

N2Y NEVER TOO YOUNG FOR COLON CANCER

Colorectal Cancer

Colon Cancer At-A-Glance*



Colon cancer is the second leading cause of cancer-related death in the U.S.



On average, your risk is about 1 in 20, although this varies widely according to individual risk factors.

50+

90% of new cases occur in people 50 or older.



People with a first-degree relative (parent, sibling or offspring) who has colon cancer have two to three times the risk of developing the disease.



There are currently more than one million colon cancer survivors in the U.S.

*Source: American Cancer Society



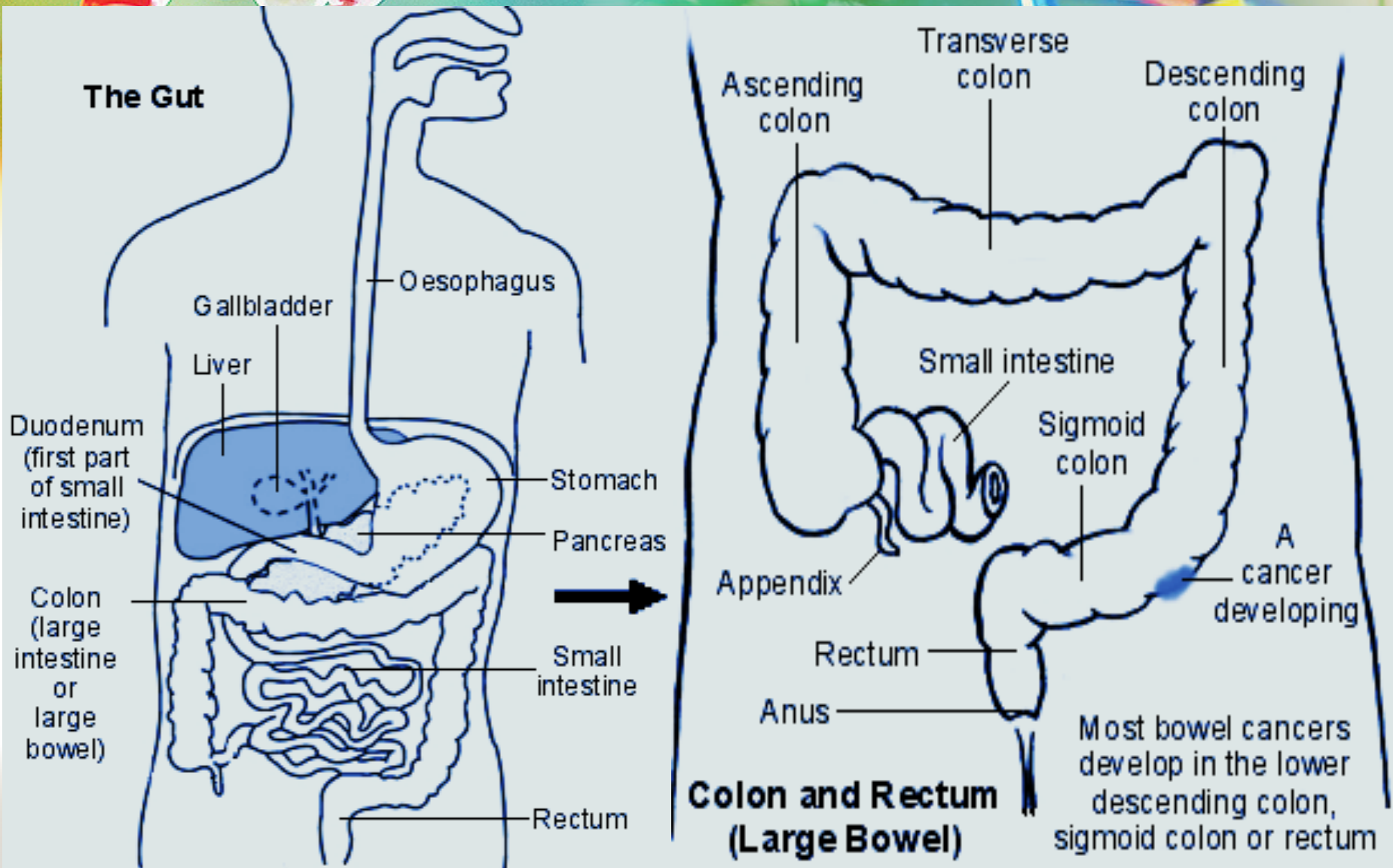
Most common Cancers

Cancer Type	Estimated New Cases	Estimated Deaths
Bladder	72,570	15,210
Breast (Female – Male)	232,340 – 2,240	39,620 – 410
Colon and Rectal (Combined)	142,820	50,830
Endometrial	49,560	8,190
Kidney (Renal Cell) Cancer	59,938	12,586
Leukemia (All Types)	48,610	23,720
Lung (Including Bronchus)	228,190	159,480
Melanoma	76,690	9,480
Non-Hodgkin Lymphoma	69,740	19,020
Pancreatic	45,220	38,460
Prostate	238,590	29,720
Thyroid	60,220	1,850

