

ORIGINAL INVESTIGATIONS

Cost-Effectiveness of Revascularization Strategies

The ASCERT Study



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ABSTRACT

BACKGROUND ASCERT (American College of Cardiology Foundation and the Society of Thoracic Surgeons Collaboration on the Comparative Effectiveness of Revascularization Strategies) was a large observational study designed to compare the long-term effectiveness of coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) to treat coronary artery disease (CAD) over 4 to 5 years.

OBJECTIVES This study examined the cost-effectiveness of CABG versus PCI for stable ischemic heart disease.

METHODS The Society of Thoracic Surgeons and American College of Cardiology Foundation databases were linked to the Centers for Medicare and Medicaid Services claims data. Costs for the index and observation period (2004 to 2008) hospitalizations were assessed by diagnosis-related group Medicare reimbursement rates; costs beyond the observation period were estimated from average Medicare participant per capita expenditure. Effectiveness was measured via mortality and life-expectancy data. Cost and effectiveness comparisons were adjusted using propensity score matching with the incremental cost-effectiveness ratio expressed as cost per quality-adjusted life-year gained.

RESULTS CABG patients (n = 86,244) and PCI patients (n = 103,549) were at least 65 years old with 2- or 3-vessel coronary artery disease. Adjusted costs were higher for CABG for the index hospitalization, study period, and lifetime by \$10,670, \$8,145, and \$11,575, respectively. Patients undergoing CABG gained an adjusted average of 0.2525 and 0.3801 life-years relative to PCI over the observation period and lifetime, respectively. The life-time incremental cost-effectiveness ratio of CABG compared to PCI was \$30,454/QALY gained.

CONCLUSIONS Over a period of 4 years or longer, patients undergoing CABG had better outcomes but at higher costs than those undergoing PCI. (J Am Coll Cardiol 2015;65:1-11) © 2015 by the American College of Cardiology Foundation.

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**ABBREVIATIONS
AND ACRONYMS**

ACCF = American College of Cardiology Foundation
CABG = coronary artery bypass graft
CAD = coronary artery disease
CI = confidence interval
DES = drug-eluting stent(s)
DRG = diagnosis-related group
ICER = incremental cost-effectiveness ratio
IPW = inverse probability-weighting
LYG = life-years gained
MI = myocardial infarction
PCI = percutaneous coronary intervention
PSBB = propensity score bin bootstrapping
QALY = quality-adjusted life-year
STS = Society of Thoracic Surgeons

While death rates attributable to coronary artery disease (CAD) have declined in recent years, CAD remains (as it has for decades) the leading cause of death and disability in the United States and the Western world (1). Whereas randomized controlled trials continue as the gold standard for comparing therapeutic choices, the available data may not be sufficient to support many therapeutic decisions. Additionally, the cost and time constraints of developing randomized controlled trials that cover all variables in all populations render their ubiquitous use impossible. Thus, in the field of comparative effectiveness research, nonrandomized data must often be considered.

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Comparisons from registry databases, though subject to treatment selection bias, can supplement randomized trials based on specific advantages, such as greater numbers, greater generalizability, and more contemporary data that can be regularly updated. Because of their size, representativeness, and reflection of real-world practice, observational databases are becoming major contributors to comparative effectiveness research (2,3).

In the area of cardiovascular disease, 2 prominent registries, the American College of Cardiology Foundation (ACCF) NCDR (National Cardiovascular Data Registry) and the Society of Thoracic Surgeons (STS) ACSD (Adult Cardiac Surgery Database), have for several years individually supplied data for several comparative effectiveness research outcomes studies (4-9). The National Heart, Lung, and Blood Institute of the National Institutes of Health awarded a grant to the ACCF in partnership with the STS to study the comparative effectiveness of percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) surgery for treating stable ischemic heart disease.

The resulting study, known as the ASCERT (American College of Cardiology Foundation-The Society of Thoracic Surgeons Collaboration on

the Comparative Effectiveness of Revascularization Strategies), compared long-term outcomes of PCI and CABG using these professional society databases as well as the Centers for Medicare and Medicaid Services 100% denominator file data (10). To further examine the comparative efficacy of CABG and PCI, we studied the relative costs and cost-effectiveness of revascularization strategies using ASCERT data.

METHODS

STUDY SUMMARY. A complete description of the ASCERT study design and methods has been published previously (11). Briefly, ASCERT was a large observational study designed to compare the long-term effectiveness of CABG and PCI to treat CAD over 4 to 5 years. The outcomes used to compare PCI and CABG were death rates, need for additional or repeat procedures, rehospitalization, and presentation of new cardiac disease conditions, such as stroke or myocardial infarction (MI).

Patients were enrolled in ASCERT based on their first eligible revascularization record (index revascularization). Data from 644 sites were available for 1,943,653 patients who underwent nonemergent isolated CABG or PCI between 2004 and 2007. The Centers for Medicare and Medicaid Services database was linked to the NCDR CathPCI and ACSD registries, yielding an analytic population of 189,793 patients, including 86,244 CABG and 103,549 PCI patients (Online Figure 1) (11).

ECONOMIC ANALYSIS PLAN AND ASSESSMENT OF COST.

