ORIGINAL RESEARCH

Associations of Self-Reported History of Depression and Antidepressant Use Before Stroke Onset With Poststroke Post–Acute Rehabilitation Care—An Exploratory Study: The BASIC (Brain Attack Surveillance in Corpus Christi) Project

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***Background*—**Prestroke depression status and post–acute rehabilitation care (PARC) are determinants of poststroke depression and function. However, little is known on how prestroke depression status affects PARC placement, a possible pathway for upstream intervention. We examined how prestroke depression status affects PARC in a population-based study.

***Methods and Results*—**Incident ischemic stroke cases were from the BASIC (Brain Attack Surveillance in Corpus Christi) Project from 2008 to 2012. Prestroke depression status was self-reported and categorized as (1) never depressed, (2) history of depression without antidepressant use before stroke onset, or (3) antidepressant use before stroke onset. PARC included home, a skilled nursing facility, or an inpatient rehabilitation facility. Confounder-adjusted multinomial regression models were used to examine the association between prestroke depression status and PARC. Adjustment for stroke severity was deferred in the main analyses because it may lie on the causal pathway. There were 548 stroke survivors (mean age 65.3 years, 48.3% female, 62.6% Mexican-American). The adjusted odds ratios comparing home discharge to a skilled nursing facility were 1.88 (95% CI: 0.86-4.11) for those with a history of depression and 2.55 (95% CI: 1.11-5.83) for those using an antidepressant at stroke onset, relative to those never depressed. The adjusted odds ratios comparing an inpatient rehabilitation facility to a skilled nursing facility were 1.17 (95% CI 0.40-3.42) and 3.28 (95% CI 1.24-8.67) for those with a history of depression and those using an antidepressant at stroke onset, respectively, relative to those never depressed.

***Conclusions*—**Antidepressant use before stroke onset may increase odds of home and inpatient rehabilitation facility discharge compared with skilled nursing facility discharge. **(*J Am Heart Assoc*. 2019;8:e013382. DOI: 10.1161/JAHA.119.013382.)**

Key Words: antidepressant • depression • epidemiology • rehabilitation • stroke

Stroke is a leading cause of long-term preventable disability in the United States.[1] By 2050, the prevalence of stroke cases is expected to more than double as the US population ages.[2] Consequently, the number of stroke survivors with related disability is estimated to increase significantly.[2]

Multiple post–acute rehabilitation care (PARC) settings exist to accommodate the spectrum of functional impairment and health states following stroke. The 4 main PARC settings include home without home health care, home with home health care, skilled nursing facility (SNF), and inpatient rehabilitation facility (IRF).[3] PARC setting is associated with subsequent disability and mortality.[3-7] Compared with post-stroke rehabilitation in a SNF, IRF-based rehabilitation is associated with improved functional outcomes, whereas home-based rehabilitation is associated with reduced mortality.[4] Stroke patients discharged to IRFs have demonstrated significantly better poststroke mobility, activities of daily living performance, and applied cognition.[8] Multidisciplinary stroke rehabilitation seems to reduce the odds of death, death or institutionalization, and death or dependency.[9] Given the influence of PARC on poststroke functional and medical

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Accompanying Data S1, Tables S1 through S13 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013382

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Clinical Perspective

What Is New?

- Antidepressant use before stroke onset may provide medical-functional protection, increasing odds of home and inpatient rehabilitation facility discharge compared with skilled nursing facility discharge.

What Are the Clinical Implications?

- In those with clinical depression at risk for stroke, adding an antidepressant to their management may improve acute poststroke rehabilitation potential in addition to helping their depression.
- When clinical teams are working with patients and families to decide the optimal post–acute rehabilitation care discharge destination, they should consider how the patient's pre- and poststroke depression status impacts the initial social and clinical evaluation acutely following stroke.
- Clinical teams should also take into account whether or not patients' pre- or acute poststroke depression status could be modified to potentially improve the patients' rehabilitation clinical pathways and recovery trajectories.

outcomes, predictors of PARC destination following acute stroke hospitalization are important to understand. A wide variety of medical, functional, sociodemographic, and environmental factors have been studied.[10] Few studies, however, have looked at the relationship between prestroke depression status and poststroke PARC discharge destination.[11]

Among those 55 and older—who make up the majority of stroke patients—the prevalence of depression is estimated to be 4.0%.[12] Evidence suggests depression is an independent risk factor for incident ischemic stroke as well as worse stroke severity. Studies have shown that those with depression had a 43% increase in risk of stroke and had a 2-point higher National Institutes of Health Stroke Scale (NIHSS) score on average compared with those without prestroke depression.[13,14] Prestroke depression is likely a significant modifiable risk factor for poststroke depression and functional impairment.[15,16] The causal and temporal relationships between poststroke depression and functional impairment may be bidirectional, with each outcome potentially a risk factor for the other.[17] Poststroke depression is estimated to affect around a third of stroke survivors.[18] Yet poststroke antidepressant use appears to have limited impact on improving functional status in those with poststroke depression.[19,20]

Knowing how prestroke depression status affects PARC could elucidate a point for upstream intervention in mitigating poststroke functional impairment and poststroke depression. Our study examined the association between prestroke depression status and PARC discharge destination in a biethnic population-based stroke study after accounting for confounding factors. We hypothesized that those with untreated history of depression at the time of stroke are less likely to be discharged to an IRF or home relative to a SNF, compared with those with no history of depression. We posit that antidepressant use before stroke may lessen SNF placement through its mood- and neuroprotective effects, although these may be subject to confounding by underlying depression effects. We examine a novel, preliminary, hypothesis-generating exploration of the impact of prestroke depression and prestroke antidepressant use on PARC placement.

Methods

Data and Cohort Study Population

Data were from the BASIC (Brain Attack Surveillance in Corpus Christi) Project for the time period 2008-2012. The data that support the findings of this study are available from the corresponding author on reasonable request. The BASIC study was approved by the Institutional Review Boards at the University of Michigan and the 2 local hospital systems. Written informed consent was obtained from all patients. Methods of this study were published elsewhere.[21] Briefly, the BASIC Project is a population-based stroke surveillance study among individuals 45 years and older in a biethnic community in Nueces County, Texas. As of April 2010 there were an estimated 340 223 people in the county (12% 65+ years old, 50.9% female, 60.6% Hispanic or Latino).[22] Stroke cases were identified via both active and passive surveillance, with details found elsewhere.[23]

This study was limited to patients with incident ischemic strokes in order to differentiate prestroke depression status from poststroke depression status, as they may have different etiologies and differentially act on stroke outcomes.[24] We also limited the study to non-Hispanic whites and Mexican-Americans given the low percentage of other ethnicities in the study sample.[21,23] The study was also limited to those who agreed to participate in the BASIC Project and survived through hospital discharge. Those discharged to hospice or palliative care (n=5, 0.7%), left against physician advice (n=4, 0.6%), or discharged to "other" units of the hospital (n=6, 0.8%) were excluded from the study.

A total of 157 patients (22.3%) were unable to communicate during the patient interview and had proxies answer their interview questions. These proxy-based interviews did not include questions on prestroke depression status (the primary exposure), so prestroke depression data were missing for these patients. We excluded these patients and restricted the sample to those who completed the interview themselves (nonproxy interviews). The subsequent final number of patients was 548.

