

Selection of Stent Type in Patients With Atrial Fibrillation Presenting With Acute Myocardial Infarction: An Analysis From the ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry—Get With the Guidelines

Amit N. Vora, MD, MPH; Tracy Y. Wang, MD, MHS, MSc; Shuang Li, MS; Karen Chiswell, PhD; Connie Hess, MD, MHS; Renato D. Lopes, MD, PhD; Sunil V. Rao, MD; Eric D. Peterson, MD, MPH

Background—Patients receiving oral anticoagulation in addition to dual-antiplatelet therapy are known to be at high risk for bleeding events; thus, the selection of a drug-eluting stent (DES) versus a bare metal stent (BMS) can have important implications for patients with atrial fibrillation (AF) presenting with acute myocardial infarction (MI).

Methods and Results—From the National Cardiovascular Data Registry ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry—Get With the Guidelines, we identified 14 427 AF patients presenting with acute MI undergoing percutaneous coronary intervention from 2008 to 2014. Temporal trends and hospital variation in DES use were examined, as were patterns of use by stroke risk (CHA₂DS₂-VASc) and bleeding risk ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation). Among patients with linked Medicare data (n=2844), multivariable Cox regression modeling was used to compare risks for a composite outcome (all-cause mortality, readmission for stroke, or MI), readmission for stroke, revascularization, and major bleeding at 1 year. A DES was used in 8414 (58.9%) MI patients with AF, increasing from 47.1% in 2008 to 67.9% in 2014, with wide variation among hospitals. DES placement was more common than BMS placement among patients at high stroke risk (CHA₂DS₂-VASc ≥2) and high bleeding risk (ATRIA ≥4). Although aspirin and a P2Y₁₂ inhibitor were prescribed for >95% of all patients regardless of stent type at discharge, warfarin was prescribed less frequently among patients receiving a DES than a BMS (31% versus 39%, *P*<0.001). The composite outcome was similar between patients with a DES or BMS at 1 year (22% versus 26%; adjusted hazard ratio: 0.88; 95% confidence interval [CI], 0.76–1.03).

Conclusions—Use of DESs among MI patients with AF has increased over time, but substantial hospital-level variation was observed. Patients with AF meeting indications for anticoagulation are more likely to receive a DES than a BMS, even among those at high predicted risk of both stroke and bleeding. (*J Am Heart Assoc.* 2017;6:e005280. DOI: 10.1161/JAHA.116.005280.)

Key Words: atrial fibrillation • myocardial infarction • stent

The management of antiplatelet and anticoagulant medications among patients with atrial fibrillation (AF) presenting with acute myocardial infarction (MI) can be

challenging. Guidelines recommend 1 year of dual-antiplatelet therapy (DAPT) for patients following acute MI; however, for patients with AF requiring percutaneous coronary intervention (PCI), the optimal antithrombotic strategy is unclear, and an important factor in determining DAPT duration may be the type of stent that is implanted during the procedure. Drug-eluting stents (DESs) have traditionally been thought to have a lower risk of longer term, in-stent restenosis at a cost of increased stent-thrombosis risk for a longer period of time following implantation, although more recent data suggest newer generation DESs may be safer.^{1–3} Although current American College of Cardiology (ACC) and American Heart Association (AHA) guidelines recommend DAPT for at least 12 months following acute coronary syndrome,⁴ minimum duration of DAPT may be driven in part by stent type in clinical practice, with at least 6 months

From the Duke Clinical Research Institute, Duke University Medical Center, Durham, NC (A.N.V., T.Y.W., S.L., K.C., R.D.L., S.V.R., E.D.P.); University of Colorado School of Medicine, Aurora, CO (C.H.).

Accompanying Table S1 and Figure S1 are available at <http://jaha.ahajournals.org/content/6/8/e005280/DC1/embed/inline-supplementary-material-1.Pdf>

Correspondence to: Amit N. Vora, MD, MPH, 2400 Pratt Street, Durham, NC. E-mail: a.vora@duke.edu

Received March 3, 2017; accepted May 26, 2017.

© 2017 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Clinical Perspective

What Is New?

- This study demonstrates significant practice variation in stent selection among atrial fibrillation patients with acute myocardial infarction undergoing percutaneous coronary intervention, with an increasing proportion of patients undergoing drug-eluting stent placement.

What Are the Clinical Implications?

- The type of implanted stent may have significant implications with respect to the type and duration of antiplatelet and anticoagulant therapies in this high-risk population, especially in patients at high ischemic and/or bleeding risk.

for patients with a DES as opposed to 30 days for patients with a bare metal stent (BMS); recent meta-analyses have suggested that a shorter duration of DAPT with DES may be reasonable.^{5,6}

It is well known that triple therapy with DAPT and an oral anticoagulant (OAC) increases bleeding risk, and clinicians must determine the most appropriate strategy to balance thrombotic complications after PCI with this increased bleeding risk. There is significant heterogeneity in the professional guidance regarding stent-type implantation among patients with AF. The ACC/AHA ST-segment-elevation MI guidelines note a class 3 recommendation (harm) in using DESs in patients unable to comply with long-term DAPT,⁷ and this may be a consideration in patients requiring long-term OAC. A North American consensus document specifically recommends avoiding DES use in patients with AF and high bleeding risk.⁸ The 2014 ACC/AHA AF guidelines allow for consideration of a BMS to minimize duration of DAPT (class 2b, level of evidence C).⁹ Although previous guidance from the European Society of Cardiology^{10,11} suggested that DESs should be avoided, more recent guidance suggests that current-generation DESs may be preferred.¹¹ The latest AF guidelines, however, provide recommendations only on antithrombotic therapy strategy, not stent-type selection.¹²

Using the NCDR[®] (National Cardiovascular Data Registry) ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry—Get With the Guidelines (ACTION Registry-GWTG), we sought to evaluate temporal trends and hospital variation in the use of DESs among patients with a history of AF who presented with acute MI. We also sought to evaluate patterns of DES use in patients stratified by stroke and bleeding risk. In a subset of patients with linkage data from Medicare claims, we evaluated 1-year rates of mortality, ischemia, and bleeding outcomes for patients receiving a DES or a BMS.

Methods

Data Source and Study Population

The ACTION Registry-GWTG is the largest quality improvement registry of acute MI in the United States and captures detailed clinical data on consecutive patients presenting with acute MI treated at each participating hospital. Details of the design and conduct of this registry have been described previously,^{13,14} and the registry is regularly and rigorously audited for data completeness and accuracy.¹⁵ Participation in the registry was approved by each hospital's institutional review board, and because data are collected without individual patient identifiers, the requirement for individual informed consent was waived.

