



ASSESSING STROKE AND BLEEDING RISK IN ATRIAL FIBRILLATION

*Consensus Statement on Appropriate
Anticoagulant Use*



ASSESSING STROKE AND BLEEDING RISK IN ATRIAL FIBRILLATION: *Consensus Statement on Appropriate Anticoagulant Use*

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Introduction

THE NUMBER OF AMERICANS AGE 65 OR OLDER is expected to increase 36% during this decade—reaching 54.8 million by 2020.¹ By 2030, there will be 72.1 million Americans aged 65 and older, and senior citizens will make up nearly 20% of the U.S. population.¹ This unprecedented and continuing aging of the population will be accompanied by a “Silver Tsunami” of age-related chronic diseases such as atrial fibrillation (AF), which increases in prevalence with age—approximately 2-3% of individuals in their 60s and 8-10% of those in their 80s have AF.²

The risk of stroke, the most-feared consequence of AF, also increases with age, with individuals over the age of 85 facing almost double the stroke risk of those aged 75-84 (increasing from 2.8% to 4.7%).³ Based on demographic factors alone, annual healthcare expenditures related to stroke can be expected to increase to \$140 billion by 2030.⁴ AF is also associated with an approximate doubling of the risk of all-cause mortality⁵ and is a contributory cause of death for around 99,000 Americans each year.⁶

Although anticoagulation is very effective at reducing AF-related strokes, a large percentage of patients do not receive stroke prophylaxis.⁷ Underuse of both ischemic stroke and bleeding risk assessment tools leads to underuse of anticoagulation for stroke prevention, and constitutes a major obstacle to optimal care. This failure to prescribe anticoagulation to high risk patients is driven by many factors, including misperceptions regarding the net clinical benefit of anticoagulant therapy, lack of incentives, time constraints, and lack of specificity as to contraindications. In addition, many healthcare providers over-estimate a patient’s bleeding risk and under-estimate the risk of ischemic stroke. This is especially true

among older adults, where the risk of bleeding events related to falls and mechanical frailty is often over-estimated.²²

The AF Optimal Treatment Task Force, led by the Alliance for Aging Research, convened an expert roundtable to discuss strategies for augmenting risk assessment and anticoagulation decision-making. The objective was to enhance the care and treatment of patients with AF, and reduce the stroke burden on the U.S. healthcare system. The roundtable participants arrived at a consensus on assessing risk and making decisions on antithrombotic therapy, identified needed health care professional and patient education materials and tools to support both risk assessment and implementation of new anticoagulation therapies, and highlighted areas requiring additional research.

Consensus Recommendations

The roundtable participants recommended a three-step approach to anticoagulation decision-making in patients with AF.

- ❖ First, a patient's **stroke risk** should be assessed using an established scoring tool (see Appendix A) and be reviewed and recorded in a chart or EMR no less than annually, as risk factors change. The most commonly used stroke risk scores are CHADS₂ and CHA₂DS₂-VASc. The latter modifies CHADS₂ to identify the lowest risk patients.
 - Those identified as intermediate or high risk should be put on an anticoagulant—warfarin or a direct thrombin inhibitor or a factor Xa inhibitor. Aspirin is not recommended for stroke prophylaxis in AF.
- ❖ Second, if the patient is at high enough risk to require anticoagulation therapy, the patient's **bleeding risk** should then be evaluated to estimate the net clinical benefit of anticoagulation, again using an available scoring tool as a starting point (see Appendix B).
 - Risk factors for ICH should be considered, including uncontrolled hypertension, concomitant antiplatelet therapy, small vessel disease and dementia. Also, while routine screening for cerebral amyloid angiopathy, leukokariosis, and ApoE genotype is not currently indicated, if previously diagnosed, these conditions should be considered.
 - For the majority of patients, the net benefit of stroke prophylaxis supersedes the “net harm” of serious bleeding events, even among older patients. Therefore, assessment of bleeding risk is not an opportunity to look for reasons not to anticoagulate, but rather an opportunity to address correctable risk factors for bleeding (examples include but are not limited to uncontrolled hypertension, anemia, renal impairment, labile INRs, concomitant prescription of aspirin or NSAIDs, ethanol abuse, reduced platelet count, and excessive fall risk). With the exception of the patient with an extremely increased risk of bleeding and a relatively low risk of stroke, those who are identified as having a high risk for bleeds should be monitored closely, and their correctable risk factors managed appropriately.
- ❖ Third, the anticoagulation decision must reflect patient preferences and values. The patient must also understand the relative benefits and risks and be involved in the net value decision.

