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ORIGINAL RESEARCH

Factors Contributing to Sex Differences in Health-Related Quality of Life After Ischemic Stroke: BASIC (Brain Attack Surveillance in Corpus Christi) Project

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BACKGROUND: Women have been reported to have worse health-related quality of life (HRQoL) following stroke than men, but uncertainty exists over the reasons for the sex difference.

METHODS AND RESULTS: We included all ischemic strokes registered with the BASIC (Brain Attack Surveillance in Corpus Christi) project (May 2010–December 2016), a population-based stroke study, who completed a 90-day outcome interview. Information on baseline characteristics was obtained from medical records and in-person interviews. HRQoL was measured by the 12-item short-form Stroke Specific Quality of Life Scale. Multivariable Tobit regression was used to estimate the mean difference in overall HRQoL scores (range, 1–5; higher indicating better HRQoL) between sexes and to identify contributing factors to the differences. We included 1061 cases with complete data on HRQoL and covariates (median age, 67 years; 51% women). In unadjusted analyses, women had poorer overall HRQoL than men (mean difference, −0.26 [95% CI, −0.40 to −0.13]). Contributors to this difference included sociodemographic/prestroke factors (eg, age, race and ethnicity, prestroke function), risk factors/comorbidities (eg, history of stroke, Alzheimer disease/dementia), and initial stroke severity. Sociodemographic/prestroke factors explained 62% of the sex difference (mean difference, −0.08 [95% CI, −0.21 to 0.04]). In a fully adjusted model that included adjustment for all confounding factors, the sex difference was eliminated and became nonsignificant (mean difference, −0.03 [95% CI, −0.16 to 0.09]).

CONCLUSIONS: Poorer HRQoL in women compared with men was observed and explained by the combination of sociodemographic and prestroke factors, including physical function before stroke and stroke severity. The findings suggest potential subgroups of women who might benefit from more targeted interventions before and after stroke to improve HRQoL.

Key Words: ischemic stroke ■ quality and outcomes ■ quality of life ■ sex characteristics

In stroke research, health-related quality of life (HRQoL) is an important patient-reported outcome measure, because it is a holistic assessment of the individual's well-being.[1] HRQoL is considered a valid indicator of service needs and intervention outcomes.[1] There is increased evidence of poorer outcomes after stroke among women compared with men.[2,3] However, uncertainty exists over the sex differences because of several limitations of the existing research, as identified by our previous reviews.[2,3] Population-based stroke incidence studies, compared with hospital-based studies, provide better external and internal validity to explore sex differences in outcomes after stroke.[4] In a recent review of sex differences in patient-reported outcome measures after stroke, few studies (2/13 published since 2007) have been specifically designed to examine the cause of sex differences in outcomes, and none of these were population based.[3]

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CLINICAL PERSPECTIVE

What Is New?

- In our large population-based study, women had worse health-related quality of life (HRQoL), measured with a stroke-specific scale, at 90 days after stroke than men.
- Poorer HRQoL in women compared with men was mostly explained by sociodemographic and prestroke factors, including physical function and cognitive status before stroke and stroke severity.
- Women had worse HRQoL related to difficulties in remembering things (psychological subdomain) than men, and this difference was not fully explained by prestroke and clinical factors.

What Are the Clinical Implications?

- The findings suggest potential subgroups of women who might benefit from more targeted interventions before and after stroke to improve HRQoL.
- Further research is needed to understand why there are sex differences in the memory subdomain of HRQoL.

Nonstandard Abbreviations and Acronyms

BASIC	Brain Attack Surveillance in Corpus Christi
IQCODE	Informant Questionnaire for Cognitive Decline in the Elderly
MD	mean difference
mRS	modified Rankin Scale
NIHSS	National Institutes of Health Stroke Scale
SS-QoL	Stroke Specific Quality of Life Scale

Several studies report worse HRQoL after stroke in women compared with men, even after adjusting for confounding factors such as age, sociodemographic factors, and stroke severity.[2,5–11] However, there is substantial variation in the outcome measurements used, adjustment for different covariates, and methods of analysis among these studies.[3] In a recent meta-analysis using individual participant data from 4 population-based studies, we found that the greatest contributors to the worse HRQoL in women were advanced age, prestroke functional limitations, and stroke severity.[12] However, even after adjustment for these factors, this study still showed poorer HRQoL among women. Given the inherent limitations of pooling data from disparate studies, there is the potential that these results could still be confounded by other unmeasured or poorly measured factors.[12] Furthermore, these analyses were limited by the fact that the available instruments (eg, EuroQol-5 dimension) were generic scales, rather than stroke-specific instruments,[12] which may bias sex differences in HRQoL, because generic instruments do not include domains specific to stroke that may be different by sex. To address some of these gaps, we aimed to identify factors contributing to sex differences in HRQoL after ischemic stroke, assessed by a stroke-specific instrument, using data from a large, ongoing, prospective population-based stroke study in the United States.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ischemic stroke survivors were identified through the ongoing BASIC (Brain Attack Surveillance in Corpus Christi) project, a population-based stroke surveillance study in Nueces County, Texas. In BASIC, we include all of the stroke events captured for the defined population of the county and follow individuals over time for their outcomes. This is in contrast to a population-based cohort study, in which a representative sample from a defined population is drawn and then followed over time for the development of stroke. Stroke cases among patients >45 years of age are obtained through active and passive surveillance. Detailed methods for BASIC have been previously published.[13]

In our analyses, we included all ischemic strokes, among Mexican American and non-Hispanic White patients, registered with the BASIC project from May 2010 to December 2016 who survived and completed a 90-day outcome interview. All patients or their proxies provided written informed consent. The BASIC study was approved by the institutional review boards at the University of Michigan and local hospitals.

Outcome Measures

HRQoL was measured by the short-form Stroke Specific Quality of Life Scale (SS-QoL; 12 items), which has been validated in the BASIC study population.[14] The scale produces 3 summary scores or domains: (1) overall QoL, (2) physical QoL, and (3) psychosocial QoL (mean score ranges 1–5 with higher scores indicating better HRQoL). The summary score is an unweighted average of all 12 item scores, and the domain scores are unweighted averages of the associated items within each domain.

Sex and Other Covariate Measures

Study factors comprised 5 groups: (1) Sociodemographics included sex (exposure factor), age, race and ethnicity (Mexican American and

non-Hispanic White), marital status, education (less than high school, high school, some colleague/vocational school, college graduate), and insurance (yes/no). (2) Prestroke factors included prestroke physical function (modified Rankin Scale [mRS]; range 1–5; higher scores represent greater functional limitations) and prestroke cognitive status (Informant Questionnaire for Cognitive Decline in the Elderly [IQCODE]; range 1–5; higher scores represent worse cognitive function with excellent accuracy for detecting preexisting dementia in stroke[15]) that were asked at the baseline interview in reference to the prestroke period. (3) Risk factors/comorbidities included history of stroke/transient ischemic attack, hypertension, diabetes, coronary artery disease/myocardial infarction, atrial fibrillation, high cholesterol, smoking, excessive alcohol consumption, cancer, chronic obstructive pulmonary disease, dementia/Alzheimer disease, epilepsy, heart failure, Parkinson disease, end-stage renal disease, and body mass index (BMI). A comorbidity index was generated as the sum of the aforementioned risk factors/comorbidities and ranged from 0 to 15. (4) Initial stroke severity was measured by the National Institutes of Health Stroke Scale (NIHSS). (5) Receipt of intravenous thrombolysis was the indicator of stroke treatment. Because of a high rate of missing data (22%), history of depression was not included in the comorbidity index and our main analyses but was included in a sensitivity analysis. Because poststroke depression was assessed at the same time as quality of life (QoL), we did not include this factor in our analyses.

