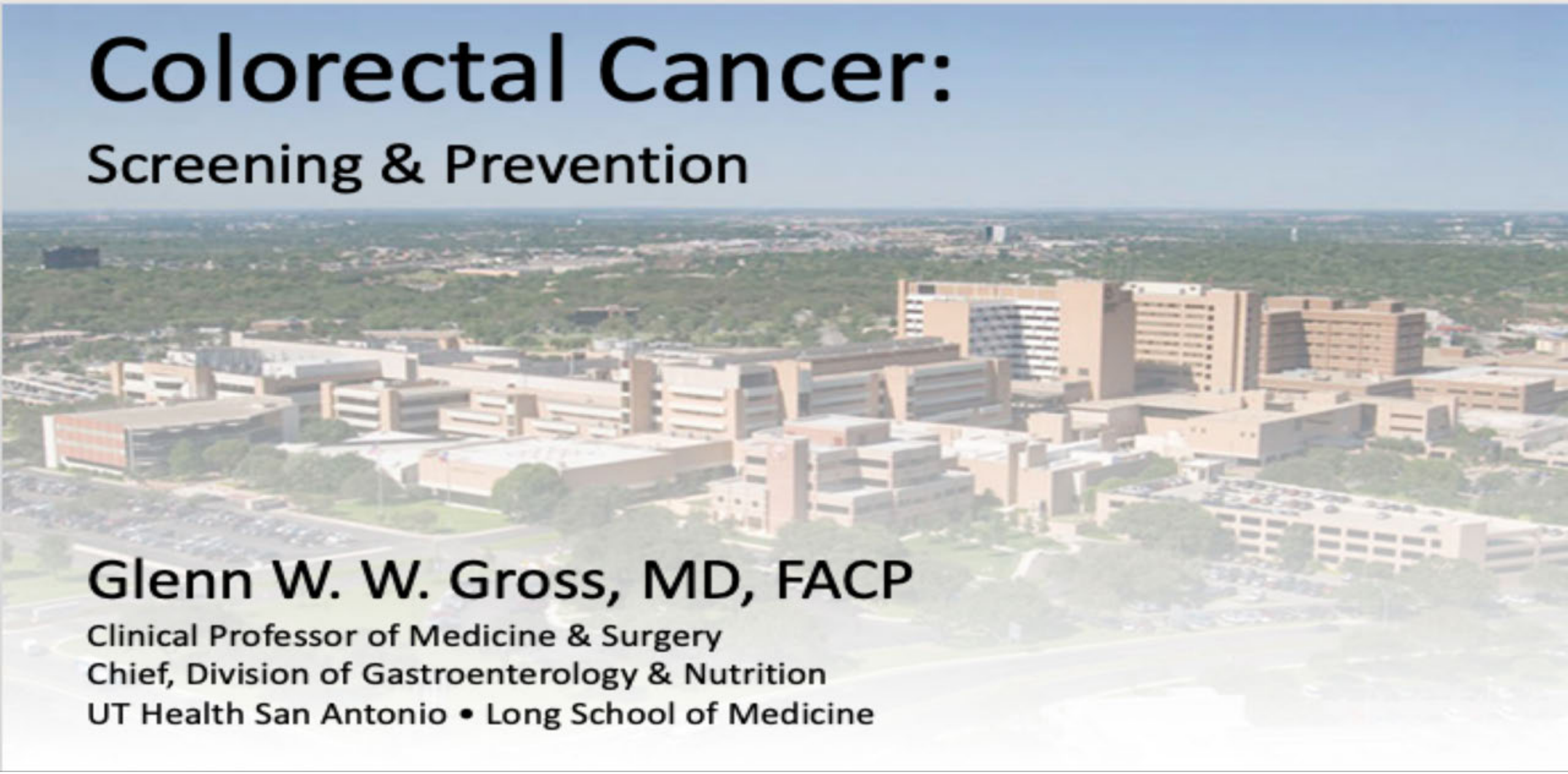
Colorectal Cancer:

Screening & Prevention



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Learning Objectives

1. Review principles of colon adenoma/cancer biology that permit successful prevention regimes

2. Describe pros/cons of screening interventions (including colonoscopy, CT colography, fecal tests)

3. State current national recommendations for colon cancer screening in average risk and selected high risk populations

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COLORECTAL CANCER – Scope of the Problem

- #2 cause of cancer mortality overall
- #3 in women (after lung, breast)
- #3 in men (after lung, prostate)

	New diagnosis	Death
Men	71,830	26,270
Women	65,000	24,040
U.S. 2014 incidence/prevalence (NCI/SEER)		

Siegel *CA Cancer J Clin* 2014;64:104-17

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COLORECTAL CANCER – Scope of the Problem

- Lifetime CRC risk: ~ 5%
- 5-yr U.S. survival (2009): 65% overall
  90% localized
- Steady ↓ in death rates since mid-1980's:
  - ↑ screening
  - Better treatments

