A Teaching Affiliate
of Harvard Medical School

Colon Cancer 2015

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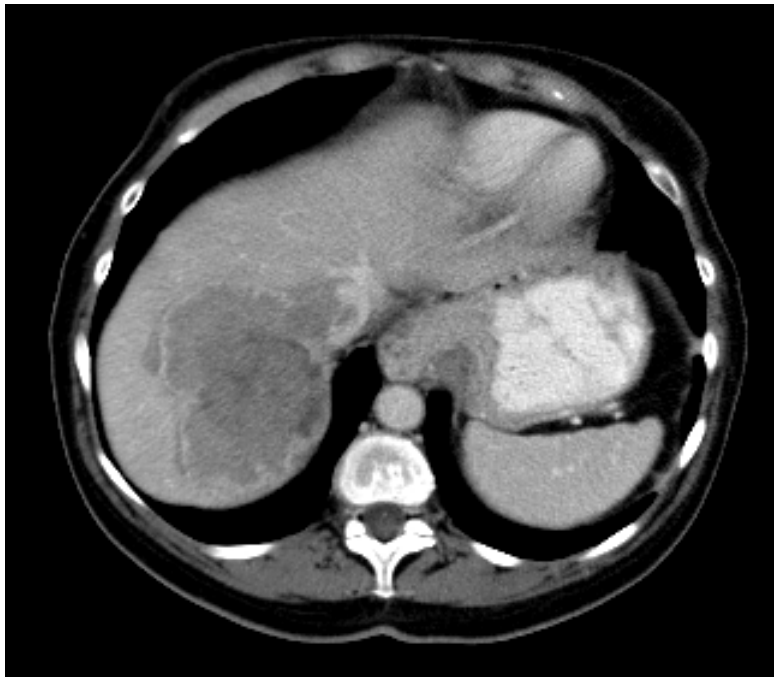
Colon Cancer Case presentation



- 72yo woman presented 1/03 abd discomfort and nausea
- Found to have Hct 30 MCV 71
- Alk Ph 150
- USG of pelvis to f/u fibroids demonstrated liver mass
- Colonoscopy: splenic flexure mass = adenocarcinoma

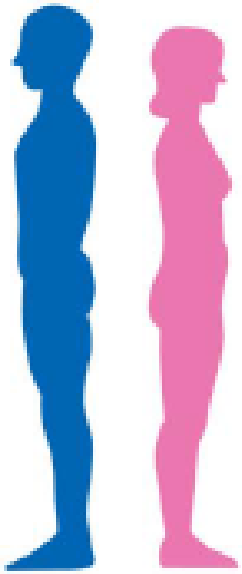
Agenda

- Statistics and Epidemiology
- Inherited Syndromes
- Approach to Screening
- Treatment

Statistics

Estimated New Cases

Males			Females		
Prostate	220,800	26%	Breast	231,840	29%
Lung & bronchus	115,610	14%	Lung & bronchus	105,590	13%
Colon & rectum	69,090	8%	Colon & rectum	63,610	8%
Urinary bladder	56,320	7%	Uterine corpus	54,870	7%
Melanoma of the skin	42,670	5%	Thyroid	47,230	6%
Non-Hodgkin lymphoma	39,850	5%	Non-Hodgkin lymphoma	32,000	4%
Kidney & renal pelvis	38,270	5%	Melanoma of the skin	31,200	4%
Oral cavity & pharynx	32,670	4%	Pancreas	24,120	3%
Leukemia	30,900	4%	Leukemia	23,370	3%
Liver & intrahepatic bile duct	25,510	3%	Kidney & renal pelvis	23,290	3%
All Sites	**848,200**	**100%**	**All Sites**	**810,170**	**100%**



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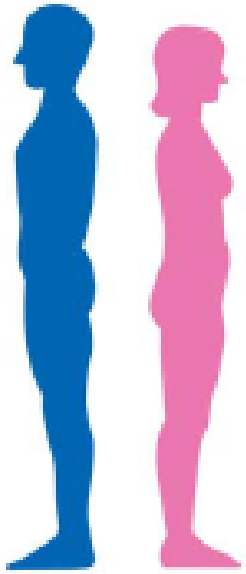
Statistics

Estimated Deaths

Males			Females		
Lung & bronchus	86,380	28%	Lung & bronchus	71,660	26%
Prostate	27,540	9%	Breast	40,290	15%
Colon & rectum	26,100	8%	Colon & rectum	23,600	9%
Pancreas	20,710	7%	Pancreas	19,850	7%
Liver & intrahepatic bile duct	17,030	5%	Ovary	14,180	5%
Leukemia	14,210	5%	Leukemia	10,240	4%
Esophagus	12,600	4%	Uterine corpus	10,170	4%
Urinary bladder	11,510	4%	Non-Hodgkin lymphoma	8,310	3%
Non-Hodgkin lymphoma	11,480	4%	Liver & intrahepatic bile duct	7,520	3%
Kidney & renal pelvis	9,070	3%	Brain & other nervous system	6,380	2%
All Sites	**312,150**	**100%**	**All Sites**	**277,280**	**100%**



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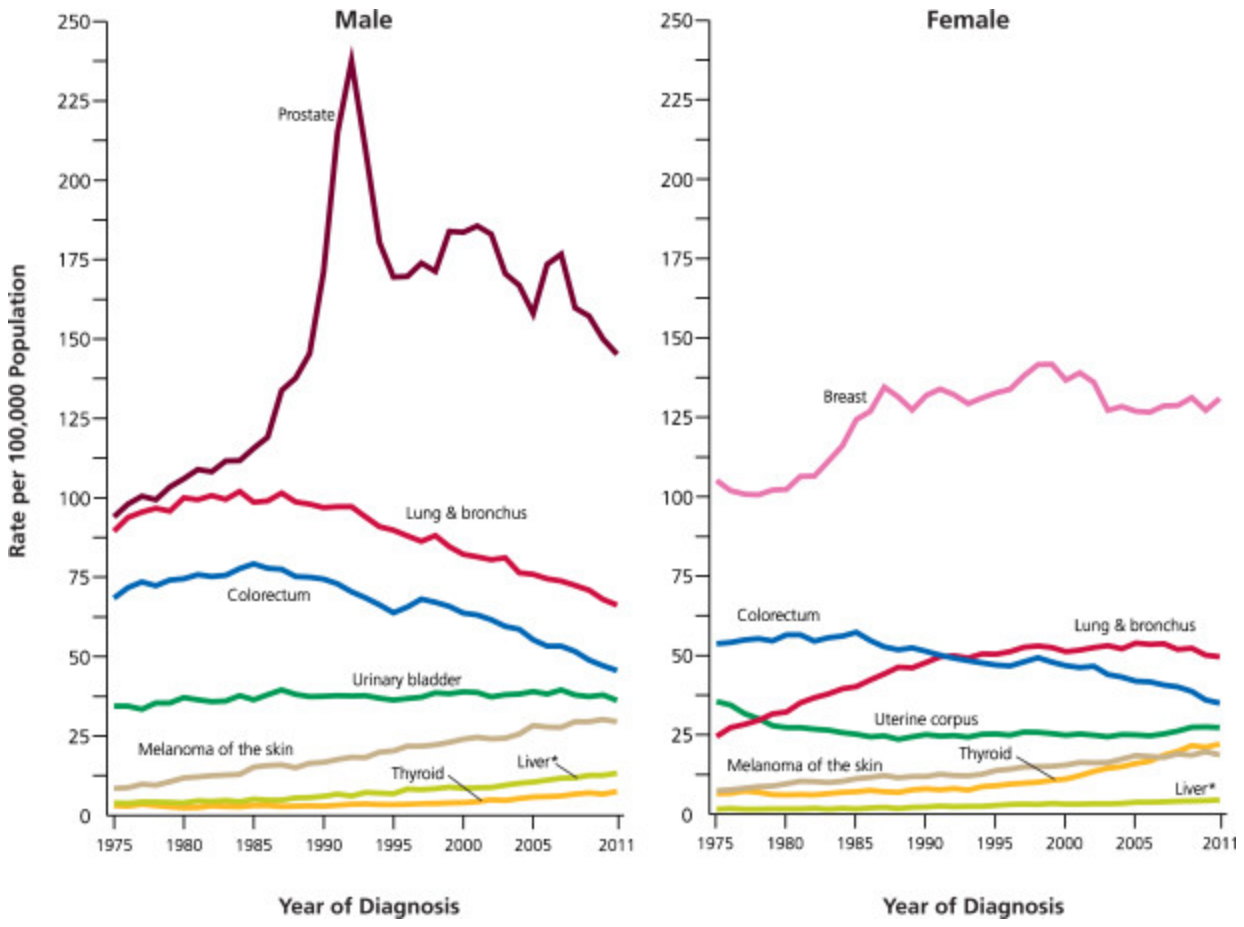
Cancer Trends



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Probability of Developing Cancer

TABLE 4. Probability (%) of Developing Invasive Cancer Within Selected Age Intervals by Sex, United States, 2009 to 2011*

		BIRTH TO 49	50 TO 59	60 TO 69	≥70	BIRTH TO DEATH
All sites†	Male	3.4 (1 in 29)	6.7 (1 in 15)	15.1 (1 in 7)	36.0 (1 in 3)	43.3 (1 in 2)
	Female	5.4 (1 in 19)	6.0 (1 in 17)	10.0 (1 in 10)	26.4 (1 in 4)	37.8 (1 in 3)
Breast	Female	1.9 (1 in 53)	2.3 (1 in 44)	3.5 (1 in 29)	6.7 (1 in 15)	12.3 (1 in 8)
Colorectum	Male	0.3 (1 in 300)	0.7 (1 in 148)	1.3 (1 in 80)	3.9 (1 in 26)	4.8 (1 in 21)
	Female	0.3 (1 in 326)	0.5 (1 in 193)	0.9 (1 in 112)	3.5 (1 in 28)	4.5 (1 in 22)
Kidney & renal pelvis	Male	0.2 (1 in 468)	0.3 (1 in 292)	0.6 (1 in 157)	1.3 (1 in 76)	2.0 (1 in 49)
	Female	0.1 (1 in 752)	0.2 (1 in 586)	0.3 (1 in 321)	0.7 (1 in 134)	1.2 (1 in 84)
Leukemia	Male	0.2 (1 in 419)	0.2 (1 in 598)	0.4 (1 in 271)	1.3 (1 in 75)	1.7 (1 in 59)
	Female	0.2 (1 in 516)	0.1 (1 in 968)	0.2 (1 in 464)	0.9 (1 in 117)	1.2 (1 in 84)
Lung & bronchus	Male	0.2 (1 in 578)	0.7 (1 in 140)	2.0 (1 in 49)	6.6 (1 in 15)	7.4 (1 in 13)
	Female	0.2 (1 in 541)	0.6 (1 in 173)	1.6 (1 in 64)	4.9 (1 in 20)	6.2 (1 in 16)
Melanoma of the skin‡	Male	0.3 (1 in 294)	0.4 (1 in 240)	0.8 (1 in 129)	2.1 (1 in 47)	3.0 (1 in 34)
	Female	0.5 (1 in 207)	0.3 (1 in 323)	0.4 (1 in 246)	0.9 (1 in 112)	1.9 (1 in 53)
Non-Hodgkin lymphoma	Male	0.3 (1 in 366)	0.3 (1 in 347)	0.6 (1 in 173)	1.8 (1 in 55)	2.4 (1 in 42)
	Female	0.2 (1 in 543)	0.2 (1 in 483)	0.4 (1 in 233)	1.4 (1 in 72)	1.9 (1 in 52)
Prostate	Male	0.3 (1 in 304)	2.3 (1 in 44)	6.3 (1 in 16)	10.9 (1 in 9)	15.0 (1 in 7)
Thyroid	Male	0.2 (1 in 585)	0.1 (1 in 827)	0.2 (1 in 653)	0.2 (1 in 464)	0.6 (1 in 174)
	Female	0.7 (1 in 135)	0.3 (1 in 288)	0.3 (1 in 306)	0.4 (1 in 263)	1.7 (1 in 60)
Uterine cervix	Female	0.3 (1 in 358)	0.1 (1 in 840)	0.1 (1 in 842)	0.2 (1 in 565)	0.6 (1 in 154)
Uterine corpus	Female	0.3 (1 in 367)	0.6 (1 in 170)	0.9 (1 in 109)	1.3 (1 in 76)	2.7 (1 in 37)

*For people free of cancer at beginning of age interval.

†All sites excludes basal cell and squamous cell skin cancers and in situ cancers except urinary bladder.

‡Probabilities are for whites.