Dependent Variable

The PARC discharge destination immediately following hospitalization for stroke (derived from UB-92 claims forms; see Data S1) was our primary outcome. The mutually exclusive PARC discharge destinations were IRF, SNF, and home (with or without home health care). PARC discharge destination was treated a priori as a nominal variable, as there is no order of appropriateness given the multiple factors involved in PARC discharge planning.[25] Treating PARC as a nominal variable also allowed testing of the global impact of antidepressant use at stroke onset, history of depression, and their joint effect on discharge destination in addition to making pairwise comparisons.

Independent Variable

Prestroke depression status was ascertained in an interview conducted shortly after stroke onset and assessed based on self-report. Prestroke depression was a priori operationalized into mutually exclusive groups: never depressed, past history of depression without current use of antidepressants (hereafter referred to as "history of depression"), or antidepressant use before stroke onset. Because stroke patients may have difficulty with assessing their prestroke health, we decided on these 3 overarching, less cognitively demanding categories to avoid misclassification from recall bias. Patients were classified as never depressed if they reported never being told they have depression and never took antidepressant medication. History of depression was defined as those not taking antidepressant medication before stroke onset but with a history of depression or antidepressant medication use. Antidepressant use before stroke onset was defined as anyone taking antidepressant medication at the time of the stroke.

Because antidepressant use (or lack of use) does not necessarily correlate with symptom severity, we conducted multiple post hoc sensitivity analyses assessing the consistency of results using the Patient Health Questionnaire 9 (PHQ-9) as the measure of prestroke depression status. The PHQ-9 screening was conducted shortly after the acute stroke, in reference to prestroke symptoms. The score was dichotomized at the cut point of $\geq$10 or $<$10 to classify prestroke depression and no prestroke depression, respectively, as well as treated as a continuous variable. Details on the measure can be found elsewhere.[26]

Covariates

The following variables were ascertained from the patient interviews: race-ethnicity (Mexican-American versus non-Hispanic white), marital status (married or living together, widowed, or single/divorced/separated), education level (dichotomized to at least 1 year of college education), routine use of medical care (see Data S1 for interview question), prestroke function via the modified Rankin Scale (mRS), and prestroke cognitive status via the validated Informant Questionnaire on Cognitive Decline in the Elderly by proxy.[27] We categorized responses to the mRS into 3 ordinal groups of disability severity because few respondents had higher levels of prestroke functional impairment (only 25 individuals in total had mRS scores of 4 or 5): no disability (scores of 0-1), slight or moderate disability (scores of 2-3), and moderately severe or severe disability (scores of 4-5). Informant Questionnaire on Cognitive Decline in the Elderly responses ranged from 1 to 5 for each category for all 16 instrument items, so a composite score was created by taking the average response score.[27] We then classified the score into 3 levels: normal cognition (score $\leq$3), cognitive impairment but no dementia (3$<$ score $<$3.44), and dementia (score $\geq$3.44).[28]

The following variables were obtained from medical record data: age, sex, insurance status (insured versus uninsured), initial stroke severity via the NIHSS, excessive alcohol use (yes or no), and comorbidity score. NIHSS was abstracted from the medical record or calculated using a validated method.[29] If NIHSS was documented in the electronic medical records, this score was used. If NIHSS was not documented, a validated algorithm making use of history and physical exam findings was used to retrospectively score the initial stroke severity. Although we planned a priori on adjusting for excessive alcohol use, we ended up not including the covariate in any models because there were too few individuals in the exposure groups; we have included this information in Table 1. As NIHSS has a nonlinear relationship with functional and neurological status[30] and is clinically often treated as a categorical variable to help with decision making (ie, give tPa or not), we classified the NIHSS into 3 ordinal levels of severity that have been shown to be predictive of PARC discharge destination to avoid violating the linearity assumption: mild (NIHSS $\leq$5), moderate (5$<$NIHSS$<$14), and severe (NIHSS $\geq$14).[31] A prestroke comorbidity score was developed by summing the number of comorbid medical conditions of the patient (range 0-11; see Data S1 for conditions).[32]

Statistical Analyses

Descriptive statistics were calculated for covariates by prestroke depression status. Differences in categorical covariates were assessed using the chi-squared test or the Fisher exact test (for cells with $<$5 counts). Differences in continuous covariates were assessed using ANOVA or a Kruskal-Wallis test (for nonnormally distributed variables).

Table 1. Participant Characteristics Stratified by Prestroke Depression Status

Covariate Characteristics	Never Depressed (n=366; 67%)	History of Depression (n=87; 16%)	Antidepressant Use Before Stroke Onset(n=95; 17%)	*P* Value*
Demographic				
Mean age, y (SD)	65.90 (11.90)	63.78 (12.61)	64.33 (11.23)	0.23
Number Mexican-American (%)	237 (64.75)	54 (62.07	52 (54.74)	0.2
Number female (%)	141 (53.56)	56 (64.37)	68 (71.6)	<0.01
Stroke severity				
Mean NIHSS score (SD)	4.59 (4.89)	5.19 (5.42)	4.31 (3.71)	0.43
NIHSS defined severity frequency, %				
Mild	262 (71.58)	52 (59.77)	66 (69.47)	0.10
Moderate	82 (22.40)	31 (35.63)	26 (27.37)	
Severe	22 (6.01)	4 (4.60)	3 (3.16)	
SES and health care access				
Frequency of uninsured, n (%)	62 (16.94)	12 (13.79)	6 (6.32)	0.02
More than high school education frequency, n (%)	126 (34.43)	37 (42.53)	37 (38.95)	0.32
Frequency of routine use of medical care, n (%)	292 (80.22)	79 (90.80)	89 (93.68)	<0.01
Prestroke health				
mRS defined functional disability frequency, n (%)				
None	234 (63.93)	43 (49.43)	21 (22.11)	<0.01
Slight or moderate	123 (33.61)	38 (43.68)	64 (67.37)	
Moderately severe or severe	9 (2.46)	6 (6.90)	10 (10.53)	
IQCODE defined cognition, frequency (%)				
Normal cognition	165 (50.00)	26 (37.68)	26 (32.50)	<0.01
Cognitive impairment	118 (35.76)	28 (40.58)	31 (38.75)	
Dementia	47 (14.24)	15 (21.74)	23 (28.75)	
Mean comorbidity score (SD)	3.23 (1.75)	3.55 (1.67)	3.83 (2.11)	0.02
Social support				
Marital status frequency, n (%)				
Married/living together	202 (55.19)	37 (42.53)	41 (43.16)	0.11
Single/divorced/separated	95 (25.96)	28 (32.18)	30 (31.58)	
Widow	69 (18.85)	22 (25.29)	24 (25.26)	
Alcohol use				
Excessive alcohol use, frequency (%)	26 (7.10)	1 (1.15)	4 (4.21)	0.08
PHQ-9–defined prestroke depression				
Mean PHQ-9 score (SD)	3.91 (4.86)	9.41 (7.49)	10.09 (7.26)	<0.01
Frequency of PHQ-9 dichotomized depression, n (%)	40 (11.27)	40 (47.06)	45 (49.45)	<0.01
PARC setting frequency, %				
Home	225 (65.03)	61 (73.49)	59 (66.29)	0.54
SNF	56 (16.18)	10 (12.05)	11 (12.36)	
IRF	65 (18.79)	12 (14.46)	19 (21.35)	

IQCODE indicates Informant Questionnaire on Cognitive Decline in the Elderly; IRF, inpatient rehabilitation facility; mRS, modified Rankin Scale; n, number; NIHSS, National Institutes of Health Stroke Scale; PHQ-9, patient health questionaire-9; SES, socioeconomic status; SNF, skilled nursing facility.
*For categorical variables, chi squared or Fisher exact test if N<5 per cell; ANOVA if continuous variable; Kruskal-Wallis if nonparametric.

