

Childhood obesity linked to increased risk of 4 of 5 newly proposed subtypes of adult-onset diabetes

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New research published in *Diabetologia* is the first study to show that childhood obesity is associated with an increased risk of four of the five

recently proposed subtypes of adult-onset diabetes. The study is by Yuxia Wei, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden, and colleagues.

In 2018, a ground-breaking study identified five novel subtypes of adult-onset diabetes: severe autoimmune diabetes (SAID, including type 1 diabetes and latent autoimmune diabetes in adults [LADA]) and four subtypes of type 2 diabetes (severe insulin-deficient diabetes [SIDD], severe insulin-resistant diabetes [SIRD], mild obesity-related diabetes [MOD] and mild age-related diabetes [MARD]). SIDD, SIRD, MOD and MARD are currently collectively classed as type 2 diabetes. These subtypes of diabetes differ in their clinical characteristics, complications and genetic backgrounds. It is unclear if they also differ in modifiable risk factors.

The prevalence of [childhood obesity](#) is rising worldwide. Childhood [adiposity](#) has been linked to several [chronic diseases](#) including type 1 diabetes in children and type 2 diabetes; however, it has never been investigated in relation to the recently proposed subtypes of adult-onset diabetes. In this study, the authors aimed to compare the effects of [childhood body size](#) on the risk of different diabetes subtypes occurring in adults. They used a [statistical technique](#) known as Mendelian randomization (MR), where [genetic information](#) is used to study the link between an environmental risk factor and a disease, while accounting for the influence of other risk factors.

The authors used data from the UK Biobank for their study. They extracted summary statistics for childhood body size from a [genome-wide association study](#) of 453,169 European participants who self-reported body size (thinner, about average, and plumper/bigger) at the age of 10 years in the UK Biobank study. The study incorporated more than 200 [genetic mutations](#) as indicators of childhood body size and linked them to LADA (267) and the other types of diabetes (275).

The results showed higher levels of childhood adiposity (children who perceive themselves as being plumper/bigger than other children compared to children who perceive themselves as being of average body size) were linked to a 62% increased risk of LADA, a doubling of the risk of SIDD, a near-tripling of the risk of SIRD, and a 7-times increased risk of MOD. The only diabetes subtype showing no association with childhood obesity was MARD.

Previous studies of this kind (using MR) have found that childhood body size is linked to a doubling of risk for both type 1 diabetes (mean age of diagnosis 16 years) and type 2 diabetes. The authors say, "We extend these findings by demonstrating that childhood adiposity is a risk factor for four out of the five recently proposed diabetes subtypes."

The authors say their study reveals potentially different mechanisms linking childhood adiposity to different diabetes subtypes. The link between childhood body size and SIRD or MOD is expected, given the adverse effects of adiposity on insulin sensitivity. Interestingly, children with higher levels of adiposity also had higher risks of LADA and SIDD, both of which are characterized by insulin deficiency. This phenomenon may be explained by the fact that impaired insulin secretion is affected jointly by excess fat around the pancreas and insulin resistance.

The authors conclude, "Our analyses indicate that childhood obesity is a risk factor for four of the five proposed novel subtypes of adult-onset diabetes, regardless of whether they are classified as being primarily characterized by autoimmunity, insulin deficiency, insulin resistance or obesity. Childhood obesity appears to be a risk factor for essentially all types of diabetes in adults, except for mild age-related [diabetes](#). This stresses the importance of preventing obesity in children."

More information: Yuxia Wei et al, Childhood adiposity and novel subtypes of adult-onset diabetes: a Mendelian randomisation and genome-

wide genetic correlation study, *Diabetologia* (2023). DOI: [10.1007/s00125-023-05883-x](https://doi.org/10.1007/s00125-023-05883-x)

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