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Association of severe mental illness with stroke outcomes and process-of-care indicators

1 **Association of severe mental illness with stroke outcomes and processes of acute care: nationwide**

2 **cohort study**

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Abstract

Background

Severe mental illness (SMI) is associated 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 processes of acute stroke care.

Method

We conducted a cohort study using routinely collected linked datasets, including adults with a first hospitalised stroke in Scotland during 1991-2014, with processes of care 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, one-year and five-year mortality and receipt of processes of care by pre-existing SMI, adjusting for sociodemographic and clinical factors. We used Cox regression to evaluate further stroke and vascular events (stroke and myocardial infarction).

Results

Among 228 699 stroke patients, 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 to 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 processes of care.

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.

2

Introduction

Background

Severe mental illness (SMI), including schizophrenia, bipolar disorder and major depression, reduces life expectancy by 10-20 years[1], which is comparable to 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 two-fold 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] Whilst 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 stroke patients 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 hospitalised stroke patients: (i) stroke mortality and further stroke and vascular event risk and (ii) processes of acute stroke care, among

69   people with prior hospitalisation for each of schizophrenia, bipolar disorder and depression,

70   compared to people with no prior hospitalisation for a mental health condition.

71   **Method**

72   **Data sources**

73   This nationwide retrospective cohort study uses data from Scotland including acute and psychiatric

74   hospital records, death records and stroke audit records (Supplementary Text 1), provided by the

75   electronic Data Research and Innovation Service (eDRIS), Public Health Scotland. Records were

76   linked by eDRIS using the Community Health Index number, a unique identifier for people registered

77   with the National Health Service, Scotland. We obtained approval to conduct this study with

78   pseudonymised, non-consented data from the National Health Service (NHS) Scotland Public Benefit

79   and Privacy Panel for Health and Social Care (reference number 1617-0179).

80   **Study populations**

81   We included all adults aged 18 or over with a diagnosis of stroke recorded in acute hospital

82   admission records. We identified index strokes from ICD-9 (430, 431, 434 and 436) and ICD-10 (I60,

83   I61, I63, I64) codes[20] recorded in a primary or secondary diagnosis field that occurred between 1991

84   and 2014, where no hospitalisation for stroke was recorded during the preceding 10 years.

85   We also defined a sub-cohort of adults with information on processes of acute stroke care. Since

86   Scottish hospital records do not contain detailed information on clinical care, we used data from the

87   Scottish Stroke Care Audit (https://www.strokeaudit.scot.nhs.uk/index.html). The audit includes

88   information on stroke patients and their care in hospitals managing acute stroke in Scotland, with

89   national coverage from 2010 onwards. We included all index strokes recorded in the stroke audit

90   between 2010 and 2014 which had a concurrent acute hospital record for stroke.

91   **Severe mental illness**

92   We determined history of a mental health condition from acute and psychiatric hospital records. We

93   identified mental health conditions from diagnosis fields of admissions that occurred after the

94   individual's 18th birthday and before their incident stroke (Supplementary Table 1). We categorised

95   people into mutually exclusive SMI groups, using a severity hierarchy when more than one diagnosis

96   was recorded: schizophrenia was considered the most severe disorder, followed by bipolar disorder

97   and then depression. We compared outcomes after stroke in people with a history of each of these

98   three disorders versus those with no prior hospitalisation record for any mental health condition

99   (Supplementary Table 1).

100   **Mortality and further stroke and vascular events**

101   Primary outcomes were 30-day, one-year and five-year mortality. Secondary outcomes included

102   mortality over the entire follow-up period and time to each of further stroke and further vascular

103   event (with a vascular event defined as either a stroke or myocardial infarction [MI]). We identified

104   deaths from Scottish death records, available up to 31 December 2018. We defined further stroke as

105   stroke occurring more than 30 days after the index stroke, ascertained from acute hospital

106   admissions using the same approach as for index strokes or death records. We defined further

107   vascular event as a stroke or MI occurring more than 30 days after the index stroke, with MIs

108   ascertained from ICD-9 (410) and ICD-10 (I21, I22) codes in the primary or secondary fields of acute

109   hospital admission records or death records.

110   **Processes of acute stroke care**

111   We defined processes of acute stroke care based on Scottish stroke care standards.[21] These

112   included: admission to stroke unit within one day of admission; brain imaging on day of admission;

113   swallow screen on day of admission; and aspirin within one day of admission for individuals with an

114   ischaemic stroke and no valid contraindication to aspirin.

115   **Covariates**

116   We defined area-based deprivation (measured by the Carstairs index[22]), urbanicity and health board

117   based on place of residence at the time of stroke (Supplementary Text 1). We ascertained history of

118   alcohol use disorder from ICD codes in diagnosis fields in hospital records prior to the date of

119   incident stroke (Supplementary Table 2). For descriptive analyses of the larger cohort, we used ICD

120   codes to identify diagnoses of atrial fibrillation (AF), diabetes and hypertension from the hospital

121   record for the incident stroke (Supplementary Table 3).

122   For the stroke audit sub-cohort we also included pathological stroke type and six case-mix variables

123   (age, whether patients lived alone and were independent in activities of daily living (ADL) before the

124   stroke and whether patients were able to communicate verbally, lift both arms and walk without

125   help from another person at first clinical assessment) that predict stroke mortality and functional

126   outcome.[23] We were also able to ascertain AF and hypertension from relevant audit questions and

127   diabetes through linkage to Scotland's diabetes register (Supplementary Text 1).

128   **Statistical analysis**

129   We used direct standardisation to calculate sex-specific age-standardised proportions for the three

130   primary mortality outcomes, by time period. To address potential issues of small numbers, we

131   aggregated age into four groups (<60, 60-69, 70-79 and ≥80 years) and time into four time periods of

132   equal duration. We used an internal standard population, which we derived from the age structure

133   of the entire nation-wide hospitalised stroke population for the period 2003-2008 (i.e. roughly the

134   mid-point of the time period of this study), to which we applied our age-specific rates for each

135   comparison group.

136   **Mortality and further stroke/vascular events**

137   We used logistic regression to model 30-day, one-year and five-year mortality, and Cox regression

138   for mortality during the entire follow-up period and for time to further stroke or vascular events. For

139   time to further stroke or vascular events, we accounted for death as a competing risk, censoring at

140   the date of death. For each outcome, model 1 included SMI, age, sex and year and model 2

141   additionally included history of alcohol use disorder, deprivation, urbanicity and health board. We

142   included age at stroke and year of admission as continuous variables modelled as fractional

143   polynomials in order to allow for non-linear relationships between these variables and the

144   outcomes[24], and the remaining covariates as categorical variables.

145 We repeated our analyses of the mortality and further event outcomes using the stroke audit sub-

146 cohort, with additional adjustment for pathological stroke type (which was poorly recorded in earlier

147 years of the acute hospital records and so was not adjusted for in the main mortality analyses),

148 diabetes, AF, hypertension and the case-mix variables.

149 For both cohorts, our analyses were based on cases with no missing data; all mortality and

150 recurrence outcome variables were complete. In the main cohort, a small number of participants

151 (0.6%) were missing data on deprivation, urbanicity and/or health board (all other variables were

152 complete). In the stroke audit sub-cohort, 4% of people were missing data for area-based

153 deprivation, urbanicity, health board, stroke type or atrial fibrillation. A further 14% of people were

154 missing data on case-mix variables, and were excluded only from analyses that adjusted for these

155 variables. There was no evidence that missing data on any variable (including the case-mix variables)

156 was associated with SMI status (Pearson's chi-squared test, p = 0.71).

157 **Acute stroke processes of care**

158 We used logistic regression to model the processes of acute stroke care outcomes in the stroke audit

159 sub-cohort. For each outcome, we included people who were eligible for the specific stroke care

160 standard and had sufficient data to determine the outcome; for example, for admission to stroke

161 unit within one day of admission we included people who survived at least one day.

162 **Sensitivity analysis of depression definition**

163 In our principal analyses, history of each mental health condition was ascertained from both acute

164 and psychiatric hospital records. This approach may have affected depression ascertainment in

165 particular, by potentially identifying people from across the depression severity spectrum, thereby

166 including a more heterogeneous group with depression. Thus, in sensitivity analyses, we repeated

167 all analyses using an alternative definition of prior depression based on psychiatric hospital

168 admission only. The definitions of prior schizophrenia and bipolar disorder were unchanged.

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

170 project.org/).

171 **Patient and public involvement**

172 This study involved the analysis of pseudonymised administrative data. At the start of the research

173 project we held a multi-stakeholder knowledge exchange event during which invited patient

174 representatives and third sector representatives had the opportunity to contribute to discussions

175 about the research project. The study advisory board includes a member from Support in Mind who

176 advised on the dissemination of study results to relevant communities.

