ORIGINAL ARTICLE

Trends in colorectal cancer incidence rates in New Zealand, 1981–2004

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Abstract

Background: Incidence rates of colorectal cancer (CRC) in New Zealand rank among the highest worldwide. Internationally, there has been evidence of a shift in colon cancer from left- to right-sided. The objective of this study was to determine trends in left- and right-sided colon and rectal cancers incidence by sex, age and ethnicity.
Methods: Using datasets created by linking data from the New Zealand Cancer Registry to the census data, we analysed a total of 47 694 CRCs from 1981 to 2004. Cancers were divided into right-sided colon (cecum to the splenic flexure); left-sided colon (descending and sigmoid colon); and rectal (rectosigmoid junction and rectum).
Results: Left- and right-sided colon, and rectal cancer incidence rates increased by 13–20% among men. In women, colon cancer rates increased by 25% for right-sided cancers, decreased by 8% for left-sided cancers and remained unchanged for rectal cancers. This corresponds with an increase in right-sided cancers from 57% to 65% of total colon cancers in women. The incidence of all CRCs increased at a faster rate among Māori than non-Māori.
Conclusion: We identified a left- to right-sided shift in colon cancer limited to women over the age of 65. While Māori trends in site distribution parallel those of their non-Māori counterparts, the rapid increase in Māori incidence rates is noteworthy. It is unclear why such shifts in CRC site distribution are occurring.

Introduction

Worldwide, colorectal cancer (CRC) is one of the most common cancers.[1] Furthermore, the incidence and mortality rates of CRC in New Zealand rank among the highest in the world.[1,2] Age, personal history of polyps, family history of CRC and inflammatory bowel disease are strong, albeit non-modifiable risk factors for the development of CRC. Data on modifiable risk factors are inconsistent but there is good evidence for the role of level of physical inactivity,[3,4] obesity[5] and diabetes mellitus (DM)[6,7] in the development of CRC.

Exploration into the evolution of CRC has led some,[8–15] but not all,[16–18] to conclude that over time there has been a shift in CRC incidence to the proximal colon, the so-called left- to right-sided shift. This finding has kindled research on site-specific aetiologies and risk factors. The proposed hypotheses suggest that the occurrence of CRC at a particular anatomic site may be associated with distinctive risk factor profiles within particular geographic and demographic groups.[19–21] As a result, studies have attempted to stratify risk by sex, age, ethnicity and income, and have reported a right-sided shift among low-income populations,[12] Caucasians,[12] African Americans,[19,22] males,[13] females[8,12,13] and/or the elderly.[12,13]

Beyond clues from socio-demographic variations in right-sided shift, studies have suggested that type 2 DM in females,[7] cigarette smoking,[23] prior cholecystectomy[24,25] and physical inactivity[3,4] increase the risk for right-sided colon cancer. Although not compelling, there is evidence that alcohol consumption,[26] type 2 DM in males[27] and dietary habits[28] are risk factors for left-sided cancers. In summary, the findings in relation to site-specific risk factors have been inconsistent, and to date, no risk factor has been identified that explains the patterns in CRC site distribution.

The aim of this study is to determine whether there has been a right-sided shift in CRC in New Zealand from 1981 to 2004. Using cancer registry data linked to the census information in a high CRC

incidence population, we investigate whether patterns in anatomic tumour location have varied by gender, age and ethnicity.

Methods

The datasets were created through linking records from the New Zealand Cancer Registry (NZCR) and records from the five yearly census of population and dwellings. The NZCR is a population-based cancer registry that collects information on all malignant tumours with the exception of non-melanotic skin cancers. Five closed non-overlapping cohorts were created of the New Zealand usual resident population (all ages) on census night 1981, 1986, 1991, 1996, 2001, followed up for incident cancer(s) until the subsequent census or in the case of the 2001 cohort, until December 31, 2004 (the most recent data available at the time of the study's record linkage). Exact time periods are as follows: March 25, 1981 to March 4, 1986; March 5, 1986 to March 5, 1991; March 6, 1991 to March 5, 1996; March 6, 1996 to March 6, 2001; and lastly, March 7, 2001 to December 31, 2004. Cohorts were created using probabilistic record linkage software (QualityStage™; IBM Corp., Armonk, NY, USA) to anonymously link census and cancer registry records within a geographic area (meshblock or census area unit) on sex, date of birth, ethnicity and country of birth. Further details on the linkage methods, process and outputs are detailed elsewhere.[29]

