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Referral challenges for early-onset colorectal cancer: a qualitative study in UK primary care

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Abstract

Background: The incidence of early onset colorectal cancer (EOCRC), in adults aged under 50 years, has increased in several Western nations. National surveys have highlighted significant barriers to EOCRC patients accessing timely care, which may be contributing to a late stage of presentation amongst this population group.

Aim: To explore awareness of the increasing incidence of EOCRC, and to understand the potential barriers or facilitators faced by general practitioners (GPs) when referring younger adults to secondary care with features suspicious for EOCRC.

Design and setting: Qualitative methodology, via virtual semi-structured interviews with seventeen GPs within Northern Ireland.

Method: Reflective thematic analysis was conducted with reference to Braun and Clarke’s framework.

Results: Three main themes were identified regarding awareness, diagnostic and referral challenges amongst participating GPs. Awareness challenges focused on perceptions of EOCRC being solely associated with hereditary cancer syndromes and colorectal cancer being a condition of older adults. Key diagnostic challenges centred around the commonality of lower gastrointestinal complaints and overlap in EOCRC symptoms with benign conditions. Restrictions in age-based referral guidance and a GP ‘guilt complex’ surrounding over-referral to secondary care summarised the referral challenges. Young women were perceived as being particularly disadvantaged with regards to delays in diagnosis.

Conclusion: This novel research outlines potential reasons, from a GP perspective, for the diagnostic delays seen in patients with EOCRC and highlights many of the complicating factors that contribute to the diagnostic process.

Key words: Colorectal neoplasms, general practice, delayed diagnosis, qualitative research, primary health care, qFIT

How this fits in:

The incidence of EOCRC has risen in many Westernised countries in recent years. Patients with EOCRC have been shown to experience longer diagnostic delays than their older counterparts. This research highlights the perceived awareness, diagnostic and referral challenges faced by GPs when younger adults present to primary care with lower gastrointestinal symptoms suspicious for EOCRC.
Introduction

The incidence of early onset colorectal cancer (EOCRC), defined as affecting adults aged under 50 years, has increased substantially in recent decades in many Westernised countries.(1, 2) A 2022 rapid review demonstrated consistent evidence of the rising trends seen globally, highlighting the need for change to suspected cancer referral guidance.(3) In the UK, incidence rates of EOCRC in 25–49 year olds have increased by 48% between 1993 and 2018.(4) Furthermore, global mortality rates from EOCRC have increased by 18% from 1990 to 2019.(5) By 2030, it is projected that EOCRC will be the leading cause of cancer-related deaths in individuals aged 20-49 years in the United States.(6)

A multitude of research has indicated a birth cohort effect with relation to people born after the 1960s having an increased risk of EOCRC.(7) Although multiple factors implicated in EOCRC have been widely debated, such as the increasing prevalence of obesity, low levels of physical activity, high processed food intake, or altered gut microbiota, there have been few conclusive findings.(8-10) The vast majority of EOCRC diagnoses are not associated with an inherited cancer syndrome and therefore sporadic, symptomatic presentation, is the most common route for diagnosis.(11,12)

Abdominal pain has been found to be a pertinent presenting feature in EOCRC patients, when accompanied by rectal bleeding and a change of bowel habit.(13-15) For this reason, the UK 2015 NICE guidance included criteria for individuals aged under 50 years presenting with rectal bleeding to include associated abdominal pain as a possible red flag cancer symptom.(16)

A survey carried out by Bowel Cancer UK as part of their ‘Never Too Young campaign’ demonstrated that four in ten patients who had asked their GP if their symptoms could be caused by bowel cancer were told they were “too young”.(17) A population-based study in England highlighted the referral challenges faced by EOCRC patients, with only 22.6% being referred through a 2-week wait (‘red flag’) referral pathway. The study theorised the lowered suspicion of cancer amongst healthcare professionals, as well as limitations in age-based referral guidelines, resulted in young patients being referred through a non-urgent pathway.(13)

