AHA/ASA Guideline 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





Writing Group Members

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



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Slide Set Prepared By A Member of the Stroke Professional Educational Committee

Debbie Summers MSN, RN, ACNS-BC, CNRN, SCRN



Guidelines for the Prevention of Stroke in Patients with Stroke and TIA

- Yearly in US 690,000 adults experience an ischemic stroke (Heart Disease and Stroke Statistics 2013)
- Estimated 240,000 will experience a transient ischemic attack (TIA)
 - Individuals are high risk for future ischemic events
 - Annual risk for future ischemic stroke or TIA is about 3-4%
 - Statement provides comprehensive and timely evidence based recommendations on the prevention of future stroke among survivors of ischemic stroke or TIA



Definition of TIA and Ischemic Stroke Subtypes

- TIA and Stroke share pathophysiologic mechanisms
- Conventional clinical definitions focal neurological symptoms or signs lasting less than 24 hours has been defined as a TIA
- One-third of those are found to have an infarct on brain imaging



Recommendations of Brain Imaging

- A transient episode of focal neurological dysfunction without acute infarction
- A stroke (CNS infarct) is based on neuropathologic, neuroimaging, and/or clinical evidence of permanent injury
- The timing and type of a diagnostic workup for TIA/Stroke is beyond the scope of this statement. Although recommendations include all patients should have brain imaging (CT or MRI) to distinguish between ischemic or hemorrhagic events



Purpose of the Guideline

- Intended for all clinicians who manage secondary prevention for Stroke and TIA
- Writing committee conducted a comprehensive review and synthesis of mostly peer reviewed literature
- This slide set will highlight the new or substantially revised classes and level of evidence (LOE) recommendations since the 2011 publication on secondary prevention
 - Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack. Stroke. 2011;42:227-276.



Definition of Classes and Levels of Evidence Used in AHA/ASA Recommendations

SIZE OF TREATMENT EFFECT

LEVEL A Multiple populations evaluated*	CLASS I Benefit >>> Risk Procedure/Treatment SHOULD be performed/ administered Recommendation that procedure or treatment is useful/effective	CLASS IIa Benefit >> Risk Additional studies with focused objectives needed IT IS REASONABLE to per- form procedure/administer treatment ■ Recommendation in favor of treatment or procedure being useful/effective	CLASS IIb Benefit ≥ Risk Additional studies with broad objectives needed; additional registry data would be helpful Procedure/Treatment MAY BE CONSIDERED ■ Recommendation's usefulness/efficacy less well established	Harm w/o B or Har Recommenda procedure or tr not useful/effec	arm dure/ Treatment No Proven Benetit Benetit to Patients imful tion that eatment is
Data derived from multiple randomized clinical trials or meta-analyses	 Sufficient evidence from multiple randomized trials or meta-analyses 	 Some conflicting evidence from multiple randomized trials or meta-analyses 	 Greater conflicting evidence from multiple randomized trials or meta-analyses 	be harmful Sufficient evi multiple randon meta-analyses	and the second
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 	 Recommenda procedure or tr not useful/effec be harmful Evidence from randomized tria nonrandomized 	eatment is tive and may n single il or
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 	 Recommenda procedure or tri not useful/effect be harmful Only expert of studies, or stan 	eatment is tive and may pinion, case
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	COR III: Harm potentially harmful causes harm
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		should not be performed/ administered/ other is not useful/ beneficial/ effective	associated with excess morbid- ity/mortality should not be performed/ administered/ other



Risk Factor Control – Hypertension

- Most important intervention for secondary prevention of ischemic stroke – present in approximately 70% of ischemic stroke
- Hypertension defined as SBP ≥ 140 mm HG or a DBP ≥ 90 mm HG



Risk Factor Control – 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 mmHg systolic or ≥ 90 mmHg diastolic (Class I, LOE B)
- Initiation of therapy for patients with pressure <140 systolic and <90 diastolic is of uncertain benefit (Class IIb, LOE C)



Hypertension Recommendations		
2014 Recommendation	Revisions (2011)	
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 \geq 140 mmHg systolic or \geq 90 mmHg diastolic. (Class I, LOE B) Initiation of therapy for patients with pressure <140 systolic and <90 systolic is of uncertain benefit. (Class IIb, LOE 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 persons who have had an ischemic stroke or TIA and are beyond the first several days. (Class I, LOE 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 mmHg and a diastolic pressure <90 mmHg. (Class IIa, LOE B) For patients with a recent lacunar stroke, it might be reasonable to target a systolic BP of <130 mm Hg. (Class IIb, LOE B)	Revised guidance for target values	

