

Shifting tides: the rising tide of early-onset cancers demands attention

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The epidemiological landscape of cancer incidence is changing. While increasing age remains a major non-modifiable risk factor for cancer, the incidence of early-onset cancers, largely accepted to be in adults aged under 50 years, is increasing. In addition, cancers historically perceived to be more common in older age groups are now being diagnosed in younger adults, including colorectal,¹ breast,² oesophageal,³ gastric⁴ and pancreatic cancers,⁵ among others.

Epidemiological evidence on early-onset cancers varies between cancer type and world region, with population-based, regional and single centre studies available in the literature. The article by Zhao *et al*⁶ aims to quantify the burden of early-onset cancers using 2019 data from the Global Burden of Disease database, offering a comprehensive overview of cancer statistics globally, and a summary of international trends.

The results show a striking increase in the global incidence of early-onset cancers between 1990 and 2019, with early-onset breast cancer having the highest incidence (13.7 per 100 000 in 2019, 95% CI 12.5 to 15 per 100 000). Early-onset nasopharyngeal and prostate cancers showed the fastest increase in incidence, with an estimated annual percentage change of 2.28% (95% CI 2.1% to 2.47%) and 2.23% (95% CI 1.97% to 2.49%), respectively. The four cancer groups with the highest death and disability-adjusted life-years burden in younger adults in 2019 were breast, tracheal/bronchus/lung, colorectal and stomach cancers. These results contrast with a more traditionally held view of 'typical' cancers in adults aged under 50 years.

An important aspect of this study is the global nature of the data. The highest age-standardised incidence rates of early-onset cancer in 2019 were in North America, Australasia and Western Europe. However, the burden of early-onset cancers in low- to middle-income countries is also of major public health concern, especially when

accounting for potential underestimation due to incomplete data collection. Disproportionately high death rates in low- to middle-income countries are shown, with the highest age-standardised death rates being observed in Oceania, Eastern Europe and Central Asia. Variation across regions is demonstrated, indicating the need to understand specific risk factors for different populations.

Risk factors identified for early-onset cancers by Zhao *et al*⁶ include dietary factors, alcohol consumption, tobacco use, physical inactivity and excess body fatness, which have also been associated with cancer in older patients.⁷ Interestingly, a high fasting plasma glucose was identified as a risk factor for early-onset cancers. This corroborates with previous observational evidence in all age groups⁸ and demonstrates another potentially modifiable risk factor in younger adults. Full understanding of the reasons driving the observed trends remains elusive, although lifestyle factors are likely contributing, and novel areas of research such as antibiotic usage, the gut microbiome, outdoor air pollution and early life exposures are being explored. It is crucial that we better understand the underlying reasons for the increase in early-onset cancers, in order to inform prevention strategies. A major global funding call in 2023—Cancer Grand Challenges—has included early-onset cancers among the nine topics of interest, in an effort to improve knowledge of their aetiology.⁹

Zhao *et al*⁶ offer a prediction of global age-standardised incidence and death rates of early-onset cancers from 2020 to 2030. Firstly, this serves as a warning for future burden on healthcare systems, which are still recovering from the impact of the COVID-19 pandemic. Secondly, the results suggest that the age group most affected is 40–49 years. Consideration of targeted early detection measures for this age group, including the potential expansion of screening, should be considered. For example, the US Preventive Services



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Task Force recommends that colorectal cancer screening should now begin at age 45.¹⁰

The main limitation of the paper, acknowledged by the authors, is the variability of data collection between countries across the world, and the completeness of the data is difficult to quantify. Nonetheless, observational data from cancer registries are essential to healthcare research and provide timely information allowing for international comparison.

While most cases of early-onset cancer appear to be sporadic, the role of hereditary syndromes needs to be better quantified. Identifying inherited cases via germline testing is important and has implications for cancer management and surveillance, both for the affected patient and their family members. A major research gap is our limited understanding of the molecular pathogenesis of sporadic early-onset cancers, and whether certain subtypes are driving the increasing incidence. For example, our working group has observed a lack of *BRAF* mutations in sporadic early-onset colorectal tumours compared with colorectal cancers in older adults.¹¹ This, in turn, suggests potentially distinct aetiologies—or, at least, distinct timings of known carcinogenic exposures—for early-onset compared with late-onset tumours, at least in some patient subgroups.

The findings of Zhao *et al*⁶ challenge perceptions of the type of cancer diagnosed in younger age groups. It is important to educate both the public and healthcare professionals regarding the possibility of certain cancers in younger adults to allow earlier diagnosis, which in turn improves outcomes. Prevention and early detection measures are urgently required, along with identifying optimal treatment strategies for early-onset cancers, which should include a holistic approach addressing the unique supportive care needs of younger patients. There is a pressing need for partnership, collaboration and resource distribution at a global level in order to achieve these aims.

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