

Daily News

SUNDAY | NOV. 12, 2023

Your backstage pass to Scientific Sessions 2023



Wu and Natarajan



Khera



Wu and Mahmoud

Distinguished Scientists, Joseph A. Vita and Nanette K. Wenger Research Goes Red Awards headline Saturday's Opening Session.

Philadelphia: Where History Meets Cardiovascular Innovation was the theme of yesterday's Opening Session, where thousands of AHA attendees from 90 countries gathered to kick off this year's Scientific Sessions that features more than 700 educational sessions and more than 4,000 abstracts.

"I hope you take advantage of the many opportunities to learn and connect with your colleagues here at Scientific Sessions," said Joseph C. Wu, MD, PhD, FAHA, AHA president. "Part of what makes this event special is the time spent

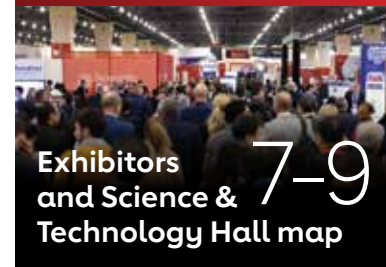
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A comprehensive view of cardiogenic shock

Weight-loss drug reduced secondary CV risk in people with overweight or obesity without diabetes

Semaglutide, a long-acting agonist of the glucagon-like peptide-1 receptor, significantly reduced cardiovascular events in people with overweight or obesity with pre-existing cardiovascular disease

without diabetes, according to Semaglutide and Cardiovascular Outcomes in Patients With Overweight or Obesity Who Do Not Have Diabetes: The SELECT trial.

Researchers revealed the trial's results during the Opening Session of Scientific Sessions 2023 on Saturday.

"This is the first drug specifically aimed at the management of overweight and obesity that has been shown to reduce cardiovascular events," said A. Michael Lincoff, MD, vice chair for research of the Robert and Suzanne Tomsich Department of Cardiovascular Medicine and an interventional cardiologist in the Sydell and Arnold Miller Family Heart, Vascular &

Thoracic Institute at the Cleveland Clinic and the study's principal investigator.

The multicenter, randomized, double-blind, placebo-controlled event-driven superiority trial enrolled 17,604 adults 45 years or older with pre-existing cardiovascular disease, such as myocardial infarction, stroke or symptomatic peripheral artery disease, and a body mass index of ≥ 27 who did not have diabetes.

Approximately 66% of patients had pre-diabetes (A1C 5.7%-6.4%).

In addition to evidence-based standard of care lipid management based on guidelines for lipid management, hypertension control and lifestyle management, patients

were randomly assigned to once weekly subcutaneous semaglutide 2.4 mg or matching placebo, with a mean follow-up of 40 months.

The primary cardiovascular efficacy composite endpoint was death from cardiovascular causes, non-fatal myocardial infarction or non-fatal stroke in a time-to-first-event analysis.

Overall, semaglutide benefited patients compared with placebo. The primary composite endpoint was reduced by 20% in patients with overweight or obesity with pre-existing cardiovascular disease in the semaglutide group compared with placebo (HR 0.80); P (two sided) <0.001 for superiority.

See **WEIGHT-LOSS DRUG**, page 6



Lincoff

Today at Sessions

Late-Breaking Science

Shocking Decisions in AFib Care

8-9:15 a.m. | Main Event I

- Efficacy and Safety of Dual Direct Current Cardioversion Versus Single Direct Current Cardioversion as an Initial Treatment Strategy in Obese Patients With Atrial Fibrillation
- Abelaclimab, a Novel Factor XI/XIa Inhibitor, Versus Rivaroxaban in Patients With Atrial Fibrillation: Primary Results of the AZALEA-TIMI 71 Randomized Trial (AZALEA-TIMI 71)
- Efficacy and Safety of Anticoagulation With Edoxaban in Patients With AHRE Durations \geq 24 Hours: The NOAH-AFNET 6 Trial (NOAH-AFNET 6)
- Apixaban for the Prevention of Stroke in Patients With Subclinical Atrial Fibrillation (ARTESIA)

Future of Lipid-Lowering Therapy — Novel Mechanisms and Approaches

3:30-4:45 p.m. | Main Event I

- Effects of Pitavastatin on Coronary Artery Disease and Inflammatory Biomarkers in HIV: Mechanistic Substudy of the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE)
- Recatimab Add-On Therapy in Patients With Non-Familial Hypercholesterolaemia and Mixed Hyperlipidemia (REMAIN-2): A Multicenter, Randomized, Double-Blind, Placebo-Controlled Phase 3 Trial (REMAIN-2)
- Efficacy and Safety of Lepodisiran: An Extended Duration Short-Interfering RNA Targeting Lipoprotein (a)
- Safety and Pharmacodynamic Effects of VERVE-101, an Investigational DNA Base Editing Medicine Designed to Durably Inactivate the PCSK9 Gene and Lower LDL Cholesterol — Interim Results of the Phase 1b heart-1 Trial

Featured Science

New Approaches to CV Therapeutics — First in Human Treatments

8-9:15 a.m. | Room 203AB

- Acute Hemodynamic Study of Oral TPN171H in Patients With Pulmonary Arterial Hypertension: A Multicenter, Randomized, Controlled, Phase 2 Clinical Trial
- Phase I Result of a Novel Antiplatelet Drug CG-0255 That Is Fast Acting, Long Lasting and Available for Either IV or Oral Administration
- Safety and Blood Pressure Lowering Effects of a Novel and Long-Acting Natriuretic Peptide Receptor 1 Agonist in Healthy Participants: A First-in-Human Clinical Study
- Safety and Efficacy of Induced Pluripotent Stem Cell-Derived Engineered Human Myocardium as Biological Ventricular Assist Tissue In Terminal Heart

Failure — BioVAT-HF-DZHK20 (BioVAT-HF-DZHK20)

- Phase 1 Gene Therapy Trial in Patients With Advanced Heart Failure Using a Novel Cardiotropic AAV Vector Targeting Protein Phosphatase Inhibitor-1

HFpEF and Amyloid — It's Prime Time!

