

# The Impact of a Stroke Prevention Clinic in Diagnosing Modifiable Risk Factors for Stroke

Mikael S. Mouradian, Muhammad S. Hussain, Harris Lari, Abdul Salam, Ambikaipakan Senthilselvan, Naeem Dean, Ashfaq Shuaib

**ABSTRACT: Objective:** To evaluate the referral patterns of patients to a stroke prevention clinic (SPC) and to test the adequacy of pre-referral diagnosis and management of modifiable risk factors for stroke. **Methods:** We collected prospective data on consecutive patients referred to the SPC at University of Alberta Hospital in Edmonton, Alberta, Canada. Outcome measures included: alternate diagnoses to stroke or transient ischemic attack (TIA), uncontrolled or undiagnosed hypertension, hyperlipidemia and diabetes, therapies, and investigations leading to carotid endarterectomy. **Results:** Two thousand and eleven patients were referred to SPC. Nearly 25% of the referrals originated from the emergency room and the rest from general physicians. Of the referrals, 68.7% were confirmed as TIA or stroke at the SPC. Among 1381 patients with TIA or stroke, 736 had history of hypertension. Uncontrolled hypertension was found in 265 patients (36.0% of those with hypertension: 95% CI: 32.5–39.5) while undiagnosed hypertension was found in 103 (15.9% of those without hypertension: 95%CI: 13.14–18.79). History of hyperlipidemia was present in 451 patients (32.6%) and 356 (78.9%: 95% CI: 75.2–82.69) of these patients were not at target for secondary prevention. Among 930 patients without history of hyperlipidemia, 739 (79.5%: 95% CI: 76.8–82.1) were diagnosed with hyperlipidemia through the SPC. Fasting blood glucose levels above 7.1 mmol/L in patients with and without history of diabetes were 221 (79.2%: 95% CI: 74.5–83.9) and 66 (6%: 95%CI: 4.6–7.4) respectively. **Conclusions:** Management of risk factors for stroke needs improvement. SPCs should consider actively managing the classical modifiable risk factors of stroke.

**RÉSUMÉ: L'impact d'une clinique de prévention de l'accident vasculaire cérébral sur le diagnostic des facteurs de risque modifiables de l'accident vasculaire cérébral. Objectif:** Évaluer le profil d'orientation de patients vers une clinique de prévention de l'accident vasculaire cérébral (CPAVC) et la pertinence du diagnostic et de la prise en charge des facteurs de risque modifiables de l'accident vasculaire cérébral (AVC). **Méthodes:** Nous avons recueilli des données prospectives sur des patients consécutifs référés à la CPAVC du University of Alberta Hospital à Edmonton, Alberta, Canada. Nous avons évalué les résultats suivants: les diagnostics autres que l'AVC ou l'ischémie cérébrale transitoire (ICT), l'hypertension, l'hyperlipidémie ou le diabète non contrôlé ou non diagnostiqué, les traitements et les évaluations menant à l'endartérectomie carotidienne. **Résultats:** Deux mille onze patients ont été référés à la CPAVC. Presque le quart de ces patients étaient référés par le service d'urgences et les autres étaient référés par des praticiens généraux. Chez 68,7% des patients le diagnostic d'ICT ou d'AVC a été confirmé à la CPAVC. Parmi les 1381 patients ayant subi une ICT ou un AVC, 736 avaient une histoire d'hypertension. Une hypertension non contrôlée a été diagnostiquée chez 265 patients (36,0% des patients hypertendus ; IC 95% : 32,5 à 39,5), un diagnostic d'hypertension non reconnue a été posé chez 103 patients (15,9% de ceux qui n'étaient pas hypertendus ; IC 95% : 13,14 à 18,79). Une histoire d'hyperlipidémie était présente chez 451 patients (32,6%) et 356 d'entre eux (78,9% ; IC 95% : 75,2 à 82,69) n'avaient pas atteint les valeurs cibles de traitement chez des patients en prévention secondaire. On a posé un diagnostic d'hyperlipidémie à la CPAVC chez 739 patients (79,5% ; IC 95% : 76,8 à 82,1) des 930 patients sans histoire d'hyperlipidémie. Une glycémie à jeun au-dessus de 7,1 mmol/L était présente chez 221 patients ayant une histoire de diabète (79,2% ; IC 95% : 74,5 à 83,9) et chez 66 patients sans histoire de diabète (6% ; IC 95% : 4,6 à 7,4). **Conclusions:** La prise en charge des facteurs de risque de l'AVC doit être améliorée. Les CPAVC devraient envisager une prise en charge active des facteurs de risque modifiables classiques de l'AVC.