The roundtable participants also recommended that education and tools at the primary care and family practitioner levels be enhanced and disseminated. These could include stroke risk assessment tools in EMR systems, awareness activities and events at medical centers, educational initiatives by payers, pocket guides, and on-line resources.

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Patient education materials, tools, and outreach must also be enhanced and promoted. Many patients are not aware that AF confers a five-fold increase in stroke risk. The U.S. healthcare system must raise awareness of AF and the associated stroke risk. Initiatives that prompt the patient to initiate a stroke prevention discussion with his or her PCP should be considered. Organizations should join forces to promote reputable on-line resources that provide accurate and objective healthcare information with a consistent message and voice.

While education of both patients and practitioners is critical, clear and consistent recommendations and incentives to comply are also necessary. With the treatment landscape rapidly changing, and treatment decisions becoming more complicated, different recommendations from various professional groups and health organizations complicates matters. A consensus promoted through these groups, guidelines, private and public payers, and other interested parties could increase anticoagulation rates.

The roundtable participants also agreed that priority should be given to collecting and analyzing real-world data on new anticoagulants to identify which patients are best suited for specific agents.

Stroke Risk Assessment

Several scoring systems—e.g., CHADS₂, CHA₂DS₂-VASc, and the Framingham Stroke Risk Score—have been developed to assess stroke risk in patients with AF. Each was developed based on data from randomized trials, and clinical and epidemiologic cohort studies, and translated a weighted, multivariate formula of stroke risk factors to a simplified, easy-to-use mnemonic device, algorithm, calculator, or on-line tool.

CHADS₂ is a widely circulated stroke assessment tool that has been validated in numerous published studies, and assigns points to a number of risk factors (congestive heart failure, hypertension, age 75 or older, diabetes mellitus, and a prior stroke or TIA). Many guidelines have recommended that the CHADS₂ score be used as an initial stroke risk assessment tool for patients with AF, and that those patients with a CHADS₂ score of 2 or more be placed on an anticoagulation regimen for stroke prophylaxis, unless there are strong contraindications.^{8,9,10,11} More recent guidelines register a preference for anticoagulation for patients with a CHADS₂ score of 1.^{8,9,11} Despite these guidelines, fewer than 60% of AF patients who are at high risk for stroke (based on their CHADS₂ scores) receive anticoagulation therapy,^{7,12} and the rate of guideline-recommended anticoagulation of octogenarians—those at greatest risk—may be as low as 30%.¹³

The cause of this under-treatment is multifactorial. First, stroke risk assessment tools may be underutilized. As a result, healthcare professionals (particularly neurologists and emergency department physicians) continue to encounter high risk AF patients who have had a stroke but were not being treated with anticoagulation.

The demands that anticoagulation therapy place on health care professionals and their office staff may be another reason for under-treatment. Warfarin, the most commonly used anticoagulant for AF, places dietary and lifestyle restrictions on the patient and requires frequent coagulation testing to monitor therapeutic intensity. This means health care professionals and their office staff have to devote time to patient education and assessment of a patient's adherence, as well as to frequent follow-up and monitoring.

Some health care professionals may also look "for any reason" not to prescribe anticoagulation. In the SAFE-II study, 88% of patients with AF treated by PCPs were not prescribed anticoagulation. Reasons why patients were not anticoagulated included: low compliance (23%), fear of hemorrhage (22%), or potential contraindication (44%), with the latter including advanced age, cognitive impairment, and falls/gait disturbance, among others.¹⁴ Some practitioners may view a bleeding event in an anticoagulated patient as more their fault than a thromboembolic event in an unanticoagulated patient. An appreciation that the risk of stroke usually exceeds the risk of bleeding in AF patients would help address this mentality.

Real or perceived bleeding risk is often incorrectly used as a reason to not prescribe anticoagulation for patients with AF. Some practitioners may not even assess a patient's stroke risk if they believe the patient is at high bleeding risk. Practitioners may also believe that aspirin is an effective alternative to warfarin, particularly in elderly patients, although trials have shown that anticoagulants are far superior to aspirin in reducing stroke risk, with little difference in bleeding risk.^{15,16} Furthermore, recent guidelines are minimizing the role of aspirin in meaningful stroke prophylaxis.^{8,9,10} The real risk of bleeding while taking an anticoagulant also may not be properly calculated due to a lack of awareness of risk factors for a dangerous bleed and lack of a consistently recommended risk assessment tool.

