In 2017, the Vanderbilt Heart & Vascular Institute (VHVI) continued to expand its innovative clinical and research programs.

We recruited additional world-renowned faculty, set new records for procedural volume in multiple areas, reached new heights in research funding, and launched several new fellowship programs.

Electrophysiology, advanced heart failure, and cardiac transplantation saw continued growth in their clinical and academic programs. We recruited Gregory Michaud, M.D., as the new director of electrophysiology. He was joined soon thereafter by two of his former colleagues: William Stevenson, M.D., and Roy John, M.D. The newly-expanded section gives Vanderbilt one of the most comprehensive electrophysiology programs in the world, with the ability to address the most complex clinical cases.

Our heart failure and transplantation program added two faculty: Lynne Stevenson, M.D., and Jonathan Menachem, M.D. For the second consecutive year, Vanderbilt was the second busiest heart transplant center in the United States, with 83 adult heart transplants.

We continued to actively recruit in other areas as well, welcoming Brian Lindman, M.D., as the new medical director of our structural heart and valve center, Melissa Levack, M.D., to our cardiac surgery program, Temujin Dinaram, M.D., to our Columbia practice, and Sheila Collins, Ph.D., to our basic science team.

Our research program continued its impressive expansion. Total NIH funding has increased by 135% since 2013. In the past year, we were awarded two new Strategically Focused Research Network grants from the American Heart Association (AHA). With these grants, Vanderbilt is one of only a few institutions to have three AHA center grants (in Prevention, Obesity, and Vascular Disease). VHVI faculty also continue to play leading roles in national precision medicine efforts, including the NIH’s “All of Us Research Program,” for which Vanderbilt is the Data and Research Center.

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Vanderbilt Heart & Vascular Institute is home to one of the leading cardiac electrophysiology programs in the world (Figure 1). In 2017, the program grew even stronger with the addition of three faculty members who have made important contributions to the field of cardiac electrophysiology: Gregory Michaud, M.D., Chief of the Arrhythmia Service, Roy John, MBBS, Ph.D., Director, Advanced Management of Ventricular Arrhythmias, and William Stevenson, M.D., Director, Cardiac Arrhythmia Clinical Research Program.

The electrophysiology program offers a comprehensive set of advanced services, making it a preferred destination for the care of patients with complex cardiac arrhythmias. Christopher Ellis, M.D., directs one of the busiest left atrial appendage closure programs in the country. VHVI offers appendage closure using both endocardial and epicardial devices, tailoring the best approach to the patient. Clinical trials assessing new devices and optimal management approaches to protecting patients from stroke are ongoing, providing patients with access to the latest technology.

The lead extraction program led by George Crossley, M.D., is one of the three busiest in the country and features an exceptional safety record.

Dan Roden, M.D., has made seminal contributions to the understanding of long QT syndrome and other inherited arrhythmia syndromes. Along with Kathy Murray, M.D., and Ben Shoemaker, M.D., few programs offer comparable breadth of experience in dealing with complicated sudden death syndromes that involve families.

Dr. Michaud is a leader in catheter ablation of atrial fibrillation (AF) and has provided important insights that enhance the success and safety of the procedure. He directs an experienced team (Pablo Saavedra, M.D., Jay Montgomery, M.D., and Sharon Shen, M.D.) that provides radiofrequency (RF) ablation, cryoablation, and hybrid endocardial/epicardial ablation approaches tailored to the individual patient. In addition, multiple ongoing clinical protocols give patients access to the latest advances.

Dr. Stevenson is a pioneer in the ablation of complex ventricular arrhythmias. His approach to identifying sites for ablation (cardiac mapping) has become a standard in the field. Along with Dr. John, Arvindh Kanagasundram, M.D., and Ashish Shah, M.D., Chairman of Cardiac Surgery, VHVI has one of the most advanced VT ablation programs in the world, offering surgical and catheter ablation, as well as approaches to modify central nervous system triggers. VHVI is one of four centers in the world offering ablation with a needle catheter, invented by
Dr. Stevenson, which is designed to intervene on sites that are inaccessible to other methods (Figure 2). Further, in many patients, severe ventricular arrhythmias are a manifestation of cardiomyopathy and heart failure. In such cases, arrhythmia management is coordinated with the cardiomyopathy and cardiac transplantation services to optimize care and outcomes.

This clinical expertise is coupled with a commitment to clinical and basic science research designed to unlock novel treatments for difficult-to-treat arrhythmias in the years ahead.