Multinomial logistic regression was used to test our hypothesis that history of depression decreases the odds of discharge to home or IRF compared with SNF as well as to explore how antidepressant use before stroke affects PARC. Figure displays the theorized causal directed acyclic graph from which we operationalized our statistical analyses. In the regression analyses we a priori chose SNF as the referent group because SNF placement is a proxy for acute poststroke debility and limited rehabilitation potential. Most research shows both IRF and home discharge to be associated with a variety of better outcomes compared with SNF.[4-6,33] Further, the interpretability of a home versus IRF comparison is difficult: discharge to home over IRF could represent the desired outcome of better medical-functional status at the time of acute care discharge or the undesired outcome of less intense poststroke rehabilitation.

We created 5 models to assess the effect of prestroke depression status on PARC, sequentially adding confounding factors by their hypothesized magnitude of biasing effect in the following order: (1) unadjusted; (2) demographic factors (age, race-ethnicity, sex); (3) socioeconomic factors (insurance status, education level); (4) prestroke medical-functional factors (comorbidity score, prestroke mRS, prestroke Informant Questionnaire on Cognitive Decline in the Elderly); and (5) marital status. We used Wald tests to assess the global effect of history of depression, antidepressant use before stroke onset, and their joint effect (history of depression or antidepressant use before stroke onset) on PARC discharge destination. Prestroke depression status may affect stroke severity, and temporally stroke severity occurs after prestroke depression,[14] so we withheld adjustment for NIHSS in our main models to avoid overadjustment bias because stroke severity may act as a mediator.[34] However, given the importance of stroke severity in determining PARC, we explored the controlled direct effect of prestroke depression status on PARC by repeating the analyses additionally adjusting for NIHSS.

We handled missing data using a combination of multiple imputation (MI) and inverse probability weighting. The combination is beneficial in cohort studies with missing data: inverse probability weighting accounts for missing data due to selective attrition, and MI imputes missing data unrelated to attrition.[35] This approach benefits from the efficiency of MI but avoids the resulting potential bias that may occur when imputing a large number of data due to selective attrition.[35] Accordingly, we employed inverse probability weighting to assign more weight to patients in the final analytic sample who were similar to those excluded due to their interview being completed by a proxy. The weights were created by taking the inverse of the probability of having a nonproxy interview (determined with a predictive logistic model used in the same cohort).[36] Fully conditional MI was used to impute the remaining missing data: 69 patients (12.6%) had missing values for the Informant Questionnaire on Cognitive Decline in the Elderly score, 30 patients (5.5%) had missing values for PARC discharge destination, and 17 patients (3.1%) had missing values for PHQ-9. Bootstrapping was used to compute 95% CIs and global Wald tests. Given the large number of sensitivity analyses conducted, we also present the Bonferroni-corrected 99.375% CIs in addition to the 95% CIs in our main analyses (Tables 2 and 3).

Sensitivity Analyses

We ran multiple sensitivity analyses to assess the robustness of our results. First, we included a dummy variable for routine

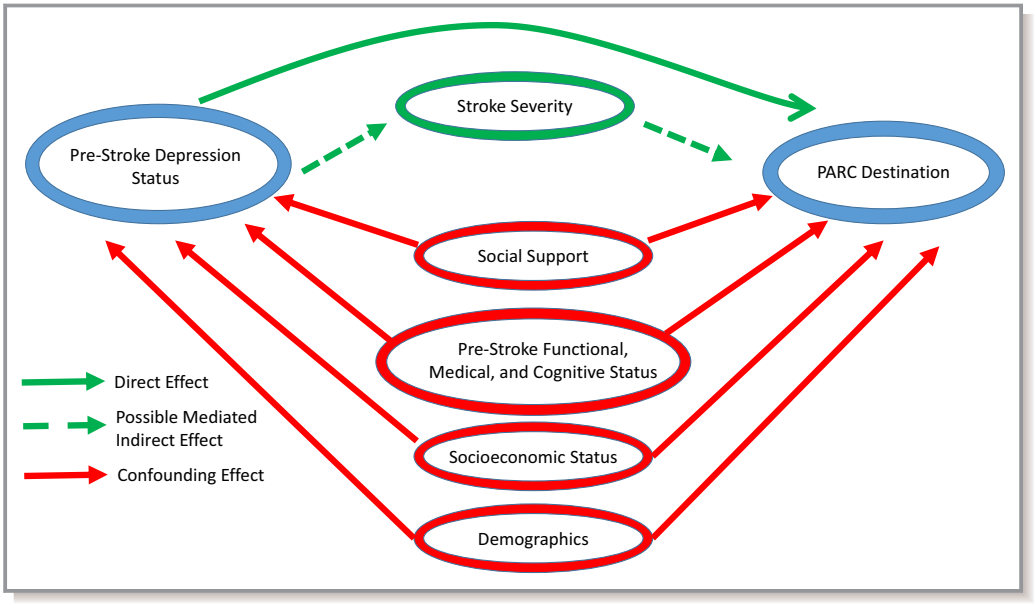

Figure. Conceptual directed acyclic graph. PARC indicates post–acute rehabilitation care.

Table 2. Results From Multinomial Regression Models of Association Between Depression Status and Odds of Discharge to Home Versus a Skilled Nursing Facility, BASIC Study, United States, 2008-2012

Model	Prestroke Depression Status, OR (95% CI)					
	History of Depression vs No History of Depression			Antidepressant Use Before Stroke Onset vs No History of Depression		
	Accounting for Attrition and Missing Data*	Bonferroni-Adjusted CIs†	Complete Case Analysis‡	Accounting for Attrition and Missing Data*	Bonferroni-Adjusted CIs†	Complete Case Analysis‡
Model 1	1.41 (0.73-2.70)	(0.56-3.49)	1.52 (0.73-3.15)	1.67 (0.82-3.42)	(0.61-4.53)	1.33 (0.66-2.71)
Model 2	1.54 (0.75-3.15)	(0.57-4.18)	1.61 (0.74-3.48)	1.69 (0.79-3.62)	(0.59-4.87)	1.33 (0.63-2.81)
Model 3	1.55 (0.76-3.21)	(0.57-4.18)	1.62 (0.75-3.52)	1.73 (0.80-3.73)	(0.59-5.07)	1.35 (0.64-2.88)
Model 4	1.79 (0.83-3.85)	(0.61-5.22)	1.64 (0.71-3.80)	2.46 (1.09-5.55)	(0.79-7.64)	2.11 (0.86-5.17)
Model 5	1.88 (0.86-4.11)	(0.63-5.59)	1.73 (0.74-4.04)	2.55 (1.11-5.83)	(0.80-8.12)	2.08 (0.84-5.14)

Model 1: unadjusted. Model 2: Model 1 + age, race, and sex. Model 3: Model 2 + insurance status and education level. Model 4: Model 3 + prestroke functional status (mRS), prestroke cognitive status (IQCODE), and comorbidity score. Model 5: Model 4 + marital status. BASIC indicates Brain Attack Surveillance in Corpus Christi; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; mRS, modified Rankin Scale; OR, odds ratio.

