

## Medical News

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## Fluctuating Cholesterol, Triglycerides Tied to Increased Dementia Risk

MEDSCAPE

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Fluctuating cholesterol and triglyceride levels in older adults are associated with a greater risk of Alzheimer's disease (AD) and Alzheimer's-related dementia (ADRD), a new study suggests.

Participants with the greatest variability in total cholesterol levels had a 19% increased risk for AD or ADRD within 12 years of baseline than those with stable levels. In addition, those with the highest variability in triglycerides had a 23% increased risk. The study did not differentiate between dementia types.

"Routine screenings for cholesterol and triglyceride levels are commonly done as part of the standard of medical care," study investigator Suzette Bielinski, PhD, a genetic epidemiologist at the Mayo Clinic in Rochester, Minnesota, said in a press release.

"Fluctuations in these results over time could help us identify who is at greater risk of dementia, help us understand mechanisms for the development of dementia, and ultimately determine whether leveling out these fluctuations could play a role in reducing dementia risk," she added. The findings were published online July 5 in *Neurology*.

Previous studies have shown a link between high cholesterol levels and increased dementia risk, but such research has usually been based on a single measurement, the researchers note. Only a few studies have examined variability of cholesterol levels over time, but they have also shown a link between varying levels and dementia risk. How the risk differs among specific types of cholesterol is not yet fully known.

To explore this question, investigators analyzed medical records in the Rochester Epidemiology Program, a medical records-linkage system in southern Minnesota and western Wisconsin.

Participants were excluded if they had a prior

diagnosis of AD/ADRD or did not have three or more lipid measurements within the baseline data collection period, leaving a final cohort of 11,571 participants. All participants were aged 60 or older. The mean age of the sample was 71, and 54% were female.

Investigators recorded participants' total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL), and high-density lipoprotein cholesterol (HDL) on at least three different days in the 5 years before the start of the study in January 2006.

The investigators then followed the cohort from baseline until incident AD/ADRD, death, or December 31, 2018, whichever came first.

Participants were divided into groups depending on the degree of variation in lipid measurements, with the lowest group having the least variation over time and the highest group having the most variation over time.

Over a mean follow-up of 10 years, 2470 (21%) of the participants developed AD/ADRD. After adjusting for variables that could affect the risk for dementia, including sex, race, education, BMI, and lipid-lowering treatments, investigators found that participants who had the most variation in total cholesterol levels had a 19% increased risk of AD/ADRD. Those with the highest variability in triglycerides had a 23% increased risk of AD/ADRD.

## Daily Aspirin Challenged in Primary Stroke Prevention: ASPREE

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Seniors who took low-dose aspirin daily for primary prevention had no reduction in the risk for first strokes in a large randomized trial that followed them for about 5 years.

But those who took aspirin at 100 mg/d, compared with placebo, did show a significant 38% jump in risk for intracranial (IC) bleeding. Rates for ischemic stroke and for hemorrhagic stroke were similar between the aspirin and control groups.

The excess IC bleeding events included hemorrhagic stroke but also dural and subdural bleeds characteristic of traumatic head injury, such as from falls, researchers say, based on their secondary analysis of the ASPREE trial. The findings applied regardless of age, sex, or cardiovascular (CV) risk factors.

This study, as much as any other, has clouded aspirin's shine as a protectant against CV events in people without a history of stroke or clinical heart disease. It adds to years of randomized trials and meta-analyses suggesting that whatever benefits it may afford in primary prevention are offset by an increased risk for major bleeding.

ASPREE's main clinical outcomes, reported in a barrage of papers in 2018, included failure to show that low-dose aspirin for primary prevention can prolong survival free of physical or mental disability over 5 years. The trial also saw significant associations between daily aspirin and risk for major bleeding, especially upper gastrointestinal bleeding, and death from any cause.

The trial, conducted in Australia and the United States, had entered 19,114 people from the community who were aged 70 years or older or at least 65 for participants in the US identifying as Black or Hispanic.

ASPREE's aspirin recipients experienced 20 fewer ischemic strokes with the trade-off of 29 extra IC bleeding events.

Although there were small numbers of hemorrhagic and non-hemorrhagic events in absolute terms, "Numerically, the bleeding events outweighed any possible prevention of ischemic events," senior author John J. McNeil added.

