

A Population-Based Study of the Incidence of Malignant Small Bowel Tumours: SEER, 1973–1990

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Background. Little is known about the incidence of cancers of the small bowel.

Methods. Data from cancer registries participating in the Surveillance, Epidemiology, and End-Results (SEER) Program from 1973 to 1990 were analysed to determine the incidence of the four major histological types of cancer occurring in the small intestine: adenocarcinomas, malignant carcinoid tumours, lymphomas and sarcomas. In addition, the incidence rate of lymphomas arising from the small intestine and stomach and adenocarcinomas from the small intestine, stomach and colon were compared over time.

Results. Small bowel tumours occurred rarely, with an average annual incidence rate of 9.9 per million people. Carcinoid tumours and adenocarcinomas were the most common histological subtypes, with average annual incidence rates of 3.8 and 3.7 per million people respectively, followed by lymphomas (1.1 per million people) and sarcomas (1.3 per million people). For all histological subtypes, men had higher rates than women. Most tumours occurred in older adults; over 90% of cases occurred in people over the age of 40. During the 18-year study period, the incidence of small bowel tumours has risen slowly. In white men, black men and black women, rises in the incidence of adenocarcinomas, malignant carcinoids and lymphomas contributed to this trend. In white women, the incidence of adenocarcinomas, was stable while malignant carcinoids and lymphomas rose. The incidence of sarcomas was steady for all groups except black women, for which it fell. The histological types were distributed by anatomical subsite; adenocarcinomas were distributed more proximally on average whereas lymphomas were more common distally. In addition, there was an association between the incidence trends of adenocarcinomas occurring in the duodenum and colon suggesting similar risk factors for cancers in these regions. There was no similar correlation for tumours in the jejunum and ileum. The incidence of lymphomas over time rose in all areas of the small intestine, paralleling a similar rise in lymphomas of the stomach.

Conclusions. Cancers of the small bowel are rare despite a slow increase over the past two decades, especially among lymphomas. Higher rates in males and whites deserve further investigation.

Keywords: small bowel, small intestine, malignancy, epidemiology, adenocarcinoma, carcinoid tumour, lymphoma, sarcoma

Cancers of the small intestine are interesting because, oddly, they are so rare. One would expect the small bowel to be a relatively frequent site of cancer because it contains some of the body's most rapidly proliferating cells, is bathed by many potential carcinogens in the diet, and is bordered by the stomach and colon which are common sites of cancer. While the small intestine constitutes 90% of the absorptive area of the

gastrointestinal tract, malignant tumours of the colon and rectum are 50 times more common.¹

This hypothesis-generating study investigates the epidemiological trends of small bowel cancer between 1973 and 1990 using population-based data from the Surveillance, Epidemiology and End-Results (SEER) Program.² A subset of these tumours (adenocarcinomas and lymphoma) are compared with trends in the stomach and colon. Because tumours of the small intestine are so uncommon, they have been investigated in the US primarily in hospital-based studies.^{3–6} There are very few population-based studies.^{1,7–10} This will be one of the first studies to compare epidemiological trends of small bowel cancer to gastric and colon cancers.

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TABLE 1 Average incidence (per million people) and percentage of small intestine cancers, by race and histology, SEER areas, 1973–1990

Histological type	Incidence (%)			
	White men	Black men	White women	Black women
Adenocarcinomas	4.0 (36.5)	4.1 (38.6)	3.4 (37.0)	4.1 (48.6)
Carcinoid	3.9 (35.8)	4.6 (44.0)	3.7 (40.2)	3.1 (36.3)
Lymphoma	1.5 (14.3)	0.8 (7.7)	0.9 (10.0)	0.4 (5.6)
Sarcoma	1.5 (13.4)	1.0 (9.7)	1.2 (12.8)	0.8 (9.5)

