Title: Thirty-day post-operative mortality after colorectal cancer surgery in England.

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ABSTRACT

Objectives: To assess the variation in risk-adjusted 30-day post-operative mortality for colorectal cancer patients between Hospital Trusts within the English NHS.

Design: Retrospective cross sectional population-based study of data extracted from the National Cancer Data Repository

Setting: All providers of major colorectal cancer surgery within the English NHS

Participants: All 160,920 individuals who underwent a major resection for a colorectal cancer diagnosed between 1998 and 2006 in the English NHS

Main outcome measures: National patterns of 30-day post-operative mortality were examined and logistic binary regression used to study factors associated with death within 30 days of surgery. Funnel plots were used to show variation between Trusts in risk-adjusted mortality.

Results: Overall 30-day mortality was 6.7% but decreased over time from 6.8% in 1998 to 5.8% in 2006. The biggest reduction in mortality was seen in 2005 and 2006. Post-operative mortality increased with age (15.0% (95%CI 14.1-15.9%) for those aged over 80), co-morbidity (24.2% (95%CI 22.0-26.5) for those with a Charlson co-morbidity score of 3 or more), stage of disease (9.9% (95%CI 9.3-10.6%) for Dukes' D patients), socio-economic deprivation (7.8% (95%CI 7.2-8.4%) for residents of the most deprived quintile) and operative urgency (14.9% (95%CI 14.2-15.7%) for patients undergoing emergency resection). Risk-adjusted control charts demonstrated that one Trust had consistently significantly better outcomes and three significantly worse outcomes than the population mean.

Conclusions: Significant variation in 30-day post-operative mortality following major colorectal cancer surgery existed between NHS hospitals in England throughout the period 1998 to 2006. Understanding the underlying causes of this variation between surgical providers will make it possible to identify and spread best practice, improve outcomes and, ultimately, reduce 30-day post-operative mortality following colorectal cancer surgery

What this paper adds

What is already known about this subject

- There is increasing demand for the NHS to publish clinical outcomes, such as post-operative mortality, to inform patient choice and improve standards.
- To be robust and informative such figures must take into account differences in the casemix of patient populations, hospital surgical workloads and be population-based.
- Previously such data have not been available.

What are the new findings?

- This study has demonstrated a method via which it is possible to assess variation in the risk-adjusted 30-day post-operative mortality for colorectal cancer patients across all hospital trusts within the English NHS.
- The study has demonstrated significant variation in this outcome between hospital Trusts.

How might it impact on clinical practice in the foreseeable future?

- Understanding the underlying causes that have lead to the significant variation in 30-day post-operative mortality rates between surgical providers will make it possible to identify and spread best practice, improve outcomes and, ultimately, reduce post-operative mortality following colorectal cancer surgery

INTRODUCTION

Colorectal cancer is the third most common cancer in the UK and, with more than 35,000 new cases diagnosed annually,(1) improving outcome is important. International comparisons demonstrate that survival from colorectal cancer in the UK is relatively poor.(2-4)

Surgery is the mainstay of colorectal cancer treatment and is generally undertaken within six months of diagnosis. International variation in survival is greatest in this period(3) suggesting that differences in the quality of care may explain some of the variation. A growing body of evidence also indicates variation in the type and quality of treatment delivered at a national level.(5;6) Focussing on the best providers, understanding their successes and optimising the delivery of care in all hospital Trusts should, therefore, significantly improve outcomes for colorectal cancer.

Institutional 30-day post-operative mortality has been suggested as one indicator of the effectiveness of multidisciplinary surgical care for colorectal tumours as it is clinically pertinent and readily understandable for the public. But reliably identifying institutions with post-operative mortality that could be considered 'outlying' (i.e. either significantly better or worse than average) is difficult for several reasons.(7-9) Firstly, unadjusted mortality estimates are difficult to interpret. Surgery inevitably carries a risk, but that risk will vary between individuals. A young patient, with an early-stage tumour and no co-morbid disease will bear a very different risk from that of an elderly, frail patient with advanced disease. Robust comparison of post-operative mortality between providers requires analyses to be 'risk-adjusted', to ensure that the impact of relevant differences between populations (such as patient age, co-morbidity and stage of disease) is taken into account. Secondly, the annual number of patients operated upon for colorectal cancer varies between institutions. Greater variability in post-operative mortality will arise by chance in institutions with smaller annual caseloads compared to units managing larger numbers. Appropriate adjustment for differences in hospital caseload is also vital if valid institutional comparisons are to be made.

