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

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

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

Evidence from several smaller trials suggesting antidepressants, namely selective serotonin reuptake inhibitors (SSRI) and tricyclic antidepressants (TCA), are effective treatments for poststroke depression.[16] 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.[17] Yet recent research documents worrisome inequities in clinical management of poststroke depression,

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

As poststroke depression is associated with impaired functional recovery,[19] poor quality of life[20] and reduced survival,[21] 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).[22]

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 accomodate potential discontinuities in and variable duration of follow-up. We assessed time trends using the Mann-Kendall test.[23] 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 Schoenfield residuals.[24]

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
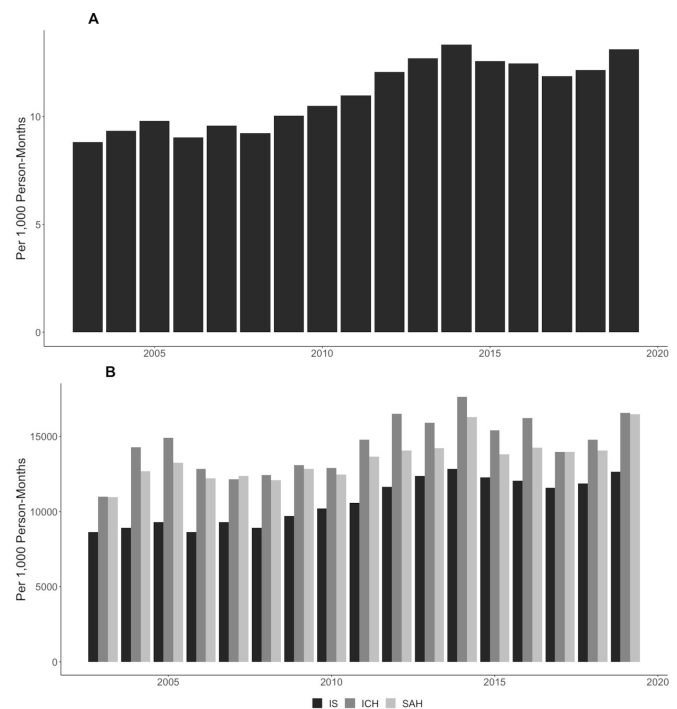

Figure 1 Depression diagnoses within 1 year of first stroke for all stroke (Panel A) and by subtype (Panel B), 2003–2020. ICH, intracerebral haemorrhage; IS, ischaemic stroke; SAH, subarachnoid haemorrhage.

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).

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%,[3 4 25] 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.[26 27]
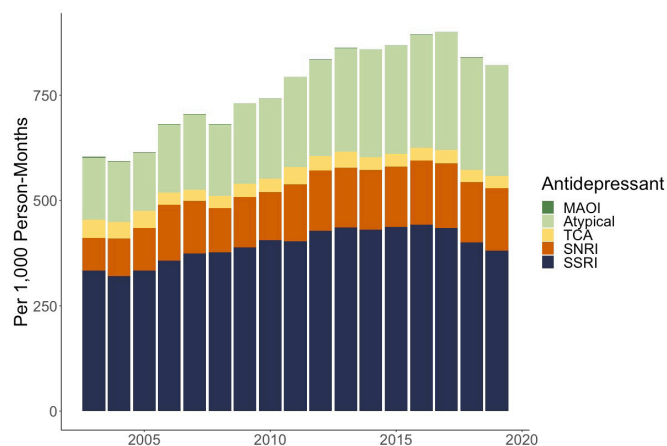

Figure 2 Prescribed antidepressants by drug class among individuals poststroke depression, 2003–2020. MAOI, monoamine oxidase inhibitor; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

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.[28] 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.[29] Our results are also generally consistent with trends in diagnosis MDD by gender, age and race/ethnicity observed in the general population.[30] 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.[31]

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.[5] 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.[32]

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.[33] 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.[34] 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,[35 36] and the TALOS trial, which showed no improvement in functional outcomes associated with early citalopram treatment.[37] 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.[38]

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.[39]

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.[40]

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.

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Supplemental Table 1. Diagnostic codes from the International Classification of Diseases for Stroke*

Stroke Type	Revision	Code	Definition
Ischemic stroke (IS)	ICD-9	362.3	Retinal vascular occlusion
	ICD-9	433.x1	Occlusion and stenosis of precerebral arteries
	ICD-9	434.x1	Occlusion of cerebral arteries
	ICD-9	436	Acute, but ill-defined, cerebrovascular disease
	ICD-10	H34.1	Central retinal artery occlusion
	ICD-10	I63.x	Cerebral infarction
	ICD-10	I64.x	Stroke, not specified as hemorrhage or infarction
Intracerebral hemorrhage (ICH)	ICD-9	431.x	Intracerebral hemorrhage
	ICD-10	I61.x	Intracerebral hemorrhage
Subarachnoid hemorrhage (SAH)	ICD-9	430.x	Subarachnoid hemorrhage
	ICD-10	I60.x	Subarachnoid hemorrhage

* Stroke classification derived from Kokotailo and Hill (2005)

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Supplemental Table 2. Diagnostic codes from the International Classification of Diseases used to identify depressive disorders

Outcome Version	Revision	Code	Definition
Major Depression[1]	ICD-9	296.2x	Major depressive disorder, single episode
	ICD-9	296.3x	Major depressive disorder, recurrent episode
	ICD-10	F32.x	Major depressive disorder, single episode
	ICD-10	F33.x	Major depressive disorder, recurrent episode
Depressive Disorders	ICD-9	293.83	Mood disorder in conditions classified elsewhere
	ICD-9	293.9	Unspecified transient mental disorder in conditions classified elsewhere
	ICD-9	296.90	Unspecified episodic mood disorder
	ICD-9	296.99	Other specified episodic mood disorder
	ICD-9	300.4	Dysthymic disorder
	ICD-9	301.10	Affective personality disorder
	ICD-9	301.12	Chronic depressive personality disorder
	ICD-9	301.13	Cyclothymic disorder
	ICD-9	309.0	Adjustment reaction with depressed mood
	ICD-9	309.1	Prolonged depressive reaction
	ICD-9	309.28	Adjustment disorder with mixed anxiety and depressed mood
	ICD-9	311	Depressive disorder, not elsewhere classified
	ICD-9	316	Psychic factors associated with diseases classified elsewhere
	ICD-10	F05.30	Mood disorder due to known physiological condition, unspecified
	ICD-10	F06	Other mental disorders due to known physiological condition
	ICD-10	F06.8	Other specified mental disorders due to known physiological condition
	ICD-10	F34.x	Persistent mood disorders
	ICD-10	F39	Unspecified mood disorders
	ICD-10	F43.21	Adjustment disorder with depressed mood
	ICD-10	F43.23	Adjustment disorder with mixed anxiety and depressed mood
	ICD-10	F54	Psychological and behavioral factors associated with disorders or diseases elsewhere classified

1. Excluding major depressive disorder, single episode in full remission (296.26, F32.5); major depressive disorder, recurrent episode in full remission (296.36, F33.4) and premenstrual dysphoric disorder (F32.81)

Supplemental Table 3. Antidepressants by drug class

Selective Serotonin Reuptake Inhibitors (SSRI)	Citalopram
	Escitalopram
	Fluoxetine
	Fluvoxamine
	Fluvoxamine CR
	Paroxetine
	Paroxetine CR
	Sertraline
Serotonin and Norepinephrine Reuptake Inhibitors (SNRI)	Desvenlafaxine
	Duloxetine
	Levomilnacipran
	Milnacipran
	Venlafaxine
	Venlafaxine XR
Tricyclic Antidepressants (TCA)	Amitriptyline
	Amoxapine
	Clomipramine
	Desipramine
	Doxepine
	Imipramine
	Maprotiline
	Nortriptyline
	Protriptyline
	Trimipramine
Monoamine Oxidase Inhibitors (MAOI)	Phenelzine
	Selegiline
	Tranylcyrpomine
Atypical Antidepressants	Buproprion
	Mirtazapine
	Nefazodone
	Trazodone
	Vilazodone
	Vortioxetine

Supplemental Table 4. Crude rates of depression diagnosis following first stroke, 2003 - 2020