177 # Results

178 **Cohort characteristics**

179 There were 238 001 people with a first-ever hospitalised stroke in Scotland between 1991 and 2014.

180 After exclusions, we included 228 699 in our cohort (Supplementary Fig. 1). Of these, 1186 (0·5%)

181 had schizophrenia, 859 (0·4%) had bipolar disorder and 7308 (3·2%) had major depression. Of people

182 hospitalised with stroke, the average age of first recorded stroke was lowest for people with

183 schizophrenia (65 years), compared to those with bipolar disorder (70 years), major depression (71

184 years) and no mental health condition (73 years). People with schizophrenia, and to a lesser extent,

185 major depression, were more likely to live in deprived areas than people without a mental health

186 condition. The proportion with diabetes recorded in the stroke admission record was broadly similar

187 across comparison groups, but people without a history of a mental health condition were more

188 likely to have AF or hypertension recorded compared to those with an SMI. Median follow-up time

189 was 2.6 years (interquartile range 0.1 to 7.7). Overall, 30-day, one-year and 5-year mortality were

190 23.3%, 39.5% and 61.3% respectively (Table 1, Supplementary Tables 4 and 5).

191 [Insert Table 1 here]

192 **Severe mental illness and absolute stroke mortality over time**

193 Absolute age-standardised sex-specific proportions of people dying within 30-days, one-year and

194 five-years of stroke were generally higher in each SMI group than those with no record of any

195 mental health condition. Mortality declined in most groups between 1991 and 2014, but tended to

196   remain higher in people with an SMI (Fig. 1). However small numbers of people with schizophrenia

197   and bipolar disorder within calendar year groups created some uncertainty with respect to patterns

198   of change over time.

199   [Insert Fig. 1 here]

200   **Severe mental illness and relative effect on stroke outcomes**

201   After adjusting for age, sex and year, each SMI was associated with greater odds of 30-day, one-year

202   and five-year mortality. Effect estimates attenuated only slightly after additional adjustment for

203   alcohol use disorder, urbanicity, area-based deprivation and health board. The association between

204   SMI and 30-day mortality was greatest in people with prior schizophrenia (OR 1.28, 95% CI 1.12 to

205   1.47) and bipolar disorder (OR 1.36, 95% CI 1.16 to 1.58) and smallest for those with major

206   depression (1.07, 95% CI 1.02 to 1.14; Table 2). Associations were slightly larger for one-year

207   mortality and larger again for five-year mortality, with effect estimates again smallest for depression

208   at one year but similar across groups at five years. Based on the results of the competing-risk Cox

209   regression models, time to further stroke and further vascular event were significantly shorter

210   among those with each SMI as compared to no mental health condition (Table 2), with associations

211   similar across SMI groups.

212   [Insert Table 2 here]

213   **Analyses of mortality and processes of acute stroke care in the stroke audit sub-cohort**

214   There were 27 606 people with confirmed first-ever stroke between 2010 and 2014 eligible for our

215   stroke audit sub-cohort (Supplementary Fig. 2). Of these, 167 had schizophrenia (0.6%), 102 had

216   bipolar disorder (0.4%) and 1078 had major depression (3.9%). Baseline characteristics were similar

217   to those of the main cohort (Supplementary Table 6). Mortality analyses in this sub-cohort produced

218   a similar pattern of results as for the main cohort. Interestingly, additional adjustment for stroke

219   type, diabetes, atrial fibrillation and hypertension did not materially alter effect estimates (Table 3).

220   Case-mix differences varied by SMI group. Compared to people without a mental health condition,

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221   all SMI groups were less likely to be independent in activities of daily living prior to their stroke and

222   patients with bipolar disorder or major depression were less likely to walk without help from

223   another person at first assessment. However, people with schizophrenia and bipolar disorder, but

224   not depression were less likely to be able to talk at first assessment (Supplementary Table 6).

225   Additional adjustment for case-mix appeared to attenuate effect estimates, such that some were no

226   longer statistically significant. However, since confidence intervals were wide, these adjusted

227   estimates cannot rule out a persistent excess risk of poor outcome in those with an SMI

228   Overall, on the day of admission 61.6% and 70.5% had brain imaging and a swallow screen,

229   respectively and within one day of admission 74.6% and 41.9% were admitted to a stroke unit and

230   received aspirin, respectively (Supplementary Tables 7 and 8). Whilst there was no evidence of

231   associations between schizophrenia, bipolar disorder and major depression and receipt of any of

232   these processes of care, lower numbers of people with SMI in this sub-cohort means that wide

233   confidence intervals do not necessarily preclude there being a reduction in receipt of care among

234   people with an SMI (Table 3).

235   [Insert Table 3 here]

Sensitivity analysis of depression definition

237   Analyses of all outcomes including processes of acute stroke care were robust to sensitivity analyses

238   in which we defined major depression according to admission to psychiatric hospitals only, with

239   results generally similar to those obtained in the main analyses (Supplementary Tables 9 and 10).

240   However, for receipt of brain imaging on day of admission and aspirin within one day of admission,

241   differences in the rates between people with major depression versus no mental health condition

242   became larger and statistically significant when defining depression in this way.

Discussion

Main findings

245   In a national cohort of hospitalised stroke patients, people with schizophrenia, bipolar disorder and

246   major depression had increased short and long-term mortality and a greater risk of further stroke

247   and vascular events, compared to those with no record of prior mental illness. The excess short-term

248   mortality was greater among those with schizophrenia and bipolar disorder than major depression,

249   but the increased long-term mortality was similar across these groups. In a sub-group where process

250   of care data were available, there did not appear to be differences in acute stroke care for those

251   with SMI.

252   **Strengths and weaknesses**

253   Our study has various strengths. It makes an important and novel contribution to the paucity of

254   literature on the association between pre-existing schizophrenia, bipolar disorder and depression

255   and stroke prognosis, particularly 30-day and one-year mortality. With the exception of one study of

256   schizophrenia and long-term post-stroke mortality[11], it is also the largest such study to date.

257   Moreover, our study makes an important contribution to the sparse data on associations between

258   SMI and processes of acute stroke care. Inclusion of national hospital admission data meant that we

259   included an unselected cohort of hospitalised stroke patients. Furthermore, Scotland has a universal

260   healthcare system and so our findings are unbiased by inequalities in access to care based on health

261   insurance provision.

262   Our study has some limitations. Whilst hospital admission records in Scotland extend as far back as

263   1980, we may still have under-ascertained history of hospital admission for SMI, which means we

264   are likely to have under-estimated associations. Given that we identified people with SMI solely from

265   hospital admission records, our findings may not be generalizable to the wider population of people

266   with SMI. If severity of SMI is associated with outcome risk then our findings reflect the association

267   among people with more severe disease. Effect estimates may be smaller for people with a SMI for

268   which they do not have a hospital admission record. There may have been selection bias in that the

269   depression group may include a heterogeneous mix of people hospitalised for major depression as

270   well as people with less severe depression hospitalised for other reasons. However, results were

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271 very similar in sensitivity analyses where we defined depression based on psychiatric hospital

272 admissions only. This aligns with the comorbidity recording practice in Scottish acute hospitals,

273 whereby depression as a comorbidity would be recorded only if it was severe enough to affect

274 patient management. We were unable to adjust for confounding by lifestyle factors such as smoking

275 and obesity or comorbidities associated with stroke mortality. Whilst we were able to adjust for

276 diabetes, hypertension and AF within our stroke audit sub-cohort, we were unable to adjust for

277 multimorbidity in general, which will likely be higher in those with SMI and potentially associated

278 with stroke outcome. Furthermore, the role of case mix, a proxy for stroke severity, in accounting for

279 the observed disparities in our study is unclear, but merits further investigation in future studies. We

280 will have under-ascertained further strokes, since we did not include strokes occurring within the

281 first 30 days of the index event or milder events assessed only in stroke outpatient clinics.

