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# Eliminating Inpatient Stool Guaiac Testing

## Quality Improvement Initiative

Stool guaiac or FOBT (fecal occult blood test) is commonly misused in the hospital to evaluate for gastrointestinal bleeding. This test is FDA approved only for the indication of outpatient colorectal cancer screening in asymptomatic individuals. We are advocating for the elimination of stool guaiac testing from the inpatient EMR. Extensive research has been published that highlights the harms of inappropriate testing, which has been the basis for eliminating the inpatient use of stool guaiac testing at many academic centers, including Parkland Health (Dallas, TX), Baylor College of Medicine, University of Missouri-Kansas City, and SSM Saint Louis University Hospital, to name a few.

## Problems with Inpatient FOBT

1. High false negative rate (30-50%) and false positive rate (12-30%)
2. Inappropriately used to evaluate for occult GI bleeding
3. Delays in appropriate care and gastroenterology consultation
4. Promotes the misconception that inpatient guaiac testing guides GI decision making regarding endoscopic evaluation

## "First, Do No Harm" – Review of the Evidence

- In one study of 2700 patients, FOBT results did not correlate with the presence of upper GI pathology. Of patients who presented with overt GI bleeding, gastroenterology consultation was delayed while awaiting FOBT results in 27% of patients *with observed melena or hematochezia.* (Chiang et al, 2011)
- A large study which reviewed 31,000 inpatient guaiac tests at Parkland Health found that only 0.5% of positive FOBT were ordered for the approved indication of CRC screening. (Gupta et al, 2018)
- Regarding the evaluation of iron deficiency anemia, the most recent AGA (American Gastroenterological Association) guidelines recommend proceeding with bidirectional endoscopy for the gastrointestinal evaluation of IDA and note that "Evidence on use of fecal occult blood testing to determine need for endoscopic evaluation is lacking". (Ko et al, 2020)

## What should we do instead?

History, physical exam (including digital rectal exam), monitor hemoglobin trend, BUN/Cr ratio, visual inspection of stool, clinical decision-making tools (i.e. Glasglow-Blatchford scores). If gastrointestinal bleeding or occult blood loss from the GI tract is suspected (i.e. iron deficiency anemia), the next step in evaluation should be consultation with a gastroenterologist to determine whether endoscopic evaluation is indicated.

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# CLINICAL PRACTICE GUIDELINES

## AGA Clinical Practice Guidelines on the Gastrointestinal Evaluation of Iron Deficiency Anemia

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This document presents the official recommendations of the American Gastroenterological Association (AGA) on the gastrointestinal evaluation of iron deficiency anemia (IDA). The guideline was developed by the AGA Institute's Clinical Guidelines Committee and approved by the AGA Governing Board. It is accompanied by a technical review that provides a detailed synthesis of the evidence from which these recommendations were formulated.[1] For a better understanding of this guideline, we recommend reading the accompanying technical review. The technical review, guideline, and clinical decision support tool are available on the AGA website (www.gastro.org) free of cost.

Development of this guideline and the accompanying technical review was fully funded by the AGA Institute without additional outside funding. Members of the Guideline Panel and Technical Review Panel were selected by the AGA Clinical Guidelines Committee Chair after careful consideration of all relevant conflict of interests and in accordance with the National Academy of Medicine (formerly the Institute of Medicine) standards for trustworthy guidelines. The guideline and accompanying technical review underwent independent peer review and were disseminated broadly during the 30-day open public comment period; comments were collated by the AGA staff and were reviewed and carefully considered by the Guideline Panel and technical review teams, respectively. All comments were addressed in an internal response document or incorporated as revisions to the final documents. In accordance with the Clinical Guidelines Committee policies, all clinical guidelines are reviewed annually at the AGA Clinical Guideline Committee meeting for new information. The next update for these guidelines is anticipated 3 years from publication (2023).

Anemia is a common diagnosis in both men and women, and iron deficiency is the most common cause of anemia worldwide. In the United States in 1999–2000, 2% of men aged 16–69 years, 12% of women aged 12–49 years, and 9% of women aged 50–69 years were iron deficient, and 4% of women aged 20-49 years and 3% of women aged 50-69 years had IDA.[2] The overall prevalence of IDA in North America in 2010 was estimated at 2.9%.[3] The etiology of IDA can include suboptimal oral intake, poor absorption of oral iron, and/or chronic blood loss from gastrointestinal and other sources. Gastrointestinal malignancy is the most serious potential cause, although other etiologies, such as peptic ulcer disease, celiac disease, inflammatory bowel disease, or other gastrointestinal tract lesions, can be detected and treated, potentially improving quality of life and patient-important outcomes.

Normal total body iron content varies between 3000 and 4000 mg, the majority of which is found in red blood cells (ie, in hemoglobin); a smaller amount of iron is found in storage compartments, including hepatic macrophages, resident bone marrow cells, and others. Iron is also bound to transferrin and other proteins, such as myoglobin, or in its storage forms as ferritin or hemosiderin. Most dietary iron absorption occurs in the duodenum and proximal jejunum. About 1–2 mg of iron is lost daily through desquamation of skin and enteric cells or through minor blood loss, which in normal individuals is balanced through intestinal absorption of dietary iron. Excess iron loss can occur through gastrointestinal bleeding, urinary losses, shedding of skin cells, or other sources of blood loss (eg, menstrual bleeding). In most adults without an obvious source of blood loss, evaluation of the gastrointestinal tract for a source of chronic blood loss or a malabsorptive process is indicated.

There is significant practice variability in the initial gastrointestinal evaluation of IDA, with uncertainty about the proper diagnostic criteria for iron deficiency in patients with anemia, the type and sequence of diagnostic evaluation with endoscopy or noninvasive testing, the utility of investigations, such as routine gastric biopsies to detect *Helicobacter pylori* infection or autoimmune atrophic gastritis,

***Abbreviations used in this paper:*** **AGA, American Gastroenterological Association; CI, confidence interval; GRADE, Grading of Recommendations Assessment, Development and Evaluation; IDA, iron deficiency anemia; PICO, population, intervention, comparator, outcome.**

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and the need for routine duodenal biopsies to detect celiac disease. In addition, the proper diagnostic evaluation likely differs according to the underlying risk of serious gastrointestinal diseases, such as malignancy, in men and women of different ages. The aim of this guideline is to outline an evidence-based approach to the initial diagnosis and evaluation of this commonly encountered clinical condition.

## Scope

In developing this guideline, the Panel prioritized clinical questions focused on the diagnosis of IDA as well as the initial gastrointestinal evaluation of chronic IDA. The target audience for this guideline includes health care professionals (primary care providers, gastroenterologists, and other specialists), policy makers, and patients. This guideline does not provide recommendations for evaluation of patients with refractory IDA despite appropriate initial evaluation and iron supplementation or recurrent IDA after initial iron repletion, due to the lack of robust evidence in the medical literature in these clinical scenarios. In patients with refractory IDA, consultation with hematology may be appropriate. In addition, management of obscure gastrointestinal bleeding, defined as persistent or recurrent bleeding of unknown origin after an appropriate endoscopic evaluation, is outside the intended scope of this guideline.

## Methods

The guideline was developed as described previously.[4] Briefly, the AGA process for developing clinical practice guidelines incorporates Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology and best practices as outlined by the National Academy of Medicine, formerly Institute of Medicine.[5] As described in detail in the technical review accompanying this guideline, clinically relevant questions for diagnosis and management of IDA were identified and framed using the PICO format, which defines a specific population (P), intervention (I), comparator (C), and outcome (O). Using the GRADE framework, recommendations are formulated based on the strength of the available evidence (Table 1), risks and benefits of different management pathways, patient preferences and values, and resource use (Table 2).[4] Optimal understanding of this guideline will be enhanced by reading applicable portions of the technical review.[1] The Guideline Panel and the authors of the technical review met face-to-face on April 30, 2019 and via teleconference on October 7, 2019 to discuss the findings from the technical review and develop the recommendations. All recommendations were based on consensus among the Guideline Panel members and voting was not performed. After the meeting, the Guideline Panel independently finalized the recommendations in this guideline document. The recommendations, quality of evidence, and strength of recommendations are summarized in Table 3.

## Recommendations

**In patients with anemia, the AGA recommends using a cutoff of 45 ng/mL over 15 ng/mL when using ferritin to diagnose iron deficiency. *Strong recommendation, high-quality evidence*.**
**Comment: In patients with inflammatory conditions or chronic kidney disease, other laboratory tests such as C-reactive protein, transferrin saturation, or soluble transferrin saturation, may be needed in conjunction with ferritin to diagnose iron deficiency anemia.**

In adults with anemia, defined as hemoglobin <13 g/dL in men and <12 g/dL in nonpregnant women,[6] determining whether the anemia is due to iron deficiency is an important step to guide appropriate diagnostic evaluation, as the evaluation of anemia without iron deficiency will differ substantially. Serum ferritin is the most commonly used test for diagnosing iron deficiency, with proposed cutoff values ranging from 15 to 100 ng/mL. Studies that use bone marrow biopsy as the gold standard for diagnosis of iron deficiency have defined the sensitivity and specificity of ferritin levels at different cutoff values. The choice of an optimal cutoff value involves a tradeoff between sensitivity and specificity at different ferritin levels. Therefore, the Technical Review Panel aimed to determine the optimal cutoff value of ferritin that would identify most patients who truly have iron deficiency (eg, maximizing sensitivity), while also providing an acceptable false-positive rate (eg, acceptable specificity) so as to best define the appropriate population in which evaluation is warranted. Optimizing the threshold ferritin level with high sensitivity will detect the great majority of patients who are truly iron deficient, minimize delays in diagnostic workup, and minimize the number of patients in whom serious underlying etiologies, such as gastrointestinal malignancy,

**Table 1.** Grading of Recommendations Assessment, Development and Evaluation Definitions for Quality of Evidence (or Certainty of Evidence)

| Quality of evidence | Definition |
|---|---|
| High | We are very confident that the true effect lies close to that of the estimate of the effect. |
| Moderate | We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. |
| Low | Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect. |
| Very Low | We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect |

**Table 2.** Grading of Recommendations Assessment, Development and Evaluation Definitions for Strength of Recommendation

| Strength of recommendation | For the patient | For the clinician |
|---|---|---|
| Strong | Most individuals in this situation would want the recommended course of action and only a small proportion would not. | Most individuals should receive the recommended course of action. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences. |
| Conditional | The majority of individuals in this situation would want the suggested course of action, but many would not. | Different choices will be appropriate for different patients. Decision aids may be useful in helping individuals in making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working towards a decision. |

might be missed. However, there are potential downsides or harms associated with evaluation of IDA, including adverse events from endoscopic procedures and higher health care utilization and cost. Therefore, the chosen threshold level also needs to have adequate specificity to minimize the number of false-positive diagnoses.

As outlined in the technical review, based on a systematic review of 55 studies, a ferritin threshold value of <45 ng/mL has a sensitivity for iron deficiency of 85% (95% confidence interval [CI], 82%–87%) with a specificity of 92% (95% CI, 91%–94%).[7] In contrast, a ferritin value of <15 ng/mL has a sensitivity of only 59% (95% CI, 55%–62%) and specificity of 99% (95% CI, 89%–99%). A ferritin threshold value of <45 ng/mL was believed to maximize sensitivity for the diagnosis of IDA with an acceptable number of false-positive diagnoses. The tradeoff between higher sensitivity and lower specificity using a threshold of 45 ng/mL instead of 15 ng/mL was believed to provide an acceptable balance of benefits of fewer missed diagnoses compared with potential harms of additional diagnostic evaluations.

In some patients, such as those with chronic inflammatory conditions or chronic kidney disease, ferritin levels may not accurately reflect body iron stores. In these situations, other clinical tests, such as the serum iron, transferrin saturation, soluble transferrin receptor, or C-reactive protein, may be useful adjunctive tests to assist in the diagnosis of iron deficiency. We did not specifically address threshold ferritin values to diagnose iron deficiency in non-anemic patients. In addition, some patients with or without iron deficiency may have gastrointestinal symptoms that would necessitate endoscopic evaluation regardless of the diagnosis of iron deficiency.

The overall quality of evidence for this recommendation was rated as high. The underlying studies are potentially at risk for bias because of the patient populations included, which did not clearly differentiate between symptomatic and asymptomatic patients.

**In asymptomatic postmenopausal women and men with iron-deficiency anemia, the AGA recommends bidirectional endoscopy over no endoscopy. *Strong recommendation, moderate-quality evidence*.**

The AGA recommends bidirectional endoscopy, including both esophagogastroduodenoscopy and colonoscopy, over no endoscopy to evaluate asymptomatic postmenopausal women and men with IDA. Bidirectional endoscopy should be performed at the same setting in these patients. This recommendation does not apply to patients who may have gastrointestinal symptoms; these patients should be evaluated by integrating the symptoms into the clinical picture. In addition, this recommendation assumes there is no other unequivocal explanation for IDA, particularly in young men, after a thorough history and physical examination. Underlying etiologies, such as frequent blood donation, nutritional deficiencies (eg, vegan or vegetarian diet), nongastrointestinal blood loss, and malabsorption syndromes should be considered and evaluated as indicated.

The Technical Review Panel identified no comparative studies of the outcomes of bidirectional endoscopy vs simple clinical observation or empiric oral iron therapy alone in any patient population. Therefore, the Guideline Panel relied on indirect evidence in formulating this recommendation. Evidence was derived from observational cohort and cross-sectional studies of the frequency of gastrointestinal findings in patients with IDA, randomized studies of endoscopic screening for colorectal cancer, and studies evaluating the risks of complications after endoscopic procedures. Pooled estimates from 18 studies on the diagnostic yield of bidirectional endoscopy in postmenopausal women and men with IDA showed detection of lower gastrointestinal malignancy in 8.9% (95% CI, 8.3%–9.5%) and upper gastrointestinal malignancy in 2.0% (95% CI, 1.7%–2.3%) of individuals.[1] These studies likely overestimate the underlying prevalence of malignancy because of referral bias and inclusion of symptomatic as well as asymptomatic patients. However, the overall evidence strongly suggests that the underlying risk of malignancy is several-fold higher than in an asymptomatic colorectal cancer screening cohort. As a

comparison, a recent meta-analysis found a prevalence of colorectal cancer of 0.8% (95% CI, 0.4%–0.7%) in individuals age 50 years and older.[8]

High-quality evidence from randomized controlled trials of flexible sigmoidoscopy[9,10] showed that endoscopic screening reduces colorectal cancer incidence and mortality. Indirectly, this suggests that detection of colorectal cancer through endoscopic evaluation of patients with IDA is important, particularly with the ongoing advances in therapy for colorectal cancer and subsequent improvements in survival. Although data on the stage distribution of gastrointestinal tract malignancy in patients with IDA are lacking, it is plausible that overall stage distribution will be somewhat later than in an asymptomatic screening cohort, potentially attenuating the benefits of earlier diagnosis seen in screening populations. There is no comparable direct evidence applicable to screening for upper gastrointestinal malignancy. Nevertheless, detection of colorectal or upper gastrointestinal cancer is a patient-important outcome regardless of its impact on mortality.