5 Leading Cancer Deaths

TABLE 9. Five Leading Types of Cancer Death by Age and Sex, United States, 2011

ALL AGES	<20	20 TO 39	40 TO 59	60 TO 79	≥80
MALE					
ALL SITES **302,231**	**ALL SITES** **1,094**	**ALL SITES** **3,984**	**ALL SITES** **54,172**	**ALL SITES** **158,118**	**ALL SITES** **84,860**
Lung & bronchus 86,738	Brain & ONS 308	Leukemia 529	Lung & bronchus 14,347	Lung & bronchus 51,951	Lung & bronchus 20,216
Prostate 27,970	Leukemia 293	Brain & ONS 491	Colorectum 5,789	Colorectum 13,088	Prostate 14,956
Colorectum 26,804	Bones & joints 107	Colorectum 442	Liver* 4,754	Prostate 11,732	Colorectum 7,480
Pancreas 18,881	Soft tissue (including heart) 80	NHL 278	Pancreas 3,676	Pancreas 10,594	Urinary bladder 4,785
Liver* 14,626	NHL 44	Soft tissue (including heart) 225	Esophagus 2,691	Liver* 7,467	Pancreas 4,510
FEMALE					
ALL SITES **274,460**	**ALL SITES** **828**	**ALL SITES** **4,407**	**ALL SITES** **50,445**	**ALL SITES** **129,632**	**ALL SITES** **89,145**
Lung & bronchus 70,219	Brain & ONS 242	Breast 1,041	Breast 11,340	Lung & bronchus 39,287	Lung & bronchus 19,694
Breast 40,931	Leukemia 226	Uterine cervix 417	Lung & bronchus 11,043	Breast 17,538	Breast 11,010
Colorectum 24,979	Soft tissue (including heart) 68	Leukemia 356	Colorectum 4,209	Colorectum 10,084	Colorectum 10,338
Pancreas 18,463	Bones & joints 67	Colorectum 344	Ovary 3,064	Pancreas 9,076	Pancreas 6,747
Ovary 14,346	Kidney & renal pelvis 23	Brain & ONS 303	Pancreas 2,578	Ovary 7,192	Leukemia 4,111

Colon Cancer

- Epidemiologic Associations
  - Western/urbanized societies
  - High meat
  - High saturated fat and cholesterol
  - Increased bowel anaerobic flora
  - Deconjugated fecal bile acid excretion
  - Diabetes Mellitus
  - Tobacco use
  - Obesity
  - Alcohol

Colon Cancer

- Epidemiologic Associations
  - Western/urbanized societies
  - High meat
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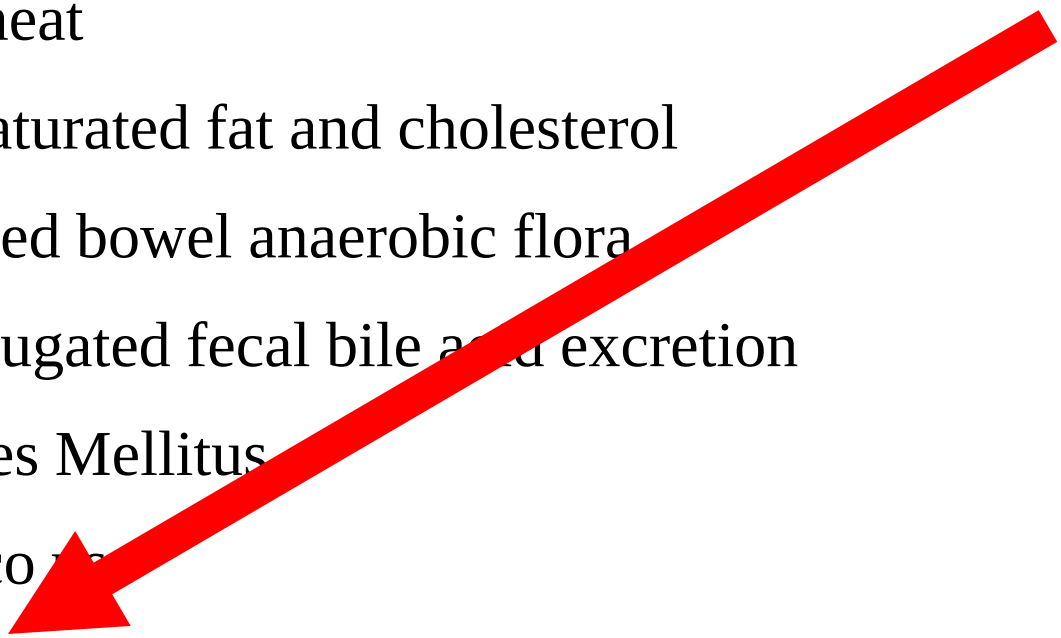
  - Increased bowel anaerobic flora
  - Deconjugated fecal bile a[illegible] excretion
  - Diabetes Mellitus
  - Tobacco [illegible]
  - Obesity
  - Alcohol



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Obesity and Cancer in Men

Table 1. RR for cancer per 5 kg/m^2 higher BMI and most likely causal mechanism: Males

Cancer type	RR	Causal mechanism
Esophageal adenocarcinoma	1.52[a]	Reflux esophagitis and chronic irritation
Thyroid	1.33[c]	Unknown
Colon	1.24[a]	Insulin
Renal	1.24[a]	In part though hypertension
Liver	1.24	Fatty liver cirrhosis
Malignant melanoma	1.17[b]	?
Multiple myeloma	1.11[a]	Inflammatory pathways—IL-6
Rectum	1.09[a]	?
Gallbladder	1.09	Chronic secretion-gallstones and irritation
Leukemia	1.08[b]	?
Pancreas	1.07	Possible insulin pathway
Non-Hodgkin's lymphoma	1.06[a]	Inflammatory pathways—IL-6
Prostate[a]	1.03	?
Lung	0.76[a]	Smoking leads to leanness and causes lung cancer
Esophageal squamous	0.71[a]	Smoking leads to leanness and causes squamous esophageal cancer

Shown is the RR for a five-point greater BMI—for example, the RR linked to a BMI of 28 compared with a BMI of 23, or a BMI of 32 compared with a BMI of 27.
[a]$p < .0001$.
[b]$p < .01$.
[c]$p < .05$.
[d]Biased to null because this includes predominantly low-grade lesions.
Abbreviations: BMI, body mass index; IL, interleukin; RR, relative risk.
Based on Figure 3 of Renehan AG, Tyson M, Egger M et al. Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. Lancet 2008;371:569–578.

Obesity and Cancer in Women

Table 2. RR for cancer per 5 kg/m^2 higher BMI and most likely causal mechanism: Females

Cancer type	RR	Causal mechanism
Endometrium	1.59[a]	Endogenous estrogen
Gallbladder	1.59[c]	Chronic secretion-gallstones and irritation
Esophageal adenocarcinoma	1.51[a]	Reflux esophagitis and chronic irritation
Renal	1.34[a]	In part through hypertension
Leukemia	1.17[c]	Unknown
Thyroid	1.14[b]	Unknown
Breast (postmenopausal)	1.12[c]	Endogenous estrogen
Pancreas	1.12[c]	Possible insulin pathway
Multiple myeloma	1.11[a]	Inflammatory pathways—IL-6
Colon	1.09[a]	Insulin
Non-Hodgkin's lymphoma	1.07	Inflammatory pathways—IL-6
Liver	1.07	Fatty liver cirrhosis
Breast (premenopausal)	0.92[b]	Irregular menstrual cycles, hormones
Lung	0.8[c]	Smoking leads to leanness and causes lung cancer
Esophageal squamous	0.57[a]	Smoking leads to leanness and causes squamous esophageal cancer

RR for a five-point greater BMI—for example, the RR linked to a BMI of 28 compared with a BMI of 23, or a BMI of 32 compared with a BMI of 27.
[a]$p < .0001$.
[b]$p < .01$.
[c]$p < .05$.
Abbreviations: BMI, body mass index; IL, interleukin; RR, relative risk.
Based on Figure 4 of Renehan AG, Tyson M, Egger M et al. Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. Lancet 2008;371:569–578.

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Colon Cancer

- Epidemiologic Associations
  - IBD
    - Risk in UC correlates with extent, duration and severity of disease
    - Risk of cancer in UC 9% at 10 yrs, 20% at 20yrs, and >35% at 30 years
    - Total colectomy eliminates the risk
  - Cholecystectomy
  - Ureterocolic anastamoses
  - Pelvic Radiation
  - Low Vit D

Colon Cancer

- Protective Factors
  - NSAIDs, folate, calcium, estrogens prevent development of polyps
    - No clear benefit for prevention of cancer
    - What is the role in patients getting adequately screened?
  - Physical activity
  - Diets high in fish and low in red meat associated with reduced incidence of colorectal cancer
  - Out of favor: anti-oxidants and fiber

Colon Cancer

- Chemoprevention with Aspirin
  - Multiple retrospective studies: reduced risk of colorectal adenomas and cancer in regular aspirin users
  - The Nurses' Health Study: regular use of aspirin (2 standard aspirin tables per day) was associated with a 25 percent reduction in the risk of an adenoma (RR 0.75, 95 percent CI 0.66 to 0.84)
  - Randomized studies of aspirin after a diagnosis of colorectal adenoma/carcinoma demonstrate reduced rate of adenomas

Colon Cancer

- Chemoprevention with Aspirin
  - BUT, the Physician's Health Study (prospective) failed to demonstrate a significant effect of aspirin use on the incidence of colorectal cancer
  - SUMMARY: The overall risk/benefit of prolonged daily aspirin for the primary prevention of colorectal cancer is unknown

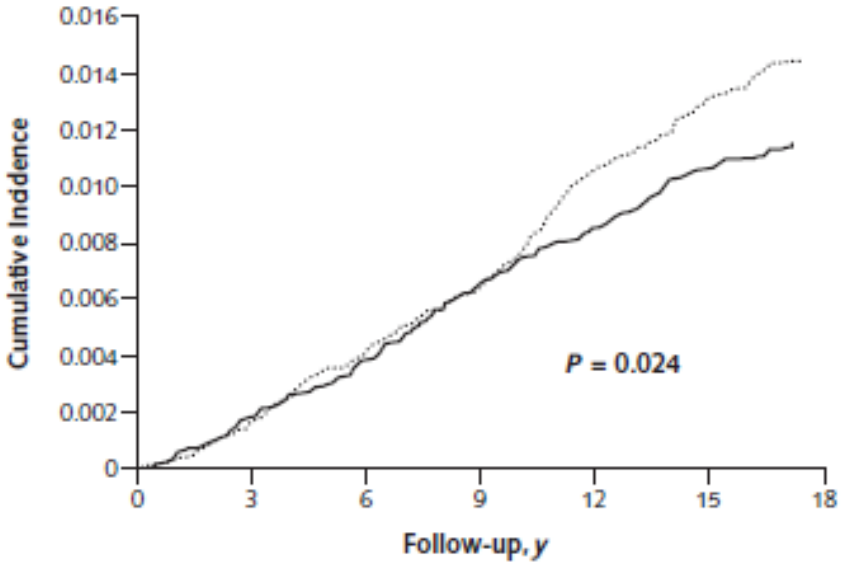
But…

Annals of Internal Medicine | ORIGINAL RESEARCH

Alternate-Day, Low-Dose Aspirin and Cancer Risk: Long-Term Observational Follow-up of a Randomized Trial

Nancy R. Cook, ScD; I-Min Lee, ScD; Shumin M. Zhang, ScD; M. Vinayaga Moorthy, PhD; and Julie E. Buring, ScD

C. Colorectal Cancer



Participants at risk, *n*

Aspirin	19 934	19 443	18 868	17 975	15 592	14 617
Placebo	19 942	19 467	18 857	17 977	15 424	14 358

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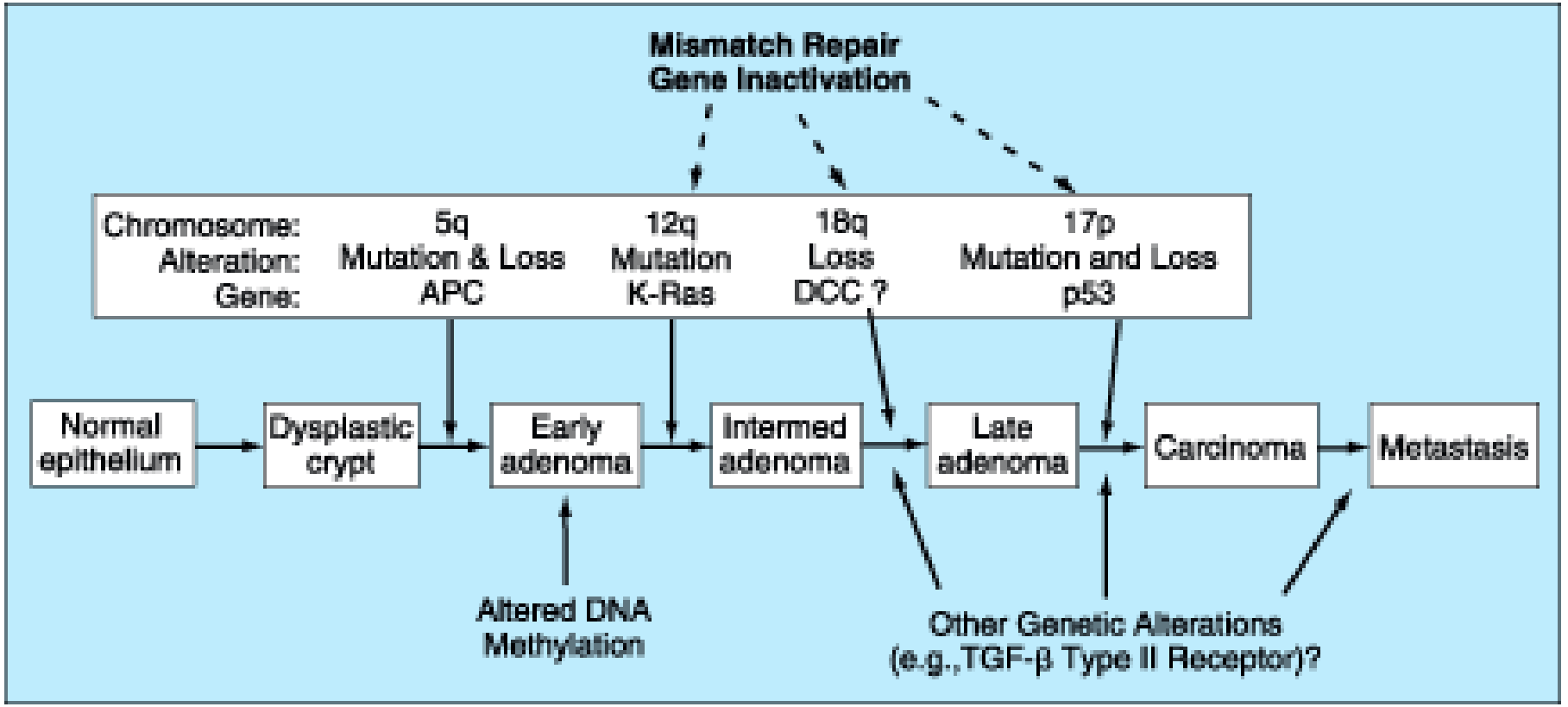
Colon Cancer

- Polyps:
  - hamartoma, hyperplastic, adenoma
- Adenomas are pre-malignant
  - Occur in 30-50% of adults
  - <1% polyps become cancer
  - Adenomatous polyps more likely to become cancer if sessile, villous, and > 1.5cm
  - Takes at least 5 yrs for polyp to become cancer
- Some hyperplastic polyps may be pre-malignant
  - Serrated polyps associated with right sided colon cancers that are braf mutant