282 **Comparison with findings from previous studies**

283 Just three previous studies have reported on the association between schizophrenia and mortality

284 within the first year after stroke, all of which included fewer patients with schizophrenia than our

285 study.[10,12,19] Findings on mortality from two of these were consistent with our results.[12,19] In contrast,

286 the smallest study reported lower 90-day mortality among people with versus without a history of

287 schizophrenia.[10] The authors matched on admission to intensive care unit and length of stay in

288 hospital, which could relate to schizophrenia status as well as the stroke event, thus results in an

289 apparent reduced mortality in people with schizophrenia. To our knowledge, no previous study has

290 reported on pre-existing depression in relation to post-stroke mortality within one year and only one

291 study (smaller than ours) examined the association between bipolar disorder and early stroke

292 mortality.[13] In contrast to our findings, the authors reported that bipolar disorder was associated

293 with 50% reduced odds of post-stroke in-hospital mortality.[13] The reason for these discordant

294 findings could potentially reflect different stroke admission and discharge patterns related to the

295 presence of bipolar disorder in the former study. Our finding that SMI is associated with higher post-

296 stroke mortality beyond one year aligns with previous studies on longer-term stroke mortality in

297   people with schizophrenia[11], bipolar disorder[14] and depression.[9] We believe our study is the first to

298   report on further stroke risk among patients with comorbid schizophrenia, bipolar disorder or

299   depression.

300   To our knowledge, just one other study has investigated these processes of stroke care with respect

301   to mental illness. The authors compared people with versus without schizophrenia and, as in our

302   study, found no differences in admission to a stroke unit or timely brain imaging.[19]

303   The reasons for the higher stroke case-fatality in people with SMI are not fully understood, but are

304   likely multifactorial. Although our analysis of the stroke audit sub-cohort did not find clear

305   differences in receipt of stroke care, these results should be interpreted with caution given their

306   wide confidence intervals. Receipt of procedures such as thrombolysis or carotid endarterectomy

307   may differ by SMI status, but existing evidence is sparse and inconsistent.[16-19,25] Stroke severity, a key

308   predictor of stroke survival, may contribute to differences in early mortality.[23] In keeping with other

309   studies[9,17,25], analysis of our stroke audit sub-cohort revealed that stroke severity is higher in those

310   with versus without SMI. Only one of these studies adjusted for stroke severity and found that it did

311   not explain the excess case-fatality among people with schizophrenia.[19] Although adjustment for

312   case-mix in our study attenuated estimates, findings were difficult to interpret given the statistical

313   uncertainty of wide confidence intervals. A higher prevalence of comorbidities and poorer lifestyle

314   factors in people with SMI likely accounts for some of the observed poorer prognosis but the

315   available data in our study did not allow for comprehensive investigation of this. Associations

316   persisted when we adjusted for diabetes, hypertension and AF in our analyses of the stroke audit

317   sub-cohort, but residual confounding is likely, partly due to under-recognition and under-treatment

318   of cardiovascular disease among people with SMI.[26] The higher risk of further vascular events and

319   long-term mortality among those with SMI observed in our study supports a need to investigate the

320   possible role of sub-optimal secondary prevention. Among lifestyle factors, smoking is particularly

321   worrying, given the high prevalence and low cessation rates among people with SMI.[27] Although

322   evidence is scant, there are reports that stroke patients with schizophrenia are less likely to be

323 prescribed anti-hypertensive, lipid-lowering or anticoagulant therapy at discharge from hospital than

324 people without schizophrenia.[19] Finally, although psychotropic medication has been linked to

325 increased mortality in stroke survivors in the long term[28], its contribution to stroke prognosis among

326 people with SMI is unknown.

327 **Implications**

328 Psychiatrists, stroke physicians, and general practitioners should be acutely aware of the poorer

329 stroke prognosis among people with SMI. Whilst further research seeks to better understand the

330 reasons for this poorer prognosis, it is important to attempt to achieve optimal primary and

331 secondary prevention in this particularly vulnerable group. More collaborative and integrated inter-

332 specialty clinical care and effective communication between secondary and primary care physicians

333 may help to reduce disparities in outcomes. Further investment in understanding the reasons for

334 these disparities is urgently needed. The mental health inequalities in physical disease occurrence

335 and outcomes have been long-neglected. Advances in healthcare record linkage present

336 opportunities to considerably accelerate our understanding of mental health inequalities in physical

337 disease, including stroke. These can for example facilitate examination of the entire clinical care

338 pathway, from point of emergency response or first clinical contact through to acute stroke care and

339 rehabilitation, since inequalities could exist at different points and accumulate along this pathway.

340 In conclusion, compared to patients without a prior hospitalisation for mental illness, those with

341 schizophrenia, bipolar disorder and depression have a far poorer stroke prognosis. We identified

342 markedly higher early and long-term mortality and further stroke and vascular event risks in these

343 vulnerable groups. We found no clear evidence of differences in receipt of acute stroke care

344 between these groups, but further research in this area is needed. Urgent action must be taken to

345 investigate and address the complex and multifactorial reasons for these observed disparities.

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Supplementary material

Supplementary material for this article has been included in a separate document.

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 datasets and the application

process are available from https://www.isdsscotland.org/Products-and-Services/eDRIS/.

Author contributions

C.J. conceived and designed this study. C.J. and K.F. acquired the data. K.F. prepared the data and

conducted the statistical analysis. All authors contributed to the interpretation of the results. C.J.

and K.F. drafted the report and all authors critically revised it for important intellectual content. C.J.

obtained funding for this project. All authors critically reviewed the draft and approved the final

draft.

Declaration of interest

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TABLES

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)
Median follow-up time (IQR), years	2.7 (0.1, 7.7)	3.0 (0.1, 7.6)	2.2 (0.1, 6.3)	2.2 (0.1, 6.5)
Sex, 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%)
Mean age at stroke (SD), years	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[†]				
N	168 387	908	628	5564
Stroke, n (%)	68 900 (40.9%)	348 (38.3%)	257 (40.9%)	2214 (39.8%)

	No mental health condition (N=219 346)	Schizophrenia (N=1186)	Bipolar disorder (N=859)	Major depression (N=7308)
Vascular event, n (%)	80 407 (47.8%)	398 (43.8%)	289 (46.0%)	2594 (46.6%)

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

Table 2: **Effect estimates for hospitalised stroke outcomes in Scotland, 1991 – 2014, comparing people with each severe mental illness versus no admission for any mental health condition**

Outcome	N	Model	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 to 1.52)	1.37 (1.18 to 1.60)	1.11 (1.05 to 1.18)
		Model 2	1.28 (1.12 to 1.47)	1.36 (1.16 to 1.58)	1.07 (1.02 to 1.14)
1-year mortality, OR (95% CI)	228 699	Model 1	1.49 (1.31 to 1.68)	1.44 (1.25 to 1.66)	1.24 (1.18 to 1.31)
		Model 2	1.40 (1.24 to 1.58)	1.41 (1.23 to 1.63)	1.17 (1.11 to 1.23)
5-year mortality, OR (95% CI)	220 287[a]	Model 1	1.80 (1.58 to 2.05)	1.53 (1.31 to 1.80)	1.55 (1.46 to 1.64)
		Model 2	1.62 (1.42 to 1.85)	1.47 (1.26 to 1.73)	1.38 (1.30 to 1.46)
All-cause mortality, HR (95% CI)	228 699	Model 1	1.45 (1.36 to 1.54)	1.36 (1.26 to 1.46)	1.26 (1.23 to 1.29)
		Model 2	1.36 (1.27 to 1.45)	1.33 (1.23 to 1.43)	1.20 (1.16 to 1.23)
Time to further stroke, HR (95% CI)	175 487[b]	Model 1	1.29 (1.16 to 1.43)	1.19 (1.05 to 1.34)	1.15 (1.10 to 1.20)
		Model 2	1.24 (1.11 to 1.38)	1.17 (1.03 to 1.32)	1.11 (1.06 to 1.16)
Time to further vascular event, HR (95% CI)	175 487[b]	Model 1	1.26 (1.14 to 1.39)	1.16 (1.03 to 1.30)	1.18 (1.14 to 1.23)
		Model 2	1.21 (1.10 to 1.34)	1.14 (1.01 to 1.28)	1.14 (1.10 to 1.19)

Model 1 is adjusted for age, sex and year. Model 2 is additionally adjusted for history of alcohol use disorder, deprivation, urbanity and health board.

HR=Hazard ratio. OR=Odds ratio.

a. Stroke admissions up to 2013 in order to ensure that all individuals have at least 5 years' follow-up.

b. Individuals who survived more than 30 days.

Table 3: Effect estimates for hospitalised 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

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

Outcome or process of acute stroke care	N	Model	Schizophrenia	Bipolar disorder	Major depression
Aspirin within one day of admission, OR (95% CI)	21 776[g]	Model 1	0.77 (0.53 to 1.09)	1.08 (0.71 to 1.63)	0.94 (0.82 to 1.08)
	21 776[g]	Model 2	0.77 (0.53 to 1.11)	1.06 (0.69 to 1.61)	0.95 (0.82 to 1.10)
	18 687[a,g]	Model 3	0.77 (0.51 to 1.13)	1.17 (0.75 to 1.83)	0.92 (0.78 to 1.07)

Model 1 is adjusted for age, sex 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 one day of admission, models 2 and 3 do not adjust for stroke type.

