Marquette General Hospital

2005 PHYSICIAN OUTCOME ANALYSIS

Colon/Rectum Cancer

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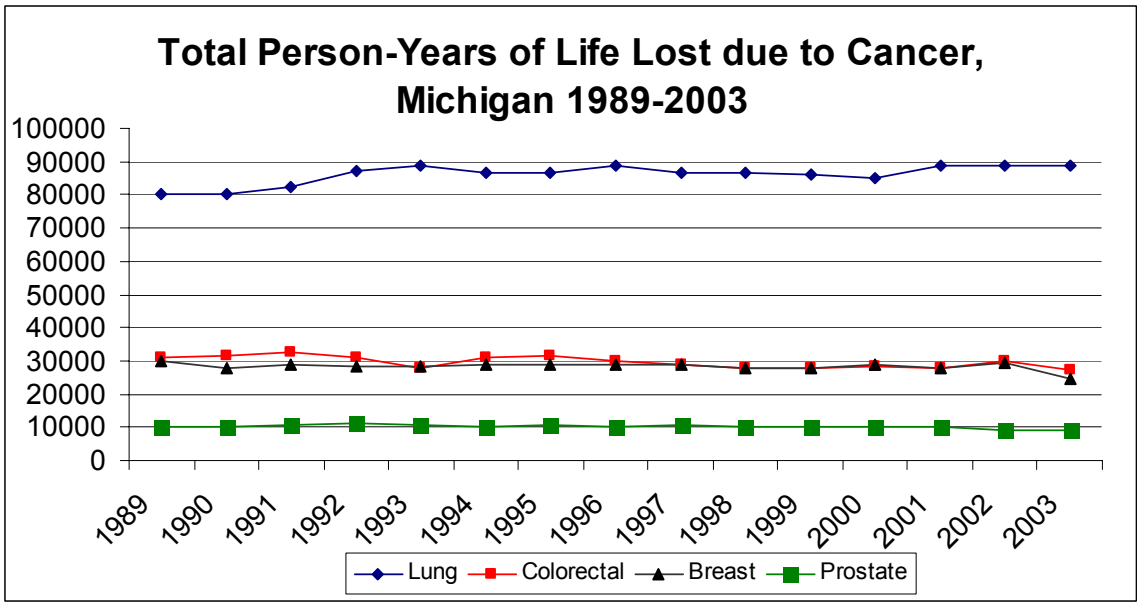
Marquette General Hospital Physician Outcome Analysis – Colon/Rectum Cancer

By: Dr. Aaron Scholnik

Cancer of the colon and rectum remains the third leading cause of cancer death in the United States and in Michigan. Carcinoma of the lung continues to be the leading cause of cancer death of both men and women. The second leading cause of cancer death in men is prostate cancer and the second leading cause of cancer death in women is breast cancer. Thus cancer of the colon and rectum remains a major cause of illness and death throughout the country, more specifically in Michigan and in the Upper Peninsula.

Graph #1



Source: The Cancer Burden In Michigan: Selected Statistics, December 2005. Developed by the Michigan Public Health Institute of the Michigan Consortium Initiative, Section 5: Human Cost p.5.

In 2005 there were 4830 new cases of cancer of the colon and rectum diagnosed in the State of Michigan and 1870 deaths from this cancer. In the year 2004, Marquette General Hospital Cancer Registry recorded 140 cases of cancers of the colon and rectum diagnosed that year and 2 deaths in 2004.

In 1996 our annual report published an extensive review of colon and rectum cancer including some of it's known causes, the genetic and mutational changes that seem to be associated with this cancer and some of the changes in early detection and in treatment that were developing. Ten years later, we can say that the state of the art has made significant strides in some areas but unfortunately has made little improvement in other areas. Similarly, our success in Michigan and Marquette General Hospital specifically show that we have made major strides in the adjuvant treatment of high risk cancer that has been surgically removed and major strides in the treatment of advanced cancer of the colon and rectum that has spread to other areas of the body. On the other hand, despite the knowledge of how to detect colon and rectum cancer when it is early and curable and despite efforts to implement this knowledge of screening and early detection we have been less than successful throughout the United States, Michigan, and the Upper Peninsula.

