

**QUALITY INDICATORS**  
**FOR THE MANAGEMENT OF STROKE AND ATRIAL FIBRILLATION**  
**FOR VULNERABLE OLDER PERSONS**

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## **INTRODUCTION**

Stroke affects 6.7% of adults over age 65 who are community dwelling(1) and 16.5% of those in nursing homes(2). An important risk factor for stroke is atrial fibrillation (AF). The proportion of strokes attributable to AF is 7.3% in persons 60 to 69 years old, 16.5% in persons 70 to 79 years old, and 31% in persons 80 to 89 years old(3), which reflects the increasing significance of AF as a contributor to stroke with increasing age. The present effort identifies potential quality indicators for stroke and AF and reviews the evidence pertaining to these indicators, emphasizing evidence germane to vulnerable elderly individuals.

## **METHODS**

The methods for developing these quality indicators, including literature review and expert panel consideration, are detailed in a preceding paper (4). For stroke, the literature review began with citations identified through the author's participation in a prior RAND effort on quality indicators for stroke in adult men.\* The structured literature review identified 42,763 titles, from which abstracts and articles were identified that were relevant to this report. Based on the literature and the authors' expertise, 29 potential quality indicators were proposed.

## **RESULTS**

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\* Golomb BA "Stroke". In: Quality of Care for Cardiopulmonary Conditions: A Review of the Literature and Quality Indicators. Eve A. Kerr, Steven M. Asch, Eric G. Hamilton, and Elizabeth A. McGlynn (eds.). MR-1282-AHRQ, 2000

Of the 29 potential quality indicators, 12 were judged valid by the expert panel process (see Quality Indicator table), 2 were merged with accepted indicators and 15 were not accepted. Three of the accepted indicators were merged into one for this report. The literature reviews that support each of the indicators judged to be valid by the expert panel process are summarized below.

## **Prevention and Screening**

### **Carotid Endarterectomy**

#### **Quality Indicator #1**

**IF** a male vulnerable elder has carotid artery symptoms, and is diagnosed with a transient ischemic attack (TIA) or nondisabling stroke, and has had carotid imaging documenting > 70% carotid stenosis on the side ipsilateral to the hemisphere producing the symptoms, and the medical record does not document that no facility is available with less than six percent 30-day morbidity and mortality, **THEN** he should receive referral for evaluation for carotid endarterectomy (CEA) within four weeks of the diagnostic study or event, whichever is later, **BECAUSE** patients with this profile may receive benefit that exceeds surgical risk from CEA if excellent surgical morbidity and mortality rates can be attained.

#### **Quality Indicator #2**

**IF** a male vulnerable elder has carotid artery symptoms and is diagnosed with a TIA or nondisabling stroke, and the medical record does not document that the patient is not a candidate for carotid surgery, **THEN** a carotid artery imaging study should be performed

within four weeks **BECAUSE** such patients who are found to have over 70% stenosis on carotid artery imaging may benefit from CEA.

### **Quality Indicator #3**

**IF** for a vulnerable elder the combined risk of surgery (patient characteristics and hospital or surgeon experience) is 10% or greater, **THEN** CEA should not be performed **BECAUSE** the surgical risk of CEA exceeds the expected benefit in this setting.

**Supporting evidence:** Benefit from CEA has been shown to exceed risk in male patients with high-grade stenosis and ipsilateral carotid artery symptoms and low surgical risk (less than 6%); and in asymptomatic patients with lower surgical risk (less than 3%)(5-7). Advancing age was not associated with an increase in the perioperative complication rate after correction for clinical severity of initial symptoms, in a RAND study of CEA(8).

Reported benefits for women are substantially less than for men, and benefits of CEA have not been demonstrated to exceed risks for women. In the ACAS study, the absolute and relative 5-year risk reductions were 8% and 66%, respectively, for men; while for women, they were 1.4% and 17%(7, 9).

