

## COLON CANCER

### Epidemiology

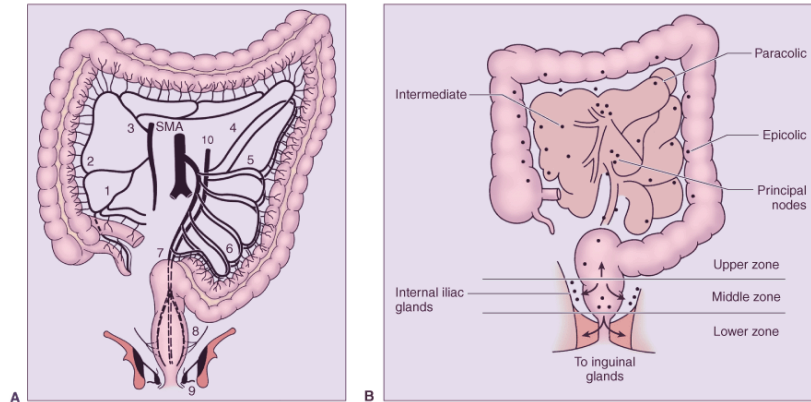
- 2nd most common cause of cancer mortality
- Lifetime risk is about 1 in 17
- Industrialized nations have the highest risks
  - South America and China are among the lowest
- Blacks > Whites > Asians > Hisp > NA
- M > F (slightly)
- Incidence increases after age 50 (90%)
- 80% are sporadic

U.S. Cancer Burden 2003 Estimates	
1,344,100 cases	556,500 deaths
220,900 prostate	157,200 lung
211,300 female breast	57,100 colorectum
171,900 lung	39,800 breast
147,500 colorectum	30,000 pancreas
65,500 ovary and endometrial	28,900 prostate
57,400 bladder	23,400 NHL
54,200 melanomas	21,900 leukemia
53,400 NHL	14,400 liver and IHBD
31,900 kidney	14,300 ovary
30,700 pancreas	13,100 brain
30,600 leukemia	13,000 esophagus

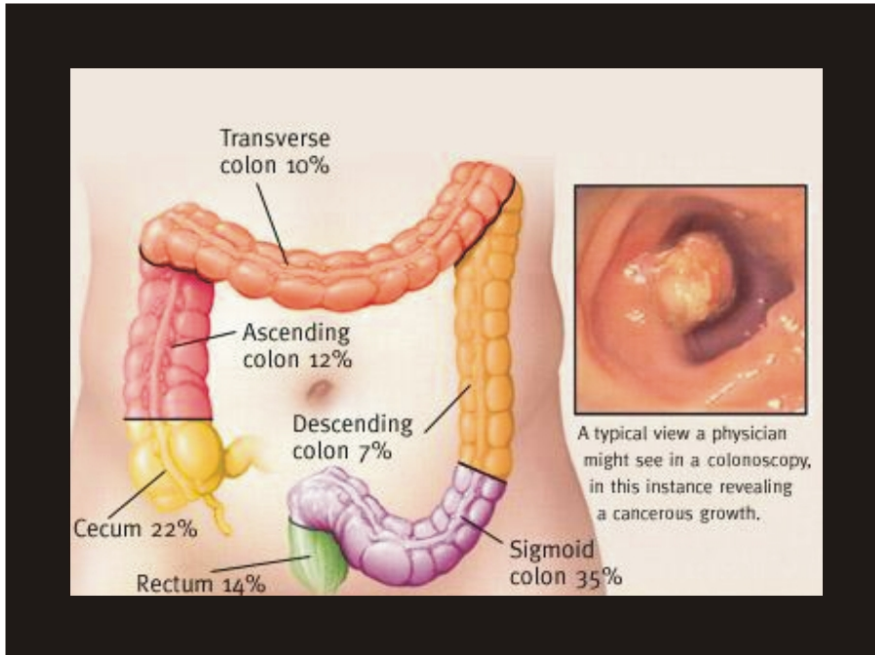
### Risk factors

- Diet
  - Red meat and animal fat
  - Folate, fiber, calcium, selenium, fruits and vegetables → ?protective
- Smoking and alcohol
- IBD
- Hereditary syndromes
- Previous carcinoma
- Polyps
- Family history
- *S. Bovis* bacteremia

## Anatomy

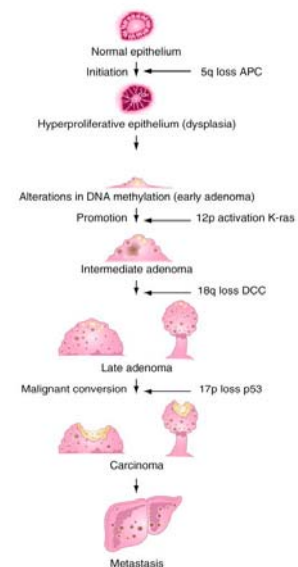


## Location



## Adenoma-Carcinoma Sequence

- Larger adenomas harbor cancer more often
- Residual benign tissue found in most cancer specimens
- Benign polyps have been observed to become cancer
- Adenomas occur more frequently in cancer patients
- Adenoma patients have increased lifetime risk of dev. cancer
- Removal of polyps decreases risk
- Populations with cancer have high prevalence of polyps
- FAP → 100% cancer
- Peak incidence of adenomas is 50; peak incidence of cancer is 60 → suggesting 10-year time span

