

Original research

# Trends and inequities in the diagnosis and treatment of poststroke depression: a retrospective cohort study of privately insured patients in the USA, 2003–2020

Holly Elser <sup>1,2</sup>, Michelle Caunca,<sup>3</sup> David H Rehkopf,<sup>4</sup> Wells Andres <sup>1</sup>,  
Rebecca F Gottesman,<sup>5</sup> Scott E Kasner,<sup>6</sup> Kristine Yaffe,<sup>7</sup> Andrea L C Schneider<sup>6,8</sup>

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/jnnp-2022-330179>).

For numbered affiliations see end of article.

## Correspondence to

Dr Holly Elser, Department of Neurology, Hospital of the University of Pennsylvania, Philadelphia, PA 19104, USA; [Holly.Elser@Pennmedicine.upenn.edu](mailto:Holly.Elser@Pennmedicine.upenn.edu)

Received 19 August 2022  
Accepted 7 November 2022  
Published Online First 18 November 2022

## ABSTRACT

**Background** Depression is a common neuropsychiatric consequence of stroke, but there is little empiric evidence regarding clinical diagnosis and management of poststroke depression.

**Methods** Retrospective cohort study among 831 471 privately insured patients with first stroke in the USA from 2003 to 2020. We identified diagnoses of poststroke depression using codes from the International Classification of Diseases. We identified treatment based on prescriptions for antidepressants. We used Cox proportional hazards regression analysis to examine rates of poststroke depression diagnosis by gender, age and race/ethnicity. Among individuals who received a diagnosis of poststroke depression, we estimated treatment rates by gender, race/ethnicity and age using negative binomial regression analysis.

**Results** Annual diagnosis and treatment rates for poststroke depression increased from 2003 to 2020 (both  $p$  for trend < 0.001). Diagnosis rates were higher in women than men (HR 1.53, 95% CI 1.51 to 1.55), lower among members of racial/ethnic minorities (vs white patients: Asian HR 0.63, 95% CI 0.60 to 0.66; Black HR 0.76, 95% CI 0.74 to 0.78; Hispanic HR 0.88, 95% CI 0.86 to 0.90) and varied by age. Among individuals diagnosed with poststroke depression, 69.8% were prescribed an antidepressant. Rates of treatment were higher in women vs men (rate ratio, RR=1.19, 95% CI: 1.17 to 1.21), lower among members of racial/ethnic minorities (vs white patients: Asian RR 0.85, 95% CI 0.80 to 0.90; Black RR 0.92, 95% CI 0.89 to 0.94; Hispanic RR 0.96, 95% CI 0.93 to 0.99) and higher among older patients.

**Conclusions** In this insured population, we identify potential inequities in clinical management of poststroke depression by gender, race/ethnicity and age that may reflect barriers other than access to healthcare.

## INTRODUCTION

Depression is a common and important neuropsychiatric consequence of stroke.<sup>1,2</sup> Pooled frequency estimates from meta-analyses suggest that the prevalence of poststroke depression is approximately 30%.<sup>3,4</sup> Yet prior research suggests poststroke depression remains underdiagnosed and undertreated in clinical practice.<sup>5</sup> This may in part reflect the challenges of differentiating poststroke depression from other common cognitive sequelae of stroke including aphasia, apathy and cognitive

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Depression is a common neuropsychiatric consequence of stroke, arising from a combination of biological and psychosocial factors. Yet there is little systematic evidence regarding current trends in clinical management of poststroke depression.

## WHAT THIS STUDY ADDS

⇒ Using claims data, we find that rates of diagnosis and treatment have increased over time. Patients who were male or who were non-white were systematically less likely to be diagnosed with or treated for poststroke depression.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings suggest inequities in clinical management that may be ameliorated with universal screening for depressive symptoms following stroke and motivates ongoing research that aims to identify the underlying mechanisms by which such inequities arise.

impairment.<sup>6</sup> The aetiology of poststroke depression is generally understood to be multifactorial, reflecting the joint effects of biological mechanisms and psychosocial factors.<sup>7,8</sup> Potential biological mechanisms include alterations in the ascending monoamine system,<sup>9</sup> glutamate-mediated excitotoxicity,<sup>10</sup> increased production of proinflammatory cytokines,<sup>11</sup> activation of the hypothalamic–pituitary–adrenal axis<sup>12</sup> and genetic susceptibility.<sup>13</sup> Relevant psychosocial risk factors include gender, history of psychiatric illness, degree of functional impairment and social isolation following stroke.<sup>14,15</sup>

Evidence from several smaller trials suggesting antidepressants, namely selective serotonin reuptake inhibitors (SSRI) and tricyclic antidepressants (TCA), are effective treatments for poststroke depression.<sup>16</sup> Therefore, guidelines issued jointly by the American Heart Association and American Stroke Association in 2016 recommend that patients with poststroke depression be treated with antidepressants in the absence of any contraindications.<sup>17</sup> Yet recent research documents worrisome inequities in clinical management of poststroke depression,



© Author(s) (or their employer(s)) 2023. No commercial re-use. See rights and permissions. Published by BMJ.

