Preventing Another Event: Role of the Hospitalist in Discharge Stroke Prevention

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Only 1 of 8 stroke patients is managed exclusively by a neurologist. Furthermore, many stroke patients harbor other vascular comorbidities and are also at risk for developing general medical complications that can lead to death following stroke. With the growing hospitalist system, it is quite clear that hospitalists are, and will increasingly be, an integral part of the care team for many hospitalized stroke patients. Because prevention remains the mainstay of treatment for ischemic stroke and TIA, it would be useful for practicing hospitalists to know the scientific evidence behind recommended therapeutic approaches to reducing vascular risk following stroke, as well as strategies for bridging the prevailing evidence–practice gap for hospitalized stroke patients, which this review article presents. *Journal of Hospital Medicine* 2007;2:31–38. © *2007 Society of Hospital Medicine.*

KEYWORDS: hospitalist, stroke, TIA, prevention.

Prevention has the greatest potential to reduce the societal burden from stroke.[1] Several therapies that specifically target the underlying atherosclerotic disease process have been shown in clinical trials to markedly lower the risk of recurrent vascular events including stroke.[2] However, there is great variability in how clinical trial data are implemented in clinical practice for ischemic stroke prevention.[3–5] This has led to a knowledge-implementation-practice gap, possibly because of the limited awareness of the scientific evidence supporting various treatments, as well as the lack of a systematic approach to hospital stroke care.[3] Our review discusses the evidence for reducing vascular risk after ischemic stroke and successful models of systematic interventions initiated during stroke hospitalization, with the goal of narrowing the stroke hospitalization evidence–practice gap.

Societal Burden

Stroke is the third-leading cause of death in the United States and the leading cause of serious long-term disability.[6] Approximately 700,000 Americans have a new stroke or recurrent strokes every year, whereas nearly 5 million live with the consequences of stroke; nearly all stroke survivors (90%) have some residual functional deficit, and approximately 40% experience moderate to severe impairment.[6] Stroke mortality is substantial, with a 30-day case fatality rate after first stroke (of any cause) of about 25%.[7,8] Indeed, four-fifths of patients do not survive for 10 years after stroke, and approximately one-third of all case fatalities occur in the first year after a stroke.[8] The estimated economic impact in 2006, US$57.9 billion, further underscores the substantial mortality and morbidity of stroke.[6] Given the limited options for acute

stroke therapies,[9] stroke prevention remains an important therapeutic goal, especially because fewer than 5% of acute stroke patients in the United States currently receive the only Food and Drug Administration–approved treatment—intravenous tissue plasminogen activator.[10] It is obvious that additional strategies are urgently needed to reduce the devastating consequences of stroke.

Why Involve the Hospitalist?

The Hospitalist system in the United States is rapidly growing.[11] Tthe Society of Hospital Medicine projects that by 2010 there will be approximately 30,000 hospitalists in the United States.[11] A member census conducted by the American Academy of Neurology in 2000 found 13,500 practicing neurologists, most of whom are concentrated in urban and metropolitan areas.[12] As such, with more than 700,000 strokes occurring each year,[6] most stroke patients in the United States will not be seen or evaluated by a neurologist. Indeed, one study indicated that only 11.3% of stroke patients are attended exclusively by a neurologist.[13] Furthermore, it is not uncommon for stroke patients to have numerous other medical issues that require attention and multidisciplinary care coordination during the hospital stay, an area where hospitalists excel. Conceivably, the ability to promptly identify and treat these non-neurological comorbidities, which account for at least 30% of the deaths from acute ischemic stroke,[14] could go a long way toward improving stroke outcomes.

Hospitalists are in the forefront of developing strategies for improving the quality of acute care and patient satisfaction, reducing medical errors, and focusing on efficient resource utilization. Translating evidence-based strategies for acute stroke care into actual practice is a mechanism for improving the quality of care, ensuring that basic care does not deviate from provider to provider or from day to day (weekdays compared to weekend days/holidays) while at the same time allowing for the individualization of care appropriate to a patient's unique needs.[15] After the acute treatment of stroke or TIA, additional measures must be initiated as soon as it is safe to do so in order to begin the process of limiting stroke progression and preventing recurrence. Secondary prevention measures require a coordinated transition in order to ensure continuation of care and follow-up as needed. After a thorough risk assessment is complete, hospitalists will need to consider a 3-pronged approach to sec-

ondary prevention that follows the national guidelines described above: pharmacotherapy, behavior modification, and, in some cases, surgical intervention.