Siegel *CA Cancer J Clin* 2014;64:104-17

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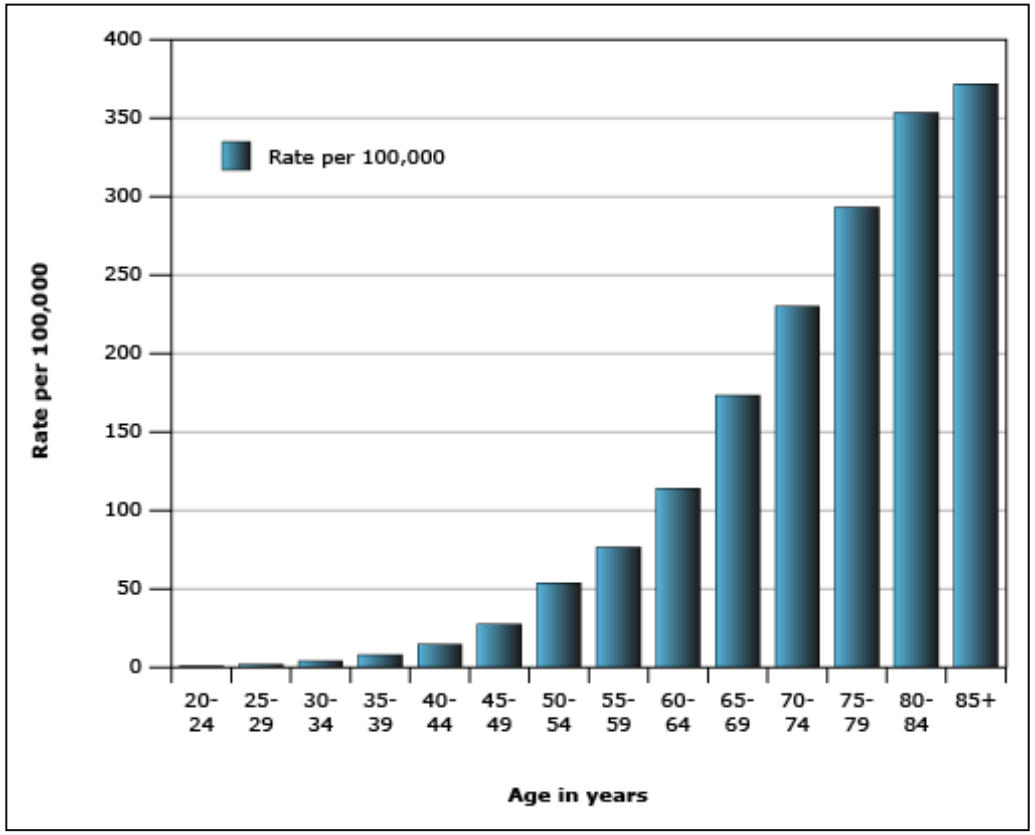
COLORECTAL CANCER – Risk Factors

- Age (90% ≥ 50 yrs old, avg age at dx 66)
- Obesity / physical inactivity / diabetes
- Long-term smoking
- Diet: high in red or processed meat
  low in fruits and vegetables
- Personal history of colorectal cancer/polyps
- Inflammatory bowel disease
- Family history of colorectal cancer or polyps
- Inherited: Lynch syndrome, FAP



15-30% of CRC

http://seer.cancer.gov/
American Cancer Society. Cancer Facts & Figures 2014
Oncoscience 2014; 1:400.

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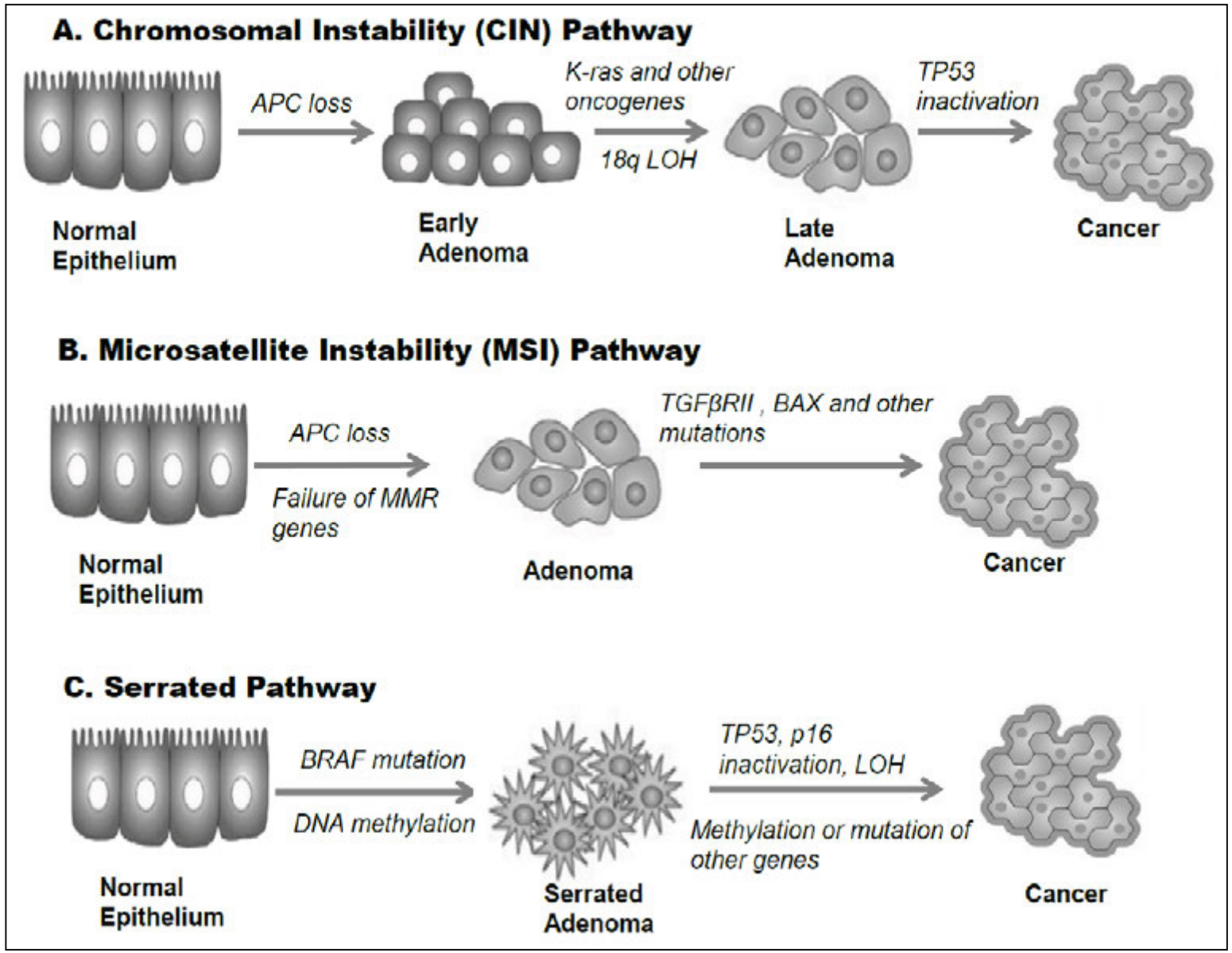
CRC Pathogenesis – Multiple Pathways



