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)

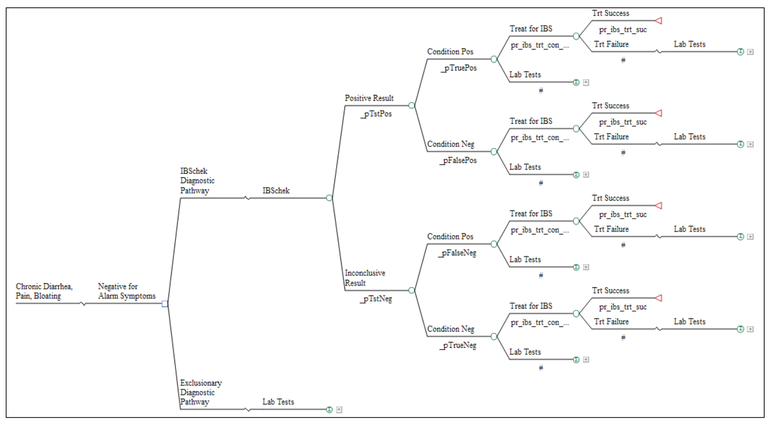
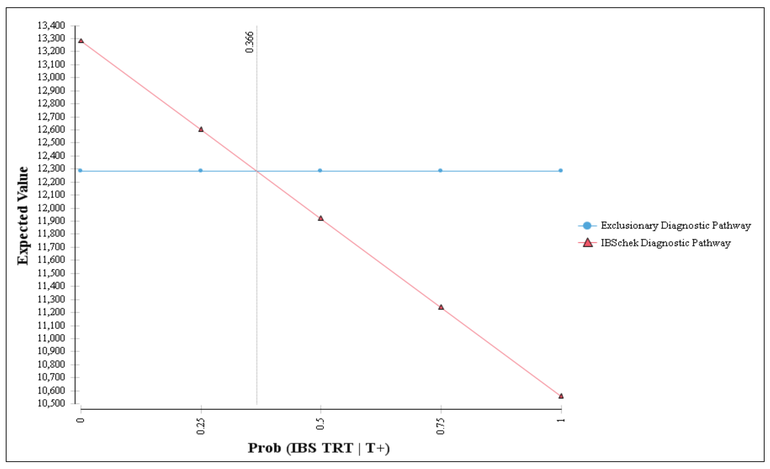


Table 1: CM Results (Model 1)

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)

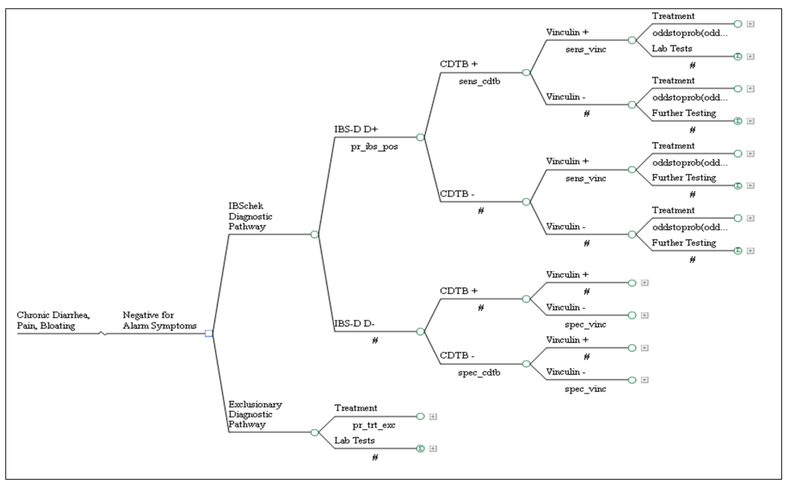


Table 2: CM Results (Model 2)

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)

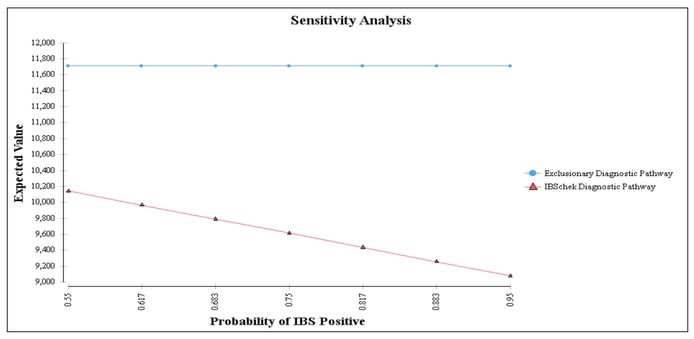


Table 4: Budget Impact Analysis (Model 2)

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.

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