Colon Cancer – The Preventable Killer

Nathan Susnow, MD

Gastroenterology of the Rockies

720-853-3771 · givisit.com





Outline

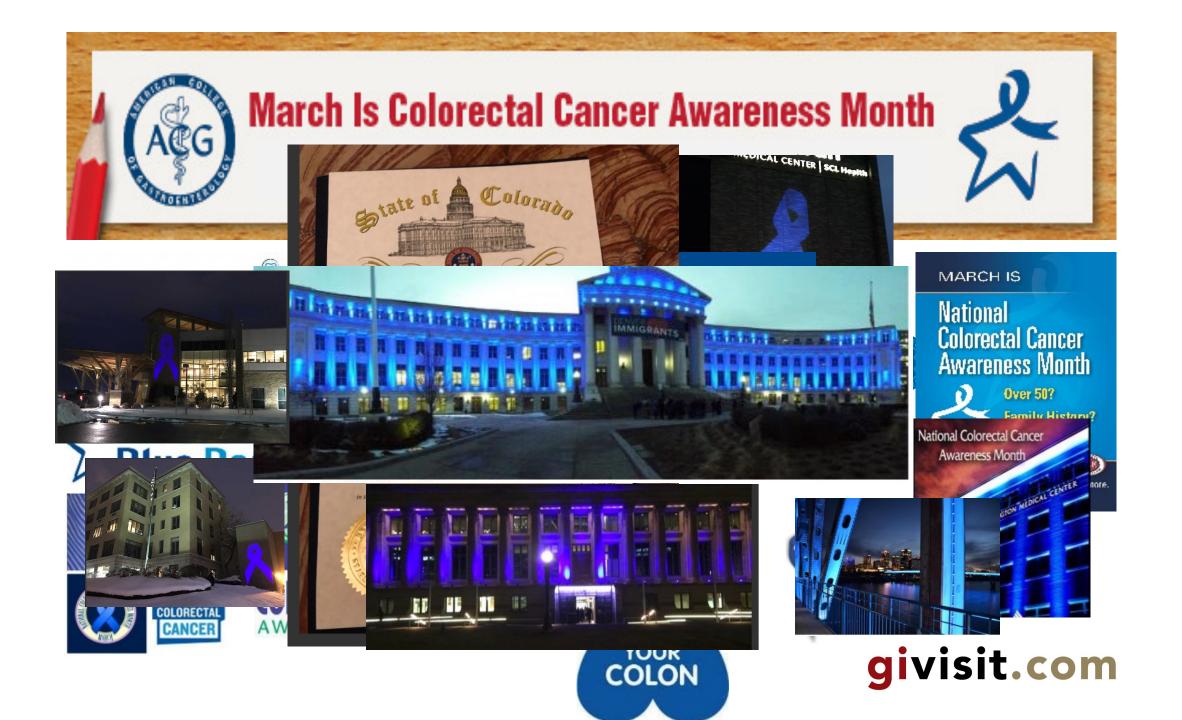


- What is colon cancer? How does it develop?
- How can we detect and/or prevent colon cancer?
- High risk groups.

My History



- College 1996-2000: Rice University, BA Chemistry
- Medical School 2000-2004: UT Southwestern, MD with distinction in research
 - Focused on cancer pathway of Barrett's Esophagus.
- Internal Medicine Residency 2004-2007: University of Colorado
 - Research elective: effect of NSAIDs on colon cancer.
- GI Fellowship 2007-2010: University of Washington
 - Research in cancer (adenocarcinoma) development at cellular level.
 - Research in HCV recurrence after liver transplant.
- Transplant Hepatology Fellowship 2010-2011: Northwestern University/Northwestern Memorial Hospital