The source for determining costs was patient-level resource use from the ASCERT study. Direct medical care costs associated with index hospitalizations were derived from resource use captured in the ACCF and STS databases; subsequent hospitalizations and subsequent outpatient procedures were obtained from the Centers for Medicare and Medicaid Services dataset. The index and subsequent hospitalizations were assigned a diagnosis-related group (DRG) in accordance with U.S. Medicare diagnostic standards. Costs for each DRG were estimated using average Medicare reimbursement rates obtained from the Medicare Part A data file. Physician costs were estimated by current procedural terminology coding

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of procedures and assigned a cost based on the Medicare fee schedule.

Lifetime costs beyond the observation period and costs not included in the hospitalization were estimated from average Medicare participant per capita expenditure, stratified by age group. Average Medicare participant per capita expenditure was \$5,276 in 2004, the base year and the latest date with available data by age. The average costs for patients ages 65 to 74 years, 75 to 84 years, and 85 years or more were \$10,778, \$16,389, and \$25,691, respectively (12). Costs (also for life-years and quality-adjusted life-years [QALY]) beyond the first year of follow-up were discounted 3% annually (13). Drug-eluting stent (DES) cost was reduced by 70%, since the DES cost was substantially reduced over the study period time.

LIFE-EXPECTANCY ESTIMATION. If death occurred during the follow-up period, life-years lost were obtained by subtracting the survival times recorded in the ASCERT database from estimated age- and sex-specific life-expectancy estimates for patients (14). We assumed that the relationship between observed age- and sex-specific mortality rates calculated from

the ASCERT patients and expected corresponding mortality rates from U.S. Life Table would continue to apply to the still-alive ASCERT patients in the future (Online Appendix, Supplement: Life Expectancy Estimation).

For patients with nonfatal MI and/or stroke events during follow-up, additional age- and sex-specific life-expectancy adjustments were made using Framingham Heart Study (13,14) risk estimations and added to the results obtained in the previous step (Online Table 1) (15-17).

The EuroSCORE II (European System for Cardiac Operative Risk Evaluation II) (18) risk was calculated to adjust the estimation of life-years lost for each treatment group and reflect the uncertainties in long-term mortality. The EuroSCORE II for each patient was estimated based on patient factors, cardiac factors, and operation factors.

QUALITY-ADJUSTED LIFE-YEARS. Life-years may be limited for comparison across studies and disciplines because a person in perfect health will derive more value for a life-year saved than a patient in impaired health will. This is addressed by calculating QALY. In ASCERT, QALY were calculated by multiplying

TABLE 1 Baseline Characteristics

	Unadjusted			Inverse Probability Weighted Adjusted			Matched Data		
	CABG (n = 86,244)	PCI (n = 103,549)	p Value	CABG (n = 86,244)	PCI (n = 103,549)	p Value	CABG (n = 43,084)	PCI (n = 43,084)	p Value
Age, yrs	73 ± 6	75 ± 7	<0.0001	74 ± 9	74 ± 8	0.49	74 ± 6	74 ± 6	0.62
Male	69	58	<0.0001	62	63	0.17	64	64	0.69
History of heart failure	12	10	<0.0001	11	11	0.07	11	11	0.31
History of MI	25	25	0.0001	25	25	0.51	24	24	0.89
Diabetes	39	34	<0.0001	36	36	0.97	37	37	0.63
Insulin-RDM	10.2	9.8	0.0069	9.7	9.9	0.35	10.1	10.0	0.66
Hypertension	85	83	<0.0001	84	84	0.58	84	84	0.37
Renal failure	6.1	6.2	0.57	6.1	6.1	0.80	6.2	6.2	0.84
Chronic lung disease	21	19	<0.0001	19	20	0.50	20	20	0.99
Cerebrovascular disease	18	16	<0.0001	17	17	0.86	17	17	0.93
Peripheral artery disease	18	15	<0.0001	16	16	0.97	16	17	0.45
BMI, kg/m ²	29 ± 6	29 ± 6	0.78	29 ± 9	29 ± 8	0.97	29 ± 6	29 ± 6	0.58
Former smoker	44	43	<0.0001	43	43	0.45	43	43	0.37
Current smoker	13	12	<0.0001	12	12	0.74	12	12	0.39
No angina	22	31	<0.0001	26	27	0.23	28	28	0.94
Stable angina	50	23	<0.0001	35	35	0.46	34	34	0.65
Unstable angina	28	47	<0.0001	39	38	0.066	38	38	0.71
Ejection fraction	53 ± 13	55 ± 13	<0.0001	54	54	0.58	54 ± 12	54 ± 13	0.43
Vessels diseased									
2	20	68	<0.0001	47	46	0.043	37	37	0.88
3	80	32		53	54		63	63	
Status urgent	35	36	<0.0001	36	35	0.051	36	36	0.43

Values are mean ± SD or %.

BMI = body mass index; CABG = coronary artery bypass graft; MI = myocardial infarction; PCI = percutaneous coronary intervention; RDM = requiring diabetes mellitus.

survival by utility, a measure of health status scaled from 0 (death) to 1 (perfect health).

QALY were estimated from published data on utilities and estimates of survival, because utility measures were not available from the ACCF or STS databases. Utility was determined on the basis of whether a patient experienced nonfatal cardiovascular

events or a stroke. The utilities were taken from the Cost-Effectiveness Analysis Registry and age-specific utility estimates were applied from population-based studies (19).

