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Circulation. published online August 14, 2012;
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

DOI: 10.1161/CIRCULATIONAHA.112.102715

Risk of Elective Major Non-Cardiac Surgery After Coronary Stent Insertion: A Population-Based Study

Running title: *Wijeysundera et al.; Surgical Outcomes After Coronary Stent Insertion*

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Journal Subject Codes: [3] Acute coronary syndromes; [4] Acute myocardial infarction; [5] Arrhythmias, clinical electrophysiology, drugs; [7] Chronic ischemic heart disease; [8] Epidemiology; [24] Catheter-based coronary interventions: stents

DOI: 10.1161/CIRCULATIONAHA.112.102715

Abstract:

Background **-** Guidelines recommend that non-cardiac surgery be delayed until 30 to 45 days after bare-metal stent implantation and one-year after drug-eluting stent implantation.

Methods and Results **-** We used linked registry data and population-based administrative healthcare databases to conduct a cohort study of 8116 patients (≥40 years) who underwent major elective non-cardiac surgery in Ontario, Canada between 2003 and 2009, and received coronary stents within 10 years before surgery. Approximately 34% (n=2725) underwent stent insertion within two years before surgery, of whom 905 (33%) received drug-eluting stents. For comparison, we assembled a separate cohort of 341,350 surgical patients who had not undergone coronary revascularization. The primary outcome was 30-day major adverse cardiac events (mortality, readmission for acute coronary syndrome or repeat coronary revascularization). The overall rate of 30-day events in patients with coronary stents was 2.1% (n=170). When the interval between stent insertion and surgery was less than 45-days, event rates were high for bare-metal (6.7%) and drug-eluting (20.0%) stents. When the interval was 45 to 180 days, the event rate for bare-metal stents was 2.6%, approaching that of intermediate-risk non-revascularized individuals. Adjusted analyses suggested that event rates were increased if this interval exceeded 180 days. For drug-eluting stents, the event rate was 1.2% once the interval exceeded 180 days, approaching that of intermediate-risk non-revascularized individuals.

Conclusions **-** The earliest optimal time for elective surgery is 46 to 180 days after bare-metal stent implantation or more than 180 days after drug-eluting stent implantation.

Key words: complications; coronary artery disease; percutaneous coronary intervention; surgery

Introduction

The management of non-cardiac surgery after percutaneous coronary intervention (PCI) and coronary stent implantation is a frequent and important concern in perioperative care. Percutaneous coronary interventions are common, with 1.2 million procedures performed every year in North America alone.[1,2] Of patients who receive coronary stents, 5% subsequently undergo non-cardiac surgery within one year,[3,4] corresponding to 60,000 patients annually in North America. The perioperative period poses important risks for such individuals. Risks of stent thrombosis and adverse cardiac events are increased due to the pro-thrombotic state induced by the surgical stress response,[5] as well as the potential disruption of anti-platelet medications. Conversely, if anti-platelet medications are continued to mitigate the risk of stent thrombosis, patients may suffer increased risks of major hemorrhage, which itself associated with increased mortality.[6]

Given these opposing risks, practice guidelines recommend that elective non-cardiac surgery be delayed until surgery can be performed safely using anti-platelet therapy with aspirin alone. The suggested delay is 30 to 45 days for bare-metal stents and one-year for drug-eluting stents.[7,8] These recommendations have important implications especially since 70% of North American patients who undergo PCI receive drug-eluting stents.[9] Specifically, many such individuals may not be able to defer their planned surgery for a year.

These recommendations are largely based on expert opinion, as well as reports that showed an increased risk of adverse cardiac events when non-cardiac surgery was performed shortly after stent implantation.[4,10-13] However, these previous reports have important limitations. Some were single-center studies with limited generalizability.[11-13] In addition, the association between non-cardiac surgery soon after PCI and adverse events may have been confounded by

the inclusion of urgent-to-emergent surgeries in several studies.[4,10,12,13] Specifically, urgent-to-emergent procedures, which are likely to necessitate non-cardiac surgery soon after PCI, are associated with an almost four-fold increased risk of mortality.[6]

Given the important implications of current guideline recommendations for the perioperative care of patients with coronary stents, and the limitations to the related literature, we conducted a population-based cohort study to evaluate the outcomes of patients who underwent elective intermediate-to-high risk non-cardiac surgery in Ontario, Canada following stent implantation.

Methods

The Cardiac Care Network of Ontario maintains a prospective clinical registry of all individuals who undergo cardiac catheterization, PCI, or coronary artery bypass grafting (CABG) surgery in Ontario, Canada.[14,15] All hospitals performing PCI are required to collect information on patients' clinical characteristics, as well as procedural information on the number of stents, characteristics of each stent, and location of stent placement. Following research ethics approval from Sunnybrook Health Sciences Centre, we conducted a retrospective cohort study by linking this registry to several population-based administrative databases, namely the Discharge Abstract Database (DAD) of the Canadian Institute for Health Information (hospital admissions), the Ontario Health Insurance Plan database (physician service claims), the Registered Persons Database (vital statistics), the Ontario Drug Benefit database (prescriptions for individuals aged 65 years and older), and the Canadian census. While these databases lack physiologic and laboratory measures (e.g. blood pressure, hemoglobin), they have been validated for many outcomes, exposures, and comorbidities.[16-20] Since the Cardiac Care Network registry is

prescribed under Ontario's health information privacy legislation, the need for informed consent was waived.

Cohort

We identified all Ontario residents who were aged 40 years or older, underwent any one of 16 pre-specified elective non-cardiac surgeries between 1 April 2003 and 31 March 2009, and underwent coronary stent implantation within 10 years before their index surgery. The included surgeries were abdominal aortic aneurysm repair, carotid endarterectomy, peripheral vascular bypass, total hip replacement, total knee replacement, large bowel resection, partial liver resection, Whipple procedure, pneumonectomy, pulmonary lobectomy, gastrectomy, esophagectomy, total abdominal hysterectomy, radical prostatectomy, nephrectomy, and cystectomy.[8,21,22] Information pertaining to the procedure performed and procedure status (elective versus non-elective) in this database is very accurate.[18] Individuals who underwent CABG surgery between the preoperative PCI and subsequent index non-cardiac surgery were excluded. In addition, we excluded low-risk ambulatory surgeries, largely because they are associated with a very low risk of major complications.[23] Furthermore, many such procedures can be performed while patients receive dual antiplatelet therapy, or delayed until dual therapy was no longer necessary.

Individuals in the cohort were categorized based on the type of stent implanted (bare-metal stent or drug-eluting stent) and duration between PCI and the index surgery. These categorizations were largely informed by practice guideline recommendations that elective non-cardiac surgery be delayed until at least 45 days after bare-metal-stent implantation, and 365 days after drug-eluting-stent implantation.[8] For individuals who underwent multiple PCI procedures before their index surgery, the categorization was based on the PCI closest to the

surgery. The nine categories were bare-metal stent within one to 45 days before surgery, bare-metal stent within 46 to 180 days before surgery, bare-metal stent within 181 to 365 days before surgery, bare-metal stent within 366 to 730 days before surgery, drug-eluting stent within one to 45 days before surgery, drug-eluting stent within 46 to 180 days before surgery, drug-eluting stent within 181 to 365 days before surgery, drug-eluting stent within 366 to 730 days before surgery, and any stent within 731 days to 10 years before surgery. Patients with remote histories of stent implantation (i.e. 731 days to 10 years before surgery) served as the control group against which we compared individuals who underwent more recent stent implantation.

