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Economic and Health Outcomes of Capsule Endoscopy: Opportunities for Improved Management of the Diagnostic Process for Obscure Gastrointestinal Bleeding

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ABSTRACT

The estimated annual incidence of gastrointestinal bleeding in the United States is approximately 100 episodes per 100,000 persons, resulting in 300,000 hospitalizations annually. Diagnostic tools such as radiologic studies and endoscopic examination often fail to identify a source of bleeding, resulting in a cycle of repetitive testing over months or even years. Costs associated with the diagnostic process, and with interim treatment for anemia and other symptoms, can be significant. The diagnostic process also takes a toll on the patient, in terms of worry, pain, and discomfort. Capsule endoscopy, a technology that received FDA clearance in August, 2001, consists of a video capsule that is ingested by the patient, and that transmits images to a wireless data recorder worn on the belt. The recorded stream of approximately 50,000 images can be reviewed on a computer workstation by a physician to identify nature and location of potential sources of bleeding. This paper presents a framework for economic analysis of this new technology. First, we present a review of the literature on the current diagnostic methods. Next, we present a conceptual model for examining contributors to costs in diagnosing obscure intestinal bleeds. We conclude by exploring the potential economic impact of the technology. Analysis of data from the first U.S. clinical trial of capsule endoscopy demonstrates its high diagnostic yield, and patient satisfaction. While further study is required, this analysis indicates that capsule endoscopy may reduce total medical utilization and costs and improve patient quality of life, when used for appropriate indications.

THE DIAGNOSIS OF OBSCURE GASTROINTESTINAL BLEEDING

THE ANNUAL INCIDENCE of gastrointestinal (GI) bleeding in the United States has been conservatively estimated at approximately 100 episodes per 100,000 persons, accounting for approximately 300,000 hospitalizations per year.[1] The actual incidence may be higher. Mass screening programs for colorectal cancer have revealed rates of fecal occult bleeding for asymptomatic individuals ranging between 2% and 8% of the at-risk population.[2]

Obscure bleeding refers to intermittent or

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chronic bleeding of unknown origin with negative endoscopy, colonoscopy, and/or small bowel series results.[3,4] Obscure bleeding can be subcategorized into either (1) obscure-occult [recurrent iron-deficiency anemia (IDA) and/or recurrent positive fecal occult blood test (FOBT) results] or (2) obscure-overt (recurrent passage of visible fecal blood).[3]

About 70–80% of small bowel bleeding cases are due to vascular lesions. Arteriovenous malformations account for about 66% of small bowel vascular lesions. Vascular lesions tend to be more common in elderly patients, patients with chronic renal failure, and patients diagnosed with inherited disorders.[5,6] Even though only about 5–7% of all GI tumors are located in the small bowel, small bowel tumors are the second most common cause of obscure bleeding.[5] The most common benign tumors of the small bowel include adenomas, leiomyomas, and lipomas. Of all malignant GI tumors, less than 2% are located in the small bowel. The most common type, adenocarcinomas, account for 40% of all small bowel carcinomas.[5]

A variety of diagnostic tools and procedures exist for identifying the source of obscure bleeding, including radiologic studies, enteroscopy, and nuclear scans.

Radiologic studies

The small bowel series, which involves x-rays after the patient has swallowed a contrast medium, has been shown to have a low diagnostic yield, about 5%, for the detection of small intestinal bleeding and a high false-negative rate of 41.6%.[7] Enteroclysis differs from small bowel series in that the contrast material is administered via a small tube placed directly in the proximal intestine.[8] Enteroclysis is not very helpful in detecting vascular lesions, but can be useful in identifying mucosal damage or small bowel tumors, since it allows for visualization of the entire small bowel, including the portion that cannot be reached by an endoscope.[5] While it is often used in combination with enteroscopy to improve diagnostic yield, the improvement may be minimal. For example, one study found a diagnostic yield of enteroscopy of 54%, versus a yield of 57% when enteroscopy was combined with enteroclysis.[9] Some disadvantages of enteroclysis compared with small bowel series include greater radiation exposure, greater patient discomfort (gagging and wretching), and longer procedure time.[10]

Push enteroscopy

Push enteroscopy, the most commonly used endoscopic diagnostic procedure for examining the small bowel, is appropriately named because the operator must "push" the diagnostic instrument through the upper GI tract into the small bowel via the oral route.[11] Several studies have indicated that the overall diagnostic yield of push enteroscopy in identifying obscure bleeding lesions is between 38% and 75%[4] (Table 1). However, these diagnostic yields may reflect all types of lesions that were identified, even including those located prior to the small bowel and not related to the source of the obscure bleed. Thus, the true diagnostic yield of push enteroscopy for work-up of obscure bleeding in the small bowel may be more in the range of 15–35%. Advantages to using push enteroscopy include its relative ease of use, time of performing the procedure (most examinations take less than 60 minutes), and the ability to obtain biopsy samples and conduct therapeutic interventions (i.e., electrocoagulation, polypectomy).[7,11] In addition, the procedure is relatively safe and has a low incidence of complications.[8]

Many of the reported complications with push enteroscopy involve the use of overtubes, which keep the enteroscope from curling in the stomach, thus allowing for deeper penetration into the small bowel. Unfortunately, the use of overtubes may cause mucosal damage to the GI tract.[11] Other disadvantages associated with enteroscopy include the need for patient sedation, and that significant patient discomfort may occur. However, the most significant disadvantage is that the enteroscope has limited reach and may only examine as little as one-third of the small bowel's total length, which is approximately 22 feet.

