Screening for Colorectal Cancer in Adults at Average Risk: A Summary of the Evidence

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Epidemiology

The U.S. Preventive Services Task Force (USPSTF) last considered its recommendations regarding colorectal cancer screening in 1996.[1] At that time, the available evidence included 1 randomized controlled trial showing that fecal occult blood testing (FOBT) reduced mortality rates,[2] a case-control study showing that persons having sigmoidoscopy were less likely to die from colorectal cancer,[3] and 1 nonrandomized controlled trial of FOBT combined with rigid sigmoidoscopy that suggested some benefit from the 2 tests together.[4] Based on this evidence, the USPSTF gave a "B" recommendation to screening for colorectal cancer with FOBT, sigmoidoscopy, or both. The USPSTF did not recommend for or against other means of screening (digital rectal examination [DRE], double contrast barium enema [DCBE], or colonoscopy) on the grounds that evidence was insufficient. The Task Force also recommended that FOBT be performed yearly but did not specify an interval for sigmoidoscopy.

Since 1996, important new evidence has emerged regarding the effectiveness of colorectal cancer screening. The USPSTF requested that the RTI-University of North Carolina-Chapel Hill Evidence-based Practice Center prepare an updated systematic evidence review to help the USPSTF evaluate new evidence on the effectiveness of different colorectal cancer screening tests as it updated its previous recommendation. In this review, we examine the evidence concerning the effectiveness of screening in adults older than 50 who are at average risk for colorectal cancer. We consider evidence about the effectiveness, accuracy, and adverse effects of DRE (with or without a single office-based FOBT), traditional 3-card FOBT (hereafter referred to as "FOBT"), sigmoidoscopy, FOBT with sigmoidoscopy, DCBE, and colonoscopy. Other tests or combinations of tests have not been well evaluated and are not discussed here. A more detailed report of our review can be found in Pignone et al,[5] available on the AHRQ Web site (www.preventiveservices.ahrq.gov). The USPSTF's

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The USPSTF recommendations based on this review can be found in Screening for Colorectal Cancer: Recommendations and Rationale (which precedes this chapter), available on the AHRQ Web site and through the AHRQ Publications Clearinghouse.

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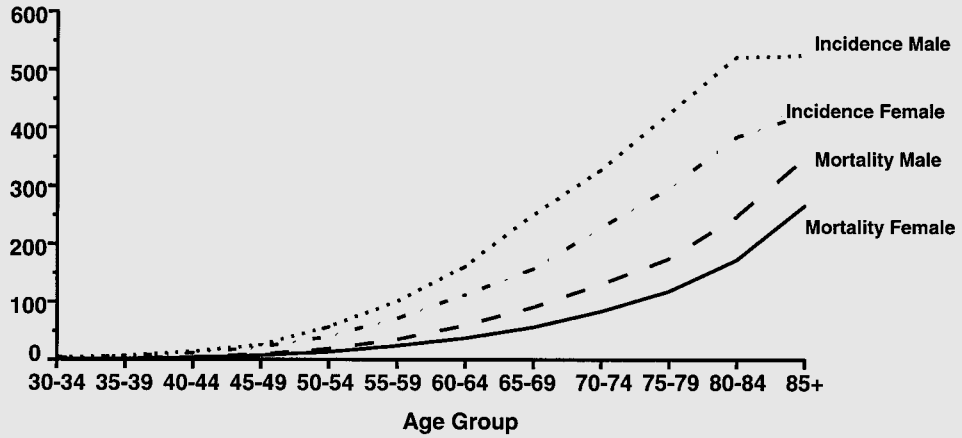
Figure 1. Cancers of the colon and rectum: average annual age-specific SEER incidence per 100,000 persons and U.S. mortality rates by gender, 1992-1996



colorectal cancer screening recommendations, which are based on this review, are also published in *Annals of Internal Medicine.*[6]

Methods

We used the second edition of the Guide to Clinical Preventive Services,[2] existing systematic reviews, focused MEDLINE literature searches from 1966 through September 2000, and hand-searches of key articles to identify the relevant literature. When available, systematic reviews were used to identify older relevant studies. Literature searches were used to identify newer studies. Detailed descriptions of the literature searches can be found in the Appendix.

To identify relevant studies, 1 reviewer examined the abstracts of the articles identified in the initial search. A second reviewer examined the excluded articles. Disagreements about inclusion were resolved by consensus. Two reviewers examined the full text of the remaining articles to determine final eligibility.

We used evidence from randomized controlled trials or observational studies that have measured patient outcomes, particularly changes in colorectal cancer mortality rates and incidence. When such data were not available, we included indirect information on screening test accuracy. Details about study inclusion are available in the Appendix.

Included articles were quality rated using the criteria developed by the USPSTF Methods Group.[7] These criteria are described in the Recommendation and Rationale Statement authored by the USPSTF.[6]

We used the final set of eligible articles to create evidence tables and a draft report. The draft report was extensively peer reviewed by the USPSTF, experts in the field, governmental agencies, and nongovernmental organizations.

Role of the Funding Agency

This evidence report was funded through a contract to the RTI-University of North Carolina Evidence-based Practice Center from the Agency for Healthcare Research and Quality (AHRQ). Staff of the funding agency contributed to the study design, reviewed draft and final manuscripts, and made editing suggestions.

Results

Our general search identified 719 articles published since 1995 on colorectal cancer screening, of which we retained 19 in our final document. Specific searches from 1966 through 2001 for

articles about the accuracy of barium enema and complications of screening yielded 621 and 839 articles, respectively. After review, we retained 13 articles about barium enema, and 19 about complications of screening. We also included 15 articles identified from the previous USPSTF review or from hand searches of other articles. Table 1 summarizes our findings.

Digital Rectal Examination

Effectiveness

A case-control study from the Kaiser Permanente Medical Care Program in northern California examined the effect of screening DRE on mortality from colorectal cancer.[8] The investigators identified patients aged 45 and older who died of distal rectal cancers between 1971 and 1986 and selected matched controls from their patient membership. They examined medical records to determine whether the patients who died and controls had undergone screening DREs within a year of cancer diagnosis. Investigators found no difference between groups after controlling for potential confounders, although the confidence interval was wide (odds ratio [OR], 0.96; 95% confidence interval [CI], 0.56 to 1.7).

Accuracy

The potential sensitivity of screening DRE is low: fewer than 10% of colorectal cancers arise within reach of the examining finger.[9] The specificity of a positive DRE has not been examined in outpatients at average risk for colorectal cancer.

In-Office Fecal Occult Blood Testing After Digital Rectal Exam

Effectiveness

No studies have examined the effect of a single in-office FOBT after DRE on colorectal cancer incidence or mortality rates.

Accuracy

A single in-office FOBT is likely to be less sensitive than the traditional 3-card home-performed FOBT because only 1 sample is taken.[10] In a large study from Japan, Yamamoto and Nakama found that the first test card detected only 58% of the cancers found with a 3-card test.[11]

A single in-office FOBT may be less specific than a properly performed 3-card FOBT because the in-office test does not allow degradation of vegetable peroxidases that sometimes produce false-positive results.[10] In addition, the potential trauma from the in-office examination itself may also result in lower specificity.[10] Two studies of poor to fair quality that used existing data to compare retrospectively the specificity of the single in-office FOBT and the 3-card home FOBT[12,13] found little difference in specificity between the 2 groups. However, the validity of these studies is limited because neither could ensure that similar patient samples received each test.

Fecal Occult Blood Testing

Effectiveness

In addition to an older randomized trial performed in Minnesota[2] that was available to the USPSTF in 1996, 2 newer randomized controlled trials (RCTs) from the United Kingdom[14] and Denmark[15] have examined the effectiveness of biennial FOBT for reducing colorectal cancer mortality. The more recent trials found reductions in mortality rates of 15% and 18%, respectively, using biennial testing. Neither trial used slides that were rehydrated prior to development (Table 2).

The Minnesota trial compared annual and biennial testing with no screening and rehydrated most test cards (83%). Cumulative mortality rates from colorectal cancer after 18 years of follow-up were 33% lower (95% CI, 17% to 49%) among people randomized to undergo annual FOBT than in a control group that was not offered screening (absolute rates: 9.5 deaths per 1,000 participants versus 14.1 deaths per 1,000 participants; difference, 4.6 deaths per 1,000 participants).[2] Biennial screening, which did not show a reduction in mortality at 13-year follow-up, produced a 21% reduction in mortality rates at 18 years (95% CI, 3% to 38%).[16] The 18-year follow-up also showed that the incidence of colorectal cancer decreased by 20% (95% CI, 10% to 30%) and 17% (95% CI,

Table 1. Characteristics of screening tests for colorectal cancer*

Screening strategy for CRC	Effectiveness in reducing incidence and mortality from CRC†	Ability to detect cancers	Likelihood of generating false-positive results	Adverse effects
Digital rectal examination	Case-control study found no difference in mortality OR: 0.96 (0.56, 1.7).[8] [Level II - poor]	Pathology data suggest <10% of CRCs are within reach of examination finger.	Unknown	No direct adverse effects known.
Office FOBT (1 card)	Unknown	Only 58% of cancers are detected on the first of 3 cards, suggesting lower sensitivity than 3-card testing.[11] [Level III - fair]	Little difference compared with 3-card testing.[12,13] [Level 3 - poor]	No direct adverse effects known.
Home FOBT (3 cards), unrehydrated	Biennial testing: 2 trials found mortality reductions of: 15% (1%, 26%)[14] and 18% (1%, 32%).[15]	One-time sensitivity 30%-40%. Unrehydrated FOBT finds about 25% of cancers.[10]	Single test specificity: 96%-98%. 5%-10% of patients will require colonoscopy over 10 years of biennial testing.[10] [Level III - good]	No direct adverse effects known.
Home FOBT (3 cards), rehydrated	Annual: 33% mortality reduction (13%, 50%)[2]; cancer incidence reduction 20% (10%, 30%).[17] Biennial: 21% mortality reduction (3%, 38%)[16]; cancer incidence reduction 17% (6%, 27%).[24] [Level I - good]	Single test accuracy for cancer = 50% (95% CI 30%, 70%); for advanced neoplasms, 24% (19%, 29%).[19] Over 13 years, rehydrated FOBT finds 50% of cancers.[2] [Level III - good]	Single test specificity: 90% Over 10 to 13 years, 38% of patients tested annually and 28% tested biennially with rehydrated FOBT required colonoscopy.[2] [Level III- good]	Inconvenience, adverse effects resulting from follow-up tests required after positive results.
Sigmoidoscopy	Small RCT found decreased CRC mortality with screening: RR 0.50 (0.10, 2.72).[20]	One-time screening detects 68%-78% of advanced neoplasia.[19,24]	N/A	< 1 in 10,000 perforation rate for diagnostic exams;

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6% to 27%) in the groups screened annually and biennially, respectively, compared with controls.[17] Differences in hydration, test frequency, duration, and effect size preclude combining the results of these trials in a meta-analysis.

