Introduction

The increasing demand for colonoscopy, and its associated costs, has led to attempts worldwide to develop prioritisation criteria and predictive systems to determine those who are most likely to benefit from colonoscopy investigation. No ideal system exists because of the issues of sensitivity and specificity, complexity and lack of generalisable features. Although there have been National Health and Medical Research Council (NHMRC) recommendations for colonoscopy indications in Australia, these are now due for review. As a result of these needs, institutions and states have developed their own guidelines, which in turn leads to variability. As a consequence, neither benchmarking nor performance indicators can be attached to colonoscopy service delivery at any level (institutional, state or nationwide).

The Victorian Department of Health and Human Services recently commissioned a group from all fields to develop transparent, reproducible categorisation guidelines for colonoscopy based on a comprehensive review of the literature and expert opinion. The basic premises built on are: age is the most important predictor for advanced neoplasia; although there are some consistently predictive symptoms/factors, most single symptoms are poorly predictive; and relevant tests improve reliability.
General principles

1. Critical factors
The following four features: iFOBT (+), anaemia, rectal bleeding and age 60 years or older, have an independent positive predictive value (PPV) for underlying colorectal cancer (CRC). In these guidelines the features are termed ‘critical factors’. The presence of a critical factor in addition to another symptom automatically increases the priority of colonoscopy to a Category 1.

2. Use of the age of 60 years
Increasing age, alone, is a risk for CRC, hence screening programs. A range of age cut-offs for greater risk have been given in the literature; however, no critical ‘tipping point’ is identified, although age greater than 55 or 60 years is common. Here we use 60 years, consistent with other groups. Although it is recognised that those under the age of 60 years may have significant pathology, the age of 60 years confers an automatic increased priority.

3. Use of ‘> 12 months’ for ‘chronic’
A good number of research papers have demonstrated that those with unchanged symptoms present for more than 12 months are very unlikely to have an underlying CRC, hence the use of this time parameter in the guidelines. Caution is advised to ensure an adequate history and investigations are undertaken to confirm stability of the chronic condition.

4. Use of symptom duration of more than six weeks
Many episodes of symptoms are self-limiting and do not require an urgent invasive colonoscopy, although a careful clinical assessment must be undertaken for any new symptom. Similar guidelines and common practice recommends a period of six weeks as reasonable, hence its use here.

5. ‘Unexplained’
This is an important qualifier that requires sound clinical judgement. An adaption of the UK’s National Institute for Health and Care Excellence (NICE) guidelines serves as a good definition: ‘Unexplained symptoms or signs are those that have not led to a diagnosis being made by a healthcare professional after initial assessment (including history, examination and any relevant investigations).’ Because a number of clinical features are non-specific and poor markers of CRC risk, it is important that common causes are sought and treated if identified. As suggested in the ‘not indicated’ column, other tests should be undertaken before requesting a low-reward and invasive colonoscopy.
iFOBT (+) (positive immunohistochemical faecal occult blood test)\textsuperscript{41,43,45–50}

iFOBT (also known as FIT – faecal immunohistochemical test) is currently recommended to assess the presence of occult colonic bleeding with a sensitivity for CRC of 79 (69–86) per cent and specificity of 94 (92–95) per cent\textsuperscript{43} compared with sensitivity 25–38 per cent and specificity 98–99 per cent\textsuperscript{45} for the guaiac-based test of choice – non-rehydrated Hemoccult II. iFOBT forms the basis of the Australian National Bowel Cancer Screening Program (NBCSP).

Although information is limited, recent evidence suggests the addition of iFOBT in assessing symptomatic patients could be useful.\textsuperscript{50–54} Due to the limitations of current evidence, quantification levels are not currently recommended. Although the use of FOBT in the 2015 NICE guidelines\textsuperscript{6} has been criticised\textsuperscript{55} it should be noted the criticism centres on the use of guaiac acid testing and not the immunohistochemical test.

A negative iFOBT does not rule out the need for a diagnostic colonoscopy but may alter the categorisation level, thus maximising specificity in diagnosing CRC and prioritising the most urgent referrals effectively.

An iFOBT is not indicated if rectal bleeding is a symptom. However, clinical judgement suggests it may be of value in resolved episodes of rectal bleeding.

It is also important to recognise that iFOBT tests for colonic bleeding; it does not test for upper gastrointestinal blood loss, which is detected by the guaiac-based tests.

