

# AHA names top heart disease and stroke research advances of 2021



As the COVID-19 pandemic continued to dominate public health headlines in 2021, vital research progressed on a variety of cardiovascular — and yes, coronavirus — fronts.

Heart disease and stroke research remains more relevant than ever. While over 800,000 Americans have died from COVID-19 in the past two years, more than 800,000 Americans die every year from cardiovascular diseases.

Some of 2021's most consequential findings addressed cardiovascular-relevant diseases such as kidney failure and obesity. Studies highlighted better ways to deliver care for stroke, heart failure and high blood pressure. And cutting-edge developments in the practice of precision medicine could improve the futures of old and young.

As a leading funder of heart- and stroke-related research, the AHA compiles an annual recap of noteworthy scientific studies. Here is an overview of 2021's pivotal developments.

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# A stubborn health challenge, obesity, meets an effective medicine

Some 650 million people worldwide have obesity, and the problem continues to grow.

But a drug developed for Type 2 diabetes, semaglutide, may help. In June, semaglutide, as a weekly under-the-skin injection, became the first drug since 2014 to be [approved](#) by the Food and Drug Administration for chronic weight management.

A series of studies in 2021 detailed potential weight loss benefits of semaglutide even in non-diabetic subjects. Investigators in an international trial called [STEP 1](#) tested semaglutide injections vs. placebo in about 1,900 patients, most of them women, who had obesity or were overweight and had at least one other weight-related risk factor (but not diabetes). After 68 weeks, the two-thirds of subjects given semaglutide lost an average of 14.9% of their body weight, compared with just 2.4% among those given the placebo, the researchers reported in the New England Journal of Medicine.

[STEP 3](#), another placebo-controlled trial, included eight weeks of a low-calorie diet at the outset and intensive behavioral therapy for 68 weeks for both study groups. Among about 600 U.S. participants, nearly 500 of them women, those given semaglutide on average lost 16% of their body weight, compared with a 5.7% average loss in the placebo group, researchers wrote in the Journal of the American Medical Association.

Another international study, [STEP 4](#), examined whether the weekly shots of semaglutide vs. placebo along with lifestyle counseling could help maintain weight loss. About 800 participants, most of them women, were treated with semaglutide for 20 weeks, charting an average 10.6% body weight loss plus other health improvements.

Then one-third were switched to placebo injections for 48 weeks. On average, those who continued on semaglutide lost 7.9% of their body weight and had additional health improvements over the additional 48 weeks, while people on placebo saw their weight increase by 6.9%, investigators reported in the Journal of the American Medical Association.

Meanwhile, doctors trying to balance the risks vs. rewards of bariatric surgery in patients with heart troubles have a [new study](#) of about 2,600 patients in Canada to help inform decision-making. That study, published in the AHA journal Circulation, used medical records to track two sets of patients with cardiovascular disease and severe obesity.

Compared with matched peers in similar health who did not have bariatric surgery, those who underwent the operation had a 42% lower risk of dying or having major cardiovascular problems such as heart attack, stroke and heart failure hospitalization. The findings require confirmation by a large-scale, randomized trial, the authors note.

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[Physician honored for promoting access to cardiology care](#)

# Clinical trials continue to expand a diabetes drug's turf

On the heels of previous successes, medicines called SGLT2 inhibitors have continued to extend their potential beyond their initial approved use to treat Type 2 diabetes.

In late 2020, the [SCORED](#) trial studied the SGLT2 inhibitor sotagliflozin in patients with Type 2 diabetes and chronic kidney disease. Compared with a placebo group, those receiving the drug had a lower risk of hospitalization/urgent care for heart failure or death from heart disease. Findings from another placebo-controlled trial released in late 2020, [SOLOIST-WHE](#), showed sotagliflozin could lower those same risks in people with diabetes and a recent worsening of heart failure.

Other research is suggesting SGLT2 inhibitors might also help patients who have heart failure with preserved ejection fraction, a condition with few available treatments ("ejection fraction" describes the strength of the heart's left ventricle). In the [EMPEROR-Preserved](#) trial testing the SGLT2 inhibitor empagliflozin in nearly 6,000 of these patients, investigators found the drug could reduce rates of cardiovascular death or hospitalization due to heart failure by over 20%. Empagliflozin appeared effective in patients both with and without diabetes, scientists reported in *The New England Journal of Medicine*.

## Drug trials score new successes in avoiding cardiovascular complications of diabetes

As Type 2 diabetes rates climb worldwide, therapies addressing diabetic complications are an urgent priority. People with Type 2 diabetes have at least double the risk of developing and dying from cardiovascular disease, and kidney disease is a common long-term complication.

