American Heart Association
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SCIENTIFIC SESSIONS 2017

DailyNews

TUESDAY, NOVEMBER 14
November 11-15 | Anaheim, California

AHA president doing well after minor heart attack

American Heart Association President John J. Warner, MD, FAHA, was away from the AHA's Scientific Sessions with his family Monday after having a minor heart attack during the organization's flagship scientific conference.

Warner, a practicing cardiologist and the CEO of UT Southwestern University Hospitals in Dallas, had the episode Monday morning. He was taken to a local hospital, where doctors inserted a stent to open a clogged artery.

He was recovering and visiting with his wife, son and daughter, all of whom attended Scientific Sessions in part to see him deliver his Presidential Address on Sunday afternoon. In that speech, the 52-year-old Warner talked about the effects of heart disease on his family. He mentioned how both his father and his father's father had heart bypass surgery in their 60s. He also lost his maternal grandfather and a great grandfather to heart disease.

He closed his speech with these lines:

"Earlier in my talk, I told you there were no old men in my family. I know this is also true in far too many other

PRESIDENT continued on page 15

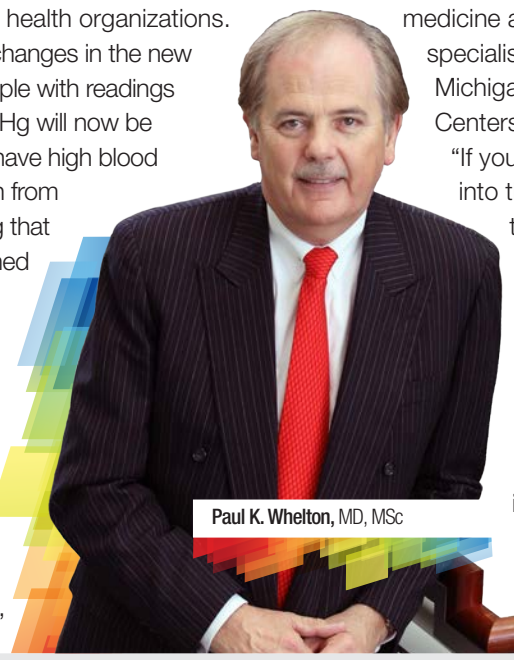
John J. Warner, MD, FAHA

New hypertension guidelines focus on prevention, early treatment

Nearly half of American adults will be diagnosed with high blood pressure under new definitions outlined in the 2017 Guideline for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults, released Monday at Scientific Sessions by the AHA, the American College of Cardiology and nine other health organizations.

Among the changes in the new guidelines, people with readings of 130/80 mm Hg will now be considered to have high blood pressure, down from 140/90 mm Hg that previously defined the condition.

The change means approximately 46 percent of U.S. adults will now be classified as having high blood pressure, compared to 32 percent under the previous definition. Blood pressure less than 120/80 mm Hg still will be considered normal, but levels above that, up to 129, will be called "elevated."



Paul K. Whelton, MD, MSc

"Yes, we will label more people hypertensive and give more medication, but we will save lives and money by not having more strokes, cardiovascular events and kidney failure," said Kenneth Jamerson, MD, professor of internal medicine and a hypertension specialist at the University of Michigan Hospitals and Health Centers in Ann Arbor.

"If you are going to put money into the healthcare system, it's to everyone's advantage if we treat and prevent on this side of it, in early treatment," added Jamerson, one of 21 experts on the guideline writing committee.

Still, the guidelines — in the works for about three years and based on hundreds of studies and clinical trials — don't suggest a massive increase in the number of people who will need to take hypertension medication. Of the estimated 14 percent increase in adults who will be classified with high blood pressure under the new guidelines, only about one in five will need medication, according to Paul K. Whelton, MD, MSc, who chaired the guideline writing committee.

Instead, the guidelines emphasize physicians should focus on a whole framework of healthier lifestyle changes for patients.

"We need to send the message that, yes, you are at increased risk and these are the things you should be doing," said Whelton, clinical professor and the Show Chwan Health System Endowed Chair in Global Public Health at Tulane University School of Public Health and Tropical Medicine in New Orleans. "I'm not saying it's easy to change our patients' lifestyles, but that should be first and foremost."

The recommendations for a heart-healthy diet include reducing salt and incorporating potassium-rich foods, such as bananas, potatoes, avocados and dark leafy vegetables. The guidelines also offer specific suggestions for weight loss,

HYPERTENSION GUIDELINES continued on page 5

Guidelines bring new implications for providers, patients

New hypertension guidelines released Monday at Scientific Sessions implicate how blood pressure is classified and measured and how hypertension is diagnosed and managed.

According to the new guidelines:

- Normal blood pressure is less than 120 mm Hg systolic and less than 80 diastolic.
- Elevated blood pressure is 120-129 systolic and less than 80 diastolic.
- A new category — Stage 1 hypertension — is 130-139 mm Hg systolic or 80-89 mmHg diastolic. Under prior guidelines, these individuals were classified as having prehypertension. Adults 65 and older fall under this same definition.

"The reason to call it Stage 1 hypertension is clear evidence of substantial elevation in risk compared to normal pressure, just about a two-fold increase in the risk of heart attack, for example," said Paul K. Whelton, MD, MSc, who chaired the 21-member multidisciplinary guideline writing committee.

The new definition will increase the prevalence of hypertension by about 14 percent in the United States and significantly more in some patient subgroups based on age, gender and ethnicity. But the number of patients needing pharmacologic therapy will rise a modest 1.9 percent, or about 4.2 million adults, 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.

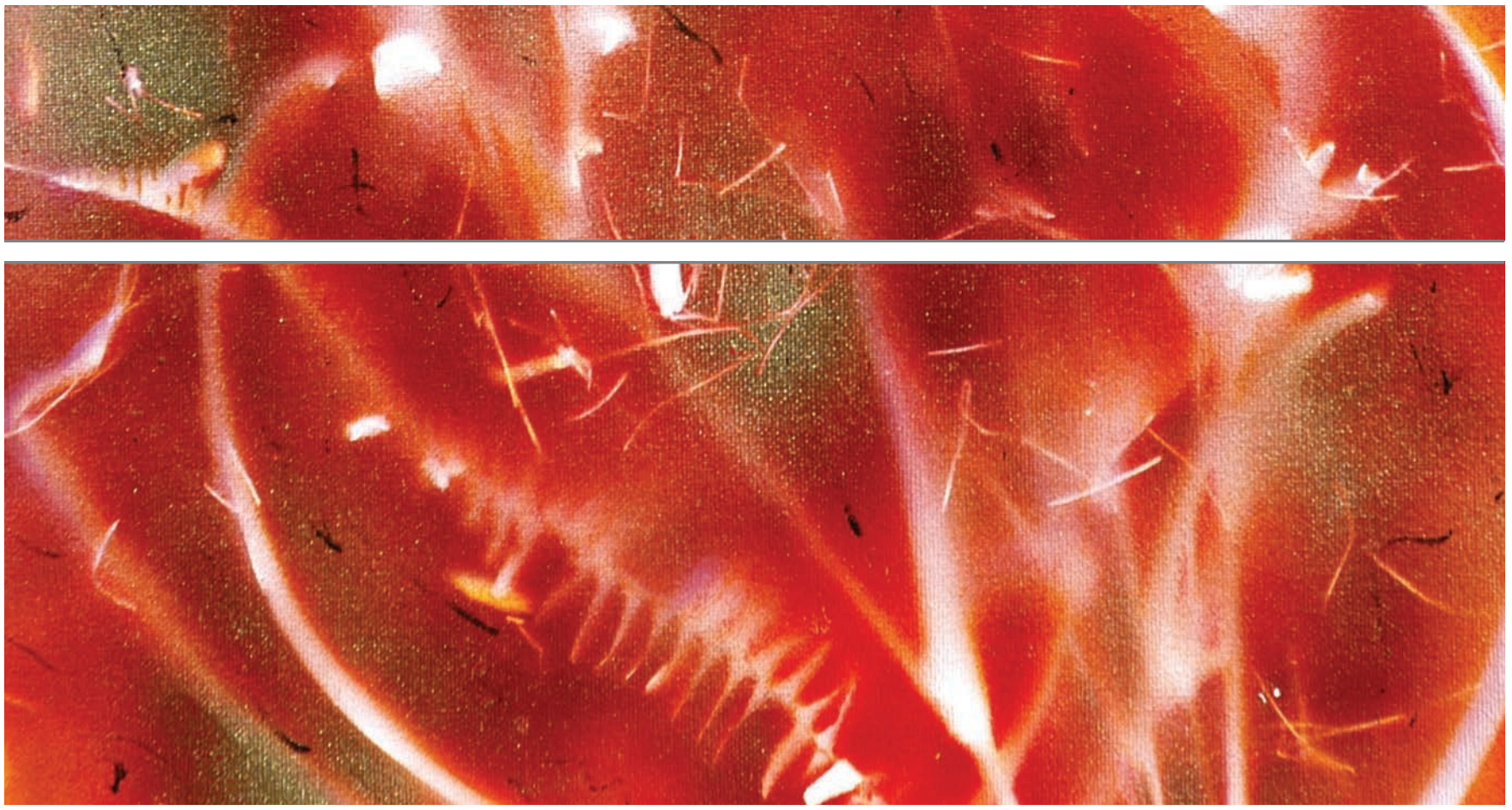
"Although we identify more people to be treated, we are more focused on who should get treated with drug therapy," Whelton said. "It's really those people with stage 1 hypertension who are at high risk who should be getting pharmacologic treatment as well as non-pharmacologic interventions. That's about 30 percent of individuals with systolic blood pressure between 130 mm Hg and 139 mm Hg."

Most people with stage 1 hypertension and elevated blood pressure should make these nonpharmacologic lifestyle changes: no tobacco use; weight loss; a DASH-type diet rich in fruits, vegetables, whole grains and low-fat dairy products; reduced sodium intake; increased potassium intake, preferably through dietary changes such as adding bananas, dark green leafy vegetables and other foods high in potassium; increased physical activity; and moderate or no alcohol consumption.

The lifestyle changes can reduce systolic blood pressure 4 mm Hg to 11 mm Hg, according to the guidelines. Diet and exercise have the greatest impact on blood pressure, Whelton said.

People with stage 1 hypertension should also be assessed for cardiovascular risk, according to the guidelines. Those at high risk should receive pharmacotherapy as well as nonpharmacologic interventions. Most can be treated with a thiazide diuretic, ACE inhibitor, angiotensin receptor blocker or calcium channel blocker. The guidelines note that once-daily medication may improve adherence compared to multiple medications each day.

IMPLICATIONS continued on page 5



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HIGHLIGHTS FROM THE PROGRAM CHAIR

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

Eric D. Peterson, MD, MPH, FAHA

After three days of walking around Scientific Sessions, your feet could probably use a break. So, take advantage of "Wear Sneakers Day" to enjoy a little extra comfort while showing your support of regular exercise.

Today's scientific program includes two Late Breaking Science sessions, beginning with "New Insights into the Risks, Benefits and Costs of Antithrombotic Therapy" at 10:45 a.m. The session will feature the latest results from the recent COMPASS, RE-DUAL PCI, POISE-2 PCI, GEMINI-ACS-1 and PRAGUE-18 trials. During the day's second Late Breaking session, "Evaluating Quality Improvement and Patient Centered Care Interventions," which begins at 3:45 p.m., investigators will present results from the SWEDEHEART, STIC2IT, ACS QUIK, ICARE-ACS, DECIDE-LVAD and STEMI ACCELERATOR-2 trials.

There are also two Frontiers in Science summits today. Beginning at 9 a.m. in rooms 154-158, ACC North, the Stem Cells Summit includes a full day of sessions featuring rapid-fire presentations by leading stem cell researchers. The Vascular Disease Summit, which begins at 3:45 p.m. in room 210D, Main Building, will feature presentations from investigators engaged in cutting-edge research and PVD "frontier science."

Recognizing the growing emphasis on individualized care, today's program also includes a special Precision Medicine Summit with sessions focusing on big data initiatives, "omics" research and technologies, and improving diagnostic precision in cardiomyopathies and heart failure. The Precision Medicine Summit begins at 9 a.m. in Hall D.

