ORIGINAL RESEARCH

Novel Testing Enhances Irritable Bowel Syndrome Medical Management: The IMMINENT Study

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ABSTRACT

Primary Study Objective: To evaluate the economic utility of a fecal biomarker panel structured to suggest alternative, treatable diagnoses in patients with symptoms of irritable bowel syndrome (IBS) by quantifying, comparing, and contrasting health service costs between tested and non-tested patients.

Study Design: Retrospective, matched cohort study comparing direct medical costs for IBS patients undergoing fecal biomarker testing with those of matched control subjects.

Methods: We examined de-identified medical and pharmacy claims of a large American pharmacy benefit manager to identify plan members who underwent panel testing, were eligible for covered benefits for at least 180 days prior to the test date, and had data available for 30, 90, and 365 days after that date. We used propensity score matching to develop population-based control cohorts for each tested cohort, comprised of records with IBS-related diagnoses but for which panel testing was not performed. Primary outcome measures were diagnostic and medical services costs as determined from claims data.

Results: Two hundred nine records from tested subjects met inclusion criteria. The only significant baseline differences between groups were laboratory costs, which were significantly higher in each tested cohort. At each follow-up time point, total medical and gastrointestinal procedural costs were significantly higher in non-tested cohorts. Within tested cohorts, costs declined significantly from baseline, while costs rose significantly in non-tested control cohorts; these differences were also significant between groups at each time point.

Conclusions: Structured fecal biomarker panel testing was associated with significantly lower medical and gastrointestinal procedural costs in this study of patients with IBS symptoms.

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BACKGROUND

Irritable bowel syndrome (IBS), a functional gastrointestinal (GI) disorder with unknown and probably multiple causes, is highly prevalent and costly. Ten to 20% of Americans suffer from IBS, with those in their prime years of productivity and employment being disproportionately affected.[1-3] The cumulative financial impact of IBS is greater than that of many other chronic illnesses, including asthma and migraine, and comparable to that of hypertension and congestive heart failure.[4]

The annual cost of IBS in the United States is estimated to be more than US $20 billion.[5] In 2005, a study of one Fortune 100 company revealed that IBS direct costs to the employer were 1.5 times higher in affected employees ($6364) than those accrued by a matched sample of controls ($4245).[4,6] This resulted in an estimated $1.9 million in costs borne by that employer alone. Furthermore, 43% more claims per beneficiary are filed with health payers on behalf of IBS patients, a positive difference that climbs to 180% for prescription claims.[4,7]

The bulk of the direct cost burden of IBS is related to excessive prescription of diagnostic procedures that (1) are administered in an unstructured, serial fashion over the course of many months or years and (2) arise from the concerns of clinicians and patients who wish to rule out every credible competing diagnosis.[8,9] IBS patients undergo significantly more diagnostic testing than matched controls, with odds ratios for common and expensive studies such as endoscopy and radiological imaging tests ranging from 2.5 to 5.7.[7] As many as 50% of patients being evaluated for IBS will undergo colonoscopy[10]; 25% of all colonoscopies performed in the United States are for evaluation of IBS symptoms.[10,11]

Despite such aggressive testing, the overwhelming majority of these procedures show normal findings in patients being assessed for IBS. Among the group of diagnoses that are typically being considered during a clinical evaluation, only maldigestion of lactose occurs at a frequency greater than 5%. Additionally, organic pathologic conditions, such as colorectal cancer and inflammatory bowel disease (IBD), occur at levels of less than 1%, and at equal or lower frequencies than they do in the general population.[12,13] Even in patients with "alarm features," for whom more invasive testing is currently recommended,[5] organic disease was identified in only 3% of patients with suspected IBS in a study of 575 subjects; 1% had gastrointestinal cancer, 1.2% had IBD, and 0.7% had malabsorption.[14]

