New study shows increased cancer mortality in people with type 2 diabetes

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New research published in *Diabetologia* shows that cancer mortality in people with type 2 diabetes is substantially higher than in the general population, by 18% for all cancers combined, 9% for breast cancer and

2.4 times for colorectal cancer. Cancer mortality in people with diabetes was also around double that in the general population for diabetes-related cancers including liver (both sexes), pancreatic (both sexes) and endometrial (women only) cancers.

The study, by Dr. Suping Ling, Leicester Real World Evidence Unit, Leicester Diabetes Research Centre, University of Leicester, and London School of Hygiene & Tropical Medicine, UK, also showed increasing breast cancer mortality rates by 4.1% per year in the younger women with type 2 diabetes across the 20-year study period from 1998-2018.

Accumulating epidemiological evidence has shown a higher risk of incidence and mortality for some types of cancer in individuals with type 2 diabetes, with prolonged exposure to the effects of increased blood sugar and insulin levels, insulin resistance and chronic inflammation being the potential underlying biological mechanisms.

Robust evidence indicates that there is a causal relationship between type 2 diabetes and pancreatic, liver and endometrial cancer. While previous studies have extensively investigated inequalities in cardiovascular outcomes among people with type 2 diabetes, less is known about whether such inequalities exist in cancer mortality rates.

In this study, the authors used a cohort of individuals aged 35 years or over who had newly diagnosed type 2 diabetes in the Clinical Practice Research Datalink, a UK general practice database, over a 20-year period between 1 January 1998 and 30 November 2018. They analyzed trends in all-cause, all-cancer and cancer-specific mortality rates by age, gender, ethnicity, socioeconomic status, obesity and smoking status. They also estimated standardized mortality ratios, comparing mortality rates in people with type 2 diabetes with the general population.

The study included 137,804 individuals with newly diagnosed type 2 diabetes with median follow-up of 8.4 years. The authors found all-cause mortality rates decreased at all ages between 1998 and 2018; cancer (all cancers combined except non-melanoma skin cancer) mortality rates also decreased for 55-year-olds (by 1.4% per year) and 65-year-olds (by 0.2% per year) but increased for 75-year-olds (by 1.2% per year) and 85-year-olds (by 1.6% per year).

The authors say that decreasing cardiovascular mortality observed in older age groups, owing to successful cardiovascular prevention and treatment in the last few decades, means that people live longer now and have a greater chance of experiencing other conditions and therefore dying from other causes (including cancer). However, diabetes screening, better management of diabetes and its complications, earlier cancer detection and improved cancer treatments seem to have benefited younger people with T2D in the same way as they have in the general population.

There were also higher "annual average percentage changes" (AAPC, the average percentage increase/decrease per year) in cancer mortality in women (1.5%) compared with men (1.0%), although women had lower cancer mortality throughout the study period. Biological factors, health-seeking behaviors, and lifestyle factors such as smoking and obesity all differ between men and women, but the relative contribution of each to cancer mortality is not known. The least deprived/wealthiest group also had a higher AAPC (1.5%) than the most deprived/poorest (1.0%)—leading to a narrowing but persistent gap by socioeconomic status.

Other key findings included higher cancer mortality AAPC for people with morbid obesity (5.8%) versus those in other weight categories (all below 1.0%), and also a higher cancer mortality AAPC for white people (2.4%) compared with an average annual percentage decrease of 3.4%

across non-white ethnicities combined. The gap in cancer mortality between smokers and non-smokers also increased, with smokers seeing an increased cancer mortality AAPC of 3.4%, while for non-smokers the AAPC fell by 1.4%.

The authors suggest current healthcare policies and structures could benefit never-smokers more than smokers—and that tailored interventions for smokers such as specific screening programs could help address increasing cancer mortality (and all-cause mortality) in smokers.

Constant upward trends in mortality rates were also observed for pancreatic, liver and lung cancer at all ages, colorectal cancer at most ages, breast cancer at younger ages, and prostate and endometrial cancer at older ages.

Compared with the general population, people with type 2 diabetes had a more than 1.5-fold increased risk of colorectal, pancreatic, liver and endometrial cancer mortality during the whole study period. Despite national reports from this period showing a decrease in breast cancer morality in the younger age ranges in this study, this new research showed also showed an increasing breast cancer mortality rates by 4.1% per year in the younger women with type 2 diabetes.

The authors suggest, "From this perspective, our results suggest that it may be helpful to extend breast cancer screening to young women with type 2 diabetes. However, given the high cost and potentially longer exposure to screening procedures, cost-effectiveness analyses are required to define the appropriate time window and identify subgroups who may benefit more."

They add that there are currently trials investigating extending the existing breast cancer screening window from 50-70 years to 47-73 years in the general population; in addition, women with a family history of

breast cancer or specific gene mutations are offered screenings from a younger age, but no current guidelines specifically consider the increased risk of breast cancer in women with diabetes.

On cancer mortality overall in people with diabetes, the authors say, "The prevention of cardiovascular disease has been, and is still considered, a priority in people with diabetes. Our results challenge this view by showing that cancer may have overtaken cardiovascular disease as a leading cause of death in people with type 2 diabetes. Cancer prevention strategies therefore deserve at least a similar level of attention as cardiovascular disease prevention, particularly in older people and for some cancers such as liver, colorectal and pancreatic cancer. Tailored interventions should also be considered for smokers, who had higher and steadily increasing cancer mortality rates. Interventions for smokers, in addition to stopping smoking could include campaigns to raise awareness of cancer and improve early detection. For people with type 2 diabetes, early cancer detection through changes to existing screening programs, or more in-depth investigations for suspected/non-specific cancer symptoms, may reduce the number of avoidable cancer deaths."

The authors conclude, "In conclusion, our findings underline the growing cancer burden in people with type 2 diabetes, particularly in older individuals, and highlight the need to prioritize cancer prevention, research and early detection and management in this population, especially for colorectal, pancreatic, liver and endometrial cancer, whose mortality rates were substantially higher in individuals with type 2 diabetes than in the general population."

More information: Suping Ling et al, Inequalities in cancer mortality trends in people with type 2 diabetes: 20 year population-based study in England, *Diabetologia* (2023). DOI: 10.1007/s00125-022-05854-8

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