

# Deciding on Anticoagulating the Oldest Old with Atrial Fibrillation: Insights from Cost-Effectiveness Analysis

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**OBJECTIVES:** To better understand the tradeoffs between the efficacy of anticoagulation with warfarin and its side effects in the oldest old with nonrheumatic atrial fibrillation (AF).

**DESIGN:** Cost-effectiveness analysis.

**SETTING:** Published literature, including meta-analyses when available, and web-based sources.

**PARTICIPANTS:** Those aged 65 to 100 with AF.

**INTERVENTION:** Anticoagulation with warfarin.

**MEASUREMENTS:** Quality-adjusted life expectancy and cost.

**RESULTS:** Anticoagulation is not effective in persons with AF who do not have other risk factors, even in the oldest old. The best argument for its use (prolongation of life at an acceptable cost) can be made in those at major risk for stroke because of previous stroke or transient ischemic attack, diabetes mellitus, and hypertension, but poor quality of life before anticoagulation and comorbidities that carry their own risks of dying diminish benefits.

The decision to anticoagulate the oldest old with AF must take into consideration the risk of hemorrhagic stroke and of death from hemorrhagic stroke that existed before anticoagulation, the increased risk of hemorrhagic stroke and of death from hemorrhagic stroke while anticoagulated, and the efficacy of anticoagulation. Cost-effectiveness is also influenced by the cost of warfarin, the risk of major extracranial bleeding, the risk (natural and anticoagulated) of death from hemorrhagic stroke, the rate of ischemic stroke, the cost of major extracranial bleeding and hemorrhagic strokes, the cost of nursing home care, and the fraction of patients with stroke who need nursing home care.

**CONCLUSION:** There is no compelling evidence to date that anticoagulation prolongs quality-adjusted life expectancy in the oldest old with nonrheumatic AF. More stud-

ies that better estimate the risk of intracranial bleeding with and without anticoagulation in the oldest old are needed before recommendations can be made. The oldest old who are most likely to benefit are those who have a high risk of stroke secondary to risk factors other than age alone, although quality of life and life expectancy related to these risk factors limit obtained benefit. Recommendations that all older persons with AF should be anticoagulated are premature. *J Am Geriatr Soc* 50:863–869, 2002.

**Key words:** Anticoagulation; atrial fibrillation; old, aged 65+; old, aged 85+; cost-effectiveness analysis

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**N**onrheumatic atrial fibrillation (AF) is most frequent in the oldest old. Although stroke due to AF is associated with age and with diseases such as diabetes mellitus and hypertension that are more common with age, and anticoagulation with warfarin has been shown in randomized trials to be effective in preventing stroke, contraindications and complications of anticoagulation also increase with age. No randomized controlled trials have specifically addressed these issues in the oldest old.

Deciding whether to anticoagulate older patients with nonrheumatic AF is a difficult and increasingly common problem for clinicians. Recent randomized trials<sup>1–6</sup> have documented the efficacy of warfarin in preventing stroke from nonrheumatic AF, but only a few of the oldest old were enrolled, and patients who were at increased risk of bleeding for conditions that become increasingly prevalent with age were excluded.

Yet the oldest old are a very important subset of those with nonrheumatic AF, because the frequency of AF increases markedly with age.<sup>7</sup> Age itself is an important risk factor for stroke for those who have AF.<sup>1</sup> The risk for other disorders strongly associated with stroke in AF, such as hypertension, diabetes mellitus, and previous stroke or transient ischemic attack (TIA), also increases with age.<sup>1</sup>

Nevertheless, the side effects of anticoagulation also increase with age.<sup>8</sup> The oldest old have an increased risk of extracranial bleeding while on warfarin.<sup>9</sup> Although studies have been inadequately powered to rigorously demon-