By contrast, a growing body of evidence suggests that, rather than being a single diagnostic entity, IBS instead represents an "umbrella" diagnosis comprised

of different, often treatable conditions.[15] Habba et al demonstrated that 98% of patients had a final diagnosis that differed from IBS, and 68% of studied patients had treatable bile acid abnormalities or related conditions.[15] Furthermore, 98% of the latter group showed a favorable response to therapy, a figure vastly higher than that generally accepted for symptomatic response in IBS in general.[15]

Others have shown a meaningful prevalence of exocrine pancreatic insufficiency (6.1%) in subjects who fulfilled concurrent Rome criteria for IBS, using fecal pancreatic elastase levels as a diagnostic tool.[16-19]

Similarly, fecal calprotectin levels have been demonstrated to effectively differentiate IBS from IBD,[20-23] and, when used as an alternative, noninvasive diagnostic testing may reduce the demand for colonoscopies and associated costs by as much as 50%, with the attendant realization of substantial cost savings.[24]

A computer-simulated economic analysis undertaken by the National Health Service in the United Kingdom showed that the use of fecal calprotectin was less costly and more diagnostically discriminative than routine blood tests—erythrocyte sedimentation rate (ESR), C reactive protein (CRP), serological markers, other neutrophil product markers, labeled white cell tests, and M2-pyruvate kinase—that are currently employed to categorize the inflammatory profiles of IBD and IBS.[25] Use of calprotectin testing resulted in fewer unnecessary endoscopies and an increase in the number of patients who were correctly diagnosed.

Many other underlying and readily treatable causes of IBS symptoms exist. These include celiac disease/gluten sensitivity, intestinal parasites and protozoans, and intestinal dysbiosis.[5,17-19,22,23,26-28] Emerging evidence suggests that there may exist a colonic microbiome pattern unique to IBS patients[29-31]; the advent of 16S ribosomal DNA polymerase chain reaction amplification may allow rapid detection of such patterns within the gut microbiome.[32-38]

We recently completed a retrospective review of 2256 records from patients who underwent simultaneous, parallel testing for a group of fecal biomarkers relevant to disorders that may produce IBS symptomatology, with treatable diagnoses suggested in 82.8% of cases.[39]

The combination of awareness of the multi-faceted nature of IBS and availability of low-cost fecal biomarker testing means that clinicians now have the ability to rapidly screen for, and in many cases identify specific, treatable diagnoses that produce the symptom constellation of IBS, while excluding dangerous conditions (such as IBD) with acceptable diagnostic accuracy.

The accurate evaluation of a broad array of GI functional biomarkers might also provide much-needed comfort to patients and clinicians alike and support implementation of symptom-based, psychosocially sensitive interventions with greater confidence. With concrete, objective laboratory information in hand that excludes significant inflammatory pathophysiology and guides a targeted treatment regimen leading to quicker improvement in patient symptoms, clinicians might be expected to order fewer expensive, invasive tests in attempts to rule out potentially significant alternative disease states. As a result, payers might in turn realize substantial cost savings.

We hypothesized that a structured, parallel, fecal biomarker panel would reduce total and GI-related diagnostic testing costs compared to the routine approach to diagnosis and managing IBS.

To test this hypothesis, we designed a retrospective cohort study to compare healthcare utilization and costs in patients whose clinicians made use of one such fecal biomarker panel (Genova Diagnostics, Asheville, North Carolina, http://www.gdx.net; detailed in Table 1), and matched controls, who received standard evaluation for IBS. The study, part of a series of investigations into the use of fecal biomarker testing in IBS, was

