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Clinical Effectiveness of Coronary Stents in the Elderly:

Results From 262,700 Patients in the American College of Cardiology-National Cardiovascular Data Registry

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Abstract

Objective: To compare outcomes in older individuals receiving drug-eluting (DES) and bare metal stents (BMS).

Background: Comparative effectiveness of DES relative to BMS remains unclear.

Methods: Outcomes were evaluated in 262,700 patients from 650 National Cardiovascular Data Registry sites during 2004-2006 using procedural registry data linked to Medicare claims for follow-up. Outcomes including death, myocardial infarction (MI), revascularization, major bleeding, stroke, death or MI, death or MI or revascularization, and death or MI or stroke, were compared using estimated cumulative incidence rates with inverse probability weighted estimators and Cox proportional hazards ratios.

Results: DES were implanted in 217,675 patients and BMS in 45,025. At 30-months, DES patients had lower unadjusted rates of death (12.9% vs. 17.9%), MI (7.3 vs. 10.0/100 pts) and revascularization (23.0 vs. 24.5/100 pts) with no difference in stroke or bleeding. After adjustment, DES patients had lower rates of death (13.5% vs. 16.5%, HR=0.75, (95% CI: 0.72, 0.79), $p < 0.001$) and MI (7.5 vs. 8.9/100 pts, HR=0.77, (95% CI: 0.72, 0.81), $p < 0.001$), with minimal difference in revascularization (23.5 vs. 23.4/100 pts; HR=0.91, (95% CI: 0.87, 0.96), stroke (3.1 vs. 2.7/100 pts, HR=0.97, (95% CI: 0.88, 1.07) or bleeding (3.4 vs. 3.6/100 pts, HR=0.91, (95% CI: 0.84, 1.00)). The DES survival benefit was observed in all subgroups analyzed and persisted throughout 30-months' follow-up.

Conclusion: In this largest ever real-world study, patients receiving DES had significantly better clinical outcomes than their BMS counterparts, without an associated increase in bleeding or stroke, throughout 30 months' follow-up and across all pre-specified subgroups.

Introduction

The dramatic reductions in restenosis and repeat revascularization associated with drug-eluting coronary artery stents (DES) compared with their bare metal (BMS) counterparts,¹ prompted swift adoption into clinical practice.² However, reports of late stent thrombosis^{3,4} and higher mortality^{5,6} resulted in release of two special FDA advisories in 2006,^{7,8} as well as subsequent studies refining event rates.^{1,6,9-13} The rarity of late DES complications means that extremely large sample sizes are required to clarify their frequency. Furthermore, the ability to examine rates of lower frequency complications in important patient subgroups is limited in smaller sample sizes.¹⁴

Accordingly, the Agency for Healthcare Research and Quality (AHRQ) and US Food and Drug Administration (FDA) commissioned the formation of a nationally-representative PCI database to determine the safety and effectiveness of DES and BMS among a contemporary ‘real world’ cohort. This was accomplished through linkage of the American College of Cardiology National Cardiovascular Data Registry (ACC-NCDR[®]) with the Centers for Medicare and Medicaid Services (CMS) national claims database. The resulting analyses will better inform national practice patterns overall and in important patient and lesion-level subgroups.

Methods

Study Population

The national ACC-NCDR[®] CathPCI Registry collects information for patients undergoing percutaneous coronary intervention (PCI) procedures. We included all CathPCI patients \geq 65 years undergoing an inpatient intracoronary stent procedure between January 1, 2004 and December 31, 2006. Patients receiving more than one stent type (ie both BMS and DES) were excluded. (Figure 1) The Duke University Medical Center Institutional Review Board granted a waiver of informed consent and authorization for this study.

Follow-Up Information

Since ACC-NCDR[®] data are limited to a single episode of care we used the research-identifiable Medicare 100% inpatient fee-for-service claims file for longitudinal patient follow-up. PCI procedure codes (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] procedure codes 00.66, 36.0x, 37.22, 37.23, and 88.5x, except 88.59) were used to identify potential index procedure matches in the Medicare files which were then linked to NCDR using indirect identifiers (non-unique fields that when used in combination may identify unique hospitalizations) to create unidentified longitudinal profiles and obtain up to 3 years follow-up. Linking rules used a hierarchy of evidence approach such that rules with the most information were applied before those with less information. Once a match was achieved for a patient, no further rules were applied. Our linking rules contained combinations of information denoting the index PCI procedure site, patient date of birth (or components thereof) or age, admission date, discharge date, and sex. In the rare event that a single ACC-NCDR[®] record could

be matched with multiple Medicare records using the same rule, no linking occurred. Sites that did not match to Medicare records were excluded as were patients whose index PCI procedure did not occur during a period of fee-for-service enrollment.

Clinical End Points

We evaluated 8 clinical endpoints: 5 events and 3 composites. Death was the only event defined both during the index PCI procedure (using ACC-NCDR[®] information) and post-discharge (using the Medicare denominator file). Clinical endpoints were defined using the Medicare claims file as the primary diagnosis for a hospital admission. The ICD-9-CM diagnosis codes used to identify events were: myocardial infarction (MI) (410.X1), stroke (430.X, 431.X, 432.X, 434.X), and bleeding (430-432, 578.X, 719.1X, 423.0, 599.7, 626.2, 626.6, 626.8, 627.0, 627.1, 786.3, 784.7, or 459.0). Revascularizations were identified using ICD-9-CM procedure codes (PCI, 36.00, 36.06, 36.07, 36.09, and coronary artery bypass graft surgery, 36.10-19). Only revascularizations occurring after discharge from the index hospitalization were included in the revascularization analysis. The composite events used in this study were: MI or death, MI or death or revascularization, and MI or death or stroke.

Statistical Analysis

Baseline and propensity matching characteristics were categorized by stent type (DES vs. BMS) and summarized as counts and percentages for categorical variables and means with standard deviations for continuous variables. Statistical significance was defined as $p \leq 0.05$, with no correction for multiple comparisons, using SAS statistical software (version 9.1; SAS Institute, Cary, NC) for all calculations.

Propensity Score Models

We used propensity scores to adjust for between-treatment group differences in baseline characteristics.¹⁵ Propensity scores represent the estimated probabilities of patients receiving drug-eluting vs. bare metal stents in our population,¹⁵ in this case conditioned upon 102 observed covariates. (Appendix) Inverse probability weighted estimators incorporating propensity scores were used to compare treatment groups.¹⁶ The propensity score model had a c-index of 0.690. In addition, the distribution of propensity scores for DES patients closely match those for BMS patients as evidenced by the 5-number summaries (min, 25th, 50th, 75th, max) describing the curves for patients receiving each type of stent: (BMS: 14.5%, 70.7%, 79.6%, 85.9%, and 99.1%) and (DES: 16.0%, 79.7%, 86.1%, 90.7%, and 99.5%). The overlap between the groups is excellent and suggests that the propensity score approach is statistically appropriate.

Inverse probability weighted estimators with monthly data partitions were used to calculate cumulative incidence rates for clinical end points (adjusted and unadjusted).^{17,18} Unadjusted estimates were based upon Kaplan-Meier estimates for treatment-specific censoring distributions; whereas adjusted estimates were based upon weights that were functions of Kaplan-Meier censoring estimates and propensity score estimates.^{17,18} Adjusted hazard ratios were calculated according to the inverse probability weighted (IPW) approach of Cole and Hernan.¹⁹ In particular we calculated two IPW Cox proportional hazards models—one with an indicator for DES as the only covariate and

one with DES plus a selected group of clinically important variables including: gender, age, diabetes, renal disease, prior revascularization, prior MI, multivessel CAD, year of procedures, and race. From these models, we estimated the adjusted hazard ratio for DES vs. BMS along with a 95% confidence intervals based on the sandwich estimated standard errors. To visually assess the proportional treatment effect assumptions we plotted the monthly cumulative incidence rates over the 30-month follow-up period. Additionally, we plotted the treatment-group specific cumulative incidence rates excluding events from the first 6 and 12 months to identify the long-term component of the treatment effect. We refer to these latter analyses as 6 and 12 month landmark analyses.

Cox Model

A Cox proportional hazards mortality model (without propensity score weighting) was developed using backward selection of the propensity score variables with a $p=0.05$ selection threshold. Forward selection was used in a sensitivity analysis for internal validation of the final model which contained 60 covariates. These models served to validate the adjusted hazard ratio estimates from the IPW Cox regression model method of Cole and Hernan.¹⁹

Subgroup Analyses

PCI status included STEMI [primary, rescue, or facilitated], urgent [non-STEMI or unstable], and elective subgroups. Within the DES group, off- vs. on-label use subgroups were examined. For patients enrolled in NCDR using version 2 of the data collection form (DCF), off-label use was defined as intervention on ACC/AHA Type C lesion, PCI status of urgent or STEMI, intervention in a previously treated lesion, use of more than two stents in a lesion, treatment of a left main or graft segment, or multi-vessel PCI. For those enrolled using DCF version 3, the off-label use definition was modified to also include device diameter ≤ 2.5 mm or >4 mm, total stented or lesion length ≥ 30 mm, and bifurcation lesions.

Sensitivity Analyses

We conducted two sensitivity analyses. For the first analysis, each of the five main outcomes were examined in a subgroup of patients fitting the inclusion and exclusion criterion from the Taxus IV and SIRIUS trials ($n=49,355$)^{20,21} using a recalibrated propensity score including 76 clinical variables with a c-index of 0.71.

The second sensitivity analysis estimated 'cause of death' after stent implantation according to the primary diagnosis of a hospitalization during which the patient expired or the most recent hospitalization within 6-months of death. Using a previously validated list of ICD-9 codes²² we examined the relative distribution of causes of death across DES and BMS patients.

Results

Between January 2004 and December 2006, 390,973 NCDR patients ≥ 65 years underwent stent implantation, and 76% were linked to longitudinal Medicare records. After exclusions, the study population included 262,700 patients from 650 sites (Figure

1). Comparison of NCDR[®] patients who did and did not match to Medicare records revealed non-match patients to be slightly younger (73 vs. 74 yrs), and more likely to be male (62% vs. 58%) and to have commercial insurance (15% vs. 3%).