**To cite:** Elser H, Caunca M, Rehkopf DH, et al. *J Neurol Neurosurg Psychiatry* 2023;**94**:220–226.

wherein patients belonging to racial/ethnic minorities, older patients, and men are less likely to receive treatment.<sup>5,18</sup>

As poststroke depression is associated with impaired functional recovery,<sup>19</sup> poor quality of life<sup>20</sup> and reduced survival,<sup>21</sup> an understanding of trends in diagnosis and treatment over time and within key population subgroups is important for clinical management of patients following stroke. In this retrospective cohort study, we present an analysis of longitudinal claims data that characterises the incidence of depression and rates of treatment following stroke among privately insured individuals followed from 2003 to 2020. The aim of this study is to provide a detailed description of the clinical management of poststroke depression over time, by stroke type and within subgroups defined by sex, age and race/ethnicity among privately insured individuals. We hypothesised that rates of both treatment and diagnosis of poststroke depression would increase over time, and further that there would be clear differences in rates of treatment by stroke type and across population subgroups.

## METHODS

The Optum Clinformatics Data Mart (CDM) is a longitudinal, deidentified commercial and Medicare Advantage claims database extending from 1 June 2003 to 30 June 2020. Member enrolment data; diagnostic codes from inpatient, outpatient and emergency department encounters; and pharmacy claims are deterministically linked across file types with a unique patient identifier. Individuals eligible for this study were aged 18 years and older with a new diagnosis of stroke between 2003 and 2020 followed for up to 365 days for depression. We identified new stroke diagnoses using codes from the International Classification of Diseases, 9th and 10th Revisions (ICD-9 and ICD-10) among individuals previously followed for at least 12 consecutive months. Consistent with stroke classification previously published by Kokotailo and Hill, stroke diagnoses were classified based on ICD codes as ischaemic stroke (IS), intracerebral haemorrhage (ICH) or subarachnoid haemorrhage (SAH) (online supplemental table 1).<sup>22</sup>

Follow-up extended from the date of stroke for up to 365 days. We aimed to minimise selection bias in our analysis by making no restrictions in eligibility based on duration or continuity of follow-up. Therefore, our analysis includes individuals with duration of follow-up less than 365 days due to end of insurance eligibility (including death and migration) or administrative censoring at the end of the study period.

### Poststroke depression

We defined poststroke depression diagnosis using codes from the ICD-9 and ICD-10 for major depressive disorder (MDD) and other depressive disorders (online supplemental table 2). We assigned the date of poststroke depression as the date of the second depression-related diagnosis within 365 days of first stroke. Because depression is episodic and occurs throughout the life course, we did not exclude individuals with a prior diagnosis of depression. For sensitivity analysis, we created three alternative outcome definitions all defined within the first 365 days after first stroke: (1) first depression-related diagnosis; (2) second diagnosis of MDD only and (3) first diagnosis of MDD only.

### Prescribed antidepressant medications

Antidepressants were identified within the first 365 days of first stroke based on generic drug names and were sub-classified as SSRI, serotonin and norepinephrine reuptake inhibitors (SNRI),

TCA, monoamine oxidase inhibitors or atypical antidepressants (online supplemental table 3). Prescriptions were standardised based on duration such that a 30-day supply counted as one prescription.

### Covariates

Covariates of interest were gender (men, women); age (18–34, 35–49, 50–64, 65 and older); imputed race and ethnicity (mutually exclusive categories of Asian, Black, Hispanic, White); US Census region (Midwest, Northeast, South, West) and depression diagnosis in the year prior to first stroke.

### Statistical analysis

First, we calculated overall and annual rates of poststroke depression diagnoses. Second, among individuals who satisfied our criteria for diagnosis of poststroke depression, we examined overall and annual rates of treatment with prescribed antidepressants. All statistical analyses were conducted using R Statistical Software V.4.0.

### Rates of poststroke depression diagnoses

We calculated overall and annual crude rates of poststroke depression diagnoses as the number of diagnoses per 1000 person-months of follow-up within the 365-day period following first stroke. We specify person-time as the denominator in calculating rates to accommodate potential discontinuities in and variable duration of follow-up. We assessed time trends using the Mann-Kendall test.<sup>23</sup> We calculated overall and annual crude rates by stroke type, gender, age category, race/ethnicity, region and among individuals with and without any depression diagnosis in the year prior to first stroke. Next, we used Cox proportional hazards regression analysis to estimate hazard ratios (HR) for poststroke depression diagnosis as a function of gender, age category, race/ethnicity and region. Models additionally included fixed effects for calendar year to account for secular trends. We estimated HRs overall and separately by stroke type. The timescale for Cox models was the duration of follow-up, and we assessed whether the assumption of proportional hazards was satisfied using Schoenfeld residuals.<sup>24</sup>

As a secondary analysis, we repeated our main analysis among individuals with and without a depression diagnosis in the year prior to first stroke. As a sensitivity analysis, we assessed the robustness of our main outcome definition by estimating HRs with alternative outcome definitions. We additionally estimated HRs for depression diagnoses within 6 months and 5 years following first stroke to evaluate the robustness of our results to alternative follow-up windows.

### Rates of treatment with antidepressant medications

In analysis restricted to individuals diagnosed with poststroke depression, we calculated the crude overall and annual rate of treatment as the number of prescribed antidepressants per 1000 person-months of follow-up in the 365 days after diagnosis of poststroke depression. As above, crude rates were calculated overall and annually by stroke type, gender, age category, race/ethnicity, region and among individuals with and without any depression diagnosis in the year prior to first stroke.

