

Abciximab provides cost-effective survival advantage in high-volume interventional practice

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Background Placebo controlled randomized trials of platelet glycoprotein (GP) IIb/IIIa blockade during percutaneous coronary intervention have demonstrated efficacy of these agents for reducing the risk of peri-procedural ischemic events. However, cost-effectiveness of this adjunctive pharmacotherapy has been scrutinized. Extrapolation of cost efficacy observations from clinical trials to “real world” interventional practice is problematic.

Methods Consecutive percutaneous coronary interventions (n=1472) performed by Ohio Heart Health Center operators at The Christ Hospital, Cincinnati, Ohio in 1997 were analyzed for procedural and long-term (6 month) outcomes and charges. Observations on cost and efficacy (survival) were adjusted for non-randomized abciximab allocation using “propensity scoring” methods.

Results Abciximab therapy was associated with a survival advantage to six months following percutaneous coronary intervention. The average reduction in mortality at 6 months was 3.4% (unadjusted) and 4.9% when adjusted for nonrandomization. The average charge increment to 6 months was \$1,512 (unadjusted) and \$950 when adjusted for nonrandomization. Patients deriving the greatest reduction in mortality also had a reduction in total cardiovascular charges to 6 months. Distinguishing demographics of this population included multi-vessel coronary intervention, coronary stent deployment, intervention within one week of myocardial infarction and lower left ventricular ejection fraction. The average cost per life year gained in this study was \$2,875 for all patients (unadjusted) and \$1,243 when adjusted for nonrandomization.

Conclusions Abciximab provides a cost effective survival advantage in high volume interventional practice which compares favorably with currently accepted standards. Clinical and procedural demographics associated with increased cost-effectiveness included multi-vessel coronary intervention, stent deployment, recent (<1 week) myocardial infarction and impaired left ventricular function.

Plaque rupture, platelet aggregation and thrombus formation are integrally involved in the pathogenesis of ischemic complications following percutaneous coronary intervention (PCI).^{1,2} The central role of the platelet in this process is underscored by the observation that therapy with aspirin can reduce the incidence of death or myocardial infarction among patients undergoing PCI.³ However, pro-coagulant activities resistant to standard doses of aspirin and unfractionated heparin persist following PCI and abrupt coronary closure still complicated 4-8% of PCI procedures prior to the advent of platelet glycoprotein (GP) IIb/IIIa receptor blockade.^{5,6} Multiple placebo controlled randomized trials of platelet GP IIb/IIIa blockade

administered during PCI have demonstrated unequivocal efficacy of these agents for reducing the risk of important peri-procedural ischemic events.⁷⁻¹¹ In this era of rising medical costs and increasing concern for cost containment, adjunctive platelet GP IIb/IIIa blockade has been scrutinized with respect to cost-effectiveness. The clinical benefit attributable to GP IIb/IIIa blockade must justify the net cost increment of therapy. In addition, the cost increment of administering GP IIb/IIIa therapy may be counter-balanced by cost decrements related to a reduced hospital length of stay and/or incidence occurrence of costly adverse clinical outcomes.¹²⁻¹⁶ This relationship is confounded by variability in patient acuity which may influence both the risk for

adverse outcomes as well as the magnitude of benefit from platelet GP IIb/IIIa therapy¹⁷ in patients undergoing PCI. Adverse events (bleeding, transfusion) related to adjunctive pharmacotherapy are also associated with incremental costs which must be included in the equation for net cost of treatment.^{13, 18}

The three currently available intravenous GP IIb/IIIa blockers have been studied in large-scale trials involving PCI with prospective economic analyses.^{12,13,18,19} However, extrapolation of cost-efficacy observations derived from these randomized controlled trials to “real world” cost-effectiveness can be problematic. For instance, randomized trials designed to determine efficacy of an adjunctive pharmacologic therapy, frequently exclude “higher risk” subsets of patients and may “protocol drive” practice pattern with pre-specified hospital lengths of stay. In addition, the yearly procedural volumes of interventional operators participating in many multi-center studies are widely discrepant. The purpose of the present study is to analyze the impact of adjunctive pharmacotherapy with abciximab platelet GP IIb/IIIa blockade during PCI on costs and clinical outcomes in a high-volume interventional practice.

Methods

Study Population

From 1/1/97 through 12/31/97, 1472 consecutive PCI procedures were performed on 1305 patients by Ohio Heart Health Center (OHHC) operators at The Christ Hospital in Cincinnati, Ohio. At the time of study, OHHC was a 26-man cardiology group with eight dedicated interventionists, all of whom performed at least 200 PCI's in 1997; the average was 280 PCI/operator. Although OHHC operators performed PCI at five Cincinnati hospitals in 1997, the present study describes only procedures performed at The Christ Hospital. Patient demographics and procedural data were prospectively collected by the interventional physician using a modified Summit database. Hospital outcomes and length of hospital stay were prospectively collated by nurses from the Quality Assurance Department of The Christ Hospital. Hospital charges were obtained from the McKesson/HBOC TrendStar decision support software system. Variables specifically assessed by the modified Summit Database included death, new Q-wave MI, urgent revascularization (PCI or coronary bypass surgery), major bleeding (intracranial, retroperitoneal or requiring

transfusion), transfusion (packed red blood cells, platelets, fresh frozen plasma) regardless of indication; vascular repair and pseudoaneurysm. Finally, Lindner Center staff made personal telephone contact with 1011 patients and/or their families to collect extensive follow-up information to 6 months following the index PCI procedure.

Statistical analysis

Standard t-tests and contingency table likelihood ratio tests were used to detect (unadjusted) treatment differences in measures of patient acuity and demographic characteristics as well as, in cost and effectiveness outcomes. Since assignment to abciximab treatment was not random at OHHC in 1997, “propensity scoring” methods²⁰ were used to estimate treatment differences “adjusted” for observed imbalances in patient acuity and demographic characteristics between treatment groups. The propensity score represents the estimated probability of abciximab use during the index PCI procedure derived from a regression model that included 15 patient characteristics (Appendix). The basic concept of propensity scoring is that outcome differences (abciximab treated minus non-abciximab treated) are computed only for patients who are “well matched” and grouped into “bins” on acuity and demographic characteristics. There was no within-bin covariate imbalance significant at the 0.05 level for any of the 15 covariates analyzed.

Adjustment for nonrandomization

To adjust for nonrandomization in this observational study, the following four steps²⁰⁻²² were taken: (1) A logistic regression model was constructed to predict the probability (propensity score) that a patient with specified characteristics would have received abciximab by OHHC in 1997. (2) All 1,011 patients followed to six months were sorted by estimated propensity score into five adjacent bins, each containing 202 or 203 patients. Bin 1 contains the 202 patients least likely to receive abciximab, while Bin 5 contains the 202 patients most likely to receive abciximab. (3) An average difference (abciximab treated minus non-abciximab treated) in cost (charge) or effectiveness (survival) was calculated within each bin. (4) An overall difference in cost or effectiveness was then calculated as a weighted average of within-bin differences, with weights proportional to sample size.