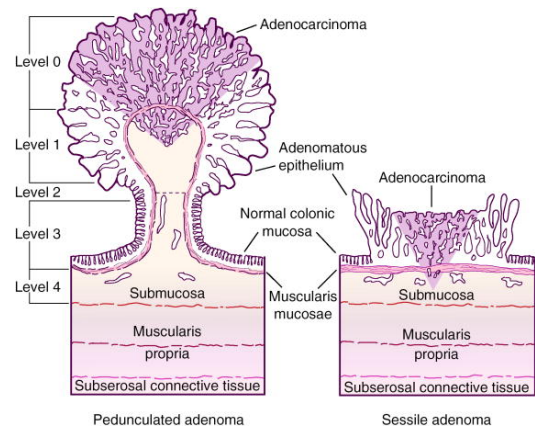


## Polyps

- Morphology
  - Tubular, villous, tubulovillous
    - Risk of malignancy; 5% - tubular, 22% - tubulovillous, 40% - villous
  - Pedunculated, flat (sessile)
    - Sessile polyp with cancer has 10% chance of lymph node metastasis
- Size
  - 0.6 – 1.5 cm = 2% chance of cancer
  - 1.6 to 2.5 = 19% chance of cancer
  - 2.6 to 3.5 = 43% chance of cancer
  - >3.5 cm = 76% chance of cancer
- Hyperplastic polyps
  - Most common
  - 90% are less than 3mm
  - Considered to have no malignant potential
  - Adenomatous changes have been found so polyps should be excised

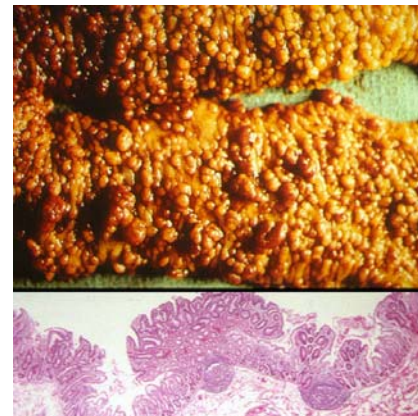
### Haggitts: Applies only to pedunculated polyps

- Level 0 – in situ
- Level 1 – head of polyp
- Level 2 – neck
- Level 3 – stalk
- Level 4 – submucosa
- Any sessile polyp is Level 4
- Excision of Level 1-3 with 2mm margin and NO poor prognostic indicator is sufficient treatment



### Familial Adenomatous Polyposis

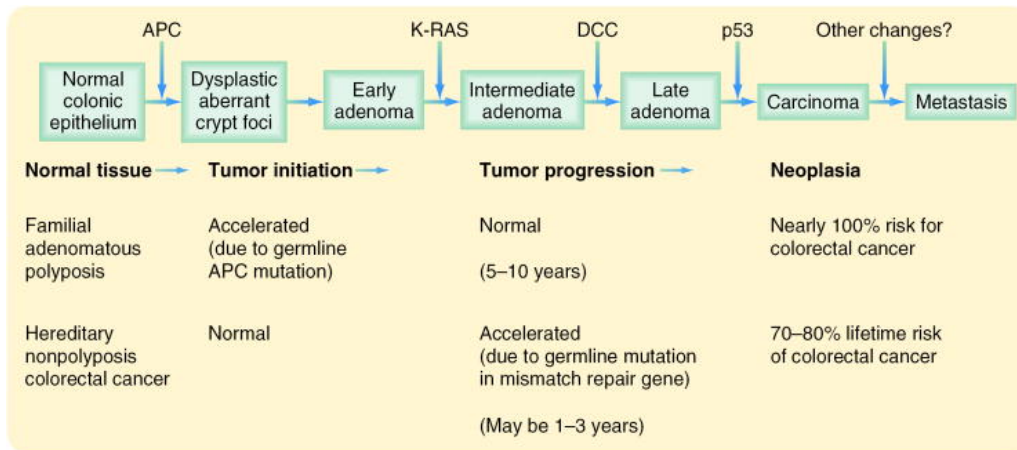
- Autosomal dominant
- Defect in APC gene
- Hundreds to thousands of polyps
- 100% cancer conversion rate – avg age 42
- Colectomies usually deferred until adulthood
- Colectomy with IRA or RPC with lifelong rectal/pouch surveillance
- Phenotypic variants
  - Gardners, Turcots, attenuated



