

# Flexible sigmoidoscopy and the changing distribution of colorectal cancer: implications for screening

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## Abstract

**Background and aims**—There has been a significant proximal shift in the distribution of colorectal cancer (CRC) in Northern Ireland over recent decades. The aim of this study was to investigate the potential implications of this proximal shift in CRC distribution on the efficacy of flexible sigmoidoscopy (FS) as a screening tool.

**Patients and methods**—The site distribution of 5153 CRCs was available from the Northern Ireland Colorectal Cancer Register for the period 1990–1997. Similar data on 1241 CRCs between 1976 and 1978 were available from a previous study. Data on the site reached by FS were obtained from a prospectively collected endoscopy database at one of Northern Ireland's main teaching hospitals for the period 1993–1998.

**Results**—There was a significant proximal shift in CRC distribution between the two periods (23.5% proximal to the splenic flexure between 1976 and 1978 *v* 36.7% between 1990 and 1997;  $p < 0.001$ ). The descending colon was visualised during 74.4% of FS examinations. By combining the observed extent of FS examination with CRC site distribution, it was calculated that FS could have visualised 68.8% of CRCs between 1976 and 1978 but only 56.0% between 1990 and 1997. Extrapolating these data to a Northern Ireland screening programme involving FS and faecal occult blood testing suggests that significantly more CRCs could have been detected between 1976 and 1978 than between 1990 and 1997 (51.7% *v* 48.2%, respectively;  $p = 0.03$ ).

**Conclusions**—This study confirms the previously documented left to right shift in CRC distribution in Northern Ireland and demonstrates that if this shift continues, FS will become less successful as a screening tool than is currently predicted. (*Gut* 2001;48:522–525)

Keywords: colorectal cancer; screening; flexible sigmoidoscopy; endoscopy

Colorectal cancer (CRC) is an important disease, being responsible for 19 000 deaths/year in the UK (450 in Northern Ireland)<sup>1,2</sup> with a cost to the National Health Service of £1 million/year/250 000 population (50% on surgery, 28% on palliative care, 10% on follow up, and 12% on other).<sup>3</sup> Despite advances in surgery and adjuvant treatment, the prognosis for CRC has not improved materially over the

past 20 years, with an average survival of three years following diagnosis.<sup>3</sup> There is also evidence suggesting that the five year survival of CRC may be worse in the UK than in other parts of Europe.<sup>4</sup> This was one of the reasons why the former chief medical officer began a programme of major reforms in the organisation of cancer services in the UK and initiated the publication of guidelines on commissioning cancer services aimed at improving outcomes in CRC.<sup>5</sup> In the USA, CRC is the second leading cause of death from cancer, with approximately 50% of patients with CRC dying of the disease and an estimated 56 000 deaths in the USA in 1998.<sup>6</sup>

Screening for CRC, which would fulfill many of the necessary criteria,<sup>7,8</sup> is an attractive proposition as surgery for early CRC is curative. However, the most acceptable and cost effective screening tool for CRC is still open to debate.<sup>9–16</sup> One potential screening strategy involves the use of flexible sigmoidoscopy (FS),<sup>13,16</sup> with an estimated reduction in mortality of 18–40%.<sup>14</sup>

There has been a well documented proximal shift in the distribution of CRC<sup>17,18</sup> in several Western countries, including Northern Ireland. If this change in CRC distribution continues, it may have a significant effect on the future usefulness of FS as a screening tool for CRC. The aim of the present study was to investigate the likely impact of the proximal shift in CRC site on the efficacy of FS as a population screening tool. This was evaluated by examining the changing distribution of CRC in Northern Ireland (population 1.68 million, 1998, General Register Office, Northern Ireland) and by examining the completion rates of FS in one of Northern Ireland's main teaching hospitals.

## Methods

Demographic, clinical, and pathological data on all new histologically confirmed cases of CRC between 1990 and 1997 were available from the Northern Ireland Colorectal Cancer Register. Tumours were categorised as proximal (caecum, ascending colon, hepatic flexure, and transverse colon), distal (splenic flexure, descending and sigmoid colon), and rectal (rectosigmoid junction and rectum). Data were available on the distribution of CRC for the years 1976–1978<sup>19</sup> where the site of the primary tumour had also been obtained from

**Abbreviations used in this paper:** CRC, colorectal cancer; FS, flexible sigmoidoscopy; NICR, Northern Ireland Cancer Registry; FOBT, faecal occult blood testing; UC, ulcerative colitis.