For information on AHA's Institute for Precision Cardiovascular Medicine, be sure to stop by the Recharge Institute Lounge for demos of the AHA Precision Medicine Platform and My Research Legacy, as well as opportunities for one-on-one discussions with precision medicine experts, including Institute staff and leadership.

Today's program also includes a special global health symposium celebrating the 50th anniversary of Fogarty International Center at National Institutes of Health. With three consecutive sessions beginning at 2 p.m. in Ballroom A, 3rd Level, Main Building, the symposium will showcase the broad reach of Fogarty-supported research and training.

And don't forget, today is your last chance to visit the exhibits in the Science and Technology Hall to learn about the latest drugs, devices, tools and technologies related to cardiac care. Check the Final Program and the Mobile Meeting Guide for the most up-to-date information on today's educational programming, networking opportunities and special events. ▼

Late-Breaking Science V: New Insights into the Risks, Benefits and Costs of Antithrombotic Therapy

LBS.05 | 10:45 a.m.-Noon Tuesday | Main Event I, Hall D, Main Building

Trial	Description
COMPASS — Costs Impact Rivaroxaban Plus Aspirin Versus Aspirin in the COMPASS Trial	COMPASS evaluated whether rivaroxaban 5 mg twice-daily, or rivaroxaban 2.5 mg twice-daily in combination with aspirin 100 mg daily, is superior to aspirin 100 mg daily for prevention of myocardial infarction, stroke or CV death in patients with stable CAD or peripheral vascular disease.
RE-DUAL PCI — Subgroup Analysis from the RE-DUAL PCI Trial: Dual Antithrombotic Therapy with Dabigatran in Patients with Atrial Fibrillation Undergoing Percutaneous Coronary Intervention	The RE-DUAL PCI trial evaluated the safety and efficacy of a dual antithrombotic therapy regimen using dabigatran and a P2Y12 platelet antagonist, and compared this with a "triple therapy" with warfarin, aspirin and a P2Y12 platelet antagonist.
POISE-2 PCI Substudy — Aspirin in Patients with Previous Percutaneous Coronary Intervention (PCI) Undergoing Noncardiac Surgery	This substudy of POISE-2 was designed to evaluate the effect of aspirin in patients with previous PCI undergoing noncardiac surgery.
GEMINI-ACS-1 — P2Y12 Inhibitor Switching in Response to Routine Notification of CYP2C19 Clopidogrel Metabolizer Status Following Acute Coronary Syndromes	This trial had an embedded feature of mandatory reporting of CYP2C19 metabolizer status for patients treated with clopidogrel or ticagrelor, with tracking of how these results influenced subsequent P2Y12 inhibitor choices.
PRAGUE-18 — One-Year Outcomes of Patients with Acute Myocardial Infarction Treated with Primary Angioplasty and Randomized to Prasugrel versus Ticagrelor	This long-term follow-up focused on a comparison of prasugrel and ticagrelor, including the safety of post-discharge, economically motivated switch from the study drugs to clopidogrel.

Late-Breaking Science VI: Evaluating Quality Improvement and Patient Centered Care Interventions

LBS.06 | 3:45-5:15 p.m. Tuesday | Ballroom CD, 3rd Level, Main Building

Trial	Description
SWEDEHEART — Improved Outcomes in Patients with Non-ST-Elevation Myocardial Infarction During 20 years are Related to Implementation of Evidence-Based Treatments – Results from the SWEDEHEART Registry 1995-2014	This study evaluated long-term data assessing the changes in outcomes and their relation to implementation of new treatments in patients with non-ST-elevation myocardial infarction (NSTEMI).
STIC2IT — Results of the Study of a Tele-Pharmacy Intervention for Chronic Diseases to Improve Treatment Adherence	This randomized trial sought to determine whether this novel, targeted, pharmacist-based intervention improves adherence and disease control.
ACS QUIK — Effect of a Quality Improvement Toolkit on Acute Myocardial Infarction in India: The ACS QUIK Cluster Randomized, Stepped Wedge Trial	ACS QUIK sought to evaluate the effect of a locally adapted, evidence-based quality improvement toolkit on process measures and outcomes among patients with acute myocardial infarction in India.
ICARE-ACS — National Implementation of a Clinical Guidance Framework for the Emergency Department Assessment of Patients with Possible Acute Coronary Syndromes	This study evaluated the safety and impact of real-life implementation of a national clinical guidance framework for the assessment of possible acute coronary syndromes.
DECIDE-LVAD — Effectiveness of a Shared Decision Making Intervention for Patients Offered a Destination Therapy Left Ventricular Assist Device for End-Stage Heart Failure	This study evaluated whether a decision support tool would improve decision quality for left ventricular assist device for destination therapy.
STEMI ACCELERATOR-2 — Regional STEMI Systems of Care: Results of the Mission: Lifeline STEMI ACCELERATOR-2 Study	This study evaluated implementation of regional systems of care to provide timely reperfusion for patients with ST-elevation MI.

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.**

8 a.m.-3 p.m.
Cardiovascular Nursing Clinical Symposium: Day Two
Room 204A, Main Building

9-10:15 a.m.
Precision Medicine Summit: The Future of Precision Medicine and Big Data
Main Event I, Hall D, Main Building

9-10:25 a.m.
Frontiers in Stem Cells: New Concepts in Progenitor Cell Biology
Rooms 154-158, ACC North

10:45 a.m.-Noon
New Insights into the Risks, Benefits, and Costs of Antithrombotic Therapy
Main Event I, Hall D, Main Building

11:40 a.m.-12:50 p.m.
Novel Perspectives that Advance Care of Older Adults with CVD
Population Forum, Science and Technology Hall

12:30-1:30 p.m.
Distinguished Scientist Lecture: Genetic and Epigenetic Determinants of the Inflamed Vessel Wall Inform New Treatments for Pulmonary Hypertension and Other Vascular Diseases
Ballroom CD, 3rd Level, Main Building

1:30-2:40 p.m.
AHA's Life's Simple 7 and 2020 Goals
Population Forum, Science and Technology Hall

2-2:30 p.m.
Paul Dudley White Lecture and Session: Post-Truth Medicine: Death and Disability by Disinformation
Room 303AB, Main Building

2-3:15 p.m.
Fogarty, NHLBI, NIH and the Future of Global Cardiovascular Health Research
Ballroom A, 3rd Level, Main Building

3:45-5 p.m.
Alexander S. Nadas Lecture and Outstanding Research Awards in Pediatric Cardiology
Room 203AB, Main Building

3:45-5 p.m.
One Size Doesn't Fit All — Difficult Decisions in Prevention Practice
Main Event I, Hall D, Main Building

5:15-7 p.m.
Frontiers in Stem Cells: Clinical Studies of Cell Therapy II
Rooms 154-158, ACC North

5:30-6:45 p.m.
Fogarty, NHLBI, NIH and the Future of Global Cardiovascular Health Research: Early Career Global Cardiovascular Research
Ballroom A, 3rd Level, Main Building

HEARTY HUMOR by Jonny Hawkins

MEMBER SPOTLIGHT

Fatima Cody Stanford, MD, MPH, MPA

Joining AHA allows obesity specialist to contribute, learn

It didn't take long for Fatima Cody Stanford to "feel at home" after a prominent, long-time AHA volunteer approached her about getting involved in the organization.

"I am thankful to have met [Sherita Hill Golden, MD, MHS, of Johns Hopkins Medicine]," said Stanford, MD, MPH, MPA. "With her prominent track record in the AHA, I believe her professionalism and encouragement bode well for improving diversity in medicine as a whole. Her long-term commitment to the AHA likely influenced her ability to continue to propel me within my career."

Stanford, an obesity medicine physician at Massachusetts General Hospital and Harvard Medical School in Boston, said one reason she became an AHA member is because of its strong voice for cardiometabolic health.

She recently joined the Council of Lifestyle and Cardiometabolic Health and the Council of Quality of Care and Outcomes Research to help address the underlying diseases or conditions — including obesity — that lead to many adverse cardiovascular events.

"I very much look forward to becoming integrated into these councils so that I may contribute my background and experience in caring for pediatric and adult patients with obesity," Stanford said. "I would like to have a special focus on obesity in one or both of these committees. I'm eager to learn how my expertise can align with others to improve the care of individuals with obesity.

"The power of organized medicine is invaluable. It's impossible to make progress with regard to patient care without a concerted and collective voice. I see the AHA as having a strong voice with regards to improving health outcomes."

In addition to contributing to AHA councils, Dr. Stanford said she's looking forward to learning from long-term members of the association.

"As a newer member, I am open to finding out more about how to maximize my membership and how to best get more involved," she said. ▼

Lasker lecturer calls for expansion of NIH New Innovator Award program

Bruce M. Alberts, PhD, says innovation is disappearing from U.S. biomedical research — and he may have a remedy to bring it back.

In his Lasker Laureate Lecture on Monday at Scientific Sessions, the biochemist urged expanding the NIH New Innovator Award program from the current 30-40 grants annually to 500.

"That would take about $1 billion out of the total $30 billion in NIH grant spending," said Alberts, the Chancellor's Leadership Chair in Biochemistry and Biophysics for Science and Education at the University of California, San Francisco. "That would be enough to encourage graduate students to plan more innovative careers."

The current funding system encourages researchers to expand what's already known instead of looking into new mysteries, Alberts said.

"Our present system strongly discourages risk-taking and prevents researchers from taking leaps into the unknown where great new discoveries can be made," he said. "In the biomedical field, the National Institutes of Health is pushing scientists into translational research, which is important, but it is not everything. You need new basic science discoveries before you can translate them."

Many genomic discoveries driving recent clinical advances originated from studies in fruit flies, Albert said. Yet, a common complaint among younger researchers is that neither the NIH nor most other funding sources are seriously considering grant proposals that aren't focused on either rodent or human biology.

Bruce M. Alberts, PhD

Age discrimination is another barrier, Albert said. In 1980, the median age of principal investigators funded by the NIH was about 36. In 2015, most PIs were 46 and older. In 2012, only 1.3 percent of key grants in the United States went to investigators under 36.

"How successful do you think Silicon Valley would be if nearly 99 percent of all investments went to innovators who were 36 years old and older?" Alberts said. "We are starting researchers out too late and losing the energy, the ambition and the innovation of young people. We need to change our incentives to encourage more younger researchers to strike out in their own direction."

The European Union provides a useful model for innovation, Alberts said. In the 20th century, much of European biomedical research had moved from innovative to copycat, driven by many of the backward incentives that are hampering U.S. research.

Young PhDs moved into an established lab, built their reputation and moved on to their own projects — which were almost always derivative. Grant review committees, in turn, focused on recognized research tracks as being more likely to produce results. Innovation suffered.

In 2007, the European Union established the European Research Council (ERC) with three grant levels. Starting grants are reserved for investigators two to seven years beyond their PhD; consolidator grants are for researchers seven to 12 years post-PhD; and advanced grants are for older researchers.

The key, Alberts said, is that the starting grant review criteria focus on novelty, interdisciplinarity and high-risk/high-gain research. Each successful applicant is funded for five years and up to €2 million, about $1.7 million. And the bulk of ERC funding is reserved for researchers 12 years or less post-PhD.

Expanding the NIH New Innovator Award program would move U.S. research in a similar direction, Albert said.

