Cause-specific mortality due to physical illness in severe mental disorders in Europe: a population-based multi-country cohort study

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Summary

Background How specific physical illnesses differentially contribute to the persistent mortality gap in severe mental illness (including schizophrenia spectrum disorders, bipolar disorder, and major depressive disorder) remains poorly understood. Using a harmonised multi-country design, we aimed to analyse excess mortality across diagnoses and causes of death to identify high-burden and high-inequity mortality patterns to inform public health prioritisation and organisation of care.

Methods In this population-based multi-country cohort study using national health registers, we identified people diagnosed with severe mental illness at age 15–65 years in five European countries (Denmark, Finland, France, Poland, and Sweden) during 2004–23 to establish excess mortality before age 75 years in relation to country-specific general population mortality. We defined cause-specific mortality using ICD-10. Random effects meta-analysis was used to pool mortality estimates representing country-specific relative mortality inequities (sex-standardised and age-standardised mortality ratios), absolute excess burden (sex-standardised and age-standardised death rates per 10 000 person-years), and the severity of premature mortality (potential years-of-life-lost before age 75 years). Subgroup analyses were conducted to test for potential effect modification.

Findings Between Jan 1, 2004, and Dec 31, 2023, there were 4 861 795 people with severe mental illness, and 561 903 deaths from any cause. All-cause mortality was 2·6-fold higher in people with severe mental illness compared with the general population (pooled standardised mortality ratio [SMR] 2·64, 95% CI 2·25–3·11). Absolute excess mortality was highest in cardiovascular disease (schizophrenia spectrum disorders: standardised excess death rate 22·08 per 10 000 person-years, 95% CI 8·77–35·39; bipolar disorder: 8·36 per 10 000 person-years, 2·96–13·75; and major depressive disorder: 9·82 per 10 000 person-years, 3·18–16·45). Relative excess mortality was highest in respiratory diseases (schizophrenia spectrum disorders: SMR 6·49; 95% CI 5·52–7·64; bipolar disorder: 2·72, 2·04–3·63; and major depressive disorder: 3·48, 2·63–4·62), followed by endocrine and metabolic diseases (schizophrenia spectrum disorders: 5·09, 4·29–6·04; bipolar disorder: 2·60, 2·26–2·98; and major depressive disorder: 3·07, 1·84–5·12), and in gastrointestinal diseases (schizophrenia spectrum disorders: 3·47, 2·58–4·67; bipolar disorder: 2·34, 2·00–2·74; and major depressive disorder: 3·48, 2·63–4·62).

Interpretation The mortality gap was characterised by distinct patterns of absolute excess mortality and relative inequality across causes of death and severe mental illness diagnoses. Considering both dimensions of excess mortality can inform public health priorities that are not apparent from either measure alone or from focusing on cause-specific numbers of deaths. Reducing premature mortality will therefore require an integrated public health approach that combines universal strategies with targeted interventions to address both high-burden causes of death and those characterised by the greatest relative inequalities.

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Introduction

Given the increasing burden of disability globally, mental disorders continue to be a public health priority.[1] Severe mental illness, including schizophrenia spectrum disorders,[2,3] bipolar disorder,[4,5] and severe major depressive disorder,[6,7] have the highest relative burden of disability and reduced life expectancy. Despite improvements in treatment of severe mental illnesses,[8,9] a substantial mortality gap persists between individuals affected by severe mental illnesses and the general population.[10] Most excess mortality is attributable to physical illnesses covering all major organ systems.[11–16]

Premature excess mortality in severe mental illness arises from a complex interaction between multiple risk

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See Online for appendix

Research in context

Evidence before this study

We searched PubMed from database inception to Jan 9, 2026, for studies on mortality in people with severe mental illness using the search terms mortality[tiab] OR death[tiab] OR died[tiab] OR "life expectancy"[tiab] OR "years of life lost"[tiab] OR "life years lost"[tiab] OR Mortality[Mesh] combined with schizophrenia[tiab] OR "bipolar disorder"[tiab] OR depression[tiab] OR depressive[tiab] OR "psychotic disorder*"[tiab] OR psychosis[tiab] OR "severe mental illness*"[tiab] OR "severe mental disorder*"[tiab] OR Schizophrenia[Mesh] OR Bipolar Disorder[Mesh] OR Depressive Disorder[Mesh] OR Psychotic Disorders[Mesh]. We did not limit the search by language. This search identified 57 997 papers. Previous research has shown that severe mental illnesses are associated with increased mortality from external causes, including suicides and accidents, and from natural causes, including cardiovascular disease. The mortality gap has not reduced during the past decades. Evidence on excess mortality in severe mental illnesses has largely been derived from single-country studies and meta-analyses combining heterogeneous designs, populations, and outcome definitions, which limits comparability across health systems and the interpretation of findings for public health decision making. Moreover, most studies have not clearly distinguished between causes that drive absolute mortality burden and those that reflect relative mortality inequities. These two dimensions imply different priorities for health policy and resource allocation.

Added value of this study

This population-based multi-country cohort study applied a harmonised transdiagnostic framework across five European countries to identify similarities and differences between severe mental illness diagnoses in somatic cause-specific mortality patterns. By integrating absolute and relative excess mortality measures within a single analytical approach, we distinguished high-burden from high-inequity causes of death and identified a dual burden pattern in excess mortality. Decomposition of excess mortality into these complementary dimensions provides an actionable evidence base for public health prioritisation and organisation of care. Our analysis including nearly 5 million people with severe mental illness showed that excess mortality was characterised by three inter-related but distinctive patterns: one of high absolute mortality rates, including cardiovascular disease and cancer; another with markedly increased relative risks, including respiratory, gastrointestinal, and endocrine and metabolic diseases; and a third pattern specific to causes contributing to greatest loss of potential years-of-life, including gastrointestinal disease, and endocrine and metabolic diseases. We also showed that excess mortality in schizophrenia spectrum disorders could reflect heterogeneous cause-specific mechanisms, whereas in bipolar disorder and severe depression, excess mortality could reflect a more generalised vulnerability.

Implications of all the available evidence

Excess mortality in severe mental illness reflects a shared dual burden of high absolute mortality from common physical conditions and markedly increased relative mortality inequalities associated with specific diseases. The more heterogeneous cause-specific mortality pattern in schizophrenia spectrum disorders, compared with the broader multisystem vulnerability observed in bipolar disorder and major depressive disorder, suggests that different combinations of targeted and universal approaches across severe mental illness diagnoses could be required in reducing the persistent mortality gap. Addressing the dual burden in excess mortality requires multilevel systemic reform rather than improvements in individual clinical care alone.

factors. For example, shared genetic predisposition, adverse health behaviours, and various social, economic, and other environmental risk factors contribute to higher rates of co-occurring physical illnesses and increased mortality risks.[17–20] Furthermore, people with severe mental illness often experience health inequity arising from substandard health care, including limited access, insufficient screening and management of modifiable risk factors, and poor management of chronic illnesses and multimorbidity.[21–24] These health system failures can lead to missed opportunities for prevention, delayed diagnosis, and ineffective treatment of both psychiatric and physical illnesses.

