American Heart Association. life is why™
SCIENTIFIC SESSIONS 2017
DailyNews
MONDAY, NOVEMBER 13
November 11-15 | Anaheim, California

New hypertension guidelines to be released today

The American Heart Association, American College of Cardiology and nine other health organizations will release new prevention, diagnosis and treatment guidelines that redefine hypertension today. The announcement will take place at 2 p.m. PST in Main Event I, Hall D. See page 5 for a preview of the announcement, and see complete coverage in Professional Heart Daily on **professional.heart.org** and in the Tuesday Scientific Sessions *Daily News*.

AHA announces partnerships to bring innovative progress to global health, drug discovery


Nancy Brown

AHA CEO Nancy Brown announced Sunday the formation of a strategic business relationship between the AHA and the XPRIZE Foundation, which is known for creating "grand challenge domains" that encourage "moonshot" thinking to solve the unimaginable — from space exploration to global literacy for children.

"Everyone here knows that cardiovascular diseases and stroke are by far the most urgent threat to worldwide health today in terms of mortality, suffering and economic burden. We also know that if diverse populations continue to be disproportionally affected, our ability to build healthier lives is compromised," Brown said during

PARTNERSHIPS continued on page 18

Study: Lower transfusion trigger not inferior to higher trigger in cardiac surgery

New data show that a more restrictive transfusion strategy during cardiac surgery is not inferior to a more liberal strategy for either death or major morbidities in moderate- to high-risk patients. Results of the Transfusion Requirements in Cardiac Surgery (TRiCS III) trial were announced Sunday during the first Late-Breaking Science session.

"Results from prior clinical trials have left us in a state of clinical equipoise," said C. David Mazer, MD, professor of anesthesia and physiology at the University of Toronto, who presented the trial. "Anemia in cardiac surgery is independently associated with adverse outcomes and red blood cell transfusions are associated with increased mortality. We needed an answer."

In the trial, researchers randomized 5,243 cardiac surgery patients at 74 sites across 19 countries to either a restrictive blood transfusion trigger of less than 7.5 g/L or a more liberal transfusion trigger of less than 9.5 g/L. The primary outcome was a composite of all-cause mortality, myocardial infarction, new renal failure with dialysis or stroke.


C. David Mazer, MD

Analysis found a 1.1 percent risk-reduction favoring the restrictive transfusion trigger, showing that the lower trigger is not inferior to the higher trigger. Secondary outcomes were similarly noninferior for the restricted trigger arm.

The only significant difference between the two arms was an expected lower use of blood products in the restricted trigger arm. Mazer estimated the reduced blood use translates to savings of about $3 million across the study population.

Subgroup analysis showed a slight superiority for the restrictive trigger in patients older than 75. Mazer said the group re-analyzed the data to confirm the age-related benefit for restricting transfusion, but could not explain the finding.

PRESERVE

Results from another late-breaking trial presented Sunday indicate that neither of two agents commonly used to prevent serious outcomes or acute kidney injury following angiography improved the primary or secondary outcomes.

Both results come from the Prevention of Serious Adverse Events Following Angiography (PRESERVE) trial.

"Earlier trials have been underpowered and provided divergent findings, but these results are very explicit: Oral NAC does not work and sodium bicarbonate works no better than isotonic saline," said Steven Weisbord, MD, MSc, associate professor of medicine and clinical and translational science at the University of Pittsburgh in Pennsylvania.

PRESERVE was designed to enroll 7,680 patients, but enrollment was halted

LATE BREAKING continued on page 17

AHA president urges colleagues to amplify the voice of patients

Early in his cardiology career, John J. Warner, MD, FAHA, worked at a clinic that catered to many of the poorest, sickest people in Dallas. The lines were so long that doctors only had time to address an immediate problem or refill a prescription before moving on to the next patient.

Driving home many nights, Warner wondered how to serve more people or at least serve them better. Years later, he got chances to help improve the overall system of care – and discovered he had quite a knack for it.

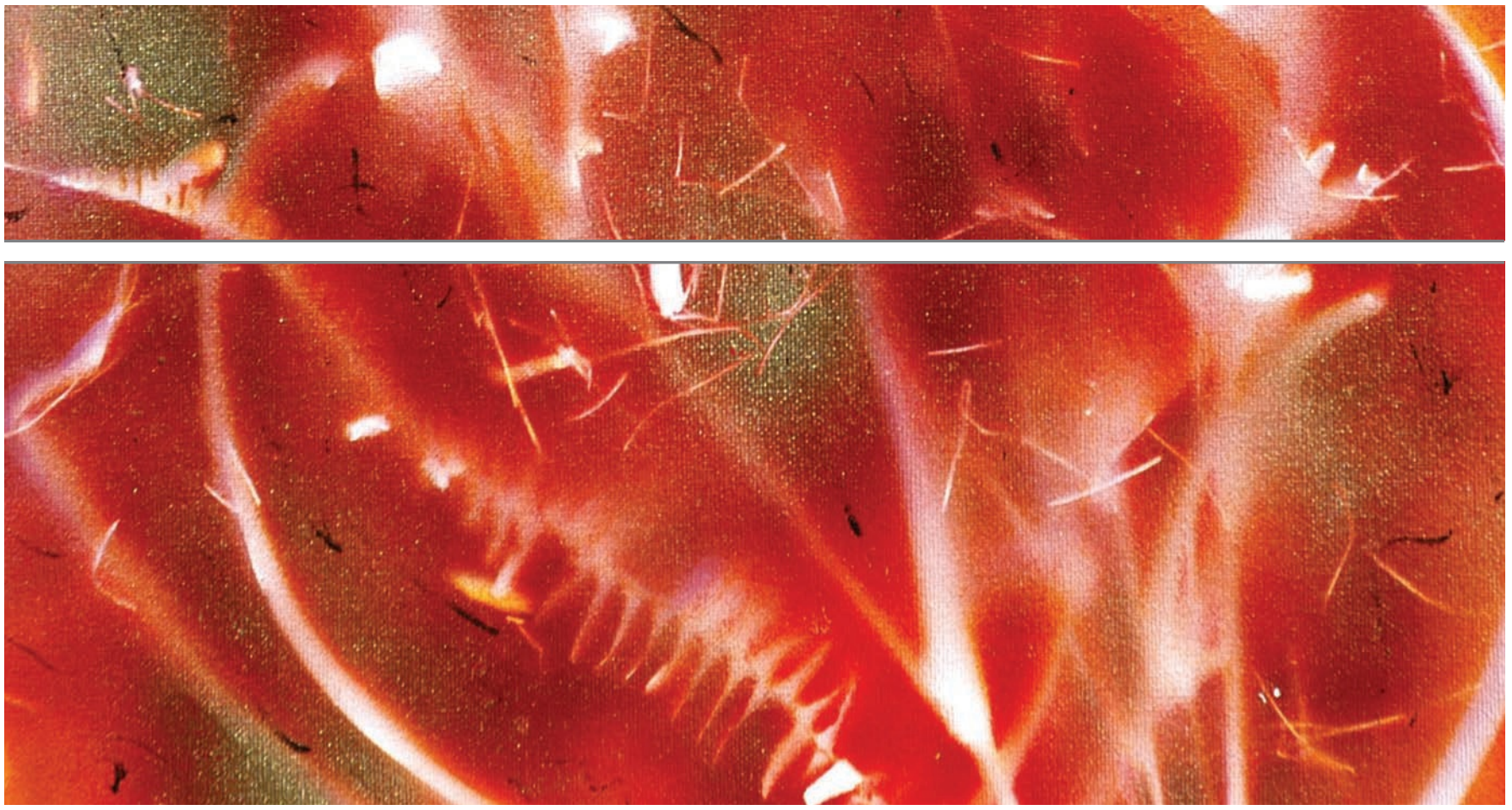
Warner was part of a team that turned Dallas smoke-free, then another that coordinated heart attack treatment across Dallas County. He oversaw design of an $800 million hospital and did such a good job that he became CEO of that healthcare system, the UT Southwestern University Hospitals. Now he's also the president of the American Heart Association, and used his address at the opening of the organization's flagship scientific event Sunday to encourage colleagues to amplify the voice of their patients.

"Caring for people, not just trying to fix their problems, this is where I think each of us individually, and the AHA collectively, have our biggest opportunities," Warner said. "As the business models of health care evolve toward rewarding the

PRESIDENT continued on page 18


John J. Warner, MD, FAHA

Tuesday is "Sneaker Day" at Scientific Sessions. Everyone is encouraged to wear athletic shoes in recognition of the importance of regular physical activity.



janssen
PHARMACEUTICAL COMPANIES
OF Johnson & Johnson

Committed to
Coronary Artery Disease (CAD)
&
Peripheral Artery Disease (PAD)

Come visit Janssen booth #2548
for more information

 November 2017 081247-171012

Janssen Pharmaceuticals, Inc.

janssen
PHARMACEUTICAL COMPANIES
OF Johnson & Johnson

HIGHLIGHTS FROM THE PROGRAM CHAIR

By Eric D. Peterson, MD, MPH, FAHA, Committee on Scientific Sessions Program Chair

Eric D. Peterson, MD, MPH, FAHA

It's "Wear Red Day!" If you packed a red shirt, tie, dress or blouse, today's the day to wear it to show your support for the AHA's mission to raise awareness of heart disease in women.

The scientific program continues today with three Late-Breaking Science sessions, beginning with "Late-Breaking Science in Prevention" at 9 a.m. This session will feature a large primary prevention trial, REAL-CAD, as well as the latest results from the REVEAL, FOURIER and CANTOS trials.

At 10:45 a.m. during the day's second Late-Breaking Science Session, "Latest Insights into Hypertension Management," investigators will present results from the Chinese BP, SPRINT and GATEWAY trials.

The final Late-Breaking Science Session of the day, "Sweet Spot in Cardiometabolic Care," begins at 3:45 p.m. and will include results from CANVAS, EXSCEL, EMPA-REG OUTCOME and a large metabolics registry, BiomarCaRE.

The highlight of the day is the release of the highly anticipated 2017 Hypertension Clinical Practice Guidelines at 2 p.m. during a Main Event session in Hall D, Main Building. Several sessions today will highlight the main recommendations and how they should impact current clinical care.

Today's schedule also includes two Frontiers in Science summits, each featuring a full day of sessions. The Arrhythmia Research Summit begins at 9 a.m. in Ballroom B, 3rd Level, Main Building, and will cover the latest research and therapeutic innovations in arrhythmia mechanisms, diagnosis and management. The Thrombosis Summit begins at 10:45 a.m. in room 225ABC, ACC North, and will explore emerging therapies and the most recent progress in thrombosis research.

Also taking place today is a special HealthTech Summit featuring a day-long series of sessions covering the latest innovations in digital healthcare solutions and health information technology. The program begins with a Main Event session at 9 a.m. in Hall D titled "Technology and Healthcare: The Road Ahead." It will feature a panel of speakers representing some of Silicon Valley's foremost leaders in health technology, including GE Ventures, Microsoft, Qualcomm and Verily Life Sciences (formerly Google Life Sciences).

Always a highlight of Scientific Sessions are the "Best of AHA Specialty Conferences" sessions, which feature some of the top basic and clinical science abstracts presented at various specialty meetings in the past year. This year's program includes six specialty conference sessions featuring abstracts from the 2017 ATVB/PVD, BCVS, EPI/Lifestyle, Hypertension, QCOR and ISC conferences. All of the sessions begin at 10:30 a.m.

That's just a taste of what's offered on a day packed with programming. Be sure to check the Final Program and the Mobile Meeting Guide for the complete schedule, including the times and locations of today's sessions, events and activities. ▼

Late-Breaking Science II: Late-Breaking Science in Prevention

LBS.02 | 9-10:15 a.m. Monday | Ballroom CD, 3rd Level, Main Building

Trial	Description
REAL-CAD — Does High-Intensity Pitavastatin Therapy Further Improve Clinical Outcomes? The REAL-CAD Study in 13,054 Patients with Stable Coronary Artery Disease	The REAL-CAD trial evaluated the efficacy of high-intensity pitavastatin therapy in patients with stable coronary artery disease in a relatively low-risk population.
REVEAL — Effects of Anacetrapib on the Incidence of New-onset Diabetes Mellitus and on Vascular Events in People with Diabetes	The HPS3/TIMI55-REVEAL trial evaluated the safety and efficacy of adding anacetrapib to an effective statin regimen in people with pre-existing cardiovascular disease.
FOURIER-PAD — Evolocumab and Outcomes in Patients with Peripheral Artery Disease	FOURIER-PAD evaluated the benefit of achieving very low LDL-C in patients with peripheral artery disease.
FOURIER-MI — Clinical Benefit of Evolocumab in Patients with a History of MI: An Analysis from FOURIER	FOURIER-MI sought to identify subsets of prior MI patients that derive greater clinical risk reduction with evolocumab.
CANTOS — Residual Inflammatory Risk and Residual Cholesterol Risk: Critical Analysis from the CANTOS Trial	CANTOS tested whether reducing inflammation among men and women who have had a prior myocardial infarction can reduce the risk of future cardiovascular events.