National risk-adjusted outcome comparisons require national data but, until now, such data have not been available. Numerous routine data sources exist that contains information about different aspects of colorectal cancer care but none contain all the data required to enable risk-adjusted comparisons of post-operative mortality. For example, cancer registry data(10) contains detailed tumour incidence and outcome information but little data on treatment. In contrast, Hospital

Episode Statistics(11) contains detailed treatment information but little information on the characteristics of the tumours. The National Cancer Intelligence Network (NCIN) has linked these data sources to create the National Cancer Data Repository (NCDR).(5;12) This resource allows the main processes and outcomes of care to be tracked for every NHS cancer patient in England.

The NCDR contains case-mix information of reasonable quality and good data on important prognostic factors such as stage, age and co-morbidity. Not all the relevant data items are complete for each patient, however, and such missing information can restrict the interpretability of institutional comparisons. Techniques such as multiple imputation have the potential to overcome some of the problems that arise from missing data.(13;14)

This study seeks to make use of the available data within the NCDR to scrutinise risk-adjusted surgical outcomes for colorectal cancer patients at a population level. It seeks to monitor national patterns and trends of 30-day post-operative mortality following major resection of colorectal cancer and, using multiple imputation(13;14) and funnel plots,(8;9) to produce robust comparisons of the performance of all NHS Hospital Trusts in England.

METHODS

The National Cancer Data Repository (NCDR) consists of pooled data from the eight population-based cancer registries that cover England, linked (using all or combinations of the identifiers of NHS number, date of birth, postcode at diagnosis and sex) to an extract of Hospital Episode Statistics (HES) including episodes of in-patient care for individuals who presented in any NHS hospital with a diagnostic code for cancer between April 1997 and June 2007.

Information was extracted from this resource on all individuals who underwent a major resection for a primary colorectal cancer diagnosed between 1 January 1998 and 31 December 2006. Information on age, sex, Dukes' stage, NHS number, postcode at diagnosis, dates of diagnosis and, where relevant, date of death, was extracted from the registry dataset for all colorectal cancers (ICD10(15) C18-C20) whilst information about patient management was derived from HES. For each colorectal cancer patient in the registry extract who could be linked to the HES dataset all in-patient episodes of care were searched to identify the date of the first major surgical resection for colorectal disease after diagnosis. Major colorectal resections were identified by OPCS4 codes(16;17) for emergency excision of appendix (H01); excision of appendix (H02); panproctocolectomy (H041); total colectomy (H05); extended right hemicolectomy (H06); right hemicolectomy (H07); transverse colectomy (H08); left hemicolectomy (H09); sigmoid colectomy (H10); colectomy (H11); sub-total colectomy (H29); excision of rectum (H33) and total exenteration of pelvis (X14). Information about the hospital Trust and the Cancer Network in which the patient was managed were derived from this episode of care. If a patient underwent two or more major colorectal resections during different episodes of treatment, the first operation was used. If a patient underwent two or more procedures during the same episode, the most radical or extensive procedure was used.

A Charlson co-morbidity score was calculated for each individual based on the diagnostic codes (excluding cancer) recorded for any hospital admissions in the year prior to diagnosis of their colorectal tumour, excluding any admission spanning the period of diagnosis. The cancer component of the Charlson index was derived for each patient from the cancer registry information in the NCDR. The score for any cancers diagnosed in the year before diagnosis of the colorectal tumour was added to scores obtained from the HES data. Higher scores indicate greater co-morbid disease. Patients were grouped into Charlson score categories of 0, 1, 2 and 3 or greater.

The urgency of surgery has been shown to have a strong influence on the risk of post-operative death(18) but this information is not recorded in HES. The method of admission is, however, available. Patients who were admitted as an emergency and underwent surgery within two days of admission were, therefore, deemed to have undergone emergency surgery while all others were considered elective.

30-day post-operative mortality (the percentage of patients dead within 30 days of surgery) was calculated for each year of diagnosis, age group, sex, Dukes' stage of the primary tumour at diagnosis, quintile of the income domain of the Index of Multiple Deprivation 2004 (derived from each patient's postcode of residence at diagnosis allocated into lower super output areas), Charlson score and Cancer Network and Trust in which the initial colorectal resection occurred. The statistical significance of any differences in post-operative mortality was assessed using the χ^2 test.

