

## Increasing Trend of Colorectal Cancer Incidence in Korea, 1999-2009

**Aesun Shin, MD, PhD<sup>1,2</sup>**  
**Kyee-Zu Kim, MPH<sup>1</sup>**  
**Kyu-Won Jung, MS<sup>2</sup>**  
**Sohee Park, PhD<sup>2</sup>**  
**Young-Joo Won, PhD<sup>2</sup>**  
**Jeongseon Kim, PhD<sup>1</sup>**  
**Dae Yong Kim, MD, PhD<sup>3</sup>**  
**Jae Hwan Oh, MD, PhD<sup>3</sup>**

<sup>1</sup>Molecular Epidemiology Branch,

<sup>2</sup>Cancer Registration and Statistics Branch,

<sup>3</sup>Center for Colorectal Cancer,

National Cancer Center, Goyang, Korea

Corresponding author: Kyu-Won Jung, MS  
 Cancer Registration and Statistics Branch,  
 National Cancer Center, 323 Ilsan-ro,  
 Ilsandong-gu, Goyang 410-769, Korea  
 Tel: 82-31-920-2170  
 Fax: 82-31-920-2179  
 E-mail: [ara@ncc.re.kr](mailto:ara@ncc.re.kr)  
 Received September 28, 2012  
 Accepted November 9, 2012

### Purpose

This study was conducted in order to demonstrate changing trends in colorectal cancer incidence according to sex, age group, and anatomical location in the Korean population.

### Materials and Methods

Data from the Korea Central Cancer Registry between 1999 and 2009 were analyzed. Annual percent changes (APCs) of sex- and age-specific incidence rates for cancer of the proximal colon (International Statistical Classification of Diseases and Related Health Problems, 10th revision [ICD-10] code C18.0-18.5), distal colon (C18.6-18.7), and rectum (C19-20), and male-to-female incidence rate ratios (IRR) were calculated.

### Results

The age-standardized incidence rate (ASR) of colorectal cancer was 27 (per 100,000) in 1999 and increased to 50.2 in 2009 among men (APC, 6.6%). The ASR for women was 17.2 in 1999 and 26.9 in 2009 (APC, 5.1%). The rectum was the most common site of cancer among both men and women during 1999 and 2009. However, the distal colon had the highest APC (10.8% among men and 8.4% among women), followed by the proximal colon (7.9% among men and 6.6% among women), and rectum (5.2% among men and 2.4% among women). The proportion of rectal cancer decreased from 51.5% in 1999 to 47.1% in 2009 among men, and from 50.5% to 42.8% among women. An increase in the male-to-female IRR was observed for distal colon cancer and rectal cancer, whereas the IRR for proximal colon cancer was stable.

### Conclusion

The rapid increase in colorectal cancer incidence is mainly attributed to the increase in colon cancer, especially distal colon cancer, and may be explained by a transition of risk factors for subsites or by the effect of colorectal cancer screening.

### Key words

Colorectal neoplasms, Incidence, Korea, Trends

## Introduction

Colorectal cancer is the third most common incident cancer among men and the second most common cancer among women worldwide [1]. Incidence rates vary 10-fold in both sexes worldwide, and the highest rates are estimated in more developed regions, such as North America and Western Europe, whereas the lowest rates are estimated in Africa (except Southern Africa) and South-Central Asia [1]. In Asia, colorectal cancer is the fourth most common incident

cancer among men and the fifth most common cancer among women [1]. Although incidence rates are relatively low in Asian countries, those for East Asian countries are relatively high [1].

In Korea, incidence of colorectal cancer has increased. Annual percentage changes in age-standardized incidence rates were 6.2% in men and 6.8% in women between 1999 and 2009 using the world standard population as a standard population [2]. In 2009, 24,986 new colorectal cancer cases (15,068 men and 9,918 women) were diagnosed, accounting for 13.0% of all cancer occurrences [2]. Colorectal cancer is the second most common cancer after stomach

cancer among men and the third most common cancer after cancers of the thyroid and breast among women [2].

There have been several reports on differences in patterns of colorectal incidence trends according to age group, sex, and anatomical location [3-5]. However, it has not been properly investigated whether colorectal cancers of a specific age group, sex, or anatomical location show more rapid increases in the Korean population. The aim of the current study was to demonstrate changing trends of colorectal cancer incidence according to age group, sex, and anatomical location.

