Colorectal Cancer Screening

Daniel C. Chung, MD
GI Unit and
GI Cancer Genetics Service
Massachusetts General Hospital

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CRC Epidemiology

- 4th most common malignancy in US (136,000 cases/yr)
- 2nd most common cause of cancer death (50,000 cases/yr)
- Cumulative lifetime risk of CRC is 6%
- Slight male predominance
- Average age of diagnosis: 65 yo
- 80% of cases occur in people without identifiable risk factors
- Prognosis is directly related to stage of disease

Colon cancer arises from a defined precursor lesion

Tubular adenoma

Tubulovillous Adenoma

High grade dysplasia (Carcinoma-in-situ)

Invasive cancer

Time ----------▸ *7-10 yrs*

Colorectal cancer (CRC) screening

1. Who to screen?
   - Average risk 75%
   - Moderate risk 20%
   - High risk 5%

2. How and how often to screen?
   - FOBT/FIT
   - Flexible sigmoidoscopy
   - Colonoscopy
   - Virtual colonoscopy
   - Molecular/genetic testing

Stool based screening tests for colon cancer

Colon cancer

Colon polyp

??

<u>Blood</u>
Hemoccult
(guaiac)
FIT

<u>Sloughed tumor cells</u>
Stool DNA
("Cologuard")

Prospective evaluation of fecal DNA testing

N = 9989 subjects referred for screening colonoscopy

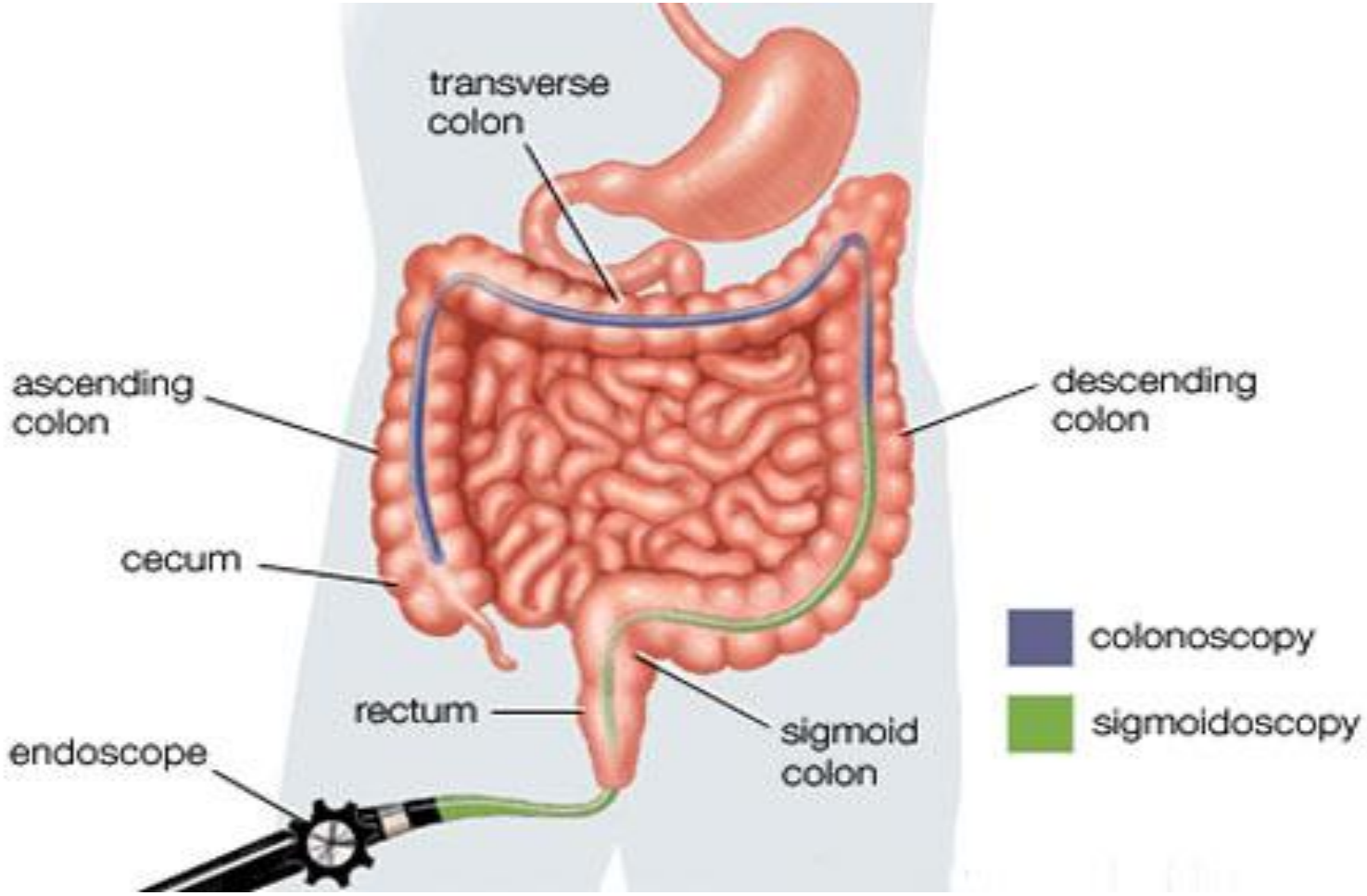
	Sensitivity (CRC)	***Sensitivity (Advanced Adenoma)***	***Specificity***
Fecal DNA	92.3%	42.4%	86.6%
FIT	73.8%	23.8%	94.9%