With the high volume of consultations within primary care, the challenge for GPs is distinguishing the rarer EOCRC cases for referral. Lower gastrointestinal (GI) tract symptoms account for one in twelve consultations in primary care, reflecting the common nature of GI complaints.(18) The overlap in symptomatology when patients present with undifferentiated symptoms shared with benign illness further contributes to the complexity of diagnosing cancer in primary care.(19)
This research aims to explore awareness of the increasing incidence of EOCRC, and to understand the potential barriers or facilitators faced by general practitioners (GPs) when referring younger adults to secondary care with features suspicious for EOCRC.
Methods

Virtual semi-structured interviews were conducted. Ethical approval was obtained from the Faculty of Medicine, Health, and Life Sciences Research Ethics Committee at Queen’s University Belfast (Reference Number: MHLS 21_55).

Participant selection and characteristics

Participants were limited to GPs practising within Northern Ireland (NI), due to specific regional referral guidance being used throughout the UK. Invitations (Supplementary File 1) to participate in semi-structured interviews were disseminated widely via NI GP mailing lists. This included practice manager and out of hours co-ordinator networks, RCGP NI newsletter and a closed NI primary care social media group, as approved by the ethics committee. Participation was voluntary and not incentivised. Twenty-three participants actively contacted the research team to express interest in participating in the study. Interviews were scheduled at participant convenience once the required written consent forms were complete and submitted. With transcription and preliminary analysis happening in parallel with further interviews, we were able to make rational decisions around data sufficiency. This point, with paucity of novelty, was achieved after seventeen interviews.

Data collection

The interview guide was collaboratively developed by the research team, using their combined expertise in qualitative research, epidemiology, and general practice, alongside patient and public involvement from the NI Cancer Consumer Forum. The final interview guide was piloted with GP academic colleagues at Queen’s University Belfast, with clarity of the study aims, to include facilitators as well as barriers to referral, addressed following piloting. The interview guide included six broad questions (Supplementary File 2). Although the interview guide provided a framework, discussions were typically guided by participant responses.

Virtual semi-structured interviews were conducted by the primary researcher (OO’N) and recorded over Microsoft Teams between June and July 2021. Interviews lasted between 20 and 43 minutes, with a median time of 31 minutes.

Interviews took place during a time of change to NI Cancer Network (NICAN) referral guidelines in June 2021. (20) Two key updates to NICAN guidelines at this time were the removal of age restrictions for referrals, and implementation of quantitative faecal immunochemical test (qFIT)-based triage.(21)
Data analysis

Data was analysed using the framework of Braun and Clarke’s thematic analysis.(22) Interviews were transcribed verbatim by OO’N. Transcription notation was adapted from formal conversational analysis transcribing conventions.(23) Further data familiarisation was achieved through repeated readings of the transcripts by OO’N and preliminary coding on a case-by-case basis. Four transcripts were picked at random and analysed independently by HR to compare and discuss codes in a reflective and collaborative manner, to enable richer interpretations and provide a consensus on the application of codes to subsequent transcripts. OO’N then coded the data on a cross-case analysis basis and grouped codes into subthemes inductively. The research team analysed the subthemes and together actively identified themes in an inductive process, identifying those most relevant to the research question.
Results

Demographics of the seventeen participating GPs are shown in Table 1. Participating GPs represented a relatively even mix of males/females, ages and practice demographics (rural, urban or mixed). The majority of participating GPs had been qualified for 11 years or more (Table 1).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n=17 (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>9 (53%)</td>
</tr>
<tr>
<td>Male</td>
<td>8 (47%)</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
</tr>
<tr>
<td>30-40</td>
<td>5 (29%)*</td>
</tr>
<tr>
<td>41-50</td>
<td>5 (29%)</td>
</tr>
<tr>
<td>51-60</td>
<td>5 (29%)</td>
</tr>
<tr>
<td>60+</td>
<td>2 (12%)</td>
</tr>
<tr>
<td>Years qualified</td>
<td></td>
</tr>
<tr>
<td>0-10</td>
<td>1 (6%)</td>
</tr>
<tr>
<td>11-20</td>
<td>7 (41%)</td>
</tr>
<tr>
<td>21-30</td>
<td>7 (41%)</td>
</tr>
<tr>
<td>30+</td>
<td>2 (12%)</td>
</tr>
<tr>
<td>Practice demographic</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>4 (24%)</td>
</tr>
<tr>
<td>Urban</td>
<td>6 (35%)</td>
</tr>
<tr>
<td>Mixed</td>
<td>7 (41%)</td>
</tr>
</tbody>
</table>

*Percentages do not total 100% due to rounding.