	American American Heart Stroke Association Association.
Hypertension Recommendations	
2014 Recommendation	Revisions (2011)
Several lifestyle modifications have been associated with BP reduction are a reasonable part of a comprehensive therapy. Patients should be educated on 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. (Class IIb, LOE C)	Revised
The optimal drug regimen to achieve the recommended level of reductions is uncertain as direct comparisons between regimens are limited. The available data indicate that diuretics or the combination of diuretics and an ACEI are useful. (Class I, LOE A)	Unchanged
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 (e.g., extracranial cerebrovascular occlusive disease, renal impairment, cardiac disease, and diabetes). (Class IIa, LOE B)	Unchanged



SPARCL only trial to date

- For the outcome of major CV events, the 5-year absolute reduction in risk was 3.5% in favor of the high-dose statin group
- There was a modestly higher rate of elevated liver enzymes and a rise in CK in the atorvastatin arm, but no cases of hepatic failure
- There was an association of statin treatment with a higher incidence of hemorrhagic stroke, similarly found in Heart Protection Study (91% relatively risk)



- The benefit of aiming for a given LDL-C target has not been definitively established in a major randomized clinical trial (RCT)
- Achieving an LDL-C level of <70 mg/dL was related to a 28% reduction in risk of stroke without a significant rise in the risk of hemorrhagic stroke in a post-hoc analysis
- Also stroke and TIA patients with ≥50% reduction in LDL-C had a 35% reduction in combined risk of nonfatal and fatal stroke



- The Treat Stroke To Target (TST) evaluating effects of targeted LDL-C should provide better evidence on management
- The lipid sub-fractions have been shown to predict future vascular events with target LDL-C achieved
 - Elevated triglyceride associated with ischemic stroke and large-artery atherosclerotic stroke
 - Low HDL-C linked to risk of ischemic stroke
 - Elevated lipoprotein (a) related to incident stroke
- Currently the efficacy of agents used to treat lipid sub-fractions has not been established



- ACC/AHA Guideline on Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults released in 2013 moved away from reliance on cholesterol measurement to select individuals for therapy and guide drug dose
- Guidelines identify 4 "statin befit groups" for drug treatment to reduce risk of atherosclerotic cardiovascular disease (ASCVD)
- Recommendations for secondary prevention consistent with ACC/AHA guidelines



Dyslipidemia Recommendations		
2014 Recommendation	Revisions (2011)	
Statin therapy with intensive lipid-lowering effects is recommended to reduce risk of stroke and CV 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, LOE B)	Revised to be consistent with ACC/AHA cholesterol guideline. Use of niacin or gemfibrozil to raise HDL has been eliminated	
Statin therapy with intensive lipid-lowering effects is recommended to reduce risk of stroke and CV 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 <i>clinical</i> ASCVD (Class I, LOE C)	Added to be consistent with the 2013 ACC/AHA cholesterol Guideline but to indicate a lower LOE 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 Guideline which include lifestyle modification, dietary and medication recommendations. (Class I, LOE A)	Revised to be consistent with the 2013 ACC/AHA cholesterol Guideline. LDL-C targets, has been eliminated to be consistent with the 2013 ACC/AHA cholesterol guideline.	



Risk Factor Control – Disorders of Glucose Metabolism & Diabetes

- In the US, 11.3% of adults have diagnoses or occult diabetes mellitus (DM)
- DM associated with increased risk for first ischemic stroke (adjusted relative risk 1.5-3.7)
- Pre-diabetes encompasses impaired fasting glucose (IFG), impaired glucose tolerance (IGT) and intermediate elevations in HBA1c (5.7-6.4%)
 - Normal fasting glucose is < 100 mg/dL (5.6 mmol/L)
 - IFG is glucose of 100 mg/dl to 125 mg/dL (6.9 mmol/L)
 - IGT is diagnosed when the 2 hour plasma glucose is ≥ 140 to 199 mg/dL (7.8 mmol/L – 11.0 mmol/L) during a 75 gram oral glucose tolerance test



Risk Factor Control – Disorders of Glucose Metabolism & Diabetes

- No major trials for secondary prevention of stroke have specifically examined interventions for prediabetes or DM; management based on non-stroke or mixed population
- Lifestyle modifications more effective than metformin in the Diabetes Prevention Program trial
- All patients with DM at risk for vascular disease benefit from statin therapy regardless of pre-treatment LDL-C
- Target BP goal of < 140 mm Hg for SBP and < 80 mm Hg for DBP



Glucose Disorders Recommendations 2014 Recommendation Revisions (2011) Patients should be screened for diabetes with New Recommendation testing of fasting plasma glucose, HbA1c, 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, HbA1c may be more accurate than other screening tests in the immediate post-event period. (Class I, LOE C)