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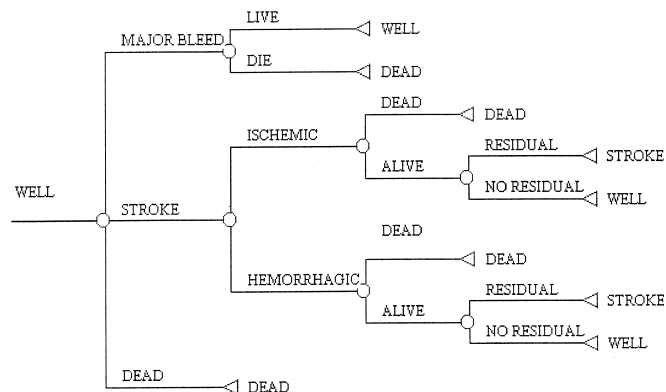
strate increased risk of intracranial bleeding, this complication is suspected and feared, because it has been demonstrated that the risk of death from intracranial bleeding in anticoagulated patients is twice the already high risk.<sup>9</sup> Although previous stroke or TIA is the greatest risk factor for recurrent stroke in patients with AF, patients with stroke residuals are also at an increased risk of falling, which may lead to intracranial and extracranial bleeding.

Several cost-effectiveness analyses of warfarin for patients with nonrheumatic AF have been published; one reports results to age 75,<sup>10</sup> the other divides the oldest old into those aged 80 to 84 and those older than 84,<sup>11</sup> neither explicitly models risk of intracerebral bleeding. This article extends previous studies while taking advantage of the new U. S. life tables that extend to age 100<sup>12</sup> to model cost-effectiveness of anticoagulation from age 65 to 100.

## METHODS

### Model

A Markov model was developed using DATA 3.5, Version 3.5.5 (TreeAge Software, Inc., Williamstown, MA). Three states were used to reflect the conditions of (1) life without a stroke, (2) life with stroke residuals, and (3) death. Patients who were well or had residuals from a stroke could continue as they were, suffer a major extracranial bleed that led to hospitalization, have a first or second stroke, or die from other causes (see Figure 1). Patients with major extracranial bleeds could fully recover or die. Strokes could be of two types: ischemic (atherosclerotic or embolic, reflecting strokes counted in the nonrheumatic AF trials) or hemorrhagic (including subdural, intracerebral, and subarachnoid hemorrhages). Patients with strokes could be left with residuals after the stroke, recover (or return to their previous stroke state, in the case of a second stroke), or die. In accord with the findings of the pooled study,<sup>1</sup> patients who have had a previous ischemic stroke or TIA are at higher risk of subsequent strokes, and risk of stroke increases with age. Indicator variables were used to study the



**Figure 1.** Possible paths and outcomes in decision analysis. Outcomes after 1 year are denoted after triangles. Outcomes are similar for patients who start off with a stroke, although the outcome WELL becomes STROKE and the outcome STROKE becomes DEAD.

effects of history of diabetes mellitus, hypertension, and previous stroke or TIA. Rates of hemorrhagic stroke and of major extracranial bleeding also increased with age. Multiplier variables were appended to all stroke and bleed rates to allow sensitivity analyses to be performed on baseline rates. The model assumed that anticoagulated patients were at higher risk of major extracranial bleeding, dying from major extracranial bleeding, intracranial bleeding, and having residuals and dying from intracranial bleeding.

The model also assumed that patients who have had two major strokes die, anticoagulation had no effect on nonembolic ischemic strokes, the efficacy of anticoagulation in preventing ischemic embolic strokes was not related to age, and patients remained anticoagulated or not regardless of their experience with stroke or bleed. The increased risk of bleeding that occurs immediately after anticoagulation commences was not included. Hospitalization was modeled as equivalent to removing 1 week of quality-adjusted life expectancy. TIAs were not modeled as a separate state, although the increased risk of stroke in patients with a history of these attacks was modeled.

### Effectiveness

The model used quality-adjusted life expectancy as the measure of effectiveness. The study of Gage et al.<sup>10</sup> determined a quality of life of .75 in patients with mild stroke residuals and .39 in patients with moderate to severe stroke residuals. Because the Framingham study indicated that patients with AF tend to have larger strokes and a higher mortality,<sup>13,14</sup> a baseline quality of life of .5 was used as the average utility for patients with residual defects after stroke. It was assumed that a major stroke with residual would halve the baseline quality of life at the start of the analysis. Quality-adjusted life expectancy was discounted at a rate of 3% per year.