## HNPCC

- Lynch I syndrome
- Autosomal dominant
- Mismatch repair genes altered
- 85% cancer penetrance
- Rapid progression to cancer
- Limited number of adenomas usually proximal to splenic flexure
- Lynch II – extracolonic manifestations
  - Usually endometrial cancer

## Adenoma-Carcinoma Sequence



## Signs & Symptoms

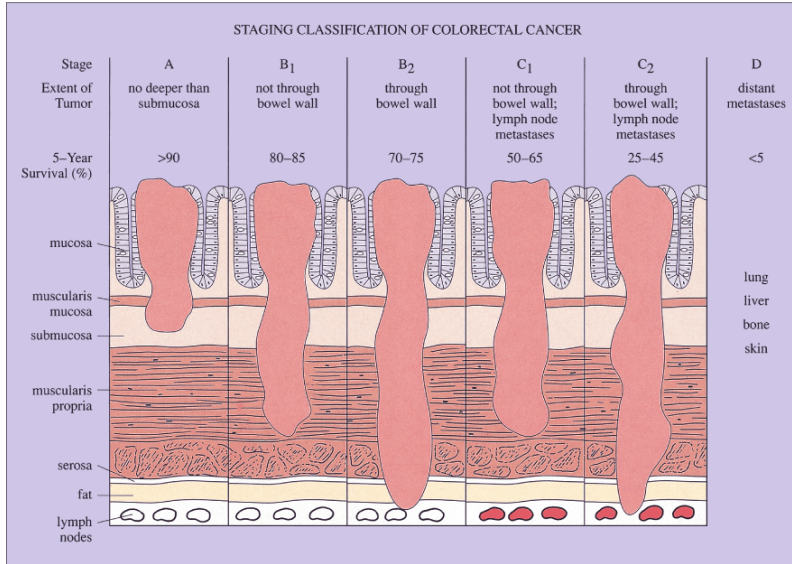
- Bleeding, abdominal pain, change in bowel habits, anorexia, wt loss, nausea, vomiting, fatigue, anemia
  - Left sided more likely to obstruct
  - Proximal cancers have occult bleeding
- Pelvic pain, tenesmus in rectal ca
- RUQ pain, hepatomegaly, ascites, lymphadenopathy in metastatic disease
- Virchow's node, Blumers shelf, Sister Mary Joseph node

## Work-up

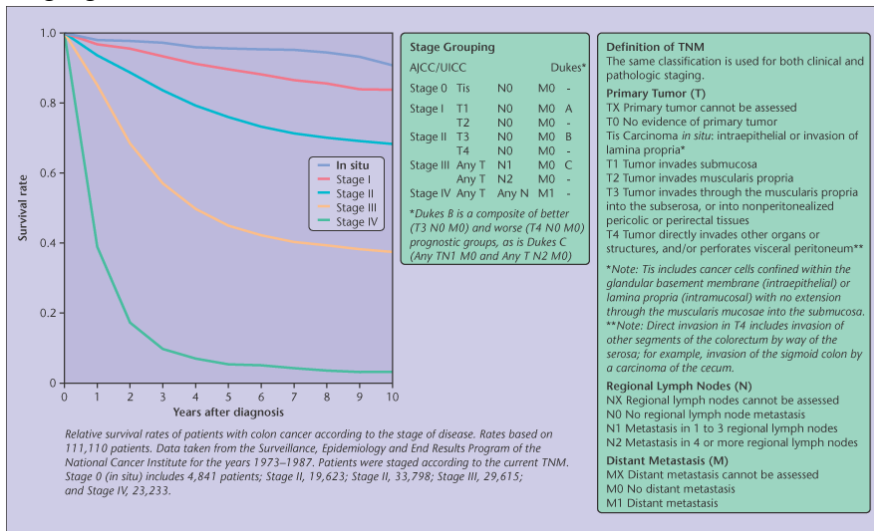
- Labs – CBC, LFTs, CEA
- Detection
  - Colonoscopy
  - Double contrast BE
  - Virtual colonoscopy
- Staging
  - CXR
  - CT/MRI

- PET - good for extrahepatic mets
- Intra-op ultrasound – best evaluation of liver

## Dukes



## Staging

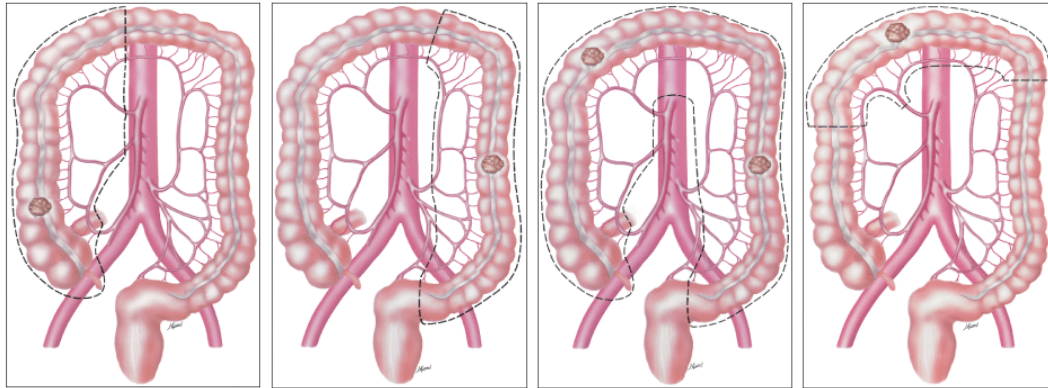


## Surgical Issues

- Bowel Prep
- Perioperative intravenous antibiotics
- Midline incision or laparoscopy
- Exploration
  - Extent of tumor
  - Liver
- Oncologic resection