Late-Breaking Science III: Latest Insights into Hypertension Management

LBS.03 | 10:45 a.m.-Noon Monday

Main Event I, Hall D, Main Building

Trial	Description
Chinese BP Trial — Time at Blood Pressure Target and the Risk of Cardiovascular Diseases and Mortality	The Chinese BP trial evaluated the time at blood pressure target and the risk of cardiovascular diseases and mortality.
SPRINT — Blood Pressure Measurement in the Systolic Blood Pressure Intervention Trial	This SPRINT trial update evaluated attended versus unattended BP measurements to determine whether the BP technique usually employed at clinical sites was associated with a difference in BP values or overtreatment.
GATEWAY — Effects of Bariatric Surgery in Obese Patients with Hypertension	GATEWAY evaluated the impact of bariatric surgery on blood pressure and antihypertensive drug withdrawn.

Late-Breaking Science IV: Sweet Spot in Cardiometabolic Care

LBS.04 | 3:45-5 p.m. Monday

Ballroom CD, 3rd Level, Main Building

Trial	Description
CANVAS — Canagliflozin for Primary and Secondary Prevention of Cardiovascular Events in Type 2 Diabetes: Results from the CANVAS Program	This CANVAS trial update evaluated canagliflozin for the comparative effects among participants with and without a history of CV disease.
EXSCEL — Effect of Exenatide Once-Weekly on Clinical Outcomes in Patients with Type 2 Diabetes Mellitus and Cardiovascular Disease: Insights from the EXSCEL Trial	This trial evaluated the safety and efficacy of exenatide once weekly in a broad population of DM patients and the present results will detail the findings in the population with a prior CV event with a deeper dive into the CV outcomes.
EMPA-REG OUTCOME — Empagliflozin Reduces Mortality and Hospitalization for Heart Failure in Patients with Type 2 Diabetes and Peripheral Artery Disease: A Sub-Analysis of the EMPA-REG OUTCOME Trial	This trial assessed the effects of empagliflozin versus placebo in addition to standard of care on cardiovascular morbidity and mortality in patients with Type 2 diabetes and established CV disease.
BiomarCaRE — Serum Metabolomic Profiles Predict Coronary Heart Disease in the General Population – The Biomarcare Consortium	This trial assessed the risk prediction capability of metabolites for incident CHD in the general population, addressing the environmental and genetic factors that reflect the heterogeneity of coronary heart disease.

TODAY AT SESSIONS

Don't miss today's highlighted presentations and events. For a complete schedule, download the Mobile Meeting Guide, see the Final Program or view the online program at **scientificsessions.org.**

9-10:15 a.m.
Technology and Healthcare: The Road Ahead
Room 303CD, Main Building

9-10:30 a.m.
Arrhythmia Research Summit: Innovations in Therapy for Ventricular Arrhythmogenesis
Ballroom B, 3rd Level, Main Building

9:30-10:45 a.m.
ReSS Main Event: Educational Innovations in Resuscitation
Rooms 154-158, ACC North

10:45-11:45 a.m.
Dickinson W. Richards Memorial Lecture: Advancing Resuscitation Science: A Combination of Courage, Compassion, Collaboration, Carpe Diem and a Little Grace
Rooms 154-158, ACC North

12:30-1:30 p.m.
Lasker Laureate Lecture: Keeping Science and Society Healthy: Challenges for Scientists
Ballroom CD, 3rd Level, Main Building

1-2:30 p.m.
Health Tech Competition
Booth 2411, Science and Technology Hall

1-4 p.m.
Cardiovascular Nursing Clinical Symposium: Day One
Room 204A, Main Building

1:30-2:45 p.m.
ReSS Main Event: Coagulopathies in Resuscitation
Room 154-158, ACC North

2-3:15 p.m.
2017 Hypertension Clinical Practice Guidelines
Main Event I, Hall D, Main Building

3:45-5 p.m.
Target: BP™ 2017 Update and Lessons Learned from Participating Practices
Ballroom A, 3rd Level, Main Building

4:30-5:30 p.m.
Oral Abstracts
Rooms 154-158, ACC North

5:15-7:15 p.m.
Clinical Practice Guidelines for Blood Pressure Management: Next Steps
Ballroom A, 3rd Level, Main Building

5:30-6:45 p.m.
Gender Disparities and Women's Cardiovascular Disease
Rooms 208AB, Main Building

HEARTY HUMOR by Jonny Hawkins

"Stop calling me a quack!"

MEMBER SPOTLIGHT
Bilal Daqaq, RN, BSN

AHA instructor credits membership for improving career opportunities

Despite his medical-surgical and cardiac care nursing experience, Bilal Daqaq, RN, BSN, needed additional qualifications to further his career. So he participated in a BLS/ACLS program, becoming an instructor — and embarking on an unexpected journey with the AHA.

"I never dreamed of the vastness and the intensity of my aspiration or of the knowledge I would have gained from the teaching experience I have had with the AHA," Daqaq said. "It is a professional pleasure to be respected, promoted and supported as I have been as an AHA instructor."

Daqaq, director of nursing training and education at Specialized Medical Center Hospital in Riyadh, Saudi Arabia, said he joined the association because it exemplifies education and its leadership knows the importance of networking, mentorship and research opportunities for members.

He will soon become a member of the Council on Cardiovascular and Stroke Nursing — hoping to help improve outcomes from sudden cardiac arrest and other emergency cardiovascular care diseases.

"AHA membership allows me to stay connected — not only to the AHA and the work the organization is striving to perform locally and nationally — but also to other investigators and, most importantly, the community members we serve," Daqaq said. "Becoming a member of the AHA affords you many opportunities in mentorship, collaboration and funding in your field of study related to cardiovascular care and resuscitation science."

Daqaq said his increasing involvement with the AHA as a professional member will benefit him for years to come. ▼

All of Us research program seeks to accelerate the drive toward precision health

The *All of Us* Research Program at the National Institutes of Health is an unprecedented research initiative to gather data over many years from 1 million or more people living in the United States, with the ultimate goal of accelerating research and improving health. The program aims to create one of the largest, richest biomedical datasets for future studies, thus accelerating scientific and medical breakthroughs to improve and save lives.

Eric Dishman

Unlike research studies that focus on a specific disease or population, *All of Us* will serve as a national research resource to inform thousands of studies, covering a wide variety of health conditions, according to program director Eric Dishman, who delivered the Lewis A. Conner Memorial Lecture Sunday at Scientific Sessions.

"Currently, we don't have the ability and often don't have enough science and research to do the kind of precision care that we need to do across all health conditions," Dishman said. "Our mission with the *All of Us* program is to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment and care — so it's not just about coming up with a better pill. If all we get out of all this talk about precision medicine stuff is more therapy and not real strategies for dealing with prevention and dealing with the social issues of health, then we will have failed."

Dishman said the program is currently in beta phase and is focused on several initial strategic objectives, including developing partnerships with key organizations such as the AHA to begin the process of ultimately recruiting "participant partners" to the *All of Us* cohort to volunteer and share information about their health, lifestyle and environment.

"This is a longitudinal study, and if we're going to get ongoing data from people, we're going to have to build a relationship with them and give them value back, as well as include them in the creation of the platform and the creation of the ethics that we're carrying forward," Dishman said. "People are going to be consented for a very long period of time and the diversity of participants we get will define what this research journey is going to be like for decades to come."

Dishman also emphasized the importance of developing the program in a way that will make it appealing and useful to a diversity of researchers.

"We don't want this to be something that just the top tier of biomedical researchers use," he said. "We want community colleges to be able to use it. We want more people to be able to use these tools, to be able to play in the biomedical sandbox without having to become a computer programmer just to do their science."

While he admitted the program is ambitious, Dishman believes the time is right for *All of Us* to succeed. Americans are engaging in improving their health and participating in health research more than ever before, he said, while electronic health records have been widely adopted, genomic analysis costs have dropped significantly, data science has become increasingly sophisticated and health technologies have become mobile.

"Think of this as the Framingham Heart Study, but larger than the town of Framingham, larger than the state of Massachusetts. It's the entire country and not just focused on cardiovascular health, but all health," Dishman said. "It's exciting to imagine what this research platform of at least a million people — hopefully many more millions over time — will do to accelerate the science, to accelerate the discoveries that are going to change people's lives." ▼

Philanthropies team up to boost CVD control

Public health authorities Sunday led a forum on a $225 million global health initiative that aims to prevent more than 100 million deaths from cardiovascular disease over the next 30 years.

Marc Jaffe, MD, vice-president of the Cardiovascular Health Initiative, joined other public health authorities to discuss Resolve to Save Lives, which is funded by Bloomberg Philanthropies, the Chan Zuckerberg Initiative and the Bill & Melinda Gates Foundation.

Tom Frieden, MD, former director of the Centers for Disease Control and Prevention and former commissioner of the New York City Health Department, is leading the effort.

The initiative, which launched in September, aims to save lives with clinical and community interventions that ultimately help prevent cardiovascular disease and help countries close gaps in epidemic preparedness and response.

According to the World Health Organization, an estimated 17.7 million people died from CVDs in 2015, representing 31 percent of global deaths. More than 75 percent occured in low-income and middle-income countries.

Resolve will work with governments to increase global control of blood pressure from 14 to 50 percent. Those measures will address a standard, evidence-based treatment protocol, access to quality medications and patient-centered services that reduce barriers to medication.

Resolve to Save Lives is an initiative of Vital Strategies, a global health organization that works in more than 60 countries. The American Heart Association is supportive of the project. ▼

Public health authorities discussed a global health initiative to prevent CVD deaths.

New hypertension guidelines to be released today

The first new comprehensive hypertension guidelines for U.S. practitioners in nearly 15 years will be rolled out at Scientific Sessions on Monday.

The guidelines will be discussed in a series of three afternoon symposia:

- "The 2017 Hypertension Clinical Practice Guidelines" begins at 2 p.m. in Main Event I, Hall D, Main Building.
- "Target: BP™ 2017 Update and Lessons Learned from Participating Practices" begins at 3:45 p.m. in Ballroom A, 3rd Level, Main Building.
- "Clinical Practice Guidelines for Blood Pressure Management: Next Steps" starts at 5:15 p.m. in Ballroom A.

About half of U.S. adults are unaware that they have hypertension or are untreated or undertreated.

"The good news is that we have made tremendous progress in the U.S. on blood pressure management, but as much as we recognize the success we have had, we have more work to do," said Paul K. Whelton, MD, MSc, who chaired the joint AHA/ACC committee that created the guidelines. "We hope the new guidelines will prove to be a valuable resource for clinicians in improving the detection, prevention and management of high blood pressure."

The last comprehensive hypertension guidelines in the United States were published in 2003 in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).

"We have an enormous amount of new information, both on the risk side of hypertension and on the treatment side from major clinical trials," said Whelton, clinical professor and the Show Chwan Health System Endowed Chair in Global Public Health at the Tulane University School of Public Health and Tropical Medicine in New Orleans, Louisiana.

"The guidelines cover everything from the classification of blood pressure and blood pressure measurement issues to diagnosis of hypertension, prevention of high blood pressure and management of hypertension in both the general population and in higher-risk populations, such as older adults, pregnant women, individuals with diabetes mellitus and those with specific comorbidities."

A 21-member multidisciplinary writing committee developed the guidelines using a precise, structured system based on a series of clinical questions addressed with comprehensive literature reviews, including systematic reviews and meta-analyses conducted by an independent evidence-review committee. Each recommendation has an assigned class to indicate its strength and a rating to show the level of supporting evidence. Extensive evidence and literature tables support each recommendation.

Paul K. Whelton, MD, MSc

One of the most important developments since the publication of JNC 7 is an appreciation for the impact of blood pressure measurements on clinical decisions, Whelton said. That's why the new guidelines focus extensively on measurement issues, including how to measure blood pressure in and outside the office, and the practical value of out-of-office measurements.

U.S. clinical practice has focused on blood pressure measurement in the office, which represents a small window on a patient's blood pressure throughout the day. Recognizing white-coat hypertension and masked hypertension are important aspects of blood pressure management, Whelton said. Those patients appear to be at similar risk for cardiovascular events as those with hypertension sustained in and out of the office.

In developing the guidelines, Whelton said the committee devoted a good deal of attention to nonpharmacological approaches to preventing and managing high blood pressure and addressed pharmacologic management in detail, including who should be treated, which drugs should be used in specific patient groups and the targets for blood pressure control. ▼

Join us for our annual awardee group photo at Scientific Sessions

If you have ever had an AHA research grant or fellowship, please join us for an **Awardee Photo** at **1:30 p.m. Tuesday** immediately following the Distinguished Scientist Lecture in **Main Event II, Ballroom CD.** The ballroom is located on the third level of the Anaheim Convention Center. AHA officers are slated to join in the photo as well. Participants will receive a special AHA Awardee lapel pin!

Baseball great Rod Carew expresses thanks for advances in care, treatment of heart disease

A secret to Baseball Hall of Famer Rod Carew's success as a hitter was how hard he studied. He kept a notebook detailing every pitch he saw from every pitcher and looked it over before every at-bat.

So Carew appreciates people who go the extra mile to be skilled at their craft. Especially when those people helped him survive heart disease.

