Impact of Atrial Fibrillation on Stroke - Related Healthcare Costs

Citation	Sussman, Matthew, Joseph Menzin, Iris Lin, Winghan J. Kwong, Michael Munsell, Mark Friedman, and Magdy Selim. 2013. "Impact of Atrial Fibrillation on Stroke - Related Healthcare Costs." Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease 2 (6): e000479. doi:10.1161/JAHA.113.000479. http://dx.doi.org/10.1161/JAHA.113.000479.
Published Version	doi:10.1161/JAHA.113.000479
Accessed	February 19, 2015 3:13:13 PM EST
Citable Link	http://nrs.harvard.edu/urn-3:HUL.InstRepos:11879588
Terms of Use	This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA

(Article begins on next page)

Impact of Atrial Fibrillation on Stroke-Related Healthcare Costs

Matthew Sussman, MA; Joseph Menzin, PhD; Iris Lin, PhD; Winghan J. Kwong, PharmD, PhD; Michael Munsell, BA; Mark Friedman, MD; Magdy Selim, MD

Background—Limited data exist on the economic implications of stroke among patients with atrial fibrillation (AF). This study assesses the impact of AF on healthcare costs associated with ischemic stroke (IS), hemorrhagic stroke (HS), or transient ischemic attack (TIA).

Methods and Results—A retrospective analysis of MarketScan claims data (2005-2011) for AF patients ≥18 years old with ≥1 inpatient claim for stroke, or ≥1 ED or inpatient claim for TIA as identified by ICD-9-CM codes who had ≥12 months continuous enrollment prior to initial stroke. Initial event- and stroke-related costs 12 months post-index were compared among patients with AF and without AF. Adjusted costs were estimated, controlling for demographics, comorbidities, anticoagulant use, and baseline resource use. Data from 23 807 AF patients and 136 649 patients without AF were analyzed. Unadjusted mean cost of the index event was $20 933 for IS, $59 054 for HS, $8616 for TIA hospitalization, and $3395 for TIA ED visit. After controlling for potential confounders, adjusted mean incremental costs (index plus 12-month post-index) for AF patients were higher than those for non-AF patients by: $4726, $7824, and $1890 for index IS, HS, TIA (identified by hospitalization), respectively, and $1700 for TIA (identified by ED) (all $P<0.01$). In multivariate regression analysis, AF was associated with a 20% (IS), 13% (HS), and 18% (TIA) increase in total stroke-related costs.

Conclusion—Stroke-related care for IS, HS, and TIA is costly, especially among individuals with AF. Reducing the risk of AF-related stroke is important from both clinical and economic standpoints. (***J Am Heart Assoc*. 2013;2:e000479 doi: 10.1161/JAHA.113.000479**)

Key Words: economics • hemorrhage • ischemic stroke • outcomes research • transient ischemic attack

Stroke among atrial fibrillation (AF) patients has been shown to be associated with increased severity, functional disability, and mortality compared with patients without AF.[1] While stroke-related costs have been estimated among a general population,[2] limited data exist on the economic implications of stroke among patients with AF. In this retrospective study, we estimate the cost of ischemic stroke (IS), hemorrhagic stroke (HS), and transient ischemic attack (TIA) among patients with AF versus those without AF from a third-party payer perspective. These data will provide a baseline estimate on the economic burden of stroke to inform future cost-benefit evaluation of interventions aimed at preventing stroke in AF patients.

From the Boston Health Economics, Inc, Waltham, MA (M. Sussman., J.M., I.L., M.M., M.F.); Daiichi Sankyo, Inc, Parsippany, NJ (W.J.K.); Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA (M. Selim.).

Correspondence to: Joseph Menzin, PhD, Boston Health Economics, Inc, 20 Fox Road, Waltham, MA 02451. E-mail: jmenzin@bhei.com

Received August 16, 2013; accepted October 28, 2013.