- No-touch technique
- Anastomosis

### Surgical Resection



- Obstructing cancer
  - Hartmans
    - 40% morbidity of colostomy closure
  - On-table lavage with primary anas.
    - Low leak rate
  - Subtotal colectomy with IRA
    - addresses risk of proximal tumors
- Perforated cancer
  - Poor prognosis
  - Assume all adhesions are malignant
  - 20% carcinomatosis risk

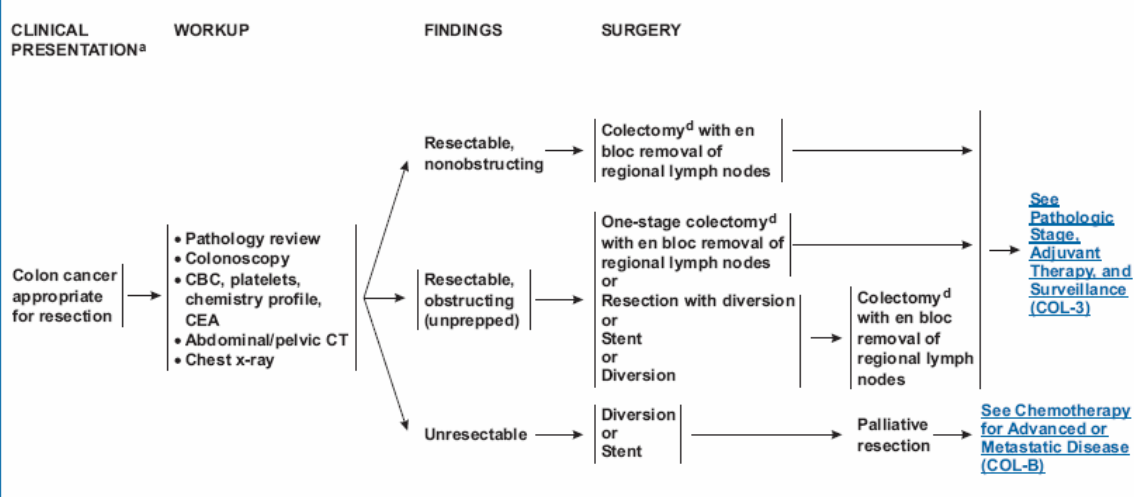
### Polyp Treatment

CLINICAL PRESENTATION <sup>a</sup>	WORKUP	FINDINGS	SURGERY
Pedunculated polyp with invasive cancer	<ul style="list-style-type: none"> <li>• Pathology review<sup>b</sup></li> <li>• Colonoscopy</li> <li>• Marking of polyp site</li> </ul>	Superficial, completely removed	None
		Deep invasion into stalk <sup>c</sup> or margins cannot be assessed or adverse pathologic findings (ie, Grade 3-4, angiolymphatic invasion, positive margins)	Colectomy <sup>d</sup> with en bloc removal of regional lymph nodes
Sessile adenomatous polyp with invasive cancer or Villous adenoma with invasive cancer or Villoglandular adenoma with invasive cancer	<ul style="list-style-type: none"> <li>• Pathology review<sup>b</sup></li> <li>• Colonoscopy</li> <li>• Marking of polyp site</li> </ul>	Single-specimen, Tis, completely removed with negative margins	None
		Fragmented specimen or margins cannot be assessed or adverse pathology, T1 or greater or margins positive	Colectomy <sup>d</sup> with en bloc removal of regional lymph nodes

[See Pathologic Stage, Adjuvant Therapy, and Surveillance \(COL-3\)](#)

[Guidelines Index](#)  
[Colon Cancer TOC](#)  
[Staging, MS, References](#)

