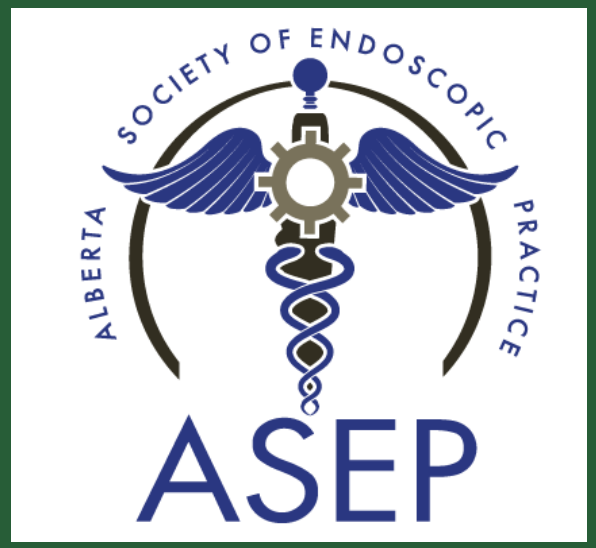
RISK FACTORS FOR COLON CANCER

Dr. Richard Sultanian, MD, MSc
Associate Clinical Professor
University of Alberta



UNIVERSITY OF ALBERTA

COI Declaration

- None

Objectives

1. To understand the importance CRC Screening

2. To recognize what patients are at risk for developing CRC

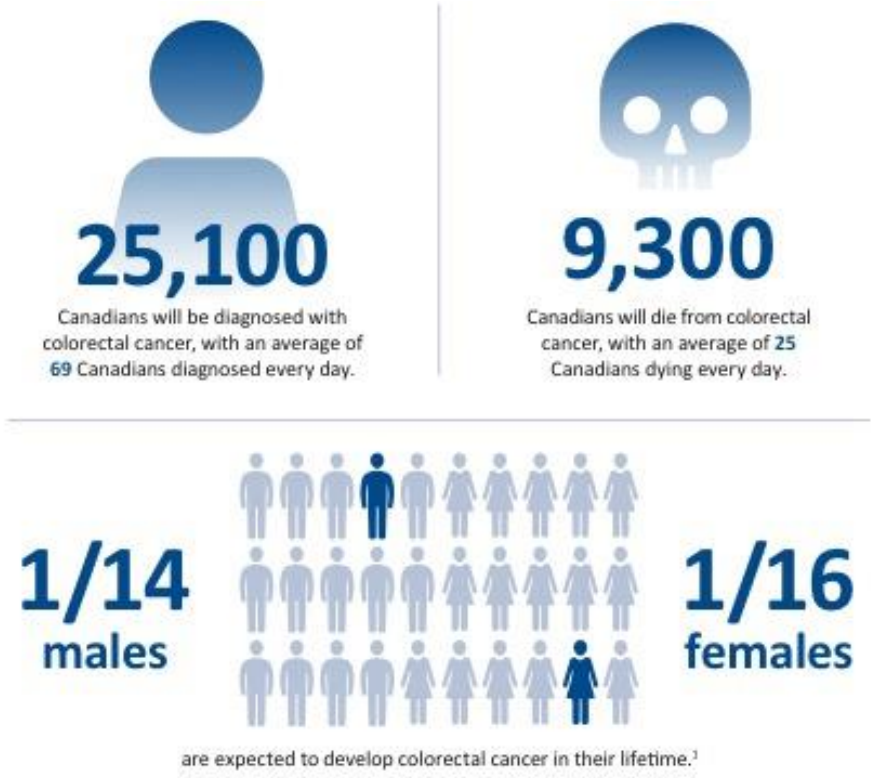
3. To discuss screening strategies for at risk populations

Importance of CRC Screening

UNIVERSITY OF ALBERTA

Importance of CRC Screening

- Why screen for CRC?

