PMD32

POTENTIAL FOR COST SAVINGS ASSOCIATED WITH A NOVEL IBS BLOOD PANEL FOR DIAGNOSING DIARRHEA PREDOMINANT IRRITABLE BOWEL SYNDROME (IBS-D): ITALIAN PERSPECTIVE

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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 Italy range from 9% - 12%
- Research has indicated that the prevalence of IBS in Italy may be greater in urban areas when compared with rural areas
- 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 , inflammatory bowel disease and colon-rectal cancer.
- 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), electrolytes dosage and liver function test (LFT)
- Also, diagnostic procedures to rule out other organic conditions may include: colonoscopy, abdominal/bowel ultrasound and abdominal CT scan
- IBS presents a significant health burden to patients and to the healthcare system in Italy both in terms of significant direct and indirect (i.e. absenteeism) costs
- 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

OBJECTIVES

- The primary aim of this study was to compare the costs associated with two differing diagnostic pathways in clinical practice in Italy: (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 analysis for the national population

Figure 1: Decision Tree Model (Model 1)

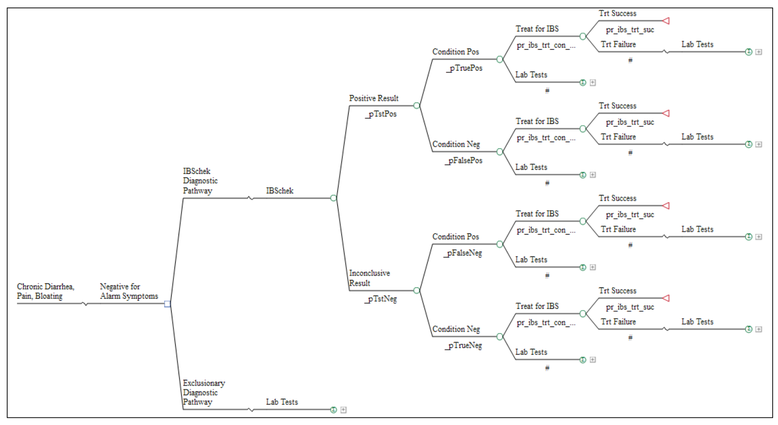
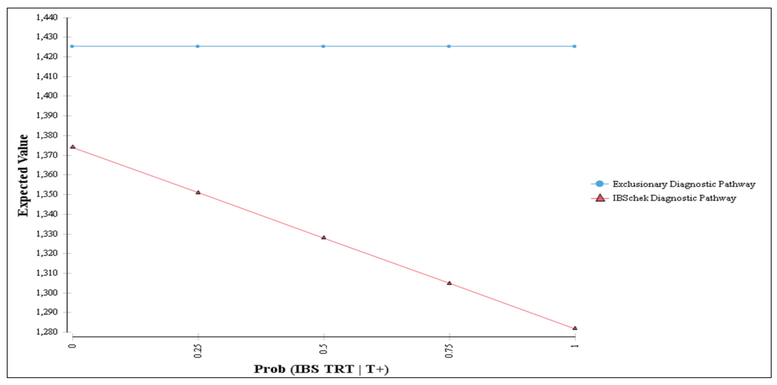


Table 1: CM Results (Model 1)

Diagnostic Pathway	Pre-test Prob Dis +	Prob (IBS TRT | T +)	Prob (IBS TRT | T -)	Expected Cost (Euros)	Cost (Savings) (Euros)
W/ IBS*chek*™	0.650	0%	0%	1374	(51)
Exclusionary	NA	NA	NA	1425	
W/ IBS*chek*™	0.650	25%	0%	1351	(74)
Exclusionary	NA	NA	NA	1425	
W/ IBS*chek*™	0.650	50%	0%	1328	(97)
Exclusionary	NA	NA	NA	1425	
W/ IBS*chek*™	0.650	75%	0%	1305	(120)
Exclusionary	NA	NA	NA	1425	
W/ IBSchek™	0.650	100%	0%	1282	(143)
Exclusionary	NA	NA	NA	1425	

Pre-Test Prob Dis +: Probability of IBS-D in Italy 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: Sensitivity for Pr (IBS TRT | T+) (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 clinical practice in Italy
- 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, ultrasound and SBFT were the most common diagnostic (instrumental) procedures reported with estimated utilization rates of 50%, 90% and 35%. Corresponding charges were €312.50, €70 and €300, respectively.
- Estimated total base case charges for the IBS diagnostic panel pathway (assumes 25% of test positive patients receive IBS-D treatment) vs the exclusionary pathway were €1,351 vs €1,425, respectively (Table 1)
- The cost savings with the IBS Diagnostic panel increases if the probability of IBS treatment increases to 50% or 75% (Table 1)
- If clinicians use the test 50% of the time for the 50% of the estimated 745,459 people who might have IBSD who seek treatment, net savings to the Italian healthcare system is €27,581,982.
- Cost neutrality occurs if 49% of the “test positive” patients seek IBS treatment
- The sensitivity analysis for the P2(IBS TRT | T+) indicates that cost savings increases as the probability of treatment increases (Figure 2)

RESULTS (CM Model 2)

- For the base-case, the CM model predicts a cost savings of €178 for the novel IBS diagnostic blood panel vs the exclusionary diagnostic pathway, due to the avoidance of downstream testing (e.g. colonoscopy, CT scans)
- A sensitivity analysis was performed for a pre-test probability of disease, for a range of values from 0.45 to 0.85; under this scenario, the cost savings range from €124 to €232
- The sensitivity analysis estimated that the cost savings with the diagnostic blood panel increase as the pre-test probability of disease increases (Figure 4)
- The BIA predicts a cost savings of 39.8 million Euros (Table 4)
- For the BIA, as the proportion seeking care is varied from 10% - 50% the cost savings varies from 13.3 million Euros to 66.3 million Euros (Table 4)

Figure 3: Decision Tree Model (Model 2)

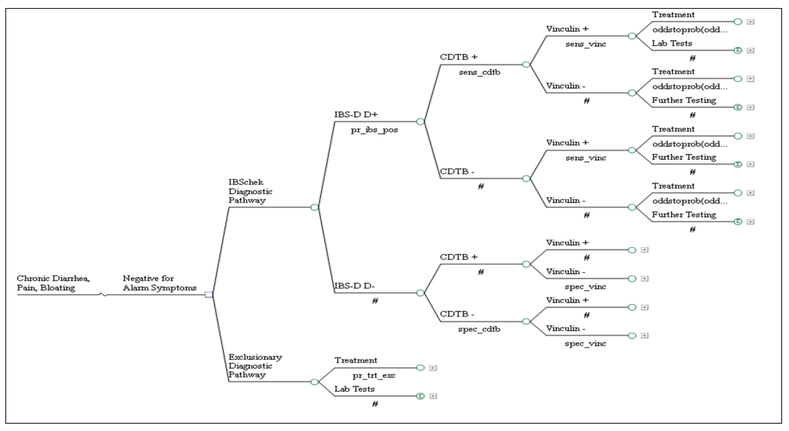


Table 2: CM Results (Model 2)

Diagnostic Pathway	Pre-test Prob Dis +	Prob (IBS TRT) Exclusionary	Expected Cost	Cost (Savings) Euros
W/ IBS*chek*™	0.450	NA	1211	(124)
Exclusionary	NA	0.350	1335	
W/ IBS*chek*™	0.550	NA	1184	(151)
Exclusionary	NA	0.350	1335	
W/ IBS*chek*™	0.650	NA	1157	(178) [1]
Exclusionary	NA	0.350	1335	
W/ IBS*chek*™	0.750	NA	1130	(201)
Exclusionary	NA	0.350	1335	
W/ IBS*chek*™	0.850	NA	1103	(232)
Exclusionary	NA	0.350	1335	