Secondary Stroke

Secondary or recurrent strokes are strokes that occur after a first stroke or TIA,[2] and the single biggest risk factor for having a stroke is already having had one.[2] Because hospitalists generally see patients after ischemic cerebrovascular events have already happened, their opportunities to intervene are mostly geared toward reducing the risk of secondary stroke (beyond enhancing the prevention of complications from the index event). Recent community-based data indicate that the short-term risk of secondary stroke is high.[16,17] After a minor stroke or TIA, the risk of recurrent stroke or TIA increases over time—8%-12% within 7 days, 12%-15% within 30 days, and 17%-19% within 90 days.[18] In the largest study of short-term risk following TIA,[19] there was an 11% risk of stroke (51% of which occurred in the 48 hours after TIA), an 13% risk of TIA, and a 25% risk of any adverse event within 90 days of the TIA.

Overall, the risk of a second cerebrovascular event is highest in the first year after a stroke/TIA (12%), declining to about 5% annually thereafter.[7] The effects of secondary stroke are more devastating than those of the primary stroke: the 30-day fatality rate after a first recurrent stroke is almost double that after the first-ever stroke (41% versus 22%).[20] The pathological factors that lead to TIA and stroke, such as platelet aggregation and subsequent thrombosis or the systolic stroke of blood against stenotic carotid plaques, are one and the same. As such, the short- and long-term risks of recurrent events after both first stroke or first TIA necessitate investigation into a patient's vascular risk and early initiation of appropriate stroke prevention strategies.[21]

Cross Risk

Because the atherothrombotic disease process is systemic in nature with a variety of manifestations, stroke patients with atherosclerosis frequently have coexistent coronary artery disease and peripheral artery disease,[22] and as such, are at risk for vascular events emanating from any of these beds in addition to that of the cervicocephalic arterial tree.[23,24] For instance, in a study of individuals in a long-term care facility, among the patients with ischemic

TABLE 1
Number Needed to Treat for Various Stroke Prevention Measures

Treatment	Relative risk reduction	Number needed to treat (1 stroke/year)
Antihypertensives	28%	51
Statins	25%	57
Aspirin	28%	77
Smoking cessation	33%	43
Carotid endarterectomy	44%	26

Adapted from Straus SE, Majumdar SR, McAlister FA. New evidence for stroke prevention: scientific review. *JAMA*. 2002;288:1388-1395.

TABLE 2
Risk Factor Control Guidelines After Stroke or Transient Ischemic Attack

Risk Factor	Recommendation
Hypertension	• Antihypertensive beyond hyperacute stroke period[60]
	• Data support diuretic or diuretic + ACEI,[28-30] but individualize based on patient characteristics
	• Antihypertensive in *all* patients regardless of history of hypertension[28]
	• Aim for average reduction of 10/5 mm HG or blood pressure < 120/80 mm Hg[28]
	• Encourage reduced intake of dietary salt
Dyslipidemia	• Statin for LDL-C goal < 100 mg/dL in those with CAD or symptomatic atherosclerosis[33,34]
	• Target LDL-C < 70 mg/dL for very high-risk persons[61]
	• Statin for stroke or TIA because of atherosclerosis regardless of LDL-C level[33,34]
	• Niacin or gemfibrozil for patients with low HDL-C[62,63]
Diabetes	• ACEIs and ARBs should be first-choice blood pressure drugs[37,38a]
	• Glucose control to near normoglycemic levels[39]
	• Target glycosylated hemoglobin ≤ 7%[64]

Adapted with permission from Sacco et al. *Stroke*. 2006;37:577-617.
[a]For additional renal protective benefit.
CAD, coronary artery disease; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

stroke, 56% had overlapping coronary artery disease, 28% had peripheral artery disease,[25] and 38% of the patients had at least 2 manifestations of their atherosclerotic disease. The take-home message here is that hospitalists also have the opportunity while treating patients hospitalized following stroke to prevent other vascular events by identifying and treating stroke patients who have systemic atherosclerosis.