Table 1 Selected Components of the Fecal Biomarker Panel

Selected Biomarkers	Description
Pancreatic elastase	Pancreatic elastase-1 (PE1) is a proteolytic enzyme secreted by the exocrine cells of the pancreas. Fecal PE1 testing provides a convenient, noninvasive, and reliable method of evaluating exocrine pancreatic function, well before steatorrhea occurs.[18,19,40,41]
Calprotectin	Calprotectin is a 36 kDa protein highly expressed in neutrophils, where it comprises up to 60% of the cytosol content. As a surrogate marker for intestinal neutrophil activity, fecal calprotectin levels >50 microg/g are considered a reliable indicator of neutrophil-mediated inflammation in the intestinal mucosa.[42,43]
Eosinophil protein X (EPX)	EPX is a cationic protein found in eosinophils. Upon degranulation, these proteins are released, mediating the eosinophilic immune response.[44-46]
Clostridium difficile	Once thought to be associated nearly exclusively with exposure to antibiotics, bowel infection with *Clostridium difficile* (*C diff*) is now recognized as being increasingly common in those without known antibiotic exposure (as many as 45.7% of people with culture-proven *C diff* infection had no antibiotic exposure in the past 90 days).[47,48]
Parasitology exam (microscopy and enzyme immunoassay)	A variety of protozoan parasitic infestations can produce symptoms of chronic diarrhea, bloating, and abdominal pain that can overlap with those of IBS; all of these organisms are also capable of causing post-infectious IBS.[49,50]
Gut microbiota	Beneficial flora controls potentially pathogenic organisms, influences nutrient production, removes toxins from the gut and stimulates the intestinal immune system (GALT).[28,51-53]

named IMMINENT (Improved Medical Management of IBS Needs Enhancement by Novel Testing) in recognition of the needs of clinicians to find better ways to understand the biology of their patients who present with symptoms consistent with IBS.

Performance characteristics of these biomarkers for diagnoses that may present as IBS have been published elsewhere for pancreatic elastase,[54-57] calprotectin,[58-60] eosinophil protein X,[61] *Clostridium difficile*,[62,63] parasitology exam,[64] with sensitivities and specificities for such diagnoses ranging from 83% to 96% and specificities in the range of 82% to 96%. The precise relationship of gut microbiota patterns to human health and disease is not yet sufficiently clear to provide specific performance characteristics.

METHODS

Objectives

The objective of the project was to evaluate the utility of the fecal biomarker panel in a clinical setting by quantifying, comparing, and contrasting health service and pharmacy costs incurred by panel-tested and –non-tested IBS patients.

Design

We chose a retrospective, matched cohort design to compare the direct medical costs incurred by IBS patients tested with the fecal biomarker panel with those of matched control subjects.

Setting

We examined the medical and pharmacy claims of a large American managed pharmacy benefit manager patient database (Medco Health Solutions, now part of Express Scripts, St Louis, Missouri).

Ethics Considerations

Because this study used only de-identified records of claims data, no protected health information could be linked to individual patients. Consent for use of medical and pharmacy claims data for research purposes was obtained by participating insurance carriers. For these reasons, institutional review board approval was not deemed necessary.

Patient Population

Case Cohorts

Medical and pharmacy claims of plan members were searched to identify a cohort of patients who had been tested with the fecal biomarker panel by Genova Diagnostics, and who had one or more IBS-related diagnoses (Table 2). Because of major administrative changes at the participating institutions, actual percentage breakdowns for each ICD-9 code are not available. In a related study of a similar population,[39] ICD-9 codes 789 (abdominal pain), 564.1 (IBS), and 797.1 (diarrhea) accounted for more than three-quarters of all records.

Records were eligible for inclusion in the study (1) if the patient had been continuously eligible to receive benefits for at least 180 days preceding and 30, 90, or 365 days following the fecal biomarker panel test date and (2) if each member's sponsoring client had approved the use of medical and pharmacy claims for research purposes. For this study, all data were de-identified prior to analysis, and no protected health information was recorded.

