Second Primary Cancers after Cancers of the Colon and Rectum in New South Wales, Australia, 1972–1991

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Abstract

Data from the New South Wales Central Cancer Registry for the period 1972–1991 were examined to determine the risk of second primary cancers after an initial invasive cancer of the colon (ICD-9 153) or rectum (ICD-9 154). The expected numbers of cancers were obtained by assuming that subjects experienced the same cancer incidence as prevailed in the corresponding general population and by applying sex-, age-, and calendar-specific rates to the appropriate person-years at risk. The relative risk (RR) of a second primary cancer was taken to be the ratio of observed:expected numbers of second cancers. After colon cancer, there was an excess of cancers of the small intestine in both sexes (RRs of 4.5 and 4.4); prostate (RR = 1.4) and kidney (RR = 1.8) in men; and breast (RR = 1.3), body of uterus (RR = 1.9), ovary (RR = 2.8), and thyroid (RR = 2.7) in women. Lung cancer occurred less frequently in men than expected (RR = 0.7). After rectal cancer, men had increased risks of cancers of the colon (RR = 1.5) and prostate (RR = 1.3) and a reduced risk of pancreatic cancer (RR = 0.3). A reciprocal relationship of increased risk was seen between cancers of the proximal (but not the distal) colon and rectum. Shared luminal risk factors for proximal colon cancer and rectal cancer and three syndromes of hereditary predisposition to colon cancer seem to be the major contributors to second primary cancers in patients with an initial colon cancer. Sources of bias have been considered.

Introduction

Colorectal cancers are common in Australia (1), as in other developed countries (2). The median age at diagnosis of 67–70 years (1) and the 5-year relative survival of approximately 50% (3) result in survival being sufficiently long for patients with one primary neoplasm to be at risk of a second, either as a consequence of treatment for the initial cancer or intensified medical surveillance resulting in earlier detection of second cancers or due to the effect of shared risk factors.

Analysis of data from cancer registries covering Connecticut (4) and Denmark (5) demonstrated associations among cancers of the colon, breast, uterine corpus, and ovary, supporting the possible influence of common hormonal or dietary factors. In a small proportion of colorectal cancers, familial clustering points to an inherited susceptibility (6).

Using data for 1972–1991 from the NSW[2] Central Cancer Registry, we have examined the incidence of second primary cancers after an initial diagnosis of cancer of the colon or rectum in NSW, where the age-standardized incidence rates (per 100,000) in 1991 were 29 (male) and 21 (female) for colon cancer and 19 (male) and 10 (female) for rectal cancer.

Patients and Methods

In 1991, NSW comprised 2.94 million males and 2.96 million females. The population-based NSW Central Cancer Registry has received statutory notifications of invasive cancer since 1972; its operation has been described previously (7). Completeness of cancer registration has not been formally assessed but is believed to be at least 95%. Only 2% of first and 2% of second primary cancers are registered solely from a death certificate. All new notifications are matched with the existing data base comparing every field and assigning a weight to each exact (and phonetic) match. Individuals identified by these procedures as possibly having a second primary cancer are reviewed by the Registry staff. With the ultimate aim of performing analyses of relative survival, the Registry has linked some cancer sites on its database with death certificates from the NSW Registrar of Births, Deaths and Marriages via two automated matching programs [one written specifically for this purpose and Automatch (8)] followed by manual checking of possible links. Persons not identified by this process as having died by December 31, 1991 are considered to be alive for the purpose of the current study (passive follow-up).

Eligible subjects for this study were NSW residents diagnosed with an invasive cancer of the colon (ICD-9 153) or rectum (ICD-9 154) in the period 1972–1991 who had been notified to the NSW Central Cancer Registry and survived for at least 2 months. Person-years of risk were accumulated for each subject beginning 2 months after the initial diagnosis of cancer and ending with the date of death, date lost to follow-up (due to migration out of NSW), date of diagnosis of second primary cancer, or the end of the study period (December 31, 1991), whichever came first. To allow a direct comparison with data from Connecticut (4) and Denmark (5), persons who were

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[2] The abbreviations used are: NSW, New South Wales; RR, relative risk; CI, confidence interval.

