



2010 Cancer Program Annual Report

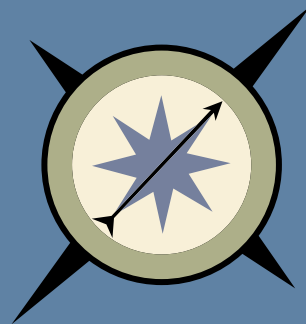




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A Message from the Medical Director

Dear Colleagues,

It is once again my honor to present the Cancer Program Annual Report and to share the accomplishments achieved by the Elkhart General Hospital Oncology Care Team over the past year. The Oncology Program continues to advance, both in terms of program scope as well as community outreach. The highlights of the past year's achievements include the following:

- We again achieved high recognition from the American College of Surgeons annual survey, earning "Accreditation with Full Commendation" – an accomplishment shared by only 41 percent of Indiana hospitals.
- Utilization of the Breast Cancer Clinic continues to grow thanks to increased awareness among members of the medical community as well as the general public. Over the past year, referrals were ten percent higher than 2009 – evidence that this innovative program is making a real difference to newly diagnosed breast cancer patients.
- "Complete and Accurate Order" – the topic of the Total Value Management (TVM) event that included our Ambulatory Infusion Center, Pharmacy and Integrated Patient Scheduling – has significantly improved the order management process and reduced patient reschedules and delays.
- The Hospital continues as an active participant in the Northern Indiana Cancer Research Consortium (NICRC), enabling us to offer the latest and most promising clinical trials to our cancer patients.

Education and awareness continue to be a major focus at Elkhart General Hospital. Important 2010 activities:

- Partnered with numerous national cancer support organizations including the American Cancer Society's *Road to Recovery*, *Reach to Recovery*, *Look Good...Feel Better*, and *I Can Cope*. This year's *I Can Cope* program drew the best community attendance in the history of the program with 60 participants per session.
- Coordinated a cervical cancer outreach program offering free screenings to 75 area women.
- Reached literally thousands of community members with free screenings, physician seminars, and information on the wide range of prevention, diagnosis and treatment programs during the Elkhart County 4-H Fair.
- Participated in numerous community outreach events including the Elkhart General Hospital Breast Cancer Awareness Event, American Cancer Society's *Making Strides Against Breast Cancer*, Susan G. Komen *Race for a Cure* and *Golf for a Cure* and the Wakarusa Community Appreciation Day.
- Offered bedside counseling smoking cessation program to all Hospital patients who smoke. It's proving to be a valuable aid in helping these people "kick the habit."
- Support group organizations continued to be an integral part of our program. These included the Cancer Survivorship Support Program, Second Saturday Coffee Survivorship Support for Breast Cancer, and the Man-to-Man Prostate Cancer Support Group.



Clearly it has been an eventful year for the Oncology Team, and it's gratifying to know that our efforts are making a real impact in the lives of cancer patients and their families throughout our community. Our goal continues to be to provide the region with the absolute best cancer program possible and we look forward to advancing this goal even further in the coming year.

Respectfully submitted,

A handwritten signature in black ink that reads "Michael Rodriguez".

Michael Rodriguez, MD, FACOG
Medical Director
Elkhart General Hospital Regional Center for Cancer Services

Oncology Care Committee 2010

The Oncology Care Committee is comprised of representatives from primary and specialty care physicians, as well as Hospital departments involved in the care of cancer patients. The multidisciplinary Committee meets regularly to review and evaluate the quality and direction of the overall cancer program, and makes recommendations for improvement.

Michael Rodriguez, MD, FACOG
Gynecological Surgical Oncologist
Medical Director, Oncology
Cancer Committee Chair

Rolan Pascual, MD
Medical Oncologist
Cancer Conference Coordinator

Michael Rotkis, MD, FACS
General & Vascular Surgeon
Cancer Liaison Physician Community Outreach Coordinator

Vicky Carter, CTR
Cancer Registrar
Cancer Registry Data Quality Control Coordinator

Beth Brew, RT(T)
Manager of Radiation Oncology
Quality Improvement Coordinator

Ann Bemiller
Cancer Registry

Heather Borsa, RD, CSO, CD
Oncology Dietitian

Joel N. Cohen, MD
Radiation Oncologist

Kathy Deka
American Cancer Society

Laurie Dubois
Community Outreach Coordinator

Danielle Dyer
Vice President of Marketing
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Peter Fretz, MD
Urologist

Alison Gratzol, RN, OCN
Manager of the Oncology Care Unit,
Ambulatory Infusion Center and Cancer
Registry

Pam Green, RN
Oncology Outpatient Care Coordinator

Ahsanul Haque, MD
Medical Oncologist

Marcie Hemenway, RN, OCN
Oncology Education

Roger Hershberger, LCSW
Oncology Experience Guide

Pam Jackson, RN
Oncology Research Nurse

James Jin, MD, PhD
Medical Oncologist

William Kaliney, MD
Pathologist

Sonja Kring, RPh
Oncology, Pharmacy

Allison Lamont, MD
Diagnostic Radiologist

Greg Losasso
Vice President of Operations

Amy Luebbehusen, PharmD
Oncology, Pharmacy

Cindie McPhie
Director of Oncology, Neuroscience
and Rehabilitation

Samir Patel, MD
Diagnostic Radiologist

William Pletcher, MD
Medical Oncologist

Kathryn Press, MD
ENT Surgeon

Kelly Puster, MD, FACS
General Surgeon

Loretta Salchert
Ribbon of Hope

Leah Schrock, LCSW
Inpatient Oncology Care Coordinator

Brion Shin, MD
Radiation Oncologist

Cancer Care Conferences 2010

Cancer Care Conferences meet every 2nd and 3rd Wednesday each month at Elkhart General Hospital. This conference is held in Auditorium A at Noon and lunch is provided. Times may change periodically if speakers are scheduled prior to case presentation.

Treatment plans are reviewed in consultation with radiologists, pathologists, surgeons, medical oncologists, radiation oncologists and other specialists. This format benefits both patients and physicians by providing forums in which experts from varied oncology disciplines can discuss different treatment options.

Cases presented in the past year were inclusive of the top five primary sites as well as Kidney, Renal Pelvis, Bladder, Lymphoma, Pancreas, Esophagus, Head and Neck, etc. A total of 24 Tumor Boards and 26 Breast Cancer Clinics or Forums were presented through the end of December 2010; totaling 122 case presentations. Physicians are encouraged to submit cases for presentation by contacting the Cancer Registry on or before Wednesday Noon the week prior to the conference at (574) 523-3454.

