GOOD NEWS!

Wake Forest University School of Medicine Cardiovascular Sciences Center

Spring 2023

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DR. GISSELLE MELÉNDEZ LEADS A STUDY AWARDED BY THE AMERICAN HEART ASSOCIATION'S STRATEGICALLY FOCUSED RESEARCH NETWORK

The American Heart Association Strategically Focused Research Network on Biologic Pathways of Chronic Psychosocial Stressors on Cardiovascular Health has awarded $15 million to research teams from 3 universities to study the biological mechanisms of chronic stress that can increase the risk of cardiovascular disease. The collaborative research project includes Ohio State University, University of California Davis and the Pauley Heart Center at Virginia Commonwealth University (VCU) with investigators at WFUSM partnering with the VCU team.

Assistant Professor of Internal Medicine and Comparative Medicine, Dr. Giselle Meléndez, MD, serves as the PI of the study at WFUSM which is a large (~$2.4 million) nonhuman primate project. Drs. Appt, Burkart, Shively and Kaplan are co-investigators. The focus of the VCU/WFUSM study is chronic psychosocial stress and cardiovascular dysfunction in cancer survivorship and it involves two basic science projects originating from the WFUSM nonhuman primate study and one clinical project at VCU. The project led by Dr. Meléndez, which is the second of the pre-clinical studies, is titled Role of chronic psychosocial stress on chemotherapy-induced cellular senescence and cardiac fibrosis. See the press release here.

CAREER CORNER

2023 SUMMER RESEARCH PROGRAMS TO INCREASE DIVERSITY IN BIOMEDICAL SCIENCE CAREERS:

The Cardiovascular Sciences Center and Sticht Center for Healthy Aging and Alzheimer’s Prevention host two summer research programs: the Excellence in Cardiovascular Sciences (EICS) program in the 31st year and the Enhancing UNderGraduate Education and Researchin AGing to Eliminate Health Disparities (ENGAGED – joint program with WSSU and WFU) in its fourth year. These programs are led by a collaborative team of faculty committed to increasing diversity in the biomedical sciences (BMS), including Drs. Tina Brinkley, Debra Diz, TanYa Gwathmey and David Soto-Pantója at WFUSM and Drs. Jill Keith (WSSU) and Gary Miller (WFU). The summer students are undergraduate students selected from across the country to participate in research topics related to aging and cardiovascular disease, as well as health disparities. Joint sessions and social activities are planned with summer trainees in programs sponsored by Biomedical Engineering, Microbiology & Immunology and Precision Medicine to provide networking and a sense of community. Many of the Cardiovascular Sciences Center members serve as program faculty and as mentors. We welcome these students to our research activities and thank the CVSC faculty who provide meaningful research experiences.
Advanced Imputation Methods

Missing data is a common occurrence in many datasets and is something you will probably run into when working with EMR data or survey data. As analytical methods advance, it has become more apparent that simple mean and mode imputation may not be appropriate for the complex datasets we work with as they can introduce bias or not meet the assumptions our predictive models need to make about the data. Two methods I often use are PPCA (Probabilistic PCA), for unsupervised analysis, and Random Forest Imputation, a supervised method. PPCA is best suited for high dimensional data where you are working with data that includes thousands of features and a handful of samples (omics data comes to mind). In a traditional predictive analysis case, random forest imputation would be more appropriate as it uses outcome data to help inform the imputation model.

Both methods use the known (non-missing) data to predict what the missing data would be so it would be wise to consider the distribution of missing data at the outset as too much could introduce random noise into the data after imputation. In most cases, it is assumed that the data is missing at random. This means the missing data can’t be explained by outside factors like data collection methods. For example, a subset of survey respondents are missing data for a set of questions because they never had the opportunity to answer them (for whatever reason). Another consideration is that these two methods only accept numeric data as input, so if your raw data includes text data you will need to consider recoding these variables.

These two methods can be implemented in R/R Studio using the “pcaMethods” and “randomForest” packages. They can also be used in other environments such as python or SAS.

Thanks for reading this edition of data tools and tips. Don’t hesitate to reach out to me if you have any questions or would like to talk more.

