

# Sleep and Circadian Rhythms in Cardiovascular Resilience:

Mechanisms, Implications, and Applications

## Program Booklet

Virtual Workshop, April 24 & 26, 2024



# Agenda



## DAY ONE:

Wednesday, April 24, 2024 | 10:00am – 4:30pm EDT

### 10:00 – 10:20 am **Welcome and Opening Remarks**

*Conceptualizing resilience and cardiovascular resilience from the NHLBI and NIH perspectives*

**Dr. David Goff, MD, PhD, FACP, FAHA, NHLBI Perspectives**

**Dr. Zorina Galis, PhD, Trans-NIH Resilience Program**

**Dr. Marishka Brown, PhD, Sleep and Circadian Rhythms Programs**

### Session 1: The Interplay of Sleep, Circadian Rhythms, and Cardiovascular Resilience

Moderator: **Dr. Don Lloyd-Jones, MD, ScM, FACC, FAHA**

### 10:20 – 10:40 am **Defining Cardiovascular Resilience and the Role of Sleep: A Cardiovascular Resilience Researcher's Perspective**

**Dr. Don Lloyd-Jones, MD, ScM, FACC, FAHA, Northwestern University**

### 10:40 – 11:00 am **Social Determinants of Sleep Health from 2017–2020: Exploring the Intersection of Race and Gender**

**Dr. Stephanie Cook, DrPH, New York University**

### 11:00 – 11:20 am **Integrating Chrononutrition and Sleep: A Pathway to Atherosclerosis Management and Cardiovascular Resilience**

**Dr. Jose Ordovas, PhD, Tufts University**

### 11:20 – 11:40 am **Intersection of Aging, Sleep and Cardiovascular Resilience**

**Dr. Pamela Lutsey, PhD, MPH, University of Minnesota**

### 11:40 – 12:00 pm **Conceptualizing Cardiovascular Resilience**

**Dr. Victoria Bautch, PhD, University of North Carolina at Chapel Hill**

12:00 – 12:30 pm **Q&A for Speakers**  
*Summary by Moderator*

12:30 – 1:00 pm **LUNCH BREAK**

## Session 2: Mechanisms Linking Sleep and Circadian Rhythms to Cardiovascular Resilience

Moderator: **Dr. Brooke Aggarwal, EdD, MS, FAHA**

1:00 – 1:20 pm **Overview of Potential Mechanisms Linking Sleep and Circadian Rhythms to Cardiovascular Resilience**  
**Dr. Brooke Aggarwal, EdD, MS, FAHA, Columbia University Irving Medical Center**

1:20 – 1:40 pm **Impact of Sleep and Circadian Disruption on Cardiovascular Outcomes from Controlled Clinical Studies**  
**Dr. Josiane Broussard, PhD, Colorado State University**

1:40 – 2:00 pm **Conceptualizing Sleep and Circadian Health and Resilience**  
**Dr. Philip Cheng, PhD, Henry Ford Health**

2:00 – 2:20 pm **Toward Mechanisms of Circadian Resilience in Cells and Synapses**  
**Dr. Jonathan Lipton, MD, PhD, Harvard University**

2:20 – 2:50 pm **Q&A for Speakers**

2:50 – 3:00 pm **BREAK**

3:00 – 3:20 pm **Mechanisms of Increased Cardiovascular Risk in Insufficient Sleep**  
**Dr. Sanja Jelic, MD, Columbia University Medical Center**

3:20 – 3:40 pm **Sleep and Leukocyte Dynamics in Cardiovascular Disease**  
**Dr. Filip Swirski, PhD, Icahn School of Medicine at Mount Sinai**

3:40 – 4:00 pm **Multilevel Determinants of Sleep and Cardiovascular Disparities: The Role of Risk and Resilience**  
**Dr. Dayna Johnson, PhD, MPH, Emory University**

4:00 – 4:30 pm **Q&A for Speakers**  
*Summary by Moderator*

## DAY TWO:

Friday, April 26, 2024 | 10:00am – 4:30pm EDT

### Session 3: Sleep and Circadian Interventions for Cardiovascular Resilience

Moderator: **Dr. Michael Grandner, PhD, MTR, CBSM, FAASM**

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| 10:00 – 10:20 am | <b>Overview: Sleep and Circadian Interventions for Cardiovascular Resilience</b><br><i>Dr. Michael Grandner, PhD, MTR, CBSM, FAASM, University of Arizona</i>  |
| 10:20 – 10:40 am | <b>Use of Light and Chronopharmacology to Improve Cardiovascular Resilience</b><br><i>Dr. Fabian Fernandez, PhD, University of Arizona</i>   |
| 10:40 – 11:00 am | <b>Opportunities for Improving Sleep to Support Cardiovascular Resilience</b><br><i>Dr. Aric Prather, PhD, University of California, San Francisco</i>   |
| 11:00 – 11:20 am | <b>System-Level Approaches to Improve Sleep Health and Cardiovascular Resilience</b><br><i>Dr. Nicole Bowles, PhD, Oregon Health and Science University</i>  |
| 11:20 – 11:40 am | <b>Q&amp;A for Speakers</b>  |
| 11:40 – 11:50 am | <b>BREAK</b>   |
| 11:50 – 12:10 pm | <b>Behavioral Sleep Health Promotion Strategies to Promote Cardiovascular Resilience</b><br><i>Dr. Kelly Baron, PhD MPH, DBSM, University of Utah</i>  |
| 12:10 – 12:30 pm | <b>Sleep Optimization: Implications for Cardiometabolic Risk and Resilience</b><br><i>Dr. Esra Tasali, MD, University of Chicago</i>   |
| 12:30 – 1:00 pm  | <b>Q&amp;A for Speakers</b><br><i>Summary by Moderator</i><br><b>Discussion:</b> Incorporating cardiovascular resilience measures into sleep research interventions and vice versa. How to incorporate CVD outcomes within sleep research? Gaps towards developing mechanistic links – what formative research is needed? How to include sex as a biological variable in mechanistic research? |
| 1:00 – 1:30 pm   | <b>LUNCH BREAK</b>   |

**Session 4: Charting the Future of Sleep Health and Cardiovascular Resilience Research; Bringing Together Perspectives from the Fields of Sleep Health, Resilience, and Cardiovascular Research**

Moderators: **All Co-Chairs**

- 1:30 – 1:50 pm      **Future Directions for Research Examining Sleep and Cardiovascular Resilience**  
Dr. Ali Azarbarson, PhD, *Harvard University*
- 1:50 – 2:10 pm      **Future Directions for Translational Research Exploring Sleep and Circadian Rhythms**  
Dr. Ron Anafi, MD, PhD, *University of Pennsylvania*
- 2:10 – 2:30 pm      **Host Resilience to Prevent Diabetes-associated Vascular Complications**  
Dr. Qing Miao, PhD, *New York University Long Island School of Medicine*
- 2:30 – 2:50 pm      **Epigenetic Studies and Protection Against Age-related Diseases**  
Dr. Rene Cortese, PhD, ATSF, *University of Missouri*
- 2:50 – 3:10 pm      **The Impact of Stress and Insomnia on Cardiovascular Functioning**  
Dr. Ivan Vargas, PhD, *University of Arkansas*
- 3:10 – 3:20 pm      **BREAK**
- 3:20 – 3:40 pm      **Q&A for Speakers**  
**Discussion #1:** Next steps, critical gaps and a research agenda
- 3:40 – 4:00 pm      **Discussion #2:** Strategies for stimulating partnerships and leveraging cutting edge technologies
- 4:00 – 4:20pm      **Discussion #3:** Implementation of sleep and circadian principles and resilience into healthcare, and the role of sex/gender, age, and other factors
- 4:20 – 4:30 pm      **Closing Remarks and Future Perspectives**  
**Co-Chairs**

# Welcome Remarks

## NHLBI Leadership



### **Dr. David Calvin Goff, Jr., MD, PhD, FACP, FAHA**

*Director, Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH)*

Dr. David Calvin Goff, Jr., serves as the Director of the Division of Cardiovascular Sciences at the National Heart, Lung, and Blood Institute, National Institutes of Health. In this role, he leads a diverse team of scientists and administrators committed to turning discovery into cardiovascular health. Dr. Goff previously served as Dean and Professor of Epidemiology at the Colorado School of Public Health and as Chair of the Department of Epidemiology and Prevention at the Wake Forest School of Medicine. He received an MD from the University of North Carolina and a PhD in epidemiology from the University of Texas-Houston School of Public Health. He trained in internal medicine at Baylor College of Medicine in Houston. He is an elected member of the American Epidemiological Society, and a Fellow of the American College of Physicians and the American Heart Association. He has published over 300 manuscripts, book chapters, and other scientific reports.