Briefly, 73.2% (1981–1986) to 81.7% (2001–2004) of eligible cancer registry records were linked to a census record, with 95.2% (1981–1986) to 96.9% (2001–2004) of these linked census-cancer records estimated to be true links. To adjust for underestimation of rates using the linked datasets, and to correct for linkage bias whereby the percentage of eligible cancer records linked varied by socio-demographic characteristics, we calculated weights for strata based on age, sex, ethnicity, small area deprivation and time since census. All analyses presented in this report use these weights, and they have been shown to satisfactorily adjust for linkage bias.[30]

Approval was granted under the Statistics New Zealand Data Integration Policy, and the Wellington Ethics Committee granted ethics approval for CancerTrends (Ref 04/10/093).

Variables

Exposures

Ethnicity was classified as Māori and non-Māori, which includes Pacific, Asian and European/Other. By the 2006 census, the New Zealand population was over 4 million; 14% classified as Māori, 7% Pacific, 9% Asian, 65% New Zealand European and 11% identifying with other ethnic groups (although largely of European descent).

Outcome

A CRC recorded in the NZCR was required to be included in this study. CRCs (ICD 10 code C18-20) were categorized into right-sided (cecum (C18.0), ascending colon (C18.2), hepatic flexure (C18.3), transverse colon (C18.4) and splenic flexure (C18.5)), left-sided (descending colon (C18.6) and sigmoid colon (C18.7)) and rectal (rectosigmoid junction (C19) and rectum (C20)). Those coded

as unspecified (C18.9) or overlapping/appendix (C18.8) were excluded.[19] A total of 47 694 CRC are analysed in this paper.

Analyses

Data were restricted to adults (25+ years) who were in their usual residence on census night. All analyses were conducted in SAS v8.2 (SAS Institute Inc., Cary, NC, USA). Person time was censored after development of the first CRC with a specific three-digit ICD code. Standardized rates and 95% confidence intervals (CIs) were calculated for sex, age and ethnicity using direct standardization to the age structure of the 2001 World Health Organization World Standard population.

Regression analysis was used to determine changes in incidence rates over time, per unit of time of 5 years, by weighted regression of the standardized rates over time (weights = inverse of the variance of the standardized rate).

Results

Table 1 shows the number of left- and right-sided colon, and rectal cancers and person-years of follow-up by time period for each sex. The overall incidence of CRC in New Zealand continues to increase. In men, there has been an increase in incidence in all sites: left-sided (19% from 1981–1986 to 2001–2004, or from our regression analysis, an increased rate of 1.13 per 100 000 per 5 years (95% CI 0.37 to 1.88)); right-sided (22%, or increased rate of 1.32 per 100 000 per 5 years (95% CI 0.77 to 1.87)); and rectal cancer (13%, or an increased rate of 1.19 per 100 000 per 5 years (95% CI 0.56 to 1.82)). There is no evidence of a shift in colon tumours from left- to right-sided among men (Fig. 1).

In women, there has been an increase in incidence of right-sided (25%, or 1.60 per 100 000 per 5 years (95% CI 1.38 to 1.82)), but a decrease in left-sided cancers (−8%, or −0.38 per 100 000 per 5 years (95% CI −0.70 to −0.05)). Incidence of rectal cancers has remained unchanged (Fig. 1). The non-overlapping CIs and divergent trends of left- and right-sided cancers indicate statistical significance. Accordingly, the percentage of all colon cancers that are right-sided increased monotonically from 57% to 65% among women.

Age

As expected, age-standardized incidence rates among those ages 65+ were considerably higher than the 25–64 age group at all sites (Table 2). Risk of CRC was stable or decreased for all sites over time for the younger age group in both sexes, although the only statistically significant trend in this group was for left-sided cancers in females (18% reduction, $P = 0.01$).

For men aged 65+ years, there was a significant increase at all sites (52%, $P = 0.02$; 35%, $P = 0.03$; and 32%, $P = 0.01$ for right-sided colon, left-sided colon and rectal cancers, respectively) without evidence of a shift to right-sided cancers. Among females 65+, there was a 58% ($P < 0.01$) increase in right-sided cancers, a non-significant increase in left-sided cancers and stable rates of rectal cancers which is consistent with a right-sided shift.