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Stroke prevention clinics (SPCs) are a relatively recent and evolving phenomenon in the delivery of specialized health care. Patients can be seen very early after a cerebrovascular event and stated targets for risk assessment such as hypertension, hyperlipidemia, smoking, atrial fibrillation, and internal carotid artery stenosis can be made. In addition, appropriate medical and surgical interventions such as antiplatelet or anticoagulation treatment, blood pressure management, cholesterol lowering agents, and carotid endarterectomy can be initiated for secondary prevention.<sup>1,2</sup> Little is known about the referral patterns to SPCs

and the extent of their involvement in screening and intervention for secondary prevention. Studies from two SPCs demonstrated

From the Division of Neurology (MM, MH, HL, AS, ND, AS), Department of Epidemiology (AS), University of Alberta, Edmonton, AB, Canada.

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Reprint requests to: Ashfaq Shuaib, 2E3.13 Walter C. Mackenzie Health Sciences Center, University of Alberta, Edmonton, Alberta, Canada T2G 2B7

inadequate management of certain modifiable risk factors, such as hypertension, hyperlipidemia, smoking and diabetes, in primary care practice despite consultations generated at SPCs.<sup>3,4</sup> Suboptimal control of vascular risk factors in patients with ischemic stroke has also been found in patient recently discharged from hospital.<sup>5</sup> Although a recent study indicates high rates of patient compliance with secondary prevention measures (via telephone interviews), the authors indicate that this does not allow statements about the quality of secondary prevention of stroke.<sup>6</sup> Despite epidemiological and drug trial results, large differences exist between the evidence and the practice in stroke prevention.<sup>7-9</sup> It is estimated that adequate control of blood pressure or blood glucose is achieved in nearly 50% of general hypertensive or diabetic population.<sup>10-13</sup> More recently published data from North America and several European countries indicate alarmingly low rates of adequate management of hypertension in the general population (in the range of 25-50% in North-America, and 5% to 10% in several European countries).<sup>14-16</sup> It is still unknown how successful SPCs will be in screening and actively managing the modifiable risk factors of stroke.<sup>2</sup> Thus, we evaluated the referral patterns of patients to a stroke prevention clinic (SPC) and assessed the adequacy of pre-referral diagnosis and management of modifiable risk factors for stroke.

## METHODS

The SPC at the University of Alberta serves a population of 1.5 million. The SPC is held daily, and the staff includes stroke neurologists and fellows, ultrasound technologist, and a nurse. The purpose of the SPC is for confirmation of cerebrovascular disease and subsequent investigation and management of modifiable risk factors for stroke in conjunction with the referring and primary care physicians. Referrals to the SPC are made by other physicians using a standardized referral form or referral letter. The referrals are triaged by the nurse coordinator. Patients are assessed in clinic to determine the etiology of their symptoms, possible risk factors, and interventions for secondary prevention are made accordingly. Patients who are candidates for

carotid endarterectomy are referred to our vascular neurosurgeons.

Data for this study was collected prospectively. The following investigations and the clinical criteria were used in assessing modifiable risk factors of stroke:

**Hypertension:** Definition of undiagnosed or uncontrolled hypertension based on the 6<sup>th</sup> report of the Joint National Committee<sup>17</sup> is given in Table 1. Two blood pressure measurements were obtained at the SPC and the recent blood pressure values from the referring physician's office, or patient's self monitoring were collected.

**Hyperlipidemia:** Definition of undiagnosed or uncontrolled hyperlipidemia based on the criteria of the National Cholesterol Education Program criteria<sup>18</sup> is given in Table 1.

**Diabetes:** Definition of undiagnosed or uncontrolled diabetes based on the report of the Expert Committee on the Diagnosis and Classification of Diabetes is given in Table 1.<sup>19</sup>

**Carotid artery stenosis:** All patients with symptoms localized to internal carotid artery (ICA) territory underwent a carotid Doppler ultrasound at the SPC. Patients with 50% to 99% ICA stenosis or occlusion on the symptomatic side underwent angiographic study. Patient candidacy for carotid endarterectomy was decided according to criteria developed by the North American Symptomatic Carotid Endarterectomy Trial Collaborators.<sup>20,21</sup>

**Cardiac source of embolization:** Electrocardiogram, Holter monitoring, or echocardiogram was obtained as indicated. Transcranial Doppler ultrasound with agitated saline was performed mainly to investigate the presence of patent foramen ovale. Issues regarding patient education and consult letters are described in a previous study from this clinic.<sup>3</sup> Referrals to other subspecialty clinics were made as necessary.

