

The Global Epidemic of Young Onset Colorectal Cancer has Arrived - Implications for Irish Healthcare

N. Ryan¹, R. Horgan ², S. O'Reilly^{1,3}.

1. Department of Medical Oncology, Cork University Hospital, Wilton, Co. Cork, Ireland.
2. Lynch Syndrome Ireland
3. Cancer Research @UCC, University College Cork, College Rd., Co. Cork, Ireland.

We are in the middle of a profound change in the epidemiology of colon cancer – one that will have transgenerational societal impacts, and requires re-imagining of how we are trying to reduce the burden of this cancer for our societies¹. By 2030 it is anticipated that young onset colorectal cancer (YO-CRC) defined as the development of colorectal cancer before 50 years of age will be the leading cause of death for adults between the ages of 20-49²⁻⁴. In the past 3 decades the rates of cancer development in this cohort have almost doubled.

At present CRC is the second most commonly diagnosed cancer in males and females in Ireland, with over 2500 new cases reported annually⁵. Globally, high income countries have the highest rates of YO-CRC however, low and middle income countries are also experiencing increasing incidence and mortality rates.⁶

YO-CRC is distinct to late onset colorectal cancer (LO-CRC) (patients diagnosed >50 years). It tends to be diagnosed at a more advanced stage possibly due to a combination of lower screening rates and delayed diagnostic testing⁷. Consequently diagnosis is often delayed by an average of 4 to 6 months⁸. Once diagnosed, these tumours are characterised by more aggressive features such as bowel obstruction clinically, distal colon or rectal locations anatomically, and signet or mucinous cell differentiation pathologically.^{9,10} Despite being more likely to tolerate aggressive anti-cancer therapy patients in this cohort tend to have similar outcomes to older ones, with similar 5 year disease free survival.^{11,12} Up to 20% of YO-CRC patients will have a germline mutation,¹³ while somatic mutation profiles also vary compared to LO-CRC patients with the presence of more KRAS and TP53 mutations noted and a lower percentage of BRAF and APC mutations.¹⁴

It is not clear why we are seeing this rising incidence in YO-CRC. Like most other cancers, smoking and alcohol use have been linked to the development of colorectal cancer, however many young patients presenting with this disease don't have these risk factors. Established risk factors such as obesity and the metabolic syndrome do not seem to be implicated.¹⁵ This has shifted the focus to the gut microbiome and its alteration by micro-processed foods as a driver for YO-CRC. Dysbiosis of gut bacteria, fungi and viruses has been implicated in CRC

tumorigenesis.¹⁶ Recent studies have examined the *Escherichia coli* (E.coli) strains producing the genotoxin colibactin. Bacterial fingerprints associated with colibactin were 3.3 times higher in patients diagnosed with CRC below age 40 than in those over 70¹⁷⁻²⁰. These mutations appeared early in tumour development suggesting that the damage may occur years – even decades- before cancer develops. This is concordant with evidence that exposure to ultra processed foods in childhood and adolescence may lead to long term changes in the gut microbiome which may increase YO-CRC risk.²¹ Paediatric exposure to antibiotics is also speculated to be a potential risk factor for development of YO-CRC.²² The role of microplastics and their synergistic carcinogenic effects with pathogenic microbiota is also a concern.²³⁻²⁶

What are the implications of these changes in CRC epidemiology for cancer care in Ireland? From a patient perspective awareness needs to increase in society that this change is occurring. This awareness impacts on public health awareness campaigns to increase representation of younger patients so that don't feel invisible. The outdated rhetoric that “you are way too young to be here” has been the offering many patients receive when they present to cancer clinics/services is not helpful as it makes patients feel like an outlier, particularly when 1 in 10 patients are YO-CRC. Awareness also needs to increase in primary care which is often the first point of contact for patients. It needs to increase in all care settings with respect to awareness of exploring family history and its significance. Finally access to approved novel agents needs to be accelerated to bring it in line with European norms, and clinical trial options need to be expanded.