Overall, 45,025 patients received one or more BMS and 217,675 received one or more DES (54% paclitaxel eluting, 46% sirolimus eluting). Unadjusted baseline characteristics show significant differences between DES and BMS, these differences were reduced following propensity score weighting (Table 1). Sixty-nine percent of DES implantations were for non-FDA-approved indications. Mean follow-up for BMS patients was slightly longer (496 ± 371 days) than for DES patients (456 ± 302 days) due to the trends in stent use over the time period studied.

Death

During the 30-month study period, 21,254 deaths occurred. Thirty-month overall mortality was higher in patients who received BMS than DES both before (17.9% vs. 12.9%; $p < 0.0001$), and after adjustment for population differences (16.5% vs. 13.5%, HR 0.75; 95% CI, 0.72 to 0.79) (Table 2). The adjusted mortality difference was statistically significant in the initial six months post-PCI, and continued to increase throughout the 30-month follow-up period (Figure 2a). The estimated hazard ratio obtained using an unweighted Cox proportional hazards mortality model with backward variable selection was similar at 0.79 with a 95% CI (0.76 to 0.81). In addition to the use of DES, other factors favorably influencing 30-month post-PCI survival included female sex and prior PCI or CABG. As expected, mortality was higher in those with diabetes, renal failure, STEMI or CHF.

Myocardial Infarction

There were 10,528 MIs during the study period. Unadjusted MI rates at 30-months were 10.0 / 100 patients in BMS vs. 7.3 / 100 patients in DES ($p < 0.0001$) with similar results following adjustment (8.9 / 100 patients vs. 7.5 / 100 patients, HR 0.77; 95% CI, 0.72 to 0.81) (Table 2). This result was driven by lower MI rates in DES patients during the first 12-months post-PCI (Figure 2b), with no difference between 12 and 30-months of follow-up. In a secondary analysis, DES patients experienced a small increase in STEMI events beyond 12 months (Figure 3).

Revascularization

Revascularization (PCI or CABG) was performed in 34,751 patients with a total of 40,427 revascularizations; 30-month unadjusted revascularization rates for BMS and DES populations were 24.5/100 patients and 23.0/100 patients ($p = 0.007$). With risk-adjustment, no difference in overall revascularization was observed in DES versus BMS patients at 30-months (23.5/100 patients vs. 23.4/100 patients, HR 0.91; 95% CI, 0.87 to 0.96) (Table 2; Figure 2c). However, revascularization rates were lower in DES patients to twelve-months post-PCI (13.3/100 patients vs. 15.2/100 patients) followed by a late rebound in revascularization procedures in the DES group between 12 and 30-months (10.2/100 patients vs. 8.2/100 patients). When CABG and PCI revascularizations were examined separately, CABG was more common in BMS than DES over the 30-month follow up period (3.7/100 patients vs. 2.5/100 patients), while the rate of PCI was similar.

Stroke and Major Bleeding

During follow-up, 4,010 strokes and 5,120 major bleeding events required hospitalization, with 59% of strokes and 49% of bleeds occurring within 6-months following PCI. Unadjusted and adjusted stroke rates were roughly 3 / 100 patients at 30-months in each group (HR 0.97; 95% CI, 0.88 to 1.07) and only a minimal difference was noted in bleeding (3.6 / 100 patients BMS vs. 3.4 / 100 patients DES, HR 0.91; 95% CI, 0.84 to 1.00) (Table 2; Figures 2d and 2e).

Composite Endpoints

Each of the composite endpoints tracked closely with its individual components, favoring DES over BMS treated patients both before and after statistical adjustment (Table 2). The unadjusted 30-month rates of death or MI (17% vs. 23%), death or MI or revascularization (32% vs. 38%), and death or MI or stroke (19% vs. 24%) were each lower in DES than BMS patients.

Subgroup Analyses

The 30-month DES survival advantage was present across all patient subgroups, independent of sex, age, comorbidities, and procedural indication or urgency (Figure 4a). This effect was somewhat less pronounced in those with a prior history of CABG and renal failure, with or without dialysis. Notably, patients receiving DES in 2005 and 2006 had a greater relative survival benefit than those receiving DES in 2004. Similarly, the 30-month risk of MI was lower in all patient subgroups except those with renal failure and insulin-dependent diabetes (Figure 4b).

Most patient subgroups experienced a slightly lower 30-month rate of revascularization with DES compared with BMS. (Figure 4c) However, no benefit was observed in patients >75 years, or with diabetes, renal failure, heart failure, or 3-vessel disease. Revascularization rates were similar in patients undergoing PCI in 2006, in contradistinction to the slightly lower DES revascularization rates from 2004 and 2005. (Figures 4d and 4e)

Sensitivity Analyses

Randomized Trial Cohort

The 49,355 NCDR[®] registry patients fitting the inclusion and exclusion criteria for the Taxus IV and SIRIUS DES randomized controlled trials had 30-month outcomes similar to those of the overall population such that those receiving DES had a lower 30-month risk of death (HR 0.62; 95% CI, 0.55 to 0.70), MI (HR 0.66; 95% CI, 0.55 to 0.80), death or MI (HR 0.64; 95% CI, 0.57 to 0.70) and revascularization (HR 0.87; 95% CI, 0.80 to 0.96) compared to BMS. No difference in stroke (HR 0.97; 95% CI, 0.74 to 1.28) or major bleeding (HR 0.87; 95% CI, 0.71 to 1.05) was noted between trial-eligible DES and BMS patients.

Cause of Death

Presumed ‘cause’ was extrapolated in 19,132 (90%) deaths using the algorithm described above, and included 8451 inpatient and 10,591 outpatient deaths. Slightly more BMS deaths were attributable to MI (15.0% vs. 13.5%, $p=0.01$) and malignancy (6.7% vs. 5.5%, $p=0.002$) while more DES deaths were more attributable to chronic lung disease (2.5% vs. 1.9%, $p=0.01$) and cerebrovascular disease (5.3% vs. 4.2%, $p=0.003$). No significant differences were found for any of the remaining diagnoses. Overall, DES patients had a lower risk of CV-only (including CHF and MI) deaths compared with BMS patients (HR 0.80; 95% CI, 0.74 to 0.86), as well as non-CV death from all other causes (HR 0.74; 95% CI, 0.70 to 0.78).

Discussion

Our study is the largest-ever observational comparison of long-term outcomes in older patients receiving BMS or DES. DES implantation was associated with lower risk of death and MI at 30-months as compared to BMS, while there were minor, if any, differences in bleeding, stroke, and overall revascularization. Our methodology allowed determination of comparative effectiveness in unselected individuals, in contemporaneous DES and BMS cohorts, with device selection and subsequent management of patients reflecting real-life, community practice.

Prespecified Outcomes

Death

Prior analyses comparing survival in DES and BMS treated patients from randomized controlled trials (RCTs) and smaller registries have produced conflicting results with relatively low precision. While no difference in late survival was demonstrated in some RCTs,^{1,23} registries and meta-analyses,^{9-11,23-28} other more recent studies have demonstrated a DES survival advantage with a point-estimate similar to that observed in our population.^{13,29-32} The higher annualized mortality rates for patients in our population receiving either DES or BMS (5.4%/year vs. 6.6%/year) than previously reported in some registries (range=1.3%/year to 4.3%/year)(23-27,33,34) is likely due to higher risk in our elderly, inpatient population, and are comparable to other Medicare cohorts.^{11,35}

Myocardial Infarction

Patients receiving DES experienced a 23% relative reduction in subsequent MI with no late increase in combined NSTEMI/STEMI risk, a result similar to several other analyses.^{1,9,11} Angiographic assessment of stent thrombosis was not possible in our data set; however, isolated analysis of STEMI events revealed a slight increase in very late (>12-months) STEMI risk in DES patients, consistent with prior literature on late stent thrombosis⁶ and the expected time-course of clopidogrel discontinuation.^{36,37}

Revascularization

Although DES have been associated with low revascularization rates,^{6,9,11,13,29-32,34} recent registry reports suggest that they may actually be as high as 15-19% over a 2-3

year follow-up,^{6,11,26} with little difference between DES and BMS patients.⁶ The higher rate of repeat revascularization in our population (24%) may be due to not censoring patients after an event, and to the inability to differentiate target lesion revascularization (TLR) from non-TLR follow-up procedures using claims data. For example, a recent report from the Duke database identified a 2-fold higher rate of overall revascularization versus target vessel revascularization in DES patients at 2 years (12.0% versus 6.6%).²⁶ Thus, the lack of anatomic data makes this database less than ideal for the comparison of revascularization between DES and BMS. An additional concern is the higher rate of late revascularization in DES compared to BMS, which tends to obscure the early benefit when examining overall DES-BMS hazard ratio. Our revascularization results should be interpreted cautiously.

Stroke and Major Bleeding

Few differences in stroke or major bleeding rates requiring re-hospitalization were observed between the overall DES and BMS populations. The anticipated greater use of clopidogrel in the DES group might have conferred a bleeding disadvantage, as has been seen in other studies;^{38,39} however, no statistically significant difference was observed in our population. Unexpectedly, although a slightly higher unadjusted rate of anemia-associated deaths was observed in DES patients, no significant adjusted or unadjusted difference in GI hemorrhage-associated deaths was evident at 30-months.

Registry Versus RCT Results: Sensitivity Analyses

The differences in outcomes between registry and RCT analyses have been previously attributed to possible differences in DES performance in a real world (registry) population as compared to a restricted RCT population; with the lack of a survival difference in RCTs being an artifact of their restricted patient populations. Since creation of a population subset fitting the inclusion and exclusion criteria of the Taxus IV and SIRIUS DES RCTs^{20,21} only sharpened the precision for each endpoint, differences in age, acuity, lesion characteristics, and off label use in the registry and RCT populations are unlikely explanations of the observed differences in results.

