

Screening for Colorectal Cancer

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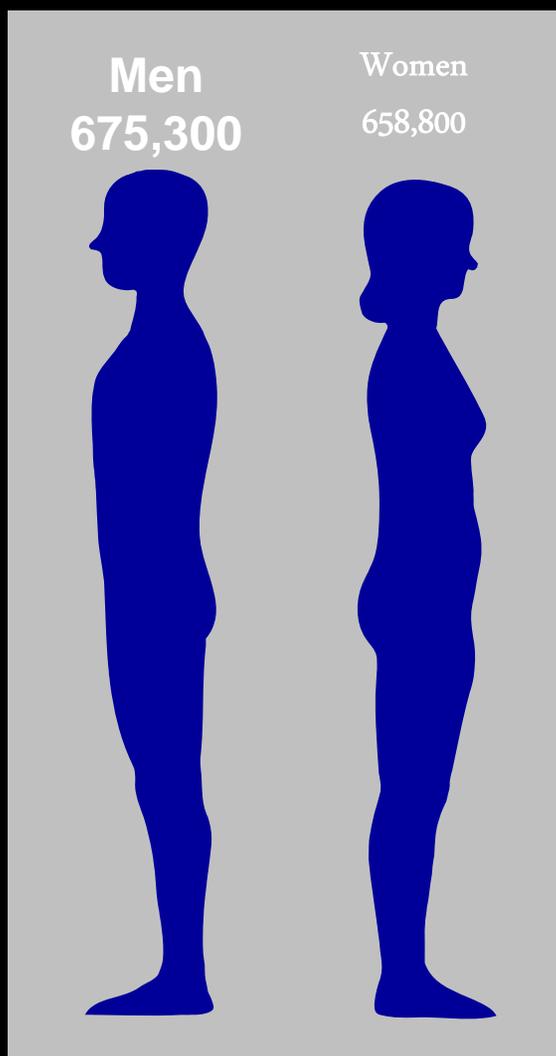
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2003 Estimated US Cancer Cases*

Prostate	222,849
Lung/bronchus	94,542
Colon/rectum	74,283
Urinary bladder	40,518
Melanoma of skin	27,012
Non-Hodgkin lymphoma	27,012
Kidney	20,259
Oral cavity	20,259
Leukemia	20,259
Pancreas	13,506
All other sites	114,801



210,816	Breast
79,056	Lung/bronchus
72,468	Colon & rectum
39,528	Uterine corpus
26,352	Ovary
26,352	Non-Hodgkin lymphoma
19,764	Melanoma of skin
19,764	Thyroid
13,176	Pancreas
13,176	Urinary bladder
62,238	All other sites

ONS=Other nervous system.

*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.

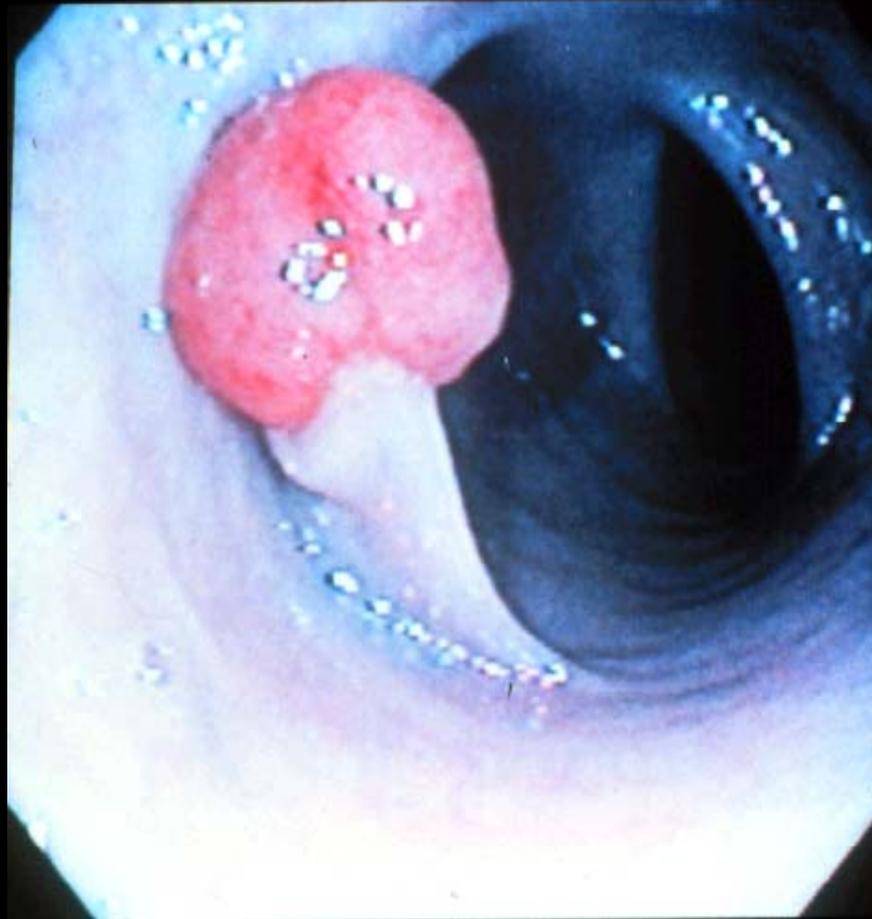
Source: American Cancer Society, 2003.