Let us first examine the advances in the treatment of metastatic or unresectable colorectal cancer. Twenty years ago someone with metastatic or unresectable colorectal cancer had an average life expectancy of only six months. Our only treatment at that time was a chemotherapy drug discovered 50 years ago at the University of Wisconsin – Madison, 5-Fluorouracil (5FU). Since that time we have made major advances by learning how to use 5FU more effectively in combination with the folic acid derivative Leucovorin and by giving 5FU as a prolonged infusion. In addition, over the last ten years four new drugs have been discovered and placed into routine clinical practice all of which, in combination with 5FU, have now increased the life expectancy of someone with advanced colorectal cancer to almost two years. Two of the new drugs, Irinotecan Hydrochloride, (Camptosar, CPT 11) and Oxaliplatin are chemotherapy agents with significant activity against colon and rectum cancer. The other two agents are "targeted" therapies against the colon cancer cell in the form of monoclonal antibodies against certain vital elements of the cancer cell or the surrounding environmental neighborhood. These two targeted therapies are known as Bevacizumab (Avastin) and Cetuximab (Erbitux). While we are still participating in clinical trials to determine the best way to combine or sequence these drugs, it appears clear that the best results are seen in patients who are exposed to all five drugs that are in our standard armamentarium now: 5FU administered by infusion and/or with Leucovorin,

Irinotecan, Oxaliplatin, Bevacizumad, and Cetuximab. In addition, new drugs including new non-cytotoxic non-chemotherapy "targeted" drugs are in development and will soon be entering clinical trials. Marquette General Hospital continues to not only use the latest proven drugs for fighting colorectal cancer but also to bring new, cutting-edge medicines and procedures to our patients, especially in the form of clinical trials and promising new treatments. A relatively new drug named Capecitabine (Xeloda) has also been developed to provide an oral form of the drug 5FU. For some patients, this oral form of chemotherapy may be preferable to prolonged IV infusions of 5FU. Capecitabine is currently being used in a number of regimens which appear of equal activity in the patient with metastatic disease and potentially in those patients undergoing adjuvant therapy.

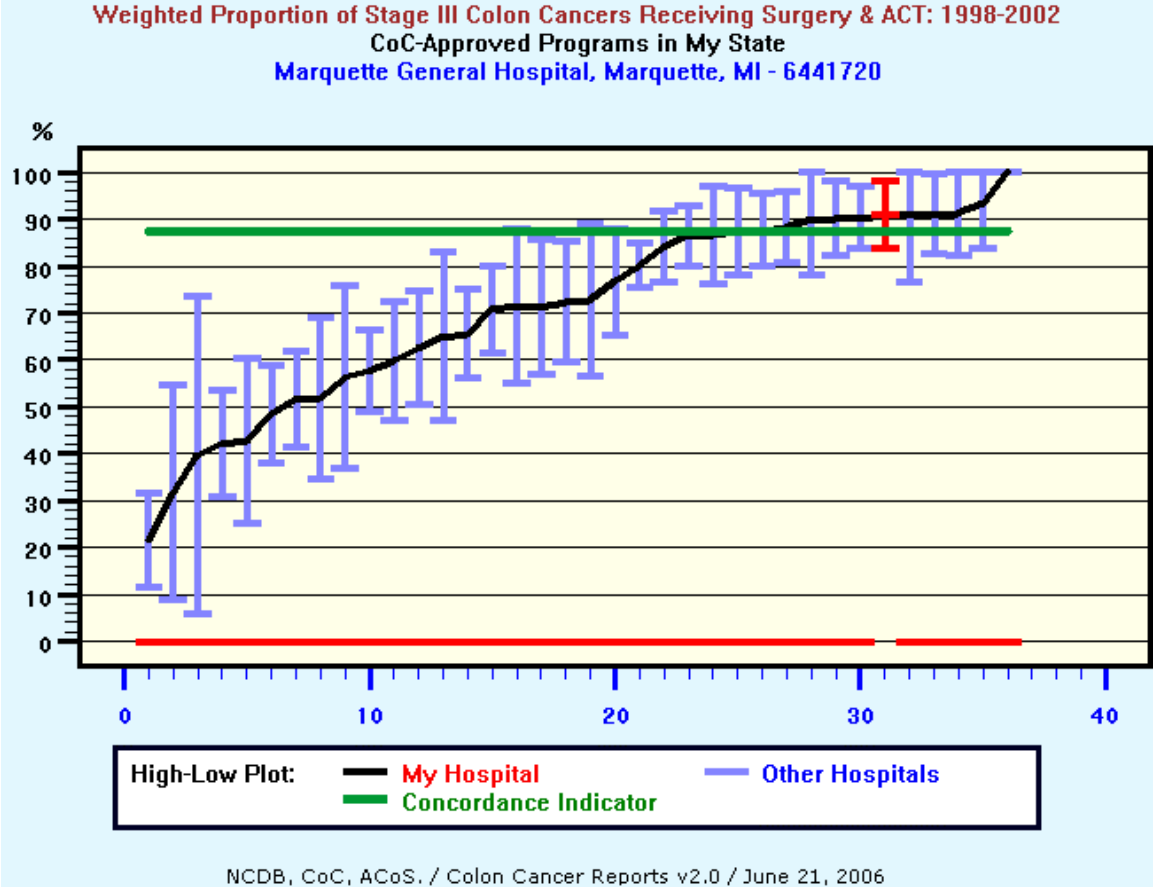
Another advance in the treatment of colorectal cancer has been the use of interventional radiology techniques which are especially useful in the treatment of metastases to the liver, the most frequent organ to which this cancer spreads. Oncology interventional radiologists can isolate the blood supply to the liver or other organs to allow specific chemotherapy or radioactive isotopes to be administered only to the areas containing cancer. These metastases of colorectal cancer to the liver can also sometimes be destroyed (ablated) using RFA (Radio Frequency Ablation) in the appropriate circumstances.