Outcomes and Comorbidities

Patients were tracked for one year after surgery for mortality, hospital readmission for an acute coronary syndrome (myocardial infarction or unstable angina), and repeat coronary revascularization (PCI or CABG surgery). The DAD (in-hospital mortality, revascularization, hospital readmission for acute coronary syndrome), Registered Persons Database (out-of-hospital mortality) and Cardiac Care Network registry (revascularization) were used to ascertain these outcomes. We identified hospitalizations for acute coronary syndromes using *International Classification of Diseases* 10th Revision diagnostic codes I21, I22, I20, I23.82 and I24.[24] The primary outcome was a major adverse cardiac event (MACE) – defined as mortality, readmission for acute coronary syndrome, or coronary revascularization – within 30 days after the index surgery. The secondary outcome was MACE within one year after surgery.

Demographic information was obtained from the Registered Persons Database, while validated algorithms were used to identify diabetes and hypertension.[17,19] The Ontario Health Insurance Plan database was used to identify anyone who required dialysis before surgery. Using the DAD, we used previously described methods to identify other comorbidities based on

International Classification of Diseases (9th or 10th Revision) codes from hospitalizations within three years preceding surgery: congestive heart failure, cerebrovascular disease, peripheral vascular disease, pulmonary disease, and chronic renal insufficiency.[25] We determined patients' socioeconomic status based on their neighborhood median income in the Canadian census, and their residence (rural versus urban) using Statistics Canada definitions.[26]

Perioperative cardiac risk was also estimated based on the Revised Cardiac Risk Index (RCRI).[27] This predictive index consists of six equally weighted components: coronary artery disease, congestive heart failure, cerebrovascular disease, diabetes, renal insufficiency, and high-risk surgery (major vascular, intra-peritoneal, or intra-thoracic procedures). It is suggested that a RCRI score of zero points corresponds to low risk, one to two points corresponds to intermediate risk, and three or more points corresponds to high risk.[28]

As an additional comparison, we used the same databases to describe the characteristics and outcomes of individuals who were aged 40 years or greater, underwent eligible surgeries during the study period, and had *not* undergone any revascularization (PCI or CABG surgery) within 10 years before their index surgery.

To describe the preoperative use of antiplatelet medications, the Ontario Drug Benefits database was used to ascertain preoperative prescriptions for thienopyridines (clopidogrel or ticlopidine) in the 100 days before the index surgery. Since these data are only available for individuals aged 65 years or older, and a 100-day look-back period was used, this analysis was performed in the subgroup aged 66 years or older.

Analyses

We used appropriate tests (analysis of variance, Kruskal-Wallis test, chi-square test) to compare the characteristics of patients who had or had not received a bare-metal stent or drug-eluting

stent within two years before their index surgeries. Descriptive statistics were used to characterize event rates of the primary and secondary outcomes among individuals who had undergone prior PCI (categorized based on stent type and PCI-to-surgery interval), and among non-revascularized individuals (categorized based on RCRI score).[27]

We then used multivariable logistic regression to determine the adjusted association between the nine categories of stent type and PCI-to-surgery interval with the primary and secondary outcomes. The reference category, against which the different categories of the primary exposure were compared, was a history of remote stenting (i.e. bare-metal or drug-eluting stent within 731 days to 10 years before surgery). The other covariates in the regression model were age, sex, surgery, congestive heart failure, cerebrovascular disease, peripheral vascular disease, hypertension, diabetes, and renal disease. Surgeries were categorized as major vascular (abdominal aortic aneurysm repair, peripheral vascular bypass), high-intermediate-risk (large bowel resection, partial liver resection, Whipple procedure, pneumonectomy, pulmonary lobectomy, gastrectomy, esophagectomy cystectomy, nephrectomy), and low-intermediate-risk (carotid endarterectomy, total hip replacement, total knee replacement, total abdominal hysterectomy, radical prostatectomy) procedures.[29] Model discrimination was measured using the c-statistic, while calibration was estimated using the Hosmer-Lemeshow statistic.

All analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC) and a two-tailed P-value less than 0.05 was used to define statistical significance.

Results

The cohort consisted of 8116 patients who underwent stent implantation within 10 years before their non-cardiac surgery. Approximately 34% (n=2725) underwent stent implantation within

two years before surgery; of these individuals, 905 (33%) received drug-eluting stents. The proportion that had received drug-eluting stents within two years before surgery varied over the study period (Online Data Supplement, **Supplemental Figure 1**). Compared to individuals with remote histories of stent implantation (i.e. 731 days to 10 years before non-cardiac surgery), patients who received bare-metal or drug-eluting stents within two years before surgery differed with regard to surgical procedure and comorbidities (**Table 1**).

The separate comparator group of patients, who were aged 40 years or greater, underwent eligible surgeries, and had not undergone coronary revascularization within 10 years before their index surgery, consisted of 341,350 individuals. Their characteristics are presented in the Online Data Supplement (**Supplemental Table 1**).

Among individuals who had undergone prior PCI, the overall risk of 30-day MACE was relatively low at 2.1% (n=170), while the risk of 1-year MACE was 9.8% (n=798). The rate of postoperative mortality was 1.2% (n=100) at 30-days and 5.2% (n=419) at one-year. The incidence of MACE over the first year following surgery is presented in **Supplemental Figure 2** (Online Data Supplement).

The unadjusted risk of cardiac events at 30-days (**Figure 1**) and one-year (Online Data Supplement, **Supplemental Figure 3**) after surgery varied based on the type of stent implanted and the time interval from stent implantation to surgery. Once the interval between PCI and surgery exceeded 45 days, the 30-day risk of MACE in a patient with a bare-metal stent approached that of an intermediate risk non-revascularized individual with one to two clinical risk factors (**Figure 1**). Once the interval exceeded 180 days, the 30-day risk of MACE in a patient with a drug-eluting stent approached that of an intermediate-risk non-revascularized individual with one risk factor (**Figure 1**).

Using multivariable logistic regression, we determined the adjusted association of coronary stent type and PCI-to-surgery time interval with postoperative MACE at 30-days (**Figure 2**) and one-year (Online Data Supplement, **Supplemental Figure 4)** after surgery. The confidence intervals were generally wide, especially with respect to adjusted odds ratios for 30-day MACE. However, these analyses were suggestive of an increased 30-day risk of MACE when surgery was performed within 45 days of either bare-metal or drug-eluting stent insertion, or within 181 to 365 days after bare-metal stent insertion (**Figure 2**).

For the subgroup aged greater than 66 years at the time of surgery (n=5381), the proportion receiving preoperative thienopyridines was 60.6% (n=734) among the 1211 individuals who received a bare-metal stent within two years before surgery, 68.9% (n=404) among the 586 individuals who received a drug-eluting stent within two years before surgery, and 12.8% (n=460) among the 3584 individuals who had received any stent within two to 10 years before surgery. The specific proportions within subgroups defined by stent type and PCI-to-surgery time interval are presented in the Online Data Supplement (**Supplemental Table 2**).

