Cost-Effectiveness of Alternative Approaches to the Management of Chronic Obstructive Coronary Artery Disease

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Chronic obstructive coronary artery disease (CAD) is a highly prevalent condition that results in premature mortality as well as substantial morbidity due to angina and reduced quality of life. Various treatment and revascularization strategies are available for managing this condition, including medical therapy, percutaneous coronary intervention, and coronary artery bypass grafting. These treatments are expensive and, given the high prevalence of chronic CAD, there is substantial cost involved in the management of this condition. Recent clinical trials comparing percutaneous coronary intervention with medical management and/or coronary artery bypass grafting, and their associated economic analyses, have generated new information regarding the relative value of these alternative treatment strategies. In this article, we review the basic concepts of cost-effectiveness analysis and the current evidence as it relates to the cost-effectiveness of percutaneous coronary intervention in the management of chronic obstructive coronary artery disease.

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More than 80 million Americans have some form of cardiovascular disease (CVD), and about 16 million suffer specifically from coronary heart disease (CHD).[1] In 2006, patients underwent an estimated 1,313,000 inpatient percutaneous coronary intervention (PCI) procedures, 448,000 inpatient coronary artery bypass grafting (CABG) procedures, and 1,115,000 inpatient diagnostic cardiac catheterizations in the United States alone.[1] The estimated direct and indirect cost of CHD projected for 2009 is $165.4 billion,[1,2] of which a substantial component is directly attributable to

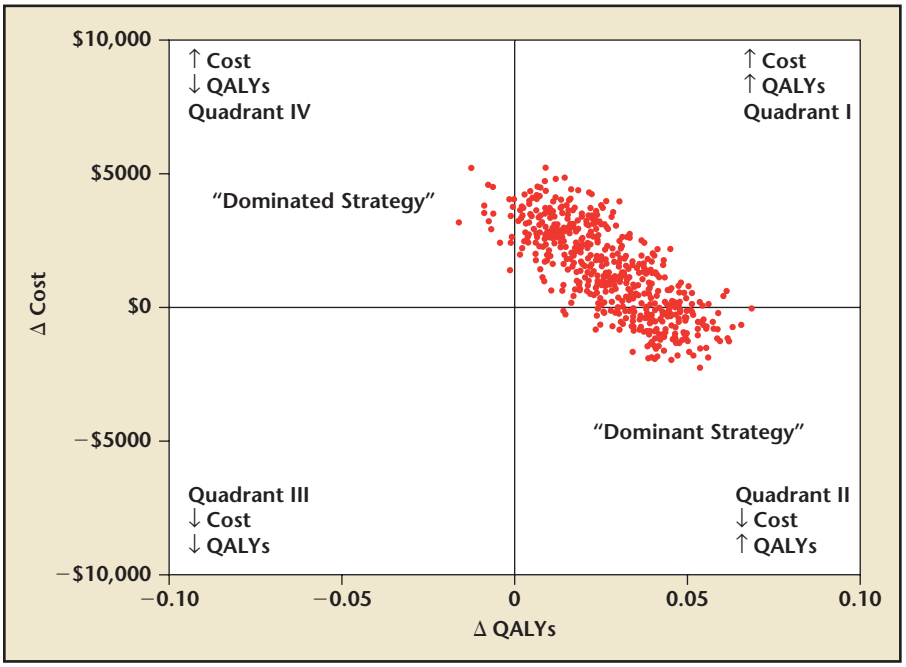
revascularization procedures and associated care.[3]

Recent clinical trials of alternative management strategies for chronic coronary artery disease (CAD),[4,5] along with rising health care costs, have set the stage for a closer inspection of economic data with respect to the benefit of revascularization strategies.[3,6] In particular, both the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluations (COURAGE) trial[4,7] and the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) study[8] have demonstrated that among selected patients with chronic CAD, revascularization in general and PCI in particular do not provide substantial benefits in terms of "hard" clinical endpoints (death or myocardial infarction [MI]) and provide, at most, modest benefits in quality of life (QoL). Consequently, there is an increasing interest in evaluating the optimal role and cost-effectiveness of revascularization strategies for patients with chronic CAD. Cost-effectiveness in the cardiovascular literature has been described in detail elsewhere[9,10] and for the purposes of this article, we briefly describe the most important concepts in contemporary economic studies.