METHODS

Data from patients diagnosed with primary small bowel cancer, lymphoma of the stomach, and adenocarcinoma of the stomach and colon registered in the SEER Program were analysed for the period between 1 January 1973 and 31 December 1990. The SEER Program of the US National Cancer Institute collects clinical, demographic and outcome information on all neoplasms in ten tumour registries from various defined areas around the US, comprising approximately 11% of the US population. Cases registered on the basis of autopsy reports or death certificates, and cases diagnosed as carcinoma *in situ* were excluded from the study. During this period, 1976 men and 1718 women were diagnosed with small bowel tumours. The tumours included in this investigation were classified into four histological categories, as used in the International Classification of Disease-Oncology:¹¹ (1) adenocarcinoma, (2) malignant carcinoid, (3) lymphoma and (4) sarcoma. The average incidence rate was calculated for the four histological groups for white men, white women, black men, and black women for three age distributions (<40, 41–60, >60 years) at 3-year intervals, then for the 18-year study period. Asians were excluded. Separate analyses were made for gastric, duodenal, jejunal and ileal lymphomas as well as for gastric, colon, duodenal, jejunal and ileal adenocarcinomas. The statistical significance of trends over time was assessed using Poisson regression.

RESULTS

The average annual age-adjusted incidence rate for malignant tumours of the small intestine in all ages was 9.9 per million people. The incidence rate was 3.7 for adenocarcinomas, 3.8 for carcinoid tumours, 1.1 for lymphomas and 1.3 for sarcomas. The age-specific incidence rate rose sharply at middle age. Over 90% of the cases occurred in men older than 40 years of age and 95% of the cases in women. On average, the annual

incidence rate for all small bowel malignancies combined was higher for men than for women, and for whites than blacks. The incidence per million people was 10.9 and 10.5 for white and black men, respectively; 9.2 and 8.4 for white and black women, respectively.

The most common histological subtypes were adenocarcinoma and carcinoid for all groups, although the per cent distribution varied by sex and race. For example, adenocarcinomas comprised nearly 50% of the cases in black women, but less than 40% of cases in other groups. Carcinoid tumours comprised the highest percentage in black men (44%) and the lowest in white men (36%). Lymphomas and sarcomas were much less common, ranging from 6 to 14% and 10 to 13% of all cases, respectively.

Although the overall incidence rate of small bowel tumours was higher in whites than blacks, black women had higher incidence rates of adenocarcinoma than white women. The incidence rate of lymphoma in white men and women was twice that in black men and women. Sarcomas were more common in whites than blacks (Table 1).

The average annual age-adjusted incidence rate for all small bowel tumours combined has risen steadily during the 18-year study period. In men, the incidence rates of adenocarcinoma, carcinoid tumour and lymphoma have all risen whereas the incidence of sarcomas has been quite stable. These trends were statistically significant with all $P \leq 0.05$. While increases from the 41–60 and >60 age groups may have contributed to the rise in adenocarcinomas ($P = 0.70$ and $P = 0.06$, respectively) and carcinoids ($P = 0.35$ and $P \leq 0.05$, respectively), all age groups are responsible for the statistically significant dramatic increase in lymphomas (all $P \leq 0.05$). In women, all age groups contributed to the rise in carcinoid tumours and lymphomas, although only trends in the 41–60 and >60 age groups were statistically significant. The incidence of adenocarcinomas and sarcomas did not change. For white men, white

