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## Diabetes and the Obesity Paradox

By ANAHAD O'CONNOR

Type 2 diabetes, a condition widely thought of as a disease of the overweight and sedentary, also develops in people who aren't overweight. And it may be deadlier in these normal-weight people, a new study shows.

In the study, which appeared in [The Journal of the American Medical Association](#), researchers reviewed data involving more than 2,500 people with Type 2 diabetes, some of whom were followed for decades. The scientists found that those who were of normal weight around the time of their diagnoses were twice as likely to die during the study period, compared with those who were overweight or obese.

The researchers could not explain why having a greater body mass index, or B.M.I., might protect someone with diabetes. But they did point out that some doctors may be prone to treating thin diabetics differently from their obese counterparts, and may be less likely to push them to make diet and exercise changes that could improve their survival.

"Normal-weight people may be treated less aggressively," said Mercedes R. Carnethon, an author of the study and an associate professor of preventive medicine at the Northwestern University Feinberg School of Medicine. "This really is an argument to treat a normal-weight person with diabetes as aggressively as you would treat an overweight or obese person with diabetes."

The findings also provide evidence that patients with Type 2 diabetes may display what researchers call the obesity paradox, the observation that people with certain chronic diseases tend to have lower mortality rates if they carry excess pounds. The phenomenon has been documented previously in people with heart failure, hypertension and kidney disease.

"We thought perhaps that the obesity paradox wouldn't apply to this population, given the strong association between overweight and diabetes," Dr. Carnethon said.

Carrying excess weight is clearly linked to Type 2 diabetes. Nationwide, [more than half of adults with the disease are obese](#), and 30 percent or more are overweight. Being obese not only makes the disease more likely, but is also associated with worse control of blood sugar levels, blood pressure and cholesterol, which in turn makes cardiovascular disease more likely.

But studies have also shown that a minority of Type 2 diabetics - perhaps 15 to 20 percent - are neither overweight nor obese, a phenomenon that researchers do not fully understand.

Some earlier studies that examined the obesity paradox may have been flawed because they classified as "normal weight" people who were in the late stages of disease and were, essentially,

"wasting away," Dr. Carnethon said. To ensure that the normal-weight diabetics in the study were not in the later stages of disease, she and her colleagues used in their analysis the weight of their subjects around the time of diagnosis, and excluded people who died within two years of the start of the research. Up to about 20 percent of the 2,625 Type 2 diabetics included in the study were considered normal weight, with a B.M.I. of 18.5 to just under 25.

Pinpointing the subjects' weight as close to the time of diagnosis as possible was also important for another reason. The authors did not want to confuse normal-weight subjects with people who had been overweight or obese but then lost the weight after learning they had diabetes. For that reason they tried to identify diabetics based on their fasting glucose levels, and excluded subjects who at the start of the study period were taking diabetes medications. And they adjusted their findings for age, gender, smoking and other factors that they thought could muddle their results.

Over all, the researchers found that people who had a normal B.M.I. at the time diabetes was diagnosed were twice as likely to die during the study period, compared with their heavier peers. They were also 30 to 50 percent more likely to die from cardiovascular disease, though there were not enough heart attacks and other cardiac events in the normal-weight group to make that finding statistically significant.

Dr. Carnethon noted that the findings were particularly important for Americans who are most at risk for normal-weight diabetes, including blacks, people of Asian heritage and older adults. She said that there may be a hereditary component to the phenomenon that causes some diabetics to be "genetically loaded," with genetic variants that predispose them to diabetes and higher mortality, as well as other illnesses.

"I think it's probable that these normal-weight adults who have diabetes have more abdominal adiposity," or fat in the midsection, she added. "That particular fat distribution is dangerous for metabolic disorders."

Whatever the underlying cause, an accompanying editorial said the findings should be viewed as a "wake-up call for timely prevention and management to reduce adverse outcomes in all patients with Type 2 diabetes." The advice may be particularly relevant to normal-weight diabetics, "who may have a false sense of protection because they are not overweight or obese," the editorial said.

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## Association of Weight Status With Mortality in Adults With Incident Diabetes

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### ABSTRACT

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**Context** Type 2 diabetes in normal-weight adults (body mass index [BMI] <25) is a representation of the metabolically obese normal-weight phenotype with unknown mortality consequences.

**Objective** To test the association of weight status with mortality in adults with new-onset diabetes in order to minimize the influence of diabetes duration and voluntary weight loss on mortality.

**Design, Setting, and Participants** Pooled analysis of 5 longitudinal cohort studies: Atherosclerosis Risk in Communities study, 1990-2006; Cardiovascular Health Study, 1992-2008; Coronary Artery Risk Development in Young Adults, 1987-2011; Framingham Offspring Study, 1979-2007; and Multi-Ethnic Study of Atherosclerosis, 2002-2011. A total of 2625 participants with incident diabetes contributed 27 125 person-years of follow-up. Included were men and women (age >40 years) who developed incident diabetes based on fasting glucose 126 mg/dL or greater or newly initiated diabetes medication and who had concurrent measurements of BMI. Participants were classified as normal weight if their BMI was 18.5 to 24.99 or overweight/obese if BMI was 25 or greater.

**Main Outcome Measures** Total, cardiovascular, and noncardiovascular mortality.

**Results** The proportion of adults who were normal weight at the time of incident diabetes ranged from 9% to 21% (overall 12%). During follow-up, 449 participants died: 178 from cardiovascular causes and 253 from noncardiovascular causes (18 were not classified). The rates of total, cardiovascular, and noncardiovascular

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mortality were higher in normal-weight participants (284.8, 99.8, and 198.1 per 10 000 person-years, respectively) than in overweight/obese participants (152.1, 67.8, and 87.9 per 10 000 person-years, respectively). After adjustment for demographic characteristics and blood pressure, lipid levels, waist circumference, and smoking status, hazard ratios comparing normal-weight participants with overweight/obese participants for total, cardiovascular, and noncardiovascular mortality were 2.08 (95% CI, 1.52-2.85), 1.52 (95% CI, 0.89-2.58), and 2.32 (95% CI, 1.55-3.48), respectively.

**Conclusion** Adults who were normal weight at the time of incident diabetes had higher mortality than adults who are overweight or obese.



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