Three main themes were identified from the data around awareness, diagnostic and referral challenges. Awareness subthemes included the perception of colorectal cancer (CRC) as a disease of older adults, as well as a presumptive hereditary cancer syndrome in younger adults. Diagnostic challenges reflected the common nature of lower GI complaints presenting to general practice and overlap with benign pathologies. A theme of young women being disadvantaged with regards to delays in diagnosis was also identified. Referral challenges included age-based guideline constraints and a ‘guilt complex’ felt by GPs when referring patients to a poorly resourced secondary care system.
Awareness challenges: Never too young

**Disease of older adults**

CRC was perceived by the majority of the participants as a disease of older adults, providing insight into why younger patients may be more likely to experience delays in referral for further investigation.

"...I suppose my radar would be mainly in the older population" P13

"I still think for most GPs age is a great reassurer...particularly in the 20s and 30s, I mean sometimes the late 40s...people think emm benign, or inflammatory bowel disease, you don’t think about cancer" P2

With participants less likely to consider the diagnosis in their immediate differentials of a younger patient, they highlighted the diagnostic uncertainty based on symptoms alone.

"I am less likely to search for it in the much younger population...there’s also the risk of overlap with the inflammatory bowel disease as some of the symptoms can be similar" P9

Perceptions were influenced by participants’ pre-existing knowledge of CRC as well as local age-based referral guidelines.

"I think eh...less than 40 and really emm... you could go up as far as 50 but I would say definitely less than 40 I really need, I need to be convinced, that I need to refer them you know.... My threshold is higher certainly" P1

"Yeah obviously the over 50s it’s easier again because it’s so much more easily quotable from the guidelines” P14

**Presumed hereditary cancer syndrome**

There was a general perception that EOCRC was associated with hereditary or genetic cancer syndromes and therefore patients without a significant family history were less readily referred.

"...he had the Lynch syndrome, that would be sort of...in my head thinking of somebody who’s very young, be related to a genetic condition” P17

"If there was a significant family history then they would be most likely be getting referred on as well you know maybe wouldn’t be hanging about as much to see if things resolve you know I’d probably refer earlier if there was that kind of thing” P1
With one participant reflecting on the routine referral of an EOCRC patient with rectal bleeding and a family history of bowel cancer rather than not referring at all due to a perceived benign diagnosis in a young patient.

“... the difficulty was I referred him routinely rather than red flag eh and one of the reasons was his mother had bowel cancer and I felt we were dealing with something like haemorrhoids here so I did routine referral probably more on the basis of his mother had bowel cancer, now it wasn’t a particularly bad family history it just seemed to be almost coincidental” p15

Diagnostic challenges: The great imitator

Commonality of GI complaints

The complexity of identifying patients with EOCRC in general practice focused on the large numbers of presentations of lower GI complaints with benign aetiology, making it difficult to identify those with sinister diagnoses.

“I guess that’s the problem you’re absolutely swamped with presentations” P10

“... a very very common presentation and that can make it quite difficult to you know...you have your differentials ...and make a decision as to what is the most likely” P17

Overlap with benign pathologies

Participants reflected on the vague presentation and typical overlap of symptoms with more common benign conditions in this age group, such as irritable and inflammatory bowel disease, and benign anorectal conditions such as haemorrhoids. Participants highlighted the difficulty of differentiating these conditions from malignant disease with the investigations and tools available in primary care.