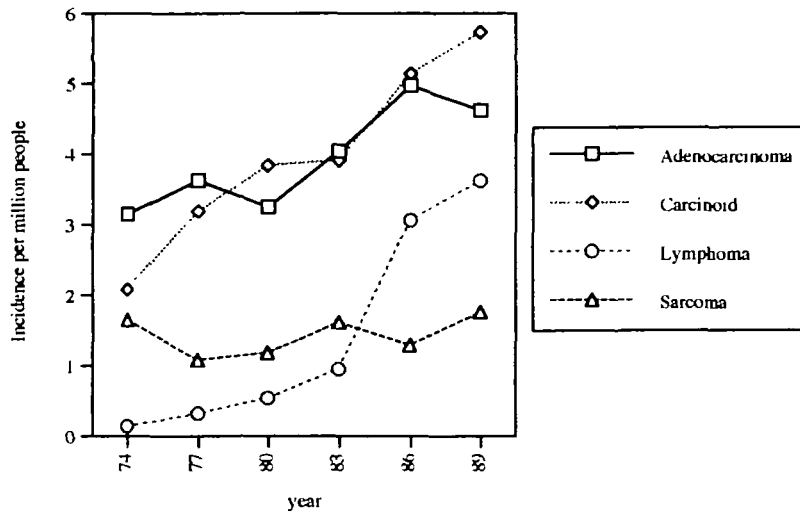


FIGURE 1 Age-adjusted incidence of cancers of the small intestine in men by histology: SEER, 1973-1990

For all values, $P \leq 0.05$.

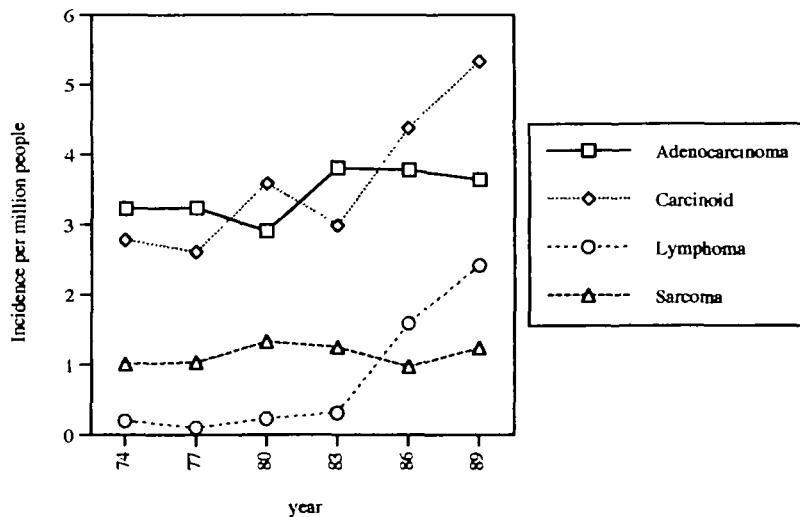


FIGURE 2 Age-adjusted incidence of cancers of the small intestine in women by histology: SEER, 1973-1990

For all values, $P \leq 0.05$.

women, black men and black women, the incidence rate of adenocarcinoma, carcinoid tumours, and lymphomas increased over time. For all trends, $P \leq 0.05$. The incidence rate of sarcoma wavered but overall, did not increase or decrease (Figures 1, 2).

Within the small intestine, the highest incidence of adenocarcinomas occurred in the duodenum

(54%; 1.8 per million population), followed by the jejunum (28%; 0.90 per million) and the ileum (18%; 0.59 per million). This compares with an average annual incidence rate of 71 per million people in the stomach, and 303 per million people in the colon. The incidence was consistently only slightly greater for males than females. There was a rise in duodenal

