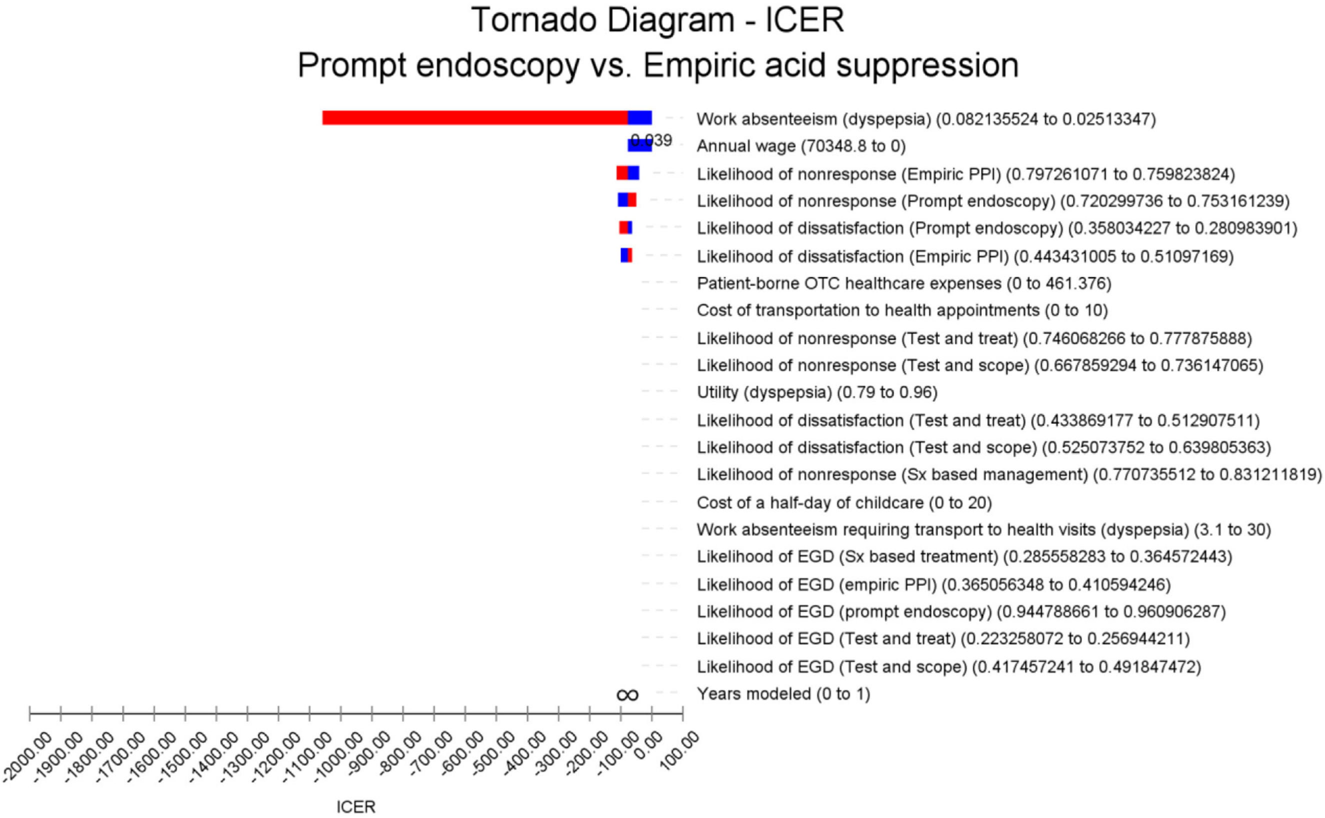
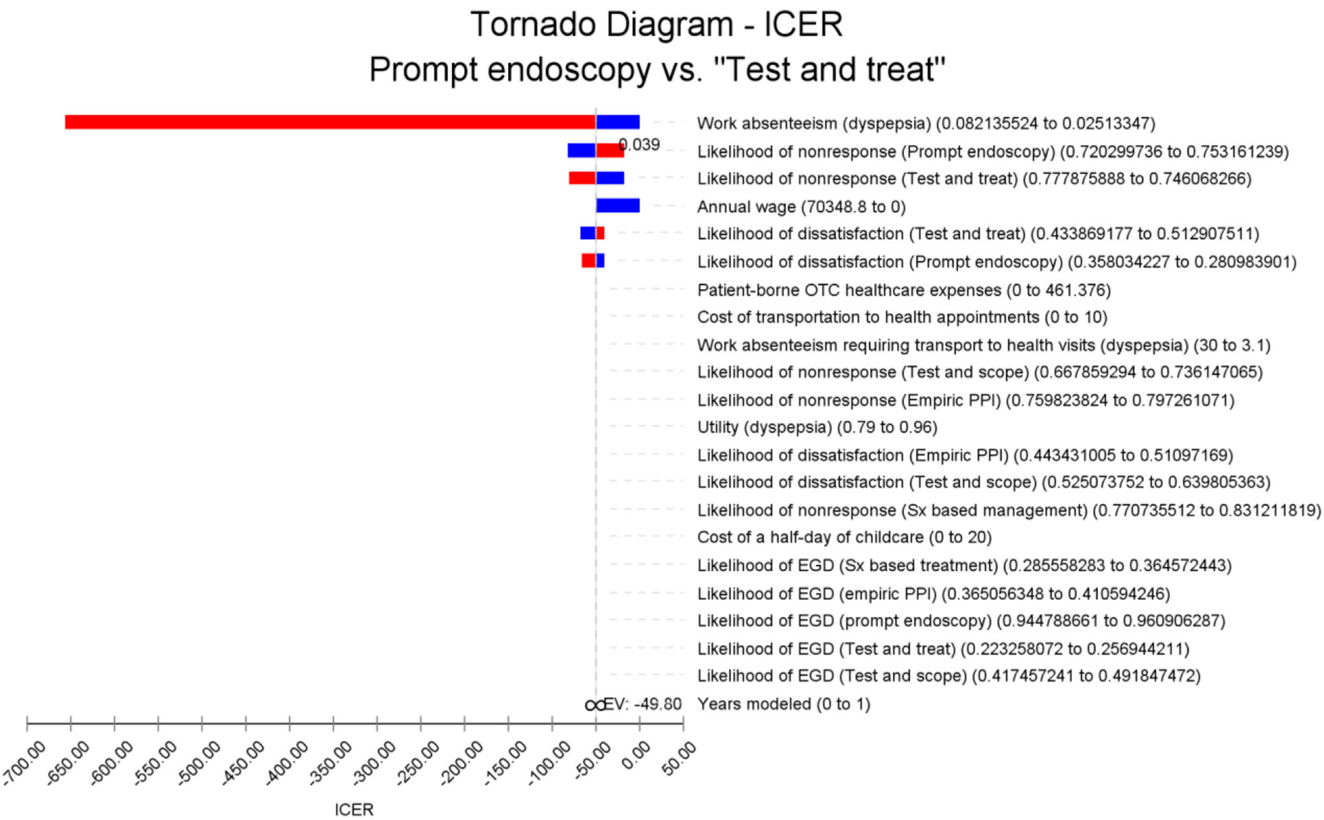
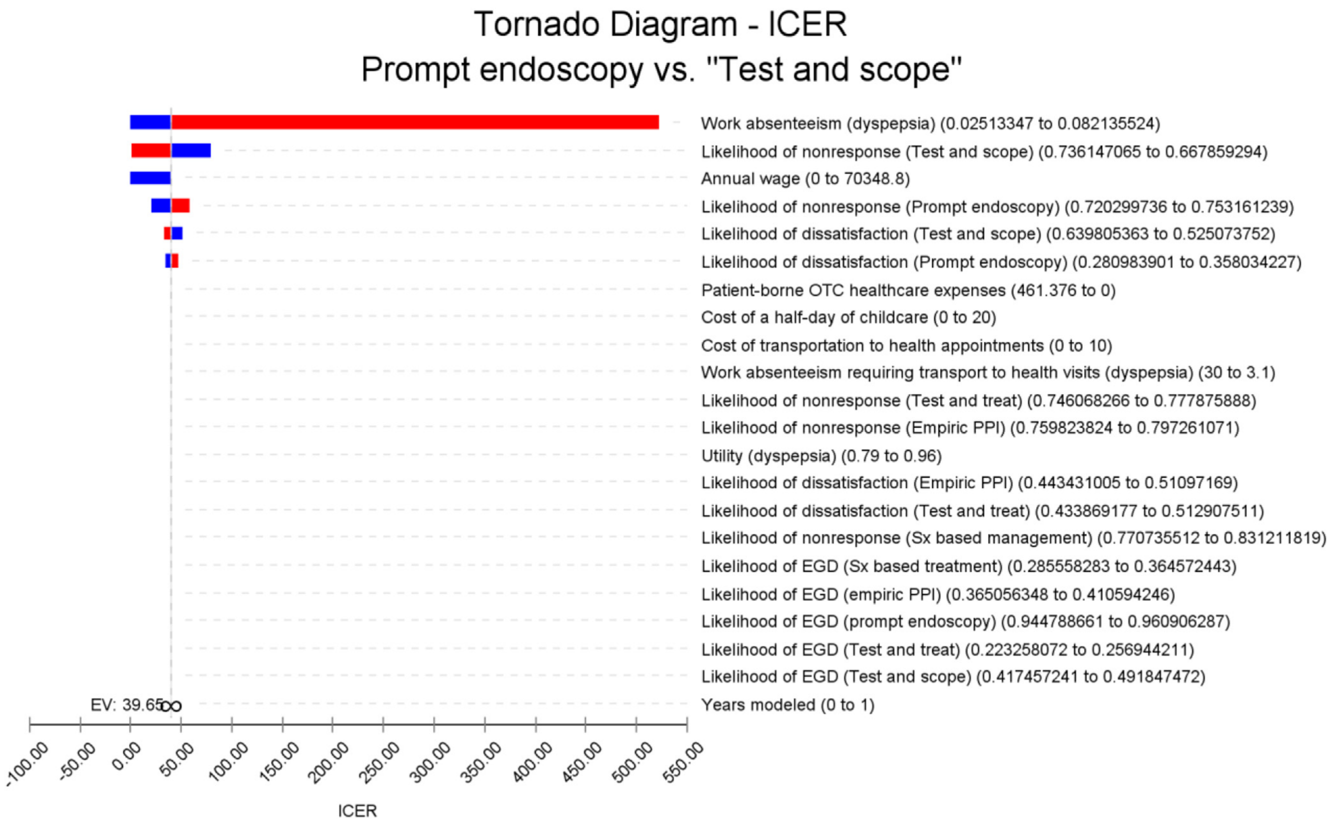