Sonde enteroscopy

Sonde enteroscopy involves transnasal insertion of a longer endoscope, which is advanced through the digestive tract to the distal

TABLE 1. YIELD FOR COMMON DIAGNOSTIC PROCEDURES FOR OBSCURE GI BLEEDING

Procedure, study	Total	Source identified	Yield (%)
Push enteroscopy[5,8,11,12]			
Foutch et al.[13] (1990)	39	15	15/39 (38)
Barkin et al.[14] (1992)	28	21	21/28 (75)
Harris et al.[15] (1994)	31	19	19/31 (61)
Schmit et al.[16] (1996)	83	49	49/83 (59)
Vakil et al.[17] (1997)	29	18	18/29 (62)
Chak et al.[6] (1998)	129	91	91/129 (71)
Shackel et al.[18] (1998)	44	23	23/44 (52)
Zaman and Katon[12] (1998)	95	39	39/95 (41)
Sonde enteroscopy[7,8,11]			
Barthel et al.[19] (1990)	18	5	5/18 (28)
Gostout et al.[20] (1991)	35	9	9/35 (26)
Morris et al.[21] (1992)	65	25	25/65 (38)
Gostout et al.[22] (1993)	24	13	13/24 (54)
Intraoperative enteroscopy[8]			
Bowden et al.[23] (1980)	18	16	16/18 (89)
Lau et al.[24] (1987)	15	12	12/15 (80)
Flickinger et al.[25] (1989)	14	13	13/14 (93)
Desa et al.[26] (1991)	12	10	10/12 (83)
Lewis et al.[27] (1991)	23	20	20/23 (87)
Ress et al.[28] (1992)	44	31	31/44 (70)
Szold et al.[29] (1992)	30	28	28/30 (93)
Lopez et al.[30] (1996)	16	14	14/16 (88)

portion of the small bowel by peristalsis, over an approximately 8-hour period. The physician slowly withdraws the endoscope while viewing the small bowel.[7] The diagnostic yield of sonde enteroscopy (Table 1) is reported to be between 26% and 54%.[8] Sonde enteroscopy is not often used today in clinical practice owing to discomfort to the patient and clinical limitations to the procedure.[5] For example, because the examination of the small bowel occurs during the withdrawal of the enteroscope, the sonde enteroscope cannot be readvanced during the procedure.[7] This limits the view to only 50–70% of the mucosal surface.[11] Further, very few types of sonde enteroscopes are available, the instrument is costly to repair, and the procedure time is significant.[7,9] Complications are uncommon, but perforations of the bowel have been reported.[8]

Intraoperative enteroscopy

Intraoperative enteroscopy is considered the "gold standard" for small bowel examination because most, if not all, of the small bowel can be visualized.[5] Because it is an invasive procedure, intraoperative enteroscopy is most often used in patients with obscure bleeding who, after multiple testing, remain undiagnosed and continue to require blood transfusions.[11] Since laparotomy is involved, the procedure requires the assistance of both an endoscopist and surgeon.[11] While the actual exam time may be as low as 30 minutes for the endoscopist,[5] preparation, intra- and postoperative surgical time and costs can be significant. Because intraoperative enteroscopy allows for the inspection of the entire mucosal surface, it has been reported that intraoperative enteroscopy has a diagnostic yield of 70–100% in patients with obscure bleeding[8] (Table 1). The array of complications that can occur with intraoperative enteroscopy show that this procedure should only be performed by experienced endoscopists and surgeons in carefully selected patients. In addition, postoperative deaths with intraoperative enteroscopy have been reported as high as 11%, but many studies fail to report mortality with intraoperative enteroscopy.[8]

Nuclear scans and angiography

Radioisotope bleeding scans may be useful in detecting bleeding sources of obscure ori-

gin. The most commonly used method is the ^{99m}Tc-labeled erythrocyte scan.[8] The sensitivity of this nuclear medicine scan can range from 50% to 90% in detecting the presence and approximate site of bleeding, pending that the test is performed during active bleeding.[5] The source must have an active bleeding rate of 0.1–0.4 mL/min to generate a positive scan result.[8] Conversely, the scan may produce a normal result if the bleeding is intermittent. The sensitivity of this test in identifying ongoing GI bleeding ranges between 30% and 86%.[5] Angiography can also be used to perform therapeutic interventions by using embolization or vasopressin infusion to treat the bleeding site.[5] The administration of anticoagulants, vasodilators, or clot-lysing agents may enhance the diagnostic yield of this procedure; however, the increased risk of bleeding complications with this technique limits its use.[8]

