

Genetic predisposition for obesity increases risk of asthma

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Credit: Karolina Grabowska from Pexels

What comes first? Do asthma sufferers put on weight because they are less active, or do they develop asthma because they are overweight, move around less and develop lung problems?

Geneticists have now entered the debate, and it looks as though people who are genetically predisposed to a high BMI also have a higher risk of developing asthma and struggle to breathe.

"We show that people who are predisposed to being overweight develop asthma more often and have lower lung function. So it appears to be important to remain at a normal weight if you want to prevent asthma and maintain normal lung function," says lead-author, Tea Skaaby, a senior scientist at the Center for Clinical Research and Prevention, Frederiksberg Hospital, Denmark.

Randomised test builds upon nature's own experiment

In the new study, which is published in the journal *Allergy*, scientists used a method known as Mendel randomization.

The method is named after Gregor Mendel—the father of genetics. It assumes that everyone is born with a genome that consists of random copies of genetic variants from the parents.

Everyone's genes are in that sense, random. And it is this randomisation that the scientists exploit in Mendel randomization.

The random assignment of genes from nature is similar to the way in which patients are randomly assigned to different groups in a clinical trial. One group receives the test medicine and the other receives a placebo. The effectiveness of the medicine is then measured by comparing the effect observed in each group.

Mendel randomization allows scientists to compare groups with different genetic mutations.

The only technique that can identify a causal relationship

Using this method, scientists are able to compare the genetics of thousands of people.

According to Lasse Folkersen, lead scientist at Sct Hans Hospital in Copenhagen, Denmark, it is the equivalent of comparing two groups of people, where one has been asked to put weight on during the experiment, and the other was asked to stay slim. The only difference is that these two groups exist naturally in the Mendel randomization experiment.

"Because the scientists have used a large database of genetic variants, they have more than 150,000 people to compare. In this way, Mendel randomization can establish a causal relationship in a large [database] and not just a random correlation," says Folkersen. He did not take part in the new study.

"Done correctly, it's perhaps the only technique that can provide a [causal relationship](#) besides human testing, which is impossible to do," he says.

Mendel randomization is not bulletproof

The scientists emphasise that the results are never 100 per cent certain. As unknown genetic variants could also play a role.

If the study does not include all of the important genetic variants and their effects, then it is difficult to draw any firm conclusions.

"It's not a bulletproof technique," says Folkersen, although he thinks that in this case the scientists have done all they could to support their

conclusions.

No practical use for the results just yet

At this stage it is unlikely that the new results will lead to any new treatments or preventative solutions just yet, says post-doc Jakob Stokholm from the Dansk Børne Astma Center (COPSAC).

"It's a step towards understanding asthma better and small pieces of the puzzle are important to come closer to preventing asthma," says Stokholm.

"We already knew that higher BMI is associated with a higher risk of asthma. So it's interesting in the big picture, but it's not knowledge that practitioners can implement," he says.

Today, Mendelian [randomization](#) is used to primarily to get a basic understanding of the relationship between genetic variations and disease or asthma and allergies, says Skaaby.

"I think that it will improve and become more concrete when we understand all of the basic mechanisms. Then we can begin to prevent [asthma](#) and allergies, and give better recommendations," she says.

More information: T. Skaaby et al. Estimating the causal effect of body mass index on hay fever, asthma and lung function using Mendelian randomization, *Allergy* (2017). [DOI: 10.1111/all.13242](https://doi.org/10.1111/all.13242)

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