### **Dr. Zorina Galis, PhD**

*Chief, Vascular Biology and Hypertension Branch, National Heart, Lung, and Blood Institute (NHLBI)*

Dr. Zorina Galis joined the NIH in 2011, leading the Vascular Biology and Hypertension Branch at the National Heart, Lung, and Blood Institute (NHLBI), where she has guided significant research from foundational discoveries to clinical trials. She has been instrumental in pioneering interdisciplinary projects and securing funding, earning recognition through NHLBI and NIH Director Awards. Her efforts include initiatives like the VITA Program, HuBMAP, the Trans-NIH Lymphatic Coordination Committee, and the NIH Underrepresented Undergraduate Summer Internship Program. Educated in Physics, Biophysics, and Cell Biology at the University of Bucharest, Pathology at McGill School of Medicine, and Vascular Medicine at Harvard, Dr. Galis has held esteemed positions in both academia and industry. At Emory School of Medicine and Georgia Institute of Technology, she secured tenured roles in Cardiology and Biomedical Engineering, and served as Chief Scientific Officer for Cardiovascular R&D at Eli Lilly and Co. Drawing on her academic research, Dr. Galis champions innovative research to enhance the understanding and resilience of the vascular system (“The Vasculome”) and the need for novel investigations into its resilience.

# Welcome Remarks

## NHLBI Leadership



### **Dr. Marishka K. Brown, PhD**

*Director, National Center on Sleep Disorder Research (NCSDR)*

As Director of the National Center on Sleep Disorder Research (NCSDR), Dr. Marishka K. Brown, leads the science of sleep and chronobiology into innovative discoveries that improve health. NCSDR, located within the National Heart, Lung, and Blood Institute (NHLBI), is the nexus of NIH sleep and circadian research activities for a network that includes professional associations, public stakeholders, and federal agencies. Dr. Brown's leadership and experience in partnership building help sustain and expand this network, bringing the benefits of NIH's scientific research into medicine and public health. Dr. Brown has dedicated her career to biomedical research that impacts health and safety for everyone. She initiated and led research programs, such as identifying abnormalities in circadian biology linked to heart, lung, and blood disorders. She spearheaded workshops showcasing how sleep impacts the immune system, lung diseases, child development, cardiovascular disease, mechanisms of early neurocognitive decline, the microbiome, and health disparities. She also chairs the working group for sleep health objectives in the Department of Health and Human Services' Healthy People 2030 initiative. Dr. Brown began her NIH career as an American Association for the Advancement of Science (AAAS) Science and Technology Policy fellow in the Office of Strategic Coordination, located within the NIH Office of the Director. Her doctorate is in pharmaceutical sciences from the University of Maryland, Baltimore. She was a postdoctoral fellow at the University of Pennsylvania's Center for Sleep and Circadian Neurobiology, where she led research on the role of the unfolded protein response in age-related sleep changes.

# Workshop Organizers



## **Dr. Yunling Gao, PhD**

*Program Director, Vascular Biology and Hypertension Branch, Division of Cardiovascular Sciences (DCVS), National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH)*

Dr. Yunling Gao is a Program Director at the Vascular Biology and Hypertension Branch, Division of Cardiovascular Sciences (DCVS) of the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH). She manages a large research grant portfolio focusing on endothelial and vascular cell biology, angiogenesis, and vascular remodeling in cardiovascular health and related diseases. She is particularly interested in exploring the impact of lifestyle choices like physical activity, diet, and sleep patterns on endothelial, vascular, and cardiovascular resilience, as well as overall health. Dr. Gao trained as a physician in China and a research scientist in the United States. She obtained her PhD at the University of Cincinnati College of Medicine and completed her postdoctoral training at Harvard Medical School and Brigham and Women's Hospital. She served as a faculty and Instructor of Medicine at the Albert Einstein College of Medicine and worked as a clinical research scientist at Eli Lilly and Company before joining the NHLBI/NIH.



## **Dr. Alfonso Alfini, PhD, MS**

*Program Director, Sleep Disorders Medicine, National Center on Sleep Disorders Research, Division of Lung Diseases, National Heart, Lung, and Blood Institute (NHLBI)*

Dr. Alfonso Alfini is a Program Director at the National Center on Sleep Disorders Research (NCSDR), in the Division of Lung Diseases (DLD), at the National Heart, Lung, and Blood Institute (NHLBI). He oversees a research portfolio that supports research on the genetic predisposition, risk factors, pathogenesis, epidemiology, diagnosis, and treatment of sleep and circadian rhythm sleep-wake disorders. He is interested in the role of lifestyle factors, particularly diet, physical activity, and sleep, in cardiometabolic and neurocognitive health. Dr. Alfini holds a doctoral degree in kinesiology and cognitive neuroscience from the University of Maryland, a master's degree in exercise science from the George Washington University, and a bachelor's degree in Human Performance and Wellness/K-12 education from Colorado Mesa University. He completed his postdoctoral training in aging and dementia at the Johns Hopkins School of Medicine and served on the faculty there in the Department of Neurology before joining the NIH.



# Workshop Co-Chairs



**Dr. Brooke Aggarwal, EdD, MS, FAHA**

*Assistant Professor of Medical Sciences, Division of Cardiology, Department of Medicine, Columbia University Irving Medical Center*

Dr. Brooke Aggarwal is a trained behavioral scientist and an Assistant Professor in the Division of Cardiology at Columbia University Irving Medical Center. Her research focuses on women's cardiometabolic health, including the influence of sleep on cardiovascular health among diverse populations of women at various life stages. Dr. Aggarwal serves as Principal Investigator of multiple national awards, including a study examining the association of sleep patterns, lifestyle, and cardiometabolic risk among women, and a study designed to conduct deep phenotyping and examine changes in markers associated with adverse weight gain during menopause using a precision medicine platform. She served as the Training Director of the American Heart Association Go Red for Women Center which is dedicated to sleep and women's health at Columbia University. She has been elected as a Fellow of the New York Academy of Medicine and as a Fellow of the American Heart Association.



**Dr. Michael Grandner, PhD, MTR, CBSM, FAASM**

*Director, Behavioral Sleep Medicine Clinic, Banner-University Medical Center, Tucson, Arizona*

Dr. Michael Grandner is a licensed clinical psychologist, board-certified in Behavioral Sleep Medicine. He is the Director of the Sleep and Health Research Program at the University of Arizona and the Director of the Behavioral Sleep Medicine Program at the Banner-University Medical Center in Tucson. Dr. Grandner is an Associate Professor of Psychiatry, Psychology, Medicine, Nutritional Sciences, and Clinical Translational Science at the University of Arizona. He has over 250 academic publications, is an elected fellow of the American Academy of Sleep Medicine, Society of Behavioral Sleep Medicine, and American Heart Association, and has won numerous awards for his work with the Sleep Research Society, American Heart Association, and other organizations.



**Dr. Donald M. Lloyd-Jones, MD, ScM, FAHA, FACC, FASPC**

*Chair, Department of Preventive Medicine, Eileen M. Foell Professor of Heart Research, Professor of Preventive Medicine, Medicine, and Pediatrics, Northwestern's Feinberg School of Medicine*

Dr. Donald M. Lloyd-Jones graduated from Swarthmore College and Columbia's College of Physicians and Surgeons, and did his internal medicine and cardiology training at Massachusetts General Hospital, where he served as chief medical resident and chief cardiac fellow. He was a fellow and then staff researcher at the Framingham Heart Study from 1997-2003. He is currently chair of the Department of Preventive Medicine, the Eileen M. Foell Professor of Heart Research, and Professor of Preventive Medicine, Medicine, and Pediatrics at Northwestern's Feinberg School of Medicine. His research interests include the study of the life course and mechanisms of cardiovascular health and healthy aging, and cardiovascular disease epidemiology, risk estimation, and prevention. He has been a frequent leader of national clinical practice guidelines and policy statements for the American College of Cardiology, American Heart Association (AHA), and NHLBI. He served as AHA President in 2021-22.

