Executive Summary: Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this guideline as an educational tool for neurologists.

Endorsed by the American Association of Neurological Surgeons and Congress of Neurological Surgeons

Walter N. Kernan, MD, Chair; Bruce Ovbiagele, MD, MSc, MAS, Vice Chair; Henry R. Black, MD; Dawn M. Bravata, MD; Marc I. Chimowitz, MBChB, FAHA; Michael D. Ezekowitz, MBChB, PhD; Margaret C. Fang, MD, MPH; Marc Fisher, MD, FAHA; Karen L. Furie, MD, MPH, FAHA; Donald V. Heck, MD; S. Claiborne (Clay) Johnston, MD, PhD; Scott E. Kasner, MD, FAHA; Steven J. Kittner, MD, MPH, FAHA; Pamela H. Mitchell, PhD, RN, FAHA; Michael W. Rich, MD; DeJuran Richardson, PhD; Lee H. Schwamm, MD, FAHA; John A. Wilson, MD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Peripheral Vascular Disease

In recognition of the morbidity of recurrent brain ischemia, the aim of the present American Heart Association/American Stroke Association (AHA/ASA) document, "Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack," is to provide clinicians with evidence-based recommendations for the prevention of future stroke among survivors of ischemic stroke or transient ischemic attack. The current average annual rate of future stroke (≈3%–4%) represents a historical low that is the result of important discoveries in prevention science. These include antiplatelet therapy and effective strategies for treatment of hypertension, atrial fibrillation (AF), arterial obstruction, and hyperlipidemia. New approaches and improvements in existing approaches are constantly emerging. To help clinicians safeguard past success and drive the rate of secondary stroke even lower, this guideline is updated every 2 to 3 years. Additional interval updates may be published, as needed, to reflect the changing state of knowledge on the approaches to prevent a recurrent stroke.

Important revisions since the last guideline are displayed in Table 1. New sections were added for sleep apnea and aortic arch atherosclerosis, in recognition of maturing literature to confirm these as prevalent risk factors for recurrent stroke. The section on diabetes mellitus (DM) has been expanded to include pre-DM. The revised guideline gives somewhat greater emphasis to lifestyle and obesity as potential targets for risk reduction. A section on nutrition was added. The sections on carotid stenosis, AF, and prosthetic heart valves have been revised substantially in a manner that is consistent with recently published AHA and American College of Chest Physicians guidelines. Sections on pregnancy and intracranial atherosclerosis have also been rewritten substantially. One section was removed (Fabry disease) in recognition of the rarity and specialized nature of this condition.

The revised guideline begins to consider clinically silent brain infarction as an entry point for secondary prevention and an event to be prevented. Brain imaging may identify evidence for clinically silent cerebral infarction, as defined by brain parenchymal injury of presumed vascular origin without a history of acute neurological dysfunction attributable to the lesion. These seemingly silent infarctions are associated with typical risk factors for ischemic stroke, increased risk for future ischemic stroke, and unrecognized neurological signs in the absence of symptoms. Clinicians who diagnose silent infarction routinely ask whether this diagnosis warrants implementation of secondary prevention measures. The writing committee, therefore, identified silent infarction as an important and emerging issue in secondary stroke prevention. Although data to guide management of patients with silent infarction are limited, the writing committee agreed to summarize these data where they could be found and incorporate them into relevant sections of this guideline.

Recommendations follow the AHA and the American College of Cardiology methods of classifying the level of certainty of the treatment effect and the class of evidence (Tables 2 and 3). The writing group prepared recommendations to be consistent with other, current AHA statements/guidelines, except where

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important new science warranted revision or differing interpretations of science could not be reconciled. Although prevention of ischemic stroke is the primary outcome of interest, many of the grades for the recommendations were chosen to reflect the existing evidence on the reduction of all vascular outcomes after stroke or transient ischemic attack (TIA), including subsequent stroke, myocardial infarction (MI), and vascular death. Recommendations in this guideline are organized to aid the clinician who has arrived at a potential explanation of the cause of the ischemic stroke in an individual patient and is embarking on therapy to reduce the risk of a recurrent event and other vascular outcomes.

Recommendations

Hypertension

1. Initiation of blood pressure (BP) therapy is indicated for previously untreated patients with ischemic stroke or TIA who, after the first several days, have an established BP ≥140 mm Hg systolic or ≥90 mm Hg diastolic *(Class I; Level of Evidence B)*. Initiation of therapy for patients with BP <140 mm Hg systolic and <90 mm Hg diastolic is of uncertain benefit *(Class IIb; Level of Evidence C)*. (Revised recommendation)
2. Resumption of BP therapy is indicated for previously treated patients with known hypertension for both prevention of recurrent stroke and prevention of other vascular events in those who have had an ischemic stroke or TIA and are beyond the first several days *(Class I; Level of Evidence A)*. (Revised recommendation)
3. Goals for target BP level or reduction from pretreatment baseline are uncertain and should be individualized, but it is reasonable to achieve a systolic pressure <140 mm Hg and a diastolic pressure <90 mm Hg *(Class IIa; Level of Evidence B)*. For patients with a recent lacunar stroke, it might be reasonable to target a systolic blood pressure (SBP) of <130 mm Hg *(Class IIb; Level of Evidence B)*. (Revised recommendation)
4. Several lifestyle modifications have been associated with BP reductions and are a reasonable part of a comprehensive antihypertensive therapy *(Class IIa; Level of Evidence C)*. These modifications include salt restriction; weight loss; the consumption of a diet rich in fruits, vegetables, and low-fat dairy products; regular aerobic physical activity; and limited alcohol consumption.
5. The optimal drug regimen to achieve the recommended level of reductions is uncertain because direct comparisons between regimens are limited. The available data indicate that diuretics or the combination of diuretics and an angiotensin-converting enzyme inhibitor is useful *(Class I; Level of Evidence A)*.
6. The choice of specific drugs and targets should be individualized on the basis of pharmacological properties, mechanism of action, and consideration of specific patient characteristics for which specific agents are probably indicated (eg, extracranial cerebrovascular occlusive disease, renal impairment, cardiac disease, and diabetes mellitus [DM]) *(Class IIa; Level of Evidence B)*.

Dyslipidemia

1. Statin therapy with intensive lipid-lowering effects is recommended to reduce risk of stroke and cardiovascular events among patients with ischemic stroke or TIA presumed to be of atherosclerotic origin and an low-density lipoprotein cholesterol (LDL-C) level ≥100 mg/dL with or without evidence for other clinical atherosclerotic cardiovascular disease (ASCVD) *(Class I; Level of Evidence B)*. (Revised recommendation)
2. Statin therapy with intensive lipid-lowering effects is recommended to reduce risk of stroke and cardiovascular events among patients with ischemic stroke or TIA presumed to be of atherosclerotic origin, an LDL-C level <100 mg/dL, and no evidence for other clinical ASCVD *(Class I; Level of Evidence C)*. (New recommendation)
3. Patients with ischemic stroke or TIA and other comorbid ASCVD should be otherwise managed according to the 2013 ACC/AHA cholesterol guidelines,[16] which include lifestyle modification, dietary recommendations, and medication recommendations *(Class I; Level of Evidence A)*. (Revised recommendation)

Disorders of Glucose Metabolism and DM

1. After a TIA or ischemic stroke, all patients should probably be screened for DM with testing of fasting plasma glucose, HbA_{1c}, or an oral glucose tolerance test. Choice of test and timing should be guided by clinical judgment and recognition that acute illness may temporarily perturb measures of plasma glucose. In general, HbA_{1c} may be more accurate than other screening tests in the immediate postevent period *(Class IIa; Level of Evidence C)*. (New recommendation)
2. Use of existing guidelines from the American Diabetes Association for glycemic control and cardiovascular risk factor management is recommended for patients with an ischemic stroke or TIA who also have DM or pre-DM *(Class I; Level of Evidence B)*.

Obesity

1. All patients with TIA or stroke should be screened for obesity with measurement of body mass index *(Class I; Level of Evidence C)*. (New recommendation)
2. Despite the demonstrated beneficial effects of weight loss on cardiovascular risk factors, the usefulness of weight loss among patients with a recent TIA or ischemic stroke and obesity is uncertain *(Class IIb; Level of Evidence C)*. (New recommendation)

Metabolic Syndrome

1. At this time, the usefulness of screening patients for the metabolic syndrome after stroke is unknown *(Class IIb; Level of Evidence C)*.
2. For patients who are screened and classified as having the metabolic syndrome, management should focus on counseling for lifestyle modification (diet, exercise, and weight loss) for vascular risk reduction *(Class I; Level of Evidence C)*.