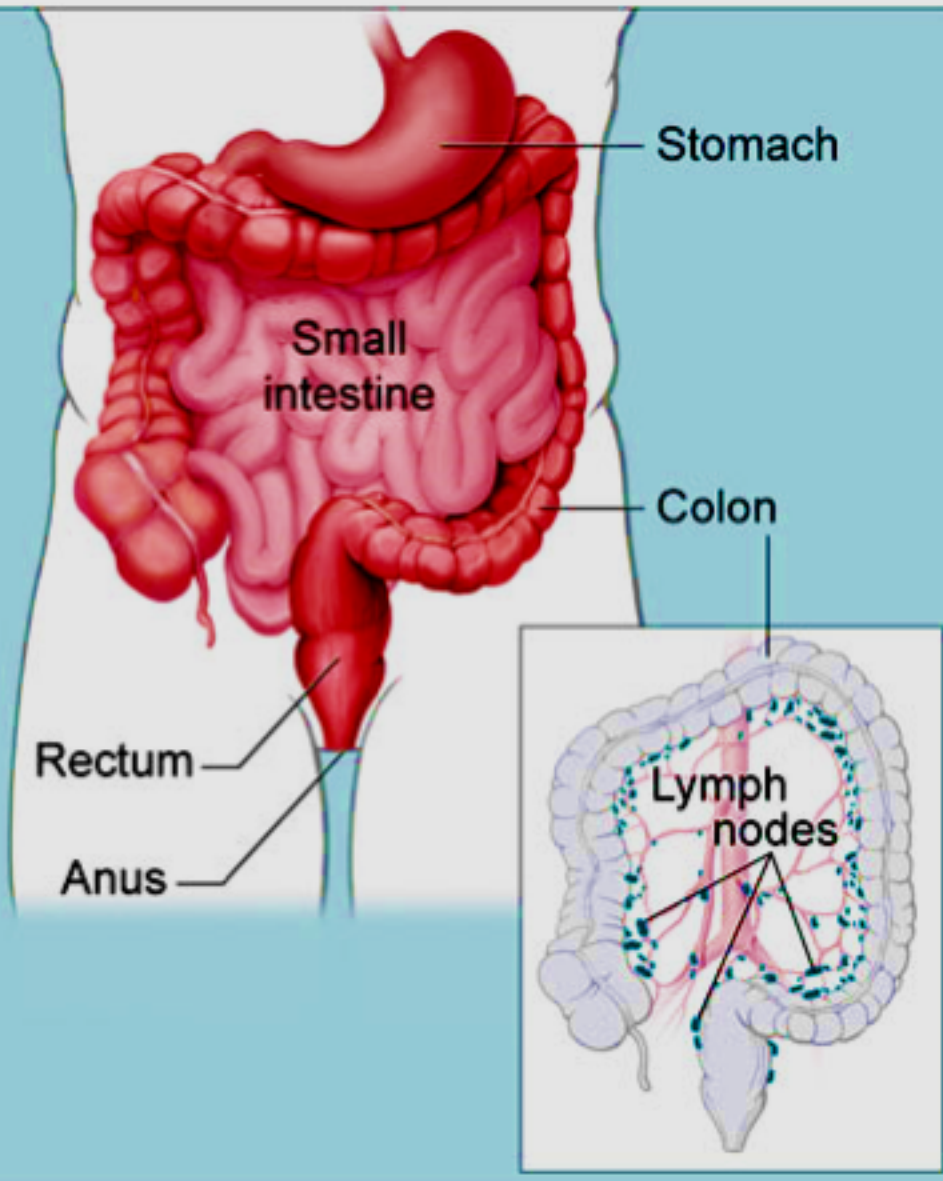
References

1. American Cancer Society: Cancer Facts and Figures 2013. Atlanta, Ga: American Cancer Society, 2013. [Also available online](#)  (PDF - 1,250 KB). Last accessed January 22, 2013.

Getting to Know Your Gut



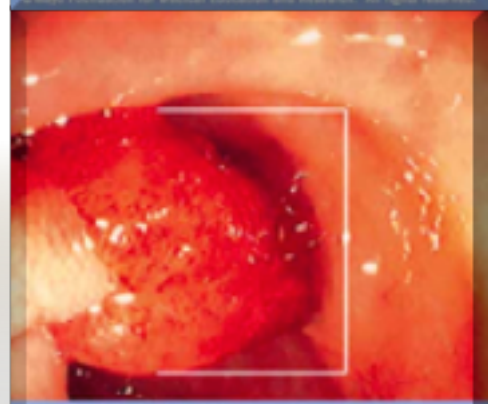
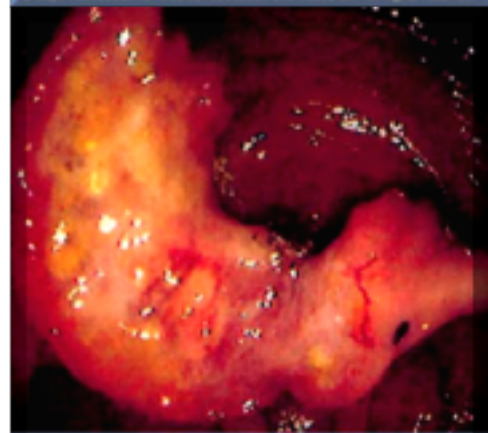
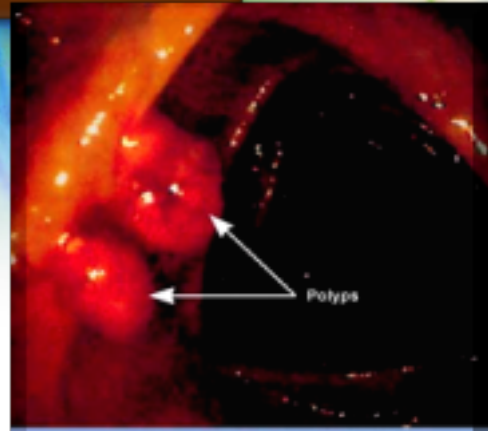
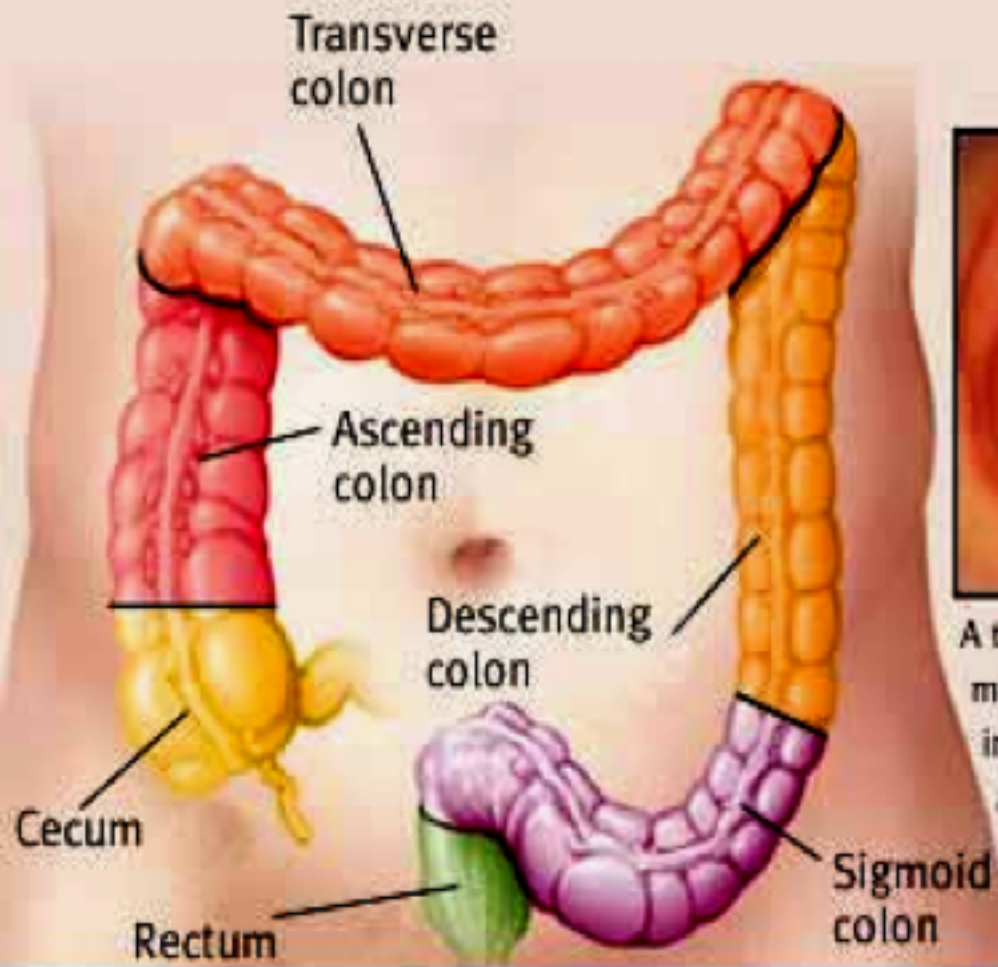
Colon and Rectum



Over Age 50

- ❑ Colorectal cancer is more likely to occur as people get older.
- ❑ More than 90 percent of people with this disease are diagnosed after age 50.
- ❑ The average age at diagnosis is 72* **in 2017 it is 63**

Colorectal Cancer



The Colorectal Cancer Problem

- ❑ Colorectal cancer is the second leading cause of cancer-related deaths in the United States
- ❑ Cancer of the large intestine accounts for 21% of all cancers in the US
- ❑ Potentially one of the most curable of gastrointestinal cancers
- ❑ **Estimated new cases and deaths** from colon and rectal cancer in the United States in 2010:
New cases: 102,900 (colon); 39,670 (rectal)
Deaths: 51,370 (colon and rectal combined)
- ❑ ~655,000 deaths worldwide per year.