Of the 160,920 cases, Dukes' stage was missing in 24,434 (15.2%) because the information had not been captured by the cancer registry while the IMD income domain score could not be derived for 404 (0.25%) because of incomplete postcode information. Analysis restricted to patients with complete data would have allowed post-operative mortality to be assessed in 136,105 (84.6%) patients, preventing Trust-level comparisons. Such estimates would also be at risk of bias with inflated standard errors. Missing data for Dukes' stage and IMD income category were imputed deterministically using the 'ICE'(19) command in Stata (version 11) with passive and substitute options and ordered logistic regression for five imputations and 10 cycles of regression switching. It was assumed that the data were 'missing at random' (MAR). Dukes' stage is MAR if, given fully observed variables, the chance of Dukes' stage being missing does not depend on the value of Dukes' stage. This assumption is made plausible because a wide range of variables were included in the imputation model, including all variables used in the analysis, all variables predictive of missing values and all variables influencing the process causing the missing data.(13) The imputation model consisted of post-operative mortality within 30 days of surgery, age at diagnosis, sex, median annual workload of the Trust, Dukes' stage, IMD income quintile, resection type (emergency or elective), admission type (emergency or elective), year of diagnosis, year of operation, Charlson co-morbidity score, site of the initial primary, hospital trust and cancer registry. For comparative purposes the models used to investigate post-operative

mortality were built using both the imputed dataset and a dataset restricted to cases with complete data.

Multilevel (random effects) binary logistic regression models were built to determine the factors associated with death within 30 days of surgery. The models were built with a hierarchy of patients clustered within hospital trusts (level 2), within cancer networks (level 3) so allowing for correlations between patient outcomes. The dependent variable, death within 30 days of surgery, was considered as a binary outcome. Covariates (explanatory variables) in the risk-adjusted model included age (per year increase), sex, site of the initial colorectal primary, IMD income quintile, year of diagnosis, Dukes' stage at diagnosis, Charlson co-morbidity score and resection type (elective or emergency). Separate analyses were undertaken for patients diagnosed during 1998-2002 and 2003-2006.

Funnel plots were used to compare 30-day mortality rates between hospital Trusts in each time period according to Speigelhalter's method.(9) Trust-specific mortality ratios were calculated from each individual's probability of death within 30 days of surgery derived from the model based on the imputed dataset. Trust-specific risk-adjusted mortality rates were subsequently calculated by multiplying the Trust-specific mortality ratios by the average national post-operative mortality rate ('the target' shown on the funnel plot as a red horizontal line). Trust mortality rates were then plotted against the Trust workload using the 'funnelcompar' command in Stata with 95% and 99.8% control limits (the inner and outer grey dashed lines respectively on the charts) around the target (the national 30-day post-operative rate represented as the red line on the chart). Hospital Trusts for which the 30-day post-operative mortality rate was more than three standard deviations from the national figure (i.e. outside the 99.8% control limits) were considered to be outliers.

RESULTS

160,920 individuals were identified with a diagnosis of colorectal cancer between 1998 and 2006 and who subsequently underwent a major resection for their disease. They were treated in 150 different hospital Trusts within 28 Cancer Networks. Of these 10,704 (6.7%) died within 30 days of the resection. Characteristics of the study population are presented in Table 1. The distribution of stage before and after imputation and amongst the imputed cases was very similar (Table 2).

