

# Progress in Colorectal Surgery

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Editors

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# Preface

In a previous publication, the authors attempted to cover not only topical issues but also difficult problems that might confront recently appointed trainees in the decisions they make that confront these individuals in their future practices.

Since that time, much of the thrust of coloproctology and government directives have centred around various aspects of colorectal cancer. The editors are thus of the opinion that they must not shy away from political incentive and have dedicated just over half of the present book to the diagnosis, presentation, and management of colorectal carcinoma.

By contrast, the editors have also tried to draw attention to the fact that many patients with benign disorders of the colorectum have symptoms which are incompatible with a constructive and useful quality of life. Crohn's disease is paramount in this respect and continues to provide challenges in both medical and surgical management. Moreover, coloproctologists continue to be vexed by the problems presented by the diagnosis and treatment of functional bowel disorders, and it is hoped that the chapters in this book will help to demystify the investigation and treatment of incontinence and constipation.

John Beynon, BSc, MS, FRCS  
Nicholas D. Carr, MD, FRCS

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# 1

## The Effective and Efficient Management of Patients with Rectal Bleeding to Identify the Few with Cancer

MICHAEL R. THOMPSON, EDWIN T. SWARBRICK, BRIAN G. ELLIS,  
IONA C. HEATH, L. FAULDS WOOD, and WENDY S. ATKIN

There are currently insufficient resources to fully investigate all patients with rectal bleeding to exclude the small possibility of cancer, and this is the dominant factor in developing strategies for the management of rectal bleeding. However, even if there were unlimited resources it may not be desirable to investigate all patients because the small risks associated with the investigative procedure might outweigh the benefits, particularly in groups at very low risk of having cancer.

The importance of efficient as well as effective delivery of healthcare was the subject of the Rock Carling Lectures delivered by Archie Cochrane in 1972 [1], and continues to be an essential aspect of clinical medicine. In the context of the management of rectal bleeding, effectiveness is achieved if all patients with colorectal cancer are promptly diagnosed, and efficiency is achieved by limiting the number of patients without cancer investigated. In view of the high prevalence of rectal bleeding in the community and the potential demand for its investigation, the efficient management of all patients presenting with rectal bleeding will profoundly affect the prompt diagnosis of those with cancer.

The management of rectal bleeding as a symptom of bowel cancer begins with advice to the general public through disease awareness campaigns, proceeds through referral guidelines to general practitioners (GPs), and finishes with the efficient use of resources for its investigation. The varying prevalence and predictive value of rectal bleeding for cancer in different cohorts of patients is important to all stages of its management.

Rectal bleeding is also important in the diagnosis of adenomatous polyps [2–7] and colitis [7] as well as colorectal cancer [2,4–11]. Overall, 40% of all colorectal cancers and 70%–80% of rectal and sigmoid cancers present with overt rectal bleeding [9–11]. It may be a sign of an early-stage curable cancer [12–15] and of large adenomatous polyps, which, with subsequent colonoscopic surveillance, may be a valuable way of reducing the prevalence and overall mortality from colorectal cancer [16]. It is perhaps not

surprising, therefore, that advice on the management of rectal bleeding stresses the importance of its detection [17,18] and prompt investigation [4,5,19].

This advice has been supported by reports that rectal bleeding has a high predictive value for cancer in primary care [4,5,19], and that it is impossible to differentiate between rectal bleeding from benign and malignant disease [4,5,19,20–24]. It is further supported by the unproven assumption that early referral of all patients with rectal bleeding will improve the survival of those with cancer [25].

These ideas have formed the basis for the current paradigm governing the approach to the management of rectal bleeding, which advises an aggressive policy of full colonic examination in all patients over the age of 40 [4,5,19]. This is partly the reason for the serious mismatch between demand and the resources for investigation—some cancer patients have long waits to be seen due to the unnecessary investigation of patients at very low risk of cancer.

We question these assumptions, and propose that it is possible to classify patients on the basis of their cancer risk for different investigation strategies.

The British government has recently introduced the “Two-Week Standard” [26], which promises that all patients suspected by their GPs of having bowel cancer will be seen within two weeks. This has focused attention on the problem, which may be partly addressed by a reconfiguration of referrals by identifying precisely which patients should qualify for urgent referral and investigation [27–30]. However, it is yet to be seen whether this will cause a greater delay in patients who do not fulfil these criteria, which in turn might exacerbate the problem with no overall benefit to all cancer patients. The introduction of referral guidelines [27–29] must not deflect the government from the long-term solution, which is for a substantial increase in hospital resources for all patients requesting and needing investigation, not just those patients at higher risk.

## 1. The High Prevalence of Rectal Bleeding in the Community

The high prevalence of all symptoms in the community, regardless of their nature, was first described in the Peckham experiment in 1946 [31] and subsequently by Wadsworth [32] and Hannay [33]. These studies demonstrated that most people have various symptoms most of the time, which they either self-treat or which resolve spontaneously without medical consultation. Only a small proportion of patients who eventually consult their doctors are referred to hospital for investigation [31–33]. This observation is also true for rectal bleeding [34–36].

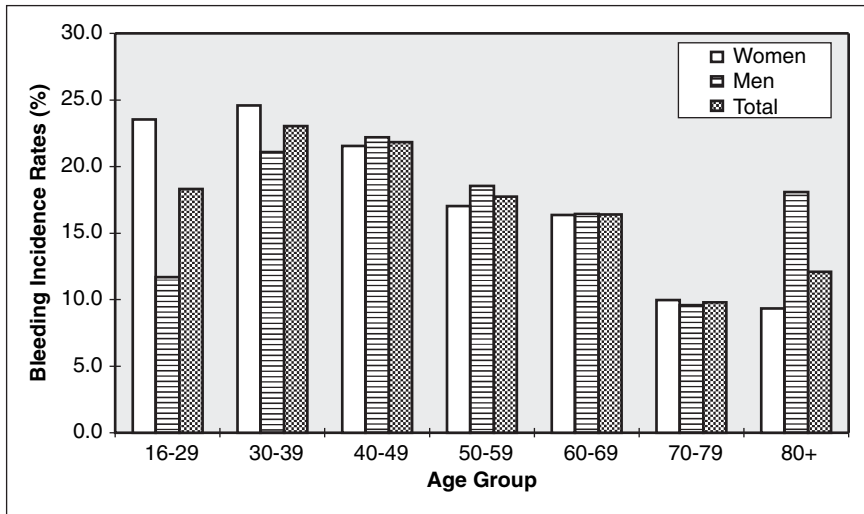


FIGURE 1.1. Incidence rates of rectal bleeding in men and women for a one year period in 1996 as a percentage of the total population.