Table 1 Characteristics of persons reported to the NSW Central Cancer Registry with an initial cancer of the colon or rectum, 1972–1991

	Colon (ICD-9 153)		Proximal colon (ICD-9 153.0, 153.1, 153.4, 153.5, 153.6)		Distal colon (ICD-9 153.2, 153.3, 153.7)		Rectum (ICD-9 154)	
	M	F	M	F	M	F	M	F
No. with first primary cancer[a]	13,506	13,925	4,606	5,502	6,442	5,759	8,603	6,475
No. who developed a second primary cancer[b]	775	547	263	230	411	231	497	279
Average age at diagnosis of first cancer (yrs)	65.7	67.9	65.9	68.9	65.5	66.0	64.9	67.1
Person-yr of follow-up	49,141	54,796	16,313	20,381	24,418	24,790	31,538	26,608
Average follow-up (yrs)	3.6	3.9	3.5	3.7	3.8	4.3	3.7	4.1

[a] Excluding those who survived less than 2 months after diagnosis of the first primary cancer or who developed a simultaneous cancer during this period.
[b] Excluding skin cancers (ICD-9 173) and those at the same site as the first primary cancer (according to three-digit ICD-9 code).

diagnosed with a second primary cancer within the first 2 months were considered to have two synchronous cancers and have been excluded from the analysis.

Person-years at risk were classified by sex, 5-year age group, 5-year period (1972–1976, 1977–1981, 1982–1986, and 1987–1991) and time since entry to the cohort (<1, 1–4, 5–9, and ≥10 years). The expected numbers of cancers were obtained by assuming that these persons experienced the same cancer incidence as prevailed in the corresponding general population and by applying sex-, age-, and calendar-specific rates to the appropriate person-years at risk. The RR of a second primary cancer was taken to be the ratio of observed (O) to expected (E) numbers of second cancers. Tests of significance and 95% CIs for the RR were calculated assuming that the cases followed a Poisson distribution.

In calculating the risk of a second primary cancer, we have excluded those cancers occurring at the same three-digit ICD-9 site as the initial tumor. This was necessary partly due to coding rules laid down by the International Association of Cancer Registries (9), which prohibit counting of a second cancer at the same three-digit ICD-9 site unless the histological type is different, and partly because of inconsistency over time in coding practices at the NSW Central Cancer Registry with respect to multiple tumors at the same three-digit site.

A subsidiary analysis was undertaken of second primary cancers after an initial cancer of the proximal colon (comprising appendix, cecum, ascending colon, hepatic flexure, and transverse colon; ICD-9 codes: 153.0, 153.1, 153.4, 153.5, and 153.6, respectively) or the distal colon (comprising splenic flexure, descending colon, and sigmoid colon; ICD-9 codes 153.2, 153.3, and 153.7, respectively).

Histological verification was available for the majority of cancers of the colon (87%) and rectum (92%).

Results

For persons diagnosed with cancer of the colon or rectum, Table 1 gives the numbers and average age of those who developed a second primary cancer (as defined in "Patients and Methods") and the duration of follow-up. Tables 2–5 provide the observed and expected numbers of subsequent tumors after cancers at each of these sites.

Colon. During the period 1972–1991, approximately equal numbers of male and female NSW residents had an initial diagnosis of cancer of the colon (Table 1). Excluding subsequent colon cancers, 775 second primary cancers developed in men (RR = 1.0) and 547 developed in women (RR = 1.1; Table 2). Significantly increased risks were found for cancer of the small intestine in both sexes (RR = 4.5 and 4.4), cancers of the prostate (RR = 1.4) and kidney (RR = 1.8) in men, and cancers of the breast (RR = 1.3), body of uterus (RR = 1.9), ovary (RR = 2.8), and thyroid (RR = 2.7) in women. Lung cancer occurred less frequently than expected in men (RR = 0.7). The reduced risks of laryngeal cancer in men and stomach cancer in women and the increased risk of kidney cancer in women bordered on statistical significance.