# Session 1

## Moderators & Speakers



**Dr. Donald M. Lloyd-Jones, MD, ScM, FAHA, FACC, FASPC**

**Moderator & Speaker**

See bio under Workshop Co-chairs.



**Dr. Stephanie Cook, DrPH, MPH**

**Speaker**

*New York University James Weldon Johnson Professor, Assistant Professor of Social and Behavioral Sciences, Assistant Professor of Biostatistics, Director, Attachment and Health Disparities Research Lab*

Dr. Stephanie Cook is the James Weldon Johnson Professor in the departments of Social and Behavioral Sciences and Biostatistics at New York University School of Public Health, and the Director of the Attachment and Health Disparities Research Lab (AHDL). Dr. Cook's substantive methodological and statistical focus is in the development and application of longitudinal study designs for determining the ways in which dynamic changes in features of minority stress are associated with changes in risk behaviors and physical health among racial/ethnic and/or sexual minority young adults. Dr. Cook aims to understand how structural- and individual-level minority stressors contribute to mental and physical health, and health behaviors across the lifespan, in the virtual and physical worlds, as well as how features of close relationships can exacerbate or buffer the negative effects of minority stress on health. Her work primarily focuses on young adults transitioning to adulthood who are at the intersection of racial/ethnic and sexual orientation status. In addition, much of her current work examines the links between minority stress (i.e., daily experiences of discrimination), biological markers of stress and disease (e.g., cortisol and C-reactive protein), and risk factors for cardiovascular disease (e.g., cardiometabolic health behaviors). She has won numerous awards for her research, service, and teaching, including the Matilda White Riley Distinguished Early-Stage Investigator Award from the NIH, the Emerging Scholar recognition from *Diverse Magazine*, and the AmStat News "Data for Good" Challenge in Human Rights Award.



**Dr. José M. Ordovás, PhD**

**Speaker**

*Professor of Nutrition, Senior Scientist, USDA-Human Nutrition Research Center on Aging, Director of the Nutrition and Genomics Laboratory, Tufts University in Boston, Massachusetts*

Dr. José M. Ordovás is a distinguished Professor of Nutrition and a Senior Scientist at the USDA-Human Nutrition Research Center on Aging at Tufts University, where he directs the Nutrition and Genomics Laboratory. In addition, he holds the position of Professor of Genetics and Pharmacology at the School of Biomedical Sciences. Beyond the United States, he spearheads the Nutritional Genomics and Epigenomics Group at IMDEA-Food in Madrid, Spain. Educated at the University of Zaragoza, Spain, where he earned his undergraduate degree in Chemistry and a doctorate in Biochemistry, Dr. Ordovás undertook postdoctoral research at eminent institutions including MIT, Harvard, and Tufts University. His research primarily explores the genetic and epigenetic underpinnings of age-related chronic diseases such as cardiovascular disease, obesity, and diabetes, focusing particularly on their interaction with environmental and lifestyle factors, notably diet. Dr. Ordovás has made substantial contributions to the field, authoring over 950 scientific articles and participating as a keynote speaker at numerous international conferences related to personalized nutrition. Acknowledged as a pioneering figure in gene-diet interactions, his achievements have been recognized with awards from the USDA, the American Society for Nutrition, the Spanish Society of Cardiology, and the Mediterranean Diet Foundation, among others. He has received honorary doctorates from the University of Cordoba and CEU-San Pablo in Madrid, and is a Fellow of the American Society for Nutrition. He has been a member of the Food and Nutrition Board of the National Academies and the FDA National Toxicology Center Advisory Committee, and is further involved in various peer review boards, and advisory panels.



**Dr. Pamela Lutsey, PhD, MPH, FAHA**

**Speaker**

*Professor, Division of Epidemiology and Community Health, School of Public Health, University of Minnesota*

Dr. Pamela Lutsey, is a Professor in the Division of Epidemiology and Community Health at the University of Minnesota (UMN). Her research focuses on identifying potentially modifiable factors that influence the risk of cardiovascular disease, dementia, and other chronic conditions. Areas of particular interest include sleep quality and quantity, nutritional biomarkers (e.g., serum magnesium), and venous thromboembolism. She is the UMN Principal Investigator of the Atherosclerosis Risk in Communities (ARIC) Study, which forms the basis for much of her research evaluating modifiable risk factors for cardiovascular disease and dementia. She is also a Co-Investigator on the Multi-Ethnic Study of Atherosclerosis (MESA), and was the UMN site-Principal Investigator of the MESA Sleep ancillary study, which collected polysomnography and actigraphy data from 2010-2013. Additionally, she conducts pharmacoepidemiology research using large administrative data sources (i.e., MarketScan, Medicare 20% sample) to compare the effectiveness of new versus established treatment strategies for venous thromboembolism and atrial fibrillation.



**Dr. Victoria L. Bautch, PhD**

**Speaker**

*Distinguished Professor of Biology, University of North Carolina Chapel Hill, Co-Director, UNC McAllister Heart Institute*

Dr. Victoria Bautch received her PhD in Biochemistry from U. Illinois Medical Center, followed by postdoctoral work at Cold Spring Harbor Laboratories, leading to a faculty position at the University of North Carolina Chapel Hill, where she is now Chapin Distinguished Professor of Biology and Co-Director of UNC McAllister Heart Institute. Dr. Bautch's early studies provided the first definitive description and live-imaging of blood vessel formation from mouse stem cells, and her group made seminal discoveries around negative regulation of VEGF signaling. Her recent work investigates flow-mediated BMP signaling and nuclear mechanotransduction in vascular biology. She's trained over 50 fellows and graduate students, served on numerous NIH review panels, served on the NIH-NHLBI Parent Committee for Program Project Grants, and she is a current member of the NIH-NHLBI Advisory Council. Dr. Bautch was President of NAVBO, she chaired a 2016 Gordon Research Conference, and co-chaired NAVBO Workshops in 2017-2019.

# Session 2

## Moderators & Speakers



**Dr. Brooke Aggarwal, EdD, MS, FAHA**

**Moderator & Speaker**

See bio under Workshop Co-chairs.



**Dr. Josiane Broussard, PhD**

**Speaker**

*Laboratory Director, Associate Professor, Colorado State University, Department of Health and Exercise Science*

Dr. Josiane Broussard, a clinical and translational scientist, explores the intersection of sleep and circadian rhythms and cardiometabolic health at both the whole body and tissue-specific levels. She received her PhD in Molecular Metabolism and Nutrition from the University of Chicago, then completed postdoctoral training with Dr. Richard Bergman in Los Angeles, CA, studying the effects of diet-induced obesity on insulin sensitivity in a large animal model. In 2015, she moved to the University of Colorado Boulder for in-depth training in clinical circadian physiology with Dr. Kenneth P. Wright, Jr. In July of 2018, she established her independent laboratory at Colorado State University to study the mechanistic underpinnings of insulin resistance due to insufficient sleep and/or circadian misalignment, as well as potential countermeasures.



**Dr. Philip Cheng, PhD**

**Speaker**

*Associate Professor of Medicine*

Dr. Philip Cheng is an Associate Professor of Medicine and a licensed psychologist at the Sleep Disorders and Research Center at Henry Ford Health, and Michigan State University Health Sciences Center in Detroit, MI. He received his PhD in Clinical Psychology from the University of Michigan, Ann Arbor. Dr. Cheng's research primarily focuses on sleep, circadian rhythms, and their roles in health and psychological functioning. He is funded by the National Institutes of Health to study phenotypes of shift work disorder, and to translate the science of circadian rhythms into clinically feasible and widely accessible interventions for night shift workers. Additionally, his work examines how digitally delivered therapies may be leveraged to enhance the accessibility of sleep treatments to those who are socially and economically disenfranchised.



