BJPsych | The British Journal of Psychiatry (2022)
221, 394–401. doi: 10.1192/bjp.2021.120

Association of severe mental illness with stroke outcomes and process-of-care quality indicators: nationwide cohort study

Kelly Fleetwood, Sarah H. Wild, Daniel J. Smith, Stewart W. Mercer, Kirsty Licence, Cathie L. M. Sudlow and Caroline A. Jackson

Background

Severe mental illness (SMI) is associated with increased stroke risk, but little is known about how SMI relates to stroke prognosis and receipt of acute care.

Aims

To determine the association between SMI and stroke outcomes and receipt of process-of-care quality indicators (such as timely admission to stroke unit).

Method

We conducted a cohort study using routinely collected linked data-sets, including adults with a first hospital admission for stroke in Scotland during 1991–2014, with process-of-care quality indicator data available from 2010. We identified pre-existing schizophrenia, bipolar disorder and major depression from hospital records. We used logistic regression to evaluate 30-day, 1-year and 5-year mortality and receipt of process-of-care quality indicators by pre-existing SMI, adjusting for socio-demographic and clinical factors. We used Cox regression to evaluate further stroke and vascular events (stroke and myocardial infarction).

Results

Among 228 699 patients who had had a stroke, 1186 (0.5%), 859 (0.4%), 7308 (3.2%) had schizophrenia, bipolar disorder and major depression, respectively. Overall, median follow-up was 2.6 years. Compared with adults without a record of mental illness, 30-day mortality was higher for schizophrenia (adjusted odds ratio (aOR) = 1.33, 95% CI 1.16–1.52), bipolar disorder (aOR = 1.37, 95% CI 1.18–1.60) and major depression (aOR = 1.11, 95% CI 1.05–1.18). Each disorder was also associated with marked increased risk of 1-year and 5-year mortality and further stroke and vascular events. There were no clear differences in receipt of process-of-care quality indicators.

Conclusions

Pre-existing SMI was associated with higher risks of mortality and further vascular events. Urgent action is needed to better understand and address the reasons for these disparities.

Keywords

Schizophrenia; bipolar affective disorders; depressive disorders; stroke; epidemiology.

Background

Severe mental illness (SMI), including schizophrenia, bipolar disorder and major depression, reduces life expectancy by 10–20 years,[1] which is comparable with the effect of smoking and greater than the effect of obesity.[2,3] In Scotland, where the present study was based, SMI reduces life expectancy by about 17 years.[4] This excess mortality largely reflects the greater burden of physical disease, particularly cardiovascular disease, in people with SMI.[1,4] Despite long recognition of the mental health inequalities in physical disease, this continues to be a shamefully neglected area of public health, with these gaps remaining unchanged or widening in recent decades.[5,6]

To date, epidemiological study of the links between SMI and physical disease has centred more on the physical disease occurrence and less on disease outcomes. This is particularly apparent for stroke. Pre-existing SMI is associated with about a twofold increased risk of stroke, with the magnitude of effect varying by mental health disorder,[1,7] but there has been little study of the association with stroke outcomes. Although post-stroke depression has been widely studied and has been linked to poorer prognosis, including increased mortality,[8] pre-existing depression in relation to stroke outcomes has rarely been studied.[9] Similarly, there are limited data on the effects of pre-existing schizophrenia[10–12] and bipolar disorder[13,14] on stroke prognosis. These studies have variously reported on long-term[9,11,13,14] and short-term mortality outcomes.[10,12,13] Although the reasons for the large physical disease burden among people with SMI are complex and not yet fully understood, suboptimal clinical care is thought to play a role.[15] A handful of studies suggest that patients who have had a stroke with pre-existing SMI may be less likely to receive interventions such as reperfusion therapies[16,17] or carotid endarterectomy,[18] but there has been almost no study of routine acute stroke care by SMI status.[19]

Objective

To address these gaps, we sought to compare, among patients who had had a stroke and were admitted to hospital: (a) stroke mortality and further stroke and vascular event risk and (b) receipt of acute stroke process-of-care quality indicators (such as timely brain scan and admission to stroke unit), among people with prior hospital admission for each of schizophrenia, bipolar disorder and depression, compared with people with no prior hospital admission for a mental health condition.

Method

Data sources

This nationwide retrospective cohort study uses data from Scotland including acute and psychiatric hospital records, death records and stroke audit records (Supplementary Text 1, available at https://doi.org/10.1192/bjp.2021.120), provided by the electronic Data Research and Innovation Service (eDRIS), Public Health Scotland.

https://doi.org/10.1192/bjp.2021.120 Published online by Cambridge University Press

Records were linked by eDRIS using the Community Health Index number, a unique identifier for people registered with the National Health Service (NHS) Scotland. We obtained approval to conduct this study with pseudonymised, non-consented data from the NHS Scotland Public Benefit and Privacy Panel for Health and Social Care (reference number 1617-0179).

Study populations

We included all adults aged 18 or over with a diagnosis of stroke recorded in acute hospital admission records. We identified index strokes from ICD-9 (430, 431, 434 and 436) and ICD-10 (I60, I61, I63, I64) codes[20] recorded in a primary or secondary diagnosis field that occurred between 1991 and 2014, where no hospital admission for stroke was recorded during the preceding 10 years.

We also defined a subcohort of adults with information on receipt of acute stroke process-of-care quality indicators. Since Scottish hospital records do not contain detailed information on clinical care, we used data from the Scottish Stroke Care Audit (https://www.strokeaudit.scot.nhs.uk/index.html). The audit includes information on patients who had had a stroke and their care in hospitals that manage acute stroke in Scotland, with national coverage from 2010 onwards. We included all index strokes recorded in the stroke audit between 2010 and 2014 that had a concurrent acute hospital record for stroke.

SMI

We determined history of a mental health condition from acute and psychiatric hospital records. We identified mental health conditions from diagnosis fields of admissions that occurred after the individual's 18th birthday and before their incident stroke (Supplementary Table 1). We categorised people into mutually exclusive SMI groups, using a severity hierarchy when more than one diagnosis was recorded: schizophrenia was considered the most severe disorder, followed by bipolar disorder and then depression. We compared outcomes after stroke in people with a history of each of these three disorders versus those with no prior hospital admission record for any mental health condition (Supplementary Table 1).