## Materials and Methods

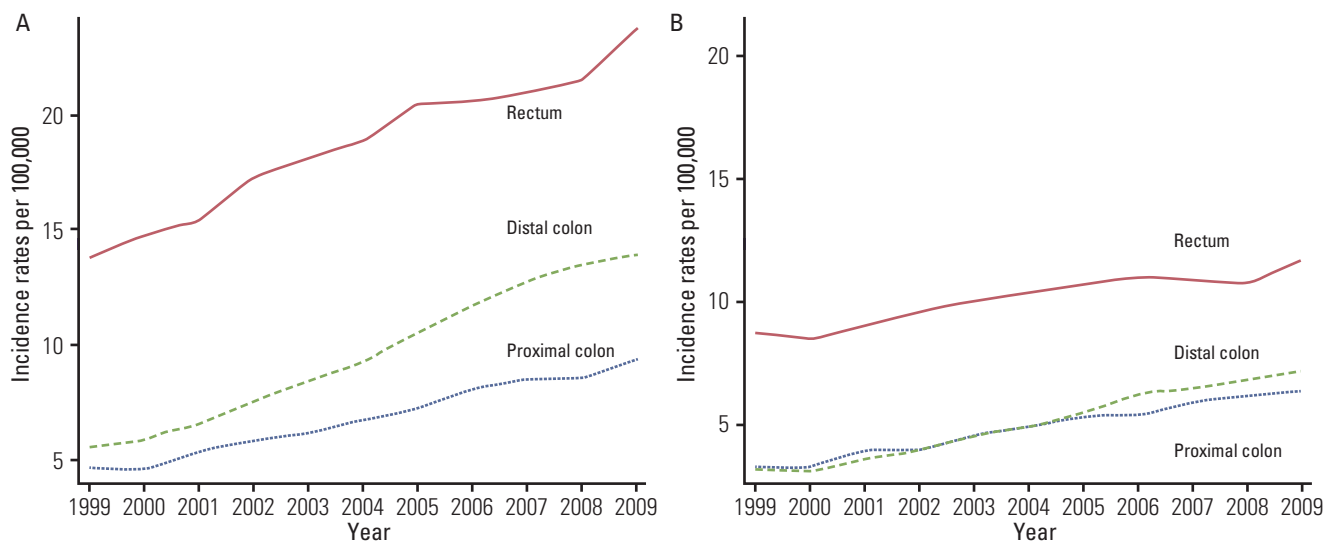
The Korea Central Cancer Registry (KCCR), a nation-wide, hospital-based cancer registry, was initiated by the Ministry of Health and Welfare, Korea in 1980. The registry collected information on approximately 80-90% of cancer cases from more than 150 training hospitals across the country, and, in 1999, the KCCR expanded cancer registration to cover the entire Korean population under the Population-Based Regional Cancer Registry program [6]. Age (five-year intervals) and sex-specific incidence rates and the number of cases of colorectal cancer between 1999 and 2009 were obtained from the Korea National Cancer Incidence Database. Anatomical subsites were defined based on the tenth version of the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) [7]. We defined the proximal colon as the cecum (C18.0), appendix (C18.1), ascending colon (C18.2), hepatic flexure (C18.3), transverse colon (C18.4), and splenic flexure of the colon (C18.5); the distal colon was defined as the descending colon (C18.6) and sigmoid colon (C18.7). The

rectum included the rectosigmoid colon (C19) and rectum (C20). Overlapping lesions of the colon (C18.8) and colon not otherwise specified (C18.9) were not included in the subsite analysis.

Age-standardized rates (ASRs) were calculated using the middle-year population of 2,000 as the standard population. The structure of the standard population is shown in Appendix 1. Annual percent changes (APCs) for the incidence rates were calculated using a linear model, according to the following formula;  $(\exp(b)-1) \times 100$ , where  $b$  is the slope of the regression of the natural logarithm of the ASR in a calendar year [8]. The 95% confidence intervals (CIs) were obtained with a standard error from the fit of the regression and the t-distribution function. All analyses were conducted by sex, subsite, and age group (10-year intervals). The R-2.12.2 (<http://cran.r-project.org>) software was used for the APC analyses. Male-to-female incidence rate ratios (IRR) were calculated using the numbers of cancer patients for each site and the sex-specific population structure for each year using Stata/SE 10.0 for Windows (Stata Corp LP, College Station, TX) [9]. Statistical significance in difference between IRRs is determined if the 95% CIs do not overlap between IRRs.

## Results

The ASRs and APCs overall and for each subsite of colorectal cancer by sex are shown in Tables 1 and 2 and Fig. 1. Among men, the ASR for colorectal cancer was 27 per 100,000 in 1999 and increased to 50.2 in 2009 (APC, 6.6%). The ASR for colorectal cancer among women was 17.2 in 1999 and 26.9 in 2009 (APC, 5.1%). The rectum was the most common cancer site among both men and women in 1999 and 2009. However, among the subsites,



**Fig. 1.** Age-standardized incidence curve for proximal colon, distal colon, and rectal cancers for male (A) and female (B) in 1999 and 2009, the Korea Central Cancer Registry.

