

# Full Report from the First Annual Heart Rhythm Society Research Forum: A Vision for Our Research Future, “Dream, Discover, Develop, Deliver”

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## 1. Introduction

The Heart Rhythm Society (HRS) organized a research forum held on December 14–15, 2010, to develop a vision for future arrhythmia research and to design practical approaches to ensure these visions are realized. The goal of the present communication is to summarize the discussions and recommendations of this research forum.

The core purpose of the HRS is to improve the health of patients with heart rhythm disorders.<sup>1</sup> In addition to the ability to end death and suffering due to bradycardia by implanting cardiac pacemakers, members of this society were largely responsible for the invention and refinement of implantable cardioverter-defibrillators (ICDs), radiofrequency catheter ablation techniques, surgical treatment of cardiac arrhythmias and improved strategies of drug therapy. Multiple clinical trials have been performed by Society members to evaluate and document the effectiveness of therapeutic approaches to various cardiac arrhythmias.

Despite these advances, heart rhythm disorders remain a major cause of mortality and morbidity in United States and in other parts of the world. Sudden cardiac death (SCD) continues to claim more than 250,000–400,000 U.S. lives annually,<sup>2,3</sup> accounting for 15–20 percent of all deaths.<sup>4,5</sup> Over 50 percent of all of coronary heart disease deaths are sudden, occurring out-of-hospital and in the emergency

room,<sup>6</sup> and survival rates from cardiac arrest remain poor.<sup>7</sup> At the same time, the percentage of the population afflicted with atrial fibrillation (AF) is growing exponentially.<sup>8,9</sup> An estimated 5.1 million people are diagnosed with AF in the United States at present, and this number is expected to rise to 7.5 million by 2020 and to 12.1 million by 2050.<sup>10</sup> The population afflicted with AF is further affected by the clinical sequelae of AF, which include thromboembolic stroke,<sup>11</sup> heart failure (HF),<sup>12</sup> cognitive dysfunction,<sup>13</sup> increased mortality,<sup>2</sup> and a lower quality of life.<sup>14</sup> Therefore, despite our best current efforts, heart rhythm disorders remain major public health problems.

In 2009, HRS embarked upon a bold strategic plan with the “big audacious goal” of “ending death and suffering due to heart rhythm disorders.” To achieve this ambitious goal, fundamental advances in our understanding of arrhythmia mechanisms are needed to facilitate the effective treatment and/or prevention of arrhythmias in our patients. Thus, research was identified as a top priority.<sup>1,15</sup> Several HRS initiatives were proposed, including efforts to establish a more robust research funding portfolio targeting early stage and transitional investigators, expanding the research focus during the Annual Scientific Sessions and more complete integration of biomedical investigation into the fabric of the Society—in short, to establish a sustainable research culture.

To ensure that heart rhythm research receives sufficient attention from its membership, the Society organized a research forum held on December 14–15, 2010. The goal of the forum was to develop a vision for future arrhythmia research and to design practical approaches to ensure these visions are realized. Attendees included HRS members and stakeholders in arrhythmia research, as well as representatives from the National Institutes of Health (NIH), National Heart, Lung and Blood Institute (NHLBI), the American Heart Association (AHA), Food and Drug Administration (FDA), Centers for Medicare & Medicaid Services (CMS), industry, patient care organizations, patient advocacy groups and affiliated scientists. Representatives from the European and Asian Pacific Heart Rhythm Associations also participated in the discussion. The attendees reaffirmed that “Ending death and suffering due to heart rhythm disorders” is the goal of HRS, and that this audacious goal can only be achieved through collaborative efforts between scientists and clinicians interested in heart rhythm research. While the forum was mainly convened to address American research, many of the issues raised cross geographic and political boundaries and the recommendations may also be readily transportable to other jurisdictions.

In his opening remarks, 2010–2011 Heart Rhythm Society President Douglas L. Packer, MD, emphasized how creating a research culture within the Society will require the participation of all Society members in each step of the research process. While research scientists play a paramount role in this process, each individual clinician must embrace

the concepts critical to progress in research. The following is a summary of the discussions in the Research Forum.

## 2. Keynote addresses

### 2.1. Exceptional opportunities in biomedical research

Francis S. Collins, MD, PhD, Director of the National Institutes of Health, provided Forum attendees with his vision regarding “exceptional opportunities” present in biomedical research today. Dr. Collins highlighted five areas that are ripe for major advances and poised to create substantial downstream benefits in relation to arrhythmia research: (1) Use of high throughput technology to understand fundamental biology, (2) Translation of basic science discoveries into new and better treatments, (3) Comparative effectiveness research and randomized trials, (4) Increasing focus on global health and (5) Reinvigorating and empowering the biomedical research community.<sup>16</sup>

Development of high-throughput technologies has allowed investigators to approach complex systems in a much more comprehensive fashion. In arrhythmia research, genome wide association studies (GWAS) have identified links between genetic variations and QT interval duration. Further development of technologies in areas such as DNA sequencing, imaging, nanotechnology, proteomics, metabolomics, small-molecule screening, and RNA interference has the potential to further revolutionize our understanding of the basic determinants of arrhythmias. Furthermore, these technologies will spur the production of massive and complex data sets requiring investments in computational biology.