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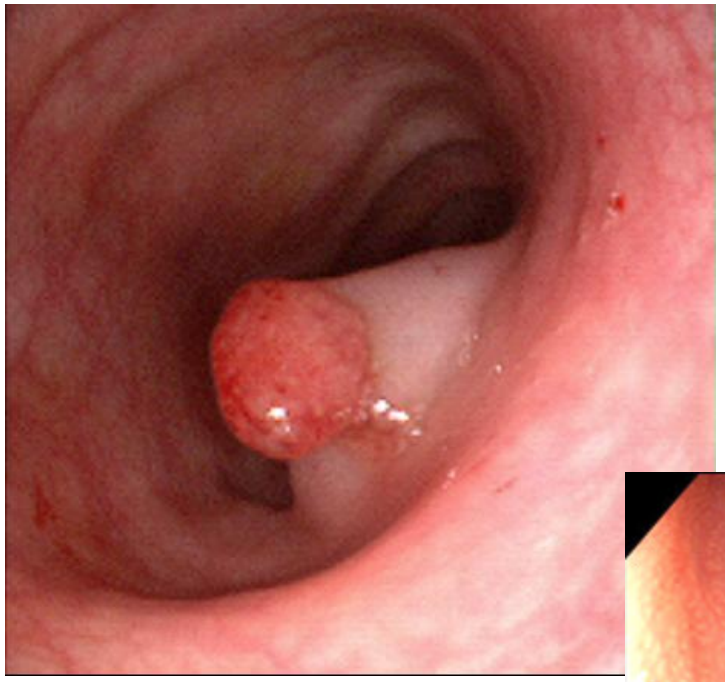
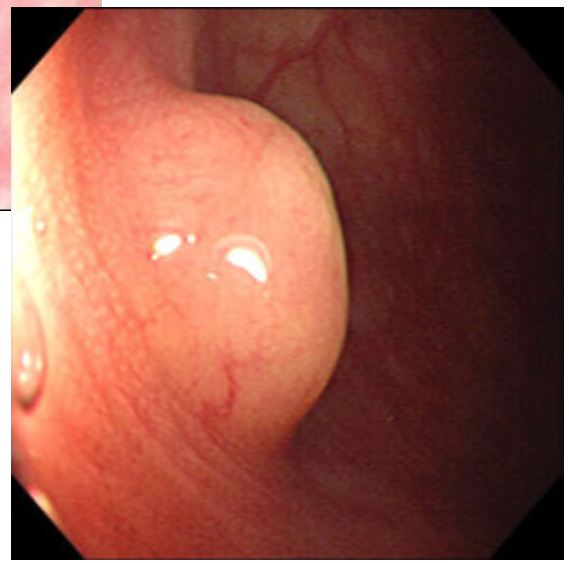
Can We Prevent Colon Cancer Deaths?