Table 1. New or Substantially Revised Recommendations for 2014*

Section	2014 Recommendation	Description of Change From 2011
Hypertension	Initiation of BP therapy is indicated for previously untreated patients with ischemic stroke or TIA who, after the first several days, have an established BP ≥140 mm Hg systolic or ≥90 mm Hg diastolic (*Class I; Level of Evidence B)*. Initiation of therapy for patients with BP <140 mm Hg systolic and <90 mm Hg diastolic is of uncertain benefit *(Class IIb; Level of Evidence C)*.	Clarification of parameters for initiating BP therapy
	Resumption of BP therapy is indicated for previously treated patients with known hypertension for both prevention of recurrent stroke and prevention of other vascular events in those who have had an ischemic stroke or TIA and are beyond the first several days *(Class I; Level of Evidence A)*.	Clarification of parameters for resuming BP therapy
	Goals for target BP level or reduction from pretreatment baseline are uncertain and should be individualized, but it is reasonable to achieve a systolic pressure <140 mm Hg and a diastolic pressure <90 mm Hg (*Class IIa; Level of Evidence B)*. For patients with a recent lacunar stroke, it might be reasonable to target a systolic BP of <130 mm Hg *(Class IIb; Level of Evidence B)*.	Revised guidance for target values
Dyslipidemia	Statin therapy with intensive lipid-lowering effects is recommended to reduce risk of stroke and cardiovascular events among patients with ischemic stroke or TIA presumed to be of atherosclerotic origin and an LDL-C level ≥100 mg/dL with or without evidence for other ASCVD *(Class I; Level of Evidence B)*.	1. Revised to be consistent with wording in the 2013 ACC/AHA cholesterol guideline[16]
	Statin therapy with intensive lipid-lowering effects is recommended to reduce risk of stroke and cardiovascular events among patients with ischemic stroke or TIA presumed to be of atherosclerotic origin, an LDL-C level <100 mg/dL, and no evidence for other clinical ASCVD *(Class I; Level of Evidence C)*.	1. Added to be consistent with the 2013 ACC/AHA cholesterol guideline[16] but to indicate a lower level of evidence when LDL-C is <100 mg/dL
	Patients with ischemic stroke or TIA and other comorbid ASCVD should be otherwise managed according to the ACC/AHA 2013 guidelines, which include lifestyle modification, dietary recommendations, and medication recommendations *(Class I; Level of Evidence A)*.	1. Revised to be consistent with the 2013 ACC/AHA cholesterol guideline[16]
Glucose disorders	After a TIA or ischemic stroke, all patients should probably be screened for DM with testing of fasting plasma glucose, HbA_{1c}, or an oral glucose tolerance test. Choice of test and timing should be guided by clinical judgment and recognition that acute illness may temporarily perturb measures of plasma glucose. In general, HbA_{1c} may be more accurate than other screening tests in the immediate postevent period *(Class IIa; Level of Evidence C)*.	New recommendation
Obesity	All patients with TIA or stroke should be screened for obesity with measurement of BMI *(Class I; Level of Evidence C)*.	New recommendation
	Given the demonstrated beneficial effects of weight loss on cardiovascular risk factors, the usefulness of weight loss among patients with a recent TIA or ischemic stroke and obesity is uncertain *(Class IIb; Level of Evidence C)*.	New recommendation
Physical inactivity	For patients who are able and willing to initiate increased physical activity, referral to a comprehensive, behaviorally oriented program is probably recommended *(Class IIa; Level of Evidence C)*.	New recommendation
Nutrition	It is reasonable to conduct a nutritional assessment for patients with a history of ischemic stroke or TIA, looking for signs of overnutrition or undernutrition *(Class IIa; Level of Evidence C)*.	New recommendation
	Patients with a history of ischemic stroke or TIA and signs of undernutrition should be referred for individualized nutritional counseling *(Class I; Level of Evidence B)*.	New recommendation
	Routine supplementation with a single vitamin or combination of vitamins is not recommended *(Class III; Level of Evidence A)*.	New recommendation
	It is reasonable to recommend that patients with a history of stroke or TIA reduce their sodium intake to less than ≈2.4 g/d. Further reduction to <1.5 g/d is also reasonable and is associated with even greater BP reduction *(Class IIa; Level of Evidence C)*.	New recommendation
	It is reasonable to counsel patients with a history of stroke or TIA to follow a Mediterranean-type diet instead of a low-fat diet. The Mediterranean-type diet emphasizes vegetables, fruits, and whole grains and includes low-fat dairy products, poultry, fish, legumes, olive oil, and nuts. It limits intake of sweets and red meats *(Class IIa; Level of Evidence C)*.	New recommendation
Sleep apnea	A sleep study might be considered for patients with an ischemic stroke or TIA on the basis of the very high prevalence of sleep apnea in this population and the strength of the evidence that the treatment of sleep apnea improves outcomes in the general population *(Class IIb; Level of Evidence B)*.	New recommendation
	Treatment with continuous positive airway pressure might be considered for patients with ischemic stroke or TIA and sleep apnea given the emerging evidence in support of improved outcomes *(Class IIb; Level of Evidence B)*.	New recommendation

(*Continued*)

Table 1. Continued

Section	2014 Recommendation	Description of Change From 2011
Carotid disease	CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery is reduced by >70% by noninvasive imaging or >50% by catheter-based imaging or noninvasive imaging with corroboration and the anticipated rate of periprocedural stroke or death is <6% *(Class IIa; Level of Evidence B)*.	Class changed from I to IIa based on outcome findings reported in a meta-analysis of comparative trials
	It is reasonable to consider patient age in choosing between CAS and CEA. For older patients (ie, older than ≈70 years), CEA may be associated with improved outcome compared with CAS, particularly when arterial anatomy is unfavorable for endovascular intervention. For younger patients, CAS is equivalent to CEA in terms of risk for periprocedural complication (ie, stroke, MI, or death) and long-term risk for ipsilateral stroke *(Class IIa; Level of Evidence B)*.	New recommendation
	CAS and CEA in the above settings should be performed by operators with established periprocedural stroke and mortality rates of <6% for symptomatic patients, similar to that observed in trials comparing CEA to medical therapy and more recent observational studies *(Class I; Level of Evidence B)*.	Class changed from IIa to I
	Routine, long term follow-up imaging of the extracranial carotid circulation with carotid duplex ultrasonography is not recommended *(Class III; Level of Evidence B)*.	New recommendation
	For patients with recurrent or progressive ischemic symptoms ipsilateral to a stenosis or occlusion of a distal (surgically inaccessible) carotid artery, or occlusion of a midcervical carotid artery after institution of optimal medical therapy, the usefulness of EC/IC bypass is considered investigational *(Class IIb; Level of Evidence C)*.	New recommendation
Intracranial atherosclerosis	For patients with recent stroke or TIA (within 30 days) attributable to severe stenosis (70%–99%) of a major intracranial artery, the addition of clopidogrel 75 mg/d to aspirin for 90 days might be reasonable *(Class IIb; Level of Evidence B)*.	New recommendation
	For patients with stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, the data are insufficient to make a recommendation regarding the usefulness of clopidogrel alone, the combination of aspirin and dipyridamole, or cilostazol alone *(Class IIb; Level of Evidence C)*.	New recommendation
	For patients with a stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, maintenance of systolic BP below 140 mm Hg and high-intensity statin therapy are recommended *(Class I; Level of Evidence B)*.	1. New cholesterol recommendation is consistent with 2013 ACC/AHA cholesterol guideline[16] 2. Class changed from IIb to I
	For patients with a stroke or TIA attributable to moderate stenosis (50%–69%) of a major intracranial artery, angioplasty or stenting is not recommended given the low rate of stroke on medical management and the inherent periprocedural risk of endovascular treatment *(Class III; Level of Evidence B)*.	New recommendation
	For patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, stenting with the Wingspan stent system is not recommended as an initial treatment, even for patients who were taking an antithrombotic agent at the time of the stroke or TIA *(Class III; Level of Evidence B)*.	New recommendation
	For patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, the usefulness of angioplasty alone or placement of stents other than the Wingspan stent is unknown and is considered investigational *(Class IIb; Level of Evidence C)*.	1. Change from 50% to 99% stenosis to 70% to 99% stenosis 2. Rewording to mention Wingspan device used in SAMMPRIS
	For patients with severe stenosis (70%–99%) of a major intracranial artery and recurrent TIA or stroke after institution of aspirin and clopidogrel therapy, achievement of systolic BP <140 mm Hg, and high-intensity statin therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stents is unknown and is considered investigational *(Class IIb; Level of Evidence C)*.	New recommendation
	For patients with severe stenosis (70%–99%) of a major intracranial artery and actively progressing symptoms after institution of aspirin and clopidogrel therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stents is unknown and is considered investigational *(Class IIb; Level of Evidence C)*.	New recommendation
AF	For patients who have experienced an acute ischemic stroke or TIA with no other apparent cause, prolonged rhythm monitoring (≈30 days) for AF is reasonable within 6 months of the index event *(Class IIa; Level of Evidence C)*.	New recommendation
	VKA therapy *(Class I; Level of Evidence A)*, apixaban *(Class I; Level of Evidence A)*, and dabigatran *(Class I; Level of Evidence B)* are all indicated for the prevention of recurrent stroke in patients with nonvalvular AF, whether paroxysmal or permanent. The selection of an antithrombotic agent should be individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including renal function and time in INR therapeutic range if the patient has been taking VKA therapy.	1. New recommendations regarding apixaban and dabigatran 2. New text regarding choice of agent