Adenoma – Carcinoma Sequence



Normal Mucosa → Adenoma → Severe Dysplasia → Cancer

Colon Polyp



Colon Cancer



Distribution of Colorectal Cancer

Colorectal Cancer



Colorectal cancer screening

First assess RISK

AVERAGE RISK INDIVIDUAL

- All patients age 50 years and older, the asymptomatic general population

HIGH RISK

- Personal history
- Family history

Colorectal Cancer Screening

Average risk

- Fecal occult blood testing (FOBT)
- Flexible sigmoidoscopy
- Barium enema
- Colonoscopy

- CT colography
- Stool genetic testing

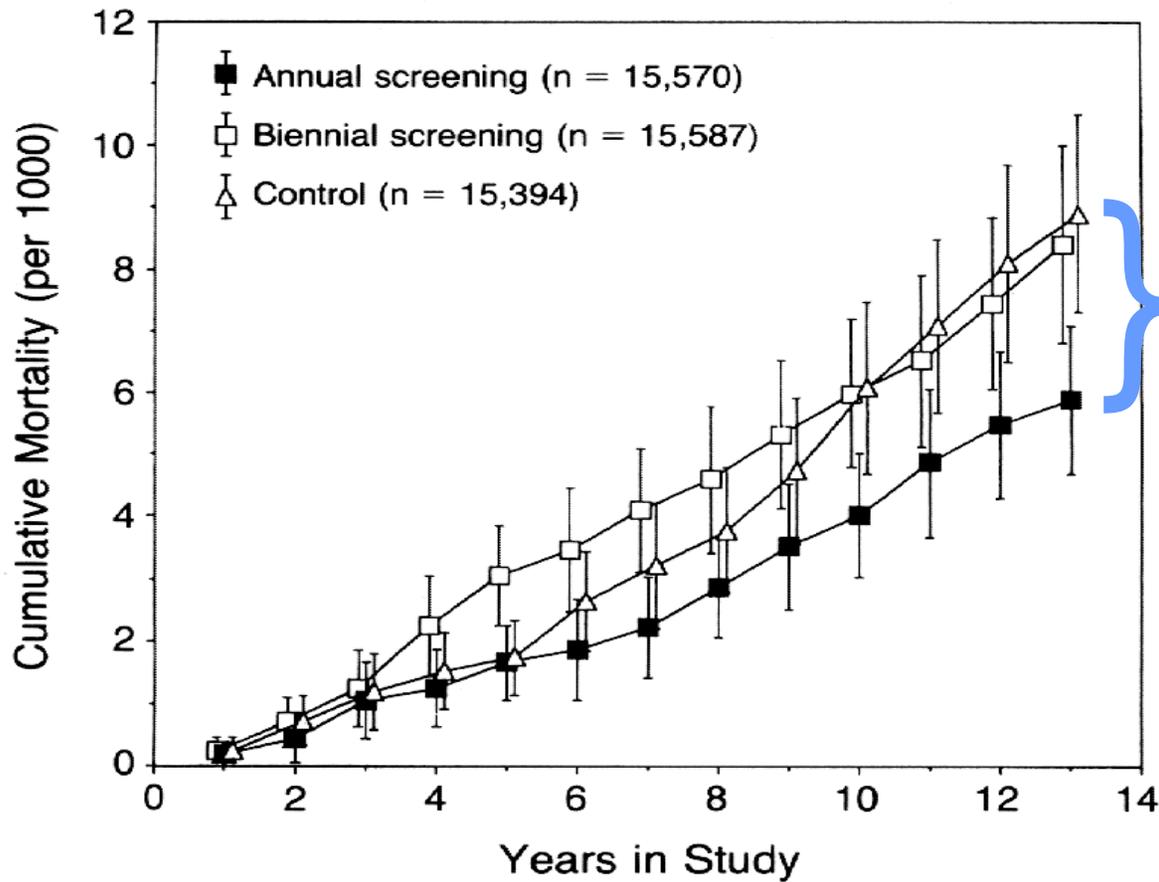


FOBT – Clinical Issues

- Test 3 consecutive stools
- Diet modification is necessary
- OK to test when patient is on low-dose ASA or warfarin in therapeutic range
- All positives lead to full colon evaluation (colonoscopy)
- Rehydration leads to higher sensitivity and lower specificity



Annual FOBT Saves Lives!



**33%
reduction**

Mandel JS et al. N Engl J Med 1993 328:1365-71.



Follow-up of Positive FOBT

- Colonoscopy recommended

HOWEVER:

- Only 52% of primary care physicians would recommend colonoscopy
- Only 29% of internal medicine residents would recommend colonoscopy