Carew overcame a serious heart attack, two episodes of cardiac arrest, a diagnosis of extreme heart failure, the implantation of a device that took over his heart's pumping for 15 months and, nearly a year ago, a heart transplant.

Rod Carew

Early in his journey, Carew partnered with the American Heart Association to promote awareness, prevention and treatment of heart disease. On Sunday, he brought his message to Scientific Sessions, speaking to supporters of the groundbreaking research that have led to success stories like his.

"I am happy to be alive. I think that's the number one thing," he said. "The treatment that I received from doctors, nurses, everybody I came into contact with was unbelievable – just unbelievable. Thank you, and thank you for all you do to help the American Heart Association. As long as I am on this earth, my wife and I are going to do the same."

Carew was joined on a panel by his wife, Rhonda, and by Dr. Dan Meyer, the surgeon who implanted the machine that kept Carew alive until his transplant, a left ventricular assist device, or LVAD, and who also has become the family's trusted friend and adviser. Dr. Gerald Marx, a pediatric cardiologist who connected the Carews and the AHA, moderated the event.

Marx pointed out that since 2005, the American Heart Association has invested nearly $62 million across 418 grants to support research broadly related to transplantation. Meyer added that "a lot of the technology that benefitted the Carews really came from research that the Heart Association has supported."

Carew often shows off the actual LVAD that was in his chest. He remains amazed that something that big could've been hooked up to his heart, and that he never felt it.

Maybe it's a good thing he didn't have his visual aid. Because Meyer said he would've brought his visual aid — the previous generation of the device, which he described as "the size of a salad plate and like 4 inches thick.

"And Rod thought his LVAD was large," Meyer said, laughing. "We thought it was unbelievable that his was so small!"

Meyer thanked the Carews for publicizing their story in hopes of helping others. Their campaign is called "Heart of 29," named for the jersey number Carew wore throughout his career. The name now has added meaning because his donor — former NFL player Konrad Reuland — was 29 when he died of a brain aneurysm.

"The future is prevention – never having to get to the point Rod did," Meyer said. "The work that Rod and Rhonda are doing to get the word out, encouraging people to know their risk factors and to get checked is already helping so many people."

Carew also talked a little baseball.

"What do you think you'd hit if you played today?" Marx said.

".285," Carew said.

"But you had a career average of .328," Marx said.

"Yeah," Carew said, "but now I'm 72 years old." ▼

Heart transplantation and LVADs improve gut dysbiosis in advanced heart failure patients, study finds

Researchers have found that left ventricular assist devices and heart transplantation might reduce endotoxemia, inflammation and oxidative stress and improve gut dysbiosis often seen in patients with advanced heart failure. Additionally, intestinal overgrowth of pathogenic bacteria and reduced microbial diversity may promote translocation of pro-inflammatory bacterial products into the systemic circulation, triggering or further exacerbating the heart failure syndrome itself.

Melana Yuzefpolskaya, MD, assistant professor of medicine and associate director of the Mechanical Circulatory Support Program at New York Presbyterian Hospital and Columbia University, presented these findings during an abstract poster session on Sunday.

"Our data demonstrated that patients with advanced heart failure present with an inflammatory phenotype concurrent with elevated markers of congestion, oxidative stress and gut dysbiosis," Yuzefpolskaya said. "Our current treatment options — LVAD and heart transplantation — appear to favorably influence the inflammatory and microbial milieu."

Melana Yuzefpolskaya, MD

The study was part of a collaboration with Paolo C. Colombo, MD, Sudhir Choudhrie Associate Professor of Cardiology and director of the Center for Advanced Cardiac Care at New York Presbyterian Hospital/Columbia University, and Ryan Demmer, PhD, MPH, FAHA, associate professor of epidemiology and community health at the University of Minnesota School of Public Health in Minneapolis.

The study included 169 patients — 65 patients had NYHA class I-III heart failure, 28 had Class IV heart failure, 28 had an LVAD for a mean duration of 1.7 years and 48 were heart transplant recipients for a mean of 6.9 years prior to study entry.

The investigators assessed serum markers of endotoxemia (lipopolysaccharide), inflammation (adiponectin, CRP and endothelin-1), interleukin-6 (IL-6), sCD14, tumor necrosis factor-alpha (TNF-alpha) and oxidative stress (isoprostane) in venous blood. Stool samples were collected from hospitalized patients and home sample kits were given to ambulatory patients. Stool samples were analyzed for bacterial DNA to assess the number of taxa between patients and the microbial community similarities between patients.

"When heart failure becomes advanced, decreased blood flow and venous congestion contribute to a shift in the microbial community, releasing endotoxins into the systemic circulation triggering an inflammatory response," Yuzefpolskaya said. "What we did not know was the effect of LVAD and heart transplantation on the degree of potential gut dysbiosis and associated levels of endotoxemia, inflammation and oxidative stress among these patients."

Advanced heart failure patients (NYHA Class IV) showed the highest levels of endotoxemia, inflammation and oxidative stress, she said. Individuals with LVADs and heart transplantation showed significantly lower levels of serum biomarkers that were similar to the levels seen in patients with more stable disease (NYHA Class I-III). Gut dysbiosis also improved after cardiac replacement therapy (LVAD and heart transplantation).

Yuzefpolskaya noted that the severe heart failure group, who were the sickest in the study, had a unique set of organisms that were not present in the other patients and a trend toward less diversity in the taxa found in the gut microbiota.

"These findings open the door to further studies that might include dietary modulation, pre/probiotics, antibiotic therapy and possibly fecal transplantation as ways to favorably alter the gut microbiome and affect heart failure outcomes," Yuzefpolskaya said. ▼

Maze procedure may improve long-term outcomes in rheumatic mitral valve surgery for Afib patients

Adding a maze procedure to rheumatic mitral valve surgery in patients with atrial fibrillation may improve clinical outcomes, according to research presented Sunday at Scientific Sessions.

Researchers from South Korea found that a concomitant maze procedure during mitral valve surgery for patients with rheumatic heart disease can reduce mortality and thromboembolic event rates. Wan-Kee Kim, MD, a cardiac surgeon at the Asian Medical Center of Korea in Seoul, reported results of the study during an abstract poster session.

The data showed improvements in thromboembolism, hemorrhage, valve explants and endocarditis.

Researchers retrospectively reviewed 1,229 patients with atrial fibrillation who were undergoing mitral valve surgery from 1997 to 2016. Of the group, 812 patients (66.1 percent) received a concomitant maze procedure, while 417 patients (33.9 percent) did not. Patients underwent one of three procedures: valve repair (161 patients), mechanical valve implant (829 patients) or bioprosthetic valve implant (239 patients).

The maze procedure gave some patients freedom from atrial fibrillation, Kim said. "In this cohort of patients who had mitral surgery over 19 years, freedom from atrial fibrillation five years after surgery was 76.5 percent in the maze group and 57.9 percent in the no-maze group," he reported. "The lower mortality and thromboembolic event rates in the maze group were probably affected by better sinus restoration effects."

Ten-year survival in the maze group was 83.2 percent, Kim said, compared to 74.4 percent in the no-maze group ($p<0.001$). In the maze group, 81 percent of patients were free from valve-related adverse events at 10 years compared to 76.6 percent in the no-maze group ($p=0.07$).

After baseline adjustment, the maze group had a significant survival advantage, with a hazard ratio for mortality of 0.69 compared to the no-maze group (95 percent CI 0.52-0.93). Thromboembolic events were also significantly less in the maze group compared to the no-maze group, with a hazard ratio of 0.49 (95 percent CI 0.32-0.75).

The survival benefit was not uniform across the three surgical procedures, Kim noted. Subgroup analyses showed a hazard ratio of 0.18 for valve repair, 0.52 for mechanical valve implant and 0.75 for bioprosthetic valve implants.

Wan-Kee Kim, MD

"Even for patients with atrial fibrillation combined with rheumatic heart disease, a concomitant maze procedure may result in better survival and protection effect against stroke with an acceptable rate of sinus rhythm restoration," Kim said. ▼

AHA Institute for Precision Cardiovascular Medicine at Recharge Institute Lounge

Learn more about the AHA's Institute for Precision Cardiovascular Medicine at the Recharge Institute Lounge in Hall D, Main Building. The lounge is open 7 a.m.-5:30 p.m. Monday and 7:30 a.m.-5:30 p.m. Tuesday, features demos of the AHA Precision Medicine Platform and My Research Legacy. You can also have one-on-one discussions with precision medicine experts, recharge your devices at multiple stations and enjoy free coffee.

HERE'S TODAY'S PRESENTATION SCHEDULE:

1-2 p.m.
AHA Precision Medicine Platform

2:05-2:30 p.m.
My Research Legacy + Meet a Heart Valve Survivor

3:15-3:45 p.m.
Amazon Web Services

LOUNGE HOURS

7 a.m.-5:30 p.m. Monday
7:30 a.m.-5:30 p.m. Tuesday

Drop by and be sure to use **#AHAprecision** on Twitter and Instagram.

Lasker lecturer wants to keep science healthy

Bruce M. Alberts, PhD, had every intention of becoming a physician. That is, until he discovered science.

"When I was an undergrad, I was taking laboratory courses three days a week," Alberts recalled. "The laboratories were like cooking, like following a recipe. It was not real science. They did not teach me anything about how science really operates."

It was not until he moved to a research lab that his eyes opened to inquiry-based science. It's this type of science, he said — the kind where people ask questions and use logic and evidence, the kind that provides an understanding of the nature of the scientific enterprise — that has the power to change the country and the world.

"Science is an amazing human invention, but most people do not understand what it takes to keep it healthy," Alberts said. "We must be vigilant and make adjustments to how it is conducted."

Alberts will present the Lasker Laureate Lecture, "Keeping Science and Society Healthy: Challenges for Scientists," at 12:30 p.m. Monday in Main Event I, Ballroom CD, Main Building.

Alberts will address several developments that threaten science's health. In recent years, for instance, the average age of biomedical scientists in the U.S. who have independent grants from the National Institutes of Health has increased dramatically, he said. Because of this shift, young scientists do not get started on their independent work until much too old an age, Alberts said, and this is very damaging to the future of the enterprise.

"We need to work to shift resources and put more resources into the hands of the best young scientists to help them test their ideas," said Alberts, who is the Chancellor's Leadership Chair in Biochemistry and Biophysics for Science and Education at the University of California, San Francisco.

It's also critical that the focus shifts from the notion that young scientists should simply continue the work of their mentors and, more generally, be conservative in how they proceed with research.

"Our current system encourages young scientists to do the same kind of research that others are already doing," Alberts said. "As someone who writes and updates textbooks every few years, I see the unfortunate result — there are a lot of fundamental biological problems out there that no one is using modern methods to attack."

Healthy science can also help society in more fundamental ways, Alberts said, like helping farmers achieve better crop yields by applying agricultural sciences, especially in impoverished communities that rely largely on manual agriculture.

Bruce M. Alberts, PhD

LECTURE PREVIEW

Lasker Laureate Lecture:
Keeping Science and Society Healthy: Challenges for Scientists

12:30-1:30 p.m. Monday
Main Event I, Ballroom CD, Main Building

"Thanks to modern communication technologies, we have huge opportunities to improve the livelihood of people with health information and farming skills through connections to local scientists and scientific knowledge," he said.

Alberts hopes his lecture will encourage attendees to pay more attention to how they can help the best young scientists productively enter the field of scientific research, as well as how they can help drive changes that exploit the potential power of science education to create healthier and more rational societies around the world. ▼

Protecting patients' circadian rhythm improves in-hospital outcomes

New data suggests that changing hospital operations to protect patients' circadian rhythm may improve both clinical outcomes and satisfaction in cardiology patients. New procedures that were trialed in a single interventional wing at Ochsner Health System's New Orleans hospital are being implemented across the institution.

These findings were presented by Richard Milani, MD, vice chair of cardiology and chief transformation officer at Ochsner Health System in New Orleans, during a poster session on Sunday.

"There's a lot of literature supporting the impact of even small changes in the circadian rhythm on clinical events," Milani said. "Disruption of circadian rhythm is very common in any hospital. There's noise. There are interruptions in sleep, whether it is collecting vital signs or lights being turned on to check on patients. Nurses wake patients up in the middle of the night to administer medications or before dawn for phlebotomy. It's all routine."

It's well known that circadian rhythms can affect cardiovascular events, Milani said, noting that there's data demonstrating the impact of even minor changes to circadian rhythms on the immune system, metabolic function and other biologic functions.

The trial at Ochsner compared 30-day readmission rates, length of stay and patient satisfaction following a stay in a

Richard Milani, MD

protected sleep environment compared to conventional care. A total of 594 cardiovascular patients were randomly admitted to an interventional wing and compared to 1,183 patients admitted to a control wing that delivered standard care.

