PMD36

IMPACT OF A NOVEL IBS DIAGNOSTIC BLOOD PANEL FOR MEXICO: COST IMPLICATIONS TO THE MEXICAN PRIVATE PRACTICE FOR DIARRHEA PREDOMINANT IRRITABLE BOWEL SYNDROME (IBS-D)

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INTRODUCTION

- Irritable Bowel Syndrome (IBS) is a chronic gastrointestinal disorder characterized by abdominal pain, bloating, discomfort and changes in bowel habit
- Prevalence estimates for IBS in Mexico range from 16% - 20%
- There are three distinct sub-types: diarrhea predominant (IBS-D), constipation predominant (IBS-C) and mixed (IBS-M)
- Diagnosing IBS-D involves a combination of symptom-based criteria (ROME III). However, diagnosing IBS-D involves differentiating this condition from organic diseases such as celiac disease and inflammatory bowel disease
- The anti-transglutaminase test (anti-tTG) is a reliable method to identify patients with celiac disease. Other diagnostic tests commonly used in the process of diagnosing patients who present with IBS-D symptoms include: complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), thyroid function test (TFT) and liver function test (LFT).
- Additional diagnostic procedures to rule out other organic conditions may include: colonoscopy, endoscopy, ultrasound and abdominal CT scan
- Therefore, IBS presents a significant health burden to patients and to the healthcare system in Mexico both in terms of significant direct and indirect (i.e. absenteeism) medical costs. According to one study, the annual direct and indirect costs associated with IBS are greater than 20 billion.
- IBS*chek* is a novel diagnostic blood panel which involves measuring antibody levels for cytolethal distending toxin B (anti-CdtB) and vinculin (anti-Vinculin)
- Animal studies have demonstrated that an IBS-like phenotype can be produced when host antibodies to CdtB cross-react with vinculin
- This biomarker has recently been validated in a large clinical trial (TARGET-3)
- This novel diagnostic blood test may provide significant benefits for patients who present with IBS-D symptoms by avoiding unnecessary testing procedures and a shorter time to diagnosis and treatment

AIMS

- The primary aim of this study was to compare the costs associated with two differing diagnostic pathways in private practice in Mexico: (1) The IBS*chek* diagnostic pathway vs. (2) the exclusionary diagnostic pathway for patients who present with IBS symptoms
- The secondary objective of this study was to extend the results of the cost-minimization model (CM) to a budget impact for two scenarios: (1) national and (2) a health plan with one million covered lives

Figure 1: Decision Tree Model (Model 1)

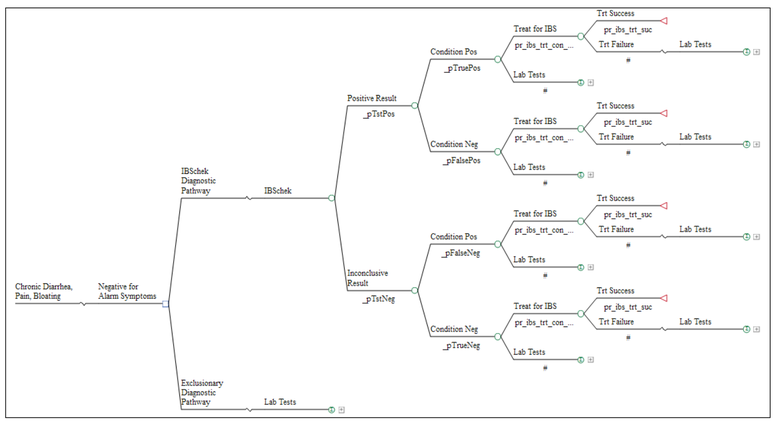
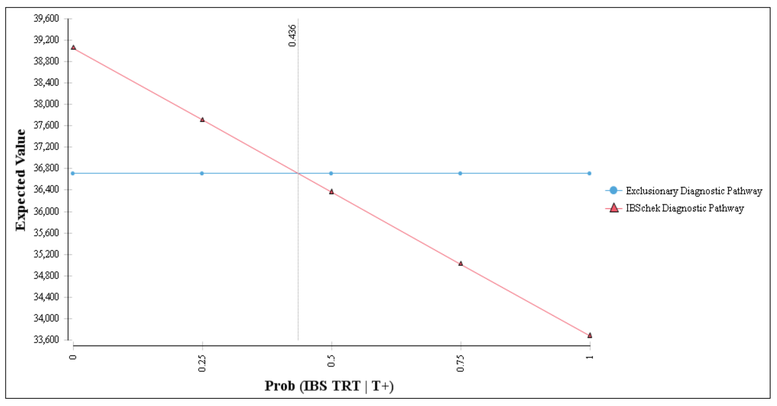


