# Colorectal Cancer – The Preventable Killer

#### **Kelly Zucker, DO** Gastroenterology of the Rockies 720-358-0832





## My History



- College: Grinnell College, BA in Biological Chemistry
- Medical School: Western University of Health Sciences, College of Osteopathic Medicine of the Pacific NW
- Internal Medicine Residency: University of Arizona-Phoenix
  - Voted by faculty as "Intern of the Year"
  - Voted by peers as "Resident of the Year"
  - Served as house staff council president
- Gastroenterology Fellowship: University of Arizona- Phoenix
  - Research and publications in liver transplant outcomes
  - Visiting fellow with ANMS (motility)
  - Served as Chief Fellow in final year of training

#### Outline



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



#### Colon Cancer is Common





President Ronald Reagan Pope John Paul II 74 72

Vince Lombardi 57



Justice Ginsburg 66



82



Sharon Osbourne 49



Darryl Strawberry 36



Chadwick Boseman 43



Kirstie Alley 70

#### Colon Cancer is Common





Jay Monahan 41



Charles Schulz 76



Elizabeth Montgomery 62



Audrey Hepburn 62



Queen Mother 66



Jackie Gleason 70

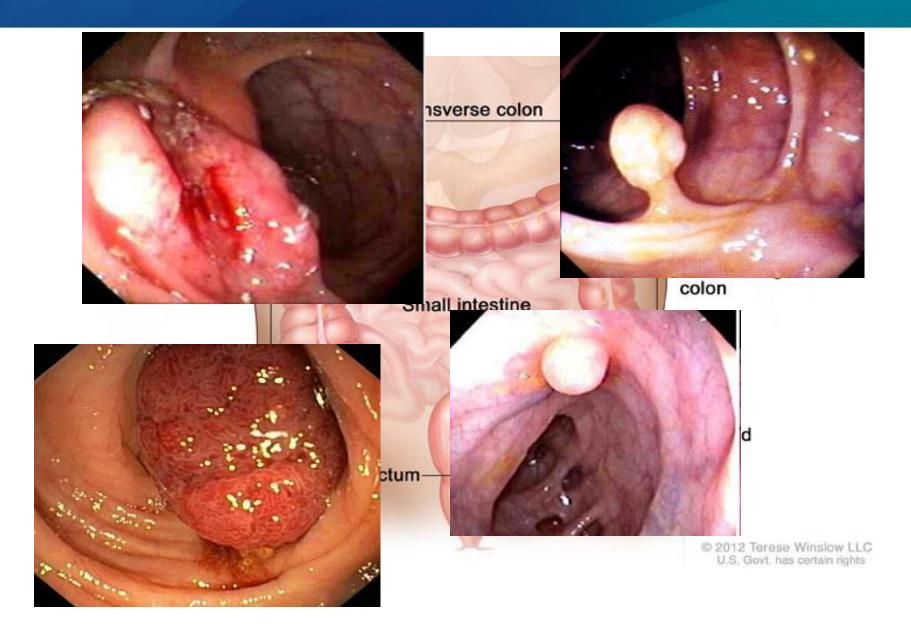


Colorectal cancer is the result of a sequence of biologic events. It is:

- Common
- Lethal
- Preventable

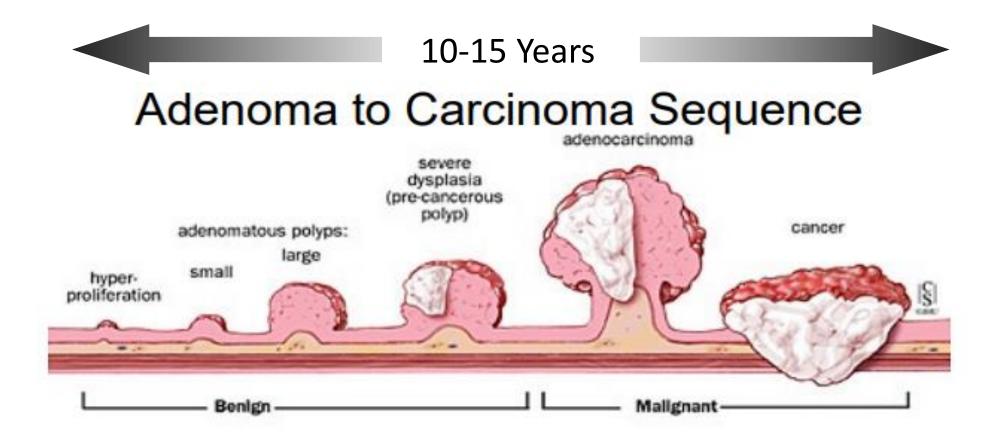
#### What is Colorectal Cancer?





