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Epidemiology of Colorectal Cancer — Incidence, Lifetime Risk Factors Statistics and Temporal Trends

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Additional information is available at the end of the chapter

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Abstract

Colorectal cancer is a major cause of morbidity and mortality in the entire world. Among cancers that affect both men and women, it accounts for >8% of all cancer incidence, making it the third most common cancer worldwide (behind lung and breast cancer). There were an estimated 14.1 million cancer cases around the world in 2012-last data available; 7.4 million were in men and 6.7 million in women. Of that, nearly 1.4 million new cases were from colorectal cancer. And, it has consistently been shown that the developed world carries the majority of the burden (Australia, New Zealand, Canada, the United States and parts of Western Europe), likely due to similarity in lifestyles and diets.

Keywords: Colon cancer epidemiology, colorectal cancer, SEER

1. Introduction

Colorectal cancer is a major cause of morbidity and mortality in the entire world. It has consistently been shown that the developed world carries the majority of the burden — this includes Australia, New Zealand, Canada, the United States and parts of Western Europe — likely due to similarity in lifestyles and diets. [9, 12]

Among cancers that affect both men and women, colorectal cancer accounts for >8% of all cancer incidence, making it the third most common cancer worldwide, behind lung and breast cancer (Table 1). [1]

	Cancer	New cases diagnosed in 2012 (1,000s)	Percent of all cancers*
Worldwide			
1	Lung	1,825	13.0
2	Breast	1,677	11.9
3	Colorectal	1,361	9.7
Men			
1	Lung	1,242	16.7
2	Prostate	1,112	15.0
3	Colorectal	746	10.0
Women			
1	Breast	1,677	25.2
2	Colorectal	614	9.2
3	Lung	583	8.8

*Excludes basal cell and squamous cell skin cancers and *in situ* carcinoma except urinary bladder. Source: GLOBOCAN 2012 v1.1, "Cancer Incidence and Mortality Worldwide"

Table 1. Cancer Incidence Worldwide

There were an estimated 14.1 million cancer cases around the world in 2012. [1] Of those cancers, 7.4 million were in men, while 6.7 million were in women. [1] Nearly, 1.4 million of those new cancer cases were from colorectal cancer. [1]

In the United States, the breakdown between genders is similar. Colorectal cancer is the third most common cancer in both women and men (after breast and prostate cancer, respectively, and lung cancer). Among both gender groups, it is the second leading cause of cancer deaths (behind lung cancer), with peak incidence being in the seventh decade of life. [24] In 2015, it is estimated that there will be 848,200 new cases of cancer among men and 810,000 among women in 2015 (Table 2). [2] Of those new cancer cases, 8% will comprise of colon and rectal cancer, with an estimated 69,090 in men and 63,610 in females. [2]

Men 848,200	Male	Female	Women 810,000
Prostate	26%	29%	Breast
Lung & bronchus	14%	13%	Lung & bronchus
Colon & rectum	8% (69,090)	8% (63,610)	Colon & rectum
Urinary bladder	7%	7%	Uterine corpus

Men 848,200	Male	Female	Women 810,000
Melanoma of skin	5%	6%	Thyroid
Non-Hodgkin lymphoma	5%	4%	Non-Hodgkin lymphoma
Kidney & renal pelvis	5%	4%	Melanoma of skin
Oral cavity & pharynx	4%	4%	Pancreas
Leukemia	4%	3%	Leukemia
Liver & intrahepatic bile duct	3%	3%	Kidney & renal pelvis
All other sites	21%	21%	All other sites

*Excludes basal cell and squamous cell skin cancers and *in situ* carcinoma except urinary bladder.

Source: American Cancer Society, —Cancer Facts and Figures 2015.|| Projected cases are based on incidence data during 1995-2011 from 49 states and the District of Columbia, as reported by the North American Association of

Central Cancer Registries (NAACCR).

Note: Estimates should not be compared with those from previous years.

Table 2. Estimated New Cancer Cases* in the U.S. in 2015

2. Clinical presentation of colorectal cancer

The importance of screening is crucial as most early-stage colorectal cancer does not typically have symptoms. In fact, colorectal cancer may be quiescently growing for as long as 5 years before symptoms appear.

2.1. Signs and symptoms

Symptoms can be specific, such as abdominal discomfort and alarming changes in bowel movements (i.e., hematochezia, diarrhea, or obstruction). More often than not, however, symptoms are usually nonspecific, such as fatigue, weight loss, and/or changes in digestion. As such, even those with some type of symptoms have been misdiagnosed with other benign conditions. These benign conditions include examples such as diverticular disease, inflammatory bowel syndrome, or hemorrhoids. [4]

The major biochemical sign is that of new onset anemia. In fact, in those older than 40 years old, a new onset anemia — specifically hypochromic and microcytic — should prompt evaluation for colorectal cancer.

