Resident Seminar
Aug 19th, 2015
Colon: Neoplastic

Scott Rieder
Dr. Colquhoun

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Objectives

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Medical Expert:

1. The biologic basis of colon neoplasia
2. Colon cancer screening (guidelines and evidence)
3. Pathology and management of polyps
4. Management of the malignant polyp
5. Presentation, diagnosis and management of colon cancer
6. Staging of colon cancer and prognosis
7. Management of colon cancer
8. Management of colon cancer emergencies
9. Role of neo-adjuvant and adjuvant care in colon cancer
10. Treatment of metastatic colon cancer
11. Post operative surveillance following curative resection of colon cancer
12. Palliation of metastatic colon cancer (role of stenting, ostomy, etc…)
13. Diagnosis and management of desmoids tumors and other FAP associated tumors

Objectives

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Collaborator:

1. Role of radiation and chemotherapy in the management of colon cancer
2. Management and palliation of colon cancer

Health Advocate:

1. Colon cancer screening
2. Screening in high risk populations
3. Post-operative surveillance of curatively resected colon cancer

Scholar:

1. Review of seminal paper

Epidemiology

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- 3rd most commonly diagnosed malignancy in Canada
- It is the 2nd leading cause of cancer death, behind lung cancer
- It is estimated that 25,000 people with diagnosed with CRC in Canada, and that over 9000 Canadians will die from CRC in 2015

Risk Factors

- Age
- Race
- Inflammatory Bowel Disease
- Family History/Genetic Syndromes
- Obesity
- High-fat diet
- Alcohol
- Smoking
- Diabetes
- Geography

CRC Incidence with age

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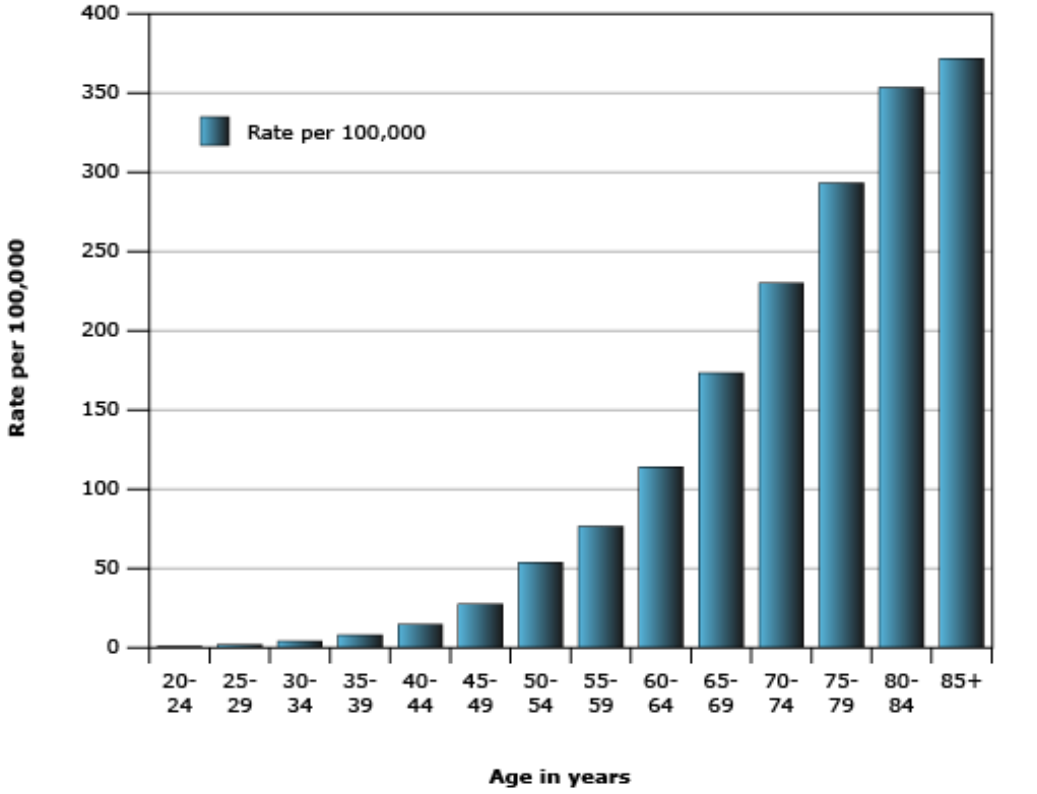
Increasing incidence of colorectal cancer with age

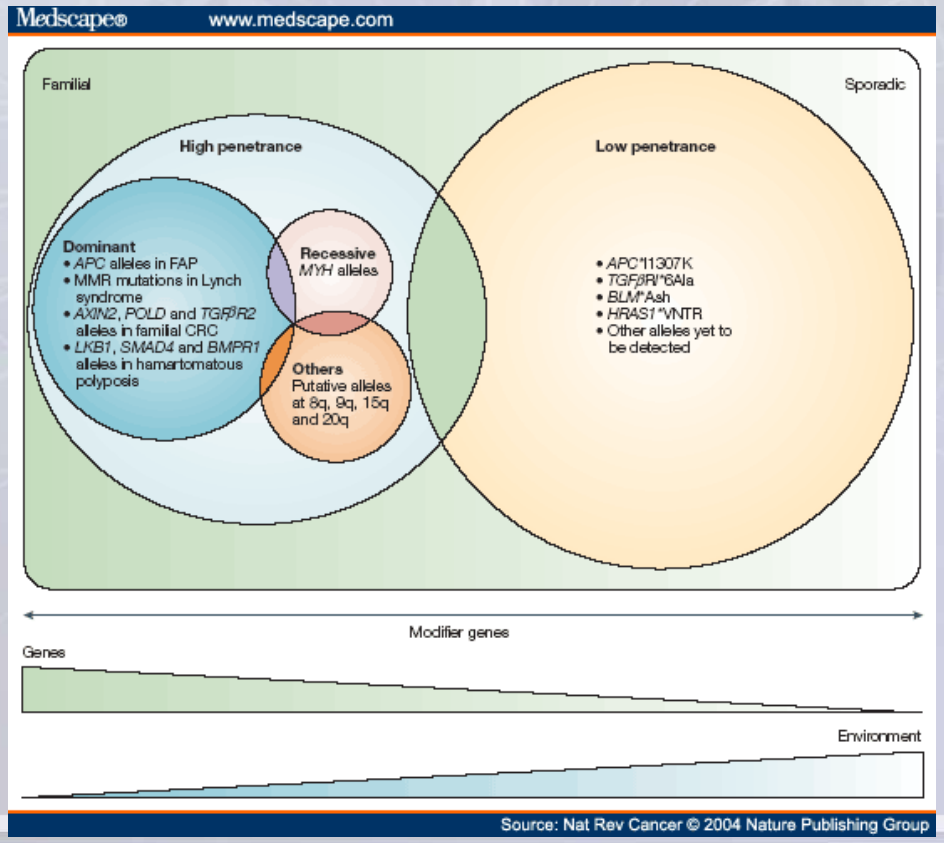


The age-specific incidence of colorectal cancer was measured between 2002 and 2006 in men and women of all races.

Data from: Surveillance, Epidemiology, and End Results (SEER) Program, 2002-2006. Available online at http://seer.cancer.gov.proxy1.lib.uwo.ca

Familial Cancer Syndromes

- It is estimated that around 15% of CRC occur in the background of a genetically inherited disorder, with FAP and HNPCC causing approximately 5% of all CRCs



Familial Cancer Syndromes

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- FAP and variants
- Cowden syndrome
- Peutz-Jeghers
- HNPCC
- MAP

Familial Adenomatous Polyposis (FAP)

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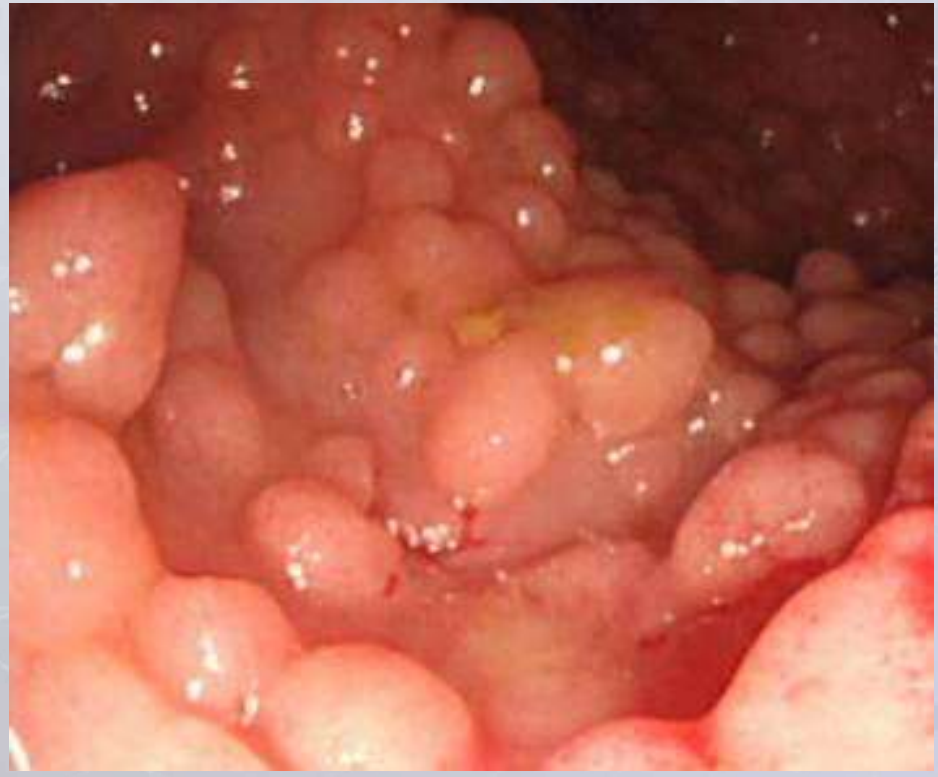

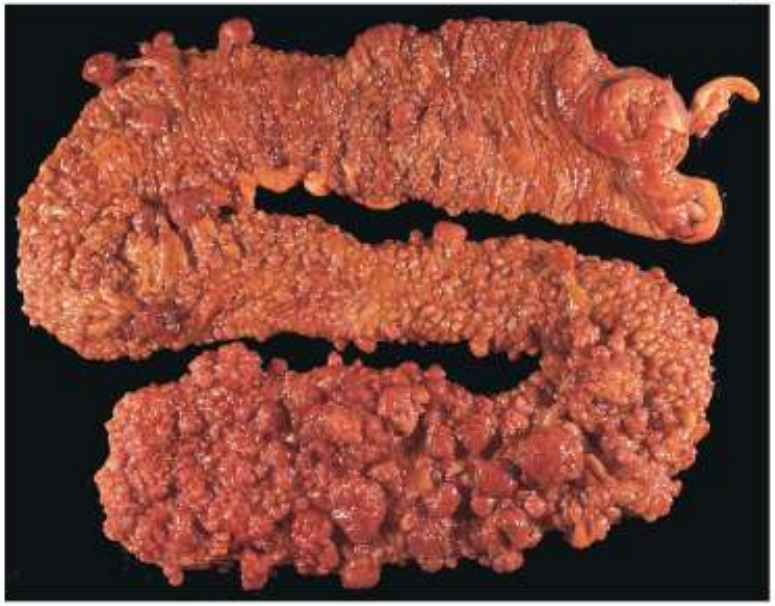

Figure 15-35 Familial adenomatous polyposis. The surface is carpeted by innumerable polypoid adenomas. (Courtesy of Dr. Tad Wieczorek, Brigham and Women's Hospital, Boston.)

Familial Adenomatous Polyposis (FAP)

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- Autosomal dominant disorder caused by mutations (>100 identified) in the adenomatous polyposis coli (APC) gene, located on the q-arm of chromosome 5
- Classic FAP is described as greater than 100 adenomatous polyps throughout the colon in a lifetime
- Polyps typically start to develop when these patients are in their teens, and lifetime risk of CRC approaches 100%
- 1/3 of newly diagnosed FAP patients are likely caused by de novo mutations or represent genetic mosaics
- The clinical presentation for FAP patients may include diarrhea, abdominal cramping/bloating and lower GI bleeds, but many are asymptomatic until they develop cancer

Genetic Screening for FAP

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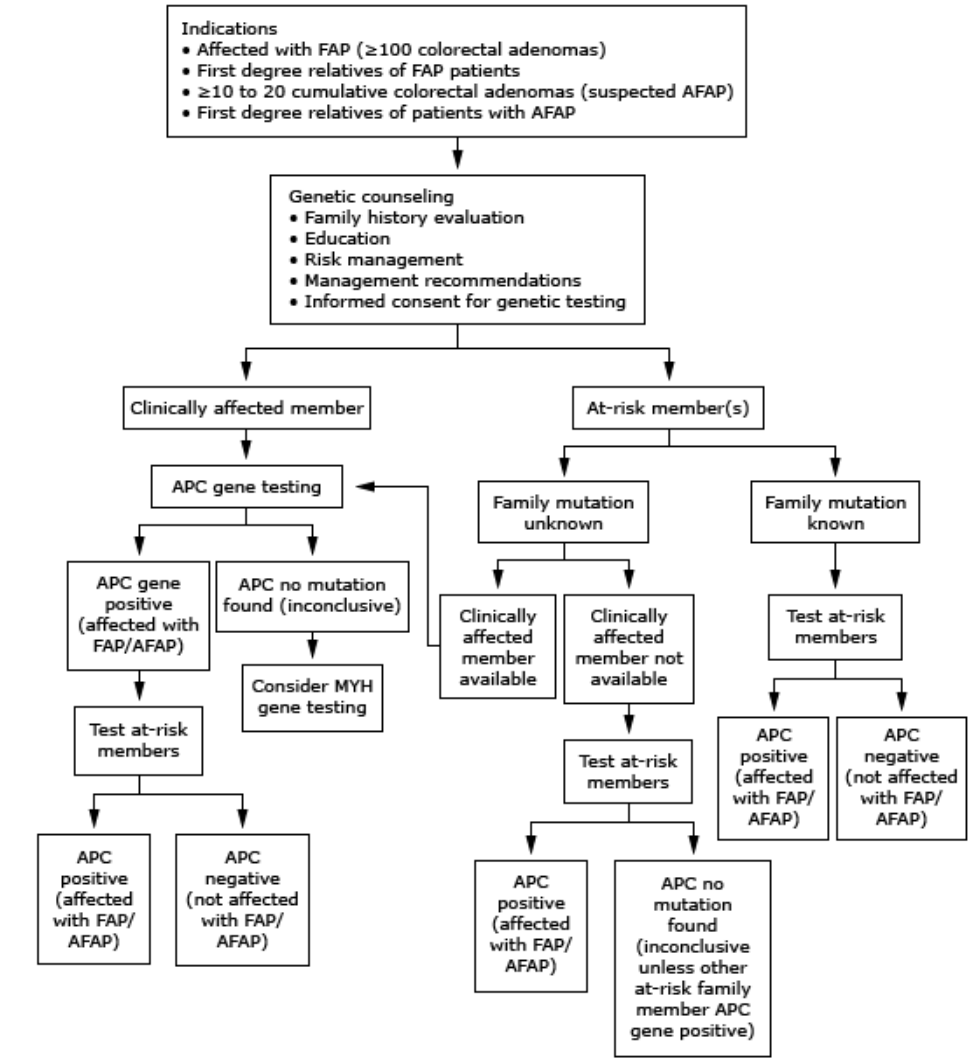
FAP gene testing algorithm



Extracolonic disease in FAP

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- Patients with FAP have many extracolonic manifestations of their disease that require close observation
- Gastric fundal polyps are common but rarely transform into gastric cancer
- Osteomas occurs in 20% of patients with FAP but require no special treatment or surveillance
- Adenomas of the small bowel, gallbladder and bile duct are also associated with FAP
- Greater than 30% of FAP patients will develop duodenal polyposis with 4-15% of FAP patients progressing to duodenal and periampullary adenocarcinoma over their lifetime
- Screening with EGD should begin at age 25 and patients should be scoped at repeat intervals according to their Spigelman stage

EGD Screening in FAP

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Table 1. Modified Spigelman's Score and Classification

Factor	Score		
	1 Point	2 Points	3 Points
No. of polyps	1-4	5-20	> 20
Polyp size, mm	1-4	5-10	> 10
Histology	Tubulous	Tubulovillous	Villous
Dysplasia	Low grade	—	High grade

NOTE. Classification: no polyp, stage 0; 1 to 4 points, stage I; 5 to 6 points, stage II; 7 to 8 points, stage III; 9 to 12 points, stage IV.