from Imperiale, NEJM, 2014

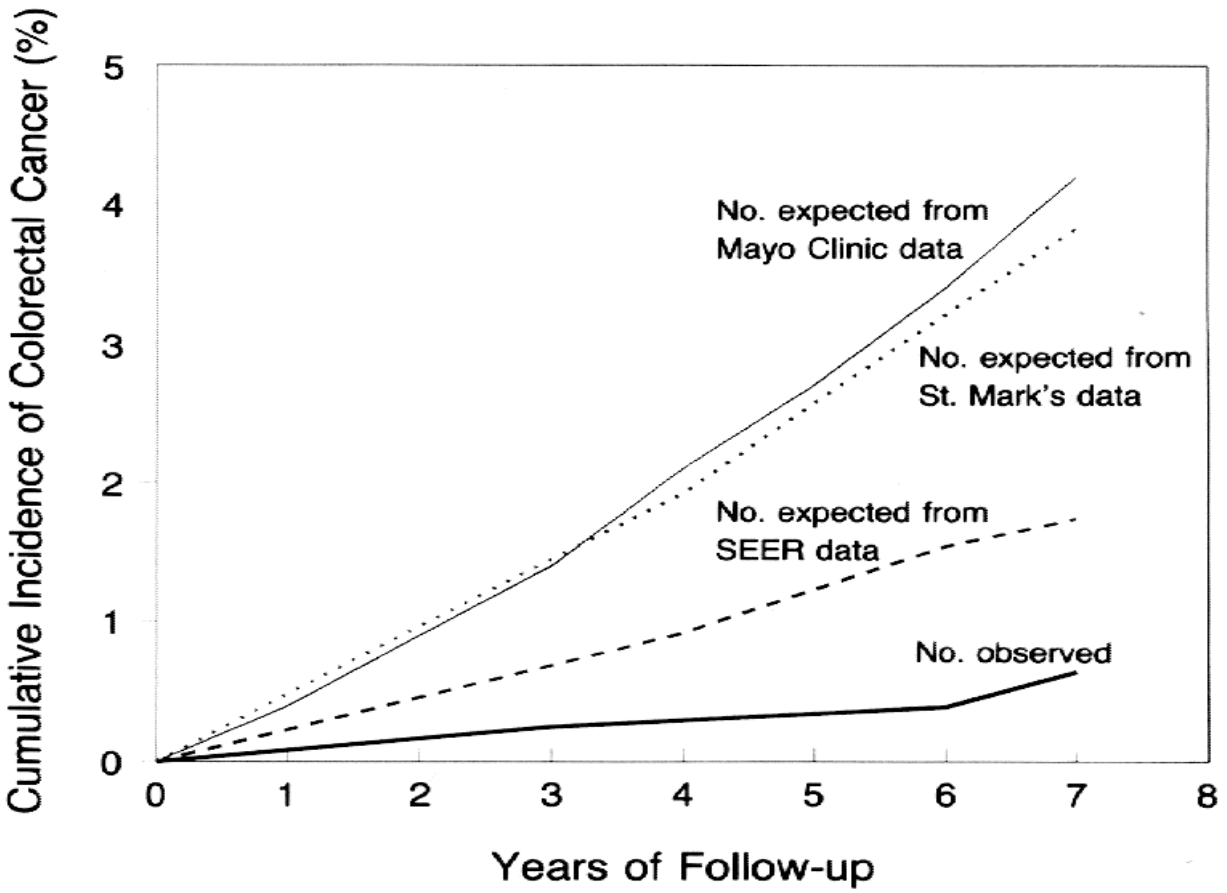
Stool tests for CRC screening

- PROS:
  - Cheaper
  - Easy to perform
  - FOBT can decrease risk of cancer death by 23%
- CONS:
  - Unpleasant to handle stool
  - Positive tests require colonoscopy
  - Potentially greater benefit from other screening tests

Colonoscopy vs. sigmoidoscopy



National Polyp Study:
polypectomy reduces incidence of CRC 76-90%



Winawer,NEJM,1993

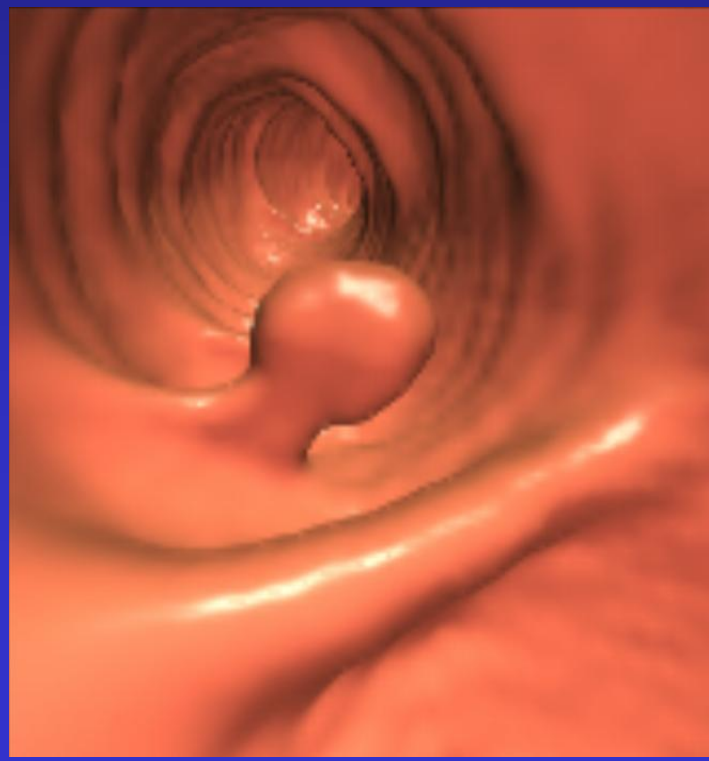
PLCO Trial (U.S.)

- 154,900 men and women randomized to screening flexible sigmoidoscopy or usual care
- Follow-up: 11.9 years
- Results: 21% reduction in CRC incidence

  26% reduction in CRC mortality

R. Schoen, NEJM, 2012

Virtual colonoscopy



Virtual colonoscopy: *performance characteristics*

Sensitivity

	Pickhardt 2003	Cotton 2004	Rockey 2005	Zalis* 2012
Polyp size				
≥ 10 mm	**94%**	**55%**	**59%**	**91%**
≥ 6 mm	**89-94%**	**39%**	**51%**	**59%**
(No. subjects)	**(1233)**	**(600)**	**(614)**	**(605)**

