

Is it time to reduce the age of screening for colorectal cancer?

Oliver Waddell, Tamara Glyn, Frank Frizelle

The incidence of bowel cancer in people aged under 50 in Aotearoa New Zealand is increasing. This is part of a worldwide trend that is occurring despite the overall incidence of bowel cancer decreasing in many countries.^{1,2} From 1995 to 2012, colon cancer in New Zealand men aged under 50 increased by 14%, and the incidence of rectal cancer increased by 18% in men and 13% in women aged under 50.³ This finding is consistent with other studies from Australia, the United States, Canada, the United Kingdom, France and Asia, which all show a rapid increase in early-onset bowel cancer.^{1,4-8} In the United States, the incidence of early-onset bowel cancer has doubled since the 1990s and by 2030 it has been estimated that more than one in 10 colon cancers and nearly one in four rectal cancers will occur in people aged under 50.^{4,5,9}

Early-onset bowel cancer is different in many ways to late-onset bowel cancer. There is a different distribution within the colon, with early-onset cancer often occurring in the distal bowel involving the rectum, rectosigmoid and sigmoid colon. Patients with early-onset bowel cancer also tend to present with more advanced disease, have a more aggressive histopathology with more poorly differentiated cancer and are more likely to have lymphatic and peri-neural involvement.^{2,5,10} Despite this, stage for stage they tend to have a better prognosis.

The aetiology of this epidemiological change is unknown;¹¹ however, it is likely to be an environmental influence, and likely associated in some way with the gut microbiota and their interaction with the gut mucosa.¹¹⁻¹⁶ With regard to early-onset colorectal cancer (EOCRC), individuals born after 1960 have an increased risk compared to previous generations,¹⁷ suggesting that shared risk factors—common across a generation—are likely to be contributing. A wide variety of loosely associated factors have been suggested to explain this trend, such as changing trends in obesity, sedentary lifestyles, smoking, Westernisation of diets and/or the use of antibiotics in early life;² the contraceptive pill in the late 1950s¹⁸ is another potential risk factor, as is the increasing level of microplastics in the environ-

ment.¹⁹ However, as yet, no proven causal relationship to any specific factor has been established.²⁰

Countries that have screening starting at age 40 seem to have avoided the impact of this shift. While direct data to show that screening populations under 50 will reduce EOCRC are lacking, there are some observational data that support this claim. A review of international trend in EOCRC incidence rates across five continents found only three countries where the incidence rates were decreasing.²¹ Two out of these three countries (Italy and Austria) have been screening patients from the age of 40 or 44 since the 1980s.²² In recent years (2003–2016), while Austria has seen rising rates of colorectal cancer (CRC) diagnosed under the age of 35, they have ongoing decreases in incidence of all age groups aged 45 and over, which may be evidence that the lower age of bowel screening is preventing the same rise across EOCRC incidence seen elsewhere.²³ Likewise, when looking at a large review of international trends in bowel cancer screening, the only other two countries who have also been screening people down to the age of 40 are China and Japan,²² neither of whom have seen a statistically significant increase in EOCRC incidence in recent years.²¹ A large systematic review including data on over 50,000 average risk screening colonoscopies found that the rates of finding CRC in patients aged 45–49 was very similar to in those aged 50–59 years, and concluded that expanding screening to this population could result in a similar impact on CRC outcomes.²⁴

Currently, the National Bowel Screening Programme is only open to people aged 60–74, whereas most countries with programmes begin screening for bowel cancer at age 50. The American Cancer Society recommends that screening should begin at age 45.²⁵ A modelling study from the United States preventative task force concluded that screening from age 45 is cost effective and results in an additional 22–27 life years gained per 1,000 people screened.²⁶

If the age of eligibility for screening in New Zealand were lowered to 40 or 45 it would be likely to result in a proportional decrease in the diagnosis

of EO CRC, as seen in countries with a lower age of screening. This is particularly important for Māori, as 30% of bowel cancer in Māori females and 25% in Māori males occurs before age 50.²⁷ Unpublished data describing the trends of all EO CRC incidence here in New Zealand over the past 25 years from 1995–2020 found that 45% of all EO CRC diagnosed were in the oldest 5-year age bracket of 45–49, meaning almost half of EO CRC

may either be prevented or diagnosed earlier if screening was lower to 45, and more so if reduced to 40. Until the cause of this avalanche can be identified and addressed, we must act to mitigate the consequences. Lowering the screening age is the most effective tool we have to combat this epidemic. This simple action would improve equity and outcomes for all New Zealanders.