Table 1: CM Results (Model 1)

Diagnostic Pathway	Setting	Pre-test Prob Dis +	Prob (IBS TRT | T +)	Prob (IBS TRT | T -)	Expected Cost (MX Pesos)	Cost (Savings) (MX Pesos)
W/ IBS*chek*™	GI	0.617	0%	0%	39044	2337
Exclusionary	GI	NA	NA	NA	36707	
W/ IBS*chek*™	GI	0.617	25%	0%	37702	995
Exclusionary	GI	NA	NA	NA	36707	
W/ IBS*chek*™	GI	0.617	50%	0%	36361	(346)
Exclusionary	GI	NA	NA	NA	36707	
W/ IBS*chek*™	GI	0.617	75%	0%	35019	(1688)
Exclusionary	GI	NA	NA	NA	36707	
W/ IBS*chek*™	GI	0.617	100%	0%	33678	(3029)
Exclusionary	GI	NA	NA	NA	36707	

Pre-Test Prob Dis +: Probability of IBS-D in Mexico in a patient consulting for Diarrhea, Bloating and Pain. Prob (IBS TRT |T+): Probability that a patient will receive treatment conditional on a positive test result. Prob (IBS TRT | T-): Probability that a patient will receive treatment conditional on a negative test result.

Figure 2: Breakeven for Pre-test Pr(D+) (Model 1)



STUDY DESIGN & METHODS

- A cost-minimization (CM) decision tree model was constructed to compare the costs associated with two possible diagnostic pathways: (1) diagnostic pathway with novel IBS diagnostic blood panel and (2) exclusionary diagnostic pathway (i.e. standard of care)
- The setting for the model is the private system in Mexico
- The model structure (CM Model 1) was based on current literature and guidance from IBS expert clinicians (Figure 1, Table 1)
- New data became available after the abstract submission; therefore the model and the results (cost-minimization and budget impact) (CM Model 2) have been updated accordingly (Figure 3, Table 2)
- The second model separates the testing procedure into four distinct levels as follows:
- Level 1: CBC + ESR + FOBT + IBSchek (in the IBS*chek* arm only)
- Level 2: LFT + TFT + Parasitological Stool + Bacterial Stool + CRP
- Level 3: Colonoscopy + Endoscopy + Celiac Panel + SBFT
- Level 4: Bile Salt Malabsorption + Pancreatitis CT Scan + Tropical Sprue
- The probability that patients will proceed to treatment was modeled as a function of the sensitivity, specificity and likelihood ratios of the individual biomarker tests (Tables 3)
- These probabilities are computed as follows:

$$Post-test\ Odds\ (D+) = Pre-test\ Odds(D+) * LR(CDTB) * LR(Vinculin)$$

$$Post-test\ \Pr(D+) = \frac{Post-test\ Odds(D+)}{1 + Post-test\ Odds\ (D+)}$$

- One-way sensitivity analyses were performed for key input variables
- For both models, a break-even analysis was performed with respect to the pre-test probability of disease (IBS-D) (Figure 2, Figure 4)
- The budget impact analysis (BIA) extrapolates results of the CM model to both: (1) the national perspective using the results of CM Model 1, and (2) to a plan of one million covered lives from CM Model 2

RESULTS (CM Model 1)

- Colonoscopy, small bowel follow through (SBFT) and endoscopy were the most common diagnostic (instrumental) procedures reported in a small physicians-based survey in Mexico, with estimated utilization rates of 78%, 62%, and 52%, respectively
- The most commonly ordered diagnostic tests (not procedural) were: complete blood count (95%), ESR (95%), thyroid function (88%), bacterial stool (85%), parasitological stool (85%), and fecal occult blood test (FOBT) (82%)
- For the base-case, the CM model predicts a cost savings of $1,688 for the novel IBS diagnostic blood panel vs the exclusionary diagnostic pathway, due to the avoidance of downstream testing (e.g. colonoscopy, CT scans) (Table 1)
- The range of additional cost (or savings) is from an additional cost of $2,337 for the IBS Diagnostic Blood Panel arm to a cost savings of $3,029 for the IBS Diagnostic Blood Panel arm (Table 1) (depending on the probability of IBS treatment conditional on a positive test)
- The break-even analysis estimated that the pre-test probability of disease would be 0.436 to attain cost neutrality (Figure 2)
- The BIA predicts a cost savings of $794,158,235 (on a national scale – for a population of 119.7 million)

