Vascular Health and Risk Management

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Costs and outcomes of noncardioembolic ischemic stroke in a managed care population

This article was published in the following Dove Press journal:
Vascular Health and Risk Management
5 October 2010
Number of times this article has been viewed

Nicole M Engel-Nitz[1]
Stephen D Sander[2]
Carolyn Harley[3]
Gabriel Gomez Rey[1]
Hemal Shah[2]

[1]Health Economic and Outcomes Research, i3 Innovus, Eden Prairie, MN, USA; [2]Health Economic and Outcomes Research, Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA; [3]Health Economic and Outcomes Research, i3 Innovus, Palo Alto, CA, USA

Purpose: To evaluate the clinical outcomes and incremental health care costs of ischemic stroke in a US managed care population.

Patients and methods: A retrospective cohort analysis was done on patients (aged 18+ years) hospitalized with noncardioembolic ischemic stroke from January 1, 2002, through December 31, 2003, identified from commercial health plan administrative claims. New or recurrent stroke was based on history in the previous 12 months, with index date defined as first date of indication of stroke. A control group without stroke or transient ischemic attack (TIA) was matched (1:3) on age, sex, and geographic region, with an index date defined as the first medical claim during the patient identification period. Patients with atrial fibrillation or mitral value abnormalities were excluded. Ischemic stroke and control cohorts were compared on 4-year clinical outcomes and 1-year costs.

Results: Of 2180 ischemic stroke patients, 1808 (82.9%) had new stroke and 372 (17.1%) had a recurrent stroke. Stroke patients had higher unadjusted rates of additional stroke, TIA, and fatal outcomes compared with the 6540 matched controls. Recurrent stroke patients had higher rates of adverse clinical outcomes compared with new stroke patients; costs attributed to recurrent stroke were also higher. Stroke patients were 2.4 times more likely to be hospitalized in follow-up compared with controls (hazard ratio [HR] 2.4, 95% confidence interval [CI]: 2.2, 2.6). Occurrence of stroke following discharge was 21 times more likely among patients with index stroke compared with controls (HR 21.0, 95% CI: 16.1, 27.3). Stroke was also predictive of death (HR 1.8, 95% CI: 1.3, 2.5). Controlling for covariates, stroke patients had significantly higher costs compared with control patients in the year following the index event.

Conclusion: Noncardioembolic ischemic stroke patients had significantly poorer outcomes and higher costs compared with controls. Recurrent stroke appears to contribute substantially to these higher rates of adverse outcomes and costs.

Keywords: burden of illness, stroke/cerebrovascular accident, cardiovascular disease, claims analysis, costs of care, health care outcomes

Background

Stroke is a major cause of serious, long-term disability, mortality, and institutionalization, and it accounts for substantial use of health care resources.[1–4] When considered separately from other cardiovascular diseases, stroke ranks third among all causes of death, following diseases of the heart and cancer.[5] Among survivors, ~15%–30% are permanently disabled and 20% require institutional care 3 months after onset.[6] As a result, stroke imposes a significant economic impact, with stroke-related costs making up as much as 3%–4% of the annual national health care budget.[1,2] For 2009, the estimated direct and indirect cost of stroke in the United States was $68.9 billion.[6]

Correspondence: Nicole M Engel-Nitz
i3 Innovus, Health Economic and Outcomes Research, An Ingenix Company, 12125 Technology Drive, Eden Prairie, MN 55344, USA
Tel +1 952 833 8048
Fax +1 952 833 6045
Email nicole.engel-nitz@i3innovus.com

submit your manuscript | www.dovepress.com
Dovepress
DOI: 10.2147/VHRM.S10851

The burden of stroke is often measured in terms of the incidence rates of first stroke, but the prevalence of total stroke (ie, first stroke plus recurrent stroke) more accurately reflects the true burden.[7,8] Nearly 30% of all strokes are recurrent events, and the risk is highest in the period immediately following a stroke.[9] It has been estimated that within 1 year after the first stroke, the risk of recurrence is 15 times the risk of stroke in the general population.[10] Of those who have had first stroke, the percentages of men and women aged 40–69 years with a recurrent stroke in 5 years are 13% and 22%, respectively. At the age of 70 years, the risk of recurrent stroke is 23% in men and 28% in women.[6] This suggests that prevention of stroke recurrence must be a primary goal of acute and long-term management of stroke.[11]

Recurrent strokes tend to inflict greater neurological impairment and more severe disability than the first stroke, and patients with recurrent strokes tend to have poorer health and economic outcomes than those with first strokes.[7,9,12] In a Medicare claims-based analysis conducted by Samsa et al[7] survival from first stroke (56.7% at 24 months) was consistently better than that for recurrent stroke (48.3% at 24 months). In addition, patients with recurrent stroke had significantly higher health care costs following their stroke compared with patients with first stroke.