9:45-11 a.m. | Room 203AB

- Effects of Semaglutide on Symptoms, Function and Quality of Life in Patients With the Obesity Phenotype of Heart Failure With Preserved Ejection Fraction: The Step-HFpEF Trial (STEP-HFpEF)
- Sodium-Glucose Cotransporter-2 Inhibitors in Transthyretin Amyloid Cardiomyopathy
- Acoramidis Improves Clinical Outcomes in Transthyretin Amyloid Cardiomyopathy Patients (ATTRIBUTE-CM)

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TCT at #AHA23

Scan the QR code for TCT at Scientific Sessions 2023 programming.

Today's Main Events



Presidential Session

1:30-3 p.m. | Main Event I

Join us for the Presidential Address featuring an inspiring Lewis A. Conner Lecture by AHA President Joseph C. Wu, MD, PhD, FAHA, an update from AHA CEO Nancy Brown and presentation of the Chairman's Award by AHA Chair Marsha Jones. The session will also feature presentations of the Eugene Braunwald Award, Research Achievement Award, Basic Research Prize, Clinical Research Prize, Population Research Prize and a special in memoriam tribute.

8-9:15 a.m. | 114/Nutter Theater
Advances of the "Polypill" in Cardiovascular Disease: From Concept to WHO Essential Medication

8-9:15 a.m. | Main Event II
Moving the Needle in Cardiogenic Shock: A Conversation With the Giants — The Intersection of Critical Care, Interventional and Heart Failure Cardiology and Cardiac Surgery

9:45-11 a.m. | Main Event II
A Confluence of Risk: Navigating the Intersection of Cardiovascular, Kidney and Metabolic Health

9:45-11 a.m. | 114/Nutter Theater
Nobel Laureate Lecture Session
Edvard I. Moser, PhD
Neural Computation of Space and Time



3:30-4:45 p.m. | Main Event II
Cardio-Oncology, "Onco-Cardiology" and Everything in Between: What Cardiologists Should Know About Cardiovascular Disease in Cancer

3:30-4:45 p.m. | 114/Nutter Theater
Paul Dudley White International Lecture and Session
Junbo Ge, MD
Panvascular Disease: What We Have Done and What We Can Do?

The prevention principle in cardio-oncology

Cardio-oncology treatment must prevent issues before they start



Herrmann



Cardinale

When it comes to cardiovascular disease in cancer, as with many other diseases, prevention is critical.

Joerg Herrmann, MD, and Daniela Cardinale, MD, PhD, FESC, will lead a discussion of prevention and all things related to cardio-oncology in a session titled, Cardio-Oncology, 'Onco-Cardiology,' and Everything in Between: What Cardiologists Should Know About Cardiovascular Disease in Cancer.

Dr. Herrmann, a cardiologist at the Mayo Clinic in Rochester, Minnesota, said prevention can be important especially in under-resourced populations.

"Disparities in cardio-oncology are just starting to be studied, and the AHA is supporting a strategically focused network on this very topic," he said. "It is much more cost effective to prevent a disease from occurring than treating it after its onset. The prevention principle applies to multiple areas of cardiology and oncology."

Dr. Cardinale, director of the cardio-oncology unit at the European Institute of Oncology in Milan, Italy, said prevention must be 360 degrees.

"Prevention can be performed at different stages of the cancer patient's treatment pathway, starting with the correction of cardiovascular risk factors and the optimization of any pre-existing heart disease," she said. "After that, in patients at a higher risk of cardiotoxicity, primary

prevention can be considered. The next step is a strict and continuous surveillance using biomarkers that can identify cardiotoxicity at the pre-clinical level, so that early intervention can be made with a cardioprotective strategy to

See **CARDIO-ONCOLOGY**, page 11

UPCOMING SESSION

Cardio-Oncology, "Onco-Cardiology," and Everything in Between: What Cardiologists Should Know About Cardiovascular Disease in Cancer

Sunday, Nov. 12 | 3:30-4:45 p.m.

Main Event II

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Trials' results suggest new approaches to reducing CVD risk and symptoms

Investigators during Late-Breaking Science Sessions on Saturday revealed surprising findings in three trials on novel approaches to reduce CVD risk. They found:

- Liberal blood transfusion strategy may improve clinical outcomes in patients with acute myocardial infarction and anemia.
- Dapagliflozin shows clinical benefit in patients with acute myocardial infarction without diabetes or chronic heart failure.
- Percutaneous coronary intervention may provide angina relief in patients with single and multivessel disease without antianginal medication.



Liberal blood transfusion for patients with myocardial infarction and anemia may be considered



Carson

Anemia is common in patients with acute myocardial infarction. Whether to transfuse or not is an everyday decision clinicians face. A restrictive red blood cell (RBC) transfusion strategy targeting a hemoglobin concentration above 7 or 8 g/dL is safe in most clinical settings outside of the coronary care unit.

But because ischemic myocardium is vulnerable, evidence suggests patients may benefit from a higher hemoglobin. Would a liberal versus restrictive transfusion strategy improve outcomes in patients with

acute myocardial infarction and anemia? That's the question asked in the Restrictive Versus Liberal Blood Transfusion in Patients With Myocardial Infarction and Anemia: Results of the MINT Trial.

The study randomized 3,506 patients with acute myocardial infarction and anemia (Hb <10 g/dL) from 144 sites throughout the United States, Canada, France, Brazil, New Zealand and Australia, with enrollment between 2017 and 2023, to a restrictive or liberal transfusion strategy.

Patients randomized to the liberal transfusion strategy arm received enough red blood cells to maintain Hb \geq 10 g/dL through hospital discharge or 30 days. Transfusion was permitted in patients randomized to the restrictive transfusion strategy arm, but not required, and only when the hemoglobin was <8 g/dL and strongly recommended for patients with Hb <7 g/dL or for ischemic symptoms not controlled with medications.

The primary outcome, a composite of all-cause mortality and recurrent myocardial infarction through 30 days following randomization, occurred

in 16.9% of patients in the restrictive transfusion group and in 14.5% in the liberal transfusion group, which yielded a relative risk of 1.16 with a lower confidence interval of 1.00 to an upper confidence interval of 1.35 (p=0.07). Cardiac death occurred in fewer patients in the restrictive transfusion group (5.5%) compared with the liberal transfusion group (3.2%). Heart failure, a major safety concern with blood transfusion post-MI, slightly favored the restrictive transfusion group, 5.8% versus 6.3% in the liberal transfusion group.