2.2. Right-sided colon cancers

Symptoms depend somewhat on the site of the tumor. In general, **right-sided colon cancers** are usually detected at an advanced stage with severe symptoms. In general, the right-sided colon cancers are commonly larger, producing vague abdominal discomfort and sometimes a palpable mass. [4, 5] Obstruction is rarely a presenting symptom, as the diameter of the right colon is larger than the left colon. [4] If the tumor involves the cecum, however, it could block the ileocecal valve causing small bowel obstruction.

Those with right-sided colon cancers are significantly older and are predominantly women (46% women versus 38% men). [6] Because of higher rates of comorbidities, survival is worse in those with right-sided carcinomas.

2.3. Left-sided colon cancers and rectal cancers

In comparison, **left-sided colon cancers and rectal cancers** tend to arise in younger, male populations with high-incidence risk. [7, 8] Cancers involving this portion of the bowel produce symptoms that range from obstruction to tenesmus, to alternating constipation and diarrhea with pencil-thin stools. [4] Often, there is blood witnessed either in the stool or coating the stool, in comparison to the right-sided colon cancers. Similarly, rectal cancers can cause obstruction and similar types of bowel movement changes as the left-sided carcinomas.

3. Risk factors of colorectal cancer

There are both modifiable and nonmodifiable risk factors associated with the incidence of colorectal cancer (Table 3).

Modifiable Risk Factors	Nonmodifiable Risk Factors
Diet	Age (≥50 years old)
Physical activity	Personal history of adenomatous colonic polyps
Body weight	Family history of colorectal cancer
Social behaviors (i.e., alcohol and cigarette smoking)	Hereditary polyposis conditions
	Personal history of inflammatory bowel disease (IBD)

Table 3. Factors Associated with Higher Risk of Colon and Rectal Cancer

Modifiable risk factors include diet, physical activity, weight, cigarette-smoking, and alcohol intake. [9] Other modifiable risk factors include low calcium content, low selenium content, and very low salt intake. [10] Occupational hazards, such as asbestos-exposure, have been linked to increased risk of colorectal cancer when compared to the rest of the general population. [10]

Socioeconomic factors, along with access to (and use of) health care services, are also important contributing risk factors. In fact, there is a disproportionately high incidence of colorectal cancers in low socioeconomic status populations. [11]

Nonmodifiable risk factors associated with higher risk of colorectal cancer include increasing age, personal history of adenomatous polyps, personal history of inflammatory bowel disease, genetic inheritance, race/ethnicity, and gender. [9] Unlike modifiable risk factors that could theoretically have been avoided, these risk factors are not considered part of the “environmental nature” of this disease. Thus, they are not controllable. They do, however, play an important role in screening and identifying susceptible patients.

3.1. Modifiable risk factors: Diet

Diets associated with high incidence of colorectal cancer include diets with high consumption of red or processed meat, diets high in fat, beer-drinking, diets low in calcium intake, and diets low in whole-grain fiber, fruits and vegetables. [9] This represents a typical “Western diet.”

On average, 40–45% of Western diets have total caloric intake made up from fatty foods (including meat products), while fat only accounts for about 10–15% of dietary makeup in lower-risk populations — China, India, and parts of Africa and South America. Consequently, it has been shown that the developed world carries the majority of the burden (Australia, New Zealand, Canada, the United States and parts of Western Europe), [9, 12] likely due to similarity in lifestyles and diets.

The hypothesis behind dietary fat as a risk factor is that the fat enhances hepatic cholesterol and bile acid synthesis resulting in increased sterols in the colon. [4] Those sterols are then converted into secondary bile acids, cholesterol metabolites, and potentially toxic metabolic compounds. [4, 13]

While the exact pathogenesis remains unknown, what is known is that these sterols and bile acid metabolites cause damage to colonic mucosa, thus enhancing proliferative activity which could lead to dysplasia. [4, 13] This has been demonstrated in animal models, where animals fed polyunsaturated and saturated fats have higher numbers of adenocarcinoma than those on a low-fat diet. [4] This has also been shown in human population studies where those with colorectal cancer tend to have higher fecal bile acid levels, [4] while a recent meta-analysis has shown that consumption of red meat and processed meat is positively associated with risk of both colon — particularly the descending and sigmoid colon — and rectal cancer. [14]

The “Western diet” also comprises of lower amounts of fiber intake. Multiple epidemiology studies have shown a geographical difference of lower colorectal cancer incidence rates in places with higher fiber intake. [9] It is even postulated that due to the ability of fiber to change the colonic pH, carcinogenesis may be impeded. [4, 9]

Dietary fiber also increases fecal bulk, thus diluting the aforementioned carcinogenic compounds and reducing transit time and mucosal contact. In fact, fiber has been found to decrease the concentration of sterol and bile acid metabolites that could be implicated in creating carcinogenic compounds. [4] Again, this has been demonstrated in animal models, where

increased fiber intake led to decreased concentration of specific bacterial metabolic enzymes that could be implicated in creating carcinogenic compounds. [4] Unfortunately, for all its experimentally demonstrative protective roles, increased fiber supplementation has been unable to prevent adenoma recurrence in several randomized-controlled trials.

