

Drug Therapy Persistence and Stroke Recurrence

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Objective: To assess the effect of persistence of use of warfarin sodium, aspirin, or clopidogrel bisulfate on stroke recurrence in a Medicaid high-risk, largely female, African American population.

Study Design: Prospective nonconcurrent cohort, longitudinal data analysis of medical and pharmacy claims of stroke patients from Medicaid managed care organizations between January 1, 2001, and December 31, 2003.

Methods: Cox proportional hazards models were used to predict the likelihood of avoiding a recurrence as a function of persistence of use of the initial medication (warfarin, aspirin, or clopidogrel) after stroke/adjusting for age, race, sex, hypertension and other comorbidities, and the pharmacotherapies prescribed. We used propensity scores to adjust for confounding by indication.

Results: Among 925 stroke patients (64.6% female, 75.1% ≥ 50 years, and 57.8% African American), hypertension and heart disease were the most prevalent comorbidities (66.1% and 65.1%, respectively); most initial strokes were nonhemorrhagic. Persistence of use of warfarin, aspirin, or clopidogrel after stroke increased the likelihood of avoiding a recurrence (hazard ratio [HR], 1.57; 95% confidence interval [CI], 1.22-2.01). Having a hemorrhagic stroke initially (HR, 0.37; 95% CI, 0.18-0.74) or having heart disease (HR, 0.82; 95% CI, 0.67-1.01), hypertension (HR, 0.63; 95% CI, 0.51-0.79), or diabetes mellitus (HR, 0.74; 95% CI, 0.60-0.91) after an initial stroke significantly decreased the likelihood of avoiding a recurrence. Patient's age, race, sex, and urban residence did not significantly predict the likelihood of avoiding a recurrence.

Conclusions: Persistence of use of the initial stroke preventive medication after stroke is effective in avoiding a recurrence. Hemorrhagic stroke, heart disease, hypertension, and diabetes increase the likelihood of a recurrence.

(*Am J Manag Care.* 2006;12:313-319)

The mortality and morbidity burden of stroke has reached high proportions in developed countries, where stroke accounts for a major share of total healthcare costs.¹⁻³ According to World Health Organization⁴ estimates, stroke was the second leading cause of death in 2002 for patients aged 60 years and older.⁴ The American Stroke Association estimates the prevalence of stroke at 2.6% (about 700 000 people experience a new or recurrent stroke each year) and the cost of stroke at \$56.8 billion, with one third attributed to indirect costs.^{5,6}

According to the National Heart, Lung, and Blood Institute and the Family Heart Study, 200 000 stroke

patients experience recurrent attacks each year.⁷ About 14% of patients who survive a first stroke or a transient ischemic attack will have another one within 1 year; the risk within 5 years is 30% to 43%.⁸ Stroke recurrence rates differ across ethnic groups; compared with white subjects, the rates are double for African American subjects and 2.6 times higher for Hispanic subjects.⁹

Risk factors for stroke recurrence include age, hypertension, diabetes mellitus, atrial fibrillation, coronary heart disease, smoking, and obesity. The risk of recurrence is 2.4 times higher for patients with a diastolic blood pressure higher than 80 mm Hg or a systolic blood pressure higher than 140 mm Hg.¹⁰ Among secondary stroke patients, 9.1% of recurrences within a year were attributable to diabetes and 4.9% to atrial fibrillation.¹¹ Those who had atrial fibrillation and were not treated with anticoagulants had a 2.1-fold increase in recurrence risk, with a 2.4 chance of higher severity.¹²

The effective treatment and management of stroke patients dramatically decrease stroke recurrence and avoid the associated morbidities; current preventive strategies include drug treatment, surgery, and lifestyle modification.^{13,14} For example, antihypertensive and statin therapies are associated with reduction of recurrence risk by 28% and 25%, respectively. Anticoagulants (eg, warfarin sodium) could reduce recurrence risk by up to 62% for stroke caused by nonvalvular atrial fibrillation, while antiplatelet therapy could reduce recurrence risk of noncardioembolic stroke by about 28%.¹⁵ To a large extent, the success of a strategy is measured by the extent of recurrence avoidance or delay. Antithrombotic therapy is recommended for the prevention of ischemic strokes (the most common [85%]

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This study was supported by a fellowship training grant from Pfizer, in collaboration with Medicaid managed care plans and the Maryland Department of Health and Mental Hygiene.