### Costs

Because the model addressed marginal cost and effectiveness, only the costs of anticoagulation and its complications and strokes related to AF and anticoagulation were modeled. Cost of warfarin administration included the average wholesale price for 5 mg warfarin,<sup>15</sup> a 50% pharmacy markup, the cost of monthly prothrombin times and every other monthly hemoglobins, blood drawing, and an extra physician visit per year. Costs of major complications of anticoagulation were modeled directly.

Charges for hospital care for patients aged 65 and older were obtained from the Healthcare Cost and Utilization Project (HCUP) 1997 Nationwide Inpatient Sample.<sup>16</sup> For strokes, the charges for the following codes from the *International Classification of Disease—Ninth Revision* were weighed by number of patients in each group: 436 (cerebrovascular accident), 434.11 (cerebral embolism with infarct), and 434.01 (cerebral thrombosis with infarct). For intracerebral bleeding, the following codes were used: 432.1 (subdural hematoma), 432.9 (intracerebral hemorrhage), 430 (subarachnoid hemorrhage), and 431 (intracerebral bleed). For extracranial bleeding, the following codes were used: 531 (acute stomach ulcer), 627.1 (postmenopausal), 534.4 (marginal ulcer), 534 (acute marginal

ulcer), 533.4 (chronic peptic disease), 533 (acute peptic ulcer), 532 (acute duodenal ulcer), 596.7 (bladder wall), 569.3 (rectal and anal), 530.82 (esophageal), and 459 (not otherwise specified).

Based on several studies,<sup>17,18</sup> the cost of hospital care for stroke was increased by 40% to account for physician and other specialty services and for specialized care required in the first year after the stroke. Ancillary costs for extracranial bleeds were assumed to be 20% more than hospital costs. The costs of physician visits and rehabilitation services for stroke were incurred in the year of the stroke. Hospital costs in patients who bled or had strokes while on anticoagulation were assumed to be the same as those occurring in patients who were not anticoagulated.

Medicaid average daily nursing home costs<sup>19</sup> were used, assuming that one-third of patients with residuals after stroke needed nursing home care. All costs were adjusted to year 2000 using the medical portion of the consumer price index and assuming a 3% increase for the last 2 years. A 3% yearly discount rate was used for all costs. Costs were modeled from a societal perspective, but the costs of lost wages (usually small in this population) and travel were not included.

**Baseline Probabilities**

Probabilities used in the initial analysis are listed in Table 1. Age-specific death rates were from the U.S. Life Tables.<sup>12</sup>

Mortality rates were increased by 20% to reflect increased mortality for those with AF.<sup>13</sup> Deaths from strokes due to AF were subtracted from total deaths.

The risks for ischemic stroke were from the pooled study,<sup>1</sup> assuming a risk of stroke of 1 per 100 person-years for patients aged 65 without other risk factors and increasing risk by 1.4 times per decade. Investigators from the Framingham study reported that strokes in AF were more likely to be severe or fatal and reported a 1-month mortality of 13% in those aged 65 to 74 and 34% in those aged 75 and older, so these values were modeled with linear interpolation between ages 70 and 80.<sup>13</sup> There was not much difference by age in the percentage of survivors who had stroke residuals, so a number-weighted average of 78 was used for the percentage of survivors who were left with stroke residuals.

The incidence of intracranial bleeding in the oldest old has not been well documented. The Stroke Prevention in Atrial Fibrillation II Study (SPAF II)<sup>20</sup> reported that anticoagulated patients aged 75 and younger (average 64) had a rate of intracranial bleeding of 0.5 per 100 per year and those older than 75 (average 80) had a rate of 1.8 per 100 per year. Therefore, the absolute risk of intracranial bleeding on warfarin was extrapolated to increase from 0.5 per 100 per year at age 65 to 9.9 per 100 per year at age 100. A recent systematic review of 1,214 patients without AF who were anticoagulated<sup>9</sup> reported that anticoagulation doubled the risk of death from intracranial hemorrhage.