Once the above mentioned chemotherapy and antibody treatments have been shown to be effective in advanced or metastatic colorectal cancer, they were then tried in patients whose cancers were resectable but were at high risk for having already spread microscopically to other areas where they might recur as metastases in the next months or years. This so-called "adjuvant chemotherapy" has undergone much the same evolution as our treatment for advanced disease. Initially we had only 5FU or 5FU with Leucovorin with which to try to improve the chances of curing patients whose visible tumor had been resected by the surgeon. Now, with the use of 5FU in various fashions along with Oxaliplatin we have further decreased the risk of colorectal cancer coming back in patients who have had surgery to remove all visible disease. Marquette General Hospital has actively participated in the clinical trials, especially those with the National

Surgical Adjuvant Breast & Bowel project (NSABP) which has delivered these advances in adjuvant therapy. These advances are so new within the last few years that we will not begin to see the true effects of these drugs reflected in increased cure rates and increased and prolonged survivals in routine clinical practice for several years.

The American College of Surgeons Commission on Cancer, the agency which accredits our cancer center and cancer centers throughout the country feels that the cardinal sign of an advanced and modern cancer center is the use of adjuvant chemotherapy in those patients who have had their colon cancer resected if that colon cancer has spread to the lymph nodes in the surgical specimen. Compared to hospitals throughout the country and within the State of Michigan, Marquette General Hospital is in the top 15 to 20% for hospitals to use this modality consistently.