Restricting the site of the initial tumor to the proximal or distal colon did not change the pattern of excess risk (data not shown), with one exception. Significantly increased RRs for rectal cancer were seen after proximal colon cancer (men, RR = 2.0; women, RR = 2.1) but not after distal colon cancer (men, RR = 0.9; women, RR =0.5; Table 4).

Rectum. An initial diagnosis of rectal cancer was made in 15,078 persons, the male:female ratio being 1.3:1 (Table 1). When second rectal cancers were excluded, 497 men and 279 women developed a further primary cancer (men, RR = 1.0; women, RR = 1.1; Table 3). Men had an excess risk of cancers of the colon (RR = 1.5) [restricted to the proximal colon (Table 4)] and prostate (RR = 1.3) and a reduced risk of pancreatic cancer (RR = 0.3). In women, there was an excess of proximal colon cancer (RR = 2.0), whereas the RRs of 0.3 for pancreatic cancer and 1.7 for endometrial cancer were marginally significant.

Changes in Risk of Second Primary Cancers over Time. The higher or lower risks for most second cancers were maintained over time, with the exception of ovarian cancer after an initial colon cancer, for which the risk fell progressively (Table 5). The increased risk for cancer of the small intestine was present in each time period [<1, 1–4.9, 5.0–9.9, and ≥10 year(s)] after an initial colon cancer in men (RRs of 5.7, 3.9, 4.6, and 4.5 based on 8 cancers in total) but not in women (RRs of 0, 10.5, 0, and 0 based on 5 cancers that occurred 1–4.9 years after the initial diagnosis). The excess of rectal cancer was seen 1–9.9 years after diagnosis of a first primary cancer of the proximal colon, with period-specific RRs of 0.3, 3.0, 2.6, and 0 for men and 0.4, 3.6, 1.6, and 0.6 for women. However, after an initial cancer of the rectum, the risk of subsequent proximal colon cancers was increased in each period (men: 3.0, 3.3, 2.7, and 1.8; women: 1.6, 1.2, 3.7, and 1.9).

Histology of Tumors. The proportions by histological type were similar for first primary cancers of the proximal (91% adenocarcinomas, 1% carcinoids, 3% carcinomas not otherwise specified, and 5% unspecified types of cancer) and distal (93, 0, 3, and 4%, respectively) colon and rectum (89, 0, 3, and 4%, respectively). Of the 13 second primary cancers of the small

Table 2 Observed (O) and expected (E) numbers of second primary cancers after diagnosis of an initial cancer of the colon (ICD-9 153) in NSW 1972–1991

Second primary cancer site ICD-9 code	Sex	O	E	O/E	(95% CI)
Oral/pharyngeal 141,143–5	M	21	16.7	1.3	(0.8–1.9)
146,148–9	F	8	7.4	1.1	(0.5–2.1)
Esophagus 150	M	13	12.5	1.0	(0.6–1.8)
	F	5	8.3	0.6	(0.2–1.4)
Stomach 151	M	35	38.4	0.9	(0.6–1.3)
	F	13	22.9	0.6	(0.3–1.0)
Small intestine 152	M	8	1.8	4.5	(1.9–8.9)
	F	5	1.1	4.4	(1.4–10)
Rectum 154	M	55	46.3	1.2	(0.9–1.6)
	F	36	31.6	1.1	(0.8–1.6)
Pancreas 157	M	23	23.6	1.0	(0.6–1.5)
	F	17	19.6	0.9	(0.5–1.4)
Larynx 161	M	6	13.0	0.5	(0.2–1.0)
	F	1	1.4	0.7	(0.0–4.0)
Lung 162	M	101	153.8	0.7	(0.5–0.8)
	F	31	36.4	0.9	(0.6–1.2)
Breast 174	F	154	116.4	1.3	(1.1–1.6)
Cervix 180	F	14	13.6	1.0	(0.6–1.7)
Body of uterus 182	F	36	19.3	1.9	(1.3–2.6)
Ovary 183	F	52	18.3	2.8	(2.1–3.8)
Prostate 185	M	243	175.2	1.4	(1.2–1.6)
Bladder 188	M	48	50.8	1.0	(0.7–1.3)
	F	14	16.6	0.8	(0.5–1.4)
Kidney 189	M	37	20.7	1.8	(1.3–2.5)
	F	21	13.6	1.6	(1.0–2.4)
Thyroid 193	M	2	1.8	1.1	(0.1–4.1)
	F	9	3.4	2.7	(1.2–5.1)
Lymphomas 200–2	M	27	27.1	1.0	(0.7–1.5)
	F	27	22.7	1.2	(0.8–1.7)
Leukemias 204–8	M	22	20.2	1.1	(0.7–1.6)
	F	17	15.9	1.1	(0.6–1.7)
All second cancers except skin and colon 140–208 (excluding 173,153)	M	775	760.8	1.02	(0.95–1.09)
	F	547	482.4	1.13	(1.04–1.23)