Bidirectional endoscopy is invasive, but the overall risk of complications is small for both upper endoscopy and colonoscopy.[11–16] In men and women older than 50 years, screening colonoscopy is already recommended in patients regardless of the presence of anemia, and the added risk of an upper endoscopy is likely minimal. Overall, the high prevalence of gastrointestinal malignancy in IDA suggests that endoscopic evaluation will lead to detection of malignancy with potential for improvement in cancer outcomes, particularly for colorectal cancer. Lastly, other potential etiologies, such as erosive esophagitis, peptic ulcer disease, celiac disease, and inflammatory bowel disease, may be detected by bidirectional endoscopy. The benefits of detection of gastrointestinal disorders and malignancy in this patient population were thought to outweigh the small risks of bidirectional endoscopy.

The overall quality of evidence for this recommendation was moderate, and its rating was downgraded for indirectness due to availability of only observational studies of the diagnostic yield of bidirectional endoscopy and differences in patient population compared to the randomized trials of screening flexible sigmoidoscopy. Studies of diagnostic yield of bidirectional endoscopy are at risk of bias due to potential referral bias.

**In asymptomatic premenopausal women with iron deficiency anemia, the AGA suggests bidirectional endoscopy over iron replacement therapy only. *Conditional recommendation, moderate-quality evidence*.**
**Comment: Patients who place a high value on avoiding the small risk of endoscopy, particularly those who are young and might have other plausible reasons for iron deficiency anemia, and a low value on the very small risk of missing a gastrointestinal malignancy would reasonably select an initial course of iron replacement therapy and no initial bidirectional endoscopy.**

The AGA suggests bidirectional endoscopy over iron replacement therapy alone for asymptomatic premenopausal women with IDA. This recommendation assumes that there is no other unequivocal explanation for IDA, particularly in younger women, after a thorough history and physical examination. Similar to postmenopausal women and men, etiologies such as frequent blood donation; other sources of blood loss, including menstrual blood loss, malabsorption syndromes; and nutritional deficiencies should be considered and investigated as indicated. Women with gastrointestinal symptoms should be evaluated as appropriate. In these patients, bidirectional endoscopy should be performed in the same setting.

In the technical review, no randomized studies comparing bidirectional endoscopy with iron replacement therapy in this patient population were identified, and the Guideline Panel relied on observational studies of the diagnostic yield of endoscopic evaluation and the harms of endoscopic evaluation to formulate this recommendation. Pooled evidence from 10 studies showed detection of lower gastrointestinal malignancy in 0.9% (95% CI, 0.3%–1.9%) and upper gastrointestinal malignancy in 0.2% (95% CI, 0%–0.9%) of premenopausal women with IDA. These are likely overestimates of the underlying prevalence of malignancy due to inclusion of symptomatic patients in the study cohorts. As a comparison, a recent meta-analysis found a prevalence of colorectal cancer of 0.1% (95% CI, 0%–0.1%) in individuals younger than 50 years, but did not estimate incidence separately for men and women.[8] It should also be noted that the incidence of colorectal cancer has increased in younger cohorts recently.[17] We did not find reliable data to define the risk of gastrointestinal malignancy in premenopausal women at different ages or with different degrees of anemia, but the prevalence of either upper or lower gastrointestinal malignancy will decrease with decreasing age in this population.

The risks of bidirectional endoscopy are likely to be small in this patient population and probably vary with patient age. Although data on endoscopy complications are limited in younger individuals, the risk of serious complications of screening and surveillance colonoscopy increases with age.[11–13] Women in the younger age groups are likely at very low risk of endoscopic complications.

Given the lack of direct data on both the prevalence of gastrointestinal malignancy and endoscopic complications in premenopausal women, it is difficult to estimate the balance of the risks compared with the potential benefits of bidirectional endoscopy. In particular, there are insufficient data to suggest a specific age or ferritin cutoff for premenopausal women who might reasonably select iron supplementation and monitoring before bidirectional endoscopy. However, particularly at younger ages, the benefit of endoscopy to detect the extremely rare gastrointestinal malignancies is likely diminished compared with the risks. Evidence that more clearly weighs benefits and harms of bidirectional endoscopy in this situation is lacking. In addition, the role of fecal occult blood testing to determine need for endoscopy in this situation is not well studied. Therefore, clinicians should discuss the tradeoff between the very small risks of a missed gastrointestinal malignancy if bidirectional endoscopy is deferred vs the small risks of endoscopy in this patient population, and shared decision making on the value of endoscopy

**Table 3.** Executive Summary Table of Recommendations

| Recommendation | Strength of recommendation | Quality of evidence |
|---|---|---|
| In patients with anemia, the AGA recommends using a cutoff of 45 ng/mL over 15 ng/mL when using ferritin to diagnose iron deficiency. | Strong | High |
| Comment: In patients with inflammatory conditions or chronic kidney disease, other laboratory tests such as C-reactive protein, transferrin saturation, or soluble transferrin saturation, may be needed in conjunction with ferritin to diagnose iron deficiency anemia. | | |
| In asymptomatic postmenopausal women and men with iron deficiency anemia, the AGA recommends bidirectional endoscopy over no endoscopy. | Strong | Moderate |
| In asymptomatic premenopausal women with iron deficiency anemia, the AGA suggests bidirectional endoscopy over iron replacement therapy only. | Conditional | Moderate |
| Comment: Patients who place a high value on avoiding the small risk of endoscopy, particularly those who are young and might have other plausible reasons for IDA, and a low value on the very small risk of missing a gastrointestinal malignancy would reasonably select an initial course of iron replacement therapy and no initial bidirectional endoscopy. | | |
| In patients with iron deficiency anemia without other identifiable etiology after bidirectional endoscopy, the AGA suggests noninvasive testing for *Helicobacter pylori,* followed by treatment if positive, over no testing. | Conditional | Low |
| In patients with iron-deficiency anemia, the AGA suggests against the use of routine gastric biopsies to diagnose atrophic gastritis. | Conditional | Very Low |
| In asymptomatic adult patients with iron deficiency anemia and plausible celiac disease, the AGA suggests initial serologic testing, followed by small bowel biopsy only if positive, over routine small bowel biopsies. | Conditional | Very Low |
| Comment: Celiac disease is a well-recognized cause of iron deficiency anemia, even in asymptomatic patients, and, therefore it must be considered in the differential diagnosis of iron deficiency anemia. | | |
| In uncomplicated asymptomatic patients with iron deficiency anemia and negative bidirectional endoscopy, the AGA suggests a trial of initial iron supplementation over the routine use of video capsule endoscopy. | Conditional | Very low |
| Comment: Caution needs to be applied in patients with comorbid conditions where the identification of small bowel pathology will change medical management, such as the use of anticoagulation and/or antiplatelet therapy. | | |

is needed. For example, women who place high value on avoiding the small risks of endoscopy and low value on the very small risk of missing a gastrointestinal malignancy may reasonably elect to pursue initial iron therapy over bidirectional endoscopy, particularly if they are young and have other plausible etiologies of the IDA. Further research is needed to define the risk of gastrointestinal malignancy as well as the diagnostic yield and adverse event rate from endoscopic procedures in this patient population.

The overall quality of evidence for this recommendation was rated as moderate due to indirectness and the availability of observational evidence only. Although there is modest benefit for detecting gastrointestinal malignancy, particularly in older premenopausal women, there is also a small risk of harm from endoscopic procedures. The balance between benefits and harms is dependent on age and other clinical considerations, and individualized decision making is needed.

**In patients with iron deficiency anemia without other identifiable etiology after bidirectional endoscopy, the AGA suggests noninvasive testing for *H pylori,* followed by treatment if positive, over no testing. *Conditional recommendation, low-quality evidence.***

The AGA suggests noninvasive testing for *H pylori*, followed by treatment if positive, over no testing. *H pylori* can cause peptic ulcer disease and is graded as a class I carcinogen by the World Health Organization due to its association with gastric adenocarcinoma.[18] *H pylori* infection is also associated with atrophic gastritis and hypochlorhydria, which can decrease iron absorption. An association between *H pylori* infection and iron deficiency has been demonstrated in observational studies.[19] Therefore, it has been hypothesized that treatment of *H pylori* infection may lead to improvement in iron deficiency.

Based on the technical review, pooled analysis of 3 randomized controlled trials showed greater improvement in mean hemoglobin in patients tested and treated for *H pylori* in conjunction with iron replacement compared with those who received iron replacement alone (mean difference, 2.2 g/dL greater improvement in hemoglobin; 95% CI, 1.3–3 g/dL).[1] In these studies, the mean improvement in ferritin was 23.2 ng/mL (95% CI, 12.2–34.3 ng/mL) greater in the *H pylori* treatment with iron replacement therapy group compared with those who received iron replacement alone. Two of these 3 randomized controlled trials were conducted in children. Therefore, testing for *H pylori,* with treatment if positive, may assist in resolution of iron

deficiency. In addition, detecting and treating *H pylori* will likely have benefits beyond resolution of iron deficiency, such as decreasing the incidence of gastric cancer.[20]

Given the benefit of identifying and treating *H pylori*, the Technical Review Panel examined different strategies for detecting this infection. Multiple methods for *H pylori* testing exist, including gastric biopsy and noninvasive tests such as serology, *H pylori* stool antigen testing, and urea breath testing.[1] Compared with a strategy of routine gastric biopsies in all patients, the overall cost savings of a strategy of urea breath testing after negative bidirectional endoscopy was substantial. The short-term harms of delayed diagnosis of *H pylori* in those with false-negative noninvasive testing were believed to be minimal. Therefore, a noninvasive testing strategy for *H pylori* after negative bidirectional endoscopy was believed to provide sufficient sensitivity and specificity with cost savings and few short-term harms, and is recommended over a strategy of routine gastric biopsies at the time of bidirectional endoscopy.

The quality of evidence for this recommendation was rated as low and was downgraded due to risk of bias, as the randomized controlled trials were not blinded. In addition, the randomized controlled trials included children primarily and evidence for benefits in adults is indirect. Lastly, there was serious imprecision in the effect estimates due to small sample size.

**In patients with iron deficiency anemia, the AGA suggests against the use of routine gastric biopsies to diagnose atrophic gastritis. *Conditional recommendation, very-low-quality evidence*.**

The AGA suggests against the use of routine gastric biopsies to diagnose autoimmune atrophic gastritis in patients with IDA. Atrophic gastritis can be associated with long-standing *H pylori* infection or can be autoimmune in etiology. Atrophic gastritis associated with *H pylori* is characterized by antral-predominant or pangastritis, with atrophy involving the antrum and potentially extending to the corpus. In autoimmune atrophic gastritis, the atrophic process is restricted to the gastric corpus, with metaplasia of the gastric body and fundus. Autoimmune atrophic gastritis leads to hypochlorhydria or achlorhydria due to destruction of parietal cells in the gastric body, potentially interfering with absorption of oral iron and subsequent IDA. In its later stages, this condition may also lead to vitamin B-12 deficiency. The diagnosis of autoimmune atrophic gastritis rests on biopsy analysis of the gastric antrum and corpus, although it can be suggested by the presence of hypochlorhydria or achlorhydria, elevated gastrin levels, and antiparietal cell or anti-intrinsic factor antibodies. Some have suggested that a serologic panel, including gastrin levels and antibodies against *H pylori*, parietal cells, and intrinsic factor, can identify patients with potential autoimmune atrophic gastritis who might benefit from endoscopy and gastric biopsies. No proven therapy for this condition is available.

The Technical Review Panel identified 6 studies that reported the prevalence of autoimmune atrophic gastritis in patients with IDA. The estimated pooled prevalence of this condition was 10.1% (95% CI, 7.6%–12.8%). However, available studies often did not differentiate atrophy due to *H pylori* infection from that due to autoimmune atrophic gastritis.[1] In addition, no evidence was found that earlier identification of autoimmune atrophic gastritis affects the clinical management of iron deficiency or long-term outcomes. Some observational studies have suggested that the risk of gastric adenocarcinoma and carcinoids may be elevated in this condition, although the degree of risk elevation is not clearly defined. The European Society of Gastrointestinal Endoscopy recommends considering endoscopic surveillance every 3–5 years, but this recommendation is based on low-level evidence.[21]

Given the lack of well-accepted management implications after a diagnosis of atrophic gastritis and insufficient evidence to demonstrate that earlier diagnosis improves patient outcomes, the use of routine gastric biopsies for this diagnosis is not supported. The use of a serologic panel to diagnose this condition would also be hindered by these concerns. The quality of evidence for this recommendation was rated as very low and was downgraded due indirectness of the evidence, risk of bias, and inconsistency.

**In asymptomatic adult patients with iron deficiency anemia and plausible celiac disease, the AGA suggests initial serologic testing, followed by small bowel biopsy only if positive, over routine small bowel biopsies. *Conditional recommendation, very-low-quality evidence.***
**Comment: Celiac disease is a well-recognized cause of iron deficiency anemia, even in asymptomatic patients, and therefore it must be considered in the differential diagnosis of iron deficiency anemia.**

The AGA suggests initial serologic testing, with small bowel biopsy only if positive, over routine small bowel biopsies in asymptomatic patients with IDA and plausible celiac disease. Patients with symptoms suggestive of celiac disease should be evaluated appropriately. Although celiac disease is a well-recognized cause of iron deficiency, consensus on the optimal diagnostic strategy in this clinical scenario is lacking. In the technical review, no randomized or observational studies were identified directly comparing routine small bowel biopsies in asymptomatic patients to targeted workup based on serologic testing and symptoms.[1] The Guideline Panel used studies on the prevalence of celiac disease in patients with IDA, the accuracy of noninvasive diagnostic testing in the general population, and the costs of small bowel biopsies and serologic testing in formulating this recommendation.