Hospital morbidity and mortality rates for male subjects depend on subject selection, and risks of surgery may be higher and achieved benefits lower in vulnerable elderly, due to lower healthy life expectancy (although very healthy elderly may do well with such surgery). Thus, use of hospital rate based on younger populations may not accurately reflect risks for vulnerable elderly. A study that examined carotid surgery in

octogenarians concluded that “results comparable to those of younger patients can be anticipated,” as perioperative acute MI death rate in the oldest group did not significantly differ from that in younger patients. However, in this study, only relatively healthy octogenarians were brought to surgery.(10) Moreover, among octogenarians, “a high ... mortality rate was apparent,” implying a worsening in the risk-benefit ratio. The long-term risk of stroke and the degree of life (or quality-of-life) enhancement after CEA in this population remain to be determined.(11)

In addition, achieved outcomes have been worse than reported outcomes for hospitals with good reported death and disability rates, possibly due in part to patient selection factors during trials. The perioperative mortality of Medicare patients following CEA was higher than that reported in trials, even in institutions that participated in the randomized studies(12). This finding raises concern that results of clinical trials may lead to unrealistic optimism regarding benefits of CEA.

## **Prevention and Screening**

### **Anticoagulation for Atrial Fibrillation**

#### **Quality Indicator #4:**

**IF** a vulnerable elder has atrial fibrillation for more than 48 –hours’ duration and has any

"high risk" condition:

- impaired left ventricular (LV) function
- female age > 76
- hypertension or systolic blood pressure (BP) > 160 mmHg

- prior ischemic stroke, transient ischemic attack (TIA), or systemic embolism

**THEN** he or she should be offered oral anticoagulant therapy, or antiplatelet therapy if the medical record documents a reason not to give anticoagulant therapy **BECAUSE** such therapy may reduce the risk of stroke.

**Supporting evidence:** In male patients under age 75 with AF, direct evidence indicates that aspirin reduces stroke outcomes compared to placebo, and warfarin improves stroke outcomes compared to aspirin, except in “low-risk” populations (those without any of several defined “high-risk” conditions), for whom risk of stroke may be low and no benefit of warfarin over aspirin (and of aspirin over placebo) has been established. In two of three individual RCTs, anticoagulants reduced stroke significantly more than did aspirin (e.g., 47% risk reduction versus aspirin, 95% CI = 28% to 61%); and 33% reduction versus aspirin (statistics not separately given for stroke) (13-15), although these studies did not select for elderly patients.

A meta-analysis based on pooled data from three RCTs (EAFT, SPAF II, AFASAK) found a statistically significant 25% reduction in risk of stroke with aspirin compared with placebo (range = 14% to 44%), although aspirin reduced stroke risk less than did warfarin.(13)

However, the only data specific to patients over age 75 with AF showed that aspirin did not clearly improve outcomes when compared to placebo (in a non-prespecified analysis).(16, 17) Similarly, warfarin did not clearly improve outcomes when compared to aspirin. Primary event rates (ischemic stroke and systemic embolism)

were assessed in two parallel randomized trials that involved 715 patients age 75 or younger and 385 patients age over 75; among those over 75, the primary event rate per year was not significantly lower with warfarin (3.6% versus 4.8%,  $p = 0.39$ ) and in this older group, the rate of all stroke with residual deficit (ischemic or hemorrhagic) was not reduced in the warfarin group (4.6% per year versus 4.3% per year in the aspirin group)(18). Increased bleeding risk with anticoagulants in older adults has been reported in several studies(19-21) and may contribute to less favorable outcomes.

In addition, effects of aspirin are gender dependent. Observational studies and randomized controlled trials have reported that risk ratios for stroke, vascular death, and overall mortality with aspirin exceeded 1.0 for women, even under conditions in which they were significantly less than 1.0 for men(22-30).

## **Quality Indicator #5**

### **Stroke Imaging before Anticoagulation**

**IF** a vulnerable elder has a presumed stroke, **THEN** a CT or MRI of the head should be obtained prior to initiation or continuation of thrombolytic treatment, anticoagulant therapy, or antiplatelet therapy **BECAUSE** identification of a hemorrhagic stroke is a relative or absolute contraindication to these treatments.

**Supporting Evidence:** Despite absence of direct data and published opinion against routine imaging(31), strong consensus and indirect rationale support the use of CT or MRI imaging of the head in patients with presumed stroke, prior to initiation of

thrombolytic, antiplatelet, or anticoagulant therapy to prevent increased death and disability. These therapies may extend existing hemorrhagic stroke or promote new hemorrhagic stroke and several (although not all) studies have found older adults to be at heightened risk of bleed or of life-threatening or fatal complications with such therapies(19-21, 32, 33).