Benign
Polyps



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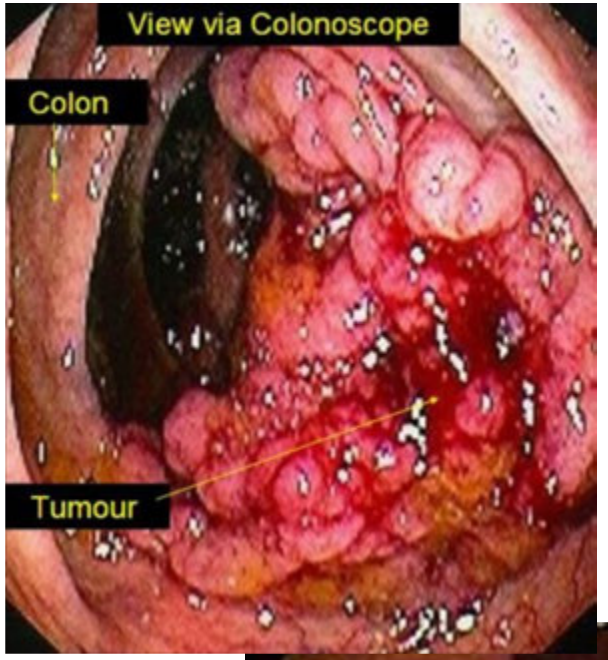
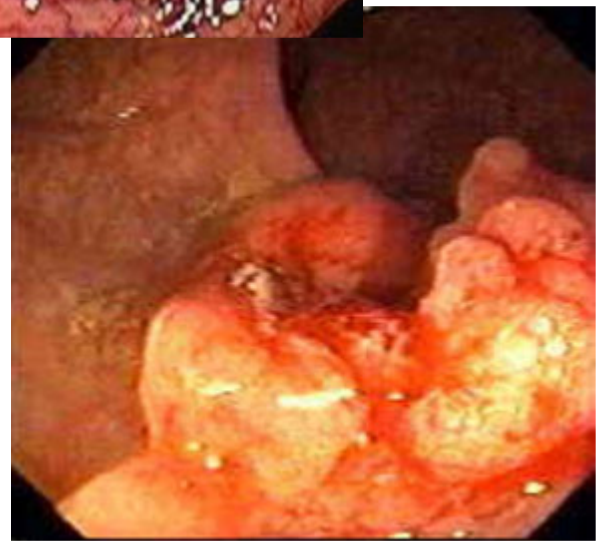
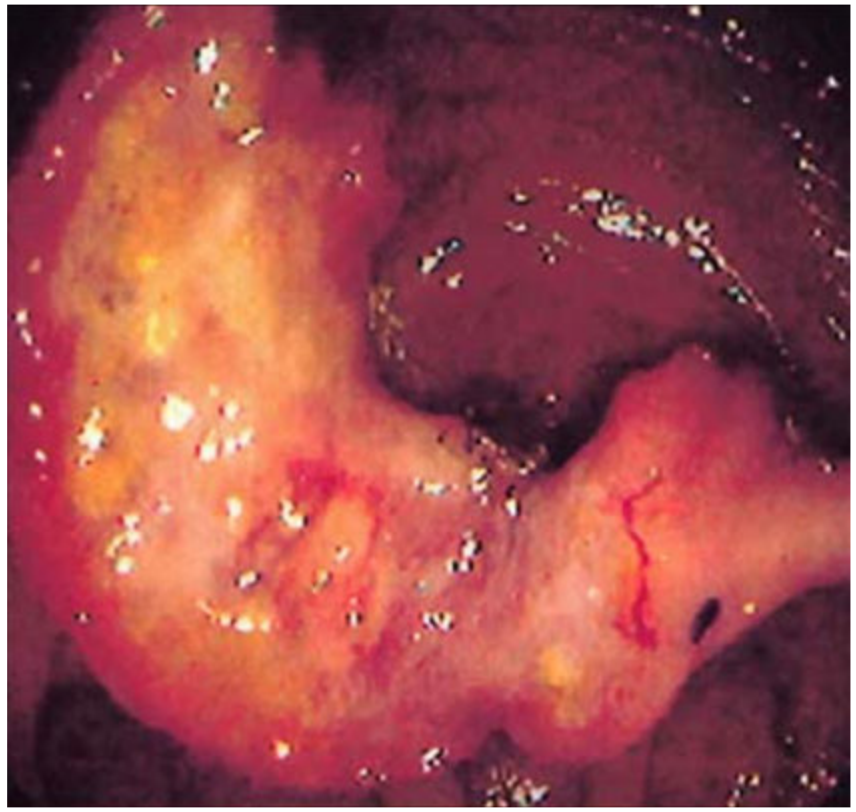


Colon Cancers





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Primary Prevention of Colorectal Cancer

"Doc, Can I Just Eat Better?"

- Diet (less red meat, more fiber)
- Regular exercise, stop smoking
- Medications: aspirin / NSAIDs
  ? calcium
  ? post-menopausal HRT
  ? statins
  anti-oxidants (no)
- Bottom Line: *Not Ready for Prime Time*

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Screening Tests for Colorectal Cancer

Tests That Detect Cancers *(Early Cancer Detection)*	Test That Detect Polyps *(Cancer Prevention)*
Fecal testing for blood	Colonoscopy
Fecal DNA testing	CT colography (virtual colonoscopy)
	Air-contrast barium enema
	Flexible sigmoidoscopy

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Colonoscopy

- Introduced 1969
- Most widely used colon cancer screening test
- 14 million performed annually
  - ~ 50-70% CRC screening/surveillance
- Allows visualization of rectum, entire colon ± distal TI
- When properly performed . . . safe, accurate, and well tolerated by most patients

Dominitz DDW-ASGE 2009

Colonoscopy

- Gold standard for colon cancer screening since Medicare coverage 1998
- IV sedation / full bowel prep
- Flexible lighted tube with camera
- Examines entire colon
- Polyps removed during procedure – “one-stop shopping”

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Polyp Removal During Colonoscopy

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So Does Colonoscopy Really Work? (prevent cancer, save lives)

- National Polyp Study (NPS)
  - 1417 patients with ≥ 1 adenoma removed
  - Mean follow-up of 5.9 years
  - 76, 88 & 90% reduction in colon cancer incidence vs. three reference groups
- 16-yr follow-up of 2602 NPS center patients 53% reduction in colon cancer mortality after removal of 1 or more adenomatous polyps

Winawer *N Engl J* Med 1993; 329:1977-1981
Zauber *N Engl J Med* 2012; 366:687-696