A second opportunity is in translational research. NIH proposes to develop the National Center for Advancing Translational Sciences, with a goal to establish focused, integrated and systematic approaches for linking basic discovery research with clinical care; to develop new tools and approaches for accelerating development of therapeutics; and to enhance translational research activities by other NIH Institutes and Centers.

A third opportunity is putting science to work for the benefit of health care. NIH is committed to improve the nation’s health system by promoting comparative effectiveness research. NIH has supported many successful randomized trials that have directly impacted the care of patients with heart rhythm disorders. Examples of NIH-supported clinical arrhythmia trials include Cardiac Arrhythmia Suppression Trial (CAST), Multicenter Unsustained Tachycardia Trial (MUSTT), Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM), Sudden Cardiac Death in Heart Failure trial (SCD-HeFT) and more recently Catheter Ablation Versus Anti-arrhythmic Drug Therapy for Atrial Fibrillation (CABANA).

A fourth opportunity is to encourage a greater focus on global health. Dr. Collins noted that cardiovascular disease is projected to increase significantly in low income populations as a cause of death, while infectious disease is projected to decrease over the next 30 years. The increasing

importance of cardiovascular diseases in the economically disadvantaged creates an opportunity for research to better address this health care challenge in the future.

Finally, there is an opportunity to reinvigorate and empower the biomedical research community through three transformative grant mechanisms. It is estimated that due to the reduced NIH budget, the overall success rate per grant application will drop below 15 percent in 2011, the lowest since 1978. Therefore, NIH is investing in (a) The Transformative R01, to support both individuals and collaborative teams with no budget limit per proposal up to budget cap for the program as a whole (\$25 million total costs per year for 5 years), (b) the NIH Director's Pioneer Award, which supports exceptionally creative individual scientists and (c) the New Investigator Award, which supports a small number of exceptionally creative new investigators to support a pipeline of outstanding and creative scientists.

## 2.2. Opportunities & challenges for embracing a research future

Susan Dentzer, Editor-in-Chief, *Health Affairs*, and Health Correspondent, PBS, provided her perspective on the challenges and opportunities for building a "culture of research" in the current environment of U.S. health care reform. In 2010, the U.S. spent \$2.6 trillion on health care overall, while health research accounted for only 5.5 percent of total health care spending.<sup>17</sup> Since 1982, growth in research and development spending has been slower than the increase in overall health care spending. There are still major disparities in health across the nation. Between 1982 and 2001, the gap in life expectancy among Americans grouped by geographic location and ethnicity has essentially remained unchanged.<sup>18</sup> A random survey in 12 metropolitan areas reported that only 54.9 percent received recommended health care according to guidelines, and this low level of performance was similar in the areas of preventive care, acute care and care for chronic conditions.<sup>19</sup>

The Patient Protection and Affordable Care Act plans to address these disparities and inadequacies in our current health care system by expanding medical coverage to a projected 32 million Americans from 2014 to 2019. Growth in national health spending is projected to be 9.2 percent in 2014, versus a growth rate of 6.6 percent in 2014 that was expected prior to the enactment of health reform legislation.<sup>20</sup> The Patient Protection and Affordable Care Act will also present new opportunities for health care systems and comparative effectiveness research. Key initiatives include the creation of the Patient-Centered Outcomes Research Institute, new centers for Medicare and Medicaid innovation, incentives for adoption of electronic health records (EHR), improved patient registries and performance reporting. A major example of how these initiatives can spur research is the current National Cardiovascular Data Registry (NCDR), which includes the CMS-mandated ICD Registry™. As of April 2010, the registry had collected data on more than 520,000 implants in the United States reflecting roughly 10,000 ICD implants per month.

Ms. Dentzer presented a vision where the U.S. Department of Health and Human Services (HHS) might build a high-performing comparative effectiveness research system. New policies and investments should exploit EHR, computerized databases, data sharing and research networks. A national database for effectiveness research studies could be established if HHS would support all of these pieces and take the lead in creating a rapid-learning culture for the U.S. health care system.<sup>21</sup> The Institute of Medicine (IOM) will also be studying potential sources of variations in health care spending and utilization across the country for individuals with Medicare, Medicaid, private insurance, or no insurance, which provides further opportunities for health systems research.

The Affordable Health Care Act will also promote shared decision-making between patients and physicians. Part of this will be through the provision of grants for the development and use of shared decision-making aids, new measures to access shared decision-making tools and the creation of shared decision-making resource centers. The CMS will provide support to test innovations that assist individuals in making informed health care choices. In conclusion, Ms. Dentzer urged HRS to take advantage of the opportunities to participate in these changes and not to underestimate the sweeping changes that will take place in our health care system over the next decade.

## 3. Discovery to practice: overcoming barriers to innovation and implementation

Development of an audacious and clear research vision requires consideration of the barriers to discovery and innovation that may be encountered in establishing that program. During the HRS research forum, several potential obstacles to program implementation were considered from NIH, FDA, Clinical Trialist, and Basic Scientist perspectives.