Basic Terminology

The general concepts of cost-effectiveness can be described by considering a comparison of a new treatment strategy versus standard of care in the "cost-effectiveness plane" (Figure 1). According to this schematic, the x-axis represents the clinical effectiveness of the new strategy, and the y-axis represents its costs. The existing standard therapy occupies the origin of the graph, and the new therapy may occupy any of the 4 quadrants.[9] As shown in Figure 1, quadrant I will locate therapies that are more expensive but also more effective than the current standard of care—a common scenario. Quadrant II identifies therapies that are less expensive and more effective than standard of care—referred to as economically "dominant." Quadrant III identifies therapies that are less effective but also less expensive than the alternative. Quadrant IV includes therapies that are less effective and more expensive than standard of care—an unfavorable combination generally referred to as economically "dominated." When a new therapy improves clinical results at increased cost (or lowers cost while sacrificing some level of effectiveness [the scenarios described in quadrants I and III in Figure 1]), the estimation of value is based upon calculation of an incremental cost-effectiveness ratio (ICER).[9]

Figure 1. *Example of a cost-effectiveness plane. The individual points represent various combinations of costs and clinical effects (generated by bootstrap resampling). QALYs, quality-adjusted life-years.*



The Cost-Effectiveness Ratio

An ICER is a quantitative method of expressing the trade-off between costs and clinical benefits described above. The generic formula for calculating an ICER is as follows:

$$\text{ICER} = \frac{(\text{Cost}_{\text{New}} - \text{Cost}_{\text{Reference}})}{(\text{Effectiveness}_{\text{New}} - \text{Effectiveness}_{\text{Reference}})}$$

The numerator, incremental costs, is not restricted to the costs of the therapies themselves, but also includes the induced costs of the treatment strategies and costs avoided due to clinical benefits.[9] For example, in the case of PCI, such induced costs might include the costs of vascular complications, repeat revascularization procedures to treat restenosis, and even bleeding complications associated with prolonged dual antiplatelet therapy. In some cases, indirect costs (eg, lost work or leisure time on the part of the patient or his or her family) may also be included as costs. The denominator—effectiveness—is defined broadly and may vary according to the specific clinical setting and audience. Potential effectiveness

measures may include standard clinical outcomes, such as mortality or complications avoided, years of life gained (ie, life expectancy), or specialized measures that take into account both QoL and life expectancy.

One metric that is commonly used in cost-effectiveness analyses is quality-adjusted life expectancy. Conceptually, quality-adjusted life expectancy is a morbidity-adjusted measure of survival that is expressed in terms of quality-adjusted life-years (QALYs). To calculate QALYs, each time interval in a given state of health is weighted by the "utility" of that health state, where utility is a theoretical construct that represents an individual's preference for that health state on a scale ranging from 0 to 1, where 1 represents perfect health and 0 represents death.[11] Thus, years of life in good health yield more QALYs than years when health status is poor.

Once a cost-effectiveness ratio is calculated, it is typically compared with cost-effectiveness ratios for other therapies in a "league table" (Table 1). In interpreting such league tables, it is important to recognize that the threshold for determining whether a therapy is economically attractive varies with the available health care budget. In the United States, for example, cost-effectiveness ratios of less than $50,000 per QALY gained are generally viewed as favorable, and ratios between $50,000 and $100,000 per QALY gained are frequently considered to be in a "gray zone." In contrast, cost-effectiveness ratios exceeding $100,000 per QALY saved are generally viewed as economically unattractive.[9] These standards do not necessarily apply to other health care systems, however. In particular, countries that spend considerably less on health care than the United States would appropriately have more stringent (lower) thresholds.[12]

Cost-Effectiveness of PCI Versus Medical Therapy

The first medical cost-effectiveness analyses began to emerge in the late 1960s,[13] but their specific application to revascularization strategies in chronic CAD—particularly by their incorporation as key endpoints in clinical trials—is a relatively recent development. One of the first studies to consider the cost-effectiveness of PCI, CABG, and medical therapy for patients with chronic CAD was performed by Wong and colleagues and published in 1990.[14] In this study, they developed a detailed decision analytic model to project overall quality-adjusted life expectancy and costs for CABG, PCI, and conservative medical therapy. Of note, data for the model were derived predominantly from observational studies

Table 1
An Example of a "League Table" Comparing the Cost-Effectiveness Ratios of Various Therapies