**Electrophysiology Cases**

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<th>Year</th>
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<td>3,332</td>
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<td>2017</td>
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*Figure 1*
Figure 2: Needle electrode successfully terminates incessant ventricular tachycardia (VT) in a patient for whom conventional approaches had failed.
New Vascular Programs

Vanderbilt’s Marfan Syndrome and Aortic Disorders Center has had an auspicious first year. Highlighting our focus on serving patients with this syndrome, we created a regional full-day Marfan Symposium in March 2017, convening patients and their families from Nashville, surrounding cities and neighboring states. Duke Cameron, an international leader in the surgical treatment of Marfan syndrome, served as keynote speaker. Working with the Marfan Foundation, the Aortic Center faculty and staff offered lectures on medical therapy and diagnosis, surgical repair strategies, potential ophthalmologic and obstetrical complications, and quality of life as it relates to Marfan Syndrome.

The Vanderbilt Marfan Syndrome and Aortic Disorders Center brings together specialists in Cardiovascular Medicine, Cardiothoracic Surgery, Vascular Surgery, Orthopedics, and Ophthalmology to harness the necessary expertise to provide the highest level of care in a collaborative, team-based approach. As an example, less than a year after the official launch of the Aortic Center (in the fall of 2016), experts from different departments came together at a critical moment to provide comprehensive, cohesive care to a high-risk aortic and obstetric patient so that both mother and child could leave the hospital together. The coordination of expertise, services, and care providers creates an environment conducive to the optimal care of patients at every level of severity. With offerings of minimally invasive therapies up to complex surgical repair, a collaborative health care team approach to patient care, and nationally recognized expertise, our center is now a premier regional site for aortic care.

The addition of the Arteriopathy Clinic to VHVI has enabled comprehensive care for the patient with complex arterial disorders, particularly fibromuscular dysplasia (FMD) and spontaneous coronary artery dissection (SCAD). Reasons for referral have ranged from questions about potential diagnoses to second opinion consults regarding ongoing symptoms or proposed procedures. In recognition of the complex medical and psychological burdens that accompany these diagnoses, which often affect young persons without traditional cardiac risk factors in the prime of their lives, the Vanderbilt SCAD Patient Symposium was held in August 2017. This symposium was a tremendous success with registrants from over 14 states who attended the meeting. The day was patient-centered and presentations were delivered in language patients could understand. Speakers were from varied disciplines including cardiology, interventional cardiology, neurology, and neurosurgery. The goal of the Arteriopathy Clinic is to provide patients insight into the diagnosis and management or surveillance strategy for these complex disorders. Patients are also provided education regarding their diagnoses, opportunities to participate in patient-centered organizations (such as the FMD Society of America and the SCAD Alliance), and opportunities to participate in research.

Referrals to the Marfan Syndrome and Aortic Disorders Center and the Arteriopathy Clinic may be obtained by calling (615) 343-9188.

Contributors

Joshua Beckman, M.D.

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The goal of the Arteriopathy Clinic is to provide patients insight into the diagnosis and management of these complex disorders.
Cardiac Transplantation

The Vanderbilt Heart Transplantation and Mechanical Support Program continues to be a national and international leader, exploring innovative approaches to improve access and outcomes in the field. Over the last three years, adult cardiac transplantation volumes at Vanderbilt have experienced dramatic growth (Figure 1).

Indeed, the Vanderbilt Heart Transplantation Program has become the second largest program in the United States, with 160 heart transplants performed in the past two years. The program recently passed 1,000 total heart transplants, a milestone achieved by only a handful of programs nationally. The number of multi-organ transplants continues to rise as well, and a rare heart-liver transplant was performed in June (only 18 heart-liver transplants were done in the entire country in 2016). Outcomes remain outstanding, with a one-year survival of 90% in 2016 and 97% in 2017.

An exciting new initiative involves the use of Hepatitis C Virus (HCV)-positive donor hearts. Under the direction of Mark Wigger, M.D., and Kelly Schlendorf, M.D., Vanderbilt now has the largest experience with HCV-positive donor hearts in the world with 33 donor hearts accepted. A report of the first 13 recipients is in press (Schlendorf K et al. “Early outcomes using hepatitis C-positive donors for cardiac transplantation in the era of effective direct-acting antiviral therapies”). The experience of the first 27 patients will be presented at the International Society for Heart and Lung Transplantation conference in 2018, along with early results for renal function, coronary allograft vasculopathy, development of anti-donor HLA antibodies, outcomes in recipients with renal dysfunction, and post-operative complications.

The group is beginning a research protocol to study the use of personalized immunosuppression based on age and several immunologic factors. The rationale for this study is outlined in an opinion piece published in the Journal of the American College of Cardiology: Heart Failure entitled “Older and wiser: personalized immunosuppression in Cardiac Transplantation”.

