

Genetic evidence that body mass increases the risk of asthma in mid-childhood

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Some of the increase in asthma risk toward the end of the 20th century could be attributed to the increase in body mass index (BMI) in mid-childhood, according to new research published in this week's *PLOS Medicine*. The study, led by Raquel Granell from the University of Bristol, UK, and colleagues, provides genetic evidence that higher fat mass and lean mass increase the risk of asthma in mid-childhood.

The incidence of [asthma](#), a chronic condition caused by inflammation of the airways, has been rising steadily over the past few decades, and it is estimated that 200-300 million adults and children worldwide are affected by asthma. The underlying causes of asthma are not known; however, some experts think obesity may be one of the causes. Obesity, like asthma, is increasingly common, and [observational studies](#) in children have reported that [body mass index](#) is positively associated with asthma. However, observational studies cannot prove that obesity causes asthma, so in this study the researchers applied a method called Mendelian randomization, which uses both genetic information and observational data, in order to assess whether BMI has a causal effect on asthma.

In a Mendelian randomization study, causality can be inferred from associations between genetic variants that are known to affect a modifiable risk factor (in this case, body [mass](#)) and the outcome of interest (childhood asthma). The researchers investigated causal effects of BMI, [fat mass](#), and lean mass on current asthma at age 7.5 years in 4,835 children enrolled in the Avon Longitudinal Study of Parents and Children (ALSPAC, a long-term health project that started in 1991). A weighted genetic score based on 32 independent BMI-related DNA sequence variations was calculated, and associations with BMI, fat mass, lean mass, and asthma were estimated. The authors found that the genetic score was strongly associated with BMI, fat mass, and lean mass, and

with [childhood asthma](#), and that the relative risk of asthma increased by 55% for every extra unit of BMI.

These findings suggest that a higher BMI increases the risk of asthma in mid-childhood, and that public health interventions designed to reduce obesity may also help to limit the global rise in asthma.

The authors note some limitations to their study, in that it is possible that the observed association between BMI and asthma reported in this study is affected by genetic pleiotropy, in which some of the genetic variants included in the BMI genetic score could also independently increase the risk of asthma. There is also some evidence that body composition (lean [body mass](#)) influences asthma through pathways not related to obesity-induced inflammation, and future studies will need to address this relationship.

The authors conclude, "environmental influences on the development of asthma in childhood have been extensively investigated in epidemiological studies, but few of these provide strong evidence for causality... [higher BMI in mid-childhood] could help explain some of the increase in [asthma risk](#) toward the end of the 20th century, although the continued rise in obesity but with a slowing in the rise in asthma prevalence in some countries implies that other non-BMI-related factors are also likely to be important."

More information: Granell R, Henderson AJ, Evans DM, Smith GD, Ness AR, et al. (2014) Effects of BMI, Fat Mass, and Lean Mass on Asthma in Childhood: A Mendelian Randomization Study. *PLoS Med* 11(7): e1001669. [DOI: 10.1371/journal.pmed.1001669](#)

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