HR=Hazard ratio. OR=Odds ratio.

a. 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).
b. Scottish Stroke Care Audit records 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.
d. Individuals who survived more than one day and had sufficient stroke unit data.
e. Individuals who survived their day of admission and had sufficient brain scan data.
f. Individuals who survived their day of admission and had sufficient swallow screen data.
g. Individuals who survived more than one day, had an ischaemic stroke, didn't have a valid contraindication to aspirin and had sufficient aspirin data.

FIGURE LEGENDS

Fig. 1: Age-standardised rates of 30-day mortality, one-year mortality and five-year mortality following a hospitalised stroke, by history of severe mental illness, 1991 – 2014. Shading represents 95% confidence intervals
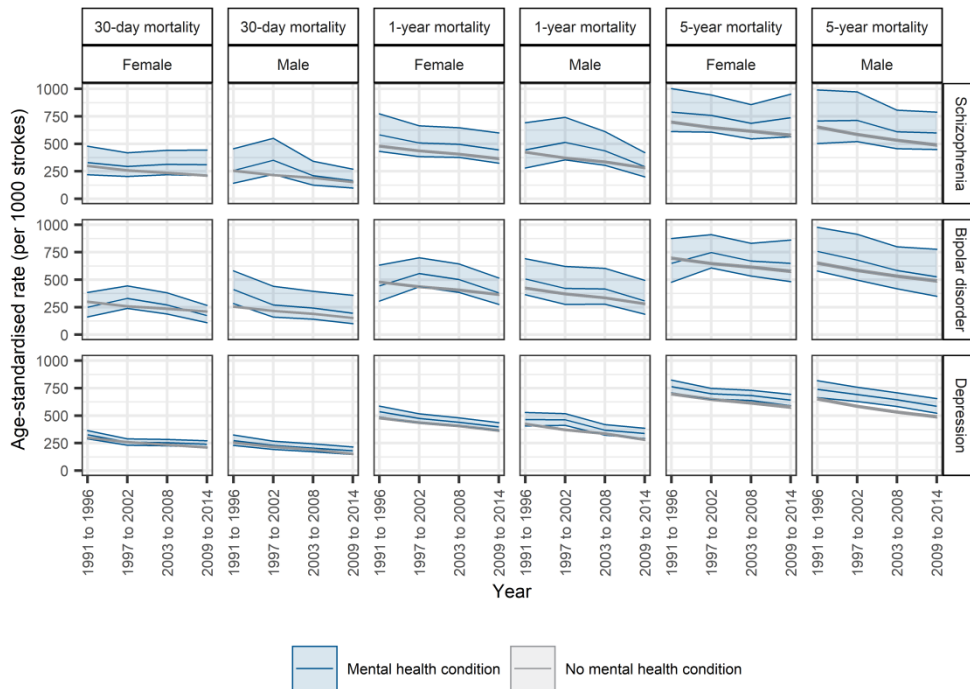
Supplementary material

Association of severe mental illness with stroke outcomes and processes of care: nationwide cohort study

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Contents

Supplementary Text 1: Data sources and covariates

This section provides supplementary information on the data sources and some of the covariates used in this study.

Data sources

Acute hospital records

The Scottish Morbidity Record General/Acute Inpatient and Day Case dataset (SMR01) includes episode level information about inpatient and day case discharges from general and acute specialities from Scottish hospitals (all NHS hospitals and NHS beds in non-NHS institutions).(1) Data is available for research from 1981 onwards. Each record includes information on the person's demographics, main diagnosis and up to five other diagnoses, recorded using ICD-9 codes up to April 1996, and subsequently using ICD-10 codes.

Psychiatric hospital records

The Scottish Mental Health Inpatient and Day Case dataset (SMR04) includes episode level information about inpatient and day case visits to mental health specialties in Scottish hospitals (all NHS hospitals and NHS beds in non-NHS institutions). Again data is available from 1981 onwards and records include information on the person's demographics and diagnoses.

Death records

This study used Scottish death records from 1991 to 2018. The records include the person's demographics, date of death, underlying cause of death and other conditions that may have contributed to their death.

Stroke audit

The Scottish Stroke Care Audit (SSCA)(2) was set up to monitor performance of hospitals against guideline based clinical standards. It includes information on stroke care in hospitals managing acute stroke in Scotland, with in-hospital data collection reaching national coverage from 2010 onwards.

Diabetes register

The Scottish Care Information – Diabetes (SCI-Diabetes) dataset is Scotland's national diabetes register. It includes approximately 99% of all patients in Scotland diagnosed with diabetes since 2004.(3)

Additional covariate information

Area-based deprivation

Area-based deprivation was measured by the Carstairs Index in line with recommendations for the analysis of deprivation in Scotland where the time frame starts prior to 1996.(4) The Carstairs Index is based on four census variables (car ownership, male unemployment, household overcrowding and low occupational social class) and calculated at the postcode sector level.(5)

Urbanicity

Urbanicity was classified according to the Scottish Government six-fold urban rural indicator.(6)

Supplementary Table 1: ICD-9 and ICD-10 codes used to identify mental health conditions.

Mental health condition[a]	ICD-10 codes (first 3 digits)	ICD-9 codes (first 4 digits)
Schizophrenia: schizophrenia and schizoaffective disorders	F20, F25	295.0-295.3, 295.6-295.9
Other psychoses: schizotypal disorders, acute and transient psychosis, delusional disorders, and other psychotic disorders	F21-F24, F28, F29	295.4, 295.5, 297.0-297.9 298.3, 298.4, 298.8, 298.9
Bipolar disorder: manic episode or bipolar affective disorder	F30-F31	296.0 296.2-296.6
Depression: depressive episode or recurrent depressive disorder	F32-F33	296.1 298.0, 300.4, 311
Other mental health conditions: including other mood disorders, neuroses, dissociative disorders, somatoform disorders, eating disorders, non-organic sleep disorders and other behavioural syndromes associated with physiological disturbances and physical factors, disorders of adult personality and behaviour, disorders of psychological development, behavioural and emotional disorders with onset in childhood and adolescence and unspecified mental disorders	F34-F69, F80-F99	293.8, 296.8, 296.9, 298.1, 298.2, 299.0-301.9, 302.1-302.9, 305.9, 306.0-309.9, 312.0-315.9 316

a. Further details on these codes can be found on the ICD-10 website (7) and in the ICD-9 book (8).
The orange rows represent the three SMI exposure groups. The comparison group comprised people with no hospitalisation record for any of the mental health conditions listed in the table.
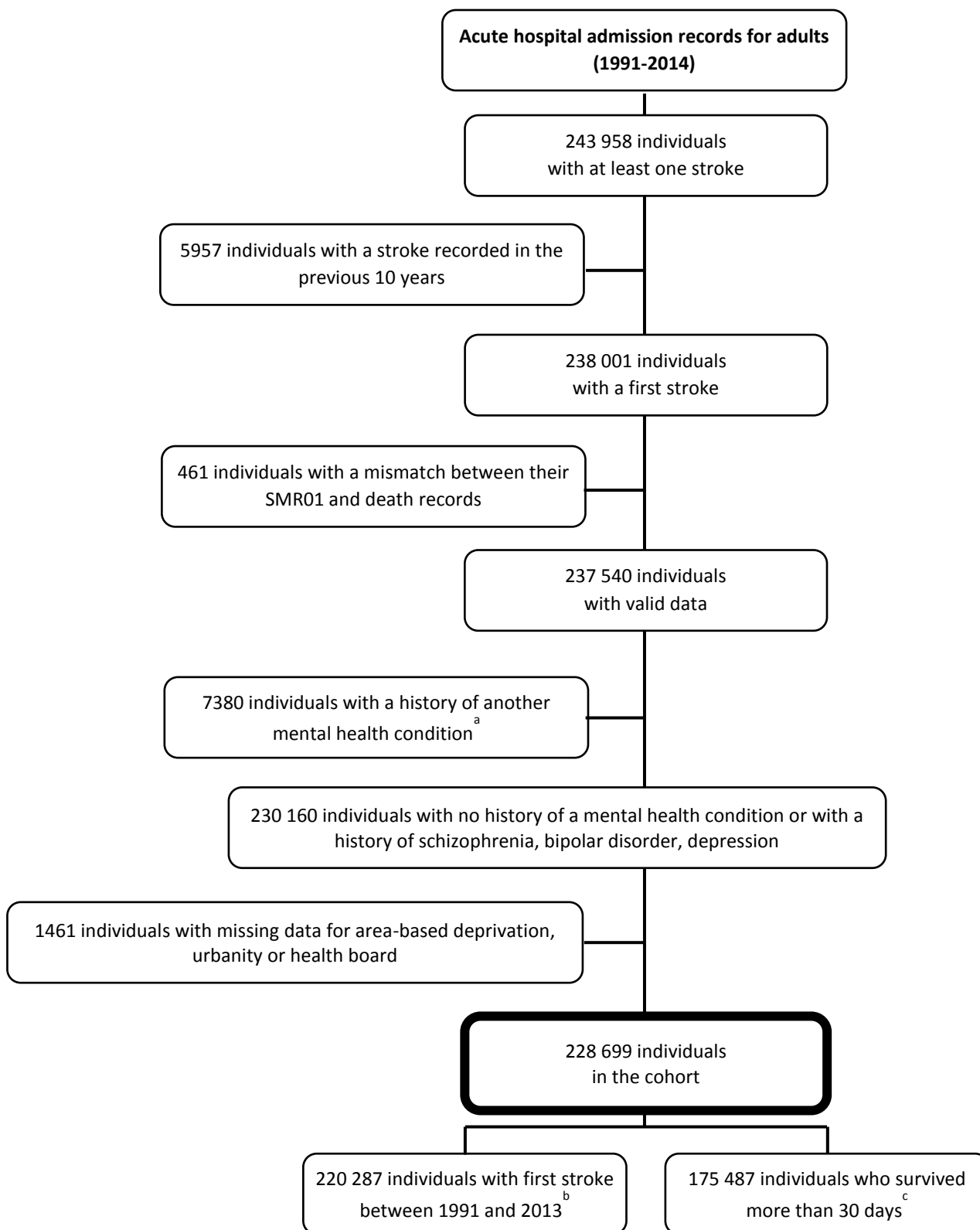
Supplementary Table 2: ICD-9 and ICD-10 codes used to identify alcohol use disorder