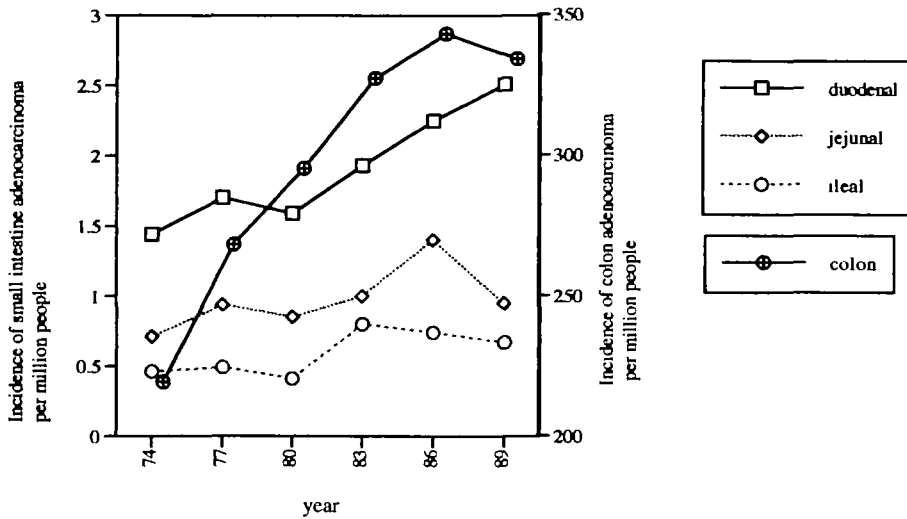


FIGURE 3A Incidence of adenocarcinomas in men by site and year: SEER areas, 1973-1990

For all values, $P \leq 0.05$.

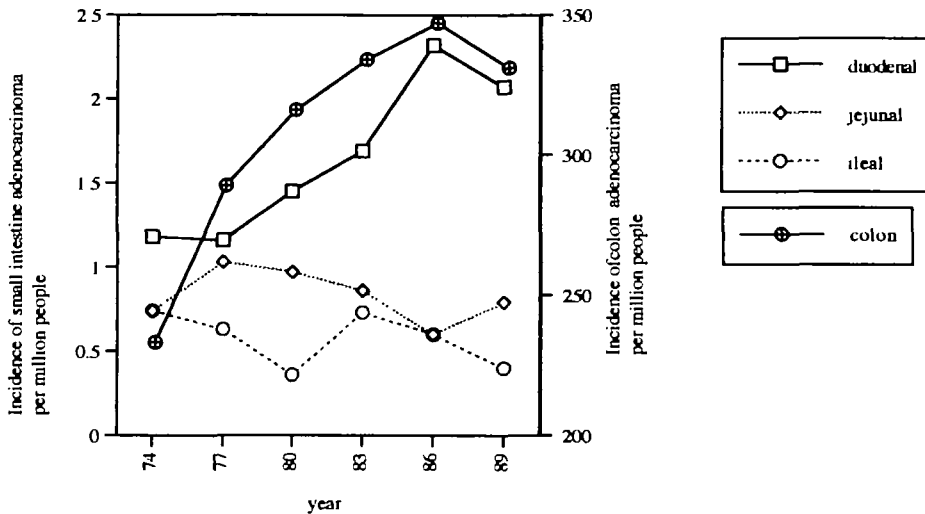


FIGURE 3B Incidence of adenocarcinomas in women by site and year: SEER areas, 1973-1990

For colon and duodenal $P \leq 0.05$, jejunal $P = 0.77$, ileal $P = 0.74$

adenocarcinomas in both men and women over the 18 years (for both, $P \leq 0.05$) and little change in jejunal and ileal types. During this period there was a statistically significant increase in colon adenocarcinoma. Meanwhile, the incidence rate of gastric adenocarcinomas rose and has recently fallen for men ($P \leq 0.05$) and for women ($P = 0.12$) (Figures 3a, 3b).

Lymphomas occurred most commonly in the ileum (53%) followed by the jejunum (35%) and duodenum (12%) with average annual incidence rates of 0.36, 0.23, and 0.09 per million people, respectively. The incidence was higher in men than women in all sites: four times greater in the duodenum, twice as great in the jejunum and three times greater in the ileum. There was a statistically significant trend for increasing

