'These are people in the prime of life': The worrying puzzle behind the rise in early-onset cancer

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David Cox

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There are rising cases of breast, colorectal and other cancers in people in their 20s, 30s and 40s. What is going on?

Over the past 10 years, rates of colorectal cancer among 25 to 49 year olds have increased in 24 different countries, including the UK, US, France, Australia, Canada, Norway and Argentina.

The investigation's early findings, presented by an international team at the Union for International Cancer Control (UICC) congress in Geneva in September 2024, were as eye-catching as they are concerning.

The researchers, from the American Cancer Society (ACS) and the World Health Organization's (WHO's) International Agency for Research on Cancer, surveyed data from 50 countries to understand the trend. In 14 of these countries, the rising trend was only seen in younger adults, with older adult rates remaining stable.

The results are the latest in a host of studies detailing a similar rise of a range of different cancers in the young.

> *To them and us it's often beyond comprehension, because who could imagine that a healthy 40 year old would develop this kind of malignancy? – Eileen O'Reilly*

Breast cancer is one form of cancer where the trend is apparent. A **new report** from the ACS found that while deaths from breast cancer in women have dropped by around 10% in the past decade, incidence rates are rising by 1% per year overall – and 1.4% per year for women under the age of 50.

Based on epidemiological investigations, it seems that this trend first began in the 1990s. **One study** found that the **global incidence of early-onset cancer had increased** by 79% between 1990 and 2019, with the number of cancer-related deaths in younger

people rising by 29%. Another report in **The Lancet Public Health** described how cancer incidence rates in the US have steadily risen between the generations across 17 different cancers, particularly in Generation Xers and Millennials.

The issue of early-onset cancers has become such a matter of concern that major organisations such as the UICC are keen to raise awareness of the trend among general practitioners to ensure that warning signs are being picked up among younger patients.

"A doctor listening to somebody above 60 who's talking about difficulty passing stool, feeling tired and bloated, is going to take those symptoms a lot more seriously than a young person in their 30s who's active and doesn't fit the typical profile of a person with cancer," says Sonali Johnson, head of advocacy at the UICC. "They might put it down to irritable bowel syndrome or work stress, so there's plenty of cases where people's symptoms are dismissed instead of being referred for blood work or a colonoscopy."

Cancer specialists say that patients presenting with diseases like pancreatic cancer, an illness where most people are diagnosed **in their early 70s**, are sometimes decades younger than would usually be expected.

"It's not uncommon for me to see someone under the age of 40 with pancreatic cancer," says Eileen O'Reilly, a gastrointestinal medical oncologist at Memorial Sloan Kettering Cancer Centre in New York. "It's almost every week, which is a scary thought. These are people in the prime of life, who are starting families and have everything to live for. The implications for society are profound."

While oncologists have typically thought of cancers in younger people as being primarily a consequence of heritable risk factors, such as the **BRCA1 and BRCA2 gene mutations** in the case of breast cancer, more and more patients have no obvious genetic predisposition. O'Reilly says that in the majority of the young-onset cases she sees, there is no obvious genetic explanation, and when studied in the lab, the tumours carried by patients in their 20s, 30s or 40s appear to be more aggressive compared with a typical pancreatic cancer patient in their 70s.

She says that this often makes their prognosis very poor, even though the patient themselves is often in otherwise good health.

"They're younger, fitter and can often handle treatment intensity better, but some have this highly aggressive form of pancreatic cancer, which causes an accelerated decline in front of your eyes," she says. "To them and us it's often beyond comprehension, because who could imagine that a healthy 40 year old would develop this kind of malignancy?"

As well as recognising the trend, cancer specialists are feeling an increasing sense of urgency to try and get to the bottom of the factors driving it. The authors of **the Lancet study** commented that if this pattern continued, it could ultimately increase the burden of disease in future, halting and even reversing decades of public health progress in combating cancer.

So what is going on?

Some researchers have suggested that components within ultra-processed foods could play a role in driving inflammation and DNA damage within the colon (Credit: Getty Images)

Perhaps the most obvious explanation points to the role of obesity and metabolic syndrome, conditions which have been associated with driving cancer risk through increasing inflammation throughout the body and causing the dysregulation of key hormonal pathways.