Incomplete risk-adjustment following biased real-world stent selection may also contribute to the survival advantage noted in this and other registry analyses. Although we used both propensity analyses and Cox proportional hazards models to adjust for differences in baseline characteristics, it is possible that unmeasured baseline population differences remained. In fact, our ‘cause of death’ sensitivity analysis did show slightly higher rates of death due to malignancy in BMS patients, suggesting that biased patient selection may have contributed to the overall mortality result, such that ‘sicker’ patients with more comorbid disease received BMS. While it is possible that the observed differences between DES and BMS patients are the sole product of unmeasured patient selection biases not reflected by this analysis, this explanation is less likely given the large number of covariates used in our propensity matching.

Strengths and Limitations

Our study has several important strengths. This represents a novel large-scale linkage between a national procedural registry and a robust claims database,

demonstrating that nationally representative analyses are feasible using clinically rich, procedural registries and a claims-based structure for follow-up. In combination, these two resources provide a powerful mechanism for tracking the post-marketing use and outcomes of novel devices and procedural innovations, at minimal cost. Importantly, the project was financed by the Agency for Healthcare Research and Quality, Cardiovascular Consortium of Effective Healthcare Program, and was independent of industry.

Data entered in NCDR[®] are intended to be used as a quality improvement tool and undergo rigorous quality control,⁴⁰ while the Medicare claims database captures all inpatient care episodes. Despite these disparate intents and the size and complexity of these two databases, our linkage rate was over 75%, adding to the generalizability of our results. We analyzed these data by three methods, IPW alone, IPW with Cox proportional hazards modeling, and standard Cox proportional hazards modeling to compare results between the different approaches. The high level of agreement between these methods enhances confidence in our findings.

Our study has several important limitations, as well. Our data are observational and therefore dependent on the accuracy and completeness of the two matched data sets. Reliance on a claims database for outcomes may be fraught with underreporting or misclassification of events. Such misclassification and underreporting should be non-differential, however, and should bias our estimates toward the null value of no overall difference. Although differences in baseline characteristics were rigorously adjusted for using propensity weighting, it is possible that additional unadjusted differences between BMS and DES patients affected results, since our analyses are limited to the data collected by ACC-NCDR[®] and Medicare. Thus we are unable to directly address some important questions which have been raised regarding the safety of stents, including whether repeat revascularization represented target lesion or vessel restenosis, the incidence of late stent thrombosis, and the impact of variations in thienopyridine use. Although the slight excess of STEMI's in DES patients after 12-months fits the time course of late stent thrombosis, these events did not translate to increased late mortality.

While the linkage rate of 76% is incomplete, it is reflective of populations known to be absent from the Medicare data set such as patients treated at Veterans Administration facilities, with Medicare Advantage insurance coverage or undergoing outpatient procedures. Our findings are drawn from hospitalized patients over age 65, an age group which accounts for approximately half of all PCI's nationally. While this cohort is likely sicker than the generally younger outpatient PCI population, the similarity in outcomes in those 65- 75 and those >75 years old suggests that these differences may have been accounted for in the risk adjustment.

Conclusions

In summary, in this large population of Medicare beneficiaries undergoing PCI at facilities participating in the ACC-NCDR[®] registry, patients who received DES had significantly lower mortality rates, including an early decrease in MI, than those who received BMS. No excess of major bleeding or stroke was noted. The survival advantage associated with DES was maintained across all subgroups analyzed and throughout the 30 months of follow-up. Drug eluting stents seem to be safe and effective in community practice in the elderly population. Longer follow up studies will need to be

conducted to further support these results and to confirm the possible effects of antiplatelet agents.

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Abbreviations

BMS, bare metal stent

DES, drug-eluting stents

ACC, American College of Cardiology

NCDR,[®] National Cardiovascular Data Registry

CMS, Centers for Medicare and Medicaid Services

AHRQ, Agency for Healthcare Research and Quality

PCI, percutaneous coronary intervention

CABG, coronary artery bypass grafting

IPW, inverse propensity weighted scoring

Tables and Figures

Table 1. Unadjusted baseline characteristics of patients in study population							
Patient Characteristics		Study Population			Study Population After Propensity Score Weighting		
		DES (217,675)	BMS (45,025)	p-value	DES* (217,675)	BMS* (45,025)	p-value
Age (mean ± SD years)		74.5±6.4	75.3±6.7	<0.001	74.7	74.8	0.03
Sex (Male)		123209 (56.6 %)	27024 (60.0)	<0.001	57.2	57.0	NS
Race	Caucasian	196260 (90.2%)	41029 (91.1%)	<0.001	90.3	90.2	NS
	African American	9051 (4.2%)	1984 (4.4%)	0.017	4.2	4.3	NS
	Asian	1885 (0.9%)	254 (0.6%)	<0.001	0.8	0.8	NS
	Hispanic	3843 (1.8%)	578 (1.3%)	<0.001	1.7	1.7	NS
	Other	6258 (2.9)	1092 (2.5%)	<0.001	2.8	2.8	NS
Hospital Region	Northeast	22642 (10.4%)	5371 (11.9%)	<0.001	10.7	10.8	NS
	South	80612 (37.0%)	15614(34.7%)	<0.001	36.6	36.8	NS
	Midwest	83956 (38.6%)	18901 (41.9%)	<0.001	39.1	39.0	NS
	West	29294 (13.5%)	4874 (10.8 %)	<0.001	13.0	13.0	NS
Hospital Setting	Rural	29951 (13.8%)	6756 (15.0%)	<0.001	14.0	13.9	NS
	Suburban	55654 (25.6%)	12658 (28.1%)	<0.001	26.0	26.4	NS
	Urban	132070 (60.7%)	25611 (56.9%)	<0.001	60.0	59.8	NS
Year Index Procedure	2004	58453 (26.9%)	19515 (43.3%)	<0.001	29.7	30.3	NS
	2005	74685 (34.3%)	9437 (21.0%)	<0.001	32.0	31.2	NS
	2006	84537 (38.8%)	16073 (35.7%)	<0.001	38.3	38.5	NS
Mean Follow-up (days ± SD)		456.4 (302.5)	495.8 (371.4)	<0.001	464.3	452.0	NS
Current smoking		25955 (11.9 %)	6108 (13.6%)	<0.001	12.2	12.3	NS
CHF		124197 (57.1%)	23112 (51.3%)	<0.001	56.1	55.7	NS
HTN		175154 (80.5 %)	35808 (79.5%)	<0.001	80.3	80.6	NS
Renal Failure	No Dialysis	10393 (4.8%)	2701 (6.0%)	<0.001	5.0	5.2	NS
	Dialysis	3380(1.6%)	854(1.9%)	<0.001	1.6	1.7	NS

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Diabetes	Non-Insulin Requiring	49874 (22.9%)	9930(22.1%)	<0.001	22.8	23.0	NS
	Insulin	20430 (9.4%)	4533 (10.1%)	<0.001	9.5	9.6	NS
Peripheral Vascular Disease		32018 (14.7%)	7776 (17.3%)	<0.001	15.2	15.5	NS
Stroke		34067(15.7%)	7908 (17.6%)	<0.001	16.0	16.5	NS
Chronic Lung Disease		39611 (18.2%)	9163 (20.4%)	<0.001	18.6	18.8	NS
Prior PCI		61974 (28.5 %)	11678(25.9 %)	<0.001	28.0	27.9	NS
Prior CABG		47777 (22.0%)	12735 (28.3%)	<0.001	23.1	23.4	NS
Prior MI		57282 (26.2%)	12941 (28.7%)	<0.001	26.8	26.9	NS
Urgency	Elective	111426 (51.2%)	20511 (45.6%)	<0.001	50.2	49.6	NS
	Urgent	82296 (37.8%)	16048 (35.6%)	<0.001	37.4	37.8	NS
	Emergent	23616 (10.9%)	8225 (18.3%)	<0.001	12.1	12.4	NS
Indication	Stable Angina	38710 (17.8%)	6129 (13.6%)	<0.001	17.1	17.0	NS
	UA/ NSTEMI	34581 (15.9%)	8413 (18.7%)	<0.001	51.3	51.0	NS
	STEMI	21170 (9.7%)	7422 (16.5%)	<0.001	10.9	11.1	NS
Pre-Procedural Shock		3675 (1.7%)	1746 (3.9%)	<0.001	2.1	2.1	NS
Pre-Procedural Aspirin		144296 (90.2%)	22790(88.8%)	<0.001	64.3	62.6	NS
Pre-Procedural Clopidogrel		173600 (80.2%)	35821(80.2%)	0.78	80.6	77.9	<0.01
Pre-Procedural IABP		637(0.2%)	172(0.4%)	<0.001	0.3	0.3	NS
Gp IIb/IIIa inhibitors		100043 (46.1%)	21726 (48.6%)	<0.001	46.9	44.7	<0.05

Multivessel PCI		34185 (15.7%)	5006 (11.1%)	<0.001	14.9	14.6	NS
Intervened Vessels	LAD	96278 (44.2%)	15259 (33.9%)	<0.001	42.4	41.7	NS
	LCX	66766 (30.7%)	13725 (30.5%)	0.43	30.6	30.7	NS
	RCA	83508 (38.4%)	20062 (44.6%)	<0.001	39.5	39.8	NS
	Graft	17412 (8.0%)	6997(15.5%)	<0.001	9.3	9.7	NS
# stents per patient	1	135961 (62.5%)	30833(68.5%)	<0.001	63.3	65.6	<0.001
	≥ 2	81714 (37.5%)	14192 (31.5%)		36.7	34.4	
# of vessels intervened	1	183490 (84.3%)	40019(88.9%)	<0.001	85.1	85.4	NS
	2	32313(14.8%)	4754(10.6%)	<0.001	14.1	13.8	NS
	3	1872(0.9%)	252(0.6%)	<0.001	0.8	0.8	NS
ACC-AHA Type C Lesions		83853 (38.5%)	18127 (40.3%)	<0.001	38.8	39.2	NS
Sirolimus-Eluting (Cypher)		100693 (46.3%)			46.3		
Paclitaxel-Eluting (Taxus)		120320 (55.3%)			55.2		
Off-Label PCI		112019 (69.2%)			77.5		

*Propensity matched comparisons reported as % of the matched population.