(*Continued*)

Table 1. Continued

Section	2014 Recommendation	Description of Change From 2011
AF cont'd	Rivaroxaban is reasonable for the prevention of recurrent stroke in patients with nonvalvular AF *(Class IIa; Level of Evidence B)*.	New recommendation
	The combination of oral anticoagulation (ie, warfarin or one of the newer agents) with antiplatelet therapy is not recommended for all patients after ischemic stroke or TIA but is reasonable in patients with clinically apparent CAD, particularly an acute coronary syndrome or stent placement *(Class IIb; Level of Evidence C)*.	New recommendation
	For patients with ischemic stroke or TIA and AF who are unable to take oral anticoagulants, aspirin alone is recommended (*Class I; Level of Evidence A*). The addition of clopidogrel to aspirin therapy, compared with aspirin therapy alone, might be reasonable *(Class IIb; Level of Evidence B)*.	1. Reworded from the 2011 text 2. Class changed from III to IIb
	For most patients with a stroke or TIA in the setting of AF, it is reasonable to initiate oral anticoagulation within 14 days after the onset of neurological symptoms *(Class IIa; Level of Evidence B)*.	New recommendation
	In the presence of high risk for hemorrhagic conversion (ie, large infarct, hemorrhagic transformation on initial imaging, uncontrolled hypertension, or hemorrhage tendency), it is reasonable to delay initiation of oral anticoagulation beyond 14 days *(Class IIa; Level of Evidence B)*.	New recommendation
	The usefulness of closure of the left atrial appendage with the WATCHMAN device in patients with ischemic stroke or TIA and AF is uncertain *(Class IIb; Level of Evidence B)*.	New recommendation
MI and thrombus	Treatment with VKA therapy (target INR, 2.5; range, 2.0–3.0) for 3 months may be considered in patients with ischemic stroke or TIA in the setting of acute anterior STEMI without demonstrable left ventricular mural thrombus formation but with anterior apical akinesis or dyskinesis identified by echocardiography or other imaging modality *(Class IIb; Level of Evidence C)*.	New recommendation
	In patients with ischemic stroke or TIA in the setting of acute MI complicated by left ventricular mural thrombus formation or anterior or apical wall-motion abnormalities with a left ventricular ejection fraction <40% who are intolerant to VKA therapy because of nonhemorrhagic adverse events, treatment with an LMWH, dabigatran, rivaroxaban, or apixaban for 3 months may be considered as an alternative to VKA therapy for prevention of recurrent stroke or TIA *(Class IIb; Level of Evidence C)*.	New recommendation
Cardiomyopathy	In patients with ischemic stroke or TIA in sinus rhythm who have left atrial or left ventricular thrombus demonstrated by echocardiography or another imaging modality, anticoagulant therapy with a VKA is recommended for ≥3 months *(Class I; Level of Evidence C)*.	New recommendation
	In patients with ischemic stroke or TIA in the setting of a mechanical LVAD, treatment with VKA therapy (target INR, 2.5; range, 2.0–3.0) is reasonable in the absence of major contraindications (eg, active gastrointestinal bleeding) *(Class IIa; Level of Evidence C)*.	New recommendation
	In patients with ischemic stroke or TIA in sinus rhythm with dilated cardiomyopathy (LV ejection fraction ≤35%), restrictive cardiomyopathy, or a mechanical LVAD who are intolerant to VKA therapy because of nonhemorrhagic adverse events, the effectiveness of treatment with dabigatran, rivaroxaban, or apixaban is uncertain compared with VKA therapy for prevention of recurrent stroke *(Class IIb; Level of Evidence C)*.	New recommendation
Valvular heart disease	For patients with ischemic stroke or TIA who have rheumatic mitral valve disease and AF, long-term VKA therapy with an INR target of 2.5 (range, 2.0–3.0) is recommended *(Class I; Level of Evidence A)*.	1. Mention of patients without AF is removed 2. Class changed from IIa to I
	For patients with ischemic stroke or TIA who have rheumatic mitral valve disease without AF or another likely cause for their symptoms (eg, carotid stenosis), long-term VKA therapy with an INR target of 2.5 (range, 2.0–3.0) may be considered instead of antiplatelet therapy *(Class IIb; Level of Evidence C)*.	New recommendation focuses on patients without AF
	For patients with rheumatic mitral valve disease who have an ischemic stroke or TIA while being treated with adequate VKA therapy, the addition of aspirin might be considered *(Class IIb; Level of Evidence C)*.	New recommendation
	For patients with ischemic stroke or TIA and native aortic or nonrheumatic mitral valve disease who do not have AF or another indication for anticoagulation, antiplatelet therapy is recommended *(Class I; Level of Evidence C)*.	Class changed from IIb to I
	For patients with ischemic stroke or TIA and mitral annular calcification who do not have AF or another indication for anticoagulation, antiplatelet therapy is recommended as it would be without the mitral annular calcification *(Class I; Level of Evidence C)*.	Class changed from IIb to I

(*Continued*)