Table 2 Diagnostic Codes for IBS-related Diagnoses

ICD-9 Code	Diagnosis
564.0	Constipation, unspecified
564.01	Slow-transit constipation
564.1	Irritable Bowel Syndrome
564.9	Functional intestinal disorder, unspecified
579.9	Unspecified intestinal malabsorption
787.91	Diarrhea
789	Abdominal pain
789.06	Abdominal pain, epigastric
789.07	Abdominal pain, generalized
536.8	Dyspepsia and other specified disorders of function of stomach
536.9	Unspecified functional disorder of stomach
558.9	Other and unspecified noninfectious gastroenteritis and colitis
787.3	Flatulence, eructation, and gas pain

This selection process resulted in identification of three longitudinally nested cohorts (Table 3). The M30 cohort (209 patients) consisted of patients with records available at 30 days after the fecal biomarker panel test date; the M90 (203 patients) consisted of members of the M30 cohort for whom data were available at 90 days after the test date; and the M365 (132 patients) consisted of M90 patients for whom data were available at 365 days after the test date.

Table 3 Summary of Selection Process

Records with fecal biomarker panel	37 945
Records matched to Express Scripts database	6892
Records eligible for study[a]	1656
Records including pharmacy data	1112
Records with data for 30 days after index date (M30)	209
Records with data for 90 days after index date M90)	203
Records with data for 365 days after index date (M365)	132

[a] Benefit eligibility preceded test date by 180 days AND carrier permits use of data for research purposes.

Control Cohorts

A population-based control cohort of patients with IBS-related diagnoses (Table 2) was created for each tested cohort. Each control cohort was created from a randomly selected pre-match pool of non-tested members who submitted a claim for one of the IBS-related diagnoses during the 30 days before or after each tested subject's test date. Similar inclusion criteria were then

applied. Following extraction of demographic and eligibility data, along with baseline pharmacy and medical utilization information, propensity score matching was applied to the pre-match pool to derive non-tested control cohorts equal in size to each tested cohort. Propensity score matching is a multivariate statistical technique that facilitates derivation of a control sample whose constituents are, on average, equivalent to treated individuals with respect to relevant covariates.[65] Thus, control cohorts were comprised of plan members whose age, gender, diagnostic code(s), and baseline medical and pharmacy utilization were statistically comparable to those of fecal biomarker panel–tested individuals. In order to optimize comparability between tested and control cohorts, a separate control cohort was generated for each tested cohort (ie, the control cohorts were not nested).

Definition of Index Date

In order to define a cut-point between baseline and follow-up periods, the index date was determined as the first date of service after the fecal biomarker panel test date for members of the tested cohort. For control cohort members (whose inclusion required a claim for one of the included ICD-9 codes within 30 days before or after the tested member's test date), the index date was the same as that of their panel-tested matched members.

Intervention

The study intervention was the use of the fecal biomarker panel in the case cohort.

Main Outcomes Measures

The primary outcome measures for this study were average net paid medical services and diagnostic costs during the baseline and follow-up periods (before and after the index date), as determined from claims data. The secondary outcome measures were average net paid pharmacy costs. To establish comparability with the 180-day baseline period, costs for the 365-day follow-up period were divided by two for both case and control cohorts.

Data Extraction

Following the creation of tested and control cohorts, medical and pharmacy claims data were extracted from the information warehouse, cleaned, reformatted, and subjected to statistical analysis. In the present context, "total medical spending" was defined as the aggregate spending for all current procedural terminology (CPT)–coded tests and procedures, including costs of the fecal biomarker panel in tested subjects.

"Total medical spending" was further broken down into the following categories:

- "Total costs for GI procedures" represented the aggregate spending for 125 GI-related CPT-coded tests and procedures (eg, upper/lower GI endoscopies/cholangiopancreatographies [ERCP]; complete list of codes available as a supplemental table online).
- Outpatient visit costs
- Office visit costs
- Laboratory costs
- Pharmacy costs
- Inpatient costs
- Statistical Analysis

All descriptive and inferential statistical analyses were conducted using "R 2.8" (R Development Core Team, 2013, Informer Technologies, Inc).[66] Continuous variables were analyzed using the Wilcoxon rank-sum test, and categorical variables were analyzed using a chi-squared test of independence. A two-sided *P* value (alpha) of .05 was used to gauge the statistical significance of all results.