Stage 0-1: Every 4 years
Stage 2: Every 2-3 years
Stage 3: 6-12 months
Stage 4: Consider resection

FAP Variants

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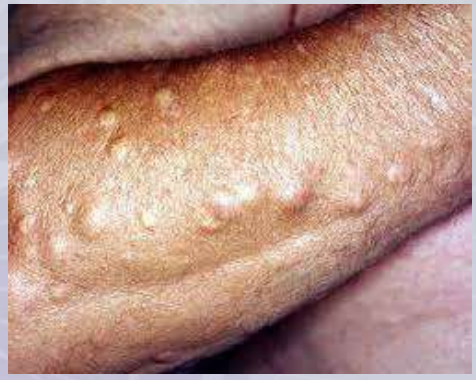
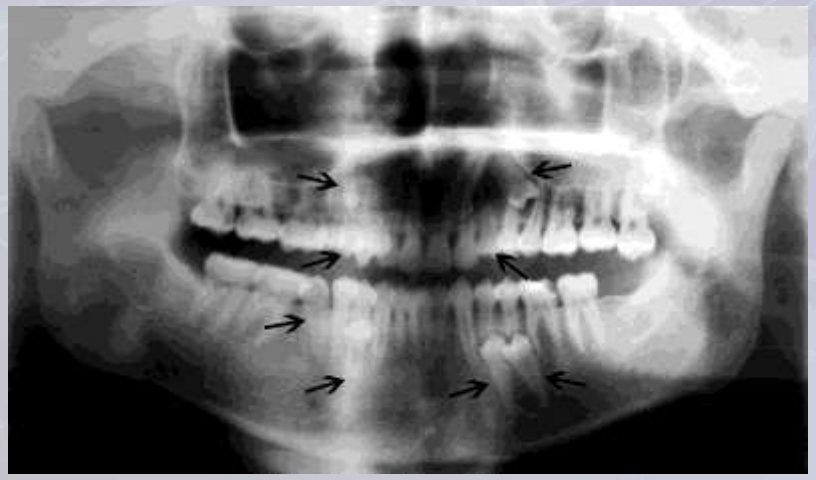
- Gardener Syndrome
- Turcott Syndrome
- Attenuated FAP

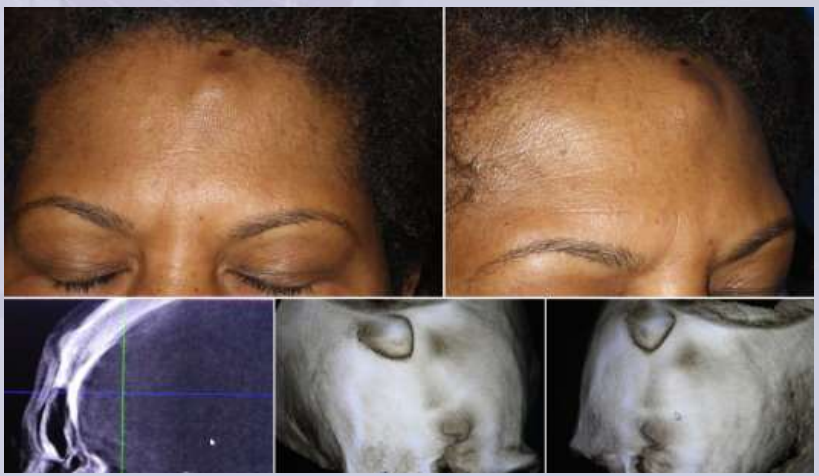
Gardener Syndrome

Described by Gardener in the 1950s in patients with FAP and is associated with extracolonic lesions including:

- **Osteomas of the face and skull**
- **Unerupted and/or supernumerary teeth**
- **Epidermal cysts, lipomas and fibromas**
- **Desmoid tumours**
- **Adrenal adenomas**
- **Nasal angiofibromas**







Gardener Syndrome

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Extracolonic malignancies associated with GS:

- **Thyroid**
- **Pancreatic**
- **Gastric**
- **Hepatoblastoma**
- **CNS**

Recommended screening in GS patients:

- **Annual thyroid exam and US, starting at age 10**
- **LFTs and abdominal US q6 months in GS children until the age of 10**
- **Generally all other screening guided by FAP principles or investigations as symptoms arise**

Desmoid Tumours in FAP

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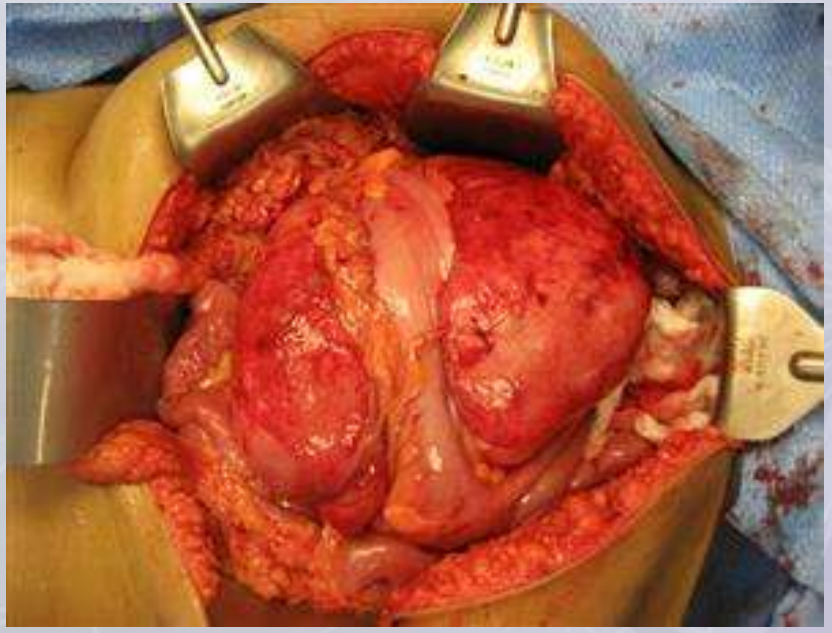

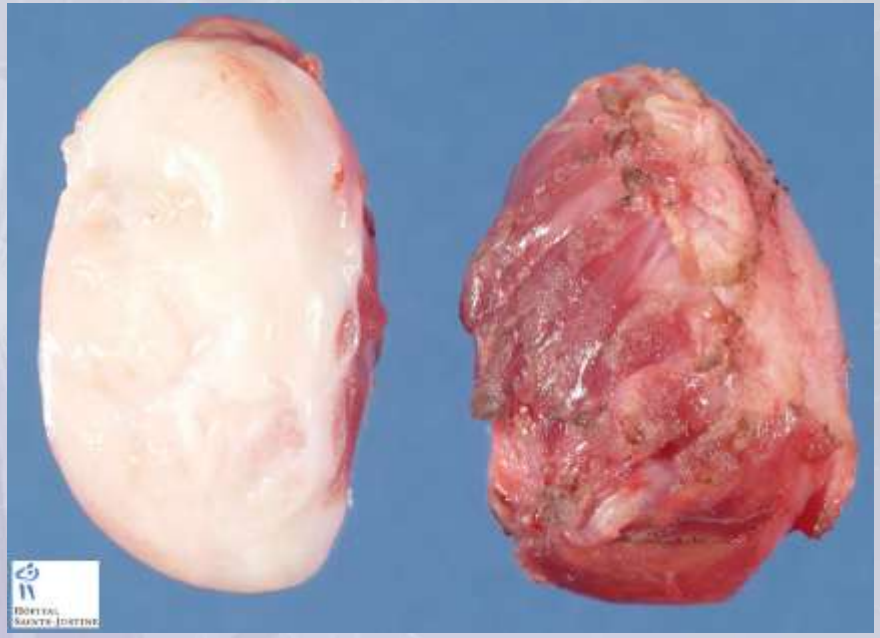

Desmoid tumours in FAP

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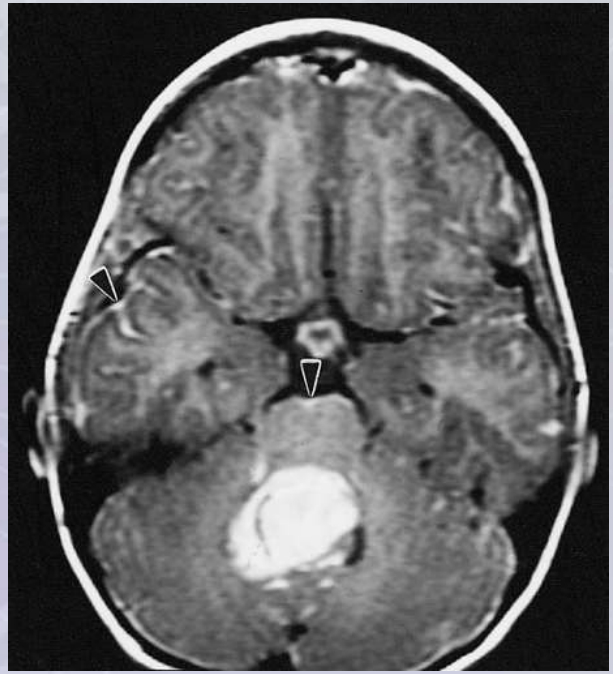
- Desmoids are fibromatous lesions that can arise in patients with FAP, primarily in the abdominal wall and within the abdomen
- Although they are benign growths, they can occasionally be locally aggressive, causing intestinal obstruction or bowel ischemia and are responsible for 9-15% of deaths in patients with FAP
- For extra-abdominal desmoids, complete surgical resection is indicated
- In FAP, patients with intra-abdominal desmoids often cannot undergo surgical resection due to the tumours being seated at the root of the mesentery, in these patients either RT or systemic therapy (tamoxifen and sulindac) is indicated

Turcott Syndrome

- First used by Turcott to describe association between FAP and brain tumours
- Through genetic studies, has been shown to be associated with both FAP (medullablastomas) and Lynch syndrome (gliomas)
- Term of historical use only

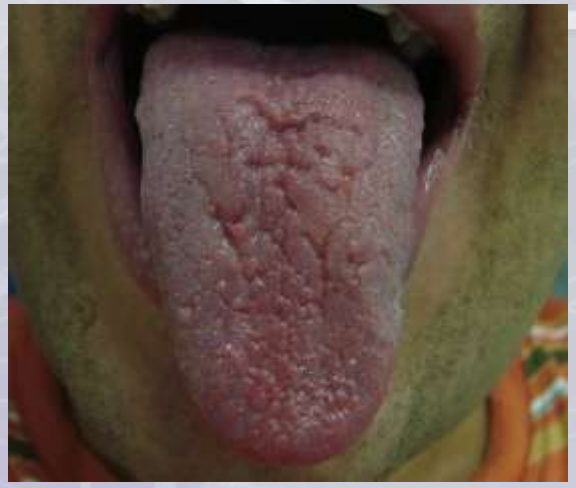


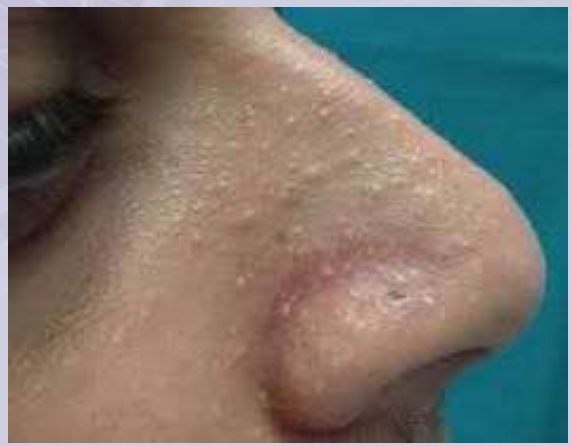
Attenuated FAP

- Less severe diagnosis than classic FAP
- Described as greater than 10-20 but less than 100 lifetime polyps
- Adenomas typically present at a later age than FAP (mean age 44)
- Lifetime risk of CRC still extremely high (~80%)

Cowden Syndrome

- Mutation in the phosphatase and tensin homolog gene (PTEN) tumour suppressor gene on chromosome 10
- Autosomal dominant inheritance
- Trichelemmomas, acral keratoses and oral papillomas are typical manifestations
- Predisposed to multiple malignancies, including:
  Breast
  Endometrial
  Renal
  Colorectal caners
- Risk of CRC ~18% higher than normal population