**Statistical Method:** Means with standard deviations were used to describe continuous variables and categorical variables were described with frequencies and percentages with 95% confidence interval. The differences between continuous variables were tested using two-independent sample t-tests. McNemar tests were used to test the changes in medication use

**Table 1: Classification of risk factors**

Hypertension	<p><i>Existing:</i> Clinical history of hypertension or use of antihypertensive medications</p> <p><i>Uncontrolled:</i> Existing hypertension with two blood pressure measurements one week apart &gt; 140/90*</p> <p><i>Undiagnosed:</i> No existing hypertension with two blood pressure measurement one week apart &gt; 140/90*</p>
Hyperlipidemia	<p><i>Existing:</i> Medical history of hyperlipidemia or use of cholesterol lowering medications</p> <p><i>Uncontrolled:</i> Existing hyperlipidemia with measured serum LDL &gt; 2.6 mmol/L<sup>†</sup> (measurement at or after SPC visit)</p> <p><i>Undiagnosed:</i> No existing hyperlipidemia with measured serum LDL &gt; 2.6 mmol/L<sup>†</sup> (measurement at or after SPC visit)</p>
Diabetes	<p><i>Existing:</i> Medical history of diabetes or use of medications for diabetes</p> <p><i>Uncontrolled:</i> Existing diabetes and a measured fasting blood glucose of &gt; 6.0 mmol/L (measurement at or after SPC visit)</p> <p><i>Undiagnosed:</i> No existing diabetes and a measured fasting blood glucose of &gt; 7.0 mmol/L<sup>‡</sup> (measurement at or after SPC visit)</p>

\* Based on JNC 6 guidelines.<sup>17</sup> † Based on National Cholesterol Education Program criteria.<sup>18</sup> ‡ Based on Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus<sup>19</sup>

**Table 2: Gender and age distribution diagnoses made at SPC**

	n (%)	Age (in years)*
Stroke or TIA (n=1381)		66.6 ±12.9
• Female	678 (49.1)	67.2 ± 13.6
• Male	703 ( 50.9)	66.1 ± 12.2
Other diagnoses (n=630)		61.9 ± 15.8
• Female	382 (60.6)	61.7 ± 16.1
• Male	248 ( 39.4)	62.3 ± 15.6

\* Mean ± Standard deviation

before index event, before seen at SPC, and before and after seen at SPC. A P-value < 0.05 was considered as statistically significant. These analysis were carried out using the statistical software SPSS.<sup>22</sup>

## RESULTS

During the 30 months from January 1999 to June of 2002, 2011 patients were seen at the SPC. From the time of referral, the mean waiting period was 12.2 days (standard deviation: 6.6; range <24 hours to 30 days). All referrals were made for a query of cerebrovascular event and/or for diagnosis and management of stroke risk factors. Among 2011 patients, 1381 referrals were confirmed as transient ischemic attack (TIA) or stroke at the SPC and the remaining 630 were diagnosed with various medical or neurological conditions other than TIA or stroke. The age of the latter group was significantly younger than the age of the TIA or stroke group ( $p < 0.001$ ). Patient demographics are summarized in Table 2. The frequencies of various symptoms in the non-TIA or stroke group that prompted a referral to SPC are summarized in Table 3.

Twenty-five percent of the referrals originated from emergency room (ER) physicians, and 75% from general practitioners. Of all ER referrals 76% were reconfirmed as TIA or stroke at the SPC (i.e. a 24% diagnostic disparity). Diagnostic disparity between the general practitioners and SPC was 36%.