From a healthcare perspective these demographic changes will impact our national bowel screening program which will need to adapt and lower the age at which screening occurs. The current framework was published in 2017, with the aim to reduce the age of Bowel Screen to 55 from 2021. This has not been implemented and is no longer in line with international guidelines which recommend that national bowel cancer screening should start at 50 years of age.²⁷ Secondly, the evolution of CRC services needs to increase allied health support such as social work, genetic counselling, psycho-oncology to make patient care less self directed and reliant on patient resilience. Many patients have significant family obligations, are at early stages of their career and lack financial security. A financial toxicity prevalence of 20% reported in a United States study of YO-CRC patients also noted its association with relationship disintegration as a consequence of financial strain in up to 50% of patients.²⁸ YO-CRC patients also express concern about specific needs such as communicating news about a diagnosis to children, dealing with long term toxicity of treatment and issues relating to fertility, sexuality and body image^{2,17}. The transgenerational impact of their deaths is also profound.^{29,30} Finally research is needed on why this trend is occurring so we can move beyond a “lifeboat” model of intervention to one of cancer prevention.

Life is led looking forward but understood looking backwards. The weight of epidemiological evidence is unambiguous that the face of CRC in Ireland is changing. Looking forward our systems need to adapt to meet the needs of patients and their families. This will require resourcing including funding and removal of institutional inertia in order to address the needs of our patients and their families.

Figure 1

Challenges for Patients with Young Onset Colorectal Cancer (YO-CRC)

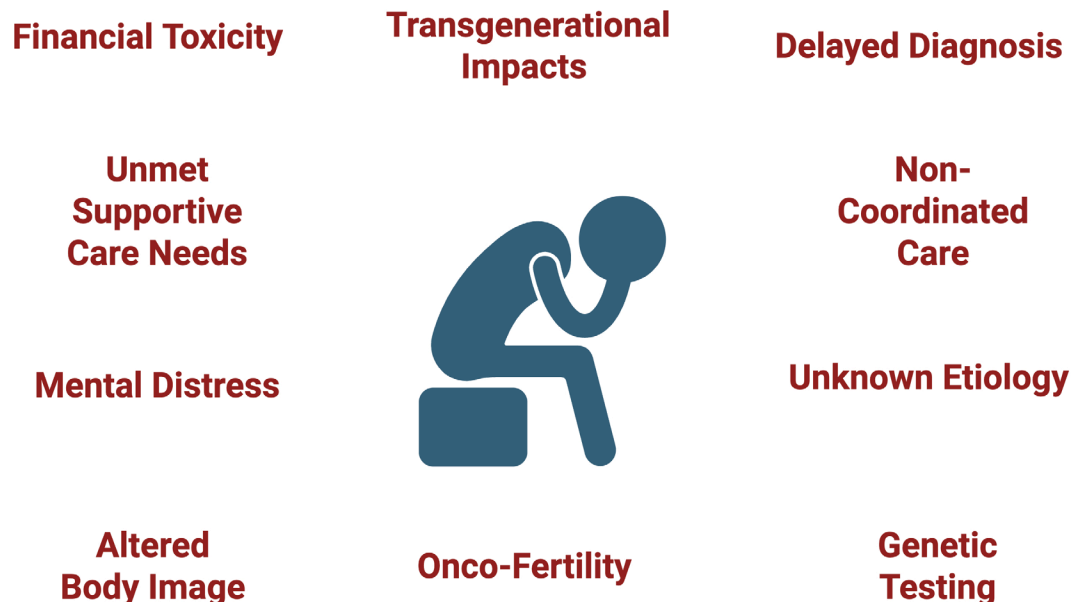


Figure created with BioRender.com

Declarations of Conflicts of Interest:

None declared.

Corresponding author:

Niamh Ryan,
 Department of Medical Oncology,

Cork University Hospital,
Wilton,
Co. Cork,
Ireland.

E-Mail: niamh.ryan14@hse.ie

References:

1. Russell, A.C.; Reid, H.; Coleman, H.G.; Santin, O. Understanding the Treatment Experiences of Adults Diagnosed with Early-Onset Colorectal Cancer: A Qualitative Study. *Psychooncology* 2024, 33, e6367
2. Spaander MCW, Zauber AG, Syngal S, Blaser MJ, Sung JJ, You YN, Kuipers EJ. Young-onset colorectal cancer. *Nat Rev Dis Primers*. 2023 Apr 27;9(1):21. doi: 10.1038/s41572-023-00432-7. PMID: 37105987; PMCID: PMC10589420.
3. Kim BJ, Hanna MH. Colorectal cancer in young adults. *J Surg Oncol*. 2023 Jun;127(8):1247-1251. doi: 10.1002/jso.27320. PMID: 37222697
4. Done JZ, Fang SH. Young-onset colorectal cancer: A review. *World J Gastrointest Oncol*. 2021 Aug 15;13(8):856-866. doi: 10.4251/wjgo.v13.i8.856. PMID: 34457191; PMCID: PMC8371519.
5. National Cancer Registry Ireland. Colorectal cancer incidence, morality, treatment and survival in Ireland 1994-2010
6. Arnold M, Sierra MS, Laversanne M, et al Global patterns and trends in colorectal cancer incidence and mortality. *Gut* 2017;66:683-691
7. Carbone, Fabio et al.. Prognosis of early-onset versus late-onset sporadic colorectal cancer: Systematic review and meta-analysis. *European Journal of Cancer*, Volume 215, 115172
8. Saraiva MR, Rosa I, Claro I. Early-onset colorectal cancer: A review of current knowledge. *World J Gastroenterol*. 2023 Feb 28;29(8):1289-1303. doi: 10.3748/wjg.v29.i8.1289. PMID: 36925459; PMCID: PMC10011966.
9. Murphy, Caitlin C. et al. Decrease in Incidence of Young-Onset Colorectal Cancer Before Recent Increase. *Gastroenterology*, Volume 155, Issue 6, 1716 - 1719.e4
10. Chang DT, Pai RK, Rybicki LA, Dimaio MA, Limaye M, Jayachandran P, Koong AC, Kunz PA, Fisher GA, Ford JM, Welton M, Shelton A, Ma L, Arber DA, Pai RK. Clinicopathologic and molecular features of sporadic early-onset colorectal adenocarcinoma: an adenocarcinoma with frequent signet ring cell differentiation, rectal and sigmoid involvement, and adverse morphologic features. *Mod Pathol*. 2012 Aug;25(8):1128-39. doi: 10.1038/modpathol.2012.61. Epub 2012 Apr 6. PMID: 22481281.

11. REACCT Collaborative. Characteristics of Early-Onset vs Late-Onset Colorectal Cancer: A Review. *JAMA Surg.* 2021;156(9):865–874. doi:10.1001/jamasurg.2021.2380
12. Zaborowski AM, Murphy B, Creavin B, Rogers AC, Kennelly R, Hanly A, Martin ST, O'Connell PR, Sheahan K, Winter DC. Clinicopathological features and oncological outcomes of patients with young-onset rectal cancer. *Br J Surg.* 2020 Apr;107(5):606–612. doi: 10.1002/bjs.11526. Epub 2020 Mar 9. PMID: 32149397.
13. Stoffel EM, Koeppe E, Everett J, Ulintz P, Kiel M, Osborne J, Williams L, Hanson K, Gruber SB, Rozek LS. Germline Genetic Features of Young Individuals With Colorectal Cancer. *Gastroenterology.* 2018 Mar;154(4):897–905.e1. doi: 10.1053/j.gastro.2017.11.004. Epub 2017 Nov 14. PMID: 29146522; PMCID: PMC5847426.
14. Rebersek, M. Gut microbiome and its role in colorectal cancer. *BMC Cancer* 21, 1325 (2021). <https://doi.org/10.1186/s12885-021-09054-2>
15. Atchade AM;Williams J; Mermelstine L; Nemesure B. Unravelling the complexities of early onset- colorectal cancer: a perspective on dietary and microbial influences. *Front. Public Health* , 4 April 2024. Sec. Environmental Health and Exposome. Vol.12-2024. <https://doi.org/10.3389/fpubh.2024.1370108>
16. Wong CC, Yu J. Gut microbiota in colorectal cancer development and therapy. *Nat Rev Clin Oncol.* 2023 Jul;20(7):429–452. doi: 10.1038/s41571-023-00766-x. Epub 2023 May 11. PMID: 37169888
17. Benjamin A Weinberg, Caitlin C Murphy, David R Freyer, K Leigh Greathouse, Jan K Blancato, Elena M Stoffel, Julia L Drewes, Anne Blaes, John M Salsman, Y Nancy You, Hannah Arem, Reetu Mukherji, Priyanka Kanth, Xin Hu, Anne Fabrizio, Marion L Hartley, Marios Giannakis, John L Marshall, Rethinking the rise of early-onset gastrointestinal cancers: a call to action, *JNCI Cancer Spectrum*, Volume 9, Issue 1, February 2025, pkaf002, <https://doi.org/10.1093/jncics/pkaf002>
18. Gerstberger, Stefanie & Lumish, Melissa & Hartner, Saskia & Shah, Farheen & Choi, Seongmin & Lum, Krystal & Cowley, Christopher & Luthra, Anisha & Jiang, Qingwen & Woo, Hyung & Mahmoud, Ahmed & Walch, Henry & Saxena, Asha & Reed, Tavis & Cercek, Andrea & Yaeger, Rona & Cristea, Ileana & McPherson, Andrew & Sánchez-Vega, Francisco & Ganesh, Karuna. (2025). Abstract 2856: Pks+ E. coli trigger intestinal stem cell plasticity and early onset colorectal cancer. *Cancer Research.* 85. 2856–2856. 10.1158/1538-7445.AM2025-2856
19. Díaz-Gay, M., dos Santos, W., Moody, S. et al. Geographic and age variations in mutational processes in colorectal cancer. *Nature* (2025). <https://doi.org/10.1038/s41586-025-09025-8>
20. Philips, C. As Rates of Some Cancers Increase in Younger People, Researchers Search for Answers. National Cancer Institute. Accessed at <https://www.cancer.gov/news->