Table 2. Unadjusted and adjusted results from time-to-event analyses for prespecified endpoints. Shown as Hazard Ratio and 95% confidence interval

Endpoint	Unadjusted	IPW Adjusted	IPW+covariates**
Death	0.67 (0.65, 0.69)	0.76 (0.72, 0.79)	0.75 (0.72, 0.79)
Death or MI	0.67 (0.65, 0.68)	0.76 (0.72, 0.79)	0.75 (0.72, 0.79)
Death or MI or Revasc	0.78 (0.75, 0.80)	0.84 (0.81, 0.87)	0.84 (0.81, 0.87)
Death or MI or Stroke	0.69 (0.67, 0.70)	0.77 (0.74, 0.81)	0.77 (0.74, 0.80)
MI*	0.66 (0.64, 0.70)	0.76 (0.72, 0.81)	0.77 (0.72, 0.81)
Revascularization*	0.89 (0.87, 0.92)	0.92 (0.87, 0.96)	0.91 (0.87, 0.96)
Stroke*	0.90 (0.84, 0.98)	0.98 (0.89, 1.07)	0.97 (0.88, 1.07)
Bleed*	0.87 (0.81, 0.93)	0.92 (0.85, 1.00)	0.91 (0.84, 1.00)
NSTEMI*	0.69 (0.66, 0.73)	0.79 (0.74, 0.85)	0.79 (0.74, 0.84)
STEMI*	0.63 (0.59, 0.68)	0.74 (0.67, 0.81)	0.74 (0.67, 0.82)

*Patients are censored after death in these analyses.

**Additional covariates included in the IPW+covariates model were: DES, sex, age > 75, race, diabetes status, renal status, prior revascularizations, prior MI, multivessel CAD, procedure year, and off-label indications.

Figure 1. Population selection—flow diagram

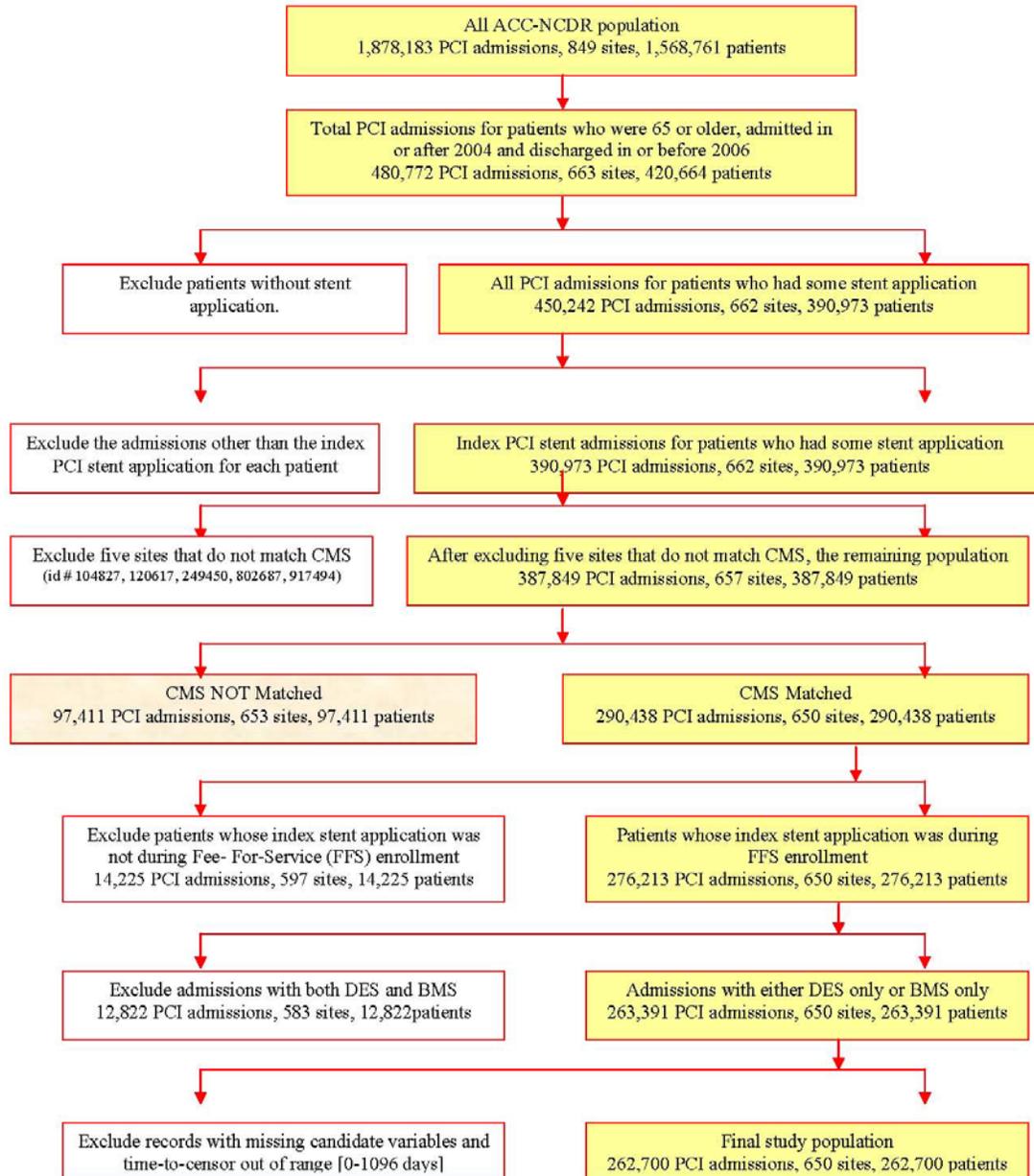


Figure 2a. Adjusted cumulative incidence for death with 6- and 12-month landmark display

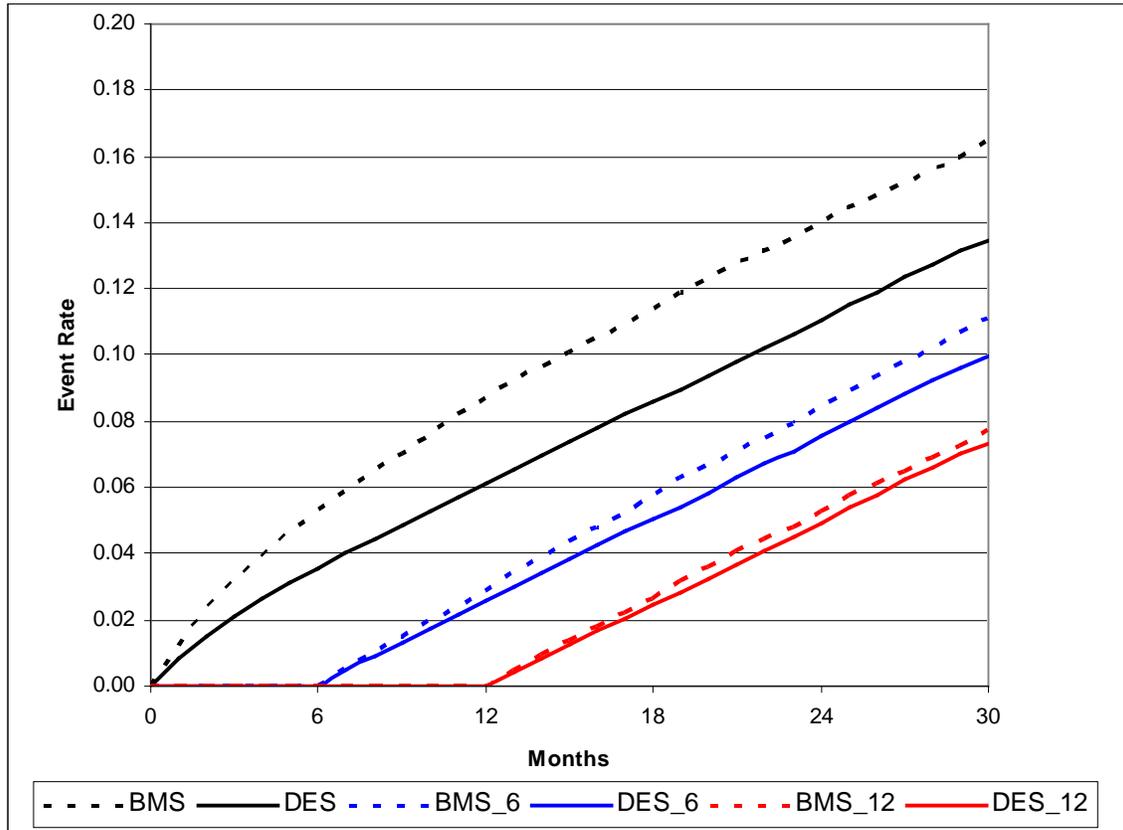


Figure 2b. Adjusted cumulative incidence for MI with 6- and 12-month landmark display

