The New Zealand PIPER Project: colorectal cancer survival according to rurality, ethnicity and socioeconomic deprivation—results from a retrospective cohort study

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ABSTRACT

AIM: To investigate differences in survival after diagnosis with colorectal cancer (CRC) by rurality, ethnicity and deprivation.

METHODS: In this retrospective cohort study, clinical records and National Collections data were merged for all patients diagnosed with CRC in New Zealand in 2007–2008. Prioritised ethnicity was classified using New Zealand Cancer Registry data; meshblock of residence at diagnosis was used to determine rurality and socioeconomic deprivation.

RESULTS: Of the 4,950 patients included, 1,938 had died of CRC by May 2014. The five-year risks of death from CRC were: Māori 47%; Pacific 59%; non-Māori-non-Pacific (nMnP) 38%. After adjustment for demographic characteristics, comorbidity and disease stage at diagnosis, compared to nMnP the relative risk (RR) for Māori was 1.1 (95%CI: 0.8–1.3) and for Pacific 1.8 (95% CI: 1.4–2.5). We found no differences in risk of death from CRC by rurality, but some differences by deprivation.

CONCLUSIONS: Disparity in outcome following diagnosis with CRC exists in New Zealand. Much of this disparity can be explained by stage of disease at diagnosis for Māori, but for Pacific peoples and those in deprived areas other factors may influence outcome. Further analyses of the PIPER data will explore the impact of any differences in management.

Survival differences following diagnosis with colorectal cancer (CRC) appear to stem from variation in the underlying disease biology, timeliness of diagnosis, treatment and follow-up.

Previous research undertaken in New Zealand has shown disparities in survival following CRC, with people living in independent urban areas, Māori (New Zealand's indigenous people), and those living in areas with greater socioeconomic deprivation having poorer survival.[1–6] New Zealand has a significant population of Pacific people, a heterogeneous group with a history of migration to New Zealand. The main Pacific ethnicities contributing to the Pacific population in New Zealand are Samoan, Cook Islands Māori, Tongan, Niuean, Fijian and

Tokelauan.[7] There is limited information on CRC outcomes for Pacific people living in New Zealand.

The timeliness of diagnosis can be inferred by the stage at diagnosis, presentation to the emergency department (ED) and presentation with obstruction. Stage at diagnosis is the strongest prognostic factor for CRC.[8] Māori patients,[1,2] Pacific patients,[9] patients living in independent urban areas and those living in areas of greater socioeconomic deprivation are more likely to present with metastatic disease. These differences in late-stage presentation will largely reflect inequity in access to and/or from primary care. However, survival disparities have been shown to exist within categories of disease stage at diagnosis, suggesting that at least some of the survival differential may be due to variation in treatment delivery.[1,2,3]

Emergency presentation has been found to be associated with higher perioperative mortality and poorer long-term survival.[10] Colorectal cancer presenting with bowel obstruction is also associated with a poor prognosis.[11] Hill et al[4] found higher proportions of Māori compared with non-Māori colon cancer patients presented with obstruction or perforation (prevalence ratio: 1.37; 95% CI: 1.01–1.85) and higher proportions of Māori also underwent emergency surgery (prevalence ratio: 1.35; 95% CI: 1.00–1.83). Data about Pacific colorectal patients' outcomes according to presentation are currently lacking; however, it is worth noting that a New Zealand study of lung cancer found a higher proportion of Pacific people presented via the ED.[12]

Identifying the factors contributing to the survival differences is important to help identify opportunities for equitable service delivery and to improve outcomes for New Zealand patients. The PIPER study (Presentations, Investigations, Pathways, Evaluation and Rx) was carried out to investigate patterns of presentation to secondary care, diagnosis, staging, treatment and follow-up, and to investigate the impact of any differences by rurality, ethnicity or deprivation on cancer survival. Here we: i) describe the disease characteristics at diagnosis; ii) compare the mode of presentation to secondary care and survival outcomes by rurality, ethnicity and deprivation; and iii) determine whether or not these differences remain after adjusting for demographic and disease characteristics at diagnosis.

Methods

The methods for the PIPER project have been previously described.[13] Briefly, data from clinical records were linked to data from the New Zealand National Databases for all patients diagnosed with CRC (ICD-10-AM codes C18-C20) in 2007–2008. We included all patients with a first confirmed diagnosis of adenocarcinoma of the colon or rectum who were resident in New Zealand at the time of diagnosis, and who presented, were diagnosed and received treatment for their primary CRC in New Zealand. Date of diagnosis was defined as the date of the first pathological report confirming CRC (where pathology was available). Colorectal cancer mortality data was complete up to 23 May 2014 (the latest date for which cause of death was coded in the New Zealand Mortality Collection at the time of data extraction) and 'all cause' mortality to 23 May 2016 (three months before the date of extraction).

Date of birth, sex and ethnicity were obtained from the New Zealand Cancer Registry (NZCR). Prioritised ethnicity was coded as Māori, Pacific and 'non-Māori-non-Pacific' (nMnP).[13,14] Rurality[15] and NZDep2006 deprivation level (a geographic area-based measure of deprivation coded 1–10 from areas of least to highest deprivation)[16] were assigned based on the meshblock of residence at time of diagnosis.[17] Rural residence included rural areas with moderate urban influence, rural areas with low urban influence, highly remote/rural areas and independent urban communities.[19] The latter are communities which are not dependent for employment on a nearby main urban area. Non-rural residence included main urban areas, satellite urban communities and rural areas with high urban influence.[19]

Comorbidity was assessed using the C3 index, calculated from hospitalisation discharge data from the National Minimum Data Set (NMDS) from the five years before diagnosis of colorectal cancer. The C3 index is a cancer-specific index of comorbidity with higher scores indicating higher comorbidity.[19] Site of primary tumour was obtained, in preferential order, from the operation note, anatomical pathology report,

colonoscopy report, radiology report or from clinic notes. T, N, and M stage were obtained from the anatomic pathology report, or if not available, in preferential order from the radiology report, outpatient clinic letter and clinical notes. For this paper, information from CT scans up to eight weeks after surgery was also used for assigning stage at diagnosis. For analysis, stage was reduced to six categories: Stage I, II, III/N1, III/N2, localised (NOS) or Stage IV. If the primary tumour site, grade or stage were unknown from PIPER data collection, NZCR data were used. The majority of the localised (NOS) patients with rectal cancer underwent neoadjuvant chemoradiation, so no surgical samples were available for staging at diagnosis. Grade, lymphovascular invasion, mucinous or synchronous tumour data were obtained from the pathology report, or if not there, from clinical notes. The two key performance indicators (KPIs) for presentation to secondary care were i) presentation to ED (collected as method of referral) and ii) presentation with obstruction. Lower proportions meeting these KPIs indicate better care.