Incremental cost-effectiveness ratio

An incremental cost effectiveness ratio (ICER), expressed as a cost per life-year gained, was calculated as follows: ICER = difference in cost (abciximab minus non-abciximab) divided by the corresponding difference in effectiveness. For the purpose of these calculations, the assumptions were: (1) cost = charges x 0.75, and (2) survival from 6 months implies an additional life-expectancy of 14 years, which are then discounted at 3%/year to yield 11.6 discounted years.^{23,24} ICER statistics were calculated for specific patient subsets (all, diabetic, non-diabetic, stent patients) using both unadjusted and adjusted (for lack of randomization) cost and survival differences. Uncertainty in ICER estimates was quantified by bootstrapping, which is a nonparametric analysis that literally redoes a study thousands of times by re-sampling (with replacement) from cost and effectiveness outcome pairs observed on individual patients.

Results

Patient and procedural demographics for 1472 consecutive PCI procedures involving 1338 patients in 1997 are shown in Table 1. Abciximab was administered during 986 procedures (70%). Abciximab-treated patients were slightly less often diabetic or hypertensive. Patients receiving abciximab were much more likely to have incurred a myocardial infarction within 30 days, or particularly 1-7 days prior to PCI. Furthermore, abciximab-treated patients had lower left ventricular ejection fractions, more coronary stenoses and coronary vessels undergoing intervention (more extensive revascularization procedure) and were more likely to have a coronary stent deployed. Abciximab was more commonly administered to patients undergoing a "first time" PCI compared with those having a repeat PCI procedure. Multivariate logistic regression analysis identified the number of vessels intervened during the index PCI, stent deployment, lower left ventricular ejection fraction and myocardial infarction within seven days prior to PCI as highly significant predictors of abciximab administration (Table 2). The presence of diabetes was a significant negative predictor for abciximab therapy. Despite the demographic profile of abciximab treated patients, a significant survival advantage was observed at six months follow-up in favor of abciximab therapy for all PCI patients, and especially for patients who had coronary stent deployment (figure 1).

No difference in major bleeding or transfusion between abciximab and non-abciximab treated patients was observed (figure 2).

Results of adjustment for covariate imbalance

Counts of patients by propensity score bin and abciximab treatment assignment are depicted in figure 3. The average reduction in mortality at six months attributed to abciximab therapy of 3.4% (unadjusted) became 4.9% when adjusted for nonrandomization (figure 4). The average charge increment to six months following abciximab therapy of \$1,512 (unadjusted) was reduced to \$950 when adjusted for nonrandomization (figure 5). The greatest reduction in mortality to six months was observed within bin 5. These patients also experienced a reduction in total cardiac charges within bin 5 when abciximab versus non-abciximab treated patients of similar acuity are compared. The distinguishing demographics of bin 5 patients are shown in Table 3 and include more frequent multi-vessel PCI, coronary stent deployment, PCI within one week of a myocardial infarction and lower left ventricular ejection fractions. Interestingly, bin 5 patients were among the least likely to be diabetic in 1997.

Cost-effectiveness of abciximab in interventional practice

The incremental cost effectiveness ratios (cost per life year gained) based on the observed survival advantage to six months attributed to abciximab are shown (unadjusted and adjusted for lack of randomization) for specific patient subsets in figure 6. The average cost per life year gained in this study of \$2,875 for all patients (unadjusted) became \$1,243 when adjusted for nonrandomization.

The bootstrap distribution for (unadjusted) cost and effectiveness outcome differences (abciximab treated minus non-abciximab treated) as well as a 95% confidence interval for the true ICER for all patients followed to 6 months is shown in Figure 7.

Comparison with contemporary clinical trials

The cost per life year gained based on one year (1.4%) survival advantage attributed to abciximab in stented patients from the EPISTENT randomized controlled trial is \$6,213.¹⁵ The \$6,213 value exceeds the \$5,193 (unadjusted) or \$1,933 (adjusted) cost per life year gained values following coronary stent deployment in the present observational study based on 3.4% (average) survival advantage at 6 months for abciximab treated patients.

This compares favorably to the absolute percentage survival advantage observed in favor of abciximab therapy in stented patients at 6 months (0.7%) and 1 year (1.4%) in the EPISTENT trial.²⁶ The greater efficacy (enhanced survival) attributable to abciximab in the present series may in part be explained by the greater acuity of patients in high volume interventional practice. More specifically, patients treated in practice were older, more often women, hypertensive, active smokers and had a higher incidence of recent myocardial infarction and more frequent requirement for multi vessel PCI (table 4). Although data regarding left ventricular function from EPISTENT are not adequate to allow comparison, EPISTENT excluded patients in cardiogenic shock or those with evolving acute myocardial infarction from enrollment. In the current series, 5.6% of patients had profound depression ($\leq 30\%$) in left ventricular ejection fraction and patients with evolving infarction were also included in the analysis. It would appear that incremental drug costs are similar and greater cost-effectiveness for abciximab in clinical practice is driven by a more pronounced survival advantage.

In comparison, the recently published economic analysis from the RESTORE placebo-controlled randomized trial of tirofiban therapy during PCI demonstrated identical cost (\$12,402 placebo versus \$12,446 tirofiban) to 30 days in both treatment arms.¹⁹ Although follow-up was reported only to 30 days, mortality was similar (0.6% placebo, 0.9% tirofiban) as was the occurrence of composite ischemic endpoints (death, myocardial infarction, repeat PCI or surgery and unplanned stent deployment) in 17.1% of placebo and 14.4% of tirofiban treated patients ($p=0.10$).^{11,19} The cost of tirofiban was estimated at \$700 (\$350/vial x 2 vials) per patient treated in this trial.¹⁹

Discussion

This study demonstrates cost-effectiveness of adjunctive abciximab therapy for PCI in high volume interventional practice. The significance of this finding lies in its direct applicability to clinical practice, outside the arbitrary, protocol-driven confines of randomized controlled trials. Acknowledging the inherent limitations to interpretation of data derived from an observational study such as ours, several important points can be made. First, abciximab therapy is associated with a survival advantage in high volume interventional practice. This observation parallels that of recently published meta-analyses²⁷ and pooled analyses²⁸ of

multiple randomized trials of abciximab therapy during PCI, as well as a survival advantage demonstrated in the EPISTENT randomized controlled trial in favor of abciximab administration in stented patients.²⁶ The majority of these clinical trials have excluded patients undergoing multi-vessel PCI or those with severely impaired left ventricular function, evolving or recent myocardial infarction and serious co-morbid conditions. Therefore, the direct relevance of observations derived from these trials to “real world” high volume interventional practice (without arbitrary exclusions) is unknown. This study, for the first time, provides observational data on a large group of consecutive patients undergoing PCI who were followed to six months. In this population, the magnitude of survival advantage demonstrated in favor of adjunctive abciximab therapy during PCI by prior clinical trials appears to be magnified, particularly after adjustment for lack of randomization.

Secondly, abciximab provides a survival advantage during PCI performed by high volume operators. Adverse outcomes following PCI have been inversely correlated with individual operator procedural volumes.²⁹⁻³¹ In general, the highest volume operators (≥ 200 PCI's/year) in the highest volume institutions (≥ 400 PCI's/year) have the lowest rates of death or urgent revascularization. Prior multi-center studies of abciximab during PCI have not been limited to high-volume operators or institutions as represented in the present series. All operators in our study performed >200 PCI's/year (average 280/operator in 1997). Thus, it appears that even high volume operators will have improved procedural outcomes following adjunctive abciximab therapy during PCI.