Winawer et al. Gastroenterol 1997;112:584

Sharma et al. Am J Gastroenterol 2000;95:1551

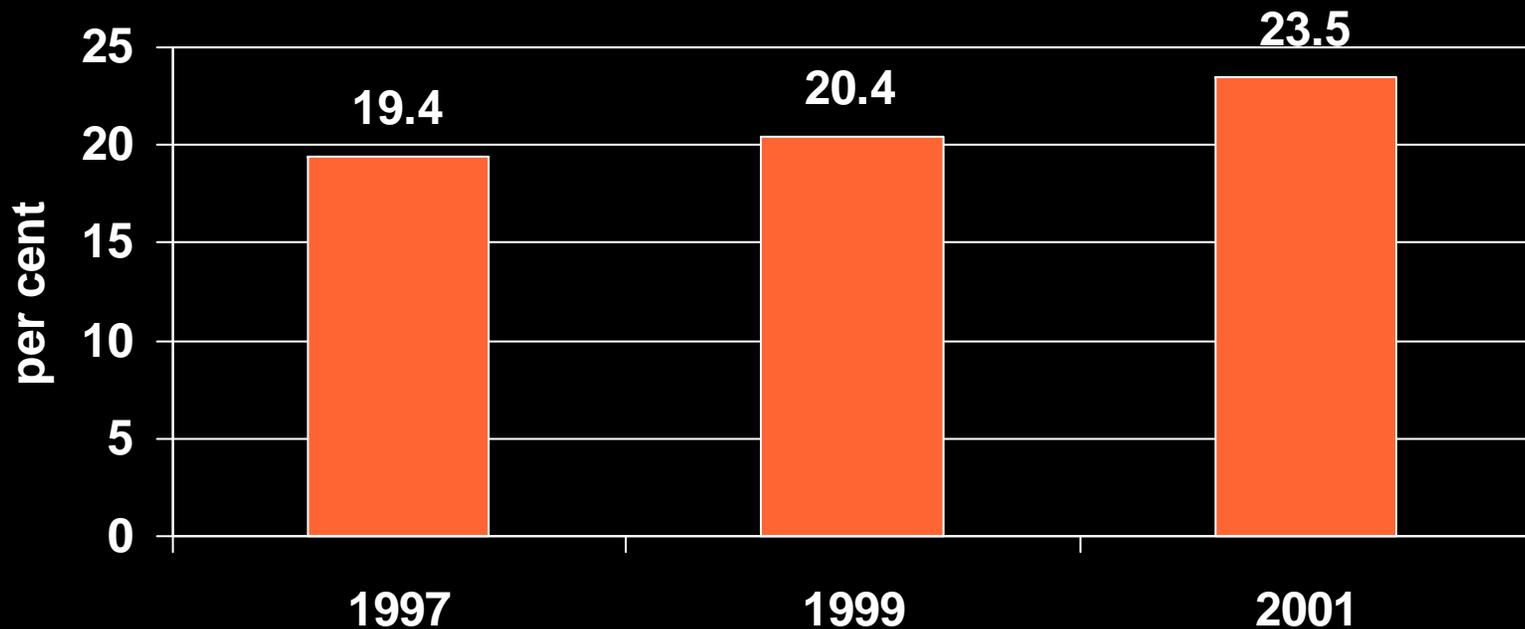
Sharma et al. Am J Gastroenterol 2000;95:1914



FOBT Utilization is Poor

CDC Behavioral Risk Factor Surveillance System

Percentage of eligible adults undergoing FOBT



MMWR Morb Mortal Wkly Rep 2003 Mar 14;52(10):193-6.



Flexible Sigmoidoscopy

PROS:

- May be done in the office
- Inexpensive, cost-effective
- Mortality from rectal cancer reduced by 60-70% in case-control studies
- Easier bowel preparation, usually done without sedation

CONS:

- Detects only one-half of adenomas
- 40% of cancers arise proximal to splenic flexure
- 75% of proximal cancers have no adenomas distal to splenic flexure
- Often limited by discomfort, poor bowel preparation

Selby et al. N Engl J Med 1992;326:653
Rex et al. Gastrointest Endosc 1999;99:727
Newcomb et al. J Natl Canc Inst 1992;84:1572

Stewart Aust NZ J Surg 1999;69:2
Painter et al. Endoscopy 1999;3:269



Flexible Sigmoidoscopy Misses 50% of Lesions

- Colonoscopy comparison studies:

46-52% of patient with advanced proximal neoplasia (> 1 cm, villous, high-grade dysplasia or cancer) had no adenomas distal to the splenic flexure

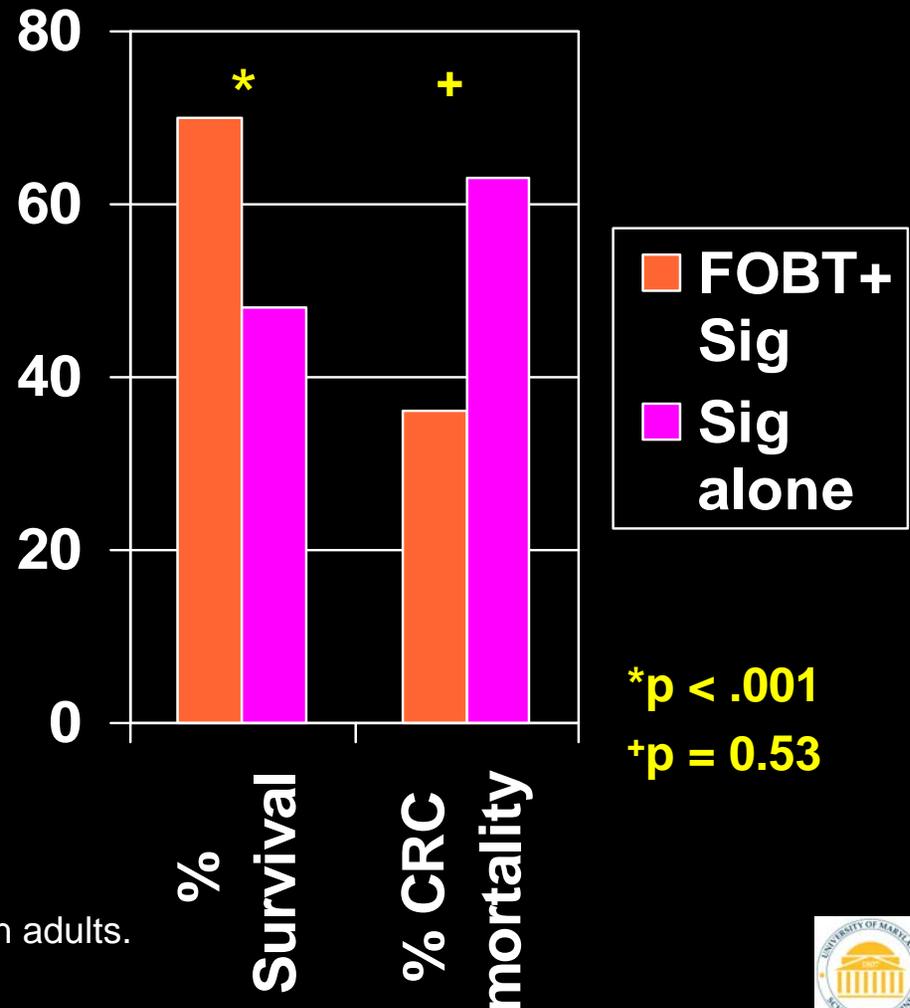
Lieberman et al. N Engl J Med 2000; 343:162-8.