## 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 2. Tubular adenoma (pedunculated).





Figure 3. Tubular adenoma (sessile).

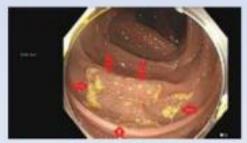


Figure 5. Tubular adenoma with high-grade dysplasia.

### Polyps



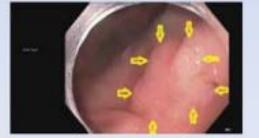
#### FIGURE 3. Advanced serrated lesions



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



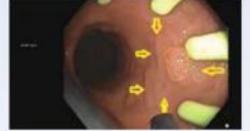
C Arrows delineate edges of a sessile serrated polyp without mucus cap



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



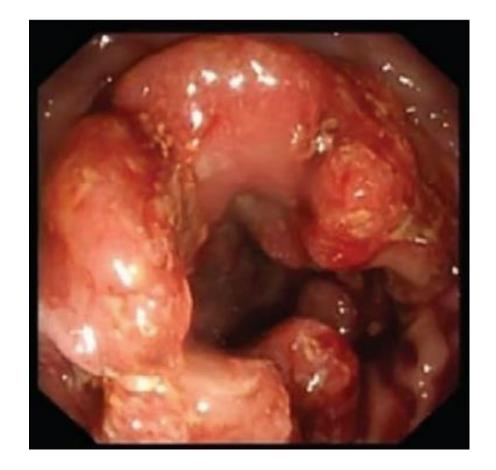
F Sessile serrated polyp with cytological dysplasia. The dysplastic portion is within the yellow line. Arrows mark the perimeter. Black object at bottom is tip of an injection catheter.