The American Gastroenterological Association (AGA) has published an algorithm for diagnosing both obscure-occult and obscure-overt bleeding[3] (Fig. 1). Initial diagnostic evaluation often involves repeated colonoscopy and upper endoscopy procedures before advancing to the small bowel. These repeat procedures often identify the bleeding source that was missed in the initial investigation.[8] It is estimated that as many as 30% of upper lesions during upper endoscopy and 3% of colonic lesions during colonoscopy are overlooked during the initial procedure.[4] Yet another study that repeated upper endoscopy and colonoscopy procedures after an initial normal examination failed to locate a bleeding lesion.[13] The decision to perform a repeat endoscopy often depends on the skill and experience of the initial endoscopist. Some investigators may elect to perform enteroscopy instead of repeating the endoscopy.[8] Despite multiple diagnostic evaluations with upper endoscopy, colonoscopy, and barium studies, approximately 5% of patients will continue to experience unidentified obscure bleeding.[31]

Because of the limitations of traditional diagnostic tests discussed above, it may take considerable time to diagnose a patient who presents with obscure GI bleeding. The median time to diagnose patients with obscure-overt bleeding has been estimated as two years, with a range from one month to eight years.[8] As a consequence of this extended time to diagnosis, patients may be forced to undergo numerous diagnostic tests and evaluations before a bleeding source can be identified. For example, in one study,[13] 39 patients undergoing push-enteroscopy for unidentified obscure bleeding had a total of 277 diagnostic tests performed, for an average of 7.3 tests per patient. At the conclusion of the study, 49% of the patients continued to have an unknown bleeding source. The cycle of repeat testing also can be associated with interim treatments, especially hospitalizations and outpatient treatments for anemia.[8] In a study of 14 patients with obscure bleeding, hospital admissions ranged from two to 10 (mean = 5), and units of blood transfused ranged from 6 to 200 (mean = 46) during the 6-year period prior to undergoing intraoperative enteroscopy.[25]

COSTS ASSOCIATED WITH DIAGNOSING OBSCURE GASTROINTESTINAL BLEEDING

The current medical literature lacks detailed information on the costs associated with diagnosing obscure GI bleeding. The most comprehensive review of the economic literature for the period 1985–1995 identified limited information of value in understanding the costs, and was not limited to obscure bleeding.[32] In Figure 2, we present a conceptual model showing how current diagnostic tools and protocols impact on costs. The model is based on literature review and consultation with clinicians, and is intended to provide a framework for conducting economic evaluation of both current and new diagnostic technologies for obscure bleed.

The model, which takes a *societal perspective*, includes a flowchart demonstrating key contributors to the direct medical costs of screening, and also identifies key indirect medical and non-medical cost categories. Although patterns of care flow may vary across provider settings (e.g., some primary care physicians may order diagnostic tests and continue to monitor care themselves, rather than referring the pa-