“You get so many of the other sort of irritable bowel type patients with any sort of quite mild symptoms and they’re in contact quite frequently you know so it’s...eh I don’t know it’s sort of that deluge of patients and sort of trying to work out which are the patients that...that have concern” P10

“It’s in that group, the diagnostic uncertainty, the chances are it’s going to be something else emm and being able to tease out, with I suppose the tools that we have” P12
"My impression is that in younger people it seems to present later, maybe...I don’t know if that’s because it tends to be more aggressive or it’s just that the sort of you know your suspicion isn’t as raised and maybe you’re more quick to say people have IBS or whatever" P11

Women most disadvantaged

Several GPs independently acknowledged that young women were most disadvantaged when it came to delays in referral and diagnosis. Potential reasons for this gender difference were discussed by participants:

“I think the under 50s emm...women with iron deficiency anaemia are often eh sort of signposted or...put into the pigeonhole of emm menstrual losses eh the altered bowel habit as well isn’t necessarily as big a red flag and ultimately it usually takes longer before you refer simply because of the overlap with irritable bowel type things” P2

“Women who are under 50 who are still menstruating as well who have iron deficiency anaemia then you’ll just put it down to that and then you’re less likely to investigate as well so you know that’s another I suppose risk factor for that being missed” P11

“...with females in particular emm gynae related issues can be...it can be difficult to discern between gynae problems and what can be bowel related problems” P17

Referral challenges: GP guilt and guidelines

GP guilt complex

Participants described a sense of guilt associated with referring patients to secondary care for further investigations and the pressure that waiting lists had on their decision making with regards to referral.

“The art is trying to sift out those guys without, without over referring, and I suppose ultimately I have, feel the...on a personal level, feel the burden of our long waiting lists and... tend to carry risk and under refer compared to some colleagues” P2

“I think one of the problems ...is that everything is getting red-flagged by you know...not from every GP, but I think probably our thresholds are too low ...they must be, sometimes very exacerbated with us... it’s the system is broken...certainly in Northern Ireland, you could have all the guidelines you like but if you don’t have the resources then what?” P16
Guideline constraints

A significant issue highlighted by participants was the constraint that guidelines, including historic NICAN referral guidance(20) put on their referral-making decisions, and sometimes the downgrade of referrals if guidelines were not met.

“The biggest problem we have is getting these patients seen because of the referral guidelines” P17

“...whenever I do a referral...a red flag referral, I have to make it fit, because if I don’t it’ll come back to me...” P4

“... if a patient fulfils it, it makes it very straightforward but I think there’s probably quite a caveat, and especially the younger patients who don’t strictly meet the criteria and that’s the problem and you might refer them...but probably knowing that the referral may well be downgraded which is probably our experience...” P7

In particular, age was identified as the main barrier to red flag referral and participants reflected that younger patients often languished on non-red flag waiting lists.

“I think most of the guidelines are all set up to be pretty clear for the over 50s and for the under 50s it gets increasingly less clear...There is no service for anybody who doesn’t meet red flag criteria” P2

“...therein lies the difficulty no matter what your age but particularly for young people or younger patients because they often don’t tend to tick the red flag box by virtue of their age and therefore they are losing out...you know potentially we are missing significant diagnoses” P12

With the long waiting lists for secondary care within the NHS, GPs felt that patients not meeting red flag criteria were particularly disadvantaged with delays in diagnosis. Participants reflected on the impact this had on patients as well as on GPs managing these patients in primary care.

“Well certainly if I’ve put in an urgent referral, I certainly hope to myself that there isn’t anything serious wrong, I’m usually aware that they don’t fit into the guidelines...but I’m aware that that doesn’t make it impossible that they have bowel cancer and I worry about the fact that urgent referrals are taking a long time to be seen” P5

“The problem is your left with carrying the can until the diagnosis is made ... at the end of the day the patient’s my responsibility and if they were doing... you know if the red flag pathway whereby they got seen and scoped within 4-6 ...I’m not going to be awfully worried about it but knowing what the waiting lists are like I know it’s back to me...” P4
Discussion