Methods

Data Source

This study used administrative claims data from the Truven Health Analytics MarketScan® Research Databases (Commercial and Medicare Supplemental), 2005-2011. The commercial database includes data from 150 contributing large self-insured employers. The Medicare Supplemental database contains the healthcare experience of individuals with Medicare supplemental insurance paid by employers. Approximately 40 million lives were analyzed, allowing for a nationally representative sample of Americans with employer-provided health insurance.

Patient Selection

We identified adult patients (≥18 years of age) with at least 1 primary inpatient diagnosis of stroke or TIA (International Classification Modification [ICD-9-CM]: 430.xx, 431.xx, 432.xx for hemorrhagic; 433.01, 433.11, 433.31, 434.xx for ischemic; 435.8, 435.9 for TIA)[2–6] or at least 1 emergency department diagnosis of TIA between January 1, 2006 and November 1, 2011. The date of the first identified stroke or

TIA diagnosis constituted the index date. Patients could not have had a stroke or TIA diagnosis in the 12 months prior to the index stroke (ie, to ensure a “baseline period” without stroke or TIA) and were required to be continuously eligible for 12 months prior to the index stroke event.

Presence of AF was based on ≥1 inpatient or ≥2 outpatient claims (separated by <1 year) associated with an AF diagnosis (ICD-9-CM: 427.31)[7,8] in the baseline period and up to 3 months after index stroke event to allow inclusion of patients who were identified to have AF after stroke occurrence.

Study Measures

The following baseline demographic and clinical characteristics were evaluated—age, sex, geographic region, metropolitan statistical area, year of index stroke diagnosis, type of stroke or TIA, comorbidities, use of oral anticoagulants (ie,

Table 1. Baseline Characteristics

Characteristic	Overall	AF Cohort	Non-AF Cohort	*P* Value*
Number of subjects	160 456	23 807	136 649	
Age, y				
Mean, SD	69 (±14.8)	77 (±11.6)	67 (±14.8)	<0.0001
Age group				
<55, N (%)	29 572 (18.4)	1048 (4.4)	28 560 (20.9)	
55 to 64, N (%)	39 376 (24.6)	3285 (13.8)	36 075 (26.4)	
65+, N (%)	91 508 (57.0)	19 474 (81.8)	72 014 (52.7)	
Female, %	51.5	50.7	51.6	0.0121
Geographic Region, %				
Northeast	12.8	15.3	12.4	<0.0001
North Central	34.6	35.3	34.4	
West	17.1	19.7	16.7	
South	35.3	29.5	36.3	
Unknown	0.2	0.3	0.2	
Metropolitan statistical area, %	84.0	84.0	82.9	<0.0001
Stroke Type, %				
Ischemic	49.9	59.9	48.2	<0.0001
TIA	36.2	27.3	37.8	
Hemorrhagic	13.9	12.8	14.1	
Type of Hemorrhagic Stroke†, %				
Subarachnoid	25.3	8.9	27.9	
Intracerebral	51.2	58.4	50.0	
Other and unspecified intracranial	23.5	32.6	22.0	
Selected Comorbidities (>5% frequency, %)				
Chronic obstructive pulmonary disease	9.7	15.0	8.8	<0.0001
Congestive heart failure (excluding left ventricular)	9.0	24.1	6.4	<0.0001
Diabetes mellitus	24.6	26.9	24.2	<0.0001
Hypertension	51.2	62.1	49.3	<0.0001
Malignancy	13.9	19.1	13.0	<0.0001
Peripheral vascular disease	9.6	15.2	8.6	<0.0001
OAC use, %	10.2	43.5	4.4	<0.0001

AF indicates atrial fibrillation; OAC, oral anticoagulant; TIA, transient ischemic attack; SD, standard deviation.
*Fisher's exact or Wilcoxon test.
†Type of hemorrhagic stroke was not tested.
Source: Truven MarketScan® Research Databases January 1, 2005 to December 31, 2011.