The Technical Review Panel compared different diagnostic strategies to identify celiac disease with sufficient sensitivity and specificity and accounting for potential harms and costs.[1] A strategy of serologic testing for celiac disease, followed by small bowel biopsies only if positive, would diagnose the large majority of patients with celiac disease with minimal short-term harm and overall cost-savings. This strategy was cost-saving compared with the

common practice of obtaining routine small bowel biopsies at the time of bidirectional endoscopy or a strategy of obtaining serologic testing after negative bidirectional endoscopy. Overall, the balance of expected benefits, harms, and costs was believed to favor initial serologic testing unless the prevalence of celiac disease is >5% in the population under consideration.

Some special considerations may alter the balance of risks and harms for these different strategies. First, epidemiologic risk factors and clinical features will alter the clinician's suspicion of underlying celiac disease. For example, celiac disease is comparatively uncommon in individuals from minority groups in the United States or in East Asian countries (eg, Japan and China). Second, suspicion for celiac disease would be increased in patients with a positive family history, a personal history of autoimmune diseases such as type 1 diabetes, or gastrointestinal symptoms. The balance of benefits, harms, and costs would change in patients with higher-risk features. In these patients, routine small bowel biopsies may be a reasonable approach, and the diagnostic strategy should be approached with shared decision making. Next, small bowel biopsies should also be taken if the duodenum appears abnormal at the time of initial upper endoscopy. Finally, if the initial serologic testing was negative, the possibility of celiac disease should be reconsidered if iron deficiency persists despite an adequate trial of iron supplementation.

The overall quality of evidence was rated as very low due to potential selection bias in the studies examining the prevalence of celiac disease in IDA. It was also rated down for indirectness, as no comparative studies of the benefits and harms of the different diagnostic approaches were identified.

**In uncomplicated asymptomatic patients with iron deficiency anemia and negative bidirectional endoscopy, the AGA suggests a trial of initial iron supplementation over the routine use of video capsule endoscopy. *Conditional recommendation, very-low-quality evidence.***
**Comment: Caution needs to be applied in patients with comorbid conditions where the identification of small bowel pathology will change medical management, such as the use of anticoagulation and/or antiplatelet therapy.**

In asymptomatic patients with IDA and negative bidirectional endoscopy, the AGA suggests a trial of initial iron supplementation over the routine use of small bowel video capsule endoscopy. No studies that directly compared small bowel investigation of any type with iron replacement therapy or clinical observation were identified, and no direct evidence that performing video capsule endoscopy reduces the risk of adverse outcomes was found. The Technical Review Panel considered studies of the diagnostic yield of small bowel evaluation in the absence of overt gastrointestinal bleeding in formulating this recommendation.

In the technical review, pooled analysis of 16 studies of the diagnostic yield of video capsule endoscopy found that small bowel malignancy was identified in 1.3% (95% CI, 0.8%–1.8%).[1] However, these studies were believed to be at very serious risk of bias due to the potential for referral bias and the inclusion of symptomatic patients. The diagnostic yield for malignancy in asymptomatic patients without overt gastrointestinal bleeding could not be determined from available evidence, and the diagnostic yield for other outcomes, such as inflammatory bowel disease, small bowel ulcers or erosions, and vascular lesions is also unknown. In addition, available studies did not include an appropriate gold standard to define the sensitivity and specificity of video capsule endoscopy. Finally, whether video capsule endoscopy leads to any change in clinical management in a clinically meaningful proportion of patients is unclear. Therefore, the evidence required to evaluate the benefits of video capsule endoscopy in IDA is not currently available.

Given the uncertainty about diagnostic yield and effect on overall clinical management in asymptomatic patients without overt gastrointestinal bleeding, as well as concerns about resource utilization, the routine use of video capsule endoscopy is not well supported. Evidence on use of fecal occult blood testing to determine need for endoscopic evaluation is lacking. A trial of adequate iron supplementation with further small bowel investigation only if iron deficiency persists may provide similar clinical outcomes, although no direct comparisons are available. Evidence on the utility of other methods of small bowel investigation, including computed tomography or magnetic resonance enterography, small bowel follow through, tagged red blood cell scintigraphy, push or deep enteroscopy, and angiography was also lacking, and did not allow for formal evidence synthesis.

This recommendation does not apply to patients who have symptoms suggestive of small bowel disease or at higher risk of small bowel pathology, such as patients with increased propensity for small bowel angioectasias, in whom diagnostic video capsule endoscopy might otherwise be indicated. Similarly, video capsule endoscopy may be indicated in select circumstances where identification of small bowel pathology may alter medical management. Examples include patients who use anticoagulation or antiplatelet medications, in whom identification of a bleeding lesion may be important for prognostic or management purposes. Likewise, patients with anemia refractory to adequate iron supplementation may be appropriate candidates for video capsule endoscopy. Also, as mentioned, this recommendation does not apply to hospitalized patients with acute or acute on chronic anemia who may warrant small bowel evaluation after negative bidirectional endoscopy due to the acute nature of anemia and potential need for transfusions.

The quality of evidence for this recommendation was rated as very low due to lack of properly designed comparative or outcomes studies, the possibility of selection or referral bias in the available studies of diagnostic yield,

and the lack of a reference standard in the studies of diagnostic yield of video capsule endoscopy.

**Question: How should iron supplementation be managed?**

Although the Technical Review Panel initially considered a PICO question on this topic, this question was ultimately determined to be outside the scope of this guideline. Although no formal recommendation is provided for this question, clinicians should recognize that several formulations of both oral and intravenous iron are available with varying costs and side effects. In most patients, an initial trial of oral iron supplementation should be given, as it is generally effective, available, inexpensive, and safe. There is no strong evidence that any of the available oral formulations is more effective or better tolerated than the others.[22] However, gastrointestinal intolerance to oral iron supplements is common, and patients with malabsorption syndromes may have limited response. Historically, a daily dose of 150–200 mg of elemental iron has been recommended, but some studies suggest that lower dosing or every-other-day dosing may improve tolerability and absorption.[23,24] Taking iron supplements with food or using enteric-coated formulations may improve tolerability but decrease absorption. Vitamin C co-administration is commonly recommended to improve oral absorption, although the evidence supporting this practice is limited.[25] A response (with improvements in hemoglobin concentration) to oral iron supplementation is typically evident within 1 month of treatment. If such a response is not seen, assessment for nonadherence (due to side effects or other reasons), malabsorption, or ongoing blood loss exceeding iron intake is needed.

Intravenous iron may be appropriate in selected patients, such as those with impaired absorption due to prior gastric surgery, with inflammatory bowel disease or chronic kidney disease, or in whom blood loss exceeds the ability to replete iron orally.[26] Consultation with a hematologist is often helpful when intravenous iron repletion is required.

### *Future Research Needs and Evidence Gaps*

Several gaps in current knowledge were identified. In premenopausal women, better understanding of the prevalence of serious gastrointestinal lesions at different ages and severity of IDA, as well as the risks of bidirectional endoscopy, is needed to inform providers about the utility of endoscopic evaluation. The role of fecal occult blood testing to determine need for endoscopic evaluation also needs further investigation. The balance of benefits and harms of gastrointestinal evaluation also needs better definition in other patient subgroups, such as patients of different ages, with different degrees of IDA, or with other clinical risk factors. Larger well-designed studies in adults should further define the utility of testing and treating for *H pylori* infection either before or after bidirectional endoscopy. Similarly, comparative outcome and cost-effectiveness studies of initial serologic testing for celiac disease vs routine small bowel biopsy are needed.

A large evidence gap is apparent regarding the outcomes and proper techniques of small bowel investigation in patients with negative bidirectional endoscopy. Well-designed studies of the diagnostic yield of video capsule endoscopy and comparative studies of outcomes of initial iron replacement vs small bowel investigation would guide future practice. In addition, there is little evidence about the role of fecal occult blood testing and the comparative efficacy of various methods of small bowel investigation, such as video capsule endoscopy, deep enteroscopy, or magnetic resonance/computed tomography enterography, in this clinical scenario. Future studies that define patient subgroups that are likely to benefit from small bowel investigation are clearly needed. Finally, further research on the utility of repeating the diagnostic evaluation in patients with persistent or recurrent IDA and negative prior evaluation is needed.

## Discussion

These practice recommendations for the initial gastrointestinal evaluation of IDA were developed using the GRADE framework, with the goal of promoting high-quality and high-value care. IDA is extremely common worldwide, and a gastrointestinal cause should be considered in all patients without an obvious etiology. There are some meaningful differences between this guideline and the British Society of Gastroenterology guideline, which does not recommend bidirectional endoscopy for premenopausal women who do not have symptoms suggesting gastrointestinal disease, a strong family history of colorectal cancer, or age older than 50 years.[27] The British guidelines also suggest that the order of endoscopic evaluation in postmenopausal women and men should be determined by the presence of symptoms and local availability of endoscopy, and that either colonoscopy or computed tomography colonography may be used for colonic evaluation. In contrast, the AGA recommends bidirectional endoscopy as the mainstay for gastrointestinal evaluation, particularly in men and in postmenopausal women for whom no other unequivocal source of iron deficiency has been identified. The outcomes and value of bidirectional endoscopy in asymptomatic premenopausal women suggest a benefit of bidirectional endoscopy over no endoscopy, but particularly in younger women, individualized decision making to balance the potential benefits of detecting a serious gastrointestinal condition vs the potential harms of endoscopy is needed. Additional etiologies that should be considered and evaluated with noninvasive testing include *H pylori* infection and celiac disease. Although other small bowel etiologies are often considered in patients with negative bidirectional endoscopy, they are relatively rare, and an initial trial of iron replacement therapy rather than routine small bowel investigation is suggested.

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# Performance of the immunochemical fecal occult blood test in predicting lesions in the lower gastrointestinal tract

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## Abstract

**Background:** Previous studies have suggested that the immunochemical fecal occult blood test has superior specificity for detecting bleeding in the lower gastrointestinal tract even if bleeding occurs in the upper tract. We conducted a large population-based study involving asymptomatic adults in Taiwan, a population with prevalent upper gastrointestinal lesions, to confirm this claim.

**Methods:** We conducted a prospective cohort study involving asymptomatic people aged 18 years or more in Taiwan recruited to undergo an immunochemical fecal occult blood test, colonoscopy and esophagogastroduodenoscopy between August 2007 and July 2009. We compared the prevalence of lesions in the lower and upper gastrointestinal tracts between patients with positive and negative fecal test results. We also identified risk factors associated with a false-positive fecal test result.

**Results:** Of the 2796 participants, 397 (14.2%) had a positive fecal test result. The sensitivity of the test for predicting lesions in the lower gastrointestinal tract was 24.3%, the specificity 89.0%, the positive predictive value 41.3%, the negative predictive value 78.7%, the positive likelihood ratio 2.22, the negative likelihood ratio 0.85 and the accuracy 73.4%. The prevalence of lesions in the lower gastrointestinal tract was higher among those with a positive fecal test result than among those with a negative result (41.3% v. 21.3%, $p < 0.001$). The prevalence of lesions in the upper gastrointestinal tract did not differ significantly between the two groups (20.7% v. 17.5%, $p = 0.12$). Almost all of the participants found to have colon cancer (27/28, 96.4%) had a positive fecal test result; in contrast, none of the three found to have esophageal or gastric cancer had a positive fecal test result ($p < 0.001$). Among those with a negative finding on colonoscopy, the risk factors associated with a false-positive fecal test result were use of antiplatelet drugs (adjusted odds ratio [OR] 2.46, 95% confidence interval [CI] 1.21–4.98) and a low hemoglobin concentration (adjusted OR 2.65, 95% CI 1.62–4.33).

**Interpretation:** The immunochemical fecal occult blood test was specific for predicting lesions in the lower gastrointestinal tract. However, the test did not adequately predict lesions in the upper gastrointestinal tract.

The fecal occult blood test is a convenient tool to screen for asymptomatic gastrointestinal bleeding.[1] When the test result is positive, colonoscopy is the strategy of choice to investigate the source of bleeding.[2,3] However, 13%–42% of patients can have a positive test result but a negative colonoscopy,[4] and it has not yet been determined whether asymptomatic patients should then undergo evaluation of the upper gastrointestinal tract.

Previous studies showed that the frequency of lesions in the upper gastrointestinal tract was comparable or even higher than that of colonic lesions[5–9] and that the use of esophagogastroduodenoscopy may change clinical management.[10,11] Some studies showed that evaluation of the upper gastrointestinal tract helped to identify important lesions in symptomatic patients and those with iron deficiency anemia;[12,13] however, others concluded that esophagogastroduodenoscopy was unjustified because important findings in the upper gastrointestinal tract were rare[14–17] and sometimes irrelevant to the results of fecal occult blood testing.[18–21] This controversy is related to the heterogeneity of study populations and to the limitations of the formerly used guaiac-based fecal occult blood test,[5–20] which was not able to distinguish bleeding in the lower gastrointestinal tract from that originating in the upper tract.

The guaiac-based fecal occult blood test is increasingly being replaced by the immunochemical-based test. The latter is recommended for detecting bleeding in the lower gastrointestinal tract because it reacts with human globin, a protein that is digested by enzymes in the upper gastrointestinal tract.[22] With this advantage, the occur-



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rence of a positive fecal test result and a negative finding on colonoscopy is expected to decrease.

We conducted a population-based study in Taiwan to verify the performance of the immunochemical fecal occult blood test in predicting lesions in the lower gastrointestinal tract and to confirm that results are not confounded by the presence of lesions in the upper tract. In Taiwan, the incidence of colorectal cancer is rapidly increasing, and *Helicobacter pylori*-related lesions in the upper gastrointestinal tract remain highly prevalent.[23] Same-day bidirectional endoscopies are therefore commonly used for cancer screening.[24] This screening strategy provides an opportunity to evaluate the performance of the immunochemical fecal occult blood test.