Additional Presentations included the following speakers at Cancer Care Conference:*

- "Advances in Treatment of Sarcoma," Daniel Rushing, MD, Clinical Professor, Department of Medicine, Division of Hematology/Oncology, Indiana University School of Medicine, Indianapolis, IN (April 21, 2010).
- "Aspects of RapidArc Radiotherapy Technology," Brion Shin, MD, Radiation Oncology, Elkhart General Hospital (August 11, 2010).
- "Spanning the Continuum of Care: Optimizing Patients Care in Non-Hodgkin Lymphoma," Steven Bernstein, MD, Professor of Medicine, Director of Lymphoma Biology Program, University of Rochester, NY (September 15, 2010).
- "The Expanding Threat of Melanoma," Christopher Touloukian, MD, Assistant Professor of Surgery, Indiana School of Medicine, Indianapolis, IN (October 13, 2010).
- "State of the Art Breast Cancer Care: The Next Decade of Novel Therapies," Rowan Chlebowski, MD, PhD, Professor of Medicine, University of California, Los Angeles, CA (November 17, 2010).
- "Chronic Myeloid Leukemia (CML) 2010: Biology Drives the Disease," Luke Akard, MD, Medical Co-Director Indiana Blood and Marrow Transplantation, St. Francis Hospital and Healthcare Center, Indianapolis, IN (December 8, 2010).
- "Urology Conference: Prostate," Peter Fretz, MD, Urology (December 15, 2010).

Medical Conferences with Cancer Related Topics:

- "Hereditary Breast and Ovarian Cancer Syndrome," Rosalie McBride, MD, OB/GYN (February 10, 2010).
- "Prostate Cancer Screening and Prevention," Timothy Roth, MD, Urology (February 24, 2010).
- "American College of Surgeons Quality Measurements for Cancer Treatment and AJCC Clinical Staging, Prognostic Indicators and NCCN Guideline Review," Michael Rotkis, MD, FACS, General and Vascular Surgery (November 10, 2010).

* Case presentations followed speakers at Cancer Care Conference with associated topic influence.

Cancer Registry

The Cancer Registry at Elkhart General Hospital has a beginning reference date of January 1, 1998 and is under the management and direction of Oncology Administration and the Cancer Committee as well as strict adherence to the American College of Surgeons Commission on Cancer program standards.

In 2010, 691 new incidences of cancer were accessioned; 648 of those cases were analytic cases with initial diagnosis and/or first course of treatment at Elkhart General Hospital. Another 43 cases were non-analytic cases of recurrent or persistent disease diagnosed and initially treated before our reference date or elsewhere. Through the Cancer Registry, recorded information for each malignancy is maintained and is inclusive but not limited to: patient demographics, primary site, histology, stage of disease, treatment, recurrence, and follow-up data. This data provides physicians and administration with statistics for research, education and strategic planning.

Confidentiality of patient identification and related medical data are strictly maintained. Only aggregate data are analyzed and published.

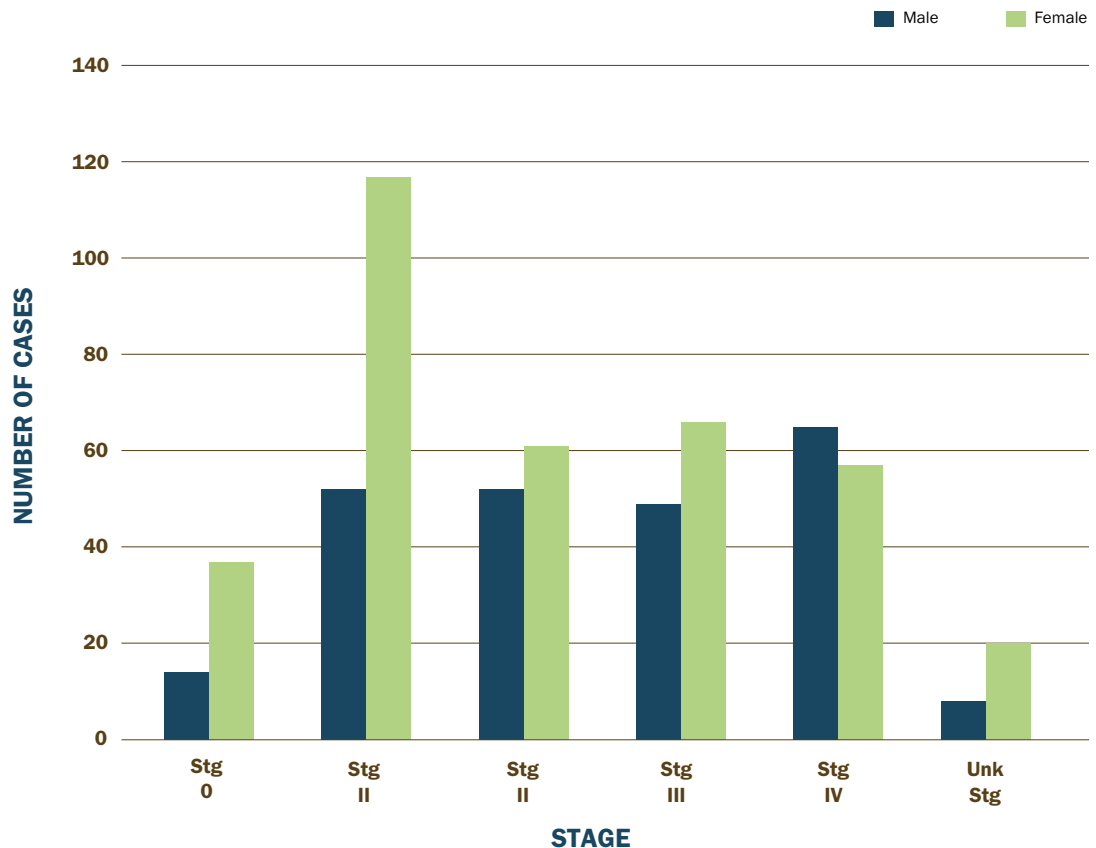
Top 5 Cancer Sites for 2009*

Site	EGH %	Indiana %	USA %
Breast	21.4	13.1	13.5
Lung	20.4	16.4	14.5
Colon	8.0	10.0	9.3
Prostate	5.4	12.6	14.2
Corpus Uteri	5.2	2.9	2.8