Table 2. Index Hospitalization and Post-Index Stroke-related Costs Among AF and Non-AF Patients

Stroke Type/Measure	Overall		AF Cohort		Non-AF Cohort		Difference (AF vs Non-AF)		
	N	Estimate	N	Estimate	N	Estimate	Unadjusted	Adjusted	*P* Value (Adjusted)
Ischemic Stroke									
Index event LOS, days	80 083	8.0 (±11.5)	14 251	8.3 (±11.7)	65 832	7.9 (±11.4)	0.4	1.1	0.0005
Index mortality rate, %		3.4		5.6		2.9	2.7	1.1	0.0011
Patients surviving index hospitalization	77 376		13 453		63 923				
Hospitalization within 30 days, %		6.5		6.9		6.4	0.5	1.4	<0.0001
Patients with continuous enrollment 12 months post-index	46 071		7072		38 999				
Stroke-related hospitalization within 12 months*, %		11.6		12.3		11.5	0.8	0.7	0.1325
Mean cost index event	80 083	$20 933 (±37 413)	14 251	$21 151 (±36 553)	65 832	$20 886 (±37 597)	$265	$3520	<0.0001
Mean 12-month total stroke-related cost*	46 071	$25 106 (±39 475)	7072	$26 602 (±41 772)	38 999	$24 835 (±39 039)	$1767	$4726	<0.0001
Hemorrhagic Stroke									
Index event LOS, days	22 275	13.7 (±20.1)	3052	10.7 (±16.1)	19 223	14.1 (±20.6)	−3.4	1.0	<0.0001
Index mortality, %		18.3		23.1		17.6	5.5	−1.3	0.1436
Patients surviving index hospitalization	18 185		2346		15 839				
Hospitalization within 30 days, %		9.7		10.0		9.6	0.4	2.8	0.0001
Patients with continuous enrollment 12 months post-index	10 010		1162		8848				
Stroke-related hospitalization within 12 months*, %		14.9		16.5		14.7	1.8	1.4	0.3179
Mean cost index event	22 275	$59 054 (±99 512)	3052	$38 028 (±66 693)	19 223	$62 384 (±103 371)	($24 356)	$2799	0.0214
Mean 12-month total stroke-related cost*	10 010	$74 462 (±113 962)	1162	$54 268 (±79 585)	8848	$77 113 (±117 479)	($22 845)	$7824	0.0019
TIA									
Patients with hospitalization index event									
Index event LOS, days	38 585	3.5 (±4.0)	4759	4.1 (±3.7)	33 826	3.4 (±4.1)	0.7	0.3	<0.0001
Index mortality, %		0.1		0.2		0.1	0.1	N/A	N/A
Patients surviving index hospitalization	38 541		4749		33 792				
Hospitalization within 30 days, %		3.2		5.0		2.9	2.1	1.2	<0.0001
Patients with continuous enrollment 12 months post-index	26 604		3047		23 557				
Stroke-related hospitalization within 12 months*, %		8.0		10.2		7.7	2.5	1.1	0.0520

Continued

Table 2. Continued

Stroke Type/Measure	Overall		AF Cohort		Non-AF Cohort		Difference (AF vs Non-AF)		
	N	Estimate	N	Estimate	N	Estimate	Unadjusted	Adjusted	*P* Value (Adjusted)
Mean cost index event	38 585	$8616 (±10 812)	4759	$9208 (±4800)	33 826	$8533 (±10 128)	$675	$846	<0.0001
Mean 12-month total stroke-related cost*	26 604	$11 931 (±15 617)	3047	$13 581 (±17 064)	23 557	$11 718 (±15 407)	$1863	$1890	<0.0001
Patients With ED Index Event									
Hospitalization within 30 days, %	19 513	8.3	1745	13.8	17 768	7.8	6.0	5.0	<0.0001
Patients with continuous enrollment 12 months post-index	12 956		1082		11 874				
Stroke-related hospitalization within 12 months*, %		8.9		14.5		8.4	6.1	5.9	<0.0001
Mean cost index event	19 513	$3395 (±3862)	1745	$2960 (±3858)	17 768	$3438 (±3860)	($478)	$274	0.0011
Mean 12-month total stroke-related cost*	12 956	$9096 (±14 091)	1082	$9651 (±15 531)	11 874	$9046 (±13 952)	$605	$1700	<0.0001