1 – Base case

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 (CD, VI)	Post-test Odds	Pr(D+)
45	0.818	5.2	2	0.6	0.8	p,p	8.509	89.5%
45	0.818	5.2	2	0.6	0.8	p,n	3.404	77.3%
45	0.818	5.2	2	0.6	0.8	n,p	0.982	49.5%
45	0.818	5.2	2	0.6	0.8	n,n	0.393	28.2%
55	1.222	5.2	2	0.6	0.8	p,p	12.711	92.7%
55	1.222	5.2	2	0.6	0.8	p,n	5.084	83.6%
55	1.222	5.2	2	0.6	0.8	n,p	1.467	59.5%
55	1.222	5.2	2	0.6	0.8	n,n	0.587	37.0%
65	1.857	5.2	2	0.6	0.8	p,p	19.314	95.1%
65	1.857	5.2	2	0.6	0.8	p,n	7.726	88.5%
65	1.857	5.2	2	0.6	0.8	n,p	2.229	69.0%
65	1.857	5.2	2	0.6	0.8	n,n	0.891	47.1%
75	3.000	5.2	2	0.6	0.8	p,p	31.20	96.9%
75	3.000	5.2	2	0.6	0.8	p,n	12.48	92.6%
75	3.000	5.2	2	0.6	0.8	n,p	3.60	78.3%
75	3.000	5.2	2	0.6	0.8	n,n	1.44	59.0%
85	5.667	5.2	2	0.6	0.8	p,p	58.93	98.3%
85	5.667	5.2	2	0.6	0.8	p,n	23.57	95.9%
85	5.667	5.2	2	0.6	0.8	n,p	6.80	87.2%
85	5.667	5.2	2	0.6	0.8	n,n	2.72	73.1%

Pre-Test Pr(D+): Probability of IBS-D in Italy 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: Sensitivity for Pre-test Pr(D+) (Model 2)

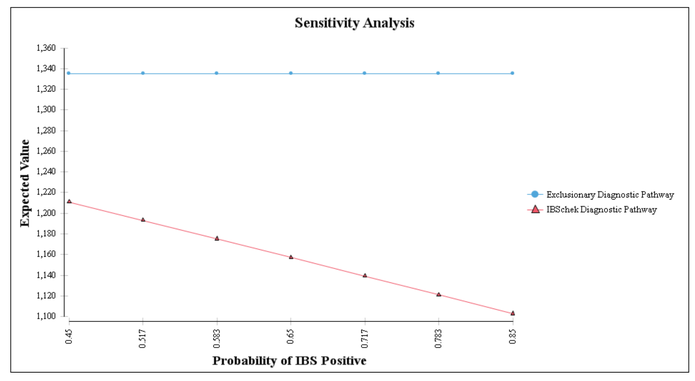


Table 4: Budget Impact Analysis (Model 2)

Covered Lives	Prevalence of IBS	Prevalence of IBS-D	18-65 Age Group %	Proportion Seeking Care	Number of Affected Individuals	Pre-test Pr(D+)	Proportion of Physicians Using IBSchek	Cost (Savings) Per IBS-D Patient	Net Cost (Savings)
61,470,000	12.0%	31%	65.2%	10%	149,092	55%	50%	€ (151)	€ (11,256,431)
61,470,000	12.0%	31%	65.2%	20%	298,184	55%	50%	€ (151)	€ (22,512,861)
61,470,000	12.0%	31%	65.2%	30%	447,275	55%	50%	€ (151)	€ (33,769,292)
61,470,000	12.0%	31%	65.2%	40%	596,367	55%	50%	€ (151)	€ (45,025,723)
61,470,000	12.0%	31%	65.2%	50%	745,459	55%	50%	€ (151)	€ (56,282,153)
61,470,000	12.0%	31%	65.2%	10%	149,092	65%	50%	€ (178)	€ (13,269,170)
61,470,000	12.0%	31%	65.2%	20%	298,184	65%	50%	€ (178)	€ (26,538,340)
61,470,000 [1]	12.0%	31%	65.2%	30%	447,275	65%	50%	€ (178)	€ (39,807,510)
61,470,000	12.0%	31%	65.2%	40%	596,367	65%	50%	€ (178)	€ (53,076,680)
61,470,000	12.0%	31%	65.2%	50%	745,459	65%	50%	€ (178)	€ (66,345,850)
61,470,000	12.0%	31%	65.2%	10%	149,092	75%	50%	€ (201)	€ (14,983,726)
61,470,000	12.0%	31%	65.2%	20%	298,184	75%	50%	€ (201)	€ (29,967,451)
61,470,000	12.0%	31%	65.2%	30%	447,275	75%	50%	€ (201)	€ (44,951,177)
61,470,000	12.0%	31%	65.2%	40%	596,367	75%	50%	€ (201)	€ (59,934,902)
61,470,000	12.0%	31%	65.2%	50%	745,459	75%	50%	€ (201)	€ (74,918,628)

CONCLUSIONS

- **Current medical literature suggests that extensive testing to diagnose IBS is often not recommended**
- **For patients who present with IBS-D symptoms in Italy, this evaluation predicts that the inclusion of a novel Diagnostic 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 Diagnostic Blood Panel arm for the diagnosis of IBS-D patients in Italy**

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DISCLOSURES

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

PMD33

INCLUSION OF A NOVEL IBS BLOOD PANEL FOR DIAGNOSING DIARRHEA PREDOMINANT IRRITABLE BOWEL SYNDROME (IBS-D): A UK PERSPECTIVE

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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 the UK range from 12% (ROME Criteria) - 22% (Manning Criteria)
- 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), as well as, 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)
- Also, diagnostic procedures to rule out other organic conditions may include: colonoscopy, endoscopy, ultrasound and abdominal CT scan
- IBS presents a significant health burden to patients and to the healthcare system in UK both in terms of significant direct and indirect (i.e. absenteeism) medical costs
- 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

OBJECTIVES

- The primary aim of this study was to compare the costs associated with two differing diagnostic pathways in private practice in the UK: (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 analysis for the national population

Figure 1: Decision Tree Model (Model 1)

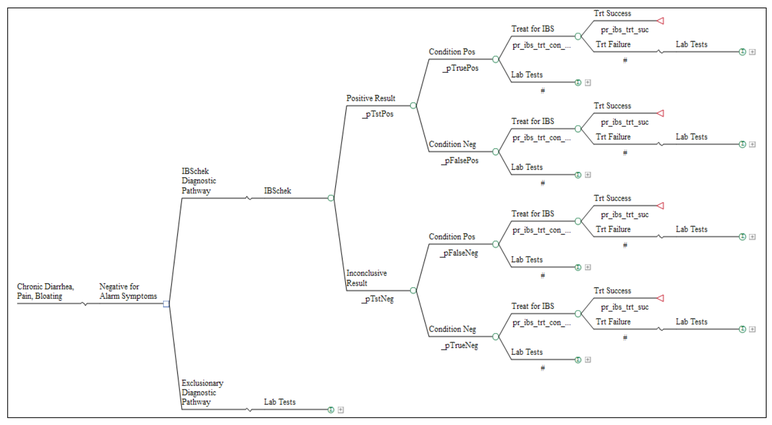
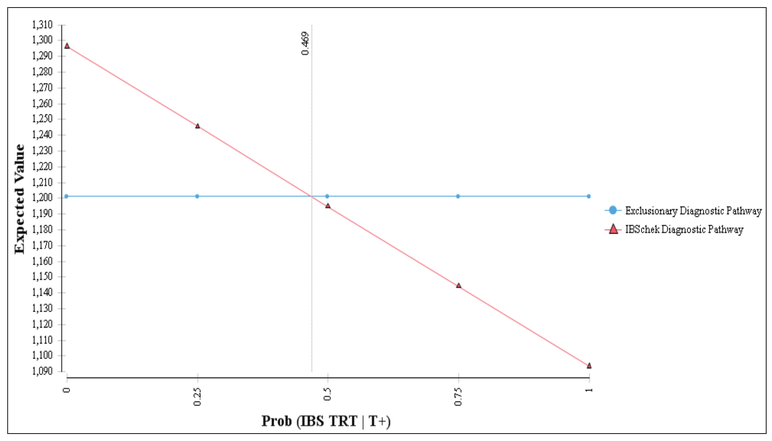


