

Low birthweight independently linked to increased risk of type 2 diabetes, including lower age at diagnosis

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Two studies published in *Diabetologia* show that lower birthweight is an independent risk factor for type 2 diabetes (T2D), and is linked to a



distinct presentation of T2D at the time of diagnosis—including younger age, a lower prevalence of overweight/obesity, and fewer people in the family with T2D.

T2D patients with lower birthweight also show higher use of diabetes drugs than those with normal birthweight, and a larger number of comorbidities including <u>high blood pressure</u>, at the time of diagnosis.

The first study is by Dr. Rasmus Wibaek, Steno Diabetes Center Copenhagen, Herlev, Denmark, and Dr. Allan Vaag, Steno Diabetes Center Copenhagen, and also Lund University, Malmö, Sweden, and colleagues.

This study included adults aged 30–60 years enrolled in the Danish Inter99 cohort in 1999–2001 (baseline examination), with information on birthweight from original birth records from 1939–1971 and without diabetes at baseline. Birth records were linked with individual-level data on age at diabetes diagnosis.

Incidence rates of T2D by age, sex and birthweight were estimated using statistical modeling, adjusting for prematurity status at birth, birth order (position in the <u>birth order</u> among any siblings), genetic risk scores for birthweight and type 2 diabetes, maternal and paternal diabetes history, <u>socioeconomic status</u> and adult body mass index (BMI).

The authors found that, among 4,590 participants, there were 492 incident T2D cases during an average follow-up of 19 years. T2D incidence rate increased with age, was higher in male participants, and decreased linearly with increasing birthweight, with each extra kg of birthweight linked to a 40% reduced risk of T2D, which continued into the highest birthweights. Notably, the absolute rate of increase in T2D incidence across age was markedly steeper in persons born with lower birth weights compared with higher birth weights.



The findings suggest that the effect of birth weight on type 2 diabetes risk is distinct and independent of genetic susceptibility to T2D and adult adiposity, and that <u>low birth weight</u> as a proxy of an adverse fetal environment is of similar etiological importance to that of genotype.

The second study, also by Dr. Vaag and first author Dr. Aleksander L. Hansen of the Steno Diabetes Center Copenhagen, and colleagues, analyzed midwife records for 6866 individuals with T2D in the Danish Centre for Strategic Research in type 2 diabetes cohort.

They assessed age at diagnosis, anthropomorphic measures (body dimensions), comorbidities, medications, metabolic variables, and family history of T2D in individuals with the lowest 25% of birthweight (3700 g), compared with a birthweight of 3000–3700 g as reference (the middle 50% of birthweights 25%-75%), using statistical modeling.

Continuous relationships across the entire birthweight spectrum were also assessed. Weighted polygenic scores (PS) for type 2 diabetes and birthweight were calculated to assess the impact of genetic predispositions.

Each 1 kg decrease in birthweight was associated with a 3.3 year younger age of diabetes onset, 1.5 kg/m² lower BMI and 3.9 cm smaller waist circumference. Compared with the reference birthweight, a birthweight of

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