Peutz-Jeghers Syndrome

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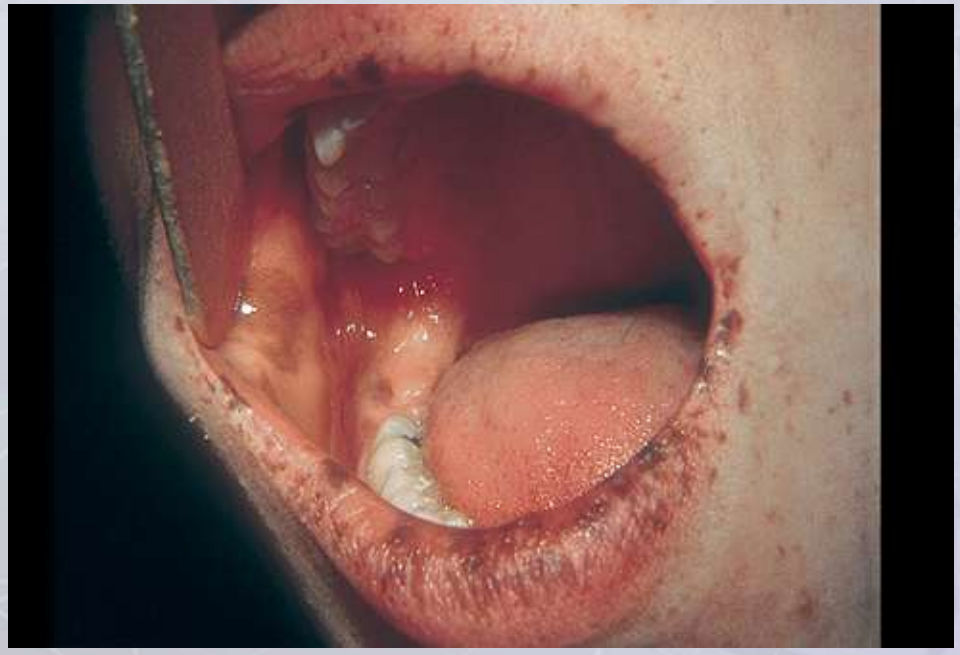
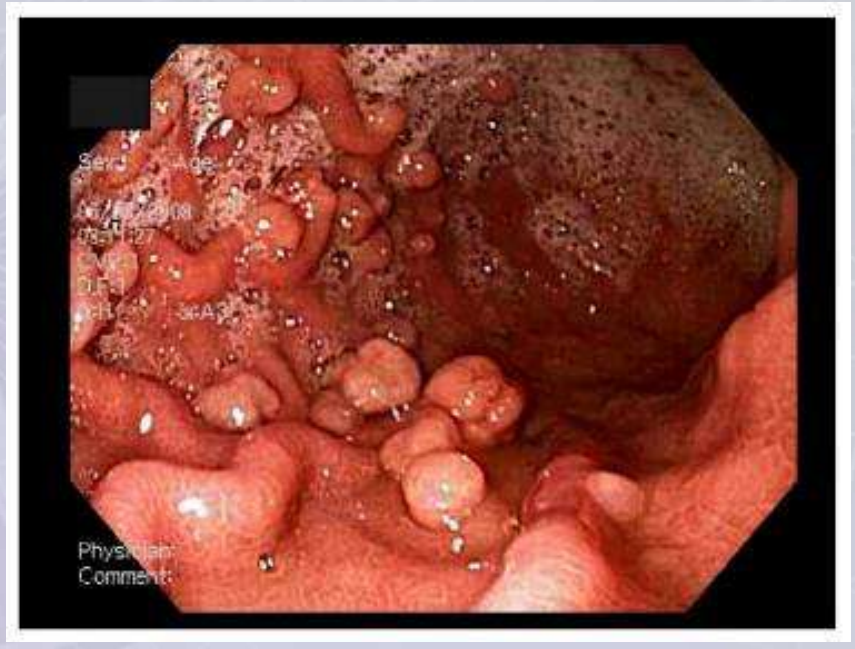
- Characterized by multiple hamartomatous polyps throughout the GI tract and pigmented mucocutaenous macules that form at a young age
- Mutation in the STK11 gene, another tumour suppressor
- Autosomal dominant inheritance
- Lifelong risk of cancers in GI tract:
  Colorectal (40%)
  Stomach (30%)
  Small bowel (13%)
  Pancreas (11-35%)
- EGD/Colonoscopy at age 8, and every 3 years after if polyps detected
- Capsule endoscopy at age 8 and q3 years for patients with multiple polyps seen in small bowel

Peutz-Jeghers Syndrome





Hereditary Nonpolyposis Colorectal Cancer

- HNPCC is the most common cause of inheritable CRC
- Autosomal dominant inheritance
- Called HNPCC when patients meet the Amsterdam criteria
- Lynch syndrome now reserved for those with identified microsatellite instability in DNA mismatch repair gene mutations (MLH1, MSH2, MSH6 and PMS2)

Amsterdam Criteria/Bethesda Guidelines

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BOX 1

Amsterdam II Criteria and Revised Bethesda Guidelines

Amsterdam II Criteria (7)

- **All criteria must be met:**
  - Three or more relatives with histologically confirmed colorectal cancer or cancer of the endometrium, small bowel, ureter, or renal pelvis, one affected relative being a first-degree relative of the other two; FAP should be excluded
  - Two or more successive generations are affected
  - At least one relative was diagnosed before the age of 50 years

Revised Bethesda Guidelines (8)

- **One or more of the following criteria must be met:**
  - Colorectal cancer before the age of 50 years
  - Synchronous or metachronous colorectal cancer or other HNPCC-related tumors[*1], regardless of age
  - Colorectal cancer with MSI-high morphology[*2] before the age of 60 years
  - Colorectal cancer (regardless of age) and a first-degree relative with colorectal cancer or an HNPCC-related tumor before the age of 50 years
  - Colorectal cancer (regardless of age) and two or more first- or second-degree relatives diagnosed with colorectal cancer or an HNPCC-related tumor (regardless of age)

[*1] HNPCC-related tumors include colorectal, endometrial, stomach, ovarian, pancreas, ureter and renal pelvis, biliary tract, and brain (usually glioblastoma as seen in Turcot syndrome) tumors, sebaceous gland adenomas and keratoacanthomas in Muir–Torre syndrome, and carcinoma of the small bowel
[*2] Presence of tumor-infiltrating lymphocytes, Crohn's-like lymphocytic reaction, mucinous/signet-ring cell differentiation, or medullary growth pattern
FAP: Familial adenomatous polyposis; HNPCC: hereditary nonpolyposis colorectal cancer; MSI: microsatellite instability

DNA MMR Genes in Lynch Syndrome

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Lifetime cancer risk related to Lynch genotypes

Cancer site	MLH1		MSH2		MSH6		PMS2	
	Men	Women	Men	Women	Men	Women	Men	Women
Any Lynch cancer	**44 to 79 percent***		**38 to 78 percent***		**25 to 47 percent***	**65 percent***	**16 to 48 percent**	**21 to 53 percent**
Colorectal	58 to 65 percent	50 to 53 percent	54 to 63 percent	39 to 68 percent	36 to 69 percent	18 to 30 percent	20 percent	15 percent
Endometrial	NA	57 to 66 percent	NA	21 percent	NA	17 to 44 percent	NA	15 percent
Ovarian	NA	20 percent	NA	24 percent	NA	1 percent		
Upper urologic tract	2.1 percent	0.4 percent	20 percent	9 percent	0.7 percent			
Gastric	6 percent*		2 percent*		6 percent	4 percent		
Small bowel¶	3 percent	6 percent	3 percent	6 percent	?			
Biliary/pancreatic	4 percent¶				?			
Brain tumors (gliomas)	1.7 percent		2.5 percent		?			
Sebaceous gland tumors	42 percent of families$^{\Delta}$		44 percent of families$^{\Delta}$		0 percent of families$^{\Delta}$			

NA: not applicable; ?: unknown.
* Not reported separately by sex.
¶ Not reported separately by genotype.
Δ Percentage of Lynch families with one or more members with sebaceous gland tumors.

Lynch Syndrome

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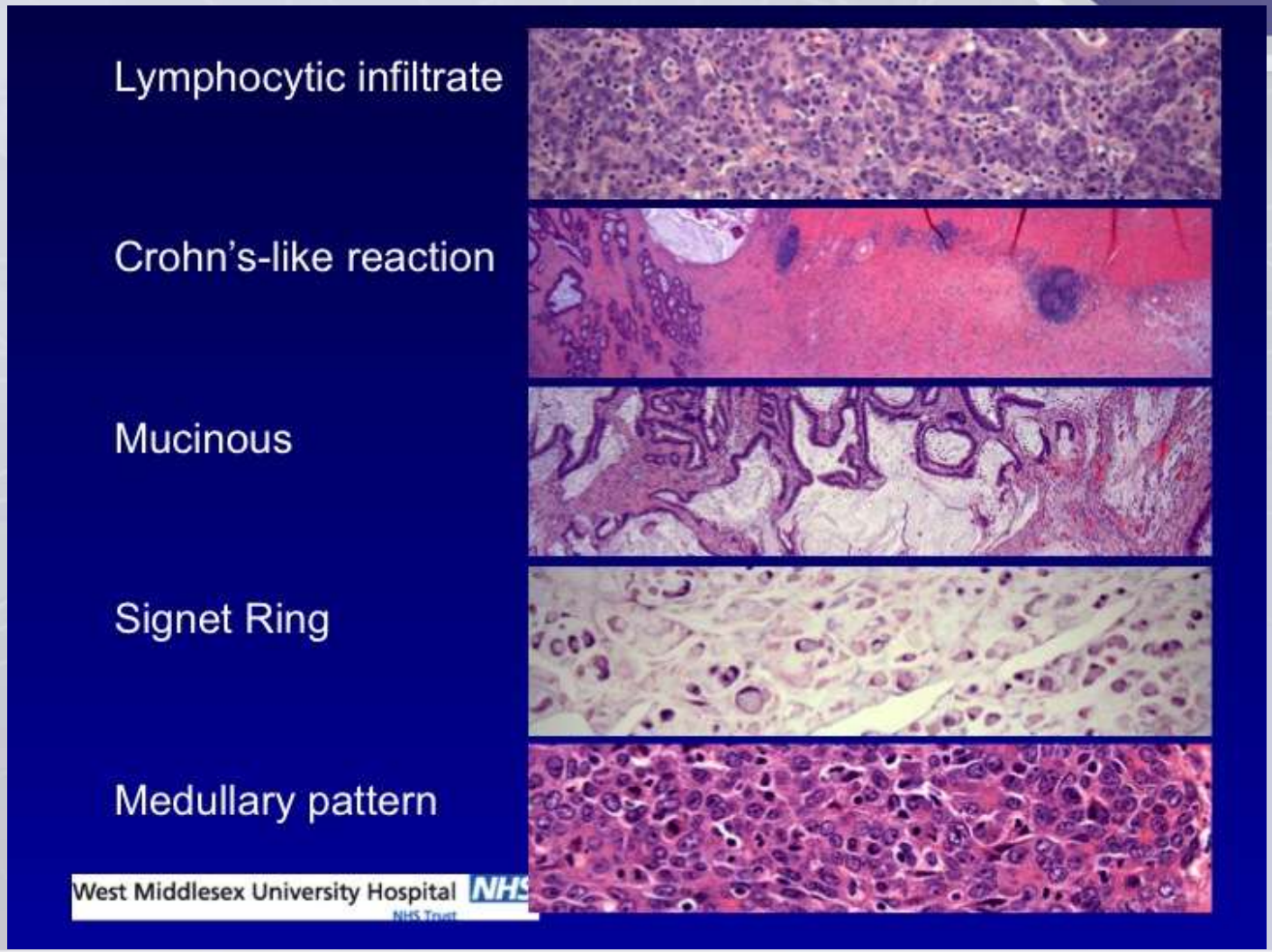
- Individuals with Lynch syndrome carry a 70% lifetime risk of CRC and occurs at an earlier age (mean 44, compared to 61-69 in sporadic CRC)
- They are also at risk for metachronous cancers, with ~10% of patients developing more than one lifetime cancer
- The adenomas in Lynch patients tend to be more proximal, flat and are more likely to contain villous histology
- There is also an accelerated polyp to cancer sequence in these patients (~35 months)
- Pathology of Lynch CRCs often demonstrates mucinous, signet ring cell or medullary histologic type cancers that are more poorly differentiated compared to sporadic CRCs
- Should undergo colonoscopic surveillance starting at age 20 every 1-2 years

Lynch Syndrome



Muir-Torre Syndrome

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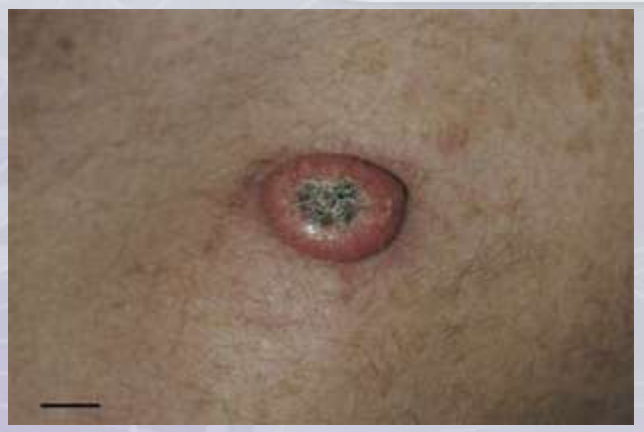
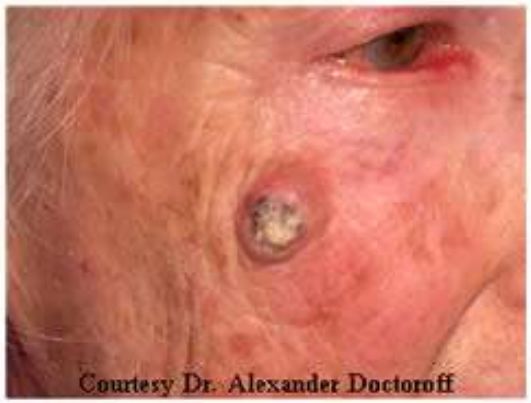
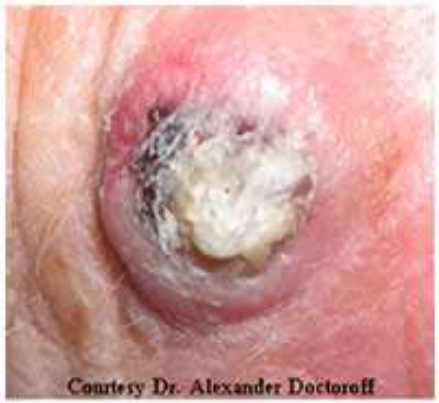
- A variant of HNPCC
- Defined as at least one sebaceous skin tumour and one visceral malignancy
- Should undergo annual skin exams in addition to typical HNPCC screening





