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Safety and Efficacy of Drug-Eluting Stents in Older Patients With Chronic Kidney Disease

A Report From the Linked CathPCI Registry–CMS Claims Database

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Objectives The purpose of this study was to determine the safety and efficacy of drug-eluting stents (DES) compared with bare-metal stents (BMS) in older patients with chronic kidney disease (CKD).

Background DES may be associated with late death and myocardial infarction (MI) secondary to stent thrombosis. However, data on outcomes in older patients with CKD are limited.

Methods We estimated the glomerular filtration rate (GFR) of 283,593 patients 65 years of age and older who underwent stent implantation between 2004 and 2007. In propensity-matched cohorts grouped by GFR, the association between DES and BMS and the risk of death, MI, revascularization, and major bleeding was examined.

Results A total of 121,446 patients (42.8%) had CKD (GFR <60 ml/min/1.73 m^2). The 30-month mortality rate for patients on long-term dialysis was 52.0%. In propensity-matched pairs, placement of a DES compared with a BMS in patients with normal renal function was associated with significant reductions in 30-month revascularization (hazard ratio [HR]: 0.91; 95% confidence interval [CI]: 0.86 to 0.95), MI (HR: 0.77; 95% CI: 0.71 to 0.83), and death (HR: 0.73; 95% CI: 0.69 to 0.77), but no difference in bleeding (HR: 0.89; 95% CI: 0.79 to 1.00). Lower MI and mortality rates were also observed after DES compared with BMS implantation in all CKD subgroups with the exception of MI in the long-term dialysis group. Decreased rates of revascularization did not extend to any subgroup of patients with CKD.

Conclusions The safety of DES compared with BMS is observed in all patients regardless of renal function and is associated with reduced rates of MI and death in some subsets of patients with CKD. (J Am Coll Cardiol 2011;58: 1859–69) © 2011 by the American College of Cardiology Foundation Open access under CC BY-NC-ND license.

Patients with chronic kidney disease (CKD) make up an increasing percentage of the population undergoing percutaneous coronary intervention (PCI). This trend is largely a result of the growing number of patients with CKD, estimated to exceed 19 million patients in the United States, and the high prevalence of coronary artery disease in these patients (1–3). However, their representation in randomized trials of PCI therapies has been historically low because of concerns about an increase in major in-hospital adverse events, short- and long-term mortality, and lower procedural success rates compared with patients with normal renal function (4–6).

The drug-eluting stent (DES) has emerged as the stent of choice in CKD patients in response to the high restenosis rates of 13% to 35% seen with bare-metal stents (BMS) in these patients (7–11). Although DES have been shown to lower restenosis and revascularization rates in patients enrolled in the randomized, controlled trials (RCTs) (12–14), >50% of DES are being placed in patient and anatomic subsets that were not included in the large pivotal RCTs

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Abbreviations and Acronyms

BMS = bare-metal stent(s)
CI = confidence interval
CKD = chronic kidney disease
DES = drug-eluting stent(s)
GFR = glomerular filtration rate
HR = hazard ratio
IPW = inverse probability–weighted
MI = myocardial infarction
NCDR = National Cardiovascular Data Registry
PCI = percutaneous coronary intervention
RCT = randomized controlled trial

(15–17). Whether these devices are safe and effective in older patients with baseline CKD or patients on long-term dialysis has not been well studied, and the recent concerns regarding increased rates of late stent thrombosis in patients with CKD after implantation of DES may offset any potential benefit of decreased revascularization (18–20).

The contemporary prevalence of CKD in older patients undergoing PCI and the relative safety and efficacy of DES compared with those of BMS in this population is unknown. Using data from the linked American College of Cardiology National Cardiovascular Data Registry (NCDR) and the Center for Medicare Services national claims databases, we evaluated the outcomes of patients with increasing severity of CKD including patients on dialysis and in these subgroups and examined the association between DES and BMS and the risks of death, myocardial infarction (MI), revascularization, and major bleeding.

Methods

Study population. The NCDR CathPCI registry, cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Interventions, was previously described (21,22). The registry catalogs data on patient and hospital characteristics, clinical presentation, treatments, and outcomes for PCI procedures from more than 1,000 sites across the United States. Data are entered into NCDR-certified software at participating institutions and exported in a standard format to the American College of Cardiology. There is a standard dataset with written definitions, uniform data entry and transmission requirements, and data quality checks. The variables were prospectively defined by a committee of the American College of Cardiology and are available online (23).

This study included all Medicare-eligible patients 65 years of age and older undergoing PCI who were enrolled in the CathPCI registry between January 1, 2004, and December 31, 2007. Only patients enrolled using version 3.0 of the data forms (contains data on baseline creatinine) were included. Patients receiving more than 1 stent type (i.e., both BMS and DES) or missing creatinine values who were not on dialysis were excluded from the analysis (Fig. 1). Patients were classified into 5 groups according to the estimated glomerular filtration rate (GFR) using the 4-component MDRD (Modification of Diet in Renal Disease study) equation incorporating age, race, sex, and serum creatinine (24). The most recent creatinine level before the day of the procedure was collected on the case report forms. Patients were classified as having normal renal function (GFR $\geq$60 ml/min/1.73 m^2), mild CKD (GFR 45 to 59 ml/min/1.73 m^2), moderate CKD (GFR 30 to 44 ml/min/1.73 m^2), severe CKD (GFR $<$30 ml/min/1.73 m^2), and long-term dialysis (as indicated by the case report form). The Duke University Medical Center Institutional Review Board granted a waiver of the informed consent and authorization for this study.