	All Stroke		IS		ICH		SAH	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	2256 / 255663	8.8 (8.5,9.2)	2049 / 236807	8.7 (8.3,9.0)	120 / 10915	11.0 (9.1,13.1)	87 / 7942	11.0 (8.8,13.5)
2004	1644 / 176201	9.3 (8.9,9.8)	1437 / 161008	8.9 (8.5,9.4)	126 / 8816	14.3 (11.9,17.0)	81 / 6377	12.7 (10.1,15.8)
2005	1725 / 176073	9.8 (9.3, 10.3)	1482 / 159070	9.3 (8.9,9.8)	157 / 10518	14.9 (12.7,17.4)	86 / 6486	13.3 (10.6,16.4)
2006	2148 / 237485	9.0 (8.7, 9.4)	1856 / 214320	8.7 (8.3,9.1)	184 / 14336	12.8 (11.1,14.8)	108 / 8829	12.2 (10.0,14.7)
2007	2902 / 302565	9.6 (9.3,9.9)	2529 / 272090	9.3 (8.9,9.7)	223 / 18351	12.2 (10.6,13.8)	150 / 1225	12.4 (10.5,14.5)
2008	3729 / 403719	9.2 (8.9,9.5)	3265 / 366012	8.9 (8.6,9.2)	294 / 23646	12.4 (11.1,13.9)	170 / 14061	12.1 (10.3,14.0)
2009	4102 / 408268	10.1 (9.7,10.4)	3578 / 367966	9.7 (9.4,10.0)	326 / 24907	13.1 (11.7,14.6)	198 / 15396	12.9 (11.1,14.8)
2010	4301 / 409894	10.5 (10.2,10.8)	3750 / 366659	10.2 (9.9,10.6)	345 / 26733	12.9 (11.6,14.3)	206 / 16501	12.5 (10.8,14.3)
2011	4477 / 407437	11.0 (10.7,11.3)	3863 / 364630	10.6 (10.3,10.9)	388 / 26253	14.8 (13.4,16.3)	226 / 16551	13.7 (11.9,15.5)
2012	5132 / 425114	12.1 (11.8,12.4)	4404 / 378242	11.6 (11.3,12.0)	465 / 28168	16.5 (15.1,18.1)	263 / 18704	14.1 (12.4,15.9)
2013	5662 / 446016	12.7 (12.34,13.0)	4902 / 396134	12.4 (12.0,12.7)	477 / 29989	15.9 (14.5,17.4)	283 / 19892	14.2 (12.6,16.0)
2014	5655 / 424022	13.3 (13.0, 13.7)	4821 / 375263	12.8 (12.5,13.2)	513 / 29061	17.7 (16.2,19.2)	321 / 1697	16.3 (14.6,18.2)
2015	6136 / 487684	12.6 (12.3,12.9)	5290 / 430353	12.3 (11.2,12.6)	516 / 33443	15.4 (14.1,16.8)	330 / 23887	13.8 (12.4,15.4)
2016	6226 / 499842	12.5 (12.2,12.8)	5281 / 438356	12.0 (11.7,12.4)	562 / 34607	16.2 (14.9,17.6)	383 / 26879	14.2 (12.9,15.7)
2017	7654 / 644794	11.9 (11.6,12.1)	6637 / 572049	11.6 (11.3,11.9)	599 / 42834	14.0 (12.9,15.1)	418 / 29911	14.0 (12.7,15.4)
2018	8730 / 717936	12.2 (11.9,12.4)	7554 / 636720	11.9 (11.6,12.1)	696 / 47061	14.8 (13.7,15.9)	480 / 34156	14.1 (12.8,15.4)
2019	8224 / 627058	13.1 (12.8,13.4)	7035 / 555163	12.7 (12.4,13.0)	674 / 40624	16.6 (15.4,17.9)	515 / 31270	16.5 (15.1,17.9)
2020	1685 / 89184	18.9 (18.0,19.8)	1429 / 77854	18.4 (17.4,19.3)	138 / 6366	21.7 (18.2,25.6)	118 / 4964	23.8 (19.7,28.4)
Total	82388 / 7138953	11.5 (11.4,11.6)	71162 / 6368698	11.2 (11.1,11.3)	6803 / 456630	14.9 (14.5,15.2)	4423 / 313625	14.1 (13.7,14.5)

Supplemental Table 5. Crude rates of depression diagnosis following first stroke by gender, 2003 - 2020

	Women		Men	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	1349 / 129849	10.4 (9.8, 11.0)	907 / 125814	7.2 (6.7, 7.7)
2004	1012 / 90599	11.2 (10.5, 11.9)	632 / 85602	7.4 (6.8, 8.0)
2005	1038 / 88650	11.7 (11.0, 12.4)	687 / 87423	7.9 (7.3, 8.5)
2006	1325 / 124516	10.6 (10.1, 11.2)	823 / 112970	7.9 (7.3, 8.5)
2007	1830 / 162418	11.3 (10.8, 11.8)	1072 / 140148	7.3 (6.8, 7.8)
2008	2337 / 215787	10.8 (10.4, 11.3)	1392 / 187931	7.6 (7.2, 8.1)
2009	2589 / 218263	11.9 (11.4, 12.3)	1513 / 190005	7.4 (7.0, 7.8)
2010	2677 / 213551	12.5 (12.1, 13.0)	1624 / 196344	8.0 (7.6, 8.4)
2011	2793 / 213786	13.1 (12.6, 13.6)	1684 / 193648	8.3 (7.9, 8.7)
2012	3205 / 223247	14.4 (13.8, 14.8)	1927 / 201867	8.7 (8.3, 9.1)
2013	3500 / 230190	15.3 (14.7, 15.7)	2162 / 215826	9.5 (9.1, 10.0)
2014	3498 / 218571	16.0 (15.5, 16.5)	2157 / 205451	10.0 (9.6, 10.4)
2015	3841 / 257035	14.9 (14.5, 15.4)	2295 / 230650	10.5 (10.1, 10.9)
2016	3913 / 264212	14.8 (14.4, 15.3)	2313 / 235630	10.0 (9.5, 10.4)
2017	4802 / 341210	14.1 (13.7, 14.5)	2852 / 303584	9.8 (9.4, 10.2)
2018	5450 / 383489	14.2 (13.8, 15.6)	3280 / 334447	9.4 (9.1, 9.7)
2019	5266 / 335310	15.7 (15.3, 16.1)	2958 / 291748	9.8 (9.5, 10.1)
2020	1075 / 47404	22.7 (21.4, 24.1)	610 / 41780	14.6 (13.5, 15.8)
Total	51500 / 3758087	13.7 (13.4, 13.8)	30888 / 3380867	9.1 (9.0, 9.2)

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Supplemental Table 6. Crude rates of depression diagnosis following first stroke by age category, 2003 - 2020