Among 1381 patients with TIA or stroke, 736 had a history of hypertension, and among those, 265 (36.0% of those with

**Table 3: Presenting complaints in patients in whom a diagnosis other than TIA or stroke was made at the SPC**

Symptom	n = 630
Dizziness / Light-headedness	133 (21%)
Numbness & tingling	113 (18%)
Memory impairment	88 (14%)
Headache	76 (12%)
Loss of consciousness	69 ( 11%)
Vertigo	50 (8%)
Blurred vision	38 ( 6%)
Limb pain	31 ( 5%)
Limb weakness	19 (3%)
Impaired gait	13 (2%)

hypertension: 95% CI: 32.5–39.5) were uncontrolled. Another 645 patients had no past history of hypertension, but 103 (16.0% of those without a past history of hypertension: 95%CI: 13.1–18.8) of those were later diagnosed with hypertension through the SPC. Overall, 27% of the patients with TIA or stroke either had uncontrolled or undiagnosed hypertension prior to their SPC visit. A history of hyperlipidemia was present in 451 patients and 356 (78.9%: 95% CI: 75.2–82.69) of these patients were not at target for secondary prevention. Among 930 patients without history of hyperlipidemia, 739 (79.5%: 95% CI: 76.8–82.1) were diagnosed with hyperlipidemia through the SPC. Among 279 patients with known diabetes, 221 (79.2%: 95% CI: 74.5–83.9) had fasting blood glucose above the target (6.0 mmol/L) and among 1102 patients without history of diabetes, 66 (6%: 95%CI: 4.6–7.4) had fasting blood glucose above 7.0 mmol/L.

Sixteen patients were diagnosed with atrial fibrillation or sick sinus syndrome. History of coronary heart disease was present in 221 (16.4%), valvular heart disease in 16 (1.2%), permanent pace maker in 14 (1.1%), and symptomatic peripheral vascular disease in 39 (2.8%) patients.

Prior to TIA or stroke, 110 patients were already on aspirin. Following stroke or TIA but before SPC visit, an additional 869 patients were started on aspirin. At the SPC visit, another 110

**Table 4: Index event indicates the clinical phenomenon that initiated referral to SPC**

Medications	Before index event n (%)	Before seen at SPC n (%)	After seen at SPC n (%)
Aspirin	110 (7.9) †	979 (70.9)	1089 (78.9) ††
Clopidogrel	12 (0.9) †	243 (17.6)	363 (26.3) ††
Aggrenox	2 (0.1) †	30 (2.2)	54 ( 3.9) ††
Warfarin	37 (2.7) †	143 ( 10.4)	140 (10.1) *

n=1381. Before index event vs. before seen at SPC, †P<0.001. Before seen at SPC vs. after seen at SPC, ††P<0.001, \*P=NS. P-values calculated from McNemar test.

patients were started on aspirin (Table 4). Similar information for clopidogrel, Aggrenox, and warfarin is given in Table 4. Warfarin was discontinued in 18 patients because of inappropriate indications. Fifteen patients were started on warfarin at SPC for atrial fibrillation. Therefore total of 33 changes were made in warfarin use (Table 4).

Of all TIA or strokes, 1194 (86.5%) events were in the carotid artery territories, and 187 (13.5%) were in the vertebrobasilar artery territories. Carotid Doppler was performed at the SPC in 1018 (85.3%) of the patients with carotid artery territory events. Digital-subtraction angiography was performed in 131 (12.8%) of these patients to further investigate the symptomatic carotid artery territory, 63 (48%) of which were performed to investigate dissections, aneurysms, or other intracerebral vascular pathologies. The remaining 68 (52%) angiograms were performed to further confirm carotid Doppler findings to assess eligibility for CEA. Of these 68 patients, 41 (60%) underwent CEA. Five of the CEAs were performed in patients with internal carotid artery (ICA) stenosis of 50% to 69%. All the remaining CEAs were performed on patients with symptomatic ICA stenosis of 70% to 99%.

## DISCUSSION

Nearly one third of the referrals to SPC were not TIA or stroke. This high rate of discordance will be seen, as the SPC serves the community by offering the experts' removal of a diagnosis of TIA or stroke in challenging cases. However, it can also be argued that these referrals delay the appropriate diagnosis and intervention for non-stroke/TIA patients, and also prolong the SPC waiting period for the patients with true TIAs or strokes. Many patients who were not diagnosed with a TIA or stroke presented with subjective or non-specific complaints such as numbness, tingling, blurred vision, or memory impairment. Elevating the knowledge base of ER physicians and general practitioners with regards to stroke syndromes may decrease the diagnostic disparity.