ICD-10 Code	Description	ICD-9 Code	Description
Mental & behavioural disorders due to use of alcohol			
F10.1	Harmful use	291.0	Delirium tremens
F10.2	Dependence syndrome	291.1	Korsakov's psychosis, alcoholic
F10.3	Withdrawal state	291.2	Other alcoholic dementia
F10.4	Withdrawal state with delirium	291.5	Alcoholic jealousy
F10.6	Amnesic syndrome	303	Alcohol dependence syndrome
Alcoholic liver disease			
K70.0	Alcoholic fatty liver	571.0	Alcoholic fatty liver
K70.1	Alcoholic hepatitis	571.1	Acute alcoholic hepatitis
K70.2	Alcoholic fibrosis and sclerosis of liver	571.2	Alcoholic cirrhosis of liver
K70.3	Alcoholic cirrhosis of liver	571.3	Alcoholic liver damage, unspecified
K70.4	Alcoholic hepatic failure		
K70.9	Alcoholic liver disease, unspecified		
Other conditions			
E24.4	Alcohol induced Pseudo-Cushing's syndrome		No equivalent code in ICD-9
E51.2	Wernicke's Encephalopathy		No equivalent code in ICD-9
G31.2	Degeneration of nervous system due to alcohol		No equivalent alcohol-specific code included in ICD-9
G62.1	Alcoholic polyneuropathy	357.5	Alcoholic polyneuropathy
G72.1	Alcoholic myopathy		No equivalent alcohol-specific code included in ICD-9
I42.6	Alcoholic cardiomyopathy	425.5	Alcoholic cardiomyopathy
K29.2	Alcoholic gastritis	535.3	Alcoholic gastritis
K85.2	Alcohol-induced acute pancreatitis		No equivalent alcohol-specific code included in ICD-9
K86.0	Alcohol-induced chronic pancreatitis		No equivalent alcohol-specific code included in ICD-9
O35.4	Maternal care for (suspected) damage to foetus from alcohol		No equivalent alcohol-specific code included in ICD-9
Y57.3	Drugs, medicaments and biological substances causing adverse effects in therapeutic use: alcohol deterrents	E947.3	Drugs, medicaments and biological substances causing adverse effects in therapeutic use: alcohol deterrents
Z50.2	Alcohol rehabilitation		No equivalent alcohol-specific code included in ICD-9
Z71.4	Alcohol abuse counselling and surveillance		No equivalent alcohol-specific code included in ICD-9

Supplementary Table 3: Comorbidities recorded during the incident stroke admission

Comorbidity	ICD-10 codes	ICD-9 codes
Atrial fibrillation	I48	427.3
Diabetes	E10-14	250
Hypertension	I10-I13, I15	401-405