Thirdly, the survival advantage observed following abciximab therapy during PCI is highly cost-effective by current standards. Indeed, the ICERs (cost per life year gained) for adjunctive abciximab administration during PCI ranged from a high of \$5,193 (unadjusted) in stented patients to a low of \$617/year of life gained (adjusted for lack of randomization) in diabetic patients. These values are extremely cost-effective when viewed in the context of accepted therapeutic standards, such as coronary bypass surgery for left main coronary disease and severe angina (\$9,200) and rtPA therapy for evolving acute myocardial infarction (\$32,700/year of life gained).²⁵ Furthermore, the calculated ICERs for abciximab in high volume interventional practice fell below those derived from randomized controlled trials such as EPILOG or EPISTENT.^{13,15} For example, in the EPISTENT trial, the estimated cost

per life year gained (based on a one year survival advantage of 1.4%) was \$6,213.¹⁵ The greater cost-effectiveness of abciximab in interventional practice appears to be, at least in part, related to the acuity of the patient population and the complexity of PCI procedures. Patients in high volume interventional practice are older, have more co-morbid conditions including recent myocardial infarction, and undergo more extensive (multi-vessel, multi-lesion) revascularization (table 4). In this scenario, increased clinical acuity appears to be associated with enhanced benefit from abciximab therapy and greater cost-effectiveness. This observation is similar to that made from the three-year follow-up of the EPIC trial,³² where patients undergoing PCI for acute coronary syndromes (unstable angina, primary or rescue angioplasty for evolving myocardial infarction) had a significant survival advantage to three years following the index procedure. Similarly, in the recently reported pooled analysis of EPIC, EPILOG and EPISTENT, patients with acute coronary syndromes derived relatively greater benefit from adjunctive abciximab administration during PCI (hazard ratio = 0.7; p=0.05) than did their counterparts who presented with a more stable symptom complex.³³

Finally, the bootstrap distribution and 95% confidence interval for the incremental cost-effectiveness ratio³⁴ of abciximab therapy in all patients having PCI in high volume interventional practice demonstrates a relatively uniform effectiveness (survival) advantage as well as a more variable cost increment incurred by treatment (figure 7). Indeed, the confidence intervals allow for a cost savings in the context of still providing a survival advantage. This study, for the first time, provides “real world” information to define a patient sub-population which derives greatest benefit (enhanced survival) from abciximab therapy at a cost savings (reduction in total cardiac charges to six months). The distinguishing demographics of these patients (bin 5) included multi-vessel PCI and stent deployment within one week of myocardial infarction and depressed left ventricular function. Remarkably, bin 5 also contained among the lowest proportion of patients with diabetes mellitus. This under-representation of diabetics in the patient population with the greatest propensity for receiving abciximab during PCI reflects the practice pattern in 1997 prior to the availability of data supporting a distinct benefit of abciximab therapy in this population. Subsequent reports have demonstrated a more marked reduction in target vessel revascularization and late mortality following

coronary stent deployment in diabetic patients^{35,36} than observed in their non-diabetic counterparts following adjunctive abciximab therapy for PCI.³⁷ Thus, the cost-efficacy observed in “bin 5” patients from the present study occurred despite a relative under-representation of diabetic patients in this population.

This study demonstrates that adjunctive abciximab therapy during PCI provides a cost-effective survival advantage in high volume interventional practice. Cost effectiveness of abciximab therapy in practice compares favorably with currently accepted standards. Clinical and procedural demographics of patients most likely to benefit from abciximab therapy include multi-vessel PCI, stent deployment, recent (<1 week) myocardial infarction and depressed left ventricular function.

Study limitations

A key feature of the present study is its observational nature; patients were not randomly assigned to abciximab treatment during PCI by OHHC at The Christ Hospital in 1997. A sophisticated statistical analysis has been employed to address the acuity imbalance that resulted from this lack of randomization. These adjustments actually magnify the relative benefit in cost-effectiveness of abciximab that was observed. The difficulties and ethical questions associated with randomizing “all comers” in the context of clinical practice are obvious.

A second limitation involves patients who were lost to six month follow-up. Of 1,305 patients analyzed in this study, 294 patients were lost to follow-up at 6 months. These patients did not differ from patients included in follow-up by either abciximab or stent usage. Demographic factors predictive of loss to follow-up included increased height and body mass index, non-Caucasian race and reduced age (table 5). These demographic factors were not predictors of mortality or cost in the present database. Furthermore, if all 294 patients lost to follow-up are assumed to have survived more than six months, death rates would be reduced proportionately across abciximab and non-abciximab treated patients, leaving the main comparisons and conclusions unchanged. Thus, although failure to achieve 100% follow-up through six months may be viewed as a limitation, it is unlikely to have materially influenced our results.

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References

1. Steel PM, Chesebro JH, Stanson AW, Holmes DR, Dewanjee MK, Badimon L, Fuster V. Balloon angioplasty. Natural history of the pathophysiological response to injury in a pig model. *Circ Res* 1985; 57:105-112.
2. Uchida Y, Hasegawa K, Kawamura K, Shibuya I. Angioscopic observation of the coronary luminal changes induced by percutaneous transluminal coronary angioplasty. *Am Heart J* 1989; 117:769-776.
3. Schwartz L, Bourassa MG, Lesperance J, Aldridge HE, Kazim F, Salvatori VA, Henderson M, Bonan R, David PR. Aspirin and dipyridamole in the prevention of restenosis after percutaneous transluminal coronary angioplasty. *N Engl J Med* 1988; 318:1714-1719.
4. Gregorini L, Marko J, Fajadet J, Bernies M, Cassagneau B, Brunell P, Bossi IM, Mannucci PM. Ticlopidine and aspirin pretreatment reduces coagulation of platelet activation during coronary dilatation procedures. *J Am Coll Cardiol* 1997;29:13-20.
5. Ellis SG, Roubin GS, King SB III, Douglas JS, Jr., Weintraub WS, Thomas RG. Angiographic and clinical predictors of acute closure after native vessel coronary angioplasty. *Circulation* 1988; 77:372-9.
6. Scott NA, Weintraub WS, Carlin SF, Tao X, Douglas JS, Jr., Lembo NJ, King SB 3d. Recent changes in the management and outcome of acute closure after percutaneous transluminal coronary angioplasty. *Am J Cardiol* 1993; 71:1159-63.
7. The EPIC investigators. Use of a monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor in high risk coronary angioplasty. *New Engl J Med* 1994;330:956-961.
8. The EPILOG Investigators. Platelet glycoprotein IIb/IIIa receptor blockade and low-dose heparin during percutaneous coronary revascularization. 1997;336:1689-1696.
9. The EPISTENT investigators. Randomised placebo-controlled and balloon-angioplasty-controlled trial to assess safety of coronary stenting with use of platelet glycoprotein IIb/IIIa blockade. *Lancet* 1998;352:87-92.
10. The IMPACT- II Investigators. Randomised placebo-controlled trial of effect of eptifibatide on complications of percutaneous coronary intervention: IMPACT-II. *Lancet* 1997;349:1422-28.
11. RESTORE investigators - effects of platelet glycoprotein IIb/IIIa blockade with tirofiban on adverse cardiac events in patients with unstable angina or acute myocardial infarction undergoing coronary angioplasty. *Circulation* 1997;96:1445-1453.
12. Mark DB, Talley JD, Topol EJ, Bowman L, Lam LC, Jollis JG, Cleman MW, Lee KL, Aversano T, Untereker WJ, Davidson-Ray L, Califf RM, for the EPIC Investigators. Economic assessment of platelet glycoprotein IIb/IIIa inhibition for prevention of ischemic complications of high risk coronary angioplasty. *Circulation* 1996; 94:629-635.
13. Lincoff AM, Mark DB, Califf RM, Tchong JE, Ellis SG, Davidson-Ray L, Anderson K, Stoner GL, Topol EJ. Economic assessment of platelet glycoprotein IIb/IIIa receptor blockade during coronary intervention in the EPILOG trial. *J Am Coll Cardiol* 1997; 29:240A.
14. Lage MJ, Barber BL, Bowman L, et al. Shorter hospital stays for angioplasty patients who receive abciximab, *J Am Coll Cardiol* 1999; 33:286A (abstract).
15. Topol EJ, Mark DB, Lincoff AM, Cohen E, Burton J, Kleiman N, Talley D, Sapp S, Booth J, Cabot CF, Anderson KM, Califf RM, for the EPISTENT Investigators*. Outcomes at 1 year and economic implications of platelet glycoprotein IIb/IIIa blockade in patients undergoing coronary stenting: results from a multicenter randomised trial. *Lancet* 1999; 354:9195:2019-24.
16. Lundstrom RJ, Colby CJ, Jindeel A, Hay RL. Abciximab in unstable coronary syndromes: benefits and costs in a group model non-profit