Accuracy

A systematic review from 1997 found that the sensitivity of a single unrehydrated FOBT for cancer was approximately 40%; its specificity appears to range from 96% to 98%. Rehydration was found to increase sensitivity to between 50% and 60% but lowered specificity to 90%.[10,18] In a recent study, Lieberman et al found that the sensitivity of rehydrated FOBT for cancer was 50% (95% CI, 30% to 70%).[19] For advanced neoplasia (cancers and polyps that are large, villous or dysplastic), sensitivity was 24% (95% CI, 19% to 29%); specificity was 94% (95% CI, 93% to 95%).

In the annual screening arm of the 13-year Minnesota trial, which used primarily rehydrated test cards and had a high initial rate of participation (about 90%), 49% of patients who developed colorectal cancer were identified through screening; and 38% of all patients had had at least 1 colonoscopy.[2] Biennial screening detected 39% of patients with cancer in the intervention group, and 28% of patients required colonoscopy. In contrast to the Minnesota trial, the 2 UK and Danish trials were population-based, 8 to 10 years in duration, used only biennial testing, and had lower rates of participation (60% to 70% of patients completed

Table 1. Characteristics of screening tests for colorectal cancer* *(continued)*

Screening strategy for CRC	Effectiveness in reducing incidence and mortality from CRC†	Ability to detect cancers	Likelihood of generating false-positive results	Adverse effects
Sigmoidoscopy *(continued)*	Case- control studies suggest 59% mortality reduction within reach of scope (31%, 75%).[3] [Level I - fair] [Level II- good]	[Level III - good]		bleeding occurs in 2.5% after diagnostic studies, 5.5% after procedures with poly-pectomy.[21] [Level III- good]
Combined FOBT and sigmoidoscopy	Nonrandomized trial found 43% mortality reduction by adding FOBT to rigid sigmoidoscopy: RR 0.57 (0.56, 1.19).[4] [Level I - fair-poor]	One-time screening detects 76% of advanced neoplasia.[19] Increased yield when sigmoidoscopy added to FOBT.[27-29] [Level III- good]	N/A	Sum of adverse effects from each test alone.
Double contrast barium enema	Unknown	One-time sensitivity for cancer or large polyps: 48% (24%-67%).[30] [Level III- fair]	One-time specificity 85% (82%, 88%).[30] [Level III- fair]	Perforations: 1 in 25,000 in study with screening and symptomatic patients.[42] [Level III- poor]
Colonoscopy	Case-control study: CRC mortality: OR: 0.43 (0.30, 0.63) CRC incidence decreased by 40-60%.[44] [Level II- fair]	Sensitivity for large adenomas: >90%; sensitivity for cancers probably higher.[45] [Level III- good]	N/A	Diagnostic procedures: perforations: 1 / 2,000 Polypectomy: perforations: 1 / 500-1,000 bleeding: 1 / 100-500 death: 1 / 20,0005 [Level III- fair-good]

*Numbers in parentheses following odds ratios (OR) and relative risks (RR) represent 95% confidence intervals (CI).

†Evidence grades for each item are in brackets. Level I: evidence from one or more controlled trials; level II: evidence from cohort or case-control studies; level III: evidence from diagnostic accuracy studies or case series. For each level, the investigators have assigned a quality score based on methods described in Harris et al 2001.7 N/A = not applicable (see text)

Note: CRC indicates colorectal cancer; FOBT, fecal occult blood test; RCT, randomized controlled trial; OR, odds ratio; RR, relative risk.

the first screening). Screening detected 27% of patients in the intervention group who developed colorectal cancer; only 5% of patients underwent colonoscopy.[14,15]

Adverse Effects

FOBT itself has few adverse effects, but false-positive FOBTs lead to further tests, such as colonoscopy, during which adverse effects may occur. The specific adverse effects of colonoscopy are described below. Theoretically, a previously negative FOBT could falsely reassure patients and lead to delayed response to the development of colorectal symptoms if a cancer were to develop, but this concern has not been evaluated empirically.

Sigmoidoscopy

Effectiveness

Thiis-Evensen et al performed a small randomized trial of sigmoidoscopy screening in Norway.[20] In 1983, 799 men and women aged 50-59 drawn from a population registry were randomly assigned to receive screening flexible sigmoidoscopy

Table 2. Trials of fecal occult testing

Trial Characteristics	Minnesota[2]		UK[14]	Denmark[15]
Frequency of testing	Annual	Biennial	Biennial	Biennial
Participants	More than 45,000 men and women ages 50-80		More than 150,000 men and women ages 45-74	More than 60,000 men and women ages 45-74
Duration of follow-up, years	18	18	8	10
Hydration of slides	Yes (83%)		No	No
Participation rate	90%	90%	60%	67%
Requiring colonoscopy	38%	28%	5%	5%
Positive predictive value	1.9%†	2.7%†	10-12%	8 - 18%
CRC mortality RRR (95% CI)	33% (17%, 49%)	21% (3%, 38%)	15% (1%, 26%)	18% (1%, 32%)
CRC mortality ARR	4.6	2.9	0.8	1.4

* Participation defined as completing at least one test.

† Mostly rehydrated slides (83%).

Note: ARR indicates absolute risk reduction per 1,000 participants; RRR, relative risk reduction.

(400 patients) or no screening (399 patients). Eighty-one percent of those offered flexible sigmoidoscopy accepted. All patients found to have polyps on sigmoidoscopy underwent immediate diagnostic colonoscopy and had surveillance examinations 2 and 6 years later. Over the 13 years of the trial, 2 colorectal cancers were diagnosed in the intervention group and 10 in the control group (RR for colorectal cancer, 0.2; 95% CI, 0.03 to 0.95). One person who was assigned to the intervention group but never had the sigmoidoscopy screening examination, died from colorectal cancer; 3 colorectal cancer deaths occurred in the control group (RR, 0.50; 95% CI, 0.10 to 2.72). The overall mortality rate was higher in the intervention group than in the control group (14% versus 9%; RR, 1.57; 95% CI, 1.03 to 2.40), mostly because of an excess of cardiovascular deaths. No clear relationship emerged between the excess deaths and any complications from the procedures.

Two ongoing randomized trials using flexible sigmoidoscopy can be expected to report their initial results within 5 years. One trial is examining the effect of once-in-a-lifetime sigmoidoscopy in the United Kingdom[21]; a second trial in the United States is examining sigmoidoscopy every 5 years with the assumption that patients are receiving FOBT as part of usual care.[22]

Two older, well-designed case-control studies that provide other important information on the effectiveness of sigmoidoscopy screening were available to the USPSTF in 1996. Using data from the Kaiser Permanente Medical Care Program in northern California,[3] Selby et al found that 9% of people who died of colorectal cancer occurring within 20 cm of the anus had previously undergone a rigid sigmoidoscopic examination, whereas 24% of persons who did not die of a cancer within 20 cm of the anus had received the test.[3] The adjusted odds ratio of 0.41 (95% CI, 0.25 to 0.69) suggested that sigmoidoscopy screening reduced the risk of death by 59% for cancers within reach of the rigid sigmoidoscope.

The investigators noted that the adjusted odds ratio for proximal colon cancer that was beyond the reach of the sigmoidoscope was 0.96.[3] This finding added support to the hypothesis that the reduced risk of death from cancers within reach of the rigid sigmoidoscope could be attributed to screening

rather than to confounding factors. The risk reduction associated with sigmoidoscopy screening did not diminish during the first 9 to 10 years after the test was performed. Although the Selby et al study mostly used rigid sigmoidoscopes, in another case-control study supporting the effectiveness of sigmoidoscopy, 75% of the examinations were performed with a flexible instrument.[23]

Accuracy

Two recent studies have examined the sensitivity of screening sigmoidoscopy for cancer or advanced adenomas in healthy patients using colonoscopy as the criterion standard. They found that sigmoidoscopy would identify 70% to 80% of patients with advanced adenomas or cancer.[19,24]

Sigmoidoscopy can produce false-positive results by detecting hyperplastic polyps that do not have malignant potential or adenomatous polyps that are unlikely to become malignant during the patient's lifetime. Because studies of diagnostic accuracy cannot measure whether small or large adenomas that are identified and removed would have gone on to become cancer, it is not possible to classify such findings in terms of their accuracy in detecting cancer. In practice, most investigators consider all adenomas to be "true positives," whether or not they would ever progress to cancer. Comparison of the specificity of sigmoidoscopy with that of other screening methods, such as FOBT, is therefore difficult.