Table 1 shows the characteristics of the population and their relationship to 30-day post-operative mortality. Due to the high numbers of individuals included in the study the majority of the differences across groups are statistically significant. Analyses undertaken on the imputed dataset and accounting for the clustering of patients with Trusts demonstrated that the 30-day post-operative mortality declined slightly from 6.9% (95% Confidence Interval (CI) 6.3-7.5%) in 1998 to 5.9% (95%CI 5.4-6.4%) in 2006. Women were significantly less likely to die post-operatively than men (6.5% (95%CI 6.1-6.9%) vs. 6.8% (95%CI 6.4-7.3%). Post-operative mortality was significantly associated with age: 1.2% (95%CI 1.0-1.4%) of patients operated upon under the age of 50 died within 30 days of surgery compared to 15.0% (95%CI 14.1-15.9%) of those over 80. Post-operative mortality was increased with more advanced tumour stage (4.2% (95%CI 3.7-4.7%) for Dukes' A tumours vs. 9.9% (95%CI 9.3-10.6%) for Dukes' D tumours, greater socio-economic deprivation (5.7% (95%CI 5.3-6.1%) in the most affluent vs. 7.8% (95%CI 7.2-8.4%) in the most deprived) and greater co-morbidity (5.4% (95%CI 5.0-5.7%) for Charlson score zero vs. 24.2% (95%CI 22.0-26.5%) for score 3 or more). Patients with colonic tumours had higher post-operative mortality than those with rectal tumours (7.7% (95%CI 7.3-8.2%) vs. 4.6% (95%CI 4.3-5.0%)). Operative urgency was also important: 14.9% (95%CI 14.2-15.7%) of patients operated as an emergency died within 30 days of surgery, compared with only 5.8% (95%CI 5.4-6.2%) of those operated upon electively.

Results of multivariable analyses examining the adjusted odds of death within 30 days of surgery are shown in Table 3. The odds of death were significantly higher for each successive decade of age (odds ratio (OR) 1.08 for each year increase in age, 95% confidence interval (CI) 1.08-1.08, $p<0.001$), Dukes' stage (OR 2.50, 95%CI 2.24-2.78 for Dukes' D vs. Dukes' A, $p<0.001$), deprivation (OR 1.32, 95%CI 1.23-1.42 for the most deprived vs. the most affluent, $p<0.001$), co-morbidity (OR 4.38, 95%CI 3.98-4.82 for Charlson co-morbidity score of 3 vs. zero, $p<0.001$) and those operated upon as an emergency (OR 2.67, 95%CI 2.53-2.82, $p<0.001$). The odds of

death were lower in women than men (OR 0.83, 95%CI 0.79-0.86) and lower for patients with rectal tumours than those with colonic tumours (OR 0.94, 95% 0.89-0.99).

The odds of death within 30 days of surgery for the various case-mix factors are shown in Table 4. A strong deprivation effect was apparent even after adjustment for the case-mix factors thought to differ between socio-economic groups such as stage, co-morbidity and emergency presentation.

For patients diagnosed during 1998-2002, unadjusted 30-day post-operative mortality was above the 99.8% control limit for eight Trusts (Figure 1A), indicating that their surgical mortality was significantly higher than expected. A further 20 Trusts were above the 95% control limit. After inclusion of all risk factors in the model (Figure 1B) eight Trusts remained above the upper 99.8% limit while 15 Trusts were above the 95% control limit. Six Trusts had significantly lower 30-day post-operative mortality than could be explained by the available case-mix information (i.e. they were below the lowest 99.8% control limit) and 19 more Trusts were below the 95% control limit. In the risk-adjusted model, five and 17 Trusts respectively remained below the lower 99.8% and 95% control limits.

Similar results were observed for patients diagnosed during 2003-2006 (Figure 2). In the risk-adjusted model, post-operative mortality in five Trusts was above the upper 99.8% control limit whilst a further 11 were above the 95% limit. Three Trusts had significantly better outcomes than expected, below the 99.8% limit, and nine Trusts were below the 95% limit.

Three trusts appeared above (and one Trust below) the 99.8% control limits in both time periods indicating consistently outlying 30-day post-operative mortality.

DISCUSSION

This retrospective population-based study is the first to provide a comprehensive, national perspective on the 30-day post-operative mortality associated with colorectal cancer surgery across England. Overall, 6.7% of the study population died within 30 days of surgery amounting to 10,704 deaths. There was significant variation across the population with post-operative mortality greater in the elderly, men, the socio-economically deprived, those with advanced stage disease at diagnosis or with additional co-morbidities and amongst those operated upon as an emergency. Significant variation, independent of case-mix, was also observed between hospital Trusts. One Trust had post-operative mortality significantly lower and three significantly higher than could be explained by the case-mix information available in both time periods examined. These hospitals were all District General Hospitals and two of those with significantly worse outcomes than expected had Foundation status.