Colon Cancer: Vogelgram



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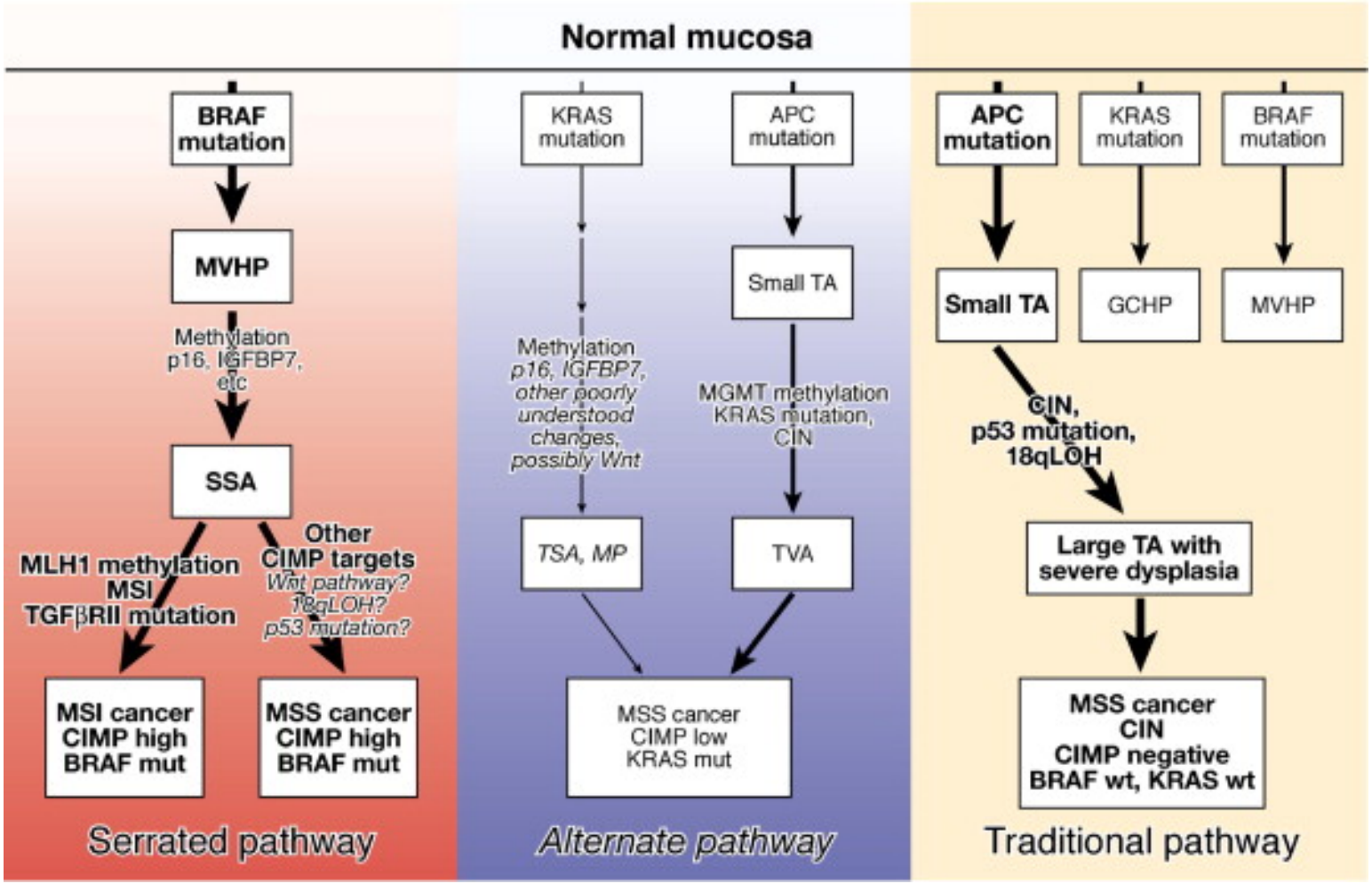
Carcinogenesis



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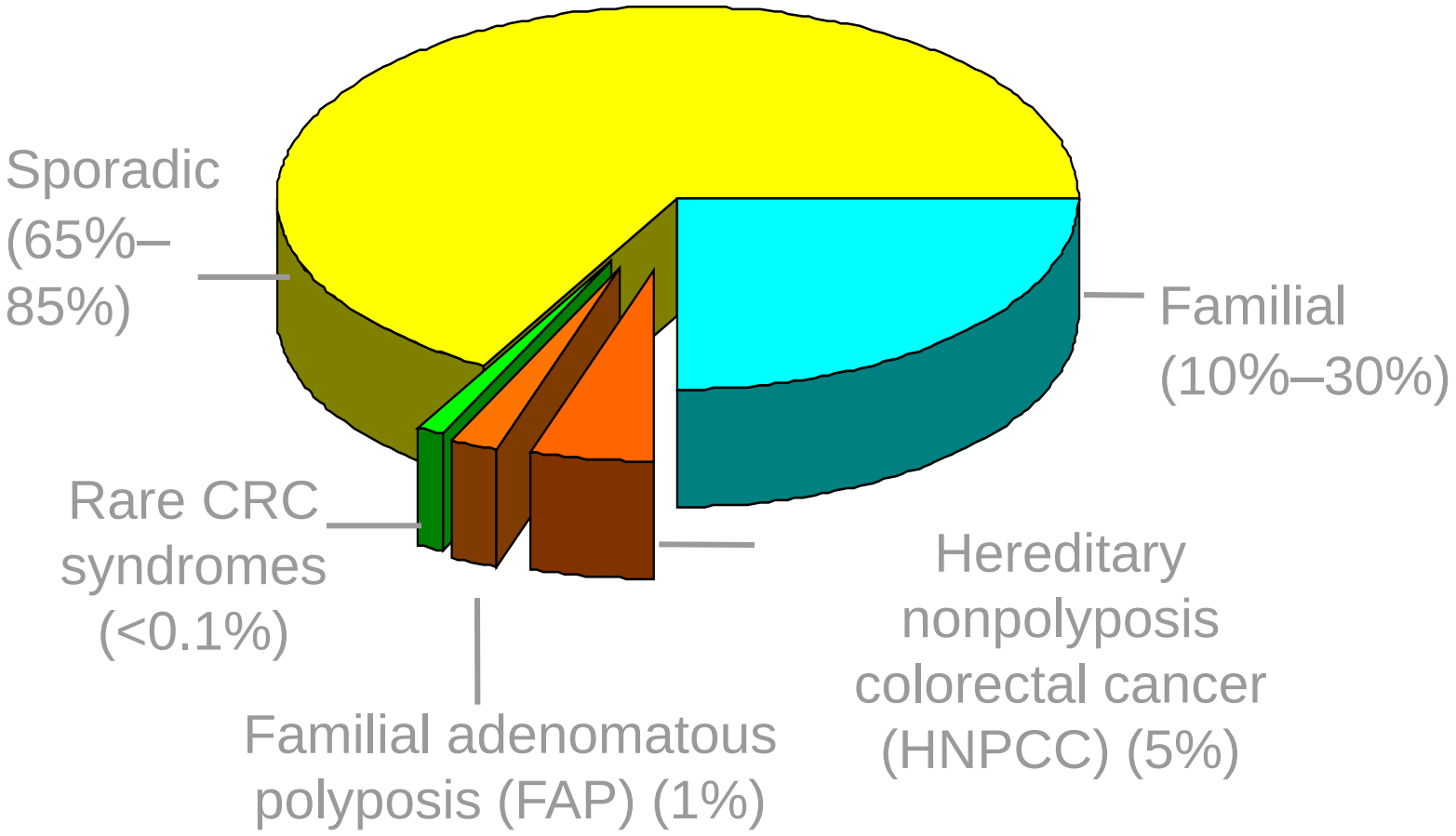
Causes of colorectal cancer



Adapted from Burt RW et al. *Prevention and Early Detection of CRC*, 1996.

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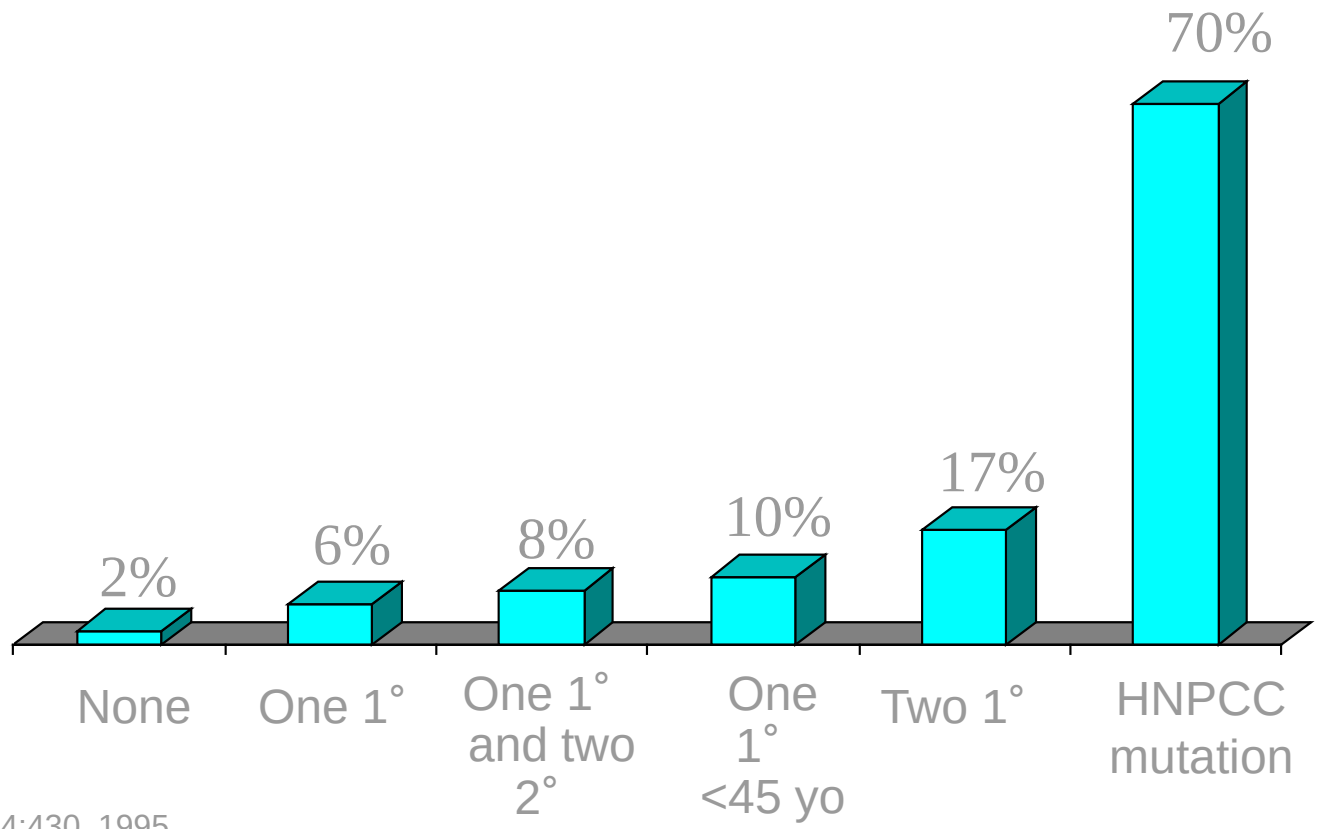
Familial Risk for Colorectal Cancer

Approximate lifetime CRC risk (%)



Aarnio M et al. *Int J Cancer* 64:430, 1995
Houlston RS et al. *Br Med J* 301:366, 1990
St John DJ et al. *Ann Intern Med* 118:785, 1993

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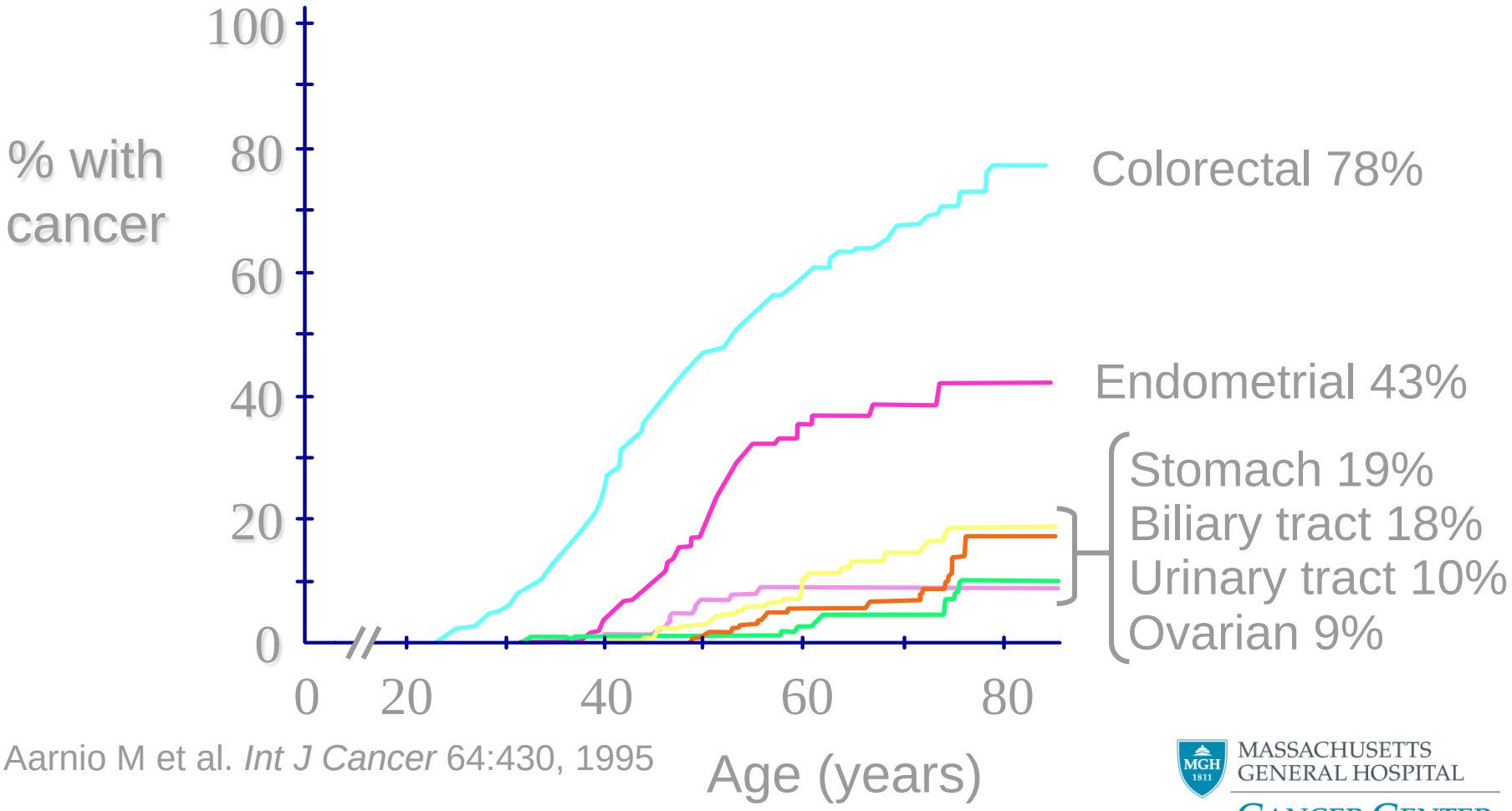
Colon Cancer Epidemiology