Adverse Effects

Estimates of bowel perforations from sigmoidoscopy have generally been in the range of 1 to 2 or fewer per 10,000 examinations, particularly since the introduction of the flexible sigmoidoscope.[25] Atkin et al recently reported initial results from a sigmoidoscopy screening trial[21] in which experienced endoscopists performed sigmoidoscopy in 1,235 asymptomatic adults aged 55-64; 288 patients had polyps removed during the examination. Adverse effects, including pain, anxiety, or any degree of bleeding, were assessed by a written questionnaire immediately after the test and by a mailed questionnaire 3 months later. Of all patients, 3.2% (40/1,235) reported bleeding, (16/288 or 5.5% after polypectomy; 24/947 or 2.5% after diagnostic studies). One patient required hospital admission; none required a transfusion. Of all patients, 14% reported moderate pain and 0.4% reported severe pain. More than 25% of patients reported gas or flatus. No perforations were reported, but 1 patient died from peritonitis after a complicated open surgical procedure to remove a severely dysplastic adenoma. A recent study of endoscopic complications from the Mayo Clinic in Arizona identified 2 perforations in 49,501 sigmoidoscopy procedures.[26]

Fecal Occult Blood Test and Sigmoidoscopy

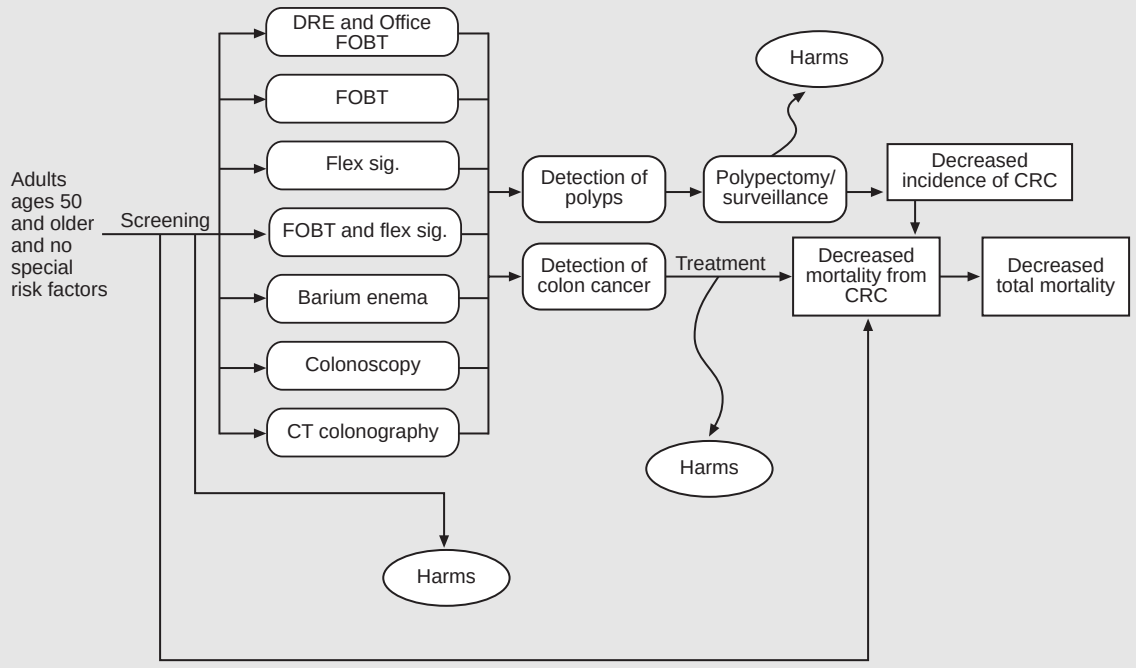
Effectiveness

Currently no randomized trials with colorectal cancer mortality as an end point have compared FOBT alone or sigmoidoscopy alone with a strategy of performing both tests.

In 1992, Winawer et al published a nonrandomized trial of more than 12,000 first-time attendees at a preventive health clinic in New York. This trial was available to the USPSTF in 1996.[4] The control group received rigid sigmoidoscopy at the first visit. All study participants were invited to return for annual rigid sigmoidoscopy re-examinations. Patients in the intervention group received rigid sigmoidoscopy and were also asked to complete Hemoccult™ (Beckerman Coulter, Fullerton, California) FOBT cards. Patients with adenomas more than 3 mm on sigmoidoscopy or who had a positive FOBT underwent full colonic examination with barium enema and colonoscopy. The control group received rigid sigmoidoscopy at the first visit and participants were invited to return for annual reexamination. Few patients continued to participate after the first examination (20% had FOBT at year 2 and 15% at year 3). Incidence of colorectal cancer and mortality were assessed over a 9-year period; follow-up data were available for 97% of subjects.

Demographic and clinical data suggest that the groups were comparable, despite the absence of

Figure 2. Colorectal cancer (CRC) screening: analytic framework



Note: CRC indicates colorectal cancer; CT, computed tomography; FOBT, fecal occult blood test; DRE, digital rectal examination; flex sig., flexible sigmoidoscopy.

randomization. More cases of colorectal cancer were detected on initial examination among intervention patients than in control patients (4.5 versus 2.5 per 1,000 participants). Incidence rates (cancers detected after the initial examination) were similar between groups (0.9 per 1,000 person-years in each group). Colorectal cancer mortality was 0.36 per 1,000 patient-years in the intervention group and 0.63 per 1,000 patient-years among controls (RR, 0.56; 95% CI, 0.25 to 1.19).

Thus, adding FOBT to rigid sigmoidoscopy appears to increase the yield of initial screening and may reduce mortality rates. Because rigid sigmoidoscopy is no longer used for screening, the generalizability of these results to the use of FOBT plus flexible sigmoidoscopy is unclear. Whether the incremental yield of combined screening will change after additional rounds of testing also remains uncertain.

Accuracy

Recent randomized trials from Europe have examined the additional diagnostic yield of performing sigmoidoscopy plus FOBT at 1 point in time for patients who were not already part of an ongoing screening program.[27-29] In each study, adding sigmoidoscopy to FOBT increased the identification of significant adenomas or cancer by a factor of 2 or more. Adding FOBT to sigmoidoscopy did not appear to identify any additional significant lesions. Winawer et al,[4] however, found an increased yield from adding FOBT to rigid sigmoidoscopy. In each study, data were limited to a single round of testing. The additional yield of this strategy may be lower after the first round of testing, but the impact of this strategy on mortality rates has not been fully evaluated.

Adverse Effects

The adverse effects of FOBT plus sigmoidoscopy are equal to the adverse effects of each test alone.

Double Contrast Barium Enema

Effectiveness

We identified no published studies that examined the effectiveness of DCBE in reducing the incidence or death from colorectal cancer.

Accuracy

Several studies have examined the accuracy of DCBE for diagnosing colorectal cancer or adenomatous polyps.[30-40] Most are of methodologically poor quality because they examined patients with symptoms or did not prospectively collect blinded data.

The National Polyp Study is a randomized trial of different intervals of surveillance after polypectomy (examinations at 1 and 3 years versus at 3 years only). In a substudy of this trial, Winawer et al compared the accuracy of DCBE with that of colonoscopy.[30] The sensitivity of DCBE for polyps smaller than 0.5 cm was 32% (95% CI, 25% to 39%); for polyps 0.6 to 1 cm, sensitivity was 53% (95% CI, 40% to 66%); for polyps larger than 1 cm, including 2 cases of cancerous polyps, sensitivity was 48% (95% CI, 24% to 67%). Of 470 patients in whom colonoscopy detected no polyps, DCBE was positive in 83 (specificity, 85%; 95% CI, 82% to 88%).

The Winawer et al study examined patients who previously had colonoscopy and removal of all polyps. Their results, therefore, may have limited generalizability for screening, because screening largely involves persons who have not had a recent colonoscopic examination and polypectomy and therefore may be more likely to have large polyps or cancers. However, the low sensitivity for large polyps and cancers found in this study is cause for concern and may limit the potential effectiveness of screening with DCBE.

Adverse Effects

The estimated risk of perforation during barium enema is low. In a study by Kewenter and Brevinge, no perforations or other complications occurred among the 1,987 screening patients undergoing barium enema as part of their screening work-up.[41] Blakeborough et al surveyed UK radiologists about the complications of barium enema during a 3-year period from 1992 through 1994.[42] All examinations were included, regardless of the indication for the procedure. Important complications of any type occurred in 1 in 10,000 examinations. Perforation occurred in 1 of 25,000 examinations; death occurred in 1 in 55,000 examinations, although whether all deaths were related to the procedure is not clear.

Colonoscopy

Effectiveness

The ability of colonoscopy to prevent colorectal cancer cases or mortality has not been measured in a screening trial. The National Polyp Study estimated that 76% to 90% of cancers could be prevented by regular colonoscopic surveillance examinations, based on comparison with historic controls.[43] However, these results should be interpreted with caution because the comparison groups were not from the same underlying population, which could introduce bias. In addition, all trial participants had polyps detected and removed, which limits generalizability of the results to the average screening population.

Muller and Sonnenberg, in a case-control study at Veterans Affairs hospitals, found that patients diagnosed with colorectal cancer were less likely to have had previous colonoscopy. The odds ratios for disease incidence were 0.47 (95% CI, 0.37 to 0.58) for colon cancers and 0.61 (95% CI, 0.48 to 0.77) for rectal cancers.[44] For colorectal cancer mortality, the odds ratio was also lower for patients with previous colonoscopy (OR, 0.43; 95% CI, 0.30 to 0.63).

Accuracy

Because colonoscopy is commonly used as the criterion standard examination, calculating sensitivity is difficult. Using tandem colonoscopic examinations, Rex et al found single-test sensitivity to be 90% for large adenomas and 75% for small adenomas (less than 1 cm); sensitivity for cancers is likely to be greater than 90%.[45]

The recent identification of flat lesions that can be missed on regular colonoscopy suggests that some histologic variants do not pass through the typical adenoma-carcinoma development sequence and thus may not be easily detectable in the precancerous phase.[46] If flat lesions account for 10% of all adenomas, sensitivity of all endoscopic screening methods may be lower than previously thought.

