

Guidelines for PRIMARY and SECONDARY PREVENTION of STROKE

STROKE PREVENTION

Preface to the Guidelines on Primary and Secondary Prevention of Stroke

- These practice guidelines provide an overview of the epidemiology and evidences associated with established and modifiable stroke risk factors, followed by recommendations for reducing stroke risk. These revised guidelines reflect current knowledge on primary and secondary stroke prevention.
- The strategy in developing these guidelines was to utilize information from several existing national consensus and evidence-based guidelines to highlight significant associations between a risk factor and stroke and how modifying the risk factor through treatment or lifestyle modification can improve outcome. This knowledge would lead to proper recommendations.
- The Stroke Prevention Writing Group members are active members of the Stroke Society of the Philippines and the Philippine Neurological Association invited by the committee chairs on the basis of each reviewer's interest, training and previous work in the relevant topic areas. Members then updated the previous editions using recently published local data. The updated working paper was submitted for initial comments by the society members, and later to key opinion leaders and institutions.
- Each major topic first discusses epidemiology (Section A) of a risk factor and its association with stroke, then highlights clinical trials or interventions on the risk factor for preventing stroke (Section B). When evidence is available, a separate subsection (Section B1) discusses primary- and secondary-prevention trials. Section C states the recommendations based on evidences.
- When available, the strength of the recommendation are included and graded according to the American Heart Association (AHA)/American Stroke Association methods of classifying levels of certainty of the treatment effect and the class of evidence (Table 1).
- Recommendations considered the cost-effective treatment of drugs with established efficacy.
- These guidelines concentrated on modifiable risk factors: hypertension, diabetes, atrial fibrillation (AF) and other specific cardiac conditions, dyslipidemia, carotid artery stenosis, peripheral arterial disease, obesity, and lifestyle (exposure to cigarette smoke, excessive alcohol use, physical inactivity and unhealthy diet).
- Other less well-documented or potentially modifiable risk factors are recognized. These include metabolic syndrome, drug abuse, oral contraceptive use, sleep-disordered breathing, migraine headache, hyperhomocysteinemia, hypercoagulability, inflammation and infection. Future editions may highlight these topics.

- Because most strokes are cerebral infarcts, these recommendations focus primarily on the prevention of ischemic stroke or transient ischemic attack (TIA).
- Although the primary outcome of interest is the prevention of stroke, many recommendations reflect the evidence on the reduction of all vascular outcome after stroke, including stroke, myocardial infarction (MI) and vascular death.
- For secondary stroke prevention, the aim is to provide comprehensive and timely evidence-based recommendations on the prevention of ischemic stroke among survivors of ischemic stroke or TIA.

Table 1. Classes and Levels of Evidence Used in AHA Recommendations

Class I	Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective
Class II	Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment
<i>Ila</i>	Weight of evidence or opinion is in favor of the procedure or treatment.
<i>Ilb</i>	Usefulness/efficacy is less well established by evidence or opinion
Class III	Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful
Level of Evidence A: Data derived from multiple randomized clinical trials Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies Level of Evidence C: Expert opinion or case studies	

I. HYPERTENSION

Hypertension awareness, treatment and control remain low. Stroke mortality rates are predicted by the prevalence of hypertension. Yet compelling data show that first stroke can be prevented by blood pressure (BP) control, among others.¹

A. Epidemiology: Hypertension is directly related to primary and secondary stroke risk. The higher the BP, the greater is the risk. Hypertension has a local prevalence of 17.4%² and is the most important modifiable risk factor for stroke. The population attributable risk (PAR) of hypertension for stroke is high at around 25%.³ Hypertensive people are three to four times more likely to have a stroke than non-hypertensive people. Furthermore, both systolic and diastolic hypertensions are risk factors.

B. Risk Modification: Treatment of hypertension substantially reduces the risk of stroke. All classes of antihypertensive drugs are effective for BP control. A meta-analysis shows BP lowering confers a 30% to 40% stroke risk reduction. A 10 to 12 mmHg SBP reduction and a 5 to 6 mmHg DBP reduction confers relative reductions in stroke risk of 38%. The treatment of isolated systolic hypertension in the elderly decreases the risk for stroke by 36%.⁴ Furthermore, small BP reductions in a population may lead to substantial reductions in stroke risk: it is estimated that a population strategy to reduce systolic BP (SBP) by 2 mmHg will reduce stroke mortality by 6%.⁵ A 3-mmHg SBP reduction reduces risk by 8%. A 5-mmHg reduction reduces risk by 14%. Similar to other cardiovascular disorders, stroke reduction is progressive as BP is reduced to at least 115/75 mmHg.⁶

B1. Primary Stroke Prevention

There is strong evidence that the control of high BP contributes to the prevention of stroke.⁵ The choice of antihypertensive agents should be individualized. BP reduction is generally more important than the specific agent used to achieve this goal.

Hypertension remains undertreated in the community, and programs to improve treatment compliance need to be developed and supported. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) provides a comprehensive, evidence based approach to the classification and treatment of hypertension (Table 2).⁵

Table 2. Classification and management of BP for adults*

BP Classification	SBP* mmHg	DBP* mmHg	Lifestyle Modification	Initial drug therapy	
				Without Compelling Indication	With Compelling Indications
Normal	<120	and <80	Encourage	No antihypertensive drug indicated.	Drug(s) for compelling indications. [‡]
Prehypertension	120-139	or 80-89	Yes		
Stage 1 Hypertension	140-159	or 90-99	Yes	Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.	Drug(s) for the compelling indications. [‡] Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.

Stage 2 Hypertension	≥ 160	or ≥ 100	Yes	Two-drug combination for most [†] (usually thiazide-type diuretic and ACEI or ARB or BB or CCB).	
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DBP, diastolic blood pressure; SBP, systolic blood pressure.

Drug abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; BB, beta-blocker; CCB, calcium-channel blocker.

*Treatment determined by highest BP category.

[†]Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.

[‡]Treat patients with chronic kidney disease or diabetes to BP goal of <80 mmHg.

B2. Secondary Stroke Prevention

The overall decrease in stroke is related to the degree of BP lowering achieved. Meta-analyses of randomized controlled trials (RCTs) confirm an approximate 30% to 40% stroke reduction with BP lowering.^{7,8} Furthermore there is a continuous association of both SBP and DBP with the risk of ischemic stroke.

The JNC 7 stresses the importance of lifestyle modifications in the overall management of hypertension. SBP reductions have been associated with weight loss; diet rich in fruits, vegetables and low-fat dairy products; regular aerobic physical activity; and limited alcohol consumption.

Data on the relative benefits of specific antihypertensive regimens for secondary stroke prevention are largely lacking. A meta-analysis showed a significant reduction in recurrent stroke with diuretics and combined diuretics and angiotensin-converting enzyme (ACE) inhibitors (ACEIs), but not with beta-blockers (BBs) or ACEIs alone.⁹ Whether a particular class of antihypertensive drug or a particular drug within a given class offers an advantage in patients after ischemic stroke remains uncertain.

With regard to stroke risk reduction, there may be beneficial non-BP-lowering properties of certain classes of BP-lowering agents, particularly from ACEIs and angiotensin-receptor blockers (ARBs).^{10,11} Among hypertensive diabetics, the use of ACEIs or ARBs reduces the risk of major vascular events and stroke by 24%.

C. Recommendation:

C1. For primary prevention

Regular screening for hypertension (at least every 2 years in most adults and more frequently in minority populations and the elderly) and appropriate management (Class I, Level A), including dietary changes, lifestyle modification and pharmacological therapy as summarized in JNC 7, are recommended.

C2. For secondary prevention

Antihypertensive treatment is recommended for both prevention of recurrent stroke and of other vascular events in patients who have had an

ischemic stroke or TIA and are beyond the hyperacute period (Class I-A).¹² Because this benefit extends to people with or without a history of hypertension, this recommendation should be considered for all ischemic stroke and TIA patients (Class IIa-B). The absolute target BP level and reduction are uncertain and should be individualized, but benefit has been associated with an average reduction of 10/5 mmHg, and normal BP levels have been defined as <120/80 mmHg by JNC 7 (Class IIa-B). BP should be adequately controlled in patients with hypertension. Physicians should check the BP of all patients at every visit. Patients with hypertension should be advised to monitor their BP at home.

Several lifestyle modifications have been associated with BP reductions and should be included as part of a comprehensive antihypertensive therapy (Class IIb-C).

The optimal drug regimen remains uncertain; however, the available data support the use of diuretics and the combination of diuretics and an ACEI (Class I-A). The choice of specific drugs and targets should be individualized on the basis of reviewed data and consideration of specific patient characteristics (e.g., extracranial cerebrovascular occlusive disease, renal impairment, cardiac disease or diabetes) (Class IIb-C). The Stroke Society of the Philippines supports the guidelines set forth by the Philippine Society of Hypertension and the JNC 7.

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II. TRANSIENT ISCHEMIC ATTACK

Conventionally, a person is diagnosed with stroke if neurological symptoms persist more than 24 hours; otherwise, a focal neurological deficit lasting <24 hours was defined as a TIA. However, with modern brain imaging, infarctions can be detected even in patients with brief symptoms. The most updated definition of stroke used by clinical trials is either symptoms lasting >24 hours or an acute clinically relevant brain lesion on imaging in patients with rapidly vanishing symptoms. The proposed new definition of TIA is a “brief episode of neurological dysfunction caused by a focal disturbance of brain or retinal ischemia, with clinical symptoms typically lasting less than 1 hour, and without evidence of infarction.”¹

A. Epidemiology: Although TIA is most correctly considered a manifestation of cerebrovascular disease and not a stroke risk factor, it is an important predictor of future strokes. Reported 90-day stroke risk associated with TIA reaches 10.5%, and the highest risk is apparent in the first week.² The risk is 4% to 8% in the first month, 12% to 13% in the first year, and 24% to 29% in 5 years.²⁻⁴ Patients with hemispheric TIA and carotid stenosis of more than 70% have a particularly poor prognosis, with a stroke rate of >40% in 2 years.^{4,5}

B. Risk Modification: The distinction between TIA and ischemic stroke has become less important in recent years because many preventive approaches are applicable in both. As the risk factors for ischemic stroke and TIA are the same, the evidences supporting that modification of a particular risk factor are found in the corresponding sections in these guidelines. Many clinical trials have demonstrated that antiplatelets reduce stroke risk after TIA or minor stroke by 18% to 41%. RCTs on antiplatelet drugs that reduce stroke, either alone or as part of a composite of vascular outcomes, include aspirin, dipyridamole, aspirin-dipyridamole combination, ticlopidine, cilostazol and clopidogrel.⁶⁻⁸ Although some studies limited subjects to those with minor strokes instead of TIA, it is reasonable to consider a similar prophylactic effect in TIA patients.