Imperiale et al. N Engl J Med 2000; 343:169-174.



Combined FOBT and Sigmoidoscopy

- Case-control trial (N=21,750) w/rigid sigmoidoscopy – improved survival
- Other trials: FS + FOBT
 - Improved yield over FOBT alone
 - Adding FOBT to FS alone may not improve yield



Winawer et al. J Natl Cancer Inst 1993;85:1311
Pignone et al. Screening for colorectal cancer in adults.
<http://www.ahrq.gov/clinic/serfiles.htm>



FOBT + Flexible Sigmoidoscopy Misses 24% of Lesions

- Colonoscopy comparison studies:

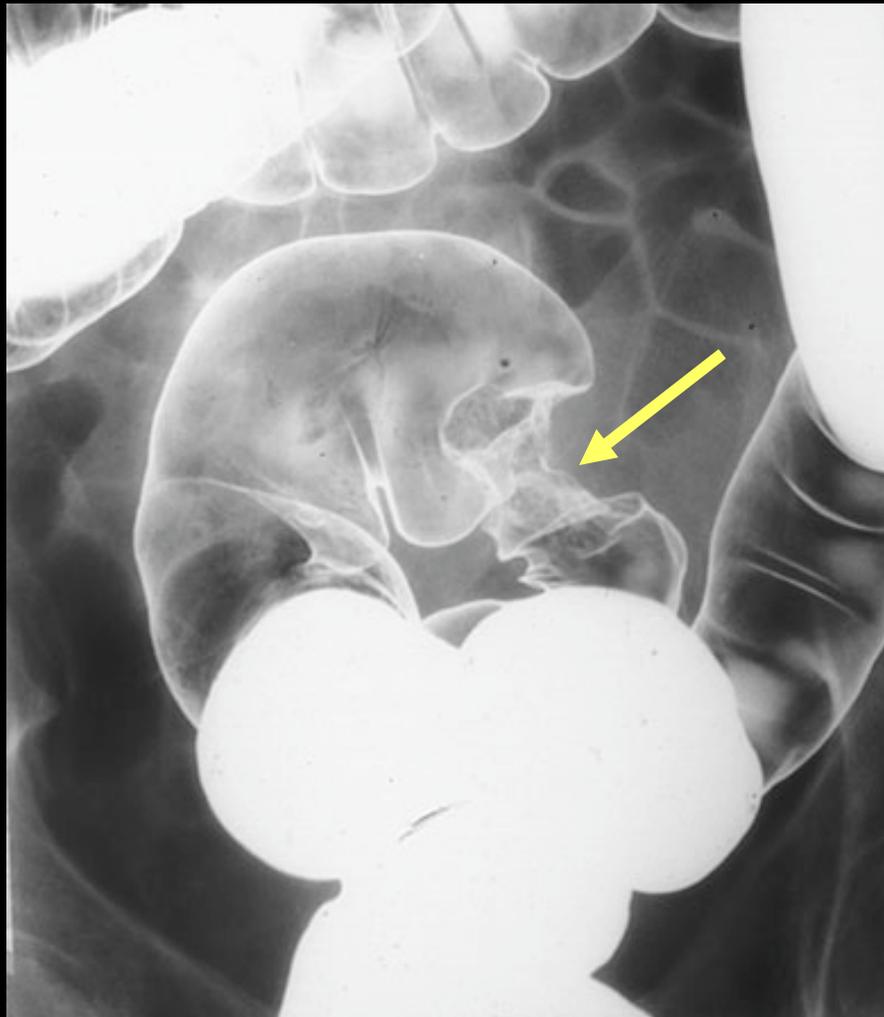
24.2% of patient with advanced proximal neoplasia (> 1 cm, villous, high-grade dysplasia or cancer) had negative FOBT and no adenomas distal to the splenic flexure.

Lieberman and Weiss. N Engl J Med 2001; 345:555-60.



Colorectal Cancer Screening: Double-Contrast Barium Enema

Colon Cancer



Double-contrast Barium Enema

PROS:

- Low cost, exams whole colon

CONS:

- Never studied as a screening test
- Missed 50% of adenomas < 1 cm in National Polyp Study
- Sensitivity for cancer in patients with positive FOBT: 50-75%
- Poor specificity; best interval unknown

Winawer et al. Gastroenterol 1997;112:599
Rex. Endoscopy 1995;27:200
Lieberman et al. N Engl J Med 2000;343:163



Colonoscopy

PROS:

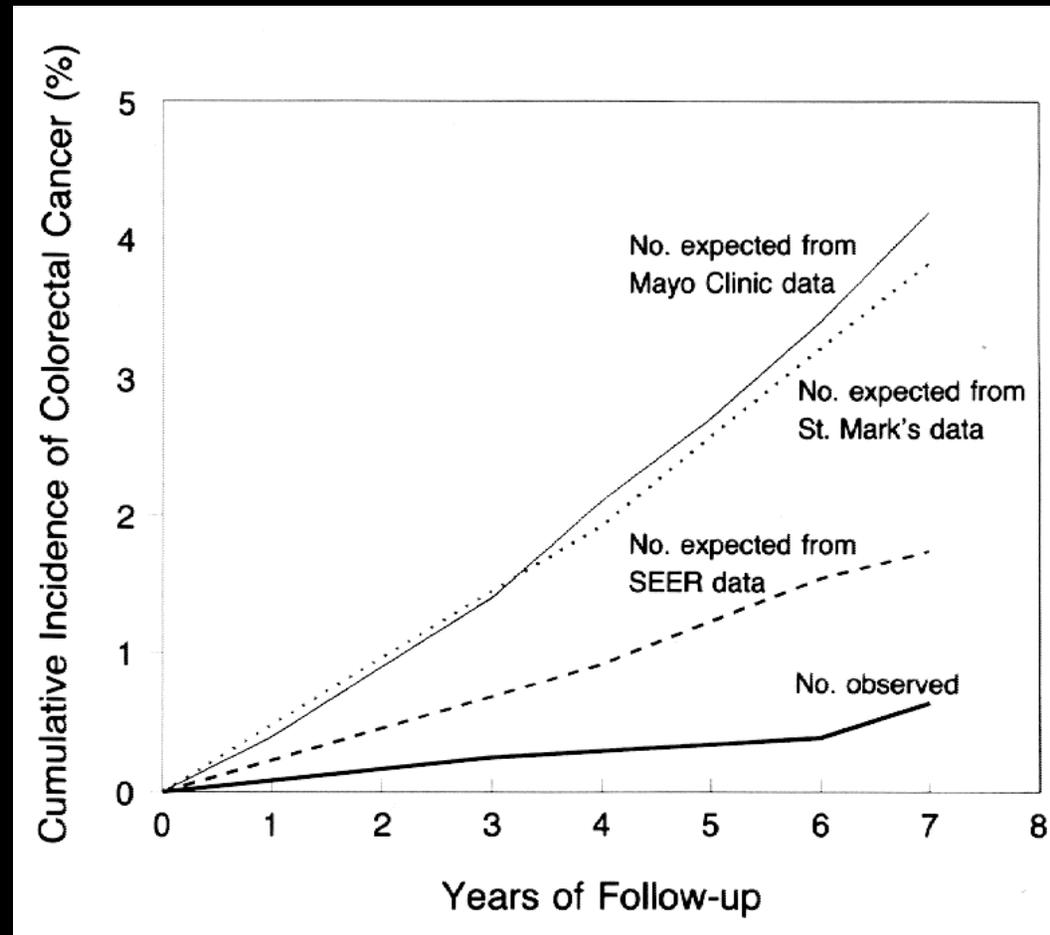
- Exams entire colon
- Therapeutic – polyps removed at time of procedure

CONS:

- Invasive, risk of complications
- Requires bowel prep, missed work, escort home
- Incomplete procedures ~5%
- Missed polyps
- Randomized trials lacking



Colonoscopic Polypectomy Reduces Colorectal Cancer Incidence



Winawer et al. N Engl J Med 1993; 329:1977-81.



Miss Rate for Colonoscopy

	Comparison group	
	Tandem Colonoscopy	CT Colography
Adenoma \leq 5 mm	27%	--
Adenoma 6 – 9 mm	13%	9%
Adenoma \geq 10 mm	6%	12%

Rex et al. Gastroenterol 1997; 112:24-28.

Pickhardt et al. N Engl J Med 2003;349:2191-2200.



Colonoscopy Complications

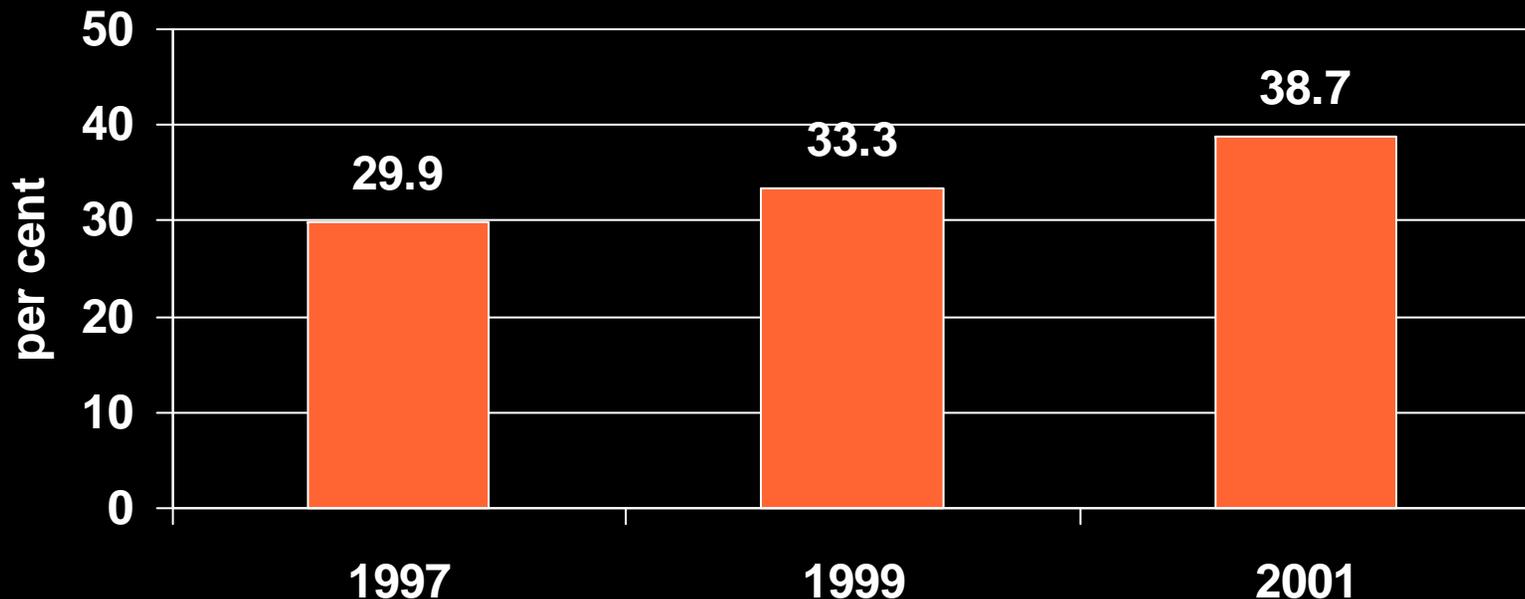
- Perforation 1-2/1000 procedures
- Bleeding 3/1000 procedures
- Mortality 1/10,000 procedures