Research had already shown that the drug finerenone could improve cardiovascular outcomes and limit renal decline in patients with Type 2 diabetes and advanced kidney disease. A new, international study expanded the list of patients who might benefit.

Like the earlier study, this one, dubbed [FIGARO-DKD](#), was conducted in people with Type 2 diabetes. But this time participants had earlier-stage kidney disease and severely elevated albumin in the urine, a marker of kidney damage, or later stage disease but moderate albuminuria. Among over 7,400 patients, finerenone reduced risk of cardiovascular death or complications by 13% compared with placebo. The reduction was primarily a result of a decrease in heart failure hospitalizations.

Another international study, [AMPLITUDE-O](#), tested the drug efpeglenatide in people with Type 2 diabetes and a history of cardiovascular disease or current kidney disease plus at least one other cardiovascular risk factor. Among over 4,000 participants, weekly under-the-skin injections of efpeglenatide were linked to risk factor

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improvements and 27% lower odds of experiencing a heart attack, stroke, or death from cardiovascular or unknown causes. Both trials were described in the *New England Journal of Medicine*.

## Precision medicine may help spare hearts in two devastating diseases

Using precise gene editing, investigators may have opened new therapeutic doors for two life-threatening diseases, transthyretin amyloidosis and Duchenne muscular dystrophy.

In transthyretin amyloidosis, also called ATTR amyloidosis, abnormal versions of the transthyretin protein, or TTR, build up in the heart, nerves and other tissues. The condition, which often goes undiagnosed, can cause symptoms including numbness and weakness, affect balance and posture, lead to cardiomyopathy and heart failure, and deprive people of their mobility and independence.

But a [small study](#), published in the *New England Journal of Medicine*, offers hope that a therapeutic agent based on the advanced gene editing technology CRISPR-Cas9 (recently recognized with a Nobel Prize) may change the course of the disease. Scientists targeted the gene defect responsible for the faulty TTR protein in six volunteers with hereditary transthyretin amyloidosis. Four weeks after the therapy was infused, concentrations of the aberrant protein in patients' blood fell on average 52% with a lower treatment dose and 87% with a higher dose.

Other research explored potential benefits of a CRISPR-Cas9-based therapy in Duchenne muscular dystrophy, which affects 1 in 5,000 boys. The disease causes severe muscle wasting and weakness, as well as cardiomyopathy and breathing complications that are common causes of death.

In a [series of experiments](#) described in the AHA journal *Circulation Research*, Dallas scientists examined whether gene editing might help protect patients' hearts. The team created induced pluripotent stem cells — a type of reprogrammed cell that can grow into different adult cell types — from a patient with Duchenne muscular dystrophy and from a healthy brother.

Gene editing allowed the patient's cells to become heart muscle cells that looked and functioned like those from the healthy brother. And in a scenario closer to how the disease appears in patients, cells that were edited later (once they became heart muscle cells) had less potential for arrhythmia, the team reported.

Also, applying their gene editing approach to a mouse model of Duchenne muscular dystrophy, the scientists showed that edited cells might improve heart abnormalities.

# Findings highlight simple successes in BP control, from kitchen table to clinic

There's no substitute for good cardiovascular health. But substitution might help — by replacing 25% of the sodium chloride in your salt shaker with potassium chloride instead.

The massive [Salt Substitute and Stroke Study](#) from China, involving 600 rural villages and nearly 21,000 people, documents the benefits in a population where eating processed food is uncommon but salt intake is high. Participants either had a history of stroke or were 60 or older with poorly controlled high blood pressure.

With an average follow-up of nearly five years, rates of stroke were 14% lower in villages assigned to use the salt mixture containing 25% potassium chloride, compared with those where regular (all-sodium-chloride) salt use continued, researchers wrote in the *New England Journal of Medicine*. Observers, however, note that elsewhere in the world, commercial food preparation — rather than salt added at home — is a major source of dietary sodium chloride.

[Another large trial](#) from China, dubbed STEP, which focused on people ages 60 to 80, sheds new light on potential benefits of tighter blood pressure control.

That trial enrolled over 8,500 people with hypertension (defined as a systolic blood pressure of 140 to 190 mmHg or taking antihypertensive medication). Those with a history of stroke were excluded. Half were assigned to intensive treatment, with a target for systolic blood pressure — the top number in a blood-pressure reading — of 110 to less than 130 mmHg. The systolic target for the rest was 130 to less than 150 mmHg.

Over more than three years of follow-up, researchers tracked whether participants died of cardiovascular disease or had a stroke, heart attack, heart failure or various other heart problems. Those outcomes occurred in just 3.5% of people with the intensive treatment goal, scientists reported in the *New England Journal of Medicine*, compared with 4.6% in the other group. The findings support current AHA and American College of Cardiology guidelines for managing high blood pressure, which set a systolic goal of less than 130 mmHg for most patients.

