

**Keywords:** colorectal cancer; population screening; early-stage disease; gFOBt; FIT

# Temporal trends in mode, site and stage of presentation with the introduction of colorectal cancer screening: a decade of experience from the West of Scotland

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**Background:** Population colorectal cancer screening programmes have been introduced to reduce cancer-specific mortality through the detection of early-stage disease. The present study aimed to examine the impact of screening introduction in the West of Scotland.

**Methods:** Data on all patients with a diagnosis of colorectal cancer between January 2003 and December 2012 were extracted from a prospectively maintained regional audit database. Changes in mode, site and stage of presentation before, during and after screening introduction were examined.

**Results:** In a population of 2.4 million, over a 10-year period, 14 487 incident cases of colorectal cancer were noted. Of these, 7827 (54%) were males and 7727 (53%) were socioeconomically deprived. In the postscreening era, 18% were diagnosed via the screening programme. There was a reduction in both emergency presentation (20% prescreening vs 13% postscreening,  $P \leq 0.001$ ) and the proportion of rectal cancers (34% prescreening vs 31% pos-screening,  $P \leq 0.001$ ) over the timeframe. Within non-metastatic disease, an increase in the proportion of stage I tumours at diagnosis was noted (17% prescreening vs 28% postscreening,  $P \leq 0.001$ ).

**Conclusions:** Within non-metastatic disease, a shift towards earlier stage at diagnosis has accompanied the introduction of a national screening programme. Such a change should lead to improved outcomes in patients with colorectal cancer.

Several large randomised control trials examining guaiac-based faecal occult blood test (gFOBt) colorectal cancer screening programmes have shown a reduction in cancer-specific mortality through the detection of early-stage disease (Mandel *et al*, 1993; Kronborg *et al*, 1996; Scholefield *et al*, 2002). Therefore, national bowel screening programmes have been introduced across the United Kingdom over the past 10 years. However, it is important to consider screening within the context of the

whole population that is being served by the screening programme. For example, the current Scottish Bowel Screening Programme (SBoSP) is targeted only at those aged between 50 and 74 years, with few over the age of 74 years opting for further testing. In addition, there is limited uptake, sensitivity and specificity of the testing algorithms in use. Therefore, clearly, not all tumours will be screen detected, and it is unclear what the overall impact on the population will be.

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Indeed, a previous single centre study from Scotland has suggested that screen-detected tumours may account for just 17% of all tumours diagnosed within a population invited to screening (Roxburgh *et al*, 2013). Additionally, it has been noted that despite the programme detecting an increased number of early-stage tumours, it may not lead to an overall stage shift to earlier disease across the population (Roxburgh *et al*, 2013).

The aim of the present study was to examine the impact that screening has had on the mode, site and stage of presentation of colorectal cancer in the West of Scotland over the past decade. The aim was to achieve this by using population statistics from the West of Scotland Managed Clinical Network (MCN) to compare cohorts before, during and after the introduction of the SBoSP.

## PATIENTS AND METHODS

The MCN covers four Health Boards (Ayrshire and Arran, Forth Valley, Greater Glasgow and Clyde and Lanarkshire) comprising 16 different hospitals and covering a population of over 2.4 million, just under half of the population of Scotland (Table 1). It was created in 2000 with the aim of improving outcomes in colorectal cancer. All patients discussed at a local hospital multidisciplinary team (MDT) with a diagnosis of colorectal cancer are included, with the clinicopathological data prospectively recorded. Details including age, sex, socioeconomic deprivation status, mode of presentation and tumour site and stage are routinely stored. For the present study, data were extracted for a period from 1st January 2003 to 31st December 2012.

The mode of presentation was defined as emergency if the patient underwent management involving a hospital admission that was unplanned. This included, but was not limited to, significant rectal bleeding, colonic obstruction and perforation. Other routes were defined as elective including screen detected, which was introduced as a data point from 2007 onwards.

Tumour site was classified according to anatomical site as per the International Classification of Disease version 10 (ICD-10). Lesions up to, but not including, the splenic flexure were classified

as right sided (C18.0–C18.4), those from splenic flexure up to, but not including, the retosigmoid junction were defined as left sided (CC18.5–C18.7) and tumours of the rectosigmoid junction and rectum were classed as rectal (C19 and C20). Tumour stage was defined according to the standard TNM (version 5) classification (Sobin and Fleming, 1997) based on histological resection of specimens and, in those who did not undergo resection, on preoperative imaging modalities. Polyp cancers, which underwent endoscopic excision only, were classified as stage I disease. Intent of procedure was collated at the time of resection as either curative or palliative by the surgical team responsible for each individual patient.