Several studies have shown that 17%–20% of patients in the community have rectal bleeding each year [34–44]. Prevalence is inversely related to age, with young women being most affected and the elderly being least affected [34–36]. Two thirds of patients who bleed each year will have had an episode in the past [36] (Figure 1.1, Figure 1.2). It has been calculated

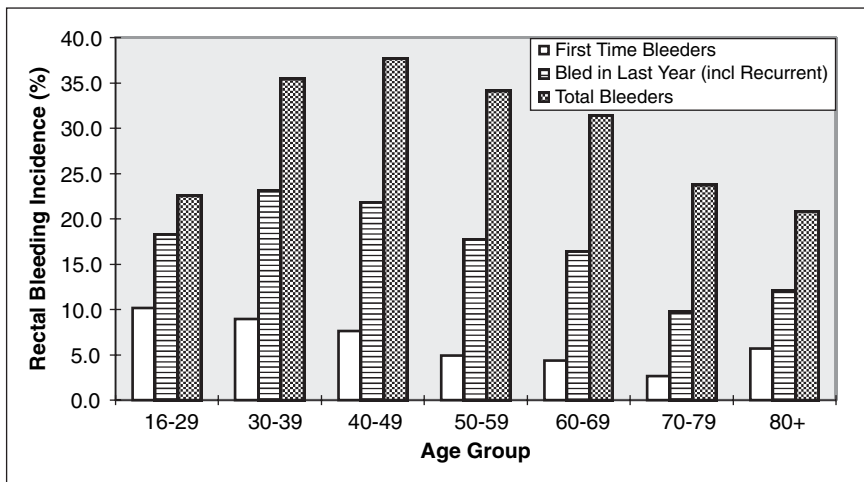


FIGURE 1.2. Incidence rates of rectal bleeding for the first time in the previous year (1996), as a percentage of the total population, and for patients having rectal bleeding at any time previously, including 1996.

that in a city with a population of 1 million people, 140 000 will have rectal bleeding each year [36].

It is fortunate that less than 15% of patients with rectal bleeding seek medical help [35,36] and only 40%–50% of those patients are referred to hospital [36]. Thus, patients seen in hospital represent the “tip of the iceberg” [33] of all patients with these symptoms and we ignore this important piece of clinical epidemiology at our peril [45]. Clearly, a great deal of selection is already occurring before referral for investigation and this needs to continue.

## 2. The Predictive Value of Rectal Bleeding for Cancer in the Community, Primary Care, and Hospital

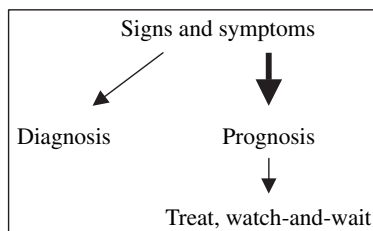
In view of the high prevalence of rectal bleeding and as a result of the considerable selection process, the predictive value of rectal bleeding for cancer varies from 1:705 in the community [23] to 1:17 in a surgical outpatient department [46].

Two studies on the predictive value of rectal bleeding in primary care have shown a 1:10 prevalence of cancer [3,5], which is considerably higher than that in the hospital study [46] and two others in primary care that showed a 1:29 and 1:30 prevalence [6,36]. It is likely that the two studies showing a higher prevalence [3,5] was the result of not all patients identified with rectal bleeding in primary care being referred for investigation. About one half of all patients with rectal bleeding in the community have an associated change in bowel habit. In two thirds of cases the change is to a decreased frequency of defaecation with straining and/or harder stools [36]. Dark red bleeding also occurs in up to 20% of patients [4,6,7,35,36] and painless (implying non-haemorrhoid-associated) rectal bleeding occurs in 80% of patients in the community and general practice [7,36]. This means that many patients with rectal bleeding from benign conditions in the community have what, at present, are considered higher risk symptoms.

## 3. The Basis of the Current Selection Process for Referral of Patients for Investigation

It is likely that at least some patients and GPs decide whether to seek investigation in hospital by adopting watch-and-wait strategies [47] that are based on the assumption that most benign conditions get better whereas symptoms from cancer persist. In general practice, “treat, watch-and-wait” strategies [47] in conjunction with “safety-netting” [48] are an integral and safe part of the diagnostic process, and are the keystones of the GP’s gate-keeper role (Figure 1.3).

FIGURE 1.3. Diagnosis in primary care: the importance of “treat, watch-and-wait” policies. Reproduced from Sackett DL, Haynes RB, Guyatt GH, Tugwell P. *Clinical Epidemiology—A Basic Science for Clinical Medicine*. 2nd ed. Boston: Little Brown & Co; 1991: 4.



The gate-keeper role saves the majority of patients with transient symptoms unnecessary investigations, which conserves hospital resources for more rapid investigation and treatment of patients with serious disease. It is crucial that the new paradigm for the management of rectal bleeding supports the GP in this important role [27–29].

The question arises: Can the selection process between the patient/GP interface and the GP/hospital interface be improved and will it improve survival from colorectal cancer?

#### 4. Will Prompt Referral and Earlier Diagnosis Improve Survival?

The term “early,” used so often in discussions of cancer therapy, is generally applied inappropriately. Although “early” refers to a dimension in time, the usual evidence assessed in the designation of “early” comes mainly from anatomy not chronometry.

Alvan F. Feinstein, *Nature*, 1966 [49]

The diagnosis of early-stage cancer results in better survival, but this should not be confused with the assumption that diagnosis early after the onset of symptoms also improves survival. This assumption is one of the reasons for the drive to promptly investigate all patients with rectal bleeding [20] and for the introduction of the “Two-Week Standard” [26], which could discourage more pragmatic “treat, watch-and-wait” approaches [29,47,48].

The rationale for early referral of patients with rectal bleeding is based on the following unproven assumptions:

- A significant number of patients currently die as a result of an avoidable delay in diagnosis and treatment.
- Delays in referral are due to patients and GPs being poorly informed of the significance of the symptoms of bowel cancer, and that this can be corrected by public awareness campaigns and better referral guidelines for GPs.
- Earlier diagnosis during the symptomatic phase of the natural history of colorectal cancer will improve survival.

There is little evidence for these assumptions, but what is certain is that encouraging more patients to have investigation for rectal bleeding will further strain already limited resources. It is therefore important to determine what proportion of patients have delay in treatment, whether it has previously been possible to persuade appropriate patients to consult their GPs earlier, and for GPs to recognise higher risk patients for referral and to determine the size of the benefit that earlier symptomatic diagnosis might achieve.