Impact of Screening Colonoscopy

- 2001-2010
  - Colorectal cancer incidence ↓ 3.4%/year

Screening Colonoscopy Utilization in U.S. Adults Aged 50-75	
2000	19%
2010	55%

Siegel *CA Cancer J Clin* 2014;64:104-17

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Limitations of Colonoscopy

- Invasive
- Potential for physical discomfort
- IV sedation (miss work, need chaperone)
- Most expensive method of screening
- Patients don’t like bowel prep
- Small risk of serious complications (bleeding, perforation)
- Not perfect: up to 10% polyps > 1cm missed

Rex *Gastroenterology* 1997;112:24–28

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Colonoscopy. . . not everybody seems to want one

- Screening rates historically low (<breast / cervical)
  - 63% of adults > age 50 screened by any means
- Public uninformed and/or resistant
- Concerns about … bowel prep, pain, indignity
- Too many options in guidelines?

CDC Behavioral Risk Factor Surveillance Survey 2008

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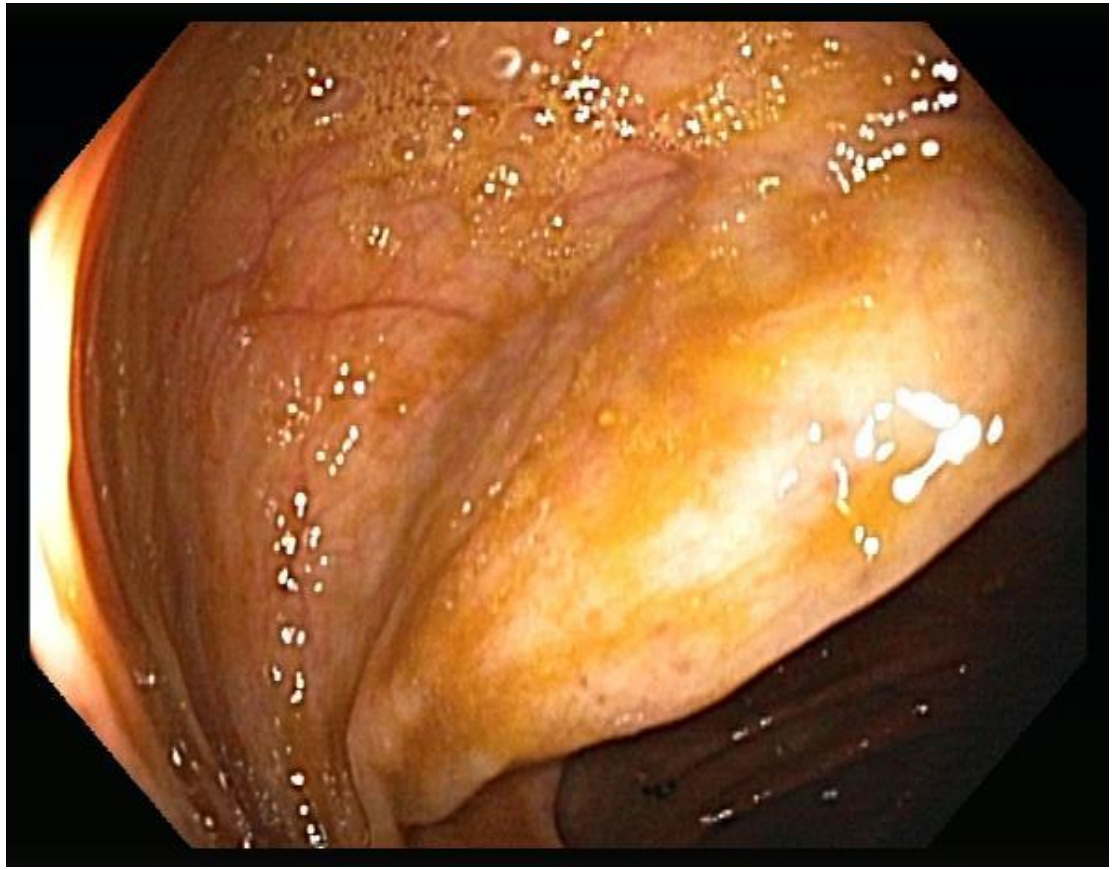
Limitations of Colonoscopy

We may not be as good as we think we are . . .

- "Interval cancers" after screening colonoscopy
  - Canadian administrative claims study
  - Colonoscopy decreased death from CRC in left colon but not the right
  - Most CSP performed by non-gastroenterologists
- It matters who does your colonoscopy (operator-dependent)
  - Cancer miss rates: 3% for GI *vs.* 13% for non-GI
    5% one GI group *vs.* 1% all other GI

Baxter *Ann Intern Med 2009;150(1):1-8*
Rex *Gastroenterology* 1997;112:17–23

- Intensified awareness of flat/subtle/atypical right-sided polyps
- Renewed emphasis on scrupulous prep and technique



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Emphasis on Quality Indicators in Colonoscopy