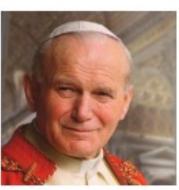


Colon Cancer is Common





President Ronald Reagan Pope John Paul II 74



72



Vince Lombardi 57



Justice Ginsburg 66



Sharon Osbourne 49



Darryl Strawberry 36



Chadwick Boseman 43

Colon Cancer is Common





Jay Monahan 41





Queen Mother 66



Elizabeth Montgomery 62



Jackie Gleason 70



Audrey Hepburn 62

The Preventable Killer

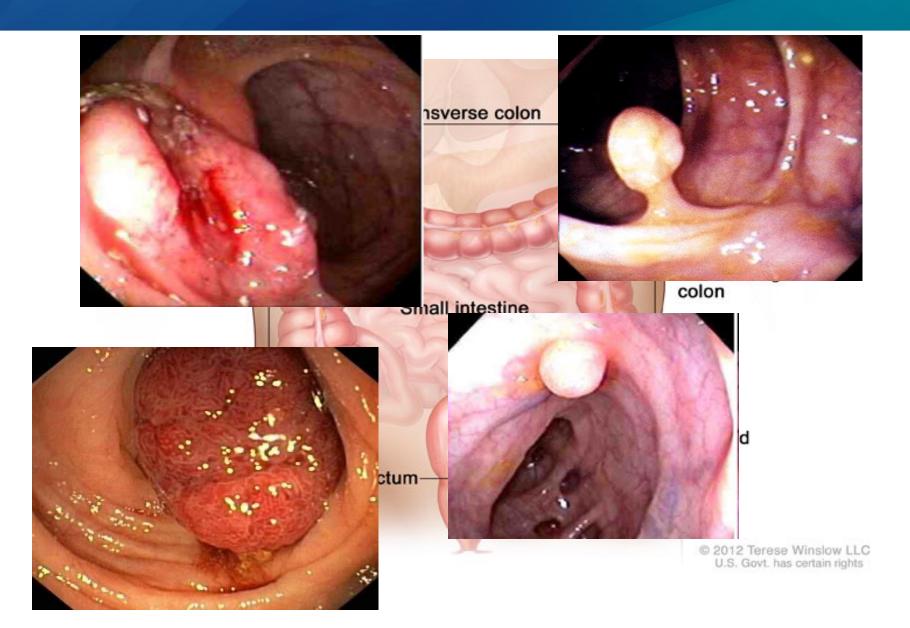


Colorectal cancer is the result of a sequence of biologic events. It is:

- Common
- Lethal
- Preventable

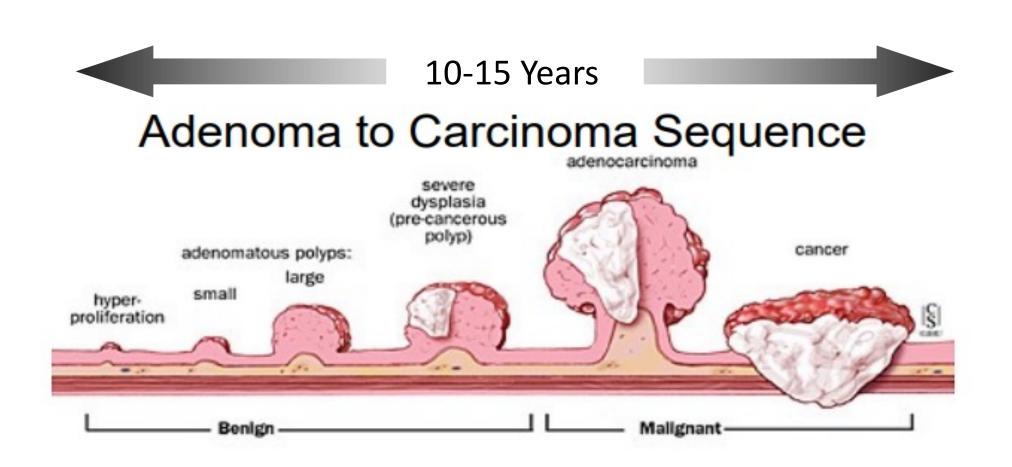
What is Colorectal Cancer?





The Adenoma Carcinoma Sequence





Fewer than 10% of all adenomas become cancerous. However, more than 95% of colorectal cancers develop from adenomas

Polyps





Figure 1. Hyperplastic polyp.



Figure 3. Tubular adenoma (sessile).



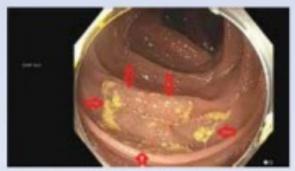
Figure 2. Tubular adenoma (pedunculated).



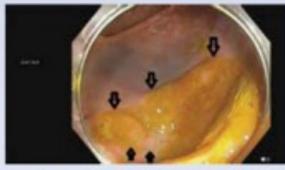
Figure 5. Tubular adenoma with high-grade dysplasia.



FIGURE 3. Advanced serrated lesions



A Arrows delineate the border of a sessile serrated polyp with adherent mucus over the lesion and debris around the perimeter



B Right colon sessile serrated polyp with thick layer of adherent mucus – arrows delineate the borders



C Arrows delineate edges of a sessile serrated polyp without mucus cap



D Sessile serrated polyp without mucus cap, flatter than the lesion seen in image C



E Extremely flat, subtle sessile serrated polyp without cytological dysplasia

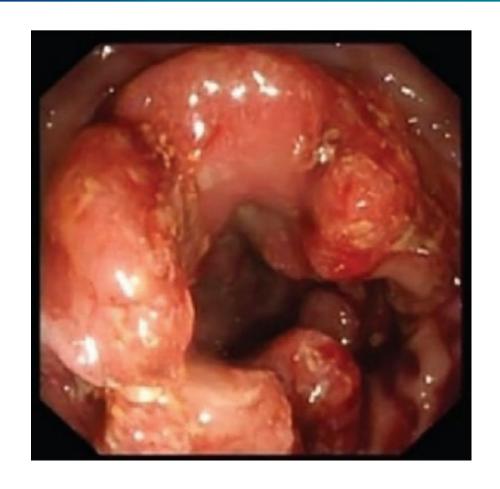


F Sessile serrated polyp with cytological dysplasia. The dysplastic portion is within the yellow line. Arrows mark the perimeter. Black object at bottom is tip of an injection catheter.