This study was presented at the 21st Annual Meeting of the International Society for Pharmacoepidemiology; August 22, 2005; Nashville, Tenn.

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type of stroke) but not for hemorrhagic strokes. Antithrombotic therapy includes anticoagulation therapy (eg, warfarin) and antiplatelet therapy (eg, aspirin, clopidogrel bisulfate, and ticlopidine hydrochloride). Practice guidelines have favored long-term anticoagulant therapy for the treatment of cardioembolic stroke, especially when it is due to atrial fibrillation. Cardioembolic stroke accounts for 20% to 25% of all ischemic strokes.¹⁶ Other noncardioembolic strokes are most commonly treated with antiplatelet therapy. For either case, however, the literature suggests an association between persistence of drug therapy and generally more favorable health outcomes.¹⁷

The objective of this study was to investigate the association between the persistence of use of stroke preventive medication given after a first stroke and the likelihood of avoiding a recurrence. Little is known about this association, especially among minority or high-risk populations who are covered by Medicaid managed care plans.^{18,19} We examined the association between the persistence of use of warfarin, aspirin, or clopidogrel and the likelihood of avoiding a stroke recurrence, adjusting for demographic and clinical confounders. We introduced a propensity score technique to adjust for confounding by indication and by population baseline risks and compared the effects of combined therapies with those of monotherapies while adjusting for persistence of the initial drug therapy after stroke.

METHODS

Population

The study population consisted of Maryland subjects covered by Medicaid. More than 400 000 people receive Medicaid coverage; about 50% are African American, 60% are female, and 50% are 17 years or younger. Medicaid recipients must enroll in 1 of 8 contracted managed care organizations.

Study Sample

All pharmacy and medical claims of stroke patients (*International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]* codes 430-438.xx) between January 1, 2001, and December 31, 2003, were obtained from Medicaid managed care organizations. To increase the likelihood of identifying new strokes, those who had a claim with an *ICD-9-CM* code for stroke during the first 6 months of the study period (January 1, 2001, to June 30, 2001) were excluded. Patients were included if they were continuously enrolled during the study period and had pharmacy and medical claims; at least 1 month of follow-up after the initial stroke; at least 1 diagnosis of stroke after June 30,

2001; and at least 1 prescription claim for warfarin, aspirin, or clopidogrel.

The mean follow-up period was 208 days (median, 152 days). The follow-up period was defined as the number of days elapsed between the first day of the first prescription after the initial stroke through the date of stroke recurrence (if applicable), the last day of plan enrollment, or the end of the study period, whichever occurred first.

Study Design

This study was a prospective nonconcurrent cohort, longitudinal data analysis of medical and pharmacy claims of stroke patients from Medicaid managed care organizations. Cox proportional hazards models were used to predict the likelihood of avoiding a stroke recurrence for these patients as a function of their persistence of use of the initial drug after stroke. We adjusted the models for age (as a categorical variable), race, sex, hypertension and other comorbidities, and the pharmacotherapies prescribed.

A previous study by Lovett et al²⁰ showed that about 4% of stroke patients will have a recurrence within 30 days and 7% within 3 months. To define stroke recurrence in the present study, the date of the primary stroke was recorded, and a subsequent claim, occurring after at least 30 days, with a diagnosis of stroke was identified as a recurrence. The absence of such a claim during the follow-up period was considered as remaining in remission.

By virtue of the study design, any given patient in the study was prescribed stroke preventive medication after the primary stroke. After that prescription, a patient may have continued taking that medication, possibly added another, switched, or discontinued altogether. The initial stroke drug prescribed after stroke was considered the index drug. For each patient, prescription claims records were analyzed for continuity of consecutive refills of the index drug, within a margin equal to the total expected length of time until the next refill (days supply) plus 15 days. Patients were considered as having discontinued their therapy if the period between their last prescription and a new prescription for the index drug was longer than the number of days supply plus 15 days. A switch was recorded for those who had a prescription claim for a stroke drug different from the index drug within 15 days after the date their last prescription was scheduled to expire. Persistence was defined as continuous refills of the same index drug until disenrollment from the plan or the end of the study period. We made note of those who added another drug and kept them in the persistence cohort. Switching to another drug was classified as nonpersistence.

