

# High Quality Fecal Occult Blood Testing (FOBT) for CRC Screening: Evidence and Recommendations

## **Rationale for use of FOBT**

High sensitivity fecal occult blood testing (FOBT) is one of the colorectal cancer screening methods recommended in guidelines from the American Cancer Society, the US Preventive Services Taskforce, and every other major medical organization. In spite of this widespread endorsement, primary care clinicians often express conviction that colonoscopy is the “gold standard” test for colorectal cancer screening and that the use of FOBT represents sub-standard care. These beliefs persist in spite of well-documented shortcomings of endoscopy (missed adenomas and cancers, higher complication rates and higher one-time costs than other screening methodologies), and the fact that access to endoscopy is limited or non-existent for a significant proportion of the U.S. population. Many clinicians are also unaware that randomized controlled trials of FOBT screening have demonstrated decreases in colorectal cancer incidence and mortality, and modeling studies suggest that the years of life saved through a high quality FOBT screening program are essentially the same as with a high quality colonoscopy based screening programs.

Recent advances in stool blood screening include the emergence of new tests and improved understanding of the impact of quality factors on testing outcomes. This document provides state-of-the-science information about high quality stool testing.

## **Types of Fecal Occult Blood Tests**

Two main types of FOBT are available – *guaiac* and *immunochemical*. Both types of FOBT have been shown to have reasonably high detection rates for colon and rectal cancers; adenoma detection rates are appreciably lower.

Guaiac-based tests have been the most commonly used in the U.S., and are the type that were used in the randomized controlled trials of colorectal cancer screening that demonstrated incidence and mortality reductions. Recent studies have found strikingly better test performance with modern, high sensitivity forms of the guaiac test (such as Hemoccult Sensa) than with older versions (Hemoccult II and others).

<b>Guaiac-based FOBT version</b>	<b>Sensitivity for Cancer*</b>	<b>Sensitivity for Adenomas*</b>
Hemoccult Sensa (high-sensitivity)	50% – 79%	21% - 35%
Hemoccult II	13% - 50%	8 % - 20%

These differences are so significant that screening guidelines now specify that only high sensitivity forms of guaiac-based tests (like Hemoccult Sensa) should be used

\*Sensitivities cited are based on review of studies that used colonoscopy as the reference standard to determine FOBT performance characteristics.

for colorectal cancer screening. Hemoccult II and similar older guaiac tests should no longer be used for colorectal cancer screening.

An alternative to guaiac-based testing is provided by *Fecal Immunochemical Tests* or “FIT”. Like guaiac-based FOBT, these tests look for hidden blood in the stool. FIT target a different portion of the hemoglobin molecule and use a different mechanism of action than do guaiac tests, making FIT more specific for human blood and for bleeding from the lower GI tract. Therefore colorectal cancer screening using FIT results in fewer false positive tests. Studies suggest that detection rates for cancer and adenomas with most FIT are similar to those achieved with high sensitivity guaiac tests like Hemoccult Sensa; both are significantly better than Hemoccult II and similar older tests.

Type of FOBT	Sensitivity for Cancer	Sensitivity for Adenomas
Immunochemical Tests (FIT)	55% – 100%	15% - 44%
High sensitivity guaiac-based tests (Hemoccult Sensa)	50% – 79%	21% - 35%

There are a number of different brands of FIT sold in the U.S., and there is no consensus that one brand is superior to another. There is some evidence that patient adherence with FIT may be higher than with guaiac FOBT; this may be a result of fewer demands placed on patients (no need for dietary and medication restrictions, and only 1 or 2 specimens required with some brands).

There are differences in cost and reimbursement between guaiac tests and FIT. Medicare currently pays \$4.61 for colorectal cancer screening using 3 specimens collected and analyzed with guaiac-based FOBT, compared to \$22.53 for screening done by FIT. However, materials for collection and processing of FIT are more expensive than the materials for guaiac-based testing. The effect of this differential varies at the practice level. Manufacturers and vendors of some brands of FIT sell test materials to individual practices, leaving test processing and patient billing in the hands of the practice. Test kits for other brands are provided to practices at no charge. These kits are returned to a reference laboratory for processing and the laboratory bills patients or their insurance company.

At present the use of FIT by U.S. physicians and patients is low. However, two major U.S. laboratories (LabCorp and Quest Labs) recently eliminated their use of guaiac tests, and now supply and process only immunochemical tests. This change may lead to a substantial increase in utilization of FIT in the U.S.

### **Quality Issues in Stool-Based Screening**

Regardless of the type of stool test selected, it is important to remember that these tests attain their full value not from one-time use as a screening test but through

\*Sensitivities cited are based on review of studies that used colonoscopy as the reference standard to determine FOBT performance characteristics.

repeat testing over time (a *program* of screening). In optimal circumstances, a correctly performed high sensitivity FOBT (immunochemical or guaiac) will detect fifty to eighty percent of cancers of the colon or rectum; adenoma detection rates are substantially lower. The potential for missing up to half of cancers present at the time of screening may raise concern unless one keeps in mind that no organization advocates the use of one-time fecal testing for colorectal cancer screening. Instead, all guidelines stress the importance of *annual* testing. Taking advantage of the relatively slow time of progression from adenoma to invasive cancer, testing on an annual basis significantly improves the likelihood of lesion detection over time. Indeed, modeling studies suggest that the potential years of life saved through a high-quality FOBT screening program are essentially the same as with a high quality colonoscopy-based screening program.