Supplementary Figure 1: Flow diagram for establishing the cohort

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                    ┌─────────────────────────────────────┐
                    │  Acute hospital admission records     │
                    │         for adults (1991-2014)        │
                    └─────────────────────────────────────┘
                                      │
                    ┌─────────────────────────────────────┐
                    │         243 958 individuals           │
                    │       with at least one stroke        │
                    └─────────────────────────────────────┘
                                      │
  ┌──────────────────────────────────┤
  │ 5957 individuals with a stroke    │
  │ recorded in the previous 10 years │
  └──────────────────────────────────┘
                                      │
                    ┌─────────────────────────────────────┐
                    │         238 001 individuals           │
                    │          with a first stroke          │
                    └─────────────────────────────────────┘
                                      │
  ┌──────────────────────────────────┤
  │ 461 individuals with a mismatch   │
  │ between their SMR01 and death     │
  │ records                           │
  └──────────────────────────────────┘
                                      │
                    ┌─────────────────────────────────────┐
                    │         237 540 individuals           │
                    │            with valid data            │
                    └─────────────────────────────────────┘
```

5957 individuals with a stroke recorded in the previous 10 years

238 001 individuals with a first stroke

461 individuals with a mismatch between their SMR01 and death records

237 540 individuals with valid data

7380 individuals with a history of another mental health condition [a]

230 160 individuals with no history of a mental health condition or with a history of schizophrenia, bipolar disorder, depression

1461 individuals with missing data for area-based deprivation, urbanity or health board

228 699 individuals in the cohort

220 287 individuals with first stroke between 1991 and 2013 [b]

175 487 individuals who survived more than 30 days [c]

a. Including other psychoses, other mood disorders, disorders of adult personality and behaviour, eating disorders, neuroses, dissociative and somatoform disorders, behavioural and emotional disorders with onset in childhood and adolescence, non-organic sleep disorders, disorders of psychosocial development and unspecified mental disorders.

b. Restricted cohort for the analysis of five-year mortality.

c. Restricted cohort for the analysis time to recurrence outcomes.

Supplementary Table 4: Number of individuals and events per group

Outcome	No MHC	Schizophrenia	Bipolar disorder	Major depression	Total
Complete cases	219 346	1186	859	7308	228 699
30-day mortality	50 959 (23.2%)	278 (23.4%)	231 (26.9%)	1744 (23.9%)	53 212 (23.3%)
1-year mortality	86 532 (39.5%)	454 (38.3%)	372 (43.3%)	3041 (41.6%)	90 399 (39.5%)
All-cause mortality	178 905 (81.6%)	941 (79.3%)	726 (84.5%)	5991 (82.0%)	186 563 (81.6%)
Complete cases (stroke admissions up to 2013)	211 370	1123	810	6984	220 287
5-year mortality	129 241 (61.1%)	666 (59.3%)	520 (64.2%)	4573 (65.5%)	135 000 (61.3%)
Complete cases (individuals who survived more than 30 days)	168 387	908	628	5564	175 487
Time to further stroke	68 900 (40.9%)	348 (38.3%)	257 (40.9%)	2214 (39.8%)	71 719 (40.9%)
Time to further vascular event	80 407 (47.8%)	398 (43.8%)	289 (46.0%)	2594 (46.6%)	83 688 (47.7%)

Supplementary Table 5: Number of individuals and events per group – sensitivity analysis (major depression based on psychiatric hospital admission records only)

Outcome	No MHC	Schizophrenia	Bipolar disorder	Major depression	Total
Complete cases	222356	1186	859	3623	228024
30-day mortality	51707 (23.3%)	278 (23.4%)	231 (26.9%)	822 (22.7%)	53038 (23.3%)
1-year mortality	87909 (39.5%)	454 (38.3%)	372 (43.3%)	1385 (38.2%)	90120 (39.5%)
All-cause mortality	181450 (81.6%)	941 (79.3%)	726 (84.5%)	2910 (80.3%)	186027 (81.6%)
Complete cases (stroke admissions up to 2013)	214238	1123	810	3495	219666
5-year mortality	131303 (61.3%)	666 (59.3%)	520 (64.2%)	2111 (60.4%)	134600 (61.3%)
Complete cases (individuals who survived more than 30 days)	170649	908	628	2801	174986
Time to further stroke	69829 (40.9%)	348 (38.3%)	257 (40.9%)	1088 (38.8%)	71522 (40.9%)
Time to further vascular event	81474 (47.7%)	398 (43.8%)	289 (46.0%)	1293 (46.2%)	83454 (47.7%)

Supplementary Figure 2: Flow diagram for establishing the stroke audit sub-cohort
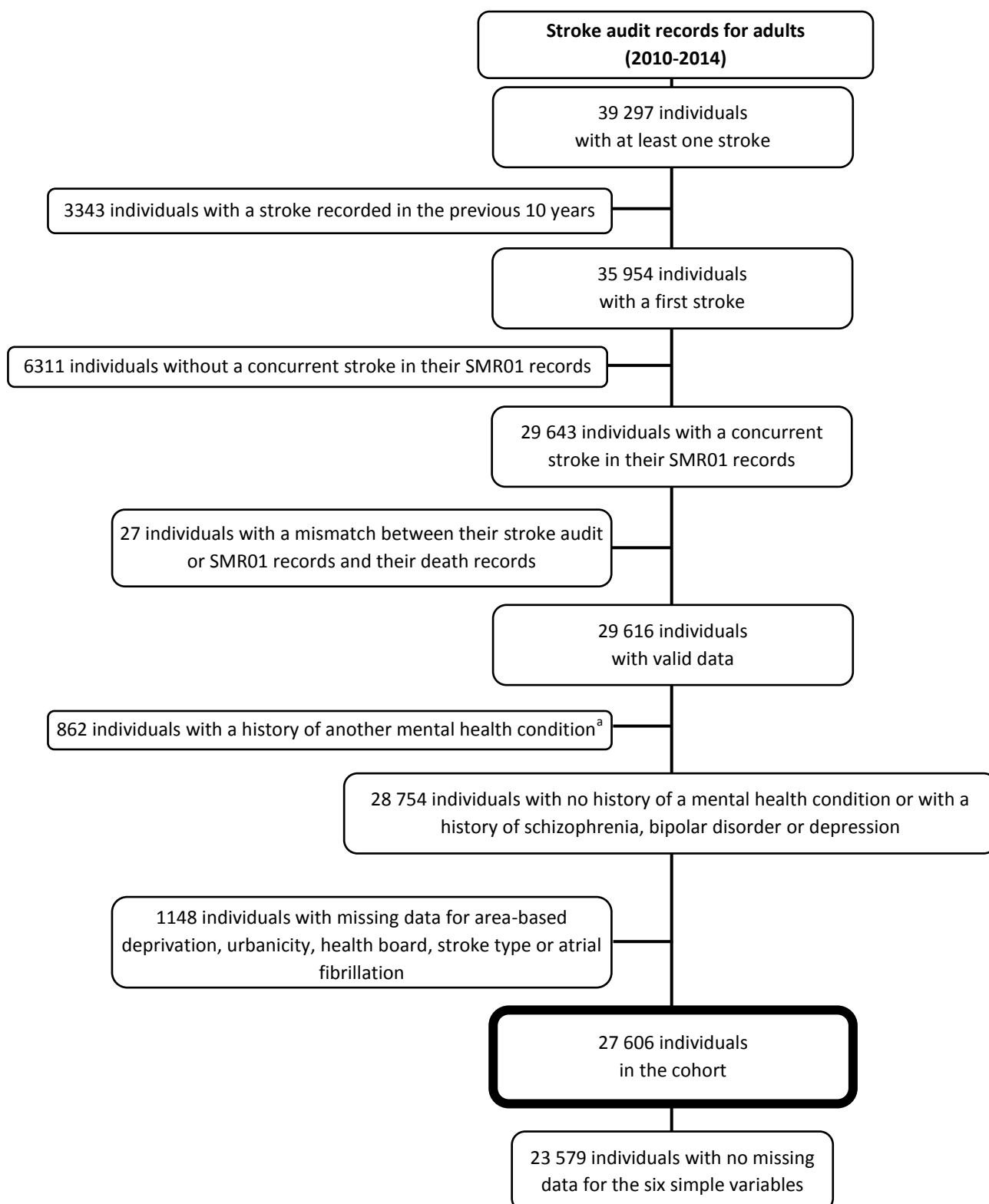
a. Including other psychoses, other mood disorders, disorders of adult personality and behaviour, eating disorders, neuroses, dissociative and somatoform disorders, behavioural and emotional disorders with onset in childhood and adolescence, non-organic sleep disorders, disorders of psychosocial development and unspecified mental disorders.

Supplementary Table 6: Baseline characteristics and outcomes for people who had a stroke in Scotland, 2010 – 2014, comparing people with each severe mental illness versus no admission for any mental health condition. Data from the stroke audit sub-cohort (excluding people with missing data in deprivation, urbanicity, health board, atrial fibrillation or stroke type)

	No mental health condition (N=26 259)	Schizophrenia (N=167)	Bipolar disorder (N=102)	Major depression (N=1078)
Median follow-up time (IQR), years	4.3 (0.8, 6.2)	4.2 (1.1, 5.9)	4.1 (0.3, 5.6)	4.2 (0.9, 6.1)
Sex, n (%)				
Female	13 078 (49.8%)	80 (47.9%)	64 (62.7%)	667 (61.9%)
Male	13 181 (50.2%)	87 (52.1%)	38 (37.3%)	411 (38.1%)
Mean age at stroke (SD), years				
Mean (SD)	73.2 (13.2)	64.6 (13.4)	68.3 (12.1)	70.1 (13.8)
Year of admission, n (%)				
2010	5113 (19.5%)	38 (22.8%)	21 (20.6%)	208 (19.3%)
2011	5137 (19.6%)	24 (14.4%)	14 (13.7%)	208 (19.3%)
2012	4959 (18.9%)	26 (15.6%)	15 (14.7%)	231 (21.4%)
2013	5494 (20.9%)	36 (21.6%)	23 (22.5%)	213 (19.8%)
2014	5556 (21.2%)	43 (25.7%)	29 (28.4%)	218 (20.2%)
Deprivation quintile, n (%)				
1 (most deprived)	5510 (21.0%)	54 (32.3%)	17 (16.7%)	267 (24.8%)
2	5400 (20.6%)	33 (19.8%)	21 (20.6%)	260 (24.1%)
3	5122 (19.5%)	34 (20.4%)	20 (19.6%)	208 (19.3%)
4	5338 (20.3%)	28 (16.8%)	20 (19.6%)	203 (18.8%)
5 (least deprived)	4889 (18.6%)	18 (10.8%)	24 (23.5%)	140 (13.0%)
Urbanity, n (%)				
Large urban area	8669 (33.0%)	69 (41.3%)	38 (37.3%)	387 (35.9%)
Other urban area	9432 (35.9%)	59 (35.3%)	36 (35.3%)	403 (37.4%)
Small town	3581 (13.6%)	20 (12.0%)	11 (10.8%)	152 (14.1%)
Rural	4577 (17.4%)	19 (11.4%)	17 (16.7%)	136 (12.6%)
History of alcohol use disorder, n (%)	1110 (4.2%)	36 (21.6%)	13 (12.7%)	233 (21.6%)
Type of stroke				
Ischaemic	23 266 (88.6%)	147 (88.0%)	NA	960 (89.1%)
Haemorrhagic	2993 (11.4%)	20 (12.0%)	NA	118 (10.9%)
Atrial fibrillation, n (%)	7381 (28.1%)	26 (15.6%)	17 (16.7%)	242 (22.4%)
