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
- IBSchek 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 panel 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 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

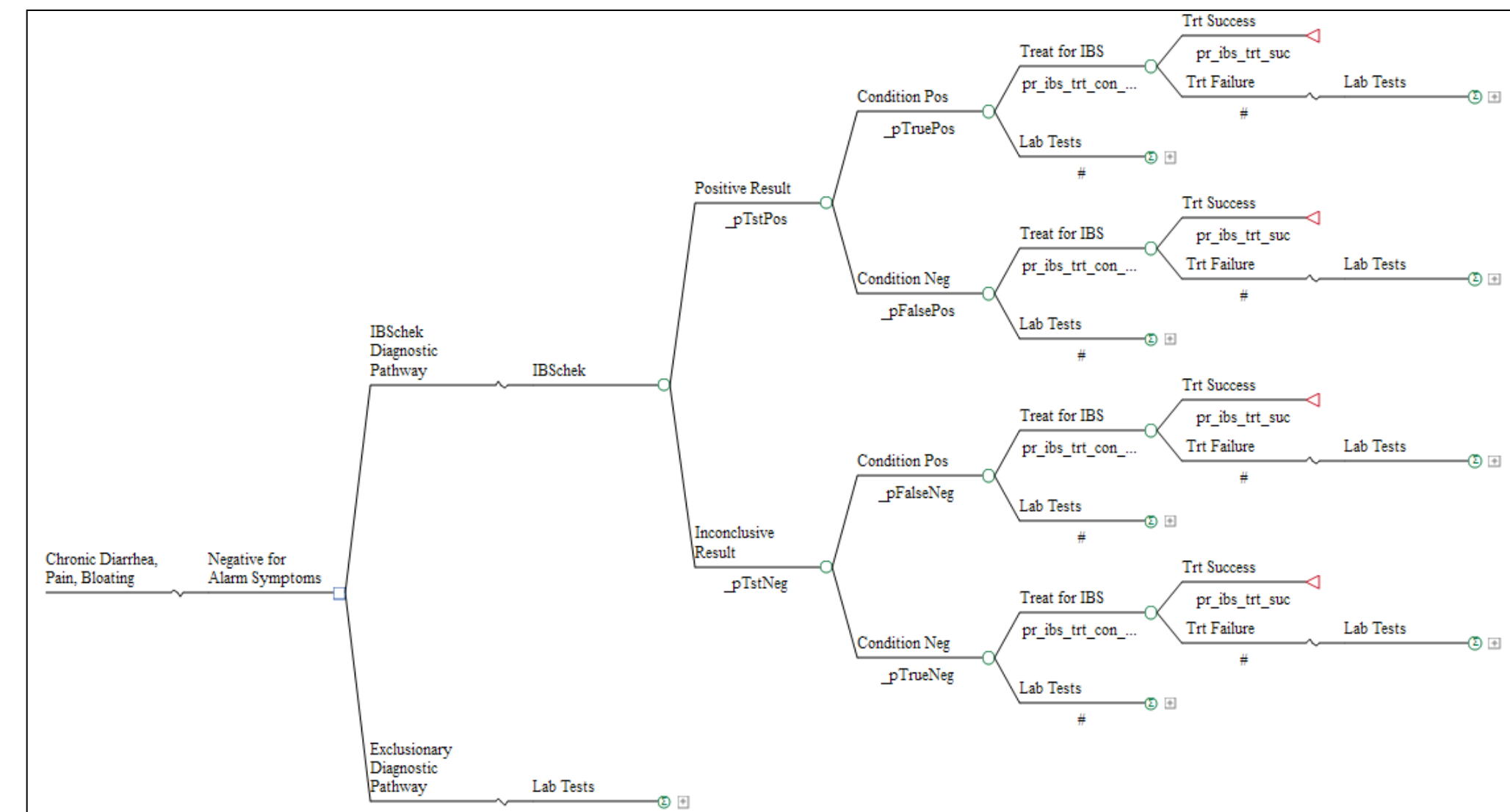## Figure 1: Decision Tree Model (Model 1)

Table 1: CM Results (Model 1)