### Short- vs Long-Term Risks

ASPREE, including a large senior population, combined with the other studies suggesting little or no advantage for aspirin in primary prevention, McNeil observed, "question whether there's much rationale for prescribing it for a long-term benefit, or benefit that might not become apparent for years afterward, when there's so many short-term risks that you have to overcome."

Indeed, ASPREE supports last year's US Preventive Services Task Force's recommendation against routine prescription of low-dose aspirin for primary prevention or any such prescription in adults 60 and

older, notes the published report.

A first stroke occurred in 4.7% of aspirin recipients and 4.6% of those on placebo, not a significant difference; nor were there significant differences in rates of ischemic stroke, hemorrhagic stroke, or fatal stroke.

The risks for IC bleeding were 1.1% and 0.8% for aspirin and placebo recipients, respectively ( $P = .03$ ).

"When you put all the data together, I think aspirin for the prevention of a first heart attack or stroke is marginally effective. But that has to be balanced against the potential risk, and this study clearly illustrates the significance of that risk," said Berger, NYU Langone Hospitals and director of the Center for the Prevention of Cardiovascular Disease at NYU Grossman School of Medicine, New York City.

The benefit of aspirin "is not as high as it once was" in an age when there are so many effective therapies that lower coronary and neurovascular risk, Berger observed. "While its absolute risk is low, the absolute benefit is also pretty low."

For populations that have been studied, he said, "the benefit of aspirin for the prevention of a first heart attack or stroke does not outweigh its risk."

Among the analysis' important features, McNeil said, is its separation of stroke and nonstroke IC bleeding events by their anatomic locations.

### An "Unrecognized Risk"

Intracranial bleeds overall as well as subdural, extradural, and subarachnoid bleeds thought to be caused by trauma were more common in the aspirin group. But the differences fell short of significance at such low incidence rates.

Subdural, extradural, and subarachnoid bleeding "are commonly caused by head strikes from falls," for which seniors are more at risk than younger adults, he observed.

"We're highlighting an unrecognized risk of aspirin, this totality of intracranial bleeds," McNeil said. "In older people, we know that bleeding risk is high, and we know the risk of head trauma is high. You put it all together and it's a statistically significant increase that doctors should be aware of."

Of the trial population (56% female, median age 74), 9525 participants were assigned to daily aspirin and 9589 to placebo and followed a median of 4.7 years.

Despite no significant differences for all strokes or

ischemic or hemorrhagic stroke separately, hazard ratios for risk for IC bleeding, including hemorrhagic stroke, were significantly increased in the aspirin group and trended up for non-stroke IC bleeding:

- All stroke: 0.97 (95% confidence interval [CI], 0.79 - 1.18;  $P = .04$ )
- Ischemic stroke, 0.89 (95% CI, 0.71 - 1.11;  $P = .28$ )
- Hemorrhagic stroke, 1.33 (95% CI, 0.87 - 2.04;  $P = .19$ )
- All IC bleeding, 1.38 (95% CI, 1.03 - 1.84;  $P = .03$ )
- Non-stroke IC bleeding, 1.45 (95% CI, 0.98 - 2.16;  $P = .07$ )

"I think the scientific community really has a lot to learn about using precision-based medicine to figure out who should be on a therapy like aspirin," Berger said.

Berger foresees a time "in the near future when we will be able to measure platelet activity or platelet genetics and tell us who would benefit from a drug like aspirin."

The field doesn't need yet another broad-based primary prevention aspirin trial, he said. "We need to start thinking about how the drug works and choose our populations wisely."

### **Snoring Could Be Harming Your Brain Health**

#### **MEDSCAPE**

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Those who snore can be aging their brains by years and hurting their brain health by depriving themselves of getting deep sleep, according to researchers with the Faculty of Medicine at the University of Paris-Cité, Paris, France.

What to Know:

- Loud snoring and obstructed breathing, often caused by sleep apnea, can lead to higher chances of exhibiting signs of stroke, Alzheimer's disease, or overall cognitive decline.
- Tiny lesions on the brain, known as white matter hyperintensities, are biomarkers that indicate brain health, becoming more prevalent with age or uncontrolled high blood pressure.
- Participants with severe sleep apnea had more white matter hyperintensities than those with mild or moderate conditions and demonstrated a decrease in the integrity of the axons of the brain

that connect nerve cells.

