Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Health Technology Assessment of Scheduled Procedures

Referral thresholds for patients with lower gastrointestinal symptoms suspected of indicating malignancy

Draft for consultation

July 2014

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The Authority's mandate to date extends across the quality and safety of the public, private (within its social care function) and voluntary sectors. Reporting to the Minister for Health and the Minister for Children and Youth Affairs, the Health Information and Quality Authority has statutory responsibility for:

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Table of Contents

1 Lower Gastrointestinal Symptoms

1.1 Scope of this health technology assessment

This health technology assessment (HTA) evaluates the appropriateness and potential impact of introducing clinical referral and diagnostic thresholds for people suspected of having colorectal cancer in Ireland. The effectiveness of these investigations may be limited unless undertaken within strict clinical criteria. This report is one of a series of HTAs of scheduled procedures. Details of the background to the request and general methodology are provided in the separate 'Background and Methods' document.[1]

The scope of this HTA is to investigate clinical referral and diagnostic thresholds that can be used in the assessment, referral and diagnosis of adults who are potentially suffering from colorectal cancer in Ireland. Inputs from an Expert Advisory Group along with a review of the clinical and cost-effectiveness literature were used to inform the criteria. Additionally, the budget impact and resource implications were assessed, as appropriate.

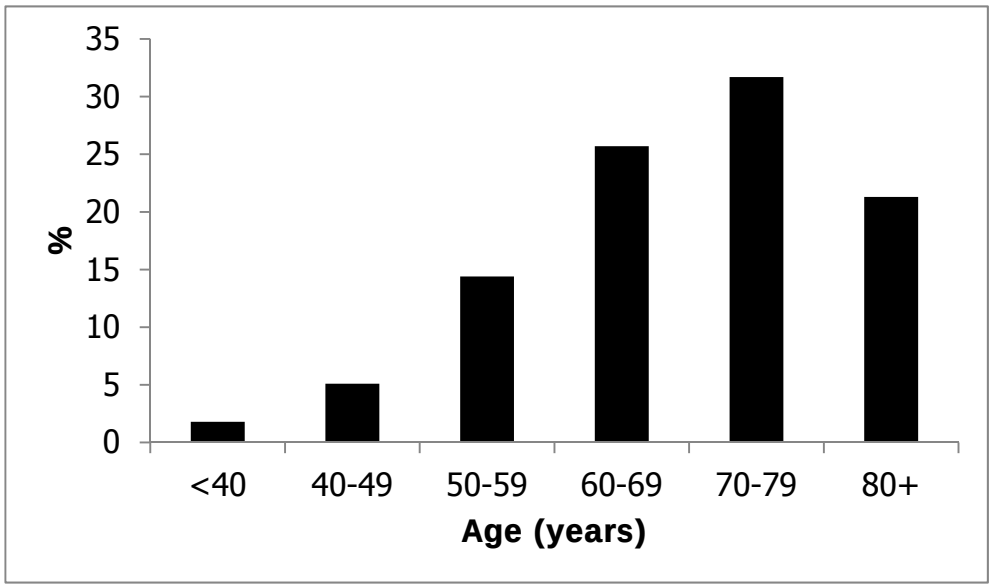
1.2 Background

The term 'colorectal cancer' encompasses malignancies of the colon and rectum and may also be termed 'bowel cancer'. According to the National Cancer Registry, there were 2,385 new cases of colorectal cancer diagnosed in Ireland in 2011 (Table 1.1). These represent 12.7% of all invasive cancers diagnosed, and colorectal cancer is the third most common invasive cancer diagnosed overall. Incidence rates of colorectal cancer in men and women are 66.1 and 44.1 per 100,000 population per year, respectively.[2] Between 2005 and 2011, 93.1% of patients diagnosed with colorectal cancer were aged 50 years or older (Figure 1.1). For those in whom the method of detection was known, >95% was on the basis of symptoms.[3] The cumulative lifetime risk of colorectal cancer in men and women is 5.1% and 3.1%, respectively. Approximately 1,040 people die of colorectal cancer in Ireland each year. Five-year relative survival from colorectal cancer improved from 50.1% between 1994 and 1999 to 60.6% between 2008 and 2010.[4]

Table 1.1 National Cancer Registry Data, Colorectal Cancer, 2005-2011[3]

Colorectal Cancer	
Year of Diagnosis	**No. Diagnosed**
2005	2,097
2006	2,154
2007	2,297
2008	2,255
2009	2,403
2010	2,373
2011	2,385
Total	**15,964**

Figure 1.1 National Cancer Registry Data, Colorectal Cancer, % of patients diagnosed with colorectal cancer by age, 2005-2011[3]



Modelling work performed by the National Cancer Registry has suggested that the incidence of colon cancer will increase by approximately 116% in women and by between 104% and 156% in males between 2010 and 2040. Similarly, its projections suggest that between 2010 and 2040 incidence rates for cancer of the rectum (and anus) will increase by between 83% and 110% for women and by between 77% and

105% for men; these projected increases are based primarily on forecasted demographic changes (increasing size of population, ageing).[5]

BowelScreen, a population-based screening programme for colorectal cancer was rolled out nationally in 2013. This consists of biennial faecal immunochemical testing (FIT), using a home test kit, for men and women between the ages of 60 and 69. The home kit is posted back to the screening programme for analysis and, if any evidence of blood is found, the person is then called for a screening colonoscopy (fibre-optic examination of the entire length of the large bowel and the last part of the small bowel). It is intended that the programme will eventually be expanded to include all those aged between 55 and 74 years.

Although it is intended that many with asymptomatic colorectal cancer will be diagnosed early through this screening service, there will remain a significant cohort who are diagnosed following presentation at their general practitioner (GP) with symptoms suggestive of colorectal malignancy. In 2008, 48% of colon and 50% of rectal and rectosigmoid cancers were stage three or four at diagnosis.[6] Symptoms which may be suggestive of underlying malignancy can included a change in bowel habit, rectal bleeding or blood in the stool, and a feeling that the bowel doesn't empty completely. Some of these symptoms can overlap with less serious and more common conditions. It has been suggested that a GP in the UK can expect to see just one new case of colorectal cancer per year.[7] It is thus important to provide guidance regarding both the selection of patients for referral and the level of urgency that needs to be attached to those referrals. Correct selection of patients can help to ensure that secondary care services are utilised appropriately, while also mitigating against missed diagnoses. This latter point is especially relevant in the case of colorectal cancer since we know that the five-year survival rate for early stage disease is greater than 90%, whereas that for those diagnosed with widespread cancer (stage four) is less than 10%.[8]

1.3 Diagnostic options, alternatives and potential complications

A number of diagnostic options are available to clinicians when investigating a patient who is suspected of having colorectal cancer, including flexible sigmoidoscopy (limited fibre-optic examination of the large bowel), colonoscopy (complete fibre-optic examination of the entire large bowel), computed tomography (CT) or magnetic resonance (MR) colonography (a 'virtual' colonoscopy using a CT or MRI scanner) and barium enema (an X-ray examination of the bowel using contrast material called

barium). Specifically in relation to rectal cancers, diagnostic alternatives include endorectal ultrasound and MRI. An analysis of colonoscopy and sigmoidoscopy versus the other diagnostic options outlined here is beyond the scope of this HTA.

The adverse event rate for *screening* colonoscopy has been estimated at 2.8 per 1,000 procedures, with a higher rate seen in colonoscopies that are not performed in this setting. Over 85% of complications are reported in patients undergoing colonoscopy with polypectomy. The colorectal cancer miss rate of colonoscopy has been reported to be as high as 6%.[9] Ireland's National Screening Service published the first edition of its guidelines for quality assurance in colorectal *screening* in 2012; these guidelines set an expected perforation rate of less than 1 per 1,000 screening colonoscopies performed, and less than 2 per 1,000 screening colonoscopies performed in conjunction with polypectomy.[10] The National Quality Assurance Programme in GI endoscopy published the updated version of its quality assurance guidelines in 2011 its maximum expected incidences for perforation are the same as those employed by the Screening Service.[11] Bleeding is the most common adverse event following polypectomy – the Irish guidelines state that this should occur in less than 1% of colonoscopies where polypectomy is carried out.

1.4 Current practice in Ireland

Patients with colorectal symptoms are generally referred by their general practitioner (GP) or by another hospital specialist to a gastroenterologist, general or colorectal surgeon. Referral or treatment thresholds (similar to those discussed in Section 2 below) may be used by GPs and hospital specialists in Ireland to identify eligible candidates for referral or treatment. However, it is unclear where such thresholds are being used, or how consistently they are being applied.

Colonoscopy and sigmoidoscopy are routine scheduled surgical procedures within the publicly-funded healthcare system in Ireland. The Hospital In-Patient Enquiry (HIPE) system was employed during this HTA to assess activity levels in relation to colonoscopy. This procedure may be coded as the principal procedure or as a secondary procedure. For consistency and completeness, data are reported to include the principal and secondary procedures (that is 'all procedures') with all data presented on this basis. The International Classification of Diseases (ICD) intervention codes used to retrieve this data are listed in Appendix 1.1; all sigmoidoscopy (flexible and rigid) and colonoscopy procedures were included. HIPE data does not permit separate analysis of colonoscopy and flexible sigmoidoscopy as both are entered on the system using the same code. Barium enema, CT and MR colonography were not included in this analysis.