#### Rex, D. PRACTICAL ADVICE FOR COLORECTAL CANCER SCREENING. GI & Hepatology News 2019

#### Colon Cancers



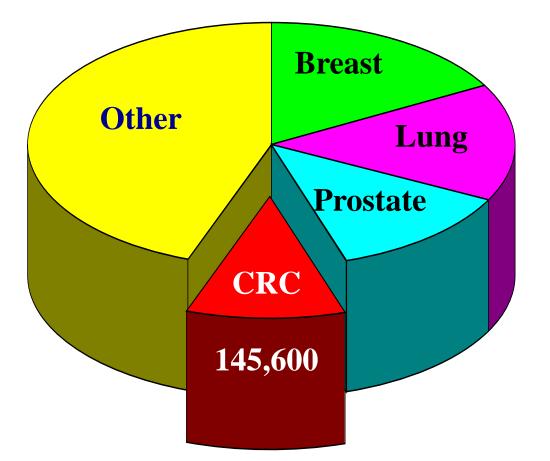




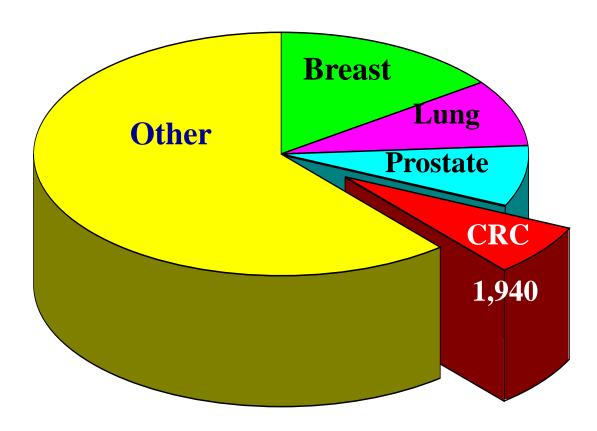
### CRC is Common



#### United States New Cases - 1,762,450

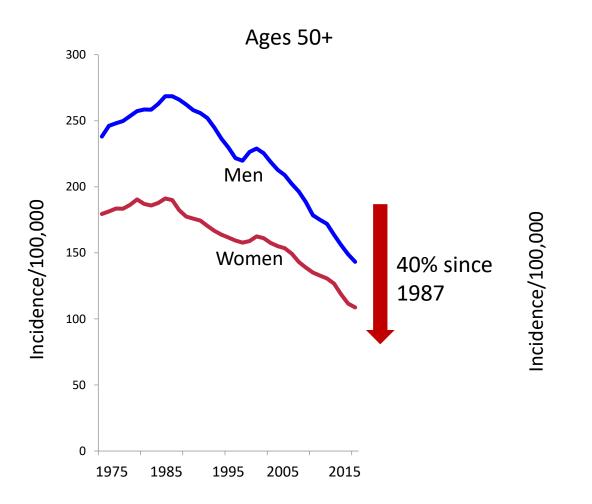


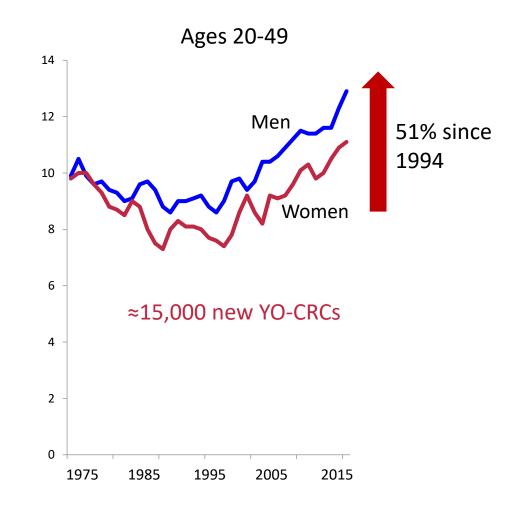
#### Colorado New Cases - 28,600



#### CRC Incidence Over Time The Good and Bad







### **CRC** Risk Factors



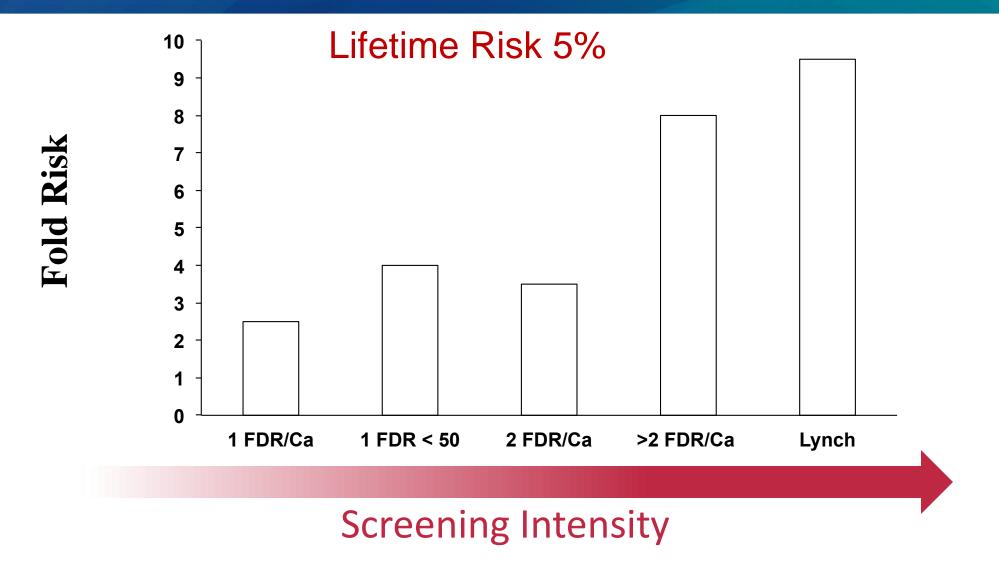
### **Demographic:**

- Country of origin
- Age
- Sex
- Race



#### Family History and CRC Risk





### **CRC** Risk Factors



#### **Demographic:**

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

#### Diet:

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

#### Lifestyle:

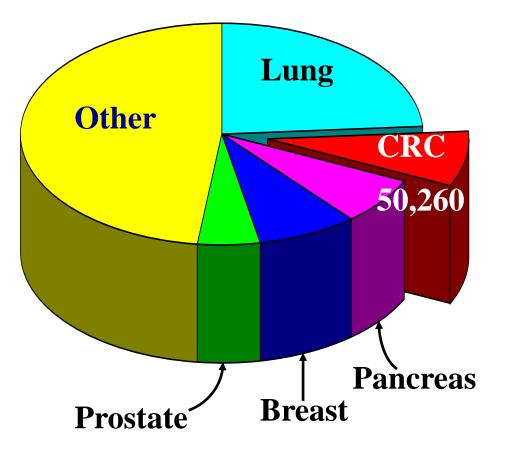
- Obesity
- Low physical activity
- Smoking
- Alcohol