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ANNOUNCEMENTS

SHVI and Dr. Esther Kim hosted the first Spontaneous Coronary Artery Dissection (SCAD) Conference and Patient Symposium, which included faculty and patients who traveled to Charlotte from 25 different states plus DC and Australia in April 2023. Day 1 was a CME-accredited event with talks delivered by esteemed internal and external faculty from multiple institutions across the country. Day 2 was a non-CME conference for patients and their loved ones organized in partnership with SCAD Alliance.

The Cardiovascular Sciences Center (CVSC) is seeking proposals for the 2023 Pilot Award Program. The projects should be those in need of support to promote new areas or technologies for cardiovascular research (basic, clinical, population), as well as to foster new collaborations, particularly across the Atrium Health System. The goal of the CVSC Pilot Program is to allow investigators (particularly early career researchers) to pursue novel and innovative ideas that will improve the likelihood of obtaining extramural funding for their research. We encourage research that uses Institutional Cores and other shared resource. The funding is also meant to allow investigators to perform critical experiments, access core facilities or improve analyses to address specific critiques raised by reviewers for already submitted and reviewed applications. Completed applications will be due ~ Spring 2024. Please contact Dr. Liliya Yamaleyeva (lyamaley@wakehealth.edu) if you need further guidance.
During the months of January to April, CVSC members were awarded 29 new grants. Below we highlight some of these awards.

**Drs. Tomar (PI) and Jadiya (Co-I)** received a NIA Administrative Supplement for R00DK120876 “Impact of mitochondrial structure on cellular homeostasis and Alzheimer’s disease” from 05/16/2023 to 04/30/2024.

**Dr. Michael Bancks (PI)** received an R01 (1R03AG077368-01) from the NIA for the project period of 01/01/2023-12/31/2024. The proposed study will assess the epidemiology of potentially inappropriate medication use and risk for mild cognitive impairment and dementia among ARIC, Look AHEAD, and MESA study populations.

**Dr. Sarah Cilvik** was awarded an R01 from the NHLBI that will start 9/1/2023 for her project titled Developmental Origins of Cardiovascular Disease in Offspring from Nonhuman Primate Pregnancies at Advanced Maternal Age. Co-investigators include **Drs. Kylie Kavanagh** (Pathology-Comparative Medicine), Matt Jorgensen (Pathology-Comparative Medicine), **Giselle Meléndez** (Cardiology), Carmen Kiper (Pediatrics-Cardiology), Joshua Nitsche (Maternal Fetal Medicine), and **Andrew South** (Pediatrics-Nephrology).

A Notice of Award was received for an NHLBI-R21 (PIs Younghan, Akbilgic, Azarbarzin) titled “Deep learning of awake and sleep electrocardiography to identify atrial fibrillation risk in sleep apnea.”

A Notice of Award was received for an NHLBI-R01 (PI Akbilgic) titled “ECG-AI Based Prediction and Phenotyping of Heart Failure with Preserved Ejection Fraction.”

A Notice of Award (PI Akbilgic) was received for WFBMI Pilot Award titled “AI-assisted prediction of Fatal Coronary Heart Disease using 12-lead ECGs.”

A Notice of Award (PI Akbilgic) was received for WFBMI-NC State Wearable Medical Technology Pilot Funding titled “Evaluation of Left Arm ECG for Deep Learning Risk Prediction of Heart Failure.”

A Notice of Award (PI Akbilgic) was received for Wake Forest Innovations Award titled “ECG-AIR: MOTHERS NEED INNOVATIVE CARE (air-MONICA).”

**Allyn Howlett, PhD**, received the Notice of Grant Award from the National Institute on Drug Abuse to renew work on “Cannabinoid Receptors and Interacting Proteins” to begin June 1, 2023, for five years of support. This is a multi-PI grant with Dr. W. Todd Lowther, Co-Director of the Structural Biology Core in the Department of Biochemistry and Molecular Biology.

**Drs. Patricia E. Gallagher and Ana Clara Melo** received a $140,130 Capital Medical Equipment Institutional Grant for the purchase of a Sartorius Incucyte Live-Cell Imaging and Analysis System to quantify complex cellular changes in real time.

