

# Colon and Rectal Cancer Summary

## Colorectal Cancer

### Background and Epidemiology

Despite the availability of approved screening and early detection tests, colorectal cancer remains the third most common malignancy in both men and women. It is estimated that 103,170 new cases of colon cancer and 40,290 new cases of rectal cancer will occur in the United States in 2012. This represents about 9% of all cancers diagnosed. It is also the second leading cause of death from cancer among American men and women combined with 51,600 deaths estimated to occur, which represents approximately 9% of all cancer deaths.

The overall incidence of colorectal cancer is very similar in men and women. Tumors of the colon are slightly more frequent in women whereas rectal cancers are more common in men.

The risk of developing colorectal tumors begins to increase at age 40 years and rises with increasing age. The median age at diagnosis in the United States is 72 years.

The incidence of colon cancers has increased by 30% in blacks since 1973 and is now higher than in whites.

The incidence of colorectal cancer tends to be higher in industrialized regions of the world and lower in less industrialized regions.

The five-year survival rates for patients with colorectal cancer have improved in recent years. The earlier the colorectal cancer is diagnosed, the lower it's stage, and the better the patients' survival. When colorectal cancer is detected early and in localized stage the 5-year survival approaches 90%, whereas if diagnosed after it has already spread to distant sites the 5-year survival may be less than 10%.

### Etiology and risk factors

Several factors have been found to be associated with colorectal cancer including nutritional factors, environmental, genetic and familial factors, as well as some preexisting diseases.

Several modifiable factors are associated with increased risk of colorectal cancer. Among these are obesity, physical inactivity, a diet high in red or processed meat, heavy alcohol consumption, long-term smoking, and possibly inadequate intake of fruits and vegetables

**Diet** Diets rich in fat and cholesterol have been linked to an increased risk of colorectal tumors. Dietary fat causes endogenous production of secondary bile acids and neutral

steroids and increases bacterial degradation and excretion of these acids and steroids, thereby promoting colonic carcinogenesis. Historically, diets rich in cereal fiber or bran and green and yellow vegetables have been said to have a protective effect, although recent studies have failed to prove a risk reduction with increasing dietary fiber intake.

A protective role has been attributed to calcium rich foods because they decrease colon-cell turnover and reduce the cancer-promoting effects of bile acid and fatty acids.

**Environment** Africans, Asians, and South Americans who emigrate from low-risk areas assume the colon cancer risk of their adopted country, suggesting an important role for environmental factors in colorectal cancer. Smoking and excessive alcohol intake increases the risk of colorectal cancer.

**Inflammatory bowel disease** Patients with inflammatory bowel disease (ulcerative colitis, Crohn's disease) have a higher incidence of colorectal carcinoma. The risk of colorectal carcinoma in patients with ulcerative colitis is associated with the duration of active disease, extent of colitis, development of mucosal dysplasia, and duration of symptoms.

**Adenomatous polyps** Colorectal tumors develop more often in patients with adenomatous polyps than in those without them. There is approximately 5% probability that cancer will be present in an adenoma; the risk correlates with the size and histology of the polyp. Adenomatous polyps <1 cm have a slightly greater than 1% chance of being malignant, in comparison with adenomas >2 cm, which have up to a 40% likelihood of malignant transformation. The potential for malignant transformation is higher for villous and tubulovillous adenomas than for tubular adenomas.

**Cancer History** Patients with a history of colorectal cancer are at increased risk to develop a second primary colon cancer. Women with a history of breast, endometrial, or ovarian cancer also have an increased chance of developing colorectal cancer.

**Genetic Factors** the risk of developing colorectal cancer is significantly increased in several forms of inherited susceptibility. Examples include: Familial adenomatous polyposis (FAP), Gardner's syndrome, Turcot's syndrome, Peutz-Jeghers syndrome, Juvenile polyposis, and Cowden's disease. Hereditary nonpolyposis colorectal cancer (HNPCC), or Lynch syndrome is the most common form of genetically determined colon cancer predisposition, accounting for 2-4% of all colorectal cancer cases. This hereditary syndrome results from germline mutations in DNA mismatch repair (MMR) genes (MLH1, MSH2, MSH6, and PMS2).