The HIPE system reports that there were approximately 74,562 patients who underwent colonoscopy or sigmoidoscopy in 2012. Of these, 65,872 (88.3%) patients were admitted for their procedure on an elective (planned) basis. This data captures procedures provided as hospital day case and inpatient procedures, as in the other HTA reports in this series. Of the 65,872 procedures carried out in the pure elective setting 63,676 (96.7%) were reported as being done on a day case basis. A total of 2,196 procedures were carried out on inpatient basis, with an average length of stay (ALOS) of 6.8 days; it is noted that a proportion of these patients would have been admitted for investigation and work-up, and would not have been in hospital for colonoscopy or sigmoidoscopy alone. It is further noted that the average length of stay for patients undergoing elective colonoscopy or sigmoidoscopy in public hospitals decreased from 8.8 days in 2005 to 6.8 days in 2012 (Figure 1.2). The average age of patients undergoing colonoscopy or sigmoidoscopy in 2012 was 54.1 years.

The 65,872 elective colonoscopies and sigmoidoscopies recorded within the HIPE system in 2012 were performed across 41 different hospital sites (range 1 – 5,362 procedures per hospital). These institutions are categorised according to their hospital groups in Table 1.2 Any variation in practice may be explained by differing catchment sizes or the availability of a gastroenterology or colorectal surgery service, hospital size or specialisation.

Table 1.2 HIPE data for elective colonoscopy and sigmoidoscopy per proposed HSE hospital group* (2012)[12]

Hospital group	Number (%) (Range)	% Day Case (Hospital Range)	Average Age (years)
Dublin North East	14,316 (21.7%) (479-4,268)	98.4 (94.8-99.7)	53.5
Dublin Midlands	12,730 (19.3%) (9-5,362)	97.8 (95.4-100)	53.6

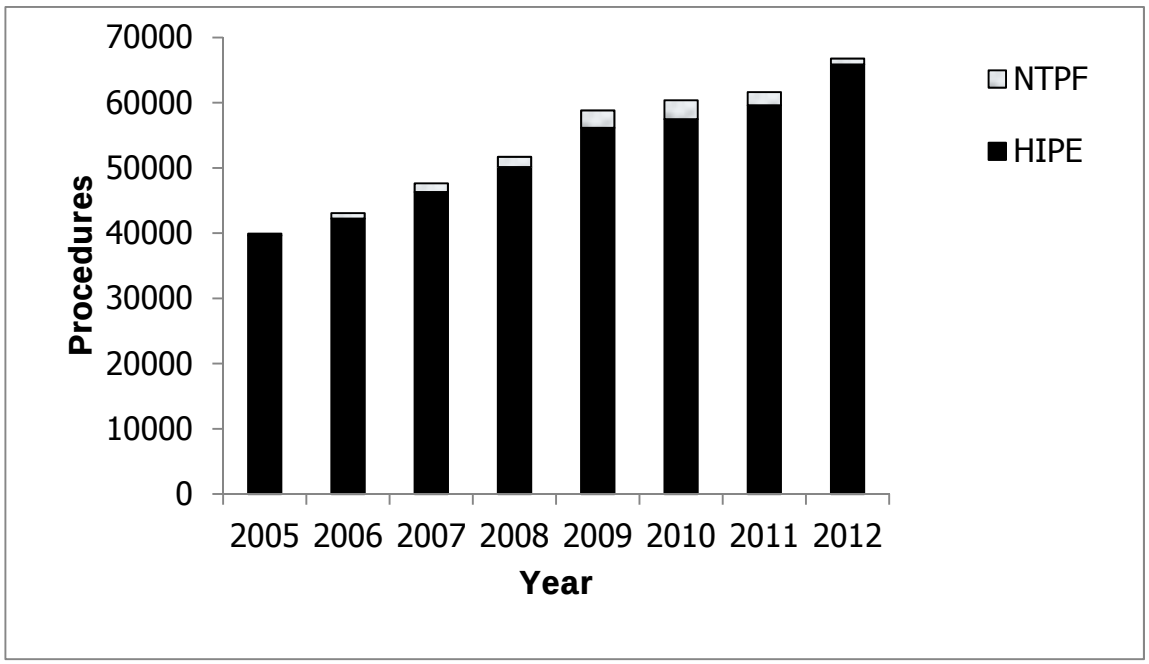
Dublin East	12,979 (19.7%) (1-2,855)	96.4 (89.8-100)	53.4
South/South West	10,984 (16.7%) (466-2,056)	93.0 (89.2-98.7)	54.9
West/North West	10,189 (15.5%) (593-2,850)	97.0 (94.1-98.6)	55.8
Midwest	4,463 (6.8%) (888-1,546)	97.2 (95.7-99.7)	55.5
Total	65,872 (100)	96.7	54.1

*Key: Range – The range in terms of number of procedures performed in individual institutions within the hospital group. NR – Not relevant * See Appendix 1.1 for HIPE codes; HIPE data include all activity in publicly-funded hospitals, including procedures in patients that used private health insurance*.

All patients who undergo a surgical procedure in Irish public hospitals have an operative diagnosis coded as part of the HIPE coding process. This is recorded as the principal diagnosis at the time of procedure, and may not be synonymous with the presumptive preoperative diagnosis. In 2012, the principal diagnosis – at the time of colonoscopy or sigmoidoscopy – was coded as 'diverticular disease of the large intestine without perforation or abscess' (9.6%); the next most frequently coded diagnoses were 'polyp of colon' (6.8%), 'gastrointestinal haemorrhage, unspecified' (6.6%), 'constipation' (4.0%) and 'gastroenteritis and colitis of unspecified origin' (4.0%).

In addition to the activity levels in public hospitals, there were 12,466 procedures procured by the public healthcare system via the National Treatment Purchase Fund (NTPF), from private hospitals, between 2005 and 2012. Data on the total number of procedures undertaken in the publicly-funded system, including the additional procedures funded by the NTPF are shown in Figure 1.2. The number of elective colonoscopies or sigmidoscopies undertaken in the publicly-funded healthcare system has increased by 67.2% from 39,936 in 2005 to 66,760 in 2012; as noted earlier, the number of colorectal cancers diagnosed annually increased by 13.7% (from 2,097 to 2,385) over approximately the same period (2005-2011).

Figure 1.2 Number of elective colonoscopies and sigmoidoscopies provided through the publicly-funded healthcare system in Ireland, 2005-2012[12]



Key: HIPE (Hospital In-Patient Enquiry Scheme) data; NTPF (National Treatment Purchase Fund) funded procedures in private hospitals. HIPE data include all activity in publicly funded hospitals, including procedures in patients that used private health insurance and procedures funded by the NTPF in public hospitals.

The length of time a patient must wait to be reviewed varies according to the referral pathway and the individual hospital and consultant to which a patient is referred. Initiatives are underway by the HSE to standardise the management of outpatient services and to ensure that there are consistent management processes across all publicly-funded healthcare facilities that provide outpatient services. This includes the publication of a protocol for the management of these services by the NTPF in January 2013 which provides the core guidance of the Outpatient Services Performance Improvement Programme.[13] The protocol specifies that patients should

be treated based on clinical urgency, with urgent referrals seen and treated first. It is intended that the definition of clinical urgency and associated maximum wait times is to be developed at speciality or condition-level and agreed by the clinical programmes. At the end of March 2014, it was reported that there were 331,281 patients on the Outpatient Waiting List database collated by the NTPF, 32.6% of whom were waiting longer than six months, with 4.9% on the list for longer than 12 months.[14] Referrals to general surgery (including ('gastrointestinal surgery') constituted 11.3% (37,436) of the total waiting list.[15]

In January 2013, the NTPF published a national waiting list management policy that outlines the standardised approach to managing scheduled care treatment for inpatient, day case and planned procedures in all publicly-funded hospitals.[16, 17] It outlines a consistent structured approach that must be adopted in the management of the waiting list; monitoring of the implementation of the policy will be routinely undertaken by the NTPF in the form of annual quality assurance reviews. Specifically in relation to GI (gastrointestinal) endoscopy (includes colonoscopy and oesophago-gastro-duodenoscopy (OGD) [fibre-optic examination of the gullet and stomach]), the HSE has stated that no patient should wait more than four weeks for an urgent colonoscopy from time of referral, and they are also monitoring the number of patients waiting greater than 13 weeks from referral to colonoscopy.[18] At the end of February 2014, there were 8,990 patients waiting for GI endoscopy; of these, 1,122 (12.5%) were waiting longer than three months, with 11 (0.1%) patients waiting longer than six months.[19] The HSE's National Performance Assurance Report, meanwhile, reported that 1,441 people were waiting over 13 weeks at the end of March 2014, 16% of the total waiting list; although this reported noted that no patients were waiting for greater than four weeks for an urgent colonoscopy, it did not comment on those patients referred for urgent upper GI endoscopy.[20]

Direct-access endoscopy is now offered at some institutions in Ireland. This has been defined as "an endoscopic procedure requested by a general practitioner and carried out without selection by a hospital consultant",[21] however, standard practice in most institutions is for the consultant to triage all referral letters to decide the procedure to be undertaken (e.g. colonoscopy or sigmoidoscopy), the timing of the procedure (within 4 or 13 weeks) and whether the patient should be initially reviewed in outpatients or proceed directly to endoscopy. A report by the Irish College of General Practitioners published in 2013, noted that 64% of GPs surveyed reported having direct access to endoscopy (57% within public system, 85% within private system).[22] While a DAE service, in the context of lower GI endoscopy, is offered by some institutions in Ireland at present, this is on an ad hoc basis and there is no formal national programme of direct-access endoscopy in place.