- health maintenance organization. *J Am Coll Cardiol* 1999; 33:41A (abstract).
17. Roe MT, Gum PA, Booth JE, Jia G, Damaraju L, Fitzpatrick SE, Kereiakes DJ, Tchong JE. Consistent and durable reduction in death and myocardial infarction with abciximab during coronary intervention in acute coronary syndromes and stable angina: a pooled analysis from EPIC, EPILOG and EPISTENT. *Circulation* 1999; 100:I-187 (abstract).
 18. Mark DB. Economics of glycoprotein IIb/IIIa inhibition. In: Lincoff AM and Topol EJ, ed. *Platelet Glycoprotein IIb/IIIa Inhibitors in Cardiovascular Disease*, Totowa, New Jersey: Human Press, 1999:253-266.
 19. Weintraub WS, Culler S, Boccuzzi SJ, Cook JR, Kosinski AS, Cohen DJ, Burnette J. Economic impact of GPIIb/IIIa blockade after high-risk angioplasty. Results from the RESTORE Trial. *J Am Coll Cardiol* 1999;34:1061-1066.
 20. D'Agostino RB Jr. Tutorial in Biostatistics: Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat in Med* 1998, 17: 2265-2281.
 21. Rosenbaum PR, Rubin DB. Reducing bias in observational studies using subclassification on the propensity score. *J Am Stat Assoc* 1984;79:516-524.
 22. Obenchain RL. PSdefine(), PSdificov() and PSdifout(): S-PLUS functions for propensity score adjustment using bins. Download from the internet at URL <http://www.math.iupui.edu/~indyasa/download.htm> 1999.
 23. Mark DB, Hlatky MA, Califf RM, et al. Cost effectiveness of thrombolytic therapy with tissue plasminogen activator as compared with streptokinase for acute myocardial infarction. *New Eng J Med* 1995, 332:1418-1424.
 24. Lipscomb J, Weinstein MC, Torrence GW. Time preference. In: Gold MR, Siegel JE, Russell LB, et al, eds. *Cost-Effectiveness in Health and Medicine*. New York, NY: Oxford University Press, 1996, 214-246.
 25. Kupersmith J, Holmes-Rovner M, Hogan A, Rovner D, Gardiner J. Cost-Effectiveness Analysis in Heart Disease, Part III: Ischemia, Congestive Heart Failure, and Arrhythmias. *Progress in Cardiovascular Diseases*. XXXVII;5:307-346.
 26. Topol EJ, Mark DB, Lincoff AM, Cohen E, Burton J, Kleiman N, Talley D, Sapp S, Booth J, Cabot CF, Anderson K, Califf RM, on behalf of the EPISTENT Investigators. Outcomes at 1 year and economic implications of platelet glycoprotein IIb/IIIa blockade in patients undergoing coronary stenting: results from a multicentre randomised trial. *The Lancet* 1999;354:2019-2024.
 27. Anderson KM, Ferguson JJ, Stoner GL, Cabot CF, Weisman HF. Long-term mortality benefit with abciximab in patients undergoing percutaneous coronary intervention (PCI). *Circulation* 1997;96:I-63 (abstract).
 28. Bhatt DL, Lincoff AM, Califf RM, Simoons ML, Tchong JE, Brener SJ, Wolski KE, Topol EJ. The benefit of abciximab of interventional cardiology is not device-specific. *Am J Cardiol* (in press).
 29. Hannan EL, Racz M, Ryan TJ, et al. Coronary angioplasty volume-outcome relationships for hospitals and cardiologists. *JAMA* 1997;279:892-8.
 30. Ellis SG, Weintraub W, Holmes D, Show R, Block PC, King SB III. Relation of operator volume and experience to procedural outcome of percutaneous coronary revascularization at hospitals with high interventional volumes. *Circulation* 1997;96:2479-84.
 31. Jollis JG, Peterson ED, Nelson CL, et al. Relationship between physician and hospital coronary angioplasty volume and outcome in elderly patients. *Circulation* 1997;95:2485-91.
 32. Topol EJ, Ferguson JJ, Weisman HF, Tchong JE, Ellis SG, Kleiman NS, Ivanhoe RJ, Whang AL, Miller DP, Anderson KN, Califf RM. Long term protection from myocardial ischemic events in a randomized trial of brief integrin B3 blockade with percutaneous coronary intervention. *J Am Med Assn* 1997;278:479-484.

33. Roe MT, Gum PA, Booth JE, Jia G, Damaraju L, Fitzpatrick S, Kereiakes DJ, Tchong JE. Consistent and durable reduction in death and myocardial infarction with abciximab during coronary intervention in acute coronary syndromes and stable angina: a pooled analysis from EPIC, EPILOG and EPISTENT. *Circulation* 1999;100:I-187 (abstract).
34. Obenchain RL. Resampling and multiplicity in cost-effectiveness inference. *J Biopharm Stat* 1999, 9:563-582.
35. Lincoff AM, Moliterno DJ, Ellis SG, Debowey D, Cabot CF, Booth JE, Godfrey NK, Topol EJ. Six month angiographic outcome with abciximab and stents: the EPISTENT angiographic substudy. *Circulation* 1998;98:I:768.
36. Lincoff AM, Califf RM, Moliterno DJ, Ellis SG, Ducas J, Kramer JH, Kleiman NS, Cohen EA, Booth JE, Sapp SK, Cabot CF, Topol EJ, for the Evaluation of Platelet IIb/IIIa Inhibition in Stenting Investigators. Complementary clinical benefits of coronary-artery stenting and blockade of platelet glycoprotein IIb/IIIa receptors. *New Engl J Med* 1999;341:319-327.
37. Bhatt DL, Marso SP, Lincoff AM, Wolski KE, Ellis SG, Topol EJ. Abciximab reduces death in diabetics following percutaneous coronary intervention. *Circulation* 1999;100:I-67 (abstract).