Relative risks and 95% confidence intervals comparing proportions were estimated using log-Poisson regression with robust standard errors to account for the binary data.[21] Cumulative incidence of death from colorectal cancer at five years after diagnosis was estimated using methods for competing risks, with death from other causes as a competing risk and censoring follow-up at 23 May 2014 for those still alive.[21–23] Overall survival was compared using Kaplan-Meier survival curves with log rank tests. Risk of death from CRC was compared using cause-specific hazard ratios estimated using the method of Fine and Grey.[24] The relationship between continuous variables and outcome was explored using fractional polynomials; a linear relationship was used unless this indicated otherwise. Regression models considered were as follows: i) Model 1 = unadjusted; ii) Model 2 = adjusted for site of initial tumour; iii) Model 3 = Model 2+ age and sex; iv) Model 4 = Model 3 + stage at diagnosis; v) Model 5 = Model 4 + tumour grade, type and presence of lymphovascular invasion at diagnosis (and presentation where relevant); vi) Model 6 = Model 5 + comorbidity. Not all model results are presented here. Multiple imputation with chained equations was used to account for missing data in the regression models.[25,26] The imputation models included all the variables in the final regression models plus the failure indicator and the Nelson-Aalen cumulative hazard.[27] Statistical analyses were carried out in STATA version 14.[27] Ethical approval for this project was granted by the Multi-Region Ethics Committee (reference number MEC/12/EXP/022).

Results

There were 5,612 patients with colorectal cancer registered on the NZCR between 1 January 2007 and 31 December 2008. Of these, 662 patients were excluded because they were: non- colorectal primary (103), non-adenocarcinoma morphology (136), recurrent disease (45), not diagnosed in 2007 or 2008 (124), not resident in New Zealand, diagnosed or treated outside New Zealand (53), had no clinical records available (196) or no pathology or radiology to confirm diagnosis (5). Rurality was unknown for 130 patients, ethnicity for 91 and deprivation for 159.

Overall, 52% of the cohort were male, the median age was 73 years (interquartile range 64 to 80 years) and the percentage of patients living in rural areas was 26%. There were 209 Māori patients and 58 Pacific patients. Demographic characteristics by rurality, prioritised ethnicity and NZDep are shown in Table 1. Of the 209 patients recorded as identifying as Māori on the Cancer Registry, six were also recorded as identifying as Pacific (these were counted as Māori for the purposes of our analysis). Māori patients were relatively more likely than non-Māori-non-Pacific (nMnP) to be from rural areas than urban areas. Pacific patients were much more likely to be living in urban areas than rural areas. Both Māori and Pacific patients were more likely to be living in areas of higher deprivation than nMnP. The comorbidity scores tended to be higher for Māori patients and Pacific patients than for nMnP, and also increased with higher deprivation levels.

In our study cohort, there were differences in disease characteristics by rurality, ethnicity, and deprivation (Tables 2A and 2B). For Māori patients, the primary tumour site

Table 1: Comparison of demographic characteristics and comorbidity by rurality, ethnicity and deprivation.

	Rurality at diagnosis				Ethnicity						Deprivation quintile (NZDep2006)											
	n=4,820				n=4,859						n=4,792											
	Urban		Rural		Māori		Pacific		nMnP		1		2		3		4		5		Total	
	n=3,543		n=1,277		n=209		n=58		n=4,592		n=972		n=973		n=1,080		n=977		n=790		n=4,950	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Age at diagnosis (yrs)																						
<40	65	(1.8)	13	(1.0)	8	(3.8)	6	(10.3)	67	(1.5)	23	(2.4)	14	(1.5)	11	(1.0)	16	(1.7)	14	(1.8)	81	(1.6)
40–49	152	(4.3)	42	(3.3)	17	(8.1)	5	(8.6)	176	(3.8)	52	(5.5)	40	(4.2)	41	(3.9)	25	(2.6)	31	(4.0)	206	(4.2)
50–59	395	(11.1)	145	(11.4)	46	(22.0)	11	(19.0)	487	(10.6)	118	(12.4)	120	(12.6)	101	(9.5)	95	(9.9)	91	(11.6)	560	(11.3)
60–69	836	(23.6)	357	(28.0)	69	(33.0)	17	(29.3)	1,119	(24.4)	269	(28.3)	246	(25.8)	243	(22.9)	233	(24.2)	175	(22.3)	1,231	(24.9)
70–79	1,172	(33.1)	434	(34.0)	49	(23.4)	10	(17.2)	1,551	(33.8)	303	(31.9)	297	(31.2)	384	(36.3)	330	(34.2)	260	(33.2)	1,639	(33.1)
>=80	923	(26.1)	286	(22.4)	20	(9.6)	9	(15.5)	1,192	(26.0)	186	(19.6)	235	(24.7)	279	(26.3)	265	(27.5)	213	(27.2)	1,233	(24.9)
Sex																						
Female	1,747	(49.3)	589	(46.1)	101	(48.3)	22	(37.9)	2,245	(48.9)	427	(43.9)	491	(50.5)	534	(49.4)	490	(50.2)	377	(47.7)	2,339	(48.5)
Male	1,796	(50.7)	688	(53.9)	108	(51.7)	36	(62.1)	2,347	(51.1)	545	(56.1)	482	(49.5)	546	(50.6)	487	(49.8)	413	(52.3)	2,551	(51.5)
Rurality																						
Urban					139	(68.1)	55	(94.8)	3,280	(73.3)	795	(81.8)	725	(74.5)	787	(72.9)	657	(67.2)	556	(70.4)	3,543	(71.6)
Rural					65	(31.9)	3	(5.2)	1,196	(26.7)	177	(18.2)	248	(25.5)	293	(27.1)	320	(32.8)	234	(29.6)	1,277	(25.8)
Unknown					5		0		116		0		0		0		0		0		130	(2.6)
Ethnicity																						
Māori	139	(4.0)	65	(5.1)							17	(1.8)	19	(2.0)	26	(2.5)	52	(5.4)	89	(11.4)	209	(4.2)
Pacific	55	(1.6)	3	(0.2)							2	(0.2)	6	(0.6)	5	(0.5)	20	(2.1)	25	(3.2)	58	(1.2)
nMnP	3,280	(94.4)	1,196	(94.6)							932	(98.0)	927	(97.4)	1,028	(97.1)	892	(92.5)	670	(85.5)	4,592	(92.8)
Unknown	69		13								21		21		21		13		6		91	(1.8)
Comorbidity																						
0	1,734	(48.9)	630	(49.3)	89	(42.6)	28	(48.3)	2,254	(49.1)	541	(55.7)	509	(52.3)	532	(49.3)	460	(47.1)	309	(39.1)	2,448	(49.5)
>0–<1	595	(16.8)	218	(17.1)	39	(18.7)	7	(12.1)	779	(17.0)	172	(17.7)	174	(17.9)	172	(15.9)	148	(15.1)	144	(18.2)	831	(16.8)
1–<2	476	(13.4)	168	(13.2)	30	(14.4)	10	(17.2)	615	(13.4)	106	(10.9)	117	(12.0)	155	(14.4)	139	(14.2)	121	(15.3)	658	(13.2)
>=2	738	(20.8)	261	(20.4)	51	(24.4)	13	(22.4)	944	(20.6)	153	(15.7)	173	(17.8)	221	(20.5)	230	(23.5)	216	(27.3)	1,013	(20.5)

