American Heart Association Atrial Fibrillation Research Summit

A Conference Report From the American Heart Association

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Atrial fibrillation (AF) poses a major global public health challenge because it is increasing in prevalence and is associated with an increased risk of stroke, dementia, heart failure, and death.[1–3] In response to the many challenges posed by AF, the American Heart Association (AHA) convened a conference in Washington, DC, on June 12–13, 2010, that included patients, nurses, physicians, and healthcare policy makers and regulators. In addition, basic, translational, population, outcomes, and clinical scientists participated (Appendix). The 22 presentations and 6 panel discussions were organized into 4 sessions: (1) Mechanisms of AF: Basic and Translational Science and Genetics; (2) Epidemiology, Outcomes, Cost, AF, and Stroke Prevention; (3) Meeting the Clinical Challenges in AF; and (4) Redefining the Therapeutic Goals of AF (Appendix). The focus of the present report is to provide an overview of the key concepts presented and the core recommendations made by the summit participants.

Mechanisms of AF: Basic and Translational Science and Genetics

Attempts to develop safe and effective pharmacological therapy for AF have focused on atrium-selective drugs that take advantage of electrophysiological differences between the atrium and ventricle.[4–7] Heterogeneous abbreviation of the effective refractory period within the atrium provides the electric substrate for development of AF. The reduced effective refractory period results from abbreviation of the atrial action potential duration, which is caused by a decrease in the calcium channel current (I_{Ca}) and an increase in the potassium channel current (I_{K1}) and the constitutively active acetylcholine-sensitive current (CA I_{KACh}).[4–7] Maintenance of AF is facilitated by structural remodeling and additional abbreviation of the effective refractory period. The principal goal of pharmacological therapy is therefore to augment the effective refractory period.

Distinctions in the ion channel currents between the atrium and ventricle open the possibility for development of atrium-specific and -selective drugs for rhythm control of AF, which might avoid ventricular proarrhythmic effects. Atrium-specific targets include I_{Kur}, I_{KACh}, and the constitutively active I_{KACh}, the most investigated of which is inhibition of I_{Kur}.[7] Recent experimental studies have identified atrium-selective I_{Na} blockers that can effectively suppress AF while exerting little or no effect in the ventricles.[5,6] Combinations of

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antiarrhythmic medications, such as amiodarone and ranolazine or dronedarone and ranolazine, are a promising avenue of investigation.[8,9] In animal models, such combinations produce potent synergistic effects that result in atrium-selective depression of sodium channel–dependent parameters and effective suppression of AF. Although synergism between atrium-selective drug combinations holds great promise, future work will be required to determine the safety and efficacy of such drug combinations in patients.

Multiple lines of evidence from basic, translational, and human studies suggest that atrial fibrosis plays an important role in the maintenance of AF.[10–13] Understanding of the mechanisms of atrial fibrogenesis will provide better targets for antifibrotic treatment of AF. There is a lack of detailed information about the biological and electrophysiological properties of fibroblasts and myofibroblasts under normal and AF conditions. Insights into signaling pathways suggest that atrial fibroblasts can be effective therapeutic targets for prevention of fibrosis.[14–16] Multiple agents with antifibrotic properties have demonstrated effects on reducing atrial fibrosis in animal models, but clinical evidence supporting their efficacy in AF prevention is currently lacking. Identification of fibroblast-specific genes will help to develop a fibroblast-specific knockout or transgenic mouse model.

Endothelin 1, a potent vasoconstrictor and mitogen involved in blood pressure regulation, may merit further investigation in AF because it modulates calcium cycling in cardiac myocytes and promotes fibroblast proliferation.[17] Because of the differential distribution of downstream signaling elements, endothelin 1 has a greater impact on atrial than on ventricular calcium cycling and contractility.[17] Interestingly, atrial endothelin 1 levels are elevated in the left atrium of patients with structural heart disease and persistent AF.[17]

Late gadolinium enhancement by cardiac magnetic resonance imaging is a highly specific and sensitive method for detecting scar in the ventricular myocardium.[18,19] Furthermore, it has been demonstrated recently that the same gadolinium-based extracellular contrast agents can be used for the quantification of extracellular remodeling and the detection of diffuse interstitial fibrosis.[20,21] Development of methods for direct assessment of myocardial collagen burden using extracellular collagen-binding contrast agents might allow imaging to characterize the presence and severity of atrial fibrosis noninvasively.