2.0 Clinical referral/treatment threshold

2.1 Review of the literature

A comprehensive review of the literature was conducted during April 2014 to identify international clinical guidelines and health policy documents describing treatment thresholds that are in place in other healthcare systems. It also considered systematic reviews and economic evaluations examining the effect of the introduction of those thresholds. The approach and general search terms are described in Appendix 1 in the 'Background and Methods' document, and a summary of the results is included in Table 2.1. A summary of the clinical guidelines identified from the search and thresholds in use elsewhere are provided in Appendices 1.3-1.6 and 1.7, respectively.

Table 2.1 Summary of literature search results

Publication Type	Number	References
Clinical Guidelines	16	23-38
Reviews	4	8, 39-41
Cost-Effectiveness Studies	3	42-44

2.2 Clinical evidence

Sixteen clinical guidelines and four systematic reviews or meta-analyses have been included for consideration in this section. The conclusions and recommendations are broadly consistent across these reports. The key document, around which many of these reports were based, and indeed around which much of the following discussion is based, is NICE's Clinical Guideline 27, entitled 'referral guidelines for suspected cancer', published in 2005.[23] This document was a follow on from the original two-week referral guideline published by the Department of Health in the UK in 2000 (Appendix 1.2).[24] Noting that while a period of 'treat, watch and wait' is reasonable in patients with equivocal symptoms who are not unduly anxious, the document then states that urgent referral is indicated for those:

- aged 40 years and older, reporting rectal bleeding with a change of bowel habit towards looser stools and/or increased stool frequency persisting for 6 weeks or more

- aged 60 years and older, with rectal bleeding persisting for 6 weeks or more without a change in bowel habit and without anal symptoms
- aged 60 years and older, with a change in bowel habit to looser stools and/or more frequent stools persisting for 6 weeks or more without rectal bleeding
- presenting with a right lower abdominal mass consistent with involvement of the large bowel, irrespective of age
- presenting with a palpable rectal mass (intraluminal and not pelvic), irrespective of age. (A pelvic mass outside the bowel would warrant an urgent referral to a urologist or gynaecologist)
- males of any age with unexplained iron deficiency anaemia and a haemoglobin of 11 g/100 ml or below
- non-menstruating women with unexplained iron deficiency anaemia and a haemoglobin of 10 g/100 ml or below.

In the context of this recommendation, 'unexplained' was taken to mean a patient whose anaemia is considered, on the basis of a history and examination in primary care, not to be related to other sources of blood loss (for example, ingestion of NSAIDs) or blood dyscrasia. It was also suggested that, for those with equivocal symptoms, a full blood count may help in identifying the possibility of colorectal cancer by demonstrating iron deficiency anaemia, which should then determine if a referral should be made and its urgency. For patients who are referred it was suggested that they should have an abdominal and digital rectal (DRE) examination, and a full blood count taken, prior to referral.[23]

The NICE guideline stated that there was insufficient evidence to support the inclusion of a positive family history of colorectal cancer as a criterion when considering whether to refer a patient. In 2011, NICE published its guidance document concerning the diagnosis and management of colorectal cancer; this did not address referral from primary care.[25] It is noted that an updated version of the 2005 guidance is to be published in 2015.

The 2005 NICE recommendations were adopted by the Association of Coloproctology of Great Britain and Ireland (ACPGBI) in its 2007 guidelines for the management of colorectal cancer.[26] This report went on to suggest that criteria indicating that patients are at low risk of colorectal cancer are:

- Rectal bleeding with anal symptoms or with an obvious external visible cause such as prolapsed piles, rectal prolapse and anal fissures

- Transient change in bowel habit for less than six weeks, particularly if this is in the form of decreased frequency of defaecation or harder stools
- Abdominal pain without iron deficiency anaemia or an easily palpable abdominal mass, and not associated with loss of appetite causing weight loss or other higher risk symptoms.

It concluded that where patients have persistent symptoms which would normally fit low-risk criteria, but there are other worrying factors such as a positive family history or a positive faecal occult blood (FOB) test, they should be seen on an urgent basis in a normal clinic.[26]

The NICE Guidelines were also adopted by the Northern Ireland Cancer Network (NICAN) in its 2012 referral guidance.[27]

A 2011 systematic review by Astin et al. noted that the 2005 guidance had been largely based upon studies which had focused on the referred population, and it was hence argued that this evidence does not pertain to the primary care population.[40] Focusing entirely on studies which had concentrated on the primary care setting, this meta-analysis reported a pooled positive predictive value (PPV) of rectal bleeding for colorectal cancer of 8.1% (95% confidence interval, 6%-11%) in those aged 50 or over; PPV estimates for abdominal pain and anaemia were 3.3% (95% CI, 0.7-16%) and 9.7% (95% CI, 3.5%-27%), respectively. Second symptoms accompanying rectal bleeding altered the strength of the association with cancer; weight loss or a change in bowel habit increased the risk further while abdominal pain decreased the risk. The authors concluded that their findings largely supported the NICE guidance.[40]

Similar work was published by Olde Bekkink et al. in 2010; the authors performed a systematic review of the diagnostic accuracy of rectal bleeding in combination with other signs, symptoms and tests.[45] Eight studies met inclusion criteria, and data on 2,323 patients were analysed; all studies had been undertaken in primary care settings. The authors concluded that no individual symptom, sign or diagnostic test in patients with rectal bleeding is likely to shift the probability of colorectal cancer to the extent of 'ruling in' or 'ruling out' the diagnosis with any degree of certainty. They went on to suggest that even 'red flag' symptoms, such as weight loss and blood mixed with stool, seem to have only modest diagnostic value; that said, they did note that the presence of these symptoms almost doubles the post-test possibility of colorectal cancer to 13%. This led the authors to conclude that these patients should certainly be referred for further investigation, but that caution is needed when counselling patients about potential diagnoses. The authors reported significant heterogeneity between studies and the use of a variety of different

reference standards (for example, colonoscopy versus sigmoidoscopy versus questionnaire), and thus the study findings need to be qualified against these limitations.[46]

Jellema et al. published their meta-analysis in 2010.[8] This examined the evidence regarding symptoms, diagnostic tests and guidelines regarding the diagnosis of colorectal malignancy. The authors included studies that had focused on primary care and, in addition, included those studies that had been performed at the interface of primary and secondary care (for example, two-week referral clinics and open access outpatient clinics); 47 cohort studies were eventually included for review, nine of which had been performed in the primary care setting. The authors reported that sensitivity was high (range 0.80-0.94, median 0.92) for the two-week referral guideline (see Appendix 1.2), but that specificity was low (median 0.42); it was hence suggested that this guideline is suitable to rule out colorectal cancer at the cost of a high number of patients needing further diagnostic testing. Specificity was consistently high for family history (range 0.75-0.98, median 0.91), weight loss (range 0.72-0.96, median 0.89), and iron deficiency anaemia (0.83-0.95, median 0.92), but all tests lacked sensitivity (medians 0.16, 0.20 and 0.13, respectively); here the authors concluded that these factors are suitable to rule in colorectal cancer, but at the cost of missing a considerable proportion of cases. The authors were unable to make firm recommendations regarding the use of diagnostic tests (for example, FOB) in primary care.[8]

One further meta-analysis that merits discussion is that by Adelstein et al., published in 2012.[39] Examining evidence up to 2008, this meta-analysis identified 40 papers that analysed the relationship between colorectal cancer and rectal bleeding; a relationship was noted, with a diagnostic odds ratio (DOR) of 2.6 reported. Based on data from 18 papers, weight loss was also associated with colorectal cancer, with a reported DOR of 2.9. No relationship was found between colorectal cancer and change in bowel habit, abdominal pain, diarrhoea or constipation. Of importance, the authors noted multiple issues with extrapolating from their findings, including the poor methodological approach taken in many of the studies, the lack of information regarding patient age, and the lack of consistency in how studies had collected their data.[39]

In 2013, a national commissioning guide for rectal bleeding in the UK was jointly published by the ACPGBI, and the Royal College of Surgeons (RCS), with NICE accrediting the process.[30] Recognising that rectal bleeding is a common symptom, and that in most cases it is due to a benign anal condition, the report also recognises that it can be a symptom of colorectal or anal cancer. The report notes that rectal bleeding has a PPV for colorectal malignancy of 8% in patients over 50 years

presenting to primary care. Primary care practitioners are advised to take particular note of the history of the condition, the presence or absence of perianal symptoms, the age of the patient, and the presence or absence of a family history of colorectal malignancy. A number of 'red flag' features are noted including the presence of an abdominal or rectal mass, weight loss, symptoms suggestive of anaemia, and an associated change in bowel habit, especially diarrhoea or increased frequency. Digital rectal examination (DRE) is advised prior to onward referral to secondary care. The document notes the following as two-week referral criteria, based on the NICE guidelines discussed above:

- aged ≥40 years with rectal bleeding and change in bowel habit towards looser and/or more frequent stools for 6 weeks or more
- aged ≥60 years with rectal bleeding persisting for 6 weeks or more without change in bowel habit and without anal symptoms
- rectal bleeding and a palpable rectal mass.