# Cancer Treatment



# Treatment by Stage

PATHOLOGIC STAGE	ADJUVANT THERAPY <sup>f</sup>	SURVEILLANCE <sup>j,k</sup>
Tis; T1, N0, M0; T2, N0, M0	None	<ul style="list-style-type: none"> <li>• History and physical every 3 mo for 2 y, then every 6 mo for a total of 5 y</li> <li>• CEA<sup>l</sup> every 3 mo for 2 y, then every 6 mo for a total of 5 y for T2 or greater lesions</li> <li>• CT may be considered for patients at high risk for recurrence.<sup>i,k</sup></li> <li>• Colonoscopy<sup>2</sup> in 1 y, repeat in 1 y if abnormal or at least every 2-3 y<sup>m</sup> if negative for polyps. If no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3-6 mo.</li> </ul>
T3, N0, M0 <sup>e</sup>	Clinical trial or Observation	
T3, N0, M0; high risk for systemic recurrence: Grade 3-4, lymphatic/vascular invasion, bowel obstruction	Consider 5-FU/leucovorin <sup>9,h</sup> or capecitabine <sup>9,h</sup> or FOLFOX <sup>9,h</sup> or Clinical trial or Observation	
T4, N0, M0; or T3 with localized perforation or close, indeterminate or positive margins	Consider 5-FU/leucovorin <sup>9,h</sup> or capecitabine <sup>9,h</sup> or FOLFOX <sup>9,h</sup> or Consider RT <sup>i</sup> or Clinical trial or Observation	

[Node positive disease, see page COL-4](#)

**FOLFOX - Infusional 5-FU/leucovorin/oxaliplatin**

See [Recurrence and Workup \(COL-9\)](#)

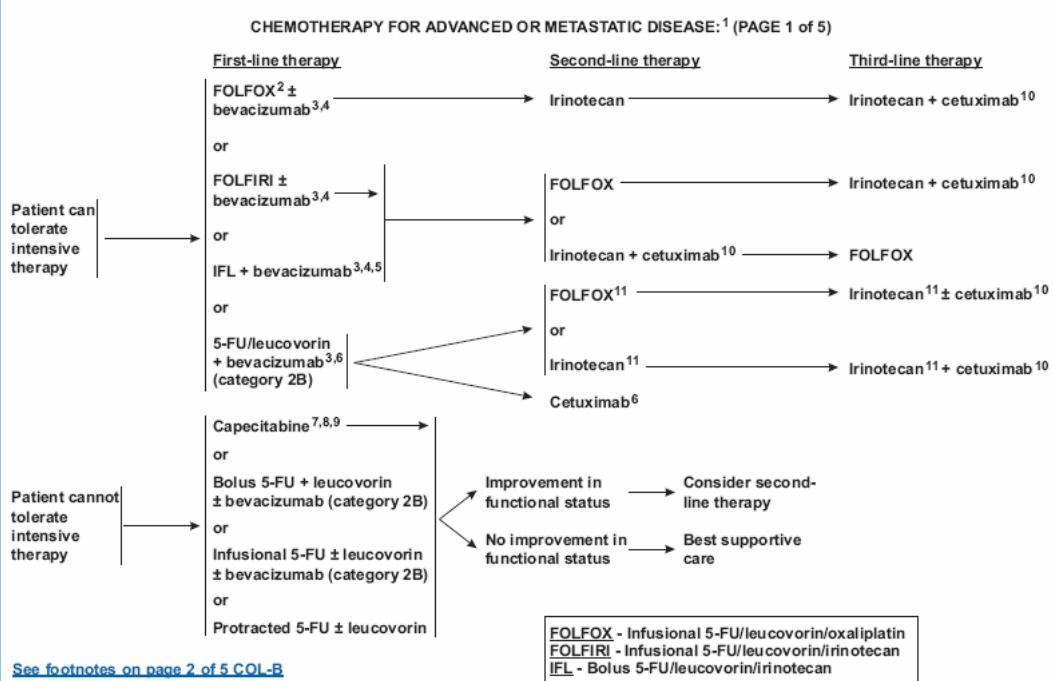
PATHOLOGIC STAGE	ADJUVANT THERAPY <sup>f</sup>	SURVEILLANCE <sup>j,k</sup>
T1-3, N1-2, M0	5-FU/leucovorin <sup>h</sup> (category 1) or Capecitabine <sup>h</sup> or FOLFOX <sup>h</sup>	<ul style="list-style-type: none"> <li>• History and physical every 3 mo for 2 y, then every 6 mo for a total of 5 y</li> <li>• CEA<sup>l</sup> every 3 mo for 2 y, then every 6 mo for a total of 5 y for T2 or greater lesions</li> <li>• CT may be considered for patients at high risk for recurrence<sup>j,k</sup></li> <li>• Colonoscopy<sup>a</sup> in 1 y, repeat in 1 y if abnormal or at least every 2-3 y<sup>m</sup> if negative for polyps. If no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3-6 mo.</li> </ul> <p style="text-align: right;"><a href="#">See Recurrence and Workup (COI-9)</a></p>
T4, N1-2, M0	5-FU/leucovorin <sup>h</sup> (category 1) or Capecitabine <sup>h</sup> or FOLFOX <sup>h</sup> or 5-FU/leucovorin + RT <sup>h,i</sup> (category 2B)	

