Exploring the Colon: Colorectal Cancer Screening

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Conflicts of Interests

- None

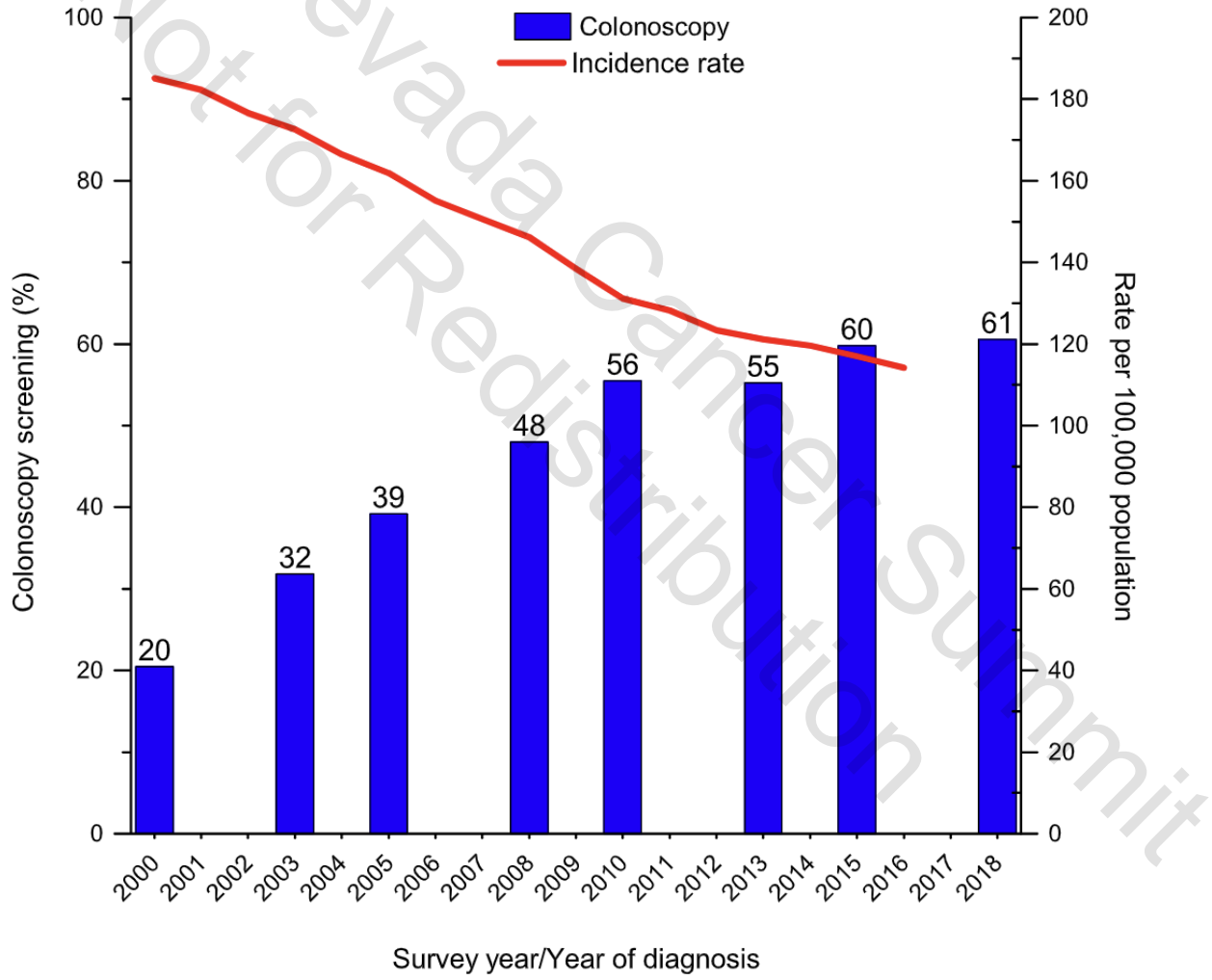
Learning Objectives

- 1. To understand the current state of colorectal cancer (CRC) incidence and mortality in the United States.
- 2. To describe the effectiveness of various screening options.
- 3. Review the current guidelines and rationale for started and stopping CRC screening and polyp surveillance in average risk individuals.

The State of Colorectal Cancer in 2024

- Third most common cancer and second leading cause of cancer death
- 153,020 people diagnosed with CRC in the US in 2024
- 53,010 will die from CRC in 2024
- 10.5% diagnosed in people younger than age 50
  - This is a 45% increase from 1992 to 2015
- Screening guidelines have shifted to starting at age 45 for average risk individuals.
- The purpose of this talk is to address how we can affect the general population.