Mortality and further stroke and vascular events

Primary outcomes were 30-day, 1-year and 5-year mortality. Secondary outcomes included mortality over the entire follow-up period and time to each of further stroke and further vascular event (with a vascular event defined as either a stroke or myocardial infarction). We identified deaths from Scottish death records, available up to 31 December 2018. We defined further stroke as stroke occurring more than 30 days after the index stroke, ascertained from acute hospital admissions using the same approach as for index strokes or death records. We defined further vascular event as a stroke or myocardial infarction occurring more than 30 days after the index stroke, with myocardial infarctions ascertained from ICD-9 (410) and ICD-10 (I21, I22) codes in the primary or secondary fields of acute hospital admission records or death records.

Process-of-care quality indicators

We defined acute stroke process-of care quality indicators based on Scottish stroke care standards.[21] These included: admission to stroke unit within 1 day of admission; brain imaging on day of admission; swallow screen on day of admission; and aspirin within 1 day of admission for individuals with an ischaemic stroke and no valid contraindication to aspirin.

Covariates

We defined area-based deprivation (measured by the Carstairs index[22]), urbanicity and health board based on place of residence at the time of stroke (Supplementary Text 1). We ascertained history of alcohol use disorder from ICD codes in diagnosis fields in hospital records prior to the date of incident stroke (Supplementary Table 2). For descriptive analyses of the larger cohort, we used ICD codes to identify diagnoses of atrial fibrillation, diabetes and hypertension from the hospital record for the incident stroke (Supplementary Table 3).

For the stroke audit subcohort we also included pathological stroke type and six case-mix variables (age, whether patients lived alone and were independent in activities of daily living (ADL) before the stroke and whether patients were able to communicate verbally, lift both arms and walk without help from another person at first clinical assessment) that predict stroke mortality and functional outcome.[23] We were also able to ascertain atrial fibrillation and hypertension from relevant audit questions, and diabetes through linkage to Scotland's diabetes register (Supplementary Text 1).

Statistical analysis

We used direct standardisation to calculate gender-specific age-standardised proportions for the three primary mortality outcomes, by time period. To address potential issues of small numbers, we aggregated age into four groups (<60, 60–69, 70–79 and ≥80 years) and time into four time periods of equal duration. We used an internal standard population, which we derived from the age structure of the entire nationwide stroke population who had been admitted to hospital for the period 2003–2008 (i.e. roughly the midpoint of the time period of this study), to which we applied our age-specific rates for each comparison group.

Mortality and further stroke/vascular events

We used logistic regression to model 30-day, 1-year and 5-year mortality, and Cox regression for mortality during the entire follow-up period and for time to further stroke or vascular events. For time to further stroke or vascular events, we accounted for death as a competing risk, censoring at the date of death. For each outcome, model 1 included SMI, age, gender and year and model 2 additionally included history of alcohol use disorder, deprivation, urbanicity and health board. We included age at stroke and year of admission as continuous variables modelled as fractional polynomials in order to allow for non-linear relationships between these variables and the outcomes,[24] and the remaining covariates as categorical variables.

We repeated our analyses of the mortality and further event outcomes using the stroke audit subcohort, with additional adjustment for pathological stroke type (which was poorly recorded in earlier years of the acute hospital records and so was not adjusted for in the main mortality analyses), diabetes, atrial fibrillation, hypertension and the case-mix variables.

For both cohorts, our analyses were based on participants with no missing data; all mortality and recurrence outcome variables were complete. In the main cohort, a small number of participants (0.6%) were missing data on deprivation, urbanicity and/or health board (all other variables were complete). In the stroke audit subcohort, 4% of people were missing data for area-based deprivation, urbanicity, health board, stroke type or atrial fibrillation. A further 14% of people were missing data on case-mix variables, and were excluded only from analyses that adjusted for these variables. There was no evidence that missing data on any variable (including the case-mix variables) was associated with SMI status (Pearson's chi-squared test, $P = 0.71$).

https://doi.org/10.1192/bjp.2021.120 Published online by Cambridge University Press

Acute stroke process-of-care quality indicators

We used logistic regression to model the association between SMI and receipt of acute stroke process-of-care quality indicators in the stroke audit subcohort. For each outcome, we included people who were eligible for the specific stroke care standard and had sufficient data to determine the outcome; for example, for admission to stroke unit within 1 day of admission we included people who survived at least 1 day.

Sensitivity analysis of depression definition

In our principal analyses, history of each mental health condition was ascertained from both acute and psychiatric hospital records. This approach may have affected depression ascertainment in particular, by potentially identifying people from across the depression severity spectrum, thereby including a more heterogeneous group with depression. Thus, in sensitivity analyses, we repeated all analyses using an alternative definition of prior depression based on psychiatric hospital admission only. The definitions of prior schizophrenia and bipolar disorder were unchanged.

All analyses were conducted using R version 3.6.1 (R Core Team, Vienna, Austria, https://www.R-project.org/).

Patient and public involvement

This study involved the analysis of pseudonymised administrative data. At the start of the research project we held a multistakeholder knowledge exchange event during which invited patient representatives and third-sector representatives had the opportunity to contribute to discussions about the research project. The study advisory board includes a member from Support in Mind who advised on the dissemination of study results to relevant communities.

Results

Cohort characteristics

There were 238 001 people with a first-ever hospital admission for stroke in Scotland between 1991 and 2014. After exclusions, we included 228 699 in our cohort (Supplementary Fig. 1). Of these, 1186 (0.5%) had schizophrenia, 859 (0.4%) had bipolar disorder and 7308 (3.2%) had major depression. Of people admitted to hospital with stroke, the average age of first recorded stroke was lowest for people with schizophrenia (65 years), compared with those with bipolar disorder (70 years), major depression (71 years) and no mental health condition (73 years). People with schizophrenia, and to a lesser extent, major depression, were more likely to live in deprived areas than people without a mental health condition (Table 1). The proportion with diabetes recorded in the stroke admission record was broadly similar across comparison groups, but people without a history of a mental health condition were more likely to have atrial fibrillation or hypertension recorded compared with those with an SMI. Median follow-up time was 2.6 years (interquartile range 0.1–7.7). For the entire study cohort, 30-day, 1-year and 5-year mortality were 23.3%, 39.5% and 61.3%, respectively (Supplementary Tables 4 and 5).