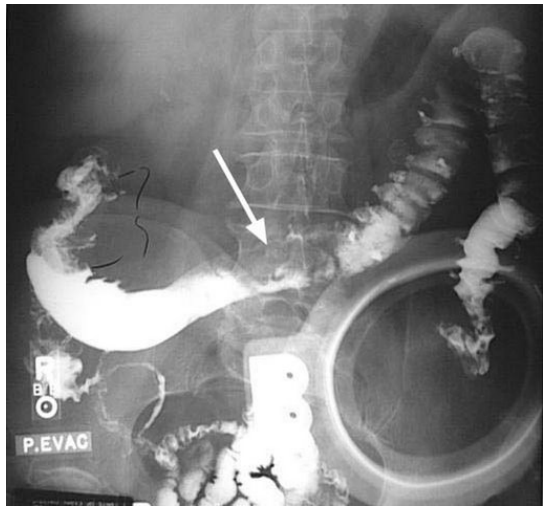
Thorough Inspection = Increased Lesion Detection

- High-quality bowel preps
- Cecal intubation ≥ 95% in screening cases
- Mean withdrawal time without intervention ≥ 6 minutes . . .*don't rush!*
- Adenoma detection rate (ADR) in asymptomatic screening patients >age 50, adenomas should be detected in: ≥ 25% men
  ≥ 15% women

Froelich Gastrointest Endosc 2005 Mar;61(3):378-84
Barclay *Clin Gastro Hepatology 2008;6(10):1091-98*

Alternative Screening: Barium Enema

- Once common, now rarely performed
- Examines entire colon, cheaper than colonoscopy, less complications
- Colonoscopy needed for all positive studies
- Poor sensitivity
  - For cancer (83%*)*
  - For polyps > 1cm (50%)
- Not proven to prevent colon cancer



Rex *Gastroenterology* 1997;112:17–23

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Alternative Screening: Flexible Sigmoidoscopy

- Examines lower third of colon
- No sedation / enema prep only
- Can be done by ML or PCP
- CRC mortality
  - ↓ 67% in examined area
  - ↓ 80% if polyps prompt colonoscopy
- Usage plummeted with screening colonoscopy

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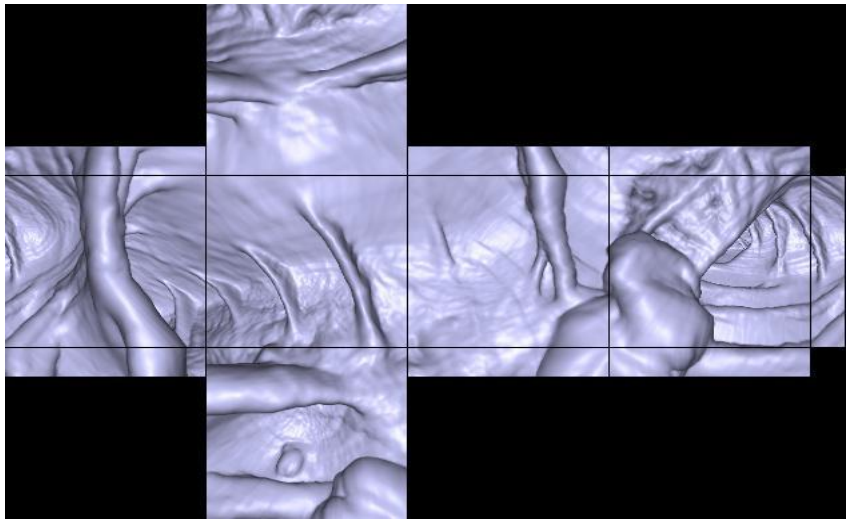
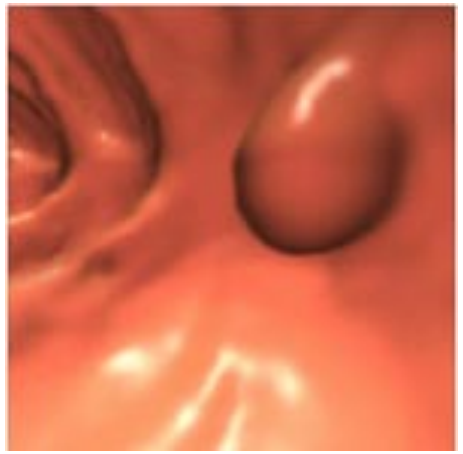
CT Colography



- CT scan w/ extensive 3D image reconstruction
- Equals traditional colonoscopy for detecting cancers and polyps > 1cm
- Still not covered by Medicare
- Current indications:
  - Failed colonoscopy
  - Patients unable to undergo colonoscopy



Pickhardt *N Engl J Med* 2003; 349:2191-2200

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CT Colography (*vs.* Colonoscopy)

Cons	Pros
Still requires bowel prep and enema tube	Image acquisition takes few seconds only
Poor detection small- and medium-sized polyps	Less invasive
Colonoscopy still required if medium/large polyps found	No IV / sedation
Cost-efficacy unproven	Safer (but not without risk)
Radiation exposure	Cheaper
Extra-colonic findings	Patient Preference

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Alternative Screening: Fecal Tests

- Stool guaiac
  - 3 stool samples
  - 32% ↓ CRC mortality over 30 yrs with annual testing
  - High false positive rate → many unnecessary tests
- Fecal immunohistochemical test (FIT) for hemoglobin
  - Only 1-2 samples needed
  - Higher sensitivity/specificity
  - Higher cost

Mandel *N Engl J Med* 1993;328:1365
Lee *Ann Intern Med 2014;160:171*

Alternative Screening: Fecal DNA Testing

- 2nd generation test (Cologuard™)
- Approved August 2014
- FIT + multi-target DNA composite:
  - DNA via gene amplification
  - Hemoglobin
  - DNA methylation patterns
- Detects cancers and (some) advanced adenomas

Imperiale *N Engl J Med* 2014;370:1287

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Alternative Screening: Fecal Tests

	Sensitivity for Colon Cancer	Sensitivity for Large Adenomas	Specificity for either
FIT	74%	24%	95%
FIT-MT DNA	92%	42%	87%
Colonoscopy	*97-100%*	*90-100%*	

Imperiale *N Engl J Med* 2014;370:1287

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Colon Cancer Screening Guidelines

- Multiple “competing” guidelines published in 2008
- All agree: offer screening to average risk individuals beginning at age 50
- After that . . .