Over the past 5 years, family history has been established as a risk factor for AF.[22] Familial forms of AF have been described, and mutations have been identified in ion channel proteins and signaling molecules; however, these genes are rare causes of AF.[23–26] Genome-wide association studies have revealed genetic risk factors for AF unanticipated by prior knowledge. In one case, the genetic variants are adjacent to a transcription factor that specifies left atrial and pulmonary vein development. How variants at this and other loci lead to AF remains unclear. Future efforts should be focused on the identification of new genetic loci, determination of the mechanism by which polymorphisms are associated with the initiation or promotion of AF, and exploration of the relation between genetic data and clinical outcomes for AF. Systems biology approaches can provide important insights by addressing the complex interactions between risk factors and disease and thus may facilitate our understanding of novel AF mechanisms. The major recommendations related to basic and translational science and AF are summarized in Table 1.

Table 1. Recommendations From the AHA Atrial Fibrillation Research Summit: Mechanisms of AF: Basic and Translational Science and Genetics

Conduct research on the mechanisms and pathogenesis of AF.
Explore the relation between genetic data and clinical outcomes for AF.
Determine the properties of sodium channel blockers (kinetics and modes of binding and unbinding, lipid solubility, molecular size, and chemical structure) that influence atrial selectivity.
Define how electrical and structural remodeling and genetics modify atrial selectivity and the utility and safety of I_{Na} blockers for treatment of AF.
Define the short-term and long-term effects of atrium-selective I_{Na} blockers.
Determine methods for direct assessment of atrial myocardial collagen burden, including extracellular collagen-binding MRI contrast agents.
Evaluate the biological, electrophysiological, and signaling properties of fibroblasts and myofibroblasts under normal and AF conditions to identify novel targets for antifibrotic therapy.
Identify biological markers that will allow antifibrotic treatment at early stages of fibrogenesis.
Identify fibroblast-specific genes to allow development of a fibroblast-specific knockout transgenic mouse model.
Determine the role of endothelin 1 in AF.

AHA indicates American Heart Association; AF, atrial fibrillation; and MRI, magnetic resonance imaging.

Epidemiology, Outcomes, Cost, AF, and Stroke Prevention

The AHA strategic plan now sets a goal of improving the cardiovascular health of all Americans by 20% in 10 years.[27] The AHA plan emphasizes primordial prevention: preventing development of risk factors for cardiovascular disease and stroke.[27] Lifestyle and health factors, including blood pressure, weight, glucose, cholesterol, smoking, diet, and physical activity, collectively known as "Life's Simple Seven," are the focus of the strategic plan.[27] The prevalence of hypertension, obesity, and diabetes mellitus, 3 major risk factors for AF,[27–31] will be favorably influenced by successful lifestyle modifications. Because AF represents one of the most potent risk factors for stroke, prevention of hypertension, obesity, and diabetes mellitus should decrease the incidence of ischemic neurological events substantially.

Several factors are associated with electric and structural atrial remodeling of the left atrium and thus are potential targets for primary prevention of AF. These risk factors can be grouped into demographic, anthropometric, behavioral, and classic cardiovascular risk factors; cardiovascular disease; pulmonary disease; and hyperthyroidism. Additionally, multiple biomarkers are associated with AF, including inflammatory (C-reactive protein, interleukin 6), oxidative stress (nicotinamide adenine dinucleotide phosphate [NADPH] oxidase, natriuretic peptides), and vasoactive peptide (endothelin 1) markers.[32] The extent to which biomarkers are causally related to AF onset, as opposed to representing an epiphenomenon of cardiovascular remodeling, remains unknown.

Systems biology approaches may provide important insights for the prediction and prevention of AF because they address the complex interactions between risk factors and disease.[33] Already, genome-wide association studies have revealed genetic risk factors for AF that were unanticipated by prior knowledge.[23–26] Because of the modest effect sizes, replicating and validating such signals will necessitate the collaboration of multiple cohorts and studies.