We included in the analysis the type of stroke, the demographic variables, the stroke preventive medication (warfarin, aspirin, or clopidogrel; excluding those who initially took enoxaparin sodium), the number of different blood pressure-lowering drugs (angiotensin-converting enzyme [ACE] inhibitors, β -blockers, calcium channel blockers, and angiotensin receptor blockers [ARBs]) or lipid-lowering drugs prescribed during the follow-up period, and the comorbidities on file after the initial stroke (patients having those comorbidities after stroke might have been diagnosed as having the same comorbidities before the occurrence of the initial stroke). Comorbidities included heart disease (*ICD-9-CM* codes 393-398.xx, 410-414.xx, and 420-429.xx), hypertension (code 401.xx), and diabetes (code 250.xx). Demographic variables included age, race, sex, and site of residence (urban or nonurban). We further differentiated between hemorrhagic (*ICD-9-CM* codes 430-432.xx) and nonhemorrhagic (codes 433-438.xx) strokes.

Statistical Analysis

Channeling bias may result when a drug is being prescribed to patients with differences in preexisting conditions.²¹ To adjust for channeling bias, we first accounted for preexisting factors that might favor prescribing one drug over another. Lack of proper adjustment for these baseline risks may result in confounding effects that lead to bias in the estimates. The propensity score method developed by Rosenbaum and Rubin²² is a technique that adjusts for channeling bias by estimating the probability of being exposed to a certain treatment given multiple covariates. We estimated these probabilities and adjusted the initial model accordingly. For this analysis, we calculated the probability of being prescribed warfarin vs aspirin or clopidogrel, given the patient's age, race, sex, site of residence, and comorbidities before the initial stroke. The rationale behind grouping aspirin and clopidogrel together is that they both fall under the therapeutic category of antiplatelet agents used for prophylaxis of stroke or transient ischemic attack, whereas warfarin is an anticoagulant used for prophylaxis and treatment of venous thrombosis and for prophylaxis of systemic embolism after myocardial infarction.²³ We created indicator variables based on the propensity of being prescribed warfarin and used these as independent variables in the initial model along with persistence, demographic variables, and comorbidities.

SAS version 9.1 software (SAS Institute, Cary, NC) was used to perform all statistical analyses; tests of statistical significance refer to the .05 α level. The study was approved by the institutional review boards of the University of Maryland and the Department of Health

and Mental Hygiene and complies with the Health Insurance Portability and Accountability Act.

RESULTS

Baseline Characteristics

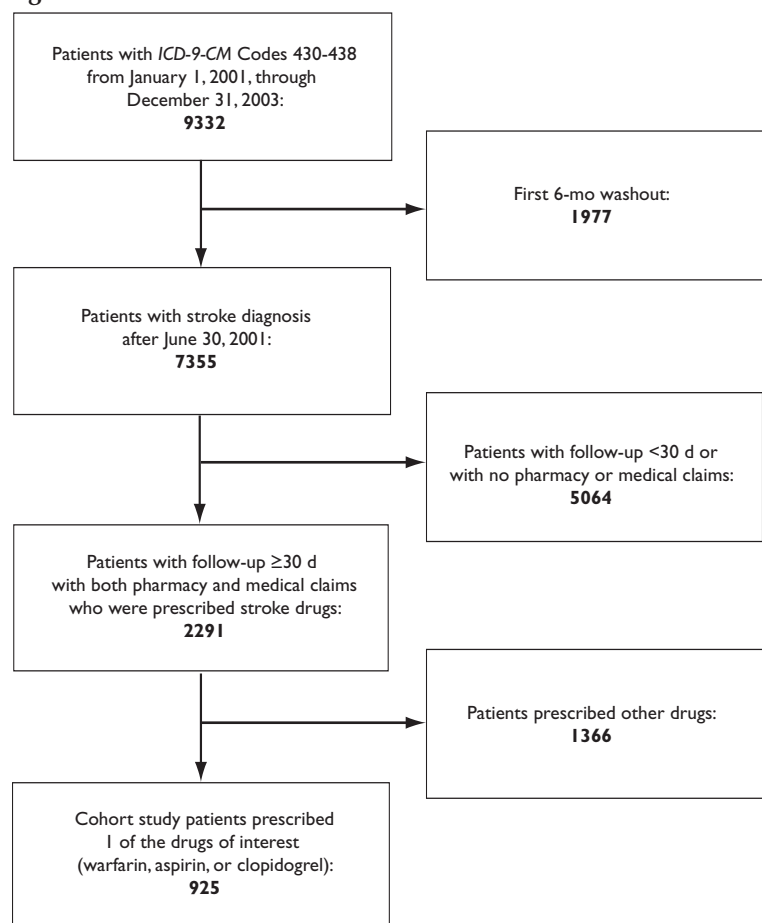
The study population consisted of 9332 continuously enrolled patients who had stroke-related medical claims with *ICD-9-CM* codes 430 through 438 in the primary, secondary, or tertiary diagnosis. Of these, 1977 patients were excluded because of a diagnosis of stroke during the first 6 months of the study period. Of the remaining 7355 subjects, 2291 had taken stroke medication after their first-ever stroke, were followed up for at least 30 days, and had both pharmacy and medical claims. Of these, 925 had been prescribed warfarin, aspirin, or clopidogrel as the initial stroke preventive drug after their first-ever stroke and had at least 1 month of follow-up since their initial stroke. The **Figure** shows how we obtained our cohort.