Next, we used negative binomial regression to model rate ratios (RR) of prescribed antidepressants as a function of gender, age category, race/ethnicity and region, with fixed effects for calendar year included to account for secular trends. We estimated RRs for all strokes combined and then separately by stroke type. In all negative binomial models, the count of unique

**Table 1** Demographic characteristics for beneficiaries by stroke type, 2003–2020

	All stroke	IS	ICH	SAH
Total	831 471 (100.0)	726 551 (100.0)	65 621 (100.0)	39 299 (100.0)
Gender				
Men	441 744 (53.1)	387 854 (53.4)	32 609 (49.7)	21 381 (54.4)
Women	389 627 (46.9)	338 697 (46.6)	33 012 (50.3)	17 918 (45.6)
Age group				
18–34	18 560 (2.2)	12 430 (1.7)	3513 (5.4)	2617 (6.7)
35–49	60 810 (7.3)	49 523 (6.8)	6263 (9.5)	5024 (12.8)
50–64	168 234 (20.2)	145 687 (20.1)	13 210 (20.1)	9337 (23.8)
65 and older	583 867 (70.2)	518 911 (71.4)	42 635 (65.0)	22 321 (56.8)
Race and ethnicity				
White	601 727 (72.4)	524 758 (72.2)	47 767 (72.8)	29 202 (74.3)
Asian	24 576 (3.0)	20 415 (2.8)	2631 (4.0)	1530 (3.9)
Black	117 665 (14.2)	105 817 (14.6)	7808 (11.9)	4040 (10.3)
Hispanic	87 503 (10.5)	75 561 (10.4)	7415 (11.3)	4527 (11.5)
Region				
Midwest	188 183 (22.6)	162 504 (22.4)	15 825 (24.1)	9854 (25.1)
Northeast	97 993 (11.8)	84 837 (11.7)	8342 (12.7)	4814 (12.2)
South	352 957 (42.4)	312 447 (43.0)	25 424 (38.7)	15 086 (38.4)
West	192 338 (23.1)	166 763 (23.0)	16 030 (24.4)	9545 (24.3)
Poststroke depression				
No	763 478 (90.1)	655 389 (90.2)	58 818 (89.6)	34 876 (88.7)
Yes	82 388 (9.9)	71 126 (9.8)	6802 (10.4)	4423 (11.3)

ICH, intracerebral haemorrhage; IS, ischaemic stroke; SAH, subarachnoid haemorrhage.

prescriptions was specified as the dependent variable with person-months of follow-up time specified as the offset. As a secondary analysis, we estimated RRs for treatment separately among individuals with and without any depression diagnosis in the 1 year prior to first stroke. As a sensitivity analysis, we estimated RRs for prescribed antidepressants within 6 months and 5 years following first stroke.

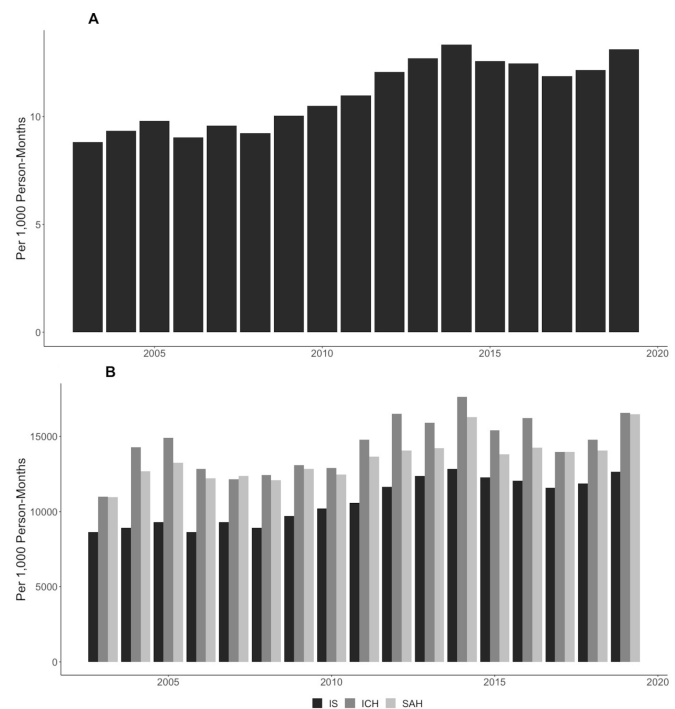
**RESULTS**

From 86 819 207 unique beneficiaries, we identified 831 471 aged 18 years or older with new stroke during the study period. Beneficiaries included in our analysis were predominantly white, aged 65 years or older and approximately half were women. Of first strokes, 87.4% were classified as IS. Although beneficiary characteristics were generally similar across stroke types, notable differences include a lesser proportion of beneficiaries over age 65 and a greater proportion of Asian beneficiaries with ICH and SAH compared with IS (table 1).