Between July 1, 2008, and March 31, 2014, we identified 554 214 eligible patients presenting with acute MI at 780 ACTION Registry-GWTG sites in the United States. We excluded patients who presented at hospitals without PCI or coronary artery bypass grafting (CABG) capabilities (n=15 494). We then excluded patients who did not undergo PCI with stent placement (n=227 465) and patients for whom the information necessary to calculate the CHA₂DS₂-VAsc or modified ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) score was missing (n=3928). We also excluded patients without a history of AF or flutter (n=292 900) within the 2 weeks before presentation, as captured on the data collection form, yielding a final study population of 14 427 patients at 652 sites nationwide.

To obtain longitudinal outcomes, patients aged ≥65 years in this registry were linked with Medicare claims data using 5 indirect identifiers in combination (date of birth, sex, hospital identifier, date of admission, date of discharge) using previously described methodology.¹⁶ Linked patients were those discharged alive with Medicare Parts A and B fee-for-service eligibility at discharge who also had Medicare Parts A and B fee eligibility for the 12 months before the index hospitalization. In addition, because the latest available linkage records available were through 2012, we focused on patients who were discharged before 2011 to allow at least 1 year for follow-up. After exclusions, 2844 patients with AF presenting with acute MI at 379 sites were evaluated for 1-year outcomes (Figure 1).

Outcomes and Definitions

The presence of AF or flutter within the 2 weeks before the index hospitalization for acute MI was denoted on the ACTION Registry-GWTG data collection form, as was the type of stent (DES versus BMS) used during the index PCI procedure. Patients receiving both DES and BMS were classified as DES patients for this analysis. We calculated the CHA₂DS₂-VAsc score using the data elements from the data collection form;

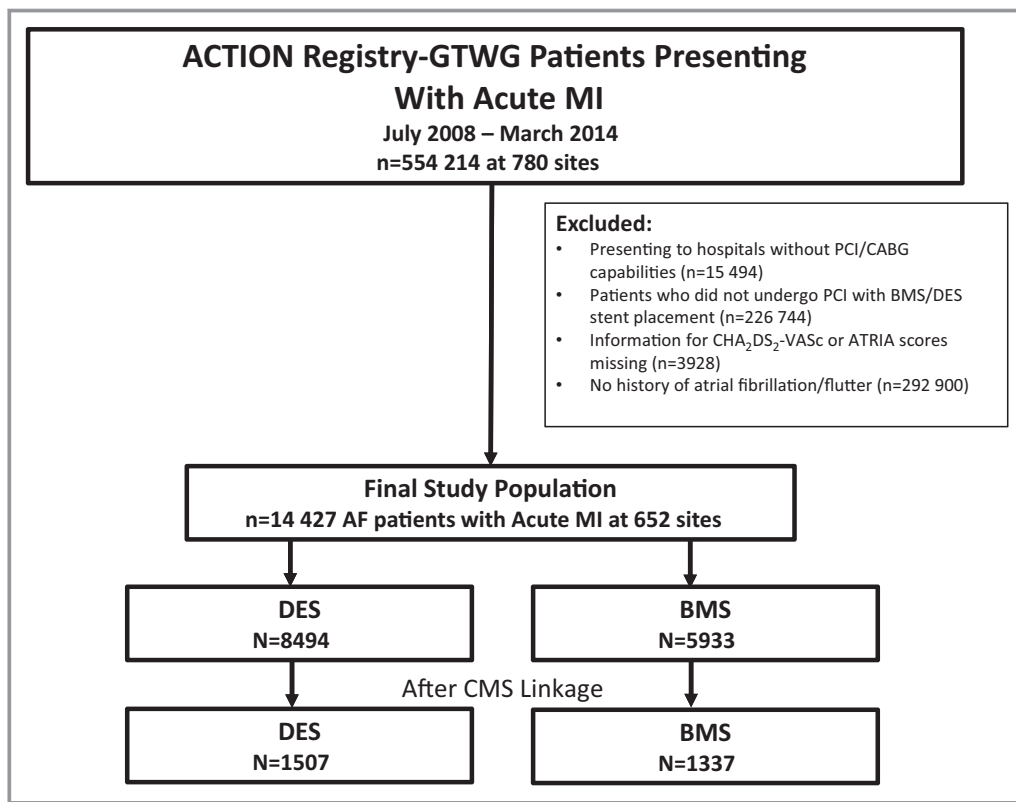


Figure 1. Study population characteristics. This figure displays the study population characteristics, including exclusions. ACTION Registry-GWTG indicates ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry—Get With the Guidelines; AF, atrial fibrillation; BMS, bare metal stent; CABG, coronary artery bypass grafting; CMS, Centers for Medicare and Medicaid Services; DES, drug-eluting stent; MI, myocardial infarction; PCI, percutaneous coronary intervention.

for this analysis, the presence of vascular disease was defined as having a history of prior MI, peripheral artery disease, prior PCI, or prior CABG. We calculated a modified ATRIA score that assigned points for anemia (hemoglobin <13 for men or <12 for women, 3 points), severe renal disease (glomerular filtration rate <30 or dialysis, 3 points), age ≥ 75 years (2 points), and hypertension (1 point). The ATRIA score assigns 1 point to history of prior bleeding, which was not captured in this registry; as such, the maximum score in this modified ATRIA model is 9 points, compared with 10 points from the actual ATRIA model.

For linked patients with longitudinal data, we evaluated 4 outcomes: (1) a composite end point including all-cause mortality and rehospitalization for MI or stroke; (2) readmission for stroke; (3) readmission for repeat revascularization; and (4) readmission for major bleeding. Readmission for MI, stroke, repeat revascularization, and major bleeding were defined using the primary *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis code and procedure codes for subsequent hospitalizations after the index hospitalization (list of diagnosis

codes is shown in Table S1). All-cause mortality was ascertained from the Medicare denominator file.

Statistical Analysis

We compared baseline demographic, presentation, in-hospital, and discharge characteristics for patients receiving a DES versus a BMS during the index presentation. Continuous variables are expressed as median values with 25th and 75th percentiles, whereas categorical values are presented as percentages. Pearson χ^2 tests were used to compare categorical variables, and Wilcoxon rank sum tests were used to compare continuous variables between 2 groups.

Temporal trends in DES use were plotted semiyearly, and the Cochran–Armitage trend test with a 2-sided *P*-value was used to test for significance. As a comparator, we evaluated DES use among patients meeting all other inclusion and exclusion criteria except for the presence of AF or flutter to demonstrate the temporal trend of DES use among non-AF patients. We identified site-level variation associated with the use of DES but excluded sites with <10 eligible patients

($n=256$ hospitals) during the study period. To evaluate for significant practice-level variation, we included hospital as a random effect in a generalized linear mixed model for DES implantation. The variance component was tested against 0 to evaluate the hypothesis that hospitals differ in their rates of DESs used. To evaluate whether hospital characteristics (including hospital type: PCI only versus surgery, academic centers, number of hospital beds, hospital region) were associated with an increased likelihood of DES implantation, we divided the remaining 396 sites into tertiles by proportion of DES use and summarized hospital characteristics by tertiles of DES use.