### 3.1. The National Institutes of Health (NIH) perspective

Michael S. Lauer, MD, Director, NHLBI, Division of Cardiovascular Sciences, reviewed past barriers to the practice of medicine that could arise again. A major barrier to the exploration of innovative concepts has been an unwillingness to depart from pre-established dogma derived from observational studies. Examples of this reluctance over the generations included practices ranging from blood-letting to the prescribing of thalidomide in pregnant women, and to the combination of aggressive chemotherapy and bone marrow transplantation for breast cancer. This has been evident in the resulting resistance to the design and conduct of definitive randomized clinical trials and adoption of their outcomes. For instance, although it was recommended in 1993 that aggressive chemotherapy and bone marrow transplantation be tested in such prospective clinical trials, it took nearly 20 years to conduct suitable investigations.<sup>22</sup> Researchers were unsuccessful in advocating for randomized clinical trials because of the *apparent* strength of observa-

tional studies to that time.<sup>23</sup> Ultimately, a randomized trial found the aggressive treatment strategy to be less effective, but only after an estimated 30,000 breast cancer patients had been treated based on observational studies alone.<sup>22</sup>

For heart rhythm disorders, these obstacles were successfully overcome with the completion of a number of large scale clinical arrhythmia trials. Over the past two decades, the CAST, MUSTT, Antiarrhythmics Versus Implantable Defibrillators (AVID), AFFIRM, and SCD-HeFT trials have aggressively tested specific treatment strategies. This has removed substantial barriers to innovation by demonstrating a clear-cut path for definitive science to establish the actual risks and benefits of therapy. The CABANA trial, now underway, will examine the utility of catheter ablation versus antiarrhythmic drug therapy for patients with AF. Randomized clinical trials and comparative effectiveness research will similarly go much further in that regard, as outlined in the recent NHLBI Conference on Comparative Effectiveness Research.<sup>24</sup> Dr. Lauer recommended that maximal progress within the HRS research program would be fostered by informing treatment decisions via these approaches.

### **3.2. Food and Drug Administration (FDA) vantage point**

Bram D. Zuckerman, MD, SUPV Medical Officer, provided an overview of the FDA perspective on the translation of discovery to practice and inherent obstacles likely to be faced. Establishment of the safety and effectiveness of medical devices, the fundamental FDA mission, requires investigator and industry partners to avoid a quick-fix mentality and move appropriately through rigorous scientific evaluations to identify a factual basis for supporting therapy. This is difficult since science is continually evolving, devices are becoming increasingly more complicated, and existing regulatory pathways initially established in 1976 are becoming outdated. The pre-market approval process was held up as a necessary first-line approach to establishing reasonable assurance of patient safety and effectiveness earlier in the drug or device evaluation process. In the discovery process, it nevertheless remains a challenge to find the right balance between potentially burdensome pre- and post-market evaluations. The FDA continues to seek an appropriate amount of premarket data to make primary decisions about the approvability of devices, which can then be supplemented with post-market information to evaluate device and operator performance in therapeutic applications. Dr. Zuckerman nevertheless proposed that more creative approaches be used to identify and correct inherent device or drug testing difficulties at an earlier stage in the process. Such efforts to decrease barriers to innovation requires 1) improving the predictability and transparency of the entire regulatory process, 2) early interaction with FDA by those presenting new discoveries, 3) providing sufficient safety information through adequate bench or animal testing and computational studies and 4) improving trial design and

execution by focusing on processes that minimizes bias and other confounding factors.

Limitations of traditional statistical approaches directed at single and composite endpoints were cited as additional barriers in the transition from discovery to device or drug development and application. In the future, a complete revolution in trial designs and approaches will likely be needed to optimize the process without compromising quality. Additional collaboration by public and private partnerships, the use of information from outside the U.S., and the development of performance goals in conjunction with professional societies will also be helpful. The clinical trials transformation initiative (CTTI) seeks to build public-private partnerships and modernize the conduct of and infrastructure for clinical trials, which should be helpful in bridging gaps in the transition process.

### **3.3. Barriers from the clinical trialist view point**

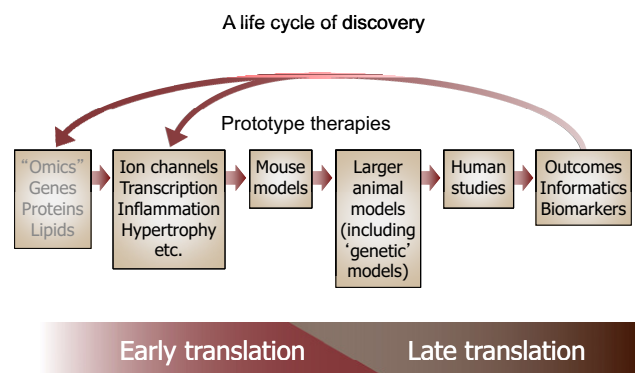
From the trialist perspective, it was considered critically important to overcome actual barriers to innovation and implementation that occur in conducting clinical trials. Participation in clinical trials requires, among other things, infrastructure, time and funding. These resources are severely limited in the current clinical practice setting. The current practice incentives in medicine focus on patient throughput, rather than participation in educational endeavors or scientific investigation. Infrastructure for conducting trials is frequently lacking as funding has eroded and as the traditional research study coordinator or nurse's time is redirected towards strictly clinical practice. All of these requirements must be viewed as affordable and acknowledgement for participation in clinical trials re-established.