### **Quality Indicator #6**

#### **Monitoring Warfarin Therapy**

**IF** a vulnerable elder is taking warfarin for AF, **THEN** an International Normalized Ratio (INR) should be checked within 4 days of the first dose and at least every 6 weeks **BECAUSE** INRs outside the target therapeutic range are associated with increased risk for stroke (low INR), and increased risk for hemorrhagic complications (high INR).

**Supporting evidence:** The risk for hemorrhagic complications is increased with warfarin; with increased INR among those taking warfarin; and particularly with INR over 3(32, 34-37). Thus, regular monitoring of individuals taking anticoagulants is desirable to maintain the INR within the 2 to 3 range. In a study of patients at increased risk for thromboembolic complications (not including AF patients)(38), a U-shaped relationship between INR and complications was seen, and no additional benefit was conferred with an INR greater than 3.

It is important to note that older adults may be at increased risk of such bleeding complications(34), as are those taking multiple medications(35). Medications that alter the risk of bleeding with coumadin are shown in Table 1(36, 39).

## **Quality Indicator #7**

### **Antiplatelet Therapy for Acute Stroke**

**IF** a vulnerable elder is diagnosed with acute atherothrombotic ischemic stroke or with a TIA, **THEN** antiplatelet treatment should be offered within 48 hours following the stroke or TIA, unless the patient is already receiving anticoagulant treatment **BECAUSE** antiplatelet treatment reduces risk of combined nonfatal and fatal vascular events in those with prior atherothrombotic cerebrovascular events.

**Supporting evidence:** Direct evidence from clinical trials and meta-analysis demonstrates that antiplatelet therapy (usually aspirin) decreases the risk of recurrent vascular events. However, data on patients over age 80 are lacking. The 1994 Antiplatelet Trialists Collaboration overview analyzed results of randomized trials of antiplatelet therapy among more than 54,000 high-risk patients with prior evidence of cardiovascular disease, including prior MI, stroke, TIA, unstable angina, stable angina, revascularization surgery, angioplasty, AF, valvular disease, and peripheral vascular disease(40). Aspirin therapy reduced the risk of subsequent vascular events (nonfatal MI, plus nonfatal stroke, plus vascular death) by about one-fourth. Significant effects were also observed among middle-aged as well as older patients, and in both men and women, hypertensive and normotensive patients, and diabetics and nondiabetics. The reduction translated to avoidance of about 40 vascular events per 1,000 patients with prior MI, stroke, or TIA treated for 2 to 3 years.

Medium-dose aspirin was the most widely tested regimen in secondary prevention (75–325 mg/d). Overall analyses showed no evidence that higher doses of aspirin or any other antiplatelet regimen were more effective than aspirin in this dose range(41).

### **Quality Indicator #8**

#### **Smoking Cessation Counseling**

**IF** a vulnerable elder has a TIA or stroke, **THEN** the medical record should document that smoking status was assessed AND that smokers were counseled to stop smoking **BECAUSE** smoking is a documented risk factor for stroke among those under age 75, and ex-smokers have a lower risk for stroke than do current smokers.

**Supporting evidence:** A meta-analysis that pooled 18 separate relative-risk estimates found that current smokers had an overall relative risk of stroke of 1.5 (1.4 to 1.6), whereas ex-smokers retained an increased relative risk, of 1.17 (1.05 to 1.30)(42). Among those over age 75, smoking is not clearly associated with increased risk for stroke or coronary artery disease risk, nor is smoking cessation after age 75 clearly related to reduction in risk. The relationship of smoking to stroke became both clinically and statistically nonsignificant in those over age 75 in this meta-analysis (age < 55: RR = 2.94[95% CI = 2.40-3.59]; age 55 to 74: RR = 1.75[95% CI = 1.56 to 1.97]; age > 75: RR = 1.11[95% CI = 0.96 to 1.28](42). The authors noted that while smoking was consistently positively related to stroke in large studies among those under age 75, several

large studies found no relationship or an inverse relationship between smoking and stroke in those over age 75(43). In this meta-analysis, neither smoking nor smoking cessation had a significant impact on stroke risk in the over-75 population.

