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Focus on Research

Molecular epidemiology and cardiovascular imaging identify disease determinants in vulnerable populations

Jorge Kizer, MD, MSc, was destined to be an outstanding physician-scientist.

During medical school at the University of Pennsylvania in the 1990s, a course in cardiovascular pathophysiology piqued his interest. Later, as a resident, when he had a chance to care for patients in the Coronary Care and Telemetry Units at Brigham and Women's Hospital, he was captivated by cardiology.

"It was the ability to intervene upon life-threatening conditions with elegant medical and procedure-based approaches, and radically change the health outlook of severely ill patients, that drew me in," said Kizer, who is now Chief of Cardiology at the San Francisco VA Health Care System (SFVAHCS) and a University of California, San Francisco (UCSF) Professor of Medicine, Epidemiology, and Biostatistics.

As Kizer diagnosed and treated cardiovascular disorders, first at Brigham and then back at the Penn Health System for a cardiology fellowship, he had the urge to understand the real disease story that lab tests and images only partly told. Kizer, who decided concurrently to pursue a Master of Science in Epidemiology, was not only a physician healer, he was a medical detective, too.

Today, Kizer, an NCIRE-supported scientist, leads a research program that combines molecular epidemiology and cardiovascular imaging to identify risk factors for heart disease, stroke, and metabolic disorders. his research also seeks to elucidate the



Jorge Kizer, MD, MSc

*Chief of Cardiology
San Francisco VA Health Care System*

*Professor of Medicine, Epidemiology and Biostatistics
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underlying mechanisms of these diseases, with the potential to inform the development of new therapies or enhance screening methods.

Two of his current studies focus on compelling, high-risk groups:

- U.S. Hispanics/Latinos have on average a higher life

expectancy than non-Hispanic whites and lower mortality in 7 of the 10 leading causes of death in the U.S., despite socio-economic disadvantage.

Hispanics in the U.S., however, are prone to a cluster of metabolic disorders, including metabolic dysfunction associated with steatotic liver disease (MASLD) and its more severe form, metabolic dysfunction associated with steatohepatitis (MASH). MASLD, and especially MASH, can lead to cirrhosis and liver cancer, and is rapidly emerging as the leading cause of liver transplants in the U.S.

- People living with HIV (PLWH) are now living longer, yet are experiencing heart disease and its complications at faster rates than people without HIV. Kizer's research among women with HIV receiving antiretroviral treatment has identified worse heart function and greater heart muscle inflammation and scarring as compared with sociodemographically similar women without HIV.

Kizer's path to his current studies, which champion research aimed at these two vulnerable groups, was serendipitous. The research journey began in the early 2000s at the Weill Cornell Medical College in New York City, where he joined a population-based study of Indigenous Peoples in the U.S.

"The Strong Heart Study included a population of Indigenous Peoples who had very high prevalences of obesity, diabetes and cardiovascular disease, which could be better investigated using cardiac and carotid ultrasound techniques," said Kizer. "It was understanding the basis for the close link between these disorders that I found enthralling; and I turned my attention to the bioactive fat hormone, adiponectin, particularly in older adults from the Cardiovascular Health Study (a National Heart, Lung and Blood-funded study)."

Kizer then moved to the Albert Einstein College of Medicine in the Bronx and started to care for patients from the borough's large population of Latinos and people living with HIV. Soon, he began collaborations with investigators in corresponding prospective cohort studies involving these populations, namely, the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) and the Women's Interagency HIV Study (WIHS). "I applied my interest in imaging to studying cardiometabolic disorders in these high-risk groups," said Kizer.

His work employed echocardiography, which uses ultrasound to look at heart and valve tissue and detect

abnormalities earlier in the disease process. Kizer also investigated adiponectin and other bioactive molecules that help with insulin sensitivity and inflammation in conditions such as obesity, type 2 diabetes and heart disease.

"The work on echocardiography identifying the prognostic value of left atrial diameter or valvular calcification for cardiovascular events and the work on bioactive molecules defining novel biomarkers for cardiometabolic disease set me on my current path," said Kizer.