#### *4.1. What Proportion of Patients Have Prolonged Delays in Treatment?*

The mean time between the onset of symptoms and treatment of bowel cancer has remained constant at approximately 7 months for rectal cancers in different countries over many years [50–56]. It is particularly disappointing that up to 20% of patients with colorectal cancer have a delay in referral and treatment of more than 1 year, and many of these patients have rectal bleeding [9,54,55,57–66].

#### *4.2. Are Delays Caused by Poorly Informed Patients and GPs, and Can This Be Improved?*

The causes of delay in referral include patient embarrassment and fear of cancer [25,34,56,67] as well as a lack of knowledge of the symptoms of colorectal cancer [67]. The delays in referral have not changed over many years in spite of disease awareness campaigns and referral guidelines for doctors in primary care. It has also been suggested that the speed of referral may be affected by the biological nature of the cancer and its effect on the symptoms. If this is correct, it may be very difficult to modulate the speed of patient consultation and primary-care doctor referral.

#### *4.3. What Is the Evidence That Earlier Diagnosis of Colorectal Cancer Improves Survival?*

A few reports [68–73], mostly based on reviews of small numbers of cancer patients, often with historical controls, have suggested an improvement in survival with shorter delays in treatment. There are more reports of an inverse relationship, with delay in treatment being associated with better outcomes [50–55,58,64,65,74,75]. This paradoxical relationship is thought to be due to biological predeterminism [49,76,77], which suggests that some slow-growing cancers may produce low grade, nondisturbing symptoms resulting in delay in referral but with good outcomes, whereas some aggressive cancers may produce more severe, rapidly progressive, and worrying symptoms resulting in rapid referral but poor survival [40,76,77]. This para-

TABLE 1.1. The symptom iceberg.

## Symptoms of rectal bleeding in the community

High prevalence: 17%–20% of the population each year
Only 15% visit their GP
Only 7% are at present investigated in hospital
More common in the younger age groups
Often associated with a change in bowel habit to decreased frequency and/or increased hardness of stool and straining
10%–20% have dark red bleeding

doxical effect makes it difficult to demonstrate the possible beneficial effect of earlier symptomatic diagnosis [50–55,57–66,70,74,78–85]. It is clear, however, that many patients die in spite of prompt treatment and substantial numbers survive in spite of delay so that the total number of patients that might benefit from earlier diagnosis could be small [50].

One study [86] determined the effect that delay in treatment had on survival after referral to hospital on the assumption that this would occur in a random fashion and would not be dependent on the biological nature of the cancer. However, this study still did not show that delay had an adverse effect on outcome, even in patients having hospital delays in treatment of over 5 months [86].

#### 4.4. Conclusion on the Benefits of Earlier Symptomatic Diagnosis

Earlier symptomatic diagnosis may be difficult to achieve for many patients with bowel cancer, and even if this could be achieved, the overall improvement in survival is likely to be small [50,54–56,58,80,81,85]. This would require a considerable increase in resources for investigating increasing numbers of symptomatic patients.

### 5. When Does the Risk of Cancer Exceed the Risk of Investigation?

Most doctors are now accustomed to balancing the benefits of treatment with its risks [87,88]. They are less familiar with this sort of analysis when deciding whether to refer low-risk patients for investigation, even though

TABLE 1.2. Predictive value of rectal bleeding for cancer.

	Community	Hospital outpatients
Predictive value of rectal bleeding for cancer	1:705	1:17



it is now accepted that before introducing screening for colorectal cancer there should be some evidence of significant overall benefit. It is possible that younger patients with lower GI symptoms are at lower risk of cancer than older asymptomatic screened patients, and similar rules to those developed for screening should be applied when deciding at what stage investigating symptomatic patients will do more good than harm.

The various disadvantages that can occur during investigation are listed in Table 1.3.

In patients at very low risk of cancer, the question must be asked: Is the risk of having a cancer greater than the risk of investigation? Or, when is the small potential benefit of earlier symptomatic diagnosis in the very few with cancer outweighed by the disadvantage of investigation in the majority without cancer (Figure 1.4).

5.1. *Summary of the Basis for Changing the Current Paradigm Governing the Management of Rectal Bleeding*

- The high prevalence of rectal bleeding in the community establishes the need for a selective policy for its investigation.
- There is no evidence that short time lags before referral reduce the chances of survival from colorectal cancer.
- Investigations can harm people, and in patients at very low risk of cancer, any benefit from earlier diagnosis to the few with cancer may be outweighed by the disadvantage of investigations to those without cancer.

TABLE 1.3. Disadvantages of investigation.

Disadvantages of investigation
Unnecessary worry of investigation and fear of cancer <sup>89,90</sup>
Labelling <sup>91</sup>
Physical harm
• Colonoscopy <sup>92,93</sup>
Risk of perforation
Risk of death 1:17000
• Barium enema 1:57000 deaths <sup>94</sup>
• False positives/unnecessary operations
• False negatives/delayed diagnosis
Costs of investigation
• Patient and caregiver costs
Time off work
Travel costs
Consuming scarce resources
• Delay in investigation of those with cancer
• Opportunity costs
Medico-legal costs

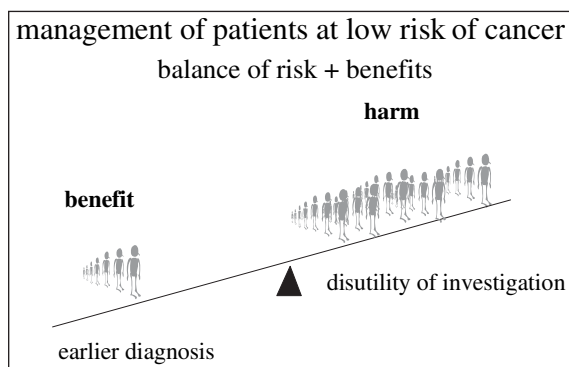


FIGURE 1.4. Management of patients at low risk of cancer.

These three fundamental points establish the need, safety, and pragmatism for new strategies to manage rectal bleeding based on careful “treat, watch-and-wait” policies [4] according to cancer risk. These are a natural and integral part of clinical diagnosis in all situations, particularly in primary care and are the keystones of the GP’s “gate-keeper” role [29]. Public awareness campaigns for patients with rectal bleeding and referral guidelines for GPs must emphasise the value of these strategies, particularly for those patients at very low risk of cancer, and to establish appropriate periods of “wait” in “treat, watch-and-wait” policies according to cancer risk [29].