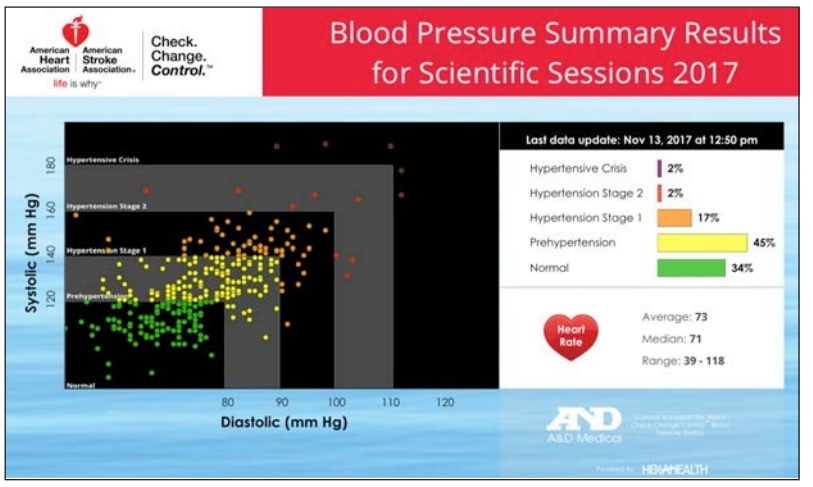
"We should encourage young people to follow their dreams in science," he said. "The message they get from faculty and funders now is that they can't do that and get funded. It shouldn't take a funding miracle to get a researcher to work on the unknown." ▼

New hypertension guidelines in action at Target: BP booth

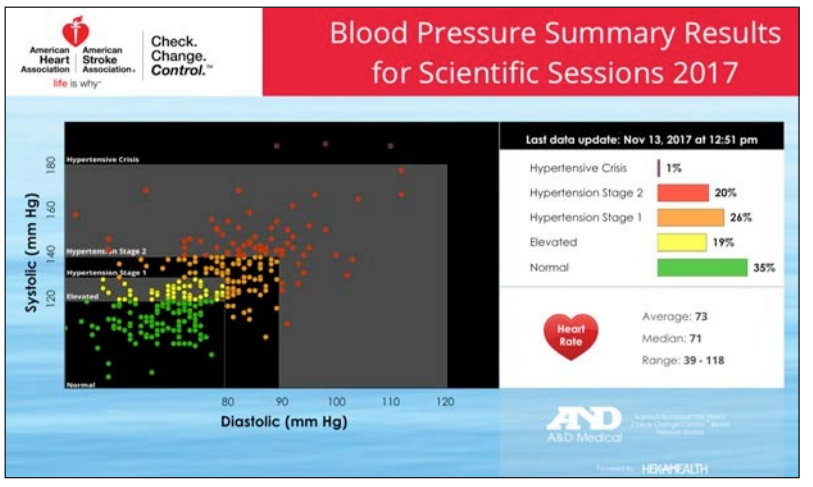
Anke Hodes, MD (pictured below), a research physician for G-Cure at the University Medical Centre Groningen in the Netherlands, and other Scientific Sessions attendees, checked their blood pressure at the Target: BP booth (721) on Monday to see firsthand how the new hypertension guidelines affect them.

Real-time charts (to the right) provide a snapshot of the aggregate results of attendees' BP readings before and after the guidelines were released. Attendees classified as hypertension Stage 2 rose by 18 percent following the guideline release (2 percent before and 20 percent after), and attendees classified as hypertension Stage 1 rose from 17 percent to 26 percent. ▼

Attendees' BP Readings Before Guidelines Release



Attendees' BP Readings After Guidelines Release



HYPERTENSION GUIDELINES continued from page 1

quitting smoking, cutting back on alcohol and increasing physical activity.

Robert M. Carey, MD, vice chair of the guideline writing committee, said he expects some controversy over how the new guidelines treat older adults, such as recommending that people over 65 be treated at the same 130/80 mm Hg goal as younger patients. A guideline early this year from the American College of Physicians and the American Academy of Family Physicians suggested patients older than 60 should be held to a standard below 150/90 mm Hg.

But Carey, a professor of medicine and a dean emeritus at the University of Virginia School of Medicine in Charlottesville, said several intensive studies since 2015 show treating older adults to a lower blood pressure goal is important.

"You have to escalate the treatment slower and monitor the side effects," he said. "But it's true there is benefit to treating ambulatory, older subjects."

According to the guidelines, it can be lifesaving: "BP-lowering therapy is one of the few interventions shown to reduce mortality risk in frail older individuals."

Under the new classification, men and women age 65 to 74 will see high blood pressure rates increase by 13 percent and 12 percent, respectively.

Here's how some other groups will be affected by the new measurements:

- High blood pressure rates nearly triple among men age 20 to 44 — up to 30 percent from 11 percent. Women in that age group will see their rates almost double, to 19 percent from 10 percent.
- Roughly three quarters of men between 55 and 74 could be diagnosed with high blood pressure.
- Black and Hispanic men will experience a 17 percent increase in rates. Asian men will see a 16 percent increase.

The new classifications and recommendations are specific in how they determine who is at risk and what they should do about it, Jamerson said.

Physicians should use a risk calculator to determine a patient's risk of heart disease in the next 10 years, he said. That, combined with the other recommendations, can prompt more thorough doctor-patient conversations to determine whether lifestyle changes alone can help, or if other medicine is needed as well.

"These new guidelines give patients a voice because it gives them an opportunity to ask healthcare providers, 'What's my risk?'" Jamerson said. "Consumers should be getting an explanation. Physicians ought to be calculating risk as they think about how to treat."

Full details are available at **professional.heart.org/hypertension.** ▼

IMPLICATIONS continued from page 1

People with a prior stroke, myocardial infarction, other major events, diabetes or chronic kidney disease are at high risk under the new guidelines.

Those who do not meet these automatic inclusion criteria should have their risk assessed, according to the guidelines. The AHA recommends using the Heart Risk Calculator at **www.cvriskcalculator.com**. People who have a 10 percent or greater risk of a major cardiovascular event in the next 10 years are considered high risk and should receive drug treatment.

Individuals with systolic blood pressure of 140 mm Hg or higher or diastolic of 90 mm Hg or higher have stage 2 hypertension and need lifestyle changes plus drug treatment with two or more agents from different classes.

A second major innovation in the guidelines is the focus on accurate blood pressure measurement in the office and at home. In-office blood pressure testing has long been the standard of care, but not all providers measure blood pressure appropriately or accurately, Whelton said. The guidelines include specific recommendations for blood pressure measurement, such as requiring patients to rest before measuring, taking multiple measurements in both arms and averaging readings to help reduce random error.

For the first time, the new guidelines emphasize the need for regular at-home blood pressure measurement to supplement in-office measurements.

"There's an increasing body of literature that what happens in the office is not always what happens outside the office," Whelton said. "One group has high blood pressure measured in the office but normal pressures outside the office. These white-coat hypertensives have a risk pattern that is more like nonhypertensives."

The more insidious problem is masked hypertension, which is when blood pressure readings in the office are normal, but elevated outside the office. People with masked hypertension have a risk pattern similar to those with sustained hypertension, Whelton said. Both groups will be missed if clinicians rely only on in-office blood pressure measurements. ▼

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Highlights FROM THE 2017 GUIDELINE FOR THE PREVENTION, DETECTION, EVALUATION AND MANAGEMENT OF HIGH BLOOD PRESSURE IN ADULTS

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

New blood pressure targets and treatment recommendations: For years, hypertension was classified as a blood pressure (BP) reading of 140/90 mm Hg or higher, but the updated guideline classifies hypertension as a BP reading of 130/80 mm Hg or higher. The updated guideline also provides new treatment recommendations, which include lifestyle changes as well as BP-lowering medications, as shown in Table 1.

TABLE 1. Classification of BP

BP Category	Systolic BP		Diastolic BP	Treatment or Follow-up
Normal	<120 mm Hg	**and**	<80 mm Hg	Evaluate yearly; encourage healthy lifestyle changes to maintain normal BP
Elevated	120-129 mm Hg	**and**	<80 mm Hg	Recommend healthy lifestyle changes and reassess in 3-6 months
Hypertension: stage 1	130-139 mm Hg	**or**	80-89 mm Hg	Assess the 10-year risk for heart disease and stroke using the atherosclerotic cardiovascular disease (ASCVD) risk calculator • If risk is less than 10%, start with healthy lifestyle recommendations and reassess in 3-6 months • If risk is greater than 10% or the patient has known clinical cardiovascular disease (CVD), diabetes mellitus, or chronic kidney disease, recommend lifestyle changes and BP-lowering medication (1 medication); reassess in 1 month for effectiveness of medication therapy – If goal is met after 1 month, reassess in 3-6 months – If goal is not met after 1 month, consider different medication or titration – Continue monthly follow-up until control is achieved
Hypertension: stage 2	≥140 mm Hg	**or**	≥90 mm Hg	Recommend healthy lifestyle changes and BP-lowering medication (2 medications of different classes); reassess in 1 month for effectiveness • If goal is met after 1 month, reassess in 3-6 months • If goal is not met after 1 month, consider different medications or titration • Continue monthly follow-up until control is achieved

TABLE 2. Hypertensive Crises: Emergencies and Urgencies (See Section 11.2 of 2017 Hypertension Guideline)

Hypertensive Crises	Systolic BP		Diastolic BP	Treatment or Follow-up
Hypertensive urgency	>180 mm Hg	**and/ or**	>120 mm Hg	Many of these patients are noncompliant with antihypertensive therapy and do not have clinical or laboratory evidence of new or worsening target organ damage; reinstitute or intensify antihypertensive drug therapy, and treat anxiety as applicable
Hypertensive emergency	>180 mm Hg + target organ damage	**and/ or**	>120 mm Hg + target organ damage	Admit patient to an intensive care unit for continuous monitoring of BP and parenteral administration of an appropriate agent in those with new/ progressive or worsening target organ damage (see Tables 19 and 20 in the 2017 Hypertension Guideline)

Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published online ahead of print November 13, 2017]. *Hypertension*. doi: 10.1161/HYP.0000000000000065.

Pharmacologic recommendations: The updated guideline recommends BP-lowering medication for those with stage 1 hypertension with clinical CVD or a 10-year risk of ASCVD 10% or greater, as well as for those with stage 2 hypertension. For stage 2, the recommendation is 2 BP-lowering medications in addition to healthy lifestyle changes, which is a more aggressive treatment standard—previous guidelines recommended starting patients on only 1 BP-lowering medication.

The guideline also updates the recommendations for specific populations. Because black adults are more likely to have hypertension than other groups, 2 or more antihypertensive medications are recommended to achieve a target of less than 130/80 mm Hg in this group, and thiazide-type diuretics and/or calcium channel blockers are more effective in lowering BP alone or in multidrug regimens. Morbidity and mortality attributed to hypertension are more common in black and Hispanic adults compared with white adults.

For adults starting a new or adjusted drug regimen to treat hypertension, follow up with them each month to determine how well they are following and responding to their prescribed treatment until their BP is under control.[2-4] For a full list of medications, see Table 18 in the 2017 Hypertension Guideline.

Emphasis on cardiovascular disease: The updated guideline provides recommendations for patients with clinical CVD and makes new recommendations for using the ASCVD risk calculator:

- Use BP-lowering medication for **primary** prevention of CVD in adults with no history of CVD ***and*** an estimated 10-year ASCVD risk less than 10% ***and*** a systolic BP of 140 mm Hg or greater ***or*** a diastolic BP of 90 mm Hg or greater.[5-9]
- Use BP-lowering medications for **secondary** prevention of recurrent CVD events in patients with clinical CVD ***and*** an average systolic BP of 130 mm Hg or greater ***or*** a diastolic BP of 80 mm Hg or greater ***and*** for **primary** prevention in adults with an estimated 10-year risk of ASCVD of 10% or greater with an average systolic BP of 130 mm Hg or greater ***or*** average diastolic BP of 80 mm Hg or greater.[5,10-17]

No prehypertension: The updated guideline eliminates the term *prehypertension* and instead uses the term *elevated BP* for a systolic BP of 120 to 129 mm Hg and a diastolic BP of less than 80 mm Hg.

More hypertension patients: Because the new definition of hypertension is lower (130/80 mm Hg), more people will be classified as having hypertension. However, most of these new patients can prevent hypertension-related health problems through lifestyle changes alone.

The new Hypertension Guideline changes the definition of hypertension, which is now considered to be any systolic BP measurement of 130 mm Hg or higher—or any diastolic BP measurement of 80 mm Hg or higher.

Hypertensive urgency vs hypertensive emergency: Hypertensive urgencies are associated with severe BP elevation in otherwise stable patients without acute or impending change in target organ damage or dysfunction. Hypertensive emergencies are severe elevations in BP associated with evidence of new or worsening target organ damage.

