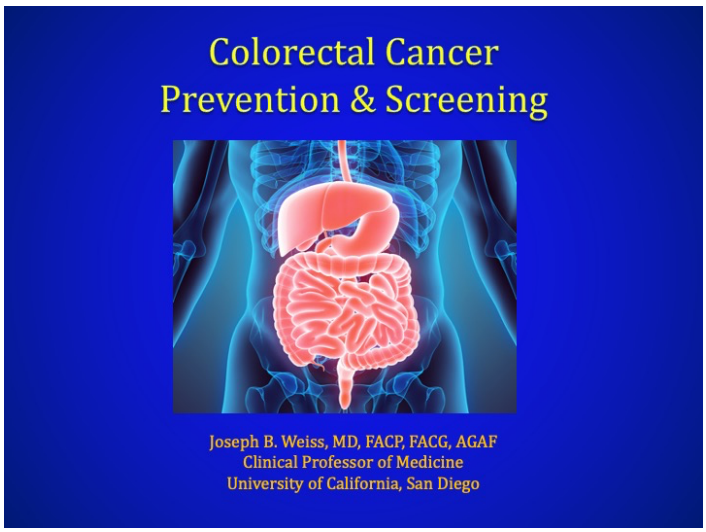


Nearly 2,500 years ago Hippocrates of Kos, traditionally considered the 'father of medicine, recognized the critical role of nutrition and diet in health and disease. As society developed, and especially when the food industry became the predominant influencer of the consumer diet, crop yield, shelf-life, and the ability to drive consumption by addictive food flavorings and convenience, made marketing the conduit to massive profitability. Unfortunately, it was not just food industry profits that became massive, as over 75% of Americans are now classified as overweight or obese. The Standard American Diet, with the all too appropriate acronym S.A.D. is a recipe for disaster and has been the diet of choice for over a generation of Americans. The Standard American Diet is over 85% processed foods and animal products. The healthy portion of the diet, vegetables, fruits, nuts, beans, and whole grains comprise only 15%.The end result of the Standard American Diet are the Standard American Diseases of Obesity, Diabetes, Cancer, Cardiovascular Diseases and Inflammation.

Diet plays a central role in human health and nutrition, including cancer. While cancer is recognized as a disease intimately tied to genes, genomics, and mutations advances in the field of epigenetics have identified the many environmental influences on the genotypic and phenotypic expression of genes. Diet plays a critical role and has been strongly associated with a variety of different cancers, including colorectal cancer (CRC). The World Health Organization has classified processed meat as Group 1 Carcinogens. Food processing can also increase carcinogenesis, such as high temperature or open flame grilling.

Obesity itself is associated with a significant increase in cancer risk, especially colorectal cancer. While increased caloric intake has accompanied the increase in portion size over the last few decades resulting in overeating, poor food choices, and reduced physical activity have also been major contributors to the virtual epidemic of overweight and obese Americans. Besides colorectal cancer these other common cancers are associated with obesity or being overweight. Alcohol is carcinogenic and is an independent risk factor for many cancers. There is no minute amount of alcohol that has not been statistically linked to an increase in cancer incidence. Alcohol in any amount is carcinogenic. Tobacco is another social habit which has a long association with a variety of cancers. After decades of public health announcements, most of the public is familiar with this message, yet tobacco use remains common.

Most of the public remains unaware of the cancer association with obesity, diabetes, alcohol, and decreased physical activity, and they would be well served to be made aware. General dietary guidelines can be very helpful, and cancer reduction is not difficult to achieve if red and processed meet, alcohol, and tobacco are eliminated, or at least restricted. Avoiding highly processed, refined, and sweetened food

should be avoided or limited. Fruits and vegetables especially if brightly and deeply colored, whole grains, legumes, and fiber rich foods should be encouraged.

Colorectal cancer (CRC) ranks only behind lung cancer as the most common malignancy among both genders. There are over 2,000,000 cases of CRC worldwide, with over 152,000 cases and 52,000 deaths in the United States alone. What many do not realize, including many specialists, is that colorectal cancer is not one single disease. There are several varieties, which are best classified based on their genomic markers, and these distinctions direct therapy, diagnosis, and prognosis. In general CRC in men occurs more often in adenomatous polyps in the more distal colon, which is why flexible sigmoidoscopy has potential value as a CRC screening measure in men, less so in women. CRC in women tends to arise in the proximal colon in sessile serrated adenomas, which are more difficult to reach, identify, and remove. These features make colonoscopy more challenging in women with higher rate of missed polyps and cancers, as well as higher morbidity and mortality.

Recognizing the different types of colorectal cancers is important when considering whether screening is recommended or not. Complicating matters further is the fact that screening is considered an investment in preventive care, and the return on that investment can be calculated several ways using a variety of variables. The most important point I want to make is that all guidelines are based on population medicine, determining what is best for the average population. No one is an average person, each individual is unique, and taking their features into account may yield a different cost benefit analysis and recommendation. The second point is that there are also a variety of stakeholders, with at times diametrically competing economic interests in the recommendations proposed. Lastly, technology is advancing rapidly, and guidelines are usually several years behind. Population based screening test recommendations are for the average risk population. They do not fully take into account the identifiable risk factors that would allow a more accurate assessment of risk, and personalized appropriate recommendations for screening. While most people will not take the time to individualize recommendations, doing so can and will save lives, the only question is at what economic cost.