Diagnostic Pathway	Setting	Pre-test Prob Dis +	Prob (IBS TRT | T +)	Prob (IBS TRT | T -)	Expected Cost(£)	Cost (Savings) (£)
W/ IBSchek™	GI	0.45	0%	0%	1296	95
Exclusionary	GI	NA	NA	NA	1201	
W/ IBSchek™	GI	0.45	25%	0%	1246	45
Exclusionary	GI	NA	NA	NA	1201	
W/ IBSchek™	GI	0.45	50%	0%	1195	(6)
Exclusionary	GI	NA	NA	NA	1201	
W/ IBSchek™	GI	0.45	75%	0%	1144	(57)
Exclusionary	GI	NA	NA	NA	1201	
W/ IBSchek™	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)
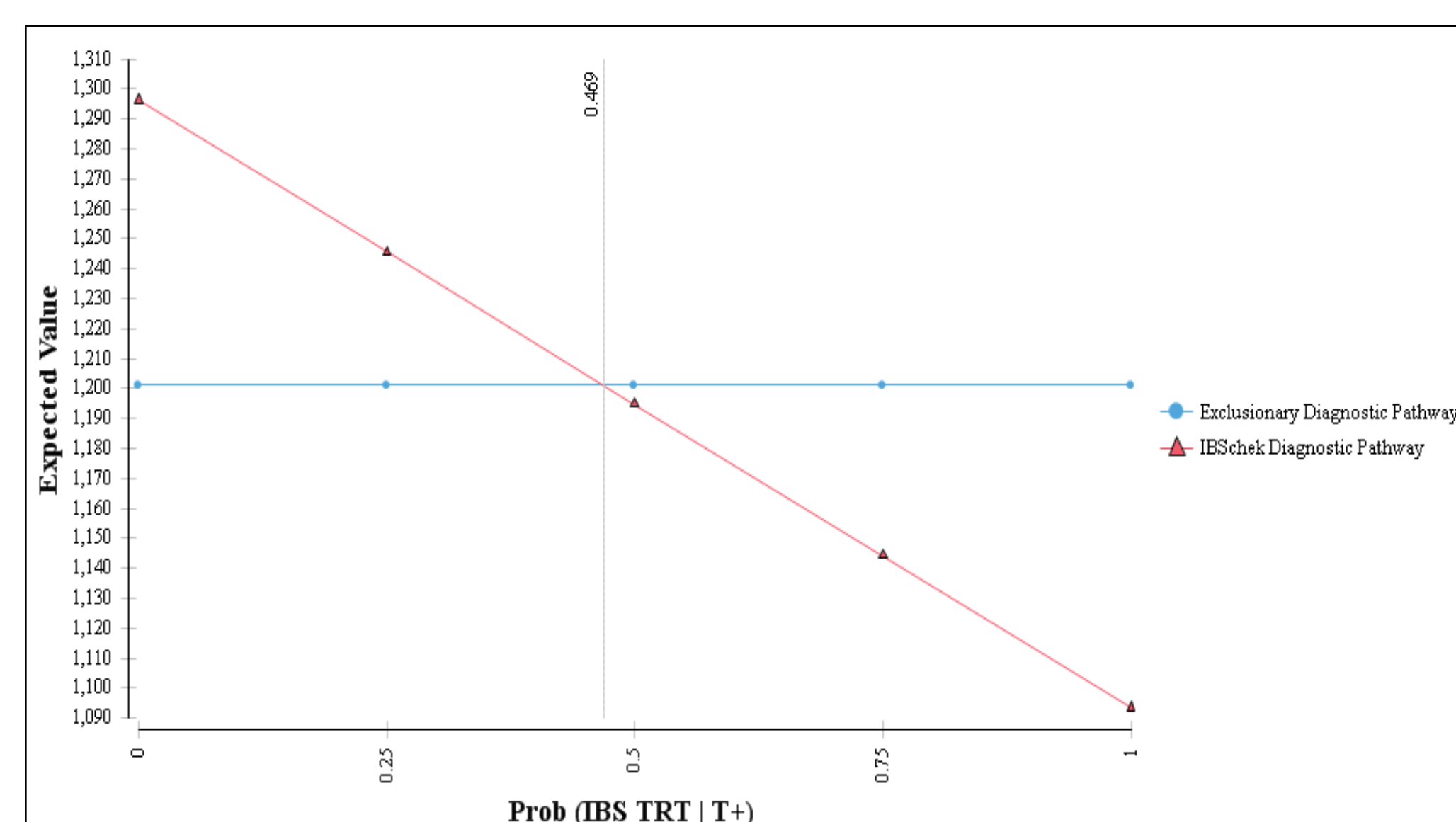
Prob (IBS TRT |T+): Probability that a patient will receive treatment conditional on a positive test result.