events/cancer-currents-blog/2025/early-onset-cancer-research-environment-genetics-support?cid=eb_govdel

21. Atchade AM;Williams J; Mermelstine L; Nemesure B. Unravelling the complexities of early onset- colorectal cancer: a perspective on dietary and microbial influences. *Front. Public Health* , 4 April 2024. Sec. Environmental Health and Exposome. Vol.12-2024. <https://doi.org/10.3389/fpubh.2024.1370108>
22. Puzzono, M., Mannucci, A., Grannò, S., Zuppardo, R. A., Galli, A., Danese, S., & Cavestro, G. M. (2021). The Role of Diet and Lifestyle in Early-Onset Colorectal Cancer: A Systematic Review. *Cancers*, 13(23), 5933. <https://doi.org/10.3390/cancers1323593>
23. Landrigan PJ, Raps H, Cropper M, Bald C, Brunner M, Canonizado EM, et al. The Minderoo-Monaco Commission on Plastics and Human Health. *Ann Glob Health*. 2023;89(1):23.
24. Seewoo BJ, Goodes LM, Thomas KV, Rauert C, Elagali A, Ponsonby AL, et al. How do plastics, including microplastics and plastic-associated chemicals, affect human health? *Nat Med*. 2024;30(11):3036-7.
25. Li C, Gillings MR, Zhang C, Chen Q, Zhu D, Wang J, et al. Ecology and risks of the global plastisphere as a newly expanding microbial habitat. *Innovation (Camb)*. 2024;5(1):100543.
26. Li S, Keenan JJ, Shaw IC, Frizelle FA. Could Microplastics Be a Driver for Early Onset Colorectal Cancer? *Cancers (Basel)*. 2023;15(13):3323
27. World Gastroenterology Organisation. Colorectal Cancer Screening Guidelines. Accessed at <https://www.worldgastroenterology.org/guidelines/colorectal-cancer-screening/colorectal-cancer-screening-english#:~:text=Colonoscopy%20for%20average%20risk%20men,colorectal%20cancer%20or%20adenomatous%20polyps>
28. Hakki L, Khan A, Ehrich F, Thompson HM, Sokolowski S, Gönen M, Aviki EM, Weiser MR. Younger Patients with Colon Cancer are More Likely to Experience Financial Toxicity Than Older Patients. *Ann Surg Oncol*. 2023 Oct;30(11):6837-6842. doi: 10.1245/s10434-023-13911-8. Epub 2023 Jul 21. PMID: 37479844; PMCID: PMC10527083.
29. Guida F, Kidman R, Ferlay J et al. Global and regional estimates of orphans attributed to maternal cancer mortality in 2020. *Nature Med* 2022. 28:2563-72. <https://doi.org/10.1038/s41591-022-02109-2>
30. Huis In 'tVeld EA, Van Assche IA, Van Calsteren K et al. Long-term development of 12- and 15- year old offspring after maternal cancer diagnosis during pregnancy: a prospective multicentre cohort study. *Ann Oncol* May 6:S0923-7534(25)00171-1. 2025. <https://doi.org/10.1016/j.annonc.2025.04.011>