Socioeconomic deprivation status was calculated from the Scottish Index of Multiple Deprivation, which is an index of relative deprivation (Scottish Government, 2009). Quintiles of deprivation were used to assign individuals to a relative deprivation category based on their postcode at their time of diagnosis, with the first quintile representing the most deprived and the fifth quintile, the least deprived. The most current version of SIMD was used at the time of data collection (i.e., SIMD 2004 for patients in 2003 to 2005, SIMD 2006 for patients in 2006, 2007 and 2008 .and so on).

The SBoSP is a biennial gFOBt/faecal immunochemical test (FIT)-based screening programme for all individuals aged 50–74 years. Details regarding the current screening algorithm have been published previously (Fraser *et al*, 2012). Briefly, all individuals aged 50–74 years are sent a preinvitation letter and then a gFOBt, and later referred for colonoscopy if this is returned and is strongly positive ( $\geq 5$  of 6 windows positive). In the case of a weakly positive gFOBt (1–4 of 6 windows positive), spoiled or untestable kit, a confirmatory FIT is sent. Individuals then proceed to colonoscopy, following preassessment by a bowel screening preassessment nurse. Screening was introduced across the four Health Boards at staged intervals (Table 1); therefore, the data were separated into five distinct time frames: 2003–2004 early pre-screening (EPrS), 2005–2006 late prescreening, 2007–2008 early introduction of screening, where the minority of the population were invited, 2009–2010 late introduction of screening, where the majority of the population were invited and 2011 to 2012 postintroduction of screening (PoS), where screening had been introduced across all four boards. This allowed for assessment not only of the impact of screening but also of the temporal changes in disease presentation and management across the area over the decade.

Permission for the study was granted by the Caldicott guardian for the data and all data were stored and analysed in an anonymised manner

**Statistical analyses.** The  $\chi^2$  test for linear trend was used to test associations between variables and calendar time. A  $P$ -value  $\leq 0.05$  was considered statistically significant. Statistical analysis was performed using the SPSS software (SPSS Inc., Chicago, IL, USA)

**Table 1. Population of NHS Health Boards across Scotland, date of screening introduction and uptake of test**

NHS Health Board	Population (est. 2009)	Screening introduction	Screening uptake (%) <sup>a</sup>
Grampian	559 210	June 2007	61
Fife	361 410	June 2007	56
Tayside	404 390	June 2007	59
<b>Ayrshire and Arran</b>	<b>372 380</b>	<b>September 2007</b>	<b>55</b>
Orkney	20 940	October 2007	63
<b>Forth Valley</b>	<b>294 140</b>	<b>December 2007</b>	<b>55</b>
Lothian	816 640	May 2008	54
Western Isles	27 420	July 2008	57
Dumfries and Galloway	151 160	December 2008	58
<b>Greater Glasgow and Clyde</b>	<b>1 199 830</b>	<b>April 2009</b>	<b>53</b>
<b>Lanarkshire</b>	<b>569 800</b>	<b>August 2009</b>	<b>48</b>
Shetland	22 790	October 2009	64
Borders	113 380	November 2009	60
Highland	318 200	December 2009	61

Abbreviation: NHS = National Health Service.

<sup>a</sup>Derived from invitations between 1st November 2010 and 31st October 2012 (Information Services Division Scotland (ISD), 2013).

## RESULTS

From 1st January 2003 to 31st December 2012, inclusive, there were 14 487 incident cases of colorectal cancer. There were 7827 (54%) males, 8142 (56%) patients were between 50 and 74 years old and 7727 (53%) patients were in the two most deprived quintiles of deprivation. Overall, 2163 (15%) patients presented to surgery as an emergency (Table 2).

On examining patient demographics over the decade of analysis, there were no changes seen in the age and sex of patients at diagnosis; however, there was a weak trend for those in PoS to be more deprived in later years ( $P = 0.057$ ). There was a significant reduction in the proportion of patients presenting to surgery as an