ESTIMATION OF COST-EFFECTIVENESS. The cost-effectiveness of CABG was expressed as the incremental cost-effectiveness ratio (ICER), defined as the

CENTRAL ILLUSTRATION Tables Demonstrating Effectiveness and Cost of Index, Over the Study Period, and Lifetime

Effectiveness: Life Years Lost and Years Gained

ITEM	CABG (N=86,244)	PCI (N=103,549)	Δ (CABG-PCI)	95% CI OF Δ
From 2004 to 2008				
Life Years Lost Due to Death (3% discount)	1.1106	1.2285	0.1178	0.0897 - 0.1459
Life Years Lost Due to Death (3% discount, adjusted by PSBB)	0.9647	1.2172	0.2525	0.2254 - 0.2772
Lifetime				
Estimated Life Years Lost (3% discount)	1.4132	1.6023	0.1891	0.1313 - 0.1949
Estimated Life Years Lost (adjusted by PSBB)	1.2248	1.5264	0.3016	0.2660 - 0.3287
Quality Adjusted Life Years Lost (3% discount, adjusted by PSBB)	0.9868	1.3669	0.3801	0.3516 - 0.4074

Costs Over Time Period Studied and Lifetime by Treatment Group

ITEM	CABG (N=86,244)	PCI (N=103,549)	Δ (CABG-PCI)	95% CI OF Δ
Index Hospitalization	\$24,422	\$13,373	\$11,049	10,175 - 12,051
Index Hospitalization (adjusted by PSBB)	\$24,290	\$13,620	\$10,670	9,624 - 11,352
From 2004 to 2008				
From 2004 to 2008	\$64,976	\$56,652	\$8,323	7,446 - 9,145
From 2004 to 2008 (adjusted by PSBB)	\$63,785	\$55,640	\$8,145	7,125 - 9,013
Lifetime				
Lifetime	\$196,256	\$187,532	\$8,724	7,121 - 9,127
Lifetime (adjusted by PSBB)	\$184,933	\$173,358	\$11,575	10,046 - 12,318

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The first table evaluates the effectiveness by reviewing life-years lost for each procedure and life-years gained with coronary artery bypass graft (CABG) compared with percutaneous coronary intervention (PCI) unadjusted and propensity score bin bootstrapping (PSBB) adjusted. The second table presents the costs indexes for hospitalization, from 2004 through 2008, and for lifetime by treatment group unadjusted and PSBB adjusted. CI = confidence interval.

additional cost of CABG divided by the life-years gained and QALY gained compared to PCI. Mean costs for each strategy were calculated as well as the mean difference. Direct medical care costs associated with index hospitalizations, subsequent hospitalizations, and total costs were considered in this analysis. Because the distribution of the differences for cost and effectiveness is typically skewed, the statistics of the difference were estimated by bootstrap analysis (17).

To reduce treatment selection bias in this observational study, propensity score bin bootstrapping methods (PSBB) were used to estimate the 95% confidence interval (CI) for the mean differences of cost and effectiveness between the 2 strategies (10,000 replicates) (20) (Online Appendix: Supplements: Propensity Model and Included Variables and PSBB Approach). Furthermore, to ensure transparency and comparability of the CABG and PCI population, 1-to-1 matching without replacement was conducted to generate an analytic population that was restricted to CABG and PCI patients matching in 3 or more decimals of propensity scores. Baseline characteristics were assessed to ensure the balance of patients for the matched population.

An observational study with a large sample size offers an important source for revealing heterogeneity of different patient characteristics, providing sufficient power to conduct subgroup cost-effectiveness analysis defined by age (≥ 75 years and < 75 years), diabetes status, anginal status (none, stable, or unstable), 2-vessel, or 3- or more vessel disease, and heart failure status. Cost-effectiveness was assessed in these subgroups using the same methods as in the overall matched analytic population.

Traditional 1-way sensitivity analyses included varying life-years gained for the CABG versus PCI group by 10% to 40%. Meanwhile, the impact of unmeasured confounding factors on cost-effectiveness has been a crucial uncertainty and was assessed (21). Probabilistic sensitivity analyses evaluated the

impact of simultaneous changes of all the variables involved in the cost and life-years gained. Monte Carlo simulation was performed to derive the differences in QALY and mean cost between the 2 treatment groups (22).

RESULTS

CLINICAL DATA SUMMARY. The study included a total of 189,793 patients, of whom 86,244 patients underwent CABG and 103,549 patients underwent PCI (Table 1). There were significant differences between these groups in both demographic and clinical characteristics prior to adjustment. A matched analytic population (n = 43,084 for each treatment group) was obtained via 1-to-1 matching in 3 or more decimals of propensity scores. Table 1 shows the comparison of baseline characteristics by treatment group with unadjusted data, adjusted by inverse probability weighted (IPW), and matched analytic population. Age, sex, and most clinical covariates were well balanced between the CABG and PCI groups for both IPW-adjusted data and matched analytic data. Note that the number of vessels diseased and urgent status were not balanced by the IPW-adjusted population, but were similar in the matched analytic population.