**Table 1. Values of Parameters Used in the Model**

Parameter	Rate at Age					Risk*	Cost \$	QOL
	65	70	80	90	100			
Ischemic stroke	1.0	1.2	1.6	1.9	2.4			
Ischemic stroke, anticoagulated	0.3	0.4	0.5	0.6	0.7			
Hemorrhagic stroke	0.3	0.4	0.9	2.1	5.0			
Hemorrhagic stroke, anticoagulated	0.5	0.8	1.8	4.2	9.9			
Major non-stroke bleed	1.0	1.2	1.6	2.2	3.0			
Major non-stroke bleed, anticoagulated	3.0	3.5	4.8	6.6	9.0			
Death from ischemic stroke (risk)	0.13	0.13	0.34	0.34	0.34			
Residual after ischemic stroke						0.78		
Death after major nonstroke bleed						0.04		
Death after hemorrhagic stroke						0.35		
Death after hemorrhagic stroke while anticoagulated						0.7		
Residual after hemorrhagic stroke						0.5		
Residual after hemorrhagic stroke while anticoagulated						1.0		
Warfarin (per year)							551	
Hospitalization								
Hemorrhagic stroke							17,454	
Ischemic stroke							9,167	
Major extracranial bleed							8,052	
Nursing Home care (per year)							30,035	
Quality of life without stroke								1.0
Quality of life with stroke with residual								0.5

Note: Efficacy of anticoagulation in preventing stroke was .69. One-week penalty for hospitalization.

\*Death from ischemic stroke was the only risk that was age adjusted.

QOL = quality of life.

There were no reliable data to assess the frequency of non-fatal intracranial hemorrhage, so the assumption was made that the risk of intracranial hemorrhage was also doubled, and, therefore, the rates from the SPAF II trial were halved to obtain the rates for the nonanticoagulated. The SPAF II investigators also reported that 71% of intracranial hemorrhages on warfarin were fatal and that all survivors had residual deficits. Because it was recently reported<sup>9</sup> that anticoagulation doubles the risk of death from intracranial hemorrhage, it was estimated that the risk of death without anticoagulants was 35% and that half of patients with intracranial hemorrhage who were not on coumadin would have residual deficits.

The incidence of major extracranial bleeding in the nonanticoagulated oldest old has not been well documented, so the same rate noted in SPAF II for patients on aspirin—1 per 100 persons per year at age 65 increasing by 3% per year—was used. Although increased risk attributable to anticoagulation is also controversial, the results from a recent systematic review that indicates that there is a threefold increase in the risk of major extracranial hemorrhage in the anticoagulated were used.<sup>9</sup> The HCUP number-weighted average of 3.7% hospital mortality for acute extracranial bleeding for patients aged 65 and older was used.

### Sensitivity Analyses

To understand the importance of all variables in the model on quality-adjusted life expectancy, all rates and probabilities were varied over a range from 50% below to 50% above the base rates (or to 1 for probabilities greater than .66). Baseline quality of life was varied from 1 to 0.5; for the latter, quality of life was assumed to drop to 0.25 after a stroke that caused residuals.