#### Failure to Get Screened!

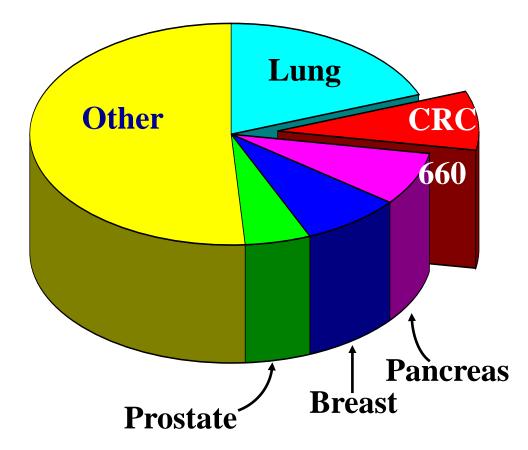
#### CRC is Lethal



#### United States Deaths- 606,880

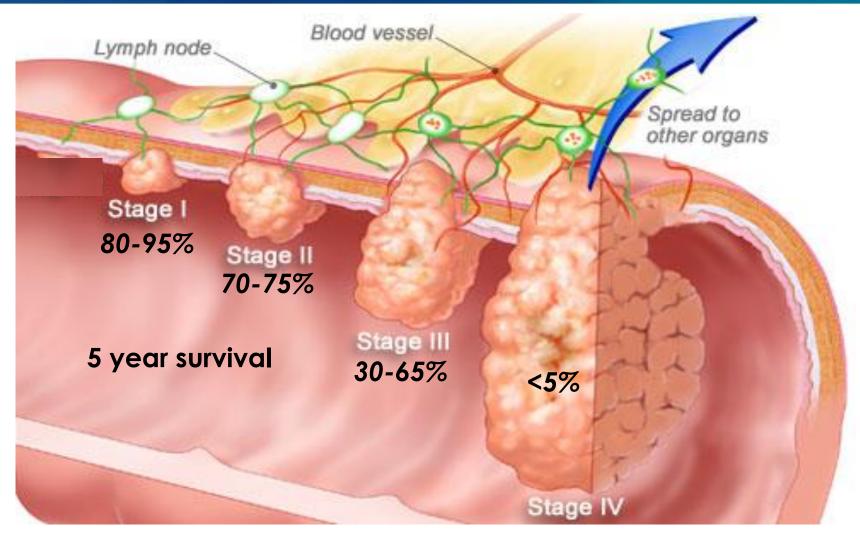


#### Colorado Deaths- 8,120



### 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

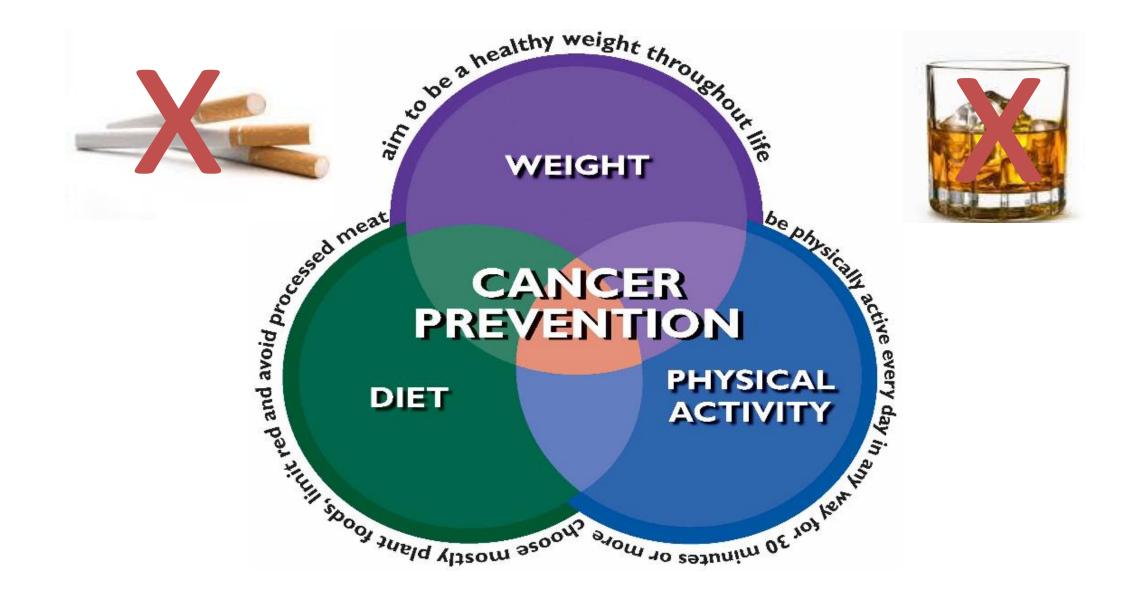
#### Diet:

- High red/processed meat
- Low fiber containing foods
- Low fruit and vegetables
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- "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