EFFECTIVENESS: LIFE-YEARS LOST, LIFE-YEARS GAINED, AND QALY LOST. The Central Illustration shows effectiveness: life-years lost in the CABG and PCI groups; life-years gained with CABG compared with those gained with PCI plus PSBB and quality-adjusted survival results over the follow-up period from 2004 through 2008; and estimated life-time results. Over the follow-up period, before adjustment, there was a significant difference in life-years lost between the groups (1.1106 and 1.2283 life-years lost for the CABG and PCI groups, respectively), resulting in 0.1178 life-years gained for CABG versus for PCI; the PSBB-adjusted years lost were 0.9647 and 1.2172 in the CABG and PCI groups,

TABLE 2 Cost-Effectiveness Analysis: PSBB Adjusted

	Δ CABG-PCI	Life-Years or QALY Gained With CABG	ICER	% CABG Dominated	% CABG Dominant	% $< \$30,000/\text{LYG}$	% $< \$50,000/\text{LYG}$	% $< \$100,000/\text{LYG}$
Life-years from 2004 through 2008	\$8,323	0.1178	\$70,647	0	0	0	0	99.0
Life-years from 2004 through 2008: 3% discount and PSBB adjusted	\$8,088	0.3088	\$26,192	0	0	70	97.0	100.0
Lifetime: 3% discount and PSBB adjusted	\$11,575	0.3016	\$38,379	0	0	3.0	91.0	99.0
Quality-adjusted lifetime: 3% and PSBB adjusted	\$11,575	0.3801	\$30,454	0	0	47.0	98.0	100.0

ICER = incremental cost-effectiveness ratio; LYG = life-years gained; PSBB = propensity score bin bootstrapping; QALY = quality-adjusted life-year(s); other abbreviations as in Table 1.

	Δ CABG-PCI	Life-Years or QALY Gained With CABG	ICER	% CABG Dominated	% CABG Dominant	% <\$30,000/LYG	% <\$50,000/LYG	% <\$100,000/LYG
Life-years from 2004 through 2008	\$8,079	0.2674	\$30,217	0	0	45.0	100.0	100.0
Lifetime: 3% discount	\$12,157	0.3172	\$38,330	0	0	0	100.0	100.0
Quality-adjusted lifetime: 3% discount	\$12,157	0.3947	\$30,803	0	0	21.0	100.0	100.0

Abbreviations as in [Tables 1 and 2](#).

respectively, resulting in 0.2525 life-years gained with CABG versus PCI.

For lifetime, unadjusted life-years lost was 1.4132 and 1.6023 in the CABG and PCI groups, respectively; the quality- and PSBB-adjusted years lost were 0.9868 and 1.3669 in the CABG and PCI groups, respectively, resulting in 0.3801 PSBB-adjusted QALY gained for CABG versus for PCI. Similar results were shown for the matched analytic population ([Online Table 2](#)).

COSTS: 2004 THROUGH 2008 AND LIFETIME. As seen in the [Central Illustration](#), index hospitalization cost remained significantly higher for the CABG group than in the PCI group, by \$11,049 before and \$10,670 after adjustment. The adjusted average total cost over the follow-up period was higher in the CABG group by \$8,145 (\$63,783 in CABG vs. \$55,640 in PCI). The difference in cost during the follow-up period (2004 through 2008) was mainly due to the difference in index hospitalization cost. This trend remained for estimated lifetime cost.

The unadjusted lifetime cost in the CABG group was \$8,742 higher than in the PCI group (\$196,256 vs. \$187,532). The PSBB-adjusted lifetime cost was \$184,933 in the CABG group and \$173,358 in the PCI group, still significantly higher for CABG by \$11,575. A similar trend was seen in the matched analytic population ([Online Table 3](#)).

COST-EFFECTIVENESS ANALYSIS FOR FOLLOW-UP AND LIFETIME. [Table 2](#) (PSBB-adjusted) and [Table 3](#) (matched analytic population) show the cost-effectiveness analysis for the follow-up period and lifetime. For lifetime, the PSBB-adjusted ICER of CABG compared to PCI was \$38,379 per life-years gained (LYG), with 3.0% and 91.0% of observations below \$30,000 and \$50,000 per LYG, respectively, and 99.0% below \$100,000 per LYG; the further quality-adjusted ICER of CABG compared to PCI was \$30,454 QALY gained, with 47.0% and 98.0% of observations below \$30,000 and \$50,000 per QALY gained, respectively, and 100% below \$100,000 per QALY gained ([Figure 1A](#)).

	Δ CABG-PCI	Life-Years or QALY Gained With CABG	ICER	% CABG Dominated	% CABG Dominant	% <\$30,000/LYG	% <\$50,000/LYG	% <\$100,000/LYG
Diabetes	\$14,069	0.5525	\$25,467	0	0	100.0	100.0	100.0
No diabetes	\$11,075	0.3051	\$36,298	0	0	0	100.0	100.0
Age >75 yrs	\$12,407	0.3863	\$32,118	0	0	1.0	100.0	100.0
Age \leq 75 yrs	\$11,806	0.4046	\$29,182	0	0	70.0	100.0	100.0
White	\$12,021	0.3999	\$30,060	0	0	46.0	100.0	100.0
Nonwhite	\$13,377	0.3511	\$38,102	0	0	0	95.0	100.0
Male	\$11,496	0.3922	\$29,309	0	0	72.0	100.0	100.0
Female	\$13,432	0.3987	\$33,693	0	0	0	100.0	100.0
No angina	\$14,914	0.5842	\$25,527	0	0	99.0	100.0	100.0
Stable angina	\$9,600	0.2262	\$42,443	0	0	0	94.0	100.0
Unstable angina	\$12,439	0.4066	\$30,484	0	0	37.0	100.0	100.0
2-vessel disease	\$10,943	0.2589	\$42,269	0	0	0	95.0	100.0
\geq 3-vessel disease	\$12,883	0.4758	\$27,080	0	0	99.0	100.0	100.0
HF	\$20,213	0.8216	\$24,602	0	0	100.0	100.0	100.0
No HF	\$11,090	0.3376	\$32,848	0	0	0	100.0	100.0

HF = heart failure; other abbreviations as in [Tables 1 and 2](#).