Focus on accurate measurements: To ensure accurate measurements, make sure the instrument you are using is properly calibrated. The updated guideline also stresses the basic processes for accurately measuring BP, including some simple yet critical actions before and during measurements. For accurate in-office measurements, do the following:

- Have the patient avoid smoking, caffeine, or exercise within 30 minutes before measurements; empty his or her bladder; sit quietly for at least 5 minutes before measurements; and remain still during measurements.
- Support the limb used to measure BP, ensuring that the BP cuff is at heart level and using the correct cuff size; don't take the measurement over clothes.
- Measure in both arms and use the higher reading; an average of 2 to 3 measurements taken on 2 to 3 separate occasions will minimize error and provide a more accurate estimate.

For more information about accurate measurements, see Tables 8 and 9 in the 2017 Hypertension Guideline.

Focus on self-monitoring: Office BPs are often higher than ambulatory or home BPs, so the updated guideline emphasizes having patients monitor their own BP for hypertension diagnosis, treatment, and management. Patients should follow these steps:

- Use the same validated instrument at the same time when measuring at home to more accurately compare results.
- Position themselves correctly, with the bottom of the cuff directly above the bend of the elbow.
- Optimally, take at least 2 readings 1 minute apart each morning before medication and each evening before supper. Ideally, obtain weekly readings 2 weeks after a treatment change and the week before a clinic visit.
- Record all readings accurately; use a monitor with built-in memory and bring it to all clinic appointments.

For clinical decision-making, base the patient's BP on an average from readings on 2 or more occasions.

Treatment recommendations: The updated guideline presents new treatment recommendations, which include lifestyle changes as well as BP-lowering medications. These lifestyle changes can reduce systolic BP by approximately 4 to 11 mm Hg for patients with hypertension, with the biggest impacts being changes to diet and exercise.

- In addition to promoting the DASH diet, which is rich in fruits, vegetables, whole grains, and low-fat dairy products, the updated guideline recommends reducing sodium intake and increasing potassium intake to reduce BP. However, some patients may be harmed by excess potassium, such as those with kidney disease or who take certain medicines. See Table 15 in the 2017 Hypertension Guideline for more information.
- Each patient's ideal body weight is the best goal, but as a rule, expect about a 1 mm Hg BP reduction for every 1 kg reduction in body weight.
- Recommendations for physical activity include 90 to 150 minutes of aerobic and/or dynamic resistance exercise per week and/or 3 sessions per week of isometric resistance exercises.
- For patients who drink alcohol, aim for reducing their intake to 2 or fewer drinks daily for men and no more than 1 drink daily for women.

New targets for comorbidities: For patients with comorbidities, the updated guideline generally recommends prescribing BP-lowering medications in patients with clinical CVD and new stage 1 or stage 2 hypertension to target a BP of less than 130/80 mm Hg (this was previously less than 140/90 mm Hg). The guideline recommends different follow-up intervals based on the stage of hypertension, type of medication, level of BP control, and presence of target organ damage.

To download the full version of the 2017 Hypertension Guideline, please visit http://professional.heart.org/hypertension.

SPRINT trial: Similar BP levels in attended, non-attended blood pressure measurements

A healthcare provider's presence or absence when blood pressure is measured resulted in similar BP levels and reduction in CVD risk, a new analysis of the SPRINT trial found.

The data, based on SPRINT staff interviews, indicate similar results whether the measurement was taken with a provider present, absent or absent part of the time.

"We saw no heterogeneity between the measurement groups," said Karen C. Johnson, MD, MPH, FAHA, vice chair of the SPRINT Steering Committee. "The use of a validated, automated blood pressure device, staff training to allow for a quiet rest period, proper positioning, use of proper cuff size and averaging multiple measurements may be more important than whether the measurement is attended or unattended."

Johnson, Endowed Professor of Women's Health in the Department of Preventive Medicine at the University of Tennessee Health Science Center in Memphis, reported the ad hoc analysis during the third Late-Breaking Science Session on Monday.

Blood pressure measurement in SPRINT is similar to methods used in virtually all recent hypertension trials and to what's recommended for clinical practice. Because 99.7 percent of SPRINT blood pressure measurements were taken with a study-provided device, Johnson said it was no surprise that having a second person in the room was of little importance in obtaining an accurate measurement.

The challenge remains translating guideline-based blood pressure measurement from the clinical study setting into clinical practice, she said. "Follow hypertension guidelines to measure blood pressure," Johnson said. "That's how you know how effective your treatment is."

Karen C. Johnson, MD, MPH, FAHA

TITRE

The more time newly diagnosed hypertension patients stay at blood pressure target, the lower their risk of subsequent events, according to a novel population study in the United Kingdom.

Researchers used the University College London CALIBER data resource to create a cohort of patients newly diagnosed with hypertension in January 1997-March 2010. They used the database to describe the average time per year spent by newly identified hypertensive patients at blood pressure care target.

Patients were at least 18 years old at baseline with no prior cardiovascular disease or hypertension diagnosis, and had at least six months of follow-up. Hypertension was defined as blood pressure at 140/90 mm Hg or higher.

Primary endpoints were a CVD composite of cardiovascular mortality, acute MI and stroke, as well as heart failure and a composite of any cardiovascular incident and death.

The cohort included 150,130 patients with a median of seven blood pressure readings during a median of five years. The average age was 52 and 56 percent were women. During follow-up, 46 percent of patients went on antihypertensive medications, 29 got dietary advice and 2 percent stopped smoking.

The time at target was not surprising, said Mar Pujades-Rodriquez, MBBS, PhD, an academic fellow in health informatics at the University of Leeds and an honorary senior researcher at University College London.

The median time at target was 2.8 months per year and only 4.5 percent of patients spent nine to 12 months at target. The less time at target, the greater the risk of cardiovascular events, Pujades-Rodriquez said.

The odds ratio for the cardiovascular disease composite ranged from 4.51 for those with no time at target to 0.7 for those who spent nine months or more per year at target. The distribution was similar for heart failure, from 3.53 for no time at target to 0.47 for nine months or longer. The association between any cardiovascular disease and death ranged from 2.57 to 0.42.

GATEWAY

Bariatric surgery can lower or eliminate the need for anti-hypertensive medications in some obese hypertensive patients, new data suggest.

The Gastric Bypass Surgery to Treat Patients with Steady Hypertension found that 83.7 percent of patients who underwent bariatric surgery had at least a 30 percent reduction in hypertensive medications at one year. Just 12 percent of patients on medical treatment had similar results.

"Over half of bariatric surgery patients — 51 percent— had a complete remission of hypertension with no antihypertensive medication use," said Carlos Aurelio Schiavon, MD, FACS, from the Center for Surgical Treatment of Morbid and Metabolic Disorders at Hospital Alemão Oswaldo Cruz in São Paulo, Brazil. "None of the patients on medical therapy only showed remission."

Observational studies and randomized trials focused primarily on diabetes have shown that antihypertensive medications are discontinued and cardiovascular events reduced after bariatric surgery.

GATEWAY is the first randomized controlled trial in a broad population of hypertensive obese patients. The 100 obese patients with hypertension were randomized to gastric bypass or medical therapy. The primary endpoints were at least a 30 percent reduction in antihypertensive while maintaining a blood pressure below 140/90 mm HG.

The bariatric surgery group had significant weight loss over several months, but reductions in antihypertensive medications were clear in the first 30 days after surgery. The underlying reasons for the improvements in hypertension are not clear, Schiavon said.

Bariatric surgery patients also showed significant improvements in metabolic and inflammatory profiles. ▼

Paul Dudley White lecturer encouraging medical community to resist disinformation

Medical research is all about hard facts and statistics, but historically — and increasingly today — there is a lot of disinformation out there.

What medical professionals should do about this problem is the focus of Tuesday's Paul Dudley White International Lecture presented by Sir Rory Collins, professor of medicine and epidemiology at the Clinical Trial Service Unit at the University of Oxford.

"The failure of the medical community, including medical journals and medical regulators, to act fast enough and robustly enough has left a long-term effect on public health," said Collins, who will deliver his lecture, "Post-Truth Medicine: Death and Disability by Disinformation," at 2 p.m. in room 303AB, Main Building.

One of the most well-known examples of disinformation in medicine was the false link between the measles, mumps and rubella vaccine and an increased risk for young children developing autism, Collins said. This disinformation led to substantially decreased immunization rates, the loss of herd immunity and increases in measles cases in Britain and the United States, he said.

Collins also will discuss statin therapy and claims of large differences in the risk of side effects based on whether one looks at observational studies or randomized clinical trials. In observational studies, where researchers assess reports among people who know they are taking a statin, claims have been made that up to 20 percent of people experience side effects. In contrast, there's a lack of increase in symptomatic side effects among people in randomized blinded trials, where people do not know whether they are taking statins or placebo.

Collins' lecture honors Paul Dudley White, who is widely regarded as the founder of preventive cardiology. White helped found the Boston Society for the Prevention and Relief of Heart Disease (now the Greater Boston Division of the American Heart Association). He joined forces with similar groups in New York City and Philadelphia, and in 1924 became one of the founders of the AHA. He served as AHA president in 1941. ▼

Sir Rory Collins

LECTURE PREVIEW

Paul Dudley White International Lecture: Post-Truth Medicine: Death and Disability by Disinformation

2-2:30 p.m. Tuesday

Room 303AB, Main Building

New data from FOURIER suggests long-term use of evolocumab may prevent recurrent CV events

The results of a follow-up analysis of data from the Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk (FOURIER) trial suggest that the addition of the PCSK9 inhibitor evolocumab to statin therapy not only reduces the risk of first major vascular events in patients with stable atherosclerotic disease, but also reduces the risk of recurrent cardiovascular events. Findings from the analysis were presented by Sabina A. Murphy, MPH, at Scientific Sessions on Monday.

"Looking at total vascular events during the 2.2-year median follow-up in the FOURIER trial, our analysis revealed more than double the number of events prevented — driven by decreases in MI, stroke and coronary revascularization — as compared with an analysis of just first events," said Murphy, director of biostatistics for the TIMI Study Group at Brigham and Women's Hospital in Boston.

In the FOURIER trial, patients with atherosclerotic cardiovascular disease who were receiving background statin therapy were randomized in a double-blind manner to continued statin therapy plus treatment with either evolocumab or placebo.

"The primary analysis of long-term cardiovascular trials often use survival analysis methods to evaluate efficacy on the first event that a patient experiences during the trial, as was done in FOURIER," Murphy said. "This is most commonly done using a standard Cox proportional hazards model, which censors patients after that first event has occurred."

To evaluate the effect of evolocumab on total events that occurred throughout the trial, the investigators used a negative binomial regression model to evaluate the total count of events that occurred in a subject. They also performed a sensitivity analysis using the Wei, Lin and Weissfeld model, which is an extension of survival models based on the Cox proportional hazard. The primary endpoint was a composite of CV death, MI, stroke, unstable angina or coronary revascularization.

There were 4,906 primary endpoint events that occurred during the course of the trial, Murphy said. Of those events, 2,907 were first primary endpoint events, which were included in the primary analysis, but there were an additional 1,999 primary endpoint events that patients experienced during the course of follow-up that were not included in the primary analysis, she said.

Among the findings of the follow-up analysis, Murphy reported that evolocumab reduced total primary endpoint events by 18 percent (incidence-rate ratio [RR] 0.82, 95 percent CI 0.75-0.90, p<0.001), including both first events (HR 0.85 [0.79-0.92], p<0.001) and subsequent events (RR 0.74 [0.65-0.85], p<0.001). Reductions in total events were driven by fewer total MIs (RR 0.74, p<0.001), fewer total strokes (RR 0.77, p=0.007) and fewer total coronary revascularizations (RR 0.78, p<0.001).

Sabina A. Murphy, MPH

"Overall, our data showed that evolocumab prevented 22 primary endpoint events per 1,000 patients treated for three years when considering first events only, and 52 such events when taking into account total vascular events," Murphy said. "We believe these data support long-term use of evolocumab in conjunction with statin therapy to reduce the risk of recurrent cardiovascular events. With continued research, we hope to more clearly define the magnitude of benefit of LDL-C lowering with evolocumab in various patient subgroups, taking into account the effect on total events." ▼

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.