Integrated, person-centred models of care have been advocated to address physical health disparities in severe mental illness,[25–27] yet identifying actionable priorities requires robust, comparable transdiagnostic evidence across health systems to identify where mortality patterns arise from shared structural deficiencies rather than disorder-specific mechanisms alone. Evidence on excess mortality in severe mental illness is still dominated by heterogeneous single-country studies with repeated analytical approaches most often based on relative risks. Furthermore, the absence of transdiagnostic epidemiological frameworks has contributed to a fragmented and siloed evidence base that does not adequately support integrated public health responses and priorities. To address these gaps, this study applied a harmonised, transdiagnostic framework across five European countries (Denmark, Finland, France, Poland, and Sweden) for direct comparison of mortality patterns in severe mental illness. Specifically, by decomposing total excess mortality, we aimed to identify both shared and diagnosis-specific mortality patterns. By jointly examining absolute burden and relative inequity, we further aimed to inform a prioritisation framework that distinguishes high-burden from high-inequity drivers of excess mortality.

Methods

Study design and participants

In this population-based multi-country cohort study, we used nationwide registers to identify people with severe mental illness and collected mortality data in five European countries (Denmark, Finland, France, Poland, and Sweden; appendix p 2). All countries followed a pre-registered harmonised protocol for preparing study cohorts and to record national mortality data. The institutions and register holders of the participating countries approved the study design.

Ethics approval and informed consent were not required because the study was based on non-identifiable administrative register data. This study follows STROBE reporting guidelines.[28]

Procedures

We defined severe mental illness using ICD-10 codes: schizophrenia spectrum disorders (F20–F29), bipolar disorder (F30–F31), and major depressive disorder (F32–F33; appendix p 7). Major depressive disorder was classified as severe if a person had inpatient contact or received disability pension due to major depressive disorder. Eligible people were aged 15–65 years at first severe mental illness diagnosis. To identify people diagnosed with a severe mental illness, we used registers covering inpatient and specialised outpatient care, sickness absences (lasting >14 days), and disability pensions, depending on data availability in each country. To reduce bias from potential over-representation of incident cases during the first years of observation, we used the first calendar years from the beginning of country-specific study periods as lead-in periods, during which prevalent cases were accumulated (appendix p 8). Country-specific general population data were obtained from national statistics institutions, and data on health system indicators from publicly available databases of Eurostat and the Organisation for Economic Co-operation and Development. We classified mortality by main cause of death using the ICD-10 codes: all-cause mortality (any cause); neoplasms (C00–D48); cardiovascular disease (I00–I99); respiratory disease (J00–J99); endocrine and metabolic diseases (E00–E99); gastrointestinal disease (K00–K93); and other natural causes not included in these categories (appendix p 7). Natural-cause mortality excluded external causes (V00–Y98) and ill-defined and unknown causes of mortality (R96–R99). We included deaths with missing ICD codes in the ill-defined and unknown causes category.

National mortality registers capture 98–100% of deaths in all included countries, but cause-of-death data quality varies (appendix p 9). Finland and Sweden have established high-quality cause-of-death data. Because Denmark does not explicitly report all relevant cause-of-death quality metrics, there was some uncertainty in data quality. In France, there was a relatively large number of non-random missing causes of death coded as unspecified causes (ICD-10 R-codes), which limits comparability in subgroup analyses. In Poland, known cause-of-death quality limitations, such as use of terminal or ill-defined codes rather than underlying medical causes in death certificates, introduce attribution bias. Furthermore, because we had cause-of-death information only for deaths that occurred in hospitals in Poland, compared with population-level data in other countries, we present cause-specific mortality separately for Poland. Because cause-of-death information was missing in 12% (45 448 of 374 866) of the deaths in France (appendix p 10), we applied multiple imputation to French mortality data and used imputed data in the analyses (appendix pp 11, 12). Because death counts of less than five were masked in Denmark, death counts do not necessarily sum to total in subgroup analyses.

For more on the **study protocol** see https://osf.io/a38u6/files/v3d6w

We stratified cohorts by sex (female, male) and 5-year age groups (15–19 years through to 70–74 years). Institutions responsible for record linkage excluded people with missing sex or age. Information on ethnicity was not available in the registers.

Statistical analysis

To focus on preventable deaths, we conducted mortality analyses for people younger than 75 years using aggregated data during the country-specific study periods (2004–22 in Denmark and Finland, 2006–22 in France, 2012–23 in Poland, and 2004–23 in Sweden). We used three complementary mortality indicators to distinguish between relative mortality inequities (sex-standardised and age-standardised mortality ratios [SMRs]), absolute excess burden (sex-standardised and age-standardised death rates per 10 000 person-years [SDRs]), and the severity of premature mortality (potential years-of-life-lost before age 75 years [PYLL]). The SDR was standardised using sex-stratified European Standard Population 2013 age distribution (appendix p 13). The SMR quantifies excess mortality relative to country-specific general populations and it reflects individual-level relative risk at the population level. Excess SDR (SDRe) was calculated as the difference between study population SDR and general population SDR. This measure reflects causes of death in which excess deaths accumulate most in absolute numbers. We calculated excess PYLL as the difference between observed and expected PYLL (calculated based on observed and expected deaths) and quantified average years-of-life-lost per excess death by dividing excess PYLL by the number of excess deaths. This measure reflects the causes of death in which excess deaths occur at younger ages and, therefore, premature loss of life is most severe. Excess deaths were calculated as observed gross excess above expected deaths, so that potential reduced mortality in some age groups did not offset the total excess mortality count.

Country-specific mortality estimates were pooled using a generic inverse-variance method in R (meta package, version 8.2.1). We estimated random effects models

because true heterogeneity across country-specific mortality estimates was expected. We used the term variability rather than heterogeneity in describing the results because variability is more appropriate in the context of mortality differences across countries. Variability in mortality estimates has been expressed using τ (tau; ie, standard deviation of effects) and the I^2 statistic. Poland was included only in pooling all-cause mortality estimates because cause-of-death data were not comparable.

Additional analyses

We conducted pre-defined additional analyses to explore potential effect modification in pooled SMR estimates. These analyses were: models stratified by sex and age group (15–34 years, 35–54 years, and 55–74 years); a sensitivity analysis of the schizophrenia spectrum disorders cohort with only individuals diagnosed with schizophrenia (ICD-10: F20); a sensitivity analysis of the bipolar disorder cohort without excluding individuals with a history of acute and transient psychotic disorders (ICD-10: F23); and a sensitivity analysis of the major depressive disorder cohort with only individuals identified from disability pensions. Furthermore, cause-specific SMR estimates for the largest cause-of-death groups within the category of other natural causes are shown separately by severe mental illness. Cause-specific mortality estimates are presented separately for Poland.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or in the decision to submit the paper for publication.