C. Recommendations: Efforts to increase public awareness and that of health workers regarding TIA and its significance should be maximized.

Evaluation of TIA should be attempted to define cause and determine prognosis and treatment. TIA patients should be expeditiously evaluated for vascular and cardiac risk factors for stroke. Hypertension, hyperlipidemia, diabetes, carotid stenosis and other modifiable risk factors should be treated, as outlined in these guidelines.

The cost and benefit of a drug should be considered when choosing an antiplatelet agent. Aspirin is the first choice unless contraindicated.

Patients who developed stroke recurrence while on aspirin, or those who cannot tolerate or have contraindications to aspirin may be given clopidogrel,

combined aspirin and dipyridamole, cilostazol, or other antiplatelets with RCT evidence of benefit. Aspirin is not recommended for primary stroke prevention, as this has no evidence especially among men.

While there is evidence of benefit of combined aspirin and clopidogrel in coronary heart disease or post-revascularization patients, this combination is not recommended for stroke prevention.

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APPENDIX OF TIA MANAGEMENT FOR STROKE PREVENTION

Since the 3rd edition of these guidelines, there have been several important trials related to antiplatelets and anticoagulants. The 2006 recommendations of the American Heart Association and the American Stroke Association are outlined below:

ASA/AHA Recommendations for Antithrombotic Therapy for Noncardioembolic Stroke or TIA (Oral Anticoagulant and Antiplatelet Therapies)

- For patients with noncardioembolic ischemic stroke or TIA, antiplatelet agents rather than oral anticoagulation are recommended to reduce the risk of recurrent stroke and other cardiovascular events (Class I-A).
- Aspirin (50 to 325 mg/day), the combination of aspirin and extended-release dipyridamole, and clopidogrel are all acceptable options for initial therapy (Class IIa- A).
- Compared with aspirin alone, both the combination of aspirin and extended-release dipyridamole and clopidogrel are safe.
- The combination of aspirin and extended-release dipyridamole is suggested over aspirin alone (Class IIa-A).
- Clopidogrel may be considered over aspirin alone on the basis of direct-comparison trials. Insufficient data are available to make evidence-based

recommendations with regard to choices between antiplatelet options other than aspirin. Selection of an antiplatelet agent should be individualized based on patient risk factor profiles, tolerance, and other clinical characteristics (Class IIb-B).

- Addition of aspirin to clopidogrel increases the risk of hemorrhage and is not routinely recommended for ischemic stroke or TIA patients (Class III-A).
- For patients allergic to aspirin, clopidogrel is reasonable (Class IIa-B).
- For patients who have an ischemic cerebrovascular event while taking aspirin, there is no evidence that increasing the dose of aspirin provides additional benefit. Although alternative antiplatelet agents are often considered for noncardioembolic patients, no single agent or combination has been well studied in patients who have had an event while receiving aspirin.

Reference: 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 [trunc]. *Stroke* 2006;37:577-617.

III. DIABETES MELLITUS

A. Epidemiology: Diabetes mellitus (DM) is a serious public health problem in the Philippines. Estimated to affect 8% of the adult population worldwide, the local prevalence of DM (fasting blood sugar >125 mg/dL) according to the 2003 National Nutrition Health Survey¹ is 4.6% (4.1% in males, 5% in females) while impaired fasting glucose is 3.2% (similar rates for males and females).

People with type 2 DM have both an increased risk of atherosclerosis and increased prevalence of atherogenic risk factors (i.e., hypertension, obesity and abnormal blood lipids). DM is a definite risk factor for stroke.² Case-control studies of stroke patients and prospective epidemiological studies have confirmed an independent effect of DM on ischemic stroke, increasing risk by 1.8- to nearly 6-fold.³ DM is frequently encountered in stroke care, being present in 15% to 33% of patients with ischemic stroke.⁴ The local RIFASAF case-control study showed a 1.6-fold higher risk for stroke among those with DM.⁵ However, data supporting DM as a risk factor for recurrent stroke are sparse.

B. Risk Modification

B1. Primary Stroke Prevention

DM has microvascular and macrovascular complications. Intensive DM therapy delays the onset and slows down the progression of microvascular complications, such as retinopathy, nephropathy and neuropathy,⁶ but not macrovascular complications.⁷ Systematic review of RCTs on intensive insulin therapy (IIT) showed that IIT can decrease the occurrence of macrovascular events by up to 42%,⁸ including stroke, myocardial infarction (MI), angina and

claudication, among patients with type 1 DM. Sub-studies on diabetic patients included in drug trials show that the use of ACEIs⁹ and ARBs¹⁰ can reduce the combined outcome of MI, stroke and cardiovascular death by 21% to 33%. Similarly, ACEIs and ARBs decrease new-onset diabetes.

Primary stroke prevention guidelines have emphasized more rigorous BP control (target BP <130/80 mmHg) among both type 1 and type 2 diabetics.¹¹ The American Diabetes Association (ADA) now recommends that all patients with diabetes and hypertension be treated with a regimen that includes either an ACEI or ARB.

Hyperlipidemia is a common comorbidity of diabetes. For any given cholesterol level, patients with diabetes have a greater frequency of cardiovascular events for which aggressive therapy of diabetic dyslipidemia is indicated, aiming for LDL<100 mg/dL or even up to 70 mg/dL among very high-risk groups.¹² The use of statins among DM patients can reduce vascular events, including stroke.^{13,14} Addition of a statin for DM patients at high risk reduces stroke risk by 24%, and in those with one additional risk factor by 48%.

Among high-risk patients with type 2 DM, the thiazolidinedione, pioglitazone, seems to reduce the composite of all cause mortality, non-fatal stroke and MI, as well as reduce the need for insulin treatment.¹⁵

B2. Secondary Stroke Prevention

Most of the available data on stroke prevention in DM patients pertain to primary prevention. However, glycemic control is consistently recommended in multiple guidelines of both primary and secondary prevention of stroke and cardiovascular disease. Among patients with type 2 DM with or without vascular events, such as stroke, multifactorial approaches involving intensive treatments to control hyperglycemia, hypertension, dyslipidemia and microalbuminuria reduce the risk of cardiovascular events.¹⁶ These approaches included behavioral measures and the use of a statin, ACEI, ARB and antiplatelet drugs, as appropriate. The beneficial role of antiplatelets among stroke patients with or without diabetes has been proven in many trials.

C. Recommendation: A long-term, intensified DM control, which includes behavioral and pharmacological modification to prevent microvascular and macrovascular complications, is recommended.

Rigorous BP and lipid control should be considered in patients with diabetes (Class IIa-B). A target BP of <130/80 mmHg (Class I-A) is recommended as part of a comprehensive risk-reduction program. An ACEI or ARB is preferred for DM patients. Adults with DM, especially those with additional risk factors, should be treated with a statin to lower the risk of a first stroke (Class I-A).

Among diabetic patients with TIA or stroke, glucose control is recommended to near-normoglycemic levels to reduce microvascular complications (Class I-A) and possibly macrovascular complications (Class IIb-B). The goal for hemoglobin A_{1c} should be 7% (Class IIa-B).

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IV. ATRIAL FIBRILLATION

A. Epidemiology: Non-valvular atrial fibrillation (NVAF) alone is associated with a three- to four-fold increase in stroke risk after adjustment for other vascular risk factors as shown in the Table 3.¹

Table 3: Epidemiology of NVAF by Age Group¹⁻⁶

Age group	Prevalence	PAR	RR	Risk reduction with treatment
50-59 y	0.5%	1.5%	4.0	Adjusted-dose warfarin vs control: 62% (CI 48%-72%); 6 trials, n=2,900. Aspirin vs placebo: 22% (CI 2%-38%); 6 trials, n=3,119. Adjusted-dose warfarin vs aspirin: 45% (CI 29%-57%); 6 trials, n=4,025.
60-69 y	1.8 %	2.8%	2.6	
70-79 y	4.8 %	9.9%	3.3	
80-89 y	8.8%	23.5%	4.5	

PAR, population-attributable risk; RR, relative risk.

The prevalence of ischemic stroke for those with NVAF but without prior TIA or stroke is 2% to 4% per year.^{3,4}

Table 3 also shows that the prevalence of NVAF increases with age. The mean age of NVAF patients is 75 years.^{1,5} Estimates of attributable risk reveal that about one quarter of strokes in the very elderly (≥ 80 years old) are due to NVAF.¹ NVAF is also associated with increased mortality after adjustment for other vascular risk factors partly because resultant strokes are large and disabling.⁷

B. Risk Modification

RCTs have established the value of antithrombotic therapies, particularly warfarin and aspirin, in reducing stroke risk in patients with NVAF (Table 3). Adjusted-dose warfarin reduces stroke by 45% compared with aspirin.⁴

The absolute risk reduction from warfarin (from 4.5% for control down to 1.4% with treatment) means the prevention of 31 ischemic strokes each year for every 1,000 patients treated. Overall, warfarin is relatively safe, with a 1.3% annual rate of major bleeding compared with 1% for placebo or aspirin. The optimal international normalized ratio (INR) for stroke prevention in AF patients appears to be 2.0 to 3.0.

The absolute risk of stroke varies 20-fold among AF patients, according to age and associated vascular diseases. Several stroke risk-stratification schemes have been developed and validated.⁸⁻¹⁰ The 2001 American College of Cardiology (ACC)/AHA/European Society of Cardiology (ESC) guidelines recommended anticoagulation for AF patients >60 years old and have a history of hypertension, DM, coronary artery disease (CAD), impaired left ventricular (LV) systolic function, heart failure or prior thromboembolism, and those >75 years old.¹¹ This stratification scheme had not been prospectively validated even though the individual factors are validated.