### **Dr. Jonathan Lipton, MD, PhD**

#### **Speaker**

*Assistant Professor of Neurology, Harvard Medical School, Faculty, Kirby Center, Boston Children's Hospital*

Dr. Jonathan Lipton is a pediatric neurologist, sleep medicine physician, and chronobiologist. Dr. Lipton was clinically trained in Child Neurology and Sleep Medicine at Boston Children's Hospital and Harvard Medical School, followed by post-doctoral studies with Mustafa Sahin where he pioneered the mechanistic investigation of circadian rhythm dysfunction in models of neurodevelopmental disorders. Dr. Lipton supervises a basic laboratory at Boston Children's Hospital dedicated to understanding the mechanistic interfaces between circadian timekeeping, sleep, and neuropsychiatric disorders. His research includes the synaptic biology of the clock system, molecular mechanisms that underlie circadian resilience in the face of external and internal perturbations, and development of platforms for bench-to-bedside approaches in circadian medicine.



### **Dr. Sanja Jelic, MD**

#### **Speaker**

*Director, Center for Sleep Medicine, Professor of Medicine, Columbia University Medical Center, New York*

Dr. Sanja Jelic is a Professor of Medicine in the Division of Pulmonary, Allergy, and Critical Care Medicine at Columbia University in New York. She received her MD degree from the University of Zagreb, Croatia, and trained in internal, pulmonary, and sleep medicine at the Albert Einstein College of Medicine and Columbia University in New York. Her research focuses on the molecular mechanisms of endothelial dysfunction in disturbed sleep, including obstructive sleep apnea and sleep deprivation. Dr. Jelic was named Herbert Irving Professor at Columbia University, received awards from the American Thoracic Society, American Academy of Sleep Medicine, and American Lung Association, and is the Director of the Center for Sleep Medicine at Columbia University Irving Medical Center. Dr. Jelic's work is funded by the NIH/NHLBI, American Heart Association, American Thoracic Society and American Academy of Sleep Medicine.



### **Dr. Fil Swirski, PhD**

#### **Speaker**

*Director, Cardiovascular Research Institute, The Arthur and Janet C. Ross Professor of Medicine, Cardiology, Professor, Diagnostic, Molecular and Interventional Radiology*

Dr. Fil Swirski is the Arthur and Janet C. Ross Professor of Medicine (Cardiology) and Professor of Diagnostic, Molecular and Interventional Radiology at the Icahn School of Medicine at Mount Sinai. As Director of the Cardiovascular Research Institute and holding secondary appointments at the Precision Immunology Institute and the BioMedical Engineering and Imaging Institute, he is a renowned figure in the fields of innate immunity, inflammation, and cardiovascular science. His work, emphasizing the interplay between the hematologic, immune, metabolic, and nervous systems, notably includes the impact of lifestyle factors like sleep, diet, and stress on cardiovascular health. After earning his PhD from McMaster University and conducting postdoctoral research at Brigham and Women's Hospital, Dr. Swirski served as a Professor at Harvard Medical School and Principal Investigator at Massachusetts General Hospital before his tenure at Mount Sinai beginning in 2021. His accolades include the Jeffrey M. Hoeg Award from the American Heart Association, the William Harvey Lecture from the European Society of Cardiology, the Martin Prize for Fundamental Research, the Howard M. Goodman Fellowship, and the Patricia and Scott Eston Research Scholar from Massachusetts General Hospital. Dr. Swirski holds an Outstanding Investigator Award from the NHLBI, an Established Investigator Award from the AHA, an investigator grant from Cure Alzheimer's Fund, and is the North American Coordinator of a Leducq Foundation Transatlantic Network of Excellence Consortium.



### **Dr. Dayna A. Johnson, PhD, MPH, MSW, MS**

#### **Speaker**

*Assistant Professor, Rollins School of Public Health, Emory University, Department of Epidemiology*

Dr. Dayna A. Johnson is a sleep epidemiologist and Assistant Professor in the Department of Epidemiology at the Rollins School of Public Health, Emory University. She received her doctorate degree in Epidemiologic Science from the University of Michigan and completed a postdoctoral fellowship in Sleep and Circadian Disorders at Harvard Medical School and Brigham and Women's Hospital. Her research aims to understand the determinants and health consequences of sleep health disparities by addressing the social and environmental determinants of sleep disorders and insufficient sleep and investigating the influence of modifiable factors such as sleep disorders and disturbances on various health outcomes. Dr. Johnson's projects include investigating associations of sleep health and sleep disorders with hypertension, diabetes, metabolic syndrome, and cognition. She is currently recruiting a cohort of 400 Black adults in Atlanta to test associations between environmental factors, sleep and circadian disruption, and cardiovascular health via ambulatory blood pressure monitoring and arterial stiffness – the ARISE Study (Assessment of Rhythms in Sleep and the Environment study, NHLBI R01). Dr. Johnson also conducts intervention studies exploring how stress reduction or home improvements can improve sleep and reduce subsequent risk for poor health outcomes. She is engaged in community partnerships to investigate the effect of environmental exposures and housing on health. Dr. Johnson has over 100 peer-reviewed publications and has been featured in several magazines, podcasts, and news programs for her expertise in sleep inequities, sleep health, and sleep disorders. Her mission is to increase awareness around the importance of sleep and eliminate sleep health inequities.



# Session 3

## Moderators & Speakers



**Dr. Michael Grandner, PhD, MTR, CBSM, FAASM**

**Moderator & Speaker**

See bio under Workshop Co-chairs.



**Dr. Fabian-Xosé Fernandez, PhD**

**Speaker**

*Associate Professor of Psychology and Neurology at the University of Arizona (UA)*

Dr. Fabian-Xosé Fernandez is an Associate Professor of Psychology and Neurology at the University of Arizona (UA). Dr. Fernandez earned his BSc in a self-tailored interdisciplinary program in Neurobiological Science from the University of Florida, Gainesville, and a PhD in Neurosciences from Stanford University. While at Stanford, he worked with a collaborative team to define the memory problems associated with chronic circadian dysrhythmia. These efforts required careful consideration of experimental design and how it could be leveraged to maximize translation of results between animals and humans. Fabian held positions in industry and at Johns Hopkins University as a research affiliate before joining the UA faculty in 2015. His laboratory has focused on important topics in the sleep and circadian sciences for over a decade.



**Dr. Aric A. Prather, PhD**

**Speaker**

*Associate Professor of Psychiatry University of California, San Francisco*

Dr. Aric A. Prather is a Professor of Psychiatry and Behavioral Sciences and directs the Behavioral Sleep Medicine Research Program at the University of California, San Francisco. Dr. Prather's research program focuses on the causes and consequences of insufficient sleep, emphasizing how sleep impacts the immune system. He is also a licensed clinical psychologist who treats sleep disorder patients, primarily those with insomnia, using cognitive behavioral therapy through the UCSF Neuro/Psych Sleep Clinic.



**Dr. Nicole Bowles, PhD**

**Speaker**

*Assistant Professor in the Oregon Institute of Occupational Health Sciences at OHSU*

Dr. Nicole Bowles is an Assistant Professor in the Oregon Institute of Occupational Health Sciences at OHSU. Her research sits at the nexus of basic science and social science, examining the modulation of sleep and circadian rhythms in humans and determining how these signaling patterns buffer the cardiometabolic responses to psychosocial and environmental stress. Dr. Bowles uses a community-based participatory framework to engage occupational populations, including on-duty Oregon firefighters and police officers, and to bring diverse populations into the laboratory, where she can control the environment and behaviors to systematically measure sleep and circadian phase. Dr. Bowles' research is currently funded by a NHLBI K01 Career Training Award and the NIOSH Total Worker Health® Program. She is also the recipient of OHSU's Women in Academic Health and Medicine Emerging Leader Award and received an honorable mention for this year's APSS DEI award.