3.2. Modifiable risk factors: Physical activity and body weight

Other modifiable risk factors are physical inactivity and excess body weight. Decreased gut motility, increased insulin resistance, lower metabolic rates, and increased circulating estrogens are all mechanisms implicated in the higher risk of colorectal cancer associated with this modifiable risk factor. [9, 10]

3.3. Modifiable risk factors: Social behaviors

Associated with a higher risk is regular consumption of cigarettes and alcohol. [10] Carcinogenic metabolites found in both tobacco and alcohol are considered promoters of tumor growth, based on experimental studies in animals. [15]

Cigarette-smoking has been attributed to 12% of colorectal cancer deaths, while alcohol consumption has been linked with early onset colorectal cancers, specifically tumors in the distal colon. [9, 16, 17] There is information showing that there is higher risk in active smokers for development of rectal cancer.[9, 18]

3.4. Nonmodifiable risk factors: Age

Increasing age carries a higher likelihood of colorectal cancer, specifically after the age of 40. [2]

Cancer incidence rises progressively after the age of 40 in the general population, with 90% of colorectal cancers occurring in those aged 50 years and older. [2] In fact, a 50-year old has 5% chance of developing cancer and 2.5% chance of dying from this cancer after the age of 80 years. [2, 9]

As such, the US Preventative Task Force (USPSTF) has defined “average risk” as those aged 50 years or more with no personal history of colorectal cancer or adenomas, no inflammatory bowel disease, and with negative family history. [19] Put in other terms, the incidence rate is more than 50 times higher in those 60–79 years old than in those less than 40 years old.

In contrast, those with “increased risk” include those with a personal history of colorectal cancer, personal history of colonic adenomas, family history of sporadic colorectal cancer, as well as family history of sporadic adenoma. [4, 9]

Finally, those with “high risk” include those with hereditary nonpolyposis colorectal cancer (Lynch syndrome), polyposis syndromes, and inflammatory bowel diseases (IBD). [4] *See below for a discussion on hereditary polyposis conditions and IBD.*

3.5. Nonmodifiable risk factors: Personal history of colonic adenomatous polyps

Carrying a personal history of adenomatous polyps has an increased risk of developing colorectal cancer, in comparison to those with no history of adenomas. In recent literature, it

was reported that 95% of sporadic colorectal cancers developed from such adenomas, usually after a protracted period, which has been estimated anywhere from 5 to 10 years. [4, 9] However, while nearly all colorectal cancer arise from adenomas, only a small minority of these dysplastic polyps actually progress to cancer (5% or less). [4]

3.6. Nonmodifiable risk factors: Family history of colonic adenomatous polyps or colorectal cancer

The majority of cases occur in those with family history of either colorectal cancer or adenomatous cancer. In fact, there is a two- to three-fold increased risk of sporadic cancer in those with first-degree relatives. This means that up to 20% of those with colorectal cancer have family members affected by this disease. [4, 9] This risk becomes even higher when there are two or more relatives involved and when those family members are affected by the disease at an age younger than 60.

3.7. Nonmodifiable risk factors: Hereditary polyposis conditions

Those with recognized inherited polyposis syndromes carry an even higher risk. Recent literature estimates that about 5–10% of sporadic colorectal cancers are the outcome of inherited conditions, such as the familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HPNCC). [4, 9]

HPNCC (also called Lynch syndrome) is thought to comprise of about 1–6% of all colorectal cancers. It carries a lifetime risk of cancer as high as 70–80%. [4, 9] FAP and its variants account for less than 1% of all colorectal cancer cases, but almost all those diagnosed with this disorder will develop cancer if the colon is not removed by the age of 40. [4]

Other hereditary conditions that are associated with sporadic colorectal cancers include Gardner's syndrome (high-risk), Turcot's syndrome (high-risk), and Peutz-Jeghers syndrome (low-to-moderate risk). [4] Appropriate screening recommendations are made for this population subtype, which will not be discussed here.

3.8. Nonmodifiable risk factors: Personal history of Inflammatory Bowel Disease (IBD)

Those with IBD — ulcerative colitis and Crohn's disease — also carry an increased risk of developing colorectal cancer. It has been estimated that the relative risk of colorectal cancer in patients with IBD ranges from 4- to 20-fold. [4, 9] Thus, appropriate screening recommendations are made for this population subtype, which will not be discussed here.