- Inherited Syndromes
  - Hereditary Non-Polyposis Colon Cancer
  - Familial Adenomatous Polyposis
  - MYH

Colon Cancer Epidemiology

- Hereditary Non-Polyposis Colon Cancer (Lynch Syndrome)
  - Autosomal dominant
  - Germline mutations in Mismatch Repair (MMR) genes leads to Microsatellite Instability (MSI)
  - Median age for tumors < 50
  - Proximal colon >> distal colon
  - May account for 5% of colon cancers

Cancer Risks in HNPCC



Aarnio M et al. *Int J Cancer* 64:430, 1995

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HNPCC

- Diagnosis
  - Amsterdam criteria
  - Bethesda criteria

Amsterdam Criteria

There should be at least three relatives with an HNPCC-associated cancer (colorectal cancer, cancer of the endometrium, small bowel, ureter, or renal pelvis)
One should be a first degree relative of the other two
At least two successive generations should be affected
At least 1 should be diagnosed before age 50
Familial adenomatous polyposis should be excluded in the colorectal cancer case(s) if any
Tumors should be verified by pathological examination

Failure to meet these criteria does *not* exclude HNPCC

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HNPCC: Bethesda Criteria

Tumors from individuals should be tested for MSI in the following situations:
1. Colorectal cancer diagnosed in a patient who is less than 50 years of age.
2. Presence of synchronous, metachronous colorectal, or other HNPCC-associated tumors*, regardless of age.
3. Colorectal cancer with the MSI-H•-like histologyΔ diagnosed in a patient who is less than 60 years of age◇.
4. Colorectal cancer diagnosed in a patient with one or more first-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under age 50 years.
5. Colorectal cancer diagnosed in a patient with two or more first- or second-degree relatives with HNPCC-related tumors, regardless of age.

Laboratory Testing for HNPCC

- Tests on the Tumor
  - Immunohistochemistry testing of the tumor
  - MSI testing
- Tests on the Blood
  - Sequence analysis

Surveillance Options for Carriers of HNPCC-Associated Mutations

Malignancy	Intervention	Recommendation
Colorectal cancer	Colonoscopy	Begin at age 20–25, repeat every 1–2 years
Endometrial cancer	• Transvaginal ultrasound • Endometrial aspirate	Annually, starting at age 25–35

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Other Surveillance in HNPCC

- Annual EGD
- Annual urinalysis with cytology
- Annual abdominal ultrasound

Clinical Features of FAP

- Estimated penetrance for adenomas >90%
- Untreated polyposis leads to 100% risk of cancer

Colon Cancer Epidemiology

- Familial Adenomatous Polyposis
  - Associated with
    - Congenital hypertophy of the retinal pigment epithelium
    - Desmoid tumors (Gardner's Syndrome)
    - Brain tumors (Turcot's Syndrome)
  - Screening of first degree relatives by age 10
  - Thousands of adenomatous polyps develop by age 20 and lead to cancer
  - Total colectomy with ileoanal anastomosis is treatment of choice

Lifetime Risk of Extra-Colonic Cancer in FAP

Site	Type of Cancer	Risk of Cancer
Small bowel: duodenum or periampulla	Carcinoma	4-12%
Small bowel: distal to the duodenum		Rare
Stomach	Adenocarcinoma	0.5%
Pancreas		~2%
Thyroid	Papillary thyroid carcinoma	~2%
CNS	Usually medulloblastoma	<1%
Liver	Hepatoblastoma	1.6% (children <age 5 years)
Bile ducts	Adenocarcinoma	Low, but increased
Adrenal gland		

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Many adenomas but no germline mutation in APC…

Consider germline mutations in ***MYH***:

•Base-excision repair gene. **Bi-allelic germline** mutations predispose to APC mutations that lead to colon adenomas, tumors.

•Family history of colon cancer shows **recessive inheritance**.

•Tens-to-hundreds of colorectal adenomas.

MGH Center for Cancer Risk Analysis
617-724-1971

- **Genetic Counselors:**
  - **6 counselors**
- **Programs:**
  - Breast and Ovarian: Leif Ellisen, MD, PhD
  - **Gastrointestinal: Daniel Chung, MD; Andy Chan, MD;**
  - Von Hippel Lindau: Othon Iliopoulos, MD
  - Melanoma: Hensin Tsao, MD, PhD
  - Psychiatry: William Pirl, MD

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Colorectal Cancer Screening

- How should I approach it?

US MultiSociety Task Force 2008

TABLE 1 Testing Options for the Early Detection of Colorectal Cancer and Adenomatous Polyps for Asymptomatic Adults Aged 50 Years and Older

Tests that Detect Adenomatous Polyps and Cancer
Flexible sigmoidoscopy every 5 years, or
Colonoscopy every 10 years, or
Double-contrast barium enema every 5 years, or
Computed tomographic colonography every 5 years
Tests that Primarily Detect Cancer
Annual guaiac-based fecal occult blood test with high test sensitivity for cancer, or
Annual fecal immunochemical test with high test sensitivity for cancer, or
Stool DNA test with high sensitivity for cancer, interval uncertain

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CA A Cancer J for Clin 2008; 58:130-160

US Multisociety Task Force, 2012 Update

2012 Recommendations for Surveillance and Screening Intervals in Individuals with Baseline Average Risk

Baseline Colonoscopy: Most Advanced Finding(s)	Recommended Surveillance Interval (years)	Quality of Evidence Supporting the Recommendation	New Evidence Stronger than 2006
No polyps	10	Moderate	Yes
Small (<10 mm) hyperplastic polyps in rectum or sigmoid	10	Moderate	No
1–2 small (<10 mm) tubular adenomas	5-10	Moderate	Yes
3–10 tubular adenomas	3	Moderate	Yes
>10 adenomas	<3	Moderate	No
One or more tubular adenomas ≥10 mm	3	High	Yes
One or more villous adenomas	3	Moderate	Yes
Adenoma with high grade dysplasia (HGD)	3	Moderate	No
Serrated lesions			
Sessile serrated polyp(s) <10 mm with no dysplasia	5	Low	NA
Sessile serrated polyp(s) ≥10 mm OR Sessile serrated polyp with dysplasia OR Traditional serrated adenoma	3	Low	NA
Serrated polyposis syndrome[a]	1	Moderate	NA

Colon Cancer Screening

- Hemoccult: gFOBT or FIT
  - 2-4% of adults with test positive and 60% will have no mucosal abnormality in their large bowel
  - 50% of pts with CRC will have a false negative study
  - Minnesota study demonstrated that screening reduces deaths from CRC
    - BUT 36% of pts assigned to annual screening underwent endoscopy and there were 20% less cancers in this subgroup

Colon Cancer Screening

- sDNA
  - Sensitivity 52-91%
  - Specificity 93-97%
  - ?interval
  - ?need for endoscopy

FIT vs sDNA

Table 1. Sensitivity and Specificity of the Multitarget Stool DNA Test and the Fecal Immunochemical Test (FIT) for the Most Advanced Findings on Colonoscopy.

Most Advanced Finding	Colonoscopy (N=9989)	Multitarget DNA Test (N=9989)		FIT (N=9989)	
		Positive Results	Sensitivity (95% CI)	Positive Results	Sensitivity (95% CI)
	no.	*no.*	%	*no.*	%
Colorectal cancer					
Any	65	60	92.3 (83.0–97.5)	48	73.8 (61.5–84.0)
Stage I to III*	60	56	93.3 (83.8–98.2)	44	73.3 (60.3–83.9)
Colorectal cancer and high-grade dysplasia	104	87	83.7 (75.1–90.2)	66	63.5 (53.5–72.7)
Advanced precancerous lesions†	757	321	42.4 (38.9–46.0)	180	23.8 (20.8–27.0)
Nonadvanced adenoma	2893	498	17.2 (15.9–18.6)	220	7.6 (6.7–8.6)
			Specificity (95% CI)		Specificity (95% CI)
All nonadvanced adenomas, non-neoplastic findings, and negative results on colonoscopy	9167	1231	86.6 (85.9–87.2)	472	94.9 (94.4–95.3)
Negative results on colonoscopy	4457	455	89.8 (88.9–90.7)	162	96.4 (95.8–96.9)

* These stages of colorectal cancer, as defined by the system recommended by the American Joint Committee on Cancer, are associated with an increased rate of cure.

† Advanced precancerous lesions include advanced adenomas and sessile serrated polyps measuring 1 cm or more.

Imperiale TF et al. N Engl J Med 2014;370:1287-1297.

Colon Cancer Screening

- Barium Enema

–DON’T DO IT

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Colon Cancer
Screening Endoscopy

- Flexible sigmoidoscopy vs Colonscopy
  - Approximately 2% of asymptomatic adults will have proximal pre-cancerous or cancerous lesions and have TOTALLY NORMAL sigmoidoscopies
  - Fecal occult blood testing plus sigmoidoscopy has a sensitivity of 75%, ie will miss 25% of lesions
  - Colonoscopy may miss lesions as much as 4% of time

Colonoscopy vs Flex Sig

Source	pts	% adequate exam	% advanced neoplasm*
Lieberman NEJM 2000	3196	97.7	5.7
Imperiale NEJM 2000	1944	97	3.1

*advanced neoplasm=carcinoma, dysplasia, or villous adenoma

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Colonoscopy vs Flex Sig

Source	% pts with proximal neoplasm if distal bowel showed		
	Advanced neoplasm	Tubular adenoma	No polyp
Lieberman NEJM 2000	14.6	6.8	2.7
Imperiale NEJM 2000	11.5	7.1	1.5

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Colonoscopy and CRC Death

Table 3. **Results of Primary Analysis: Odds Ratio for the Association Between Colonoscopy and Colorectal Cancer Death***

Model	Odds Ratio (95% CI)			
	All Cancer	Right-Sided Cancer	Left-Sided Cancer	Undefined Site of Cancer
Attempted colonoscopy				
None	1.00	1.00	1.00	1.00
Any	0.69 (0.63–0.74)	1.07 (0.94–1.21)	0.39 (0.34–0.45)	0.90 (0.75–1.08)
Completeness of colonoscopy				
None	1.00	1.00	1.00	1.00
Complete	0.63 (0.57–0.69)	0.99 (0.86–1.14)	0.33 (0.28–0.39)	0.90 (0.73–1.10)
Incomplete	0.91 (0.78–1.07)	1.35 (1.07–1.69)	0.63 (0.49–0.81)	0.91 (0.61–1.35)

* Conditional logistic regression, adjusted for Charlson Comorbidity Index score.

Baxter, N. N. et. al. Ann Intern Med 2009;150:1-8

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Colonoscopy and CRC Death

Table 4. **Results of Analysis Stratified by Age and Sex: Odds Ratio for the Association Between Colonoscopy and Colorectal Cancer Death***

Variable	Odds Ratio (95% CI)			
	All Cancer	Right-Sided Cancer	Left-Sided Cancer	Undefined Site of Cancer
Stratified by age at diagnosis				
<70 y				
No colonoscopy	1.00	1.00	1.00	1.00
Complete colonoscopy	0.47 (0.39–0.55)	0.92 (0.72–1.18)	0.22 (0.16–0.30)	0.52 (0.33–0.84)
Incomplete colonoscopy	0.78 (0.58–1.05)	1.14 (0.75–1.73)	0.53 (0.33–0.86)	0.92 (0.38–2.21)
≥70 y				
No colonoscopy	1.00	1.00	1.00	1.00
Complete colonoscopy	0.72 (0.64–0.81)	1.03 (0.86–1.22)	0.41 (0.33–0.50)	1.06 (0.84–1.33)
Incomplete colonoscopy	0.98 (0.81–1.17)	1.46 (1.11–1.93)	0.68 (0.51–0.92)	0.92 (0.59–1.43)
Stratified by sex				
Men				
No colonoscopy	1.00	1.00	1.00	1.00
Complete colonoscopy	0.59 (0.52–0.67)	1.02 (0.84–1.25)	0.33 (0.26–0.41)	0.80 (0.60–1.07)
Incomplete colonoscopy	0.75 (0.58–0.96)	1.01 (0.67–1.51)	0.56 (0.39–0.081)	1.00 (0.55–1.84)
Women				
No colonoscopy	1.00	1.00	1.00	1.00
Complete colonoscopy	0.68 (0.59–0.78)	0.96 (0.79–1.17)	0.33 (0.25–0.44)	1.03 (0.76–1.38)
Incomplete colonoscopy	1.05 (0.86–1.29)	1.57 (1.19–2.08)	0.71 (0.50–1.00)	0.85 (0.50–1.44)

* Conditional logistic regression, adjusted for Charlson Comorbidity Index score.

Baxter, N. N. et. al. Ann Intern Med 2009;150:1-8

US Preventive Services Task Force March 2008
When to stop?

SCREENING FOR COLORECTAL CANCER
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Adults Age 50 to 75 Years*	Adults Age 76 to 85 Years*	Adults Older Than 85 Years*
Recommendation	Screen with high-sensitivity FOBT sigmoidoscopy, or colonoscopy Grade: A	Do not screen routinely Grade: C	Do not screen Grade: D
	For all populations, evidence is insufficient to assess the benefits and harms of screening with computed tomographic colonography and fecal DNA testing. Grade: I (Insufficient evidence)		

U.S. Preventive Services Task Force, Ann Intern Med 2008;0:0000605-200811040-00243-E-243

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Colon Cancer Screening
Average Risk

- Colonoscopy beginning at age 50 every 10 years
- If pathology found, follow the recommendation of the gastroenterologist
  - For low risk adenoma, they will recommend repeat screening at 5 years
  - For high risk adenoma, they will recommend repeat screening at 3 years

Colon Cancer
Increased Risk

•Have you ever had colorectal cancer or an adenomatous polyp?

•Have you had inflammatory bowel disease (ulcerative colitis or Crohn's disease)?

•Has a family member had colorectal cancer or an adenomatous polyp? If so, how many, was it a first-degree relative (parent, sibling, or child), and at what age was the cancer or polyp first diagnosed?