The guide goes on to suggest that investigation of rectal bleeding should be considered in patients who do not meet the NICE guidelines for suspected malignancy in the following circumstances:

- strong family history of colorectal malignancy
- anxiety about colorectal malignancy
- persistent rectal bleeding despite treatment for haemorrhoids
- rectal bleeding in patients with a past history of pelvic radiotherapy
- assessment of suspected inflammatory bowel disease.

Finally, the document notes that referral for screening colonoscopy or genetics assessment may be appropriate when rectal bleeding has triggered access to medical care, but the primary concern is a strong family history of colorectal cancer.[30]

In 2011 Cancer Care Ontario published its referral guidelines, based on expert evaluation of current literature.[31] This document categorises referral into urgent (two weeks), semi-urgent (four weeks) and other, based on referral time guidelines published by the Canadian Association of Gastroenterology in 2006.[28] The full algorithm is included in Appendix 1.3. Briefly, urgent referral was suggested for those with a palpable rectal mass or with an abnormal imaging result suspicious for colorectal cancer, with semi-urgent referral suggested for those with unexplained rectal bleeding and at least one of the following characteristics or combinations of symptoms:

- Dark rectal bleeding

- Rectal bleeding mixed with stool
- Rectal bleeding in the absence of perianal symptoms
- Rectal bleeding and change in bowel habits
- Rectal bleeding and weight loss
- Unexplained iron-deficiency anaemia (haemoglobin of ≤11 g/100 ml for males or ≤10 g/100 ml for non-menstruating females and iron below normal range).[31]

The Scottish Intercollegiate Guidelines Network (SIGN) published its updated guidelines regarding colorectal cancer in 2011 (Appendix 1.5).[29] This guideline states that assessment of risk can be made using the patient's age and the presence or absence of presenting symptoms and signs. Specifically, it notes that less than 1% of colorectal cancers occur in patients under the age of 40 with incidence increasing significantly thereafter, reaching a peak in the eighth decade. Although the 2005 NICE guidance recommended referral for those aged 60 or over with bleeding in isolation, the SIGN report suggests that patients over the age of 40 who present with new onset, persistent or recurrent rectal bleeding should be referred for investigation; NICE had recommended that, for patients aged between 40 and 60 years, only those with rectal bleeding ***and*** a change in bowel habit or increased stool frequency should be referred.[23] High risk features recognised by SIGN as warranting referral were adapted from the 2007 Scottish referral guidelines for suspected cancer[47], as follows:

- Persistent rectal bleeding without anal symptoms
- Persistent change in bowel habit (>6 weeks)
- Significant family history
- Right sided abdominal mass
- Palpable rectal mass
- Unexplained iron deficiency anaemia
- Patients with persistent diarrhoea
- Patients in whom there is clinical doubt.

In 2009, the New Zealand Guidelines Group (NZGG) published its management guidelines regarding suspected cancer in primary care.[33] This report adopted the aforementioned NICE guideline above.[23] In addition, they went on to state that patients at low risk of colorectal cancer with a significant symptom (rectal bleeding or a change in bowel habit) and a normal rectal examination, no anaemia and no abdominal mass, should be managed by a strategy of treat, watch and review in three months; as noted, NICE had discussed the option of a treat, watch and wait policy, but did not put a timeframe on when a review should take place. Unlike the NICE guidance, the New Zealand report included a statement on patients with a left-sided abdominal mass; they suggested that faecal loading should first be excluded as

the cause, and that a referral should then be made for a surgical opinion. Finally, this report also differed from the NICE guidance in that it made specific reference to those with known high risk factors (for example, familial adenomatous polyposis (FAP), hereditary non-polyposis colorectal cancer (HNPCC), other familial colorectal syndromes, or a past history of lower gastrointestinal cancer); it suggested if these patients have any unexplained gastrointestinal symptom they should be referred to a specialist.[33]

In 2012, New Zealand published its referral criteria for direct access outpatient colonoscopy.[32] These criteria categorised patients into those who require a colonoscopy within two weeks, those requiring intervention within six weeks, and finally those for whom a colonoscopy is not indicated (Appendix 1.4). It suggests that in referring a patient for colonoscopy the referrer should:

- inform the patient about the procedure
- ensure they are willing to undergo the procedure
- consider the ability of the patient to tolerate both the bowel preparation and the procedure
- consider the presence of multiple comorbidities or advanced malignancy (generally referral implies they are well enough to tolerate further treatment)
- if the patient has had a colonoscopy in the preceding five years, ensure there is a clear indication to repeat the procedure (the 'miss' rate of lesions > 1cm following a well performed colonoscopy is approximately 6 %).

In 2005, the Australian Health and Medical Research Council in conjunction with the Australian Cancer Network published its clinical practice guidelines for colorectal cancer.[37] This document identified three sets of signs and symptoms which raise the possibility of colorectal cancer, namely (1) rectal bleeding, (2) bowel or abdominal symptoms, and (3) iron deficiency anaemia. Specific recommendations regarding referral were not discussed. Similarly, the American Society of Colon and Rectal Surgeons published its guidelines for the management of colon cancer in 2012 – again, referral recommendations were not included.[38]

In 2012, the American Society for Gastrointestinal Surgery (ASGE) published its guidelines on the appropriate use of GI endoscopy.[34] These were not specific to colorectal cancer however, and instead were a set of principles which the ASGE felt should guide decision-making when considering the need for colonoscopy in general terms (Appendix 1.5). Finally, the European Panel on the Appropriateness of Gastrointestinal Endoscopy (EPAGE) published its updated guidelines in relation to

bleeding per rectum and diarrhoea in 2009[35, 36]; its recommendations are depicted in Appendix 1.6.

The use of referral thresholds by Primary Care Trusts (PCTs) in the English NHS has been common practice for several years. As part of the changes to the NHS brought about by the Health and Social Care Act 2012, PCTs and Strategic Health Authorities (SHAs) ceased to exist on 31 March 2013. Their responsibilities were taken over by Clinical Commissioning Groups (CCGs) and the NHS Trust Development Authority. A number of national commissioning guidelines have been published including the one on rectal bleeding discussed above.[30] However, the thresholds that were previously developed by these trusts are likely to represent ongoing practice at a local level while new commissioning guides are being established. A summary of specific thresholds from a sample of two NHS PCT and CCG areas is provided in Appendix 1.7.

To summarise, much of the published evidence and international guidance has been shaped around the 2005 NICE referral criteria for suspected cancer. Although this guidance was equivocal on the relevance of family history when considering the need to refer, succeeding guidance has suggested that a positive family history should be incorporated into the decision making process and should influence the clinician towards making a referral. There is general agreement across guidelines regarding which symptoms warrant referral.

2.3 Cost-effectiveness evidence

In 2012, Tilson et al. published an analysis of the cost of care for colorectal cancer in Ireland.[44] Taking a healthcare payer perspective, the study was performed as part of the HTA which evaluated the potential effectiveness and cost-effectiveness of a population based colorectal cancer screening programme in Ireland; this HTA was published by HIQA in 2009.[48] Tilson et al. estimated cost data by modelling separate treatment pathways for each stage of colon and rectal cancer, based on national data and international guidelines. Costs as calculated by Tilson et al. are reproduced in Table 2.2. All costs were adjusted to the year 2008 using the Consumer Price Index for health (Central Statistics Office [www.cso.ie]), and any costs derived from other jurisdictions (e.g. UK) were converted to Euro using the average annual exchange rate published by the European Central Bank. Costs of follow up in years two to five post surgery were discounted at an annual rate of four percent (the standard discount rate recommended for Ireland). For the purposes of this report, all costs have been updated to 2012 prices using the Consumer Price Index. The overall stage-weighted costs for diagnosis, treatment and follow-up of colorectal cancer were €1,611, €35,415 and €2,026, respectively. Costs were estimated for

colonoscopy (€640), CT colonography (€542), rigid sigmoidoscopy (€890), MRI pelvis (€460), and transrectal ultrasound (€158). A biopsy, with histopathological analysis was costed at €129 and an outpatient visit was calculated to cost €167. Total costs were most sensitive to the cost of chemotherapy and biological agents, the duration of treatment with biological agents and recurrence rates for stage 2 and 3 cancers.[44]

Table 2.2 Cost of care for colorectal cancer in Ireland. Tilson et al.[44]*

	Stage 1	Stage 2	Stage 3	Stage 4	Overall Stage-Weighted Cost
Colorectal Cancer	€23,356	€36,659	€48,151	€36,090	€39,049
(95% Confidence Interval)	(€20,607-€28,190)	(€29,861-€47,360)	(€39,980-€61,706)	(€32,315-€42,361)	(€33,369-€48,294)

*Costs as reported by Tilson et al. have been updated to 2012 prices.

