Cost-effectiveness of Endoscopy in Irritable Bowel Syndrome

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Background: It is unknown to what extent at what expense flexible sigmoidoscopy and colonoscopy add to the diagnosis of irritable bowel syndrome (IBS). The aim of the study was to assess the incremental cost-effectiveness of endoscopic procedures in the workup for IBS.

Methods: Using the Bayes formula, we calculated the increase in diagnostic certainty for a consecutive number of tests. We also calculated the incremental cost-effectiveness ratio, which corresponds to the test costs divided by the increment in diagnostic certainty.

Results: The diagnosis of IBS can be established with a relatively high probability of more than 80% relying on relatively inexpensive and noninvasive tests only. Flexible sigmoidoscopy or colonoscopy constitute the most costly portion of any workup for IBS, which amounts to 50% to 75% of the overall costs. Because of their high incremental cost-effectiveness ratio, endoscopic procedures should not be used at the beginning of the diagnostic workup. This outcome of the analysis remains largely unaffected within reasonable ranges of the sensitivity and specificity of various tests.

Conclusions: In the diagnosis of IBS, inexpensive, noninvasive tests should be used first to rule out other diagnoses. Despite their high incremental cost-effectiveness ratio, flexible sigmoidoscopy and colonoscopy are indicated when a serious organic disease is reasonably likely and needs to be ruled out.

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IRRITABLE BOWEL syndrome (IBS) affects 15% to 20% of the US population,1 of whom only 30% seek medical attention for this condition.2-4 Its diagnosis is based primarily on the occurrence of typical symptoms.5 In the absence of any specific biochemical markers, symptoms constitute the only positive test modality for diagnosis of IBS. Studies6-9 have shown the sensitivity associated with typical symptoms to vary between 42% and 94% and the specificity to vary between 55% and 94%. To improve the diagnostic probability, physicians must resort to ruling out other potential organic diseases, such as inflammatory bowel disease, microscopic colitis, gastrointestinal infections, lactose intolerance, intestinal malabsorption, endocrine disorders, and colorectal cancer.10,11 This requires multiple laboratory tests, stool studies, radiologic small bowel followthrough, and flexible sigmoidoscopy or colonoscopy.11-13 The expenditures rise as a result of the multitude of tests necessary to rule out other medical conditions and to increase the certainty associated with the specific diagnosis of IBS. It was estimated that the excess medical cost for diagnosing IBS in the United States in 1992 was $8 billion.14 The present study focuses on the cost-effectiveness of endoscopic procedures in the workup of IBS. How much do flexible sigmoidoscopy and colonoscopy add to establishing a diagnosis of IBS and at what expense? The aim of our study was to assess the incremental cost-effectiveness of endoscopic procedures in the workup for IBS.

Figure 1 shows a decision tree of various possible test sequences. Each box symbolizes a different test of the sequence. The dollar amount inside the box represents the cumulative costs spent on tests. The number in the right upper corner represents the remaining population (of the initial 1000 patients) with a test sequence that is still suggestive of IBS and to whom the next test will be applied. The rest of the initial population has dropped out because one of the tests has suggested another diagnosis than IBS. The percentage value inside the box represents the cumulative probability for IBS. The cumulative probability is calculated by repetitive ap-
METHODS

GENERAL DECISION MODEL

The diagnosis of IBS is assumed to be based on a sequence of 6 consecutive tests: (1) history and physical examination, (2) general laboratory panel, (3) hydrogen breath test, (4) radiologic small bowel follow-through, (5) flexible sigmoidoscopy, and (6) colonoscopy. The order of tests can be permuted in many different ways, and the diagnostic work-up can be stopped after any given number of tests. The increment in diagnostic certainty for a consecutive number of tests is calculated using the Bayes formula. The incremental cost-effectiveness ratio (ICER) corresponds to the increment in test costs divided by the increment in diagnostic certainty. For the purpose of the present analysis, the ICER is defined as costs per 1% increase in the probability of having IBS. We also calculate the average cost-effectiveness ratio (ACER) of establishing 1 diagnosis of IBS, ie, the total costs of all diagnostic tests in the entire patient population divided by the number of correct diagnoses.

TEST COSTS

The Table lists the physician and facility costs associated with the 6 diagnostic procedures. The procedures are assigned code numbers from the Physicians’ Current Procedural Terminology (CPT), using the code numbers to assign costs to each test. The costs represent the average payments allowed for each coded procedure by the Health Care Financing Administration during fiscal year 2000. Except for laboratory tests, the dollar amount reflects physician plus facility cost. In the case of colonoscopy, CPT codes reflect the endoscopy plus one set of biopsy specimens taken during the procedure. The costs for the biopsy include the professional fees of a surgical pathologist. No polypectomy or costs of potential complications resulting from endoscopy are considered. Biopsy costs were not added to the cost of flexible sigmoidoscopy because rectal biopsies were found to be unnecessary in the investigation of IBS by MacIntosh and coworkers, and in general they are less likely to be done routinely.