At both local and national levels, the process of start up of a trial center is bogged down in extensive and growing institutional review board (IRB) requirements, ethics reviews, management of intellectual property, and the time required to negotiate contracts between primary study coordinating centers and individual clinical trial centers. Each of these regulatory and legal components is excessively burdensome, and central IRBs and/or contracting centers may be of substantial benefit in minimizing these barriers.

A shortage of cardiovascular specialists and inadequate research training also creates barriers.<sup>25</sup> The collection of research data, limitations of medical records and quality control all similarly loom large as barriers to conducting trials. Within the U.S., each of these barriers contributes to incremental concern about the "globalization" of clinical trials to international sites.<sup>26</sup> Integrated reporting with the creation of mega-databases may be an alternative, where information gathered in the process of clinical care is readily available for clinical trials and registries<sup>27</sup> as well as for quality, performance and public reporting purposes. In each of these, the clinician remains at the middle of the reporting process but should be supported, in turn, by the practice organization.

Clinical trial funding remains an ever increasing barrier to the successful transfer of ideas from discovery, develop-

## Opportunity: Where does “basic” or early translational science fit in the HRS missions?



ment, and design to the actual idea or product deployment.<sup>25</sup> Available NIH funds are limited, as are foundation dollars. Industry money has also been viewed as “tainted” by the apparent accompanying conflicts of interest. Such a view may be inappropriate, provided the oversight is in place to maintain study quality and avoid exclusive control of clinical trials by industry.<sup>28</sup>

Finally, dealing with the time demands of clinical practice should be possible through providing protected or compensated time, along with clinical trial infrastructure incentives, to facilitate the successful identification and recruitment of appropriate patients for specific clinical trials. The development of clinical research within thematic areas to support a “learning health care system”<sup>29</sup> must be more carefully considered to bridge over gaps in research and eliminate unnecessary barriers to progress. These issues are further reviewed in the Work Shop Summary of the IOM’s Forum on Drug, Discovery, Development, and Translation.<sup>30</sup>

### 3.4. The investigator perspective

Our ability to reach the goal “to end suffering and death from arrhythmias” will require improved understanding of arrhythmia mechanisms in order to create better approaches to arrhythmia prevention and treatment. Fundamental and clinical investigations will undoubtedly lead to the development of novel diagnostic techniques that will help to identify those at great risk of arrhythmic disease<sup>3</sup> and to target this population with increasingly efficacious and individualized therapies. Collectively, scientists will need to embody a broad set of skills to study very basic arrhythmia mechanisms, at the level of molecules and cells, and integrated systems, including animal models and patients. It is convenient to consider discovery domains as having early and late translational components (Fig 1). Taken together, early and late translational research contributes to a “life cycle of discovery” where therapeutic outcomes in patients provide feedback

(through evidence from patient satisfaction, cost, quality measures, morbidity, mortality and biomarkers) that informs early and late phases of translation.

One of the most tenuous phases in the arrhythmia research pipeline is in early translational research. Early stage translational research has traditionally relied primarily on financial support from NIH and private foundations. The amount of NIH money for research, including cardiovascular research, has not grown significantly over the past half decade when indexed to inflation,<sup>31</sup> and the recent increase in research funding related to the American Recovery and Reinvestment Act of 2009 (ARRA) economic stimulus package, which was minimal in overall scope, is now over. At the same time, the capacity for private foundations to fund early stage research has been challenged by the recession. The AHA, traditionally a major source of research funding for young cardiovascular scientists, has reduced the fraction of its budget dedicated to research to 20 percent. Late stage translational research tends to be more expensive than early stage translational research, and is typically performed with industry funding or by public private partnerships. Because of the greater amount of money required, funding from HRS will be less likely to impact the late stage translation than the early stage translation.

Clearly, there are multiple methods through which the Society might support arrhythmia researchers. A strong, vibrant national meeting with cutting-edge science and a sufficient number of travel awards for the most promising trainees can help to attract new scientists to the field. Early and late stage investigators will benefit from accessible databases with informatics support. Investigators, particularly early stage investigators, may benefit from mentoring in grant writing, laboratory management and career-building. HRS will need to identify and resolve current obstacles that prevent skilled and talented scientists from selecting and continuing arrhythmia research.

## 4. HRS research vision (achievements, obstacles, and opportunities)

### 4.1. Societal advantage

The North American Society of Pacing and Electrophysiology (NASPE) was formed in 1979 and transitioned to its current name, the Heart Rhythm Society, in 2004. Research has always been a major focus of the Society’s mission, and the focus on research has paid off. Breakthrough developments in pacemakers, ICDs, radiofrequency catheter ablations, resynchronization therapy and comparative effectiveness research in antiarrhythmic drugs have revolutionized the care of patients with heart rhythm disorders. A recent survey of HRS members shows that a large percentage of members are actively participating in clinical trials. Due to its associated hospital networks, diverse patient populations and membership that includes highly trained physicians, basic scientists and allied health providers, HRS provides unique and exceptional opportunities for clinicians, clinician-scientists, basic scientists and allied health providers to leverage their areas of expertise in the areas of opportunity

highlighted by Dr. Collins and Ms. Dentzer. The ultimate goal is to transform HRS into the pre-eminent global leader in innovative clinical research and health care delivery in heart rhythm disorders.