SMI and absolute stroke mortality over time

Absolute age-standardised gender-specific proportions of people dying within 30 days, 1 year and 5 years of stroke were generally higher in each SMI group than those with no record of any mental health condition. Mortality declined in most groups between 1991 and 2014, but tended to remain higher in people with an SMI (Fig. 1). However, small numbers of people with schizophrenia and bipolar disorder within calendar year groups created some uncertainty with respect to patterns of change over time.

SMI and relative effect on stroke outcomes

After adjusting for age, gender and year, each SMI was associated with greater odds of 30-day, 1-year and 5-year mortality. Effect estimates attenuated only slightly after additional adjustment for alcohol use disorder, urbanicity, area-based deprivation and health board. The association between SMI and 30-day mortality was greatest in people with prior schizophrenia (odds ratio (OR) = 1.28, 95% CI 1.12–1.47) and bipolar disorder (OR = 1.36, 95% CI 1.16–1.58) and smallest for those with major depression (OR = 1.07, 95% CI 1.02–1.14; Table 2). Associations were slightly larger for 1-year mortality and larger again for 5-year mortality, with effect estimates again smallest for depression at 1 year but similar across groups at 5 years. Based on the results of the competing-risk Cox regression models, time to further stroke and further vascular event were significantly shorter among those with each SMI as compared with no mental health condition (Table 2), with associations similar across SMI groups.

Analyses of mortality and acute stroke process-of-care quality indicators in the stroke audit subcohort

There were 27 606 people with confirmed first-ever stroke between 2010 and 2014 eligible for our stroke audit subcohort (Supplementary Fig. 2). Of these, 167 had schizophrenia (0.6%), 102 had bipolar disorder (0.4%) and 1078 had major depression (3.9%). Baseline characteristics were similar to those of the main cohort (Supplementary Table 6). Mortality analyses in this subcohort produced a similar pattern of results as for the main cohort. Interestingly, additional adjustment for stroke type, diabetes, atrial fibrillation and hypertension did not materially alter effect estimates (Table 3). Case-mix differences varied by SMI group. Compared with people without a mental health condition, all SMI groups were less likely to be independent in ADL prior to their stroke and patients with bipolar disorder or major depression were less likely to walk without help from another person at first assessment. However, people with schizophrenia and bipolar disorder, but not depression were less likely to be able to talk at first assessment (Supplementary Table 6). Additional adjustment for case mix appeared to attenuate effect estimates, such that some were no longer statistically significant. However, since confidence intervals were wide, these adjusted estimates cannot rule out a persistent excess risk of poor outcome in those with an SMI.

Overall, on the day of admission 61.6% and 70.5% had brain imaging and a swallow screen, respectively, and within 1 day of admission 74.6% and 41.9% were admitted to a stroke unit and received aspirin, respectively (Supplementary Tables 7 and 8). Although there was no evidence of associations between schizophrenia, bipolar disorder and major depression and receipt of any of these process-of-care quality indicators, lower numbers of people with SMI in this subcohort means that wide confidence intervals do not necessarily preclude there being a reduction in receipt of care among people with an SMI (Table 3).

Sensitivity analysis of depression definition

Analyses of all outcomes including processes of acute stroke care were robust to sensitivity analyses in which we defined major depression according to admission to psychiatric hospitals only, with results generally similar to those obtained in the main analyses (Supplementary Tables 9 and 10). However, for receipt of brain imaging on day of admission and aspirin within 1 day of admission, differences in the rates between people with major depression versus

https://doi.org/10.1192/bjp.2021.120 Published online by Cambridge University Press

Table 1 Baseline characteristics and outcomes for people who were admitted to hospital with a stroke in Scotland, 1991–2014, comparing people with each severe mental illness *versus* no admission for any mental health condition

	No mental health condition (*n* = 219 346)	Schizophrenia (*n* = 1186)	Bipolar disorder (*n* = 859)	Major depression (*n* = 7308)
Follow-up time, years: median (IQR)	2.7 (0.1–7.7)	3.0 (0.1–7.6)	2.2 (0.1–6.3)	2.2 (0.1–6.5)
Gender, *n* (%)				
Female	117 069 (53.4)	634 (53.5)	558 (65.0)	4742 (64.9)
Male	102 277 (46.6)	552 (46.5)	301 (35.0)	2566 (35.1)
Age at stroke, years: mean (s.d.)	72.7 (13.5)	65.4 (13.5)	70.3 (12.4)	71.2 (14.0)
Year of admission, *n* (%)				
1991–1995	51 126 (23.3)	183 (15.4)	185 (21.5)	1216 (16.6)
1996–2000	50 417 (23.0)	245 (20.7)	156 (18.2)	1431 (19.6)
2001–2005	45 421 (20.7)	250 (21.1)	201 (23.4)	1723 (23.6)
2006–2010	40 725 (18.6)	291 (24.5)	177 (20.6)	1590 (21.8)
2011–2014	31 657 (14.4)	217 (18.3)	140 (16.3)	1348 (18.4)
Deprivation quintile, *n* (%)				
1 (most deprived)	49 623 (22.6)	364 (30.7)	161 (18.7)	1802 (24.7)
2	45 339 (20.7)	260 (21.9)	173 (20.1)	1603 (21.9)
3	43 651 (19.9)	231 (19.5)	187 (21.8)	1479 (20.2)
4	43 326 (19.8)	196 (16.5)	183 (21.3)	1338 (18.3)
5 (least deprived)	37 407 (17.1)	135 (11.4)	155 (18.0)	1086 (14.9)
Urbanity, *n* (%)				
Large urban area	78 175 (35.6)	479 (40.4)	334 (38.9)	2750 (37.6)
Other urban area	75 461 (34.4)	429 (36.2)	269 (31.3)	2476 (33.9)
Accessible small town	19 542 (8.9)	99 (8.3)	73 (8.5)	629 (8.6)
Remote small town	9131 (4.2)	42 (3.5)	33 (3.8)	351 (4.8)
Accessible rural	22 478 (10.2)	87 (7.3)	93 (10.8)	612 (8.4)
Remote rural	14 559 (6.6)	50 (4.2)	57 (6.6)	490 (6.7)
History of alcohol use disorder, *n* (%)	7256 (3.3)	194 (16.4)	91 (10.6)	1191 (16.3)
Type of stroke				
Ischaemic	79 832 (36.4)	463 (39.0)	296 (34.5)	2672 (36.6)
Haemorrhagic	32 117 (14.6)	150 (12.6)	113 (13.2)	941 (12.9)
Unclassified	107 397 (49.0)	573 (48.3)	450 (52.4)	3695 (50.6)
Atrial fibrillation recorded at stroke admission, *n* (%)	24 363 (11.1)	58 (4.9)	60 (7.0)	668 (9.1)
Diabetes recorded at stroke admission, *n* (%)	19 619 (8.9)	120 (10.1)	80 (9.3)	712 (9.7)
Hypertension recorded at stroke admission, *n* (%)	43 142 (19.7)	161 (13.6)	113 (13.2)	1260 (17.2)
30-day mortality, *n* (%)	50 959 (23.2)	278 (23.4)	231 (26.9)	1744 (23.9)
1-year mortality, *n* (%)	86 532 (39.5)	454 (38.3)	372 (43.3)	3041 (41.6)
5-year mortality[a]				
n	211 370	1123	810	6984
n (%)	129 241 (61.1)	666 (59.3)	520 (64.2)	4573 (65.5)
Further events during follow-up[b]				
n	168 387	908	628	5564
Stroke, *n* (%)	68 900 (40.9)	348 (38.3)	257 (40.9)	2214 (39.8)
Vascular event, *n* (%)	80 407 (47.8)	398 (43.8)	289 (46.0)	2594 (46.6)