Using the calculated $\text{CHA}_2\text{DS}_2\text{-VASc}$ and modified ATRIA scores, we divided patients by predicted stroke and bleeding risk, respectively. A $\text{CHA}_2\text{DS}_2\text{-VASc}$ score of ≥ 2 denoted high stroke risk, and a modified ATRIA score ≥ 4 denoted high bleeding risk. Rates of DES implantation were compared for patients with high versus low ischemic and bleeding risk.

In the linked analysis, unadjusted rates of the 1-year composite end point of mortality and readmission for MI or stroke were estimated using the product limit method (Kaplan–Meier). The failure curves between patients with DESs and those with BMSs were compared using the log-rank test. The unadjusted cumulative incidence of each nonfatal adverse outcome of interest (readmission for stroke, readmission for repeat revascularization, readmission for major bleeding) was compared using Gray's method to account for mortality as a competing risk for readmission.^{17,18} We then used multivariable Cox proportional hazards models to compare risk-adjusted outcomes between patients receiving a DES versus a BMS. For the readmission outcomes within 1 year of discharge, follow-up was censored at last follow-up or at death, if occurring before the event of interest. The resulting hazard ratios (HRs) estimated the cause-specific effect among patients still alive and at risk. Robust standard errors were used to adjust for within-hospital clustering, as patients treated at the same hospital tended to have more similar responses relative to patients treated at other hospitals. Outcomes were adjusted for the following variables based on the previously validated ACTION Registry-GWTG mortality risk model¹⁹: demographics (age, sex, body mass index, race [white versus nonwhite]), medical history (hypertension, dyslipidemia, diabetes mellitus, prior MI, prior heart failure, prior PCI, prior CABG, stroke, peripheral artery disease), discharge medications (any P2Y₁₂ inhibitor, beta blockers, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, statin), signs and symptoms at presentation (ST-segment–elevation MI versus non–ST-segment–elevation MI, heart failure, cardiogenic shock, multivessel disease [≥ 2 versus 1 and 0], ejection fraction), laboratory results (baseline hemoglobin [g/dL], baseline serum creatinine [mg/dL], initial troponin [times the upper

limit of normal]), the number of admissions in the year before the index admission, and socioeconomic status (median household income in the past 12 months denoted in 2011 inflation-adjusted dollars, proportion of patients with a bachelor's degree or higher). All continuous variables were fitted with restricted cubic spline, with 3 knots at 10%, 50%, and 90% of their empirical distribution. Given that the safety profiles of first- versus second-generation DESs may be different from that of BMSs, we performed a sensitivity analysis by dividing our study duration into 2 time periods—2008 to 2010 and 2011 to 2014—based on when operators in the United States transitioned from first- to second-generation DESs.²⁰

Statistical significance was defined as $P<0.05$. All analyses were performed by the NCDR data analysis center at the Duke Clinical Research Institute using SAS software (versions 9.3 and 9.4).

Results

After exclusions, we identified 14 427 patients with a history of AF presenting with acute MI who underwent PCI (Figure 1). Overall, DESs were used in 8494 (58.9%) patients. The proportion of patients receiving a DES increased from 47.1% in 2008 to 67.9% in 2014 ($P<0.001$). For comparison, among patients in the ACTION Registry-GWTG who met other inclusion and exclusion criteria but did not have AF ($n=292$ and $n=900$, respectively), the overall rate of DES use was 70.4%, increasing from 58.9% in 2008 to 79.1% in 2014 (Figure 2).

Patients receiving a DES were younger (median age 72 versus 75 years, $P<0.001$) and less often female. They more often had a history of diabetes mellitus and prior MI and revascularization with either PCI or CABG but less often had a history of prior stroke. Prior to admission, DES patients were more often treated with aspirin and a P2Y₁₂ inhibitor but less often treated with warfarin than BMS patients; however, 24.8% of patients receiving a DES were on warfarin at home. On admission, patients eventually receiving a DES less often presented with ST-segment elevation MI, heart failure, or cardiogenic shock on admission (Table 1).

Table 2 describes in-hospital characteristics of patients receiving a DES versus a BMS. Patients receiving a DES had smaller infarct size, as measured by peak troponin, and were less likely to develop heart failure, cardiogenic shock, stroke, or major bleeding (all $P<0.001$) compared with patients receiving a BMS. They were also less likely to receive blood transfusion ($P<0.001$). Differences were statistically significant but clinically modest.

There were similar rates of discharge on DAPT between patients receiving a DES versus a BMS (Table 3). DES patients

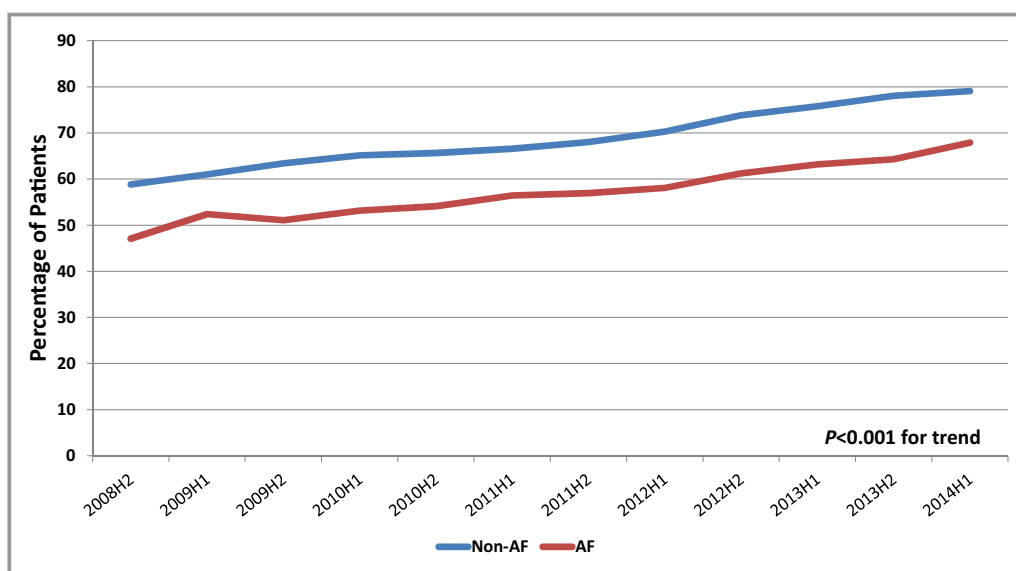


Figure 2. Temporal trends in drug-eluting stent (DES) use. This figure shows the percentage of DES use among patients with atrial fibrillation (AF) and acute myocardial infarction by half-year (H) during the study period.

were more likely to be discharged on a higher potency P2Y₁₂ inhibitor such as prasugrel or ticagrelor (17.0% versus 9.6%, $P<0.001$). Only 34.0% of patients were discharged on warfarin, with lower rates among patients receiving DESs than BMSs (30.8% versus 39.0%, $P<0.001$).