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                    ┌─────────────────────────┐
                    │    OBSCURE BLEEDING      │
                    └────────────┬────────────┘
        ┌───────────────────────────┴───────────────────────────┐
┌─────────────────────┐                              ┌─────────────────────┐
│   OBSCURE-OCCULT     │                              │   OBSCURE-OVERT      │
│ Recurrent or persistent │                          │ Recurrent or persistent │
│ IDA and/or positive FOBT │                         │   visible bleeding   │
└─────────────────────┘                              └──────────┬──────────┘
                                                     ┌──────────────────────┐
                                                     │  ACTIVELY BLEEDING?  │
                                                     └──────────────────────┘
                                                       NO          YES
```
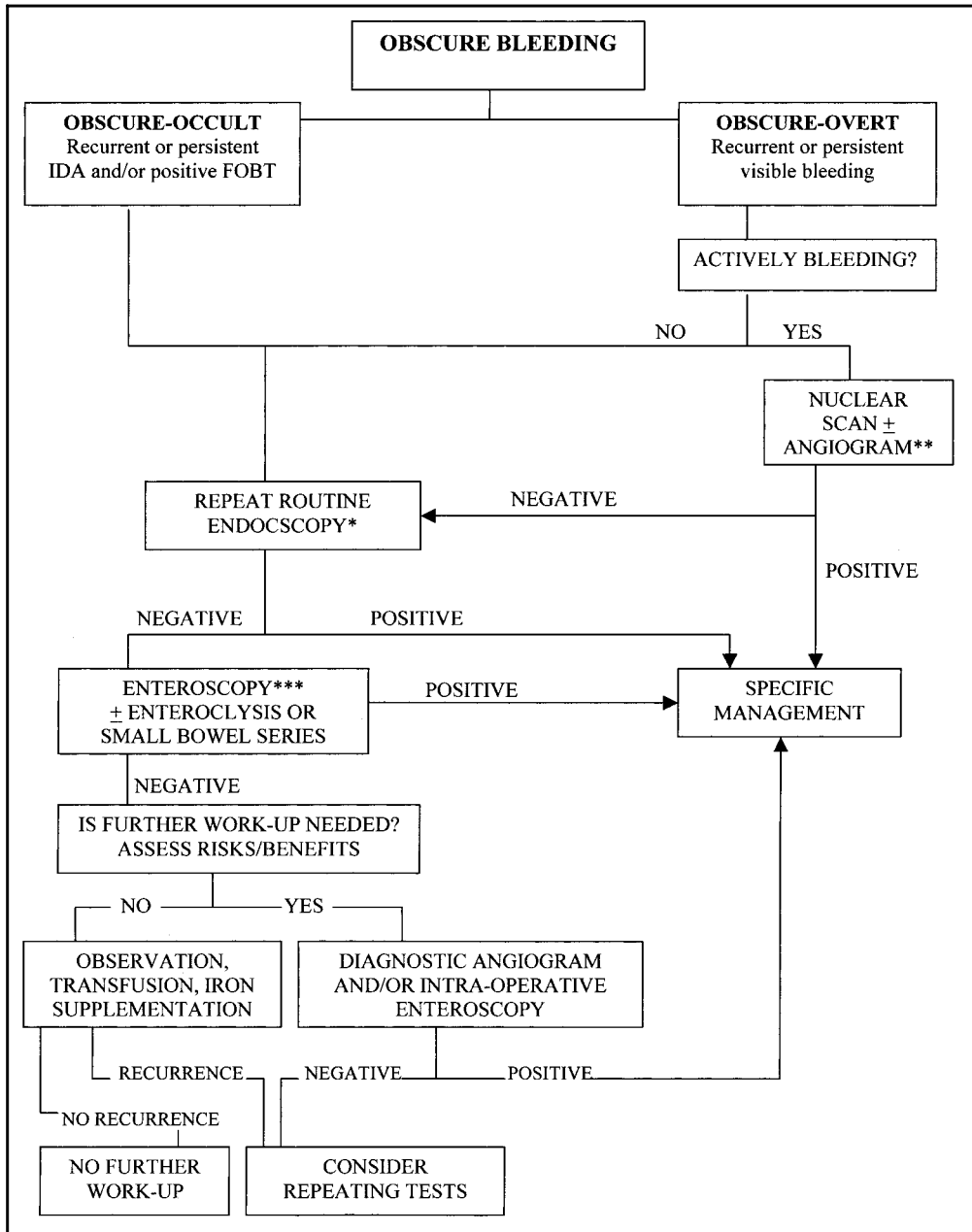

FIG. 1. American Gastroenterological Association algorithm for evaluation of obscure bleeding, published January, 2000. *The decision to repeat upper endoscopy and/or colonoscopy may depend on the skill and expertise of the initial endoscopist; push enteroscopy can replace upper endoscopy at this juncture; and small bowel biopsy is indicated in patients with clinical or endoscopic evidence of celiac sprue or unexplained IDA. **Repeat routine endoscopy may be performed in actively bleeding patients at the discretion of the endoscopist. ***Push enteroscopy and/or Sonde enteroscopy may be performed, depending on operator and institution expertise; enteroclysis can complement enteroscopy and improve the diagnostic yield.

tient to gastroenterology for work-up), the categories of contributors to cost are expected to be similar across settings, systems, and geographic regions.

Direct medical costs

A bleeding event, as noted previously, may be defined as a positive finding on an occult screening exam, or the visible presence of blood
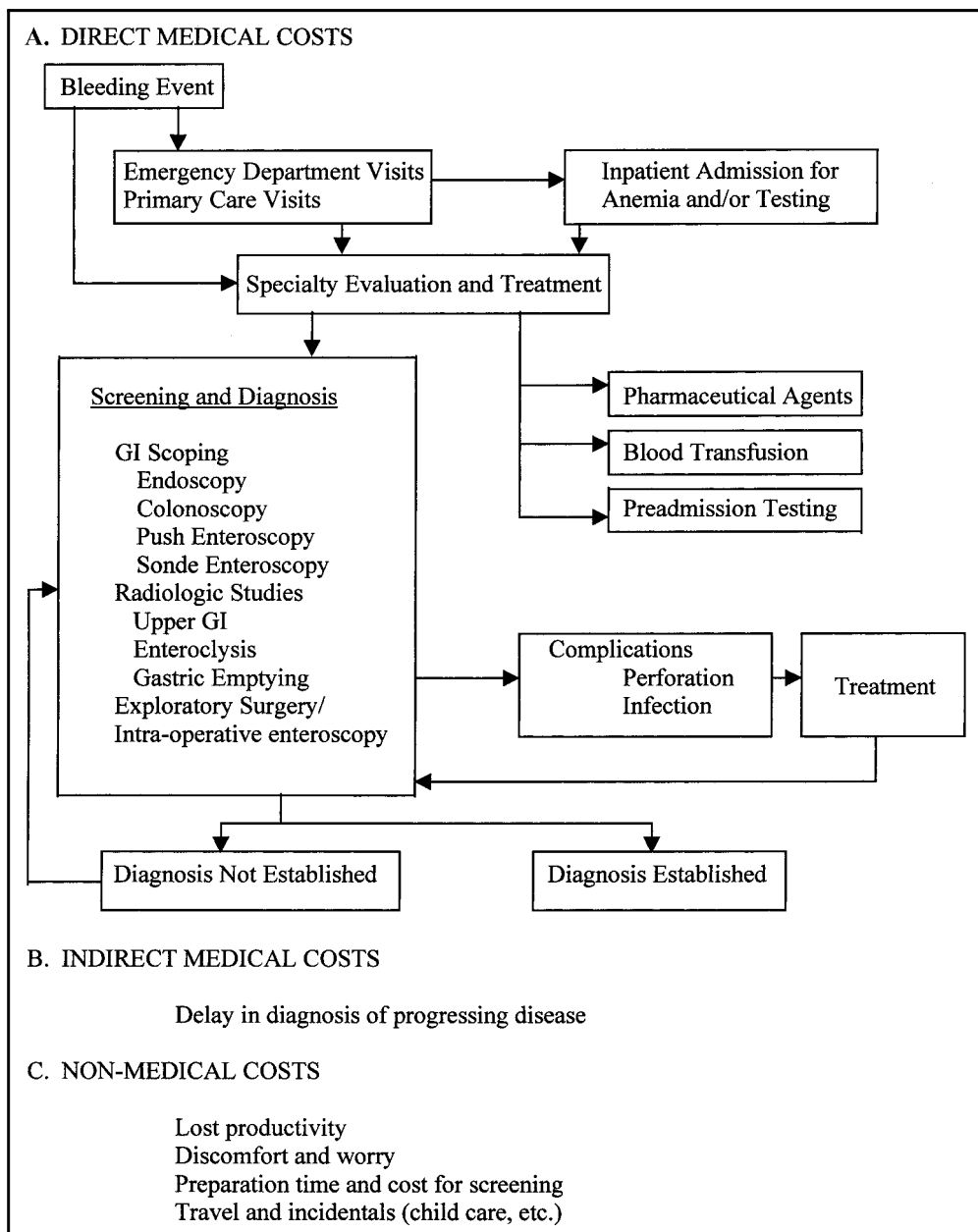
A. DIRECT MEDICAL COSTS

Bleeding Event

Emergency Department Visits
Primary Care Visits

Inpatient Admission for
Anemia and/or Testing

Specialty Evaluation and Treatment

Pharmaceutical Agents

Blood Transfusion

Preadmission Testing

Screening and Diagnosis

GI Scoping
  Endoscopy
  Colonoscopy
  Push Enteroscopy
  Sonde Enteroscopy
Radiologic Studies
  Upper GI
  Enteroclysis
  Gastric Emptying
Exploratory Surgery/
Intra-operative enteroscopy

Complications
Perforation
Infection

Treatment

Diagnosis Not Established

Diagnosis Established

B. INDIRECT MEDICAL COSTS

Delay in diagnosis of progressing disease

C. NON-MEDICAL COSTS

Lost productivity
Discomfort and worry
Preparation time and cost for screening
Travel and incidentals (child care, etc.)

FIG. 2.   Costs associated with diagnosing obscure bleeds.

in the stool. An initial bleeding event, or repeat episodes, may trigger visits to a healthcare provider. Typically, the initial presentation (or identification of occult blood) will take place in a primary care provider setting or an emergency department. Initial evaluation may be conducted by the intake provider (e.g., a family physician performing a flexible sigmoidoscopic exam), but the typical case of obscure bleed ultimately will be referred to gastroenterology for work-up. In some cases, "intake" also may result in inpatient admission for acute treatment of severe anemia.

As noted in the previous section, a range of diagnostic tests are available for clinical work-up, including endoscopy and other gastroenterologic scoping methods, radiologic studies, and exploratory surgery. A series of tests and examinations, including repeat administrations of the same diagnostic exam, are typically needed in order to rule out potential sources of bleeding, and to establish the site(s) of bleed-

ing. In some cases, exploratory surgery, including intraoperative enteroscopy, may be warranted. When these diagnostic procedures are performed on an inpatient or same-day surgery basis, cost may be increased by requirements for preadmission testing. In addition, because of their invasive nature, these diagnostic examinations can result in complications requiring treatment, ranging from pain and discomfort to perforation or infection.

Concurrent with diagnostic work-up, which may take place over weeks, months, or even years until a source of bleeding can be established, treatment may be required. Pharmaceutical interventions, including over-the-counter medications, may include iron supplementation for mitigating the impact of bleeding, stool softeners and laxatives, and, in some cases, sedation to control anxiety.

Indirect medical costs