## Methods

### Study design

For this prospective cohort study, we enrolled consecutive patients aged 18 years or more who voluntarily underwent bidirectional endoscopies as part of a self-paid medical check-up at the Far Eastern Memorial Hospital in Taiwan between August 2007 and July 2009. They were recruited through advertisements for health promotion purposes. Before the examination, a self-administered questionnaire was used to collect information on the participants' demographic characteristics, social habits, clinical symptoms, and medical and medication histories. The examination protocol included an immunochemical fecal occult blood test, a face-to-face interview, blood chemistry tests, colonoscopy and esophagogastroduodenoscopy.

To ensure that the study population was asymptomatic and that bleeding was occult, we excluded people who had overt gastrointestinal symptoms (e.g., dysphagia or abdominal pain that normally would require an immediate medical evaluation) and overt gastrointestinal bleeding (e.g., hematemesis, tarry stool, melena and hematochezia). We also excluded people who reported a history of malignant disease, polyps in the colon, inflammatory bowel disease or bowel surgery.

The hospital ethics committee approved the study protocol (no. 97024), and people who met the inclusion criteria provided informed consent.

### Fecal occult blood test

A one-step commercial immunochemical fecal occult blood test kit with a brush-type sampler (OC-Light, Eiken Chemical Co. Ltd., Tokyo, Japan) was given to all participants. The test has a positive cutoff level of 50 ng/mL. Participants were asked to collect stool samples within two days before the bowel preparation started for the screening endoscopies. They brought the stool samples to the hospital on the screening day; within 24 hours the samples were sent to the laboratory, where they were tested immediately.

### Endoscopic examinations

Participants were given sodium phosphate (Fleet; C.B. Fleet Company Inc., Lynchburg, Virginia, USA) for bowel preparation, which they took at least four hours before the endoscopic examinations. The endoscopies were performed with the use of a standard colonoscope (CF-H260AZI; Olympus, Tokyo, Japan) and esophagogastroduodenoscope (GIF-H260Z; Olympus) by two of us (T.-H.C. and C.-H.T.), who were experienced endoscopists who had each performed at least 3000 colonoscopies. The two endoscopists were blinded to the results of the fecal tests.

Endoscopic findings were recorded on a standardized reporting form. They included information on the quality of bowel preparation; completeness of the colonoscopy; number, size and localization of lesions; and whether a biopsy was performed. Participants with an incomplete colonoscopy or poor bowel preparation were excluded from analyses.

Lesions that were identified as important were confirmed clinically. We defined important lesions in the lower gastrointestinal tract as colorectal cancer, colonic adenoma, carcinoid, colitis or ulcer, angiodysplasia and submucosal tumour. Hyperplastic polyps and hemorrhoids were not included in the definition. Important lesions in the upper gastrointestinal tract included cancer, esophageal varix, ulcer of at least 0.5 cm in diameter with a perceptible depth, angiodysplasia, submucosal tumour, and reflux esophagitis with a severity of at least Los Angeles class C or D.[25]

### Statistical analysis

For descriptive findings, we present quantitative data as means and standard deviations, and categorical variables as percentages. Differences in demographic characteristics between participants with positive and negative fecal test results were determined using the Student *t* test or the $\chi^2$ test.

To determine the performance of the immunochemical fecal occult blood test, we used the test results and the colonoscopic findings to construct a $2 \times 2$ table and calculated the sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios, accuracy and corresponding 95% confidence intervals (CIs). Because the immunochemical fecal test is specific for detecting bleeding in the lower gastrointestinal tract, we hypothesized that its specificity for predicting lesions in the colon would be high.

We set a minimally acceptable level of speci-

ficity at 85%, a level achieved by the guaiac-based test (Hemoccult SENSA, Beckman Coulter Inc., USA) in our institution. Assuming that the specificity of an immunochemical-based test should reach at least 90%, we determined that a sample size of 750 participants with a negative finding on colonoscopy would be required to detect this difference at $\alpha = 0.05$, $\beta = 0.1$ and a single-tail hypothesis. Knowing that the prevalence of colon lesions in our population is about 20%,[28] we determined that an overall sample size of 940 participants would suffice.

We then compared the prevalence rates of lesions in the lower and upper gastrointestinal tracts between participants with positive and negative fecal test results. To test our theory that the fecal test result is not confounded by the presence of a lesion in the upper gastrointestinal tract, we hypothesized that the prevalence of lesions in the colon would be higher among participants with a positive fecal test result than among those with a negative test result. In contrast, we hypothesized that the prevalence of lesions in the upper gastrointestinal tract would

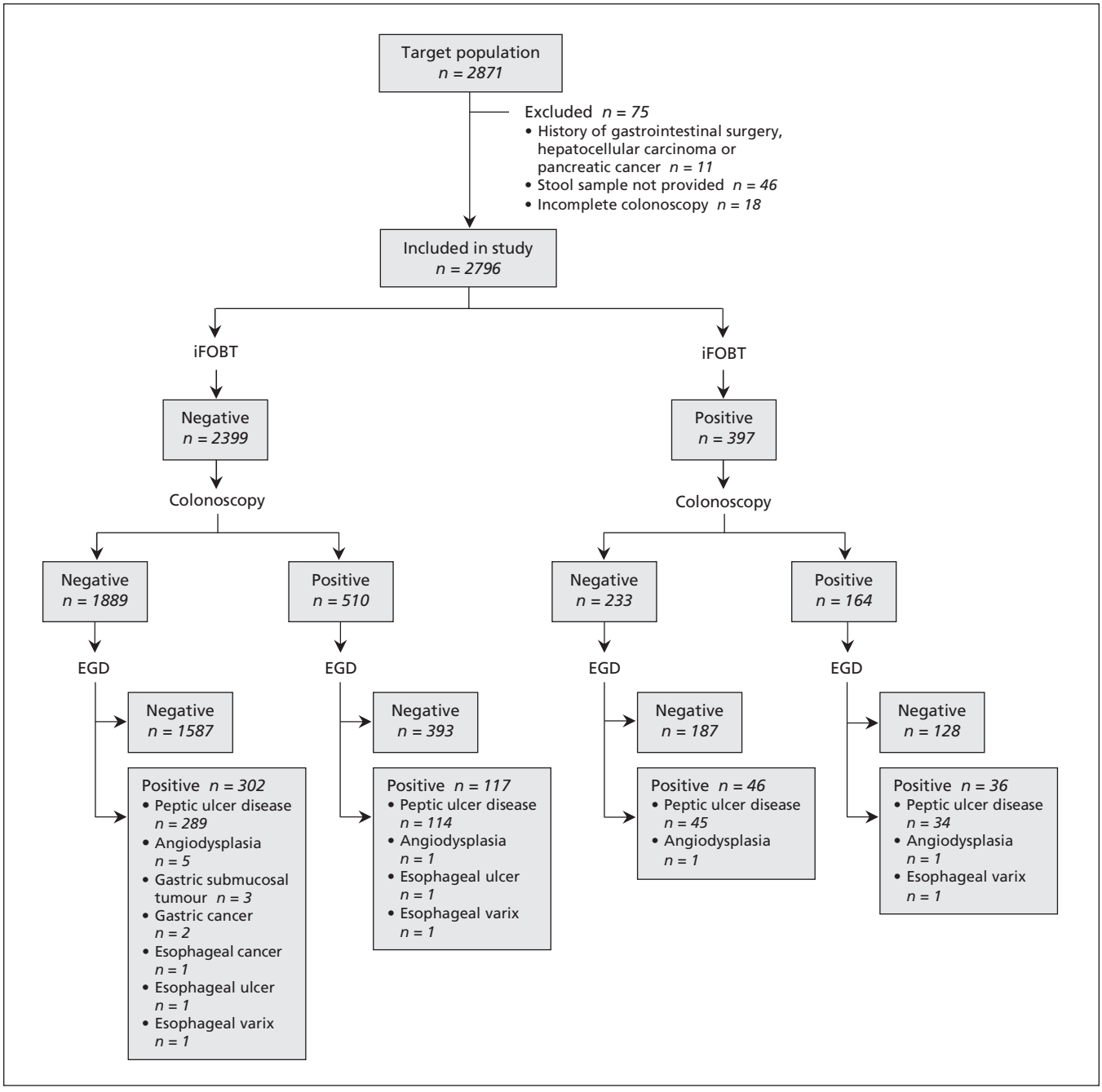


**Figure 1: Study flow of asymptomatic participants undergoing immunochemical fecal occult blood test (iFOBT), colonoscopy and esophagogastroduodenoscopy (EGD).**

be similar among those with positive and negative fecal test results. We assessed statistical differences using the $\chi^2$ test.

We evaluated the association between a positive fecal test result and a positive finding on colonoscopy using multivariable logistic regression analysis and controlling for the presence of lesions in the upper gastrointestinal tract. Results were expressed as adjusted odds ratios (ORs) and 95% CIs. Because malignant disease commonly causes occult gastrointestinal bleeding, we compared rates of fecal test positivity between participants with colon cancer and those with esophageal or gastric cancer, expecting the former to be higher.

Finally, we identified risk factors associated with a positive fecal test result and a negative finding on colonoscopy using the backward elimination method in a multivariable logistic regression model. Odds ratios greater than 1.0 indicated an increased risk of a false-positive fecal test result. A two-tailed *p* value of less than 0.05 indicated statistical significance.

## Results

### Participant characteristics

Of the 2871 consecutive people who volunteered to undergo the screening endoscopies during the study period, we excluded 75 because they had a history of gastrointestinal surgery ($n = 8$), hepatocellular carcinoma ($n = 2$) or pancreatic cancer ($n = 1$), they did not provide a stool sample ($n = 46$), or they had an incomplete colonoscopy ($n = 18$) (Figure 1). The remaining 2796 participants (1654 men and 1142 women) were included in the study. The mean age was 49.0 (standard deviation 11.2) years. Overall, 397 (14.2%) of the participants had a positive result of the immunochemical fecal occult blood test. The characteristics of the participants did not differ significantly between those with a positive fecal test result and those with a negative result except that a higher proportion of those with a positive result used antiplatelet drugs (Table 1).

**Table 1:** Demographic characteristics of 2796 study participants, by result of immunochemical fecal occult blood test

| Characteristic | Fecal test result: Positive *n = 397* | Fecal test result: Negative *n = 2399* | Total *n = 2796* |
|---|---|---|---|
| Age, yr | | | |
| Mean (SD) | 50.5 (12.5) | 48.7 (10.9) | 49.0 (11.2) |
| Range | 19–84 | 20–84 | 19–84 |
| Male sex, no. (%) | 244 (61.5) | 1410 (58.8) | 1654 (59.2) |
| Body mass index, kg/m$^2$ | | | |
| Mean (SD) | 24.4 (3.6) | 24.0 (3.4) | 24.1 (3.4) |
| Range | 16.5–39.0 | 13.9–41.4 | 13.9–41.4 |
| Chronic comorbid disease,* no. (%) | 101/364 (27.8) | 461/1955 (23.6) | 562/2319 (24.2) |
| Current smoker, no. (%) | 95/364 (26.1) | 431/1956 (22.0) | 526/2320 (22.7) |
| Alcohol use, no. (%) | 104/364 (28.6) | 595/1956 (30.4) | 699/2320 (30.1) |
| Use of antiplatelet drugs,† no. (%) | 29/364 (8.0) | 72/1954 (3.7) | 101/2318 (4.4) |
| Hemoglobin, g/L | | | |
| Mean (SD) | 145 (18) | 147 (16) | 146 (16) |
| Range | 83–189 | 85–193 | 83–193 |
| Platelet count, $\times 10^9$/L | | | |
| Mean (SD) | 254.6 (67.2) | 248.1 (58.6) | 249.0 (60.0) |
| Range | 109–570 | 76–695 | 76–695 |

Note: SD = standard deviation.
*Includes diabetes mellitus, hypertension and cardiovascular disease.
†Regular use of low-dose acetylsalicylic acid ($n = 77$), clopidogrel ($n = 13$), low-dose acetylsalicylic acid and clopidogrel ($n = 3$) or non-steroidal anti-inflammatory drug ($n = 8$).

**Table 2:** Performance of immunochemical fecal occult blood test in predicting lesions in the lower gastrointestinal tract among the 2796 participants

| Outcome | Performance measure (95% CI): Sensitivity, % | Specificity, % | Positive predictive value, % | Negative predictive value, % | Positive likelihood ratio | Negative likelihood ratio | Accuracy, % |
|---|---|---|---|---|---|---|---|
| Colorectal cancer | 96.4 (95.1–97.7) | 86.6 (85.3–87.9) | 6.8 (4.3–9.3) | 99.9 (99.8–100) | 7.21 (6.41–8.12) | 0.04 (0.01–0.28) | 86.7 (85.3–88.1) |
| Adenoma | 21.4 (18.1–24.7) | 88.9 (87.6–90.2) | 34.9 (26.7–43.1) | 80.3 (78.7–81.9) | 1.93 (1.59–2.34) | 0.88 (0.85–0.92) | 74.2 (72.6–75.8) |
| Colorectal cancer or adenoma | 24.8 (21.4–28.2) | 88.9 (87.6–90.2) | 39.2 (34.4–44.0) | 80.2 (78.6–81.8) | 2.23 (1.86–2.67) | 0.85 (0.81–0.89) | 74.4 (72.8–76.0) |
| Any important lesion | 24.3 (21.1–27.5) | 89.0 (87.7–90.3) | 41.3 (36.5–46.1) | 78.7 (77.1–80.3) | 2.22 (1.85–2.65) | 0.85 (0.81–0.89) | 73.4 (71.8–75.0) |

Note: CI = confidence interval.

### Specificity of fecal test

Lesions were more prevalent in the lower gastrointestinal tract (24.1%) than in the upper tract (17.9%); colon cancer was more prevalent than upper gastrointestinal cancers. Performance of the immunochemical fecal occult blood test in predicting lesions in the lower gastrointestinal tract is shown in Table 2. The test's specificity was almost 90% for colorectal cancer, adenoma or any important lesion. The sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios, and accuracy of the fecal test were all significant for lesions in the lower gastrointestinal tract.