**Dr. Simon Mahler (PI) and Co-Is Jason Stoppyra, Anna Snavely, Nick Ashburn, Tara Hashemian, Doug Easterling, Matt Belford, Amresh Hanchate, Dave Pearson, Santosh Rao, Joe Miller, James McCord, and Wake Forest QPRO** have been awarded a 5-year R01 grant from AHRQ. This grant directly addresses how best to care for moderate risk patients in the era of high sensitivity troponins and will ensure that Wake Forest remains at the cutting edge and continues to lead the development of best practices for ED chest pain risk stratification in the U.S. and beyond.

**Dr. Andrew South** received a WFUSM CTSI Ignition Fund Pilot Award (5/2023 – 8/2023) for the project titled “The Relationship Between Preexisting Undernutrition and the Development of Chronic Kidney Disease and Cardiovascular Disease.” This pilot award provides funds to perform a rat model of undernutrition. The study is led by Learner-PI Kayla McMillian for her master’s thesis.
Dalane Kitzman, MD of Wake Forest and Nicole Cyrille-Superville, MD of Sanger Heart & Vascular Institute received Notice of Grant Award of $1.5M from the National Heart, Lung, and Blood Institute to support the development of the Wake Forest — Atrium Health HeartShare Clinical Center. The HeartShare Project is a $50M national effort to study heart failure treatment. As one of a planned 6 national clinical care centers, Wake Forest — Atrium Health is also positioned to receive further NIH funding in support of serving as a core laboratory for multiple aspects of the project.

Dr. Meléndez was awarded an NIAID R21 (1R21 AI68902-01A1) for her project “A novel, genetic model of IL-6 trans-signaling to interrogate cardiac fibrosis pathology.”

The 2023 CVSC Pilot Awards went to the following:

Saraschandra Vallabhajosyula, MD – Dept. of Medicine. $20,000. “Differences in Healthcare Delivery, Management and Outcomes of Cardiogenic Shock from Heart Failure versus Acute Myocardial Infarction” Co-Investigators – Olivia N Gilbert, MD MSc, P Matthew Belford, MD, David X Zhao, MD, PhD, David M Herrington, MD, MHS

Rong Chen, PhD – Dept of Physiology and Pharmacology. $20,000. “Interactions between the renin-angiotensin and dopamine system in the brain” Co-investigator – Liliya Yamaleyeva, MD, MS

Mark C. Chappell, PhD – Hypertension Center. $20,000. “Prorenin, renin and the prorenin receptor in septic shock patients: potential biomarkers of disease of severity” Co-investigators – Ashish Khanna MD, Christopher Schaich, PhD, MHS

Dr. Esther Kim was named chair of the Council on Peripheral Vascular Disease at the American Heart Association.

Pictured left to right: FMDSA President Brad Daar, Dr. Heather Gornik and Ester Kim. Two of the FMDSA Founders, Rich and Susan Gould and Executive Director, Pam Mace.
Dr. Sarah Civlik was invited to give a talk at the Center for Reproductive Health Sciences Seminar Series at Washington University School of Medicine in St. Louis, MO on April 7, 2023. Her presentation was titled “Adverse Pregnancy Outcomes and Developmental Programming in Nonhuman Primate Pregnancies at Advanced Maternal Age.”

Drs. Vallabhajosyula and Akbilgic presented at the Internal Medicine Grand Rounds on March 16, 2023. The title of the talk was “Most Influential Papers in Cardiovascular Medicine.”

Dr. Akbilgic presented “Artificial Intelligence to Unlock the Potential of Electrocardiogram in Disease Detection and Risk Prediction” at the NC State Advanced Self-Powered Systems of Integrated Sensors and Technologies (ASSIST) Center, April 12, 2023.

Dr. Xuewei Zhu was invited to present a seminar at the Center for Cardiovascular Research (CCR) at Washington University School of Medicine in their weekly CCR Seminar Series on April 27, 2023. Her seminar was titled “Regulation of Macrophage Immunometabolism in Acute and Chronic Inflammatory Diseases.”

