Original Research

A Predictive Model to Estimate Cost Savings of a Novel Diagnostic Blood Panel for Diagnosis of Diarrhea-predominant Irritable Bowel Syndrome

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ABSTRACT

Purpose: A high incidence of irritable bowel syndrome (IBS) is associated with significant medical costs. Diarrhea-predominant IBS (IBS-D) is diagnosed on the basis of clinical presentation and diagnostic test results and procedures that exclude other conditions. This study was conducted to estimate the potential cost savings of a novel IBS diagnostic blood panel that tests for the presence of antibodies to cytolethal distending toxin B and anti-vinculin associated with IBS-D.

Methods: A cost-minimization (CM) decision tree model was used to compare the costs of a novel IBS diagnostic blood panel pathway versus an exclusionary diagnostic pathway (ie, standard of care). The probability that patients proceed to treatment was modeled as a function of sensitivity, specificity, and likelihood ratios of the individual biomarker tests. One-way sensitivity analyses were performed for key variables, and a break-even analysis was performed for the pretest probability of IBS-D. Budget impact analysis of the CM model was extrapolated to a health plan with 1 million covered lives.

Findings: The CM model (base-case) predicted $509 cost savings for the novel IBS diagnostic blood panel versus the exclusionary diagnostic pathway because of the avoidance of downstream testing (eg, colonoscopy, computed tomography scans). Sensitivity analysis indicated that an increase in both positive likelihood ratios modestly increased cost savings. Break-even analysis estimated that the pretest probability of disease would be 0.451 to attain cost neutrality. The budget impact analysis predicted a cost savings of $3,634,006 ($0.30 per member per month).

Implications: The novel IBS diagnostic blood panel may yield significant cost savings by allowing patients to proceed to treatment earlier, thereby avoiding unnecessary testing. (*Clin Ther*. 2016;38:1638–1652) © 2016 The Authors. Published by Elsevier HS Journals, Inc.

Key words: budget impact analysis, colonoscopy, cost-minimization, diarrhea-predominant irritable bowel syndrome, IBS diagnostic blood panel.

INTRODUCTION

Irritable bowel syndrome (IBS) is a common relapsing gastrointestinal (GI) disorder characterized by abdominal pain and discomfort, bloating, and changes in bowel habit.[1,2] IBS is the most common functional GI disorder in the population and has a prevalence that ranges from 5% to 15%.[3–8] The prevalence of IBS was 10.5% in a large survey of patients from community-based practices,[8] and a recent meta-analysis reported a pooled global prevalence of 11.2%.[7] Within the overall prevalence, IBS is subclassified according to the predominant bowel habit to include diarrhea-predominant IBS (IBS-D), constipation-predominant IBS, mixed subtype IBS, or unclassified IBS.[4] In the large survey of patients in community-based practices, symptom profiles were evenly divided between those patients with predominant diarrhea (25.4%) and constipation (24.1%), with more women than men typically affected by IBS.[8]

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Chronic diarrhea associated with IBS-D may also be common among individuals with celiac disease or inflammatory bowel disease (IBD). The anti-tissue transglutaminase antibody is a reliable biomarker selective for celiac disease[9]; however, differentiating IBS from IBD relies on excluding organic disease origins. Although the diagnosis of IBS is based on clinical findings that meet Rome criteria (eg, Rome III),[10] these common criteria do not distinguish IBS from IBD.[11] Importantly, the process of exclusion used for a definitive IBS-D diagnosis can be laborious, time-consuming, and costly.[12]

Common diagnostic testing for IBS can include laboratory tests (thyroid and liver function, C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], celiac panel, and complete blood cell [CBC] counts) and procedures, such as endoscopy, hydrogen breath test, ultrasound, and/or abdominal/pelvic computed tomography (CT) scans.[12] In a retrospective cohort study of patients diagnosed with IBS, blood tests were performed in 49% of patients, imaging and endoscopic procedures in 47%, colon tests in 37%, and sigmoidoscopy in 18%.[13] Although the current battery of laboratory tests is useful for the differentiation of IBD and IBS-D, none is associated with biomarkers that have been linked to IBS-D. ESR and CRP are used to investigate biomarkers associated with inflammation and thereby are tests of exclusion for IBS-D.

A recent systematic review reported evidence suggesting that CRP level has significant utility for the differential diagnosis of IBS-D and IBD whereas ESR did not. If the CRP level was ≤ 0.5, the probability that the patient had IBD was then $\leq 1\%$.[14] A prospective study investigated the performance of several laboratory tests for the diagnosis of IBS-D; this study found the sensitivity and specificity of CRP to be 64% and 92%, respectively, for the discrimination of IBS-D and IBD.[15] Including (and beyond just considering) the costs associated with reaching a definitive diagnosis, the health care burden of IBS is substantial.[16] It contributes 3.5 million physician office visits, even though a low proportion (10%–25%) of patients with IBS seek medical treatment. According to 1 study, annual direct and indirect costs of IBS exceed $20 billion.[17] Unfortunately, IBS is a heterogeneous disease, and, until now, there has been no reliable biomarker (organic) that is selective for IBS.[4,11]

Increased understanding of the pathophysiology of IBS by the lead author and others has helped lead to the development of a novel IBS diagnostic blood panel (Commonwealth Laboratories, Inc, Salem, MA).[18–24] The biomarker consists of a simple blood test measurement of circulating antibodies to cytolethal distending toxin B (anti-CdtB) and vinculin (anti-vinculin). Studies in a postinfectious animal model have shown that an IBS-like phenotype was produced when host antibodies to CdtB cross-reacted with vinculin in the host gut.[25] This IBS diagnostic blood panel was recently validated in a large study that enrolled patients with IBS-D (n = 2375), IBD (n = 142), or celiac disease (n = 121) and healthy control subjects (n = 43).[21] In that study, anti-CdtB and anti-vinculin titers were significantly higher in patients with IBS-D than in patients with IBD, celiac disease, and healthy subjects (all comparisons, $P < 0.001$). In that study, optimization demonstrated that for anti-CdtB (optical density ≥ 2.80), the sensitivity, specificity, and likelihood ratio were 43.7%, 91.6%, and 5.2, respectively. For anti-vinculin, optimization demonstrated (optical density ≥ 1.68) that the sensitivity, specificity, and likelihood ratio were 32.6%, 83.8%, and 2.0. This diagnostic test is currently available to providers who are responsible for diagnosing and managing patients with various GI disorders.

The IBS diagnostic blood panel may have beneficial economic implications for the diagnosis and management of patients suspected of having IBS-D; however, this possibility has not been studied. Indeed, a reduction in the time interval or number of diagnostic procedures used from symptom presentation to treatment initiation for a definitive IBS-D diagnosis may reduce patient morbidity and cost burden associated with performing a battery of exclusionary tests.[26,27] The objective of the present study, therefore, was to apply a cost-minimization (CM) decision tree model to compare the costs associated with 2 diagnostic pathways: the novel IBS diagnostic blood panel pathway and the exclusionary diagnostic pathway (current standard of care).

MATERIALS AND METHODS

Physician Surveys

Two surveys were developed and completed by expert gastroenterologists in the United States. The physician characteristics are reported (see **Supplemental Table I** in the online version at http://dx.doi.org/10.1016/j.clinthera.2016.05.003). The first survey addressed physician characteristics, patient characteristics, patient insurance type, distribution of patients with IBS according to