Risk Factors

The first step in any approach to stroke prevention is the identification of predisposing risk factors. Several of the known biological and lifestyle risk factors associated with cerebrovascular disease were identified decades ago from large longitudinal studies.[2] Certain stroke risk factors are nonmodifiable and therefore cannot be the target of intervention. 26 Treatment of the various stroke risk factors could have a substantial impact on reducing the burden of stroke. Table 1 shows the number needed to treat to prevent one stroke per year by modification of the individual stroke risk factor.

Guidelines for Secondary Stroke Prevention

Several organizations have published guidelines for the prevention of secondary stroke based on clinical evidence and expert consensus. Key guidelines include those published by the American Stroke Association (ASA),[2] American College of Chest Physicians (ACCP),[27] and the National Stroke Association. Although these guidelines are broad—addressing many components of stroke prevention and care—each contains recommendations specifically applicable to secondary prevention in most stroke patients who the hospitalist will encounter. Some provide hospital-based guidelines that focus on care protocols and systems processes (ie, ASA

Stroke Systems Guidelines), whereas others are therapy-based guidelines (i.e, ACCP Guidelines on Antithrombotic Therapy for Ischemic Stroke). In the next few sections, we discuss common risk factors for and causes of secondary stroke and the prevailing guideline recommendations for modifying them. Discussion of the management of rare causes of ischemic stroke such as arterial dissection, vasculitis, patent foramen ovale, and so forth is beyond the scope of this article.

Hypertension, Dyslipidemia, and Diabetes

Table 2 shows the current national guideline recommendations for the management of premier vascular risk factors—hypertension, dyslipidemia, and diabetes—in ischemic stroke and TIA patients.[2] Antihypertensive therapy is recommended for the prevention of secondary stroke and other vascular events in patients who have experienced an ischemic stroke or TIA and are beyond the hyperacute period.[28,29] Such treatment should be considered for all ischemic stroke and TIA patients regardless of history of hypertension.[28] Although available data support the use of diuretics and the combination of diuretics plus an angiotensin-converting en-

zyme inhibitor,[28,30] selection of specific medications should be individualized according to a patient's comorbid conditions.[29] It is also important to note that despite the proven benefit of beta blockers in the secondary prevention of recurrent cardiac events, current evidence shows no clear benefit from the use of beta blockers in the prevention of stroke.[29,31]

For ischemic cerebrovascular disease patients with dyslipidemia or symptomatic atherosclerosis, cholesterol management should be according to the current Adult Treatment Panel (ATP) guidelines.[32] Statins should be the first-line treatment.[33,34] Ischemic stroke or TIA patients whose underlying stroke mechanism is presumed to be atherosclerosis should be considered for statin therapy even if they have normal cholesterol levels and no evidence of atherosclerosis.[33,34] The recent Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) study was the first study to specifically investigate the effect of statins in patients with a prior stroke but with normal cholesterol levels and no evidence of coronary heart disease. It found that treatment with atorvastatin 80 mg/day (vs. placebo) was associated with a 16% reduction in relative risk of recurrent stroke.[34]

The care of an ischemic stroke or TIA patient who has diabetes warrants more rigorous control of blood pressure and lipids.[35,36] Such patients usually require more than one antihypertensive drug. ACEIs and angiotensin receptor blockers (ARBs) are more effective in reducing the progression of renal disease and are the recommended first-choice medications for these patients.[37,38] The target for glucose control should be reaching near-normoglycemic levels.[39]

Large-Artery Atherosclerosis

In selected at-risk stroke patients, surgical techniques (eg, carotid endarterectomy [CEA], carotid angioplasty and/or stenting [CAS]) may reduce the rate of recurrent stroke.[40−44] For patients who have had ischemic cerebrovascular events in the preceding 6 months and who have ipsilateral severe (70%-99%) cervical carotid artery stenosis, CEA done by a surgeon is recommended; it has a perioperative morbidity and mortality of less than 6%.[40] For those with ipsilateral moderate (50%-69%) cervical carotid stenosis, CEA should be considered, and whether to operate should be decided on the basis of the patient's age, sex, comorbidities, and severity of initial symptoms.[41] Analyses of endarterectomy

trials indicated that the benefit from CEA is greatest if performed within 2 weeks of a patient's last ischemic event, the advantage it confers rapidly falling with increasing delay.[45] From the hospitalist's standpoint, it is of prime importance to ensure that patients admitted to the hospital with a TIA or ischemic stroke are not discharged before it has been established whether have severe carotid stenosis that requires a revascularization procedure. If carotid stenosis is less than 50%, CEA is not recommended.[41]