Follow-up information. The CathPCI registry only covers pre-hospital testing and in-hospital outcomes, so we used the Medicare 100% inpatient fee-for-service claims file for longitudinal patient follow-up. The CathPCI Registry-CMS Claims Database linking rules were previously described (25).

Clinical endpoints. We evaluated 4 primary clinical endpoints: death, MI, repeat revascularization, and follow-up bleeding (26,27). Death was defined both during the index PCI procedure (using American College of Cardiology NCDR information) and post-discharge (using the Medicare denominator file). Other clinical endpoints were defined post-discharge only with the Medicare claims file as the primary diagnosis for the hospital admission. The ICD-9 CM diagnosis codes used to identify events were MI (410.X1) (26,27), major bleeding (430 through 432 [intracerebral], 578.X [gastrointestinal tract], 719.1X [hemarthrosis], 423.0 [hemopericardium], 599.7 [hematuria], 626.2, 626.6, 626.8, 627.0, 627.1 [vaginal], 786.3 [hemoptysis], 784.7 [epistaxis], or 459.0 [hemorrhage not otherwise specified]), and revascularizations (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 hospital stay were included in the revascularization analysis.

Statistical analysis. Differences between groups were compared using chi-square tests for categorical variables and the Wilcoxon rank sum or Kruskal-Wallis test for continuous variables. Event rates were calculated based on Kaplan-Meier censoring estimates. Kaplan-Meier event curves, stratified by CKD subgroup, were generated and presented as cumulative incidence curves. To evaluate the independent effect of CKD severity on outcomes, we used a Cox proportional hazards model adjusted with variables from the NCDR PCI mortality model (28,29). Patients with normal renal function were used as the referent group in all comparisons.

Propensity scores were developed for the receipt of DES within each CKD subgroup such that the receipt of a DES is the dependent variable conditioned on 102 observed covariates. We then matched each DES recipient to a BMS control within each CKD subgroup by using the estimated logit of the propensity score using a