The medical costs identified above are associated with the process of ruling out potential sources of bleeding and determining both the site and etiology of bleeding. Additional medical costs may result from delayed treatment, (e.g., the delay in identifying a small bowel malignancy). The published literature has yet to address this issue from an economic perspective.

Non-medical costs

In addition to the costs associated with medical care, consideration must be given to the humanistic and societal costs of the diagnosis process for obscure bleed. Main categories of these costs include:

- Lost workplace and non-workplace productivity, associated with time spent scheduling medical appointments, preparing for examination, undergoing testing and treatment, and recuperation.
- Worry and decreased quality of life, associated with concern over the lack of a diagnosis, potential for the cause of bleeding to be life-threatening, and being subjected to repeat testing.
- Pain and discomfort associated with preparation for testing (fasting, clearing the GI

tract), the testing procedure, and recuperation.
- Travel, parking, child-care, and other out-of-pocket costs for the patient.

ECONOMIC ANALYSIS OF CAPSULE ENDOSCOPY

Description of the technology and acquisition costs

Capsule endoscopy is a new diagnostic technology, FDA-cleared for the diagnosis of obscure bleeding in 2001. The manufacturer of capsule endoscopy technology is Given Imaging Ltd., a GI diagnostics company headquartered in Yoqneam, Israel. The Given Diagnostic Imaging System includes the M2A® Capsule Endoscope, the DataRecorder, Sensor Array, and RAPID™ (Reporting and Processing of Images and Data) WorkStation. The Capsule Endoscope is a disposable video endoscope measuring 11×26 mm. Like traditional endoscopes, the Capsule Endoscope contains an integrated light source, video chip, energy source, and transmitter. Like the sonde endoscope, it is ingested by the patient and advances through the GI tract through peristalsis. It provides direct color video images of the GI mucosa at a rate of 2 images per second for approximately 8 hours. The capsule is naturally excreted. The Sensor Array is worn on the abdomen and receives images and data from the capsule endoscope. The sensors pass the video images to the DataRecorder, which the patient wears on a belt. The ambulatory belt permits patients to continue with normal daily activities during the examination. After approximately 8 hours, the patient procedure is complete, and the DataRecorder can download approximately 50,000 images with localization and diagnostic data to the RAPID WorkStation. The RAPID WorkStation is equipped with Given's proprietary RAPID Application Software, which processes the data downloaded from the DataRecorder. The output allows physicians to view the endoscopy video, save individual images and short video clips, save findings, and print reports. The physician endoscopy review time is approximately 1.5 hours.

A complete installation of the capsule en-

doscopy technology at a clinical site requires an initial supply of disposable capsules, one or more DataRecorders with Sensor Array, and a WorkStation for reading images and data from the recorder. Given's current pricing for the technology includes $19,950 in fixed costs for the WorkStation and DataRecorder kit with Sensor Array, and variable costs of $450 for each disposable Capsule Endoscope. The fixed cost of acquiring the technology is similar to the acquisition cost of other diagnostic technologies for obscure bleed. For example, the average cost for a traditional enteroscope is approximately $29,000.

From a provider's perspective, the cost of the technology per test will depend in part on the volume of procedures performed, as illustrated in Table 2. The cost in Table 2 is based on the pricing above, and the assumption that a site would purchase one recorder for every 100 procedures performed in a year. The workstation and recorder costs are amortized over 3 years, although for the purposes of simplicity of presentation, a discount rate is not applied.

As can be seen, the cost driver for economic analysis of the Given technology to a large extent is the variable cost of the disposable Capsule Endoscope ($450). Additional costs for the technology include labor time and facility overhead allocation for:

- Physician or nurse to prepare the patient with thorough explanation of procedure instructions

- Physician or nurse to prepare the patient by shaving the abdomen to place the Sensor Array
- Nurse or technician to disinfect the Sensor Array, DataRecorder, and recorder belt
- Nurse or technician to set up and attach Sensor Array, DataRecorder, and recorder belt for patient
- Physician to discuss ingestion technique and introduce Capsule Endoscope to patient