RESULTS (CM Model 2)

- For the base-case, the CM model predicts a cost savings of $5,805 for the novel IBS diagnostic blood panel vs the exclusionary diagnostic pathway, due to the avoidance of downstream testing (e.g. colonoscopy, CT scans). If only direct costs are considered, the cost savings are reduced to $4,180 (Table 2)
- A sensitivity analysis was performed for a pre-test probability of disease value of 0.75; under this scenario, the cost savings increases to $8,917; if only direct costs are considered, the cost savings are reduced to $7,292
- The break-even analysis estimated that the pre-test probability of disease would be 0.367 to attain cost neutrality (Figure 4)
- The BIA predicts a cost savings of $15,209,100 (for a health plan of one million covered lives)
- For the BIA, as the proportion seeking care is varied from 10% - 50% the cost savings varies from $7.6 million to $38.0 million

Figure 3: Decision Tree Model (Model 2)

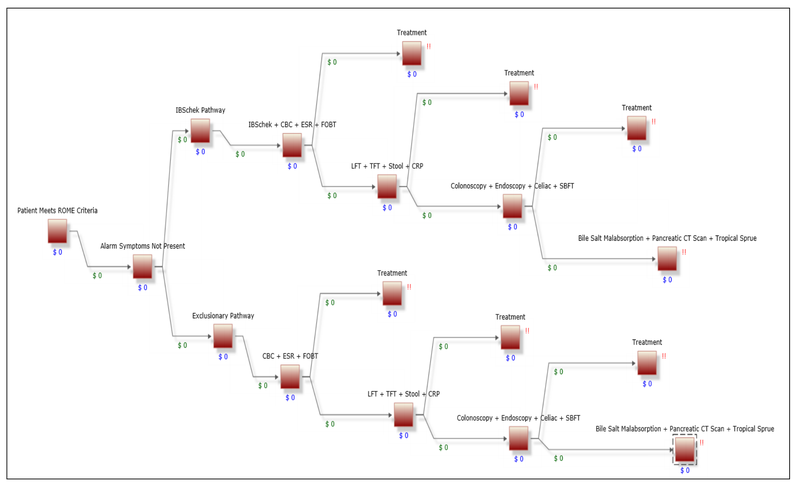


Table 2: CM Results (Model 2)

Direct Costs	Indirect Costs	Pre-test Probability of Disease [3]	IBS*chek*™ Expected Cost [1,2]	Exclusionary Arm Expected Cost [1,2]	Difference	Percentage Decrease
Y	Y	0.617	29,737	35,542	5,805	16.3%
Y	N	0.617	26,603	30,783	4,180	13.6 %
N	Y	0.617	3,134	4,759		
Y	Y	0.750	26,625	35,542	8,917	25.1 %
Y	N	0.750	23,491	30,783	7,292	23.7 %
N	Y	0.750	3,134	4,759		

1 – Probability of Rifaximin success = 0.41
2 – Probability of Amitriptyline Success = 0.66
3 – Sensitivity analysis for pre-test probability of IBS-D = 0.75

Table 3: Pre-test & Post-test Pr(D+) (Model 2)

Pre-Test Pr(D+)	Pre-Test Odds(D+)	LR+ CdtB	LR+ VINC	LR- CdtB	LR- VINC	Test Results (CdtB, VINC)	Post-test Odds	Pr(D+)
50%	1.00	5.2	2	0.6	0.8	p,p	10.400	91.2%
50%	1.00	5.2	2	0.6	0.8	p,n	4.160	80.6%
50%	1.00	5.2	2	0.6	0.8	n,p	1.200	54.5%
50%	1.00	5.2	2	0.6	0.8	n,n	0.480	32.4%
61.7%	1.61	5.2	2	0.6	0.8	p,p	16.754	94.4%
61.7%	1.61	5.2	2	0.6	0.8	p,n	6.702	87.0%
61.7%	1.61	5.2	2	0.6	0.8	n,p	1.933	65.9%
61.7%	1.61	5.2	2	0.6	0.8	n,n	0.773	43.6%
70%	2.33	5.2	2	0.6	0.8	p,p	24.267	96.0%
70%	2.33	5.2	2	0.6	0.8	p,n	9.707	90.7%
70%	2.33	5.2	2	0.6	0.8	n,p	2.800	73.7%
70%	2.33	5.2	2	0.6	0.8	n,n	1.120	52.8%
71.2%	2.472	5.2	2	0.6	0.8	p,p	25.71	96.3%
71.2%	2.472	5.2	2	0.6	0.8	p,n	10.28	91.1%
71.2%	2.472	5.2	2	0.6	0.8	n,p	2.97	74.8%
71.2%	2.472	5.2	2	0.6	0.8	n,n	1.19	54.3%
75%	3	5.2	2	0.6	0.8	p,p	31.20	96.9%
75%	3	5.2	2	0.6	0.8	p,n	12.48	92.6%
75%	3	5.2	2	0.6	0.8	n,p	3.60	78.3%
75%	3	5.2	2	0.6	0.8	n,n	1.44	59.0%