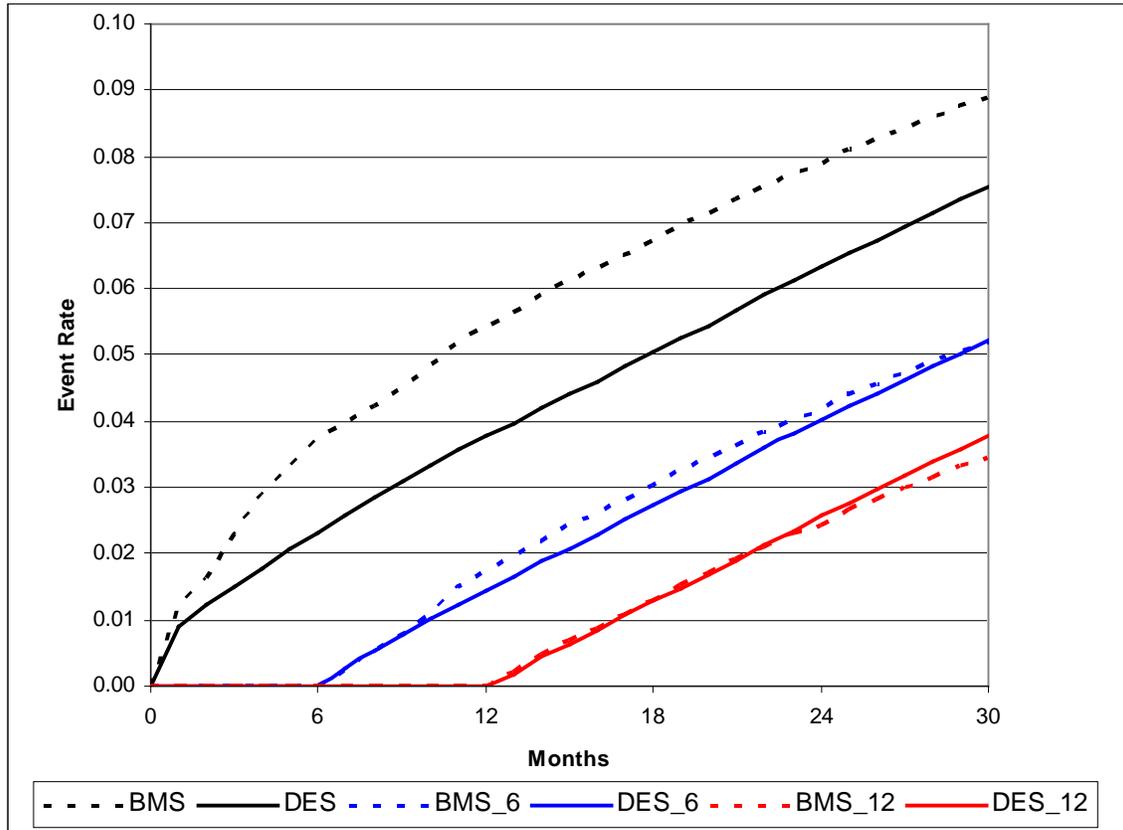


Figure 2c. Adjusted cumulative incidence for revascularization with 6- and 12-month landmark display

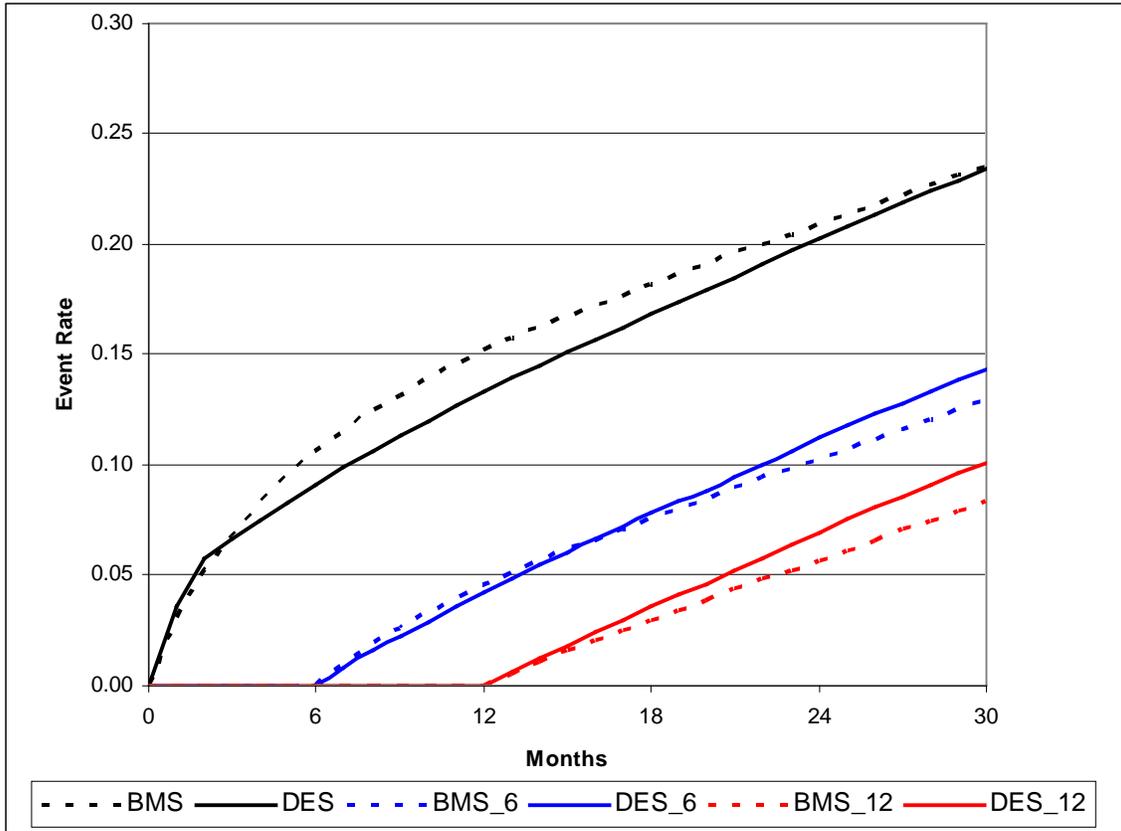


Figure 2d. Adjusted cumulative incidence for bleeding with 6- and 12-month landmark display

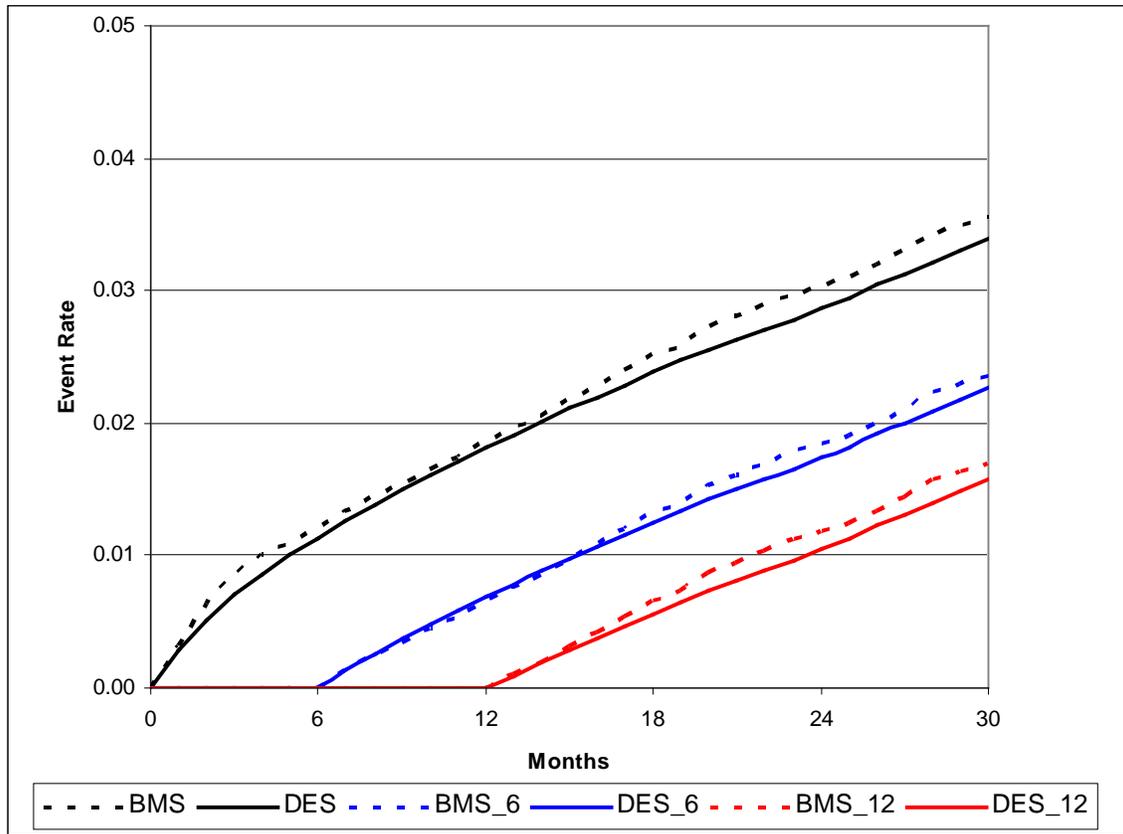


Figure 2e. Adjusted cumulative incidence for stroke with 6- and 12-month landmark display

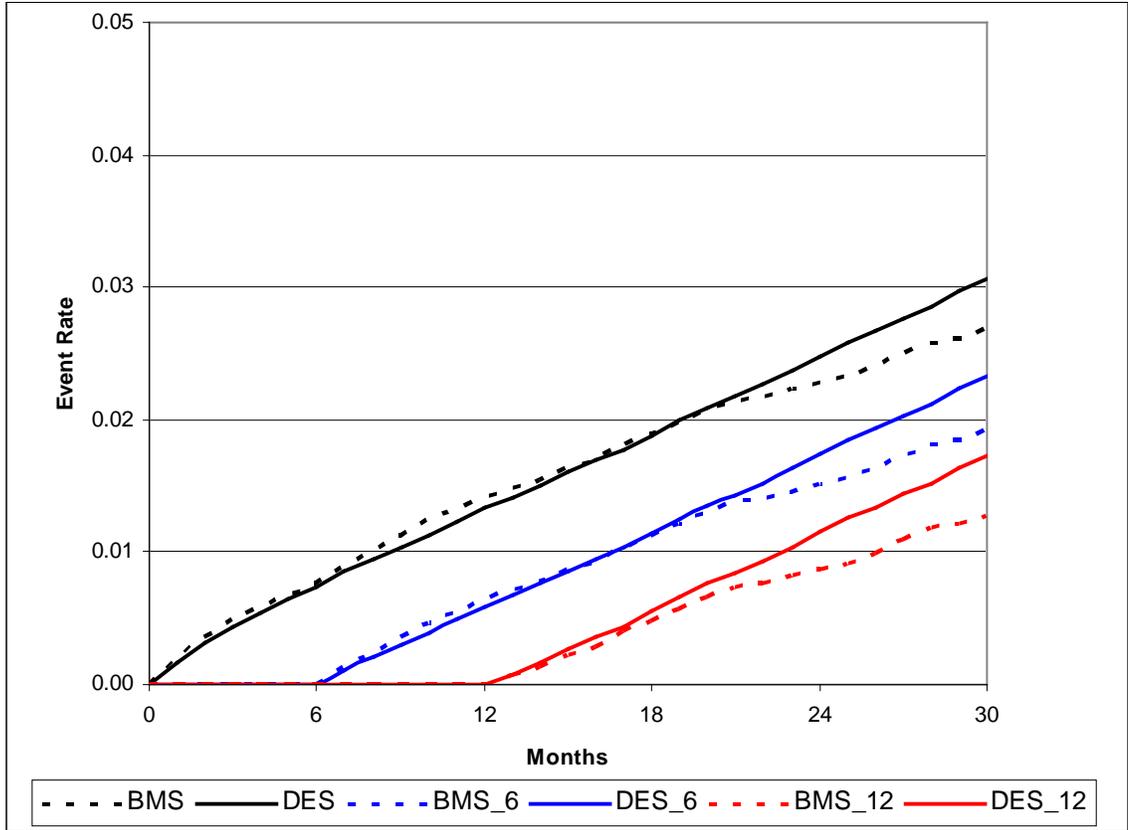


Figure 3. Adjusted cumulative incidence for STEMI with 6- and 12-month landmark display