RESULTS

Patient Populations

A total of 209 fecal biomarker panel-tested subjects who met the study's criteria for inclusion at 30 days following the index date (M30 cohort) were identified. Of those, 203 met criteria for inclusion in the 90-day (M90) cohort, and 132 of those met criteria for inclusion in the 365-day (M365) cohort (Table 3). An equal-sized and statistically comparable non-tested control group was developed for each case cohort by matching for age, gender, diagnosis code, and baseline medical and pharmacy utilization characteristics, as described above.

Baseline Characteristics

Baseline characteristics of the study populations are shown in Table 4. No differences were found between the tested and non-tested groups for age or gender. Similarly, analysis of the use of 30 medications commonly prescribed for IBS patients, of 41 common diagnosis codes, and of 14 common CPT codes revealed no significant differences (*P* values .1261 to 1.0000). A table of these medications, diagnoses, and CPT codes is available in the online supplemental materials.

In the 30 days prior to the index date, average total medical costs were significantly higher in the tested cohort. Baseline laboratory costs were significantly higher at all three time intervals in all tested cohorts. No significant differences were found between the tested and non-tested cohorts for other baseline medical costs incurred for the 30, 90, or 180 days preceding testing.

Medical Costs

Table 5 shows the comparison of costs following the index date for the three cohorts. Total Medical Costs were significantly higher at each time period following the index date for the non-tested control cohorts. Within the tested cohorts, total medical costs declined significantly from baseline, while costs rose significantly in the non-tested control cohorts; these differences were significant between groups at each time point as well.

Average total GI-procedure costs were significantly higher in the non-tested control cohorts at all three

Table 4 Baseline Characteristics and Average Costs Prior to Index Date

Baseline Characteristic	Cohort	Tested	Control	*P* value
Age (y)	M30	52.7	51.7	.4022
	M90	52.93	53.27	.8755
	M365[b]	53.05	53.49	.7716
Gender (% male)	M30	13.4	13.4	1.0000
	M90	12.81	13.30	.8829
	M365[b]	12.88	12.12	.8524
Total medical costs (USD)	M30	546.77	369.95	.0199[a]
	M90	1065.37	882.71	.2510
	M365[b]	1822.59	1473.57	.5401
Total GI procedure costs, including GI imaging studies (USD)	M30	22.15	41.57	.4227
	M90	76.80	41.97	.9893
	M365[b]	98.16	77.38	.4410
Total pharmacy costs (USD)	M30	511.72	203.84	.4725
	M90	2520.83	604.82	.9800
	M365[b]	4793.94	1263.96	.9176
Outpatient visit costs[c] (USD)	M30	82.63	94.30	.4399
	M90	180.11	178.42	.0616
	M365[b]	360.14	437.54	.2894
Office visit costs (USD)[d]	M30	266.40	110.88	.5408
	M90	537.80	357.21	.6262
	M365[b]	736.26	522.63	.3774
Laboratory costs (USD)	M30	121.19	18.12	.0000[a]
	M90	163.86	44.46	.0000[a]
	M365[b]	220.99	62.24	.0001[a]

Baseline characteristics of tested cohorts and control subjects, as well as baseline costs determined for the indicated periods (30, 90, and 365 days) prior to the index date. Significant differences ($P < 0.05$) occurred only in total medical costs for the M30 cohort and for laboratory costs, which were consistently higher for tested cohorts compared with controls.

[a] $P<.05$.

[b] Baseline data for the M365 cohort represent data for the 180-day eligibility period.

[c] Outpatient costs included outpatient hospital, ambulatory care, and same day surgical center costs.

[d] Office costs included physician office and in-home care costs.

Abbreviations: GI, gastrointestinal; USD, US dollars.

time intervals. The change in spending from baseline was significant between groups at each time point.

Average total outpatient visit costs were significantly lower at all time points in the fecal biomarker panel–tested cohorts compared with the non-tested groups. The change from baseline was significant between groups only at the 30-day observation.