Discussion

In this population-based study, we found that the risk of perioperative MACE was highest when major elective non-cardiac surgery was performed less than 45 days after coronary stent implantation. The earliest optimal time for performing surgery appeared to be from 46 to 180 days after bare-metal-stent implantation, or more than 180 days after drug-eluting-stent implantation. Thus, these findings help inform clinical decision-making regarding the timing of major elective non-cardiac surgery following recent PCI.

Implications

Our findings suggest that elective non-cardiac surgery can be performed reasonably safely in carefully selected patients once at least six months had elapsed since drug-eluting-stent implantation. There may also be an "optimal" time window for performing surgery within the year following bare-metal-stent implantation, namely from 46 to 180 days after PCI. While the presence of this "optimal" window is not certain, especially because its associated adjusted odds ratio is imprecise, this window is biologically plausible. It represents the period when re-endothelialization is largely complete after bare-metal-stent implantation,[30] but when in-stent restenosis has yet to completely manifest itself.[31] Conversely, once more than one year has elapsed since either bare-metal or drug-eluting stent implantation, physicians can reassured that the associated perioperative cardiac risk has reached a plateau, with risks similar to that of individuals with remote histories of previous PCI (i.e. two to 10 years before surgery).

Importantly, our results also indicate that the *absolute* magnitude of short-term postoperative risk is not unreasonable during these periods, namely 45 to 180 days after bare-metal stent implantation and more than 180 days after drug-eluting-stent implantation. Specifically, perioperative risks during these intervals approach that of an intermediate risk non-revascularized patient with one to two risk factors. This absolute risk is important for clinicians to consider when weighing the risks of proceeding with elective surgery following PCI against the risks of *not* operating in individuals who require surgery for conditions such as cancer.

Our study has implications for current guideline recommendations pertaining to the perioperative care of patients with coronary stents. While our results do support the recommendation to delay elective non-cardiac surgery until at least 30 to 45 days have elapsed since bare-metal-stent implantation, they further suggest that excessive delays are not helpful. Specifically, short-term perioperative cardiac risk might rise once more than 180 days have

elapsed since PCI. Conversely, whereas guidelines recommend that surgery be delayed until one year after drug-eluting-stent implantation,[8] our findings instead suggest that surgery can be performed reasonably safely following a six-month delay.

Our results have both important similarities and differences with respect to previous investigations of non-cardiac surgery following coronary stent implantation. We confirmed observations of substantially increased risk when surgery is performed within six weeks of coronary stent implantation.[4,10,12,13] In addition, our study is largely consistent with previous research showing that cardiac risk is relatively low if elective surgery is delayed by six months or more after drug-eluting-stent implantation.[32-34] Our findings also corroborate a prior study where discontinuation of dual antiplatelet therapy after six months was not associated with increased rates of stent thrombosis following drug-eluting-stent implantation.[35]

Conversely, our findings differ from some prior studies with respect to rates of perioperative MACE.[4,10,36] In two prospective cohort studies, Vincenzi *et al*. reported an adverse event rate of 44% while Godet *et al*. reported a 12% rate of postoperative myocardial necrosis.[4,36] These differences may be explained, in part, by their inclusion of urgent-to-emergent surgeries (28% in the study by Vincenzi *et al*. and 8% in the study by Godet *et al*.). These studies also differed from our investigation with respect to the definition of adverse events. Vincenzi *et al*. included a broad range of complications – including cardiac death, myocardial infarction, repeat revascularization, bleeding, sepsis, and elevated troponin concentrations without clinical evidence of myocardial infarction– in their reported event rate. If only cardiac death, myocardial infarction and repeat revascularization were considered, the event rate was 22% instead.[4] Similarly, while Godet *et al*. reported a 12% rate of elevated troponin concentrations, the rate of myocardial infarction or death was 4%.[36]

In a previous study that used administrative databases, Cruden *et al*. reported a 14% rate of postoperative death or ischemic events. Notably, the adverse event rate remained elevated at 11% rate even when surgery was performed more than one year after PCI.[10] These differences may be explained the investigators' use of administrative data to identify postoperative in-hospital cardiac complications. Previous research has shown that administrative data generally do not accurately capture in-hospital complications.[37] In contrast, the components of our primary outcome – mortality, readmission for acute coronary syndrome, or revascularization – are accurately captured by administrative databases.[18,24] Notably, rates of postoperative death, which are generally accurately captured by administrative data, in the study by Cruden *et al*. were considerably lower at only 0.6%.

The major strength of our study is the generalizability associated with its population-based sample. Additionally, the cohort only included elective procedures, thereby focusing the analysis on the clinically relevant situation where physicians must decide whether to delay elective surgery to minimize perioperative risk related to coronary stents. Conversely, for non-elective procedures, surgery usually proceeds regardless of the interval since recent PCI, and the main issue is how best to manage patients' antiplatelet medications.

Our study also has several limitations. *First*, despite being one of the largest evaluations of non-cardiac surgery following stent implantation, event rates were relatively low, thereby limiting our statistical power. Many estimates from multivariable analyses therefore had wide confidence intervals, and smaller subgroups within patients who underwent prior PCI (e.g. strata defined by RCRI score) could not be evaluated. *Second*, administrative databases generally do not accurately capture in-hospital complications.[37] We could not therefore ascertain several postoperative complications that are directly relevant to this study, such as non-fatal myocardial

infarction, stent thrombosis, and clinically significant bleeding. Nonetheless, the primary outcome includes all significant sequelae of a postoperative myocardial infarction, namely death, repeat revascularization or hospital re-admission for acute coronary syndrome. *Third*, our databases did not capture in-hospital medications or outpatient aspirin use; furthermore, they did not describe whether patients had briefly discontinued their aspirin or thienopyridine use before surgery. Indeed, the absence of information on in-hospital medications may explain the paradoxically lower rate of thienopyridine use among patients who had non-cardiac surgery less than 45 days after stent insertion (Online Data Supplement, **Supplemental Table 1**). *Fourth*, the PCI registry lacked some detailed procedural information (e.g. bifurcational stenting, poor run-off) that may have influenced both patients' perioperative risks and clinicians' willingness to discontinue anti-platelet therapy earlier than recommended by practice guidelines.

Fifth, survivor bias and unmeasured confounding may explain, in part, the lower event rates among individuals with longer delays between PCI and non-cardiac surgery. For example, when compared to anyone who underwent surgery shortly after PCI, such patients would have to survive longer after PCI without dying or needing repeat revascularization. Thus, any individual with unstable coronary artery disease requiring repeat revascularization would either be excluded if CABG was performed, or reclassified as having a shorter interval from PCI to surgery. In addition, the performance of elective surgery sooner after PCI may have been a marker of more urgent procedures that were themselves associated with increased perioperative risk. *Sixth*, changing practice guidelines might explain, in part, the reduced risk of MACE when surgery was performed more than six months following drug-eluting stent insertion. Specifically, prior to the updating of perioperative practice guidelines in 2007,[7] PCI-specific guidelines recommended clopidogrel therapy for only three months after sirolimus stent implantation, and six months after

paclitaxel stent implantation.[38] Performance of surgery more than six months after drug-eluting stent implantation may therefore be a marker of more compliant physicians whose patients generally had better overall outcomes.