Colon Cancer
Screening Made Easy

•Have you ever had colorectal cancer or an adenomatous polyp? → Colonoscopy q 3-5years

•Have you had inflammatory bowel disease (ulcerative colitis or Crohn's disease)?

•Has a family member had colorectal cancer or an adenomatous polyp? If so, how many, was it a first-degree relative (parent, sibling, or child), and at what age was the cancer or polyp first diagnosed?

Colon Cancer
Screening Made Easy

•Have you ever had colorectal cancer or an adenomatous polyp? → Colonoscopy q 3-5years

•Have you had inflammatory bowel disease (ulcerative colitis or Crohn's disease)? → refer to Gastroenterology

•Has a family member had colorectal cancer or an adenomatous polyp? If so, how many, was it a first-degree relative (parent, sibling, or child), and at what age was the cancer or polyp first diagnosed?

Colon Cancer
Screening Made Easy

Has a family member had colorectal cancer or an adenomatous polyp? If so, how many, was it a first-degree relative (parent, sibling, or child), and at what age was the cancer or polyp first diagnosed?

- Begin screening at least 10 years younger than the youngest member in the family with colon cancer
- Begin screening at age 40 if first degree relative had colon cancer <60
- Refer to High Risk Genetics if HNPCC suspected

Colon Cancer: Screening
CT Colonography

- Appears to be just as good for lesions that are 1cm in size
- Very good for patients who have incomplete colonoscopies
- Still have to give GI prep
  - Novel preps under investigation
- Not able to biopsy

Colon Cancer
Clinical Presentation

- Nearly half of colon cancers are found in the right side of the colon
  - Trend is for unknown reasons
  - Different biology (e.g. braf mutation)
- Presenting symptoms (ie bleeding, change in bowel habits, anemia, obstuction) depend on location
- Clinical pearls

Colon Cancer
Clinical Presentation

- Clinical pearls
  - If you feel something on rectal exam, never assume that it is an internal hemorrhoid

Colon Cancer
Clinical Presentation

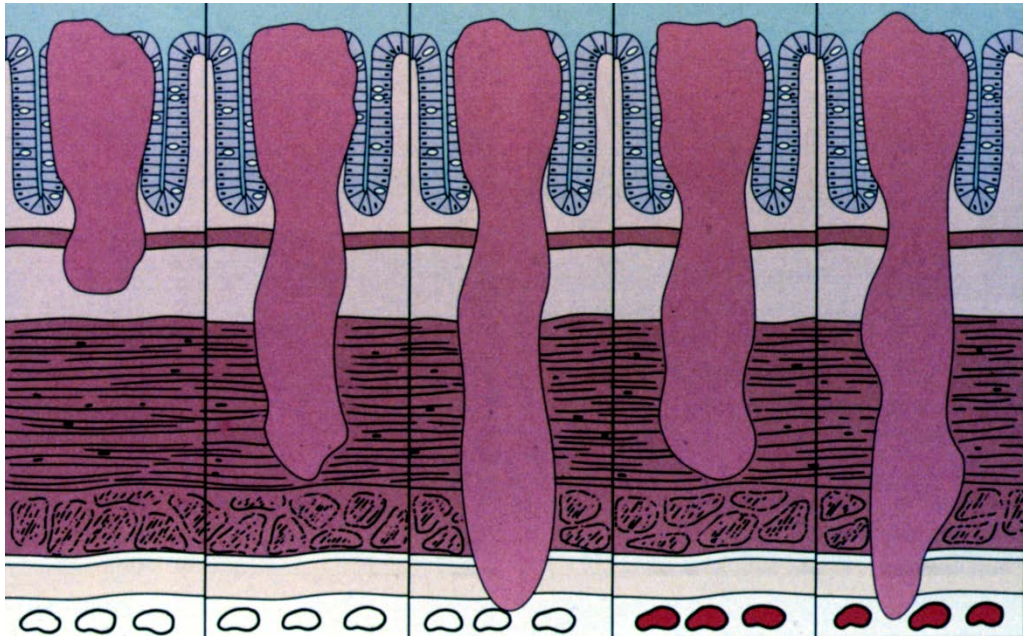
- Clinical pearls
  - If you feel something on rectal exam, never assume that it is an internal hemorrhoid
  - A walled off perforation from a colon cancer can masquerade as diverticulitis

Colon Cancer
Clinical Presentation

- Clinical pearls
  - If you feel something on rectal exam, never assume that it is an internal hemorrhoid
  - A walled off perforation from a colon cancer can masquerade as diverticulitis
  - If an Fe def anemia workup has been done and nothing found, repeat the colonoscopy…right sided lesions could have been missed

Staging of Colorectal Cancer

	No deeper than submucosa	Not through bowel wall	Through bowel wall	Not through bowel wall: lymph node metastases	Through bowel wall: lymph node metastases	Distant metastases
5-year survival	>90%	>90%	80%	70-90%	40-80%	20%



Mucosa
Muscularis mucosa
Submucosa
Muscularis propria
Serosa
Fat
Lymph nodes

Liver
Lung
Bone
Skin
Brain

Adapted from Skarin AT, ed. *Atlas of Diagnostic Oncology.* 3rd ed. St. Louis, Mo: Mosby Inc; 2003:155.

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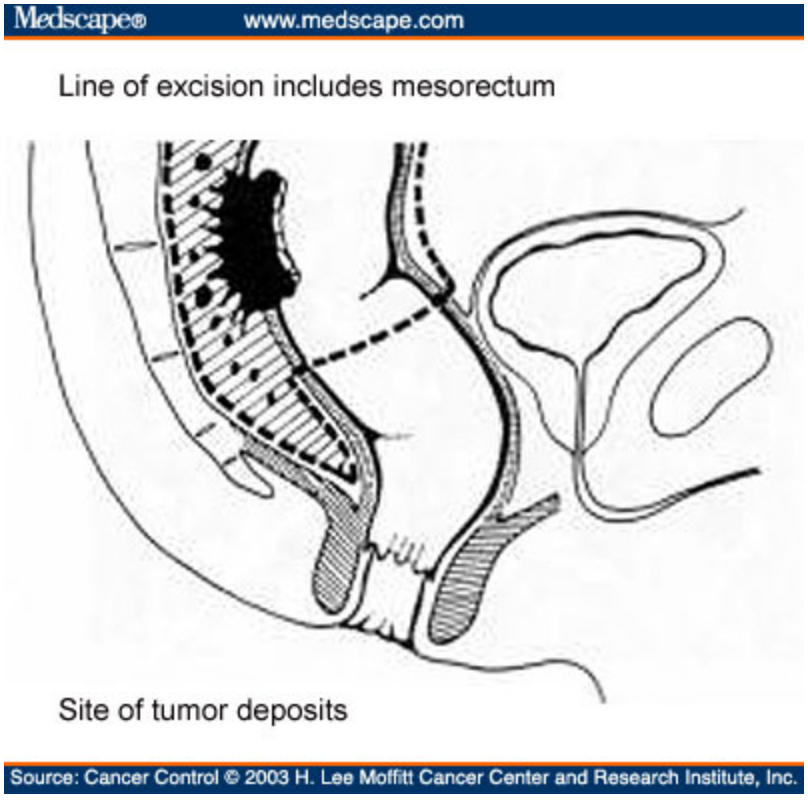
Colon Cancer Treatment

- Stage I: surgery
  - Laparoscopic or open colectomy
- Stage II: surgery + ?chemotherapy
- Stage III: surgery + chemotherapy
- Stage IV: chemotherapy + ?surgery
  - Patients with isolated liver or lung metastases can be cured with surgical resection

Rectal Cancer:
Total Mesorectal Excision



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Rectal Cancer Treatment

- Stage I: surgery
- Stage II: surgery + chemotherapy + radiation
- Stage III: surgery + chemotherapy + radiation
- Stage IV: chemotherapy + ?surgery

Colorectal Cancer Surveillance

- Colonoscopy 1 year after diagnosis and then every 3-5 years
- For stage 2 and 3, every 3 month CEA/LFTs/physical exam and annual CT for 3 years. Then follow annually with cea and LFTs until year 5
- Lifestyle/Dietary Changes: Very good retrospective or observational evidence
  - Exercise, ASA, Vit D
  - ?Red meat

Colorectal Cancer:

3 reasons for seeing an oncologist

- Be Cured
- Live Longer
- Feel Better

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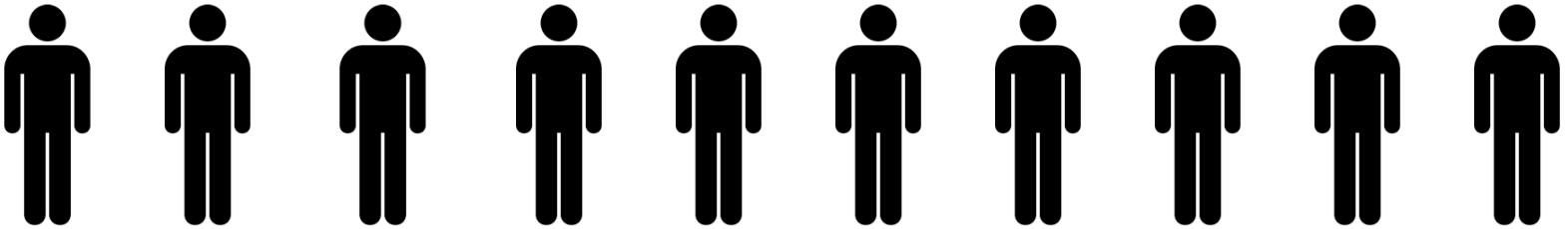
How to Explain to Patients
Stage 3c



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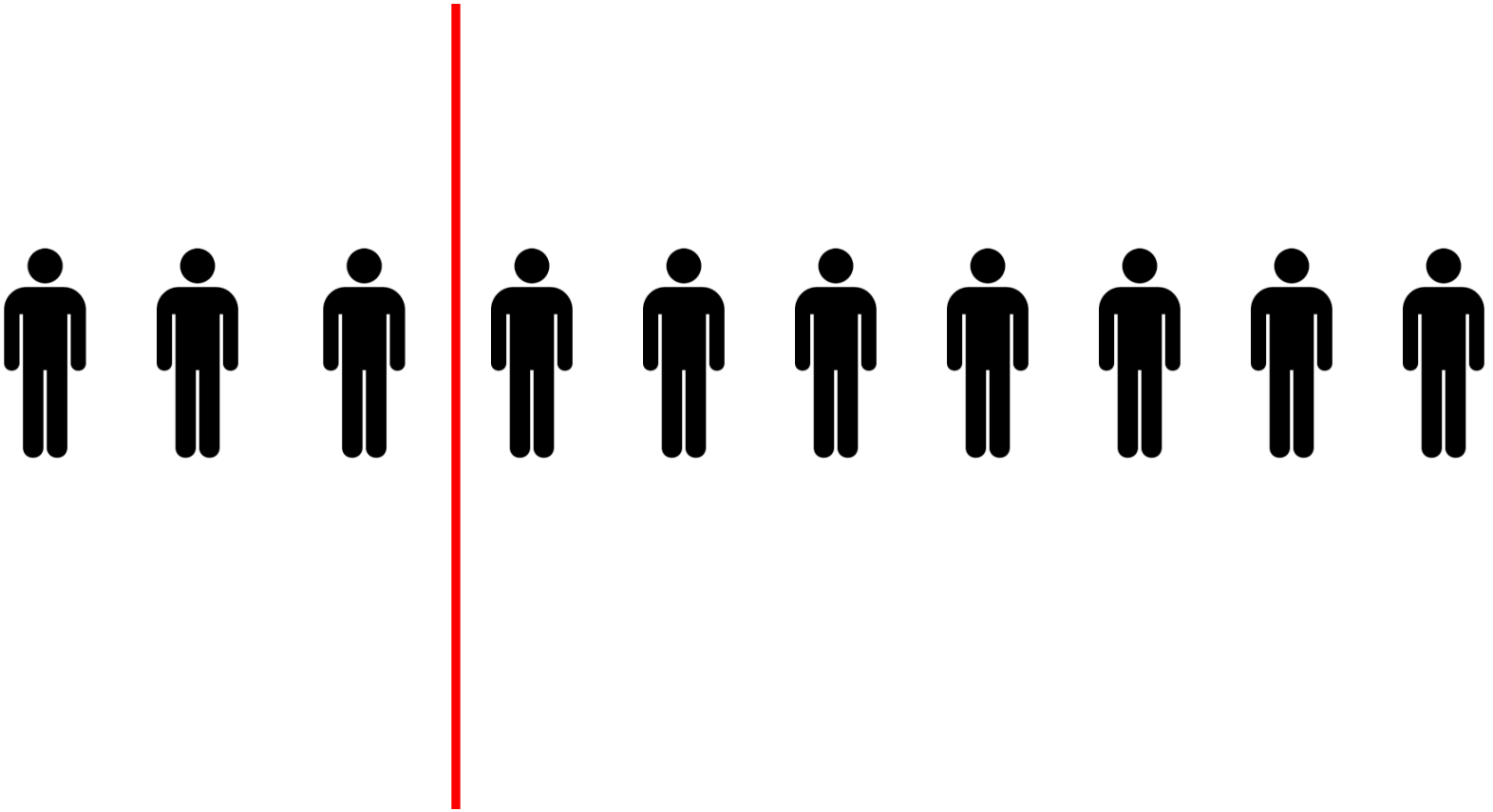
How to Explain to Patients
Stage 3c