Statistical Analysis

Analyses were conducted in SAS 9.4 (SAS Institute). Continuous variables were described as means with SD (prestroke mRS), or medians with interquartile range (age, BMI, and NIHSS). Categorical variables were represented as counts with percentages. We used *t* tests for comparing means, Wilcoxon tests for comparing medians, and χ^2 tests for comparing categorical data to make comparisons between men and women. When there are bounded outcomes, regular regression methods can misestimate standard error leading to biased inferences.[16] Because the short-form SS-QoL scores are bounded (see Figure S1 through S4 for the distribution of outcome data), Tobit regression can help minimize the misestimation of standard errors.[16] Therefore, Tobit regression was used to estimate the mean differences (MDs) in HRQoL scores for women compared with men, separately for overall, physical, and psychological QoL. The model building procedures included generating a base model (Model 1) with age and sex, and then adding each individual covariate to the model to assess its confounding role on the age-adjusted association between sex and HRQoL.[13] A covariate was considered a confounder if the inclusion of the variable changed the magnitude of the coefficient for the age-adjusted sex difference by ≥5%.[13] The confounding effect could be either a positive change (leading to a reduction in sex difference) or a negative change (resulting in an increase in sex difference). We then performed further analyses by adding to Model 1 race and ethnicity and the sociodemographic factors that met the criteria of being confounders (forming Model 2). Because of the important role of race and ethnicity on patient-reported outcomes after stroke,[17] this covariate was forced into Model 2 regardless of meeting the criteria for being a confounder. Functional limitations before stroke have been identified as an important confounding factor to the sex differences in outcomes after stroke.[12,13] Model 3 was formed by adjusting for prestroke factors in Model 2, including prestroke mRS (categorical: 0–1, 2–3, and ≥4) and cognition status (categorical IQCODE: ≤3, >3 to <3.44, and ≥3.44), regardless of meeting the confounding criteria above. Other factors that met our criteria of being confounders were then added to Model 3, including risk factors/comorbidities (forming Model 4). Stroke severity is an established confounding factor to the sex differences in HRQoL after stroke,[12] and therefore, Model 4 was further adjusted for stroke severity and other stroke-related factors that met criteria for being confounders (forming Model 5). The final model (Model 6) included sex, age, race and ethnicity, prestroke mRS and IQCODE, stroke severity, and all of the identified confounding factors. We tested whether the continuous covariates required transformations using fractional polynomials in multivariable modeling[18] to get the best model fit. Age and BMI were modeled linearly. Initial NIHSS scores were modeled as natural logarithm of (NIHSS+1) given the highly skewed distribution.[18] We tested the interactions between sex and all other covariates. In the final multivariable model, statistical interactions were assessed by a test of statistical significance of sex×covariate product terms. A 2-tailed *P* value ≤0.05 was considered statistically significant. A clinically important difference in the total SS-QoL score of 4.7 has been identified for the original version of SS-QoL,[19,20] but the clinically important difference for the short form is lacking.[14] According to the Cohen rule of thumb, the size of effect size estimates range from a small to large effect, with 0.2 SD as small, 0.5 SD as medium. and 0.8 SD as large.[21] A study by Norman and colleagues provided an interpretation of changes in HRQoL using one-half of 1 SD,[22] which falls between these extremes and is a medium effect. We therefore used the rule of 0.5 SD for determining if the MDs between men and women in HRQoL scores were clinically important.[22] Our main findings were based on a complete-case analysis. We also conducted sensitivity analysis to examine the effect of missing data

on the robustness of the association between sex and HRQoL when compared with the complete-case analysis.

Sensitivity Analysis

Multiple imputation using chained equations[23] (m=50 imputations) combined with inverse probability weighting was used to impute missing data on any of the SS-QoL items or covariates among those who completed the 90-day outcome interview, under the assumption that covariates were missing at random. Of note, prestroke depression was not included as a covariate in the imputed analyses because the data were only available among those without a proxy interview and had high rate of missingness (22%). We did not impute the data for those who refused to participate or were lost to follow-up. The combined approach of multiple imputation and inverse probability weighting was used to minimize selection bias by filling in missing values for the study sample, and accounting for differential attrition by generating inverse probability weights.[24] The effect of imputation was examined by comparing crude and adjusted effect estimates between the complete-case and imputed data set analyses.

We also performed a sensitivity analysis that was limited to those with prestroke depression data including this covariate to understand its impact on the sex differences in HRQoL after stroke. Using similar model building procedures outlined above, each individual covariate, including prestroke depression, was first added to the base model (Model 1; age adjusted) to assess its confounding role. We then performed further analyses (Models 2–6) with depression being considered as a comorbidity and added in Model 4 together with relevant significant confounding factors.

Subdomain Analyses

The impacts of stroke may differ between women and men on the 12 items forming the scale.[12] We quantified sex differences in subdomain scores in unadjusted and fully adjusted models after accounting for confounding factors using the same methods above.

RESULTS

Of a total of 3158 patients with ischemic stroke from May 2010 to December 2016, 2108 (66.8%) agreed to participate in the interview portion of the BASIC study. At 90 days, 262 participants (13.5%) had died. Among 1846 participants who survived until 90 days after stroke, 1426 completed their outcome interview, and 420 (22.8%) could not be located or refused to participate (Figure S2). Of the 1426, 1334 (51.1% women) were Mexican American and non-Hispanic White and included in our analyses (Table 1). About 21% of the interviews (n=283) were completed by proxy respondents, with some difference by sex of the stroke survivors (men 19.1% versus women 23.5%). Women (median age, 69 years versus men 66 years) were less likely to be married at stroke onset compared with men (P<0.0001; Table 1). Men were more likely to have completed high school or higher education (P=0.005), be former or current smokers (P<0.001) and excessive alcohol consumers (P<0.001) than women. Women, compared with men, had higher BMI (P=0.001) and more prestroke functional limitations, both physically (categorical mRS; P<0.0001) and mentally (categorical IQCODE; P=0.003). Women were more likely to have a history of congestive heart failure (P=0.005), prestroke depression (P<0.001), and Alzheimer disease/dementia (P=0.003; Table 1), whereas men were more likely to have coronary artery disease/myocardial infarction (P<0.001). More men had at least 3 comorbidities compared with women (51.7% versus 45.2%; P=0.020). Clinically important differences (0.5 SD) in overall (0.55 SD), physical (0.65 SD), psychological QoL (0.58 SD) and the 12 individual scale items of the BASIC registrants are presented in Tables S1 through S4.

The sample for the complete-case analysis was n=1061 cases after excluding 205 participants (20.5%) who completed the outcome interview but were missing data on some SS-QoL items or covariates. Women, compared with men, were more likely to have statistically significant poorer HRQoL in overall: mean 3.11±1.10 versus men 3.35±1.09; physical: 2.68±1.27 versus men 2.89±1.30; and psychological QoL: 3.53±1.17 versus men 3.82±1.13; P-values <0.001 (Tables S1 through S4). In unadjusted models, the MD was −0.26 (95% CI, −0.40 to −0.13) for overall QoL; MD was −0.28 (95% CI, −0.47 to −0.09) for physical QoL; and MD was −0.33 (95% CI, −0.49 to −0.17) for psychological QoL (Table 2). The sex differences after adjusting for age remained statistically significant in all domains (overall, physical, and psychological) of HRQoL (Model 1; Table 2).