*N=548 for all models after accounting for attrition and missing data.

†α=0.00625, with a 99.375% CI.

‡N=518 for models 1 to 3 when only analyzing complete cases. N=451 for models 4 to 5 when only analyzing complete cases.

use of medical care in socioeconomic status–adjusted models to control for our primary measure potentially capturing healthcare access rather than depression. Next, we reran our main model treating mRS as a continuous variable to see if that would impact the result. Similarly, we reran our mediation analysis treating NIHSS as a continuous variable.

We also ran multiple sensitivity analyses incorporating PHQ-9. We repeated the analyses using the dichotomized PHQ-9 score in place of the 3-category prestroke depression status to check for consistency of our primary findings and to allow for comparison with earlier work using a dichotomous exposure.[11] Next, we repeated the analyses using PHQ-9 score as a continuous exposure in order to assess for a dose-response relationship. This analysis also allowed us to assess potential selection bias that might have occurred if those who chose not to participate in BASIC were the most depressed with highest PHQ-9 scores. In every model, we confirmed linearity of PHQ-9 with the resulting logits using the Box-Tidwell test. Next, to explore confounding by indication and account for antidepressant use (or lack of use) not necessarily correlating with depressive symptoms, we used dichotomous antidepressant use before stroke onset as the exposure and adjusted for continuous PHQ-9 and routine use of medical care. Last, we repeated the main analysis comparing odds of IRF versus home discharge to aid in our interpretation and comparison with previous studies.

Table 3. Results From Multinomial Regression Models of Association Between Depression Status and Odds of Discharge to Inpatient Rehabilitation Facility Versus Skilled Nursing Facility, BASIC Study, United States, 2008-2012

Model	Prestroke Depression Status, OR (95% CI)					
	History of Depression vs No History of Depression			Antidepressant Use Before Stroke Onset vs No History of Depression		
	Accounting for Attrition and Missing Data*	Bonferroni-Adjusted CIs†	Complete Case Analysis‡	Accounting for Attrition and Missing Data*	Bonferroni-Adjusted CIs†	Complete Case Analysis‡
Model 1	0.83 (0.32-2.16)	(0.22-3.13)	1.03 (0.42-2.57)	2.02 (0.88-4.61)	(0.63-6.43)	2.02 (0.93-4.41)
Model 2	0.98 (0.36-2.67)	(0.24-3.95)	1.16 (0.45-2.97)	2.20 (0.92-5.27)	(0.65-7.40)	1.61 (0.68-3.82)
Model 3	0.97 (0.36-2.65)	(0.24-3.86)	1.14 (0.45-2.95)	2.15 (0.89-5.20)	(0.63-7.34)	1.57 (0.66-3.74)
Model 4	1.12 (0.39-3.19)	(0.26-4.87)	1.27 (0.46-3.51)	3.14 (1.20-8.21)	(0.82-11.99)	3.13 (1.14-8.61)
Model 5	1.17 (0.40-3.42)	(0.26-5.21)	1.32 (0.47-3.68)	3.28 (1.24-8.67)	(0.85-12.71)	3.09 (1.12-8.54)

Model 1: unadjusted. Model 2: Model 1 + age, race, and sex. Model 3: Model 2 + insurance status and education level. Model 4: Model 3 + prestroke functional status (mRS), prestroke cognitive status (IQCODE), and comorbidity score. Model 5: Model 4 + marital status. BASIC indicates Brain Attack Surveillance in Corpus Christi; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; mRS, modified Rankin Scale; OR, odds ratio.

*N=548 for all models after accounting for attrition and missing data.

†α=0.00625, with a 99.375% CI.

‡N=518 for models 1 to 3 when only analyzing complete cases. N=451 for models 4 to 5 when only analyzing complete cases.

Results

Our analytic sample was composed of 548 stroke patients: 366 (66.8%) patients were never depressed, 87 (15.9%) had a history of depression, and 95 (17.3%) were taking antidepressants at the time of stroke.

Descriptive statistics are presented in Table 1. Those using an antidepressant before stroke onset were more likely to be female, insured, more disabled, to have dementia, and to have more comorbidities. On average, those with a history of depression were less likely to use alcohol excessively. Those who were never depressed were more likely to be male, have normal cognition, less likely to have dementia, and more likely to be married or living with a partner. With respect to PARC, 345 patients (63.0%) went home, 77 (14.1%) went to a SNF, and 96 (17.50%) went to an IRF. On average, those with a history of depression and those taking antidepressants before their stroke had similar depression symptom severity, with mean PHQ-9 scores of 9.41 and 10.09, respectively, compared with 3.91 for those with no history of depression.

Table 2 presents the sequentially adjusted associations of prestroke depression status with the odds of discharge to home compared with SNF, relative to those never depressed. In the unadjusted model (Model 1), history of depression was associated with increased odds of discharge to home (odds ratio [OR] 1.41, 95% CI 0.73-2.70), as was antidepressant use before stroke onset (OR 1.67, 95% CI 0.82-3.42), but these associations did not reach significance. The history of depression–home association increased with each sequentially adjusted model (Model 5, OR 1.88, 95% CI 0.86-4.11), as did the antidepressant use before stroke onset and home association (Model 5 OR 2.55, 95% CI 1.11-5.83), which reached significance. The association of history of depression and home discharge increased with adjustment for stroke severity (Table 4, Model 3, OR 2.19, 95% CI 0.95-5.11). The association between antidepressant use before stroke onset and home discharge relative to SNF was attenuated with adjustment for stroke severity (Table 4, Model 3, OR 2.03, 95% CI 0.85-4.83).

Table 3 presents the sequentially adjusted associations of prestroke depression status with odds of discharge to IRF compared with SNF, relative to those never depressed. In the unadjusted model history of depression was inversely associated with discharge to IRF (Model 1, OR 0.83, 95% CI 0.32-2.16), and antidepressant use before stroke onset was associated with higher odds of discharge to IRF (Model 1, OR 2.02, 95% CI 0.88-4.63), although neither association reached statistical significance. Sequential adjustment qualitatively changed the association between history of depression and odds of discharge to IRF (Model 5, OR 1.17, 95% CI 0.40-3.42). For those using an antidepressant at stroke onset, the association increased after adjustment for demographics

Table 4. Results from Multinomial Regression Model of Association Between Depression Status and Odds of Discharge to Home vs Skilled Nursing Facility: Exploring Mediation by Stroke Severity

Model	Prestroke Depression Status, OR (95% CI) After Adjusting for Stroke Severity		
	None	History of Depression	Antidepressant Use Before Stroke Onset
Model 1	1.00 (Ref)	1.86 (0.85-4.08)	1.50 (0.67-3.36)
Model 2	1.00 (Ref)	2.03 (0.89-4.64)	1.98 (0.84-4.65)
Model 3	1.00 (Ref)	2.19 (0.95-5.11)	2.03 (0.85-4.83)

Model 1: adjusted for NIHSS, age, sex, race, insurance status, and education level. Model 2: Model 1 + prestroke functional status (mRS), prestroke cognitive status (IQCODE), and comorbidity score. Model 3: Model 2 + marital status. BASIC indicates Brain Attack Surveillance in Corpus Christi; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; Ref, reference value.