Since publication of the 2001 ACC/AHA/ESC guideline, the so-called CHADS₂ stratification scheme has been proposed and validated.⁸ CHADS₂ stands for Congestive heart failure (CHF), Hypertension, Age >75 years, DM, and prior Stroke or TIA. The CHADS₂ score was derived from independent predictors of stroke risk in patients with NVAF as shown on Table 4. The score

gives 1 point each for CHF, hypertension, age >75 years, and DM; and 2 points for prior stroke or TIA. The score was validated in a large cohort study and in clinical trials.^{3,8,9} In this scheme, stroke risk of NVAF patients was reliably predicted as low (usually comprises half of patients), moderate (25% of patients) or high (25%).³ The validation study shows that patients with prior stroke or TIA and no other risk factors average 10.8 strokes per 100 patient-years, and that in the Stroke Prevention in Atrial Fibrillation (SPAF),¹² patients with prior stroke or TIA without other risk factors had a stroke rate of 5.9%/year. Therefore, patients with stroke or TIA in the setting of AF should be treated with warfarin unless contraindicated.

LV dysfunction, left atrial size, mitral annular calcification (MAC), spontaneous echo contrast, and left atrial thrombus by echocardiography also predict increased thromboembolic risk.

Anticoagulation is particularly underused in elderly patients with NVAF.¹³ Although the attributable risk of stroke associated with AF increases with age,² elderly (≥ 75 years old) AF patients have about twice the risk of serious bleeding complications during anticoagulation compared with younger patients. Nevertheless, anticoagulation is still warranted if their risk of ischemic stroke without warfarin is greater than their risk of bleeding. In addition to age, poorly controlled hypertension and concomitant aspirin or non-steroidal anti-inflammatory drug use confer higher bleeding risk during anticoagulation. Therefore, age alone is not a contraindication to anticoagulation of high-risk AF patients.

No data are available to address the question of when to initiate oral anticoagulation in an AF patient after a stroke or TIA. In general, initiation is recommended within 2 weeks of an ischemic stroke or TIA; however, for patients with large infarcts or uncontrolled hypertension, further delays may be appropriate. For AF patients with ischemic stroke or TIA despite therapeutic anticoagulation, no data indicate that either increasing the intensity of anticoagulation or adding an antiplatelet agent provides additional protection from future ischemic events.

Table 4: NVAF Risk Stratification and Treatment Recommendations: Risk Stratification by CHADS₂ Scheme

CHADS ₂ Score*	Risk Level	Stroke Rate (%/year)	Treatment Recommendations
0	Low	1.0	Aspirin (75-325 mg/day)
1	Low-moderate	1.5	Warfarin INR 2.0-3.0 or aspirin (75-325 mg/day) [†]
2	Moderate	2.5	Warfarin INR 2.0-3.0 [†]
3	High	5.0	Warfarin INR 2-3 [‡]
≥ 4	Very high	>7.0	

CHF, hypertension, age >75 years, or diabetes=1 point. Stroke or TIA=2 points. All NVAf patients with prior stroke or TIA should be considered high risk and treated with anticoagulants; the CHADS₂ scheme should be applied for primary prevention.

†Consider patient preferences, bleeding risk and access to good INR monitoring. For those with score=1, the number needed to treat with warfarin to prevent one stroke over 1 year is around 100. Excellent anticoagulation control is essential to achieve this benefit.

‡If patient is >75 years old, an INR target of 1.6 -2.5 is recommended by some experts.

C. Recommendations: Antithrombotic therapy with warfarin or aspirin is recommended to prevent stroke in NVAf patients according to assessment of absolute stroke risk, estimated bleeding risk, patient preferences, and access to high-quality anticoagulation monitoring. For risk stratification and treatment recommendations, the CHADS₂ scheme (Table 4) should be followed (Class I-A).

Warfarin (INR=2.0-3.0) is recommended for high-risk (>4% annual stroke risk) AF patients provided there are no clinically significant contraindications to oral anticoagulants (Class I-A).

For patients with ischemic stroke or TIA with persistent or paroxysmal (intermittent) AF, anticoagulation with adjusted-dose warfarin (INR=2.5 [2.0-3.0]) is recommended (Class I-A). In patients unable to take oral anticoagulants, aspirin 325 mg/day is recommended (Class I-A).

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V. ACUTE MYOCARDIAL INFARCTION (WITH LEFT VENTRICULAR THROMBUS) AND CARDIOMYOPATHY

Acute MI with LV Thrombus

A. Epidemiology: Stroke or systemic embolism are less common among uncomplicated MI patients but can occur in up to 12% of patients with acute MI complicated by an LV thrombus. Acute MI is associated with up to 5% risk of ischemic stroke within 2 weeks. The rate is higher in those with anterior than inferior infarcts and may reach 20% in those with large anteroapical infarcts.¹ The incidence of embolism is highest during the period of active thrombus formation in the first 1 to 3 months, yet the embolic risk remains substantial even beyond the acute phase in patients with persistent myocardial dysfunction, CHF or AF.

B. Risk Modification: An overview of trials on anticoagulation after MI has shown that INR of 2.5 to 4.8 may increase hemorrhagic stroke 10-fold, whereas INR below 2.0 may not be effective in preventing ischemic stroke. An INR range of 2.0 to 3.0 with a target of 2.5 is recommended. Two studies of MI patients (n= 4,618) found that warfarin (INR=2.8-4.8) reduced ischemic stroke risk by 55% and 40%, respectively, compared with placebo, over 37 months.^{2,3}

Statins for secondary prevention in patients with established atherosclerosis (CAD, thrombotic cerebral stroke, peripheral arterial disease or prior revascularization) significantly reduced overall risk of stroke, total mortality, cardiovascular death, MI and revascularization when total cholesterol is ≥ 190 mg/dL or LDL is ≥ 100 mg/dL. Stroke Prevention by Aggressive Reduction in Cholesterol Levels study (SPARCL) showed that patients previously documented to have stroke or TIA and no history of coronary heart disease benefited from atorvastatin 80 mg in reducing fatal stroke and TIA.⁴

C. Recommendations: Oral anticoagulation for MI patients is recommended if they have one or more of the following conditions: persistent AF, decreased LV function (e.g., ejection fraction [EF] 28%) or when LV thrombi are detected within several months after MI. Antiplatelets is not recommended to prevent a first stroke after an MI.

For patients with ischemic stroke or TIA due to acute MI in whom LV mural thrombus was identified by echocardiography or another form of cardiac imaging, oral anticoagulation is reasonable, aiming for an INR of 2.0 to 3.0 for at least 3

months and up to 1 year (Class IIa-B). Aspirin should be used concurrently for ischemic CAD during oral anticoagulant therapy in doses up to 160 mg/d (Class IIa-A). For patients with established atherosclerosis and total cholesterol \geq 190 mg/dL or LDL \geq 100 mg/dL, statins are recommended. Furthermore, adherence to the 2005 Clinical Practice Guidelines for the Management of Dyslipidemia in the Philippines is recommended.⁵

For patients with stroke or TIA but without coronary heart disease, statin therapy should be administered to prevent recurrence of stroke and TIA.

Cardiomyopathy

A. Epidemiology: Two large studies found that the incidence of stroke is inversely proportional to EF.^{6,7} In the Survival and Ventricular Enlargement (SAVE) study, patients with EF of 29% to 35% (mean=32%) had a 0.8% stroke rate per year, whereas the yearly rate in those with EF \leq 28% (mean=23%) was 1.7%. There was an 18% incremental increase in stroke risk for every 5% decline in EF. A retrospective analysis of data from the Studies of Left Ventricular Dysfunction (SOLVD) trial, which excluded patients with AF, found a 58% increase in risk of thromboembolic events for every 10% decrease in EF among women (p=0.01) but no increased risk in men.⁸

In patients with non-ischemic dilated cardiomyopathy, the rate of stroke appears similar to that associated with cardiomyopathy resulting from ischemic heart disease.

B. Risk Modification: Warfarin is sometimes prescribed to prevent cardioembolic events in patients with cardiomyopathy. However, no RCT has demonstrated the efficacy of anticoagulation. Considerable controversy surrounds the use of warfarin in patients with cardiac failure or reduced LVEF.^{9,10}

Warfarin appears to reduce the risk of ischemic stroke in patients with non-ischemic cardiomyopathy and in those with ischemic heart disease.¹¹ Aspirin reduces the stroke rate by around 20%.¹² Potential antiplatelet therapies used to prevent recurrent stroke include aspirin (50 to 325 mg/day), combined aspirin and extended-release dipyridamole (25mg/200 mg twice daily), and clopidogrel (75 mg daily).

C. Recommendation: For patients with ischemic stroke or TIA who have dilated cardiomyopathy, either warfarin (INR=2.0-3.0) or antiplatelet therapy may be considered for prevention of recurrent events (Class IIb-C).

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VI. VALVULAR HEART DISEASE and PROSTHETIC HEART VALVES

A. Epidemiology

Annual rates of systemic thromboembolism (TE) in different valvular diseases are shown in Table 5¹⁻⁴:

Table 5: Incidence of systemic thromboembolism in valvular heart disease

	Alone (No AF)	With AF (vs without AF)
1. Prosthetic valve	20%	Increased
2. Rheumatic mitral regurgitation	7.7%	22%
3. Rheumatic mitral stenosis	1.5%-4.0%	Increased by 7-18x
4. Mitral valve prolapse	<2%	Increased
5. Aortic valve	Not increased	Increased

Patients with paroxysmal or persistent AF and valvular heart diseases such as mitral stenosis are at highest risk for future embolic events.

B. Risk Modification: Antithrombotic therapy can reduce the likelihood of stroke and systemic embolism in patients with valvular heart disease. The rate of TE in patients with mechanical heart valves is 4.4 per 100 patient-years without antithrombotic therapy; 2.2 per 100 patient-years with antiplatelet drugs; and 1 per 100 patient-years with warfarin. With or without AF, all patients with mechanical heart valves require anticoagulation with target anticoagulation levels varying according to type and position of the valve, and the presence of other risk

factors. The risk of TE in patients with native valvular heart diseases or mechanical or biological heart-valve prostheses must be balanced with the risk of bleeding. Nevertheless, because the frequency and permanency of consequences of TE events are usually greater than the outcome of hemorrhagic complications, anticoagulant therapy is generally recommended, particularly when associated with AF.⁵

Rheumatic Mitral Valve Disease

a. Epidemiology: The annual rate of TE in rheumatic mitral regurgitation (MR) and stenosis (MS) without AF are 7.7% and 1.5% to 4% respectively. The presence of AF increases TE by 22% in MR patients and by seven- to 18-fold in MS patients.