was the descending colon for 48% compared with 36% for Pacific and 37% for nMnP. For Pacific patients, the site of the primary tumour was the rectum for 40%, compared with 29% for Māori and 24% for nMnP. For nMnP patients a higher percentage had a tumour in the ascending colon (31%) compared with Māori (17%) and Pacific patients (21%). There were no marked differences in stage at diagnosis between urban and rural patients. However, stage varied by ethnicity; the percentages with metastatic disease at diagnosis were 35% for Māori, 31% for Pacific and 23% for nMnP. Comparisons within localised stage are difficult due to the differences in primary treatment for tumours in the colon versus rectum. Many patients with rectal cancer receive neoadjuvant chemoradiation therapy, so pathological T and N stage are unknown at diagnosis. There were differences in degree of tumour differentiation (grade) by rurality and ethnicity, with rural and nMnP patients having the higher percentages with poorly or undifferentiated tumours. Differences by deprivation were less clear, but patients living in areas of high deprivation were slightly more likely to have tumours in the descending colon, well or moderately differentiated tumours and metastatic disease. Mucinous vs non-mucinous adenocarcinoma, lymphovascular invasion and perineural invasion were not documented in available clinical notes for a large percentage of patients (21%, 28% and 43% respectively), so our ability to assess the impact of these factors was limited.

Presentation key performance indicators

Overall 31% of patients presented directly to the ED. The percentages were very similar for urban and rural patients (Table 3). Māori patients were the most likely to present to ED (45%) followed by Pacific (35%) then nMnP (30%). The differences were attenuated after controlling for demographic characteristics and disease variables (such

Table 2A: Comparison of disease characteristics at diagnosis by rurality and ethnicity.

	Rurality of residence at diagnosis				**Ethnicity**					
	n=4,820				n=4,859					
	Urban		**Rural**		**Māori**		**Pacific**		**nMnP**	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Tumour site										
Ascending colon	1,106	(31.2)	364	(28.5)	35	(16.7)	12	(20.7)	1,439	(31.3)
Transverse colon	277	(7.8)	105	(8.2)	12	(5.7)	2	(3.4)	370	(8.1)
Descending colon	1,304	(36.8)	499	(39.1)	101	(48.3)	21	(36.2)	1,697	(37.0)
Colon (NOS)	54	(1.5)	10	(0.8)	5	(2.4)	2	(3.4)	60	(1.3)
Rectum	856	(24.2)	309	(24.2)	61	(29.2)	23	(39.7)	1,086	(23.6)
Stage pre-chemoradiation										
I	289	(8.3)	137	(10.9)	10	(4.9)	2	(3.4)	404	(8.9)
II	734	(21.0)	263	(20.9)	30	(14.6)	6	(10.3)	956	(21.1)
III N1	410	(11.7)	179	(14.2)	29	(14.1)	7	(12.1)	556	(12.3)
III N2	243	(6.9)	61	(4.8)	11	(5.3)	3	(5.2)	290	(6.4)
Localised (NOS)	1,007	(28.8)	319	(25.3)	55	(26.7)	22	(37.9)	1,284	(28.3)
Metastatic	817	(23.3)	302	(23.9)	71	(34.5)	18	(31.0)	1,046	(23.1)
Unknown	43		16		3		0		56	
Tumour grade										
Well	587	(19.6)	118	(10.9)	26	(14.7)	16	(31.4)	676	(17.5)
Moderate	1,784	(59.7)	712	(66.0)	122	(68.9)	25	(49.0)	2,358	(60.9)
Poor	580	(19.4)	242	(22.4)	29	(16.4)	8	(15.7)	792	(20.5)
Undifferentiated	39	(1.3)	7	(0.6)	0	(0.0)	2	(3.9)	45	(1.2)
Unknown	553		198		32		7		721	
Mucinous tumour										
Yes	382	(13.8)	137	(13.5)	15	(9.8)	6	(16.2)	490	(13.6)
No	2,389	(86.2)	878	(86.5)	138	(90.2)	31	(83.8)	3,117	(86.4)
Unknown	772		262		56		21		985	
Lymphovascular invasion										
Yes	866	(33.6)	236	(26.9)	53	(38.7)	16	(47.1)	1,042	(31.8)
No	1,712	(66.4)	641	(73.1)	84	(61.3)	18	(52.9)	2,239	(68.2)
Unknown	965		400		72		24		1,311	

*All patients (both rectal and colon cancer) who had neo-adjuvant chemotherapy are classified as localised or metastatic.

Table 2B: Comparison of disease characteristics at diagnosis by deprivation.