- 1. The optimal level of glucose control (i.e., HbA1c < 6% or 6.5%) should be for prevention of macrovascular disease
 - This may be modestly effective for preventing non-fatal coronary heart disease (CHD) events (MI) compared to current targets (HbA1c < 7%-8%)
- 2. Intensive treatment does not appear to reduce all-cause mortality or stroke risk and increases risk for severe hypoglycemia



Obesity Recommendations		
2014 Recommendation	Revisions (2011)	
All should be screened for obesity with measurement of BMI. (Class I, LOE C)	New Recommendation	
Given the demonstrated beneficial effects of weight loss on cardiovascular risk factors, weight loss may be considered in patients with a recent TIA or ischemic stroke and obesity. (Class IIb, LOE C)	New Recommendation	

- Obesity is defined as a BMI of ≥ 30 kg/m² and an established risk for CHD and premature mortality
- Recent epidemiologic studies suggest that the risk increases in a nearlinear fashion starting at a BMI of 20 kg/m² such that 1 kg/m² increase in BMI is associated with a 5% increase in risk for stroke



Metabolic Syndrome

- Components include: overweight, hypertriglyceridemia, low HDL-C, high BP, and hyperglycemia
- Recommendations
 - usefulness of screening patients for the metabolic syndrome after stroke is unknown. (Class IIb, LOE C)
 - If classified as having the metabolic syndrome, focus on counseling for life-style modification Class I, LOE C)
 - Preventive care is management of the components (particularly dyslipidemia and hypertension) (Class I, LOE A)



Physical Inactivity Recommendations		
2014 Recommendation	Revisions (2011)	
For those who are capable of engaging in physical activity, at least 3-4 sessions per week of moderate-vigorous intensity aerobic physical exercise is reasonable to reduce stroke risk factors. Session should last an average of 40 minutes. Moderate-intensity exercise is typically defined as sufficient to break a sweat or noticeably raise heart rate (e.g. walking briskly, using an exercise bicycle). Vigorous-intensity exercise includes activities such as jogging. (Class IIa, LOE C)	Further specification of levels of exercise recommended. Revision to be concordant with 2013 AHA/ACC Guideline on lifestyle management	
For patients who are able and willing to initiate increased physical activity, referral to a comprehensive, behaviorally oriented program is probably recommended. (Class IIa, LOE C)	New Recommendation	



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Nutrition Recommendations	
2014 Recommendation	Revisions (2011)
Reasonable to conduct a nutritional assessment looking for signs of over-nutrition or under-nutrition. (Class IIa, LOE C)	New Recommendation
Patients with signs of under-nutrition should be referred for individualized nutritional counseling. (Class I, LOE B)	New Recommendation
Routine supplementation with a single vitamin or combination of vitamins is not recommended. (Class III, LOE A)	New Recommendation
It is reasonable to recommend reducion of sodium intake to less than about 2.4 grams per day. Further reduction to less than 1.5 grams per day is also reasonable and is associated with even greater BP reduction. (Class IIa, LOE C)	New Recommendation
It is reasonable to counsel patients to follow a Mediterranean-type diet over a low-fat diet. The Mediterranean-type diet emphasizes vegetables, fruits, and whole grains and includes low-fat dairy products, poultry, fish, legumes, and nuts. It limits intake of sweets and red meats. (Class IIa, LOE C)	New Recommendation



Sleep Apnea Recommendations		
2014 Recommendation	Revisions (2011)	
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, LOE 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, LOE B)	New Recommendation	

- 1. Sleep apnea is present in approximately 1/2 to 3/4 of stroke or TIA patients
- 2. The American Academy of Sleep Medicine's Adult Obstructive Sleep Apnea Task Force recommends the use of polysomnography
- 3. Sleep apnea is associated with poor outcomes among stroke/TIA patients including: higher mortality, delirium, depressed mood and worse functional outcome

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Cigarette Smoking & Alcohol Consumption

- Newer research has extended concerns over smoking by showing that exposure to environmental tobacco smoke or passive ("second-hand") smoke also increases the risk of stroke
- Light to moderate alcohol consumption has been associated with a reduced risk of first-ever stroke (1/drink/day for women) and (2/drinks/day for men)
- Elevated stroke risk with heavier alcohol and greater risk of hemorrhagic stroke



Cigarette Smoking Recommendations

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
It is reasonable to advise patients after TIA or ischemic stroke to avoid environmental (passive) tobacco smoke	Class IIa; Level of Evidence B
Counseling, nicotine products, and oral smoking cessation medications are effective in helping smokers to quit	Class I; Level of Evidence A).