Dr. Joseph Yeboah was invited to participate as a speaker at the 83rd Scientific Sessions of the American Diabetes Association panel titled “Above and Beyond the Regular Lipid Panel—Are Additional Measurements Really Needed?” The title of his presentation is “When to use Coronary Artery Calcium and New Imaging to Complement Lipid Panels.”

Drs. Akbilgic, Herrington and Soliman’s et al abstract has been accepted as a moderated poster presentation at the 2023 ESC in Amsterdam, Netherlands.


Dr. Andrew South’s research team presented 22 abstracts at the Pediatric Academic Societies Annual Meeting in April 2023 in Washington, DC, including 75% first-authored by learners (3 undergraduate students), 80% by women, and 25% by learners who are underrepresented in the biomedical sciences.

Dr. Dermot Phelan presented to NBA leadership and NBA team cardiologists at the NBA Combine in Chicago on May 19, 2023. His presentation was titled “Echocardiographic Quality in the National Basketball Association” and showcased all of SHVI’s work thus far on echo quality assurance for the league.

The following 7 abstracts from SHVI were presented at the 2023 ACC’s Cardiovascular Summit and 1 was awarded the best abstract award.

- Sanger Heart & Vascular Institute – Perfect Care Improves Patient Outcomes After Surgery. Shannon Crotwell, RN / Maya Gantt, RN / Yolanda Cousen, APP / Leslie Doyle, RN / James Reynolds, MBA / Larry Watts, MD / John Frederick, MD / Thomas Maxey, MD / William Downey, MD / Troy Leo, MD / Geoffrey Rose, MD / Kevin Lobdell, MD
- Sanger Heart & Vascular Institute – Health Equity Evaluation of the EVAR Patient’s Journey. Elizabeth Ross, MSN / Ethan Shi / Frank Arko, MD / Charles Briggs, MD / Stephanie Irausquin, PhD / William Downey, MD
- Leveraging Implantable Devices with Heart Failure Risk Stratification Features to Manage More Patients and Decrease Cost. Meghan Emig, MPAS, PA-C / Sanjeev Gulati, MD, FACC / Elizabeth Davenport, MSN, RN / Satish Misra, MD / Kelsey Guffey, MSN, MBA, RN
- Expanding Access to Efficient Evaluation for Advanced Heart Therapy Referral Leveraging a 3-Day Process. Taylor Foster, MBA / Joseph Mishkin, MD, FACC / Meghan Emig, MPAS, PA-C / Sarah Caldwell, CMA / Susan Bernardo, BSN, RN, CCTC / Hani Nabi, BSN
- Implementation of a 72-Hour Outpatient Cardiology Follow-up Pathway for Moderate Risk Chest Pain Patients Presenting to the ED. David Pearson, MD, MS, MBA / William Downey, MD / Sanjeev Gulati, MD, FACC / Christina Lesassier, MSN, RN / Carolyn Miller, MHA, FACHE / Kelsey Guffey, RN / Kamala Swayampakala, PhD
- Implementation of Advanced Practice Provider – Led Inpatient Service to Provide Cost-Effective Cardiovascular Care. Ashley McDaniel, AGACNP-BC, FNP-C / Sanjeev Gulati, MD, FACC / Troy Leo, MD, MHCM, FACC / Carolyn Miller, MHA, FACHE
- Best Abstract Award
  Reducing the Risks: A Quality Improvement Project for the Prevention of Atrial Fibrillation in Cardiac Surgery Patients. Sherry Saxohnhouse, MD, MS, FHR, FACC / Theresa Remolina, BS, RVT, RDMS / John Frederick, MD / Douglas Haden, MD


Dr. Jonathan Ray, a research fellow in Dr. Liliya Yamaleyeva’s lab, presented his work as a poster titled “Sex differences in middle cerebral artery reactivity and hemodynamics in 6-month-old Sprague-Dawley rats independent from systemic arterial stiffness or blood pressure” at the America Physiology Summit in Long Beach, CA in April 20-23, 2023
Congratulations to **Kimber Potts, NP** on receiving the Hero Award for Trust! A huge thank you to Kimber for all you do for Atrium Health Wake Forest Baptist Cardiology!

