 334–341 (2015).
18. Correll, C. U. et al. Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls. *World Psychiatry* **16**, 163–180 (2017).
19. Crump, C., Winkleby, M. A., Sundquist, K. & Sundquist, J. Comorbidities and mortality in persons with schizophrenia: a Swedish national cohort study. *Am. J. Psychiatry* **170**, 324–333 (2013).
20. Westman, J. et al. Increased cardiovascular mortality in people with schizophrenia: a 24-year national register study. *Epidemiol. Psychiatr. Sci.* **27**, 519–527 (2018).
21. Drevinskaite, M. et al. Cancer mortality and morbidity among patients with schizophrenia: a hospital-based cohort study, 1992-2020. *Acta Psychiatr. Scand.* **149**, 234–243 (2024).
22. Zhuo, C., Tao, R., Jiang, R., Lin, X. & Shao, M. Cancer mortality in patients with schizophrenia: systematic review and meta-analysis. *Br. J. Psychiatry* **211**, 7–13 (2017).
23. Davis W. A., Bruce D. G., Starkstein S. E., Davis T. M. E. Temporal trends in mortality associated with comorbid Type 2 diabetes and schizophrenia: the fremantle diabetes study. *J. Clin. Med.*12. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9820984/. 2023[cited 2024 Mar 5].
24. Lluch, E. & Miller, B. J. Rates of hepatitis B and C in patients with schizophrenia: a meta-analysis. *Gen. Hosp. Psychiatry* **61**, 41–46 (2019).
25. Girardi, P. et al. Causes of mortality in a large population-based cohort of psychiatric patients in Southern Europe. *J. Psychiatr. Res.* **136**, 167–172 (2021).
26. Liu, N. H. et al. Excess mortality in persons with severe mental disorders: a multilevel intervention framework and priorities for clinical practice, policy and research agendas. *World Psychiatry* **16**, 30–40 (2017).
27. Vancampfort, D. et al. Promotion of cardiorespiratory fitness in schizophrenia: a clinical overview and meta-analysis. *Acta Psychiatr. Scand.* **132**, 131–143 (2015).
28. Suetani, S. et al. Increased rates of respiratory disease in schizophrenia: a systematic review and meta-analysis including 619,214 individuals with schizophrenia and 52,159,551 controls. *Schizophr. Res.* **237**, 131–140 (2021).
29. Peritogiannis, V., Ninou, A. & Samakouri, M. Mortality in schizophrenia-spectrum disorders: recent advances in understanding and management. *Healthcare.* **10**, 2366 (2022).
30. De Hert, M., Detraux, J., van Winkel, R., Yu, W. & Correll, C. U. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. *Nat. Rev. Endocrinol.* **8**, 114–126 (2011).
31. Taipale, H. et al. 20-year follow-up study of physical morbidity and mortality in relationship to antipsychotic treatment in a nationwide cohort of 62,250 patients with schizophrenia (FIN20). *World Psychiatry* **19**, 61–68 (2020).
32. Solmi, M. et al. Antipsychotics use is associated with greater adherence to cardiometabolic medications in patients with schizophrenia: results from a nationwide, within-subject design study. *Schizophr. Bull.* **48**, 166–175 (2022).
33. Barber, S. & Thornicroft, G. Reducing the mortality gap in people with severe mental disorders: the role of lifestyle psychosocial interventions. *Front. Psychiatry* **9**, 463 (2018).
34. Wilkinson, S. T. et al. Pharmacological and somatic treatment effects on suicide in adults: a systematic review and meta-analysis. *Depress Anxiety* **39**, 100–112 (2022).
35. Solmi, M. et al. Disparities in cancer screening in people with mental illness across the world versus the general population: prevalence and comparative meta-analysis including 4 717 839 people. *Lancet Psychiatry* **7**, 52–63 (2020).
36. Solmi, M. et al. Disparities in screening and treatment of cardiovascular diseases in patients with mental disorders across the world: systematic review and meta-analysis of 47 observational studies. *Am. J. Psychiatry* **178**, 793–803 (2021).
37. Arvaniti, A. et al. Health service staff's attitudes towards patients with mental illness. *Soc. Psychiatry Psychiatr. Epidemiol.* **44**, 658–665 (2009).
38. Metiniai mirties priežasčių duomenys [Internet]. Available from: https://www.hi.lt/mirties-priezasciu-statistika-metiniai-mirties-priezasciu-duomenys/. [cited 2024 Nov 29].

AUTHOR CONTRIBUTIONS

Conceptualisation, Mingaile Drevinskaite, Arunas Germanavicius and Giedre Smailyte; Data curation, Giedre Smailyte; Formal analysis, Auguste Kaceniene; Methodology, Auguste Kaceniene and Giedre Smailyte; Project administration, Giedre Smailyte; Supervision, Giedre Smailyte; Writing – original draft, Mingaile Drevinskaite; Writing – review & editing, Mingaile Drevinskaite, Auguste Kaceniene, Arunas Germanavicius and Giedre Smailyte.

COMPETING INTERESTS

The authors declare no competing interests.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the authors did not use any generative AI or AI-assisted technologies.

ETHICAL APPROVAL

This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Vilnius regional biomedical research ethics committee (approval number No. 2022/6-1449-915 on 14 June 2022).

INFORMED CONSENT

Patients' consent was waived to this study.

ADDITIONAL INFORMATION

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