The key to a new paradigm governing the management of rectal bleeding therefore depends on the identification of patients at higher and low risk of cancer on the basis a simple history and examination [27–30].

## 6. Can Symptoms and Signs Be Used to Determine Cancer Risk in the Community and in Primary Care?

The challenge for providing advice for public awareness campaigns and the new referral guidelines is to identify criteria determining cancer risk that maintain high sensitivity for cancer, that is, include the majority of patients with cancer, with as little loss of specificity as possible, which means including a minority of patients with benign disease [27–30].

It is important to understand that “as sensitivity increases, a point is reached at which very small increases in sensitivity are accompanied by very large decreases in specificity, i.e., the number of false-positive results increases. An increase in the number of false-positive tests increases patient anxiety, the costs of ‘*investigation*’ and the risk associated with unnecessary ‘*investigation*’” [95].

The implication of this is that there will be an exponential increase in the number of patients needing to be investigated to capture the last few cancer patients with less common symptom profiles.

### *6.1. The Common Age, Symptom, and Sign Profiles of Rectal Bleeding in Patients with Established Cancer*

It is likely that the common age, symptom, and sign profiles of rectal bleeding in patients with established cancer will have higher predictive values than those occurring less commonly.

It is clear from many previous articles [9–11,53,54,60–63,65] that colorectal cancer presents with more than one symptom or one sign. For example, it is now clear that approximately 75% of cancer patients presenting with rectal bleeding also have a change in bowel habit, and another 20% have bleeding without anal symptoms or with a palpable anorectal mass [11,15,46]. This means that as little as 5% of cancer patients present with rectal bleeding, anal symptoms, no persistent change in bowel habit, and no palpable anorectal mass; the common symptom pattern in patients bleeding from piles [11,46].

### *6.2. The Symptom Patterns with the Highest Predictive and Diagnostic Values*

#### 6.2.1. Rectal Bleeding with a Change in Bowel Habit

Several studies in primary care [2,5–7] and in a surgical outpatient department [46] have shown that patients presenting with both rectal bleeding and a change in bowel habit have up to a 5 times greater risk of cancer as compared with patients presenting with rectal bleeding as a single symptom (Table 1.4).

#### 6.2.2. Rectal Bleeding and No Perianal Symptoms

Two studies, one in primary care [7] and one in a surgical outpatient department [46], have shown that patients presenting with rectal bleeding and no anal symptoms have up to a 4 times greater risk of cancer compared with those patients presenting with anal symptoms (Table 1.4). This occurs in patients whether or not their rectal bleeding is associated with a change in bowel habit.

### *6.3. The Diagnostic Value of the Other Characteristics of Rectal Bleeding*

#### 6.3.1. Dark Red Bleeding

Three recent studies have shown dark red bleeding to have a predictive value of 9%–13% compared with 4%–8% for bright red bleeding [5–7,19] (Table 1.5).

TABLE 1.4. The predictive and diagnostic value of the symptom combinations of rectal bleeding.

Symptom	Study	Sensitivity	Specificity	LR	95% CI	PPV change in bowel habit	
						With	Without
Rectal bleeding with a change in bowel habit	Fijten <sup>6*</sup>	89%	78%	4.0	2.9–5.5	11%	0.4%
	Ellis <sup>7*</sup>	100%	58%	2.4	1.6–2.7	9%	0%
	Dodds <sup>97**</sup>	75%	65%	2.13	2.0–2.3	13%	3%
Symptom	Study	Sensitivity	Specificity	LR	95% CI	PPV anal symptoms	
						With	Without
Rectal bleeding without anal symptoms	Ellis <sup>7*</sup>	64%	78%	2.9	1.6–4.3	2%	11%
	Dodds <sup>97**</sup>	59%	73%	2.2	2.0–2.5	4%	13%

\*Primary-care population.

\*\*Hospital population.

LR, likelihood ratio (sensitivity/1-specificity); PPV, positive predictive value.

### 6.3.2. The Manifestation of Rectal Bleeding

The way rectal bleeding is noticed and bleeding of recent onset are either of no or little diagnostic value [7,19], although blood mixed with the stool has been shown to be of value in 2 studies [5,6] and of no value in 2 others [7,19]. Sudden, self-limiting, large-volume, fresh bleeding after defaecation can be very frightening and is a common reason for referral to a surgical outpatient clinic, but paradoxically is probably of diagnostic value in identifying patients at very low risk of cancer [7]. This is contrary to what many patients and GPs understandably feel.

### 6.3.3. Palpable Rectal Mass

Forty to eighty percent of rectal cancers, most of which present with rectal bleeding, have a palpable rectal mass [7,10,24,49,96]. This is a crucially

TABLE 1.5. The diagnostic value of dark red bleeding.

Symptom	Study	Sensitivity	Specificity	LR	95% CI	PPV color	
						Dark	Bright
Dark red Bleeding	Ellis <sup>7*</sup>	27%	88%	2.3	0.8–5.3	9%	4%
	Metcalf <sup>5*</sup>	37%	70%	1.25	0.5–3.2	11%	8%
	Chave <sup>98**</sup>	37%	83%	2.08	1.8–2.5	13%	5%

\*Primary-care population.

\*\*Hospital population.

LR, likelihood ratio (sensitivity/1-specificity); PPV, positive predictive value.

important physical sign for a small number of cancer patients presenting with rectal bleeding who otherwise have a low-risk symptom pattern, that is, rectal bleeding with anal symptoms without a change in bowel habit.

#### *6.4. The Nature of the Change in Bowel Habit*

The nature of the change in bowel habit in 80%–90% of patients with colorectal cancer is to increased frequency and/or looser stools [7,11,46]. It is likely that this type of change in bowel habit will have higher diagnostic value [97] than a change in bowel habit to decreased frequency and harder stools, which is extremely common in patients with rectal bleeding from benign disease in the community [32].

#### *6.5. The Effect of Age on the Diagnostic Value of Rectal Bleeding*

The prevalence of rectal bleeding in the community is highest in the 20–40 age group and decreases with age (Figure 1.1, Figure 1.2). In contrast, 85% of patients with colorectal cancer are over the age of 60 with less than 1% below the age of 40 [98]. This means that rectal bleeding is of much greater significance in patients over the age of 60 years [4–8,46].