**Dr. Kelly Glazer Baron, PhD, MPH, DBSM**

**Speaker**

*Professor, Division of Public Health, Licensed Clinical Psychologist, Director, Behavioral Sleep Medicine Program, Department of Family and Preventive Medicine, Adjunct Associate Professor, Departments of Psychology and Psychiatry*

Dr. Kelly Glazer Baron is a Professor in the Division of Public Health, Department of Family and Preventive Medicine. She is a clinical psychologist with specialty training in Behavioral Sleep Medicine. Prior to her position at the University of Utah, Dr. Baron held faculty positions at the Feinberg School of Medicine at Northwestern University and Rush University Medical School. Dr. Baron completed her bachelor's degree with honors and distinction at the Ohio State University, her master's degree and PhD in clinical psychology at the University of Utah, and her predoctoral residency in health psychology at Rush University Medical School. After graduate school, she completed a postdoctoral fellowship in health services research as well as a MPH degree at Northwestern University. Dr. Baron conducts NIH-funded research, including sleep interventions among patients with hypertension and studies examining the role of circadian timing on appetite regulation. Dr. Baron is the training director of the behavioral sleep medicine program patients for non-drug treatment for sleep disorders, including treatments for insomnia, circadian disorders, problems using CPAP treatment in sleep apnea, and other sleep issues.



## **Dr. Esra Tasali, MD**

### **Speaker**

*Professor of Medicine, Director, U Chicago Sleep Center*

Dr. Esra Tasali is a Professor of Medicine at the University of Chicago and the Director of the UChicago Sleep Center. She has clinical training in pulmonary, sleep medicine, and endocrinology. Dr. Tasali is an internationally recognized sleep medicine expert with over 20 years of research experience. Her work has significantly contributed to our understanding of how sleep duration and quality are linked to energy metabolism and cardiometabolic disease risk. Her recent publication demonstrating that sleep extension reduces caloric intake in a real-world setting has garnered significant attention in the scientific community and the public worldwide given its important implications for the prevention or reversal of obesity. She is the recipient of several awards for her pioneering work on the role of sleep in cardiometabolic risk. She currently serves as the chair of the Sleep Disorders Research Advisory Board at the National Institute of Health.

# Session 4

## Moderators & Speakers



**Dr. Donald M. Lloyd-Jones, MD, ScM, FAHA, FACC, FASPC**

**Dr. Brooke Aggarwal, EdD, MS, FAHA**

**Dr. Michael Grandner, PhD, MTR, CBSM, FAASM**

### **Moderators**

See bios under Workshop Co-chairs.



**Dr. Ali Azarbarzin, PhD**

### **Speaker**

*Assistant Professor of Medicine Harvard University*

Dr. Ali Azarbarzin is an Assistant Professor of Medicine at Harvard Medical School and a lead investigator at the Brigham and Women's Hospital, where he directs the Sleep Apnea Health Outcomes Group. Dr. Azarbarzin's research interests lie in the area of physiological consequences of sleep apnea, ranging from markers of cardiovascular and neurocognitive health outcomes to identifying individuals who benefit most from treatment.



**Dr. Ron Anafi, MD, PhD**

### **Speaker**

*Assistant Professor of Medicine, University of Pennsylvania*

Dr. Ron Anafi is an Assistant Professor of Medicine at the University of Pennsylvania. As an undergraduate at Tulane University, he studied biomedical engineering and philosophy. He traveled north for the University of Minnesota's MD/PhD program, where he completed his graduate degree in mechanics, humorously noting he still cannot fix his car! His graduate research with Ted Wilson focused on the mechanics of asthmatic bronchoconstriction. After an internal medicine residency at the University of Vermont, he moved to the University of Pennsylvania for clinical training in sleep medicine, remaining for a postdoctoral fellowship in circadian bioinformatics working with Dr. John Hogenesch. His lab uses techniques from machine learning, engineering, and systems biology to understand how sleep and molecular rhythms influence physiology in the brain and body. He sees patients at the Penn Sleep Center.



### **Dr. Qing Robert Miao, PhD**

#### **Speaker**

*Professor of Foundations of Medicine, Diabetes and Obesity Research Center, New York University Long Island School of Medicine*

Dr. Qing Robert Miao is well recognized for his research on elucidating the biological functions of the Nogo-B receptor and its roles in the pathogenesis of human diseases. Nogo-B receptor (NgBR) is a cell surface receptor identified by Dr. Miao during his postdoctoral training in Dr. William Sessa's laboratory at the Yale School of Medicine. His work at the Medical College of Wisconsin demonstrated that NgBR is a vital gene required for development, and loss of NgBR causes early embryonic lethality. In 2019, Dr. Miao was recruited to NYU Grossman Long Island School of Medicine from the Medical College of Wisconsin. Dr. Miao's research program is innovative and impactful, bridging the gap between bench and bedside, strengthening the translational aspect of his research through collaboration with clinical colleagues. By identifying physiological defects in NgBR tissue-specific knockout mice, Dr. Miao's team has established unique animal models to study the effects of metabolites on epigenetic regulation and host resilience. These models have been instrumental in elucidating the novel underlying mechanisms of several human diseases, including cerebrovascular malformations, nonalcoholic fatty liver diseases, obesity-induced diabetes, and diabetes-associated vascular complications. His contribution to the field is evidenced by continuous success in NIH funding and the Mid-Career Investigator Award from the American Heart Association's Council on Peripheral Vascular Disease.



### **Dr. Rene Cortese, PhD**

#### **Speaker**

*Assistant Professor, Departments of Pediatrics and Obstetrics, Gynecology and Women's Health, School of Medicine, University of Missouri, Columbia, MO*

Dr. Rene Cortese studies epigenetics of complex diseases to understand how they develop, progress, are inherited, and can be treated. His research focuses on multiomics studies on phenotype modulation in Children's and Women's Health, epigenetics mechanisms involved in the Developmental Origin of Diseases, epigenomics of Sleep Disorders, and epigenomics profiling in circulating DNA in bodily fluids. Dr. Cortese received his MSc in Biological Sciences from the University of Buenos Aires, Argentina, and earned his PhD at the University of Bonn, Germany. He completed his Post-doctoral Fellowship in Epigenetics at the Krembil Family Epigenetics Laboratory CAMH, in Toronto, Canada. He has over 35 publications and 6 patents and has worked in genetics/epigenetics for over 15 years in both academia and industry.



**Dr. Ivan Vargas, PhD**

**Speaker**

*Assistant Professor of Psychological Science at the University of Arkansas*

Dr. Ivan Vargas is an Assistant Professor of Psychological Science at the University of Arkansas. He completed a postdoctoral fellowship at the Behavioral Sleep Medicine Program and the Center for Sleep and Circadian Neurobiology at the University of Pennsylvania School of Medicine. Dr. Vargas' research interests focus on the etiology and treatment of insomnia, including the evaluation of behavioral interventions for sleep, such as cognitive-behavioral therapy for insomnia (CBT-I). His research is currently supported by an NIH career development award funded by the National Heart, Lung, and Blood Institute (K23HL141581).

# Abstracts



## Session 1

### Defining Cardiovascular Resilience and the Role of Sleep: A Cardiovascular Resilience Researcher's Perspective

*Donald M. Lloyd-Jones, MD, ScM, FAHA, FACC, FASPC*

In cardiovascular epidemiology, cardiovascular resilience is often considered retrospectively by identifying outliers—individuals who defy expectations by not developing cardiovascular disease despite having multiple adverse risk factors, or a single severely adverse factor. Defining cardiovascular resilience in real time or prospectively is more challenging. In 2010, the American Heart Association introduced a formal definition for “cardiovascular health (CVH),” a novel construct intended to assess health status—rather than risk—measurable, monitorable, and modifiable at both individual and population levels. Originally termed “Life’s Simple 7™,” this construct assessed a range of seven health behaviors and physiological factors, including diet, physical activity, smoking status, body mass index, blood cholesterol, blood glucose, and blood pressure. In 2022, the CVH scoring system was updated to enhance sensitivity to inter-individual differences and intra-individual changes, and sleep was incorporated as a new metric, thus evolving into “Life’s Essential 8™.” Substantial research has demonstrated that maintaining high levels of CVH or improving CVH at any life stage correlates with better longevity, a longer health span free of cardiovascular disease and other major chronic conditions, reduced morbidity, lower healthcare costs, and improved quality of life. Therefore, the CVH construct may serve as a robust, current indicator of cardiovascular and general health resilience. Recent studies are exploring how both qualitative and quantitative sleep metrics contribute to cardiovascular health.