Original Investigation

October 11, 2018

Association of Obesity With Risk of Early-Onset Colorectal Cancer Among Women

Po-Hong Liu, MD, MPH¹; Kana Wu, MD, MPH, PhD²; Kimmie Ng, MD, MPH³; [et al](#)[➤ Author Affiliations](#)

JAMA Oncol. 2019;5(1):37-44. doi:10.1001/jamaoncol.2018.4280

Key Points

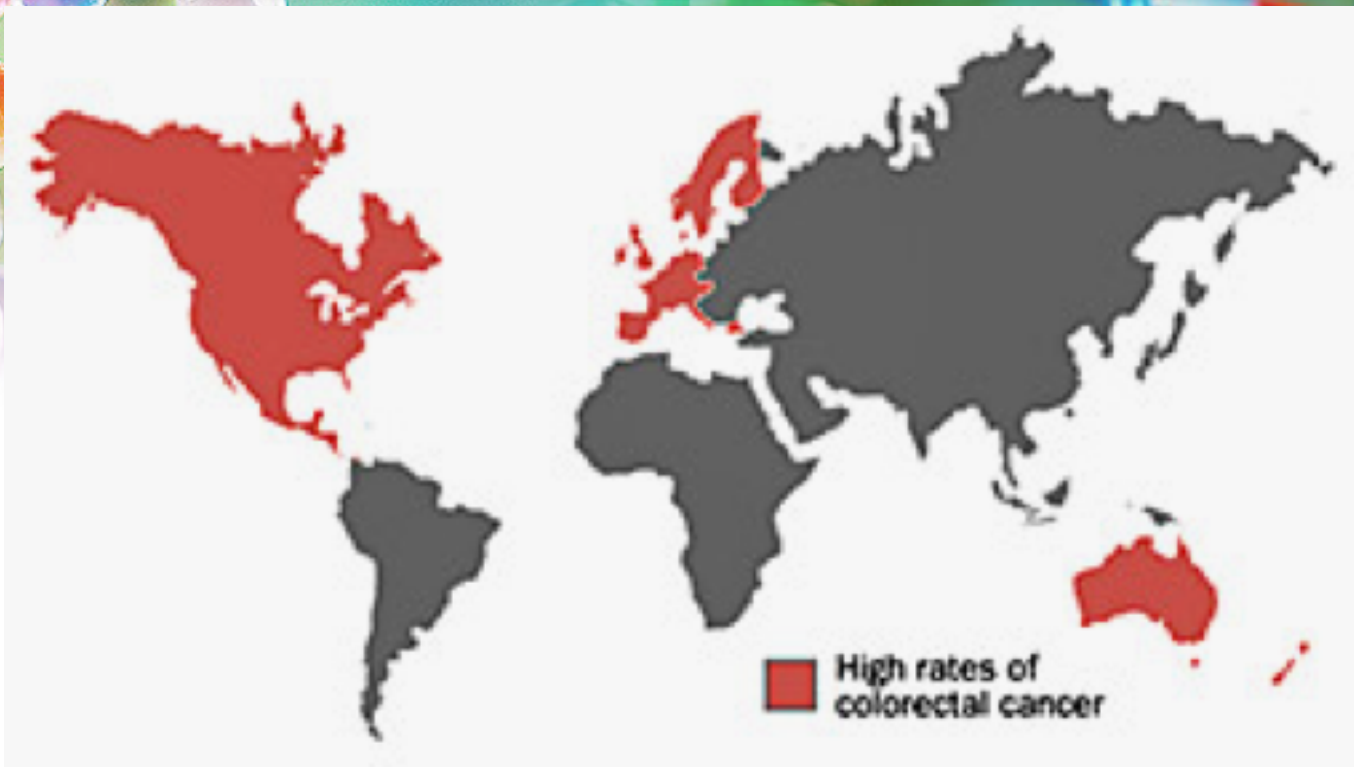
Question Is obesity associated with early-onset colorectal cancer, which may have etiologic differences from late-onset colorectal cancer?

Findings In a prospective cohort study of 85 256 women, those with obesity (body mass index ≥ 30) had a nearly doubled risk of early-onset colorectal cancer compared with women with a body mass index of 18.5 to 22.9.

Meaning The findings suggest that obesity is associated with an increased risk of early-onset colorectal cancer; further investigations are needed to identify whether this association is causal.



Geographic Distribution of Sporadic Colon Cancer

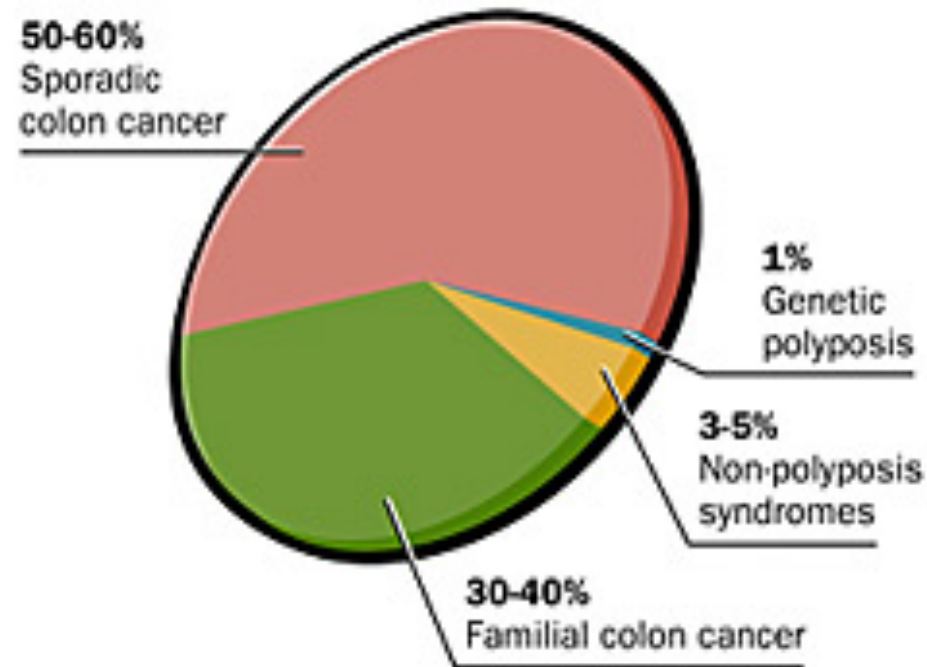


- ❑ There is great variability in the worldwide incidence and mortality rates of colon cancer.
- ❑ Industrialized nations appear to have the greatest risk while most developing nations have lower rates.
- ❑ North America, Western Europe, Australia and New Zealand have high rates for colorectal neoplasms