TEST CHARACTERISTICS

The sensitivity and specificity for each of the tests were obtained from the literature. The characteristics of taking a history are estimated based on the sensitivity and specificity reported for the Manning and Rome criteria. The combined sensitivity of multiple blood and stool tests is calculated as the weighted average of each individual test for a positive gastrointestinal diagnosis, using various disease prevalence rates as weights (see formula 1). In general, the normal range of each laboratory test is set to include 95% of all true-negative results, ie, a 95% specificity. Bessette and coworkers report a sensitivity of 61% for the small bowel follow-through in detecting small bowel tumors; they also cite other studies that report sensitivity ranging from 53% to 83%. Others have reported overall sensitivities of more than 90% for the small bowel follow-through. The median value of 70% is taken to estimate the general sensitivity associated with any small bowel disease. For the hydrogen breath test, we use the median sensitivity and specificity values reported to test for bacterial overgrowth and lactase deficiency. The sensitivity (sens) and specificity of colonoscopy and flexible sigmoidoscopy are calculated as the weighted average of these tests for inflammatory colitis, diverticular disease, and colon cancer, again using disease prevalence (prev) as weight:

\[
sens = \frac{\sum prev_i \times sens_i}{\sum prev_i}
\]

The literature values for sensitivity and specificity show a large spread, which can be partly explained by the trade-offs between sensitivity and specificity. As indicated by the receiver operating characteristic of each test, a sensitivity value can be increased at the expense of lowering the corresponding specificity value.

In Figure 2, the cumulative costs are plotted against the cumulative probability of diagnosing IBS. The numbers next to each test represent the remaining population undergoing each particular test. Four possible sequences are shown. History plus physical examination, laboratory test panel, hydrogen breath test, and small bowel follow-through yield a diagnostic probability of 83% at the expense of $398. Panel A depicts a flat curve that starts to rise steeply only after the inclusion of flexible sigmoidoscopy and colonoscopy into the diagnostic work-up. Flexible sigmoidoscopy increases the overall probability by 6% at the expense of almost doubling the cumulative costs. The inclusion of colonoscopy raises the probability by an additional 7% at the expense of yet again doubling the cumulative costs. Leaving out flexible sigmoidoscopy, as suggested by panel B, and going directly from small bowel
INCREMENTS IN DIAGNOSTIC CERTAINTY

Since IBS affects 15% of the adult population, of whom one third seek medical attention, the point prevalence of this condition in a general patient population is estimated as 5%. This is used as a starting value for the pretest probability (P0) of IBS in a given patient. The prevalence of IBS in combination with the sensitivity (sens) and specificity (spec) values taken from the Table are then keyed into the Bayes formula to calculate the positive predictive value (P1) associated with a positive first test result, i.e., a positive history of symptoms:

\[
P1 = \frac{P0 \times sens}{P0 \times sens + (1 - P0) \times (1 - spec)}
\]

\[
= \frac{0.05 \times 0.67}{0.05 \times 0.67 + (1 - 0.05) \times (1 - 0.70)}
\]

\[
\approx 0.11
\]

The positive predictive value (P1) serves as an updated pretest probability value for the second round of tests, for instance, the laboratory test panel. The increase in disease probability after each test is calculated by repetitive use of the Bayes formula. Except for the history and physical examination, the sensitivity and specificity values of all subsequent tests relate to a positive diagnosis other than IBS, whereas IBS itself is included in the group of negative diagnoses. In other words, all subsequent tests are designed to rule out diagnoses in the differential other than IBS. Therefore, the Bayes formula for a negative predictive value is used to calculate the upgrade in diagnostic probability (P2) after the second test, for instance,

\[
P2 = \frac{P1 \times spec}{P1 \times spec + (1 - P1) \times (1 - sens)}
\]

\[
= \frac{0.11 \times 0.95}{0.11 \times 0.95 + (1 - 0.11) \times (1 - 0.85)}
\]

\[
\approx 0.43
\]

P2 is subsequently entered as pretest probability into a third Bayes formula to calculate the negative predictive value of IBS (P3) associated with a third round of diagnostic testing. This procedure is repeated according to the number of tests used in trying to establish the diagnosis. The values P1−P0, P2−P1, P3−P2, and so on correspond to the increments in diagnostic certainty with respect to IBS.