A **recent study** found that accumulating excess body weight between the ages of 18 and 40 is associated with a greater risk of up to 18 different cancers, while **the Lancet report** found that 10 of the 17 cancers which are growing in prevalence among the young in the US are obesity-related malignancies such as kidney, ovarian, liver, pancreatic and gallbladder cancers as well as myeloma.

"The overall evidence points to lifestyle change," says Shuji Ogino, professor of pathology and epidemiology at Harvard University who has been investigating the rise of early-onset cancers. "Every one of us has thousands of genetic variants, some of which give a very small increased risk of cancer, which rises when combined with some environmental changes. We know that eating too much sugar and processed food, having consistently high blood glucose and becoming insulin resistant not only raises your risk of diabetes but also cancer."

But obesity alone doesn't represent the full story. O'Reilly says that many of the younger pancreatic cancer patients she sees are fit and apparently healthy, with no clear explanations for why they should have fallen unwell. "It certainly always strikes me that the traditional things we think about mostly don't apply to these people," she says. "They appear often healthy, vibrant and extremely physically fit."

> “ *Ogino feels that a heavily overlooked connection is the marked change in sleep patterns around the world which has occurred in 50-100 years.*

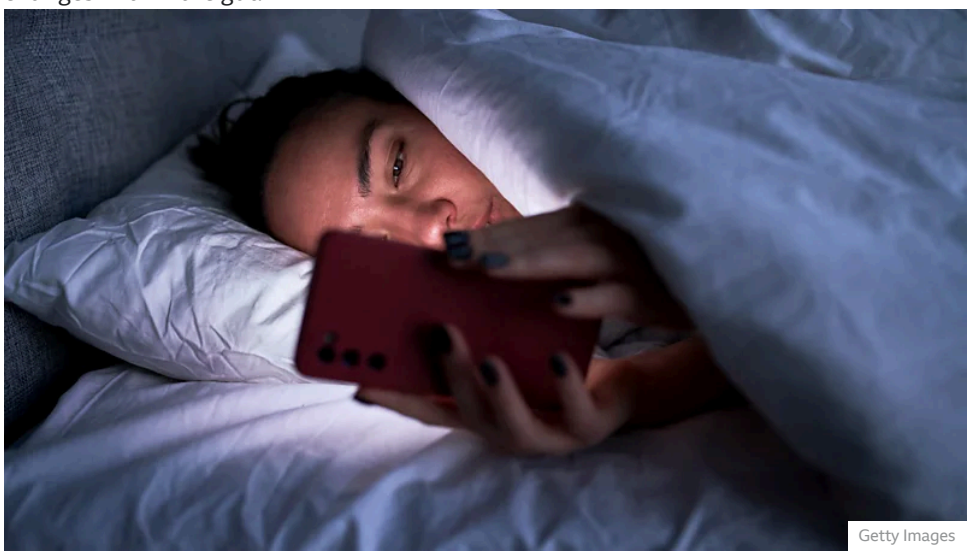
Ogino believes that this may reflect the emergence of some different carcinogens, ones which have previously drawn less attention. While epidemiologists have long focused on the link between smoking and cancer, smoking prevalence has declined markedly in recent decades with the WHO **finding** that globally just one-in-five adults consume tobacco products now, compared with one-in-three in 2000.

Instead, Ogino feels that a heavily overlooked connection is the marked change in sleep patterns around the world which has occurred in 50-100 years. **One study** found that the average sleep duration of children and adolescents declined by 60 minutes per night between 1905 and 2008, while shift work **has become** increasingly prevalent in recent decades in Australia, China, Japan, Europe and North and South America. A **2021 study** using data from the English Longitudinal Study of Ageing, a database which contains information from more than 10,000 people over the age of 50, found an association between poor sleep quality and greater risk of cancer.

Some scientists have **even argued** that our near permanent exposure to artificial light, either through streetlights or mobile phones and tablets, represents a novel carcinogen through triggering disruptions in the body's biological clock, something that has been linked to breast, colon, ovarian and prostate cancer. **Studies** have even suggested that continued light exposure during nighttime hours through shift work may facilitate cancer growth through lowering levels of the hormone melatonin.

"We are exposed a lot to artificial light at night, even from when we are babies," says Ogino. "And in Japan, for instance, a substantial fraction of the population stay up to midnight every night. Shift work has become more common with things like 24-hour convenience stores."