Risk Factors for Colorectal Cancer

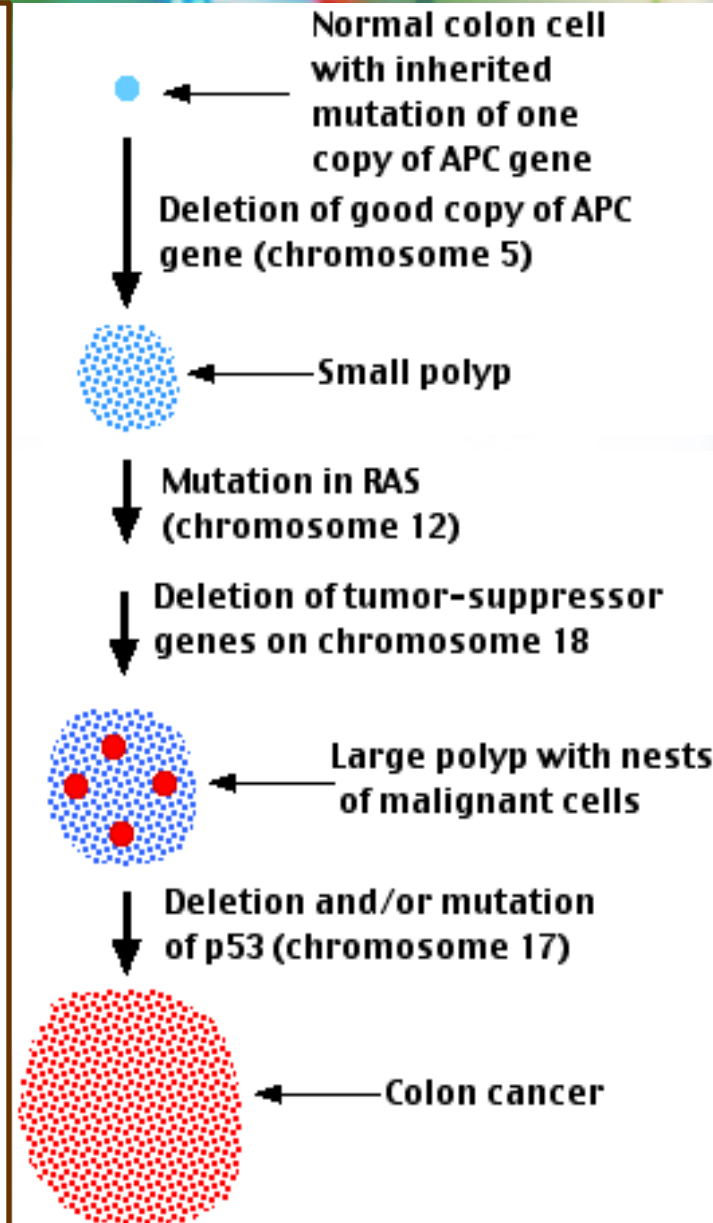
- Most people who develop colorectal cancer have no identifiable risk factors.
- Polyps** (non-cancerous growths that can become cancerous over time). Most colon cancers develop from polyps.
- Family history** of colon or rectal cancers, chronic colitis, or colon polyps. Unless it is treated, an inherited condition called Familial Polyposis puts a person at very high risk.
- Age.** Colon and rectal cancers occur most often in people over age 50.
- Having long term inflammation of the colon (diseases called **ulcerative colitis or Crohn's disease**)
- Eating a **diet** high in fat and low in fiber
- Physical inactivity**

Incidence of types of colorectal cancer in the United State



Progression of Colon Cancer

- ❑ Begins with the development of **polyps** in the epithelium of the colon. Polyps are **benign** growths
- ❑ As time passes, the polyps may get bigger
- ❑ At some point, nests of malignant cells may appear within the polyps
- ❑ If the polyp is not removed, some of these malignant cells will escape from the primary tumor and metastasize throughout the body.
- ❑ **At Least 2 Gene Mutations Involved**
 1. Deletion of a healthy copy of the **APC** (adenomatous polyposis coli) tumor suppressor gene on chromosome 5, or p53 (chromosome 17)
 2. A mutant proto-oncogene (often **RAS**).



Colon cancer's stages

Colon cancer is one of the most common types of cancer. It is very treatable, if caught early. Stages of a tumor and risk factors:

Stage 0

Cancer has not grown beyond inner layer of colon wall

Stage 1

Grown to outer layer of wall

Stage 2

Tumor is through wall, not spread to lymph nodes

Colon

Large intestine

Liver

Stomach

Small intestine

Stage 3

Spread to lymph nodes

Stage 4

Cancer spreads to distant sites in body, such as liver or lung

How tumor begins

- Normal tissue forms a polyp projecting from colon wall
- Over time, polyp becomes a tumor

Colon

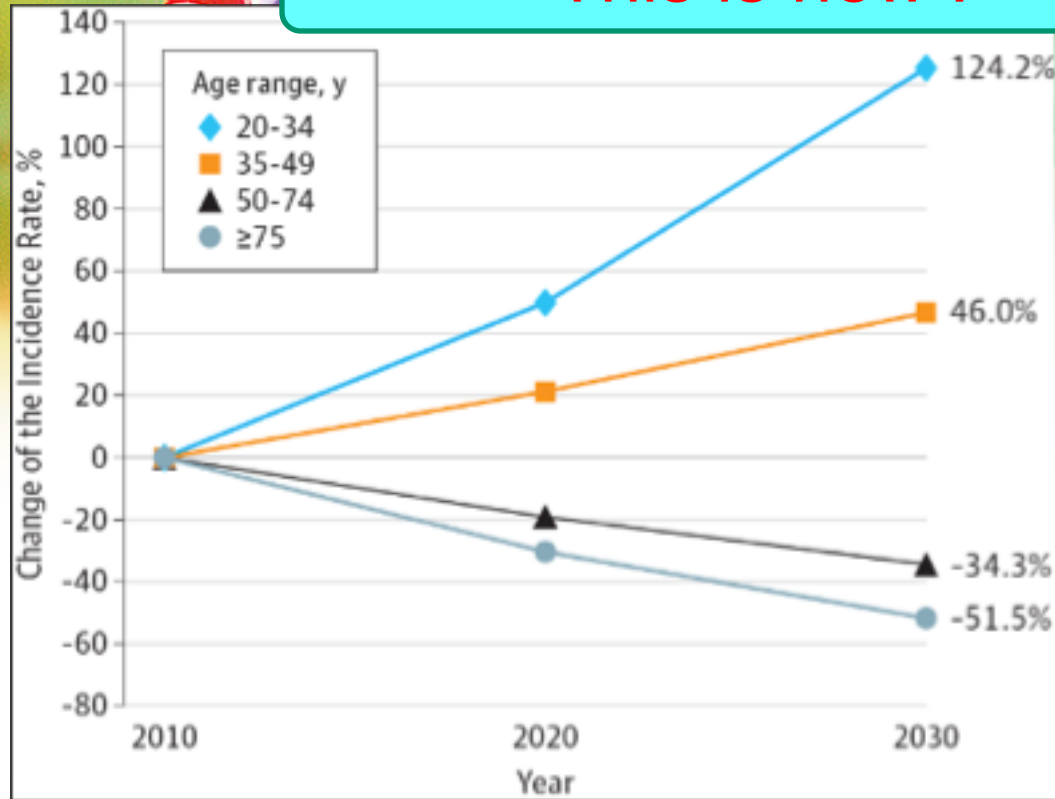
Risk factors

Age, family history of colon cancer, patients with ulcerative colitis or Crohn's disease

Colorectal Cancer Risk Factors



This is new !



Older decreased ?
Better screening

Colorectal cancer and age

- The median age at diagnosis for colon cancer is 68 in men and 72 in women; for rectal cancer it is 63 years of age in both men and women.
- As a result of rising colon and rectal cancer incidence rates in younger age groups coincident with declining rates in older age groups, the proportion of cases diagnosed in individuals younger than age 50 increased from 6% in 1990 to 11% in 2013.
- Most of these cases (72%) occur in people who are in their 40s.

Colorectal cancer doesn't care how old you are

The truth is you're never too young, and colorectal cancer is on the rise in those under age 50



One in 10 are diagnosed before age 50

A recent survey of young cancer survivors indicated

82%

were initially misdiagnosed

73%

were diagnosed at a later stage

50%

felt their symptoms were ignored

62%

did not have family history

67%

saw at least two doctors before diagnosis

What can you do?



Know the signs and symptoms



Listen to your body and speak up if something is not right



Know your family health history

What are the warning signs?