Endoscopic Screening Rates are Low

CDC Behavioral Risk Factor Surveillance System

Percentage of eligible adults undergoing screening lower endoscopy within 5 years



MMWR Morb Mortal Wkly Rep 2003 Mar 14;52(10):193-6.



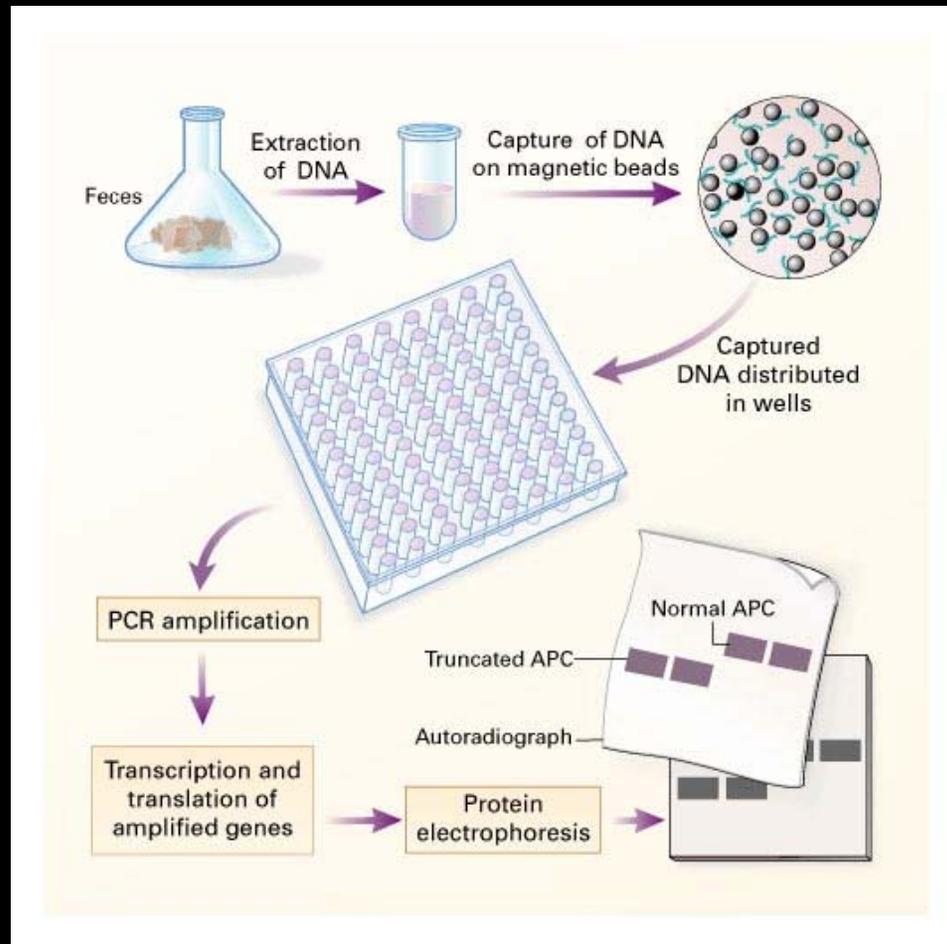
Cost-Effectiveness of Colorectal Cancer Screening

Screening method	Cost-effectiveness ratio (cost per life-years saved)
FOBT annually	\$ 5,691 - \$17,805
Flexible sigmoidoscopy every 5 years	\$12,477 - \$19,068
FOBT annually + flexible sigmoidoscopy every 5 yrs	\$13,792 - \$22,518
Double contrast barium enema every 5 years	\$11,168 - \$25,624
Colonoscopy every 10 yrs	\$ 9,038 - \$22,012

Pignone et al. Ann Int Med 2002;137:96-104.