Anticoagulation of patients at low or intermediate risk for stroke based on the CHADS₂ scale adds complexity to treatment decisions. In the U.S., the new ACCP Guidelines recommend that AF patients with

a CHADS₂ score of 1 receive an anticoagulant rather than aspirin.⁸ In this lower-risk group, patient concerns about bleeding risk and/or dietary and lifestyle restrictions may play an important role in underuse of anticoagulation. Increasingly, patients are turning to on-line healthcare news sites, patient forums, and blogs to inform their healthcare decisions. Some of these sources may over-emphasize the potential complications associated with warfarin and the newer oral anticoagulants, leading some patients to oppose taking them.

The conundrum of anticoagulating lower-risk patients has also led to some divergence in the U.S., Canadian, and European guidelines. The 2010 European guidelines now recommend that the CHA₂DS₂-VASc score be used to refine risk stratification, especially for lower-risk patients.⁹ The CHA₂DS₂-VASc scheme incorporates CHADS₂ risk factors, but further stratifies age >65, and assigns a point for vascular disease (e.g., past myocardial infarction, peripheral arterial disease, or aortic atherosclerosis), and a point for female gender. The net effect of CHA₂DS₂-VASc is to increase the proportion of atrial fibrillation patients for whom anticoagulation is recommended.¹⁷

In effect, the CHA₂DS₂-VASc score subdivides the CHADS₂ score category of 0 into a very low risk score category of 0, and higher risk categories.^{18,19} The European guidelines have used the CHA₂DS₂-VASc approach to recommend against anticoagulation for a relatively small group of AF patients with a score of 0, and to recommend considering anticoagulation for all others.⁹ The need to identify and anticoagulate high-risk patients is paramount. However, further refinement of stroke risk stratification could result in identifying patients who are truly at low risk for a stroke and who presumably have a low net clinical benefit from anticoagulation. European and Canadian guidelines are shifting towards identifying truly low risk patients who do not need antithrombotic therapy.^{9,11}

Using any of the stroke assessment tools is better than not assessing stroke at all, as that will reduce cases where high risk patients are not anticoagulated. Thus, the roundtable participants recommended that the first course of action must be stroke risk assessment (using one of the available scoring tools, e.g., CHADS₂, CHA₂DS₂-VASc, Framingham) for all patients with AF, including those with paroxysmal AF. Since risk factors are dynamic, and, therefore, risk profiles can change over time (e.g., as individuals age), stroke risk assessment should be reviewed at least annually, and recorded in patients' charts or electronic medical records. Participants agreed that the specific stroke assessment tool used was secondary to the assessment itself. It was noted that the most commonly used stroke risk scores are

CHADS₂ and CHA₂DS₂-VASc. The latter modifies CHADS₂ to identify the lowest risk patients. Proper use of these tools would lead to greater use of appropriate stroke prophylaxis treatments in the US.

Bleeding Risk Assessment

Bleeding risk assessment tools specific to the AF patient population—e.g., HAS-BLED, ATRIA, HEMORR₂HAGES—have been less prominent than stroke risk assessment. Similar to the stroke risk assessment tools, they strive to balance simplicity and multivariate predictability. A problem with bleeding risk scores is that they generally do not provide health care professionals with a clear, consistent message with regard to anticoagulation. Canadian and European AF guidelines recommend the use of HAS-BLED to assist in the decision whether to anticoagulate.^{9,11} In the U.S., a bleeding risk assessment tool has not been endorsed by medical societies. Incorporation of bleeding risk tools into anticoagulation decision-making is complicated by the fact that stroke and bleeding risk tend to be correlated, although bleeding events generally have less impact on patients' lives than strokes. The category of bleeding events that is as severe as ischemic strokes (and sometimes even more severe) is intracranial hemorrhages (ICH), in particular intracerebral bleeding.