After excluding hospitals with <10 eligible patients during the study period (256 hospitals), we evaluated hospital-level variation in DES use. Figure 3 demonstrates the hospital level of percentage of DES use with an exact 95% binomial confidence interval (CI) for the remaining 396 hospitals rank-ordered by percentage of DES use. There was significant hospital level variation in the proportion of DESs used, with the median hospital utilizing DESs in 60.2% of patients (interquartile range: 50.0–73.7%) but ranging from 0% to 100%. Hospitals in the highest tertile of DES use had modestly fewer beds and were less likely to have CABG capability (Table 4).

We examined DES selection among patients classified as high versus low predicted bleeding and stroke risk. The median modified ATRIA score was 3 (interquartile range: 1–4). Overall, 4595 (31.9%) patients were at high bleeding risk, classified by a modified ATRIA score ≥ 4 . Among these patients, 2573 (56.0%) underwent DES placement, whereas 60.2% of patients at low bleeding risk (modified ATRIA score <4) underwent DES placement. The median CHA₂DS₂-VASc score in our study population was 4 (interquartile range: 3–5); 12 812 patients (88.8%) had a CHA₂DS₂-VASc score ≥ 2 . Among these patients, 7492 (58.5%) underwent DES placement, whereas among the 1615 patients at low stroke risk, 62.0% received a DES (Figure 4).

Among a subset of patients with Medicare-linked data (n=2844), the unadjusted cumulative incidence of the composite outcomes of all-cause mortality and readmission for MI or stroke was 22.9% among DES patients versus 26.9% among BMS patients ($P=0.02$), although this difference was attenuated after multivariable adjustment (adjusted HR: 0.88; 95% CI, 0.76–1.03). Rates of mortality were lower in patients receiving a DES (16.1% versus 20.9%, $P=0.001$) but were similar after multivariable adjustment. Rates of readmission for stroke at 1 year were similar between DES and BMS patients before and after multivariable adjustment (2.9% versus 2.6%, $P=0.69$; adjusted HR: 1.14; 95% CI, 0.70–1.88), as were rates of readmission for repeat revascularization (10.8% versus 9.0%, $P=0.13$; adjusted HR: 1.08; 95% CI, 0.84–1.39) and readmission for major bleeding (9.7% versus 9.0%, $P=0.55$; adjusted HR: 1.09; 95% CI, 0.87–1.36; Table 5). Cumulative incidence curves are shown in Figure S1.

We performed a sensitivity analysis to evaluate whether outcomes differed across generation of DES by dividing our study period into 2 periods when first-generation DESs (2008–2010) and second-generation DESs (2011–2014) were more broadly used. Our results were broadly consistent with the primary analysis ($P=0.66$, interaction for composite outcome). These results are shown in Table S1.

Discussion

Our study represents the first national examination of stent selection among patients with a history of AF presenting with

Table 1. Patient Characteristics According to Stent Type

	BMS (n=5933)	DES (n=8494)	P Value
Demographics			
Age, y	75 (65–83)	72 (63–80)	<0.001
Female	34.8	33.2	0.04
BMI, kg/m ²	27.6 (24.2–32.0)	28.5 (25.1–32.9)	<0.001
Race			0.32
White	88.2	88.8	
Black	6.7	5.8	
Asian	1.0	1.1	
Other	0.6	0.6	
Hispanic ethnicity	3.2	3.3	0.63
Clinical characteristics			
Prior myocardial infarction	28.4	33.1	<0.001
Prior heart failure	24.8	24.1	0.29
Prior PCI	25.7	36.9	<0.001
Prior CABG	18.2	22.1	<0.001
Prior stroke	14.2	11.3	<0.001
Peripheral arterial disease	14.3	15.2	0.15
Diabetes mellitus	34.4	39.4	<0.001
Hypertension	84	84.6	0.32
Dyslipidemia	65.6	71.3	<0.001
Smoker	22.8	21.9	0.23
Home antithrombotic therapy			
Aspirin	45.6	53.8	<0.001
P2Y ₁₂ receptor inhibitor	11.8	21.8	<0.001
High potency	0.52	1.6	<0.001
Warfarin	33.4	24.8	<0.001
Presentation features			
STEMI (vs non-STEMI)	49.3	35.6	<0.001
Signs of heart failure on admission	22.5	20.7	0.01
Cardiogenic shock on admission	10.0	6.5	<0.001
Initial creatinine, mg/dL	1.1 (0.9–1.4)	1.1 (0.9–1.4)	0.005
Initial hemoglobin, g/dL	13.5 (12.0–14.9)	13.7 (12.3–15.0)	<0.001
Initial troponin (times ULN)	1.9 (0.4–14.0)	1.6 (0.4–10.0)	<0.001

Data are expressed as number (percentage) of patients for categorical variables and median (interquartile range) for continuous variables. BMI indicates body mass index; BMS, bare metal stent; CABG, coronary artery bypass grafting; DES, drug-eluting stent; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; ULN, institutional upper limit of normal.

Table 2. In-Hospital Characteristics*

	BMS (n=5933)	DES (n=8494)
Peak troponin	81.5 (15.5–419)	53.7 (10.4–272.7)
Left ventricular ejection fraction <40% (%)	32.4	28.3
Peak creatinine (among nondialysis)	1.3 (1.0–1.7)	1.2 (1.0–1.6)
Adverse event		
Cardiogenic shock	8.2	5.6
Heart failure	10.1	8.2
Stroke	1.5	0.8
Major bleeding	15.3	12.1
Blood transfusion	10.2	6.9

BMS indicates bare metal stent; DES, drug-eluting stent.

*All $P < 0.001$.

acute MI. The rate of DES implantation has increased significantly over time, with more than two-thirds of AF patients now receiving a DES during their hospitalization for acute MI. However, there is significant hospital-level variation in the rate of DES implantation among MI patients, and, paradoxically, those at highest risk of stroke and bleeding were most likely to receive a DES. After adjusting for patient and presentation characteristics, there were no observed differences in adverse cardiovascular or bleeding outcomes between patients receiving a DES versus a BMS.