## COVID-19 puts young people's heart health in the headlines

For children and young adults, the pandemic has posed special challenges in the form of rare but serious conditions linked to the virus or to two of the vaccines. Experts have acted quickly to characterize those conditions.

In the journal *Circulation*, European investigators presented a [heart-focused snapshot](#) of a newly emerging, coronavirus-related condition — multisystem inflammatory syndrome in children. MIS-C can cause dangerous inflammation in the heart, lungs, kidneys, brain, skin, eyes and other organs.

The study, involving 286 young patients with MIS-C from across Europe, captured the new syndrome's most common cardiac implications: arrhythmias, shock, reduced ejection fraction, dilated coronary arteries and fluid buildup in the pericardial sac around the heart. Inflammatory markers were raised in most of the children, the scientists noted. And nearly two-thirds had evidence of previous infection with the virus that causes COVID-19.

Other research sought to better understand cases of myocarditis, or heart muscle inflammation, arising after vaccination with either of the new mRNA vaccines, from Pfizer-BioNTech or Moderna. Leveraging nationwide data in the wake of a brisk immunization campaign in Israel, one [massive study](#) found only 136 definite or probable myocarditis cases, one fatal, among over 5 million people ages 16 and older who were given the Pfizer vaccination from December 2020 through May 2021.

Risk was highest within a week after the second dose in the two-shot series. In all, almost 4 in 100,000 boys or men, and fewer than 1 in 100,000 girls or women, developed myocarditis within 30 days after their second Pfizer dose, the researchers calculated. But those odds were almost 11 in 100,000 in men ages 20 to 24 and 15 in 100,000 among males ages 16 to 19, the group with the highest rate.

The [other study](#), of 2.5 million patients at a major health care provider and insurer in Israel, pinpointed 54 myocarditis cases in a five-month window and highlighted medical details of the cases.

Overall, the risk of myocarditis after vaccination was low, the studies concluded. Most cases were mild or moderate and eventually resolved. Both studies were published in the *New England Journal of Medicine*.

The American Heart Association continues to [recommend](#) vaccination against COVID-19 in adults and eligible children and notes that ongoing research clearly shows a far greater risk of heart complications, stroke and blood clotting problems after COVID-19 infection than after vaccination.

## Fighting the flu heads off cardiovascular and other risks, too

Vaccinating people against the flu within 72 hours of a heart attack or invasive coronary procedure may yield health benefits beyond flu season, [research published in \*Circulation\*](#) found.

An international team of investigators gave 1,272 heart patients a flu shot and 1,260 a saline placebo, then tracked their health for a year. Compared with the placebo group, those who were vaccinated were 28% less likely

to have a heart attack or a dangerous clot in a coronary stent or die of any cause, the study found. They also were 41% less likely to die of cardiovascular disease.

## Stroke advances address the need for speed

As the saying goes, time is brain: Fast treatment that removes a blockage and restores blood flow can minimize the damage stroke inflicts.

Two studies in 2021 examined efforts to shave minutes off the time from stroke onset to initiation of therapy. Both reported better patient outcomes.

One study conducted in Houston and six other U.S. urban centers [examined mobile stroke units](#), ambulances with specially trained staff, a CT scanner and laboratory testing equipment that allows for stroke diagnosis and treatment in the vehicle. Staff in the mobile unit can give patients tPA, a clot-dissolving medicine that can save lives and reduce disability when administered promptly. Mobile stroke units can also help determine, before reaching the hospital, which patients are candidates for endovascular thrombectomy, or EVT, which removes the blockage in the brain that caused the stroke.

The study focused on 1,047 patients eligible for tPA. Compared with usual emergency medical services, additional dispatch of a mobile stroke unit was linked to more patients receiving tPA, plus substantially shortened times from stroke onset to the start of treatment, and led to more patients returning to normal activities by 90 days later, researchers reported in the *New England Journal of Medicine*.

Meanwhile, in stroke patients believed to have a blockage in one of their major brain arteries, expediting their transfer for angiography to quickly image those arteries and remove any clots was linked to less severe disability later, a [study from Spain](#) found. Among 174 patients in the study who were within six hours of stroke onset, roughly half were transferred directly to a Barcelona hospital's angiography suite, bypassing the emergency department and conventional imaging.

Upon arrival at the hospital, the direct-transfer patients underwent EVT and had blood flow in the brain restored more quickly, the study in *JAMA Neurology* showed.