In 2011, Beggs et al. published the results of their cost analysis of a 'straight to colonoscopy' (direct access) service in the UK.[49] Patients were referred based on the aforementioned 2005 NICE criteria.[23] A total of 317 patients were seen over a one year period; the authors reported that 44 (13.9%) did not meet any of the criteria for urgent colonoscopy when assessed by the colonoscopist; the paper notes, however, that these patients did warrant referral and investigation. Prices were based on the 2004-2005 NHS tariff; a new outpatient consultation in a colorectal surgery clinic was costed at £144 Pounds Sterling (GBP£); the tariff per colonoscopy was GBP£438. The authors reported that the cost for the 317 patients through the 'straight to colonoscopy' service was GBP£159,958; using decision-tree analysis, the authors then hypothesised that the total cost of using an 'out-patient appointment first' system would have been GBP£186,134. The 'straight to colonoscopy' service was thus estimated to have saved GBP£82.57 per patient. It should be noted that patient characteristics (for example, age and disease severity) were not reported.

In 2008, Hassan et al. published their analysis of the cost-effectiveness of colonoscopy based on the appropriateness of the indication.[43] Appropriateness was taken to mean conforming with the aforementioned ASGE and the original EPAGE guidelines for colonoscopy.[34, 50] Using a decision-analysis model, the authors assessed the clinical and economic consequences of referring or not referring a patient with an appropriate or inappropriate indication to colonoscopy, in relation to the eventual detection of colorectal cancer. This was performed using a hypothetical population of 100,000 US adults aged 60 years, and taking 2007 Medicare cost data; no discounting was employed as the authors noted that all investigation and

treatment costs would occur in the one year. Based on pooled data from 12 studies, the authors estimated that 1,075 colorectal cancers would be detected when referring all 100,000 inappropriate hypothetical cases to colonoscopy, resulting in 376 (0.4%) cancer-related deaths and the related loss of 7,527 years of life. The number of colonoscopies to be performed to detect one case of cancer was 93. In the hypothetical population of 100,000 sixty year old subjects with an appropriate indication for colonoscopy, meanwhile, it was calculated that 5,569 cancers would be detected when performing the requested colonoscopy, corresponding to 18 colonoscopies needing to be performed to detect one case of cancer. The incremental cost-effectiveness of performing colonoscopy for an inappropriate and appropriate indication, compared to no endoscopy, was $31,807 and $6,154 United States dollars (USD$), respectively. The authors concluded, given the relatively high prevalence of colorectal cancer in patients for whom colonoscopy generally is not indicated according to established guidelines, as well as the marked decrease in survival associated with the diagnostic delay, that even colonoscopy for an inappropriate indication could be considered cost-effective (using a threshold of $150,000 per life year gained) and argued therefore that the guidelines should not be employed as exclusive criteria in selecting patients for colonoscopy.

To summarise, there is limited data regarding the cost-effectiveness of different referral practices in the symptomatic population suspected of harbouring colorectal malignancy. It is clear that the costs associated with delayed diagnosis are significant and hence the final threshold must seek to avoid missing those who have a malignancy while also attempting to streamline referral such that those who require urgent investigation can be attended to in a timely manner.

2.4 Budget impact and resource implications

The number of elective lower GI endoscopies provided through the publicly-funded healthcare system has increased by approximately 67% since 2005. The current estimated annual national cost of elective lower GI endoscopies is €50 million, with an average weighted cost per inpatient case of €6,310, and an average weighted cost per day case patient of €569, based on the latest Casemix costs (Appendix 1.8). This markedly higher cost for inpatients reflects the previously noted reality that many of these patients are in hospital for reasons other than their elective endoscopy, and many will have a protracted length of stay. The estimated annual national cost of elective lower GI endoscopies performed solely in the day case setting is €36.2 million.

2.5 Advice on clinical referral / treatment threshold

Taking account of the available evidence that exists in relation to lower gastrointestinal symptoms and the associated risk of malignancy, the following threshold criteria are advised for referral and treatment within the publicly-funded healthcare system in Ireland:

An abdominal and digital rectal examination should be offered to all patients with symptoms suggestive of colorectal cancer. A positive finding should expedite referral, but a negative rectal examination should not rule out the need to refer. Prior to referral to secondary care, all symptomatic patients should have at least a full blood count. Imaging, however, is not required

Patients with one or more of the following signs or symptoms should be referred for **urgent review and or investigation (including sigmoidoscopy, colonoscopy, or CT colonography as appropriate) within four weeks** in secondary care:

- palpable abdominal or rectal mass
- unexplained rectal bleeding (benign anal causes excluded or treated)
- unexplained iron deficiency anaemia
- altered bowel habit for (more than)(≥) six weeks,
    - with rectal bleeding – all ages should be referred
    - without rectal bleeding – those aged (greater than) (≥)50 years should be referred
- abnormal abdominal imaging (result suspicious for colorectal cancer)
- unexplained weight loss

Patients who do not fit the referral criteria above, but;

- who have persistent symptoms which do not respond to treatment, OR
- whose symptoms recur after stopping treatment, OR
- where based on clinical judgement, there remains a high level of suspicion of colorectal cancer

should be referred for review and or investigation in secondary care within four weeks.

Patients aged less than 50 years of age who present with altered bowel habit for more than (≥) six weeks, without rectal bleeding, should be referred for review and or investigation in secondary care within thirteen weeks.

Patients with new onset of symptoms who do not fit the referral criteria above, but who have known high risk factors (for example, FAP, HNPCC, other familial colorectal syndromes, or a past history of lower gastrointestinal cancer) should be referred for review and or investigation in secondary care within four weeks.

Patients who do not meet the above criteria should remain under the care of the general practitioner who will manage conservative treatment of the patient.

3 Discussion

Draft referral thresholds have been developed based on a comprehensive review of the literature and international referral guidelines. While referral thresholds may currently be used on an informal, improvised, and or unplanned basis within the Irish system, this has not been done consistently. The need for standardisation in referral practices is driven by an increasing pressure on the public healthcare system, and by the need to ensure consistency of clinical practice. In particular, while the Health Service Executive has stated that no patient should wait more than four weeks for an urgent colonoscopy from time of referral, the definition of urgent in this setting has not previously been defined.

As noted, the number of elective colonoscopies and sigmoidoscopies performed annually in Ireland increased by greater than 67% between 2005 and 2012. Over approximately the same time frame (2005-2011), the number of colorectal cancers diagnosed annually increased by 13%. The threshold set out in this report aims to ensure that all patients with symptoms suggestive of underlying malignancy are seen urgently, while simultaneously aiming to avoid unnecessary referral of patients who can be managed in the primary care setting. It is intended that this threshold will provide clarity to general practitioners (GPs) in making decisions regarding referral, while providing room for clinical judgement to supersede in individual cases.

In addition, it is noted that while development of this threshold should aid in defining who should be referred for urgent review, the mechanisms around its practical implementation remain to be fully clarified. It is clear that the National Healthlink Project, which permits the secure transmission of clinical patient information between GPs and hospitals, has facilitated improved communication of referrals between primary and secondary care. It is thus suggested that one mechanism through which this referral threshold might be implemented would be through its integration in the form of a standardised referral form into this Project.

It is evident that triage of referrals made to symptomatic colorectal services remains a significant component of a consultant's clinical workload in secondary care. It is suggested that this service may be better utilised by resourcing specialist nurses, under the supervision of a lead clinician, to perform this triage function. This system has been implemented successfully for rapid access oncology clinics in other specialties (for example, rapid access lung clinics), and has the potential to free up clinician time for other clinical activities. An alternative, but similar approach, which might be adopted is that taken by BowelScreen, in which each individual scheduled

for colonoscopy is contacted by phone by a BowelScreen nurse who coordinates the written consent process as part of the colonoscopy pre-assessment process.[10]

As noted, HIPE data does not allow separation of colonoscopy from flexible sigmoidoscopy for analytic purposes. While beyond the scope of this current work, it would be interesting to assess the extent to which the relative proportion of these procedures differs by hospital group, and to compare the average age at which patients undergo these procedures by hospital group. Any variation identified could present one potential avenue for better utilisation of existing resources, given that flexible sigmoidoscopy is a quicker, less resource-intensive procedure.

