NEJM: REACT reveals that silent atherosclerosis already affects 1 in 13 young adults aged 18 to 29 and progresses rapidly from the menopause

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The research, presented in a Hot Line session at the European Society of Cardiology Congress in Munich and published simultaneously in The New England Journal of Medicine, proposes a paradigm shift towards prevention based on early detection through vascular imaging

Atherosclerosis, the process underlying most cardiovascular diseases, begins long before the first symptoms appear. An international study led by Professor Henning Bundgaard, Professor of Cardiology at Rigshospitalet in Copenhagen, Denmark, and Dr. Borja Ibáñez, Scientific Director of the Centro Nacional de Investigaciones Cardiovasculares Carlos III, CNIC, cardiologist at Hospital Universitario Fundación Jiménez Díaz and a group leader at CIBERCV, shows that the disease can already be detected in apparently healthy young adults and is much more common than previously thought.

The results, presented in a Hot Line session at ESC Congress 2026 and published simultaneously in *The New England Journal of Medicine*, show that 57.1% of the more than 16,000 participants included in the study had atherosclerotic plaques, despite having no symptoms or previous diagnosis of cardiovascular disease.

The data come from the first phase of REACT, one of the largest studies conducted to date to map the presence of silent atherosclerosis throughout adult life. REACT is an international initiative funded by the Novo Nordisk Foundation and developed through collaboration between Rigshospitalet and other Danish hospitals and CNIC in Spain. Professor Bundgaard explains that “the vision of REACT is to transform primary cardiovascular prevention through a precision medicine approach based on the early identification of atherosclerosis”.

The Novo Nordisk Foundation granted up to **EUR 23 million** to support the first phase of the initiative.

Atherosclerosis is the main cause of cardiovascular disease and typically presents as heart attacks, strokes or sudden death. While not all individuals with atherosclerotic plaques will develop symptomatic disease, nearly 20 million people worldwide die from cardiovascular disease every year, and most of these deaths are caused by atherosclerosis. However, atherosclerosis can remain silent for decades while plaques progressively develop in the arteries

Professor Ibáñez stated that “the REACT study is based on a simple but revolutionary idea: moving from the current model, which estimates the probability of cardiovascular disease on the basis of traditional risk factors such as blood pressure, cholesterol and smoking, towards a new paradigm in which the disease is detected directly through imaging before it causes symptoms. In this model, preventive interventions and the treatment of risk factors could be guided by the actual presence of silent atherosclerosis rather than relying solely on an indirect estimate of risk. The first step in this ambitious endeavour was to determine the actual prevalence of silent atherosclerosis in all three major vascular territories and across the entire adult lifespan, something that we are reporting now”.

REACT is expected to run for eight years across two phases. Phase 1 (REACT-DETECT) began in 2024 and, if granted, Phase 2 (REACT-PROTECT) will run from 2027 to 2032. The present findings arise from Phase1, which represents the most complete atlas of the presence of silent atherosclerosis in different regions of the body at different ages, both in women and men.

Atherosclerosis detected in young adults

In the first phase, 16,808 people aged 18 to 70 were recruited in Denmark and Spain. None of the participants had a known **history** of atherosclerotic cardiovascular disease. Each participant underwent advanced imaging to detect atherosclerotic plaques in the carotid, femoral and coronary arteries. Cardiovascular risk factors, blood biomarkers, samples for omics studies and retinal images were also analysed, generating one of the most comprehensive databases on atherosclerosis developed to date.

The results show that the disease is already present in very young adults. Approximately 1 in 13 people aged 18 to 29 years had atherosclerosis in at least one artery. This proportion increased progressively with age, reaching 9 in 10 people aged 60 to 70 years.

An important finding was that most people with atherosclerosis in the coronary arteries also had the disease in the arteries of the neck or legs, specifically the carotid or femoral arteries. This has important implications for screening because examining the carotid and femoral arteries using ultrasound is easier, faster and non-invasive compared to CT scannings.

“In the paradigm we propose, portable ultrasound devices usable by any healthcare professional will become the standard tool for atherosclerosis screening from the early stages of adult life,” Dr Ibáñez said.

Differences between women and men

The study also reveals important differences between women and men. In men, prevalence began to increase at younger ages, with an atherosclerotic profile five to ten years ahead of that observed in women.

In women, the sharpest increase was observed between the ages of 40 and 60, a period that broadly coincides with the menopausal transition. These findings highlight the importance of studying preventive strategies adapted to sex and stage of life.

Another of the study's most relevant findings is that the conventional methods currently used to estimate cardiovascular risk, including risk scores such as SCORE2, identify only a small proportion of people who already have silent atherosclerosis.

According to Dr Ibáñez, the results underline the need to move towards a new approach to cardiovascular prevention.

"For decades, we have estimated cardiovascular risk using factors such as age, blood pressure and cholesterol. This study shows that we can now go one step further and detect the disease directly before it causes a heart attack or stroke."

He added: "The future of cardiovascular prevention must be more precise and personalised. If we identify atherosclerosis in its earliest stages, we will be able to intervene sooner, tailor treatment more effectively and reduce the burden of cardiovascular disease."

Professor Bundgaard believes the results represent a unique opportunity to transform cardiovascular prevention.

"Until now, preventive decisions have been based on an estimate of risk, but we did not know whether the disease was already present. REACT shows that atherosclerosis can be detected decades before clinical manifestations appear and provides the most comprehensive atlas of the evolution of the disease across adult life."

The future of cardiovascular prevention must be more precise and personalised

Professor Bundgaard added that the results provide the scientific foundation needed to evaluate a new preventive model.

"Identifying and treating silent atherosclerosis as early as possible is essential to reducing the global burden of cardiovascular disease. Our results support prospective studies evaluating whether a preventive strategy guided by imaging, including the use of portable ultrasound, can improve current standards. If confirmed, this would bring precision medicine to the most common cardiovascular disease."

If funded, the second phase of REACT, planned for 2027 to 2032, will take the research one step further. The investigators will launch a large randomised clinical trial to evaluate whether an imaging-guided precision prevention strategy can halt or reduce the systemic progression of atherosclerosis – with the long-term view to markedly reduce heart attacks, strokes and other cardiovascular events more effectively than the current practice. The investigators are also expanding the scope of REACT beyond Europe. "REACT is expanding its impact around the world. We have established close collaborations with India, Singapore, Tanzania and Mexico to validate these results in populations across the globe," Dr Ibáñez said.

REACT expands on the PESA-CNIC-Santander study, led by Dr. Valentín Fuster, Director General of CNIC, who is also directly involved in REACT.

"PESA has shown us that atherosclerotic disease is present in many middle-aged people and is associated with lifestyle patterns. In REACT, we wanted to investigate how it emerges at much younger ages. For years, we have proposed that early intervention in atherosclerosis could not only

prevent its progression but might even make it possible to cure the disease. REACT will answer this question," Dr Fuster said.

- *Bundgaard H, García-Lunar I, Kofoed KF, Hasselbalch R, Pérez-García CN, Kunkel JB, et al. Prevalence of silent atherosclerosis across adult life. N Engl J Med. 2026. doi:10.1056/NEJMoa2609059.*

- REACT - Prevalence of silent atherosclerosis across adult life' presented during HOT LINE 2 at ESC Congress 2026 on 29 August from 08:15 to 09:45 in Munich (Main Auditorium – Hall B3).

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