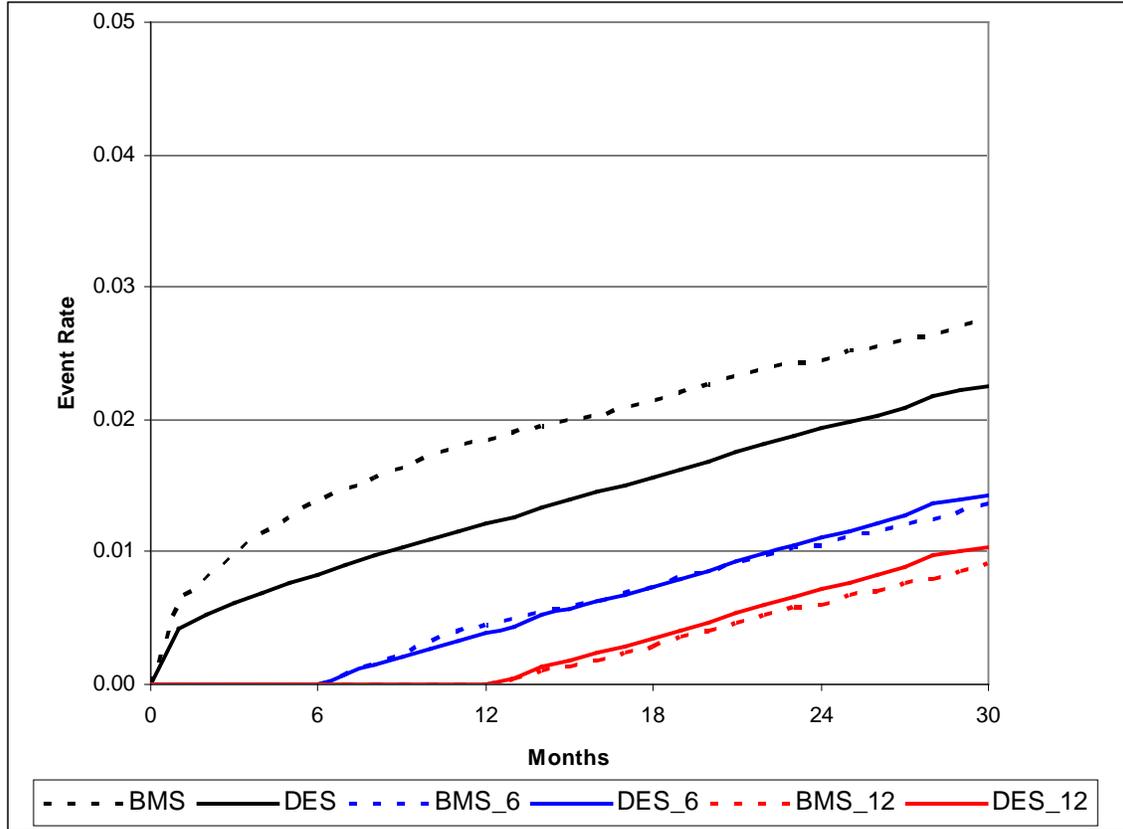


Figure 4a. Subgroup results—forest plot of hazard ratios for death
 Points to the left of the vertical line favor DES.

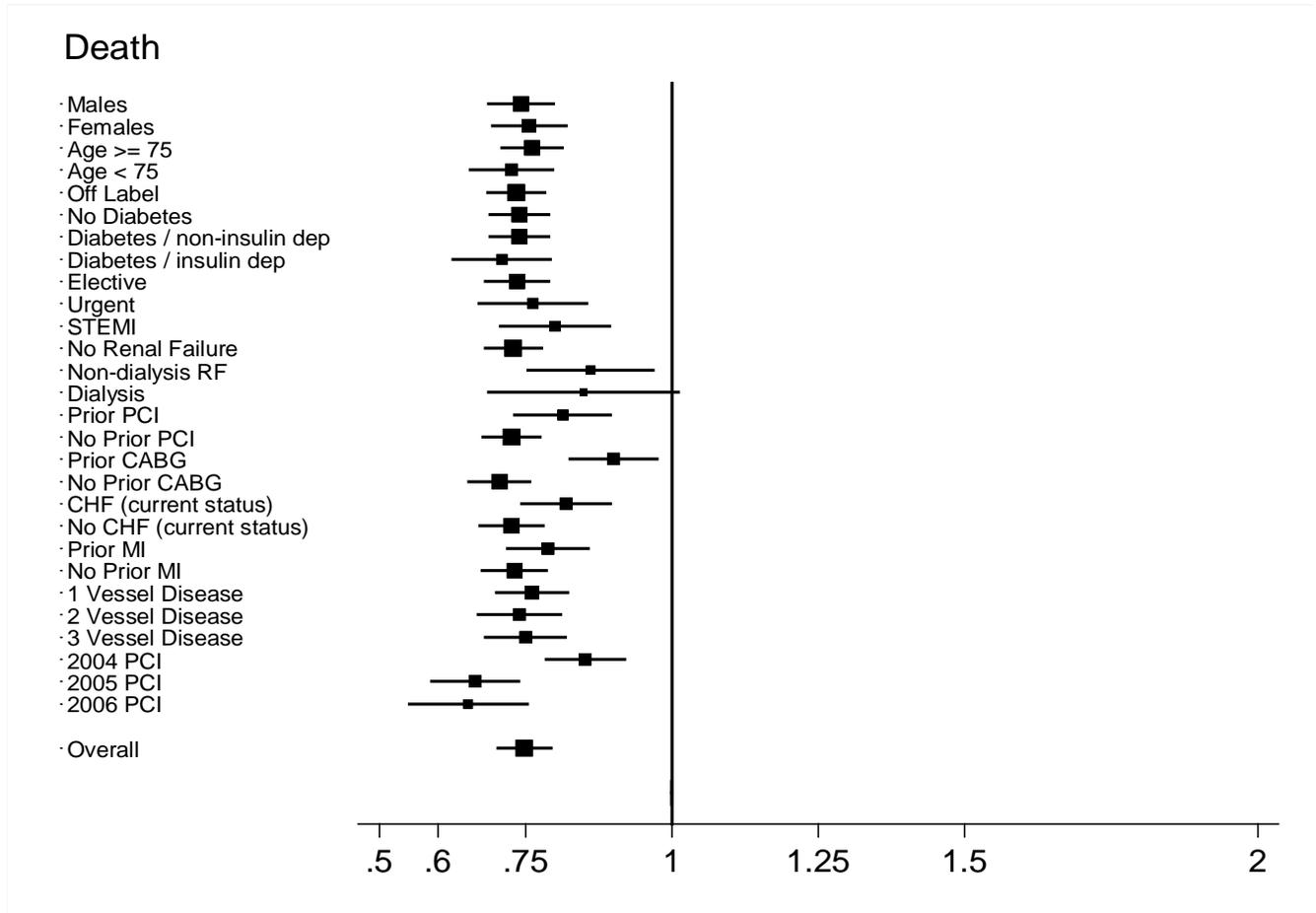


Figure 4b. Subgroup results—forest plot of hazard ratios for MI
 Points to the left of the vertical line favor DES.