Table 1: CM Results (Model 1)

Diagnostic Pathway	Setting	Pre-test Prob Dis +	Prob (IBS TRT | T +)	Prob (IBS TRT | T -)	Expected Cost(£)	Cost (Savings) (£)
W/ IBS*chek*™	GI	0.45	0%	0%	1296	95
Exclusionary	GI	NA	NA	NA	1201	
W/ IBS*chek*™	GI	0.45	25%	0%	1246	45
Exclusionary	GI	NA	NA	NA	1201	
W/ IBS*chek*™	GI	0.45	50%	0%	1195	(6)
Exclusionary	GI	NA	NA	NA	1201	
W/ IBS*chek*™	GI	0.45	75%	0%	1144	(57)
Exclusionary	GI	NA	NA	NA	1201	
W/ IBS*chek*™	GI	0.45	100%	0%	1094	(107)
Exclusionary	GI	NA	NA	NA	1201	

Pre-Test Prob Dis +: Probability of IBS-D in the UK 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: Sensitivity for Pr (IBS TRT | T+) (Model 1)



Prob (IBS TRT |T+): Probability that a patient will receive treatment conditional on a positive test result.

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 are gastroenterologists within the national healthcare system in the UK
- 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 (Figures 3,4; Tables 2 - 4)
- For both models (CM 1 and CM 2), the probabilities for test utilization were taken from an IBS survey of practicing gastroenterologists
- Country specific costs were used to populate both models
- 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 (Table 2)
- For both models, a sensitivity 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 2 to the national population (Table 4)
- TreeAge Pro 14 was used for cost-minimization modeling; Microsoft Excel 2010 was used for budget impact modeling

RESULTS (CM Model 1)

- Gastroscopy, flexible sigmoidoscopy, and colonoscopy were the most common diagnostic (instrumental) procedures reported with estimated utilization rates of 55%, 55% and 35%, respectively
- Corresponding charges were £200, £400 and £400, respectively
- Net savings in the base case of £57 favored the IBS diagnostic blood panel pathway (assumes 75% of test positive patients receive IBS-D treatment) vs the exclusionary pathway (Table 1)
- As the pre-test probability of IBS treatment conditional on a positive test is ranged from 0% to 100%, the cost or savings range from an additional cost of £95 (for diagnostic blood panel arm) to a cost savings of £107 (for the diagnostic blood panel arm)
- The sensitivity analysis for the probability of treatment conditional on a positive test indicates that the break-even occurs when this probability is equal to 0.469 (Figure 2)
- If clinicians use the test 50% of the time for the 30% of the estimated 446,382 people who might have IBS-D who seek treatment, the net potential savings to NHS is £12,721,891

RESULTS (CM Model 2)

- For the base-case, the CM model predicts a cost savings of £102 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 2)
- A sensitivity analysis was performed for a pre-test probability of disease, for a range of values from 0.25 to 0.65; under this scenario, the cost savings range from £53 to £152 (Table 2)
- The sensitivity analysis estimated that the cost savings with the diagnostic blood panel increase as the pre-test probability of disease increases (the pre-test probability of disease is varied from 0.25 to 0.65) (Figure 4)
- The BIA predicts a cost savings of £22.8 million for the arm with the diagnostic blood panel (Table 4)
- For the BIA, as the proportion seeking care is varied from 10% - 50% the cost savings varies from £7.6 million to £37.9 million (Table 4)

Figure 3: Decision Tree Model (Model 2)

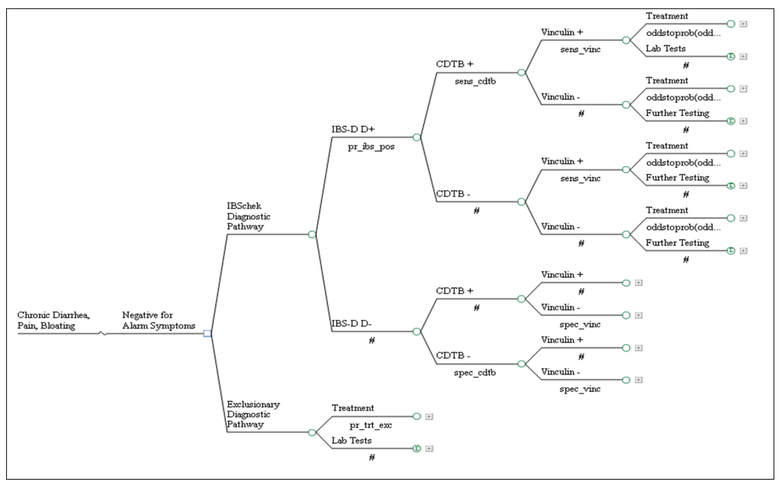


Table 2: CM Results (Model 2)

Diagnostic Pathway	Setting	Pre-test Prob Dis +	Prob (IBS TRT) Exclusionary	Expected Cost (Pounds)	Cost (Savings) Pounds
W/ IBS*chek*™	GI	0.25	NA	1094	(53)
Exclusionary	GI	NA	0.350	1147	
W/ IBS*chek*™	GI	0.35	NA	1070	(77)
Exclusionary	GI	NA	0.350	1147	
W/ IBS*chek*™	GI	0.45	NA	1045	(102) [1]
Exclusionary	GI	NA	0.350	1147	
W/ IBS*chek*™	GI	0.55	NA	1020	(127)
Exclusionary	GI	NA	0.350	1147	
W/ IBS*chek*™	GI	0.65	NA	995	(152)
Exclusionary	GI	NA	0.350	1147	