	18 – 34 Years		35 – 49 Years		50 – 64 Years		65 and Older	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	100 / 7937	12.6 (10.3,15.3)	383 / 29450	13.0 (11.7,14.4)	758 / 73198	10.3 (9.6,11.1)	1015 / 145079	7.0 (6.6,7.4)
2004	88 / 7190	12.2 (9.8,15.1)	318 / 24618	12.9 (11.5,14.4)	536 / 53905	9.9 (9.1,10.8)	702 / 90489	7.8 (7.2,8.4)
2005	81 / 7159	11.3 (9.0,14.0)	342 / 25403	13.5 (12.1,15.0)	615 / 56230	10.9 (10.1,11.8)	687 / 87281	7.9 (7.3,8.5)
2006	100 / 8398	11.9 (9.7,14.5)	393 / 30372	12.9 (11.7,14.3)	724 / 67518	10.7 (10.0,11.5)	931 / 131198	7.1 (6.6,7.6)
2007	117 / 9749	12.0 (9.9,14.4)	472 / 31417	15.0 (13.7,16.4)	838 / 76053	11.0 (10.3,11.8)	1475 / 185346	8.0 (7.6, 8.4)
2008	101 / 9537	10.6 (8.6,12.9)	467 / 34110	13.7 (12.5,15.0)	975 / 86138	11.3 (10.6,12.0)	2186 / 373933	8.0 (7.6, 8.3)
2009	136 / 10201	13.3 (11.2,15.6)	449 / 33289	13.5 (12.3,14.8)	1058 / 85250	12.4 (11.7,13.2)	2459 / 279528	8.8 (8.5,9.2)
2010	124 / 9892	12.5 (10.4,14.9)	471 / 33035	14.3 (13.0,15.6)	1135 / 86780	13.1 (12.3,13.9)	2571 / 280187	9.2 (8.8,9.5)
2011	125 / 10046	12.4 (10.4,14.8)	453 / 30644	14.8 (13.5,16.2)	1149 / 88900	12.9 (12.2,13.7)	2750 / 277845	9.9 (9.5,10.3)
2012	152 / 10567	14.4 (12.2,16.8)	527 / 31446	16.8 (15.4,18.2)	1366 / 92259	14.8 (14.0,15.6)	3087 / 290841	10.6 (10.2,11.0)
2013	139 / 10134	13.7 (11.5,16.2)	451 / 30151	15.0 (13.6,16.4)	1362 / 87972	15.5 (14.7,16.3)	3710 / 317758	11.7 (11.3,12.1)
2014	134 / 9540	14.0 (11.8,16.6)	439 / 28119	15.6 (14.2,17.1)	1339 / 84572	15.8 (15.0,16.7)	3743 / 301791	12.4 (12.0,12.8)
2015	140 / 10608	13.2 (11.1,15.6)	476 / 30195	15.8 (14.4,17.2)	1254 / 90657	13.8 (13.1,14.6)	4266 / 356224	12.0 (11.6,12.3)
2016	121 / 8834	13.7 (11.4,16.3)	464 / 30546	15.2 (13.8,16.6)	1397 / 92104	15.2 (14.4,16.0)	4244 / 368358	11.5 (11.1,11.9)
2017	165 / 9752	16.9 (14.5,19.7)	482 / 33549	14.4 (13.1,15.7)	1635 / 113643	14.4 (13.7,15.1)	5372 / 487850	11.0 (10.7,11.3)
2018	168 / 10434	16.1 (13.8,18.7)	505 / 36457	13.9 (12.7,15.1)	1663 / 116860	14.2 (13.6,14.9)	6394 / 554186	11.5 (11.3,11.8)
2019	147 / 8485	17.3 (14.7,20.3)	464 / 29471	15.7 (14.3,17.2)	1464 / 99370	14.7 (14.0,15.5)	6149 / 489732	12.6 (12.2,12.9)
2020	20 / 1141	17.5 (10.7,26.9)	89 / 3891	22.9 (18.4,28.1)	277 / 14064	19.7 (17.5,22.1)	1299 / 70089	18.5 (17.5,19.6)
Total	2158 / 159603	13.5 (13.0,14.1)	7645 / 526163	14.5 (14.2,14.9)	19545 / 1464573	13.3 (13.2,13.5)	53040 / 4987715	10.6 (10.5,10.7)

Supplemental Table 7. Crude rates of depression diagnosis following first stroke by race and ethnicity, 2003 - 2020

	Asian		Black		Hispanic		White	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	35 / 3784	9.2 (6.5,12.8)	245 / 35794	6.8 (6.0,7.8)	103 / 14810	7.0 (5.7,8.4)	1873 / 201275	9.3 (8.9,9.7)
2004	17 / 3248	5.2 (3.1,8.4)	154 / 22404	6.9 (5.8,8.0)	101 / 11354	8.9 (7.3,10.8)	1372 / 139196	9.9 (9.3,10.4)
2005	20 / 3247	6.2 (3.8,9.5)	163 / 23360	7.0 (6.0,8.1)	97 / 11704	8.3 (6.7,10.1)	1445 / 137763	10.5 (10.0,11.0)
2006	26 / 5104	5.1 (3.3,7.4)	194 / 32725	5.9 (5.1,6.8)	133 / 17733	7.5 (6.3,8.9)	1795 / 181923	9.9 (9.4,10.3)
2007	57 / 7524	7.6 (5.7,9.8)	295 / 39009	7.6 (6.7,8.5)	218 / 27526	7.9 (6.9,9.0)	2332 / 228506	10.3 (9.8,10.6)
2008	68 / 11721	5.8 (4.5,7.3)	417 / 52716	7.9 (7.2,8.7)	293 / 44427	6.6 (5.8,7.4)	2951 / 294856	10.0 (9.7,10.4)
2009	74 / 12189	6.1 (4.8,7.6)	464 / 54855	8.5 (7.7,9.3)	408 / 46785	8.7 (7.9,9.6)	3156 / 294440	10.7 (10.3,11.1)
2010	82 / 11576	7.1 (5.7,8.9)	503 / 54851	9.2 (8.4,10.0)	392 / 44098	8.9 (8.0,9.8)	3324 / 299469	11.1 (10.7,11.5)
2011	77 / 12322	6.2 (4.9,7.8)	526 / 55561	9.5 (8.7,10.3)	421 / 40030	10.5 (9.5,11.6)	3453 / 299522	11.5 (11.1,11.9)
2012	78 / 12822	6.1 (4.8,7.6)	615 / 59585	10.3 (9.5,11.2)	430 / 41407	10.4 (9.5,11.4)	4009 / 311300	12.9 (12.5,13.3)
2013	120 / 16180	7.4 (6.2,8.9)	673 / 61705	10.9 (10.1,11.8)	565 / 46350	12.2 (11.2,13.2)	4304 / 321781	13.4 (13.0,13.8)
2014	124 / 15362	8.1 (6.7,9.6)	657 / 55242	11.9 (11.0,12.8)	590 / 48828	12.1 (11.1,13.1)	4284 / 304590	14.1 (13.6,14.5)
2015	163 / 17755	9.2 (7.8,10.7)	724 / 65221	11.1 (10.3,11.9)	655 / 54970	11.9 (11.0,12.9)	4594 / 349738	13.1 (12.8,13.5)
2016	153 / 17292	8.8 (7.5,10.4)	707 / 67787	10.4 (9.7,11.2)	647 / 56066	11.5 (10.7,12.5)	4719 / 358697	13.2 (12.8,13.5)
2017	147 /20726	7.1 (6.0,8.3)	1100 / 104640	10.5 (9.9,11.1)	895 / 81161	11.0 (10.3,11.7)	5512 / 438267	12.6 (12.2,12.9)
2018	194 / 24009	8.1 (7.0,9.3)	1141 / 112470	10.1 (9.6,10.7)	1020 / 90564	11.2 (10.6,12.0)	6375 / 490894	13.0 (12.7,13.3)
2019	166 / 21186	7.8 (6.7,9.1)	1122 / 96388	10.1 (9.6,10.7)	895 / 76002	11.8 (11.0,12.6)	6041 / 433482	13.9 (13.6,14.3)
2020	37 / 2868	12.9 (9.1,17.7)	225 / 13705	16.4 (14.4,18.7)	168 / 10244	16.4 (14.0,19.1)	1255 / 62368	20.1 (19.0,21.3)
Total	1638 / 218815	7.5 (7.1,7.9)	9925 / 1008107	9.8 (9.7,10.0)	8031 / 764054	10.5 (10.3,10.7)	62794 / 5148067	12.2 (12.1,12.3)

Supplemental Table 8. Crude rates of depression diagnosis following first stroke by U.S. Census Region, 2003 - 2020