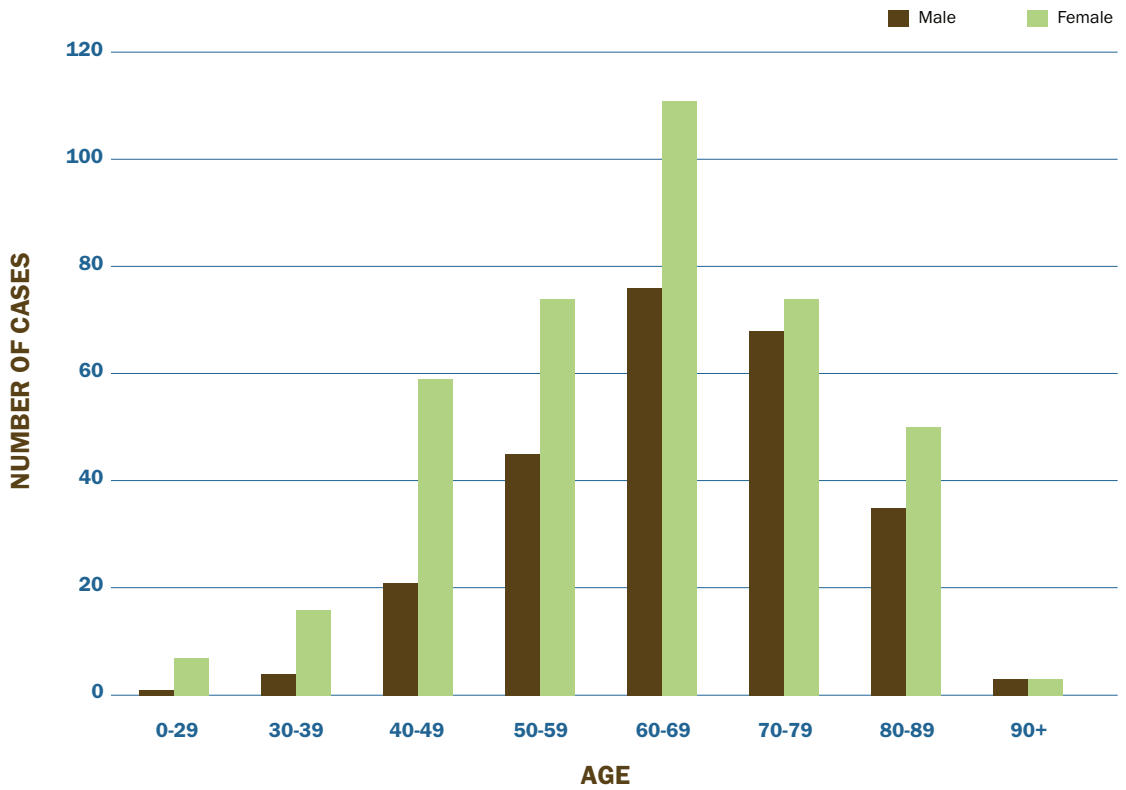
*Based on American Cancer Society's 2010 Cancer Facts & Figures

Each patient in the database is followed annually in order to acquire necessary information on disease recurrences, subsequent treatment and survival data that is vital for continued patient care. The program standard requires a 90 percent annual follow-up rate with Cancer Registry currently maintaining an average monthly follow up rate of 97 percent.

Male vs. Female by Best AJCC Stage 2009 Cases

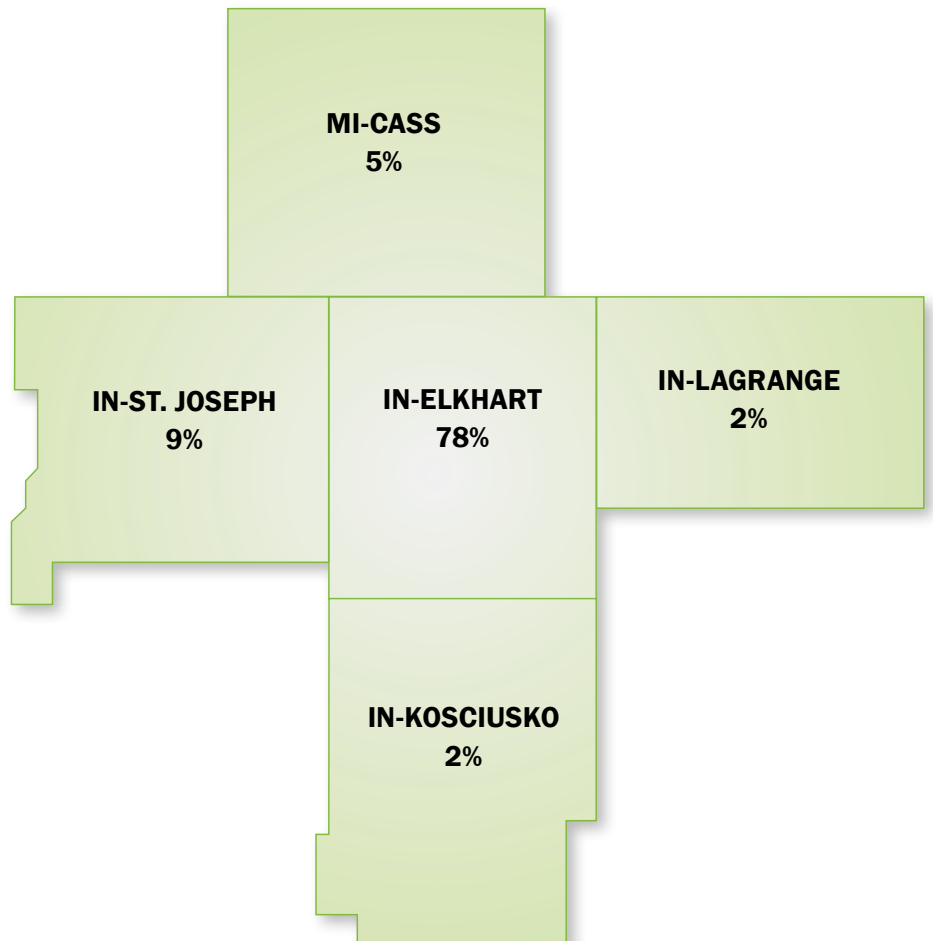


Male vs. Female Age at Diagnosis 2009 Cases



Distribution by State/County 2009 Cases

NOTE: 4 percent of patients reside in counties outside of the service areas shown.



Cancer Registry

Registry Accomplishments for 2010:

- Maintained bimonthly Cancer Care Conferences as multidisciplinary case presentations and lectures.
- Submitted required data to National Cancer Database October 20, 2010 timely and free of errors.
- Reported required cancer cases to the Indiana State Cancer Registry within six months of diagnosis on a monthly basis.
- Implemented the use of required revised 2010 Cancer Registry tools: 7th Edition American Joint Committee on Cancer (AJCC) Staging Manual; Collaborative Staging (CSv2) Manual; National Cancer Institute Hematopoietic Database; Facility Oncology Registry Data Standards (FORDS) Manual; and Multiple Primary and Histology (MPH) Rules.
- Collaborated with Cancer Registry abstracting software provider (METRIQ) to incorporate CSV2 upgrade.
- Completed the required SARS annual update.
- Participated in successful Commission on Cancer Accreditation Survey.
- Partnered with William Kaliney, MD, Pathology, on a Colorectal Carcinoma Study with comparisons to National Data.
- Maintained ongoing quality review of data via annual physician review of 10% analytic cases inclusive of cancer registrar collaborative stage review, monthly state edits and periodic internal audits.
- Instrumental in supplying data for Continuous Quality Improvement (“benchmark”), physician requests for research, Administration, Marketing and Planning, Community Outreach, Education and Cancer Care Conferences.

- Attendance for continued education and maintenance of CTR; Coordinator of Cancer Registry:

Indiana State Department of Health (ISDH) Educational Offerings

9/29/10 “Collaborative Stage V2 Workshop.”

American College of Surgeons (ACoS) Commission on Cancer Webinars

5/20/10; “AJCC 7th Edition Staging Series: Shaping the Future; An Overview Presentation of the 7th Edition AJCC Cancer Staging Manual.”

8/27/10; “Coding and Using the New Class of Case Categories.”