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)
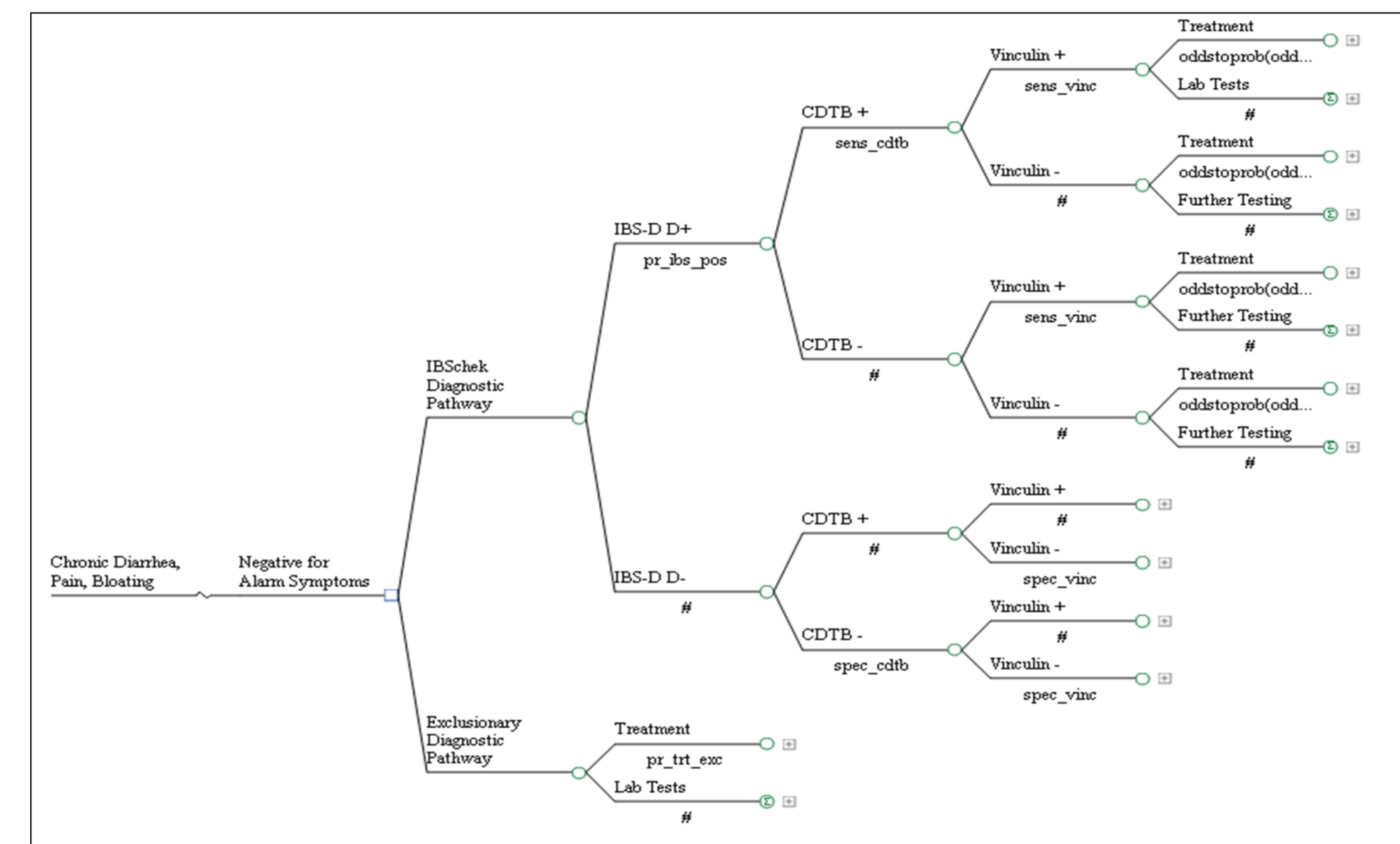
Figure 3: Decision Tree Model (Model 2)

Table 2: CM Results (Model 2)

Diagnostic Pathway	Setting	Pre-test Prob Dis +	Prob (IBS TRT) Exclusionary	Expected Cost (Pounds)	Cost (Savings) Pounds
W/ IBSchek™	GI	0.25	NA	1094	(53)
Exclusionary	GI	NA	0.350	1147	
W/ IBSchek™	GI	0.35	NA	1070	(77)
Exclusionary	GI	NA	0.350	1147	
W/ IBSchek™	GI	0.45	NA	1045	(102) [1]
Exclusionary	GI	NA	0.350	1147	
W/ IBSchek™	GI	0.55	NA	1020	(127)
Exclusionary	GI	NA	0.350	1147	
W/ IBSchek™	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 IBSchek) Probability for the patient to be IBS-D positive. n: negative. p: positive