4. Statistics

4.1. Methods

The following statistical data were obtained from the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute (NCI), specifically from the data

previously published in the *SEER Cancer Statistic Review (CSR) 1975–2012*, which was released in April 23, 2015. The NCI funds for the program through Centers for Disease Control and Presentation (CDC), National Program of Cancer Registries, and involved states’ contributions.

The SEER program was conceptualized in 1973, with a mission to report the “most recent cancer incidence, mortality, survival, prevalence, and lifetime risks statistics. It originally only represented about 10% of the US population.

Since then, it has expanded to include the following population-based cancer registries: Alaska Native Tumor Registry, Arizona Indians, Cherokee Nation, Connecticut, Detroit, Georgia Center for Cancer Statistics (Atlanta, Greater Georgia, Rural Georgia), Greater Bay Area Cancer Registry (San Francisco-Oakland, San Jose-Monterey), Greater California, Hawaii, Iowa, Kentucky, Los Angeles, Louisiana, New Jersey, New Mexico, Seattle-Puget Sound, and Utah. This translates to approximately 26% of African Americans, 41% of Hispanics, 43% of American Indians and Alaska Natives, 54% of Asians, and 71% of Hawaiian/Pacific Islanders. It is published annually, with 2012 being the most recent year for which data are available.

4.2. Temporal trends in the united states

How common is this cancer? It is estimated that there will be 132,700 new colorectal cancer cases in 2015. [21] This comprises 8% of all new cancer cases (Figure 1). [21] Of those new cancer cases, there will be an estimated 49,700 deaths. [21] This comprises 8.4% of all cancer deaths (Table 4).

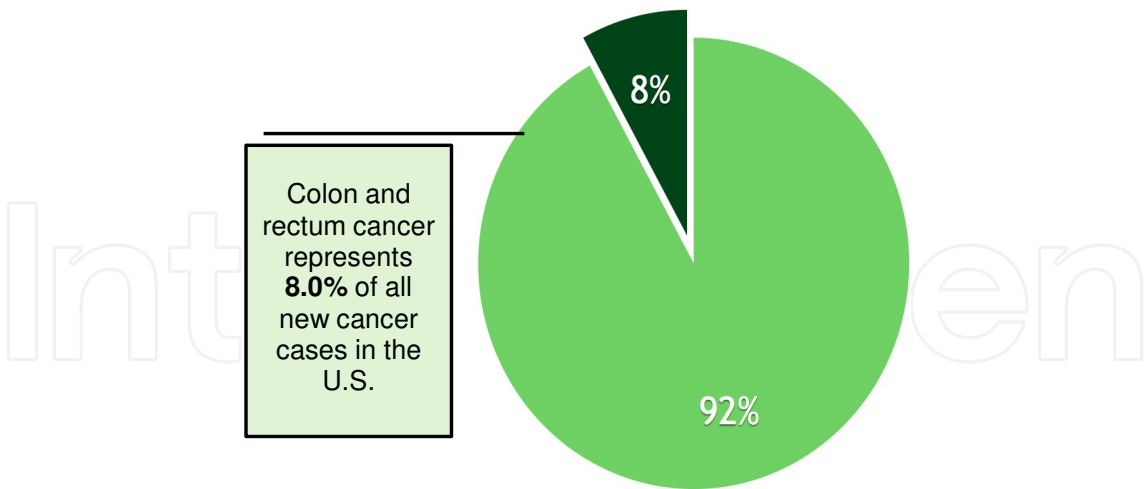


Figure 1. Colon and rectum cancer in the U.S.

Who gets this cancer? Colorectal cancer is more common in men than in women. In 2014, there were a total of 135,260 people diagnosed with colorectal cancer: 70,099 men versus 65,161 women. [22] Based on SEER 18, this means that 48.9 per 100,000 persons new cases were male, while 37.1 per 100,000 persons were female. [20]

Common Type of Cancer	Estimated New Cases 2015	Estimated Deaths 2015
Breast cancer (female)	231,840	40,290
Lung and bronchus cancer	221,200	158,040
Prostate cancer	220,800	27,540
Colon & rectal cancer	132,700	49,700
Bladder cancer	74,000	16,000
Melanoma of the skin	73,870	9,940
Non-Hodgkin Lymphoma	71,850	19,790
Thyroid cancer	62,450	1,950
Kidney & renal pelvis cancer	61,560	14,080
Endometrial cancer	54,870	10,170

