Supplementary Methods

Model Transition Probabilities and Calibration

Probability of cancer-related death. Cancer-specific survival for T1b EAC treated with ET has only been reported in small studies with a wide range of estimates. Therefore, we calculated our own estimates of cancer-specific death for esophagectomy and ET on the basis of data from the November 2014 linkage of the SEER database by the National Cancer Institute. Patients were included if they had non-metastatic EAC diagnosed between January 1, 2000 and December 31, 2011 that could be classified as T1 cancer. A cancer was classified as EAC by using International Classification of Diseases for Oncology codes 8050, 8140–8147, 8160–8162, 8180–8221, 8250–8507, 8514, 8520–8551, 8560, 8570–8574, 8576, and 8940–8941. Patients were classified into T subgroups by mapping the extension of disease variables to the appropriate stage by using the seventh edition of the American Joint Committee on Cancer Staging Manual, which is based on whether they only invaded the lamina propria or muscularis mucosa (T1a) or invaded the submucosa (T1b). Because of the small number of T1b tumors in the database, T1 tumors that were categorized as T1NOS were combined into the T1b group. Kaplan-Meier survival curves of T1a, T1b, and T1NOS tumors showed worst outcomes for T1NOS (treated with either ET or esophagectomy), suggesting that these tumors are likely T1b or higher stage rather than T1a (Supplementary Figure 1). Exclusion criteria included cancers that were not the first primary cancer diagnosis, had evidence of lymph node involvement (N1), and lacked treatment information on receipt of surgery or local therapy. Patients were also excluded if they received radiotherapy treatment before surgery or local therapy or they were not continuously eligible for Medicare Part A and B for 13 months before diagnosis.

Patients who received esophagectomy or ET on the basis of Medicare claims were included (Supplementary Table 1). Because use of both SEER and Medicare claims may enhance identification of cancer surgery, patients receiving ET according to SEER with no Medicare claims for esophagectomy were classified in the ET group, and those receiving esophagectomy according to SEER were classified in the surgery group.

The comorbidity score was estimated by applying the adaptation by Deyo et al of the Charlson comorbidity index to Medicare inpatient, outpatient, and physician claims during the 13-month period before cancer diagnosis and classified into the groups 0, 1, and 2+.[26]

Survival was measured from cancer diagnosis to death or December 31, 2013, whichever came first. Patients were identified as having died of their cancer on the basis of the cause of death variable in SEER. Cancer-specific survival curves were generated by using Kaplan-Meier. All statistical analyses were performed by using SAS software, version 9.4 (SAS Institute, Inc, Cary, NC).

Kaplan-Meier curves were generated to compare overall survival between treatment groups, with those alive on December 31, 2013 censored (Figure 2). Hazard rates were calculated on the basis of the Kaplan-Meier curves of cancer-specific survival. Procedural mortality was excluded from these rates and accounted for as a separate input in the model. Thirty-day surgical mortality was estimated from the Steyerberg score, a validated risk score for mortality from esophagectomy derived from data from the SEER-Medicare database (Supplementary Methods).[18] Kaplan-Meier curves were generated to compare overall survival between treatment groups (Figure 2). Hazard rates were calculated on the basis of the Kaplan-Meier curves of cancer-specific survival. Procedural mortality was excluded from these rates and accounted for as a separate input in the model. Non–cancer-related death was predicted from the probability of death on the basis of age multiplied by the relative risk of death based on Charlson comorbidity index.[24,26]