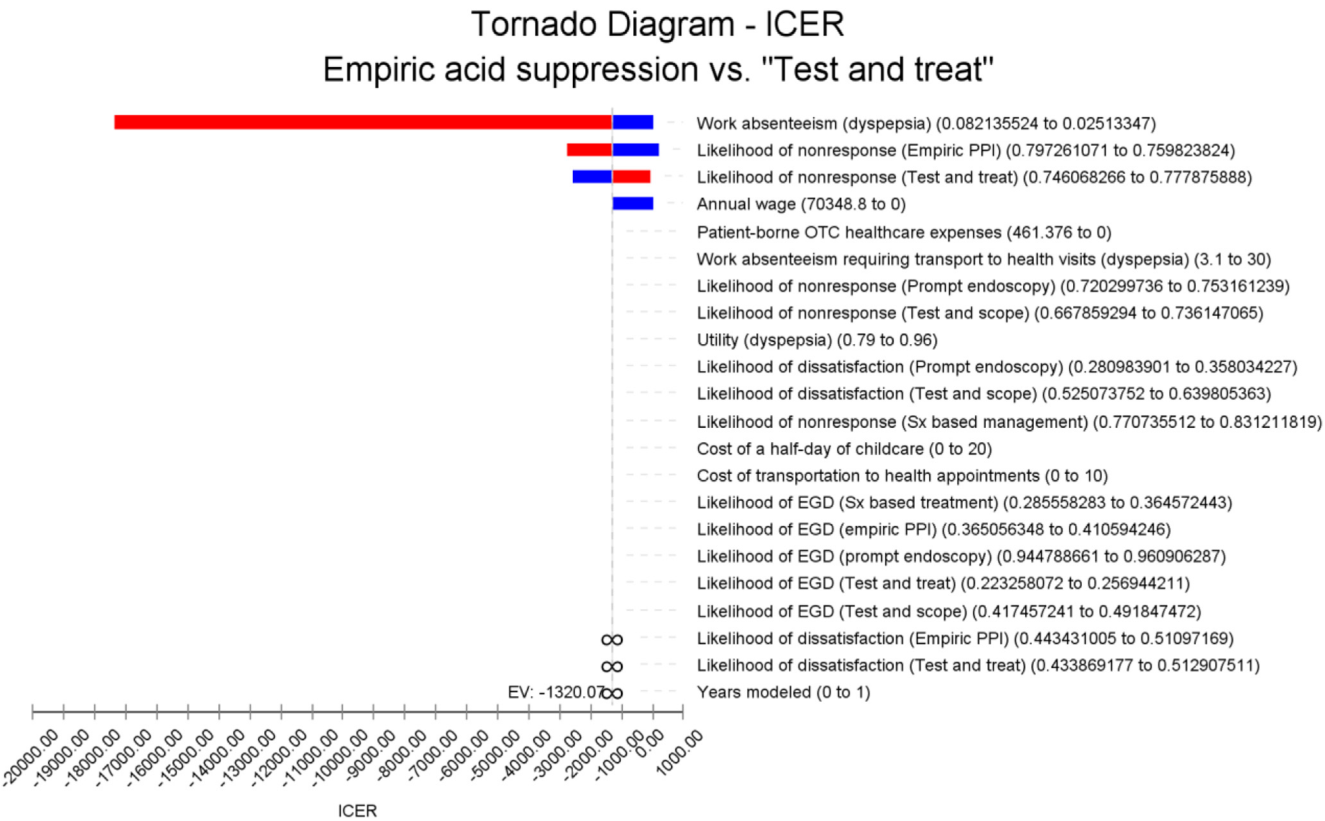
Supplementary Figure 1. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of prompt endoscopy compared with empiric acid suppression from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against empiric acid suppression, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Prompt endoscopy was preferred across almost all ranges for all variables. However, both strategies would be equally preferred among patients with no workdays missed because of dyspepsia. EGD, esophagogastroduodenoscopy; ICER, incremental cost-effectiveness ratio; OTC, over-the-counter; PPI, proton pump inhibitor; Sx, symptoms.



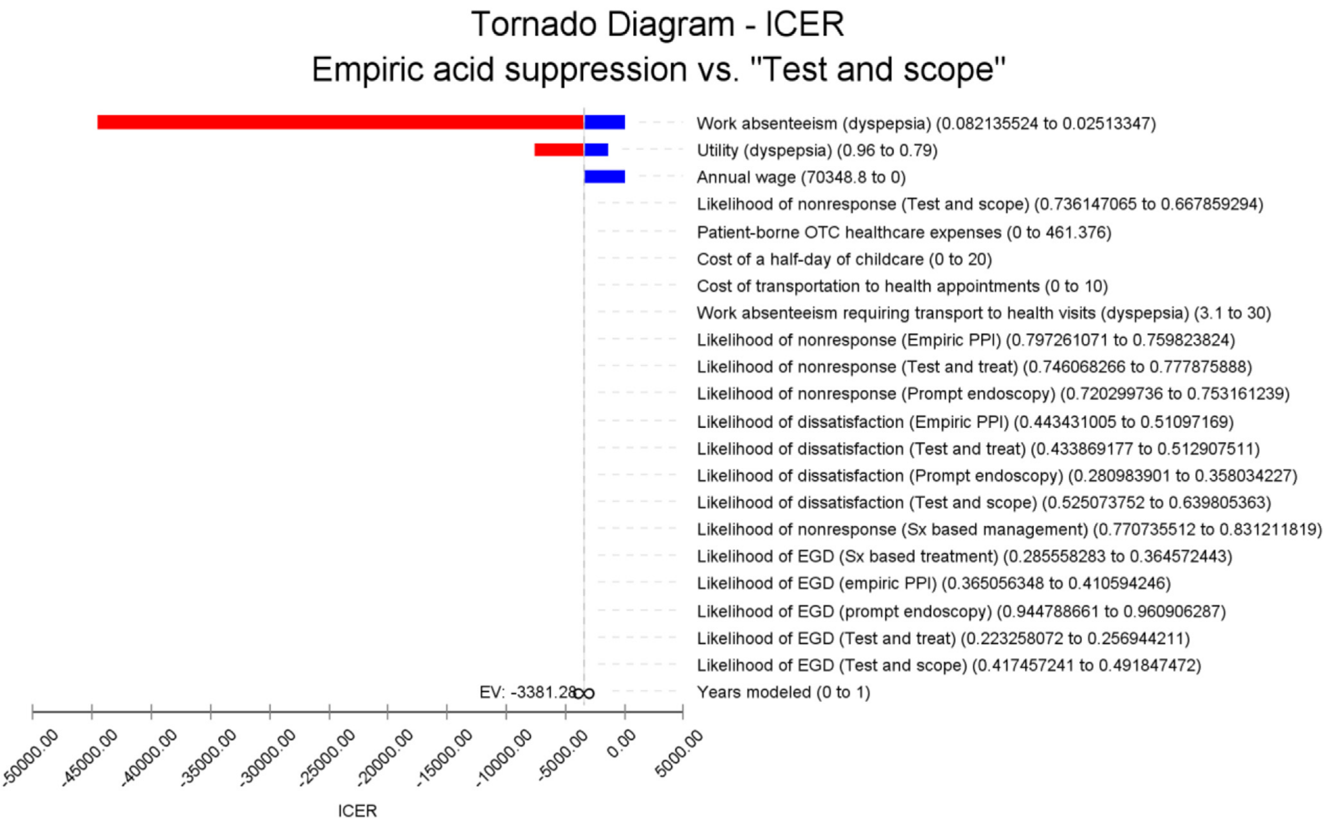
Supplementary Figure 2. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of prompt endoscopy compared with test-and-treat from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against test-and-treat, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Prompt endoscopy was preferred across almost all ranges for all variables. However, both strategies would be equally preferred among patients with no workdays missed because of dyspepsia. EV, expected value.



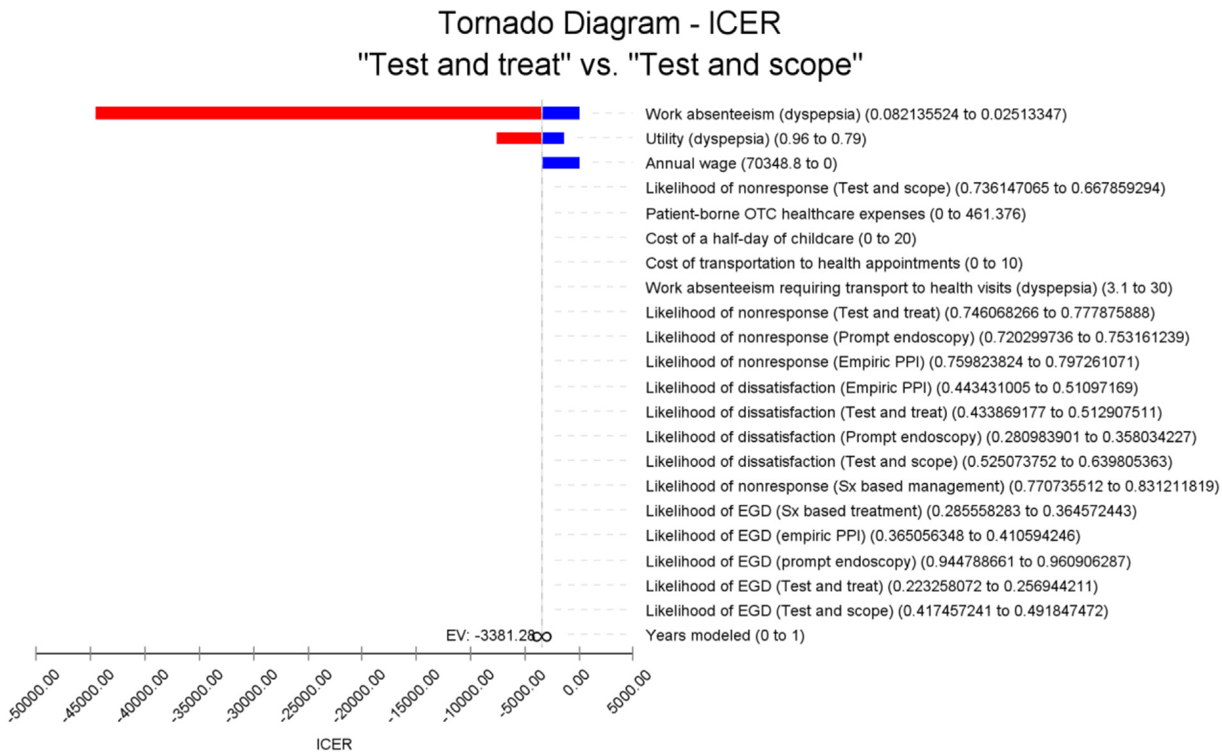
Supplementary Figure 3. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of prompt endoscopy compared with test-and-scope from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, expected value.



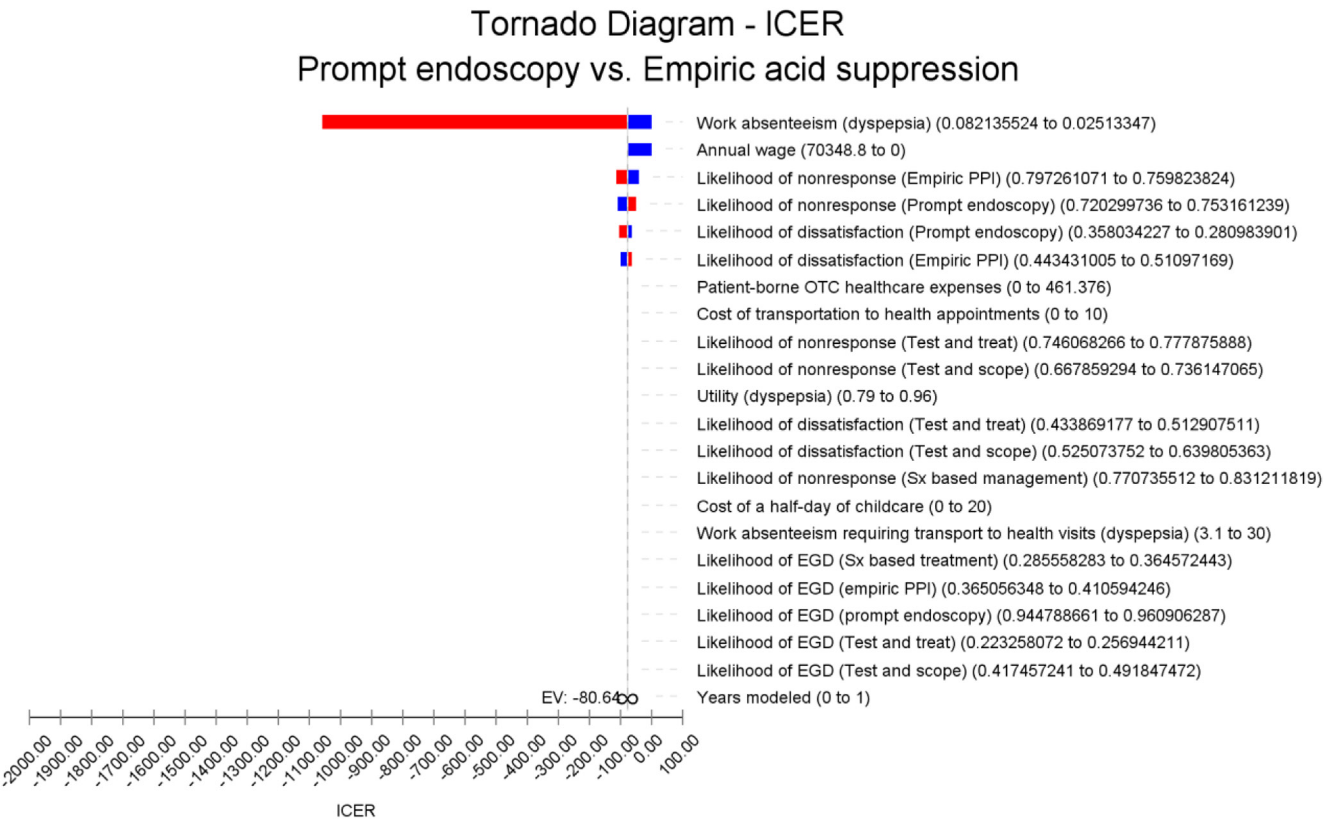
Supplementary Figure 4. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of empiric acid suppression compared with test-and-treat from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for empiric acid suppression referenced against test-and-treat, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-treat was preferred across all ranges for all variables. EV, expected value.