Summary

This qualitative study highlights some of the important challenges faced by GPs when assessing and referring younger patients with lower GI symptoms suspicious for cancer. With the worrying increasing trends in EOCRC seen globally and often late stage at diagnosis seen in these patients, (24-26) the need to identify challenges and implement change is necessary to protect future generations. The interviews in this study provide an insight into factors contributing to these delays. The complexity of making a diagnosis in general practice is multi-factorial. The commonality of the presentation as well as the overlap in symptomatology with benign conditions adds to this complexity. Furthermore, an ingrained perception of CRC being a disease of older adults and younger patients being associated with hereditary cancer syndromes lowers GPs’ suspicions. The barriers that primary care face with regards to referral guidance also complicates the diagnostic process in many younger patients, compounded by long waiting lists and an underlying feeling of guilt amongst many GPs about over-referring to secondary care. Unique diagnostic challenges were particularly noted around young women with potential EOCRC, with presumptive menstrual causes for iron deficiency anaemia and women being more readily diagnosed with irritable bowel syndrome.

Strengths and limitations

The authors believe this to be novel research into the unique GP perspective and understanding why there may be delays in primary care with regards to EOCRC patients in a UK region. Our research design was strengthened by the mix of expertise within the research team and robust involvement of the patient and public perspective. A methodological strength of the data analysis was the independent coding of some reports by an experienced qualitative researcher as a second reviewer.

Limitations to this research include the potential for regional specific challenges, given that the study was limited to GPs practise in NI. However, we feel that the majority of the themes identified are likely to be theoretically transferable to other UK regions, and indeed internationally. We have also acknowledged that the timing of the interviews occurred during a period of change to local referral guidance, with age-specific criteria being removed from red flag guidance.(21) However, it is likely that the long-standing age-based criteria may influence decision making by GPs into the future and ingrained perceptions may transcend guidelines.
Comparison with existing literature

It is well documented that patients with EOCRC experience longer diagnostic delays compared with their older counterparts.\textsuperscript{(27, 28)} A European retrospective case-case study found that only 40.7\% of EOCRC patients were diagnosed within six months from symptom-onset compared to 85.6\% of patients over the age of 50.\textsuperscript{(29)} GPs are more likely to suspect cancer in older patients, with younger age and female gender being found to be factors that contribute to GPs’ cognitive bias with regards to first impression cancer risk. \textsuperscript{(30)} Although hereditary cancer syndromes or family history of CRC are significant risk factors for the disease,\textsuperscript{(31)} the majority of EOCRC are known to be sporadic.\textsuperscript{(32)} Low levels of suspicion amongst GPs in young patients without a family history of CRC was identified as a potential barrier to further investigation and referral within our study. To our knowledge, this novel finding on misperceptions of family history and inherited cancer syndromes amongst EOCRC patients by GPs has not been previously reported.

A large UK study of 36 primary care practices in the mid-1990s found that GI symptoms accounted for 1 in 12 consultations, and of those symptomatic patients, nearly half were diagnosed with a functional bowel disorder including irritable bowel syndrome (IBS).\textsuperscript{(18)} With an estimated 11\% of the global population affected by IBS,\textsuperscript{(33)} the difficulty is trying to identify sinister pathology particularly with the overlap in benign symptoms. An English data-linkage study has found that women with CRC and abdominal symptoms in the pre-diagnostic year were twice as likely to be diagnosed with a benign condition compared to men with similar symptoms.\textsuperscript{(34)} Women aged 40-59 years with a new onset benign diagnosis were at particularly high risk of an emergency presentation of their CRC diagnosis.\textsuperscript{(34)} The theme of perceptions of CRC being a diagnosis of older patients, as well as prioritisation of common conditions by GPs were also highlighted as potential barriers to timely diagnosis of EOCRC in a UK mixed-methods study.\textsuperscript{(35)} This study also identified a possible sex disparity, with females more likely to report a misdiagnosis of IBS and psycho-emotional diagnoses such as stress.\textsuperscript{(35)}