Surgical mortality. This score incorporates the major risk-conferring and protective factors that predict the surgical mortality for a patient: age, number of comorbidities, whether patients had received neo-adjuvant therapy with radiation or chemotherapy, and hospital volume of esophagectomies per year (with higher volume conferring protection against surgical mortality). For our model, the input for number of comorbidities was the Charlson comorbidity index. All patients were assumed to have not received neoadjuvant therapy. Hospital volume was set at "very high."
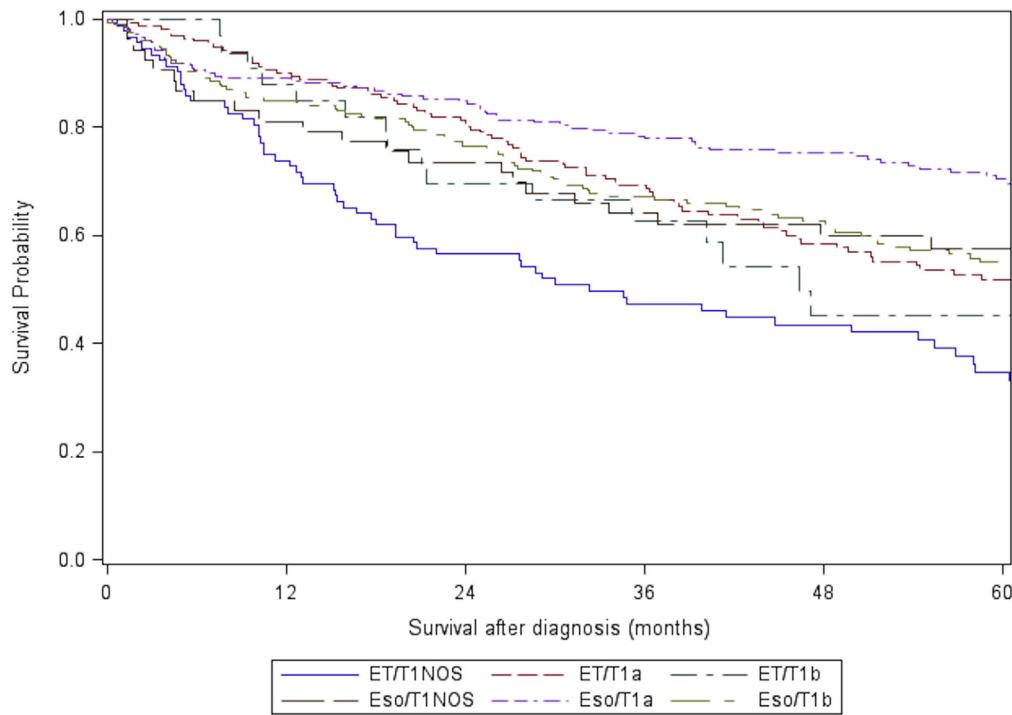
Supplementary Figure 1. Kaplan-Meier curves of overall survival for T1a, T1b, and T1NOS cancers treated with ET or esophagectomy. Data obtained from the SEER-Medicare database. ESO, esophagectomy.
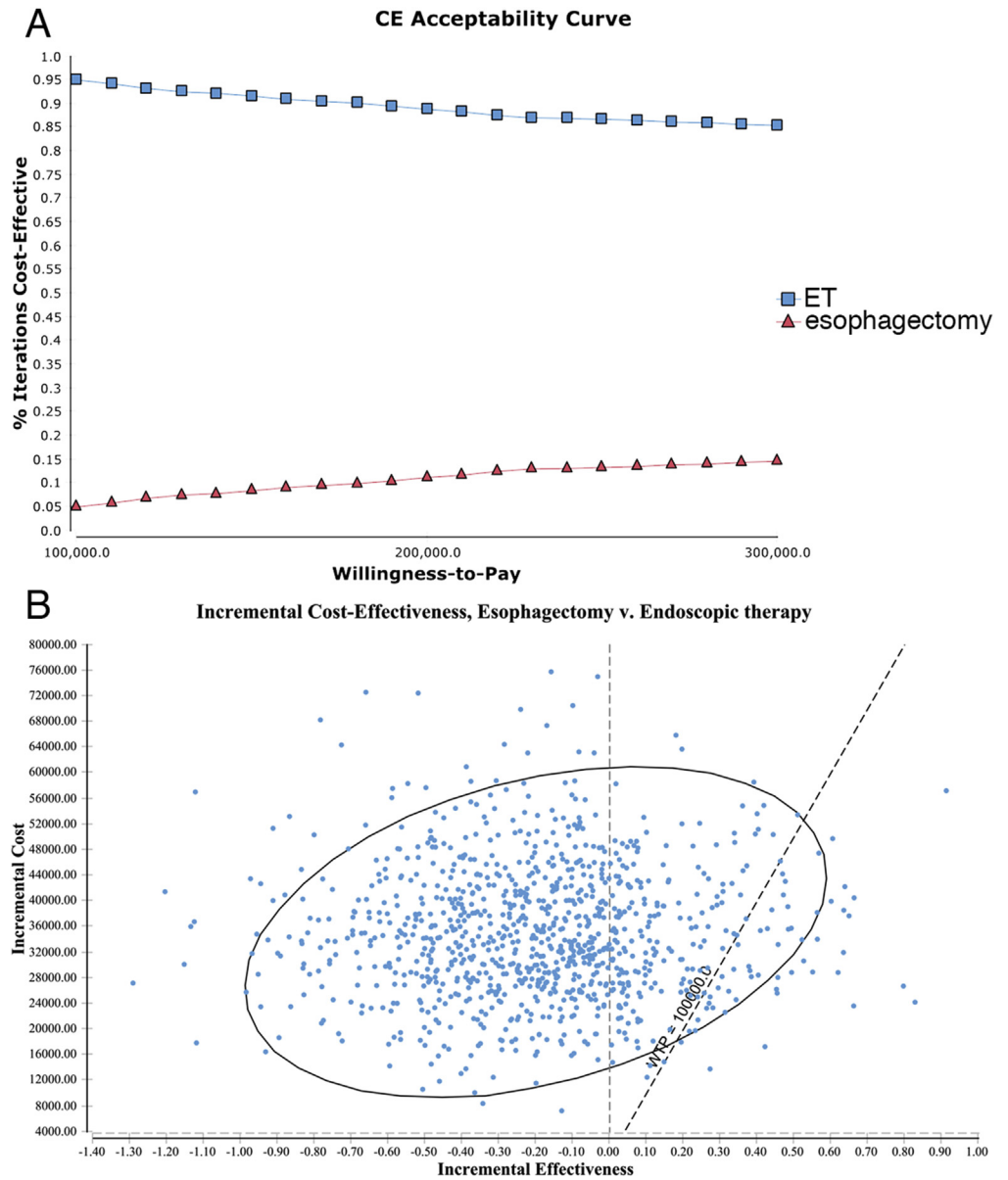
Supplementary Figure 2. Results of probabilistic sensitivity analysis for T1a EAC. *(A)* Cost-effectiveness acceptability curve. *(B)* ICER scatter plot; iterations to the right of the willingness-to-pay line found esophagectomy cost-effective. CE, Cost-effective.