Diabetes, n (%)	4801 (18.3%)	35 (21.0%)	22 (21.6%)	210 (19.5%)
Hypertension recorded at stroke admission, n (%)	8601 (32.8%)	35 (21.0%)	22 (21.6%)	282 (26.2%)
Case-mix variables[a]				
N	22 437	145	90	907
Living alone before stroke, n (%)	8789 (39.2%)	59 (40.7%)	37 (41.1%)	420 (46.3%)
Independent in ADL before stroke, n (%)	19 240 (85.8%)	98 (67.6%)	66 (73.3%)	660 (72.8%)
Able to talk at first assessment, n (%)	16 418 (73.2%)	86 (59.3%)	58 (64.4%)	667 (73.5%)
Able to lift arms at first assessment, n (%)	13 759 (61.3%)	83 (57.2%)	55 (61.1%)	522 (57.6%)
Able to walk unassisted at first assessment, n (%)	10 554 (47.0%)	67 (46.2%)	37 (41.1%)	379 (41.8%)
30-day mortality, n (%)	3432 (13.1%)	25 (15.0%)	17 (16.7%)	142 (13.2%)
1-year mortality, n (%)	7071 (26.9%)	41 (24.6%)	30 (29.4%)	281 (26.1%)
5-year mortality[b]				

	No mental health condition (N=26 259)	Schizophrenia (N=167)	Bipolar disorder (N=102)	Major depression (N=1078)
N	20 703	124	73	860
n (%)	10 275 (49.6%)	67 (54.0%)	40 (54.8%)	449 (52.2%)
Further events during follow-up[c]				
N	22 827	142	85	936
Stroke, n (%)	6977 (30.6%)	43 (30.3%)	26 (30.6%)	312 (33.3%)
Vascular event, n (%)	7634 (33.4%)	47 (33.1%)	28 (32.9%)	346 (37.0%)
Brain imaging on day of admission[d]				
N	25 943	164	102	1065
n (%)	15 996 (61.7%)	97 (59.1%)	65 (63.7%)	634 (59.5%)
Swallow screen on day of admission[e]				
N	25 805	158	101	1061
n (%)	18 187 (70.5%)	113 (71.5%)	71 (70.3%)	740 (69.7%)
Admission to stroke unit within one day[f]				
N	25 792	164	102	1060
n (%)	19 251 (74.6%)	112 (68.3%)	79 (77.5%)	775 (73.1%)
Aspirin within one day[g]				
N	20694	130	91	861
n (%)	8686 (42.0%)	48 (36.9%)	41 (45.1%)	349 (40.5%)
Received thrombolysis, n (%)	3792 (14.4%)	10 (6.0%)	14 (13.7%)	133 (12.3%)

NA=Not available. Counts less than 10 are not available in order to protect the identity of individuals.

a. Based on the 23 579 individuals with complete information on the case-mix variables.

b. Based on the 21 760 individuals with their first stroke between 2010 and 2013.

c. Based on 23 990 individuals who survived more than 30 days.

d. Based on the 27 274 individuals who survived their day of admission and had sufficient brain imaging data.

e. Based on the 27 125 individuals who survived their day of admission and had sufficient swallow screen data.

f. Based on the 27 118 individuals who survived more than one day and had sufficient stroke unit data.

g. Based on the 21 776 individuals who survived more than one day, had an ischaemic stroke, didn't have a valid contraindication to aspirin and had sufficient aspirin data.

Supplementary Table 7: Number of individuals and events per group for the stroke audit sub-cohort

Outcome	No mental health condition	Schizophrenia	Bipolar disorder	Major depression	Total
Complete cases	26 259	167	102	1078	27 606
30-day mortality	3432 (13.1%)	25 (15.0%)	17 (16.7%)	142 (13.2%)	3616 (13.1%)
1-year mortality	7071 (26.9%)	41 (24.6%)	30 (29.4%)	281 (26.1%)	7423 (26.9%)
Mortality during follow-up	14 575 (55.5%)	93 (55.7%)	58 (56.9%)	636 (59.0%)	15 362 (55.6%)
Complete cases (stroke admissions up to 2013)	20 703	124	73	860	21 760
5-year mortality	10 275 (49.6%)	67 (54.0%)	40 (54.8%)	449 (52.2%)	10 831 (49.8%)
Complete cases (individuals who survived more than 30 days)	22 827	142	85	936	23 990
Time to further stroke	6977 (30.6%)	43 (30.3%)	26 (30.6%)	312 (33.3%)	7358 (30.7%)
Time to further vascular event	7634 (33.4%)	47 (33.1%)	28 (32.9%)	346 (37.0%)	8055 (33.6%)
Complete cases (individuals who survived more than one day and had sufficient stroke unit data)	25 792	164	102	1060	27 118
Admission to stroke unit within one day of admission	19 251 (74.6%)	112 (68.3%)	79 (77.5%)	775 (73.1%)	20 217 (74.6%)
Complete cases (Individuals who survived their day of admission and had sufficient brain scan data)	25 943	164	102	1065	27 274
Brain scan on day of admission	15 996 (61.7%)	97 (59.1%)	65 (63.7%)	634 (59.5%)	16 792 (61.6%)
Complete cases (Individuals who survived their day of admission and had sufficient swallow screen data)	25 805	158	101	1061	27 125
Swallow screen on day of admission	18 187 (70.5%)	113 (71.5%)	71 (70.3%)	740 (69.7%)	19111 (70.5%)
Complete cases (individuals who survived more than one day, had an ischaemic stroke, didn't have a valid contraindication to aspirin and had sufficient aspirin data)	20 694	130	91	861	21 776
Aspirin within one day of admission	8686 (42.0%)	48 (36.9%)	41 (45.1%)	349 (40.5%)	9124 (41.9%)

Supplementary Table 8: Number of individuals and events per group for the stroke audit sub-cohort – sensitivity analysis (major depression based on psychiatric hospital admission records only)

Outcome	No mental health condition	Schizophrenia	Bipolar disorder	Major depression	Total
Complete cases	26 715	167	102	476	27 460
30-day mortality	3493 (13.1%)	25 (15.0%)	17 (16.7%)	63 (13.2%)	3598 (13.1%)
1-year mortality	7193 (26.9%)	41 (24.6%)	30 (29.4%)	122 (25.6%)	7386 (26.9%)
Mortality during follow-up	14 853 (55.6%)	93 (55.7%)	58 (56.9%)	262 (55.0%)	15 266 (55.6%)
Complete cases (stroke admissions up to 2013)	21 065	124	73	389	21 651
5-year mortality	10 472 (49.7%)	67 (54.0%)	40 (54.8%)	189 (48.6%)	10 768 (49.7%)
Complete cases (individuals who survived more than 30 days)	23 222	142	85	413	23 862
Time to further stroke	7114 (30.6%)	43 (30.3%)	26 (30.6%)	121 (29.3%)	7304 (30.6%)
Time to further vascular event	7786 (33.5%)	47 (33.1%)	28 (32.9%)	137 (33.2%)	7998 (33.5%)
Complete cases (individuals who survived more than one day and had sufficient stroke unit data)	26 236	164	102	471	26 973
Admission to stroke unit within one day of admission	19 568 (74.6%)	112 (68.3%)	79 (77.5%)	346 (73.5%)	20 105 (74.5%)
Complete cases (Individuals who survived their day of admission and had sufficient brain scan data)	26 390	164	102	472	27 128
Brain scan on day of admission	16 277 (61.7%)	97 (59.1%)	65 (63.7%)	266 (56.4%)	16 705 (61.6%)
Complete cases (Individuals who survived their day of admission and had sufficient swallow screen data)	26 253	158	101	468	26 980
Swallow screen on day of admission	18 498 (70.5%)	113 (71.5%)	71 (70.3%)	319 (68.2%)	19 001 (70.4%)
Complete cases (individuals who survived more than one day, had an ischaemic stroke, didn't have a valid contraindication to aspirin and had sufficient aspirin data)	21 058	130	91	381	21 660
Aspirin within one day of admission	8844 (42.0%)	48 (36.9%)	41 (45.1%)	134 (35.2%)	9067 (41.9%)

Supplementary Table 9: Odds ratios and hazard ratios for outcomes following stroke in Scotland, 1991 – 2014. Ratios compare individuals with a severe mental illness to individuals without a history of a mental health condition. Sensitivity analysis for models 1 and 2 with major depression only identified using psychiatric hospital admission records