We assessed the confounding role of individual covariates by adding each factor to the base model with age and sex (see Figure S3 for visual illustration on percentage of change of female effect on age-adjusted mean difference in overall QoL). Confounding factors of the age-adjusted association between sex and HRQoL were consistent for all domains of HRQoL (Table 2). They included marital status (other than married/living together), education (high school or higher), higher BMI, smoking, history of stroke/transient ischemic attack, presence of Alzheimer disease/dementia, presence of coronary artery disease/myocardial infarction, comorbidity index (>3), prestroke mRS (>2), and initial stroke severity (natural logarithm [NIHSS+1]). Race and ethnicity were important contributing factors to the sex differences in psychological QoL but

Table 1. Baseline Characteristic of BASIC Registrants by Sex, May 2010 to December 2016, for Stroke (n=1334)

Characteristic	Men		Women		*P* value*
	N or median	% or (Q1–Q3)	N or median	% or (Q1–Q3)	
No. of cases	652	48.90	682	51.10	
Proxy	124	19.05	160	23.46	0.057†
Sociodemographics					
Age, y, median (IQR)	66	(58–74)	69	(59–80)	<0.001†
Race and ethnicity					0.689
Non-Hispanic White	244	37.42	247	36.22	
Mexican American	408	62.58	435	63.78	
Marital status					<0.001†
Married/living together	381	58.44	241	35.34	
Other (single, widowed, divorced/separated)	271	41.56	441	64.66	
Education					
Less than high school	194	29.98	243	35.74	0.005†
High school	190	29.37	185	27.21	
Vocational school/some college	135	20.87	160	23.53	
College or more	128	19.78	92	13.53	
Health insurance	584	89.57	635	93.11	0.028†
Prestroke mRS‡, mean	1.46	1.31	1.95	1.45	<0.001†
Prestroke mRS, categorical‡					<0.001†
0–1	330	50.61	259	37.98	
2–3	277	42.48	316	46.33	
4+	45	6.9	107	15.69	
IQCODE, categorical§					0.003†
≤3, normal cognition	309	54.79	265	44.99	
>3 and <3.44, mild impairment	160	28.37	212	35.99	
≥3.44, severe impairment	95	16.84	112	19.02	
Body mass index, median (IQR)	28.24	(25.1–32.3)	29.12	(25.06–34.28)	0.001†
Risk factors/comorbidities					
Individual comorbidities‖					
Smoking	323	49.77	197	29.01	<0.001†
Parkinson	9	1.39	10	1.47	>0.999
Alzheimer/dementia	43	6.60	77	11.29	0.003†
Prestroke depression‖	139	26.73	250	47.53	<0.001†
Excessive alcohol consumption	68	10.48	21	3.09	<0.001†
Congestive heart failure	40	6.16	72	10.59	0.005†
COPD	62	9.55	76	11.18	0.379
Cancer	71	10.94	94	13.82	0.131
Atrial fibrillation	80	12.33	102	15.00	0.181
History of stroke/TIA	183	28.20	211	30.98	0.293
Hypertension	539	82.67	557	81.67	0.686
High cholesterol	338	52.00	354	52.06	0.999
Epilepsy	21	3.24	18	2.65	0.636

(*Continued*)

Table 1. Continued

Characteristic	Men		Women		*P* value*
	N or median	% or (Q1–Q3)	N or median	% or (Q1–Q3)	
End-stage renal disease	24	3.70	36	5.29	0.205
Diabetes	326	50.15	339	49.71	0.914
CAD/MI	233	35.74	169	24.78	<0.001†
Comorbidity index, median (IQR)	4	(2–5)	3	(2–5)	0.571
≥3 comorbidities	337	51.69	308	45.16	0.020†
Stroke-related factors					
Stroke severity, NIHSS, median (IQR)¶	3	(1.0–6.0)	3	(1.0–6.0)	0.647
Log (NIHSS+1)¶	1.39	(0.69–1.95)	1.61	(1.1–2.2)	0.006†
Treated with intravenous thrombolysis¶	81	12.42	97	14.24	0.370

CAD indicates coronary artery disease; COPD, chronic obstructive pulmonary disease; IQCODE, Informant Questionnaire for Cognitive Decline in the Elderly; IQR, interquartile range; MI, myocardial infarction; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; and TIA, transient ischemic attack.

*t test for comparing means, Wilcoxon tests for comparing medians, and χ^2 test for comparing groups.

†Statistical significant results ($P \leq 0.05$).

‡Missing n=34 cases (2.5%).

§Missing n=181 cases (13.6%).

‖Depression and/or with past or current antidepressant medication; missing n=288 cases (22%).

¶Missing n≤6 cases (0.5%).

not the other domains (Table 2). In overall QoL, sociodemographic factors explained 32% of the sex difference (MD, −0.15 [95% CI, −0.29 to −0.01]; Table 2). Further adjustment for prestroke mRS decreased the magnitude of the sex difference by 30% to 62% (MD, −0.08 [95% CI, −0.21 to 0.04]). In the final fully adjusted model for overall QOL that included further adjustment for risk factors/comorbidities and stroke severity, the sex difference was mostly (85%) accounted for by confounders, with MD being −0.03 (95% CI, −0.16 to 0.09). In the fully adjusted models, the identified confounding factors (Table 2) accounted for 63% of the difference in physical QoL (MD, −0.10 [95% CI, −0.28 to 0.09]; Table 2) and 85% of the difference in psychological QoL (MD, −0.04 [95% CI, −0.17–0.09]) in women compared with men. It is important to note that all of the unadjusted and adjusted estimates for sex differences were below the clinically important thresholds determined in Tables S1 through S4.

No statistically significant interactions between sex and other covariates were observed. Sensitivity analyses using multiple imputation combined with inverse probability weighting (n=1334 participants) to account for missing data for the subjects with either missing outcome and covariates showed similar direction of the association between sex and HRQoL, with minimal change in the magnitude of the sex difference compared with the main findings (Table S2). In the imputed analyses, race and ethnicity were found to be confounding factors to the sex differences in overall, physical, and psychological QoL. Prestroke cognitive status was an additional factor that consistently confounded the association between sex and the HRQoL outcomes in the analyses that used imputation.

In our sensitivity analysis, which was limited to those with prestroke depression data (n=828 participants), history of depression was found to be an additional confounding factor that had the greatest impact on the sex differences in overall, physical, and psychological HRQoL after stroke. Compared with the main findings, the sensitivity analysis revealed similar magnitude and direction of the association between sex and HRQoL in multivariable models (Table S3).

Subdomain Analyses

Women reported significantly lower physical QoL in 4 items: doing daily work, buttoning buttons, walking, and taking a shower (Table 3, unadjusted). The differences became nonsignificant after accounting for all confounding factors (Table 3, fully adjusted**)**. In terms of psychological QoL, women, compared with men, were more likely to be affected in 2 items: feelings of burden to my family and memory, in both unadjusted and age-adjusted models (Table 3). The sex differences in psychological QoL remained statistically significant in the memory subdomain after accounting for all significant confounding factors (Table 3, fully adjusted model). However, it is again important to note that the sex differences in 12 SS-QoL items in adjusted analyses were below the clinically important thresholds determined in Tables S1 through S4.

Table 2. Impact of Covariates on Age-Adjusted MD in QoL at 90 Days After Stroke for Women Compared With Men Using Tobit Regression