intestine that occurred after an initial colon cancer, 12 were adenocarcinomas and 1 was a carcinoid (the expected numbers were 8 and 5, respectively); of the 13 preceding cancers of the colon, 12 were adenocarcinomas and 1 was a carcinoma not otherwise specified. Of the second primary cancers of the kidney after colon cancer, the excess was for transitional cell carcinomas of the renal pelvis and ureter (RR = 3.4 and 95% CI, 2.0–5.4 in men; RR = 2.0 and 95% CI, 0.9–3.6 in women) rather than for renal cell cancers (RR = 1.3, not significant, for men and women).

Discussion

This analysis of population-based data from NSW has demonstrated, in both men and women, a reciprocal relationship of increased risk between cancers of the proximal colon and rectum. Twice the expected rate of rectal cancer followed an initial cancer of the proximal colon, whereas a 2–3-fold excess of proximal colon neoplasms was seen after a first primary rectal cancer. No such relationship was seen between cancer of the distal colon and rectum in either sex. The only other similar study, in which the proximal and distal colon were analyzed separately, showed a stronger association of proximal than distal colon cancers with rectal cancer (10). No explanation was provided.

Surgical practice in the 1970s and 1980s in Australia entailed resection of the proximal third of the rectum in the operation for cancer of the sigmoid colon and removal of one-half to two-thirds of the distal sigmoid colon for rectal cancer. The rectum was not resected during surgery for cancers of the descending colon or splenic flexure.[3] Because some 84% of NSW patients with cancer of the colon or rectum were treated by surgery,[4] the most plausible explanation for our seemingly paradoxical finding is that the expected numbers of cases in a subset of the population who have a significant part of the tissue at risk removed surgically will be reduced. Accordingly, a correction has to be applied in estimating the expected number of cases when calculating an RR for these patients. If it is assumed that second primary cancers occur along the length of the distal colon or rectum with the same frequency as first primary cancers and that the expected number will decrease in proportion to the amount of the tissue resected, then the revised RR for rectal cancer after an initial cancer of the distal colon would be 1.6 (95% CI, 1.0–2.5) for men and 0.9 (95% CI, 0.4–1.9) for women, and the revised RR for cancer of the distal colon after a first primary cancer of the rectum would be 1.2 (95% CI, 0.6–2.0) and 0.4 (95% CI, 0.1–1.3), respectively (compare the figures shown in Table 4). Bearing in mind that these figures are no more than estimates, it seems that the

[3] M. Killingback, personal communication.
[4] Unpublished data from the NSW Central Cancer Registry for the period 1972–1984.

