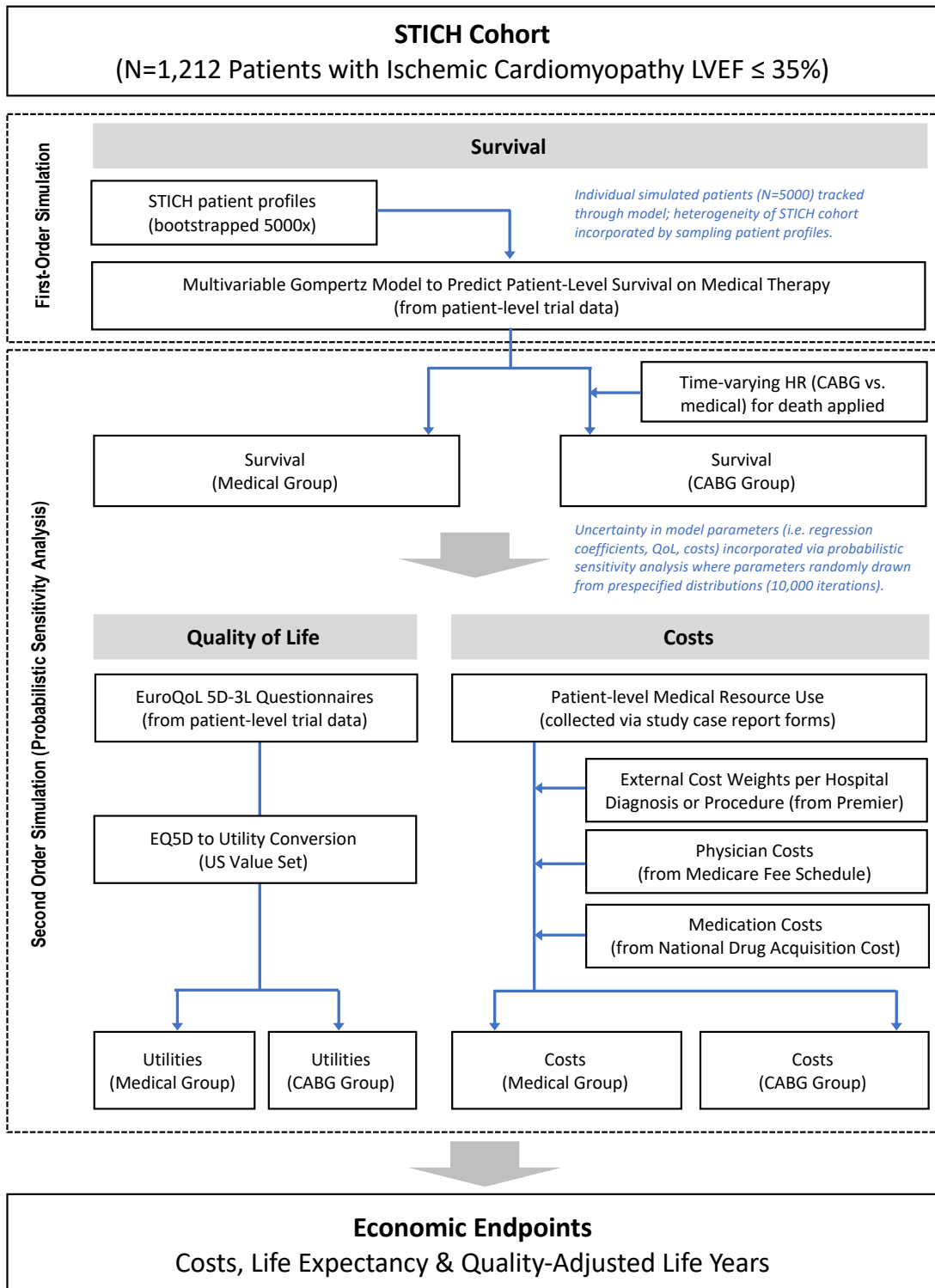
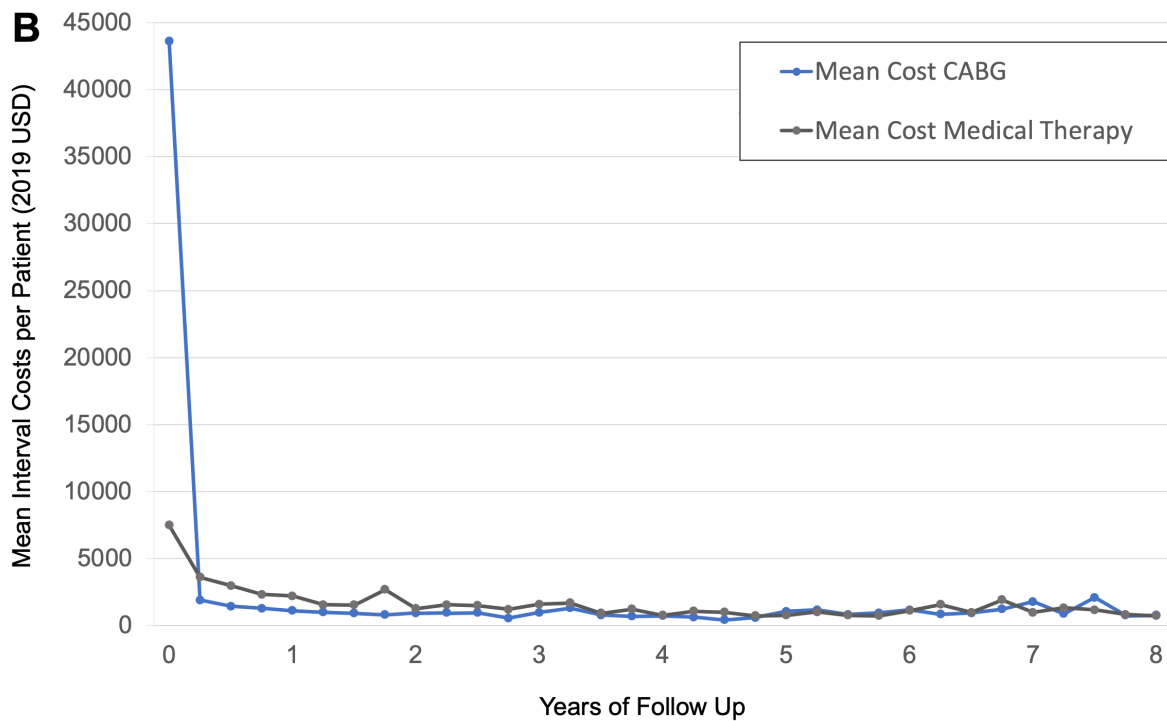