In patients presenting to a surgical outpatient department [42], the prevalence of cancer varied from 50% in patients over 80 with the highest risk symptom profile (rectal bleeding with a change in bowel habit, no abdominal pain, and no perianal symptoms) to 1:888 in patients below the age of 50 with the lowest risk symptom profile (rectal bleeding without a change in bowel habit, with perianal symptoms, and no other significant diagnostic factors), a 444-fold difference in cancer prevalence [46] (Table 1.6).

### **7. New Management Strategies for Investigating Rectal Bleeding**

These new data on the predictive values of age, symptom, and sign profiles of rectal bleeding suggest it is now sensible to discard the idea that all cancer patients presenting with rectal bleeding have nonspecific symptoms. In the future, different management strategies with different speeds of referral should be introduced on the basis of cancer risk assessment as determined by a simple history and examination (Table 1.7, Table 1.8).

Fast-track referral is appropriate for patients with higher risk criteria, but only after symptoms have persisted for 6 weeks [27–29]. For patients at low risk of cancer, longer “treat, watch-and-wait” policies are appropriate, both in the community, perhaps with help from a pharmacist, and also in primary care [27–29]. If these patients do need referral, this should be to a routine

TABLE 1.6. The effect of age on the prevalence of cancer in patients with rectal bleeding and other symptoms.

Age	Rectal bleeding (all patients)	Plus a change in bowel habit	Plus a change in bowel habit but no abdominal pain or anal symptoms	No change in bowel habit and no anal symptoms	No change in bowel habit with anal symptoms*
<39	1:268	1:73	1:26	1:148	0.633
40–49	1:83	1:32	1:9	1:122	1:255
50–59	1:26	1:13	1:6	1:62	1:178
60–69	1:10	1:6	1:3	1:13	1:100
70–79	1:8	1:6	1:3	1:8	1:47
≥80	1:5	1:4	1:2	1:6	1:18
Total number of patients	5442	2063	331	810	2544
Total number of cancers	347	261	97	49	16
Overall	1:16	1:8	1:3	1:17	1:159

\*Not including patients with a palpable rectal or abdominal mass and those with iron-deficiency anaemia below 10g.

Personal data from a study of 8000 surgical outpatients (Thompson MR, Swarbrick ET, Ellis BG, et al. In: Cunningham D, Topham C, Miles A, eds. *The Effective Management of Colorectal Cancer*. 2nd ed. London: Aesculapius Medical Press; 2000: 173).

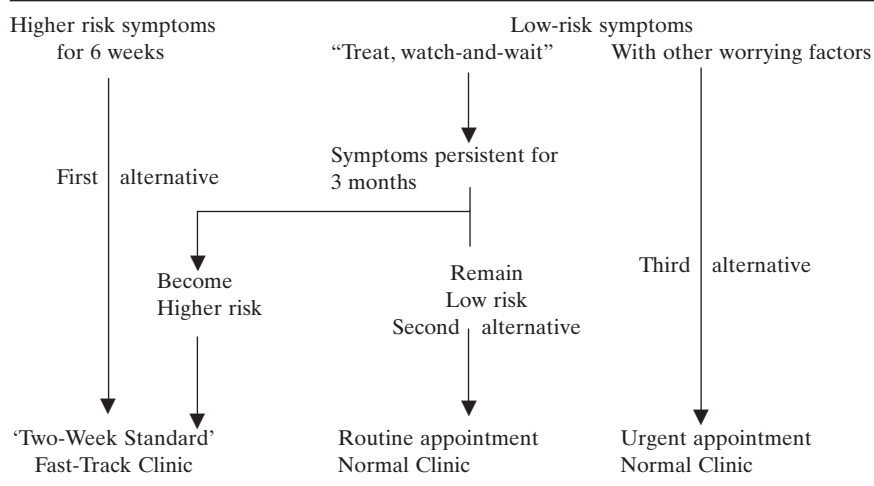
TABLE 1.7. Management of rectal bleeding.

Old paradigm	New paradigm
Patients with colorectal cancer present with nonspecific rectal bleeding, and therefore all patients with this symptom over a certain age should have prompt and full colonic investigation.	There are large differences in the predictive value of rectal bleeding for cancer according to its association with other symptoms and signs and the age of the patient. Different management strategies with different speeds of referral should be adopted according to cancer risk so that patients with transient low-risk symptoms from benign disease avoid investigation.

TABLE 1.8. Criteria determining the management strategy [29].

Higher-risk symptoms
• Rectal bleeding with a <i>persistent</i> change in bowel habit to looser stools and/or increased frequency of defaecation for at least 6 weeks.
• Rectal bleeding <i>persistently</i> without anal symptoms in patients over the age of 60.
Low-risk symptoms
• Rectal bleeding <i>with</i> anal symptoms and <i>without</i> a change in bowel habit and <i>no</i> anal mass (or with a transient change in bowel habit, particularly to decreased frequency of defaecation, harder stools and straining).

TABLE 1.9. The three alternative methods for referral.



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clinic, where the waiting time will depend on the available resources and the numbers of patients referred with low risk symptoms (Table 1.9).

7.1. Management of Recurrent Rectal Bleeding Over Prolonged Periods of Time Following Negative Investigations

Some patients have recurrent bleeding [32] over long periods of time and may have had previous investigations in hospital. If patients have already had a flexible sigmoidoscopy within the previous 3 years, they can be safely managed by longer watch-and-wait strategies, but if these symptoms persist, even if they remain low-risk symptoms, they need to be re-referred to a routine clinic, and if flexible sigmoidoscopy is again normal, they may need examination by colonoscopy.

8. “Treat, Watch-and-Wait” Strategies for Patients at Low Risk of Cancer

Approximately 5%–10% of patients presenting with rectal bleeding from a colorectal cancer will present with low-risk symptoms and these patients will continue to be diagnosed in routine clinics. Careful “treat, watch-and-wait” management strategies are therefore needed in primary care to avoid excessive time lags before referral of these low-risk patients. This means

that all patients with persistent symptoms, even if low risk, must eventually be investigated, and it is likely that the only long-term solution to the management of rectal bleeding is to develop more resources so that all patients referred are investigated promptly, not just those with higher risk symptoms.

“Treat, watch-and-wait” strategies must be with the agreement of the patient, who will need to understand the overall benefit to the majority of patients with transient symptoms of avoiding unnecessary investigations [29]. Patients who are not happy with this arrangement can still be referred routinely to a normal clinic, and others may be given written information about what constitutes higher risk symptoms so they can self-refer back at an earlier stage if these develop [48]. If patients are overly anxious with low-risk symptoms or in younger age groups with persistent higher risk symptoms (i.e., rectal bleeding without anal symptoms), there is a third alternative route for referral, an urgent appointment in a routine clinic [27–29]. This mode of referral must be kept to a minimum to ensure that all patients referred in this way are seen promptly.