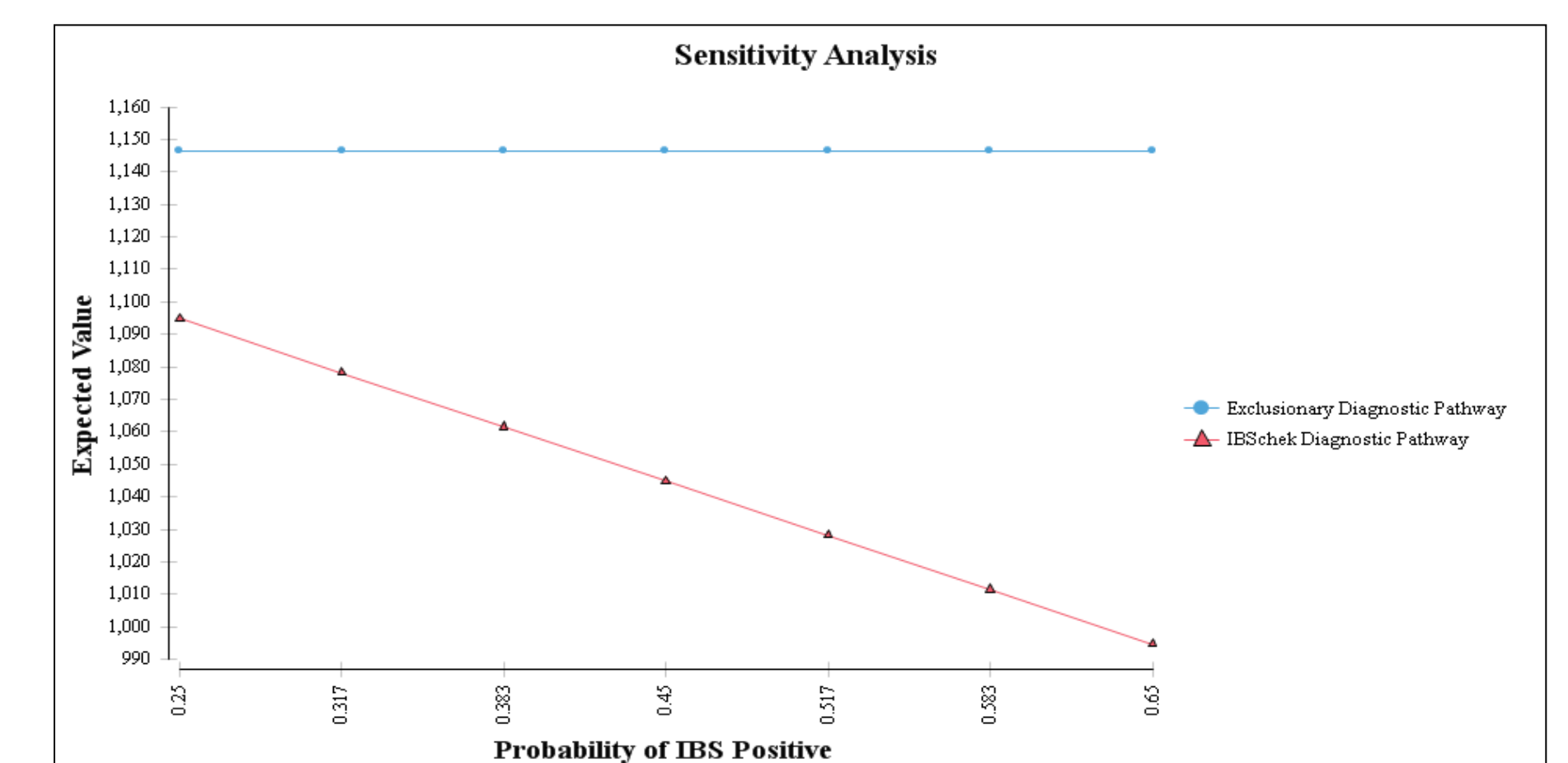## Figure 4: Sensitivity for Pre-test Pr(D+) (Model 2)

Table 4: Budget Impact Analysis (Model 2)

Covered Lives [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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DISCLOSURES