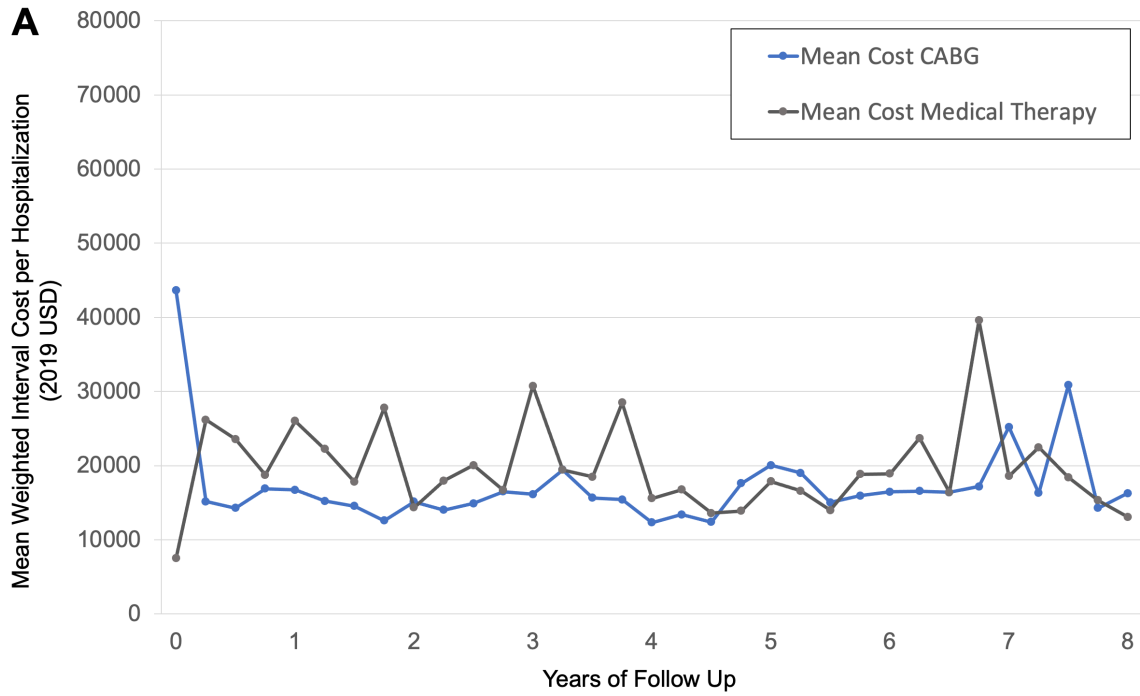