- Physician or nurse to receive patient for disassembly of components and receive feedback
- Physician or nurse to prepare WorkStation and download DataRecorder for image processing
- Physician or nurse to recharge DataRecorder batteries and reprocess equipment
- Physician to review capsule endoscopy video and diagnostic data for 1.5 hours

The intensity of review by a professional of capsule endoscopy of the small intestine is significant, owing to the number of images (more than 50,000) that are relayed by the Capsule Endoscope. The labor involved in the test mirrors a gastroenterologist's activity in performing sonde enteroscopy. While total physician time required for the capsule endoscopy of the small intestine review exceeds that of sonde enteroscopy, this time can be spread over hours or days, and images can be viewed repeatedly, unlike other forms of enteroscopy.

From a payor perspective, CPT code 44376 is used for sonde enteroscopy and is described as

Number of tests per year	Capsule cost	Workstation cost	Recorder cost	Total cost	Equipment cost per test
25	11,250	4,833	1,817	17,900	716
50	22,500	4,833	1,817	29,150	583
75	33,750	4,833	1,817	40,400	539
100	45,000	4,833	1,817	51,650	517
150	67,500	4,833	3,633	75,967	506
200	90,000	4,833	3,633	98,467	492
250	112,500	4,833	3,633	120,967	484

TABLE 2. RELATIONSHIP BETWEEN VOLUME OF TESTS PERFORMED AND EQUIPMENT COST (IN DOLLARS) — *per test*

"Small intestinal endoscopy, enteroscopy beyond second portion of duodenum, including ileum; diagnostic." As shown in the 2001 edition of *Medical Fees in the United States*, published by Practice Management Information Corporation (PMIC), the national average for the usual and customary professional fee for CPT 44376 is $847. The fees vary regionally. For example, in Long Island, New York, the usual and customary fee is $1,185 for the same procedure. In 2001, the average Medicare professional fee reimbursement for CPT 44376 was $320 nationally, and $383 in New York. A separate CPT code for capsule endoscopy of the small intestine and an HCPCS code for the Capsule itself have yet to be established.

How might the cost of capsule endoscopy compare with the cost of diagnosing obscure bleeding patients with traditional exams? Since the procedural cost of sonde enteroscopy and capsule endoscopy are similar, in order to answer this question effectively, one must consider the diagnostic yield and *cost-effectiveness* of capsule endoscopy compared with traditional diagnostic tools.

The potential for cost savings

The placement of capsule endoscopy within a clinical guideline needs to be sensitive to both the effectiveness of the test and its cost-effectiveness. The conceptual care flow model presented in the previous section is useful in identifying potential areas for cost savings that could result from the introduction of capsule endoscopy into the clinical diagnosis tool kit for obscure bleeds:

- Improved diagnostic yield and reduction in the occurrence of repeat, inconclusive testing, associated not only with the clarity of the images obtained by the Capsule, but also with the Capsule's ability to traverse the entire small bowel (whereas endoscopic exams leave part of the small bowel unexamined)
- Improved diagnostic precision in being able to confirm the source of bleeding, and/or rule-out certain etiologies
- Earlier diagnosis of potentially adverse conditions, such as malignancies of the small bowel

- Reduced complications associated with the diagnostic procedure, such as intestinal tears resulting from placement of the enteroscope, and/or infection
- Reduced losses in productivity associated with undergoing testing and repetitive examinations, and reduced losses in quality of life associated with both testing and worry
- Reduced pain and discomfort associated with the diagnostic procedures

Clinical trial data analysis

The first U.S. trial of capsule endoscopy provides data confirming the potential cost savings and quality of life improvement associated with the new technology. In this trial, patients with obscure GI bleeding of unknown origin despite repeated testing were examined using capsule endoscopy, which was followed within one week by push enteroscopy, so that the diagnostic yield of the two procedures could be compared. Push enteroscopy was selected for comparison as the most equivalent diagnostic procedure in the current clinical toolkit. Although intraoperative enteroscopy, as discussed above, is the diagnostic gold standard, it is less often performed, particularly in early stages of diagnosing obscure bleeding, owing to its higher cost, risk, and patient impact.