Alcohol Consumption Recommendations

	Class I; Level of Evidence C
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



- Three major trials have shown superiority of CEA plus medical therapy over medical therapy alone for symptomatic patients with high-grade stenosis (>70% angiographic stenosis) (ECST, NASCET, VACS)
- Role of CEA less clear with symptomatic stenoses in the 50% to 69%
- 5-year rate of any ipsilateral stroke was 15.7% patients surgically treated compared with 22.2% in medical treated patients.
 - CEA justification with patient selection criteria and a review of patient risk-benefit ratio – defined in guidelines



Carotid Disease Recommendations		
2014 Recommendation	Revisions (2011)	
Carotid artery stenting (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 ICA is reduced by more than 70% by noninvasive imaging or more than 50% by catheter-based imaging or non-invasive imaging with corroboration, and the anticipated rate of periprocedural stroke or death is less than 6%. (Class IIa, LOE 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 (i.e., over about 70 years), CEA may be associated with improved outcome compared with CAS, particularly when arterial anatomy is unfavorable for endovascular intervention. For younger patient, CAS is equivalent to or possibly better than CEA in terms of risk for periprocedural complication (i.e., stroke, MI, death) or long term risk for ipsilateral stroke. (Class IIa, LOE B)	New recommendation	



Carotid Disease Recommendations		
2014 Recommendation	Revisions (2011)	
CAS and CEA in the above settings should be performed by operators with established periprocedural stroke and mortality rates of less than 6% for symptomatic patients, similar to that observed in trials comparing CEA to medical therapy and more recent observational studies. (Class I, LOE B)	Class changed from Class IIa to Class I	
Routine, long term follow-up imaging of the extracranial carotid circulation with carotid duplex ultrasonography is not recommended. (Class III, LOE 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 mid-cervical carotid artery after institution of optimal medical therapy, the usefulness of EC/IC bypass is considered investigational. (Class IIb, LOE C)	New Recommendation	



Intracranial Atherosclerosis Recommendations

2014 Recommendation	Revisions (2011)
If stroke or TIA (within 30 days) due to severe stenosis (70-99%) of a major intracranial artery, the addition of clopidogrel 75 mg per day to aspirin for 90 days might be reasonable. (Class IIb, LOE B)	New Recommendation
If stroke or TIA due to 50-99% stenosis of a major intracranial artery, the data are insufficient to made a recommendation regarding the usefulness of clopidogrel alone, combination aspirin and dipyridamole, or cilostazol. (Class IIb, LOE C)	New Recommendation
If stroke or TIA due to 50-99% stenosis of a major intracranial artery, maintaining systolic BP below 140 mm Hg and high intensity statin therapy are recommended. (Class I, LOE B)	Consistent with 2013 ACC/AHA cholesterol guideline. Class changed from IIb to I



- Three trials demonstrated optimal timing of carotid revascularization after a non-disabling stroke
 - Median time from randomization to surgery was 2-14 days and /13 of perioperative stroke attributed to surgery occurred during this time
- In medically treated patients the stroke risk was greatest in the first 2 weeks and then declined within 2-3 years approaching the rate observed for asymptomatic patients
- The writing group recommends surgery within 2 weeks if no patient contraindication
 - A detailed review of the data on non disabling stroke patients with surgical treatment of ≥70% had a risk reduction of stroke or death within 30 day of 30% within first 2 weeks to 18% at 2-4 weeks and 11% at 4-12 weeks



- Early trials did not use embolic devices and either stenting or medical management were comparable.
- Embolic protection devices were adopted to reduce periprocedural stroke rates and the SAPPHIRE trial compared safety and efficacy of CAS with embolic device to CEA.
 - 30 day combined stroke, death, and MI rates were 9.9% for surgery versus 4.4% for stenting
 - One year stroke or death for surgery was 20.1% and 12% for stenting
 - Despite difference the conclusion was that CAS was non-inferior to CEA in the high risk patient cohort
- Morbidity and mortality in both treatment arms were high enough that there was question to benefit of either procedure compared to medical management in asymptomatic patients



- A more current comparison of CAS and CEA available is the Carotid Revascularization Endarterectomy versus Stent Trial (CREST). The hazard ratio for the primary outcome; CAS compared with CEA
 - Rose from 0.6 (95% CI, 0.31-1.18) for patients younger than 65 years to 1.08 (95% CI, 0.65-1.78) for patients 65-74 years to 1.63 (95% CI, 0.99-2.69) for patients age 75 years or older
 - Risk of MI did not increase with age in either treatment group.
 - The age at which the hazard ratio was 1.0 was about 70 years for the primary outcomes and 64 years for stroke
 - There was no difference between CAS and CEA in periprocedural events amongst men, but there was a non-statistically significant trend towards fewer events with women and CEA
- Cochrane reviews in 2012 showed similar interaction between age and treatment effect



