

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-TG) 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
- IBScheKTM is a novel diagnostic blood panel which involves measuring antibody levels for cytotoxin 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 IBScheK 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)

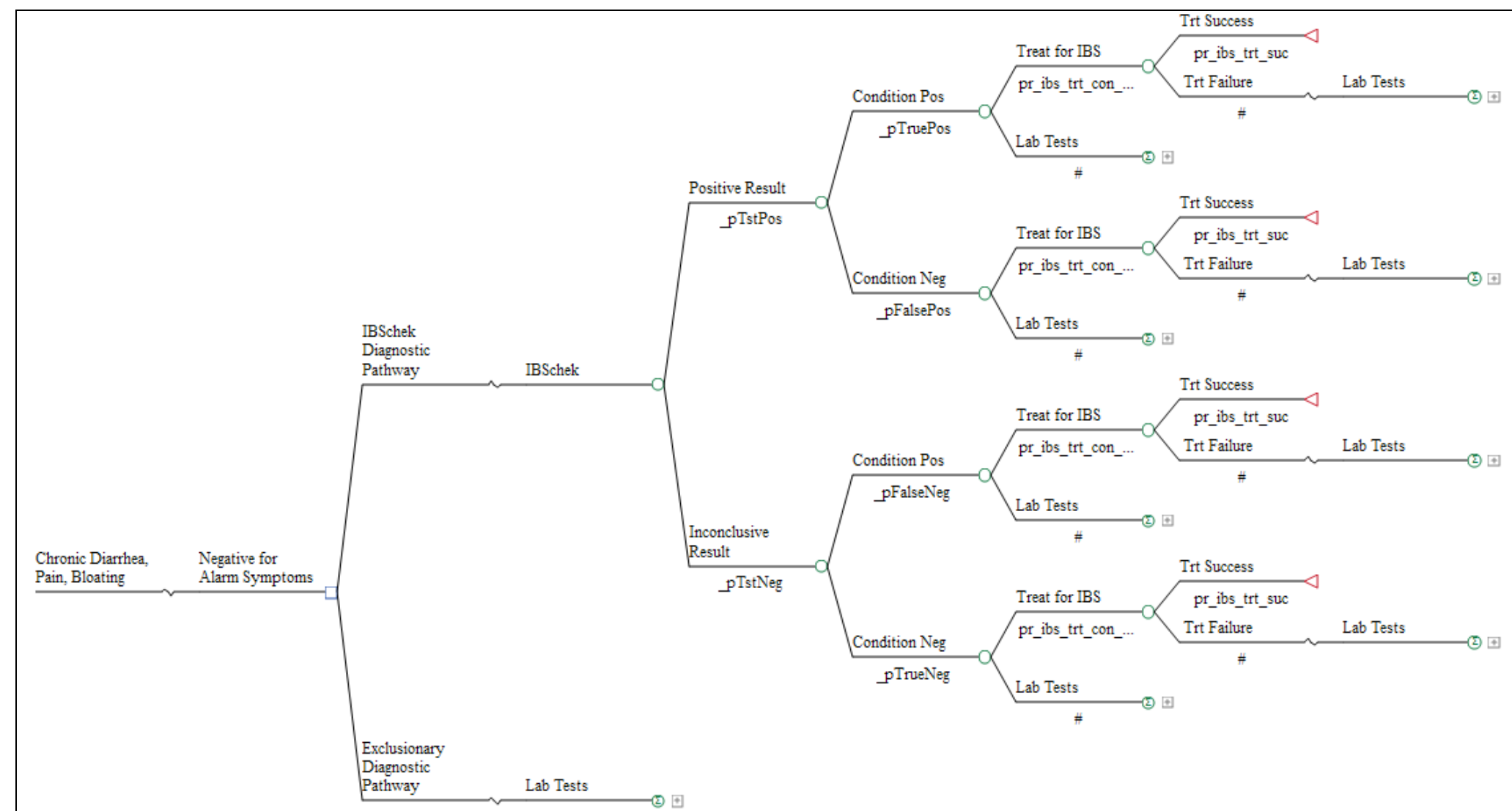
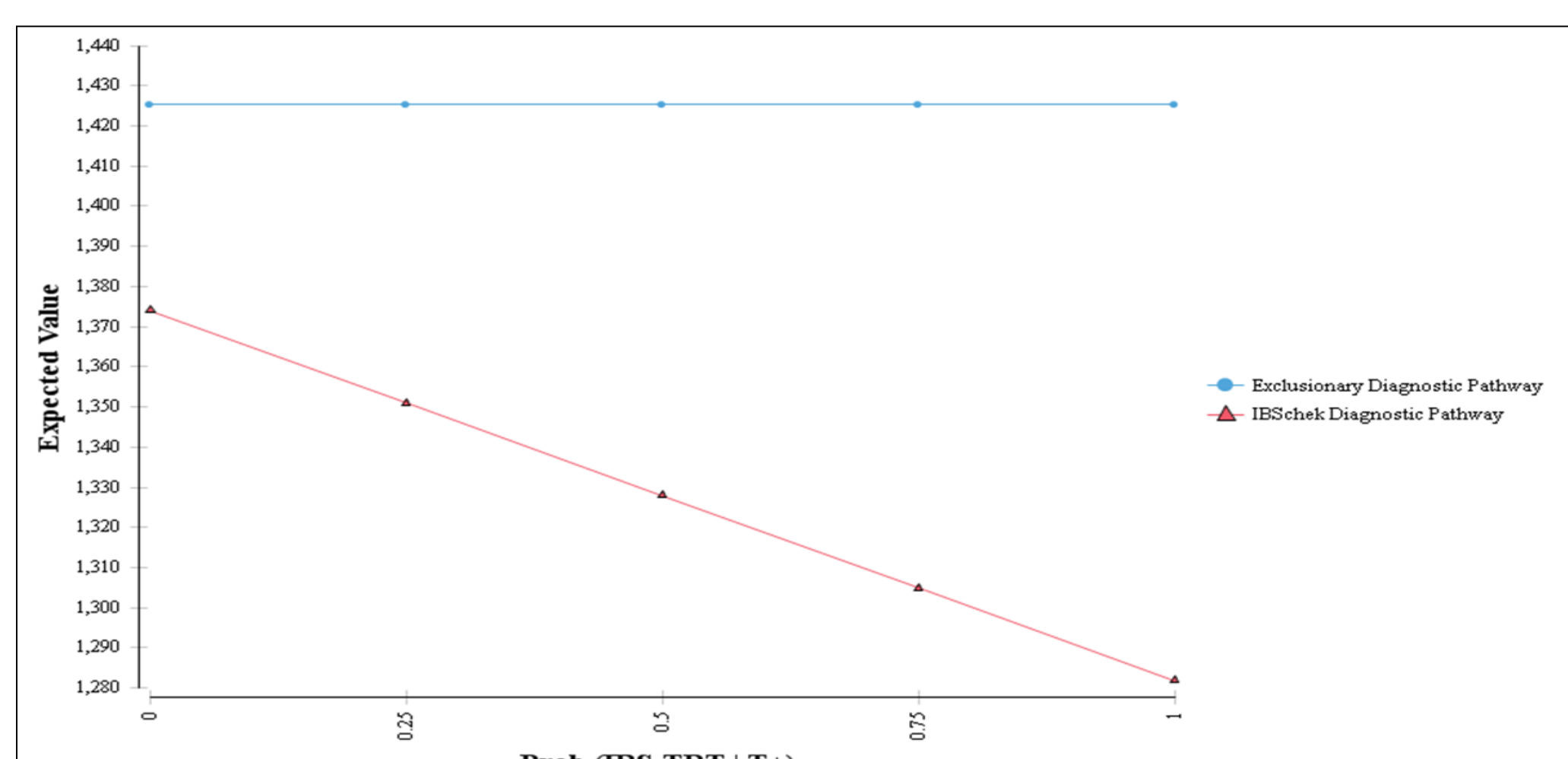