Although risk-prediction models to identify individuals at increased risk of AF exist, several areas of uncertainty remain.[2] AF is more common in whites than in other racial groups,[26] but the mechanisms underlying these racial differences are unknown. Potential explanations include variation in diagnosis by race, presence of competing risks in minorities, different susceptibility to AF risk factors, and genetic determinants.[2,24–26] It is uncertain whether AF risk-prediction instruments developed in whites are generalizable to blacks or other ethnic groups. In addition, the proper translation of imaging tests, biomarkers, and genomic markers into clinical practice for improved risk prediction is uncertain. The development of genomic and clinical phenotypes that can distinguish different AF subtypes by functional burden, prognosis, and response to treatment would represent a fundamental advance. Classification into mechanistic and pathogenetic subtypes might allow targeted prevention and treatment in the future.

The outcomes of patients with AF can be improved by prompt diagnosis, appropriate treatment, adherence to practice guidelines, quality research that includes comparative effectiveness research, proper utilization of registries, and translation of research findings into better decision making. Evidence-based guidelines from the AHA/American Stroke Association emphasize the need for antithrombotic therapy, in particular warfarin, in eligible patients.[3,30] The efficacy of warfarin at reducing stroke in patients with AF has been well established by randomized clinical trials.[3] Indeed, the AHA Get With The Guidelines (GWTG) program has identified use of antithrombotic therapy among patients with AF as the key performance metric. Although more patients are being treated with antithrombotic therapy over time, community statistics continue to show large numbers of AF subjects who are not treated with antithrombotic therapy. Despite its demonstrated efficacy, warfarin use is associated with many challenges. Thus, novel vitamin K antagonists are in development. Dabigatran, a direct thrombin inhibitor studied in the RE-LY trial (Randomized Evaluation of Long-Term Anticoagulation Therapy), proved superior to warfarin without an increased incidence of major bleeding.[34] Several factor Xa inhibitors are being examined in phase 3 trials.[34–36] The comparative efficacy of these agents versus warfarin and their impact on utilization require further evaluation.

Data from large healthcare systems and electronic medical records may provide key data on practice patterns in AF management and contribute to improving the outcomes of patients with AF.[37] Such "real-world data" will facilitate comparative effectiveness research and may allow comparisons of the effectiveness of treatments as used in routine clinical practice. Given the important health policy implications of conclusions about the comparative effectiveness of various diagnostic and treatment approaches, caution should be exercised in drawing either positive or negative conclusions from observational analyses alone, although such findings may be instrumental in directing definitive prospective randomized trials that are sufficiently powered for noninferiority conclusions. The large numbers of patients in these databases also may allow examination of understudied subgroups. Several AF registries are being developed, including SAFARI (Safety of Atrial Fibrillation Ablation Registry Initiative), a national registry of AF catheter ablation procedures, and ORBIT-AF (Outcomes Registry for Better Informed Treatment of Atrial Fibrillation), whose primary objective is to assess real-world patterns of care and outcomes of patients with AF.[38] The major recommendations related to AF prevention and stroke prevention, epidemiology, outcomes, and cost are summarized in Table 2.

Table 2. Recommendations From the AHA Atrial Fibrillation Research Summit: Epidemiology, Outcomes, Cost, AF, and Stroke Prevention

Encourage international, multiinstitutional, multidisciplinary teams to collaborate in research and integrate approaches to AF prevention.
Determine the cause of variation in AF epidemiology, presentation, risk factors, and prognosis by age, sex, and race/ethnicity.
Develop strategies to detect and monitor AF more effectively in individuals and large populations.
Develop more accurate clinical, imaging, biomarker, and genomic phenotyping to more rigorously classify AF.
Evaluate AF risk-prediction instruments and the added clinical utility of novel markers.
Systematically ascertain the burden and impact of AF in all regions of the world.
Conduct randomized clinical trials of primordial, primary, and secondary AF prevention.
Refine stratification for risk of systemic thromboembolism, intracranial hemorrhage, and other major bleeding.
Improve implementation of proven stroke prevention guidelines, particularly in underserved populations.
Characterize the clinical outcomes, cost, and impact on quality of life and utilization of antithrombotic therapy of new anticoagulants.
Design, fund, and conduct rigorous comparative effectiveness and safety studies of AF therapeutic approaches.
Create and realign meaningful provider, institutional, and payer incentives to encourage participation in databases and registries.
Develop better models of cost in AF management that include quality of life, patient/provider adherence, clinical outcomes, and healthcare utilization.
Develop methods to facilitate the use of cost-effectiveness models by clinicians.