*Laxative free exams

CT Colonography: limitations

- **No therapeutic capabilities**
- **Detection rate of small, flat polyps is low**
- **Discomfort from air insufflation**
- **Pre-procedure laxative preparation required**
- **Not reimbursed by insurance**

CRC Screening: *Average risk patient*

- Men and women over age 50
- No symptoms (bleeding)
- No risk factors for CRC (Family history)

*Tests that detect polyps and cancer (** preferred)*

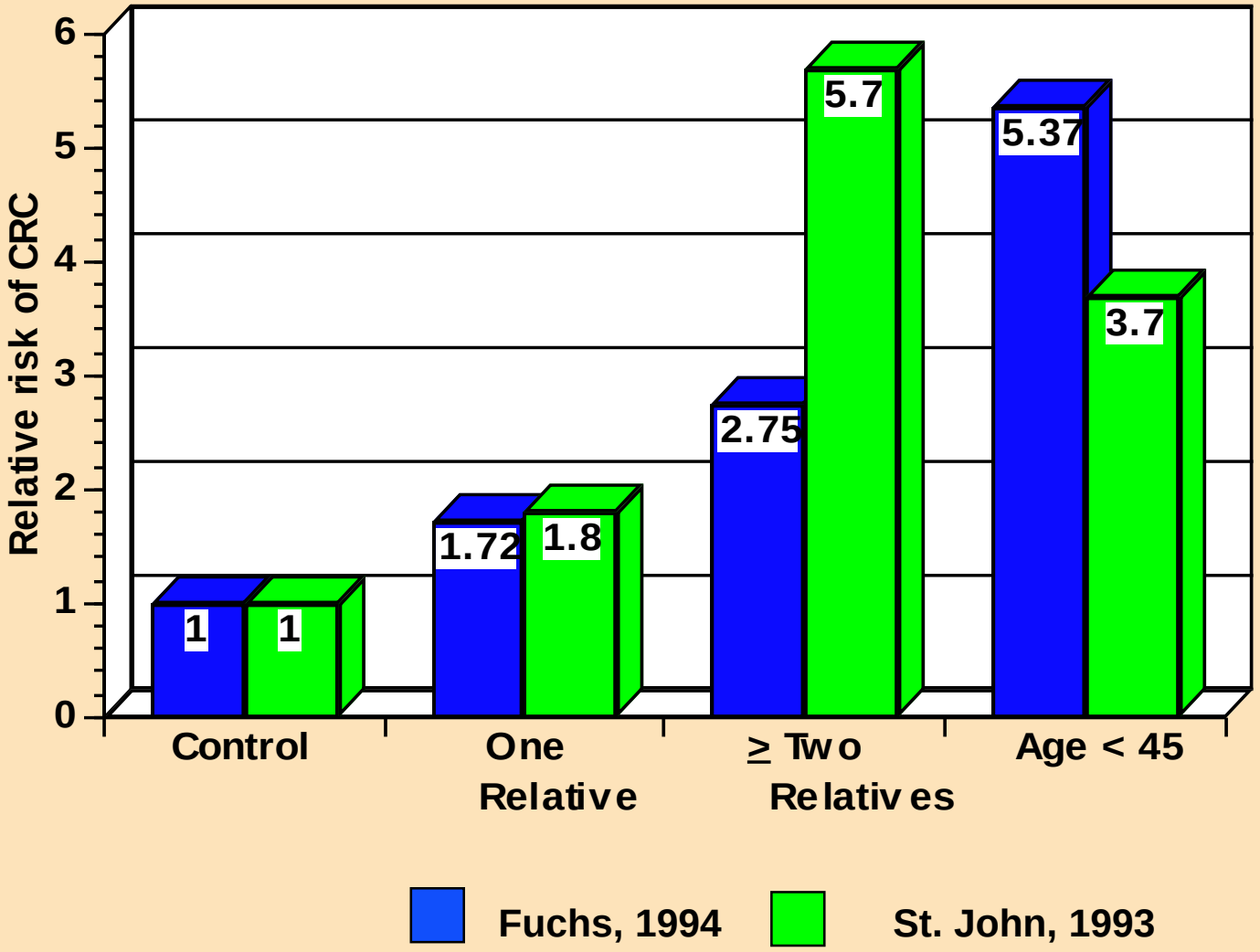
- Flex Sig every 5 yrs
- Colonoscopy every 10 yrs
- Virtual colonoscopy every 5 yrs