SUPPLEMENTAL MATERIALS

Supplemental Figure I. Schematic of Individual Patient Simulation Model



Supplemental Figure II. (A) Mean weighted interval hospitalization cost, given hospitalization, by Treatment. (B) Mean interval costs per patient in overall cohort, by Treatment. Note: Costs do not include physician fees.



Supplemental Table I. Parametric Gompertz Survival Model

Functional form of the survivor function:

$$S(t) = \exp(-(\lambda/\gamma) \cdot \exp(\gamma \cdot t) - 1)$$

where:

$$\lambda \text{ (scale)} = \exp(k + \beta_{\text{age}} \cdot \text{age} + \beta_{\text{sex}} \cdot \text{sex} + \beta_{\text{smoker}} \cdot \text{smoker} + \beta_{\text{NYHA}} \cdot \text{NYHA class} + \beta_{\text{diabetes}} \cdot \text{diabetes} + \beta_{\text{LVEF}} \cdot \text{LVEF} + \beta_{\text{creatinine}} \cdot \text{creatinine} + \beta_{\text{Hgb}} \cdot \text{Hgb} + \beta_{\text{MRseverity}} \cdot \text{MR severity} + \beta_{\text{vessels}} \cdot \text{vessels})$$

$$K \text{ (constant)} = -5.530693$$

$$\gamma \text{ (shape)} = 0.0031644$$

Covariate (β)	Coefficient	Standard Error	Univariate Wald χ^2 Test
Age	0.0164	0.0058	9.63
Female Sex	-0.3072	0.1730	3.05
Smoker	0.2762	0.1247	7.64
NYHA class	0.1849	0.0752	16.82
Diabetes	0.1177	0.1053	1.44
Left ventricular ejection fraction	-0.2175	0.0064	21.49
Creatinine	0.2574	0.0930	22.93
Hemoglobin	-0.0567	0.0314	4.50
Mitral Regurgitation Severity (none, trace/mild, mod-severe)	0.2052	0.0649	13.45
Number of Vessels (>75% Stenosis)	0.0674	0.0626	3.83
K (Constant)	-5.5307	0.7171	N/A
γ (Shape)	0.0032	0.0015	N/A

Supplemental Table II. Base case clinical and utility inputs

Variable	Base Case Input	Range[†]	Distribution	Reference
<i>Clinical Inputs</i>				
Hazard Ratio of all-cause death (CABG vs. Medical Therapy)			Log-normal	Trial
Over entire follow up period	0.84	0.73-0.97		
≤ 60 days	2.55	1.4-4.6		
61 days to 365 days	0.75	0.50-1.12		
366 days to 2 years	1.00	0.66-1.51		
≥ 2 years	0.74	0.63-0.89		
<i>Utilities</i>				
Medical Therapy			Beta	Trial, ²²
Baseline	0.723	± 0.244		
4 months	0.774	± 0.226		
12 months	0.776	± 0.240		
24 months	0.781	± 0.259		
36 months	0.815	± 0.216		
CABG			Beta	Trial, ²²
Baseline	0.693	± 0.258		
Utility Increments (CABG vs Med)				
4 months	0.047	0.013-0.081		
12 months	0.052	0.018-0.086		
24 months	0.044	0.006-0.081		
36 months	0.036	-0.001-0.074		
<i>Costs (2019 USD)</i>				
Annual Cost of Office Visits	3,407	3,014 - 3,800	Gamma	²⁵
Annual Medication Costs	4,773	4,419 - 5,128	Gamma	²⁵

† Uncertainty range reported as ± standard deviations or 95% confidence intervals unless otherwise specified.

Supplemental Table III. Cost of hospitalizations and inpatient procedures during trial follow-up period

	Number of Visits / Procedures		Cost Weights† (2019 USD)		
	CABG	Medical Therapy	Mean	10 th Percentile	90 th Percentile
Procedures‡					
Heart Transplant	1	4	272,339	175,184	425,043
Left Ventricular Assist Device	2	1	242,811	154,486	331,716
Coronary Artery Bypass Grafting	2	93	46,577	29,853	68,724
Implantable Cardioverter Defibrillator	90	117	38,845	24,456	55,551
Cardiac Resynchronization Therapy	13	12	28,305	17,862	40,591
Pacemaker	11	6	22,075	12,666	35,151
Percutaneous Coronary Intervention	48	66	19,145	11,184	30,412
Coronary Angiography	50	97	13,208	6,224	23,955
Hospitalization					
Acute myocardial Infarction	43	71	9,061	3,943	16,515
Arrhythmia	117	99	8,192	3,263	16,362
Stroke	37	30	12,024	4,939	23,165
Heart Failure	255	303	8,014	3,732	14,096
Other cardiovascular	68	63	8,533	3,314	17,005
Infection	109	67	16,106	6,215	30,806
Gastrointestinal	52	65	11,162	4,747	20,438
Pulmonary	46	26	10,465	4,391	19,348
Renal	32	24	8,765	3,827	16,372
Malignancy	28	23	13,599	5,155	26,103
Other non-cardiovascular	207	184	11,313	4,174	22,193