Number	Intervention Versus Comparator in Target Population	$/QALY Gained
1.	Warfarin versus aspirin in 65-year-old with nonvalvular atrial fibrillation and high risk for stroke	Cost-saving
2.	Warfarin versus aspirin in 65-year-old with nonvalvular atrial fibrillation and medium risk for stroke	$8800
3.	Warfarin versus aspirin in 65-year-old with nonvalvular atrial fibrillation and low risk for stroke	$410,000
4.	Thrombolytic therapy with intracoronary streptokinase versus conventional therapy in patients with electrocardiographic evidence of myocardial infarction and a duration of symptoms not exceeding 4 hours	$4800
5.	Captopril therapy versus no captopril in 70-year-old patients surviving myocardial infarction	$5900
6.	Magnetic resonance angiographic preoperative evaluation versus conventional angiographic preoperative evaluation in patients with limb-threatening peripheral vascular disease	$30,000
7.	Thrombolytic therapy with tissue plasminogen activator versus thrombolytic therapy with streptokinase in patients presenting within 6 hours after onset of symptoms of acute myocardial infarction	$32,000
8.	Implantable cardioverter defibrillator–only regimen with relative risk reduction of 20% versus amiodarone-only regimen in 57-year-old survivors of cardiac arrest at high risk for ventricular fibrillation, ventricular tachycardia, or nonarrhythmic cardiac death	$80,000
9.	Screening for carotid disease, with carotid endarterectomy if positive versus no screening for carotid endarterectomy in 65-year-old men with no symptoms of carotid disease	$130,000
10.	Dual air bags versus driver-side air bag only in driving population (and passengers)	$69,000

Adapted with permission from Chapman RH et al.[32]

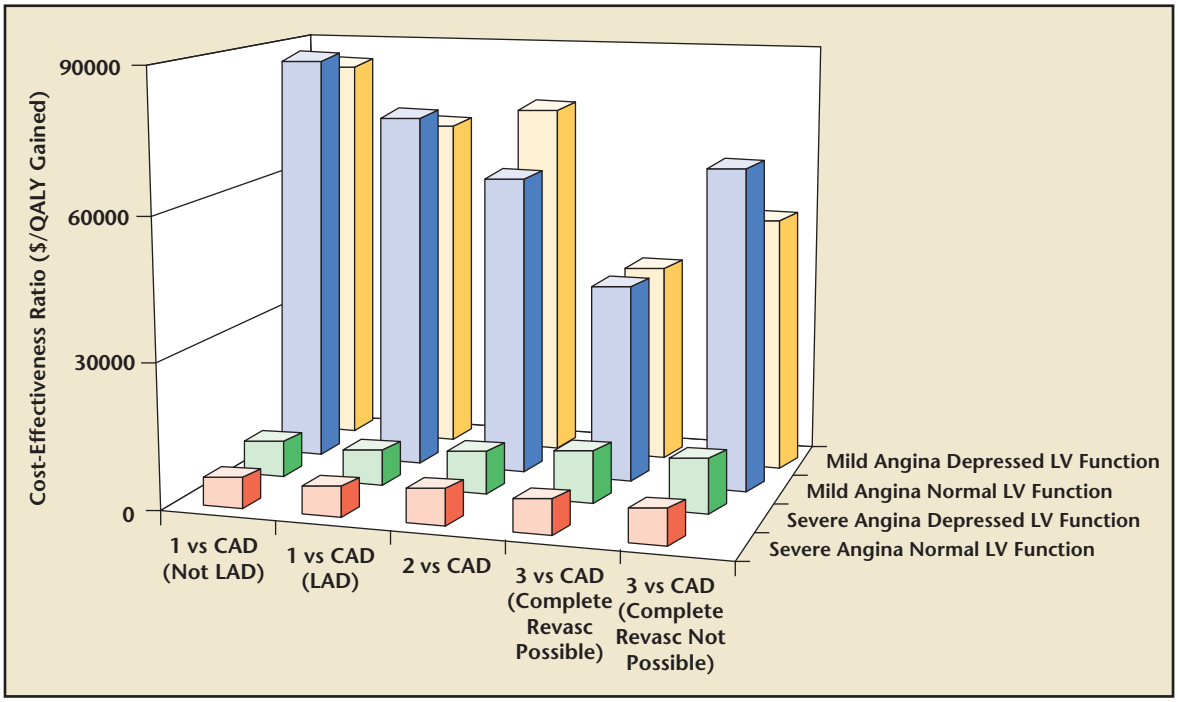
and a small number of clinical trials comparing CABG with medical therapy because these were the only data available at the time of the study.[14]

Although technological advances in the past 2 decades have called into question many of the specific results of this study, several of its basic principles are of enduring value. In particular, the concept that the effectiveness (in terms of quality-adjusted life expectancy) and cost-effectiveness of revascularization therapy varies with specific patient characteristics—including the extent of CAD, whether left ventricular function is normal or impaired, and the severity of angina and its impact on a patient's QoL—remains valid even today.

In terms of our understanding of the cost-effectiveness of PCI for patients with chronic CAD, several of their specific results are worth noting as well. First of all, they projected that the cost-effectiveness of PCI would vary with the extent of underlying CAD. For patients with 1- or 2-vessel disease and severe angina, they projected that PCI would be reasonably cost-effective compared with medical therapy, with ICERs ranging from $6000 to $9000 per QALY gained (Figure 2). On the other hand, for patients with complex 3-vessel disease, they found that bypass surgery was probably the most effective therapy in the long-run (due to improved survival) and was reasonably cost-effective, particularly for patients with complex anatomy that renders complete revascularization via PCI technically challenging (Figure 2).