There are therefore three alternative routes or speeds of referral dependent on cancer risk and the concern of the patient and the GP (Table 1.9).

## 9. Conclusion

The current lack of resources for investigating rectal bleeding means that the efficient management of patients without cancer is the key to the effective diagnosis of those with cancer.

The traditional assumption suggesting that all patients with rectal bleeding over the age of 40 years seeking medical advice should have prompt and full colonic investigation should now be reviewed. The high prevalence of rectal bleeding in the community, especially in patients below the age of 60 years, means that selection of patients for investigation may always be necessary, both because it is unlikely that at least in the near future there will be sufficient resources to meet the demand for its investigation, and because in younger patients at low risk the possible benefit to the very few with cancer from earlier symptomatic diagnosis may be outweighed by the harm of full colonic imaging for the great majority who do not have cancer. The key to better selection of patients for investigation, and therefore efficient as well as effective diagnosis of colorectal cancer in patients with rectal bleeding, is a clear understanding of the diagnostic value of symptom and sign profiles in determining cancer risk and how this is affected by age. This will enable higher risk patients to be identified, who should be encouraged to have prompt investigation and, just as important, those at very low risk who can initially self-care [45] or be managed by their GPs in primary care for more prolonged periods of time.



Every patient at low risk of cancer successfully managed in the community or in primary care will conserve the investigative resources for those at higher risk, who can then be seen, investigated, and treated more quickly. This strategy, even if it does not increase the overall survival of cancer patients, will ensure a higher quality of care for all patients, not just those with cancer. The greatest challenge for the new guidelines will be to construct safe "treat, watch-and-wait" policies for those patients at low risk to ensure that the few with cancer do not suffer excessive time lags before referral.

Every patient with low-risk symptoms and signs successfully treated in the community or in primary care may enable a patient with cancer to be seen and treated more quickly.

## References

1. Cochrane AL. *Effectiveness and efficiency; random reflections on health services*. London: The Nuffield Provincial Hospitals Trust 1972. Printed by Burgess & Son (Abingdon Berks Limited).
2. Norreland N, Norreland H. Colorectal cancer and polyps in patients aged 40 years and over who consult a GP with rectal bleeding. *Fam Pract*. 1996;13:160–165.
3. Chapuis PH, Goulston KJ, Dent OF, Tait AD. Predictive value of rectal bleeding in screening for rectal and sigmoid polyps. *Br Med J*. 1985;290:1546–1548.
4. Goulston KJ, Cook I, Dent OF, and General Practitioners and Specialists Associated with the Concord Hospital Gastroenterology Unit. How important is rectal bleeding in the diagnosis of bowel cancer and polyps? *Lancet* 1986; 2:261–265.
5. Metcalf JV, Smith J, Jones R, Record CO. Incidence and causes of rectal bleeding in general practice as detected by colonoscopy. *Br J Gen Pract*. 1996;46:161–164.
6. Fijten GH, Starmans R, Muris JWM, Schouten HJA, Blijham GH, Knottnerus JA. Predictive value of signs and symptoms for colorectal cancer in patients with rectal bleeding in general practice. *Fam Pract*. 1995;12:279–286.
7. Ellis BG, Jones M, Thompson MR. Rectal bleeding in general practice: who needs referral? *Colorect Dis*. 1999;1(suppl 1):23–24.
8. Wauters H, Van Casteren V, Buntinx F. Rectal bleeding and colorectal cancer in general practice: diagnostic study. *BMJ*. 2000;321:998–999.
9. McSherry CK, Cornell GN, Glenn F. Carcinoma of the colon and rectum. *Ann Surg*. 1969;169:502–509.
10. Shallow TA, Wagner FB, Colcher RE. Clinical evaluation of 750 patients with colon cancer. Diagnostic survey and follow-up covering a 15-year period. *Ann Surg*. 1955;142:164–175.
11. Ellis B, Baig MK, Cripps NPJ, et al. Common modes of presentation of colorectal cancer patients. *Colorect Dis*. 1999;1(suppl 1):24.
12. Chapuis PH, Dent OF, Fisher R, et al. A multivariate analysis of clinical and pathological variables in prognosis after resection of large bowel cancer. *Br J Surg*. 1985;72:698–702.

13. Armstrong-James D, Moss S, Bygrave S, Thompson MR. Colorectal cancer patients presenting with rectal bleeding have earlier stage tumours and longer pre-diagnosis history [abstract]. *Gut* 1997;40(suppl 1):A50. Abstract TH199.
14. Rafferty TL, Samson N. Carcinoma of the colon: a clinical correlation between presenting symptoms and survival. *Am J Surg.* 1980;46:600–606.
15. Tsavellas G, Pond C, Thompson MR. Colorectal cancer patients with rectal bleeding have earlier stage disease and better outcomes. *Colorect Dis.* 2000; 2(suppl 1):41.
16. Atkin WS, Morson BC, Cuzick J. Long-term risk of colorectal cancer after excision of rectosigmoid adenomas. *N Engl J Med.* 1992;326:658–662.
17. Dent OF, Goulston KJ, Zubrzycki J, Chapuis PH. Bowel symptoms in an apparently well population. *Dis Colon Rectum.* 1986;29:243–247.
18. Goulston K, Chapuis P, Dent O, Bokey L. Significance of bowel symptoms. *Med J Aust.* 1987;146:631–633.
19. Mant A, Bokey EL, Chapuis Ph, et al. Rectal bleeding. Do other symptoms aid in diagnosis? *Dis Colon Rectum.* 1989;32:191–196.
20. Keddie N, Hargreaves A. Symptoms of carcinoma of the colon and rectum. *Lancet* 1968;2:749–750.
21. Curless R, French J, Williams GV, James OFW. Comparison of gastrointestinal symptoms in colorectal carcinoma patients and community controls with respect to age. *Gut* 1994;35:1267–1270.
22. Byles JE, Redman S, Hennrikus D, Sanson-Fisher RW, Dickinson J. Delay in consulting a medical practitioner about rectal bleeding. *J Epidemiol Community Health.* 1992;46:241–244.
23. Holliday HW, Hardcastle JD. Delay in diagnosis and treatment of symptoms colorectal cancer. *Lancet* 1979;1:309–311.
24. MacArthur C, Smith A. Factors associated with speed of diagnosis, referral and treatment in colorectal cancer. *J Epidemiol Community Health.* 1984;38: 122–126.
25. McLennan I, Hill J. How can doctors diagnose colorectal cancer earlier? By increasing patient's awareness of the disease and investigating them promptly when they present. *BMJ.* 1993;306:1707.
26. Great Britain: Department of Health. London: *The new NHS—Modern Dependable.* Published by the Department of Health 1997. London: The Stationery Office; 1997. (Command paper Cm 3807)
27. [www.acpgbi.org.uk](http://www.acpgbi.org.uk)
28. Referral guidelines for colorectal cancer. *Colorect Dis.* 2002;4:287–297.
29. Thompson MR, Heath I, Ellis BG, et al. Identifying and managing patients at low risk of bowel cancer in general practice. *BMJ.* 2003;327:263–265.
30. Selvachandran SN, Hodder RJ, Ballal MS, Cade D. Prediction of colorectal cancer by a patient consultation questionnaire and scoring system: a prospective study. *Lancet* 2002;360:278–283.
31. Pearse IH, Crocker LH. *The Peckham Experiment: A Study of the Living Structure of Society.* London: Scottish Academic Press Ltd; 1985.
32. Wadsworth MEJ, Butterfield WJH, Blaney R. *Health and Sickness, The Choice of Treatment. Perception of Illness and Use of Services in an Urban Community.* London: Camelot Press Ltd; 1971.
33. Hannay DR. *The Symptom Iceberg: A Study of Community Health.* London: Routledge & Kegan Paul; 1979.