	Overall QoL			Physical QoL			Psychological QoL		
	MD	95% CI	Δ(%)*	MD	95% CI	Δ(%)*	MD	95% CI	Δ(%)*
Raw model	−0.262	−0.400 to −0.125	NA	−0.280	−0.466 to −0.094	NA	−0.330	−0.489 to −0.172	NA
Base model: age-adjusted Model 1	−0.219	−0.355 to −0.083	NA	−0.265	−0.453 to −0.078	NA	−0.251	−0.405 to −0.097	NA
Model 1+each covariate									
Marital status (other than married/living together)	−0.163	−0.303 to −0.023	26†	−0.199	−0.391 to −0.006	25†	−0.190	−0.348 to −0.032	24†
Ethnicity (MA)	−0.210	−0.343 to −0.076	4	−0.256	−0.440 to −0.071	4	−0.239	−0.389 to −0.089	5
Education, high school or higher	−0.201	−0.334 to −0.067	8†	−0.243	−0.427 to −0.060	8†	−0.232	−0.383 to −0.081	8†
BMI	−0.198	−0.335 to −0.061	10†	−0.227	−0.415 to −0.039	15†	−0.234	−0.389 to −0.080	7†
Alzheimer/dementia	−0.189	−0.323 to −0.055	14†	−0.237	−0.422 to −0.051	11†	−0.213	−0.363 to −0.063	15†
CAD/MI	−0.241	−0.378 to −0.104	−10†	−0.297	−0.485 to −0.108	−12†	−0.266	−0.421 to −0.111	−6†
Comorbidity index (>3)	−0.250	−0.384 to −0.116	−14†	−0.306	−0.490 to −0.122	−15†	−0.280	−0.431 to −0.128	−11†
IQCODE, categorical	−0.212	−0.347 to −0.078	3	−0.255	−0.440 to −0.070	4	−0.249	−0.400 to −0.097	1
Prestroke mRS >2, categorical	−0.108	−0.235 to 0.019	51†	−0.151	−0.332 to 0.030	43†	−0.115	−0.255 to 0.025	54†
Current/former smoker	−0.242	−0.381 to −0.103	−11†	−0.302	−0.493 to −0.111	−14†	−0.265	−0.423 to −0.108	−6†
Congestive heart failure	−0.198	−0.333 to −0.063	10†	−0.245	−0.431 to −0.058	8†	−0.225	−0.376 to −0.073	10†
History of stroke/TIA	−0.203	−0.336 to −0.070	7	−0.246	−0.430 to −0.062	7†	−0.234	−0.384 to −0.084	7†
COPD	−0.215	−0.351 to −0.079	2	−0.263	−0.450 to −0.076	1	−0.246	−0.399 to −0.092	2
High cholesterol	−0.219	−0.355 to −0.083	0	−0.265	−0.452 to −0.078	0	−0.251	−0.405 to −0.098	0
Health insurance	−0.220	−0.356 to −0.083	0	−0.266	−0.453 to −0.078	0	−0.252	−0.405 to −0.098	0
Hypertension	−0.224	−0.360 to −0.089	−2	−0.274	−0.460 to −0.087	−3	−0.254	−0.408 to −0.101	−1
Diabetes	−0.222	−0.357 to −0.087	−1	−0.270	−0.455 to −0.084	−2	−0.253	−0.405 to −0.101	−1
Cancer	−0.219	−0.356 to −0.083	0	−0.266	−0.453 to −0.078	0	−0.252	−0.405 to −0.098	0
Atrial fibrillation	−0.218	−0.354 to −0.082	0	−0.265	−0.452 to −0.078	0	−0.250	−0.403 to −0.096	0
Stroke severity, ln NIHSS+1	−0.176	−0.305 to −0.047	20†	−0.225	−0.408 to −0.042	15†	−0.198	−0.341 to −0.055	21†
Intravenous thrombolysis	−0.220	−0.356 to −0.084	0	−0.268	−0.455 to −0.081	−1	−0.251	−0.405 to −0.098	0
Model 2, Model 1+race and ethnicity, marital status, education	−0.150	−0.285 to −0.014	32†	−0.183	−0.371 to 0.005	31†	−0.175	−0.329 to −0.022	30†
Model 3, Model 2+prestroke mRS, IQCODE	−0.084	−0.211 to 0.043	62†	−0.116	−0.299 to 0.066	56†	−0.094	−0.235 to 0.047	62†
Model 4, Model 3+risk factors/comorbidities identified as confounders (Δ ≥5%)	−0.061	−0.188 to 0.067	72†	−0.124	−0.312 to 0.063	53†	−0.072	−0.211 to 0.067	71†
Model 5, Model 4+ln NIHSS+1‡	−0.032	−0.155 to 0.091	85†	−0.098	−0.283 to 0.088	63†	−0.038	−0.169 to 0.093	85†
Model 6, full model‡	−0.032	−0.155 to 0.091	85†	−0.098	−0.283 to 0.088	63†	−0.038	−0.169 to 0.093	85†

Negative scores indicate worse QoL in women (n=1061). BMI indicates body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; IQCODE, Informant Questionnaire for Cognitive Decline in the Elderly; ln, natural logarithm; MA, Mexican American; MD, mean difference; MI, myocardial infarction; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; QoL, quality of life; and TIA, transient ischemic attack.

*Percent change of coefficient of sex difference (age-adjusted β – covariate-adjusted β)/age-unadjusted β×100.

†Δ ≥5%.

‡Full model included sex, age, race and ethnicity, prestroke mRS and IQCODE, stroke severity, and all the identified confounding factors (Δ ≥5%): marital status, education, BMI, Alzheimer/dementia, CAD/MI, comorbidity index (>3), current/former smoker, history of stroke/TIA, and congestive heart failure.

Table 3. Sex Difference in Specific SS-QoL Items in the BASIC Project, May 2010 to December 2016, for Stroke (n=1061)

Items	Unadjusted		Age adjusted		Fully adjusted model*	
	MD	95% CI	MD	95% CI	MD	95% CI
Psychological quality of life, 6 items						
I felt I was a burden to my family.	−1.073†	−1.829 to −0.318†	−1.065†	−1.825 to −0.305†	−0.463	−1.245 to 0.319
My physical condition interfered with my social life.	−0.757	−1.675 to 0.160	−0.573	−1.490 to 0.343	0.271	−0.649 to 1.190
I was too tired to do what I wanted to do.	−0.727	−1.494 to 0.041	−0.651	−1.421 to 0.119	−0.019	−0.802 to 0.765
I was discouraged about my future.	−0.135	−0.885 to 0.615	−0.167	−0.921 to 0.587	0.410	−0.371 to 1.190
My personality has changed.	−0.533	−1.178 to 0.112	−0.558	−1.207 to 0.090	−0.380	−1.053 to 0.293
I had trouble remembering things.	−1.103†	−1.710 to −0.496†	−1.001†	−1.607 to −0.394	−0.749†	−1.368 to −0.130†
Physical quality of life, 6 items						
Did you have to repeat yourself so others could understand you?	−0.029	−0.305 to 0.247	0.009	−0.268 to 0.285	0.204	−0.064 to 0.472
Did you have to stop and rest more than you would like when walking/using the wheelchair?	−0.658†	−0.942 to −0.374†	−0.562†	−0.842 to −0.281†	−0.242	−0.508 to 0.024
Did you have trouble buttoning buttons?	−0.715†	−1.256 to −0.175†	−0.474	−1.001 to 0.052	0.080	−0.431 to 0.591
Did you have trouble seeing the television well enough to enjoy a show?	−0.288	−0.916 to 0.340	−0.144	−0.774 to 0.486	0.250	−0.395 to 0.895
Did you have trouble doing daily work around the house?	−2.485†	−3.455 to −1.515†	−2.020†	−2.950 to −1.089†	−0.711	−1.571 to 0.149
Did you need help taking a bath or shower?	−2.112†	−3.313 to −0.911†	−1.381†	−2.504 to −0.259†	0.291	−0.734 to 1.316

Negative scores indicate worse quality of life in women. BASIC indicates Brain Attack Surveillance in Corpus Christi; MD, mean difference; and SS-QoL, Stroke Specific Quality of Life Scale.

*Covariates included in models are described in Table 2.

†Statistically significant results.

Again, sensitivity analyses using multiple imputation (n=1334 participants) showed similar trends in the associations between sex and HRQoL subdomain scores, with minimal change in the magnitude for sex difference compared with the main findings (Table S4).

DISCUSSION

In our large population-based study, differences between women and men in HRQoL at 90 days after stroke were present, confirming previous findings.[2,3,12] Identifying the factors that contribute to the sex difference is important to inform clinical and policy decisions on ways to improve stroke management to ameliorate these differences that affect women. In this study, poorer HRQoL among women after stroke compared with men was mostly (62%) explained by sociodemographic (race and ethnicity, marital status, educational level) and prestroke function (prestroke mRS). Other important contributing factors included stroke risk factors (high BMI, smoking), presence of comorbidities (eg, history of stroke/transient ischemic attack, Alzheimer disease/dementia, congestive heart failure), and initial stroke severity. In our imputed analyses that accounted for missing data on HRQoL and covariates, prestroke cognitive function was an additional factor that confounded the association between sex and overall, physical, and psychological QoL after stroke. We tested the interactions between sex and all other covariates, but no significant interactions were observed. In this study, there was some evidence of residual differences in HRQoL between men and women after accounting for confounding factors, but they were small and unlikely to be clinically important. The current findings suggest that more intense and specific interventions could target subgroups of women who are at increased risk of poor QoL following stroke (eg, being older, socioeconomically disadvantaged, and functionally disabled) to improve their outcomes. Resilience has particular relevance for patients diagnosed with cardiovascular diseases, including stroke.[25] In addition to responding to the traumatic nature of the condition, patients are expected to navigate life after stroke including engaging in new behaviors such as adherence to medication, changing health behaviors (eg, diet, exercise), and adhering to rehabilitation programs, which may be more challenging for women who are more likely to be older, widowed, and have prestroke functional and cognitive deficits.[25] Targeted interventions to build and enhance resilience among women with stroke have potential to improve patient outcomes and reduce sex differences in HRQoL after stroke.