The specificity of colonoscopy with biopsy is generally reported to be 99% or 100%, but this assumes that all detected adenomas represent true-positive results. As with sigmoidoscopy, most detected adenomas, especially small adenomas, will never develop into cancer. If detection of an adenoma that will not become cancer is considered a false positive result that subjects a patient to risk without benefit, then the actual specificity of colonoscopy would be much lower.

Adverse Effects

Colonoscopy, which uses sedation and requires skilled support personnel, is more expensive than other screening tests and has a higher risk of procedural complications than other screening tests, particularly when polypectomy is performed. Use of conscious sedation adds the risk of complications attributable to the sedative agent.

In our systematic review of studies examining the principal complications of colonoscopy,[5] we focused on hemorrhage and perforation but noted the less frequent complications of death, infections, sedation-related events, and chemical colitis. Two recent studies examined the incidence of complications from colonoscopy performed in screening populations. In the study in Veterans Affairs medical centers by Lieberman et al, 10 of 3,121 patients (0.3%) had major complications during or immediately following the procedures, including 6 who had bleeding requiring hospitalization and 1 each with a stroke, myocardial infarction, Fournier gangrene, and thrombophlebitis.[19] Three other patients died within 1 month, probably from causes unrelated to the procedure. In the study by Imperiale et al of employees of a large corporation, 1,994 people aged 50 and older underwent colonoscopy.[24] One (0.05%) had a perforation not requiring surgery; 3 (0.15%) had bleeding that required emergency room visits but not admission or surgery.

Apart from these 2 screening studies, most of the studies examining colonoscopy complications are retrospective reviews of endoscopy records from U.S. university hospitals that recorded only immediate complications of the procedure and included a mixture of screening and diagnostic procedures.[19,24,26,47-61] A prospective study that also included a patient questionnaire administered 10 days after the procedure identified several additional important complications that occurred outside the hospital, suggesting that hospital record review alone may underestimate actual complication rates.[47]

Despite these limitations of reporting and nonscreening study populations, these studies provide a useful approximation of the complication rates that can be expected from colonoscopy. For diagnostic procedures, perforation rates were low (0.029% to 0.61%) and bleeding was not reported in enough studies to generate an estimate of its frequency. For therapeutic procedures, complication rates were higher (perforations, 0.07% to 0.72%; bleeding, 0.2% to 2.67%). Deaths occurred infrequently (reported rates from 1 in 30,000 to 1 in 3,000 with higher rates in studies with older patients and more symptomatic patients). The rate of screening related death may be on the lower end of this range; one cost-effectiveness analysis estimated it to be 1 per 20,000 patients.[18] Other clinically relevant complications were identified and reported too infrequently and measured too inconsistently to allow accurate estimation of their true incidence.

Discussion

Our systematic review supports the effectiveness of screening as a means of reducing colorectal cancer mortality. For biennial FOBT, 3 high-quality RCTs have shown disease-specific mortality rate reductions of 15% to 21% over 8 to 13 years. Annual FOBT with rehydrated slides appears to produce larger reductions in mortality rates (33% in one trial). Case-control studies have shown that sigmoidoscopy and possibly colonoscopy are also associated with decreased death from colorectal cancer. The combined strategy of FOBT and sigmoidoscopy was supported by 1 nonrandomized trial showing a borderline statistically significant 43% reduction in mortality rates when FOBT was added to rigid sigmoidoscopy.[4] This strategy was also supported by indirect evidence showing increased yield with both tests compared with FOBT alone. DCBE has not been studied as extensively as other methods for screening; further data are required in screening populations.

Although colorectal cancer screening is supported by strong direct and indirect evidence, no trials have compared different screening strategies head-to-head using colorectal cancer incidence or mortality rates as the endpoint of interest. Some groups have interpreted recent evidence showing the superior single-test accuracy of colonoscopy as proving its broader superiority and have recommended it as the procedure of choice for screening. However, these analyses have not always considered differences in yield over time, complications, and real-world performance, which may not always favor colonoscopy.[62,63] One possibility would be to perform a trial of colonoscopy. However, the cost of such a trial, particularly if colonoscopy were to be compared to other screening modalities rather than to no screening, would be quite high, and many years of follow-up would be required. In the face of good general evidence supporting screening but uncertainty about the most effective method for doing so, providers and patients may benefit from discussing the pros and cons of the different methods and incorporating patients' preferences in the decision about how to screen.[64]

Several areas of colorectal cancer screening and prevention warrant additional research. One is the critical need to learn more about adherence to screening among informed patients. Furthermore, we need better data on the real-world complication rates of colonoscopic screening and polypectomy, including whether complications become more or less likely as procedure volume increases. DCBE should be studied in a screening population. The accuracy of novel screening techniques, including virtual colonoscopy and genetic stool tests (or other novel noninvasive tests) should be evaluated in screening populations.

Additional means of prevention, including chemopreventive agents such as nonsteroidal anti-inflammatory drugs, calcium, or estrogen also warrant further study. Behavioral factors, including physical activity, dietary fat, dietary fiber, and fruit and vegetable consumption, appear to be related to colorectal cancer incidence; further research would clarify whether these relationships are causal or the result of uncontrolled confounding.

Despite its apparent effectiveness, colorectal cancer screening is currently underused by age-eligible adults. The multiple reasons for low utilization include patient-, provider-, and system-specific barriers.[65] Effective colon cancer screening requires ongoing efforts to ensure test ordering and adherence. Screening with FOBT, for example, may require offering annual testing to 500 to 1,000 people for 10 years to prevent 1 death from colorectal cancer.[2] Although this level of effort may seem inefficient or low in yield, the potential benefit is large and the costs per person are small. To achieve high rates of screening in real-world settings rather than in trials, which focused strictly on one aspect of preventive care, colorectal cancer screening must be integrated with other care needs, including other preventive services.

Several strategies have shown effectiveness in raising screening rates in primary care settings over the short term. Effective strategies include reminder systems, patient decision aids, and special screening clinics.[66] Further research is needed to determine whether such systems can maintain their effect over

time and to identify novel means of reaching people at risk who currently are not served, or are underserved, by the existing health care system.

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References

1. U.S. Preventive Services Task Force. *Guide to Clinical Preventive Services.* 2nd ed. Washington, DC: Office of Disease Prevention and Health Promotion; 1996.
2. Mandel J, Bond J, Church T, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. *N Engl J Med.* 1993;328:1365-1371.
3. Selby J, Friedman G, Quesenberry C, Weiss N. A case-control study of screening sigmoidoscopy and mortality from colorectal cancer. *N Engl J Med.* 1992;326:653-657.
4. Winawer S. Screening for colorectal cancer with fecal occult blood testing and sigmoidoscopy. *J Natl Cancer Inst.* 1993;85:1311-1318.
5. Pignone MP, Rich M, Teutsch SM, Berg AO, Lohr KN. *Screening for Colorectal Cancer in Adults.* Systematic Evidence Review. No. 7 (Prepared by the RTI-UNC Evidence-based Practice Center under Contract No. 290-97-0011). Rockville, MD: Agency for Healthcare Research and Quality. July 2002. (Available on the AHRQ Web site at: www.ahrq.gov/clinic/serfiles.htm).
6. U.S. Preventive Services Task Force. Screening for Colorectal Cancer: Recommendations and Rationale. *Ann Intern Med.* 2002;137(2):129-131.
7. Harris RP, Helfand M, Woolf SH, et al. Current methods of the U.S. Preventive Services Task Force: a review of the process. *Am J Prev Med.* 2001;2(suppl 3):21-35.
8. Herrinton LJ, Selby JV, Friedman GD, Quesenberry CP, Weiss NS. Case-control study of digital-rectal screening in relation to mortality from cancer of the distal rectum. *Am J Epidemiol.* 1995;142:961-964.
9. Winawer SJ, Fletcher RH, Miller L, et al. Colorectal cancer screening: clinical guidelines and rationale. *Gastroenterology.* 1997;112:594-642.
10) Ransohoff DF, Lang CA. Screening for colorectal cancer with the fecal occult blood test: a background paper. American College of Physicians. *Ann Intern Med.* 1997;126:811-822.
11. Yamamoto M, Nakama H. Cost-effectiveness analysis of immunochemical occult blood screening for colorectal cancer among three fecal sampling methods. *Hepatogastroenterology.* 2000;47(32), 396-399.
12. Eisner MS, Lewis JH. Diagnostic yield of a positive fecal occult blood test found on digital rectal examination. Does the finger count? *Arch Intern Med.* 1991;151:2180-2184.
13. Bini EJ, Rajapaksa RC, Weinshel EH. The findings and impact of nonrehydrated guaiac examination of the rectum (FINGER) study: a comparison of 2 methods of screening for colorectal cancer in asymptomatic average-risk patients. *Arch Intern Med.* 1999;159:2022-2026.
14. Hardcastle J, Chamberlain J, Robinson M, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. *Lancet.* 1996;348:1472-1477.
15. Kronborg O, Fenger C, Olsen J, Jorgensen D, Sondergaard O. Randomised study of screening for colorectal cancer with faecal-occult-blood test. *Lancet.* 1996;348:1467-1471.
16. Mandel JS, Church TR, Ederer F, Bond JH. Colorectal cancer mortality: effectiveness of biennial screening for fecal occult blood. *J Natl Cancer Inst.* 1999;91:434-437.
17. Mandel JS, Church TR, Bond JH, et al. The effect of fecal occult-blood screening on the incidence of colorectal cancer. *N Engl J Med.* 2000;343:1603-1607.
18. Wagner J, Tunis S, Brown M, Ching A, Almeida R. Cost-effectiveness of colorectal cancer screening in average-risk adults. In: Young G, Rozen P, Levin B, eds. *Prevention and Early Detection of Colorectal Cancer.* London: Saunders; 1996:321-356.
19. Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G. Use of colonoscopy to screen

asymptomatic adults for colorectal cancer. Veterans Affairs Cooperative Study Group 380. *N Engl J Med.* 2000;343:162-168.