Colon Cancers



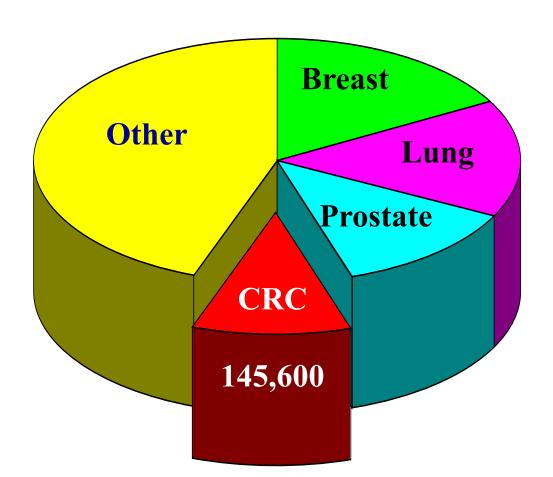




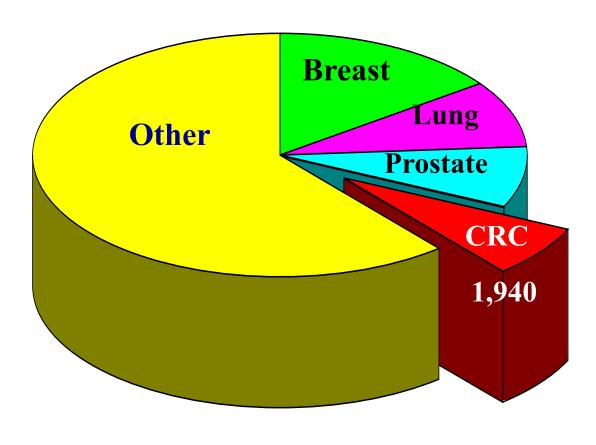
CRC is Common



United States New Cases - 1,762,450

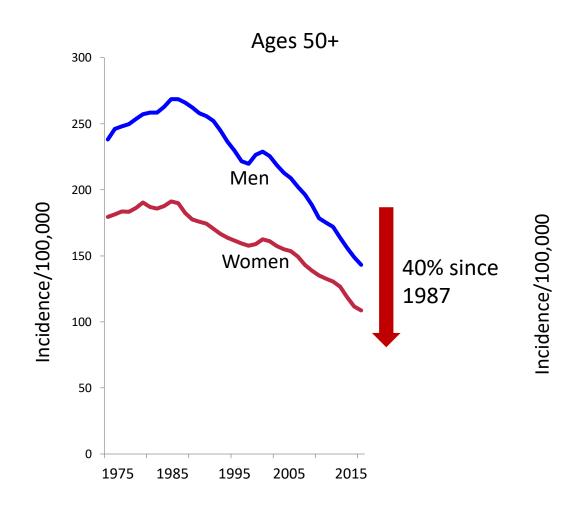


Colorado New Cases - 28,600

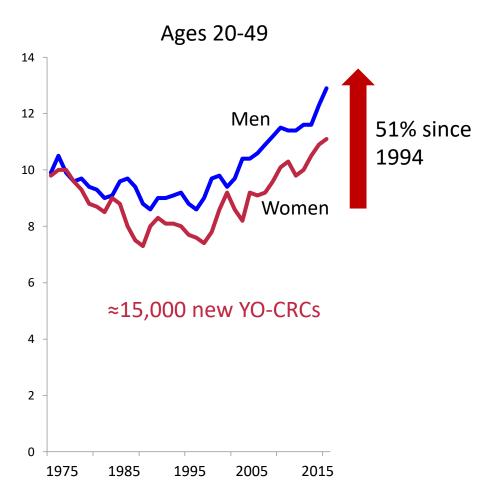


CRC Incidence Over Time The Good and Bad





Siegel R: Source:-SEER 9 delay-adjusted rates, 1975-2012; 2-yr moving average.



New Screening Age: 45!

CRC Risk Factors

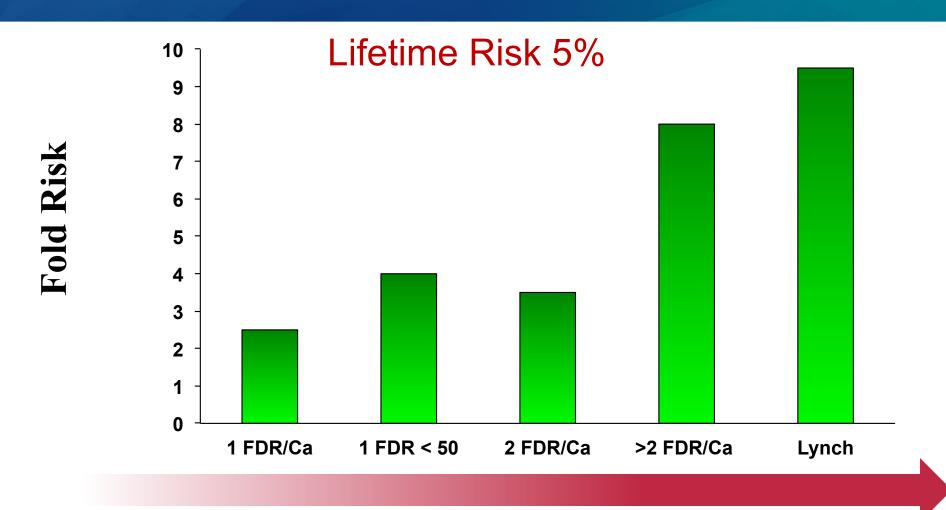


Demographic:

- Country of origin
- Age
- Sex
- Race/Ethnicity
- Socioeconomic status (SES)
- Family history

Family History and CRC Risk





Screening Intensity

CRC Risk Factors



Demographic:

- Country of origin
- Age
- Sex
- Race/Ethnicity
- Family history

Lifestyle:

- Obesity
- Low physical activity
- Smoking
- Alcohol

Diet:

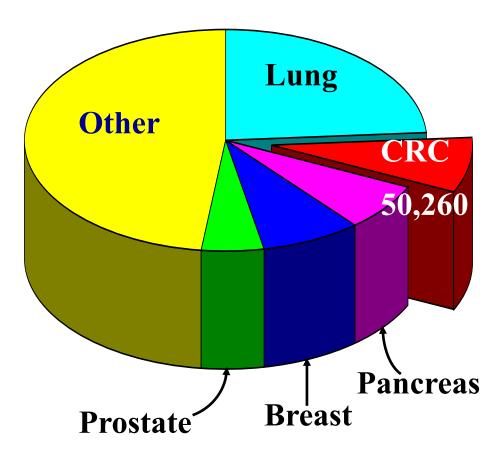
- High red/processed meat
- Low fiber containing foods
- Low fruits and vegetables
- Charred/Broiled/Grilled foods
- "Ultra-processed Foods"

Failure to Get Screened!

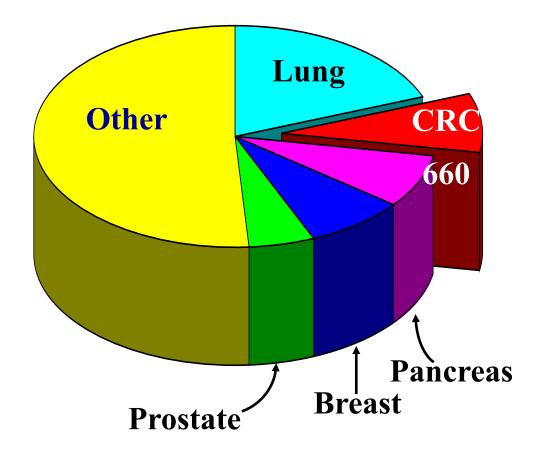
CRC is Lethal



United States Deaths- 606,880

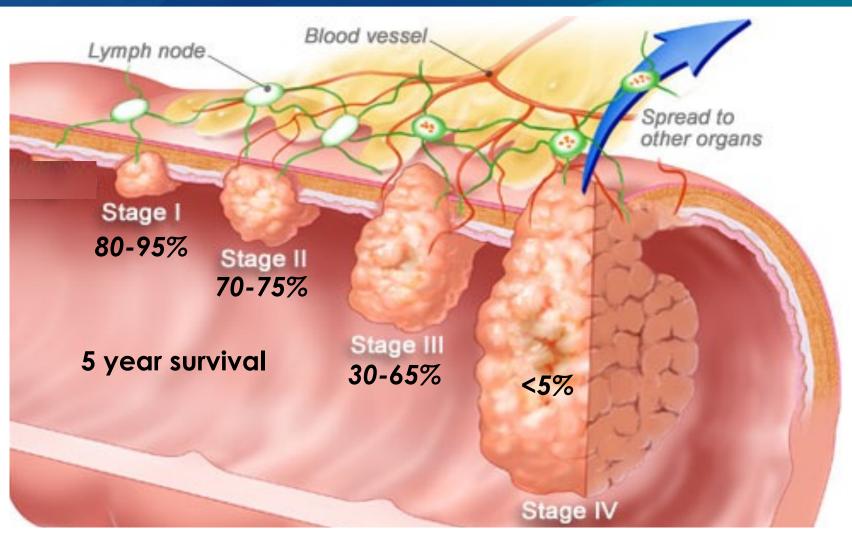


Colorado Deaths- 8,120



CRC Staging





Early Detection is Critical.