(Model 2, OR 2.20, 95% CI 0.92-5.27) but decreased after adjustment for socioeconomic status (Model 3, OR 2.15, 95% CI 0.89-5.20). With the subsequent adjustments, the association strengthened (Model 5, OR 3.28, 95% CI 1.24-8.67) and became significant. With additional adjustment for stroke severity, the association between antidepressant use before stroke onset and IRF discharge relative to SNF was attenuated (Table 5, Model 3, OR 2.56, 95% CI 0.94-7.00), and the association between history of depression and IRF discharge relative to SNF was attenuated toward the null (Table 5, Model 3, OR 0.99, 95% CI: 0.32-3.01). Bonferroni-corrected CIs produced null results in all models for both the relation between prestroke depression status and odds of home versus SNF as well as IRF versus SNF.

Wald testing for global effect showed antidepressant use before stroke onset to have a statistically significant effect ($P<0.05$) on the discharge destination in the fully adjusted

Table 5. Results From Multinomial Regression Model of Association Between Depression Status and Odds of Discharge to Inpatient Rehabilitation Versus Skilled Nursing Facility: Exploring Mediation by Stroke Severity

Model	Prestroke Depression Status, OR (95% CI) After Adjusting for Stroke Severity		
	None	History of Depression	Antidepressant Use Before Stroke Onset
Model 1	1.00 (Ref)	0.85 (0.30-2.40)	1.76 (0.72-4.33)
Model 2	1.00 (Ref)	0.92 (0.31-2.76)	2.44 (0.90-6.55)
Model 3	1.00 (Ref)	0.99 (0.32-3.01)	2.56 (0.94-7.00)

Model 1: adjusted for NIHSS, age, sex, race, insurance status, and education level. Model 2: Model 1 + prestroke functional status (mRS), prestroke cognitive status (IQCODE), comorbidity score. Model 3: Model 2 + marital status. BASIC indicates Brain Attack Surveillance in Corpus Christi; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; IRF, inpatient rehabilitation facility; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; Ref, reference value; SNF, skilled nursing facility.

multinomial model (Model 5). History of depression did not have a statistically significant effect ($P>0.15$) on discharge destination in the fully adjusted multinomial model (model 5). Wald testing for the global effect of prestroke depression status (effect of antidepressant use at stroke onset or history of depression) on discharge destination approached statistical significance ($P=0.14$).

In sensitivity analyses inclusion of routine use of medical care as a confounder did not significantly affect the estimates (Tables S1 and S2). Treating mRS as a continuous variable in our main models produced similar results, although antidepressant effect estimates were slightly attenuated (Tables S3 and S4). Treating prestroke NIHSS as a continuous variable in our mediation analyses produced similar effect estimates (Tables S5 and S6). PHQ-9 dichotomization–defined prestroke depression was associated with increased odds of discharge to home and IRF compared with SNF (Tables S7 and S8). A 5-unit increase in PHQ-9 score was associated with a small increase in the odds of discharge to home and IRF relative to SNF in all models (Tables S9 and S10). Antidepressant use before stroke onset, adjusted for depression severity and routine use of medical care, was associated with increased odds of discharge to an IRF and home over a SNF, with the former association increased and the latter association attenuated relative to the primary analyses' results (Tables S11 and S12). Neither history of depression nor antidepressant use before stroke onset seemed to affect the odds of an IRF discharge relative to home discharge (Table S13).

Discussion

This study investigated the association of prestroke depression status with PARC discharge destination using data from a population-based stroke study. Because PARC destination likely impacts both poststroke functional status and poststroke depression status, knowing how prestroke depression status affects PARC discharge destination could inform clinical decision making with respect to poststroke rehabilitation destination with the goal of preventing functional decline and poststroke depression. After adjustment for confounding factors, antidepressant use before stroke onset was associated with increased odds of discharge to home and an IRF compared with a SNF. Results of the sensitivity analyses were consistent with our primary analyses with respect to the direction of effects, speaking to the robustness of our findings.

The only previous study on this topic found prestroke depression to be associated with greater odds of discharge to an institution (IRF or SNF) rather than to home.[11] There were methodologic differences between our study and this earlier study that are important to consider when the findings are compared. First, the study by Nuyen et al was conducted in the Netherlands, representing a different population as well as differences in acute and rehabilitation care. Second, we chose to separate SNF and IRF as unique outcomes because they provide different levels of rehabilitation and medical care and have different resulting costs and outcomes.[6,7] Third, rather than using a dichotomous exposure of depressed or not depressed, we made antidepressant use before stroke onset a unique exposure group to distinguish possible prestroke antidepressant medication effects from prestroke depression effects. Fourth, we adjusted for a comprehensive set of potential confounders. Fifth, we used a combination of MI and inverse probability weighting to get more valid effect estimates in the setting of missing data, whereas the previous study assumed data to be missing completely at random and excluded those missing prestroke depression status data.

Our finding of antidepressant use before stroke onset being associated with reduced frequency of SNF placement highlights the potential role of selective serotonin reuptake inhibitors (SSRIs) in stroke recovery. Although our study did not distinguish type of antidepressant, guidelines recommend SSRIs as a common first-line treatment in the elderly,[37] so we believe a large proportion were SSRIs. Animal-based studies have shown that SSRIs contribute to neuroplasticity, neurogenesis, and neural protection in the time surrounding ischemia.[38] The Sertraline Anti-Depressant Heart Attack Randomized Trial showed SSRI administration to be associated with decreased endothelial and platelet biomarkers in post–acute coronary syndrome patients with depression.[39] This potential downregulation of the coagulation-fibrinolysis cascade in conjunction with potential SSRI-induced vasodilation[40] could be a mechanism for the prevention of secondary subclinical vascular changes and minimization of damage to the ischemic penumbra and reduced infarct volume. This could lead to diminished damage during the stroke, preventing the decline in functional status and severe disability with little rehabilitation potential that often leads to SNF placement.