The post-operative mortality of 6.7% seen in this study is notably higher than that previously reported for the UK. Data submitted to the most recent National Bowel Cancer Audit Programme (NBOCAP) report recorded post-operative mortality of 4.7% for all surgical cases.(5) Submission to this audit is, however, voluntary resulting in incomplete case ascertainment. In addition, it is not possible to calculate post-operative mortality across all surgically resected cases submitted due to incomplete or inaccurate reporting of dates of surgery and (prior to 2009) death. In consequence, it is likely that, due to under-reporting, the results from the NBOCAP audits are biased.

The post-operative mortality of English colorectal cancer patients determined in this study is also significantly higher than that reported from other countries. 30-day post-operative mortality from population-based studies in Scandinavia, Canada and the USA ranged from 2.7% (for rectal cancers alone) to 5.7%.(20-25) Whilst there are undoubtedly big differences between the populations in these international studies that make comparison to the UK difficult, the post-operative mortality from these reports are consistently below the 6.7% found in this study. This suggests that either the NHS may have fundamentally worse post-operative outcomes than some other comparable health services or the operative risk of patients differs between countries. Understanding and minimising these differences could significantly reduce the number of premature deaths caused by this disease across the country.

A strong relationship between socio-economic deprivation and post-operative mortality was observed with those who resided in more deprived areas having significantly greater risk of death within 30 days of surgery than those who resided in more affluent areas. This effect remained despite adjustment for stage of disease, co-morbidity and urgency of surgical resection. This finding mirrors other studies that have shown socio-economic gradients in both the long and short-term outcomes of colorectal cancer.(22;26;27) In contrast, there is evidence to suggest that in a randomised trial setting where patients were given equal treatment this gradient disappeared(28) although it is possible this may be partially explained by the participants of randomised trials being of a better prognosis than those who are not. Further evidence is required, therefore, before it is possible to determine whether inequalities in care may account for some of the socio-economic disparities observed in 30-day post-operative mortality. Understanding the causes of the gradient and minimising it has the potential, however, to significantly improve outcomes from colorectal cancer.

A limitation of this study is that is based on routine health data in the form of linked routine cancer registry and HES and the quality and accuracy of coding within these resources has been questioned.(29) A recent study, however, identified colorectal cancer patients enrolled in a randomised trial within the NCDR and found excellent agreement in the information recorded in both datasets with regard to both treatment and outcomes.(30) This demonstrated that the data within the NCDR were sufficient to monitor 30-day post-operative mortality across the country.

Another potential limitation of the study is that the case-mix adjustment was inadequate due to the routine nature of the data upon which it was based. The NCDR does not contain detailed information about every aspect of a patient or their care that could influence the risk of post-operative death and, in consequence, it is possible that some unmeasured prognostic factor is confounding our results. These analyses do, however, include adjustment for many of the most important factors known to influence outcome such as age, co-morbidity, stage of disease and socio-economic deprivation and, as such, the results should not be dismissed. Previous studies have demonstrated that routine data can be used to identify divergent practice(31;32) and the linked data upon which this study is based are much more comprehensive than any previously available. Furthermore, it is hoped that the NBOCAP data will soon be incorporated into the NCDR. These data contain information such as anaesthetic risk scores that are not currently available in the NCDR but that could significantly influence post-operative outcomes. The availability of such data could, in the future, help refine the models further.

Currently, the NCDR is limited by the timeliness of the routine data available. Efforts are being made across the NHS to increase the timeliness of data it collects and it is a priority for the NCIN to improve the temporality of the NCDR. In the future, therefore, it is hoped that timelier reporting can be achieved.

Many factors may influence 30-day post-operative mortality. These may relate to the patient (for example, stage of disease or level of co-morbidity) or the institution offering care (such as the specialisation of the operating team, the quality of post-operative care or the availability of beds in high dependency and intensive care units). Examining how these factors vary in relation to 30-day post-operative mortality rates may provide evidence to help explain the variability seen across English NHS Trusts, amongst socio-economic groups and between countries. Whilst this study has identified providers with outlying 30-day post-operative mortality, however, it is not possible to determine from the data available what aspects of care or, indeed, if the quality of care within these units is deficient. The outlying status could be explained by problems in data quality, chance or, as discussed previously, case-mix factors not quantified in this study. Institutions with outlying status should not, however, be ignored but efforts made to determine why they appear to have significantly better or worse post-operative mortality than other units. With this information it should then be possible to learn from those achieving good outcomes, by seeking the underlying causes, adding to and spreading the adoption of best practice guidelines,(33-36) improving poor outcomes and, ultimately, reducing post-operative mortality following colorectal cancer surgery.