"With the advent of new technologies for large-scale measurement of biochemical markers in blood, particularly metabolomics and proteomics, for assessment of the gut microbiome, and for evaluation of gene regulation and expression (epigenetics and transcriptomics), unprecedented opportunities have arisen to unravel the molecular mechanisms underlying cardiometabolic diseases and identify novel therapeutic targets," he said. "That is the direction I am currently taking in these cohorts."

His study of MASLD and MASH, which has completed magnetic resonance imaging (MRI) of fibrosis, inflammation, and fat buildup in the liver among more than 1,600 Latino adults, is evaluating how acculturation, lifestyle, psychosocial and sociocultural factors interact with genetics in the development of fatty liver disease. Kizer's investigation also examines the impact of these factors on heart muscle disease assessed in the same MRI scans, as well as the link between liver and heart fibrosis and the candidate molecular pathways responsible.

Kizer has also embarked on a study of diet, metabolism and MASLD/MASH—in collaboration with researchers at UCSF and Albert Einstein College of Medicine in New York—to identify host and bacteria produced metabolic products of diet that contribute to liver fibrosis.

For the study of cardiovascular disease associated with HIV infection, Kizer and Albert Einstein of College of Medicine co-researchers are using "multi-omics" to examine the role of the gut microbiome and metabolic and inflammatory factors in heart and vascular disease in people living with HIV.

The study will build off ongoing research with some 3,000 participants from the national Multicenter AIDS Cohort Study/Women's Interagency HIV Study Combined Cohort Study. Echocardiography and carotid ultrasound are used to understand the impact

of HIV on heart and vascular disease.

“Identifying molecular pathways that lead to liver and heart disease, and applying genetic information to support causation, can streamline the development and testing of appropriate therapies to prevent these disorders,” said Kizer. “Determining the role of social determinants and genetics in liver and heart disease can

identify improved strategies for intervention at the community and individual level for these disorders.”

“Delineating the specific gut microbes and their molecular products driving cardiometabolic disease can lead to the use of pre- or pro-biotic therapies or novel drugs for prevention and treatment,” he said.

Q and A: An Interview with Dr. Aoife O’Donovan

Q: Your research seeks to answer, “How does traumatic stress cause ill health?” How did you become interested in this topic?

A: My interest in health psychology stemmed from my experiences as a trainee reporter at a newspaper in my home county of Cork in Ireland. I was tasked with writing a series of articles about people living with different forms of chronic illness.

One of the most striking things about those interviews was that the interviewees’ quality of life seemed far more impacted by the stressors in their lives, than by their objective physical symptoms. This was really eye opening for me; and it led me to drop a potential career in journalism for health psychology.

Q: What brought you to the San Francisco VA Health Care System (SFVAHCS)?

A: As a visiting graduate student at the University of California, San Francisco (UCSF) Center for Health and Community, I was studying the effects of chronic stressors on the immune system and biological aging with Dr. Elissa Epel (Professor and Vice Chair in the UCSF Department of Psychiatry and Behavioral Sciences). Although



Aoife O’Donovan, PhD

Research Psychologist

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Associate Professor in Residence of Psychiatry and Behavioral Sciences

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Director

Trauma and Health Research on Immunity, Vitality, and Emotions (THRIVE) Laboratory

University of California, San Francisco

Faculty Member

Translational Psychedelic Research Program (TrPR)

University of California, San Francisco

Faculty Member

Stress and Health Research Program (SHRP)

Northern California Institute for Research and Education

*San Francisco VA Health Care System
University of California, San Francisco*

accumulating research was showing potent effects of chronic stress on biological indicators of health, we knew relatively little about how traumatic stress impacts biological systems.

Given that the San Francisco VA is a world leader in trauma and post-traumatic stress disorder (PTSD) research, it emerged as an ideal place for me to get the additional training I needed to pursue this new line of study. After my first meeting with the Stress and Health Research Program Director, Dr. Thomas Neylan, I was hooked on furthering our understanding of how traumatic stress and PTSD impact biological systems and health.

Q: You direct the Trauma and Health Research on Immunity, Vitality, and Emotions (THRIVE) Laboratory at the SFVAHCS. What are its key research projects?

