Lucky genes can help protect people with obesity from some disease

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Geneticists have revealed why some people with obesity remain relatively healthy, while others suffer from life-changing ailments such as type 2 diabetes and heart disease.

Anyone with a BMI over 30 is considered obese rather than just overweight, and although people with obesity all have a few extra kilos in common, two people with the same BMI can have very different amounts of fat, and that fat can be distributed in different places throughout the body. Fat stored under the skin, like a paunch or a double chin, is considered less harmful than fat stored around organs such as the liver and heart. It's the genes we're born with that determine how and where this fat is stored—what scientists refer to as having "favorable" or "unfavorable" adiposity.

"Some people have unlucky fat genes, meaning they store higher levels of fat everywhere, including under the skin, liver and pancreas. That's associated with a higher risk of diseases such as type 2 diabetes," said Dr. Hanieh Yaghootkar, a lecturer in biosciences at Brunel University London, who led the research. "Others are luckier and have genes that mean higher fat under the skin but lower liver fat and a lower risk of diseases like type 2 diabetes."

Using a technique known as Mendelian randomization, the team found that of the 37 diseases they tested, 12—including coronary artery disease , stroke and type 2 diabetes—were directly related to the genes that determine whether or not a person has a "favorable adiposity," while nine could be said to be unrelated to someone's adiposity and were most likely a result of simply carrying too much weight, such as having deep vein thrombosis or arthritic knees.

However, the researchers caution that regardless of whether someone has a favorable or unfavorable adiposity, being obese is a serious hazard to a person's health, with even those with a favorable adiposity still at a heightened risk of diseases such as gallstones, adult-onset asthma and psoriasis.

They also found some other diseases previously thought to be related to

someone's weight, such as Alzheimer's, appear to be unconnected.

"To better prevent and measure risk of disease, it is important to understand if obesity is a casual risk factor and if it is causal, which consequences of it—be they metabolic, mechanical or psychological—are deriving the risk," said Dr. Yaghootkar.

She added, "Our results also provide evidence that everyone will benefit from losing their extra fat even if they are metabolically healthy."

The researchers say the results will help medical doctors determine if they should be targeting the adverse effects of someone's obesity, or be trying to get them to shed a few pounds. "For example, there are many treatments that can lower the high-fat levels in the blood and around the organs that do not affect the extra weight a person carries," said Prof. Timothy Frayling, Professor of Human Genetics at the University of Exeter.

"In contrast, for other conditions, it may be more important to reduce the extra weight, as much as or more than the damaging high sugar and fat levels in the blood."

The study, published in the journal *eLife*, funded by Diabetes UK, and run in collaboration with the University of Winchester, used data from Finland's FinnGen project and the UK Biobank, which collected information from 500,000 individuals aged 37 to 73 between 2006 and 2010 from across the UK. One in four are already considered by the NHS to be "very overweight" and at increased risk of getting seriously ill.

Dr. Susan Martin, a postdoctoral research fellow at Exeter who was involved in the research, said, "While it's important that we identify the causes of obesity-related disease, good genes is still no substitute for a

healthy lifestyle. A favorable adiposity will only go so far—if you're obese, the advice is to still try and shift the excess weight where you can."

Provided by Brunel University