Table 3 Observed (O) and expected (E) numbers of second primary cancers after diagnosis of an initial cancer of the rectum (ICD-9 154) in NSW, 1972–1991

Second primary cancer site ICD-9 code	Sex	O	E	O/E	(95% CI)
Oral/pharyngeal 141,143–145	M	13	10.9	1.2	(0.6–2.0)
146,148–149	F	3	3.6	0.8	(0.2–2.5)
Esophagus 150	M	6	7.7	0.8	(0.3–1.7)
	F	3	3.8	0.8	(0.2–2.3)
Stomach 151	M	18	23.3	0.8	(0.5–1.2)
	F	10	10.4	1.0	(0.5–1.8)
Small intestine 152	M	1	1.1	0.9	(0.0–5.1)
	F	1	0.5	1.8	(0.1–10)
Colon 153	M	73	48.8	1.5	(1.2–1.9)
	F	38	34.6	1.1	(0.8–1.5)
Pancreas 157	M	4	14.3	0.3	(0.1–0.7)
	F	3	9.0	0.3	(0.1–1.0)
Larynx 161	M	8	8.4	1.0	(0.4–1.9)
	F	1	0.7	1.4	(0.0–8.0)
Lung 162	M	87	95.9	0.9	(0.7–1.1)
	F	25	17.7	1.4	(0.9–2.1)
Breast 174	F	64	56.1	1.1	(0.9–1.5)
Cervix 180	F	7	6.7	1.1	(0.4–2.2)
Body of uterus 182	F	16	9.5	1.7	(1.0–2.7)
Ovary 183	F	10	8.9	1.1	(0.5–2.1)
Prostate 185	M	129	102.2	1.3	(1.1–1.5)
Bladder 188	M	26	30.8	0.8	(0.6–1.2)
	F	11	7.8	1.4	(0.7–2.5)
Kidney 189	M	17	12.8	1.3	(0.8–2.1)
	F	10	6.6	1.5	(0.7–2.8)
Thyroid 193	M	1	1.1	0.9	(0.0–5.0)
	F	4	1.6	2.5	(0.7–6.3)
Lymphomas 200–202	M	21	16.6	1.3	(0.8–1.9)
	F	15	10.8	1.4	(0.8–2.3)
Leukemias 204–208	M	10	12.2	0.8	(0.4–1.5)
	F	11	7.3	1.5	(0.8–2.7)
All second cancers except	M	497	483.5	1.03	(0.94–1.12)
(excluding 173,154)	F	279	248.9	1.12	(0.99–1.26)
140–208 (excluding 173, 154)					

Table 4 Observed (O) and expected (E) numbers of first and second primary cancers of the proximal colon, distal colon, and rectum in NSW, 1972–1991

First primary site	Second primary site	Sex	O	E	O/E	(95% CI)
Proximal colon[a]	Rectum	M	31	15.6	2.0	(1.3–2.8)
		F	26	12.4	2.1	(1.4–3.1)
Rectum	Proximal colon	M	49	17.1	2.9	(2.1–3.8)
		F	29	14.3	2.0	(1.4–2.9)
Distal colon[b]	Rectum	M	21	23.1	0.9	(0.6–1.4)
		F	7	13.6	0.5	(0.2–1.1)
Rectum	Distal colon	M	14	22.2	0.6	(0.3–1.1)
		F	3	12.8	0.2	(0.1–0.7)

[a] Proximal colon comprises appendix, cecum, ascending colon, hepatic flexure, and transverse colon (ICD-9 codes 153.0, 153.1, 153.4, 153.5, and 153.6).
[b] Distal colon comprises splenic flexure, descending colon, and sigmoid colon (ICD-9 codes 153.2, 153.3, and 153.7).

reciprocal association between rectal cancer and colon cancer is stronger for proximal than for distal tumors of the colon.

Exposure to shared luminal risk factors could explain a predilection for cancer of the rectum after colon cancer as shown in Connecticut (4), Finland (11), and Sweden (12) and for cancer of the colon after rectal cancer as seen in Connecticut (4) and Sweden (12). However, the perception now held that the etiology of cancers at these two sites is somewhat different could account for the relative weakness of the association and the failure to demonstrate it in Denmark (5) and South Australia (13).

It has been suggested that right (proximal)- and left (distal)-sided colon cancers should be considered separately because their embryonic origins are different, and the incidence of right-sided cancers has increased to a greater extent than that of left-sided tumors (14–16). Moreover, it is possible that reproductive (17), familial (18), and dietary (19) factors have a differential effect, whereas genetic alterations indicate that proximal and distal colon carcinomas might differ in the genetic mechanisms of their initiation and/or progression (20).