As summarized in **Table 1**, the study population was primarily female (64.6%), 50 years or older (75.1%), and African American (57.8%) and most commonly had hypertension (66.1%) and heart disease (65.2%). Most initial strokes were nonhemorrhagic. The mean \pm SD age of the cohort was 54.18 \pm 9.32 years.

Patients who initially took clopidogrel had the highest stroke recurrence rate (51.0%), followed by those who initially took aspirin (45.8%) (**Table 2**). Those who initially took warfarin had the highest persistence rate (84.1%), followed by the individuals who initially took clopidogrel (79.1%). The highest switch rate (2.5%) was seen among those who were initially prescribed warfarin.

Predictors of the Likelihood of Avoiding a Stroke Recurrence

Cox proportional hazards models were used to predict the likelihood of avoiding a stroke recurrence among patients who initially took warfarin, aspirin, or clopidogrel. The strength of this time-dependent approach is in the adjustment for factors such as age, race, sex, site of residence, drug persistence, use of blood pressure-lowering and lipid-lowering drugs after stroke, and presence of heart disease, hypertension, and diabetes. As summarized in **Table 3**, patients who continued the initially prescribed drug after stroke vs those who were nonpersistent (hazard ratio [HR], 1.57; 95% confidence interval [CI], 1.22-2.01; $P < .001$), and initially took clopidogrel vs aspirin (HR, 1.41; 95% CI, 1.10-1.82; $P = .007$), and took 1 or 2 blood pressure-lowering drugs vs 0 (HR, 1.39; 95% CI, 1.12-1.73; $P = .003$), were more likely to avoid a recurrence. Hemorrhagic stroke vs

Figure. Cohort Determination

ICD-9-CM indicates *International Classification of Diseases, Ninth Revision, Clinical Modification*.

nonhemorrhagic (HR, 0.37; 95% CI, 0.18-0.74; $P = .005$), heart disease (HR, 0.82; 95% CI, 0.67-1.01; $P = .06$), hypertension (HR, 0.63; 95% CI, 0.51-0.79; $P < .001$), and diabetes (HR, 0.74; 95% CI, 0.60-0.91; $P = .004$) significantly decreased the chances of remaining in remission. For example, a patient with hypertension has only about two thirds (63%) the chance of someone without hypertension to avoid a recurrence. After adjusting for clinical confounders, patient's age, race, sex, and urban residence were not significant predictors of remission. The results were not affected when we included age as a continuous variable or when we included different categories of age.

Because the use of ACE inhibitors or ARBs might be associated with stroke recurrence, we ran the same model introducing an indicator variable for ACE inhibitor and ARB use. Although not significant, the results demonstrated that, if patients were prescribed ACE inhibitors or ARBs independently, they were more likely to avoid a recurrence. However, patients who were

prescribed both or who switched between ACE inhibitors and ARBs were significantly less likely to stay in remission (HR, 0.42; 95% CI, 0.22-0.81; $P = .01$).