Conclusions

In this population-based study, the earliest optimal time for performing elective non-cardiac surgery appeared to be from 46 to 180 days after bare-metal-stent implantation, or more than 180 days after drug-eluting-stent implantation. In addition to being relevant to future practice guidelines, these findings will help inform clinical decision-making when weighing the risks of operative versus non-operative therapy in patients being considered for major elective non-cardiac surgery following recent coronary stent implantation.

Funding Sources: Dr. Wijeysundera is supported by a Clinician-Scientist Award from the Canadian Institutes of Health Research. Drs. Wijeysundera, Wąsowicz and Beattie are supported by Merit Awards from the Department of Anesthesia at the University of Toronto. Dr. Wąsowicz is supported by a Canadian Anesthesiologists' Society Career Scientist Award from the Canadian Anesthesia Research Foundation. Dr. Beattie is R. Fraser Elliot Chair of Cardiac Anesthesia at the University Health Network. Dr. Ko is supported by a New Investigator Award from the Canadian Institutes of Health Research. The authors acknowledge that the clinical registry data used in this publication are from the Cardiac Care Network of Ontario and its member hospitals. The Cardiac Care Network of Ontario serves as a support to the Ontario healthcare system, including the Ontario Ministry of Health and Long-Term Care, and is dedicated to improving the quality, efficiency, access, and equity of adult cardiovascular services in Ontario, Canada. The Cardiac Care Network of Ontario is funded by the Ontario Ministry of Health and Long-Term Care. The analysis for this study was supported by operating grant MOP (102487) from the Canadian Institutes of Health Research. This study was also supported in part by the Institute for Clinical Evaluative Sciences, which is itself supported in part by the Ontario Ministry of Health and Long-Term Care. The study sponsor had no role in the design and conduct of the study; analysis and interpretation of the data; and preparation, review, or approval of the manuscript. The opinions, results, and conclusions are those of the authors, and no endorsement by the Ontario Ministry of Health and Long-Term Care or the Institute for Clinical Evaluative Sciences is intended, or should be inferred.

Conflict of Interest Disclosures: None.

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DOI: 10.1161/CIRCULATIONAHA.112.102715

Table 1. Characteristics of main study cohort*

	BMS 0-2 Years before Surgery (n=1820)	DES 0-2 Years before Surgery (n=905)	Stent 2-10 Years before Surgery (n=5391)	P-Value
Demographics				
Female sex	590 (32.4%)	314 (34.7%)	1,681 (31.2%)	0.09
Age (y), mean (SD)	69.1 (9.3)	68.8 (9.5)	69.2 (9.0)	0.45
Income quintile				
First (lowest)	364 (20.1%)	175 (19.3%)	1,009 (18.8%)	
Second	325 (17.9%)	196 (21.7%)	1,133 (21.1%)	
Third	387 (21.3%)	175 (19.3%)	1,097 (20.4%)	0.12
Fourth	371 (20.5%)	165 (18.2%)	1,084 (20.1%)	
Fifth (highest)	366 (20.2%)	194 (21.4%)	1,057 (19.6%)	
Missing	7 (0.4%)	0 (0%)	11 (0.2%)	
Rural residence	314 (17.3%)	152 (16.8%)	974 (18.1%)	0.54
Comorbid disease				
Congestive heart failure	202 (11.1%)	71 (7.8%)	313 (5.8%)	<0.001
Cerebrovascular disease	116 (6.4%)	57 (6.3%)	212 (3.9%)	<0.001
Peripheral vascular disease	369 (20.3%)	169 (18.7%)	817 (15.2%)	<0.001
Hypertension	1,501 (82.5%)	779 (86.1%)	4,640 (86.1%)	<0.001
Diabetes mellitus	591 (32.5%)	372 (41.1%)	1,939 (36.0%)	<0.001
Pulmonary disease	163 (9.0%)	81 (9.0%)	436 (8.1%)	0.41
Renal disease	113 (6.2%)	60 (6.6%)	290 (5.4%)	0.19
Procedure				
AAA repair	161 (8.8%)	48 (5.3%)	323 (6.0%)	
Carotid endarterectomy	92 (5.1%)	68 (7.5%)	265 (4.9%)	
Peripheral vascular bypass	157 (8.6%)	89 (9.8%)	350 (6.5%)	
Total hip replacement	304 (16.7%)	137 (15.1%)	964 (17.9%)	
Total knee replacement	482 (26.5%)	279 (30.8%)	1,929 (35.8%)	
Large bowel surgery	280 (15.4%)	130 (14.4%)	563 (10.4%)	<0.001
Liver resection	17 (0.9%)	6 (0.7%)	29 (0.5%)	
Whipple procedure	6 (0.3%)	8 (0.9%)	24 (0.4%)	
Lung resection	67 (3.7%)	21 (2.3%)	155 (2.9%)	
Gastrectomy or esophagectomy	33 (1.8%)	13 (1.4%)	85 (1.6%)	
Abdominal hysterectomy	73 (4.0%)	47 (5.2%)	215 (4.0%)	
Radical prostatectomy	59 (3.2%)	26 (2.9%)	277 (5.1%)	
Nephrectomy	70 (3.8%)	25 (2.8%)	47 (0.9%)	
Cystectomy	19 (1.0%)	8 (0.9%)	47 (0.9%)	
Revised Cardiac Risk Index				
1 point	597 (32.8%)	317 (35.0%)	2,181 (40.5%)	
2 points	756 (41.5%)	343 (37.9%)	2,193 (40.7%)	<0.001
3 points	351 (19.3%)	181 (20.0%)	800 (14.8%)	
4 or more points	116 (6.4%)	64 (7.1%)	217 (4.0%)	

Abbreviations: AAA, abdominal aortic aneurysm; BMS, bare-metal-stent; DES, drug-eluting-stent; SD, standard deviation