Additional adjustment for stroke severity resulted in estimates for the associations with antidepressant use before stroke onset with discharge to home and IRF attenuating by 26% and 28%, respectively. The sensitivity analysis isolating antidepressant effects from prestroke depression severity yielded increased odds of discharge to home and an IRF over a SNF. The attenuation of the results that follow additional adjustment for stroke severity suggests that antidepressants may decrease stroke severity, subsequently lowering SNF placement. Thus, our results may in part reflect the vascular effects of prestroke antidepressant use. However, few studies have examined the association between prestroke SSRIs and ischemic stroke severity, and the results of those studies have been mixed.[41-43] Consistent with the animal and biomarker studies' findings, a Cochrane Review of the effect of SSRIs on

poststroke outcomes summarized the evidence as indicating that poststroke SSRIs seem to mitigate dependence, disability, and neurological impairment following stroke.[44] Yet, the results of the recent FOCUS (Fluoxetine or Control Under Supervision) randomized control trial showed no significant benefit in functional status at 6 months poststroke when fluoxetine was given 2 to 15 days poststroke in those without depression.[45]

There are major differences between the populations and research question of our study and the FOCUS trial that warrant discussion. First, the FOCUS trial excluded those with prestroke depression on an SSRI before stroke onset and had few participants with a diagnosis of previous depression, which prevents drawing conclusions on the effect of prestroke depression status on outcomes or its effects on stroke severity. Second, we explored the effects of antidepressant use before stroke onset on an acute poststroke outcome, whereas the FOCUS trial examined poststroke SSRIs' effect on long-term functional outcomes. Although it answers a very important question on poststroke SSRIs for long-term functional recovery, the FOCUS trial does not address the impact of prestroke depression status or prestroke antidepressant use on PARC or other acute poststroke outcomes. It does not provide information on the effects of antidepressants or prestroke depression on stroke severity, other potential peristroke mediators, or their effect on acute poststroke mood or motivation. Further, the mean time of randomization in the FOCUS trial was about 7 days poststroke for both trial arms, which limits inference on prestroke or acute poststroke antidepressant effects or its impact on PARC destination (which is often decided before 7 days). Nonetheless, the results from the FOCUS trial make it less likely that our results signify that antidepressants improve acute poststroke functional recovery and subsequent PARC placement independent of other peristroke mediating factors. More research is needed to better delineate depression and the peri- and intrastroke effects of antidepressants.

Another hypothesis that could explain our results is that antidepressant use before stroke onset may decrease acute poststroke depression and improve motivation, leading to greater rehabilitation potential and less need for SNF-based care. Because there is a bias toward undertreating depression in older adults,[12] poststroke depression may be unrecognized in the acute-care setting and thus influence discharge planning. Those using antidepressants before stroke onset may have improved motivation and mood symptoms immediately following a stroke, leading to better rehabilitation potential and less SNF placement.

Of note, the associations of antidepressant use before stroke onset with PARC strengthened in magnitude and only reached statistical significance after adjustment for variables that likely portend higher SNF placement (being female, having more comorbidities, having dementia), pointing to the countervailing influences and complexity of multiple factors in determining PARC. As a result, a causal mediation analysis on how stroke severity, acute poststroke mood, and acute poststroke disability mediate the association of antidepressant use before stroke onset with decreased SNF placement would be informative in delineating potential causal mechanisms and pathways.

We hypothesized and expected history of depression to be associated with decreased odds of home and IRF discharge given the lower prestroke functional status and higher rates of poststroke depression associated with prestroke depression.[16] The observed, counterintuitive increase in odds of home discharge relative to SNF in those patients with a history of depression as compared with those with no history of depression is surprising. We do not have a great explanation for these results, as earlier literature suggests that acute poststroke depression is associated with a worse acute functional status,[46] and we would expect prestroke depression to yield similar results, portending a higher likelihood of SNF placement. In hip fracture patients there is some evidence to suggest that depression does not impact change in functional status in an IRF but rather reflects a poorer baseline.[47] It is possible that this phenomenon holds for stroke patients as well and thus does not influence discharge destination decision making as we hypothesized. It may also be that those with depression may not be able to complete the intensive rehabilitation regimen required for inpatient rehabilitation and may prefer to return home following a stroke. Although we took numerous steps to account for healthcare access as a confounder, it is still possible that those who received a diagnosis of prestroke depression before stroke were more likely to have unmeasured social support or economic/healthcare access, which helped them avoid SNF placement. We must note that there may be no clinically meaningful effect because the association between history of depression and home discharge does not reach statistical significance regardless of adjustment for stroke severity. More research is needed to delineate the interrelations among prestroke depression, stroke severity, poststroke depression, and their influence on PARC placement and long-term functional outcomes.

There are limitations to our study that warrant discussion. We may have been underpowered to detect some associations. However, antidepressant use before stroke onset reached statistical significance for pairwise comparisons (home versus SNF and IRF versus SNF), and in the global Wald tests for effect on discharge destination. Some models may have overfitted the data; acknowledging this, we incrementally added covariates to the models, adjusting for the hypothesized strongest confounders first. Given the multiple sensitivity analyses and models examined, our results

are prone to type 1 error. We have included Bonferroni-corrected CIs in our main analyses to adjust for multiple comparisons and urge further research to examine how prestroke depression affects rehabilitation care pathways.

Recall bias of prestroke depression status as a function of impaired cognition both secondary to and independent of stroke is possible. The retrospective patient-reported ascertainment of prestroke depression status may differentially misclassify depression status by discharge destination, as older adults may fail to recognize their symptomatology and underreport their depression.[48]This could lead to the misclassification of depressed individuals as having no history of depression when they in fact do, hence biasing our results toward the null and minimizing the effect of prestroke depression history on PARC. We used the categorical bins of "no history of depression," "history of depression," and "antidepressant use at stroke onset" to mitigate this possibility by allowing for easier, less cognitively demanding self-ascertainment of prestroke depression history. Although using the PHQ-9 poststroke in reference to prestroke symptomology has never been validated and may be biased by the acute trauma from the stroke itself, our cross-tabulation of PHQ-9 with our primary measure showed congruence, and our sensitivity analysis results were consistent with our primary findings. These 2 factors reassure us to some extent of the validity of our exposure measurement.

Conversely, these 2 poststroke self-reported measurements of prestroke depression may lead to overreporting of prestroke depression in the context of an acute stroke. Thus, we may fail to see an association between prestroke depression and the increased odds of SNF placement. If this were the case, though, we would hypothesize that those discharged to a nursing facility would be most inclined to overreport prestroke depression, and we fail to see that association. Nonetheless, we urge caution in overinterpreting our results and recommend that further research be done using prospective, clinically ascertained prestroke depression status.

Our exposure variable may capture healthcare access rather than prestroke depression, as access to mental health care varies widely. However, healthcare access is high in the study community.[49] We adjusted for insurance status in our primary analysis, and our sensitivity analysis adjusting for routine use of medical care produced consistent results. Our measure of antidepressant use before stroke onset may be subject to confounding by indication; however, our sensitivity analysis examining PHQ-9–adjusted antidepressant use before stroke onset as the exposure was consistent with our primary findings. Antidepressants are often used for the treatment of many psychiatric and nonpsychiatric conditions other than depression (eg, anxiety, obsessive-compulsive disorder, chronic pain, peripheral neuropathy, migraines, insomnia), which may in part explain the larger proportion of individuals taking antidepressants before stroke compared with those with a history of depression. The PHQ-9–adjusted antidepressant use before stroke sensitivity analysis also helped to mitigate any potential misclassification of antidepressant use for 1 of these nondepression indications by adjusting for depression severity, and the results were consistent with our primary analyses. It may be that those who chose not to participate in the study are different with respect to both their prestroke depression status and PARC. We theorized that the group choosing not to participate was more likely to be severely depressed and to have high PHQ-9 scores on average. However, our analysis using continuous PHQ-9 as the exposure showed increased odds of discharge to home and IRF relative to SNF. Nonetheless, as some of the results of the sensitivity analyses were attenuated compared with our primary results, it is possible that the primary findings are biased away from the null.