Although the literature provides some evidence of the incremental costs and adverse clinical outcomes associated with recurrent stroke in a Medicare patient population, the extent to which the findings apply to a younger, commercially insured population has not been fully explored. This claims-based retrospective analysis was designed to evaluate clinical outcomes and costs associated with noncardioembolic ischemic stroke compared with the general managed care population. Furthermore, the study explored the relative impact of new versus recurrent stroke.

Methods

Data source

This was a retrospective administrative claims data study using eligibility, medical, and pharmacy claims data from a large US managed care plan affiliated with i3 Innovus. The individuals covered by this health plan were geographically diverse across the United States, with enrollees in all four US Census regions. The plan provides fully insured coverage for physician, hospital, and prescription drug services. The data are linked longitudinally using an encrypted patient ID.

The database contained enrollment and claims data for 10.7 million commercial health plan enrollees during the identification period of January 1, 2002, through December 31, 2003. Claims data for the assessment of patient characteristics and outcomes among those identified and retained for analysis ranged from January 1, 2001, through December 31, 2005.

Sample selection

Patients were selected for the ischemic stroke cohort if they were aged at least 18 years, were hospitalized for ischemic stroke during the 2-year identification period, and had no diagnostic evidence during the identification period of atrial fibrillation (AF) or mitral valve abnormalities (ICD-9-CM codes 427.31, 746.5, 396.0, 396.1, 394.2, 394.0, 424.0, 391.1, 392.0, 398.90, 398.99). Inpatient hospital claims were examined for evidence of stroke based on a qualifying diagnosis code (ICD-9-CM codes 362.31–362.34, 430.xx–432.xx, 433.x1, 434.x1, 436.xx, and 438.xx) in the primary diagnosis position on a claim.[7] Patients were included in the stroke cohort if they had a diagnosis for ischemic stroke; patients without ischemic stroke either during the index hospitalization or during the pre-index period were excluded. Patients were categorized as new ischemic stroke patients if the hospitalization was for ischemic stroke and there was no evidence of any prior stroke during the pre-index period. Patients were categorized as recurrent stroke patients if there was evidence of ischemic stroke in the 12-month period prior to the index stroke hospitalization (pre-index period). Qualifying stroke patients were required to be continuously enrolled in the health plan with medical and pharmacy benefits for 12 months prior to the admission date for the index hospitalization. Variable follow-up observation was permitted until the earliest of death (identified from discharge hospital claims), 48 months of observation, or December 31, 2005.

A general population of adult control subjects with at least 1 month of enrollment during the identification period was randomly selected from the database. An index date was set based on the first service date on a medical claim during the patient identification period. Potential controls were retained if they met the 12-month pre-index continuous enrollment requirement and had no evidence of stroke, transient ischemic attack (TIA), AF, or mitral valve abnormalities during the pre-index period. The non stroke control population was matched 3:1 to stroke patients on age, sex, and geographic region.

Outcome variables

Outcomes were measured in the claims data during the variable follow-up period from the day following discharge among stroke patients or control patients with an index hospitalization, or from the index date among control patients not hospitalized on index. Two types of outcomes were analyzed for this study. First, clinical outcomes including hospitalization, stroke, TIA, and death were assessed in the variable follow-up period (up to 4 years). Second, index hospitalization, medical, pharmacy, and total costs of health care services were examined in the year following stroke. Costs were calculated as the patient and health plan paid amounts for services delivered (regardless of direct relationship to the condition of 'stroke') in the 12 months following discharge or index date among those with no hospitalization on index. Costs were adjusted to 2005 values based on the medical component of the Chained Consumer Price Index[13] and were converted to a per-patient-per-year measure to account for the variable observation in the 12 months following the index date.

Independent variables

Stroke and control cohorts were the primary variable of interest. In addition, age, gender, and US Census region in which the patient lived were derived from the enrollment data. Claims from the pre-index period were assessed for evidence of comorbid illnesses, specifically hypertension, diabetes, TIA, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), and myocardial infarction (MI).

Statistical methods

Bivariate comparisons between the stroke cohort and the control cohort were conducted for all study variables. For comparison of mean, *t*-tests were used for continuous measures and χ^2 tests of differences in proportions were used for dichotomous or ordinal variables. All results are also shown for new and recurrent stroke patients, although no testing was performed. Costs, mortality, additional stroke, and additional hospitalization were further analyzed using appropriate multivariable statistical methods. Time to hospitalization, time to stroke, and time to death were analyzed using time-to-event analysis techniques to allow for differing follow-up times. Specifically, Cox proportional hazard models were estimated and Kaplan–Meier curves were presented for each of these outcomes. Wilcoxon and Log-rank tests were performed for the Kaplan–Meier analyses to test for differences across the cohorts. Tests of the proportionality assumption were performed for the Cox proportional hazards models to determine whether the hazards remained constant over time.