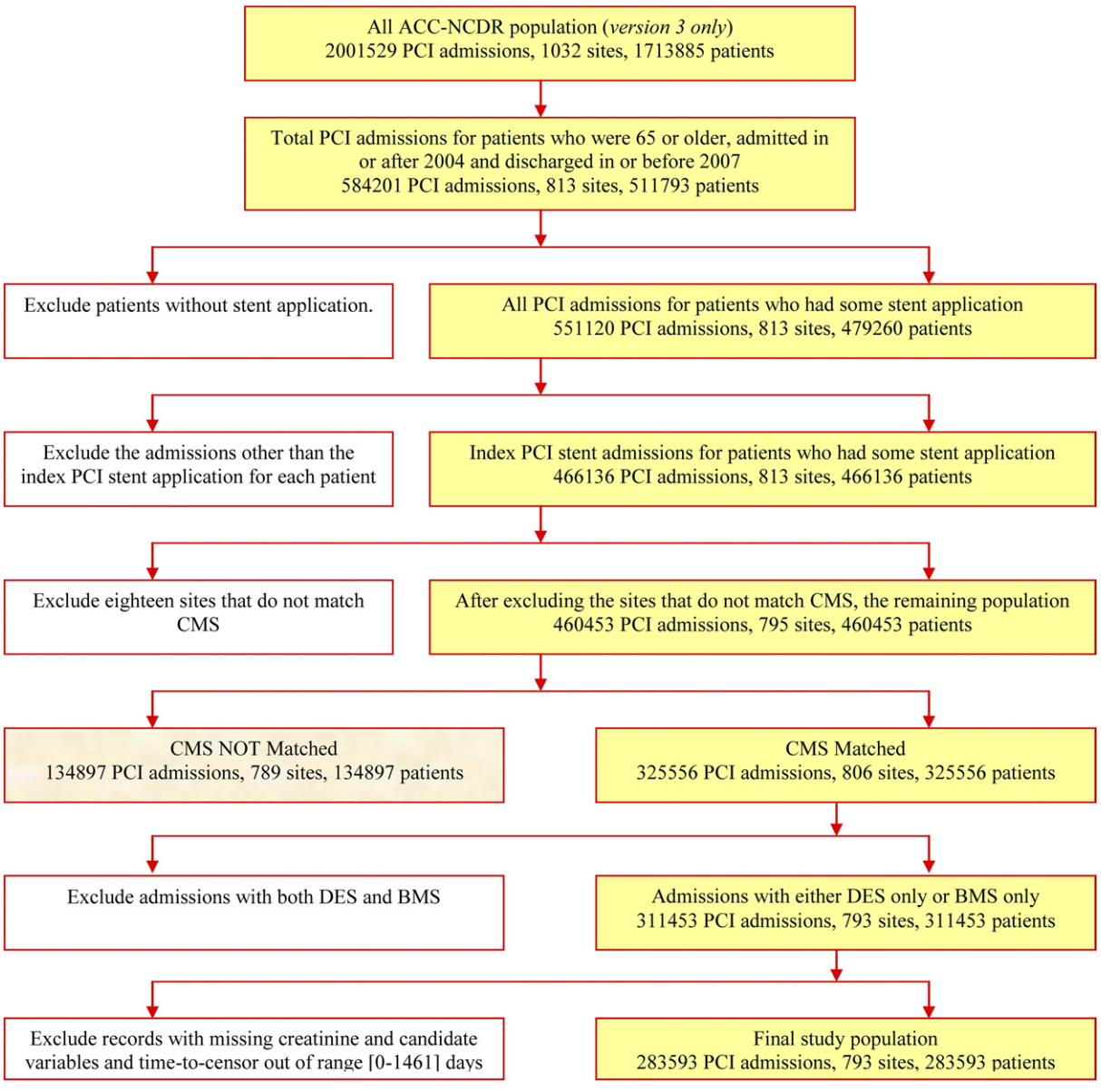

Figure 1 **Population Selection: Flow Diagram**

ACC–NCDR = American College of Cardiology–National Cardiovascular Data Registry; BMS = bare-metal stent; CMS = Centers for Medicare and Medicaid Services; DES = drug-eluting stent(s); PCI = percutaneous coronary intervention.

"greedy" 5-to-1 digit-matching algorithm. Using the matched pairs in each subgroup, the reduction in the risk of the outcome was compared between the DES and the BMS groups with the use of a Cox regression model, with stent type as the sole predictor. Analyses were performed using SAS software version 9.0 (SAS Institute Inc., Cary, North Carolina).

Sensitivity analyses. To further assess the robustness of our findings, we performed a series of additional sensitivity analyses. First, we also used inverse probability–weighted (IPW) estimators incorporating propensity scores to compare treatment groups. IPW estimators require fewer distributional assumptions and handle censored data (30). Adjusted hazard ratios (HRs) were calculated according to the IPW approach of Cole and Hernan (31). Second, because propensity matching cannot be expected to balance unmeasured confounders that are unrelated to the measured confounders, we estimated the magnitude of odds ratios between an unmeasured confounder and exposure that would invalidate our results (32). We varied the prevalence of a potential confounder between 0.3 and 0.7 and assumed a strong association of the confounder to the outcome

Table 1 HRs for Death, MI, Revascularization, and Bleeding According to CKD Subgroup at 30 Months

Outcome	GFR ≥60 ml/min/1.73 m² Normal (n = 162,417)	GFR 45–59 ml/min/1.73 m² Mild CKD (n = 73,751)	GFR 30–44 ml/min/1.73 m² Moderate CKD (n = 34,004)	GFR <30 ml/min/1.73 m² Severe CKD (n = 8,509)	Dialysis (n = 5,182)
Death*	10.5	13.8	22.0	32.7	51.9
Unadjusted HR	1.0†	1.31 (1.27–1.35)	2.29 (2.22–2.37)	3.73 (3.55–3.91)	6.63 (6.31–6.97)
Adjusted HR‡		1.11 (1.08–1.15)	1.45 (1.40–1.51)	1.87 (1.76–1.98)	3.55 (3.36–3.74)
MI*	5.6	6.6	9.0	13.7	19.5
Unadjusted HR	1.0†	1.21 (1.15–1.26)	1.61 (1.53–1.71)	2.31 (2.12–2.52)	3.75 (3.43–4.11)
Adjusted HR‡		1.06 (1.01–1.11)	1.14 (1.07–1.20)	1.34 (1.21–1.49)	2.11 (1.91–2.31)
Revascularization*	18.2	18.4	18.1	20.7	23.9
Unadjusted HR	1.0†	1.02 (1.00–1.04)	0.99 (0.96–1.03)	1.02 (0.96–1.09)	1.22 (1.13–1.32)
Adjusted HR‡		1.02 (1.00–1.05)	0.97 (0.94–1.01)	0.97 (0.90–1.04)	1.13 (1.04–1.23)
Major bleeding*	3.0	3.7	4.9	6.3	9.6
Unadjusted HR	1.0†	1.21 (1.14–1.29)	1.73 (1.61–1.86)	2.32 (2.06–2.61)	3.20 (2.79–3.66)
Adjusted HR‡		1.09 (1.02–1.16)	1.31 (1.21–1.42)	1.59 (1.38–1.82)	2.27 (1.97–2.60)

Values are % or HR (95% confidence interval). *Kaplan-Meier event rate. †This group served as the reference group. ‡Covariates used are listed in the Online Appendix.
CKD = chronic kidney disease; GFR = glomerular filtration rate; HR = hazard ratio; MI = myocardial infarction.

because weaker associations would require stronger associations between the unmeasured confounder and the exposure so that the reported magnitudes are conservative.

Results

Severity of CKD and outcomes. Between January 1, 2004, and December 31, 2007, 460,453 patients 65 years of age and older underwent stent implantation, and 70.7% were linked to Medicare longitudinal records. After exclusions (Fig. 1), the study population included 283,593 patients from 793 sites. Comparison of NCDR patients who did and did not match to Medicare records revealed nonmatch patients (Online Table 1) to be slightly younger (age 73.6 years vs. 74.7 years) and more likely to be men (61.8% vs. 58.0%) and to live in the Western United States (24.3% vs. 14.3%).