A

CE Acceptability Curve

B

Incremental Cost-Effectiveness, Esophagectomy v. Endoscopic therapy
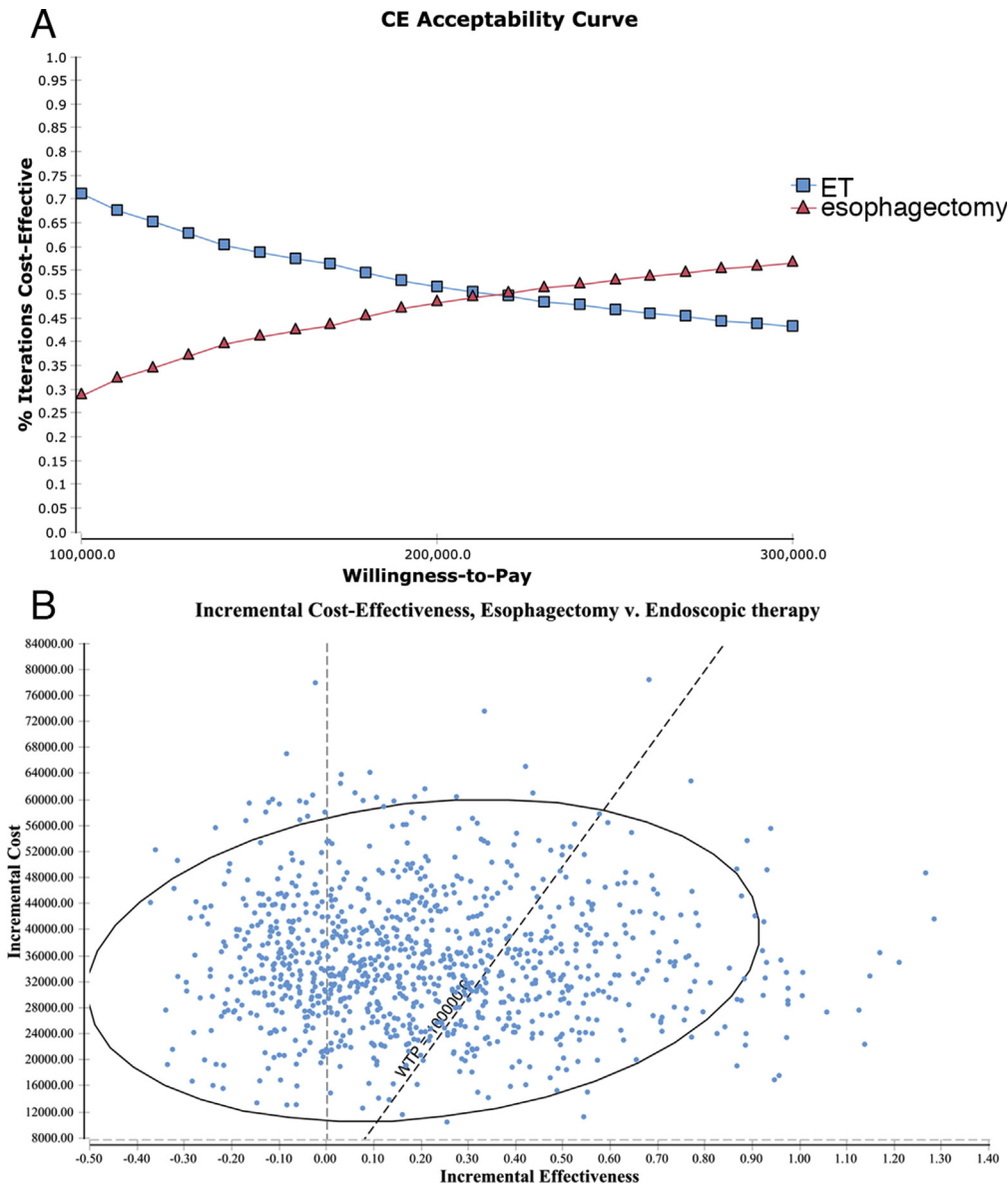
Supplementary Figure 3. Results of probabilistic sensitivity analysis for T1b EAC. (A) Cost-effectiveness acceptability curve. More than 50% of iterations found esophagectomy cost-effective at a willingness-to-pay of $220,000. (B) ICER scatter plot; iterations to the right of the willingness-to-pay line found esophagectomy cost-effective. CE, Cost-effective.