34. Crossland A, Jones R. Rectal bleeding: prevalence and consultation behaviour. *BMJ*. 1995;311:486–488.
35. Talley NJ, Jones M. Self-reported rectal bleeding in a United States community; prevalence, risk factors, and health care seeking. *Am J Gastroenterol*. 1998; 11:2179–2183.
36. Thompson JA, Pond CL, Ellis BG, Beach A, Thompson MR. Rectal bleeding in general and hospital practice: the tip of the iceberg. *Colorect Dis*. 2000;2 :288–293.
37. Jones ISC. An analysis of bowel habit and its significance in the diagnosis of carcinoma of the colon. *Am J Proctol*. 1976;27:45–46.
38. Kewenter J, Haglind, Smith L. Value of a risk questionnaire in screening for colorectal neoplasm. *Br J Surg*. 1989;76:280–283.
39. Silman AJ, Mitchell P, Nicholls RJ, et al. Self-reported dark red bleeding as a marker comparable with occult blood testing in screening for large bowel neoplasms. *Br J Surg*. 1983;70:721–724.
40. Farrands PA, Hardcastle JD. Colorectal screening by a self-completion questionnaire. *Gut* 1984;25:445–447.
41. Chapuis PH, Goulston KJ, Dent OF, Tait AD. Predictive value of rectal bleeding in screening for rectal and sigmoid polyps. *BMJ*. 1985;290:1546–1548.
42. Dent OF, Goulston KJ, Zubrzycki J, Chapuis PH. Bowel symptoms in an apparently well population. *Dis Colon Rectum*. 1986;29:243–247.
43. Jones R, Lydeard S. Irritable bowel syndrome in the general population. *BMJ*. 1992;303:87–90.
44. Fijten G, Blijham GH, Knottnerus JA. Occurrence and clinical significance of overt blood loss per rectum in the general population and in medical practice. A review. *Br J Gen Pract*. 1994;44:320–325.
45. Jones R. Self care. *BMJ*. 2000;320:596.
46. Thompson MR, Swarbrick ET, Ellis BG, et al. Strategies for the efficient management of all patients with lower gastrointestinal symptoms to achieve effective diagnosis of colorectal cancer. In: Cunningham D, Topham C, Miles A, eds. *The Effective Management of Colorectal Cancer*. 2nd ed. London: Aesculapius Medical Press; 2000: 173.
47. Sackett DL, Haynes RB, Guyatt GH, Tugwell P. *Clinical Epidemiology—A Basic Science for Clinical Medicine*. 2nd ed. Boston: Little Brown & Co; 1991: 4.
48. Neighbour R. *The Inner Consultation. How to Develop an Effective and Intuitive Consulting Style*. Lancaster: MTP Press Limited; 1987.
49. Feinstein AR. Symptoms as an index of biological behaviour and prognosis in human cancer. *Nature*. 1966;209:241–245.
50. Baig MK, Whatley P, Thompson MR. Delays during stages of referral diagnosis and treatment of colorectal cancer: their relationship to mortality. *Colorect Dis*. 1999;1(suppl 1):3.
51. Copeland EM, Miller LD, Jones RS. Prognostic factors in carcinoma of the colon and rectum. *Am J Surg*. 1968;116:875–881.
52. Pescatori M, Maria G, Beltrani B, Mattana C. Site, emergency and duration of symptoms in the prognosis of colorectal cancer. *Dis Colon Rectum*. 1982; 25:33–40.
53. Mulcahy HE, O'Donoghue DP. Duration of colorectal cancer symptoms and survival: the effect of confounding clinical and pathological variables. *Eur J Cancer*. 1997;33:1461–1467.