Pre-Test Pr(D+): Probability of IBS-D in Mexico in a patient consulting for Diarrhea, Bloating and Pain. LR: Likelihood Ratio. CdtB: Distending Cytotoxin B. VINC: Vinculin. Pr(D+): Imputation of the post-test probability of disease as the probability that a patient will be treated for IBS-D (after IBS*chek*) Probability for the patient to be IBS-D positive. n: negative. p: positive

Figure 4: Breakeven for Pre-test Pr(D+) (Model 2)

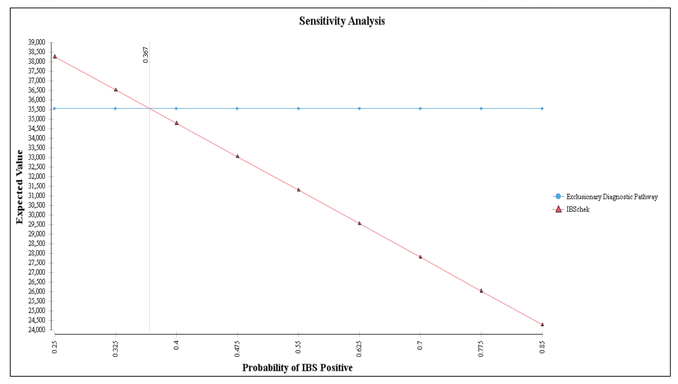


Table 4: Budget Impact Analysis (Model 2)

Covered Lives [1,2]	Prevalence of IBS-D [3]	18-65 Age Group %	Proportion Seeking Care	Number of Affected Individuals	Pre-test Pr(IBS D+)	Proportion of Physicians Using IBS*chek*	Cost (Savings) Per IBS-D Patient	Net Cost (Savings)
1,000,000	20%	65.50%	10%	2,620	61.7%	50%	($5,805)	($7,604,550)
1,000,000 [4]	20%	65.50%	20%	5,240	61.7%	50%	($5,805)	($15,209,100)
1,000,000	20%	65.50%	30%	7,860	61.7%	50%	($5,805)	($22,813,650)
1,000,000	20%	65.50%	40%	10,480	61.7%	50%	($5,805)	($30,418,200)
1,000,000	20%	65.50%	50%	13,100	61.7%	50%	($5,805)	($38,022,750)
1,000,000	20%	65.50%	10%	2,620	75.0%	50%	($8,917)	($11,681,270)
1,000,000	20%	65.50%	20%	5,240	75.0%	50%	($8,917)	($23,362,540)
1,000,000	20%	65.50%	30%	7,860	75.0%	50%	($8,917)	($35,043,810)
1,000,000	20%	65.50%	40%	10,480	75.0%	50%	($8,917)	($46,725,080)
1,000,000	20%	65.50%	50%	13,100	75.0%	50%	($8,917)	($58,406,350)

1 – Assumption: HMO with 1 million covered lives.
2 - IBS Prevalence = 20.0%
3 – IBS-D Prevalence within IBS in Mexico =20.0% (IBS Physician Survey (Administered by AHRM Inc. (April – June of 2015))
4 – Base case results

CONCLUSIONS

- Current medical literature suggests that extensive testing to diagnose IBS is often not necessary
- For patients who present with IBS symptoms in the private practice setting in Mexico, this evaluation predicts that the inclusion of a novel Blood Panel in the diagnostic process has the potential for significant cost savings due to the avoidance of downstream testing
- Sensitivity analyses indicate that the pre-test probability of disease (IBS-D) has a significant impact on the magnitude of the cost outcomes
- Both models predict significant cost savings for the treatment arm including the novel IBS Diagnostic Blood Panel

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DISCLOSURES

This study was sponsored by Commonwealth Diagnostics International, Inc. Salem, MA, USA. All authors met the ISPOR authorship criteria. Neither honoraria nor payments were made for authorship.

Dr. Mark Pimentel and Dr. Max Schmulson have acted as scientific consultants for Commonwealth Laboratories, LLC and Commonwealth Diagnostics International, Inc.