Table 1. Continued

Section	2014 Recommendation	Description of Change From 2011
Valvular heart disease cont'd	For patients with mitral valve prolapse who have ischemic stroke or TIAs and who do not have AF or another indication for anticoagulation, antiplatelet therapy is recommended as it would be without mitral valve prolapse *(Class I; Level of Evidence C)*.	1. Change in wording 2. Class changed from IIb to I
Prosthetic HV	For patients with a mechanical aortic valve and a history of ischemic stroke or TIA before its insertion, VKA therapy is recommended with an INR target of 2.5 (range, 2.0–3.0) *(Class I; Level of Evidence B)*.	Modified to focus on aortic valve
	For patients with a mechanical mitral valve and a history of ischemic stroke or TIA before its insertion, VKA therapy is recommended with an INR target of 3.0 (range, 2.5–3.5) *(Class I; Level of Evidence C)*.	1. New recommendation focuses on mitral valve 2. INR target is revised for the mitral valve
	For patients with a mechanical mitral or aortic valve who have a history of ischemic stroke or TIA before its insertion and who are at low risk for bleeding, the addition of aspirin 75 to 100 mg/d to VKA therapy is recommended *(Class I; Level of Evidence B)*.	New recommendation
	For patients with a bioprosthetic aortic or mitral valve, a history of ischemic stroke or TIA before its insertion, and no other indication for anticoagulation therapy beyond 3 to 6 months from the valve placement, long-term therapy with aspirin 75 to 100 mg/d is recommended in preference to long-term anticoagulation *(Class I; Level of Evidence C)*.	New recommendation specifically addresses timing of TIA or stroke in relation to valve replacement and recommends aspirin in preference to anticoagulation
Antiplatelet therapy	The combination of aspirin and clopidogrel might be considered for initiation within 24 hours of a minor ischemic stroke or TIA and for continuation for 21 days *(Class IIb; Level of Evidence B)*.	New recommendation
	For patients with a history of ischemic stroke or TIA, AF, and CAD, the usefulness of adding antiplatelet therapy to VKA therapy is uncertain for purposes of reducing the risk of ischemic cardiovascular and cerebrovascular events *(Class IIb; Level of Evidence C)*. Unstable angina and coronary artery stenting represent special circumstances in which management may warrant DAPT/VKA therapy.	New recommendation
Aortic arch atheroma	For patients with an ischemic stroke or TIA and evidence of aortic arch atheroma, antiplatelet therapy is recommended *(Class I; Level of Evidence A)*.	New recommendation
	For patients with an ischemic stroke or TIA and evidence of aortic arch atheroma, statin therapy is recommended *(Class I; Level of Evidence B)*.	New recommendation
	For patients with ischemic stroke or TIA and evidence of aortic arch atheroma, the effectiveness of anticoagulation with warfarin, compared with antiplatelet therapy, is unknown *(Class IIb; Level of Evidence C)*.	New recommendation
	Surgical endarterectomy of aortic arch plaque for the purposes of secondary stroke prevention is not recommended *(Class III; Level of Evidence C)*.	New recommendation
PFO	For patients with an ischemic stroke or TIA and a PFO who are not undergoing anticoagulation therapy, antiplatelet therapy is recommended *(Class I; Level of Evidence B)*.	Class changed from IIa to I
	For patients with an ischemic stroke or TIA and both a PFO and a venous source of embolism, anticoagulation is indicated, depending on stroke characteristics *(Class I; Level of Evidence A)*. When anticoagulation is contraindicated, an inferior vena cava filter is reasonable *(Class IIa; Level of Evidence C)*.	New recommendations
	For patients with a cryptogenic ischemic stroke or TIA and a PFO without evidence for DVT, available data do not support a benefit for PFO closure *(Class III; Level of Evidence A)*.	Class changed from IIb to III
	In the setting of PFO and DVT, PFO closure by a transcatheter device might be considered, depending on the risk of recurrent DVT *(Class IIb; Level of Evidence C)*.	New recommendation
Homocysteinemia	Routine screening for hyperhomocysteinemia among patients with a recent ischemic stroke or TIA is not indicated *(Class III; Level of Evidence C)*.	New recommendation
	In adults with a recent ischemic stroke or TIA who are known to have mild to moderate hyperhomocysteinemia, supplementation with folate, vitamin B_6, and vitamin B_{12} safely reduces levels of homocysteine but has not been shown to prevent stroke (*Class III; Level of Evidence B*).	Class changed from IIb to III
Hypercoagulation	The usefulness of screening for thrombophilic states in patients with ischemic stroke or TIA is unknown *(Class IIb; Level of Evidence C)*.	New recommendation
	Anticoagulation might be considered in patients who are found to have abnormal findings on coagulation testing after an initial ischemic stroke or TIA, depending on the abnormality and the clinical circumstances *(Class IIb; Level of Evidence C)*.	Substantial rewording Class changed from IIa to IIb

(*Continued*)

Table 1. Continued

Section	2014 Recommendation	Description of Change From 2011
Hypercoagulation cont'd	Antiplatelet therapy is recommended in patients who are found to have abnormal findings on coagulation testing after an initial ischemic stroke or TIA if anticoagulation therapy is not administered *(Class I; Level of Evidence A)*.	Represents a more firm recommendation for antiplatelet therapy in the circumstance described
Antiphospholipid antibodies	Routine testing for antiphospholipid antibodies is not recommended for patients with ischemic stroke or TIA who have no other manifestations of the antiphospholipid antibody syndrome and who have an alternative explanation for their ischemic event, such as atherosclerosis, carotid stenosis, or AF *(Class III; Level of Evidence C)*.	New recommendation
	For patients with ischemic stroke or TIA who have an antiphospholipid antibody but who do not fulfill the criteria for antiphospholipid antibody syndrome, antiplatelet therapy is recommended *(Class I; Level of Evidence B)*.	Clarifies circumstances in which antiplatelet therapy is recommended over anticoagulation
	For patients with ischemic stroke or TIA who meet the criteria for the antiphospholipid antibody syndrome but in whom anticoagulation is not begun, antiplatelet therapy is indicated *(Class I; Level of Evidence A)*.	New recommendation
Sickle cell disease	For patients with sickle cell disease and prior ischemic stroke or TIA, chronic blood transfusions to reduce hemoglobin S to <30% of total hemoglobin are recommended *(Class I; Level of Evidence B)*.	Class changed from IIa to I
Pregnancy	In the presence of a high-risk condition that would require anticoagulation outside of pregnancy, the following options are reasonable: a. LMWH twice daily throughout pregnancy, with dose adjusted to achieve the LMWH manufacturer's recommended peak anti-Xa level 4 hours after injection, or b. Adjusted-dose UFH throughout pregnancy, administered subcutaneously every 12 hours in doses adjusted to keep the midinterval aPTT at least twice control or to maintain an anti-Xa heparin level of 0.35 to 0.70 U/mL, or c. UFH or LMWH (as above) until the 13th week, followed by substitution of a VKA until close to delivery, when UFH or LMWH is resumed *(Class IIa; Level of Evidence C)*.	More detail is provided that is intended to be consistent with the recent statement by the American College of Chest Physicians[18]
	For pregnant women receiving adjusted-dose LMWH therapy for a high-risk condition that would require anticoagulation outside of pregnancy, and when delivery is planned, it is reasonable to discontinue LMWH ≥24 hours before induction of labor or cesarean section *(Class IIa; Level of Evidence C)*.	New recommendation
	In the presence of a low-risk situation in which antiplatelet therapy would be the treatment recommendation outside of pregnancy, UFH or LMWH, or no treatment may be considered during the first trimester of pregnancy depending on the clinical situation *(Class IIb; Level of Evidence C)*.	New recommendation
Breastfeeding	In the presence of a high-risk condition that would require anticoagulation outside of pregnancy, it is reasonable to use warfarin, UFH, or LMWH *(Class IIa; Level of Evidence C)*.	New recommendation
	In the presence of a low-risk situation in which antiplatelet therapy would be the treatment recommendation outside of pregnancy, low-dose aspirin use may be considered *(Class IIb; Level of Evidence C)*.	New recommendation
Implementation	Monitoring achievement of nationally accepted, evidence-based guidelines on a population-based level is recommended as a basis for improving health-promotion behaviors and reducing stroke healthcare disparities among high risk groups *(Class I; Level of Evidence C)*.	New recommendation
	Voluntary hospital-based programs for quality monitoring and improvement are recommended to improve adherence to nationally accepted, evidence-based guidelines for secondary stroke prevention *(Class I; Level of Evidence C)*.	New recommendation

ACC indicates American College of Cardiology; AF, atrial fibrillation; AHA, American Heart Association; aPTT, activated partial thromboplastin time; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CAS, carotid angioplasty and stenting; CEA, carotid endarterectomy; DAPT, dual-antiplatelet therapy; DM, diabetes mellitus; DVT, deep vein thrombosis; EC/IC, extracranial/intracranial; HbA_{1c}, hemoglobin A_{1c}; HV, heart valve; INR, international normalized ratio; LDL-C, low-density lipoprotein cholesterol; LMWH, low-molecular-weight heparin; LV, left ventricular; LVAD, left ventricular assist device; MI, myocardial infarction; PFO, patent foramen ovale; SAMMPRIS, Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis; STEMI, ST-elevation myocardial infarction; TIA, transient ischemic attack; UFH, unfractionated heparin; and VKA, vitamin K antagonist.

*Includes recommendations for which the class was changed from one whole number to another and recommendations for which a change in wording significantly changed meaning. This table does not list removed recommendations.

3. Preventive care for patient with the metabolic syndrome should include appropriate treatment for individual components of the syndrome, which are also stroke risk factors, particularly dyslipidemia and hypertension *(Class I; Level of Evidence A)*.

Physical Inactivity

1. For patients with ischemic stroke or TIA who are capable of engaging in physical activity, at least 3 to 4 sessions per week of moderate- to vigorous-intensity aerobic physical

Table 2. Applying Classification of Recommendations and Level of Evidence

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT	SIZE OF TREATMENT EFFECT			
	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	**CLASS IIa** *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	**CLASS IIb** *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	**CLASS III** *No Benefit* or **CLASS III** *Harm* Procedure/Test / Treatment COR III: No benefit — Not Helpful / No Proven Benefit COR III: Harm — Excess Cost w/o Benefit or Harmful / Harmful to Patients
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit: is not recommended; is not indicated; should not be performed/ administered/ other; is not useful/ beneficial/ effective COR III: Harm: potentially harmful; causes harm; associated with excess morbidity/mortality; should not be performed/ administered/ other
Comparative effectiveness phrases†	treatment/strategy A is recommended/indicated in preference to treatment B treatment A should be chosen over treatment B	treatment/strategy A is probably recommended/indicated in preference to treatment B it is reasonable to choose treatment A over treatment B		

A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Although randomized trials are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as sex, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use.