There were 162,147 patients (57.2%) with normal renal function, 73,751 (26.0%) with mild CKD, 34,004 (12.0%) with moderate CKD, 8,509 (3.0%) with severe CKD, and 5,182 (1.8%) on long-term dialysis who underwent PCIs. The prevalence of mild, moderate, and severe CKD patients increased with increasing age, whereas the prevalence of dialysis patients decreased (Fig. 2). The proportions of patients with coexisting comorbidities at baseline increased with increasing severity of CKD (Online Table 2).

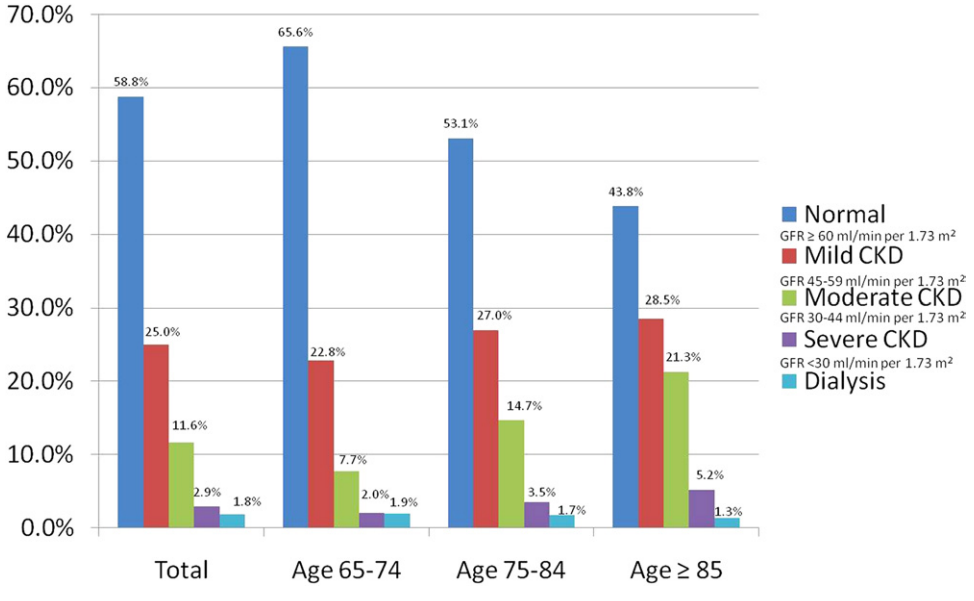

Figure 2 Prevalence of CKD by Age

CKD = chronic kidney disease; GFR = glomerular filtration rate.

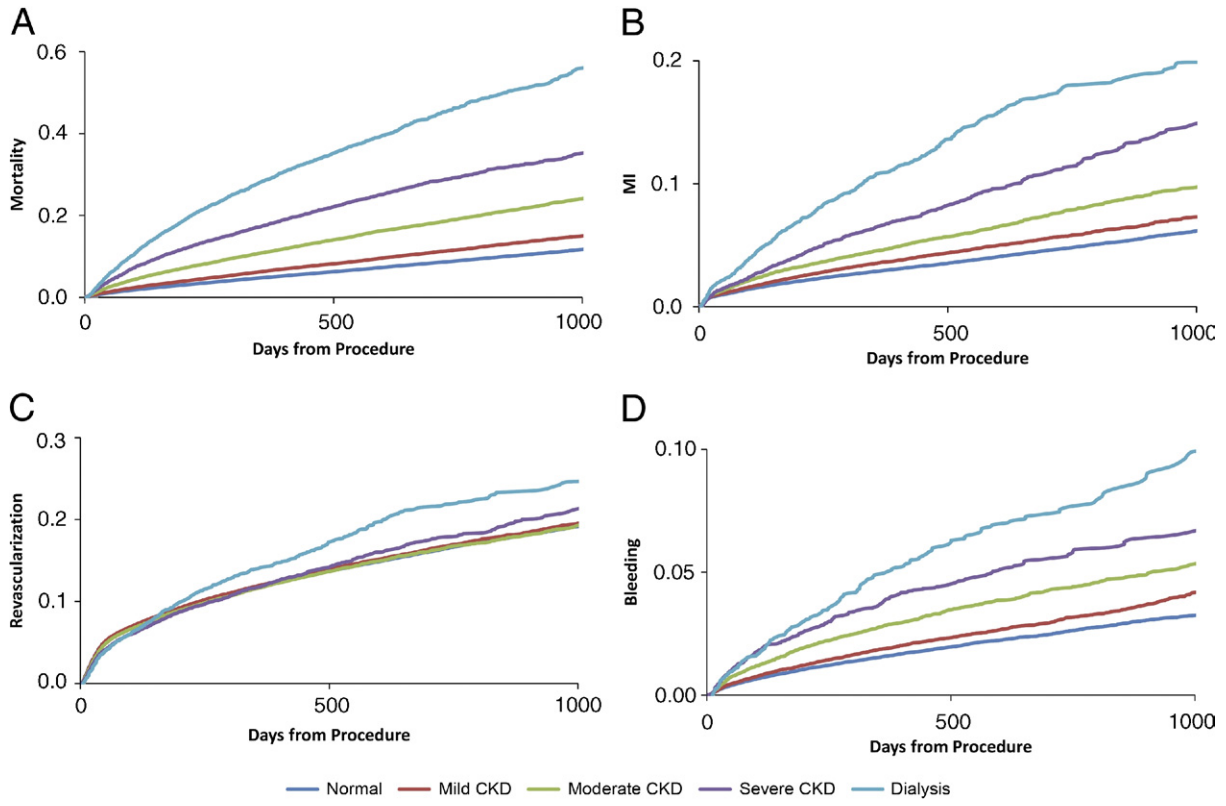

Figure 3 **Stratified Cumulative Incidence Curves by Severity of CKD**

Cumulative incidence for death **(A)**, myocardial infarction (MI) **(B)**, revascularization **(C)**, and major bleeding **(D)**. CKD = chronic kidney disease.