**Rates of poststroke depression diagnosis**

There were 11.5 diagnoses of poststroke depression per 1000 person-months of follow-up (95% CI 11.4 to 11.6) within the first 365 days after first stroke. Diagnosis rates increased gradually from 2003 (8.8, 95% CI 8.5 to 9.2) to 2019 (13.1, 95% CI 12.8 to 13.4) (p for trend <0.001). Rates of diagnosis were higher for ICH (14.9, 95% CI 14.5 to 15.2) and SAH (14.1, 95% CI 13.7 to 14.5) than for IS (11.2, 95% CI 11.1 to 11.3) as evidenced by non-overlapping 95% CIs (figure 1, online supplemental table 4). Diagnosis rates were higher in women than in men, among beneficiaries ages 18–49, among white beneficiaries in the Northeast (online supplemental tables 5–8) and among individuals with a diagnosis of depression in the 1 year prior to stroke (36.9, 95% CI 36.6 to 37.2) as compared with those without (6.1, 95% CI 6.0 to 6.1) (online supplemental table 9).

In Cox proportional hazards regression analysis, women were more likely to be diagnosed with poststroke depression than men (HR 1.53, 95% CI 1.51 to 1.55). Compared with individuals ages 18–34, rate of diagnosis was higher among those 35–49 (HR 1.10, 95% CI 1.04 to 1.15), lower among those 65 and



**Figure 1** Depression diagnoses within 1 year of first stroke for all stroke (Panel A) and by subtype (Panel B), 2003–2020. ICH, intracerebral haemorrhage; IS, ischaemic stroke; SAH, subarachnoid haemorrhage.

**Table 2** HR for association between demographic characteristics and depression following first stroke, 2003–2020

	All stroke HR (95% CI)	IS HR (95% CI)	ICH HR (95% CI)	SAH HR (95% CI)
Sex				
Male	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Female	1.53 (1.51 to 1.55)	1.55 (1.53 to 1.58)	1.39 (1.33 to 1.46)	1.40 (1.32 to 1.49)
Age group				
18–34	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
35–49	1.10 (1.04 to 1.15)	1.05 (1.00 to 1.12)	1.38 (1.23 to 1.56)	1.24 (1.08 to 1.42)
50–64	1.01 (0.96 to 1.05)	0.99 (0.94 to 1.05)	1.22 (1.09 to 1.36)	1.10 (0.97 to 1.25)
65 and older	0.75 (0.72 to 0.79)	0.74 (0.70 to 0.78)	0.92 (0.83 to 1.02)	0.89 (0.78 to 1.01)
Race and ethnicity				
White	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Asian	0.63 (0.60 to 0.66)	0.64 (0.60 to 0.67)	0.55 (0.48 to 0.65)	0.54 (0.44 to 0.66)
Black	0.76 (0.74 to 0.78)	0.77 (0.75 to 0.79)	0.65 (0.60 to 0.71)	0.80 (0.72 to 0.89)
Hispanic	0.88 (0.86 to 0.90)	0.89 (0.87 to 0.91)	0.85 (0.78 to 0.92)	0.79 (0.71 to 0.88)
Region				
Midwest	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Northeast	1.22 (1.19 to 1.25)	1.22 (1.19 to 1.25)	1.25 (1.16 to 1.34)	1.19 (1.08 to 1.30)
South	0.87 (0.86 to 0.89)	0.88 (0.86 to 0.89)	0.83 (0.79 to 0.89)	0.87 (0.81 to 0.94)
West	0.73 (0.71 to 0.74)	0.73 (0.71 to 0.74)	0.68 (0.63 to 0.73)	0.73 (0.67 to 0.80)

ICH, intracerebral haemorrhage; IS, ischaemic stroke; SAH, subarachnoid haemorrhage.

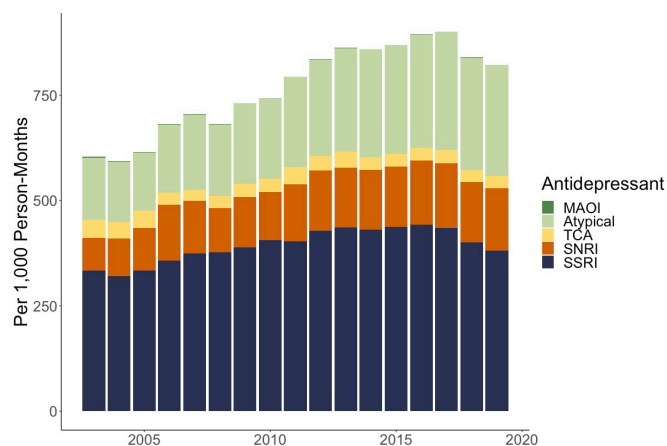
older (HR 0.75, 95% CI 0.72 to 0.79) and similar among those ages 50–64 (HR 1.01, 95% CI 0.96 to 1.05). Compared with white beneficiaries, diagnosis rates were lower among beneficiaries who were Asian (HR 0.63, 95% CI 0.60 to 0.66), Black (HR 0.76, 95% CI 0.74 to 0.78) or Hispanic (HR 0.88, 95% CI 0.86 to 0.90) (table 2). This general pattern remained consistent across stroke types, among those with and without prior depression diagnosis, and in sensitivity analyses (online supplemental tables 10–12).

### Rates of treatment with antidepressant

Of the 82 388 individuals diagnosed with poststroke depression, there were 57 542 (69.8%) who were prescribed an antidepressant. As with diagnoses, rates of treatment with prescribed antidepressants increased gradually over the study period (p for trend <0.001). Treatment rates were higher for IS (815, 95% CI 814 to 816) than for ICH (744, 95% CI 740 to 747) or SAH

(766, 95% CI 762 to 750). SSRI comprised approximately half of prescriptions over the study period (figure 2, online supplemental tables 13 and 14). Treatment rates were generally higher among women, beneficiaries ages 50–64 and 65 and older, for white beneficiaries, and in the West (online supplemental tables 15–18). Treatment rates were increased among individuals diagnosed with poststroke depression who had also received a depression diagnosis in the year prior to stroke (online supplemental table 19).