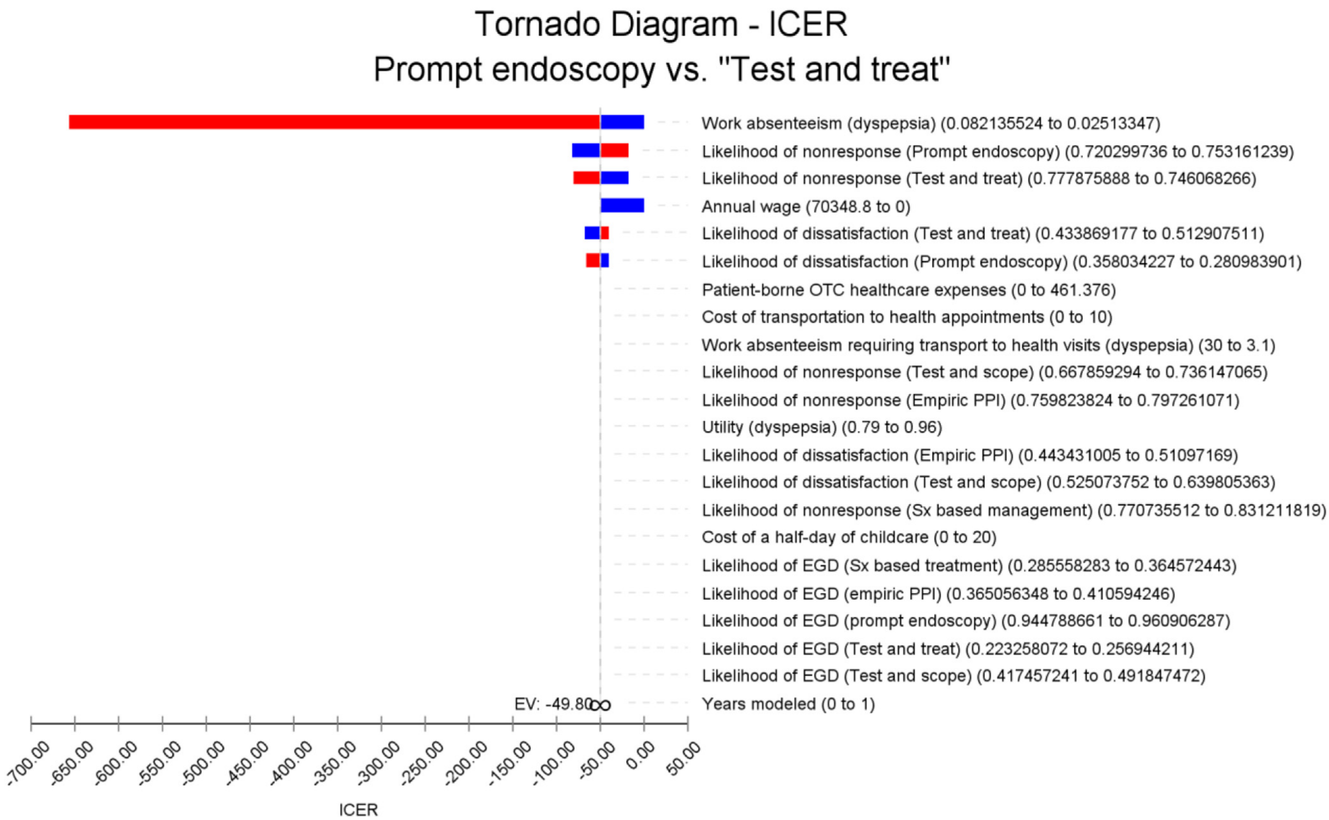
Supplementary Figure 5. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of empiric acid suppression compared with test-and-scope from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for empiric acid suppression referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, expected value.



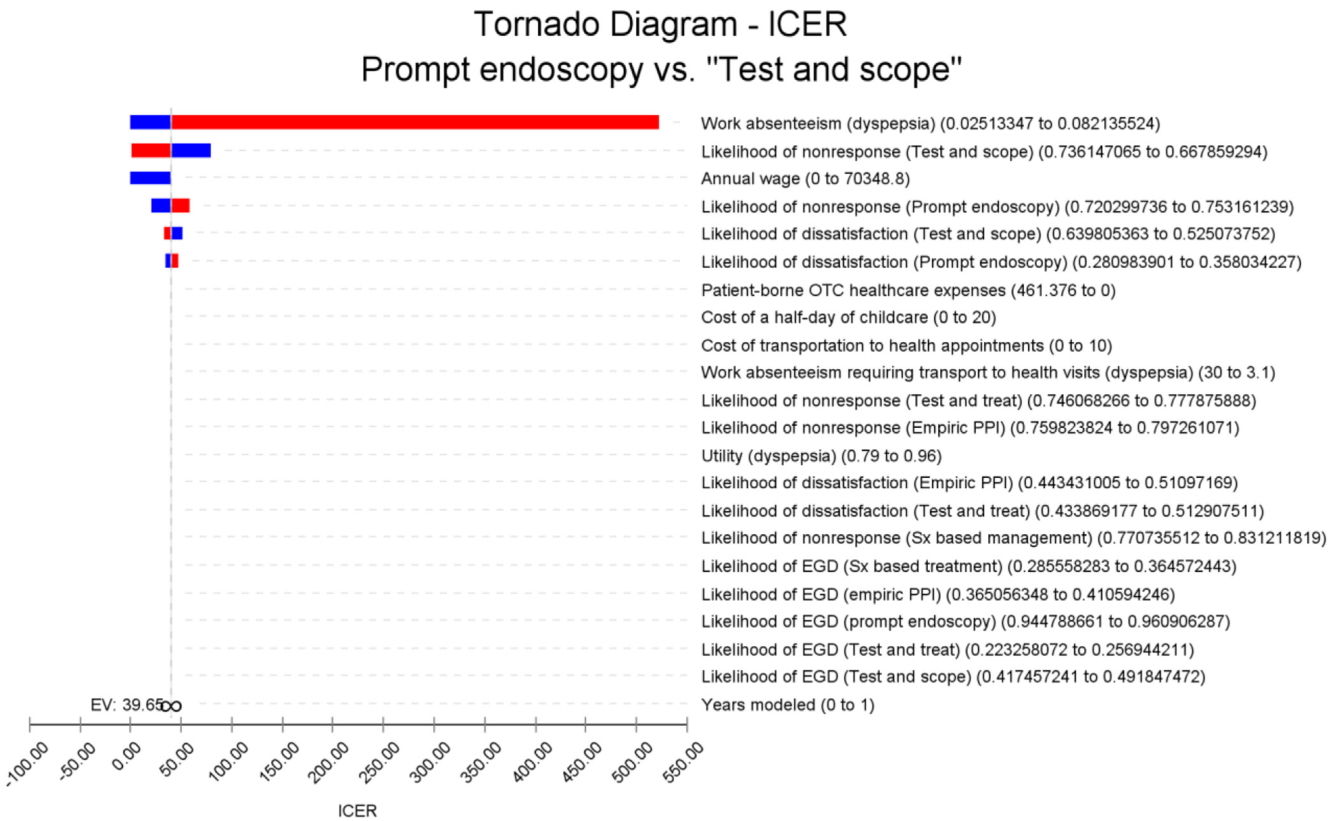
Supplementary Figure 6. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of test-and-treat compared with test-and-scope from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for test-and-treat referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, expected value.



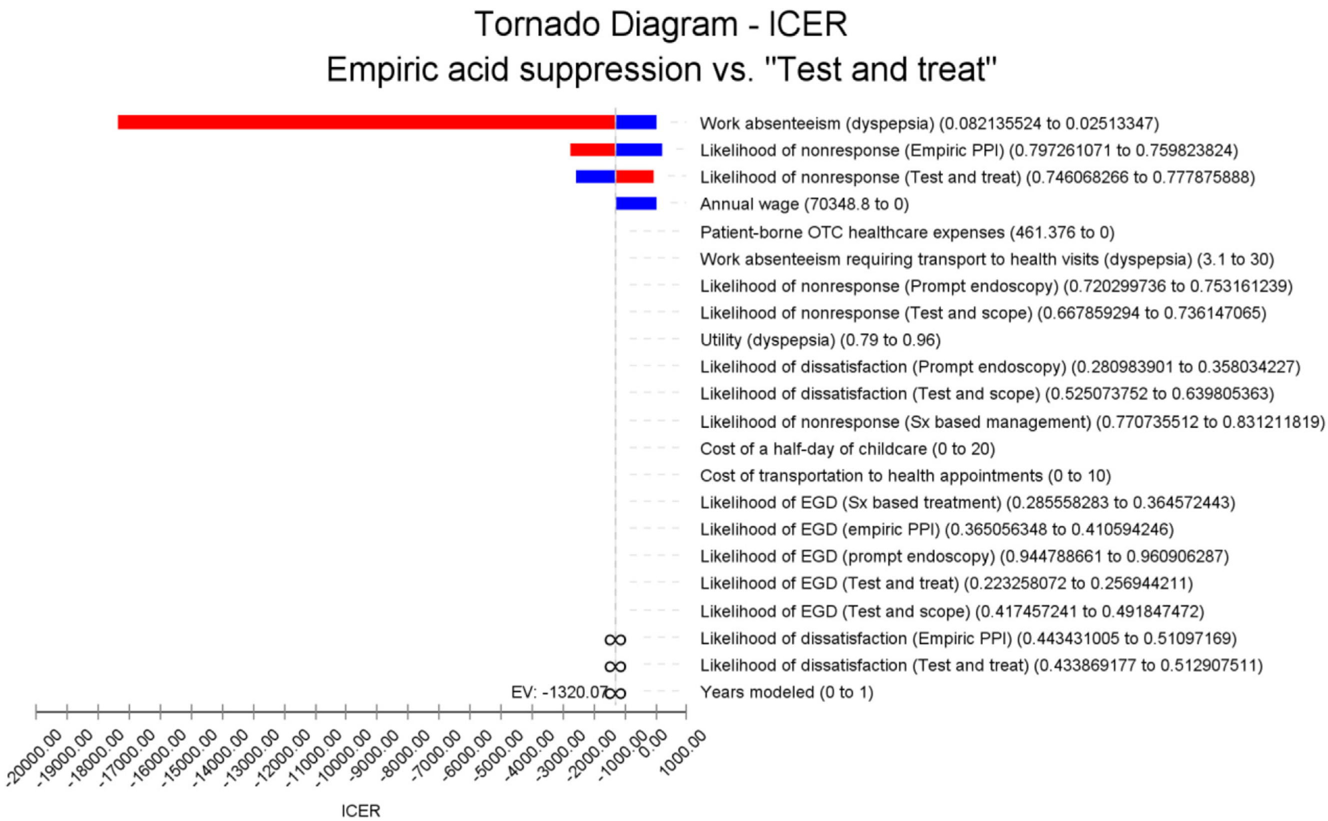
Supplementary Figure 7. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of prompt endoscopy compared with empiric acid suppression from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against empiric acid suppression, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Prompt endoscopy was preferred across all ranges for all variables. EV, expected value.