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the pathology request and result forms and from operative records. Although data for both periods were not available from a single source, the method of data collection for both periods was based on pathology request forms within the relatively closed community of Northern Ireland. As an independent check on the current site distribution of CRC in Northern Ireland, data were also obtained from the Northern Ireland Cancer Registry (NICR). It collects data on a wide range of cancers, including CRC. The NICR obtains information on cancer automatically from hospital pathology laboratories, the hospital patient administration system, and the registrar general's office. Data were available on the site distribution of CRC for the period 1993–1995.

Data on FS were obtained from a prospectively collected endoscopy database (Endoscopy Record Systems, Micromed, UK) in the Royal Victoria Hospital, Northern Ireland, for the period 1 November 1993 to 27 April 1998. Comprehensive patient demographics and endoscopy details were entered at the time of examination and data stored on disk for later retrieval and analysis. Those examinations carried out for assessment of colitis were excluded. The "level reached" during FS is that recorded by the endoscopist.

FS has previously been defined as complete when the long view of the descending colon is visualised.<sup>13</sup> It is assumed that such a "complete" examination will diagnose all abnormalities distal to and including the splenic flexure. Although such an assumption is likely to overestimate the efficacy of FS as a screening tool, this assumption will be used in the present study. Similarly, it will be assumed that once the ascending colon is reached, all abnormalities in the proximal colon will be diagnosed. Multiple CRCs will be treated as rectal tumours as they are likely to be diagnosed on FS.

#### STATISTICAL ANALYSIS

Differences in proportions were assessed using a  $\chi^2$  test for contingency tables with Yates' continuity correction. Significance was accepted at the 5% level.

#### Results and modelling

The change in distribution of CRC over the period 1976–1978 to 1990–1997 is shown in table 1.<sup>18</sup> These data show a significant increase in the percentage of tumours diagnosed proximal to the splenic flexure (23.6% in 1976–1978 *v* 36.7% in 1990–1997;  $p < 0.001$ ,  $\chi^2 = 76.33$ ,  $df = 1$ ). As there are a similar number of unknown sites in each period, these will be excluded in future discussion.

Table 1 Distribution of colorectal cancer (CRC) diagnosed between 1976–78 and 1990–97

Site	No (%) CRC/site 1976–78 <sup>18</sup>	No (%) CRC/site 1990–97
Proximal	292 (23.6)	1890 (36.7)
Distal	339 (27.2)	1398 (27.1)
Rectal	551 (44.4)	1643 (31.9)
Unknown	59 (4.8)	183 (3.5)
Multiple	0 (0.0)	39 (0.8)
Total	1241 (100)	5153 (100)

The NICR contained data on 2767 CRCs for the years 1993–1995. This larger number of CRCs per year (922.3/year in the database of NICR *v* 644.1/year in the Northern Ireland CRC registry) reflects a difference in the methods of collecting data. The NICR data were based on histology in 82.5% of cases, imaging in 3.3% of cases, and others (for example, death certificate, clinical diagnosis) in 14.2% of cases. Of the 2767 CRCs in the NICR, 764 (27.6%) were proximal to the splenic flexure, 560 (20.2%) distal colon, 895 (32.4%) rectal, and 548 (19.8%) of unknown site. The percentage of CRCs proximal to the splenic flexure appears small due to the large number of unknown sites (where the diagnosis was histologically proved in 62.2% of cases). If the latter are excluded, these data are broadly comparable with the Northern Ireland CRC registry (the percentage of CRCs of known site proximal to the splenic flexure is 34.4% in the NICR *v* 38.3% in the Northern Ireland CRC registry). If the actual site distribution among the cases with unknown sites were comparable with known sites, our conclusions would not be materially different. In the future discussion the CRC distribution will be based on the Northern Ireland CRC register.

Indications for carrying out flexible sigmoidoscopies undertaken at the Royal Victoria Hospital are shown in table 2. Table 3 shows the level reached during FS, as determined by the endoscopist. The sigmoid colon was reached 98.8% of the time with the acute bend of the sigmoid/descending colon successfully manoeuvred approximately 74.4% of the time and the terminal ileum actually reached on 1.6% of occasions when the initial aim of the endoscopy was FS. It is probable that a colonoscope was used in such extensive FS examinations. As the aim of the study was to anticipate the likely benefit of FS as a screening tool, the completion rate has not been adjusted

Table 2 Indications for flexible sigmoidoscopy (often multiple)

Indication	No
Rectal bleeding	312
Anaemia	51
Abdominal pain	170
Abdominal mass	1
Change in bowel habit	346
Abnormal barium enema	64
Positive FOBT	8
Polyp follow up	47
Cancer follow up	18
Surveillance (including UC)	17
Miscellaneous	83
Total	117

FOBT, faecal occult blood test; UC, ulcerative colitis.