Of the 21 patients enrolled in the trial, one female was excluded owing to a technology malfunction. Of the remaining 20 patients, 11 were females and nine were males. The mean age was 61 years. The patients in the trial had significant history of bleeding: The mean length of time since first recognition of bleeding was 2.7 years, after excluding one outlier who had gone 12 years since first bleed. Table 3 summarizes a few of the key utilization measures for history between initial occurrence of bleeding and entry into the trial. Because actual cost and charge data are not available from the trial, costs from a payer reimbursement perspective are imputed based on average Medicare fees. For example, for hospitalizations, the average Medicare reimbursement for DRG 174 (GI hemorrhage with complications or comorbid conditions) was $4,264. Commercial reimbursements would be significantly

higher. Transfusion costs are based on prior economic analysis.[33]

As demonstrated in Table 3, the costs associated with diagnosing obscure bleeding and treating anemia and other symptoms can be significant. Furthermore, data on other utilization contributing to direct medical costs, such as physician visits, emergency department visits, and prescriptions, were not collected as part of the trial. Therefore, *these figures significantly underestimate the total cost of diagnosis and ameliorative treatment* prior to capsule endoscopy.

Two experienced gastroenterologists independently reviewed the image stream recorded from capsule endoscopy. Confirmation of a bleeding site was based on agreement from both physicians' assessments. A bleeding site was found through the capsule endoscopy exam in 12 of the 20 patients participating in the clinical trial (60% yield), and push enteroscopy found the cause of bleeding in seven of 20 patients (35% yield). The fact that capsule endoscopy provided a negative diagnosis in eight of the 20 patients is also a meaningful diagnostic result. Since the Capsule was able to view the entire small intestine in all 20 patients, it was the only diagnostic tool able to provide a negative diagnostic result short of intra-operative exploratory surgery. The negative diagnostic result in these eight patients suggests that the cause of bleeding is not within the small intestine. The push enteroscope provided a negative result in 13 of the 20 patients, but the result is not as meaningful since only one-third of the 22-foot small intestine could be viewed.

The case for the effectiveness of capsule endoscopy is even further strengthened when considering that the 20 cases in the trial were all patients with lengthy history of bleeding and failed efforts to determine the bleeding source. The patients in this study averaged more than 10 procedures without any diagnostic finding prior to capsule enteroscopy. This large number of ineffective procedures is consistent with the published literature cited earlier in this paper. These findings do suggest that capsule endoscopy may be an appropriate approach to work-up prior to enteroscopy.

Perhaps most compelling in discussing the effectiveness of capsule endoscopy as a diagnostic tool for obscure bleed is the data obtained from the clinical trial on patient-reported outcomes. Patients completed a survey tool regarding their experience with both capsule endoscopy and enteroscopy. Table 4 summarizes the findings, demonstrating significantly higher patient satisfaction with capsule endoscopy when compared with traditional enteroscopy.

DISCUSSION AND CONCLUSION

Review of the literature on current diagnostic tools for obscure bleeding of the small intestine and examination of the data from the first U.S. clinical trial of capsule endoscopy suggest that this new technology potentially has significant clinical, economic, and humanistic benefits.

Clinically, capsule endoscopy appears to have a diagnostic yield that is higher than other endoscopic examinations of the small intestine.

TABLE 3.   PRIOR COSTS (IN DOLLARS) FOR SELECTED DIAGNOSTIC TESTS AND TREATMENTS FOR PATIENTS SUBSEQUENTLY ENROLLED IN THE CAPSULE ENDOSCOPY CLINICAL TRIAL

Procedure	Number of events	Estimated cost/event	Total cost	Cost per patient
Colonoscopy	73	660	48,180	2,409
Gastroscopy	83	590	48,970	2,449
Enteroscopy	22	590	12,980	649
Diagnostic radiology	38	220	8,360	418
Transfusion (red blood cell units)	588	500	294,000	14,700
Inpatient hospitalizations	61	4,264	260,104	13,005
Total			672,594	33,630

	Number of subjects responding		
	None or minimal	Moderate to extreme	p *value*[a]
Difficulty in swallowing capsule			
Capsule endoscopy	20	1	
Enteroscopy	4	17	<0.001
Pain during the procedure			
Capsule endoscopy	19	2	
Enteroscopy	16	5	0.003
Discomfort during the procedure			
Capsule endoscopy	20	1	
Enteroscopy	8	13	<0.001
Pain after the procedure			
Capsule endoscopy	20	1	
Enteroscopy	18	3	.002