Stool DNA Testing



Schwartz. N Engl J Med 2002;346:302-4

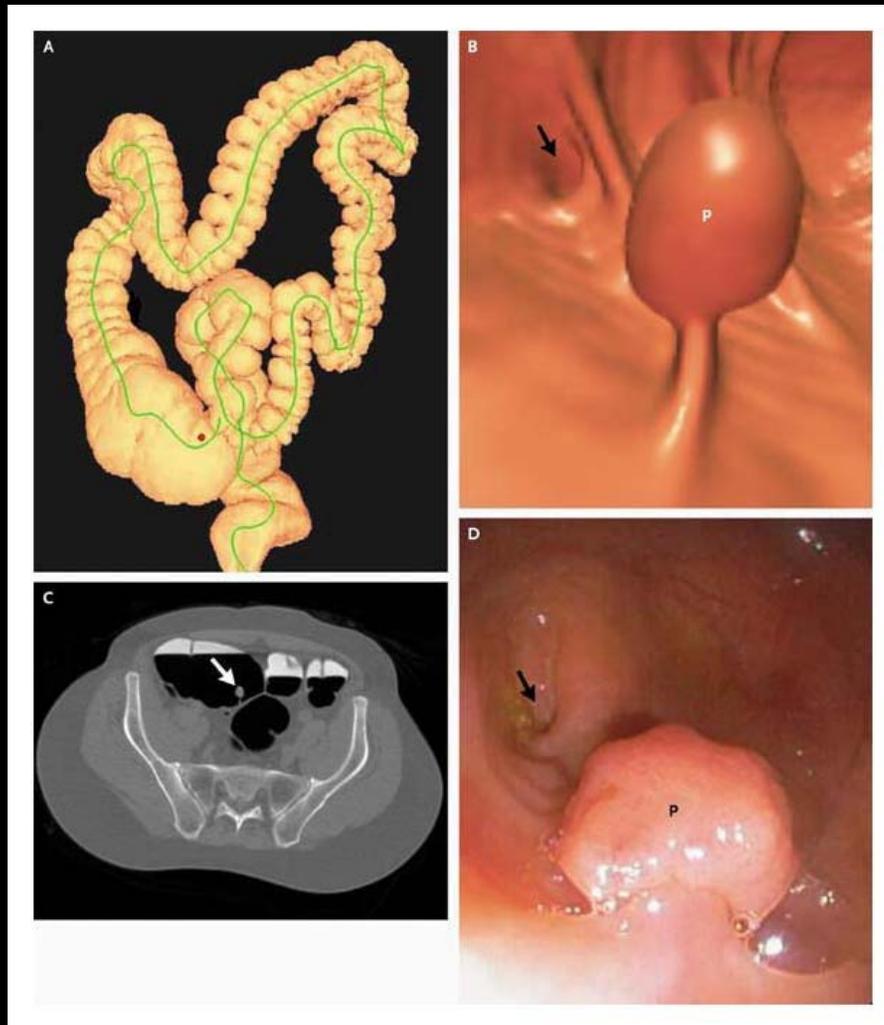


Stool DNA Testing

- Pros
 - No sedation or preparation necessary
 - Home-based (patient mails sample)
 - No risk
- Cons
 - Low sensitivity of current tests for detection of cancers (50-70%) or polyps (27-74%)
Ross. Practical Gastroenterol 2004:28-34.
 - Cost (? frequency of exam)
 - Not therapeutic
 - Not covered by insurance



CT Colography/Virtual Colonoscopy



**Solitary 16-mm
Pedunculated Cecal
Polyp in a 55-Year-Old
Man at Average Risk for
Colorectal Neoplasia**

Pickhardt et al. N Engl J Med
2003;349:2191-2200



Virtual Colonoscopy Technique

1. Cleanse bowels vigorously

- Liquid/low fiber diet x 24-36 hrs
- Sodium phosphate, PEG or equivalent
- Bisacodyl tablets + suppository
- Oral stool tagging optional



Virtual Colonoscopy Technique

2. Inflate colon

Old method =>
50 hand-bulb squeezes
of room air (78% N)

New method =>
Electronic CO₂
insufflator



**Adequately
distended
colon crucial**



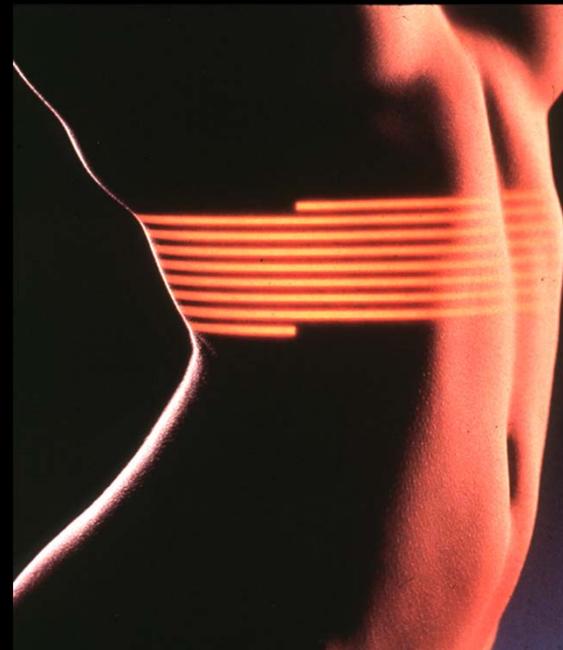
Virtual Colonoscopy Technique

3. Scan Abdomen

Multi-detector (4-16
slice) helical CT

Scan time: < 20 sec
1-mm slices

Scan patient prone
and supine



Virtual Colonoscopy Technique

4. Analyze data

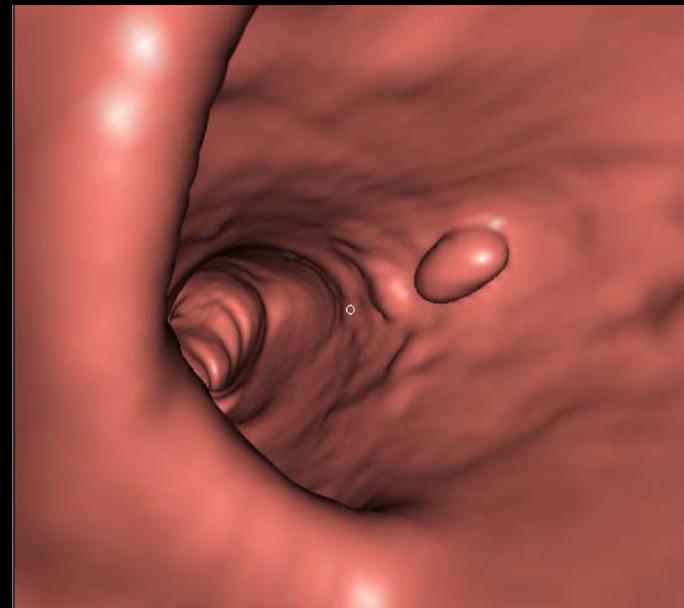
2-D image review, 3-D
for problem solving
or vice versa