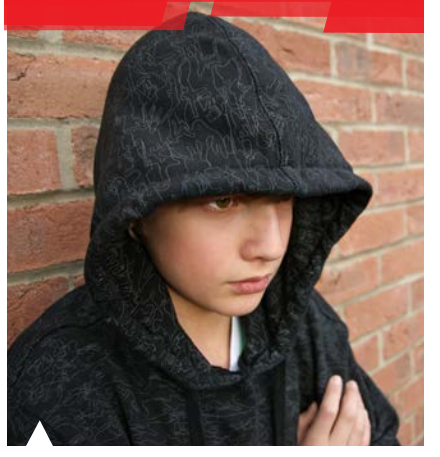
The interventional wing adjusted operating procedures in order to protect patients' sleep cycles. Changes included a reduction in nighttime noise, a delay in routine phlebotomy from 5 a.m. to 6 a.m., passive vital sign monitoring instead of active monitoring that required waking patients and the use of red-enriched lighting after sunset instead of standard white sources to reduce light disturbances.

While hospital staff members are familiar with patient complaints about nighttime interruptions, Milani said they may not be aware of the potential adverse effects that can stem from disturbing patients. Practices such as early morning phlebotomy, he noted, likely grew out of attempts to ensure that lab results were ready for physicians who preferred to conduct hospital rounds early in the morning. Turning on lights to check on patients during the night, he added, can be seen as a safety and quality-of-care issue.

The results of the study were surprising, Milani said. Patients in the sleep-protected wing had an 18 percent reduction in 30-day readmission (p=0.03) and a 17 percent improvement in satisfaction scores (p=0.03). Patients with better sleep also showed significant improvements in length of stay and the need for pain medication, as well as non-significant trends toward improved survival.

"All of the things we did are doable at no or low cost. There was nothing in this intervention that requires you to spend a lot of money or blow up your hospital and reconfigure your wards," Milani said. "These are changes that almost any hospital system can implement. Getting more sleep and higher-quality sleep in the hospital may seem like a small thing, but it's meaningful to patients. This is one of those rare one-and-done changes that can make a major difference in patient outcomes and satisfaction." ▼

MOOD, MEMORY AND TEEN HEART DISEASE



Adolescents with single-ventricle congenital heart disease (SVHD) show brain-related functional deficits, particularly in mood and memory. Hippocampi are key brain structures of mood and memory circuitry, but their integrity in SVHD adolescents is unclear. Researchers in Los Angeles used high-resolution, T1-weighted MRI to evaluate the effect of hippocampal volumes in SVHD and control adolescents.

The study's findings will be presented during an Abstract Rapid Fire Oral session at 3 p.m. Monday in the Science and Technology Hall, Clinical II Forum.

Cardiorespiratory fitness may help protect against age-related carotid enlargement

Good levels of cardiorespiratory fitness may help protect against cardiovascular disease by attenuating the enlargement of arteries associated with age. Longitudinal data presented during a poster session on Sunday suggest that the protective effect seen from improved physical fitness may be due in part to physical changes in arteries and improved maintenance of arterial lumens.

"We know that elastic arteries, such as the carotid, undergo remodeling with age," said Yuko Gando, PhD, a researcher in the Section of Physical Activity Research of the National Institutes of Biomedical Innovation, Health and Nutrition in Tokyo, Japan, who presented the poster.

The commonly observed expansion of the arterial lumen is an adaptive process in response to long-term hemodynamic stresses, Gando explained. Expansion of the arteries is also associated with increased cardiovascular events.

At the same time, she said, it's well recognized that higher levels of physical fitness, especially cardiorespiratory fitness, protect against cardiovascular disease. However, little evidence has been uncovered that might explain the mechanisms by which fitness protects against cardiovascular events. Gando said this might be the first prospective study of carotid enlargement in individuals over time and the relationship between cardiorespiratory fitness and physiological changes in the carotid arteries.

Researchers used five-year longitudinal data from Japan's Nutrition and Exercise Intervention Study, an ongoing prospective study sponsored by the National Institute of Health and Nutrition. The study cohort included 256 healthy men and women aged 27 to 67 years at the start of the observation period. Cardiorespiratory fitness was assessed at baseline using peak oxygen uptake during an incremental cycle exercise test. Carotid size was measured by B-mode ultrasonography at baseline and at five years.


Yuko Gando, PhD

After adjusting for baseline age and sex, baseline peak oxygen uptake was inversely associated with changes in carotid lumen diameter over the five-year observation period (β = -0.15, p=0.035), Gando reported. The inverse association persisted after adjusting for baseline systolic blood pressure, body mass index and hemoglobin A1C (β =-0.18, p=0.017).

Gando noted that additional studies are required to investigate the mechanisms underlying the observed relationships between cardiorespiratory fitness and age-related arterial remodeling, including longer observational studies as well as interventional trials. Her group also plans to focus on the interactions between cardiorespiratory fitness and nutrition on age-related arterial remodeling.

"What we can say for now is that these prospective data show that cardiorespiratory fitness is very clearly inversely associated with arterial enlargement and that maintaining a high level of fitness may have a protective effect by limiting this age-related remodeling," Gando said. "That makes the maintenance of a higher level of cardiorespiratory fitness an important element in primary prevention strategies for people in all age groups." ▼

Claiming CME/CE at Scientific Sessions

Healthcare professionals attending Scientific Sessions can claim and print CME/CE certificates when they have attended all of the sessions for the meeting. **Physicians, nurses and EMS must claim credit by May 15, 2018. Pharmacists must claim credit by Dec. 15, 2017. ABIM MOC credit is available and must be claimed by Dec. 15, 2017.**

1. Go to **learn.heart.org**.
2. Click "Activities in Progress" in the left-hand navigation. You will be prompted to sign in using your American Heart Association username and password. You can create an account if you don't have one.
3. Review the "Activity Overview and "Activity Material" tabs.
4. Complete the evaluation.
5. Claim your credit(s).

International attendees can obtain their attendance verification certificate at the registration center. For a full list of conference accreditation statements and credit hours, visit **scientificsessions.org**.

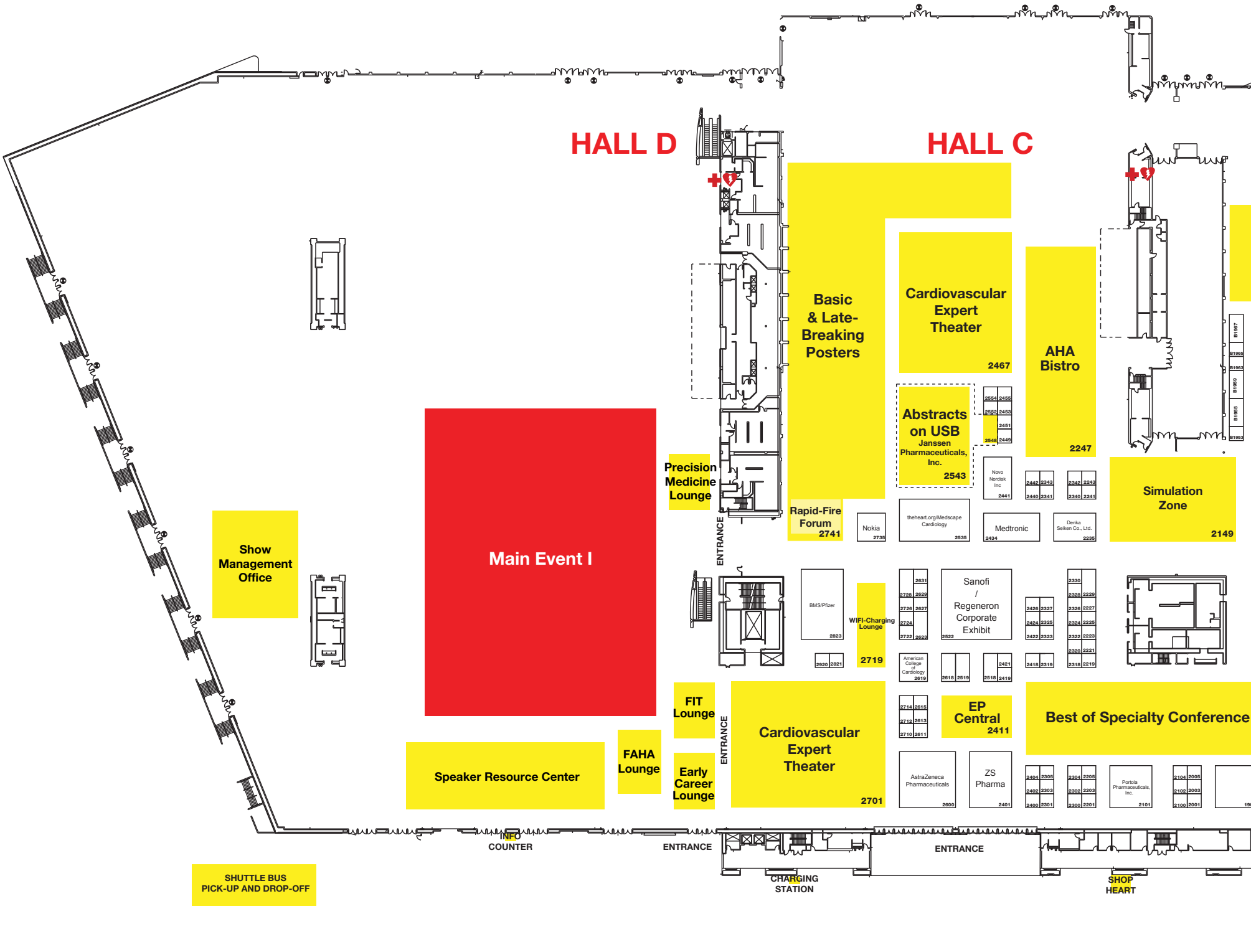
2017 Scientific Sessions Exhibitors

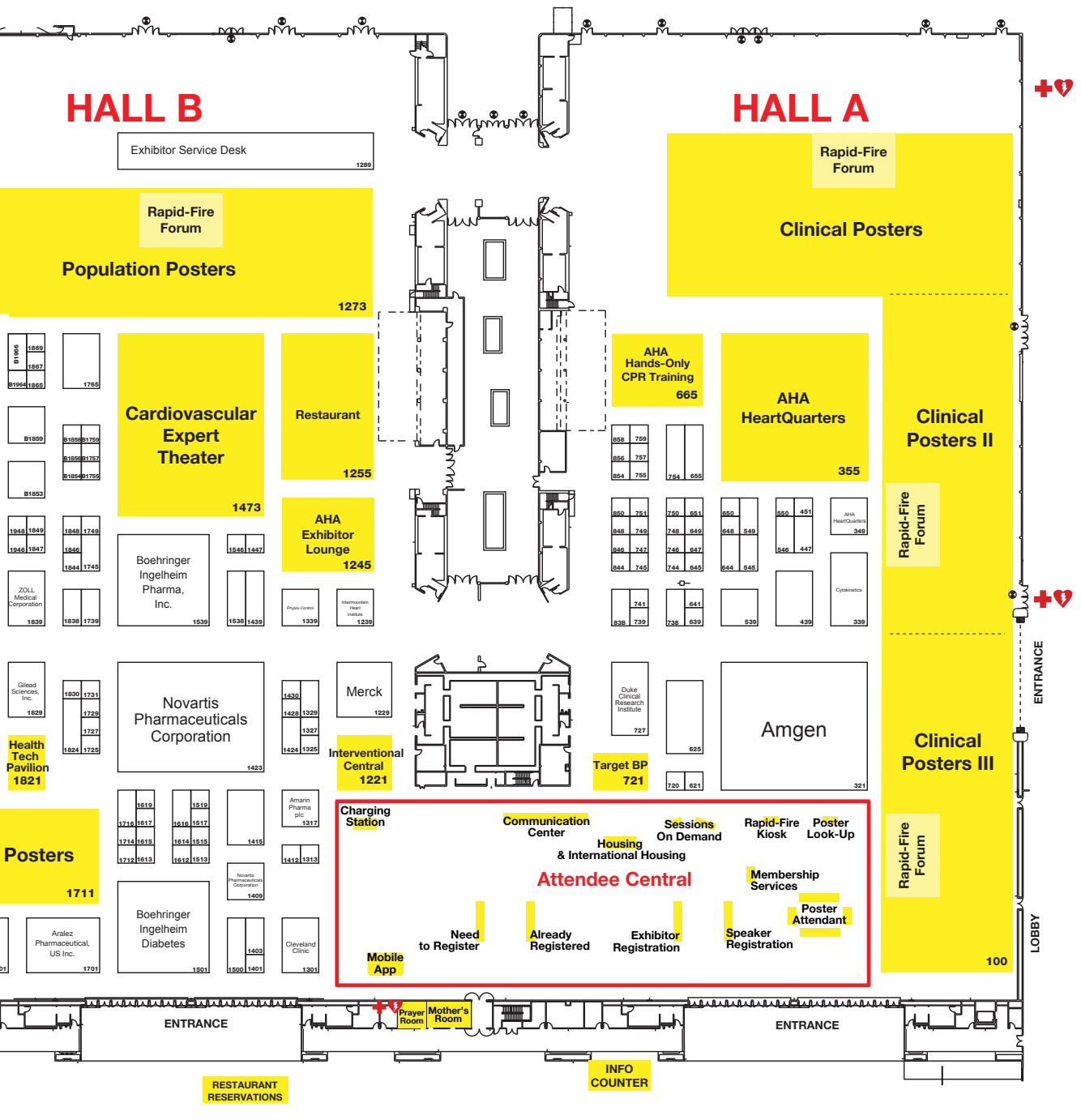
Science & Technology Hall Hours

Monday	10 a.m.-4:30 p.m.
Tuesday	10 a.m.-3 p.m.