Appendix

Propensity Score Variables

Patient characteristics included in the propensity score included continuous measures (age, height, left ventricular ejection fraction and number of coronary vessels intervened at the index procedure) and “indicator” (0=no; 1=yes) variables (female gender; black race; prior Q-wave myocardial infarction; diabetes; hypertension; current smoker; recent myocardial infarction [evolving \leq 24 hours; acute 1-7 days; or recent \leq 30 day] and stent use).

Table 1: Patient and Procedural Demographics for 1472 Consecutive Percutaneous Coronary Intervention

(n)	Abcix (986)	No Abcix (486)	P-value
Age yrs (\pm SE)	61.4 \pm 0.38	61.3 \pm 0.54	0.96
Weight Kg (\pm SE)	84.9 \pm 0.60	84.7 \pm 0.86	0.84
% Female	34.1	36.4	0.38
% Diabetics	21.0	25.9	0.03
% Hypertension	70.2	76.3	0.01
% Smoke	58.0	58.2	0.88
% MI \leq 30 Days	31.8	20.8	<0.0001
1-7 Days	17.3	5.8	.0001
\leq 1 Day	13.1	12.7	
LVEF % (\pm SD)	50.7 \pm 0.35	52.1 \pm 0.50	0.03
# Stenoses Rx			
1 (%)	62.3	80.4	
\geq 2 (%)	37.2	19.6	<0.0001
# Vessels Rx			
2 (%)	27.9	15.8	
3 (%)	6.0	1.4	
4 (%)	1.7	0.2	<0.0001
% Stent	69.5	60.0	<0.0001
% First Procedure	93.7%	79.2%	<0.0001

(MI=Myocardial Infarction; LVEF=Left Ventricular Ejection Fraction)

Table 2: Most Significant Predictors of Abciximab Use by Multivariable Logistic Regression

	Coefficient	Std Error	p-value
Stent	0.550	0.150	0.0003
Diabetes	-0.377	0.173	0.03
MI <7 Days	1.830	1.041	0.07
LVEF	-0.0181	0.00785	0.02
# Vessels PCI	0.755	0.138	<0.0001

(MI=Myocardial Infarction; LVEF=Left Ventricular Ejection Fraction; PCI=Percutaneous Coronary Intervention)

Table 3: Distinguishing Demographics by Propensity Score Bin

	BIN 1	BIN 2	BIN 3	BIN 4	BIN 5
Total Patients	202	202	203	202	202
Abciximab Patients	110	125	132	161	182
Proportion Stent	0.21	0.74	0.82	0.76	0.80
Proportion Acute MI (<7 days)	0.00	0.00	0.02	0.14	0.56
Number of Vessels PCI	1.00	1.07	1.17	1.64	2.06
Ejection Fraction	54.31	53.57	51.59	48.80	46.41
Proportion Diabetic	0.42	0.24	0.09	0.24	0.14

(MI=Myocardial Infarction; PCI=Percutaneous Coronary Intervention)

Table 4: Comparative Demographics for PCI Patients

	EPISTENT (n=2374)	Lindner/OHHC (n=1011)
Mean age	59.5	62.5
Diabetic	20.5%	22.5%
Male gender	75%	65%
Smokers	36.6%	57.4%
Hypertension	52.5%	72.0%
Myocardial infarction		
≤ 12 hrs	1%	14.5%
≤ 7 days	16.4%	26.9%
# Native vessels attempted		
1	2103 (88.6%)	688 (68.1%)
2	197 (8.3%)	257 (25.4%)
≥ 3	7 (0.3%)	62 (6.1%)

OHHC = Ohio Heart Health Center

Table 5: Comparative Demographic Proportions for Patients by Follow-up Status

	No Follow-up (n=294)	Follow-up (n=1011)
ReoPro	0.721	0.702
Stent	0.690	0.668
Gender (Female)	0.354	0.348
Height*	172.4	171.4
Weight	86.03	84.64
Body Mass Index*	28.82	28.81
Race (Black)*	0.041	0.013
Age*	57.83	62.45
Diabetes	0.228	0.225
Hypertension	0.663	0.720
Current Smoking	0.619	0.574
Prior Q-Wave MI	0.003	0.003
Major Bleed	0.003	0.008
Transfusion	0.010	0.009
Acute MI (All)	0.354	0.282
≤7 Days	0.156	0.145
<24 Hrs	0.170	0.124
<30 days	0.014	0.008
# Coronary Lesions Intervened	1.248	1.304
LV Ejection Fraction	50.224	50.937

*p <0.05

MI = Myocardial Infarction; LV = Left Ventricular

FIGURE LEGENDS

Figure 1: Mortality (percent) in hospital and to six months following percutaneous coronary intervention by Ohio Heart operators at The Christ Hospital in 1997. Data are shown for all interventions and for patients having coronary stent deployment.

Figure 2: Incidence occurrence of major bleeding and transfusion in hospital for all interventions and for patients having coronary stent deployment by pharmacologic treatment strategy.

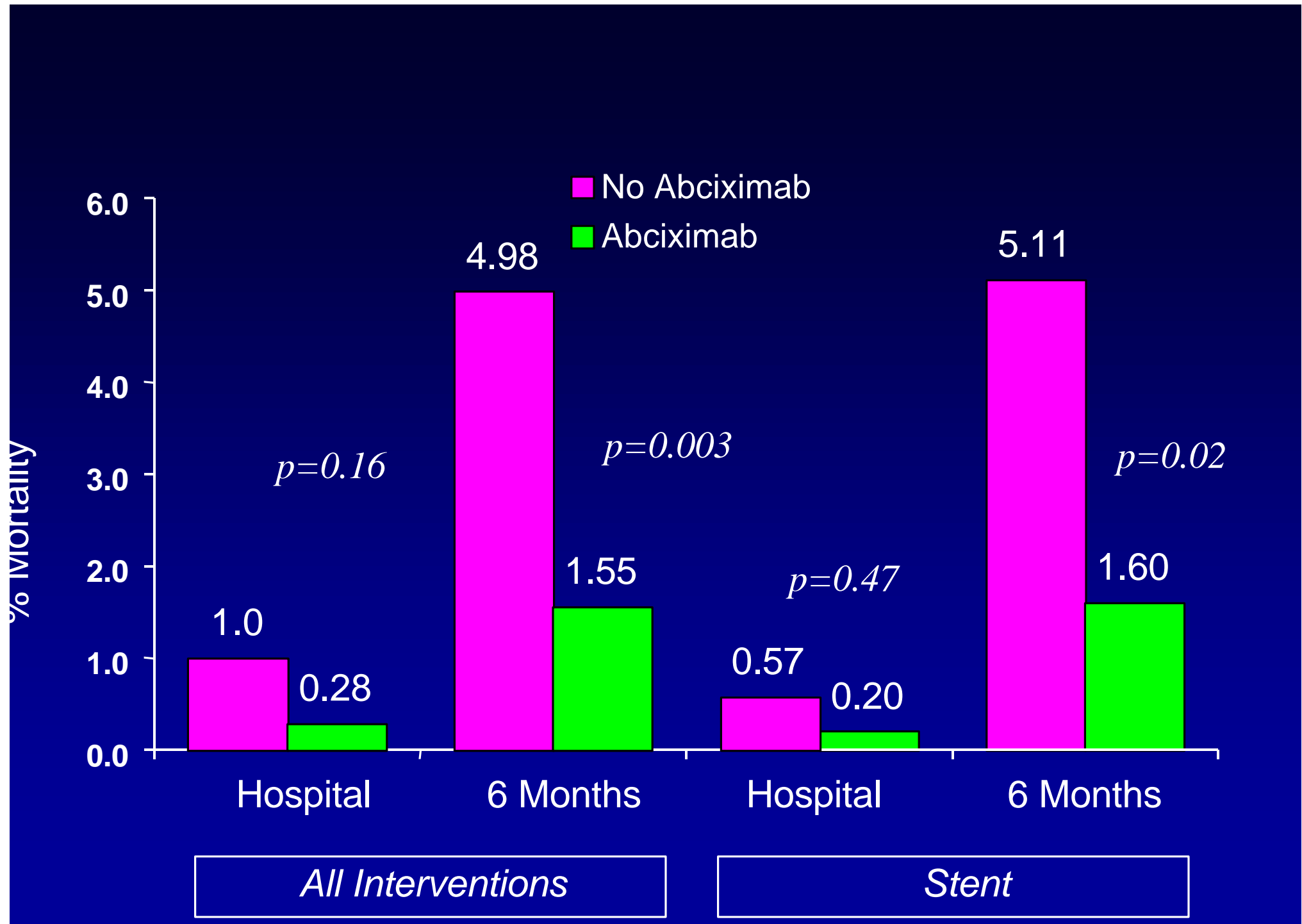
Figure 3: Patient counts by propensity score bin and abciximab treatment assignment. Patients in bin 1 were least likely to receive abciximab, while those in bin 5 were most likely to be administered abciximab by OHHC at Christ Hospital in 1997.