National Cancer Registrars Association (NCRA) Webinars

2/23/10; “What’s New in FORDS in 2010?”

6/14/10; “Collaborative Staging v2; GYN.”

6/28/10; “Hematopoietic and Lymphoid Neoplasms Project Training: Background.”

6/28/10; “Hematopoietic and Lymphoid Neoplasms Project Training: Disease Presentations and Diagnostic Process.”

6/29/10; “Hematopoietic and Lymphoid Neoplasms Project Training: Moving Through the Rules.”

Elkhart General Hospital Medical Topics

2/10/10; “Hereditary Breast and Ovarian Cancer Syndrome,” Rosalie McBride, MD, OB/GYN.

2/24/10; “Prostate Cancer Screening and Prevention,” Timothy Roth, MD, Urology.

11/10/10; “American College of Surgeons Quality Measurements for Cancer Treatment and AJCC Clinical Staging, Prognostic Indicators and NCCN Guideline Review,” Michael Rotkis, MD, FACS, General and Vascular Surgery.

12/15/10; “Urology Conference: Prostate”, Peter Fretz, MD, Urology.

Indiana Cancer Registrars Association Annual Fall Conference

11/4/10-11/5/10; “Planting the Seeds of Change.”

2010 Annual Report Primary Site Table Based on 2009 Statistics

Primary Site	Total	Male	Female	Class of Case			AJCC Staging					Unk or N/A
				Analytic*	Non-analytic**	In-situ	I	II	III	IV		
Lip	1	1	0	1	0	0	0	0	0	1	0	
Tongue	4	3	1	4	0	0	1	0	0	3	0	
Nasopharynx	1	0	1	1	0	0	0	1	0	0	0	
Tonsil	3	3	0	3	0	0	0	0	0	3	0	
Oropharynx	1	1	0	1	0	0	0	0	0	1	0	
Hypopharynx	3	1	2	3	0	0	0	1	0	2	0	
Oral Cavity & Pharynx	13	9	4	13	0	0	1	2	0	10	0	
Esophagus	11	10	1	11	0	0	1	1	1	6	2	
Stomach	4	1	3	4	0	0	0	1	1	0	2	
Small Intestine	4	1	3	3	1	0	0	0	0	0	3	
Colon Excluding Rectum	53	24	29	52	1	7	13	11	12	7	2	
Rectum & Rectosigmoid (Junction)	14	8	6	14	0	2	3	2	3	2	2	
Anus, Anal Canal and Anorectum	1	1	0	1	0	0	0	0	0	0	1	
Liver and Intrahepatic Bile Duct	8	6	2	8	0	0	1	1	2	0	4	
Gallbladder	3	2	1	3	0	1	1	1	0	0	0	
Other Biliary	3	3	0	3	0	0	0	1	0	2	0	
Pancreas	13	9	4	12	1	0	0	1	3	8	0	
Digestive System	114	65	49	111	3	10	19	19	22	25	16	
Larynx	11	8	3	132	0	0	6	1	1	3	0	
Lung & Bronchus	135	70	65	11	3	1	28	8	38	52	5	
Respiratory System	146	78	68	143	3	1	34	9	39	55	5	
Bones & Joints	1	0	1	0	1	0	0	0	0	0	1	
Soft Tissue (Including Heart)	6	1	5	5	1	0	0	0	1	0	5	
Melanoma - Skin (Excluding Basal & Squamous)	15	12	3	12	3	1	6	3	2	0	0	
Breast	144	0	144	139	5	28	42	36	18	6	9	
Cervix Uteri	12	0	12	10	2	0	3	2	3	2	0	
Corpus Uteri, NOS	36	0	36	34	2	0	18	2	8	3	3	
Ovary	14	0	14	14	0	0	3	1	7	3	0	
Vagina	1	0	1	1	0	0	0	0	0	1	0	
Vulva	5	0	5	4	1	0	1	0	1	1	1	
Other Female Genital Organs	1	0	1	1	0	0	1	0	0	0	0	
Female Genital System	69	0	69	64	5	0	26	5	19	10	4	
Prostate Gland	47	47	0	36	11	0	0	32	3	1	0	
Testis	3	3	0	3	0	0	3	0	0	0	0	
Male Genital System	50	50	0	39	11	0	3	32	3	1	0	
Urinary Bladder	23	18	5	20	3	8	5	5	1	1	0	
Kidney & Renal Pelvis	21	16	5	16	5	0	8	2	4	2	0	
Ureter	1	0	1	1	0	0	0	1	0	0	0	
Other Urinary Organs	2	2	0	2	0	1	1	0	0	0	0	
Urinary System	47	36	11	39	8	9	14	8	5	3	0	
Brain	4	0	4	4	0	0	0	0	0	0	4	
Cranial Nerves, Other Nerves	8	2	6	8	0	0	0	0	0	0	8	
Brain & Other Nervous System	12	2	10	12	0	0	0	0	0	0	12	
Thyroid	10	1	9	10	0	0	4	2	1	2	1	
Other Endocrine (Including Thymus)	4	0	4	3	1	0	0	0	0	0	3	
Endocrine System	14	1	13	13	1	0	4	2	1	2	4	
Hodgkin Lymphoma	6	3	3	6	0	0	1	1	2	2	0	
Non-Hodgkin Lymphoma	27	8	19	27	0	0	7	2	7	9	2	
Lymphomas	33	11	22	33	0	0	8	3	9	11	2	
Multiple Myeloma	6	2	4	6	0	0	0	0	0	0	6	
Lymphocytic Leukemia	4	1	3	2	2	0	0	0	0	0	2	
Myeloid & Monocytic Leukemia	4	2	2	4	0	0	0	0	0	0	4	
Leukemia	8	3	5	6	2	0	0	0	0	0	6	
Mesothelioma	2	1	1	2	0	0	1	0	0	0	1	
Unknown or Ill Defined Site	11	5	6	10	1	0	0	0	0	0	10	
TOTAL	691	279	412	648	43	49	159	119	120	124	77	

*Analytic = First diagnosed and/or first course of treatment at this institution. **Non-analytic = First diagnosed and first course of treatment elsewhere.

Colorectal Carcinoma Study

Colorectal carcinoma (CRC) is the third most common cancer diagnosed among men and women in the United States and the second leading cause of death from cancer. It is estimated that approximately 150,000 men and women will be diagnosed with CRC in 2010 and close to 50,000 will die from this disease. If the cancer is diagnosed while confined to the muscular wall of the bowel five year survival is approximately 90 percent, but only 68 percent for regional disease (including regional lymph node involvement) and only 10 percent if distant metastases are present.¹ CRC incidence and mortality rates are highest in African Americans. Overall CRC rates are higher in men despite race and ethnicity.⁶ Recent trends in the incidence and mortality of CRC reveal decreasing rates, which have been attributed to reduced exposure to risk factors, routine screening of individuals at increased risk for CRC, prevention through polypectomies and improved treatment after diagnosis. Despite these trends, even greater incidence and mortality improvements could be achieved if a greater proportion of adults received regular screening. Although randomized trials and observational studies have demonstrated mortality reductions associated with early detection of invasive disease, a majority of U.S. adults are not receiving regular age and risk appropriate screening or have never been screened at all.