	Midwest		Northeast		South		West	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	1056 / 102223	10.3 (9.7,11.0	282 / 27233	10.4 (9.2,11.6)	775 / 110442	7.0 (6.5,7.5)	143 / 15765	9.1 (7.7,10.7)
2004	704 / 65424	10.8 (10.0,11.6)	204 / 19686	10.4 (9.0,11.9)	631 / 78639	8.0 (7.4,8.7)	105 / 12452	8.4 (6.9,10.2)
2005	714 / 61940	11.5 (10.7,12.4)	199 / 19641	10.1 (8.8,11.6)	677 / 79654	8.5 (7.9,9.2)	135 / 14838	9.1 (7.7,10.7)
2006	743 / 65823	11.7 (10.9,12.5)	217 / 19683	11.0 (9.6,12.6)	887 / 104508	8.5 (7.9,9.1)	301 / 49164	6.1 (5.5,6.9)
2007	769 / 65823	11.7 (10.9,12.5)	422 / 26389	16.0 (14.5,17.6)	1199 / 127090	9.4 (8.9,10.0)	512 / 83263	6.1 (5.6,6.7)
2008	812 / 65484	12.4 (11.6,13.3)	474 / 29659	16.0 (14.9,17.5)	1368 / 157396	8.7 (8.2,9.2)	1075 / 151180	7.1 (6.6,7.4)
2009	930 / 67091	13.9 (13.0,14.8)	503 / 31115	16.1 (14.8,17.6)	1473 / 160345	9.2 (8.7,9.7)	1196 / 149716	8.0 (7.5,8.5)
2010	1009 / 78524	12.9 (12.1,13.7)	482 / 30337	15.9 (14.5,17.4)	1691 / 167186	10.1 (9.6,10.6)	1119 / 133848	8.4 (7.9,8.9)
2011	1114 / 86472	12.9 (12.1,13.7)	510 / 31087	16.5 (15.0,17.9)	1755 / 170825	10.3 (9.8,10.8)	1098 / 119051	9.2 (8.7,9.8)
2012	1307 / 92575	14.1 (13.4,14.9)	693 / 42235	16.4 (15.2,17.7)	2078 / 177938	11.7 (11.2,12.2)	1054 / 112365	9.4 (8.8,10.0)
2013	1330 / 97754	13.6 (12.9,14.4)	1049 / 66079	15.9 (14.9,16.9)	2146 / 169960	12.6 (12.9,14.0)	1137 / 112222	10.1 (9.6,10.7)
2014	1357 / 94967	14.3 (13.5,15.1)	1063 / 63477	16.7 (15.8,17.8)	2090 / 156143	13.4 (12.8,14.0)	1145 / 109435	10.4 (9.9,11.1)
2015	1414 / 113882	12.4 (11.8,13.1)	1135 / 67252	16.9 (15.9, 17.9)	2405 / 193371	12.4 (11.9,12.9)	1182 / 113180	10.4 (9.9,11.1)
2016	1525 / 116219	13.1 (12.5,13.8)	1020 / 67252	15.3 (14.4,16.3)	2542 / 203472	12.5 (12.0,13.0)	1139 / 113449	10.0 (9.5,10.6)
2017	1739 / 135634	12.8 (12.2,13.4)	1081 / 74730	14.5 (13.6,15.3)	3538 / 297014	11.9 (11.5,12.3)	1396 / 137416	9.4 (8.9,10.0)
2018	1893 / 142196	13.3 (12.7,13.9)	1507 / 90259	15.7 (15.9,17.6)	3956 / 338861	11.7 (14.2,15.0)	1374 / 146620	9.4 (8.8,9.9)
2019	1736 / 124793	13.9 (13.3,14.6)	1445 / 83439	17.3 (16.4,18.2)	3808 / 291148	13.1 (12.7,13.5)	1235 / 127679	9.7 (9.1,10.2)
2020	385 / 18363	21.0 (18.9,23.1)	297 / 11504	25.8 (23.0,28.9)	764 / 41612	18.4 (17.1,20.0)	239 / 17706	13.5 (11.9,15.3)
Total	20537 / 1593493	12.9 (12.7,13.1)	12583 / 800508	15.7 (15.4,16.0)	33783 / 3025603	11.1 (11.0,11.3)	15485 / 1719350	9.0 (8.9,9.1)

Supplemental Table 9. Crude rates of depression diagnosis among individuals with and without a diagnosis of depression in the year prior to first stroke, 2003–2020

	Prior Depression Dx		No Prior Depression Dx	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	740 / 10488	70.55 (65.73 – 75.63)	1516 / 245175	6.18 (6.88 – 6.50)
2004	760 / 17587	43.21 (40.26 – 46.32)	884 / 158614	5.57 (5.21 – 5.95)
2005	828 / 20150	41.09 (38.39 – 43.92)	897 / 155923	5.75 (5.38 – 6.14)
2006	1052 / 28795	36.53 (34.40 – 38.77)	1096 / 208690	5.25 (4.95 – 5.57)
2007	1561 / 40580	38.47 (36.62 – 40.38)	1341 / 261985	5.12 (4.85 – 5.40)
2008	1879 / 50629	37.11 (35.48 – 38.80)	1850 / 353090	5.24 (5.00 – 5.48)
2009	2219 / 61794	35.91 (34.46 – 37.41)	1883 / 346474	5.44 (4.19 – 5.69)
2010	2436 / 68766	35.42 (34.06 – 36.83)	1865 / 341128	5.47 (5.22 – 5.72)
2011	2582 / 71920	35.90 (34.55 – 37.29)	1895 / 335515	5.65 (5.40 – 5.91)
2012	2976 / 82069	36.26 (34.99 – 37.56)	2156 / 343045	6.29 (6.02 – 6.56)
2013	3335 / 87018	38.33 (37.06 – 39.62)	2327 / 358998	6.48 (6.22 – 6.75)
2014	3392 / 87825	38.62 (37.36 – 39.92)	2263 / 336196	6.73 (6.46 – 7.01)
2015	3651 / 101814	35.86 (34.73 – 37.02)	2485 / 385870	6.44 (6.19 – 6.70)
2016	3666 / 104795	34.98 (33.88 – 36.11)	2560 / 395047	6.48 (6.23 – 6.74)
2017	4450 / 129806	34.28 (33.30 – 35.29)	3204 / 514988	6.22 (6.01 – 6.44)
2018	5176 / 147124	35.18 (34.25 – 36.14)	3554 / 570812	6.23 (6.02 – 6.43)
2019	5019 / 136279	36.83 (35.84 -37.84)	3205 / 490778	6.53 (6.31 – 6.76)
2020	1065 / 21095	50.49 (47.57 – 53.53)	620 / 68090	9.11 (8.41 – 9.85)
Total	46787 / 1268535	36.88 (36.56 – 37.21)	35601 / 5870419	6.06 (6.00 – 6.13)

Supplemental Table 10. Hazard ratios (HR) for demographic characteristics and post-stroke depression among individuals with and without a diagnosis of depression in the year prior to first stroke

	Prior Depression Dx HR (95% CI)	**No Prior Depression Dx** HR (95% CI)
Sex		
Male	1 (Ref)	1 (Ref)
Female	1.12 (1.10 – 1.14)	1.29 (1.27 – 1.32)
Age Group		
18 to 34	1 (Ref)	1 (Ref)
35 to 49	1.00 (0.94 – 1.07)	1.05 (0.98 – 1.13)
50 to 64	0.96 (0.90 – 1.01)	0.91 (0.86 – 0.97)
65 and older	0.79 (0.74 – 0.83)	0.80 (0.75 – 0.85)
Race and Ethnicity		
White	1 (Ref)	1 (Ref)
Asian	0.95 (0.89 – 1.02)	0.68 (0.63 – 0.73)
Black	0.91 (0.89 – 0.94)	0.70 (0.78 – 0.83)
Hispanic	0.93 (0.90 – 0.96)	0.90 (0.87 – 0.94)
Region		
Midwest	1 (Ref)	1 (Ref)
Northeast	1.33 (1.29 – 1.37)	1.17 (1.13 – 1.21)
South	0.92 (0.90 – 0.94)	0.85 (0.83 – 0.88)
West	0.77 (0.75 – 0.80)	0.69 (0.67 – 0.71)

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Supplemental Table 11. Hazard ratios (HR) for demographic characteristics and post-stroke depression with alternative follow-up duration

	Six Months HR (95% CI)	One Year HR (95% CI)	Five Years HR (95% CI)
Sex			
Male	1 (Ref)	1 (Ref)	1 (Ref)
Female	1.51 (1.49 – 1.54)	1.53 (1.51 – 1.55)	1.56 (1.55 – 1.58)
Age Group			
18 to 34	1 (Ref)	1 (Ref)	1 (Ref)
35 to 49	1.08 (1.02 – 1.14)	1.10 (1.04 – 1.15)	1.09 (1.05 – 1.14)
50 to 64	0.98 (0.94 – 1.04)	1.01 (0.96 – 1.05)	1.02 (0.99 – 1.06)
65 and older	0.73 (0.69 – 0.76)	0.75 (0.72 – 0.79)	0.80 (0.78 – 0.83)
Race and Ethnicity			
White	1 (Ref)	1 (Ref)	1 (Ref)
Asian	0.64 (0.61 – 0.68)	0.63 (0.60 – 0.66)	0.60 (0.57 – 0.62)
Black	0.76 (0.74 – 0.77)	0.76 (0.74 – 0.78)	0.77 (0.75 – 0.78)
Hispanic	0.86 (0.84 – 0.88)	0.88 (0.86 – 0.90)	0.89 (0.88 – 0.91)
Region			
Midwest	1 (Ref)	1 (Ref)	1 (Ref)
Northeast	1.27 (1.24 – 1.31)	1.22 (1.19 – 1.25)	1.16 (1.14 – 1.18)
South	0.86 (0.84 – 0.88)	0.87 (0.86 – 0.89)	0.90 (0.89 – 0.91)
West	0.70 (0.68 – 0.72)	0.73 (0.71 – 0.74)	0.77 (0.76 – 0.78)