#### 4.2. Annual scientific sessions

The Society's Annual Scientific Sessions has become the preferred national meeting for a majority of the clinicians and investigators focused on heart rhythm disorders. Among the physicians who attend Annual Scientific Sessions, 52 percent did not attend other conferences. In 2009, Postertown was initiated, creating a novel venue for scientific discourse between junior and senior investigators, as well as a forum for interaction between investigators and clinicians. In addition, the Basic and Translational Research Forum attracted participants to a full-day symposium focused on electrical remodeling and arrhythmia mechanisms. The annual Douglas P. Zipes Lecture was incorporated into the symposium as the keynote lecture.<sup>32,33</sup>

#### 4.3. Early career awards and funding

Most successful clinician-scientists report an early interest in research.<sup>34</sup> Consequently, recruiting and/or redirecting talented early career researchers to a focus on arrhythmia research has the potential to provide enormous value and "return on investment" for HRS. Development efforts that target funding of graduate student stipends, post-doctoral fellowships and early faculty investigators engaged in the most promising arrhythmia science have a high potential to shore up the early pipeline for new knowledge and candidate arrhythmia therapies.

The Society currently actively funds research fellowship awards for those with an excellent track record in their early careers. When recently surveyed, the overwhelming majority (84 percent) of prior HRS Research Fellowship award recipients reported that the fellowship had been very valuable in their career development. Almost all (98 percent) indicated that some of their current professional time was devoted to research, and 55 percent devote at least half of their time to research. Prior recipients were equally distributed across investigative disciplines, with 54 percent participating in basic science, 50 percent in translational research, and 46 percent in clinical research. More than half have gone on to receive a Career Development Award (K Award) and 44 percent were subsequent recipients of at least one NIH Research Project Grant (R01). These results support the success of our current research funding efforts and demonstrate our ability as a society to train future investigators.

Although the present HRS Research Fellowship program has successfully facilitated the early stage of many young careers, these awards do not yet address the transition from career awards to independent funding, a major hurdle in the lifecycle of an investigator where attrition often occurs. The number of new investigators funded by the NIH did not keep pace with the increasing volume of applications that occurred during the time of NIH prosperity.<sup>35</sup> As a result,

the average age when a first independent NIH grant is received has climbed from 34.2 years to 41.7 years.<sup>36</sup> NIH has responded to this concern by creating NIH-wide initiatives for Early Stage Investigators that include separate extended pay lines and accelerated resubmissions. The Society can provide arrhythmia researchers with a competitive advantage at this critical time. An HRS program could leverage existing federal programs for identification of highly meritorious awards in arrhythmia research, thus improving the efficiency and limiting the administrative cost of the program. These awards could then be utilized as a supplement to career awards to provide preliminary data for an R01 application, or as bridge funding during this vulnerable period when an independent research effort is being established.

#### 4.4. Driving clinical research in heart rhythm disturbances

In a recent survey of Society membership,<sup>37</sup> the overwhelming majority of respondents value clinical research highly and 74 percent wish to increase their participation in clinical trials as sites. However, many respondents indicated that their participation in trials was limited by factors such as the lengthy process of obtaining IRB approval and lack of appropriately trained research staff, as well as challenges with securing protected time and funding. In order to promote clinical research, HRS could establish a clinical trial network (HRS.Trialnet) (see Section 5.2) that would organize its membership into a consortium of clinical research sites and pair member sites with subscribed trials from the NIH, industry and private industry-initiated studies. In addition to facilitating traditional clinical trials in heart rhythm disturbances, this network could also be a resource for conducting large-scale registries, comparative effectiveness research, and establishing a collection of biospecimens. When the concept of an HRS clinical trial network was introduced to Society members, 73 percent agreed that this was an important concept.

### 5. Working groups/recommendations

Attendees of the HRS Research Forum were organized into four working groups. These groups further considered the obstacles and opportunities present in each focus area, in an effort to arrive at formal recommendations to present to the HRS leadership. A summary of these discussions and recommendations follows.

#### 5.1. Leadership roles and collaborations

HRS recognizes and supports the importance of research education broadly. The Association of American Universities, Association of Public Land-grant Universities, and The Science Coalition recently performed public opinion research to analyze how registered voters feel about the federal government's role in and proposed cuts to scientific research. The pollsters found that the number of voters who think the federal government should increase its spending in scientific research has declined steadily from 45 percent in

1997 to 36 percent in 2011. Therefore, societies such as HRS will need to increase public awareness of the favorable impact that research has on the public health in the U.S. and throughout the world.

Second, advances in treatment of cardiac arrhythmias require fundamental discovery. Today there is an appropriate emphasis on translational research and establishing “proof-of-concept” in targeted patient populations. However, translational research will not be successful if there is insufficient basic discovery to translate.