	Deprivation quintile (NZDep2006)										
	n=4,792										
	1			**2**		**3**		**4**		**5**	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
Tumour site											
Ascending colon	312		(32.1)	289	(29.7)	352	(32.6)	291	(29.8)	215	(27.2)
Transverse colon	68		(7.0)	88	(9.0)	89	(8.2)	69	(7.1)	65	(8.2)
Descending colon	342		(35.2)	359	(36.9)	394	(36.5)	385	(39.4)	316	(40.0)
Colon (NOS)	9		(0.9)	17	(1.7)	12	(1.1)	8	(0.8)	18	(2.3)
Rectum	250		(25.7)	237	(24.4)	245	(22.7)	232	(23.7)	194	(24.6)
Stage pre-chemoradiation*											
I	88		(9.2)	90	(9.4)	111	(10.4)	82	(8.5)	52	(6.7)
II	182		(19.0)	195	(20.3)	227	(21.3)	225	(23.3)	164	(21.0)
III N1	119		(12.4)	127	(13.2)	127	(11.9)	125	(12.9)	87	(11.2)
III N2	68		(7.1)	61	(6.3)	73	(6.9)	55	(5.7)	47	(6.0)
Localised (NOS)	275		(28.6)	278	(28.9)	281	(26.4)	257	(26.6)	225	(28.8)
Metastatic	228		(23.8)	211	(21.9)	246	(23.1)	222	(23.0)	205	(26.3)
Unknown	12			11		15		11		10	
Tumour grade											
Well	138		(16.5)	148	(18.2)	166	(18.2)	136	(16.4)	114	(17.4)
Moderate	509		(60.9)	494	(60.8)	562	(61.5)	500	(60.5)	416	(63.4)
Poor	179		(21.4)	160	(19.7)	176	(19.3)	184	(22.2)	119	(18.1)
Undifferentiated	10		(1.2)	11	(1.4)	10	(1.1)	7	(0.8)	7	(1.1)
Unknown	136			160		166		150		134	
Mucinous tumour											
Yes	100		(12.8)	99	(13.0)	117	(13.5)	104	(13.5)	97	(16.6)
No	681		(87.2)	665	(87.0)	749	(86.5)	666	(86.5)	486	(83.4)
Unknown	191			209		214		207		207	
Lymphovascular invasion											
Yes	231		(32.3)	229	(32.6)	226	(29.3)	230	(32.8)	178	(32.7)
No	484		(67.7)	473	(67.4)	546	(70.7)	472	(67.2)	366	(67.3)
Unknown	257			271		308		275		246	(31.1)

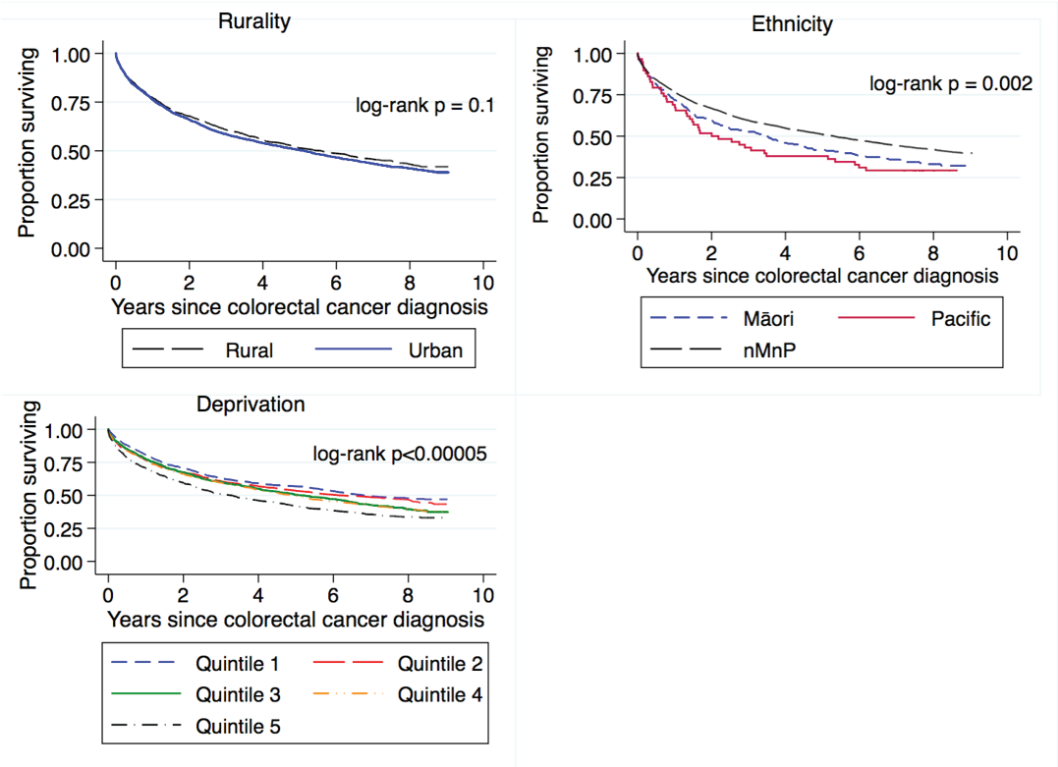
*All patients (both rectal and colon cancer) who had neo-adjuvant chemotherapy are classified as localised or metastatic.

Table 3: Comparison of presentation to secondary care by ethnicity, rurality and deprivation. KPIs are presentation directly to ED and presentation with obstruction.