One-way sensitivity analyses varying the definition of persistence were conducted to test for robustness of the results. In the first analysis, patients were considered as nonpersistent if the period between the last prescription and the new prescription was longer than the number of days supply plus 10 days, as opposed to 15 days. The estimated persistence effect was similar and statistically significant (HR, 1.61; 95% CI, 1.28-2.01; $P < .001$), and all other estimates had the same significance level and direction as the original model. We also found no significant difference in the results when the definition of nonpersistence was changed from 15 days to 20 days (HR, 1.67; CI, 1.27-2.19; $P < .001$).

Propensity Score Model

To adjust for confounding factors, a propensity score model was developed to predict the likelihood of being prescribed warfarin vs aspirin or clopidogrel. Patients diagnosed as having preexisting heart disease (OR, 1.90; 95% CI, 1.38-2.61; $P < .001$), were more likely to be prescribed warfarin. Those with preexisting hypertension (OR, 0.62; 95% CI, 0.50-0.85; $P < .001$) and diabetes (OR, 0.56; 95% CI, 0.40-0.77; $P < .001$) were less likely to initially take

warfarin. The type of stroke, use of blood pressure-lowering or lipid-lowering drugs, or patient's age, race, and sex did not significantly predict the type of drug prescribed. The results of the Hosmer-Lemeshow goodness-of-fit test indicated that the fit of this model was adequate ($P = .29$). The next step was to compute the estimated propensities and to include them in the original Cox proportional hazards model.

Table 4 gives the results of the Cox proportional hazards model after adjusting for the propensity of being prescribed warfarin. The higher the propensity of being prescribed warfarin vs aspirin or clopidogrel (HR, 0.24; 95% CI, 0.08-0.76; $P = .02$), the lesser the likelihood of avoiding a recurrence, after adjusting for blood pressure-lowering and lipid-lowering drugs, comorbidities, and demographic variables. In addition, patients who continued taking the initially prescribed drug after stroke (HR, 1.52; 95% CI, 1.18-1.95; $P = .001$) and those who took 1 or 2 blood pressure lowering drugs

(HR, 1.36; 95% CI, 1.09-1.68; $P = .006$) were more likely to avoid a recurrence. Hemorrhagic stroke (HR, 0.42; 95% CI, 0.20-0.86; $P = .02$), hypertension (HR, 0.59; 95% CI, 0.48-0.74; $P < .001$), and diabetes (HR, 0.68; 95% CI, 0.54-0.85; $P < .001$) significantly decreased the chances of staying in remission. We also ran the model after adjusting for the propensity of being prescribed clopidogrel. The results were consistent with the previous findings; the higher the propensity of being prescribed clopidogrel vs aspirin or warfarin (HR, 7.80; 95% CI, 1.92-31.65; $P = .004$), the higher the likelihood of avoiding a recurrence.

DISCUSSION

The major finding of this study is that persistence of use of the initial stroke preventive medication taken after a first stroke is a significant predictor of stroke recurrence. On average, our results show that 79.7% of stroke patients covered by Medicaid continue taking the initial drug prescribed after stroke. Our results are consistent with those of Sappok et al,¹⁸ who investigated the determinants of persistence of use of antithrombotic medication and showed that 87.6% of patients persisted during 1 year. Other studies found persistence rates of

66.7% for antithrombotic medication after 3 months of follow-up²⁴ and 92.6% for aspirin after 3 months and 84% after 1 year.²⁵ Nonpersistence of anticoagulant regimens varied from 10% to 26% in randomized trials^{26,27}; our 16% nonpersistence rate is comparable.