1 – Base case

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

Pre-Test Pr(D+)	Pre-Test Pr(D+)	Pre-Test Odds(D+)	LR+ CDTB	LR+ VINC	LR- CDTB	LR- VINC	Test Results (CD, VI)	Post-test Odds	Pr(D+)
25	25%	0.333	5.2	2	0.6	0.8	p,p	3.467	77.6%
25	25%	0.333	5.2	2	0.6	0.8	p,i	1.387	58.1%
25	25%	0.333	5.2	2	0.6	0.8	i,p	0.400	28.6%
25	25%	0.333	5.2	2	0.6	0.8	i,i	0.160	13.8%
35	35%	0.538	5.2	2	0.6	0.8	p,p	5.600	84.8%
35	35%	0.538	5.2	2	0.6	0.8	p,i	2.240	69.1%
35	35%	0.538	5.2	2	0.6	0.8	i,p	0.646	39.3%
35	35%	0.538	5.2	2	0.6	0.8	i,i	0.258	20.5%
45	45%	0.818	5.2	2	0.6	0.8	p,p	8.509	89.5%
45	45%	0.818	5.2	2	0.6	0.8	p,i	3.404	77.3%
45	45%	0.818	5.2	2	0.6	0.8	i,p	0.982	49.5%
45	45%	0.818	5.2	2	0.6	0.8	i,i	0.393	28.2%
55	55%	1.222	5.2	2	0.6	0.8	p,p	12.71	92.7%
55	55%	1.222	5.2	2	0.6	0.8	p,i	5.08	83.6%
55	55%	1.222	5.2	2	0.6	0.8	i,p	1.47	59.5%
55	55%	1.222	5.2	2	0.6	0.8	i,i	0.59	37.0%
65	65%	1.857	5.2	2	0.6	0.8	p,p	19.31	95.1%
65	65%	1.857	5.2	2	0.6	0.8	p,i	7.73	88.5%
65	65%	1.857	5.2	2	0.6	0.8	i,p	2.23	69.0%
65	65%	1.857	5.2	2	0.6	0.8	i,i	0.89	47.1%

Pre-Test Pr(D+): Probability of IBS-D in UK 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: Sensitivity for Pre-test Pr(D+) (Model 2)

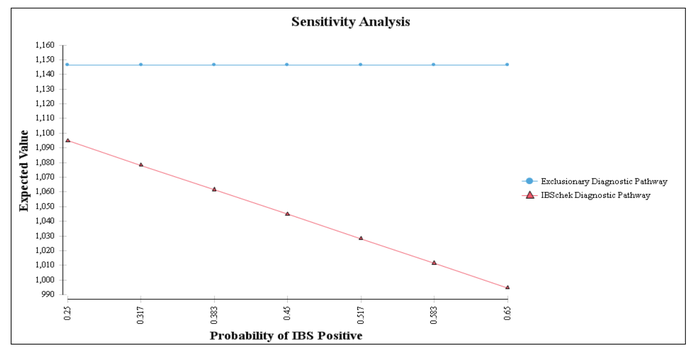


Table 4: Budget Impact Analysis (Model 2)

Covered Lives [1-3]	Proportion Seeking Care	Number of Affected Individuals	Pre-test Pr(D+)	Proportion of Physicians Using IBSchek	Cost (Savings) Per IBS-D Patient	Net Cost (Savings)
64,100,000	10%	148,794	35%	50%	-£ 77.00	-£ 5,728,570
64,100,000	20%	297,588	35%	50%	-£ 77.00	-£ 11,457,141
64,100,000	30%	446,382	35%	50%	-£ 77.00	-£ 17,185,712
64,100,000	40%	595,176	35%	50%	-£ 77.00	-£ 22,914,283
64,100,000	50%	743,970	35%	50%	-£ 77.00	-£ 28,642,854
64,100,000	10%	148,794	45%	50%	-£ 102.00	-£ 7,588,496
64,100,000	20%	297,588	45%	50%	-£ 102.00	-£ 15,176,992
64,100,000 [4]	30%	446,382	45%	50%	-£ 102.00	-£ 22,765,489
64,100,000	40%	595,176	45%	50%	-£ 102.00	-£ 30,353,985
64,100,000	50%	743,970	45%	50%	-£ 102.00	-£ 37,942,482
64,100,000	10%	148,794	55%	50%	-£ 127.00	-£ 9,448,422
64,100,000	20%	297,588	55%	50%	-£ 127.00	-£ 18,896,844
64,100,000	30%	446,382	55%	50%	-£ 127.00	-£ 28,345,266
64,100,000	40%	595,176	55%	50%	-£ 127.00	-£ 37,793,688
64,100,000	50%	743,970	55%	50%	-£ 127.00	-£ 47,242,110

1 – Prevalence = 12.0%
2 - Prevalence of IBS-D within IBS = 31%
3 – Proportion of the population within 18-65 age group = 65.4%
4 – Base case results

CONCLUSIONS

- Current medical literature suggests that extensive testing to diagnose IBS is often not recommended
- For patients who present with IBS-D symptoms in the UK, this evaluation predicts that the inclusion of a novel Diagnostic 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 cost outcomes
- Both cost minimization models predict significant cost savings for the Diagnostic Blood Panel arm

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PMD34

A NOVEL IBS DIAGNOSTIC BLOOD PANEL CAN ENHANCE A POSITIVE DIAGNOSTIC STRATEGY VERSUS A STRATEGY OF EXCLUSION FOR PATIENTS WITH DIARRHEA PREDOMINANT IRRITABLE BOWEL SYNDROME (IBS-D): COST IMPLICATIONS FOR DENMARK

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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
- A recently published article (2013) estimated the prevalence of IBS (i.e. meeting the ROME III criteria) at 16% in Denmark; the IBS-D subtype was estimated to be 33% of the IBS population
- 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)
- Also, diagnostic procedures to rule out other organic conditions may include: colonoscopy, endoscopy, ultrasound and abdominal CT scan
- IBS presents a significant health burden to patients and to the healthcare system in Denmark both in terms of significant direct and indirect (i.e. absenteeism) medical costs
- 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

OBJECTIVES

- The primary aim of this study was to compare the costs associated with two differing diagnostic pathways in gastroenterology practice in Denmark: (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 analysis for the national population

Figure 1: Decision Tree Model (Model 1)

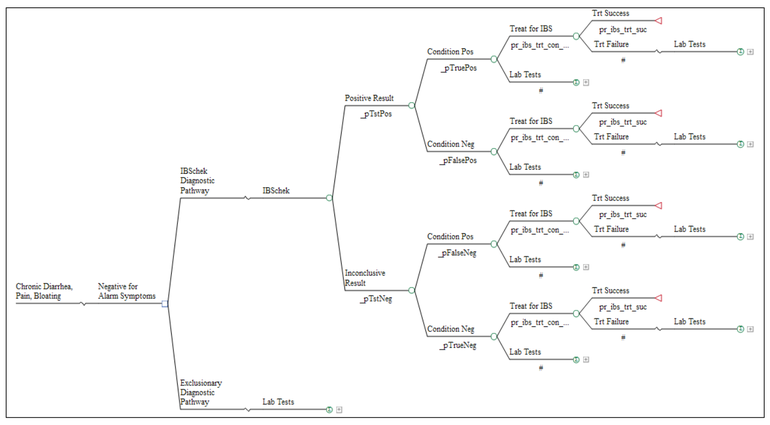
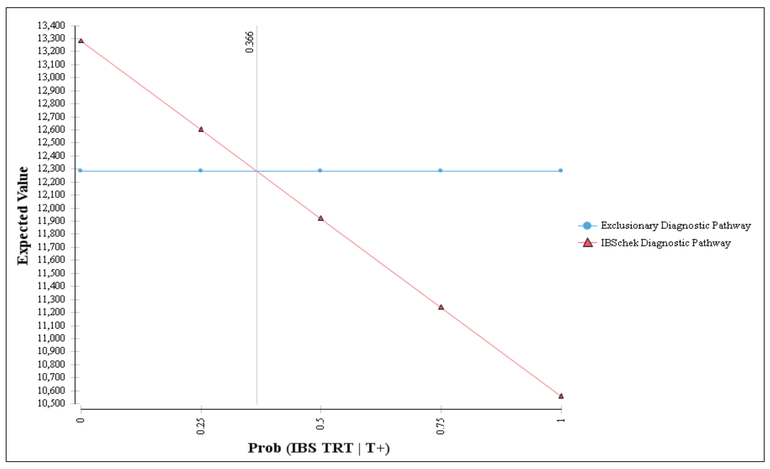