	Presentation			Adjusted for tumour site			Adjusted for confounders below*		
	n	(%)	(95%CI)	RR	(95%CI)	p-value	RR	(95%CI)	p-value
Presentation to ED	1,417	(30.6)	(0.29, 0.32)						
Urban	1,041	(30.9)	(29.4, 32.5)	1.0	reference		1.0	reference	
Rural	376	(30.4)	(27.9, 33.0)	1.0	(0.9, 1.1)	0.9	1.0	(0.9, 1.1)	0.4
Māori	87	(44.6)	(37.8, 51.7)	1.6	(1.3, 1.8)	<0.0005	1.5	(1.2, 1.7)	<0.0005
Pacific	20	(34.5)	(23.5, 47.6)	1.3	(0.9, 1.8)	0.1	1.2	(0.8, 1.6)	0.4
nonM-nonP	1,307	(30.4)	(29.0, 31.7)	1.0	reference		1.0	reference	
Urban Māori	53	(40.8)	(32.6, 49.4)	1.4	(1.1, 1.7)	0.001	1.3	(1.1, 1.6)	0.006
Rural Māori	34	(52.3)	(40.2, 64.2)	1.9	(1.5, 2.4)	<0.0005	1.8	(1.4, 2.2)	<0.0005
Pacific	20	(34.5)	(23.4, 47.6)	1.3	(0.9, 1.8)	0.1	1.2	(0.8, 1.6)	0.4
Urban nonM-nonP	963	(30.9)	(29.3, 32.5)	1.0	reference		1.0	reference	
Rural nonM-nonP	339	(29.3)	(27.8, 32.0)	1.0	(0.9, 1.1)	0.6	1.0	(0.9, 1.1)	0.8
Deprivation quintile									
1	246	(27.1)	(24.3, 30.0)	1.0	reference		1.0	reference	
2	266	(28.9)	(26.0, 31.9)	1.1	(0.9, 1.2)	0.4	1.1	(0.9, 1.2)	0.4
3	315	(30.5)	(27.7, 33.3)	1.1	(1.0, 1.3)	0.1	1.1	(1.0, 1.3)	0.1
4	297	(31.3)	(28.4, 34.3)	1.2	(1.0, 1.3)	0.04	1.1	(1.0, 1.3)	0.1
5	283	(37.0)	(33.6, 40.5)	1.4	(1.2, 1.6)	<0.0005	1.3	(1.1, 1.5)	<0.0005
Presentation with obstruction									
Total	892	(19.3)	(18.2, 20.5)						
Urban	606	(17.8)	(16.6, 19.1)	1.0	reference		1.0	reference	
Rural	286	(23.4)	(21.2, 25.6)	1.3	(1.2, 1.5)	<0.0005	1.3	(1.2, 1.5)	<0.0005
Māori	46	(23.5)	(18.0, 29.9)	1.2	(0.9, 1.5)	0.3	1.1	(0.8, 1.4)	0.6
Pacific	10	(17.2)	(9.5, 29.3)	1.0	(0.6, 1.7)	0.9	0.9	(0.5, 1.7)	0.8
nonM-nonP	838	(19.3)	(18.2, 20.6)	1.0	reference		1.0	reference	
Urban Māori	28	(21.1)	(14.9, 28.8)	1.1	(0.8, 1.5)	0.6	1.0	(0.7, 1.4)	0.9
Rural Māori	18	(29.5)	(19.4, 42.2)	1.6	(1.1, 2.4)	0.03	1.4	(0.9, 2.2)	0.09
Pacific	10	(17.2)	(9.4, 29.3)	1.1	(0.6, 1.9)	0.8	1.0	(0.6, 1.8)	0.97
Urban nonM-nonP	566	(18.0)	(16.7, 19.4)	1.0	reference		1.0	reference	
Rural nonM-nonP	264	(23.0)	(20.7, 25.6)	1.3	(1.1, 1.5)	<0.0005	1.3	(1.1, 1.5)	<0.0005
Deprivation quintile									
1	160	(17.4)	(15.1, 20.0)	1.0	reference		1.0	reference	
2	168	(18.1)	(15.8, 20.7)	1.0	(0.8, 1.2)	0.8	1.0	(0.9, 1.2)	0.7
3	209	(20.2)	(17.8, 22.7)	1.1	(0.9, 1.4)	0.2	1.2	(1.0, 1.4)	0.1
4	185	(19.5)	(17.1, 22.1)	1.1	(0.9, 1.3)	0.4	1.1	(0.9, 1.3)	0.4
5	169	(22.0)	(19.2, 25.1)	1.2	(1.0, 1.5)	0.03	1.2	(1.0, 1.5)	0.04

* Adjusted for location of primary tumour, age at diagnosis, sex, stage at diagnosis, grade, mucinous tumour, lymphovascular invasion and comorbidity. Missing data were imputed for all the regression models.

Figure 1: Overall survival after diagnosis with colorectal cancer by rurality, ethnicity and deprivation (unadjusted).



as stage and grade) at diagnosis, but Māori patients (particularly rural Māori) and those in the highest quintile of deprivation were still significantly more likely to present directly to ED. The overall percentage of patients presenting with obstruction was 19.3%. Patients from rural areas were significantly more likely to present with obstruction than those from urban areas (RR 1.3; 95% CI: 1.2–1.5). There was no evidence of a difference by ethnicity, but we also examined the risk for urban and rural Māori separately. While the risk ratio (relative to urban nMnP) was higher for rural than urban Māori the confidence intervals were wide. Those living in the quintile of highest deprivation were more likely to present with obstruction (RR 1.2; 95%CI: 1.0–1.5). Adjustment for confounding made little difference to the patterns for deprivation.

Overall survival

For overall survival, follow-up was complete to 23 January 2016, giving 7–9 years of follow-up. The total number of deaths from any cause was 2,871. The overall five-year survival for the complete cohort of CRC patients was 51%, 95% CI (50–53%). Comparisons by stage of disease are shown in Appendix 1.

Comparisons of overall survival by rurality, ethnicity and deprivation are show in in Figure 1. There were no differences by rurality, but there were differences by ethnicity and deprivation. The five-year overall survival was 42% (95% CI: 35–48%) for Māori, 37% (95%CI: 26–50%) for Pacific patients and 51% (95% CI: 50–52%) for nMnP. Median survival was 3.5 years (95% CI: 2.2–4.5 years) for Māori, 2 years (95% CI: 1.3–5.1 years) for Pacific patients and 5.3 years (95% CI: 4.9–5.7 years) for nMnP.

Risk of death from colorectal cancer

Follow-up for cause-specific death was complete to 23 May 2014, giving 5–7 years of follow-up. The overall five-year cumulative incidence of death from CRC was 37.8% (95% CI: 36.4–39.1%) (Table 4). We found no evidence of a difference in risk of death from colorectal cancer by rurality (p=0.6) (Figure 2). The cumulative incidence for Pacific patients was 58.6% (95%

Figure 2: Cumulative incidence of death from colorectal cancer by rurality, ethnicity and deprivation.