Third, achievement of the goal to end death and suffering from heart rhythm disorders would also benefit from strategic influence over national research funding directions and priorities. New treatments for cardiac arrhythmias, such as AF and ventricular tachycardia/ventricular fibrillation (VT/VF), would benefit from prospectively established national programs that integrate basic, translational, and clinical research to achieve new breakthroughs in treatment.

Fourth, accredited training programs in clinical cardiac electrophysiology are not yet effectively incorporating this potential pool of clinical investigators into a nationally organized research consortium. Moreover, most trainees and program directors do not appreciate the vital role these new physicians could serve to rapidly test new therapies under the aegis of a national and collaborative clinical research mandate. This mandate could correct the current approach of subjecting patients to new but unproven treatments that are billed to third-party payers by requiring the establishment of benefit of new treatment options using common protocols through nationally organized clinical research programs prior to allowing referrals for new therapies.

### 5.1.1. Recommendations

- Develop an educational kit that emphasizes the importance of research; explains where it is performed; details funding sources; describes the training requirements of scientists and physician-scientists; defines basic, translational, and clinical investigation; provides examples of success and stresses its impact on the economy.
- Utilize the educational kit to advocate and build awareness of research among HRS members, government, patients, media, and the public.
- Engage HRS members to identify two or three heart rhythm abnormalities that should be targeted for a comprehensive basic, translational, and clinical research strategic plan.
- Identify gaps of fundamental knowledge in these selected rhythm disorders that become the focus for new discovery.
- Champion basic research to allow the future performance of meaningful translational research.
- Collaborate with the NIH, FDA, and industry to develop novel and budgeted NIH-sponsored and integrated basic, translational, and clinical research programs targeted to

these new discovery needs and their translation to clinical medicine.

- Further enrich training programs in clinical cardiac electrophysiology by developing and mandating practical education in clinical research emphasizing the critical role HRS clinicians and allied health professionals must assume to facilitate enrollment of patients in clinical trials.
- Embrace and advocate for a culture change among HRS physicians and allied health professionals to enroll or refer patients for enrollment in clinical trials as a better alternative to performing procedures in areas where questions remain regarding the efficacy and safety of the therapy.
- As a Society, take the initiative to work together with NIH, FDA, other professional societies, patient advocacy organizations and industry to identify and favorably impact the current roadblocks to performing clinical research.

### 5.2. Clinicians and clinical trials: HRS.trialNet

This Working Group identified the fundamental need for a mechanism enabling clinical investigators to more effectively identify active trials and sites for participation, for patients to easily identify studies relevant to their heart rhythm condition, and for study sites to identify such patients on a regional and national basis. Based on the central position of research in the Society’s Strategic Plan<sup>37</sup> and the pre-eminent international position of HRS within the field, the Working Group recommended that HRS facilitate clinical research in heart rhythm disorders by creating HRS.TrialNet. Subsequent to the Research Forum, HRS convened a Working Group that met in March 2011 to further discuss the implementation of HRS.TrialNet. The recommendations from both these meetings are outlined below.

#### 5.2.1. Recommendations

- Develop a HRS.TrialNet with the following mission statement: “To leverage the pre-eminent position of Heart Rhythm Society to foster and facilitate novel clinical trials and comparative effectiveness research in heart rhythm disorders.”
- Provide a database of member sites that detail clinical volume, expertise and interests, research infrastructure, IRB and contracting timelines, past performance and site cost. It was recommended that the database include elements that capture measures of quality, such as whether a particular site has well-trained research coordinators and infrastructure, information on data integrity and summary data on prior audits from regulatory bodies or sponsors. Domain-specific indices may also be included, such as procedural times, or numbers of board-certified physicians.
- Provide normative and comparative data from the database.
- Develop a database of ongoing clinical trials in heart rhythm disorders, providing a more focused but more detailed resource than general trial databases.

- Provide training and possibly certification of coordinators and sites.
- Facilitate the development of uniform IRB language or possibly a centralized IRB process.
- Serve as a liaison to related societies and patient advocacy groups to enhance access to patient populations for clinical trials.
- Provide an accessible resource for efficiently conducting large-scale registries, comparative effectiveness research, trials requiring specific phenotyping, collecting biospecimens or expanding small trials from single-center to a few sites.
- Design and launch a pilot project in the near term to demonstrate the feasibility and potential of HRS.TrialNet in a scalable fashion enabling growth to encompass all desired components of the Initiative over time. To this end, the Group decided that the most feasible pilot would involve creation of a scalable relational database to pair study sites with ongoing trials.
- Consider the inclusion, during the initial phase of HRS.TrialNet implementation, of roundtable discussions between the Society and clinicians from countries currently underrepresented in clinical trials. The roundtables could be convened during the next fiscal year, each having the objective of refining and adapting TrialNet to best meet the goals of these constituents. The eventual goal is to expand the HRS.TrialNet into the preeminent global network to conduct clinical trials in Heart Rhythm disorders.
- Compete successfully for NHLBI funding for Arrhythmia Trial Net studies, ranging from registries to comparative effectiveness research comparable to those ongoing in the current Heart Failure [Trial.net](#).