Medical or pharmaceutical costs are difficult to model because of the skewed nature of the distribution of costs (ie, many subjects have minimal or no costs during the study period whereas a few subjects have extremely high costs). Therefore, to compensate for the skewed distribution, we estimated costs using a generalized linear model with gamma distribution and log link. For the disease cohort variable, the coefficients from the generalized linear modeling specification represent the ratio of expected costs in the disease cohort versus the control cohort. This method avoids potential difficulties introduced by transformation (eg, calculating the log of the costs) and retransformation of the dependent variable.[14] Independent variables included the presence of stroke during the baseline period, age, gender, geographic region, and comorbid illness. Interaction terms between age and gender were tested and included in the models where statistically significant.

SAS software (v. 8.2; SAS Institute Inc., Cary, NC) was used for creation of the analytic dataset and descriptive analyses, and STATA software (v. 9; StataCorp LP, College Station, TX) was used for multivariate analyses.

Results

Patient characteristics

Of the 10.7 million health plan enrollees in the research database during the identification period from January 1, 2002, to December 31, 2003, 39,446 patients were identified with ischemic stroke, hemorrhagic stroke, unknown stroke, or TIA. From this group, patients were excluded due to mitral valve abnormality, AF, age, application of the 12-month pre-index continuous enrollment requirement, and finally down to patients with ischemic stroke on the index date. These patients were then matched 3:1 to controls. The final sample retained 2180 ischemic stroke patients, including 1808 new stroke patients and 372 recurrent stroke patients, and 6540 control patients.

Table 1 shows the demographic and baseline characteristics of the study cohorts. Mean age of both the stroke and control cohorts was 59 (SD 13) years. More than half of all study patients were 55 years of age or older. Men represented 58.49% of the stroke and control cohorts. Within the stroke cohort, new stroke patients were more likely to be male (59.07%) compared with the recurrent stroke patients (55.65%). The recurrent stroke subgroup had a larger percentage of patients 65 years of age or older. The distribution across the four geographic regions was similar between the stroke and control cohorts, and across new and recurrent stroke patients; reflective of the distribution of the research database population, the majority of the patients were either from the Midwest (41.4%) or South (40.4%).

Table 1 Demographic characteristics

	Stroke cohort (N = 2180)	New stroke (N = 1808)	Recurrent stroke (N = 372)	Control cohort (N = 6540)
Days of observation, mean ± SD	571 ± 433*	587 ± 432	489 ± 429	900 ± 446
Pre-index costs, mean ± SD	$8085 ± $17,340*	$7014 ± $16,054	$13,293 ± $21,860	$3142 ± $7264
Age, mean ± SD	59 ± 13	59 ± 13	60 ± 13	59 ± 13
Age group, n (%)				
18–24	13 (0.6)	12 (0.7)	1 (0.3)	39 (0.6)
25–34	51 (2.3)	42 (2.3)	9 (2.4)	153 (2.3)
35–44	190 (8.7)	159 (8.8)	31 (8.3)	570 (8.7)
45–54	513 (23.5)	433 (24.0)	80 (21.5)	1539 (23.5)
55–64	794 (36.4)	665 (36.8)	129 (34.7)	2382 (36.4)
65+	619 (28.4)	497 (27.5)	122 (32.8)	1857 (28.4)
Sex, n (%)				
Female	905 (41.5)	740 (40.9)	165 (44.35)	2715 (41.5)
Male	1275 (58.5)	1068 (59.1)	207 (55.65)	3825 (58.5)
Region, n (%)				
Northeast	220 (10.1)	185 (10.2)	35 (9.41)	659 (10.1)
Midwest	902 (41.4)	748 (41.4)	154 (41.40)	2705 (41.4)
South	880 (40.4)	724 (40.0)	156 (41.94)	2641 (40.4)
West	178 (8.2)	151 (8.4)	27 (7.26)	535 (8.2)
Comorbid illness, n (%)				
Hypertension	1179 (54.1)*	908 (50.2)	271 (72.9)	1838 (28.1)
Diabetes	602 (27.6)*	481 (26.6)	121 (32.5)	654 (10.0)
TIA	196 (9.0)*	83 (4.6)	113 (30.3)	62 (1.0)
COPD	189 (8.7)*	134 (7.4)	55 (14.8)	250 (3.8)
CHF	138 (6.3)*	84 (4.7)	54 (14.5)	160 (2.5)
MI	54 (2.5)*	26 (1.4)	28 (7.5)	42 (0.6)

Notes: All comparisons are relative to the control cohort and are computed by *t*-test for continuous measures or χ^2 test for dichotomous or ordinal measures. *$P < 0.001$.
Abbreviations: CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; TIA, transient ischemic attack.