	Schizophrenia spectrum disorders	Bipolar disorder	Severe depression	Severe mental illness combined
Number of people	1 460 483	669 727	2 731 585	4 861 795
Females	652 236 (45%)	413 859 (62%)	1 692 389 (62%)	2 758 484 (57%)
Mean age at index diagnosis	38 (15)	41 (14)	43 (16)	41 (15)
Source of index diagnosis*				
Inpatient contact	610 884 (42%)	239 734 (36%)	1 992 972 (73%)	2 843 590 (58%)
Outpatient contact	420 359 (29%)	195 720 (29%)	NA	616 079 (13%)
Disability pension	414 375 (28%)	217 187 (32%)	738 613 (27%)	1 370 175 (28%)
Sickness absence	14 865 (1%)	17 086 (3%)	NA	31 951 (1%)
Country of residence				
France	778 831 (53%)	389 410 (58%)	2 143 679 (78%)	3 311 920 (68%)
Poland	372 376 (25%)	105 947 (16%)	92 446 (3%)	570 769 (12%)
Finland	118 918 (8%)	56 038 (8%)	205 886 (8%)	380 842 (8%)
Sweden	96 887 (7%)	89 614 (13%)	231 170 (8%)	417 671 (9%)
Denmark	93 471 (6%)	28 718 (4%)	58 404 (2%)	180 593 (4%)

Data are N (%) or mean (SD). NA=not applicable due to the definition of severe depression. *Information on outpatient contacts, sickness absence, and disability pensions not available in all countries.

Table: **Characteristics of cohorts**

Results

Countries varied in population size and in relation to various health system indicators, including health system resources, service use and delivery, health-care coverage and access, mortality outcomes, and health-related risk factors (appendix p 14). Avoidable mortality, both preventable and treatable mortality, was highest in Poland, and lowest in Sweden and France.

Between Jan 1, 2004, and Dec 31, 2023, there were 4 861 795 people (2 758 484 [57%] women; mean age 41 [SD 15] years at index diagnosis) in the combined severe mental illness cohort (table). The schizophrenia spectrum disorders cohort included 1 460 483 people (652 236 [45%] women; mean age 38 [SD 15] years), the bipolar disorder cohort included 669 727 people (413 859 [62%] women; mean age 41 [SD 14] years), and the severe major depressive disorder cohort included 2 731 585 people (1 692 389 [62%] women; mean age 43 [SD 16] years; table). People with severe mental illness were identified mainly through inpatient and outpatient contacts, but the relative contribution of different registers varied by country (eg, due to data availability; appendix p 15). More than half of the people in each severe mental illness cohort were residents of France.

In the general population reference cohort, there were 6 507 185 deaths from any causes, with neoplasms and cardiovascular disease having the highest death rates, followed by gastrointestinal disease and respiratory disease (appendix p 16). Mortality in severe mental illness, overall and across severe mental illness groups, mirrored the general population pattern (appendix pp 16–17).

There were 148 562 excess deaths from any causes in the schizophrenia spectrum disorders cohort (SDRe 105·29 per 10 000 person-years [95% CI 85·42–125·17]), 29 992 excess deaths in the bipolar disorder cohort (52·36 per 10 000 person-years [34·17–70·54]), and 181 741 excess deaths in the severe major depressive disorder cohort (70·29 per 10 000 person-years [56·95–85·00]) when Poland was included (figure 1). Both absolute and relative excess mortality were lowest in Poland and highest in Sweden and Denmark. All-cause mortality was 2·6-fold higher in the severe mental illness population compared with the general population (SMR 2·64; 95% CI 2·25–3·11). Each excess death contributed, on average, more than 19 years-of-life-lost before age 75 years (excess PYLL/excess deaths [PYLLe/De] 19·55; 95% CI 18·52–20·57).

For cause-specific excess mortality from natural causes, in absolute numbers, excess deaths accumulated in causes in which the background mortality was also highest, namely neoplasms and cardiovascular disease (appendix p 18). In contrast, causes of death, such as respiratory disease, gastrointestinal disease, and endocrine and metabolic disease, had the highest shares of excess deaths relative to background mortality. Of all

	Observed deaths	Expected deaths	SMR (95% CI)	SDRe/10 000 person-years	Excess deaths	Excess PYLL	PYLLe/De, years (95% CI)
Schizophrenia spectrum disorders							
Poland	50 770	21 675	2·34 (2·32–2·36)	87·60 (85·33–89·87)	29 093	522 851	17·97 (17·76–18·18)
Finland	23 097	6698	3·45 (3·41–3·49)	107·22 (100·24–110·20)	16 399	308 082	18·79 (18·49–19·09)
France	111 142	31 631	3·51 (3·49–3·53)	92·42 (91·18–93·66)	79 513	1 655 093	20·82 (20·67–20·97)
Denmark	14 571	3610	4·04 (3·97–4·11)	127·65 (123·19–132·11)	10 962	213 920	19·51 (19·14–19·88)
Sweden	16 462	3869	4·25 (4·19–4·31)	112·02 (108·48–115·56)	12 595	237 025	18·82 (18·48–19·16)
Overall	216 042	67 483	3·45 (2·58–4·61)	105·29 (85·42–125·17)	148 562	2 936 971	19·18 (17·85–20·51)
Variability			I^2=100%, τ=0·23 (0·14–0·69)	I^2=99%, τ=15·93 (8·52–43·86)			I^2=99%, τ=1·06 (0·74–3·71)
Bipolar disorder							
Poland	7299	4889	1·49 (1·46–1·52)	33·62 (29·70–37·54)	2410	51 464	21·35 (20·48–22·22)
France	34 043	15 351	2·22 (2·20–2·24)	51·21 (49·35–53·07)	18 692	382 338	20·45 (20·15–20·75)
Finland	5675	2480	2·29 (2·23–2·35)	56·21 (52·07–60·35)	3196	67 894	21·24 (20·49–21·99)
Sweden	6201	2601	2·38 (2·32–2·44)	47·20 (44·03–50·37)	3601	77 734	21·59 (20·87–22·31)
Denmark	3429	1338	2·56 (2·47–2·65)	74·14 (68·12–80·16)	2093	30 836	14·73 (14·08–15·38)
Overall	56 647	26 659	2·15 (1·65–2·80)	52·36 (34·17–70·54)	29 992	610 266	19·87 (16·26–23·48)
Variability			I^2=100%, τ=0·21 (0·12–0·60)	I^2=97%, τ=14·50 (7·02–36·31)			I^2=99%, τ=2·89 (1·60–8·13)
Severe depression							
Finland	24 053	12 533	1·93 (1·91–1·95)	53·27 (51·23–55·31)	11 520	233 312	20·25 (19·87–20·63)
Poland	8134	4071	2·00 (1·96–2·04)	74·87 (69·33–80·41)	4062	87 918	21·64 (20·96–22·32)
Denmark	7181	2771	2·59 (2·53–2·65)	72·34 (68·18–76·50)	4412	78 324	17·75 (17·21–18·29)
France	229 681	82 125	2·80 (2·79–2·81)	70·55 (69·80–71·30)	147 554	2 891 122	19·59 (19·49–19·69)
Sweden	20 165	5972	3·38 (3·33–3·43)	84·15 (81·65–86·65)	14 193	266 840	18·80 (18·48–19·12)
Overall	289 214	107 472	2·48 (1·85–3·33)	70·98 (56·95–85·00)	181 741	3 557 516	19·60 (17·79–21·41)
Variability			I^2=100%, τ=0·24 (0·13–0·69)	I^2=99%, τ=11·16 (6·20–34·46)			I^2=96%, τ=1·44 (0·60–3·37)
Severe mental illness overall	**561 903**	**201 614**	**2·64 (2·25–3·11)**	**76·29 (61·79–90·80)**	**360 295**	**7 104 753**	**19·55 (18·52–20·57)**