†For comparative effectiveness recommendations (Class I and IIa; Level of Evidence A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

exercise are reasonable to reduce stroke risk factors. Sessions should last an average of 40 minutes. Moderate-intensity exercise is typically defined as sufficient to break a sweat or noticeably raise heart rate (eg, walking briskly, using an exercise bicycle). Vigorous-intensity exercise includes activities such as jogging *(Class IIa; Level of Evidence C)*. (Revised recommendation)

2. For patients who are able and willing to initiate increased physical activity, referral to a comprehensive, behaviorally oriented program is reasonable *(Class IIa; Level of Evidence C)*. (New recommendation)
3. For individuals with disability after ischemic stroke, supervision by a healthcare professional such as a physical therapist or cardiac rehabilitation professional, at least on initiation of an exercise regimen, may be considered *(Class IIb; Level of Evidence C)*.

Nutrition

1. It is reasonable to conduct a nutritional assessment for patients with a history of ischemic stroke or TIA, looking for signs of overnutrition or undernutrition *(Class IIa; Level of Evidence C)*. (New recommendation)
2. Patients with a history of ischemic stroke or TIA and signs of undernutrition should be referred for

Table 3. Definition of Classes and Levels of Evidence Used in AHA/ASA 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
Class IIa	The weight of evidence or opinion is in favor of the procedure or treatment
Class IIb	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
Therapeutic recommendations	
Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses
Level of Evidence B	Data derived from a single randomized trial or nonrandomized studies
Level of Evidence C	Consensus opinion of experts, case studies, or standard of care
Diagnostic recommendations	
Level of Evidence A	Data derived from multiple prospective cohort studies using a reference standard applied by a masked evaluator
Level of Evidence B	Data derived from a single grade A study or one or more case-control studies, or studies using a reference standard applied by an unmasked evaluator
Level of Evidence C	Consensus opinion of experts

AHA/ASA indicates American Heart Association/American Stroke Association.

individualized nutritional counseling *(Class I; Level of Evidence B)*. (New recommendation)

3. Routine supplementation with a single vitamin or combination of vitamins is not recommended *(Class III; Level of Evidence A)*. (New recommendation)
4. It is reasonable to recommend that patients with a history of stroke or TIA reduce their sodium intake to less than ≈2.4 g/d. Further reduction to <1.5 g/d is also reasonable and is associated with even greater BP reduction *(Class IIa; Level of Evidence C)*. (New recommendation)
5. It is reasonable to counsel patients with a history of stroke or TIA to follow a Mediterranean-type diet instead of a low-fat diet. The Mediterranean-type diet emphasizes vegetables, fruits, and whole grains and includes low-fat dairy products, poultry, fish, legumes, olive oil, and nuts. It limits intake of sweets and red meats *(Class IIa; Level of Evidence C)*. (New recommendation)

Sleep Apnea

1. A sleep study might be considered for patients with an ischemic stroke or TIA on the basis of the very high prevalence of sleep apnea in this population and the strength of the evidence that the treatment of sleep apnea improves outcomes in the general population *(Class IIb; Level of Evidence B)*. (New recommendation)
2. Treatment with continuous positive airway pressure might be considered for patients with ischemic stroke or TIA and sleep apnea given the emerging evidence in support of improved outcomes *(Class IIb; Level of Evidence B)*. (New recommendation)

Cigarette Smoking

1. Healthcare providers should strongly advise every patient with stroke or TIA who has smoked in the past year to quit *(Class I; Level of Evidence C)*.
2. It is reasonable to advise patients after TIA or ischemic stroke to avoid environmental (passive) tobacco smoke *(Class IIa; Level of Evidence B)*.
3. Counseling, nicotine products, and oral smoking cessation medications are effective in helping smokers to quit *(Class I; Level of Evidence A)*.

Alcohol Consumption

1. Patients with ischemic stroke, TIA, or hemorrhagic stroke who are heavy drinkers should eliminate or reduce their consumption of alcohol *(Class I; Level of Evidence C)*.
2. Light to moderate amounts of alcohol consumption (up to 2 drinks per day for men and up to 1 drink per day for nonpregnant women) may be reasonable, although nondrinkers should not be counseled to start drinking *(Class IIb; Level of Evidence B)*.

Extracranial Carotid Disease

1. For patients with a TIA or ischemic stroke within the past 6 months and ipsilateral severe (70%–99%) carotid artery stenosis as documented by noninvasive imaging, carotid endarterectomy (CEA) is recommended if the perioperative morbidity and mortality risk is estimated to be <6% *(Class I; Level of Evidence A)*.
2. For patients with recent TIA or ischemic stroke and ipsilateral moderate (50%–69%) carotid stenosis as documented by catheter-based imaging or noninvasive imaging with corroboration (eg, magnetic resonance angiogram or computed tomography angiogram), CEA is recommended depending on patient-specific factors, such as age, sex, and comorbidities, if the perioperative morbidity and mortality risk is estimated to be <6% *(Class I; Level of Evidence B)*.
3. When the degree of stenosis is <50%, CEA and carotid angioplasty and stenting (CAS) are not recommended *(Class III; Level of Evidence A)*.
4. When revascularization is indicated for patients with TIA or minor, nondisabling stroke, it is reasonable to perform the procedure within 2 weeks of the index event rather than delay surgery if there are no contraindications to early revascularization *(Class IIa; Level of Evidence B)*.
5. CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications associated with endovascular intervention when the diameter of the lumen of the internal carotid artery

is reduced by >70% by noninvasive imaging or >50% by catheter-based imaging or noninvasive imaging with corroboration and the anticipated rate of periprocedural stroke or death is <6% *(Class IIa; Level of Evidence B)*. (Revised recommendation)

6. It is reasonable to consider patient age in choosing between CAS and CEA. For older patients (ie, older than ≈70 years), CEA may be associated with improved outcome compared with CAS, particularly when arterial anatomy is unfavorable for endovascular intervention. For younger patients, CAS is equivalent to CEA in terms of risk for periprocedural complications (ie, stroke, MI, or death) and long-term risk for ipsilateral stroke *(Class IIa; Level of Evidence B)*. (New recommendation)
7. Among patients with symptomatic severe stenosis (>70%) in whom anatomic or medical conditions are present that greatly increase the risk for surgery or when other specific circumstances exist such as radiation-induced stenosis or restenosis after CEA, CAS is reasonable *(Class IIa; Level of Evidence B)*. (Revised recommendation)
8. CAS and CEA in the above settings should be performed by operators with established periprocedural stroke and mortality rates of <6% for symptomatic patients, similar to that observed in trials comparing CEA to medical therapy and more recent observational studies *(Class I; Level of Evidence B)*. (Revised recommendation)
9. Routine, long-term follow-up imaging of the extracranial carotid circulation with carotid duplex ultrasonography is not recommended *(Class III; Level of Evidence B)*. (New recommendation)
10. For patients with a recent (within 6 months) TIA or ischemic stroke ipsilateral to a stenosis or occlusion of the middle cerebral or carotid artery, extracranial/intracranial (EC/IC) bypass surgery is not recommended *(Class III; Level of Evidence A)*.
11. For patients with recurrent or progressive ischemic symptoms ipsilateral to a stenosis or occlusion of a distal (surgically inaccessible) carotid artery, or occlusion of a midcervical carotid artery after institution of optimal medical therapy, the usefulness of EC/IC bypass is considered investigational *(Class IIb; Level of Evidence C)*. (New recommendation)
12. Optimal medical therapy, which should include antiplatelet therapy, statin therapy, and risk factor modification, is recommended for all patients with carotid artery stenosis and a TIA or stroke, as outlined elsewhere in this guideline *(Class I; Level of Evidence A)*.

