



FECAL IMMUNOCHEMICAL TESTING (FIT) TO SCREEN FOR COLORECTAL CANCER

A Technology Assessment

INTRODUCTION

The California Technology Assessment Forum is requested to review the scientific evidence for the use of fecal immunochemical testing (FIT) as a modality for colorectal cancer screening.

BACKGROUND

In the United States in 2007 there will be an estimated 153,760 new cases of colorectal cancer and an estimated 52,180 deaths from this disease.¹ Colorectal cancer is the third most common cancer (excluding non-melanoma skin cancers) in both men and women in the U.S., as well as the second most common cause of cancer-specific deaths overall.¹ With its high prevalence and serious consequences, colorectal cancer is an excellent candidate for population-based screening.² In addition, it meets other commonly accepted criteria for population-based screening: colorectal cancer has a detectable pre-clinical phase in the form of pre-cancerous adenomatous polyps, and treatment of pre-symptomatic disease is more effective than treatment after symptoms develop.²⁻⁴ Five year survival is excellent (90%) for individuals diagnosed in the earliest stage of the disease, but only 39% of colorectal cancers are diagnosed that early.^{1, 5} It is estimated that appropriate testing could save more than half of the expected annual deaths from colorectal cancer.^{5, 6} Yet, rates of screening for colorectal cancer greatly lag behind those for breast and cervical cancer.⁵ What has been demonstrated is that screening for colorectal cancer can reduce colorectal cancer specific mortality, and may in fact reduce the actual incidence of colorectal cancer. This has been shown directly for guaiac fecal occult blood testing (GFOBT),⁷⁻⁹ and is often presumed to be true for colonoscopy since the reduction in mortality in the GFOBT studies was attained via early detection and polypectomy on colonoscopy. However, the actual risk-benefit ratio of colonoscopy as a screening test has not been established in clinical trials.

Fecal Immunochemical Testing (FIT)

The guaiac FOBT (GFOBT) test detects the peroxidase activity of heme either as intact hemoglobin or free heme and is not specific for human hemoglobin. Heme is present in red meat and peroxidase activity is present in fresh fruits and vegetables such as radishes, turnips and broccoli. These foods, therefore, have the potential to produce false-positive results especially when using HemoccultSensa, a GFOBT that has been altered to detect lower levels of peroxidase activity and to improve readability.^{10, 11} FIT, also known as immunochemical fecal occult blood testing (iFOBT), use specific antibodies to human hemoglobin, albumin, or other blood components. Some use monoclonal



and polyclonal antibodies to detect the intact globin protein portion of human hemoglobin. The labeled antibody attaches to the antigens of any human globin present in the stool, resulting in a positive test result.¹² Globin does not survive passage through the upper gastrointestinal tract; therefore, FIT detection of globin is specific for occult bleeding from the large bowel. In addition, FITs do not react with nonhuman globin or with food such as uncooked fruits and vegetables that may have peroxidase activity. Thus, the theoretical advantages of this method over GFOBT include advantages of the test characteristics themselves: higher human hemoglobin sensitivity leading to higher sensitivity for detection of cancerous or pre-cancerous lesions and thus fewer false negatives and higher specificity for human hemoglobin leading to fewer false positive tests and thus fewer unnecessary colonoscopies. The advantages for individuals undergoing the test which could lead to higher rates of screening participation include not having to adhere to dietary restrictions prior to testing, potentially needing fewer samples and in the case of the newer brush-based tests (e.g. InSure), the possible increased ease of obtaining the sample.^{12, 13} The new FIT have already replaced GFOBT in some parts of the world, including Italy, France, Australia and Japan. However, they are not yet being used extensively in the United States. This review intends to examine the existing data for improved test characteristics and participation in screening populations.

TECHNOLOGY ASSESSMENT (TA)

TA Criterion 1: The technology must have final approval from the appropriate government regulatory bodies.

Several FITs have been cleared by the FDA for marketing. To name a few, they are: Innovacon Flipcard™ Fecal Occult Blood Test Device (Innovacon, Inc., San Diego, CA); InSure Quik Fecal Immunochemical Test (Enterix Inc., Edison, NJ); Hemoccult® ICT (Beckman Coulter, Inc., Fullerton, CA); QuickVue® FIT Test (Quidel, San Diego, CA); Hemosure One-Step Immunological Fecal Occult Blood Test (WHPM, Inc., Beverly, MA); Instant-View Fecal Occult Blood Rapid Test (Alfa Scientific Designs, Inc., Poway, CA); Hema Screen Specific FIT (Immunostics, Inc. Ocean, NJ); Monohaem (Silenus Laboratories Proprietary Ltd., Wilmington, DE); Occultech (YD Diagnostics Corp., Annandale, VA). Most commercially available immunochemical tests are CLIA waived.