Table 1: CM Results (Model 1)

Diagnostic Pathway	Setting	Pre-test Prob Dis +	Prob (IBS TRT | T +)	Prob (IBS TRT | T -)	Expected Cost (kr)	Cost (Savings) (kr)
W/ IBS*chek*™	GI	0.750	0%	0%	13280	996
Exclusionary	GI	NA	NA	NA	12284	
W/ IBS*chek*™	GI	0.750	25%	0%	12599	315
Exclusionary	GI	NA	NA	NA	12284	
W/ IBS*chek*™	GI	0.750	50%	0%	11918	(366)
Exclusionary	GI	NA	NA	NA	12284	
W/ IBS*chek*™	GI	0.750	75%	0%	11237	(1047)
Exclusionary	GI	NA	NA	NA	12284	
W/ IBS*chek*™	GI	0.750	100%	0%	10557	(1727)
Exclusionary	GI	NA	NA	NA	12284	

Pre-Test Prob Dis +: Probability of IBS-D in the Denmark 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: Sensitivity for Pr (IBS TRT | T+) (Model 1)



Prob (IBS TRT |T+): Probability that a patient will receive treatment conditional on a positive test result

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 are gastroenterologists within the national healthcare system in Denmark
- 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 (Figures 3,4; Tables 2 - 4)
- For both models (CM 1 and CM 2), the probabilities for test utilization were taken from an IBS survey of practicing gastroenterologists
- Country specific costs were used to populate both models
- Indirect costs were included (time off work only)
- 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 (Table 2)
- For both models, a sensitivity 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 2 to the national population (Table 4)
- TreeAge Pro 14 was used for cost-minimization modeling; Microsoft Excel 2010 was used for budget impact modeling

RESULTS (CM Model 1)

- Sigmoidoscopy, colonoscopy, SBFT were the most common diagnostic procedures reported with estimated utilization rates of 35%, 35% and 15% (corresponding charges were kr4819, kr4819 and kr1861)
- The base case for the pre-test probability of disease (IBS-D) was estimated to be 0.75
- Estimated total base case charges for the IBS diagnostic blood panel pathway (assumes 75% of test positive patients receive IBS-D treatment) vs the exclusionary pathway were kr11,237 vs kr12,284 (a cost savings of kr1047 for the diagnostic blood panel) (Table 1)
- As a sensitivity analysis, the probability that patients will proceed to treatment was varied from 0% to 100%; the outcomes ranged from an additional cost of kr996 (for the diagnostic blood panel) to a cost savings of kr1727 (for the diagnostic blood panel) (Table 1)
- If clinicians use the test 50% of the time for the 30% of the estimated 57,490 people who might have IBS-D who seek treatment, net savings to the Danish healthcare system is kr30,095,980 (BIA from model 1)
- Cost neutrality occurs if 37% of the "test positive" patients seek IBS treatment

RESULTS (CM Model 2)

- For the base-case, the CM model predicts a cost savings of kr2098 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 2)
- A sensitivity analysis was performed for a pre-test probability of disease, for a range of values from 0.55 to 0.95; under this scenario, the cost savings range from kr1568 to kr2633 (Table 2)
- The sensitivity analysis estimated that the cost savings with the diagnostic blood panel increase as the pre-test probability of disease increases (the pre-test probability of disease is varied from 0.55 to 0.95) (Figure 4)
- The BIA predicts a cost savings of kr60.3 million for the arm with the diagnostic blood panel (Table 4)
- For the BIA, as the proportion seeking care is varied from 10% - 50% the cost savings varies from kr20.1 million to kr100.5 million (Table 4)

Figure 3: Decision Tree Model (Model 2)

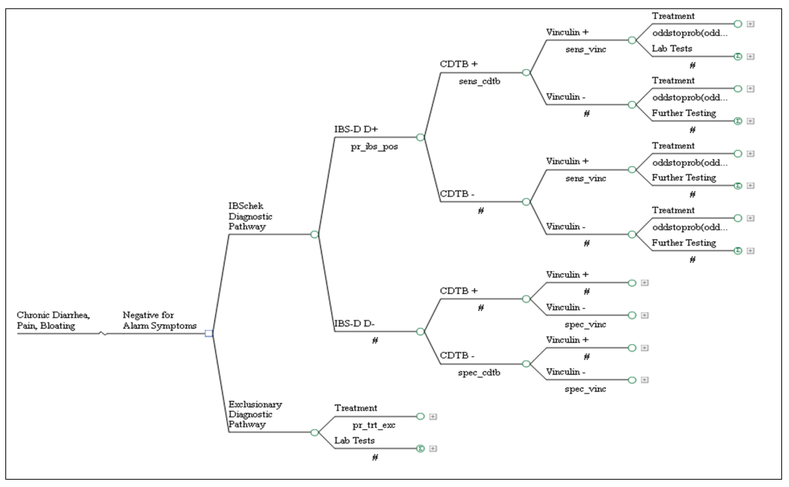


Table 2: CM Results (Model 2)

Diagnostic Pathway	Setting	Pre-test Prob Dis +	Prob (IBS TRT) Exclusionary	Expected Cost Krone	Cost (Savings) Krone
W/ IBS*chek*™	GI	0.55	NA	10142	(1568)
Exclusionary	GI	NA	0.350	11710	
W/ IBS*chek*™	GI	0.65	NA	9878	(1832)
Exclusionary	GI	NA	0.350	11710	
W/ IBS*chek*™	GI	0.75	NA	9612	(2098) [1]
Exclusionary	GI	NA	0.350	11710	
W/ IBS*chek*™	GI	0.85	NA	9346	(2364)
Exclusionary	GI	NA	0.350	11710	
W/ IBS*chek*™	GI	0.95	NA	9077	(2633)
Exclusionary	GI	NA	0.350	11710	

1 – Base case

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 (CD, VI)	Post-test Odds	Pr(D+)
55%	1.222	5.2	2	0.6	0.8	p,p	12.711	92.7%
55%	1.222	5.2	2	0.6	0.8	p,i	5.084	83.6%
55%	1.222	5.2	2	0.6	0.8	i,p	1.467	59.5%
55%	1.222	5.2	2	0.6	0.8	i,i	0.587	37.0%
65%	1.857	5.2	2	0.6	0.8	p,p	19.314	95.1%
65%	1.857	5.2	2	0.6	0.8	p,i	7.726	88.5%
65%	1.857	5.2	2	0.6	0.8	i,p	2.229	69.0%
65%	1.857	5.2	2	0.6	0.8	i,i	0.891	47.1%
75%	3.000	5.2	2	0.6	0.8	p,p	31.200	96.9%
75%	3.000	5.2	2	0.6	0.8	p,i	12.480	92.6%
75%	3.000	5.2	2	0.6	0.8	i,p	3.600	78.3%
75%	3.000	5.2	2	0.6	0.8	i,i	1.440	59.0%
85%	5.667	5.2	2	0.6	0.8	p,p	58.93	98.3%
85%	5.667	5.2	2	0.6	0.8	p,i	23.57	95.9%
85%	5.667	5.2	2	0.6	0.8	i,p	6.80	87.2%
85%	5.667	5.2	2	0.6	0.8	i,i	2.72	73.1%
95%	19.000	5.2	2	0.6	0.8	p,p	197.60	99.5%
95%	19.000	5.2	2	0.6	0.8	p,i	79.04	98.8%
95%	19.000	5.2	2	0.6	0.8	i,p	22.80	95.8%
95%	19.000	5.2	2	0.6	0.8	i,i	9.12	90.1%