**Table 1.** Age-standardized colorectal cancer incidence rates<sup>a)</sup> per 100,000 and APC by subsites in male, the Korea Central Cancer Registry, 1999-2009

	Sites (ICD-10 code)			
	Overall (C18.0-C20)	Proximal colon (C18.0-C18.5)	Distal colon (C18.6-C18.7)	Rectum (C19-C20)
Year				
1999	27.0	4.6	5.4	13.8
2000	28.2	4.5	5.8	14.8
2001	30.5	5.3	6.5	15.4
2002	33.9	5.8	7.5	17.3
2003	36.0	6.1	8.4	18.2
2004	38.6	6.7	9.2	18.9
2005	41.9	7.2	10.5	20.5
2006	44.0	8.0	11.7	20.6
2007	45.8	8.5	12.8	21.0
2008	47.0	8.5	13.5	21.6
2009	50.2	9.4	13.9	23.7
APC	6.61	7.88	10.77	5.23
95% CI	6.46-6.76	7.69-8.08	10.54-11.00	5.05-5.41
p-value	<0.001	<0.001	<0.001	<0.001

APC, annual percent change; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th revision; CI, confidence interval. <sup>a)</sup>Age adjusted to the Korean population in 2000.

**Table 2.** Age-standardized colorectal cancer incidence rates<sup>a)</sup> per 100,000 and APC by subsites in female, the Korea Central Cancer Registry, 1999-2009

	Sites (ICD-10 code)			
	Overall (C18.0-C20)	Proximal colon (C18.0-C18.5)	Distal colon (C18.6-C18.7)	Rectum (C19-C20)
Year				
1999	17.2	3.3	3.2	8.8
2000	17.1	3.4	3.2	8.5
2001	18.5	4.0	3.7	9.1
2002	19.7	4.1	4.0	9.6
2003	21.3	4.6	4.6	10.1
2004	22.3	4.9	5.0	10.4
2005	23.8	5.4	5.5	10.7
2006	24.7	5.4	6.3	11.1
2007	25.2	6.0	6.5	10.9
2008	25.7	6.3	6.9	10.8
2009	26.9	6.4	7.2	11.7
APC	5.13	6.56	8.39	2.41
95% CI	4.97-5.28	5.97-7.14	7.28-9.51	1.42-3.41
p-value	<0.001	<0.001	0.003	0.244

APC, annual percent change; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th revision; CI, confidence interval. <sup>a)</sup>Age adjusted to the Korean population in 2000.

rectal cancer showed the lowest increase. Cancer of the distal colon showed the highest APC (10.8% among men and 8.4% among women), followed by the proximal colon (7.9% among men and 6.6% among women) and rectum (5.2% among men and 2.4% among women). As a result, the proportion of rectal cancer decreased from 51.5% in 1999 to 47.1% in 2009 among men, and

from 50.5% in 1999 to 42.8% in 2009 among women, whereas the proportion of proximal and distal colon cancers increased among both men and women (Appendix 2). In all subsites, significantly higher APCs were observed among men, compared with women. As a result, the male-to-female IRRs showed a significant increase between 1999 and 2009 for overall colorectal cancer (1.20 in 1999

to 1.51 in 2009), distal colon cancer (1.32 to 1.60), and rectal cancer (1.22 to 1.67), whereas the IRR for proximal colon cancer did not show a significant change (1.09 to 1.16) (Table 3).

The ASRs and APCs for colorectal cancer subsites by age group are shown in Tables 4 and 5. For overall colorectal cancer, men who were in their 60s showed the highest increase, whereas, for women, those in their 80s showed the highest increase. Distal colon cancer consistently showed the highest APC in most age groups among both men and women, except for women in their 80s, who showed the highest APC for proximal colon cancer. Among women, for almost every subsite, the most notable increases in incidence were

observed for the oldest age group. Proximal colon cancer in men also showed the highest APC in the oldest age groups, whereas APCs were significantly higher only in the 60s for distal colon cancer and 40s and 60s for rectal cancer. However, the APCs showed narrow ranges of between 10.1 and 11.7 for distal colon cancer and between 4.7 and 5.8 for rectal cancer among men over 40 years old.