* Values are expressed as number (percentage) unless indicated otherwise

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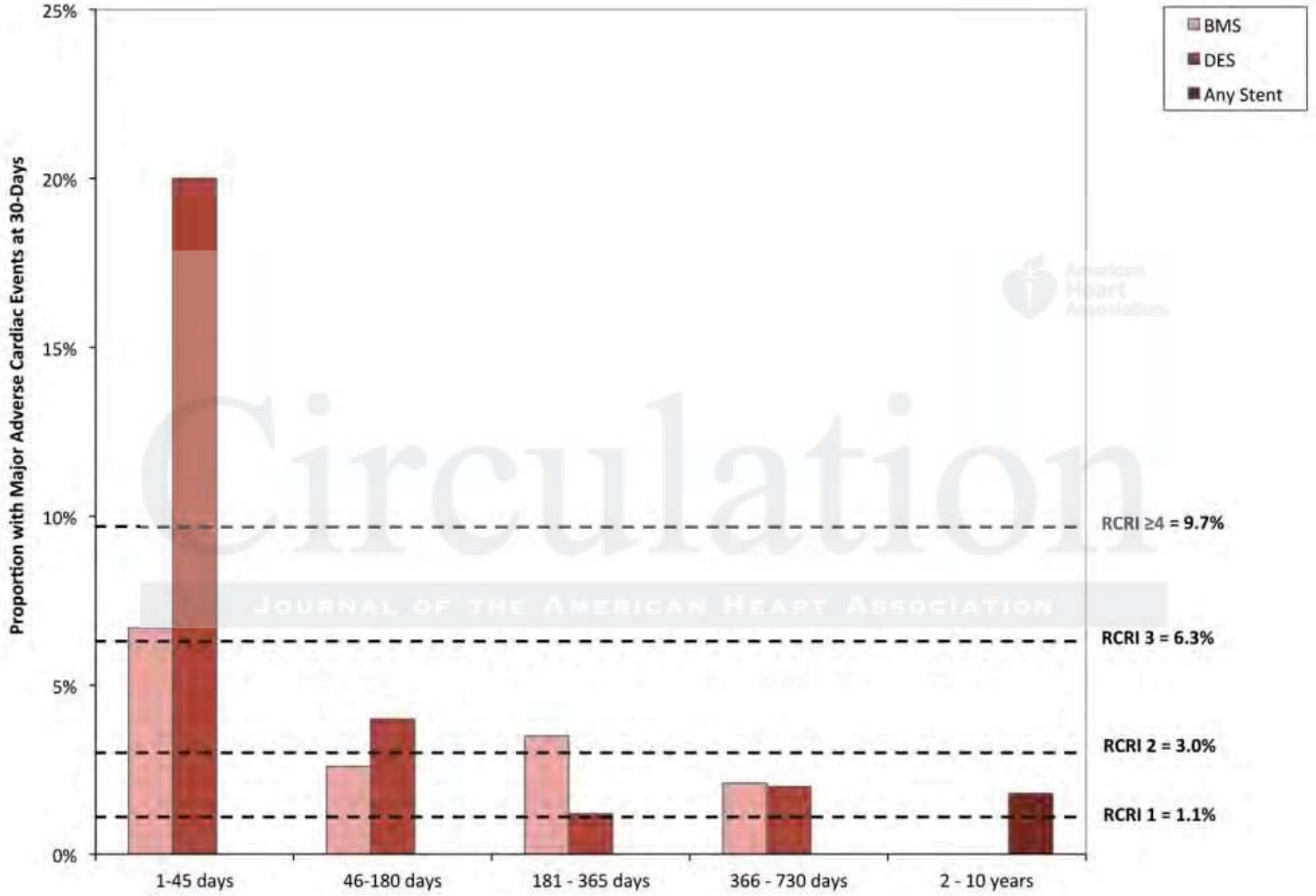
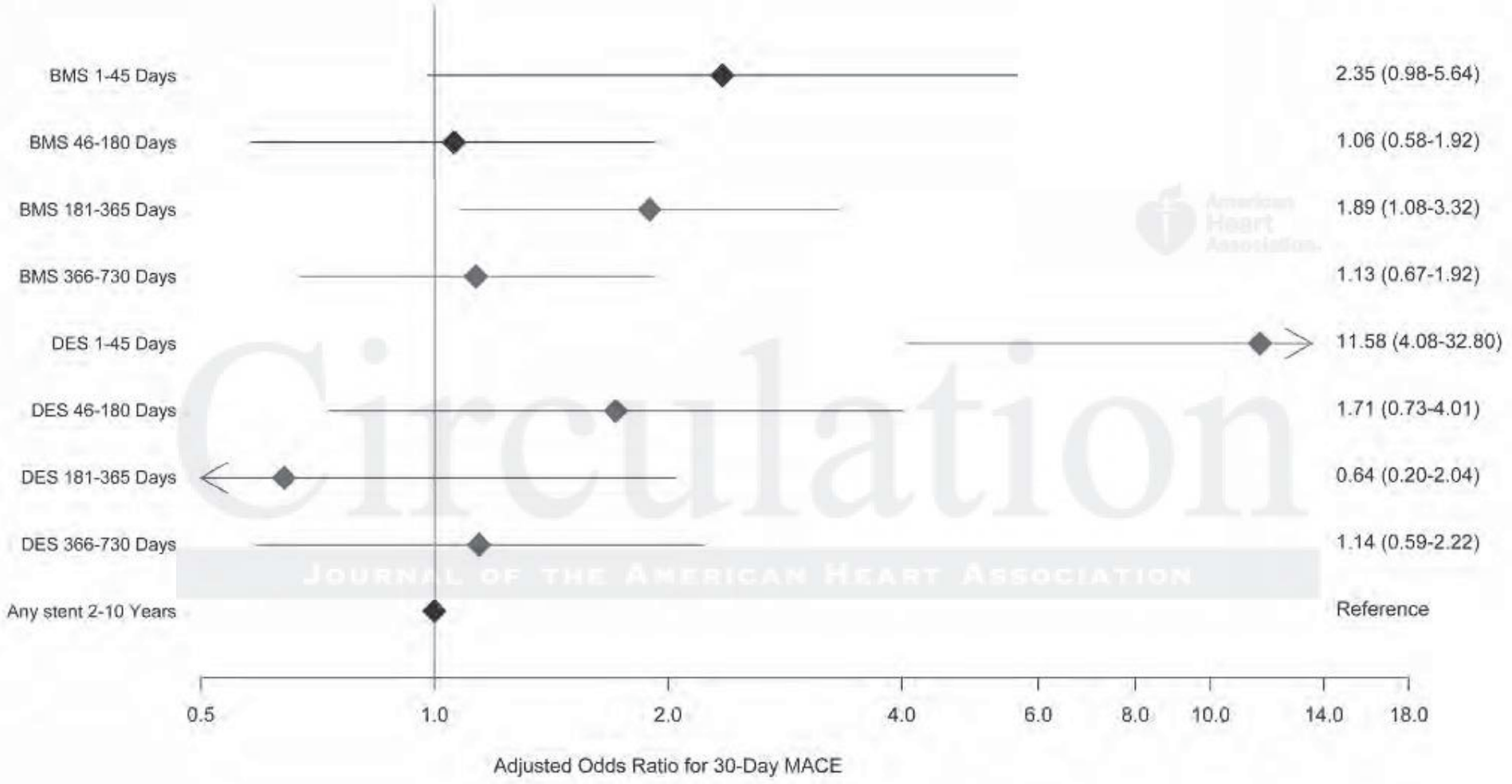
Figure Legends:

Figure 1. Proportion of patients with major adverse cardiac events within 30 days after elective non-cardiac surgery. Proportion of patients with major adverse cardiac events (death, readmission for acute coronary syndrome, coronary revascularization) within 30 days after elective non-cardiac surgery, based on the interval between the most recent coronary stent insertion and subsequent non-cardiac surgery. The red columns represent proportions for individuals who received bare metal stents (BMS), drug eluting stents (DES), or either type of stent (for stent insertions two to 10 years before non-cardiac surgery). For comparison, the horizontal dashed lines represent event rates for individuals who did *not* undergo coronary revascularization within 10 years before non-cardiac surgery, and had been stratified by their Revised Cardiac Risk Index scores.