†Cost weights exclude physician fees, and are reported for inpatient procedures (see Table S3B for cost weights for outpatient / day procedures). ‡Admission and procedural categories are defined hierarchically. That is, if a patient had more than one procedure per visit, procedures were attributed based on highest drivers of cost. For hospitalization, encounters were classified as cardiovascular-related or non-cardiovascular. The hierarchical structure is represented in the listed order of the table.

Supplemental Table IV. Cost of outpatient hospital procedures during trial follow-up period

	Number of Visits / Procedures		Cost Weights† (2019 USD)		
	CABG	Medical Therapy	Mean	10 th Percentile	90 th Percentile
Procedures†					
Implantable Cardioverter Defibrillator	31	31	30,327	19,872	47,336
Cardiac Resynchronization Therapy	13	18	18,197	12,182	25,999
Pacemaker	13	15	13,463	7,966	20,343
Percutaneous Coronary Intervention	7	7	12,805	8,524	17,821
Coronary Angiography	46	70	6,386	4,601	9,751

†Cost weights exclude physician fees

Supplemental Table V. Comparison of undiscounted Life Years estimated by parametric model compared to Life Years from trial using restricted mean survival time.

Time Horizon	Medical Management		CABG	
	RMST	Model*	RMST	Model*
1 year	0.93 (0.92 - 0.95)	0.95	0.91 (0.89 - 0.93)	0.93
3 year	2.55 (2.48 - 2.62)	2.56	2.53 (2.45 - 2.60)	2.56
5 year	3.88 (3.74 - 4.01)	3.89	3.94 (3.80 - 4.08)	3.95
10 year	6.11 (5.82 - 6.40)	6.14	6.51 (6.21 - 6.80)	6.55

*Modelled LYs were estimated using a bootstrap (N=20,000) of individual patient risk profiles from STICH. Abbreviations: CABG – coronary artery bypass grafting; RMST – restricted mean survival time.

Supplemental Table VI. Model inputs for Sensitivity and Subgroup Analyses

Variable	Base Case Input	Range (95% CI)	Distribution	Reference
Subgroup Analysis (LVEF ≤ 28% vs. > 28%)				
HR of all-cause death (CABG vs. Medical Therapy) if LVEF ≤ 28%			Log-normal	Trial
Over entire follow up period	0.77	0.64-0.92		
≤ 60 days	2.18	1.08-4.41		
61 days to 365 days	0.62	0.37-1.06		
366 days to 2 years	0.89	0.54-1.48		
≥ 2 years	0.68	0.54-0.86		
HR of all-cause death (CABG vs. Medical Therapy) if LVEF > 28%				
Over entire follow up period	0.89	0.71-1.11		
≤ 60 days	3.32	1.07-10.3		
61 days to 365 days	0.95	0.50-1.81		
366 days to 2 years	1.13	0.56-2.32		
≥ 2 years	0.78	0.60-1.02		
Subgroup Analysis (0-2 Vessel Disease vs. 3 Vessel Disease)				
HR of all-cause death (CABG vs. Medical Therapy) if 0-2 Vessel Disease			Log-normal	Trial
Over entire follow up period	0.93	0.78-1.11		
≤ 60 days	3.88	1.68-8.94		
61 days to 365 days	0.77	0.44-1.35		
366 days to 2 years	1.05	0.62-1.80		
≥ 2 years	0.83	0.67-1.03		
HR of all-cause death (CABG vs. Medical Therapy) if 3 Vessel Disease				
Over entire follow up period	0.68	0.54-0.86		
≤ 60 days	1.29	0.52-3.21		
61 days to 365 days	0.70	0.39-1.27		
366 days to 2 years	0.91	0.47-1.75		
≥ 2 years	0.60	0.45-0.80		
Sensitivity Analysis – Alternate Quality of Life Extrapolation				
CABG – Mean Utility in STICH	0.800	0.794-0.806	Beta	Trial, ²²
Medical Management – Mean Utility in STICH	0.785	0.779-0.791	Beta	Trial, ²²