The highest male-to-female IRRs for overall colorectal cancer were observed for the oldest age groups, whereas the lowest IRRs were observed for younger age groups (Table 6). However, significant increases in male-to-female IRRs were observed in their 50s and 60s between 1999 and 2009. In the subsite-specific analyses,

**Table 3.** Male-to-female colorectal cancer IRR by subsites, the Korea Central Cancer Registry, 1999 and 2009

Year	Sites (ICD-10 code)			
	Overall (C18.0-C20)	Proximal colon (C18.0-18.5)	Distal colon (C18.6-18.7)	Rectum (C19-C20)
1999				
IRR	1.20	1.09	1.32	1.22
95% CI	1.15-1.24	0.99-1.19	1.20-1.44	1.15-1.29
2009				
IRR	1.51	1.16	1.60	1.67
95% CI	1.48-1.55	1.10-1.23	1.53-1.68	1.60-1.73

IRR, incidence rate ratios; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th revision; CI, confidence interval.

**Table 4.** Incidence rates per 10,000 (1999 and 2009) and APC of colorectal cancer by subsite and age groups in male, the Korea Central Cancer Registry, 1999-2009

Sites (ICD-10 code)	Age groups (yr)					
	30-39	40-49	50-59	60-69	70-79	≥ 80
Overall (C18-C20)						
1999	6.0	20.3	59.8	125.5	206.4	232.9
2009	10.3	33.1	114.7	257.1	377.5	389.4
APC	5.29	6.08	6.51	6.82	6.75	5.84
95% CI	5.03-5.55 <sup>a)</sup>	5.82-6.35 <sup>a)</sup>	6.29-6.73 <sup>a)</sup>	6.10-7.54 <sup>a)</sup>	6.56-6.94 <sup>a)</sup>	5.60-6.08 <sup>a)</sup>
Proximal colon (C18.0-C18.5)						
1999	1.5	4.1	10.5	21.1	32.5	30.3
2009	2.4	5.8	18.5	45.6	82.4	77.6
APC	5.18	4.11	6.28	9.13	10.20	10.37
95% CI	4.63-5.73 <sup>a)</sup>	3.88-4.34 <sup>a)</sup>	5.92-6.64 <sup>a)</sup>	8.81-9.44 <sup>a)</sup>	9.89-10.51 <sup>a)</sup>	9.77-10.96 <sup>a)</sup>
Distal colon (C18.6-C18.7)						
1999	1.2	3.3	11.7	27.1	44.9	41.7
2009	1.8	7.9	31.8	78.9	102.3	104.6
APC	6.90	10.11	10.83	11.74	10.73	10.50
95% CI	6.34-7.47 <sup>a)</sup>	9.70-10.53 <sup>a)</sup>	10.50-11.16 <sup>a)</sup>	11.52-11.95 <sup>a)</sup>	10.26-11.20 <sup>a)</sup>	10.13-10.86 <sup>a)</sup>
Rectum (C19-C20)						
1999	2.9	11.1	32.5	65.9	99.5	102.4
2009	5.8	17.3	57.9	164.6	117.0	166.6
APC	5.85	5.82	5.15	5.66	5.08	4.73
95% CI	5.35-6.36 <sup>a)</sup>	5.55-6.10 <sup>a)</sup>	4.90-5.40 <sup>a)</sup>	5.39-5.93 <sup>a)</sup>	4.89-5.26 <sup>a)</sup>	4.35-5.12 <sup>a)</sup>

APC, annual percent change; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th revision; CI, confidence interval. <sup>a)</sup>p < 0.001.

**Table 5.** Incidence rates per 10,000 (1999 and 2009) and annual percent change (APC) of colorectal cancer by subsite and age groups in female, the Korea Central Cancer Registry, 1999-2009

Sites (ICD-10 code)	Age groups (yr)					
	30-39	40-49	50-59	60-69	70-79	≥80
Overall (C18-C20)						
1999	5.7	15.7	42.0	76.5	115.7	106.7
2009	8.1	25.0	64.2	121.1	179.6	211.3
APC	4.26	5.10	5.34	4.46	4.84	6.73
95% CI	3.77-4.76 <sup>a)</sup>	4.87-5.33 <sup>b)</sup>	5.08-5.60 <sup>b)</sup>	4.03-4.90 <sup>b)</sup>	4.58-5.10 <sup>b)</sup>	6.52-6.95 <sup>b)</sup>
Proximal colon (C18.0-C18.5)						
1999	1.0	2.4	8.3	15.5	24.6	16.2
2009	1.3	4.3	13.7	32.3	48.1	56.9
APC	3.41	6.26	6.40	7.62	8.29	12.66
95% CI	2.55-4.28	5.72-6.81 <sup>b)</sup>	6.14-6.66 <sup>b)</sup>	7.28-7.96 <sup>b)</sup>	7.84-8.73 <sup>b)</sup>	12.32-13.00 <sup>b)</sup>
Distal colon (C18.6-C18.7)						
1999	1.2	3.1	9.0	14.6	16.7	14.5
2009	2.3	7.9	19.0	32.1	42.6	44.5
APC	7.97	9.76	9.91	9.52	9.91	11.86
95% CI	7.47-8.49 <sup>b)</sup>	9.40-10.12 <sup>b)</sup>	9.38-10.43 <sup>b)</sup>	9.16-9.88 <sup>b)</sup>	9.52-10.29 <sup>b)</sup>	11.41-12.32 <sup>b)</sup>
Rectum (C19-C20)						
1999	3.2	9.0	21.5	40.1	54.4	43.7
2009	4.2	11.9	28.8	49.9	74.8	80.9
APC	3.23	3.29	3.12	2.35	3.15	6.42
95% CI	2.52-3.94 <sup>a)</sup>	3.05-3.5 <sup>b)</sup>	2.86-3.38 <sup>b)</sup>	2.18-2.51 <sup>b)</sup>	2.90-3.40 <sup>b)</sup>	6.02-6.83 <sup>b)</sup>