Recurrent embolism occurs in 30% to 65% of patients with rheumatic mitral valve disease who have a history of a previous embolic event.⁶⁻⁸ Between 60% to 65% of these recurrences develop within the first year, most within 6 months.^{6,7}

b. Risk Modification: Although not evaluated in randomized trials, multiple observational studies have reported that long-term anticoagulant therapy effectively reduces the risk of systemic embolism in patients with rheumatic mitral valve disease.^{3,9} Long-term anticoagulant therapy in patients with MS who had left atrial thrombus identified by transesophageal echocardiography can result in the disappearance of the thrombus.¹⁰

c. Recommendations: For patients with rheumatic mitral valve disease or prosthetic valve without prior stroke or TIA, oral anticoagulation with coumadin is recommended unless contraindicated.

For patients with ischemic stroke or TIA who have rheumatic mitral valve disease, whether or not AF is present, long-term warfarin therapy is reasonable, with a target INR of 2.5 (range; 2.0-3.0) (Class IIa-C).

Antiplatelet agents should not routinely be added to warfarin to avoid the additional bleeding risk (Class III-C). Aspirin 80 mg/day is suggested for patients with ischemic stroke or TIA with rheumatic mitral valve disease, whether or not AF is present, who have recurrent embolism while receiving warfarin (Class IIa-C)

Mitral Valve Prolapse

a. Epidemiology: Mitral valve prolapse (MVP) is the most common form of valve disease in adults.¹¹ Thromboembolic phenomena have been reported in patients with mitral valve prolapse in whom no other source could be found.¹²⁻¹⁶ The annual rate of TE in those with MVP and no AF is less than 2%. AF increases TE risk.

b. Risk Modification: No randomized trials have addressed the efficacy of selected antithrombotic therapies for this subgroup of stroke or TIA patients. The evidence on the efficacy of antiplatelet agents for general stroke and TIA patients was used to reach these recommendations.

c. Recommendation: For patients with MVP who had ischemic stroke or TIA, antiplatelet therapy is reasonable (Class IIa-C).

Mitral Annular Calcification

a. Epidemiology: Although the incidence of systemic and cerebral embolism is not clear, thrombus has been found on heavily calcified annular tissue upon autopsy.¹⁷⁻²²

b. Risk Modification: From observations and in the absence of randomized trials, anticoagulant therapy may be considered for patients with MAC and a history of TE.

c. Recommendations: For patients with ischemic stroke or TIA in whom MAC is not documented to be calcific, antiplatelet therapy may be considered (Class IIb-C).

For patients with MR due to MAC and without AF, antiplatelet or warfarin therapy may be considered (Class IIb-C).

Aortic Valve Disease

a. Epidemiology: Clinically detectable systemic embolism in isolated aortic valve disease is increasingly recognized because of microthrombi or calcific emboli.²³ In an autopsy study of 165 patients with calcific aortic stenosis, systemic embolism was found in 31 patients (19%). In the absence of associated mitral valve disease or AF, systemic embolism in patients with aortic valve disease is uncommon. TE increases in patients with aortic valve disease.

b. Risk Modification: No randomized trials on selected patients with stroke and aortic valve disease exist.

c. Recommendation: For patients with ischemic stroke or TIA and aortic valve disease but no AF, antiplatelet therapy may be considered (Class IIb-C)

Prosthetic Heart Valves

b. Epidemiology: The annual percentage of occurrence of systemic TE in those with prosthetic heart valves is 20%. The risk increases with AF.

c. Risk Modification: A variety of mechanical heart valve prostheses are available for clinical use, all of which require antithrombotic prophylaxis.

The most convincing evidence that oral anticoagulants are effective in patients with prosthetic heart valves comes from patients randomized to

treatment for 6 months with either warfarin in uncertain intensity or one of two aspirin-containing platelet-inhibitor regimens.²⁴

In two randomized studies, concurrent treatment with dipyridamole and warfarin reduced the incidence of systemic embolism,^{25,26} and the combination of dipyridamole (450 mg/day) and aspirin (3.0 g/d) reduced the incidence of TE in patients with prosthetic heart valves.²⁷ A randomized study of aspirin 1.0 g/day plus warfarin versus warfarin alone in 148 patients with prosthetic heart valves found a significant reduction of embolism in the aspirin-treated group.²⁸ Another trial showed that the addition of aspirin 100 mg/day to warfarin (INR=3.0-4.5) improved efficacy compared with warfarin alone.²⁹

The ESC guidelines recommend anticoagulant intensity in proportion to the TE risk associated with specific types of prosthetic heart valves.³⁰ For first-generation valves, an INR of 3.0 to 4.5 was recommended; an INR of 3.0 to 3.5 was recommended for second-generation valves in the mitral position, whereas an INR of 2.5 to 3.0 was advised for second-generation valves in the aortic position. The 2004 American College of Chest Physicians recommended an INR of 2.5 to 3.5 for patients with mechanical prosthetic valves, and 2.0 to 3.0 for those with bioprosthetic valves and low-risk patients with bileaflet mechanical valves (such as the St. Jude Medical device) in the aortic position.³¹ Similar guidelines have been promulgated conjointly by the ACC and the AHA.^{11,32}

d. Recommendations: For patients who have modern mechanical prosthetic heart valves, with or without ischemic stroke or TIA, oral anticoagulants should be administered to an INR target of 3.0 (range; 2.5-3.5) (Class I-B).

For patients with mechanical prosthetic heart valves who had an ischemic stroke or systemic embolism despite adequate therapy with oral anticoagulants, aspirin 75 to 100 mg/day in addition to oral anticoagulants and maintenance of the INR at 3.0 (range; 2.5-3.5) are reasonable (Class IIa-B).

For patients with ischemic stroke or TIA who have bioprosthetic heart valves with no other source of thromboembolism, anticoagulation with warfarin (INR=2.0-3.0) may be considered (Class IIb-C).

Table 6. Summary of Recommendations for Patients With Cardioembolic Stroke or TIA

Risk Factor	Recommendation	Class/Level of Evidence
AF	For patients with ischemic stroke or TIA with persistent or paroxysmal (intermittent) AF, anticoagulation with adjusted-dose warfarin (target INR=2.5 [2.0-3.0]) should be administered	Class I-A
	In patients unable to take oral anticoagulants, aspirin 325 mg/day is recommended.	Class I-A

Acute MI and LV thrombus	For patients with ischemic stroke caused by acute MI with LV mural thrombus identified by echocardiography or another form of cardiac imaging, oral anticoagulation is reasonable (INR=2.0-3.0 for at least 3 months up to 1 year).	Class IIa-B
	Aspirin up to 160 mg/day (preferably enteric-coated) should be used concurrently for patients with ischemic CAD during oral anticoagulant therapy.	Class IIa-A
Cardiomyopathy	For patients with ischemic stroke or TIA who have dilated cardiomyopathy, either warfarin (INR=2.0-3.0) or antiplatelet therapy may be considered to prevent recurrent events.	Class IIb-C
MVP	For patients with MVP who have ischemic stroke or TIA, long-term antiplatelet therapy is reasonable.	Class IIa-C
MAC	For patients with ischemic stroke or TIA and MAC not documented to be calcific, antiplatelet therapy may be considered.	Class IIb-C
	Among patients with MR due to MAC, without AF, antiplatelet or warfarin therapy may be considered.	Class IIb-C
Aortic valve disease	For patients with ischemic stroke or TIA and aortic valve disease who do not have AF, antiplatelet therapy may be considered.	Class IIa-C
Prosthetic heart valves	For patients with ischemic stroke or TIA who have modern mechanical prosthetic heart valves, oral anticoagulants are recommended, with an INR target of 3.0 (range; 2.5-3.5).	Class I-B
	For patients with mechanical prosthetic heart valves who had an ischemic stroke or systemic embolism despite adequate therapy with oral anticoagulants, aspirin 75 to 100 mg/day in addition to oral anticoagulants maintained at INR of 3.0 (range; 2.5-3.5) is reasonable.	Class IIa-B
	For patients with ischemic stroke or TIA who have bioprosthetic heart valves with no other source of TE, anticoagulation with warfarin (INR=2.0-3.0) may be considered.	Class IIb-C

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VII. CHOLESTEROL

A. Epidemiology: Epidemiological and observational studies have not shown a definite correlation between serum cholesterol levels and the incidence of stroke.^{1,2} According to the Asia Pacific Cohort Studies Collaboration,³ the relationship between cholesterol and stroke risk is more complex, with a stronger positive association with ischemic stroke and a weaker negative association with hemorrhagic stroke. However, this trend in hemorrhagic stroke was not seen in the HPS and combined data from the Long-term Intervention with Pravastatin in Ischaemic Disease study (LIPID) and the Cholesterol and Recurrent Event study. Furthermore, low cholesterol is common in patients with weight loss, severe handicap, or severe and chronic illness, which may be confounding factors for the demonstrated trend between hemorrhagic stroke and low total cholesterol.

B. Risk Modification

B1. Primary Stroke Prevention

A meta-analysis of 13 lipid-lowering trials prior to statin use showed no change in risk for total stroke.⁴ With the advent of statins, a meta-analysis of CARE, LIPID, HPS, the Scandinavian Simvastatin Survival Study (4S), the Prospective Study of Pravastatin in the Elderly at Risk study (PROSPER), the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), the Kyushu Lipid Intervention Study (KLIS), the GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE), and the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) showed that the overall relative risk reduction is 21% (ARR=9%).⁵ The greater the LDL reduction, the greater the intima-media thickness and stroke risk reduction.⁶

Statins conferred an important and large relative reduction in cardiovascular events including stroke among hypertensive patients who are not conventionally deemed dyslipidemic.⁷ Pretreatment with statins seem to reduce clinical severity in patients with stroke, especially among diabetics.^{8,9}

B2. Secondary Stroke Prevention

HPS showed a 19% reduction in major vascular events, but the decrease was due to reduction in coronary events and not in stroke recurrence.¹⁰

The Stroke Prevention with Aggressive Reduction of Cholesterol Levels (SPARCL), a large-scale statin RCT in patients with a history of stroke or TIA without CAD, and have mildly elevated lipid levels (mean LDL=133 mg/dL).¹¹ The trial showed that atorvastatin 80 mg/day significantly reduced stroke by 16% in this patient subgroup.