While screening has documented value, prevention has an even more attractive approach and value proposition. Avoiding colon polyps and cancers reduces the need for screening tests, invasive procedure, and the risk of complications and expense. Further refinements are expected, and some of the most recent research has identified specific microbiome populations that may place a role in CRC pathogenesis as well. CRC risk reduction has been associated with the following: aspirin 50% lower risk, NSAIDs 50% lower risk, fruits 15% lower risk, vegetables 15% lower risk, calcium, magnesium, Vitamin D, garlic, fish, metformin, estrogen hormone replacement therapy, selenium, folate, resistant starch, fiber, Vitamin B6 (pyridoxine). Coffee and statins may also reduce the risk, but the data is not yet clear.

General recommendations are that average risk screening begin at age 45 with either fecal immunochemical test (FIT) performed every year, multi-target stool DNA with FIT (Cologuard) every three years, or high-quality colonoscopy every 10 years. The best screening test is the one that gets done, and a regular schedule with compliance is key. There are many nuances and distinctions as to how to define a high-quality colonoscopy, and many receive a colonoscopy with a poor preparation or other limitations. Because of these limitations it is not unusual for CRC to develop in the interval of screening examinations, up to a 7% rate of interval CRC has been reported. Screening allows the diagnosis of premalignant polyps, and the removal of these polyps at colonoscopy is an easy, fast, and low risk way to avoid a cancer that may develop years in the future.

Screening can also identify a polyp that already contains a cancer, or a cancer that is at the early stages within the colon or rectum itself. When colorectal cancer is identified at stage I the 5-year survival rate is 94%, at stage II it is 82%, at stage III 67%, and at stage IV 11%. Advances in therapy, such as immunotherapy, may further improve numbers, but it is clear that later stages of disease have much

lower 5-year survival rates. Low screening compliance is associated with poor prognosis, and over one half of all CRC deaths are attributed to missed screening opportunities. There are a number of options for CRC screening, and each has advantages and disadvantages. While choice enhances compliance for many, for others it becomes an issue that leads to decision paralysis. When offered with knowledgeable and compassionate guidance the choices allow selection of the CRC screening method that is most likely to result in compliance. While all of the screening tests have different rates of sensitivity and specificity, the 'bottom line' is that the best CRC screening test for an individual is the one that will get done!

The public health outreach to encourage CRC screening has designated March as colon cancer awareness month each year. The risk factors and warning signs are listed, but these warning signs often appear to late in the course of the disease. Routine annual CRC screening beginning at age 45 is prudent, especially in African Americans. Easy, safe, reliable, and inexpensive fecal immunochemical test (FIT) of stool for occult blood is the most common screening test employed. Even for those without a family history raising additional concerns, a once in a lifetime saliva genomic test for over 150 otherwise hidden genetic predispositions, including the CRC risk of Lynch Syndrome and the BRAC 1 & 2 genes, is available for under $200. Genomic tests for CRC using cell free tumor cell DNA are now commercially available but not yet covered by insurance.

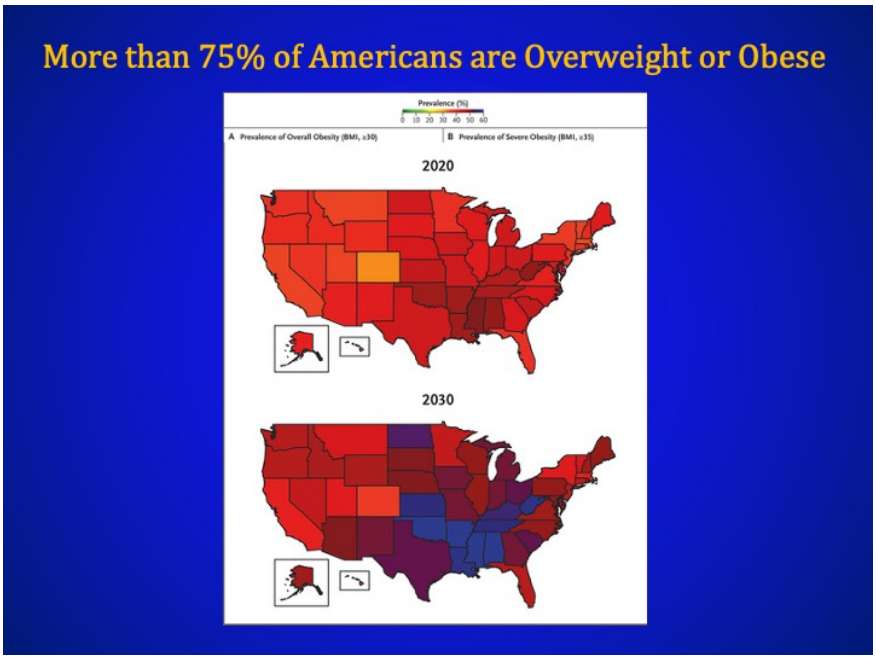
Advances in genomics and tumor biology have identified a growing large number of oncogenes, tumor suppressor genes, and other markers of cancer predisposition or development. In CRC there are over a dozen that have been identified and appear to follow a cascade of mutations leading to cancer. They are also being used to pinpoint therapy for the precision medicine of modern oncology. Many cancers that used to be identified only by their organ of origin, are now being reclassified based on their genomic markers.