## Signs and symptoms

During the early stages of colorectal cancer, patients may be asymptomatic or complain of vague abdominal discomfort and flatulence, which may be attributed to gallbladder disease or peptic ulcer disease. Minor changes in bowel movements, with or without rectal bleeding are also noted; they are frequently ignored or attributed to hemorrhoids or other benign disorders.

Right colon lesions often produce vague abdominal aching, anemia due to chronic blood loss, generalized weakness, and weight loss.

Left colon cancers may cause constipation alternating with diarrhea; abdominal pain; and obstructive symptoms such as nausea and vomiting.

Rectal cancers may present with change in bowel movements; rectal fullness; bleeding; urgency; and tenesmus.

Pelvic pain is seen at later stages of the disease and usually indicates local extension of the tumor.

## Screening and diagnosis

### Screening

American Cancer Society guidelines on screening for early detection of colorectal adenomas and cancer in average risk individuals begin at age 50 years.

Screening can result in the detection and removal of colorectal polyps before they become cancerous, as well as the detection of cancer that is at an early stage. Thus colorectal cancer screening reduces mortality both by decreasing the incidence of cancer and by detecting cancers at early, more curable stages.

Colonoscopy every 10 years provides the opportunity to visualize, sample, and/or remove significant lesions from the entire colon.

Fecal occult blood testing (FOBT) annually and flexible sigmoidoscopy every 5 years together is preferred over either test alone. All positive tests should be followed up by colonoscopy.

Double-contrast barium enema every 5 years is an alternative if colonoscopy is unavailable or not feasible for the patient. All positive tests should be followed up with colonoscopy.

Individuals at increased risk or high risk of colorectal cancer are recommended to start screening at an earlier age and/or be screened more often.

## Diagnosis

Initial work-up for patients suspected of having colorectal tumors should include colonoscopy with biopsy of any detected lesions. After biopsy proof of malignancy is obtained adequate staging prior to definitive treatment requires: CT scan of the chest, abdomen and pelvis with contrast, CBC, comprehensive metabolic profile, and measurement of carcinoembryonic antigen (CEA) level.

## Pathology

**Adenocarcinomas** constitute 90%-95% of all large bowel neoplasms. Other tumor types are far less common and include: squamous cell carcinomas, small-cell carcinomas, carcinoid tumors, adenosquamous and undifferentiated tumors. Nonepithelial tumors, such as sarcomas and lymphomas, are exceedingly rare.

## Staging and prognosis

The TNM staging system of the 7<sup>th</sup> edition of the American Joint Committee on Cancer's (AJCC) Cancer Staging Manual (Table1), which is based on the depth of tumor invasion in the bowel wall, the number of lymph nodes involved, and the presence or absence of distant metastases, is used to help guide treatment recommendations and provides prognostic information.

**Pathologic stage** is the single most important prognostic factor following surgical resection of colorectal tumors. The prognosis for early stage (I and II) is favorable overall, in contrast to the prognosis for advanced stages (III and IV).

## Treatment

### Surgery

Primary treatment of localized disease relies primarily on surgical resection of the bowel with the adjacent draining lymph nodes. The need for adjuvant systemic chemotherapy with or without concurrent irradiation depends on tumor location and stage of disease.

### Neoadjuvant therapy

For rectal cancers approaching the anal sphincter, preoperative irradiation often combined with concurrent chemotherapy will significantly reduce the size of the majority of tumors. This approach may allow for sphincter-preserving surgery in many patients.

### Adjuvant therapy for colon cancer

The natural history and patterns of failure following curative resection are different for colon and rectal cancers. Locoregional failure as the only site of recurrence is more common in rectal cancer, whereas colon cancer tends to recur in the peritoneum, liver, and other distant sites, with a lower rate of local failure.

Systemic chemotherapy is the principal adjuvant therapy for colon cancer following a curative resection. An analysis of survival data from patients treated with Stage III colon

cancer reveals a significant survival advantage for adjuvant chemotherapy. Category 1 treatment options include FOLFOX, and CapeOx.

### **Adjuvant therapy for rectal cancer**

Local recurrence alone or in combination with distant metastases occurs in up to 50% of patients with rectal cancer. Nodal metastases and deep bowel wall penetration are significant risk factors for locoregional failure. Postoperative chemotherapy with radiation therapy is a standard of care for patients with Stage II or Stage III rectal cancer.