APC, annual percent change; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th revision; CI, confidence interval. <sup>a)</sup> $p < 0.05$ , <sup>b)</sup> $p < 0.001$ .

the changes in male-to-female IRRs between 1999 and 2009 showed a statistically significantly increase for rectal cancer among men and women in their 50s, and 60s and for distal colon cancer among those in their 60s.

## Discussion

Incidence of colorectal cancer has increased in most countries, except for the United States and some areas of Japan [10]. The most significant increases have been observed in Eastern European countries and most Asian countries [10]. Although the Korean population has experienced a rapid increase in colorectal cancer incidence, it has not been properly investigated whether the increasing pattern differs according to age group, sex, or anatomical location. There have been suggestions that colorectal cancer incidence by subsite differs according to race, sex, age group, and time period [4,11,12]. In our study, rectal cancer accounted for the highest proportion among all subsites and ranged from 41% to 51% of all colorectal cancers. This result is consistent in part with a report from the US, which showed that the rectum (C19.9 and C20.9) was the most common subsite for male Asians and Pacific Islanders living in the US (35%), whereas the proximal colon was the most common site for Whites and Blacks among both men and women,

as well as female Asians and Pacific Islanders [11,12]. However, in the current study, the APC for rectal cancer was the lowest among the subsites included, thus, it appears that the proportion of rectal cancer has decreased among both men and women in Korea. Instead, colon cancer, particularly distal colon cancer, has shown a rapid increase. We expect that the proportion of rectal cancer will continue to decrease in the future, and the proportion will eventually reach a level similar to that of Western countries.

One study suggested that incidence of colorectal cancer has increased among younger age groups in the US population, although overall incidence of colorectal cancer has declined [4]. The increases observed in the younger population were mainly attributed to rectal cancer [4]. In our study, we did not find clear evidence for a more rapid increase in overall incidence of colorectal cancer or rectal cancer in younger age groups, compared to older age groups in women. In men, however, it is worthy of mention that, unlike proximal colon cancer and distal colon cancer, where the APCs were lowest in their 30s and 40s, the APCs of rectal cancer in men in their 30s and 40s were statistically higher than those for men in their 70s and 80s.

It is notable that although the incidence was higher among men than among women, the APCs were also higher among men than among women for most subsites. As a result, the male-to-female IRR for overall colorectal cancer increased from 1.20 in 1999 to 1.51 in 2009. A high male-to-female IRR was observed for most

**Table 6.** Male-to-female colorectal cancer IRR by subsites and age groups, the Korea Central Cancer Registry, 1999 and 2009

Sites (ICD-10 code)	Age groups (yr)					
	30-39	40-49	50-59	60-69	70-79	≥80
<b>Overall (C18-C20)</b>						
1999						
IRR	1.07	1.26	1.41	1.63	1.85	2.35
95% CI	0.89-1.28	1.12-1.43	1.29-1.54	1.51-1.76	1.68-2.03	1.96-2.81
2009						
IRR	1.28	1.29	1.76	2.11	2.11	1.91
95% CI	1.11-1.49	1.19-1.40	1.67-1.86	2.01-2.22	2.00-2.23	1.75-2.09
<b>Proximal colon (C18.0-C18.5)</b>						
1999						
IRR	1.54	1.69	1.27	1.37	1.32	1.87
95% CI	1.04-2.32	1.27-2.27	1.04-1.55	1.15-1.62	1.07-1.62	1.22-2.86
2009						
IRR	1.76	1.35	1.36	1.41	1.71	1.36
95% CI	1.26-2.50	1.11-1.64	1.20-1.54	1.27-1.56	1.55-1.90	1.13-1.63
<b>Distal colon (C18.6-C18.7)</b>						
1999						
IRR	1.05	1.04	1.29	1.85	2.68	2.88
95% CI	0.70-1.57	0.79-1.38	1.07-1.56	1.57-2.19	2.17-3.31	1.93-4.31
2009						
IRR	0.82	1.01	1.68	2.46	2.40	2.35
95% CI	0.60-1.11	0.87-1.18	1.51-1.86	2.25-2.70	2.17-2.66	1.97-2.81
<b>Rectum (C19-C20)</b>						
1999						
IRR	0.93	1.23	1.51	1.64	1.83	2.34
95% CI	0.72-1.18	1.05-1.44	1.34-1.70	1.49-1.82	1.61-2.08	1.84-2.98
2009						
IRR	1.38	1.46	2.01	2.34	2.20	2.06
95% CI	1.13-1.68	1.31-1.64	1.86-2.18	2.17-2.52	2.04-2.38	1.80-2.35