AHA indicates American Heart Association; AF, atrial fibrillation.

Meeting the Clinical Challenges and Redefining the Therapeutic Goals of AF

Antiarrhythmic drugs are likely to remain essential components of any comprehensive therapeutic strategy of maintaining sinus rhythm in patients with AF.[39] Recently, drug development for AF has emphasized multichannel blockers with less potential toxicity than amiodarone, including novel ion channel targets (eg, I_{Kur} blockers, late I_{Na} blockers, calcium current modulators), and non–ion-channel therapeutic targets (eg, fibrosis, gap junctions, and inflammation).[40,41]

Novel approaches being evaluated to prevent AF are the use of statins, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and omega-3 fatty acids.[42] In addition to improving clinical outcomes in patients with heart failure and prior myocardial infarction, angiotensin-converting enzyme inhibitors and angiotensin receptor blocker agents appear to prevent the atrial electric and structural remodeling associated with AF through hemodynamic, antiproliferative, antiinflammatory, antioxidant, and antiapoptotic effects.[42] These agents have been shown to be antisympathetic and to prevent the development of left atrial stretch and interstitial fibrosis, as well as adverse atrial electric remodeling. However, these effects have not yet been clearly translated into clinical benefit, because there have been mixed results for the efficacy of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in prevention of AF. The evidence-based medicine that supports the use of these agents to prevent AF is insufficient to merit incorporating their use into clinical practice guidelines. Similarly, statins have been shown to possess antiinflammatory, antiischemic, antioxidant, and antiarrhythmic effects while having a beneficial effect on modulation of autonomic tone; however, there have been mixed results related to the efficacy of statins in the prevention of AF. Other potential targets for prevention of AF are aldosterone and endothelin 1 antagonists, but no meaningful clinical data are available.[42]

An important issue related to AF clinical trial design is the selection of optimal monitoring approaches and end point definitions.[39] Traditional end points for AF drug trials have been time to first symptomatic recurrence and total recurrences over time. The total burden of AF, however, may be a better measure of the effectiveness of therapy. Use of this end point will require better understanding of the advantages and disadvantages of intermittent monitoring, 30-day full-disclosure monitors, and implantable loop recorders to quantify the burden of AF and the correlation of AF burden with clinically important end points such as mortality, stroke, and quality of life. The prognostic significance of asymptomatic episodes of AF and the clinical implications of the burden of AF remain unknown.[39]

Although intermediate end points are more easily measured, adequate rate control and the number and timing of AF recurrences do not necessarily correspond to the clinical value of a drug and the patient's prognosis.[39,43,44] Recurrent AF as an outcome may be satisfactory in young patients with highly symptomatic AF; however, AF recurrence fails to tell us about the effects of a given therapy on the most important outcomes, including stroke incidence, cardiovascular morbidity, cardiovascular mortality, total mortality, healthcare costs, New York Heart Association functional class, quality of life, and exercise tolerance.

The ATHENA trial (A Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg BID for the Prevention of Cardiovascular Hospitalization or Death From Any Cause in Patients With Atrial Fibrillation/Atrial Flutter) showed that antiarrhythmic drug therapy decreases cardiovascular hospitalizations.[45] The major mechanism of dronedarone benefit is probably linked to a combination of decreasing the recurrence of AF and decreasing heart rate, particularly the ventricular response in the presence of AF.[45] However, other effects that antiarrhythmic drugs may have on cardiovascular and noncardiovascular mortality or morbidity, as well as extracardiac effects, remain uncertain.[46] Assessment of rhythm control should be focused not only on recurrence of symptomatic arrhythmias but also on objective measurements of cardiovascular morbidity, mortality, hospitalizations, functional status, quality of life, and cost.[39]