A: At the THRIVE Lab, our long-term goal is to identify better interventions to reduce or eliminate the adverse effects of traumatic stress on health. In pursuit of this goal, we aim to clarify the adverse health effects of traumatic stress, uncover the mechanisms by which traumatic stress causes ill health, and test new interventions.

Some of our projects use VA electronic health record data to uncover the health effects of trauma and PTSD. Using this data, we found that VA patients with PTSD and other psychiatric disorders had higher risk for both infectious and chronic diseases. In ongoing work, THRIVE Lab Associate Director, Dr. Kristen Nishimi, is elucidating the relationship between PTSD and autoimmune disorders using VA electronic health record data.

Other projects are focused on furthering our understanding of immune system abnormalities in PTSD. These abnormalities likely contribute to symptoms of PTSD, as well as to the doubling of risk for cardiovascular and autoimmune disorders observed in PTSD. We are currently funded by the National Institute of Mental Health to examine the effects of inflammatory activity on fear learning and memory processes that underlie some PTSD symptoms.

Q: What are some potential interventions that you are investigating?

A: Unfortunately, PTSD treatments are not available to all who need them and don't work for all who can access them. One of our goals is to develop an app-based intervention that can reduce some symptoms of PTSD and be widely available.

We have been funded by the Department of Defense to develop such an app and are currently focused on personalizing the intervention we deliver on this app. Some of the most exciting research

happening in psychiatry is focused on psychedelic therapy. Together with Drs. Josh Woolley and Ellen Bradley from TrPR, THRIVE Lab Postdoctoral Researcher, Dr. Parker Kelley, and I are working to uncover the biological effects of psychedelic drugs. The goal of this work is to understand how psychedelic therapy works so that we can identify those most likely to benefit and personalize the treatment.

Q: What makes your laboratory unique?

A: One of the best things about THRIVE Lab is that we have been able to recruit people with a variety of backgrounds to create a truly interdisciplinary team. Moreover, the labs at the SFVAHCS and UCSF ensure that we have access to some of the best scientists across disciplines, including psychology, psychiatry, epidemiology, data science, and others. With this interdisciplinary team, we can tackle challenging research questions and get closer to the ultimate goal of identifying better interventions for trauma-exposed people.

Q: During the COVID-19 pandemic, VA scientists were called upon to conduct research about what was then new and mysterious. Your COVID-19 studies informed your current research. Please explain.

A: The COVID-19 pandemic presented the global scientific community with extraordinary challenges. Our piece of the puzzle was to work to uncover the effects of the pandemic among people with PTSD. In 2020, we launched a

longitudinal study with almost 900 trauma-exposed subjects whom we are still following today.

The data we collected from surveys in 2020 and 2021 facilitated understanding of how people with PTSD were struggling to adjust to COVID-19 restrictions. In other work, we employed the VA's electronic health record data to show that VA patients living with PTSD had much greater health risks during the first two years of the pandemic. This work is also still ongoing and has led us to thinking a lot about how stressors and PTSD impact the risk and outcomes of infectious diseases.

Q: Why is the SFVAHCS an ideal place to conduct this kind of research?

A: The SFVAHCS is a phenomenal environment for a PTSD researcher. We typically have 15-20 faculty members who are dedicated to PTSD research, as well as a host of outstanding trainees who come here to learn about trauma and PTSD. If I have a specific question about PTSD, one of my colleagues likely is one of the best people in the world to answer. On top of that, the VA as an institution does an excellent job of screening patients for PTSD symptoms, which means that we have the necessary data to study the health impact of the condition.

Q: How does your work with Veterans motivate you?

A: A life in research can be so rewarding, but it can also be tough. We fail a lot—we fail to get grants, our papers are rejected, and some-

times, our ideas don't pan out—it can be challenging to stay motivated. However, working at the SFVAHCS and seeing the Veterans who come in for their

medical care is a constant reminder of why it is important to do this work.

Q: What would most people be

surprised to know about you?

A: I grew up in Ireland, and I really dislike potatoes.

Research Community News

Alzheimer's Disease Neuroimaging Initiative Celebrates 20 Years!

The Alzheimer's Disease Neuroimaging Initiative (ADNI) study celebrates 20 years as an active project!

