

Metabolically 'healthy' obesity still linked to higher risk of cardiovascular disease

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Women who are obese and who have been metabolically healthy for decades are still at higher risk of developing cardiovascular disease compared to metabolically healthy women of normal weight, according to an observational study that followed over 90000 American women for up to 30 years, published in *The Lancet Diabetes & Endocrinology*

journal.

The findings indicate that obesity is a risk factor for cardiovascular [disease](#), regardless of whether or not women develop any of the common metabolic diseases such as [high blood pressure](#) or type 2 diabetes.

The study also found that the majority of metabolically healthy women are likely to become metabolically unhealthy over time, even if they were [normal weight](#).

"Our large cohort study confirms that metabolically healthy obesity is not a harmless condition, and even women who remain free of metabolic diseases for decades face an increased risk of cardiovascular events," explains Professor Matthias Schulze from the German Institute of Human Nutrition Potsdam-Rehbruecke, Nuthetal, Germany, who led the research.

"What's more, we observed that most healthy women are likely to develop type 2 diabetes, high blood pressure, or high cholesterol over time, irrespective of their BMI, putting them at much higher risk for cardiovascular disease."

Obesity (BMI of more than 30kg/m²) affects almost all of the [cardiovascular disease risk](#) factors, particularly those related to [metabolic syndrome](#) including high blood pressure, poor blood sugar control or diabetes, and abnormal blood fats, which double the risk of cardiovascular disease such as heart attacks and stroke. However, some people with obesity seem to be free of these metabolic abnormalities—estimates suggest as many as a third of obese people might be metabolically healthy.

Whether this so called 'metabolically health obesity' is associated with a higher risk of cardiovascular disease has been hotly debated for many

years. It remains unclear how changes or maintenance of metabolic status affect the development of cardiovascular disease in both normal weight and overweight/obese individuals.

To investigate this further, Schulze and colleagues examined the association between obesity and cardiovascular disease incidence in 90257 women (initially free from cardiovascular disease) from the Nurses' Health Study—a study tracking the health of female nurses (aged 30-55 years) in the USA since 1976.

Participants were divided into groups by BMI category, [metabolic health](#) (defined as the absence of three metabolic risk factors—type 2 diabetes, high blood pressure, and high blood cholesterol), and change in metabolic health status, and followed for 30 years between 1980 and 2010. Participants were sent questionnaires every two years to update their BMI and metabolic health status, as well as to assess their lifestyle, health behaviour, and medical history.

The researchers adjusted for a range of factors that may have influenced the results including age, diet, smoking status, physical activity, alcohol consumption, ethnicity or race, highest education level, menopausal status, aspirin use, and family history of heart attack or diabetes.

During an average follow-up of 24 years, 6306 new cases of cardiovascular disease, including 3304 heart attacks and 3080 strokes were recorded.

Cardiovascular disease risk was especially high in all metabolically unhealthy women, regardless of their BMI. Metabolically unhealthy normal weight women were around 2.5 times more likely to develop cardiovascular disease compared to normal weight women with no metabolic abnormalities, whilst those with 'metabolically healthy obesity' were also at higher risk of cardiovascular disease (39% higher risk).

Importantly, the majority of women who were initially metabolically healthy obese (84%), and around two-thirds (68%) of normal weight metabolically healthy women, converted to unhealthy phenotypes over 20 years.

Furthermore, even women who maintained metabolically healthy obesity over 20 years still had a 57% higher [risk](#) of developing cardiovascular disease compared with normal weight metabolically healthy women.

"Long-term maintenance of metabolic health is a challenge for overweight/obese, but also for normal-weight women," says Professor Schulze. "Our findings highlight the importance of preventing the development of metabolic diseases, and suggest that even individuals in good metabolic health may benefit from early behavioural management to improve their diet and increase physical activity in order to guard against progression to poor metabolic health."

The authors acknowledge that their findings show observational associations rather than cause and effect. They note some limitations, including that the study included mainly [women](#) of European descent, so the findings cannot be generalised to other ethnic groups and men; and that their definition of metabolic health (the absence of three [metabolic diseases](#)), may identify a different subgroup than in other studies. However, key strengths include the large cohort, repeated measurements, and long follow up time.

Writing in a linked Comment, Professor Carl Lavie from the University of Queensland School of Medicine, New Orleans, USA and colleagues discuss whether fitness is more important than fatness, pointing out that, "Those with metabolically healthy obesity and decent levels of cardiorespiratory fitness have a quite good overall prognosis from [cardiovascular disease](#) and overall survival."

He adds: "Drastic efforts are needed to prevent obesity in the first place and, especially, to prevent conversion to more severe degrees of obesity and the metabolic syndrome. Public health policies aiming to increase cardiorespiratory fitness through physical activity and exercise will further contribute to improve people's [health](#). It is prudent to remind ourselves that an ounce of prevention is better than a pound of cure."

More information: *The Lancet Diabetes & Endocrinology* (2018).
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