"Although we can't claim a liberal transfusion strategy is superior based on our primary outcome, most of the MINT results suggest that patients with acute myocardial infarction and anemia may potentially benefit from a liberal transfusion strategy without undue risk of harm," said Jeffrey L. Carson, MD, MACP, the study's principal investigator, Distinguished Professor of Medicine and Richard C. Reynolds, MD, chair in General Internal Medicine at Rutgers, Robert Wood Johnson Medical School.

After the presentation, the study will be published in the *New England Journal of Medicine*.

Innovative trial shows dapagliflozin reduces risk of adverse cardiometabolic outcomes in patients with acute myocardial infarction



James

Dapagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, conferred a significant clinical benefit in patients with myocardial infarction and any degree of left ventricular dysfunction, according to a Registry-Based Randomized Trial of Dapagliflozin in Patients With Acute Myocardial Infarction Without Diabetes (DAPA-MI Trial).

The registry-based, double-blind, placebo-controlled trial enrolled 4,017 people hospitalized for myocardial infarction without

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Meet the Trialist is a series of extended conversations with select researchers discussing current discoveries and the latest data in clinical trials | Located in the Science & Technology Hall, Level 2

known diabetes or established heart failure at 39 sites in Sweden and 64 sites in the United Kingdom from December 2020 to March 2023. Patients were randomized to dapagliflozin 10 mg versus placebo once daily in addition to standard therapy to evaluate the effect on a composite of cardiometabolic outcomes over a median follow-up of 12 months.

At baseline, 72% had ST-elevation myocardial infarction, 9% prior myocardial infarction and 2% prior stroke.

The primary endpoint, a hierarchical composite of death, hospitalization for heart failure, non-fatal myocardial infarction, atrial fibrillation/flutter, new diagnosis of Type 2 diabetes, New York Heart Association Functional Classification at the last visit and body weight decrease $\geq 5\%$ at the last visit, was determined using the win ratio statistical analysis method. Analysis of the primary hierarchical composite of cardiometabolic outcomes resulted in 34% more wins for dapagliflozin than placebo, with a win ratio of 1.34 (95% CI, 1.20 to 1.50, $p < 0.001$). Treatment effect was consistent across pre-specified subgroups.

“Patients with diabetes and heart failure have an indication for dapagliflozin therapy based on evidence from previous trials,” said Stefan James, MD, the study’s lead researcher and professor of cardiology at Uppsala University in Sweden. “Similarly, in patients with acute MI and impaired left ventricular function without prior diabetes and chronic heart failure, dapagliflozin demonstrated significant benefit with regards to improvement in cardiometabolic outcomes compared with placebo.

“The DAPA-MI trial has provided several new learnings on the cardiometabolic benefits of dapagliflozin. We have pioneered the Registry-Based Randomized Clinical Trial set up in a large blinded cardiovascular outcome trial recruiting more than 4,000 patients with acute myocardial infarction in only two countries,

which is an outstanding achievement. Dapagliflozin should be considered as part of standard secondary prevention therapy for patients with acute myocardial infarction and any degree of left ventricular dysfunction.” The study will be published in the *New England Journal of Medicine Evidence* following the presentation.

Percutaneous coronary intervention reduced angina symptoms



Rajkumar

Percutaneous coronary intervention (PCI) significantly reduced angina symptoms in patients with single and multivessel disease and little or no tolerated antianginal medication, according to Objective Randomized Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina (ORBITA-2).

The multicenter, double-blind, placebo-controlled trial conducted in 14 U.K. centers enrolled 301 patients with angina or angina equivalent symptoms, severe coronary stenosis in ≥ 1 vessel and evidence of ischemia: stress imaging or invasive physiology and clinical eligibility for PCI.

At enrollment, patients completed angina and quality of life questionnaires and reported their angina symptom frequency daily using a customized smartphone application. Antianginal medications were stopped. Patients were randomized 1:1 to PCI or a placebo procedure.

Patients then entered a blinded follow-up period in which they and the medical and research teams were blinded to treatment allocation. Antianginal medication

initiation and up-titration for angina was triggered by patient conduct and managed by the blinded research team. After 12 weeks of follow-up, angina and quality of life questionnaires, treadmill testing and dobutamine stress echocardiology were repeated prior to unblinding and the return to routine clinical care.

The primary endpoint was an angina symptom score, which was a composite ordinal clinical outcome scale of angina health status derived from the number of episodes of angina reported by the patient on a given day, the units of antianginal medication prescribed on that day and high-level category overrides for unblinding due to intolerable angina, acute coronary syndrome and death.

Following randomization, patients in the PCI arm had a significantly lower angina symptom score than those in the placebo arm.

“The benefit of angioplasty compared to placebo was equivalent to one full dose of antianginal medication,” said Christopher Rajkumar, MD, MRC, clinical research training fellow in interventional cardiology at Imperial College London and the study’s first author.

Still, a significant percentage of patients (59%) had angina symptoms after undergoing PCI.

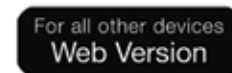
“This isn’t a procedure that works for everybody,” said Rasha Al-Lamee, MD, BHF, intermediate research fellow and reader in interventional cardiology at Imperial College London and the study’s chief investigator. “But for patients in whom it does, the benefits are likely to be as soon as the next day.

Overall, “ORBITA-2 showed us that PCI should be included early on in shared decision-making when discussing angina therapy options,” Dr. Al-Lamee said. “For the most benefit from PCI, you have to offer it early in their treatment algorithm.” The study will be published in the *New England Journal of Medicine* after the presentation. •



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ARIES HeartMate-3 9:45-10:15 a.m. Sunday, Nov. 12 <i>CardioTalk II</i>	VERVE-101 9:45-10:15 a.m. Monday, Nov. 13 <i>CardioTalk I</i>	ESPRIT 9:45-10:15 a.m. Monday, Nov. 13 <i>CardioTalk II</i>	SPEC-AI Nigeria 1:30- 2 p.m. Monday, Nov. 13 <i>CardioTalk I</i>	ARISE 1:30- 2p.m. Monday, Nov. 13 <i>CardioTalk II</i>
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**Paul Dudley
White
International
Lecture**

**“Panvascular
Disease: What We
Have Done and
What We Can Do?”**



Junbo Ge,
Fundan University

**Sunday, Nov. 12
3:30–4:45 p.m.
114/Nutter Theater**

WEIGHT-LOSS DRUG

continued from page 1

Patients in the semaglutide group lost 9.4% of their body weight compared with 0.9% for those on placebo.

