Increasing incidence of colorectal cancer in young patients

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Colorectal cancer is the third most common cancer worldwide, and the second leading cause of cancer-related mortality. In 2018, there were an estimated 1·8 million new colorectal cancers diagnosed, with 881,000 associated deaths.

The incidence patterns and epidemiology of colorectal cancer have changed in recent decades. Although colorectal cancer remains an age-associated disease, the number of colorectal cancers diagnosed in patients under the age of 50 years has been steadily increasing worldwide. In addition to the increased incidence, these young individuals tend to present with more advanced disease and to have a less favourable prognosis.

Early-onset colorectal cancer is a diagnosis of bowel cancer in individuals under the age of 50. In New Zealand, the incidence of early-onset bowel cancer has increased by 2.9% per year over the past 10 years.

Epidemiology

Over recent decades, the incidence of early-onset colorectal cancer has increased worldwide. The increase in incidence rates has been shown in all age groups under the age of 50 years. While most data demonstrating this trend has come from European and Western countries, there is emerging evidence of an increase in incidence of early-onset colorectal cancer from Taiwan, Japan, Hong Kong and South Korea.

As colorectal cancer remains an age-associated disease, the absolute incidence rates of early-onset colorectal cancer are higher in age groups approaching the age of 50. However, if the rate of changing incidence over the last few decades is considered, the steepest rise in incidence is observed in younger age groups.

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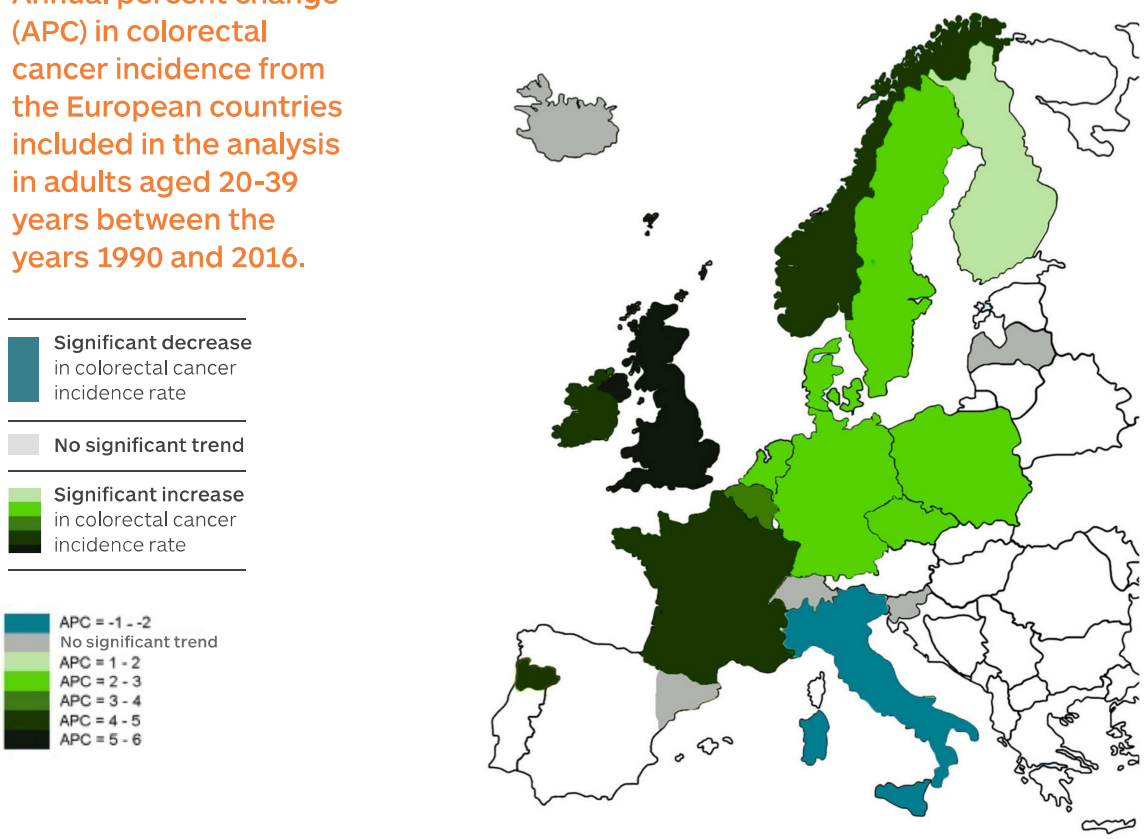
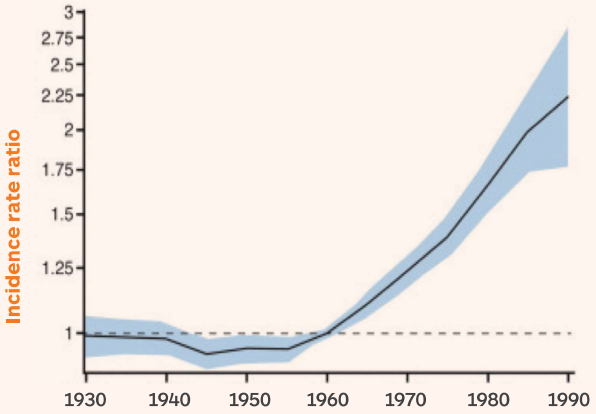
As an example, a European study analysed cancer registry data from 20 European nations and showed that in the 20-29 year age group the incidence of colorectal cancer had increased at a rate of 7.9% per year from 2004 to 2016. By contrast, in the 40-49 year age group the annual increase in incidence was only 1.6%.