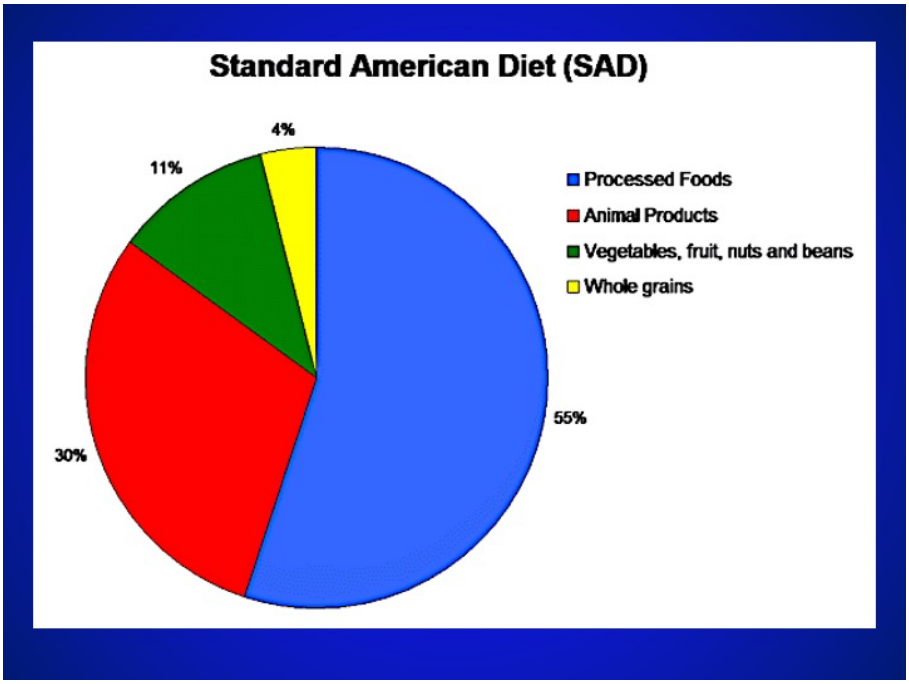
Colon polyps are very common, occurring in over 50% of the population over age 60, and the majority do not go on to cancer. The greater the size of the polyp, the great the risk, large polyps larger than 2.5 cm have a 50% incidence of cancer within the polyp. It usually takes years for polyps to progress to that size, allowing the 10-year interval between screening colonoscopies. Fecal immunochemical test (FIT) has replaced the old guaiac test for occult blood. It is specific for human hemoglobin, nearly always of colonic origin because it requires microbial degradation of hemoglobin. There are variations in sensitivity and reliability, laboratory-based tests are preferred but are more expensive at 4100 to $150, but less expensive CLIA waived home use tests ($20 to $45) may well be acceptable, clinical trials are ongoing.

Multitarget stool DNA includes a FIT test as well as specific gene markers to identify cancers and polyps. It is more sensitive and specific than FIT for polyps but is much more expensive at around $500 to $650. Standard to repeat at three years in an average risk individual. CT and MRI virtual colonoscopy. Comparable to colonoscopy in identifying cancer and polyps > 1cm. Less expensive, faster, no sedation required, low dose radiation, advancing technology to avoid prep with ability to tag stool and then digitally subtract it from images. Has additional advantage over colonoscopy which fails and cannot reach cecum in about 5% of cases. There are also many areas that the colonoscopist does not inspect because of instrument and visualization limitations. Virtual colonoscopy does not have these limitations yet has still not gained popularity.

Cell free DNA blood tests specifically for CRC, as well as a panel for over 50 different cancers are now commercially available but not covered by insurance. Cost is usually just under $1,000. Expect rapid advances, competition, and price decreases. Anticipate that this technology will eventually dominate the marketplace with high accuracy, high compliance as a simple blood test, no stool, no colonoscopy, no 'explosive' colon blow-out prep, no sedation, no lost work time, high reproducibility, full insurance coverage. Colonoscopy remains the gold standard for higher risk individuals and polypectomy. As a screening test for the average risk population it is grossly overpromoted.

Most primary care practitioners are not aware of its downsides, and its title as the gold standard should refer to its financial prowess in generating revenue for colonoscopists, endoscopy centers, and hospitals. Complication rate around 2% most are minor but life-threatening complications (bleeding, perforation, aspiration, cardiopulmonary, etc.) and death occur with regularity at a rate of approximately 1 in 1,000. Miss rate for cancers around 5%, polyps >6mm 10 to 20%, polyps <5 mm around 45%. Incomplete exams by not reaching cecum 5%, poor preparation limiting view 20%, anatomical challenges especially women with abdominal or pelvic surgery over 10% unable to complete exam and over 50% limited views of proximal colon where most dangerous pathology occurs. Very expensive ranging from $2,500 to $15,000 if include professional fees, facility fees, anesthesiologist, pathologist, pharmacy, time off from work transportation, etc.