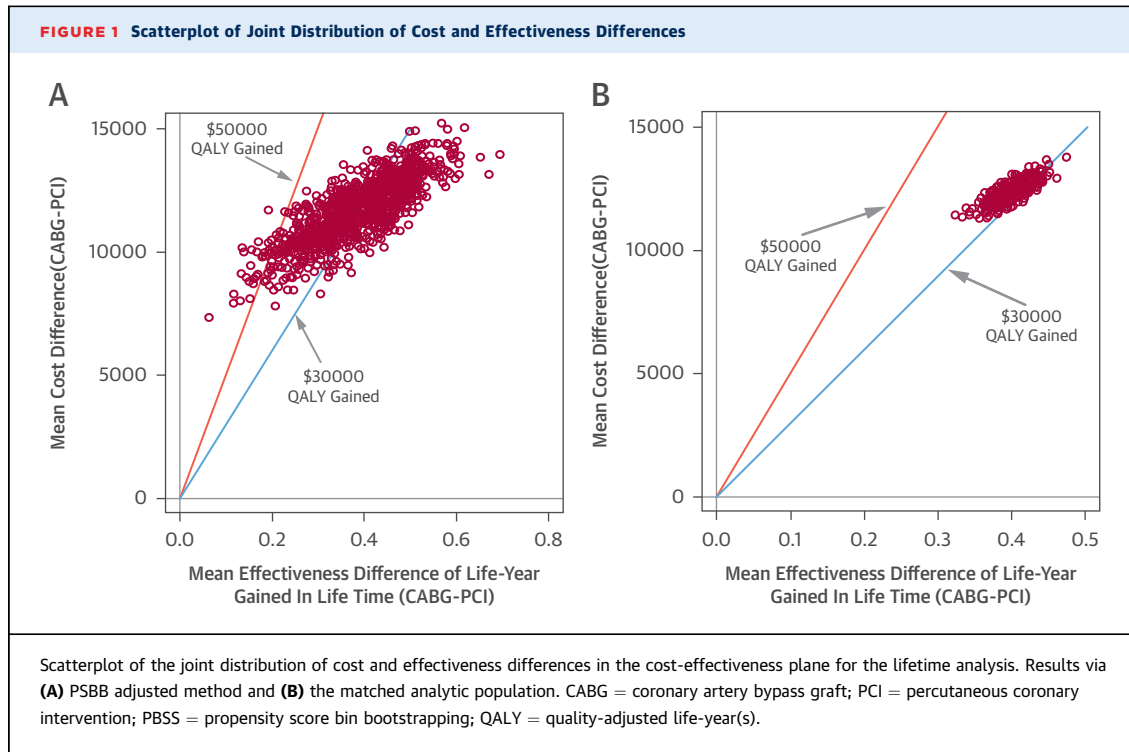
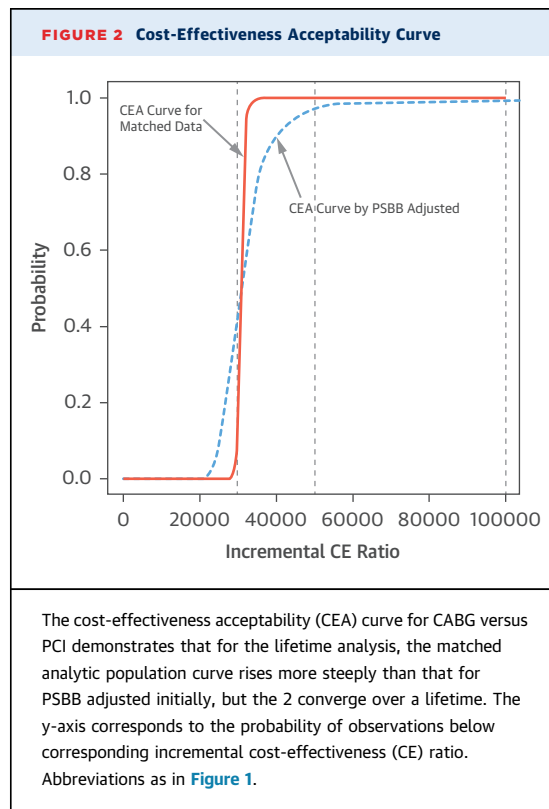
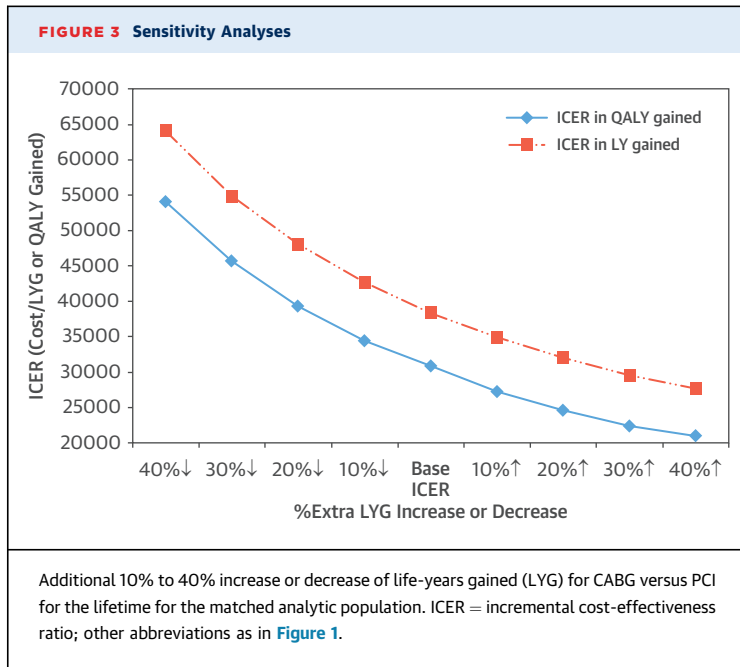