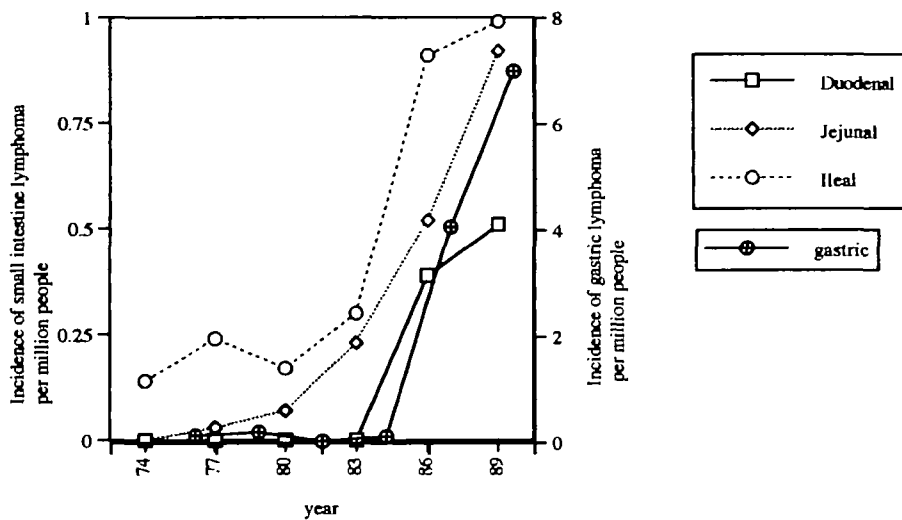


FIGURE 4A Incidence of lymphoma in men by site and year: SEER areas, 1973–1990

For all values, $P \leq 0.05$.

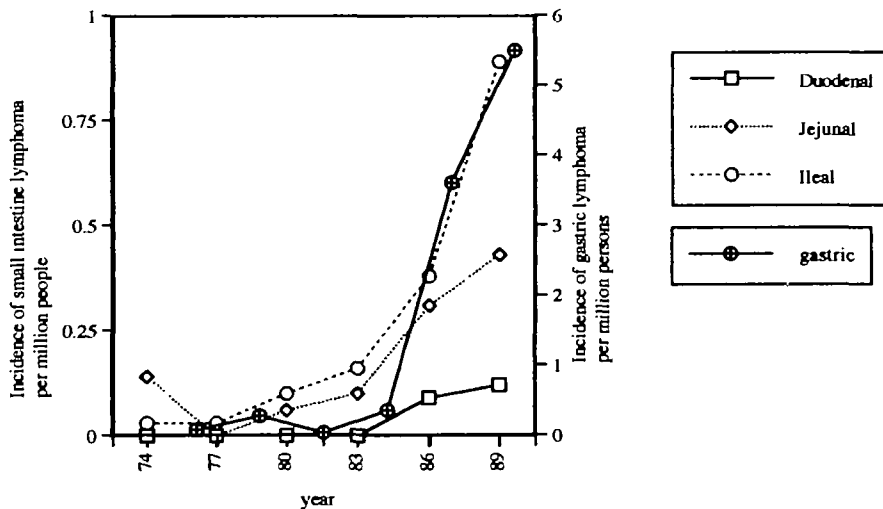


FIGURE 4B Incidence of lymphoma in women by site and year: SEER areas, 1973–1990

For all values, $P \leq 0.05$.

incidence of lymphoma in all segments of the small intestine in both males and females with all $P \leq 0.05$. The incidence of gastric lymphoma also rose over the same time period with $P \leq 0.05$ (Figures 4a, 4b).

DISCUSSION

Malignant small bowel tumours occur infrequently in the US with an average annual incidence rate of 9.9 per

million people. This study shows that the majority of these cancers are adenocarcinomas and carcinoid tumours; nearly all tumours occur in adults; and that the different histological types seem to have unique epidemiological characteristics. This is consistent with previous population-based^{1,7,9,10} and hospital-based^{3–6} studies.

We also found that these tumours occur more frequently in men than women and in whites than blacks,

although there was variation for each histological subtype. In addition, we found a trend over time for increasing incidence of small bowel tumours overall, and specifically for adenocarcinoma, carcinoid and lymphoma in white men, black men, and black women and carcinoid and lymphoma in white women. Although the increasing incidence of carcinoid tumours in blacks was previously noted,¹⁰ the other findings are new. The reason for these findings (higher rates in males and whites) are unknown. Presumably they reflect variations in life-style and sociocultural factors, e.g. diet. Higher rates in males may suggest occupational factors while higher rates in whites may reflect socioeconomic variables.