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Overland Park, KS 66213
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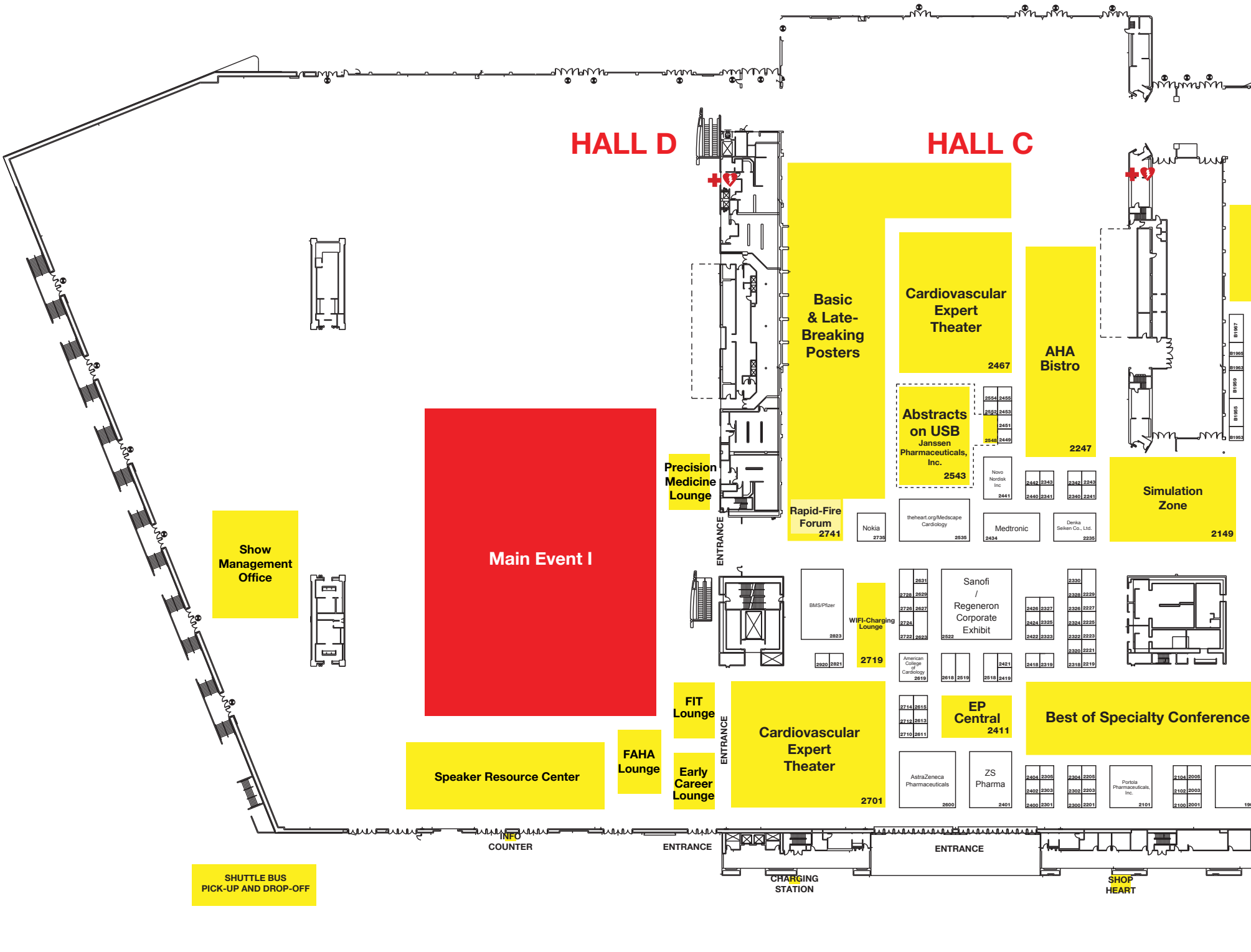
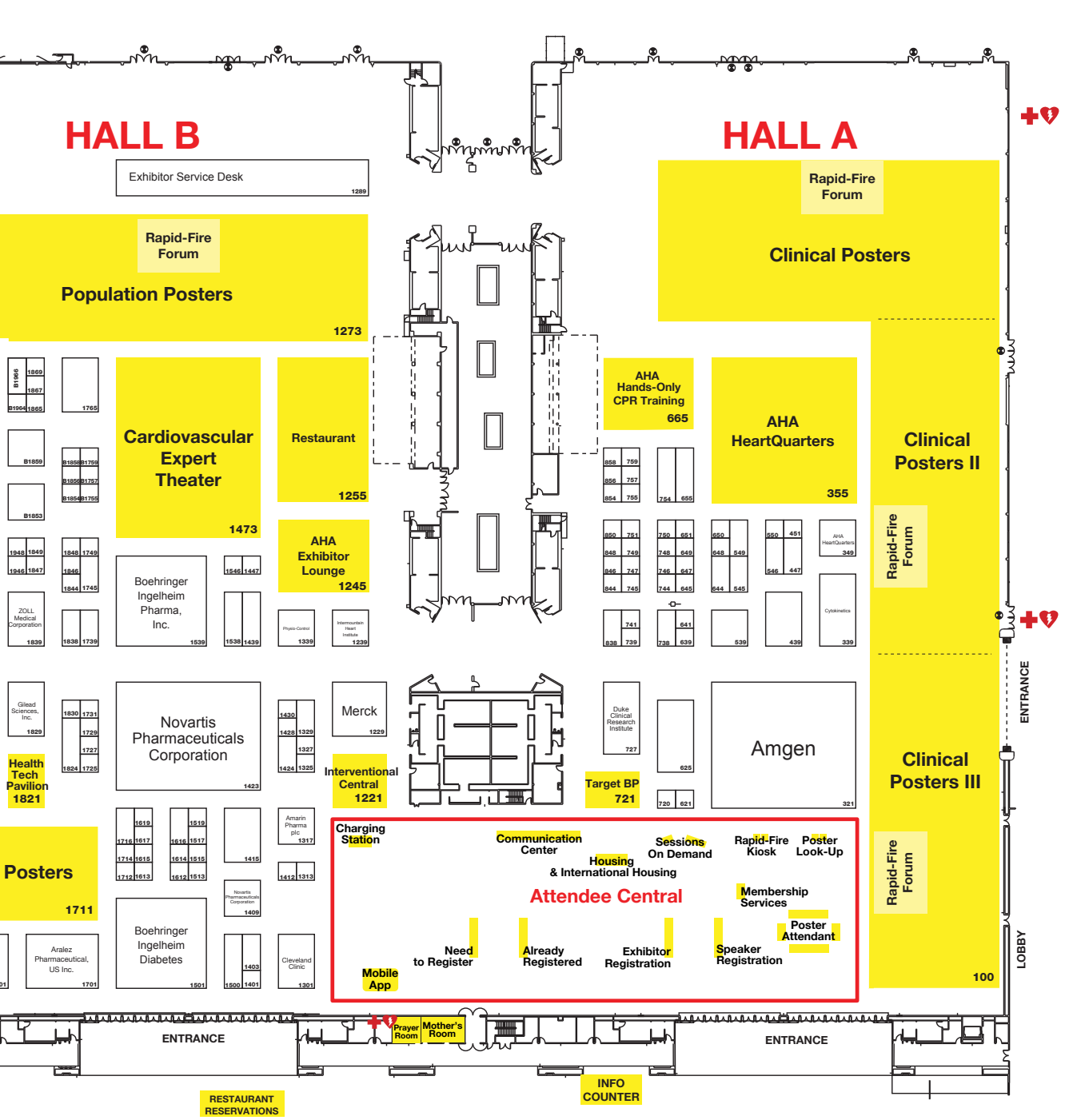
2017 Scientific Sessions Exhibitors

Science & Technology Hall Hours
Tuesday 10 a.m.-3 p.m.

Hall Breaks
Tuesday 10:15-10:45 a.m. and Noon-2 p.m.





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SCIENTIFIC SESSIONS 2017

TUESDAY'S THEATER PRESENTATIONS

CARDIOVASCULAR EXPERT THEATER BOOTH 1473

Noon-12:45 p.m.
Cardiovascular Disease: From Risk Factors to Clinical Discussions
Supporter: Amgen, Inc.
Presenter: Alan S. Brown, MD

CARDIOVASCULAR EXPERT THEATER BOOTH 2467

Noon-12:45 p.m.
Advancements in the Management of Patients with Type 2 Diabetes: Results from a Large Cardiovascular Outcomes Trial
Supporter: Novo Nordisk
Presenters: Robert Chilton, DO, FACC, FAHA, and Carol Wysham, MD

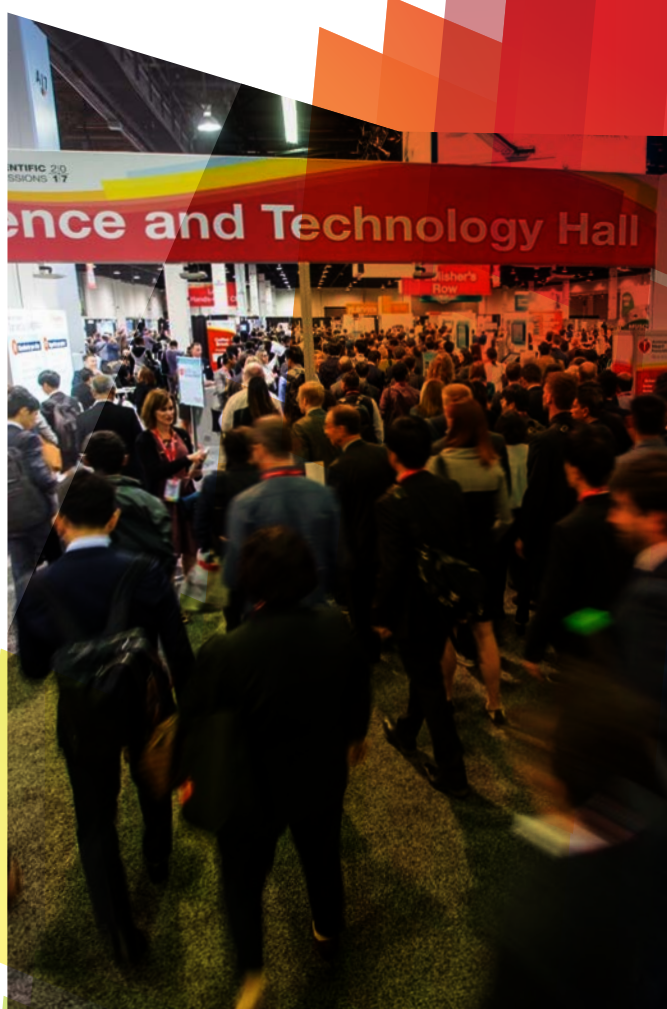
CARDIOVASCULAR EXPERT THEATER BOOTH 2701

10:15-11:15 a.m.
Spotlight Series: Stroke Work-up: Atrial Fibrillation
Supporter: American Heart Association
Presenter: Nazem Akoum, MD, MS, FAHA, FACC, FHRS

1:15-2:30 p.m.
Spotlight Series: The Management of Heart Failure: A Practical but Guideline-directed Approach
Supporter: American Heart Association
Presenter: Mariell Jessup, MD, FAHA

HEARTQUARTERS THEATER BOOTH 335

10-11 a.m.
Cardiovascular Center of Excellence – Benefits to the Community
Presenters: CVCOE Developers



Study: Physical activity associated with greater gray matter volumes in older adults

Higher levels of lifestyle physical activity are significantly associated with greater gray matter volumes in older adults, according to results of a cross-section study presented by Shannon Halloway, PhD, RN, during an abstract oral session on Monday.

The abstract was selected as one of this year's Cardiovascular Stroke Nursing Best Abstract Award winners.

