The Prudent Prescriber

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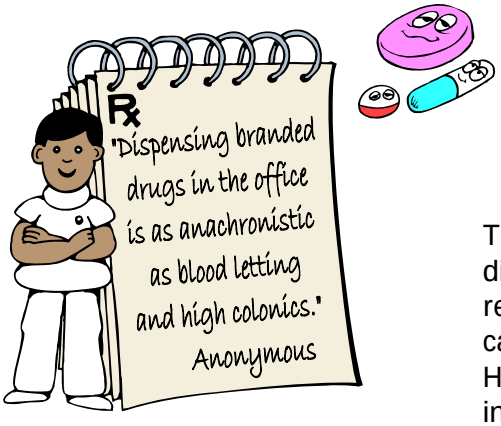


Screening for Colorectal Cancer: USPSTF and Beyond

This month, I'll invoke editorial privilege to discuss a non-pharmaceutical topic: the latest recommendations on screening for colorectal cancer. My thanks to Drs. Jake Dodge and Donald Hess of Williamsport, Pennsylvania for stimulating interest in this topic. Keep in mind that this entire review is focused only on asymptomatic adults at average risk for colorectal cancer.

What's new with the USPSTF recommendations?

"The USPSTF concludes with high certainty that screening for colorectal cancer in average risk, asymptomatic adults aged 50 to 75 years is a substantial net benefit (A recommendation)."

The USPSTF found no head to head studies demonstrating that *any of the screening strategies it considered are more effective than others*. Therein, they list the following acceptable tests in *no particular order of preference.*

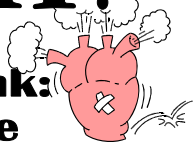
☑ Guaic-based fecal occult blood testing
☑ Fecal immunochemical testing (FIT)
☑ Multitargeted stool DNA testing (FIT-DNA)
☑ Colonoscopy
☑ Computed tomography colonography (CTC)
☑ FS plus FIT
☑ Flexible sigmoidoscopy (FS)

Pharm Reps ≠ Rational Prescribing
(PR) (RP)

Antibiotics do NOT

help acute bronchitis

CHF?

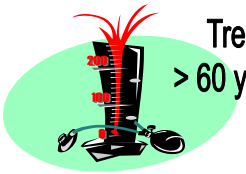


Think:
Ace
Aldactone
B-blocker
Dig
Diuretic

Avoid these expensive "me-too" drugs:

Intermezzo
Vimovo
Livalo
Pristiq
Viibyrd
Edarbi
Daliresp

ß-blockers in post-MI save lives



Treat patients > 60 years to 150/90

Pill splitters save BIG

The USPSTF guidelines:

- do not consider the costs of providing a service.

* point out that the modest differences in effectiveness among the seven possible tests are overshadowed by the population based benefit of additional screening tests performed when patients have the widest choice of testing methods.

What are the operating characteristics of the common screening tests?

(Flexible sigmoidoscopy and double contrast barium enema will not be discussed because of their current infrequent use.)

Guiac based testing:

⊙ Requires 3 consecutive samples and dietary restrictions. A single test finds less than 50% of cancers and less than 20% of adenomas. (Lieberman. JAMA Int Med Jan2014)

⊙ Five older, large RCTs (n= 419,966) with 11-30 years of follow-up, doing annual or biennial screening, compared to no screening resulted in a reduction in CRC disease specific mortality of relative risk (RR) of 0.91 at 19.5 years and RR of 0.78 at 30 years. (Linn. JAMA June 21, 2016)

⊙ Annual screening with Hemoccult II resulted in reduced CRC mortality, compared with placebo, of RR of 0.68 after 11 rounds of testing. (NEJM. 2013:369 (12):1106-1114.) The more sensitive Hemoccult SENSA is now recommended.

FIT:

⊙ Sensitivity: 60%-85% and specificity: >90% for CRC and <50% for advanced adenomas. *

⊙ Efficacy with a single stool sample; no special diet; repeat annually. *

⊙ The FDA approved OC-Light and OC FIT-CHEK tests have the most evidence to support their use. (Lin. JAMA. 2016; 315(23):2576-2594.)