Average office visit costs were significantly lower in the fecal biomarker panel-tested group only at the 90-day observation, while the change in office visit costs from baseline was significantly less between the groups at 30 and 90 days.

Average total laboratory testing costs did not differ significantly between groups at any of the three time points, but at 30 and 90 days, the non-tested cohorts showed a smaller increase in cost changes from baseline, while at 365 days, the panel-tested cohort costs had declined significantly more than those recorded for the non-tested group (Table 5).

Average total pharmacy costs did not significantly differ between the tested and non-tested cohorts at any of the time periods. Similarly, the groups did not significantly differ with respect to inpatient costs at any time point.

STUDY LIMITATIONS

This study has the limitations associated with retrospective analyses. There is the possibility of selection bias in that the decision to use the CDSA 2.0 test was made by the treating physician in a non-random fashion, albeit before the study data were collected. It is possible that these physicians may represent more integrative practices than is typical of the physician community in general, potentially influencing habits regarding other testing and resource utilization. Similarly, while the creation of the matched cohorts was undertaken using rigorous and well-established techniques, it is impossible to say with certainty that the tested and control cohorts were identical in all respects other than the assignment of the intervention. Because of these constraints, no conclusions regarding causality may be drawn.

However, we believe that the findings presented here represent important preliminary stages in understanding the impact of fecal biomarker testing on cost and resource utilization in the large population of patients with symptoms potentially representing IBS. These findings should be viewed as hypothesis-generating and should be further explored in prospective, appropriately controlled studies.

DISCUSSION

The growing recognition that IBS symptoms arise, not as the result of a single diagnosis (of exclusion or otherwise), but rather as manifestations of a sizable group of underlying treatable organic conditions,[15] creates an imperative to rapidly and inexpensively establish or exclude such diagnoses. This is especially important in light of the substantial costs and low diagnostic yields associated with existing, invasive testing that is often performed in serial fashion and aimed at excluding dangerous GI conditions that occur with extremely low frequency in patients manifesting IBS symptoms.[7-14]

The expansion of fecal biomarker testing offers an opportunity to take a structured, parallel approach to lower-cost, less invasive diagnostic maneuvers that may lower the cost of diagnosing and treating IBS, a disease whose aggregate healthcare expenditures rival those of other chronic, debilitating conditions.

In a companion publication, we report an analysis of 2256 patients who underwent evaluation for IBS, of which 82.8% had results suggesting a treatable GI diagnosis.[39] These findings reflect those of previous studies of individual clinical entities capable of pro-

Table 5 Average Medical Costs After Index Date by Cohort

Cohort	Post-testing			Change From Baseline		
	Tested (USD)	Control (USD)	*P* value	Tested (USD)	Control (USD)	*P* (between groups)
Total Medical Costs						
M30	323.70	821.62	.0000[a]	–106.42	451.67	.0000[a]
M90	720.01	1249.68	.0022[a]	–228.10	366.97	.0079[a]
M365[b]	1433.42	1799.92	.0478[a]	–272.59	326.35	.0043[a]
GI Procedure Costs, Including GI Imaging Studies						
M30	23.97	153.34	.0000[a]	1.82	111.77	.0006a
M90	51.22	206.65	.0001[a]	–25.58	164.68	.0014a
M365[b]	55.44	160.48	.0008[a]	–42.72	83.10	.0008[a]
Outpatient Visit Costs						
M30	485.25	1309.82	.0142[a]	402.63	1215.52	.0149[a]
M90	431.79	517.95	.0448[a]	251.69	339.53	.206
M365[b]	83.88	236.44	.0170[a]	–276.27	–201.10	.8450
Office Visit Costs						
M30	960.12	1373.69	.0587	693.72	1262.81	.0080[a]
M90	762.07	1042.84	.0445[a]	224.27	685.64	.0296[a]
M365[b]	226.87	234.10	.1064	–536.39	–288.53	.5403
Laboratory Costs						
M30	263.25	95.77	.2651	115.05	77.64	.0111[a]
M90	215.45	78.44	.3016	51.59	33.98	.0042[a]
M365[b]	66.77	43.05	.3625	–154.22	–21.19	.0001[a]