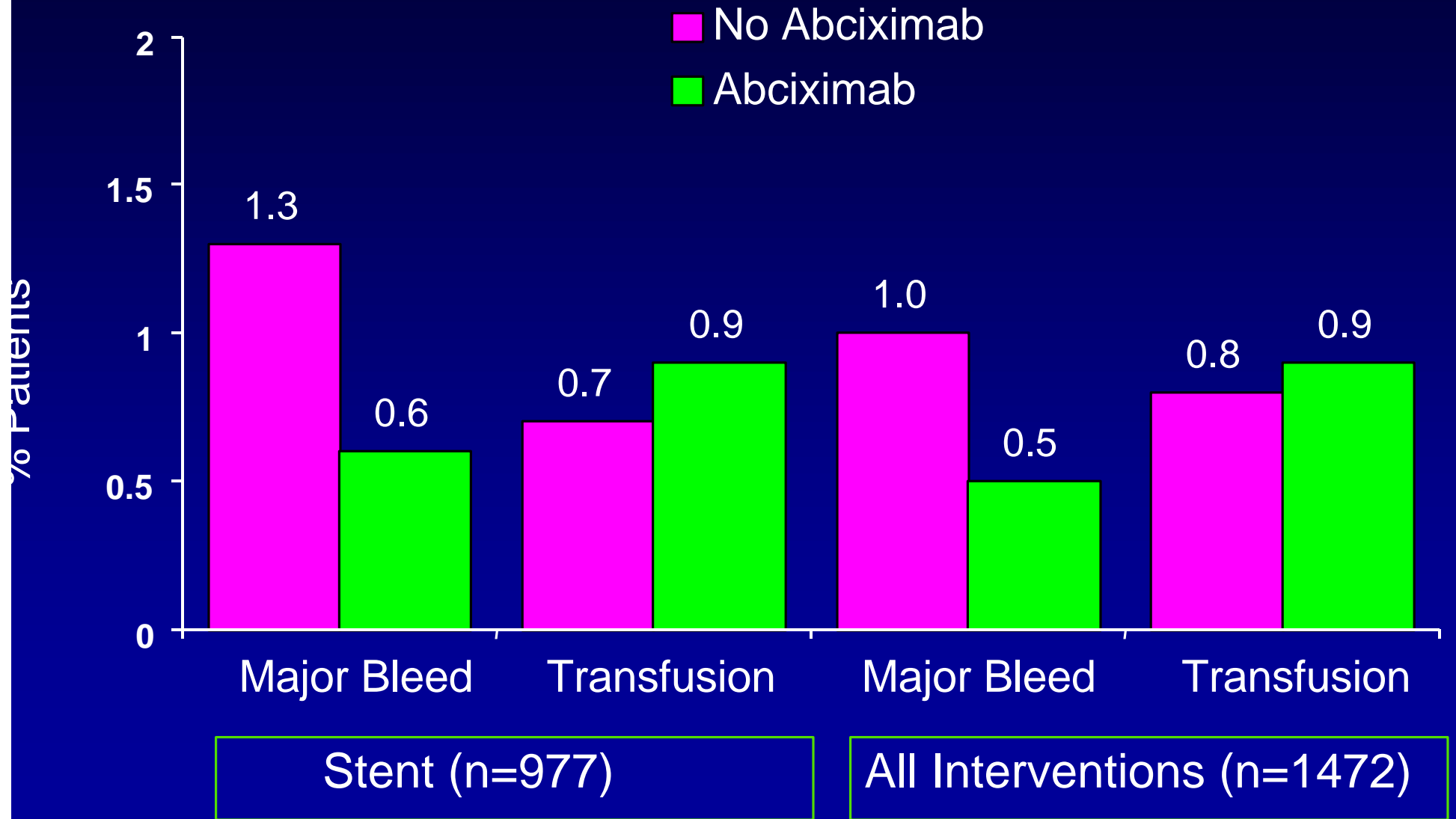
Figure 4: Mortality by propensity score bin and abciximab treatment assignment.