### **Preoperative vs. postoperative chemoradiation therapy**

Preoperative chemoradiation therapy may be preferred to postoperative adjuvant treatment, particularly in patients with T3 or T4 lesions. Such treatment may enhance resectability and may be associated with a lower frequency of complications compared with postoperative treatment.

## **Treatment of Advanced Colorectal Cancer**

The current management of disseminated metastatic disease involves various active drugs either in combination or as single agents: 5-FU/LV, capecitabine, irinotecan, oxaliplatin, bevacizumab, cetuximab, panitumumab, ziv-aflibercept, and regorafenib. The treatment of metastatic colorectal cancer (CRC) has in recent years made significant advances. The addition of biologic agents, such as vascular endothelial growth factor (VEGF) inhibitors and epidermal growth factor (EGFR) inhibitors has further enhanced the options of conventional chemotherapy. These advances have increased the median overall survival of advanced CRC from 6 months with best supportive care, to 12 months with 5-FU, to around 2 years if all active agents can be used in the course of disease.

### **Post-treatment follow-up**

Patients who have completed therapy for colorectal cancer require monitoring for potential treatment-related effects, recurrent disease, and possible new cancers. Patients are usually seen every 3 months for the first two years and then every 6 months for a total of five years. Colonoscopy is repeated in 1 year.

## **SURVIVORSHIP**

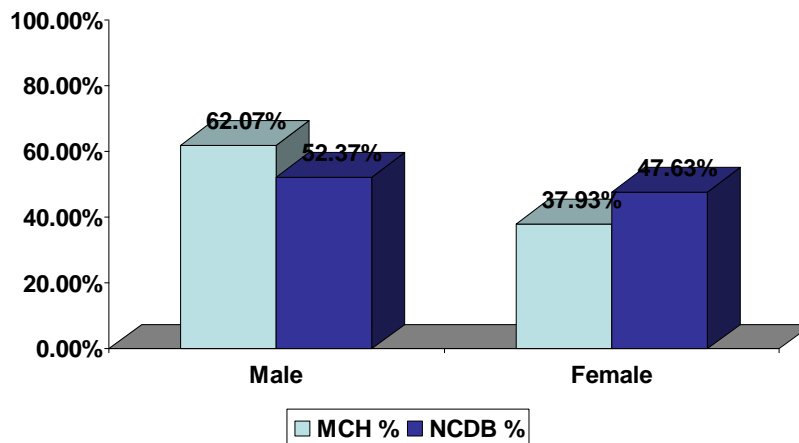
The prescription for survivorship includes an overall summary of all treatments received. The clinical course and effects of treatments are described. Other recommendations include disease- prevention measures and early disease detection through periodic screening. Evidence also indicates that certain lifestyle characteristics, such as smoking cessation, maintaining a healthy body mass index (BMI), engaging in regular exercise, and making certain dietary choices are associated with improved outcomes after treatment of colon cancer.

## Summary of Medical Center Health System Experience

The summary of the data from patients diagnosed and treated with colorectal cancer at Medical Center Health System (MCHS) is presented and compared to national data from the National Cancer Database (NCDB) in the following sections. MCHS data is based on 58 patients who were diagnosed with colorectal cancer in 2012. All data from the NCDB are cases diagnosed in 2011, from all types of facilities.

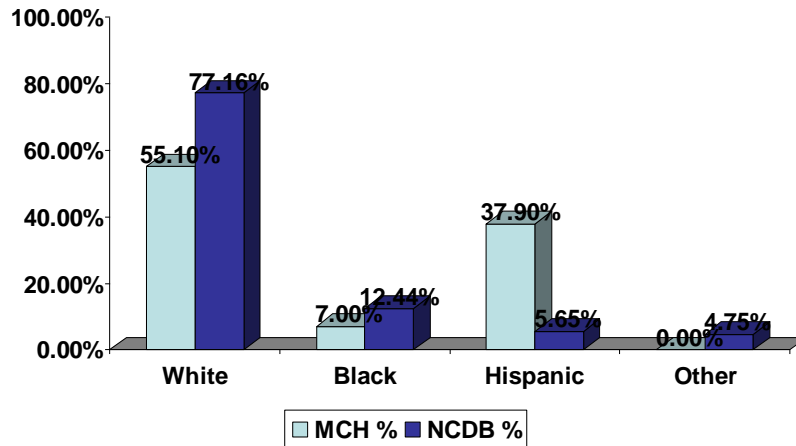
Colorectal cancer is usually reported as affecting males and females with similar incidence. However, both the NCDB data as well as data from MCHS shows a slightly increase incidence in males than females as shown in Table 2.