The number of patients with a positive test result (N1) is determined by the fraction of true-positive test results (sens) in patients with IBS (P0) and the fraction of false-positive test results (1−spec) in subjects without IBS (1−P0):

\[
(4) N1 = P0 \times sens + (1 - P0) \times (1 - spec)
\]

Equation 4 corresponds to the denominator of the Bayes formula of equation 2 multiplied by the initial patient population (N0). Applying equation 4 to an initial population of N0=1000 patients yields a positive history of symptoms in the following:

\[
(5) N1 = 1000 \times [0.05 \times 0.67 + (1 - 0.05) \times (1 - 0.70)] \approx 319
\]

Similarly, the number of patients with possible IBS after a negative laboratory panel corresponds to the denominator of equation 3 multiplied by the remaining patient population after applying the first test (N1):

\[
(6) N2 = N1 \times [P1 \times spec + (1 - P1) \times (1 - sens)]
\]

\[
N2 = 319 \times [0.11 \times 0.95 + (1 - 0.11) \times (1 - 0.85)] \approx 75
\]

SENSITIVITY ANALYSIS

The primary focus of the present analysis relates to the incremental cost-effectiveness of flexible sigmoidoscopy and colonoscopy. Besides the sensitivity and specificity of both procedures, this value depends largely on the pretest probability achieved through other means before embarking on endoscopic procedures. In a sensitivity analysis, the pretest probability varied between 80% and 98%.

follow-through to colonoscopy provides only moderate relief with respect to the overall expenses.

The 2 sequences outlined in the 2 bottom panels (C and D) indicate that performing endoscopy early during the workup does not represent a valid option, because it adds large costs to the early workup without pushing the diagnostic probability beyond 70%. Inexpensive tests at the onset of the diagnostic workup function as a sieve to exclude patients without IBS and increase its a priori probability before using the more expensive tests. The test sequences of panels A and C, as well as panels B and D, contain identical tests, resulting in the same medical outcome. In the 2 lower panels (C and D), flexible sigmoidoscopy and colonoscopy, respectively, are used as early as the third diagnostic test. Shifting endoscopy toward the beginning of the diagnostic workup leads to a larger number of patients undergoing endoscopy. In the sequence of panel A, for instance, only 31 subjects undergo flexible sigmoidoscopy compared with 75 patients in panel C. Similarly, only 31 subjects undergo colonoscopy in the sequence of panel B compared with 75 in panel D. The total cost of testing in the entire patient population corresponds to the sum of patients associated with each test in Figure 2 multiplied by the respective test costs. The ACER corresponds to the total cost divided by the number of correct diagnoses of IBS. Although sequences A and C lead to identical medical outcomes, their ACERs are $18382 and $24686 per diagnosis, respectively. Similarly, the identical outcomes of the 2 sequences B and D are associated with ACERs of $12724 and $14355 per diagnosis, respectively.

The sequences depicted in Figures 1 and 2 are restricted to the analyses of true test results. The cumulative costs of diagnosing IBS may become further inflated by the contribution of false tests. For instance, the atypical description of bowel symptoms may convince the phy-
sician to pursue diagnoses other than IBS and invest in many unnecessary tests. Similarly, a false-positive sign of ileal obstruction or inflammation may mislead the physician to rule out a diagnosis of inflammatory bowel disease, intestinal lymphoma, or tumor before returning to the workup for IBS. No systematic analysis can predict the variety and types of erroneous and occasionally convoluted workups that may ensue from false test results. A false-positive diagnosis of IBS would not contribute to the cost of IBS itself but add to the costs of other differential diagnoses.

Under baseline conditions, history and physical examination, laboratory tests, hydrogen breath test, and small bowel follow-through reach a probability value of 83%, with a total of $398 spent on diagnostic workup. The ICER of all 4 tests, compared with the baseline prevalence rate of 5%, is $398/(83%−5%)=$510 per 1% increase in diagnostic probability. The ICER of flexible sigmoidoscopy is $5846 for this step alone. Colonoscopy alone is associated with an ICER of $8246, whereas the combination of both endoscopic procedures is associated with an ICER of $9338. A higher pretest probability leads to lower increments in diagnostic certainty achieved through endoscopy and, hence, a higher ICER. Figure 3 shows the relation between pretest probability and the ICER of endoscopic procedures. When varying the pretest probability, one notices a change in the incline for each of the series at 94%, when the ICER becomes steeper. This indicates that the expenditures become much greater for smaller gains in probability beyond this probability.