In regression analysis, treatment rates were increased in women compared with men (RR 1.19, 95% CI 1.17 to 1.21). By age, we observed the strongest association among beneficiaries ages 50–64 (RR 1.49, 95% CI 1.41 to 1.58) compared with those ages 18–34. By race and ethnicity, treatment rates were reduced among Asian, Black and Hispanic beneficiaries as compared with white beneficiaries (table 3). This pattern of findings persisted in secondary and sensitivity analyses (online supplemental tables 20 and 21).



**Figure 2** Prescribed antidepressants by drug class among individuals poststroke depression, 2003–2020. MAOI, monoamine oxidase inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

### DISCUSSION

In this retrospective cohort study, we examined trends in diagnosis and treatment of poststroke depression among privately insured US adults followed from 2003 to 2020. We focused first on rates of depression diagnosis following stroke. Whereas pooled frequency estimates from meta-analyses suggest the prevalence of poststroke depression is approximately 30%,<sup>3 4 25</sup> the estimated rate of poststroke depression diagnoses in this analysis is demonstrably lower at 11.5 diagnoses per 1000 person-months of follow-up. This equates roughly to a 1-year prevalence of 13.9%. This may reflect the fact that our outcome measure relies on diagnoses of depression rather than direct measures of depressive symptoms. A novel contribution of our analysis is separate consideration of trends in poststroke depression diagnoses across major stroke types. We found that the rates of poststroke depression diagnosis were consistently higher for ICH and SAH than for IS, in contrast with some prior evidence that the risk of poststroke depression does not vary significantly between individuals by stroke type.<sup>26 27</sup>

**Table 3** Rate ratios for prescribed antidepressants among individuals with depression diagnosis following first stroke, 2003–2020

	All stroke RR (95% CI)	IS RR (95% CI)	ICH RR (95% CI)	SAH RR (95% CI)
Sex				
Male	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Female	1.19 (1.17 to 1.21)	1.18 (1.16 to 1.20)	1.24 (1.15 to 1.34)	1.24 (1.17 to 1.32)
Age group				
18–34	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
35–49	1.27 (1.19 to 1.35)	1.23 (1.14 to 1.32)	1.42 (1.18 to 1.71)	1.26 (1.07 to 1.47)
50–64	1.49 (1.41 to 1.58)	1.46 (1.36 to 1.56)	1.56 (1.31 to 1.85)	1.44 (1.25 to 1.67)
65 and older	1.23 (1.16 to 1.30)	1.19 (1.11 to 1.28)	1.28 (1.08 to 1.52)	1.25 (1.09 to 1.44)
Race and ethnicity				
White	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Asian	0.85 (0.80 to 0.90)	0.86 (0.81 to 0.92)	0.79 (0.61 to 1.02)	0.78 (0.64 to 0.95)
Black	0.92 (0.89 to 0.94)	0.93 (0.90 to 0.95)	0.81 (0.71 to 0.92)	0.80 (0.72 to 0.89)
Hispanic	0.96 (0.93 to 0.99)	0.97 (0.94 to 1.00)	0.93 (0.83 to 1.05)	0.89 (0.81 to 0.98)
Region				
Midwest	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Northeast	0.99 (0.96 to 1.02)	0.99 (0.96 to 1.02)	1.01 (0.90 to 1.14)	0.99 (0.90 to 1.09)
South	1.18 (1.15 to 1.20)	1.17 (1.15 to 1.20)	1.19 (1.09 to 1.30)	1.18 (1.10 to 1.27)
West	1.36 (1.32 to 1.39)	1.36 (1.32 to 1.39)	1.39 (1.26 to 1.54)	1.36 (1.25 to 1.48)

ICH, intracerebral haemorrhage; IS, ischaemic stroke; SAH, subarachnoid haemorrhage.

Rates of poststroke depression diagnosis were higher among women and patients between 35 and 49 years of age, but were consistently decreased among Asian, Black and Hispanic patients. Our findings by gender are consistent with research suggests that poststroke depression is more prevalent among women.<sup>28</sup> These findings are consistent with prior analysis of US Medicare data from 2016 to 2017 in which female patients and white patients were more likely to be diagnosed with depression after stroke.<sup>29</sup> Our results are also generally consistent with trends in diagnosis MDD by gender, age and race/ethnicity observed in the general population.<sup>30</sup> This is despite key clinical differences between MDD and poststroke depression that include increased likelihood of cognitive impairment and decreased likelihood of anhedonia and sleep-wake cycle disturbance in poststroke depression.<sup>31</sup>

We then focused on treatment of poststroke depression. There is evidence to suggest that many patients with poststroke depression go untreated with inequities in treatment across demographic subgroups. In analysis of cross-sectional study data from 2005 to 2011 from the National Ambulatory Medical Care Survey, Bhattacharjee *et al* found that approximately half of stroke patients received no treatment, and that white patients were four times as likely to be treated than patients belonging to racial and ethnic minorities.<sup>5</sup> In a nationally representative sample of patients with stroke from the Medical Expenditure Panel Survey 2004–2017, Dong *et al* found that two-thirds of patients with stroke who screened positive for depression received no outpatient treatment and that older, male, non-Hispanic Black and Hispanic patients were less likely to receive any treatment.<sup>32</sup>