20. Thiis-Evensen E, Hoff GS, Sauar J, Langmark F, Majak BM, Vatn MH. Population-based surveillance by colonoscopy: effect on the incidence of colorectal cancer: Telemark Poly Study I. *Scand J Gastroenterol.* 1999;34:414-420.

21. Atkin WS, Hart A, Edwards R, et al. Uptake, yield of neoplasia, and adverse effects of flexible sigmoidoscopy screening. *Gut.* 1998;42:560-565.

22. Kramer BS, Gohagan J, Prorok PC, Smart C. A National Cancer Institute sponsored screening trial for prostatic, lung, colorectal, and ovarian cancers. *Cancer.* 1993;71:589-593.

23. Newcomb PA, Norfleet RG, Storer BE, Surawicz TS, Marcus PM. Screening sigmoidoscopy and colorectal cancer mortality. *J Natl Cancer Inst.* 1992;84:1572-1575.

24. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. *N Engl J Med.* 2000;343:169-174.

25. Nelson RL, Abcarian H, Prasad ML. Iatrogenic perforation of the colon and rectum. *Dis Colon Rectum.* 1982;25:305-308.

26. Anderson ML, Pasha TM, Leighton JA. Endoscopic perforation of the colon: lessons from a 10-year study. *Am J Gastroenterol.* 2000;95:3418-3422.

27. Verne JE, Aubrey R, Love SB, Talbot IC, Northover JM. Population based randomized study of uptake and yield of screening by flexible sigmoidoscopy compared with screening by faecal occult blood testing. *BMJ.* 1998;317:182-185.

28. Berry DP, Clarke P, Hardcastle JD, Vellacott KD. Randomized trial of the addition of flexible sigmoidoscopy to faecal occult blood testing for colorectal neoplasia population screening. *Br J Surg.* 1997;84:1274-1276.

29. Rasmussen M, Kronborg O, Fenger C, Jorgensen OD. Possible advantages and drawbacks of adding flexible sigmoidoscopy to hemoccult-II in screening for colorectal cancer: a randomized study. *Scand J Gastroenterol.* 1999;34:73-78.

30. Winawer SJ, Stewart ET, Zauber AG, et al. A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. *N Engl J Med.* 2000;342:1766-1772.

31. Ott DJ, Scharling ES, Chen YM, Wu WC, Gelfand DW. Barium enema examination: sensitivity in detecting colonic polyps and carcinomas. *South Med J.* 1989;82:197-200.

32. Rex DK, Rahmani EY, Haseman JH, Lemmel GT, Kaster S, Buckley JS. Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice. *Gastroenterology.* 1997;112:17-23.

33. Johnson CD, Carlson HC, Taylor WF, Weiland LP. Barium enemas of carcinoma of the colon: sensitivity of double- and single-contrast studies. *Am J Roentgenology.* 1983;140:1143-1149.

34. Bloomfield JA. Reliability of barium enema in detecting colonic neoplasia. *Med J Aust.* 1981;1:631-633.

35. Teefey SA, Carlson HC. The fluoroscopic barium enema in colonic polyp detection. *Am J Roentgenology.* 1983;141:1279-1281.

36. Brady AP, Stevenson GW, Stevenson I. Colorectal cancer overlooked at barium enema examination and colonoscopy: a continuing perceptual problem. *Radiology.* 1994;192:373-378.

37. Strom E, Larsen JL. Colon cancer at barium enema examination and colonoscopy: a study from the county of Hordaland, Norway. *Radiology.* 1999;211:211-214.

38. Brekkan A, Kjartansson O, Tulinius H, Sigvaldason H. Diagnostic sensitivity of X-ray examination of the large bowel in colorectal cancer. *Gastrointest Radiol.* 1983;8:363-365.

39. Glick S, Wagner JL, Johnson CD. Cost-effectiveness of double-contrast barium enema in screening for colorectal cancer. *Am J Roentgenology.* 1998;170:629-636.

40. Myllyla V, Paivansalo M, Laitinen S. Sensitivity of single and double contrast barium enema in the detection of colorectal carcinoma. *Rofo: Fortschritte auf dem Gebiete der Rontgenstrahlen und der Nuklearmedizin.* 1984;140:393-397.

41. Kewenter J, Brevinge H. Endoscopic and surgical complications of work-up in screening for colorectal cancer. *Dis Colon Rectum.* 1996;39:676-680.

42. Blakeborough A, Sheridan MB, Chapman AH. Complications of barium enema examinations: a survey of UK Consultant Radiologists 1992 to 1994. *Clin Radiol.* 1997;52:142-148.

43. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy.

The National Polyp Study Workgroup. *N Engl J Med.* 1993;329:1977-1981.

44. Muller AD, Sonnenberg A. Protection by endoscopy against death from colorectal cancer: a case-control study among veterans. *Arch Intern Med.* 1995;155:1741-1748.

45. Rex DK, Cutler CS, Lemmel GT, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology.* 1997;112:24-28.

46. Rembacken BJ, Fujii T, Cairns A, et al. Flat and depressed colonic neoplasms: a prospective study of 1000 colonoscopies in the UK. *Lancet.* 2000;355:1211-1214.

47. Newcomer MK, Shaw MJ, Williams DM, Jowell PS. Unplanned work absence following outpatient colonoscopy. *J Clin Gastroenterology.* 1999;29:76-78.

48. Eckardt VF, Kanzler G, Schmitt T, Eckardt AJ, Bernhard G. Complications and adverse effects of colonoscopy with selective sedation. *Gastrointest Endosc.* 1999;49:560-565.

49. Zubarik R, Fleischer DE, Mastropietro C, et al. Prospective analysis of complications 30 days after outpatient colonoscopy. *Gastrointest Endosc.* 1999;50:322-328.

50. Wexner SD, Forde KA, Sellers G, et al. How well can surgeons perform colonoscopy? *Surg Endosc.* 1998;12:1410-1414.

51. Farley DR, Bannon MP, Zietlow SP, Pemberton JH, Ilstrup DM, Larson DR. Management of colonoscopic perforations. *Mayo Clinic Proc.* 1997;72:729-733.

52. Foliente RL, Chang AC, Youssef AI, Ford LJ, Condon SC, Chen YK. Endoscopic cecal perforation: mechanisms of injury. *Am J Gastroenterol.* 1996;91:705-708.

53. Gibbs DH, Opelka FG, Beck DE, Hicks TC, Timmcke AE, Gathright JBJ. Postpolypectomy colonic hemorrhage. *Dis Colon Rectum.* 1996;39:806-810.

54. Ure T, Dehghan K, Vernava AM III, Longo WE, Andrus CA, Daniel GL. Colonoscopy in the elderly. Low risk, high yield. *Surg Endosc.* 1995;9:505-508.

55. Lo AY, Beaton HL. Selective management of colonoscopic perforations. *J Am Coll Surg.* 1994;179:333-337.

56. Rosen L, Bub DS, Reed JF III, Nastasee SA. Hemorrhage following colonoscopic polypectomy. *Dis Colon Rectum.* 1993;36:1126-1131.

57. DiPrima RE, Barkin JS, Blinder M, Goldberg RI, Phillips RS. Age as a risk factor in colonoscopy: fact versus fiction. *Am J Gastroenterol.* 1988;83:123-125.

58. Nivatvongs S. Complications in colonoscopic polypectomy: lessons to learn from an experience with 1576 polyps. *Am Surg.* 1988;54:61-63.

59. Brynitz S, Kjaergard H, Struckmann J. Perforations from colonoscopy during diagnosis and treatment of polyps. *Annales Chirurgiae et Gynaecologiae.* 1986;75:142-145.

60. Webb WA, McDaniel L, Jones L. Experience with 1000 colonoscopic polypectomies. *Ann Surg.* 1985;201:626-632.

61. Macrae FA, Tan KG, Williams CB. Towards safer colonoscopy: a report on the complications of 5000 diagnostic or therapeutic colonoscopies. *Gut.* 1983;24:376-383.

62. Rex DK, Johnson DA, Lieberman DA, Burt RW, Sonnenberg A. Colorectal cancer prevention 2000: screening recommendations of the American College of Gastroenterology. American College of Gastroenterology. *Am J Gastroenterol.* 2000;95:868-877.

63. Podolsky DK. Going the distance: the case for true colorectal-cancer screening. *N Engl J Med.* 2000;343:207-208.

64. Woolf SH. The best screening test for colorectal cancer: a personal choice. *N Engl J Med.* 2000;343:1641-1643.

65. Vernon SW. Participation in colorectal cancer screening: a review. *J Natl Cancer Inst.* 1997;89:1406-1422.

66. Balas EA, Weingarten S, Garb CT, Blumenthal D, Boren SA, Brown GD. Improving preventive care by prompting physicians. *Arch Intern Med.* 2000;160:301-308.

Methods Appendix

Search Strategies

To update the evidence on screening for colorectal cancer, we performed 3 separate literature searches using MEDLINE: 1 general update from January 1995 to December 2001 and 2 focused searches for evidence related to barium enema and complications of screening that used search dates from 1966 through December 2001. All searches were limited to "human" subjects.

For the general search, we combined the MeSH headings "colorectal neoplasms" or "occult blood" or "sigmoidoscopy" or "colonoscopy" with the term "mass screening." This search produced 719 results, of which we retained 19 in the final document.

To identify articles on the use of barium enema, we combined the exploded MeSH terms "colorectal neoplasms" and "barium sulfate" and "enema," which yielded 621 results. We retained 13 articles in our final data set.

For studies about the complications of screening, we combined the exploded MeSH terms colonoscopy/ae [Adverse Effects] and sigmoidoscopy/ae [Adverse Effects], intestinal perforation, intraoperative complications, postoperative complications, or gastrointestinal hemorrhage, with a search combining the test names and the keyword "complications." Our search yielded 839 articles, of which we retained 16.