**FOLFOX - Infusional 5-FU/leucovorin/oxaliplatin**

Liver Mets

FINDINGS	SURGERY	ADJUVANT THERAPY (6 mo preferred)	SURVEILLANCE
Synchronous liver metastases	Resectable <sup>d</sup> → Colectomy with en bloc removal of regional lymph nodes, intraoperative ultrasound (IOUS), synchronous liver resection or Colectomy with en bloc removal of lymph nodes with subsequent liver resection, IOUS or Colectomy with neoadjuvant chemotherapy (FOLFIRI or FOLFOX [category 2B]) and staged liver resection	5-FU/leucovorin <sup>n</sup> or FOLFIRI <sup>n</sup> or FOLFOX <sup>n</sup> or Continuous IV 5-FU or Capecitabine <sup>o</sup> or Hepatic artery infusion therapy ± systemic 5-FU/leucovorin (category 2B) or continuous IV 5-FU or Consider observation, if patient received neoadjuvant therapy	If patient stage IV, NED: • CEA every 3 mo x 2 y, then every 6 mo x 3-5 y (if elevated preoperatively) • Chest x-ray or chest CT every 3-6 mo x 2 y, then every 6-12 mo up to a total of 5 y (category 2B) • Abdominal/pelvic CT scan every 3-6 mo x 2 y, then every 6-12 mo up to a total of 5 y • Colonoscopy <sup>a</sup> in 1 y, repeat in 1 y if abnormal or at least every 2-3 y <sup>m</sup> if negative for polyps. If no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3-6 mo.
	Unresectable → Consider limited colon resection if substantial risk of obstruction and/or if liver burden low ± ablative therapy (category 2B)	<a href="#">See Chemotherapy for Advanced or Metastatic Disease (COI-B)</a>	

**FOLFOX - Infusional 5-FU/leucovorin/oxaliplatin**  
**FOLFIRI - Infusional 5-FU/leucovorin/irinotecan**



## Laparoscopy

The NEW ENGLAND JOURNAL of MEDICINE

### ORIGINAL ARTICLE

## A Comparison of Laparoscopically Assisted and Open Colectomy for Colon Cancer

The Clinical Outcomes of Surgical Therapy Study Group\*

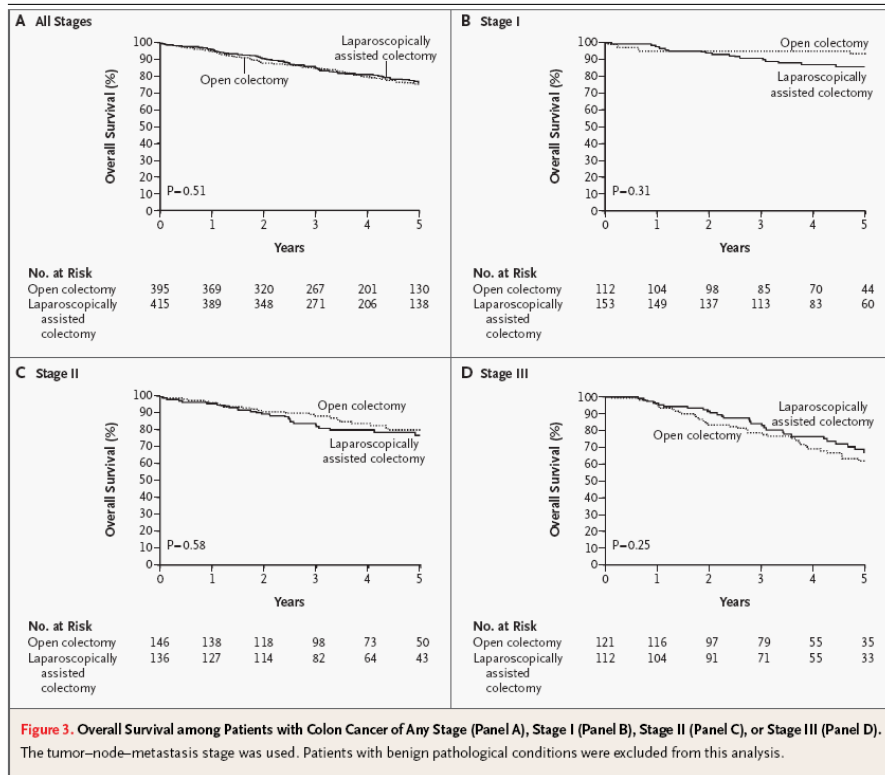
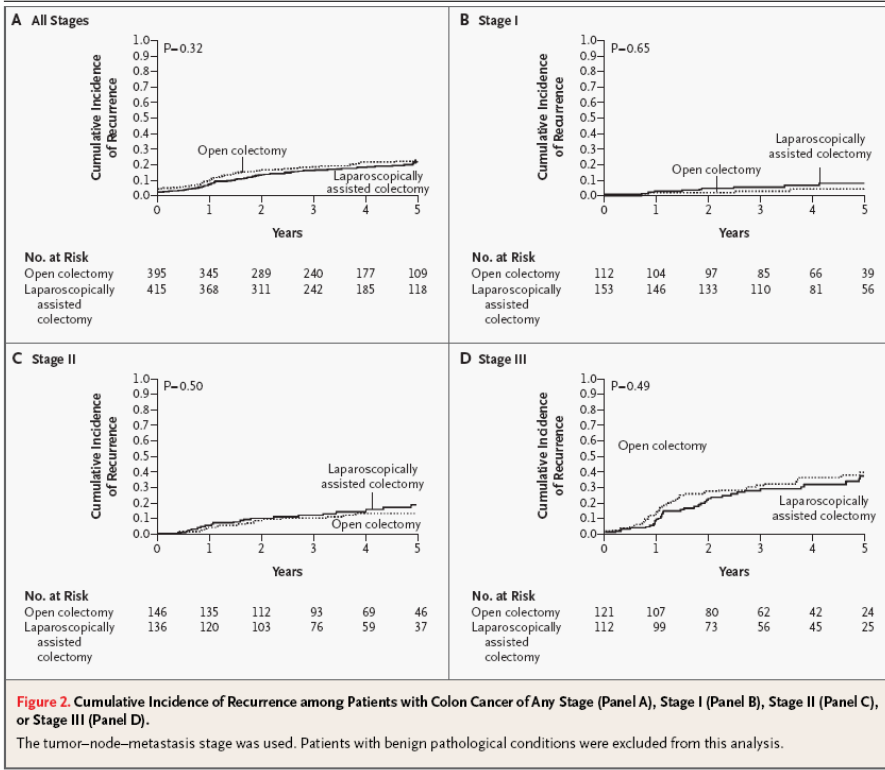
- Short Term
  - Bowel function
  - Hospital stay
  - Analgesia
  - Earlier recovery
  - Wound benefit
- Long Term
  - ?Hernias
  - ?Bowel obstruction
  - ?Immune function
  - ?Oncologic outcome

