Cancer is becoming the leading cause of death in diabetes

DOI:
10.1016/S0140-6736(23)00445-2

Document Version
Final published version

2 Roser M, Ortiz-Ospina E, Ritchie H. Life expectancy. October, 2019. https://ourworldindata.org/life-expectancy (accessed Jan 21, 2023).
3 Hasell J, Roser M, Ortiz-Ospina E, Arriagada P. Poverty. 2022. https://ourworldindata.org/poverty (accessed Jan 21, 2023).
4 Pinker S. Enlightenment now: the case for reason, science, humanism, and progress. New York, NY: Viking Press, 2018.
5 Chiolero A, Anker D. Yes, we can—a cure for public health catastrophism. *Am J Public Health* 2021; **111:** 1371–72.

Cancer is becoming the leading cause of death in diabetes

In their Seminar on type 2 diabetes, Ehtasham Ahmad and colleagues[1] highlighted the current and future global burden of disease and correctly stated that the increased risk of premature death from this chronic condition is mainly driven through the detrimental effects on vascular integrity. Accordingly, many national guidelines recommend secondary prevention of cardiovascular disease.

We would like to draw attention to three studies from the past 10 years indicating that cancer is, or is predicted to become, the leading cause of diabetes-related death. An Australian study from 2014 reported on cause-specific mortality trends in over 1·1 million people with diabetes (1997–2010), and noted that cardiovascular disease was the most common contributor to death, but rates had declined.[2] By contrast, cancer deaths had increased, becoming the second most common cause of death in Australia. In 2021, Pearson-Stuttard and colleagues[3] evaluated causes of death trends in over 300 000 individuals with diabetes in England (2001–18). They concluded that "the decline in vascular death rates has been accompanied by….a transition…to cancers as the leading contributor to diabetes-related death". Similarly, mortality trends in Swedish National Diabetes Registry data predict that cancer will be the leading cause of death among individuals with diabetes by 2030.[4]

This changeover reflects declining cardiovascular disease mortality through improved prevention, coupled with increasing cancer-related mortality, in part reflecting increased cancer incidence secondary to the survival advantage afforded through cardiovascular disease prevention. It is time to widen secondary prevention efforts in people with diabetes to reducing cancer incidence and, among those with diabetes who develop cancer, improving cancer survival, ultimately avoiding many premature deaths.

We declare no competing interests.

*Mengying Wang, Matthew Sperrin, Martin K Rutter, *Andrew G Renehan*
andrew.renehan@manchester.ac.uk

Division of Cancer Sciences (MW, AGR) and Division of Diabetes, Endocrinology and Gastroenterology (MKR), Faculty of Biology, Medicine and Health, and Centre for Health Informatics, and Division of Informatics, Imaging and Data Science (MS), School of Medical Sciences, University of Manchester, Manchester M20 4BX, UK; Manchester Cancer Research Centre, National Institute for Health Research, Manchester Biomedical Research Centre, Manchester, UK (MW, AGR); Diabetes, Endocrinology and Metabolism Centre, Manchester University NHS Foundation Trust, Manchester Academic Health Sciences Centre, Manchester, UK (MKR)

1 Ahmad E, Lim S, Lamptey R, Webb DR, Davies MJ. Type 2 diabetes. *Lancet* 2022; **400:** 1803–20.
2 Harding JL, Shaw JE, Peeters A, Guiver T, Davidson S, Magliano DJ. Mortality trends among people with type 1 and type 2 diabetes in Australia: 1997–2010. *Diabetes Care* 2014; **37:** 2579–86.
3 Pearson-Stuttard J, Bennett J, Cheng YJ, et al. Trends in predominant causes of death in individuals with and without diabetes in England from 2001 to 2018: an epidemiological analysis of linked primary care records. *Lancet Diabetes Endocrinol* 2021; **9:** 165–73.
4 Bjornsdottir HH, Rawshani A, Rawshani A, et al. A national observation study of cancer incidence and mortality risks in type 2 diabetes compared to the background population over time. *Sci Rep* 2020; **10:** 17376.

Authors' reply

We thank Mengying Wang and colleagues for their very insightful comments on our Seminar on type 2 diabetes.[1] They have drawn our attention to the fact that cancer is, or is predicted to become, the leading cause of diabetes-related death in the coming years, overtaking cardiovascular disease. We acknowledge that cancer rates are rising in people with type 2 diabetes. Indeed, in January, 2023, our team at Leicester Diabetes Research Centre published data demonstrating a transition from cardiovascular disease to cancer deaths in type 2 diabetes.[2]

Cancer and type 2 diabetes are known to share many common risk factors, including ageing, obesity, unhealthy diet, physical inactivity, alcohol, and smoking. Diabetes along with obesity induces metabolic abnormalities leading to the release of various inflammatory cytokines, immune mediators, hormones, and growth factors.[3] These abnormal metabolic substrates are implicated as risk factors for development of cancer and its mortality.[4]

We agree with Wang and colleagues that better primary and secondary prevention of cardiovascular disease has meant that people with type 2 diabetes now live longer, which consequently has led to longer exposure to the detrimental effects of hyperglycaemia, insulin resistance, and chronic inflammation, all potentially associated with an increased risk of cancer in people with type 2 diabetes. It is also worth remembering that although vascular mortality rates have generally declined over the years in people with type 2 diabetes,[5] the evidence is less clear for cancer in the context of type 2 diabetes and more robust data are needed for accurate trends across different geographical regions of the world and ethnicities.

We strongly agree that now is the correct time to widen general prevention efforts in people with diabetes to reduce cancer incidence and specifically for people with type 2 diabetes, early cancer detection could reduce the number of avoidable cancer deaths. In summary, although the prevention of cardiovascular disease is still considered a priority in people with type 2 diabetes, we do emphasise the