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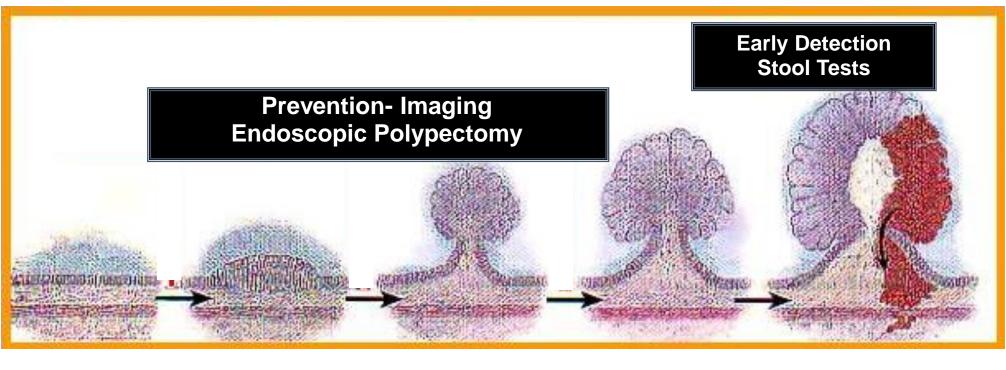
#### Protective Factors:

• Aspirin for selected groups

Screening

### Screening - Prevention and Early Detection





Normal epithelium

Abnormal epithelium

Small adenoma Large adenoma Colon carcinoma

## The Adenoma Carcinoma Sequence

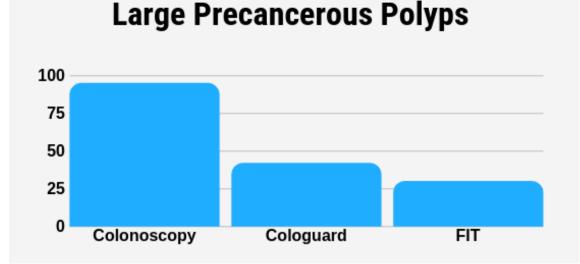




## Cologuard (FIT+ DNA)



- 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)