### **Quality Indicator #9**

#### **Thrombolytic Therapy**

**IF** a vulnerable elder is started on thrombolytic therapy for a stroke, **THEN** all of the following should be true:

- a head CT or MRI should precede initiation of thrombolytic therapy;
- sulcal effacement, mass effect, edema, or possible hemorrhage should not be present on neuroimaging;
- time from symptom onset to initiation of thrombolytic therapy should be documented in the medical record and should not exceed 3 hours;
- absence of absolute contraindications to thrombolysis should be documented in the medical record;
- tissue plasminogen activator (tPA) should be used; AND
- National Institute of Neurological Disorders and Stroke (NINDS) exclusion criteria should not be present

**BECAUSE** thrombolysis has reduced the risk of combined death and disability only if these conditions have been met.

**Supporting Evidence:** Randomized clinical trial data have reported mixed results on the use of thrombolytic therapy for acute stroke patients. The Cochrane Stroke Review Group examined all completed and unconfounded, truly randomized or quasi-randomized trials comparing thrombolytic agents with control started within 14 days of the stroke onset in patients with definite ischemic stroke(44). Outcomes assessed included death and dependency at the end of the trial follow-up periods; all deaths during the scheduled treatment and follow-up period; symptomatic intracranial hemorrhage; death due to intracranial hemorrhage; and, in patients randomized within 3 hours of the stroke, data on death or dependency and case fatality during follow-up. Twelve trials with 3,435 patients were included. There was an excess of deaths within the first two weeks (OR = 1.99; 95% CI = 1.56 to 2.53) and during follow-up (OR = 1.36; 95% CI = 2.73 to 4.80), which was the main cause of the excess deaths. Thrombolysis and aspirin in a factorial randomized design showed a definite excess of deaths, but only in patients randomized to thrombolysis plus aspirin; some variation in death rates in other trials may have been due to variation in use of aspirin and heparin, which was not randomly allocated. Despite the excess of deaths, the combined outcome of death or dependency was reduced in the thrombolytic group at the end of follow-up (OR = 0.75; 95% CI = 0.63 to 0.88)(44).

Others also view the evidence favoring thrombolysis as equivocal. The 1997 AHA Prevention Conference IV: Prevention and Rehabilitation of Stroke, Executive Summary, refers to the five recent clinical trials of thrombolytic therapy as “conflicting”(45). A recent editorial in the special Stroke issue of the Journal of the American Medical Association refers to published recommendations for the use of

thrombolytic treatments as “premature”(46). Moreover, a study in the same issue found that the majority of sampled physicians (including emergency physicians, neurologists, and general radiologists) did not achieve a level of sensitivity for identification of intracerebral hemorrhage sufficient to permit safe selection of candidates for thrombolytic therapy(47), consistent with the stated concerns of the ECASS study group(48).

Because of the demonstrated harm that may occur with thrombolysis outside restricted conditions, if thrombolytic treatment is undertaken, the above guidelines should be employed, reflecting those conditions in which thrombolytic therapy may be associated with benefit exceeding risk.

### **Quality Indicator #10**

#### **Admission to Stroke Unit**

**IF** a vulnerable elder is admitted to the hospital with a diagnosis of acute ischemic or hemorrhagic stroke, **THEN** he or she should be admitted to a specialized acute or combined acute and rehabilitative stroke unit, or transferred to a specialized stroke unit if such a unit is available in the hospital **BECAUSE** admission to stroke units improves multiple outcomes, including length of hospital stay, functional status, quality of life, need for institutionalization, and risk for mortality.

**Supporting Evidence:** A systematic review of randomized trials in the Stroke Unit Trialists’ Collaboration and the Cochrane Review confirms the benefits of stroke unit (SU) admission(49-51). These trials compared the effect of organized SU care with that

of general medical ward (GMW) care in reducing death, dependency, and need for institutionalization in patients hospitalized with acute stroke. (Dependency was defined as need for physical assistance with transfers, feeding, dressing or toileting.