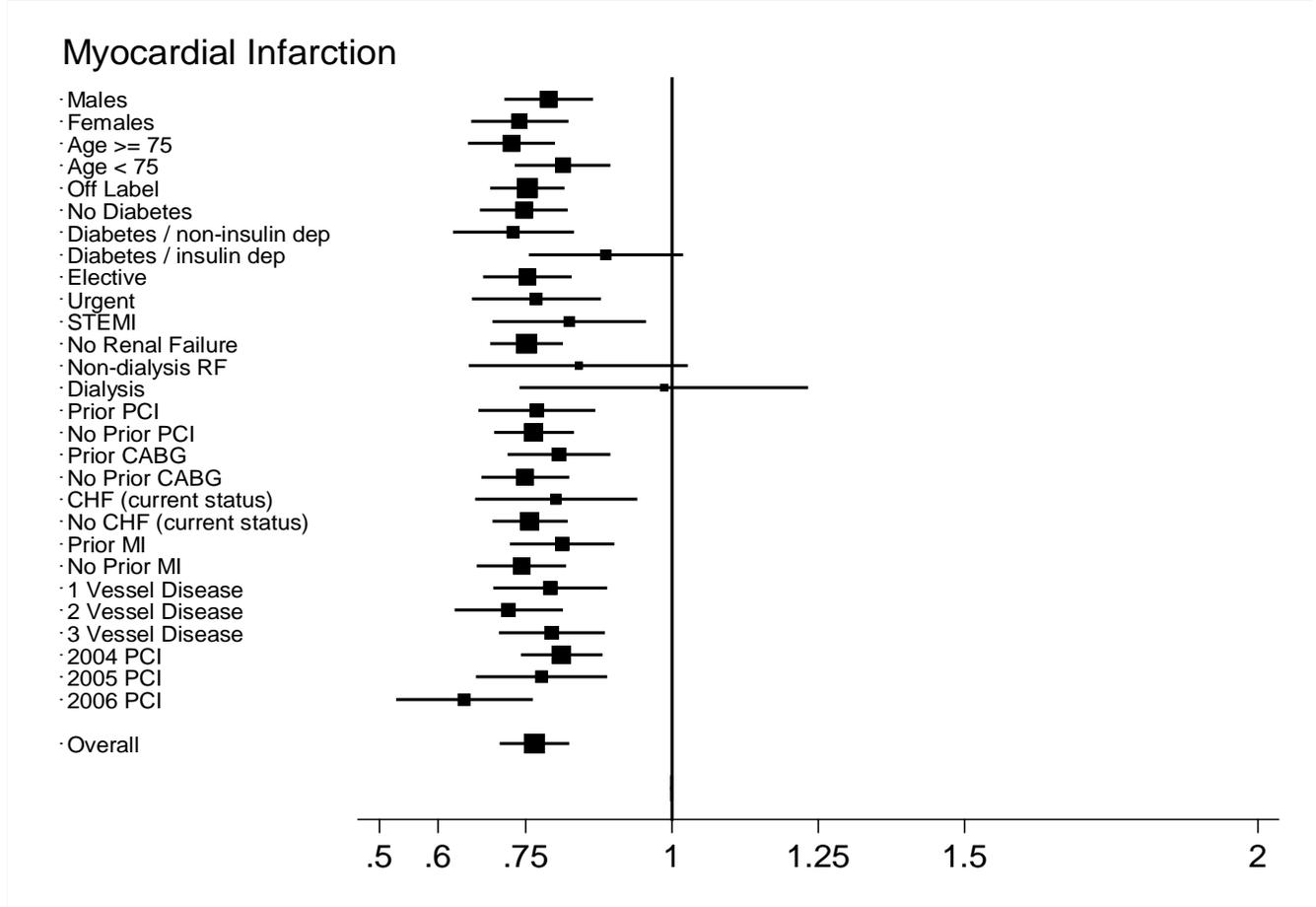


Figure 4c. Subgroup results—forest plot of hazard ratios for revascularization
 Points to the left of the vertical line favor DES.

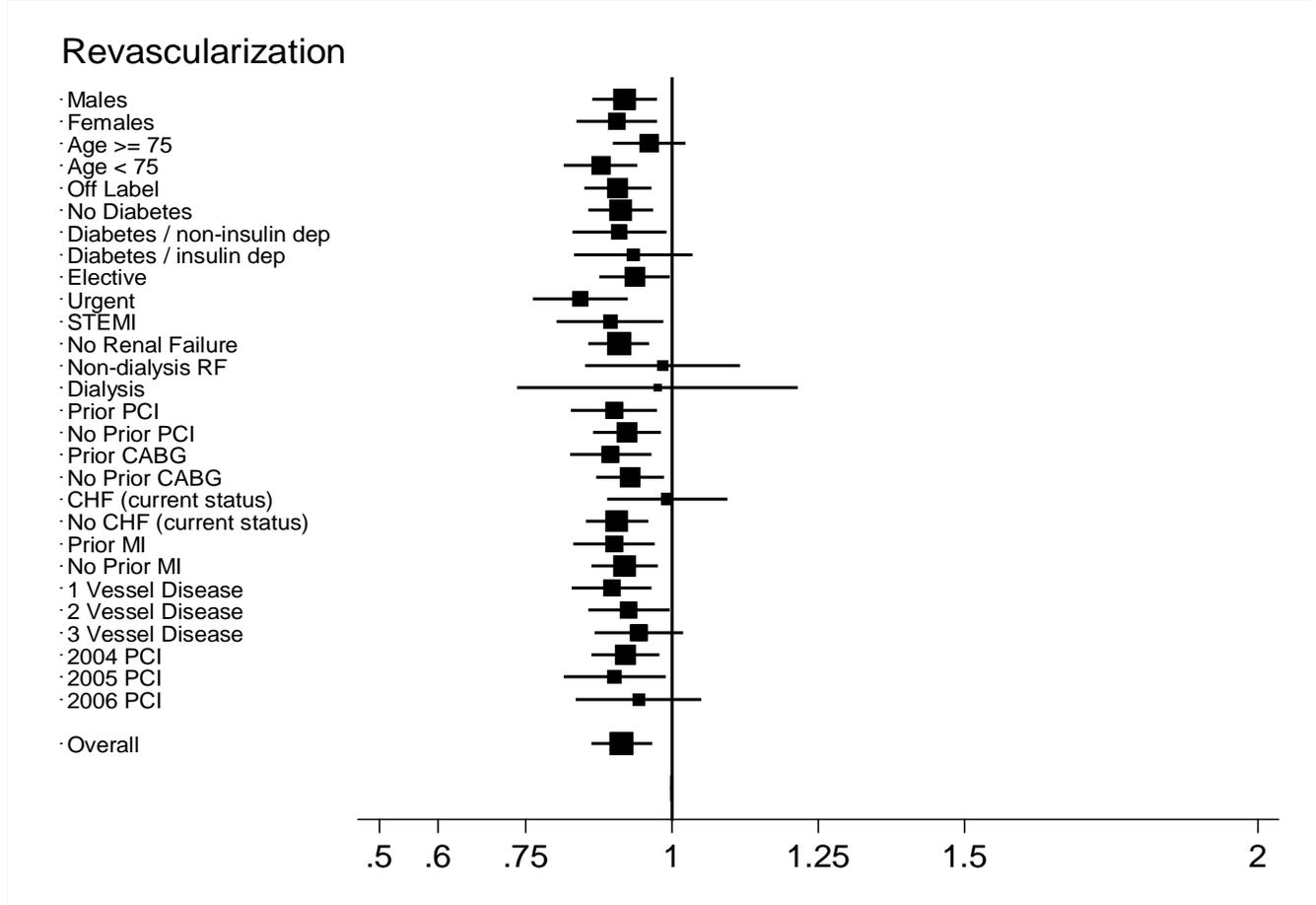


Figure 4d. Subgroup results—forest plot of hazard ratios for major bleeding
Points to the left of the vertical line favor DES.