Statins are likely to reduce stroke risk by stabilizing and /or repressing plaque. Statins also have pleiotropic (anti-inflammatory, antioxidant) effects that further justify their use in the primary and secondary prevention of cerebrovascular disease.¹²⁻¹⁴ Statins have a favorable safety profile and are not associated with increased hemorrhagic stroke or cancer risk.⁵

C. Recommendations

C1. Primary Stroke Prevention

Therapeutic lifestyle changes are recommended as an essential modality in clinical management.² These include smoking cessation, weight management, regular physical activity and adequate BP monitoring and control.¹⁵ For patients at any level of cardiovascular risk, especially those with established atherosclerosis, a low-fat, low-cholesterol diet is recommended for life.

High-risk hypertensive patients and those with CAD should be treated with lifestyle measures and a statin, even with normal LDL levels (Class I-A).^{16,17}

Adults with diabetes, especially those with additional risk factors, should receive statins to lower the risk of a first stroke (Class I-A).¹⁶

Patients with coronary artery disease and low HDL may be treated with weight reduction, increased physical activity, smoking cessation, and possibly niacin or fibrates (Class IIa-B).^{3,16}

C2. Secondary Stroke Prevention

Statins are recommended in patients with coronary heart disease or symptomatic atherosclerotic disease to lower cholesterol levels to LDL < 100 mg/dL (< 70 mg/dL for very high-risk persons) (Class I-A).^{16,18-20}

Patients with ischemic stroke or TIA presumed to be due to atherosclerosis but without preexisting indications for statins are reasonable candidates for statin treatment to reduce the risk of vascular events (Class IIa-B).¹⁶

Patients with ischemic stroke or TIA and low HDL may be considered for treatment with niacin or fibrates (Class IIb-B).^{3,16}

Lastly, adherence to the statements of the *2005 Clinical Practice Guidelines for the Management of Dyslipidemia in the Philippines* is recommended. These are¹⁵:

1. To reduce the overall cardiovascular risk, all patients, regardless of their present morbid condition or risk profile, should be advised on the need for the following:

- Smoking cessation;
- Weight management;
- Regular physical activity; and
- Adequate blood pressure monitoring and control.

2. For patients at any level of cardiovascular risk, especially those with established atherosclerosis, a low-fat, low-cholesterol diet is recommended for life.
3. In poorly nourished and elderly patients, correction of nutritional deficiencies can be achieved even with a low-fat, low-cholesterol diet.
4. For low-risk patients without evidence of atherosclerosis, drug therapy is not recommended, regardless of lipid levels. Risk factors include hypertension, familial hypercholesterolemia, left ventricular hypertrophy, smoking, family history of premature CAD, male sex, age >55 years, proteinuria, microalbuminuria, BMI ≥ 25 . Low risk patients have <3 risk factors. The presence of familial hypercholesterolemia warrants treatment even without other risk factors.
5. For patients without established atherosclerosis but with ≥ 3 risk factors and total cholesterol ≥ 190 mg/dL or LDL ≥ 100 mg/dL, statins may be recommended.
6. For diabetic patients without evidence of atherosclerosis and with total cholesterol ≥ 190 mg/dL or LDL ≥ 100 mg/dL, statins are recommended.
7. Fibrates may be recommended as an alternative to statins in diabetic patients with HDL ≤ 35 mg/dL and LDL ≤ 90 mg/dL.
8. For patients with established atherosclerosis and total cholesterol ≥ 190 mg/dL or LDL ≥ 100 mg/dL, statins are recommended.
9. Fibrates may be recommended as an alternative to statins if HDL ≤ 35 mg/dL and LDL ≤ 90 mg/dL.
10. In patients without risk factors and history or symptoms of established atherosclerosis, screening for lipid levels is not recommended.
11. In patients without established atherosclerosis but with ≥ 3 risk factors, lipid profile may be recommended.
12. In patients with established atherosclerosis or diabetes, the use of lipid profile for screening is recommended.

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VIII. CAROTID STENOSIS

A. Epidemiology: Extracranial carotid artery disease accounts for 15% to 20% of all ischemic strokes.¹ Individuals with carotid stenosis often have more widespread atherosclerotic disease with a high prevalence of coronary heart disease and claudication.^{2,3}

The stroke risk due to carotid artery stenosis is determined primarily by symptom status and is related to lesion severity. Patients with symptomatic severe carotid stenosis have an annual stroke risk of 13% to 15%, compared with 1% to 2% in those with no history of prior stroke or TIA or those with asymptomatic lesions.⁴⁻⁶ In addition, echolucent or ulcerated plaques, hypertension and progressive lesions are associated with increased risk of neurological events.⁷

B. Risk Modification

B1. Primary Stroke Prevention

The role of carotid endarterectomy (CEA) in asymptomatic cases requires special consideration. Among patients with asymptomatic carotid artery stenosis of 60% to 99% enrolled in the Asymptomatic Carotid Artery Stenosis Study (ACAS), CEA combined with best medical treatment reduced the 5-year ipsilateral-stroke risk from 11% to 5.1% (RRR=53%).⁵ The Asymptomatic Carotid Surgery Trial (ACST) supports the results of ACAS, showing a small but definite reduction in the risk of stroke with surgery among patients with at least 60% stenosis (5-year stroke risk of 11.8% in the medical arm compared with 6.4% in the combined CEA and medical treatment arm).⁶ For asymptomatic patients to benefit from surgery, there should be an exceptionally low perioperative complication rate (< 3%).⁵⁻⁷

Neither ACAS nor ACST showed increasing benefit from surgery with increasing degree of asymptomatic stenosis within the 60%-to-99% range.^{5,6,8}

B2. Secondary Stroke Prevention

Among symptomatic patients with 70% stenosis or greater but without near occlusion, combined CEA and medical treatment provide up to 16% absolute-risk reduction or 61% relative-risk reduction in ipsilateral and perioperative stroke over medical treatment alone (over 5 years).^{4,9-11}

There was a trend toward benefit with surgery at 2 years (ARR=5.6 %) among patients with near-total carotid occlusion, but this was seen only for in the short term (-1.7% over 5 years).⁹

CEA was harmful for symptomatic patients with less than 30% stenosis. It had had no effect among patients with 30% to 49% stenosis, and was of marginal benefit in patients with 50% to 69% stenosis. Greater benefit was seen in men, those ≥ 75 years old, those with hemispheric symptoms (compared with those with transient monocular blindness) and those were randomized within 2 weeks of a TIA or a non-disabling ischemic stroke.^{4,9-11}

Meta-analysis of five completed or terminated RCTs comparing endovascular treatment and CEA (Carotid and Vertebral Artery Transluminal Angioplasty Study [CAVATAS], Kentucky, Leicester, Wallstent, Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy [SAPPHIRE]) found no difference in the odds of death or any stroke at 30 days and at one year between the two groups.¹² As yet, there is no evidence on the long-term efficacy of angioplasty and stenting available from any of the studies. Several international trials such as the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST),¹³ International Carotid Stenting Study (ICSS),¹⁴ Stent-protected Percutaneous Angioplasty of the Carotid versus Endarterectomy (SPACE)¹⁵ and Endarterectomy versus Angioplasty in patients with severe Symptomatic Stenosis (EVA-3s)¹⁶ are awaiting completion.

C. Recommendations: Antiplatelets, statins and modification of stroke risk factors for all patients with carotid artery disease (Class I-C).

At present, mass screening for high-grade asymptomatic carotid stenosis is not cost-effective. However it is reasonable to do screening using non-invasive tests (e.g., carotid duplex) in patients at risk for significant carotid disease, such as those who survived a stroke, or those who have carotid bruit, peripheral vascular disease, and/or CAD. It is also reasonable to consider CEA for patients with asymptomatic stenosis of >60% if the patient has a life expectancy of at least 5 years and the perioperative risk can be reliably documented to be <3% (Class I-A).

CEA combined with optimal medical management is recommended for patients with recent TIA or stroke and ipsilateral severe carotid artery stenosis (70%-99%) if perioperative risk of <6% can be attained (Class I-A).

For symptomatic patients with 50% to 69% stenosis, CEA is recommended depending on patient-specific factors, such as age, gender, comorbidities and severity of initial symptoms (Class I-A). When the degree of stenosis is <50%, there is no indication for CEA (Class III-A).^{17,18}

Since benefit from CEA is dependent on the degree of stenosis, measurement must be accurate and reliable. In deciding for surgical intervention, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method of angiographically defining the degree of stenosis is recommended (i.e., % stenosis = {1-[diameter of stenosis/diameter of distal internal carotid artery]} x 100%).¹⁹

In patients with concomitant carotid and coronary artery disease, available data at this time are insufficient to declare superiority of timing CEA either before or simultaneous with coronary-artery bypass grafting (CABG).

Unless results of ongoing studies are reported, carotid angioplasty and stenting (CAS) remains to be a second option to CEA. The endovascular approach is favored in certain cases (e.g., stenosis is difficult to access surgically; restenosis after CEA or medical conditions exist that greatly increase the risk of surgery) (Class IIb-B). CAS is reasonable when performed by operators with established periprocedural morbidity and mortality rates of <6% (Class IIb-B).¹⁸

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IX. INTRACRANIAL STENOSIS

A. Epidemiology: Atherosclerotic intracranial stenoses are responsible for ischemic stroke in 5% to 10% of Caucasian patients, and in up to 33% of Asian, Hispanic and African patients.¹⁻⁶ Other risk factors for intracranial atherosclerosis include age, hypertension, smoking, diabetes, lipid disorders and metabolic syndrome.⁷⁻¹²

The annual risk of stroke among patients with symptomatic intracranial stenosis ranges from 3% to 15% (approximate annual values are: 7.6% for the carotid siphon, 7.8% for the middle cerebral artery [MCA], 2%-7% for the vertebral artery and 11% in the basilar artery).¹³⁻¹⁸ In contrast, asymptomatic MCA stenosis appears to have a benign prognosis with a low risk of ipsilateral stroke (1.4% annually) in medically treated Caucasian patients.¹⁹⁻²⁰

B. Risk Modification: There is currently no data available.

Among patients with stroke or TIA caused by a 50% to 99% stenosis of a major intracranial artery, the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) study showed that warfarin does not confer an advantage over aspirin in terms of stroke reduction (2-year ischemic stroke rate of 19.7% for aspirin vs. 17.2% for warfarin).¹⁶

In the Trial of cilOstazol in Symptomatic intracranial arterial Stenosis (TOSS), adding cilostazol to aspirin was superior to aspirin monotherapy in preventing progression of intracranial arterial stenosis.²¹ Continued trials are warranted to confirm the efficacy of cilostazol in preventing progression and further vascular events in patients with symptomatic intracranial arterial stenosis.