Table 1: CM Results (Model 1)

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

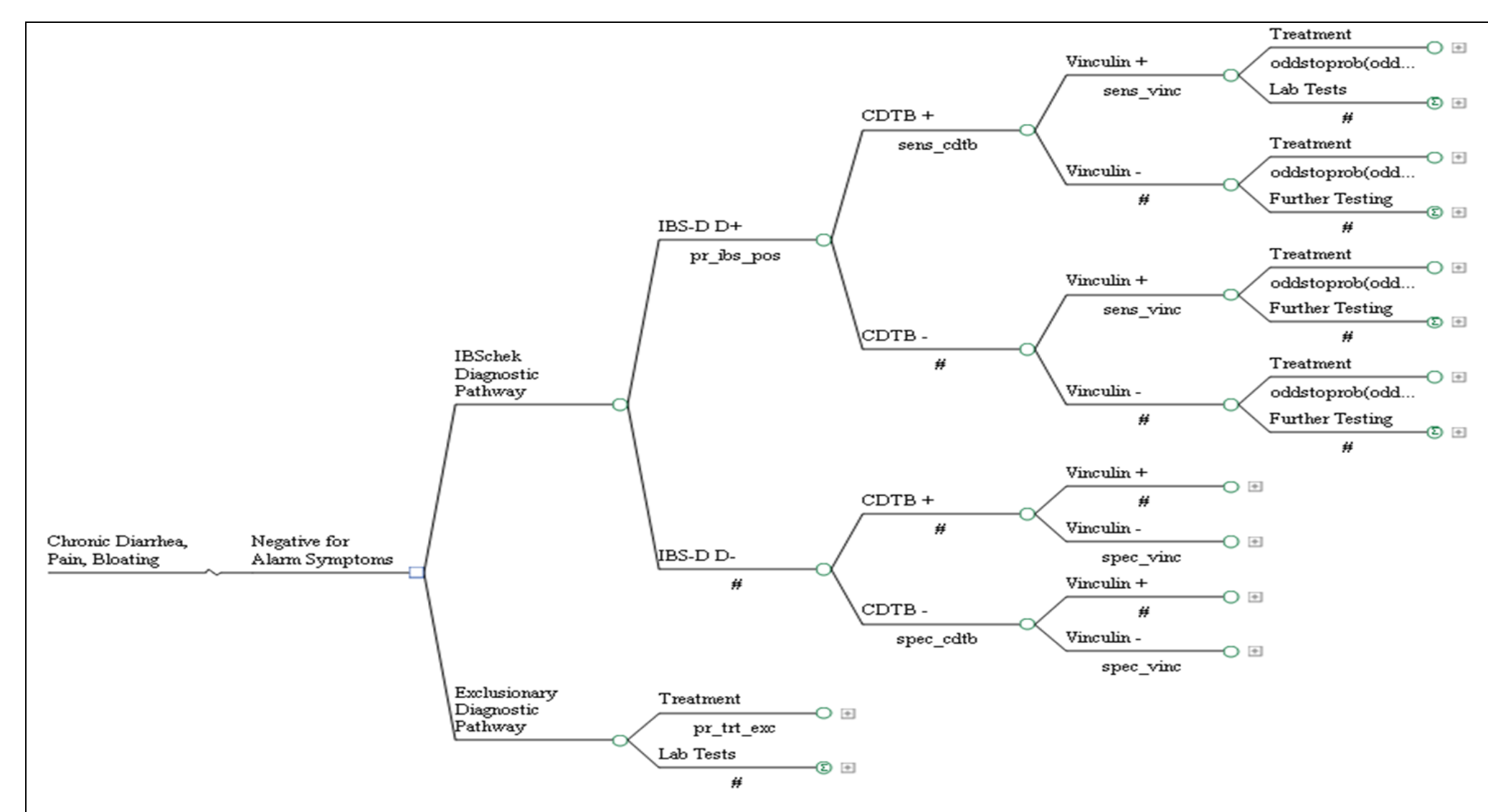


Table 2: CM Results (Model 2)

Diagnostic Pathway	Pre-test Prob Dis +	Prob (IBS TRT) Exclusionary	Expected Cost	Cost (Savings) Euros
W/ IBScheK TM	0.450	NA	1211	(124)
Exclusionary	NA	0.350	1335	
W/ IBScheK TM	0.550	NA	1184	(151)
Exclusionary	NA	0.350	1335	
W/ IBScheK TM	0.650	NA	1157	(178) [1]
Exclusionary	NA	0.350	1335	
W/ IBScheK TM	0.750	NA	1130	(201)
Exclusionary	NA	0.350	1335	
W/ IBScheK TM	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, V)	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	2.729	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	31.200	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 IBScheK) Probability for the patient to be IBS-D positive. n: negative. p: positive