- Anemia
- Rectal bleeding, dark or black stool
- Change in bowel habits
- Diarrhea and/or constipation
- Narrowing of stool
- Persistent abdominal discomfort (cramps, gas, pain, or feeling bloated)
- Unexplained weight loss
- Weakness or fatigue
- Nausea or vomiting
- If you have Crohn's, Colitis, or IBS, you are at a higher risk

ccalliance.org | Helpline: (877) 422-2030

The Colorectal Cancer Alliance is a national organization committed to ending colorectal cancer within our lifetime. We are your allies — a national network of passionate survivors, caregivers and advocates dedicated to helping you and your family navigate all aspects of the disease, from diagnosis and treatment to a lifetime of progression-free survival. We are a community of people eager to share experiences, address your concerns, and answer your questions. We understand the different stages of the colorectal cancer journey because we've been there. We are here for you when you need us because we believe tomorrow can't wait.



Colorectal cancer

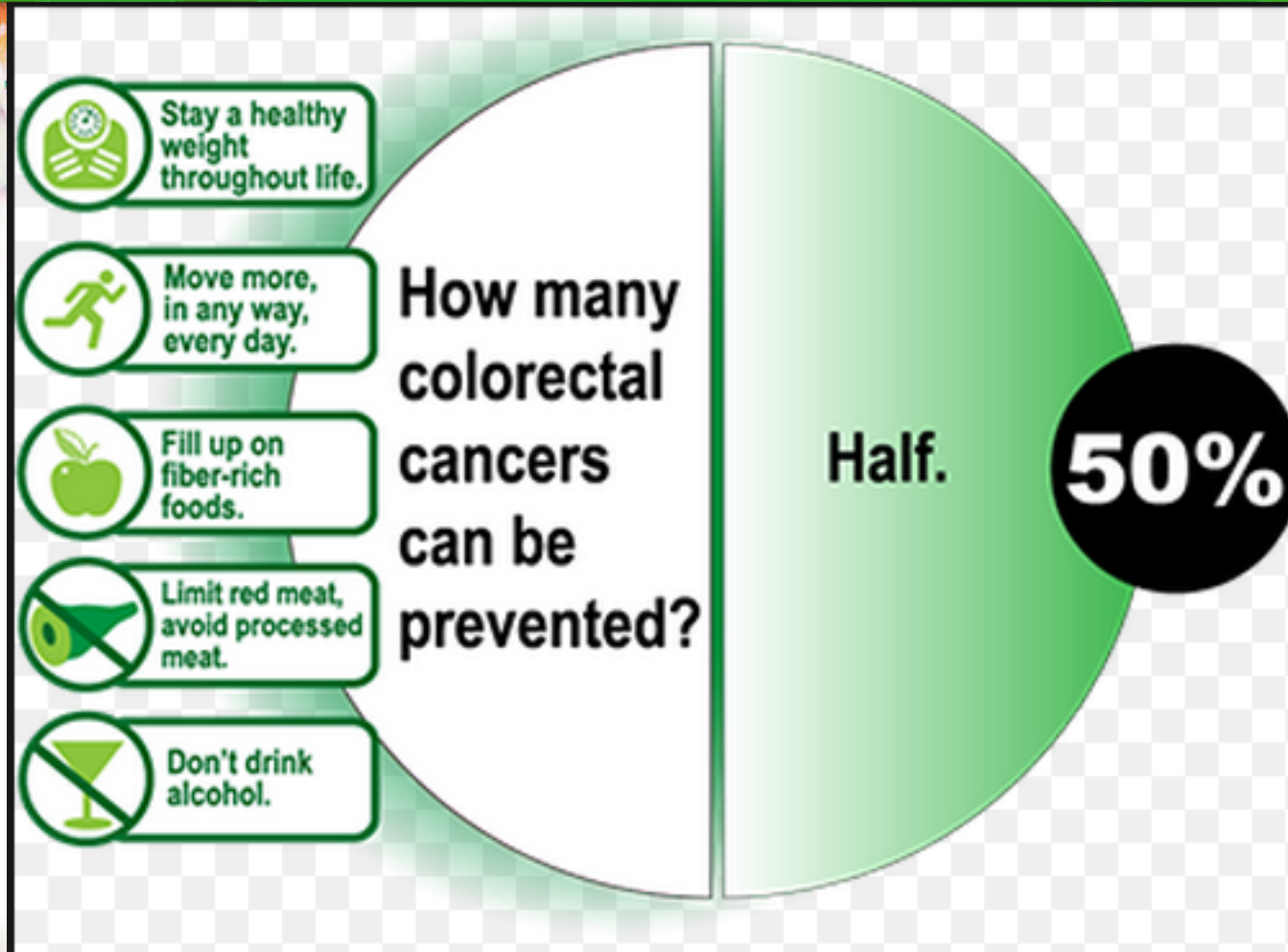
Factors that increase risk

Heredity and Medical History	RR
Family history	
• 1 FDR	2.2
• >1 relative	4.0
• Relative with cancer <45 years	3.9
Inflammatory bowel disease	
• Crohn's disease	2.6
• Ulcerative colitis	
◇ Colon	2.8
◇ Rectum	1.9
Diabetes	1.2
Behavioral Factors	RR
Alcohol consumption	1.6
Obesity	1.2
Red meat	1.2
Processed meat	1.2
Smoking	1.2

Factors that decrease risk

Lifestyle factors	RR
Physical activity (colon)	0.7
Dairy consumption	0.8
Fruit consumption	0.9
Vegetable consumption	0.9
Total dietary fiber (10g/day)	0.9
Aspirin use	0.5

Colorectal Cancer Risk



- B Catenin other half
See below

Screening Recommendations

- ❑ Beginning at the age of 50 years, persons at average risk for colorectal cancer undergo one of the following screening regimens:
- ❑ 1. **Fecal occult blood** testing annually.
- ❑ 2. **Flexible sigmoidoscopy** every five years.
- ❑ 3. Fecal occult blood testing annually plus flexible sigmoidoscopy every five years.
- ❑ 4. **Double-contrast barium** enema every five to 10 years.
- ❑ 5. **Colonoscopy** every 10 years.

TABLE 2

Summary of Characteristics of Screening Tests Discussed in the AHCPR Report*

Screening method	Overall performance	Complexity †	Potential effectiveness	Evidence of effectiveness	Screening test risk
Fecal occult blood test	Intermediate for cancers Low for polyps	Lowest	Lowest	Strongest	Lowest
Flexible sigmoidoscopy	High for up to one half of the colon	Intermediate	Intermediate	Intermediate	Intermediate
Fecal occult blood test plus flexible sigmoidoscopy	Same as for flexible sigmoidoscopy	Intermediate	Intermediate	Intermediate	Intermediate
Double-contrast barium enema	High	High	High	Weakest	Intermediate
Colonoscopy	Highest	Highest	Highest	Weakest	Highest