The safety profile was also favorable: 16.6% of patients in the semaglutide group stopped the drug due to adverse events, compared with 8.2% in the placebo group (P<0.001).

“Semaglutide was well tolerated,” Dr. Lincoff said. “The majority of adverse events were gastrointestinal, including diarrhea, nausea and GI upset, which is a known effect of the drug.”

A substantial cardiovascular risk is associated with overweight and obesity independent of diabetes, Dr. Lincoff said.

“In patients with pre-existing cardiovascular disease and overweight or obesity, but without diabetes, weekly subcutaneous semaglutide superimposed upon standard of care will help improve cardiovascular outcomes,” he said. The study will be published in the *New England Journal of Medicine* following the presentation. •

Changing the course of medicine

Scientists dedicated to the research and results of the polypill share exciting progress and prospects

The development of the polypill has had life-changing effects on patients with cardiovascular disease. Though the development process proved challenging, the remarkable results have been worth it — with more to come.

Experts will address these efforts and outlooks in-depth during the session, *Advances of the “Polypill” in Cardiovascular Disease: From Concept to WHO Essential Medication*.

Professor Sir Nicholas Wald and Professor Malcolm Law initially proposed the novel concept of the polypill two decades ago, with 2023 marking its 20th anniversary. The unconventional idea of a fixed dose combination medication that could be administered to entire populations and reduce cardiac events was met with some early hesitation and uncertainty. It also provoked curiosity and enthusiasm.

Creation and validation

The Spanish National Center for Cardiovascular Research (CNIC) and its general director, Valentin Fuster, MD, PhD, helped create the polypill and led the recent large-scale SECURE trial. Dr. Fuster, who is also physician-in-chief at Mount Sinai Hospital and president of Mount Sinai Heart in New York City, will chair the session. Additional speakers include José María Castellano, MD, PhD, Daniel

José Piñeiro, MD, and Clara Chow, MBBS, PhD.

“The main purpose of the polypill was to make the initiation and continuation of evidence-based prevention treatments easier for patients at high risk of cardiovascular disease,” said Dr. Chow, professor of medicine and academic director of the Westmead Applied Research Centre and academic co-director of Charles Perkins Centre Westmead in Sydney.

Currently, the polypill is given to people who have already had a heart attack or stroke episode and need intervention to prevent recurring cardiac events. At the time of concept, drug adherence for cardiovascular disease was less than 50%, and a single combination pill sounded like the simple, magical answer. Of course, it was far from simple to devise.

“We had to develop 50 polypills before we could get to one,” Dr. Fuster said.

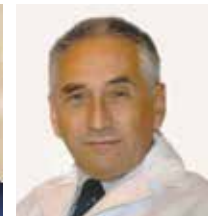
The polypill combines three essential drugs: aspirin, statin and ace inhibitor. Once scientists reached the correct synthesis, they began to study its efficacy. Over four years, the SECURE



Fuster



Castellano



Piñeiro

UPCOMING SESSION

Advances of the “Polypill” in Cardiovascular Disease: From Concept to WHO Essential Medication
Sunday, Nov. 12 | 8–9:15 a.m. | Nutter Theater

trial followed 2,500 patients in seven countries who’d had a recent cardiovascular event. Half of these were given the polypill, and the control half were given the medications separately.

In the end, the polypill proved effective not only in lowering the risk of secondary adverse events by 24%, but also in reducing cardiovascular mortality by 33% — largely due to increased adherence.

“The SECURE study findings suggest that the polypill could become an integral element of strategies to prevent recurrent cardiovascular events in patients who have had a heart attack,” Dr. Fuster said. “By simplifying treatment and improving adherence, this approach has the potential to reduce the risk of recurrent cardiovascular disease and death on a global scale.”

See **POLYPILL**, page 13

Competition ignites innovation

New and emerging technology solutions took center stage, literally, at yesterday’s Health Tech Competition, where innovators presented their technology focused on health impact and sustainability in the middle of the Science & Technology Hall.

“(This competition) serves as a platform to highlight groundbreaking technologies against the backdrop of the Super Bowl of scientific meetings where the cardiovascular and scientific community come together,” said Nancy Brown, AHA CEO. “We are thrilled with the number of

submissions we have received, nearly 60 this year, marking the highest number ever. We have only five finalists, which was a very tough task, who will present solutions designed to better prevent, treat or diagnose heart disease and stroke.”

Finalists, who presented in alphabetical order, had seven minutes to pitch their innovation to judges, followed by a 10-minute Q&A. Today’s presentations focused on the business impact of their technology. The finalists will return to the Health Innovation Pavilion at 11:15 a.m. tomorrow for another round of presentations focusing on the science and evidence of their products.

The finalists’ technologies are:

- **Aintheven:** First pediatric and young adult ECG interpretation tool powered by AI to help identify cardiac risk in the 12-18 age group.
- **CardieX:** Device technology that adds arterial health assessment to a BP monitor for detection of early vascular aging (EVA).
- **Cardiosense:** Non-invasive hemodynamic monitoring platform for virtual HF management and early detection of heart disease.
- **PyrAmes:** Non-invasive passive blood pressure monitoring, Always On, offering continuous monitoring for patients of all ages.
- **RCE Technologies:** Real-time cardiac injury assessment and monitoring for ruling out acute cardiac events quicker. •

#AHA23 Exhibitors

Abbott	Health Innovation Pavilion	
Accurant Biotech		1442
ADInstruments		3111
Adult Congenital Heart Association		3121
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American Academy of Sleep Medicine		949
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Science & Technology Hall

Science & Technology Hall Hours

Sunday, Nov. 12
9 a.m.-5 p.m.

Monday, Nov. 13
9 a.m.-3 p.m.



Don't miss today's Early Innovator Spotlight Programming

Located in CardioTalk I
AHA Early Innovators Spotlight 5 | Clinical and Population Science
 9:45-11:12 a.m., Sunday

AHA Early Innovators Spotlight 6 | Basic Science
 11:30 a.m.-12:57 p.m., Sunday

Visit the Membership Lounge

Located in the Heart Hub
 Members may stop by for special career development programming and to learn about other opportunities as an AHA member. While you are there, relax, play board games, watch some football and grab a complimentary snack or beverage.