The mortality rate for AF patients on warfarin who have an intracerebral hemorrhage (i.e., hemorrhagic stroke) can be up to 50%,²⁰ with high disability rates for those who survive. This high mortality rate may be one reason many PCPs prioritize bleeding risk over stroke prevention. However, the hemorrhagic stroke rate for patients taking warfarin was only 0.5 per 100 patient years (versus 0.3 for patients taking aspirin) in one study.²¹ Subdural hemorrhage on warfarin is also a potentially life-threatening event. However, the fear that an anticoagulated elderly patient may fall and suffer such a hemorrhage may be exaggerated. Importantly, for elderly patients, the risk of ischemic stroke off anticoagulants is, in general, greater than the risk of intracranial hemorrhage on anticoagulants.²²

Identifying specific risk factors for intracranial hemorrhage is a priority. More research is needed into specific risks associated with ICH, including the effects of biological (versus chronological) age, frailty, and specific findings on brain imaging.

Some conditions that may predispose anticoagulated patients to ICH, but that are not included in the bleeding risk assessment tools include the following: small vessel disease, cerebral amyloid angiopathy (which typically affects individuals aged 75 or over), leukokariosis, and presence of particular ApoE

genotypes (which are associated with an increased risk of CNS bleeding due to the presence of cerebral amyloid angiopathy). While routine screening for these conditions is not currently indicated, they should be considered if previously diagnosed. In addition, patients with lower CHADS₂ scores who have coronary stents and are on dual antiplatelet therapy, as well as those with uncontrolled hypertension, may not be optimal candidates for anticoagulation. This decision is especially complicated by patients with both coronary artery disease and AF, who need antiplatelet agents to prevent restenosis of an artery or occlusion of a stent, yet also need oral anticoagulants to prevent stroke. In this case, triple therapy—despite exposure to increased bleeding risk—may be the best solution until better ways to deal with this critical unmet clinical need are found.

The roundtable participants recommended that bleeding risk for all patients with AF be assessed (using one of the available scoring tools e.g., HAS-BLED, ATRIA, HEMORR₂HAGES) *following* stroke risk assessment, and that bleeding risk be assessed annually and recorded in the patient's chart or electronic medical record. Since bleeding risk assessment tools have not had the same degree of validation as stroke risk assessment tools, most roundtable participants felt that no one tool should be endorsed, as that could dissuade practitioners from considering all factors that could lead to an intracranial hemorrhage. That is, if one particular tool were recommended, some practitioners may assume the tool encapsulates all risk factors and not consider other risk factors unique to the patient.

The roundtable participants were united in the opinion that the net benefit of ischemic stroke prevention through anticoagulation supersedes bleeding risk concerns for most patients with AF.²³ Therefore, the assessment of bleeding risk is not an opportunity to look for reasons not to anticoagulate, but rather an opportunity to address correctable risk factors for bleeding (examples include but are not limited to uncontrolled hypertension, anemia, renal impairment, labile INRs, concomitant prescription of aspirin or NSAIDs, ethanol abuse, reduced platelet count, and excessive fall risk). With the exception of the patient with an extremely increased risk of bleeding and a relatively low risk of stroke, those that are identified as having a high risk for bleeds should be monitored closely and their correctable bleeding risk factors should be managed.

The anticoagulation decision must also reflect patient preferences and values. For instance, low or intermediate risk patients might value stroke prevention over other considerations. The cost of anticoagulant drugs, along with the risks and benefits associated with each, should be discussed so that

the patient can make an informed decision. The patient needs to understand the relative benefits and risks and must be involved whenever possible in the net value decision.

Anticoagulant Options

Warfarin, a vitamin K antagonist, has been an effective stroke prevention therapy for decades. However, the patient's international normalized ratio (INR) must be maintained between 2.0 and 3.0 to optimize ischemic stroke prevention and minimize bleeding risk. Given this narrow therapeutic range and since changes in concomitant medications and dietary intake of vitamin K can affect the INR, frequent testing is critical. The burden of undertaking these repeated lab tests, as well as dietary and lifestyle restrictions, are thought to decrease patient adherence. Thus, the medical community has developed an infrastructure—incorporating ancillary health care professionals, anticoagulation clinics, patient education materials, and self-monitoring—to manage AF patients on warfarin. This infrastructure and support have led to better efficacy and reduced complications. However, despite warfarin's efficacy in ischemic stroke prevention, both health care professionals and patients have been hoping for alternative anticoagulant therapies for many reasons, but especially because of the difficulty in maintaining optimal INR levels—due in large measure to the interaction of warfarin with so many drugs and foods, as well as the variability of dose response.