IQR, interquartile range.
a. Based on the 220 287 individuals with their first stroke between 1991 and 2013.
b. Based on the 175 487 individuals who survived more than 30 days.

no mental health condition became larger and statistically significant when defining depression in this way.

Discussion

Main findings

In a national cohort of patients admitted to hospital with a stroke, those with schizophrenia, bipolar disorder and major depression had increased short- and long-term mortality and a greater risk of further stroke and vascular events, compared with those with no record of prior mental illness. The excess short-term mortality was greater among those with schizophrenia and bipolar disorder than major depression, but the increased long-term mortality was similar across these groups. In a subgroup where process of care data were available, there did not appear to be differences in receipt of acute stroke process-of-care quality indicators for those with SMI.

Strengths and weaknesses

Our study has various strengths. It makes an important and novel contribution to the paucity of literature on the association between pre-existing schizophrenia, bipolar disorder and depression and stroke prognosis, particularly 30-day and 1-year mortality. With the exception of one study of schizophrenia and long-term post-stroke mortality,[11] it is also the largest such study to date. Moreover, our study makes an important contribution to the sparse data on associations between SMI and processes of acute stroke care. Inclusion of national hospital admission data meant that we included an unselected cohort of patients admitted to hospital with a stroke. Furthermore, Scotland has a universal healthcare system and so our findings are unbiased by inequalities in access to care based on health insurance provision.

Our study has some limitations. Although hospital admission records in Scotland extend as far back as 1980, we may still have under-ascertained history of hospital admission for SMI, which

https://doi.org/10.1192/bjp.2021.120 Published online by Cambridge University Press