Wong and colleagues[14] also found that the cost-effectiveness of PCI for chronic CAD varies substantially with the severity of angina at baseline as well as the extent of underlying ischemia (Figure 2). For example, for patients with severe angina and single-vessel CAD, PCI was projected to be reasonably cost-effective (ICER = $6000 per QALY gained), whereas the ICER for patients with single-vessel disease and only mild angina was projected to be far less favorable (ICER = $87,000 per QALY gained). On the other hand, among patients with mild angina, the cost-effectiveness of PCI was projected to vary from $41,000 per QALY gained to $87,000 per QALY gained, depending on the extent of underlying CAD and ischemia (more cost-effective with more extensive CAD and greater ischemic burden). Although the relevance of their specific conclusions and cost-effectiveness ratios to contemporary practice may certainly be questioned, recent studies such as COURAGE and Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) (described in detail below) suggest that the general

Figure 2. *Cost-effectiveness ratios of percutaneous transluminal coronary angiography by clinical patient subsets. CAD, coronary artery disease; LAD, left anterior descending; LV, left ventricular; QALY, quality-adjusted life-year; Revasc, revascularization. Adapted from Wong JB et al.*[14]



principles underlying these findings remain unchanged even in the era of aggressive secondary coronary prevention and drug-eluting stents.

Finally, Wong and colleagues[14] used their model to estimate the impact of patient age on the cost-effectiveness of revascularization. Although intuition might suggest that revascularization at an early age would provide greater and longer benefits (and, thus, superior cost-effectiveness), their results suggest a different conclusion. Based on the epidemiologic data underlying their model, it appears that the dominant factor underlying the cost-effectiveness of revascularization for chronic CAD—whether by PCI or CABG—is the underlying coronary event rate. Because coronary event rates increase substantially with age, their model suggests that revascularization therapy is somewhat more cost-effective among older as compared with younger patients—all things being equal. In light of numerous data from observational registries suggesting that the elderly are less likely to undergo revascularization than younger patients in a variety of settings,[15] these findings certainly suggest that advanced age should not be considered a deterrent from PCI or CABG, when appropriate, and that efforts to reverse this apparent risk-treatment disparity should be encouraged.

Newer Insights—The COURAGE Trial

The first study to formally evaluate the costs and cost-effectiveness of elective PCI for chronic obstructive CAD in the era of contemporary medical therapy was the COURAGE trial.[4,7] In COURAGE, costs were assessed from the perspective of the US health care system by multiplying counts of resources by average US Medicare reimbursement rates (for hospitalizations, major cardiovascular procedures, and physician services). Costs for medications were included as well, but indirect costs such as lost productivity were not. One novel feature of COURAGE was that utility weights were assessed directly from each study participant at regular intervals to allow the calculation of QALYs.

The main findings of the study were that during the observed follow-up period (a median of 4.6 years), total in-trial costs were $34,843 for the PCI plus optimal medical therapy (OMT) group and $24,718 for the OMT-only group (a difference of $10,125), with in-trial quality-adjusted life expectancies of 3.56 and 3.51 QALYs, respectively (a difference of 0.05 QALYs). The within-trial cost-effectiveness ratio was thus $206,229 per QALY gained (ie, $10,125 per 0.05 QALYs) with PCI plus OMT compared with OMT alone. When the in-trial event data were used to project lifetime costs, utilities, and life expectancy, these values changed only minimally, and the lifetime cost-effectiveness ratio was $168,019 per QALY gained for initial PCI. Bootstrap analysis demonstrated that the cost-utility ratio remained more than $50,000 per QALY in 89.9% of trial replicates and more than $100,000 per QALY in 64.6%. Based on these findings, the authors concluded that PCI for chronic stable CAD is not an economically attractive strategy in the current health care environment.[4]

Given the overall results of COURAGE, the results of the economic analysis are not particularly surprising. The improvement in overall quality-adjusted life expectancy was modest because there were no differences in hard outcomes (which might otherwise have been expected to translate into substantial gains in life expectancy for the trial population), and the QoL benefits that were observed were limited. The finding that treatment costs were substantially higher with PCI is also fairly intuitive given the high upfront costs of the PCI procedures. It is somewhat surprising, however, that PCI did not result in substantial reductions in follow-up cost. Indeed, over the approximately 5-year follow-up period, "downstream" costs were only $1285 per patient lower with initial PCI plus OMT versus OMT alone—reflecting the fact that there were no differences in the incidence of bypass surgery during follow-up and limited reductions in the need for subsequent PCI procedures in the initial PCI group as well.

