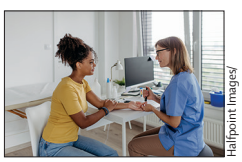
Young adult-onset type 2 diabetes heralds a poor prognosis



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Younger-onset type 2 diabetes is rapidly increasing in prevalence, with the majority presenting in adulthood aged 18–39 years.[1] This change in diabetes topography presents a challenge to health-care professionals that is hindered by a paucity of research to inform clinical practice. In the UK, the fastest rate of increase in new type 2 diabetes cases (40% between 2016 and 2023) is in people younger than 40 years,[2] which reflects the scale of this looming crisis. Comprehension of the natural history, phenotypic characteristics, and complication risk, assessed longitudinally over time, can help to inform which areas of care require clinical attention and direct future research.

Insights into this understanding are provided in *The Lancet Diabetes & Endocrinology* by Beryl Lin and colleagues in the analysis from the landmark UK Prospective Diabetes Study (UKPDS) of glucose-lowering therapies in adults with newly diagnosed type 2 diabetes recruited between 1977 and 1991.[3] In this report, the trajectory of clinical characteristics, incidence of diabetes-related complications, and mortality risk of younger-onset type 2 diabetes (mean age of diagnosis: 35 years, constituting 9·4% of study population) were compared to older-onset (mean age of diagnosis: 54 years) type 2 diabetes, observed over a median duration of 18 years. Only those with no autoantibodies for type 1 diabetes were studied. Compared with those diagnosed above age 40 years, the younger-onset cohort had higher levels of obesity with poorer glycaemic control, greater insulin resistance, and a more rapid decline in insulin secretory capacity. The younger-onset cohort had a higher 5-year incidence of diabetes-related complications and mortality at any given age.

Although younger-onset type 2 diabetes was an uncommon diagnosis when the UKPDS was undertaken, it confirms that in young adults, type 2 diabetes presents a much more serious biological phenotype than when it develops later in life, being associated with the combination of failing insulin secretion, increasing insulin resistance, and greater obesity. These conclusions are strengthened by the long duration of the UKPDS in a well characterised type 2 diabetes population. While other studies have shown more rapid decline in insulin secretion in a younger-onset subgroup,[4] few have shown the concurrent presence of higher insulin resistance with prevailing obesity. In the UKPDS population, the BMI of the newly diagnosed, younger-onset cohort was 30 kg/m^2, which was lower than has been documented in recent studies (around 35 kg/m^2),[5] highlighting the temporal progression of obesity in young adults over four decades.

The heightened risk of diabetes complications, despite a similar length of follow-up to the older-onset group, shows the elevated lifetime risk in young adult-onset type 2 diabetes, which is more prominent for retinal and renal complications, revealing an aggressive phenotype. It is debatable whether the elevated propensity to develop complications relates to diabetes duration or to adverse biological predisposition.[6] The predominant factor might depend on the type of complication. Regardless of the cause, the message is clear: aggressive management is imperative in young adult-onset type 2 diabetes. A recent UK study showed that individuals diagnosed with type 2 diabetes at age 45 years had an 80% chance of developing cardiorenal disease in their lifetime.[7] It is likely that those diagnosed below age 40 years will possess a similar or even higher risk of these complications. The rationale for using lifetime, rather than short-term (10 years), risk assessment for cardiovascular disease is justified to avoid misclassifying younger-onset type 2 diabetes as a low-risk condition.[8]

Provision of comprehensive and intensive diabetes management is essential to improve the prognosis of young people with type 2 diabetes. Faced with reduced life expectancy, active treatment of cardiovascular risk factors should mitigate loss of life years, potentially with greater benefit in young adults.[9] In 2023, the National Health Service England launched a national initiative, the T2Day programme, to improve care of young people living with type 2 diabetes through optimisation of diabetes management, including weight, glycaemia, and cardiovascular risk interventions. The study by Lin and colleagues[3] clearly supports the fundamental principles of care espoused by this programme.

Information that could assist management of younger-onset type 2 diabetes include the effect of newer medications (SGLT2-inhibitors, GLP-1 agonists, and dual GIP/GLP-1 agonists) on glycaemic durability,

For more on the **T2Day programme** see https://www.england.nhs.uk/2023/08/nhs-rolls-out-world-first-programme-to-transform-diabetes-care-for-under-40s/

weight loss, and prognostic outcomes. A limitation of the UKPDS is that it predated the use of therapies that can modify cardiometabolic and mortality risk. Effective weight management is important since people with type 2 diabetes younger than 40 years are likely to have obesity or gain weight.[10] More challengingly, ascertainment of innovative service models tailored to deliver holistic care that is culturally sensitive and clinically responsive to the complex medical and psychosocial needs of these young individuals is crucial. This is important since ethnic minority groups are now disproportionately represented in the younger-onset cohort, in contrast to the largely White population in the UKPDS.

Formulation of national guidelines to inform clinicians of evidence-based and cost-effective interventions for young people with type 2 diabetes is urgently needed since complications are occurring at an economically productive age. More research in this younger-onset population is crucial to fulfil this objective.

We declare no competing interests.

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1 NHS England. National Diabetes Audit 2021–22: young people with type 2 diabetes, detailed analysis report. https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-audit-yt2/young-people-with-type-2-diabetes-detailed-report-2021-22 (accessed Aug 14, 2024).
2 Diabetes UK. Reverse the trend report: reducing type 2 diabetes in young people. London: Diabetes UK, 2024.
3 Lin B, Coleman RL, Bragg F, Maddaloni E, Holman RR, Adler AI. Younger-onset compared with later-onset type 2 diabetes: an analysis of the UK Prospective Diabetes Study (UKPDS) with up to 30 years of follow-up (UKPDS 92). *Lancet Diabetes Endocrinol* 2024; published online Oct 23. https://doi.org/10.1016/S2213-8587(24)00242-0.
4 Ke C, Stukel TA, Shah BR, et al. Age at diagnosis, glycemic trajectories, and responses to oral glucose-lowering drugs in type 2 diabetes in Hong Kong: a population-based observational study. *PLoS Med* 2020; **17:** e1003316.
5 Dibato J, Montvida O, Ling J, Koye D, Polonsky WH, Paul SK. Temporal trends in the prevalence and incidenc0e of depression and the interplay of comorbidities in patients with young- and usual-onset type 2 diabetes from the USA and the UK. *Diabetologia* 2022; **65:** 2066–77.
6 Sajjadi SF, Sacre JW, Carstensen B, Ruiz-Carmona S, Shaw JE, Magliano DJ. Evaluating the incidence of complications among people with diabetes according to age of onset: findings from the UK Biobank. *Diabet Med* 2024; **41:** e15349.
7 Zhang R, Mamza JB, Morris T, et al. Lifetime risk of cardiovascular-renal disease in type 2 diabetes: a population-based study in 473,399 individuals. *BMC Med* 2022; **20:** 63.
8 Moran GM, Bakhai C, Song SH, Agwu JC. Type 2 diabetes: summary of updated NICE guidance. *BMJ* 2022; **377:** o775.
9 Kianmehr H, Zhang P, Luo J, et al. Potential gains in life expectancy associated with achieving treatment goals in US adults with type 2 diabetes. *JAMA Netw Open* 2022; **5:** e227705.
10 Katsoulis M, Lai AG, Diaz-Ordaz K, et al. Identifying adults at high-risk for change in weight and BMI in England: a longitudinal, large-scale, population-based cohort study using electronic health records. *Lancet Diabetes Endocrinol* 2021; **9:** 681–94.