### Social Determinants of Sleep Health from 2017–2020: Exploring the Intersection of Race and Gender

*Dr. Stephanie Cook, DrPH, MPH*

Racial/ethnic differences significantly influence sleep health, with minorities often experiencing fewer minutes of sleep compared to their white counterparts. This study employs an Intersectionality Framework to examine variations in sleep duration among different racial/ethnic groups of men and women over time. Data from 5,280 participants were analyzed, collected through the All of Us Research Program. Sleep duration was measured using daily summaries from participants’ Fitbit devices, which were worn for at least 10 hours per day. Sociodemographic characteristics, including gender, race, and ethnicity, along with covariates such as BMI, heart condition, and substance use, were assessed through self-reported questions. A three-way interaction model analyzing gender, race, and time revealed significant disparities in sleep duration. Black and Asian participants slept 42 minutes ( $p < 0.001$ , 95%CI -53.7, -31.9) and 39 minutes ( $p < 0.001$ , 95%CI -56.4, -23.5) less on average than white participants,

respectively. Gender-related differences were also significant, with trajectories of sleep decreasing more sharply for Black, Hispanic, and Asian women compared to white women, and Black males experiencing a steeper decline in sleep duration compared to white males. The findings underscore pronounced longitudinal disparities in sleep duration across different racial/ethnic and gender groups. Future research should adopt an intersectional approach to uncover the underlying processes exacerbating these disparities. Such insights are crucial for developing sleep interventions tailored to meet the unique needs of racial/ethnic minority groups. Moreover, future studies should explore resilience or protective factors that mitigate the impact of poor sleep across these diverse groups.

## **Integrating Chrononutrition and Sleep: A Pathway to Atherosclerosis Management and Cardiovascular Resilience**

*Dr. Jose M Ordovas, PhD*

The interplay between chrononutrition and sleep is increasingly acknowledged as pivotal for cardiovascular health, particularly in managing atherosclerosis and enhancing cardiac resilience. Chrononutrition, aligning food intake with the body's circadian rhythms, profoundly impacts metabolic processes such as lipid metabolism and glucose regulation. When combined with quality sleep—a crucial restorative process that regulates heart rate, blood pressure, and endothelial function—the potential for cardiovascular benefit is magnified. Evidence suggests that synchronized sleep routines and timed meals optimize metabolic health and reduce cardiovascular risks like hypertension, atherosclerosis, and heart failure. In contrast, misaligned eating patterns disrupt these benefits and are linked to metabolic and cardiovascular disease onset. The discussion also touches on the significance of interindividual variability, where chrononutrition emerges as an aspect of precision nutrition, acknowledging that dietary responses can vary based on genetic, metabolic, and environmental factors. The future of cardiovascular health strategy is shaped by a transdisciplinary approach, integrating technological advances for a nuanced understanding of these interactions. This progressive view aims to shift preventive strategies, offering customized care to enhance cardiovascular resilience, thereby improving life quality and reducing the burden of heart diseases with evidence-based interventions.

## **Intersection of Aging, Sleep and Cardiovascular Resilience**

*Dr. Pamela Lutsey, PhD, MPH*

Aging, sleep and cardiovascular resilience are intertwined. It is well-established that risk of cardiovascular disease (CVD) increases with age. Similarly, sleep architecture and the pervasiveness of sleep disorders also change with age. Older adults tend to have shorter sleep duration, more awakenings, less slow wave sleep, and a higher prevalence of obstructive sleep apnea (OSA). Biological aging relates to the cellular and molecular processes underlying age-related physiologic changes. Sleep may directly affect biological aging through numerous pathways. Cross-sectional data from observational studies have reported that participants with OSA are more likely to have accelerated biological aging, as quantified by shorter leukocyte telomere length and greater epigenetic age. Similarly, a higher number of insomnia symptoms has been associated with epigenetic age acceleration and late differentiated T cells. Circadian rhythms also undergo age-related changes, which may have implications for cardiovascular resilience and risk. Aging-related changes in sleep quality and quantity may directly influence cardiovascular resilience and risk. Rigorous research is needed to evaluate whether treatment of sleep disorders can improve cardiovascular reliance, particularly among older adults.



## Conceptualizing Cardiovascular Resilience

*Dr. Victoria Bautch, PhD*

Resilience, defined broadly, is the ability of living systems to maintain or return to homeostasis in response to stressors or challenges. Refining this broad definition to specifically study cardiovascular resilience is an active focus within the cardiovascular research community. The challenge lies in working across different scales and integrating outcomes over biological systems. This presentation will address several concepts that inform cardiovascular resilience, from the cellular to the tissue level, including circadian rhythms in cardiovascular biology. The examples provided will demonstrate that the endothelial cell is a critical control node in cardiovascular resilience. These discussions will set up questions whose answers aim to integrate various scales of cardiovascular resilience, fostering a deeper understanding of the mechanisms at play.

## Session 2

### Overview of Potential Mechanisms Linking Sleep and Circadian Rhythms to Cardiovascular Resilience

*Dr. Brooke Aggarwal, EdD, MS, FAHA*

Sleep and circadian rhythms may be linked to cardiovascular resilience through a variety of potential mechanisms, including physiological, behavioral, and psychological aspects. For example, there are daily rhythms and circadian systems that regulate blood pressure, which, if disturbed, can lead to hypertension. Multiple dimensions of sleep, including both short and long sleep duration, poor sleep quality, and sleep variability, have been shown to potentially reduce cardiovascular resilience through increased inflammation, hypertension, obesity, arterial stiffness, endothelial dysfunction, and risk for type 2 diabetes. Poor sleep and circadian misalignment may also negatively impact diet and physical activity, key behaviors for maintaining optimal cardiovascular health. Additionally, psychosocial risk factors for cardiovascular disease such as stress, depressive symptoms, and anxiety have been shown to increase after periods of even mild sleep deprivation or commonly experienced sleep disturbances. These mechanisms may have important implications for the cardiovascular health and resilience of a large segment of the population who are not meeting recommendations for nightly sleep duration, shift workers, and/or people living with sleep or circadian disorders.

### Impact of Sleep and Circadian Disruption on Cardiovascular Outcomes from Controlled Clinical Studies

*Dr. Josiane Broussard, PhD*

Cardiometabolic dysfunction encompasses a variety of abnormalities and diseases, including insulin resistance,  $\beta$ -cell dysfunction, atherogenic dyslipidemia, nonalcoholic fatty liver disease, type 2 diabetes, and cardiovascular disease. The primary therapy for managing these complications emphasizes lifestyle modifications aimed at weight loss through increased exercise and reduced caloric intake. Emerging evidence also highlights the significance of interventions focused on sleep and circadian timing as crucial for mitigating cardiometabolic dysfunction. Specifically, the timing of behaviors such as sleep, food intake, and physical activity can influence the relationships between physiological changes and cardiometabolic health. However, our understanding of how the circadian timing of these behaviors affects cardiometabolic outcomes is still developing and represents a burgeoning field of biomedical research. There is a need for rigorous, highly-controlled studies to further our knowledge of how the timing of behaviors impacts cardiometabolic health.

## Conceptualizing Sleep and Circadian Health and Resilience

*Dr. Philip Cheng, PhD*

The evidence for the importance of sleep and circadian rhythms for health and wellness is clear; however, most existing research has focused on how disruptions to healthy sleep are risk factors for disease. Research examining the roles that sleep and circadian rhythms may have in promoting resilience is still emergent. One challenge in resilience research is the complexity of resilience as a construct. Indeed, there are ongoing debates about what does and does not constitute resilience. This talk will operationalize resilience using an established model that breaks it into three sub-components: resistance, recovery, and adaptation. Emergent evidence implicating sleep and circadian rhythms as contributing factors to each of the three components of resilience will be presented, including an exploration of potential multilevel mechanisms through which sleep and circadian rhythms contribute to resilience. We will aim to discuss practical implications for research and clinical applications, including exploration of future directions and expanded conceptualizations of resilience.