In conclusion, the thresholds above are unlikely to represent a major change from current practice, but rather a standardisation of referral and treatment criteria across all areas of the publicly-funded healthcare system. As with all thresholds, it is imperative that there are opportunities for appeal mechanisms to ensure good governance.

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5 Appendices

Appendix 1.1 – HIPE ICD-10AM/ACHI list of intervention codes for colonoscopy procedures

Intervention code	Description
3207500	Rigid Sigmoidoscopy
3208400	Fibreoptic colonoscopy to hepatic flexure
3208402	Colonoscopy to hepatic flexure with tattooing
3209000	Fibreoptic colonoscopy to caecum
3209002	Colonoscopy to caecum with tattooing
3207501	Rigid sigmoidoscopy with biopsy
3207800	Rigid sigmodioscopy; polypectomy ≤9 polyps
3208100	Rigid sigmoidoscopy; polypectomy ≥10 polyps
3208401	Fibreoptic colonoscopy to hepatic flexure; biopsy
3208700	Fibreoptic colonoscopy to hepatic flexure; polypectomy
3209001	Fibreoptic colonoscopy to caecum with biopsy
3209300	Fibreoptic colonoscopy to caecum with polypectomy

Appendix 1.2 The Department of Health (UK) higher risk criteria ('Two week referral guideline')[24]

Criteria (when at least one criterion is positive the patient should be referred):

- Rectal bleeding with a change in bowel habit to looser stools and/or increased frequency of defecation persistent for 6 weeks. Age threshold: all ages.
- Change in bowel habit as above without rectal bleeding and persistent for 6 weeks. Age threshold: over 60 years.
- Rectal bleeding persistently without anal symptoms (includes soreness, discomfort, itching, lumps and prolapse as well as pain). Age threshold: over 60 years.
- A definite palpable right-sided abdominal mass. Age threshold: all ages.
- A definite palpable rectal mass (not pelvic). Age threshold: all ages.
- Unexplained iron deficiency anaemia. In men: below 11g/dl, all ages. In women: below 10 g/dl, post menopausal.

Appendix 1.3 Canadian Association of Gastroenterology, Referral Guidelines, 2006[31]

Referral and wait time recommendations for the following indications are based on evidence of the relative predictability for colorectal cancer of single or combined signs, symptoms, or diagnostic investigations and by weighing this with the predictability for colorectal cancer of a positive faecal occult blood test (FOBT) in the Ontario CRC Screening Program. The referral wait times also align with the recommendations developed by the Canadian Association of Gastroenterology. In many jurisdictions, organized Diagnostic Assessment Programs (DAPs) with centralized referral access may facilitate timely tests and specialist appointments.

1. URGENT REFERRAL

Referring physicians should send a referral to a colorectal cancer DAP or a specialist competent in endoscopy within 24 hours, expect a consultation within 2 weeks, and expect a definitive diagnostic workup to be completed within 4 weeks of referral, if a patient has at least one of the following:

- Palpable rectal mass suspicious for CRC
- Abnormal abdominal imaging result suspicious for CRC

2. SEMI-URGENT REFERRAL

Referring physicians should send a referral to a colorectal cancer DAP or a specialist competent in endoscopy within 24 hours, expect a consultation within 4 weeks, and expect a definitive diagnostic work up to be completed within 8 weeks of referral, if a patient has at least one of the following:

- Unexplained rectal bleeding in patients with at least one of the following characteristics or combinations of symptoms:
- Dark rectal bleeding
- Rectal bleeding mixed with stool
- Rectal bleeding in the absence of perianal symptoms
- Rectal bleeding and change in bowel habits
- Rectal bleeding and weight loss

Unexplained iron-deficiency anemia (hemoglobin of ≤110 g/L for males or ≤100 g/L for non-menstruating females and iron below normal range)

Referring physicians should include information that may increase the likelihood

of colorectal cancer in the consultation request:

- Patients aged 60 years and older
- Male patients
- The presence of two or more signs or symptoms
- Patients with a personal history of colorectal polyps or IBD or a first-degree family history of CRC

3. If the unexplained signs or symptoms of patients do not meet the criteria for referral but, based on clinical judgement, there remains a:

high level of suspicion of colorectal cancer, then:

- then refer to a CRC DAP or a specialist competent in endoscopy

low level of suspicion of colorectal cancer, then:

- treat the sign and/or symptom if applicable. Review and ensure resolution of symptoms within four to six weeks. If signs and/or symptoms have not resolved in four to six weeks, then confer with or refer to a colorectal cancer DAP or specialist competent in endoscopy.

- a Fecal Occult Blood Test (three stool sample FOBT non-ColonCancerCheck) may be ordered in the absence of recent CRC screening and in the absence of current active rectal bleeding. If the result is positive, refer semiurgently. A negative result does not rule out CRC.

In situations where wait times for specialists to perform colonoscopy are considered excessive, referring physicians may order (depending on locally available resources):

- Computed tomographic (CT) colonography
- Double-contrast barium enema (DCBE)

This is best done in coordination with the colorectal cancer DAP or specialist, if possible. Normal or negative results should not lead to a cancellation of the consult with the colorectal cancer DAP or specialist. Positive results may facilitate more timely investigation of a patient.

Appendix 1.4 New Zealand Criteria for direct access outpatient colonoscopy[32]

Two week category

- Known or suspected CRC (on imaging, or palpable, or visible on rectal examination), for preoperative procedure to rule out synchronous pathology
- Unexplained rectal bleeding (benign anal causes treated or excluded) with iron deficiency anaemia (haemoglobin below the local reference range)*
- Altered bowel habit (looser and/or more frequent) > six weeks duration plus unexplained rectal bleeding (benign anal causes treated or excluded) aged ≥ 50 years

Six week category

- Altered bowel habit (looser and/or more frequent) > six weeks duration, aged ≥ 50 years
- Altered bowel habit (looser and/or more frequent) > six weeks duration plus unexplained rectal bleeding (benign anal causes treated or excluded), aged 40-50 years
- Unexplained rectal bleeding (benign anal causes treated or excluded) aged ≥ 50 years
- Unexplained iron deficiency anaemia (haemoglobin below local reference range)*
- Family History plus one or more of altered bowel habit (looser and/or more frequent) > six weeks duration plus unexplained rectal bleeding (benign and anal causes treated or excluded), aged ≥ 40 years
- Family History plus one or more of altered bowel habit (looser and/or more frequent) > six weeks duration plus unexplained rectal bleeding (benign and anal causes treated or excluded), aged ≥ 25 years
- Suspected/assessment inflammatory bowel disease (consider FSA)
- Imaging reveals polyp > 5mm

Not accepted

- Acute diarrhoea < six weeks duration - likely infectious aetiology and self-limited
- Rectal bleeding aged less than 50 years (normal haemoglobin[JM1]

[E2]) - consider FSA or flexible sigmoidoscopy if no anal cause

- Irritable bowel syndrome (may require specialist assessment)
- Constipation as a single symptom
- Uncomplicated computed tomography (CT) proven diverticulitis without suspicious radiological features
- Abdominal pain alone without any 'six week category' features
- Decreased ferritin aged < 50 years with normal haemoglobin
- Abdominal mass - refer for appropriate imaging
- Metastatic adenocarcinoma unknown primary - six percent is due to CRC and in the absence of clinical, radiological, or tumour marker evidence of CRC, colonoscopy is not indicated.

* The indication of iron deficiency anaemia requires a haemoglobin level below the local reference range in association with a low ferritin level. Menstruation is the commonest cause of iron deficiency anaemia in women - or women aged less than 55 years a menstrual history should be obtained prior to referral. Coeliac disease and urinary loss should also be excluded.