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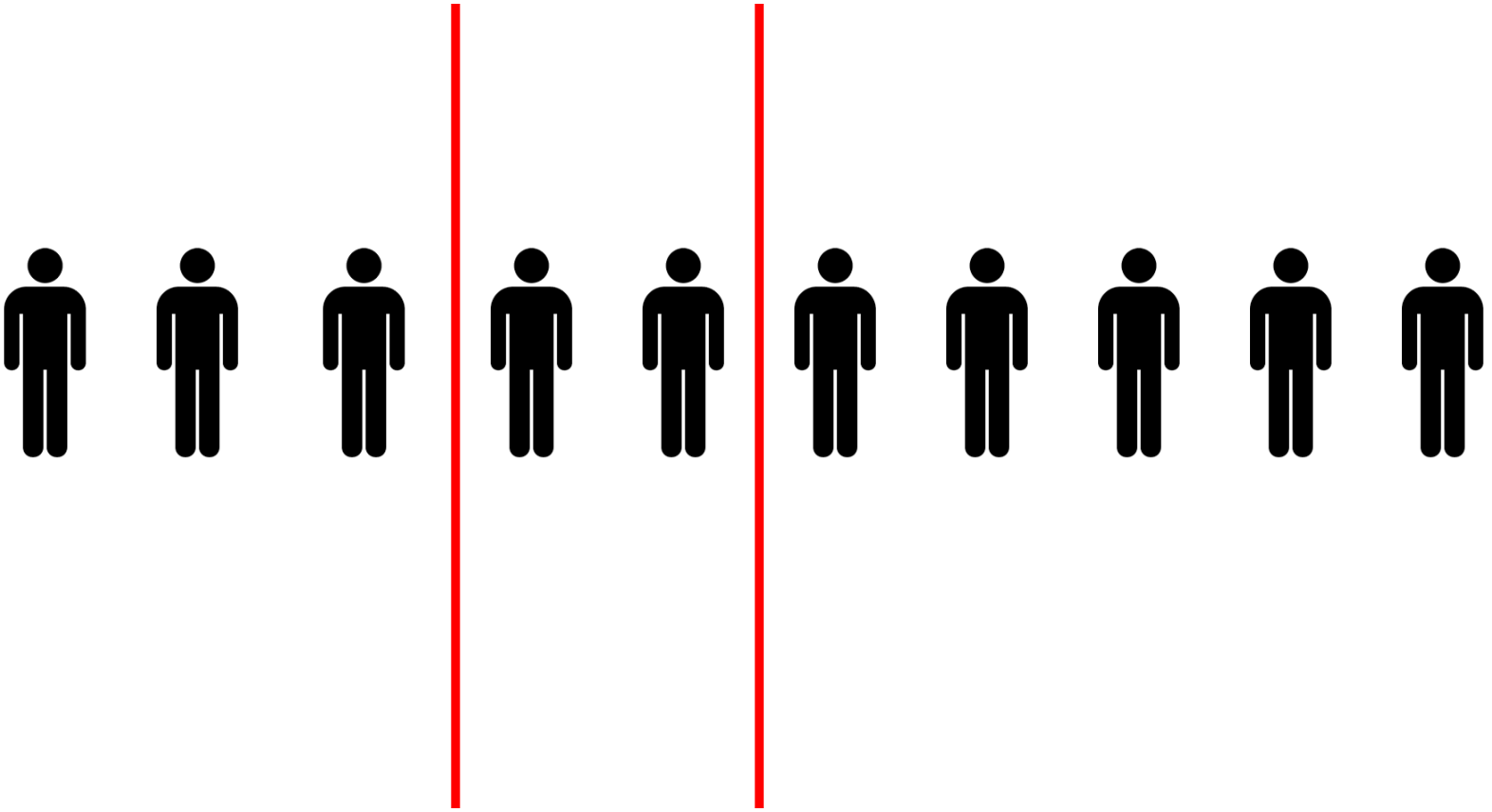
How to Explain to Patients
Stage 3c



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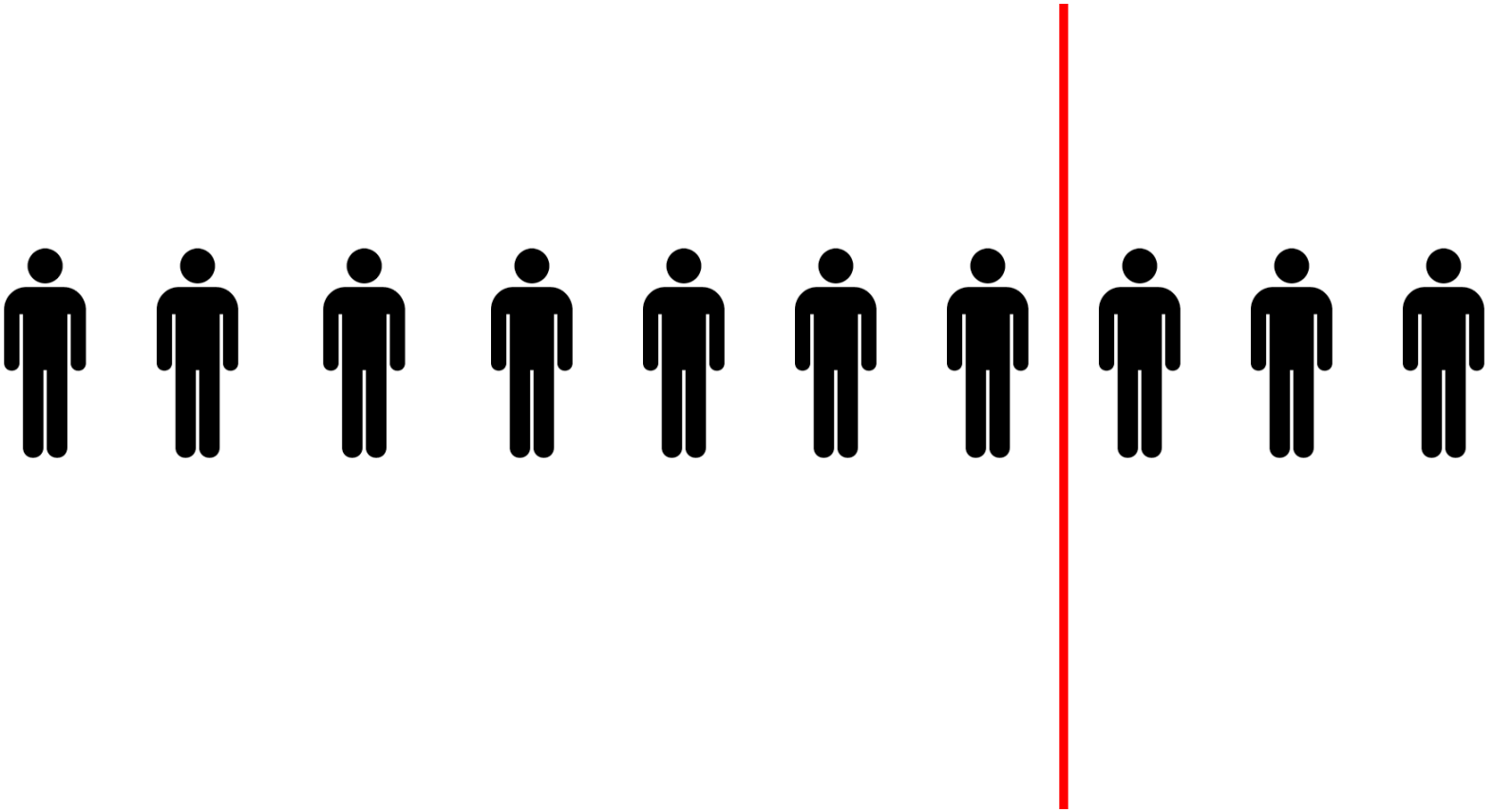
How to Explain to Patients
Stage 3a



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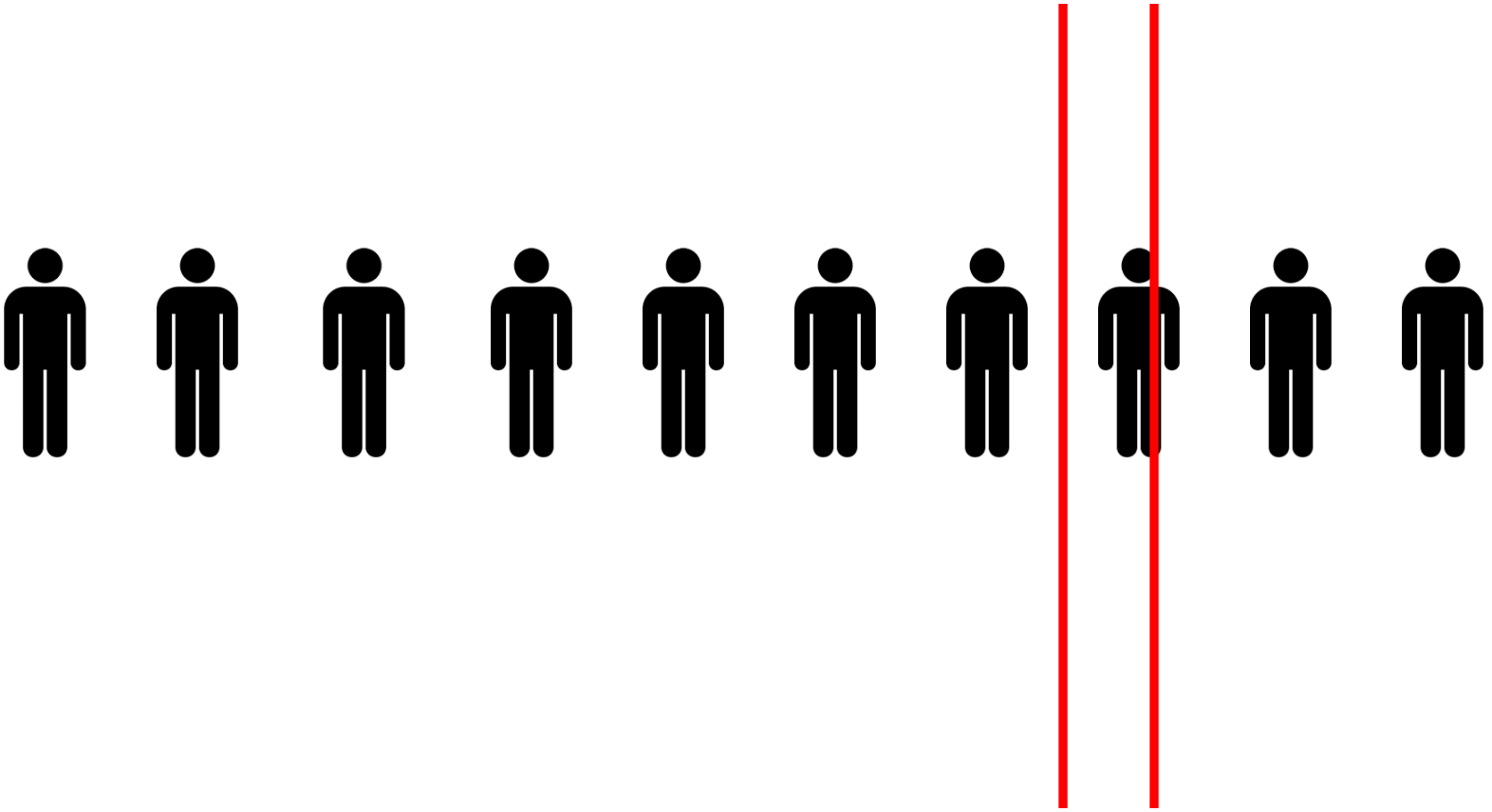
How to Explain to Patients
Stage 3a



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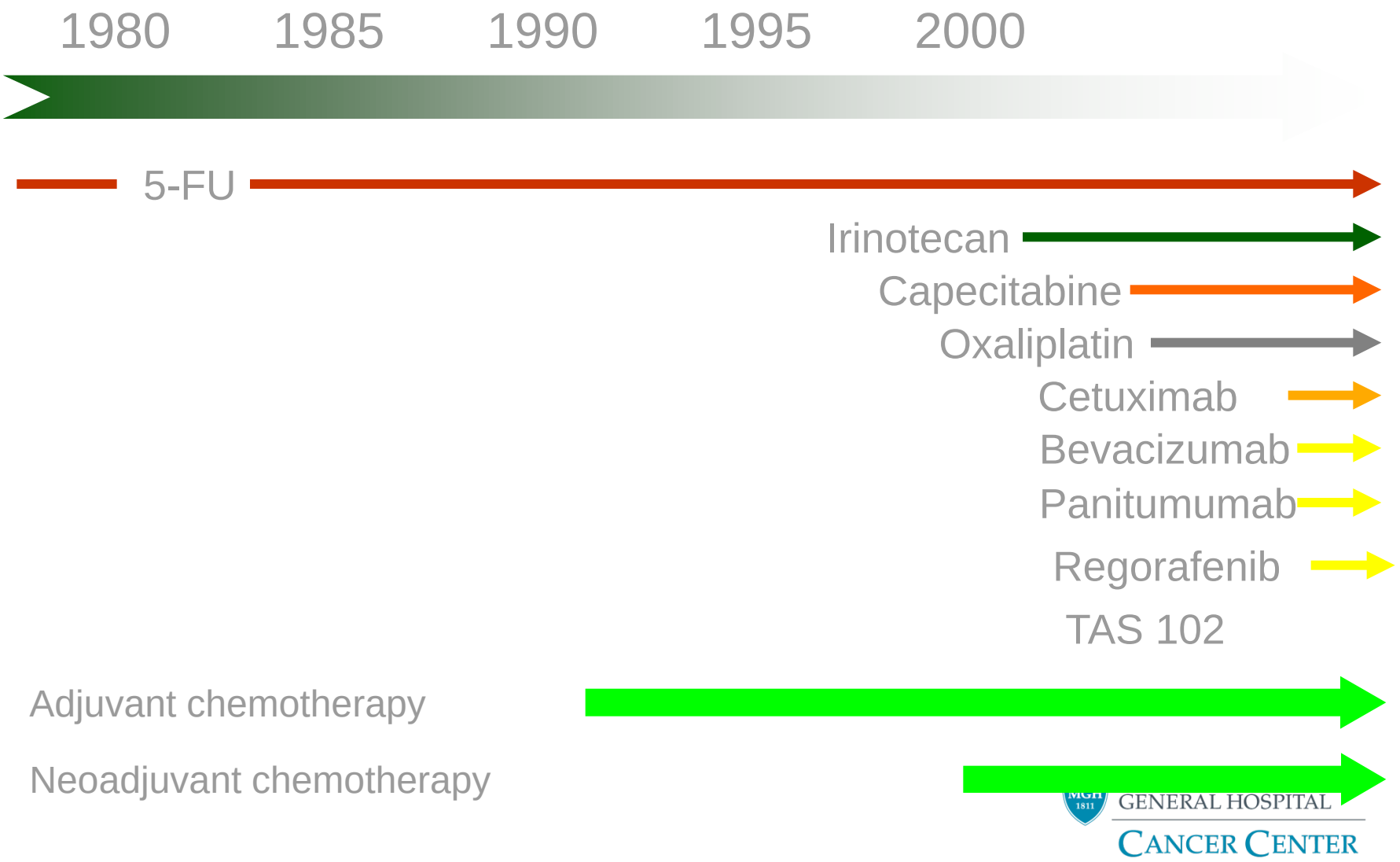
Advances in the Treatment of Colorectal Cancer