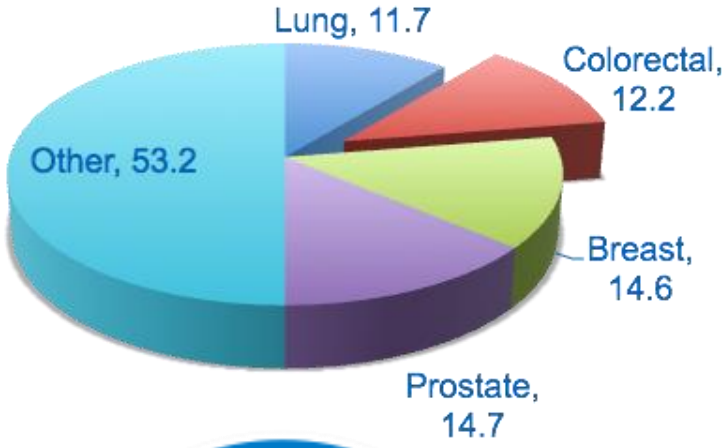


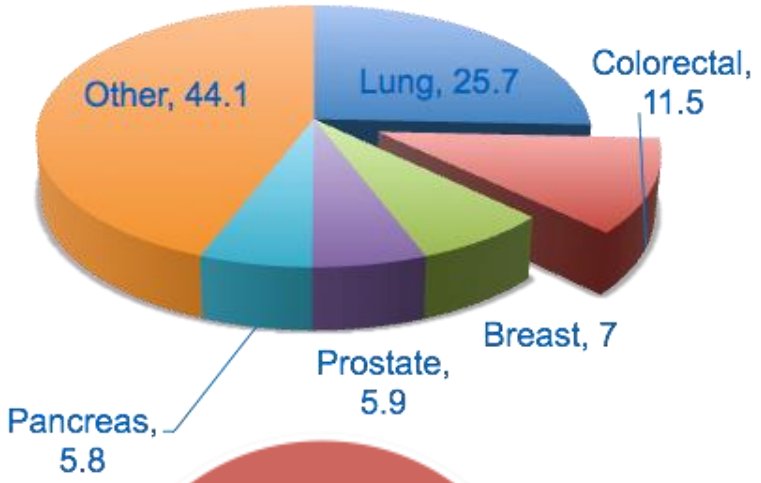
UNIVERSITY OF ALBERTA

Colorectal Cancer Screening in Canada, Monitoring and Evaluation of Quality Indicators-Results Report Jan 2019-Dec2020

Importance of CRC Screening

- Why screen for CRC?





Colorectal Cancer is the 3rd most diagnosed cancer in Alberta

Colorectal Cancer is the 2nd lethal cancer in Alberta

UNIVERSITY OF ALBERTA

Preventing CRC through Screening

- Screening allows for diagnosis of CRC prior to the development of advanced malignancy
  - lead to lower incidence of metastatic disease and death
- Ideally allows diagnosis and treatment of pre-malignant polyps BEFORE cancer develops

Corley D et al NEJM 2014 370:2539-41

Preventing CRC through Screening

- Incidence and mortality of CRC is decreasing
  - CRC is 90% preventable with early intervention
- In 2009, less than 36% of Albertans between 50 - 74 years received appropriate screening
- 31% increase in colorectal cancer screening since 2009
  - FIT

Preventing CRC through Screening

- Import question remain
  - Are we screening the right patients?
  - Are we over screening some populations and ignoring other at risk populations?
  - What populations are at an increased risk of CRC?

What patients are at risk for colorectal cancer?

What causes increased risk of CRC?

- Combination of environmental and genetic factors
  - Majority of CRC is sporadic, but other RF for CRC are important to recognize

- Genetic Factors
  - Hereditary CRC Syndrome (Lynch, FAP etc.)
  - Associated condition - IBD, acromegaly, metabolic syndrome
- Environmental factors
  - Diet, occupation

UNIVERSITY OF ALBERTA

1. Barkun A et al. Clinical Gastro Hep 2022

Hereditary CRC Syndrome

- As many as 12% of patients with CRC carry pathogenic mutations[1]
- Study of 1058 patients with CRC
  - 105 had one or more mutations identified
  - Majority (74%) were non-Lynch related (*APC*, biallelic *MUTYH*, *BRCA1* and *BRCA2*, *PALB2*, *CDKN2A*, and *TP53*)
- High incidence in younger patients[2]
  - 14% of patient under 50 have a genetic predisposition
  - Comprehensive genetic screening panel for young patients with CRC