Length of follow-up varied widely between the cohorts. Controls had the longest average follow-up available with 900 (SD 446) days compared with 571 (SD 433) days for the stroke cohort ($P < 0.001$). Within the stroke cohort, new stroke patients averaged 587 (SD 432) days of follow-up, and recurrent stroke patients averaged 489 (SD 429) days of follow-up.

The stroke cohort was significantly more likely to have pre-existing comorbid disease compared with the control cohort. Hypertension was common, present in 54.1% of stroke patients, compared with 28.10% of control patients ($P < 0.001$). Diabetes was also highly prevalent, identified in 27.6% of stroke patients compared with 10.0% of controls ($P < 0.001$). All comorbid conditions were more prevalent in recurrent stroke patients compared with new stroke patients.

Unadjusted analysis

Stroke patients had a significantly higher rate of incident hospitalization during follow-up compared with controls. A total of 752 (34.5%) stroke patients were hospitalized in follow-up for a rate of 307 incident hospitalizations per 1000 patient-years. Comparatively, 21.2% of control patients were hospitalized at a rate of 100 per 1000 patient-years. Patients with recurrent stroke had the highest rate of hospitalization (382 incident hospitalizations per 1000 patient-years) compared with new stroke patients, who had 294 incident hospitalizations per 1000 patient-years. A total of 340 stroke patients (15.6%) experienced a subsequent stroke following index hospital discharge for an incident rate of 115 strokes per 1000 patient-years. This was a substantially higher rate compared with the control patients (5 strokes per 1000 patient-years). The rate of fatal stroke was 6 per 1000 patient-years for all stroke patients compared with <1 for control subjects. Among recurrent stroke patients, additional stroke had an incident rate of 165 per 1000 patient-years, whereas fatal strokes had an incident rate of 8 per 1000 patient-years. New stroke patients were comparatively less likely to experience an additional stroke (107 strokes and 5 fatal strokes per 1000 patient-years).

The incidence of post-index date TIA was higher among stroke patients than that in controls (186 incident TIA events versus 9 incident TIA events per 1000 patient-years). Similarly, the rates of MI and fatal MI were higher among stroke patients compared with general-population controls (11 incident MIs versus 6 incident MIs per 1000 patient-years; 2 fatal MIs versus <1 fatal MI per 1000 patient-years); however, this did not reach statistical significance. Recurrent stroke patients had the highest risk of all-cause mortality (86 deaths per 1000 patient-years), followed by new stroke patients and controls (37 deaths and 4 deaths per 1000 patient-years, respectively) (Table 2).

The average cost of index hospitalization was $15,634 (SD $27,536) for new stroke patients and $17,121 (SD $53,693) for recurrent stroke patients (Table 3). Among the 168 (2.6%) patients in the control cohort with a hospitalization on the index date, the average cost of hospitalization was $11,281 (SD $29,052). Patients in the stroke cohort had significantly greater costs in the first year following the index event compared with controls. Medical costs averaged $23,725 (SD $58,227) per stroke patient compared with an average of $5142 (SD $16,619) per control. Similarly, pharmacy costs averaged $2950 (SD $3549) per stroke patient compared with an average of $1388 ($2302) per control. Total combined costs were $26,675 (SD $58,605) per stroke patient per year. Recurrent stroke patients had 38% higher costs compared with new stroke patients, averaging $34,639 per patient in the first year following discharge from the index hospitalization compared with $25,036 per new stroke patient.

Adjusted analysis

After adjusting for covariates, results from the Cox proportional hazards model suggested that stroke patients were 2.4 times more likely to be hospitalized in follow-up compared with control subjects (HR 2.4; 95% CI: 2.2–2.6) (Table 4). Older age was associated with a greater risk of hospitalization, with a 2% increase in hazard of being hospitalized for each additional year of age ($P < 0.001$). Patients who were male and who lived in the Northeast had a lower hazard of being hospitalized by 8% (95% CI: 0.8, 1.0) and 13% (95% CI: 0.7, 1.0), respectively. In addition, patients with pre-index comorbid conditions had higher hazards of being hospitalized over the follow-up compared to patients without these conditions. Specifically, the hazard of hospitalization was higher by 26% for hypertension (95% CI: 1.1, 1.4), 28% for diabetes (95% CI: 1.1, 1.4), and 29% for TIA (95% CI: 1.1, 1.4). Patients with COPD faced even higher increases in the risk of hospitalization, with a 57% increased hazard compared to patients without COPD (95% CI: 1.3, 1.8). CHF and MI also conferred additional risk of hospitalization by 79% and 50%, respectively (CHF 95% CI: 1.5, 2.1; MI 95% CI: 1.1, 2.1). Cox proportional hazards model results indicated that occurrence of stroke following discharge was 21 times more likely among stroke patients compared with control subjects (95% CI: 16.1–27.3) (Table 5). No other covariates were significant predictors of subsequent stroke in this model. Being in the stroke cohort was predictive of death in follow-up after adjusting for covariate (Table 6); stroke patients were 1.8 times more likely to die in follow-up compared with control patients (95% CI: 1.3–2.5). Diagnosis of TIA in the pre-index period was the only other covariate that was statistically significant in the model; patients with pre-index TIA had a hazard of dying that was 2.3 times that of patients without prior TIA (95% CI: 1.3, 4.0).