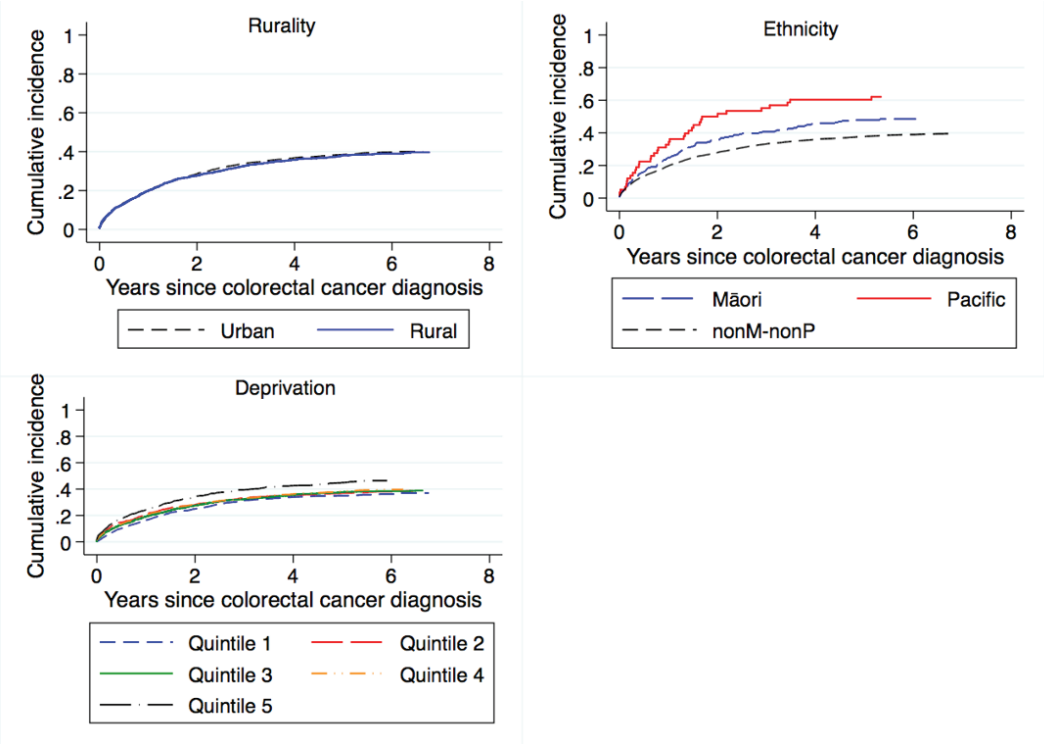


Table 4: Comparison of risk of death from colorectal cancer by rurality, ethnicity and deprivation.

	Deaths from CRC	Five-year cumulative incidence		Adjusted for tumour site			Adjusted for age, sex, tumour site and stage			Adjusted for age, sex, disease and comorbidity*		
	(n)	Risk (%)	(95% CI)	RR	(95%CI)	p-value	RR	(95%CI)	p-value	RR	(95%CI)	p-value
Overall	1,938	37.7	(36.4, 39.1)									
Urban	1,411	38.4	(36.8, 40.0)	1.0	reference		1.0	reference		1.0	reference	
Rural	500	38.0	(35.3, 40.6)	1.0	(0.9, 1.1)	0.6	1.0	(0.9, 1.2)	0.5	1.0	(0.9, 1.1)	0.7
Māori	101	47.4	(40.4, 53.9)	1.3	(1.1, 1.6)	0.006	1.1	(0.9, 1.4)	0.2	1.1	(0.8, 1.3)	0.6
Pacific	36	58.6	(44.9, 70.0)	1.9	(1.4, 2.7)	<0.0005	2.0	(1.5, 2.7)	<0.0005	1.8	(1.4, 2.5)	<0.0005
nMnP	1,799	37.8	(36.3, 39.2)	1.0	reference		1.0	reference		1.0	reference	
Urban Māori	68	47.5	(39.0, 55.5)	1.3	(1.0, 1.6)	0.06	1.2	(0.9, 1.5)	0.2	1.1	(0.8, 1.4)	0.7
Rural Māori	33	50.8	(38.1, 62.1)	1.5	(1.0, 2.1)	0.04	1.1	(0.7, 1.6)	0.6	1.1	(0.8, 1.5)	0.6
Pacific	36	58.6	(44.9, 70.0)	1.9	(1.4, 2.7)	<0.0005	2.0	(1.5, 2.7)	<0.0005	1.9	(1.4, 2.5)	<0.0005
Urban nMnP	1,306	38.4	(36.7, 40.1)	1.0	reference		1.0	reference		1.0	reference	
Rural nMnP	466	37.7	(35.0, 40.5)	1.0	(0.9, 1.1)	0.7	1.1	(0.9, 1.2)	0.4	1.0	(0.9, 1.2)	0.6
Deprivation quintile												
1	355	34.8	(31.9, 37.9)	1.0	reference		1.0	reference		1.0	reference	
2	372	36.9	(34.0, 40.0)	1.1	(0.9, 1.3)	0.2	1.3	(1.1, 1.4)	0.002	1.3	(1.1, 1.5)	0.002
3	416	37.6	(34.7, 40.5)	1.1	(0.9, 1.3)	0.2	1.1	(1.0, 1.3)	0.1	1.1	(1.0, 1.3)	0.1
4	387	38.2	(35.1, 41.2)	1.1	(1.0, 1.3)	0.1	1.1	(1.0, 1.3)	0.1	1.1	(1.0, 1.3)	0.2
5	366	44.8	(41.3, 48.1)	1.4	(1.2, 1.6)	<0.0005	1.3	(1.1, 1.5)	0.001	1.3	(1.1,1.5)	0.004

* Adjusted for location of primary tumour, age at diagnosis, sex, stage at diagnosis, grade, mucinous tumour, lymphovascular invasion and comorbidity. Missing data were imputed for all the regression models.