- Deep sleep is one of the best indicators of sleep quality and the study found that for every 10% decrease in deep sleep, the white matter hyperintensities increased, equivalent to the brain aging 2.3 years.
- The same 10% reduction of deep sleep was also associated with reducing the integrity of axons, and that decrease was similar to the effect of the brain appearing 3 years older.

### **Higher Step Counts Tied to Fewer Symptoms in Heart Failure**

#### **MEDSCAPE**

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Higher daily step counts, as measured by actigraphy, were linked to heart failure symptoms and health status, although reductions in step counts were not, in a new study.

Daily step counts between 1000 and 5000 were significantly associated with symptoms and physical limitations, as reflected in Kansas City Cardiomyopathy Questionnaire (KCCQ) total symptom (TS) and physical limitation (PL) scores.

Participants whose step counts increased by 2000 steps per day demonstrated a 5.2-point increase in their KCCQ-TS scores and a 5.33-point increase in their KCCQ-PL scores, with higher scores reflecting improvement.

However, declines in step counts were not associated with significant declines in KCCQ-PL scores.

The findings are not yet ready to be implemented into practice, first author Jessica R. Golbus, MD, of the University of Michigan. However, she said, they "suggest that clinicians should interpret improvements in step counts as indicative of improving health status, though should not necessarily be as concerned with reductions in step count.

"I would certainly, however, still encourage clinicians to discuss decrementing physical activity levels with their patients, though an intervention may not necessarily be warranted," she added.

The investigators analyzed data from the Canagliflozin: Impact on Health Status, Quality of Life and Functional Status in Heart Failure (CHIEF-HF) trial, a randomized, controlled trial that enrolled participants with heart failure who had a smartphone.

Participants were given a Fitbit Versa 2 and

completed serial KCCQs via the smartphone app.

The researchers assessed the relationship between daily step count and KCCQ-TS and KCCQ-PL scores at baseline, as well as changes in the scores between 2 and 12 weeks.

The study included 425 patients. The mean age was 63.5 years, 44.5% were women, and 83.3% were White; 40.9% had reduced ejection fraction, 59.1% had preserved ejection fraction, and 27.5% had type 2 diabetes.

At 2 weeks, the mean KCCQ-TS score was 62.7, and the mean KCCQ-PL score was 55.7.

KCCQ-TS scores increased by 2.5 points on average, and KCCQ-PL scores by 4 points through 12 weeks.

When categorized by 25-point ranges, the step count increased with increasing scores for both KCCQ-TS and KCCQ-PL. Those with KCCQ-TS scores of 0 to 24 averaged 2437.6 steps daily, and those with scores of 75 to 100 averaged 4870.9 steps daily.

Similarly, participants with KCCQ-PL scores of 0 to 24 averaged 2301.5 steps daily, and those with scores of 75 to 100 averaged 5351.9. The relationship remained significant after adjustment.

There were nonlinear relationships between activity and KCCQ scores: Daily step counts below 5000 steps were associated with KCCQ scores, but there was little association with counts above 5000 steps.

Compared with participants who walked 2000 steps per day, those who walked 1000 had KCCQ-TS scores that were 3.11 points lower; participants who walked 3000 had KCCQ-TS scores that were 2.89 points higher.

Similarly, participants who walked 1000 steps per day had KCCQ-PL scores that were 5.36 points lower than those who walked 2000 steps, and those who walked 3000 steps had KCCQ-PL scores that were 4.97 points higher.

After adjustment, change in daily step counts was significantly associated with a change in KCCQ-PL scores from baseline through 12 weeks; for example, participants whose step counts increased by 2000 steps per day experienced a 5.33 increase in their KCCQ-PL scores relative to participants whose step counts did not change.

"New Kid on the Block"

"A study with longer follow-up among patients from a broader background would provide confidence on the generalizability of the findings," said Frederick

Ho, PhD, a lecturer in public health at the University of Glasgow, who is a volunteer spokesperson for the American Heart Association. He led a recent study that showed accelerometer-measured physical activity was associated with a lower risk of heart failure. "It'd also be interesting to validate the findings using different types of wearable devices."