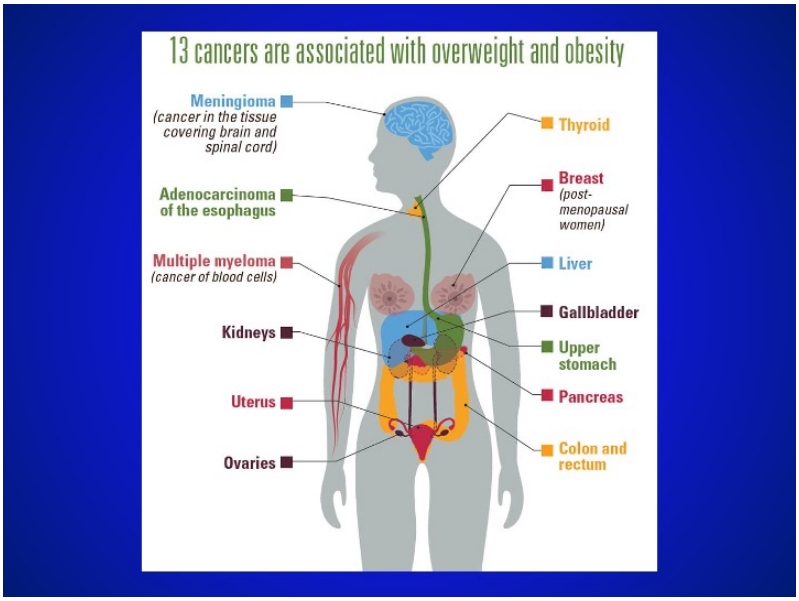




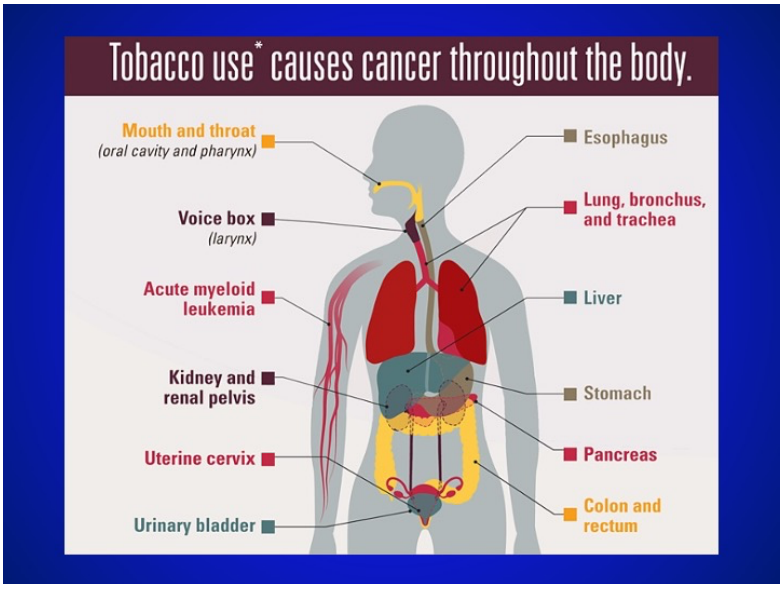

WORST CANCER CAUSING FOODS
Refined sugars and grains , hydrogenated oils, and nitrates are ingredients in food that are known to promote cancer development. The following food are the absolute worst and should be avoided.
1. Hotdogs
2. Processed Meats and Bacon
3. Doughnuts
4. French Fries
5. Chips, Crackers and Cookies


The World Health Organization has classified processed meats like bacon, salami, hotdogs and ham as
GROUP 1 CARCINOGENS


Portion Distortion
20 YEARS AGO
TODAY
DIFFERENCE
333 Calories
590 Calories
257 MORE CALORIES
Lifting weights for 1 HOUR AND 30 MINUTES burns approximately 257 calories* *Based on 130-pound person
500 Calories
850 Calories
350 MORE CALORIES
Playing golf (while walking and carrying your clubs) for 1 HOUR burns approximately 350 calories* *Based on 160-pound person
1 cup spaghetti with sauce and 3 small meatballs
2 cups spaghetti with sauce and 3 large meatballs
500 Calories
1,025 Calories
525 MORE CALORIES
Housecleaning for 2 HOURS AND 35 MINUTES burns approximately 525 calories* *Based on 130-pound person
20 YEARS AGO
TODAY
DIFFERENCE
Coffee, 8 oz (with whole milk and sugar)
Mocha Coffee, 16 oz (with steamed whole milk and mocha syrup)
45 Calories
350 Calories
305 MORE CALORIES
Walking 1 HOUR AND 20 MINUTES burns approximately 305 calories* *Based on 130-pound person
1.5 oz
4 oz
210 Calories
500 Calories
290 MORE CALORIES
Vacuuming for 1 HOUR AND 30 MINUTES burns approximately 290 calories* *Based on 130-pound person
1.5 diameter
3.5 diameter
55 Calories
275 Calories
220 MORE CALORIES
Washing a car for 1 HOUR AND 15 MINUTES burns approximately 220 calories* *Based on 130-pound person


13 cancers are associated with overweight and obesity
Meningioma
(cancer in the tissue covering brain and spinal cord)
Adenocarcinoma of the esophagus
Multiple myeloma
(cancer of blood cells)
Kidneys
Uterus
Ovaries
Thyroid
Breast
(post-menopausal women)
Liver
Gallbladder
Upper stomach
Pancreas
Colon and rectum

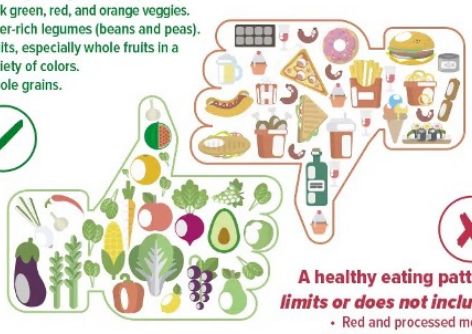

ALCOHOLIC BEVERAGES
INCREASE RISK
OF THESE CANCERS:
Mouth, Pharynx, Larynx
Esophageal
Breast
Colorectal
Stomach
Liver
For cancer prevention, AICR recommends not drinking alcohol.
If you do drink, limit your alcoholic beverages to 2 for men and 1 for women a day.
www.aicr.org
Sources: AICR/WCRF's Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective (2007), Continuous Update Project reports (ongoing).
American Institute for Cancer Research


Tobacco use* causes cancer throughout the body.
Mouth and throat
(oral cavity and pharynx)
Voice box
(larynx)
Acute myeloid leukemia
Kidney and renal pelvis
Uterine cervix
Urinary bladder
Esophagus
Lung, bronchus, and trachea
Liver
Stomach
Pancreas
Colon and rectum

Diet Guidelines for Cancer Prevention

A healthy eating pattern *includes*:

- A variety of vegetables, especially dark green, red, and orange veggies.
- Fiber-rich legumes (beans and peas).
- Fruits, especially whole fruits in a variety of colors.
- Whole grains.