IRR, incidence rate ratios; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th revision; CI, confidence interval.

subsites across ethnic groups in the US population [11]. Our study also showed that the lowest male-to-female IRR was observed for proximal colon cancer, indicating that the proportion of proximal colon cancer was higher among women than men. This result is consistent with results reported from the US [11], Germany [13], and Japan [14]. Traditionally, differences in the distribution of colorectal cancer subsites between men and women have been explained by the role of female hormonal factors [15,16].

Rapid increases in colorectal cancer incidence and the stabilization of colorectal cancer mortality in the Korean population could be explained by introduction of colorectal cancer screening. Colorectal cancer screening programs were introduced in 2004 as a part of the National Cancer Screening Program for Medical Aid recipients and National Health Insurance beneficiaries in the lower income bracket [17]. The fecal occult blood test (FOBT) is provided free of charge as a primary modality for men and women aged 50 years or older. FOBT-positive individuals were provided follow-up by either colonoscopy or double-contrast barium enema [17]. The

participation rate was only 10.5% in 2004, however, it increased to 21.1% in 2008 [17]. According to the Korea National Cancer Screening Survey, which covers organized and opportunistic cancer screening programs, lifetime screening rates for colorectal cancer were 25.3% in 2004 and 54.2% in 2010, whereas screening rates by recommended guidelines were 19.9% in 2004 and 35.5% in 2010 [18].

In the early phase of screening, increases in incidence are due to detection of prevalent cancers. However, the introduction of colorectal cancer screening cannot completely explain the differential increase in colorectal cancer incidence by subsite. FOBT usually has a higher sensitivity for advanced neoplasia, including colorectal cancer and advanced colorectal adenomas, in the left vs. right colon [19]. This explains in part the increase in the rate of distal colon cancer, but not the low increase in rectal cancer. In addition, the National Cancer Screening Program Guidelines recommend colonoscopy or double-contrast barium enema as a follow-up modality for FOBT positive patients [17]. Sigmoidoscopy, which is

used as a screening tool for an average-risk population in the US [20], is not considered as a follow-up modality in Korea. Therefore, there is little possibility that screening-detected cancers are more likely to be distal colon and rectal cancer.

A transition in risk factors may explain the differential increase in colorectal cancer according to incidence according to subsite. In a large insurance database-based study, frequent alcohol consumption and high consumption amount were more strongly associated with risk of distal colon cancer among men and risk of rectal cancer risk among women [21]. High body mass index ( $BMI \geq 25 \text{ kg/m}^2$ ) was associated with increased risk for distal colon cancer among men and for proximal colon cancer among women. In addition, frequent meat intake was associated with proximal colon cancer risk among men and risk of proximal colon and rectal cancer among women [21]. Daily alcohol consumption in Korea increased from 10.6 g in 1999 to 17.3 g in 2007 among men and from 1.4 g in 1999 to 2.9 g in 2007 among women [22]. The proportion of adult men with a BMI of  $25 \text{ kg/m}^2$  and was 25.1% in 1998 and increased to 35.3% in 2008 [22]. Daily per capita meat consumption was 6.6 g in 1969 and increased to 95.1 g in 2005 [23]. In contrast, the cigarette smoking rate in the adult population decreased from 75.1% in 1992 to 43.1% in 2009 among men and from 5.1% in 1992 to 3.9% in 2009 among women [24]. Cigarette smoking has shown a stronger association with risk of rectal cancer than colon cancer [25].

In our subsite analysis, we excluded overlapping lesions of the colon (C18.8) and colon not otherwise specified (C18.9). The proportions of C18.8 did not change between 1999 and 2009 (1.0% for men and 0.8% for women), however, the proportions of C18.9 during the same period decreased from 9.8% to 5.5% among men and from 11.1% to 5.9% among women. Improved accuracy in topology classification may explain in part the increase in the incidence of distal colon cancer, however, the changes exceeded the

portion that might be explained by improved accuracy in topology coding.