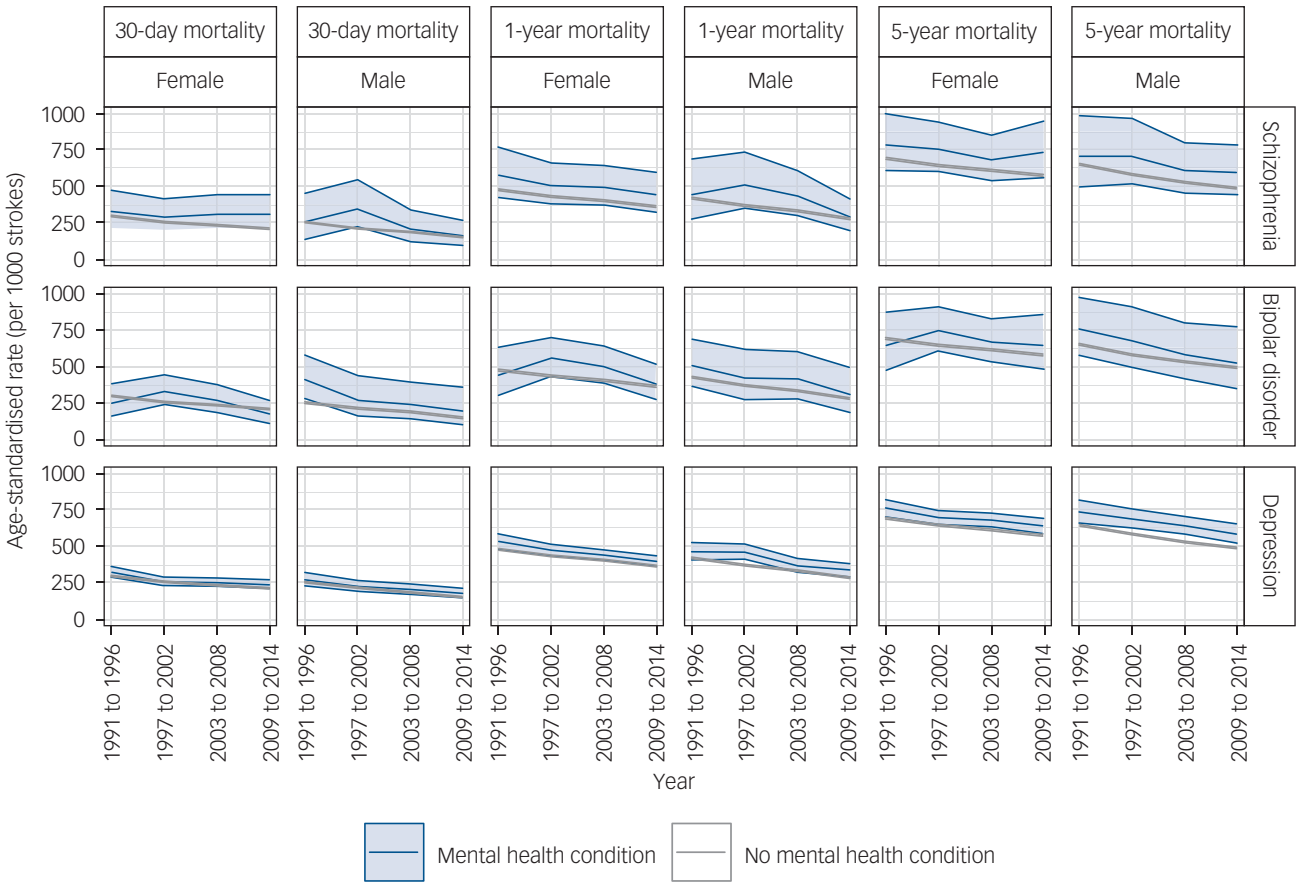

Fig. 1 Age-standardised rates of 30-day mortality, 1-year mortality and 5-year mortality following a hospital admission for stroke, by history of severe mental illness, 1991–2014 for men and women separately.

Shading represents 95% confidence intervals.

Table 2 Effect estimates for admissions to hospital for stroke outcomes in Scotland, 1991–2014, comparing people with each severe mental illness versus no admission for any mental health condition[a]

Outcome, model	*n*	Schizophrenia	Bipolar disorder	Major depression
Number of individuals per group	226 699	1186	859	7308
30-day mortality, OR (95% CI)	228 699			
Model 1		1.33 (1.16–1.52)	1.37 (1.18–1.60)	1.11 (1.05–1.18)
Model 2		1.28 (1.12–1.47)	1.36 (1.16–1.58)	1.07 (1.02–1.14)
1-year mortality, OR (95% CI)	228 699			
Model 1		1.49 (1.31–1.68)	1.44 (1.25–1.66)	1.24 (1.18–1.31)
Model 2		1.40 (1.24–1.58)	1.41 (1.23–1.63)	1.17 (1.11–1.23)
5-year mortality, OR (95% CI)	220 287[b]			
Model 1		1.80 (1.58–2.05)	1.53 (1.31–1.80)	1.55 (1.46–1.64)
Model 2		1.62 (1.42–1.85)	1.47 (1.26–1.73)	1.38 (1.30–1.46)
All-cause mortality, HR (95% CI)	228 699			
Model 1		1.45 (1.36–1.54)	1.36 (1.26–1.46)	1.26 (1.23–1.29)
Model 2		1.36 (1.27–1.45)	1.33 (1.23–1.43)	1.20 (1.16–1.23)
Time to further stroke, HR (95% CI)	175 487[c]			
Model 1		1.29 (1.16–1.43)	1.19 (1.05–1.34)	1.15 (1.10–1.20)
Model 2		1.24 (1.11–1.38)	1.17 (1.03–1.32)	1.11 (1.06–1.16)
Time to further vascular event, HR (95% CI)	175 487[c]			
Model 1		1.26 (1.14–1.39)	1.16 (1.03–1.30)	1.18 (1.14–1.23)
Model 2		1.21 (1.10–1.34)	1.14 (1.01–1.28)	1.14 (1.10–1.19)

OR, odds ratio; HR, hazard ratio.
a. Model 1 is adjusted for age, gender and year. Model 2 is additionally adjusted for history of alcohol use disorder, deprivation, urbanity and health board.
b. Stroke admissions up to 2013 in order to ensure that all individuals have at least 5 years' follow-up.
c. Individuals who survived more than 30 days.

means we are likely to have underestimated associations. Given that we identified people with SMI solely from hospital admission records, our findings may not be generalisable to the wider population of people with SMI. If severity of SMI is associated with outcome risk then our findings reflect the association among people with more severe disease. Effect estimates may be smaller

https://doi.org/10.1192/bjp.2021.120 Published online by Cambridge University Press

Table 3 Effect estimates for admissions to hospital for stroke outcomes and processes of acute stroke care, in Scotland, 2010–2014, based on data from the Scottish Stroke Care Audit and comparing people with each severe mental illness versus no admission for any mental health condition[a]