Hall Breaks

Monday	10:15-10:45 a.m., Noon-2 p.m. and 3:15-3:45 p.m.
Tuesday	10:15-10:45 a.m. and Noon-2 p.m.





American Heart Association.
life is why™

SCIENTIFIC SESSIONS 2017

MONDAY'S THEATER PRESENTATIONS

CARDIOVASCULAR EXPERT THEATER BOOTH 1473

Noon-12:45 p.m.
The Underlying Thrombotic Risk in Patients with Atherosclerotic Vascular Disease
Supporter: Janssen Pharmaceuticals, Inc.
Presenter: Marc Bonaca, MD, MPH

1:15-2 p.m.
The Repatha Patient Journey
Supporter: Amgen, Inc.
Presenter: Harold Bays, MD, FTOS, FACC, FACE, FNLA

CARDIOVASCULAR EXPERT THEATER BOOTH 2467

Noon-12:45 p.m.
For International Attendees: The LDL Paradigm Sponsored by Amgen
Supporter: Amgen, Inc.

1:15-2 p.m.
Optimizing Treatment to Improve Outcomes: Implementing the New Guideline for Managing Heart Failure with Reduced Ejection Fraction
Supporter: Novartis
Presenters: Gregg C. Fonarow, MD, FAHA, FACC, FHFSA; Roberta Bogaev, MD; and Beth Davidson, DNP, ACNP, CHFN, CCRN

CARDIOVASCULAR EXPERT THEATER BOOTH 2701

Noon-12:45 p.m.
Persistent Vascular Risk: Reducing Thrombotic CV Events in the Management of Patients with Systemic Atherothrombosis
Supporter: Aralez Pharmaceuticals, US, Inc.
Presenter: Seth J. Baum, MD, FACC, FACPM, FAHA, FNLA, FASPC

1:15-2 p.m.
A Closer Look at New, Real-World Evidence for an OAC with Reversal
Supporter: Boehringer Ingelheim Pharmaceuticals, Inc.
Presenter: Todd Villines, MD, FACC

3:15-4 p.m.
Awaken a Transformation in Type 2 Diabetes Management
Supporter: Janssen Pharmaceuticals, Inc.
Presenter: Matthew Budoff, MD, FACC, FAHA

HEARTQUARTERS THEATER BOOTH 335

10-10:45 a.m.
Heart Valve Education Center
Presenters: Mark Ridder, Debra North

11a.m.-Noon
Cardiovascular Center of Excellence
Presenter: Bob McNamara, MD, MHS, FAHA, FACC, FASE, Associate Professor, Section of Cardiovascular Medicine, Yale

12:15-12:45 p.m.
Visualizing Complex Results in the Age of Big Data: Examples from the Global Burden of Disease Study
Presenter: Greg Roth, MD, MPH, DPhil, Institute of Health Metrics and Evaluation, University of Washington

1-1:30 p.m.
Social Media and Crowdsourcing in Health Research
Presenter: Benjamin Ranard, MD, Duke University School of Medicine

2:15-2:45 p.m.
Social Determinants of Health Presentation-Multicultural Markets
Presenters: Francesca Martinez, Bry Mabry, Arika Cason

3-3:30 p.m.
Research Funding Opportunities
Presenter: Steven R. Houser, PhD, FAHA, Temple University School of Medicine & AHA Immediate Past-President

3:30-4 p.m.
CVD Research at the Edges of Hard Science: The Biology of Social Determinants and the Impact on Cardiovascular Health
Presenter: Michelle A. Albert, MD, MPH, UCSF School of Medicine

No additional bleeding risk from DOACs in AF patients presenting with myocardial infarction, study finds

The results of an analysis of data from the National Cardiovascular Data Registry showed no additional risk of in-hospital bleeding for atrial fibrillation patients presenting with a myocardial infarction who were on no oral anticoagulation at home, warfarin or direct oral anticoagulants (DOACs).

The findings from the study were presented during an Abstract Rapid Fire Oral session on Sunday by Christopher Madias, MD, co-director of the Cardiac Arrhythmia Center at Tufts University Medical Center in Boston.

"There's a perceived higher bleeding risk from being on direct-acting oral agents and undergoing PCI, but our data suggest that it's safe to revascularize these patients urgently," Madias said.

Researchers compared outcomes for 6,471 patients with an ST elevation MI and 19,954 NSTEMI patients treated at 761 U.S. hospitals reporting to the ACTION Registry® from January 2015 through December 2016. All patients had a prior history of AF.

In the STEMI group, 71.3 percent were not on any anticoagulation therapy at home, 15.7 percent were on warfarin and 13 percent were on DOACs. In the NSTEMI group, 61.9 percent were not on anticoagulation at home, 22.8 percent were on warfarin and 15.4 percent were on DOACs.

Madias reported that rates of angiography within 24 hours of presentation and frequency of primary PCI were similar between the three groups for STEMI patients. NSTEMI patients who were not on anticoagulation at home were more likely to undergo angiography or PCI within 24 hours of presentation compared to patients with either form of oral anticoagulation.

"One of the unexpected findings was, in the patients on oral anticoagulation, especially those on direct-acting oral anticoagulants, we saw a reduced risk of in-hospital mortality compared to patients who were not on any blood thinners at home," Madias said. "However, we have to interpret these data with caution, given that this is a retrospective, observational study and unmeasured confounders could not be accounted for."

Also of note, he added, patients who were on home anticoagulation therapy — whether they were on warfarin or on DOACs — tended to be prescribed the same oral anticoagulant upon discharge.

"The major take-home message from these data suggest that patients with atrial fibrillation on home oral anticoagulation, including with direct oral anticoagulants, can be managed as safely as patients who are not on blood thinners during the peri-infarction period," Madias said. ▼

MEDIATING MITOPHAGY DURING ISCHEMIA

Activation of mitophagy, its underlying mechanism and its functional significance have not been clearly demonstrated in the heart during ischemia. Researchers examined the roles that two key regulators of autophagy, Atg7 and Ulk1, play in mediating mitophagy during energy stress in the heart.

The study results will be presented during an Abstract Rapid Fire Oral session at 1:30 p.m. Monday in the Science and Technology Hall, Basic Forum.

Novel protein exhibits promising rescue effect in heart failure models

Researchers have identified a micropeptide that appears to reverse heart failure in multiple mouse models. The new peptide is one of dozens of proteins so small they had been misannotated as noncoding RNAs, according to Catherine A. Makarewich, PhD, a post-doctoral research fellow at UT Southwestern in Dallas, who described this finding during an oral abstract session on Sunday.

"We found ways to search noncoding RNA transcripts to look for small, conserved, open reading frames that code for functional peptides," Makarewich said. "This one — dwarf open reading frame, or DWORF — has just 34 amino acids, which makes it the third smallest full-length protein in the mouse genome. It significantly increases calcium cycling and contractility in cardiac muscle. Overexpressing DWORF can completely rescue several animal models of heart failure."

The researchers found DWORF in slow-twitch skeletal muscle, but Makarewich said the protein is most highly expressed in cardiac muscle. In cardiomyocytes, it binds to SERCA2a (sarcoplasmic/endoplasmic reticulum Ca(2+)ATPase 2), which regulates and enhances calcium ion reuptake into the sarcoplasmic reticulum and increases contractility. Enhanced SERCA2a activity accelerates contractility, increasing cardiac output.

A key feature of DWORF is its ability to preferentially bind to SERCA2a and displace phospholamban (PLN), which acts as an inhibitor of SERCA activity and reduces contractility, Makarewich explained.

"DWORF competes for the same binding site as PLN, so when you overexpress DWORF it displaces PLN and relieves its inhibitory effects, which means you have enhanced calcium cycling in cardiomyocytes and enhanced contractility," Makarewich said. "Other groups have shown that gene deletion of phospholamban can rescue heart failure models, so we thought that outcompeting phospholamban for binding sites on SERCA2a might have similar effects. It does."

The researchers created a mouse model that overexpresses DWORF in cardiac tissue and crossed the over-expressers with the well-characterized muscle LIM protein (MLP) knockout mouse model of dilated cardiomyopathy. The result was complete restoration of cardiac function. DWORF also prevented the pathological remodeling, extensive fibrosis and ultrastructural defects that are typical of the heart failure model.

Catherine A. Makarewich, PhD

"The rescue effect of DWORF is breathtaking," Makarewich said. "The effect is clear and complete. At this time, we don't know what else DWORF might be doing, so we have a considerable amount of work left to do."

Another interesting facet, she noted, is DWORF's apparent specificity. While most proteins are active in multiple sites and pathways, DWORF seems to bind only with SERCA2a and almost exclusively in cardiac tissue. Unlike phospholamban and other micropeptides, Makarewich said it does not even bind with itself.

In the case of phospholamban, self-binding creates oligomers that sequester it from binding with SERCA2a. Because DWORF does not form similar oligomers, more of the protein remains in an active state and binds with SERCA2a to enhance cardiomyocyte contractility.

"We are seeing a big picture of DWORF as an enhancer of SERCA2a activity and cardiac contractility," Makarewich said. "We hope it can have beneficial effects in additional models of heart failure. We intend to test it on many different animal models before considering its clinical potential. But so far in our work, DWORF has robustly rescued all the heart failure phenotypes we have tested it with." ▼

DailyNews

The American Heart Association's Scientific Sessions 2017 *Daily News* is published by TriStar Publishing, Inc., as a service to American Heart Association Scientific Sessions attendees.

American Heart Association
7272 Greenville Avenue
Dallas, TX 75231
Phone: (214) 570-5935
scientificsessions.org

TriStar Publishing, Inc.
7285 W. 132nd Street,
Suite 300
Overland Park, KS 66213
Phone: (913) 491-4200
tristarpub.com

Achieving NT-proBNP goal associated with reverse left ventricular remodeling, study finds

Heart failure patients who achieved an NT-proBNP goal of less than 1,000 pg/ml after one year of medical therapy had a significantly greater reversal of adverse left ventricular remodeling than patients who failed to meet this goal, according to the results of research presented on Sunday at Scientific Sessions.

Kirkwood Adams, MD, of the division of cardiology at the University of North Carolina-Chapel Hill, presented the research for Melissa Daubert, MD, assistant professor at Duke University School of Medicine in Durham, North Carolina.

Adams reported that patients who attained the NT-proBNP goal showed significant improvements in ejection fraction, end-systolic volume, end-diastolic volume and global left ventricular strain. Patients in the study achieving the NT-proBNP goal also had a significantly lower rate of death and heart failure hospitalization a year after treatment.

"We have known that decreasing levels of natriuretic peptides, such as NT-proBNP, are associated with improved clinical outcomes in heart failure patients with reduced ejection fraction," Daubert said before the meeting. "This study shows that the improved outcomes seen with lowering NT-proBNP may be explained, at least in part, by reverse LV remodeling."

The findings are from a pre-specified substudy of the Guiding Evidence Therapy Using Biomarker Intensified Treatment in Heart Failure (GUIDE-IT) trial. GUIDE-IT was designed to compare usual care for heart failure to a biomarker-guided strategy that aimed for NT-proBNP levels of less than 1,000 pg/ml. The main trial was stopped early after 894 patients (planned for 1,100 patients) were enrolled due to lack of efficacy in the biomarker-guided treatment group compared with usual care.

Daubert was the principal investigator for the Echo Substudy that assessed the impact of biomarker-guided therapy on cardiac structure and function compared to usual care in heart failure patients with systolic dysfunction. The substudy enrolled 269 patients, 117 of whom had both baseline and one-year echocardiograms.

A total of 53 patients achieved the goal of NT-proBNP less than 1,000 pg/ml at one year and 64 patients did not. After one year, patients who achieved the goal had an absolute increase in ejection fraction of 9.9 percent compared to those who did not meet goal ($p<0.001$). Patients who achieved goal had an absolute reduction of 24.6 ml/m2 in indexed end-systolic volume ($p<0.001$), a 22.0 ml/m2 reduction in indexed end-diastolic volume ($p=0.006$), and a 2.8 percent absolute improvement in global left ventricular strain ($p=0.003$).

"We found that the clinical characteristics of these two groups of patients were strikingly different at baseline," Daubert said. "Patients who achieved goal were more likely to have a nonischemic cardiomyopathy, while those who did not achieve goal were more likely to have an ischemic cardiomyopathy."

The analysis also demonstrated that the rate of death or heart failure hospitalization after 12 months was significantly higher in patients who did not achieve NT-proBNP goal ($p<0.001$).

"We now have some mechanistic insight into why these patients improve when they achieve NT-proBNP goal," Daubert said. "This study was also able to quantify for the first time the change in NT-proBNP needed to get meaningful change in cardiac structure and function."

Reducing NT-proBNP levels by an absolute value of 1,000 pg/ml decreased indexed end-systolic volume by at least 17 ml/m2, Daubert noted, and increased ejection fraction by almost 7 percent.