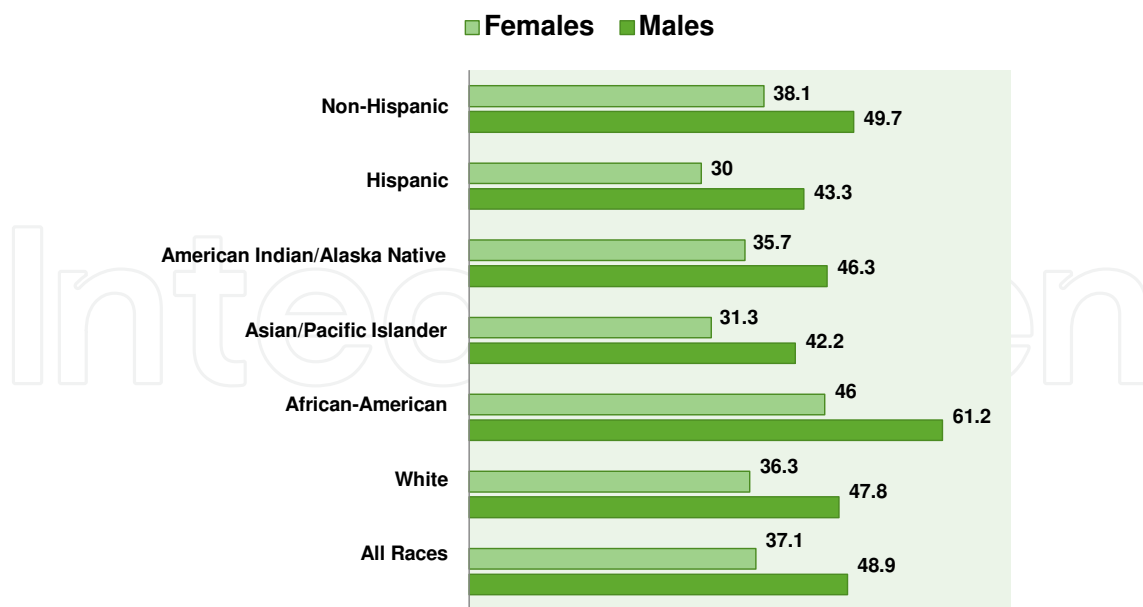
Source: SEER 2015

Table 4. Comparison of Common Cancers

While colorectal cancer is more common in men than in women, the gender bias is smaller when all races are included. However, the gender bias remains wide when race and ethnicity are factored in. The greatest divide was found in African American males versus females, with 61.2 per 100,000 new cases in black men versus 46.0 per 100,000 new cases in black women. [20]

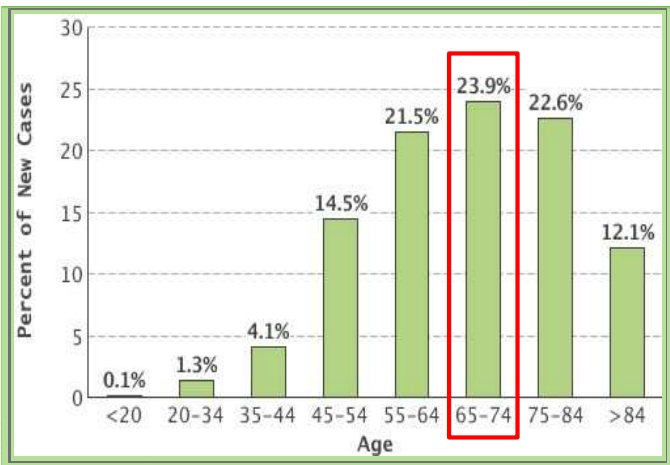
Other race/ethnicities also showed a divide, but not as wide. Hispanic male new cases were 30/100,000 while female new cases were 43.3/100,000. American Indian/Alaska Native male new cases were 35.7/100,000 while female new cases were 46.3/100,000. Asian/Pacific Islander male new cases were 31.3/100,000 while female new cases were 42.2/100,000. White male new cases were 36.3/100,000 while female new cases were 47.8/100,000 (Table 5). [20]

At what age is this cancer most frequently diagnosed? Colorectal cancer is most frequently diagnosed among those aged 65–74 years old. [20] This age group comprises 23.9% of new cases. [20] The median age is 68 years old (Table 6; Figure 2).



Source: SEER 18 2008-2012, Age Adjusted

Table 5. Number of New Colon and Rectal Cancer Cases/100,000 Persons by Race/Ethnicity & Sex



Source: SEER 2015

Table 6. Percent of Deaths by Age Group

There is different distribution based on age at diagnosis in different gender groups. In women, colon cancer tends to arise in an older population (mean age being 73 years old; Figure 2; in comparison, colon cancer tends to arise in a younger population in men (mean age being 69 years old; Figure 2). [9]

In the younger age groups (all races, both sexes), those <20 years old comprised of 0.1% of new cases; 20–34 years old comprised of 1.3%; 45–54 years old comprised of 14.5%; 55–64 years old comprised of 21.5%.