There remain many limitations to the randomized controlled trials evaluating catheter ablation of AF compared with antiarrhythmic agents.[47,48] Further trials are needed to evaluate catheter ablation of AF versus the strategy of rate control or rhythm control. Mortality, freedom from recurrent AF, costs, resource utilization, cost-effectiveness, and impact on quality of life should be included as end points. The Catheter Ablation versus Antiarrhythmic Drug Therapy for Atrial Fibrillation Trial (CABANA) is an ongoing multicenter study of catheter ablation versus pharmacological therapy as treatment of symptomatic AF.[49] This multicenter randomized study is intended to address many of the limitations of previous studies. Nonetheless, like other clinical trials, CABANA will provide only limited insight into important aspects of this procedure such as the techniques, safety, and long-term effectiveness of AF ablation in routine clinical practice. There is a need to address the limitations of available data and other key concerns about the safety of AF ablation with robust registry data.[38] As noted for catheter ablation of AF, complications, mortality, freedom from recurrent AF, costs, resource utilization, cost-effectiveness, and impact on quality of life should be included as end points for the maze procedure and other surgical approaches to AF.[48,50,51] Additionally, prospective multicenter clinical trials are needed to better define the relative safety and efficacy of various surgical tools and techniques for surgical ablation of AF.[48,50,51]

The investigation of advanced approaches to AF management requires an understanding of the complex interplay between AF and heart failure. The prevalences of both conditions are increasing in concert, particularly with an aging population.[52] Heart failure and AF frequently coexist, with heart failure representing an important risk factor for developing AF and AF contributing importantly to the morbidity of patients with heart failure, particularly those without left ventricular dilation and with preserved left ventricular ejection fractions.[1,2] Both the hemodynamic and neurohormonal perturbations of heart failure likely contribute to the pathogenesis of AF via both mechanical and structural changes within the atria. A number of studies have suggested that inhibition of the renin-angiotensin-aldosterone axis reduces the incidence of AF, an effect that may be mediated via reduced atrial stretch, prevention of adverse atrial remodeling, or both.[42] Research into prevention and management of AF should consider the interaction of these 2 conditions, exploration of mechanistic interactions, examination of relationships between treatment effects on both arrhythmic and heart failure–related end points, and addressing the expanding population in which these 2 conditions coexist.

A substantial body of clinical and experimental data indicates that sleep apnea and AF commonly coaggregate.[53–56] Estimates from population-based research suggest that individuals with moderate to severe sleep apnea are

Table 3. Recommendations From the AHA Atrial Fibrillation Research Summit Meeting: Meeting the Clinical Challenges and Redefining the Therapeutic Goals in AF

Evaluate the efficacy and safety of agents with antifibrotic properties.
Evaluate alternative upstream therapies (statins, ACE inhibitors/ARBs, fish oil) to prevent onset and recurrences of AF.
Evaluate efficacy and safety of atrium-selective I_{Na} blocker combinations shown to exert potent synergistic actions in experimental models of AF (ie, ranolazine and dronedarone combination).
Identify appropriate end points for observational studies, comparative effectiveness studies, and clinical trials of AF.
Evaluate whether the burden of AF and benefits of therapies are related to symptoms, QOL, functional status, and cardiovascular outcomes.
Develop a QOL metric that is specific to patients with AF and one that can measure the effect of AF on symptoms as well as outcomes.
Develop methods to efficiently measure AF burden, outcomes, and cost rather than process metrics.
Explore the interactions between AF and heart failure, including mechanistic interactions and relationships between treatment effects on both arrhythmic and heart failure–related end points; develop management strategies that address the expanding population in which these 2 conditions coexist.
Identify the heart rates and duration of AF that result in tachycardia-induced cardiomyopathy.
Compare rhythm control by use of antiarrhythmic drug therapy with catheter ablation of AF.
Conduct clinical and mechanistic studies defining the interactions among sleep apnea–mediated changes in cardiac structure, autonomic function, and inflammation and their impact on AF.
Define strategies for prevention of postoperative AF.
Systematically evaluate strategies for a surgical cure of AF.
Provide both provider and health system incentives to design and embed quality and performance improvement in EMRs, track application of evidence-based therapies and improve patient outcomes.
Design and research decision support tools to enhance clinicians' abilities to implement evidence-based treatment and guidelines.