The UK's cardiothoracic surgeons have openly reported their surgical outcomes since 1998 and the publication of these results have demonstrably improved outcomes for cardiothoracic surgical mortality across the country.(37;38) It is intended that the development of the NCDR will enable national 30-day post-operative mortality to be reported annually at both a Trust and (as the NCDR also contains information about the consultant overseeing each surgical event), potentially, surgeon level (although it should be emphasised that post-operative mortality should be treated as a colorectal team or Trust event and the operating surgeon should not be vilified). The NCIN plans to work collaboratively with the Association of Coloproctology of Great Britain and Ireland (ACPGBI), therefore, to disseminate these findings to hospital Trusts and Cancer Networks and use them to inform care. The reduction in 30-day post-operative mortality over the study period is welcomed but our findings show that there was wide variation across the NHS and considerable

scope for improvement. It is now time for colorectal cancer, and subsequently other cancer teams, to follow the cardiothoracic example in order to improve outcomes. The NCDR provides the means by which this process can start.

FIGURES & TABLES

Table 1: Characteristics of the study population

Characteristic		Total	Dead within 30 days of surgery			
			Overall		Multilevel	
			n	%	%	(95%CI)
Age	≤50	9,552	112	1.2	1.2	(1.0 , 1.4)
	51-60	22,436	438	2	1.9	(1.7 , 2.2)
	61-70	43,695	1,669	3.8	3.9	(3.5 , 4.2)
	71-80	57,373	4,344	7.6	7.6	(7.1 , 8)
	>80	27,864	4,141	15	15.0	(14.1 , 15.9)
Sex	Male	88,789	6,037	6.8	6.8	(6.4 , 7.3)
	Female	72,131	4,667	6.5	6.5	(6.1 , 6.9)
Year of diagnosis	1998	18,018	1,231	6.8	6.9	(6.3 , 7.5)
	1999	18,076	1,276	7.1	7.1	(6.5 , 7.7)
	2000	18,075	1,249	6.9	6.9	(6.4 , 7.5)
	2001	17,296	1,195	6.9	6.9	(6.4 , 7.5)
	2002	17,336	1,213	7	7.0	(6.5 , 7.5)
	2003	17,498	1,155	6.6	6.6	(6 , 7.1)
	2004	17,869	1,230	6.9	6.9	(6.4 , 7.4)
	2005	18,421	1,086	5.9	6.0	(5.5 , 6.4)
	2006	18,331	1,069	5.8	5.9	(5.4 , 6.4)
Cancer site	Colon	104,023	7,933	7.6	7.7	(7.3 , 8.2)
	Rectosigmoid	13,555	748	5.5	5.6	(5.1 , 6.2)
	Rectum	43,342	2,023	4.7	4.6	(4.3 , 5)
Charlson co-morbidity score	0	137,924	7,333	5.3	5.4	(5.0 , 5.7)
	1	13,618	1,754	13	13.1	(12.2 , 14.1)
	2	6,551	946	14	14.7	(13.2 , 16.3)
	≥3	2,827	671	24	24.2	(22.0 , 26.5)
Dukes' stage	A	17,151	606	3.5	4.2	(3.7 , 4.7)
	B	53,711	3,122	5.8	6.2	(5.8 , 6.6)
	C	51,390	3,247	6.3	7.1	(6.7 , 7.6)
	D	14,234	1,287	9	9.9	(9.3 , 10.6)
	Unknown	24,434	2,442	10	-	-
IMD income category	Most affluent	31,538	1,790	5.7	5.7	(5.3 , 6.1)
	2	35,139	2,113	6	6.0	(5.5 , 6.5)
	3	34,409	2,320	6.7	6.8	(6.4 , 7.2)
	4	31,889	2,358	7.4	7.3	(6.9 , 7.8)
	Most deprived	27,541	2,122	7.7	7.8	(7.2 , 8.4)
	Unknown	404	1	0.2	-	-
Operation type	Elective	145,480	8,401	5.8	5.8	(5.4 , 6.2)
	Emergency	15,440	2,303	15	14.9	(14.2 , 15.7)

Table 2 Dukes' stage distribution by co-variable category, and before and after imputation