TA Criterion 1 is met.

TA Criterion 2: The scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes.

The Medline database, Cochrane clinical trials database, Cochrane reviews database and the Database of Abstracts of Reviews of Effects (DARE) were searched using the key words 'colorectal cancer', cross-referenced with the

keywords 'screening' and 'immunochemical'. The search was performed for the period from 1966 through March 2007. The bibliographies of systematic reviews and key articles were manually searched for additional references. The abstracts of citations were reviewed for relevance and all potentially relevant articles were reviewed in full. Although there were many publications in high-risk or mixed-risk populations,¹⁴⁻³⁴ there were only five publications which studied screening in average-risk populations.³⁵⁻³⁹ The bulk of this review will focus on those five studies- their designs are summarized in Table 1.

Level of Evidence: 3, 5

TA Criterion 2 is met

TA Criterion 3: The technology must improve the net health outcomes.

Studies of High-risk Populations

In our review, we encountered 18 published studies of FIT in high-risk populations, ranging from diagnostic accuracy studies to cohort studies.^{14-22, 25-31, 33, 34} The high-risk populations in these studies ranged from those with a family history of colorectal cancer to those undergoing colonoscopy for symptoms; or colorectal cancer surveillance to retrospective studies of those diagnosed with colorectal cancer on endoscopy. The largest two studies were published in 1995 and 2007.^{15, 21} In the 1995 paper, Robinson et al studied GFOBT and FIT (HemeSelect) results for 808 high-risk asymptomatic patients (personal or family history of colorectal cancer or long-standing colitis history) undergoing colonoscopy. This study found a 70% sensitivity for carcinoma and a 44% sensitivity for large (≥ 1 cm) adenoma by FIT, compared to a 33% and 18% sensitivities by GFOBT. In contrast, FIT had a lower overall specificity (88%) compared to GFOBT (98%).²¹ In the recent 2007 paper, Levi et al studied 3-sample FIT (Hemodia OC) results in 1,000 high-risk patients (positive GFOBT, personal or family history of colorectal cancer, symptomatic bowel changes) undergoing colonoscopy; they did not compare the FIT results to those for GFOBT. This study found a sensitivity of 94.1% for cancer and 67% for any significant neoplasia, and a specificity of 87.5% for cancer and 91.4% for any significant neoplasia.¹⁵

Studies of Mixed-risk Populations

Our review found three studies of mixed-risk (high and average/population-based) populations.^{23, 24, 32} In the earliest of these, St. John et al compared the results for two GFOBT (Hemoccult II and Hemoccult II SENSE) and an FIT (HemeSelect) in 1,512 individuals with mixed presentation/risk (107 with colorectal cancer, 50 healthy young subjects, 1,079 subjects with a family history of colorectal cancer, and 276 community volunteers). They found very few cancers or adenomas in the patients without a history of colorectal cancer. In the cancer population they found a high sensitivity for HemeSelect (97.2% compared to 93.5% for Hemoccult SENSE and 88.8% for Hemoccult II), and



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a lower sensitivity for large ($\geq 1\text{cm}$) adenoma (75.6% vs. 60.0% vs. 42.2%).²⁴ In 2000, Rozen et al compared GFOBT (Hemoccult SENSAs) to FIT (FexSure OBT) results for 1410 patients with mixed-risk (screening and symptomatic combined) undergoing colonoscopy or flexible sigmoidoscopy. They found that the sensitive GFOBT was a more sensitive test than FIT for significant neoplasia (carcinoma or adenoma $\geq 1\text{cm}$) – 50% versus 35% - and less specific – 95% versus 99%. These authors concluded that the HemoccultSENSAs was a better test for population based screening.³² Smith et al found the opposite when comparing HemoccultSENSAs to FIT (InSure) in a largely screening population (2,351 average risk and 161 high-risk) who underwent colonoscopy. This study found a sensitivity of 82.4% for cancer and 44.4% for large ($\geq 1\text{cm}$) adenoma using FIT in the screening group as compared to 47.1% and 33.3% using GFOBT in the screening group. It also found a slightly higher false positive rate for FIT compared to GFOBT (3.4% versus 2.5%).²³ This study was unique in that the FIT it studied used the brush-sampling of toilet-bowl water near the stool rather than the spatula technique of directly smearing the stool.