Annual percent change (APC) in colorectal cancer incidence from the European countries included in the analysis in adults aged 20-39 years between the years 1990 and 2016.



In order to understand these trends better, modelling studies can be considered. The Period Cohort Modelling aims to determine the effect of a birth cohort in the incidence of early-onset colorectal cancer. This modelling has shown that the incidence rate for those aged 50-54 years nowadays in the USA is similar to the incidence rate of older age groups when we compare data of people born in the 1970s and 1980s. The inflection point for this effect is for individuals born after 1960. This observed birth cohort effect suggests shared risk factors across a generation might be contributing to early-onset colorectal cancer risk.

Colorectal cancer incidence has steadily increased across successive birth cohorts since 1960.



Clinical and pathological features and risk factors

Early-onset colorectal cancer manifests differently from late-onset colorectal cancer. Most patients with early-onset colorectal cancer present with symptoms, and are more likely to present with rectal bleeding (28.8% vs 23.2%, p<0·01) and abdominal pain (41.2% vs 27.2%, p<0·01) when compared with patients with late-onset colorectal cancer, who are more likely to be diagnosed incidentally (14.6% vs 5.2%, p<0·01).

Unfortunately, despite being more likely to present with symptoms, younger people experience a significantly longer interval in proceeding to investigation. Those diagnosed with colorectal cancer under the age of 50 years have been shown to have experienced symptoms for more than 250 days on average before being investigated, in contrast to those aged over 50 years who have an average investigation interval of 150 days.

Younger individuals are more likely to be diagnosed with left sided colon cancer, particularly rectal cancer. Disease tends to be more aggressive, with advanced histological features such as mucinous or signet-ring histology (12.6% vs 10.8%, p<0·01) and poor or no differentiation (20.4% vs 18%, p<0·01), compared with late-onset colorectal cancers.

Furthermore, early-onset colorectal cancer is diagnosed at a more advanced stage than late-onset disease. This difference in stage at presentation cannot simply be explained by a longer time between the onset of symptoms and diagnosis. An example of this is the fact that younger patients with stage III or IV disease have shorter symptom and workup periods compared with those with stage I or II disease. Thus, advanced stage at diagnosis is not likely only explained by longer dwell time or time to diagnosis.

An important clinical clue that can help in the diagnosis of colorectal cancer in younger patients is family history: recent studies have shown that up to 35% of patients with early-onset colorectal cancer have a family history of colorectal cancer or advanced colorectal polyps.