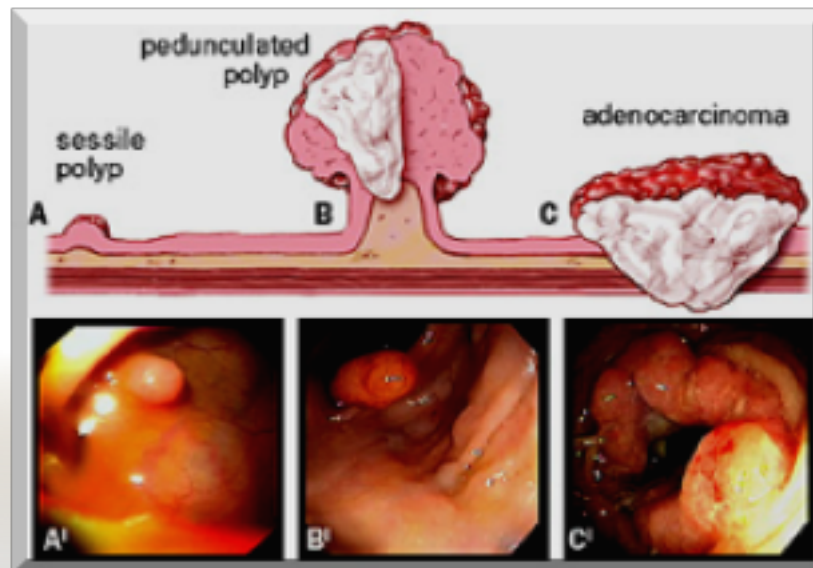
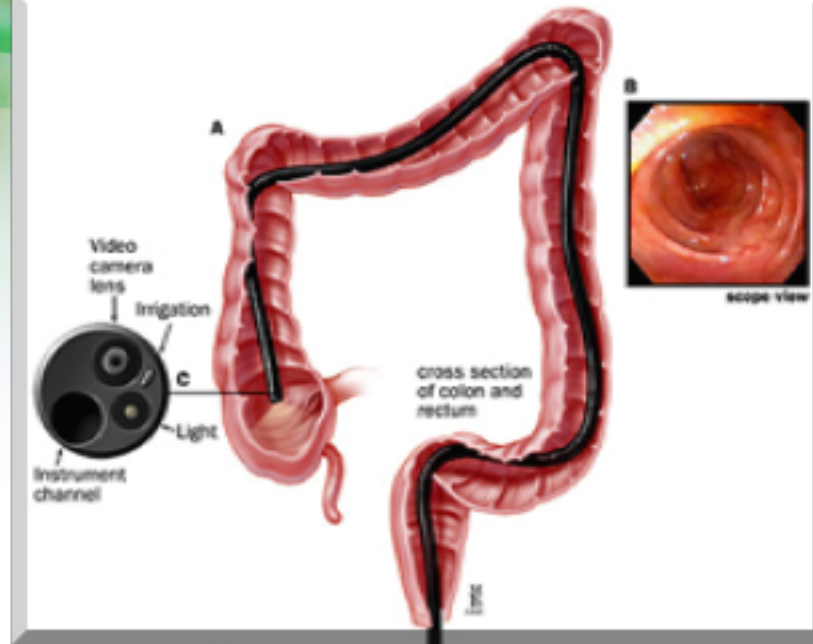
AHCPR = Agency for Health Care Policy and Research.

*—The cost of these screening tests (also an important characteristic) varies, but the costs of the screening strategies (lifetime programs of screening and follow-up of abnormal test results) are comparable.

†—Complexity includes patient preparation, inconvenience, facilities and equipment needed, and patient discomfort.

Colonoscopy

- ❑ **Colonoscopy** is the most widely used diagnostic method to study the colon and has the highest diagnostic sensitivity and specificity of all available tests.
- ❑ **Ninety to 95%** of the colon can be examined in most studies
- ❑ Test usually takes 60 minutes or less to complete and may be both diagnostic and therapeutic.
- ❑ Offers the flexibility of performing **biopsy** of suspicious regions and the ability to perform endoscopic **polypectomy**
- ❑ The sensitivity of colonoscopy for the detection of polyps greater than or equal to 1 cm and tumors is greater than 95%
- ❑ Colonoscopy is the preferred procedure for diagnosis of symptomatic patients and is the “**gold standard**” for the diagnosis of colorectal neoplasms





Cell. 1991 Aug 9;66(3):589-600.

Identification and characterization of the familial adenomatous polyposis coli gene.

Groden J, Thliveris A, Samowitz W, Carlson M, Gelbert L, Albertsen H, Joslyn G, Stevens J, Spirio L, Robertson M, et al.

Department of Human Genetics, University of Utah Health Sciences Center, Salt Lake City 84132.

Abstract

DNA from 61 unrelated patients with adenomatous polyposis coli (APC) was examined for mutations in three genes (DP1, SRP19, and DP2.5) located within a 100 kb region deleted in two of the patients. The intron-exon boundary sequences were defined for each of these genes, and single-strand conformation polymorphism analysis of exons from DP2.5 identified four mutations specific to APC patients. Each of two aberrant alleles contained a base substitution changing an amino acid to a stop codon in the predicted peptide; the other mutations were small deletions leading to frameshifts. Analysis of DNA from parents of one of these patients showed that his 2 bp deletion is a new mutation; furthermore, the mutation was transmitted to two of his children. These data have established that DP2.5 is the APC gene.

Wnt , B catenin: oncogenes

APC: tumor suppressor

(a) Normal cell (without Wnt protein).

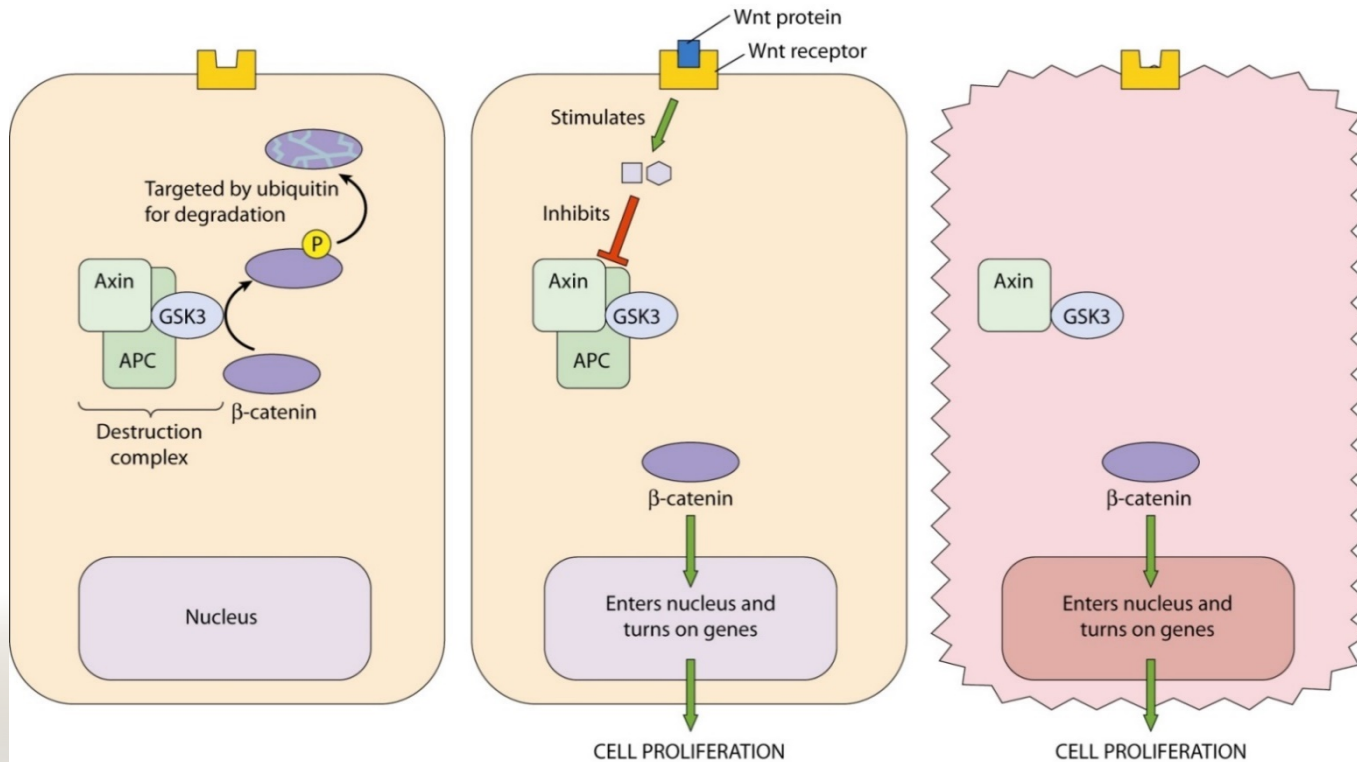
In the absence of a growth-signaling Wnt protein, β -catenin is targeted for degradation by the axin-APC-GSK3 destruction complex, which catalyzes the phosphorylation of β -catenin. The phosphorylated β -catenin is then linked to ubiquitin, thereby marking the phosphorylated β -catenin for degradation by proteasomes. The resulting absence of β -catenin maintains the Wnt pathway in the OFF position.