Clinical Presentation

Patients who are symptomatic and are subsequently diagnosed as having CRC can present with blood in the stool, rectal bleeding and/or change in bowel habits. Both constipation and diarrhea can be the earliest symptoms of CRC as well as fatigue and weakness due to anemia from blood loss.

Risk Factors

Various risk factors for CRC include: 1) family history of CRC in a first degree relative less than 60 years of age or in two or more first degree relatives at any age; 2) prior patient history of colon polyps (tubular adenomas) or 3) chronic inflammatory bowel diseases including Crohn's Disease and Ulcerative Colitis. Individuals with family histories of CRC in a first degree relative (brother, sister, father, mother or child) under 60 years of age have greater than a two-fold (200 percent) increased risk for developing CRC.^{4,7} Other potential risk factors include:

- Dietary factors (high fat and/or low fiber diets, high calorie diets, high meat protein diets);
- Smoking (cigarettes, pipes, cigars);
- High alcohol consumption due to its byproduct acetaldehyde, a recognized carcinogen;
- Prior radiation to abdomen which can increase CRC risk two-four fold (200-400 percent);
- Low serum levels of selenium (found in seafood and cereal grains) are associated with increased risk of colorectal, prostate and breast cancers; and
- Miscellaneous genetic factors
 - Familial Adenomatous Polyposis (FAP) either with established diagnosis or strong clinical evidence;
 - Genetic or clinical diagnosis of Hereditary Non-Polyposis Colorectal Cancer (HNPCC).

CRC Screening

More than 90 percent of people who are diagnosed with CRC are 50 or older and the average age at diagnosis is 64 years. Approximately one in four people by the age of 50 have colon polyps (tubular adenomas) which are colon cancer precursors. CRC screening, particularly after the age of 50 years, is an excellent colon cancer prevention method.

The main goal of CRC screening is to reduce mortality through a reduction in the incidence of advanced disease at diagnosis. Modern CRC screening can achieve this goal through the detection of early-stage adenocarcinomas as well as the detection and removal of tubular adenomas (adenomatous polyps); the latter accepted by most experts in the field as nonobligate precursor lesions. Tubular adenomas are common in adults over the age of 50 years but the majority will not develop into adenocarcinoma. Their histology and size mainly determine their clinical significance. Approximately 1/2 to 2/3 of colorectal polyps are tubular adenomas and they are associated with higher risk for development of CRC. Many CRC screening studies evaluate the detection rate of invasive CRC as well as advanced tubular adenomas. Advanced adenomas are conventionally defined as 1) polyps greater than or equal to 10 mm (1 cm) in greatest dimension or 2) histologically having high grade (severe) dysplasia or a significant villous component to the adenoma. Those with significant villous components also tend to be larger and often sessile polyps. Although the evidence for the importance of colorectal polyps in the development of CRC is largely indirect, it is nevertheless extensive and convincing.

Today there is a range of options for CRC screening in the average risk population. There are two general categories: stool tests which include tests for occult blood or exfoliated tumor cell DNA; and structural examinations, which include digital rectal examination (DRE), flexible sigmoidoscopy (FSIG), colonoscopy, double-contrast barium enema (DCBE) and computed tomographic colonography (CTC). Stool tests are best suited for the detection of invasive adenocarcinoma although they may also be positive in cases of larger

or advanced adenomas. Structural examinations can achieve the dual goals of detecting adenocarcinoma as well as colorectal polyps. These tests may be used alone or in combination to improve sensitivity. Although these various methods for CRC screening differ in their degrees of sensitivity, potential mortality reductions, cost effectiveness and acceptability, they all when applied in a systematic program of regular screening have the potential to greatly reduce deaths from CRC.

Over the past 30 years the American Cancer Society (ACS) has gradually updated and refined its guidelines for CRC screening including adding screening recommendations for high risk individuals in 1997. The evidence base to support screening colonoscopy or fecal occult blood testing (FOBT) with colonoscopy follow up in positive patients is substantial. Randomized control trials have shown significant reduction in incidence and mortality rates for CRC in both patients screened with FOBT and colonoscopy as follow up as well as screening colonoscopy alone. If a colonoscopy is used as the primary screening, it has been recommended that a colonoscopy every 10 years is acceptable in average risk patients beginning at age 50 years.¹ Despite these guidelines and attempts at improving the screening for CRC, many barriers to CRC screening remain. Some of these include lack of public knowledge about testing options and probability that uninsured individuals are substantially less likely to be screened for CRC. At least one study found that among the individuals at high risk for CRC, African Americans were half as likely to have undergone a colonoscopy screening, even after accounting for differences in education, income and health insurance status.⁴

Primary Prevention

Avoidance or elimination of some of the above potential risk factors and increasing protective factors will help to prevent the development of colon polyps and CRC. Factors that may lower the risk of developing CRC include hormone replacement therapy (when both estrogen and progesterone are used). However, this therapy has other adverse side effects including increased risk for breast cancer, heart disease and vascular thrombosis. Non steroidal anti-inflammatory

Colorectal Carcinoma Study CONTINUED

drugs (NSAIDs) may in some people lower the risk of CRC. These medications block the biochemical abnormalities in prostaglandin homeostasis in colorectal neoplasms and can cause involution of small adenomas, known precursors of CRC. Other possible factors that may lower the risk include the use of multivitamins that include high doses of folic acid and diets that are low in fat and high in fiber, fruits and vegetables. So far it has not been shown that the use of statins (cholesterol lowering medications) significantly affects the risk of CRC despite some initial reports to the contrary.⁶

Histopathologic Features of CRC

Traditionally CRC has been graded according to the degree of glandular differentiation from G1 (well differentiated) to G2 (moderately differentiated) to G3 (poorly differentiated) to G4 (undifferentiated) types. Although the degree of differentiation has been shown to correlate with the aggressiveness of the tumor with well differentiated tumors behaving best and undifferentiated doing worst, there are certain subtypes that have unique characteristics and behaviors. Signet ring cell carcinoma is defined by the presence of less than 50 percent of tumor cells with prominent intracytoplasmic vacuoles and many singly invasive tumor cells. These tumors are commonly poorly differentiated and more aggressive than usual CRCs. Mucinous adenocarcinoma is characterized by less than 50 percent of the lesion associated with abundant mucin production. Many high-frequency microsatellite instability (MSI-H) carcinomas are of this histologic type. Medullary carcinoma is characterized by sheets of malignant cells without gland formation and with a prominent infiltrate of intraepithelial lymphocytes. These tumors are invariably associated with MSI-H and have a favorable prognosis compared to other poorly differentiated and undifferentiated carcinomas.⁷

Molecular Genetics

The development of most CRCs is thought to begin from a colorectal epithelial cell with a mutational inactivation of the adenomatous polyposis coli (APC)

suppressor gene. This interferes with E-cadherin (cell adhesion) homeostasis and causes dysregulation of transcription of other genes. Included in this process is activation of proto-oncogenes such as “c-myc” and “ras” and inactivation of additional suppressor genes. These inactivated genes are commonly present on chromosomes 18 and 17.⁷

Microsatellite Instability (MSI) Some CRCs have extensive nucleotide insertions or deletions in numerous unstable repeated sequences in tumor DNA, termed microsatellite instability. If two or more of the common microsatellite markers show MSI, the tumor is classified as high-frequency microsatellite instability (MSI-H). If only one marker shows MSI, the tumor is classified as low-frequency microsatellite instability (MSI-L). If no markers show MSI, the tumor is classified as microsatellite stable (MSS). MSI-H tumors are characteristic of hereditary non-polyposis colorectal cancer syndrome (HNPCC) due to germline mutation of one of groups of DNA mismatch repair genes followed by somatic inactivation of the other allele. Sporadic MSI-H tumors comprise approximately 15 percent of all colorectal carcinomas.