Stroke patients had significantly higher costs compared with control patients in the year following the index event controlling for age, gender, region, and comorbid conditions (Table 7). Total costs were 3.8 times higher among stroke patients compared with control patients, ranging from 3.4 times to 4.3 times higher ($P < 0.001$). Compared to patients without these comorbid condition, hypertension, diabetes, COPD, and CHF, all were associated with higher costs in follow-up, with cost ratios ranging from 1.2 higher

Table 2 Unadjusted rates of clinical events during follow-up period

Patients with an event (%) [rate per 1000 patient-years]	Total ischemic stroke cohort (*N* = 2180)	New stroke (N = 1808)	Recurrent stroke (*N* = 372)	Control cohort (N = 6540)
Hospitalization	752 (34.5) [307]	619 (34.2) [294]	133 (35.8) [382]	1387 (21.2) [100]
Any stroke	340 (15.6) [115]	272 (15.0) [107]	68 (18.3) [165]	73 (1.1) [5]
Fatal stroke	19 (0.9) [6]	15 (0.8) [5]	4 (1.1) [8]	3 (0.1) [0]
Hemorrhagic stroke	45 (2.1) [13]	33 (1.8) [12]	12 (3.2) [25]	14 (0.2) [1]
Fatal hemorrhagic stroke	5 (0.2) [1]	4 (0.2) [1]	1 (0.3) [2]	1 (0.0) [0]
TIA	483 (22.1) [186]	388 (21.5) [173]	95 (25.5) [266]	138 (10.0) [9]
MI	38 (1.7) [11]	32 (1.8) [11]	6 (1.6) [12]	101 (1.5) [6]
Fatal MI	7 (0.3) [2]	5 (0.3) [2]	2 (0.5) [4]	5 (0.1) [0]
All-cause mortality	151 (6.9) [44]	108 (6.0) [37]	43 (11.6) [86]	69 (1.1) [4]

Abbreviations: MI, myocardial infarction; TIA, transient ischemic attack.

Table 3 Cost of hospitalization for stroke and first year follow-up costs (per patient per year)

Mean ± SD	Stroke cohort (N = 2180)	New stroke (N = 1808)	Recurrent stroke (N = 372)	Control cohort (N = 6540)
Index hospitalization costs	\$15,888 ± \$33,466*	\$15,634 ± \$27,536	\$17,121 ± \$53,693	\$11,281 ± \$29,052[a]
1-year follow-up costs				
Medical costs	\$23,725 ± \$58,227*	\$22,099 ± \$53,690	\$31,625 ± \$76,138	\$5142 ± \$16,619
Pharmacy costs	\$2950 ± \$3549*	\$2937 ± \$3577	\$3014 ± \$3416	\$1388 ± \$2302
Combined medical and pharmacy	\$26,675 ± \$58,605*	\$25,036 ± \$54,052	\$34,639 ± \$76,586	\$6530 ± \$17,167

Notes: All comparisons are relative to the control cohort and are computed by *t*-test. [a]Mean costs reported for 168 control subjects with a hospitalization on the index date. *$P < 0.001$.

for diabetes (95% CI: 1.1, 1.5) to 1.6 higher for CHF (95% CI: 1.2, 2.1). Increasing age was associated with a small (<1% per year of age) but statistically significant increase in cost ($P < 0.001$).

Discussion

The results of our study are consistent with those reporting significant adverse clinical and cost consequences of non-cardioembolic ischemic stroke in other patient populations. Moreover, the study supports previous research showing that patients with recurrent stroke generally fare worse and cost more than patients experiencing first ischemic stroke, which may be related to the overall severity of the stroke for recurrent compared with first stroke. Severe strokes cost twice as much as mild strokes, despite similar diagnostic testing. In a population study of stroke costs within 30 days of an acute event, the average cost was \$7200 for mild ischemic strokes and \$12,400 for severe ischemic strokes (4 or 5 on the Rankin Disability Scale).[15] Inpatient hospital cost for an acute stroke event accounts for 70% of first-year poststroke cost.[16] The largest components of acute care cost are room charges (50%), medical management (21%), and diagnostic costs (19%).[17] Comorbidities such as ischemic heart disease may also predict higher costs.[18]

In our managed care population, the recurrent stroke patients had poorer outcomes on all measures. Although the study designs differed, our findings were consistent with those of Samsa et al[7] which pertained exclusively to a Medicare patient population. The interpretation of the results comparing recurrent and new stroke requires some caution. Our recurrent stroke subgroup represented approximately 17% of all strokes based on a 12-month pre-index evaluation. This estimate is below the national rate of 29% reported by the American Heart Association.[6] The difference between the estimates likely stems from the limited pre-index evaluation. Prior strokes may have occurred in a larger population than were identified in only the 12 months evaluated. In addition, the impact of inappropriately designating some patients as new stroke patients rather than recurrent stroke patients may falsely inflate adverse outcomes and costs among new stroke patients. However, despite this risk, the differentials between new and recurrent stroke patients in clinical outcomes and costs were substantial.