⊙ Cheap ~$23 (Medicare pays) *

* Lieberman JAMA Int Med Jan 2014

FIT/DNA (Cologuard):

⊙ Cologuard includes an immunochemical assay (similar to the FIT), molecular assays for DNA (KRAS) mutations, and methylation biomarkers associated with colorectal neoplasia.

⊙ One study (n=9989)(NEJM. 2014; 370(14): 1287-1297) compared Cologuard with OC FIT-CHEK. Cologuard had better sensitivity for finding both CRC (92%) and advanced adenomas (42%) than the OC FIT-CHEK, but poorer specificity, 84% for CRC and 86%-87% for advanced adenomas.

⊙ Mail in stool sample; no prep; $493; repeat every 3 years if negative.

⊙ Evidence is lacking on the appropriate follow-up of abnormal results from FIT–DNA screening when the initial diagnostic colonoscopy is negative. There is a concern that FIT-DNA may generate inappropriate use of surveillance colonoscopy because of the genetic component of this test.

CT Colonography:

⊙ Only one radiologist in Grand Junction is doing CT colonography. He describes it as a useful test, but has performed it primarily in patients who have failed colonoscopy or have had a previous colonoscopy perforation.

⊙ Studies of CT colonography test performance found that the sensitivity to detect adenomas >10 mm or larger ranged from 67% to 94% and specificity ranged from 86% to 98%. (Agency for Healthcare Research and Quality; 2016. (AHRQ publication 14–05203–EF–1)

⊙ The USPSTF recommends CT colonography every five years.

⊙ CTC involves no conscious sedation and uses the same prep used for colonoscopy. In addition, the issues of extra-colonic findings (incidence of 40%-70% and 5%-37% require diagnostic follow-up) Serial testing every five years would deliver significant radiation.·

⊙ Pricey, but no one will/can tell me the cost.

Colonoscopy:

Colonoscopy is the final common pathway for all other positive CRC screening tests. It is considered by many to be the gold standard of CRC screening. **However, there is no randomized clinical trial or other high quality evidence showing that colonoscopy reduces CRC mortality.** (Lieberman JAMA Int Med Jan 2014)

⊙ An observational study (Zauber. NEJM. 366;(8) February 23, 2012) involving 2,602 patients who had adenomas removed during colonoscopy, suggested a 53% reduction in CRC mortality.

⊙ Sensitivity to detect adenomas 6mm or greater ranged from 75% to 93%.

⊙ The serious complications of colonoscopy include: perforation 4/10,000; major bleeding 8/10,000.

⊙ Other disadvantages of colonoscopy include unpleasant preparation, discomfort of the procedure, lost work time; patients must ask a friend or family member for a ride and high cost.

⊙ In the US, moderate sedation is often being replaced by deep sedation using propofol. Use of anesthesia services is associated with a 46% increased complication risk, although the absolute rate of serious complications remains low. (Cooper JAMA Intern Med 2013; 173 (7): 551–556.)

Digital Rectal Exam:

⊙ **One in four CRCs is in the rectum, and many are within an examiner's reach on** digital rectal examination. However there is little evidence to support the effectiveness of digital rectal examination (DRE) for the detection of rectal cancer, and DRE is not recommended in colorectal screening guidelines.

What are others saying?

⊙ In contrast to the USPSTF, the American Cancer Society, the US Multi-Society Task Force for Colorectal Cancer, the American College of Radiology and the American Gastroenterological Association declare a preference for a test that can result in the detection of early cancer and adenomatous polyps, ie…sigmoidoscopy or colonoscopy.

⊙ The American College of Gastroenterology recommends colonoscopy as the single preferred screening strategy.

⊙ In 2015, the American College of Physicians recommended four strategies:
1) annual high sensitivity FOBT or FIT,
2) flexible sigmoidoscopy every five years,
3) high sensitivity FOBT or FIT every three years plus flexible sigmoidoscopy every five years, or
4) colonoscopy every 10 years.

