People who vape had worrisome changes in cardiovascular function, even as young adults

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Adults who regularly used electronic nicotine delivery devices, or e-cigarettes, displayed worrisome changes in heart and blood vessel function and performed significantly worse on exercise stress testing

than people who did not use any nicotine products, according to two separate analyses of preliminary research to be presented at the American Heart Association's Scientific Sessions 2022. The meeting, held in person in Chicago and virtually, Nov. 5-7, 2022, is a premier global exchange of the latest scientific advancements, research and evidence-based clinical practice updates in cardiovascular science.

Researchers from the Cardiac and LUng E-cig Smoking (CLUES) Study will present two abstracts that compared outcomes among people who vaped, those who smoked traditional, combustible cigarettes and people who reported not using any nicotine products.

The CLUES study was conducted by researchers at the University of Wisconsin between March 2019–March 2022. It was designed to examine the short-term effects of vaping and cigarette smoking in regular nicotine users, compared with similar matched peers who didn't use nicotine in any form. The 395 study participants included:

- 164 people who reported exclusively using electronic cigarettes for an average of 4.1 years, and 80% reported using the most recent generation of vaping devices (average age of 27.4 years, 39% female, 86% reported white race);
- 117 people who exclusively smoked traditional, combustible cigarettes for an average of 23 years (average age of 42.8 years, 44% female, 56% reported white race); and
- 114 adults who reported never smoking or vaping and who currently had negative urine tests for nicotine use (average age of 30.8 years, 50% female, 69% reported white race).

In the first report (Abstract SU3138—Acute Effects Of Nicotine-containing Product Challenges On Cardiovascular And Autonomic Function Among Electronic Cigarette Vapers, Combustible Cigarette Smokers, And Controls: The Clues Study), researchers assessed blood

pressure, heart rate, the diameter of the brachial artery in the arm and heart rate variability before and up to 15 minutes after the participants either vaped or smoked. Researchers then compared the before-and-after measures to measurements taken 10 to 15 minutes apart in the participants who reported never vaping or smoking.

The investigators found that, compared with people who did not use any nicotine, people who vaped and those who smoked combustible cigarettes had:

- greater increases in heart rate, meaning their hearts beat faster. Among those who vaped and those who smoked they experienced an approximately 4 beat per minute (bpm) increase in heart rate after vaping or smoking, whereas people who reported no nicotine use had no changes in heart rate;
- greater increases in both systolic (top number) and diastolic (lower number) blood pressure. People who vaped and those who smoked experienced increases in blood pressure from approximately 122/72 mm Hg to approximately 127/77 mm Hg after vaping or smoking, whereas those who never used nicotine products had no change in blood pressure measures.

After vaping or smoking, people who used these nicotine-containing products also experienced greater constriction of the brachial artery and worse measures of heart rate variability, indicating the activation of the body's sympathetic nervous system. The sympathetic nervous system helps activate the fight-or-flight response. It becomes more active when a person is stressed or in danger, increases heart rate and blood pressure, creates a greater need for oxygen by the heart and creates dysfunction in artery walls.

"Immediately after vaping or smoking, there were worrisome changes in blood pressure, heart rate, heart rate variability and blood vessel tone

(constriction)," said lead study author Matthew C. Tattersall, D.O., M.S., an assistant professor of medicine at the University of Wisconsin School of Medicine and Public Health and the associate director of preventive cardiology at UW Health in Madison, Wisconsin. "These findings suggest worse cardiovascular disease risk factors right after vaping or smoking, and activation of the sympathetic nervous system may play a role in the adverse responses seen immediately after using e-cigarettes and after exercise testing 90 minutes later."

In the second analysis (Abstract SA3142—Differences In Treadmill Exercise Stress Testing Parameters Among Electronic Cigarette Vapers, Combustible Cigarette Smokers, And Controls: The Clues Study) of the same participants, those who vaped and those who smoked were compared with the group of participants who did not smoke or use e-cigarettes to assess how they performed on exercise stress testing, which is known to predict cardiovascular disease outcomes. Treadmill stress tests were performed approximately 90 minutes after participants had either vaped or smoked and 90 minutes after those who reported no nicotine use had rested.