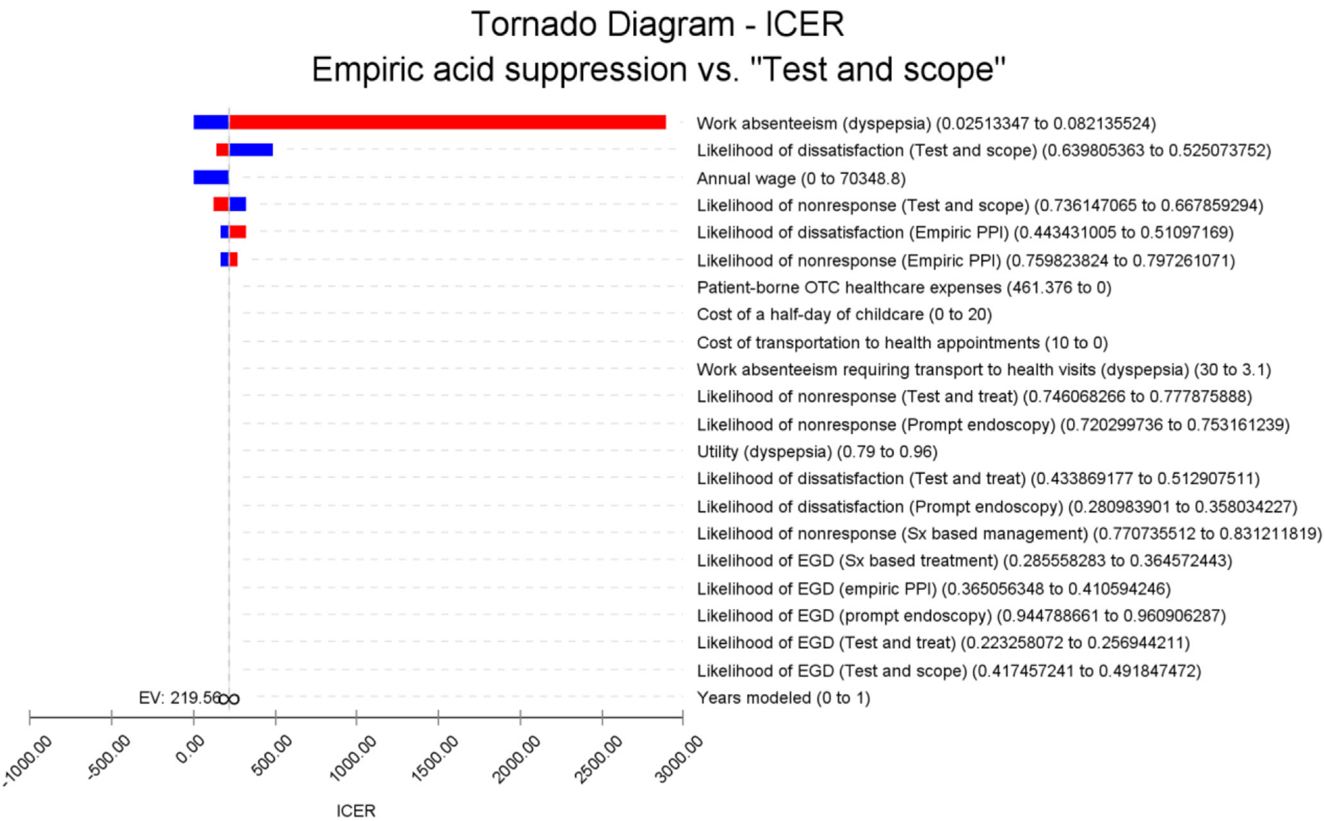
Supplementary Figure 8. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of prompt endoscopy compared with test-and-treat from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against test-and-treat, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Prompt endoscopy was preferred across all ranges for all variables. EV, Expected Value.



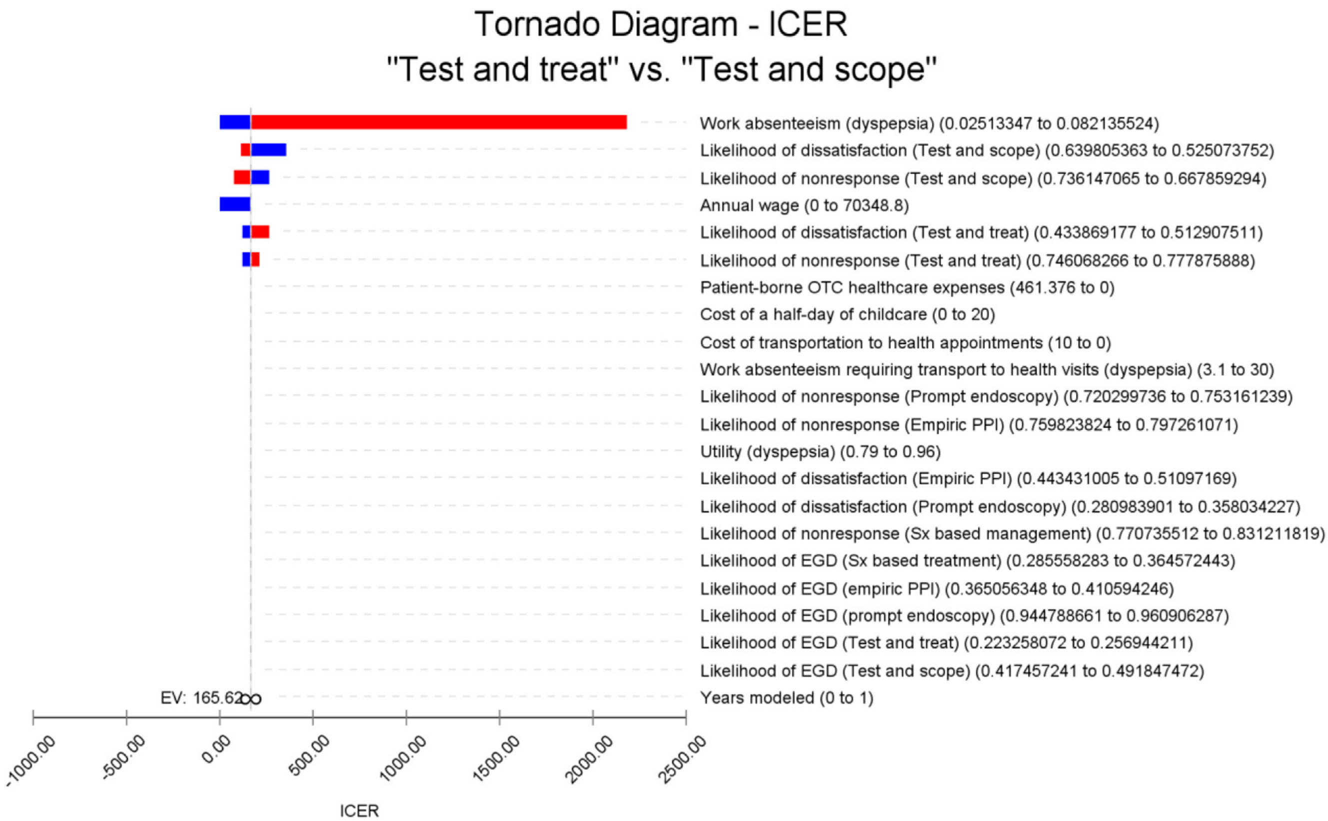
Supplementary Figure 9. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of prompt endoscopy compared with test-and-scope from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Prompt endoscopy was preferred across all ranges for all variables. EV, Expected Value.



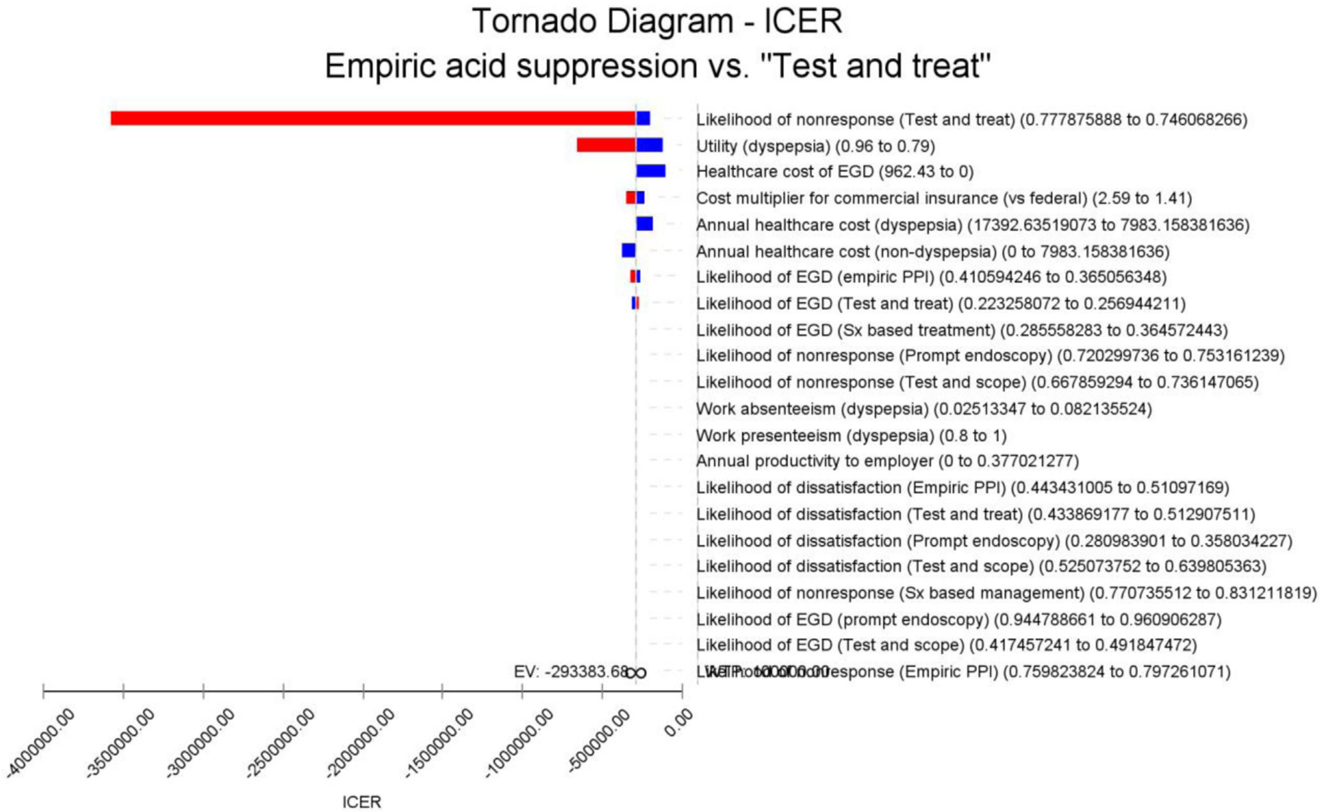
Supplementary Figure 10. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of empiric acid suppression compared with test-and-treat from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for empiric acid suppression referenced against test-and-treat, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-treat was preferred across all ranges for all variables. EV, Expected Value.



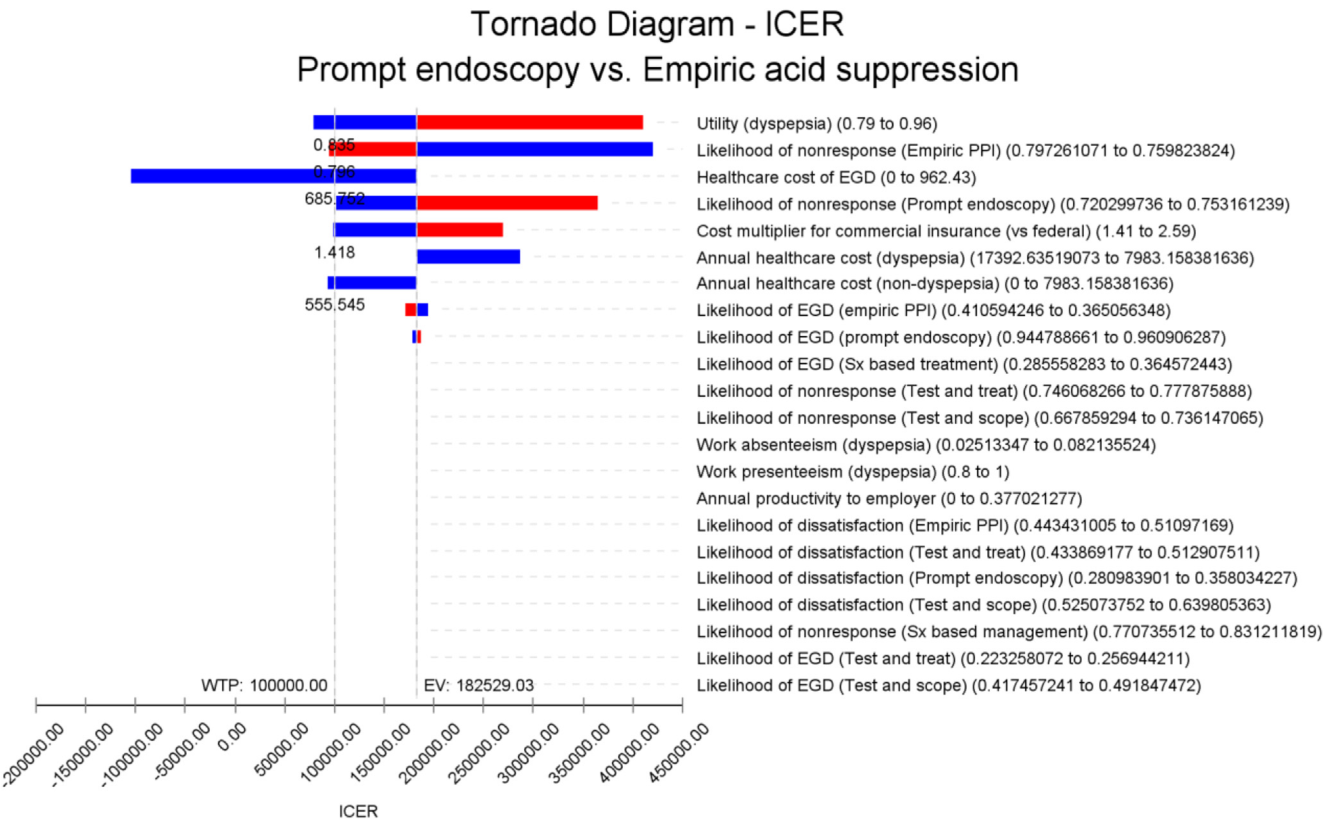
Supplementary Figure 11. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of empiric acid suppression compared with test-and-scope from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for empiric acid suppression referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, Expected Value.