A newer, less invasive form of carotid artery revascularization is CAS,[46] which is performed by operators with established periprocedural morbidity and mortality rates of 4%-6% and may be considered in those with:

- Symptomatic severe stenosis (>70%) that is difficult to access surgically.[2]
- Medical issues that greatly increase the risks of surgery, such as clinically significant cardiac disease, severe pulmonary disease, contralateral carotid occlusion, contralateral laryngeal nerve palsy, radiation-induced stenosis or restenosis after carotid endarterectomy, and more than 80 years old.[43]

Angioplasty and/or stenting may also be considered when patients with symptomatic extracranial vertebral stenosis are having symptoms despite optimal medical risk factor treatments.[2] Among those with hemodynamically significant stenosis of the major intracranial vasculature (basilar, middle cerebrals, distal carotids, and vertebrals) experiencing symptoms despite optimal medical risk factor treatments, angioplasty and/or stenting is considered experimental.[2]

The degree of arterial stenosis can be assessed by ultrasound, magnetic resonance angiogram (MRA), computed tomography angiogram (CTA), and conventional catheter angiogram, the last of which remains the gold standard. A carotid ultrasound performed at a certified vascular laboratory or by an experienced radiology technologist that shows less than 50% stenosis need not be followed up with another neuroimaging test. Generally, MRA tends to overestimate the degree of arterial stenosis but is a useful screening tool. In the event that an MRA reveals more than 50% stenosis, another diagnostic modality such as a carotid duplex, CTA, or conventional catheter angiogram should be performed to confirm this finding.

Antithrombotic Treatment
Cardioembolic Stroke Mechanism
Although it can sometimes be difficult to determine the precise mechanism underlying a patient's stroke or TIA, those who have a high-risk source of cardiogenic embolism should generally be treated with anticoagulant medications to prevent recurrence.[2] Among ischemic cerebrovascular event patients with persistent or paroxysmal atrial fibrillation, anticoagulation with adjusted-dose warfarin (target international normalized ratio [INR] of 2.5; range, 2.0-3.0) should be administered.[47] The ASA recommends initiating oral anticoagulation within 2 weeks of an ischemic stroke or TIA but indicates that further delays may be appropriate for patients with large infarcts or uncontrolled hypertension.[2] For patients unable to take oral anticoagulants, aspirin 325 mg/day should be given instead. Among patients who suffered an ischemic stroke or TIA because of an acute myocardial infarction in whom left ventricular mural thrombus is identified by echocardiography or another form of cardiac imaging, oral anticoagulation should be considered, aiming for an INR of 2.0-3.0 for at least 3 months and up to 1 year.[2] Patients receiving oral anticoagulation who also have ischemic coronary artery disease should be prescribed aspirin as well, in doses up to 162 mg/day.[2]

Noncardioembolic Stroke Mechanism
For ischemic stroke or TIA patients who have no high-risk source of cardiogenic embolism, antiplatelet agents rather than oral anticoagulation are generally recommended to reduce the risk of recurrent stroke and other cardiovascular events.[48–50] Acceptable options for initial therapy include:

- Aspirin (50 to 325 mg/day)[48];
- Combination of aspirin (50 mg) and extended-release dipyridamole (400 mg) daily[49,51];
- Clopidogrel (75 mg) daily.[50]

The combination of aspirin and extended-release dipyridamole is suggested instead of aspirin alone, and clopidogrel may be considered instead of aspirin alone.[49,51] However, currently there is not enough data to make evidence-based recommendations for choosing between antiplatelet drugs beyond aspirin.[2] Furthermore, there is no evidence that increasing the dose of aspirin for patients who have had an ischemic stroke while taking aspirin provides additional benefit.[2] The selection of an antiplatelet agent must be individualized, giving due consideration to a patient's presumed stroke mechanism, risk factor profile, and tolerance.