It is possible that the effects of prestroke depression status on PARC vary by age or that the direct effect of prestroke depression status on PARC is conditional on level of stroke severity. We hypothesized that the effects of prestroke depression status would be most salient in those with moderately severe strokes where there is not an obvious PARC discharge destination as with mild or severe strokes. Unfortunately, we were underpowered to test for effect modification by age or stroke severity. Future research should explore these possible interactions. As with all observational studies, our study is subject to residual confounding particularly related to the construct of social support. However, we accounted for a large breadth of likely sources of confounding that were not present in the previous study.[11]

Conclusions

Our exploratory, hypothesis-generating study reveals new insight into the impact of prestroke depression status on PARC discharge destination. Antidepressant use before stroke onset may provide medical-functional protection, increasing the odds of home and IRF discharge compared with SNF discharge. We encourage research to investigate the causal pathway from antidepressant use before stroke onset to stroke severity and PARC placement as well to ascertain how untreated prestroke depression impacts rehabilitation care pathways and subsequent outcomes.

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Disclosures

None.

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SUPPLEMENTAL MATERIAL

Data S1.

UB-92 codes for respective PARC destinations:

The codes below from UB-92 claims forms were used to determine post-stroke PARC destination:

1. IRF = DISPUB92 62
2. SNF = DISPUB92 3, 61
3. Home = DISPUB92 1, 6, 8

Routine use medical care based off the following interview question:

"Do you have a routine place or physician you see for routine medical needs?"

Conditions Accounted for in the Comorbidity Score:

Hypertension, diabetes mellitus, coronary artery disease, atrial fibrillation, hyperlipidemia, myocardial infarction, cancer, chronic obstructive pulmonary disease, Alzheimer's disease, epilepsy, congestive heart failure, Parkinson's disease, end-stage renal disease.

Sensitivity Analyses: Results from the Sensitivity Analysis Examining the Effect of Inclusion of Routine Use of Medical Care on the Model Effect Estimates

Table S1. Results from multinomial regression model of the association between depression status and odds of discharge to home versus skilled nursing facility, accounting for proxy-based nonresponse and adjusting for routine use of medical care, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	Pre-Stroke Depression Status, OR (95% CI)		
	None	History of Depression	Antidepressant Use Prior to Stroke Onset
Model 1	1.00 (Ref)	1.59 (0.77, 3.30)	1.83 (0.67, 5.04)
Model 2	1.00 (Ref)	1.79 (0.83, 3.85)	2.53 (.89, 7.23)
Model 3	1.00 (Ref)	1.87 (0.85, 4.08)	2.62 (0.91, 7.57)

Model 1: Adjusted for age, sex, race, insurance status, education level, and routine use of medical care

Model 2: Model 1 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 3: Model 2 + marital status

Table S2. Results from multinomial regression model of the association between depression status and odds of discharge to inpatient rehabilitation facility versus skilled nursing facility, accounting for proxy-based nonresponse and adjusting for routine use of medical care, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	Pre-Stroke Depression Status, OR (95% CI)		
	None	History of Depression	Antidepressant Use Prior to Stroke Onset
Model 1	1.00 (Ref)	0.99 (0.31, 3.18)	2.37 (0.78, 7.18)
Model 2	1.00 (Ref)	1.12 (0.34, 3.68)	3.34 (1.03, 10.86)
Model 3	1.00 (Ref)	1.17 (0.35, 3.90)	3.49 (1.06, 11.46)

Model 1: Adjusted for age, sex, race, insurance status, education level, and routine use of medical care

Model 2: Model 1 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 3: Model 2 + marital status

Results from the Sensitivity Analysis Examining the Effect of Modeling mRs as a Continuous Variable

Table S3. Results from multinomial regression model of the association between depression status and odds of discharge to home versus skilled nursing facility, accounting for proxy-based nonresponse, using continuous mRs as a covariate rather than categorized, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	Pre-Stroke Depression Status, OR (95% CI)		
	None	History of Depression	Antidepressant Use Prior to Stroke Onset
Model 1	1.00 (Ref)	1.83 (0.86, 3.90)	2.35 (0.82, 6.72)
Model 2	1.00 (Ref)	1.93 (0.89, 4.19)	2.44 (0.85,7.02)

Model 1: Adjusted for age, sex, race, insurance status, education level, pre-stroke functional status (**continuous mRs**), pre-stroke cognitive status (IQCODE), comorbidity score

Model 2: Model 2 + marital status

Table S4. Results from multinomial regression model of the association between depression status and odds of discharge to IRF versus skilled nursing facility, accounting for proxy-based nonresponse, using continuous mRs as a covariate rather than categorized, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	Pre-Stroke Depression Status, OR (95% CI)		
	None	History of Depression	Antidepressant Use Prior to Stroke Onset
Model 1	1.00 (Ref)	1.15 (0.35, 3.78)	2.91 (0.91, 9.27)
Model 2	1.00 (Ref)	1.23 (0.37, 4.07)	3.07 (0.95, 9.88)

Model 1: Adjusted for age, sex, race, insurance status, education level, pre-stroke functional status (**continuous mRs**), pre-stroke cognitive status (IQCODE), comorbidity score

Model 2: Model 2 + marital status

Results from the Sensitivity Analysis Examining the Effect of Modeling NIHSS as a Continuous Variable

Table S5. Results from multinomial regression model of the association between depression status and odds of discharge to home versus skilled nursing facility, accounting for proxy-based nonresponse and adjusting for continuous NIHSS, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012.

	Pre-Stroke Depression Status, OR (95% CI) After Adjusting for Stroke Severity		
	None	History of Depression	Antidepressant Use Prior to Stroke Onset
Model 1	1.00 (Ref)	1.88 (0.83, 4.29)	1.35 (0.48, 3.80)
Model 2	1.00 (Ref)	2.00 (0.85, 4.74)	1.72 (0.58, 5.14)
Model 3	1.00 (Ref)	2.21 (0.91, 5.38)	1.77 (0.58, 5.35)

Model 1: Adjusted for **continuous NIHSS**, age, sex, race, insurance status, and education level

Model 2: Model 1 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 3: Model 2 + marital status

Table S6. Results from multinomial regression model of the association between depression status and odds of discharge to IRF versus skilled nursing facility, accounting for proxy-based nonresponse and adjusting for continuous NIHSS, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012.

