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Press release

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Heart Attack and Stroke Risk Also Elevated in Women with Obesity Who Are Metabolically Healthy

Potsdam-Rehbruecke – Women with obesity are at increased risk of cardiovascular disease, even if they are considered to be metabolically healthy. Moreover, women of normal weight are at risk of heart attack or stroke if they suffer from a metabolic disease such as diabetes or high blood pressure. These are the results of an analysis conducted by scientists of the German Institute of Human Nutrition (DIfE), Harvard University and University Hospital Tübingen based on 90,257 data records of a large U.S. cohort study. The researchers have now published their findings in the journal The Lancet Diabetes & Endocrinology.

Overweight and obesity* can lead to metabolic disorders such as diabetes, high blood pressure and hypercholesterolemia and are therefore risk factors for heart attacks and strokes. However, there is also the phenomenon of "the healthy obese", that is, people who do not develop metabolic disorders despite obesity. On the other hand, there are "unhealthy normal-weight people", who despite their normal weight have a similarly increased risk of cardiovascular disease as metabolically unhealthy obese people. So far it has been unclear how metabolic risk factors change over decades in metabolically healthy people depending on body weight and what heart attack and stroke risk results from this.

The team of scientists led by Matthias Schulze and Nathalie Eckel of DIfE evaluated data from 90,257 women who participated in the Nurses' Health Study**, a large U.S. longitudinal study. The women were observed for up to 30 years with regard to their body weight, their metabolic health and the occurrence of heart attack and stroke. All women who were not diagnosed with high blood pressure, diabetes or hypercholesterolemia were considered to be metabolically healthy.

As the study shows, metabolically healthy women with overweight or obesity are at an increased risk of cardiovascular disease compared to metabolically healthy, normal-weight women. However, if at least one risk factor was present, the risk of disease increased in all women regardless of body weight. Over the course of 20 years, more than 80 percent of metabolically healthy obese women developed at least one risk factor. Moreover, only about one third of the normal-weight women remained metabolically healthy. High blood pressure and diabetes were the metabolic diseases which contributed significantly to a 2-3 fold increased risk of heart attack and stroke.

"We observed that obese women had an increased risk of cardiovascular disease even if they remained metabolically healthy for over 10 or even 20 years," said first author Nathalie Eckel. "Obesity therefore represents a serious risk of disease, regardless of whether one has had no metabolic abnormalities for years. There is still no clear evidence that there is a subgroup of people with obesity who do not have an increased risk." The results confirm an earlier study by the scientists in which they systematically evaluated studies to find an appropriate definition of healthy obesity***.

"We were also surprised that such a high proportion of metabolically healthy, normal-weight women suffer from either high blood pressure, diabetes or a disorder of the lipid metabolism over the course of 20 years," said Matthias Schulze,

who heads the Department of Molecular Epidemiology at DIfE and coordinates the epidemiological research of the DIfE within the framework of the German Center for Diabetes Research (DZD). “Because these diseases significantly affect the risk of heart attack and stroke, it is important to maintain metabolic health through a healthy lifestyle and a healthy diet in the long term – regardless of whether you are normal-weight or overweight," Schulze added.

Original Publication:

Eckel N, Li Y, Kuxhaus O, Stefan N, Hu FB, Schulze MB. Transition from metabolic healthy to unhealthy phenotypes and association with cardiovascular disease risk across BMI categories in 90 257 women (the Nurses’ Health Study): 30 year follow-up from a prospective cohort study. Lancet Diabetes Endocrinol 2018.
(http://dx.doi.org/10.1016/S2213-8587(18)30137-2)

The study was funded by the German Federal Ministry of Education and Research (BMBF) and the German Center for Diabetes Research (DZD).

Background Information:

* The Body Mass Index (BMI) is used to classify body weight. The BMI is the ratio of weight (in kg) and height (in m) squared (kg/m²). Overweight is present at a BMI of ≥ 25 kg/m2. Obesity starts at a BMI of ≥ 30 kg/m2. (Source: weight classification in adults based on the BMI according to WHO, 2000)

** The Nurses’ Health Study is a U.S. cohort study investigating relationships between diet and chronic conditions such as type 2 diabetes, cardiovascular disease and cancer. It is considered one of the world's most important epidemiological longitudinal studies. The study was started in 1976 with approximately 122,000 nurses and since then includes biennial surveys on health status and major risk factors.

*** Eckel N, Meidtner K, Kalle-Uhlmann T, Stefan N, Schulze MB. Metabolically healthy obesity and cardiovascular events: A systematic review and meta-analysis. Eur J Prev Cardiol. 2016 Jun;23(9):956-66
(http://journals.sagepub.com/doi/abs/10.1177/2047487315623884)

The German Institute of Human Nutrition Potsdam-Rehbrücke (DIfE) is a member of the Leibniz Association. It investigates the causes of nutrition-associated diseases in order to develop new strategies for prevention, treatment and nutritional recommendations. Its research interests include the cause and consequences of the metabolic syndrome, a combination of obesity, hypertension (high blood pressure), insulin resistance and lipid metabolism disorder, the role of nutrition for healthy aging and the biological bases of food choices and dietary behavior. DIfE is also a partner of the German Center for Diabetes Research (DZD), which has been funded by the German Federal Ministry of Education and Research (BMBF) since 2009. More information under http://www.dife.de.

The Leibniz Association connects 93 independent research institutions. Its focus ranges from the natural, engineering and environmental sciences to the economic, spatial and social sciences and the humanities. Leibniz Institutes are dedicated to socially, economically and ecologically relevant questions. They conduct knowledge- and application-oriented research, also in the collaborative Leibniz Research Alliances, provide or maintain scientific infrastructures and offer research-based services. The Leibniz Association focuses on knowledge transfer, especially with the Leibniz Research Museums. It advises and informs policy makers in government, academia, industry and the general public. Leibniz institutions maintain close cooperation with universities - e.g. in the form of the Leibniz Science Campi, with industry and other partners at home and abroad. They are subject to a transparent and independent

assessment procedure. Due to their nationwide importance, the federal government and the states jointly support the institutes of the Leibniz Association. The Leibniz Institutes employ around 19,100 people, including 9,900 scientists. The total budget of the institutes is more than 1.9 billion euros. More details under https://www.leibniz-gemeinschaft.de/en.

The German Center for Diabetes Research (DZD) is one of six German Centers of Health Research. It brings together experts in the field of diabetes research and combines basic research, epidemiology and clinical applications. By adopting an innovative, integrative approach to research, the DZD aims to make a substantial contribution to the successful, personalized prevention, diagnosis and treatment of diabetes mellitus. The members of the association are Helmholtz Zentrum München – German Research Center for Environmental Health, the German Diabetes Center Düsseldorf (DDZ), the German Institute of Human Nutrition Potsdam-Rehbruecke (DIfE), the Institute of Diabetes Research and Metabolic Diseases of Helmholtz Zentrum München at the University of Tübingen, and the Paul Langerhans Institute Dresden of Helmholtz Zentrum München at the University Medical Center Carl Gustav Carus of TU Dresden, associated partners at the universities in Heidelberg, Cologne, Leipzig, Lübeck and Munich, and other project partners. More information under https://www.dzd-ev.de/en.

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Till Budde/DIfE