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# Children born underweight found to be at increased risk of disease if they develop obesity

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Scientists at the University of Copenhagen have discovered a link between birth weight and the risk of health complications from obesity

during childhood. The findings highlight the need for prevention and treatment approaches for children with obesity who were born with a lower birth weight.

Hundreds of millions of people live with obesity, which is normally measured as a higher-than-optimal body mass index (BMI). While an elevated BMI increases the risk of a range of cardiometabolic diseases and is responsible for around five million deaths a year, according to the World Health Organization, not everyone is equally at risk.

Scientists at the University of Copenhagen have now discovered that children born with a low birth weight are especially at risk of health complications if they later develop obesity. The research appears in *eBioMedicine*.

"Our study shows that the link between low birth weight and cardiometabolic disease risk can be detected already in childhood—and that this is the case for both the actual birth weight and the genetic determinants of birth weight," says Sara Stinson, Postdoctoral research fellow, and first author of the study.

"It also supports the theory that individuals who were born [with] low birth weight, or who are genetically predisposed to low birth weight, may be more vulnerable to health hazards—such as excess visceral fat—throughout the course of life."

## Interrogating the link between disease risk and birth weight

Scientists have already discovered that people born with a high birth weight are more at risk of developing a higher-than-optimal BMI later in life. On the other hand, there is strong evidence that people born with a

low birth weight, or who have a genetic predisposition to low birth weight, have an increased risk of cardiometabolic diseases like type 2 diabetes.

What is less well understood is how and when in life people with these risk factors actually develop cardiometabolic disease. It is also unclear how overweight and obesity play a role in the development of cardiometabolic disease, depending on birth weight.

To learn more, the team of scientists analyzed a Danish cohort called The HOLBÆK Study of more than 4,000 children and adolescents with and without obesity. The cohort contains a wide variety of health-related data including birth weight, BMI, clinical evaluations, blood samples, biomarkers, and a polygenic score for birth weight—a calculation that combines the effect of many genetic variants related to birth weight.

## Underdeveloped subcutaneous fat increases disease risk

The scientists showed that developing obesity as a child presents more health risks if the child is born underweight. One example is sensitivity to the hormone insulin, which helps to regulate blood sugar levels. Low insulin sensitivity is a risk factor for type 2 diabetes.

"If we look at measures of insulin sensitivity, we see that being born with a low birth weight does not have an adverse effect in children with normal weight. However, in children with obesity, we see near normal insulin sensitivity in children born with a high birth weight and drastically decreased insulin sensitivity in children with low birth weight," says Ph.D. Student Pauline Kromann Reim, from the Novo Nordisk Foundation Center for Basic Metabolic Research at the University of Copenhagen and second author of the study.

The reason could be—literally—skin deep. The body normally stores fat in fat cells beneath the skin, called subcutaneous fat. But these fat stores may be underdeveloped in children who are born underweight, and they can therefore not expand as needed to store more fat.

Instead, their body stores fat, called visceral fat, around their organs. While subcutaneous fat is not dangerous for the body—but is essential for its proper functioning—higher levels of visceral fat have a range of negative health impacts including an increased risk of type 2 diabetes.

The scientists also found a link between low birth weight and increased levels of fat in the liver, which decreases insulin sensitivity and could explain why low birth weight individuals are—already in childhood—at a higher risk of developing type 2 diabetes. Blood samples from people with low birth weight also had higher levels of obesity-related biomarkers in their blood.

## Low birth weight children need tailored prevention and treatment

Based on the findings, Clinical Associate Professor Jens Christian Holm from The Children's Obesity Clinic, Copenhagen University Hospital Holbæk, and co-senior author on the paper, calls for prevention and treatment approaches that are tailored specifically for children with obesity who were born with a lower birth weight.

"Such targeted strategies could potentially reduce their risk of developing obesity-related cardiometabolic complications," says Christian Holm.

"Early intervention and more precision in who to treat and who not to treat are key elements in the battle of cardiometabolic disease," adds

Professor Torben Hansen from the Novo Nordisk Foundation Center for Basic Metabolic Research at the University of Copenhagen, and co-senior author on the paper.

**More information:** Sara Stinson et al, The interplay between birth weight and obesity in determining childhood and adolescent cardiometabolic risk, *eBioMedicine* (2024).

Provided by University of Copenhagen