## Toward Mechanisms of Circadian Resilience in Cells and Synapses

*Dr. Jonathan Lipton, MD, PhD*

Circadian rhythms are essential multi-scale organizers of cellular and organismal timekeeping, aligning biological functions with the earth's light/dark cycles. These biological clocks are believed to bolster biological resilience by enabling predictability and adaptability, anticipating and compensating for environmental changes. Although primarily known for regulating the sleep/wake cycle, circadian rhythms influence various cognitive behaviors, including learning, memory, mood regulation, and attention, yet the underlying mechanisms remain unclear. Disruptions in these rhythms have been implicated in a range of neurodevelopmental and neurodegenerative disorders, highlighting their critical role in maintaining homeostasis. This presentation will explore recent findings from my laboratory, including both reported and unpublished work, that identify the core clock protein BMAL1 as a crucial organizer of rhythmic synaptic function. Our studies show that BMAL1's interaction with the key synaptic enzyme CaMKII $\alpha$  at synapses introduces biochemical and functional rhythms independently of its traditional role in the canonical circadian clock. We hypothesize that synaptic BMAL1 contributes to neurological resilience by timing energetically demanding neural processes, such as synaptic plasticity and neurotransmission, to occur at the most suitable times of day. We also speculate that similar mechanisms could enhance cellular resilience in non-neural systems.

## Mechanisms of Increased Cardiovascular Risk in Insufficient Sleep

*Dr. Sanja Jelic, MD*

More than a third of US adults sleep less than the recommended 7-8 hours per night, increasing cardiovascular risk, particularly pronounced in women. Healthy sleep prevents oxidative stress, a key contributor to endothelial dysfunction and cardiovascular disease progression. Insufficient sleep, like other cardiovascular risk factors such as cigarette smoking and hypertension, triggers intracellular oxidative stress. In model organisms, sleep restriction amplifies oxidative stress and activates the antioxidant response via the nuclear factor (erythroid-derived 2)-like 2 (Nrf2), which stimulates genes with the antioxidant response element (ARE). Overexpression of antioxidant genes has rescued severely sleep-deprived *Drosophila*, highlighting the protective role of the Nrf2-ARE pathway against cardiovascular diseases. In a rigorous, randomized crossover study using freshly harvested endothelial cells (ECs), we observed that mild, prolonged sleep restriction mimicking real-life conditions increases endothelial oxidative stress and inflammation, leading to endothelial dysfunction in healthy women. Remarkably, despite significantly increased endothelial oxidative stress, endothelial antioxidant responses were absent following sleep restriction. Through an

unbiased RNA sequencing approach in harvested ECs, we identified a reduction in the expression of endothelial Defective in Cullin Neddylation-1 Domain Containing 3 (DCUNID3), a protein essential for facilitating the Nrf2-mediated antioxidant response in ECs. This novel mechanism elucidates the lack of endothelial antioxidant response to sleep restriction-induced oxidative stress. Furthermore, curtailing sleep by delaying bedtime diminishes the expression of endothelial DCUNID3 regulator serum response factor, a transcription factor crucial for priming cortical responses to sleep restriction. These findings provide direct evidence that reducing sleep duration, a common behavior among adults, detrimentally impacts vascular health.

## **Sleep and Leukocyte Dynamics in Cardiovascular Disease**

### **Influence of Sleep on Brain-Body Communication**

*Dr. Filip Swirski, PhD*

Sleep profoundly affects our health. While it is well documented that good sleep hygiene can keep us healthy and may even prolong our lives, it is less clear how sleep affects communication between our tissues, cells, and their products. Our work investigates how the brain perceives environmental fluctuations and controls immune, metabolic, and circulatory systems. Using tools of neuroscience, immunology, hematology, and vascular biology, we aim to uncover fundamental mechanisms underlying brain-body communication in response to lifestyle factors. In this talk, I will discuss how sleep controls leukocyte dynamics and function and, more broadly, how it modulates brain-body communication.

## **Multilevel Determinants of Sleep and Cardiovascular Disparities: The Role of Risk and Resilience**

*Dr. Dayna Johnson, PhD, MPH*

Sleep is not equitable. Historically minoritized individuals have a high prevalence of sleep disorders and adverse sleep health. Research supports that social determinants of health contribute to sleep health inequities. Furthermore, sleep is socially patterned. Neighborhoods with high rates of crime, violence, disadvantage, pollution, inopportune light exposure, and noise, where historically minoritized individuals are most likely to reside, are associated with adverse sleep health. Additionally, discrimination, racism, and stress burdens are linked with poor sleep health among these populations. While extensive evidence identifies risk factors for adverse sleep health, research also supports factors that promote healthy sleep. A growing body of literature indicates that neighborhood social cohesion, safety, and individual-level social support are associated with healthy sleep, which in turn is linked to better cardiovascular health. Emerging research suggests that sleep disparities contribute to cardiovascular inequities. Therefore, incorporating resilience into sleep interventions may help reduce these cardiovascular disparities. Future research should explore factors that promote sleep health among those most at risk and examine the subsequent impact on cardiovascular health.

## Session 3

### Overview: Sleep and Circadian Interventions for Cardiovascular Resilience

*Dr. Michael Grandner, PhD, MTR, CBSM, FAASM*

Interventions designed to enhance cardiovascular resilience through improved sleep and circadian health can operate at multiple levels. These interventions may target enhancements in sleep and circadian health directly and/or alleviate related symptoms and disorders. For instance, strategies might include the use of light, melatonin, or other zeitgebers to modify, consolidate, or strengthen circadian rhythms. Alternatively, pharmacological and behavioral approaches could aim to alleviate sleep symptoms, enhance sleep quality, improve daytime functioning related to sleep health, or address sleep disorders. Interventions might also indirectly improve cardiovascular resilience by tackling social, behavioral, environmental, and biological determinants of sleep and circadian health. This could encompass individual-level factors like attitudes, health status, and mental health; social-level factors such as workplace dynamics, family interactions, and neighborhood conditions; and societal-level influences including health disparities, public policies, and economic conditions. Additionally, technology plays a crucial role in the development of intervention components (e.g., generative AI), assessment tools (e.g., sensors and behavioral inputs), and the delivery of interventions (e.g., enhancing interactivity, broadening dissemination, and reducing accessibility barriers).

### Use of Light and Chronopharmacology to Improve Cardiovascular Resilience

*Dr. Fabian Fernandez, PhD*

A recent NHLBI Workshop on Circadian Rhythm of Blood Pressure and Chronotherapy for Hypertension (2021) concluded that the efficacy of bedtime administration of antihypertensive medications was unclear. However, in this presentation, I will summarize clinical data that contradict these findings. Focused on dosing strategies that optimize drug availability to coincide with early morning surges in heart rate and blood pressure—which are times of increased risk for stroke and myocardial infarction—researchers from two major pharmaceutical companies have developed proprietary antihypertensive formulations. These formulations, which were FDA-approved and began widespread use in the mid-2000s, exemplify the practical applications of circadian medicine. Looking ahead, these advances provide valuable lessons for enhancing cardiovascular system resilience through the synchronized use of environmental interventions and vascular disease medications, aligning treatment with the 24-hour biological clock.

### Opportunities for Improving Sleep to Support Cardiovascular Resilience

*Dr. Aric Prather, PhD*

There is growing evidence that insufficient sleep and sleep disturbances can negatively impact cardiovascular health, yet it remains unclear whether sleep interventions promote cardiovascular resilience. Opportunities for improving sleep health span multiple levels, ranging from policies that can shape sleep at the population level to individual-level interventions, including medications, technology use, and behavioral interventions known to reduce sleep disturbances and regulate circadian biology. This presentation aims to review the medications and select technologies that have been shown to reduce sleep disturbances and improve sleep quality, with potential implications for cardiovascular resilience. Specifically, I will review common medications used to treat insomnia and their potential risks to cardiovascular health. Additionally, this presentation will explore emerging technologies that may improve sleep, including bedroom technologies such as the use of white and/or colored noise, tools to support optimal thermoregulation, and emerging devices developed to augment sleep neurophysiology, including transcutaneous vagal nerve stimulation, closed-loop sensory stimulation, and transcranial magnetic stimulation. The goal of this selective review is to generate discussion on how these tools may be used to support cardiovascular resilience.