Anaemia\textsuperscript{5,35,36,56–60}

A number of studies have looked at anaemia as an ‘alarm’ feature for underlying CRC risk with an overall PPV of 9.7 (3.5–27) per cent.\textsuperscript{36} Although the lowest levels of haemoglobin and highest degree of iron deficiency are more likely to be associated with CRC, many of those with malignancy will not have these advanced features, hence our use of ‘anaemia’ instead. The specific level of haemoglobin is not included due to the variability in the literature and ‘below the lowest limit for gender’ is suggested as with other groups. Importantly, when anaemia is combined with another symptom or factor, the likelihood of an underlying CRC is increased.

Many groups have used iron deficiency as a qualifier for anaemia and therefore as an indication for colonoscopy. A specific decision has been made not to limit to iron-deficiency anaemia (IDA) in these guidelines. The assessment of iron deficiency may be variable or misleading, leaving the possibility of missed diagnosis. With respect to ferritin, isolated low levels are poorly predictive of CRC, and ferritin levels may even be high in the presence of CRC.

One of the important extra elements of a presentation with anaemia, iron deficiency or otherwise, is whether or not there is a likely cause found. With anaemia, it is important that a ‘likely cause’ is considered, investigated and treated where appropriate before ordering a diagnostic colonoscopy. Clearly, if there are ‘critical factors’, associated symptoms or findings consistent with CRC, a likely cause is unable to be identified, or if the identified cause has been treated with no response, then a colonoscopy would be indicated, regardless of age. Failure to investigate IDA has been recognised as delaying a CRC diagnosis.\textsuperscript{60}

Age alone, associated with anaemia, does carry a very slightly increased risk of an underlying CRC, hence inclusion in Category 3 without any other feature or finding.

The role of upper gastrointestinal endoscopy in assessing anaemia is acknowledged, and it should be considered. The British Society of Gastroenterology guidelines provide a useful flow chart for rational investigation of both iron deficiency and anaemia (Figure 1).\textsuperscript{64}
Evidence of iron deficiency anaemia
- Low Hb
- Low ferritin
- Microcytosis
- Hypochromia

Check coeliac serology (tTG Ab)
-ve

Pre-menopausal woman

Colonoscopy or CT colography and OGD

Normal

Manage detected condition

Yes

Upper GI symptoms

OGD

Normal

No

Yes

Family history of colorectal cancer*

Colonoscopy or CT colography

Normal

Yes

Iron replacement. Investigate further if response inadequate

No

Confirm coeliac disease with OGD and small bowel biopsy

Yes

No

Manage detected condition

Source: Goddard et al. 2011.64

CT = computed tomography scan;
GI = gastrointestinal;
Hb = haemoglobin;
OGD = oesophagogastroduodenoscopy;
tTG Ab = tissue transglutaminase antibody
Row 3

Rectal bleeding\textsuperscript{5,23,35,36,61}

Rectal bleeding is the strongest single symptom predictive of underlying CRC (PPV 2.4 per cent). This likelihood is increased further if, in addition to the bleeding, the patient’s age is over 50 years (PPV 8.1 per cent) or if another symptom or clinical finding is present: abnormal rectal examination (8.5 per cent), diarrhoea (6.8 per cent), a second presentation (6.8 per cent), loss of weight (4.7 per cent), anaemia (3.6 per cent) or constipation (2.4 per cent). Although dark rectal bleeding and mucus have also been suggested as predictive, they have not been included separately, although the importance is recognised and they should be noted.

All rectal bleeding should be assessed by rectal examination, proctoscopy and sigmoidoscopy. Although it is accepted that generalists may not be comfortable performing the latter procedures, all clinicians should perform rectal examinations at first presentation to prevent diagnostic delay. If the history suggests an anorectal cause for the bleeding, then a rigid or flexible sigmoidoscopy should be undertaken and any anorectal causes (such as haemorrhoids) identified and treated before considering colonoscopy. It is suggested that this decision be specialist-only to minimise the opportunity for missed diagnosis. Colonoscopy should be reserved for unexplained rectal bleeding, bleeding associated with other symptoms, explained rectal bleeding in patients 50 years of age or older, or failure to stop bleeding with treatment of anorectal conditions.