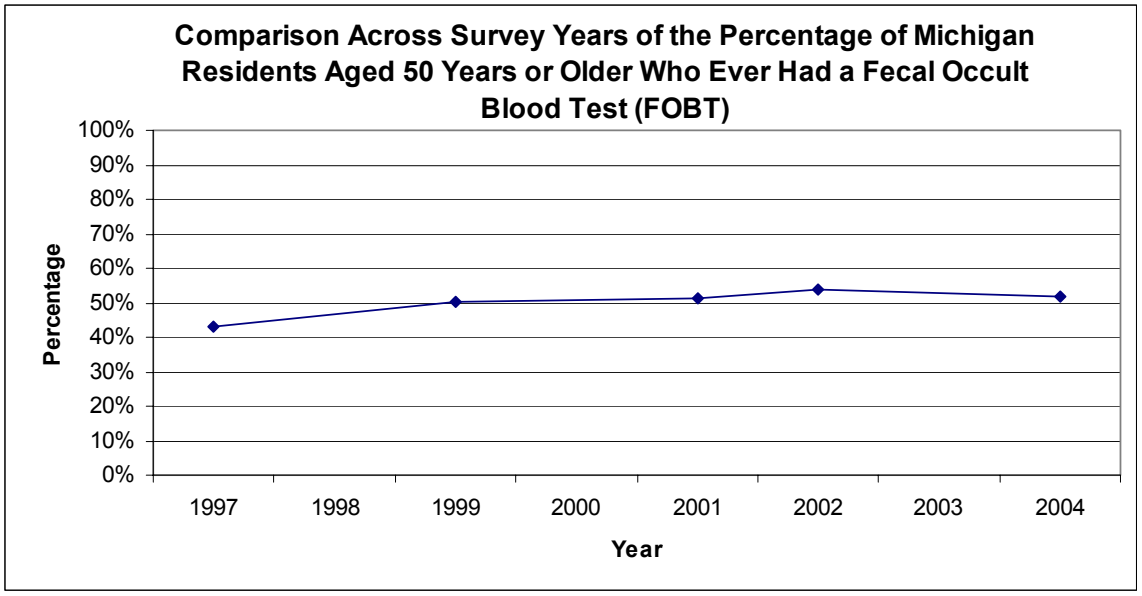
Graph #2



Conversely, Marquette General Hospital shows one of the lowest rates of surgery alone as the only curative modality for patients whose colorectal cancer has spread to the lymph nodes that were resected indicating that the entire spectrum of cancer services is the most modern and up-to-date and comprehensive.

One of the characteristics of colorectal cancer is that the colon is an organ which can be observed carefully and tested frequently for the first signs of cancerous or pre-cancerous lesions. Many studies have shown that the simple use of annual "stool cards" for testing the stool for hidden (occult) blood in minute amounts can increase the curability of cancer of the colon and rectum by allowing us to find it in an earlier stage when it has not yet spread. In addition, there are new developments in the science of stool testing such as the use of DNA probes for the abnormal genes found in cancerous and pre-cancerous lesions of the colon and rectum which are excreted into the stool which may be even more sensitive and more specific for colon cancer. Unfortunately, even a simple test as this is frequently not accepted by the patients and sometimes not always recommended by their physicians.

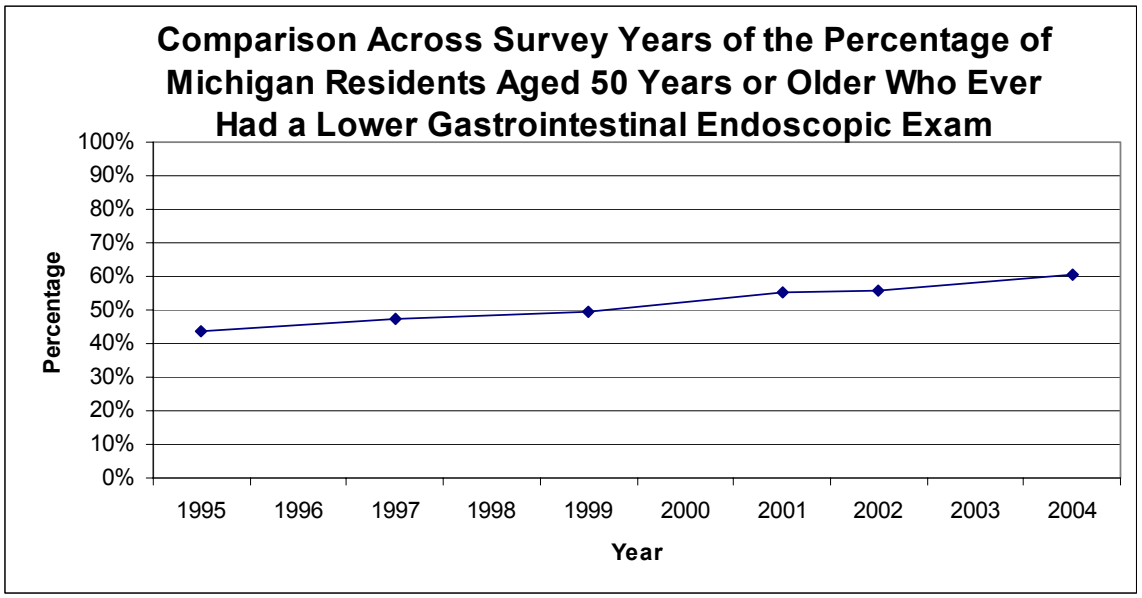
Graph #3



Source: The Cancer Burden In Michigan: Selected Statistics, December 2005. Developed by the Michigan Public Health Institute of the Michigan Consortium Initiative, Section 4: Cancer-related Behavioral Risk Factors: Colorectal Cancer pg16.