### Prevalence of gastrointestinal lesions by positivity of fecal test

Endoscopic findings are summarized in Table 3. Lesions in the lower gastrointestinal tract were more frequent among participants with a positive immunochemical fecal test result than among those with a negative result (41.3% v. 21.3%, $p < 0.001$). The frequency of lesions in the upper gastrointestinal tract was similar in both groups (20.7% and 17.5%, $p = 0.12$). Of the 397 participants with a positive fecal test result, 233 (58.7%) had a negative finding on colonoscopy; of these, 46 (19.7%) had an important lesion in the upper gastrointestinal tract, which was most often a peptic ulcer (97.8%).

The presence of a lesion in the lower gastrointestinal tract was significantly associated with positivity of the fecal test (adjusted OR 2.59, 95% CI 2.07–3.23). The presence of a lesion in the upper tract was not associated with the test's positivity (adjusted OR 1.14, 95% CI 0.87–1.49).

Among participants found to have a malignant lesion, almost all who had colon cancer had a positive fecal test result (27/28, 96.4%). In contrast, none of the three participants found to have esophageal or gastric cancer had a positive fecal test result ($p < 0.001$).

**Table 3:** Endoscopic findings among the 2796 participants, by result of immunochemical fecal occult blood test

| Finding | Fecal test result; no. (%) of participants | |
|---|---|---|
| | Positive *n = 397* | Negative *n = 2399* |
| **Lower gastrointestinal tract** | | |
| Lesion | 164 (41.3) | 510 (21.3) |
| Advanced colon cancer | 10 (2.5) | 0 |
| Early colon cancer | 17 (4.3) | 1 (0.0) |
| Tubular adenoma | 116 (29.2) | 458 (19.1) |
| Tubulovillous adenoma | 9 (2.2) | 13 (0.6) |
| Villous adenoma | 4 (1) | 2 (0.1) |
| Carcinoid | 0 | 1 (0.0) |
| Colitis or ulcer | 6 (1.5) | 19 (0.8) |
| Angiodysplasia | 1 (0.3) | 13 (0.6) |
| Submucosal tumour | 0 | 3 (0.1) |
| Peutz–Jegher syndrome | 1 (0.3) | 0 |
| No lesion | 233 (58.7) | 1889 (78.7) |
| **Upper gastrointestinal tract** | | |
| Lesion | 82 (20.7) | 419 (17.4) |
| Advanced esophageal cancer | 0 | 1 (0.0) |
| Advanced gastric cancer | 0 | 1 (0.0) |
| Early gastric cancer | 0 | 1 (0.0) |
| Esophageal varix | 1 (0.3) | 2 (0.1) |
| Esophageal ulcer | 0 | 2 (0.1) |
| Gastric ulcer | 57 (14.4) | 293 (12.2) |
| Duodenal ulcer | 11 (2.8) | 70 (2.9) |
| Gastric or duodenal ulcer | 11 (2.8) | 40 (1.7) |
| Angiodysplasia | 2 (0.5) | 6 (0.3) |
| Gastric submucosal tumour | 0 | 3 (0.1) |
| No lesion | 315 (79.3) | 1980 (82.6) |

### Risk factors associated with a false-positive fecal test result

Use of antiplatelet drugs and having a low hemoglobin concentration were the only factors associated with a positive result of the immunochemical fecal occult blood test among participants with a negative finding on colonoscopy (Figure 2). These risk factors remained significant after adjustment for confounding variables (adjusted OR 2.46, 95% CI 1.21–4.98 for use of antiplatelet drugs; 2.65, 95% CI 1.62–4.33, for low hemoglobin concentration).

## Interpretation

We found that the specificity of the immunochemical fecal occult blood test was almost 90% for predicting colorectal cancer, adenoma or any important lesion in the lower gastrointestinal tract. These findings support those of previous studies showing that the immunochemical fecal test is a specific diagnostic tool.[26–34] Also, the test's sensitivity was 25% for neoplasms in the colon and 96% for colorectal cancer, findings that are consistent with most results of previous studies evaluating the immunochemical fecal test in either Eastern or Western populations (see Appendix 1 at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.101248/-/DC1).

Previous studies invited asymptomatic participants with a negative result of the immunochemical fecal occult blood test to undergo

colonoscopy to validate the test results.[26–30] We took the additional step of adding esophagogastroduodenoscopy to clarify the effect of lesions in the upper gastrointestinal tract on the fecal test results. In our study, the prevalence of lesions in the upper tract was consistently about 20% whether among participants with a positive immunochemical fecal test result, a negative fecal test result, or a positive fecal test result and a negative finding on colonoscopy. In addition, the rate of positivity of the fecal test was substantially higher among participants with colon cancer than among those with malignant lesions in the upper gastrointestinal tract. Furthermore, regression analyses showed a lack of association between positivity of the fecal test and the presence of a lesion in the upper gastrointestinal tract. These findings indicate that the immunochemical fecal occult blood test cannot predict the presence of lesions in the upper gastrointestinal tract.

Among participants with a negative finding on colonoscopy, risk factors associated with a false-positive result of the immunochemical fecal occult blood test has rarely been addressed. Bleeding from hemorrhoids is one of the commonly speculated causes of a false-positive result. However, in our study, the prevalence of hemorrhoids was similar among those with a positive fecal test result (61/397, 15.4%) and those with a negative test result (318/2399, 13.3%). In addition, the regression analyses showed a lack of association between positivity of the immunochemical fecal test and the presence of hemorrhoids among participants with a negative finding on colonoscopy. These findings indicate that hemorrhoids should not be used to explain a positive immunochemical fecal test result or hamper the indication for colonoscopy.

Recently, the effect of antiplatelet drugs on the performance of the immunochemical fecal occult blood test has attracted attention, because studies conducted in Western populations have shown that such use may increase the sensitivity of the test in detecting neoplasms in the colon with no or minimal change in specificity.[29,30,35] However, in our study, although a low proportion of participants used antiplatelet drugs, their false-positive test rate did increase, such that the sensitivity was increased (32.3% v. 24.3% for the whole study population), but the specificity was reduced (72.9% v. 89.0%) (see Appendix 1).

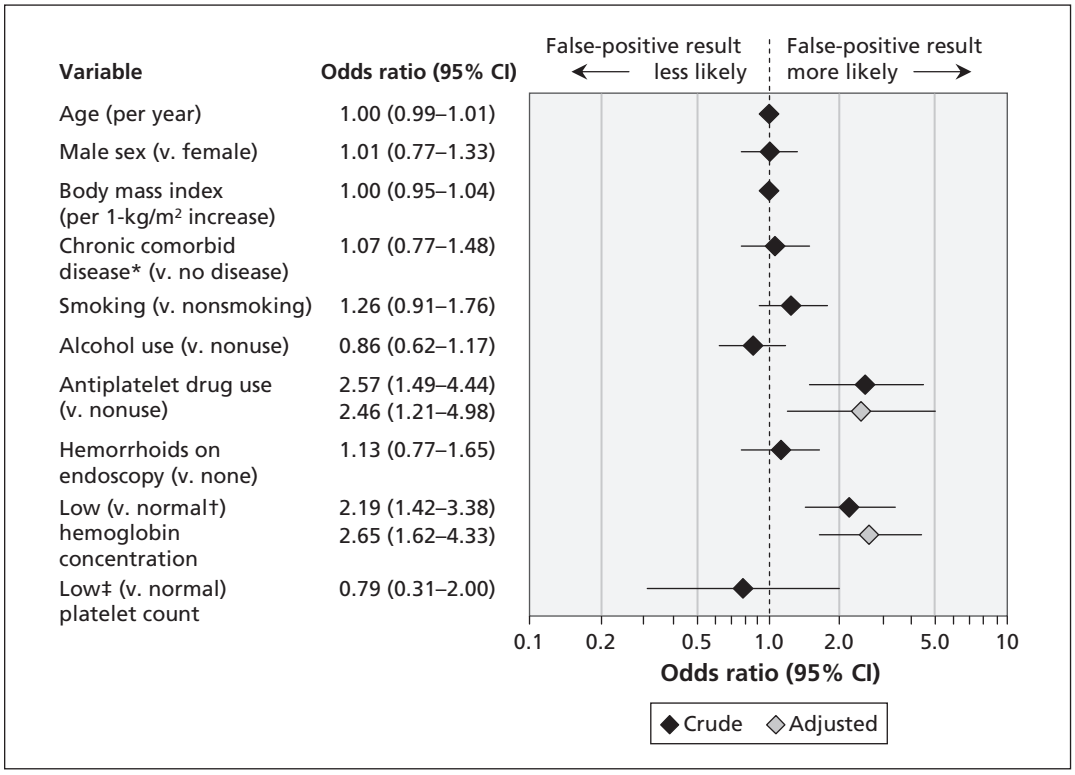


**Figure 2: Risk factors associated with 233 false-positive results of the immunochemical fecal occult blood test among 2122 participants with a negative finding on colonoscopy. The multivariable model adjusted for all variables shown in the forest plot. An odds ratio greater than 1.0 indicates an increased risk of a false-positive result. CI = confidence interval. *Includes diabetes mellitus, hypertension and cardiovascular disease. †Normal hemoglobin concentration: < 120 g/L in women and < 130 g/L in men. ‡Low platelet count: < 150 × $10^9$/L.**

## Limitations

Our study has limitations. First, although we identified antiplatelet use and low hemoglobin concentration as risk factors associated with a false-positive immunochemical fecal test result, the performance of our multiple logistic regression model remains limited in accurately predicting the possibility of such a false-positive result. Also, low hemoglobin concentration appears to be a result rather than a cause. Therefore, it is worthwhile to investigate whether the participants, especially those who were using antiplatelet drugs, had other sources of bleeding, such as small-bowel lesions.

Second, the immunochemical fecal occult blood test does not adequately predict lesions in the upper gastrointestinal tract. Such lesions were present in 20% of the participants in our study who had a false-positive fecal test result and in 6% to 42% of participants in previous studies (see Appendix 2, at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.101248/-/DC1). A pan-detecting assay based on stool samples is a recent development that offers an intriguing research opportunity for simultaneous multiple cancer screenings.[36] A combination of immunochemical fecal occult blood test and a stool antigen test for *H. pylori*[37] is an approach that may help to realize this goal in a population in which lesions in both the lower and upper gastrointestinal tracts are equally prevalent.[38,39] This topic warrants further investigation.

## Conclusion

Our findings confirm that the immunochemical fecal occult blood test is specific for predicting lesions in the lower gastrointestinal tract but it does not adequately predict lesions in the upper tract. Among participants who had a negative colonoscopy, a false-positive result of the immunochemical fecal test was associated with the use of antiplatelet drugs and a low hemoglobin concentration.

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# Eliminating In-Hospital Fecal Occult Blood Testing: Our Experience with Disinvestment

The fecal occult blood test has an unimpeachable role in population-wide colorectal cancer screening. More than 5 decades ago, soon after commercial availability of the test, its use was extended for workup of altered stool color (example, melena) or anemia. Although this practice was debatable even then, current imaging and endoscopic tools have revolutionized our approach, rendering the fecal occult blood test irrelevant to modern hospital practice.[1-3] Yet the routine use of fecal occult blood tests in hospitalized patients has persisted, sometimes reflexively with rectal examinations. Fecal occult blood tests are of 2 types: guaiac-based tests measuring heme, and immunochemical tests measuring globin.[3] They are used to detect the microscopic presence of hemoglobin in stool but are plagued by poor accuracy. False-positive results can occur with nongastrointestinal bleeding sources (epistaxis, swallowed hemoptysis), mucosal inflammation without bleeding (inflammatory bowel disease), certain foods (vegetables containing peroxidase, and meats), toxins (such as alcohol), or clinically insignificant bleeding caused by antiinflammatory drugs.[3] False-negative results, such as those caused by slow or intermittent bleeding, ingestion of antioxidants such as vitamin C, or upper gastrointestinal bleeding in which globin is denatured, preclude their ability to convincingly rule out important pathology.[3] Multiple samples need to be sent for increased sensitivity, and visual misinterpretation of results can occur.[3] Inappropriate testing and interpretation not only leads to increased costs of testing but can lead to patient harm through incorrect downstream management decisions and unnecessary interventions. Studies have questioned the utility of having fecal occult blood tests available as an orderable test in the inpatient setting.[4-8]

Therefore, we aimed to determine the use of fecal occult blood tests at the Parkland Health and Hospital System, an 870-bed safety net hospital in Dallas, Texas. Using these data, and with support from multidisciplinary stakeholders, we implemented stepwise interventions to abandon the use of fecal occult blood tests at our hospital.

## METHODS AND RESULTS

In 2015 we performed a retrospective review of medical records from January 1, 2011 to December 31, 2014 to determine the number of fecal occult blood tests performed on patients in the emergency room and on inpatients (collectively termed in-hospital use). Fecal occult blood tests could be performed as a point-of-care test or in the laboratory. Additionally, we reviewed the medical records of 400 randomly selected patients with a positive fecal occult blood test result to determine the indication for testing.

Over the initial 4-year period, a total of 31,790 fecal occult blood tests were performed in the hospital (mean 7948 tests per year) (**Figure**). A majority were performed in the emergency room (71%, vs 29% inpatient) and as a point-of-care test (76%, vs 24% in the laboratory). Overall, 17% of fecal occult blood test results were positive. The indications for testing in the 400 randomly selected patients with positive fecal occult blood test results were as follows: history of dark stools 132 (33%), anemia 96 (24%), overt gastrointestinal bleeding 48 (12%), nonbloody diarrhea 23 (6%), colon cancer screening 2 (0.5%), and unknown 99 (25%). When indications were unknown, 82 (82%) were sent reflexively after a digital rectal examination. Of the patients with anemia, only 36 (38%) had supportive laboratory evidence of iron deficiency (low mean corpuscular volume or low iron and ferritin levels) at the time of fecal occult blood test. In all 400 instances, the use of fecal occult blood testing was not evidence based or recommended by guidelines. The laboratory cost of fecal occult blood testing to the hospital was approximately $5 per test, leading to direct testing costs of approximately $40,000 per year alone.