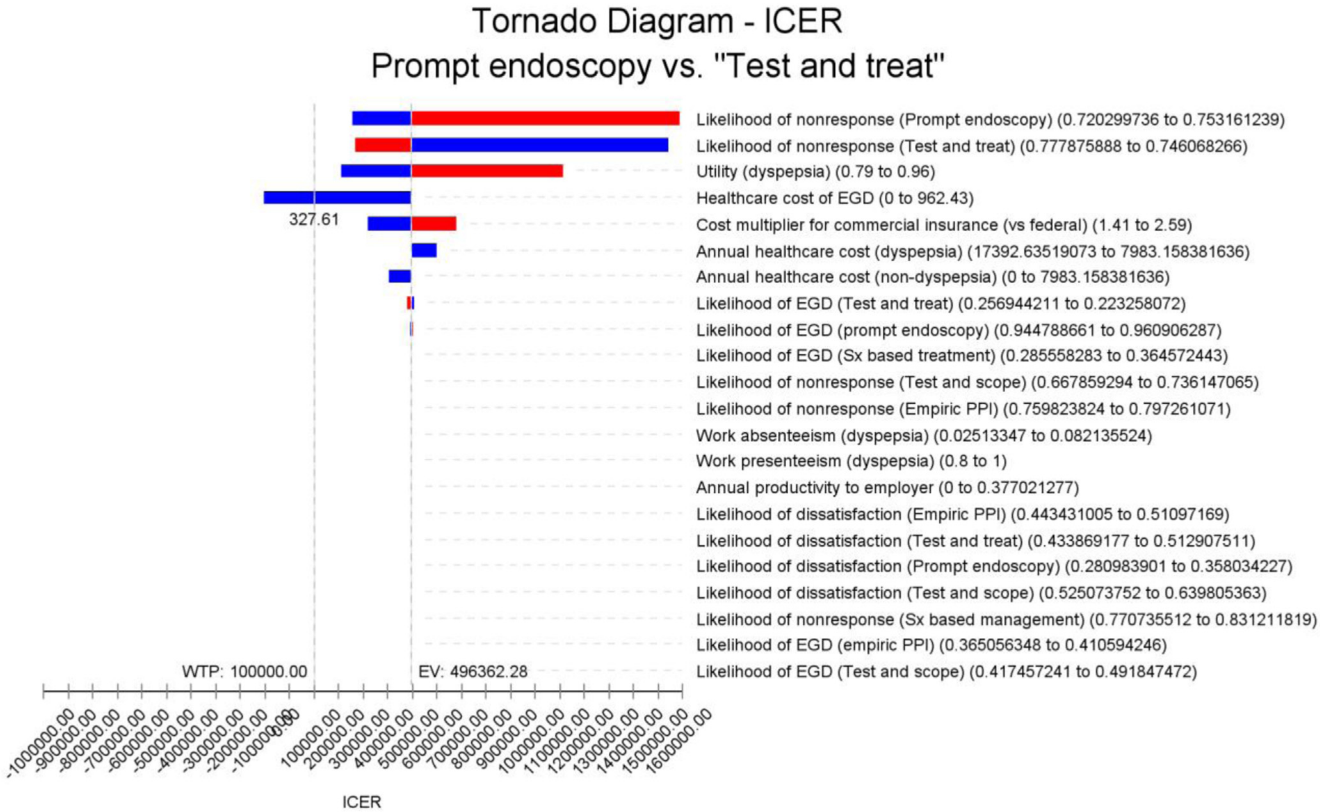
Supplementary Figure 12. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of test-and-treat compared with test-and-scope from a patient perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for test-and-treat referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, Expected Value.



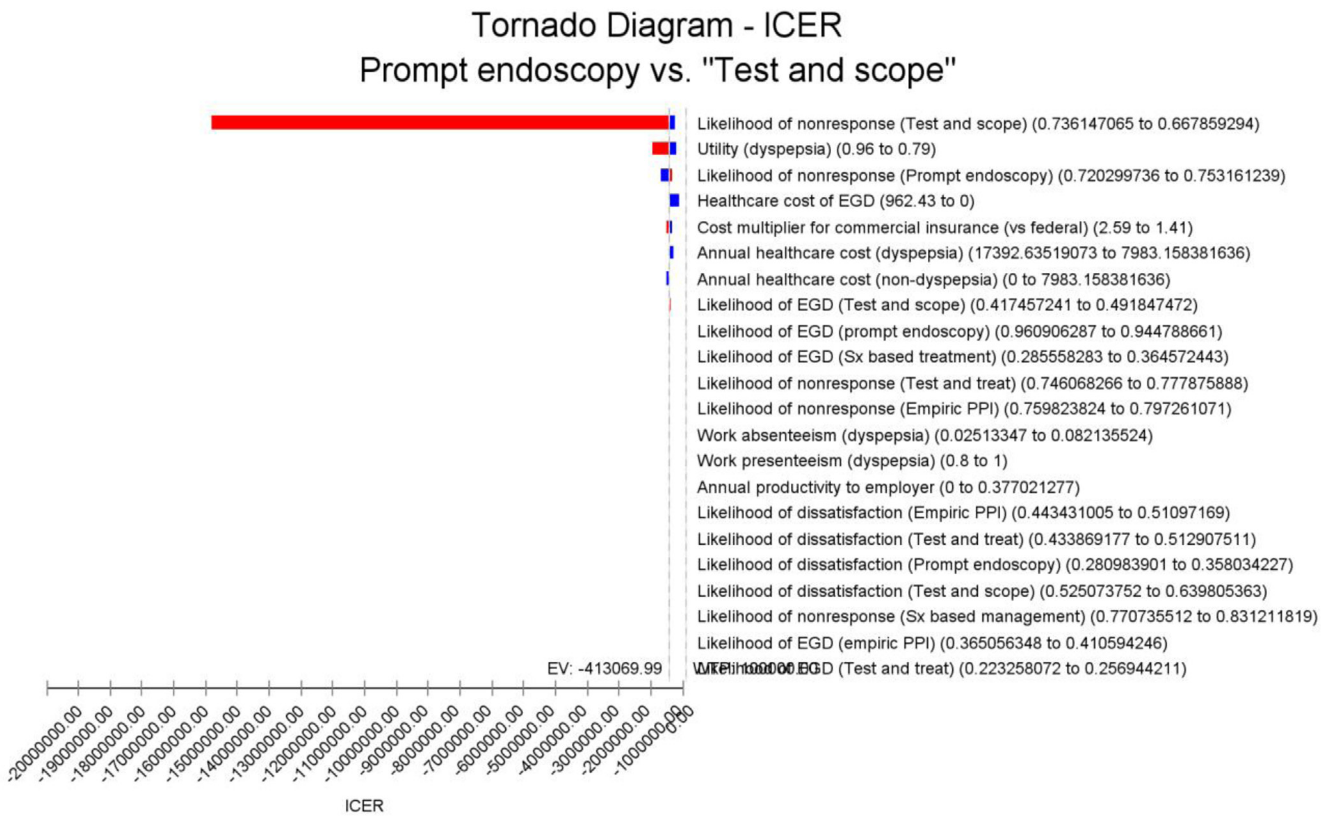
Supplementary Figure 13. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of empiric acid suppression compared with test-and-treat from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for empiric acid suppression referenced against test-and-treat, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-treat was preferred across all ranges for all variables. EV, expected value.



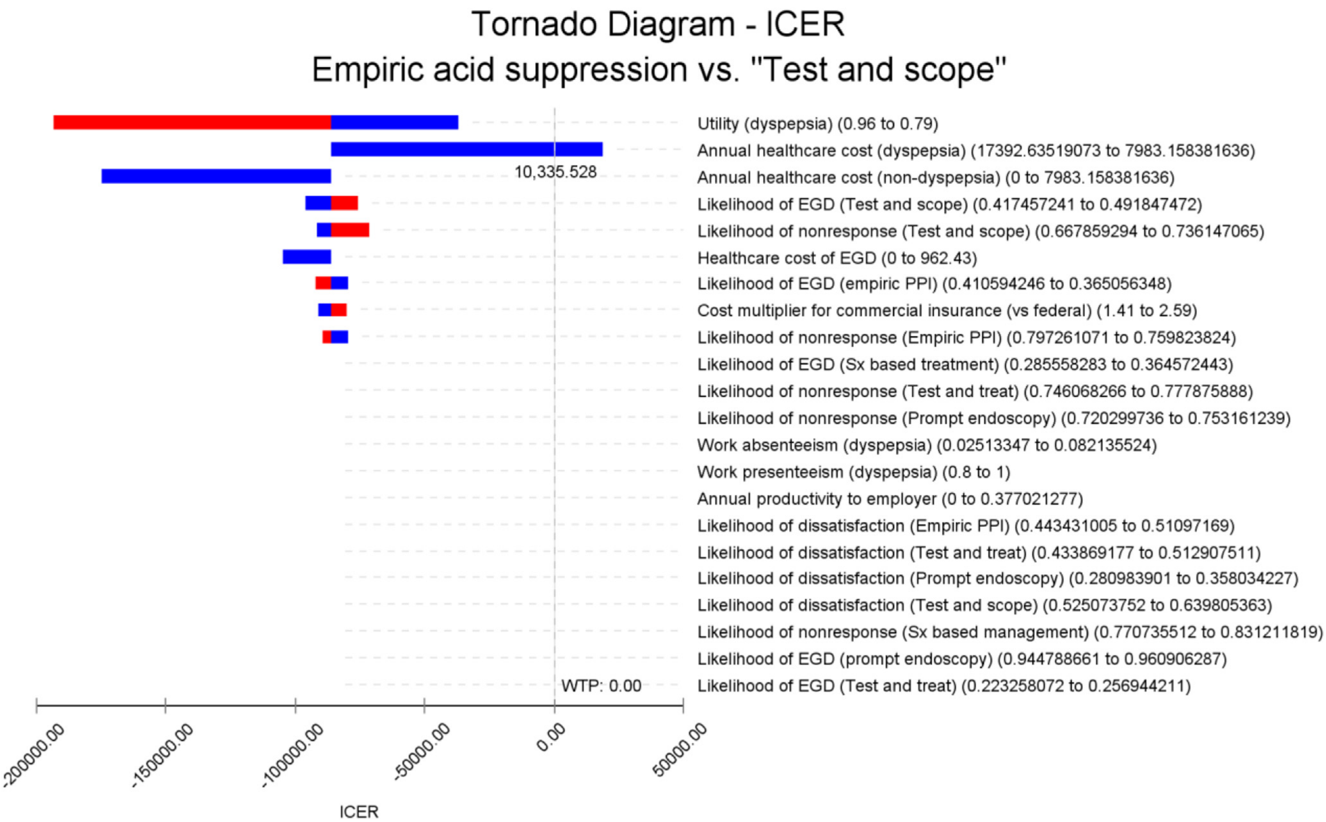
Supplementary Figure 14. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of prompt endoscopy compared with empiric acid suppression from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against empiric acid suppression, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. WTP, willingness to pay. EV, expected value.