COMPETING INTERESTS

Frank Frizelle is the Editor in Chief of the *New Zealand Medical Journal* and a Medical Advisor to Bowel Cancer New Zealand.

AUTHOR INFORMATION

Oliver Waddell: Department of Surgery, University of Otago Christchurch, New Zealand.

Tamara Glyn: Department of Surgery and Critical Care, University of Otago Christchurch; Department of Surgery, Te Whatu Ora Waitaha.

Frank Frizelle: Editor in Chief *NZMJ*; Professor of Surgery; Clinical Director of General Surgery; Department of Surgery, University of Otago Christchurch, New Zealand.

CORRESPONDING AUTHOR

Oliver Waddell: Department of Surgery, University of Otago Christchurch, New Zealand.
E: Droliverwaddell@gmail.com

REFERENCES

- Chittleborough TJ, Gutlic I, Pearson JF, et al. Increasing Incidence of Young-Onset Colorectal Carcinoma A 3-Country Population Analysis. *Dis Colon Rectum*. 2020;63(7):903-910. doi:10.1097/DCR.0000000000001631.
- REACCT Collaborative; Zaborowski AM, Abdile A, et al. Characteristics of Early-Onset vs Late-Onset Colorectal Cancer: A Review. *JAMA Surg*. 2021;156(9):865-874. doi:10.1001/jamasurg.2021.2380.
- Gandhi J, Davidson C, Hall C, et al. Population-based study demonstrating an increase in colorectal cancer in young patients. *Br J Surg*. 2017;104(8):1063-1068. doi:10.1002/bjs.10518.
- Bailey CE, Hu CY, You YN, et al. Increasing disparities in the age-related incidences of colon and rectal cancers in the United States, 1975-2010. *JAMA Surg*. 2015;150(1):17-22. doi:10.1001/jamasurg.2014.1756.
- Stoffel EM, Murphy CC. Epidemiology and Mechanisms of the Increasing Incidence of Colon and Rectal Cancers in Young Adults. *Gastroenterology*. 2020;158(2):341-353. doi:10.1053/j.gastro.2019.07.055.
- Patel P, De P. Trends in colorectal cancer incidence and related lifestyle risk factors in 15-49-year-olds in Canada, 1969-2010. *Cancer Epidemiol*. 2016;42:90-100. doi:10.1016/j.canep.2016.03.009.
- Young JP, Win AK, Rosty C, et al. Rising incidence of early-onset colorectal cancer in Australia over two decades: report and review. *J Gastroenterol Hepatol*. 2015;30(1):6-13. doi:10.1111/jgh.12792.
- Chauvenet M, Cottet V, Lepage C, et al. Trends in colorectal cancer incidence: a period and birth-cohort analysis in a well-defined French population. *BMC Cancer*. 2011;11:282. doi:10.1186/1471-2407-11-282.
- Siegel RL, Miller KD, Fedewa SA, et al. Colorectal cancer statistics, 2017. *CA Cancer J Clin*. 2017;67(3):177-193. doi:10.3322/caac.21395.
- Baran B, Mert Ozupek N, Yerli Tetik N, et al. Difference Between Left-Sided and Right-Sided Colorectal Cancer: A Focused Review of Literature. *Gastroenterology Res*. 2018;11(4):264-273. doi:10.14740/gr1062w.
- Fuchs CS, Giovannucci EL, Colditz GA, et al. A prospective study of family history and the risk of colorectal cancer. *N Engl J Med*. 1994 Dec 22;331(25):1669-74. doi: 10.1056/NEJM199412223312501.
- Atuma C, Strugala V, Allen A, Holm L. The adherent gastrointestinal mucus gel layer: thickness and physical state in vivo. *Am J Physiol Gastrointest Liver Physiol*. 2001 May;280(5):G922-9. doi: 10.1152/ajpgi.2001.280.5.G922.
- Coleman OI, Haller D. Microbe-Mucus Interface in the Pathogenesis of Colorectal Cancer. *Cancers (Basel)*. 2021 Feb 4;13(4):616. doi: 10.3390/cancers13040616.
- Johansson ME, Phillipson M, Petersson J, et al. The inner of the two Muc2 mucin-dependent mucus layers in colon is devoid of bacteria. *Proc Natl Acad Sci U S A*. 2008 Sep 30;105(39):15064-9. doi: 10.1073/pnas.0803124105.
- Korpela, K. Diet, Microbiota, and Metabolic Health: Trade-Off Between Saccharolytic and Proteolytic Fermentation. *Annu Rev Food Sci. Technol*. 2018;9:65-84. doi: 10.1146/annurev-food-030117-012830.
- Purcell RV, Pearson J, Aitchison A, et al. Colonization with enterotoxigenic *Bacteroides fragilis* is associated with early-stage colorectal neoplasia. *PLoS One*. 2017 Feb 2;12(2):e0171602. doi: 10.1371/journal.pone.0171602.
- REACCT Collaborative. Microsatellite instability in young patients with rectal cancer: molecular findings and treatment response. *Br J Surg*. 2022 Feb 24;109(3):251-255. doi: 10.1093/bjs/znab437.
- Liao PV, Dollin J. Half a century of the oral contraceptive pill: historical review and view to the future. *Can Fam Physician*. 2012 Dec;58(12):e757-60.
- Li S, Keenan JI, Shaw IC, Frizelle FA. Could Microplastics Be a Driver for Early Onset Colorectal Cancer? *Cancers (Basel)*. 2023 Jun 24;15(13):3323. doi: 10.3390/cancers15133323. PMID: 37444433; PMCID: PMC10340669.
- Murphy CC, Singal AG. Establishing a research