Flexible sigmoidoscopy is recommended by some as the routine first investigation for rectal bleeding, especially if the blood is bright. It is very important to note that this investigation is both readily available and should not require patients to be placed on a waiting list. A good model of care is for the assessment to take place in a dedicated ‘rectal bleeding clinic’. Such a clinic can streamline both diagnosis and treatment. The necessity for a total colonoscopy can therefore be rapidly established and colonoscopy categorisation guidelines followed.

There is no role for iFOBT where there is overt rectal bleeding. Having said that, there may be a role in those for whom bleeding is intermittent to further stratify risk.

Row 4

Altered bowel habit\textsuperscript{5,23,35,36,61,62}

One of the challenges with this row is defining what is covered by ‘altered bowel habit’. In a number of the symptom reviews this definition is not specific. Is altered bowel habit simply diarrhoea or constipation or a change from a normal pattern of evacuation? We therefore include all but do recommend sound clinical judgement.

Most single symptoms are not strongly associated with likelihood of underlying CRC. However, as mentioned in the Rectal bleeding section (row 3), the presence of another symptom or finding increases the significance. Confusing the picture is the fact that the very common condition irritable bowel syndrome also presents with altered bowel habit and abdominal pain, so, first, a careful clinical assessment is required and consideration of extra tests (such as iFOBT, faecal calprotectin and full blood count) before requesting a diagnostic colonoscopy. This is particularly true of longstanding changes to bowel habit.

It is important to note that chronic constipation or diarrhoea (> 12 months) with no other symptoms are extremely unlikely to harbour an underlying cancer, hence the recommendation for full clinical assessment by a specialist before requesting a colonoscopy.

Short-term symptoms (< six weeks) can also be problematic because they are often self-limiting, infective or inflammatory in nature. Here too, careful clinical assessment is required, and in the case of diarrhoea, tests to rule out infective causes are recommended. If considering inflammatory bowel disease (IBD) a rigid/flexible sigmoidoscopy should be undertaken first (as per the IBD section below – row 8).
Abdominal pain (unexplained)\textsuperscript{5,23,36,61}

Literature is poor for this ill-defined symptom, with a PPV of 3.3 per cent (0.7–16) as a single symptom. This is a direct result of abdominal pain being a common symptom with a multitude of non-cancerous causes, irritable bowel syndrome being a frequent culprit. In addition, a number of non-abdominal causes need to be considered.

The word ‘unexplained’ is pivotal in the approach to this symptom. As a result, careful clinical assessment is required to explore all causes of abdominal pain before requesting a diagnostic colonoscopy. In particular, the presence of another symptom or finding needs to be sought and other diagnostic investigations undertaken first. Notable here is the explained abdominal pain of an episode of diverticulitis. A stratified approach to a follow-up colonoscopy is recommended, with the procedure being reserved for those who have atypical computed tomography (CT) findings, persistent symptoms after discharge, greater than average risk of CRC (such as a significant family history) or other clinical features (age, symptoms, examination or investigations) that would suggest a colonoscopy is appropriate. The role of iFOBT is unclear from the literature but may be of value.

As with rectal bleeding, the length of time present and the frequency of attacks of abdominal pain influence the risk of CRC. A history of less than 12 months and attacks of pain occurring weekly have a higher risk.\textsuperscript{23}

The ‘Not indicated’ column gives some guidance to an approach.

Weight loss (unexplained)\textsuperscript{5,23,36,61}

Our review of the literature has not revealed a universally accepted absolute measure for or definition of ‘significant weight loss’. Some have suggested more than 7 kg, others have looked at percentage of body weight lost and still others have used ‘clinically significant’ loss of weight without further specification. We therefore recommend sensible clinical judgement of what is both significant and unexplained in the context of the individual’s unique circumstances.

Studies have shown that weight loss as a single symptom is not a good discriminator, with a PPV of 1.2 per cent (95 per cent confidence interval 0.9–1.6). However, when combined with another symptom or finding, it carries increased significance (for example: Hb < 10 g/dl; PPV 4.7 per cent, abnormal rectal or abdominal examination PPV 6.4–7.4 per cent). As a result, the risk of underlying CRC is stratified by the presence of ‘critical factors’ and other symptoms in the guideline.

As with ‘Abdominal pain’ (row 5), the qualifier here is ‘unexplained’. Thus, full clinical assessment and other investigations are required to rule out common causes of loss of weight before requesting a colonoscopy. These should also include iFOBT, full blood count and iron studies. It is estimated that one-tenth of patients with involuntary weight loss will have gastrointestinal cancer. Malabsorption syndromes, IBD and coeliac disease should also be considered and tested for.