U. S. Preventive Services Task Force

- Simulation decision model
- Identifying premalignant lesions (prevention) not valued over cancer detection
- For adults aged 50-75, three screening strategies:
  - Annual FOBT
  - Flex Sig every 5 yrs + FOBT every 3 yrs
  - Colonoscopy every 10 yrs
- Insufficient evidence for CT colography, fecal DNA, ACBE

Ann Intern Med 2008;149:627

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American Cancer Society/Multi-Society Task Force

- More inclusive list of recommended tests
  - No test unequivocally superior
  - “the best test is the one patients will take”
  - Incorporating patient preferences may ↑ rates of screening
- Stop screening when estimated life expectancy < 10 years

Strategies Endorsed for Early Detection + Prevention	Strategies Endorsed for Early Detection
Colonoscopy every 10 yrs	FOBT (guaiac) annually
CT colography every 5 yrs	FIT annually
Flex Sig every 5 yrs	
ACBE every 5 yrs	

Levin *CA Cancer J Clin* 2008;58:130

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American College of Gastroenterology

- Endorsed all options in ACS-MSTF guideline, but . . .
- Colonoscopy designated as “preferred strategy” for screening/cancer prevention
- FIT “preferred strategy” for screening/cancer detection for patients who “decline a cancer prevention test”
- Screening ends at age 75
- Recommend begin screening at age 45 in African-Americans

Rex *Am J Gastroenterol* 2009;104:739

American Cancer Society – May 2018 Update

- Lower age of initial screening to 45
- Screen till age 75 unless life expectancy < 10 years
- Individualize between 75-85 based on health, preferences
- No screening after age 85

Strategies Endorsed for Early Detection + Prevention	**Strategies Endorsed for Early Detection**
Colonoscopy every 10 yrs	FOBT (guaiac) annually
CT colography every 5 yrs	FIT annually
Flex Sig every 5 yrs	*Multi-target fecal DNA every 3 yrs*
~~ACBE every 5 yrs~~	

Levin *CA Cancer J Clin* 2008;58:130

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What Does Medicare Currently Cover?

Test	Coverage Frequency
Fecal Occult Blood or FIT	annually
Flexible Sigmoidoscopy	every 4 years, or 10 years after a previous colonoscopy
Colonoscopy	every 10 years, or 4 years after a previous flexible sigmoidoscopy
Barium Enema	every 4 years (if done instead of colonoscopy or flexible sigmoidoscopy)
Multi-target fecal DNA	every 3 years

Not covered: CT colography

www.cancer.org/healthy/findancerearly/cancerscreeningguidelines

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Follow-Up Intervals After Surveillance Colonoscopy

Baseline colonoscopy: most advanced finding(s)	Recommended surveillance interval (*y*)
No polyps	10
Small (<10 mm) hyperplastic polyps in rectum or sigmoid	10
1–2 small (<10 mm) tubular adenomas	5–10
3–10 tubular adenomas	3
>10 adenomas	<3
One or more tubular adenomas ≥10 mm	3
One or more villous adenomas	3
Adenoma with HGD	3
Serrated lesions	
Sessile serrated polyp(s) <10 mm with no dysplasia	5
Sessile serrated polyp(s) ≥10 mm	3
OR	
Sessile serrated polyp with dysplasia	
OR	
Traditional serrated adenoma	
Serrated polyposis syndrome[a]	1

Gastroenterology 2012; 143: 844.

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What About After the First Surveillance Exam?

Findings at Baseline Colonoscopy	Findings at 1st Surveillance	Interval for 2nd Surveillance (y)
Low Risk Adenoma (LRA) - 1-2 adenomas - < 10mm in size	HRA	3
	LRA	5
	No adenoma	10
High Risk Adenoma (HRA) - 3 or more adenomas - Advanced Adenoma(s) • *≥ 10mm in size* • *high grade dysplasia* • *villous histology*	HRA	3
	LRA	5
	No adenoma	5

US Multi-Society Task Foce Update
Lieberman et al *Gastroenterology* 2012:143:844

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Surveillance – Increased Risk Patients
Family History of Colorectal Cancer

Condition	Age to Begin Colonoscopy	Interval
Single FDR with CRC or advanced adenoma* at age ≥ 60	40	Every 10 years
Singe FDR with CRC or advanced adenoma at age < 60 **or** Two FDR with CRC or advanced adenoma at any age	Age 40 or 10 yrs younger than youngest affected relative	Every 5 years
***Advanced adenoma = adenoma ≥ 1cm in size, or HGD, or villous histology**		

US Multi-Society Task Force Update
Rex et al *Am J Gastroenterol 2017*

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Surveillance – Increased Risk Patients
Hereditary Syndromes

Condition	Age to Begin Colonoscopy	Interval
Classic FAP (Familial Adenomatous Polyposis), Gardner's	At diagnosis	Annually, until colectomy
Lynch Syndrome(s)	Age 20-25	Every 2 yrs, annually after age 40