DESs have been shown to decrease the risk of in-stent restenosis by inhibiting neointimal hyperplasia compared with BMS, but longer duration DAPT is generally required to mitigate the increased risk of in-stent thrombosis, particularly in older generation DESs. Although current guidelines

Table 3. Discharge Medications and Interventions

	BMS (n=5933)	DES (n=8494)	P Value
Discharge medications*			
Aspirin	98.5	98.4	0.52
P2Y ₁₂ receptor inhibitor	96.3	96.3	0.82
High-potency (%)	9.6	17	<0.001
Warfarin	39.0	30.8	<0.001
Beta blocker	96.7	96.8	0.98
ACE inhibitor or ARB	74.6	75.7	0.21
Statin	93.3	94.1	0.15

Data are expressed as number (percentage) of patients for categorical variables and median (interquartile range) for continuous variables. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BMS, bare metal stent; DES, drug-eluting stent.

*Discharge therapies are expressed as proportion of use among patients without documented contraindications to each treatment.

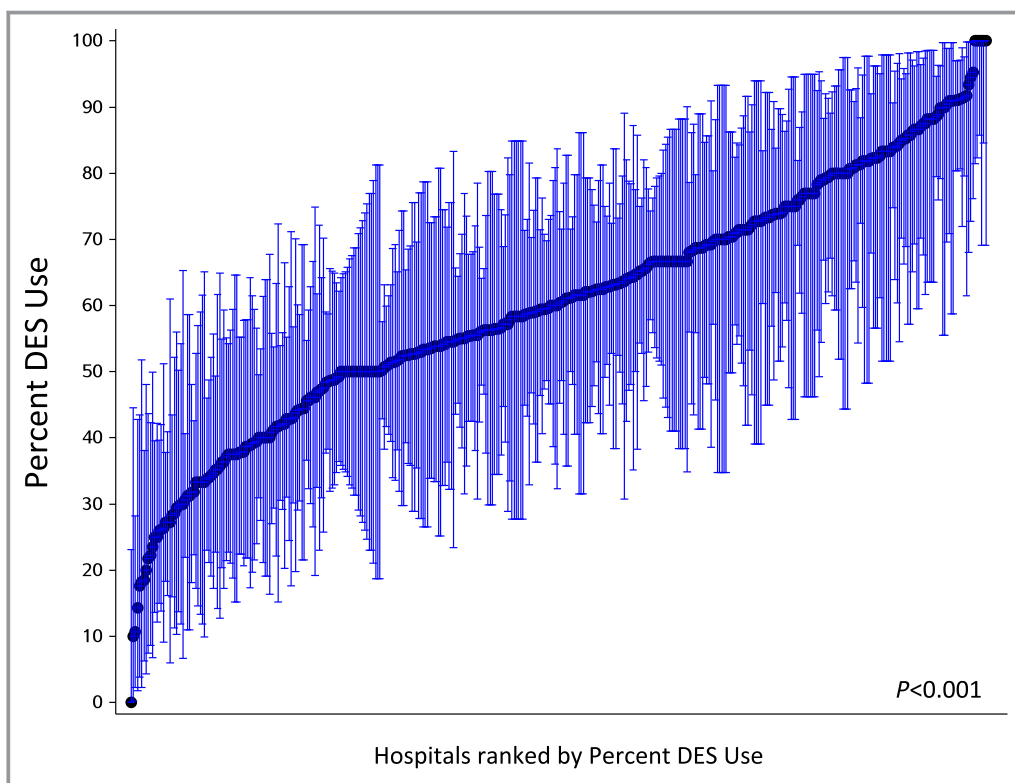


Figure 3. Hospital-level variation in drug-eluting stent (DES) use. This figure rank-orders hospitals by percentage of DES use with exact 95% binomial confidence intervals.

recommend 12 months of DAPT following an acute MI,^{7,21} a provider’s willingness to interrupt therapy might be affected by stent type and the risk of possible stent thrombosis. Consequently, stent selection may have important implications for the type and duration of antithrombotic therapy following acute MI, particularly in patients with a history of AF requiring lifelong anticoagulation. Despite some evidence that

shorter duration of DAPT may be reasonable,^{22,23} current ACC/AHA guidelines still recommend 12 months of DAPT following DES placement but 30 days for patients treated with a BMS. This is different from the current European guidelines, which tailor antithrombotic strategy to bleeding risk and favor short-duration triple therapy in patients at high risk of bleeding. Although the current North American

Table 4. Hospital Characteristics by Tertile of Drug-Eluting Stent Use Presented at the Patient Level*

	Lowest Tertile (132 Sites)	Middle Tertile (133 Sites)	Highest Tertile (131 Sites)
Number of beds	407 (285–705)	398 (271–530)	362 (235–488)
Region			
West	7.9	15.3	14.7
Northeast	9.0	6.9	4.9
Midwest	34.8	30.8	27.6
South	48.3	46.9	52.8
Surgery capability	93.4	92.9	90.1
Academic	23.3	27.0	21.2

*All $P < 0.001$.

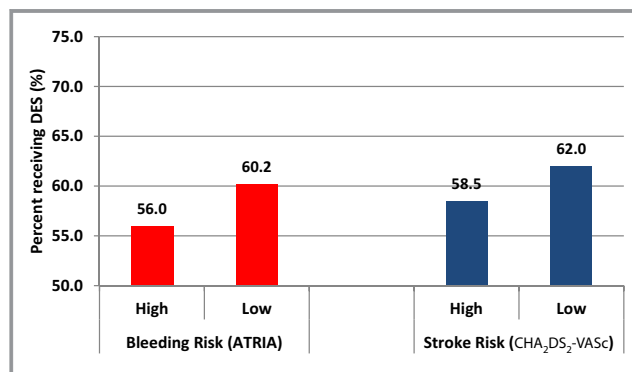


Figure 4. Drug-eluting stent (DES) use by stroke and bleeding risk. This figure reports the percentage of DES use stratified by predicted stroke and bleeding risk. Low stroke risk is defined as a CHA₂DS₂-VASc score <2, and a low modified ATRIA score is defined as <4.

Table 5. Outcomes at 1 Year in Patients With Medicare-Linked Data

	Unadjusted Cumulative Incidence (%)			Adjusted Hazard	
	DES	BMS	P Value	Adjusted HR (95% CI)	P Value
Composite end point	22.9	26.9	0.02	0.88 (0.76–1.03)	0.11
Mortality	16.1	20.9	0.001	0.85 (0.71–1.01)	0.07
Readmission for MI	7.7	6.2	0.12	0.96 (0.72–1.28)	0.78
Rehospitalization for stroke	2.9	2.6	0.69	1.14 (0.70–1.88)	0.59
Rehospitalization for repeat revascularization	10.8	9.0	0.13	1.08 (0.84–1.39)	0.54
Rehospitalization for major bleeding	9.7	9.0	0.55	1.09 (0.87–1.36)	0.45

BMS indicates bare metal stent; CI, confidence interval; DES, drug-eluting stent; HR, hazard ratio; MI, myocardial infarction.

consensus guidelines recommend avoiding DESs in patients who are at high risk of bleeding or unable to comply with DAPT, European guidance now suggests DES placement for all patients, coupled with shorter duration DAPT; no randomized data support this strategy.