Appendix 1.5 Referral Guidelines

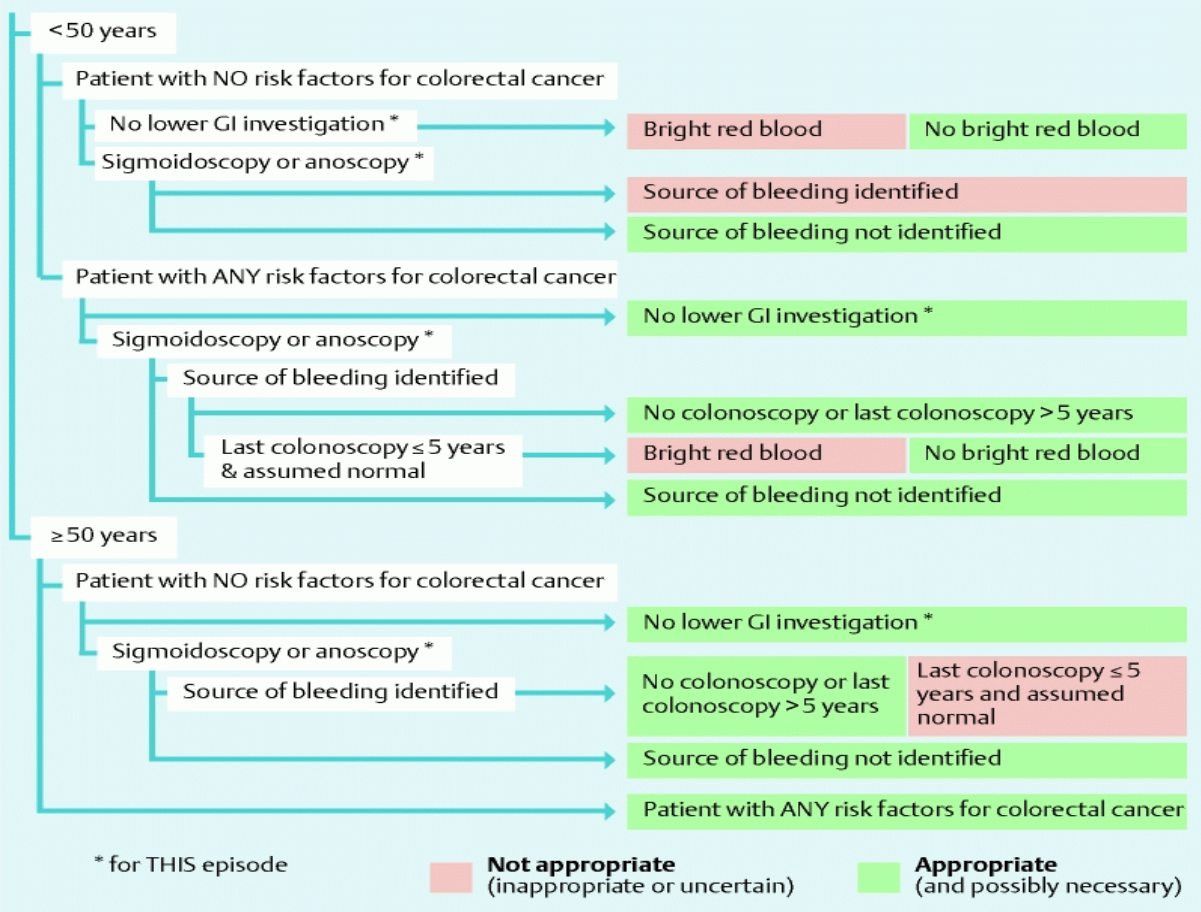
SIGN[29]	**SIGN Referral Thresholds for patients suspected of having colorectal cancer** ▪ Patients over the age of 40 who present with new onset, persistent or recurrent rectal bleeding should be referred for investigation. ▪ Patients under the age of 40 with low-risk features and transient symptoms a watch and wait policy is recommended. ▪ Review of the patient by a regional clinical genetics service is recommended for accurate risk assessment if family history of colorectal cancer is the principal indication for referral for investigation ▪ General practitioners should perform an abdominal and rectal examination on all patients with symptoms indicative of colorectal cancer. A positive finding should expedite referral, but a negative rectal examination should not rule out the need to refer. ▪ All symptomatic patients should have a full blood count. In cases of anaemia the presence of iron deficiency should be determined. All patients with unexplained iron deficiency anaemia should be referred for endoscopic investigation of upper and lower gastrointestinal tracts.
ASGE[34]	**Colonoscopy is generally indicated in the following circumstances:** Evaluation of an abnormality on barium enema or other imaging study that is likely to be clinically significant, such as a filling defect and stricture. Evaluation of unexplained GI bleeding: ▪ Hematochezia. ▪ Melena after an upper GI source has been excluded. ▪ Presence of fecal occult blood. Unexplained iron deficiency anaemia.

	Screening and surveillance for colonic neoplasia: ▪ Screening of asymptomatic, average-risk patients for colonic neoplasia. ▪ Examination to evaluate the entire colon for synchronous cancer or neoplastic polyps in a patient with treatable cancer or neoplastic polyp. ▪ Colonoscopy to remove synchronous neoplastic lesions at or around the time of curative resection of cancer followed by colonoscopy at 1 year and, if normal, then 3 years, and, if normal, then 5 years thereafter to detect metachronous cancer. ▪ Surveillance of patients with neoplastic polyps. ▪ Surveillance of patients with a significant family history of colorectal neoplasia. For dysplasia and cancer surveillance in select patients with long-standing ulcerative or Crohn's colitis. ▪ For evaluation of patients with chronic inflammatory bowel disease of the colon, if more precise diagnosis or determination of the extent of activity of disease will influence management. Clinically significant diarrhoea of unexplained origin. Intraoperative identification of a lesion not apparent at surgery (eg, polypectomy site, location of a bleeding site). Treatment of bleeding from such lesions as vascular malformation, ulceration, neoplasia, and polypectomy site. Intraoperative evaluation of anastomotic reconstructions typical of surgery to treat diseases of the colon and rectum (eg, evaluation for anastomotic leak and patency, bleeding, pouch formation). As an adjunct to minimally invasive surgery for the treatment of diseases of the colon and rectum. Management or evaluation of operative complications (eg, dilation of anastomotic strictures). Foreign body removal.

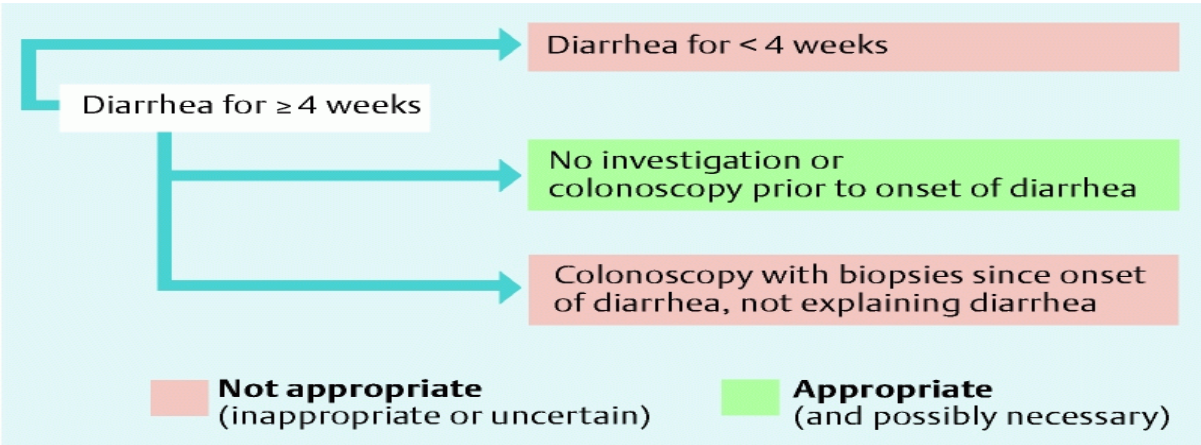
	Excision or ablation of lesions. Decompression of acute megacolon or sigmoid volvulus. Balloon dilation of stenotic lesions (eg, anastomotic strictures). Palliative treatment of stenosing or bleeding neoplasms (eg, laser, electrocoagulation, stenting). Marking a neoplasm for localization. **Colonoscopy is generally not indicated in the following circumstances:** Chronic, stable, irritable bowel syndrome or chronic abdominal pain; there are unusual exceptions in which colonoscopy may be done once to rule out disease, especially if symptoms are unresponsive to therapy. Acute diarrhoea. Metastatic adenocarcinoma of unknown primary site in the absence of colonic signs or symptoms when it will not influence management. Routine follow-up of inflammatory bowel disease (except for cancer surveillance in chronic ulcerative colitis and Crohn's colitis). GI bleeding or melaena with a demonstrated upper GI source. **Colonoscopy is generally contraindicated in:** Fulminant colitis. Documented acute diverticulitis.

Appendix 1.6 – EPAGE Guidelines

Appropriateness of colonoscopy in Europe (EPAGE II) – Iron-deficiency anemia and hematochezia[35]



Appropriateness of colonoscopy in Europe (EPAGE II) – Chronic Diarrhoea[36]



Appendix 1.7 Primary Care Trust/Clinical Commissioning Group Referral Thresholds, UK

Vale of York Clinical Commissioning Group (CCG) – Change in bowel habit and/or rectal bleeding[51]

Exclude Red Flag Symptoms

Try to establish the most likely diagnosis and refer accordingly as either 2 week wait, urgent or routine referral

2 week wait criteria:

- Definite palpable right-sided abdominal mass (to exclude caecal tumour)
- Definite rectal mass on PR exam
- Unexplained iron deficiency anaemia with:
    - Hb<11g/dl in men
    - Hb<10g/dl in non-menstruating women
- 40-60 yrs old with persistent (>6 weeks) rectal bleeding and a change to looser/more frequent stools
- 60 yrs or over with persistent (>6 weeks) rectal bleeding (in the absence of anal symptoms) and/or change to looser/more frequent stools

Urgent referral:

- Rectal bleeding in the absence of anal symptoms/haemorrhoids
- Blood mixed with stool and or clots
- Rectal bleeding and associated change to looser stool (any age)
- Unexplained weight loss
- Strong family history of colorectal cancer. (1st degree relative with colorectal cancer <50 yrs old or two 1st degree relatives with colorectal cancer at any age)
- Iron deficiency anaemia (see separate guideline)

Routine referral:

Patients with persistent low-risk symptoms which do not respond to treatment, or which recur after stopping treatment, should be referred.