AHA indicates American Heart Association; AF, atrial fibrillation; ACE, angiotensin-converting enzyme; ARBs, angiotensin receptor blockers; QOL, quality of life; and EMRs, electronic medical records.

approximately 4-fold more likely to have AF than those without apnea and that the occurrence of apneas during sleep may serve as a trigger of paroxysms of AF.[57–59] These observations suggest that sleep apnea contributes to AF incidence and recurrence or that there are common mechanisms, such as altered autonomic tone, linked to the pathogenesis of both conditions. Because sleep apnea prevalence appears to be increasing in conjunction with the obesity epidemic, it is possible that unrecognized and untreated sleep apnea may be a significant contributor to the rising population burden of AF. Sleep apnea may provide a new intervention target for the prevention and management of AF. Reversal of sleep apnea–associated hypoxemia, intrathoracic swings, and autonomic imbalance may attenuate triggers for AF.

Multifaceted strategies to facilitate the process of improving clinical care have emerged, with an emphasis on evidence-based medicine, clinical practice guidelines, quality metrics and performance measures, and patient outcomes.[60] By facilitating measurements of cardiovascular healthcare quality, performance measurement sets may serve as vehicles to accelerate appropriate translation of scientific evidence into clinical practice. Application of performance measures related to AF should provide a mechanism through which the quality of medical care can be measured to improve patient outcomes. The major clinical recommendations related to AF are summarized in Table 3.

Conclusions

Although considerable progress has been made in understanding the mechanisms of AF and preventive and treatment strategies, it is evident that much remains unknown. Prevention and treatment of AF will ultimately depend on understanding the pathophysiology in the individual patient. Understanding of several key aspects of AF, including the patterns of its occurrence in different populations, risk factors, and underlying pathophysiology, will result in identification and testing of prevention and treatment strategies. A concerted effort is thus needed on several fronts, as outlined by the recommendations in Tables 1, 2, and 3, to optimally predict, prevent, and treat AF and thereby improve patient outcomes.

Sources of Funding

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Appendix

Session I: Epidemiology, Outcomes, Cost, AF, and Stroke Prevention

Section Editor: Sana M. Al-Khatib, MD, Duke University, Durham, NC. *Moderators:* Mark A. Hlatky, MD, Stanford School of Medicine, Stanford, CA; Elaine Hylek, MD, MPH, Massachusetts General Hospital, Boston, MA.

Translating Evidence Into Practice: Reducing Death and Disability Due to Stroke—In Perspective of Ideal Health and Prevention: Ralph L. Sacco, MS, MD, FAHA, FAAN, University of Miami, Miami, FL.

Prediction and Prevention of AF: The Decade Ahead: Emelia J. Benjamin, MD, ScM, FAHA, Boston University Schools of Medicine and Public Health, Boston, MA.

The Global Burden of AF: Sumeet S. Chugh, MD, Cedars-Sinai Medical Center, Los Angeles, CA.

AF in Ethnic Minorities: What Are the Unanswered Questions? Alvaro Alonso, MD, MPH, PhD, University of Minnesota, Minneapolis, MN.

Utilizing Health Maintenance Organizations and Electronic Medical Records to Advance Knowledge in AF: Alan S. Go, MD, Kaiser Permanente of Northern California, Oakland, CA.

Improving Patient Outcomes in AF: Registries, Comparative Effectiveness: Sana M. Al-Khatib, MD, Duke University, Durham, NC.

Developing Better Models of Cost in AF Management: Brian F. Gage, MD, Washington University, St Louis, MO.

New Developments in Anticoagulation for AF: Michael D. Ezekowitz, MBChB, DPhil, FRCP, FAHA, MD, Lankenau Institute for Medical Research, Wynnewood, PA.