54. Barillari P, de Angelis R, Valabrega S, et al. Relationship of symptom duration and survival in patients with colorectal carcinoma. *Eur J Surg Oncol.* 1989;15: 441–445.
55. McDermott F, Hughes E, Pihl E, Milne B, Price A. Symptom duration and survival prospects in carcinoma of the rectum. *Surg Gynecol Obstet.* 1981;153: 321–326.
56. Holliday HW, Hardcastle JD. Delay in diagnosis and treatment of symptomatic colorectal cancer. *Lancet* 1979;2:309–311.
57. Tamoney HJ Jr, Caldarelli RA. Cancer of the right colon. An analysis of 211 patients. *Dis Colon Rectum.* 1966;9:13–19.
58. McDermott FT, Hughes ESR, Pihl E, Milnes BJ, Price AB. Prognosis in relation to symptom duration in colon cancer. *Br J Surg.* 1981;68:846–849.
59. Clarke AM, Jones ISC. Diagnostic accuracy and diagnostic delay in carcinoma of the large bowel. *NZ Med J.* 1970;71:341–347.
60. Jolly KD, Scott JP, MacKinnon MJ, Clarke AM. Diagnosis and survival in carcinoma of the large bowel. *Aust NZ J Surg.* 1982;52:12–16.
61. Turnbull PRG, Isbister WH. Colorectal cancer in New Zealand: a Wellington study. *Aust NZ J Surg.* 1979;49:365–367.
62. Bassett ML, Bennett SA, Goulston KJ. Colorectal cancer. A study of 230 patients. *Med J Aust.* 1979;1:589–592.
63. Schillaci A, Cavallaro A, Nicolanti V, Ferri M, Gallo P, Stipa S. The importance of symptom duration in relation to prognosis of carcinoma of the large intestine. *Surg Gynecol Obstet.* 1984;158:423–426.
64. Khubchandani M. Relationship of symptom duration and survival in patients and carcinoma of the colon and rectum. *Dis Colon Rectum.* 1985;28:585–587.
65. Polissar L, Sim D, Francis A. Survival of colorectal cancer patients in relation to duration of symptoms and other prognostic factors. *Dis Colon Rectum.* 1981; 24:364–369.
66. Wessex Colorectal Cancer Audit. Final Report on behalf of the Wessex Colorectal Cancer Working Group. October 2000. *South-West Cancer Intelligence Service.* Hampshire, U.K.
67. Hackett TP, Cassem NH, Raker JW. Patient delay in cancer. *N Eng J Med.* 1973;289:14–20.
68. Robinson E, Mohilever J, Zidan J, Sapir D. Colorectal cancer: incidence delay in diagnosis and stage of disease. *Eur J Cancer Clin Oncol.* 1986;22:157–161.
69. Rowe-Jones D, Aylett S. Delay in treatment in carcinoma of colon and rectum. *Lancet* 1965;2:973–976.
70. Welch CE, Burke JF. Carcinoma of the colon and rectum. *N Engl J Med.* 1962; 266:846; 211–9.
71. Rubin M, Zer M, Dintsman M. Factors influencing delay in treatment of cancer of rectum and colon in Israel. *Israel J Med Sci.* 1980;16:641–645.
72. Launoy G, Le Courtour X, Gignoux M, Pottier D, Dugleux G. Influence of rural environment on diagnosis, treatment and prognosis of colorectal cancer. *J Epidemiol Community Health.* 1992;46:365–367.
73. Clarke JP, Kettlewell MGW, Dehn TCB. Changing patterns of colorectal cancer in a regional teaching hospital. *Ann R Coll Surg Engl.* 1992;74:291–293.
74. Chapuis PH, Dent OF, Fisher R, et al. A multivariate analysis of clinical and pathological variables in prognosis after resection of large bowel cancer. *Br J Surg.* 1985;72:698–702.

75. Baig MK, Whatley P, Thompson MR. Does early diagnosis and prompt treatment of symptomatic colorectal cancer improve survival. *Gut* 1998;42(suppl 1): A93.
76. Macdonald I. Biological predeterminism in human cancer. *Surg Gynecol Obstet.* 1951;92:443–452.
77. Macdonald I. The individual basis of biologic variability in cancer. *Surg Gynecol Obstet.* 1958;106:227–229.
78. Ragland JJ, Londe AM, Spratt JS Jr. Correlation of the prognosis of obstructing colorectal carcinoma with clinical and pathologic variables. *Am J Surg.* 1971; 121:552–556.
79. Stubbs RS, Long MG. Symptom duration and pathologic staging of colorectal cancer. *Eur J Surg Oncol.* 1986;12:127–130.
80. Irvin TT, Greaney MG. Duration of symptoms and prognosis of carcinoma of the colon and rectum. *Surg Gynecol Obstet.* 1997;144:883–886.
81. Slaney G. Results of treatment of carcinoma of the colon and rectum. In: Irvine WT, ed. *Modern Trends in Surgery* 3. London: Butterworths; 1971:69–89.
82. Kyle SM, Isbister WH, Yeong ML. Presentation, duration of symptoms and staging of colorectal carcinoma. *Aust NZ J Surg.* 1991;61:137–140.
83. Ratcliffe R, Kiff RS, Kingston RD, Walsh SH, Jeacock J. Early diagnosis in colorectal cancer. Still no benefit? *J R Coll Surg Edinb.* 1989;34:152–155.
84. Dent OF, Chapuis PH, Goulston KJ. Relationship of survival to stage of the tumour and duration of symptoms in colorectal cancer. *Med J Aust.* 1983; 1:274–275.
85. Goodman D, Irvin TT. Delay in the diagnosis and prognosis of carcinoma of the right colon. *Br J Surg.* 1993;80:1327–1329.
86. Baig MK, Whatley P, Thompson MR. Delay in diagnosis and treatment of colorectal cancer of colorectal cancer: does it affect outcome? *Colorect Dis.* 1999;1(suppl 1):3.
87. Muir Gray JA. *Evidence-Based Healthcare: How to Make Health Policy and Management Decisions.* New York: Churchill Livingstone; 1997.
88. Sackett DL, Haynes RB, Guyatt GH, Tugwell P. *Clinical Epidemiology—A Basic Science for Clinical Medicine.* 2nd ed. Boston: Little Brown & Co; 1991: 283–302.
89. Marshall KG. Prevention. How much harm? How much benefit? 3. Physical psychological and social harm. *Can Med Assoc.* 1996;155:169–170.
90. Haynes RB, Sackett DL, Taylor DW, Gibson ES, Johnson AL. Increased absenteeism from work after detection and labelling of hypertensive patients. *N Engl J Med.* 1978;299:741–744.
91. MacDonald LA, Sackett DL, Haynes RB, Taylor DW. Labelling in hypertension: a review of the behavioural and psychological consequences. *J Chron Dis.* 1984;37:933–942.
92. Williams CB. Colonoscopy. *Br Med Bull.* 1986;42:265–269.
93. Waye JD, Kahn O, Auerbach ME. Complications of colonoscopy and flexible sigmoidoscopy. *Gastrointest Endosc Clin N Am.* 1996;6:343–377.
94. Blakeborough A, Sheridan MB, Chapman AH. Complications of barium enema examinations: a survey of UK consultant radiologists 1992 to 1994. *Clin Radiol.* 1997;52:142–148.
95. Muir Gray JA. *Evidence-Based Healthcare: How to Make Health Policy and Management Decisions.* New York: Churchill Livingstone; 1997:39.

96. Staniland JR, Ditchburn J, De Dombal FT. Clinical presentation of diseases of the large bowel. A detailed study of 642 patients. *Gastroenterology* 1976;70: 22–28.
97. Chave H, Flashman K, Senapati A, Cripps NPJ, Thompson MR. Characteristics of the change in bowel habit in patients with colorectal cancer. *Colorect Dis.* 2000;2(suppl 1):1–2.
98. Cancer Research UK. Large Bowel Cancer Factsheet. April 2004. *Cancer Research UK*. London.