The theme of young women being disproportionately disadvantaged when it comes to delays in diagnosis has also been highlighted in other reports. The Bowel Cancer UK’s ‘Never Too Young Report’ in 2015 found that 20\% of patients with EOCRC presented to their GP five or more times before referral, with 54\% of male patients being referred after fewer than three consultations compared to only 35\% of females.\textsuperscript{(36)} Younger women have previously been found to be more likely to experience missed opportunities for diagnosis of CRC than men\textsuperscript{(37)} and experience longer overall clinical delays.\textsuperscript{(38)} Interestingly, unlike late onset CRC, which has a slight male predominance, rates of EOCRC have been found to be similar in both sexes.\textsuperscript{(39)} Siegel et al demonstrated that since 1994,
both sexes have seen incidence rates increase >50%.(40) GPs need to have increased awareness of EOCRC affecting both males and females to a similar extent. Our research has highlighted some of the potential reasons for sex differences seen with referral patterns, including iron deficiency anaemia being attributed to menstrual losses and an overlap between bowel and gynaecological symptomatology.

Another highlighted theme identified guideline constraints and a poorly resourced secondary care system as potential barriers to onward referral. Delays within primary care relating to accessibility, referral pathways and resources were also identified in a European cross-sectional survey as potential barriers to timely cancer diagnoses.(41) Furthermore, the concept of a GP ‘guilt complex’ with regards to referral was noted in a UK-based primary care study which investigated all-age CRC suspicions in GPs.(42) Amongst patients meeting urgent referral criteria, that UK study found key barriers to referral included a fear of over-referral or unnecessary referrals with participants wishing to avoid being identified as having a high referral rate.(42) With NICE referral guidance having an estimated 3% cancer pick-up rate (16), the perception that referrals should amount to a high level of cancer diagnoses is skewed but it is interesting that GPs feel this pressure with regards to their referrals.

Research exploring variations in suspected cancer referral pathways across ten different jurisdictions in the International Cancer Benchmarking Partnership concluded that allowing more flexibility with referral pathways, with greater access to investigations and open channels of communication with secondary care may improve cancer diagnostic delays.(43) The authors exemplified the Australian system, as having flexibility with referrals and direct access to investigations in part as to their success with higher cancer survival and earlier stage at diagnosis compared to international counterparts.(43) Waiting lists for secondary care within the NHS are significant at present and particularly within NI.(44) It is important to address accessibility to investigations and secondary care to improve the diagnostic journey for patients presenting to primary care.

**Implications for research and practice**

This research aimed to gain a deeper understanding of why patients with EOCRC experience longer diagnostic delays. This research has the potential to alter practice through challenging longstanding perceptions and addressing areas of health care professional deficits of awareness and knowledge of EOCRC. By acknowledging the unique diagnostic challenges faced by EOCRC patients, and particularly women, we hope to improve their diagnostic journey. It is imperative that GPs have
access to tools to aid decision making with regards to onward referrals, or improved diagnostic pathways.

The future for early diagnosis may be found in the implementation of risk stratification tools in primary care, as evaluated in a recent English cohort study incorporating blood test trends to identify patients at high risk of cancer. Future research should evaluate the introduction of symptomatic qFIT use in NICAN primary care referral guidance (21) and the removal of age-based restrictions, and potential impact on earlier diagnosis of EOCRC patients. QFIT use in symptomatic patients has been found to have a high level of sensitivity for CRC with the benefit of identifying a truly low risk cohort of patients who can be managed in primary care, with approval of its use in primary care. The introduction of Rapid Diagnostic Centres following recommendations in the 2022 NI Cancer Strategy (47), and their perceived impact on GP referrals for cancer diagnoses (including EOCRC) also requires future study. (48)

A multi-faceted approach is required to enable GPs to make more timely diagnoses, optimal utilisation of secondary care services, and ultimately improve EOCRC patient experiences and outcomes.

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Ethical approval: Ethical approval was obtained from the Faculty of Medicine, Health, and Life Sciences Research Ethics Committee at Queen’s University Belfast (Faculty REC Reference Number: MHLS 21_55).

Competing interests: None declared

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