⊙ In 2016 the Canadian Task Force on Preventive Healthcare recommended that adults age 50 to 74 years be screened for colorectal cancer with FOBT or FIT every two years or flexible sigmoidoscopy every 10 years. **It recommended against using colonoscopy as a primary screening test.**

⊙ **The Council of the European Union recommends only FOBT for screening.** (Lansdorp-Voglelaar Endoscopy 2012; 44 supplement 3: SE 15.)

What about CRC screening in older patients?

⊙ "The decision to screen for colorectal cancer in adults aged 76 to 85 years should be an individual one, taking into account the patient's overall health and prior screening history (USPSTF C recommendation)." Screening patients ages 76 to 85 years will be more efficient in those patients who have never had screening colonoscopy compared to those who have previously had the procedure.

⊙ The USPSTF does not recommend routine screening for colorectal cancer in adults 86 years and older. In this age group competing causes of mortality preclude a mortality benefit that would outweigh the harms.

⊙ Colonoscopy carries increased risk in older adults, with significant complications incurring in 0.3% of 600 veterans ages 70 to 75 years undergoing colonoscopy screening. (Lieberman New England Journal of Medicine 2000; 343:162.)

Adherence to Screening:

⊙ In 2012 in the United States, 65.1% of the adults between ages 50 and 75 years were up to date with CRC screening and 27.7% had never been screened.
(MMWR 2013; 62:881.)

⊙ In the NordicICC study, where participation was totally free and set up in convenient settings, adherence for colonoscopy was a disappointing 40% overall.

⊙ The effectiveness of fecal tests depends on the extent to which the results are followed up. Some studies have shown that 25% to 35% of patients with positive test results do not undergo a colonoscopy.
(Lieberman JAMA Internal Medicine January 2014)

⊙ Compliance with annual stool testing is low: Almost 1/2 of the uninsured population who had an initial screening stool guaic failed to have a second screening procedure for colon cancer over a two-year period.
(Annals of Family Medicine 2010; 8:397.)

⊙ Although all relevant authorities recommend an interval of ten years between normal screening colonoscopies, in a study of 24,071 Medicare patients who had a negative screening colonoscopy, 23.5% underwent a repeat colonoscopy in seven years or less with no clear indication for the early repeated examination. (Goodwin. Arch Intern Med. 171(105), August 8/22, 2011)

What is coming?

⊙ There are three large, long term randomized controlled trials looking at colonoscopy as screening and preventive tools in normal risk individuals.

NordicICC, finishing in June 2026
COLONPREV, finishing in November 2021
CONFIRM, finishing in September 2027

My Take :

⊙ To date, no method of screening for colorectal cancer has been shown to reduce all cause mortality in any age group. **There is no evidence to suggest that people live longer by participating in a CRC screening program.** Should we advise all patients undergoing colorectal cancer screening of this fact?

⊙ The concept of colonoscopic removal of precancerous polyps seems logical, but we have been misled by observational data in the past. It may be the people who undergo CRC screening with adenoma removal are healthier in other ways. Recall the "healthy user" bias led to the mistaken belief that estrogen prevented heart disease. It is also possible that many colonic adenomas may be similar to ductal carcinoma in situ for breast cancer, many of which never progress to cancer.
(Esserman. JAMA 2013; 310 (8): 797–798.)

⊙ Different screening methods may be more or less attractive for patients based on their features. **As clinicians, we should engage our patients in shared decision-making about the screening strategy that will most likely result in getting the job done over time.**

⊙ Increasing screening rates depends on 1) clinicians recommending a menu of tests, 2) patient and clinician reminders, 3) decision aids, and 4) monitoring to avoid both underutilization and overutilization of screening. (Pignone. American J Med 2009; 122:419)

⊙ **Who does the best job of colonoscopy in your community?** In the NordicICC trial, performance differed significantly between the 35 endoscopists. Recommended benchmarks for cecal intubation (95%) and adenoma detection (25%) were not met by 17.1% and 28.6% of the endoscopists, respectively.

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