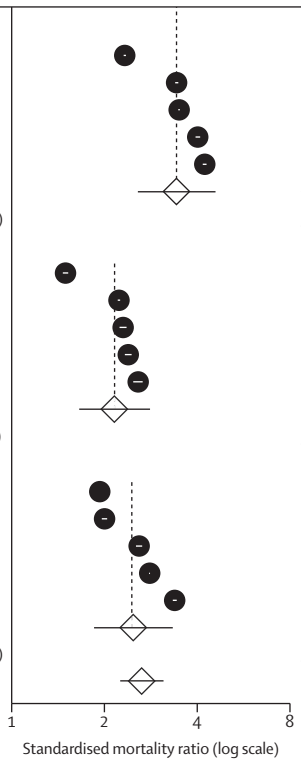

Figure 1: **All-cause mortality in severe mental illness**
Estimates are from random effects models with tau (τ) on the log scale for SMR and with gross excess mortality. PYLL=potential years-of-life-lost. PYLLe/De=excess PYLL/excess deaths. SDRe=standardised excess death rate. SMR=standardised mortality ratio.

deaths due to natural causes, share of excess deaths was highest in people with schizophrenia spectrum disorders (79 361 [68%] of 117 337 people) and lowest in people with bipolar disorder (14 610 [44%] of 33 053 people; appendix p 18).

Physical illnesses represented 61% (219 463 of 360 295) of all excess deaths and 54% (3 823 910 of 7 104 753 years) of all excess life-years-lost (figures 1, 2). Excess mortality from natural causes was highest in schizophrenia spectrum disorders (figure 2) both in absolute (SDRe 79·76 per 10 000 person-years) and relative terms (SMR 3·37; 95% CI 3·05–3·73), followed by major depressive disorder (SDRe 44·23 per 10 000 person-years; SMR 2·24; 95% CI 1·53–3·30), and bipolar disorder (SDRe 33·28 per 10 000 person-years; SMR 1·91; 95% CI 1·58–2·31). Each excess death from natural causes contributed, on average, about 15 life-years-lost (PYLLe/De 15·45; 95% CI 13·88–17·03).

In schizophrenia spectrum disorders, cardiovascular disease had the highest excess death rate (SDRe 22·08 per 10 000 person-years; 95% CI 8·77–35·39), about twice the excess rate in respiratory disease (11·09 per 10 000 person-years; 2·55–19·62; figure 2). Relative excess mortality was highest in respiratory disease, which was about six-fold higher than in the general population (SMR 6·49; 95% CI 5·52–7·64), and nearly twice the relative excess in cardiovascular disease (3·55; 2·72–4·64). High relative excess mortality was also observed in endocrine and metabolic diseases (5·09; 4·29–6·04) and in gastrointestinal diseases (3·47; 2·58–4·67). Cardiovascular disease contributed more than twice the number of excess PYLL compared with respiratory disease (280 230 years *vs* 128 585 years). In contrast, respiratory, endocrine and metabolic, and gastrointestinal diseases combined contributed about 19% more excess PYLL (334 174 years) than cardiovascular disease alone. The highest number of life-years-lost per excess death was from gastrointestinal disease (PYLLe/De 18·51; 95% CI 15·40–21·63), and lowest from respiratory disease (13·08; 10·48–15·47).

In bipolar disorder, cardiovascular disease had the highest excess death rate (SDRe 8·36 per 10 000 person-years; 95% CI 2·96 to 13·75), about twice the rate in respiratory disease (3·90 per 10 000 person-years; –1·47 to 9·26). Relative excess mortality was consistently between two-to-three-fold higher than in the general population, except in neoplasms in which it was about 20% higher (figure 2). Relative excess mortality was highest in respiratory disease (SMR 2·72; 95% CI 2·04 to 3·63), followed by endocrine and metabolic disease

(2·60; 2·26 to 2·98), and gastrointestinal disease (2·34; 2·00 to 2·74). Cardiovascular disease contributed about 2·6-times the number of excess PYLL compared with respiratory disease (PYLL 49 907 years *vs* 19 320 years). Respiratory disease, endocrine and metabolic disease, and gastrointestinal disease combined contributed about 31% more excess PYLL (65 176 years) compared with cardiovascular disease alone. Highest number of