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 Sessions OnDemand™
 Overflow Theater (Sunday-Monday)

AED = AED LOCATIONS

Metabolic risk factors can complicate kidney, cardiovascular health, according to panel

Combinations of risk factors, kidney disease and cardiovascular disease can be difficult to treat

A growing number of people have combinations of metabolic risk factors, chronic kidney disease and cardiovascular disease — possibly leading to a complicated diagnosis and treatment.

Chiadi Ndumele, MD, PhD, MHS, FAHA, associate professor of medicine at Johns Hopkins Hospital in Baltimore, Maryland, said historic levels of metabolic risk factors such as obesity and diabetes are disproportionately prevalent in disenfranchised populations, leading to a high burden of cardiovascular kidney metabolic (CKM) syndrome.

Dr. Ndumele will address those concerns during Sunday’s session, *A Confluence of Risk: Navigating the Intersection of Cardiovascular, Kidney and Metabolic Health*.

Janani Rangaswami, MD, FACP, FCRS, FAHA, professor of medicine at George Washington University School of Medicine in Washington, D.C., and Sheryl L. Chow, PharmD, FCCP, FAHA, FHFSa, associate professor at Western University of Health Sciences in Pomona, California, will also lead the panel discussion.

“In addition to causing diabetes, obesity leads to the development of high blood pressure, abnormal lipids and systemic inflammation,” Dr. Ndumele said. “In turn, high blood pressure and diabetes are the most common causes of chronic kidney diseases. Metabolic risk factors and chronic kidney disease each increase cardiovascular disease risk, and a synergistic increase is seen when both are present. Additionally, cardiovascular disease, particularly

heart failure, increases risk for worsening chronic kidney disease.”

The primary consequence of this interplay between metabolic risk factors, chronic kidney disease and the cardiovascular system is

premature mortality, usually from heart disease and stroke. And the medical community needs to address it right away, Dr. Ndumele said.

“It is believed that the high burden of CKM syndrome in the population has caused a plateau, and possibly even an uptick, in previously declining cardiovascular mortality rates over several decades,” he said. “Therefore, addressing the interplay between metabolic risk factors, chronic kidney disease and cardiovascular disease reflected by CKM syndrome is a public health emergency.”

More therapies are now available at the physician’s disposal to deal with CKM syndrome, Dr. Ndumele said.

“First, a recognition that excess adiposity is at the root of most CKM syndrome is important,” he said. “We have increasingly effective strategies for addressing obesity, through support for lifestyle modification, obesity pharmacotherapies and bariatric surgery, which can help reduce the pipeline of individuals with CKM syndrome.”

He said there’s also an increasing number of therapies with beneficial metabolic and kidney effects that can lower cardiovascular risk.

“For individuals with Type 2 diabetes, agents like SGLT2 inhibitors and GLP-1RAs have both beneficial and metabolic

effects and reduce the risk of heart disease,” Dr. Ndumele said. “SGLT2 inhibitors, in addition to renin-angiotensin system inhibitors and finerenone, have protective effects against adverse kidney events and adverse cardiovascular events. Health care providers need more guidance on how and when to utilize these agents, which the clinical algorithms on CKM health developed by AHA have started to provide.”

For people with CKM syndrome, Dr. Ndumele said an interdisciplinary approach to care is critical.

“Many individuals with multi-organ impairment see multiple providers, which can lead to fragmented care, differing — and even conflicting — recommendations from different subspecialists, and challenges with navigating the health system,” he said.

This care can be value-based with support for health care professionals from a CKM interdisciplinary team using a CKM coordinator to communicate guidance. Or it can be volume-based to make sure high-risk patients with existing severe disease or who are at high risk for major adverse events are being referred to specialists to help optimize care.

“These complementary approaches can help to optimize interdisciplinary care for individuals with multi-organ impairment,” Dr. Ndumele said. •



Ndumele



Rangaswami



Chow

UPCOMING SESSION

A Confluence of Risk: Navigating the Intersection of Cardiovascular, Kidney and Metabolic Health

Sunday, Nov. 12 | 9:45-11 a.m. | Main Event II

Today’s Industry Events

Industry events provide a unique opportunity for companies in the field of cardiology to share their latest advances in cardiovascular practices, services and technologies.

Sunday, Nov. 12



See the Mobile Meeting Guide App for more details.

TIME	LOCATION	SUPPORTER	TITLE
9:30-10:15 a.m.	Learning Studio I	Cytokinetics, Inc	Elevating the Impact of Obstructive Hypertrophic Cardiomyopathy: A Conversation Between Providers and Patients
	Learning Studio II	Bristol-Myers Squibb	Facing Obstructive HCM Together: Provider and Patient Conversation
11:15 a.m.–Noon	Learning Studio I	Sanofi	CHANGE of Beat in AFib: How Can Cardiologists and Electrophysiologists Navigate an Evolving Treatment Paradigm?
	Learning Studio II	Novartis Pharmaceuticals Corporation	Elevated Lipoprotein(a): Raise Your Game and Lower Your (Risk) Score?
	Heart Theater	Bristol-Myers Squibb	A Review of Long-Term Outcomes for Cardiac Myosin Inhibition in Adults With NYHA Class II-III Obstructive HCM
12:30-1:15 p.m.	Learning Studio I	Merck & Co.	Addressing Risk of HF Rehospitalization With an Additional Guideline-Recommended Medication
	Learning Studio II	Amgen Inc	Don't Keep Your ASCVD Patients Waiting: Are You Prioritizing LDL-C to Reduce Risk?
	Heart Theater	Recor Medical	Introduction to uRDN and Building a Multidisciplinary Team to Manage Hypertension
3:15-4 p.m.	Learning Studio I	Agepha Pharma	Targeting Residual Inflammatory Risk for Atherosclerosis Treatment and Prevention
	Learning Studio II	Kiniksa Pharmaceuticals	Breaking the Cycle of Recurrent Pericarditis: A Targeted Approach for Pain Relief, Inflammation Resolution and Flare Prevention
	Heart Theater	Bristol Myers Squibb – Pfizer Alliance	Let's Get to the Heart of It: Explore How Evidence Generation and Select Methodological Approaches Can Help Inform Clinical Practice in Patients With Nonvalvular Atrial Fibrillation (NVAF)



Nobel Laureate Edvard Moser, PhD

Studying how our brain helps us find our way from point A to point B



Most of us take navigating for granted. Somehow, our brain knows where we are and how to tell us where we are going without a lot of conscious thought. We know where we are in relation to landmarks around us, such as trees and streets, without questioning it.