Studies of Screening Populations

In addition to the study described above by Smith et al which did present data separately on a screening population, our review found five other studies which focused on FIT in screening (average risk or community-based) populations. The results of these studies are detailed in Table 2. Two of these studies are essentially very large diagnostic accuracy studies which tested FIT against a gold-standard of colonoscopy.^{37, 38} Both studies had similar findings to those in high-risk populations in that sensitivity was considerably higher for cancers than for large adenomas, and both had sensitivity and specificity for cancer higher than those reported in the earlier GFOBT studies.⁷⁻⁹ Nakama et al compared sensitivity and specificity for 1-sample, 2-sample, and 3-sample FIT and found that there was significant increase in sensitivity with both the 2-sample and 3-sample FIT as compared to the 1-sample, with only small decreases in specificity.

The remaining three studies compared FIT to GFOBT and only had gold-standard colonoscopy results for those participants with a positive test.^{35, 36, 39} Two of these studies followed participants over two-years and assessed disease via registry and medical record data. Allison et al³⁵ found that sensitive GFOBT (Hemoccult II SENSAs) had the highest sensitivity, but lowest specificity for predicting cancer and overall neoplasia; FIT had nearly as good sensitivity and much improved specificity; and use of the FIT as a confirmation test for the sensitive GFOBT performed the best. (See Table 2) However, use of FIT in this manner may not accrue any of the theoretical benefits of improved screening participation. In this study all participants underwent dietary restriction and had 3-samples collected for each test studied. In their evaluation of a population-based screening program in Italy, Zappa et al³⁹ used a proportional incidence analysis to assess the impact of population screening with FIT versus GFOBT (Hemoccult II). In this analysis, the authors use the proportion of the observed two-year incidence of colorectal



cancer in each of the screening groups to the expected two-year incidence of colorectal cancer in the absence of screening to estimate the sensitivity of each screening test. Using this analytic technique, the authors estimate that the sensitivity of the FIT in detecting cancer is much greater than that of the GFOBT (82% versus 50%). Although a creative approach, it is unclear how well this analytic technique accurately estimates test performance. Likewise, in a multivariable regression analysis, the authors estimate more than a two-fold increased rate in interval cancers (cancers diagnosed after a negative screening test) in the GFOBT screened group compared to the FIT screened group. In the last of these studies, Guittet et al³⁶ evaluated a French population-based screening program, evaluating the ratio of sensitivities and ratio of false positive rates for FIT compared with GFOBT (Hemoccult II) at different quantitative hemoglobin cutoffs for the FIT (Immudia). They found that the FIT was most beneficial as compared to the GFOBT at the higher cutoffs of 50 or 75ng/ml rather than the more sensitive 20ng/ml cutoff.

Screening Participation

Our review found two publications evaluating screening participation and FIT. One study⁴⁰, by Ko et al, compared rates of card return to a Veterans Affairs based general medical clinic for FIT (FlexSure OBT, which uses the spatula method of specimen collection) compared to GFOBT (HemoccultSENSA) and found no significant difference in participation rate (48% versus 47%). The other study, by Cole et al, compared participation rates for three randomized groups invited to participate by mail in Australia; screening groups were GFOBT (Hemoccult), and two FIT (FlexSure OBT using spatula sampling method or InSure using brush sampling) .⁴¹ The authors designed this study to assess the impact on participation of 1) no dietary restrictions (FlexSure compared to GFOBT) and 2) easier sampling method (InSure compared to FlexSure). This study found significant difference in participation rates by screening test, with the lowest rate for GFOBT (23.4%) the highest rate for FIT InSure (39.6%) and the rate for FIT FlexSure (30.5%). However, none of the rates in this study were particularly high, and they were all lower than in the VA study by Ko et al.

TA Criterion 3 is met.