Tests that primarily detect cancer

- Stool occult blood or FIT annually
- Stool DNA every 3 years

ACS/US Multisociety Task Force on CRC, ACR: CA Cancer Journal, 2008

RISK OF COLON CANCER: ROLE OF FAMILY HISTORY



CRC Screening: *Moderate Risk Patient*

Family History of CRC/polyps

- CRC or polyps in 1st degree relative < 60 or two 1st degree relatives of any age:

  Colonoscopy at age 40, or 10 yrs before youngest case. Then every 5 years.

- CRC or polyps in 1st degree relative ≥ 60 or two 2nd degree relatives of any age :

  Average risk recommendations,
  but start screening at age 40

“Hereditary Colon Cancer”

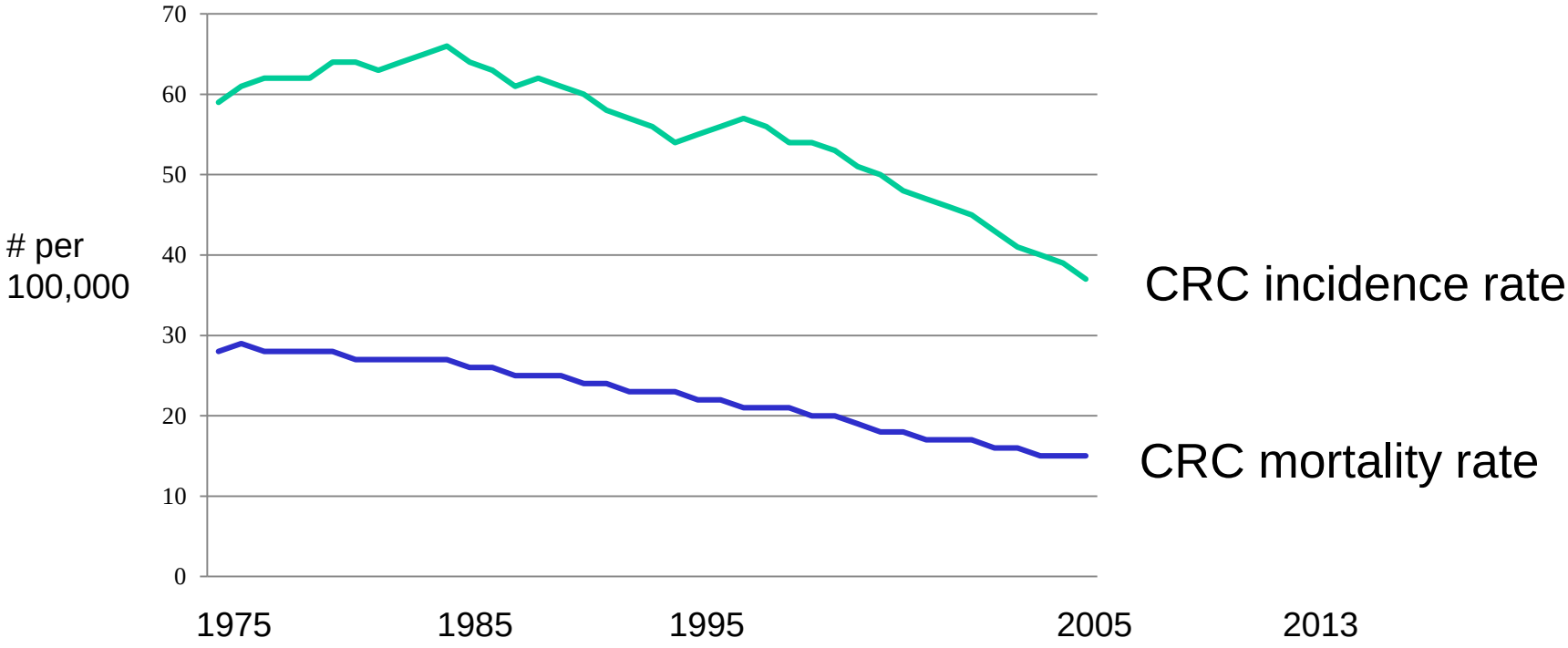
- Those with a very strong family history may have a condition known as “Hereditary Colon Cancer”
- Very high risk of colon cancer (up to 80%)
- Increased risk of other tumors (up to 50%)
  - Uterus, Stomach, Small intestine
- Increased risk of cancer in family members