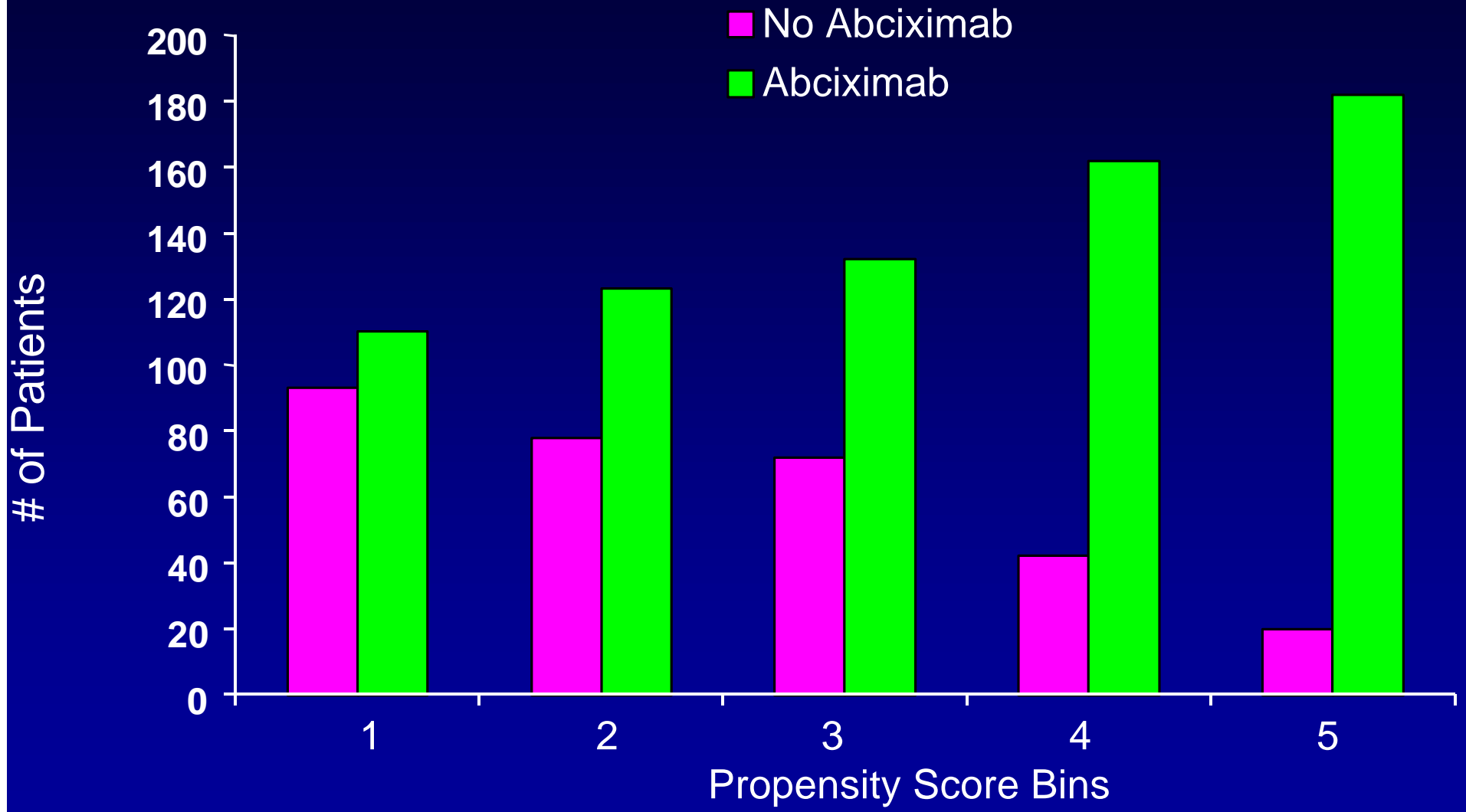
Figure 5: Cardiac charges to six months by propensity score bin and abciximab treatment assignment.

Figure 6: Incremental cost effectiveness ratios by patient subsets unadjusted and adjusted (for lack of randomization).

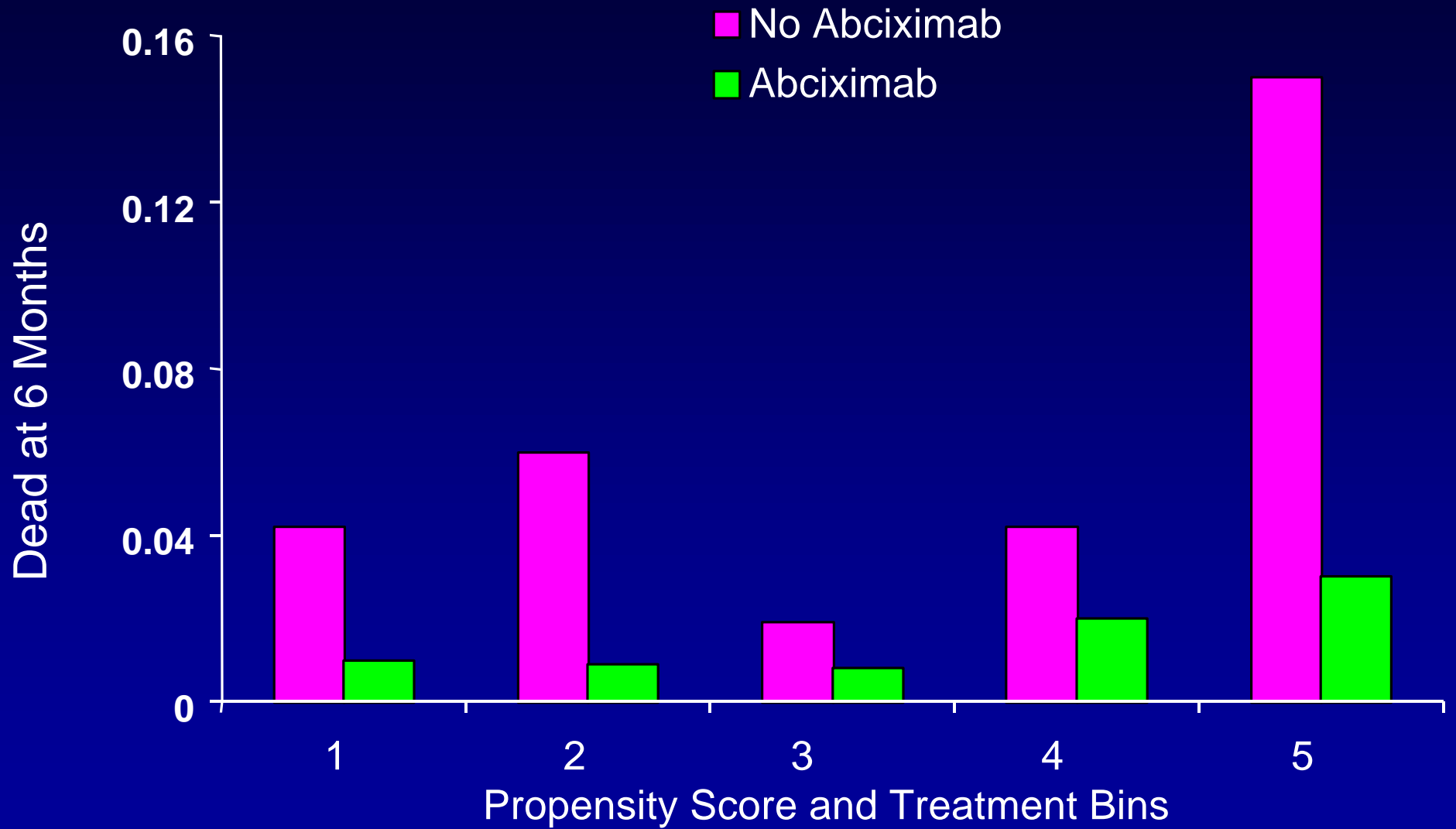
Figure 7: Bootstrap distribution of average cost and effectiveness outcome differences (abciximab treated minus non-abciximab treated) and a 95% confidence interval of (-1153, +8191) for cost per life year gained for all patients followed to six months following percutaneous coronary intervention. Only 1,000 bootstrap replications are shown here, but 5.8% of the 25,000 bootstrap replications performed yielded a negative cost difference (reduced total cost due to abciximab treatment).