### Incidence by Gender



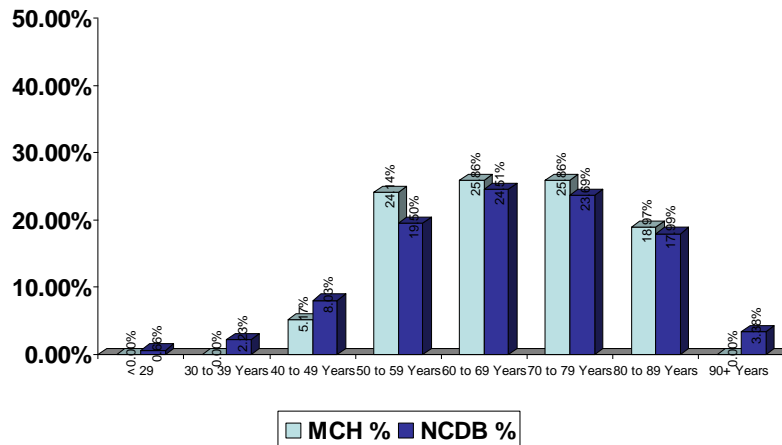
The incidence by race/ethnicity of patients diagnosed with colorectal cancer are shown in Table 3. NCDB data shows Caucasians representing 77% of the total cases and Hispanics 5.6% of cases. At MCHS 55% of cases were reported in Caucasians and 37.9% in Hispanics. This difference is likely a reflection of regional demographics with a higher percentage Hispanic population locally than is seen nationally.

## Incidence by Race/Ethnicity



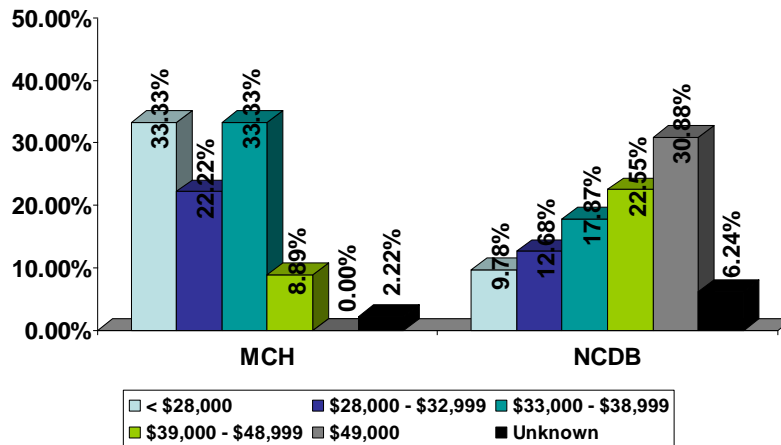
The age at diagnosis of colorectal cancer increases significantly starting at around age 50 as is seen in both the NCDB and MCHS data. This is seen in Table 4.

## Incidence by Age



The median household income of patients diagnosed with colorectal cancer at MCHS is lower than that of patients from the NCDB database, as is shown in Table 5.