A healthy eating pattern *limits or does not include*:

- Red and processed meats.
- Sugar-sweetened beverages.
- Highly processed foods.
- Refined grain products.
- Alcohol.

SOURCE: AMERICAN CANCER SOCIETY GUIDELINE FOR DIET AND PHYSICAL ACTIVITY FOR CANCER PREVENTION

To Screen or Not To Screen?

National ,regional, and demographic variation.
Guidelines are based on general populations, not personalized or precise.
Economic conflicts (provider vs insurer).
Guidelines often not current with advances (e.g. cell free DNA).
Guidelines variable influenced by stakeholders.

- American Association for the Study of Liver Disease (AASLD)
- American College of Gastroenterology (ACG)
- American Gastroenterological Association (AGA)
- American College of Surgeons (ACS)
- American Society of Clinical Oncology (ASCO)
- American Society for Gastrointestinal Endoscopy (ASGE)
- American College of Radiology (ACR)
- National Comprehensive Cancer Network (NCCN)
- European Society of Medical Oncology (ESMO)
- American Cancer Society (ACS)
- National Cancer Institute (NCI)
- National Clinical Guideline Center (NCGC)
- US Preventive Services Task Force (USPSTF)

Cancer of Colon & Rectum

2,000,000+ worldwide CRC cases each year

150,000+ United States CRC cases each year

52,000+ deaths from CRC in United States each year

Most common cancer for screening promotion

Screening can identify precancer polyps

Increasing incidence in younger population

Multiple screening options

Cancer of Colon & Rectum – Increased Risk

- Age
- Familial adenomatosis polyposis (FAP)
- Hereditary non-polyposis colorectal cancer (HNPCC) - Lynch syndrome
- MUTYH-associated polyposis (MAP)
- Family history 80% increase first degree
- Alcohol 70% increased risk
- Obesity 50% increased risk
- Hyperlipidemia 50% increased risk
- Tobacco 25% increased risk
- Male 25% increased risk
- African American 20% increased risk
- Family history 20% if not first degree
- Red processed meat 15% increased risk
- Sedentary lifestyle 15% increased risk
- Colon polyps - adenoma, sessile serrated
- Ulcerative colitis
- Hereditary breast and ovarian cancer syndrome (BRCA1, BRCA2)
- Diabetes mellitus
- Acromegaly
- Crohn disease
- Cystic fibrosis
- Antibiotics
- High fat foods
- Low fiber diet
- High temperature grilling/cooking
- Abdominal/pelvic radiation
- Hypertension
- Iron deficiency
- Transplant immunosuppression
- Cholecystectomy
- Androgen deprivation therapy
- Ureterocolic anastomosis
- Coronary heart disease

Cancer of Colon & Rectum – Reduced Risk

- Aspirin 50% lower risk
- NSAIDs 50% lower risk
- Fruits 15% lower risk
- Vegetables 15% lower risk
- Calcium
- Magnesium
- Vitamin D
- Garlic
- Fish
- Metformin
- Hormone replacement therapy
- Selenium
- Folate
- Resistant starch
- Fiber
- Vitamin B6 (pyridoxine)
- Coffee?
- Statins?

Colon & Rectal Cancer Screening

Average risk screening begin age 45

- Fecal immunochemical test (FIT) - annual
- Multi target stool DNA test - every 3 years
- Colonoscopy every 10 years

Higher risk screening

- Genetic syndromes
- Family history
- Inflammatory bowel disease
- Colon polyp history

REDUCE YOUR RISK OF CANCER

CONSUME **LESS** OF	EAT **MORE** OF
	
• Saturated fats • Processed meat • Red meat • Salt-cured & smoked food • Food with preservatives • Alcoholic beverages	• Fruits & vegetables • Whole grains • Dark green & orange vegetables • Foods rich with Vitamins A, C, and E

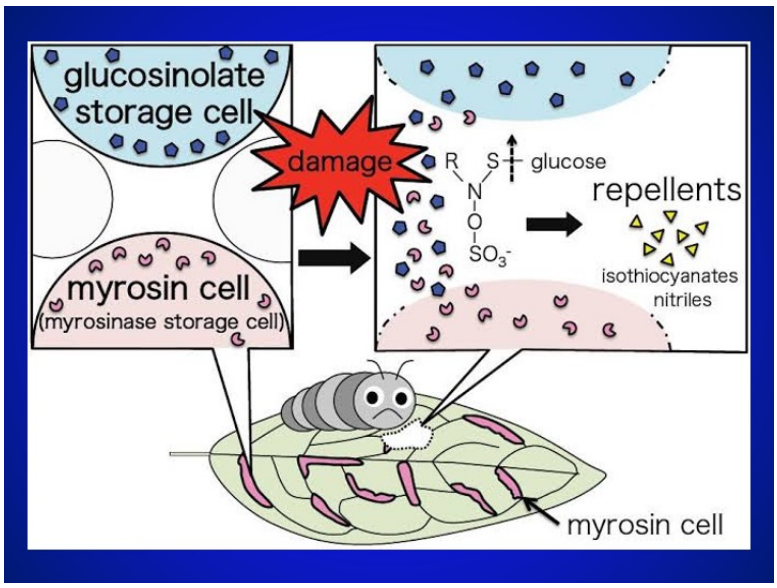
Studies show vegetarians live longer

A pesco vegetarian has a 19% lower risk of death compared to a non-vegetarian.

WHAT ARE CRUCIFEROUS VEGETABLES?

