Age at prediabetes diagnosis and risk of developing type 2 diabetes and cancer

Age at diagnosis of prediabetes influences the association with developing type 2 diabetes, cancer and mortality, with the highest risk in people diagnosed with prediabetes at age 75 years and above, according to this study of data from nearly 330 000 people published in *The Lancet Diabetes & Endocrinology*. Cancer rates were only slightly higher in those who progressed to type 2 diabetes compared with those who remained in prediabetes, with maximal differences around 4 and 5 cases per 1000 person-years in men and women, respectively. Smoking, BMI, socioeconomic status and ethnicity had smaller influences on progression rates. There were no significant differences in rates and transitions between men and women, and the median age of prediabetes diagnosis was 63.5 years in women and 60.1 years in men. It is hoped these data can help target cancer prevention and screening services and motivate people to make lifestyle changes to reduce their risks of progression to type 2 diabetes.

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Previous studies have suggested an increased risk of breast, colorectal, endometrial, gallbladder, liver and pancreatic cancers associated with type 2 diabetes. Around 30% of deaths are due to cancer, and almost half of all cancer deaths can be prevented through risk factor modification. Cancer and diabetes are closely linked; globally, almost 6% of cancer incidence is attributable to type 2 diabetes and overweight or obesity (Pearson-Stuttard et al, 2018).

In the present study of people diagnosed with prediabetes over a 20-year period in England, Zaccardi and colleagues sought to quantify the trajectories from prediabetes to cancer, including the possible interim development of type 2 diabetes and death, with a view to better targeting of cancer prevention and screening. It also sought to take into consideration key socioeconomic factors which may influence cancer development, such as age, BMI and smoking.

The study

Data from the Clinical Practice Research Datalink GOLD database were used to identify people aged 18–100 years with a new first diagnosis of prediabetes from 1 January 1998 to 30 November 2018. Hospital Episode Statistics death registrations were used to identify deaths.

HbA_{1c} 42–47 mmol/mol, fasting blood glucose 5.5–6.9 mmol/L, or a coded diagnosis of prediabetes or non-diabetic hyperglycaemia were used to identify the 328 049 people (47% women and 53% men) with prediabetes included in the study. Age, BMI and smoking status at diagnosis of prediabetes, as well as ethnicity (white vs non-white) were recorded.

The median age of prediabetes diagnosis was 63.5 years in women and 60.1 years in men. The dates of diagnosis of type 2 diabetes, cancer or death, if any of these occurred, were collected and used to identify seven transitions (*Figure 1*, overleaf) in men and women separately.

Results

Over a median of 7.7 years' follow-up, cancer incidence rates were higher in people who were older at prediabetes diagnosis (age ≥75 years versus <55 years). Cancer incidence rates were marginally higher in those with type 2 diabetes versus those with prediabetes; over 10 years, the lowest additional cancer risk was only 1.3 extra cases per 1000 person-years, while the highest additional risk was 4.1 and 4.8 cases per 1000 person-years in women and men, respectively.

At 10 years after prediabetes diagnosis, the likelihood of the specific outcomes, according to sex and age at prediabetes diagnosis, ranged as follows:

- Persisting prediabetes ranged from 23.2% (men aged ≥75 years) to 72.1% (men aged <55 years).
- Death ranged from 1.2% (women aged <55 years) to 38.7% (women aged ≥75 years).

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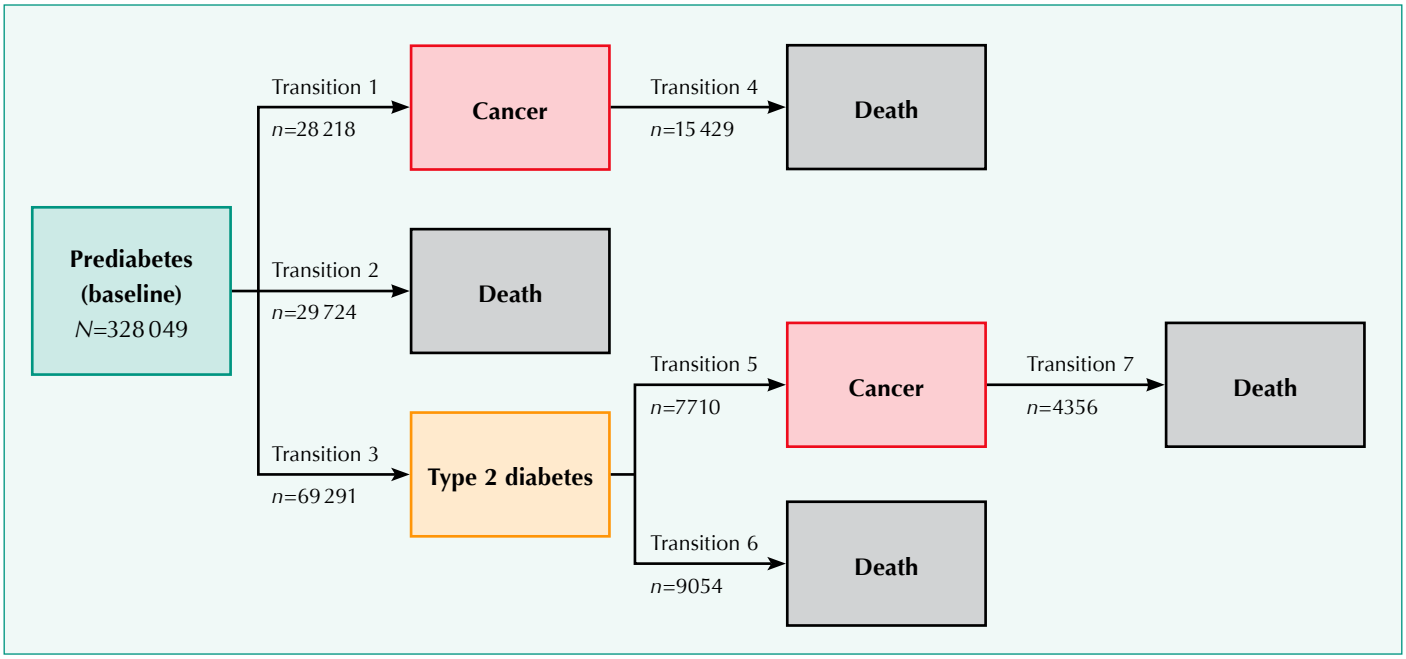