### Test Characteristics and Costs*

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Item</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Cost, $†</th>
</tr>
</thead>
<tbody>
<tr>
<td>99245</td>
<td>Office consultation</td>
<td>67</td>
<td>70</td>
<td>198</td>
</tr>
<tr>
<td>82270</td>
<td>Fecal occult blood test</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>80050</td>
<td>General laboratory panel†</td>
<td>46</td>
<td></td>
<td></td>
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<tr>
<td>89552</td>
<td>Sedimentation rate</td>
<td>4</td>
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<td>87072</td>
<td>Stool culture</td>
<td>10</td>
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</tr>
<tr>
<td>87177</td>
<td>Stool ova and parasites</td>
<td>12</td>
<td></td>
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</tr>
<tr>
<td>86674</td>
<td>Stool Giardia fecal antigen</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Laboratory Tests</strong></td>
<td></td>
<td>85</td>
<td>95</td>
<td><strong>96</strong></td>
</tr>
<tr>
<td>74251</td>
<td>SBFT (enteroclysis)</td>
<td>70</td>
<td>92</td>
<td>78</td>
</tr>
<tr>
<td>91065</td>
<td>Hydrogen breath test</td>
<td>58</td>
<td>87</td>
<td>26</td>
</tr>
<tr>
<td>45330</td>
<td>Flexible sigmoidoscopy</td>
<td>60</td>
<td>70</td>
<td>381</td>
</tr>
<tr>
<td>45380</td>
<td>Colonoscopy with biopsy</td>
<td>743</td>
<td></td>
<td></td>
</tr>
<tr>
<td>88305</td>
<td>Surgical pathology</td>
<td>71</td>
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<tr>
<td><strong>Total Colonoscopy</strong></td>
<td></td>
<td>70</td>
<td>80</td>
<td><strong>84</strong></td>
</tr>
</tbody>
</table>

† Expenditures for all tests except laboratory tests include professional and facility cost.
‡ Includes serum electrolytes, coagulation, liver and kidney function tests, albumin, complete blood cell count, and thyroid-stimulating hormone.
The objective of performing medical tests is to increase the diagnostic probability associated with a given diagnosis. Most diagnoses can be ascertained by a sequence of one or few positive test results. Irritable bowel syndrome constitutes a diagnostic conundrum, because its workup is mainly composed of negative test results. Except for a set of specific symptoms that may be ascertained through careful history taking, IBS can only be approached in an indirect fashion by ruling out other differential diagnoses. The large variety of diagnoses associated with abdominal pain harbors the potential risk of turning the workup for IBS into a rather expensive medical exercise. Our analysis suggests that the diagnosis of IBS can be established with a relatively high probability by relying on relatively inexpensive and noninvasive tests only. Endoscopic procedures should not be used at the beginning of the diagnostic process.

Figure 2. The cumulative cost and probability of irritable bowel syndrome (IBS) associated with various diagnostic paths. The numbers represents the number of patients subjected to each consecutive test. H&P indicates history and physical examination; lab, laboratory tests as indicated in the Table; H2BT, hydrogen breath test; SBFT, small bowel follow-through; FS, flexible sigmoidoscopy; and colon, colonoscopy.

Figure 3. Incremental cost-effectiveness ratio (ICER) of endoscopic procedures plotted against the pretest probability achieved by nonendoscopic means. The ICER is given in US dollars per 1% increase in the diagnostic probability of irritable bowel syndrome (IBS).
workup, and they should be reserved for patients in whom high diagnostic certainty is deemed necessary. Flexible sigmoidoscopy or colonoscopy constitute the most costly portion of any workup for IBS, which amounts to 50% to 75% of the overall costs. This outcome of the analysis remains largely unaffected by the sensitivity and specificity of various tests. In general, a better diagnosis of IBS by means other than endoscopy increases the ICER of subsequent endoscopy.

The present analysis uses the Bayes formula to calculate the increment in diagnostic certainty achieved through a sequence of consecutive tests. In strictly mathematical terms, the repeated application of Bayes formula requires that the tests are statistically independent. In reality, such conditions are rarely met. For instance, inflammatory bowel disease may lead to intestinal obstruction, visible on the small bowel follow-through, and crampy abdominal pain. Obviously, some of the pain may stem from the intestinal obstruction, and the 2 signs are not independent of each other. Similarly, rectal cancer could result in 4 related signs—constipation, anemia plus positive fecal occult blood test result, and a positive finding during sigmoidoscopy. The erroneous assumption of test independence tends to overestimate the cumulative probability of multiple tests and the diagnostic increment associated with individual tests. These types of errors concern mostly the diagnostic contribution exerted by the 2 endoscopic procedures. Obviously, flexible sigmoidoscopy and colonoscopy constitute similar tests, and the actual contribution of a colonoscopy after a flexible sigmoidoscopy may be much smaller than calculated here based on its sensitivity and specificity alone.