Cruciferous vegetables are vegetables in the family Brassica, and they are some of the most nutritionally dense foods we eat. Among others, this family includes:

- BROCCOLI
- KALE
- ARUGULA
- CABBAGE
- RADISH
- HORSERADISH
- WATERCRESS
- COLLARD GREENS
- BRUSSELS SPROUTS
- CAULIFLOWER
- TURNIP
- RUTABAGA
- MUSTARD
- WASABI



Significantly fewer patients survive when they are diagnosed in a later stage[2,3]

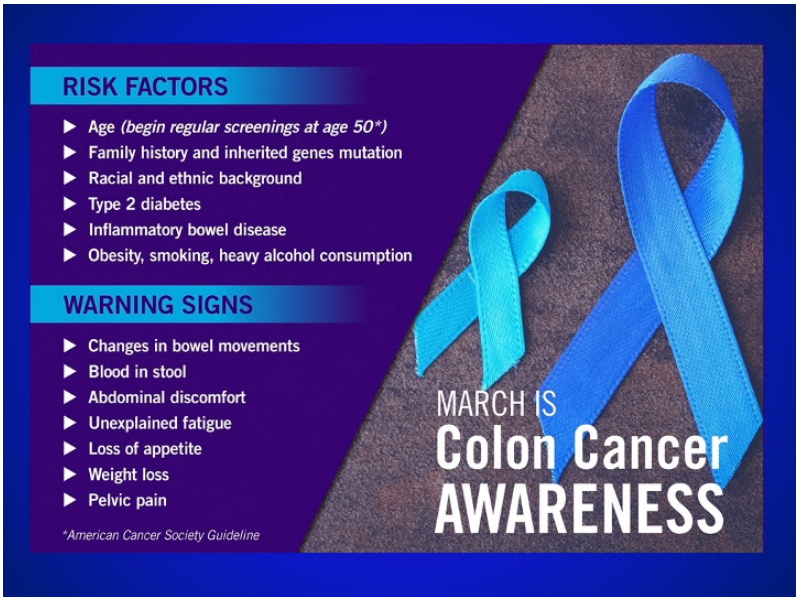
5-YEAR SURVIVAL RATE
BASED ON STAGE OF DIAGNOSIS[2,3]

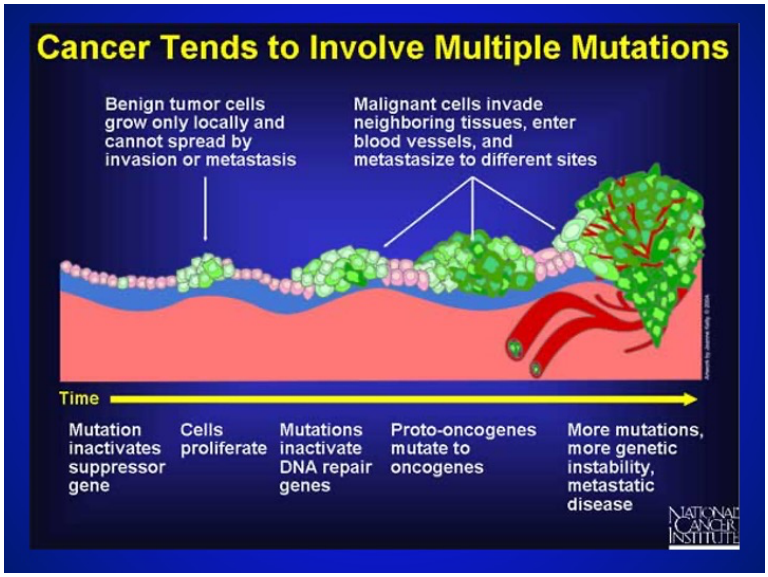
Early Stage (I-II)	90%
Late Stage (IV)	14%

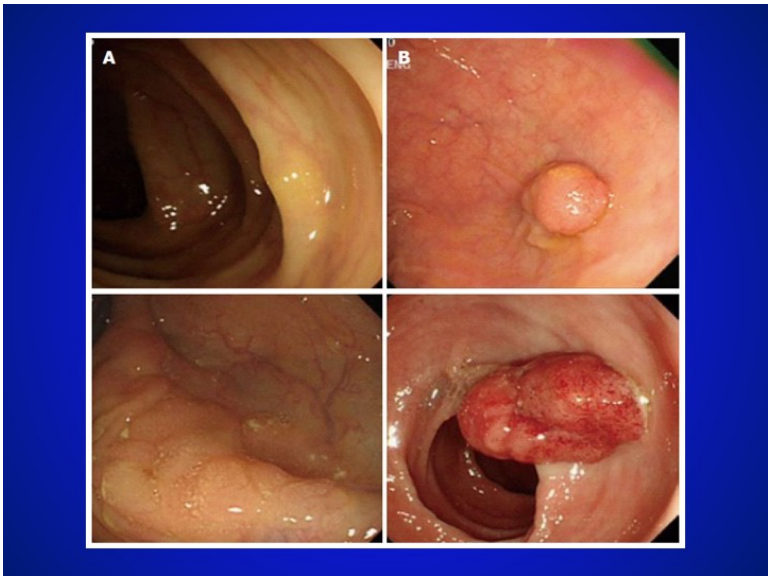
Sadly, low screening compliance may contribute to over half of patients getting diagnosed after their disease has spread.[4,5]

Many factors can prevent patient follow-through[7-10]

	Stool-based test	Colonoscopy
Barriers	• Discomfort or disgust with handling stool • Inconvenience of collecting and mailing stool sample • Apprehension about accurately completing a test at home	• Fear of an invasive procedure and associated risk • Discomfort with bowel prep • Burden and time required for an inpatient procedure, including prep and recovery time
Compliance rates	14-67%[11,12]	38-50%[8,12]