Consistent with the published literature, we identified that factors including age,[2,3,12] sociodemographics (eg, race,[5,26] marital status,[5] and education[5]), and prestroke physical function,[27] confounded the relationship

between sex and HRQoL. Among these factors, we observed that prestroke mRS accounted for the greatest attenuation in the magnitude of sex differences in all dimensions of HRQoL, which was followed by marital status and the presence of Alzheimer disease/dementia. Targeting modifiable cardiovascular disease risk factors before and after stroke, prevention of frailty,[28] and clinical management in elderly stroke survivors and those with functional limitations,[29] who are mostly women, could promote healthy aging and better stroke outcomes.[30,31] In our sensitivity analysis, prestroke depression was also found to confound the association between sex and HRQoL after stroke, although these results should be interpreted with caution given the degree of missing data. Strategies to more effectively manage comorbid depression may be one pathway to reducing stroke outcome disparities in women, but this requires further study.

Similar to the findings of previous research,[2,3,12] we found that stroke severity was an important confounder of the association between sex and HRQoL, although the difference between men and women in NIHSS scores was small. The minimal difference in stroke severity may be because the men and women in this study had similar distributions of age (median, men 66 versus women 69 years), and the median age among the study population was younger than other cohorts (67 versus 72 years).[32] By contrast, a meta-analysis of sex differences in stroke severity conducted on 8 population-based studies showed that women were 35% more likely to have severe ischemic strokes (NIHSS>7) compared with men.[32] The sex difference in severity was mostly explained by the fact that women were older than men (74.5 versus 70.0 years) when the stroke occurred.[32] Although insightful, these analyses only examined the sex difference in total NIHSS score but not subdomains. This limits our understanding about which aspects might impact women the most. The same score can be achieved with different deficits, and women who have different types of strokes affecting different function may have more of a HRQoL impact. Further research is needed to explore the roles of NIHSS subdomains on the association between sex and HRQoL after stroke.

Our study found that prestroke cognitive status (IQCODE) was potentially a contributing factor to the sex differences in HRQoL in our analyses accounting for missing data. This was because of women having greater mild and severe cognitive impairment before stroke compared with men. This finding is relevant in that research has shown that many adults with mild cognitive impairment, particularly older adults, might not receive evidence-based treatments for stroke, thus impacting their outcomes.[33] In contrast to our measure of prestroke cognitive function, other studies tended to measure cognitive impairment after stroke, which was found to be associated with poorer HRQoL following stroke.[26,34] Although poststroke cognitive impairment may reflect prestroke cognitive decline, it is possible that survivors of stroke may show no cognitive deficits or may decline, initially decline and then improve, remain stable, or progress to dementia over time.[35] Because prestroke cognitive performance is a potentially important indicator of outcomes,[36] we encourage the inclusion of prestroke cognitive assessment in future studies, particularly those focused on sex differences in HRQoL after stroke.[33]

When we examined the subdomains of HRQoL, we found that women, compared with men, had lower HRQoL related to difficulties in remembering things (psychological QoL). This finding was consistent with previous research.[37,38] The sex difference was not fully explained by prestroke factors and clinical factors, suggesting that other factors may contribute, such as poststroke mood disorders[12] and cognitive decline.[26,34] Further research is needed to understand why there are sex differences in the memory subdomain of HRQoL.

The study has several strengths. It was based on population-based stroke study that overcomes the limitation of selection bias of hospital-based studies.[39] We examined a wide range of potential factors that may contribute to the sex differences in HRQoL, particularly prestroke cognitive status, that are less often measured in stroke research, using a stroke-specific HRQoL instrument (SS-QoL). Several limitations should also be acknowledged. Because of a lack of information on clinically important difference for the short-form SS-QoL (12 items; score range, 1–5),[14] we used the rule of 0.5 SD[22] (eg, 0.55 for overall score SS-QoL; Tables S1 through S4) for determining if the sex differences in HRQoL were clinically meaningful, which has some limitations and may not reflect the true clinically important differences.[40] There is a possibility that self-reported HRQoL can vary across different populations; future studies should consider cultural and contextual factors to determine whether the sex differences in HRQoL are clinically meaningful. We performed multiple imputations to account for missing data on SS-QoL items and covariates (20.5%). The comparable results between imputed and complete-case analyses suggests that the possibility of bias is minimal but not fully eliminated. Poststroke depression has been found to be a potential contributing factor to sex differences in HRQoL[12]; however, we did not include this factor in our analyses because it was assessed at the same time as QOL. We did not have details of clinical treatments while in the hospital (except for intravenous thrombolysis) and other poststroke factors such as rehabilitation outcomes. It is noted that our previous analyses in the same study have reported poorer functional[13] and cognitive outcomes[41] at 90 days following stroke

among women compared with men, that were mostly explained by prestroke factors, but no statistically significant difference between sex in the prevalence of depression.[24]

CONCLUSIONS

We found that poorer overall QoL after stroke among women compared with men was mostly explained by sex differences in sociodemographics, prestroke functional limitations, and stroke severity. The findings suggest potential subgroups of women who might benefit from more targeted interventions before and after stroke to improve HRQoL.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Tables S1–S4
Figures S1–S3

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SUPPLEMENTAL MATERIAL

Table S1. Quality of life (n=1,061) of BASIC registrants, May 2010 – Dec 2016 for stroke

	All					Women		Men		p-value
Domain/Subdomain	**Median**	**IQR**	**Mean**	**SD**	**Clinically important difference ***	**Mean**	**SD**	**Mean**	**SD**	
Overall	3.25	(2.33, 4.25)	3.23	1.10	0.55	3.11	1.10	3.35	1.09	**0.0003**
Physical domain	2.67	(1.67, 3.83)	2.78	1.29	0.65	2.68	1.27	2.89	1.30	**0.0092**
Psychological domain	4.00	(2.83, 4.67)	3.67	1.16	0.58	3.53	1.17	3.82	1.13	**<.0001**
Psychological subdomain										
I felt I was a burden to my family.	3.00	(1.00, 5.00)	3.12	1.77	0.89	2.98	1.78	3.27	1.75	**0.0074**
My physical condition interfered with my social life.	2.00	(1.00, 5.00)	2.26	1.75	0.87	2.52	1.76	2.70	1.79	0.0946
I was too tired to do what I wanted to do.	2.00	(1.00, 5.00)	2.63	1.75	0.87	2.52	1.70	2.75	1.78	**0.0349**
I was discouraged about my future	2.00	(1.00, 5.00)	2.96	1.77	0.89	2.95	1.79	2.97	1.76	0.8548
My personality has changed	2.00	(1.00, 5.00)	2.94	1.74	0.87	2.85	1.74	3.02	1.73	0.1102
I had trouble remembering things	2.00	(1.00, 5.00)	2.44	1.65	0.82	2.27	1.58	2.62	1.70	**0.0006**
Physical subdomain										
Did you have to repeat yourself so others could understand you?	4.00	(3.00, 5.00)	3.84	1.24	0.62	3.82	1.27	3.86	1.21	0.6158
Did you have to stop and rest more than you would like when walking/using the wheelchair?	3.00	(1.00, 5.00)	3.33	1.40	0.70	3.14	1.40	3.53	1.37	**<.0001**
Did you have trouble buttoning buttons?	4.00	(2.00, 5.00)	3.63	1.57	0.78	3.49	1.60	3.77	1.52	**0.0048**
Did you have trouble seeing the television well enough to enjoy a show?	5.00	(5.00, 5.00)	4.46	1.09	0.55	4.43	1.13	4.50	1.04	0.2358
Did you have trouble doing daily work around the house?	3.00	(1.00, 5.00)	3.02	1.80	0.90	2.74	1.75	3.30	1.81	**<.0001**
Did you need help taking a bath or shower?	5.00	(2.00, 5.00)	3.75	1.70	0.85	3.57	1.73	3.93	1.65	**0.0004**

SD=Standard deviation; *0.5 SD; IQR=Interquartile range

Table S2. Impacts of covariables on aged-adjusted mean difference (MD) in quality of life (QoL) at 90 days after stroke for women compared to men using imputed results (n=1,334) using multiple imputation. Negative scores indicate worse QoL in women.