Previous studies have shown that wrist-worn wearables might overestimate light-intensity activities compared to hip-worn devices, he noted. "I'd imagine that the findings would be slightly different due to different types of devices, but the overall premise should remain."

Terminology and reporting features need to be standardized, and preferred methods of implementation need to be established, including how to wear the devices, he suggests.

Further research is needed to validate that "accelerometers and their digitally processed movement 'counts' actually measure activity and that this measured activity has clinical relevance."

## **Continuous Glucose Monitoring Might Help In Managing Postoperative Hypoglycemia**

**Medscape**

**July 28, 2023**

Continuous glucose monitors (CGMs) may help curb the severity of hypoglycemia after weight-loss operations and even other gastrointestinal procedures, according to recent findings from a small study published online in the journal *Diabetes, Obesity, and Metabolism*.

Hypoglycemia is a chronic and persistent complication common in patients following bariatric surgery, affecting as many as 30% of people who undergo a sleeve gastrectomy or Roux-en-Y gastric bypass.

The symptoms of hypoglycemia, including light headedness, heart palpitations, difficulty concentrating, and confusion, can mimic anxiety disorders, arrhythmia, and dumping syndrome.

If a postoperative patient experiences these symptoms within a few hours following a meal or exercising, "primary care doctors should consider the possibility that hypoglycemia may be a contributor," said Mary-Elizabeth Patti, MD, director of the Hypoglycemia Clinic at the Joslin Diabetes Center in

Boston and senior author of the new study.

"In fact, hypoglycemia is a possible diagnosis even among those who underwent [operations other than bariatric, including] fundoplication or other upper gastrointestinal or esophageal surgeries," she said.

To understand how CGM could benefit patients, Patti and colleagues recruited 22 participants who had undergone bariatric surgery more than 8 years prior and had post-bariatric hypoglycemia. Their mean age was 51 years, 90% were women, 82% were diagnosed with level 3 hypoglycemia, and none had type 1 or 2 diabetes.

All participants experienced neuronal dysfunction with symptoms like fatigue, concentration difficulties, and confusion. More than 90% had received medical nutrition therapy for post-bariatric hypoglycemia in the past.

CGM data were collected in the 22 individuals in two sequential phases: masked (no access to sensor glucose or alarms) and unmasked (access to sensor glucose and alarms for low or rapidly declining sensor glucose). Twelve participants wore a CGM (Dexcom G4 device) for a total of 28 days, whereas 10 wore a CGM (the Dexcom G6 device) for a total of 20 days.

The team observed that the percentage of time when the participants' blood glucose was below 70 mg/dL — the definition of hypoglycemia — was significantly lower during the unmasked phase.

Though CGM devices are not sensitive enough to serve as a diagnostic tool for hypoglycemia, "the alarms on CGM devices can provide some much-needed awareness," Patti said. "After a detailed diagnosis, CGM devices can be a helpful tool to assess dietary patterns and make modifications that could reduce the severity of post-bariatric hypoglycemia."

If a patient frequently experiences hypoglycemia, they may not sense when their glucose levels drop, also known as hypoglycemia unawareness, according to Patti. Studies have found that post-bariatric hypoglycemia remains under diagnosed because most patients are asymptomatic.

"The use of CGM devices may improve safety in post-bariatric hypoglycemia, particularly for patients with hypoglycemia unawareness," the researchers conclude.

Patients are more vulnerable to hypoglycemia after a sleeve gastrectomy or gastric bypass surgery because

these procedures involve removing the pylorus. This valve plays a crucial role in only allowing small portions of food to enter the intestine and prevents sudden spikes in blood glucose.

Without the pylorus, large amounts of food directly enter the intestine and soon result in large amounts of glucose getting absorbed. "The pancreas then goes into overdrive and produces a lot of insulin, which continues reducing sugar levels," Machineni said. "That is what causes hypoglycemia."

Patti and her team are next working on research using CGM-derived data to investigate how different types of meals, physical activities, and other factors could influence glucose metabolism patterns in patients with hypoglycemia.