(b) Normal cell (with Wnt protein).

The Wnt pathway is normally turned ON by Wnt proteins, which bind to and activate cell surface Wnt receptors. The activated receptors stimulate proteins that inactivate the axin-APC-GSK3 destruction complex, thereby protecting β -catenin from degradation. The β -catenin then enters the nucleus and activates a variety of target genes, including those that control cell proliferation.

(c) Cancer cell (independent of the presence or absence of Wnt protein).

Some cancer cells have loss-of-function mutations in the APC gene. In the absence of functional APC protein, the destruction complex cannot form and β -catenin therefore accumulates, entering the nucleus and locking the Wnt pathway in the ON position.



Tumor typing / B(Beta) catenin mutations

Medscape Medical News > Oncology

Only Half of Colorectal Cancers Linked to Obesity and Inactivity

Zosia Chustecka

Feb 26, 2013



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Obesity and physical inactivity have been increasingly linked to colorectal cancer, but a new study suggests that these risk factors are only important in about half of all cases.

The study, published online February 26 in *Cancer Research*, found that increased body weight and decreased levels of physical activity are only associated with an increased risk for colorectal cancer that tests negative for the **biomarker** CTNNB1. This subtype accounted for 54% of the cases tested.

For CTNNB1-positive colorectal cancer, which accounted for the remaining 46% of cases tested, no such association was found. It appears that these cancers are independent of those lifestyle factors, senior author Shuji Ogino, MD, PhD, associate professor of pathology at the Dana-Farber Cancer Institute and

associate professor of epidemiology at the Harvard School of Public Health in Boston, Massachusetts, told *Medscape Medical News*.

marker distinguishes between *lifestyle* and genetic cancer

Studies Link Daily Doses of Aspirin to Reduced Risk of Cancer

By RONI CARYN RABIN
Published: March 20, 2012

Taking aspirin every day may significantly reduce the risk of many cancers and prevent [tumors](#) from spreading, according to two new studies published on Tuesday.



Tim Boyle/Getty Images
Drawbacks of daily doses of aspirin include a risk of gastrointestinal bleeding.

The findings add to a body of evidence suggesting that cheap and widely available aspirin may be a powerful if overlooked weapon in the battle against [cancer](#). But the research also poses difficult questions for doctors and public health officials, as regular doses of aspirin can cause [gastrointestinal bleeding](#) and other side effects. Past studies have suggested that the drawbacks of daily use may outweigh the benefits, [particularly in healthy patients](#).

One of the new studies examined patient data from dozens of large, long-term randomized controlled trials involving tens of thousands of men and women. Researchers at the University of Oxford found that after three years of daily aspirin use, [the risk of developing cancer was reduced by almost 25 percent when compared with a control group not taking aspirin](#). After five years, the risk of dying of cancer was reduced by 37 percent among those taking aspirin.

RECOMMEND

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PRINT

REPRINTS

SHARE



- Toxicity/bleeding..... screening first



- 25% **DECREASE** from aspirin therapy
- **BUT** only for those with mutation
- Highlights genomic/ personal medicine

HarvardScience ▶ Health & Medicine ▶

Aspirin's impact on colorectal cancer

Gene mutation key to dramatic increase in rate of survival



Aspirin therapy can extend the life of colorectal cancer patients whose tumors carry a mutation in a key gene, but it has no effect on patients who lack the mutation, Harvard-affiliated [Dana-Farber Cancer Institute](#) scientists report in the Oct. 25 issue of the New England Journal of Medicine.

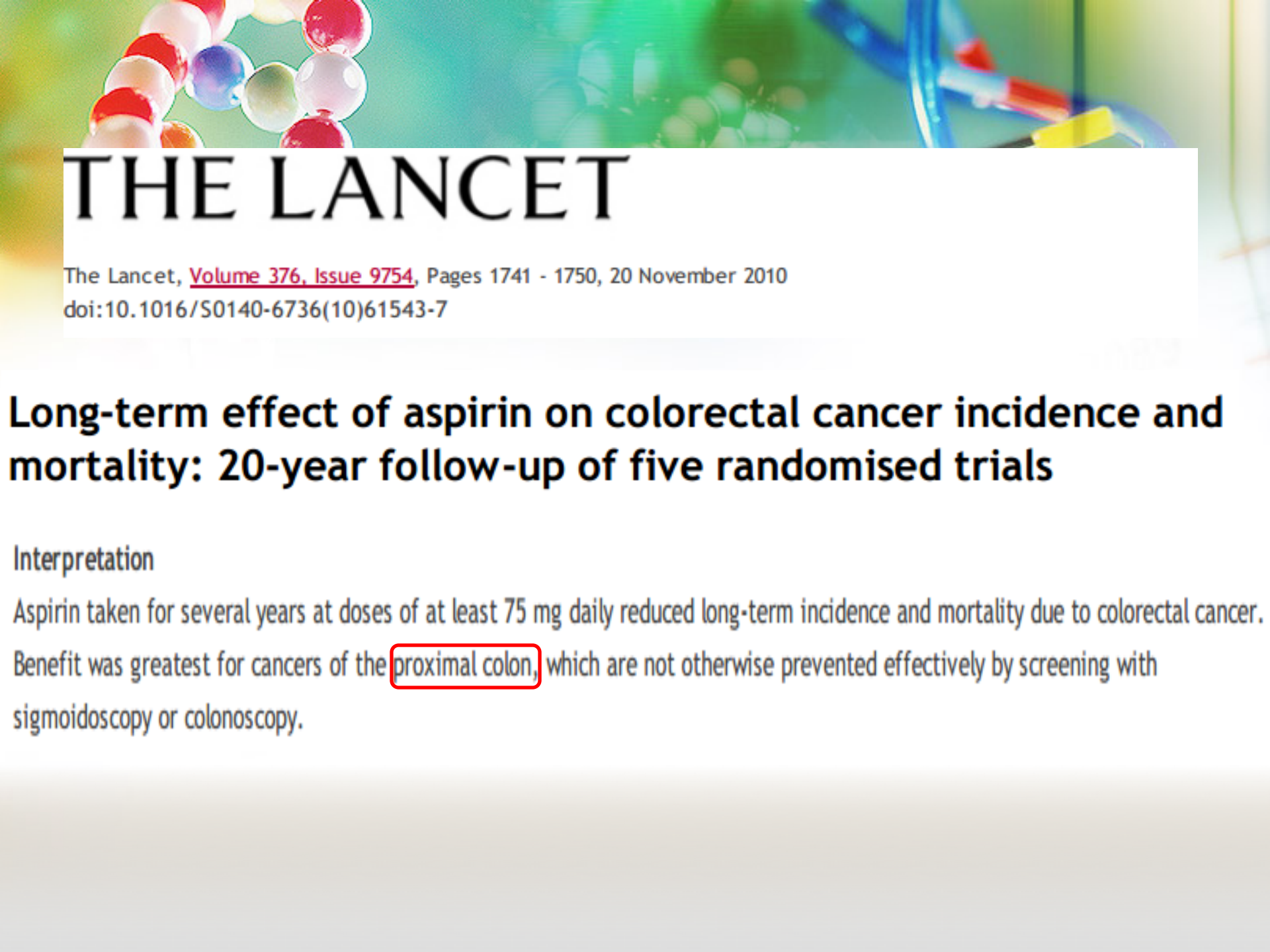
In a study involving more than 900 patients with colorectal cancer, the researchers found that, for patients whose tumors harbored a mutation in the gene [PIK3CA](#), aspirin use produced a sharp jump in survival: five years after diagnosis, 97 percent of those taking aspirin were still alive, compared with 74 percent of those not using aspirin. By contrast, aspirin had no impact on five-year survival rates among patients without a [PIK3CA](#) mutation.