CI: 44.9–70.0%), for Māori patients 47.4% (95% CI: 40.4–53.9%), and for nMnP 37.8% (95% CI: 36.3–39.2%). After adjusting for demographic variables and disease variables at diagnosis the relative risk of death from CRC for Māori relative to nMnP was attenuated from 1.3 to 1.1 and was no longer statistically significant (p=0.5). The observed relative risk for rural Māori patients was higher than that for urban Māori patients, however the difference was not statistically significant. For Pacific patients, the crude relative risk of 1.9 remained high after adjustment for confounding (RR 1.8; 95% CI: 1.4–2.5; p<0.0005). Patients living in areas with NZDep2006 scores in the most deprived quintile had a 40% higher risk of death from CRC than those in the least deprived quintile. The RR was only slightly reduced by control of confounding. We also found that after control for confounding by age, sex, tumour site and stage, those living in areas of moderate deprivation (deciles 3 and 4) were 30% more likely to die from CRC than those in the least deprived deciles.

Discussion

In this study we have found clear evidence that among people diagnosed with colorectal cancer the risk of death from their cancer differs by ethnicity and deprivation, but found no evidence of a difference by rurality. Pacific patients had the worst outcomes, with a five-year cumulative incidence of death from CRC of 59%, and a risk two-fold higher than that for nMnP. This increased risk in Pacific patients was not explained by differences in measures of disease at diagnosis, although the numbers were small and the confidence interval correspondingly wide. Māori patients also had a higher risk of death from CRC than nMnP, with a five-year cumulative incidence of 47%, and a risk 30% higher than nMnP. Much of the increased risk for Māori was explained by differences in measured disease at diagnosis. For deprivation, an increased risk was present for the most deprived quintile (40% higher risk than the least deprived) and this increase was attenuated only slightly by adjusting for confounding. Furthermore, adjustment for confounding revealed a higher risk in deprivation deciles 3 and 4 compared to the least deprived.

Our study included all patients registered on the NZCR diagnosed in 2007 and 2008, hence gives a full picture of the experience of the colorectal cancer population across New Zealand. The data collection from clinical records from both public and private hospitals meant we had extended information regarding the disease at diagnosis, including more accurate information on stage and grade than was available from the National Collection databases. This increased our ability to distinguish factors affecting timeliness of diagnosis from those affecting treatment after diagnosis.

However, the data collection was retrospective, which limited available data to those collected for clinical purposes. Several variables including smoking, aspirin use, family history, body mass index, diet, performance status and perineural invasion were not consistently recorded in notes. There was very little information on CEA at diagnosis, tumour budding or on currently known genetic biomarkers such as MSI (approximated by MMR status by IHC assessment), K- & N-RAS and BRAF. Information on other potentially explanatory factors such as diet is not recorded in clinical notes. Our measure of comorbidity was based on hospital discharge data, so is likely to underestimate comorbidity, especially in those who experience greater barriers in accessing health services. As a consequence, uncontrolled confounding may explain some of the difference in risk of death from colorectal cancer between groups.

Our measures of ethnicity, rurality and deprivation relied on routinely collected data. The ethnicity classifications from the Cancer Registry are updated continuously, and have been demonstrated to be accurate in this age group compared with self-report census data.[28] In order to make the comparisons in this paper we used prioritised ethnicity, although we could have used total ethnicity categories, where Māori and Pacific are categorised within either or both ethnic groups with which they identify (so groups are not mutually exclusive). In fact this decision only affected six patients, so is unlikely to have had an important impact on the results. Further papers are planned looking separately at the experiences of Maori and of Pacific people with colorectal

cancer. The measures of rurality, and deprivation used were based on mesh block of residence at diagnosis in this paper, and as such may not fully capture the circumstances of individuals. More detailed information was beyond the scope of this study, but future papers may explore the impact of changing residence if numbers allow.

Disentangling the differing impacts of late stage presentation and treatment after entering secondary care on risk of CRC death is not straightforward. Some variables such as age and comorbidity act on both sections of the path. For the presentation KPIs, presentation to ED and presentation with obstruction, Māori patients were still more likely to present to ED after controlling for confounding, but we found no difference for Pacific patients. Hill et al also found a higher proportion of Māori with colon cancer (compared with non-Māori) underwent emergency surgery, although the difference in that study was not statistically significant.[3] We did not measure emergency surgery directly, and it is possible that presentation to ED is a poor surrogate for this as patients with greater socioeconomic deprivation may present to ED rather than a GP. There was little difference in the proportion presenting with obstruction by ethnicity, suggesting that acute presentation is a poor surrogate for obstruction and more likely to reflect engagement with primary care and/or diagnostic pathways. People living in rural areas were more likely to have presented with obstruction than those in urban areas. This difference was not explained by our measures of demographic and clinical characteristics, but did not appear to translate to worse outcomes. Furthermore, controlling confounding by stage at diagnosis is difficult for rectal cancer. Many patients receive neoadjuvant chemoradiation (CRT), and reliable TNM stage is not available until surgical and histological examination following CRT. Because of the heterogeneity of pre-operative treatment strategies for rectal cancer, we used stage as known before any treatment for this paper, so could only classify rectal cancer stage as localised versus metastatic. The impact of chemoradiation will be addressed in a future paper. Given the relatively high proportion of Pacific patients with rectal cancer, some confounding by disease stage at diagnosis is likely to remain at this point.

Our results suggest that much of the poorer survival outcome for Māori patients results from delays in diagnosis; the largest attenuation in relative risk (from 1.4 to 1.1) occurred with adjustment for disease stage (data not shown). However, the confidence interval includes up to a 20% decrease and a 30% increase in risk compared with non-Māori-non-Pacific, so it is still possible that differences in outcome due to differences in treatment after diagnosis may occur. It is likely that there is residual confounding by stage, smoking status, comorbidity and BMI, but it is difficult to know the extent of this. In contrast, a study of patients diagnosed between 1996 and 2003, which also used clinical record data, Hill et al found worse survival for Māori patients, which was not explained by either demographic characteristics or disease at diagnosis including stage at diagnosis. They found evidence of differences in both access to and quality of care for Māori patients which explained about a third of the survival disparity.[3] For Pacific patients, post-diagnosis differences in care are likely to be influencing survival, although here as well we cannot rule out residual confounding. For patients with rectal cancer, which is more common in Pacific patients, stage at diagnosis is not well defined for those having neo-adjuvant chemoradiation, so we were unable to control fully for this confounding. Differences in outcome may also reflect underlying differences in tumour biology. We found differences in tumour location and grade by ethnicity, and while we were able to control for the two measures in the analysis there may be other aspects of tumour biology that affect outcome that we have not accounted for. We also note that the overall number of Pacific patients in this study is small. The KPIs relating to treatment and management will be explored in further papers and may identify areas for improvement for both Māori and Pacific patients.