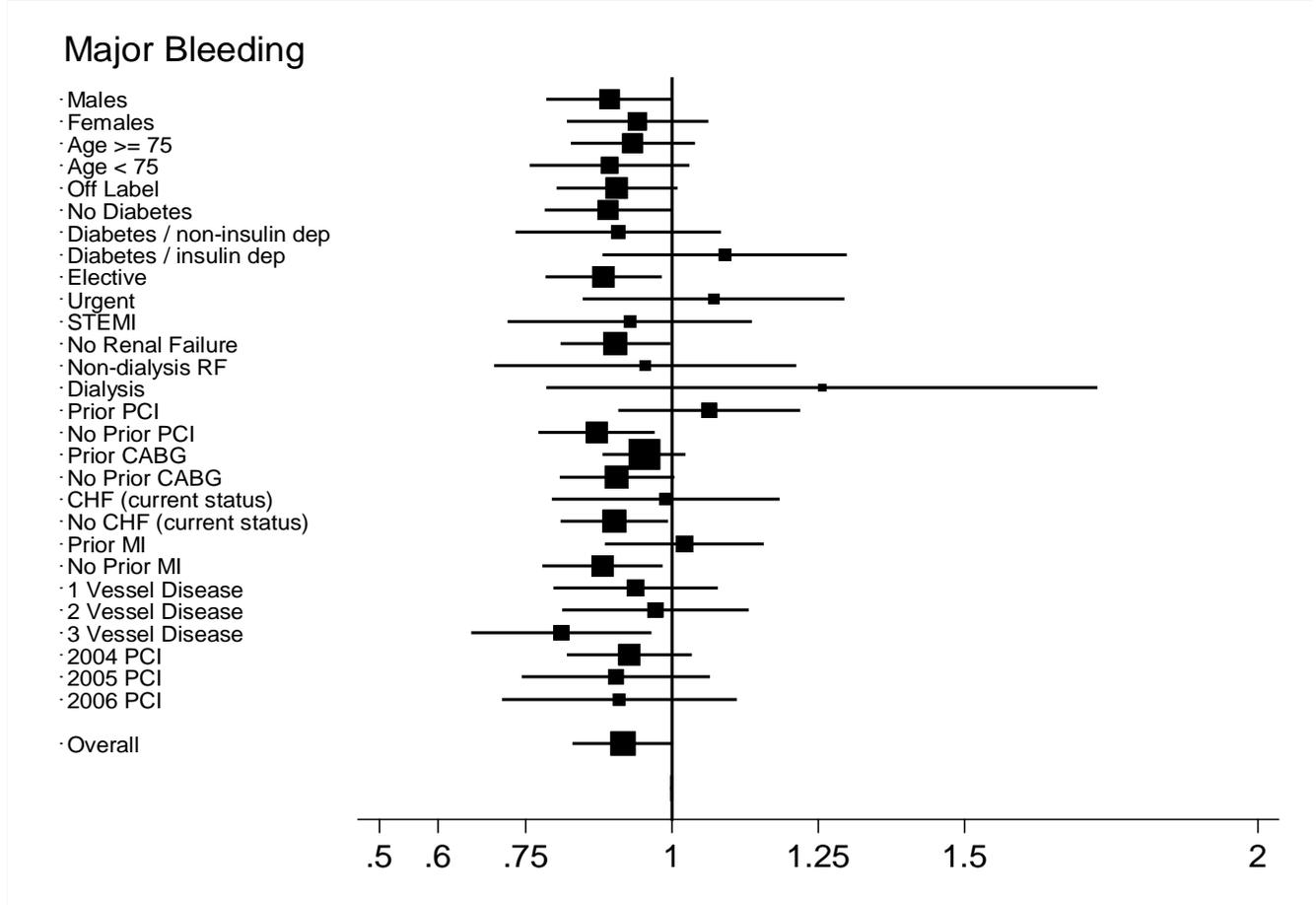
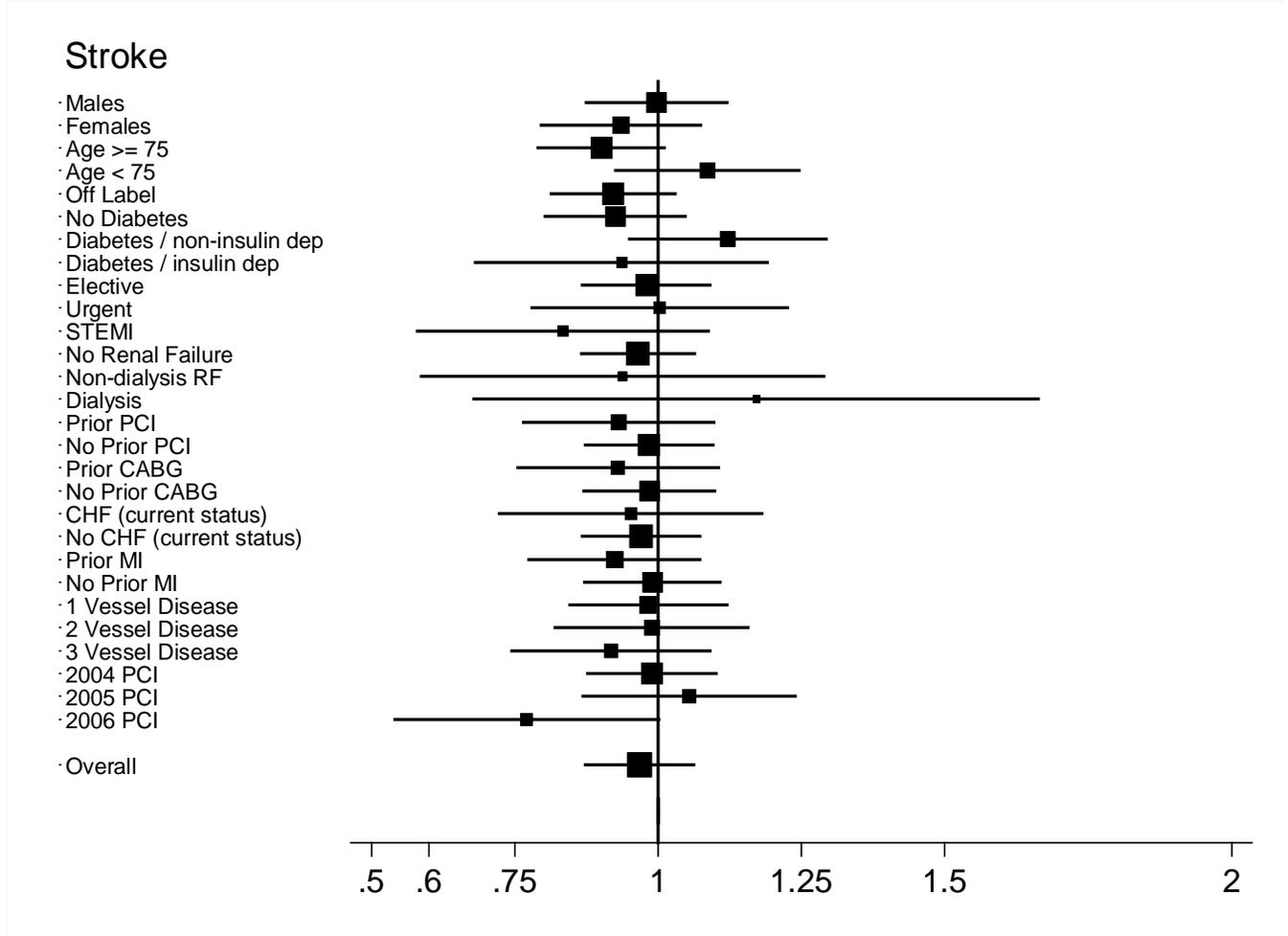


Figure 4e. Subgroup results—forest plot of hazard ratios for stroke
 Points to the left of the vertical line favor DES.



Appendix. Covariates Used in the Propensity Score Model

OR>1 indicates more DES; OR<1 indicates more BMS

Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
Age<75	0.981	0.980	0.983
Race, white	0.940	0.880	1.004
Gender, Male	1.123	1.097	1.149
HTN	0.989	0.963	1.017
Prior PCI	1.110	1.081	1.140
Prior CABG	1.032	0.995	1.070
Prior MI	0.951	0.926	0.975
Prior Valve Surgery	0.864	0.797	0.937
Cerebrovascular Dz	0.947	0.920	0.975
Peripheral Vasc Dz	0.928	0.901	0.956
Chronic Lung Dz	0.904	0.880	0.930
Hyperlipidemia	1.102	1.075	1.129
Family History of CAD	0.992	0.967	1.018
Any CHF	0.973	0.946	1.001
CHF	0.971	0.937	1.007
Cardiogenic Shock	0.818	0.761	0.879
RHC Procedure	0.936	0.890	0.985
LHC Procedure	0.985	0.957	1.013
IABP	0.608	0.565	0.653
Pre-Procedural IABP	1.194	0.982	1.451
Highest Risk Segment in Graft	0.804	0.702	0.920
Lesion Risk	1.018	0.993	1.044
Previously Treated Lesion	1.522	1.411	1.643
% Pre-Stenosis	1.000	0.998	1.001
Some Lesion Segment in Graft	0.836	0.640	1.092
NIDDM	1.012	0.986	1.039
IDDM	0.953	0.918	0.989
Non-Dialysis RF	0.935	0.892	0.980
Dialysis	0.867	0.800	0.939
Urgent	1.096	1.054	1.140
STEMI	0.783	0.719	0.852
2 Vessel Disease	0.986	0.954	1.020

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Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
3 Vessel Disease	0.852	0.808	0.897
Payor-Government	0.861	0.808	0.918
Payor-Missing	0.695	0.420	1.151
Former Tobacco Use	0.954	0.932	0.977
Current Tobacco Use	0.854	0.825	0.885
2 Vessel PCI	1.411	1.244	1.600
3 Vessel PCI	1.638	1.245	2.155
EF	1.005	1.004	1.006
EF-missing	0.883	0.861	0.907
PCI Status-Urgent	1.041	1.015	1.069
PCI Status-Emergency	0.858	0.818	0.901
PCI Status-Salvage	0.504	0.417	0.610
DeNovo Lesion	1.226	1.120	1.341
Restenosis	1.394	1.246	1.560
DeNovo/Restenosis	1.612	1.416	1.834
Subacute Thrombosis	0.851	0.678	1.068
Highest Risk Lesion Length	1.020	1.019	1.022
Lesion Length-missing	0.954	0.820	1.111
Prox-RCA/mid-LAD/Prox-LCx Intervened	1.110	1.081	1.139
Prox-LAD	1.328	1.269	1.390
Highest Risk Lesion Characteristic	1.282	1.054	1.560
Pre-PCI TIMI 1 flow	1.246	1.191	1.304
Pre-PCI TIMI 2 flow	1.239	1.190	1.290
Pre-PCI TIMI 3 flow	1.238	1.191	1.286
Suburban Hospital	1.006	0.972	1.041
Urban Hospital	1.134	1.099	1.171
Private/Community Hospital	0.660	0.602	0.723
University Hospital	0.674	0.611	0.744
Region—West	1.312	1.265	1.361
Region—Northeast	1.038	1.001	1.077
Region—South	1.141	1.113	1.170
Acute Thrombosis	1.015	0.948	1.087
Prior Cardiac Transplant	1.003	0.758	1.327
Atypical Chest Pain	1.116	1.062	1.174
Stable Angina	1.329	1.277	1.382

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Odds Ratio Estimates			
Effect	Point Estimate	95% Wald Confidence Limits	
Unstable Angina	1.213	1.171	1.256
NSTEMI	0.988	0.934	1.046
STEMI	1.099	1.002	1.205
Symptom Onset <6 hrs	1.025	0.971	1.081
Symptom Onset 6-12 hrs	1.038	0.961	1.122
Symptom Onset 12-24 hrs	1.010	0.932	1.094
Symptom Onset 24-48 hrs	1.015	0.930	1.107
Symptom Onset 2-7 Days	0.976	0.903	1.056
% Left Main Stenosis	0.998	0.997	0.998
% Left Main Stenosis-missing	0.948	0.882	1.019
% Proximal LAD Stenosis	1.000	1.000	1.000
% Proximal LAD Stenosis-missing	1.028	0.959	1.102
% Mid-LAD Stenosis	1.001	1.001	1.001
% Mid-LAD Stenosis-missing	1.060	1.001	1.122
% Prox-LCx Stenosis	1.000	1.000	1.001
% Prox-LCx Stenosis-missing	0.881	0.846	0.918
% Prox-RCA Stenosis	1.001	1.000	1.001
% Prox-RCA Stenosis-missing	0.995	0.935	1.059
# of Stents	1.029	1.012	1.046
Bifurcation Lesion	1.331	1.270	1.396
Bifurcation Lesion-missing	0.812	0.489	1.347
LCx PCI	1.005	0.890	1.135
LAD PCI	1.168	1.034	1.319
RCA PCI	0.857	0.757	0.970
IVUS Use	0.964	0.909	1.023
Procedural Year, 2004	0.931	0.849	1.020
Procedural Year, 2005	1.540	1.498	1.584
Any Off Label Lesion	0.756	0.731	0.783
Race, black	0.825	0.760	0.896
Race, Hispanic	1.138	1.018	1.272
Race, Asian	1.206	1.037	1.401
Contraindication to Aspirin	0.706	0.649	0.768
Contraindication to Platelet Inhibitor	0.626	0.544	0.720
Contraindication to Anti-thrombotic	0.824	0.759	0.895
Coumadin Use, yes	0.887	0.838	0.940