This milestone was commemorated at a reception during the Alzheimer's Association International Conference (AAIC) 2024, in Philadelphia, Pennsylvania, July 28th-August 1st.

NCIRE-supported Principal Investigator, Dr. Michael Weiner, provided the keynote presentation, with recognition given to the many collaborators and people who have allowed the ADNI to flourish for the past two decades, including NCIRE-supported Co-Investigators, Drs. Duygu Tosun-Turgut and Rachel Nosheny.

The ADNI study actively supports the investigation and development of treatments that slow or stop the progression of Alzheimer's disease (AD). Researchers at over 60 clinical sites in the U.S. and Canada collect data to study the progression of AD in the human brain across normal aging, mild cognitive impairment (MCI), and Alzheimer's disease and dementia. Visit <https://adni.loni.usc.edu/> to learn more about the history of ADNI and the researchers who lead the study.

Dr. Daniel Mathalon receives UCSF Royer Prize for Excellence in Psychiatry

Congratulations to NCIRE-supported Principal Investigator, Dr. Daniel Mathalon, for being recognized by the University of California, San Francisco (UCSF) with the J. Elliott Royer Award for Excellence in Psychiatry!

The Royer Award for Excellence in Academic Psychiatry was awarded to Dr. Daniel Mathalon in recognition of his long track record of outstanding contributions as a mentor, educator, clinician, and researcher to the UCSF Department of Psychiatry and Behavioral Sciences (DPBS) and the San Francisco VA Health Care System (SFVAHCS).

The award was presented at the UCSF Psychiatry faculty meeting on September 17, 2024.

Drs. Salomeh Keyhani and Carolyn Gibson head new Center for Data to Discovery and Delivery Innovation!

NCIRE-supported Principal Investigators, Drs. Salomeh Keyhani and Carolyn Gibson, will be the Director and Associate Director, respectively, of the Center for Data to Discovery and Delivery Innovation (3DI), a new Health Systems Research Center of Innovation (COIN) funded by the San Francisco VA Health Care System (SFVAHCS) through an award from the Veterans Affairs (VA) Office of Research and Development in partnership with NCIRE.

3DI is focused on improving health by supporting research and training that advance patient-centered health behavior change. The Center brings together a multidisciplinary group of 25 core investigators from the School of Medicine and the School of Nursing at the University of California, San Francisco (UCSF). The Center will partner with numerous centers, programs, and institutes across UCSF, including the UCSF institute for Health Policy Studies, the UCSF Center for Tobacco Control Research and Education, the UCSF Osher Center for Integrative Health, and the UCSF UC Berkeley Joint Program in Computational Precision Health.

New Federal Funding Awards

Congratulations to the following Principal Investigators for your recently funded awards!

Duygu Tosun-Turgut, PhD

Project Title: MVP Data Integration into the ADSP Phenotype Harmonization Consortium
Sponsor: NIH via subaward from Vanderbilt University Medical Center
Activation Date: 5/15/2024

Xuhui Liu, MD

Project Title: Improving Cardiac and Diaphragm Function with Beta-3 Adrenergic Receptor Agonist in Duchenne Muscular Dystrophy
Sponsor: Dept. of the Army – USAMRAA
Activation Date: 7/11/2024

Linda Chao, PhD

Project Title: Feasibility of Tele-Singing at Home for Older Adults with Mild Cognitive Decline
Sponsor: National Institute on Aging
Activation Date: 9/5/2024

Rebecca Sudore, MD

Project Title: Mapping the Complex Processes and Outcomes of Care Planning
Sponsor: NIH via subaward from Indiana University
Activation Date: 9/5/2024

Michael Weiner, MD

Project Title: Evaluating SARS-CoV-2 spike antigen-induced coagulopathy and neuroinflammation as mechanistic drivers of neurologic PASC
Sponsor: NIH via subaward from UCSF
Activation Date: TBD

Bruce Ovbiagele, MAS, MBA, MD

Project Title: CiLostAzol for pReventIon of recurrent sTroke in Africa (CLARITY-Africa)
Sponsor: National Institute of Neurological Disorders and Stroke
Activation Date: TBD

Funding Opportunities

Industry Opportunities

Please contact Newton Ong, newton.ong@ncire.org, or Adan Pinedo, adan.pinedo@ncire.org, for further information on the following Industry Opportunities.