Extracranial Vertebrobasilar Disease

1. Routine preventive therapy with emphasis on antithrombotic therapy, lipid lowering, BP control, and lifestyle optimization is recommended for all patients with recently symptomatic extracranial vertebral artery stenosis *(Class I; Level of Evidence C)*.
2. Endovascular stenting of patients with extracranial vertebral stenosis may be considered when patients are having symptoms despite optimal medical treatment *(Class IIb; Level of Evidence C)*.
3. Open surgical procedures, including vertebral endarterectomy and vertebral artery transposition, may be considered when patients are having symptoms despite optimal medical treatment *(Class IIb; Level of Evidence C)*.

Intracranial Atherosclerosis

1. For patients with a stroke or TIA caused by 50% to 99% stenosis of a major intracranial artery, aspirin 325 mg/d is recommended in preference to warfarin *(Class I; Level of Evidence B)*. (Revised recommendation)
2. For patients with recent stroke or TIA (within 30 days) attributable to severe stenosis (70%–99%) of a major intracranial artery, the addition of clopidogrel 75 mg/d to aspirin for 90 days might be reasonable *(Class IIb; Level of Evidence B)*. (New recommendation)
3. For patients with stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, the data are insufficient to make a recommendation regarding the usefulness of clopidogrel alone, the combination of aspirin and dipyridamole, or cilostazol alone *(Class IIb; Level of Evidence C)*. (New recommendation)
4. For patients with a stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, maintenance of SBP below 140 mm Hg and high-intensity statin therapy are recommended *(Class I; Level of Evidence B)*. (Revised recommendation)
5. For patients with a stroke or TIA attributable to moderate stenosis (50%–69%) of a major intracranial artery, angioplasty or stenting is not recommended given the low rate of stroke with medical management and the inherent periprocedural risk of endovascular treatment *(Class III; Level of Evidence B)*. (New recommendation)
6. For patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, stenting with the Wingspan stent system is not recommended as an initial treatment, even for patients who were taking an antithrombotic agent at the time of the stroke or TIA *(Class III; Level of Evidence B)*. (New recommendation)
7. For patients with stroke or TIA attributable to severe stenosis (70%–99%) of a major intracranial artery, the usefulness of angioplasty alone or placement of stents other than the Wingspan stent is unknown and is considered investigational *(Class IIb; Level of Evidence C)*. (Revised recommendation)
8. For patients with severe stenosis (70%–99%) of a major intracranial artery and recurrent TIA or stroke after institution of aspirin and clopidogrel therapy, achievement of SBP <140 mm Hg, and high-intensity statin therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stent is unknown and is considered investigational *(Class IIb; Level of Evidence C)*. (New recommendation)
9. For patients with severe stenosis (70%–99%) of a major intracranial artery and actively progressing symptoms after institution of aspirin and clopidogrel therapy, the usefulness of angioplasty alone or placement of a Wingspan stent or other stents is unknown and is considered investigational *(Class IIb; Level of Evidence C)*. (New recommendation)

10. For patients with stroke or TIA attributable to 50% to 99% stenosis of a major intracranial artery, EC/IC bypass surgery is not recommended *(Class III; Level of Evidence B)*.

Atrial Fibrillation

1. For patients who have experienced an acute ischemic stroke or TIA with no other apparent cause, prolonged rhythm monitoring (≈30 days) for atrial fibrillation (AF) is reasonable within 6 months of the index event *(Class IIa; Level of Evidence C)*. (New recommendation)
2. Vitamin K antagonist (VKA) therapy *(Class I; Level of Evidence A)*, apixaban *(Class I; Level of Evidence A)*, and dabigatran *(Class I; Level of Evidence B)* are all indicated for the prevention of recurrent stroke in patients with nonvalvular AF, whether paroxysmal or permanent. The selection of an antithrombotic agent should be individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions, and other clinical characteristics, including renal function and time in international normalized ratio (INR) therapeutic range if the patient has been taking VKA therapy. (Revised recommendation)
3. Rivaroxaban is reasonable for the prevention of recurrent stroke in patients with nonvalvular AF *(Class IIa; Level of Evidence B)*. (New recommendation)
4. For patients with ischemic stroke or TIA with paroxysmal (intermittent), persistent, or permanent AF in whom VKA therapy is begun, a target INR of 2.5 is recommended (range, 2.0–3.0) *(Class I; Level of Evidence A)*.
5. The combination of oral anticoagulation (ie, warfarin or one of the newer agents) with antiplatelet therapy is not recommended for all patients after ischemic stroke or TIA but is reasonable in patients with clinically apparent coronary artery disease, particularly an acute coronary syndrome or stent placement *(Class IIb; Level of Evidence C)*. (New recommendation)
6. For patients with ischemic stroke or TIA and AF who are unable to take oral anticoagulants, aspirin alone is recommended *(Class I; Level of Evidence A)*. The addition of clopidogrel to aspirin therapy, compared with aspirin therapy alone, might be reasonable *(Class IIb; Level of Evidence B)*. (Revised recommendation)
7. For most patients with a stroke or TIA in the setting of AF, it is reasonable to initiate oral anticoagulation within 14 days after the onset of neurological symptoms *(Class IIa; Level of Evidence B)*. (New recommendation)
8. In the presence of high risk for hemorrhagic conversion (ie, large infarct, hemorrhagic transformation on initial imaging, uncontrolled hypertension, or hemorrhage tendency), it is reasonable to delay initiation of oral anticoagulation beyond 14 days *(Class IIa; Level of Evidence B)*. (New recommendation)
9. For patients with AF and a history of stroke or TIA who require temporary interruption of oral anticoagulation, bridging therapy with an low-molecular-weight heparin (LMWH) (or equivalent anticoagulant agent if intolerant to heparin) is reasonable, depending on perceived risk for thromboembolism and bleeding *(Class IIa; Level of Evidence C)*.
10. The usefulness of closure of the left atrial appendage with the WATCHMAN device in patients with ischemic stroke or TIA and AF is uncertain *(Class IIb; Level of Evidence B)*. (New recommendation)

Acute MI and Left Ventricular Thrombus

1. Treatment with VKA therapy (target INR, 2.5; range, 2.0–3.0) for 3 months is recommended in most patients with ischemic stroke or TIA in the setting of acute MI complicated by left ventricular (LV) mural thrombus formation identified by echocardiography or another imaging modality *(Class I; Level of Evidence C)*. Additional antiplatelet therapy for cardiac protection may be guided by recommendations such as those from the American College of Chest Physicians. (Revised recommendation)
2. Treatment with VKA therapy (target INR, 2.5; range, 2.0–3.0) for 3 months may be considered in patients with ischemic stroke or TIA in the setting of acute anterior ST-segment MI without demonstrable LV mural thrombus formation but with anterior apical akinesis or dyskinesis identified by echocardiography or other imaging modality *(Class IIb; Level of Evidence C)*. (New recommendation)
3. In patients with ischemic stroke or TIA in the setting of acute MI complicated by LV mural thrombus formation or anterior or apical wall-motion abnormalities with an LV ejection fraction <40% who are intolerant to VKA therapy because of nonhemorrhagic adverse events, treatment with an LMWH, dabigatran, rivaroxaban, or apixaban for 3 months may be considered as an alternative to VKA therapy for prevention of recurrent stroke or TIA *(Class IIb; Level of Evidence C)*. (New recommendation)

Cardiomyopathy

1. In patients with ischemic stroke or TIA in sinus rhythm who have left atrial or LV thrombus demonstrated by echocardiography or another imaging modality, anticoagulant therapy with a VKA is recommended for ≥3 months *(Class I; Level of Evidence C)*. (New recommendation)
2. In patients with ischemic stroke or TIA in the setting of a mechanical LV assist device, treatment with VKA therapy (target INR, 2.5; range, 2.0–3.0) is reasonable in the absence of major contraindications (eg, active gastrointestinal bleeding) *(Class IIa; Level of Evidence C)*. (New recommendation)
3. In patients with ischemic stroke or TIA in sinus rhythm with either dilated cardiomyopathy (LV ejection fraction ≤35%) or restrictive cardiomyopathy without evidence of left atrial or LV thrombus, the effectiveness of anticoagulation compared with antiplatelet therapy is uncertain, and the choice should be individualized *(Class IIb; Level of Evidence B)*. (Revised recommendation)