Table 4 Cox proportional hazards analysis of time to hospitalization

	Cox proportional hazards model				
	Hazard ratio	SE	*P* value	95% CI lower	95% CI upper
Stroke	2.368	0.116	0.000	2.152	2.606
Age	1.023	0.002	0.000	1.019	1.027
Male	0.918	0.040	0.050	0.842	1.000
Midwest	1.037	0.050	0.453	0.944	1.138
Northeast	0.826	0.065	0.015	0.708	0.963
West	0.909	0.078	0.268	0.768	1.076
Hypertension	1.259	0.061	0.000	1.146	1.383
Diabetes	1.281	0.072	0.000	1.148	1.430
TIA	1.288	0.131	0.013	1.055	1.572
COPD	1.568	0.122	0.000	1.347	1.826
CHF	1.753	0.155	0.000	1.475	2.085
MI	1.495	0.251	0.017	1.076	2.078

Abbreviations: CHF, congestive heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; SE, standard error; TIA, transient ischemic attack.

Table 5 Cox proportional hazards analysis of time to stroke

	Cox proportional hazards model				
	Hazard ratio	SE	*P* value	95% CI lower	95% CI upper
Stroke	20.964	2.826	0.000	16.096	27.304
Age	1.031	0.004	0.000	1.023	1.039
Male	0.841	0.084	0.082	0.692	1.022
Midwest	1.023	0.112	0.833	0.825	1.269
Northeast	0.886	0.151	0.477	0.634	1.237
West	0.899	0.177	0.590	0.611	1.323
Hypertension	1.028	0.111	0.797	0.832	1.270
Diabetes	1.066	0.125	0.588	0.846	1.342
TIA	1.175	0.205	0.355	0.834	1.655
COPD	1.255	0.205	0.163	0.912	1.728
CHF	1.355	0.258	0.111	0.933	1.968
MI	1.334	0.420	0.361	0.719	2.474

Abbreviations: CHF, congestive heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; SE, standard error; TIA, transient ischemic attack.

Table 6 Cox proportional hazards analysis of time to death

Outcome	Cox proportional hazards model				
	Hazard ratio	SE	*P* value	95% CI lower	95% CI upper
Stroke	1.808	0.310	0.001	1.291	2.531
Age	0.990	0.006	0.099	0.979	1.002
Male	1.102	0.166	0.520	0.820	1.479
Midwest	0.965	0.156	0.825	0.703	1.324
Northeast	1.230	0.316	0.420	0.744	2.034
West	1.540	0.458	0.147	0.859	2.759
Hypertension	0.947	0.145	0.719	0.702	1.277
Diabetes	0.883	0.154	0.474	0.627	1.242
TIA	2.290	0.643	0.003	1.321	3.969
COPD	1.392	0.278	0.098	0.941	2.060
CHF	1.082	0.220	0.697	0.727	1.611
MI	1.006	0.322	0.984	0.537	1.885

Abbreviations: CHF, congestive heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; SE, standard error; TIA, transient ischemic attack.

As in other studies, clinical outcomes such as hospitalization, additional stroke, and death were substantially higher among stroke patients compared with controls and among recurrent stroke patients compared with new stroke patients. Although our measurement period was different from that used by Samsa et al[7] and by Vickery et al,[19] trends in reported outcomes were similar. TIA and stroke were the most common clinical events occurring in the follow-up period. However, compared with Vickery et al,[19] our rates of subsequent stroke were much lower.

This study confirms previous reports that patients with ischemic stroke and TIA are more at risk for recurrent cerebrovascular events compared with cardiac events.[20–22] In a retrospective study of patients with ICD codes for ischemic stroke/TIA, Brown et al[21] reported that cardiac events at 2 years had occurred in 7.7% of patients. Acute MI was the most common cardiac event reported. We found similar rates of MI (1.7%) compared with results reported by Vickery et al (1.5%).[19]