But deep within our brain, a lot of activity is going on that creates an internal mental map, which in turn helps us find our way around. Nobel Laureate Edvard Moser, PhD, professor at the Norwegian University of Science and Technology in Trondheim, Norway, has spent much of his life studying those regions of the brain and how they work. He'll bring his expertise to Sunday's Nobel Laureate Lecture with his presentation, "Neural Computation of Space and Time."

Prior to Scientific Sessions 2023, Scientific Sessions *Daily News* visited with Dr. Moser about his research, findings and finding our direction.

Q You have been studying neuroscience and neurophysiology for almost 40 years. How did you first get involved in that area?

Dr. Moser: As a young psychology student, I was inspired by pioneering studies on the neural basis of memory as well as vision, which I learned about in undergraduate classes in 1984-1985. This motivated me to approach professor Per Andersen, PhD, at the University of Oslo, a leading figure in Norwegian neuroscience at the time, highly recognized for his work on the physiology of neurons in a brain structure called the hippocampus. I did my PhD with him (as did my long-time collaborator and fellow professor May-Britt Moser, PhD), and through this work was introduced to John O'Keefe, PhD, FRS, FMedSci, who had discovered place cells. Dr. O'Keefe taught me the basics on place cells, enough for Dr. May-Britt Moser and me to

set up a lab in Trondheim, Norway, some years later.

Q In 2005, you and Dr. May-Britt Moser discovered a type of cell close to the hippocampus that is important for determining relative position. What went into that discovery, and what did it mean for the field of neuroscience?

Dr. Moser: We discovered grid cells, a specialized cell in the brain's entorhinal cortex that is active each time an animal (or human being) is at a certain subset of positions in the environment. These positions form, for each cell, a hexagonal lattice spanning the entire available space. Grid cells are thought to serve as a coordinate system for mapping of spatial position, which animals use to find their way in the environment.

We were familiar with John O'Keefe's discovery of place cells and wanted to understand how they are generated. We explored brain areas with strong neural projections into the place cell area, including the entorhinal cortex. We expected to observe some sort of spatial tuning also in the inputs from this area, like in place cells themselves, but were surprised by the lattice-like firing of the entorhinal cells, which no one expected.

It provided insights into an entirely new system for position coding in the brain, located primarily in the entorhinal cortex. (We discovered many other spatial cell types there later). Second, it opened the doors for studies of neural coding or computation. We and others proposed models for how the hexagonal firing could be generated, inspiring an entire new branch of computational neuroscience. Investigators explore coding in grid cells as a gateway to understanding high-level cognitive functions in the brain.

Q You, along with Dr. May-Britt Moser and Dr. O'Keefe, won the Nobel Prize in Physiology or Medicine in 2014 for research

UPCOMING SESSION

Nobel Laureate: Edvard Moser, PhD | Neural Computation of Space and Time

Sunday, Nov. 12 | 9:45-11 a.m.
114/Nutter Theater

related to that discovery. What did it mean to you to receive that award?

Dr. Moser: It brought attention to the major advances that had been made over the past few decades in understanding the neural computations underlying cognitive functions. Grid cells provide an easy access route to a high-level brain function — spatial coding and navigation — and I think the prize has drawn attention to the advances in mechanisms of cognition for the more general public. Of course, I am honored that our work was recognized, at the same time as I am fully aware that we have been standing on the shoulders of giants.

Q Your presentation at Scientific Sessions is titled, "Neural Computation of Space and Time." Can you give us a peek at what you'll be discussing and what attendees might take away from it?

Dr. Moser: I will discuss the neural basis of space and time coding in the entorhinal cortex. Space and time perception are brain functions that have a strong innate contribution: They determine how we experience the world. I will show how space is coded by collective activity in hundreds to thousands of neurons in the medial entorhinal cortex, whereas equally large assemblies of neurons encode the passage of time in the lateral entorhinal cortex, in a very different manner from what we observe in the space-coding system.

I hope people will get a glimpse into the very fast advances that take place today in neuroscience — that they will appreciate how a synergy between new technological developments and an increasing need for theory and models drive the field forward. •

CARDIO-ONCOLOGY

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prevent the development of clinical cardiotoxicity, or at least reduce its magnitude."

One area that cardiologists need to be aware of is the diverse spectrum of drug safety (or toxicity). This includes

"It is much more cost effective to prevent a disease from occurring than treating it after its onset. The prevention principle applies to multiple areas of cardiology and oncology."

– Daniela Cardinale, MD, PhD, FESC

cardiomyopathy, vascular disease and arrhythmias. When it comes to arrhythmias, one has to mention the buzzword of QTc prolongation, said Dr. Herrmann.

"Multiple drugs have been and are being tested for this measure. It is relatively easy to obtain measure and is of clinical significance (predisposition to fatal arrhythmias)," he said. "A number of the newer generation of drugs called tyrosine kinase inhibitors can prolong the QT interval, and in combination with electrolyte abnormalities due to vomiting and diarrhea as well as in combination with other drugs in cancer patients, can become really problematic."

Dr. Cardinale said managing possible interactions between antiarrhythmic drugs and anticoagulant drugs with some new and even some older drugs may be tricky.

"The most frequent and feared form of cardiotoxicity remains cardiac dysfunction," she said. "Other forms of toxicity include vascular toxicity resulting in hypertension, acute coronary syndromes and thrombo-embolic episodes."

A key tool in cardiotoxicity assessment is cardiac imaging, and artificial intelligence has started to make inroads in that area. Dr. Cardinale said it is still too early to say how much of an impact it will have.

"Artificial intelligence seems to be able to make a great contribution to the clinician at different levels," she said. "For now, however, it is just a great potential. We need to understand the correct and most effective application to our clinical practice." •



David Morrow, MD, MPH, FAHA,
and Susanna Price, MD, PhD

A comprehensive view of cardiogenic shock



Cardiogenic shock, a life-threatening condition in which a person's heart can't pump enough blood to meet the needs of the body, is most often caused by a serious heart attack or advanced heart failure. Historically, data related to cardiogenic shock have been limited, inconsistent and challenging to interpret. As a result, varying treatment recommendations exist around best practices.