## Household Income

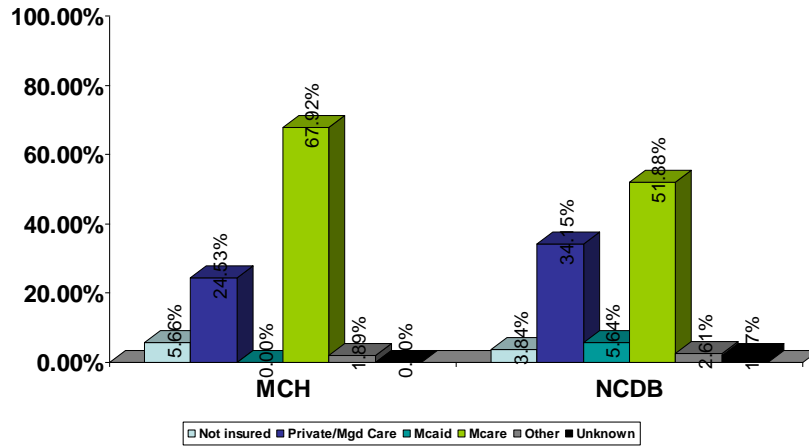


NOTE: MCHS 2011 data per NCDB statistical tool

Medicare was the most common form of insurance for patients diagnosed at MCHS as well as from the NCDB database. A greater percent of patients diagnosed at MCHS were uninsured, while a greater percent of patients in the NCDB database had private or managed care insurance as can be seen in Table 6.



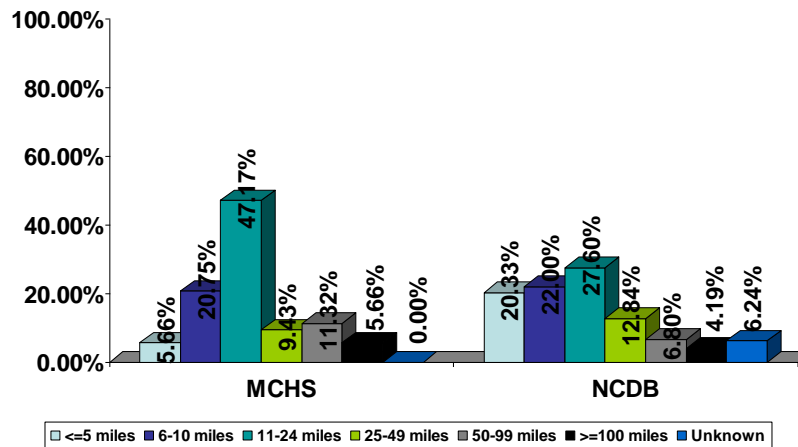
# Insurance Status



NOTE: MCHS 2011 data per NCDB statistical tool

A higher percentage of MCHS patients diagnosed with colorectal cancer traveled greater than 11 miles for care, compared to patients nationally as is shown in Table 7.

# Incidence by Distance Traveled



NOTE: MCHS 2011 data per NCDB statistical tool

Nationally a greater percentage of patients are diagnosed with stages 0 and 1 colorectal cancer, and a greater percentage of MCHS patients are diagnosed with stage II disease.

The encouraging data is that despite the differences previously shown in household income, insurance status, and travel distance for care, the incidence of more advanced, higher stage colorectal cancer is remarkably similar when comparing MCHS and NCDB data. The stage at the time of initial diagnosis of colorectal cancer is shown in Table 8.

## Incidence by Stage

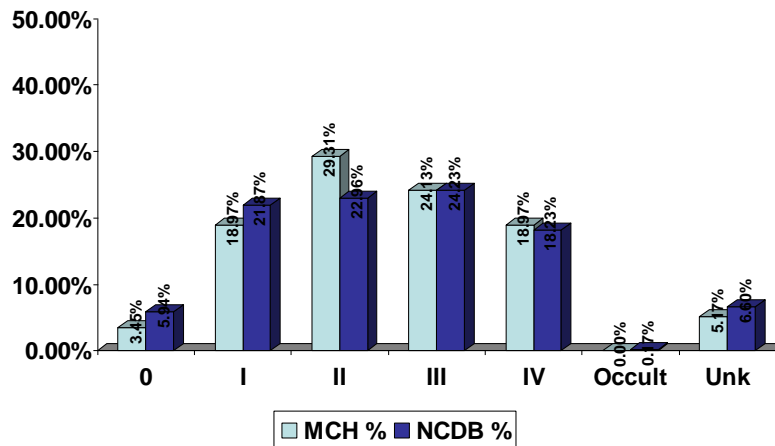
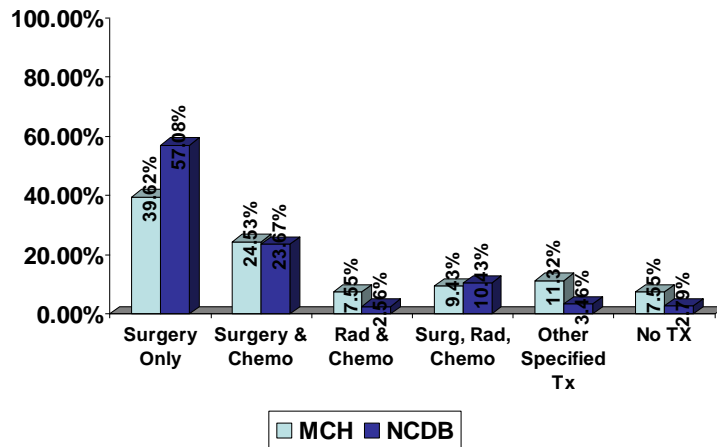