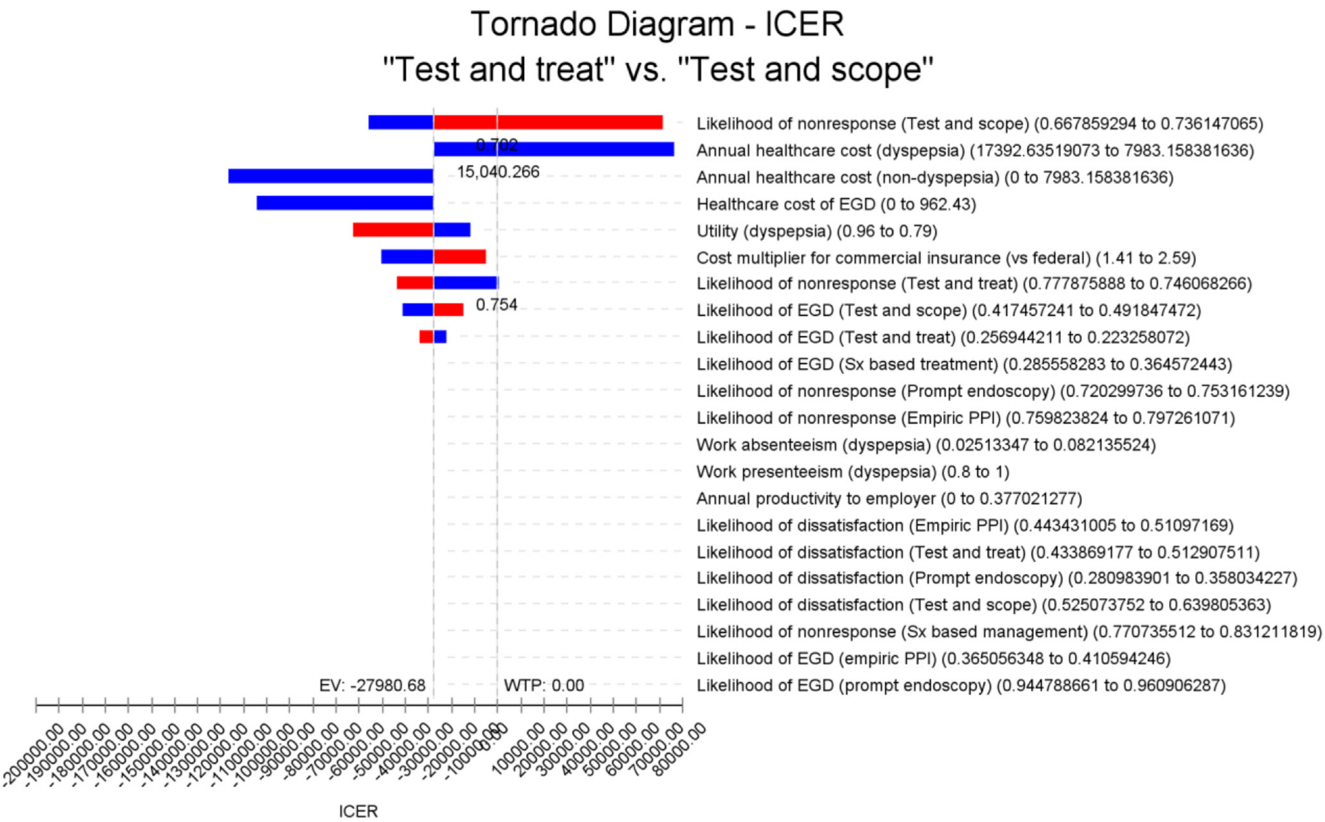
Supplementary Figure 15. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of prompt endoscopy compared with test-and-treat from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against test-and-treat, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, expected value.



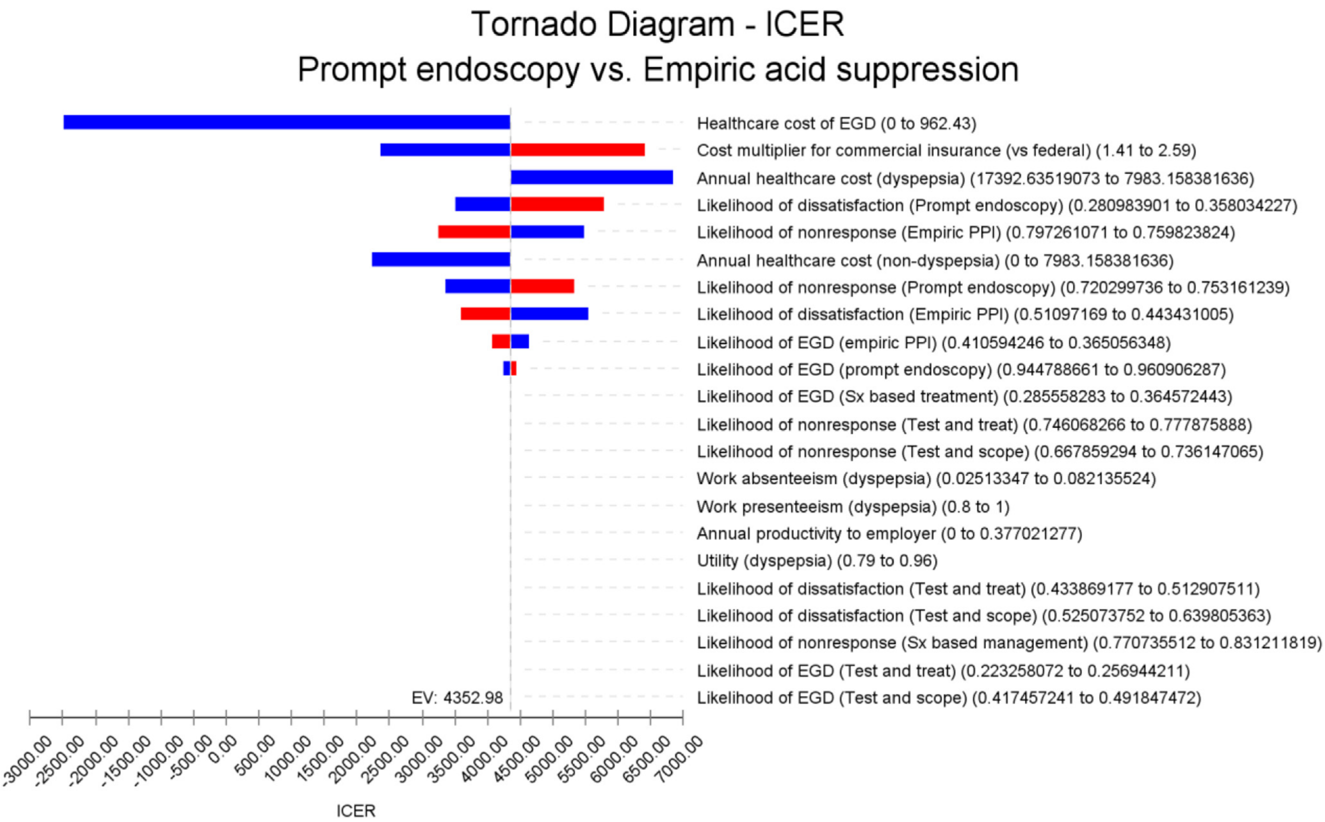
Supplementary Figure 16. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of prompt endoscopy compared with test-and-scope from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, expected value.



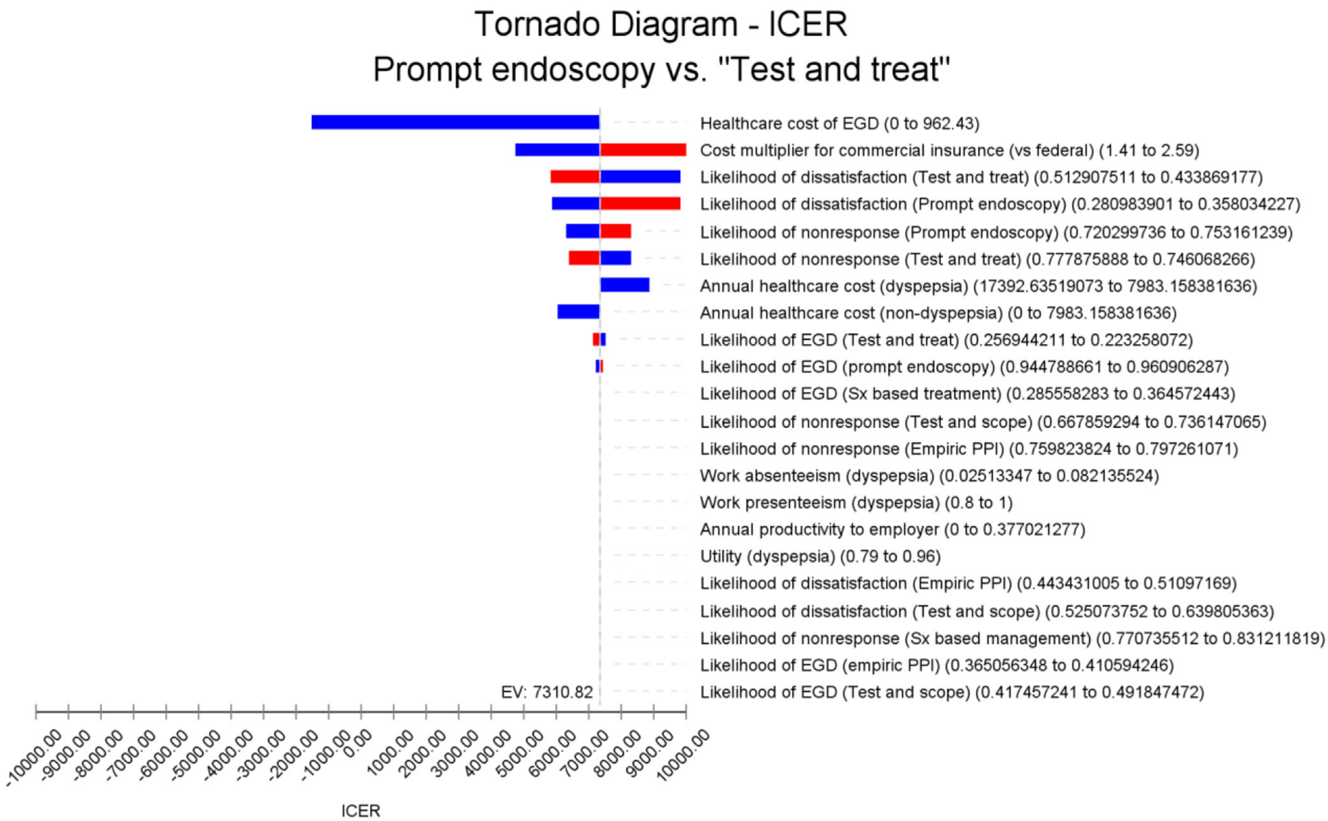
Supplementary Figure 17. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of empiric acid suppression compared with test-and-scope from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for empiric acid suppression referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, expected value.