CRC is Preventable – Modifiable Risk Factors



Demographic:

- Country of origin
- Age
- Sex
- Race/Ethnicity
- Family history

Lifestyle:

- Obesity
- Low physical activity
- Smoking
- Alcohol

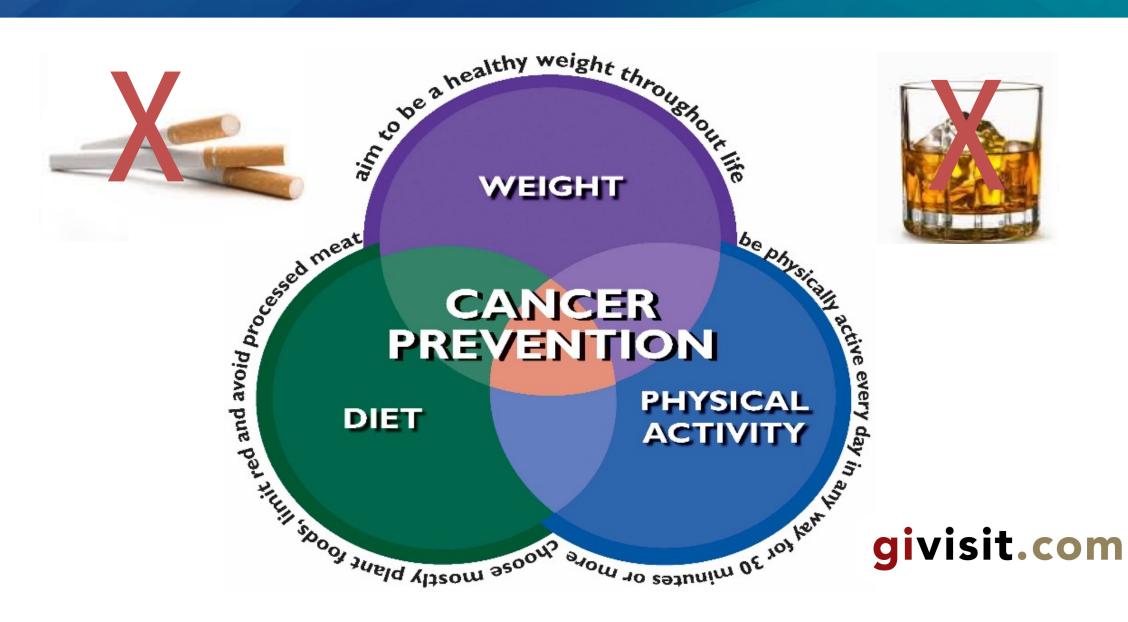
Diet:

- High red/processed meat
- Low fiber containing foods
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- Charred/Broiled/Grilled foods
- "Ultra-processed Foods"



CRC Prevention





Risk Factors



Demographic:

- Country of origin
- Age
- Sex
- Race/Ethnicity
- SES
- Family history

Lifestyle:

- Obesity
- Low physical activity
- Smoking
- Alcohol

Diet:

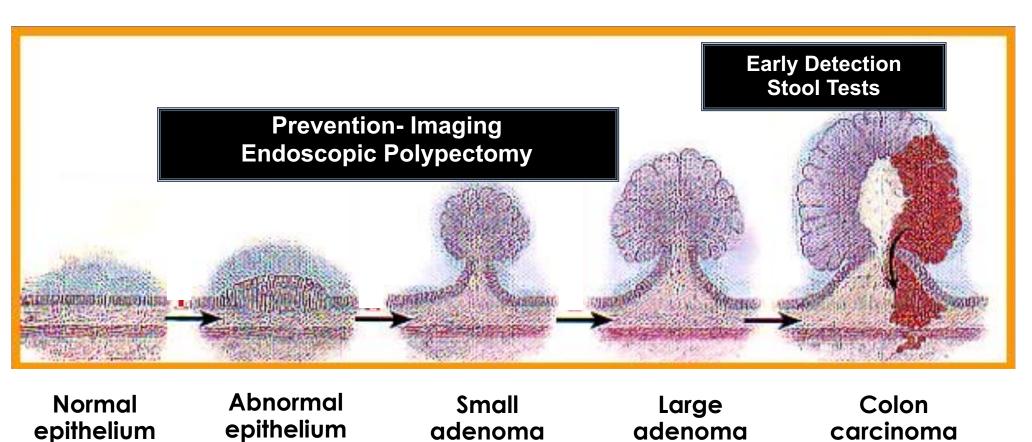
- High red/processed meat
- Low fiber containing foods
- Low fruit and vegetables

Protective Factors:

- Aspirin for selected groups
- Screening

Screening - Prevention and Early Detection





The Adenoma Carcinoma Sequence

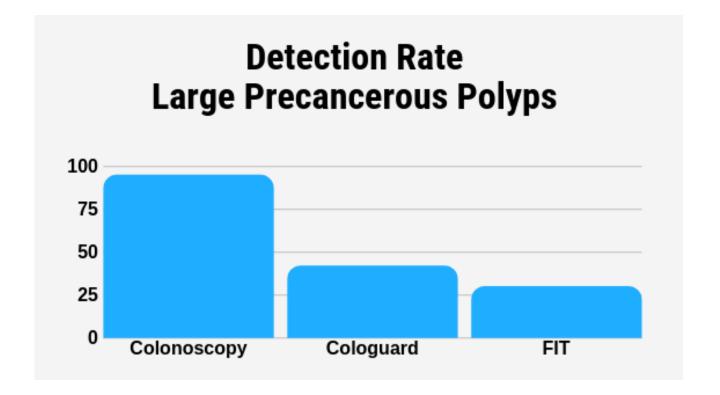




Cologuard (FIT+ DNA)



- Non-invasive assessment for cancer DNA and/or blood in stool.
 - Stool sample mailed in.
 - Negative (no blood or DNA detected).
 - Positive (blood and/or DNA detected).