Characteristic		Stage at diagnosis				
		A	**B**	**C**	**D**	**Unknown**
Age at diagnosis	≤50	9.4	25.7	33.8	12.8	18.2
	51 to 60	11.0	28.3	33.8	11.2	15.7
	61 to 70	11.4	31.2	32.6	9.4	15.4
	71 to 80	11.0	35.3	31.1	8.2	14.6
	≥81	9.0	39.7	30.5	6.1	14.7
Sex	Male	11.1	32.9	31.7	8.8	15.5
	Female	10.1	34.0	32.2	8.9	14.9
Operation	Elective	11.6	33.5	31.4	8.3	15.2
	Emergency	1.8	31.9	37.3	14.2	14.8
IMD income category	1	11.5	32.3	32.0	8.7	15.5
	2	11.2	33.3	32.1	8.6	14.8
	3	10.4	34.2	31.8	8.7	14.9
	4	10.2	33.5	32.0	8.8	15.6
	5	9.8	33.5	31.7	9.7	15.4
	Unknown[1]	11.4	34.7	36.6	11.6	5.7
Cancer site	Colon	7.6	36.7	32.1	9.9	13.6
	Rectosigmoid	11.8	30.7	33.3	10.0	14.3
	Rectum	17.6	26.3	31.0	6.0	19.2
Year of diagnosis	1998	8.5	31.0	28.2	8.6	23.7
	1999	10.1	30.9	30.3	8.9	19.9
	2000	10.4	33.1	31.8	8.8	15.9
	2001	11.3	34.7	32.8	9.9	11.4
	2002	10.9	34.5	34.2	9.2	11.2
	2003	11.2	33.9	32.6	8.7	13.6
	2004	10.4	31.8	30.4	8.4	19.0
	2005	11.5	35.1	34.5	8.7	10.2
	2006	11.8	35.5	32.6	8.4	11.7
Charlson co-morbidity score	0	10.9	33.1	31.8	9.0	15.3
	1	8.2	34.7	33.7	8.7	14.7
	2	10.6	35.5	31.9	7.6	14.5
	3	9.2	37.4	31.9	6.1	15.5
Dukes' stage distribution	Before imputation (all)	10.7	33.4	31.9	8.9	15.2
	Before imputation (staged cases only)	12.6	39.4	37.7	10.4	-
	After imputation	12.7	39.5	37.4	10.4	-
	Across imputed cases	13.5	40.0	36.3	10.1	-

[1] IMD income category information was missing in only a small proportion of cases (n=404, 0.25%)

Table 3: Multivariable analyses showing the odds of death within 30 days of surgery

Characteristic		Complete case analysis[2]			Multiple imputation analysis[3]		
		OR	95% CI	P-value	OR	95% CI	P-value
Age at diagnosis (per year)		1.08	(1.07, 1.08)	<0.001	1.08	(1.08, 1.08)	<0.001
Year of diagnosis (per advancing year)		0.99	(0.98, 1.00)	<0.001	0.97	(0.97, 0.98)	<0.001
Sex	Male	1.00	-	<0.001	1.00	-	<0.001
	Female	0.81	(0.77, 0.85)		0.83	(0.79, 0.86)	
Operation	Elective	1.00	-	<0.001	1.00	-	<0.001
	Emergency	2.61	(2.46, 2.77)		2.67	(2.53, 2.82)	
Dukes' stage at diagnosis	A	1.00	-	<0.001	1.00	-	<0.001
	B	1.28	(1.17, 1.4)		1.23	(1.12, 1.35)	
	C	1.53	(1.39, 1.68)		1.54	(1.40, 1.69)	
	D	2.63	(2.37, 2.93)		2.50	(2.24, 2.78)	
IMD income category	Most affluent	1.00	-	<0.001	1.00	-	<0.001
	2	1.04	(0.96, 1.12)		1.03	(0.96, 1.10)	
	3	1.13	(1.05, 1.22)		1.11	(1.04, 1.19)	
	4	1.24	(1.15, 1.34)		1.22	(1.13, 1.30)	
	Most deprived	1.37	(1.26, 1.49)		1.32	(1.23, 1.42)	
Cancer site	Colon	1.00	-	<0.001	1.00	-	0.0021
	Rectosigmoid	0.83	(0.76, 0.91)		0.88	(0.82, 0.96)	
	Rectum	0.92	(0.86, 0.98)		0.94	(0.89, 0.99)	
Charlson co-morbidity score	0	1.00	-	<0.001	1.00	-	<0.001
	1	2.12	(1.99, 2.26)		2.05	(1.94, 2.18)	
	2	2.46	(2.26, 2.68)		2.43	(2.25, 2.62)	
	≥3	4.51	(4.06, 5.01)		4.38	(3.98, 4.82)	