The EC-IC Bypass Trial failed to show clinical benefit of revascularization procedure (extracranial-intracranial anastomosis) in patients with atherosclerotic disease of the carotid artery and MCA.¹⁷ Bypass-patency rate was 96%, but fatal and non-fatal stroke occurred more frequently and earlier among those randomized to surgery.

Single-center experiences suggest that intracranial angioplasty and/or stenting can be performed with a high degree of technical success.²² Acceptable anatomical and clinical results of up to 6 months were obtained in small groups of medically refractory patients with strokes attributable to intracranial stenosis enrolled in the Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVA) and WingSpan trials.²³⁻²⁴ Further studies are needed in larger cohorts with longer follow-up periods to fully determine the effectiveness of interventional catheter-based procedures for intracranial stenosis.

C. Recommendation: Patients with intracranial stenosis should be counseled regarding optimal medical therapy (antiplatelets, statins) and aggressive management of stroke risk factors.^{22,25}

Further studies are warranted to evaluate short and long-term efficacy of angioplasty and or stenting in patients with hemodynamically significant intracranial stenosis (>50%) and symptoms despite medical therapy.²⁵ (Class IIb-C)

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X. SMOKING

A. Epidemiology

A1. Prevalence

Asian countries have the highest prevalence of smoking in the world: 72% in Korean men, 63% in Chinese men and 58% in Japanese men.¹ The 2003 NNHeS survey showed that the prevalence of smoking in Filipinos is 56.3% in males and 12.1% in females.² Two national surveys on Filipino adolescents revealed that one in five adolescents current smoking, males having a higher rate than females (37.3% vs. 6.3%).^{3,4}

A2. Smoking as Stroke Risk Factor

A meta-analysis of 32 studies estimated the relative risk for cerebral infarct to be 1.9 for smokers versus nonsmokers.⁵ Case control and prospective studies have shown that cigarette smoking is an independent predictor of stroke, with a dose-response relationship affecting both men and women.⁶⁻⁸ The Framingham Heart Study showed that the relative risk of stroke in heavy smokers (>40 cigarettes/day) was twice that of light smokers (<10 cigarettes/day), and the risk increased with the number of cigarettes smoked.⁹ The large cohort study of U.S. male physicians showed heavy smokers (>20 cigarettes/day) had a relative risk of 2.71 for total nonfatal stroke, and 1.46 for fatal stroke.¹⁰

Studies also suggest a dose-response relationship between pack-years of smoking and carotid-artery intima-media wall thickness.¹¹ Smoking only one cigarette increases heart rate, blood pressure and cardiac index, and decreases arterial distensibility.¹² In addition, both active and passive smoke are associated with the development of atherosclerosis.¹³

Stroke also increases the risk of hemorrhagic stroke. In men, current smokers of <20 cigarettes/day had relative risks of 1.65 for total hemorrhagic strokes, 1.60 for intracerebral hemorrhage (ICH), and 1.75 for subarachnoid hemorrhage (SAH) compared to those who never smoked.¹⁴ Current smokers of ≥ 20 cigarettes/day had relative risks of 2.36 for total hemorrhagic stroke, 2.06 for ICH and 3.22 for SAH.

In women, current smokers of <15 cigarettes/day had a relative risks of 1.93 for total hemorrhagic stroke, 2.5 for ICH and 1.70 for SAH.¹⁵ Women who smoked ≥ 15 cigarettes/day had relative risks of 3.29 for total hemorrhagic stroke, 2.67 for ICH and 4.02 for SAH.

A3. Smoking Potentiates Effects of Other Stroke Risk Factors

A synergistic effect on the risk of cerebral infarction exists between the use of oral contraceptives (OC) and smoking. With nonsmoking women who do not use OC as reference group, the odds for cerebral infarction were 1.3 times greater for women who smoked but did not use OC, 2.1 times greater for nonsmoking OC users, and 7.2 times greater for OC users who smoked.¹⁶

A similar impact on hemorrhagic stroke is observed. The odds for hemorrhagic stroke were 1.6 times greater for women smoked but did not use OC, 1.5 times greater for nonsmoking OC users, and 3.7 times greater for OC users who smoked.¹⁷

A4. Environmental Tobacco Smoke and Passive Smoking

Like outdoor air pollution, the effects of second-hand smoke are large and rapid. Several studies suggest that environmental tobacco smoke is a substantial risk factor for stroke, with risk approaching the doubling found seen with active smoking.¹⁸ Passive smoking may exert detrimental effects on vascular homeostasis. Cohort studies showed an elevated prevalence of stroke among women nonsmokers living with husbands who smoked, and prevalence increased with increasing intensity and duration of husbands' smoking.¹⁹

B. Risk Modification: Both the Framingham Heart Study and the Nurses Health Study showed that 5 years after cessation of smoking, risk ratios normalized.^{9,20} However, another study showed that the risk reduction was dependent on the quantity of cigarettes smoked before stopping: light smokers (<20 cigarettes/day) reverted back to normal values but heavy smokers retained twice the incidence of stroke as non smokers.²¹ Switching to pipe or cigar smoking confers little benefit, emphasizing the need for complete cessation of smoking.²² A combination of nicotine replacement therapy, social support and skills training seems to be the most effective approach to smoking cessation.^{23,24}

C. Recommendations: Smoking cessation for all current smokers is recommended (Class I-C).²⁵ Nonsmokers are also advised not to start smoking. Exposure to environmental tobacco smoke should be minimized (Class IIa-C). Republic Act No. 9211 or The Tobacco Regulation Act of 2003 should be implemented to protect the populace from hazardous products, promote the right to health and instill health consciousness. Effective behavioral and pharmacological treatments should be advised and encouraged for nicotine dependence (Class IIa-B).

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XI. EXCESSIVE ALCOHOL

A. Epidemiology: There is a direct, dose-dependent effect of the consumption of alcohol on the risk of hemorrhagic stroke but the association with ischemic stroke varies with different studies.¹⁻⁴ Most studies suggest a J-shaped association between alcohol and ischemic stroke: a protective effect with light to moderate drinking, and an elevated risk with heavy consumption.⁵⁻⁸ While the protective effect of light consumption alcohol is evident among Caucasians, this is not evident among Asians.^{2,4-6,9-11} Moderate alcohol consumption decreased risk of ischemic stroke in a multiethnic population.¹² Heavy alcohol use, either daily or in binges, is related to excess of stroke risk.¹³

B. Risk Modification: Alcohol consumption of up to two drinks per day was protective against ischemic strokes in Caucasians, Blacks and Hispanics, but consumption above five drinks per day increased the risk of ischemic stroke.¹⁴

C. Recommendations: Moderate intake of alcohol in those who drink alcohol and have no health contraindications to its use. Consumption of alcohol, up to 30 mL (or 28 grams) of ethanol per day, equivalent to 60 mL or two jiggers of 100-proof whiskey, one glass of wine (240 mL) or two bottles of beer (720 mL), or two drinks per day for men and one drink per day for non-pregnant women, may reduce the risk of ischemic stroke (Class IIb-C).

Patients with ischemic stroke or TIA who are heavy drinkers should eliminate or reduce their consumption of alcohol (Class I-A).

Those who do not customarily drink alcohol should not be encouraged to do so.

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XII. PERIPHERAL ARTERIAL DISEASE

Peripheral arterial disease (PAD) is characterized by arterial stenosis and occlusion of the peripheral arterial bed. It can be symptomatic or asymptomatic. Symptomatic PAD ranges from intermittent claudication (IC) to chronic limb ischemia. Regardless of symptomatology, PAD is an indicator of diffuse systemic atherosclerosis. Risk factors include smoking, DM, dyslipidemia, hypertension and hyperhomocysteinemia, which considerably and frequently overlap and coexist with coronary and cerebrovascular disease. There are numerous reports on the increased risk of MI, stroke and cardiovascular death in patients with PAD.^{1,2}

A. Epidemiology: The prevalence of PAD is highly age dependent. Using objective testing with ankle-brachial index (ABI) in a U.S. population showed the prevalence was 2.5% in people aged <60 years old, while among the 60- to 69-year age group the prevalence is 8.3%, and is 18.8% in those >70 years old.³

There is a 20% to 60% increased risk for MI and a two- to six-fold increased risk of death due to coronary artery events in PAD patients.⁴⁻⁸ The risk of stroke is increased by approximately 40%. In the Atherosclerosis Risk in Communities (ARIC) study, men with PAD were four to five times more at risk of stroke and TIA than those without PAD.⁸

In addition, all-cause mortality rate is 61.8% after 10 years in men with PAD compared with 16.9% in unaffected men.⁶ The corresponding mortality rates for women were 33.3% and 11.6%, respectively. The increase in total mortality was due to a sharp increase in cardiovascular mortality, which persisted even

after adjusting for pre-existing CAD and cerebrovascular disease at baseline. The risk was proportional to the severity of PAD.

Local studies reported that 2% of Filipinos aged 55 years and older have IC, and approximately 5% have PAD upon ABI confirmation. In a study on Filipino patients aged 40 years or older and confined in the intensive care unit for heart attack, stroke or type 2 DM, 30% had silent PAD.⁹ The 2003 NNHeS reported a PAD prevalence of 1.6% among Filipinos aged 20 years and above.¹⁰

B. Risk Modification: In lower-extremity PAD, adverse cardiovascular events may be reduced with lifetime modification or elimination of risk factors, such as cigarette smoking, diabetes mellitus, dyslipidemia and hypertension. Exercise and a non-atherogenic diet are strongly advised

B1. Smoking Cessation

No prospective RCTs have shown the effects of smoking cessation on cardiovascular events. Only observational studies have shown that the risk of death, MI and limb loss is greater in individuals who continue to smoke than those who stop smoking.¹¹⁻¹³

B2. Diabetes Mellitus

It is still unclear whether blood glucose control decreases the risk of adverse cardiovascular events in those with lower-extremity PAD. Analysis of the Diabetes Control and Complication Trial (DCCT) showed that the use of intensive insulin therapy on type 1 DM patients only reduced risk of IC, peripheral revascularization and amputation by 22%, which was not statistically significant.¹⁴ The 10-year United Kingdom Prospective Study (UKPDS) showed that aggressive treatment (using sulfonylureas or insulin) in type 2 DM patients reduced the risk of MI by 16% (borderline significance) compared with conventional treatment, but did not reduce the risk of death or stroke.¹⁵

B3. Dyslipidemia

Treatment of dyslipidemia in patients with systemic atherosclerosis can reduce future adverse cardiovascular events.¹⁶ In the HPS, which included 6,748 PAD patients, there was a 25% reduction of cardiovascular events in the simvastatin-treated group.