**Detection Rate** 

#### Cologuard (Fit + DNA)



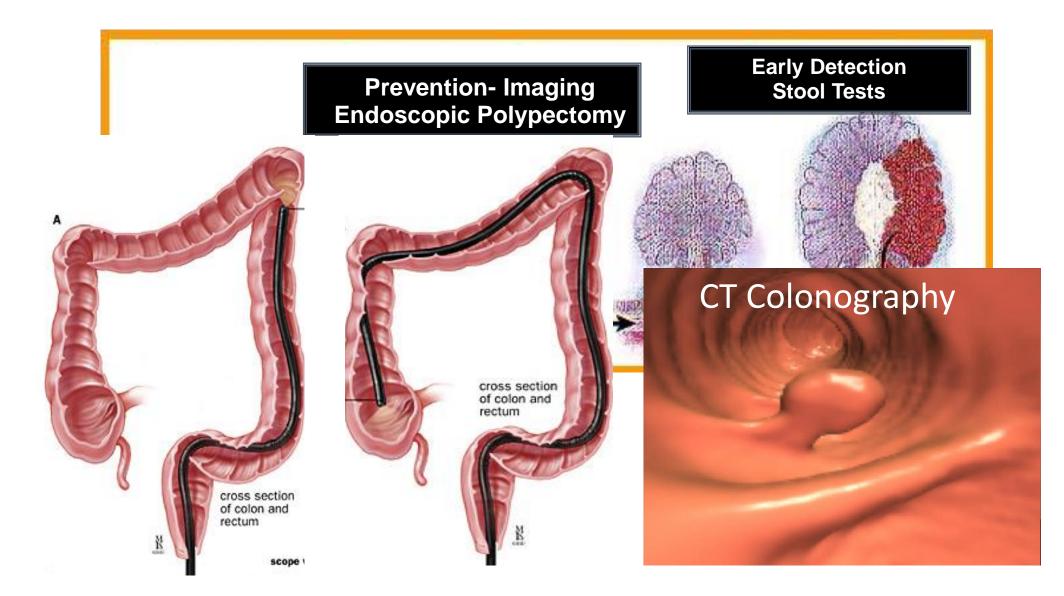
Test	Finds Colon Cancer	Finds High Risk Polyps (>10mm)	False Positives	False Negatives (Cancer Miss Rate)
FIT-fecal DNA	92%	42%	12%	Misses 1 in 13 Cancers
Fit Testing	75-80%	30%-40%	<4%	Misses 1 in 5 Cancers
Colonoscopy	95%	>95%		0-6%** Interval Cancers

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.

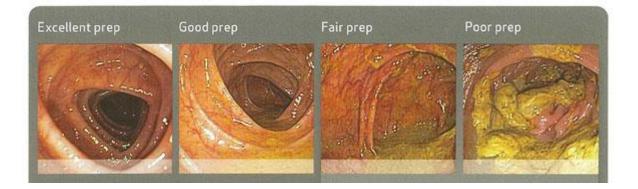
### The Adenoma Carcinoma Sequence





## 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
- 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 8 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%

### 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.
  - 1/3<sup>rd</sup> 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 worked for those who had it
  - Works better when done well

### GI Genius



- GI of the Rockies: 1<sup>st</sup> in Colorado to incorporate.
  - Improves ADR + cancer detection 13% in randomized controlled trials





### CRC Screening - Risk Groups



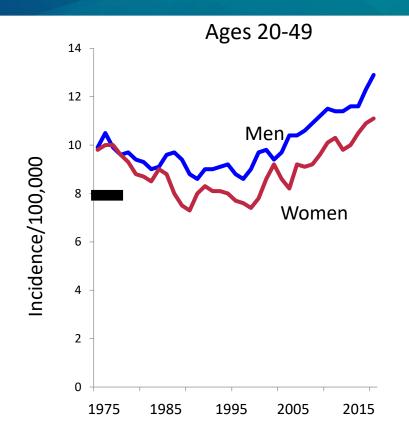
#### Average risk:

- 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



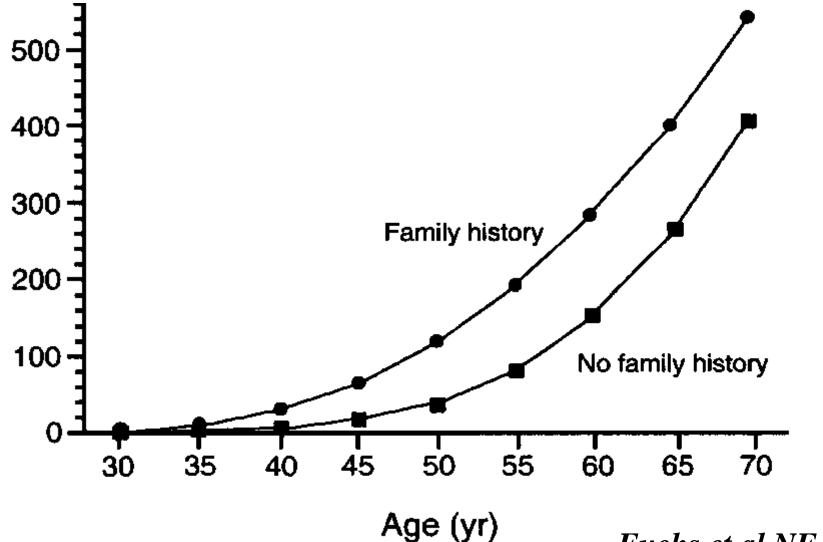
- USPSTF 2021 "recommends offering CRC screening starting at age 45 years and continuing until age 75.... multiple screening strategies to choose from" (a recommendation). Individualize screening age 76-85.
- American Cancer Society 2018 "recommends that adults aged **45 years** and older with average 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

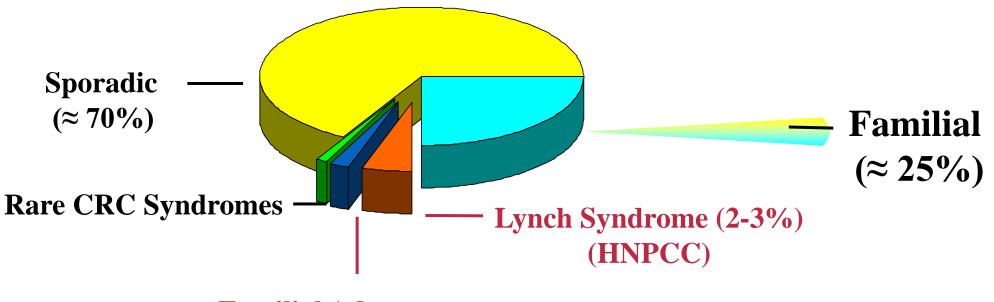
#### Family History of CRC Increases Risk Boulder Community Health



Fuchs et al NEJM 1994

#### Familial and Hereditary CRC



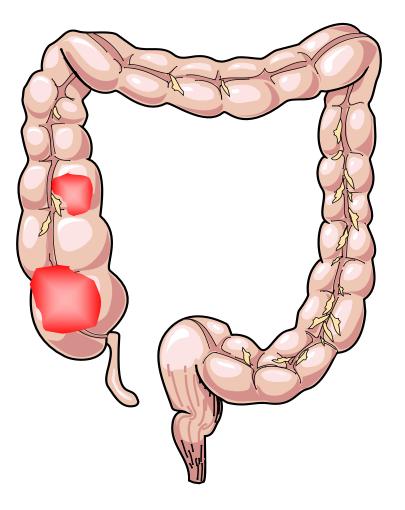


Familial Adenomatous Polyposis (<1%)

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

### 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



Boulder Community Health

### 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:
  - 4<sup>th</sup> most common cancer in US and CO
  - Decreasing overall, but increasing in the young
- Lethal:
  - 2<sup>nd</sup> 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

#### Thank You!



## **Questions?**





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