Split colon, Fillet views

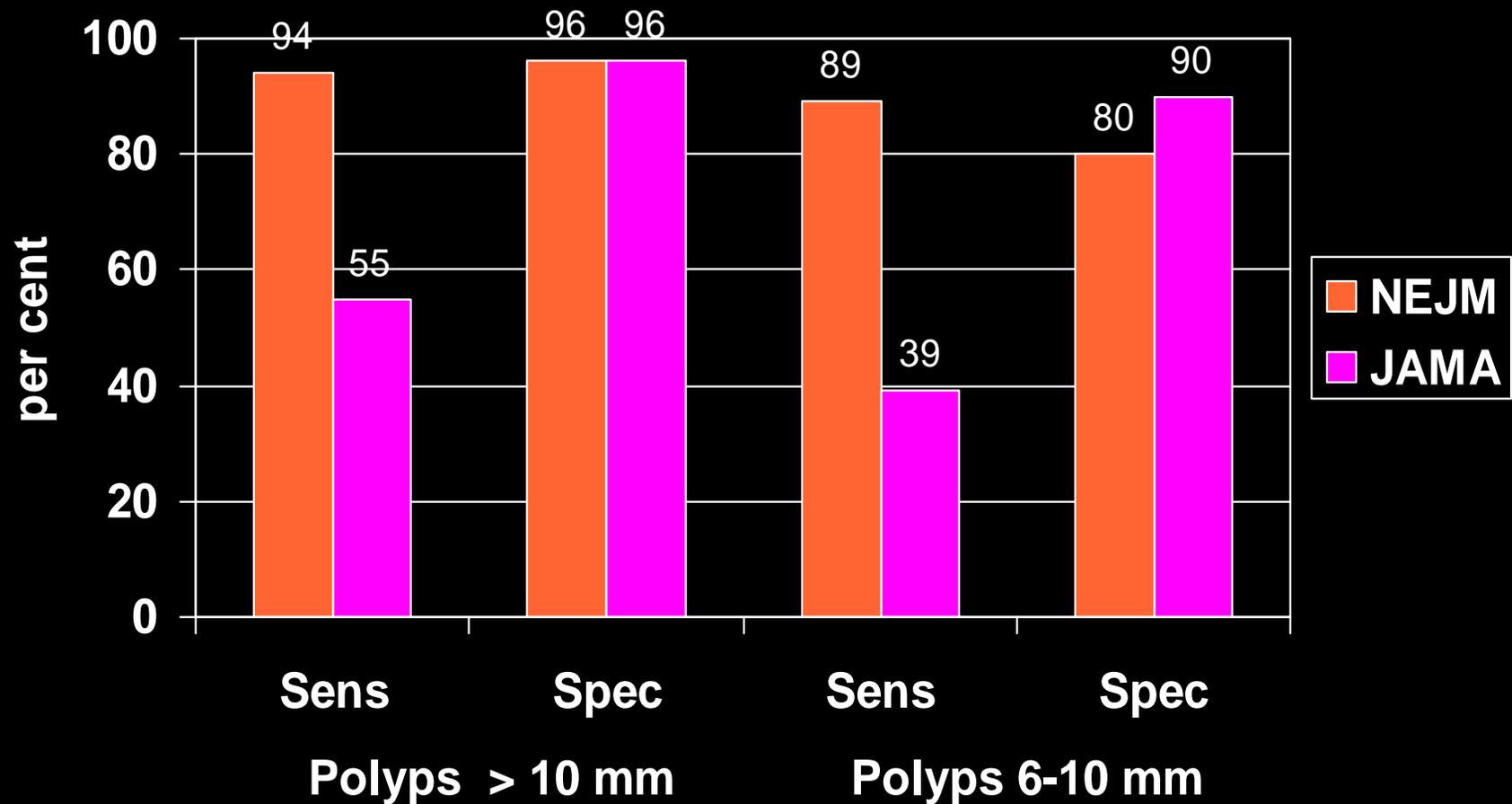
Computer-assisted
detection



Display on CT Workstation



Virtual Colonoscopy Results are Variable!



Pickhardt et al. N Engl J Med 2003;349:2191
Cotton et al. JAMA 2004, 291:1731



Problems with Virtual Colonoscopy

- Polyps < 8mm difficult
- Preparation still needed: stool and fluid can simulate/obscure polyps
- Lack of mucosal detail: flat polyps can be missed (same with colonoscopy)
- Steep learning curve for radiologist
- Specialized equipment needed
- Radiation dose



Strengths of Virtual Colonoscopy

- No sedation necessary
- Low risk
- Fast: 20 min vs. 25 min for colonoscopy (plus 60-min recovery)
- Detection of extracolonic lesions
- Option for failed colonoscopy or unsuitable patients



How to Improve Virtual Colonoscopy

- Well trained readers – Accreditation programs necessary
- Double read all cases during learning curve
- Careful attention to technique – well distended colon and good prep
- Use “State-of-the-Art” workstation and computer-aided diagnosis (CAD) to optimize lesion detection



“If, after the age of fifty, you wake up in the morning and nothing hurts, this is strong evidence that you have died during the night.”

- A. Paukner



Colorectal Cancer Screening

- **Fecal occult blood test (FOBT) every year, or**
- **Flexible sigmoidoscopy every 5 years, or**
- **A fecal occult blood test every year plus flexible sigmoidoscopy every 5 years (*recommended by the American Cancer Society*), or**
- **Double-contrast barium enema every 5 to 10 years, or**
- **Colonoscopy every 10 years (*recommended by the American College of Gastroenterology*).**