It is also known that colonoscopy not only can find cancers when they are very early, it can also prevent cancers by discovering the polyps which are the pre-cancerous lesions in the majority of cancers and allowing them to be resected thru the colonoscope. Once again, unfortunately, many patients have not availed themselves of this technology and the reluctance of third party payers (insurance, health plans, etc.) to pay for these relatively expensive colonoscopy tests has frustrated the ability to improve the early detection rate for colon and rectal cancers.

Graph #4

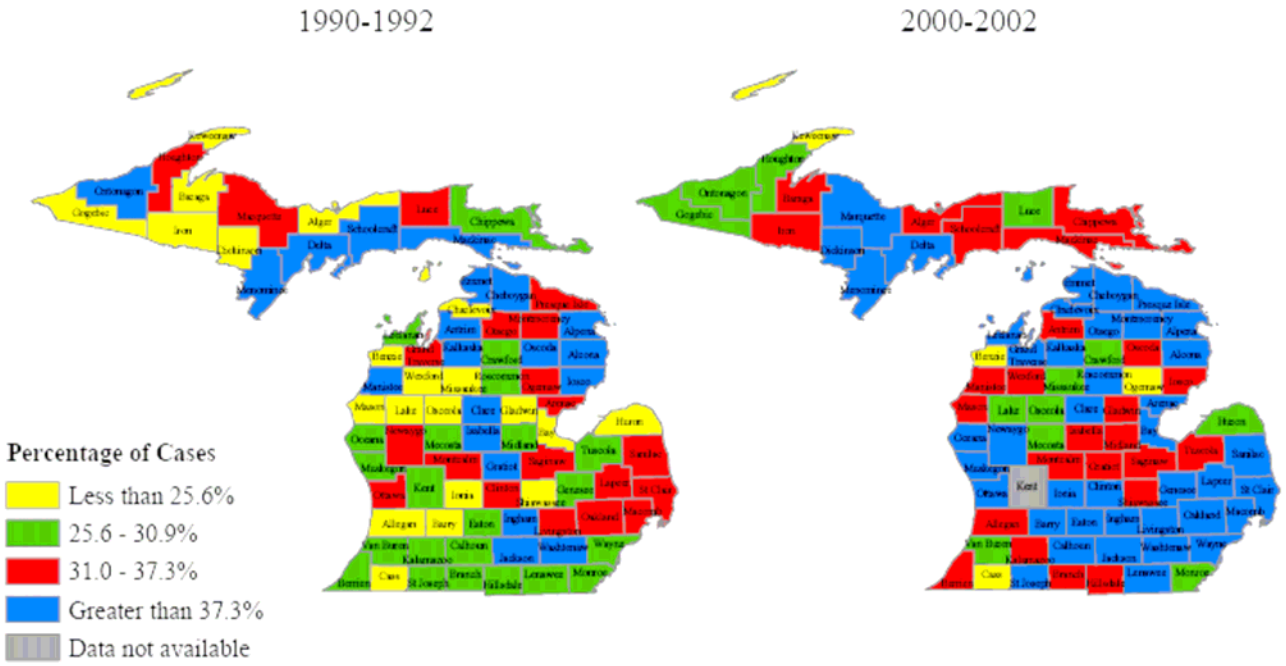


Source: The Cancer Burden In Michigan: Selected Statistics, December 2005. Developed by the Michigan Public Health Institute of the Michigan Consortium Initiative, Section 4: Cancer-related Behavioral Risk Factors: Colorectal Cancer pg17.