Table 3 Level reached during flexible sigmoidoscopy between 1993 and 1998, as determined by the endoscopist

Site reached	No	%
Terminal ileum	15	1.6
Caecum	18	2.0
Ascending colon	30	3.3
Hepatic flexure	31	3.4
Transverse colon	71	7.8
Splenic flexure	229	25.0
Descending colon	681	74.4
Sigmoid colon	904	98.8
Rectum	915	100

Table 4 Reasons for failure of completion of flexible sigmoidoscopy in relation to sex (data missing for 36 cases)

	Men (No (%))	Women (No (%))
Incomplete		
Technical	48 (10.4)	83 (13.1)
Disease	36 (7.8)	44 (7.0)
Poor preparation	2 (0.4)	1 (0.2)
Total	86 (18.7)	128 (20.2)
Complete	289 (62.7)	376 (59.5)

Table 5 Potential number of colorectal cancers (CRCs) detected by flexible sigmoidoscopy (FS) (excluding those of unknown site and categorising multiple tumours as rectal as they are likely to be detected by FS)

Site	% of FS viewing site	No CRC potentially detected by FS/site (total No CRC/site)	
		1976-78	1990-97
Proximal	3.3	9.6 (292)	62.4 (1890)
Distal	74.4	252.2 (339)	1040.1 (1398)
Rectal	100	551.0 (551)	1682.0 (1682)
Total		812.9 (1182)	2784.5 (4970)

for failure due to poor bowel preparation. Also, as examinations for colitis activity were excluded and only nine strictures identified during the study period, adjustment for failure due to the presence of disease (presumably of lower incidence in the general population than in this selected subgroup) would have little effect on the overall completion rates.

There was no significant difference in crude completion rates between men and women (289/375 *v* 376/504, respectively;  $p=0.40$ ,  $\chi^2=0.58$ ,  $df=1$ ) (table 4).

It is possible to estimate the number of CRCs which could be detected by FS in Northern Ireland by excluding those where the site is unknown and assuming: (1) the observed FS completion rate in this study would apply to a population screening programme, (2) everyone with CRC underwent FS, (3) that FS is 100% sensitive for CRC, and (4) no other diagnostic tests were applied. Under these assumptions, the observed left to right shift in CRC distribution means that whereas FS could have directly visualised 68.8% (812.9/1182) of cancers between 1976 and 1978, only 56.0% (2784.5/4970) could have been similarly visualised between 1990 and 1997 ( $p<0.001$ ,  $\chi^2=63.38$ ,  $df=1$ ) (table 5).

When estimating the potential benefit of FS as a screening tool, the following limitations

Table 6 Potential number of colorectal cancers (CRCs) detected by a screening programme combining flexible sigmoidoscopy (FS) with faecal occult blood testing (FOBT) (excluding those of unknown site and categorising multiple tumours as rectal as they are likely to be detected by FS)

Site	% of CRC possibly detected by FS	No (%) CRC potentially detected by screening programme	
		1976-78	1990-97
Proximal	3.3	9.6	62.4
Distal	74.4	252.2	1040.1
Rectal	96.5	531.7	1623.1
Subtotal		793.6	2725.6
	22.6% of undiagnosed proximal CRCs detected indirectly <sup>23</sup>	+63.8	+413.0
Subtotal		857.4	3138.6
	51% non-compliant <sup>13</sup>	-437.3	-1600.1
	25% of remaining undiagnosed CRCs detected by FOBT <sup>28, 29</sup>	+190.5	+858.0
Total		610.6 (51.7)	2396.5 (48.2)

need to be taken into account: (1) FS has a 96.5% sensitivity rate in the rectosigmoid area for CRC (one study examining the use of both FS and double contrast barium enema following a positive faecal occult blood test (FOBT) showed that two of 57 CRC in the rectosigmoid area viewed by FS were missed),<sup>20</sup> and (2) FS screening programmes are likely to have a 38% compliance rate in Ireland<sup>21</sup> and 49% in the UK.<sup>13</sup> Such low compliance rates may be improved by appropriate educational programmes aimed at increasing public awareness of CRC and the advantages of screening combined with more accessible FS, such as community clinics offering complete FS with no unnecessary delay.<sup>22</sup>

Factors which may increase the diagnostic yield of an FS screening programme include follow up of any abnormality found during FS with a complete colonoscopy. One study has shown that 22.6% (81/358) of proximal CRCs have a synchronous distal abnormality<sup>23</sup> whereas another has shown it may be as high as 34.5% (40/116).<sup>24</sup> Another method of increasing the diagnostic yield of an FS screening programme would be the additional use of FOBT to detect proximal CRCs. However, FOBT is unlikely to provide additional benefit to a FS screening programme<sup>25</sup> because: (1) FOBT may have a low sensitivity for asymptomatic proximal lesions,<sup>21, 26</sup> (2) it may be necessary to repeat FOBT every one to two years, requiring intensive patient follow up, and (3) compliance is likely to be low. However, a Japanese study of 11 333 colonoscopies carried out as part of a health checkup suggested that FS as a screening tool on its own would have missed 73.7% of proximal high risk tumours but would have missed only 62.0% when combined with immunological FOBT.<sup>27</sup> The use of FOBT will therefore be included in the following discussion.