Table 2. Surgical, Pathological, and Postoperative Data.

Variable	Open Colectomy (N=428)	Laparoscopically Assisted Colectomy (N=435)	P-Value
Length of incision — cm			<0.001
Median	18	5	
Range	3–35	2–35	
Duration of surgery — min			<0.001
Median	95	150	
Range	27–435	35–450	
Proximal margin — cm			0.38
Median	12	13	
Range	3–50	2–78	
Distal margin — cm			0.09
Median	11	10	
Range	1–42	2–40	
Conversion to open from laparoscopically assisted colectomy			—
No. (%)	—	90 (21)	
Reasons for conversion — no. (%)			
Not applicable	428 (100)	0	
Not converted	—	345 (79)	
Advanced disease	—	22 (5)	
Complicating disease	—	3 (1)	
Inadequate margins of resection	—	4 (2)	
No visualization of critical structures	—	12 (3)	
Unable to mobilize colon	—	10 (2)	
Adhesions	—	14 (3)	
Intraoperative complications	—	4 (1)	
Other	—	21 (5)	
Other organs resected — no. (%) <sup>b</sup>	62 (14)	33 (8)	0.001
Abdominal-wall adhesions — no. (%)	106 (25)	149 (34)	0.002
Bowel adhesions — no. (%)	58 (14)	95 (22)	0.001
Pelvic adhesions — no. (%)	59 (14)	66 (15)	0.53
Other types of intraabdominal disease — no. (%)	44 (10)	51 (12)	0.48
Duration of use of oral analgesics — days			0.02
Median	2	1	
Interquartile range	1–3	1–2	
Duration of use of parenteral narcotics — days			<0.001
Median	4	3	
Interquartile range	3–5	2–4	
Duration of hospitalization — days			<0.001
Median	6	5	
Interquartile range	5–7	4–6	
30-Day mortality — no. (%)	4 (1)	2 (<1)	0.40
Complications — no. (%)			
Overall	85 (20)	92 (21)	0.64
Intraoperative <sup>†</sup>	8 (2)	16 (4)	0.10
Postoperative (before discharge)	80 (19)	81 (19)	0.98
Grade of postoperative complications — no./total no. (%)			0.73
1	44/80 (55)	42/81 (52)	
2	33/80 (41)	24/81 (42)	
3	0/80 (0)	2/81 (2)	
4	3/80 (4)	3/81 (4)	

\* Other organs resected included the gallbladder (10 patients in each group), gynecologic organs (24 in the open-colectomy group and 8 in the laparoscopic-surgery group), liver (9 and 1, respectively), the bladder and abdominal wall (6 and 3, respectively), small bowel (4 and 6, respectively), and other (9 and 5, respectively).