At the same time, Ogino says that there is unlikely to be a single risk factor involved in many of these cases of early-onset cancer, but instead a confluence of factors converging to drive disease. Combined with shifts in lifestyle, many cancer scientists believe that a key driving force for these illnesses is the consequences of various toxic changes within the gut.



Some scientists have argued our exposure to artificial light, such as through smartphones, could represent a novel (Credit: Getty Images)

In June 2023, Frank Frizelle, a colorectal surgeon at Christchurch Hospital, New Zealand, issued something of a call-to-arms for colorectal cancer specialists around the world, calling for greater investigation of the potential link between ingesting high amounts of microplastics and developing premature bowel cancer.

His provocatively titled **paper,** "Could microplastics be a driver for early-onset colorectal cancer?", argued that the emergence of colorectal cancer as an increasingly problematic disease in the under 50s matches the timeframe over which microplastics have become exponentially more present in the environment. His suggestion is that the presence of these tiny plastic particles may disrupt the colonic mucus layer, which protects the lining of the bowel from various pathogens and toxins from our food.

"Micro and nanoplastics may allow the mucus layer to be permeated in some way, like putting a series of pin holes in a condom," he says. "If we can prove this to be true, it might be size related, like carbon particles and lung disease."

At present, this is still mostly speculative, but Frizelle is far from the only scientist to have linked toxic changes within the gut to potentially carcinogenic processes. Other researchers have suggested that certain components within ultra-processed foods may play a role in driving inflammation and DNA damage within the colon, from **food colourants** to **emulsifiers**, although, as with microplastics, the evidence still remains relatively limited.

Because the colon is connected to the stomach and the wider gastrointestinal tract as well as the immune system, marked changes within the gut are not only associated with colorectal cancer, but also a range of solid tumours **including breast cancer** as well as **blood cancers**.

Researchers are probing whether use of antibiotics could be a factor. As for microplastic exposure, antibiotic use around the world has risen in recent decades. In particular, the doses of antibiotics consumed by children under the age of five **increased** from 9.8 per 1,000 people in 2000 to 14.3 in 2018. Overall, the global per-capita consumption of antibiotics **grew across** all age groups between 2000 and 2015, something which O'Reilly believes is a key cause for concern.

Given the ability of antibiotics to wipe out large swathes of bacterial species and thus drastically reshape the gut microbiome in potentially harmful ways, greater antibiotic exposure has previously been **linked to** lung cancer, lymphomas, pancreatic cancer, renal cell carcinoma and multiple myeloma.

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"The bacteria that live in the gut have been selected by some sort of Darwinian process and they're part of the immune surveillance which allows our immune system to recognise abnormal cells, foreign particles, and prevent the genesis of malignancies in the first place," says O'Reilly. "It's still not known, but the idea is that greater antibiotic exposure could mean that immune surveillance is not working as effectively as it should."

One of the potential consequences of excessive antibiotics is that wiping out so-called commensal bacteria, species which are native to the gut, creates a chasm which can then be filled by more malevolent microbes. In the last 10 years, Ogino and his collaborators around the world have published **numerous studies** on certain opportunistic pathogens which **seem to be capable** of invading the gut and driving cellular changes which increase the risk of cancer progression.

In particular, Ogino and others have found that a bacterium called *Fusobacterium nucleatum* seems to be capable of driving **pre-cancerous intestinal growths** as well as the **development** of more aggressive tumours. Other studies have shown that certain species of *E. coli* appear **to be capable** of driving cancer development and simultaneously suppressing the body's immune response.

As with sleep and obesity, Ogino says, the factors driving early-onset cancer are multifactorial from childhood to adulthood and likely combine synergistically to gradually increase disease risk in early adulthood. He points out that while most of us carry some form of *E. coli,* his research has shown that these bacteria tend to flourish most when we're also consuming a so-called "Western diet", high in ultra-processed foods, indicating that diet will also play a key role.

We are still some way from being able to pin down exactly why different groups of people have ended up developing early-onset cancers. But O'Reilly says that it is vital for scientists to try and study them in greater detail, to try and avoid a global health catastrophe in years to come.

"There's an enormous need for research to try and understand what's going on and what's inciting these diseases at a much earlier stage," she says. "I find it an incredibly scary observation that we're seeing incidence of pancreatic cancer and other solid organ cancers going up in the young. To me, it's a looming public health crisis."

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