1. Win AK et al. Gastro 2014. 146: 1208
2. Pearlman R et al. JAMA Oncol 2017. 3: 464

Familial adenomatous polyposis syndrome

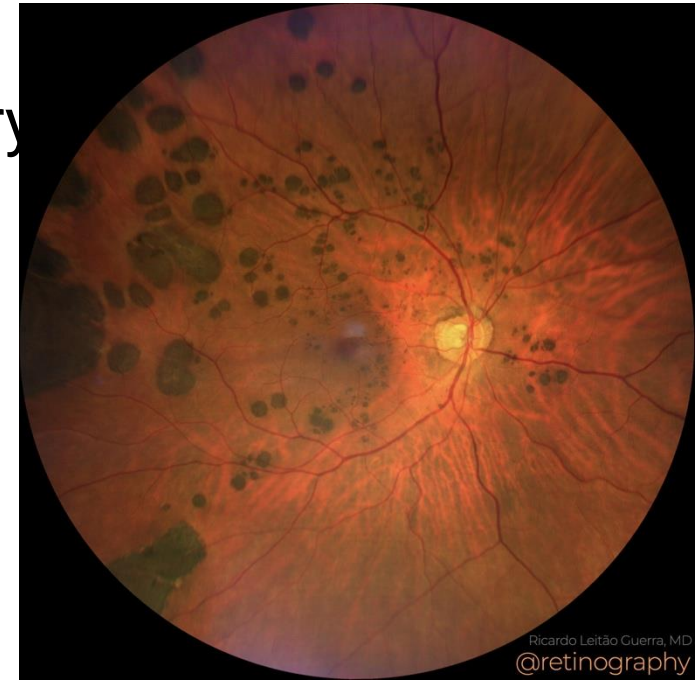
- Accounts for <1% of CRC
- Onset: Childhood
- Mutation: APC (occurs in 6-8% of Ashkenazi Jews)
- Presentation
  - Innumerous colonic polyps/ CRC in 90% of untreated patients by age 45
  - Extracolonic malignancy – Gastric, ampullary, small bowel, pancreatic, brain (medulla blastoma), papillary thyroid, pancreatic and more
- **Attenuation FAP**: Later onset presentation but same genetic mutation, decreased volume of polyposis and less chance of CRC

Familial adenomatous polyposis syndrome

- CRC Screening: start at 10-13yo q1-2y
- Other screening
  - EGD with side viewer q1-3y
  - MRI brain
  - US thyroid/abdo/pelvis q3y
- Colectomy
  - Documented or suspected colorectal cancer
  - Adenomas with HGD, size >1cm
  - Marked increases in polyp number or inability to manage high polyp

CHRPE

- Congenital hypertrophy of retinal pigmented epithelium
- Dx by ophthalmology
- Association with APC mutation and FAP, but this association is low
- Recommendations
  - Initiate screening after dx, and if features/family history suggestive of FAP, proceed accordingly



UNIVERSITY OF ALBERTA

Lynch Syndrome

- Accounts for 3% of CRC
- Onset: late teens/early 20s
- Mutation: 6 MMR genes (*hMLH1*, *hMSH2*, *hMSH6*, or *hPMS2*)
- Presentation
  - Numerous colonic polyps/ CRC in 90% of untreated patients by age 45
  - Extracolonic malignancy – Endometrial, ovary, stomach, small bowel, hepatobiliary system, brain and renal pelvis or ureter, and possibly breast and prostate

Lynch Syndrome

- CRC Screening: start late teens q1-3
- Other screening
  - EGD with side viewer q1-3y
  - MRI brain
  - US abdo/pelvis q3y
- Colectomy
  - Documented or suspected colorectal cancer
  - Adenomas with HGD, size >1cm
  - Marked increases in polyp number or inability to manage high polyp