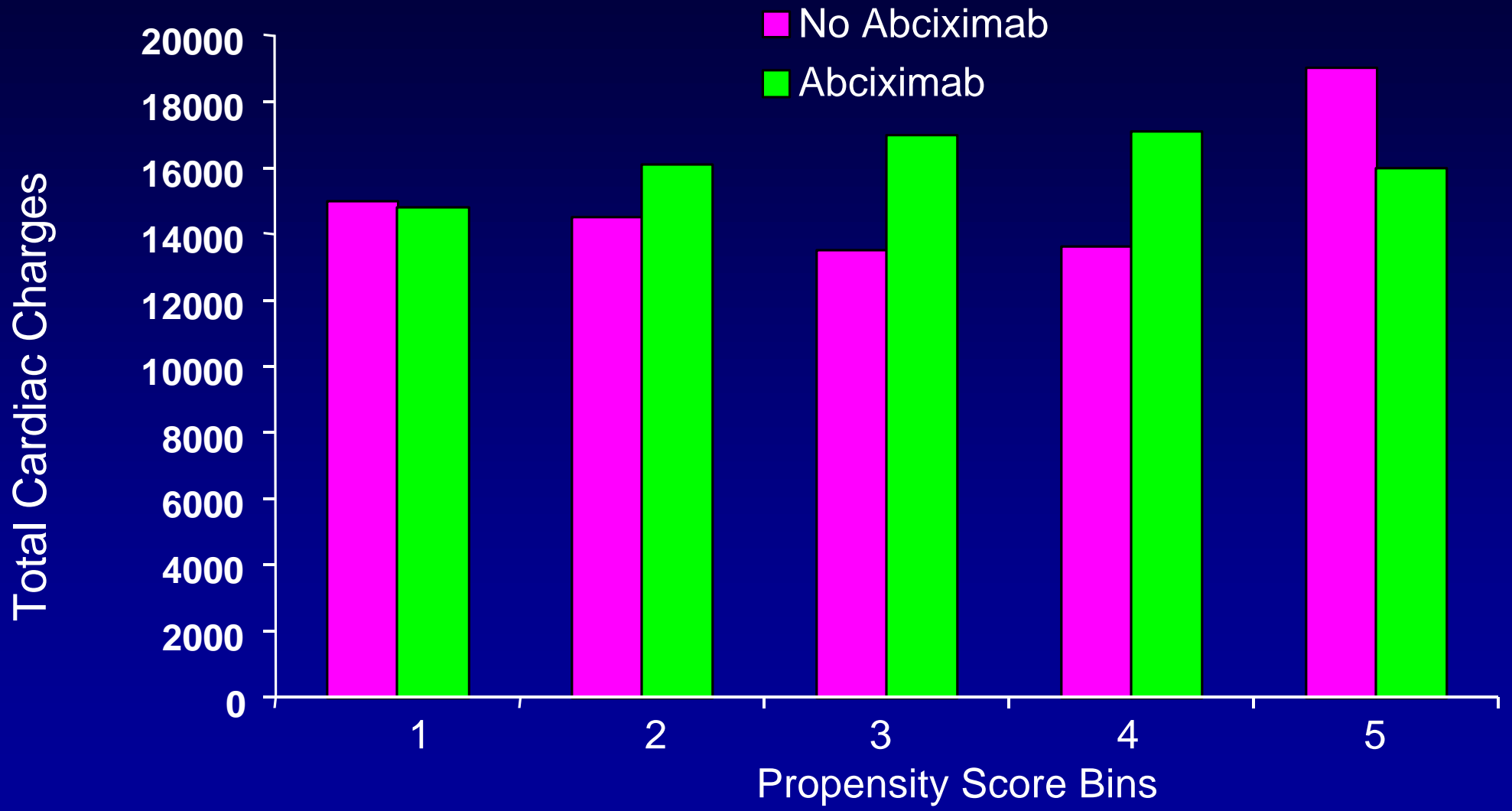




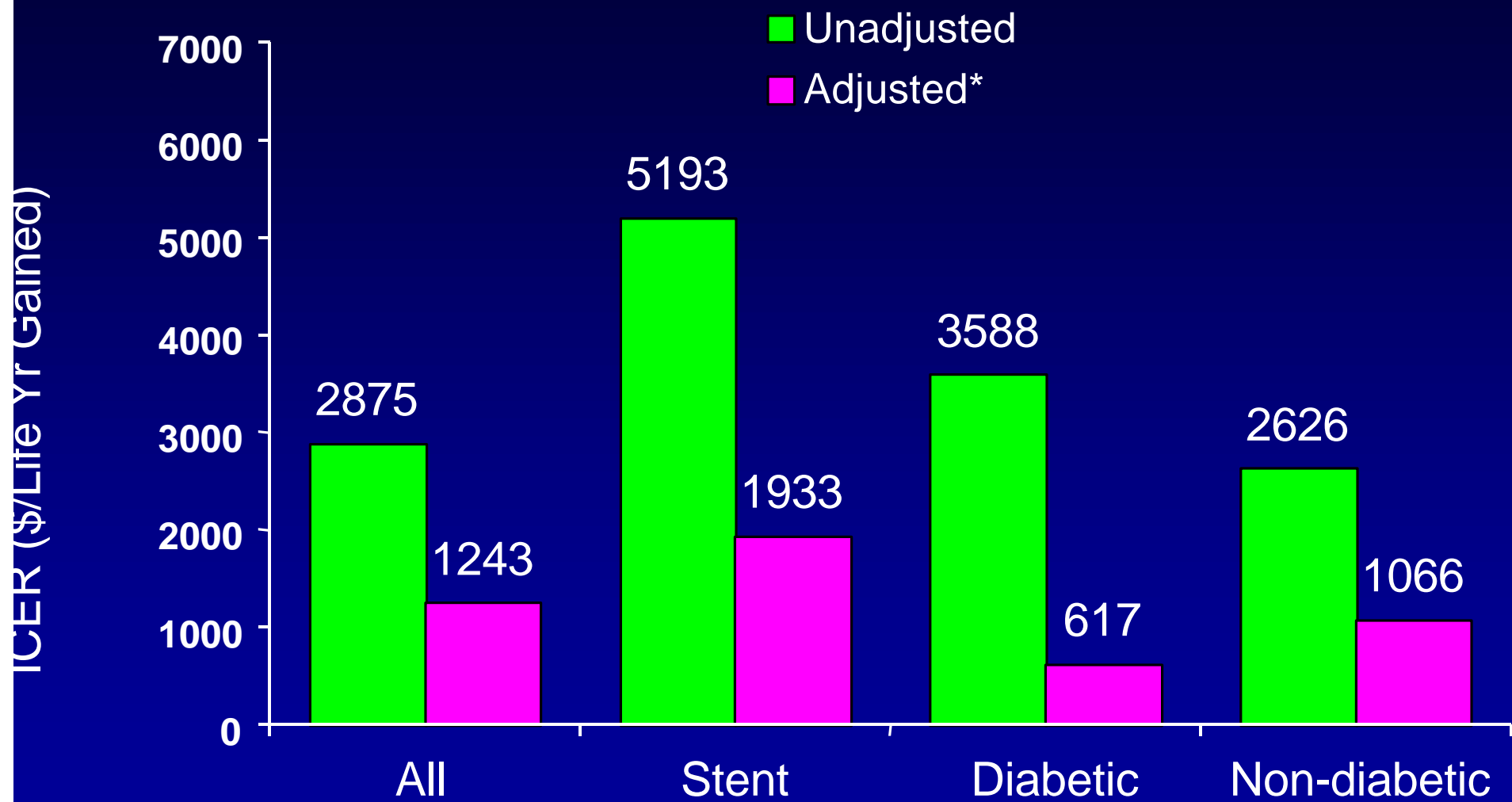
Matched = equal predicted probability of receiving abciximab



Average Reduction: 3.4% (adjusted to 4.9%)



Average charge increment: \$1,512 (adjusted to \$950)



for non-randomization