Trends in Colonoscopy Prevalence and CRC Incidence Rates 2000 to 2016



Factors that influence screening recommendations.

- Age
  - 2018 American Cancer Society changed recommendations to begin at 45.
  - 2021 United States Preventative Services Task Force recommended 45 as well.
  - 2021 American College of Gastroenterology followed with age 45.
- Race and Sex
  - Black Americans, Native Americans, and Alaskan Native individuals have the highest incidence and mortality rates
  - Men have 33% higher mortality from CRC than females.
- Hereditary CRC syndromes
- Acromegaly
- Renal Transplantation with long term immunosuppression

Risk factors for CRC development-

but do not influence screening recommendations.

- Obesity is a risk factor for development CRC
  - Especially when weight gain occurs between early adulthood and midlife.
  - Risk was highest for those in the highest weight gain category.
  - Obesity also increases risk of death
- Diabetes mellitus: 38% higher
  - Even when controlling for smoking, obesity, and physical activity
- Insulin Resistance
  - Insulin is an important growth factor for colonic mucosal cells and stimulates tumor cells.
  - Plasma concentrations of insulin-like growth factor and IGF binding protein 3 influence the risk of CRC
- Diabetes also increased risk of mortality after diagnosis of CRC.

Risk factors for CRC development-

but do not influence screening recommendations.

- Red and processed meats: Data is not consistent
  - High temperature cooking (e.g. BBQ, pan-frying)
  - Perhaps by the production of polyaromatic hydrocarbons and other carcinogens
  - Lean red meat may be associated with less risk
  - WHO International Agency for Research on Cancer classified processed meats as carcinogenic to humans
  - Sausages, bacon, ham, beef jerky, corned beef, and other smoked, salted, fermented, or cured meats are considered group 1 carcinogens.
  - Other group 1 carcinogens: asbestos, cigarettes, and alcohol.

Risk factors for CRC development-

but do not influence screening recommendations.

- Tobacco: Increased risk of polyp formation, development of CRC (greatest in the rectum), and mortality.
- Alcohol: Significant risk for moderate and heavy drinkers, but not light drinkers.
- Use of androgen deprivation therapy.
- Cholecystectomy
- CAD
- Ureterocoloic anastomoses for bladder surgery, endometrial cancer
- Gastrointestinal microbiome
- Prolonged sitting

Protective Factors

- Physical activity
- Diet
- Fiber
- Regular use of ASA or NSAIDs and hormone replacement therapy in postmenopausal females
- Folate and folic acid
- Vitamin B6
- Calcium and dairy products
- Vitamin D
- Magnesium
- Garlic
- Fish consumption
- Coffee

Why does it have to be so complicated?

- Wake up early.
- Get outside and move.
- Get some sun.
- Eat your fruits and veggies
- Eat your lean proteins, fish>chicken>meat
- How your food was treated is how your food will treat you.
- Be aware of all the levels of processing.
- Limit processing as much as possible.
- Go outside again and move.
- Get to bed early and sleep well.

Types of tests for CRC screening

- Stool based testing
  - Detecting hemoglobin in blood
  - DNA alterations suggestive of malignancy
- Direct Visualization
  - Endoscopy
  - Capsule endoscopy
  - Radiologic imaging
- We will review the characteristics of individual tests used for CRC screening.

Selecting a screening test

- Tests for CRC differ with regard to
  - Sensitivity
  - Specificity
  - Effectiveness
  - Convenience
  - Safety
  - Availability
  - Cost (one time cost and cumulative cost over time)

Stool-Based Tests

- Fecal Immunochemical (FIT) for blood
- Guaiac-based fecal occult blood test (gFOBT)
- Multitarget stool DNA tests with fecal immunochemical testing (Cologuard)

- For practical purposes please consider only FIT or the DNA stool tests, gFOBT have several barriers (diet, collection, 3 samples) without any advantages over FIT.