In modeling the path toward a diagnosis of IBS, we considered only true-positive and true-negative test results that helped to improve the probability of this particular diagnosis. False tests would prolong the diagnostic chain and inflate the costs of the diagnosis. More tests would also add to the overall risk of adverse effects and complications associated with any lengthy medical workup involving multiple procedures. Since errors occur randomly and their financial consequences are difficult to predict, we decided to restrict the cost analysis to Medicare reimbursement for various medical costs. In ignoring these additional costs, our analysis of diagnosing IBS underestimates the true cost of consecutive testing. The analysis focuses on the implications of advancing the workup toward a correct diagnosis of IBS, but it cannot measure the cost-effectiveness of excluding other diagnoses, such as colorectal cancer, diverticulitis, or inflammatory bowel disease. Foremost, there would be no reason to restrict the benefit of exclusion to gastrointestinal disease, and the diagnostician could well claim the benefit of having excluded in essence an entire textbook of medicine in each individual patient. One would need to know the myriad costs associated with the entirety of other diagnoses and quantify all gains in terms of quality-adjusted life-years achieved through each individual test. Besides the difficulties in accumulating such information, the results would be compromised by the arbitrariness of what diagnoses or parameters to consider. The analysis of IBS would become overwhelmed by other issues, and its outcome would be extremely sensitive to minor changes in the underlying assumptions. The general benefit of endoscopy in the workup of gastrointestinal disease or the cost-effectiveness of colonoscopy in colorectal cancer reside outside the realm of the present analysis.

The model shows that 4 relatively simple, noninvasive tests can achieve a diagnostic probability of more than 80%. Such a value may provide sufficient diagnostic certainty in a young patient with a history of similar symptoms during a prolonged period. Patients with IBS fall into the age range of 30 to 55 years.6,7,14,27,28 The prevalence and incidence of IBS decline with increasing age, and during a 5-year follow-up patients tend to recover from their symptoms of IBS.29 Most patients have their symptoms for more than 2 years.3 This pattern is in striking contrast to colorectal cancer, where most cases occur after the age of 50 years. These patients also present with a shorter history that tends to worsen over time.

Besides colorectal cancer, the need to rule out inflammatory bowel disease or microscopic colitis represents another reason to schedule an endoscopic procedure in patients with abdominal symptoms. Hamm and coworkers30 analyzed the results of endoscopy in 306 patients who met the Rome criteria for IBS. Only 7 patients presented with colonic abnormalities, of whom 3 had inflammatory bowel disease, 1 had intestinal obstruction, and 3 had colonic polyps. Vanner and coworkers31 reported that in the absence of alarm signs, such as weight loss, nocturnal symptoms, blood mixed with stool, recent antibiotic use, family history of colon cancer, or relevant abnormalities on physical examination, the Rome criteria had a sensitivity of 65% and a specificity of 100%.

These citations from the last 2 paragraphs should not be misinterpreted, however, to indicate that flexible sigmoidoscopy or colonoscopy can be generally dispensed within the workup for irritable bowel. Similarly, the high ICER of endoscopy must not be mistaken as an argument against its use in the diagnosis of IBS. Toward the end of all diagnostic workups, increasing amounts of money are spent on confirming a suspected diagnosis and raising its probability by a few points only. This law of diminishing return permeates a large variety of medical and nonmedical endeavors. In a previous decision analysis, it was shown that a diagnostic test remains indicated as long as the pretest probability (P) of a given disease exceeds the ratio of test cost (T) to disease cost (C), that is, P > T/C.32 In the case of colorectal cancer or inflammatory bowel disease, for instance, the overall costs of the disease outweigh the costs of a single endoscopy by a factor of 50 or more, for which the ratio is 2% or less. In other words, a gap in the diagnostic probability between 80% and 100% may be large in some patients and represent an intolerable risk. An endoscopic procedure that would help in bridging this gap and eliminating the risk of serious organic disease may well justify its high ICER.

In conclusion, endoscopic procedures represent the most costly portion in the workup for IBS, contributing to 50% to 75% of the total cost. They should be scheduled at the end of a diagnostic chain, using less expensive tests first to rule out other differential diagnoses. Despite their high ICER, however, the utilization of en-
doscopic procedures is indicated in all patients in whom, besides diagnosing IBS, ruling out a serious organic disease is necessary.

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