Institutionalization included nursing home placement, residential care placement, or hospitalization at the end of the rehabilitation period.) The review included randomized controlled trials of dedicated SUs, mixed assessment and rehabilitation units, and GMW (usual) care that included the outcomes noted above. The review identified 24 trials, 6 of which were ongoing and 18 of which had information available on 3,249 patients.

Mortality was significantly reduced in the SU group at the final interview (median follow-up = 1 year; mortality = 21% versus 25%; OR = 0.81; 95% CI = 0.68 to 0.96;  $2p < .05$ ); the odds ratio for the combined adverse outcome of death or institutionalization at final review was 0.75 (95% CI = 0.65 to 0.87;  $2p < .0001$ ); and for the combined adverse outcome of death or dependency, the odds ratio was 0.71 (95% CI = 0.61 to 0.84), with a trend toward reduction in dependency. The odds ratios for resuming independent living at home for those in SUs compared to those receiving usual care were 1.41 (95% CI = 1.19 to 1.67;  $p < .01$ ); for institutional care, 0.83 (95% CI = 0.68 to 1.03); and for death, 0.80 (95% CI = 0.67 to 0.95)(50). Benefits were even more pronounced in older patients (those over age 75); moreover, benefits are present for those with minor, moderate, or severe stroke; and for women and for men(49-52). Older adult patients benefited at least as greatly as did younger stroke patients in the measured outcome of combined death and institutional care (OR = 0.64, for age over 75; 95% CI = 0.49 to 0.85, versus OR = 0.78, for age 75 or less; 95% CI = 0.63 to 0.97) (51).

A host of individual RCTs has demonstrated significant improvement in outcomes in patients admitted to specialized SUs compared with GMWs. These outcomes have included improved functional status(53-56) , shorter hospital stay(53-57), reduced mortality(54, 56-58), improved quality of life(55), reduced neurological deficit(56), and increased discharge home (or reduced dependency)(54, 56, 57).

## **DISCUSSION**

Producing quality indicators for the vulnerable elderly frequently depends on evidence derived from younger subjects in whom the risks and benefits of interventions may differ; moreover, inferences regarding the direction and magnitude of these risk-benefit differences may vary. While the indicators presented here represent a panel's judgment based on existing evidence, in order that high quality evidence may guide future indicators for the vulnerable elderly, studies directed to the elderly, and including vulnerable elders, should be strongly considered. AF and stroke are concentrated in the elderly and older elders; focusing on these populations in studies of stroke and AF is particularly desirable. This effort examined the relationship between processes and outcomes of care, toward development of explicit criteria to evaluate quality of care for AF and stroke in the vulnerable elderly. The ten quality indicators judged valid for use as measures of quality of stroke and AF care for vulnerable elders can potentially serve as a basis to compare the care provided by different health care delivery systems as well as the change in care over time.

**Table 1: Drugs that influence the effect of warfarin(36, 39):**

**A. Drugs that influence the effect of warfarin by altering plasma levels**

- Phenylbutazone, sulfinpyrazone, disulfiram, metronidazole, trimethoprim-sulfamethoxazole, cimetidine, omeprazole, amiodarone (which increase warfarin levels by reducing its clearance)
- Cholestyramine, barbiturates, rifampin, and carbamazepine (which reduce warfarin levels by increasing clearance)
- HMG-CoA reductase inhibitors

**B. Drugs that affect the action, or hemorrhagic potential, of warfarin without affecting plasma levels**

- Second- and third-generation cephalosporins, clofibrate, heparin, and ancrod (which potentiate the anticoagulant effect without affecting plasma levels of warfarin)
- Erythromycin, anabolic steroids, topical testosterone, ketoconazole, fluconazole, piroxicam, tamoxifen, quinidine, high-dose vitamin E, phenytoin, and propafenone (which potentiate the effect by unestablished mechanisms)
- Sulfonamides, broad-spectrum antibiotics, nafcillin, and sucralfate (which antagonize the effect by unknown mechanisms)
- Aspirin and other nonsteroidal anti-inflammatory drugs
- Ticlopidine

- Penicillins (in high doses) such as carbenicillin, and moxalactam (which potentiate the effects by interfering with platelet action)

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