It was recommended that the broad HRS membership be engaged to guide final development of HRS.Trialnet, in particular by providing features that would be of value to different constituencies.

### 5.3. Advancing research careers

As outlined by several speakers in the Forum, a steady flow of young investigators is critical to the continued development of new strategies and therapies for reducing morbidity and mortality of cardiac arrhythmias. HRS has the opportunity to play an important role in the development of young investigators, but there are many challenges to establishing programs to attain this goal. Attracting clinical and basic investigators into electrophysiology research careers is an important first step.

Many medical students and physicians receive minimal exposure to cardiac electrophysiology. By the time they begin training in cardiology fellowship, they are often following other paths in cardiology, fostered by encounters during medicine training. Incorporating research opportunities and training into clinical electrophysiology training programs is challenging. Providing protected time for research, while ensuring adequate clinical training, is difficult

for many programs. By the time a physician has completed clinical electrophysiology training, substantial educational debts are common, increasing the pressure to enter private practice. Even in academic environments, clinical electrophysiologists are subject to pressures to build and maintain clinical volume that reduce the time available for research pursuits. The Society recognizes these factors and is potentially in a position to aid investigators. However, HRS is currently seen primarily as a professional society, with a limited profile for fostering and supporting research.

#### 5.3.1. Recommendations

A number of potential programs have been suggested by which the Society could foster the development and retention of investigators focused on arrhythmia research:

- Creation of a new HRS-sponsored Early Faculty Transition Award: This new incremental two-year grant program would support junior faculty in the critical transition to independent investigator.
  - 1) The program could leverage existing federal programs for identification of highly meritorious awards in arrhythmia research, thus improving the efficiency and limiting the administrative cost of the program. Junior faculty that have been awarded a K Award (i.e., K08, K23, AHA Scientist Development Grant or equivalent) will be eligible to apply for this award after the second year of funding. The K Award submission and an update including published and in press papers with a description of the relevance of the research to the mission of the Society will constitute the application.
  - 2) The Early Faculty Transition award could be tied to institutional commitments for support and then be utilized to obtain additional protected time, preliminary data, and/or bridge funding prior to obtaining an R01. This prestigious award would provide our very best junior investigators with a competitive advantage in applying for independent funding.
  - 3) There could also be an option to extend the funding to the period beyond the K Award, with the goal of facilitating creation of a research program that would successfully compete for RO1 funding.
- The need also exists for HRS-sponsored Bridging Awards for investigators facing significant gaps in research funding who received meritorious scores on NIH applications that were not funded due to current low pay lines. This future award would require additional successful fundraising in order to be viable.
- Create an HRS-sponsored mentorship network. Such a program would allow mentors outside a trainee's institution to link up with mentees, potentially at the Society's Annual Scientific Sessions or other educational programs. As part of this mentorship network, HRS could create a white paper on "How to be an Effective Mentee" for junior investigators.



- Increase advocacy for heart rhythm research at early stages of development. Potential HRS initiatives that would increase interest in research and awareness of Heart Rhythm disturbances at an early stage in training could include:
  - Travel awards for early-stage clinicians, which would provide funding for cardiology residents to travel to the Annual Scientific Sessions.
  - Sponsorship of a retreat for cardiology residents who wish to explore the possibility of a career in cardiac electrophysiology.
  - Pilot educational programs and health fairs aimed at science students, even as early as high school, to increase awareness of the public health implications of cardiac arrhythmias.

#### 5.4. Mechanisms for supporting and funding research

Fundamental advances in understanding the pathophysiology and improving the treatment of cardiac arrhythmias and cardiovascular disease are critically needed for the Society to reach its big audacious goal of “ending death and suffering due to heart rhythm disorders.” These advances can only be made if we are able to support and fund the research that makes such advances possible. Some of the opportunities and challenges associated with generating the support for this mission are as follows.

##### 5.4.1. Recommendations

- Enhance awareness of the HRS “brand.” For potential donors to consider supporting the Heart Rhythm Society, they must not only be aware of the Society but must also think of the HRS *first* when issues related to rhythm disorders come to mind. We propose a series of steps that may enhance awareness of the HRS brand, and develop the HRS as a destination for major philanthropic gifts:
  - Enhance awareness of the HRS by co-branding rhythm related education and research efforts with the AHA, ACC, industry and other interested organizations. Build bridges with the leadership of these organizations, with a focus on synergy of efforts.
  - Develop multi-media educational campaigns that use iconic individuals to simultaneously target awareness of the limitations of current technology to prevent sudden cardiac death or atrial fibrillation while building awareness of the HRS mission and brand.
  - Consider public educational campaigns that highlight the role of HRS support in the scientific advances made by clinicians and scientists currently involved in heart rhythm research who received early career research support by the HRS.
- Simultaneously focus on enhancing the role of the HRS in supporting heart rhythm research and awareness of the Heart Rhythm Foundation (which has as its mission to enhance the prevention and treatment of cardiac rhythm disorders by supporting the research, education and ad-

vocacy efforts of the Society) as a top destination for philanthropy. For donors to consider major gifts, they must be convinced that their funds will support research that makes a difference.