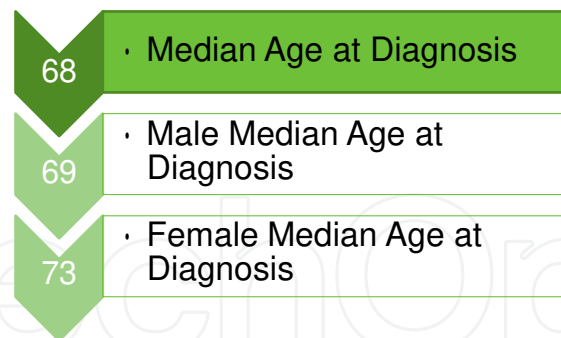


Figure 2. Median age at which colorectal cancer is most frequently diagnosed.

In the older age groups (all races, both sexes), 75–84 years old comprised of 22.6% (75–84 years old) and those >84 years old comprised of 12.1%. [20]

What are the survival rates? Based on the data from SEER 18 2005–2011, relative survival statistics show that 64.9% of people survive 5 years or more after being diagnosed with colon or rectal cancer (all races/sexes, Figure 3). [20, 22]

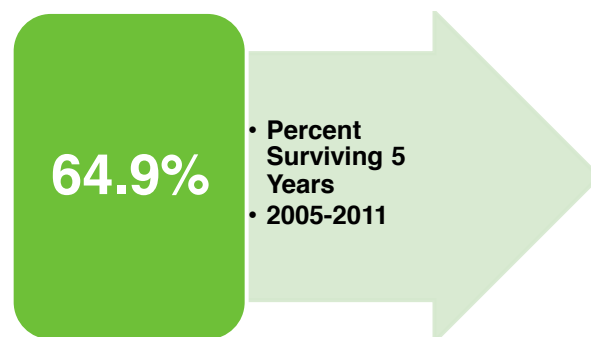


Figure 3. Relative survival rate of colon or rectal cancer.

Does staging influence survival rates? Cancer stage at diagnosis will determine both treatment options and has a strong influence on the length of survival. Obviously, the earlier the cancer is caught, the better the chance of survival.

Current statistics show that 39.5% of colon and rectal cancers are diagnosed at the local stage (confined to primary site), with a 5-year survival for localized colon and rectal cancer being very high at 90.1% [20] (Table 7).

Thirty-six percent of cancers in the regional stage (those spread to regional lymph nodes) have a 70.8% 5-year relative survival rate. [20] Twenty percent of cancers in the distant stage (those that metastasized) carry a 13.1% 5-year relative survival rate. [20] Lastly, those that are unstaged (5%) have a 34.5% 5-year survival rate [20] (Table 7).

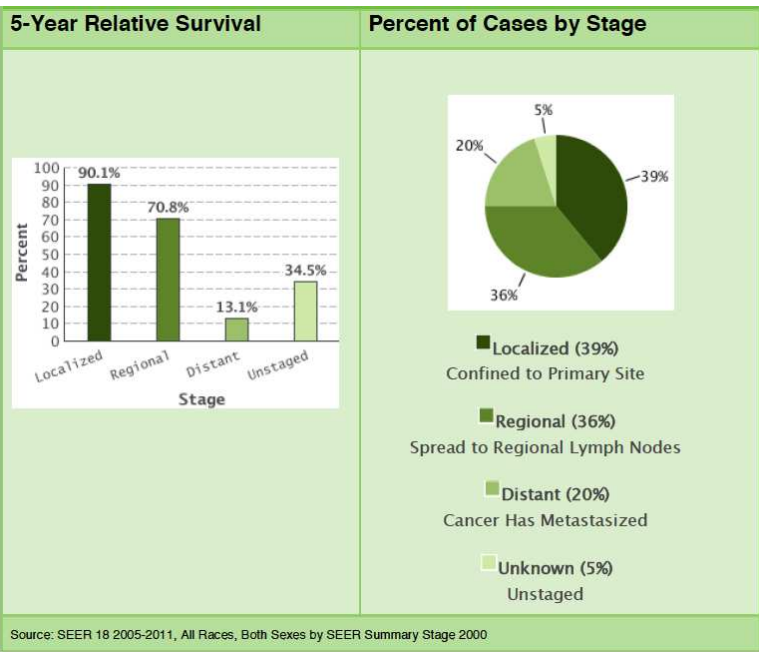


Table 7. 5-Year Relative Survival and Percent of Colon and Rectal Cancer Cases by Stage at Diagnosis [20]

Does the site of cancer change the incidence? Distribution of colon cancers also vary. This suggests that there are different pathogenic etiologies and carcinogenic mechanisms involved in different sites of the colon (and rectum).