Table 7 Generalized linear modeling of per-patient-per-year total costs

	Generalized linear model				
	Cost ratio (ExpB)	SE	*P* value	95% CI lower	95% CI upper
Stroke	3.821	0.242	0.000	3.375	4.325
Age	1.008	0.002	0.000	1.004	1.013
Male	1.011	0.054	0.838	0.911	1.122
Midwest	0.939	0.054	0.276	0.838	1.052
Northeast	0.945	0.087	0.539	0.788	1.133
West	1.006	0.101	0.951	0.827	1.224
Hypertension	1.348	0.081	0.000	1.198	1.516
Diabetes	1.247	0.100	0.006	1.065	1.460
TIA	1.064	0.167	0.692	0.782	1.447
COPD	1.445	0.177	0.003	1.137	1.836
CHF	1.560	0.235	0.003	1.162	2.094
MI	1.327	0.338	0.266	0.806	2.186

Abbreviations: CHF, congestive heart failure; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ExpB, exponentiated coefficients; MI, myocardial infarction; SE, standard error; TIA, transient ischemic attack.

Similar to our study, Samsa et al[7] found that in a Medicare population, recurrent stroke patients experienced a greater cost burden in 1 year following the index event compared with new stroke patients. All stroke patients had substantially higher costs than controls. Samsa et al[7] reported that the cost burden for new and recurrent stroke the first year, including index hospitalization, was approximately $29,000 and $32,000, respectively. At the time of the Samsa[7] study, Medicare did not cover outpatient pharmacy costs, which represented ~11% of total cost in our study. In addition, other technological changes that have increased the cost of health care in general are likely contributing to the overall higher burden of illness observed in our study. Interestingly, according to the American Heart Association, 36% of direct health care costs are allocated toward nursing home care. Because the commercial health plan covers only limited short-term nursing home care, our study probably underestimates the overall true burden of stroke.[23]

In addition to the limitations described above in the interpretation of our data, additional limitations may impact the results reported here. First, as with all studies relying on retrospective administrative claims data, there are limits to the degree to which claims data can accurately capture an individual's medical history. Also, although comorbid conditions were considered controls in the modeling, the underlying health status of the stroke cohort may have been considerably worse than the control patients, resulting in the inappropriate attribution of rate and cost differentials to the presence of stroke. However, because stroke may occur in otherwise healthy adults and the major comorbidities contributing to excess costs were accounted for in the analysis, including hypertension and diabetes, we believe that the substantial burden of stroke is accurately reflected in this analysis. It is possible that the study underestimated the cost burden of stroke; the stroke population had a shorter length of follow-up than the control cohort, and it is not known how large the health care costs were for patients who disenrolled from the health plan and switched to another insurer or became uninsured. In addition, since the measure of mortality was based upon hospital discharge status in the claims, additional deaths may have occurred outside the inpatient setting that would not have been identified for the study. Estimates of re-hospitalization were based upon the identification of claims for inpatient sites of service (excluding nursing homes or skilled nursing facilities), but it is possible that some acute rehabilitation hospitals may have been included in this measure.

Results of this analysis are primarily applicable to managed care settings. The plans used for analysis, however, are discounted fee-for-service plans rather than capitated or gatekeeper models. They include a wide geographic distribution across the United States and thus provide the capability for generalization to managed care populations on a national level. However, these results cannot be extrapolated to represent the association between stroke and clinical and cost outcomes in a solely Medicare patient population or among the uninsured. As discussed previously, the inability to identify costs after patients disenrolled from the health plan also suggests that this finding may somewhat under-represent costs for ischemic stroke patients; health care systems in which the payers are responsible for patients' costs throughout their life span may face a higher cost burden. In addition, these results may not be generalizable to cardioembolic stroke; this analysis was limited to patients without AF or mitral valve abnormalities, as the intense management required for AF or valve abnormalities may result in different clinical outcomes, utilization patterns, and costs for this subset of patients than those experienced by patients with noncardioembolic stroke.

The findings of this study highlight the need for an urgent approach to diagnosis and treatment in order to prevent noncardioembolic ischemic stroke and stoke recurrence. Because treatment of patients with acute ischemic stroke is challenging and presents its own risks to the patient,[24] prevention is a crucial strategy. Evidence-based and consensus-based guidelines advocate the use of antiplatelet agents, anticoagulants (where appropriate), and antihypertensive medications for the prevention of secondary stroke.[25]

In conclusion, noncardioembolic ischemic stroke patients represent a significant burden on the managed care system, and despite its relatively lower prevalence rate, recurrent stroke disproportionately contributes to higher costs and negative clinical outcomes.

Acknowledgment

This work was financially supported by Boehringer Ingelheim Pharmaceuticals, Inc.

Disclosure

Dr Sanders and Dr Shah are employees of Boehringer Ingelheim Pharmaceuticals, Inc., a manufacturer of medications that prevent stroke.