## Conclusion

The rapid increase in colorectal cancer incidence in Korea between 1999 and 2009 is mainly attributed to increases in colon cancer, especially distal colon cancer. Increases in the proportion of colon cancer may be explained by a transition in risk factors for subsites and the effect of colorectal cancer screening programs. The male-to-female IRRs were higher for distal colon and rectal cancer and increased between 1999 and 2009 due to more rapid changes in male colorectal cancer incidence.

## Conflicts of Interest

Conflict of interest relevant to this article was not reported.

## Acknowledgments

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (2010-0010276) and a research grant from the National Cancer Center of Korea (1010160).

## References

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. GLOBOCAN 2008 v1.2, Cancer incidence and mortality worldwide: IARC Cancer Base No. 10 [Internet]. Lyon: International Agency for Research on Cancer; 2010 [cited 2012 Nov 30]. Available from: <http://globocan.iarc.fr>.
2. Jung KW, Park S, Kong HJ, Won YJ, Lee JY, Seo HG, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2009. *Cancer Res Treat*. 2012;44:11-24.
3. Gupta AK, Melton LJ 3rd, Petersen GM, Timmons LJ, Vege SS, Harmsen WS, et al. Changing trends in the incidence, stage, survival, and screen-detection of colorectal cancer: a population-based study. *Clin Gastroenterol Hepatol*. 2005;3:150-8.
4. Meyer JE, Narang T, Schnoll-Sussman FH, Pochapin MB, Christos PJ, Sherr DL. Increasing incidence of rectal cancer in patients aged younger than 40 years: an analysis of the surveillance, epidemiology, and end results database. *Cancer*. 2010;116:4354-9.
5. Meza R, Jeon J, Renehan AG, Luebeck EG. Colorectal cancer incidence trends in the United States and United Kingdom: evidence of right- to left-sided biological gradients with implications for screening. *Cancer Res*. 2010;70:5419-29.
6. Shin HR, Won YJ, Jung KW, Kong HJ, Yim SH, Lee JK, et al. Nationwide cancer incidence in Korea, 1999-2001; first result using the national cancer incidence database. *Cancer Res Treat*. 2005;37:325-31.
7. World Health Organization. International statistical classification of diseases and related health problems. 10th rev. ed. Geneva: World Health Organization; 1992-1994.
8. Altekruse SF, Kosary CL, Krapcho M, Neyman N, Aminou R, Waldron W, et al. SEER cancer statistics review, 1975-2007. Bethesda: National Cancer Institute; 2010.
9. Boyle P, Parkin DM. Statistical methods for registries. In: Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet RG, editors. *Cancer registration: principles and methods*. Lyon: IARC Press; 1991. p. 126-58.
10. Center MM, Jemal A, Ward E. International trends in colorectal cancer incidence rates. *Cancer Epidemiol Biomarkers Prev*. 2009;18:1688-94.
11. Murphy G, Devesa SS, Cross AJ, Inskip PD, McGlynn KA, Cook MB. Sex disparities in colorectal cancer incidence by anatomic subsite, race and age. *Int J Cancer*. 2011; 128:1668-75.
12. Wu X, Chen VW, Martin J, Roffers S, Groves FD, Correa CN, et al. Subsite-specific colorectal cancer incidence rates and stage distributions among Asians and Pacific Islanders in the United States, 1995 to 1999. *Cancer Epidemiol Biomarkers Prev*. 2004; 13:1215-22.
13. Benedix F, Kube R, Meyer F, Schmidt U, Gastinger I, Lippert H, et al. Comparison of 17,641 patients with right- and left-sided colon cancer: differences in epidemiology, perioperative course, histology, and survival. *Dis Colon Rectum*. 2010;53:57-64.
14. Toyoda Y, Nakayama T, Ito Y, Ioka A, Tsukuma H. Trends in colorectal cancer incidence by subsite in Osaka, Japan. *Jpn J Clin Oncol*. 2009;39:189-91.
15. Chlebowski RT, Wactawski-Wende J, Ritenbaugh C, Hubbell FA, Ascensao J, Rodabough RJ, et al. Estrogen plus progestin and colorectal cancer in postmenopausal

women. *N Engl J Med.* 2004;350:991-1004.