The most common tumor locations in decreasing order are the descending colon (40–42%), rectosigmoid and rectum (30–33%), cecum and ascending colon (25–30%), and transverse colon (10–13%). [22, 23] In other words, 50% of colon cancers are within reach of a flexible sigmoidoscope [24] (Table 8).

Who dies from this cancer? As with all cancers, the death rates increase with age. Among both gender groups, it is the second leading cause of cancer deaths — behind lung cancer — with peak incidence being in the seventh decade of life. [2, 20]

In the United States, colorectal cancer is the second leading cause of death. [2] Unfortunately, each year there are >55,000 deaths (26,804 men; 24,979 women). [20]

The percent of deaths is highest among those aged 75–84 at 26.6%. [20] The median age at death is 73 years old (Figure 4). [20] This age group comprises 26.6% of all colorectal cancer deaths [20] (Table 9).

In the younger age groups (all races, both sexes), percent of deaths in those <20 years old comprised of 0% of new cases; 20–34 years old comprised of 0.7%; 35–44 years old comprised of 2.5%; 45–54 years old comprised of 9.3%; 55–64 years old comprised of 17.9%.

In the older age groups (all races, both sexes), percent of deaths in those 65–74 years old comprised of 22.1% and those >84 years old comprised of 21.0%. [20]

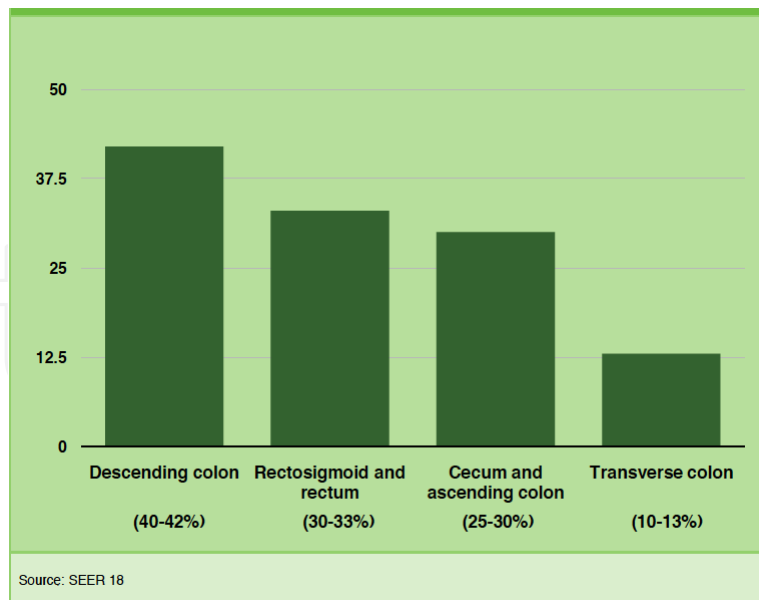
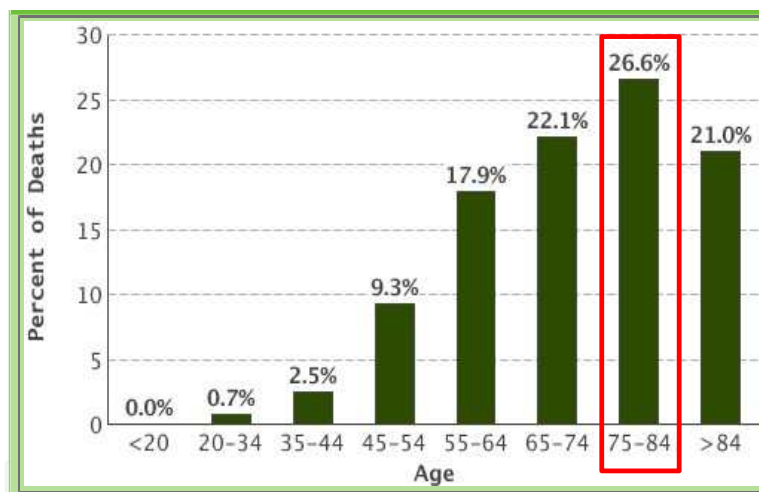


Table 8. Incidence Rates of Colon and Rectal Cancer by Location [20]