	Observed deaths (%)	Expected deaths (%)	SMR (95% CI)	SDRe/10 000 person-years	Excess deaths (%)	Excess PYLL (%)	PYLLe/De, years (95% CI)
Schizophrenia spectrum disorders							
Neoplasms	34 170 (29)	18 742 (49)	1·87 (1·77–1·97)	12·61 (10·36–14·87)	15 436 (20)	275 657 (20)	15·35 (10·55–20·14)
Variability			I^2=87%, τ=0·03 (0·01–0·14)	I^2=72%, τ=1·12 (0·38–5·08)			I^2=99%, τ=2·99 (1·90–10·80)
Gastrointestinal disease	9245 (8)	2812 (7)	3·47 (2·58–4·67)	5·85 (3·56–8·14)	6436 (8)	125 000 (9)	18·51 (15·40–21·63)
Variability			I^2=98%, τ=0·18 (0·09–0·66)	I^2=93%, τ=1·37 (0·66–5·07)			I^2=91%, τ=1·86 (0·92–7·28)
Cardiovascular disease	25 794 (22)	7927 (21)	3·55 (2·72–4·64)	22·08 (8·77–35·39)	17 873 (23)	280 230 (21)	14·95 (11·58–18·33)
Variability			I^2=99%, τ=0·17 (0·10–0·65)	I^2=100%, τ=8·35 (5·58–32·46)			I^2=99%, τ=2·10 (1·25–8·25)
Endocrine and metabolic diseases	5846 (5)	1139 (3)	5·09 (4·29–6·04)	4·25 (2·08–6·42)	4707 (6)	80 589 (6)	16·57 (14·23–18·91)
Variability			I^2=86%, τ=0·10 (0·04–0·37)	I^2=95%, τ=1·32 (0·62–4·73)			I^2=83%, τ=1·31 (0·52–5·54)
Respiratory disease	10 889 (9)	1755 (5)	6·49 (5·52–7·64)	11·09 (2·55–19·62)	9137 (12)	128 585 (10)	13·08 (10·48–15·47)
Variability			I^2=95%, τ=0·10 (0·05–0·38)	I^2=99%, τ=5·31 (2·36–13·87)			I^2=97%, τ=1·60 (0·94–6·58)
Other natural causes	31 393 (27)	5636 (15)	5·38 (4·47–6·46)	20·06 (10·87–29·26)	25 772 (33)	460 139 (34)	15·70 (11·48–19·91)
Variability			I^2=98%, τ=0·11 (0·06–0·41)	I^2=99%, τ=5·73 (2·98–17·20)			I^2=99%, τ=2·63 (1·58–10·00)
All natural causes	117 337 (100)	38 011 (100)	3·37 (3·05–3·73)	79·76 (62·49–97·03)	79 361 (100)	1 350 200 (100)	15·65 (11·40–19·89)
Variability			I^2=98%, τ=0·06 (0·03–0·22)	I^2=97%, τ=10·69 (4·80–28·06)			I^2=100%, τ=2·66 (1·68–10·00)
Bipolar disorder							
Neoplasms	11 650 (35)	9590 (51)	1·22 (1·13–1·30)	3·15 (1·42–4·89)	2293 (16)	44 908 (18)	15·73 (9·49–21·98)
Variability			I^2=58%, τ=0·04 (<0·00–0·16)	I^2=49%, τ=0·69 (<0·00–4·24)			I^2=97%, τ=3·81 (2·32–13·70)
Cardiovascular disease	6849 (21)	3749 (20)	1·97 (1·56–2·49)	8·36 (2·96–13·75)	3112 (21)	49 907 (20)	14·54 (9·58–19·51)
Variability			I^2=95%, τ=0·14 (0·07–0·53)	I^2=96%, τ=3·30 (1·91–11·51)			I^2=97%, τ=3·06 (1·70–10·00)
Gastrointestinal disease	2887 (9)	1275 (7)	2·34 (2·00–2·74)	3·51 (0·72–6·30)	1620 (11)	30 416 (12)	17·76 (14·22–21·30)
Variability			I^2=84%, τ=0·09 (0·03–0·39)	I^2=93%, τ=1·69 (0·80–6·25)			I^2=74%, τ=1·92 (0·55–8·22)
Endocrine and metabolic diseases	1461 (4)	568 (3)	2·60 (2·26–2·98)	1·66 (0·53–2·79)	903 (6)	15 440 (6)	15·58 (8·87–22·29)
Variability			I^2=29%, τ=0·06 (<0·00–0·34)	I^2=67%, τ=0·52 (0·18–2·45)			I^2=93%, τ=3·93 (2·06–13·27)
Respiratory disease	2355 (7)	882 (5)	2·72 (2·04–3·63)	3·90 (–1·47–9·26)	1480 (10)	19 320 (8)	12·19 (7·57–16·81)
Variability			I^2=91%, τ=0·17 (0·08–0·64)	I^2=94%, τ=3·26 (1·22–9·29)			I^2=95%, τ=2·76 (1·49–10·00)
Other natural causes	7851 (24)	2659 (14)	2·81 (1·97–4·02)	9·08 (2·37–15·79)	5202 (36)	87 125 (35)	13·47 (8·30–18·63)
Variability			I^2=97%, τ=0·22 (0·10–0·76)	I^2=97%, τ=4·10 (1·97–11·63)			I^2=98%, τ=3·19 (2·03–11·78)
All natural causes	33 053 (100)	18 723 (100)	1·91 (1·58–2·31)	33·28 (13·55–53·01)	14 610 (100)	247 116 (100)	14·96 (9·84–20·08)
Variability			I^2=98%, τ=0·12 (0·06–0·40)	I^2=97%, τ=12·19 (5·44–31·85)			I^2=99%, τ=3·19 (1·98–11·25)
Severe depression							
Neoplasms	94 535 (44)	46 303 (52)	1·62 (1·07–2·45)	9·97 (–0·56–20·50)	48 239 (38)	876 861 (39)	15·63 (12·51–18·75)
Variability			I^2=100%, τ=0·26 (0·16–1·15)	I^2=100%, τ=6·61 (4·28–24·90)			I^2=99%, τ=1·91 (1·30–9·93)
Cardiovascular disease	35 463 (17)	17 204 (19)	2·14 (1·42–3·20)	9·82 (3·18–16·45)	18 265 (15)	303 967 (14)	14·97 (11·13–18·81)
Variability			I^2=100%, τ=0·25 (0·13–0·95)	I^2=99%, τ=4·14 (2·23–13·20)			I^2=99%, τ=2·39 (1·45–10·00)
Respiratory disease	12 612 (6)	3964 (5)	2·88 (1·70–4·88)	3·90 (0·64–7·16)	8654 (7)	122 032 (6)	12·17 (9·10–15·24)
Variability			I^2=99%, τ=0·33 (0·16–1·17)	I^2=98%, τ=2·01 (0·89–6·93)			I^2=97%, τ=1·87 (1·18–8·65)
Endocrine and metabolic diseases	8503 (4)	2623 (3)	3·07 (1·84–5·12)	2·38 (0·88–3·87)	5882 (5)	105 388 (5)	17·27 (13·06–21·48)
Variability			I^2=98%, τ=0·32 (0·15–1·12)	I^2=93%, τ=1·06 (0·49–3·94)			I^2=87%, τ=2·48 (0·96–8·75)
Gastrointestinal disease	21 473 (10)	6022 (7)	3·48 (2·63–4·62)	6·03 (4·27–7·78)	15 458 (12)	288 470 (13)	17·27 (14·47–20·07)
Variability			I^2=99%, τ=0·18 (0·09–0·67)	I^2=93%, τ=1·06 (0·49–3·94)			I^2=95%, τ=1·68 (0·93–7·23)
Other natural causes	41 920 (20)	12 935 (15)	2·93 (1·69–5·05)	9·48 (2·99–15·97)	28 994 (23)	529 876 (24)	15·59 (11·78–19·40)
Variability			I^2=100%, τ=0·34 (0·17–1·24)	I^2=100%, τ=4·06 (2·37–13·86)			I^2=99%, τ=2·36 (1·58–10·00)
All natural causes	214 506 (100)	89 051 (100)	2·24 (1·53–3·30)	44·23 (23·96–64·50)	125 492 (100)	2 226 594 (100)	15·74 (12·31–19·17)
Variability			I^2=100%, τ=0·24 (0·14–1·04)	I^2=100%, τ=12·72 (7·97–46·46)			I^2=100%, τ=2·15 (1·40–10·00)
Severe mental illness overall							
All natural causes	364 896 (100)	145 785 (100)	2·44 (2·03–2·93)	52·49 (37·61–67·37)	219 463 (100)	3 823 910 (100)	15·45 (13·88–17·03)

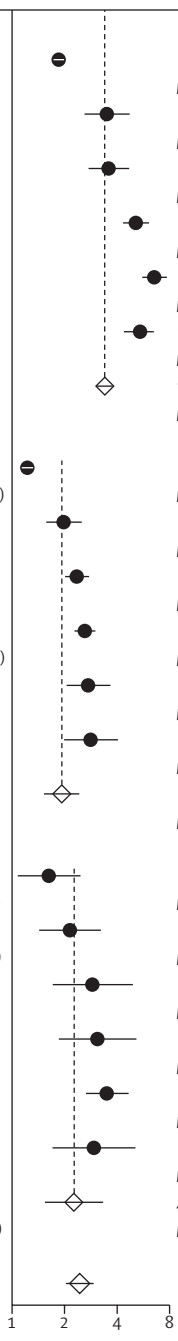

Figure 2: **Cause-specific mortality from natural causes by severe mental illness**
Estimates are from random effects models with Poland excluded, tau (τ) on the log scale for SMR, and with gross excess mortality. PYLL=potential years-of-life-lost. PYLLe/De=excess PYLL/excess deaths. SDRe=standardised excess death rate. SMR=standardised mortality ratio.

life-years-lost per excess death was from gastrointestinal disease (PYLLe/De 17·76; 95% CI 14·22 to 21·30) and lowest from respiratory disease (12·19; 7·57 to 16·81).

