

## **EASD ABSTRACT (3200 characters excluding spaces)**

**Broad changes in body mass index between age 10 and adulthood are associated with type 2 diabetes risk independently of adult body mass index.**

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**Keywords:** BMI, type 2 diabetes, childhood body size, UK Biobank

Background and aims: Obesity is a strong risk factor for type 2 diabetes, but the condition occurs across the body mass index (BMI) range. Age, sex, ethnic differences, varying body fat distribution and genetic factors all contribute to differences in type 2 diabetes risk independently of BMI. Here, we used the UK Biobank to test the hypothesis that an additional factor, approximate change in BMI between childhood and adulthood, would contribute to type 2 diabetes risk.

Materials and methods: We used data from 371,903 individuals of European ancestry in the UK Biobank, with a measure of adult BMI, self-reported perceived relative body size at age 10 and genetic data available. First, we validated the perceived body size at age 10 by investigating the association with a BMI genetic risk score. We then stratified individuals based on their adulthood BMI into overweight and obese. Logistic regression models were used to calculate the odds of type 2 diabetes for individuals who were thin at age 10 and were either now overweight or obese in comparison to overweight or obese individuals who perceived themselves to be average or plump at age 10.

Results: Individuals in the overweight BMI range (25-30 kg/m<sup>2</sup>) but who reported being thin, average and plump at age 10 had an average BMI of 27.2, 27.3 and 27.5 kg/m<sup>2</sup> respectively. Despite these very similar current BMIs, individuals who on average had moved up these broad BMI centiles were at 1.53 [95%CI: 1.44, 1.62] higher odds of diabetes than someone who had remained in an average BMI centile. Obese individuals ( $\geq 30$  kg/m<sup>2</sup>) who reported being thin, average and plump at age 10 had an average BMI of 33.6, 33.5 and 34.9 kg/m<sup>2</sup> respectively. Despite slightly lower current BMI, the prevalence of type 2 diabetes was highest in those people, who on average had moved up the broad BMI centiles, with individuals who were thin at age 10, average at age 10 and plump at age 10 having a type 2 diabetes prevalence of 14.6%, 11.0% and 12.3% respectively. This equated to an odds ratio of type 2 diabetes of 1.07 [95%CI: 1.01, 1.13] for the group of people moving up

these broad BMI centiles compared to those staying at the same broad centile. These findings were independent of an individuals birthweight and current BMI. Conclusions: These findings suggest that individuals who remain in higher BMI centiles throughout life may adapt to excess weight in ways that lower the risk of type 2 diabetes in comparison to individuals of similar adult BMI that have moved up the BMI centiles since childhood.