Hereditary Nonpolyposis Colorectal Cancer (HNPCC)

HNPCC (also termed Lynch Syndrome) is an autosomal dominant disorder where predisposed individuals have a high lifetime risk of developing CRC (70-85 percent), endometrial carcinoma (50 percent) and certain other cancers including small intestine and kidney (below 15 percent). CRCs are often diagnosed at an early age (mean, 45 years) and are located in the proximal colon in 2/3 of patients. Medullary carcinoma morphology is also common. In over 90 percent of patients the tumors exhibit MSI as described above. The diagnostic criteria (Amsterdam criteria) for HNPCC include: there should be at least three relatives with an HNPCC-associated cancer (either colorectal, endometrial, small intestine, ureter or renal pelvis); one patient should be a first degree relative of the other two; and at least two successive generations should be affected and at least one tumor should be diagnosed before the age of 50 years.⁷

“The test of a civilization is the way it cares for its helpless members.”

Pearl Buck (1892-1973)

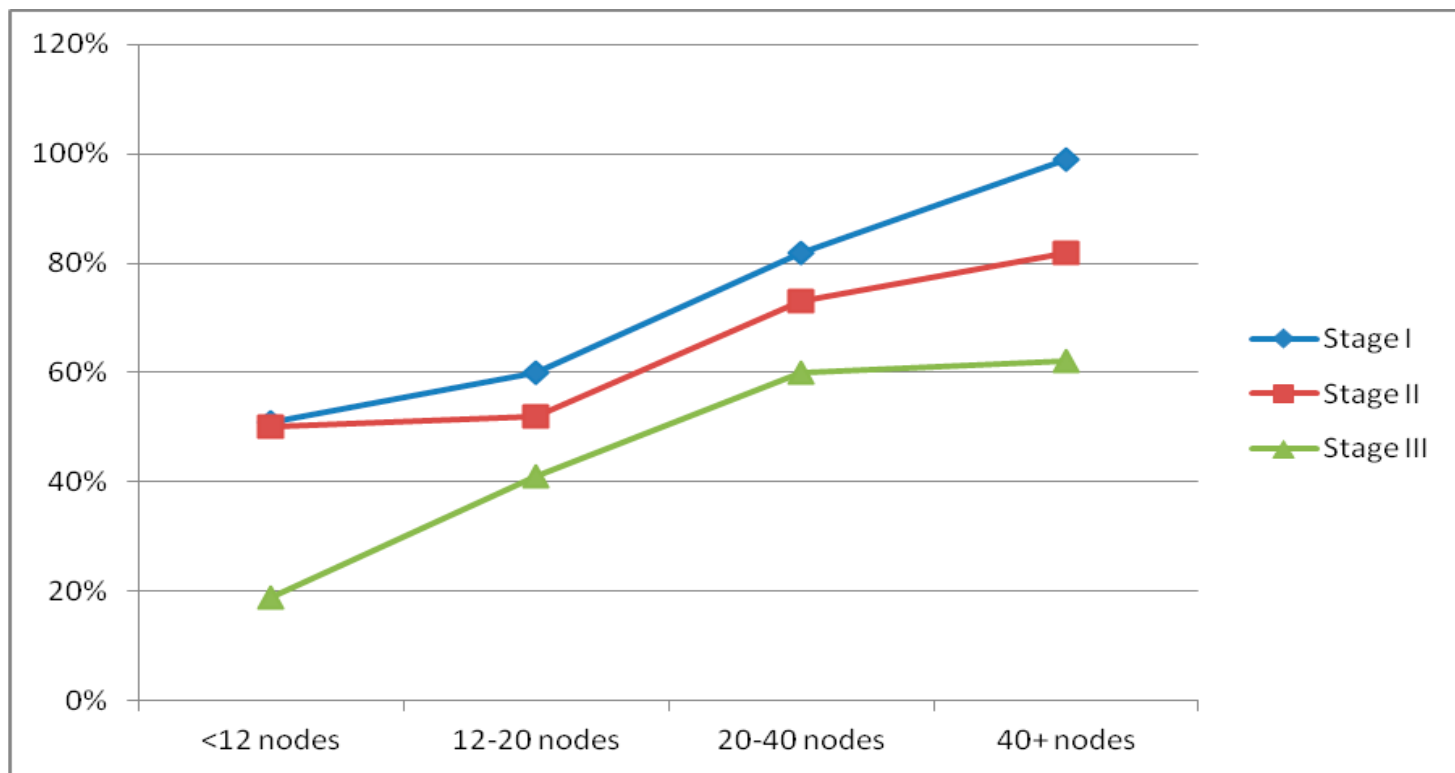


Familial Adenomatous Polyposis (FAP) Familial adenomatous polyposis is an autosomal dominant disorder that is characterized by numerous adenomatous colorectal polyps that have an intrinsic tendency to progress to adenocarcinoma. It is caused by germline mutation in the Adenomatous Polyposis Coli (APC) gene located on the long arm of chromosome 5. Gardner Syndrome is a variant of FAP that also includes multiple epidermoid cysts, osteomas, dental anomalies and desmoid tumors. The reported incidence of FAP varies between one in 7,000 to one in 30,000 births. These patients have at least 100 colorectal tubular adenomas (adenomatous polyps) and often begin developing multiple adenomas between the ages of 10 and 20. The most important clinical feature of this disorder is the invariable development of one or more of these polyps into colorectal adenocarcinoma, where the mean age of CRC development is approximately 40 years. The most commonly used commercially available test for FAP involves identification of the mutant APC allele by in vitro

detection of the truncated APC protein. This technique is referred to as in vitro protein synthesis (IVPS) testing. IVPS testing is able to detect mutation carriers in about 80 percent of affected families. Screening of gene carriers usually involves sigmoidoscopy every one to two years beginning between age 10 and 12.^{7,10}