## RESULTS

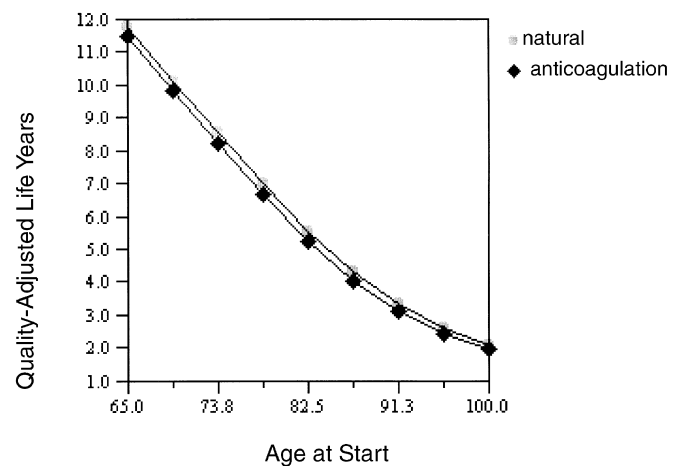
### Influence of Variables

Sensitivity analyses indicate that the most influential variables affecting quality-adjusted life expectancy are risk of hemorrhagic stroke and death from hemorrhagic stroke before anticoagulation, increased risk of hemorrhagic stroke and death from hemorrhagic stroke during anticoagulation, and efficacy of anticoagulation.

The variables most affecting cost are cost of warfarin, efficacy of anticoagulation, risk of major extracranial bleeding, risk (natural and anticoagulated) of death from hemorrhagic stroke, natural rate of ischemic and hemorrhagic stroke, risk of hemorrhagic stroke in anticoagulated patients, cost of major extracranial bleeding and hemorrhagic stroke, cost of nursing home care, and fraction of patients with stroke who need nursing home care. These variables are also the ones that most affect cost-effectiveness ratios, although the order of their importance is slightly different.

### Age

At baseline values for the parameters in the model (Table 1), anticoagulation leads to worse outcomes at any age, although the differences in outcomes are small (Figure 2). For example, the quality-adjusted life expectancy of 65-year-olds with AF who are not anticoagulated is 11.75 quality-adjusted life years (qalys), compared with 11.48 qalys for those who are anticoagulated; and that for a 100-year-old is 2.07 qalys

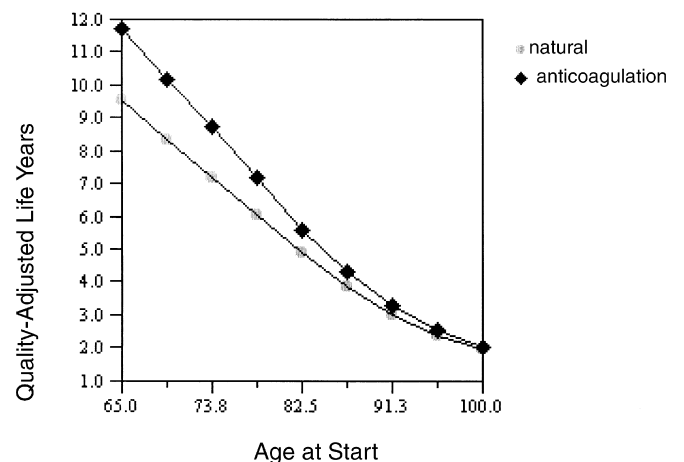


**Figure 2.** Quality-adjusted life expectancy in older persons with nonrheumatic atrial fibrillation who have no other risk factors, with and without anticoagulation.

and 1.95 qalys, respectively. Even if it is assumed that there is no age-related increase in risk of hemorrhagic stroke, risk of hemorrhagic stroke with anticoagulation, or risk of mortality from stroke by using values for 65-year-olds for all older persons, anticoagulation still leads to worse outcomes, although the life expectancy versus age curves are nearly superimposable.

### Risk Factors

Anticoagulation has a major effect in prolonging quality-adjusted life expectancy in older patients with AF with excellent quality of life and a history of previous stroke or TIA, diabetes mellitus, and hypertension (Figure 3). For example, the life expectancy of 65-year-olds with AF who are not anticoagulated is 9.52 qalys, compared with 11.70 qalys for those who are anticoagulated, whereas that for 100-year-olds is 1.94 qalys and 2.02 qalys, respectively. Both the absolute and the relative quality-adjusted life expectancy gained with



**Figure 3.** Quality-adjusted life expectancy in older persons with nonrheumatic atrial fibrillation who have a history of diabetes mellitus and hypertension and who have had a previous stroke or transient ischemic attack, with and without anticoagulation.

anticoagulation decrease with age. For a 65-year-old with all three risk factors, there is a 23% increase in qalys with anticoagulation, compared with 4% for a 100-year-old.