#### **PSIM NEWS CORNER:**

##### **MEET and greet with Royal College of Physicians:**

Secretary General PSIM Dr. Somia Iqtadar met the Royal College of Physicians President Dr Sarah Clarke, Vice President Global Dr Mumtaz Patel and Director Education and Training Dr Tom Baker along with education team for future collaborations. PSIM annual International Conference 2024, Global Women Leaders Program and many upcoming collaborative PSIM-RCP courses with accreditation were discussed.

##### **Advocacy for the World Dengue Day Seminar:**

Advocacy for the World Dengue Day Seminar was held by the Pakistan Society of Internal Medicine in collaboration with the World Health Organization Pakistan on 15<sup>th</sup> of June at PC hotel Lahore with an aim to celebrate and dedicate 1 day to this most important fastest going mosquito disease i.e dengue and celebrate it as an international health day just like we celebrate world TB day, world asthma day, world malaria day etc. The event was moderated by Dr. Hina Ltif and well attended by government officials and national and international dignitaries. Minister Health Punjab, Prof. Dr. Javed Akram who is also president of PSIM, highlighted the need to take necessary measures to control this disease. The speaker Dr. Somia Iqtadar, Representative Pakistan Dengue Advisory Group (DAG) International Society of Neglected Tropical Diseases (ISNTD) presented the data regarding the burden of dengue in Pakistan and emphasized the need to dedicate a day

worldwide to this disease

Director General Health Services Punjab DR. MUHAMMAD ILYAS, Minister Primary and secondary Health: Dr. Jamal Nasir and World Representative WHO Dr. Palitha Mahipala also showed concern over the issue. Dr. Mahipala also appreciated the efforts of PSIM and GOP in trying to control this deadly disease. Prof. Dr. Aftab Mohsin presented Vote Of Thanks which was followed by Signing of World Dengue Day Petition.

### **Diabetes Prevention and Management CME Program by PSIM Gujrat Chapter**

Diabetes Prevention and Management CME Program was held by PSIM Gujrat Chapter in July to highlight the importance of diabetes prevention. It was well attended by faculty, General physicians, trainees and students of Gujrat and surrounding areas. The session was moderated by Dr. Sami Ullah Mumtaz and Minister Health Punjab Prof. Javed Akram was the chief guest of the session. Dr. Somia Iqtadar, Secretary General PSIM briefed about PSIM and its role in creating awareness of different diseases. Prof. AZIZ UR REHMAN and Prof. Aftab Mohsin gave a detailed talk on diabetes prevention and management. Prof. Sajid abaidullah and Prof. Tariq waseem along with Dr. M afzaal chaudhary (Gujrat chapter head) chaired the event. Minister Health Punjab Prof. Javed Akram appreciated the efforts of everyone in managing and preventing diabetes.

### **Inter-society dialogue for Cardiometabolic risk prevention and control**

Inter-society dialogue for Cardiometabolic risk prevention and control was held in Karachi where presidents and a secretary's of 8 medical societies including the Pakistan Cardiac Society, Pakistan Hypertension League, Pakistan Society of Internal Medicine, Pakistan Society of Interventional Cardiology, Pakistan Endocrine Society, Pakistan Society of Nephrology, Pakistan Society of Neurology and Pakistan Stroke Society deliberated on a way forward. PSIM was represented by Prof Javed Akram founder President and Dr. Somia Iqtadar founder Secretary General of the society.

### **1st Ever Medicine Review Board (4th Program) Mentor-Mentee Program**

4<sup>th</sup> Program of Mentor-Mentee Program - 1st Ever

Medicine Review Board in collaboration with PharmEvo held in Karachi on 22<sup>nd</sup> July at Agha Khan University for the young physicians or fellows of Medicine in training facilitated by Dr. Ainan Arshad secretary Karachi chapter. A big number of Experts in the field of Medicine was on board. This Preparatory Course gave trainees and residents in the field of medicine a first-hand experience from the subject's leading experts to prepare for their fellowship exams. The program was well attended and appreciated by the residents.







گجرات پاکستان سوسائٹی آف انٹرنل میڈیسن کے ذریعہ منعقد کی جانے والی کارڈیو میٹابولک ریسک کے موضوع پر سیمینار اور کانفرنس کے شرکاء کا گروہی تصویر (پانچویں نمبر)۔