Pre-Test Pr(D+): Probability of IBS-D in Denmark 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. i:inconclusive, p:positive

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

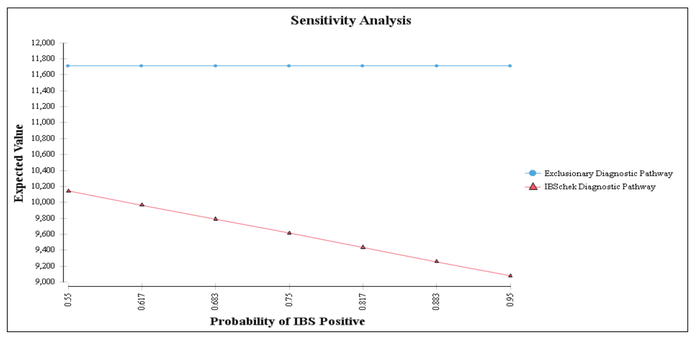


Table 4: Budget Impact Analysis (Model 2)

Covered Lives [1-3]	Proportion Seeking Care	Number of Affected Individuals	Pre-test Pr(D+)	Proportion of Physicians Using IBS*chek*™	Cost (Savings) Per IBS-D Patient	Net Cost (Savings)
5,627,000	20%	38,327	65%	50%	kr. -1,832	kr. -17,553,593
5,627,000	20%	38,327	65%	50%	kr. -1,832	kr. -35,107,186
5,627,000	30%	57,490	65%	50%	kr. -1,832	kr. -52,660,779
5,627,000	40%	76,653	65%	50%	kr. -1,832	kr. -70,214,372
5,627,000	50%	95,817	65%	50%	kr. -1,832	kr. -87,767,965
5,627,000	10%	19,163	75%	50%	kr. -2,098	kr. -20,102,313
5,627,000	20%	38,327	75%	50%	kr. -2,098	kr. -40,204,626
5,627,000 [4]	30%	57,490	75%	50%	kr. -2,098	kr. -60,306,940
5,627,000	40%	76,653	75%	50%	kr. -2,098	kr. -80,409,253
5,627,000	50%	95,817	75%	50%	kr. -2,098	kr. -100,511,567
5,627,000	10%	19,163	85%	50%	kr. -2,633	kr. -25,228,499
5,627,000	20%	38,327	85%	50%	kr. -2,633	kr. -50,456,998
5,627,000	30%	57,490	85%	50%	kr. -2,633	kr. -75,685,497
5,627,000	40%	76,653	85%	50%	kr. -2,633	kr. -100,913,996
5,627,000	50%	95,817	85%	50%	kr. -2,633	kr. -126,142,495

1 – Prevalence = 16.0%
2 - Prevalence of IBS-D within IBS = 33%
3 – Proportion of the population within 18-65 age group = 64.5%
4 – Base case results

CONCLUSIONS

- Current medical literature suggests that extensive testing to diagnose IBS is often not recommended
- For patients who present with IBS-D symptoms in Denmark, this evaluation predicts that the inclusion of a novel Diagnostic 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 cost outcomes
- Both cost-minimization models predict significant cost savings for the Diagnostic Blood Panel arm

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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 has acted as scientific consultants for Commonwealth Laboratories, LLC and Commonwealth Diagnostics International, Inc.

PMD35

COST-MINIMIZATION FOR A NOVEL IBS DIAGNOSTIC BLOOD PANEL VERSUS STANDARD EXCLUSIONARY DIAGNOSTIC TESTING FOR DIARRHEA PREDOMINANT IRRITABLE BOWEL SYNDROME: A UNITED STATES PERSPECTIVE

Pimentel M[1], Purdy C[2], Magar R[3]

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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
- A published article (2005) estimated the prevalence of irritable bowel syndrome to be 14.1% (medically diagnosed 3.3%; undiagnosed, but meeting irritable bowel syndrome criteria 10.8%)
- IBS has a significant impact on the sufferer's health and quality of life; also, there are significant social and economic ramifications
- 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)
- Also, diagnostic procedures to rule out other organic conditions may include: colonoscopy, endoscopy, ultrasound and abdominal CT scan
- IBS presents a significant health burden to patients and to the healthcare system in the US both in terms of significant direct and indirect (i.e. absenteeism) medical costs
- IBS*chek*™ is a novel diagnostic blood panel (for IBS-D) 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

OBJECTIVES

- The primary aim of this study was to compare the costs associated with two differing diagnostic pathways in gastroenterology practice in the US: (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 analysis for a health plan

Figure 1: Decision Tree Model (CM1)

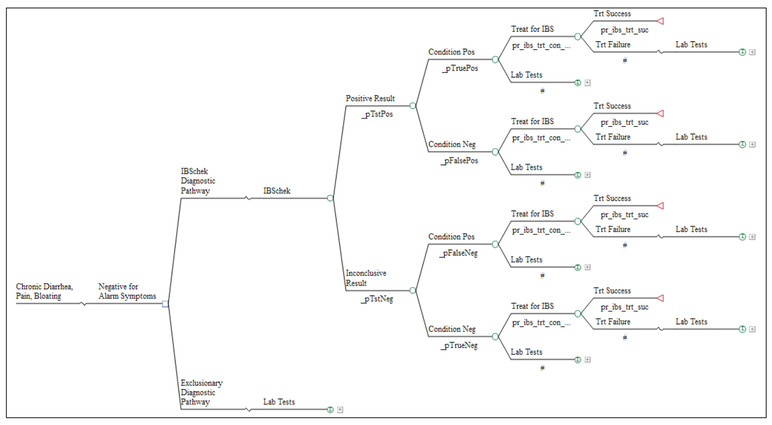
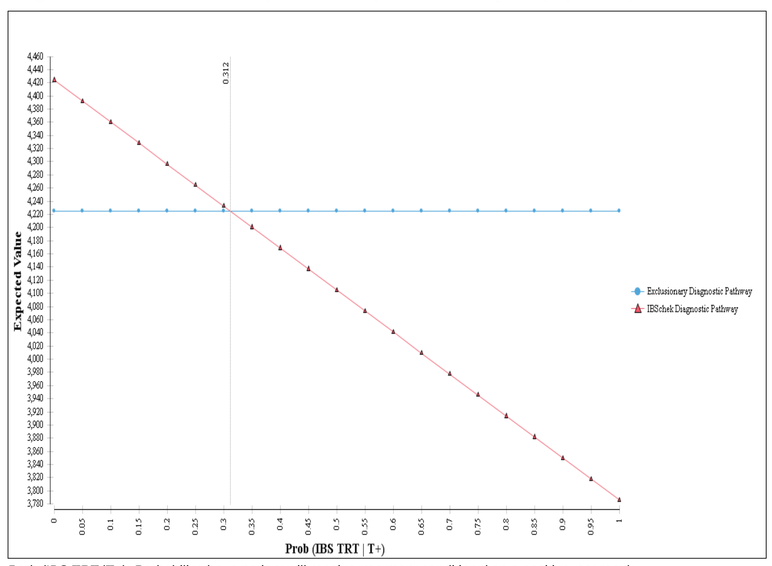


Table 1: CM Results (CM1)