Recommendation Summary

Population	Recommendation	Grade (What's This?)
Adults aged 50 to 59 years with a $\geq 10\%$ 10-year CVD risk	The USPSTF recommends initiating low-dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer (CRC) in adults aged 50 to 59 years who have a 10% or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.	B
Adults aged 60 to 69 years with a $\geq 10\%$ 10-year CVD risk	The decision to initiate low-dose aspirin use for the primary prevention of CVD and CRC in adults aged 60 to 69 years who have a 10% or greater 10-year CVD risk should be an individual one. Persons who are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years are more likely to benefit. Persons who place a higher value on the potential benefits than the potential harms may choose to initiate low-dose aspirin.	C
Adults younger than 50 years	The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults younger than 50 years.	I
Adults aged 70 years or older	The current evidence is insufficient to assess the balance of benefits and harms of initiating aspirin use for the primary prevention of CVD and CRC in adults aged 70 years or older.	I

See the [Clinical Considerations](#) section for guidance on aspirin dosage.



THE LANCET

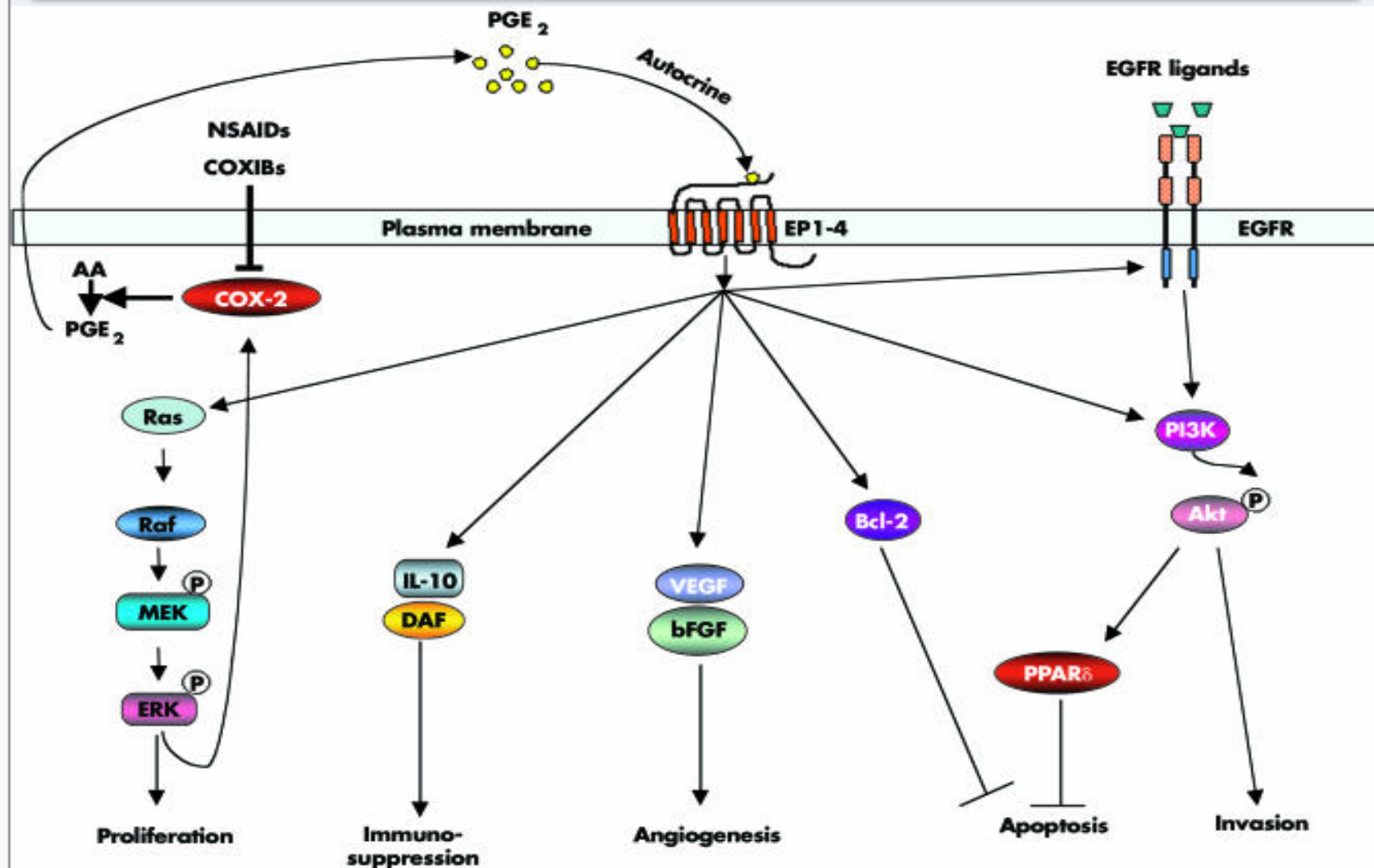
The Lancet, [Volume 376, Issue 9754](#), Pages 1741 - 1750, 20 November 2010
doi:10.1016/S0140-6736(10)61543-7

Long-term effect of aspirin on colorectal cancer incidence and mortality: 20-year follow-up of five randomised trials

Interpretation

Aspirin taken for several years at doses of at least 75 mg daily reduced long-term incidence and mortality due to colorectal cancer. Benefit was greatest for cancers of the **proximal colon**, which are not otherwise prevented effectively by screening with sigmoidoscopy or colonoscopy.

Aspirin lowers colorectal cancer rates



The USPSTF is an independent panel of non-Federal experts in prevention and evidence-based medicine and is composed of primary care providers (such as internists, pediatricians, family physicians, gynecologists/obstetricians, nurses, and health behavior specialists).

The USPSTF conducts scientific evidence reviews of a broad range of clinical preventive health care services (such as screening, counseling, and preventive medications) and develops recommendations for primary care clinicians and health systems. These recommendations are published in the form of "Recommendation Statements."

Current Recommendation

Release Date: October 2008

- The USPSTF recommends screening for colorectal cancer using fecal occult blood testing, sigmoidoscopy, or colonoscopy in adults beginning at age 50 years and continuing until age 75 years. The risks and benefits of these screening methods vary.
Grade: [A Recommendation](#).
- The USPSTF recommends against routine screening for colorectal cancer in adults ages 76 to 85 years. There may be considerations that support colorectal cancer screening in an individual patient.
Grade: [C Recommendation](#).
- The USPSTF recommends against screening for colorectal cancer in adults older than age 85 years.
Grade: [D Recommendation](#).
- The USPSTF concludes that the evidence is insufficient to assess the benefits and harms of computed tomographic colonography and fecal DNA testing as screening modalities for colorectal cancer.
Grade: [I Statement](#).



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Stool DNA tests

Instead of looking for blood in the stool, these tests look for certain abnormal sections of DNA (genetic material) from cancer or polyp cells. Colorectal cancer cells often contain DNA mutations (changes) in certain genes. Cells from colorectal cancers or polyps with these mutations are often shed into the stool, where tests may be able to detect them.

Although stool DNA tests have been used for colorectal screening in the past, they are no longer available in the US.