4. In patients with ischemic stroke or TIA in sinus rhythm with dilated cardiomyopathy (LV ejection fraction ≤35%), restrictive cardiomyopathy, or a mechanical LV assist device who are intolerant to VKA therapy because of nonhemorrhagic adverse events, the effectiveness of treatment with dabigatran, rivaroxaban, or apixaban is uncertain compared with VKA therapy for prevention of recurrent stroke *(Class IIb; Level of Evidence C)*. (New recommendation)

Mitral Stenosis, Mitral Regurgitation, Mitral Prolapse, Mitral Annular Calcification, and Aortic Valve Disease

1. For patients with ischemic stroke or TIA who have rheumatic mitral valve disease and AF, long-term VKA therapy with an INR target of 2.5 (range, 2.0–3.0) is recommended *(Class I; Level of Evidence A)*. (Revised recommendation)
2. For patients with ischemic stroke or TIA who have rheumatic mitral valve disease without AF or another likely cause for their symptoms (eg, carotid stenosis), long-term VKA therapy with an INR target of 2.5 (range, 2.0–3.0) may be considered instead of antiplatelet therapy *(Class IIb; Level of Evidence C)*. (New recommendation)
3. For patients with rheumatic mitral valve disease who are prescribed VKA therapy after an ischemic stroke or TIA, antiplatelet therapy should not be routinely added *(Class III; Level of Evidence C)*.
4. For patients with rheumatic mitral valve disease who have an ischemic stroke or TIA while being treated with adequate VKA therapy, the addition of aspirin might be considered *(Class IIb; Level of Evidence C)*. (New recommendation)
5. For patients with ischemic stroke or TIA and native aortic or nonrheumatic mitral valve disease who do not have AF or another indication for anticoagulation, antiplatelet therapy is recommended *(Class I; Level of Evidence C)*. (Revised recommendation)
6. For patients with ischemic stroke or TIA and mitral annular calcification who do not have AF or another indication for anticoagulation, antiplatelet therapy is recommended as it would be without the mitral annular calcification *(Class I; Level of Evidence C)*. (Revised recommendation)
7. For patients with mitral valve prolapse who have ischemic stroke or TIAs and who do not have AF or another indication for anticoagulation, antiplatelet therapy is recommended as it would be without mitral valve prolapse *(Class I; Level of Evidence C)*. (Revised recommendation)

Prosthetic Heart Valve

1. For patients with a mechanical aortic valve and a history of ischemic stroke or TIA before its insertion, VKA therapy is recommended with an INR target of 2.5 (range, 2.0–3.0) *(Class I; Level of Evidence B)*. (Revised recommendation)
2. For patients with a mechanical mitral valve and a history of ischemic stroke or TIA before its insertion, VKA therapy is recommended with an INR target of 3.0 (range, 2.5–3.5) *(Class I; Level of Evidence C)*. (New recommendation)
3. For patients with a mechanical mitral or aortic valve who have a history of ischemic stroke or TIA before its insertion and who are at low risk for bleeding, the addition of aspirin 75 to 100 mg/d to VKA therapy is recommended *(Class I; Level of Evidence B)*. (New recommendation)
4. For patients with a mechanical heart valve who have an ischemic stroke or systemic embolism despite adequate antithrombotic therapy, it is reasonable to intensify therapy by increasing the dose of aspirin to 325 mg/d or increasing the target INR, depending on bleeding risk *(Class IIa; Level of Evidence C)*. (Revised recommendation)
5. For patients with a bioprosthetic aortic or mitral valve, a history of ischemic stroke or TIA before its insertion, and no other indication for anticoagulation therapy beyond 3 to 6 months from the valve placement, long-term therapy with aspirin 75 to 100 mg/d is recommended in preference to long-term anticoagulation *(Class I; Level of Evidence C)*. (New recommendation)
6. For patients with a bioprosthetic aortic or mitral valve who have a TIA, ischemic stroke, or systemic embolism despite adequate antiplatelet therapy, the addition of VKA therapy with an INR target of 2.5 (range, 2.0–3.0) may be considered *(Class IIb; Level of Evidence C)*. (Revised recommendation)

Antiplatelet Agent

1. For patients with noncardioembolic ischemic stroke or TIA, the use of antiplatelet agents rather than oral anticoagulation is recommended to reduce the risk of recurrent stroke and other cardiovascular events *(Class I; Level of Evidence A)*.
2. Aspirin (50–325 mg/d) monotherapy (*Class I; Level of Evidence A*) or the combination of aspirin 25 mg and extended-release dipyridamole 200 mg twice daily *(Class I; Level of Evidence B)* is indicated as initial therapy after TIA or ischemic stroke for prevention of future stroke. (Revised recommendation)
3. Clopidogrel (75 mg) monotherapy is a reasonable option for secondary prevention of stroke in place of aspirin or combination aspirin/dipyridamole *(Class IIa; Level of Evidence B)*. This recommendation also applies to patients who are allergic to aspirin.
4. The selection of an antiplatelet agent should be individualized on the basis of patient risk factor profiles, cost, tolerance, relative known efficacy of the agents, and other clinical characteristics *(Class I; Level of Evidence C)*.
5. The combination of aspirin and clopidogrel might be considered for initiation within 24 hours of a minor ischemic stroke or TIA and for continuation for 21 days *(Class IIb; Level of Evidence B)*. (New recommendation)
6. The combination of aspirin and clopidogrel, when initiated days to years after a minor stroke or TIA and continued for 2 to 3 years, increases the risk of hemorrhage relative to either agent alone and is not recommended for routine long-term secondary prevention after ischemic stroke or TIA *(Class III; Level of Evidence A)*.

7. For patients who have an ischemic stroke or TIA while taking aspirin, there is no evidence that increasing the dose of aspirin provides additional benefit. Although alternative antiplatelet agents are often considered, no single agent or combination has been adequately studied in patients who have had an event while receiving aspirin *(Class IIb; Level of Evidence C)*.
8. For patients with a history of ischemic stroke or TIA, AF, and coronary artery disease, the usefulness of adding antiplatelet therapy to VKA therapy is uncertain for purposes of reducing the risk of ischemic cardiovascular and cerebrovascular events *(Class IIb; Level of Evidence C)*. Unstable angina and coronary artery stenting represent special circumstances in which management may warrant dual antiplatelet therapy/VKA therapy. (New recommendation)

Oral Anticoagulant

1. For patients with noncardioembolic ischemic stroke or TIA, the use of antiplatelet agents rather than oral anticoagulation is recommended to reduce the risk of recurrent stroke and other cardiovascular events *(Class I; Level of Evidence A)*.

Aortic Arch Atheroma

1. For patients with an ischemic stroke or TIA and evidence of aortic arch atheroma, antiplatelet therapy is recommended *(Class I; Level of Evidence A)*. (New recommendation)
2. For patients with an ischemic stroke or TIA and evidence of aortic arch atheroma, statin therapy is recommended *(Class I; Level of Evidence B)*. (New recommendation)
3. For patients with ischemic stroke or TIA and evidence of aortic arch atheroma, the effectiveness of anticoagulation with warfarin, compared with antiplatelet therapy, is unknown *(Class IIb; Level of Evidence C)*. (New recommendation)
4. Surgical endarterectomy of aortic arch plaque for the purposes of secondary stroke prevention is not recommended *(Class III; Level of Evidence C)*. (New recommendation)

Arterial Dissection

1. For patients with ischemic stroke or TIA and extracranial carotid or vertebral arterial dissection, antithrombotic treatment with either antiplatelet or anticoagulant therapy for at least 3 to 6 months is reasonable *(Class IIa; Level of Evidence B)*.
2. The relative efficacy of antiplatelet therapy compared with anticoagulation is unknown for patients with ischemic stroke or TIA and extracranial carotid or vertebral arterial dissection *(Class IIb; Level of Evidence B)*.
3. For patients with stroke or TIA and extracranial carotid or vertebral arterial dissection who have definite recurrent cerebral ischemic events despite medical therapy, endovascular therapy (stenting) may be considered *(Class IIb; Level of Evidence C)*.
4. Patients with stroke or TIA and extracranial carotid or vertebral arterial dissection who have definite recurrent cerebral ischemic events despite medical therapy and also fail or are not candidates for endovascular therapy may be considered for surgical treatment *(Class IIb; Level of Evidence C)*.