Diagnostic Pathway	Setting	Pre-test Prob Dis +	Prob (IBS TRT | T +)	Prob (IBS TRT | T -)	Expected Cost	Cost (Savings)
W/ IBS*chek*™	GI	0.763	0%	0%	4424	199
Exclusionary	GI	NA	NA	NA	4225	
W/ IBS*chek*™	GI	0.763	25%	0%	4265	40
Exclusionary	GI	NA	NA	NA	4225	
W/ IBS*chek*™	GI	0.763	50%	0%	4105	(120)
Exclusionary	GI	NA	NA	NA	4225	
W/ IBS*chek*™	GI	0.763	75%	0%	3945	(280)
Exclusionary	GI	NA	NA	NA	4225	
W/ IBS*chek*™	GI	0.763	100%	0%	3786	(439)
Exclusionary	GI	NA	NA	NA	4225	

Pre-Test Prob Dis +: Probability of IBS-D in the US 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: Sensitivity for Pr (IBS TRT | T+) (CM1)



Prob (IBS TRT |T+): Probability that a patient will receive treatment conditional on a positive test result

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 are gastroenterologists within the US
- 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 (Figures 3-6; Tables 2,3)
- For both models (CM 1 and CM 2), the probabilities for test utilization were taken from an IBS survey of practicing gastroenterologists
- Country specific costs (US) were used to populate both models
- 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 (Table 2)
- For both models, a sensitivity 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 2 to a health plan with 1 million covered lives (Table 3)
- TreeAge Pro 14 was used for cost-minimization modeling; Microsoft Excel 2010 was used for budget impact modeling

RESULTS (CM Model 1)

- Colonoscopy, endoscopy, computed tomography and ultrasound were the most common diagnostic procedures reported with estimated utilization rates of 0.625, 0.400, 0.306 and 0.294
- The corresponding charges were $2,727, $1,375, $2,175 and $370.50
- The base case for the pre-test probability of disease (IBS-D) was estimated to be 0.763
- The CM model predicts a base case savings of $280 per patient for the diagnostic pathway that includes the novel IBS diagnostic blood panel
- Sensitivity analyses predict a range of cost savings of $120 to $439
- Budget impact analysis predicts a base case savings of $1,080,232 to the plan or $0.09 on a per member per month basis for the diagnostic pathway with the novel IBS diagnostic blood panel
- The time dependent model indicates that the potential cost savings associated with the novel IBS blood test are attenuated over time

RESULTS (CM Model 2)

- For the base-case, the CM model predicts a cost savings of $509 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 2)
- A sensitivity analysis was performed for a pre-test probability of disease, for a range of values from 0.363 to 0.963; under this scenario, the outcomes range from an additional cost of $142 for the diagnostic blood panel to a cost savings of $840 for the diagnostic blood panel (Table 2)
- The sensitivity analysis for the pre-test probability of disease indicates that the break-even occurs at 0.451 (Figure 4)
- The sensitivity analysis for the probability of IBS treatment in the exclusionary branch of disease indicates that the break-even occurs at 0.652 (Figure 5)
- The sensitivity analysis for the probability of treatment success indicates there is no break-even for this variable (Figure 6)
- For the BIA, as the proportion seeking care is varied from 10% - 100% the cost savings varies from $0.06 to $0.61 PMPM (Table 3)

Figure 3: Decision Tree Model (CM2)

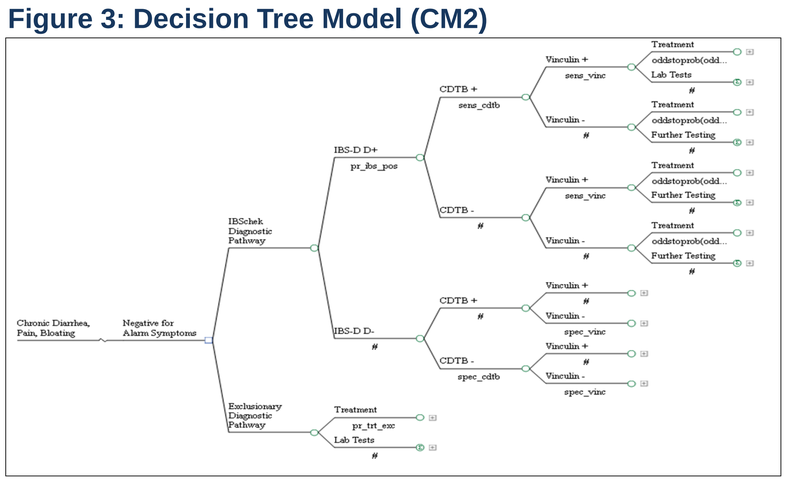


Table 2: CM Results (Model 2)

Diagnostic Pathway	Setting	Pre-test Prob Dis +	Prob (IBS TRT) Exclusionary	Expected Cost	Cost (Savings)
W/ IBS*chek*™	GI	0.363	NA	4141	142
Exclusionary	GI	NA	20.0	3999	
W/ IBS*chek*™	GI	0.463	NA	3980	(19)
Exclusionary	GI	NA	20.0	3999	
W/ IBS*chek*™	GI	0.563	NA	3817	(182)
Exclusionary	GI	NA	20.0	3999	
W/ IBS*chek*™	GI	0.663	NA	3654	(345)
Exclusionary	GI	NA	20.0	3999	
W/ IBS*chek*™	GI	0.763	NA	3490	(509) [1]
Exclusionary	GI	NA	20.0	3999	
W/ IBS*chek*™	GI	0.863	NA	3325	(674)
Exclusionary	GI	NA	10.0	3999	
W/ IBS*chek*™	GI	0.963	NA	3159	(840)
Exclusionary	GI	NA	0.0	3999	

1 – Base case

Figure 4: Sensitivity for Pre-Test Pr(D+) (CM2)

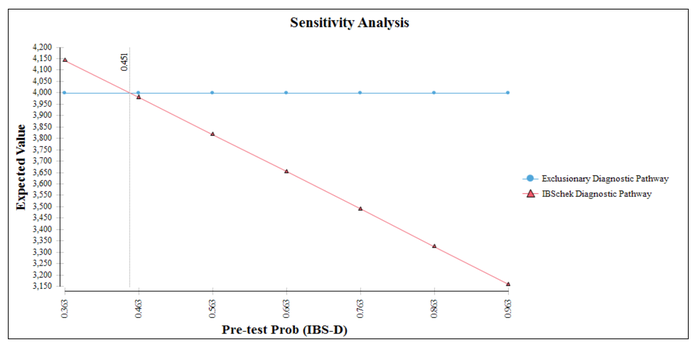


Figure 5: Sensitivity for Pr(IBS TRT | Exc Br) (CM2)

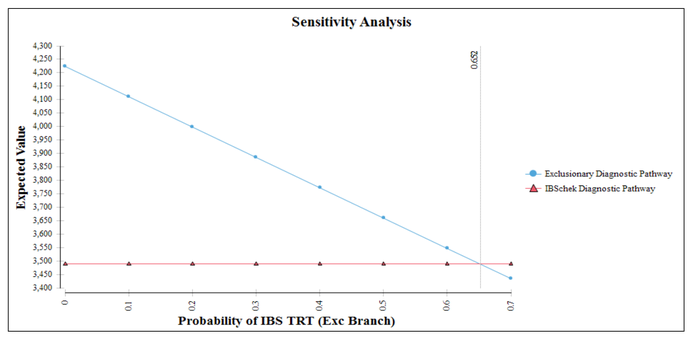


Figure 6: Sensitivity for Pr(TRT Success) (CM2)