Among many risk factors stroke, management of hypertension<sup>23,24</sup> hyperlipidemia,<sup>25</sup> atrial fibrillation<sup>26</sup> and carotid endarterectomy for symptomatic carotid stenosis<sup>20</sup> have been shown to offer secondary prevention of stroke in randomized trials. However, a large number of patients have either uncontrolled or undiagnosed risk factors, particularly hypertension. There are multiple reasons for this, including underdiagnosis, patient compliance, and conditions that may be resistant to treatment. Starting late 1970s, the incidence of stroke severity and stroke mortality has decreased in the United States. This has been partly attributed to better detection and management of hypertension.<sup>27</sup> However, it is estimated that in the United States almost half of the individuals with hypertension remain hypertensive.<sup>28</sup> A recent study from Canada estimated that nearly 60% of individuals with hypertension are not managed according to the Canadian hypertension recommendations.<sup>29</sup> The current evidence about the benefit of adequate blood pressure management in primary and secondary prevention of stroke should be vigorously practiced.<sup>23,24,30</sup> Although their effectiveness has yet to be proven, SPCs should be actively involved in the screening and management of hypertension.

Similarly, a significant number of patients were not at the appropriate target LDL cholesterol level for secondary prevention. This is concerning finding, especially in view of the results of Heart Protection Study.<sup>25</sup> Our data indicates that the diagnosis and management of hyperlipidemia in the stroke population is suboptimal. The exact cause of this disparity between current recommendations and the reality in the community is unknown. Recently, it was shown that in patients with coronary heart disease, only 37% of the eligible patients received lipid lowering drugs, and nearly 60% were screened according to National Cholesterol Education Program guidelines.<sup>31,32</sup> Considering that secondary prevention concepts in stroke are more recently developed as compared to that for coronary heart disease, it is hoped that over time screening and adequate management of hyperlipidemia for secondary prevention of stroke will improve in community practice. Once again, SPCs should take a leading role in this aspect of stroke prevention as well.

Diagnosis of diabetes was missed in relatively fewer patients. However the success rate of adequate glycemic control among diabetics was low. This finding highlights the need to develop a working partnership between metabolic clinics, general practitioners and SPCs, especially when NCEP-III guidelines are considered, where diabetes is classified as a coronary artery disease equivalent.<sup>19</sup>

Following a TIA or stroke, aspirin was prescribed in large number of patients by community practice or ER physicians. Although through the SPC, 254 changes or additions were made in antiplatelet prescriptions, the use of these medications closely followed the general guidelines. Warfarin was discontinued in 18 patients because of inappropriate indications. This is concerning, especially considering that only few clear indications exist for the long term use of this medication in stroke or TIA.

Patients presenting with carotid artery territory stroke or TIA were thoroughly investigated for symptomatic carotid disease and only 41 patients with anterior circulation TIA or stroke underwent CEA. The great majority of surgical interventions were performed on symptomatic ICA stenosis of 70-99%. The five patients with 50% to 69% ICA stenosis who underwent CEA had multiple risk factors for stroke. No patient was screened or underwent carotid endarterectomy for asymptomatic ICA stenosis. This is in agreement with the recent recommendations of Canadian Stroke Consortium.<sup>33</sup> A recent published audit on CEA performed in a Canadian health care region reflects this practice.<sup>34</sup>

In conclusion, in the community practice many patients remain undiagnosed or sub-optimally managed for hypertension, hyperlipidemia and diabetes, following cerebrovascular ischemic events. While extended involvement of SPCs in screening and managing the conventional risk factors of stroke seems to be necessary, additional studies are needed to assess the effectiveness of SPCs in managing the common risk factors of stroke such as hypertension and hyperlipidemia.

## REFERENCES

1. Wolf PA, Clagett PA, Easton JD, et al. Preventing ischemic stroke in patients with prior stroke and transient ischemic attack. *Stroke* 1999;30:1991-1994.
2. Straus SE, Majumdar SR, McAlister FA. New evidence for stroke prevention. Scientific review. *JAMA* 2002;288:1396-1398.