Figure 2. Adjusted association of stent type and time interval from stent insertion to surgery with major adverse cardiac events within 30 days after elective non-cardiac surgery. The diamonds represent adjusted odds ratios (OR) for 30-day major adverse cardiac events, while the error bars are 95% confidence intervals (CI). The corresponding numerical values for these point estimates and CIs are presented on the right. The arrows denote CIs that extend beyond the scale of this graph. The reference category for the adjusted odds ratios was a remote history of stent insertion (i.e. bare-metal or drug-eluting stent within 731 days to 10 years before surgery). The adjusted ORs were derived from a logistic regression model that adjusted for age, sex, surgery, congestive heart failure, cerebrovascular disease, peripheral vascular disease, hypertension, diabetes mellitus, and renal disease. This model had reasonable discrimination (c-index 0.71) and good calibration (Hosmer-Lemeshow statistic P=0.63).





SUPPLEMENTAL MATERIAL

Supplemental Table 1: Characteristics of individuals who were aged 40 years or greater, underwent eligible surgeries during the study period, and had not undergone any coronary revascularization procedure within 10 years before their index non-cardiac surgery.

	RCRI: 0 points (n=206,774)	RCRI: 1 point (n=103,490)	RCRI: 2 points (n=24,945)	RCRI: 3 points (n=4,841)	RCRI: ≥4 points (n=1,066)
Demographics					
Female sex	145,008 (70.1%)	54,405 (52.6%)	10,104 (40.5%)	1,763 (36.4%)	379 (35.6%)
Age (y), mean (SD)	61.7 (12.5)	66.1 (11.3)	69.6 (10.1)	71.9 (9.6)	72.8 (9.5)
Income quintile					
First (lowest)	33,681 (16.3%)	19,538 (18.9%)	5,442 (21.9%)	1,213 (25.2%)	250 (23.4%)
Second	40,336 (19.6%)	21,572 (20.9%)	5,494 (22.1%)	1,064 (22.1%)	284 (26.7%)
Third	41,491 (20.1%)	20,654 (20.0%)	4,974 (20.0%)	887 (18.4%)	205 (19.3%)
Fourth	43,693 (21.2%)	20,819 (20.2%)	4,651 (18.7%)	911 (18.9%)	175 (16.5%)
Fifth (highest)	47,039 (22.8%)	20,609 (20.0%)	4,294 (17.3%)	748 (15.5%)	146 (13.7%)
Missing	534 (0.3%)	298 (0.3%)	90 (0.4%)	18 (0.4%)	6 (0.5%)
Rural residence	34,690 (16.8%)	16,267 (15.7%)	3,908 (15.7%)	807 (16.7%)	187 (17.5%)
Comorbid disease					
Coronary artery disease	0 (0.0%)	5,196 (5.0%)	6,498 (26.0%)	3,266 (67.5%)	895 (84.0%)
Congestive heart failure	0 (0.0%)	832 (0.8%)	1,367 (5.5%)	1,176 (24.3%)	652 (61.2%)
Cerebrovascular disease	0 (0.0%)	2,134 (2.1%)	2,138 (8.6%)	993 (20.5%)	343 (32.2%)
Peripheral vascular disease	803 (0.4%)	7,755 (7.5%)	5,073 (20.3%)	1,576 (32.6%)	475 (44.6%)
Hypertension	105,222 (50.9%)	67,268 (65.0%)	20,200 (81.0%)	4,333 (89.5%)	1,005 (94.3%)

Diabetes	0 (0.0%)	39,637 (38.3%)	18,411 (73.8%)	3,786 (78.2%)	903 (84.7%)
Pulmonary disease	5,963 (2.9%)	6,092 (5.9%)	2,719 (10.9%)	916 (18.9%)	305 (28.6%)
Renal disease	0 (0.0%)	954 (0.9%)	2,074 (8.3%)	1,395 (28.8%)	559 (52.4%)
Procedure					
AAA repair	0 (0.0%)	3,874 (3.7%)	2,007 (8.0%)	516 (10.7%)	90 (8.4%)
Carotid endarterectomy	2,406 (1.2%)	2,025 (2.0%)	800 (3.2%)	175 (3.6%)	31 (2.9%)
Peripheral vascular bypass	0 (0.0%)	3,616 (3.5%)	2,789 (11.2%)	907 (18.7%)	315 (29.5%)
Total hip replacement	45,562 (22.0%)	10,790 (10.4%)	1,345 (5.4%)	270 (5.6%)	53 (5.0%)
Total knee replacement	74,568 (36.1%)	25,485 (24.6%)	2,836 (11.4%)	430 (8.9%)	62 (5.8%)
Large bowel surgery	0 (0.0%)	29,539 (28.5%)	8,700 (34.9%)	1,448 (30.0%)	331 (31.1%)
Liver resection	0 (0.0%)	1,603 (1.5%)	511 (2.0%)	66 (1.4%)	9 (0.8%)
Lung resection	0 (0.0%)	4,972 (4.8%)	1,386 (5.6%)	265 (5.5%)	41 (3.8%)
Gastrectomy, esophagectomy, or Whipple procedure*	0 (0.0%)	3923 (3.8%)	1374 (5.5%)	190 (3.9%)	41 (3.8%)
Abdominal hysterectomy	69,261 (33.5%)	7,830 (7.6%)	407 (1.6%)	51 (1.1%)	8 (0.8%)
Radical prostatectomy	14,977 (7.2%)	2,623 (2.5%)	155 (0.6%)	8 (0.2%)	0 (0.0%)
Nephrectomy	0 (0.0%)	5,655 (5.5%)	2,084 (8.4%)	389 (8.0%)	72 (6.8%)
Cystectomy	0 (0.0%)	1,555 (1.5%)	551 (2.2%)	126 (2.6%)	13 (1.2%)

Abbreviations: AAA, abdominal aortic aneurysm; RCRI, Revised Cardiac Risk Index

* These categories were combined to prevent small cell numbers and thereby preserve the anonymity of these administrative healthcare data