In addition to these searches, we used peer review, hand searching of the bibliographies of included articles and other systematic reviews, as well as articles from the 1996 document, which yielded another 15 references for our final document.

Eligibility criteria

We developed eligibility criteria to guide decisions about inclusion of articles. In general, we sought to identify and include the highest quality evidence available. The Table shows the criteria for each specific topic.

Appendix Table. Eligibility criteria

Test	Type of studies included
DRE	diagnostic accuracy, observational
FOBT	RCTs
Sigmoidoscopy	RCTs, observational studies
FOBT + sigmoidoscopy	controlled trials, observational studies, diagnostic accuracy studies
Barium Enema	diagnostic accuracy studies
Colonoscopy	observational studies, diagnostic accuracy studies
Adverse effects (any test)	case series, observational studies, RCTs

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Screening for Breast Cancer

Recommendations and Rationale

U.S. Preventive Services Task Force

This statement summarizes the current U.S. Preventive Services Task Force (USPSTF) recommendations on screening for breast cancer and the supporting scientific evidence, and it updates the 1996 recommendations contained in the Guide to Clinical Preventive Services, second edition.[1] Explanations of the ratings and of the strength of overall evidence are given in Appendix A and Appendix B, respectively. The complete information on which this statement is based, including evidence tables and references, is available in the article Breast Cancer Screening: A Summary of the Evidence for the U.S. Preventive Services Task Force[2] (which follows this recommendation) and in the Systematic Evidence Review[3] on this topic. These documents can be obtained through the USPSTF Web site (www.preventiveservices.ahrq.gov), and through the National Guideline Clearinghouse (www.guideline.gov). The summary of the evidence and the recommendation statement are also available in print through the AHRQ Publications Clearinghouse (call 1-800-358-9295 or e-mail ahrqpubs@ahrq.gov).

To update their recommendations on screening for breast cancer, the USPSTF reviewed the evidence regarding the effectiveness of mammography, clinical breast examination, and breast self-examination in reducing breast cancer mortality. The USPSTF did not review the evidence regarding genetic screening, surveillance of women with prior breast cancer, or formal evaluation of new screening modalities that have not been studied in the general population. A meta-analysis using a Bayesian random effects model was conducted for the USPSTF to obtain a summary of relative risk estimates of the effectiveness of screening with mammography, either alone or in combination with clinical breast examination, in reducing breast cancer mortality. Clinical studies that evaluated breast self-examination were included in the review.

Note: These recommendations were first released on February 21, 2002. Subsequent to their release, a 2002 publication provided additional data on outcomes and methods of 4 mammography trials conducted in Sweden.[4] The additional follow-up data have been incorporated into the numeric estimates of the effectiveness of mammography in this statement, which differ minimally from those cited in the February 2002 release. Overall ratings of study quality were not affected.

This was first released on the AHRQ Web site on Septemeber 3, 2002, and an abridged version of this recommendation also appeared in *Ann Intern Med.* 2002;137(5 Part 1):344-346.

Summary of Recommendations

- The U.S. Preventive Services Task Force (USPSTF) recommends screening mammography, with or without clinical breast examination (CBE), every 1-2 years for women aged 40 and older. **B recommendation.**

The USPSTF found fair evidence that mammography screening every 12-33 months significantly reduces mortality from breast cancer. Evidence is strongest for women aged 50-69, the age group generally included in screening trials. For women aged 40-49, the evidence that screening mammography reduces mortality from breast cancer is weaker, and the absolute benefit of mammography is smaller, than it is for older women. Most, but not all, studies indicate a mortality benefit for women undergoing mammography at ages 40-49, but the delay in observed benefit in women younger than 50 makes it difficult to determine the incremental benefit of beginning screening at age 40 rather than at age 50. The absolute benefit is smaller because the incidence of breast cancer is lower among women in their 40s than it is among older women. The USPSTF concluded that the evidence is also generalizable to women aged 70 and older (who face a higher absolute risk for breast cancer) if their life expectancy is not compromised by comorbid disease. The absolute probability of benefits of regular mammography increase along a continuum with age, whereas the likelihood of harms from screening (false-positive results and unnecessary anxiety, biopsies, and cost) diminish from ages 40-70. The balance of benefits and potential harms, therefore, grows more

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favorable as women age. The precise age at which the potential benefits of mammography justify the possible harms is a subjective choice. The USPSTF did not find sufficient evidence to specify the optimal screening interval for women aged 40-49 (see Clinical Considerations).

- The USPSTF concludes that the evidence is insufficient to recommend for or against routine CBE alone to screen for breast cancer. **I recommendation.**

No screening trial has examined the benefits of CBE alone (without accompanying mammography) compared to no screening, and design characteristics limit the generalizability of studies that have examined CBE. The USPSTF could not determine the benefits of CBE alone or the incremental benefit of adding CBE to mammography. The USPSTF therefore could not determine whether potential benefits of routine CBE outweigh the potential harms.

- The USPSTF concludes that the evidence is insufficient to recommend for or against teaching or performing routine breast self-examination (BSE). **I recommendation.**

The USPSTF found poor evidence to determine whether BSE reduces breast cancer mortality. The USPSTF found fair evidence that BSE is associated with an increased risk for false-positive results and biopsies. Due to design limitations of published and ongoing studies of BSE, the USPSTF could not determine the balance of benefits and potential harms of BSE.

Clinical Considerations

- The precise age at which the benefits from screening mammography justify the potential harms is a subjective judgment and should take into account patient preferences. Clinicians should inform women about the potential benefits (reduced chance of dying from breast cancer), potential harms (eg, false-positive results, unnecessary biopsies), and limitations of the test that apply to women their age. Clinicians should tell women that the balance of benefits and potential harms of mammography improves with increasing age for women between the ages of 40 and 70.
- Women who are at increased risk for breast cancer (eg, those with a family history of breast cancer in a mother or sister, a previous breast biopsy revealing atypical hyperplasia, or first childbirth after age 30) are more likely to benefit from regular mammography than women at lower risk. The recommendation for women to begin routine screening in their 40s is strengthened by a family history of breast cancer having been diagnosed before menopause.
- The USPSTF did not examine whether women should be screened for genetic mutations (eg, BRCA1 and BRCA2) that increase the risk for developing breast cancer, or whether women with genetic mutations might benefit from earlier or more frequent screening for breast cancer.
- In the trials that demonstrated the effectiveness of mammography in lowering breast cancer mortality, screening was performed every 12-33 months. For women aged 50 and older, there is little evidence to suggest that annual mammography is more effective than mammography done every other year. For women aged 40-49, available trials also have not reported a clear advantage of annual mammography over biennial mammography. Nevertheless, some experts recommend annual mammography based on the lower sensitivity of the test and on evidence that tumors grow more rapidly in this age group.
- The precise age at which to discontinue screening mammography is uncertain. Only 2 randomized controlled trials enrolled women older than 69 and no trials enrolled women older than 74. Older women face a higher probability of developing and dying from breast cancer but also have a greater chance of dying from other causes. Women with comorbid conditions that limit their life expectancy are unlikely to benefit from screening.
- Clinicians should refer patients to mammography screening centers with proper accreditation and quality assurance standards to ensure accurate imaging and radiographic interpretation.

Clinicians should adopt office systems to ensure timely and adequate follow-up of abnormal results. A listing of accredited facilities is available at http://www.fda.gov/cdrh/mammography/certified.html.

- Clinicians who advise women to perform BSE or who perform routine CBE to screen for breast cancer should understand that there is currently insufficient evidence to determine whether these practices affect breast cancer mortality, and that they are likely to increase the incidence of clinical assessments and biopsies.

Scientific Evidence

Epidemiology and Clinical Consequences

Breast cancer is the most common non-skin malignancy among women in the United States and second only to lung cancer as a cause of cancer-related death. In 2001, an estimated 192,200 new cases of breast cancer were diagnosed in American women, and 40,200 women died of the disease.[5] The risk for developing breast cancer increases with age beginning in the fourth decade of life. The probability of developing invasive breast cancer over the next 10 years is 0.4% for women aged 30-39, 1.5% for women aged 40-49, 2.8% for women aged 50-59, and 3.6% for women aged 60-69.5 Individual factors other than age that increase the risk for developing breast cancer include family history or a personal history of breast cancer, biopsy-confirmed atypical hyperplasia, and having a first child after age 30.[6]

Accuracy and Reliability of Screening Tests

The USPSTF examined the test characteristics of mammography, CBE, and BSE. Precise estimates of sensitivity and specificity of screening are made more difficult by the varied criterion standards in available studies. Estimating the predictive value of positive and negative tests is also difficult because studies have been conducted on populations with a widely varying prevalence of breast cancer.

Mammography

Estimates of the sensitivity of mammography vary with the methods used to calculate it.[2] In a good quality systematic review, the first round of mammography detected 77% to 95% of cancers diagnosed over the following year, but only 56% to 86% of cancers diagnosed over the next 2 years.[3,7] Sensitivity is lower among women who are younger than 50, have denser breasts, or are taking hormone replacement therapy.[3]

In screening trials, the false-positive rate of the initial round of mammography was 3% to 6% (ie, specificity 94% to 97%).[3] Specificity is increased with a shorter screening interval and the availability of prior mammograms.[3] In a large study in a health maintenance organization, the rate of false-positive mammograms (those requiring some additional follow-up) was higher in women aged 40-59 (7% to 8%) than in women aged 60-79 (4% to 5%).[8]

The probability that an abnormal mammogram is due to cancer increases with age. A large study in Northern California estimated positive predictive values for abnormal mammograms at 2% to 4% among women aged 40-49, 5% to 9% among women aged 50-59, and 7% to 19% among women aged 60 and older.[3,9] Positive predictive values were also higher among women with a family history of breast cancer in 2 studies.[3]

Clinical Breast Examination

In a recent good quality review of data from clinical trials, the sensitivity of CBE ranged from 40% to 69%, specificity from 86% to 99%, and positive predictive value from 4% to 50%, using mammography and interval cancer as the criterion standard.[10] In a large community study, only 4% of women with an abnormal CBE were subsequently diagnosed with cancer.[11]

Breast Self-examination

The accuracy of BSE is largely unknown. Available evidence shows sensitivity ranging from 26% to 41% compared with CBE and mammography.[3] Specificity of BSE is largely unknown.