Quality of life before stroke has a marked effect on benefit and cost-effectiveness of anticoagulation (Figure 4). For example, compared with a life expectancy of 11.70 qalys for older persons with a quality of life of 1 who have all three major risk factors, anticoagulated 65-year-olds with a quality of life of .5 would have a quality-adjusted life expectancy of 6.07 qalys, a .9 (17%) life expectancy increase over the nonanticoagulated, whereas 100-year-olds would have a life expectancy of 1.3 qalys (a 3% increase).

The benefits of anticoagulation in patients with other combinations of risk factors for stroke are intermediate to those of patients without other risk factors and those of patients with all risk factors and are detailed in Table 2. For those with only one risk factor, life expectancy with anticoagulation is better at younger ages, but thresholds are reached whereby anticoagulation is no longer the preferred strategy. For example, for patients with diabetes mellitus alone, a 65-year-old has a life expectancy of 11.41 qalys compared with 11.51 qalys for those who are anticoagulated; a threshold is reached after age 71, when qalys gained are actually less for those who are anticoagulated: 2.04 qalys without anticoagulation and 1.96 qalys with anticoagulation. For those with hypertension alone and a previous stroke or TIA alone, the results are quite similar, although thresholds are reached at ages 68 and 82, respectively.

For those with two risk factors, outcomes for patients with diabetes mellitus and hypertension are similar to those with a history of a previous stroke or TIA alone, but the threshold at which anticoagulation is no longer the preferred course is reached at age 85. All other two-way combinations that include a history of previous stroke or TIA have better outcomes with anticoagulation, although thresholds are reached in nonagenarians.

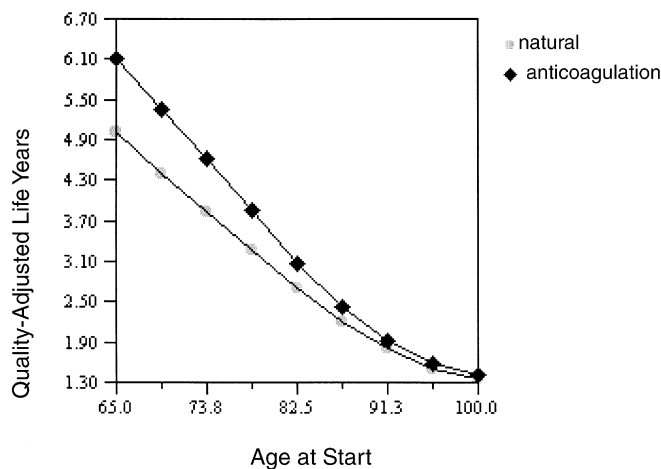


Figure 4. Quality-adjusted life expectancy in older persons with nonrheumatic atrial fibrillation who have a history of diabetes mellitus and hypertension and who have had a previous stroke or transient ischemic attack and who have a quality of life of 0.5, with and without anticoagulation.

Table 2. Quality-Adjusted Life Expectancy in Patients with Atrial Fibrillation by Risk Factor Combinations and Age

Risk factor	Age	Anticoagulation	
		No	Yes
None	65	11.8	11.5
	100	2.1	2.0
History of diabetes mellitus	65	11.4	11.5
	100	2.0	2.0
History of high blood pressure	65	11.5	11.5
	100	2.1	2.0
History of stroke or TIA	65	11.1	11.5
	100	2.0	2.0
Diabetes mellitus and high blood pressure	65	10.9	11.6
	100	2.0	2.0
Diabetes mellitus and stroke or TIA	65	10.4	11.6
	100	2.0	2.0
High blood pressure and stroke or TIA	65	10.5	11.6
	100	1.2	2.0
Diabetes mellitus and high blood pressure and stroke or TIA	65	9.5	11.7
	100	1.9	2.0

TIA = transient ischemic attack.