FIT – Fecal Immunochemical Test for blood

- Directly measures hemoglobin in the stool.
- Small single sample of stool into a container.
- Frequency yearly.
- No restrictions to medications or diet
- ASA and other NSAIDs generally do not need to be held.
- Advantages: Convenient, easy, inexpensive
- FIT can be positive due to an upper gastrointestinal bleed and therefore be a false positive for CRC screening.
- Cost: $15-50

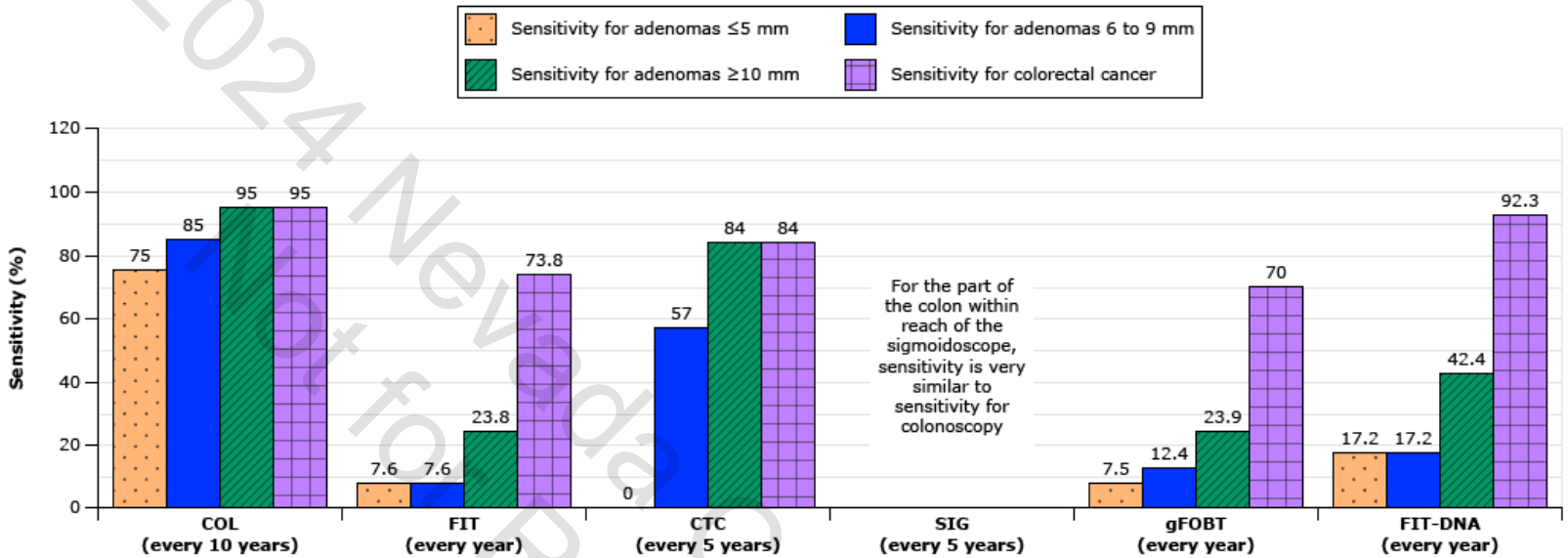
Multitarget stool DNA tests with FIT (Cologuard)

- Composite of tests:
  - molecular assays to test for DNA mutations (KRAS)
  - Gene amplification technique to test for methylation biomarkers associated with colorectal neoplasia
  - FIT to test for hemoglobin from blood.
- Must collect a full stool sample, not a smear like FIT. Must analyzed within 72 hours.
- No dietary or medication restrictions.
- Testing is recommended every 3 years, although optimal interval is unknown.
- 13% false positive rate, that means 1 in 10 positive cologuards will incorrectly identify cancer or polyps.
- 1 in 10 cologuards will result in an unnecessary colonoscopy.
- Cost: $500-1000 every 3 years.
- As of 2023, Medicare and insurance plans will cover a colonoscopy following a positive cologuard result.

Endoscopic visualization: Colonoscopy

- Most commonly used CRC screening test in the United States
- Definitive test for detection of precancerous adenomas and CRC
- Performed by a trained physician.
- Performed every 10 years for average risk patients.
- Requires a change of diet, a vigorous bowel preparation, sedation is usually required and is invasive
- Risks: Bleeding, perforation, and infection.
- Preferred test for high risk patients.
- If lesions are detected they are immediately removed.
- Cost: $1500 every 10 years.