**Table 2. Temporal trends in colorectal cancer presentation with the introduction of screening**

	All patients		Pre-screening				Screening introduction				Postscreening		P-value
	n (14 487)	%	Early		Late		Early		Late		2011–2012		
			2003–2004		2005–2006		2007–2008		2009–2010				
			n (2380)	%	n (2384)	%	n (3098)	%	n (3282)	%	n (3343)	%	
<b>Age (years)</b>													
≤50	751	5	129	5	129	5	172	6	139	4	182	5	0.584
50–74	8142	56	1250	53	1368	57	1702	55	1897	58	1925	58	
≥75	5299	37	851	35	793	33	1202	39	1224	37	1229	37	
Unknown	295	2	150	6	94	4	22	1	23	1	6	0	
<b>Sex</b>													
Female	6364	44	1017	42	1054	44	1384	45	1416	43	1493	45	0.169
Male	7827	54	1213	51	1236	52	1692	55	1843	56	1843	55	
Unknown	296	2	150	6	94	4	22	1	23	1	7	0	
<b>Deprivation category</b>													
1 (most deprived)	4329	30	667	28	706	30	935	30	978	30	1043	31	0.057
2	3398	23	545	23	555	23	732	24	776	24	790	24	
3	2370	16	364	15	380	16	529	17	557	17	540	16	
4	1921	13	307	13	300	13	406	13	433	13	475	14	
5 (least deprived)	2072	14	247	16	349	15	474	15	514	16	488	15	
Unknown	297	2	150	6	94	4	22	1	24	1	7	0	
<b>Presentation to surgery</b>													
Emergency	2163	15	480	20	431	18	414	13	420	13	418	13	≤0.001 <sup>b</sup>
Elective													
Symptomatic	8948	62	1849	78	1868	78	1910	62	1729	53	1592	47	
Screen detected <sup>a</sup>	1200	8	—	—	—	—	107	3	486	15	607	18	
Did not undergo procedure	2056	14	30	1	56	2	624	20	642	20	704	21	
Unknown	115	1	21	5	29	3	43	1	5	0	22	1	
<b>Site of tumour</b>													
Right colon	4857	34	753	32	811	34	1048	34	1099	34	1146	34	0.001
Left colon	4827	33	790	33	736	31	997	32	1165	35	1139	34	
Rectum	4647	32	825	34	818	34	996	32	983	30	1025	31	
Multiple/unknown	156	1	12	1	19	1	57	2	35	1	33	1	
<b>Management Intent</b>													
Curative intent	9980	68	1797	76	1744	73	1972	64	2238	68	2229	67	≤0.001 <sup>c</sup>
Palliative procedure	1877	13	440	18	389	16	337	11	334	10	377	11	
Did not undergo procedure	2056	14	30	1	56	2	624	20	642	20	704	21	
Unknown/other	574	4	113	5	195	8	165	5	68	2	33	1	

<sup>a</sup>Recorded from 2007 onwards.<sup>b</sup>Emergency vs all elective (including screen detected).<sup>c</sup>Curative vs palliative resection.

emergency over the timeframe from 20% EPrS to 13% PoS ( $P \leq 0.001$ ) (Table 2).

On examining tumour characteristics, there was a reduction in the proportion of rectal cancers diagnosed over the timeframe from 34% EPrS to 31% PoS ( $P = 0.001$ ). Comparing procedure intent, excluding those who did not undergo a procedure, more patients underwent a procedure with a curative intent in later years (76% EPrS vs 84% PoS,  $P \leq 0.001$ ) (Table 2). Overall, 3379 (23%) patients had incomplete TNM staging information and 708 (5%) patients had evidence of distant metastatic disease. These were subsequently excluded from analysis and stage I–III disease was examined independently. Over the timeframe, there was a shift among those without distant metastases towards a higher proportion of stage I cancers in later years (17% EPrS vs 28% PoS,  $P \leq 0.001$ ) (Table 3).

Patients with colorectal cancer diagnosed in the PoS timeframe were further examined to compare screen-detected and non-screen-detected disease (Table 4). Patients with screen-detected disease were more likely to be younger ( $P \leq 0.001$ ), male ( $P \leq 0.001$ ), less deprived ( $P = 0.002$ ) and present electively ( $P \leq 0.001$ ). In addition screen-detected tumours were more likely to be distal ( $P \leq 0.001$ ), of an earlier stage ( $P \leq 0.001$ ) and managed with a curative intent ( $P \leq 0.001$ ).

## DISCUSSION

The results of the present study provide an overview of the changes in mode, site and stage of colorectal cancer presentation in a single geographical area over the past decade, accompanying the introduction of a national screening programme. The results show a reduction in emergency presentation, a reduction in the proportion of rectal cancers and a shift among those without distant metastases to earlier stage at diagnosis. Furthermore, an overall increase in the proportion of patients managed with a curative intent has been identified.