Investigations prior to referral:

Dependent of the most likely diagnosis in the differential, but will usually include FBC, U&E, CRP, celiac screen

Management

Management will depend on the most likely diagnosis of those in the differential.

NHS B&NES & Wiltshire Two Week Wait Referral Process[52]

All referral forms will be triaged by a clinician to decide the most appropriate diagnostic procedure.

Patients may have lower gastro-intestinal endoscopy at their first appointment and must therefore be suitable for a day case procedure.

Would the patient be able to manage oral bowel preparation at home [ ] Yes [ ] No

Is the patient suitable for a day case procedure [ ] Yes [ ] No

If your patient is NOT suitable, please indicate this as part of the accompanying information

- 40 years and older with rectal bleeding and change in bowel habit which is defined as change to loose stools &/or increased frequency of defecation persisting for 6 weeks or more.
- 60 years and older with rectal bleeding persisting 6 weeks or more without change in bowel habit, as defined above, or anal symptoms.
- 60 years and older with change in bowel habit, as defined above, for 6 weeks or more.
- Palpable rectal mass
- Lower abdominal mass consistent with involvement of the large bowel.
- Men with unexplained iron deficiency anaemia and haemoglobin of 11g/100ml or below.
- Non-menstruating women with unexplained iron deficiency anaemia and haemoglobin of 10g/100ml or below.

  Duration of symptoms _____
  Abdominal pain present? [ ] Yes [ ] No
  HB_____ Ferritin_____
  MCV_____ CREA_____

If your patient does not meet any of these criteria, or if the patient has severe symptoms, please contact the colorectal team to discuss the referral.

Appendix 1.8
HSE inpatient and day case acute hospital activity and costs for elective lower GI endoscopies procedures summarised by diagnosis-related group (based on 2011 costs and 2012 activity)[53]

DRG code	Description	No.	% of Total	Cost / inpatient (€)	Cost / Day Case(€)
G48C	Colonoscopy; Sameday	40610	61.65	654	550
G46C	Complex Gastroscopy; Sameday	11057	16.79	942	619
Z40Z	Endoscopy W Diagnoses of Other Contacts W Health Services; Sameday	6615	10.04	423	466
G11Z	Anal and Stomal Procedures	2135	3.24	3461	1130
Q61B	Red Blood Cell Disorders W/O Catastrophic or Severe CC	1731	2.63	2563	416
G48B	Colonoscopy W/O Catastrophic or Severe CC	768	1.17	3681	550
K40C	Endoscopic or Investigative Procedure for Metabolic Disorders; Sameday	545	0.83	516	520
G46B	Complex Gastroscopy W/O Catastrophic CC	471	0.72	5111	619
Z64B	Other Factors Influencing Health Status; Sameday	340	0.52	333	304
J67B	Minor Skin Disorders; Sameday	133	0.2	242	351
R62B	Other Neoplastic Disorders W/O CC	114	0.17	4598	969
G70B	Other Digestive System Diagnoses W/O Catastrophic or Severe CC	106	0.16	1663	442
Z64A	Other Factors Influencing	89	0.14	5119	304

	Health Status				
G02B	Major Small and Large Bowel Procedures W/O Catastrophic CC	88	0.13	13084	1324
G48A	Colonoscopy W Catastrophic or Severe CC	87	0.13	8783	550
N62Z	Menstrual and Other Female Reproductive System Disorders	48	0.07	1058	395
Q61A	Red Blood Cell Disorders W Catastrophic or Severe CC	40	0.06	5474	416
H63B	Disorders of Liver Excep Malig; Cirrhosis; Alcoholic Hepatitis W/O Cat/Sev CC	36	0.05	2542	531
K40B	Endoscopic or Investigative Proc for Metabolic Disorders W/O Catastrophic CC	30	0.05	7132	520
G60B	Digestive Malignancy W/O Catastrophic CC	28	0.04	4262	722
G12C	Other Digestive System OR Procedures W/O CC	25	0.04	4791	1668
G02A	Major Small and Large Bowel Procedures W Catastrophic CC	25	0.04	27413	1324
R61C	Lymphoma and Non-Acute Leukaemia; Sameday	20	0.03	712	846
G61B	GI Haemorrhage W/O Catastrophic or Severe CC	20	0.03	2372	544
L41Z	Cystourethroscopy; Sameday	20	0.03	897	425
H61B	Malignancy of Hepatobiliary System; Pancreas W/O Catastrophic CC	15	0.02	4813	824
G01B	Rectal Resection W/O Catastrophic CC	14	0.02	15013	3844

801C	OR Procedures Unrelated to Principal Diagnosis W/O CC	14	0.02	7379	1759
J11Z	Other Skin; Subcutaneous Tissue and Breast Procedures	14	0.02	4211	689
F74Z	Chest Pain	14	0.02	1028	570
M60B	Malignancy; Male Reproductive System W/O Catastrophic or Severe CC	13	0.02	4703	683
G12B	Other Digestive System OR Procedures W Severe or Moderate CC	12	0.02	8536	1668
D67B	Oral and Dental Disorders Except Extractions and Restorations; Sameday	12	0.02	498	539
M64Z	Other Male Reproductive System Diagnoses	11	0.02	1251	563
M40Z	Cystourethroscopy; Sameday	11	0.02	696	496
J68C	Major Skin Disorders; Sameday	11	0.02	318	288
G01A	Rectal Resection W Catastrophic CC	10	0.02	31668	3844
A06B	Trach W Vent >95 hours W/O Cat CC or Trach/Vent >95 hours W Cat CC	10	0.02	55270	
Z01B	OR Procedures W Diagnoses of Other Contacts W Health Services W/O Cat/Sev CC	10	0.02	4322	1501
Q60C	Reticuloendothelial and Immunity Disorders W/O Cat or Sev CC W/O Malignancy	10	0.02	4177	1036
L67B	Other Kidney and Urinary Tract Diagnoses W/O Catastrophic or Severe CC	10	0.02	3116	511

H64B	Disorders of the Biliary Tract W/O CC	10	0.02	1629	382
L65B	Kidney and Urinary Tract Signs and Symptoms W/O Catastrophic or Severe CC	10	0.02	2020	300
G10B	Hernia Procedures W/O CC	9	0.01	3727	1613
G05C	Minor Small and Large Bowel Procedures W/O CC	9	0.01	8049	1535
F65B	Peripheral Vascular Disorders W/O Catastrophic or Severe CC	9	0.01	2470	570
H60B	Cirrhosis and Alcoholic Hepatitis W Severe or Moderate CC	8	0.01	5450	729
M61Z	Benign Prostatic Hypertrophy	8	0.01	3724	397
Q02B	Other OR Procedure of Blood and Blood Forming Organs W/O Cat or Sev CC	7	0.01	4802	1071
B82C	Chronic and Unspecified Paraplegia/Quadriplegia W or W/O OR Pr W/O Cat/Sev CC	7	0.01	10275	1529
N60B	Malignancy; Female Reproductive System W/O Catastrophic CC	7	0.01	4729	1238
E42B	Bronchoscopy W/O Catastrophic CC	7	0.01	6343	735
G46A	Complex Gastroscopy W Catastrophic CC	7	0.01	14475	619
T64C	Other Infectious and Parasitic Diseases W/O CC	7	0.01	2337	434
H62B	Disorders of Pancreas Except for Malignancy W/O Catastrophic or Severe CC	7	0.01	2570	390

H08B	Laparoscopic Cholecystectomy W/O Closed CDE W/O Cat or Sev CC	6	0.01	4922	2691
G10A	Hernia Procedures W CC	6	0.01	6806	1613
G05B	Minor Small and Large Bowel Procedures W Severe or Moderate CC	6	0.01	9592	1535
Q62Z	Coagulation Disorders	6	0.01	6520	882
R61B	Lymphoma and Non-Acute Leukaemia W/O Catastrophic CC	6	0.01	6906	846
E71B	Respiratory Neoplasms W/O Catastrophic CC	6	0.01	5104	696
Z63B	Other Surgical Follow Up and Medical Care W/O Catastrophic CC	6	0.01	3391	440

*Key: DRG- Diagnostic-related group; W-with; W/O-without; CC-complication or comorbidity. Data summary from HSE National Casemix Programme Ready Reckoner, 2013 based on the 2011 inpatient and day case costs reported by 38 hospitals participating in the programme that year. Activity is based on the latest 2012 HIPE data. *Note the remaining diagnosis-related groups accounted for five or fewer of the procedures each.*

Published by the Health Information and Quality Authority.

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