As in a recent analysis of United States Surveillance Epidemiology End Results (SEER) data (21), this population-based study was able to identify two sets of associations that are best explained by shared hereditary factors previously recognized in family studies, one with hereditary nonpolyposis colon cancer and the other with familial adenomatous polyposis coli. A marked excess risk of adenocarcinomas of the small intestine was found after an initial colon (but not rectal) cancer in men and women in the present study. Increased risks of cancer of the small intestine were also seen after cancers of the colon (men, RR = 10.2; women, RR = 5.1) and rectum (men, RR = 3.8; women, RR = 2.0 not significant) in Sweden (12). A reciprocal relationship between adenocarcinoma of the small bowel and colorectal cancers with risks ranging from 4–9-fold has been reported from the United States SEER data, in which adenocarcinomas accounted for 36% of small intestinal tumors (22).

Table 5 Observed (O) and expected (E) numbers of second primary cancers in NSW, 1972–1991, by period since initial diagnosis

First primary cancer	Second primary cancer:	Sex	Period (yrs)	O	E	O/E	(95% CI)
Colon	Breast	F	<1	25	22.2	1.1	(0.7–1.7)
(ICD-9 153)	(ICD-9 174)		1–4	66	49.1	1.3	(1.0–1.8)
			5–9	38	29.4	1.3	(0.9–1.8)
			≥10	25	15.6	1.6	(1.0–2.4)
	Body of uterus	F	<1	5	3.8	1.3	(0.4–3.1)
	(ICD-9 182)		1–4	13	8.3	1.6	(0.8–2.7)
			5–9	15	4.9	3.1	(1.7–5.1)
			≥10	3	2.4	1.2	(0.3–3.6)
	Ovary	F	<1	18	3.6	5.1	(3.0–8.0)
	(ICD-9 183)		1–4	25	7.8	3.2	(2.1–4.8)
			5–9	7	4.6	1.5	(0.6–3.2)
			≥10	2	2.4	0.8	(0.1–3.0)
	Prostate	M	<1	41	32.7	1.3	(0.9–1.7)
	(ICD-9 185)		1–4	92	74.3	1.2	(1.0–1.5)
			5–9	66	44.5	1.5	(1.1–1.9)
			≥10	44	23.6	1.9	(1.3–2.5)
	Kidney	M	<1	6	4.1	1.5	(0.5–3.2)
	(ICD-9 189)		1–4	14	9.0	1.6	(0.9–2.6)
			5–9	10	5.0	2.0	(1.0–3.6)
			≥10	7	2.5	2.8	(1.1–5.8)
	Lung	M	<1	15	32.1	0.5	(0.3–0.8)
	(ICD 162)		1–4	48	68.6	0.7	(0.5–0.9)
			5–9	28	36.6	0.8	(0.5–1.1)
			≥10	10	16.5	0.6	(0.3–1.1)
	Thyroid	F	<1	0	0.7	0	
	(ICD-9 193)		1–4	8	1.4	5.6	(2.4–11)
			5–9	0	0.8	0	
			≥10	1	0.4	2.4	(0.1–13)
Rectum	Colon	M	<1	16	9.8	1.6	(0.9–2.7)
(ICD-9 154)	(ICD-9 153)		1–4	35	21.2	1.7	(1.2–2.3)
			5–9	14	11.8	1.2	(0.7–2.0)
			≥10	8	6.0	1.3	(0.6–2.6)
	Pancreas	M	<1	1	3.0	0.3	(0.0–1.9)
	(ICD-9 157)		1–4	2	6.3	0.3	(0.0–1.2)
			5–9	1	3.4	0.3	(0.0–1.7)
			≥10	0	1.7	0	
	Prostate	M	<1	27	19.2	1.4	(0.9–2.1)
	(ICD-9 185)		1–4	52	42.7	1.2	(0.9–1.6)
			5–9	33	25.7	1.3	(0.9–1.8)
			≥10	17	14.5	1.2	(0.7–1.9)