Figure 3 shows the Kaplan-Meier cumulative incidence curves stratified by CKD severity. Increasing severity of CKD was associated with increasing mortality rates. Mortality rates were extremely high in patients with severe CKD, with 30-month mortality rates of 32.7% (95% confidence interval [CI]: 31.2 to 34.1) and peaked in patients on long-term dialysis at 51.9% (95% CI: 49.8 to 54.0). Increasing severity of CKD was also associated with increasing rates of MI, revascularization, and bleeding (Table 1).

Using patients with normal renal function (GFR ≥60 ml/min/1.73 m^2) as the reference group, there was a graded increase in the association of CKD severity with adjusted rates of death, MI, and major bleeding (Table 1). Dialysis patients had the highest adjusted rates of death (adjusted HR: 3.55; 95% CI: 3.36 to 3.74), MI (adjusted HR: 2.11; 95% CI: 1.91 to 2.31), and major bleeding (adjusted HR: 2.27; 95% CI: 1.97 to 2.60). Significant increases in revascularization were only seen in the dialysis group (adjusted HR: 1.13; 95% CI: 1.04 to 1.23).

DES cohort compared with BMS cohort. The baseline characteristics of the 283,593 patients who underwent PCIs grouped by both CKD severity and type of stent received are shown in Online Table 2. Overall, 65,063 patients (22.9%) received a BMS. In the entire study population, BMS patients were significantly older with a higher prevalence of smoking and history of congestive heart failure, peripheral arterial disease, stroke, and chronic lung disease compared with patients treated with DES. In all subgroups examined, patients receiving DES were more likely to have had a previous PCI and to present for an elective PCI.

DES propensity cohort compared with BMS propensity cohort. After propensity-score matching, there were 121,942 matched pairs overall (60,971 patients who received DES and 60,971 who received BMS). The patient characteristics and clinical factors of the propensity-matched population are shown in Table 2. The standardized differences between the 2 groups within each CKD stratum were less than 10%, indicating good balance of the covariates. Compared with BMS, DES treatment was associated with lower 30-month death rates in patients with normal renal function (12.2% vs. 14.7%, $p < 0.001$), mild CKD (15.1% vs. 18.6%, $p < 0.001$), moderate CKD (24.1% vs. 26.6%, $p < 0.001$), and severe CKD (33.7% vs. 33.7%, $p = 0.04$) and patients on long-term dialysis (48.9% vs. 56.4%, $p < 0.001$) (Table 3, Fig. 4).

Overall, MI rates at 30 months were lower in the DES compared with the BMS patients (7.2% vs. 8.2%, $p < 0.001$). The use of DES compared with BMS was also

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Table 2 Demographics and Baseline Characteristics of Propensity Matched Population

	GFR ≥60 ml/min/1.73 m² Normal				GFR 45–59 ml/min/1.73 m² Mild CKD			
	DES (n = 33,648)	BMS (n = 33,648)	p Value	Standardized Difference	DES (n = 15,977)	BMS (n = 15,977)	p Value	Standardized Difference
Age, yrs	74.4 ± 6.4	74.5 ± 6.6	0.688	−0.6	76.2 ± 6.6	76.1 ± 6.8	0.613	0.2
Male	22,205 (66.0)	22,198 (66.0)	0.955	0.0	8,290 (51.9)	8,295 (51.9)	0.955	−0.1
Current smoking	5,234 (15.6)	5,267 (15.7)	0.726	−0.3	2,006 (12.6)	1,977 (12.4)	0.623	0.5
CHF (previous or current)	24,128 (71.7)	24,211 (72.0)	0.477	−0.5	12,028 (75.3)	12,033 (75.3)	0.948	−0.1
HTN	26,110 (77.6)	26,126 (77.6)	0.882	−0.1	13,317 (83.4)	13,291 (83.2)	0.697	0.4
Renal failure								
No dialysis	370 (1.1)	357 (1.1)	0.628	0.4	707 (4.4)	721 (4.5)	0.705	−0.4
Dialysis								
DM								
Non–insulin-dependent	7,374 (21.9)	7,240 (21.5)	0.210	1.0	3,649 (22.8)	3,693 (23.1)	0.558	−0.7
Insulin-dependent	2,232 (6.6)	2,226 (6.6)	0.926	0.1	1,554 (9.7)	1,543 (9.7)	0.835	0.2
PVD	4,847 (14.4)	4,806 (14.3)	0.652	0.3	2,651 (16.6)	2,676 (16.7)	0.707	−0.4
Stroke	5,069 (15.1)	5,028 (14.9)	0.658	0.3	2,868 (18.0)	2,879 (18.0)	0.873	−0.2
Chronic lung disease	6,801 (20.2)	6,741 (20.0)	0.564	0.4	3,282 (20.5)	3,288 (20.6)	0.934	−0.1
Previous PCI	7,831 (23.3)	7,789 (23.1)	0.701	0.3	3,902 (24.4)	3,901 (24.4)	0.990	0.0
Previous CABG	7,813 (23.2)	7,684 (22.8)	0.238	0.9	4,061 (25.4)	4,008 (25.1)	0.495	0.8
Previous MI	8,155 (24.2)	8,133 (24.2)	0.843	0.2	4,262 (26.7)	4,247 (26.6)	0.849	0.2
Indication								
No symptoms, no angina	5,064 (15.1)	4,993 (14.8)	0.441	0.6	2,292 (14.3)	2,268 (14.2)	0.698	0.4
Atypical chest pain	2,279 (6.8)	2,297 (6.8)	0.784	−0.2	1,043 (6.5)	1,018 (6.4)	0.567	0.6
Stable angina	4,749 (14.1)	4,725 (14.0)	0.788	0.2	2,131 (13.3)	2,172 (13.6)	0.504	−0.7
Unstable angina	10,510 (31.2)	10,415 (31.0)	0.426	0.6	4,795 (30.0)	4,792 (30.0)	0.965	0.0
NSTEMI	6,209 (18.5)	6,256 (18.6)	0.644	−0.4	3,158 (19.8)	3,108 (19.5)	0.478	0.8
STEMI	4,835 (14.4)	4,962 (14.7)	0.166	−1.1	2,556 (16.0)	2,619 (16.4)	0.341	−1.1
Multivessel PCI	3,693 (11.0)	3,733 (11.1)	0.623	−0.4	1,860 (11.6)	1,845 (11.5)	0.793	0.3
Off-label PCI	18,147 (78.8)				8,376 (79.7)			