Effectiveness of Early Detection

The USPSTF reviewed 8 randomized controlled trials (RCTs) of mammography (4 of mammography alone and 4 of mammography plus CBE) that have reported results with 11- 20 years of follow-up.[4,12-21] The USPSTF found important methodological limitations in each trial, but rated only one trial as "poor" based on established criteria used by the USPSTF to evaluate the quality of evidence for screening tests.[22] The most serious problems concerned the assembly and maintenance of comparable groups, methods for ascertaining outcomes, and generalizability to routine practice. The USPSTF concluded that the flaws were problematic but unlikely to negate the reasonably consistent and significant mortality reductions observed in these trials.

Imperfections in these mammography trials have been recognized and discussed in the literature and by the original investigators for many years. Recently, a 2001 Cochrane Collaboration review[23] of the same trials concluded that 6 of the 8 trials were "flawed" or of "poor" quality and that the pooled results from the remaining 2 better quality trials did not support a benefit from mammography. Although the USPSTF was concerned about many (but not all) of the flaws identified in the Cochrane review, it did not consider the presence of flaws sufficient reason in itself for rejecting trial results. Instead, it examined whether observed mortality reductions in the trials were likely to be explained by the biases potentially introduced by such flaws. Studies rated to be of "fair" quality by the USPSTF contained flaws that were considered unlikely to account for observed benefits (or lack of benefits).

The trials[4,12-21] reported mortality reductions ranging from no significant effect to a 32% reduction in breast cancer mortality. The meta-analysis performed for the USPSTF on the most current published data found that the pooled effect size of the combined trials was sizable and statistically significant. After excluding data from one trial rated as poor quality by the USPSTF,[17] the summary relative risk (RR) of breast cancer death among women of all ages randomized to screening in the remaining 7 trials was 0.84 (95% CI, 0.77-0.91).

Earlier subgroup analyses from these mammography trials raised questions about whether screening is effective in women younger than 50. Seven trials enrolled women aged 40-49. Six of these were rated by the USPSTF to be of at least "fair" quality, but only 1 of these was designed to specifically address the benefits of screening in this age group: it reported no reduction in breast cancer mortality with annual mammography and CBE.[18,20] Of the remaining 5 fair-quality trials that included women younger than 50, 1 trial has reported significant mortality reduction with screening in this age group,[4,13] 3 have reported non-significant mortality reductions,[4,12,15,16] and 1 found no benefit.[14] In a meta-analysis performed for the USPSTF pooling results for women aged 40-49 in the 6 fair-quality trials, the summary relative risk of breast cancer mortality was 0.85 (95% CI 0.73-0.99) among screened women after 13 years of observation.[2] These results are similar to prior meta-analyses based on older data.

Because these data represent a subgroup analysis of trials not designed to test the benefits of beginning screening at a specific age, questions remain about the additional benefits of beginning screening before age 50. On average, the time until mortality benefits begin to be observed in these trials is longer in women younger than 50 than in older women (8 years vs 4 to 6 years) and some of the observed benefits could be due to screening after age 50.[3,4] Analyses of individual studies suggest that at least some of the mortality reduction is due to early detection of tumors before age 50, but definitive estimates of the proportion of benefits due to early screening cannot be made.[3,24]

Clinical Breast Examination

No study has compared CBE to no screening. The reductions in breast cancer mortality in studies using mammography alone are comparable to those using mammography plus CBE.[3]

Breast Self-examination

The role of BSE in reducing breast cancer mortality has been evaluated in 1 Chinese[25] and 1 Russian[26] RCT and 1 non-randomized controlled trial of BSE education in the United Kingdom.[27]

None of the 3 trials has demonstrated a reduction in breast cancer mortality or significant improvements in the number or stage of cancers detected, with follow-up ranging from 5 to 14 years; follow-up is continuing in 1 trial that observed a slight non-significant reduction in mortality in the BSE group at 9 years.[26] In a good-quality nested case-control analysis from a Canadian screening study, the overall practice of BSE was not associated with a reduction in mortality.[28] Although none of these studies provides support for BSE, the USPSTF concluded that these studies did not exclude a possible benefit, due to their limited duration of follow-up and questions about whether results from other countries are generalizable to women in North America.

When To Stop Screening

Although there are no trial data directly evaluating screening in women older than 74, 2 RCTs suggest benefits among women enrolled in screening trials up to ages 70 and 74.[15,16] Because risk for breast cancer is high after age 70, the benefits of mammography could be important. However, this is offset by the fact that some older women (especially the very old and those with comorbid illness) will die from other causes before they observe any benefits from early detection.

Screening Interval

In clinical trials, mortality reductions occurred in programs with screening intervals ranging from 12-33 months, with no clear difference due to interval.[3] Data suggest that breast cancer grows more rapidly in women younger than 50, and the sensitivity of mammography is lower in this age group; thus, shorter screening intervals have been advocated for women aged 40-49. Among the trials showing or suggesting a benefit of screening in women younger than 50, screening intervals that ranged from 12-33 months appeared to achieve comparable results, providing no direct evidence of incremental benefits over annual screening.[3]

Potential Harms of Screening

Similar to other cancer screening tests, the large majority (80% to 90%) of abnormal screening mammograms or CBEs are false-positives.[3] These may require follow-up testing or invasive procedures such as breast biopsy to resolve the diagnosis, and can result in anxiety, inconvenience, discomfort, and additional medical expenses.[3] In 1 large community study, 6.5% of screening mammograms required some additional follow-up and, over a 10-year period, 23% of all women had experienced at least 1 abnormal mammogram.[8] The cumulative risk for a false-positive result after 10 mammograms was estimated to be 49%.[8] The proportion of false-positive results that lead to biopsy varies substantially in different settings.[29] In screening trials, 1% to 6% of all women screened underwent biopsy, and the proportion of biopsies that revealed cancer ranged from 12% to 78%.[3] In 2 RCTs, BSE education resulted in a nearly 2-fold increase in false-positive results, physician visits, and biopsies for benign disease.[25,26]

The consequences of false-positive mammograms are uncertain. Most, but not all, studies report increased anxiety from an abnormal mammogram.[2] At the same time, some studies report that women in the United States may be willing to accept a relatively high number of false-positive results in the population in return for the benefits of mammography.[2,30] Studies do not indicate that false-positive results diminish adherence to subsequent screening.[3]

False-negatives also occur with mammograms and CBE. Although false-negative results might provide false reassurance, the USPSTF found no data indicating these led to further delays in diagnosis.[3]

Some experts view the over-diagnosis and treatment of ductal carcinoma in situ (DCIS) as a potential adverse consequence of mammography. Although the natural history of DCIS is variable, many women in the United States are treated aggressively with mastectomy or lumpectomy and radiation.[2] Given the dramatic increase in the incidence of DCIS in the past 2 decades (750%) and autopsy series suggesting that there is a significant pool of DCIS among women who die of other causes,[3] screening may be increasing the number of women undergoing treatment for lesions that might not pose a threat to their health.

A final potential concern about mammography is radiation-induced breast cancer, but there are few data to directly assess this risk. A 1997 review, using risk estimates provided by the Biological Effects of Ionizing Radiation report of the National Academy of Sciences, estimated that annual mammography of 100,000 women for 10 consecutive years beginning at age 40 would result in up to 8 radiation-induced breast cancer deaths.[31]

Recommendations of Others

Nearly all North American organizations support mammography screening, although groups vary in the recommended age to begin screening, the interval for screening, and the role of CBE. The American Medical Association (AMA),[32] the American College of Obstetricians and Gynecologists (ACOG),[33] the American College of Radiology (ACR),[34] and the American Cancer Society (ACS),[35] all support screening with mammography and CBE beginning at age 40. The Canadian Task Force on Preventive Health Care (CTFPHC),[36] the American Academy of Family Physicians (AAFP),[37] and the American College of Preventive Medicine (ACPM)[38] recommend beginning mammography for average-risk women at age 50. AAFP and ACPM recommend that mammography in high-risk women begin at age 40, and AAFP recommends that all women aged 40-49 be counseled about the risks and benefits of mammography before making decisions about screening.[37,38] A 1997 Consensus Development Panel convened by the National Institutes of Health concluded that the evidence was insufficient to determine the benefits of mammography among women aged 40-49. This panel recommended that women aged 40-49 should be counseled about potential benefits and harms before making decisions about mammography.[39] In 2001, the CTFPHC concluded there was insufficient evidence to recommend for or against mammography in women 40-49.[40]

Organizations differ on their recommendations for the appropriate interval for mammography. Annual mammography is recommended by AMA, ACR, and ACS.[32,34,35] Mammography every 1-2 years is recommended by AAFP, ACPM, and the CTFPHC.[36-38] ACOG recommends annual mammography every 1-2 years for women aged 40-49 and annually for women aged 50 and older.[33]

In their 2001 report, the Canadian Task Force on Preventive Health Services recommends against teaching BSE to women aged 40-69.[41] The AMA, ACOG, ACS, and AAFP support teaching BSE.