A 2014 review by **Dr. Mark Chappell et al** has more views than 99% of all other Frontier articles.


Congratulations to the following list of individuals from the Section of Cardiovascular Medicine recognized for their achievements!

- **Manrique Alvarez, MD, FACC, FASC** - Master Teacher Award
- **Luke Peters, MD, FACC** – Class of 2024 - Best Inpatient Clerkship Teacher
- **Barbara Pisani, DO, FACC, FAHA** - Class of 2024 - Best Inpatient Clerkship Teachers
- **David Zhao, MD, PhD** - Class of 2024 - Best Inpatient Clerkship Teachers
- **Brandon Stacey, MD** - Class of 2023 and Class of 2025 - Annual Teaching Award
- **Aysha Amjad, MBBS** - 2023 Clinical Excellence Award
- **Karl Richardson, MD** - Promotion to Associate Professor
- **Robert Applegate, MD** - Retired
- **Michael Kutcher, MD** - Retired
- **Heng-Jie Cheng, MD, PhD, FAHA** - Retired
- **Che-Ping Cheng, MD, PhD, FAHA** - Retired
- **Frederic Kahl, MD** - Retiring

**Dr. E. Ann Tallant** retired after thirty-one years of service to the University and School of Medicine in the Section of Hypertension, Department of Surgery, with secondary appointments in the Department of Physiology and Pharmacology and Department of Cancer Biology. She is recognized for exceptional contributions as a researcher, mentor and leader; for innovation in translational research focused on the development of novel therapeutics to treat and prevent cancer and cardiovascular disease; for exceptional mentorship of graduate students, fellows, staff scientists and faculty, particularly from under-represented groups; and for an exemplary record of professional scholarship with over 280 abstracts, articles and book chapters, two awarded patents and more than $27 million in research funding. Dr. Tallant will continue to contribute to the university and the department as an Emeritus Professor.

**Dr. Oguz Akbilgic** was invited to become a member for the Statisticians Group of American Diabetes Association’s Diabetes Care Journal.

**Dr. Oguz Akbilgic** was invited to become a member for NCI-DOE Collaboration Computational Resources of Cancer Research Portal, Community Engagement Working Group.

**Dr. Andrew South** is the new Chair of the Membership Committee of the AHA Council on the Kidney in Cardiovascular Disease.

B. Hadley Wilson MD, Executive Vice Chair of Sanger Heart & Vascular Institute, advanced to president of the American College of Cardiology (ACC). The ACC is a 56,000-member national cardiovascular (CV) professional society dedicated to advancing research, education, and clinical care in CV medicine and surgery. The ACC also advises the US Congress and the Centers for Medicare and Medicaid on health policy matters. Dr. Wilson’s term continued through March 2023.

The William, Jeff, and Jennifer Gross Family Foundation provided a $2 million gift to endow Dr. William (Bill) Downey as chair and medical director of The Jenny & Jeff Gross Family Center for Cardiovascular Care Transformation. Dr. Downey, who is also the vice chair of quality care and transformation at SHVI, is the first named chairholder and will continue his groundbreaking CV research and development of programmatic needs for the Center. This is the third gift to SHVI from the Gross family in support of the Center, and their previous generosity has supported initiatives such as a virtual Hypertension Bootcamp and creation of an advanced analytics team to focus on enterprise-wide quality improvement.

SHVI received a $2 million donation from The Dowd Foundation to develop the Dowd Cardio-Oncology Center of
Excellence, opening at SHVI Kenilworth by the end of 2023. This program will offer improved care models and advance novel research efforts for vulnerable patient populations. Dr Jai Singh is the Director for the Center and leading a pilot study to evaluate the effect of supervised cardiac rehabilitation in patients with cardiac amyloidosis. SHVI will also be joining the Global Cardio-Oncology Registry (G-COR), the first prospective international observational registry in the field.

SHVI received a donation of $300,000 from the Tysinger Family Fund for Excellence in Cardiovascular Care. Mr. Tim Tysinger was the recipient of a heart transplant in October 2021 at SHVI and wanted to share his gratitude for his entire care team. His generosity will enable SHVI to create a full-time ICU nurse educator position, a critical role for the training and recruitment of additional nurses.