Table 1 Number of colorectal cancers and person-years of follow-up by site and sex for those aged 25+ years (47 694 total colorectal cancers)

| | Males | | | Females | | |
	Right colon	Left colon	Rectal	Right colon	Left colon	Rectal
1981–1986†						
Total cancers	1 215	1 074	1 686	1 662	1 149	1 242
Person-years	4 309 024	4 309 512	4 307 881	4 556 671	4 557 967	4 557 666
1986–1991						
Total cancers	1 392	1 236	1 881	1 893	1 272	1 284
Person-years	4 662 273	4 662 563	4 661 070	4 972 980	4 974 209	4 974 302
1991–1996						
Total cancers	1 548	1 377	2 094	2 118	1 248	1 455
Person-years	4 937 950	4 938 387	4 936 651	5 343 537	5 345 630	5 345 132
1996–2001						
Total cancers	1 758	1 623	2 334	2 466	1 416	1 569
Person-years	5 304 041	5 304 327	5 302 566	5 810 385	5 812 888	5 812 460
2001–2004						
Total cancers	1 647	1 326	1 956	2 307	1 122	1 344
Person-years	4 131 298	4 131 789	4 130 655	4 606 380	4 608 527	4 608 177

†Time periods are non-overlapping; please refer to Methods section for exact dates.

Ethnicity

Table 3 shows the age-standardized incidence rates of CRC for males and females by ethnicity. Despite having considerably lower incidence rates of CRC than non-Māori at each site for all time periods, Māori men and women had a higher relative increase in incidence over the study period. The difference was particularly marked for left-sided disease among males with relative increases of 11% ($P = 0.07$) for non-Māori and 127% ($P = 0.06$) for Māori males, and rectal disease with relative increases of 6% ($P = 0.10$) for non-Māori and 82% ($P < 0.01$) for Māori males.

Significant increases were seen in right-sided cancers in both non-Māori (21%, $P < 0.01$) and Māori women (66%, $P = 0.04$), compared with non-significant changes in left-sided cancers (−12%, $P = 0.07$ and 16%, $P = 0.13$ for non-Māori and Māori, respectively) and rectal cancers (−1%, $P = 0.69$ and 39%, $P = 0.30$, respectively). Consequently, right-sided tumours increased as a percentage of all colonic tumours for both non-Māori (58% to 66%) and Māori women (45% to 54%), albeit the latter increase being non-monotonic and erratic. Non-Māori men had relative increases in incidence at all sites, with no change in site distribution. Māori men had larger increases in incidence rates at all sites relative to non-Māori men but lacked statistical precision, thus precluding any conclusion of shift in tumour location.

Discussion

From our study of 47 694 CRC from 1981 to 2004 in an unscreened New Zealand population,[31,32] we found an increase in CRC for both sexes, restricted to those 65+ years of age. While there is no evidence for a left- to right-sided shift in men, we identify a right-sided shift in both non-Māori and Māori women aged 65+ years.

We found an increasing incidence of CRC for those aged 65+, but no change or a reduction in incidence among the younger population. This is consistent with a birth cohort analysis of CRC in New Zealand which concluded that the incidence rates of CRC have been declining for successive cohorts born from 1943 to 1953.[33] The high

CRC incidence rates seen in the 65+ age group may be the result of early-life exposures and risk factors, although how such early-life risk factors would give rise to a right-sided shift, and differentiate by sex, is unresolved.

The only other New Zealand study that investigated a shift in CRC reported a right-sided shift in both sexes that was more pronounced in the elderly. However, this was a small study that only compared data from two consecutive 4-year time periods and likely does not accurately represent the trends over time.[10]

A number of international population-based studies have reported a left- to right-sided shift in CRC among both older men and women.[10–12,14,15] For example, in Norway, Larsen and Bray found evidence of a left- to right-sided shift in both sexes seen among the older population (55–74 years).[15] These authors also carried out a birth cohort analysis and concluded that there have been rapid increases in right-sided colon cancer among generations born from 1900 with stabilization of colon cancer at both sites in generations born after 1955. Similarly, Singh *et al*. analysed 40 years of colon cancer data from Canada, and reported an increase in rates of right-sided colon cancer in both sexes, largely among the older population (>70 years).[14] Saltzstein and Behling investigated CRC incidence from 1988 to 2003 in California and reported a left- to right-sided shift in both sexes, but more pronounced among women.[12]