![Figure 1](image-url)

**Contributors**

**JoAnn Lindenfeld, M.D.**

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**Mark Wigger, M.D.**

**Kelly Schlendorf, M.D.**
the current era” (Richa Gupta M.D., MPH, Kelly Schlendorf, M.D., and JoAnn Lindenfeld M.D.).

There are also exciting developments in the use of mechanical circulatory support as a bridge to transplantation. For 50 years, cold storage for limited periods of time has been the cornerstone of organ preservation. However, the emergence of ex vivo perfusion has the potential to reshape this paradigm. Led by Ashish S. Shah, M.D., Chairman of Cardiac Surgery and Surgical Director of the Heart Transplant program, Vanderbilt will participate in the EXPAND trial. Utilizing the Transmedics Organ Care System (OCS), our heart transplant team will recover and resuscitate hearts felt to be unusable. The portable OCS system allows investigators to safely support hearts for extended periods of time and over a larger geographic area (Figure 2).

Figure 2: Transmedics Organ Care System.
New arrivals

- **Brian Lindman, M.D.**, was recently recruited from Washington University in St. Louis as the Medical Director of the Structural Heart and Valve Center and Associate Professor of Medicine.

- **Melissa Levack, M.D.**, just completed her cardiac surgery training at Cleveland Clinic, where she developed particular expertise in valve and aortic surgery. She is an Assistant Professor of Cardiac Surgery.

Clinical program

The structural heart and valve program at VHVI continues to grow. We have an active multidisciplinary heart valve clinic in which patients are seen by both a cardiologist and cardiac surgeon to determine what treatment options are most appropriate for each patient. The decisions and recommendations are discussed and reviewed in our weekly valve conference. Procedural volumes have grown every year, with 245 percutaneous valve cases performed in 2017.

Over the last two years, **Joseph Fredi, M.D.**, has led our adoption of accessing the abdominal aorta through the inferior vena cava (“transcaval approach”). Transcaval access to the aorta has emerged as a valuable alternative strategy for catheter based valve interventions in patients whose aorto-iliac arterial anatomy precludes a standard transfemoral arterial approach. To date, 35 transcaval procedures have been performed with excellent results and minimal bleeding complications. **Dr. Fredi** spearheads our innovation in transcatheter therapies for mitral and tricuspid valve disease, and is joined on the interventional side by **Mark Robbins, M.D.**, and **Marshall Crenshaw, M.D.**, in the performance of transcatheter aortic valve replacement (TAVR) procedures. **Clay Kaiser, M.D.**, and **Ben Barton, M.D.**, provide surgical expertise and collaboration in our transcatheter program. **Jeff Carr, M.D.**, offers expertise in the performance and interpretation of cardiac CT used in our pre-procedural planning for these procedures. **Dr. Lindman** and **Michael Baker, M.D.**, provide interventional echocardiographic guidance for transcatheter valve interventions, which are also supported by our colleagues in cardiac anesthesiology.

To date, **35 transcaval procedures have been performed** with excellent results and minimal bleeding complications.

Research program

**Dr. Lindman** is the principal investigator for several multicenter research studies coordinated and led by Vanderbilt, including:
• **Multicenter registry study for development of risk prediction models for outcomes after TAVR:** Vanderbilt is coordinating a multicenter registry funded by the Doris Duke Charitable Foundation that includes 10 other high-volume valve centers in the United States. Clinical, imaging, frailty, quality of life, and survival data are collected on patients undergoing TAVR, and blood is banked for biomarker analyses. Nearly 1,000 patients have been enrolled and the study is in a final follow-up phase. One activity is the development of models to predict survival and quality of life after TAVR.

• **ACTIVE AFTER TAVR (NCT03270124):** The goal of this multicenter study is to obtain pilot and feasibility data on novel tools (accelerometer and iPad-based computerized adaptive testing to assess quality of life) that could be used as efficacy endpoints in future adjunctive therapy trials after TAVR. We will also evaluate the feasibility and efficacy of a pragmatic in-home exercise strategy to increase daily activity and improve quality of life after TAVR.

• **Biobank core lab for the EARLY TAVR study:** The EARLY TAVR trial (Edwards Lifesciences) is a randomized, multicenter strategy trial comparing early valve replacement versus clinical surveillance with deferred valve replacement in patients with severe asymptomatic aortic stenosis. Under the direction of Dr. Lindman and Yan Ru Su, Ph.D., the Cardiovascular Core Lab for Translational and Clinical Research is serving as the biobanking core lab for the EARLY TAVR trial. This will facilitate numerous analyses to evaluate how biomarkers may be helpful in the clinical management of patients with aortic stenosis.