	Early-onset colorectal cancer (age <50 years)	**Late-onset** colorectal cancer (age ≥50 years)
Presenting with symptoms (%)	85–95.6	33.9–79
Duration of symptoms (days)	243	154
Family history of bowel cancer (%)	14–33.5	8.3–19.3
Location (%)		
Right colon	16.2–39.9	28.5–53.5
Left colon	24.0–53.0	28.9–48.5
Rectum	23.5–49.1	20.0–35.2
Histology (%)		
Mucinous	8.1–15	4.7–16.
Signet-ring cells	1–13	0.9–4
Poor or no differentiation	7.2–27.9	3.2–18.9

Source: *PLEASE PROVIDE*

Risk factors and cause of the rising incidence

There is a significant body of evidence supporting typical risk factors associated with overall risk of colorectal cancer in older individuals. Some of these risk factors appear to play a role in early-onset colorectal cancer. Such typical risk factors include smoking, obesity, increased consumption of processed meat, and excess alcohol use.

Unique risk factors for early-onset colorectal cancer have also been identified: sedentary lifestyle, high consumption of ultra-processed food, and increased consumption of sugar-sweetened beverages.

Ongoing research is needed to understand the complex interplay of how these exposures modulate colorectal cancer risk over time. Prospective cohort studies, with detailed collection of diet, lifestyle, and environmental exposures, along with longitudinal biospecimen collection, will provide the opportunity to analyse biomarkers to help shed light on colorectal cancer pathogenesis.

Early detection and prevention of early-onset colorectal cancer

Although there are many hypotheses, it is not yet understood why the rise in early-onset colorectal cancer is being seen. What we do know based on current available evidence is that patients with early-onset colorectal cancer appear to present more commonly with symptoms, and many report a family history of bowel cancer. There also seems to be a longer interval between the onset of symptoms and the diagnosis of bowel cancer. This represents an opportunity for clinicians to be aware of the possibility of colorectal cancer in younger individuals, and to proceed to investigation in a more timely manner.

Prompt symptom evaluation
The cause of the delay in the investigation of symptoms is likely to be multi-factorial, including delays in seeking care, barriers to accessing care, and systematic health system dismissal when symptoms are present in otherwise healthy young individuals.

An example of this is rectal bleeding. Although bleeding is the most common presenting symptom of early-onset colorectal cancer, it is one of the most common presenting complaints to primary care physicians and gastroenterologists. And although it is often caused by benign pathology such as haemorrhoids or fissures, it can also be the presentation of more proximal pathology. Furthermore, bleeding haemorrhoids can obscure subtle symptoms suggestive of a more proximal source.

The US Multi-society Task Force on Colorectal Cancer recommends that all unexplained symptoms of rectal bleeding or iron deficiency anaemia in younger individuals should be promptly and thoroughly investigated with a colonoscopy. This recommendation is based on a study that showed that early-onset colorectal cancer was 10 times more commonly diagnosed in young individuals who presented with iron deficiency anaemia or haematochezia.

Thorough collection and action on family history of colorectal cancer
Approximately 16% of all patients with early-onset colorectal cancer have an associated hereditary syndrome and an additional 35% have a family history of colorectal cancer. Identifying the group of individuals who would benefit from screening based on their family history will help to reduce the burden of early-onset colorectal cancer.

Conclusion

The incidence of colorectal cancer in patients under the age of 50 years is rising worldwide, without an obvious cause. Ongoing research will help to elucidate pathogenesis and inform our approach to screening of average-risk individuals. Given that up to 35% of patients with early-onset disease report some family history of colorectal cancer, and over 95% present with symptoms, it is essential to continue collecting and acting on family history of colorectal cancer and promptly evaluating symptoms.

Take home message

- The incidence of colorectal cancer in patients under the age of 50 is increasing worldwide.
- The most common presenting symptoms in younger patients are haematochezia and abdominal pain.
- Family history of colorectal cancer and advanced colonic polyps is a significant risk factor for early-onset colorectal cancer.

More information

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