We estimate that approximately 70% of patients with a diagnosis of poststroke depression were treated with any antidepressant. The discrepancy between our findings and theirs may reflect the fact that our analysis includes only individuals with health insurance. We find that prescribing rates increased gradually over the study period. Rates of treatment were highest for IS, perhaps reflecting the risk of intracerebral and intracranial haemorrhage related to SSRI exposure.<sup>33</sup> We further noted that while SSRIs comprised half of prescriptions, the proportion of

SNRI and atypical antidepressants prescribed increased over time. We nevertheless identified potentially inequities in treatment rates across demographic subgroups. Specifically, patients who were male, ages 18–34, and members of racial/ethnic minorities were less likely to be treated.

Taken together, our findings and those of prior studies suggest persistent inequities in treatment of poststroke depression. In this insured population, the presence of inequities suggests persistent barriers to treatment. These may include systematic differences in attitudes, preferences and treatment-seeking propensity, inadequate poststroke follow-up, inconsistencies in depression screening, provider bias or limited access to mental healthcare resources. As many of these barriers are potentially modifiable, future research should aim to identify the predominant mechanisms underlying these differences.

Notably, this study includes several years of follow-up before and after publication in 2011 of the influential FLAME trial.<sup>34</sup> The FLAME trial examined the effects of early prescription of fluoxetine with physiotherapy among patients ages 18–85 with IS and hemiplegia or hemiparesis recruited from nine stroke centres in France. The trial results suggested that the combination of fluoxetine and physiotherapy led to enhanced motor recovery, suggesting an important role for fluoxetine in the management of patients post stroke. We do not observe a clear or sudden increase in rates of SSRI prescribing after 2011. Interestingly, rates of prescribed antidepressants decreased after 2017, perhaps in part reflecting the influence of the subsequent FOCUS and AFFINITY trials, which showed no improvement in functional outcomes associated with fluoxetine after acute stroke,<sup>35 36</sup> and the TALOS trial, which showed no improvement in functional outcomes associated with early citalopram treatment.<sup>37</sup> In the more recent EFFECTS trial, while enrollees treated with fluoxetine showed no improvement in functional outcomes as compared with placebo controls, the proportion of depression was decreased among those treated with fluoxetine. These findings from the EFFECTS trial underscore that while SSRI may not be effective in improving functional outcomes, they nevertheless may be among the most effective tools to mitigate depression following stroke.<sup>38</sup>

## Limitations

Data for this study were derived from commercial and Medicare Advantage claims, and therefore, may not generalise to uninsured and Medicare-eligible individuals who experience stroke. Specific details regarding plan type, deductibles and coinsurance and reimbursement rates may influence rates of diagnosis and treatment over time and across subgroups but were not available in these data. Similarly, our measures of treatment for depression are based on filled prescriptions for antidepressants, which may systematically underestimate prescribing rates and does incorporate information on medication adherence. Our analysis does not specifically address the potential for competing risk due to mortality. Nevertheless, results were consistent across sensitivity analyses with varying duration of follow-up (6 months, 1 year, 5 years), suggesting that lost to follow-up over time does not constitute a substantial source of bias.

It is difficult to accurately identify prior depression in administrative data where follow-up is limited by duration of insurance eligibility. We did not exclude individuals with depression diagnosis prior to first stroke in our main analyses. Annual rates of diagnosis and treatment were higher for individuals with a prior diagnosis of depression. In regression analysis, however, we observed similar trends by gender, race/ethnicity and age among individuals with and without prior depression diagnosis. We aimed to minimise selection bias in our analysis by making no restrictions in eligibility based on duration or continuity of follow-up. These data did not include information on stroke or depression severity, which may be an important determinant of treatment with antidepressants.<sup>39</sup>

Diagnosis of poststroke depression may be complicated by concurrent cognitive symptoms including aphasia, agnosia, apraxia and memory disturbance. Our analysis relies on diagnostic codes from outpatient, inpatient and emergency department encounters to measure depressive disorders following stroke. Our analysis may systematically underestimate the true burden of depressive symptoms in stroke patients as compared with self-report tools. However, our results were robust to several alternative specifications for poststroke depression and remained consistent when we alternatively examined poststroke depression in the 6 months and 5 years following first stroke. Finally, our analysis of treatment rates does not consider therapeutic modalities beyond prescribed antidepressants, although there is evidence that psychotherapy may be beneficial for stroke patients with depression.<sup>40</sup>

## CONCLUSIONS

This retrospective cohort study examines trends in diagnosis and treatment of poststroke depression among privately insured patients from 2003 to 2020. Rates of poststroke depression diagnoses and treatment increased over the study period. Poststroke depression was diagnosed more frequently among women, older and white beneficiaries. In analysis restricted to individuals diagnosed with poststroke depression, differences in treatment persisted. Beneficiaries who were male, ages 18–34, and members of racial/ethnic minorities were less likely to be prescribed an antidepressant. In this insured population, differences in clinical management of poststroke depression across population subgroups may reflect barriers other than access to healthcare. Future research may aim to identify the predominant mechanisms that explain systematic differences in poststroke depression treatment that we and others have observed.