Also a concern with warfarin, even with effective management, is the risk of bleeding. The introduction of two novel agents (dabigatran and rivaroxaban) over the past 18 months—with apixaban awaiting an FDA approval decision in 2012, and edoxaban in very advanced stages of development—changes the treatment paradigm for patients with AF. These new agents offer greater convenience and timely anticoagulation, as they have better pharmacodynamic predictability than warfarin. They have very few food and drug interactions—for example, there is no limitation on the consumption of green, leafy vegetables which is a major complaint of those taking warfarin. There is also no need for routine anticoagulation monitoring. Thus patients for whom regular INR testing—in clinics or through self-testing—is not feasible or whose time in therapeutic range is low despite careful adherence to dosing and follow-up recommendations, may be the best candidates for the new and emerging anticoagulant treatments.

Whether this greater convenience will translate to improved patient adherence has not yet been proven. In fact, some practitioners believe that not having monthly laboratory coagulation blood draws could actually decrease patient adherence. Additionally, the need for routine monitoring of the patient is not completely eliminated, since renal function must be monitored at least annually, especially since so many AF patients are elderly.

The new agents lower the risk of ICH, and, thereby, favorably shift the balance between the risks of stroke and bleeding. However, a minority of participants felt uncertain about whether the new agents confer a clinically important efficacy and safety benefit compared to well-controlled warfarin.

The management of each new agent will likely be nuanced, offering options for personalized medicine, but also potentially complicating treatment decisions in the near term, particularly as the full extent of risks unique to each novel agent may not be known for some time. Additionally, some evidence suggests that dabigatran may not protect against myocardial infarction (MI) as well as warfarin.²⁴

Priority should be given to educating healthcare professionals on the benefits and risks associated with the new agents. Allied professionals who typically spend more time on patient education and support need to be fully conversant with the many considerations in the use of the new agents—including mechanisms of metabolism and excretion, half-lives, occasional interactions with other medications, lifestyle restrictions, etc. Given the relatively short half-lives of the new anticoagulants, patient adherence is critical. Patient education emphasizing the need for compliance will likely require a team effort, with the prescribing physician having the initial discussion with the patient, and pharmacists, nurses, and physician assistants handling follow-up phone calls or office visits. Reputable on-line resources should also be used as an additional resource for patients and their families.

There is some evidence in laboratory tests in healthy volunteers that coagulation in the presence of rivaroxaban can be normalized using clotting factor concentrates, but this has not yet been confirmed in patients with AF. No clinical studies have tested efficacy for reversal or reduction of bleeding complications.²⁵ While there are currently no reversal agents for the new drugs, their relatively short half-lives may make the issue less concerning.

Cost is another consideration for all parties (providers, patients, and payers). Cost-effectiveness analysis of dabigatran prior to FDA approval of the agent suggested that dabigatran's incremental cost-

effectiveness ratio (ICER) would be \$45,372 per quality-adjusted life years (QALY), below the generally accepted threshold of \$50,000 per QALY for cost effectiveness. Of note, the per-unit cost used in this analysis was higher than dabigatran's price following introduction in the U.S.²⁶ As cost can be a factor in patients' compliance with drug regimes, a patient's ability—and willingness—to pay for the novel therapies is a key consideration in the anticoagulation decision.

The roundtable participants did not include considerations for “bridging” a patient from warfarin to one of the new agents. There was general agreement that patients who are well-managed on warfarin should have the option of continuing on it, and that all patients should be offered the new drugs and advised about their benefits and risks.

In the long term, the new oral anticoagulants may increase the proportion of patients with AF who are anticoagulated, and reduce the rates of bleeding complications. However, it will likely be many years before sufficient real-world data are available to develop profiles for which patients are best suited for which therapy. In the meantime, roundtable participants recommended that health care professionals include patient preferences in the choice of anticoagulation therapy for stroke prophylaxis. This discussion should include consideration of cost, as the new agents are currently priced considerably higher than warfarin.

Methods to Increase Appropriate Use of Anticoagulants in Patients with AF

Over the course of the roundtable discussion, several initiatives that have fostered greater stroke risk assessment and/or better patient management were presented.

In the United Kingdom, the use of stroke risk assessment tools at the PCP and family practitioner levels is increasing, as these providers are incentivized to record stroke risk scores, and place AF patients at high risk for stroke on antithrombotic therapy. The latter reflects an important change in policy language to specify anticoagulation compared to previous text that was interpreted as suggesting that aspirin is equivalent to warfarin. The widespread use of electronic health records (EHRs) has also been a factor in increased stroke risk assessment performed by PCPs and family practitioners.