Examining the impact of screening on overall TNM stage at presentation using population-based data sets can be problematic. This is because of high number of patients with incomplete staging information and limited information on those with metastatic disease. For example, in a recent population study examining tumours diagnosed within and without the English Bowel Cancer Screening Programme, 25% of cases were unstaged (Morris *et al*, 2012), similar to the present study. In addition, patients who do not have complete staging information are more likely to die closer to their time of diagnosis, implying the presence of more advanced disease (Downing *et al*, 2013).

**Table 3. Temporal trends in TNM stage of colorectal cancer at presentation with the introduction of screening (non-metastatic disease only)**

Stage	All patients		Prescreening				Screening introduction				Postscreening		P-value
	n (10400)	%	Early		Late		Early		Late		2011–2012		
			2003–2004	2005–2006	2007–2008	2009–2010	n (2219)	%					
I	2134	17	348	17	329	17	367	18	461	22	629	28	≤0.001
II	4124	40	791	40	803	40	884	42	834	40	812	37	
III	4142	43	860	43	860	43	821	40	823	39	778	35	

Abbreviation: TNM = tumour node metastasis.

The MCN has been created to improve outcome in colorectal cancer through delivery of high-quality care with a focus on surgical outcomes. Data are collated following local MDT discussion; therefore, information on patients with metastatic disease who are managed palliatively is poorly captured. It is recognised that this limitation of the data set is particularly true in the early cohorts. For example, only 1% of patients in the EPrS timeframe did not undergo a procedure compared with 20% of patients in PoS timeframe. Furthermore, examining stage IV disease across the timeframe actually showed an increase from 3% (EPrS) to 9% (PoS) with a concurrent rise in unstaged disease from 13% (EPrS) to 25% (PoS) (data not presented). However, this clearly identifies a failure in capture of metastatic or incompletely staged patients of the MCN data set.

Therefore, to maintain data quality when examining stage, the present study chose to focus only on those without distant metastases. When this was considered separately, a clear trend towards larger proportions of node-negative and stage I disease following screening introduction was seen. It has been reported that tumours detected through the screening pathway are of an earlier stage compared with non-screen detected and the present study supports this finding (Morris *et al*, 2012; Roxburgh *et al*, 2013). In addition, despite only accounting for 18% of all tumours diagnosed, an overall impact on the population has been noted. Such a change may well be associated not only with the test itself but also with an overall improvement in the knowledge and attitudes of the population with the widespread publication of screening information. However, a degree of caution should be exercised in interpreting this stage shift among those without distant metastases, as it has been shown that the proportion of stage I disease may well reduce with successive screening rounds (Steele *et al*, 2009). Hence, further work examining the impact on stage at a population level as subsequent rounds of screening occur is required for clarification.

Emergency presentation has long been associated with both poorer short-term (Anderson *et al*, 1992; McArdle and Hole, 2004) and long-term outcomes (McMillan *et al*, 2010; Gunnarsson *et al*, 2011). This disparity has been shown to exist even when node-negative disease is examined independently (Oliphant *et al*, 2014). The reason for this poorer outcome appears multifactorial incorporating elements such as tumour characteristics (Wong *et al*, 2008), preoperative patient morbidity (Skala *et al*, 2009), use of a specialist surgeon (Biondo *et al*, 2010) and the presence of an elevated host preoperative systemic inflammatory response (Crozier *et al*, 2009). There is evidence from the Nottingham gFOBT screening trial that emergency presentation is reduced in a population undergoing screening (Scholefield *et al*, 1998). In addition, the Coventry arm of the population pilot study reported similar findings, with emergency admissions from colorectal cancer reducing from 29% in 1999 to 16% in 2004, with a concomitant improvement in 30-day mortality, following screening

introduction (Goodyear *et al*, 2008). Interestingly, the present study showed a reduction in the proportion of emergency presentation before the introduction of screening; however, little change occurs during its rollout and widespread adoption. It therefore questions the impact that screening itself has had on overall emergency presentation in our geographical area. This is in keeping with a recently published cohort study, which has shown that emergency admissions are reduced when comparing participants and non-participants in screening; however, they remain similar comparing cohorts invited and not invited to screening (Libby *et al*, 2014). Therefore, it appears that it is participation and not invitation that is the key determinant in reducing emergency admissions.