Some editorialists have questioned the relevance of the COURAGE trial because relatively few patients (< 5%) received drug-eluting stents at the time of their initial revascularization procedures.[16] Although it is tempting to speculate that greater use of DES would have led to different results, it seems unlikely that this would have dramatically altered the cost-effectiveness results. To address these important concerns, the COURAGE investigators included a sensitivity analysis that incorporated both the proven benefits of DES (a reduction in the need for subsequent revascularization procedures) and their costs (higher procedural and medication-related costs for extended dual antiplatelet therapy). Although the cost-effectiveness of PCI was improved in this hypothetical scenario, the resulting cost-utility ratio was still more than $150,000 per QALY in both in-trial and lifetime analyses. Once again, these results are not surprising because DES have not been shown in randomized trials to either lower costs[17,18] or improve survival.[19] Although these results remain speculative, they suggest

that it is unlikely that widespread use of DES in COURAGE would have had dramatic impact on the overall cost-effectiveness results.

Despite the high quality of the data and methods underlying the COURAGE trial and its associated economic analysis, there are still important caveats that should temper the impact of its findings. The most important limitation of the COURAGE trial, however, is whether its results can be readily extrapolated to the overall population with chronic CAD. Although the inclusion criteria for COURAGE were quite broad and would be expected to encompass a large proportion of the patients who undergo elective PCI, it appears likely that the actual population enrolled in the trial was quite different. Like other randomized trials of entrenched therapies, COURAGE had difficulty with recruitment, ultimately enrolling fewer than 10% of patients who were screened for the trial over a significantly longer period of enrollment than was originally projected, thus suggesting that the population enrolled in the trial was quite different than the population screened.[3,7] The slow recruitment for the trial may also be an indication of the difficulty the COURAGE investigators faced in randomizing patients with multiple severe stenoses or disabling angina[3]—precisely those populations that would be expected to derive the greatest benefit from PCI. Indeed, almost 42% of patients enrolled in the trial had either mild angina or no anginal symptoms (based on Canadian cardiovascular angina class), and the median duration of angina preceding enrollment was 5 months. This finding suggests a population of patients with very stable angina overall,[3] which is further supported by the low rate of cardiac death in the COURAGE population (approximately 0.5% per year). In light of the previous findings of Wong and colleagues[14] regarding the key determinants of cost-effectiveness of elective PCI, it is thus tempting to speculate that the results of COURAGE (both clinical and economic) might have been far more favorable for PCI had it enrolled either a more symptomatic or higher-risk patient population (Figure 2).

Cost-Effectiveness of PCI Versus CABG

For patients with milder forms of CAD, the clinical question tends to focus on the comparison of PCI versus medical therapy, but for patients with more extensive CAD (eg, multivessel disease, reduced left ventricular function) or complex anatomic features (eg, diffuse lesions, chronic total occlusions, left main disease), the more relevant comparison is between PCI and bypass surgery. To date, at least 9 studies have compared percutaneous transluminal coronary angioplasty (PTCA) (balloon angioplasty only) costs with those of CABG, including published reports from at least 6 randomized clinical trials. The main studies are summarized in Table 2.

Although each of these studies has specific inclusion and exclusion criteria and has used different time frames and cost measurement techniques, several general observations can still be made. First, the initial hospital cost for PCI is approximately 30% to 50% lower than that of bypass surgery. Despite the substantial initial cost savings with multivessel PCI, however, over a 3- to 5-year follow-up period, much of these initial cost savings are lost due to the need for repeat revascularization (PCI or bypass surgery) in approximately 50% of PCI patients.[20,21]

For example, Weintraub and colleagues[22,23] have reported 3- and 8-year economic data for the 386 patients randomized to balloon angioplasty or bypass surgery in the Emory Angioplasty versus Surgery Trial (EAST). Initial hospital costs and professional charges for the PTCA group averaged $17,212 per patient compared with $29,640 per patient for the CABG group. By the end of 3 and 8 years of follow-up, however, mean costs for the PTCA group had increased to 91% and 95% of those for bypass surgery, and the difference was no longer statistically significant. In patients with focal 2-vessel disease, however, the 3-year cost of PTCA remained significantly lower than for bypass surgery ($20,875 vs $23,639; $P < .001$); 8-year data for this subset have not been reported.