"This gives providers a target," she said. "If they can move NT-proBNP by at least 1,000 pg/ml, they will potentially see beneficial effects on the structure and function of the heart. As long as the patient is tolerating medications, they can feel confident that the patient is likely undergoing positive changes in left ventricular remodeling." ▼

Study analysis: Increasing low-risk lifestyle factors could add years to U.S. life expectancy

A new analysis of existing population studies suggests that improving lifestyle could make a significant difference in life expectancy — women could expect to add nearly 15 years and men more than 12 years of life by increasing the number of low-risk lifestyle factors.

Yanping Li, MD, a research scientist at the Harvard T.H. Chan School of Public Health in Boston, presented the findings from the study Sunday during the Robert Levy Memorial Lecture/Lifestyle and Cardiometabolic Health Young Investigator Award session.

"It's not because of genetics that Americans live shorter lives than almost anyone else in the developed world — it's because not enough people in this country apply a healthy lifestyle," Li said. "We have found that moving to a healthy lifestyle could make the life expectancy of Americans almost the same as the Japanese, who have the longest life expectancy, according to the World Health Organization."

Researchers analyzed data from the Nurses' Health Study (1980-2014) and the Health Professionals Follow-up Study (1986-2014) to estimate hazard ratios associated with five low-risk lifestyle factors: never smoking, body mass index between 18.5 and 24.9, at least 30 minutes of moderate to vigorous exercise daily, moderate alcohol intake and a diet quality score in the upper 40 percent.

"What we know in looking at lifestyle patterns over the past 30 years is that the portion of Americans following a healthy lifestyle is getting less and less, especially when it comes to obesity and lack of physical activity," Li said. "Smoking and the composition of the diet have improved a little, but the improvement is too small compared to the worsening patterns we see in obesity and physical activity."

Recognizing that healthcare professionals are more likely to follow lifestyle recommendations than the average person, the research team used data from the Nurses' Health Study and the Health Professionals Follow-up Study to determine hazard ratios associated with each of the five factors included in the analysis. Between them, the two studies followed more than 123,000 individuals for up to 34 years.

Using data from National Health and Nutrition Examination Survey 2013-2014, the researchers estimated the nationwide distribution of the five low-risk factors that were studied. Age-specific death rates for Americans were derived from the Centers for Disease Control and Prevention's Wide-ranging OnLine Data for Epidemiologic Research (WONDER) database.


Yanping Li, MD

The two healthcare professionals studies documented 41,859 deaths, including 13,721 deaths from cancer and 10,639 deaths from cardiovascular disease. There was a linear association between the number of low-risk factors and lower mortality rates. Hazard ratios for no risk factors versus all five risk factors were 0.26 for all-cause mortality, 0.35 for cancer mortality and 0.18 for cardiovascular disease mortality.

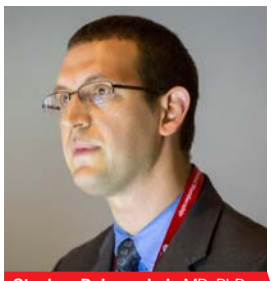
For all U.S. adults, the population-attributable risk was 60.7 percent for all-cause mortality, 51.7 percent for cancer mortality and 70.7 percent for cardiovascular mortality. The average life expectancy at age 50 was 14.9 years longer for women with five low-risk factors compared to no low-risk factors, and 12.4 years longer for men.

"It's not that hard to plan a healthy lifestyle — the hard part is keeping to a healthy lifestyle, especially over years and decades," Li said. "Lifestyle is not just individual behavior, but also a reflection of the food, physical and policy environments. Prevention should be a top priority for national health policy, and preventive care should be an indispensable part of the healthcare system." ▼

New studies demonstrate benefits of DASH diet, reduced sodium intake

Two abstracts presented on Sunday show that combining the Dietary Approaches to Stop Hypertension (DASH) diet and reductions in dietary sodium can provide blood pressure effects greater than those seen with major classes of antihypertensive medications, and that daily intervention can reduce daily sodium intake.

Stephen P. Juraschek, MD, PhD, instructor of medicine at Beth Israel Deaconess Medical Center/Harvard Medical School in Boston, presented results of a study suggesting that the blood pressure-reducing effects of diet and dietary sodium reduction are related to baseline blood pressure.


Stephen P. Juraschek, MD, PhD

"When comparing the low-sodium DASH diet to the high-sodium control diet, we saw blood pressure reductions of 20 mm Hg for individuals with baseline systolic pressure of 150 mm Hg and above," Juraschek said. "The combination of these dietary changes had effects comparable or larger than those reported for ACE inhibitors, calcium channel blockers and other antihypertensive medications. Starting with systolic blood pressure in the 120-129 mm Hg range and going up, the trend was striking — the higher the baseline blood pressure, the greater the benefit."

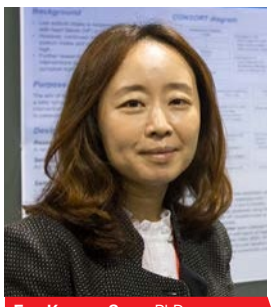
Researchers compared the effects of three different levels of dietary sodium — 50, 100 and 150 mmol/day at 2,100 kcal per day over four weeks for a DASH diet — versus a typical U.S. diet control diet. Low versus high-sodium diet, DASH versus control diet, and low sodium-DASH versus high-sodium control diet were studied across four different strata of systolic blood pressure: less than 120-129 mm Hg, 130-139 mm Hg, 140-149 mm Hg, and 150 mm Hg or higher, in 412 participants. The mean age of the study group was 48 years, mean blood pressure was 135/86, 57 percent were women and 57 percent were black. The study participants were not taking antihypertensive medications.

Both the DASH diet and sodium reduction lowered systolic blood pressure whether baseline blood pressure was low or high. However, the blood pressure lowering effect was greater in groups with higher baseline systolic blood pressure. The combination of low sodium and the DASH diet showed the greatest blood pressure lowering effects: -5.3 mm Hg for baseline systolic blood pressure below 130 mm Hg, -7.5 for baseline systolic blood pressure of 130-139 mm Hg, -9.7 for baseline systolic blood pressure of 140-149 mm Hg, and -20.8 for baseline systolic blood pressure of 150 mm Hg and higher ($p<0.001$ for trend across groups).

The key, Juraschek said, is maintaining dietary changes over the long term. One of the continuing barriers to reducing dietary sodium is the high amount of sodium in our food supply, as well as a general lack of awareness of the sodium content of common foods such as bread, canned/processed foods and fast food.

"For clinicians, raising awareness is an important step, such as encouraging patients to look more closely at nutrition information on labels," Juraschek said. "The salt we knowingly add to our foods from a salt shaker only accounts for a fraction of our total dietary sodium intake. The majority of the sodium we consume is already in foods that we buy."

Further supporting the benefits of reducing dietary sodium intake, Eun Kyeung Song, PhD, of the University of Ulsan in South Korea, presented the results of a study suggesting that patient education about the sodium content of foods combined with daily self-monitoring and regular feedback can reduce sodium intake and have a significant effect on symptom burden in heart failure patients.


Eun Kyeung Song, PhD

"Adherence to a low-sodium diet remains poor," Song said. "Most patients with heart failure are not aware of low-sodium diet guidelines and do not know how to follow a low-sodium diet. Patients also do not understand the link between high-sodium intake and worsening symptoms."

Researchers compared three interventions in a group of 109 patients with NYHA class III/IV heart failure whose baseline daily sodium intake was >3 g — usual care, a telephone monitoring group that received phone calls every two weeks encouraging restricted sodium intake and a self-monitoring group that completed daily checklists of both heart failure symptoms and consumption of high-sodium foods from an individualized list based on a food diary compiled at the beginning of the study.

Song reported that the self-monitoring group showed a significant reduction in daily sodium intake ($p=0.007$) and a significant reduction in physical symptom burden ($p=0.035$). Compared to the usual care group, the telephone-monitoring group did not show any improvement in sodium intake or physical symptom burden.

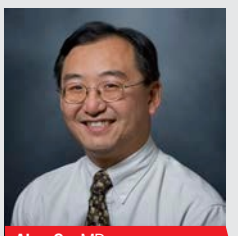
"Healthcare providers need to help heart failure patients understand the associations of sodium intake with symptom burden," Song said. "Clinicians need to encourage patients with heart failure to engage in self-monitoring for daily sodium intake and symptoms." ▼

Research networks reps to update attendees on progress, innovation in speeding translation of science to patient care

Representatives from the AHA's Strategically Focused Research Networks will update attendees on the progress and innovation occurring across the networks in a special session Tuesday morning.

Alan Go, MD, chair of the Prevention SFRN Oversight Advisory Committee, will moderate and provide a brief overview in the "SFRN Information Session," which begins at 9 a.m. in room 212AB, Main Building.

"When I think about the investment from the AHA in the Strategically Focused Research Networks, what most impresses me is the attempt to tackle large problems by bringing together people across basic science, clinical science and population science to accelerate our progress and deliver on the bench-to-bedside promise," Go said. "We talk about bench-to-bedside all the time, but this is a deliberate effort by the AHA to speed up that process."


Alan Go, MD

Translating ideas from basic science to clinical research and eventually to real-world populations is often slow, Go said.

"These networks are really intended to leapfrog a lot of the delays that occur by having people work together in a more coordinated, deliberate fashion," he said. "The goal is to take on very big problems — prevention, cardiovascular disease in women, pediatric obesity and hypertension, heart failure, atrial fibrillation, etc."

In addition to learning how the networks function, attendees will get information about unique training opportunities within the networks.

"That's another big benefit of this — to train the next generation of transdisciplinary cardiovascular researchers," Go said.

For more information, visit **professional.heart.org** and hover over "Research Programs" and then choose "Strategically Focused Research Programs" from the drop-down menu. ▼

2017 Unofficial Satellite Events

Monday, Nov. 13

6:30-8:30 a.m.
Industry-supported Symposium
Getting to the Heart of Type 2 Diabetes Care: Seeking Better Outcomes in Patients with Cardiovascular Disease
Sponsored by Paradigm Medical Communications, LLC
Supported by Novo Nordisk Inc.
Hilton Anaheim, Pacific Ballroom A
Registration: www.paradigmmc.com/649

6:30-9:30 p.m.
Industry-supported Symposium
Applying PCSK9 Inhibitors to Optimize Outcomes in Patients with Dyslipidemia
Sponsored by AcademicCME and the Elsevier Office of Continuing Medical Education
Supported by Amgen Inc.
Hilton Anaheim, California Ballroom D
Registration: academiccme.com/PCSK9

7-9 p.m.
Industry-supported Symposium
Providing Quality Care for Patients with Heart Failure
Sponsored by Vindico Medical Education
Supported by Novartis Pharmaceuticals Corporation
Anaheim Marriott, Platinum Ballrooms 5 & 6
Registration: VindicoCME.com/111317

7-9 p.m.
Social Event
University of Iowa Reception
Sponsored by University of Iowa Hospitals and Clinics
Supported by University of Iowa Hospitals and Clinics
Hyatt Regency Orange County

7-9:30 p.m.
Industry-supported Symposium
From Clinical Trials to Clinical Practice: Applying Cardiovascular Outcome Trial Data to Real World T2DM Management
Sponsored by Creative Educational Concepts
Supported by AstraZeneca
Anaheim Marriott, Marquis Ballroom Northeast
Registration: www.ceconcepts.com/live/278

7-9:30 p.m.
Industry-supported Symposium
The Role of the Cardiologist for Successfully Managing Atrial Fibrillation Patients
Sponsored by AtriCure
Supported by MediaSphere Medical
Anaheim Marriott
Registration: www.innovationsincrm.com/aha

7-10 p.m.
Nonprofit Symposium
Machine Learning Vulnerable Patient Project
Sponsored by SHAPE
Hilton Anaheim
Registration: shapesociety.org

7:30-9 p.m.
Industry-supported Symposium
Preventing Pulmonary Embolism and Stroke: A New Era of Enhanced DOAC Efficacy and Safety
Sponsored by Medscape Education
Supported by Portola Pharmaceuticals, Inc.
Anaheim Marriott, Grand Ballroom E & F
Registration: www.medscape.org/townhall/preventing-pe-and-stroke

Tuesday, Nov. 14

6:30-8:30 a.m.
Industry-supported Symposium
Severe Hypocholesterolemia: Review of Clinical Trials to Improve Outcomes
Sponsored by Potomac Center for Medical Education and Rockpointe
Supported by Amgen
Anaheim Marriott, Platinum Ballroom 3 & 4
Registration: www.cvent.com/d/wtq951

7:30-9 a.m.
Industry-supported Symposium
Renal Denervation and Blood Pressure Control: A Clinical Trial Update
Sponsored by Cardiovascular Research Foundation
Supported by Medtronic
Hilton Anaheim, Pacific A
Registration: rdn-htn.com

7-9 p.m.
Industry-supported Symposium
Cornerstones in Cardioprevention: Rediscovering the Utility of Aspirin
Sponsored by Medscape, LLC
Supported by Bayer Consumer Health
Anaheim Marriott, Platinum Ballroom 5 & 6 (Ground Floor)
Registration: www.medscape.org/townhall/aspirin-benefits

LATE BREAKING continued from page 1

at 5,177 following a pre-planned interim analysis. There were no differences across study groups, no differences across primary endpoints and no differences across secondary endpoints, Weisbord said.