In major depressive disorder, cardiovascular disease had the highest excess death rate (SDRe 9·82 per 10 000 person-years; 95% CI 3·18–16·45), about 63% higher than in gastrointestinal disease (6·03 per 10 000 person-years; 4·27–7·78), and about 2·5-times the rate in respiratory disease (3·90 per 10 000 person-years; 0·64–7·16; figure 2). Relative excess mortality was consistently between two-fold and three-fold higher than in the general population. Relative excess mortality was highest in gastrointestinal disease (SMR 3·48; 95% CI 2·63–4·62), followed by endocrine and metabolic disease (3·07; 1·84–5·12), and respiratory disease (2·88; 1·70–4·88). Cardiovascular disease contributed about 5% higher number of excess PYLL compared with gastrointestinal disease (303 967 years *vs* 288 470 years). Gastrointestinal disease, respiratory disease, and endocrine and metabolic disease combined contributed about 70% more excess PYLL (515 890 years) compared with cardiovascular disease alone. The highest number of life-years-lost per excess death was from gastrointestinal disease (PYLLe/De 17·27; 95% CI 14·47–20·07) and from endocrine and metabolic disease (17·27; 13·06–21·48), and lowest from respiratory disease (12·17; 9·10–15·24).

Incorporating premature years-of-life-lost and joint contributions refined the interpretation of excess mortality patterns across severe mental illnesses. Although cardiovascular disease remained the leading contributor to absolute excess deaths, analysis of PYLL showed a more distributed burden across conditions with respiratory, endocrine and metabolic, and gastrointestinal diseases jointly accounted for having a substantially larger share of premature mortality than suggested by death counts alone. This combined contribution exceeded that of cardiovascular disease. A substantial proportion, about a third in schizophrenia spectrum disorders and bipolar disorder, and about one fifth in major depressive disorder of absolute excess mortality, came from the category of other natural causes (figure 2). Breakdown of this cause-of-death group showed high relative excess across all cause-specific categories (appendix p 19). Excess mortality due to physical illnesses showed a consistent dual burden pattern across severe mental illnesses, with high absolute mortality from common diseases alongside marked relative mortality inequalities for specific conditions (figure 3). Cardiovascular disease accounted for the largest absolute excess mortality burden across severe mental illnesses, whereas respiratory and endocrine or metabolic diseases showed the highest relative excess despite lower absolute excess death rates. When combining burden and inequity dimensions of excess mortality, schizophrenia spectrum disorders showed the most heterogeneous excess mortality

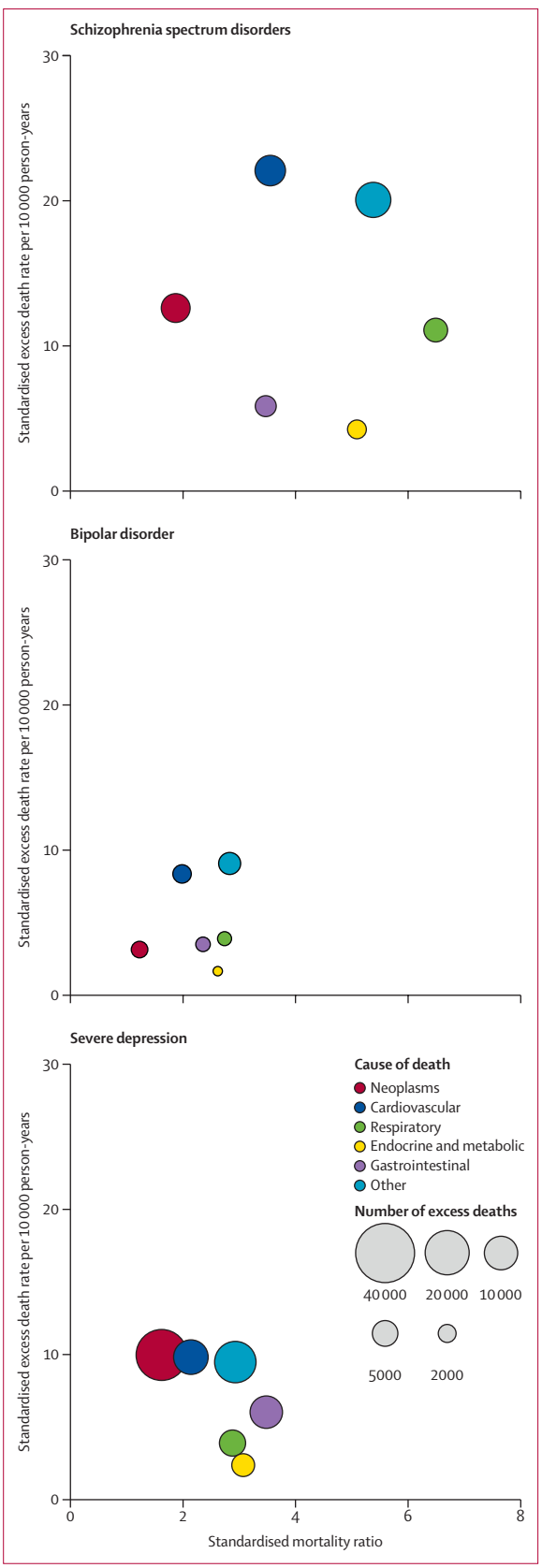

***Figure 3*: Absolute excess mortality, relative excess mortality, and total excess mortality burden by natural causes of death and severe mental illness**
Estimates are from random effects models with Poland excluded. The size of the circle indicates the total excess mortality burden as absolute number of excess deaths.

pattern, bipolar disorder an intermediate pattern with less spread across dimensions, and major depressive disorder with most clustered pattern. As dual burden pattern was seen across all severe mental illnesses, it was most evident in schizophrenia spectrum disorders, with cardiovascular disease, respiratory disease, and endocrine and metabolic diseases particularly contributing to this pattern.

Cause-specific mortality burden varied substantially between countries (figure 4), as indicated by the high I^2 statistic values, but in absolute terms, differences were small to moderate (appendix pp 20–22). Cross-country variability was largest in deaths due to cardiovascular disease and respiratory disease.

In terms of additional analyses, no significant differences were observed between females and males in all-cause and natural-cause mortality (test for subgroup differences, all p values >0·30; appendix p 23). In age-stratified models, relative excess mortality was highest in younger age groups (aged 15–34 years and 35–54 years) compared with the oldest age group (age 55–74 years; appendix p 24). This finding applied to all three severe mental illnesses and all-cause and natural-cause mortality, with significant age group differences in most cause-of-death groups (p values ≤0·0011). Sensitivity analyses by cohort definitions did not show significant differences in all-cause mortality in schizophrenia spectrum disorders or bipolar disorder (test for subgroup differences, p=0·65 and p=0·95, respectively; appendix p 25). When the major depressive disorder cohort was defined only through disability pensions, all-cause mortality was significantly lower compared to when the major depressive disorder cohort was defined using information on both inpatient contacts and disability pensions (test for subgroup differences, p=0·0055; appendix p 25), meaning that people identified from inpatient contacts had significantly higher excess mortality than people identified from disability pensions. In Poland, hospital-based relative excess mortality from natural causes was highest in people diagnosed with schizophrenia spectrum disorders and lowest in people diagnosed with bipolar disorder (appendix p 26), which was consistent with population-based excess mortality in other countries. However, Poland differed in magnitude and relative contribution of causes. Consistent with other countries, respiratory disease had the highest relative excess mortality but, unlike in other countries, it was followed by cardiovascular disease. Furthermore, other cause-of-death groups did not show a consistent pattern across severe mental illnesses.