Keractoacanthoma on the cheek



Close up of the keratoacanthoma lesion

MUTYH-Associated Polyposis

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- Affected individuals typically have multiple colonic polyps and have had APC mutations excluded
- MUTYH genes are responsible for repairing oxidative damage to DNA, and individuals with MAP have biallelic mutations in MUTYH
- Lifetime risk of CRC in these patients is 70-75%
- Also at risk of developing duodenal and gastric polyps
- In patients with diagnosed MAP and a colon cancer, total colectomy is indicated

Polyp to Cancer Sequence

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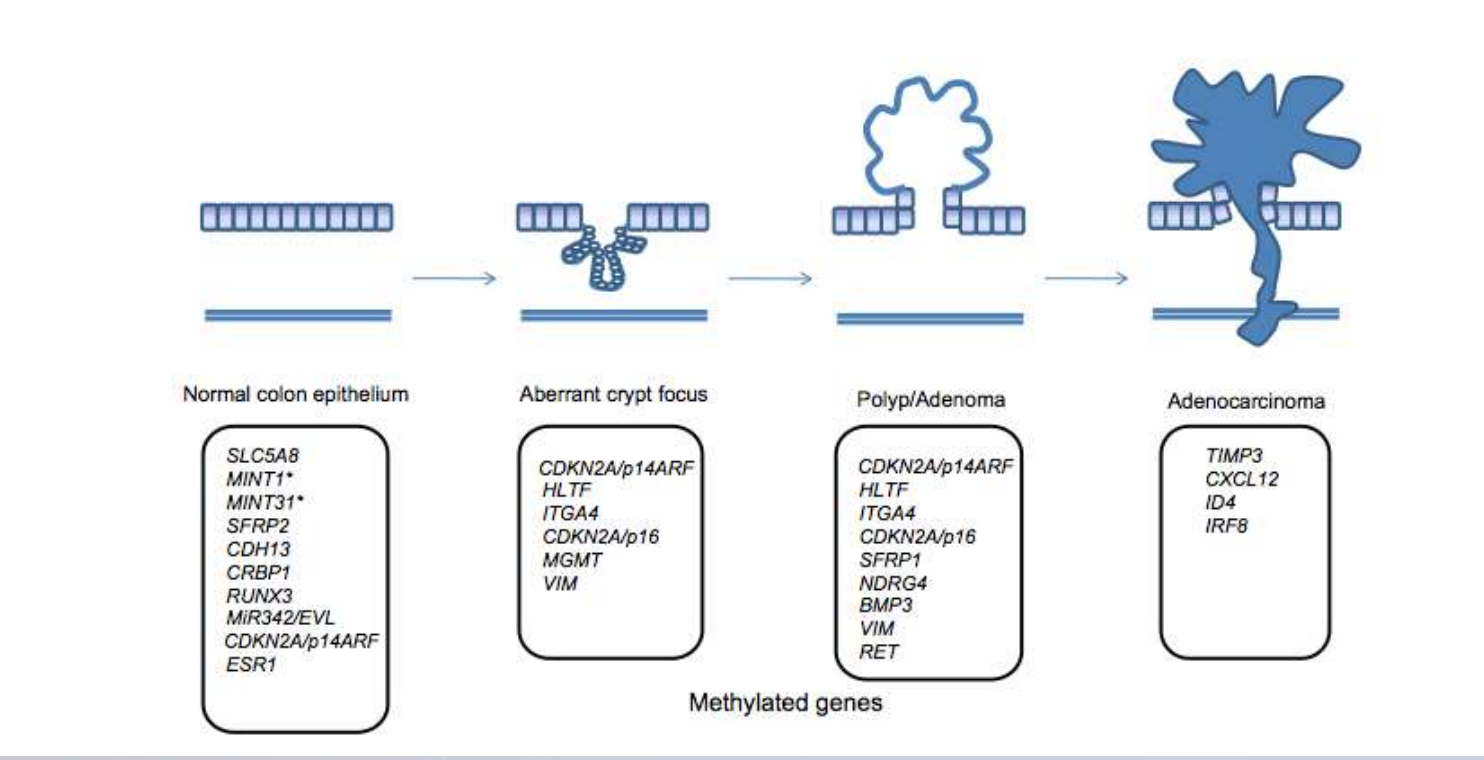
- Almost all CRC cancers arise from benign neoplasms



Rationale for CRC Screening

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- Screening for and removing premalignant can reduce death by CRC
- Adenoma to cancer sequence takes between 10-15 years in an an average risk patient
- Screening methods include stool testing, cross-sectional imaging and direct visualization
- NCCN generally recommends colonoscopy over other methods as the primary screening tool for CRC

Screening Test Characteristics

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Summary of the characteristics of screening tests for colorectal cancer

Screening test	Test performance (sensitivity, specificity)	Complexity	Potential effectiveness	Direct evidence of effectiveness	Screening test risk
Fecal occult blood test	Intermediate for cancers, low for polyps	Lowest	Lowest	Strong	Lowest
Fecal immunochemical test for hemoglobin	Intermediate for cancers, low for polyps	Low	Low	Weak	Lowest
Flexible sigmoidoscopy	High for up to half of the colon	Intermediate	Intermediate	Strong	Intermediate
FOBT + flexible sigmoidoscopy	Same as flexible sigmoidoscopy and FOBT	Intermediate	Intermediate	Weak	Intermediate
Colonoscopy	Highest	Highest	Highest	Intermediate	Highest
Computed tomographic colonography	High (similar to colonoscopy)	High	High	Weak	Low

The costs of the screening tests themselves, also an important characteristic, vary, but the costs of the screening strategies (lifetime programs of screening and follow-up of abnormal test results) are comparable. Complexity involves patient preparation, inconvenience, facilities and equipment needed, and patient discomfort.

Data updated according to joint multi-society guidelines 2008. Adapted from Winawer SW, Fletcher RH, Mille L, et al. AGA guidelines: Colorectal cancer screening: Clinical guidelines and rationale. Gastroenterology 1997; 112: 594.

Screening Guidelines – Average Risk

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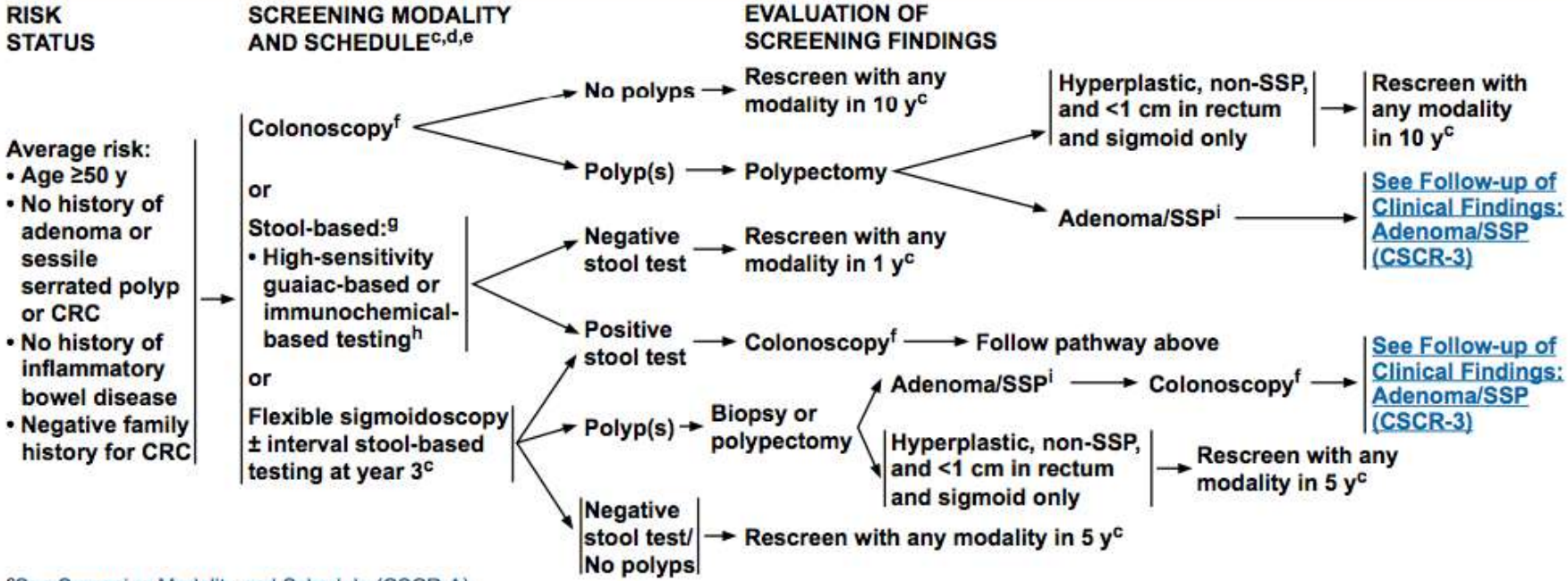
National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2015
Colorectal Cancer Screening

NCCN Guidelines Index
Colorectal Screening TOC
Discussion



[c] See Screening Modality and Schedule (CSCR-A).

[d] Currently there is not a consensus on the use of CT colonography (CTC) as a primary screening modality, and it is evolving with regards to recommended/ programmatic frequency, polyp size leading to referral for colonoscopy, and protocol for evaluating extra colonic lesions. Also unclear is what follow-up is required for a patient with a positive CTC and a negative colonoscopy. CTC may also not be as sensitive as colonoscopy to detect clinically significant lateral spreading tumors (Togashi K, et al. World J Gastroenterol 2014;20:17552-7). Despite these uncertainties, CTC is being utilized in clinical practice. The current data available suggest that, if CTC is negative/no polyps, then repeat CTC in 5 y, and if positive/polyps lesions, colonoscopy should be performed.

[e] CRC screening should be performed as part of a program that includes a systematic method for identifying those who are eligible for and wish to undergo screening, standard methods for administering the screening tests at agreed upon intervals, standardized reporting of the results, and a mechanism for follow-up of those with a positive test.

[f] If colonoscopy is incomplete or preparation is suboptimal, consider other screening modality or repeat colonoscopy within 1 year (Johnson D, et al. Gastro 2014;147:903–924.).

[g] Stool DNA testing has recently been approved by the FDA as a primary screening modality for colorectal cancer (Imperiale TF, et al. N Engl J Med 2014;370:1287-1297). At this time, there are limited data available to determine an appropriate interval between screening.

[h] Recent studies have demonstrated that FIT is more sensitive than high-sensitivity guaiac-based testing. However, regular guaiac-based stool testing has been shown to reduce CRC mortality in randomized trials (category 1).

[i] SSPs without dysplasia are generally managed like adenomas; SSP-cd are managed like high-risk adenomas and may need even more frequent surveillance.(Rex D, et al. Am J Gastro 2012;107:1315-1329; Leiberman D, et al. Gastroenterology 2012;143:844-857).

Increased Personal History/Adenoma/SSP

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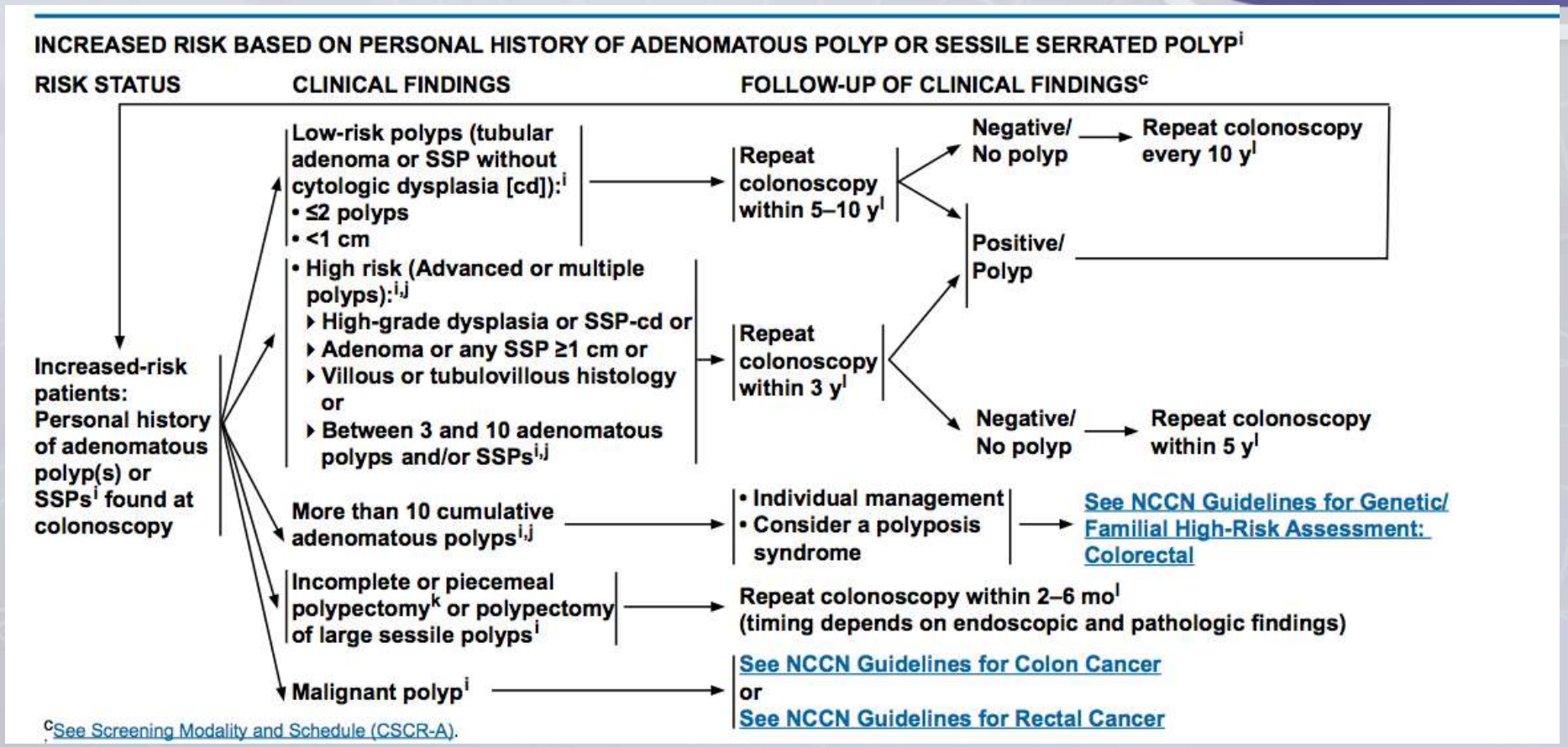