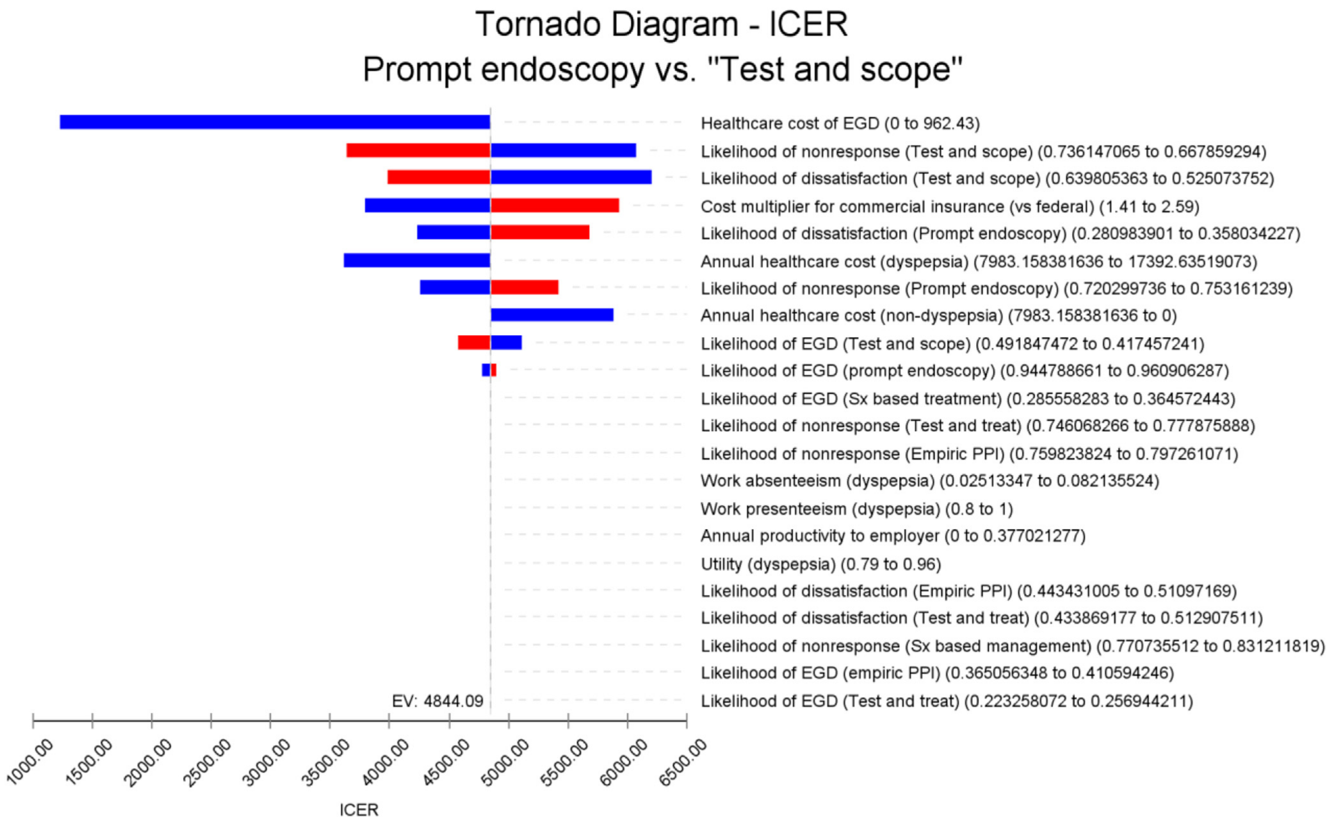
Supplementary Figure 18. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-effectiveness of test-and-treat compared with test-and-scope from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for test-and-treat referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, expected value.



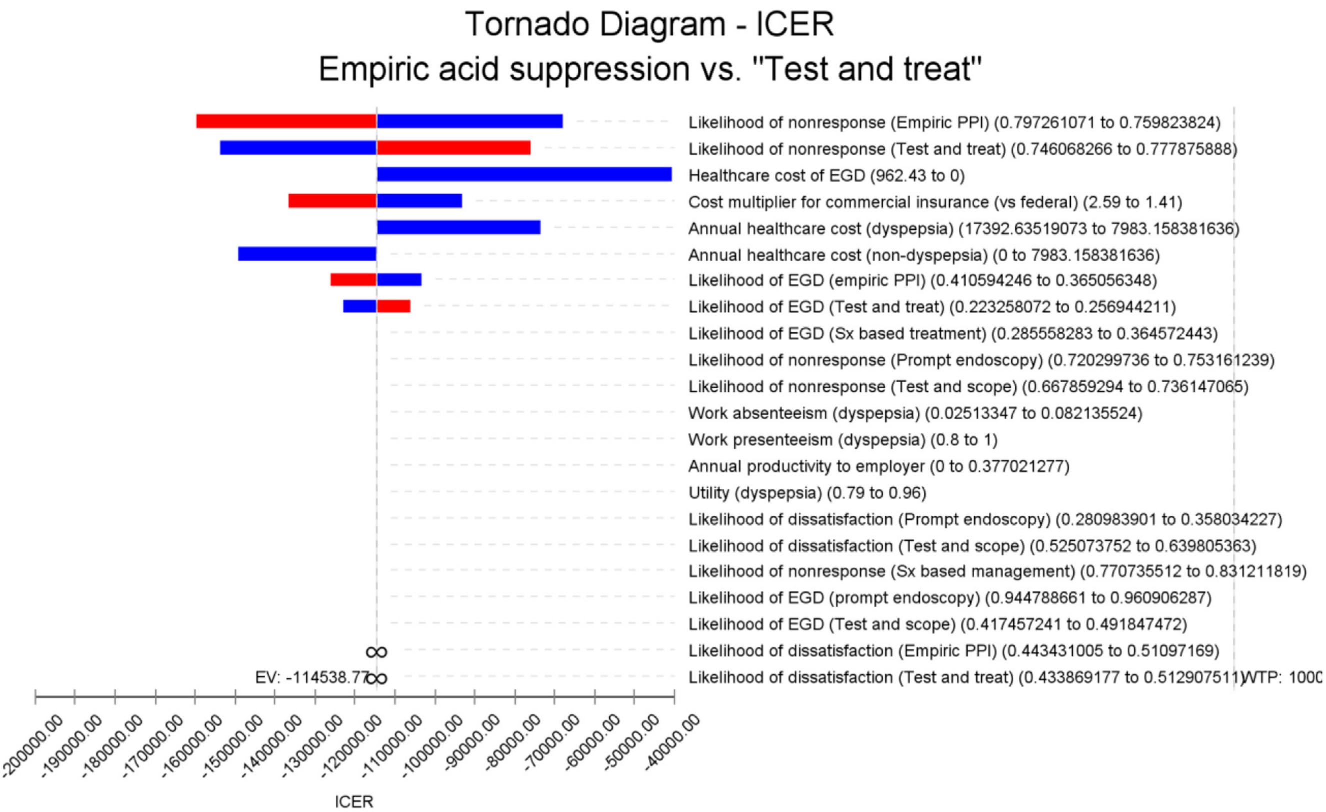
Supplementary Figure 19. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of prompt endoscopy compared with empiric acid suppression from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against empiric acid suppression, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Prompt endoscopy was preferred across all ranges for all variables. EV, expected value.



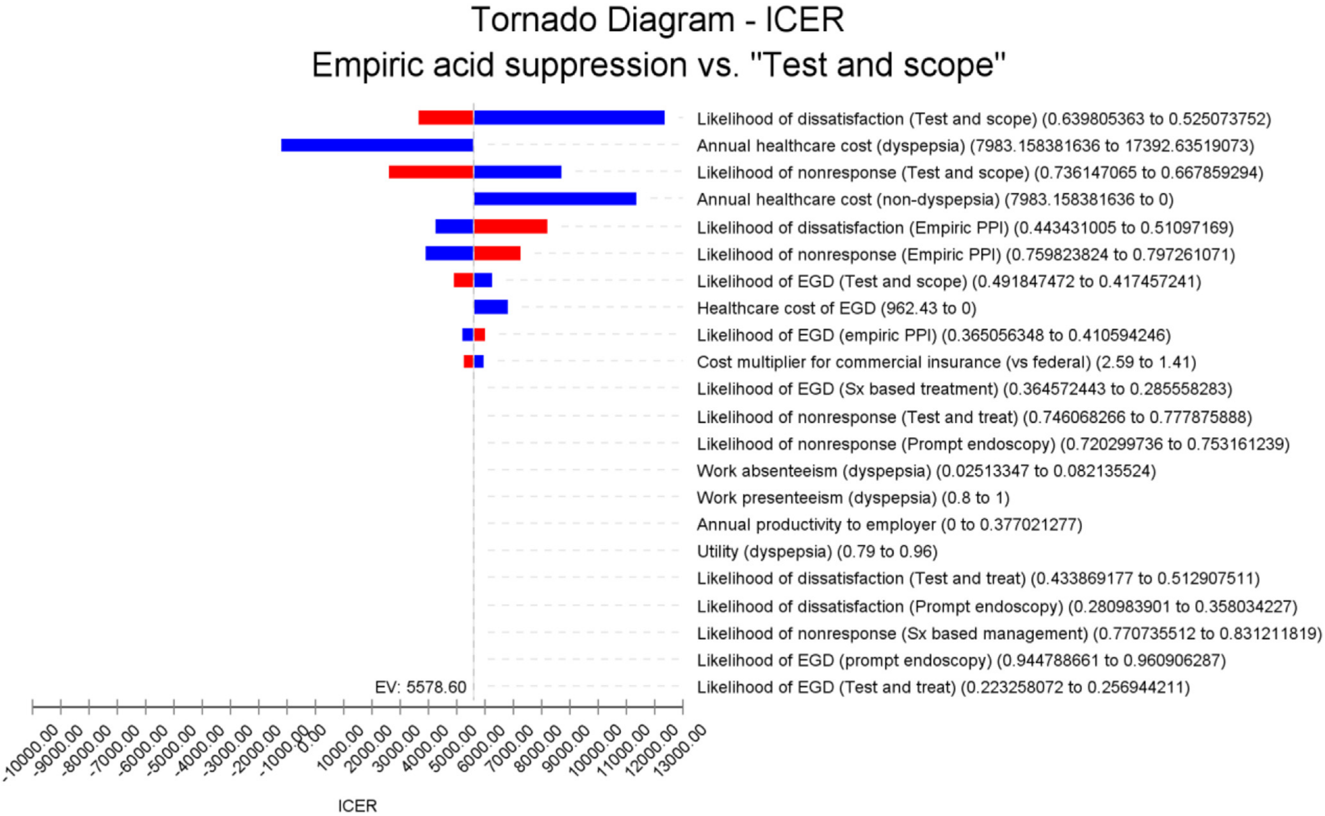
Supplementary Figure 20. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of prompt endoscopy compared with test-and-treat from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against test-and-treat, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Prompt endoscopy was preferred across all ranges for all variables. EV, expected value.



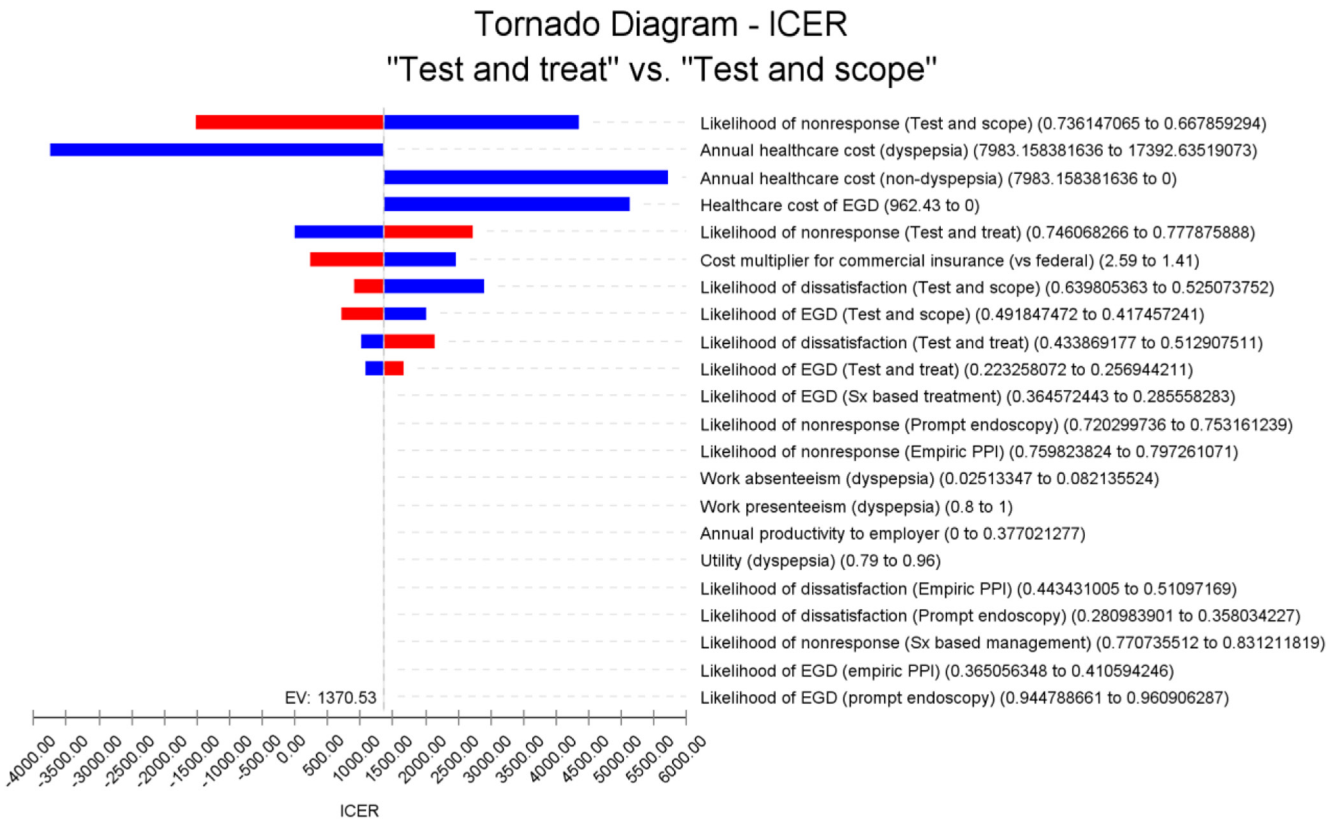
Supplementary Figure 21. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of prompt endoscopy compared with test-and-scope from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for prompt endoscopy referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Prompt endoscopy was preferred across all ranges for all variables. EV, expected value.