Other Genetic mutations

- Many other genetic mutations potentially associated with CRC
  - CHEK-2, MUTYH
  - Variable phenotypic presentation/penetrance
  - Less clear evidence basic guidelines
  - Colonoscopy q1-3 years
- BCA1/2
  - Inconclusive association with CRC
  - No society recommendations for early CRC screening

Other Polyposis Syndromes

- Sessile serrated polyposis syndrome
  - No known genetic markers, no recommendations for genetic screening
  - Diagnosis:
    - >20 SSP throughout the colon, >5 proximal to the rectum
    - At least 2 >10mm in size
  - Colonoscopy:
    - start 10y younger than affected family members
    - Subsequent intervals based on endoscopic findings

Other Polyposis Syndromes

- Juvenile polyposis syndrome (Peutz Jeghers Syndrome
  - Hamartomatous polyposis syndrome throughout GI tract
  - Many extra-intestinal cancers (breast, ovarian, pancreas, testicular)
  - Genetic cause: autosomal dominant STK11 mutation
  - Diagnosis:
    - 2 or more hamartomatous polyps
    - Hyperpigmentation of the mouth, lips, nose and genitals
    - First degree family members affected
  - Endoscopy q1-3 y
    - start early teens or at time of diagnosis (genetic or otherwise)
    - Consider CT/MR enterography and VCE

Associated Conditions Requiring Increased Screening

Inflammatory Bowel Disease

- Ulcerative colitis
  - Well documented association
    - Dependent on severity, extent and duration of disease
  - Colonoscopy
    - Q3y for disease >10y
    - Q2y for disease >20y
    - Q1y for disease >10y
  - Increased risk of CRC if associated with PSC
- Crohns Disease
  - Less correlation than US
  - Thought to be similar RF if pancolonic CD

Previous Radiation Exposure

- Leads to increased CRC risk, especially is childhood exposure
- Limited society guideless for initiation and frequency of colonoscopy

- Some studies demonstrate a small increase in incidence of rectal cancer in pt who had radiation for prostate CA
  - Not felt to be significant enough to warrant early or increased frequency of colonoscopy

Other Conditions

- Acromegaly
  - Increased risk vs general population
  - Recommendations: Start CRC screening at time of diagnosis
- Cystic Fibrosis
  - Increased risk vs general population
  - Significant increase post-lung transplant (2-5x general population)
  - Screening at 40 or post-transplant
- Solid organ transplant
  - Increased risk due to immunosuppression but no formal recommendations for early or increased frequency of screening

Risk Factors that DO NOT Alter CRC Screening

Conditions NOT Altering Screening

- Obesity
  - Increases with time and severity of obesity
  - Not significant enough to warrant early screeing
- DM2
  - Meta-analysis 16 studies demonstrated a 20-35% increase in CRC[1]
  - Thought to be secondary to high IGF accelerating polyp growth
- Red Meat /Processed Meats[2]
  - Long term consumption (especially grilled)
  - Polyaromatic compounds and other carcinogens released during charring, preservation, pickling

1. Yurhara et al. Am J Gastro 2011. 106: 1911
2. Pearlman R et al. JAMA Oncol 2017. 3: 464

Other Conditions NOT Altering Screening

- Tobacco
  - Increased risk of polyps
  - Increased incidence and mortality from CRC (especially rectal)
- Alcohol
  - Increased incidence in moderate (2-3/d) and heavy drinkers (>4/d)
  - Thought to be secondary to decreased folate intake and absorption
- Cholecystectomy
  - Slight increase in incidence of right sided cancers
  - Thought to be secondary to altered bile acid composition post-chole

Take Home Messages

- Be mindful of conditions that increase risk for CRC!
- Genetic syndromes, while rare, are very important to recognize
  - Remember there are extraintestinal cancers that needs screening as well
- Increase incidence and awareness of SSP syndrome
  - Require more frequent and careful screeing
- IBD, especially UC, is a significant risk for CRC
  - Utilize advanced techniques such as electronic and topical chromoendoscopy
- Counsel patients that have modifiable RF
  - Lifestyle change is more effective than increasing screening

Questions?