Patent Foramen Ovale

1. There are insufficient data to establish whether anticoagulation is equivalent or superior to aspirin for secondary stroke prevention in patients with patent foramen ovale (PFO) *(Class IIb; Level of Evidence B)*.
2. For patients with an ischemic stroke or TIA and a PFO who are not undergoing anticoagulation therapy, antiplatelet therapy is recommended *(Class I; Level of Evidence B)*. (Revised recommendation)
3. For patients with an ischemic stroke or TIA and both a PFO and a venous source of embolism, anticoagulation is indicated, depending on stroke characteristics *(Class I; Level of Evidence A)*. When anticoagulation is contraindicated, an inferior vena cava filter is reasonable *(Class IIa; Level of Evidence C)*. (New recommendation)
4. For patients with a cryptogenic ischemic stroke or TIA and a PFO without evidence for deep vein thrombosis (DVT) available data do not support a benefit for PFO closure *(Class III; Level of Evidence A)*. (Revised recommendation)
5. In the setting of PFO and DVT, PFO closure by a transcatheter device might be considered, depending on the risk of recurrent DVT *(Class IIb; Level of Evidence C)*. (New recommendation)

Hyperhomocysteinemia

1. Routine screening for hyperhomocysteinemia among patients with a recent ischemic stroke or TIA is not indicated *(Class III; Level of Evidence C)*. (New recommendation)
2. In adults with a recent ischemic stroke or TIA who are known to have mild to moderate hyperhomocysteinemia, supplementation with folate, vitamin B_6, and vitamin B_{12} safely reduces levels of homocysteine but has not been shown to prevent stroke *(Class III; Level of Evidence B)*. (Revised Recommendation)

Hypercoagulable States

1. The usefulness of screening for thrombophilic states in patients with ischemic stroke or TIA is unknown *(Class IIb; Level of Evidence C)*. (New recommendation)
2. Anticoagulation might be considered in patients who are found to have abnormal findings on coagulation testing after an initial ischemic stroke or TIA, depending on the abnormality and the clinical circumstances *(Class IIb; Level of Evidence C)*. (Revised recommendation)
3. Antiplatelet therapy is recommended for patients who are found to have abnormal findings on coagulation testing after an initial ischemic stroke or TIA if anticoagulation therapy is not administered *(Class I; Level of Evidence A)*. (Revised recommendation)
4. Long-term anticoagulation might be reasonable for patients with spontaneous cerebral venous sinus thrombosis or a recurrent ischemic stroke of undefined origin

and an inherited thrombophilia *(Class IIb; Level of Evidence C)*.

Antiphospholipid Antibodies

1. Routine testing for antiphospholipid antibodies is not recommended for patients with ischemic stroke or TIA who have no other manifestations of the antiphospholipid antibody syndrome (APS) and who have an alternative explanation for their ischemic event, such as atherosclerosis, carotid stenosis, or AF *(Class III; Level of Evidence C)*. (New recommendation)
2. For patients with ischemic stroke or TIA who have an antiphospholipid antibody but do not fulfill the criteria for APS, antiplatelet therapy is recommended *(Class I; Level of Evidence B)*. (Revised recommendation)
3. For patients with ischemic stroke or TIA who meet the criteria for the APS, anticoagulant therapy might be considered depending on the perception of risk for recurrent thrombotic events and bleeding *(Class IIb; Level of Evidence C)*. (Revised recommendation)
4. For patients with ischemic stroke or TIA who meet the criteria for the APS but in whom anticoagulation is not begun, antiplatelet therapy is indicated *(Class I; Level of Evidence A)*. (New recommendation)

Sickle Cell Disease

1. For patients with sickle cell disease and prior ischemic stroke or TIA, chronic blood transfusions to reduce hemoglobin S to <30% of total hemoglobin are recommended *(Class I; Level of Evidence B)*. (Revised recommendation)
2. For patients with sickle cell disease and prior ischemic stroke or TIA for whom transfusion therapy is not available or practical, treatment with hydroxyurea may be considered *(Class IIb; Level of Evidence B)*. (Revised recommendation)
3. For adults with sickle cell disease and ischemic stroke or TIA, general treatment recommendations cited elsewhere in this guideline are reasonable with regard to the control of risk factors and the use of antiplatelet agents *(Class IIa; Level of Evidence B)*.

Cerebral Venous Sinus Thrombosis

1. Anticoagulation is reasonable for patients with acute cerebral venous sinus thrombosis, even in selected patients with intracranial hemorrhage *(Class IIa; Level of Evidence B)*. (Revised recommendation)
2. In cerebral venous sinus thrombosis patients without a recognized thrombophilia, it is reasonable to administer anticoagulation for ≥3 months, followed by antiplatelet therapy *(Class IIa; Level of Evidence C)*. Recommendations for patients with a recognized thrombophilia are discussed elsewhere in this document.

Pregnancy

1. In the presence of a high-risk condition that would require anticoagulation outside of pregnancy, the following options are reasonable[18]:
   a. LMWH twice daily throughout pregnancy, with dose adjusted to achieve the LMWH manufacturer's recommended peak anti-Xa activity 4 hours after injection, or
   b. Adjusted-dose unfractionated heparin (UFH) throughout pregnancy, administered subcutaneously every 12 hours in doses adjusted to keep the midinterval activated partial thromboplastin time at least twice control or to maintain an anti-Xa heparin level of 0.35 to 0.70 U/mL, or
   c. UFH or LMWH (as above) until the 13th week, followed by substitution of a VKA until close to delivery, when UFH or LMWH is resumed. *(Class IIa; Level of Evidence C)* (Revised recommendation)
2. For pregnant women receiving adjusted-dose LMWH therapy for a high-risk condition that would require anticoagulation outside of pregnancy, and when delivery is planned, it is reasonable to discontinue LMWH ≥24 hours before induction of labor or cesarean section[18] *(Class IIa; Level of Evidence C)*. (New recommendation)
3. In the presence of a low-risk situation in which antiplatelet therapy would be the treatment recommendation outside of pregnancy, UFH or LMWH, or no treatment may be considered during the first trimester of pregnancy depending on the clinical situation *(Class IIb; Level of Evidence C)*. (New recommendation)
4. In the presence of a low-risk situation in which antiplatelet therapy would be the treatment recommendation outside of pregnancy, low-dose aspirin (50–150 mg/d) is reasonable after the first trimester of pregnancy *(Class IIa; Level of Evidence B)*. (Revised recommendation)

Breastfeeding Women

1. In the presence of a high-risk condition that would require anticoagulation outside of pregnancy, it is reasonable to use warfarin, UFH, or LMWH *(Class IIa; Level of Evidence C)*. (New recommendation)
2. In the presence of a low-risk situation in which antiplatelet therapy would be the treatment recommendation outside of pregnancy, low-dose aspirin use may be considered *(Class IIb; Level of Evidence C)*. (New recommendation)

Anticoagulation After Intracranial Hemorrhage

1. The decision to restart antithrombotic therapy after intracranial hemorrhage (ICH) related to antithrombotic therapy depends on the risk of subsequent arterial or venous thromboembolism, the risk of recurrent ICH, and the overall status of the patient and must therefore be individualized to each patient. For patients with a comparatively lower risk of cerebral infarction (eg, AF without prior ischemic stroke) and a higher risk of recurrent ICH (eg, elderly patients with lobar ICH or presumed amyloid angiopathy) or with very poor overall neurological function, an antiplatelet agent may be considered for prevention of ischemic stroke *(Class IIb; Level of Evidence B)*.

2. For patients who require resumption or initiation of anticoagulation after an acute ICH, subarachnoid hemorrhage, or subdural hematoma, the optimal timing is uncertain. For most patients, however, it might be reasonable to wait ≥1 week *(Class IIb; Level of Evidence B)*.
3. For patients with hemorrhagic cerebral infarction, continuation of anticoagulation may be considered, depending on the specific clinical scenario and underlying indication for anticoagulant therapy *(Class IIb; Level of Evidence C)*.

Special Approaches in High-Risk Populations

1. Monitoring achievement of nationally accepted, evidence-based guidelines on a population-based level is recommended as a basis for improving health-promotion behaviors and reducing stroke healthcare disparities among high-risk groups *(Class I; Level of Evidence C)*. (New recommendation)
2. Voluntary hospital-based programs for quality monitoring and improvement are recommended to improve adherence to nationally accepted, evidence-based guidelines for secondary stroke prevention *(Class I; Level of Evidence C)*. (New recommendation)

References

References are available in the full text of this guideline: http://stroke.ahajournals.org/cgi/reprint/STR.0000000000000024.