SHVI’s Heart Transplantation team performed 51 adult heart transplants in 2022, placing the program amongst the top 20 centers in the US. 1-year survival in the program exceeded 98%, compared to a national average of <92%.

Dr. Jonathan Schwartz and Dr. Markus Scherer performed the first-ever live structural heart case at Atrium Health --- 3D ICE-guided LAAO with a WATCHMAN FLX device.

SHVI’s cardiovascular program at Carolinas Medical Center was recognized on the Fortune/PINCAI 2023 list of the nation’s 50 Top Cardiovascular Hospitals. This designation is awarded based solely on objective, publicly reported data on clinical outcomes, the efficiency of care, and the patient experience.

The Marfan Foundation has recognized the efforts of SHVI’s Marfan and genetic aortopathy program. This work was a collaboration among the SHVI, Levine Children’s, and Wake Forest Baptist teams.

Dr. Esther Kim was awarded the Founders Award by the Fibromuscular Dysplasia Society of America (FMDSA) in May 2023. This award is for those who have taken extraordinary measures to advance FMD awareness, research, and treatment.

Dr. Jonathan Schwartz was elected to the ACC’s Healthcare Innovation Council and the SCAI’s Structural Heart Disease Council (Spring 2023). He also presented at both the 2023 Cardiovascular Research Technologies (CRT) meeting and the Scottsdale Interventional Forum (SIF) (Spring 2023).

Dr. Esther Kim was named chair of the Council on Peripheral Vascular Disease at the American Heart Association.

Dr. Dermot Phelan has been invited to join the following organizations:
- Cardiology representative on the National Football League General Medical Board (2023-present)
- Chair of the Cardiology Advisory Task Force for the National Football League (2023-present)
- Chair of the American Society of Echocardiography Advocacy Committee (2023-2025)
- Course chair of the ACC’s “Care of the Athletic Heart” (2023)

Anna Soloshenko, a Wake Forest University undergraduate student mentored by Dr. Liliya Yamaleyeva, successfully defended her Biochemistry Honors thesis and graduated with a B.S. degree with honors in Biochemistry and Molecular Biology. She has been accepted to the Wake Forest University School of Medicine Class of 2027!

Recent studies funded by the NIH Human Placenta Project from Dr. Yamaleyeva’s lab are featured on NIH website under Human Placenta Project Findings: “Identifying High-Risk Pregnancies with Photoacoustic Imaging of Placental Oxygen”.

Dr. Jeffrey Willey launched mice to the International Space Station (ISS) as a lead scientist for the first ever official NASA - Japanese Space Agency rodent research collaboration aboard the ISS as part of a NASA grant. Two Molecular Medicine PhD students served as leaders for the project as well, Chirayu Patel and Kaitlyn Reno. They tested if artificial gravity could protect against musculoskeletal damage by housing the mice in a centrifuge module that spun the mice at different gravitational levels, like on Mars. PBS reached out after reading about the work on https://school.wakehealth.edu/features/research/scientists-and-students-study-the-risks-of-space-travel and will be doing a story on their research.

Based on their findings, NASA wants to test whether housing conditions aboard the ISS can impact musculoskeletal health and performance in rodents. Therefore, NASA funded Dr. Willey et al to fly mice to the ISS again next with SpaceX and perform another mission. NASA grant: 80NSSC23K0918. Title: Rodent Research Standard Housing Mission: Multidisciplinary Approach to Understanding Spaceflight Responses. Willey: Institutional PI. Start Date: June 1, 2023.
PUBLICATIONS

Between the months of January-April, Cardiovascular Sciences Center members published 123 manuscripts. Of these, 10 were CVSC first author publications. Below we highlight publications from the CVSC and SHVI.


* Impact factor of 23


Dr. Jonathan Schwartz was a co-author of the Triluminate clinical trial, which showed that tricuspid transcatheter edge-to-edge repair was safe and reduced the severity of tricuspid regurgitation in patients with severe tricuspid regurgitation.