In early 2015, when these results were reviewed, an educational campaign regarding the appropriate use of fecal occult blood tests was launched. Hospital-wide periodic discussions were held among a multi-departmental team including members from internal medicine, the emergency department, surgery, pathology, laboratory services, and leadership. This resulted in 2-minute announcements once per week before

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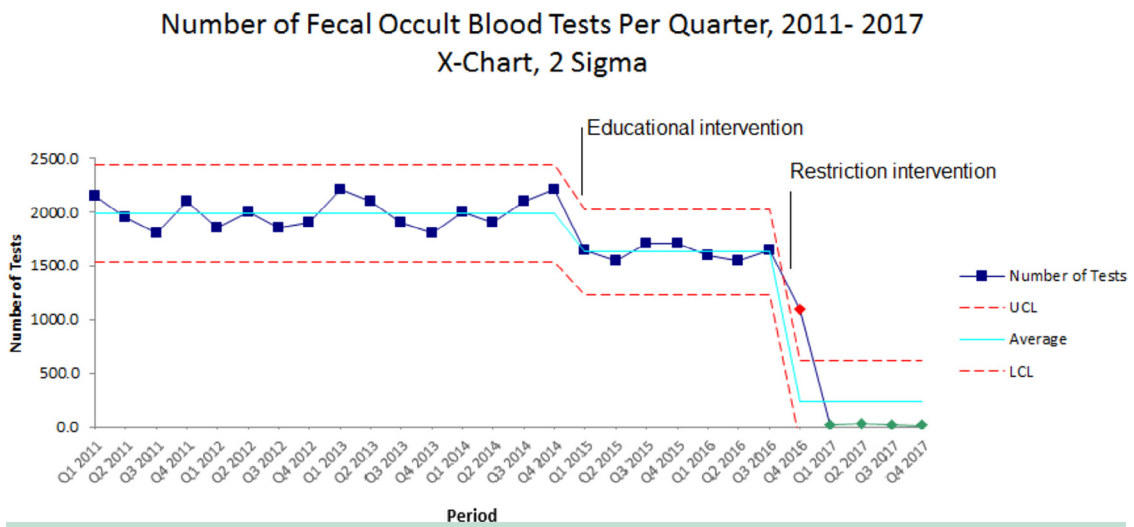


**Figure** Statistical Process Control Chart showing the number of fecal occult blood tests ordered per quarter at Parkland Hospital, Dallas, Texas from 2011 to 2017. An educational intervention was implemented in January 2015, resulting in slightly decreased use, and a restriction intervention was implemented in November 2016, resulting in significant reduction in testing throughout 2017. LCL = lower confidence limit; Q1 = quarter 1; Q2 = quarter 2; Q3 = quarter 3; Q4 = quarter 4; UCL = upper confidence limit.

the noon conference for house staff, and weekly e-mails regarding the appropriate use of fecal occult blood tests were sent, over a 2-month period. House staff interested in gastroenterology gave a couple of hour-long noon lectures on the appropriate use of fecal occult blood tests. Every time the gastroenterology service was consulted with the results of a fecal occult blood test, the gastroenterology fellow and attending physician contacted the ordering provider regarding the correct interpretation and use of the test. The impact of this intervention on fecal occult blood test ordering rates was monitored, and a slight decrease in ordering was noted in 2015 and early 2016 compared with a baseline of 4 years prior (**Figure**).

Although we observed a reduction in testing, we were unsatisfied with these results. We debated among ourselves and eventually proposed complete elimination of fecal occult blood tests for hospitalized patients. Disinvestment or de-adoption of a medical practice is a heavily understudied discipline and has proven to be exceptionally difficult, even when clear evidence exists supporting disinvestment. Keeping this in mind, we adhered to the following principles while seeking support and presenting this initiative throughout the hospital.

## Focus on Direct Medical Harm Rather Than Just Cost Saving

The first step was gathering and summarizing data on the futility of fecal occult blood tests and how patients experienced direct harm. Change introduced with the primary intention of saving costs can be viewed by physicians with suspicion, lest it negatively impact the quality of care.[9] We appealed to the nonmaleficence of physicians by collecting data on patients in the hospital who did not receive an urgent colonoscopy owing to a false-negative fecal occult blood test result and patients who received an unnecessary colonoscopy or upper endoscopy owing to a false-positive test result. We also presented data on how, in a majority of cases, the results of the test did not alter the management plan but delayed appropriate care.

## Establish Consensus Internally (Within the Gastroenterology Department) Before Advertising This Initiative

We realized the need to present a unified face to the rest of the hospital. The initiative was initially presented to just the gastroenterology faculty, some of whom reacted with skepticism. Review of the published literature and the data at our hospital helped the discussions, and eventually all faculty agreed that there was no utility of the test for hospitalized patients. We were then ready to present this to the rest of the hospital.

## Phenomenon of "Defer to the Experts"

The emergency medicine, internal medicine (including hospitalist), and surgery services, who form a bulk of our hospital's practice, were happy to let go of the test because the gastroenterology service (experts in the field) were the ones recommending this change. Furthermore, the feedback we received was that sometimes the test was ordered with the belief that gastroenterologists would want the test. We believe having a senior gastroenterologist as the team leader, who would personally go and present this proposal at the multi-departmental laboratory utilization committee meeting, was critical in being able to engage and convince people of the futility of this test. We believe that trying to effect change from the outside—for example, internal medicine physicians trying to change

a primarily gastroenterology practice—would in contrast be more difficult.

## Building Support

We realized it was important to engage and get support from several stakeholders—not just the people who order the test but also those who perform it. Thus, we also spoke with the nursing staff, who sometimes performed the test as part of standing orders, and with oncologists, who were sometimes consulted for a positive fecal occult blood test result (incorrect method of colon cancer screening after a rectal examination). This initiative was supported by both nurses and oncologists.

## Top–Down Approach (vs Bottom–Up Approach)

The focus of Choosing Wisely and other such initiates has been on change originating at the grassroots level, with trainees and frontline clinicians leading change based on recommendations from medical societies. Although admirable and encouraging, the impact of these initiatives has been modest.[10-12] We engaged the hospital leadership early and presented the patient harm that was caused by continuing the test and the potential cost savings to the hospital if the test was abolished. We found that informed, educated directives coming from the "top" to individual departmental leadership were helpful to our cause.

Over 6 months, with continuous discussion, we could garner enough support for the Medical Executive Committee, consisting of physician leaders from different departments, to agree to abolish the test. Fecal occult blood tests were removed as an orderable test from the inpatient computerized provider order entry system in November 2016. Fecal occult blood test use immediately decreased by 98% (**Figure**), although minimal use persists because a few divisions acquire their own point-of-care kits for select cases.

# DISCUSSION

Disinvestment or de-adoption is the processes of withdrawing certain healthcare resources (practices, medications, procedures, technologies) that deliver little or no gain relative to their cost.[13] Eliminating an unnecessary clinical test is the holy grail of disinvestment. Unfortunately, despite overwhelming evidence, de-adoption continues to be a vexing problem internationally.[14] Some of the challenges are policy driven; Elshaug et al[13] have compiled key challenges in disinvesting low-value care practices. These include lack of dedicated resources to build and support disinvestment policy mechanisms; lack of reliable administrative mechanisms to identify and prioritize practices with uncertainty regarding their effectiveness; political, clinical, and social challenges to removing an established technology; lack of published studies that clearly demonstrate that existing technologies/practices provide little or no benefit; and inadequate resources to support a research agenda to advance disinvestment methods. Changing established low-value hospital practices is difficult, and different approaches, including education, peer review, and feedback have been attempted. However, as shown in our study, these approaches by themselves are insufficient to significantly and consistently modify ingrained ordering practices. Contributing to this difficulty are the facts that research in this area is poorly coordinated, without a common language, and devoid of a conceptual framework.[15] We hope that our approach can inspire and help other institutions to take up this challenge until a more robust and widely applicable framework for disinvestment is developed.

We can place our interventions and results in the context of the elegant behavior system framework developed by Michie et al.[16] In this behavioral change wheel, capability, opportunity, and motivation interact to generate behavior ("COM-B" system). This forms the hub around which are positioned a total of 9 possible intervention functions affecting 1 or more of these conditions; around which are placed 7 categories of policy that could enable those interventions. Capability is having the necessary knowledge and skills to engage in the activity concerned. Opportunity includes all factors outside the individual that allow or prompt a behavior. Motivation is the brain process that energizes and directs behavior, beyond goals and conscious decision making, including habit, emotional responding, and analytical decision making. Capability and opportunity influence motivation, and all 3 individually interact bidirectionally with behavior. Education and restriction are 2 of the 9 possible interventions around the COM-B hub. Our initial initiative (education) likely affected the capability (psychological) and the motivation of providers. This influenced their behavior of fecal occult blood testing, resulting in the 16% reduction in ordering that we observed. However, our educational initiative had limited impact owing to its relatively limited scope and the unaffected opportunity to obtain the test. Abolishing the test (restriction) denied clinicians the opportunity to order the test. Restriction and education together hit all 3 variables of the COM-B system that influence ultimate behavior, leading to a successful change in practice.

Our study confirmed the reasons for inappropriate use of fecal occult blood tests. Similar to other studies, we show that fecal occult blood tests in hospitalized patients are often obtained to evaluate dark-colored stools (suspected melena), anemia, diarrhea, or routinely during rectal examinations.[17] However, almost all tests are unnecessary because results are irrelevant to the next steps of care. The use of fecal occult blood tests in patients with overt gastrointestinal bleeding, or its routine use after a rectal examination, demonstrate its largely perfunctory nature. Melena or black tarry stools indicates bleeding from the upper gastrointestinal tract and is a clinical diagnosis based on visual inspection of stools; fecal occult blood tests may in fact confound the diagnosis. Similarly, the workup of iron deficiency anemia without overt gastrointestinal bleeding and without another clear source of blood loss is gastrointestinal endoscopy, irrespective of fecal occult blood test results.[3] Blood loss may be intermittent, and a negative test does not rule out gastrointestinal blood loss. If anemia is not iron deficient, chronic gastrointestinal blood

loss is less likely, and other reasons for anemia should be considered. Indeed, more than half the patients with anemia who underwent fecal blood tests in our study did not have laboratory evidence of iron deficiency at the time of the testing. A positive fecal occult blood test result in the setting of non–iron deficiency anemia should not immediately prompt endoscopy. In one study only one-third of hospitalized patients with a positive fecal occult blood result test underwent further gastrointestinal testing, and a majority of them underwent an endoscopy even before testing resulted.[8] Physicians may feel compelled to perform endoscopy to evaluate a positive fecal occult blood test result even if they believed endoscopy would be low-yield.

When sufficient medical evidence exists, modifying the "opportunity" to order a test, such as elimination or restriction, along with education and support from hospital leadership, becomes necessary. We provide our experience with deadopting inpatient use of fecal occult blood tests. It has been more than 17 years since studies confirmed the futility of in-hospital fecal occult blood tests and initiated its long demise.[4] We have waited long enough. It is time to write the obituary for in-hospital fecal occult blood tests.

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# Fecal Occult Blood Testing in Hospitalized Patients with Upper Gastrointestinal Bleeding

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*The "Things We Do for No Reason" (TWDFNR) series reviews practices which have become common parts of hospital care but which may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent "black and white" conclusions or clinical practice standards, but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.*

## CASE REPORT

A 47-year-old man with a history of alcohol abuse, cirrhosis, and grade II esophageal varices is admitted for treatment of alcohol withdrawal. He reports having some dark-colored stools a week prior to admission, but his stools since then have been normal in color. A repeat hemoglobin is stable, but a fecal occult blood test is positive. What should be done next?

## BACKGROUND

The US Preventive Services Task Force and the American College of Gastroenterology recommend fecal occult blood testing (FOBT) as one method for colorectal cancer (CRC) screening in average risk populations.[1,2] FOBTs can be divided into guaiac-based tests (gFOBTs), which measure heme, and fecal immunochemical tests (FITs), which measure the globin portion of human hemoglobin (Hb). In gFOBTs, heme present in the sample reacts with a hydrogen peroxide developer to oxidize guaiac, producing a blue color.[3] Screening gFOBT was shown to decrease mortality from CRC in several landmark studies in the 1990s, but its sensitivity is poor, ranging from 30% to 57%.[4] Because the guaiac-induced color change is determined visually, interpretation of gFOBT results are subject to error. In a survey of 173 medical providers, 12% did not accurately interpret gFOBT results.[5] In light of these limitations, recent guidelines support the use of newer FITs for CRC screening. FITs utilize antibodies directed against the human globin moiety and demonstrate an increased sensitivity when compared with gFOBTs (by 32% to 62%) for detecting neoplasm.[6] While evidence supports the use of FOBTs in CRC screening, providers use these tests for nonvalidated purposes, including the evaluation of suspected acute upper gastrointestinal bleeding (UGIB).

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## WHY YOU MIGHT THINK FOBT IS HELPFUL FOR EVALUATION OF INPATIENTS WITH SUSPECTED ACUTE UGIB

Given the incidence (up to 100 per 100,000 persons per year) and high mortality of UGIB (up to 20,000 deaths annually in the United States),[7] there would ideally be a noninvasive test available to help guide management. In evaluating a patient with possible acute UGIB, FOBT affords several theoretical benefits. FOBT is quick, inexpensive, and can be performed by any health professional. In contrast, the primary diagnostic procedure for UGIB, esophagogastroduodenoscopy (EGD), carries procedural and sedation-related risks, can be costly and time-consuming, and requires consultation from subspecialty providers.