Values are mean ± SD or n (%).

BMS = bare-metal stent; CABG = coronary artery bypass graft; CHF = congestive heart failure; DES = drug-eluting stent; DM = diabetes mellitus; HTN = hypertension; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary artery intervention; PVD = peripheral vascular disease; STEMI = ST-segment elevation myocardial infarction; other abbreviations as in Table 1.

associated with lower adjusted 30-month MI rates in patients with normal renal function or mild, moderate, or severe CKD. This pattern was not observed in patients on long-term dialysis. Revascularization rates at 30 months were slightly lower in the DES compared with BMS patients (18.1% vs. 18.4%, $p < 0.001$). There appeared to be a differential reduction in revascularization rates for DES compared with BMS (interaction $p < 0.01$) in patients with normal renal function only, whereas patients with mild, moderate, or severe CKD and patients on dialysis did not show significant differences. Major bleeding rates at 30 months were slightly lower in the DES compared with the BMS subgroup (3.9% vs. 4.1%, $p = 0.04$). After adjustment, DES use in the severe CKD subgroup was associated with significant reductions in the incidence of 30-month rates of hospitalization for bleeding, whereas no differences were seen in the other groups.

Sensitivity analyses. Comparison of DES and BMS using IPW adjustment yielded findings consistent with the propensity analysis (Fig. 4). Sensitivity analysis of residual confounding indicated that an unmeasured confounder would need to be associated with a greater than 9-fold increase in the odds of selecting a DES with a large protective effect on mortality (HR: 0.50) to eliminate the significant associations of our findings.

Discussion

In the largest observational real-world study evaluating older patients undergoing PCI, we found that pre-existing kidney disease was a common condition, prevalent in more than one-third of older patients and is associated with increased risk of death, MI, revascularization, and major bleeding after PCI. Our study demonstrates a very high mortality in patients with severe CKD and patients on long-term dialysis, with nearly 1 in 3 (32.7%) and more than one-half (52.0%), respectively, dying within 3 years. Despite these high adverse event rates, we observed a significant reduction in risk-adjusted mortality, MI, and revascularization associated with the use of DES compared with BMS in patients with normal renal function and most subgroups of patients with CKD, but not patients on long-term dialysis. Importantly, we did not detect a significant safety hazard with the use of DES compared with BMS across the spectrum of high-risk elderly patients with CKD.

The association between CKD and cardiovascular outcomes has been the focus of many studies over the past decade. Most of the data have been consistent, with our study showing worsened short- and long-term clinical outcomes including death in a dose-dependent fashion with increasing serum creatinine during and after PCI

