Colorectal Cancer: The Preventable Killer

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Relevant Conflicts of Interest:
Co-Investigator (past)- CRC screening trial for stool DNA test
Co-Investigator (current)- CRC Screening trial of colonoscopy vs FIT
Co-Author- Modeling studies commissioned by ACS for current guidelines

Colorectal Cancer is the result of a sequence of biologic events; It is
• Common
• Lethal
• Preventable

What is Colorectal Cancer?
The Adenoma Carcinoma Sequence

10-15 Years

Normal epithelium
Abnormal epithelium
Small adenoma
Large adenoma
Colon carcinoma

CRC is Common

United States
New Cases- 1,762,450

Large adenoma
Colon carcinoma
10-15 Years

The Adenoma Carcinoma Sequence

Other
Breast
Lung
Prostate

CRC
145,600

Colorado
New Cases- 28,600

Other
Breast
Lung
Prostate

CRC
1,940

CRC Incidence Over Time
The Good and Bad

Ages 50+

Men
Women

40% since 1987

Ages 20-49

Men
Women

51% since 1994

≈15,000 new YO-CRCs

CRC Risk Factors

Demographic
- Country of origin
- Age
- Sex
- Race/Ethnicity
- SES
- Family History

Siegel R: Source:-SEER 9 delay-adjusted rates, 1975-2012; 2-yr moving average.
Family History and CRC Risk

Lifetime Risk 5%

Family History and CRC Risk

Demographic
- Country of origin
- Age
- Sex
- Race/Ethnicity
- SES
- Family History

Diet
- High Red/Processed Meat
- Low Fiber Containing foods
- Fruits and Vegetables

Lifestyle
- Obesity
- Low Physical Activity
- Smoking
- Alcohol

Failure to Get Screened

CRC Risk Factors

CRC is Lethal

United States
Deaths- 606,880

Colorado
Deaths- 8,120

CRC Staging

Early Detection is Critical

5 year survival

Stage I 80-95%
Stage II 70-75%
Stage III 30-65%
Stage IV <5%
CRC is Preventable - Modifiable Risk Factors

Demographic
- Country of origin
- Age
- Sex
- Race/Ethnicity
- SES
- Family History

Lifestyle
- Obesity
- Low Physical Activity
- Smoking
- Alcohol

Risk Factors

Diet
- High Red/Processed Meat
- Low Fiber Containing foods
  - Low Fruit and Vegetable

Protective Factors
- Aspirin for selected groups
- Screening

Screening - Prevention and Early Detection

Normal epithelium
Abnormal epithelium
Small adenoma
Large adenoma
Colon carcinoma

Endoscopic Polypectomy
Stool Tests
The Adenoma Carcinoma Sequence

Early Detection Stool Tests

Prevention-Imaging Endoscopic Polypectomy

Early Detection Stool Tests

CT Colonography

CRC Screening- Risk Groups

- Average risk
  - No personal or FH of colonic neoplasia or IBD
  - Start CRC screening at age 45/50, stop at age 75-85
  - Options for screening
    - hsFOBT/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 by 60-80%

Current 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 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 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
- State legislatures decide which guidelines insurers in their state must follow - Colorado is currently a USPSTF state

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 (12-25), annual colonoscopy

Family History of CRC Increases Risk

Fuchs et al NEJM 1994

Familial and Hereditary CRC

- Sporadic (≈ 70%)
- Familial (≈ 25%)
- Rare CRC Syndromes
  - Lynch Syndrome (2-3%) (HNPCC)
  - 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) by age 25
- 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
- Attenuated FAP is different

**What Is GROCK Doing?**
- Routine cancer family history
- Test all biopsies of CRCs for DNA MMR deficiency
- Outreach to family members of patients with CRC or advanced colonic polyps
- G &RA Clinic
  - Complete risk evaluation
  - Screening and prevention recommendations
  - Genetic counseling and testing when appropriate

**Colorectal Cancer: The Preventable Killer**
- Sequential progression from polyp to cancer
- Common -
  - 4<sup>th</sup> most common cancer in US and CO
  - Decreasing but increasing in the young
- Lethal
  - 2<sup>nd</sup> most common cause of cancer death in US/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