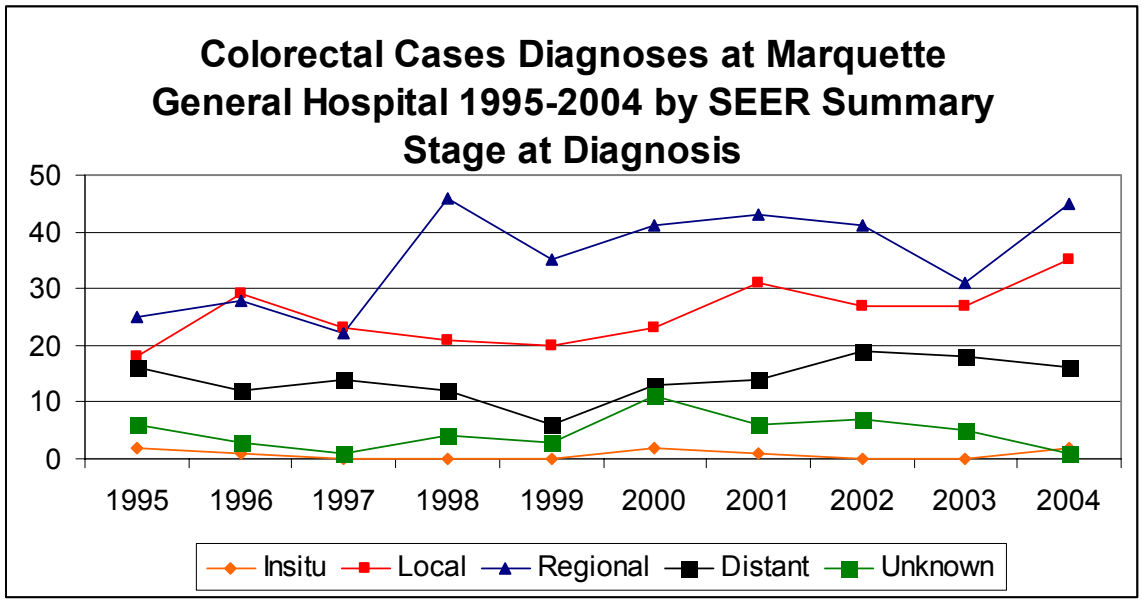
Theoretically, if cancers are discovered earlier then the cure rate will improve. Improved cure rate will occur because the cancers are found in an earlier stage when they have not yet had a chance to spread. Therefore, if screening were being done regularly in the majority of patients, then the stage at diagnosis of colon and rectal cancer should have decreased (improved) over the last decade or more. Unfortunately, we can see from this graph that this has not happened as quickly as it should.

Map Graph #5

Percentage of Colorectal Cancer Cases Localized at Diagnosis by County



Graph #6



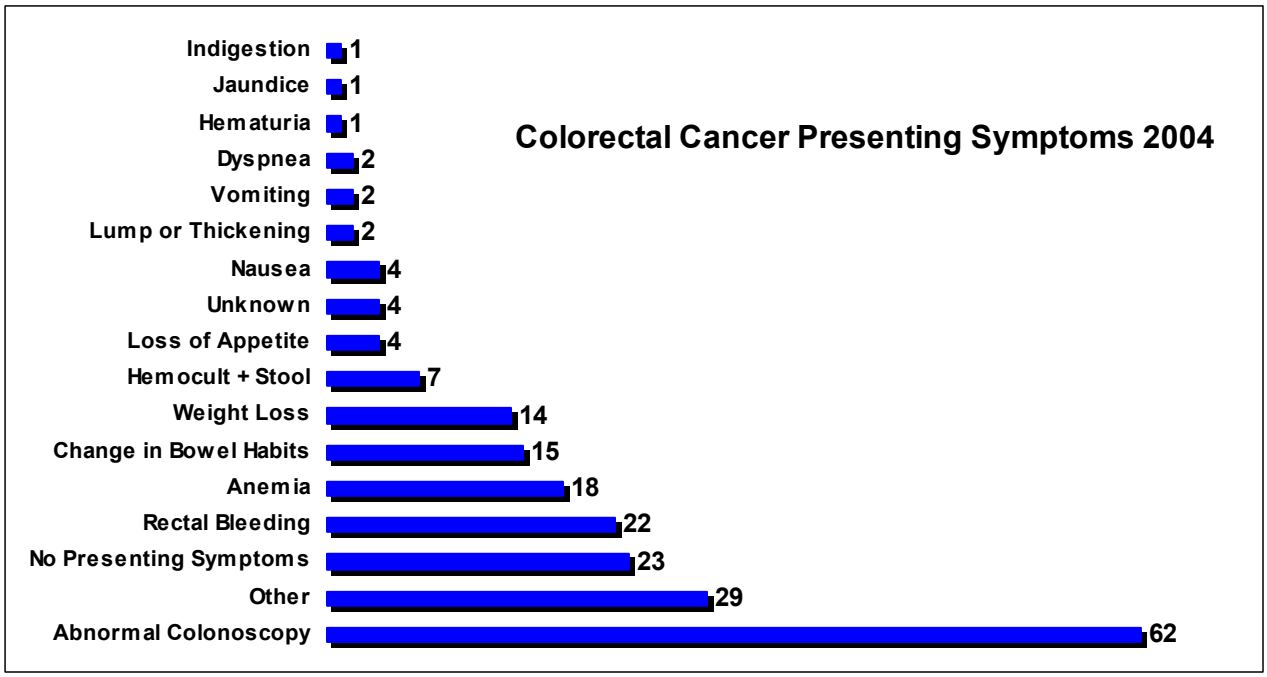
Source: Marquette General Health System, Cancer Research Department; .Tumor Registry Data