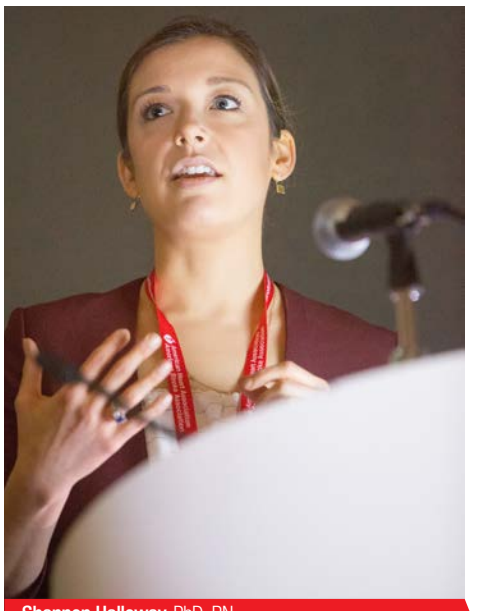
In this study, researchers conducted a secondary analysis of data from the Rush Memory and Aging Project (MAP), an epidemiological study that examines common chronic conditions of old age with questionnaires, performance tests and clinical evaluations. The purpose of the secondary analysis was to examine the cross-sectional association between physical activity, as measured by an accelerometer, and gray matter volumes, as measured by MRI.

"We know that physical activity can improve cognitive function in older adults," said Halloway, of Rush University Medical Center in Chicago. "A specific subcategory of physical activity is lifestyle physical activity, which refers to activities that a person carries out in the course of daily life. Lifestyle physical activity can be measured with a wearable device, such as an accelerometer. Older adults often prefer programs that focus on lifestyle physical activity rather than structured exercise programs that take place in the gym."

Participants in the study were 262 older adults from the Rush MAP cohort. Average age was 81 years and exclusion criteria included diagnosis or symptoms of dementia or mild cognitive impairment per clinical evaluation, history of brain surgery and structural brain abnormalities atypical to aging.

Total counts of physical activity per day were assessed using an Actical accelerometer worn continuously for 10 consecutive days on the nondominant wrist. Gray matter volumes were measured using Freesurfer brain imaging analysis software on high-resolution T1-weighted anatomical MRI data.

The researchers conducted models examining the effects of total daily lifestyle physical activity on three measures of gray matter volumes — subcortical gray matter volume, total cortex volume and total gray matter volume. The analysis controlled for demographics, depressive symptoms, body mass index and physical disability. These are known factors that can impact physical activity and, at times, gray matter, Halloway said.


Shannon Halloway, PhD, RN

Halloway reported that multivariate general linear models indicated that higher levels of total daily physical activity were associated with larger volumes of all gray matter volume variables, ($F[2, 215]=3.61$, $p=.027$), including subcortical gray matter ($\beta=.17$, $p=.01$) and total gray matter ($\beta=.11$, $p=.05$). There were no significant effects for total cortex volume.

"Our findings with a device measure of lifestyle physical activity confirmed results from earlier self-report structured exercise and gray matter studies," Halloway said. "Unexpectedly, though, the relation between lifestyle physical activity and total cortex volume in our analyses was not significant. However, we controlled for multiple health status variables, which earlier studies did not include."

Because this was a cross-sectional study only, Halloway said future research using longitudinal designs or a randomized controlled trial of lifestyle physical activity intervention is needed to further explore these relationships.

"Moving forward, our goal is to develop and test behavioral interventions that focus on lifestyle physical activity for older adults at increased risk for cognitive decline due to cardiovascular disease," Halloway said. "We are currently completing pilot testing of a walking intervention for older women with cardiovascular disease that aims to improve cognition." ▼

Risk prediction tool may help to identify childhood cancer survivors at increased risk of CVM

Using prospective data from the National Cancer Institute's Surveillance, Epidemiology and End Results program, a multinational group of researchers developed a risk prediction tool that can help clinicians identify long-term childhood cancer survivors (CCS) at increased risk of cardiovascular mortality (CVM).

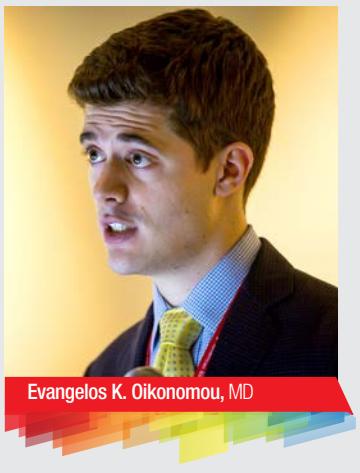
Evangelos K. Oikonomou, MD, a PhD student in the Division of Cardiovascular Medicine at the University of Oxford in the United Kingdom, presented the findings in an oral abstract presentation Monday.

Over the past couple of decades, a growing and effective armamentarium in cancer therapy has led to improved survival rates in children diagnosed with malignant neoplasms, Oikonomou noted. However, he noted that an expanding body of evidence suggests that long-term childhood cancer survivors are at increased cardiovascular risk compared to the general population.

"There is no prognostic model to date to estimate the risk of hard cardiovascular endpoints among long-term childhood cancer survivors," Oikonomou said. "Such a tool would be invaluable in primary care to improve the longitudinal follow-up and care of an ever-increasing population of patients."

In the study using data from the SEER program (1973-2013), long-term CCS (age at diagnosis ≤19 years, and survival ≥5 years) were identified and followed up over a median time period of 12.3 (range: 5 to 40.9) years. Independent predictors of CVM were combined into a risk score, which was initially developed in a derivation group (n=22,374 CCS in seven registries) and subsequently validated in an independent group of patients (n=6,437 CCS in two registries).

In the derivation group, the researchers found that older age at diagnosis, male sex, non-white race, a history of lymphoma versus other malignancies and radiotherapy were independently associated with an increased risk of CVM in long-term CCS ($p<0.05$ for all).


Evangelos K. Oikonomou, MD

A risk score derived from this model — the Childhood and Adolescence Cancer Survivor CardioVascular (CHACS-CV) score (range 0-8) — showed good discrimination for prediction of CVM (Harrell's C-index [95 percent CI]: 0.73 [0.68-0.78], $p<0.001$) and identified a high-risk group (CHACS-CV≥6), with cumulative incidence of CVM over 30 years of 6 percent (95 percent CI: 4.3-8.1 percent) compared to 2.6 percent (95 percent CI: 1.8-3.7 percent), and 0.7 percent (95 percent CI: 0.5-1 percent) in the mid- (CHACS-CV=4-5) and low-risk (CHACS-CV≤3) groups, respectively ($P_{log\text{-}rank}<0.001$). In the validation set, the respective cumulative incidence rates were 4.7 percent, 3.1 percent and 0.8 percent ($P_{log\text{-}rank}<0.001$).

While the CHACS-CV score was validated within the SEER database, Oikonomou noted that further external validation is needed to determine the generalizability of the score. Additionally, he said, the integration of more detailed exposure variables (*e.g,* chemotherapy and radiotherapy regimens, doses, etc.), which were unavailable in the SEER database, will likely further improve the diagnostic value of the score.

"Based on our current findings, we propose the use of the CHACS-CV score as a first-line and cost-effective screening tool to help healthcare providers caring for long-term childhood cancer survivors identify those patients at increased cardiovascular risk who might benefit from early cardiovascular screening and risk reduction strategies," Oikonomou said. ▼

Childhood predictors of adult aortic stiffness and cardiac hypertrophy vary by race, study finds

Researchers have identified childhood metabolic and hemodynamic risk factors associated with future young-adult aortic stiffness and middle-age adult cardiac hypertrophy that differ between blacks and whites.

Justin P. Zachariah, MD, MPH, FAHA, described the findings from a study exploring the "primordial prevention" links between early-life risk factors on subsequent vascular function and consequent cardiac remodeling in an abstract presentation on Monday.

Participants for this study were sampled from the Bogalusa Heart Study, an ongoing community-based prospective study that began enrolling black and white children in 1973.

"In our sample, we observed that in adulthood, blacks had more cardiac hypertrophy and stiffer aortae compared to whites," said Zachariah, assistant professor at Texas Children's Hospital in Houston. "Taking all participants together, stiffer aortae in young adulthood were associated with higher low-density lipoprotein cholesterol and higher mean arterial pressure in childhood. Cardiac hypertrophy in middle age was associated with higher body mass index, higher triglycerides in childhood and stiffer aortae in young adulthood."

The sample participants had at least three study visits over the life course, including at least one visit in childhood, one visit in young adulthood where ultrasound for aorta-femoral pulse wave velocity (afPWV) was performed and another visit in middle age where echocardiographic left-ventricular mass referenced to body surface area (LVMI) was measured (n=1081; 24-44 years of age; 31 percent black; 57 percent female; mean follow-up 27 years). Demographic, anthropometric, hemodynamic and metabolic variables were extracted from each visit.

"We employed multivariable adjusted regression models, which incorporate multiple measurements from variable numbers of visits at variable visit intervals, to determine the associations between childhood and/or cumulative life course traits and aortic stiffness or cardiac hypertrophy," Zachariah said. "Additionally, race-based differences in the relation between the traits and outcomes were formally tested."

Justin P. Zachariah, MD, MPH, FAHA

Zachariah reported higher afPWV was associated with childhood LDL-C in blacks (standardized regression coefficient 0.17; p<0.01) and whites (0.1; p<0.01), while mean arterial pressure was associated only in whites (0.08; p=0.04). Higher LVMI was associated with childhood BMI in blacks (0.27; p<0.001) and whites (0.34; p<0.001), while LDL-C (0.1; p=0.02), TG (-0.14; p<0.01), glucose (0.12; p<0.01) and afPWV (0.11, p<0.01) were associated only in whites.

"The primordial prevention paradigm suggests modifying early life-course risk factors for the development of aortic stiffness and, in turn, cardiac hypertrophy, could prevent CVD events," Zachariah said. "Encouragingly, our previous work demonstrates pediatric lifestyle modification can alter lipid traits with or without weight change."

Zachariah noted that the findings are observational and would benefit from confirmation in other pediatric and adult cohorts.

Exploring racial differences in cross-cultural or international study groups may help disentangle effects specific to local culture or sociodemographic disadvantage versus other biopsychosocial mechanisms," he said. ▼

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!

CANTOS: Anti-IL1β biologic may reduce recurrent cardiac events

Anti-inflammatory therapy with canakinumab to target the interleukin-1β innate immunity pathway may reduce recurrent cardiovascular events even without lowering lipid levels, according to late-breaking study results presented Monday at Scientific Sessions.

In the study, patients who showed high initial response to treatment as measured by hsCRP levels had the greatest reduction in subsequent cardiovascular events. Patients with better hsCRP response also had reduced risk for incident lung cancer and lung cancer mortality.

"There has been growing evidence that reducing inflammation might reduce the risk of cardiovascular disease, but there has never been proof that atherosclerosis is an inflammatory disease," said Paul M. Ridker, MD, MPH, FACC, FAHA. "Now we have seen that reducing inflammation using canakinumab reduces cardiovascular events out to five years. And we have a tool that allows us to predict who is most likely to respond to biologic treatment."

Ridker, the Eugene Braunwald Professor of Medicine at Harvard Medical School in Boston, presented results of a sensitivity analysis of the Canakinumab Anti-Inflammatory Thrombosis Outcomes Study (CANTOS). The primary outcome of CANTOS presented earlier this year reduced CV event rates with no change in lipid levels.

In data presented Monday, a subset of patients whose hsCRP levels fell below 2mg/L after canakinumab had a 25 percent reduction in MACE, a 31 percent reduction in cardiovascular mortality and a 31 percent reduction in all-cause mortality. Patients whose hsCRP remained above 2 mg/L had only a 5 percent reduction in MACE.

The data also showed a direct relationship between individual response to canakinumab and subsequent CV events. The lower the hsCRP levels, the greater reduction in CV events. The results were consistent at all doses of canakinumab used in the trial.


Paul M. Ridker, MD, MPH, FACC, FAHA

REAL-CAD

Patients tolerate high-dose pitavastatin and high-intensity therapy produces better cardiac outcomes compared to lower-dose therapy in patients with stable coronary artery disease, new data from Japan show.

"Western trials have consistently shown that higher-intensity statins are more effective than low-intensity treatment," said Hiroaki Shimokawa, MD, PhD, of Tokohu University Graduate School of Medicine in Tohoku, Japan. "But there's no clear evidence regarding high-intensity efficacy in Asian populations. Most of the high-intensity statin doses seen in the AHA/ACC guidelines are not even approved in Japan."