In the Randomized Intervention Treatment of Angina (RITA) study, initial hospital costs in the PTCA arm were 52% lower than in the CABG group, at £3592 and £6192, respectively.[24] This difference narrowed considerably during follow-up, and by 5 years, aggregate costs in the PTCA group were 95% of those in the group initially treated with coronary bypass surgery, at £8842 and £9268, respectively, due to 6-fold higher follow-up procedural costs in the PTCA arm.[25]

Results of a 5-year economic substudy of the Bypass Angioplasty Revascularization Investigation (BARI) have been reported as well.[21] To date, this study represents the largest and most comprehensive economic evaluation of alternative revascularization strategies for patients with multivessel coronary disease. Among 934 patients randomized to initial PTCA or bypass surgery, initial medical care costs were 35% lower with PTCA ($21,113 vs $32,347). Over the first 3 years of follow-up, this cost difference narrowed progressively such that by the end of

Table 2
Cost Studies Comparing PCI Versus Bypass Surgery

Study	Date	Method	N	Diseased Vessels	Cost Measure	Time Period When Costs Assessed	PTCA Cost	CABG Cost
PTCA Versus CABG trials								
Reeder et al[33]	1979–1981	OBS	168	1,2,3	Medical charges	Initial hospitalization	$7571	$12,154
						1 year	$11,384	$13,387
Kelly et al[34]		OBS	163	1,2,3	Hospital and doctor charges	1 year	$7689	$13,559
EAST[22,23]	1987–1990	RCT	384	2,3	Hospital costs and doctor charges	Initial hospitalization	$17,212	$29,640
						3-year total	$25,458	$31,035
						8-year total	$44,491	$46,548
RITA[24]	1993–1994	RCT	999	2,3	Hospital costs	Initial hospitalization		
						London center	£3753	£7319
						Non-London center	£3024	£5722
					Hospital, procedural, and medication costs	2-year total		
						London center	£6916	£8739
						Non-London center	£5448	£6498
BARI[20,21]	1988–1995	RCT	952	2,3	Hospital and out-patient costs, and doctor fees	Initial revascularization	$21,113	$32,347
						5-year total	$56,225	$58,889
						5-year total among 2-vessel disease patients	$52,930	$58,498
						5-year total among 3-vessel disease patients	$60,918	$59,430
						12-year total	$120,750	$123,000
						12-year total for patients with diabetes	$150,100	$151,100
BMS PCI Versus CABG trials								
ARTS[26]	1997–1998	RCT	1200	2,3	Hospital costs and doctor fees	Initial revascularization	7366 EU	11,295 EU
						1-year total	10,665 EU	13,638 EU
SoS[28]	1997–1999	RCT	967	2,3	Hospital and out-patient costs	Initial revascularization	£4205	£7396
						1-year total	£6419	£8914
DES PCI Versus CABG trials								
SYNTAX[30]	2005-2007	RCT	1800	2,3	Hospital costs, doctor fees, and out-patient costs	Initial revascularization	$27,000*	$33,000*
						1-year total costs	$36,000*	$40,000*

*The SYNTAX trial costs are preliminary and unpublished.
ARTS, Arterial Revascularization Therapy Study; BARI, Bypass Angioplasty Revascularization Investigation; BMS, bare-metal stent; CABG, coronary artery bypass grafting; DES, drug-eluting stent; EAST, Emory Angioplasty versus Surgery Trial; OBS, observational study; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; RCT, randomized clinical trial; RITA, Randomized Intervention Treatment of Angina; SYNTAX, Synergy between PCI with Taxus and Cardiac Surgery; SoS, Stent or Surgery.

5 years of follow-up, aggregate costs with PTCA remained slightly (5%) but significantly lower than with bypass surgery ($56,225 vs $58,889; $P = .047$). Subgroup analysis demonstrated that PTCA remained approximately $6000 less expensive than CABG for patients with 2-vessel disease, but that 5-year costs were no different for patients with 3-vessel disease. Because bypass surgery was associated with a trend toward improved survival in BARI, formal cost-effectiveness analysis was performed to determine whether routine CABG would be economically attractive for such patients. The BARI investigators found the ICER for bypass surgery as compared with angioplasty to be $26,000 per year of life gained. Surgery appeared

particularly cost-effective in the treatment of patients with diabetes because of their significantly improved survival.

More recently, the BARI investigators reported 12-year cost and QoL results.[20] At 12 years, costs for patients assigned to initial CABG were approximately $2000 higher than for patients who underwent initial PTCA ($123,000 vs $120,750 per patient), whereas cumulative life expectancy was 8.58 versus 8.42 years, respectively—yielding a highly attractive cost-effectiveness ratio of $14,300 per life-year gained for CABG over PTCA.[20] Whether the availability of coronary stents and their benefits on both the acute and long-term results of PCI have altered the balance of costs and benefits of PCI versus CABG in patients with multivessel disease is less certain—particularly from the perspective of the US health care system. Although prospective economic analyses were performed alongside both the Arterial Revascularization Therapy Study (ARTS)[26,27] and the Stent or Surgery (SoS) trial,[28] to date, published data from these studies are limited to 1 to 3 years of follow-up and have been based on costs and measures of resource utilization from non-US health care systems.[26-28]