Inflammatory Bowel Disease Screening

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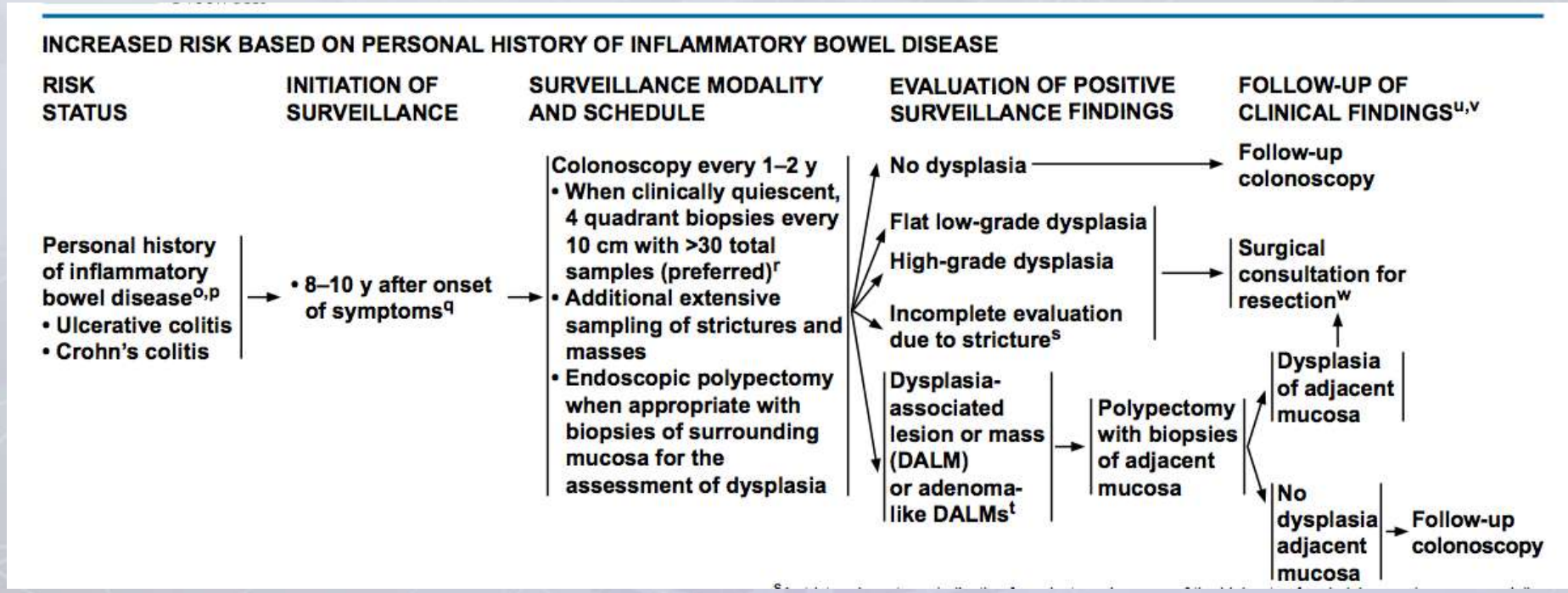


Endoscopic Appearance of Colonic Polyps

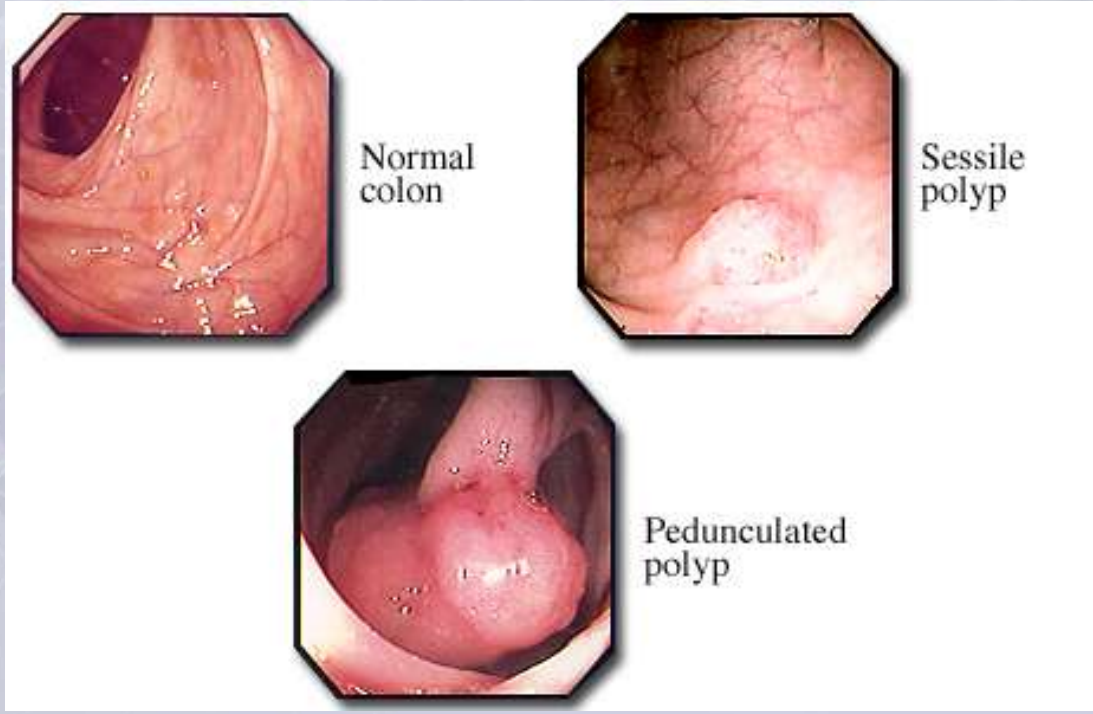
- Polyps may be classified in part by their morphology:

Penduculated

Sessile

Flat

Depressed



Pathology of Colonic Polyps

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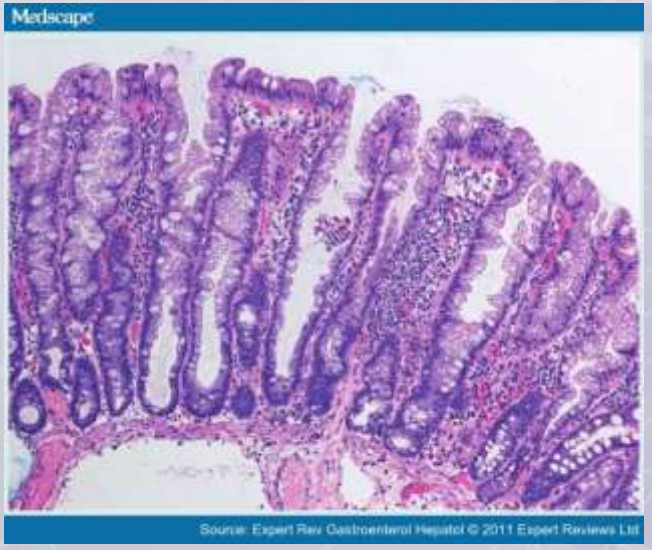
- **Hyperplastic** - most common non-neoplastic polyp in colon, typically found in rectosigmoid and less than 5mm in size, generally carry very low risk of malignant transformation
- **Serrated Adenoma** – More prevalent in proximal colon, lack typical dysplasia seen in adenomas but develop foci of dysplasia within the polyp, tend to be large and flat (more difficult to remove endoscopically)
- **Tubular Adenoma** – 80% of all colonic polyps, characteristic branches of adenomatous epithelium
- **Villous Adenoma –** 10% of all colonic polyps, characteristic long narrow glands extending to center of polyp
- **Tubulovillous Adenoma** – A combination of tubular and villous pathology

Pathology of Colonic Polyps



Hyperplastic polyp with saw tooth pattern

Pathology of Colonic Polyps

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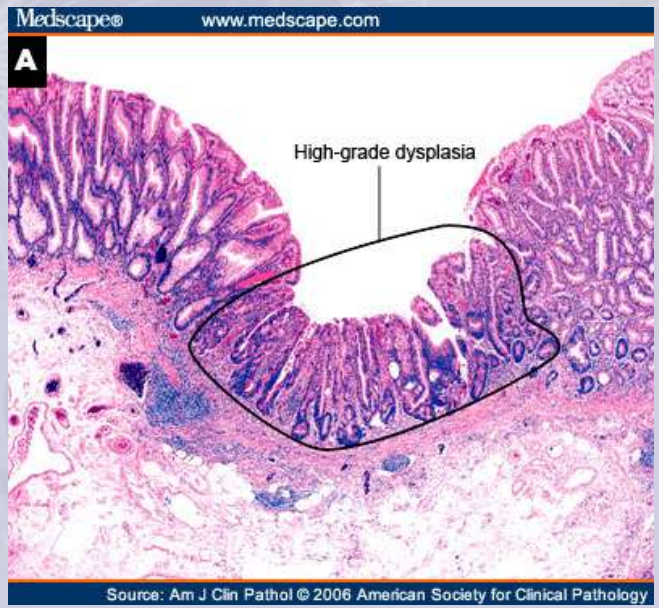
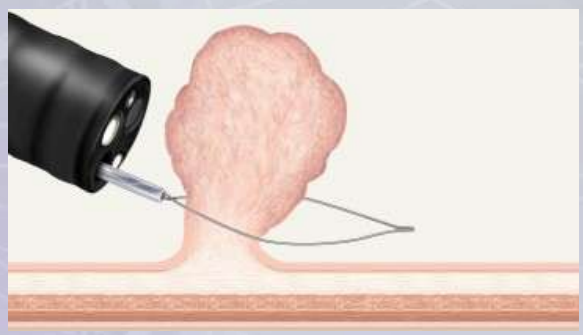
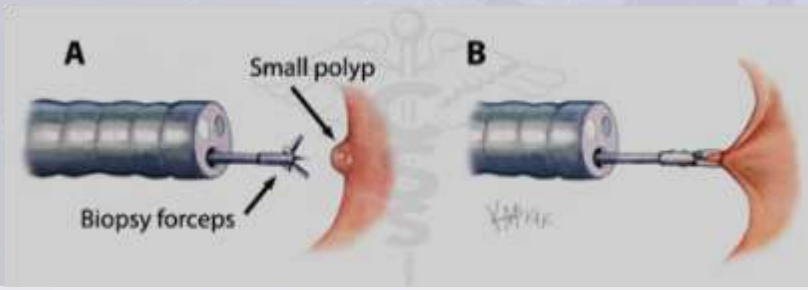
- All adenomas are dysplastic, but are graded as having either high-grade or low-grade dysplasia
- Risk factors that increase the risk of high-grade dysplasia and malignancy:
  Size (>1cm)
  Villous Histology
  Number of colonic polyps

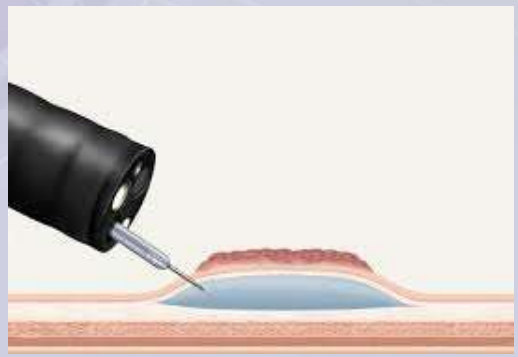


Management of Colonic Polyps

- When a polyp is detected, endoscopic polypectomy is generally recommended when feasible, and can be achieved through a variety of means:
  Cold/hot biopsy
  Cold/hot snare
  Piecemeal excision
  Fulguration with cautery or APC
  Injection assisted mucosal resection
  Submucosal dissection
  Surgical resection







Management of Colonic Polyps

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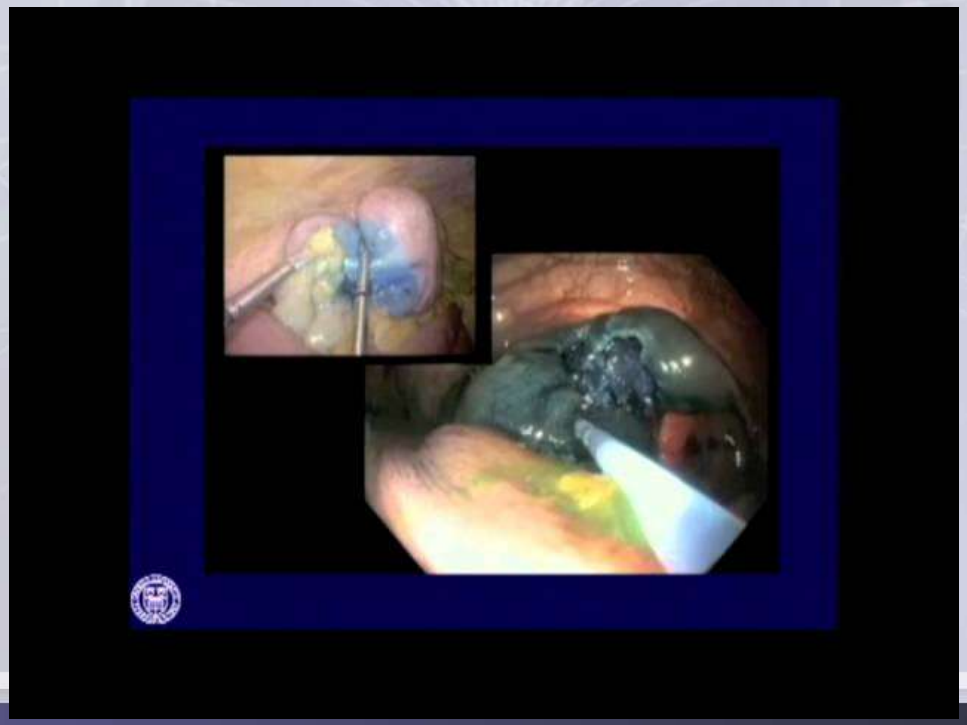
- A new approach to previously unresectable polyps is to combine the endoscopic resection with laparoscopic assistance
- Specimen sent for frozen to ensure no malignacy
- May reduce morbidity of formal resection in selected patients