	Overall QoL				Physical QoL				Psychological QoL			
	MD	95%	CI	Δ(%)*	MD	95%	CI	Δ*	MD	95%	CI	Δ(%)*
Raw model	-0.248	-0.370	-0.125		-0.258	-0.424	-0.093		-0.308	-0.450	-0.165	
Age-adjusted model (1)	-0.208	-0.330	-0.086		-0.247	-0.414	-0.081		-0.232	-0.371	-0.095	
Model 1 + each covariate												
Marital status (other than married/living together)	-0.169	-0.293	-0.044	**19**	-0.204	-0.374	-0.034	**17**	-0.187	-0.329	-0.046	**19**
Ethnicity (MA)	-0.197	-0.317	-0.077	**5**	-0.236	-0.400	-0.071	**5**	-0.219	-0.355	-0.083	**6**
Education (≥ high school)	-0.190	-0.310	-0.070	**9**	-0.226	-0.390	-0.062	**8**	-0.213	-0.350	-0.077	**8**
BMI	-0.191	-0.314	-0.068	**8**	-0.218	-0.385	-0.051	**12**	-0.219	-0.358	-0.080	**6**
Alzheimer/Dementia	-0.182	-0.302	-0.063	**12**	-0.223	-0.387	-0.058	**10**	-0.201	-0.336	-0.067	**13**
CAD/MI	-0.226	-0.349	-0.103	**-9**	-0.274	-0.441	-0.107	**-11**	-0.245	-0.385	-0.106	**-6**
Comorbidity index (>3)	-0.244	-0.364	-0.124	**-18**	-0.296	-0.459	-0.132	**-20**	-0.267	-0.404	-0.130	**-15**
IQCODE, categorical	-0.199	-0.320	-0.078	**5**	-0.235	-0.400	-0.070	**5**	-0.226	-0.363	-0.089	3
Pre-stroke mRS (>2)	-0.102	-0.218	0.013	**51**	-0.141	-0.303	0.021	**43**	-0.101	-0.229	0.027	**56**
Current/former smoker	-0.232	-0.356	-0.107	**-11**	-0.284	-0.454	-0.115	**-15**	-0.249	-0.390	-0.107	**-7**
Congestive heart failure	-0.186	-0.308	-0.065	**10**	-0.226	-0.391	-0.060	**9**	-0.207	-0.343	-0.070	**11**
History of stroke/TIA	-0.197	-0.316	-0.077	**5**	-0.234	-0.398	-0.071	**5**	-0.220	-0.356	-0.085	**5**
COPD	-0.205	-0.327	-0.083	1	-0.245	-0.411	-0.079	1	-0.231	-0.369	-0.092	1
High cholesterol	-0.208	-0.330	-0.086	0	-0.248	-0.414	-0.082	0	-0.233	-0.371	-0.094	0
Health insurance	-0.209	-0.331	-0.087	0	-0.247	-0.414	-0.081	0	-0.235	-0.373	-0.097	-1
Hypertension	-0.214	-0.335	-0.093	-3	-0.257	-0.422	-0.092	-4	-0.237	-0.375	-0.099	-2
Diabetes	-0.204	-0.325	-0.083	2	-0.244	-0.409	-0.079	1	-0.228	-0.365	-0.091	2
Cancer	-0.208	-0.330	-0.086	0	-0.247	-0.413	-0.080	0	-0.234	-0.372	-0.095	-1
Atrial fibrillation	-0.207	-0.329	-0.085	0	-0.247	-0.413	-0.081	0	-0.232	-0.370	-0.094	0
Stroke severity; ln(NIHSS+1)	-0.166	-0.282	-0.050	**20**	-0.210	-0.373	-0.048	**15**	-0.179	-0.307	-0.050	**23**
Intravenous thrombolysis	-0.209	-0.331	-0.087	0	-0.250	-0.416	-0.083	-1	-0.233	-0.372	-0.095	-1

Table S2. Impacts of covariables on aged-adjusted mean difference (MD) in quality of life (QoL) at 90 days after stroke for women compared to men using imputed results (n=1,334) using multiple imputation. Negative scores indicate worse QoL in women.

	Overall QoL				Physical QoL				Psychological QoL			
	MD	95%	CI	Δ(%)*	MD	95%	CI	Δ*	MD	95%	CI	Δ(%)*
Model 1 + ethnicity, marital status, education (2)	-0.151	-0.273	-0.029	**28**	-0.184	-0.352	-0.017	**25**	-0.167	-0.305	-0.028	**28**
Model 2 + pre-stroke mRS, IQCODE (3)	-0.078	-0.194	0.038	**63**	-0.112	-0.276	0.052	**55**	-0.075	-0.204	0.054	**68**
Model 3 + significant risk factors/comorbidities (3)	-0.064	-0.179	0.052	**69**	-0.131	-0.299	0.037	**47**	-0.060	-0.187	0.066	**74**
Model 4 + ln (NIHSS+1)	-0.038	-0.149	0.074	**82**	-0.109	-0.275	0.056	**56**	-0.028	-0.148	0.091	**88**
Full model†	-0.038	-0.149	0.074	**82**	-0.109	-0.275	0.056	**56**	-0.028	-0.148	0.091	**88**

NIHSS=National Institutes of Health Stroke Scale; mRS: modified Rankin score; CAD=Coronary artery disease; MI=Myocardial infarction; TIA=transient ischemic attack; MA=Mexican Americans; COPD=chronic obstructive pulmonary disease

* % change of coefficient of sex difference (age-adjusted β – covariate-adjusted β) / age-unadjusted β *100

† Full model included sex, age, ethnicity, and potential confounders (being associated with QoL, associated with sex, and Δ ≥5%) that are bold in column Δ

Table S3. Sensitivity analysis limiting those with pre-stroke depression data. Impacts of covariates on aged-adjusted mean difference (MD) in quality of life (QoL) at 90 days after stroke for women compared to men using tobit regression. Negative scores indicate worse QoL in women (n=828)