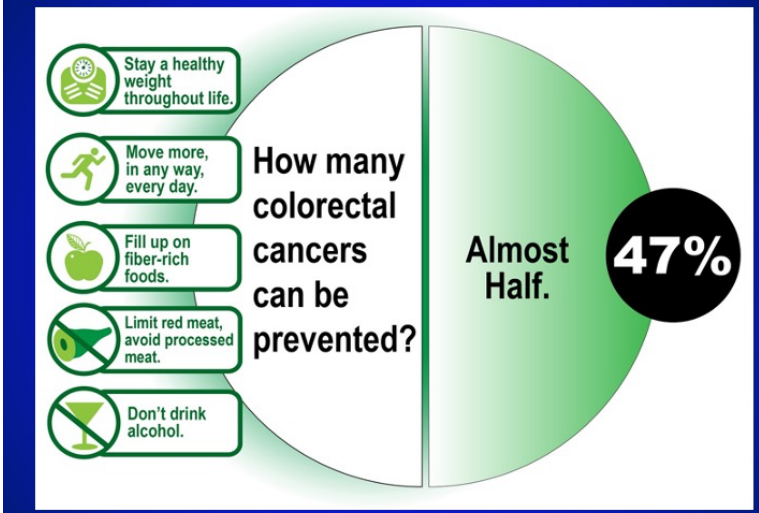

RISK FACTORS
Age (begin regular screenings at age 50*)
Family history and inherited genes mutation
Racial and ethnic background
Type 2 diabetes
Inflammatory bowel disease
Obesity, smoking, heavy alcohol consumption
WARNING SIGNS
Changes in bowel movements
Blood in stool
Abdominal discomfort
Unexplained fatigue
Loss of appetite
Weight loss
Pelvic pain
*American Cancer Society Guideline
MARCH IS
Colon Cancer
AWARENESS


Cancer Tends to Involve Multiple Mutations
Benign tumor cells grow only locally and cannot spread by invasion or metastasis
Malignant cells invade neighboring tissues, enter blood vessels, and metastasize to different sites
Time
Mutation inactivates suppressor gene
Cells proliferate
Mutations inactivate DNA repair genes
Proto-oncogenes mutate to oncogenes
More mutations, more genetic instability, metastatic disease
NATIONAL CANCER INSTITUTE

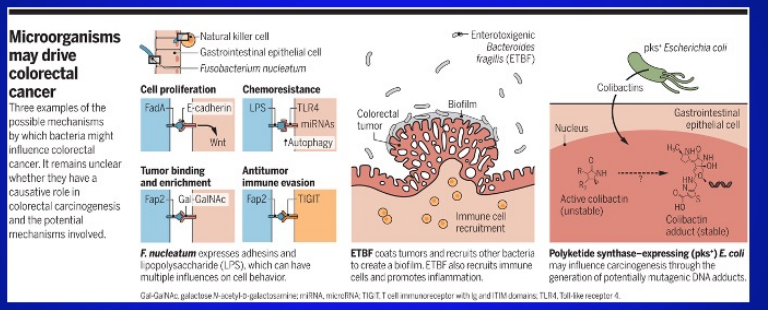

A
B

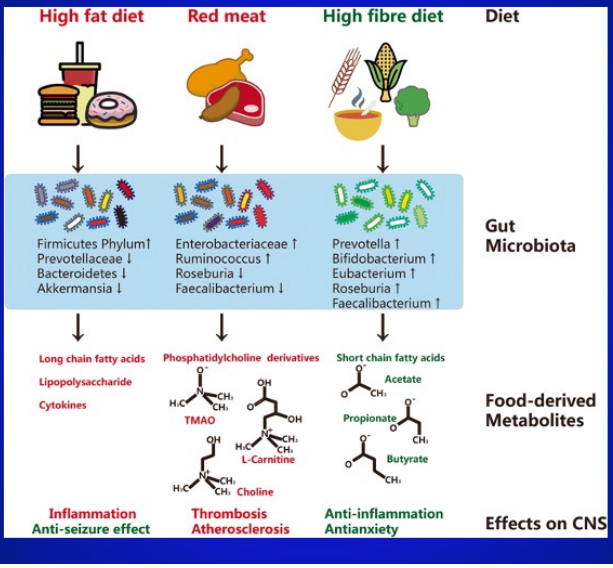
Colon Polyps & Cancer

- 50% of population over age 60 have colon polyps
- 50% of polyps great than 1 inch (2.5 cm) have cancer
- Probably began 10-15 years earlier as single polyp/cancer cell
- Average age at diagnosis: men 68, women 72
- On average lose 15 years of additional life span, up to 50 years
- Preventive measures are proven and have additional benefits
- Screening just once every ten years reduces the risk
- Alternative non-invasive tests include urine, blood, stool, capsule colonoscopy, virtual colonoscopy



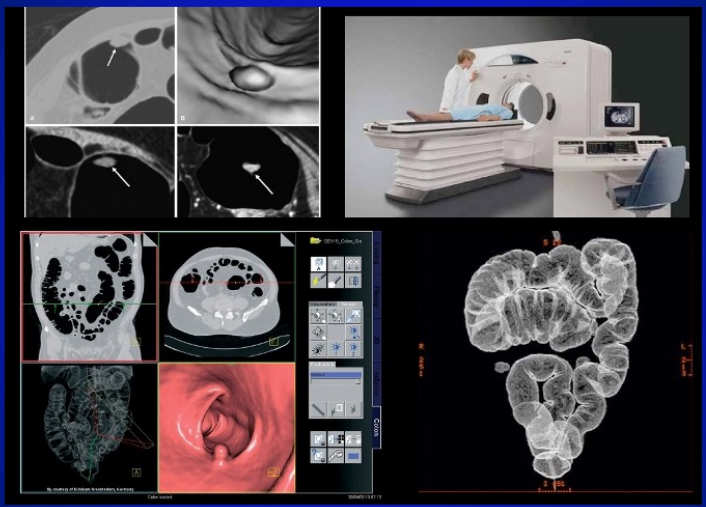
IF YOU WERE BORN IN THE 90'S... YOU HAVE 2X THE RISK OF COLON CANCER AND 4X THE RISK OF RECTAL CANCER THAN THOSE BORN IN 1950.