Discomfort after the procedure			
Capsule endoscopy	20	1	
Enteroscopy	17	4	0.003
Overall discomfort with the procedure			
Capsule endoscopy	19	2	
Enteroscopy	4	17	<0.001
	Positive	Negative	
Overall impression			
Capsule endoscopy	21	0	
Enteroscopy	9	12	<0.001
Preference for procedure			
Capsule endoscopy	21	0	
Enteroscopy	6	15	<0.001

TABLE 4. PATIENT SURVEY FINDINGS

[a]All comparisons, using two-sided paired *t* tests, were statistically significant.

This is not surprising, since the video images that are relayed from the capsule to the Recorder can be examined multiple times by one clinician or multiple clinicians, and the Capsule transmits images through the entire small bowel, including areas not viewable by other endoscopic tools. In one of the 21 cases in the first U.S. trial of capsule endoscopy, the technology malfunctioned. As the technology is more widely diffused into practice, the failure rate will need to be monitored, since it may impact on the estimates of cost and effectiveness. The literature contains little information on the failure rate of other endoscopic technologies. In addition, the diagnostic tool is only as good as the clinician who reviews the images, and further research will be needed on overall diagnostic yield as the technology is diffused to providers in a variety of settings. However, the retained data in a digital format, which can be viewed by multiple clinicians, provide exciting opportunities for training and for quality improvement.

Economically, the data from the first U.S. trial suggests a potential net cost savings associated with capsule endoscopy, through earlier diagnosis, reduction in repetitive diagnostic procedures, and reduction in intermediate treatment costs pending diagnosis and resolution. The capsule endoscopy technology on a per-unit cost is comparable to other current endoscopic procedures. Providers who invest in the new technology will require training, and professional standards for use may need to be developed and monitored to ensure that inappropriate utilization does not result in a net increase in payors' reimbursements.

Finally, but most importantly from a societal perspective, the technology has great *humanistic* advantages. As demonstrated from clinical

trial data, capsule endoscopy results in less pain, discomfort, and anxiety. The ability to establish an early diagnosis also averts needless worry, inconvenience, and out-of-pocket costs to the patient.

These principles are illustrated by many of the 20 cases in the first U.S. clinical trial. For example, the clinical summary for patient HPO is presented:

> A 45-year-old attorney who has no significant past medical history, developed obscure GI bleeding 7 months prior to referral. He had 3 episodes of maroon blood per rectum and was hospitalized three times. His hemoglobin fell to 7 grams and he was transfused 3 units of packed cells. Prior evaluation included 2 colonoscopies, 2 upper endoscopies, a push enteroscopy, and a bleeding scan. All tests were negative. Capsule endoscopy revealed a tumor in the ileum. Subsequent push enteroscopy to 2.5 meters failed to reach this lesion and the exam was therefore normal. The patient underwent directed laparoscopy and a 1.5 cm tumor was found in the distal ileum. The lesion was a carcinoid. In this case, capsule endoscopy identified a tumor that was not diagnosable by any other means.

In summary, capsule endoscopy is a promising new technology on many levels. Its diagnostic yield is high, with the potential to result in earlier diagnosis. This in turn can result in more timely treatment and lower overall utilization and cost. While further study is needed, it also appears that capsule endoscopy may greatly improve patient safety and reduce the occurrence of adverse events associated with more invasive exploratory diagnostic procedures. Humanistic outcomes, such as patient comfort, satisfaction, quality of life, and productivity, all appear to be significantly improved as well.

The cost per capsule endoscopy exam and the clinical activity and intensity appear similar to those of sonde enteroscopy. However, the potential overall cost savings may be significant, and the cost-effectiveness of capsule endoscopy, when used appropriately, may prove

to be highly favorable. Clearly, broad acceptance, adoption, and diffusion of new technologies needs to be driven by *evidence*. However, the business case and outcomes data presented above suggest that this new technology already has a place in the diagnostic toolkit, and that the need for further economic evaluation should not come at the expense of making this FDA-cleared technology available immediately, for the work-up of obscure intestinal bleeding.

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