Table 3 shows that the cost-effectiveness results for matched analytic populations were similar to those using the PSBB-adjusted method. For lifetime, the quality-adjusted ICER of CABG compared to PCI was \$30,803 QALY gained, with 21.0% and 100.0% of observations below \$30,000 and \$50,000 per QALY gained, respectively (Figure 1B). Using a common threshold such as \$50,000 per QALY gained, results from both the PSBB-adjusted and matched analytic population approaches illustrated that CABG provided moderate to high probability of better clinical benefit, which means CABG will often be a cost-effective strategy (Figure 2).

SUBGROUP ANALYSIS. Subgroup lifetime cost-effectiveness analyses were performed for the matched analytic population. Similar results were obtained for all patients via PSBB (not shown). Results in Table 4 demonstrate differences in terms of patient features (Online Appendix: Supplement: Subgroup Analysis). For instance, ICER were \$42,443 per QALY and \$42,269 per QALY for stable angina and 2-vessel disease patients, respectively, and both with 0% of observation below \$30,000 per QALY.

SENSITIVITY ANALYSIS. There is uncertainty regarding years of life lost due to early death and the impact of nonfatal MI or stroke on subsequent life expectancy.





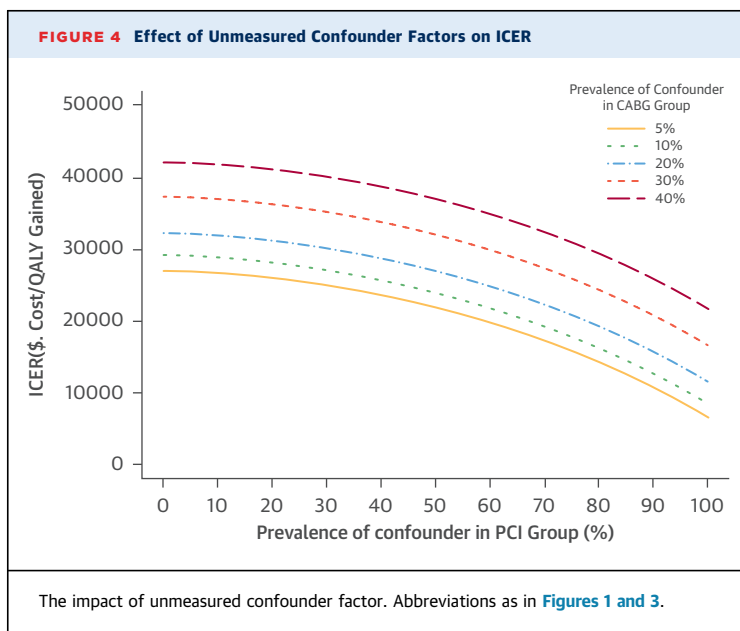
Thus, for the matched analytic population over a lifetime, if the quality-adjusted benefit of CABG relative to PCI decreased by 10%, 20%, 30%, and 40%, the ICER would increase from \$30,803 to \$34,400, \$39,330, \$45,660, and \$54,100 per QALY gained, respectively. In contrast, if the estimated and adjusted QALY gained with CABG relative to PCI increased by 10%, 20%, 30%, and 40%, the ICER