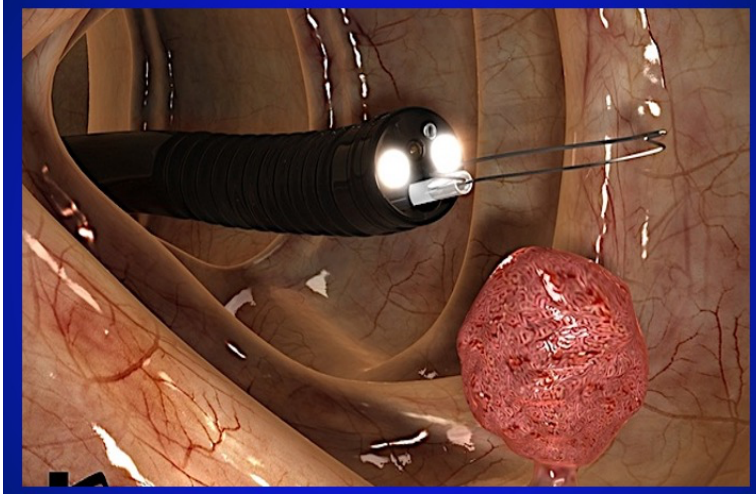




What is a FIT Home Stool Test?

- FIT is also called a Fecal Immunochemical Test
- It finds blood in the stool that is not visible to the eye
- You can pick up the FIT from a lab (with a form from your healthcare provider)
- You do not have to change your diet or medications for the test

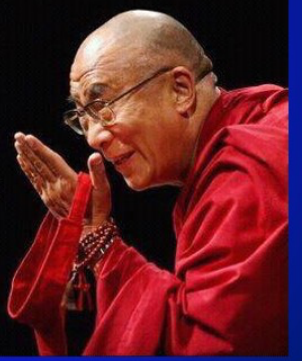




Prevent Colon Cancer

- Avoid Tobacco
- Avoid Alcohol
- Physical Activity
- Maintain healthy weight
- Avoid red meats, smoked and processed foods, nitrites
- Increase fresh fruits, vegetables, dairy, fish, garlic, fiber
- Avoid inflammation, stress, environmental toxins
- Nutrients: calcium, selenium, folate, Vitamins D & E, omega-3
- Genetics – select biological parents well
- Probiotics?
- Aspirin, Metformin
- Regular Screening Tests

The Dalai Lama, when asked what surprised him most about humanity, answered "Man. Because he sacrifices his health in order to make money. Then he sacrifices money to recuperate his health. And then he is so anxious about the future that he does not enjoy the present; the result being that he does not live in the present or the future; he lives as if he is never going to die, and then dies having never really lived."



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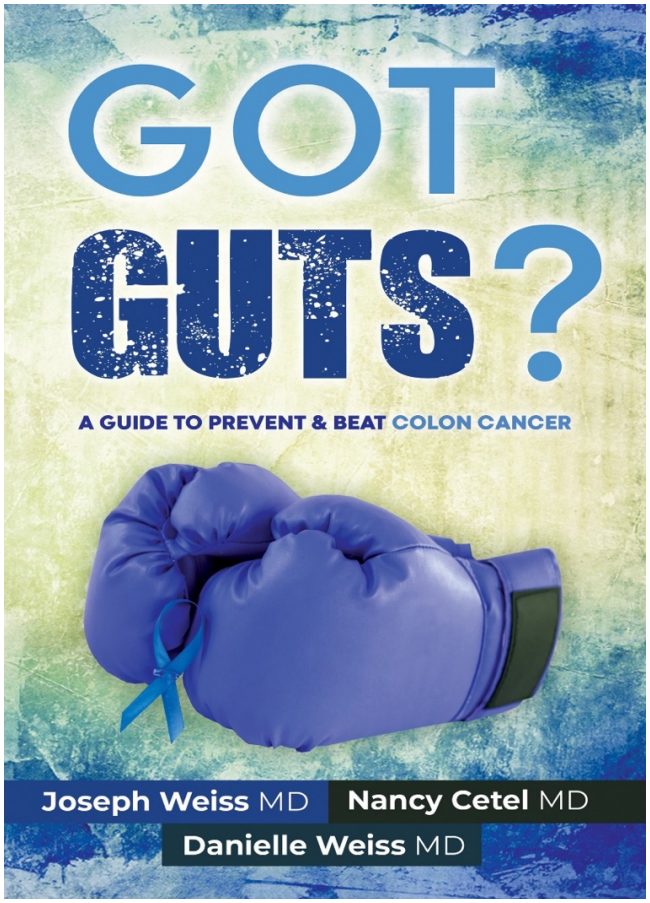

I have coauthored a comprehensive yet concise guide for the primary care physician and educated patient on how to prevent and beat colon cancer. Send me an e-mail at weisscme@ucsd.edu requesting your complimentary copy, and I will send you a PDF publisher's proof of the complete volume at no charge. The book is copyrighted, this gift is for your personal use, but is available to others by purchase through Amazon and other booksellers.