Vanderbilt is also participating as an enrolling site for several national TAVR trials, including:

• **Medtronic Low Risk TAVR Trial:** This trial is enrolling patients with severe aortic stenosis at low risk for surgery. Notably, asymptomatic patients can be included if they meet certain inclusion criteria. Randomization is to TAVR versus surgical AVR.

• **TAVR UNLOAD:** This multicenter strategy trial will compare TAVR + optimal medical therapy to optimal medical therapy alone in patients with moderate aortic stenosis and left ventricular dysfunction. It will test the hypothesis that unloading the ventricle when aortic stenosis is less severe is important in patients with impaired cardiac function.

VHVI offers state-of-the-art treatments for advanced valvular heart disease, using a patient-centered approach to select the optimal transcatheter or open surgical strategy.
The way we practice medicine is changing. We are moving to a model where “average” treatments, often identified across huge populations, will be complemented by a “precision” medicine approach that incorporates differences among patients into treatment decisions. While a lot of the buzz is around using genetics, the full precision medicine paradigm extends beyond genetics to integrate molecular, clinical, environmental, and behavioral information with the goal of improving our ability to predict which treatments will work best for specific patients, advance our understanding of underlying disease mechanisms, and discover novel diagnostic, preventive, and therapeutic approaches. The transition to precision medicine will not only require important scientific discoveries, but also innovations in the way health care is delivered, including improved integration of electronic health records (EHRs) and enhanced engagement of patients and providers. Vanderbilt University Medical Center (VUMC) is a national and international leader in efforts to meet these challenges. These initiatives are led by Dan Roden, M.D., Senior Vice President of Personalized Medicine and a senior faculty member at VHVI, in partnership with Joshua Denny, M.D., Professor of Biomedical Informatics and Medicine.

Denny leads the Precision Medicine Initiative (now called “All of Us”) Data and Research Center, supported by a $75 million award – the largest in VUMC history – from the National Institutes of Health (NIH). The All of Us Research Program, launched in 2015, is an unprecedented effort to improve our understanding of how differences between individuals can affect health and disease by gathering longitudinal data for at least one million individuals in the United States. Transformative in scale, All of Us will help enable precision medicine by providing researchers and patients a powerful platform to conduct research, develop new technologies, evaluate policies related to precision medicine, and deliver precision medicine to participants.

Roden and Denny also lead Vanderbilt’s participation in the Electronic Medical Records and Genomics (eMERGE) network. Supported by the National Human Genome Research Institute (NHGRI), eMERGE is a national collaboration across medical centers with DNA biorepositories coupled to EHRs to enable large scale genetic research. VUMC spearheaded this effort as the coordinating center for eMERGE since the network started 10 years ago and many in the field think that it was work in eMERGE that led to the creation of the All of Us program. eMERGE investigators have made important contributions to our understanding of the clinical impact of genetic variation, and are advancing precision medicine by developing protocols to return genetic information to patients and clinicians and tools for clinical decision support. The network is also addressing the cost-effectiveness of precision approaches and the ethical and legal implications of incorporating genetic information into the clinical environment.

An important goal of precision medicine is prediction of drug response and toxicity. Under Roden’s leadership, VUMC has been a site in the NIH’s Pharmacogenomics Research Network since 2001, and recently was one of only three sites to be successfully renewed. Current work at the Vanderbilt site has three major objectives: use of induced pluripotent stem cells (iPSCs) to study drug-induced cardiac arrhythmias (led by Roden), detection and prevention of adverse drug events using the EHR (Denny), and studies of immune-mediated drug reactions like the Stevens Johnson Syndrome, led by Elizabeth Phillips, M.D., Professor of Medicine.

Ultimately, scientific discoveries must be translated to the bedside to impact patient care, and VHVI and VUMC are among the first in the world to implement precision medicine into routine clinical care. As part of the VUMC Pharmacogenomic Resource of Enhanced Decisions in Care and Treatment (PREDICT) program, patients are “preemptively” genotyped for variants known...
to modify efficacy and/or toxicity risk for multiple commonly used drugs to help tailor therapy. Pharmacogenetic data are embedded in the EHR and presented to clinicians, with appropriate clinical support, when a relevant drug is prescribed. To date, PREDICT includes more than 14,000 patients, including more than 2,600 patients who have had genotype-informed selection of antiplatelet therapy after coronary stent placement.

The vision of Precision Medicine is very appealing, but there are many challenges to be addressed to determine how best to implement that vision. Through scientific advances ranging from molecular mechanisms to clinical implementation, VHVI and VUMC are leading the way.