16. Yoo KY, Tajima K, Inoue M, Takezaki T, Hirose K, Hamajima N, et al. Reproductive factors related to the risk of colorectal cancer by subsite: a case-control analysis. *Br J Cancer.* 1999;79:1901-6.
17. Choi KS, Lee HY, Jun JK, Shin A, Park EC. Adherence to follow-up after a positive fecal occult blood test in an organized colorectal cancer screening program in Korea, 2004-2008. *J Gastroenterol Hepatol.* 2012;27:1070-7.
18. Lee EH, Lee HY, Choi KS, Jun JK, Park EC, Lee JS. Trends in Cancer Screening Rates among Korean Men and Women: Results from the Korean National Cancer Screening Survey (KNCSS), 2004-2010. *Cancer Res Treat.* 2011;43:141-7.
19. Haug U, Knudsen AB, Brenner H, Kuntz KM. Is fecal occult blood testing more sensitive for left- versus right-sided colorectal neoplasia? A systematic literature review. *Expert Rev Mol Diagn.* 2011;11:605-16.
20. Smith RA, Cokkinides V, Brooks D, Saslow D, Brawley OW. Cancer screening in the United States, 2010: a review of current American Cancer Society guidelines and issues in cancer screening. *CA Cancer J Clin.* 2010;60:99-119.
21. Shin A, Joo J, Bak J, Yang HR, Kim J, Park S, et al. Site-specific risk factors for colorectal cancer in a Korean population. *PLoS One.* 2011;6:e23196.
22. Korea Centers for Disease Control and Prevention. The Fourth Korea National Health and Nutritional Examination Survey (KNHANES IV-2), 2008. Seoul: Korea Centers for Disease Control and Prevention; 2009.
23. Kim J, Shin A, Lee JS, Youn S, Yoo KY. Dietary factors and breast cancer in Korea: an ecological study. *Breast J.* 2009;15:683-6.
24. National Cancer Center, Ministry of Health and Welfare. Cancer facts and figures 2010 in the Republic of Korea. Goyang, Seoul: National Cancer Center, Ministry of Health and Welfare; 2010.
25. Liang PS, Chen TY, Giovannucci E. Cigarette smoking and colorectal cancer incidence and mortality: systematic review and meta-analysis. *Int J Cancer.* 2009;124:2406-15.

**Appendix 1.** Mid-year population in 2000, Korea

Age group (yr)	No. of population	Weight
Total	47,534,124	1
0-4	3,262,382	0.068632
5-9	3,546,106	0.074601
10-14	3,156,497	0.066405
15-19	3,826,940	0.080509
20-24	3,923,161	0.082534
25-29	4,491,340	0.094487
30-34	4,479,771	0.094243
35-39	4,411,157	0.0928
40-44	4,067,761	0.085576
45-49	2,897,028	0.060946
50-54	2,318,703	0.04878
55-59	2,088,513	0.043937
60-64	1,796,705	0.037798
65-69	1,301,094	0.027372
70-74	883,475	0.018586
75-79	587,065	0.01235
80-84	309,500	0.006511
≥ 85	186,926	0.003932

Source: Korean Statistical Information Service (<http://www.kosis.kr>).

**Appendix 2.** The number of colorectal cancer cases by subsites, the Korea Central Cancer Registry, 1999 and 2009

	Year	Sites (ICD-10 code)					Rectum (C19-C20)
		Overall (C18.0-C20)	Proximal colon (C18.0-18.5)	Distal colon (C18.6-18.7)	Overlapping lesion of colon (C18.8)	Colon, not otherwise specified (C18.9)	
Male	1999	5,310	932	1,069	54	521	2,734
	2000	5,789	943	1,185	41	563	3,057
	2001	6,525	1,144	1,394	59	599	3,329
	2002	7,470	1,294	1,660	64	611	3,841
	2003	8,352	1,424	1,936	73	671	4,248
	2004	9,392	1,630	2,237	105	796	4,624
	2005	10,606	1,810	2,670	115	790	5,221
	2006	11,600	2,105	3,078	126	823	5,468
	2007	12,648	2,350	3,543	119	819	5,817
	2008	13,668	2,466	3,910	138	854	6,300
	2009	15,068	2,808	4,185	146	829	7,100
Female	1999	4,404	850	806	35	491	2,222
	2000	4,566	896	835	40	545	2,250
	2001	5,143	1,101	1,017	35	493	2,497
	2002	5,613	1,166	1,116	46	555	2,730
	2003	6,309	1,387	1,326	62	570	2,964
	2004	6,821	1,526	1,484	53	607	3,151
	2005	7,609	1,727	1,731	65	690	3,396
	2006	8,180	1,833	2,031	71	604	3,641
	2007	8,656	2,099	2,188	74	602	3,693
	2008	9,186	2,275	2,397	76	600	3,838
	2009	9,918	2,402	2,600	80	591	4,245

ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th revision.