Estimated sensitivity, specificity, and cancer-specific deaths averted for each colorectal cancer screening strategy



Test specificity	86	96.4	88	87	92.5	89.8
Colorectal cancer deaths averted per 1000 40-year-olds (n)*	22 to 24	20 to 23	16 to 24	16 to 21	20 to 23	21 to 24

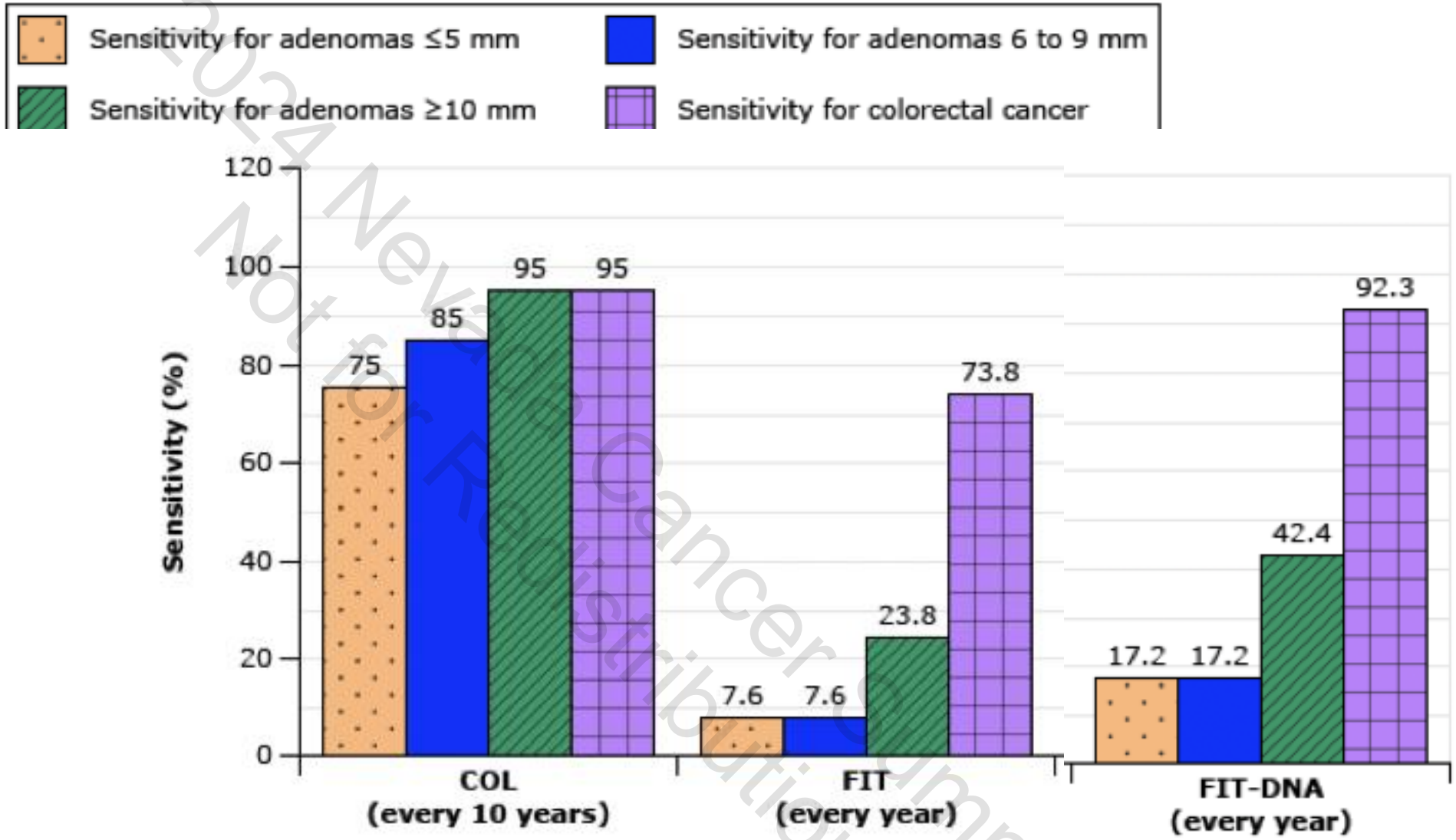
Sensitivity, specificity, and cancer-specific deaths averted for each screening strategy.

COL: colonoscopy; FIT: fecal immunochemical test; CTC: computed tomography colonography; SIG: sigmoidoscopy; gFOBT: guaiac-based fecal occult blood test; FIT-DNA: multitargeted stool DNA test.

* Assumes screening from ages 50 to 75 years, including 100% adherence, complete follow-up without delay, and appropriate surveillance. Ranges reflect results from 3 models.

Data from:

1. *Zauber A, Knudsen A, Rutter CM, et al. Evaluating the Benefits and Harms of Colorectal Cancer Screening Strategies: A Collaborative Modeling Approach. AHRQ Publication No. 14-05203-EF-2. Rockville, MD: Agency for Healthcare Research and Quality; October 2015.*
2. *Knudsen AB, Zauber AG, Rutter CM, et al. Estimation of Benefits, Burden, and Harms of Colorectal Cancer Screening Strategies: Modeling Study for the US Preventive Services Task Force. JAMA 2016; 315:2595.*



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Blood Based Test for Colorectal Screening

- 10,258 person study, 7861 were eligible
- Cell-free DNA blood based test
- Primary outcome: Sensitivity for CRC.
- Secondary outcome: Sensitivity for polyps.
- There was an 83.1% sensitivity of the participants with CRC detected by colonoscopy who had a positive blood test.
- There was a 13.2% sensitivity for detection of polyps with a positive blood test in those who had already underwent colonoscopy.