For each outcome, this table presents a summary of the results of the sensitivity analysis for models 1 and 2. In the sensitivity analysis, major depression is only identified using psychiatric hospital admission records. Thus fewer people are included in the major depression group, and the overall cohort is smaller. The results for schizophrenia and bipolar disorder differ slightly between the main analysis and the sensitivity analysis because the comparison group has changed (some people who were included in the major depression group for the main analysis are included in the no mental health admission group for the sensitivity analysis).

Outcome	Model	N	Schizophrenia	Bipolar disorder	Major depression
30-day mortality, OR (95% CI)	Model 1	228 024	1.33 (1.16 to 1.52)	1.37 (1.17 to 1.60)	1.09 (1.01 to 1.18)
	Model 2	228 024	1.28 (1.11 to 1.47)	1.35 (1.16 to 1.58)	1.04 (0.96 to 1.13)
1-year mortality, OR (95% CI)	Model 1	228 024	1.48 (1.31 to 1.67)	1.44 (1.25 to 1.65)	1.16 (1.08 to 1.24)
	Model 2	228 024	1.39 (1.23 to 1.58)	1.41 (1.22 to 1.62)	1.08 (1.00 to 1.16)
5-year mortality, OR (95% CI)	Model 1	219 666[a]	1.79 (1.57 to 2.04)	1.52 (1.30 to 1.78)	1.34 (1.24 to 1.45)
	Model 2	219 666[a]	1.60 (1.41 to 1.83)	1.46 (1.25 to 1.71)	1.18 (1.09 to 1.27)
All-cause mortality, HR (95% CI)	Model 1	228 024	1.44 (1.35 to 1.54)	1.35 (1.26 to 1.45)	1.22 (1.18 to 1.27)
	Model 2	228 024	1.35 (1.27 to 1.44)	1.32 (1.23 to 1.42)	1.14 (1.10 to 1.18)
Time to further stroke, HR (95% CI)	Model 1	174 986[b]	1.28 (1.16 to 1.43)	1.18 (1.05 to 1.34)	1.11 (1.04 to 1.17)
	Model 2	174 986[b]	1.24 (1.11 to 1.37)	1.16 (1.03 to 1.31)	1.06 (1.00 to 1.12)
Time to further vascular event, HR (95% CI)	Model 1	174 986[b]	1.26 (1.14 to 1.39)	1.15 (1.03 to 1.29)	1.14 (1.08 to 1.20)
	Model 2	174 986[b]	1.21 (1.09 to 1.33)	1.14 (1.01 to 1.28)	1.09 (1.03 to 1.15)

Model 1 is adjusted for age, sex and year. Model 2 is adjusted for age, sex, year, history of alcohol use disorder, deprivation, urbanity and health board. HR=Hazard ratio. OR=Odds ratio.

a. Stroke admissions up to 2013 in order to ensure that all individuals have at least 5 years' follow-up.
b. Individuals who survived more than 30 days.

Supplementary Table 10: Odds ratios and hazard ratios for outcomes and processes of care following stroke in Scotland, 2010 – 2014, based on data from the stroke audit sub-cohort. Ratios compare individuals with a severe mental illness to individuals without a history of a mental health condition. Sensitivity analyses for models 1, 2 and 3 based on data from the stroke audit sub-cohort

For each outcome, this table presents a summary of the sensitivity analysis where major depression is only identified using psychiatric hospital admission records. For this sensitivity analysis, fewer people are included in the major depression group, and the overall cohort is smaller. The results for schizophrenia and bipolar disorder differ slightly between the main analysis and the sensitivity analysis because the comparison group has changed (some people who were included in the major depression group for the main analysis are included in the no mental health admission group for the sensitivity analysis).

Outcome	Model	N	Schizophrenia	Bipolar disorder	Major depression
30-day mortality, OR (95% CI)	Model 1	27 460	1.89 (1.19 to 2.88)	1.84 (1.04 to 3.06)	1.24 (0.94 to 1.62)
	Model 2	27 460	1.80 (1.12 to 2.77)	2.05 (1.16 to 3.44)	1.19 (0.89 to 1.57)
	Model 3	23 449[a]	1.05 (0.60 to 1.79)	1.76 (0.90 to 3.25)	1.14 (0.80 to 1.60)
1-year mortality, OR (95% CI)	Model 1	27 460	1.62 (1.10 to 2.34)	1.73 (1.09 to 2.70)	1.23 (0.98 to 1.54)
	Model 2	27 460	1.50 (1.01 to 2.19)	1.83 (1.14 to 2.85)	1.17 (0.93 to 1.47)
	Model 3	23 449[a]	0.97 (0.60 to 1.52)	1.51 (0.87 to 2.53)	1.08 (0.82 to 1.41)
5-year mortality, OR (95% CI)	Model 1	21 651[b]	2.70 (1.82 to 4.01)	2.24 (1.35 to 3.73)	1.47 (1.17 to 1.85)
	Model 2	21 651[b]	2.32 (1.55 to 3.47)	2.23 (1.34 to 3.73)	1.28 (1.01 to 1.61)
	Model 3	18 132[a,b]	1.69 (1.06 to 2.70)	1.80 (0.99 to 3.28)	1.24 (0.94 to 1.63)
Mortality during follow-up, HR (95% CI)	Model 1	27 460	1.84 (1.50 to 2.26)	1.51 (1.17 to 1.96)	1.32 (1.17 to 1.50)
	Model 2	27 460	1.71 (1.40 to 2.11)	1.60 (1.24 to 2.08)	1.24 (1.09 to 1.40)
	Model 3	23 449[a]	1.27 (1.01 to 1.59)	1.46 (1.11 to 1.92)	1.14 (0.99 to 1.30)
Time to further stroke, HR (95% CI)	Model 1	23 862[c]	1.45 (1.08 to 1.96)	1.22 (0.83 to 1.80)	1.10 (0.92 to 1.32)
	Model 2	23 862[c]	1.33 (0.99 to 1.80)	1.21 (0.82 to 1.79)	1.04 (0.87 to 1.25)
	Model 3	20 481[a,c]	1.21 (0.88 to 1.67)	1.06 (0.69 to 1.61)	1.01 (0.83 to 1.23)
Time to further vascular event, HR (95% CI)	Model 1	23 862[c]	1.45 (1.09 to 1.94)	1.22 (0.84 to 1.76)	1.16 (0.98 to 1.37)
	Model 2	23 862[c]	1.34 (1.00 to 1.79)	1.21 (0.83 to 1.75)	1.10 (0.92 to 1.30)
	Model 3	20 481[a,c]	1.21 (0.89 to 1.64)	1.03 (0.68 to 1.55)	1.08 (0.89 to 1.29)
Admission to stroke	Model 1	26 973[d]	0.73 (0.53 to 1.03)	1.16 (0.74 to 1.89)	0.95 (0.77 to 1.17)

Outcome	Model	N	Schizophrenia	Bipolar disorder	Major depression
unit within one day of admission, OR (95% CI)	Model 2	26 973[d]	0.78 (0.56 to 1.11)	1.31 (0.83 to 2.16)	0.97 (0.78 to 1.20)
	Model 3	23 097[a,d]	0.86 (0.60 to 1.26)	1.24 (0.77 to 2.08)	0.98 (0.78 to 1.24)
Brain imaging on day of admission, OR (95% CI)	Model 1	27 128[e]	0.79 (0.57 to 1.08)	0.99 (0.66 to 1.50)	0.76 (0.64 to 0.92)
	Model 2	27 128[e]	0.77 (0.56 to 1.07)	0.96 (0.64 to 1.47)	0.79 (0.65 to 0.96)
	Model 3	23 189[a,e]	0.73 (0.51 to 1.05)	1.01 (0.64 to 1.62)	0.81 (0.65 to 1.01)
Swallow screen on day of admission, OR (95% CI)	Model 1	26 980[f]	1.05 (0.74 to 1.50)	0.95 (0.62 to 1.48)	0.91 (0.75 to 1.11)
	Model 2	26 980[f]	1.13 (0.80 to 1.63)	1.00 (0.65 to 1.56)	0.90 (0.74 to 1.11)
	Model 3	23 102[a,f]	1.08 (0.75 to 1.60)	1.12 (0.70 to 1.85)	0.85 (0.68 to 1.07)
Aspirin within one day of admission, OR (95% CI)	Model 1	21 660[g]	0.76 (0.53 to 1.09)	1.08 (0.71 to 1.63)	0.75 (0.60 to 0.92)
	Model 2	21 660[g]	0.77 (0.53 to 1.10)	1.06 (0.69 to 1.61)	0.75 (0.60 to 0.93)
	Model 3	18 583[a,g]	0.77 (0.51 to 1.13)	1.17 (0.75 to 1.82)	0.70 (0.54 to 0.88)

Model 1 is adjusted for age, sex and year. Model 2 is adjusted for age, sex, year, history of alcohol use disorder, deprivation, urbanity, health board, stroke type, diabetes, history of atrial fibrillation, and hypertension. Model 3 is adjusted for age, sex, year, history of alcohol use disorder, deprivation, urbanity, health board, stroke type, diabetes, history of atrial fibrillation, hypertension, 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 one day of admission, models 2 and 3 do not adjust for stroke type because this process of care was only assessed amongst people with an ischaemic stroke. HR=Hazard ratio. OR=Odds ratio.

a. 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).
b. Stroke audit records 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.
d. Individuals who survived more than one day and had sufficient stroke unit data.
e. Individuals who survived their day of admission and had sufficient brain imaging data.
f. Individuals who survived their day of admission and had sufficient swallow screen data.
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