- agenda for early-onset colorectal cancer. *PLoS Med.* 2018 Jun 1;15(6):e1002577. doi: 10.1371/journal.pmed.1002577.
21. Siegel RL, Torre LA, Soerjomataram I, et al. Global patterns and trends in colorectal cancer incidence in young adults. *Gut.* 2019 Dec;68(12):2179-2185. doi: 10.1136/gutjnl-2019-319511.
 22. Schreuders EH, Ruco A, Rabeneck L, et al. Colorectal cancer screening: a global overview of existing programmes. *Gut.* 2015 Oct;64(10):1637-49. doi: 10.1136/gutjnl-2014-309086.
 23. Gartlehner G, Schernhammer E, Lax SF, et al. Screening for colorectal cancer. *Wien Klin Wochenschr.* 2023. <https://doi.org/10.1007/s00508-023-02209-0>.
 24. Kolb JM, Hu J, DeSanto K, et al. Early-Age Onset Colorectal Neoplasia in Average-Risk Individuals Undergoing Screening Colonoscopy: A Systematic Review and Meta-Analysis. *Gastroenterology.* 2021 Oct;161(4):1145-1155.e12. doi: 10.1053/j.gastro.2021.06.006.
 25. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin.* 2018;68(4):250-281. doi:10.3322/caac.21457.
 26. Knudsen AB, Rutter CM, Peterse EFP, et al. Colorectal Cancer Screening: An Updated Modeling Study for the US Preventive Services Task Force. *JAMA.* 2021 May 18;325(19):1998-2011. doi: 10.1001/JAMA.2021.5746.
 27. McLeod M, Harris R, Paine SJ, et al. Bowel cancer screening age range for Māori: what is all the fuss about? *N Z Med J.* 2021;134(1535):71-77.