Extracranial Atherosclerosis Recommendations	
2014 Recommendation	Revisions (2011)
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 more than 70% by noninvasive imaging or more than 50% by catheter-based imaging or non-invasive imaging with corroboration, and the anticipated rate of periprocedural stroke or death is less than 6%. (Class IIa, LOE B)	Revised Recommendation,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 (i.e., over about 70 years), CEA may be associated with improved outcome compared with CAS, particularly when arterial anatomy is unfavorable for endovascular intervention. For younger patient, CAS is equivalent to CEA in terms of risk for periprocedural complication (i.e., stroke, MI, death) or long term risk for ipsilateral stroke. (Class IIa, LOE B)	New Recommendation



Extracranial Atherosclerosis Recommendations	
2014 Recommendation	Revisions (2011)
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, LOE B)	Revised Recommendation
CAS and CEA in the above settings should be performed by operators with established peri-procedural stroke and mortality rates of less than 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
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



Extracranial Atherosclerosis Recommendations2014 RecommendationRevisions (2011)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 mid-cervical
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 Recommendations	
2014 Recommendation	Revisions (2011)
If stroke or TIA due 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, LOE B)	New Recommendation
If stroke or TIA due 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 on an antithrombotic agent at the time of the stroke or TIA. (Class III, LOE B)	New Recommendation
If stroke or TIA due to severe stenosis (70-99%) of a major intracranial artery, the usefulness of angioplasty alone or placement of stents other than Wingspan is unknown and is considered investigational. (Class IIb, LOE C)	Change from 50% to 99% stenosis to 70% to 99% stenosis Rewording to mention Wingspan device used in SAMMPRIS



Intracranial Atherosclerosis Recommendations	
2014 Recommendation	Revisions (2011)
Patients with severe stenosis (70-99%) of a major intracranial artery and recurrent TIA or stroke after institution of aspirin and clopidogrel and achievement of systolic BP < 140 mmHg and high-intensity statin therapy, the usefulness of angioplasty alone or placement of Wingspan or other stents is unknown and is considered investigational. (Class IIb, LOE C)	New Recommendation
Patients with severe stenosis (70-99%) of a major intracranial artery and actively progressing symptoms after institution of aspirin and clopidogrel, the usefulness of angioplasty alone or placement of Wingspan or other stents is unknown and is considered investigational. (Class IIb, LOE C)	New Recommendation



Atrial Fibrillation

- Affects about 2.7 million Americans
- Increasing prevalence with age; leading heart arrhythmia in the elderly
- In the US this arrhythmia is responsible for > 70,000 ischemic strokes/yearly (about 10%-12% of all ischemic strokes)
- About 10% of patients with acute ischemic stroke or TIA will have new AF detected during their hospitalization.
- An additional 11% may be found to have AF (if tested) within 30 days of discharge by continuous ECG monitoring.



Atrial Fibrillation Recommendations	
2014 Recommendation	Revisions (2011)
For patients who have experienced an acute ischemic stroke or TIA with no other apparent etiology, prolonged rhythm monitoring (approximately 30 days) for atrial fibrillation is reasonable within six months of the index event. (Class IIa, LOE C)	New Recommendation
Vitamin K agonist (VKA) therapy (Class I, LOE A), apixaban (Class I, LOE A), and dabigatran (Class I, LOE B) are all indicated for the prevention of first and recurrent stroke in patients with nonvalvular AF, 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.	New recommendations regarding apixaban and dabigatran New text regarding choice of agent.



Atrial Fibrillation Recommendations	
2014 Recommendation	Revisions (2011)
Rivaroxaban is reasonable for the prevention of first and recurrent stroke in patients with nonvalvular AF. (Class IIa, LOE B)	New Recommendation
The combination of oral anticoagulation (i.e., 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, LOE C)	New Recommendation
The addition of clopidogrel to aspirin therapy, compared with aspirin therapy alone, is of uncertain net benefit for patients with a contraindication to VKA therapy. (Class IIb, LOE B)	Reworded from the 2011 text 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, LOE B)	New Recommendation



Atrial Fibrillation Recommendations	
2014 Recommendation	Revisions (2011)
In the presence of high risk for hemorrhagic conversion (i.e., 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, LOE B)	New Recommendation
The usefulness is uncertain for closure of the left atrial appendage with the WATCHMAN device in patients with ischemic stroke or TIA and atrial fibrillation. (Class IIb, LOE B)	New Recommendation



Acute MI and LV Thrombus

- Patients with large anterior MI associated with an LV ejection fraction <40% and anteroapical wall motion abnormalities are at an increased risk for developing LV mural thrombus (stasis of blood in the ventricle and endocardial injury with associated inflammation)
- No studies have examined the efficacy and safety of the newer antithrombotic agents(dabigitran, rivoraxaban, apixaban or fondaparinux) for prevention of LV thrombus or stroke in patients with acute MI.