## WHY FOBT IS NOT HELPFUL FOR EVALUATION OF INPATIENTS WITH SUSPECTED ACUTE UGIB

While FOBTs are valuable as screening tests for CRC in the outpatient setting, their use has been extended to diagnose gastrointestinal (GI) bleeding in the inpatient setting without supporting data. As is true for many screening tests, FOBT is associated with a high incidence of false-positive results, or type I errors.[8,9] False-positive FOBT results can occur from ingested blood via extra-intestinal sources (eg, epistaxis, gingival bleeding, pharyngitis, hemoptysis), or in medical conditions with intestinal mucosal inflammation (eg, esophagitis, gastritis, inflammatory bowel disease). False-positive results can also be due to clinically insignificant GI blood loss induced by medications (eg, aspirin, nonsteroidal anti-inflammatory drugs), alcohol,[10] or by ingestion of meats, fruits, or vegetables containing peroxidase (eg, broccoli, cauliflower).[11]

Outpatients using FOBTs for cancer screening are advised to hold medications and avoid foods that may lead to false-positive results. Despite institution of these restrictions, false-positive rates are still high, as 37% to 53% of CRC screening patients with a positive FOBT have a subsequent negative colonoscopy, and only 11% to 21% of these patients have a source of bleeding identified on subsequent EGD.[12] False-positive results might be even higher in the inpatient setting, where patients typically do not adhere to these restrictions. A review of FOBTs performed in 3 acute care hospitals revealed that 65% of patients tested were on

**TABLE.** Causes of Inaccurate Fecal Occult Blood Test Results

| | gFOBT | FIT |
|---|---|---|
| False-Positive Results | Ingestion of nonhuman heme (eg, meat products)<br>Ingestion of peroxidases (eg, broccoli)<br>Ingestion of non-GI blood (eg, epistaxis)<br>Use of aspirin, NSAIDs, or anticoagulant medication | Use of aspirin, NSAIDs, or anticoagulant medication |
| False-Negative Results | Ingestion of antioxidants (eg, Vitamin C) | Bleeding from the upper GI or proximal lower GI tracts |
| Additional Considerations | Potential for visual misinterpretation<br>Low sensitivity (requires multiple samples) | Potential for visual misinterpretation (qualitative tests only)<br>Varying test characteristics depending on manufacturer |

NOTE: Abbreviations: FIT, fecal immunochemical test; FOBT, fecal occult blood testing; gFOBT, guaiac-based FOBT; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs.

at least one medication that impacted the validity of gFOBT results, and 98% had no evidence of dietary restriction prior to testing.[13]

The use of FOBTs (particularly FITs) is also subject to false-negative results, or type II errors. While FITs have increased specificity for lower GI bleeding, their ability to detect UGIB is limited, because most Hb is digested in the small intestine and not present in rectal stool.[14] In a study of more than 2,700 patients, FIT results were not correlated with the presence of upper GI pathology.[15] False-negative results are less common with gFOBTs, although these may occur with low volume, slow or intermittent bleeding,[16] or with ingestion of substances that inhibit oxidation, such as vitamin C.[17]

Beyond these test limitations, studies suggest that the majority of inpatient FOBT results do not impact immediate medical decision-making or management. In one study, only 34% of hospitalized patients with a positive FOBT underwent further GI studies, with the majority of those patients (60%) receiving endoscopy before the results of the FOBT were known.[18] In another study of 201 FOBTs performed on hospitalized patients, those with negative results underwent further GI evaluation at a higher rate than those with positive results (41% vs 38%).[8] This aligns with a study that revealed the majority of patients suspected of having a GI bleed underwent endoscopic evaluation regardless of the FOBT result.[9]

## WHEN MIGHT FOBT BE HELPFUL?

FOBT currently has a role in CRC screening and may have a role in the evaluation of anemia of unknown etiology to evaluate for occult GIB, although the yield is likely low.[13] In one retrospective analysis of inpatients with unexplained anemia, 43.6% of FOBTs were positive, but a potential GI cause was found in only 6.8% of patients.[9] Patients with anemia from an unknown etiology should have a workup based on the history, physical, and complete blood count indices. While iron deficiency anemia warrants eventual evaluation for occult blood loss, noncritical anemia in an otherwise stable patient does not require an inpatient evaluation. When FOBT is used in the outpatient setting, patients can be counseled on proper dietary and medication modifications prior to testing.

## WHAT WE SHOULD DO INSTEAD

A careful history, physical examination, and visual inspection of the stool remain the foundation of establishing UGIB as the etiology of anemia. Observed melena (either by passed stool or a rectal examination) has a likelihood ratio (LR) of 25 for UGIB; a patient's self-report of stools that sounds melenic (black or tarry) has an LR of 5-6.[19] An upper GI source may be further supported by an elevated blood urea nitrogen (BUN) to creatinine ratio, as blood is absorbed through the small bowel and patients may have concomitant decreased renal perfusion. A BUN to creatinine ratio of >30 is associated with a positive LR (LR+) of 7.5 for UGIB.[19] Recall that the higher the LR+, and the lower the negative LR (LR-), the better the test is at ruling in and out the diagnosis, respectively. LR+ of 2–10 and LR− of 0.1–0.5 represent a modestly helpful diagnostic test, whereas LR+ >10 and LR- <0.1 are considered robust. These are generalizations only, as value of LR+/LR- depends on pretest probability.

Clinical decision tools, such as the Glasgow-Blatchford and Rockall scores, utilize the history, physical examination, laboratory results, and pretest probability for high-grade peptic ulcer stigmata to estimate the severity of an UGIB and risk for adverse outcomes, respectively. Notably, these scoring systems do not include FOBT results. Despite the relatively inexpensive cost per FOBT ($3.03 per unit),[20] this test's poor specificity when used in the inpatient setting has the potential to lead to significant, unnecessary downstream expense (as well as the potential for procedural risk and anxiety for patients). Given that the incidence of acute UGIB is approximately 100 per 100,000 persons per year,[7] based on the United States population in 2016,[21] there were 323,936 patients with UGIB. If each patient underwent an FOBT, the direct expense would be nearly a million dollars. Nonetheless, the number of patients getting a FOBT in the inpatient setting for a suspected UGIB (or for other indications) is unknown, and the direct costs of the tests itself likely represent a fraction of the healthcare expenditures associated with this practice. Allowing that only a third of patients with positive



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FOBTs in the inpatient setting typically undergo EGD,[22] overuse of this test would lead to a high number of unnecessary EGDs, and potentially colonoscopies or additional diagnostic procedures (eg, capsule endoscopy). In light of the false-positive results associated with FOBT, and lack of diagnostic utility, this brief cost analysis suggests FOBT is a low-value test for suspected UGIB in the inpatient setting, and there are potential significant cost savings if FOBTs are withheld.

Although Gastroccult[23] may be considered for the detection of occult blood in gastric juice, its package insert states: "As with any occult blood test, results with the Gastroccult test cannot be considered conclusive evidence of the presence or absence of upper gastrointestinal bleeding or pathology." As with any diagnostic evaluation, we would only recommend this test if it would change management.

## RECOMMENDATIONS

- FOBT should not be performed to diagnose UGIB.
- When there is clinical suspicion of acute GI bleeding, the best diagnostic tools are a good history, physical examination, and visual inspection of the stool by the clinician to determine the presence of hematochezia or melena.
- Deferring FOBT to the ambulatory setting may improve test performance characteristics.

## CONCLUSION

Revisiting our patient, for all of the reasons discussed above, there is no indication for FOBT as it would not affect management. Based on a careful history and physical examination, our patient would likely require upper endoscopy either as an inpatient or an outpatient depending on his clinical course.

FOBT is validated as an outpatient colon cancer screening tool in asymptomatic patients, not for inpatient evaluation of acute GIB. Given the poor positive predictive value for a positive FOBT in an acute GIB scenario, the potential risk for unnecessary treatments or procedures is real. Conversely, a negative FOBT (particularly FIT) does not rule out GI bleeding and risks a false sense of security that may result in under-treatment. In most scenarios in which FOBT is performed, clinicians can make decisions based on a composite of history, physical exam, visual inspection of the stool, and laboratory investigation. Until further research substantiates the utility of FOBT for this purpose, we would recommend against the routine use of FOBT for evaluating UGIB in hospitalized patients.

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Do you think this is a low-value practice? Is this truly a "Thing We Do for No Reason"? Let us know what you do in your practice and propose ideas for other "Things We Do for No Reason" topics. Please join in the conversation online at Twitter (#TWDFNR)/ Facebook and don't forget to "Like It" on Facebook or retweet it on Twitter. We invite you to propose ideas for other "Things We Do for No Reason" topics by e-mailingTWDFNR@hospitalmedicine.org.

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# An Audit of the Utility of In-Patient Fecal Occult Blood Testing

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**OBJECTIVES:** Recent surveys of physician practice have suggested the existence of excessive, inappropriate use of the fecal occult blood test (FOBT). We studied the implementation of this test in hospitalized patients.

**METHODS:** We performed a retrospective chart review of 1000 randomly selected patients who had been discharged from the Medicine service at four teaching hospitals. Patient demographics, clinical presentation, presence or absence of overt GI bleeding, and use of medications that might affect the FOBT were recorded. Reviewers assessed whether patients who had FOBT would have been candidates for colon resection if asymptomatic colon cancer had been found.

**RESULTS:** Digital rectal examination was documented in 44.8% of patients; the findings were recorded in only 9%. A total of 421 patients had FOBT on admission, usually on stool obtained at digital rectal examination. Of the patients with a positive FOBT, 17% had active GI bleeding. Only 41.1% of patients with a positive FOBT were referred to the gastroenterology service. In 70.5% of patients, FOBT could be considered inappropriate because of factors such as age, active GI bleeding, or use of aspirin or other nonsteroidal anti-inflammatory drugs.

**CONCLUSIONS:** The FOBT, which is validated only for colorectal cancer screening, is often performed inappropriately in patients admitted to the hospital. This test should be restricted in hospital practice. It would be preferable to identify patients who are appropriate candidates for colorectal cancer screening at the time of hospital discharge and to advise them about the appropriate performance of the FOBT at home. (Am J Gastroenterol 2001;96:1256–1260. © 2001 by Am. Coll. of Gastroenterology)

## INTRODUCTION

The fecal occult blood test (FOBT) is currently an integral part of colorectal cancer screening (CRCS). Indeed, CRCS is the only indication for which the FOBT has been validated. Current CRCS guidelines recommend annual FOBT starting at age 50 yr in individuals at average risk for colorectal cancer (CRC) (1, 2). However, these guidelines also state that the FOBT should be performed only on samples of spontaneously voided stool and in patients who adhere to specific dietary and medication restrictions (1, 2). A recent study found that the FOBT, when performed on stool samples obtained at digital rectal examination (DRE), was not associated with an increase in the rate of false-positive results (3). However, controlled trials demonstrating that FOBT reduces CRC mortality were performed on samples of spontaneously voided stool that had been obtained after appropriate dietary advice and medication restriction (1).

Although the FOBT has been validated only for CRCS, primary care physicians (4), internal medicine residents (5), and gastroenterologists (6) use this test for reasons other than CRCS in patients with specific GI symptoms, and do so without adequate patient preparation in terms of dietary and medication restriction. This indiscriminate use of the FOBT might lead to an excessive number of false-positive results and subsequently to unnecessary follow-up diagnostic testing. Current guidelines stress that colonoscopy is the appropriate test with which to follow-up a positive screening FOBT (1, 2). However, colonoscopy is expensive, is not universally available, and is associated with a small but finite risk, particularly in frail or elderly patients. Performing colonoscopy to evaluate a positive FOBT result obtained under inappropriate test conditions may result in a low diagnostic yield. Thus, limited health-care resources may be expended for little or no tangible benefit. As recent surveys had suggested that the FOBT was being used excessively and inappropriately (4–6), we decided to assess how this

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test was being applied in teaching hospitals. Accordingly, we undertook this multicenter in-patient audit in various regions of the United States.

## MATERIALS AND METHODS

We devised a simple checklist to be applied to a retrospective in-patient chart review of randomly selected patients at four US teaching hospitals. These were Rush-Presbyterian-St. Luke's Medical Center (Chicago, IL), Cook County Hospital (Chicago, IL), the Hospital of the University of Pennsylvania (Philadelphia, PA), and the Veterans Affairs Medical Center (Houston, TX). Each has an internal medicine residency and gastroenterology fellowship program. One or two medical residents or gastroenterology fellows (S.K., S.N., A.H., P.M., V.J.V., A.W.) at each institution undertook the chart reviews. Reviewers made unscheduled visits to medical floors of the hospitals and selected charts at random from those of patients who had been discharged within the previous 2 days.

Chart reviewers were unaware of any specific study hypothesis. They were asked to record data objectively from the chart so that we could assess the in-patient use of the FOBT. They recorded the patient's demographic information, presenting complaint, and presence or absence of overt GI bleeding (defined as any one or more of hematemesis, "coffee-ground" emesis, melena, hematochezia, or bright red rectal bleeding) at the time of admission. The chart was also reviewed to see if information had been collected from the patient regarding a past history of colon polyps, CRC, previous GI bleeding, or other GI disorders. Information was collected about family history of CRC and previous colonoscopy, flexible sigmoidoscopy, or barium enema. Medications that were recorded included aspirin, other nonsteroidal anti-inflammatory drugs (NSAIDs), anticoagulants, and vitamin C supplements. Whether or not the patient had received DRE at the time of admission was recorded and, if so, by whom. Any reported findings on DRE were recorded, as well as whether an FOBT was performed on the stool sample obtained by DRE and, if so, the result. It was also noted whether the FOBT was repeated in any patient who had a positive FOBT on DRE at the time of admission. For those patients in whom at least one FOBT was positive, the chart was reviewed to ascertain whether an in-patient gastroenterology consultation had been arranged and, if so, what investigations had been suggested to investigate the positive FOBT further. The results of any investigations recommended by the gastroenterology service were ascertained and noted. The resident or fellow who performed the chart review assessed, based only upon the information obtained from the chart, whether the patient would have been a suitable candidate for colectomy, had an early or asymptomatic colon cancer been detected. If the reviewer thought that the patient would not have been a suitable candidate, he or she was asked to explain the reason for that assessment. We considered FOBT inappropriate if the patient was not in the recommended age group for CRCS in average-risk individuals, or if the patient had been taking aspirin or another NSAID at the time of admission, or if the patient had presented to hospital with active GI bleeding. Otherwise, the FOBT was considered potentially to be appropriate.

**Table 1.** Summary of Disposition and Outcome of the Patients Whose Charts Were Reviewed Based on the Performance of In-Patient FOBT

| |
|---|
| 1000 in-patient charts reviewed |
| DRE documented in 448 of 1000 (44.8%) |
| FOBT on stool sample obtained at DRE in 421 of 448 (94.0%) |
| FOBT positive in 214 of 421 (50.8%) |
| Gastroenterology consultation in 88 of 214 patients with positive FOBT (41.1%) |
| Colonoscopy performed in 60 of 214 patients with positive FOBT (28.0%) |
| Colorectal neoplasia found in 17 of 214 patients with positive FOBT (7.9%) |

One checklist was completed for each chart reviewed. All data were entered onto a computer spreadsheet (Excel 97; Microsoft, Redmond, WA) for subsequent statistical analysis at the University of Arkansas for Medical Sciences (Little Rock, AR) using SPSS version 8 (SPSS, Chicago, IL).