[a] Indicates statistical significance at *P*<.05.
[b] Costs shown for 365-day cohorts have been divided by 2 for comparison with baseline data, which were collected over 180 days.

ducing symptoms of IBS in patients meeting concurrent Rome criteria.[15-23,67]

The present retrospective study demonstrates the potential economic utility of a systems biology–based fecal biomarker panel in the evaluation and management of patients presenting with symptoms consistent with IBS. Average total medical and GI procedure costs were significantly lower in panel-tested cohorts at each post-testing time point compared with those in the non-tested control cohorts. Similarly, the amount of cost reduction from baseline was significantly greater at each time point for the tested cohorts. Average outpatient visit costs were also significantly lower in the tested cohorts compared with non-tested controls.

The apparent impact of the fecal biomarker panel on laboratory costs is potentially instructive. Average total medical costs were moderately, though significantly, higher in the tested group at 30 days prior to the index date compared with non-tested subjects. This appears to reflect the fact that the cost of the fecal biomarker panel itself is included in the 30-day baseline for the tested, but obviously not for the non-tested, cohorts. Indeed, average laboratory costs at all three baseline time intervals were moderately but significantly higher in the tested compared with the non-tested cohorts, each of which includes the one-time cost of the fecal biomarker panel.

That one-time increase in cost is sharply offset, however, by the net savings realized in the average total medical costs in the tested cohort compared with non-tested controls. For example, at the 30-day time point, average total medical costs fell by $106 in the tested group, while rising by $452 in the non-tested group, representing a total net average monthly savings of $558. Additional savings were realized at the 90-day time point, with a drop of $228 in the tested group and an increase of $367 in the non-tested group, for a total net average 3-month savings of $595. The savings at 1 year may be estimated by doubling the figures in Table 5 for the M365 group because the actual total costs for the 1 year of follow-up were divided by 2 for statistical comparison with the 180-day baseline data collection period. This calculation produces an average annual per-member savings of $1198, achieved by reducing costs by $546 in the tested group, while total costs rose by $652 in the non-tested group.

Thus, on a per-member-per-month (PMPM) basis, cost savings range from an estimated $100 (using the 365-day figure divided by 12) to an estimated $558 (using only the 30-day figure).

These projections support the conclusions of a 2010 British National Health Service study, which demonstrated an incremental cost savings of £13,464 in a computer-simulated cohort of 1000 patients for whom fecal calprotectin was compared with erythrocyte ESR and CRP in blood as indicators of inflammation that determined the need for further workup, especially endoscopy, in discriminating between IBS and IBD.[25]

Others have demonstrated the value of seeking or excluding other individual causes of IBS symptomatology, such as bile acid malabsorption, pancreatic exocrine insufficiency, celiac disease/gluten intolerance,

intestinal dysbiosis, and parasite infestations.[5,26-28] To our knowledge, however, the current study is the first in which the cost-effectiveness of a parallel, multiple-component fecal biomarker panel has been systematically evaluated.[10,12-14,68-70] This small initial investigation supports our hypothesis that a structured, parallel, fecal biomarker panel was associated with significantly lower total medical and diagnostic costs compared to a standard approach to managing IBS.

That stated, the study was not a randomized, controlled clinical trial, so conclusions regarding causality cannot be made. Nonetheless, we believe that these findings represent an important first step in establishing the value of parallel testing with a fecal biomarker panel in the IBS arena. Further prospective, randomized clinical studies with well-defined quantitative and qualitative outcomes measures appear justified.

From this preliminary, retrospective study we conclude that the use of a fecal biomarker panel was associated with significantly reduced total and GI procedure-related medical costs of this sample of subjects undergoing evaluation for IBS. Further studies, using a randomized, controlled clinical trial approach, are warranted.

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