Shimokawa presented results of the Randomized Evaluation of Aggressive or Moderate Lipid Lowering Therapy with Pitavastatin in Coronary Artery Disease (REAL-CAD) trial on Monday.

REAL-CAD compared 1 mg/day pitavastatin against 4 mg/day in more than 13,000 patients across multiple centers in Japan. The mean age of patients was 68; 91 percent had coronary revascularization, 93 percent were on aspirin and 45 percent were on DAPT.

Patients on the higher dose showed sharp and consistent declines in lipid parameters and hsCRP, Shimokawa reported. High-intensity patients also had a 19 percent reduction in the primary endpoint of cardiovascular mortality, myocardial infarction, ischemic stroke or unstable angina requiring emergency hospitalization. Adding a secondary endpoint of coronary revascularization gave high-dose patients a 17 percent advantage compared to low-dose patients.

High-dose patients had higher rates of muscle-related complaints, but the overall rate was less than 2 percent.

REVEAL

Patients taking the cholesteryl ester transfer protein (CETP) inhibitor anacetrapib have reduced risk for coronary events regardless of whether they also have diabetes, according to a late-breaking study presented Monday.

In the trial, anacetrapib was also associated with a numerical reduction in the risk of non-onset diabetes. An extension to assess longer-term efficacy and safety is ongoing.

Louise Bowman, MD, joint principal investigator for the Randomized Evaluation of the Effects of Anacetrapib through Lipid Modification (REVEAL), detailed the cardiovascular effects of the CTEP inhibitor in patients with diabetes.

Diabetes increases cardiovascular risk and the risk of vascular death, said Bowman, associate professor of clinical trials at Oxford University in the United Kingdom. Diabetes is also associated with low HDL cholesterol and elevated triglycerides.

FOURIER

Two updates of Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk (FOURIER) trial were presented Monday.

The first evaluated the effects in patients with peripheral artery disease and the second examined clinical benefits in patients with a prior MI.

FOURIER randomized 27,564 high-risk, stable patients with a prior MI or stroke or symptomatic PAD who were on background statin therapy to evolocumab or placebo. Subjects were followed for a median 2.2 years.

Evolocumab reduced LDL-cholesterol by 59 percent, an absolute reduction of 56 mg/dl, compared to placebo. Patients with PAD were older than the typical FOURIER patient and had more risk factors, including hypertension, smoking and diabetes, said Marc. P. Bonaca, MD, MPH, associate physician at Brigham and Women's Hospital in Boston. They had about a 60 percent higher primary endpoint rate than other patients, and an 80 percent higher major event rate.

Data showed that evolocumab reduced LDL cholesterol by a median 62 mg/dl. Patients on evolocumab also had significant reductions in primary endpoint and major cardiac events.

Mark S. Sabatine, MD, the Lewis Dexter, MD, Distinguished Chair in Cardiovascular Medicine and professor at Harvard Medical School in Boston, reviewed the clinical benefit of evolocumab in patients with prior MI.

The benefits of treatment tended to be greater in higher-risk patients such as those closer to their most recent MI, with multiple MIs or with multi-vessel CAD, Sabatine reported. A patient's history of coronary disease can be used to identify those most likely to benefit from PCSK9 inhibition, he said. ▼

Distinguished Scientist Lecture to address underlying causes of PAH research

Marlene Rabinovitch, MD, FAHA, focuses her research on discovering the fundamental mechanisms responsible for the loss and obliteration of blood vessels that cause pulmonary arterial hypertension.

Rabinovitch, the Dwight and Vera Dunlevie Professor of Pediatric Cardiology at Stanford University School of Medicine in California, will explore that topic further Tuesday at 12:30 p.m. during the Distinguished Scientist Lecture in Ballroom CD, on the 3rd Level in the Main Building.

Pulmonary arterial hypertension is most challenging in its idiopathic form because there is no underlying medical disorder associated with it, Rabinovitch said. PAH has no signs, and symptoms aren't present until the disease is at a very advanced stage and a patient has extensive blood vessel damage, she said.

"Treatment of PAH is particularly challenging when the disease is advanced," Rabinovitch said. "The current standard of care for PAH is to try to open as many non-obliterated vessels as possible using vasodialator agents."

While those therapies can improve survival and quality of life, they do not directly address the mechanisms that cause the progressive occlusive changes in the pulmonary arteries, she said. Over time, symptoms increase and heart failure necessitates lung transplantation. The disease will not be curable "until we find treatment that can reverse the underlying pathology," Rabinovitch said.

Rabinovitch has contributed to the field of pediatric cardiology for more than 35 years, working to improve understanding and management of congenital heart disease, PAH and other causes of vascular and heart damage.

To learn more about the underlying PAH mechanisms, Rabinovitch and her team turned to a genetic breakthrough that identified a *BMPR2* mutation in 70 percent of patients with a familial form of PAH, and in 20 percent of those with sporadic cases of idiopathic PAH.

During her lecture, she also will discuss the discovery of an enzyme produced by smooth muscle cells and neutrophils that degrade elastic fibers causing vascular stiffness. This enzyme not only appears to be a key determinant of progressive loss and occlusion of the pulmonary arteries, but is also elevated in coronary and other diseased blood vessels.

"The enzyme is released with relatively minor provocation of PAH cells," she said. "We need to understand what causes a viral-like response in PAH inflammatory cells associated with elevated production and release of the elastic fiber degrading enzyme."

Rabinovitch also will show how some of the discoveries in her laboratory are resulting in Phase I and II clinical trials that could influence how patients are treated in the future. ▼


Marlene Rabinovitch, MD, FAHA

LECTURE PREVIEW

Distinguished Scientist Lecture: Genetic and Epigenetic Determinants of the Inflamed Vessel Wall Inform New Treatments for Pulmonary Hypertension and Other Vascular Diseases

12:30-1:30 p.m. Tuesday
Ballroom CD, 3rd Level, Main Building

PRESIDENT continued from page 1

families, not just in the U.S., but around the world. I believe the people in this room have the power — and even the duty — to change that. Together, we can make sure old men and old women are regulars at family reunions. … In other words, I look forward to a future where people have the exact opposite experience of my family, that children grow up surrounded by so many healthy, beloved, elderly relatives that they couldn't imagine life any other way."

Warner, a longtime AHA volunteer, began his one-year term as the organization's volunteer leader in July. Thus far, he's represented the organization everywhere from the nation's capital to Panama and Beijing. Scientific Sessions is usually among the highlights of a president's tenure.

"John wanted to reinforce that this incident underscores the important message that he left us with in his presidential address yesterday — that much progress has been made, but much remains to be done. Cardiac events can still happen anytime and anywhere," said Nancy Brown, chief executive officer of the AHA.

Warner spent the bulk of his medical career as an interventional cardiologist, often performing the procedure he underwent Monday morning.

His extensive training in cardiac catheterization came at Duke. In 2003, he returned to UT Southwestern — where he'd done his residency after medical school — to lead the cath lab. He took on other leadership roles over the years, then began expanding his influence beyond his hospital system by working with the AHA.

Warner played a lead role in turning the nation's ninth-largest city smoke-free and in setting up a chain of survival for people who suffer a particular type of heart attack in Dallas County.

"I began to see the health of my community in a different way," he said in Sunday's speech. "Being part of this effort helped me realize that the voices of doctors, nurses and healthcare leaders needed to be heard within the community. … I vowed to do more of this, to broaden my involvement in my community and to make a difference on a larger scale."

A great opportunity came in 2010, when UT Southwestern decided to build an $800 million hospital. Warner became the physician lead on its design. His efforts were so lauded that he became CEO of the healthcare system in 2012, the same year the hospital opened.

The toughest part of making that move, he said in his speech, was ending his days as an interventional cardiologist.

"You don't want a guy who wears a suit all day dropping by the cath lab to put in your stent," he said, laughing.

Warner was born in Lubbock and raised in West Texas. His primary passions as a youth were science and sports, especially running.

He attended Abilene Christian on a track and cross-country scholarship and was part of several NCAA championship teams. During a specific race, he realized he'd be better off trying to become a doctor than trying to make the Olympics.

He went to medical school at Vanderbilt University in Nashville, Tennessee, initially thinking he'd go into sports medicine. Cardiology captivated him for a variety of reasons, including his family history.

"The first time I heard the phrase 'heart attack' was at age 6, when my great grandfather died suddenly," he said in his speech. "Like many such victims, he had no known heart disease and his death came as a shock to our family. Later, during my residency, both of my grandfathers died of cardiovascular disease. … After my son was born and we were introducing him to his extended family, I realized something very disturbing: There were no old men on either side of my family. None. All the branches of our family tree cut short by cardiovascular disease." ▼

Precision Cardiovascular Medicine Institute Lounge

Tuesday is the last day to visit the Recharge Institute Lounge to learn more about the AHA's Institute for Precision Cardiovascular Medicine. Drop by the lounge at 10 a.m. for a 30-minute demo of the AHA Precision Medicine Platform, or stop in for a free cup of coffee or to recharge your devices at one of the lounge's charging stations.

HOURS

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

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Fogarty: Global cardiovascular research benefits all countries


Thomas A. Gaziano, MD, MSc

The Fogarty International Center will commemorate its 50th anniversary with a session Tuesday that explores the history, future and benefits of global cardiovascular research.

"Fogarty, NHLBI, NIH and the Future of Global Cardiovascular Health Research," which begins at 2 p.m. in Ballroom A, 3rd Level, Main Building, includes lectures from key thought leaders in global health and will showcase the importance of supporting open research in other countries.

"About 15 years ago, Fogarty recognized that cardiovascular disease is important globally and is not just a high-income-country problem," said Thomas A. Gaziano, MD, MSc, an organizer of the event and director of the Global Cardiovascular Health Policy and Prevention Unit at Brigham and Women's Hospital in Boston.

Though Fogarty helps focus NIH research, training and funding internationally, research dollars invested abroad benefit recipient institutions and U.S. funding agencies, Gaziano said.

The NIH and the NHLBI have provided major funding for centers in Africa, India, China and Latin America to study questions that have importance locally. The centers also improve understanding of cardiovascular disease globally and create local training opportunities.

"People understandably want to know what the U.S. gets out of research dollars spent in these countries," Gaziano said. "Not only is there better understanding of chronic disease in different settings, but there are a variety of developing technologies such as mobile health that have major applications in the U.S. as well as in developing countries."

While Fogarty first focused on infectious disease and vaccine research, 1993's groundbreaking Disease Control Priorities in Developing Countries (DCP) helped identify the major sources of chronic disease in low- and middle-income countries. The World Bank also funded the publication to systematically assess the cost-effectiveness of various interventions.

"We're at a crossroads in trying to understand where U.S. policy is in relation to global research and what the status of global health research really is," Gaziano said. "While our first goal is to recognize Fogarty and its continuing role in global cardiovascular disease research, the second goal is to recognize the NIH and the National Heart, Lung, and Blood Institute as major supporters of cardiovascular research in low-income-country settings through funding to support centers of excellence." ▼

Community-based, self-care intervention program improves CVD risk factors

The results of a randomized controlled trial presented Monday show that a community-based, culturally appropriate self-care cardiovascular disease risk-reduction intervention program was effective in promoting improvement of multiple CVD risk factors.

The results of the trial were presented by Debra K. Moser, PhD, RN, professor and Linda C. Gill Chair of Cardiovascular Nursing and director of the RICH Heart Program at the University of Kentucky College of Nursing in Lexington.

"Participants in our study came from the Central Appalachia area of Kentucky — an underserved, socioeconomically distressed region known for having some of the worst health disparities in the country, including cardiovascular disease," Moser said.

The study enrolled 352 individuals living in the region who were at risk for cardiovascular disease by virtue of having two or more CVD risk factors. In collaboration with an advisory board of lay community members, business owners, church leaders and healthcare providers, the researchers developed an intervention program to address six CVD risk factors: tobacco use, blood pressure, lipid profile, body mass index, depressive symptoms and physical activity levels. Participants in the trial were randomized to either the intervention program or usual care (referral to a primary care provider).