Sunday morning's in-depth session, Moving the Needle in Cardiogenic Shock: A Conversation With the Giants — The Intersection of Critical Care, Interventional and Heart Failure Cardiology and Cardiac Surgery, seeks to expand the conversation on the subject.

Prior to the session, cardiac experts and session moderators David Morrow, MD, MPH, FAHA, and Susanna Price, MD, PhD, provided valuable analysis on the evolution of this life-threatening condition to *Scientific Sessions Daily News*. Dr. Morrow is the director of the Levine Cardiac Intensive Care Unit (CICU) at Brigham and Women's Hospital in Boston and co-chair of the AHA's Cardiogenic Shock Registry Steering Committee. Dr. Price is a consultant cardiologist and intensivist based at Royal Brompton Hospital in London and chair of the National Health Service (NHS) Pan-London Cardiogenic Board.

"We are nowhere near to having cardiogenic shock 'solved,'" said Dr. Morrow. "If we hope to improve outcomes, it is essential for us to have a better understanding of the landscape of cardiogenic shock care, its varied clinical presentations, applied interventions, processes of care and outcomes."

Q In reviewing the past and present of cardiogenic shock, what have been some of the biggest breakthroughs and developments?

Dr. Morrow: It's sobering that our biggest breakthrough in managing shock was nearly 25 years ago with the demonstration that early revascularization improves survival in patients with cardiogenic shock due to acute myocardial infarction. Now, a quarter decade later, despite multiple shots on goal with new clinical trials, we have not yet found new treatments that have impacted hard outcomes.

However, we have made substantial recent progress in refining our definitions and classification of cardiogenic shock and its complications, giving us a more refined common language that has promise to reduce variability in clinical trials and perhaps overcome some of the pitfalls that arise in

studying such a heterogeneous population. Additionally, coordinated multidisciplinary team-based care has emerged as a likely important factor in improving cardiogenic shock care.

Dr. Price: The developments in interventional cardiology have been extraordinary, such that we can now undertake many cardiovascular interventions (including valve implantation, EP interventions and congenital heart disease interventions) using catheter-based techniques. Unfortunately, although there have been developments in acute mechanical circulatory support, the advances have not been so extensive. Nonetheless, these all add up to game-changers within the management of cardiogenic shock.

I would also add that the widespread availability of echocardiography in the ICU has transformed our ability to assess and guide interventions in these most critically ill patients.

Q What innovations are on the horizon that will continue to advance cardiogenic shock?

Dr. Morrow: I see three major areas for near-term progress:

1. **Dedicated shock registries:** There are several registries dedicated to cardiogenic shock that are making successful headway in gathering these data with important opportunities for expansion to capture cardiogenic shock more comprehensively in the next few years. For example, the AHA recently launched the Cardiogenic Shock Registry powered by Get With The Guidelines, which underscores its commitment to advancing care of patients with this life-threatening syndrome.
2. **Deep phenotyping:** A commonly held belief is that more targeted interventions aimed at the driving pathobiology for an individual patient may be more successful. Therefore, comprehensive phenotyping integrating clinical characteristics, invasive hemodynamics, imaging and biomarkers is an area of intense interest in the field, and one in which we are starting to make some headway with much more to come.
3. **Pragmatic clinical trials:** Implementation of randomized clinical trials in cardiogenic shock is not easy. One of our major shortcomings has been the paucity of rigorously designed, adequately powered clinical trials. Encouragingly, there is a renewed commitment to the initiation and conduct of randomized trials of therapies for cardiogenic shock and an openness to innovative pragmatic trial designs that may enable a next generation of trials in the field.

Dr. Price: I would also add a fourth:

4. **Early recognition:** Combining deep phenotyping, genomics, proteomics and metabolomics with standard monitoring and leveraging advances in artificial intelligence (AI) will hopefully allow early

recognition of the declining patient or high-risk patient in ways we don't yet recognize.

Q Why is multidisciplinary collaboration so important in this area?

Dr. Morrow: I often say that shock care is a team-based sport. One of the most important pieces of evidence from the past five years has been the coalescence of data from multiple observational studies showing an association between implementation of shock teams and lower mortality rates in cardiogenic shock. It takes a substantial commitment of time and resources to make shock teams work 24/7 x 365.

We still need to tease out the critical elements and processes that constitute an effective shock team framework and potentially drive the association with more favorable outcomes.

Dr. Price: I agree. Additionally, training the next generation and transferring knowledge and skills is going to be vital. Communication was facilitated during the pandemic, allowing rapid convening of remote multidisciplinary teams and bringing expertise to the bedside no matter where the patient finds himself or herself. This was a game-changer.

Q Why should members attend this session, and what do you want them to take away from it?

Dr. Morrow: Cardiogenic shock is a profoundly morbid culmination or complication of so many cardiovascular disorders. Because of that, we anticipate that this forward-looking session will be of broad interest to specialists, clinicians and researchers committed to advancing care of this challenging syndrome.

Dr. Price: Cardiogenic shock, which represents one of the most extreme manifestations of acute cardiovascular disease, is at the cutting edge of the interface

between cardiology, critical care and extracorporeal support. The potential to change outcomes in these critically ill patients is extraordinary, knowledge is expanding rapidly and this session represents the opportunity to hear some of the very best outlining and debating of the latest advances in the field.

The extensive session includes a panel of specialists who will join Drs. Morrow and Price to address a breadth of interests on cardiogenic shock, from registries and clinical trials to pathophysiology and equity. They are:

- Judith S. Hochman, MD, MA, FAHA
- JoAnn Lindenfeld, MD
- Venu Menon, MD, FAHA
- Robert Roswell, MD
- Holger Thiele, MD

Cardiogenic Shock Registry

In 2022, the American Heart Association created the Cardiogenic Shock Registry powered by Get With The Guidelines®. The registry is designed to help researchers, clinicians and regulators better understand the clinical symptoms of shock types, treatment patterns and outcomes. It will provide a foundation for working toward improving the quality and consistency of care in patients in U.S. hospitals with cardiogenic shock symptoms.