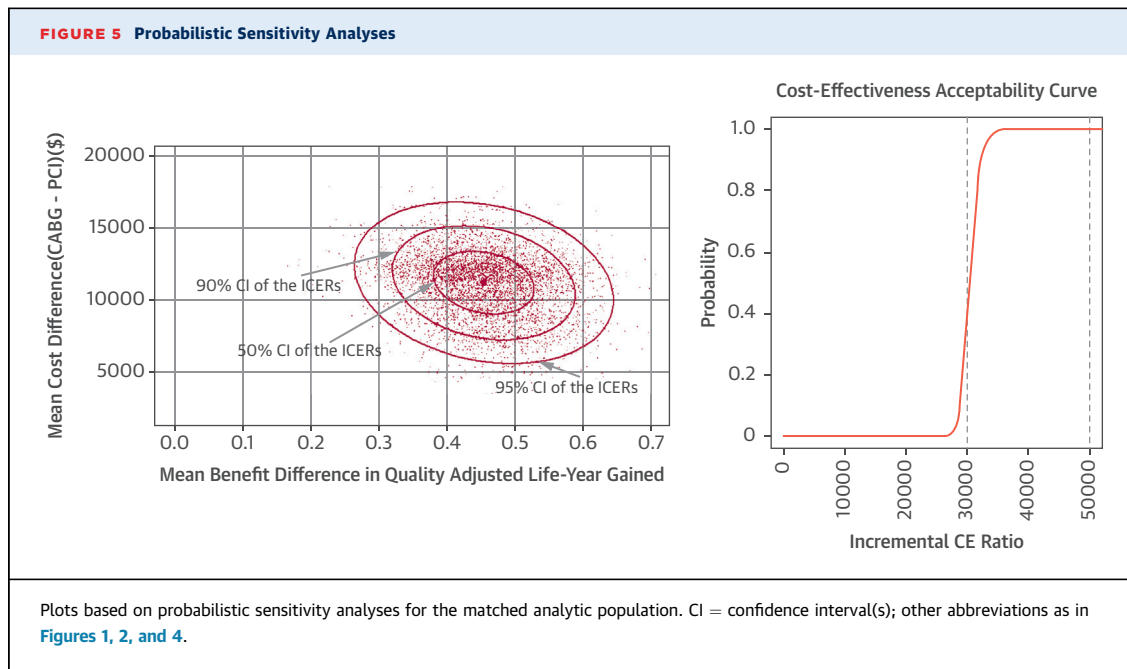
would decrease from \$30,803 to \$27,240, \$24,550, \$22,280, and \$20,930 per QALY gained, respectively ([Figure 3](#)).

[Figure 4](#) represents the impact of a single unmeasured confounder on the ICER as a combination of cost and effectiveness, to account for the advantage of CABG over PCI detected in the study. From the adjusted survival analysis in ASCERT, if an unmeasured risk factor was present in 10% of the patients in the CABG group and in 20%, 35%, or 50% of the PCI patients, then the hazard ratio that would be required for the observed decreased risk with CABG would be 4.25, 2.09, and 1.65, respectively ([11](#)). The unmeasured confounder could also have affected the observed cost difference, ranging from a decrease of 20% to an increase of 10% ([23](#)). If the prevalence due to the confounder in PCI was 50%, the ICER of CABG versus PCI would change from \$24,000, to \$28,000, to \$33,000, to \$38,000, and to \$41,000 per QALY gained for the prevalence of the confounder in CABG with 5%, 10%, 20%, 30%, 40%, respectively.

To account for uncertainties regarding years of life lost due to early death, the impact of nonfatal MI or stroke on subsequent life expectancy and the estimation of cost due to differences in the use of resources, a probabilistic sensitivity analysis was conducted to assess the robustness of the estimates for matched analytic population. The results of EuroSCORE II are shown in the [Online Appendix: Supplement: EuroSCORE II](#). The distributional assumptions of the cost data were based on the actual data in this study and their ranges come from relevant literature, with probabilities of effectiveness ([Online Table 4](#)) derived from other cardiovascular studies and resources such as the American Heart Association Heart Disease and Stroke Statistical Update ([1](#)). [Figure 5A](#) presents the contour plot of simulated distribution of mean differences in cost and effectiveness using matched analytic population and quality adjustment, based on the probabilistic sensitivity analysis over a lifetime. The ellipses indicate 50%, 95%, and 99% CI of the simulated lifetime ICER. It reveals that the IPW-adjusted lifetime QALY gained could range from 0.27 to about 0.65 years for the CABG group compared with those for the PCI group; on the other hand, the cost for the CABG group would always be significantly larger, varying from \$5,500 to \$17,800, indicating a better clinical benefit for CABG but at increased cost.

The cost-effectiveness acceptability curve ([Figure 5B](#)) illustrates that the variation the ICER considered in this sensitivity analysis was greater than noted purely by the play of chance in the base case;





specifically, compared with 21.0% of observations below \$30,000 per QALY gained, and 100% below \$50,000 per QALY gained for the base case, there was a 33% probability of CABG being cost-effective at the \$30,000 threshold and 100% at the \$50,000 threshold. The probability of CABG being dominated by PCI was <1%. Sensitivity trends were similar for all patients adjusted using the PSBB approach.

DISCUSSION

We performed a cost-effectiveness analysis of ASCERT; the main clinical results showed that there was a long-term survival advantage in older patients with nonemergent multivessel CAD who were selected to have CABG rather than PCI. The present economic analysis shows CABG is more expensive than PCI is, almost entirely due to the initial procedural costs (Central Illustration). It is reasonable to conclude that, after the study period, resource use and costs would largely track in parallel. A long-term survival advantage among patients in the CABG group was converted into QALY gained (Central Illustration), but the point estimates for the ICER for potential CABG benefit were below common benchmarks (Tables 2 and 3).

To address selection bias in this large observational study, analyses were conducted through both PSBB and a matched analytic population. PSBB captured the information from all patients

with balance achieved for measured confounders via propensity score adjustment. The 1-to-1 matched analytic population indeed had better risk factor balance between the CABG and PCI groups, but approximately one-third of the patients were excluded from the analysis. Nonetheless, the similarity of results from PSBB method and matched analytic population enhances the results' reliability.