AF indicates atrial fibrillation; ED, emergency department; TIA, transient ischemic attack; LOS, length of stay.
*Only patients with 12 months continuous enrollment post index; includes index event cost.
Source: Truven MarketScan® Research Databases January 1, 2005 to December 31, 2011.

warfarin, dabigatran, and rivaroxaban), inpatient and ED resource use, and duration of follow-up.

Outcomes included index hospitalization length of stay (LOS), index event costs (all costs occurring throughout the timeframe of the index hospitalization or ED visit), hospitalization rates within 30 days of index event, stroke-related hospitalization rates 12 months post-index, and stroke-related costs 12 months post-index for all components of medical care. Stroke-related costs and hospitalizations were required to list a stroke/TIA ICD-9-CM code.

Costs data reflect the total gross payments to all providers associated with a given medical event. Total stroke-related costs were derived by summing all payments associated with a stroke/TIA admission (based on primary or any ICD-9-CM diagnosis code) over the 12-month follow-up period for all places of service (eg, inpatient, outpatient, emergency department, skilled nursing facility, home health care, durable medical equipment). Stroke-related laboratory and pharmacy costs (ie, the presence of select medications, including anticoagulants such as warfarin, dabigatran, and rivaroxaban, as well as antiplatelets and rate/rhythm control medications) were included in the calculation of total costs.

Follow-up analysis included those patients who were continuously enrolled for 12 months following the index event.

Statistical Analyses

We compared adjusted index event LOS and stroke-related cost between patients with and without AF using a generalized linear model with a negative binomial distribution and a log link, controlling for age, sex, geography, year of index diagnosis, selected comorbidities (based on >5% frequency), oral anticoagulant (OAC) use, and baseline hospital and ED use. Given common characteristics observed in healthcare cost data, such as a highly skewed distribution from the small percentage of patients with extremely high expense rates, the generalized linear model is highly recommended for models using administrative claims data.[9] Regression coefficients from the generalized linear model help to quantify the relationship between 12-month stroke-related costs and the selected patient characteristics (eg, when exponentiated using a base of *e*, the coefficient represents a percentage increase/decrease in costs compared to patients without the characteristic). Adjusted stroke-related hospitalization rates were estimated using a logistic regression controlling for the same covariates included in the generalized linear model.

Results

We identified 160 456 patients with stroke or TIA, 23 807 (14.8%) of whom had AF (Table 1). Of the AF patients, 43.5% were on an oral-anticoagulant in the baseline period. There

Table 3. Generalized Linear Model Predicting Stroke-Related Costs in the 12 Months Following the Index Event, by Stroke Type