Fewer studies have investigated site distribution by ethnicity. Cucino *et al*. found increased proportions in right-sided cancers among black males and whites of both sexes from the Department of Veterans Affairs database and increased right-sided cancers for both sexes in blacks and whites from the SEER database of the National Cancer Institute.[11] On the other hand, a study by Demers *et al*. looking at 22 years of CRC data from Michigan, USA, reported a right-sided shift only in African Americans (both sexes) and concluded that such shifts may be related to ethnic-specific changes in environmental exposures.[19]

It is not clear why there may be variations in CRC subsite trends over time and between countries or regions. One possibility is that differential screening uptake may impact site distribution. One study
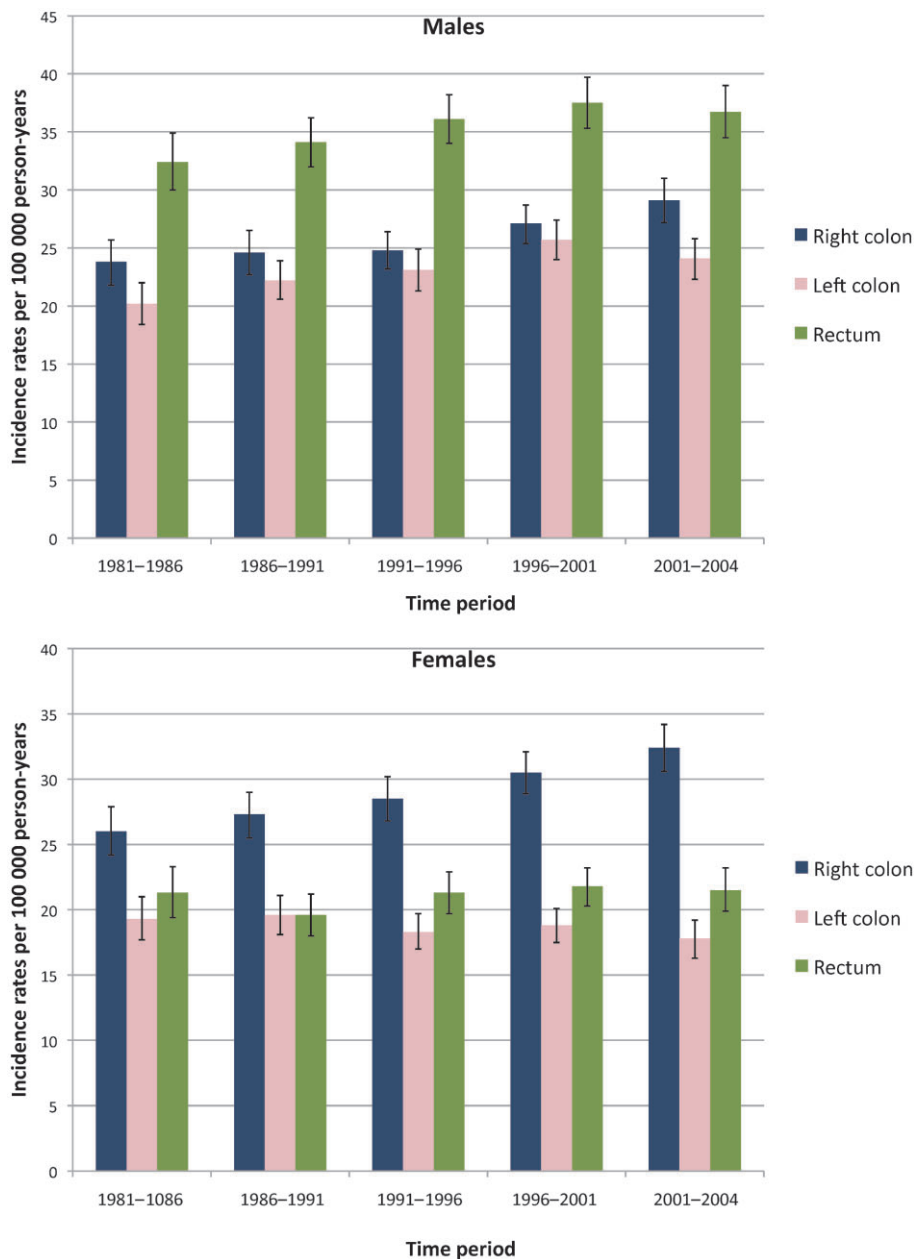
suggests that polypectomies have led to a disproportionate decrease in incidence of left-sided cancers and therefore an increased proportion of right-sided cancers.[12] There is also some evidence that colonoscopy differentially reduces mortality from cancers on the left compared with right.[34] Such theories do not help explain our findings, as there is no significant utilization of screening,[31,32] and certainly no clear increased utilization by women in New Zealand.