The Malignant Polyp

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- Resected polyps with malignant foci represent a challenge to both the patient and surgeon on whether or not to proceed to surgical resection
- Some guiding principles to not proceed to segmental colectomy include:
  Low grade malignancies
  No lymphovascular invasion
  Polyp specimen resected en mass
  Negative (>2mm) margin
- If all of these criteria are not met, surgical resection should be strongly considered, based on clinical acumen, patient wishes and patient factors

Presentation of colon cancer

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- Generally colon cancer presents in one of three ways:

  Symptoms from tumour (local or metastatic)

  Routine screening or surveillance

  Surgical emergency

Presentation of colon cancer

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- Common symptoms include:

  Altered bowel habits (typically for left-sided cancer/rectal cancers
  Hematochezia (rectal and sigmoid)
  Anemia
  Abdominal pain and bloating

- Typically patients who present symptomatic have a worse prognosis than those picked up on routine screening or found incidentally
- Patients presenting with obstruction and perforation carry the worst prognosis, including those with node-negative disease

Diagnosis of colon cancer

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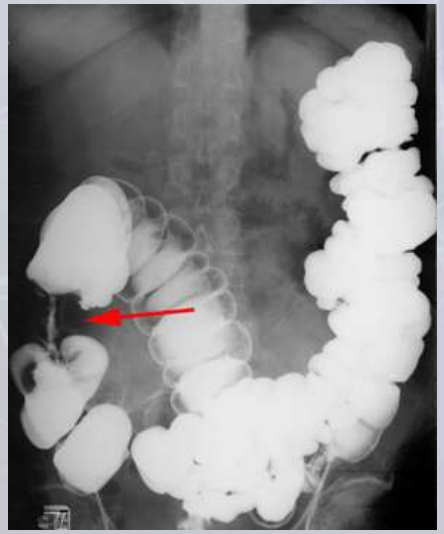
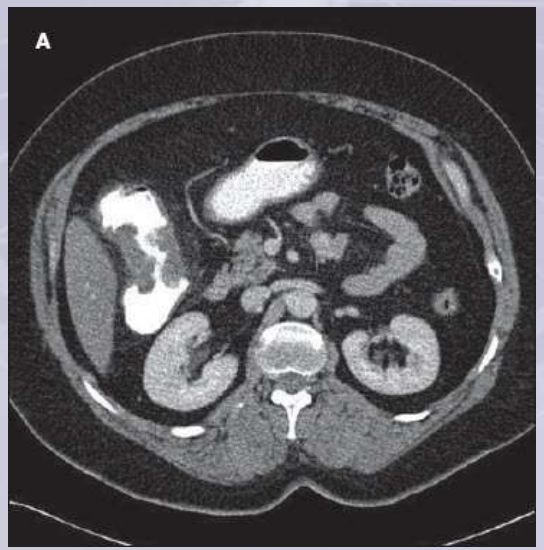
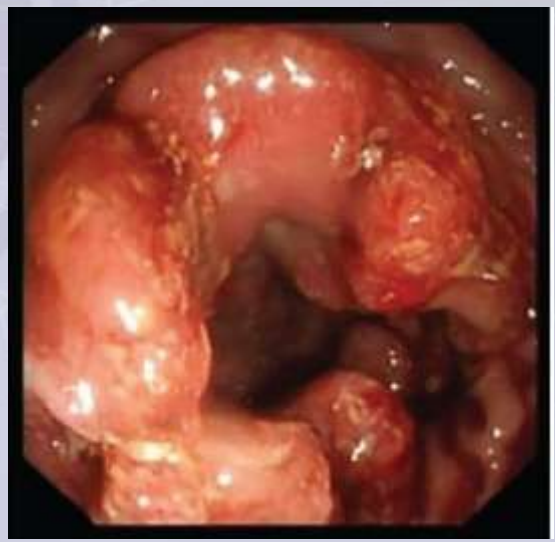
- If a colon cancer is suspected or being screened for; barium enema, CT colonography or colonoscopy may be utilized for diagnosis
- Colonoscopy is preferred as it is the only method that can achieve tissue diagnosis
- Most common colon cancer is adenocarcinoma







Staging of CRC

- Once a diagnosis of CRC has been established, patients should be sent for a CT scan of their chest, abdomen and pelvis to assess for metastatic disease
- Carcinoembryonic antigen (CEA) level, a glycoprotein produced in the GI tract during neonatal development and secreted by CRC cancers, should be drawn
- CEA is not a tool for diagnosis or staging, it is used for follow-up after treatment

Staging of CRC

STAGE	DESCRIPTION
TUMOR-NODE-METASTASIS (TNM) SYSTEM	
Primary Tumor	
TX	Primary tumor cannot be assessed
T0	No evidence of tumor in resected specimen (prior polypectomy or fulguration)
Tis	Carcinoma in situ
T1	Invades into submucosa
T2	Invades into muscularis propria
T3/T4	Depends on whether serosa is present
Serosa Present	
T3	Invades through muscularis propria into subserosa; invades serosa (but not through); invades pericolic fat within the leaves of the mesentery
T4	Invades through serosa into free peritoneal cavity or through serosa into a contiguous organ
NP Serosa (distal two thirds of rectum, posterior left or right colon)	
T3	Invades through muscularis propria
T4	Invades other organs (vagina, prostate, ureter, kidney)
Regional Lymph Node Involvement	
NX	Nodes cannot be assessed (e.g., local excision only)
N0	No regional node metastases
N1	1–3 positive nodes
N2	4 or more positive nodes
N3	Central nodes positive
Distant Metastasis	
MX	Presence of distant metastases cannot be assessed
M0	No distant metastases
M1	Distant metastases present

Stage		Description	
0	Tis	N0	M0
I	T1,2	N0	M0
IIA	T3	N0	M0
IIB	T4	N0	M0
IIIA	T1,2	N1	M0
IIIB	T3,4	N1	M0
IIIC	Any T	N2	M0
IV	Any T	Any N	M1

DUKES STAGING SYSTEM CORRELATED WITH TNM SYSTEM	
Dukes A	T1, N0, M0 (stage I)
	T2, N0, M0 (stage I)
Dukes B	T3, N0, M0 (stage II)
	T4, N0, M0 (stage II)
Dukes C	T (any), N1, M0; T (any), N2, M0 (stage III)
Dukes D	T (any), N (any), M1 (stage IV)

Prognosis

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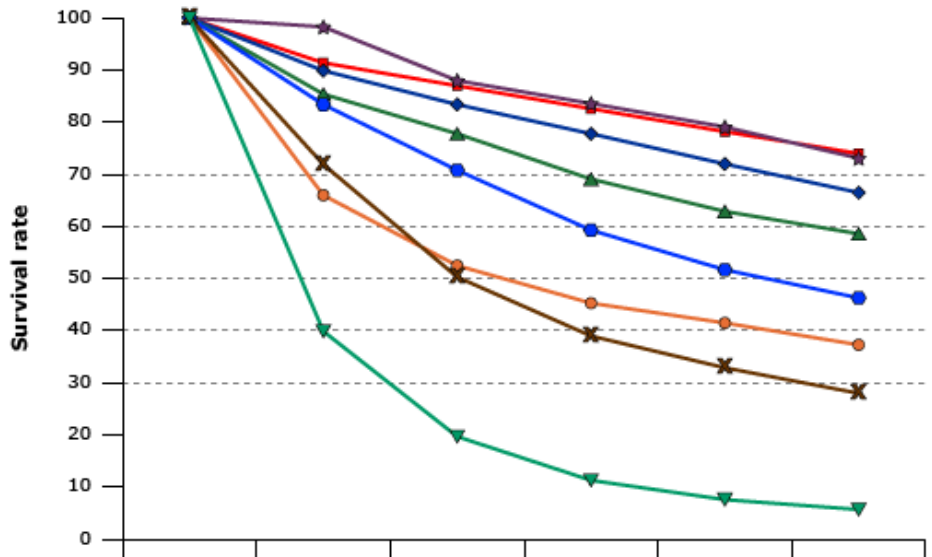
Observed survival rates for 28,491 cases with adenocarcinoma of the colon



	0	1	2	3	4	5
I	100.0	91.4	87.0	82.6	78.2	74.0
IIA	100.0	89.9	83.4	77.8	72.0	66.5
IIB	100.0	85.4	77.8	69.1	62.9	58.6
IIC	100.0	66.0	52.5	45.3	41.5	37.3
IIIA	100.0	98.3	88.0	83.6	79.1	73.1
IIIB	100.0	83.4	70.8	59.3	51.7	46.3
IIIC	100.0	71.9	50.3	39.0	32.9	28.0
IV	100.0	39.9	19.7	11.3	7.6	5.7

Years from diagnosis

Data from the SEER 1973-2005 Public Use File diagnosed in years 1998-2000. Stage I includes 7417; Stage IIA, 9956; Stage IIB, 997; Stage IIC, 725; Stage IIIA, 868; Stage IIIB, 1492; Stage IIIC, 2000; and Stage IV, 5036.

Management of CRC

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- Currently surgical resection is the only way to achieve cure in CRC
- Principle of surgical resection is to remove the primary cancer along with the major vascular pedicles and lymphatic drainage of the diseased segment of colon and to remove en bloc any invasion of the cancer to adjacent structures
- Both open and laparoscopic approaches to resection have demonstrated equivalent cure rates and no difference in perioperative complications
- After full workup, plan for treatment can be done alone with the surgeon or in conjunction with a multi-disciplinary team depending on the complexity

Segmental colon resection

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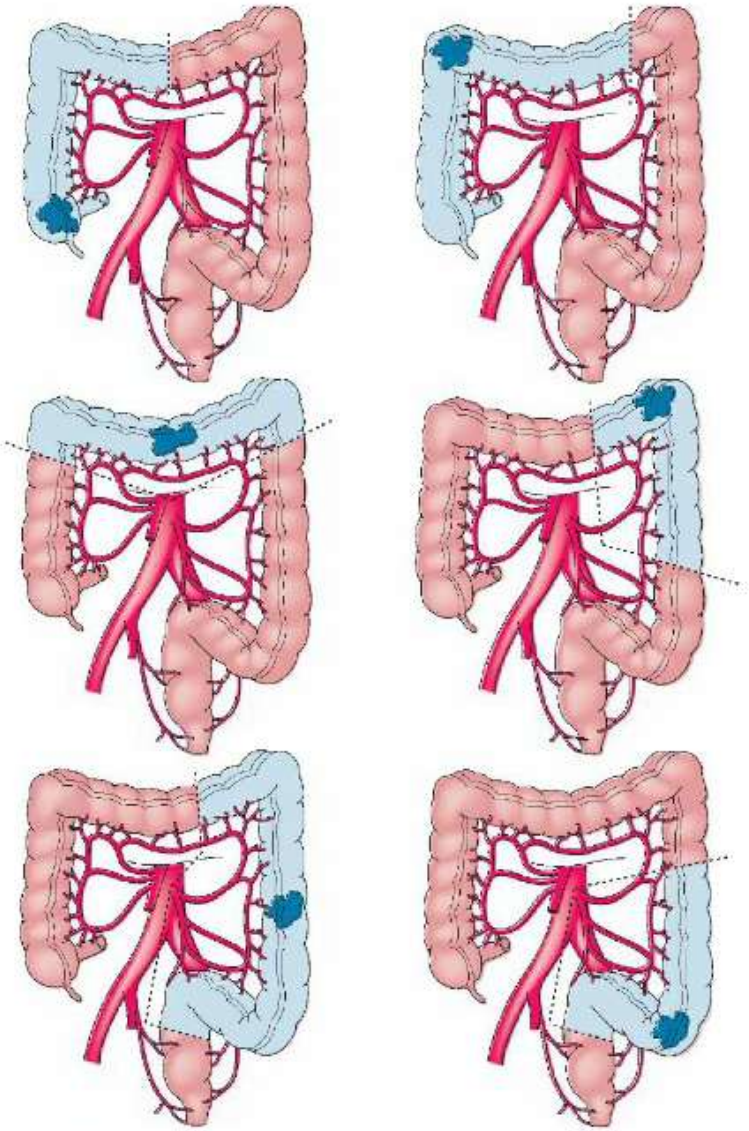
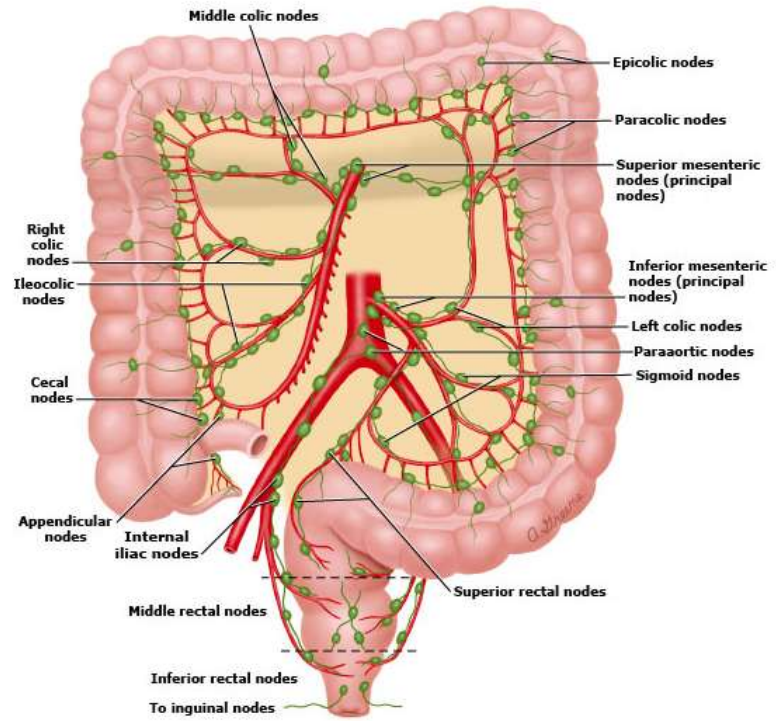


FIGURE 68.10. Segmental resections for cancers of the colon and upper third of the rectum.