Cologuard (Fit + DNA)



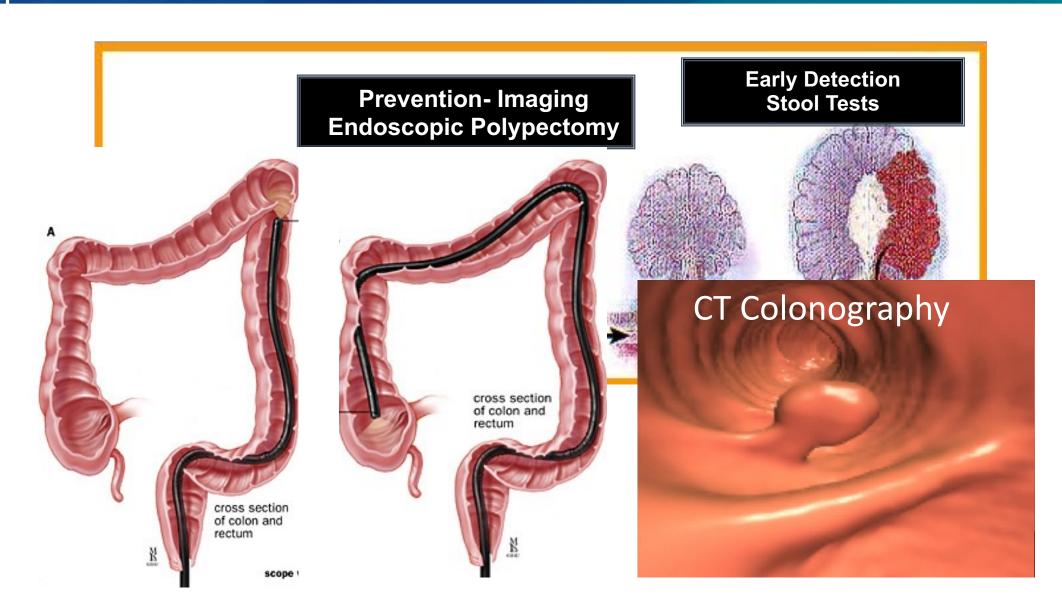
Test	Finds Colon Cancer	Finds High Risk Polyps (>10mm)	False Positives	False Negatives (Cancer Miss Rate)
FIT-fecal DNA	92%	42%	12%	Misses 1 in 13 Cancers
Fit Testing	75-80%	30%-40%	<4%	Misses 1 in 5 Cancers
Colonoscopy	95%	>95%		0-6%** Interval Cancers

Robertson DJ, Lee JK, Boland CR, et al. Gastrointest Endosc. 2017;85(1):2-21.e3.

Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. N Engl J Med. 2014;370(14):1287-1297.

The Adenoma Carcinoma Sequence

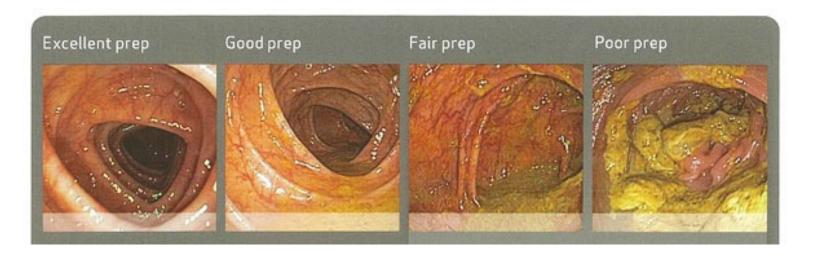




Colonoscopy Quality



- Exam Effectiveness, Patient Factors:
 - Split dose prep.
 - Good compliance with instructions.
 - Low residue diet a couple days prior to exam.
 - Avoid constipation prior to starting prep.
 - Discuss pre-existing GI issues with your scheduler in case modifications need to be made.
 - Read through instructions carefully.



Colonoscopy = Prevention



- Most effective colorectal cancer prevention test.
- Detects 3x more advanced lesions than FIT.
- Detects 2x more advanced lesions than FIT-DNA.
- Single test with diagnosis and resection.
- Only test able to be performed at 10-year intervals.