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Supplemental Table 12. Hazard ratios (HR) using alternative outcome definitions for post-stroke depression [1]

	Main Outcome Definition HR (95% CI)	Alternative 1 HR (95% CI)	Alternative 2 HR (95% CI)	Alternative 3 HR (95% CI)
Sex				
Male	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Female	1.53 (1.51 – 1.55)	1.60 (1.58- 1.63)	1.63 (1.60 – 1.66)	1.52 (1.50 – 1.54)
Age Group				
18 to 34	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
35 to 49	1.10 (1.04 – 1.15)	1.15 (1.09 – 1.22)	1.10 (1.03 – 1.17)	1.14 (1.09 – 1.18)
50 to 64	1.01 (0.96 – 1.05)	1.17 (1.11 – 1.23)	1.08 (1.02 – 1.15)	1.07 (1.04 – 1.11)
65 and older	0.75 (0.72 – 0.79)	0.88 (0.84 – 0.92)	0.74 (0.71 – 0.80)	0.84 (0.81 – 0.87)
Race and Ethnicity				
White	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Asian	0.63 (0.60 – 0.66)	0.63 (0.60 – 0.67)	0.60 (0.56 – 0.64)	0.64 (0.62 – 0.67)
Black	0.76 (0.74 – 0.78)	0.76 (0.74 – 0.77)	0.75 (0.73 – 0.78)	0.77 (0.76 – 0.78)
Hispanic	0.88 (0.86 – 0.90)	0.99 (0.97 – 1.01)	0.93 (0.90 – 0.96)	0.84 (0.81 – 0.87)
Region				
Midwest	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Northeast	1.22 (1.19 – 1.25)	1.09 (1.05 – 1.11)	1.18 (1.14 – 1.22)	1.13 (1.05 – 1.15)
South	0.87 (0.86 – 0.89)	0.98 (0.96 – 0.99)	0.97 (0.95 – 0.99)	0.88 (0.87 – 0.89)
West	0.73 (0.71 – 0.74)	0.94 (0.92 – 0.96)	0.85 (0.83 – 0.88)	0.79 (0.77 – 0.80)

1. **Alternative 1:** First diagnosis of major depressive disorder in 365 days; **Alternative 2:** Second diagnosis of major depressive disorder in 365 days; **Alternative 3:** First depression-related diagnosis in 365 days; **Main Outcome Definition:** Second depression-related diagnosis in 365 days.

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Supplemental Table 13. Prescribed antidepressants among individuals with post-stroke depression overall and by stroke type, 2003 – 2020

	All Stroke		IS		ICH		SAH	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	13223 / 21901	603.8 (597.2, 610.2)	11971 / 19832	603.6 (596.8,610.4)	703 / 1210	581.0 (552.6,609.0)	550 / 859	640.3 (607.2,672.4)
2004	9387 / 15810	593.8 (586.0, 601.4)	8215 / 13783	596.0 (587.8,604.2)	738 / 1248	591.3 (563.5,618.8)	434 / 779	557.1 (521.4,592.4)
2005	10049 / 16361	614.2 (606.7, 621.7)	8708 / 14026	620.8 (612.8,628.9)	923 / 1546	597.0 (572.1,621.6)	418 / 790	529.1 (493.6,564.4)
2006	14076 / 20664	681.2 (674.8, 687.5)	12269 / 17938	684.0 (677.1,690.8)	1109 / 1711	648.2 (625.0,670.8)	698 / 1015	687.7 (658.2,716.1)
2007	19932 / 28266	705.2 (699.8, 710.5)	17622 / 24615	715.9 (710.2,721.5)	1285 / 2121	605.8 (584.7,626.7)	1025 / 1530	667.0 (645.7,693.5)
2008	25000 / 36713	681.0 (676.1, 685.7)	21951 / 32187	681.2 (676.8,687.1)	1985 / 2858	694.5 (677.3,711.4)	1065 / 1669	638.1 (614.5,661.2)
2009	29212 / 39984	730.6 (726.2, 734.9)	25778 / 34861	739.5 (734.8,744.1)	2051 / 3072	667.6 (650.7,684.3)	1383 / 2052	674.0 (653.2,694.2)
2010	30949 / 41703	742.1 (737.9, 746.3)	27303 / 36421	749.6 (745.2,754.1)	2182 / 3262	668.9 (652.5,685.1)	1464 / 2020	724.8 (704.7,744.1)
2011	34825 / 43911	793.1 (789.3, 796.9)	30591 / 38119	802.5 (798.5,806.5)	2662 / 3673	724.7 (710.0,739.1)	1571 / 2119	741.4 (722.2,760.0)
2012	42246 / 50578	835.3 (832.0, 838.5)	36469 / 43451	839.3 (835.8,842.8)	3671 / 4529	810.6 (798.8,821.9)	2106 / 2598	810.6 (795.0,825.5)
2013	45857 / 53156	862.7 (859.7, 865.6)	40185 / 46011	873.4 (870.3,876.4)	3496 / 4443	786.9 (774.5,798.8)	2176 / 2702	805.0 (789.5,819.7)
2014	45936 / 54663	858.6 (855.7, 861.6)	40934 / 46763	875.4 (872.3,878.3)	3475 / 4750	731.6 (718.7,744.1)	2526 / 3150	801.9 (787.6,815.7)
2015	52406 / 60366	868.1 (865.4, 870.8)	45923 / 52190	880.0 (877.1,882.7)	3681 / 4865	756.6 (744.3,768.6)	2802 / 3312	846.0 (833.3,858.1)
2016	54055 / 60477	893.8 (891.3, 896.3)	46614 / 51598	903.4 (900.8,905.9)	4347 / 5181	839.0 (828.7,848.9)	3094 / 3699	836.4 (824.1,848.2)
2017	67502 / 74981	900.3 (898.1, 902.4)	59549 / 65377	910.9 (908.6,913.0)	4672 / 5578	837.6 (827.6,847.2)	3281 / 4026	815.0 (802.6,826.8)
2018	71880 / 85522	840.5 (838.0, 842.9)	62934 / 74032	850.1 (847.5,852.7)	5223 / 6672	782.8 (772.7,792.7)	3722 / 4818	772.5 (760.4,784.3)
2019	47722 / 58128	821.0 (817.8, 824.1)	41199 / 49589	830.8 (827.5,834.1)	3548 / 4805	738.4 (725.7,750.8)	2974 / 3735	796.3 (783.0,809.1)
2020	3215 / 3785	849.5 (837.6, 860.7)	2764 / 3215	859.7 (847.2,871.5)	249 / 312	798.1 (749.2,841.2)	203 / 258	786.8 (731.7,835.2)
Total	618747 / 766970	806.7 (805.9, 807.6)	540981 / 664007	814.7 (813.8,815.7)	46000 / 61834	743.9 (740.4,747.4)	31493 / 41128	765.7 (761.6,759.8)

Supplemental Table 14. Crude rates of prescribed antidepressants by drug class, 2003 - 2020