We found that this lack of clear evidence and the conflicting guidelines statements led to considerable variability in community practice. Nevertheless, we also found an overall trend toward greater use of DESs among AF patients over time. There may be a number of possible explanations for these trends. First, DES technology has improved during the study period, and coupled with refinements in stent-deployment technologies, current-generation DESs may have a similar or lower rate of stent thrombosis than BMSs.^{1,2,24–26} More recently, the Norwegian Coronary Stent Trial (NORSTENT) demonstrated a slightly lower rate of stent thrombosis with DESs compared with BMSs, although overall rates of stent thrombosis were very low.³ In addition, a number of studies have demonstrated that shorter duration of DAPT may not increase overall ischemic risk in this patient population.^{22,23} Therefore, investigators may feel more comfortable using DESs with a shorter duration of DAPT, particularly in patients at high risk of bleeding. The substantial practice variation that we observed in this study, however, suggests that the evidence base for stent selection in this high-risk population remains ill-defined, and there is no clear consensus about the benefits of a DES versus a BMS in patients currently on an OAC.

Despite current guidelines recommending risk stratification, particularly for bleeding, when selecting stent type, we report overall modest differences in DES use across the strata of bleeding and stroke risk, with DESs used more frequently than not among patients at increased risk of bleeding. For patients at high stroke risk requiring lifelong anticoagulation, we felt that further risk stratification by bleeding risk may affect DES selection, but the overall difference in DES use was modest between patients with high versus low bleeding risk. Conversely, DES use is only slightly higher among patients at

low stroke risk who likely do not require anticoagulation, highlighting the lack of overall risk assessment prior to stent selection.

Our study also highlights the implications for DES use with respect to antithrombotic therapy strategy at discharge. In our study, there was almost universal discharge on DAPT. Although most patients were discharged on aspirin and clopidogrel, there was a small but sizeable proportion of patients discharged on more potent P2Y₁₂ inhibitors despite a class 3 recommendation for their use among patients requiring an OAC. This suggests that these patients may be exposed to higher bleeding risk by combining a more potent antiplatelet agent with an OAC or may be subjected to downstream switching as the P2Y₁₂ inhibitor is transitioned to clopidogrel once an OAC is added. In addition, a minority of patients were discharged on warfarin, regardless of the type of stent implanted. This result is concordant with a prior analysis from the DANISH Registry that analyzed antithrombotic therapy selection for AF patients with an indication for DAPT, although that analysis also did not capture information on stent-type selection.²⁷ Although our study does not capture discharge on novel OAC agents, none are currently recommended for use in combination with DAPT. Our analysis suggests either that providers may be underestimating stroke risk in AF patients by implanting DESs and discharging patients without OACs or that the operators understand that the daily risk of stroke, even in high-risk patients, is low enough that treatment with DAPT for 1 month followed by reinstatement of OAC may not increase stroke risk. A number of trials are currently evaluating antithrombotic strategy among patients with AF undergoing PCI^{28–30}; however, because all of these trials allow for stent selection at the discretion of the investigator, information gleaned about the effect of stent selection in optimizing patient outcomes in this population may be limited.

Our study must be considered in light of a number of important limitations. First, we did not capture individual provider rationale for stent selection. We also retrospectively

calculated the CHA₂DS₂-VASc and the modified ATRIA scores; because we did not capture a history of prior hemorrhage, the maximum ATRIA score is 9 instead of 10. The lack of data on prior hemorrhage may affect the overall validity of the ATRIA score. Although it is possible that operators may have used another method of risk stratification, both the CHA₂DS₂-VASc and ATRIA scores have been well validated to accurately stratify stroke and bleeding risk in patients with AF. Next, we did not capture information on any of the novel OACs (dabigatran, rivaroxaban, apixaban, edoxaban); however, none are currently indicated for use in this patient population. In addition, because this information is not captured, the overall proportion of patients on an OAC coupled with DAPT is likely higher than what we reported in this study. Moreover, the ACTION Registry-GWTG does not capture information regarding stent generation. The second-generation DESs, which were predominantly used during most of the study period for this analysis, have a more favorable safety profile than first-generation DESs. Finally, because this analysis is observational, we are unable to draw causal inferences from these results, and we cannot exclude the possibility of unmeasured confounding.

Conclusions

Among AF patients presenting with acute MI, the use of DES has increased over time with substantial hospital-level variation. Paradoxically, patients with the highest risk of stroke and bleeding were most likely to receive a DES. After multivariable adjustment, we observed no differences in rates of adverse cardiovascular or bleeding outcomes between patients receiving a DES versus a BMS.

Acknowledgments

Partners and Sponsors: The ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry—Get With the Guidelines is an initiative of the American College of Cardiology Foundation and the American Heart Association, with partnering support from the Society of Chest Pain Centers, the American College of Emergency Physicians, and the Society of Hospital Medicine.

Sources of Funding

This research was supported by the American College of Cardiology Foundation's National Cardiovascular Data Registry (NCDR). The views expressed in this article represent those of the author(s), and do not necessarily represent the official views of the NCDR or its associated professional societies identified at www.ncdr.com. Role of the Sponsor: The funding sources had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data;

preparation, review, or approval of the article; and decision to submit the article for publication.

Disclosures

Dr Vora was funded by NIH T-32 training grant T32 HL069749 and L30 HL124592. However, no relationships exist related to the analysis presented. Dr Wang reports research funding from AstraZeneca, Gilead, Lilly, The Medicines Company, and Canyon Pharmaceuticals (all significant); educational activities or lectures (generates money for Duke) for AstraZeneca (modest); consulting (including CME) for Medco (modest) and American College of Cardiology (significant). Dr Hess reports research funding from Gilead Sciences, Inc. Dr Lopes reports research funding from Bristol-Myers Squibb and Glaxo Smith Kline (all significant); consulting for Bayer (modest), Boehringer Ingelheim (modest), Bristol-Myers Squibb (modest), Merck (modest), Pfizer (significant), and Portola (modest). Dr Rao reports research funding from Bellerophon; consulting for Terumo Medical, The Medicines Company, and ZOLL. Dr Peterson reports research funding for the American College of Cardiology, American Heart Association, Eli Lilly & Company, Janssen Pharmaceuticals, and Society of Thoracic Surgeons (all significant); consulting (including CME) for Merck & Co. (modest), Boehringer Ingelheim, Genentech, Janssen Pharmaceuticals, and Sanofi-Aventis (all significant). The remaining authors have no disclosures to report.