Telix Pharmaceuticals

Prospective Observational Multicenter Registry Study to Assess the Impact and Long Term Outcomes of 68Ga-PSMA-11 PET/CT (Illuccix) Imaging Evaluations for VA PCa Patients with Newly Diagnosed, or Suspected Recurrent Prostate Cancer or are candidates for Radioligand Therapy for Prostate Cancer.

NuView Life Sciences

A clinical trial of a new non-invasive diagnostic test for prostate cancer to replace PSA tests. Lead PI of multi-site study or PI of study site.

Bristol Myers Squibb

A Phase 3, Randomized, Open-label Study of Nivolumab + Relatlimab Fixed-Dose Combination with Chemotherapy Versus Pembrolizumab with Chemotherapy as First Line Treatment for Participants with Stage IV or Recurrent Non-squamous Non-Small Cell Lung Cancer.

Please visit the Office of Sponsored Research page on the NCIRE SharePoint at <https://ncire.sharepoint.com/> or click [here](#) for the full list of Industry Opportunities.

Federal Funding Opportunities

Please contact Jessica Schmidt, jessica.schmidt@ncire.org, for further information on the following Federal Funding Opportunities.

NIH: [Clinical and Translational Science Award \(UM1 Clinical Trial Optional\)](#)

(PAR-24-272)

National Center for Advancing Translational Sciences

- Application Deadlines: March 13, 2025; May 28, 2025; September 29, 2025

NIH: [HEAL Initiative: Pain Research Enhancement Program \(PREP\) \(R15 Clinical Trial Optional\)](#)

Funding Opportunities continued

(RFA-AT-25-001)

National Center for Complementary and Integrative Health

National Institute on Alcohol Abuse and Alcoholism

National Institute on Aging

National Institute of Arthritis and Musculoskeletal and Skin Diseases

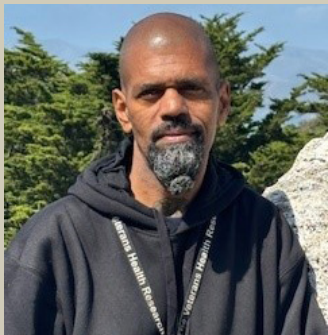
Eunice Kennedy Shriver National Institute of Child Health and Human Development

National Institute of Neurological Disorders and Stroke

- Application Deadlines: November 19, 2024; October 28, 2025; October 27, 2025

Please visit the Office of Sponsored Research page on the NCIRE SharePoint at <https://ncire.sharepoint.com/> or click [here](#) for the full list of Federal Funding Opportunities.

In the Helix



Angelo (Charles) Dangerfield
Buyer II/Materials Handler II, NCIRE

Q: If you could have a meal with anyone (alive or deceased), who would it be?

A: If I could have a meal with anyone alive or deceased, it would be Gopi Krishna. I'm into my DNA stuff, so I thought about an ancestor from maybe the early 1800s whom I could ask questions. I could learn a lot more from Gopi Krishna.

Q: What is your favorite time of the day and why?

A: My favorite time of the day is morning. I like the morning because there are less people out, and the fact that it's the morning means that I was blessed to see another day.

Q: If you had to play one album forever, which one would it be?

A: The album one is hard to answer. I started with "Thriller" (Michael Jackson). Then I went to "What's Going On" (Marvin Gaye). "Purple Rain" and "Dirty Mind" (Prince) were next, but I ended up staying with "Off the Wall" (Michael Jackson).



Liliana Moore
Research Assistant III, NCIRE

Q: If you could have a meal with anyone (alive or deceased), who would it be?

A: My sister! She moved to Denver a few years ago and I miss living in the same city as her. We often joke that we wish we could teleport to each other's kitchens to have dinner together on a more regular basis.

Q: What is your favorite time of the day and why?

A: My favorite time of day is the golden hour. I love going on a walk or playing at a brewery with my band while watching the sunset.