MI and Thrombus Recommendations	
2014 Recommendation	Revisions (2011)
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-elevation MI without demonstrable left ventricular mural thrombus formation but with anterior apical akinesis or dyskinesis identified by echocardiography or other imaging modality. (Class IIb, LOE C)	New Recommendation
In patients with ischemic stroke or TIA in the setting of acute MI complicated by left ventricular mural thrombus formation and/or anterior or apical wall motion abnormalities with a left ventricular ejection fraction < 40% who are intolerant to VKA therapy due to non-hemorrhagic adverse events, treatment with 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, LOE C)	New Recommendation



Cardiomyopathy

- Patients with ischemic or non-ischemic dilated cardiomyopathy are at an increased risk for stroke.
- About 10% of patients with ischemic stroke have an LV ejection fraction of < 30%
- A meta-analysis of 4 trials (n=3681) demonstrated that warfarin was associated with a 41% RRR of stroke (pooled ratio 0.59; 95% CI, 0.41- 0.85; p=0.004)
- There is no available data of the use of the newer anticoagulant agents for prevention of stroke in patients with cardiomyopathy or mechanical assist devices.



Cardiomyopathy Recommendations	
2014 Recommendation	Revisions (2011)
In patients with ischemic stroke or TIA in sinus rhythm that have left atrial or left ventricular thrombus demonstrated by echocardiography or another imaging modality, anticoagulant therapy with a vitamin K antagonist is recommended for at least three months. (Class I, LOE 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 (e.g. active gastrointestinal bleeding). (Class IIa, LOE 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 due to non-hemorrhagic adverse events, the effectiveness of treatment with dabigatran, rivaroxaban, or apixaban is uncertain compared with VKA therapy for prevention of recurrent stroke. (Class IIb, LOE C)	New Recommendation



Valvular Heart Disease Recommendations	
2014 Recommendation	Revisions (2011)
For patients who have rheumatic mitral valve disease and AF, long-term vitamin K antagonist (VKA) therapy with an INR target range of 2.5 (range 2.0 to 3.0) is recommended. (Class I, LOE A)	Mention of patients without AF removed. Class changed from Ila to I
For patients who have rheumatic mitral valve disease without AF or another likely cause for their symptoms (e.g., carotid stenosis), long-term VKA therapy with an INR target range of 2.5 (range 2.0 to 3.0) may be considered over antiplatelet therapy. (Class IIb, LOE C)	New recommendation focuses on patients without AF
For patients with rheumatic mitral valve disease who have an ischemic stroke or TIA while on adequate VKA therapy, addition of aspirin might be considered. (Class IIb, LOE C)	New Recommendation



Valvular Heart Disease

- The magnitude of risk for brain embolism from a diseased heart valve depends on the nature and severity of the disease.
- Persons at high risk may be suitable for anticoagulation, while others may be treated with antiplatelets or no therapy.
- Secondary prevention of stroke in the setting of mitral stenosis, mitral valve regurgitation and mitral valve prolapse, mitral annular calcification and aortic valve disease are addressed in this guideline.



Valvular Heart Disease Recommendations	
2014 Recommendation	Revisions (2011)
For patients with ischemic stroke or TIA native aortic or non- rheumatic mitral valve disease who do not have AF or another indication for anticoagulation, antiplatelet therapy is recommended. (Class I, LOE C)	Class changed from IIb to I
For patients with mitral annular calcification who do not have AF or another indication for anticoagulation, antiplatelet therapy is recommended as it would be without the mitral annual calcification. (Class I, LOE C)	Class changed from IIb to I
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 MVP. (Class I, LOE C)	Change in wording Class changed from IIb to I



Prosthetic Heart Valves (Mechanical and Bioprosthetic)

- All patients with mechanical heart valves are at an increased risk for thromboembolism.
 - The risk can be reduced with the use of oral vitamin K antagonists.
 - INR intensity will depend on location of the valve, type of mechanical valve, and other factors that increase the risk for embolism.
- Bioprosthetic valves are associated with a lower rate of thromboembolism than mechanical valves.
 - The risk is not uniform and is affected by specific patient features.
 - These patients who have had a thromboembolic stroke after placement of a bioprosthetic valve may be at risk for recurrence.