B4. Hypertension

In PAD patients, antihypertensive treatment may diminish perfusion to the limb and exacerbate symptoms of limb ischemia. However, most patients do not experience any worsening of symptoms with appropriate antihypertensive therapy needed to reduce risk of cardiovascular events.

The use of beta-blockers has been controversial in the treatment of PAD patients. However, a meta-analysis of 11 placebo-controlled studies in patients with PAD showed that beta-blockers did not adversely affect walking capacity.¹⁷

The Heart Outcomes Prevention Evaluation (HOPE), which included 4,051 PAD patients randomized to ramipril or placebo, reported risk reduction for MI,

stroke or vascular death by 25%, similar to that achieved in the overall study population.¹⁸

C. Recommendations: Individuals with risk factors for PAD, regardless of whether they are symptomatic and asymptomatic, should be identified and ABI measured. Therapeutic interventions to diminish the increased risk of MI, stroke and death may be given (Class I-B). Treatment used in the management of atherosclerotic conditions, such as CAD and cerebrovascular disease, as recommended in the other sections of these guidelines, may reduce the risk of stroke.

Those with PAD who smoke should be advised to quit. Smoking cessation interventions, including behavior modification therapy or nicotine replacement therapy, should be offered (Class I-B).

Reducing HbA_{1c} to <7% through tight glycemic control may reduce microvascular complications and improve cardiovascular outcomes (Class IIa-C).

Statins are indicated for all patients with PAD (Class I-B), and treatment should aim to reduce serum cholesterol to < 70mg/dL when at very high risk of ischemic events (Class IIa-B). Treatment with fibric acid derivatives can be useful for PAD patients with low HDL, normal LDL and elevated triglycerides (Class IIa-C).

Antihypertensive treatment should aim to reduce BP to <140/90 mmHg, or <130/80 mmHg for those with DM or chronic renal disease (Class I-A). Beta-blockers are effective and are not contraindicated in PAD patients (Class I-A). It is reasonable to use ACEIs for those with symptomatic PAD to reduce cardiovascular risk (Class IIa-B). ACEIs may be considered for asymptomatic PAD patients to reduce cardiovascular risk (Class IIb-C).

Antiplatelets are indicated to reduce risk of MI, stroke and vascular death in PAD patients (Class I-A). Daily aspirin 75 to 325 mg is considered safe and effective in reducing the risk of MI, stroke or vascular death (Class I-A). Clopidogrel 75 mg/day is recommended as an alternate to (Class I-B). Oral anticoagulation therapy with warfarin is not indicated to reduce the risk of adverse cardiovascular events in patients with PAD (Class III-C).

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XIII. PHYSICAL INACTIVITY

A. Epidemiology: Physical inactivity is a growing public health problem that may have a major impact on the prevalence of atherothrombotic cardiovascular disease in the coming decades. The relative risk of cardiovascular disease associated with physical inactivity ranges from 1.5 to 2.4, a risk increase similar to those observed with high blood cholesterol, high BP or cigarette smoking.¹ Physical inactivity is a risk factor for stroke, DM, colon and breast cancer, obesity, hypertension, osteoporosis and depression.²⁻⁶ Local data shows the odds ratio for stroke associated with physical inactivity is 1.23.⁷

B. Risk modification

B1. Primary Stroke Prevention

Physical activity is defined as any bodily movement produced by skeletal muscles that result in energy expenditure beyond resting expenditure. Physical activity reduces stroke risk in both genders and across all racial/ethnic and age groups (OR; 0.37).^{8,9} The Framingham Heart Study, the Honolulu Heart Program, and the Oslo Study have shown the protective effect of physical activity for men.¹⁰⁻¹² There seems to be a graded linear relation between the volume of physical inactivity and total stroke.¹³ The Physicians' Health Study showed a lower total stroke risk associated with vigorous exercise (five times a week or more) among men (RR; 0.86).¹⁴ The Harvard Alumni Study showed a decrease in total stroke risk in men who were highly physically active (RR; 0.82).¹⁵

For women, the Nurses' Health Study and the Copenhagen City Heart Study showed an inverse association between level of physical activity and stroke incidence.^{16,17} Physical activity (in sports, leisure time or at work) also reduced risk of ischemic strokes, in particular.^{9,18}

The protective effect of physical activity may be partly mediated by BP reduction, improvement of lipid profiles (reduces triglyceride, increases HDL, and decreases LDL:HDL ratios), improvement of glucose homeostasis and insulin sensitivity, and improvement in body composition and weight.^{3,4,19} Other benefits of physical activity include reduction in blood coagulability,²⁰⁻²² improvement of coronary blood flow,²³ augmentation of cardiac function,²⁴ enhancement of endothelial function,²⁵⁻²⁷ improvement of autonomic tone,²⁸ and reduction of systemic inflammation.²⁹

B2. Secondary Stroke Prevention

The cardiac response to acute exercise among stroke survivors has been documented in some studies. Stroke patients achieve significantly lower maximal workloads, heart rate and BP responses than control subjects during progressive exercise testing to volitional fatigue.^{30,31} Furthermore, stroke survivors are often deconditioned and predisposed to a sedentary lifestyle that limits performance of activities of daily living, increases the risk for falls, and may contribute to a heightened risk for recurrent stroke and cardiovascular disease. Thus, the major rehabilitation goals for the stroke patient are: (1) to prevent complications of prolonged inactivity; (2) to decrease recurrent stroke and cardiovascular events, and; (3) to increase aerobic fitness.

Stroke patients can increase their cardiovascular health and fitness with regular aerobic exercise.³² In a RCT of 42 hemiparetic stroke survivors, vigorous aerobic exercise training three times per week for 10 weeks significantly improved peak oxygen consumption and workload, submaximal exercise, BP response, exercise time and sensorimotor function.³³ In a study of 35 stroke patients with multiple comorbidities who underwent 12 weeks of a 1-hour/day, 3-days/week exercise program of combined cardiovascular, strength and flexibility training, the exercise group had significant gains in peak oxygen uptake, strength and improvements in body composition compared with controls.³⁴ In a RCT involving 88 men with CAD and disability, two-thirds of whom were stroke survivors, a 6-month home exercise training program significantly increased peak

left ventricular ejection fraction and HDL, and decreased resting heart rate and total serum cholesterol.³⁵

C. Recommendations

C1. Primary Stroke Prevention

Increased physical activity is associated with a reduction in stroke risk, and is recommended (Class I-B). It is important to recognize that physical education in school may form the starting point for an active lifestyle later in life.

At least 30 minutes of moderate-intensity aerobic exercise on most days of the week (preferably all days) is recommended as part of a healthy lifestyle (Class IIa-B). Healthy people should be advised to choose enjoyable activities that fit into their daily routine, preferably for 30 to 45 minutes, four to five times weekly, at an intensity to maintain 60% to 80% of the average maximum heart rate. Additional benefits are gained from vigorous-intensity activity.³⁶

C2. Secondary Stroke Prevention

Exercise for stroke patients is recommended and should be tailored to individual needs and limitations. In general, aerobic training at 40% to 70% of peak oxygen consumption or heart rate reserve may be advised to stroke survivors.³⁷ Continuous or accumulated aerobic training for 20 to 60 minutes daily, three to seven days a week, depending on the patient's level of fitness, is advised.

Persons with known or suspected cardiovascular, respiratory or neurological disorders should consult a physician before beginning or significantly increasing physical activity. Adaptive programs for post-stroke patients depending on neurological deficits are recommended.³⁸

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XIV. OBESITY

A. Epidemiology: The World Health Organization defined “overweight” as having a body mass index (BMI) $>25 \text{ kg/m}^2$ and “obesity” with a BMI $>30 \text{ kg/m}^2$ for the general population.¹ However, the National Institute for Health and Clinical Excellence (NICE) recommends that overweight or obesity among Asian adults should be set at 23 and 27.5 kg/m^2 respectively.²

Waist circumference (WC) is positively correlated with disease risk, and is one of the most practical measurements for assessing abdominal fat mass (central obesity). For Asians, the cutoff points are 90 cm (35 inches) for males and 80 cm (32 inches) for females.²

Another measure of abdominal fat deposition is the waist-hip ratio (WHR), defined as the waist circumference divided by the hip circumference. Elevated WHR is defined as >0.95 in males and >0.85 in females.³

In the Philippines, the prevalence of obesity based on BMI has increased from 4.6% to 5.0% between 1998 to 2003.⁴ Obesity is increasingly being recognized as a modifiable risk factor for cardiovascular disease, particularly ischemic heart disease.⁵ Primary prevention studies documenting the specific impact of obesity on stroke have varied results. In men, findings from the Physicians’ Health Study have shown that an increasing BMI is associated with a steady increase in ischemic stroke, independent of hypertension, diabetes and cholesterol.⁶ Among women, data are inconsistent, with some studies showing association, while others, none.^{7,8}

Several studies suggest that abdominal obesity, rather than general obesity, is more related to stroke risk.^{9,10} In the Northern Manhattan Study, a significant and independent association between abdominal obesity (elevated WHR) and ischemic stroke was found in all racial/ethnic groups, whereas BMI did not show any significant association with ischemic stroke.⁹ Furthermore, persons with elevated BMI or WHR have increased carotid artery intima-media thickness and cross-sectional intima-media area, which are two preclinical predictors of atherosclerosis.¹¹

B. Risk Factor Modification

B1. Primary Stroke Prevention

Epidemiological studies indicate that increased body weight and abdominal fat are directly associated with stroke risk. Weight reduction is recommended because it lowers BP (Class I-A) and may thereby reduce the risk of stroke. Modest weight loss (e.g., 10% of the initial body weight over 6 months) is realistic and attainable.¹² It is better to maintain a moderate loss over the long term than to achieve a greater weight loss that cannot be maintained.