Rex *Am J Gastroenterol* 2009;104:739

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Surveillance – Increased Risk Patients
Inflammatory Bowel Disease

- After 8-10 yrs of colitis annual or biannual colonoscopies with multiple biopsies at regular intervals
- HGD in flat mucosa, confirmed by an expert pathologist, is an indication for colectomy
- LGD in flat mucosa may also be an indication for colectomy
- Emerging alternative: chromoendoscopy with biopsy of detected abnormalities

ACG Practice Guideline 2010 – Kornbluth *et al*

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Surveillance – Increased Risk Patients
After Colon Cancer Resection

- Initial surveillance colonoscopy 1-yr post-op
- 2nd surveillance colonoscopy 3 years later (4 yrs post-op)
- 3rd surveillance colonoscopy 5 years later (9 yrs post-op)… and every 5 yrs thereafter, till surveillance not appropriate

US Multi-Society Task Force

Am J Gastroenterol advance online publication, 12 February 2016; doi:10.1038/ajg.2016.22

Rex *Am J Gastroenterol* 2009;104:739

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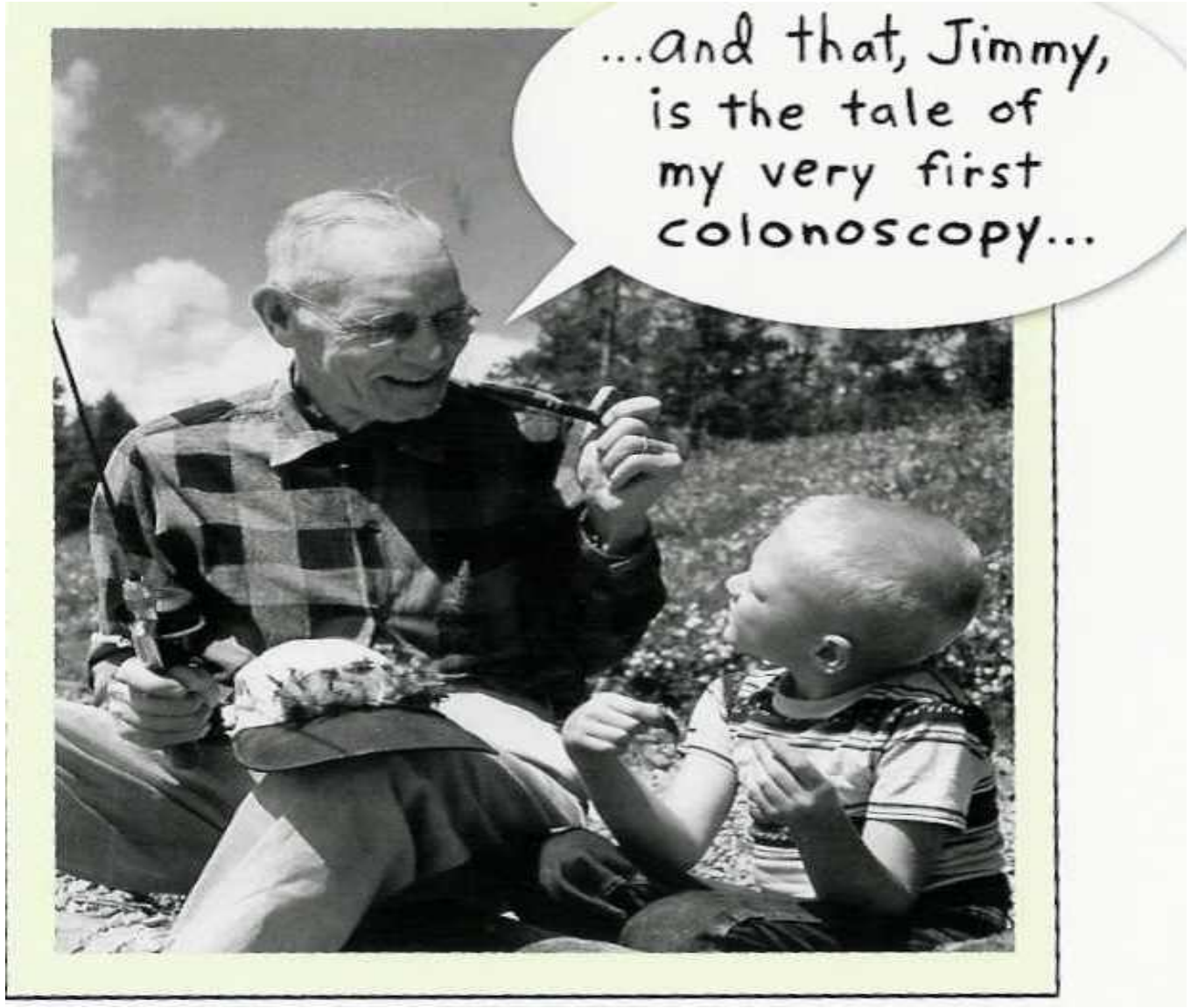
In Conclusion . . .

- Colorectal cancer is a serious national health problem and largely preventable
- Colon cancer rates are decreasing, most likely due to increased screening
- Colonoscopy is the dominant and most effective form of screening, but many patients resist having one
- Beneficial screening and cancer detection alternatives exist, and any screening is better than no screening
- Start screening at age 50, earlier in high risk patients

Thanks for your attention!



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