In another study, [STROKE-AF](#), researchers sought a better understanding of the risk of atrial fibrillation — a type of irregular heartbeat that increases stroke risk — in patients who had already had a [Print](#) due to a blockage in large or small blood vessels.

Over 400 participants at 33 U.S. sites were assigned to usual care including external heart monitoring, or to long-term monitoring with an inserted cardiac device within 10 days of their stroke. After a year, Afib had been detected in 12% of those with the inserted monitor, compared with fewer than 2% of those receiving usual care, the investigators reported in the *Journal of the American Medical Association*.

# Heart-health issues in pregnancy put mothers, infants and adolescents at risk

Cardiovascular disease is the No. 1 cause of maternal death in the U.S. Risk factors that arise before pregnancy can threaten pregnancy outcomes and raise cardiovascular dangers later. And a recent study finds that pre-pregnancy heart health is getting worse.

[Researchers analyzed](#) over 31.6 million U.S. birth certificates from 2011 to 2019, focusing on four cardiovascular-related data points collected about mothers — prepregnancy smoking, body mass index, and presence of high blood pressure or diabetes — assigning one point for each optimal metric. In 2011, 42.1% of women had ideal scores of 4 but in 2019, only 37.7% did, the research team reported in the *American Journal of Preventive Cardiology*.

Black women, women on Medicaid and those receiving support from WIC — the Special Supplemental Nutrition Program for Women, Infants, and Children — were least likely to have ideal scores for cardiovascular health in 2019, the study found. Hispanic women, meanwhile, had the greatest decline in prepregnancy heart-health scores over the study period.

Rates of obesity and diabetes are on the rise among young adults, the study notes, and are disproportionately high among Hispanic people. Future studies, the authors say, should include more factors associated with heart health and aim to capture how social factors that influence health, including structural racism, are related to women's health before pregnancy.

Other research indicates that poor maternal heart health can echo far beyond pregnancy and the postpartum months — and into children's adolescence.

In a [study of over 2,300 mothers](#) and their children in the U.S., Canada and four other nations, poor maternal heart health at an average of 28 weeks into pregnancy was linked to poorer heart health in the children later, at ages 10 to 14. The research was described in the *Journal of the American Medical Association*.

Maternal health was scored based on five measures of cardiovascular health: body mass index, blood pressure, total cholesterol, glucose level and smoking status. Children were scored on those factors minus smoking status. Only about one-third of mothers had top scores reflecting all ideal metrics; about 42% of children did.

As gestational health scores for the mothers worsened, the prevalence of ideal scores among the children declined. This suggests a general profile of cardiovascular health during pregnancy (rather than just focusing on individual risk factors) may shed light on fetal health and help identify newborns at risk for poor heart health later, the authors wrote.



# Studies scrutinize the risk of extra anti-clotting treatments

Two studies in 2021 took new looks at old habits related to the use of antiplatelet medicines.

An international trial called [MASTER DAPT](#) examined outcomes for over 4,500 patients after coronary angioplasty and implantation of a particular type of biodegradable, drug-eluting stent. Among patients who were at high risk of bleeding, shortening the time they received dual antiplatelet therapy to one month appeared to lower that risk without worsening cardiovascular outcomes including heart attack, stroke and death, scientists reported in the New England Journal of Medicine.

[Research from Michigan](#), meanwhile, suggests a need to review aspirin use in patients taking a direct oral anticoagulant, or DOAC — any of several anti-clotting drugs that are an alternative to a vitamin K antagonist like warfarin.

The study first looked at records of 3,280 people who were being treated for atrial fibrillation or blood clotting in the veins (venous thromboembolism) but had no recent heart attack or history of heart valve replacement. Nearly one-third were taking aspirin on top of a DOAC although they had no clear reason to, investigators reported in JAMA Internal Medicine. Records of two matched groups of patients, over 2,000 in total, who were using a DOAC revealed that over an average of almost 21 months, those also taking aspirin had a higher risk of bleeding problems and related hospitalizations without an improvement in clotting rates.

## A pill packed with drugs for cholesterol and BP may help prevent heart disease

In the challenge of preventing cardiovascular disease, a one-pill-fits-all approach could have a broad public health impact.

A [large international study](#) published in the New England Journal of Medicine found that such a "polypill," taken with aspirin, was associated with a 31% lower risk of cardiovascular death or events including heart attack, stroke, cardiac arrest and heart failure, compared with placebo. The polypill contained four drugs: simvastatin, which is used to treat high cholesterol and triglycerides, and the blood pressure medicines hydrochlorothiazide, atenolol and ramipril.

Research subjects — men 50 or older and women 55 or older — did not have established cardiovascular disease, but scoring suggested they had at least an intermediate risk level.

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