Table 1. Published Studies of FIT in Screening Populations

Study (Author, year)	Study Type	Population	FIT	Comparison GFOBT	Gold Standard
Allison, 1996	Cohort; 3 samples; +dietary restrictions	California Kaiser Permanente Screening Population ≥50 N=8,104	HemeSelect	Hemoccult II; Hemoccult II Sensa	Colonoscopy or Flexible sigmoidoscopy only for positive test. Everyone followed for 2 years: Colorectal Cancer or polyp ≥ 1cm in the two years after screening identified in cancer registry / pathology records data.
Nakama 1999	Case Series; 3 samples; No dietary restrictions	Japanese Outpatient Asymptomatic Population ≥ 40 N=4,611	MonoHaem	None	Colonoscopy for all participants
Zappa 2001	Cohort: Biannual screening; Unclear number of samples or dietary restrictions	Italian population-based screening Age 50-70 N=41,774	HemeSelect / Immudia, Hem SP	Hemoccult II	Colonoscopy (or combination colonoscopy and double contrast barium enema) for positive test only Everyone followed for 2 years; neoplasm (CRC or polyp ≥ 1cm)
Morikawa 2005	Case Series; 1 sample; No dietary restrictions	Japanese Outpatient Asymptomatic Population age 20-91 (avg. age 48) N=21,805	Magstream 1000/Hem SP	None	Colonoscopy for all participants
Guittet 2007	Cohort; 2 sample FIT; 3 sample GFOBT; No dietary restrictions	French population-based screening Age 50-74 N=10,304	Immudia, Hem SP	Hemoccult II	Colonoscopy only for positive test.

Table 2. Results of Published Studies of FIT in Screening Populations

Study	Analysis	Disease detection	Results																																								
Allison, 1996 N=8,104	Compared 3-sample FIT to two different 3-sample GFOBTs and to sensitive GFOBT with FIT confirmation (combined); 2 year cancer registry & pathology follow-up	35 cancers 107 polyps \geq 1cm	<table border="0"> <thead> <tr> <th><u>Sensitivity</u></th> <th><u>Cancer</u></th> <th><u>Polyp\geq 1cm</u></th> <th><u>Overall</u></th> </tr> </thead> <tbody> <tr> <td>FIT</td> <td>66.8 (51.1-86.4)</td> <td>66.7 (57.0-76.3)</td> <td>67.2 (58.8-75.5)</td> </tr> <tr> <td>HO</td> <td>37.1 (19.7-54.6)</td> <td>30.8 (21.6-40.1)</td> <td>32.4 (24.3-40.4)</td> </tr> <tr> <td>HOS</td> <td>79.4 (64.3-94.5)</td> <td>68.6 (59.2-77.9)</td> <td>71.2 (63.3-79.1)</td> </tr> <tr> <td>Combined</td> <td>65.6 (47.6-83.6)</td> <td>50.0 (39.8-60.2)</td> <td>53.7 (44.9-62.5)</td> </tr> </tbody> </table> <table border="0"> <thead> <tr> <th><u>Specificity</u></th> <th><u>Cancer</u></th> <th><u>Polyp\geq 1cm</u></th> <th><u>Overall</u></th> </tr> </thead> <tbody> <tr> <td>FIT</td> <td>94.4 (93.8-94.9)</td> <td>95.2 (94.7-95.7)</td> <td>95.2 (94.7-95.7)</td> </tr> <tr> <td>HO*</td> <td>97.7 (97.3-98.0)</td> <td>98.1 (97.7-98.4)</td> <td>98.1 (97.7-98.4)</td> </tr> <tr> <td>HOS**</td> <td>86.7 (85.9-87.4)</td> <td>87.5 (86.7-88.2)</td> <td>87.5 (86.7-88.2)</td> </tr> <tr> <td>Combined</td> <td>97.3 (96.9-97.6)</td> <td>97.9 (97.6-98.2)</td> <td>97.9 (97.6-98.2)</td> </tr> </tbody> </table>	<u>Sensitivity</u>	<u>Cancer</u>	<u>Polyp\geq 1cm</u>	<u>Overall</u>	FIT	66.8 (51.1-86.4)	66.7 (57.0-76.3)	67.2 (58.8-75.5)	HO	37.1 (19.7-54.6)	30.8 (21.6-40.1)	32.4 (24.3-40.4)	HOS	79.4 (64.3-94.5)	68.6 (59.2-77.9)	71.2 (63.3-79.1)	Combined	65.6 (47.6-83.6)	50.0 (39.8-60.2)	53.7 (44.9-62.5)	<u>Specificity</u>	<u>Cancer</u>	<u>Polyp\geq 1cm</u>	<u>Overall</u>	FIT	94.4 (93.8-94.9)	95.2 (94.7-95.7)	95.2 (94.7-95.7)	HO*	97.7 (97.3-98.0)	98.1 (97.7-98.4)	98.1 (97.7-98.4)	HOS**	86.7 (85.9-87.4)	87.5 (86.7-88.2)	87.5 (86.7-88.2)	Combined	97.3 (96.9-97.6)	97.9 (97.6-98.2)	97.9 (97.6-98.2)
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<p>Morikawa 2005 N=21,805</p>	<p>Assessed 1-sample FIT with gold standard colonoscopy in all participants</p>	<p>79 cancers 648 adenomas and high grade dysplasia</p>	<table border="0"> <thead> <tr> <th>Sensitivity</th> <th>Cancer</th> <th>Polyp\geq 1cm and high grade dysplasia</th> </tr> </thead> <tbody> <tr> <td>FIT</td> <td>65.8 (55.4-76.3)</td> <td>27.1 (23.9-30.3)</td> </tr> <tr> <th>Specificity</th> <th>Cancer</th> <th>Polyp\geq 1cm and high grade dysplasia</th> </tr> <tr> <td>FIT</td> <td>94.6 (94.3-94.9)</td> <td>95.1 (94.8-95.4)</td> </tr> </tbody> </table>	Sensitivity	Cancer	Polyp \geq 1cm and high grade dysplasia	FIT	65.8 (55.4-76.3)	27.1 (23.9-30.3)	Specificity	Cancer	Polyp \geq 1cm and high grade dysplasia	FIT	94.6 (94.3-94.9)	95.1 (94.8-95.4)												
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TA Criterion 4: The technology must be as beneficial as any established alternatives.