To date, the only study to formally evaluate the cost-effectiveness of stenting versus CABG from the perspective of the US health care system was based on an economic model that used data from the BARI trial.[29] Using this model and extrapolating the clinical benefits of bare-metal stents over balloon angioplasty based on clinical trials conducted in patients with single-vessel disease, Yock and colleagues[29] projected that although stents led to reduced rates of target lesion revascularization in the short-term, these benefits (along with the added costs of stents) were not sufficient to substantially alter the previous results of the BARI analyses. They therefore concluded that, compared with bare-metal stents, bypass surgery remains the preferred form of initial revascularization for most patients with multivessel disease.[29]

Impact of Drug-Eluting Stents on the Cost-Effectiveness of Multivessel PCI Versus CABG

Whether the introduction and widespread adoption of drug-eluting stents has had a substantial impact on the cost-effectiveness of multivessel PCI is currently unknown. However, preliminary data from the SYNTAX trial[5] suggest that by further reducing the incidence of restenosis, drug-eluting stents may have finally achieved the goal of matching the clinical benefits of CABG with a less invasive and less costly procedure—at least for certain patients with 3-vessel and left main disease. The SYNTAX trial was the most ambitious clinical trial of percutaneous versus surgical coronary revascularization that has been performed to date. A total of 1800 patients with either 3-vessel coronary disease, left main disease, or both were randomized to bypass surgery or PCI with paclitaxel-eluting TAXUS stents. Both QoL and health economic data were collected prospectively, and 1-year results for these analyses were presented at the 2009 American College of Cardiology Scientific Session in Orlando, FL.[30]

QoL was assessed at baseline, 1 month, 6 months, and 12 months using a combination of disease-specific and generic instruments. The primary QoL endpoint, the angina frequency subscale of the Seattle Angina Questionnaire (SAQ), improved substantially for both groups by 1 month. However, at both 6- and 12-month follow-up, there were small but statistically significant differences in favor of CABG. On the other hand, as assessed by the SF-36® health status instrument, both physical and mental health were substantially better with PCI at the 1-month time point. These PCI-related benefits were largely resolved at the 6- and 12-month time points, however. Utility assessment demonstrated a significant early benefit with PCI but no late benefit with CABG; as a result, total quality-adjusted life expectancy actually favored PCI (by 0.02 QALYs) at the 1-year assessment.

From an economic perspective, SYNTAX provided several important insights as well. First, the cost of the initial PCI procedures was more than $14,000 per patient—reflecting the use of an average of 4.6 drug-eluting stents per patient as well as the fact that about 14% of patients required staged procedures. Nonetheless, given the marked reduction in hospital length of stay and procedural complications, as well as lower physician fees, the overall initial revascularization cost was still about $6000 per patient lower with PCI than CABG. On the other hand, over the ensuing year, follow-up costs were about $2500 per patient lower with CABG than with the initial PCI—reflecting a reduced need for repeat revascularization procedures as well as lower medical therapy costs (largely related to the cost of dual antiplatelet therapy among the DES patients). Nonetheless, total 1-year costs remained about $3500 per patient lower with initial PCI. Thus, at 1-year, PCI with drug-eluting stents was an economically dominant strategy with both lower overall health care costs and improved quality-adjusted life expectancy.[30]

Although these results apply to the "average" SYNTAX patient, subgroup analyses demonstrated important

differences in cost-effectiveness according to specific patient characteristics—most notably, angiographic complexity as assessed by the SYNTAX score.[5] For patients with the lowest and intermediate tertiles of SYNTAX scores (≤ 33), the 1-year cost-effectiveness results were either strongly or moderately in favor of PCI. On the other hand, for patients with the greatest extent of disease and highest angiographic complexity (SYNTAX score > 33), the 1-year costs of CABG were virtually identical to those of PCI, and quality-adjusted life expectancy tended to favor CABG as well; the resulting ICER for CABG versus PCI was already favorable at about $49,000 per QALY gained. Thus, even at this early follow-up stage, the SYNTAX economic analysis would suggest that CABG should be the preferred initial management strategy on both *clinical and economic* grounds for patients with highly complex coronary anatomy. It is important to acknowledge that these results are preliminary and have been published only in abstract form. Moreover, given the natural history of patients with multivessel coronary disease, it may be premature to base health policy or reimbursement decisions on 1-year follow-up data. Indeed, 5-year follow-up of the SYNTAX population is ongoing and will be essential to the completion of the economic assessment.