Table 1. Demographic and Clinical Characteristics of Stroke Patients, by Recurrence Status*

Characteristic	Cohort (n = 925)	Recurrence (n = 442)	No Recurrence (n = 483)	P†
Age, mean ± SD, y				
<40	63.00 ± 6.81	26.00 ± 41.27	37.00 ± 58.73	.17
40-49	167.00 ± 18.05	74.00 ± 44.31	93.00 ± 55.69	.14
50-59	362.00 ± 39.13	173.00 ± 47.79	189.00 ± 52.21	.40
>59	333.00 ± 36.00	169.00 ± 50.75	164.00 ± 49.25	.74
Sex				
Male	327 (35.4)	154 (47.1)	173 (52.9)	.32
Female	598 (64.6)	288 (48.2)	310 (51.8)	.81
Race				
White	332 (35.9)	148 (44.6)	184 (55.4)	.05
African American	535 (57.8)	264 (49.3)	271 (50.7)	.79
Other	58 (6.3)	30 (51.7)	28 (48.3)	.79
Stroke type				
Hemorrhagic	33 (3.6)	8 (24.2)	25 (75.8)	.003
Nonhemorrhagic	892 (96.4)	434 (48.7)	458 (51.3)	.42
Comorbidities before first stroke				
Heart disease	555 (60.0)	234 (42.2)	321 (57.8)	<.001
Hypertension	595 (64.3)	270 (45.4)	325 (54.6)	.02
Diabetes	365 (39.5)	156 (42.7)	209 (57.3)	.006
Comorbidities after first stroke				
Heart disease	602 (65.1)	268 (44.5)	334 (55.5)	.007
Hypertension	611 (66.1)	272 (44.5)	339 (55.5)	.007
Diabetes	388 (41.9)	164 (42.3)	224 (57.7)	.002

*Data are given as number (percentage) of patients unless otherwise indicated.
 †Comparison of proportions with vs without recurrence using χ^2 test.

Table 2. Stroke Recurrence, Persistence of Drug Therapy, and Switch Rates by Index Drug*

Index Drug	Cohort	Recurrence		Persistence		Switched Drug				
		Yes	No	Yes	No	Aspirin	Clopidogrel	Enoxaparin	Warfarin	
Aspirin	286 (30.9)	131 (45.8)	155 (54.2)	218 (76.2)	61 (21.3)	7 (2.4)	0	5 (71.4)	1 (14.3)	1 (14.3)
Clopidogrel	363 (39.2)	185 (51.0)	178 (49.0)	287 (79.1)	70 (19.3)	6 (1.7)	2 (33.3)	0	0	4 (66.7)
Warfarin	276 (29.8)	126 (45.7)	150 (54.3)	232 (84.1)	37 (13.4)	7 (2.5)	3 (42.9)	4 (57.1)	0	0
Total	925 (100.0)	442 (47.8)	483 (52.2)	737 (79.7)	168 (18.2)	20 (2.2)	5 (25.0)	9 (45.0)	1 (5.0)	5 (25.0)

*Data are given as number (percentage) of patients.

Table 3. Factors Associated With the Likelihood of Avoiding a Stroke Recurrence

Factor	Hazard Ratio (95% Confidence Interval)*	P
Persistence of use of the initial stroke preventive drug	1.57 (1.22-2.01)	<.001
Initially took clopidogrel vs aspirin	1.41 (1.10-1.82)	.007
Initially took warfarin vs aspirin	1.05 (0.80-1.38)	.70
Hemorrhagic stroke	0.37 (0.18-0.74)	.005
Lipid-lowering drug	0.96 (0.77-1.20)	.73
Prescribed ≤2 blood pressure-lowering drugs vs 0	1.39 (1.12-1.73)	.003
Prescribed ≥3 blood pressure-lowering drugs vs 0	0.83 (0.64-1.08)	.17
Heart disease after stroke	0.82 (0.67-1.01)	.06
Hypertension after stroke	0.63 (0.51-0.79)	<.001
Diabetes after stroke	0.74 (0.60-0.91)	.004
African American race vs white or other	1.21 (0.97-1.50)	.08
Male sex	0.95 (0.78-1.15)	.59
Age >60 y	1.11 (0.92-1.35)	.28
Urban residence	1.05 (0.84-1.31)	.68

*Cox proportional hazards regression.