"The current standard of care for preventing contrast-associated acute kidney injury should be intravenous saline and no use of NAC," he concluded.

DACAB

Dual therapy with ticagrelor plus aspirin is more effective than either aspirin or ticagrelor in maintaining patency of saphenous vein grafts in coronary arterial bypass grafting, according to results from the Efficacy and Safety of Dual Acetylsalicylic Acid Plus Ticagrelor or Ticagrelor Alone Antiplatelet Strategy After Coronary Artery Bypass Surgery at 12 Months: Randomized Multicentre Trial.

Dual antiplatelet therapy (DAPT) has been found to reduce MACE in patients with acute coronary syndrome who undergo CABG, but this is the largest trial to date on DAPT and saphenous vein graft patency.

In the trial, 500 patients with acute coronary syndrome scheduled for CABG at six Chinese hospitals were randomized to DPAT, ticagrelor or aspirin. One-year follow up rates were high, between 92.2 percent and 94.9 percent. The primary outcomes were saphenous vein graft patency and non-occlusion. Secondary outcomes included MACE, recurrence of angina, atrial fibrillation and bleeding.

"Combination treatment gives better outcomes at one year than either agent alone," said Qiang Zhao, MD, of Jian Tong University School of Medicine in Shanghai, China. "Aspirin alone had the worst outcomes in both patency and MACE as well as cardiovascular mortality, myocardial infarction and stroke."

As expected, there were more bleeding events in the DAPT arm than the single-agent arms, but bleeds were minimal in all three arms, Zhao added.

BRUISE CONTROL-2

Continuous or interrupted use of direct oral anticoagulation (DOAC) are both effective strategies for limiting device pocket hematoma following pacemaker or defibrillator implantation, according to results from A Randomized Controlled Trial of Continued versus Interrupted Novel Oral Anti-Coagulant at the Time of Device Surgery (BRUISE CONTROL-2).

Surgeons might prefer one strategy over the other depending on the situation, said co-principal investigator David H. Birnie, MD, director of the arrhythmia service at the University of Ottawa Heart Institute in Ontario.

An earlier trial, BRUISE CONTROL, found that uninterrupted anticoagulation with warfarin showed 80 percent fewer pocket hematomas compared to interrupted anticoagulation, Birnie said.

"With the new generation of DOACs, we had to do a new trial," he said. "DOACs are currently used in the majority of patients with atrial fibrillation."

Major clinical trials with DOACs have found that brief interruptions for procedures or surgery are associated with a three-fold increase in stroke and systemic embolism, Birnie said. But device pocket hematomas can require a prolonged halt to anticoagulation, which increases the risk of thromboembolism and is associated with increased risk of device pocket infection.

BRUISE CONTROL-2 was designed for 846 patients, but was stopped early after a second pre-specified interim analysis. A total of 662 patients were enrolled between April 2013 and June 2017 — 328 in the continuous DOAC arm and 334 in the interrupted DOAC arm.

The primary or secondary outcomes between the two arms were similar, Birnie reported. He added that scenarios in which interruption of anticoagulation might lead to unacceptable harm or patients with high stroke risk might favor continuous DOAC.

ABRIDGE-J

The Ablation Preoperative Dabigatran in use Envision in Japan (ABRIDGE-J) trial compared the efficacy and safety of minimally interrupted dabigatran to uninterrupted warfarin for catheter ablation for nonvalvular atrial fibrillation. Patients in the dabigatran arm had anticoagulation interrupted for one or two doses to allow for ablation.

There were no thromboembolic events in the dabigatran group and one event in the warfarin group in the first 90 days following ablation, reported principle investigator Ahihiko Nagami, MD, PhD, of the University of Tsukuba in Japan. Dabigatran also showed a significant reduction in the risk for major bleeding compared to warfarin.

"Anticoagulation with minimally interrupted dabigatran was associated with fewer bleeding complications than uninterrupted warfarin with no increase in thromboembolic events," Nagami said. ▼

PRESIDENT continued from page 1

quality of care we are providing, as opposed to the quantity of work we are doing, more and more of our success will be defined by diseases we prevent, rather than by diseases we treat."

Warner's first step toward impacting public health outside of his hospital came when he joined the AHA's Dallas board.

His timing was good. A local push to make the city smoke-free had stalled. There was a theory that a prominent clinician with a personal story to tell could help make a difference. Warner had a grandfather who'd been a longtime smoker before dying of heart disease. He and others with compelling personal tales swayed the nation's ninth-largest city to spare hundreds and thousands of people the dangers of second-hand smoke.

"Being part of this effort helped me realize that the voices of doctors, nurses and healthcare leaders needed to be heard within the community," he said. "Speaking to the city council took only 30 minutes, but it helped effect a major change in a major city. I vowed to do more of this, to broaden my involvement in my community and to make a difference on a larger scale."

Next, he was part of an AHA team that connected every link in the chain of survival for people who suffer STEMI. Coordination included standardizing EMS equipment and protocols. Another component was "Don't Die of Doubt," a campaign urging people to call 911 and to seek help for chest pain more quickly.

"All told, this work produced exactly what we hoped – patients presenting earlier in their (heart attacks), then entering a system more prepared to care for them quickly," Warner said. "It also reinforced the AHA's unique ability to move past barriers and convene critical partners to transform the health of communities."

Building the hospital was the next evolution. He said it "truly transformed me. It also expanded my definition of a healthcare team."

A key part of his master plan was listening to everyone who'd be part of that team: patients, their families and everyone who works at the hospital, from doctors and nurses to chaplains and valet parkers.

The result was an award-winning hospital that's filled with patients.

"We created more than just a building," he said. "We actually transformed the care we deliver by truly putting patients first."

Warner brought that approach to the CEO office. While he struggled with the decision to give up working in the catheter lab for the board room, he did so "to impact more patients more of the time."

His call to action in Sunday's address was for others to seek opportunities to try making an impact in their community or country.

"For decades, we have been focused on improving the cardiovascular health of populations around the world," Warner said. "And with cardiovascular disease being the No. 1 killer of both men and women worldwide, even small improvements in cardiovascular health will save the lives of many." ▼

PARTNERSHIPS continued from page 1

the Opening Session of Scientific Sessions. "The AHA and XPRIZE Foundation will reimagine and bring to life health and well-being for people everywhere, not just for privileged populations."

Brown said the AHA and XPRIZE will invite creative people from the United States and around the globe to design a roadmap, including prizes that can inspire courageous thinking and breakthrough solutions.

"Bringing together the brightest minds in science and industry, innovators and the voices of the underserved, we will solve seemingly unsolvable problems by redefining what the future can look like for people everywhere," Brown said.

Brown also announced the launch of the AHA Center for Accelerated Drug Discovery, part of a new strategic business relationship with the Lawrence Livermore National Laboratory. The goal is to combine world-class technology and high-impact biology to develop a comprehensive reference atlas of cell-protein targets to accelerate drug discovery.

"It takes 10 years, on average, for a new medicine to be commercialized in the marketplace and an average cost of $2.6 billion," Brown said. "Imagine if we could reduce the time to market by half."

Leveraging one of the world's most powerful computer facilities at LLNL, the goal is to create a simulated environment that precisely predicts how drugs bind to their target proteins and to generate a robust drug discovery pipeline. Just as cloud technology is empowering researchers to find new answers, Brown said machine-learning will allow the biomedical community to validate targeted drug hypotheses that have higher probabilities of success while reducing time to market.

"The AHA's leading science combined with Lawrence Livermore National Laboratory's leading-edge computational engines will speed progress and give rise to high-value treatments, making therapeutic innovations more readily available and more affordable," Brown said. ▼

REPATHA® (evolocumab)

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Please see package insert for full Prescribing Information

1. INDICATIONS AND USAGE

1.1 Primary Hyperlipidemia

REPATHA is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low density lipoprotein cholesterol (LDL-C).

1.2 Homozygous Familial Hypercholesterolemia

REPATHA is indicated as an adjunct to diet and other LDL-lowering therapies (e.g., statins, ezetimibe, LDL apheresis) for the treatment of patients with homozygous familial hypercholesterolemia (HoFH) who require additional lowering of LDL-C.

1.3 Limitations of Use

The effect of REPATHA on cardiovascular morbidity and mortality has not been determined.

4. CONTRAINDICATIONS

REPATHA is contraindicated in patients with a history of a serious hypersensitivity reaction to REPATHA [*see Warnings and Precautions (5.1)*].

5. WARNINGS AND PRECAUTIONS

5.1 Allergic Reactions

Hypersensitivity reactions (e.g., rash, urticaria) have been reported in patients treated with REPATHA, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic reactions occur, discontinue treatment with REPATHA, treat according to the standard of care, and monitor until signs and symptoms resolve.

6. ADVERSE REACTIONS

The following adverse reactions are also discussed in other sections of the label:

• Allergic Reactions [*see Warnings and Precautions (5.1)*]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Adverse Reactions in Patients with Primary Hyperlipidemia and in Patients with Heterozygous Familial Hypercholesterolemia

REPATHA is not indicated for use in patients without familial hypercholesterolemia or atherosclerotic CVD [*see Indications and Usage (1.1)*].

The data described below reflect exposure to REPATHA in 8 placebo-controlled trials that included 2651 patients treated with REPATHA, including 557 exposed for 6 months and 515 exposed for 1 year (median treatment duration of 12 weeks). The mean age of the population was 57 years, 49% of the population were women, 85% White, 6% Black, 8% Asians, and 2% other races.

Adverse Reactions in a 52-Week Controlled Trial

In a 52-week, double-blind, randomized, placebo-controlled trial (Study 2), 599 patients received 420 mg of REPATHA subcutaneously once monthly [*see Clinical Studies (14.1)*]. The mean age was 56 years (range: 22 to 75 years), 23% were older than 65 years, 52% women, 80% White, 8% Black, 6% Asian, and 6% Hispanic. Adverse reactions reported in at least 3% of REPATHA-treated patients, and more frequently than in placebo-treated patients in Study 2, are shown in Table 1. Adverse reactions led to discontinuation of treatment in 2.2% of REPATHA-treated patients and 1% of placebo-treated patients. The most common adverse reaction that led to REPATHA treatment discontinuation and occurred at a rate greater than placebo was myalgia (0.3% versus 0% for REPATHA and placebo, respectively).

Table 1. Adverse Reactions Occurring in Greater than or Equal to 3% of REPATHA-treated Patients and More Frequently than with Placebo in Study 2

	Placebo (N=302) %	REPATHA (N=599) %
Nasopharyngitis	9.6	10.5
Upper respiratory tract infection	6.3	9.3
Influenza	6.3	7.5
Back pain	5.6	6.2
Injection site reactions†	5.0	5.7
Cough	3.6	4.5
Urinary tract infection	3.6	4.5
Sinusitis	3.0	4.2
Headache	3.6	4.0
Myalgia	3.0	4.0
Dizziness	2.6	3.7
Musculoskeletal pain	3.0	3.3
Hypertension	2.3	3.2
Diarrhea	2.6	3.0
Gastroenteritis	2.0	3.0

†includes erythema, pain, bruising

Adverse Reactions in Seven Pooled 12-Week Controlled Trials

In seven pooled 12-week, double-blind, randomized, placebo-controlled trials, 993 patients received 140 mg of REPATHA subcutaneously every 2 weeks and 1059 patients received 420 mg of REPATHA subcutaneously monthly. The mean age was 57 years (range: 18 to 80 years), 29% were older than 65 years, 49% women, 85% White, 5% Black, 9% Asian, and 5% Hispanic. Adverse reactions reported in at least 1% of REPATHA-treated patients, and more frequently than in placebo-treated patients, are shown in Table 2.

Table 2. Adverse Reactions Occurring in Greater than 1% of REPATHA-treated Patients and More Frequently than with Placebo in Pooled 12-Week Studies

	Placebo (N=1224) %	REPATHA† (N=2052) %
Nasopharyngitis	3.9	4.0
Back pain	2.2	2.3
Upper respiratory tract infection	2.0	2.1
Arthralgia	1.6	1.8
Nausea	1.2	1.8
Fatigue	1.0	1.6
Muscle spasms	1.2	1.3
Urinary tract infection	1.2	1.3
Cough	0.7	1.2
Influenza	1.1	1.2
Contusion	0.5	1.0

†140 mg every 2 weeks and 420 mg once monthly combined

Adverse Reactions in Eight Pooled Controlled Trials (Seven 12-Week Trials and One 52-Week Trial)

The adverse reactions described below are from a pool of the 52-week trial (Study 2) and seven 12-week trials. The mean and median exposure durations of REPATHA in this pool of eight trials were 20 weeks and 12 weeks, respectively.

Local Injection Site Reactions

Injection site reactions occurred in 3.2% and 3.0% of REPATHA-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising. The proportions of patients who discontinued treatment due to local injection site reactions in REPATHA-treated patients and placebo-treated patients were 0.1% and 0%, respectively.

Allergic Reactions

Allergic reactions occurred in 5.1% and 4.7% of REPATHA-treated and placebo-treated patients, respectively. The most common allergic reactions were rash (1.0% versus 0.5% for REPATHA and placebo, respectively), eczema (0.4% versus 0.2%), erythema (0.4% versus 0.2%), and urticaria (0.4% versus 0.1%).