Colonoscopy Risks - Screening



- Cardiopulmonary Risks < 1%
- Perforation 0.03-0.07% risk.
 - 1 in 2,000 (0.05%) considered standard of care.
 - Me: 2 perforations in 12 years, performing approximately 1,000 colonoscopies/year.
 - 1 perforation was not screening.
 - 1 perforation was delayed after resection of large polyp.
- Bleeding after polyp removal: 0.5%
 - Higher with large polyp removal.
- Death attributable to colonoscopy: 1 in 15,000
- Lifetime odds of death:
 - MVC 1 in 101
 - Fall 1 in 102
 - Gun 1 in 221
 - Drowning 1 in 1,024

Colonoscopy Quality



- High-definition colonoscope.
- Careful exam of the entire colon.
 - At least 6 min (usually closer to 10) spent withdrawing the scope and searching.
 - Experienced Endoscopist:
 - > 95% cecal intubation rate.
 - Adenoma Detection Rate (ADR)
 - Lower limit > 20% women, > 30% men.
 - US Average ADR 39%
- My metrics Oct. 2021-Sept. 2022:
 - Withdrawal time: 11.2 min
 - ADR male: 66%
 - ADR female 62%
 - Cecal intubation rate > 95%

GI Genius



- GI of the Rockies: 1st in Colorado to incorporate.
 - Improves ADR + cancer detection 13% in random controlled trials.





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CRC Screening - Risk Groups



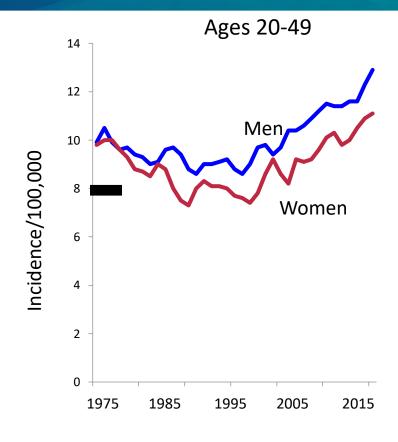
Average risk:

- No personal or FH of colonic neoplasia or IBD.
- Start CRC screening at age 45, stop at age 75-85.
- Options for screening:
 - FOBT/FIT annually
 - FIT/DNA every 3 years
 - Flexible Sigmoidoscopy every 5 years
 - CT Colonography every 5 years
 - Colonoscopy every 10 years
- If done, CRC cases and deaths decrease by 60-80%.

Previous Screening Guidelines



- USPSTF 2016 "recommends CRC screening starting at age 50 years and continuing until age 75.... multiple screening strategies to choose from" (a recommendation). Individualize screening age 76-85.
- ACS 2017 Repeated modeling studies using current incidence and mortality rates for the young.



• **Conclusion:** Starting at age 45 led to a 4-8% decrease in number of new CRCs, and an 8-11% decrease in CRC deaths with a 12-17% increase in the number of colonoscopies needed, compared to starting at age 50.

Current Screening Guidelines



- USPSTF 2021 "recommends offering CRC screening starting at age 45 years and continuing until age 75.... multiple screening strategies to choose from" (a recommendation). Individualize screening age 76-85.
- American Cancer Society 2018 "recommends that adults aged 45 years and older with average risk of colorectal cancer undergo regular screening" and continuing until age 75 with any of multiple screening strategies. Individualize screening age 76-85.
- Colorado HOR passed House Bill 20-1103 in 2020.

CRC Screening - Risk Groups

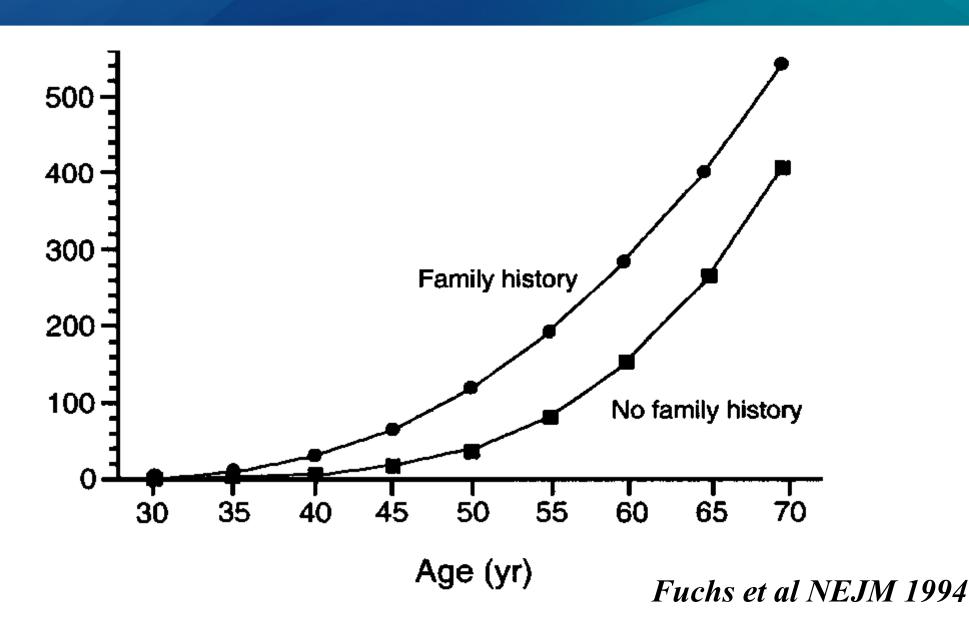


- Increased risk FDRs of patients with CRC
 - Start at age 40 or earlier depending on # and age of CRCs in family - colonoscopy is preferred.