Supplementary Table 1. SEER-Medicare Current Procedural Terminology Codes

Data source	Variable/code	Endoscopic therapy	Surgery
Medicare	International Classification of Diseases, 9th revision-Clinical Modification procedure code	42.33	42.40–42.42, 42.50–42.59, 42.60–42.69, 43.5, 43.99
	Current Procedural Terminology code	43217, 43216, 43228, 43250, 43251, 43257, 43258, 96570, 96571	43100, 43101, 43107, 43108, 43112, 43113, 43116, 43117, 43118, 43119, 43121, 43122, 43123, 43124
SEER	Surgery of primary site (sxprif1) variable	10–14, 20–27	30, 40, 50–55, 80

SEER, Surveillance Epidemiology and End Results.

Supplementary Table 2. Deterministic Sensitivity Analyses of Selected Parameters for T1a Patients

Parameter	Unadjusted life years	QALYs	ICER, $
Age (y)			
60			
Esophagectomy	10.57	7.80	Dominated
ET	9.82	7.83	
85			
Esophagectomy	4.25	2.93	Dominated
ET	4.29	3.20	
CCI			
1			
Esophagectomy	4.68	3.34	Dominated
ET	4.76	3.66	
2			
Esophagectomy	2.98	2.13	Dominated
ET	3.16	2.44	
Female			
Esophagectomy	7.73	5.19	Dominated
ET	7.50	5.44	
Utility of post-esophagectomy state			
0.8			
Esophagectomy	—	4.41	Dominated
ET	—	5.22	
1			
Esophagectomy	—	5.49	130,861.44
ET	—	5.22	
Utility of post-ET state			
0.88			
Esophagectomy	—	4.95	168,500.56
ET	—	4.74	
1			
Esophagectomy	—	4.95	Dominated
ET	—	5.38	
Cost of esophagectomy, $			
25,000			
Esophagectomy	—	—	Dominated
ET	—	—	
Age (y) and CCI			
60, 0			
Esophagectomy	10.57	7.80	Dominated
ET	9.82	7.83	
85, 2			
Esophagectomy	1.20	0.82	Dominated
ET	1.31	0.98	
Utilities of post-esophagectomy and post-ET states			
0.8, 0.88			
Esophagectomy	—	4.41	Dominated
ET	—	4.74	
1, 0.88			
Esophagectomy	—	5.49	46,445.80
ET	—	4.74	
0.8, 1.0			
Esophagectomy	—	4.41	Dominated
ET	—	5.38	
1.0, 1.0			
Esophagectomy	—	5.49	Dominated
ET	—	5.38	

CCI, Charlson comorbidity index; ET, endoscopic therapy; ICER, incremental cost-effective ratio; QALY, quality-adjusted life year.