References

1. U.S. Preventive Services Task Force. *Guide to Clinical Preventive Services.* 2nd ed. Washington, DC: Office of Disease Prevention and Health Promotion; 1996.
2. Humphrey LL, Helfand M, Chan BKS. Breast cancer screening: a summary of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2002;137:347-360.
3. Humphrey LL, Chan BKS, Detlefsen S, Helfand M. *Screening for Breast Cancer.* Systematic Evidence Review No. 15 (Prepared by the Oregon Health & Science University Evidence-based Practice Center under Contract No. 290-97-0018). Rockville, MD: Agency for Healthcare Research and Quality. September 2002. (Available on the AHRQ Web site at: www.ahrq.gov/clinic/serfiles.htm).
4. Nystrom L, Andersson I, Bjurstam N, Frisell J, Nordenskjöld B, Rutqvist LE. Long-term effects of mammography screening: updated overview of the Swedish randomized trials. *Lancet.* 2002;359(9310):909-919.
5. American Cancer Society. Cancer facts and figures, 2001-2002. Atlanta, Georgia: American Cancer Society. Available at: http://www.cancer.org. Accessed February 18, 2002.
6. National Cancer Institute. Surveillance, Epidemiology, and End Results Program 1995-1997. Available at: http://www.nci.nih.gov. Accessed February 18, 2002.

7. Mushlin AI, Kouides RW, Shapiro DE. Estimating the accuracy of screening mammography: a meta-analysis. *Am J Prev Med.* 1998;14(2):143-153.

8. Elmore JG, Barton MB, Moceri VM, et al. Ten-year risk of false positive screening mammograms and clinical breast examinations. *N Engl J Med.* 1998;338(16):1089-1096.

9. Kerlikowske K, Carney PA, Geller B, et al. Performance of screening mammography among women with and without a first-degree relative with breast cancer. *Ann Intern Med.* 2000;133(11):855-863.

10. Barton MB, Harris R, Fletcher SW. Does this patient have breast cancer? The screening clinical breast examination: should it be done? How? *JAMA.*1999;282(13):1270-1280.

11. Bobo JK, Lee NC, Thames SF. Findings from 752,081 clinical breast examinations reported to a national screening program from 1995 through 1998. *J Natl Cancer Inst.* 2000;92(12):971-976.

12. Shapiro S. Periodic screening for breast cancer: the HIP Randomized Controlled Trial Health Insurance Plan. *J Natl Cancer Inst Monogr.* 1997;22:27-30.

13. Bjurstam N, Bjorneld L, Duffy SW, et al. The Gothenburg breast screening trial: first results on mortality, incidence, and mode of detection for women ages 39-49 years at randomization. *Cancer.* 1997;80(11):2091-2099.

14. Frisell J, Lidbrink E, Hellstrom L, Rutqvist LE. Followup after 11 years: update of mortality results in the Stockholm mammographic screening trial. *Breast Cancer Research & Treatment.* 1997;45:263-270.

15. Andersson I, Janzon L. Reduced breast cancer mortality in women under age 50: updated results from the Malmo Mammographic Screening Program. *J Natl Cancer Inst Monogr.* 1997;22:63-67.

16. Tabar L, Vitak B, Chen HH, et al. The Swedish Two-County Trial twenty years later: updated mortality results and new insights from long-term follow-up. *Radiol Clin North Am.* 2000;38(4):625-651.

17. Alexander FE, Anderson TJ, Brown HK, et al. 14 years of follow-up from the Edinburgh randomised trial of breast-cancer screening. *Lancet.* 1999;353(9168):1903-1908.

18. Miller AB, Baines CJ, To T, Wall C. Canadian National Breast Screening Study: 1. Breast cancer detection and death rates among women aged 40 to 49 years [published erratum appears in *Can Med Assoc J.* 1993;148(5):718]. *CMAJ.* 1992;147:1459-1476.

19. Miller AB, Baines CJ, To T, Wall C. Canadian National Breast Screening Study: 2. Breast cancer detection and death rates among women aged 50 to 59 years [published erratum appears in *Can Med Assoc J.* 1993;148(5):718]. *CMAJ.* 1992;147:1477-1488.

20. Miller AB, To T, Baines CJ, Wall C. The Canadian National Breast Screening Study: update on breast cancer mortality. *J Natl Cancer Inst Monogr.* 1997;22:37-41.

21. Nystrom L, Rutqvist LE, Wall S, et al. Breast cancer screening with mammography: overview of Swedish randomized trials. *Lancet.* 1993;341(8851):973-978.

22. Harris RP, Helfand M, Woolf SH, et al. Methods of the third U.S. Preventive Services Task Force. *Am J Prev Med.* 2001;20(suppl 3):21-35.

23. Olsen O, Gøtzsche PC. Screening for breast cancer with mammography (Cochrane Review). In: *The Cochrane Library,* Issue 3 2002. Oxford: Update Software. Available at: http://www.cochrane.org/cochrane/revabstr/ab001877.htm. Accessed August 14, 2002.

24. Cox B. Variation in the effectiveness of breast screening by year of follow-up. *J Natl Cancer Inst Monogr.* 1997;22:69-72.

25. Thomas DB, Gao DL, Self SG, et al. Randomized trial of breast self-examination in Shanghai: methodology and preliminary results. *J Natl Cancer Inst.* 1997;89(5):355-365.

26. Semiglazov VF, Moiseenko VM, Manikhas AG, et al. Interim results of a prospective randomized study of self-examination for early detection of breast cancer. Russia/St.Petersburg/World Health Organization. *Vopr Onkol.* 1999;45(3):265-271.

27. UK Breast Cancer Detection Working Group. 16-year mortality from breast cancer in the UK trial of early detection of breast cancer. *Lancet.* 1999;353(9168):1909-1914.

28. Harvey BJ, Miller AB, Baines CJ, Corey PN. Effect of breast self-examination techniques on the risk of death from breast cancer. *CMAJ.* 1997;157(9):1205-1212.

29. Fletcher SW, Harris RP, Gonzalez JJ, et al. Increasing mammography utilization: a controlled study. *J Natl Cancer Inst.* 1993;85:112-120.

30. Schwartz LM, Woloshin S, Sox HC, Fischhoff B, Welch HG. U.S. women's attitudes to false positive mammography results and detection of ductal carcinoma in situ: cross sectional survey. *Br Med J.* 2000;320(7250):1635-1640.

31. Feig SA, Hendrick RE. Radiation risk from screening mammography of women aged 40-49 years. *J Natl Cancer Inst Monogr.* 1997(22):119-124.

32. American Medical Association. Report 16 of the Council on Scientific Affairs (A-99). Mammographic Screening for Asymptomatic Women. June 1999. Available at: http://www.ama-assn.org/ama/pub/article/2036-2346.html. Accessed January 2002.

33. American College of Obstetricians and Gynecologists. Primary and preventive care: periodic assessments. ACOG Committee Opinion 246. Washington, DC: ACOG, 2000.

34. Feig SA, D'Orsi CJ, Hendrick RE, et al. American College of Radiology guidelines for breast cancer screening. *Am J Roentgenol.* 1998;171(1):29-33.

35. ACS guidelines for the early detection of breast cancer: update 1997. *CA Cancer J Clin.* 1997;47(3):150-153.

36. Canadian Task Force on the Periodic Health Examination. Ottawa (Canada): Health Canada; 1994:788-795 (reaffirmed by the Canadian Task Force on the Periodic Health Examination 1999). Available at: http://www.ctfphc.org/index.html. Accessed February 18, 2002.

37. Periodic Health Examinations: Summary of AAFP Policy Recommendations & Age Charts. Availabel at: http://www.aafp.org/exam. Accessed January 2002.

38. Ferrini R, Mannino E, Ramsdell E, Hill L. Screening mammography for breast cancer: American College of Preventive Medicine practice policy statement. *Am J Prev Med.* 1996;12(5):340-341.

39. Breast Cancer Screening for Women Ages 40-49. NIH Consensus Statement Online 1997 Jan 21-23; 15(1):1-35. Available at: http://odp.od.nih.gov/consensus/cons/103/103_statement.htm. Accessed December 12, 2001.

40. Jolie Ringash and the Canadian Task Force on Preventive Health Care. Preventive health care, 2001 update: screening mammography among women aged 40-49 years at average risk of breast cancer. Available at: http://www.ctfphc.org). Accessed August 15, 2002.

41. Nancy Baxter and the Canadian Task Force on Preventive Health Care. Preventive health care, 2001 update: should women be routinely taught breast self-examination to screen for breast cancer? *CMAJ.* 2001;164(3):1837-1846.

Appendix A
U.S. Preventive Services Task Force - Recommendations and Ratings

The Task Force grades its recommendations according to one of 5 classifications (A, B, C, D, I) reflecting the strength of evidence and magnitude of net benefit (benefits minus harms):

A. The USPSTF strongly recommends that clinicians routinely provide [the service] to eligible patients. *The USPSTF found good evidence that [the service] improves important health outcomes and concludes that benefits substantially outweigh harms.*

B. The USPSTF recommends that clinicians routinely provide [the service] to eligible patients. *The USPSTF found at least fair evidence that [the service] improves important health outcomes and concludes that benefits outweigh harms.*

C. The USPSTF makes no recommendation for or against routine provision of [the service]. *The USPSTF found at least fair evidence that [the service] can improve health outcomes but concludes that the balance of benefits and harms is too close to justify a general recommendation.*

D. The USPSTF recommends against routinely providing [the service] to asymptomatic patients. *The USPSTF found at least fair evidence that [the service] is ineffective or that harms outweigh benefits.*

I. The USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing [the service]. *Evidence that [the service] is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.*

Appendix B
U.S. Preventive Services Task Force - Strength of Overall Evidence

The USPSTF grades the quality of the overall evidence for a service on a 3-point scale (good, fair, poor):

Good: Evidence includes consistent results from well-designed, well-conducted studies in representative populations that directly assess effects on health outcomes.

Fair: Evidence is sufficient to determine effects on health outcomes, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies, generalizability to routine practice, or indirect nature of the evidence on health outcomes.

Poor: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information on important health outcomes.

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