	SSRI		SNRI		TCA		MAOI		Atypical	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	7320 / 21901	334.2 (328.0,340.5)	1687 / 21901	77.0 (73.5,80.6)	937 / 21901	42.8 (40.1, 45.5)	42 / 21901	0.2 (0.1,0.3)	3237 / 21901	147.8 (143.1,152.6)
2004	5072 / 15810	320.8 (313.5,328.1)	1419 / 15810	89.7 (85.3,94.3)	620 / 15810	39.2 (36.2,42.4)	16 / 15810	0.1 (0.1, 0.2)	2260 / 15810	143.0 (137.5,148.5)
2005	5451 / 16361	333.2 (325.9,340.5)	1665 / 16361	101.8 (97.2,106.5)	673 / 16361	41.1 (38.1,44.3)	6 / 16361	0.4 (0.1,0.7)	2254 / 16361	137.8 (132.5,143.1)
2006	7377 / 20664	357.0 (350.5,363.6)	2736 / 20664	132.4 (127.8,137.1)	621 / 20664	30.1 (27.8,32.5)	13 / 20664	0.6, 0.3,1.1)	3328 / 20664	161.1 (156.1,166.1)
2007	10585 / 28266	374.4 (368.8,380.2)	3541 / 28266	125.3 (121.4,129.2)	710 / 28266	25.1 (23.3,27.0)	38 / 28266	0.1 (0.1,0.2)	5058 / 28266	179.0 (174.4,183.5)
2008	13853 / 36713	377.3 (372.5,382.5)	3843 / 36713	104.7 (101.6,107.9)	1066 / 36713	29.0 (27.3,30.8)	44 / 36713	1.2 (0.9,1.6)	6195 / 36713	168.7 (164.9,172.6)
2009	15557 / 39984	389.1 (384.3,393.9)	4783 / 39984	119.6 (116.5,122.8)	1236 / 39984	30.9 (29.3,32.7)	14 / 39984	0.4 (0.2,0.6)	7623 / 39984	190.6 (186.8,194.5)
2010	16930 / 41703	406.0 (401.2,410.7)	4754 / 41703	114.0 (111.0,117.1)	1311 / 41703	31.4 (29.8,33.2)	24 / 41703	0.6 (0.4,0.9)	7931 / 41703	190.2 (186.4,194.0)
2011	17727 / 43911	403.7 (399.1,408.3)	5937 / 43911	135.2 (132.0,138.4)	1783 / 43911	40.6 (38.8,42.5)	14 / 43911	0.3 (0.2,0.5)	9364 / 43911	213.3 (209.4,217.1)
2012	21656 / 50578	428.2 (423.9,432.5)	7228 / 50578	142.9 (139.9,146.0)	1770 / 50578	35.0 (33.4,36.6)	75 / 50578	1.5 (1.2,1.9)	11516 / 50578	227.7 (224.0,231.4)
2013	23170 / 53156	435.9 (431.7,440.1)	7546 / 53156	142.0 (139.0,145.0)	2041 / 53156	38.4 (36.8,40.1)	28 / 53156	0.5 (0.4,0.8)	13072 / 53156	245.9 (242.3,249.6)
2014	23588 / 54663	431.5 (427.4,435.7)	7751 / 54663	141.8 (138.9,144.7)	1615 / 54663	29.5 (28.1,31.0)	11 / 54663	0.2 (0.1,0.4)	13971 / 54663	255.6 (251.9,259.3)
2015	26411 / 60366	437.5 (433.6,441.5)	8656 / 60366	143.4 (140.6,146.2)	1804 / 60366	29.9 (28.5,31.3)	30 / 60366	0.5 (0.3,0.7)	15504 / 60366	256.8 (253.4,260.3)
2016	26748 / 60477	442.3 (438.3,446.3)	9253 / 60477	153.0 (150.1,155.9)	1838 / 60477	30.4 (29.0,31.8)	74 / 60477	1.2 (1.0,1.5)	16143 / 60477	266.9 (263.4,270.5)
2017	32640 / 74981	435.3 (431.8,438.9)	11489 / 74981	153.2 (150.7,155.8)	2390 / 74981	31.9 (30.6,33.2)	37 / 74981	0.5 (0.3,0.7)	20946 / 74981	279.3 (276.1,282.6)
2018	34214 / 85522	400.1 (396.8,403.4)	12341 / 85522	144.3 (142.0,146.7)	2446 / 85522	28.6 (27.5,29.7)	26 / 58128	0.5 (0.4,0.7)	22834 / 85522	267.0 (264.0,270.0)
2019	22116 / 58128	380.5 (376.5,384.4)	8670 / 58128	149.1 (146.3,152.1)	1698 / 58128	29.2 (27.9,30.6)	26 / 58128	0.4 (0.3, 0.7)	15212 / 58128	261.7 (258.1, 265.3)
2020	1451 / 3785	383.3 (367.8,399.1)	622 / 3785	164.4 (152.7,176.5)	96 / 3785	25.3 (20.6,30.9)	1 / 3785	0.1 (0.0, 0.1)	1046 / 3785	276.3 (262.2,291.0)
Total	311865 / 766970	406.6 (405.5,407.7)	103921 / 766970	135.5 (134.7,136.3)	24655 / 766970	32.1 (31.8,32.5)	538 / 766970	0.7 (0.6, 0.8)	177494 / 766970	231.4 (230.4,232.4)

Supplemental material

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Supplemental Table 15. Crude rates of prescribed antidepressants by gender, 2003 - 2020

	Women		Men	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	8319 / 13238	628.4 (620.1,636.7)	4904 / 8663	566.0 (555.6,576.6)
2004	6098 / 9809	621.7 (612.0,631.3)	3289 / 6002	548.0 (535.3,560.6)
2005	6623 / 10011	661.6 (652.2,670.8)	3426 / 6350	539.5 (527.2,551.8)
2006	9160 / 12802	715.5 (707.6,723.3)	4916 / 7861	625.3 (614.6,636.1)
2007	13490 / 18132	744.0 (737.6,750.3)	6442 / 10133	635.7 (626.3,645.1)
2008	16894 / 23280	725.7 (719.9,731.4)	8106 / 13434	603.4 (595.1,611.7)
2009	19955 / 25752	774.9 (769.7,780.0)	9258 / 14232	650.4 (642.6,658.3)
2010	20961 / 26307	796.8 (791.9,801.6)	9989 / 15396	648.8 (641.2,656.3)
2011	23319 / 27971	833.7 (829.3,838.0)	11506 / 15939	721.8 (714.8,728.8)
2012	28090 / 32089	875.4 (871.7,879.0)	14156 / 18489	765.7 (759.5,771.7)
2013	30285 / 33398	906.8 (903.6,909.9)	15572 / 19758	788.1 (782.4,793.8)
2014	31985 / 34269	933.3 (930.7,936.0)	14951 / 20393	733.1 (727.0,739.2)
2015	35997 / 38438	936.5 (932.4,937.3)	16409 / 21928	748.3 (741.0,752.6)
2016	36279 / 38505	942.2 (939.8,944.5)	17776 / 21972	809.0 (803.8,814.2)
2017	45461 / 47538	956.3 (954.4,958.1)	22041 / 27443	803.2 (798.4,807.8)
2018	48015 / 54384	882.9 (880.2,885.6)	23865 / 31138	766.4 (761.7,771.1)
2019	31849 / 37452	850.4 (846.7,854.0)	15873 / 20677	767.7 (761.8,773.4)
2020	2185 / 2407	907.9 (895.5,919.0)	1030 / 1378	747.5 (723.6,770.2)
Total	414966 / 485782	854.2 (853.2,855.2)	203508 / 281188	723.7 (722.1,725.4)

Supplemental Table 16. Crude rates of prescribed antidepressants by age category, 2003 - 2020