Stroke Type	Ischemic Stroke*			Hemorrhagic Stroke†			TIA‡		
Predictor Variable	Coefficient	Standard Error	*P* Value	Coefficient	Standard Error	*P* Value	Coefficient	Standard Error	*P* Value
Intercept	10.392	0.0209	<0.0001	11.048	0.0548	<0.0001	9.2636	0.02	<0.0001
AF cohort	**0.1847**	0.0125	<0.0001	**0.1179**	0.038	0.0019	**0.1717**	0.0147	<0.0001
Hemorrhage Subtype (vs Other and unspecified intracranial hemorrhage)									
Subarachnoid hemorrhage	—	—	—	**0.7295**	0.0301	<0.0001	—	—	—
Intracerebral hemorrhage	—	—	—	**0.1843**	0.0255		—	—	—
Age Group (vs <55)									
55 to 64	−**0.0955**	0.0132	<0.0001	−**0.0192**	0.0273	<0.0001	**0.0424**	0.0119	<0.0001
65+	−**0.5977**	0.012		−**0.7795**	0.0269		−**0.0967**	0.0109	
Metropolitan Statistical Area	**0.0586**	0.0111	<0.0001	−0.0436	0.0282	0.1218	**0.0732**	0.0103	<0.0001
Female	0.0132	0.0082	0.1068	**0.0536**	0.0204	0.0087	−**0.0253**	0.0079	0.0014
Geographic Region (vs Northeast)									
North Central	−**0.2087**	0.0134	<0.0001	−**0.1533**	0.0329	<0.0001	−**0.1483**	0.0133	<0.0001
West	**0.1261**	0.0153		**0.3305**	0.0362		**0.0171**	0.0145	
South	−**0.0824**	0.0136		−**0.0661**	0.0329		−**0.063**	0.0132	
Year of Stroke Diagnosis (vs 2006)									
2007	0.0274	0.0134	<0.0001	0.0687	0.034	0.0707	0.0022	0.013	<0.0001
2008	**0.0665**	0.0134		**0.1376**	0.0341		−0.0084	0.013	
2009	**0.0925**	0.013		**0.12**	0.0324		0.0237	0.0126	
2010	**0.0396**	0.0131		**0.0862**	0.033		0.0087	0.0129	
2011	0.0682	0.029		0.0789	0.0715		−**0.1114**	0.0309	
OAC use	−0.0016	0.0158	0.918	−0.0242	0.0369	0.5122	−**0.0889**	0.0159	<0.0001
Selected Comorbidities									
Acute MI	**0.1037**	0.0343	0.0025	0.164	0.1009	0.1041	0.0711	0.0335	0.0336
CHF	0.0027	0.0158	0.8629	**0.1395**	0.0466	0.0027	**0.0475**	0.0162	0.0034
CKD	**0.0646**	0.0231	0.0052	−0.0743	0.0672	0.2691	**0.1763**	0.025	<0.0001
COPD	−0.0216	0.0145	0.1343	−0.0369	0.0416	0.3745	0.0153	0.014	0.2742
Diabetes mellitus	**0.036**	0.0094	0.0001	0.0209	0.0276	0.4495	**0.1089**	0.0095	<0.0001

Continued

Table 3. Continued

Stroke Type	Ischemic Stroke*			Hemorrhagic Stroke†			TIA‡		
Predictor Variable	Coefficient	Standard Error	*P* Value	Coefficient	Standard Error	*P* Value	Coefficient	Standard Error	*P* Value
Hypertension	0.0152	0.0084	0.0721	0.0257	0.0219	0.2412	**0.0443**	0.0082	<0.0001
Liver disease	0.0061	0.0294	0.8345	0.0309	0.0601	0.6067	**0.1147**	0.0263	<0.0001
Malignancy	−0.0263	0.0123	0.0327	−0.0388	0.0323	0.2293	0.0179	0.0119	0.1314
Peripheral vascular	**0.0367**	0.0142	0.0098	0.0009	0.042	0.9828	**0.0607**	0.0142	<0.0001
All-Cause Baseline Resource Use									
Had hospitalization	0.028	0.011	0.0109	**−0.0818**	0.0288	0.0045	**0.0401**	0.0106	0.0002
Had ED visit in baseline	**0.0368**	0.0109	0.0008	−0.0454	0.0275	0.0984	**0.0489**	0.0099	<0.0001

Note: Bolded parameters are significant ($P<0.01$). AF indicates atrial fibrillation; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; OAC, oral anticoagulant.
*N=46 071; ratio of deviance to degrees of freedom=1.1185.
†N=10 010; ratio of deviance to degrees of freedom=1.1574.
‡N=39 560; ratio of deviance to degrees of freedom=1.0977.
Source: Truven MarketScan® Research Databases January 1, 2005 to December 31, 2011.

were differences in terms of demographic and clinical characteristics between the AF and non-AF groups. In the AF cohort, mean age was 77 years (±11.6) compared to a mean age of 67 years (±14.8) in the non-AF cohort ($P<0.01$) (Table 1). Prevalence of selected comorbidities was also higher in the AF cohort ($P<0.01$).