Emergency Colon Surgery

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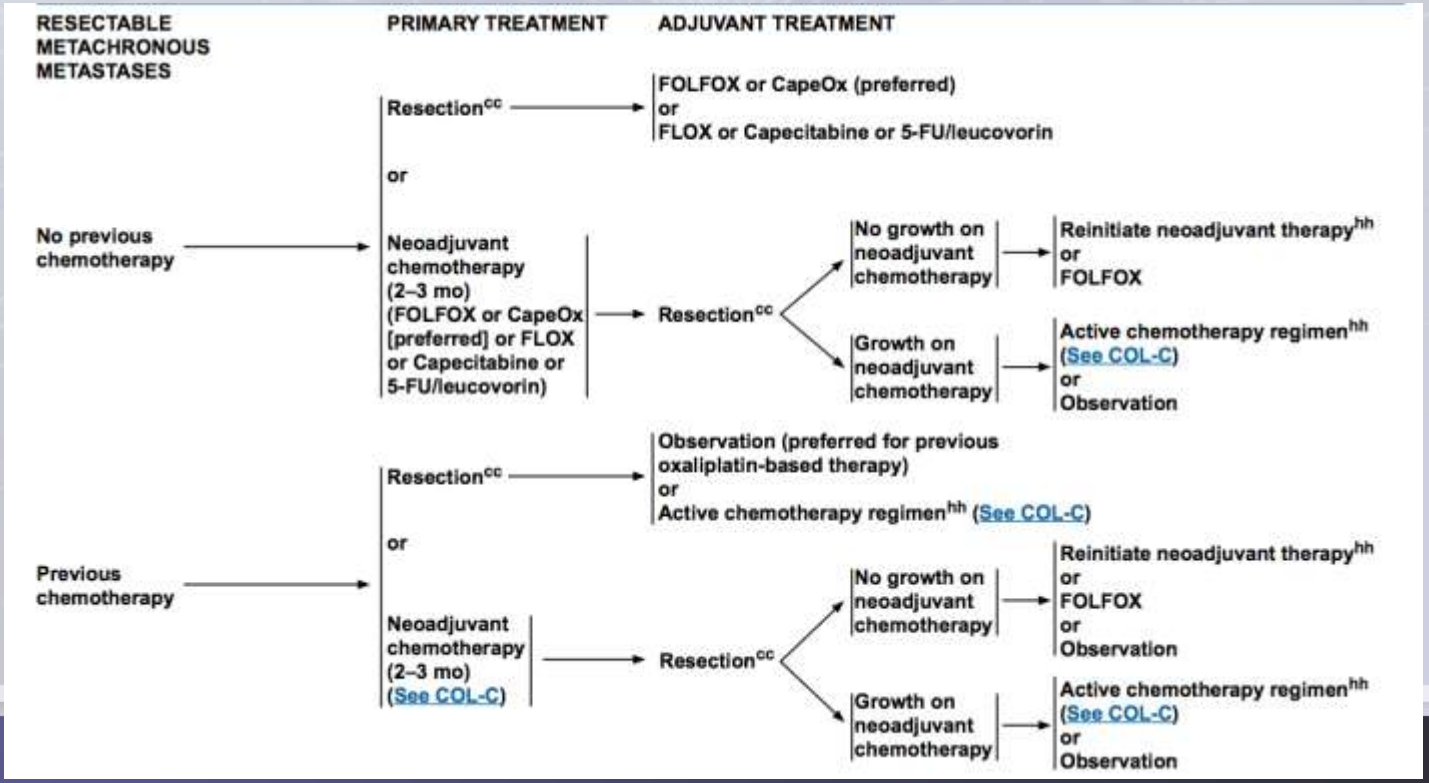
- Patients may present with colonic obstruction, or with colonic perforation and peritonitis
- Urgent operations are indicated in the setting of complete obstruction, perforation with frank contamination, peritonitis or sepsis
- In these setting, primary anastomosis post resection may not be feasible and an ostomy may be brought out
- In patients with a near-obstructing mass, a colonic stent may be considered as a bridge to planned surgery, although this is generally reserved for patients are high risk for surgery and would benefit from medical optimization

Neo-adjuvant therapy

- Preoperative radiotherapy generally does not play a role in colon cancers for curative intent (very different from rectal cancer)
- Patients presenting with potentially resectable metastatic disease (typically lung and liver mets) may go for neoadjuvant chemotherapy prior to resection



Principes of Pathologic Review

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- After resection of the primary tumour, several pathologic features of the tumour need to be reported to aid in possible adjuvant therapy as well as timing of followup:
  Grade
  T-stage (depth of penetration)
  Number of nodes evaluated and positive nodes
  Margins (Proximal, distal, and radial)
  Lymphovascular invasion
  Perineural invasion
  Extranodal tumour deposits

Adjuvant therapy for CRC

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- The role of adjuvant therapy depends on the stage of disease and patient factors, however in general

stage one – no role for adjuvant therapy

stage two – adjuvant therapy may offer some benefit, but studies still unclear

Predicted five year DFS estimates for patients with node-negative colon cancer

Disease stage	Low grade		High grade	
	Surgery alone, percent	Surgery and chemo, percent	Surgery alone, percent	Surgery and chemo, percent
T3N0	73 (69 to 76)	77 (74 to 80)	65 (60 to 70)	70 (65 to 74)
T4N0	60 (54 to 68)	66 (59 to 73)	51 (43 to 60)	57 (49 to 66)

stage three/four – adjuvant therapy has proven benefit
Radiation therapy can be added to T4 tumours affixed to other structures or with positive resection margin

Adjuvant therapy for CRC

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- First line therapy typically involves treatment with FOLFOX or FOLFIRI +/- avastin

  FOL – Folinic acid, Allows for purine/pyrimidine synthesis in the setting of 5-FU therapy
  F – Fluorouracil (5-FU), Blocks synthesis of thymidine
  OX – Oxaliplatin – Platinum-based cytotoxic agent that prevents DNA transcription and replication
  IRI – irinotecan, a topoisomerase inhibitor

  Avastin – Bevacizumab, monoclonal antibody that inhibits VEG-F

Adjuvant therapy for CRC

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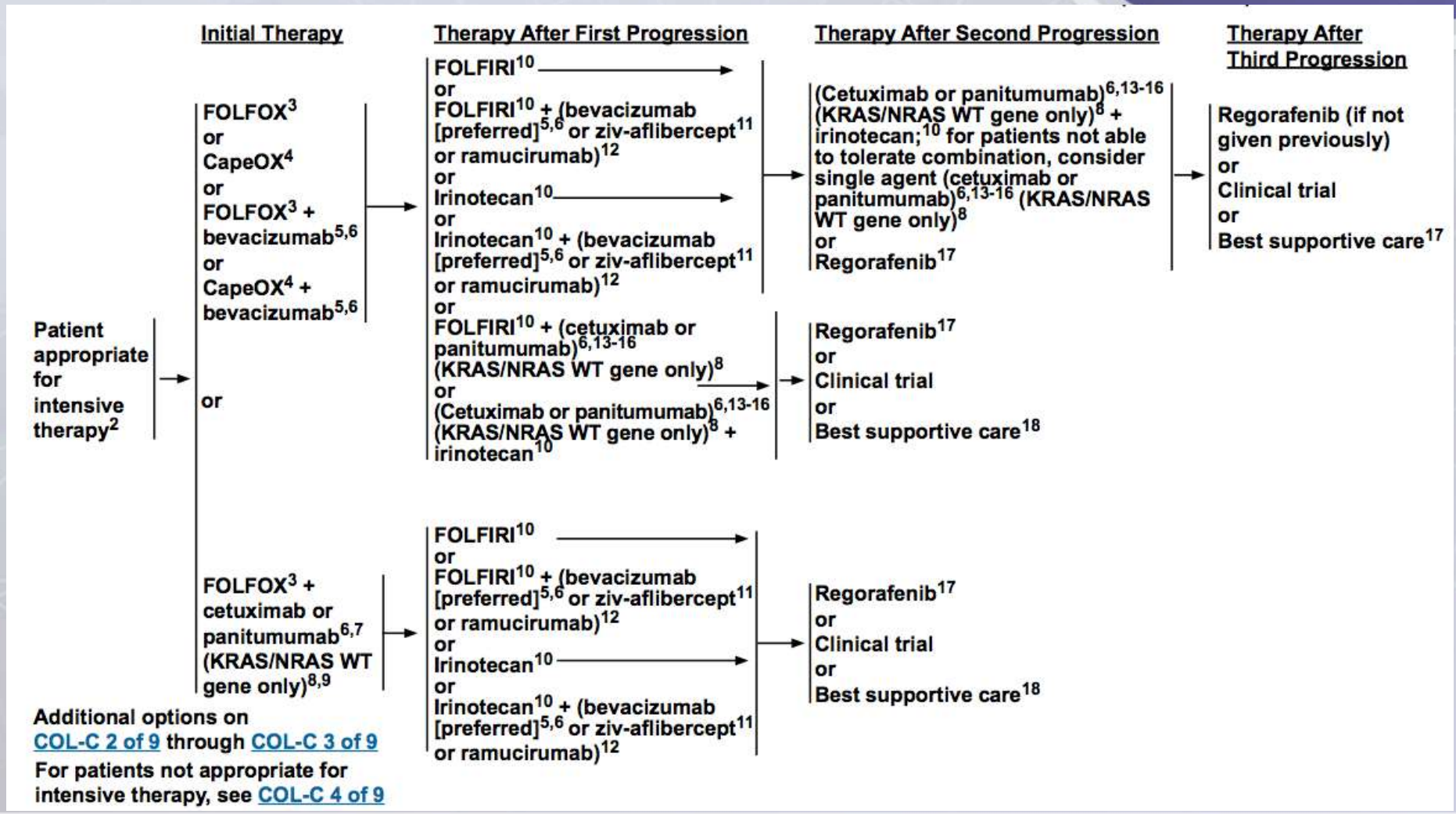
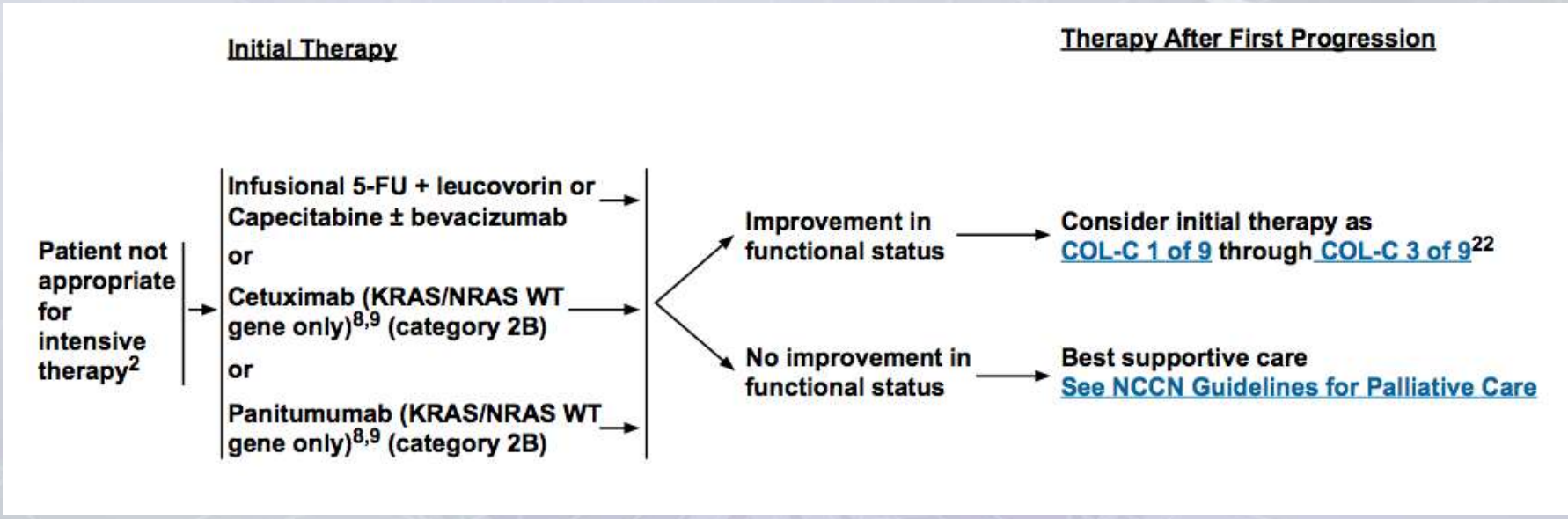


Additional options on COL-C 2 of 9 through COL-C 3 of 9

For patients not appropriate for intensive therapy, see COL-C 4 of 9

Nonoperative metastatic disease



Capecitabine – Oral prodrug to 5-FU

Panitumumab – Inhibits EGFR and subsequently cell growth

Postoperative follow-up

GUIDELINES FOR SURVEILLANCE STUDIES AFTER RESECTION OF STAGE II OR III COLORECTAL CANCER[a]

TEST	RECOMMENDATIONS
Carcinoembryonic	If patient is medically fit to undergo liver resection for liver metastases, evaluate antigen every 2–3 mo for 2 y or more; an elevated result warrants further evaluation for metastatic disease but does not justify systemic therapy for presumed disease
History and physical examination	Every 3–6 mo for first 2–3 y, biannually for next 2 years, and annually thereafter
Colonoscopy	After initial clearing colonoscopy to rule out synchronous lesions, surveillance colonoscopy at first year postoperatively. If normal, thereafter, every 3–5 y to detect new cancers and polyps
Computed tomography	Individualized
Chest roentgenography	Individualized

[a]Endorsed by the American Society of Clinical Oncology.

Palliative CRC

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- Although resection and cure is not an option with these patients, there are interventions offered by surgeons to alleviate symptoms and prolong life
- Generally complications of diffuse disease include obstruction, perforation and bleeding
- Surgical options include primary resection and anastomosis, diverting ostomy and surgical bypass
- Colonic stenting has a role in large bowel obstructions secondary to CRC who are not ideal operative candidates

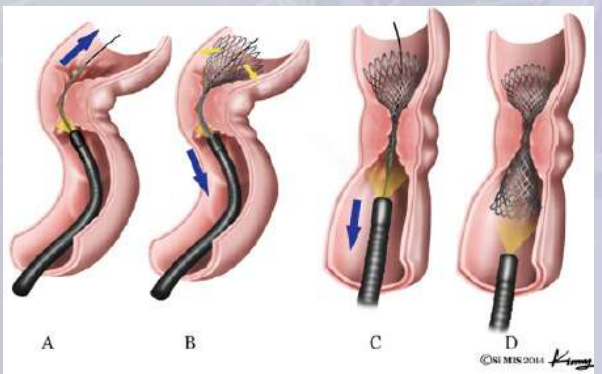
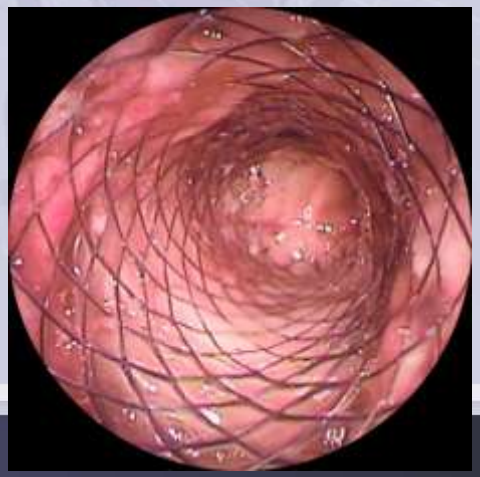


Figure 1 Technique of SEMS placement in acute colorectal obstruction. A: Passing stent and guide wire through lesion with contrast injection. B: Partial stent deployment. C: Pull back stent and scope until fair part of stent reach upper border. D: Fully deployment of SEMS.