The core scientific aims of the registry include:

- Study cardiogenic shock, including diagnosis, treatment and outcomes among patients in real-world acute care clinical settings throughout the United States.
- Provide high-quality evidence that helps inform clinicians, researchers, federal agencies, the industry and other health care stakeholders on best practices for treating cardiogenic shock patients.
- Develop streamlined longitudinal research infrastructure for pragmatic clinical trials and other translational, clinical and implementation science.
- Create and pilot evidence-based performance metrics for national benchmarking.
- Promote systems-of-care metrics for cardiogenic shock patients that strive for health equity. •

POLYPILL

continued from page 6

Progressive prevention

The fixed dose polypill's positive outcomes on risk and adherence proved vital in managing cardiovascular disease. It also significantly lowers the medication cost for patients, Dr. Fuster said.

"For those that meet the population's priority health care needs, it can save lives, decrease suffering and improve quality of life," he said. "It's already in 40 countries and evolving rapidly."

In July 2023, the World Health Organization (WHO) announced

a landmark decision to add fixed dose combination drugs for the prevention of cardiovascular disease to its Model List of Essential Medicines (EML). Dr. Fuster said this act signifies the polypill's extensive efficacy and will aid in the global production and distribution of it in mass quantities.

"The importance of the (WHO Essential Medicine) listing is recognizing the importance and need for this treatment and addressing the huge gap in implementation of cardiovascular disease prevention treatments around the world," Dr. Chow said.

Dr. Fuster said his next challenge

is to examine future possibilities for the polypill and discover the next big breakthrough.

"We already know that the polypill is significant with secondary prevention of heart attacks," he said. "Can we move it to primary prevention? Could we test people who have never had a cardiovascular event but are at very high risk, then use the polypill to control risk factors in advance?"

He also hopes to apply the concept of the polypill to other cardiovascular conditions with low adherence, such as heart failure that requires patients to take four separate medications. •



Do you know your number?

Lp(a) Testing Booth #401

Saturday, Nov. 11
9 a.m.-4:30 p.m.

Sunday, Nov. 12
9 a.m.-5 p.m.

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OPENING SESSION

continued from page 1

catching up with old friends and also making new ones.”

Dr. Wu led off the Opening Session by recognizing what makes the American Heart Association community special: its members, who make critical contributions to the scientific community each year.

First, Dr. Wu congratulated the Distinguished Scientists Award recipients (profiled in yesterday’s *Daily News* on pages 14-15), before announcing the winners of the

Joseph A. Vita Award and the Nanette K. Wenger Award.

The award named for Dr. Joseph A. Vita, who was the first editor-in-chief of the AHA’s open access journal, *JAHA: Journal of the American Heart Association*, is especially meaningful to Dr. Wu, he said, because he was its inaugural recipient in 2018.

Each year, the award recognizes the contributions of a mid-career investigator whose work, published in the AHA journals during the last five years, has had great impact in cardiovascular biology or

cardiovascular health.

This year, the honor went to Pradeep Natarajan, MD, MMSc, who is a world leader in large-scale genetic analysis of coronary artery disease and preventive cardiology. His notable scientific contributions include the interpretation of whole genome sequences for coronary artery disease risk, such as through polygenic risk scoring, as well as discovering new genes responsible for coronary artery disease. His work has informed clinical practice and drug development programs, Dr. Wu said.

The Dr. Nanette K. Wenger Research Goes Red® Award recognizes the best article about cardiovascular disease and stroke in women published each year in an AHA journal. The award, which empowers women to contribute to health research, was presented to Zainab Mahmoud, MD, MSc, for her article, “Racial Disparities in Specific Cardiovascular Outcomes,” which showed the profound and widening racial disparities in maternal mobility and mortality in the U.S. in Black women compared to white women.

Following the awards recognitions, Amit Khera, MSc, FACC, FAHA, welcomed attendees to Scientific Sessions and offered his tips for making the most of the next few days.

“On behalf of the (CSSP) Committee, we want to ensure that each of you has an amazing experience over the next three days,” Dr. Khera said. “We want this to be a really enriching experience, and dare I say, even a little fun ... This is my 22nd Scientific Sessions, and I know from experience that you can spend the first two days learning the lay of the land. By the time you get comfortable, it’s time to go home. We certainly don’t want that to happen to you, so I want to offer you some tips on how to navigate this meeting. And rather than tell you, we’re going to show you.”

In a short video, Dr. Khera took everyone behind the scenes to cover the highlights as well as the hidden gems of the meeting, from the Heart Hub, Membership Lounge and Simulation Zone in the Science & Technology Hall to the Poster Hall featuring 4,000 posters, to the Main Events hall, synonymous with late-breakers. The video included cameos from a few AHA VIPS, such as Bob Harrington, MD, FAHA, past president who said nothing beats the excitement of being at Scientific Sessions.

“In 2019, we used the phrase ‘you want to be in the room where it happens,’ and that applies so well to late-breaking clinical trials,” Dr. Harrington said. “We want to be in the room. There’s an energy. There’s excitement. You can turn to the person next to you and have a conversation about what you just heard and what you just saw. Sure, you can watch on your computer screen at home, but it’s not the same. You want to be in the room where it happens.” •


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A home for all things health technology at Scientific Sessions

Visit the **Health Innovation Pavilion**, located in the Heart Hub. Attend the three-day Health Tech & Innovation Summit and engage with companies and start-ups showcasing their products and services. Also featured:

- Updates from the Health Tech Advisory Group
- Health Tech Competition (see details below)
- Health tech researchers
- Next generation imaging and AI analysis
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- Updates from the Innovators Network
- Best practices in digital coaching
- Digital tools in cardiac rehabilitation

Join us for the 2023 Health Tech Competition

Competition Days
 Day 1: Health Tech Competition
 Date: Nov. 11, 2023
 Time: 11:15 a.m.-1:15 p.m. ET
 Location: Health Innovation Pavilion

Day 2: Health Tech Competition
 Date: Nov. 12, 2023
 Time: 11:15 a.m.-1:15 p.m. ET
 Location: Health Innovation Pavilion

Watch as finalists pitch their health tech start-up to top physicians, industry leaders and VIPs who can help take companies to the next level.




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Alviar



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Carlos L. Alviar MD, FACC, director of Cardiac and Coronary Care Unit and director of the Extracorporeal Membrane Oxygenation Program at Bellevue Hospital Center, and Christopher Barnett, MD, MPH, professor of medicine at the University of California, San Francisco, served as volunteer champions for the Critical Care Cardiology Simulations.

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