Cost-Effectiveness

In patients with AF who have histories of previous stroke or TIA, diabetes mellitus, and hypertension, anticoagulation saves money and extends life. In 65-year-olds it saves \$1,434 while increasing life expectancy by 2.2 qalys, whereas in 85-year-olds it saves \$1,767 while adding .5 qaly. Even using the results of our analysis at face value (ignoring the uncertainty of estimates at this age), the maximal cost of anticoagulation is not very high compared with other life-extending treatments; for example, for 95-year-olds with hypertension and previous stroke or TIA, the marginal cost effectiveness ratio is \$30,000 per qaly saved.

DISCUSSION

The decision analysis suggests that anticoagulation is not effective in prolonging quality-adjusted life expectancy in patient with AF without other risk factors at any age and that it is effective only for some subgroups who have other risk factors for stroke. Even for the oldest old who are at the greatest risk for embolic stroke—those who have had previous stroke or TIA and have a history of diabetes mellitus and hypertension the decision to anticoagulate is still quite close to that not to anticoagulate, and the results are based on parameters whose values are uncertain.

The decision to anticoagulate is quite sensitive to age-related risk of bleeding with and without anticoagulation, such as increased risk of intracranial bleeding and death from intracranial bleeding with and without warfarin, yet the baseline risks used in the model for these parameters are uncertain. The nonrheumatic AF studies of the efficacy of warfarin did not enroll enough of the oldest old to have been adequately powered to give precise estimates of these risks.

The analysis suggests that an important factor that limits the absolute benefit that can accrue to even the oldest old at the highest risk of embolic stroke is the competing risk of death from other illnesses in the oldest old.

Even in those at the highest risk for stroke, the absolute and percentage increases in remaining life expectancy with anticoagulation decrease with advancing age. This analysis also suggests that those who have a history of stroke or TIA, diabetes mellitus, and hypertension should be considered for anticoagulation even if they are younger than 65.

Baseline quality of life before anticoagulation also has an important influence on quality-adjusted life expectancy gained with anticoagulation. This is a crucial consideration in deciding on anticoagulating the oldest old because the Beaver Dam Health Outcomes Study, a community-based study of quality of life, listed self-reported quality of well-being scores ranging from .67 to .71 for those aged 65 to 74 and from .58 to .66 for those aged 85 and older.<sup>21</sup>

The findings of this study are consistent with a recent meta-analysis of patients with nonrheumatic AF that suggests a beneficial effect of anticoagulation in patients with a history of previous stroke or TIA<sup>22</sup> and the cost-effectiveness analysis of Thomson et al.<sup>11</sup> However the present study cautions against extrapolating these results to the oldest old and is consistent with the conclusion of a recent review that, "Additional studies of the tolerability of anticoagulation in older patients with AF are needed."<sup>23</sup> Although data on the efficacy of anticoagulation in decreasing stroke are quite robust, it cannot automatically be inferred that because strokes are decreased, quality-adjusted life expectancy is improved or that a treatment that is beneficial at one age is also beneficial at another age or over a lifetime.

The present study is consistent with the SPAF II<sup>20</sup> findings that the benefits of anticoagulation in the oldest old are countermanded by the increased risk of intracerebral risk with anticoagulation, especially considering that several other observational studies have suggested that the risk of bleeding complications<sup>24–29</sup> and death<sup>30</sup> are greater in the anticoagulated oldest old.

Our cost-effectiveness analysis is consistent with previous analyses in suggesting that anticoagulation saves health-care costs and extends life for high-risk groups, shortens life for those without risk factors, and, for those with most combinations of risk factors, the costs are not prohibitive. For example, Thomson et al.<sup>11</sup> reported a maximum cost-effectiveness ratio of £6,000 (approximately \$9,000), whereas we report that in most cases the costs to society are less than \$30,000 per qaly. The results across studies are not directly comparable because Gage et al.<sup>10</sup> do sensitivity analyses using risk as a continuous variable, whereas the study of Thomson et al.<sup>11</sup> uses 1,512 risk combinations, and the present study uses 288. Using risk as a continuous variable necessarily leads to very high cost-to-effectiveness ratios as effectiveness decreases toward zero.