Other antiplatelet guidelines for noncardioembolic stroke/TIA patients include that:

- Adding aspirin to clopidogrel increases the risk of hemorrhage and should not be routinely recommended for ischemic stroke or TIA patients.[52,53]
- Clopidogrel is a reasonable alternative for aspirin-intolerant patients.[50]

Education for Behavior Modification
It is crucial to discharge patients with the tools they need to make important lifestyle changes. Patients can significantly reduce their stroke risk by making changes in their everyday patterns of behavior. As much education as possible about smoking cessation, exercise, diet, and the warning signs of stroke should be provided often as possible during hospitalization for a stroke and need not be left to nurses. Stroke education is extremely important so patients understand the need to call for emergency medical services immediately if they even suspect they are having stroke symptoms because of the very narrow window of opportunity for treatment of an acute stroke.[54] All patients should be encouraged to make lifestyle adjustments such as ceasing smoking, reducing alcohol intake, and controlling weight. Smoking cessation appears to be effective in preventing secondary stroke (33% reduction in relative risk),[44] and initiating smoking cessation counseling during hospitalization for stroke may result in a high rate of adherence to smoking cessation, at least in the short term.[55] Table 3 displays current national guideline recommendations on lifestyle modification approaches.[2]

Evidence–Practice Gap
There are now many secondary stroke prevention modalities, and there is a copious amount of data validating the efficacy of quite a few of them.[2] Yet there is a large gap in implementing evidence-based secondary prevention strategies.[3–5] TIA and ischemic stroke patients are often discharged from the hospital without being prescribed any preventive medications, despite the data supporting the use of antiplatelet agents, anticoagulants, and antihypertensives for prevention of secondary stroke.[4] In addition, several behavioral interventions could help patients to avoid stroke recurrence,[2] but quite often stroke patients are not educated about them

TABLE 3
Behavior Modification Recommendations after Ischemic Stroke or TIA

Risk Factor	Recommendation
Smoking	• Smoking cessation • Avoid environmental smoke • Counseling, nicotine products, and oral smoking cessation medications
Alcohol	• Eliminate or reduce alcohol consumption • Light to moderate levels—2 drinks/day for men, 1 drink/day for nonpregnant women may be considered
Obesity	• Weight reduction goal: BMI 18.5-24.9 kg/m^2 and waist circumference < 35 inches for women, < 40 inches for men • Encourage weight management through balance of caloric intake, physical activity, behavioral counseling
Physical Activity	• At least 30 minutes of moderate-intensity physical exercise most days of the week • Supervised therapeutic exercise regimen for those with residual disability

Adapted with permission from Sacco et al. *Stroke.* 2006;37:577-617.
BMI is body mass index.

TABLE 4
Tools for Bridging the Stroke Prevention Evidence–Practice Schism

Tool	Description
AHA Get with the Guidelines—Stroke (www.strokeassociation.org)	• Focuses on care team protocols to facilitate appropriate in-hospital and discharge stroke treatment utilization • Identifies champions to lead, develop, and mobilize teams to optimally implement evidence-based stroke treatment in acute care hospitals • Utilizes standardized admission orders, patient educational materials, data monitoring • Provides resources to help hospitals obtain JCAHO certification
UCLA Stroke PROTECT (Preventing Recurrence of Thromboembolic Events through Coordinated Treatment) program (http://strokeprotect.mednet.ucla.edu)	• Integrates 8 proven secondary stroke prevention measures into standard stroke care provided during hospitalization • Applies quality improvement measures through preprinted admission orders, care maps, discharge protocols, educational materials, patient self-assessment logs, and data monitoring tools
JCAHO Disease Specific Certification for acute stroke care (http://www.jointcommission.org/)	• Designates eligible hospitals as "primary stroke centers" • Promotes compliance with consensus-based national standards • Encourages effective use of established clinical practice guidelines to manage and optimize stroke care • Fosters an organized approach to performance measurement and improvement activities

AHA, American Heart Association; UCLA, University of California, Los Angeles; JCAHO, Joint Commission on Accreditation of Hospital Organizations.

during the acute care period.[4] Poor discharge treatment utilization limits the effectiveness of proven therapies, resulting in lost opportunities to reduce the burden of secondary stroke.