Finally, in applying the results of studies such as BARI, ARTS, and SYNTAX, it is important to recognize that most clinical trials of PCI versus CABG have been performed among patients who were suitable candidates for either revascularization technique. The clinical and economic results of coronary revascularization procedures may differ, however, among patients with multiple comorbidities who are at increased risk of both fatal and nonfatal complications of CABG. In the Angina With Extremely Serious Operative Mortality Evaluation (AWESOME) trial,[31] 445 patients at high risk of CABG-related complications (prior open heart surgery, age older than 70 years, left ventricular ejection fraction less than 0.35, MI within 7 days, or requirement for ongoing intra-aortic balloon counterpulsation) were randomized to PCI or CABG. At 5-year follow-up, there was a trend toward improved survival with PCI (75% vs 70%; $P = .21$), whereas total medical care costs (as assessed from the perspective of the US Medicare program) were substantially higher with CABG ($100,522 vs $81,790; $P = .0012$). These findings (which were replicated in about 90% of bootstrap simulations) demonstrate that for patients with refractory angina who are at high risk of CABG-related complications, PCI is the preferred management strategy on *both* clinical and economic grounds.

Final Thoughts

As demonstrated by this review, cost-effectiveness analysis is a powerful tool that can provide important insights to help guide both individual clinical decisions and overall administrative or policy decisions. However, one should also understand the limitations of such studies before applying their results to the development of clinical guidelines or reimbursement policies. Just as with clinical decision-making, there is no single "cost-effective" solution for a given problem for all patients and situations. In particular, the cost-effectiveness of coronary revascularization strategies varies substantially according to a broad range of patient and anatomic factors as well as the specific characteristics of the local health care environment. Nonetheless, data from clinical trials, observational studies, and carefully constructed disease-simulation models have demonstrated a number of important principles in this regard.

One general principle is that the cost-effectiveness of coronary revascularization varies with a number of patient-related factors including age, symptom level, extent of CAD, and degree of underlying ischemia. For patients with chronic CAD, PCI clearly leads to modest improvements in QoL (angina relief). Nonetheless, compared with aggressive medical therapy, the extent of benefit is relatively modest and time-limited (2-3 years). Formal economic analyses suggest that the cost-effectiveness of an initial PCI approach is relatively unfavorable and that a compromise approach of initial medical therapy followed by PCI for patients whose symptoms persist at an unacceptable level can provide a reasonable balance between clinical benefit to the individual and economic value to society.

For patients with multivessel disease (where the decision is related mainly to the type of revascularization rather than whether to revascularize or not), CABG was traditionally the favored approach given improved angina relief, the suggestion of improved survival for high-risk patient subsets (such as patients with diabetes), and comparable long-term costs. However, recent data suggest that with the development of drug-eluting stents, the balance may now favor DES for patients with 3-vessel and left main disease with less complex anatomy (eg, SYNTAX score < 33), whereas bypass surgery remains favored on both clinical and economic grounds for patients with more extensive disease and highly complex anatomy.

Finally, it is important to recognize that the results of economic analyses are not static. Similar to clinical

guidelines, the insights derived from cost-effectiveness analyses require continuous updating because of improvements in both medical care and procedural outcomes as well as changes in the costs of resources over time. Despite these limitations, cost-effectiveness analysis serves an important goal of providing a formal analytic framework for balancing the costs of therapies with their clinical benefits and thus helping to meet the challenge of continuing to improve health outcomes and the quality of care in the face of increasingly scarce health care resources. ■

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Main Points

- Recent clinical trials of alternative management strategies for chronic coronary artery disease (CAD), along with rising health care costs, have set the stage for a closer inspection of economic data with respect to the benefit of revascularization strategies.
- The main findings of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluations (COURAGE) trial were that total in-trial costs were $34,843 for the percutaneous coronary intervention (PCI) plus optimal medical therapy (OMT) group and $24,718 for the OMT-only group.
- The most important limitation of the COURAGE trial is whether its results can be readily extrapolated to the overall population with chronic CAD.
- In the Bypass Angioplasty Revascularization Investigation (BARI) trial, initial medical care costs were 35% lower with percutaneous transluminal coronary angioplasty than with bypass surgery ($21,113 vs $32,347). By the end of 5 years of follow-up, however, these cost savings diminished to 5% (due to need for repeat revascularization).
- Preliminary data from the Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trial suggest that by further reducing the incidence of restenosis, drug-eluting stents may have achieved the goal of matching the clinical benefits of coronary artery bypass grafting (CABG) with a less invasive and less costly procedure—at least for certain patients with 3-vessel and left main disease.
- The Angina With Extremely Serious Operative Mortality Evaluation (AWESOME) trial demonstrated that for patients with refractory angina who are at high risk of CABG-related complications, PCI is the preferred management strategy on *both* clinical and economic grounds.

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