Four outcome measures were collected and analyzed during and after the stress test:

- Metabolic equivalents (METS), a measure of exercise ability or fitness: 1 MET is sitting at rest quietly, whereas a brisk walk is 3-4 METS, which is 3-4 times the energy the body uses at rest. Achieving lower METS measured on a stress test is associated with higher cardiovascular risk.
- Rate-pressure product, which is a measure of work conducted by the heart at peak exercise levels, meaning the workload on the heart. Achieving a higher rate means the heart can work harder.
- Heart rate reserve, a measure of the resting heart rate versus maximum predicted heart rate with exercise—i.e., how much

reserve the heart can harness, with higher reserve meaning better cardiac fitness.
- 60-second heart rate recovery, a measure of how fast the heart rate recovers after exercise: the faster the heart rate recovers, the better cardiac shape a person is in and the better their long-term cardiovascular prognosis.

People who vaped and those who smoke cigarettes performed significantly worse on all the 4 exercise parameters, compared to the group who reported no nicotine use. In addition, when compared to people who did not use nicotine, those who smoked or vaped regularly:

- had less exercise ability as noted by lower peak METS (9.8 for people who vaped, 9.3 for people who smoked and 11.1 for people who did neither);
- achieved a lower cardiac workload when exercising at their maximum level;
- had lower heart rate reserve, indicating poorer fitness (87% for people who vaped, 85% for people who smoked and 91% for people who did neither); and
- experienced slower heart rate recovery after finishing the exercise test (25.2 bpm for people who vaped, 22.4 for people who smoked and 28.1 for people who did neither).

"People who vaped clearly performed worse on all four exercise parameters compared to their peers who did not use nicotine, even after adjusting for age, sex and race/ethnicity," said lead author of the study, Christina M. Hughey, M.D., a fellow in cardiovascular medicine at UW Health, the integrated health systems of the University of Wisconsin-Madison. "The exercise performance of those who vaped was not significantly different than people who used combustible cigarettes, even though they had vaped for fewer years than the people who smoked and were much younger."

"Our findings from the CLUES study raise concerns about the potential harms of chronic use of electronic nicotine delivery systems, particularly for cardiovascular disease," said CLUES principal investigator James H. Stein, M.D., FAHA, director of preventive cardiology at UW Health and the Robert Turrell Professor in Cardiovascular Research at the University of Wisconsin School of Medicine and Public Health in Madison. "We did not study the long-term effects of vaping, use of vaping as a smoking cessation aid or the effectiveness or safety of vaping in that context. However, these findings are concerning because they indicate vaping may increase cardiovascular risk. The message for people who smoke combustible cigarettes is the same as always—try to quit using tobacco and nicotine products and seek support from your physician and community to increase your chances of success."

The CLUES Study was an observational, product challenge study. This means that individuals were observed, and certain outcomes were measured before and after product use, so the findings cannot confirm a cause-and-effect relationship between the use of nicotine-containing products and the cardiovascular measurements taken. Because the people who smoked in the studies were older, had used nicotine-containing products for many more years (average use of 23 years those who smoked combustible cigarettes vs. 4 years for those who used e-cigarette products) and were more likely to be from underrepresented races and ethnicities than those who vaped, the researchers were unable to directly compare the effects of vaping to smoking. Most of the people who vaped self-identified as white adults, so the results on the effects of vaping may not be generalizable to people from other racial and ethnic groups.

"These studies add to the growing body of science that shows similar cardiovascular injury among people who use e-cigarettes and those who smoke combustible cigarettes. Additionally, it shows this cardiovascular risk is seen even among younger people who have a shorter history of

nicotine use," said Aruni Bhatnagar, Ph.D., FAHA, co-director of the American Heart Association's National Institutes of Health/Food and Drug Administration-funded Tobacco Center of Regulatory Science and a professor of medicine, biochemistry and molecular biology at the University of Louisville in Louisville, Kentucky. "People should know that e-cigarettes and combustible cigarettes contain addictive nicotine and toxic chemicals that may have adverse effects on their cardiovascular system and their overall health."

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More information: Abstract SU3138: www.abstractsonline.com/pp8/?_… 1/presentation/11057

Abstract SA3142: www.abstractsonline.com/pp8/?_… 1/presentation/15491

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