We will need to renew our efforts for early detection and find new ways to educate our patients as well as the third party payers about the benefits of screening and early detection and will need to find ways to make this testing as acceptable and easily accessible to entire population at risk (which means everybody) as is the mammogram for detecting breast cancer or the blood PSA test for detecting prostate cancer.

In this regard, Marquette General Hospital and the Upper Peninsula in general are no better or worse than the entire State of Michigan or indeed the entire United States. Major efforts are under way thru the Michigan Cancer Consortium, MCC (of which Marquette General Hospital is a charter member) and it's ColoRectal Awareness Network (CRAN) to increase the rate of colorectal cancer screening and early detection and thus eventually to "downstage" cases found and eventually to increase the cure rate and overall survival of those patients who developed potentially curable and also potentially life-threatening illness. Refer to Appendix 1 for the Michigan Cancer Consortium Guidelines for the Early Detection of Colorectal Cancer and Recommendations for Follow-Up of Abnormal Colorectal Cancer Screening Results and Diagnostic Evaluation of Rectal Bleeding. Also available on MCC website: htpp:www.michigancancer.org/WhatWeDo/ColorectalCancer.cfm.

One promising sign that the tide is beginning to shift is a comparison of the presenting symptoms of colorectal cancer in 1996 and 2004. As we can see the abnormal colonoscopy was the most frequent presenting sign or symptom. Hopefully, the increasing use of colonoscopy as a screening tool on asymptomatic patients will eventually lower the stage and increase the cure rate of this disease.

Graph #7



Source: Marquette General Health System, Cancer Research Department; .Tumor Registry Data

APPENDIX

Michigan Cancer Consortium Guidelines for the Early Detection of Colorectal Cancer
February 2, 2005
Recommendations for Colorectal Cancer Screening (Table 1)

Based on Guidelines of the American Cancer Society (2004), the U.S. Multisociety Task Force (2003), and the U.S. Preventive Services Task Force (2002)

- **If patient reports rectal bleeding a diagnostic evaluation is recommended (See Table 3.)**
- **Screening should continue regardless of age; however, discontinuing screening is reason able in patients whose age or comorbid conditions limit life expectancy.**

Table 1 AVERAGE RISK

Risk Category	Recommendation[1]	Age to Begin	Interval
All people ages 50 and over not in the categories below	- Fecal occult blood test (FOBT)* - Flexible sigmoidoscopy (FS) - Flexible sigmoidoscopy plus FOBT - Double Contrast Barium Enema (DCBE) - Colonoscopy (CS) *Virtual Colonoscopy*[2]	Age 50	- FOBT every year - FS every 5 years - FOBT every year & FS every 5 years - DCBE every 5 years - CS every 10 years

MODERATE RISK

Risk Category	Recommendation	Age to Begin	Interval
People with single, small (< 1 cm) adenomatous polyps	Colonoscopy[3]	At time of initial polyp diagnosis	Colonoscopy 3-6 years after initial polyp removal; if normal, as per average-risk recommendations (above)
People with one large (≥ 1 cm) adenomatous polyp *or* multiple adenomatous polyps of any size	Colonoscopy[3]	At time of initial polyp diagnosis	Colonoscopy *within* 3 years after initial polyp removal; if normal, repeat exam in 3 years; if normal then, the patient can thereafter be screened as per average-risk guidelines.
Personal history of curative-intent resection of colorectal cancer	Colonoscopy[3]	Within 1 year after resection	If normal, colonoscopy in 3 years; if still normal, colonoscopy every 5 years. Colorectal cancer or other visceral cancers[4] at a young age should be considered for counseling for genetic testing.
Colorectal cancer or adenomatous polyp in first-degree relative before age 60 (parent, sibling, or child) Colorectal cancer or adenomatous polyps in two *or* more first-degree relatives of *any* age	Colonoscopy[3]	Age 40 (or 10 years before the youngest case in the family, whichever is earlier)	Every 5 years. Counseling to consider genetic testing, with referral to a specialist/specialty center.[4]
Colorectal cancer in any other relatives not included above (e.g., grandparent, aunt, uncle)	As per average risk recommendations (above)		