## Author affiliations

- <sup>1</sup>Department of Neurology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA
- <sup>2</sup>Center for Population Health Sciences, Stanford University, Stanford, California, USA
- <sup>3</sup>Department of Neurology, University of California, San Francisco, California, USA
- <sup>4</sup>Epidemiology and Population Health, Stanford University, Stanford, California, USA
- <sup>5</sup>National Institute of Neurological Disorders and Stroke Intramural Research Program, National Institutes of Health, Bethesda, Maryland, USA
- <sup>6</sup>Department of Neurology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA
- <sup>7</sup>Departments of Psychiatry, Neurology and Epidemiology, University of California, San Francisco, California, USA
- <sup>8</sup>Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA

**Twitter** Holly Elser @ElserHolly, Michelle Caunca @michelle\_caunca, David H Rehkopf @drehkopf, Rebecca F Gottesman @gottesman\_lab, Kristine Yaffe @KristineYaffe and Andrea L C Schneider @ASchneiderMDPhD

**Contributors** HE: conceptualised and designed the study, acquired and analysed the data, drafted the manuscript, revised the manuscript critically for important intellectual content, and is accountable for the overall content as guarantor. MC: conceptualised and designed the study, assisted with data interpretation, and revised the manuscript critically for important intellectual content. DR: assisted in data acquisition, assisted with data interpretation, and revised the manuscript critically for important intellectual content. WA: assisted with data interpretation and revised the manuscript critically for important intellectual content. RFG: assisted with data interpretation and revised the manuscript critically for important intellectual content. SK: assisted with data interpretation and revised the manuscript critically for important intellectual content. KY: assisted with data interpretation and revised the manuscript critically for important intellectual content. ALCS: conceptualised and designed the study, assisted with data interpretation and revised the manuscript critically for important intellectual content. All authors provided final approval for the manuscript and have confidence in the integrity of the contributions of their coauthors.

**Funding** Data for this project were accessed using the Stanford Center for Population Health Sciences Data Core. ALCS was supported by the National Institute of Neurological Disorders and Stroke project grant K23NS123340. KY was supported by the National Institute on Aging project grant R35AG071916. RFG was supported by the National Institute of Neurologic Disorders and Stroke Intramural Research Program.

**Disclaimer** The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing interests** None declared.

**Patient consent for publication** Not applicable.

**Ethics approval** This study received approval from the Institutional Review Boards at the University of Pennsylvania (Protocol #849356) and at Stanford University (Protocol #61688). A waiver of consent was granted for this project as it involved deidentified administrative claims data for more than 800 000 individuals.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data may be obtained from a third party and are not publicly available.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

## ORCID iDs

Holly Elser <http://orcid.org/0000-0003-1781-904X>  
Wells Andres <http://orcid.org/0000-0001-6375-7367>

## REFERENCES

- 1 Taylor-Rowan M, Momoh O, Ayerbe L, *et al*. Prevalence of pre-stroke depression and its association with post-stroke depression: a systematic review and meta-analysis. *Psychol Med* 2019;49:685–96.
- 2 Skajaa N, Adelborg K, Horváth-Puhó E, *et al*. Stroke and risk of mental disorders compared with matched general population and myocardial infarction comparators. *Stroke* 2022;53:2287–98.