Debra K. Moser, PhD, RN

"The intervention was delivered to groups of 10 or fewer people over a six-week period, during which they participated in a series of modules designed to educate, provide the skills and motivation for behavior change and promote self-care to address the different risk factors," Moser said. "For example, we introduced people to different sorts of foods at the sessions and taught them how to adapt their favorite recipes to healthier versions. We also encouraged physical activity and mapped out safe walking paths and safe activity areas for them in the community where they lived."

The targeted CVD risk factors were measured at baseline, then four and 12 months post-intervention. Linear mixed models analysis was used to compare outcomes between the groups across time.

Among their findings, Moser reported that the intervention produced improvement in systolic and diastolic BP (p=0.002 and p=0.001 for group X time interaction [GXT]), total cholesterol (p=0.026 GXT), high density lipoprotein (p=0.026 GXT), body mass index (p=0.017 GXT), smoking status (p=0.001 GXT), physical activity (p=0.001 GXT) and depressive symptoms (p=0.019 GTX) compared to the control group. All improvements were maintained through 12 months. There were no differences seen across time by group in low-density lipoprotein or triglyceride levels.

"One of the big reasons we think the intervention was effective is because we really didn't tell people that they had to make these huge and immediate changes in their lifestyles — we simply tried to introduce healthier behavior into what people were already doing [and] what they were already eating on a daily basis," Moser said. "A great thing about the program is it doesn't require specialized personnel to deliver the intervention and it doesn't require a lot of specialized resources. It's a program that could be easily adaptable to all sorts of practices in all kinds of settings that want to improve their ability to provide preventive services." ▼

Text messaging program improves patient adherence to dietary recommendations

Results from a randomized controlled trial demonstrated that a lifestyle-focused text-message intervention program improved dietary patterns in patients with coronary heart disease. The most recent findings from the TEXT ME Study were presented Monday in an abstract poster session by Karla Santo, MD. Santo was selected as one of this year's Paul Dudley White International Scholars for the work presented in this abstract.


Karla Santo, MD

In the TEXT ME Study, 710 patients with CHD (mean age 57.6 ± 9.2 years, 82 percent male) were randomized to receive either usual care (control group) or a text-message program (intervention group), which consisted of semi-personalized text messages providing information, advice, motivation and support for patients to improve their diet, increase their physical activity levels and encourage smoking cessation, if relevant.

"The messages were delivered by an automated message software program, with patients receiving four messages per week for six months, including at least one message per week focused on dietary recommendations and general healthy eating tips," said Santo, a research fellow at the George Institute for Global Health and PhD candidate at the University of Sydney in Australia.

The patients' dietary patterns were assessed, both at baseline and at six months, using a self-reported questionnaire to determine how well they were adhering to dietary guideline recommendations, including consumption of vegetables, fruits, fish, unsaturated fat oils and spreads, takeaway foods, salt and alcohol drinks.

At baseline, 54 percent of the patients were meeting four or more of the dietary recommendations (intervention 53 percent versus control 56 percent, p=0.3762). At six months, Santo reported that 93 percent of patients in the intervention group were achieving at least four of the eight guideline recommendations, compared to 76 percent of patients in the control group (p<0.0001). Specifically, she noted, the text messages had the most impact on consumption of vegetables, fruits and fish, and reduced consumption of takeaway foods and salt.

"We know that a healthy diet plays an important role in primary and secondary prevention of CHD, so it's important to encourage and regularly reinforce adherence to a healthy diet, especially for those patients with a previous history of CHD," Santo said. "This text-message program is a simple and scalable intervention to reinforce healthy eating behaviors that can be delivered to a large number of people at a low cost. It can be especially useful in reaching those people who cannot attend healthcare facilities on a regular basis or who live in rural and remote areas."

Santo said her group is currently conducting a larger trial of the text-messaging program with longer patient follow-up, as well as investigating the efficacy of a mobile app designed to improve medication adherence. ▼

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Rehab program associated with significant survival benefit in premature CAD

The completion of a cardiac rehabilitation program has been found to be significantly associated with reduced mortality in patients with premature coronary artery disease, according to research presented Monday at Scientific Sessions. However, only about a third of CR potential candidates actually complete the program, according to Michael Khoury, MD.

"Cardiac rehabilitation is an established strategy that is widely used to help prevent repeat cardiac events in those with coronary artery disease," said Khoury, of the University of Alberta in Edmonton, Canada. "However, the effectiveness of cardiac rehab in patients with premature coronary artery disease, defined as men younger than 55 years old or women younger than 65 years, has not been well established. That was the motivation for our study."


Michael Khoury, MD

To carry out the study, the researchers linked data from two different databases in Alberta, Canada — Total Cardiology-Rehabilitation (TC-R) and Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH). They analyzed data on all subjects in Calgary, Canada, with premature CAD (>/=1 vessel CAD on angiogram in women <65 and men <55 years) between 1996-2016. Logistic regression models were constructed to assess predictors of CR referral and completion. A Cox proportional hazard model evaluated the associations between CR status (not referred; referred, did not complete; completed CR) and survival. All models were adjusted for available demographics, disease severity and co-morbidities.

A total of 11,119 subjects (3,608 women; median age: men, 49.7; women, 56.9 years) with premature CAD were identified. Nearly two-thirds of subjects (7,071 or 63.1 percent) were referred and 3,982 (56.3 percent of those referred) completed CR. In the overall cohort, only 35 percent of eligible patients completed cardiac rehab, Khoury said.

"We also found that men were more likely than women to be referred and to complete cardiac rehab," Khoury added. "Additionally, patients with diabetes and those who were current smokers were also less likely to complete cardiac rehab."

Median follow-up was 9.5 years (IQR 5.2, 14.4), and there were 1,329 deaths. In a fully adjusted model, Khoury reported that CR completion predicted better survival (HR 0.48, 95 percent CI 0.41, 0.56), but referral alone did not (HR 0.87, 95 percent CI 0.74, 1.01).

"Given the significant survival benefit associated with the successful completion of a cardiac rehabilitation program, we must increase our efforts to improve referral and completion of this established and beneficial prevention strategy," Khoury said. ▼

Cardiac rehabilitation may protect against abdominal aortic aneurysm expansion

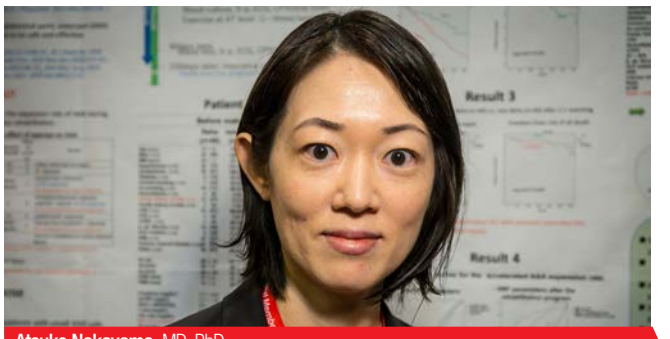
In patients with a small abdominal aortic aneurysm (AAA), cardiac rehabilitation via a well-modified, supervised exercise program may protect against AAA expansion, according to the results of a study presented during an abstract poster session on Monday. Atsuko Nakayama, MD, PhD, presented the findings.

"A previous experimental study using AAA-modeled mice suggested that a protective effect of cardiac rehabilitation was achieved through the preservation of endothelial integrity, reduction in inflammation and oxidative stress and inhibition of the osteogenic pathway," said Nakayama, a research associate at the University of Tokyo Hospital in Japan. "In real-world practice, however, we are hesitant to recommend exercise training for AAA patients because we worry that exercise might elevate their blood pressure and trigger rupture of the aneurysm."

In the study, Nakayama and her colleagues sought to determine whether a modified exercise program, in which excessive blood pressure elevation was carefully avoided, has a beneficial effect on AAA expansion rate. The risk of AAA repair surgery, major adverse cardiac events and mortality in long-term follow-up were also evaluated.

The researchers conducted a cohort study on 1,515 patients who were diagnosed as having small AAA before surgery at two high-volume hospitals in Tokyo from 2004 to 2015, Nakayama said. They used propensity score matching to compare the mortality and clinical outcomes, including AAA expansion rate between two groups — a rehabilitation group (Reha) and a non-rehabilitation group (non-Reha).

Background characteristics were similar between the two groups and the average AAA size was 41 mm. The rehabilitation group participated in a carefully supervised and monitored exercise program, with particular caution given to maintaining stable systolic blood pressure during the exercise.


Atsuko Nakayama, MD, PhD

Among their findings, Nakayama reported the risk for AAA repair was significantly lower in the Reha group, before and after propensity score matching (HR, 0.43; 95 percent CI, 0.25-0.72; p=0.001 and HR, 0.22; 95 percent CI, 0.12-0.42; p<0.001). Moreover, the expansion rate of AAA was slower in the Reha group (before matching: Reha group, 2.3 ± 3.7 mm/yr versus non-Reha group, 3.8 ± 3.4 mm/yr; p=0.008; after matching: Reha group, 2.1 ± 3.0 mm/yr versus non-Reha group, 4.5 ± 4.0 mm/yr, p<0.001). Additionally, the elevation of blood pressure during exercise was positively related to the AAA expansion rate after the rehabilitation program (r=0.569, p<0.001).

"In this cohort study, we also observed that exercise improved the level of C-reactive protein (CRP), but we couldn't find the relation between inflammation and an expansion rate of AAA," Nakayama said. "While further research is needed to determine the long-term effectiveness of cardiac rehabilitation in AAA patients, based on these findings we believe our supervised cardiac rehabilitation program, which was safely performed, clearly suppressed the recurrence of major cardiovascular events as well as the expansion of the abdominal aortic aneurysm." ▼

Plasma microRNAs associated with dysregulated cardiac remodeling in AF

A data analysis of the Framingham Heart Study Offspring Cohort revealed several microRNAs associated with heart disease are also associated with left atrial functional index (LAFI) and atrial fibrillation.

These findings suggest that an underlying framework of microRNA-mediated cardiac electrical and structural remodeling promotes vulnerability to AF, according to study results presented in an abstract poster session Monday by Aditya Vaze, MD.

"The purpose of our study was to evaluate the novel genetic pathways that contribute to the development of atrial fibrillation," said Vaze, a resident physician at the University of Massachusetts Medical School in Worcester and author of the study "Relations Between Plasma microRNAS, Echocardiographic Markers of Atrial Remodeling, and Atrial Fibrillation: Data From the Framingham Offspring Study."

"Our goal was to measure the association between plasma microRNAs, molecules involved in gene regulation during cardiac development and in diverse cardiovascular pathology, and left atrial functional index, an echocardiographic marker of pathological atrial structure and function, as well as the association with atrial fibrillation," she said.

Building on prior research that identified microRNAs associated with AF, the investigators analyzed data from 1,840 Framingham Offspring Cohort participants who underwent genomic profiling and echocardiographic measurements between 2005 and 2008. They quantified expression of 340 miRNAs from plasma using high-throughput quantitative reverse-transcriptase PCR (RT-qPCR) and related plasma miRNA levels to LAFI and then AF. Models were adjusted for the CHARGE-AF risk score and Bonferroni correction for multiple testing was employed.

FHS Offspring participants included in the analysis had a mean age of 66.6±9.3 years, 54 percent were women, 8 percent had AF at the time of examination, 6 percent developed AF over seven years of follow-up and the mean LAFI was 31.2 ± 14.2. As a result of their analysis, the investigators identified 73 miRNAs that were associated with LAFI, including four that were also associated with AF: microRNAs-106b, 26a-5p, 324a-3p and 20a-5p.

"A very important finding was that, as the levels of these microRNAs decreased, there was a corresponding decrease in left atrial function, as well as an increased risk for atrial fibrillation," Vaze said. "Our goal is to further investigate the genetic pathways that these microRNAs regulate in order to better understand the pathophysiology of atrial fibrillation on a molecular and cellular level."

If their findings are validated in other cohort studies, the investigators said they believe the findings could form the basis for developing therapies that target microRNAs to reduce pathological atrial remodeling and, ultimately, decrease the risk of atrial fibrillation. ▼

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/

The conference is coming to a close

Don't miss your chance to aim low in a game of *CholesterBall* at **booth 321**

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]

*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