References

1. Kereiakes DJ, Yeh RW, Massaro JM, Driscoll-Shempp P, Cutlip DE, Steg PG, Gershlick AH, Darius H, Meredith IT, Ormiston J, Tanguay JF, Windecker S, Garratt KN, Kandzari DE, Lee DP, Simon DI, Iancu AC, Trebacz J, Mauri L. Stent thrombosis in drug-eluting or bare-metal stents in patients receiving dual antiplatelet therapy. *JACC Cardiovasc Interv*. 2015;8:1552–1562.
2. Valgimigli M, Patialiakas A, Thury A, McFadden E, Colangelo S, Campo G, Tebaldi M, Ungi I, Tondi S, Roffi M, Menozzi A, de Cesare N, Garbo R, Meliga E, Testa L, Gabriel HM, Airolidi F, Ferlini M, Liistro F, Dellavalle A, Vranckx P, Briguori C. Zotarolimus-eluting versus bare-metal stents in uncertain drug-eluting stent candidates. *J Am Coll Cardiol*. 2015;65:805–815.
3. Bona KH, Mannsverk J, Wiseth R, Aaberge L, Myreng Y, Nygard O, Nilsen DW, Klow NE, Uchto M, Trovik T, Bendz B, Stavnes S, Bjornerheim R, Larsen AI, Slette M, Steigen T, Jakobsen OJ, Bleie O, Fossum E, Hanssen TA, Dahl-Eriksen O, Njolstad I, Rasmussen K, Wilsgaard T, Nordrehaug JE. Drug-eluting or bare-metal stents for coronary artery disease. *N Engl J Med*. 2016;375:1242–1252.
4. Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, Granger CB, Lange RA, Mack MJ, Mauri L, Mehran R, Mukherjee D, Newby LK, O'Gara PT, Sabatine MS, Smith PK, Smith SC Jr. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2016;68:1082–1115.
5. Bangalore S, Kumar S, Fusaro M, Amoroso N, Attubato MJ, Feit F, Bhatt DL, Slater J. Short- and long-term outcomes with drug-eluting and bare-metal coronary stents: a mixed-treatment comparison analysis of 117 762 patient-years of follow-up from randomized trials. *Circulation*. 2012;125:2873–2891.
6. El-Hayek G, Messerli F, Bangalore S, Hong MK, Herzog E, Benjo A, Tamis-Holland JE. Meta-analysis of randomized clinical trials comparing short-term versus long-term dual antiplatelet therapy following drug-eluting stents. *Am J Cardiol*. 2014;114:236–242.
7. O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-

- Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;61:e78–e140.
8. Faxon DP, Eikelboom JW, Berger PB, Holmes DR Jr, Bhatt DL, Moliterno DJ, Becker RC, Angiolillo DJ. Antithrombotic therapy in patients with atrial fibrillation undergoing coronary stenting: a North American perspective: executive summary. *Circ Cardiovasc Interv*. 2011;4:522–534.
 9. January CT, Wann LS, Alpert JS, Calkins H, Cleveland JC, Cigarroa JE, Conti JB, Ellnor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM, Yancy CW. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*. 2014;64:e1–e76.
 10. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kolh P, Le Heuzey JY, Ponikowski P, Rutten FH. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Europace*. 2010;12:1360–1420.
 11. Lip GY, Windecker S, Huber K, Kirchhof P, Marin F, Ten Berg JM, Haeusler KG, Boriani G, Capodanno D, Gilard M, Zeymer U, Lane D, Storey RF, Bueno H, Collet JP, Fauchier L, Halvorsen S, Lettino M, Morais J, Mueller C, Potpara TS, Rasmussen LH, Rubboli A, Tamargo J, Valgimigli M, Zamorano JL. Management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous coronary or valve interventions: a joint consensus document of the European Society of Cardiology Working Group on Thrombosis, European Heart Rhythm Association (EHRA), European Association of Percutaneous Cardiovascular Interventions (EAPCI) and European Association of Acute Cardiac Care (ACCA) endorsed by the Heart Rhythm Society (HRS) and Asia-Pacific Heart Rhythm Society (APHRS). *Eur Heart J*. 2014;35:3155–3179.
 12. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, Castella M, Diener H-C, Heidbuchel H, Hendriks J, Hindricks G, Manolis AS, Oldgren J, Popescu BA, Schotten U, Van Putte B, Vardas P, Agewall S, Camm J, Baron Esquivias G, Budts W, Carerj S, Casselman F, Coca A, De Caterina R, Deftereos S, Dobrev D, Ferro JM, Filippatos G, Fitzsimons D, Gorenek B, Guenoun M, Hohnloser SH, Kolh P, Lip GYH, Manolis A, McMurray J, Ponikowski P, Rosenhek R, Ruschitzka F, Savelieva I, Sharma S, Suwalski P, Tamargo JL, Taylor CJ, Van Gelder IC, Voors AA, Windecker S, Zamorano JL, Zeppenfeld K. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Eur Heart J*. 2016;37:2893–2962.
 13. Peterson ED, Roe MT, Chen AY, Fonarow GC, Lytle BL, Cannon CP, Rumsfeld JS. The NCDR ACTION Registry-GWTG: transforming contemporary acute myocardial infarction clinical care. *Heart*. 2010;96:1798–1802.
 14. Peterson ED, Roe MT, Rumsfeld JS, Shaw RE, Brindis RG, Fonarow GC, Cannon CP. A call to ACTION (acute coronary treatment and intervention outcomes network): a national effort to promote timely clinical feedback and support continuous quality improvement for acute myocardial infarction. *Circ Cardiovasc Qual Outcomes*. 2009;2:491–499.
 15. Messenger JC, Ho KK, Young CH, Slattery LE, Draoui JC, Curtis JP, Dehmer GJ, Grover FL, Mirro MJ, Reynolds MR, Rokos IC, Spertus JA, Wang TY, Winston SA, Rumsfeld JS, Masoudi FA. The National Cardiovascular Data Registry (NCDR) data quality brief: the NCDR data quality program in 2012. *J Am Coll Cardiol*. 2012;60:1484–1488.
 16. Hammill BG, Hernandez AF, Peterson ED, Fonarow GC, Schulman KA, Curtis LH. Linking inpatient clinical registry data to Medicare claims data using indirect identifiers. *Am Heart J*. 2009;157:995–1000.
 17. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics*. 1986;42:121–130.
 18. Gray RJ. A class of K-sample tests for comparing the cumulative incidence of a competing risk. *Ann Stat*. 1988;16:1141–1154.
 19. Chin CT, Chen AY, Wang TY, Alexander KP, Mathews R, Rumsfeld JS, Cannon CP, Fonarow GC, Peterson ED, Roe MT. Risk adjustment for in-hospital mortality of contemporary patients with acute myocardial infarction: the acute coronary treatment and intervention outcomes network (ACTION) registry-get with the guidelines (GWTG) acute myocardial infarction mortality model and risk score. *Am Heart J*. 2011;161:113–122.e2.
 20. Baber U, Giustino G, Wang T, Grines C, McCoy LA, Saha-Chaudhuri P, Best P, Skelding KA, Ortega R, Chieffo A, Mehilli J, Tcheng J, Mehran R. Comparisons of the uptake and in-hospital outcomes associated with second-generation drug-eluting stents between men and women: results from the CathPCI Registry. *Coron Artery Dis*. 2016;27:442–448.
 21. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ; American College of Cardiology/American Heart Association Task Force on Practice G, Society for Cardiovascular A, Interventions, Society of Thoracic S and American Association for Clinical C. 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;64:e139–e228.
 22. Gilard M, Barragan P, Noryani AA, Noor HA, Majwal T, Hovasse T, Castellant P, Schneeberger M, Maillard L, Bressolette E, Wojcik J, Delarche N, Blanchard D, Jouve B, Ormezzano O, Paganelli F, Levy G, Sainsous J, Carrie D, Furber A, Berland J, Darremont O, Le Breton H, Lyuyx-Bore A, Gommeaux A, Cassat C, Kermarrec A, Cazaux P, Druelles P, Dauphin R, Armengaud J, Dupouy P, Champagnac D, Ohlmann P, Endresen K, Benamer H, Kiss RG, Ungi I, Boschat J, Morice MC. 6- versus 24-month dual antiplatelet therapy after implantation of drug-eluting stents in patients nonresistant to aspirin: the randomized, multicenter ITALIC trial. *J Am Coll Cardiol*. 2015;65:777–786.
 23. Schulz-Schupke S, Byrne RA, Ten Berg JM, Neumann FJ, Han Y, Adriaenssens T, Tolg R, Seyfarth M, Maeng M, Zrenner B, Jacobshagen C, Mudra H, von Hodenberg E, Wohrle J, Angiolillo DJ, von Merzljak B, Rifatov N, Kufner S, Morath T, Feuchtenberger A, Ibrahim T, Janssen PW, Valina C, Li Y, Desmet W, Abdel-Wahab M, Tiroch K, Hengstenberg C, Bernlochner I, Fischer M, Schunkert H, Laugwitz KL, Schomig A, Mehilli J, Kastrati A. ISAR-SAFE: a randomized, double-blind, placebo-controlled trial of 6 vs. 12 months of clopidogrel therapy after drug-eluting stenting. *Eur Heart J*. 2015;36:1252–1263.
 24. Byrne RA, Joner M, Kastrati A. Stent thrombosis and restenosis: what have we learned and where are we going? The Andreas Gruntzig Lecture ESC 2014. *Eur Heart J*. 2015;36:3320–3331.
 25. Tada T, Byrne RA, Simunovic I, King LA, Cassese S, Joner M, Fusaro M, Schneider S, Schulz S, Ibrahim T, Ott I, Massberg S, Laugwitz KL, Kastrati A. Risk of stent thrombosis among bare-metal stents, first-generation drug-eluting stents, and second-generation drug-eluting stents: results from a registry of 18 334 patients. *JACC Cardiovasc Interv*. 2013;6:1267–1274.
 26. Palmerini T, Benedetto U, Bacchi-Reggiani L, Della Riva D, Biondi-Zoccai G, Feres F, Abizaid A, Hong MK, Kim BK, Jang Y, Kim HS, Park KW, Genereux P, Bhatt DL, Orlandi C, De Servi S, Petrou M, Rapezzi C, Stone GW. Mortality in patients treated with extended duration dual antiplatelet therapy after drug-eluting stent implantation: a pairwise and Bayesian network meta-analysis of randomised trials. *Lancet*. 2015;385:2371–2382.
 27. Lamberts M, Gislason GH, Olesen JB, Kristensen SL, Schjerning Olsen A-M, Mikkelsen A, Christensen CB, Lip GYH, Køber L, Torp-Pedersen C, Hansen ML. Oral anticoagulation and antiplatelets in atrial fibrillation patients after myocardial infarction and coronary intervention. *J Am Coll Cardiol*. 2013;62:981–989.
 28. Study apixaban to vitamin K antagonist for the prevention of stroke or systemic embolism and bleeding in patients with non-valvular atrial fibrillation and acute coronary syndrome/percutaneous coronary intervention. 2015. Available at: <http://clinicaltrials.gov>. Accessed March 29, 2017.
 29. Evaluation of dual therapy with dabigatran vs. triple therapy with warfarin in patients with AF that undergo a PCI with stenting (REDUAL-PCI). 2015.
 30. Gibson CM, Mehran R, Bode C, Halperin J, Verheugt F, Wildgoose P, van Eickels M, Lip GY, Cohen M, Husted S, Peterson E, Fox K. An open-label, randomized, controlled, multicenter study exploring two treatment strategies of rivaroxaban and a dose-adjusted oral vitamin K antagonist treatment strategy in subjects with atrial fibrillation who undergo percutaneous coronary intervention (PIONEER AF-PCI). *Am Heart J*. 2015;169:472–478.e5.

SUPPLEMENTAL MATERIAL

Table S1. Sensitivity analysis of outcomes based on time period

Outcome	N	Adjusted*			P-value
		HR	95% CI for HR (Lower)	95% CI for HR (Upper)	
Composite of mortality/readmission of MI/Stroke					
Year 2008 -- 2010	1696	0.86	0.71	1.05	0.1314
Year 2011 -- 2014	1148	0.92	0.73	1.16	0.4666
Readmission of Stroke					
Year 2008 -- 2010	1696	1.09	0.61	1.95	0.7797
Year 2011 -- 2014	1148	1.22	0.57	2.60	0.6061
Readmission of Repeat Revascularization					
Year 2008 -- 2010	1696	1.19	0.87	1.62	0.2825
Year 2011 -- 2014	1148	0.95	0.65	1.38	0.7836
Readmission of Major Bleeding					
Year 2008 -- 2010	1696	1.01	0.75	1.35	0.9602
Year 2011 -- 2014	1148	1.25	0.85	1.85	0.2503

Model of outcome:**P-value for the interaction**

Composite of mortality and readmission of MI / Stroke	0.66
Readmission of Stroke	0.80
Readmission of Repeat Revascularization	0.35
Readmission of Bleeding	0.40

Figure S1. Cumulative incidence curves for: A) the composite endpoint (all-cause mortality, rehospitalization for stroke, rehospitalization for MI); B) all-cause mortality; C) rehospitalization for MI; D) rehospitalization for stroke; E) rehospitalization of repeat revascularization; F) rehospitalization for bleeding. Abbreviations: BMS, bare metal stent; CABG, coronary artery bypass grafting; DES, drug eluting stent; MI, myocardial infarction