- 3 Ayerbe L, Ayis S, Wolfe CDA, *et al.* Natural history, predictors and outcomes of depression after stroke: systematic review and meta-analysis. *Br J Psychiatry* 2013;202:14–21.
- 4 Hackett ML, Pickles K. Part I: frequency of depression after stroke: an updated systematic review and meta-analysis of observational studies. *Int J Stroke* 2014;9:1017–25.
- 5 Bhattacharjee S, Axon DR, Goldstone L, *et al.* Patterns and predictors of depression treatment among stroke survivors with depression in ambulatory settings in the United States. *J Stroke Cerebrovasc Dis* 2018;27:563–7.
- 6 Douven E, Köhler S, Rodriguez MMF, *et al.* Imaging markers of post-stroke depression and apathy: a systematic review and meta-analysis. *Neuropsychol Rev* 2017;27:202–19.
- 7 Robinson RG, Jorge RE. Post-Stroke depression: a review. *Am J Psychiatry* 2016;173:221–31.
- 8 Villa RF, Ferrari F, Moretti A. Post-Stroke depression: mechanisms and pharmacological treatment. *Pharmacol Ther* 2018;184:131–44.
- 9 Terroni L, Amaro E, Iosifescu DV, *et al.* Stroke lesion in cortical neural circuits and post-stroke incidence of major depressive episode: a 4-month prospective study. *World J Biol Psychiatry* 2011;12:539–48.
- 10 Sanacora G, Treccani G, Popoli M. Towards a glutamate hypothesis of depression: an emerging frontier of neuropsychopharmacology for mood disorders. *Neuropharmacology* 2012;62:63–77.
- 11 Ferrari F, Villa RF. The neurobiology of depression: an integrated overview from biological theories to clinical evidence. *Mol Neurobiol* 2017;54:4847–65.
- 12 Åström M, Olsson T, Asplund K. Different linkage of depression to hypercortisolism early versus late after stroke. A 3-year longitudinal study. *Stroke* 1993;24:52–7.
- 13 Kohen R, Cain KC, Mitchell PH, *et al.* Association of serotonin transporter gene polymorphisms with poststroke depression. *Arch Gen Psychiatry* 2008;65:1296–302.
- 14 Hackett ML, Anderson CS, Auckland Regional Community Stroke (ARCOS) Study Group. Frequency, management, and predictors of abnormal mood after stroke: the Auckland regional community stroke (ARCOS) study, 2002 to 2003. *Stroke* 2006;37:2123–8.
- 15 Paolucci S, Gandolfo C, Provinciali L, *et al.* The Italian multicenter observational study on post-stroke depression (DESTRO). *J Neurol* 2006;253:556–62.
- 16 Schmid AA, Kroenke K, Hendrie HC, *et al.* Poststroke depression and treatment effects on functional outcomes. *Neurology* 2011;76:1000–5.
- 17 Winstein CJ, Stein J, Arena R, *et al.* Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American stroke association. *Stroke* 2016;47:e98–169.
- 18 Medeiros GC, Roy D, Kontos N, *et al.* Updated review. *Gen Hosp Psychiatry* 2020;2020:70–80.
- 19 Blöchl M, Meissner S, Nestler S. Does depression after stroke negatively influence physical disability? A systematic review and meta-analysis of longitudinal studies. *J Affect Disord* 2019;247:45–56.
- 20 Hilari K, Needle JJ, Harrison KL. What are the important factors in health-related quality of life for people with aphasia? A systematic review. *Arch Phys Med Rehabil* 2012;93:S86–95.
- 21 Mead GE, Hsieh C-F, Lee R, *et al.* Selective serotonin reuptake inhibitors for stroke recovery: a systematic review and meta-analysis. *Stroke* 2013;44:844–50.
- 22 Kokotailo RA, Hill MD. Coding of stroke and stroke risk factors using International classification of diseases, revisions 9 and 10. *Stroke* 2005;36:1776–81.
- 23 McLeod AL. Kendall rank correlation and Mann-Kendall trend test. R package Kendall; 2005.
- 24 Kleinbaum DG, Klein M. *Survival analysis*. Vol 3. Springer, 2010.
- 25 Hackett ML, Yapa C, Parag V, *et al.* Frequency of depression after stroke: a systematic review of observational studies. *Stroke* 2005;36:1330–40.
- 26 De Ryck A, Brouns R, Geurden M, *et al.* Risk factors for poststroke depression: identification of inconsistencies based on a systematic review. *J Geriatr Psychiatry Neurol* 2014;27:147–58.
- 27 Kutlubaev MA, Hackett ML. Part II: predictors of depression after stroke and impact of depression on stroke outcome: an updated systematic review of observational studies. *Int J Stroke* 2014;9:1026–36.
- 28 Poynter B, Shuman M, Diaz-Granados N, *et al.* Sex differences in the prevalence of post-stroke depression: a systematic review. *Psychosomatics* 2009;50:563–9.
- 29 Mayman N, Stein LK, Erdman J, *et al.* Risk and predictors of depression following acute ischemic stroke in the elderly. *Neurology* 2021;96:e2184–91.
- 30 Kessler RC, Berglund P, Demler O, *et al.* The epidemiology of major depressive disorder: results from the National comorbidity survey replication (NCS-R). *JAMA* 2003;289:3095–105.
- 31 Gainotti G, Azzoni A, Marra C. Frequency, phenomenology and anatomical-clinical correlates of major post-stroke depression. *Br J Psychiatry* 1999;175:163–7.
- 32 Dong L, Sánchez BN, Skolarus LE, *et al.* Ethnic differences in prevalence of post-stroke depression. *Circ Cardiovasc Qual Outcomes* 2018;11:e004222.
- 33 Hackam DG, Mirkobrada M. Selective serotonin reuptake inhibitors and brain hemorrhage: a meta-analysis. *Neurology* 2012;79:1862–5.
- 34 Chollet F, Tardy J, Albuher J-F, *et al.* Fluoxetine for motor recovery after acute ischaemic stroke (FLAME): a randomised placebo-controlled trial. *Lancet Neurol* 2011;10:123–30.
- 35 Dennis M, Mead G, Forbes J, *et al.* Effects of fluoxetine on functional outcomes after acute stroke (FOCUS): a pragmatic, double-blind, randomised, controlled trial. *Lancet* 2019;393:265–74.
- 36 Hankey GJ, Hackett ML, Almeida OP, *et al.* Safety and efficacy of fluoxetine on functional outcome after acute stroke (AFFINITY): a randomised, double-blind, placebo-controlled trial. *Lancet Neurol* 2020;19:651–60.
- 37 Kraglund KL, Mortensen JK, Damsbo AG, *et al.* Neuroregeneration and vascular protection by citalopram in acute ischemic stroke (TALOS). *Stroke* 2018;49:2568–76.
- 38 Lundström E, Isaksson E, Näsman P, *et al.* Safety and efficacy of fluoxetine on functional recovery after acute stroke (effects): a randomised, double-blind, placebo-controlled trial. *Lancet Neurol* 2020;19:661–9.
- 39 Mortensen JK, Johnsen SP, Andersen G. Prescription and predictors of post-stroke antidepressant treatment: a population-based study. *Acta Neurol Scand* 2018;138:235–44.
- 40 Hackett ML, Anderson CS, House A, *et al.* Interventions for treating depression after stroke. *Cochrane Database Syst Rev* 2008;241 Suppl 1.