The small intestine is only one of several cancer sites found to excess in kindreds with hereditary nonpolyposis colon cancer, the others being endometrium, ovary, and less commonly, stomach, renal pelvis, and ureter (23). Indeed, in the present study, increased RRs after colon cancer were found for endometrium (RR = 1.9), ovary (RR = 2.8), and renal pelvis and ureter (men, RR = 3.4; women, RR = 2.0) but not for stomach (men, RR = 0.9; women, RR = 0.6).

The excess of thyroid cancer (RR = 2.7) after colon cancer in women was seen also in women (RR = 4.7) in Osaka (10) and in men (RR = 2.9) in Connecticut (4). Thyroid cancer is one of the extracolonic cancers associated with familial adenomatous polyposis coli (24), the others are adenocarcinoma of the duodenum, adrenal carcinoma (not examined here), and pancreatic cancer (men, RR = 1.0; women, RR = 0.9 in this study).

Some people with colon cancer carry a hereditary predisposition to cancers of the breast, body of uterus, and ovary (6), but these cancers also share common hormonal or dietary factors. This may account for the reciprocal relationship between colon and each of these three female cancers in Connecticut (4), the association between cancers of the colon, uterus, and ovary in Denmark (5), and excesses, after colon cancer, of breast (12), endometrial (10–12), and ovarian (10, 11) cancers in other populations. The falling trend in incidence of second primary ovarian cancers after colon cancer also seen in Connecticut (4) and Denmark (5), in which the excess risks (RRs of 2.4 and 2.6, respectively) were eliminated within 5 years of the initial diagnosis of colon cancer, suggests a decreasing intensity of medical surveillance, but there is no other reason to postulate this explanation.

A reciprocal relationship exists between cancers of the body of uterus and ovary after colorectal cancer and *vice versa* (25), but not with cancer of the renal pelvis (26).

An increased risk for prostate cancer after a first primary colon cancer was shown also in Connecticut (4), Sweden (12), and South Australia (13). Because autopsy rates are low in Australia, detection of latent tumors at death is an unlikely explanation for the NSW finding, although it played a role in the Swedish data. The proposition of shared lifestyle factors, as suggested by the positive correlation of their incidence rates internationally (2), is not supported by a reciprocal relationship; there was no excess of colorectal cancer after an initial prostate cancer in NSW (26), Connecticut (4), or Denmark (5).

Colon cancer is associated with higher socioeconomic status (27), which in turn is negatively linked with smoking.

This is likely to explain the deficit of lung cancer after colon cancer, but not the marked deficit of pancreatic cancer after rectal cancer.

It is possible that the risk of second primary cancer has been underestimated as a result of the migration of NSW residents to another Australian state or to another country. However, the magnitude of this bias seems to be small; during the year preceding the 1986 census, 1.3% of persons at least 15 years of age migrated interstate, more than three-fourths of whom were 20–39 years old (28), an age group in which cancer is uncommon. In the same period, permanent migration overseas accounted for 0.1% of the entire NSW population and 0.06% of those more than 50 years old.[5]

A more important source of bias is likely to be medical surveillance, either the detection and removal of precancerous lesions or the advance of the time of diagnosis of indolent or slowly growing cancers. The former would apply especially to the rectum and distal colon and may have contributed to the lower than anticipated observed:expected ratio of second cancers at these sites. Advancing the time of diagnosis, a plausible outcome of increased medical surveillance for prostate (4, 12) and possibly small intestinal cancer is generally associated with an RR that falls over time. This pattern was not seen in men for either cancer; there were too few female cases of cancer of the small intestine to draw any conclusions. We have no data to indicate whether the second primary tumors were of low grade or early stage at the time of diagnosis.

Shared luminal risk factors for proximal colon cancer and rectal cancer and three syndromes of hereditary predisposition to colon cancer seem to be the major contributors to second primary cancers in patients with an initial colon cancer.

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