In the U.S., some practitioners have had success with framing the need for anticoagulation in terms of five-year stroke risk. Patients presented with the annual stroke risk associated with their CHADS₂ score

may view the information in light of the likelihood of not having a stroke. For instance, a patient whose CHADS₂ score implies a 6% annual stroke risk may interpret the information as a 94% chance they can be free of stroke without anticoagulation. Presenting a five-year stroke risk of 30%, however, often forces the patient to take the anticoagulant discussion (and decision) more seriously.

Other U.S. practitioners have found that having the patient initiate the discussion makes the patient more receptive to anticoagulant therapy. One academic center cross-referenced records of ECGs with those in the pharmacy database, and found that only about 18% of AF patients were anticoagulated. Letters were sent to patients indicating that they could be at risk for stroke, and recommended that patients initiate a conversation with their PCP at the next office visit. After six months, the percentage of anticoagulated patients increased to 64%.

For patients on warfarin, self-testing can also lead to greater patient satisfaction, and, presumably, increased adherence and time in therapeutic range. One anticoagulation clinic evaluated self-testing of INR levels. At the beginning of the study, only 62% of patients would recommend warfarin to a friend. After six months, all patients recommended warfarin for stroke prevention.²⁷ Interestingly, some guidelines are now recommending self-management strategies over outpatient INR monitoring for those who demonstrate competency in self-management.

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This consensus document was supported by the efforts of the AF Optimal Treatment Task Force:

Alliance for Aging Research

The Anticoagulation Forum

Atrial Fibrillation Association

Clot Care

The Heart Rhythm Society

Mended Hearts

The Men's Health Network

National Forum for Heart Disease and Stroke Prevention

National Stroke Association

Preventive Cardiovascular Nurses Association

The Society for Women's Health Research

StopAfib.org

Appendix A: Stroke Risk Assessment Scoring Tools

CHADS₂ Score

Letter	Clinical Characteristic	Points Awarded
C	<u>C</u> ongestive heart failure	1
H	<u>H</u> ypertension	1
A	<u>A</u> ge ≥75	1
D	<u>D</u> iabetes mellitus	1
S₂	<u>S</u> troke/TIA/TE	2
Maximum score		6
<p>TIA = transient ischemic attack; TE = thromboembolism 0 points = low risk 1 point = intermediate risk 2 or more points = high risk Annual Adjusted Stroke Rate 0 points = 1.9% 1 point = 2.8% 2 points = 4% 3 points = 5.9% 4 points = 8.5% 5 points = 12.5% 6 points = 18.2%</p>		

CHA₂DS₂-VaSc Score

Letter	Clinical Characteristic	Points Awarded
C	<u>C</u> ongestive heart failure/LV dysfunction	1
H	<u>H</u> ypertension	1
A₂	<u>A</u> ge ≥75	2
D	<u>D</u> iabetes mellitus	1
S₂	<u>S</u> troke/TIA/TE	2
V	<u>V</u> ascular disease	1
A	<u>A</u> ge 65 - 74	1
Sc	<u>S</u> ex category (i.e. female sex)	1
Maximum score		9
<p>LV = left ventricular; TIA = transient ischemic attack; TE = thromboembolism; vascular disease = prior myocardial infarction, peripheral artery disease, or aortic plaque 0 points = low risk 1 point = intermediate risk 2 or more points = high risk Annual Adjusted Stroke Rate 0 points = 0% 1 point = 1.3% 2 points = 2.2% 3 points = 3.2% 4 points = 4.0% 5 points = 6.7% 6 points = 9.8% 7 points = 9.6% 8 points = 6.7% 9 points = 15.2%</p>		

Framingham Heart Study

Clinical Characteristic	Points Awarded
Age, y	
55 - 59	0
60 - 62	1
63 - 66	2
67 - 71	3
72 - 74	4
75 - 77	5
78 - 81	6
82 - 85	7
86 - 90	8
91 - 93	9
> 93	10
Gender	
Male	0
Female	6
Systolic Blood Pressure, mmHg	
< 120 mmHg	0
120 - 139	1
140 - 159	2
160 - 179	3
> 179	4
Diabetes	
No	0
Yes	5
Prior Stroke or TIA	
No	0
Yes	6
Maximum score	31
TIA= transient ischemic attack Predicted 5-Year Risk of Stroke 0-1 points = 5% 18 points = 28% 2-3 points = 6% 19 points = 31% 4 points = 7% 20 points = 34% 5 points = 8% 21 points = 37% 6-7 points = 9% 22 points = 41% 8 points = 11% 23 points = 41% 9 points = 12% 24 points = 48% 10 points = 13% 25 points = 51% 11 points = 14% 26 points = 55% 12 points = 16% 27 points = 59% 13 points = 18% 28 points = 63% 14 points = 19% 29 points = 67% 15 points = 21% 30 points = 71% 16 points = 24% 31 points = 75% 17 points = 26%	