	Overall QoL				Physical QoL				Psychological QoL			
	MD	95%	CI	Δ(%)*	MD	95%	CI	Δ(%)*	MD	95%	CI	Δ(%)*
Raw model	-0.212	-0.353	-0.07	NA	-0.254	-0.462	-0.045	N/A	-0.246	-0.393	-0.098	NA
Base model: Age-adjusted model (1)	-0.205	-0.347	-0.063	NA	-0.266	-0.475	-0.056	N/A	-0.22	-0.367	-0.073	NA
Model 1 + each covariate												
Marital status (other than married/living together)	-0.143	-0.289	0.002	**30**	-0.199	-0.413	0.016	**25**	-0.151	-0.3	-0.001	**31**
Ethnicity (MA)	-0.206	-0.346	-0.065	0	-0.267	-0.475	-0.059	-1	-0.22	-0.365	-0.076	0
Education (≥ high school)	-0.193	-0.334	-0.053	**6**	-0.252	-0.458	-0.046	**5**	-0.208	-0.353	-0.064	5
BMI	-0.175	-0.317	-0.032	**15**	-0.225	-0.436	-0.015	**15**	-0.188	-0.335	-0.041	**15**
Alzheimer/Dementia	-0.2	-0.342	-0.058	3	-0.258	-0.466	-0.049	3	-0.216	-0.362	-0.069	2
Depression	-0.077	-0.219	0.065	**62**	-0.066	-0.273	0.141	**75**	-0.125	-0.274	0.024	**43**
CAD/MI	-0.229	-0.372	-0.086	**-12**	-0.298	-0.508	-0.088	**-12**	-0.235	-0.383	-0.087	-7
Comorbidity index (>3)	-0.239	-0.378	-0.1	**-17**	-0.311	-0.516	-0.106	**-17**	-0.249	-0.397	-0.105	**-13**
IQCODE, categorical	-0.21	-0.351	-0.069	-3	-0.27	-0.478	-0.063	-2	-0.228	-0.374	-0.082	-4
Pre-stroke mRS (>2)	-0.106	-0.242	0.03	**48**	-0.141	-0.353	0.055	**47**	-0.112	-0.251	0.026	**49**
Current/former smoker	-0.238	-0.383	-0.093	**-16**	-0.31	-0.522	-0.097	**-17**	-0.249	-0.398	-0.099	**-13**
Congestive heart failure	-0.184	-0.324	0.043	**10**	-0.244	-0.452	-0.036	**8**	-0.193	-0.336	-0.051	**12**
History of stroke/TIA	-0.196	-0.335	-0.057	4	-0.255	-0.461	-0.049	4	-0.21	-0.353	-0.068	4
COPD	-0.197	-0.339	-0.055	4	-0.258	-0.467	-0.048	3	-0.211	-0.357	-0.065	4
High cholesterol	-0.204	-0.347	-0.062	0	-0.265	-0.473	-0.056	0	-0.22	-0.366	-0.073	0
Health insurance	-0.205	-0.348	-0.063	0	-0.266	-0.475	-0.057	0	-0.22	-0.367	-0.074	0
Hypertension	-0.213	-0.355	-0.071	-4	-0.277	-0.486	-0.069	-4	-0.225	-0.371	-0.079	-2
Diabetes	-0.217	-0.358	-0.077	**-6**	-0.281	-0.488	-0.074	**-6**	-0.232	-0.377	-0.087	**-6**
Cancer	-0.202	-0.344	-0.059	2	-0.261	-0.47	-0.052	2	-0.218	-0.365	-0.072	1
Atrial fibrillation	-0.207	-0.349	-0.064	-1	-0.268	-0.477	-0.059	-1	-0.221	-0.368	-0.076	-1
Stroke severity; ln(NIHSS+1)	-0.17	-0.309	-0.031	**17**	-0.227	-0.433	-0.021	**15**	-0.181	-0.323	-0.04	**18**
Intravenous thrombolysis	-0.203	-0.346	-0.061	1	-0.263	-0.472	-0.054	1	-0.219	-0.365	-0.072	1

Table S3. Sensitivity analysis limiting those with pre-stroke depression data. Impacts of covariates on aged-adjusted mean difference (MD) in quality of life (QoL) at 90 days after stroke for women compared to men using tobit regression. Negative scores indicate worse QoL in women (n=828)

	Overall QoL				Physical QoL				Psychological QoL			
	MD	95%	CI	Δ(%)*	MD	95%	CI	Δ(%)*	MD	95%	CI	Δ(%)*
Model 1 + race/ethnicity, marital status, education (2)	-0.138	-0.281	0.004	**32**	-0.192	-0.403	0.019	**28**	-0.146	-0.293	0.002	**33**
Model 2 + pre-stroke mRS, IQCODE (3)	-0.078	-0.215	0.059	**62**	-0.125	-0.331	0.081	**53**	-0.075	-0.215	0.064	**66**
Model 3 + significant risk factors/comorbidities bolded in column Δ: (4)	-0.025	-0.166	0.116	**88**	-0.021	-0.163	0.121	**92**	-0.048	-0.192	0.097	**78**
Model 4 + ln (NIHSS+1) (5)	0.004	-0.134	0.142	**102**	-0.007	-0.131	0.144	**98**	-0.018	-0.158	0.122	**92**
Full model† (6)	0.004	-0.134	0.142	**102**	-0.007	-0.131	0.144	**98**	-0.018	-0.158	0.122	**92**

NIHSS=National Institutes of Health Stroke Scale; mRS: modified Rankin score; CAD=Coronary artery disease; MI=Myocardial infarction; TIA=transient ischemic attack; MA=Mexican Americans; COPD=chronic obstructive pulmonary disease

*% change of coefficient of sex difference (age-adjusted β – covariate-adjusted β) / age-unadjusted β *100

†Full model included sex, age, race/ethnicity, pre-stroke mRS and IQCODE, stroke severity, and all the identified confounding factors (Δ ≥5%) that are bolded in column Δ: marital status, education, pre-stroke mRS, BMI, Depression, CAD/MI, Comorbidity index (>3), current/former smoker, congestive heart failure, and diabetes

Table S4. Sex difference in specific SSQoL items in BASIC project on the imputed data set, May 2010 – Dec 2016 for stroke (n=1,334) using multiple imputation

Items	Unadjusted			Age-adjusted			Fully-adjusted model*		
	MD	95% CI		MD	95% CI		MD	95% CI	
Psychological Quality of life									
I felt I was a burden to my family.	**-0.978**	**-1.613**	**-0.343**	**-0.986**	**-1.625**	**-0.348**	-0.464	-1.120	0.191
My physical condition interfered with my social life.	-0.617	-1.407	0.173	-0.469	-1.260	0.322	0.234	-0.562	1.030
I was too tired to do what I wanted to do.	**-0.771**	**-1.445**	**-0.096**	**-0.713**	**-1.391**	**-0.036**	-0.241	-0.931	0.449
I was discouraged about my future	-0.057	-0.695	0.581	-0.093	-0.734	0.549	0.393	-0.271	1.057
My personality has changed	-0.534	-1.117	0.049	-0.562	-1.148	0.023	-0.380	-0.986	0.226
I had trouble remembering things	**-1.073**	**-1.614**	**-0.533**	**-0.978**	**-1.519**	**-0.437**	**-0.789**	**-1.341**	**-0.236**
Physical Quality of Life									
Did you have to repeat yourself so others could understand you?	-0.020	-0.268	0.227	0.018	-0.229	0.266	0.218	-0.022	0.457
Did you have to stop and rest more than you would like when walking/using the wheelchair?	**-0.565**	**-0.817**	**-0.314**	**-0.481**	**-0.730**	**-0.232**	-0.208	-0.445	0.029
Did you have trouble buttoning buttons?	**-0.573**	**-1.047**	**-0.098**	-0.354	-0.819	0.111	0.219	-0.231	0.670
Did you have trouble seeing the television well enough to enjoy a show?	-0.115	-0.626	0.395	-0.013	-0.526	0.500	0.354	-0.172	0.881
Did you have trouble doing daily work around the house?	**-2.257**	**-3.055**	**-1.459**	**-1.857**	**-2.625**	**-1.089**	-0.696	-1.410	0.017
Did you need help taking a bath or shower?	**-2.174**	**-3.201**	**-1.147**	**-1.448**	**-2.404**	**-0.492**	0.028	-0.848	0.904

MD: mean difference; Negative scores indicate worse quality of life in women

*covariates included in models were those changed the magnitude of the MD by 5%

Figure S1. Distribution of quality of life (QoL) scores (total, physical and mental) of BASIC registrants, May 2010 – Dec 2016 for stroke