In the overall sample, 49.9% of patients had IS, 13.9% had HS, and 36.2% had TIA (12.2% identified with ED; 24.0% identified with hospitalization). Compared to the non-AF cohort, the AF cohort had higher rates of IS, intracerebral hemorrhage, and other intracranial hemorrhage and lower rates of TIA and subarachnoid hemorrhage (Table 1).

Among IS and TIA patients, the AF cohort had longer index hospitalization LOS than the non-AF cohort (8.3 versus 7.9 for IS; 4.1 versus 3.4 for TIA), but the opposite was true for HS patients (10.7 versus 14.1 days). Among patients surviving the index event, hospitalization within 30 days of discharge was significantly more common among AF patients, regardless of index stroke type (OR=1.248 $P<0.05$ for IS; OR=1.424 $P<0.05$ for HS; OR=1.425 $P<0.05$ for TIA).

Unadjusted mean cost of index event was $20 933 (±$37 413) for IS, $59 054 (±$99 512) for HS, $8616 (±10 812) for TIA with index hospitalization, and $3395 (±3862) for TIA with index ED visit (Table 2). Adjusted mean incremental costs (index plus 12-month post-index) for AF patients were significantly higher than those for non-AF patients by: $4726, $7824, and $1890 for index IS, HS, TIA (identified by hospitalization), respectively, and $1700 for TIA (identified by ED) (all $P<0.01$). In the multivariate regression predicting stroke-related follow-up costs (index plus 12-month post-index), AF was associated with significant increases in total stroke-related costs among patients with IS (20%), HS (13%), and TIA (19%) (all $P<0.01$) (Table 3).

Discussion

In this study, we estimate the direct cost of stroke-related medical care among patients with AF versus those without AF using a large payer database. After controlling for potential confounders, adjusted mean incremental costs (index plus 12-month post-index) for AF patients were significantly higher than those for non-AF patients, with results from a generalized linear model demonstrating the statistical significance of this relationship. This study is subject to the general limitations of basing case ascertainment on ICD-9-CM codes from billing data, including coding errors and potential underestimation of event occurrence. We only counted follow-up costs for medical care that listed stroke/TIA as a diagnosis; also, this likely underestimates the full costs experienced by patients, because some stroke-related services may be coded for specific complications rather than strictly stroke or TIA.

However, our index hospitalization and post-index stroke-related cost findings are consistent with estimates reported from previous studies using various sources of data.[3,10]

While limited data exist on the relationship between AF and stroke-related costs from a US perspective, multiple published studies have attempted to evaluate this relationship with non-US data sources. For instance, a 2008 article published by Ghatnekar and colleagues evaluated the impact of AF on stroke-related inpatient costs over a 3-year follow-up period in Sweden.[11] Due to a higher observed mortality rate during the index stroke hospitalization, patients with AF had a shorter mean follow-up period than those without the disease, resulting in a non-significant difference in costs between the 2 cohorts over the full follow-up period. The effect of AF on stroke-related inpatient costs became statistically significant once only patients surviving the index event were included in the regression analysis (€818 higher, $P<0.01$), a criterion also employed in our study. An analysis of data from the Berlin Acute Stroke Study also established a significant relationship between the presence of AF and higher total direct costs within 1 year of an index stroke event (€2982 higher, $P<0.001$), with resource use and cost data obtained from a patient self-report survey.[12] In addition to providing data from a US perspective, our study adds to this body literature by providing estimates on stroke-related costs for all components of medical care (eg, inpatient, outpatient, rehabilitation) to third-party payers stratified by stroke type.

Our findings provide current estimates of the cost of various stroke types, including ischemic stroke, hemorrhagic stroke, and TIA. These results demonstrate the high economic burden of stroke to payers, especially in persons with AF. Therefore, reducing the risk of AF-related stroke may be important from both a clinical and economic standpoint. Professional guidelines recommend oral anticoagulant therapy for the prevention of stroke in patients with AF.[13] Data from this analysis will be useful when evaluating the cost-effectiveness of clinical interventions designed to prevent stroke among those with AF, such as new developments in anticoagulant therapy.