	Pre-Stroke Depression Status, OR (95% CI) After Adjusting for Stroke Severity		
	None	History of Depression	Antidepressant Use Prior to Stroke Onset
Model 1	1.00 (Ref)	1.08 (0.32, 3.62)	1.78 (0.58, 5.45)
Model 2	1.00 (Ref)	1.17 (0.34, 4.01)	2.42 (0.73, 8.05)
Model 3	1.00 (Ref)	1.33 (0.38, 4.70)	2.55 (0.76, 8.60)

Model 1: Adjusted for **continuous NIHSS**, age, sex, race, insurance status, and education level

Model 2: Model 1 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 3: Model 2 + marital status

Results from the Sensitivity Analysis Examining the Effect of Modeling History of Depression as a PHQ-9 Defined Dichotomous Exposure

Table S7. Results from multinomial regression model of the association between PHQ-9 dichotomized depression status and odds of discharge to home versus skilled nursing facility, accounting for proxy-based nonresponse, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	Pre-Stroke Depression Status, OR (95% CI)	
	No depression (PHQ-9 <10)	Depression (PHQ-9 ≥10)
Model 1	1.00 (Ref)	2.01 (1.06, 3.81)
Model 2	1.00 (Ref)	1.60 (0.81, 3.15)
Model 3	1.00 (Ref)	1.86 (0.91, 3.79)
Model 4	1.00 (Ref)	2.22 (1.04, 4.73)
Model 5	1.00 (Ref)	2.30 (1.06, 5.00)

Model 1: Unadjusted

Model 2: Model 1 + age, race and sex

Model 3: Model 2 + education level and insurance status

Model 4: Model 3 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 5: Model 4 + marital status

Table S8. Results from multinomial regression model of the association between PHQ-9 dichotomized depression status and odds of discharge to inpatient rehabilitation facility versus skilled nursing facility, accounting for proxy-based nonresponse, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	Pre-Stroke Depression Status, OR (95% CI)	
	No depression (PHQ-9 <10)	Depression (PHQ-9 ≥10)
Model 1	1.00 (Ref)	1.85 (0.86, 4.00)
Model 2	1.00 (Ref)	1.77 (0.79, 3.95)
Model 3	1.00 (Ref)	1.93 (0.86, 4.39)
Model 4	1.00 (Ref)	2.23 (0.92, 5.38)
Model 5	1.00 (Ref)	2.33 (0.94, 5.73)

Model 1: Unadjusted

Model 2: Model 1 + age, race and sex

Model 3: Model 2 + education level and insurance status

Model 4: Model 3 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 5: Model 4 + marital status

Results from the Sensitivity Analysis Examining the Dose-Response Effect of Increasing Continuous PHQ-9 Score

Table S9. Results from multinomial regression model of the association between 5-unit increase in PHQ-9 score and change in odds of discharge to home versus skilled nursing facility, accounting for proxy-based nonresponse, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	5-Unit increase in PHQ-9 Score, OR (95% CI)
Model 1	1.21(0.85, 1.27)
Model 2	1.13 (0.82, 1.28)
Model 3	1.17 (0.92, 1.47)
Model 4	1.26 (0.98, 1.63)
Model 5	1.27 (0.99, 1.64)

Model 1: Unadjusted

Model 2: Model 1 + age, race and sex

Model 3: Model 2 + education level and insurance status

Model 4: Model 3 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 5: Model 4 + marital status

Table S10. Results from multinomial regression model of the association between 5-unit increase in PHQ-9 score and change in odds of discharge to inpatient rehabilitation facility versus skilled nursing facility, accounting for proxy-based nonresponse, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	5-Unit increase in PHQ-9 Score, OR (95% CI)
Model 1	1.18 (0.80, 1.33)
Model 2	1.18 (0.80, 1.35)
Model 3	1.20 (0.91, 1.57)
Model 4	1.29 (0.95, 1.75)
Model 5	1.30 (0.96, 1.78)

Model 1: Unadjusted

Model 2: Model 1 + age, race and sex

Model 3: Model 2 + education level and insurance status

Model 4: Model 3 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 5: Model 4 + marital status

Results from the Sensitivity Analysis Exploring the Isolated Effects of Antidepressant use prior to Stroke Onset and Confounding by Indication

Table S11. Results from multinomial regression model of the association between dichotomized pre-stroke anti-depressant use and odds of discharge to home versus skilled nursing facility, adjusting for depression severity and routine use of medical care, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	Pre-Stroke Anti-Depressant Status, OR (95% CI)	
	No Antidepressant use prior to Stroke Onset	Antidepressant use prior to Stroke Onset
Model 1	1.00 (Ref)	1.99 (0.82, 4.85)
Model 2	1.00 (Ref)	1.52 (0.65, 3.54)
Model 3	1.00 (Ref)	1.52 (0.55, 4.21)
Model 4	1.00 (Ref)	1.97 (0.82, 4.75)
Model 5	1.00 (Ref)	2.01 (0.83, 4.90)

Model 1: Adjusted for continuous PHQ-9 score

Model 2: Model 1 + age, race and sex

Model 3: Model 2 + education level, insurance status, and routine use of medical care

Model 4: Model 3 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 5: Model 4 + marital status

Table S12. Results from multinomial regression model of the association between dichotomized pre-stroke anti-depressant use and odds of discharge to inpatient rehabilitation facility versus skilled nursing facility, adjusting for depression severity and routine use of medical care, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	Pre-Stroke Anti-Depressant Status, OR (95% CI)	
	No Antidepressant use prior to Stroke Onset	Antidepressant use prior to Stroke Onset
Model 1	1.00 (Ref)	2.09 (0.82, 5.28)
Model 2	1.00 (Ref)	2.22 (0.86, 5.74)
Model 3	1.00 (Ref)	2.18 (0.72, 6.64)
Model 4	1.00 (Ref)	2.94 (1.06, 8.11)
Model 5	1.00 (Ref)	3.02 (1.09, 8.41)

Model 1: Adjusted for continuous PHQ-9 score

Model 2: Model 1 + age, race and sex

Model 3: Model 2 + education level, insurance status, and routine use of medical care

Model 4: Model 3 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score

Model 5: Model 4 + marital status

Results from the sensitivity analysis examining the effects of history of depression and antidepressant use prior to stroke onset on inpatient rehabilitation facility vs. home discharge

Table S13. Results from multinomial regression model of the association between depression status and odds of discharge to inpatient rehabilitation facility versus home, accounting for proxy-based nonresponse, the Brain Attack Surveillance in Corpus Christi study, United States, 2008-2012. N = 548.

	Pre-Stroke Depression Status, OR (95% CI)		
	None	History of Depression	Antidepressant Use Prior to Stroke Onset
Model 1	1.00 (Ref)	0.58 (0.22, 1.52)	1.24 (0.70, 2.20)
Model 2	1.00 (Ref)	0.63 (0.24, 1.69)	1.34 (0.73, 2.46)
Model 3	1.00 (Ref)	0.62 (0.23, 1.65)	1.27 (0.69, 2.36)
Model 4	1.00 (Ref)	0.62 (0.23, 1.68)	1.30 (0.65, 2.61)
Model 5	1.00 (Ref)	0.62 (0.23, 1.69)	1.31 (0.65, 2.64)

Model 1: Unadjusted
Model 2: Model 1 + age, race and sex
Model 3: Model 2 + insurance status, and education level
Model 4: Model 3 + pre-stroke functional status (mRs), pre-stroke cognitive status (IQCODE), comorbidity score
Model 5: Model 4 + marital status