Outcome or process of acute stroke care, model	*n*	Schizophrenia	Bipolar disorder	Major depression
Number of individuals per group, *n*	27 606	167	102	1078
30-day mortality, OR (95% CI)				
Model 1	27 606	1.89 (1.19–2.88)	1.84 (1.04–3.06)	1.15 (0.95–1.38)
Model 2	27 606	1.80 (1.12–2.77)	2.05 (1.15–3.44)	1.07 (0.88–1.30)
Model 3	23 579[b]	1.05 (0.60–1.78)	1.75 (0.90–3.24)	1.01 (0.80–1.27)
1-year mortality, OR (95% CI)				
Model 1	27 606	1.62 (1.10–2.34)	1.74 (1.09–2.70)	1.16 (0.99–1.34)
Model 2	27 606	1.49 (1.00–2.17)	1.83 (1.15–2.85)	1.06 (0.91–1.24)
Model 3	23 579[b]	0.96 (0.60–1.51)	1.50 (0.87–2.52)	0.91 (0.75–1.09)
5-year mortality, OR (95% CI)				
Model 1	21 760[c]	2.72 (1.84–4.04)	2.26 (1.36–3.77)	1.61 (1.37–1.88)
Model 2	21 760[c]	2.34 (1.57–3.51)	2.25 (1.35–3.77)	1.39 (1.18–1.63)
Model 3	18 227[b,c]	1.70 (1.06–2.71)	1.82 (1.00–3.30)	1.29 (1.07–1.56)
Mortality during follow-up, HR (95% CI)				
Model 1	27 606	1.85 (1.51–2.27)	1.52 (1.18–1.97)	1.34 (1.24–1.45)
Model 2	27 606	1.72 (1.40–2.12)	1.61 (1.24–2.08)	1.25 (1.15–1.35)
Model 3	23 579[b]	1.27 (1.01–1.59)	1.46 (1.11–1.93)	1.11 (1.02–1.22)
Time to further stroke, HR (95% CI)				
Model 1	23 990[d]	1.46 (1.08–1.97)	1.23 (0.84–1.81)	1.21 (1.08–1.36)
Model 2	23 990[d]	1.34 (0.99–1.81)	1.22 (0.83–1.79)	1.12 (1.00–1.26)
Model 3	20 594[b,d]	1.22 (0.89–1.67)	1.06 (0.70–1.61)	1.03 (0.91–1.17)
Time to further vascular event, HR (95% CI)				
Model 1	23 990[d]	1.46 (1.09–1.94)	1.22 (0.84–1.77)	1.25 (1.12–1.39)
Model 2	23 990[d]	1.34 (1.01–1.79)	1.21 (0.84–1.76)	1.16 (1.04–1.29)
Model 3	20 594[b,d]	1.21 (0.89–1.65)	1.03 (0.68–1.55)	1.07 (0.95–1.21)
Admission to stroke unit within 1 day of admission, OR (95% CI)				
Model 1	27 118[e]	0.73 (0.52–1.02)	1.15 (0.74–1.88)	0.92 (0.80–1.06)
Model 2	27 118[e]	0.78 (0.56–1.10)	1.31 (0.83–2.15)	0.97 (0.84–1.12)
Model 3	23 227[b,e]	0.86 (0.60–1.25)	1.24 (0.77–2.07)	1.01 (0.86–1.18)
Brain imaging on day of admission, OR (95% CI)				
Model 1	27 274[f]	0.79 (0.57–1.08)	0.99 (0.66–1.50)	0.88 (0.77–1.00)
Model 2	27 274[f]	0.77 (0.56–1.07)	0.96 (0.64–1.47)	0.89 (0.78–1.02)
Model 3	23 319[b,f]	0.73 (0.51–1.05)	1.01 (0.64–1.62)	0.90 (0.78–1.05)
Swallow screen on day of admission, OR (95% CI)				
Model 1	27 125[g]	1.05 (0.74–1.50)	0.95 (0.62–1.48)	0.97 (0.85–1.12)
Model 2	27 125[g]	1.13 (0.80–1.63)	1.00 (0.65–1.56)	0.98 (0.85–1.13)
Model 3	23 231[b,g]	1.09 (0.75–1.61)	1.12 (0.70–1.86)	1.01 (0.87–1.18)
Aspirin within 1 day of admission, OR (95% CI)				
Model 1	21 776[h]	0.77 (0.53–1.09)	1.08 (0.71–1.63)	0.94 (0.82–1.08)
Model 2	21 776[h]	0.77 (0.53–1.11)	1.06 (0.69–1.61)	0.95 (0.82–1.10)
Model 3	18 687[b,h]	0.77 (0.51–1.13)	1.17 (0.75–1.83)	0.92 (0.78–1.07)

OR, odds ratio; HR, hazard ratio.
a. Model 1 is adjusted for age, gender and year. Model 2 is additionally adjusted for history of alcohol use disorder, deprivation, urbanity, health board, stroke type, diabetes, history of atrial fibrillation and hypertension. Model 3 is adjusted for all factors included in model 2, plus living alone before the stroke, independence in activities of daily living before the stroke, ability to communicate verbally at first clinical assessment, ability to lift both arms at first clinical assessment and ability to walk without help from another person at first clinical assessment. For aspirin within 1 day of admission, models 2 and 3 do not adjust for stroke type.
b. Records with complete data on the six simple variables (age, living alone before the stroke, independence in activities of daily living before the stroke, ability to communicate verbally at first clinical assessment, ability to lift both arms at first clinical assessment and ability to walk without help from another person at first clinical assessment).
c. Scottish Stroke Care Audit records up to 2013 in order to ensure that all individuals have at least 5 years' follow-up.
d. Individuals who survived more than 30 days.
e. Individuals who survived more than 1 day and had sufficient stroke unit data.
f. Individuals who survived their day of admission and had sufficient brain scan data.
g. Individuals who survived their day of admission and had sufficient swallow screen data.
h. Individuals who survived more than 1 day, had an ischaemic stroke, did not have a valid contraindication to aspirin and had sufficient aspirin data.

for people with a SMI for which they do not have an hospital admission record. There may have been selection bias in that the depression group may include a heterogeneous mix of people admitted to hospital for major depression as well as people with less severe depression admitted for other reasons. However, results were very similar in sensitivity analyses where we defined depression based on psychiatric hospital admissions only. This aligns with the comorbidity recording practice in Scottish acute hospitals, whereby depression as a comorbidity would be recorded only if it was severe enough to affect patient management.

We were unable to adjust for confounding by lifestyle factors such as smoking and obesity or comorbidities associated with stroke mortality. Although we were able to adjust for diabetes, hypertension and atrial fibrillation within our stroke audit subcohort, we were unable to adjust for multimorbidity in general, which will likely be higher in those with SMI and potentially associated with stroke outcome. Furthermore, the role of case mix, a proxy for stroke severity, in accounting for the observed disparities in our study is unclear, but merits further investigation in future studies. We will have under-ascertained further strokes, since we did not include strokes occurring within the first 30 days of the index event or milder events assessed only in stroke out-patient clinics.

Comparison with findings from previous studies

Just three previous studies have reported on the association between schizophrenia and mortality within the first year after stroke, all of which included fewer patients with schizophrenia than our study.[10,12,19] Findings on mortality from two of these were

https://doi.org/10.1192/bjp.2021.120 Published online by Cambridge University Press

consistent with our results.[12,19] In contrast, the smallest study reported lower 90-day mortality among people with versus without a history of schizophrenia.[10] The authors matched on admission to intensive care unit and length of stay in hospital, which could relate to schizophrenia status as well as the stroke event, thus results in an apparent reduced mortality in people with schizophrenia.

To our knowledge, no previous study has reported on pre-existing depression in relation to post-stroke mortality within 1 year and only one study (smaller than ours) examined the association between bipolar disorder and early stroke mortality.[13] In contrast to our findings, the authors reported that bipolar disorder was associated with 50% reduced odds of post-stroke in-hospital mortality.[13] The reason for these discordant findings could potentially reflect different stroke admission and discharge patterns related to the presence of bipolar disorder in the former study. Our finding that SMI is associated with higher post-stroke mortality beyond 1 year aligns with previous studies on longer-term stroke mortality in people with schizophrenia,[11] bipolar disorder[14] and depression.[9] We believe our study is the first to report on further stroke risk among patients with comorbid schizophrenia, bipolar disorder or depression.