Acknowledgments

The authors thank Lauren Lee for her contribution to study design and review of results.

Sources of Funding

This study was funded by Daiichi Sankyo, Inc.

Disclosures

Dr Kwong is an employee of the study sponsor. All other authors have no financial disclosures to report.

References

1. Lin HJ, Wolf PA, Kelly-Hayes M, Beiser AS, Kase CS, Benjamin EJ, D'Agostino RB. Stroke severity in atrial fibrillation. The Framingham Study. *Stroke*. 1996; 27:1760–1764.
2. Roberts CS, Gorelick PB, Ye X, Harley C, Goldberg GA. Additional stroke-related and non-stroke-related cardiovascular costs and hospitalizations in managed-care patients after ischemic stroke. *Stroke*. 2009;40: 1425–1432.
3. Burton TM, Lacey M, Liu F, Yu Y, Monsalvo JL, Lang K, Sander S. One-year follow-up healthcare costs of patients hospitalized for transient ischemic attack or ischemic stroke and discharged with aspirin plus extended-release dipyridamole or clopidogrel. *J Med Econ*. 2012;15:1217–1225.
4. Lee WC, Christensen MC, Joshi AV, Pashos CL. Long-term cost of stroke subtypes among medicare beneficiaries. *Cerebrovasc Dis*. 2007;23: 57–65.
5. Engel-Nitz NM, Sander SD, Harley C, Rey GG, Shah H. Costs and outcomes of noncardioembolic ischemic stroke in a managed care population. *Vasc Health Risk Manag*. 2010;6:905–913.
6. Roumie CL, Mitchel E, Gideon PS, Varas-Lorenzo C, Castellsague J, Griffin MR. Validation of ICD-9 codes with a high positive predictive value for incident strokes resulting in hospitalization using Medicaid health data. *Pharmacoepidemiol Drug Saf*. 2008;17:20–26.
7. Naccarelli GV, Johnston SS, Dalal M, Lin J, Patel PP. Rates and implications for hospitalization of patients ≥65 years of age with atrial fibrillation/flutter. *Am J Cardiol*. 2012;109:543–549.
8. Jensen PN, Johnson K, Floyd J, Heckbert SR, Carnahan R, Dublin S. A systematic review of validated methods for identifying atrial fibrillation using administrative data. *Pharmacoepidemiol Drug Saf*. 2012;21(suppl 1): 141–147.
9. Blough D, Ramsey SD. Using generalized linear models to assess medical care costs. *Health Serv Outcomes Res Methodol*. 2000;1:185–202.
10. Qureshi AI, Suri MF, Nasar A, Kirmani JF, Ezzeddine MA, Divanni AA, Giles WH. Changes in cost and outcome among US patients with stroke hospitalized in 1990 to 1991 and those hospitalized in 2000 to 2001. *Stroke*. 2007;38:2180–2184.
11. Ghatnekar O, Glader EL. The effect of atrial fibrillation on stroke-related inpatient costs in Sweden: a 3-year analysis of registry incidence data from 2001. *Value Health*. 2008;11:862–868.
12. Bruggenjurgen B, Rossnagel K, Roll S, Andersson FL, Selim D, Muller-Nordhorn J, Nolte CH, Jungehulsing GJ, Villringer A, Willich SN. The impact of atrial fibrillation on the cost of stroke: the berlin acute stroke study. *Value Health*. 2007;10:137–143.
13. You JJ, Singer DE, Howard PA, Lane DA, Eckman MH, Fang MC, Hylek EM, Schulman S, Go AS, Hughes M, Spencer FA, Manning WJ, Halperin JL, Lip GY. Antithrombotic therapy for atrial fibrillation: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141: e531S–e575S.