Session II: Mechanisms of AF: Basic and Translational Science and Genetics

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Atrioventricular Distinctions in Ion Channels as the Basis for Development of Atrial-Selective Drugs in the Management of AF: Charles Antzelevitch, PhD, FACC, FAHA, FHRS, Masonic Medical Research Laboratory, Utica, NY.

Sleep Apnea, Experimental Hypertension, and AF: Autonomic and Structural Considerations: Susan Redline, MD, MPH, Brigham and Women's Hospital, Boston, MA.

Novel MRI Markers of Cardiac Fibrosis: Michael Jerosch-Herold, PhD, Brigham and Women's Hospital, Boston, MA.

Fibrosis and AF: Lixia Yue, PhD, University of Connecticut Health Center, Farmington, CT.

Mechanisms of AF in Hypertrophy, Endothelin, Angiotensin Signaling: David R. Van Wagoner, PhD, FAHA, Cleveland Clinic, Cleveland, OH.

Novel Pathways for Pharmacological Treatment and Prevention of AF: Peng-Sheng Chen, MD, Indiana University School of Medicine, Indianapolis, IN.

Session III: Meeting the Clinical Challenges in AF

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Therapies to Prevent AF: Statins, ACE-I/ARB, Omega-3 Fatty Acids: Anne B. Curtis, MD, FHRS, FACC, FAHA, The State University of New York, University at Buffalo.

Strategies for AF Management: Reevaluating Rate and Rhythm Control: Ken A. Ellenbogen, MD, FAHA, Virginia Commonwealth University, Richmond, VA.

New Pharmacological Agents for AF: John P. DiMarco, MD, PhD, University of Virginia Health System, Charlottesville, VA.

Ablation of AF: Addressing the Gaps in Knowledge: Douglas L. Packer, MD, Mayo Clinic, Rochester, MN.

Session IV: Redefining the Therapeutic Goals of AF

New Initiatives From the NHLBI: Yves D. Rosenberg, MD, MPH, National Heart, Lung, and Blood Institute, Bethesda, MD.

Prevention of Postoperative AF and Advancing the Surgical Frontier for Cure of AF: Richard Lee, MD, Northwestern Medical Center, Chicago, IL.

Developing and Validating Standardized and Quantitative Approaches to Understanding the Burden of Asymptomatic and Symptomatic AF on Quality of Life: Eric N. Prystowsky, MD, FAHA, St Vincent Hospital, Indianapolis, IN.

AF Clinical Guidelines, Performance Measures, and Quality Metrics: Improving Clinical Outcomes in AF Patients: N.A. Mark Estes III, MD, FAHA, Tufts University, Boston, MA.

Disclosures

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Douglas L. Packer	Mayo Clinic	Biosense Webster*; Boston Scientific*; CryoCath*; EP Limited*; Medtronic*; Minnesota Partnership for Biotechnology*; NIH*; Siemens AG*	None	None	None	Financial interest in mapping technology licensed to St Jude Medical†	Biosense Webster*; Boston Scientific*; CyberHeart*; Medtronic*; Sanofi-Aventis*; St Jude Medical*; Toray Industries*	None
Sunny S. Po	University of Oklahoma Health Sciences Center	None	None	Biosense*	None	None	None	None

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Advisory Group Disclosures, *Continued*

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Eric N. Prystowsky	The Care Group	Sanofi-Aventis†; fellowship support from Boston Scientific†, Medtronic†, and St Jude†	None	None	None	CardioNet†; Stereotaxis†	Boehringer Ingelheim†; Medtronic†; Sanofi-Aventis†; Stereotaxis†	None
Susan Redline	Case Western Reserve University/ Brigham and Women's Hospital	Received contract from Dymedix Inc to perform apnea/hypopnea sensor validation studies; receive CPAP units by Philips Respironics for use in NIH-funded research	None	None	None	None	None	None
Yves Rosenberg	National Institutes of Health	None	None	None	None	None	None	None
Ralph L. Sacco	University of Miami	None	None	None	None	None	None	None
David R. Van Wagoner	Cleveland Clinic	GlaxoSmithKline†	None	None	None	None	None	None
Kathryn A. Wood	Duke University School of Nursing	None	None	None	None	None	None	None
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This table represents the relationships of advisory group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (1) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (2) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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