## System-Level Approaches to Improve Sleep Health and Cardiovascular Resilience

*Dr. Nicole Bowles, PhD,*

Workplace characteristics such as long work hours, commute time, job strain, shift work, and noise levels have been linked with insomnia and cardiovascular disease. Conversely, the workplace also offers assets that enhance our quality of life, including social support, a sense of purpose, opportunities for skills and knowledge development, and health insurance. Considering that a significant portion of adults are employed and spend a considerable amount of their time at work, leveraging and expanding these benefits through health promotion initiatives can mitigate poor health behaviors, enhance safety, improve employees' quality of life, and consequently benefit the employer's financial standing. Initiatives that engage all stakeholders from the outset of program development are more likely to be adopted and sustained. Additionally, programs that adopt the hierarchy of controls and aim for strategies that eliminate occupational hazards or reorganize work through engineering or administrative controls tend to be most effective. This session will focus on studies that have specifically evaluated system-level approaches in the workplace that influence sleep and/or cardiovascular health, as well as the gaps and challenges in this field.

## Behavioral Sleep Health Promotion Strategies to Promote Cardiovascular Resilience

*Dr. Kelly Baron, PhD MPH, DBSM*

Although at least one-third of the adult population is affected by short sleep duration, most behavioral sleep medicine interventions have traditionally focused on specific sleep disorders such as insomnia. Short sleep duration is known to escalate cardiometabolic risk factors, including risks for diabetes and hypertension. This presentation will explore the development and testing of a sleep extension intervention that utilizes consumer wearables and brief coaching to extend sleep duration among adults who typically experience short sleep. The process will include obtaining user feedback to shape the intervention design, refining the approach through pilot studies, and then deploying it in a fully powered study targeted at populations with elevated blood pressure. This talk will also address the gaps in the intervention's delivery and discuss potential adaptations of the intervention aimed at managing short sleep duration and reducing cardiovascular risk among populations facing health disparities.

## Session 4

### Physiological Consequences of Sleep Disordered Breathing and Cardiovascular Outcomes

#### Obstructive Sleep Apnea and Cardiovascular Risk: Beyond the Apnea-Hypopnea Index

*Dr. Ali Azarbarzin, PhD*

Obstructive Sleep Apnea (OSA) is diagnosed and managed by a metric called the apnea-hypopnea index (AHI). While epidemiological studies have established OSA as a risk factor for cardiovascular outcomes, the magnitude of risk is highly variable among individuals with OSA, when defined by the AHI. OSA treatment can improve some outcomes, but results of randomized trials are disappointing, likely due to the limitations of current diagnostic and intervention strategies, as highlighted by the Agency for Healthcare Research and Quality. The AHI quantifies the total number of respiratory events (apnea or hypopnea), disregarding important information on the characteristics and physiological consequences of respiratory events, including degrees of ventilatory deficit and associated hypoxemia, cardiac autonomic response, and cortical activity. Over the last several years, novel methodologies have been proposed to better quantify the magnitude of OSA-related breathing disturbance and its physiological consequences. As a result, stronger associations with cardiovascular outcomes have been observed. The focus of this presentation is to discuss these novel methods and their ability to predict adverse cardiovascular outcomes.

## Future Directions for Translational Research Exploring Sleep and Circadian Rhythms

*Dr. Ron Anafi, MD, PhD,*

In mice, daily rhythms modulate the expression of thousands of transcripts, proteins, and metabolites, indicating profound influences of sleep and wakefulness on both brain and body. These distinct yet interrelated systems significantly impact metabolic, autonomic, and immune pathways essential for cardiovascular health. Disease states can alter physiological rhythms, and emerging data suggests that medications in current use may be modifying these daily patterns. Consequently, sleep and circadian scientists hypothesize that treatments could be timed to enhance therapeutic benefits or that physiological rhythms themselves might serve as viable therapeutic targets. However, the translation of these discoveries to human health has been gradual, with the limited clinical studies conducted so far producing mixed outcomes. This presentation will focus on emerging methods to: (1) understand physiological rhythms in human health and disease; (2) develop electronic and molecular biomarkers to better phenotype patients who might benefit from sleep and circadian therapeutics; and (3) target sleep and molecular rhythms to optimize health.

## Host Resilience to Prevent Diabetes-associated Vascular Complications

*Dr. Qing Miao, PhD*

The susceptibility of diabetes patients to severe lung injury and higher mortality suggests that hyperglycemia may compromise the host resilience needed to prevent acute lung injury (ALI). We used published single-nucleus RNA-seq data to reveal a significant decrease in the number of endothelial cells expressing NRF2 and the Nogo-B receptor (NgBR) in the lungs of patients with severe ALI. While the role of NRF2 in oxidative stress response and resilience is well-established, the function of NgBR as a resilience factor in lung endothelial cells (ECs) remains unexplored. To determine NgBR resilience, we noted that NgBR gradually decreases in the lung ECs isolated from diabetic mice, corresponding to increased blood glucose levels. The genetic depletion of NgBR in ECs results in damage to endothelial junctions and severe hemorrhage in the lungs of NgBR-inducible endothelial cell-specific knockout (iecko) mice. The connection between the decreased NgBR expression in the lung ECs of diabetic mice and the severity of lipopolysaccharide (LPS)-induced ALI has been further elucidated by various interventions to restore NgBR expression and the NgBR-mediated pathway. Our findings suggest that NgBR loss in diabetic lung ECs impairs the integrity of the lung vasculature and exacerbates the pathogenesis of lung injury.

## Epigenetic Studies and Protection Against Age-related Diseases

*Dr. Rene Cortese, PhD, ATSF*

Sleep disorders impact billions worldwide, affecting children, adults, and the elderly across both sexes, imposing multi-organ morbidity risks and increasing overall mortality. There is growing evidence that sleep disorders contribute to cellular pathways that mimic accelerated biological aging and senescence, which are closely linked to the pathophysiology of age-related diseases. Epigenetic studies have emerged as a vital research area for understanding the pathophysiology of sleep disorders and their associated morbidities, providing new avenues for therapeutic and diagnostic advancements. This presentation will focus on the latest advances in understanding the epigenetic mechanisms involved in sleep disorders. Research on obstructive sleep apnea (OSA) has shown that patients with OSA experience systemic epigenetic age acceleration compared to controls, and that adherent treatment can significantly decelerate epigenetic aging, whereas no changes are seen in controls. Additionally,

multi-phenotype and multi-omics studies using animal models have demonstrated that senolytics treatment significantly improves the cellular, molecular, and physiological effects of intermittent hypoxia exposure, which mimics OSA, across cardiovascular, metabolic, and cognitive domains. These findings support the notion that sleep disorders promote systemic senescence that is reversible with treatment and highlight the potential for personalized therapeutic interventions based on understanding the cellular and molecular mechanisms involved.

## **The Impact of Stress and Insomnia on Cardiovascular Functioning**

### **Chronic Insomnia and Its Impact on Cardiovascular Health**

*Dr. Ivan Vargas, PhD*

Chronic insomnia is one of the most prevalent sleep disorders in the general population and a significant risk factor for cardiovascular disease. Stressors are the primary precipitating factors in the onset of insomnia, but over time, as insomnia transitions from acute to chronic, it itself becomes a chronic stressor. This ongoing stress leads to chronic activation of biological stress responses, resulting in a state of hyperarousal. The hypothalamic-pituitary-adrenal axis, the primary neuroendocrine system regulating hormonal responses to stress, is a critical link between insomnia and poor cardiovascular health. This presentation will provide an overview of an etiological model of insomnia, explore potential mechanisms that explain the link between insomnia and cardiovascular health, including the role of stress, and discuss the potential for behavioral sleep interventions to augment treatment for cardiovascular disease.