## Prediabetes: much more than just a risk factor

On Feb 6, 2025, Diabetes UK reported that more than 12 million people in the UK are now living with diabetes or prediabetes. The total includes 4.6 million with diabetes (90% type 2 diabetes, 8% type 1 diabetes, and 2% other forms), 1.3 million with undiagnosed diabetes, and 6.3 million with prediabetes. The numbers keep rising year after year—4.6 million new cases have been diagnosed this year, up from 4.4 million last year.

With 5-10% of people per year with prediabetes progressing to type 2 diabetes, tackling the spiralling global epidemic of type 2 diabetes will only be possible with a renewed focus on and greater commitment to prevention programmes targeting prediabetes and its progression. The UK is by no means alone in facing the challenge of a growing population with prediabetes. In the USA, data from the Centres for Disease Control and Prevention (CDC) show that 38% of adults (aged 18 years and older) were living with prediabetes in 2021 (98 million), a proportion rising to 49% in those aged 65 years and older. Globally, the situation is similar. According to the International Diabetes Federation (IDF) Atlas, 10th Edition, 541 million adults around the world were living with prediabetes in 2021—a number similar to the number of people living with diabetes.

Prediabetes (also referred to as impaired fasting glucose, impaired glucose tolerance, impaired glucose regulation, and non-diabetic hyperglycaemia) is defined by a fasting glucose level of 100-125 mg/dL, a glucose level of 140-199 mg/dL measured 2 h after a 75 g oral glucose tolerance test, or an  $HbA_{1c}$  of 5.7% to 6.4%or 6.0% to 6.4%, as per proposals from the American Diabetes Association (ADA), WHO, and the International Expert Committee. Although people with the highest scores on the diagnostic tests are at greatest risk of progressing to type 2 diabetes, prediabetes is more than just a reading on a glycaemic scale. This condition is a serious health issue, closely tied to metabolic syndrome and associated with cardiovascular disease and mortality. In a 2020 meta-analysis of 129 studies including more than 10 million individuals, compared with normoglycaemia in the general population, prediabetes was associated with an increased relative risk of all-cause mortality (13%), cardiovascular disease (15%), coronary heart disease (16%), and stroke (14%), over a median follow-up of 9.8 years. Some of these risks became more pronounced when prediabetes was compared with normoglycaemia in the population with pre-existing atherosclerotic cardiovascular disease. For example, over a median follow-up of 3·2 years, prediabetes was linked to a 36% increase in all-cause mortality and 37% increase in cardiovascular disease.

Major risk factors for prediabetes include overweight and obesity, older age (45 years and older), genetic predisposition, unhealthy diet, physical inactivity, socioeconomic deprivation, and having current or previous conditions (eg, metabolic dysfunction-associated steatotic liver disease or gestational diabetes). Race and ethnicity are also contributing factors, with Asian, Black, and Hispanic adults at higher risk of prediabetes than White adults.

Prediabetes can be treated or reversed by intensive lifestyle modification involving calorie restriction and increased physical activity, or, less effectively, by metformin in some groups. In the 2024 STEP 10 trial in people with obesity and prediabetes, 81% of participants treated with semaglutide 2·4 mg reverted to normoglycaemia compared with only 14% in the placebo group. This result suggests that GLP-1 receptor agonists could, in the future, offer hope for people in whom lifestyle change is unsuccessful.

Prediabetes is the last point on the glycaemic spectrum at which type 2 diabetes can still be halted. Yet, prediabetes has long been viewed as just a risk factor rather than a key opportunity for prevention. The rising number of people with prediabetes worldwide, which directly fuels the type 2 diabetes epidemic, is a looming public health crisis that must be addressed. Early detection and treatment of prediabetes is essential to prevent crippling already overstretched and underfunded health-care systems from surging type 2 diabetes cases and mitigate the economic burden on societies of treating this costly condition and its complications. Given the differing definitions and diagnostic criteria for prediabetes, a single, universally accepted, sensitive, and cost-effective blood test is urgently required to facilitate wider adoption of screening for prediabetes. Until then, educating people about their risk of type 2 diabetes and targeting those most at risk of progression for treatment should be a priority. 

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For the **Diabetes UK report** see https://www.diabetes.org.uk/ about-us/news-and-views/onefive-adults-now-live-diabetesor-prediabetes-uk

For more on **prediabetes** see **Series** *Lancet* 2023; **379:** 2279–90

For more on **prediabetes in the USA** see https://www.cdc.gov/
diabetes/php/data-research/
index.html

For more on the **global prevalence of prediabetes** see https://diabetesatlas.org/

For more on diagnosis and management of prediabetes see JAMA 2023; **329**: 1206–16

For prediabetes, all-cause mortality and cardiovascular disease see BMJ 2020; 370: m2297

For more on prediabetes prevalence by race and ethnicity see Front Public Health 2023; 11: 1277657

For the **STEP 10 trial** see **Articles** Lancet Diabetes Endocrinol 2024; **12:** 631–42

For more on individual risk of type 2 diabetes see Editorial Lancet Diabetes Endocrinol 2023; 11: 879