The reasons for these care gaps are multifactorial and can be traced to patient and provider issues as well as to health care delivery processes. Our understanding of the reasons for this gap is improving. Generally speaking, preventive services are used less frequently than those services or treatment modalities that provide immediate relief or economic benefit. The benefit of most preventive services is more readily seen at a population level than at a individual level and accrues slowly over time. It becomes more difficult to stress prevention in a health care system driven by technology-based acute care.[3]

Current clinical management of acute stroke patients has stroke specialists and hospital physicians focusing on the acute management and diagnostic workup during hospitalization. Initiation of long-term treatment is often deferred to after discharge, when the patient resumes long-term primary care follow-up.[54] This deferred approach may result in therapy not being initiated or being initiated less efficiently and at a time (weeks or months after the initial presentation) when the stroke event and underlying atherosclerotic disease may no longer be the focus of either the patient or the primary care physician.[54]

Initiating medications during the acute stroke hospitalization phase sends the patient the message that these therapies are important for preventing recurrence and are an essential part of their treatment.[54] More important, hospital initiation of secondary prevention therapies has been shown to be a strong predictor of these therapies continuing to be used after discharge[56] and is associated with better clinical outcomes.[57–59] Table 4 shows some of the resources available to assist hospitalists in overcoming the evidence–practice gap in stroke treatment.

CONCLUSIONS

The acute stroke hospitalization setting provides the ideal opportunity for hospitalists to not only institute evidence-based prevention therapies for recurrent stroke but also to have the undivided attention of patients and their families. Furthermore, it may be risky to assume that relevant therapy when deferred will be initiated in a timely fashion, if at all, after hospital discharge. As part of an effective continuum of care, hospitalists have an important role not just in the management of acute ischemic stroke, but also in long-term reduction of vascular risk.