Despite the proven value of stool testing in reducing colorectal cancer incidence and mortality there are challenges to the integrity of stool-based screening as it is currently applied in clinical practice. In order to achieve the test and program sensitivity levels discussed above it is imperative that fecal occult blood testing be performed correctly. Manufacturers' instructions for most tests available in the U.S. recommend home collection of stool samples. Multiple samples are also recommended for most of these tests. This approach helps address the intermittent pattern of bleeding demonstrated by many cancers and adenomas. Failure to collect and analyze multiple specimens markedly limits the effectiveness of guaiac FOBT. This was clearly illustrated by a well-designed study which compared the sensitivity of guaiac-based fecal testing of a single sample of stool obtained during a digital rectal exam (DRE) with the findings from three specimens collected at home by the same patients. All patients subsequently underwent colonoscopy. The results of this study were startling. Less than 1 out of 20 of the cancers and significant adenomas found at colonoscopy were detected by the single stool sample obtained at DRE. Detection rates were more than four times greater using the recommended three card home collection method. Similar studies have not been performed with immunochemical tests, but there is no evidence to suggest that in-office sampling with this method is an effective approach to colorectal cancer screening.

Unfortunately FOBT screening in the U.S. is not always performed in the prescribed manner. Investigators from the National Cancer Institute and the Centers for Disease Control and Prevention recently surveyed more than twelve hundred primary care physicians across the U.S. regarding their practices around fecal testing and follow up. Twenty-five percent of respondents who order FOBT for colorectal cancer screening use exclusively in-office FOBT; an additional fifty-three percent use in-office testing in some cases. In addition, although guidelines unequivocally recommend colonoscopy for follow up of all positive FOBTs, studies have found that up to a third of patients who have been told by their physician of a positive FOBT report that their doctor followed this positive with a repeat FOBT, or they had **no** diagnostic work-up for this finding.

### **Characteristics of High Quality FOBT Screening Programs**

On the basis of the evidence discussed above guidelines from the American Cancer Society, the US Preventive Services Taskforce, and other organizations endorse the use of either a high sensitivity guaiac-based FOBT or an FIT for the prevention and early detection of colorectal cancer, within the context of a high quality program of screening.

High quality FOBT screening programs are characterized by the following features:

<b>Quality Characteristic</b>	<b>Rationale</b>
Use only high sensitivity guaiac-based FOBTs (such as <i>Hemoccult Sensa</i> ) or fecal immunochemical tests (FIT).	Sensitivity for cancer is 2-3 times higher with high sensitivity guaiac tests or FIT when compared to older stool guaiac tests (such as Hemoccult II) in most studies.
Eliminate the use of Hemoccult II and other older forms of guaiac-based FOBT.	Sensitivity for cancer is less than 25% in many studies of Hemoccult II (compared to sensitivity of >50% for highly sensitive guaiac-based tests and FIT)
Never use in-office FOBT at the time of digital rectal exam as a screening test for colorectal cancer.	Studies have shown that a guaiac FOBT obtained on a single stool sample obtained at the time of in-office digital rectal exam may miss up to 95% of cancers and significant adenomas. There is no evidence that this would be an appropriate method for collection of stool for FIT either.
Perform tests only on stool specimens collected by patients at their home; the number of specimens to be collected and the collection process should follow manufacturers' recommendations.	Studies that demonstrated decreases in incidence and mortality with FOBT screening utilized home collection and analysis of specimens based on manufacturers' instructions.
Repeat stool tests annually.	One-time use of a highly sensitive guaiac test or FIT may miss up to 50% of cancers (and a higher proportion of adenomas). Annual testing significantly improves lesion detection over time.
Follow up all patients with positive stool tests with colonoscopy.	Stool-based screening results in decreased colorectal cancer incidence and mortality only when screen-detected abnormalities are assessed and managed appropriately.

## **Conclusion**

Screening with high sensitivity FOBT (guaiac or immunochemical) can lead to decreases in colorectal cancer incidence and mortality. However, getting the best results from any screening test requires that the test be used as directed, and screen detected abnormalities be assessed and managed appropriately. Modern forms of FOBT hold promise, but there is considerable room for improvement in both the utilization of these tests and the follow up of abnormal findings. Clinicians can substantially improve the outcomes of stool-based screening by switching to a high sensitivity guaiac-based FOBT or FIT, and by incorporating additional key quality elements into their practices.

For additional information please visit:

[cancer.org/colonmd](http://cancer.org/colonmd) and [ncrt.org/about/provider-education/crc-clinician-guide/](http://ncrt.org/about/provider-education/crc-clinician-guide/)

## **References**

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