Discussion

Our findings on nearly 5 million people with severe mental illness have showed that excess mortality was characterised by three distinctive patterns—one of high absolute mortality rates mirroring the leading causes of death in the general population, another with markedly increased relative risks, and a third pattern specific to causes contributing to greatest loss of potential years-of-life. Overall, this excess mortality profile could reflect inequities in access to health care, in addition to differences in the quality and timeliness of care provided. The cause-specific mortality pattern in schizophrenia spectrum disorders suggested contribution of disease-specific underlying mechanisms in determining the excess mortality burden, whereas in bipolar disorder and major depressive disorder, excess mortality burden could be determined more by generalised vulnerability affecting equally across causes. Integrating multiple complementary mortality measures and considering joint cause contributions shifted the focus from a single dominant driver of excess mortality to a wider transdiagnostic pattern of premature mortality across multiple organ systems. These findings highlight the shared and differential cause-specific mechanisms underlying the persistent mortality gap experienced by people with severe mental illness and have potential implications for public health strategies aimed at reducing the mortality gap.

Our results confirm that mortality is about two-fold to three-fold higher in people diagnosed with severe mental illness compared with the general population,[3–7] and that excess mortality in severe mental illness was mainly driven by the same preventable and treatable conditions that are the leading causes of death in the general population, including most cancers, ischaemic heart disease, cerebrovascular disease, congestive heart failure, chronic obstructive pulmonary disease, chronic liver disease, and type 2 diabetes. These conditions are amenable to primary prevention through established interventions targeting modifiable risk factors, such as hypertension, dyslipidaemia, obesity, tobacco smoking, and harmful alcohol use. However, because people with severe mental illness experience inequities related to health-care access and quality,[22–24] strengthening primary prevention to reduce disease onset must be accompanied by improved secondary prevention. Integrated care models emphasising early detection, chronic disease management, and use of effective lower risk-profile pharmacotherapy could help reduce disproportionately increased mortality from treatable conditions.[14,19,22–24] Nearly half of the absolute mortality burden came from external causes of death, including unintentional injuries, poisonings, and suicides. Because external causes contribute a substantial proportion of excess deaths, particularly at younger ages, continuous risk assessment remains essential.[10] Consistent with previous research, sex-stratified models showed similar associations in females and males, whereas relative excess mortality was highest in younger age groups across most causes.

Focusing on high absolute mortality alone overlooks a substantial proportion of excess mortality burden attributable to various other physical conditions.

Respiratory disease, endocrine and metabolic diseases, and gastrointestinal disease contributed fewer deaths in absolute terms than cardiovascular disease but showed substantially higher relative excess mortality. In addition to increased relative risks, gastrointestinal and endocrine and metabolic diseases also contributed to excess mortality through deaths occurring, on average, at younger ages compared with other disease groups.

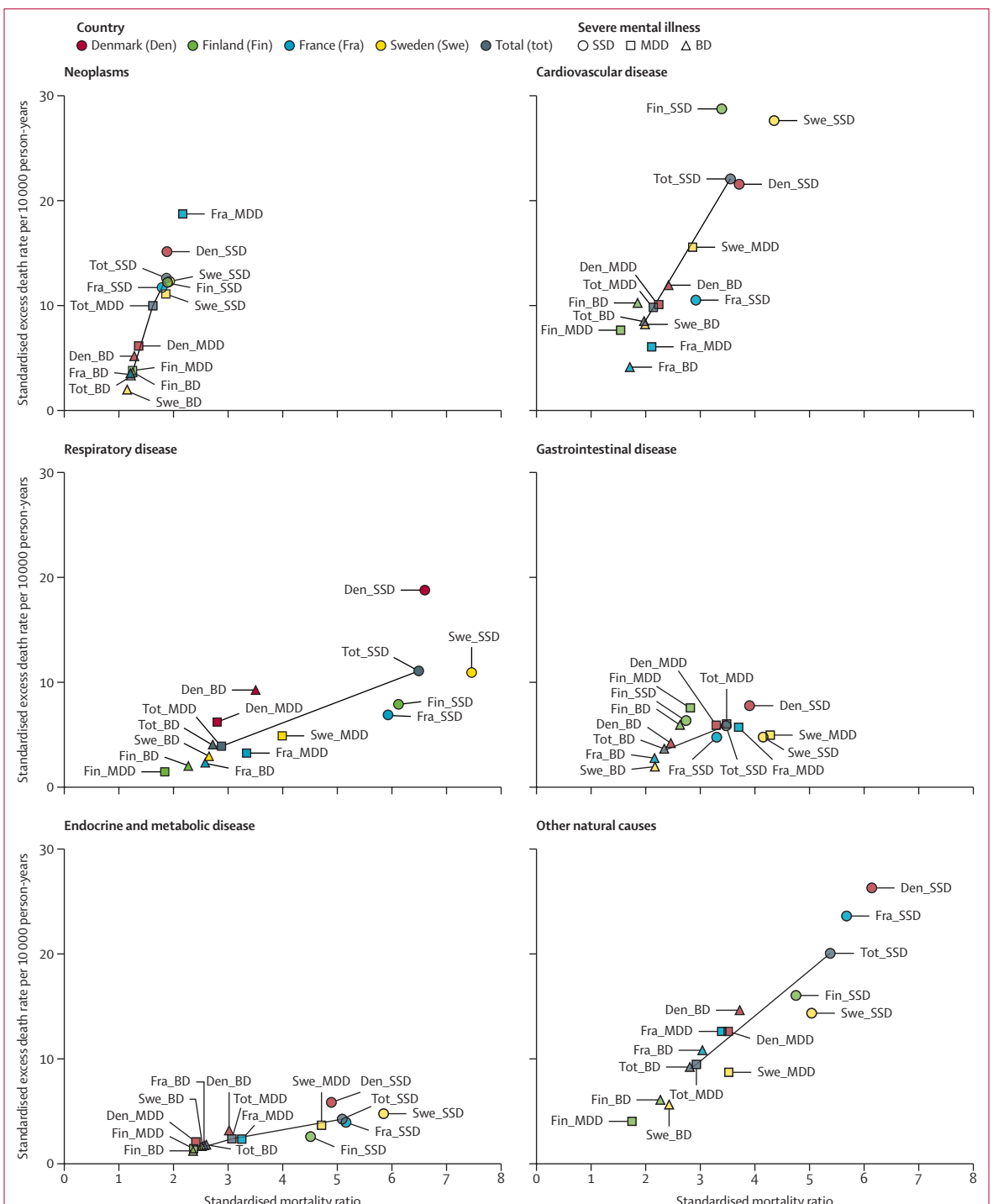

Figure 4: **Absolute excess mortality and relative excess mortality by natural cause of death group, country, and severe mental illness**
Estimates are from random effects models with Poland excluded. The solid grey lines connect disease-specific pooled estimates and are provided as visual aids. BD=Bipolar disorder. MDD=Severe depression. SSD=Schizophrenia spectrum disorders.