KRAS KRAS is a type of proto-oncogene that encodes one of the proteins in epidermal growth factor receptor (EGFR) signaling pathway. This pathway is important in the development and progression of several types of cancers, including CRC. Analysis of multiple recent clinical trials has shown that the presence of a mutation in either codon 12 or 13 of KRAS is strongly associated with the lack of response to treatment with Epidermal Growth Factor Receptor (EGFR) antibodies in patients with metastatic CRC. It has been recommended that patients with advanced CRC be tested for the presence of KRAS mutations if anti-EGFR antibody therapy is to be considered. Therapy should be given to those with normal (non-mutated or wild type) KRAS.^{7,9}

Figure 1



5-Year Survival for Elkhart General Hospital Patients 2000-2005

Prognostic Factors in CRC

As applying to cancers in other locations, in CRC localized tumors (contained within the intestinal wall) in general behave better than those with regional spread (to serosal surface or beyond). Multiple lymph node metastases, particularly to lymph nodes further away from the primary tumor, are associated with poorer survival. Inflammatory reaction to the tumor (as in medullary tumor type) is associated with improved prognosis. Other features of CRC that have been shown to also be of prognostic value in some studies include angiolymphatic invasion, perineural space involvement, and extramural venous involvement.⁷

Colorectal Carcinoma in Patients Treated at Elkhart General Hospital 2000-2005

From 2000-2005, 254 patients with colorectal carcinoma (215 with colon carcinoma and 39 with rectal carcinoma) were treated at Elkhart General Hospital. There was slight male predominance with 52 percent males (131 patients) and 48 percent females (123 patients). Most patients had single tumors with three having two separate adenocarcinomas and one patient having four separate invasive colon carcinomas.

The patients with colon carcinoma (215 patients) were separated according to prognostic factors (T – representing the initial extent of the primary tumor at the time of excision; N – lymph node status; and M – presence or absence of metastatic carcinoma). They were then classified into pathologic stages and the five

year survivals for these patients were compared with the national survival rates. (Figure 1).

Stage 0 patients (Tis N0 M0) – 11 of the 12 patients with Stage 0 survived five years (92 percent). The exception was a patient who subsequently was diagnosed with small cell carcinoma of the lung and died as a result of his lung cancer. The national statistics are also greater than 90 percent.

Stage I patients (T1 N0 M0 and T2 N0 M0) – 14 of the 16 patients with Stage I survived five years (87.5 percent). One of the two patients died as a result of metastatic gastric adenocarcinoma. The national 5 year survival rate for Stage I is 74 percent.^{1,5,8}

Stage II patients – 59 out of 88 patients with Stage II survived five years. Elkhart General patients survival for the sub-stages compared to the national statistics was:

Stage IIA (T3 N0 M0)	EGH (69%)	National (67%)
Stage IIB (T4a N0 M0)	EGH (54%)	National (58%)
Stage IIC (T4b N0 M0)	EGH (40%)	National (37%)

Stage III patients – 51 out of 82 patients with Stage III survived five years.

Stage IIIA (T1-T2 N1/N1c M0; T1 N2a M0)	EGH (71%)	National (73%)
Stage IIIB (T3-T4a N1/N1c M0; T2-3 N2a M0; T1-2 N2b M0)	EGH (58%)	National (48%)
Stage IIIC *(T4a N2a M0; T3-4a N2b M0; T4b N1-2 T4b)	EGH (18%)	National (28%)

**In Stage IIIC the statistic may be misleading because there were only 11 patients in this category at Elkhart General.*

Stage IV patients – 1 out of 17 patients with Stage IV survived five years. This percentage (5.9 percent) compares to 5.7 percent nationally.

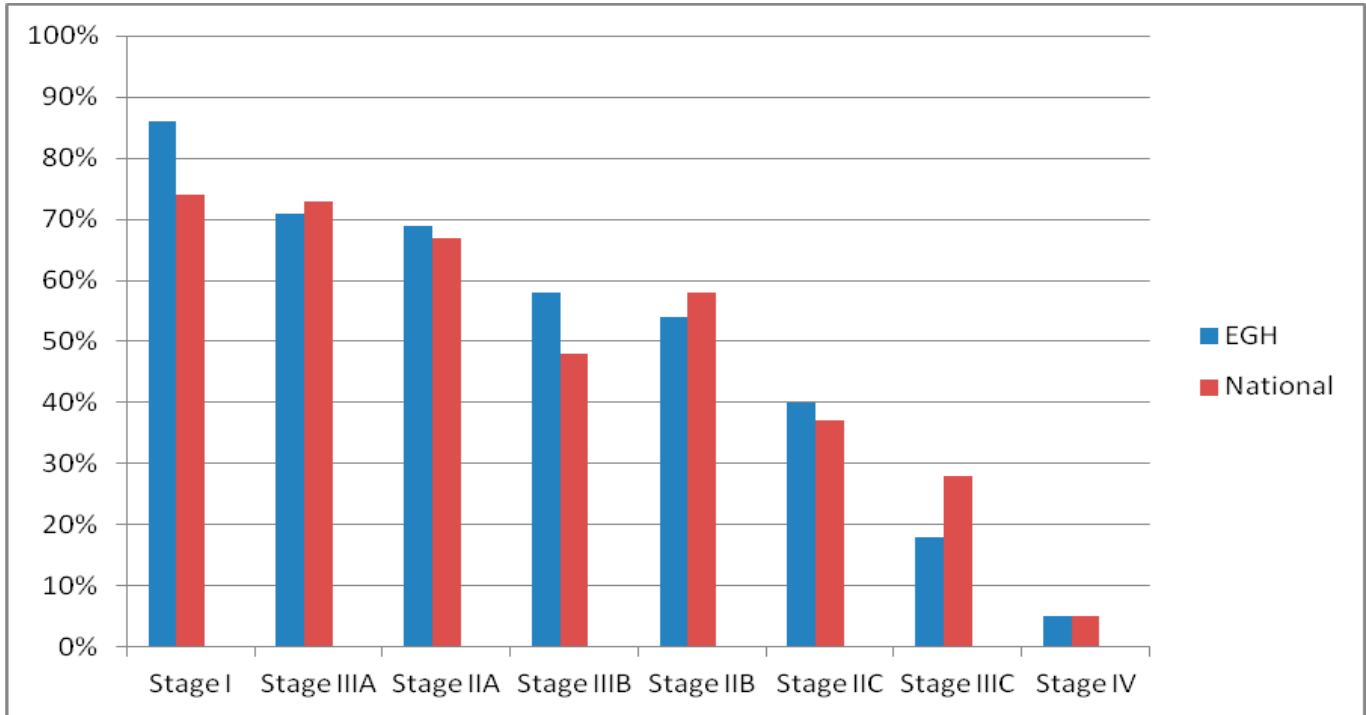
Lymph Node Status

Not only is lymph node status (i.e. whether regional lymph nodes are involved by metastatic tumor or not) important, but also the number of lymph node(s) identified has been shown to have prognostic importance. Studies have shown that the total number of lymph nodes recovered from colorectal resection specimen is an independent prognostic factor.^{2,3} Most authors agree that perhaps the main reason for this



is down-staging of CRC patients in whom fewer lymph nodes are identified. It has also been postulated that the number of regional lymph nodes identified may be related to the degree of immune response to the patients' tumors (i.e. the more the immune response the more grossly identifiable lymph nodes present). Both the College of American Pathologists (CAP) and the American College of Surgeons (ACoS) have recommended that pathologists attempt to identify a minimum number of 12 lymph nodes in traditional colorectal resection specimens.