Table 9 shows the first course of treatment for patients diagnosed with colorectal cancer. Nationally, a greater percentage of patients were treated with surgery only. Also shown is the greater percentage of patients who elected no active treatment when diagnosed with colorectal cancer at MCHS when compared to the NCDB data. These differences in part might be explained by the greater percentage of very early stage disease diagnosed nationally, a difference in colon and rectal cancer case mix, and the overall small sample size in the subcategories of MCHS patients.

## First Course of Treatment

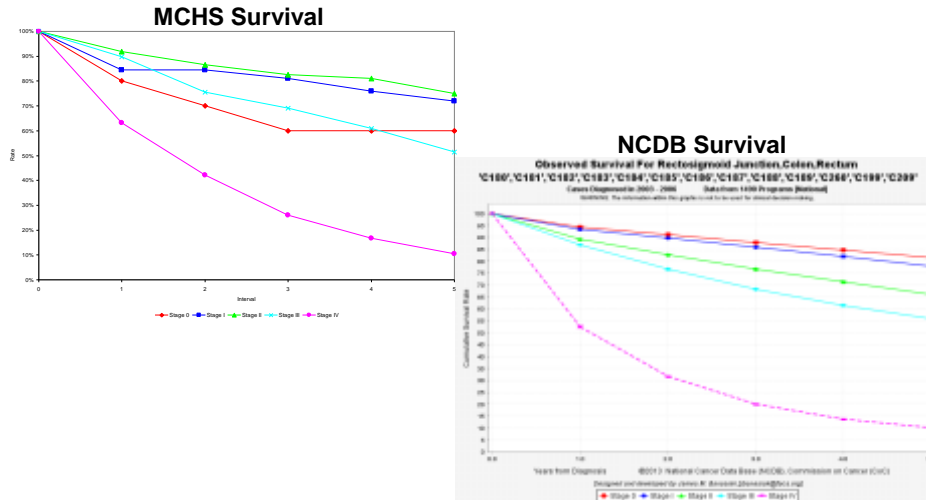


The overall 5 year survival rates of patients diagnosed with colorectal cancer is shown in Table 10. The survival data is presented by stage at the time of diagnosis and follows patients out to 5 years.

The survival for patients diagnosed with early stage colorectal cancer is good with about 80% survival for MCHS patients diagnosed with stage I and II disease which is similar to the national data. Small total numbers of patients diagnosed with stage 0 disease at MCHS may explain the difference seen.

On the other hand, patients diagnosed with advanced and metastatic colorectal cancer have a similarly poor overall survival according to both MCHS and NCDB data.

## Observed 5-Year Survival For Colorectal Cancer MCHS vs NCDB



In order to continue to improve the survival of patients with colorectal cancer at MCHS and nationally, early detection remains essential.

The American Cancer Society as well as other published national guidelines recommends screening for early detection of colorectal adenomas and cancer in average risk individuals beginning at age 50 years. Screening colonoscopy provides an opportunity to visualize, sample, and/or remove precancerous polyps from the colon. Removing precancerous polyps is an effective means to prevent colorectal cancer.

Screening colonoscopy is also able to detect cancer at an early stage of disease, before symptoms develop, and when the cure of colorectal cancer is excellent and the treatment is often less intense.

Joseph G. Kaczor M.D.  
Chairman, Cancer Committee  
Medical Center Health System