Table 2

GFR 30–44 ml/min/1.73 m² Moderate CKD				GFR <30 ml/min/1.73 m² Severe CKD				Dialysis			
DES (n = 7,944)	BMS (n = 7,944)	p Value	Standardized Difference	DES (n = 2,066)	BMS (n = 2,066)	p Value	Standardized Difference	DES (n = 1,336)	BMS (n = 1,336)	p Value	Standardized Difference
78.1 ± 6.7	78.0 ± 6.9	0.392	1.3	77.9 ± 6.8	77.8 ± 6.9	0.638	1.2	74.0 ± 6.3	74.1 ± 6.4	0.782	−1.9
3,706 (46.7)	3,708 (46.7)	0.975	−0.1	819 (39.6)	819 (39.6)	1.000	0.0	775 (58.0)	784 (58.7)	0.724	−1.4
786 (9.9)	803 (10.1)	0.653	−0.7	206 (10.0)	224 (10.8)	0.359	−2.9	131 (9.8)	131 (9.8)	1.000	0.0
6,289 (79.2)	6,289 (79.2)	1.000	0.0	1,718 (83.2)	1,716 (83.1)	0.934	0.3	1,065 (79.7)	1,075 (80.5)	0.628	−1.9
6,935 (87.3)	6,928 (87.2)	0.868	0.3	1,861 (90.1)	1,859 (90.0)	0.917	0.3	1,234 (92.4)	1,232 (92.2)	0.885	0.6
1,453 (18.3)	1,445 (18.2)	0.869	0.3	1,157 (56.0)	1,159 (56.1)	0.950	−0.2				
								1,336 (100.0)	1,336 (100.0)		.
2,072 (26.1)	2,034 (25.6)	0.491	1.1	519 (25.1)	541 (26.2)	0.433	−2.4	357 (26.7)	357 (26.7)	1.000	0.0
1,161 (14.6)	1,176 (14.8)	0.737	−0.5	468 (22.7)	460 (22.3)	0.766	0.9	490 (36.7)	487 (36.5)	0.904	0.5
1,754 (22.1)	1,714 (21.6)	0.442	1.2	543 (26.3)	541 (26.2)	0.944	0.2	518 (38.8)	502 (37.6)	0.524	2.5
1,831 (23.0)	1,799 (22.6)	0.545	1.0	518 (25.1)	514 (24.9)	0.886	0.4	352 (26.3)	361 (27.0)	0.694	−1.5
1,831 (23.0)	1,790 (22.5)	0.438	1.2	526 (25.5)	501 (24.2)	0.368	2.8	379 (28.4)	368 (27.5)	0.635	1.8
1,982 (24.9)	2,003 (25.2)	0.701	−0.6	476 (23.0)	439 (21.2)	0.166	4.3	338 (25.3)	331 (24.8)	0.755	1.2
2,287 (28.8)	2,211 (27.8)	0.181	2.1	512 (24.8)	507 (24.5)	0.857	0.6	393 (29.4)	383 (28.7)	0.670	1.6
2,437 (30.7)	2,397 (30.2)	0.490	1.1	635 (30.7)	629 (30.4)	0.839	0.6	451 (33.8)	452 (33.8)	0.967	−0.2
1,156 (14.6)	1,109 (14.0)	0.286	1.7	305 (14.8)	286 (13.8)	0.399	2.6	271 (20.3)	278 (20.8)	0.745	−1.3
461 (5.8)	476 (6.0)	0.613	−0.8	85 (4.1)	83 (4.0)	0.875	0.5	105 (7.9)	102 (7.6)	0.824	0.9
937 (11.8)	930 (11.7)	0.863	0.3	196 (9.5)	204 (9.9)	0.674	−1.3	131 (9.8)	135 (10.1)	0.801	−1.0
2,284 (28.8)	2,290 (28.8)	0.916	−0.2	562 (27.2)	555 (26.9)	0.806	0.8	402 (30.1)	389 (29.1)	0.573	2.2
1,812 (22.8)	1,832 (23.1)	0.706	−0.6	535 (25.9)	564 (27.3)	0.307	−3.2	329 (24.6)	334 (25.0)	0.831	−0.8
1,294 (16.3)	1,307 (16.5)	0.780	−0.4	383 (18.5)	374 (18.1)	0.717	1.1	97 (7.3)	98 (7.3)	0.945	−0.3
982 (12.4)	1,009 (12.7)	0.518	−1.0	271 (13.1)	280 (13.6)	0.680	−1.3	192 (14.4)	197 (14.7)	0.784	−1.1
4,206 (81.9)				1,000 (79.1)				772 (81.3)			

(5,9,33–36). Our study included more than 5,000 dialysis patients and provides important insights into clinical outcomes in this poorly studied population. Compared with patients with normal renal function, those on dialysis had a 3.6-fold increased risk of death, a 2.1-fold increased risk of MI, and a 2.3-fold increased risk of major bleeding at 30-month follow-up. Long-term dialysis patients also had higher rates of repeat revascular-

Table 3 Death, MI, Revascularization, and Bleeding Rates at 30 Months

	KM Rate, %					
	Overall (N = 127,308)	GFR ≥60 ml/min/1.73 m² Normal (n = 72,174)	GFR 45–59 ml/min/1.73 m² Mild CKD (n = 31,990)	GFR 30–44 ml/min/1.73 m² Moderate CKD (n = 16,148)	GFR <30 ml/min/1.73 m² Severe CKD (n = 4,266)	Dialysis (n = 2,730)
Death						
DES	16.1	11.9	15.0	24.7	34.6	53.2
BMS	18.8	14.6	18.6	26.8	34.1	55.9
p value	<0.001	<0.001	<0.001	0.002	0.125	0.066
Any MI						
DES	6.9	5.7	6.5	9.6	15.0	22.9
BMS	8.1	7.0	7.3	11.9	12.8	21.2
p value	<0.001	<0.001	<0.001	0.007	0.026	0.463
Revascularization						
DES	18.0	17.8	18.1	17.6	19.4	23.9
BMS	18.5	18.7	17.5	18.3	20.1	23.8
p value	<0.001	<0.001	0.100	0.909	0.431	0.959
Bleeding						
DES	4.2	3.5	4.4	5.9	4.7	10.7
BMS	4.1	3.4	4.0	5.6	9.5	7.5
p value	0.462	0.162	0.255	0.874	0.002	0.261

KM = Kaplan-Meier; other abbreviations as in Tables 1 and 2.