Another source for inconsistent findings is the variation in categorization of left and right colon. For example, Vobecky *et al*. used a classification that included five groups – caecum, ascending colon, transverse and descending colon (as one group), sigmoid colon, and rectum – while Demers *et al*. used three groups – right colon from caecum to splenic flexure, left colon from descending to sigmoid colon, and rectum.[8,19] Such variation in categorization may result in

contradicting conclusions even if identical data are used. To allow for reproducibility and comparison between studies, it would be useful to standardize the categorization of left and right colon. However, such classification errors are presumably non-differential by sex, age and ethnicity, and therefore would not affect patterns of varying site distribution by these demographic groups.

Strengths and limitations

This study allowed us to investigate CRC incidence for the entire New Zealand population over a 24-year period. The resulting comprehensive database enabled us to identify trends and populations at risk for CRC. By using data from the entire New Zealand (census night) population as well as data from NZCR, it was possible to overcome undercounting of Māori on cancer registry data.[35]

Table 2 Trends in age-standardized right- and left-sided colon, and rectal cancer incidence rates per 100 000 person-years (95% CI) by sex and age

| | Males | | Females | |
	25–64	65+	25–64	65+
Right colon				
1981–1986†	12.5 (11.3–13.7)	86.9 (79.8–94.0)	14.8 (13.5–16.1)	90.9 (83.3–98.5)
1986–1991	13.6 (12.4–14.9)	86.9 (78.9–94.9)	15.1 (13.7–16.5)	97.9 (91.1–105.0)
1991–1996	12.8 (11.6–13.9)	96.2 (89.4–103.0)	15.5 (14.3–16.8)	106.0 (98.0–113.0)
1996–2001	13.2 (12.1–14.3)	110.0 (103.0–117.0)	14.8 (13.6–16.0)	123.0 (116.0–130.0)
2001–2004	11.3 (10.2–12.3)	132.0 (123.0–142.0)	12.9 (11.7–14.1)	144.0 (135.0–152.0)
% change	−10	52	−13	58
P (trend)	0.36	**0.02***	0.22	**<0.01**
Left colon				
1981–1986	11.6 (10.4–12.7)	72.8 (65.5–80.0)	13.1 (11.7–14.5)	59.7 (53.7–65.6)
1986–1991	13.9 (12.7–15.2)	73.9 (67.4–80.4)	13.1 (11.9–14.4)	58.8 (53.4–64.2)
1991–1996	13.2 (12.1–14.4)	83.0 (75.7–90.2)	12.2 (11.1–13.4)	55.9 (50.3–61.6)
1996–2001	13.0 (12.0–14.1)	102.0 (95.0–109.0)	12.0 (11.0–13.1)	62.9 (57.9–67.8)
2001–2004	11.8 (10.7–12.8)	98.1 (90.9–105.0)	10.8 (9.8–11.8)	64.9 (58.4–71.3)
% change	2	35	−18	9
P (trend)	0.92	**0.03**	**0.01**	0.25
Rectal				
1981–1986	19.3 (17.6–20.9)	112.0 (103.0–121.0)	13.0 (11.8–14.2)	73.1 (63.8–82.4)
1986–1991	21.9 (20.3–23.5)	114.0 (105.0–123.0)	12.1 (10.9–13.3)	62.7 (56.6–68.8)
1991–1996	20.9 (19.4–22.5)	134.0 (125.0–144.0)	12.9 (11.7–14.1)	71.7 (65.3–78.1)
1996–2001	22.5 (21.0–24.0)	132.0 (124.0–141.0)	13.3 (12.2–14.4)	73.5 (67.7–79.3)
2001–2004	18.9 (17.6–20.3)	148.0 (138.0–158.0)	13.1 (11.9–14.2)	74.5 (68.3–80.6)
% change	−2	32	1	2
P (trend)	0.83	**0.01**	0.39	0.25

*Significant values (P < 0.05) indicated in bold font. †Time periods are non-overlapping; please refer to Methods section for exact dates.