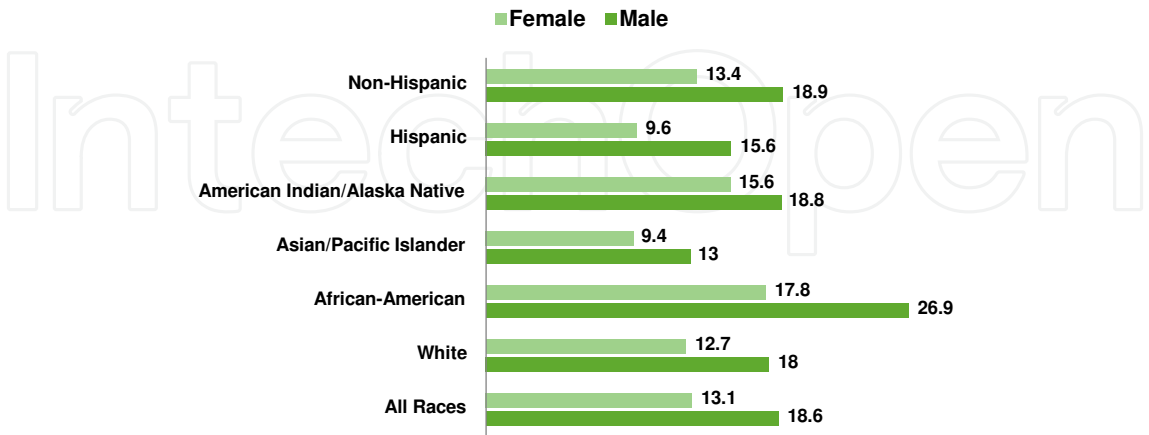
Source: SEER 18 2008-2012, All Races/Both Sexes

Table 9. Percent of Deaths by Age Group

As more males are diagnosed each year than females, there are more male number of deaths than females. In all races, there were 18.6 number of deaths per 100,000 males versus 13.1 number of deaths per 100,000 females.

The divide between the genders was even greater when race and ethnicity were factored in. African American males had the highest number of deaths per 100,000: 26.9 (versus 17.8/100,000 females). [25] Males who were identified as non-Hispanic (but not white or black) had the second highest number of deaths (18.9/100,000), followed by American Indian/Alaska

native (18.8/100,000) and whites (18.0/100,000). Black females had the higher number of deaths per 100,000 (17.8), followed by American Indian/Alaska native (15.6), non-Hispanic (13.4), and whites (12.7) [20] (Table 10).

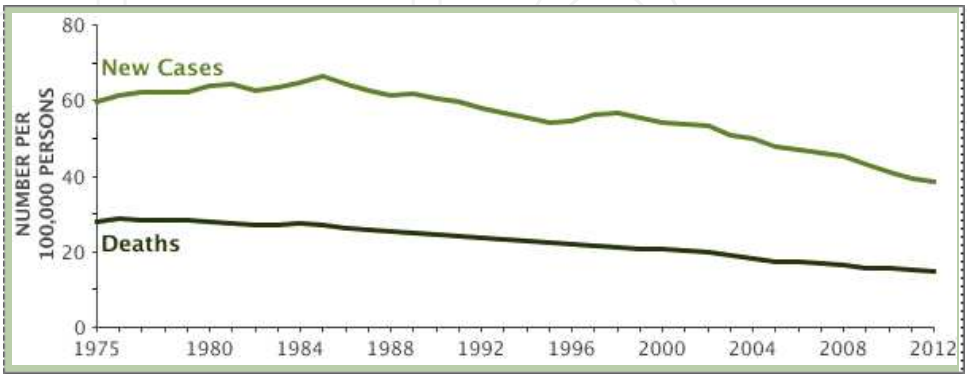


Source: U.S. 2008-2012, Age-Adjusted

Table 10. Number of Colon and Rectal Cancer Deaths per 100,000 Persons by Race/Ethnicity & Sex

What are the projection rates of colorectal cancer? Rates of new colon and rectal cancer diagnosis have been falling each year, over the past 10 years. [26] This is true not only for the United States but also for New Zealand, Australia, and Western Europe.[9] Despite these numbers, the death rate has not changed significantly, however (Table 11).

Year	1975	1980	1985	1990	1995	1999	2003	2007
5-Year	48.6%	51.1%	58.0%	60.8%	59.7%	64.5%	65.3%	66.5%
Relative Survival								



Source: SEER 9 Incidence & U.S. Mortality 1975-2012, all races/both sexes/rates are age-adjusted

Table 11. Incidence & U.S Mortality 1975-2012

5. Conclusion

Although new diagnosis rates of colorectal cancer have lowered significantly in both women and men since 1975, more can be done in terms of screening. The drama in these numbers is that colorectal cancer is a preventative cancer, both in screening and in identification of modifiable (i.e., theoretically preventable) risk factors. In fact, if everyone aged 50 years or older had regular screening tests, at least 60% of deaths from this cancer could have been avoided. [3, 19] And with the knowledge that the 5-year survival is close to 90% when colorectal cancer is diagnosed at an early stage, the statistics becomes even more dramatic. **Bottom-line:** colorectal cancer is susceptible to screening and aggressive campaigns toward educating the public dictate the future of its incidence and survival.

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