B2. Secondary Stroke Prevention

Although no study has demonstrated that weight reduction will reduce stroke recurrence in patients who have suffered a previous stroke or TIA, losing weight significantly improves BP, fasting glucose values, serum lipids and physical endurance.¹³ Because obesity is a contributing factor to other risk factors associated with recurrent stroke, promoting weight loss and maintenance of a healthy weight is important. Exercise and a diet rich in fruits and vegetables can help control weight and reduce the risk of stroke, MI and death.^{14,15}

C. Recommendation: Weight reduction should be considered for all overweight patients to maintain the following goals: BMI=18.5 to 22.9 kg/m²; WHR_≤0.95 in males and _≤0.85 in females; and WC_≤90 cm (35 inches) in males and _≤80 cm (32 inches) in females.¹⁶

Gradual and moderate weight loss is encouraged for overweight and obese patients. Clinicians should encourage weight management as early as childhood through an appropriate balance of caloric intake, physical activity, exercise and behavioral counseling.

Table 7. Weight classifications and associated comorbidities risk according to BMI and waist circumference in adult Asians¹⁶

Classification	BMI (kg/m ²)	Risk of comorbidities	
		Waist circumference	
		<90 cm (men) <80 cm (women)	≥90 cm (men) ≥80 cm (women)
Underweight	<18.5	Low*	Average
Normal range	18.5-22.9	Average	Increased
Overweight (at risk)	23-24.9	Increased	Moderate
Obese I	25-29.9	Moderate	Severe
Obese II	≥30	Severe	Very severe

* But increased risk of other clinical problems

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XV. DIET

A. Epidemiology: Although dietary factors may be risk factors for stroke, their role is poorly defined. Homocysteine may be associated with stroke and is associated with deficiency of dietary intake of folate, vitamins B6 and B12 (observed in case-control studies but not clearly in prospective studies).¹ In ecological and some prospective studies, a higher level of sodium intake is associated with an increased risk of stroke.²⁻⁵ Higher potassium intake is also associated with reduced stroke risk in prospective studies.^{6,7} However, several methodological limitations, particularly difficulties in estimating dietary electrolyte intake, hinder risk assessment and may lead to false-negative results in observational studies.

B. Risk Modification: Prospective studies show that increased fruit and vegetable consumption is associated with a dose-related reduced stroke risk. Fruits and vegetables may contribute to stroke prevention through antioxidant mechanisms or elevation of potassium levels.⁷⁻¹⁰ Increase sodium intake is associated with hypertension, and reduction in salt consumption may significantly lower BP and reduce stroke mortality.

The 2006 AHA Guidelines recommend a well-balanced diet containing ≥ 5 servings of fruits and vegetables per day to reduce stroke risk. The DASH diet, which emphasizes fruit, vegetables and low-fat dairy products and is reduced in saturated and total fat, also lowers BP and is recommended (Class I- A).¹¹

C. Recommendations: While awaiting more definitive data, reducing intake of sodium and increasing intake of potassium to help lower BP is recommended (Class I-A). The recommended sodium intake is ≤ 2.3 g/day (100 mmol/day), and the recommended potassium intake is ≥ 4.7 g/day (120 mmol/day).

It seems prudent to limit excess saturated fat and to replace vitamins B6 and B12 and folate when such deficiencies are identified

A diet rich in fruits and vegetable is advised (Class IIb-C).

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APPENDIX OF DIET MODIFICATION FOR STROKE PREVENTION

The FNRI-DOST and the Nutritionists-Dietitians Association of the Philippines (NDAP) provide a simple diet guide that clinicians can in advising patients on dietary fat modification. However, patients requiring intensive dietary interventions for whatever reason or condition should be referred to a nutritionist/dietitian for individualized counseling.

Simple Dietary Plan for Fat Modification (2000)

The Biomedical Nutrition Research Division, FNRI-DOST, and NDAP

Some pointers to observe in planning meals:

1. Choose freely from fruits, vegetables, cereals, root crops, bread, dried beans and nuts.
2. Eat fish as main dish at least three times a week.
3. May eat chicken meat as a substitute to fish at least three to four times a week.

4. For other kinds of meat, use lean parts and prepare as boiled, baked, broiled, or roasted. Trim off any visible fat.
5. Use evaporated filled milk or skimmed milk instead of whole milk and avoid whole milk products such as cheese, butter, cream, etc. Use margarine made with allowed vegetable oil.
6. Use unsaturated fats and oils such as corn oil, soybean oil, peanut butter, etc.
7. Limit eggs to only three per week.
8. Avoid rich desserts such as cakes, pastries, cookies, pies, ice cream and chocolates.
9. Always read the nutrition labels of packaged/processed foods.

Food selection guide

Food group	Allowed	Restricted/avoided
Fats and oils	<i>In prescribed amounts:</i> Olive, canola, corn, soybean, palm, sunflower and peanut oils. Coconut oil.	<ul style="list-style-type: none"> • Fats and oils from animal foods, butter. Hydrogenated vegetable oils (e.g., margarine, lard, shortening, spread) • Meat and chicken fat drippings used for sauces, bacon fat, "chicharon"
Meat, fish, poultry, eggs, milk, dry beans	<p><i>Eat frequently*:</i> Fish (fresh, frozen or canned in water, tomato or vinegar); chicken breast without skin or fat. Dried beans, lentils, fresh or frozen sweetpeas; "vege-meat", tokwa, taho, tofu & other bean products;</p> <p><i>Eat occasionally**:</i> Very lean, well-trimmed cuts of beef, pork, veal, lamb; crabmeat, shrimp without head; whole eggs up to 3 pieces per week, eggwhite as desired, may be cooked in allowed fat; Skimmed milk or low fat milk or cheese</p>	<ul style="list-style-type: none"> • Fish roe, crabfat "aligui" shrimp head, oyster, clams. • Fatty meats: cold cuts, canned or frozen meats, sausages.; fatty poultry with skin; internal organs (liver, kidney, heart, tripe, sweetbreads) • Whole milk/cow's milk and cheese made from whole milk
Vegetable	<p>All vegetables prepared without fat or with allowed fats only.</p> <p><i>Eat frequently*:</i> Green leafy and yellow vegetables (they are good sources of beta-carotene, vitamin C, calcium, iron and dietary fiber among others)</p>	Buttered, creamed, fried vegetables in restricted fats or cooked with fatty meat and sauces.
Fruit	<p>All fruits; adjust fat allowance when using avocado.</p> <p><i>Eat frequently*:</i> Vitamin C-rich fruits and deep colored fruits</p>	Avocado in moderation (due to its high fat content)
Rice, corn, rootcrops, noodles, bread and cereals	<p>All cereals, roots/tubers, certain noodles/pasta, wheat bread, "pan de sal" except those restricted</p> <p><i>Eat frequently*:</i> Oatmeal, cold cereals, corn and sweet potato</p>	<ul style="list-style-type: none"> • Croissants, muffins, crackers, biscuits, waffles, pancakes, doughnut, rolls made with whole egg, butter, margarine or fat of unknown composition • Fresh mami or miki noodles • Potato chips, french fries, popcorn

Desserts	Fat-free/low-fat/light dessert. Fresh or canned fruits in light syrup only. Plain cakes with no icing (angel or sponge cakes), meringue, yogurt, sherbet	Rich dessert especially those made with cream, butter, solid shortening, lard, whole egg, chocolate cookies and pies made from cream fudge, ice cream; pastillas from whole milk, yema
Soups	Fat-free broths made from meat or chicken stock. Soups prepared with skimmed/low-fat milk.	Cream soups, fatty broth or stock
Beverage	<ul style="list-style-type: none"> • Coffee (not more than 3 cups black), decaffeinated coffee, tea, carbonated beverages in moderation. • Alcoholic drinks: not more than 1 jigger for women and not more than 2 jiggers for men 	<p>Soda fountain beverages such as milk shake, malted milk and chocolate drinks.</p> <p>Alcoholic drinks in moderation.</p>
Miscellaneous	<ul style="list-style-type: none"> • Nuts (peanuts, walnut, almond, cashew, pili, etc.) preferably boiled, roasted/baked, consume in moderation. • Nondairy cream in moderation • Spices and seasonings in moderation. Sauce made with allowed fats and skimmed milk, vinegar, pickles, mustard, catsup, banana sauce. 	<ul style="list-style-type: none"> • Sauces and gravies with restricted fats or milk; regular mayonnaise • Butter-dipped foods. • Packed dinners or “instant foods” of unknown fat content.

*Eat frequently – at least 4 to 5 times a week.

**Eat occasionally – at most, once a month.

APPENDIX TO STROKE PREVENTION

Independent Risk Factors for Stroke Among Filipinos (RIFASAF data)

Variable	Odds Ratio	95% Confidence Interval	P-Value
Hypertension	6.01	4.48-8.05	0.000
Diabetes	1.60	1.10-2.32	0.014
Atrial Fibrillation	1.91	0.51-7.19	0.337
Myocardial Infarction	4.67	1.18-18.52	0.029
Rheumatic Heart Disease	3.69	1.05-12.99	0.042
Smoking	1.36	1.00-1.86	0.053
Snoring	3.37	2.49-4.58	0.000
Stress	1.69	1.25-2.29	0.001
Frequent Alcohol Intake	1.75	1.14-2.70	0.011

Statistical model derived using multiple regression analysis (Strata v. 5.0)

The odds ratio estimates the risk of a patient for stroke if the variable (risk factor) is present compared with a similar person without the risk factor.

Reference: Roxas A, for the Philippine Neurological Association and Department of Health. Risk factors for stroke among Filipinos. *Phil J Neurol* 2002;6:1-7.

Philippine Prevalence for Atherosclerosis Risk Factors (≥ 20 years old) (2003 National Nutrition Health Survey)

Risk Factor	Basis	Prevalence (%)
Hypertension	BP or history	17.4
Diabetes	FBS >125 mg/dL or history or use of anti-diabetes medication	4.6
Stroke	History	1.4
Hypercholesterolemia	TC ≥ 240 mg/dL	8.5
Current Smoking (M/F)	History	56.3 / 12.1
Obesity: BMI	BMI ≥ 30	4.8
Obesity: Waist Hip Ratio (M/F)	1.0 for men; 0.85 for women	12.1 / 54.8
Angina Pectoris	History or questionnaire	12.1
Peripheral Arterial Disease	Questionnaire or ankle-brachial index	8.9

Reference: Dans AL, Morales DD, Abola TB, Roxas J, et al; for NNHeS 2003 Group. National Nutrition and Health Survey (NNHeS): Atherosclerosis-related Diseases and Risk Factors. *Phil J Int Med* 2005;43;103-115.