Review of CRCs excised at Elkhart General Hospital from 2000–2005 revealed that out of a total of 254 cases, 210 specimens contained pericolonic or perirectal tissue where lymph nodes are accessible for examination. The other 44 cases were either limited resections (e.g. polypectomies alone), those treated without definitive surgery or patients who had definitive surgeries performed elsewhere. In the 210 specimens that contained pericolonic fat, there were only 12 specimens where less than 12 lymph nodes were identified. In eight cases, the specimens were short or limited colonic segments (often removed for superficial cancers arising in polyps) and two cases were associated with preoperative neoadjuvant therapy (where lymph nodes are often extremely small due to therapy). In only two patients of 210 total patients (1 percent), were there less than 12 lymph nodes identified without justification.



5-Year Survival vs. Total Lymph Nodes - Elkhart General Hospital 2000-2005

Total of 254 CRC patients:

- 44 cases with either limited resections (e.g. polypectomies alone) and/or patients treated elsewhere;
- 210 patients with definitive surgical excisions with accessible lymph nodes;
- 12 patients with less than 12 lymph nodes;
- Eight patients with short or limited excisions (e.g. superficial tumors);
- Two patients with preoperative neoadjuvant chemotherapy/radiation; and
- Two patients with less than 12 lymph nodes (no justifiable explanation).

The mean number of lymph nodes identified in these 210 patients was 31.2; with a range of 5 to 148. Partly responsible for the high number of identified lymph nodes in Elkhart General Hospital, colorectal resections is the procedure that our histopathology laboratory has used for over 20 years. It is designated “lymph node

clearing” where the pericolonic fat is exposed to several hours of chemical digestion leaving the intact lymph nodes much easier to grossly identify. We have provided this method to several other laboratories to aid in their lymph node recovery.

The 5-year survival of patients with Stage I, Stage II and Stage III colon carcinomas was evaluated in these patients at Elkhart General Hospital. Their 5-year survival was compared to the total number of lymph nodes recovered within these two tumor stages. (Figure 2).

This data in Elkhart General Hospital CRC patients supports the premise that the total number of lymph nodes recovered in these specimens is an independent prognostic factor. This is a controversial topic in the medical literature and further studies may better clarify this issue. However, as noted above the ACoS and CAP have recommended that a minimum number of 12 lymph nodes be removed and that pathologists make every attempt to identify additional lymph nodes when 12 are not seen initially.



Dr. William Kaliney is a graduate of the Northwestern University Medical School. He completed a residency at Case Western Reserve University Hospitals and is certified by the American Board of Pathology in Anatomic and Clinical Pathology.

Summary

Much progress has been made in recent years in the diagnosis and treatment of CRC. This study provides supportive evidence that CRC patients at Elkhart General Hospital have comparable (and in certain tumor stages better) survival rates compared to the national averages. Molecular genetic testing to assist in determining individuals at increased risk for CRC and helping to personalize patient's therapies, also is now becoming available. Despite these diagnostic and therapeutic advances, other challenges remain including better public education concerning the importance of CRC screening (and cancer screening in general) to improve early diagnosis and subsequent patient prognosis.

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Sincerely,

William Kaliney, MD
Pathologist

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Cancer Program Practice Profile Reports (CP³R): For Colon and Rectal Cancers Diagnosed 2004 - 2008

Elkhart General Hospital, Elkhart, IN

The National Quality Forum (NQF) brought public and private payers together with consumers, researchers, and clinicians to broaden consensus on performance measures for breast and colorectal cancer. The performance rates shown in the Cancer Program Practice Profile Reports (CP³R) match the specifications of the colon and rectal cancer care measures endorsed by the NQF in April, 2007. The Commission on Cancer

has been actively engaged in this process. The CoC has instituted the CP³R as a facility feedback mechanism to promote awareness of the importance of charting and coding accuracy in line with evidence based practice guidelines. In light of the national movement towards Pay for Performance (P4P), these reports provide CoC-Approved programs with the ability to examine program-specific colon and rectal cancer care practices.

Select Colorectal Measures		Performance Rates				
		2004	2005	2006	2007	2008
COLON	Adjuvant chemotherapy is considered or administered within 4 months (120 days) of diagnosis for patients under the age of 80 with AJCC Stage III (lymph node positive) colon cancer. [ACT]	100%	100%	100%	100%	100%
	At least 12 regional lymph nodes are removed and pathologically examined for resected colon cancer. [12RLN]	88.5%	92.6%	95%	91.7%	100%
	<i>State of Indiana performance rates for at least 12 regional lymph nodes are removed and pathologically examined for resected colon cancer. [12RLN]</i>	49.6%	49.7%	61.9%	75.1%	78.3%
RECTAL	Radiation therapy is considered or administered within 6 months (180 days) of diagnosis for patients under the age of 80 with clinical or pathologic AJCC T4N0M0 or Stage III receiving surgical resection for rectal cancer. [AdjRT]	100%	100%	100%	100%	NA*

Interpreting This Table: The estimated performance rates shown above provides the cancer program with an indication of the proportion of colorectal patients treated according to recognized standards of care by diagnosis year. These proportions are computed based on data directly reported from the registry to the NCDB. This Cancer Program Practice Profile Reports (CP³R) application provides cancer programs with the opportunity to examine data to determine if the performance rates are representative of the care provided at the institution.

*Limited Sampling.



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Telephone Directory

Treatment and Clinical Services

Ambulatory Infusion Center	296-6444
Breast Cancer Clinic	389-5654
Breast Care Center	296-6571
Oncology Care Unit	523-3112
Radiation Oncology Center	523-7857
Regional Center for Cancer Services	800-643-5719

Ancillary Services

Center for Behavioral Medicine	523-3347
Center for Pain Management	523-3232
Individual Nutrition Counseling	523-3444
Home Care and Infusion Therapy	800-284-8999
Home Medical Equipment	888-517-3100
Inpatient Rehabilitation Services	523-3443
Mammography Scheduling	523-3444
Nursing Education	523-3257
Outpatient Rehabilitation Services	523-3242
Outpatient Pharmacy	523-3101

Professional Education/Research

Cancer Conferences	523-3454
Cancer Registry	523-3454
Continuing Medical Education	523-4826

Patient and Family Support

Cancer Support Group Information	523-6553
Case Management	523-3257
Chaplaincy Services	523-3142
Financial Assistance	296-6571
Patient Accounts	523-7818
Ribbon of Hope Cancer Support & Ministry	389-7379

Community Services

American Cancer Society	800-227-2345
Cancer Care Counseling Line	800-813-HOPE
Cancer Information	888-344-6773
Community Education Programs	523-3303
Health Information Center	888-344-6773
KME National Breast Cancer Organization	800-221-2141
National Cancer Institute Info Line	800-4CANCER
Physician Referral Line	888-344-6773
United Cancer Services	875-5158

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