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

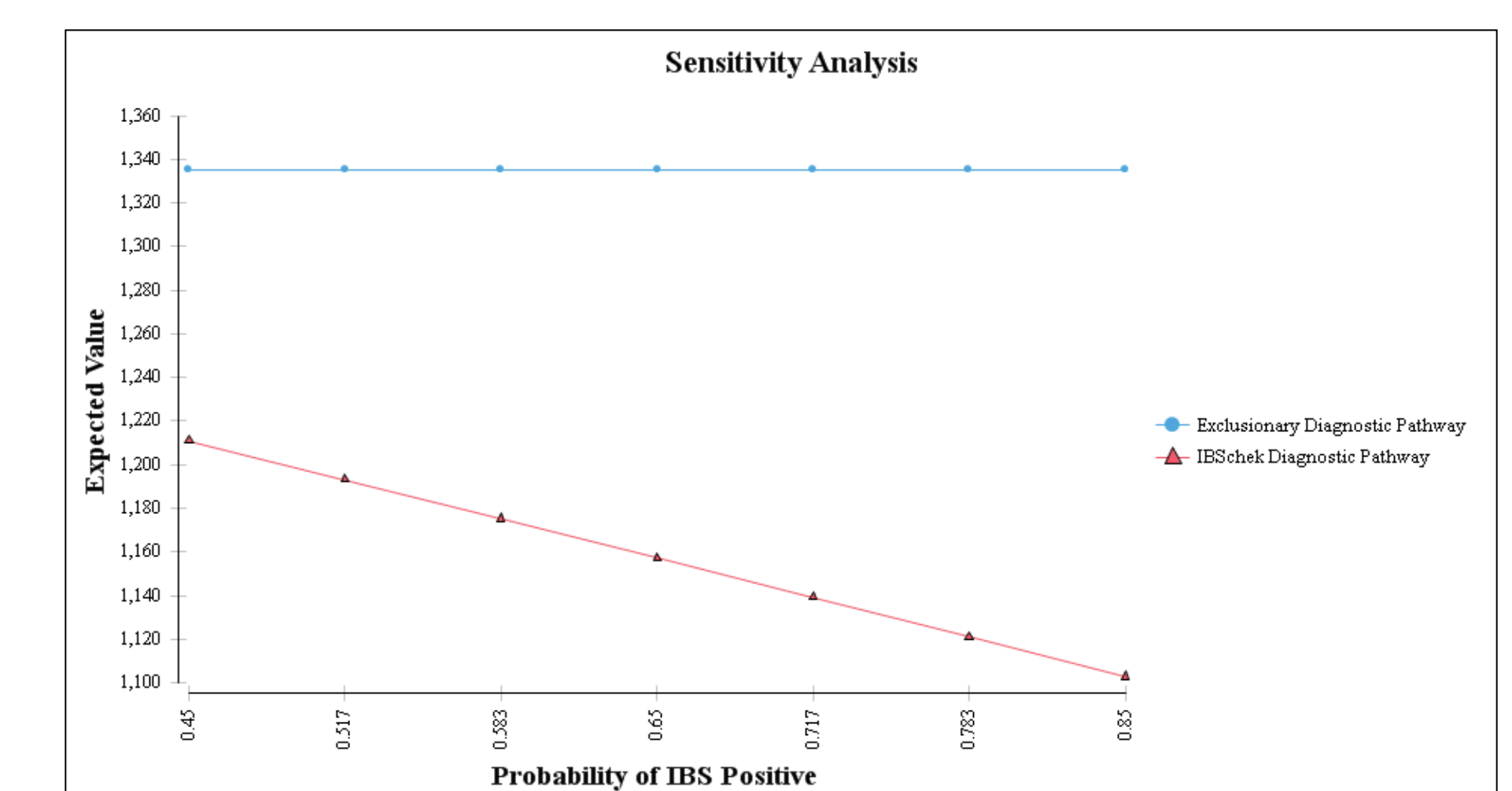


Table 4: Budget Impact Analysis (Model 2)

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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