Q: If you had to play one album forever, which one would it be?

A: This is an impossible question to answer since I love listening to such a wide variety of music! However, some top contenders would be "Songs About Jane" (Maroon 5), "Get the Picture" (Smash Mouth), "Gold Medal" (The Donna's), and "Little Voice" (Sarah Bareilles).

If you know an NCIRE employee and would like to be featured in *In the Helix*, contact us at dna@ncire.org.

Message from the Chief Executive Officer

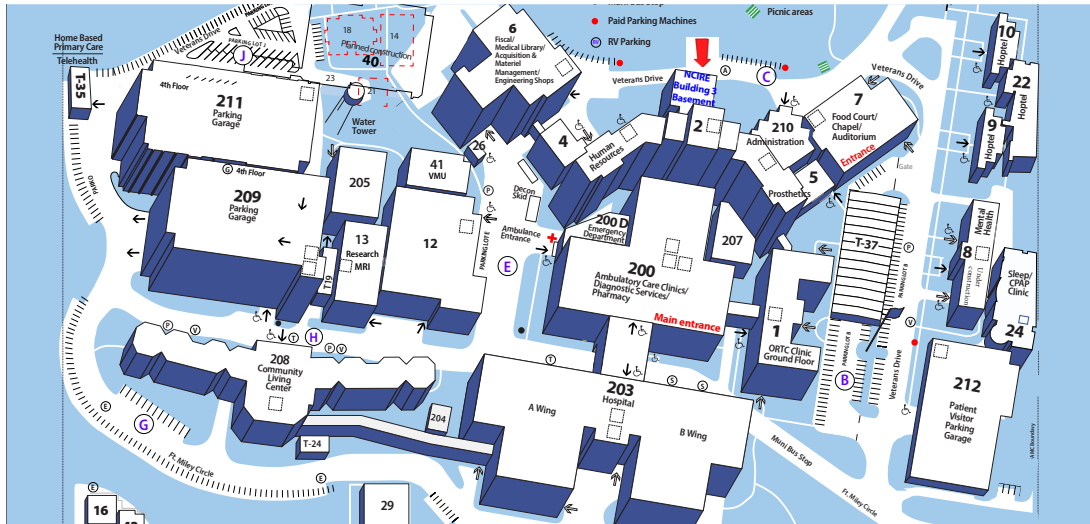
The transition from summer to fall is always magical. In every leaf, there's a whisper of autumn's charm, and as we enter the autumnal months, I hope this season offers some enchantment for you.

With the 24th volume, we have remarkable contributors for the Fall 2024 Newsletter: Jorge Kizer, MD, MSc and Aoife O'Donovan, PhD. We appreciate the time they have dedicated to sharing their research.

NCIRE is approaching the end of fiscal year 2024, ending on September 30, 2024. We will be working to close the 2024 financials, build the fiscal 2025 financial projections, and will begin work on the 2024 financial audit.

The 2024 annual NCIRE Principal Investigator and Research Community Satisfaction Survey closed at the end of July. The response rate was 44%. The full 2024 survey results can be found [here](#). Over the next year we will work to continue to facilitate and support research by: 1) providing consistent administrative and IT support, 2) building awareness on the organization's allocation of resources, and 3) providing timely training and educational opportunities that will support research and staff.

We are looking forward to hosting an Open House on Thursday, October 17, 2024, 2 pm to 4 pm to provide an opportunity for you to personally meet members of the NCIRE Core Staff Team. Please join us in Building 3 – Basement.



Thank you for taking time to read our Fall 2024 Newsletter.

Rebecca Rosales, MBA, CRA
Chief Executive Officer

About NCIRE

NCIRE - The Northern California Institute for Research and Education has one mission and one goal: Advancing Veterans Health. We sustain a scientific community of clinicians and researchers and support nearly 200 researchers who have joint faculty appointments at the University of California, San Francisco (UCSF) and the San Francisco VA Health Care System (SFVAHCS) and are working to foster innovation through leadership in the field of Veterans health research. Our broad portfolio of projects receives generous support from the National Institutes of Health, the Department of Defense, and individual donors, making us the largest nonprofit research institute devoted to Veterans health in the US.

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