Figure 1. Transitions and outcomes at 10 years' follow-up (men and women combined).

- Developing type 2 diabetes and remaining in this state (without cancer or death) ranged from 7.9% (men ≥75 years) to 24.0% (women <55 years).
- Developing cancer ranged from 1.9% (men <55 years) to 7.8% (men aged 65 to <75 years).

Older age (>75 years at diagnosis) was associated with higher cancer rates, and the highest transition rates in both men and women were to death following a cancer diagnosis. Younger age (<55 years) was associated with less transition to type 2 diabetes during the timeframe of the study. 10 years post-diagnosis, 25–30% of those in the ≥75 age range and 70% of those aged <55 years were still in prediabetes.

There were no significant differences in rates and transitions between men and women, but the median age of prediabetes diagnosis was 63.5 years in women and 60.1 years in men.

Higher BMI was associated with a lower likelihood of persisting prediabetes at 10 years, with a relative risk of 0.67 when those with BMI ≥40 were compared to those with BMI <25 kg/m^2. Smoking, socioeconomic status and ethnicity showed independent associations with different trajectories of developing type 2 diabetes, cancer or death; however, the associations were generally of smaller magnitude.

In the 10 years following the diagnosis of prediabetes, time spent with prediabetes was lowest in men aged ≥75 years at diagnosis (5.34 years), and highest in men aged <55 years (8.34 years). As expected, BMI, smoking, socioeconomic status and ethnicity also impacted the amount of time spent in each state during the study.

Discussion

The postulated mechanism for the increased cancer risk observed in people with type 2 diabetes in previous studies is that high insulin levels and insulin resistance stimulate cancer-related signalling pathways. Hyperglycaemia begins in the prediabetes state, and a previous meta-analysis has demonstrated increased cancer risk in people with prediabetes (Schlesinger et al, 2022).

This large study demonstrated only small differences in cancer rates between those with type 2 diabetes and those with prediabetes. In contrast, age at diagnosis of prediabetes had a significant impact on the likelihood of persisting prediabetes, progression to type 2 diabetes, and development of cancer and mortality. To some extent, this can usefully be incorporated into screening programmes to ensure those at highest risk are targeted.

Strengths of the study include the use of multistate modelling, which can better mimic

the natural history of disease progression and provide a more accurate and detailed understanding of the full course and interactions of these diseases. Use of a primary care database was an additional strength, as a recent publication from Leeds highlights that clinical coding in secondary care, including cancer centres, may be inaccurate in coding those with type 2 diabetes, whereas coding of type 2 diabetes in primary care is more consistent due to incentive schemes (Zucker et al, 2025).

Implications for practice

This paper provides a wealth of UK data. People with prediabetes often ask about their risk of developing type 2 diabetes, and people diagnosed with type 2 diabetes ask how this will influence risk of chronic conditions including cancers. This study provides data on the potential trajectories towards the development of cancer, type 2 diabetes and death, and how these associations are impacted by age and BMI in a UK population. It is hoped we may be able to use these data in a non-threatening, informational way, to help people understand their risks and perhaps motivate them to choose to make lifestyle changes and to lose weight.

Most people, particularly those diagnosed with prediabetes under the age of 55 years, did not develop either type 2 diabetes or cancer over the ensuing 10 years in this study, but we know from other studies that risk of cardiovascular disease is increased (Cai et al, 2020); therefore, their overall health risks are higher than those with normoglycaemia. What we may have given less thought to is the impact of chronic hyperglycaemia in prediabetes on inflammation, signalling pathways and supporting tumour growth, and how this may impact cancer risk. We will also have an important role in helping people cope with the psychological and physical impact of having both type 2 diabetes and cancer.

People with prediabetes may spend less than 2 hours with a healthcare professional each year unless they choose to attend a formal diabetes prevention programme; for the remainder of the time, they have sole responsibility for their health. Any information and education we share can make an impact, and hopefully we can harness the data in this study, turn it into a useful format, and make time to share key messages to motivate people to make lifestyle changes.

Going forward, screening strategies and support for people who develop prediabetes should take into account the age at diagnosis, and target prevention and screening appropriately at older people as well as younger people. ■

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Trajectories of type 2 diabetes and cancer in 330 000 individuals with prediabetes: 20-year observational study in England

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