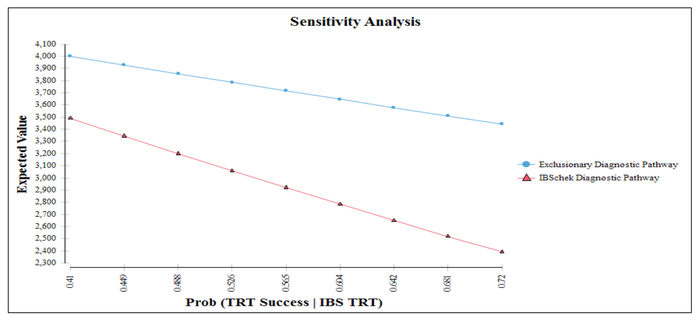


Table 3: Budget Impact Analysis (CM2)

Covered Lives [1-5]	Proportion Seeking Care	Number of Individuals Seeking Care	Net Cost if 100% of Patients Diagnosed with Exclusionary Path	Net Cost if 50% Exclusionary Path, 50% IBS*chek*™	Cost (Savings)	Cost (Savings) PMPM
1,000,000	10%	2,856	$ 11,421,144	$ 10,694,292	$ (726,852)	$ (0.06)
1,000,000	20%	5,712	$ 22,842,288	$ 21,388,584	$ (1,453,704)	$ (0.12)
1,000,000	30%	8,567	$ 34,259,433	$ 32,079,132	$ (2,180,302)	$ (0.18)
1,000,000	40%	11,423	$ 45,680,577	$ 42,773,424	$ (2,907,154)	$ (0.24)
1,000,000	50%	14,279	$ 57,101,721	$ 53,467,716	$ (3,634,006)	$ (0.30)
1,000,000	60%	17,135	$ 68,522,865	$ 64,162,008	$ (4,360,858)	$ (0.36)
1,000,000	70%	19,991	$ 79,944,009	$ 74,856,300	$ (5,087,710)	$ (0.42)
1,000,000	80%	22,846	$ 91,361,154	$ 85,546,847	$ (5,814,307)	$ (0.48)
1,000,000	90%	25,702	$ 102,782,298	$ 96,241,139	$ (6,541,159)	$ (0.55)
1,000,000	100%	28,558	$ 114,203,442	$ 106,935,431	$ (7,268,011)	$ (0.61)

1 – Assumption: HMO with 1 million covered lives.
2 - IBS Prevalence = 14.1% (Hungin AP, Chang L, Locke GR, Dennis EH, Barghout V. Irritable bowel syndrome in the United States: prevalence, symptom patterns and impact. Aliment Pharmacol Ther. 2005 Jun 1;21(11):1365-75.6)
3 – IBS-D Prevalence within IBS =32.2% (IBS Physician Survey (Administered by AHRM Inc. (April – June of 2015))
4 – Proportion of US population within 18-64 age group (62.9%) (http://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf)
5 – Pre-test probability of disease estimated to be 0.763 (from cost-minimization model)

CONCLUSIONS

- Current medical literature suggests that extensive testing to diagnose IBS is often not recommended
- For patients who present with IBS-D symptoms in the US, this evaluation predicts that the inclusion of a novel Diagnostic 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 cost outcomes
- Both cost-minimization models predict significant cost savings for the Diagnostic Blood Panel arm

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DISCLOSURES

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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)

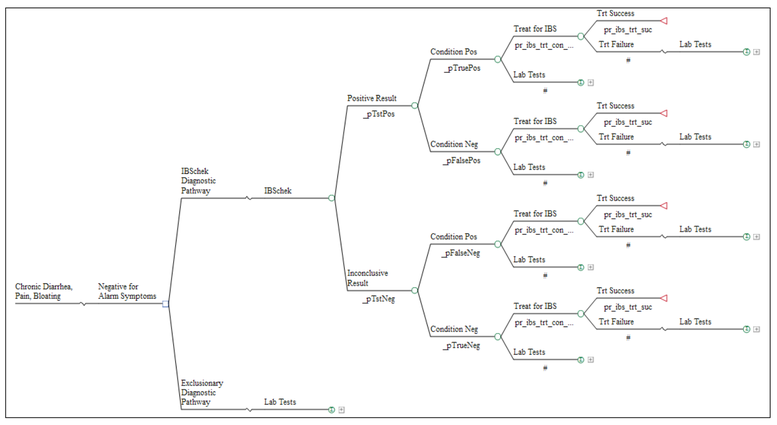
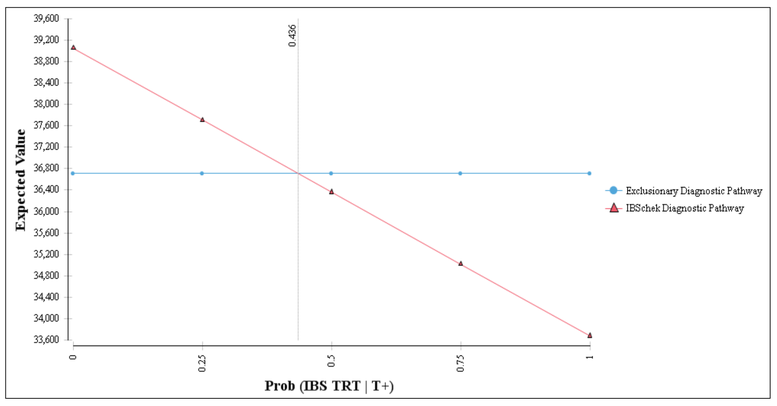


Table 1: CM Results (Model 1)

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)

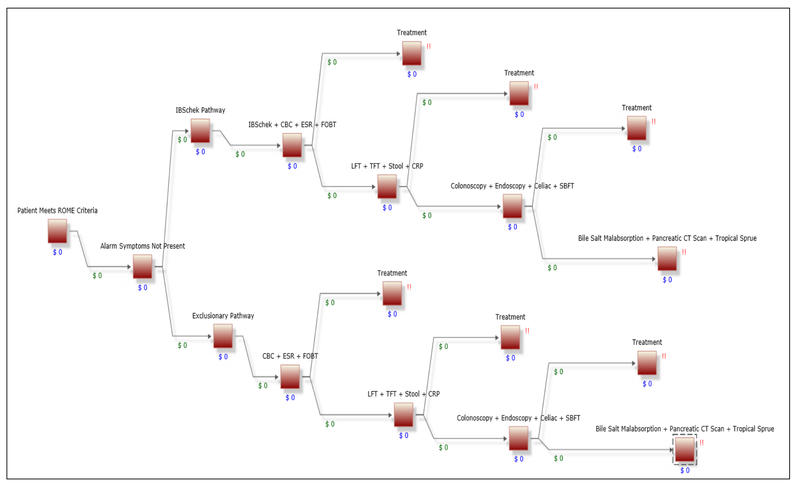


Table 2: CM Results (Model 2)

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)

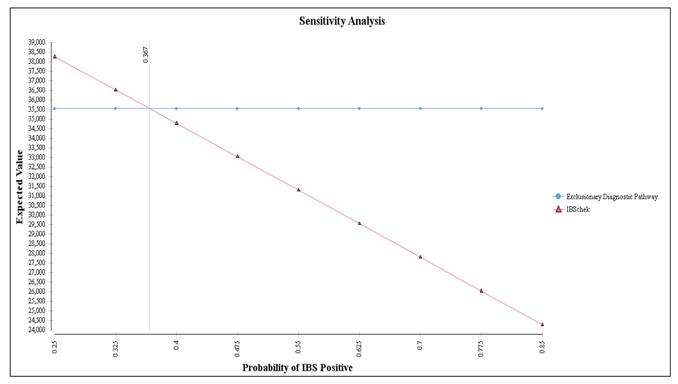


Table 4: Budget Impact Analysis (Model 2)

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

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