## RESULTS

A total of 1000 in-patient charts were reviewed. Of the entire group, 57% of patients were men, with a mean age of 58 yr (range 17–101 yr). The racial composition was 32.9% white, 49.0% black, 7.6% Hispanic, and 1.9% Asian or other; race was not recorded in the remaining 8.6%.

### *Performance and Documentation of Digital Rectal Examination*

In all, 448 (44.8%) of the charts documented that patients had DRE performed by an emergency room physician or medical resident at the time of admission. The actual physical findings on DRE were recorded in only 9% of patients. Of the patients who had DRE, 421 (94.0%) had FOBT performed on the stool sample obtained (Table 1). These patients had a mean age of 60 yr (range 20–101 yr). FOBT was positive in 214 (50.8%) of those who had the test on DRE at the time of admission. Of those patients, 17% had presented to hospital with overt GI bleeding, compared with 8% of the entire group of 1000.

### *Past and Family History of Colorectal Neoplasia*

A past history of adenomatous colon polyps or colon cancer was documented in 2.4% each of the entire group. However, information on these conditions had not been recorded in 47.6% and 39.5% of patients, respectively. Only 3.2% of the patients had a documented positive family history of CRC, and 65% had no known family history; in the remaining 31.8%, this information was not documented in the chart.

**Table 2.** Appropriateness of the FOBT and Subsequent Diagnostic Evaluation*

| 297 Patients (70.5%) Considered Inappropriate | 124 Patients (29.5%) Considered Potentially Appropriate |
|---|---|
| 150 Patients aged <50 yr | |
| 51 Patients aged >80 yr | |
| 28 Patients aged 50–80 yr but with active GI bleeding | Patients aged 50–79 yr |
| 68 Patients aged 50–80 yr, without active GI bleeding but taking aspirin or a nonaspirin NSAID | No overt GI bleeding<br>Not taking aspirin or nonaspirin NSAID |
| FOBT positive in 158/297 patients (53.2%) | FOBT positive in 56/124 patients (45.2%) |
| 75/158 (47.5%) had GI consultation | 13/56 (23.2%) had GI consultation |
| 48/158 (30.4%) had colonoscopy | 12/56 (21.4%) had colonoscopy |

* FOBT on DRE in 421 patients.

### *Previous Lower GI Investigations*

A total of 77 patients (7.7%) had had colonoscopy within 1–172 months (mean 18 months) of hospital admission. Of the 56 patients who had colonoscopy within the preceding 5 yr, 53 still had FOBT on admission to the hospital. Previous flexible sigmoidoscopy was documented for 12 patients (mean age 59 yr; range 25–81 yr) within the preceding 1–60 months (mean 12 months). Of these, 11 (91.7%) had FOBT on hospital admission; the one patient who did not have FOBT was 34 yr of age. Previous barium enema was documented for 35 patients (mean age 66 yr; range 29–84 yr) within the preceding 1–108 months (mean 44 months). Of these, 24 (68.6%) had FOBT performed on hospital admission.

### *Use of Medications That Might Affect Interpretation of the FOBT*

At the time of admission, 22.9% of the patients had been using aspirin, whereas 75.1% denied aspirin use. This information was not recorded for 2.0% of patients. The daily dose of aspirin was ≥325 mg in 160 patients (69.9%), 81 mg in 33 patients (14.4%), and unrecorded in 36 patients (15.7%). Among the patients who had FOBT at the time of admission, 225 (53.4%) had been taking aspirin. Of those, the daily dose was 81 mg for 33 patients, ≥325 mg for 159, and not recorded for the remaining 33. A total of 85 patients (8.5%) were taking a nonselective NSAID other than aspirin, whereas 895 patients (89.5%) denied NSAID use; this information was not recorded in 20 patients (2%). Of the patients who had FOBT on admission, 61 had been taking NSAIDs; only one patient had used a COX-2–specific NSAID. In all, 79 patients (7.9%) were taking warfarin at the time of admission. The warfarin dose was not recorded in the chart in 30 cases; in the remaining 49, the mean daily dose was 4.4 mg (range 0.5–12 mg). Use of vitamin C supplements was recorded in 33 patients; the dose was usually not recorded or was part of a multivitamin preparation.

### *Follow-Up of Positive FOBT Results and Diagnostic Yield*

In the 214 patients who had a positive FOBT at the time of admission, the test was initially repeated in 31%; another 7% had at least one additional FOBT performed during the admission. Consultation with the gastroenterology service was obtained for only 88 (41.1%) of the patients with a positive FOBT (Table 1). Subsequent endoscopic studies in patients with a positive FOBT included esophagogastroduodenoscopy (EGD) in 80, colonoscopy in 60, and flexible sigmoidoscopy in three. Many patients had both EGD and colonoscopy, whereas the remainder either had no further diagnostic evaluation or had investigations other than endoscopy. In 70.5% of the patients who had FOBT on DRE at the time of admission, the test may have been considered inappropriate because of the age of the patient, the presence of active GI bleeding, or the use of aspirin or another NSAID. Details are listed in Table 2, which illustrates the distribution of inappropriate and potentially appropriate testing, the rate of test positivity, and subsequent diagnostic evaluation.

The diagnostic yield from subsequent endoscopic evaluation was CRC in four patients, undiagnosed rectal mass (possibly cancer) in another three, and colon polyps in 11, one of whom also had rectal cancer (Fig. 1). Thus, for 214 patients with a positive FOBT on admission to the hospital, 60 (28.0%) received colonoscopy, and definite or probable colorectal neoplasia was found in 17 (7.9%) (Table 1, Fig. 1). Other endoscopic diagnoses obtained in patients with a positive FOBT included esophagitis in 10, esophageal cancer in one, esophageal or gastric varices in 13, gastric ulcer in six, gastric cancer in four, duodenal ulcer in 11, and colonic diverticulosis in 13. Two patients with negative FOBT underwent colonoscopy; one had colon polyps.

### *Suitability of Patients for Surgery for Early/Asymptomatic Colorectal Cancer*

Of the patients who had received FOBT, reviewers independently considered that 17.1% would not have been suitable candidates for surgery for early or asymptomatic colon cancer because of severe or advanced coexisting medical conditions or advanced age. The mean age of those patients was 69 yr (range 34–101 yr).

## DISCUSSION

The results of this in-patient audit support and lend credence to recent surveys of physician practice (4–6). Although the

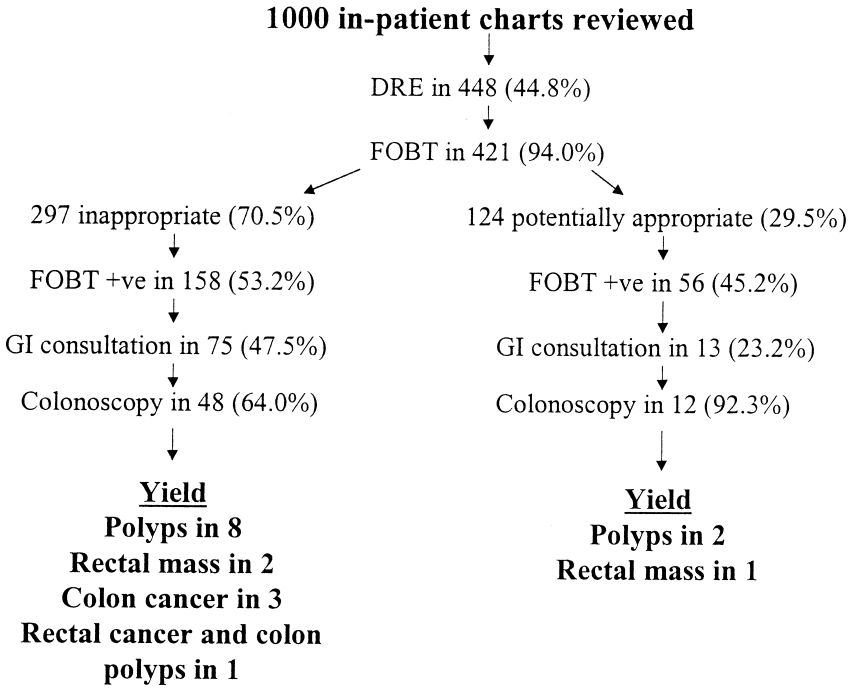


**Figure 1.** Flow diagram illustrating diagnostic yield of in-patient FOBT based on the appropriateness of the test (see text and Table 2). +ve = positive.

FOBT has been validated only for CRCS, we have confirmed that it is frequently performed for other reasons and without adequate preparation of patients in terms of dietary and medication restrictions.

Of the patients in this study, less than half had documentation of DRE at the time of admission. Furthermore, the findings on DRE were usually not recorded in the chart. These are alarming findings, as DRE is an essential component of the physical examination that may detect mass lesions of the rectum or prostate and that can, without FOBT, determine whether melena or bright red blood is present. It may be that residents perform DRE solely to obtain a stool sample for FOBT. If so, this would represent a major deficiency in their training.

Physicians who perform FOBT on stool obtained at DRE in a patient presenting acutely to hospital cannot know what diet the patient had been taking and will often not know whether the patient had recently taken any medication that might influence the interpretation of the test. Many of the patients in this study who received FOBT at the time of hospital admission had been taking aspirin or another NSAID.

A survey of primary care physicians (4) found that 69% considered the FOBT to be an appropriate part of the evaluation of hematemesis and that 74% performed it to evaluate rectal bleeding. In a subsequent survey of internal medicine residents, 83% performed FOBT in patients being assessed in the emergency room; 68%, 77%, and 81%, respectively, performed it for further evaluation of rectal bleeding, hematemesis, and melena (5). In this current in-patient audit, FOBT was performed on 89% of patients presenting with overt GI bleeding. FOBT was performed more frequently in these patients than in the group as a whole, suggesting that the decision to perform FOBT on stool obtained at DRE is in part dependent on presentation with active GI bleeding. This is clearly an inappropriate use of the test.

The FOBT seems, therefore, to be performed almost routinely in patients who are admitted to hospital, irrespective of whether the patient is a suitable candidate for CRCS. Of the patients included in this survey, 339 were aged $<50$ yr. Of the patients who had FOBT on admission to hospital, 150 were aged $<50$ yr (Table 2); assuming that they were at average risk for CRC, they would not be considered candidates for CRCS based on current national guidelines (1, 2). Had they been at increased risk for CRC, alternative forms of screening would have been more appropriate than FOBT (1, 2) and would have been indicated irrespective of the FOBT result.

Of the patients included in this survey, 107 were aged $\geq 80$ yr and 15 were aged $\geq 90$ yr. Of the patients who had FOBT at the time of admission, 51 were aged $\geq 80$ yr (Table 2). Although current guidelines do not specify an age limit to CRCS, it is probably inappropriate to continue the process into advanced age (1). The residents and fellows who performed the independent chart surveys considered that 17.1% of patients who had an in-patient FOBT would not have been candidates for surgery if early or asymptomatic colon cancer had subsequently been found. These assessments were usually made on the basis of advanced age of the patient or the presence of other serious medical problems.

Although these subjective assessments may have been biased by the reviewers' perceptions of the senior investigators' opinions, the reviewers were not aware of any primary study hypothesis. They knew only that the study aimed to examine how the FOBT was being used in hospital practice.

The performance of the FOBT in elderly patients might lead to colonoscopy as a further diagnostic evaluation for positive results, many of which will be false-positives. However, a recent survey of Medicare beneficiaries with a positive FOBT found that only 34% subsequently received any form of appropriate diagnostic testing (7), further emphasizing the futility of the FOBT as it is often currently performed. Elderly patients with iron deficiency anemia may require investigation for chronic GI blood loss. Such patients should undergo all endoscopic procedures that are clinically appropriate irrespective of the FOBT result. A recent study confirmed that endoscopy will usually find a cause for chronic GI blood loss in elderly patients, but that the FOBT is generally unhelpful (8).

We found that the diagnostic yield from follow-up investigations for a positive FOBT was quite low. Definite or probable colorectal neoplasia was detected in 17 patients (Fig. 1). The patient with rectal cancer and colon polyps had presented with lower GI bleeding. In the three patients with a rectal mass, this had been detected by DRE alone; furthermore, each had other indicative symptoms including constipation, proctalgia, and perianal pain. One patient with colon cancer had presented with constipation and weight loss. Only one patient with colon cancer had presented without GI symptoms. Therefore, it is likely that appropriate physical examination and diagnostic evaluation of the patients' presenting symptoms would have detected all but one of these definite or presumed cancers without the performance of FOBT.

Some patients were diagnosed with upper GI conditions after documentation of a positive FOBT. However, it is doubtful whether the positive FOBT *per se* led to these diagnoses. Specialist consultation and the relevant endoscopic examinations would probably have been performed irrespective of the FOBT result because of the specific upper GI symptoms–most notably, bleeding—that these patients had.

There are some potentially serious consequences of the continued, widespread, inappropriate use of the FOBT in hospitalized patients. Residents in training may continue to apply it inappropriately when they are in practice, as borne out by a recent survey of primary care physicians (4). They could also become disillusioned with the utility of the test and could fail to recommend it to their patients who are suitable candidates for CRCS.

The availability of the FOBT has subsequently been restricted at one of the hospitals that participated in this study. Some may argue, however, that there will still be an occasional requirement to perform FOBT in the hospital. One example might be when there was doubt whether black stool was due to melena or to another cause such as vegetable matter or a medication that contained iron or bismuth. However, this will usually be evident without FOBT. It might be argued that in-patient FOBT is the only opportunity for CRCS in some patients who might not be able or willing to comply with the test at home after hospital discharge. However, such patients may also be too sick or frail to undergo appropriate diagnostic testing to investigate a positive screening FOBT, as suggested by the recent follow-up of Medicare beneficiaries (7).

Whenever possible, patients who are suitable candidates for CRCS should be identified at the time of discharge and, after giving informed consent, should be instructed on the proper performance of the FOBT at home. They will also require advice about the necessary dietary and medication restrictions, which many physicians currently do not provide (4, 5). Focused educational efforts on restricting the FOBT to its proper role in CRCS should be directed at residents in training, emergency room physicians, and primary care providers.

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