To our knowledge, just one other study has investigated these particular acute stroke process-of-care quality indicators with respect to mental illness. The authors compared people with versus without schizophrenia and, as in our study, found no differences in admission to a stroke unit or timely brain imaging.[19] The reasons for the higher stroke case fatality in people with SMI are not fully understood, but are likely multifactorial. Although our analysis of the stroke audit subcohort did not find clear differences in receipt of stroke care, these results should be interpreted with caution given their wide confidence intervals. Receipt of procedures such as thrombolysis or carotid endarterectomy may differ by SMI status, but existing evidence is sparse and inconsistent.[16–19,25] Stroke severity, a key predictor of stroke survival, may contribute to differences in early mortality.[23]

In keeping with other studies,[9,17,25] analysis of our stroke audit subcohort revealed that stroke severity is higher in those with versus without SMI. Only one of these studies adjusted for stroke severity and found that it did not explain the excess case fatality among people with schizophrenia.[19] Although adjustment for case mix in our study attenuated estimates, findings were difficult to interpret given the statistical uncertainty of wide confidence intervals. A higher prevalence of comorbidities and poorer lifestyle factors in people with SMI likely accounts for some of the observed poorer prognosis but the available data in our study did not allow for comprehensive investigation of this. Associations persisted when we adjusted for diabetes, hypertension and atrial fibrillation in our analyses of the stroke audit subcohort, but residual confounding is likely, partly as a result of under-recognition and undertreatment of cardiovascular disease among people with SMI.[26]

The higher risk of further vascular events and long-term mortality among those with SMI observed in our study supports a need to investigate the possible role of suboptimal secondary prevention. Among lifestyle factors, smoking is particularly worrying, given the high prevalence and low cessation rates among people with SMI.[27] Although evidence is scant, there are reports that patients who had a stroke with schizophrenia are less likely to be prescribed antihypertensive, lipid-lowering or anticoagulant therapy at discharge from hospital than people without schizophrenia.[19] Finally, although psychotropic medication has been linked to increased mortality in stroke survivors in the long term,[28] its contribution to stroke prognosis among people with SMI is unknown.

Implications

Psychiatrists, stroke physicians and general practitioners should be acutely aware of the poorer stroke prognosis among people with SMI. While further research seeks to better understand the reasons for this poorer prognosis, it is important to attempt to achieve optimal primary and secondary prevention in this particularly vulnerable group. More collaborative and integrated inter-specialty clinical care and effective communication between secondary and primary care physicians may help to reduce disparities in outcomes. Further investment in understanding the reasons for these disparities is urgently needed. The mental health inequalities in physical disease occurrence and outcomes have been long-neglected. Advances in healthcare record linkage present opportunities to considerably accelerate our understanding of mental health inequalities in physical disease, including stroke. These can, for example, facilitate examination of the entire clinical care pathway, from point of emergency response or first clinical contact through to acute stroke care and rehabilitation, since inequalities could exist at different points and accumulate along this pathway.

In conclusion, compared with patients without a prior hospital admission for mental illness, those with schizophrenia, bipolar disorder and depression have a far poorer stroke prognosis. We identified markedly higher early and long-term mortality and further stroke and vascular event risks in these vulnerable groups. We found no clear evidence of differences in receipt of acute stroke care between these groups, but further research in this area is needed. Urgent action must be taken to investigate and address the complex and multifactorial reasons for these observed disparities.

Kelly Fleetwood, Usher Institute, University of Edinburgh, UK;; **Sarah H. Wild**, Usher Institute, University of Edinburgh, UK; **Daniel J. Smith**, Institute of Health and Wellbeing, University of Glasgow, UK; **Stewart W. Mercer**, Usher Institute, University of Edinburgh, UK; **Kirsty Licence**, Information Services Division, National Services Scotland, NHS Scotland, UK; **Cathie L. M. Sudlow**, Usher Institute, University of Edinburgh, UK; **Caroline A. Jackson**, Usher Institute, University of Edinburgh, UK

Correspondence: Caroline A. Jackson. Email: caroline.jackson@ed.ac.uk

First received 31 Mar 2021, final revision 7 Jul 2021, accepted 23 Jul 2021

Supplementary material

To view supplementary material for this article, please visit https://doi.org/10.1192/bjp.2021.120. Supplementary material for this article has been included in a separate document.

Funding

The NHS Scotland Chief Scientist Office (HIPS/16/59) funded this study.

Acknowledgments

D.J.S. acknowledges support from an MRC Mental Health Data Pathfinder Award (MC_PC_17217) and a Lister Institute Prize Fellowship (2016–2021). We acknowledge the support of the eDRIS Team (Public Health Scotland) for their involvement in obtaining approvals, provisioning and linking data, and the use of the secure analytical platform within the National Safe Haven.

Data availability

Researchers can request access to a wide range of Scottish records by contacting the electronic Data Research and Innovation Service (eDRIS). Details of the available data-sets and the application process are available from https://www.isdscotland.org/Products-and-Services/eDRIS/.

Author contributions

C.A.J. conceived and designed this study. C.A.J. and K.F. acquired the data. K.F. prepared the data and conducted the statistical analysis. All authors contributed to the interpretation of

https://doi.org/10.1192/bjp.2021.120 Published online by Cambridge University Press

the results. C.A.J. and K.F. drafted the report and all authors critically revised it for important intellectual content. C.A.J. obtained funding for this project. All authors critically reviewed the draft and approved the final draft.

Declaration of interest

The authors declare funding from the NHS Scotland Chief Scientist Office for the submitted work.

References

1 Chesney E, Goodwin GM, Fazel S. Risks of all-cause and suicide mortality in mental disorders: a meta-review. *World Psychiatry* 2014; **13**: 153–60.

2 Grover SA, Kaouache M, Rempel P, Joseph L, Dawes M, Lau DC, et al. Years of life lost and healthy life-years lost from diabetes and cardiovascular disease in overweight and obese people: a modelling study. *Lancet Diabetes Endocrinol* 2015; **3**: 114–22.