There are several clinically accepted alternatives for screening for colorectal cancer, including colonoscopy, flexible sigmoidoscopy, double contrast barium enema, and GFOBT. All of these methods are equally endorsed by the US Preventive Services Task Force and the American Cancer Society.^{4, 42} There have been randomized control trials which have established that screening for colorectal cancer, at least with GFOBT, saves lives.⁷⁻⁹ It is widely assumed that this decrease in mortality due to GFOBT was gained via colonoscopy, and thus that screening with colonoscopy also saves lives.^{3, 42} None of the published FIT studies have assessed mortality. However, any mortality benefit would be gained, just as it is with GFOBT, via colonoscopic evaluation in positive screened cases to find and treat pre-cancerous lesions and early-stage cancers early. Given the data from the large observational trials, it appears that FIT is at least as good as, if not better than, GFOBT at accurately identifying significant neoplasia.

TA Criterion 4 is met.

TA Criterion 5: The improvement must be attainable outside the investigational settings.

Three of the five studies in screening populations evaluated large-scale screening programs that were already in place outside of the research setting. Two of these were in communities in France and Italy,^{36, 39} and one in an outpatient clinical setting in Japan.³⁷

TA Criterion 5 is met.

CONCLUSION

In conclusion, the various FIT that have been studied around the world do appear to be more sensitive and only a little less specific than the traditional Hemocult II GFOBT. They also appear to be more specific than the sensitive GFOBT, HemocultSENSA. In this regard, they have test characteristics that are somewhat improved over GFOBT.

However, in regard to their theoretical advantage of being easier to use and therefore improving participation rate, the data is limited. The randomized clinical trials (RCT) which did show higher participation rates, particularly for the brush-sampling technique of the InSure FIT, had low overall participation rates; while the other study with better overall participation rates did not show any improvement in participation rates. Thus, while the theoretical



advantages may make a difference for some, there may be others for whom the sampling requirements of either type of FOBT will remain too challenging to participate in, even without dietary restrictions, and particularly with the spatula method of sampling.

Other areas of uncertainty remain in the best use of FIT. Studies have focused on different specific tests and it is not clear that they are all equivalent. In addition to differences in sampling technique (most of the studies have been of spatula-sampling methods and not of the brush-sampling method), there may also be differences in assays and cutoff points which could make the results not generalizable to all FIT brands. It is encouraging, however, that all of the studies of screening populations show positive results for FIT in terms of sensitivity and specificity, despite differences in brands studied. Only one study evaluated the number of samples necessary for best results, and it appears that two samples are better than one. Both this finding and the early work on hemoglobin concentration cutoffs for positivity deserve further study for a uniform recommendation regarding the best use of these tests.