- Hereditary Syndromes
 - Start much earlier (age 12-25) annual colonoscopy.

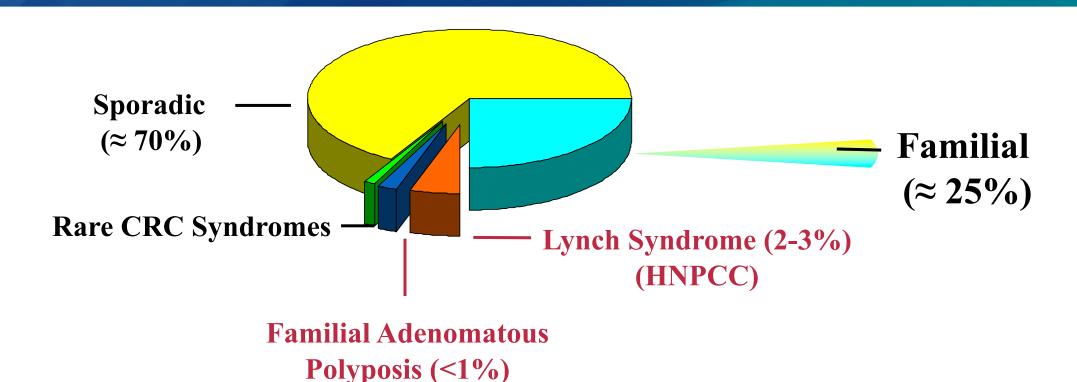
Family History of CRC Increases Risk Boulder Community Health





Familial and Hereditary CRC

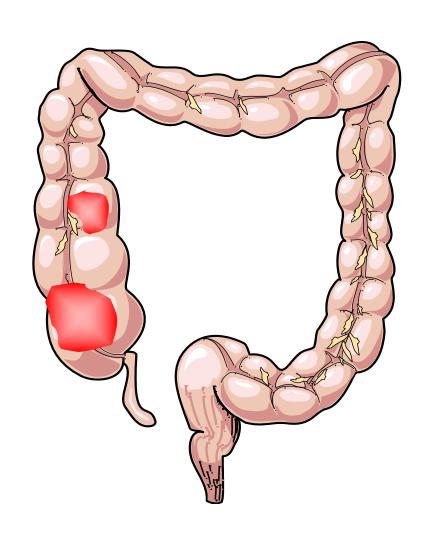




Lynch Syndrome



- Autosomal Dominant 3% of CRCs
- High CRC risk up to 50%
- Early onset 44 yrs
- Proximal location 65%
- Other cancers (Uterus, Ovary)
- Under recognized (<5%)
- Genetic testing (MMR genes)
- Screening works
 - Annual colonoscopy age 25 or earlier



Familial Adenomatous Polyposis



- Rare 1/7,000 to 1/22,000
- Autosomal Dominant
- High CRC risk ≈100%
- Easily recognized
- Genetic testing or screening around age 12
- Surveillance annually



Colorectal Cancer – The Preventable Killer



- Sequential progression from polyp to cancer
- Common:
 - 4th most common cancer in US and CO
 - Decreasing but increasing in the young
- Lethal:
 - 2nd most common cause of cancer death in US and CO
 - Strongly dependent on stage at diagnosis
- Preventable:
 - Prudent lifestyle changes
 - Screening is most effective prevention, as well as early detection strategy
- Familial and hereditary CRC require special attention

Take Home Points



- Colonoscopy can prevent colon cancer.
 - Start at age 45 average risk.
 - Only test recommended for + family history.
 - Every 10 years, sooner if adenomatous polyps/hx colon cancer/fam hx.
 - Let your doctor know if you have a family history of colon or other cancers.
- If no colonoscopy, then:
 - FIT yearly or Cologuard (FIT-Fecal DNA) every 3 years.
 - Misses some cancers and most high-risk polyps.



Questions?



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Nordic Study (NEJM)- Oct. 2022



- 85,000 people in Norway, Poland, Sweden, Netherlands.
 - One colonoscopy vs no screening.
 - Randomized from population (not from PCP or advertisement). Sent a single letter inviting to screening.
 - Primary Endpoints: Colorectal Cancer incidence and mortality after 10-15 years and all-cause mortality.
 - 1/3rd of endoscopists had ADR < 25%, below minimum acceptable standard in US.
 - Average US ADR is 40%.

Nordic Study (NEJM) Results



 Risk of colon cancer 18% lower in group invited to undergo screening.

No decreased risk of death overall.

Is colonoscopy ineffective?

Nordic Study (NEJM) Limitations



- Only 42% of those invited actually had a colonoscopy.
 - All of those invited are included in outcome analysis.
- Of those who actually had colonoscopy:
 - 31% reduced colon cancer risk.
 - 50% reduced risk of death.
- Average follow-up period only 5 years.
 - Too short to see benefits of polyp removals over time.
- Colonoscopy works for those who had it.
 - It works better when done well.