To estimate the likely sensitivity of a FS screening programme in Northern Ireland, one might assume a 96.5% sensitivity rate in the rectosigmoid area,<sup>20</sup> an expected 49% compliance rate,<sup>13</sup> indirect detection of 22.6% of proximal CRCs during follow up of any synchronous distal abnormalities,<sup>23</sup> and the possibility of an additional 25% of CRCs being detected by concurrent use of non-rehydrated FOBT.<sup>28, 29</sup> In a combined FS and FOBT screening programme it is difficult to know whether patients non-compliant with FS would be compliant with FOBT. For the purposes of the following discussion, FOBT will be assumed to detect 25% of the CRCs not detected (either directly or indirectly) by FS. Such a population screening programme applied to Northern Ireland could have detected significantly more CRCs in 1976-1978 than in 1990-1997 (51.7% *v* 48.2%, respectively;  $p=0.03$ ,  $\chi^2=4.41$ ,  $df=1$ ) (table 6).<sup>13, 23, 28, 29</sup> This decrease in sensitivity of 3.5% means that in 1997, when there were 669 surgically treated CRCs in Northern Ireland, 23.4 fewer cancers would have been detected by such a screening programme as a result of the left to right shift in CRC distribution (345.9 *v* 322.5;  $p=0.20$ ,  $\chi^2=1.50$ ,  $df=1$ ).

## Discussion

This study has examined the potential number of CRCs which could be diagnosed by a screening programme consisting of FS and FOBT. It has not attempted to assess the detection rate of polyps which would be of greater interest to a long term screening programme. However, the changes observed in the distribution of CRC can realistically be assumed to reflect earlier changes in the distribution of potentially neoplastic polyps, allowing conclusions to be made regarding the potential usefulness of FS as a screening tool.

This study has also not attempted to identify the cause of the proximal shift in CRC distribution in Northern Ireland. What is clear is that clinicians in Northern Ireland are currently confronted with a group of patients where an increasing percentage of tumours are proximal to the splenic flexure. Whatever the reason for this shift, it has important implications for screening of CRC.

A problem with any such study on sigmoidoscopy/colonoscopy completion rates is that there is no way of confirming the exact anatomical site reached. However, our results are in keeping with other recently reported studies, for example, 75.2% (8671/11531) of FS carried out for CRC screening in an American study achieved a depth of >40 cm and only 34.2% (3942/11 531) achieved a depth of 60 cm.<sup>30</sup> Another American study revealed that 80% (144/180) of FS achieved a depth of >40 cm and this was reduced to 70% when the aim of the FS was screening.<sup>31</sup> In the latter case the reasons for incomplete FS were technical 51%, disease 15%, and poor preparation/stool 34%. One method for increasing FS completion rates may be to use a colonoscope to ensure adequate scope length to reach the splenic flexure.

In addition to any change in the sensitivity of FS for detecting CRC, any programme leading to positive screening tests for CRC would require follow up colonoscopy to fully visualise the bowel and treat premalignant lesions. On top of the burden of the screening programme itself, this could have considerable implications for limited financial and endoscopy resources. Any endoscopy based screening programme will require a substantial investment in endoscopy facilities and trained staff. It has been estimated<sup>14</sup> that FS will have a 10–20% positivity rate if repeated five yearly from 50 to 65 years old, that annual rehydrated FOBT from 50 to 65 years old will have a 30% positivity rate (with 15 positive tests per life saved),<sup>32</sup> and that their combined use will have a 50% positivity rate. If 50% of people may ultimately need a colonoscopy, it may be more practical to offer everyone a once off diagnostic colonoscopy at a selected age.

Although CRC screening is an attractive proposition with a 30% reduction in mortality<sup>9</sup> saving 5700 lives/year in the UK, this study confirms the previously documented left to right shift in CRC distribution in Northern Ireland<sup>18</sup> and demonstrates that if this shift continues, FS will become less successful as a screening tool than is currently predicted.

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