Supplementary Table 3. Deterministic Sensitivity Analyses of Selected Parameters for T1b Patients

Parameter	Unadjusted life years	QALYs	ICER, $
Age (y)			
60			
Esophagectomy	7.89	5.85	58,359.19
ET	6.54	5.24	
65			
Esophagectomy	7.30	5.34	74,856.05
ET	6.16	4.87	
70			
Esophagectomy	6.61	4.77	96,630.52
ET	5.65	4.40	
80			
Esophagectomy	4.74	3.32	362,530.82
ET	4.25	3.22	
85			
Esophagectomy	3.74	2.58	1,467,245.16
ET	3.43	2.56	
CCI			
1			
Esophagectomy	4.07	2.90	1,774,990.15
ET	3.74	2.88	
2			
Esophagectomy	2.71	1.93	Dominated
ET	2.63	2.03	
Sex			
Female			
Esophagectomy	6.24	4.20	133,581.96
ET	5.41	3.94	
Utility of post-esophagectomy state			
0.8			
Esophagectomy	—	3.63	Dominated
ET	—	3.85	
1			
Esophagectomy	—	4.52	52,658.07
ET	—	3.85	
Utility of post-ET state			
0.88			
Esophagectomy	—	4.07	60,845.34
ET	—	3.50	
1			
Esophagectomy	—	4.07	331,649.61
ET	—	3.97	
Cost of esophagectomy, $			
26,600	—	—	96,108.44
28,200	—	—	103,288.97
Age (y) and CCI			
60, 0			
Esophagectomy	7.89	5.85	58,359.19
ET	6.54	5.24	
60, 1			
Esophagectomy	6.62	4.92	99,447.70
ET	5.68	4.57	
60, 2			
Esophagectomy	5.26	3.92	278,961.05
ET	4.71	3.80	
65, 0			
Esophagectomy	7.30	5.34	74,856.05
ET	6.16	4.87	

Supplementary Table 3. Continued

Parameter	Unadjusted life years	QALYs	ICER, $
65, 1			
Esophagectomy	5.87	4.31	160,379.03
ET	5.16	4.09	
65, 2			
Esophagectomy	4.45	3.28	2,221,110.14
ET	4.10	3.26	
70, 0			
Esophagectomy	6.61	4.77	96,630.52
ET	5.65	4.40	
70, 1			
Esophagectomy	5.04	3.64	272,124.81
ET	4.50	3.52	
70, 2			
Esophagectomy	3.61	2.62	Dominated
ET	3.38	2.65	
80, 0			
Esophagectomy	4.74	3.32	362,530.82
ET	4.25	3.22	
80, 1			
Esophagectomy	3.08	2.16	Dominated
ET	2.92	2.22	
80, 2			
Esophagectomy	1.86	1.30	Dominated
ET	1.88	1.43	
85, 0			
Esophagectomy	3.74	2.58	16,233.98
ET	3.43	2.56	
85, 1			
Esophagectomy	2.18	1.51	Dominated
ET	2.12	1.59	
85, 2			
Esophagectomy	1.15	0.79	Dominated
ET	1.19	0.89	
Utilities of post-esophagectomy and post-ET states			
0.8, 0.88			
Esophagectomy	—	3.63	262,131.92
ET	—	3.50	
1, 0.88			
Esophagectomy	—	4.52	34,417.06
ET	—	3.50	
0.8, 1.0			
Esophagectomy	—	3.63	Dominated
ET	—	3.97	
1.0, 1.0			
Esophagectomy	—	4.52	63,957.14
ET	—	3.97	

CCI, Charlson comorbidity index; ET, endoscopic therapy; ICER, incremental cost-effective ratio; QALY, quality-adjusted life year.

Supplementary Table 4. Probabilistic Sensitivity Analyses

Parameters	Mean	Distribution	Sources
Age (y)	75	Uniform (60–85)	SEER-Medicare, see
Sex	Male	Uniform (male, female)	Materials & Methods
Charlson comorbidity index	0	Uniform (0–2)	[24]
Probabilities			
Esophagectomy surgical mortality	0.071633	Beta (alpha = 24.93, beta = 323.07)	[18]
Endoscopic therapy mortality	4.73E-05	Beta (alpha = 10, beta = 211391.92)	[32]
Utilities			
Resectable cancer, before therapy	0.84	Uniform (0.68–0.92)	[27]
Post-esophagectomy			
0–1 mo	0.7	Uniform (0.70–1)	[23,27,28,32]
1+ mo	0.9	Uniform (0.8–1)	[23,27,32]
Post-ET	0.97	Uniform (0.88–1)	[23,27,33]
Costs ($)			
Esophagectomy	40,163.89	Gamma (alpha = 16, lambda = 0.00040)	[27,32,34]
ET (per session)	1037.46	Gamma (alpha = 16, lambda = 0.015)	[27,32]
Surveillance endoscopy	746.43	Gamma (alpha = 16, lambda = 0.021)	[27,32]
Clinic visit	125.33	Gamma (alpha = 16, lambda = 0.13)	[27,32,34]

ET, endoscopic therapy.