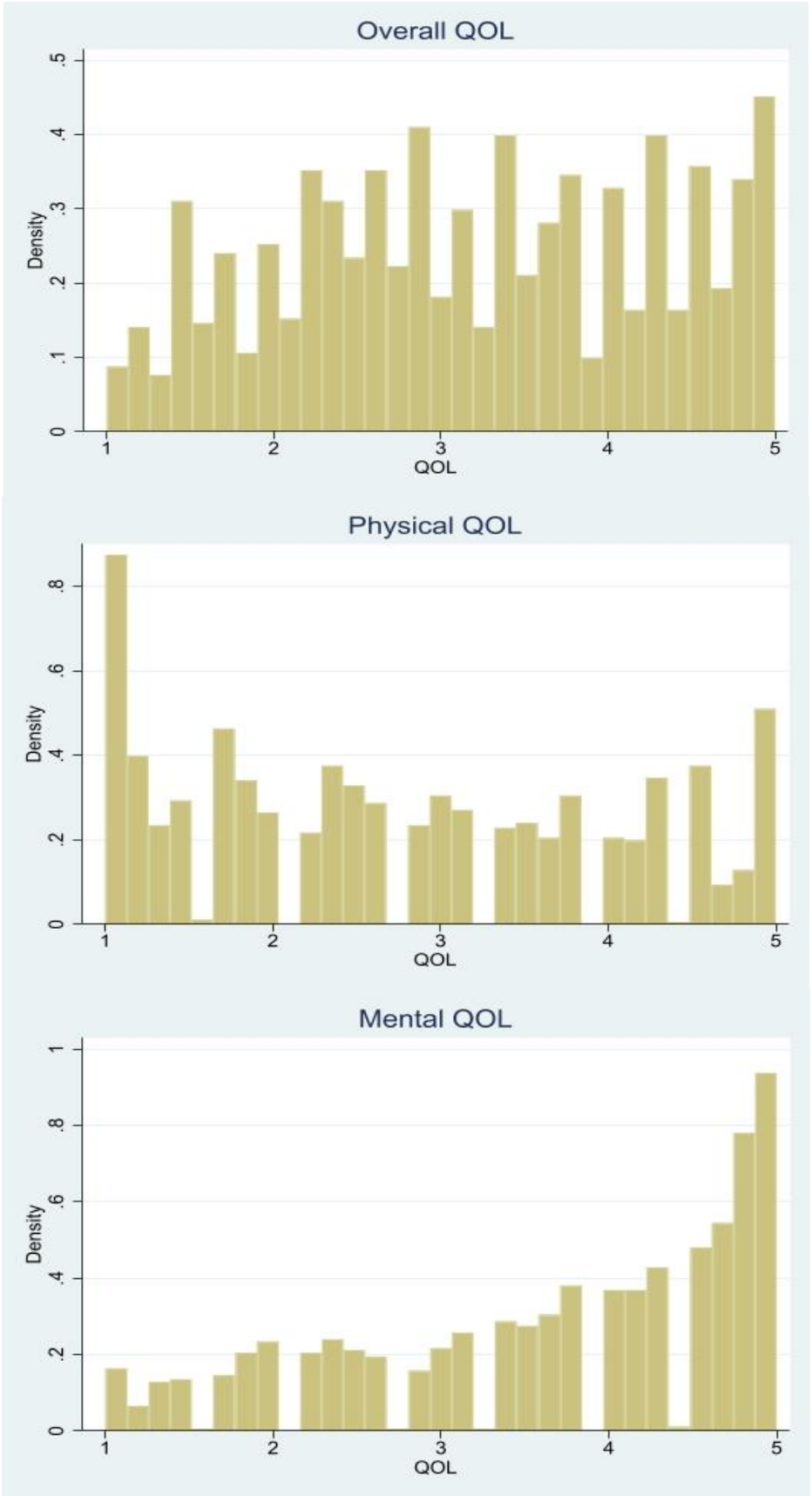

Figure S2. Sample construction and attrition, Brain Attack Surveillance in Corpus Christi project (BASIC), United States, May 2010– Dec 2016

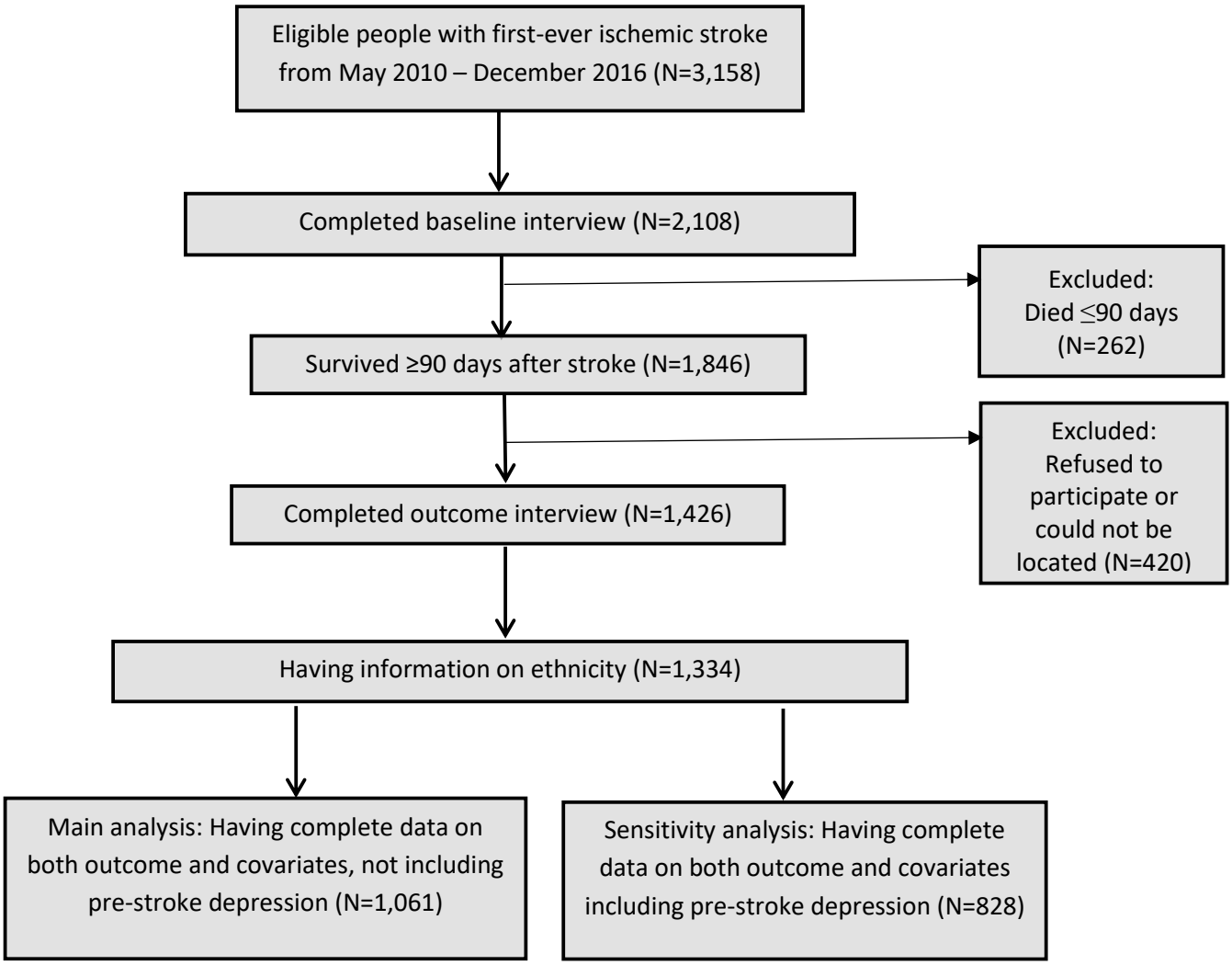

Figure S3. Impacts of covariates on aged-adjusted mean difference in overall quality of life at 90 days after stroke for women compared to men (--- denoting 5% change; ● denoting covariates meeting criteria for being confounding factors; - denoting covariates not meeting criteria for being confounders). mRS: modified Rankin score; CAD=Coronary artery disease; MI=Myocardial infarction; TIA=transient ischemic attack; COPD=chronic obstructive pulmonary disease; BMI=Body mass index