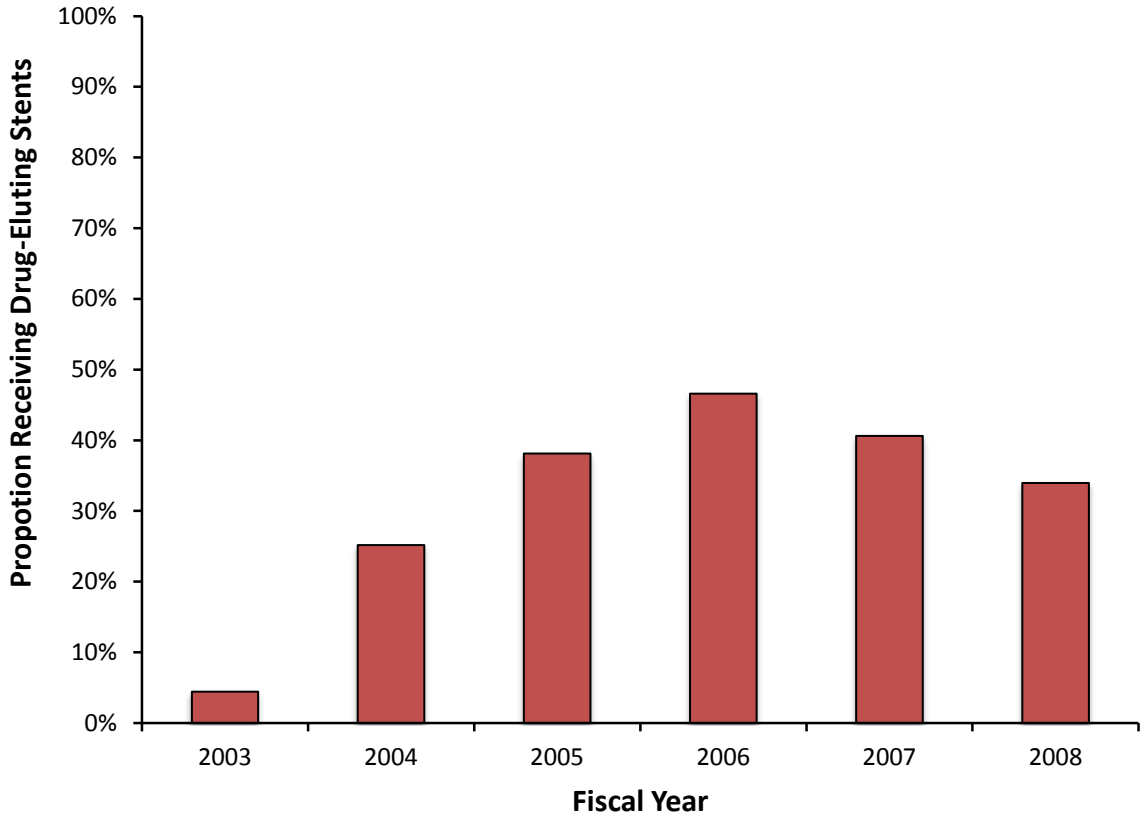
Supplemental Table 2: Proportion of individuals aged 66 years or older who were receiving thienopyridines (clopidogrel or ticlopidine) before elective non-cardiac surgery*

Stent Type	Interval between Stent Insertion and Surgery	Total Number	Patients Receiving Thienopyridines before Surgery (%)
BMS	1 to 45 days	63	47 (74.6%)
	46 to 180 days	337	286 (84.9%)
	181 to 365 days	285	206 (72.3%)
	366 to 730 days	526	195 (37.1%)
DES	1 to 45 days	15	11 (73.3%)
	46 to 180 days	98	88 (89.8%)
	181 to 365 days	161	141 (87.6%)
	366 to 730 days	312	164 (52.6%)
BMS or DES	2 to 10 years	3584	460 (12.8%)

Abbreviations: BMS, bare metal stent; DES, drug-eluting stent

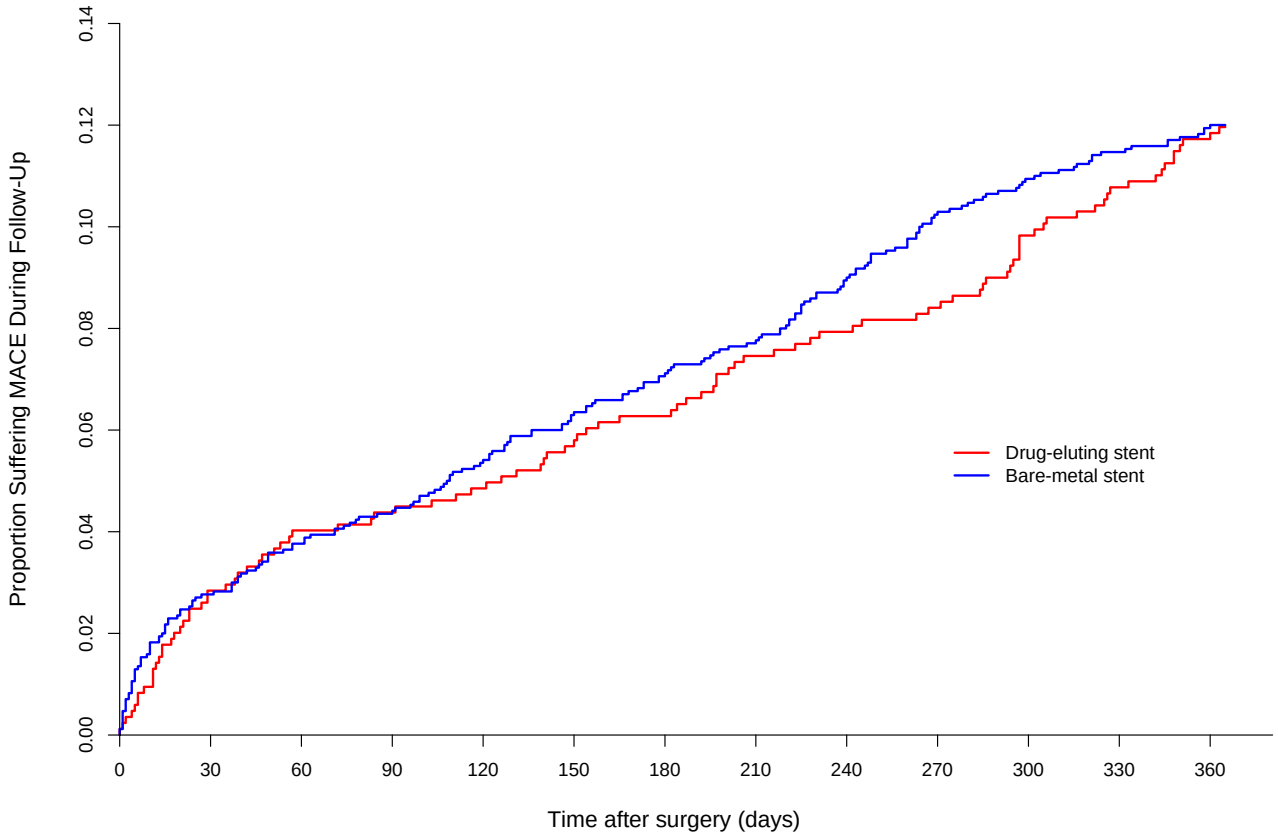
* Defined as presence of one or more relevant outpatient prescriptions within 100 days before admission for index non-cardiac surgery

Supplemental Figure 1: Proportion with drug-eluting stents among patients who received coronary stents within two years before major elective non-cardiac surgery