HIGH RISK

Risk Category	Recommendation (Includes referral to a specialist/specialty center)	Age to Begin	Interval
Family history of familial adenomatous polyposis	Early surveillance with endoscopy, counseling to consider genetic testing	Puberty	If familial polyposis is confirmed, colectomy is indicated; otherwise, endoscopy every 1-2 years
Family history of hereditary non-polyposis colon cancer (HNPCC)	Colonoscopy and counseling to consider genetic testing	Age 21	Every 1-2 years until age 40, then every year
Inflammatory bowel disease[5]	Colonoscopies with biopsies for dysplasia	8 years after the start of colitis	Every 1-2 years

[1] Digital rectal examination should be done at the same time as sigmoidoscopy or colonoscopy.

[2] Virtual colonoscopy is still being evaluated. The choice of procedure should depend on the medical status of the patient and the relative quality of the medical examinations available in a specific community.

[3] If a colonoscopy is not available, not feasible, or not desired by the patient, a virtual colonoscopy or DCBE can be used.

[4] Personal or family history of visceral cancers, such as endometrial, ovarian, gastric, hepatobiliary, or small bowel cancer or transitional-cell carcinoma of the renal pelvis or ureter, may be suggestive of HNPCC. See above section on HNPCC.

[5] The available scientific evidence is much stronger for ulcerative colitis than it is for other forms of inflammatory bowel disease, such as Crohn's disease.

*FOBT is defined as the at-home procedure of collecting two samples from three consecutive bowel movements.

Michigan Cancer Consortium Guidelines for the Early Detection of Colorectal Cancer

February 2, 2005

Recommendations for Follow-Up of Abnormal Colorectal Cancer Screening Results (Table 2)

and

Recommendations for Diagnostic Evaluation of Rectal Bleeding (Table 3)

Table 2

Abnormal Screening Test Result	Recommended Procedure	Future Screening Protocol
Abnormal Fecal Occult Blood Test (If only one of the three cards tests positive, this is considered a positive test. Proceed to recommended procedure and do not repeat FOBT.)	Colonoscopy	Reassess risk status based upon results of colonic exam and follow appropriate future screening protocol.
Abnormal Flexible Sigmoidoscopy	**If biopsy done:** If hyperplastic polyp: colonoscopy not necessary If adenoma: colonoscopy **OR** **If no biopsy done:** colonoscopy	Reassess risk status based upon results of biopsy and follow appropriate protocol.
Abnormal Double Contrast Barium Enema **OR** Abnormal Virtual Colonoscopy	Colonoscopy	Reassess risk status based upon results of biopsy and follow appropriate protocol.
Abnormal Colonoscopy	Biopsy or Polypectomy	Reassess risk status based upon results of biopsy and follow appropriate protocol.
Incomplete Colonoscopy	Double Contrast Barium Enema *Virtual Colonoscopy*[1]	Reassess risk status based upon results and follow appropriate protocol.

Table 3

Symptom Reported by Patient	Recommended Procedure	Future Screening Protocol
Bright red rectal bleeding on tissue, in bowl, or on stool	**Age 50 and up:** Colonoscopy or flexible sigmoidoscopy with double contrast barium enema. **Age 40-50:** If obvious anorectal disease and no risk factors: flexible sigmoidoscopy. Otherwise: colonoscopy or flexible sigmoidoscopy with double contrast barium enema **Below age 40:** If obvious anal source and no risk factors: treat symptomatically. If recurrent symptoms, then flexible sigmoidoscopy. Further testing if clinically indicated	Reassess risk status based upon results of colonic exam and follow appropriate future screening protocol.
Burgundy blood marbled into the stool	Colonoscopy	Reassess risk status based upon results of colonic exam and follow appropriate future screening protocol.

[1] Virtual colonoscopy is still being evaluated. The choice of procedure should depend on the medical status of the patient and the relative quality of the medical examinations available in a specific community.