The increase in adenocarcinoma in men may be related to the rise of adenocarcinomas of the colon over the same time period. Adenocarcinomas of these two regions have numerous associations,¹²⁻¹⁵ including our finding that duodenal adenocarcinoma has incidence trends similar to that of the colon. Despite the finding that tumours in the jejunum and ileum do not share this relationship, the overall trend of adenocarcinoma of the small intestine may reflect the majority of cases which occurred in the duodenum. It may be that different risk factors operate in different segments of the small bowel. For example, Crohn's disease is known to raise the risk of small bowel adenocarcinomas, but only in the ileum. Small bowel tumours do not show a clear relationship with the pattern of gastric malignancies.

Increases in the incidence of malignant carcinoid tumours may be real but should be reviewed cautiously. The rise in incidence of these tumours, which are indolent and often discovered at surgery, may simply reflect the swelling case-load of abdominal surgery or improvements in laparotomy techniques. Increases may also reflect more accurate diagnosis after classification guidelines were established in 1981.¹⁰

The dramatic climb of lymphomas in all regions of the small intestine which parallels increases in lymphomas of the stomach may reflect a common aetiology. Although immunosuppressed states, such as those found in HIV-positive, AIDS and transplant patients, are a risk factor for lymphoma,¹⁶ whether this relates to the rise in intestinal lymphomas is uncertain.

It is unclear why cancers occur so rarely in the small intestine. Certain characteristics inherent in the small intestine may protect it from the cancers that occur in the adjacent stomach and colon. Lowenfels proposed some possibilities: the rapid transit time of liquid contents of the small intestine results in less exposure of the mucosa to potential carcinogens; carcinogens are diluted by the large volume of enteric secretions and this liquid may be less irritating to the bowel than the solid stool against the colonic mucosa; plentiful

quantities of IgA are secreted by regional lymphocytes contributing to local immunosurveillance and may decrease malignant potential; and the small metabolically inactive bacterial population in the small intestine may not be capable of transforming food products into carcinogens.¹³ High levels of regional microsomal enzymes such as benzopyrene hydrolase may serve to detoxify potential carcinogens.^{17,18}

On the other hand, small bowel tumours also share some risk factors of colon and gastric cancers. Small and large bowel malignancies have some common characteristics. Their international incidence rates covary with each other.¹³ Adenocarcinomas from both sites arise from adenomatous polyps and show an association with familial adenomatous polyposis.¹⁵ In addition, there is an increased risk for adenocarcinomas of the small intestine in individuals with colorectal cancer, and vice versa,¹⁴ and in individuals with previous adenocarcinomas.¹² Similarly, our findings that the trend for rising incidence of small bowel adenocarcinomas is similar to the trend of colon adenocarcinomas. Although Lowenfels found no correlation between small bowel and gastric cancers, salted and cured foods have been implicated in causing small intestine and gastric cancers.⁸ *Helicobacter pylori* has been closely linked to gastric cancer, but is unrelated to colorectal cancer.¹⁹ Its relationship to small bowel malignancies, especially by subsite, is unknown and merits further research. In addition, our results show that lymphomas of the stomach and small intestine all seem to be rising.

Part of the difficulty in elucidating the preventative and causative agents of small bowel tumours lies in the beast itself; different regions of the small intestine seem to react to carcinogenesis differently. For example, adenocarcinomas in the duodenum, but not the jejunum or ileum, are correlated with cancers in the colon. This is logical since the duodenum, jejunum and ileum each varies by function, histological and biochemical make-up and the composition of food end-products which flow through it. In addition, the four main histological types of cancer each act differently. Adenocarcinomas prefer the duodenum and jejunum whereas lymphomas tend toward the ileum. Because there are so many variables, small intestinal cancer should not be considered as one uniform disease.

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