Although the greatest uncertainty is in the differential life expectancy, these results are robust to variations in relative gain in life expectancy with CABG, both before and after PSBB adjustment, and for the matched analytic population.

It is natural to evaluate our findings in the context of results from other health economic studies. In 2006, on the basis of a Department of Veterans Affairs Cooperative Study randomizing high-risk patients with medically refractory myocardial ischemia, a cost-effectiveness assessment of CABG (n = 227) versus PCI (n = 218) for high-risk patients showed that PCI was less costly and at least as effective for the urgent revascularization of medically refractory, high-risk patients over 5 years. After 5 years, average total costs were \$81,790 for PCI versus \$100,522 for CABG patients, a difference of \$18,732 (95% CI: \$9,873 to \$27,831), whereas survival at 5 years was 0.75 for PCI patients versus 0.70 for CABG patients (p = 0.21) (23). The FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal

Management of Multivessel Disease) trial was a 5-year study between 2005 and 2010 of 1,800 patients with diabetes and multivessel CAD who were randomly assigned to CABG or PCI with DES at 140 centers throughout the world. Investigators reported that CABG was associated with 0.66 QALY gained and higher costs of approximately \$5,400 per patient; lifetime cost-effectiveness of CABG was therefore \$8,132 per QALY gained, which is significantly lower than the commonly used benchmark of \$50,000 per QALY gained for considering a treatment to be cost-effective (24). The SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) trial randomized 1,800 patients with left-main or 3-vessel CAD to CABG (n = 897) or DES-PCI (n = 903) between 2005 and 2007. Over a lifetime horizon, CABG remained more costly than DES-PCI with a favorable ICER of \$16,537/QALY gained (25). Our ASCERT results demonstrated a similar trend, but exhibited some discrepancy in ICER values. The discrepancy may be due to the change of survival rate of CABG versus PCI, such as no difference in survival between groups at 1 year, but significant better benefit in survival in CABG group at 4 years. The differences over a lifetime may reflect diverse assumptions in estimating life expectancy in both arms of the studies.

Using professional society databases, we demonstrated the distinct advantages of linking clinical and administrative databases. Clinical databases are well suited to risk adjustment and the identification of clinically important subgroups, but lack long-term outcome information. Administrative datasets have limited capacity for clinical considerations, but they do provide long-term information on outcomes as well as cost of care. Linking the clinical data with administrative data capitalizes on the distinct advantages of each dataset to create a powerful analytic tool for observational studies.

STUDY LIMITATIONS. ASCERT is a nonrandomized observational study, and although PSBB/IPW adjustment created CABG and PCI populations demonstrating excellent balance, enabling a more valid comparison, there remains a potential for unmeasured confounders to have influenced the estimation of both clinical outcomes and cost. Although our cost-effectiveness analysis sought a societal basis, costs such as DRG-based values were estimated from a payer perspective. It is also not generally possible to account for all costs and for all utilization. Resource use beyond the trial period is based on a model, not on direct measurement. For instance, costs beyond

the period of observation were estimated from average Medicare participant expenditures stratified by age.

For patients still alive at the end of the follow-up period, we applied a Monte Carlo simulation method to estimate the life expectancy on the basis of the observed mortality rate and the U.S. Life Tables (2009) and converted to life-year lost for each procedure. Our methods are an estimate both of patients' health status (utility) and projected survival. We used Framingham data, an external database, to estimate nonfatal events related to life expectancy. The Framingham database, however, may not reflect multiple advances in medical care, specifically in cardiovascular medicine, that have occurred since that database was created. Projection of life expectancy for disease-specific patients and cost beyond the observational period must be based on models developed from the literature. Evaluation of utility, used to quality adjust survival, is also problematic, with utility estimates not directly from the dataset. Although propensity matching balanced the patients, some important covariates that should have been included in the propensity model could have been missed. It is likely that the accurate estimation of difference in life expectancy was limited. Despite these limitations, the results of our sensitivity analyses were robust, suggesting that the results are unlikely to be severely affected as long as there is a survival benefit of CABG in keeping with the ASCERT results.

Finally, there is no scientific basis for a threshold to establish whether a therapy is cost-effective. The commonly used threshold of \$50,000 is an approximation of societal "willingness to pay."

CONCLUSIONS

This study shows that over a period of 4 years or longer, CABG is associated with better outcomes but at higher cost than PCI among older patients with 2- or 3-vessel CAD. Under the assumption that our analysis has fully accounted for both measured and unmeasured confounding, in patients with stable ischemic heart disease, CABG will often be considered cost-effective at thresholds of \$30,000 or \$50,000/QALY.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Comparison of PCI and CABG surgery allow assessment of the effectiveness of the 2 procedures for treatment of patients with multivessel disease. Observational and clinical trial data have demonstrated a survival advantage associated with CABG, but surgery is more expensive, due almost entirely to the initial costs associated with the operation.

TRANSLATIONAL OUTLOOK: Analyses that link clinical and administrative databases can be applied to other aspects of patient management to enhance insights from observational studies and clinical registries about the relative value of various options and inform shared decision making between patients and providers.

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KEY WORDS coronary artery bypass graft, incremental cost-effectiveness ratio, percutaneous coronary intervention, stable ischemic heart disease

APPENDIX For supplemental sections, tables, and a figure, please see the online version of this article.