References

1. Holloway RG, Benesch CG, Rahilly CR, Courtright CE. A systematic review of cost-effectiveness research of stroke evaluation and treatment. *Stroke*. 1999;30(7):1340–1349.
2. Evers SM, Ament AJ, Blaauw G. Economic evaluation in stroke research: a systematic review. *Stroke*. 2000;31(5):1046–1053.
3. Dewey HM, Thrift AG, Mihalopoulos C, et al. Cost of stroke in Australia from a societal perspective: results from the North East Melbourne Stroke Incidence Study (NEMESIS). *Stroke*. 2001;32(10):2409–2416.
4. Kavanagh S, Knapp M, Patel A. Costs and disability among stroke patients. *J Public Health Med*. 1999;21(4):385–394.
5. Asplund K, Stegmayr B, Peltonen M. From the twentieth to the twenty-first century: a public health perspective on stroke. In: Ginsberg MD, Bogousslavsky J, editors. *Cerebrovascular Disease Pathophysiology, Diagnosis, and Management*. Chapter 64, Vol. 2. Malden (MA): Blackwell Science; 1998:901–918.
6. Lloyd-Jones D, Adams R, Carnethon M, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics – 2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2009;119(3):e21–e181.
7. Samsa GP, Bian J, Lipscomb J, Matchar DB. Epidemiology of recurrent cerebral infarction: a medicare claims-based comparison of first and recurrent strokes on 2-year survival and cost. *Stroke*. 1999;30(2):338–349.
8. Broderick J, Brott T, Kothari R, et al. The Greater Cincinnati/Northern Kentucky stroke study: preliminary first-ever and total incidence rates of stroke among Blacks. *Stroke*. 1998;29(2):415–421.
9. Ovbiagele B. The emergency department: first line of defense in preventing secondary stroke. *Acad Emerg Med*. 2006;13(2):215–222.
10. Burn J, Dennis M, Bamford J, Sandercock P, Wade D, Warlow C. Long-term risk of recurrent stroke after a first-ever stroke: the Oxfordshire Community Stroke Project. *Stroke*. 1994;25(2):333–337.
11. Leira EC, Chang KC, Davis PH, et al. Can we predict early recurrence in acute stroke? *Cerebrovasc Dis*. 2004;18(2):139–144.
12. Hier DB, Foulkes MA, Swiontoniowski M, et al. Stroke recurrence within 2 years after ischemic infarction. *Stroke*. 1991;22(2):155–161.
13. Bureau of Labor Statistics, US Department of Labor. Chained consumer price index; 1999. https://www.policyarchive.org. Accessed 2009 Oct 6.
14. Manning WG. The logged dependent variable, heteroscedasticity, and the retransformation problem. *J Health Econ*. 1998;17(3):283–295.
15. Leibson CL, Hu T, Brown RD, Hass SL, O'Fallon WM, Whisnant JP. Utilization of acute care services in the year before and after first stroke: a population-based study. *Neurology*. 1996;46(3):861–869.
16. Taylor TN, Davis PH, Torner JC, Holmes J, Meyer JW, Jacobson MF. Lifetime cost of stroke in the United States. *Stroke*. 1996;27(9):1459–1466.
17. Diringer MN, Edwards DF, Mattson DT, et al. Predictors of acute hospital costs for treatment of ischemic stroke in an academic center. *Stroke*. 1999;30(4):724–728.
18. Matz R. Cost-effective, risk-free, evidence-based medicine. *Arch Intern Med*. 2003;163(8):884–892.
19. Vickery BG, Rector TS, Wickstrom SL, et al. Occurrence of secondary ischemic events among persons with atherosclerotic vascular disease. *Stroke*. 2002;33(4):901–906.
20. di Pasquale G, Andreoli A, Pinelli G, et al. Cerebral ischemia and asymptomatic coronary artery disease: a prospective study of 83 patients. *Stroke*. 1986;17(6):1098–1101.
21. Brown DL, Lisabeth LD, Roychoudhury C, Ye Y, Morgenstern LB. Recurrent stroke risk is higher than cardiac event risk after initial stroke/transient ischemic attack. *Stroke*. 2005;36(6):1285–1287.
22. Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. *JAMA*. 2000;284(22):2901–2906.

23. Rosamond W, Flegal K, Friday G, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics – 2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2007;115(5):e69–e171. Erratum in: *Circulation*. 2007; 115(5):e172.
24. Weinberger J. Adverse effects and drug interactions of antithrombotic agents used in prevention of ischaemic stroke. *Drugs*. 2005;65(4): 461–471.
25. Sacco RL, Adams R, Albers G, et al. American Heart Association; American Stroke Association Council on Stroke; Council on Cardiovascular Radiology and Intervention; American Academy of Neurology. Guidelines for prevention of stroke in patients with ischemic stroke or transient ischemic attack: a statement for healthcare professionals from the American Heart Association/American Stroke Association Council on Stroke. Co-sponsored by the Council on Cardiovascular Radiology and Intervention: the American Academy of Neurology affirms the value of this guideline. *Stroke*. 2006;37(2):577–617.