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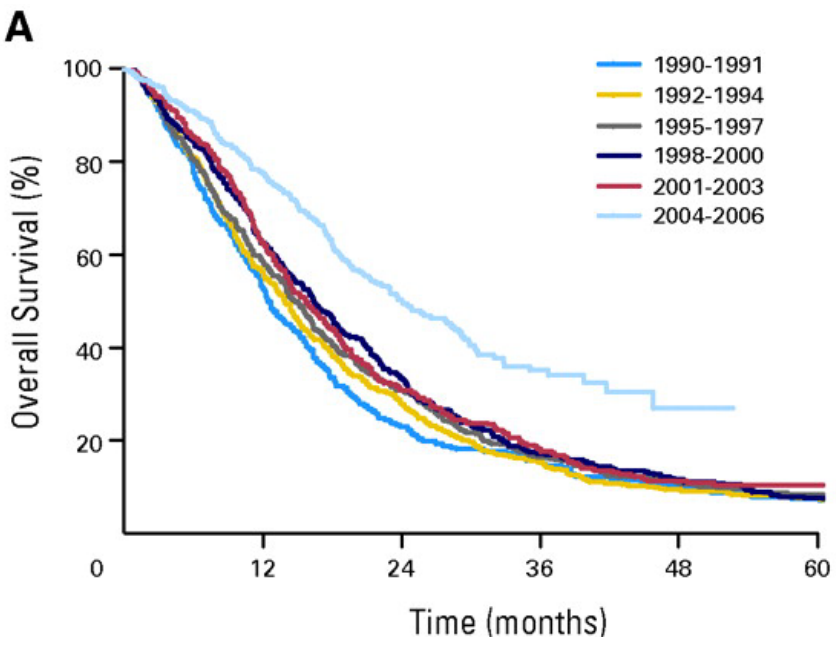
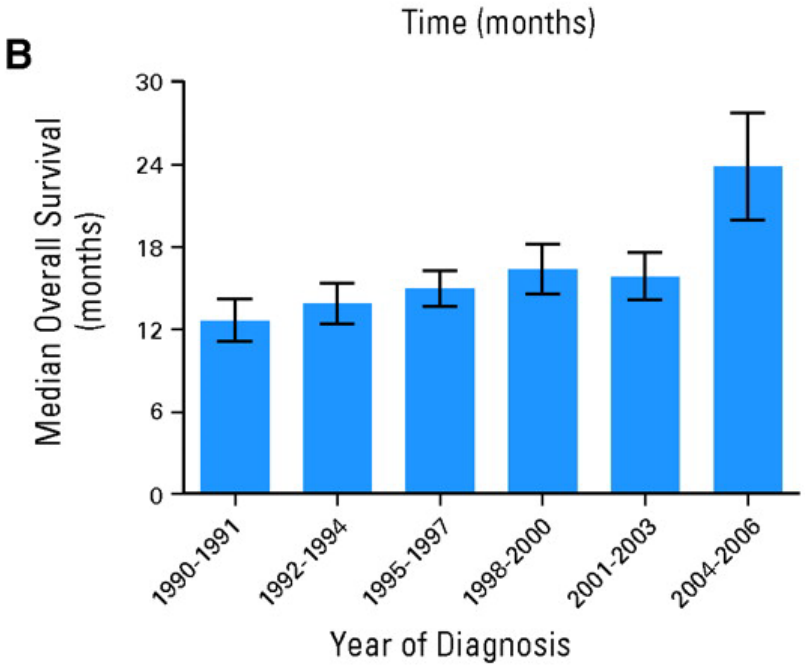
Stage 4 Colon Cancer: Improved Survival





Kopetz et al JCO 2012

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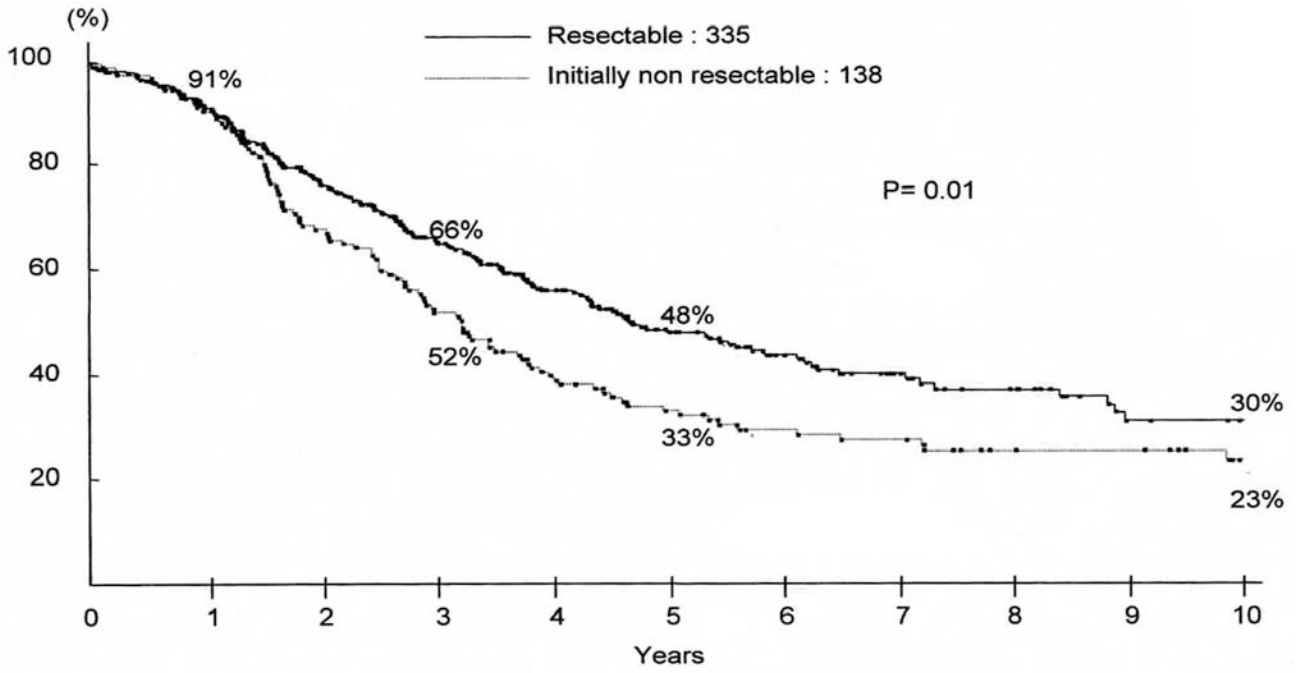
Overall Survival for Liver Resection

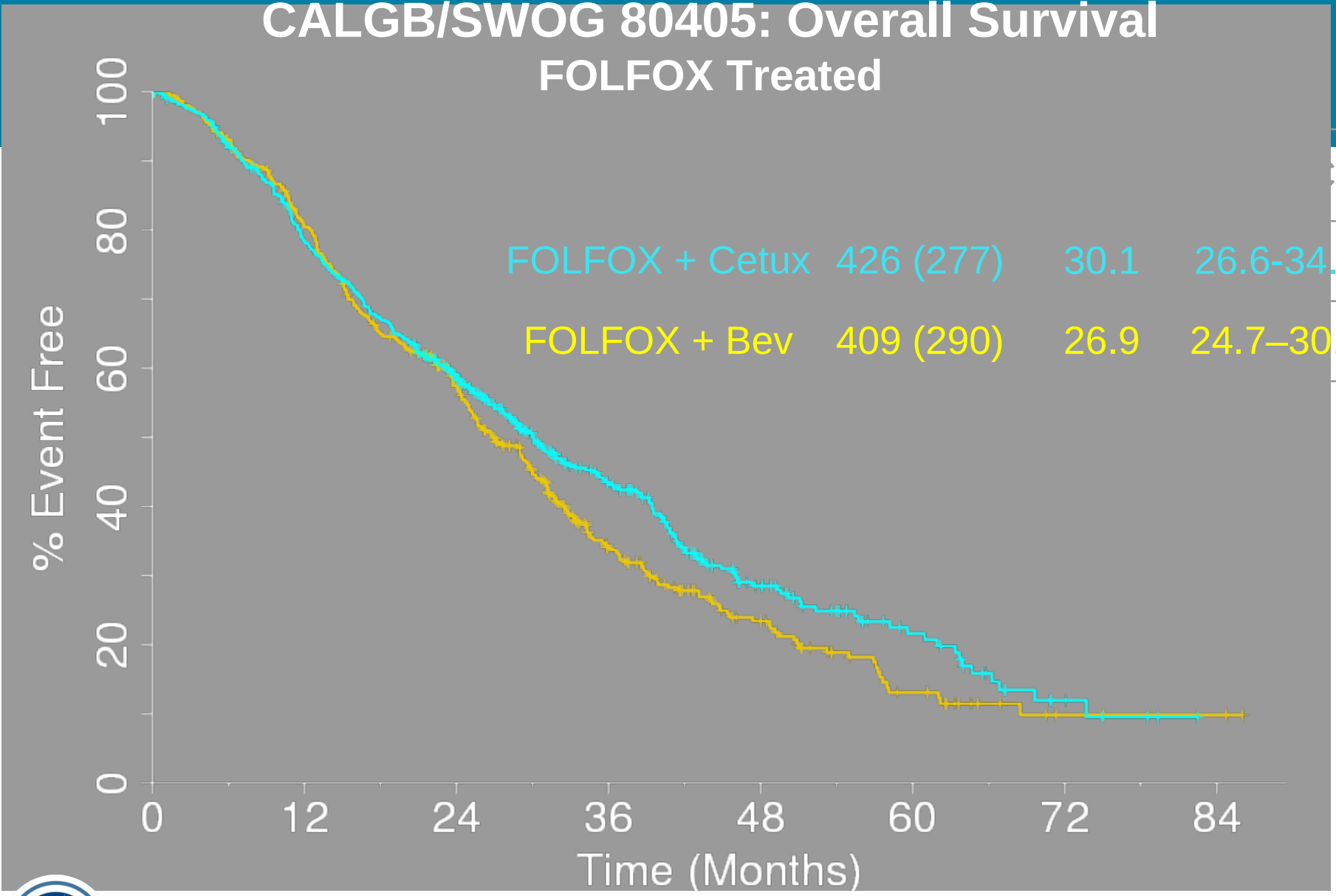


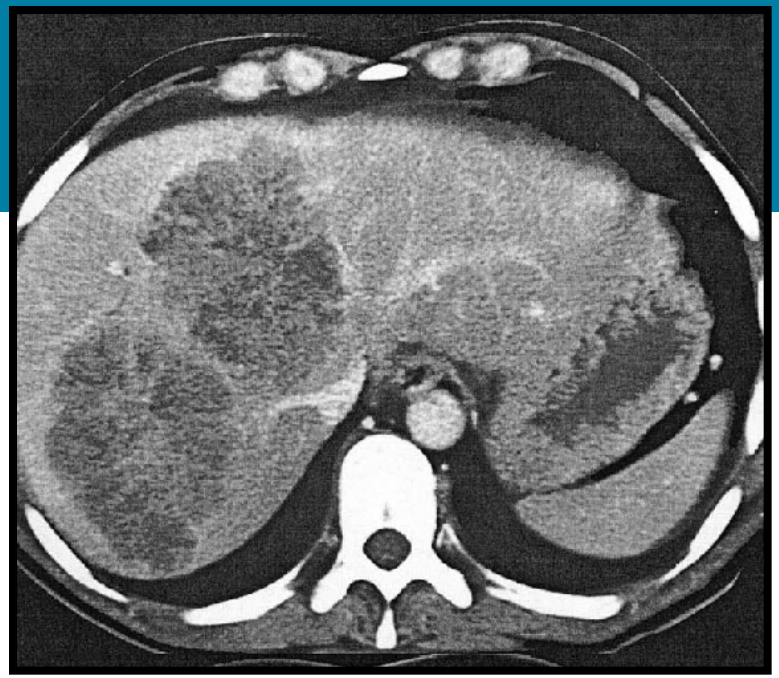
No Pts at risk	0 Yr	1 Yr	3 Yrs	5 Yrs	8 Yrs	10 Yrs
Non resectable	138	124	69	37	18	12
Resectable	335	282	168	90	32	17

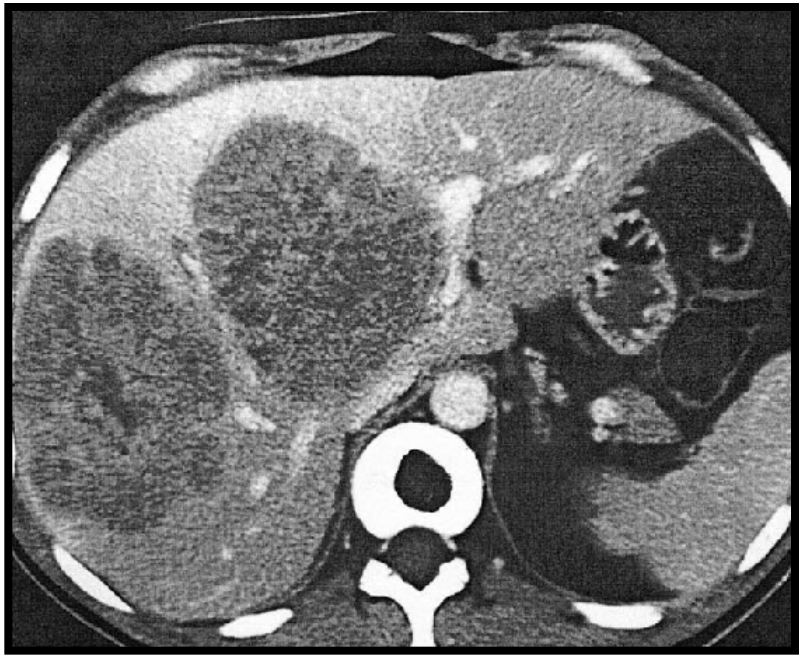
Adam R, et al., *Ann Surgery.* 2004 Oct;240(4):644-57.