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REFERENCES

1. Gorelick P. Stroke prevention: windows of opportunity and failed expectations? A discussion of modifiable cardiovascular risk factors and a prevention proposal. *Neuroepidemiology*. 1997;16(4):163-173.
2. Sacco RL, Adams R, Albers G, et al. 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;37:577-617.
3. Holloway R, Benesch, C., Rush, SR. Stroke prevention: narrowing the evidence-practice gap. *Neurology*. 2000;54:1899-1906.
4. Reeves MJ, Arora S, Broderick JP, et al. Acute stroke care in the US: results from 4 pilot prototypes of the Paul Coverdell National Acute Stroke Registry. *Stroke*. 2005;36:1232-1240.
5. Ovbiagele B, Hills NK, Saver JL., Johnston, SC. Lipid Assessment and treatment patterns in hospitalized TIA and ischemic stroke patients. *J Hosp Med*. 2006;1:214-220.
6. Thom T, Haase N, Rosamond W, et al. Heart disease and stroke statistics—2006 update. A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2006;113(6):e85–e151.
7. Hankey GJ. Long-term outcome after ischaemic stroke/transient ischaemic attack. *Cerebrovasc Dis*. 2003;16(Suppl 1):14-19.
8. Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-year survival after first-ever stroke in the perth community stroke study. *Stroke*. 2003; 34:1842-1846.
9. NINDS rt-PA Stroke Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med*. 1995;333:1581-1587.
10. Nilasena D, Kresowik TF, Wiblin RT, Piskac AF, Kresowik RA, Brenton, MA. Assessing patterns of t-PA use in acute stroke. *Stroke*. 2002;33:354.
11. Growth of hospital medicine nationwide. Available at: http://www.hospitalmedicine.org/Content/NavigationMenu/ Media/GrowthofHospitalMedicineNationwide/Growth_of_ Hospital_M.htm. Accessed April 12, 2006.
12. American Academy of *Neurology*. Available at: http://www. aan.com/students/medical/faq.cfm. Accessed June 25, 2006.
13. Ringel SP. The neurologist's role in stroke management. *Stroke*. 1996;27:1935-1936.
14. Brott T. Prevention and management of medical complications of the hospitalized elderly stroke patient. *Clin Geriatr Med*. 1991;7:475-482.
15. Matchar DB, Samsa GP, Matthews JR, et al. The Stroke Prevention Policy Model: linking evidence and clinical decisions. *Ann Intern Med*. 1997;127:704-711.
16. Coull A, Lovett JK, Rothwell, PM. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. *BMJ*. 2004;328:326.
17. Kleindorfer D, Panagos P, Pancioli A, et al. Incidence and short-term prognosis of transient ischemic attack in a population-based study. *Stroke*. 2005;36:720-723.
18. Coull AJ, Lovett JK, Rothwell PM. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. *BMJ*. 2004;328:326.
19. Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. *JAMA*. 2000;284:2901-2906.
20. Hardie K, Hankey GJ, Jamrozik K, Broadhurst RJ, Anderson C. Ten-year risk of first recurrent stroke and disability after first-ever stroke in the Perth Community Stroke Study. *Stroke*. 2004;35:731-735.
21. Adams HP. New strategies for prevention of ischemic stroke: the LIFE study. *Curr Neurol Neurosci Rep*. 2003;3(1):46-51.
22. Espinola-Klein C, Rupprecht HJ, Blankenberg S, et al. [Manifestations of atherosclerosis in various vascular regions. Similarities and differences regarding epidemiology, etiology and prognosis]. *Med Klin*. 2002;97(4):221-228.
23. Rauch U, Osende JI, Fuster V, Badimon JJ, Fayad Z, Chesebro JH. Thrombus formation on atherosclerotic plaques: pathogenesis and clinical consequences. *Ann Intern Med*. 2001;134(3):224-238.
24. Caplan L. Prevention of strokes and recurrent strokes. *J Neurol Neurosurg Psychiatry*. 1998;64:716.
25. Ness J, Aronow WS. Prevalence of coexistence of coronary artery disease, ischemic stroke, and peripheral arterial disease in older persons, mean age 80 years, in an academic hospital-based geriatrics practice. *J Am Geriatr Soc*. 1999;47:1255-1256.
26. Sacco R, Wolf PA, Gorelick, PB. Risk factors and their management for stroke prevention: outlook for 1999 and beyond. *Neurology*. 1999;53(7 Suppl 4):S15–S24.
27. Albers G, Amarenco, P., Easton, JD., Sacco, RL., Teal, P. Antithrombotic and thrombolytic therapy for ischemic stroke: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. Sep 2004;126(3 Suppl):483S–512S.
28. Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. *Lancet*. 2001;358:1033-1041.
29. Rashid P, Leonardi-Bee J, Bath P. Blood pressure reduction and secondary prevention of stroke and other vascular events: a systematic review. *Stroke*. 2003;34:2741-2748.
30. Post-stroke antihypertensive treatment study. A preliminary result. PATS Collaborating Group. *Chin Med J (Engl)*. 1995; 108:710-717.

31. Lindholm LH, Carlberg B, Samuelsson O. Should beta blockers remain first choice in the treatment of primary hypertension? A meta-analysis. *Lancet.* 2005;366:1545-1553.

32. Grundy S, Cleeman JI, Merz CN, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation.* 2004;110(2):227-239.

33. Heart Protection Study Collaborative Group. Effects of cholesterol-lowering with Simvastatin on stroke and other major vascular events in 20, 536 people with cerebrovascular disease or other high-risk conditions. *Lancet.* 2004;363:757-767.

34. Welch K, et al. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) study. Presented at the 15th European Stroke Conference, Brussels, Belgium, May 16-19, 2006.

35. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38: UK Prospective Diabetes Study Group. *BMJ.* 1998;317:703-713.

36. Collins R, Armitage J, Parish S, Sleigh P, Peto R, for the Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet.* 2003;361:2005-2016.

37. Lewis E, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy: the Collaborative Study Group. *N Engl J Med.* 1993;329:1456-1462.

38. Lewis E, Hunsicker LG, Clarke WR, for the Collaborative Study Group. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med.* 2001;345:861-869.

39. Ohkubo Y, Kishikawa H, Araki E., et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract.* 1995;28:103-117.

40. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med.* 1991;325:445-453.

41. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. *N Engl J Med.* 1998;339:1415-1425.

42. Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA.* 1995;273:1421-1428.

43. Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med.* 2004;351:1493-1501.

44. Straus SE, Majumdar SR, McAlister FA. New evidence for stroke prevention: scientific review. *JAMA.* 2002;288:1388-1395.

45. Rothwell PM, Eliasziw M, Gutnikov SA, Warlow CP, Barnett HJ. Endarterectomy for symptomatic carotid stenosis in relation to clinical subgroups and timing of surgery. *Lancet.* 2004;363:915-924.

46. Alhaddad IA. Carotid artery surgery vs. stent: a cardiovascular perspective. *Catheter Cardiovasc Interv.* 2004;63:377-384.

47. Reynolds MW, Fahrbach K, Hauch O, et al. Warfarin anticoagulation and outcomes in patients with atrial fibrillation: a systematic review and metaanalysis. *Chest.* 2004;126:1938-1945.

48. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ.* 2002;324:71-86.

49. Diener HC, Cunha L, Forbes C, Sivenius J, Smets P, Lowenthal A. European Stroke Prevention Study. 2. Dipyridamole and acetylsalicylic acid in the secondary prevention of stroke. *J Neurol Sci.* 1996;143(1-2):1-13.

50. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). CAPRIE Steering Committee. *Lancet.* 1996;348:1329-1339.

51. Halkes PH, van Gijn J, Kappelle LJ, Koudstaal PJ, Algra A. Aspirin plus dipyridamole versus aspirin alone after cerebral ischaemia of arterial origin (ESPRIT): randomised controlled trial. *Lancet.* 2006;367:1665-1673.

52. Diener HC, Bogousslavsky J, Brass LM, et al. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomised, double-blind, placebo-controlled trial. *Lancet.* 2004;364:331-337.

53. Bhatt DL, Fox KA, Hacke W, et al. Clopidogrel and aspirin versus aspirin alone for the prevention of atherothrombotic events. *N Engl J Med.* Apr 20 2006;354(16):1706-1717.

54. Ovbiagele B, Saver JL, Fredieu A, et al. PROTECT: A Coordinated Stroke Treatment Program to Prevent Recurrent Thromboembolic Events. *Neurology.* Vol 63; 2004:1217-1222.

55. Ovbiagele B, Saver J, S., Fredieu A, et al. In-hospital initiation of secondary stroke prevention therapies yields high rates of adherence at follow up. *Stroke.* 2004;35:2879-2883.

56. Aronow H, Novaro GM, Lauer MS, et al. In-hospital initiation of lipid-lowering therapy after coronary intervention as a predictor of long-term utilization: a propensity analysis. *Arch Intern Med.* 2003;163:2576-2582.

57. Muhlestein JB, Anderson JL, Horne BD, et al. Early effects of statins in patients with coronary artery disease and high C-reactive protein. *Am J Cardiol.* 2004;94:1107-1112.

58. Fonarow GC, Gawlinski A, Moughrabi S, Tillisch JH. Improved treatment of coronary heart disease by implementation of a Cardiac Hospitalization Atherosclerosis Management Program (CHAMP). Am J Cardiol. Apr 1 2001;87(7):819-822.

59. Fonarow GC, Gheorghiade M, Abraham WT. Importance of in-hospital initiation of evidence-based medical therapies for heart failure-a review. *Am J Cardiol.* 2004;94:1155-1160.

60. Lawes CM, Bennett DA, Feigin VL, Rodgers A. Blood pressure and stroke: an overview of published reviews. *Stroke.* 2004;35:1024.

61. Cannon C, Braunwald E, McCabe, CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med.* 2004;350:1495-1504.

62. Meyers CD, Kamanna VS, Kashyap ML. Niacin therapy in atherosclerosis. *Curr Opin Lipidol.* 2004;15:659-665.

63. Bloomfield Rubins H, Davenport J, Babikian V, et al. Reduction in stroke with gemfibrozil in men with coronary heart disease and low HDL cholesterol: The Veterans Affairs HDL Intervention Trial (VA-HIT). *Circulation.* 2001;103:2828-2833.

64. Reichard P, Nilsson BY, Rosenqvist U. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. *N Engl J Med.* 1993;329:304-309.