3. Mouradian M, Majumdar SR, Senthilselvan A, Khan K, Shuaib A. How well are hypertension, hyperlipidemia, diabetes, and smoking managed after stroke or transient ischemic attack? *Stroke* 2002;33:1656-1659.
4. Joseph LN, Babikian VL, Allen NC, Winter MR. Risk factor modification in stroke prevention: the experience of a stroke clinic. *Stroke* 1999;30:16-20.
5. Kalra L, Perez I, Melboun A. Stroke risk management. Changes in mainstream practice. *Stroke* 1998;29:53-57.
6. Sappok T, Faulstich A, Stuckert E, et al. Compliance with secondary prevention of ischemic stroke. A prospective evaluation. *Stroke* 2001;32:1884-1889.
7. Holloway RG, Benesch C, Rush SR. Stroke prevention. Narrowing the evidence-practice gap. *Neurology* 2000;54:1899-1906.
8. Holloway RG, Rush SR. Quality improvement in stroke prevention. In: The prevention of stroke, Gorelick PB, Alter M. editors, Parthenon Publishing, 2002; 141-147.
9. Goldstein LB. Gaps in professional and community knowledge about stroke prevention and treatment. In: Gorelick PB, Alter M. (Eds). The Prevention of Stroke, New York, Parthenon Publishing, 2002: 149-154.
10. Marques-Vidal P, Tuomilehto J. Hypertension awareness, treatment and control in the community: is the "rule of halves" still valid? *J Hum Hypertens* 1997;11:213-220.
11. Joffers MR, Ghadrian P, Fodod JG, et al. Awareness, treatment and control of hypertension in Canada. *Am J Hypertens* 1997;10:1097-1102.
12. Colhoum HM, Dong W, Poulter NR. Blood pressure screening, management and control in England: results from the health survey for England 1994. *J Hypertens* 1998;16:747-752.
13. Lantino-Ang LC. Epidemiology of diabetes in Western Pacific region: focus on Philippines. *Diabetes Res Clin Pres* 2000;50:S29-S34.
14. Ihab H, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1998-2000. *JAMA* 2003;290:199-206.
15. Lloyd DM, Evans JC, Larson MG, et al. Differential control of systolic and diastolic blood pressure. *Hypertension* 2000;36:594-599.
16. Wolf-Maier K, Cooper KS, Benegas JR, et al. Hypertension prevalence and blood pressure levels in 6 European countries, Canada and the United States. *JAMA* 2003;289:2362-2369.
17. Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure: the sixth report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure. *Arch Intern Med* 1997;157:2413-2446.
18. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *J Am Med Assoc* 2001;285:2486-2497.
19. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 2000;23;Suppl. 1:S4-S19.
20. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;325:445-453.
21. Barnett H.J.M, Taylor D.W, Eliasziw M, et al. Meldrum H.E. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. *N Engl J Med* 1998;339:1415-1425.
22. Statistical Packages for Social sciences SPSS (Release 11.01, Standard Version, copy right © SPSS inc., 1989-2001.
23. PROGRESS Collaborative Group. Randomized trial of a perindopril-based blood pressure-lowering regimen among 6105 individuals with previous stroke or transient ischemic attack. *Lancet* 2001;358:1033-1041.
24. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic. *JAMA* 2002;288:2981-2997.
25. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20536 high-risk individuals: a randomized placebo-controlled trial. *Lancet* 2002;360:7-22.
26. Saxena R, Koudstall P. Anticoagulants versus antiplatelet therapy for preventing stroke in patients with nonrheumatic atrial fibrillation and a history of stroke or transient ischemic attack. *Cochrane Database Syst Rev* 2004;CD000187.
27. Bonita R, Beaglehole R. The enigma of the decline in stroke deaths in the United States. The search for an explanation. *Stroke* 1996;27:370-372.
28. Joint National Committee: The Fifth Report of the Joint National Committee on detection, evaluation, and treatment of high blood pressure. NIH Publication no. 93-1088. NIH, Bethesda, MD, 1993.
29. Khan N, Chockalingam A, Campbel NRC. Lack of control of high blood pressure and treatment recommendations in Canada. *Can J Cardiol* 2002;18:657-661.
30. PATS Collaborating Group. Post-stroke antihypertensive treatment study: a preliminary result. *Chin Med J* 1995;108:710-717
31. Majumdar SR, Gurwitz JH, Soumerai S. Undertreatment of hyperlipidemia in the secondary prevention of coronary artery disease. *J Gen Intern Med* 1999;14:711-717.
32. Folkis JP, Zyzanski SJ, Schwartz JM, Suhan PS. Physician noncompliance with the 1993 National Cholesterol Education Program (NCEP-ATPII) guidelines. *Circulation* 1998;98:851-855.
33. Perry JR, Szalai JP, Norris JW. For the Canadian Stroke Consortium. Consensus against both endarterectomy and routine screening for asymptomatic carotid artery stenosis. *Arch Neurol* 1997;54:25-28.
34. Auditing carotid endarterectomy: A regional experience. Findlay JM, Nykolyn L, Lubkey TB, et al. *Can J Neurol Sci* 2002;29:326-332.