	18 – 34 Years		35 – 49 Years		50 – 64 Years		65 and Older	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	538 / 968	555.7 (523.8,587.4)	2483 / 3745	663.1 (647.6,678.2)	5397 / 7417	727.7 (717.4,737.8)	4805 / 9772	491.7 (481.8,501.7)
2004	324 / 835	387.4 (354.8,422.0)	1869 / 3118	599.4 (582.0,616.7)	3629 / 5258	609.2 (677.5,702.7)	3566 / 6599	540.3 (528.3,552.5)
2005	378 / 794	475.9 (440.8,511.5)	1912 / 3205	596.7 (579.3,613.6)	4233 / 5974	708.6 (696.9,720.1)	3526 / 6388	552.0 (357.7,377.1)
2006	308 / 887	347.1 (315.9,379.6)	2649 / 3819	693.5 (678.7,708.2)	5316 / 7077	751.2 (740.9,761.2)	5803 / 8880	653.5 (643.5,663.3)
2007	580 / 1083	535.9 (505.3,565.6)	2811 / 4577	614.2 (599.9,628.3)	6095 / 8360	729.1 (719.4,738.6)	10446 / 14246	733.3 (725.9,740.5)
2008	439 / 949	462.7 (430.5,494.9)	2951 / 4636	636.4 (622.5,650.4)	7155 / 9715	736.6 (719.4,738.6)	14455 / 21414	675.0 (668.7,681.3)
2009	658 / 1288	510.9 (483.2,538.5)	2979 / 4373	681.2 (667.2,695.0)	8288 / 10465	792.0 (784.1,799.7)	17287 / 23857	724.6 (718.9,730.3)
2010	596 / 1155	516.2 (486.8,545.2)	3198 / 4530	706.0 (692.5,719.2)	8857 / 11222	789.3 (781.6,796.8)	18298 / 24797	737.9 (732.4,743.4)
2011	675 / 1211	556.9 (528.9,585.6)	3029 / 4313	702.3 (688.4,715.9)	9835 / 11268	872.9 (866.5,878.9)	21285 / 27118	784.9 (780.0,789.8)
2012	769 / 1453	529.5 (503.2,555.2)	3780 / 5253	719.5 (707.2,731.7)	11782 / 13584	867.3 (861.5,873.0)	25915 / 30288	855.6 (851.6,859.6)
2013	713 / 1182	603.4 (574.7,631.2)	3291 / 4215	780.6 (768.0,793.2)	12093 / 13084	924.2 (919.6,928.7)	29760 / 34674	858.3 (854.6,861.9)
2014	660 / 1288	512.2 (484.7,540.0)	3069 / 4189	732.5 (719.0,746.0)	11717 / 13141	891.6 (886.2,896.9)	31490 / 36044	873.7 (870.2,877.1)
2015	802 / 1360	589.8 (563.0,616.0)	3767 / 4587	821.3 (809.8,832.2)	11539 / 12273	940.2 (935.9,944.3)	36297 / 42146	861.2 (857.9,864.5)
2016	755 / 1064	710.1 (681.3,736.7)	3913 / 4246	921.6 (913.1,929.5)	12965 / 13239	979.3 (976.7, 981.7)	36422 / 41928	868.7 (865.4,871.9)
2017	951 / 1571	605.5 (580.7,629.6)	3448 / 4424	779.4 (766.9,791.5)	15875 / 15844	1002 (987.2,1017)	47227 / 53142	888.7 (886.0,891.4)
2018	1008 / 1647	612.2 (588.0,635.6)	3867 / 4742	815.4 (804.1,826.4)	16649 / 16119	1033 (1018, 1048)	50355 / 63013	799.1 (796.0,802.2)
2019	709 / 996	711.6 (682.6,739.8)	2999 / 3345	896.6 (885.7,906.7)	10210 / 10113	1010 (991.0,1028)	33803 / 43674	774.0 (770.0,777.9)
2020	28 / 53	521.5 (386.4,667.0)	216 / 188	1148 (1008, 1302)	672 / 643	1046 (971.4, 1123)	2300 / 2902	792.6 (777.3,807.2)
Total	10891 / 19785	550.5 (543.5,557.4)	52230 / 71505	730.4 (727.2,733.7)	162309 / 184796	878.3 (876.8,879.8)	393043 / 490885	800.7 (799.6,801.8)

Supplemental Table 17. Crude rates of prescribed antidepressants by race and ethnicity, 2003 - 2020

	Asian		Black		Hispanic		White	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	205 / 375	545.6 (494.7,597.8)	1164 / 2458	473.5 (453.7,493.5)	532 / 1050	506.5 (476.0,537.3)	11323 / 18019	628.4 (621.3,635.5)
2004	15 / 124	117.1 (69.3,19.2)	648 / 1566	413.7 (389.3,438.6)	447 / 956	467.2 (435.6,499.8)	8278 / 13164	628.8 (620.5,637.1)
2005	87 / 191	458.2 (383.4,529.0)	666 / 1408	473.0 (446.7,499.5)	386 / 929	415.3 (383.6,448.0)	8910 / 13833	644.1 (636.1,652.1)
2006	122 / 278	438.7 (379.6,499.4)	1315 / 1966	668.8 (647.6,689.7)	610 / 1233	495.2 (466.5,523.0)	12029 / 17187	699.9 (693.0,706.7)
2007	313 / 569	550.2 (508.1,591.5)	1804 / 2828	637.8 (619.9,655.6)	1340 / 2146	624.4 (603.5,645.0)	16475 / 22722	725.1 (719.2,730.9)
2008	431 / 647	667.1 (628.3,702.4)	2456 / 4163	589.9 (574.8,605.0)	1940 / 2943	659.2 (641.7,676.3)	20173 / 28961	696.6 (691.2,701.8)
2009	516 / 724	712.2 (678.2,745.4)	3163 / 4534	697.8 (684.0,711.0)	2622 / 3994	656.5 (641.5,671.2)	22911 / 30733	745.5 (740.6,750.3)
2010	559 / 807	692.2 (659.6,724.4)	3139 / 4791	655.2 (641.5,668.7)	2720 / 3923	711.2 (696.7,725.3)	24462 / 32183	760.0 (755.4,764.7)
2011	556 / 742	749.5 (716.5,780.1)	3683 / 4901	751.5 (739.1,763.5)	3336 / 4153	803.4 (790.9,815.3)	27249 / 34115	798.7 (794.4,803.0)
2012	489 / 798	612.8 (578.0,646.7)	4443 / 5925	749.9 (738.6,760.9)	3441 / 4413	779.7 (767.2,791.9)	33873 / 39442	858.8 (855.3,862.2)
2013	734 / 1087	675.3 (646.5,703.0)	4852 / 6047	802.4 (792.1,812.4)	4839 / 5617	861.6 (852.2,870.4)	35431 / 40405	876.9 (873.7,880.1)
2014	992 / 1193	831.9 (809.0,852.3)	4905 / 6158	796.4 (786.2,806.5)	4749 / 5835	813.9 (803.7,823.8)	36290 / 41476	875.0 (871.7,878.1)
2015	1230 / 1595	771.4 (749.7,791.6)	5253 / 6991	751.3 (741.1,761.5)	6116 / 6603	926.3 (919.7,932.4)	39807 / 45177	881.1 (878.1,884.1)
2016	995 / 1453	684.9 (660.2,708.6)	5149 / 6612	778.6 (768.5,788.7)	6019 / 6326	951.2 (945.9,956.6)	41892 / 46085	909.0 (906.4,911.6)
2017	1379 / 1496	922.2 (907.0,934.9)	9083 / 10409	872.6 (866.1,879.0)	8043 / 8817	912.2 (906.1,918.0)	48996 / 54259	903.0 (900.5,905.5)
2018	1363 / 1880	725.2 (704.2,745.1)	8478 / 10856	781.0 (773.0,788.7)	8239 / 10066	818.5 (810.8,826.0)	53799 / 62720	857.8 (855.0,860.5)
2019	802 / 1173	683.6 (656.2,710.3)	5719 / 7664	746.2 (736.3,755.9)	5511 / 6243	882.8 (874.5,890.6)	35690 / 43049	829.1 (825.7,832.8)
2020	83 / 87	957.5 (886.4,987.3)	427 / 500	854.0 (820.0,883.8)	367 / 392	935.2 (907.3,958.3)	2338 / 2806	833.3 (818.9,846.8)
Total	10873 / 15219	714.4 (707.2,721.6)	66346 / 89778	739.0 (736.1,741.9)	61327 / 75637	810.8 (808.0,813.6)	479927 / 586337	818.5 (817.5,819.5)

Supplemental Table 18. Crude rates of prescribed antidepressants by region, 2003 - 2020