CALGB/SWOG 80405: Overall Survival

FOLFOX Treated







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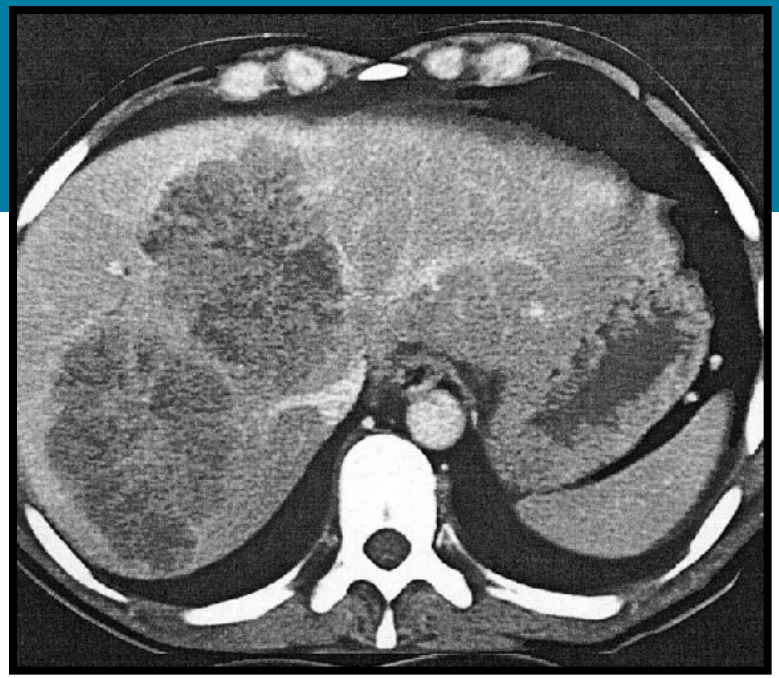
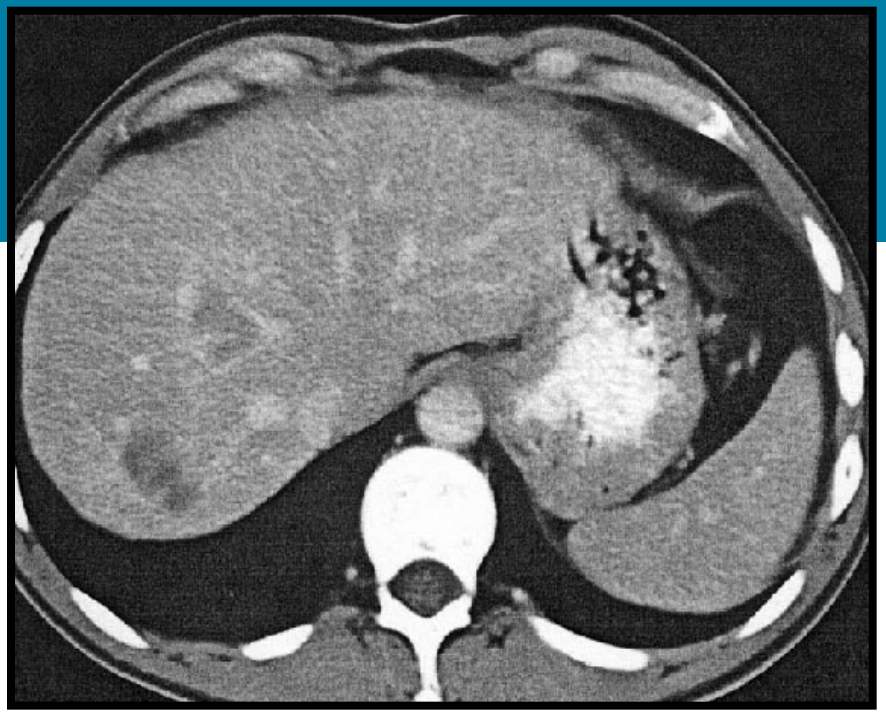
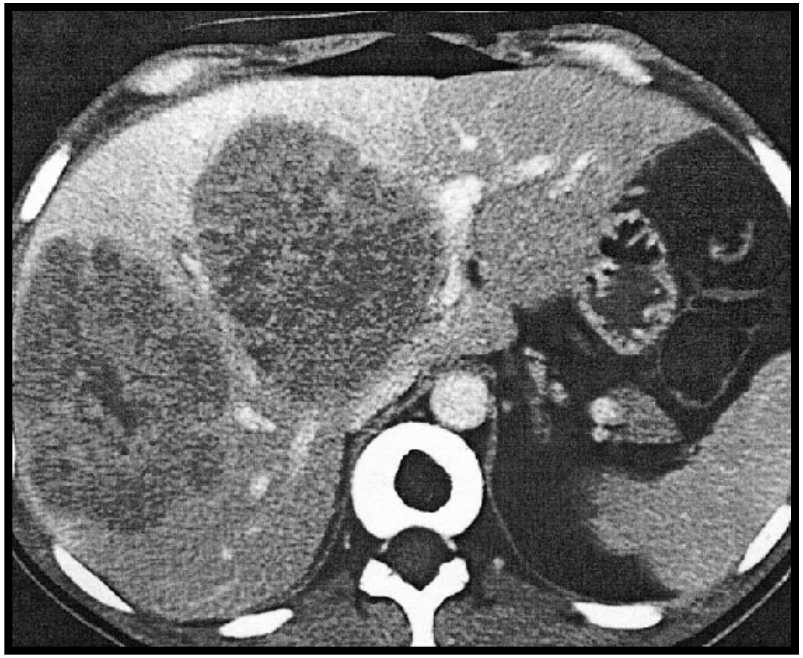
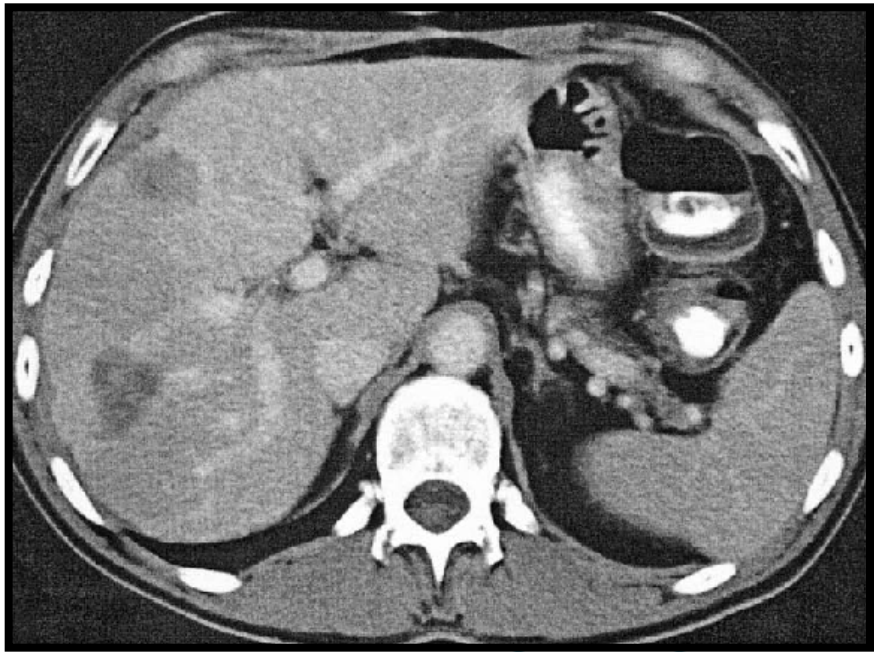
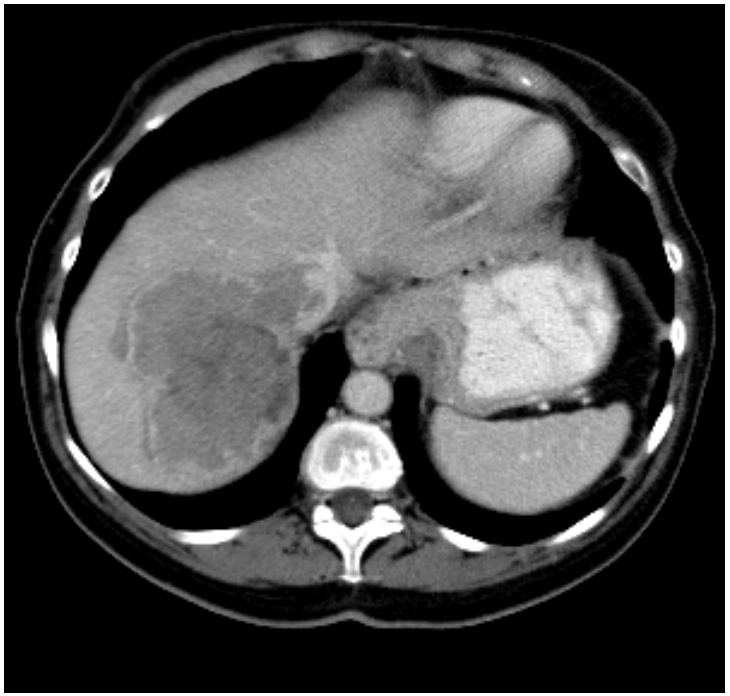








Colon Cancer Case presentation



- Left hemicolectomy for T4, N1, M1 colon cancer
- Treated with chemotherapy

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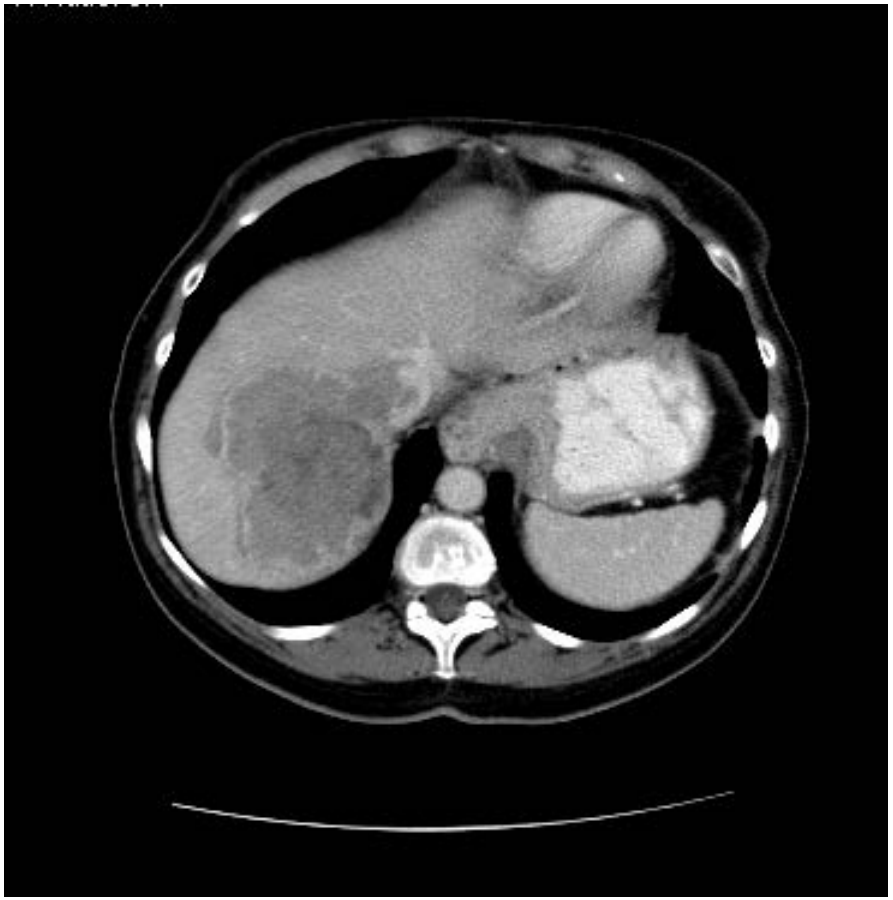
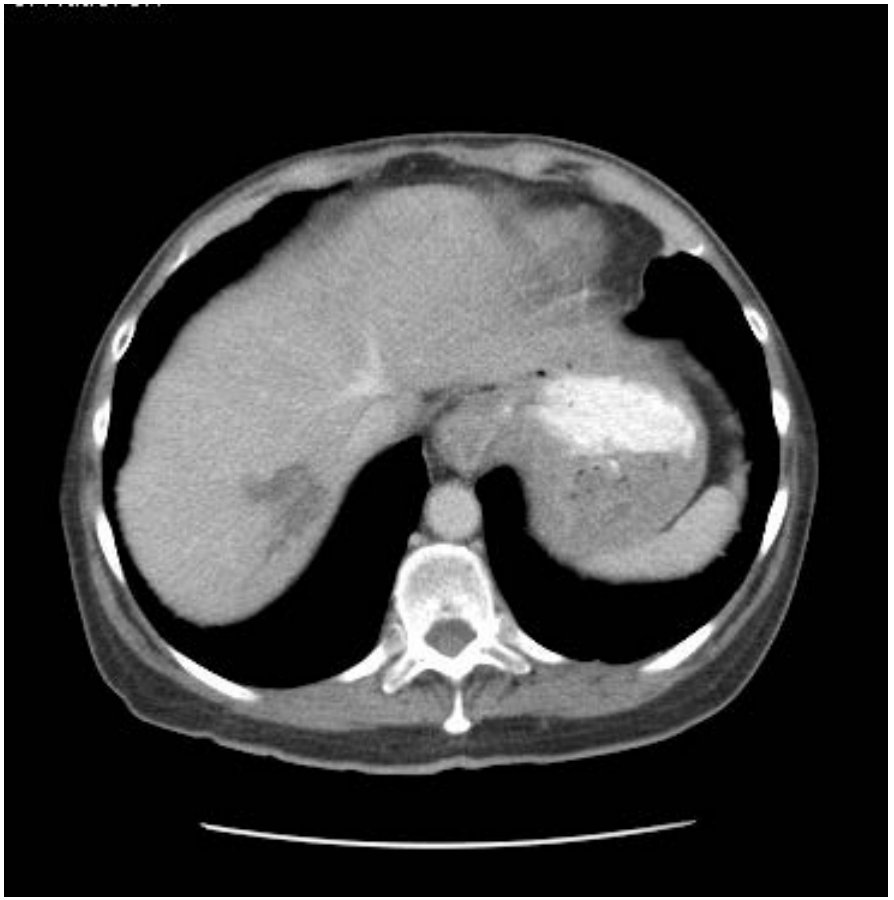
Colon Cancer Case presentation





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Colorectal Cancer Summary

- Obesity and Exercise
- Colonoscopy: Left >>Right
- Identification of high risk patients is key in offering appropriate screening
- All stage III and some stage II patients will get 6 months of adjuvant therapy
- Treatment of metastatic disease has changed dramatically in last 10 years