Neurocognitive Events

In placebo-controlled trials, neurocognitive events were reported in less than or equal to 0.2% in REPATHA-treated and placebo-treated patients.

Low LDL-C Levels

In a pool of placebo- and active-controlled trials, as well as open-label extension studies that followed them, a total of 1988 patients treated with REPATHA had at least one LDL-C value < 25 mg/dL. Changes to background lipid-altering therapy were not made in response to low LDL-C values, and REPATHA dosing was not modified or interrupted on this basis. Although adverse consequences of very low LDL-C were not identified in these trials, the long-term effects of very low levels of LDL-C induced by REPATHA are unknown.

Musculoskeletal Events

Musculoskeletal adverse reactions were reported in 14.3% of REPATHA-treated patients and 12.8% of placebo-treated patients. The most common adverse reactions that occurred at a rate greater than placebo were back pain (3.2% versus 2.9% for REPATHA and placebo, respectively), arthralgia (2.3% versus 2.2%), and myalgia (2.0% versus 1.8%).

Adverse Reactions in Patients with Homozygous Familial Hypercholesterolemia

In a 12-week, double-blind, randomized, placebo-controlled trial of 49 patients with HoFH (Study 4), 33 patients received 420 mg of REPATHA subcutaneously once monthly [*see Clinical Studies (14.3)*]. The mean age was 31 years (range: 13 to 57 years), 49% were women, 90% White, 4% Asian, and 6% other. The adverse reactions that occurred in at least two (6.1%) REPATHA-treated patients, and more frequently than in placebo-treated patients, included:

• Upper respiratory tract infection (9.1% versus 6.3%)
• Influenza (9.1% versus 0%)
• Gastroenteritis (6.1% versus 0%)
• Nasopharyngitis (6.1% versus 0%)

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The immunogenicity of REPATHA has been evaluated using an electrochemiluminescent bridging screening immunoassay for the detection of binding anti-drug antibodies. For patients whose sera tested positive in the screening immunoassay, an in vitro biological assay was performed to detect neutralizing antibodies.

In a pool of placebo- and active-controlled clinical trials, 0.1% of patients treated with at least one dose of REPATHA tested positive for binding antibody development. Patients whose sera tested positive for binding antibodies were further evaluated for neutralizing antibodies; none of the patients tested positive for neutralizing antibodies.

There was no evidence that the presence of anti-drug binding antibodies impacted the pharmacokinetic profile, clinical response, or safety of REPATHA, but the long-term consequences of continuing REPATHA treatment in the presence of anti-drug binding antibodies are unknown.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to REPATHA with the incidence of antibodies to other products may be misleading.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data available on use of REPATHA in pregnant women to inform a drug-associated risk. In animal reproduction studies, there were no effects on pregnancy or neonatal/infant development when monkeys were subcutaneously administered evolocumab from organogenesis through parturition at dose exposures up to 12 times the exposure at the maximum recommended human dose of 420 mg every month. In a similar study with another drug in the PCSK9 inhibitor antibody class, humoral immune suppression was observed in infant monkeys exposed to that drug in utero at all doses. The exposures where immune suppression occurred in infant monkeys were greater than those expected clinically. No assessment for immune suppression was conducted with evolocumab in infant monkeys. Measurable evolocumab serum concentrations were observed in the infant monkeys at birth at comparable levels to maternal serum, indicating that evolocumab, like other IgG antibodies, crosses the placental barrier. FDA's experience with monoclonal antibodies in humans indicates that they are unlikely to cross the placenta in the first trimester; however, they are likely to cross the placenta in increasing amounts in the second and third trimester. Consider the benefits and risks of REPATHA and possible risks to the fetus before prescribing REPATHA to pregnant women.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

In cynomolgus monkeys, no effects on embryo-fetal or postnatal development (up to 6 months of age) were observed when evolocumab was dosed during organogenesis to parturition at 50 mg/kg once every 2 weeks by the subcutaneous route at exposures 30- and 12-fold the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC. No test of humoral immunity in infant monkeys was conducted with evolocumab.

8.2 Lactation

Risk Summary

There is no information regarding the presence of evolocumab in human milk, the effects on the breastfed infant, or the effects on milk production. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for REPATHA and any potential adverse effects on the breastfed infant from REPATHA or from the underlying maternal condition. Human IgG is present in human milk, but published data suggest that breast milk antibodies do not enter the neonatal and infant circulation in substantial amounts.

8.4 Pediatric Use

The safety and effectiveness of REPATHA in combination with diet and other LDL-C-lowering therapies in adolescents with HoFH who require additional lowering of LDL-C were established based on data from a 12-week, placebo-controlled trial that included 10 adolescents (ages 13 to 17 years old) with HoFH [*see Clinical Studies (14.3)*]. In this trial, 7 adolescents received REPATHA 420 mg subcutaneously once monthly and 3 adolescents received placebo. The effect of REPATHA on LDL-C was generally similar to that observed among adult patients with HoFH. Including experience from open-label, uncontrolled studies, a total of 14 adolescents with HoFH have been treated with REPATHA, with a median exposure duration of 9 months. The safety profile of REPATHA in these adolescents was similar to that described for adult patients with HoFH.

The safety and effectiveness of REPATHA have not been established in pediatric patients with HoFH who are younger than 13 years old.

The safety and effectiveness of REPATHA have not been established in pediatric patients with primary hyperlipidemia or HeFH.

8.5 Geriatric Use

In controlled studies, 1420 patients treated with REPATHA were ≥ 65 years old and 171 were ≥ 75 years old. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment

No dose adjustment is needed in patients with mild to moderate renal impairment. No data are available in patients with severe renal impairment [*see Clinical Pharmacology (12.3)*].

8.7 Hepatic Impairment

No dose adjustment is needed in patients with mild to moderate hepatic impairment (Child-Pugh A or B). No data are available in patients with severe hepatic impairment [*see Clinical Pharmacology (12.3)*].

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of evolocumab was evaluated in a lifetime study conducted in the hamster at dose levels of 10, 30, and 100 mg/kg administered every 2 weeks. There were no evolocumab-related tumors at the highest dose at systemic exposures up to 38- and 15-fold the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC. The mutagenic potential of evolocumab has not been evaluated; however, monoclonal antibodies are not expected to alter DNA or chromosomes.

There were no adverse effects on fertility (including estrous cycling, sperm analysis, mating performance, and embryonic development) at the highest dose in a fertility and early embryonic developmental toxicology study in hamsters when evolocumab was subcutaneously administered at 10, 30, and 100 mg/kg every 2 weeks. The highest dose tested corresponds to systemic exposures up to 30- and 12-fold the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC. In addition, there were no adverse evolocumab-related effects on surrogate markers of fertility (reproductive organ histopathology, menstrual cycling, or sperm parameters) in a 6-month chronic toxicology study in sexually mature monkeys subcutaneously administered evolocumab at 3, 30, and 300 mg/kg once weekly. The highest dose tested corresponds to 744- and 300-fold the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC.

13.2 Animal Toxicology and/or Pharmacology

During a 3-month toxicology study of 10 and 100 mg/kg once every 2 weeks evolocumab in combination with 5 mg/kg once daily rosuvastatin in adult monkeys, there were no effects of evolocumab on the humoral immune response to keyhole limpet hemocyanin (KLH) after 1 to 2 months exposure. The highest dose tested corresponds to exposures 54- and 21-fold higher than the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC. Similarly, there were no effects of evolocumab on the humoral immune response to KLH (after 3 to 4 months exposure) in a 6-month study in cynomolgus monkeys at dose levels up to 300 mg/kg once weekly evolocumab corresponding to exposures 744- and 300-fold greater than the recommended human doses of 140 mg every 2 weeks and 420 mg once monthly, respectively, based on plasma AUC.

This Brief Summary is based on the REPATHA® Prescribing Information v3, 07/16

AMGEN®

REPATHA® (evolocumab)
Manufactured by: Amgen Inc.
One Amgen Center Drive
Thousand Oaks, California 91320-1799
U.S. License Number 1080
Patent: http://pat.amgen.com/repatha/

PAID ADVERTISEMENT

Are you maximizing your conference experience?

Take the next step at **booth 321**, or one of these talks:

Repatha®: Take the Next Step*
with William Cromwell, MD, FAHA, FNLA
on Monday, November 13 from
11:00 AM – 11:30 AM at **booth 321**

The Repatha® Patient Journey*
with Harold Bays, MD, FTOS, FACC, FACE, FNLA
on Monday, November 13 from
1:15 PM – 2:00 PM
Product Theater at **booth 1473**

Repatha® is the #1 prescribed PCSK9 inhibitor[1,†]

For adults with clinical ASCVD
on **maximally tolerated** statin therapy as an adjunct to diet[2]

HELP YOUR PATIENTS
ESCAPE HIGH LDL-C

ADD REPATHA® AND MAXIMIZE LDL-C LOWERING

Repatha® every 2 weeks + statin delivered
UP TO **77%** **ADDITIONAL LDL-C REDUCTION**
compared to placebo + statin[2,3]

Results from a 12-week study in patients with ASCVD. At week 12, LDL-C was reduced 63% to 77% (mean 71%) with Repatha® 140 mg every 2 weeks + statin more than with placebo + statin. Maximum-dose statins used were atorvastatin 80 mg, rosuvastatin 40 mg, and simvastatin 40 mg.[2,3]

*This event is not part of the official Scientific Sessions 2017 as planned by the AHA Committee on Scientific Sessions Program.

†Based on IMS (TRx) data for the period of September 11, 2015 to June 2, 2017.

ASCVD = atherosclerotic cardiovascular disease;
PCSK9 = proprotein convertase subtilisin/kexin type 9.

Indication

- Repatha® is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with clinical atherosclerotic cardiovascular disease (CVD), who require additional lowering of low density lipoprotein cholesterol (LDL-C).
- The effect of Repatha® on cardiovascular morbidity and mortality has been published. Inclusion of the results in the approved labeling is under evaluation with the FDA.

Important Safety Information

- **Contraindication:** Repatha® is contraindicated in patients with a history of a serious hypersensitivity reaction to Repatha®.
- **Allergic reactions:** Hypersensitivity reactions (e.g. rash, urticaria) have been reported in patients treated with Repatha®, including some that led to discontinuation of therapy. If signs or symptoms of serious allergic reactions occur, discontinue treatment with Repatha®, treat according to the standard of care, and monitor until signs and symptoms resolve.
- **Adverse reactions:** The most common adverse reactions (> 5% of Repatha®-treated patients and more common than placebo) were: nasopharyngitis, upper respiratory tract infection, influenza, back pain, and injection site reactions.

  In a 52-week trial, adverse reactions led to discontinuation of treatment in 2.2% of Repatha®-treated patients and 1% of placebo-treated patients. The most common adverse reaction that led to Repatha® treatment discontinuation and occurred at a rate greater than placebo was myalgia (0.3% versus 0% for Repatha® and placebo, respectively).
- **Adverse reactions from a pool of the 52-week trial and seven 12-week trials:** Local injection site reactions occurred in 3.2% and 3.0% of Repatha®-treated and placebo-treated patients, respectively. The most common injection site reactions were erythema, pain, and bruising. The proportions of patients who discontinued treatment due to local injection site reactions in Repatha®-treated patients and placebo-treated patients were 0.1% and 0%, respectively.

  Allergic reactions occurred in 5.1% and 4.7% of Repatha®-treated and placebo-treated patients, respectively. The most common allergic reactions were rash (1.0% versus 0.5% for Repatha® and placebo, respectively), eczema (0.4% versus 0.2%), erythema (0.4% versus 0.2%), and urticaria (0.4% versus 0.1%).

  Neurocognitive events were reported in less than or equal to 0.2% in Repatha®-treated and placebo-treated patients.

  In a pool of placebo- and active-controlled trials, as well as open-label extension studies that followed them, a total of 1,988 patients treated with Repatha® had at least one LDL-C value < 25 mg/dL. Changes to background lipid-altering therapy were not made in response to low LDL-C values, and Repatha® dosing was not modified or interrupted on this basis. Although adverse consequences of very low LDL-C were not identified in these trials, the long-term effects of very low levels of LDL-C induced by Repatha® are unknown.

  Musculoskeletal adverse reactions were reported in 14.3% of Repatha®-treated patients and 12.8% of placebo-treated patients. The most common adverse reactions that occurred at a rate greater than placebo were back pain (3.2% versus 2.9% for Repatha® and placebo, respectively), arthralgia (2.3% versus 2.2%), and myalgia (2.0% versus 1.8%).
- **Immunogenicity:** Repatha® is a human monoclonal antibody. As with all therapeutic proteins, there is a potential for immunogenicity with Repatha®.

Please see Brief Summary of full Prescribing Information on adjacent page.

References: 1. Data on file, Amgen; 2017. **2.** Repatha® (evolocumab) Prescribing Information, Amgen. **3.** Data on file, Amgen; 2015.

AMGEN Cardiovascular

Repatha® (evolocumab) injection 140 mg/mL

Visit **booth 321**
or www.RepathaHCP.com for more information