Laparoscopic vs Open for CRC

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ORIGINAL ARTICLE

A Comparison of Laparoscopically Assisted and Open Colectomy for Colon Cancer

The Clinical Outcomes of Surgical Therapy Study Group*

ABSTRACT

BACKGROUND

Minimally invasive, laparoscopically assisted surgery was first considered in 1990 for patients undergoing colectomy for cancer. Concern that this approach would compromise survival by failing to achieve a proper oncologic resection or adequate staging or by altering patterns of recurrence (based on frequent reports of tumor recurrences within surgical wounds) prompted a controlled trial evaluation.

METHODS

We conducted a noninferiority trial at 48 institutions and randomly assigned 872 patients with adenocarcinoma of the colon to undergo open or laparoscopically assisted colectomy performed by credentialed surgeons. The median follow-up was 4.4 years. The primary end point was the time to tumor recurrence.

RESULTS

At three years, the rates of recurrence were similar in the two groups — 16 percent among patients in the group that underwent laparoscopically assisted surgery and 18 percent among patients in the open-colectomy group (two-sided P=0.32; hazard ratio for recurrence, 0.86; 95 percent confidence interval, 0.63 to 1.17). Recurrence rates in surgical wounds were less than 1 percent in both groups (P=0.50). The overall survival rate at three years was also very similar in the two groups (86 percent in the laparoscopic-surgery group and 85 percent in the open-colectomy group; P=0.51; hazard ratio for death in the laparoscopic-surgery group, 0.91; 95 percent confidence interval, 0.68 to 1.21), with no significant difference between groups in the time to recurrence or overall survival for patients with any stage of cancer. Perioperative recovery was faster in the laparoscopic-surgery group than in the open-colectomy group, as reflected by a shorter median hospital stay (five days vs. six days, P<0.001) and briefer use of parenteral narcotics (three days vs. four days, P<0.001) and oral analgesics (one day vs. two days, P=0.02). The rates of intraoperative complications, 30-day postoperative mortality, complications at discharge and 60 days, hospital readmission, and reoperation were very similar between groups.

CONCLUSIONS

In this multi-institutional study, the rates of recurrent cancer were similar after laparoscopically assisted colectomy and open colectomy, suggesting that the laparoscopic approach is an acceptable alternative to open surgery for colon cancer.

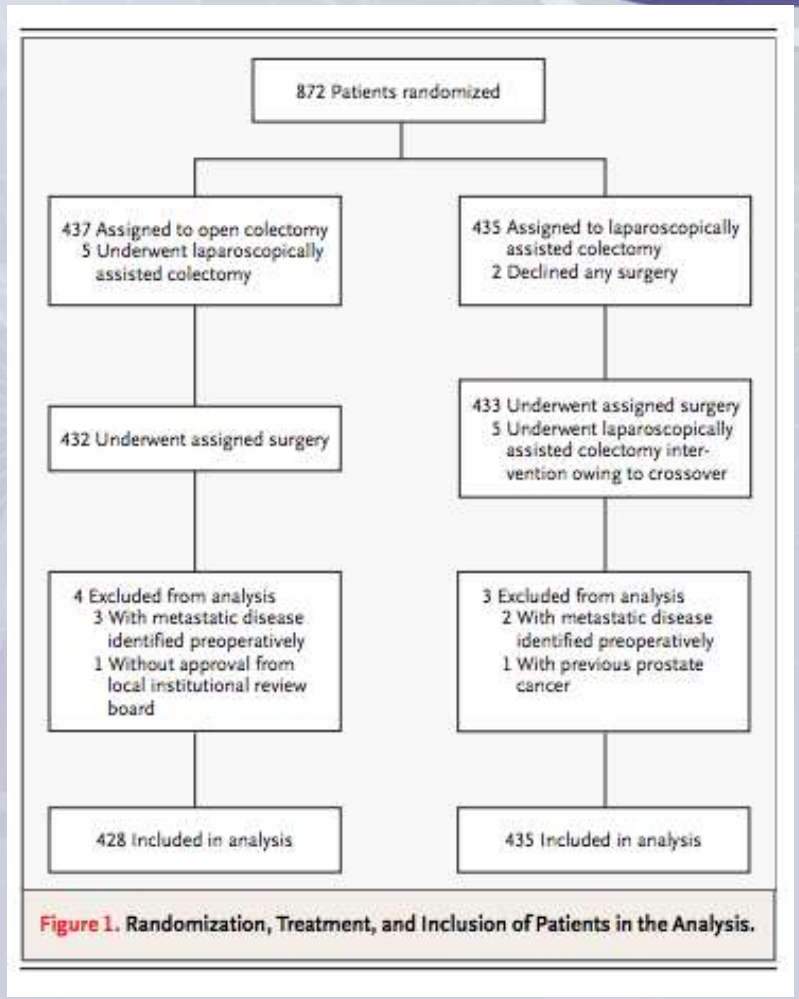

Figure 1. Randomization, Treatment, and Inclusion of Patients in the Analysis.

Laparoscopic vs Open for CRC

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Table 1. Baseline Characteristics of the Patients and Tumors.

Characteristic	Open Colectomy (N=428)	Laparoscopically Assisted Colectomy (N=435)
Age — yr		
Median	69	70
Range	29–94	28–96
Female sex — no. (%)	220 (51)	212 (49)
American Society of Anesthesiologists class — no. (%)		
1 or 2	367 (86)	373 (86)
3	61 (14)	62 (14)
Location of primary tumor — no. (%)		
Right side of colon	232 (54)	237 (54)
Left side of colon	32 (7)	32 (7)
Sigmoid colon	164 (38)	166 (38)
TNM stage — no. (%)*		
0	33 (8)	20 (5)
I	112 (26)	153 (35)
II	146 (34)	136 (31)
III	121 (28)	112 (26)
IV	16 (4)	10 (2)
Unknown	0	4 (1)
Depth of invasion — no. (%)		
Submucosal, not muscle wall	59 (14)	67 (15)
Muscle wall, not serosal or perirectal	76 (18)	105 (24)
Serosal	237 (55)	226 (52)
Beyond serosa or perirectal fat, involvement of contiguous structure	23 (5)	12 (3)
Not applicable (benign pathological findings)	33 (8)	20 (5)
Unknown	0	5 (1)
Grade of differentiation — no. (%)		
1 (Well)	44 (10)	36 (8)
2 (Moderately)	271 (63)	315 (72)
3 (Poorly)	72 (17)	51 (12)
4 (Undifferentiated)	6 (1)	5 (1)
Not applicable (benign pathological findings)	33 (8)	20 (5)
Unknown	2 (<1)	8 (2)
No. of previous operations — no. (%)		
0	233 (54)	246 (57)
1	120 (28)	113 (26)
>1	37 (9)	41 (9)
Unknown	38 (9)	35 (8)

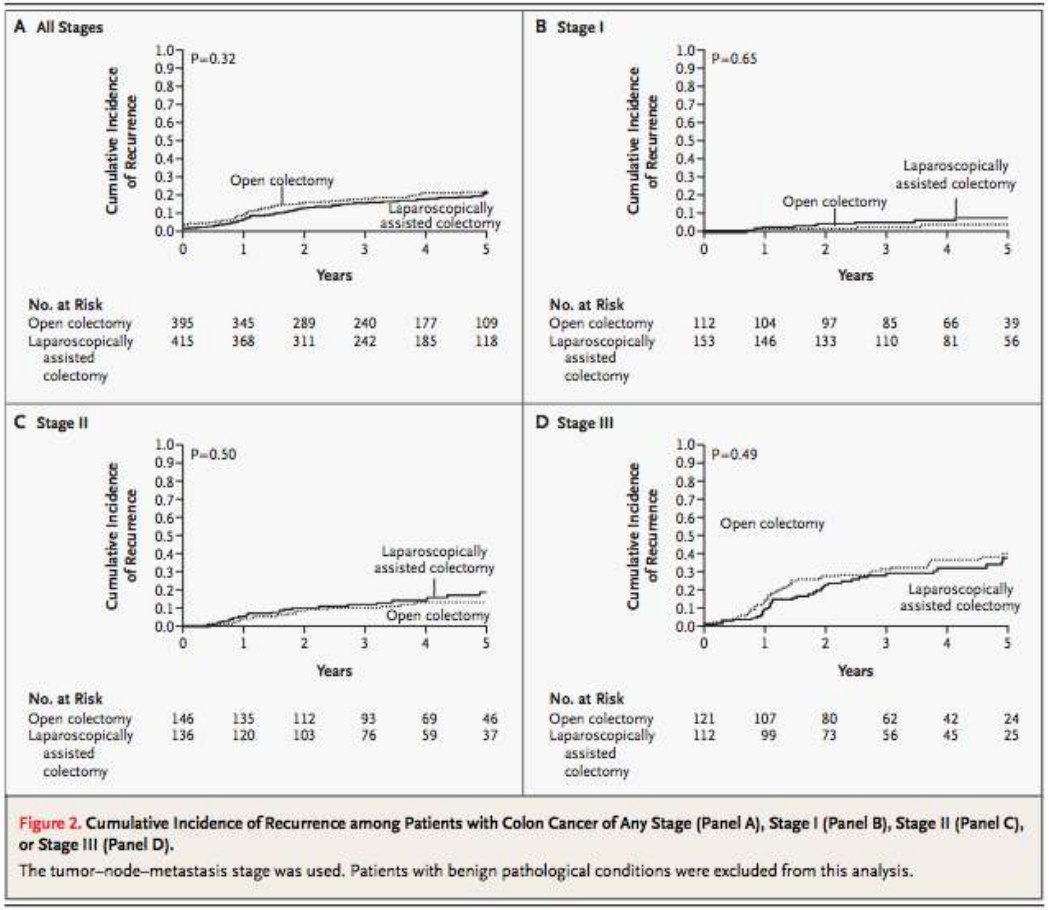

Figure 2. Cumulative Incidence of Recurrence among Patients with Colon Cancer of Any Stage (Panel A), Stage I (Panel B), Stage II (Panel C), or Stage III (Panel D).

The tumor–node–metastasis stage was used. Patients with benign pathological conditions were excluded from this analysis.

Laparoscopic vs Open for CRC

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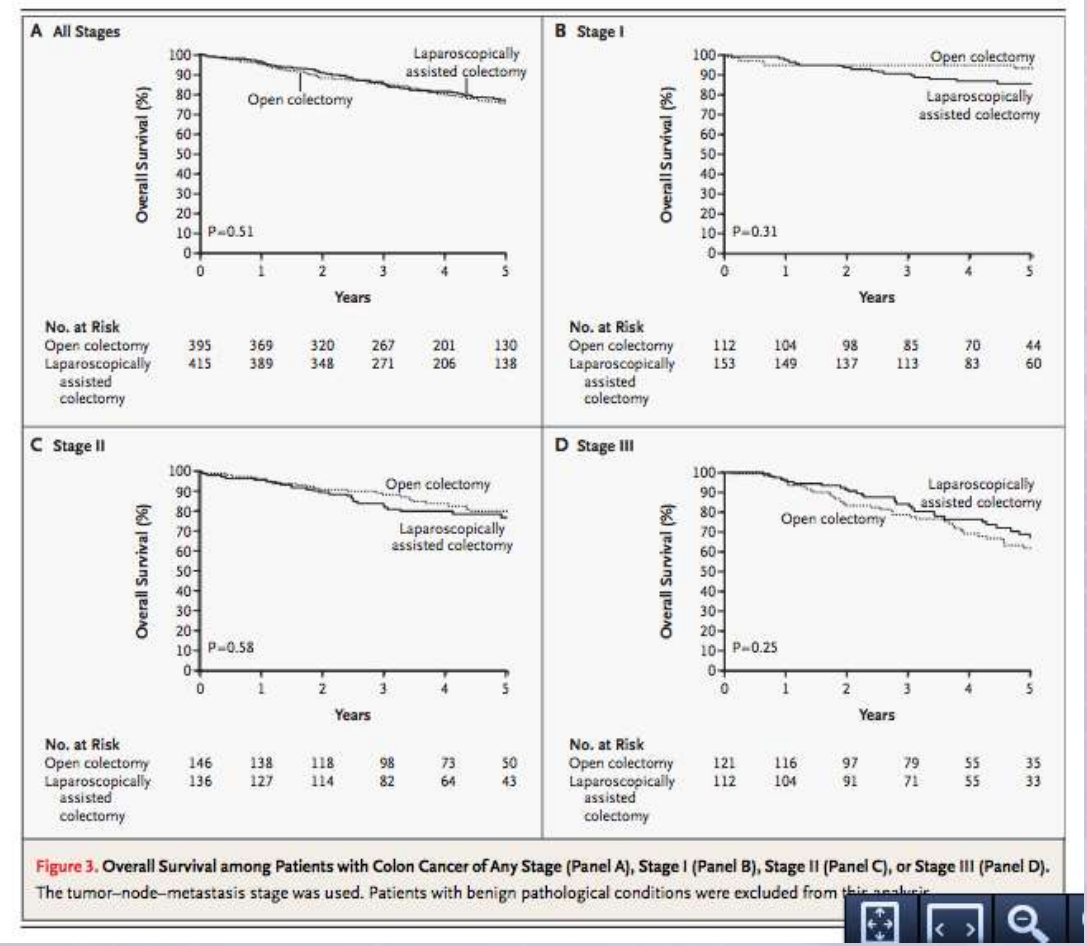

Figure 3. Overall Survival among Patients with Colon Cancer of Any Stage (Panel A), Stage I (Panel B), Stage II (Panel C), or Stage III (Panel D).
The tumor–node–metastasis stage was used. Patients with benign pathological conditions were excluded from their analysis.

No difference in perioperative complications, recurrence or 5 year survival

Thanks for your attention

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