Mass palpable (abdominal or rectal) or present on rigid/flexible sigmoidoscopy

Clearly these findings demand an early colonoscopy. The only caveat being noted in the ‘Not indicated’ column where the place of CT scan needs considering.
Possible inflammatory bowel disease (IBD)\textsuperscript{38,39,63}

A number of patients will fall into this diagnostic category and do require a diagnostic colonoscopy to confirm IBD or to reassess for previously treated IBD. One of the challenges will often be to resolve the dilemma of whether the patient has IBD, irritable bowel syndrome or a malabsorption condition.

To help stratify risk, a complete assessment needs to be undertaken (including rigid/flexible sigmoidoscopy) and simple investigations for iFOBT, faecal calprotectin, inflammatory markers (CRP and ESR), full blood count, iron studies and serum albumin.

Faecal calprotectin estimation has been demonstrated to be very helpful in differentiating irritable bowel syndrome from IBD. This calcium- and zinc-binding protein is derived predominantly from neutrophils and is therefore related to inflammation in the gastrointestinal tract, even if inflammatory markers are normal. In adults, a positive result was 93 per cent sensitive and 94 per cent specific for IBD. In addition, a normal result had a negative predictive value (NPV) of 96 per cent for the exclusion of symptomatic organic gastrointestinal disease.

A review of treatment effect is not deemed of utmost urgency in most instances, hence categorising it as Cat 2. Any surveillance categorisation should be determined by following the Cancer Council Australia algorithm at \textless www.cancer.org.au\textgreater (search ‘colonoscopic surveillance intervals’).

Low MCV/MCH or ferritin\textsuperscript{39,58,63–66}

These are included because colonoscopies are often requested for this indication; however, in isolation the indices are poorly predictive of CRC. The guidelines suggest these factors should be considered in terms of other clinical features, with priority determined by a critical factor or other symptoms.

Primary of unknown origin\textsuperscript{8}

In the absence of any critical factors, symptoms or clinical signs, there is a very low likelihood of diagnostic colonoscopy identifying an occult CRC, hence the recommendation to investigate further and elsewhere prior to colonoscopy, unless relevant critical factors or other symptoms or findings are present. The importance of a full clinical assessment is highlighted.

Abnormal imaging

Clearly, the nature of the imaging findings, combined with the clinical picture, will determine the likelihood of underlying colorectal pathology and urgency of colonoscopy. The follow-up of CT-proven diverticulitis is an area of contention. If imaging is typical for uncomplicated diverticulitis, symptoms have completely resolved after a six-week period and the individual after full assessment (history, examination and investigations) is at average risk of CRC, colonoscopy is not indicated. Consideration should be given to iFOBT as an adjunct.
Surveillance colonoscopy (adenoma, colorectal cancer, inflammatory bowel disease) or on the basis of family history

Many colonoscopies are either not needed or performed too frequently, which burdens our health system and places patients at needless extra risk. As a result it is important that all surveillance colonoscopies are warranted, at any point in time. To this end, referring doctors are directed to the Cancer Council Australia website at <http://www.cancer.org.au/health-professionals/clinical-guidelines/colorectal-cancer.html>, where the following four documents can help determine the correct approach for patients.

- Algorithm for colonoscopic surveillance intervals – adenomas
- Algorithm for colonoscopic surveillance intervals – following surgery for colorectal cancer
- Algorithm for colorectal cancer screening – family history
- Algorithm for colonoscopic surveillance intervals – IBD.

Clearly if a symptom should arise in a surveillance patient, then the urgency will be guided by the criteria identified in the categorisation guidelines above.

The colonoscopy categorisation guidelines will not handle the booking of surveillance patients, but placing this group in Cat 2 should ensure a timely surveillance colonoscopy is undertaken. Prolonged waiting times for an elective surveillance defeats the purpose of surveillance. As a result, the recommendation is that Cat 2 surveillance patients waiting more than 60 days beyond their due booking date should be upgraded to Cat 1 so that excessive delays to timely surveillance are prevented.

Polyp > 2 cm for excision

A polyp larger than 2 cm is highly likely to be malignant in nature, hence Cat 1 categorisation. Smaller polyps still require removal but not as urgently, hence categorise as Cat 2 as per NHMRC guidelines.

References