When to suspect Hereditary Colon Cancer

- Colon cancer in 2 or more family members
- Colon cancer before age 50, polyp before age 45
- More than 10 cumulative polyps
- Colon cancer in conjunction with other cancers: uterine

- Genetic testing can be used to diagnose "Hereditary Colon Cancer"

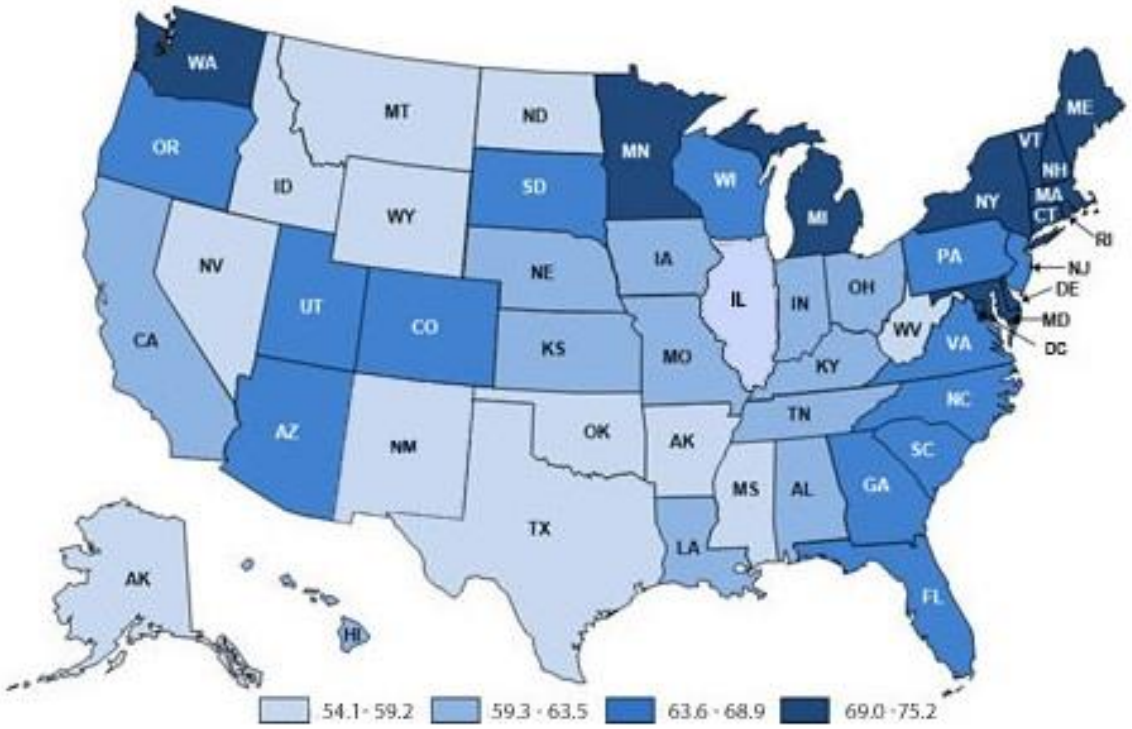
CRC incidence and mortality are falling in the US



SEER data

Participation with CRC screening guidelines

Percentage of Adults Aged 50–75 Years Who Reported Being Up-to-Date* with Colorectal Test Screening, by State
Behavioral Risk Factor Surveillance System, United States, 2010



Overall rate of participation: 65%

Key points

- Everyone requires colon cancer screening
- There are many options for CRC screening
- Accurate risk stratification is key, and this depends upon a careful family history
- High-risk families should have a genetic evaluation