Table 4. Factors Associated With the Likelihood of Avoiding a Stroke Recurrence Using Propensity Score Modeling

Factor	Hazards Ratio (95% Confidence Interval)*	P
Persistence of use of the initial stroke preventive drug	1.52 (1.18-1.95)	.001
Probability of being prescribed warfarin	0.24 (0.08-0.76)	.02
Hemorrhagic stroke	0.42 (0.20-0.86)	.02
Lipid-lowering drug	0.98 (0.78-1.22)	.84
Prescribed ≤2 blood pressure-lowering drugs vs 0	1.36 (1.09-1.68)	.006
Prescribed ≥3 blood pressure-lowering drugs vs 0	0.83 (0.64-1.08)	.18
Heart disease after stroke	0.89 (0.72-1.09)	.27
Hypertension after stroke	0.59 (0.48-0.74)	<.001
Diabetes after stroke	0.68 (0.54-0.85)	<.001
African American race vs white or other	1.09 (0.87-1.36)	.46
Male sex	0.91 (0.75-1.11)	.37
Age >60 y	1.05 (0.86-1.29)	.62
Urban residence	0.82 (0.64-1.05)	.11

*Cox proportional hazards regression.

Although the absolute recurrence rates are 25% for hemorrhagic stroke and 49% for ischemic stroke, the adjusted model shows a higher risk of recurrence associated with hemorrhagic stroke. Perhaps much of the risk after ischemic stroke can be better accounted for by the covariates included in our model. In addition, patients who have primary intracerebral hemorrhage are at risk for ischemic stroke, transient ischemic attack, and recurrent hemorrhage.²⁸

The results of this analysis are consistent with other studies that found that patients who initially take clopidogrel vs aspirin after their initial stroke are less likely to have a recurrence. Indeed, in a large randomized controlled trial of patients at risk for ischemic events, clopidogrel was associated with fewer adverse effects and better stroke prevention efficiency (about 8.7% relative risk reduction compared with aspirin).²⁹ Perhaps because of drug cost considerations, clopidogrel is not commonly the first choice for antiplatelet therapy. However, in our sample, clopidogrel was one of the most prescribed medications, likely because of the uniform coverage for all drugs, with at most a \$1 copayment.

This analysis shows that patients who were prescribed 1 or 2 blood pressure-lowering drugs after stroke are more likely to stay in remission than those who do not take any. Indeed, there is evidence that an association exists between the number and combination of antihypertensive drugs and cardiovascular outcomes.³⁰

Our results demonstrate that patients who had a diagnosis of heart disease, hypertension, or diabetes after their initial stroke were less likely to stay in remission. Those results are consistent with the literature reporting that hypertension is the most significant risk factor for secondary stroke¹⁰ and that 9.1% of recurrences are attributable to diabetes and 4.9% to atrial fibrillation.¹¹

Compared with national averages,³¹ our sample population was younger and included more African Americans and more women, reflecting the demographic profile of patients covered by Medicaid.³² The results show a stroke incidence of 231 cases per 100 000, which is comparable to other studies documenting an incidence rate for initial stroke among white subjects in Rochester, Minn, of 179 cases per 100 000³³ and incidence rate of 288 cases per 100 000 among African Americans in the greater Cincinnati, Ohio, area.³⁴ The recurrence rate in our study, however, was 48% (within a mean of 208 days), which is higher than the rate of 14% (within a year) reported in the literature.⁸ Our results may reflect the general morbidity burden among Medicaid populations, as well as their healthcare access and socioeconomic status.

While this study allowed the observation of large populations, it does not include clinical indicators per se because of the nature of the data, but it provides evidence-based results to guide managed care interventions. In addition, there might be issues of internal and external validity. Investigations have shown that there may be some diagnostic coding errors in some Medicaid data³⁵; however, we tested the integrity of our data and found the data valid. Furthermore, because this study was conducted based on Medicaid data from one state, the results may not be comparable to those of patients in other state Medicaid, Medicare, commercial, or other types of plans. Another limitation was the application of the 6-month window to exclude patients who had prior stroke. Despite the exclusion of 1977 patients, the included patients might still have had a stroke before January 1, 2001. Finally, because the data were extracted from a claims data set, they may not have captured all episodes of care, specifically the use of over-the-counter drugs.

In conclusion, persistence of use of the initial stroke preventive medication after stroke is effective in avoiding a recurrence. Hemorrhagic stroke, heart disease, hypertension, and diabetes significantly raise the risk of a recurrence.

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