Appendix B: Bleeding Risk Assessment Scoring Tools

HAS-BLED Score

Letter	Clinical Characteristic	Points Awarded
H	<u>H</u> ypertension	1
A	<u>A</u> bnormal renal &/or liver function (1 point each)	1 or 2
S	<u>S</u> troke history	1
B	<u>B</u> leeding	1
L	<u>L</u> abile INRs	1
E	<u>E</u> lderly (age ≥ 65)	1
D	<u>D</u> rugs or alcohol (1 point each)	1 or 2
Maximum score		9
<p>Hypertension = systolic BP ≥ 160 mmHg; Abnormal renal function = presence of chronic dialysis or renal transplantation or serum creatinine ≥ 200 μmol/L; Abnormal liver function = chronic hepatitis disease (e.g., cirrhosis) or biochemical evidence of significant hepatic derangement (e.g., bilirubin > 2x upper limit of normal, in association with AST/ALP/ALP > 3x upper limit normal, etc.); Bleeding = previous bleeding history or predisposition to bleeding (e.g., bleeding diathesis, anemia, etc.); Labile INRs = unstable/high INRs or poor time in therapeutic range (e.g., < 60%); Drugs or alcohol = concomitant use of drugs, such as antiplatelet agents, non-steroidal anti-inflammatories, or alcohol abuse, etc.; INR = international normalized ratio</p> <p>Annual Adjusted Bleeding Rate 0 points = 1.13% 1 point = 1.02% 2 points = 1.88% 3 points = 3.74% 4 points = 8.70% 5 points = 12.50% Any score = 1.56%</p>		

ATRIA Score

	Clinical Characteristic	Points Awarded
	Anemia	3
	Severe renal disease	3
	Age ≥ 75	2
	Bleeding history	1
	Hypertension	1
Maximum score		10
<p>Severe renal disease = glomerular filtration rate < 30 ml/min or dialysis-dependent ATRIA = Anticoagulation and Risk Factors in Atrial Fibrillation 0 - 3 points = low risk 4 points = intermediate risk 5 - 10 points = high risk</p> <p>Annual Adjusted Bleeding Rate 0 - 3 points = 0.8% 4 points = 2.6% ≥ 5 points = 5.8%</p>		

HEMORR₂HAGES Score

	Clinical Characteristic	Points Awarded
H	<u>H</u> epatic or renal disease	1
E	<u>E</u> thanol abuse	1
M	<u>M</u> alignancy	1
O	<u>O</u> lder (age >75)	1
R	<u>R</u> educed platelet count or fxn	1
R₂	<u>R</u> ebleeding risk	2
H	<u>H</u> ypertension (uncontrolled)	1
A	<u>A</u> nemia	1
G	Genetic factors	1
E	Excessive fall risk*	1
S	Stroke	1
Maximum score		12
*Including neuropsychiatric disease 0 – 1 points = low risk 2 – 3 points = intermediate risk ≥4 points = high risk Annual Adjusted Bleeding Rate 0 points = 1.9% 1 point = 2.5% 2 points = 5.3% 3 points = 8.4% 4 points = 10.4% ≥ 5 points = 12.3%		

Outpatient Bleeding Risk Index (OBRI)

	Clinical Characteristic	Points Awarded
	Age ≥ 65 years	1
	History of GI bleeding	1
	History of stroke	1
	One or more comorbid conditions	1
Maximum score		4
Comorbid conditions = recent MI, anemia (hematocrit <30%), renal impairment (creatinine level >1.5mg/dL), or diabetes mellitus 0 points = low risk 1 – 2 points = intermediate risk ≥3 points = high risk		

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Principal funding for the expert roundtable and this consensus document came from Daiichi Sankyo. The Alliance for Aging Research maintained all editorial control and no statement in this document should be construed as being a statement or position of Daiichi Sankyo, Inc.