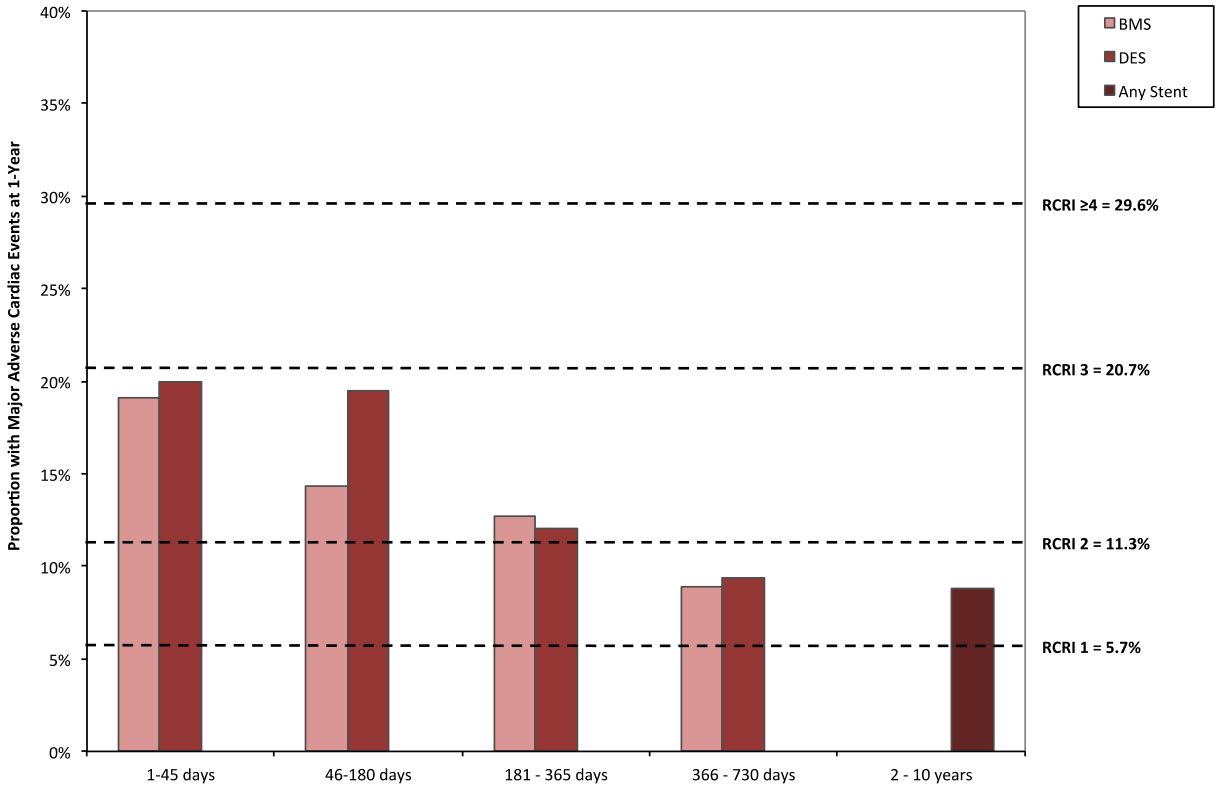
Legend: Proportion of patients with drug-eluting stents, among individuals who received coronary stents within two years before major elective non-cardiac surgery. The columns represent proportions for each fiscal year of the study – from fiscal year 2003 (1 April 2003 to 30 March 2004) to fiscal year 2008 (1 April 2008 to 30 March 2009)

Supplemental Figure 2: Time to first major adverse cardiac event within one year after major elective non-cardiac surgery



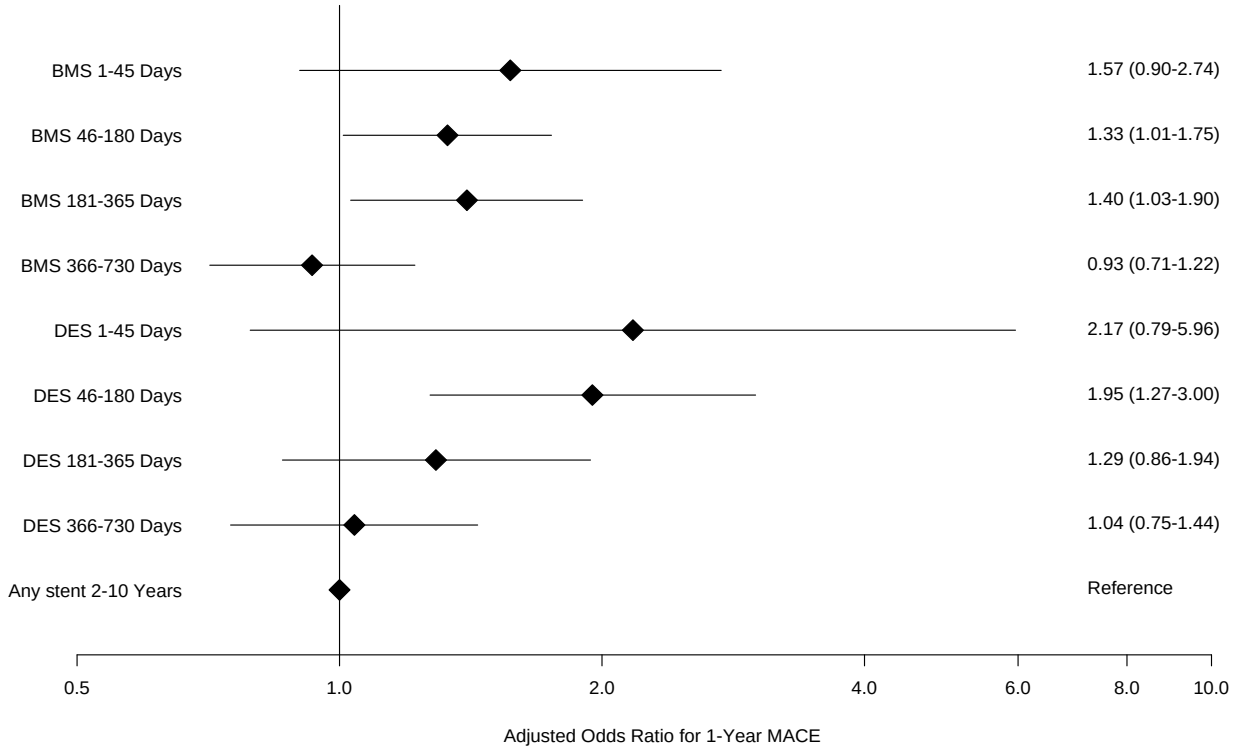
Legend: Proportion suffering adverse cardiac events among patients who underwent coronary stent implantation within two years before non-cardiac surgery, as stratified by type of stent implanted.

Supplemental Figure 3: Proportion of patients with major adverse cardiac events within one year after elective non-cardiac surgery



Legend: Proportion of patients with major adverse cardiac events (death, readmission for acute coronary syndrome, coronary revascularization) within 365 days after elective non-cardiac surgery, based on the interval between the most recent coronary stent insertion and subsequent non-cardiac surgery. The red columns represent proportions for individuals who received bare metal stents (BMS), drug eluting stents (DES), or either type of stent (for stent insertions two to 10 years before noncardiac surgery). For comparison, the horizontal dashed lines represent event rates for individuals who did *not* undergo coronary revascularization within 10 years before non-cardiac surgery, and had been stratified by their Revised Cardiac Risk Index scores.

Supplemental Figure 4: Adjusted association of stent type and time interval from stent insertion to surgery with major adverse cardiac events within one year after elective non-cardiac surgery.



Legend: The diamonds represent adjusted odds ratios (OR) for 1-year major adverse cardiac events, while the error bars are 95% confidence intervals (CI). The corresponding numerical values for these point estimates and CIs are presented on the right. The reference category for the adjusted odds ratios was a remote history of stent insertion (i.e. bare-metal or drug-eluting stent within 731 days to 10 years before surgery). The adjusted ORs were derived from a logistic regression model that adjusted for age, sex, surgery, congestive heart failure, cerebrovascular disease, peripheral vascular disease, hypertension, diabetes mellitus, and renal disease. This model had a c-index of 0.67 and good calibration (Hosmer-Lemeshow statistic P=0.42).