Those who are at the greatest risk for embolic stroke based on the clinical indicators delineated in the pooled study<sup>1</sup> have the most to gain from anticoagulation, although the indicators of "history of hypertension" and "history of diabetes" are vague. For example, use of these indicators implies that a patient with a history of moderate hypertension that has been adequately controlled for many years is at the same risk as someone with uncontrolled severe hypertension, a supposition that contradicts clinical understanding of disease. In addition, indicators such as history of diabetes mellitus and hypertension are not proximate causes of emboli but are most likely surrogates for other factors that lead to in-

creased formation of emboli. The SPAF study<sup>4</sup> has suggested that left atrial size, as determined by echocardiography, may be a better marker of risk for stroke in AF than clinical risk factors, although this study did not adjust for the clinical factors used in the pooled study.<sup>1</sup> Better tests of the risk of stroke and better understanding of the risks of bleeding with and without anticoagulation might help us target those who would most benefit from anticoagulation, although there probably will be groups for which the decision is difficult.<sup>31</sup> However, even in patients who are at high risk for stroke, the present analysis suggests that anticoagulation might not be beneficial for the oldest old.

The analysis strongly suggests that we need better data on the risks and benefits of anticoagulation—especially on the risk of intracerebral bleeding and its complications—for the oldest old with AF. Such a study will be difficult to conduct. It will have to include thousands of the oldest old with AF from many different centers. It also could be designed to separate the effect of duration of hypertension and diabetes mellitus, pretreatment level of blood pressure and hemoglobin A1C, extent of control of hypertension and diabetes mellitus, and the independent role of echocardiography in delineating risk for stroke.

The present study has several limitations. A decision model is a tradeoff between simplifying assumptions (listed in the Methods section) that keep it tractable and the complexity of the real world, and therefore the results of these analyses cannot be exact. The model does not differentiate between the major types of intracerebral bleeding—intracerebral hemorrhage, subdural hematoma, and subarachnoid hemorrhage—each of which has different age-related risks and increased risks with anticoagulation (and different clinical risk factors). However, AF studies so far have been underpowered for accurate estimates of intracerebral bleeding; accurate estimation of subtypes of bleeding would require even larger studies.

The model also uses as its baseline parameters risks and rates for bleeding and stroke from randomized studies that required patients to be at low risk of complications for inclusion. Early studies of bleeding complications in anticoagulation clinics reported higher risks of bleeding in community populations than those reported in randomized trials. In addition, the risk of major bleeding with and without anticoagulation is constantly changing. Newer treatments for other conditions (such as cyclo-oxygenase-2 inhibitors for arthritis) and better control of warfarin treatment such as with self-monitoring<sup>32</sup> may decrease the risk of major bleeding, albeit not the risk of complications once major bleeding does occur.

Although the analysis adjusts for increased mortality in those with AF, it does not adjust for higher mortality in those with risk factors and therefore overestimates the benefits of anticoagulation for them.

Decision-maker preferences are important in deciding whether to use anticoagulation in patients with AF,<sup>33</sup> and they were not considered in this analysis. However, the results of the analysis should be useful for decision makers in helping them understand the benefits obtained from anticoagulation in different clinical situations.

The estimates of charges that we used based on the HCUP study should be quite accurate, although they do not differentiate between costs of bleeding in anticoagulated versus nonanticoagulated patients, and they were converted

to costs using the cost-to-charge ratio at one teaching hospital. In addition, the fraction of patients with strokes secondary to AF who need long-term nursing home care is not well established.

In summary, there is no compelling evidence that anticoagulation prolongs quality-adjusted life expectancy in the oldest old with nonrheumatic AF. More studies that better estimate the risk of major bleeding with and without anticoagulation in the oldest old are needed before blanket recommendations can be made. The oldest old who are most likely to benefit are those who have a high risk of stroke secondary to risk factors other than age alone. Recommendations that all older persons with AF should be anticoagulated are premature.

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