[2] Analyses based on only those individuals for whom all casemix variables were available (n=136,105)
[3] Analyses based on all individuals with missing casemix data being imputed (n=160,290)

Table 4: The results of the additive logistic regression models (based on the imputed dataset) investigating the odds of death within 30 days of surgery

Characteristic		**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**
Age at diagnosis (per year)		1.08	1.08 - 1.08	1.08	1.07 - 1.08	1.08	1.08 - 1.08	1.08	1.08 - 1.08
Sex	Male	1.00	-	1.00	-	1.00	-	1.00	-
	Female	0.78	0.75 - 0.81	0.82	0.79 - 0.86	0.82	0.79 - 0.86	0.83	0.79 - 0.86
Year of diagnosis		0.98	0.97 - 0.98	0.97	0.96 - 0.98	0.97	0.96 - 0.98	0.97	0.97 - 0.98
Cancer site	Colon	1.00	-	1.00	-	1.00	-	1.00	-
	Rectosigmoid	0.77	0.71 - 0.84	0.82	0.76 - 0.89	0.83	0.76 - 0.9	0.88	0.82 - 0.96
	Rectum	0.7	0.67 - 0.74	0.77	0.73 - 0.81	0.82	0.78 - 0.86	0.94	0.89 - 0.99
IMD income category	Most affluent	1.00	-	1.00	-	1.00	-	1.00	-
	2	1.03	0.97 - 1.11	1.03	0.96 - 1.1	1.03	0.96 - 1.1	1.03	0.96 - 1.10
	3	1.14	1.07 - 1.22	1.12	1.05 - 1.2	1.12	1.05 - 1.2	1.11	1.04 - 1.19
	4	1.26	1.18 - 1.35	1.22	1.14 - 1.31	1.22	1.14 - 1.31	1.22	1.13 - 1.30
	Most deprived	1.42	1.32 - 1.52	1.35	1.26 - 1.45	1.35	1.25 - 1.45	1.32	1.23 - 1.42
Charlson score	0			1.00	-	1.00	-	1.00	-
	1			2.04	1.93 - 2.16	2.02	1.91 - 2.14	2.05	1.94 - 2.18
	2			2.34	2.17 - 2.53	2.38	2.2 - 2.56	2.43	2.25 - 2.62
	≥3			4.13	3.76 - 4.54	4.23	3.85 - 4.65	4.38	3.98 - 4.82
Dukes' stage	A					1.00	-	1.00	-
	B					1.31	1.2 - 1.44	1.23	1.12 - 1.35
	C					1.7	1.55 - 1.87	1.54	1.40 - 1.69
	D					2.86	2.57 - 3.19	2.50	2.24 - 2.78
Operation type	Elective							1.00	-
	Emergency							2.67	2.53 - 2.82

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AUTHOR CONTRIBUTIONS

Eva Morris, James Thomas, Phil Quirke and David Forman were instrumental in accessing and managing the data upon which this study is based. James Thomas, Eva Morris, Paul Finan and Phil Quirke produced a clinically sound algorithm to extract data from the NCDR for this study and Faye Taylor, Eva Morris, Bernard Rachet and Michel Coleman were responsible for its statistical analysis. Clinical interpretation of the results was undertaken by Phil Quirke, Michel Coleman and Paul Finan. All authors were involved in drafting and revising the paper and all authors approved the final version.

COMPETING INTEREST DECLARATION

All authors have completed the Unified Competing Interest form at www.icme.org/coi_disclosure.pdf and declare that they have not had support from a company for the submitted work; have a relationship with any companies that might have an interest in the submitted work in the previous three years; their spouses, partners or children have no financial relationships that may be relevant to the submitted work; and they do not have any non-financial interests that may be relevant to the submitted work.

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ETHICAL APPROVAL

Ethical approval was obtained from the Fife, Forth Valley & Tayside Research Ethics Service in September 2008 (Reference number 08/S0501/66)

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