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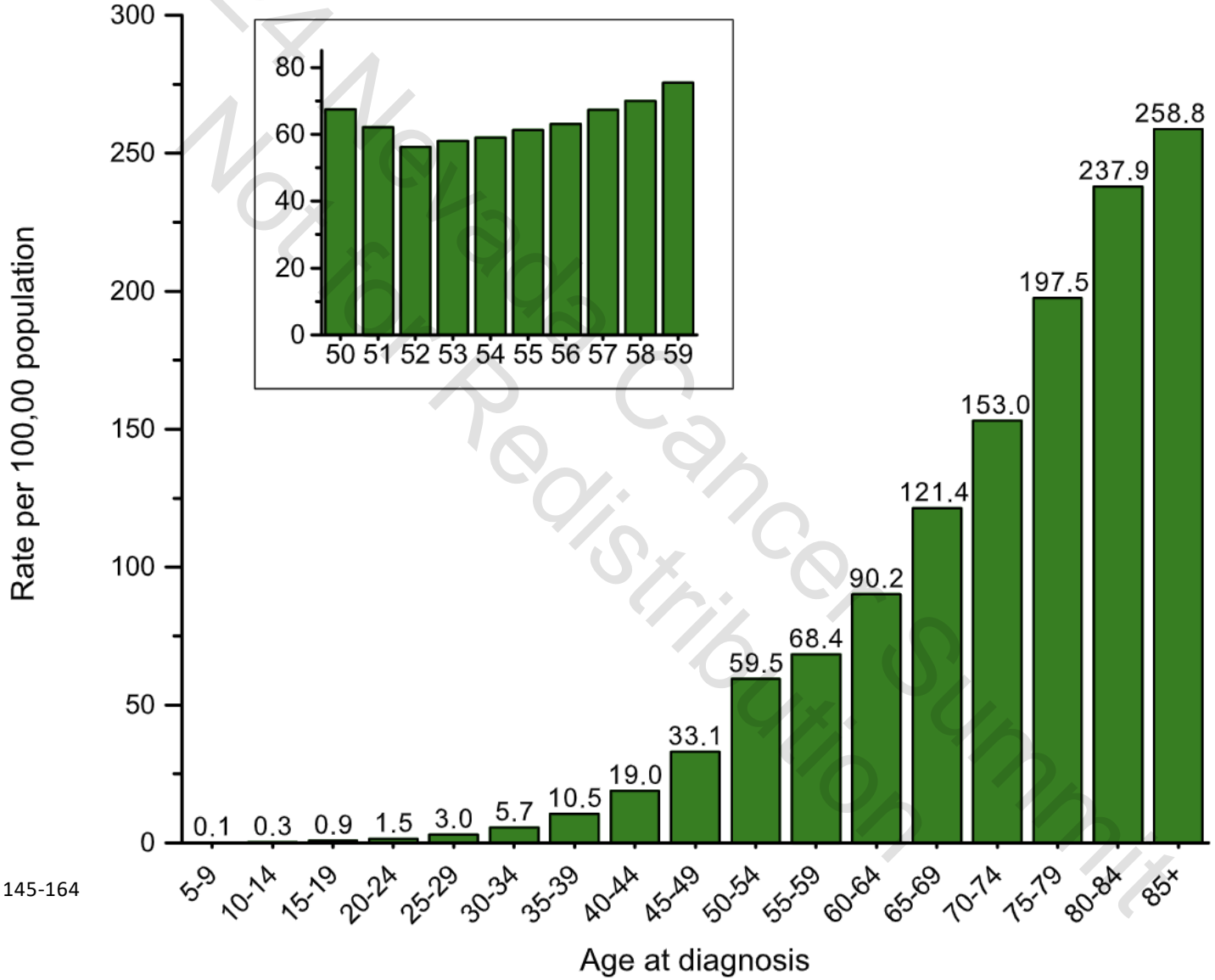
When to stop screening?

- Each patient is different

Age Specific CRC Incidence Rates, United States, 2012 to 2016.



Seigel R et al. CA Cancer J Clinicians 2020: 70; 145-164

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