In the present study, only 18% of all patients in the PoS cohort presented through the screening programme. This is on the background of an overall uptake of screening in our geographical region of 52%, with lower uptake in the most deprived cohorts (Mansouri *et al*, 2013). Higher rates of emergency presentation are associated with socioeconomic deprivation and elderly age (Gunnarsson *et al*, 2013). However, such deprived patients are less likely to choose to participate in screening (Steele *et al*, 2010; von Wagner *et al*, 2011) and patients over the age of 74 years are currently not routinely invited to screening. Moreover, it has previously been shown that those patients who are socioeconomically deprived have a worse outcome following a diagnosis of colorectal cancer (Kelsall *et al*, 2009; Oliphant *et al*, 2013). Hence, the current screening programme may underserve the very people who do worse. Efforts to improve uptake of the programme should therefore be made to target such subgroups. One of the concerns raised regarding screening is that it may widen the gap in outcomes that has been created by socioeconomic deprivation and this may be associated with its effect on the rate of emergency presentation.

**Strengths and limitations.** The strengths of the present study are its size and the prospectively collected core data set including data on emergency presentation. It is recognised that there are issues with utilising population-based databases such as missing data. Nevertheless, such prospective data sets provide an opportunity to examine overall trends. Furthermore, there are additional tumour and host variables that determine outcome independent of TNM stage, which would be of interest to explore; however, these were not collected prospectively over the time period. This is particularly relevant for stage II disease, where outcome can be varied (Roxburgh *et al*, 2014; Park *et al*, 2015). Further work with mature follow-up and detailed tumour and host information is required to assess the impact on outcome in particular in stage II disease. A further limitation is utilising data over a decade, where staging modalities may have altered. For example, changes in the sensitivity of CT in detecting metastatic disease or changes in the approach to the pathological processing of specimens may have led to a comparative understaging of those in the earlier cohorts (i.e., a



**Table 4. Comparison of screen- and non-screen-detected colorectal cancer in the postscreening era (2011/12)**

	All patients (3343)		Screen detected (672)		Non-screen detected (2671)		P-value
	n	%	n	%	n	%	
<b>Age (years)</b>							
≤ 50	182	5	1	0	182	7	≤ 0.001
50–74	1925	58	607	90	1318	49	
≥ 75	1229	37	64	10	1165	44	
Unknown	6	0	0	0	6	0	
<b>Sex</b>							
Female	1493	45	246	37	1247	47	≤ 0.001
Male	1843	55	425	63	1418	53	
Unknown	7	0	1	0	6	0	
<b>Deprivation category</b>							
1 (most deprived)	1043	31	192	29	851	32	0.002
2	790	24	150	22	640	24	
3	540	16	97	14	443	17	
4	475	14	115	17	360	14	
5 (least deprived)	488	15	117	17	371	14	
Unknown	7	0	1	0	6	0	
<b>Site of tumour</b>							
Right colon	1146	34	171	25	975	37	≤ 0.001
Left colon	1139	34	284	42	855	32	
Rectum	1025	31	214	32	811	30	
Multiple/unknown	33	1	3	0	30	1	
<b>Management intent</b>							
Curative intent	2229	67	600	89	1629	61	≤ 0.001 <sup>a</sup>
Palliative procedure	377	11	27	4	350	13	
Did not undergo procedure	704	21	40	6	664	25	
Unknown/other	33	1	5	1	28	1	
<b>Presentation to surgery</b>							
Emergency	418	13	12	2	406	15	≤ 0.001 <sup>b</sup>
Elective	2199	65	607	90	1592	60	
Did not undergo procedure	704	21	40	6	664	25	
Unknown	22	1	13	2	9	0	
<b>Stage</b>							
I	629	19	256	38	373	14	≤ 0.001
II	812	24	164	24	648	24	
III	778	23	155	23	623	23	
IV	295	9	24	4	271	10	
Unknown/other	829	25	73	11	756	28	

<sup>a</sup>Curative vs palliative resection.<sup>b</sup>Emergency vs elective presentation.

more attentive approach to lymph node examination in later years). However, such bias is difficult to avoid when examining historical data. Finally, our definition of emergency presentation includes those admitted with acute bleeding. Recently, it has been reported that those patients with colorectal cancer who present with GI bleeding have a better outcome than others, and as such grouping these along with colonic perforation and obstruction is suboptimal (Alexiusdottir *et al*, 2013). Nevertheless, this was the definition of an emergency as coded prospectively in the data set and therefore precluded more detailed analysis.

In conclusion, examining population data from the West of Scotland over the past decade has identified that the SBoSP now accounts for 18% of all tumours encountered in clinical practice. Over the past decade, accompanying the introduction of screening, there has been a reduction in the rate of emergency presentation, a rise in the proportion of operative procedures performed with a curative intent and, in patients with no evidence of distant metastases, a shift towards an increased number of earlier stage

tumours. These changes are likely to improve outcomes overall in the West of Scotland for patients presenting with colorectal cancer; however, there is a need for high-quality follow-up to establish this.

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