3 Jha P, Ramasundarahettige C, Landsman V, Rostron B, Thun M, Anderson RN, et al. 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med* 2013; **368**: 341–50.

4 Ajetunmobi O, Taylor M, Stockton D, Wood R. Early death in those previously hospitalised for mental healthcare in Scotland: a nationwide cohort study, 1986–2010. *BMJ Open* 2013; **3**: e002768.

5 Jackson CA, Kerssens J, Fleetwood K, Smith DJ, Mercer SW, Wild SH. Incidence of ischaemic heart disease and stroke among people with psychiatric disorders: retrospective cohort study. *Br J Psychiatry* 2020; **217**: 442–9.

6 Lee EE, Liu J, Tu X, Palmer BW, Eyler LT, Jeste DV. A widening longevity gap between people with schizophrenia and general population: a literature review and call for action. *Schizophr Res* 2018; **196**: 9–13.

7 Correll CU, Solmi M, Veronese N, Bortolato B, Rosson S, Santonastaso P, 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* 2017; **16**: 163–80.

8 Bartoli F, Di Brita C, Crocamo C, Clerici M, Carrà G. Early post-stroke depression and mortality: meta-analysis and meta-regression. *Front Psychiatry* 2018; **9**: 530.

9 Naess H, Lunde L, Brogger J, Waje-Andreassen U. Depression predicts unfavourable functional outcome and higher mortality in stroke patients: the Bergen Stroke Study. *Acta Neurol Scand* 2010; **122** (Suppl 190): 34–8.

10 Kang JH, Xirasagar S, Lin HC. Lower mortality among stroke patients with schizophrenia: a nationwide population-based study. *Psychosom Med* 2011; **73**: 106–11.

11 Tsai K-Y, Lee C-C, Chou Y-M, Su C-Y, Chou FH-C. The incidence and relative risk of stroke in patients with schizophrenia: a five-year follow-up study. *Schizophr Res* 2012; **138**: 41–7.

12 Yung NCL, Wong CSM, Chan JKN, Or PCF, Chen EYH, Chang WC. Mortality in patients with schizophrenia admitted for incident ischemic stroke: a population-based cohort study. *Eur Neuropsychopharmacol* 2020; **31**: 152–7.

13 Chen PH, Kao YW, Shia BC, Lin HC, Kang JH. Adverse stroke outcomes among patients with bipolar disorder. *PLoS One* 2019; **14**: e0213072.

14 Wu H-C, Chou FH-C, Tsai K-Y, Su C-Y, Shen S-P, Chung T-C. The incidence and relative risk of stroke among patients with bipolar disorder: a seven-year follow-up study. *PLoS One* 2013; **8**: e73037.

15 Firth J, Siddiqi N, Koyanagi A, Siskind D, Rosenbaum S, Galletly C, et al. The lancet psychiatry commission: a blueprint for protecting physical health in people with mental illness. *Lancet Psychiatry* 2019; **6**: 675–712.

16 Bongiorno DM, Daumit GL, Gottesman RF, Faigle R. Comorbid psychiatric disease is associated with lower rates of thrombolysis in ischemic stroke. *Stroke* 2018; **49**: 738–40.

17 Willers C, Sunnerhagen KS, Lekander I, von Euler M. The association of pre-stroke psychosis and post-stroke levels of health, resource utilization, and care process: a register-based study. *Front Neurol* 2018; **9**: 1042.

18 Bongiorno DM, Daumit GL, Gottesman RF, Faigle R. Patients with stroke and psychiatric comorbidities have lower carotid revascularization rates. *Neurology* 2019; **92**: e2514–21.

19 Sheehan K, Fang J, Porter J, Casaubon L, Kurdyak P, Kapral M. Quality of care and mortality following stroke in individuals with schizophrenia. *Eur Stroke J* 2019; **4** (suppl): 103.

20 Woodfield R, Grant I. U.K. biobank stroke outcomes group, U.K. biobank follow-up and outcomes working group, sudlow CLM. Accuracy of electronic health record data for identifying stroke cases in large-scale epidemiological studies: a systematic review from the UK biobank stroke outcomes group. *PLoS One* 2015; **10**: e0140533.

21 Scottish Stroke Care Audit. *Scottish Stroke Care Standards 2013*. Information Services Division, NHS National Services Scotland, 2013 (https://www.strokeaudit.scot.nhs.uk/Quality/130311_ScottishStrokeCareStandards_2013_FinalVersion.pdf).

22 Brown D, Allik M, Dundas R, Leyland AH. *Carstairs Scores for Scottish Postcode Sectors, Datazones & Output Areas from the 2011 Census*. MRC /CSO Social and Public Health Sciences Unit, University of Glasgow, 2014 (http://www.sphsu.mrc.ac.uk/carstairs_2011_report.pdf).

23 Counsell C, Dennis M, McDowall M, Warlow C. Predicting outcome after acute and subacute stroke. *Stroke* 2002; **33**: 1041–7.

24 Royston P, Sauerbrei W. *Multivariable Model-Building: A Pragmatic Approach to Regression Anaylsis Based on Fractional Polynomials for Modelling Continuous Variables*. John Wiley & Sons, Ltd, 2008.

25 Hoyer C, Schmidt HL, Kranaster L, Alonso A. Impact of psychiatric comorbidity on the severity, short-term functional outcome, and psychiatric complications after acute stroke. *Neuropsychiatr Dis Treat* 2019; **15**: 1823–31.

26 Smith DJ, Langan J, McLean G, Guthrie B, Mercer SW. Schizophrenia is associated with excess multiple physical-health comorbidities but low levels of recorded cardiovascular disease in primary care: cross-sectional study. *BMJ Open* 2013; **3**: e002808.

27 Prochaska JJ, Das S, Young-Wolff KC. Smoking, mental illness, and public health. *Ann Rev Public Health* 2017; **38**: 165–85.

28 Jennum P, Baandrup L, Iversen HK, Ibsen R, Kjellberg J. Mortality and use of psychotropic medication in patients with stroke: a population-wide, register-based study. *BMJ Open* 2016; **6**: e010662.

EXTRA CONTENT ONLINE

https://doi.org/10.1192/bjp.2021.120 Published online by Cambridge University Press