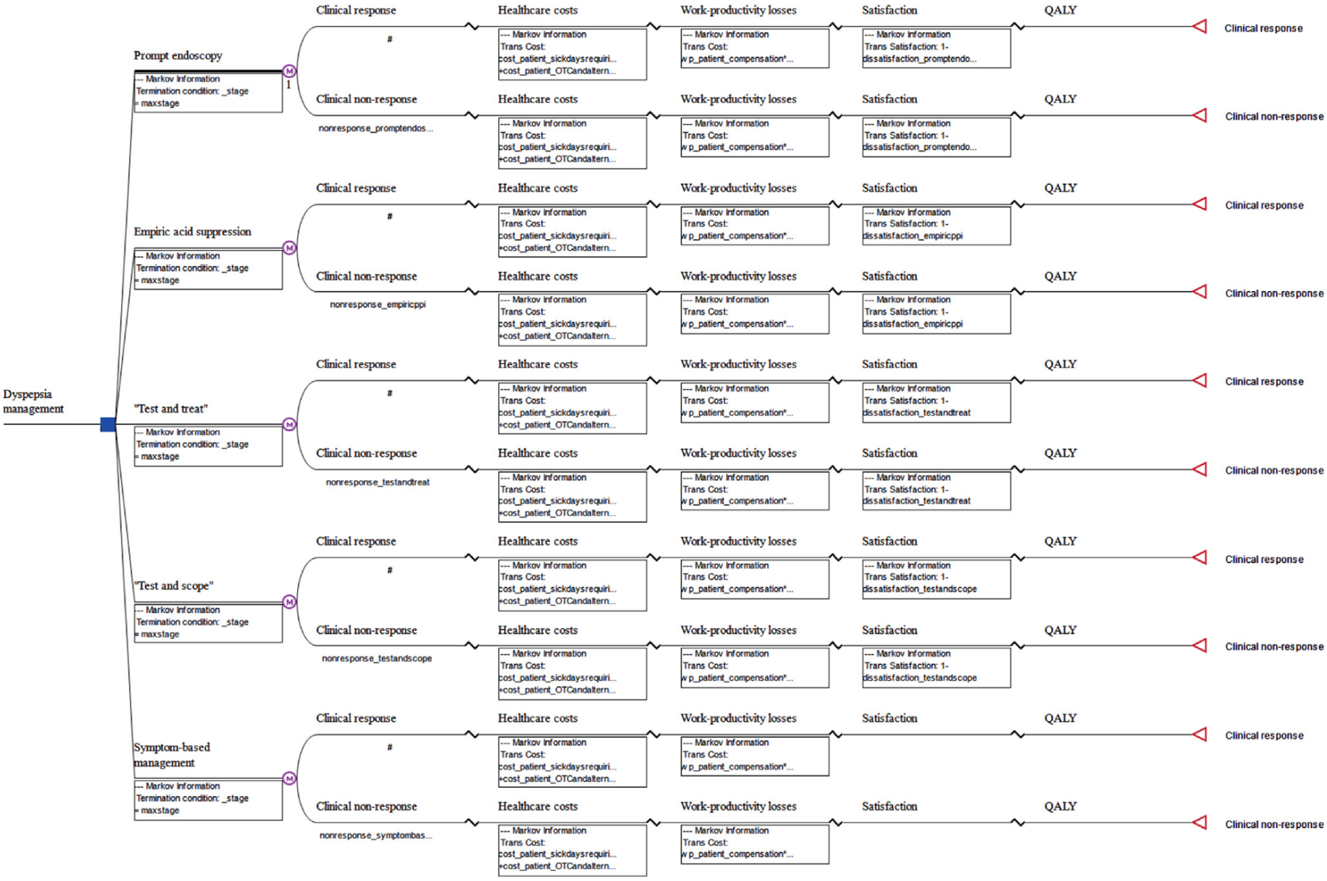
Supplementary Figure 22. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of empiric acid suppression compared with test-and-treat from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for empiric acid suppression referenced against test-and-treat, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-treat was preferred across all ranges for all variables. EV, expected value.



Supplementary Figure 23. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of empiric acid suppression compared with test-and-scope from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for empiric acid suppression referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, expected value.



Supplementary Figure 24. Multiple one-way sensitivity analyses to assess the influence of the range of model inputs on cost-satisfaction of test-and-treat compared with test-and-scope from an insurer perspective. Results are presented as a tornado diagram. ICER is presented on the x-axis for test-and-treat referenced against test-and-scope, with each *horizontal bar* representing how ICER changes throughout the expected range for each model input. Test-and-scope was preferred across all ranges for all variables. EV, expected value.



Supplementary Figure 25. Model diagram. Ranges for model input estimates were derived from the 5th and 95th percentile beta distributions for binomial data. Ranges for health utility estimates were modeled on the basis of established differences between mild and severe dyspepsia in the literature. Ranges for costs were more extensively modeled across the full range from $0 to largest estimate in the literature. We did not model greater costs, because these patients would more likely reflect quaternary referral settings rather than general gastroenterology and therefore outside the scope of our study. Ranges for work absenteeism were modeled from 0 days to 30 full sick-days taken per year, which exceeds the median estimate in the literature of 3.93 days missed annually because of dyspepsia. EV, expected value.

Supplementary Table 1. Final Model Assumptions Developed on Post-Meeting Survey Using Modified Delphi Expert Consensus Methods

Model assumptions	Appropriateness ratings: Mean (1–9)	No. of uncertain ratings	No. of inappropriate ratings
Basic model design			
We will perform a cost-minimization analysis to rank diagnostic and management strategies for uninvestigated dyspepsia based on costs.	8.0	0	0
We will model our study over 1 year. A longer 5-year time horizon will be tested in sensitivity analysis, recognizing that we will need to extrapolate 1-year data because of the lack of longer-term outcomes data.	8.3	0	0
Analysis will be performed from insurer (ie, practice/health system reimbursement) and patient perspectives.	8.3	0	0
Our base-case patient will be a commercially insured individual with uninvestigated dyspepsia, younger than 60 years of age with moderate to severe symptoms, without pyrosis or alarm features, and without prior trial of empiric proton pump inhibitor (PPI) therapy.	8.0	0	0
Diagnostic and management strategies included in our analysis			
Four competing diagnostic/management strategies will be evaluated: prompt endoscopy, test-and-treat (test for *H pylori* and eradication treatment in those who test positive), test-and-scope (test for *H pylori* and perform endoscopy in those who test positive), empirical acid suppression (8-week PPI trial).	7.8	1	0
Patients undergoing endoscopy with resulting normal findings and negative *H pylori* testing will receive a PPI trial. We will explore other approaches to managing functional dyspepsia (ie, neuromodulators) in sensitivity analysis.	8.3	0	0
Patients in the test-and-treat strategy with negative *H pylori* testing will subsequently be managed with a PPI trial.	8.5	0	0
Patients undergoing a PPI trial will receive 8 weeks of omeprazole 20 mg twice daily by prescription. We will evaluate over-the-counter omeprazole, other proton pump inhibitors, and a shorter 4-week trial in sensitivity analysis.	8	0	0
Patients who respond to PPI will remain on PPI, and patients who do not respond to PPI will stop the PPI.	8	0	0
Patients who do not respond to the treatments assigned to each strategy will subsequently receive symptom-based management.	7.3	1	0
We recognize significant variation in management of functional dyspepsia based on predominant symptom, subtypes of functional dyspepsia, and patient preferences toward dietary, drug, and psychological approaches.	8.5	0	0
As such, among patients failing a PPI, we define symptom-based management according to representative average medical and pharmacy costs at a population level. These costs will be informed by prospective observational studies following pooled commercially insured populations, varied in sensitivity analysis.	8.0	0	0
Costs and outcomes			
All patients will incur the costs associated with any endoscopy, *H pylori* testing, or drug treatments that are listed for each dyspepsia management strategy.	8.8	0	0
Patients who do not respond to treatment will be burdened with additional direct healthcare utilization costs for additional tests and treatment trials.	8.5	0	0
We will define these additional healthcare utilization costs using large observational studies following patients receiving usual care for dyspepsia.	8.3	0	0
We will define clinical response based on the likelihood of remaining symptomatic.	8.3	0	0
Clinical response in functional dyspepsia is immediate and remains stable over time for the purposes of modeling.	8.0	0	0

Supplementary Table 1. Continued

Model assumptions	Appropriateness ratings		
	Mean (1–9)	No. of uncertain ratings	No. of inappropriate ratings
Efficacy of each management strategy will be considered relative to 1-year observational outcomes among dyspeptic patients.	8.3	0	0
We will not specifically model the likelihood of receiving an endoscopy with each intended strategy, because we will already capture the costs associated with treatment non-response in our model.	7.8	1	0
Work productivity costs			
Patients who do not respond to dyspepsia treatment will incur work productivity costs associated with functional dyspepsia.	8.3	0	0
Patients who respond to dyspepsia treatment will no longer incur any work productivity costs related to their dyspepsia illness.	8.5	0	0
Effectiveness			
We will measure QALYs in a secondary cost-effectiveness analysis.	8.5	0	0
Treatment response will represent a return to complete health.	8.5	0	0
Treatment non-response will represent ongoing health burden as defined in a large observational burden-of-illness study of patients with functional dyspepsia.	8.5	0	0
Treatment satisfaction			
We will perform a secondary cost-effectiveness analysis to assess the dollars spent to improve treatment satisfaction scores with each dyspepsia management strategy.	8.3	0	0

NOTE. Ratings of 1–3 represent inappropriateness of the model assumption, 4–6 represent uncertainty, and 7–9 represent appropriate model assumptions.

Supplementary Table 2. Cost-Effectiveness of Dyspepsia Management Strategies Among Patients Aged 21–47

Management strategy	Annual cost ($)	Annual effectiveness	Incremental cost	Incremental effectiveness
Patient perspective				
Symptom-based management	2570	0.94	Reference	Reference
Test-and-scope	2540	0.94	($30)	0.00
Prompt endoscopy	2550	0.94	($20)	0.00
Test-and-treat	2558	0.94	($12)	0.00
Empiric acid suppression	2563	0.94	($7)	0.00
Insurer perspective				
Symptom-based management	15,527	0.94	Reference	Reference
Test-and-scope	14,842	0.94	($685)	0.00
Test-and-treat	14,992	0.94	($535)	0.00
Prompt endoscopy	16,121	0.94	$594	0.00
Empiric acid suppression	15,432	0.94	($95)	0.00

Supplementary Table 3. Cost-Effectiveness of Dyspepsia Management Strategies Among Patients Aged 48–59

Management strategy	Annual cost ($)	Annual effectiveness	Incremental cost	Incremental effectiveness
Patient perspective				
Symptom-based management	2570	0.94	Reference	Reference
Test-and-scope	2540	0.95	($30)	+0.01
Prompt endoscopy	2550	0.95	($20)	0.00
Test-and-treat	2558	0.95	($12)	0.00
Empiric acid suppression	2563	0.95	($7)[a]	0.00
Insurer perspective				
Symptom-based management	15,527	0.94	Reference	Reference
Test-and-scope	14,842	0.95	($685)	+0.01
Test-and-treat	14,992	0.95	($535)	0.00
Prompt endoscopy	16,121	0.95	$594	0.00
Empiric acid suppression	15,432	0.95	($95)	0.00