Prosthetic HV Recommendations	
2014 Recommendation	Revisions (2011)
For patients with a mechanical aortic valve and a history of ischemic stroke or TIA prior to its insertion, VKA therapy is recommended with an INR target of 2.5 (range 2.0 to 3.0). (Class I, LOE B)	Modified to focus on aortic valve
For patients with a mechanical mitral valve and a history of ischemic stroke or TIA prior to its insertion, VKA therapy is recommended with an INR target of 3.0 (range 2.5 to 3.5). (Class I, LOE C)	New recommendation focuses on mitral valve 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 prior to its insertion and who are at low risk for bleeding, addition of aspirin 75mg to 100 mg daily to VKA therapy is recommended. (Class I, LOE B)	New Recommendation



Prosthetic HV Recommendations	
2014 Recommendation	Revisions (2011)
For patients with a bioprosthetic aortic or mitral valve, a history of ischemic stroke or TIA prior to its insertion and no other indication for anticoagulation therapy beyond 3-6 months from the valve placement, long-term therapy with aspirin 75mg to 100 mg daily is recommended in preference to long-term anticoagulation. (Class I, LOE C)	New recommendation specifically addresses timing of TIA or stroke in relation to valve replacement and recommends aspirin over anti-coagulation
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 to 3.0) may be considered. (Class IIb, LOE C) (Modified recommendation)	Wording is revised to specify that VKA therapy may be warranted when TIA or stroke events occur after valve replacement.



Antiplatelet Therapy for Noncardioembolic Stroke or TIA

- Four antiplatelet agents have been approved by the FDA for prevention of vascular events among patients with ischemic stroke or TIA.
 - Aspirin, combination aspirin/dipyridamole, clopidogrel or ticlopidine.
 - On average, these agents reduce the RR of stroke, MI or death by about 22%
 - There are important differences between these that have direct implications for therapeutic selection



Antiplatelet Therapy Recommendations	
2014 Recommendation	Revisions (2011)
The combination of aspirin and clopidogrel might be considered for initiation within 24 hours of a minor ischemic stroke or TIA and continuation for 90 days. (Class IIb, LOE 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, LOE C) Unstable angina and coronary artery stenting represent special circumstances where management may warrant DAPT/VKA therapy.	New Recommendation



Treatment for Stroke Patients with other Specific Conditions

Aortic Arch Atheroma Patent Foramen Ovale Hyperhomocysteinemia Hypercoagulable States Antiphospholipid Antibodies Sickle Cell Disease Pregnancy and Breast Feeding



Aortic Arch Atheroma Recommendations	
2014 Recommendation	Revisions (2011)
For patients with an ischemic stroke or TIA and evidence of aortic arch atheroma, antiplatelet therapy is recommended. (Class I, LOE A)	New Recommendation
For patients with an ischemic stroke or TIA and evidence of aortic arch atheroma, statin therapy is recommended. (Class I, LOE 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, LOE C)	New Recommendation
Surgical endarterectomy of aortic arch plaque for the purposes of secondary stroke prevention is not recommended. (Class III, LOE C)	New Recommendation



Patent Foramen Ovale Recommendations	
2014 Recommendation	Revisions (2011)
For patients with an ischemic stroke or TIA and a PFO who are not on anticoagulation therapy, antiplatelet therapy is recommended. (Class I, LOE 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, LOE A). When anticoagulation is contraindicated, an inferior vena cava filter is reasonable (Class IIa, LOE C).	New Recommendations
For patients with a cryptogenic ischemic stroke or TIA and a	Revised
PFO without evidence for DVT, available data does not support a benefit for PFO closure. (Class III, LOE A)	Recommendation
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, LOE C)	New Recommendation



Homocysteinemia Recommendations	
2014 Recommendation	Revisions (2011)
Routine screening for hyperhomocysteinemia among patients with a recent ischemic stroke or TIA is not indicated. (Class III, LOE C)	New Recommendation

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Hypercoagulation Recommendations	
2014 Recommendation	Revisions (2011)
The usefulness of screening for thrombophilic states in patients with ischemic stroke or TIA is unknown. (Class IIb, LOE 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, LOE C)	Substantial rewording Class changed from Ila to Ilb
Antiplatelet therapy is recommended in patients who are found to have abnormal findings on coagulation testing after an initial ischemic stroke or TIA who are not placed on anticoagulation. (Class I, LOE A)	Represents a more firm recommendation for antiplatelet therapy in the circumstance described

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Antiphospholipid Antibodies Recommendations	
2014 Recommendation	Revisions (2011)
Routine testing for anti-phospholipid antibodies is not recommended for patients who have no other manifestations of the anti-phospholipid antibody syndrome and who have an alternative explanation for their ischemic event, such as atherosclerosis, carotid stenosis, or AF. (Class III, LOE 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, LOE 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, anticoagulant therapy might be considered depending on the perception of risk for recurrent thrombotic events and bleeding. (Class IIb, LOE C)	Adds detailed guidance for anticoagulation in the APAS and changes class from IIa to IIb
For patients who meet the criteria for the antiphospholipid antibody syndrome but are not placed on anticoagulation, antiplatelet therapy is indicated (Class I, LOE A).	New Recommendation