Table 3 Trends in age-standardized right- and left-sided colon, and rectal cancer incidence rates per 100 000 person-years (95% CI) by ethnicity (25+ years)

| | Non-Māori | | Māori | |
	Male	Female	Male	Female
Right colon				
1981–1986†	26.4 (24.9–27.9)	29.8 (28.3–31.3)	12.3 (7.9–16.7)	8.7 (5.0–12.4)
1986–1991	27.7 (26.2–29.2)	30.6 (29.1–32.0)	10.7 (5.7–15.8)	12.9 (8.5–17.3)
1991–1996	28.2 (26.8–29.6)	31.9 (30.4–33.3)	10.7 (6.5–14.8)	13.2 (8.7–17.7)
1996–2001	29.3 (27.9–30.6)	33.9 (32.5–35.3)	18.0 (13.7–22.3)	14.2 (10.3–18.1)
2001–2004	31.4 (30.0–32.9)	36.2 (34.7–37.8)	19.5 (14.6–24.4)	14.4 (10.7–18.2)
% change	19	21	59	66
P (trend)	**<0.01***	**<0.01**	0.11	**0.04**
Left colon				
1981–1986	23.1 (21.7–24.5)	21.5 (20.2–22.8)	8.1 (3.8–12.5)	10.7 (6.7–14.8)
1986–1991	24.7 (23.3–26.0)	22.1 (20.7–23.4)	12.3 (7.4–17.2)	9.0 (5.3–12.7)
1991–1996	25.2 (23.9–26.6)	20.1 (18.9–21.3)	14.5 (8.9–20.1)	10.8 (6.5–15.0)
1996–2001	26.8 (25.5–28.1)	20.6 (19.5–21.7)	23.6 (18.1–29.1)	11.5 (8.7–14.3)
2001–2004	25.7 (24.4–27.0)	19.0 (17.8–20.1)	18.4 (13.9–22.9)	12.4 (8.7–16.1)
% change	11	−12	127	16
P (trend)	0.07	0.07	0.06	0.13
Rectal				
1981–1986	36.2 (34.5–37.9)	23.0 (21.7–24.4)	17.6 (11.2–24.0)	10.5 (5.4–15.5)
1986–1991	37.5 (35.8–39.3)	21.4 (20.1–22.6)	20.1 (14.7–25.4)	11.3 (7.3–15.3)
1991–1996	38.1 (36.4–39.8)	22.0 (20.8–23.3)	27.8 (21.3–34.3)	19.4 (13.4–25.4)
1996–2001	39.3 (37.7–40.9)	22.6 (21.4–23.8)	31.1 (23.7–38.5)	19.2 (14.9–23.4)
2001–2004	38.2 (36.5–39.8)	22.8 (21.6–24.1)	32.0 (26.0–38.0)	14.6 (10.9–18.2)
% change	6	−1	82	39
P (trend)	0.10	0.69	**<0.01**	0.30

*Significant values (P < 0.05) indicated in bold font. †Time periods are non-overlapping; please refer to Methods section for exact dates.

However, the study has limitations. Statistical imprecision becomes a problem when stratifying by ethnicity. It was not possible to link all cancer records back to the census, and so weighting for linkage bias was undertaken; we are confident that this will have adjusted for bias due to misclassification of the cancer outcome. The Cancer Registry Act, which came into effect in 1994, required mandatory registration of all cancers, and there was an increase in CRC registrations following its introduction, and probably reflects improved notification or may reflect a 'holding over' of registrations from one year to the next but this probably impacted ethnic groups,

and site distribution in a similar manner. In addition, changes in the distribution of ethnicities within the non-Māori group may slightly distort the observed trends.

Conclusions

Overall, the incidence of CRC in New Zealand continued to increase. We have identified a left- to right-sided shift in colon cancer in both Māori and non-Māori women, particularly those above 65+ years. Men have had an increase in CRC incidence at all sites, without evidence of a shift. Māori have a lower incidence of CRC but their incidence rates are increasing more rapidly, leading to the possibility that their rates of CRC may meet or exceed those of non-Māori with time. These findings are of interest for two reasons. First, a shift from left to right is consistent with findings elsewhere, and may provide aetiological clues for left- and right-sided colon cancers. Second, these findings could be considered as part of the decision-making process relating screening methods in the context of planning for a national screening programme in New Zealand.

Acknowledgements

Statistics New Zealand security statement

Access to the data in this study was provided by Statistics New Zealand in a secure environment designed to give effect to the confidentiality provisions of the Statistics Act 1975. The results in this study and any errors contained therein are those of the author, not Statistics New Zealand.

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