	Midwest		Northeast		South		West	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	6109 / 10181	600.1 (590.4,609.6)	1784 / 2788	639.9 (621.7,657.7)	4365 / 7538	579.1 (567.8,590.2)	965 / 1394	692.1 (667.3,716.4)
2004	4219 / 6758	624.3 (612.6,635.9)	946 / 1988	475.6 (453.7,498.1)	3563 / 6056	588.4 (575.8,600.8)	660 / 1009	654.0 (623.9,683.5)
2005	4271 / 6796	628.5 (616.8,640.0)	894 / 1738	514.3 (490.6,538.1)	4049 / 6515	621.5 (609.6,633.3)	835 / 1312	636.8 (609.7,662.5)
2006	4473 / 6839	654.0 (642.6,665.3)	1528 / 2078	735.2 (715.8,754.2)	5861 / 8775	667.8 (658.0,677.8)	2215 / 2972	745.5 (729.2,760.9)
2007	4631 / 7316	633.1 (621.8, 644.1)	3192 / 4237	753.4 (740.1,766.3)	8295 / 11689	709.6 (701.3,717.9)	3814 / 5024	759.1 (747.1,770.9)
2008	4899 / 7856	623.7 (612.8,634.3)	2807 / 4585	612.1 (597.9,626.4)	8968 / 13613	658.8 (650.7,666.7)	8326 / 10659	781.1 (773.2,788.9)
2009	6044 / 9042	668.4 (658.6,678.1)	3277 / 4844	676.5 (663.1,689.7)	10691 / 14320	746.6 (739.4,753.7)	9201 / 11778	781.2 (773.6,788.6)
2010	6777 / 9741	695.7 (686.5,704.8)	3173 / 4413	719.1 (705.5,732.2)	12166 / 16380	742.7 (736.0,749.4)	8833 / 11169	790.8 (783.2,798.4)
2011	7658 / 10902	702.5 (693.8,711.0)	3956 / 4913	805.2 (793.9,816.2)	13306 / 16883	788.1 (781.9,794.3)	9905 / 11212	883.4 (877.3,889.3)
2012	8709 / 12802	680.3 (672.1,688.4)	5438 / 6854	793.3 (783.6,802.9)	17210 / 20276	848.8 (843.8,853.7)	10889 / 10646	1023 (1005,1041)
2013	8417 / 12779	658.6 (650.4,666.9)	6921 / 9477	730.3 (721.2,739.2)	16921 / 19126	884.7 (880.1,889.2)	13598 / 11775	1155 (1137,1173)
2014	8905 / 12983	685.9 (677.8,693.9)	6948 / 9962	697.5 (688.3,706.5)	18623 / 20155	923.4 (920.2,927.6)	12460 / 11562	1078 (1060,1096)
2015	9768 / 14163	689.7 (682.0,697.3)	7313 / 10536	694.1 (684.2,702.9)	22508 / 23584	954.4 (951.6,957.0)	12817 / 12083	1061 (1043,1078)
2016	11140 / 14871	749.1 (742.1,756.1)	6975 / 9746	715.7 (706.6,724.6)	22840 / 24508	931.9 (928.7,935.1)	13099 / 11352	1154 (1135,1173)
2017	12486 / 16728	746.4 (739.7,753.0)	7625 / 10510	725.5 (716.9,734.0)	32478 / 34522	940.8 (938.2,943.3)	14913 / 13220	1128 (1111,1145)
2018	14442 / 18354	786.9 (780.9,792.8)	9482 / 14488	654.5 (646.7,662.2)	32811 / 38551	851.1 (847.5,854.6)	15145 / 14130	1072 (1056,1088)
2019	9698 / 12295	788.8 (781.5,796.0)	7455 / 10356	719.8 (711.1,728.5)	22430 / 26202	856.0 (851.7,860.3)	8139 / 9275	877.5 (870.7,884.1)
2020	774 / 905	855.5 (830.6,877.5)	451 / 623	723.6 (687.0,758.7)	1498 / 1668	897.8 (882.6,912.2)	492 / 588	836.7 (804.3,865.7)
Total	133421 / 191309	697.4 (695.3,699.5)	80164 / 1441348	702.3 (553.6,558.7)	258583 / 310363	833.2 (831.8,834.5)	146306 / 151160	967.9 (967.0,968.8

Supplemental Table 19. Crude rates of prescribed antidepressants among individuals with and without a diagnosis of depression in the year prior to first stroke, 2003–2020

	Prior Depression Dx HR (95% CI)		No Prior Depression Dx HR (95% CI)	
	Events / PM	Rate (95% CI) Per 1,000 PM	Events / PM	Rate (95% CI) Per 1,000 PM
2003	5411 / 7388	732.4 (722.2–742.5)	7812 / 14513	538.3 (530.1–546.4)
2004	5218 / 7329	712.0 (701.4–722.3)	4169 / 8481	491.4 (480.9–502.3)
2005	5747 / 8012	717.3 (707.3–727.1)	4302 / 8349	515.3 (504.5–526.0)
2006	8112 /10253	791.2 (783.2–799.0)	4964 / 10411	572.8 (463.3–582.4)
2007	12587 / 15547	809.6 (803.3–815.8)	7345 / 12718	577.5 (468.9–586.1)
2008	14239 / 18751	759.4 (753.2–765.5)	10761 / 17963	599.0 (591.9–606.2)
2009	18397 / 22314	824.5 (819.4–829.4)	10816 / 17671	612.1 (608.3–622.8)
2010	19847 / 23973	827.9 (823.1–832.6)	11102 / 17730	626.2 (619.0–633.3)
2011	22950 / 25836	888.3 (884.4–892.1)	11874 / 18074	657.0 (650.0–663.9)
2012	28006 / 30126	929.6 (926.7–932.5)	14240 / 20452	696.3 (690.0–702.6)
2013	31747 / 32307	982.7 (981.2–984.1)	14110 / 20849	676.8 (670.4–683.1)
2014	32504 / 33468	971.2 (969.3–973.0)	14431 / 21194	680.9 (674.6–687.2)
2015	36907 / 36979	998.1 (997.5–998.5)	15499 / 23387	662.7 (656.6–668.8)
2016	37863 / 36459	1038.5 (1028.6–1048.5)	16192 / 24018	674.1 (668.2–680.1)
2017	45862 / 44563	1029.1 (1020.2–1038.1)	21640 / 30418	711.4 (706.3–716.5)
2018	50085 / 52208	959.3 (957.6–961.0)	21795 / 33314	654.2 (649.1–659.3)
2019	34496 /36851	936.1 (933.5–938.6)	13226 / 21277	621.6 (615.1–628.1)
2020	2365 / 2367	999.2 (997.0–999.9)	851 / 1418	599.7 (574.1–625.8)
Total	412345 / 444732	927.2 (926.4–927.9)	206129 / 322238	639.7 (638.0–641.3)

Supplemental Table 20. Rate ratios for prescribed antidepressants among individuals with and without a diagnosis of depression in the year prior to first stroke, 2003–2020

	Prior Depression Dx HR (95% CI)	**No Prior Depression Dx** HR (95% CI)
Sex		
Male	1 (Ref)	1 (Ref)
Female	1.12 (1.10 – 1.14)	1.17 (1.13 – 1.20)
Age Group		
18 to 34	1 (Ref)	1 (Ref)
35 to 49	1.24 (1.15 – 1.34)	1.27 (1.14 – 1.42)
50 to 64	1.46 (1.36 – 1.57)	1.46 (1.32 – 1.62)
65 and older	1.24 (1.15 – 1.33)	1.26 (1.14 – 1.39)
Race and Ethnicity		
White	1 (Ref)	1 (Ref)
Asian	0.90 (0.84 – 0.98)	0.83 (0.75 – 0.91)
Black	0.98 (0.95 – 1.01)	0.86 (0.82 – 0.89)
Hispanic	1.00 (0.97 – 1.03)	0.90 (0.86 – 0.94)
Region		
Midwest	1(Ref)	1 (Ref)
Northeast	1.02 (0.99 – 1.06)	0.91 (0.87 – 0.96)
South	1.18 (1.15 – 1.21)	1.18 (1.14 – 1.22)
West	1.33 (1.29 – 1.37)	1.40 (1.34 – 1.45)

Supplemental material

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Supplemental Table 21. Rate ratios for prescribed antidepressants following first stroke with alternative follow-up duration, 2003-2020

	Six Months HR (95% CI)	One Year HR (95% CI)	Five Years HR (95% CI)
Sex			
Male	1 (Ref)	1 (Ref)	1 (Ref)
Female	1.16 (1.13 – 1.18)	1.19 (1.17 – 1.21)	1.20 (1.18 – 1.22)
Age Group			
18 to 34	1 (Ref)	1 (Ref)	1 (Ref)
35 to 49	1.28 (1.19 – 1.37)	1.27 (1.19 – 1.35)	1.28 (1.20 – 1.36)
50 to 64	1.40 (1.31 – 1.49)	1.49 (1.41 – 1.58)	1.52 (1.43 – 1.62)
65 and older	1.11 (1.04 – 1.18)	1.23 (1.16 – 1.30)	1.25 (1.17 – 1.32)
Race and Ethnicity			
White	1 (Ref)	1 (Ref)	1 (Ref)
Asian	0.89 (0.83 – 0.95)	0.85 (0.80 – 0.90)	0.83 (0.78 – 0.89)
Black	0.91 (0.88 – 0.93)	0.92 (0.89 – 0.94)	0.92 (0.89 – 0.94)
Hispanic	0.95 (0.92 – 0.98)	0.96 (0.93 – 0.99)	0.95 (0.92 – 0.98)
Region			
Midwest	1 (Ref)	1 (Ref)	1 (Ref)
Northeast	0.97 (0.94 – 1.01)	0.99 (0.96 – 1.02)	1.00 (0.98 – 1.03)
South	1.20 (1.17 – 1.23)	1.18 (1.15 – 1.20)	1.17 (1.14 – 1.19)
West	1.35 (1.31 – 1.39)	1.36 (1.32 – 1.39)	1.28 (1.25 – 1.32)