Sickle Cell Disease Recommendations	
2014 Recommendation	Revisions (2011)
For patients with sickle cell disease and prior ischemic stroke or TIA, chronic blood transfusions to reduce hemoglobin S to <30% of total hemoglobin is recommended. (Class I, LOE B)	Class changed from Ila to I



Pregnancy Recommendations	
2014 Recommendation	Revisions (2011)
 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 h in doses adjusted to keep the mid-interval aPTT at least twice control or to maintain an anti-Xa heparin level of 0.35 to 0.70 units/mL or c. UFH or LMWH (as above) until the 13th week, followed by substitution of a vitamin K antagonist until close to delivery when UFH or LMWH is resumed. (Class IIa, LOE C) 	More detail is provided which is intended to be consistent with the recent statement by the American College of Chest Physicians



Pregnancy Recommendations	
2014 Recommendation	Revisions (2011)
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 \geq 24 h prior to induction of labor or cesarean section. (Class IIa, LOE C)	
In the presence of a low risk situation where antiplatelet therapy would be the treatment recommendation outside of pregnancy, low dose aspirin, UFH or LMWH, or no treatment may be considered during the first trimester of pregnancy depending on the clinical situation (Class IIb, LOE C)	New Recommendation



Breast Feeding Recommendations	
2014 Recommendation	Revisions (2011)
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, LOE C)	New Recommendation
In the presence of a low risk situation where antiplatelet therapy would be the treatment recommendation outside of pregnancy, low dose aspirin use may be considered. (Class IIb, LOE C)	New Recommendation



Anticoagulation after Intracranial Hemorrhage

- The decision to restart antithrombotic therapy is 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 infarctions (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, and antiplatelet agent may be considered for prevention if ischemic stroke. (Class IIb, LOE B)
- For patients who require resumption or initiation of anticoagulation after an acute ICH, SAH, or SDH, the optimal timing is uncertain. For most patients, however, it might be reasonable to wait <a> 1 week. (Class IIb, LOE B)
- 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, LOE C)



SPECIAL APPROACHES TO IMPLEMENTING GUIDELINES AND THEIR USE IN HIGH-RISK POPULATIONS



Special Populations at High Risk

- Special approaches to reduce the burden of recurrent stroke in high-risk populations defined by older age, socioeconomic position, and ethnicity
 - Many trials do not include sufficient patients > 80
 - Socioeconomically disadvantaged because of limited access to care
- Death rate has declined by 11% in the US, not all groups have benefited equally, examples include
 - African Americans were less likely to receive smoking cessation counseling
 - Black patients had lower odds relative to white patients in receiving IV thrombolysis
 - Studies have suggested worse post stroke outcomes in women



Special Populations at High Risk

- Expert panels show the need for a multilevel approach to include the patient, provider, and organization delivery health care
- The NINDS Stroke Disparities Planning Panel, convened in June 2002, developed strategies and program goals that include establishing data collection systems and exploring effective community impact programs and instruments in stroke prevention
- With the increased attention to new models of care delivery designed to address the needs and costs of the highest risk, medically ill populations, Accountable Care Organizations may find new solutions to improve secondary prevention of cardiovascular disease and stroke



Special Populations at High Risk

- Expanding the medical home to include a neighborhood of specialists may help foster greater collaboration between primary and specialty care and make progress toward the goal of eliminating existing disparities
- Utilizing data from quality improvement registries to identify gaps in guideline-based treatment and design targeted interventions to address those gaps reflect a likely future evolution in the use of continuous quality improvement strategies for secondary prevention.



High Risk Patient Implementation Recommendations

2014 Recommendation	Revisions (2011)
Monitoring achievement of nationally-accepted, evidence based guidelines on a population based level is recommended as a basis for identifying areas to target for quality improvement interventions (Class I, LOE C)	New Recommendation
Voluntary hospital-based programs for quality monitoring and improvement are recommended to improve adherence with nationally-accepted, evidence-based guidelines for secondary stroke prevention. (Class I, LOE C)	New Recommendation



Guideline Implementation Strategies

- National consensus guidelines are published by many professional societies and governmental agencies to increase healthcare providers' awareness of evidence-based approaches to disease management.
- This method of knowledge dissemination assumes an increased awareness of guideline content and can lead to substantial changes in physician behavior and ultimately patient behavior and health outcomes.
- Unfortunately experience suggests otherwise.
 - Compliance with secondary stroke and CAD prevention strategies based on guideline dissemination did not produce dramatic improvements in the 1990s to 2000s.
 - Specific examples include: control of BP, hypercholesterolemia.
- Guideline dissemination <u>must</u> be coupled with effective dissemination strategies to change healthcare provider practice.
- Implementation strategies include (to improve quality of practice): enabling strategies (office reminders), reinforcing strategies (feedback – Example: the AHA Get With the Guidelines program), and predisposing strategies (practice guidelines).