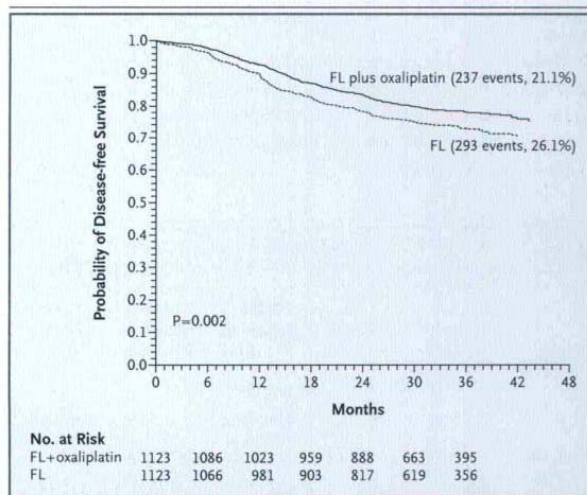
<sup>†</sup> Intraoperative complications included splenic injury (two in the open-colectomy group), bleeding (one in the open-colectomy group and eight in the laparoscopic-surgery group), bowel injury (two and six, respectively), and miscellaneous (three and two, respectively).



ORIGINAL ARTICLE

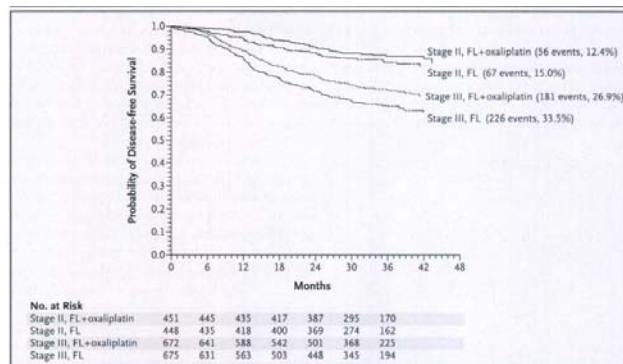
## Oxaliplatin, Fluorouracil, and Leucovorin as Adjuvant Treatment for Colon Cancer

Thierry André, M.D., Corrado Boni, M.D., Lamia Mounedji-Boudiaf, M.D., Matilde Navarro, M.D., Josep Taberero, M.D., Tamas Hickish, M.D., Clare Topham, M.D., Marta Zaninelli, M.D., Philip Clingan, M.D., John Bridgewater, M.D., Isabelle Tabah-Fisch, M.D., and Aimery de Gramont, M.D., for the Multicenter International Study of Oxaliplatin/5-Fluorouracil/Leucovorin in the Adjuvant Treatment of Colon Cancer (MOSAIC) Investigators



**Figure 1.** Kaplan–Meier Estimates of Disease-free Survival in the Group Given Fluorouracil and Leucovorin (FL) and the Group Given FL plus Oxaliplatin, According to the Intention to Treat.

The hazard ratio for recurrence in the group given FL plus oxaliplatin, as compared with the FL group, was 0.77 (95 percent confidence interval, 0.65 to 0.91;  $P=0.002$ ).



**Figure 2.** Kaplan–Meier Estimates of Disease-free Survival in the Group Given Fluorouracil and Leucovorin (FL) and the Group Given FL plus Oxaliplatin, According to the Stage of Disease and the Intention to Treat.

## Liver Mets

- 20% have mets at time of diagnosis
- 75-90% of hepatic mets have inc CEA
- Repeat colonoscopy
- Pre-op eval
  - Determine resectability
    - Anatomic resection vs destructive techniques
  - General medical condition
  - Residual parenchyma
  - Biology of disease
- Synchronous liver mets
  - Staged vs simultaneous

## Clinical Score for Predicting Recurrence After Hepatic Resection for Metastatic Colorectal Cancer

### Analysis of 1001 Consecutive Cases

Yuman Fong, MD,\*† Joseph Fortner, MD,† Ruth L. Sun, BA,\*† Murray F. Brennan, MD,† and Leslie H. Blumgart, MD, FRCS\*†

From the \*Hepatobiliary Service and the †Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York City, New York

**Table 5. CLINICAL RISK SCORE FOR TUMOR RECURRENCE**

Score	Survival (%)					Median (mo)
	1-yr	2-yr	3-yr	4-yr	5-yr	
0	93	79	72	60	60	74
1	91	76	66	54	44	51
2	89	73	60	51	40	47
3	86	67	42	25	20	33
4	70	45	38	29	25	20
5	71	45	27	14	14	22

Each risk factor is one point: node-positive primary, disease-free interval <12 months, >1 tumor, Size >5 cm, CEA >200 ng/ml.

**Table 2. OVERALL PERIOPERATIVE RESULTS**

	All Resections	Lobectomy or More	Less than Lobectomy
Number	1001	631	370
Hospital stay (median days)	9 (0-70)	10 (1-70)	8 (4-35)
30-day mortality	28 (2.8%)	26 (4.1%)	2 (0.5%)
Complications (%)	31	37	20
1-yr survival (%)	89	85	93
3-yr survival (%)	57	53	75
5-yr survival (%)	37	33	40
Median survival (mo)	42	39	46

Dipen Maun, M.D.  
August 15, 2005