RECOMMENDATION

It is recommended that use of Fecal Immunochemical Tests (FIT) as a screening modality for colorectal cancer annually in individuals for whom screening is clinically appropriate and recommended meets CTAF criteria 1-5 for safety, effectiveness and improvement in health outcomes.

The CTAF panel voted unanimously in favor of this recommendation.

June 20, 2007



RECOMMENDATIONS OF OTHERS

Blue Shield Blue Cross Association (BCBSA)

In 2004 the BCBSA Technology Evaluation Center conducted an assessment of this technology. The Medical Advisory Panel determined that TEC criteria were not met.

Centers for Medicare and Medicaid Services (CMS)

In November 2003, CMS issued a National Coverage Determination on Screening Immunoassay Fecal Occult Blood Test.. “CMS concludes that there is adequate evidence to determine that the immunoassay fecal occult blood test (FIT) is an appropriate and effective colorectal cancer screening fecal occult blood test for Medicare beneficiaries aged 50 years and older.”

American Gastroenterological Association (AGA)

The AGA provided opinion in support of the use of this technology and testimony at the meeting.

American Cancer Society (ACS)

Cancer Screening in the United States, 2007, A Review of Current Guidelines, Practices, and Prospects was published this year and is available online at www.caonline.amcancersoc.org. The recommendations for colorectal screening support the use of FIT or gFOBT as part of a screening program.

Association of Northern California Oncologists (ANCO)

ANCO has indicated that it does not have a position regarding the use of this technology and that a representative will not attend the meeting. In addition, the American Society of Clinical Oncology does not have a policy or guideline statement on this specific technology.

Medical Oncology Association of Southern California (MOASC)

MOASC has provided an opinion in favor of the use of this technology. A representative was not available to provide testimony at the meeting.

United States Preventive Health Services Task Force (USPSTF)

The USPSTF Screening for colorectal cancer: recommendations and rationale was published in the Annals of Internal Medicine in 2002 and is available online at www.guideline.gov. There is no mention of FIT in the recommendation. However, the guideline notes: “Proven methods of FOBT screening use guaiac-based test cards prepared at home by patients from three consecutive stool samples and forwarded to the clinician.”



American Academy of Family Physicians (AAFP)

The AAFP recommends colorectal cancer screening for men and women 50 years of age or older. The AAFP references the USPSTF guideline.

American Society of Gastrointestinal Endoscopy (ASGE)

ASGE guideline: colorectal cancer screening and surveillance (2006) speak of FOBT in general terms and do not specifically refer to FIT technology.

Multispecialty guideline:

Colorectal cancer screening and surveillance: clinical guidelines and rationale-update based on new evidence published in the journal *Gastroenterology* 2003 is available at www.guideline.gov. This guideline does not differentiate between gFOBT and FIT in its recommendation. This guideline was developed by the American College of Gastroenterology, the American College of Physicians, the American Gastroenterological Association Institute, and the American Society for Gastrointestinal Endoscopy.

World Health Organization recommendation for choice of FOBT:

At present, there is no extensively studied FOBT that fulfills the needs for all target populations worldwide. Choice of FOBT should take into account population dietary compliance and colonoscopy resources: The more sensitive newer tests should be used if dietary compliance is good (in the case of guaiac tests) and colonoscopy resources are adequate for diagnostic workup of people who test positive. Immunochemical tests remove the difficulties created by diet and drug restrictions and are more amenable to standardized development and quality control. (Young GP, St. John JB, Winawer SJ, et al.: Choice of fecal occult blood tests for colorectal cancer screening: recommendations based on performance characteristics in population studies. *Am J Gastroenterol* 2002, 97:2499–2507.)

ABBREVIATIONS USED IN THIS ASSESSMENT:

FIT: Immunochemical Fecal Occult Blood Testing

DARE: Database of Abstracts of Reviews of Effects

FIT: Fecal Immunochemical Tests

RCT: Randomized Clinical Trials

GFOBT: Guaiac Fecal Occult Blood Testing

ELISA test: Enzyme-linked Immunosorbent Assay

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