We did not find any evidence of disparity in survival outcomes by rurality. This is consistent with findings from other New Zealand studies including a recent study in New Zealand breast cancer patients.[2,29] Similarly a study of colorectal cancer patients

in South Australia found no difference in survival for patients living in rural vs urban areas.[30] In contrast, a large study in the US using SEER data found evidence of small differences in outcome by population density, with people from large metropolitan areas and rural areas having the worst outcomes.[31] It is worth noting that the underlying impact of rurality and remoteness may vary between countries depending on the extent of remoteness and the way in which health services are organised. It is plausible that those living in the most remote areas of New Zealand are less likely to have timely access to cancer care, but a study including more people from remote areas would be required to address that. We also considered using distance of travel to the treatment centre as a measure of rurality, but excluded this due to the complex relationship with socioeconomic status and the small numbers living substantial distances from a cancer treatment centre. Differences in outcome due to variations in surgical procedure volume have been demonstrated in the US,[32] but the observed differences were small, and this study would not have been large enough to detect them.

Patients living in areas with the greatest deprivation experienced worse survival outcomes after colorectal cancer diagnosis. Some of this can be explained by late stage presentation, but differences still occur. Again, it is likely that there is residual confounding by smoking status, comorbidity and BMI. Both Māori and Pacific patients are more likely to live in the high deprivation areas. However, numbers were too small in this study to explore separate roles of deprivation and ethnicity. We also found, unexpectedly, that outcomes were worse for patients in the second decile of deprivation than in areas of least deprivation. The cause of this is unclear, but given the number of comparisons in this paper some false positive findings would not be surprising.

International comparisons of CRC-specific outcomes after diagnosis are complicated by a number of factors, including differences in screening practices[33] and differences in statistical methods. However, Beckman et al in a study in South Australia found a five-year cumulative incidence of death from CRC of 32% using similar statistical methods to ours in a population wide linkage study (as compared to our 38%).[30] Our results are also consistent with findings from other studies, which have shown higher cause-specific or relative mortality in New Zealand than in Australia.[34]

Conclusions

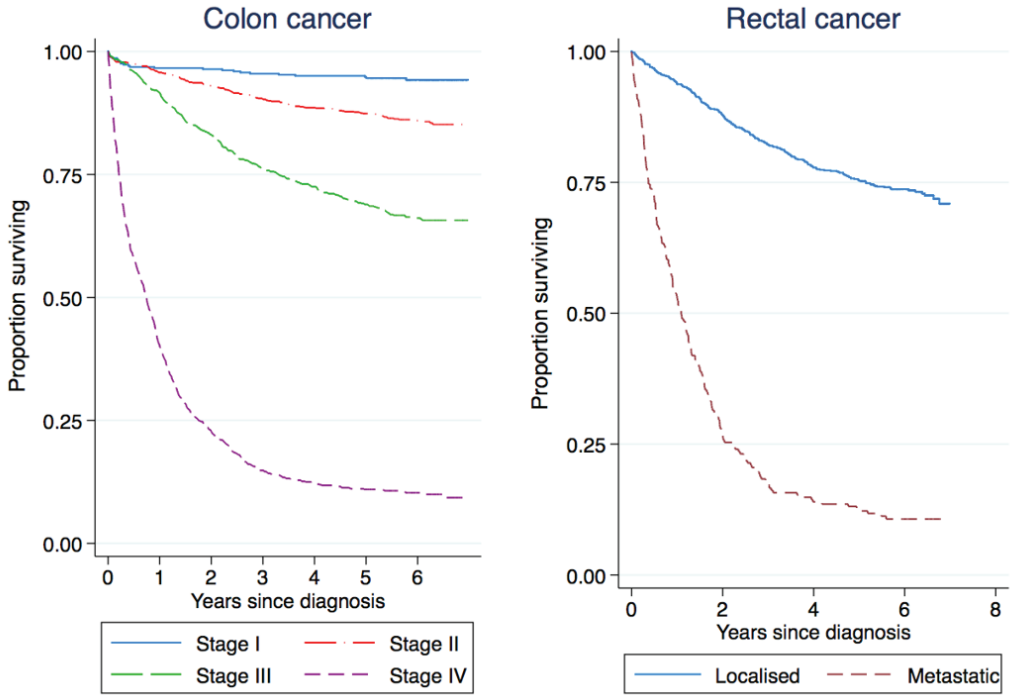
Disparity in outcomes following diagnosis of CRC exists in New Zealand. Māori and Pacific patients and those residing in the most deprived areas are at increased risk of death. The increased risk of death from CRC is significantly worse for Pacific patients. Some of the differential in survival is likely to be due to factors affecting presentation to secondary care, as evidenced by the later stage at presentation and presentation to ED. Improving access to early detection, through both screening and reducing barriers to existing care, is therefore important for reducing inequity. However, particularly for Pacific patients, the differential persists after taking into account disease at presentation, indicating that differences in management after diagnosis also impact on survival. Further analyses of the PIPER data will explore where these differences occur.

Appendix

Survival by stage for patients with colon and rectal cancer.

Among the 3,713 patients with colon cancer, stage was unknown for 41 and known as localised only for 433. Based on those with known stage, the five-year overall survival percentages were (Figure 1A): stage I 80%, 95% CI (76 –84); stage II 71%, 95%CI (70–74); stage III N1 63%, 95% CI (59–67); stage III N2 50%, 95% CI (44–56); stage IV 6%, 95% CI (5–8). Among the 1,195 with rectal cancer, stage was unknown for 17. At diagnosis patients were classified as localised or metastatic only (due to the varied use of neoadjuvant chemoradiation in many of those with localised disease). The five-year overall survival percentages for patients with rectal cancer were (Figure 1B): localised 65%, 95% CI (62–68); metastatic 10%, 95% CI (7–15).

Appendix Figure 1: Overall survival after diagnosis with colorectal cancer by stage at diagnosis.



Competing interests:
The authors disclose that the work included in this publication received funding from the Health Research Council of New Zealand and the Ministry of Health. Dr Sarah Derrett discloses reimbursement of costs to attend Bowel Cancer New Zealand meetings outside of the submitted work. There are no other conflicts of interest to declare.

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