Consequently, these disease groups contributed equally, or more, to total excess burden than cardiovascular disease alone. Furthermore, a wide range of additional causes collectively accounted for about one-third of all excess deaths and life-years-lost. Overall, these findings support a multilevel approach that combines population-wide risk factor reduction with improved and more integrated health care for high-risk groups, while also addressing wider social and structural factors that shape health outcomes. Future work should aim to establish how upstream social determinants of health shape these pathways.

Combined evaluation of absolute and relative excess mortality has potential, important implications for public health prioritisation, because different patterns imply different intervention strategies. Causes with high absolute but moderate relative excess mortality could reflect failures in system-level prevention, detection, and treatment and can be addressed through scaling up and strengthening shared care pathways. Causes with high relative excess mortality could indicate areas where universal approaches are insufficient and where more targeted interventions are required. Causes with both high absolute and high relative excess mortality probably require a combination of population-wide and targeted strategies. In our study, excess mortality in people with schizophrenia spectrum disorders showed a marked dual burden of high absolute and high relative excess mortality, whereas excess mortality in people diagnosed with bipolar disorder and major depressive disorder was more evenly distributed across causes. This pattern could suggest a greater contribution of disease-specific mechanisms in schizophrenia spectrum disorders, whereas the more uniform pattern in bipolar disorder and major depressive disorder could reflect broader vulnerability driven by shared determinants. From a transdiagnostic perspective, psychiatric epidemiology would benefit from moving beyond a predominantly relative-risk framework towards an integrated approach that jointly quantifies relative inequalities alongside absolute excess burden.[29,30] Such an approach would strengthen the basis for public health prioritisation and organisation of care by ensuring that epidemiological estimates reflect both disparity and population impact in a form directly usable for intervention planning and resource allocation.

The number of included countries in our study did not allow direct cross-country comparisons. Excess mortality patterns in the Nordic countries are well described, whereas excess mortality in France and Poland is less often reported. France has comparable high-resource context with the Nordic countries, which could have partly explained the largely comparable excess mortality patterns observed between France and the Nordic countries. Poland had lower Healthcare Access and Quality Index scores and higher avoidable mortality in the general population, particularly from treatable causes, compared with countries with higher health system performance. Nevertheless, all-cause excess mortality was consistently lower in Poland, with a magnitude similar to that reported previously.[31] This observation might not only reflect higher reference population mortality affecting relative risk measures, but also possible under-identification and diagnostic misclassification of severe mental illness in routine health-care data, differences in universal health-care coverage, access, and quality, and differences in the quality of cause-of-death attribution.[31] For example, in Poland, death records often capture only the immediate cause; intermediate causes and the full causal chain are frequently missing, and cause-of-death information is not centrally integrated across institutions. Infrequent autopsies and the use of terminal codes or broad categories (nearly 60% of deaths are coded as cardiovascular disease), together with limited awareness of psychiatric illness history and diagnostic overshadowing, could further reduce specificity and distort the cause-of-death profile. These data quality concerns limit direct comparisons between Poland and the other included countries.

The strengths of our study include the use of high-quality nationwide health registers capturing people diagnosed with severe mental illness and the use of harmonised methods to collect and analyse country-specific mortality. Our transdiagnostic approach across severe mental illnesses enabled direct comparison of cause-specific mortality patterns across severe mental illnesses. We explicitly distinguished between population burden and relative inequity, which enabled us to provide a decomposition of the drivers of the mortality gap and to highlight an underlying dual burden in excess mortality.

As in all register-based studies, there are limitations that should be acknowledged. Cross-country variability in cause-specific mortality patterns should be interpreted with caution because these could partly reflect differences in cause-of-death ascertainment and coding practices across countries. Because health registers are collected for administrative purposes, the information available did not allow us to analyse potential factors associated with various causes of death. Because we had cause-specific natural-cause mortality only from four countries, we were not able to conduct meta-regression to identify potential country-level factors explaining cross-country differences in mortality estimates. However, because cross-country differences in mortality across severe mental illness groups mirrored cross-country differences in general population mortality, the factors explaining mortality differences are probably more related to general population determinants than to severe mental illness-specific factors. Our results are consistent with various other multi-country meta-analyses on relative excess mortality,[3–7,10] but the countries included are not representative of all European countries, which limits generalisability of the results. Multiple imputation of missing cause-of-death information in the French data produced a consistent distribution of causes of death and imputation did not change the direction or interpretation

of mortality estimates, but the limited number of covariates available in the registers could have introduced some uncertainty into the imputed estimates. Data from Denmark did not include disability pensions and sickness absences for case identification, which could have affected the country-specific estimates particularly in major depressive disorder. Although we adopted a transdiagnostic public health framework to identify shared mortality patterns and prioritisation targets across severe mental illness diagnoses, the mechanisms underlying excess mortality are likely heterogeneous across disorders and causes of death, involving differing combinations of biological, behavioural, socioeconomic, treatment-related, and other health system factors. Our study cannot disentangle these pathways and, therefore, the observed associations should not be interpreted mechanistically.

Excess mortality in people with severe mental illness was characterised by three complementary dimensions, including leading causes of absolute excess, relative excess, and premature excess mortality. Addressing the persistent mortality gap in people with severe mental illness requires integrated physical and psychiatric care alongside policies that tackle upstream social determinants.[32] Public health strategies should target both causes contributing the greatest absolute number of deaths and those with the largest inequities.[33] This transdiagnostic equity-weighted framework requires multilevel systemic reform rather than improvements in individual clinical care alone. Integrating prevention and treatment of physical illnesses in psychiatric care will provide opportunities to address shared risk factors across severe mental illnesses and shared underlying aetiological mechanisms across various competing causes of death.

Contributors

LB, HT, and TTG designed the study. TTG, HT, VP, VO, MZ, EAR, and JBV accessed and verified the underlying country-specific data. TTG did the statistical analysis, and wrote the first draft of the manuscript. AH, AK, EAR, EM-R, HT, JBV, JT, LB, MM, MZ, REN, TTG, UI, VO, and VP equally reviewed and revised the manuscript for important intellectual content. LB acquired funding and provided project oversight. All authors were responsible for the decision to submit the manuscript for publication.

Declaration of interests

HT has, within the past 3 years, received grants from Janssen, and speaking fees from Gedeon Richter, Janssen, Lundbeck, Otsuka, and Teva. MM has, within the past 3 years, received speaking fees from Lundbeck, Rovi, Johnson and Johnson, Viatris, Fidia, and Angelini. REN has, within the past 3 years, been an investigator for Compass Pharmaceuticals and Boehringer Ingelheim for clinical trials, and has received speaking fees from Lundbeck, Teva Pharmaceuticals, Janssen-Cilag, and Boehringer Ingelheim. All other authors declare no competing interests.

Data sharing

The data that support the findings of this study can be obtained from the institutions maintaining the registers used in this study. Restrictions apply to the availability of these data.

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