- Create a rigorous system of peer-review for awards that will fund outstanding basic scientists and physician investigators committed to careers focused on heart rhythm related research. Consider the support of outstanding proposals that do not quite meet the threshold needed for NIH support. Provide enough funds in these awards that they are both prestigious and helpful. It may be useful to make the funds flexible so that they can be used either to increase protected time (clinical researchers) or used for supplies (basic scientists).
- Re-focus the mission of the Heart Rhythm Foundation as the primary funding mechanism for HRS-supported research efforts. This will help to delineate the philanthropic efforts of the society from industry-supported activities. Recruit professional fund raisers who can target affluent and influential donors for philanthropy. Involve Society member scientists and/or physicians in the call process, to highlight the donation to bench (or trial) connection.
- Improve partnerships with patient advocacy groups. Many of these groups are interested in supporting research but have little or no infrastructure for the critical review or support of research. HRS could manage the review and administration of awards that are supported by both the Society and the advocacy group. It would be straightforward for the awards to recognize both groups.

## 6. Conclusion

Recent advances in genomics, bioinformatics and pharmacology offer the potential to dramatically improve our understanding of the fundamental mechanisms of arrhythmogenesis and thus to pursue more mechanistically based treatment and prevention strategies. Due to long-term budgetary constraints, federal funding of heart rhythm research faces enormous challenges. For those passionate about the Society’s mission, this is an exciting time — we have a unique opportunity to have a major impact on the training and conduct of heart rhythm related research that will bring us ever closer to the goal of ending death and suffering due to heart rhythm disorders.

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**Author Disclosures:** Report from the First Annual Heart Rhythm Society Research Forum

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Mark E. Anderson, MD, PhD	None	None	NIH (f), Fondation Leduq (f)	None	Allosteros Therapeutics (b)	Allosteros Therapeutics (b) (intellectual property rights)
Michael E. Cain, MD	None	None	None	None	None	
Glenn I. Fishman, MD	None	None	National Institutes of Health (f), New York State (f)	None	American Heart Association – Founders (a) Topera, Inc. (a)	
Sanjiv M. Narayan, MD, PhD	American College of Associate Cardiology (Associate editor for JACC) (c), St. Jude Medical (b), Biotronik (b), Medtronic Corporation (b), Gilead, Inc. (b)	None	None	St. Jude Medical (e), Biotronik (c), Medtronic Corporation, (d), Boston Scientific (d), Biosense Webster (c)		University of California, San Diego (owns intellectual property) (a), Topera, Inc. (ownership/partnership/principal), (e)
Jeffrey E. Olgin, MD	None	None	Medtronic (f), Zoll (f), Gilead (f), NIH (f)	Medtronic (d), Biotronik (d), Biosense Webster (d), St. Jude (d), Boston Scientific (d)	None	
Peter M. Spooner, PhD	None	None	NIH/NHLBI, Leduqq Fondation	None	None	Johns Hopkins University (salary) (f), US Patent on Cardiac Risk Genotype (a)
William G. Stevenson, MD	None	None	None	None	None	American Heart Association (Editor) (d), Patent for Needle Ablation, Consigned to Brigham and Women's Hospital (a)
David R. Van Wagoner, PhD	None	None	NIH (f), Fondation Leduqq European North American AF Research Alliance (f)	None	None	

**Author Disclosures:** Report from the First Annual Heart Rhythm Society Research Forum

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Douglas L. Packer, MD	Biosense Webster, Inc. (Speaker/Adv. Board) (a), Cardialysis (Adv. Board) (a), Endosense (Adv. Board) (a), CyberHeart (Adv. Board) (a), Medtronic CryoCath LP (Speaker/Adv. Board) (a), Sanofi-Aventis (Speaker/Adv. Board) (a), Siemens AG (Adv. Board) (a), St. Jude Medical (Speaker/Adv. Board) (a), GE Healthcare (Adv. Board) (a), Philips Healthcare (a), CardioFocus (Adv. Board) (a), InnerPulse (Adv. Board) (a), Coherex (Adv. Board) (a), OrthoMcNeill (Adv. Board) (a), NACCME (a), Skyline Ventures (Adv. Board) (a), Toray Industries (Adv. Board) (a), Imricor (Adv. Board) (a)	None	NIH (f), Medtronic CryoCath LP (f), Siemens AcuNav (a), Thermedical (EP Limited) (d), Endosense (a), EpiEP (c), EP Advocate (b), Population Health Research Institute-Hamilton Health Sciences General Hosp. (a), St. Jude Medical (f), Minnesota Partnership for Biotechnology and Medical Genomics/ University of Minnesota (f), Biosense Webster (f), Inc., Boston Scientific (a)	None	None	Blackwell Publishing (royalty) (b), St. Jude Medical (royalty) (e)

(a) = \$0.  
 (b) = <\$10,000.  
 (c) = >\$10,000 to <\$25,000.  
 (d) = >\$25,000 to <\$50,000.  
 (e) = >\$50,000 to <\$100,000.  
 (f) = >\$100,000.