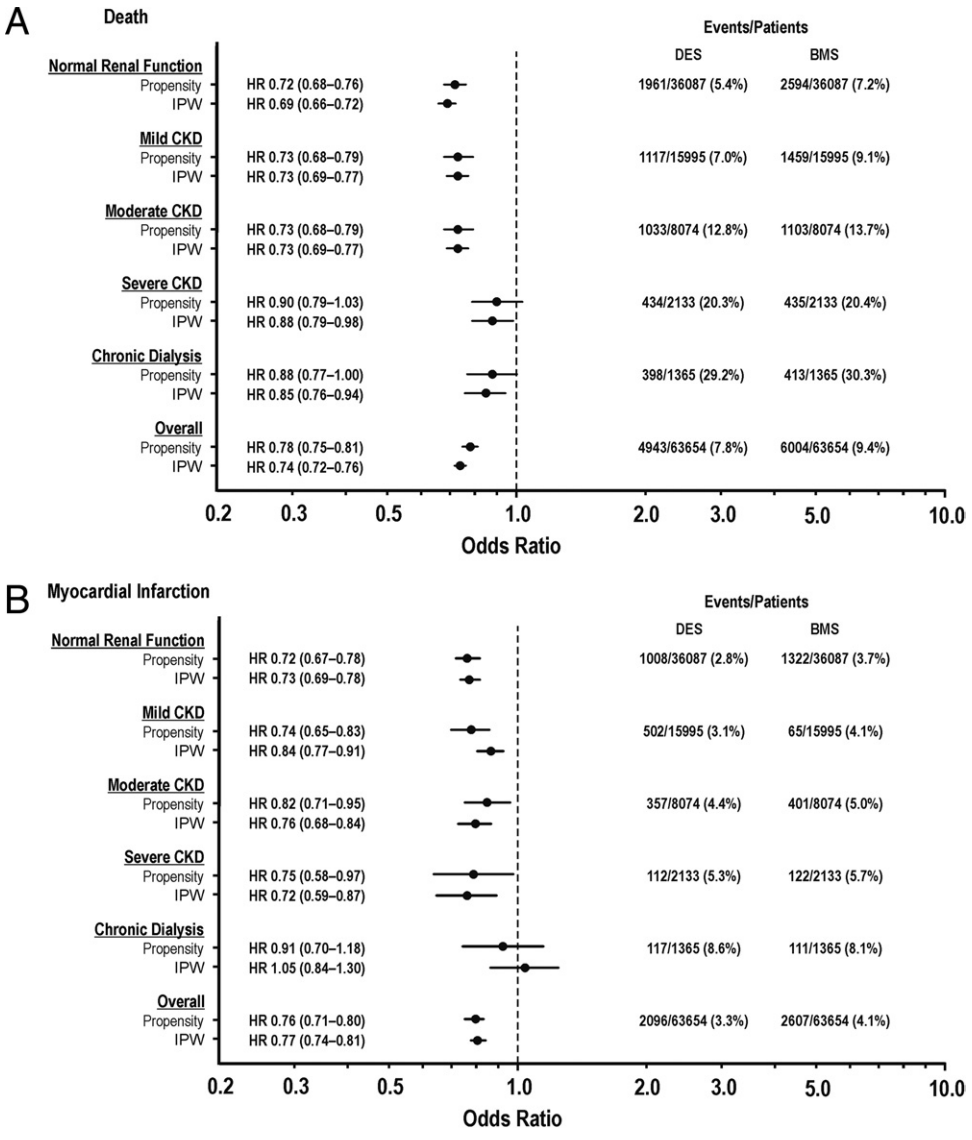

Figure 4 **Safety and Efficacy Outcomes at 30-Month Follow-Up**

Shown are the propensity-matched and inverse probability–weighted (IPW) hazard ratios (HRs) and the 95% confidence intervals stratified by baseline kidney function. Death **(A)**, myocardial infarction **(B)**, revascularization **(C)**, major bleeding **(D)**. Abbreviations as in Figures 1 and 2.

ization in follow-up, a pattern that was not seen in mild, moderate, or severe CKD patients.

Evidence of DES safety and efficacy has primarily come from both RCTs and large-scale observational registry studies (34,36–39). Kirtane et al. (40) highlighted the differences in RCTs compared with observational studies in a comprehensive meta-analysis showing that in RCTs, DES (compared with BMS) were associated with no detectable differences in overall mortality or MI, with a significant 55% reduction in target vessel revascularization. In contrast, observational studies have consistently shown that DES use was associated with significant reductions in mortality, MI, and target vessel revascularization compared with BMS. The differences in the results of RCTs and observational studies highlight the advantages and disadvantages of different study designs. Where observational studies falter with regard to unmeasured confounders, they have strength in the number of patients enrolled, the power to detect differences in low-rate safety endpoints, and excellent external generalizability. RCTs eliminate bias through randomization but apply to restricted trial populations with inadequate statistical power to detect important differences in low-frequency outcomes such as mortality. Therefore, the findings from RCTs and observational studies should be viewed as complementary.

Our results suggest that the use of DES in patients 65 years of age and older with normal renal function and

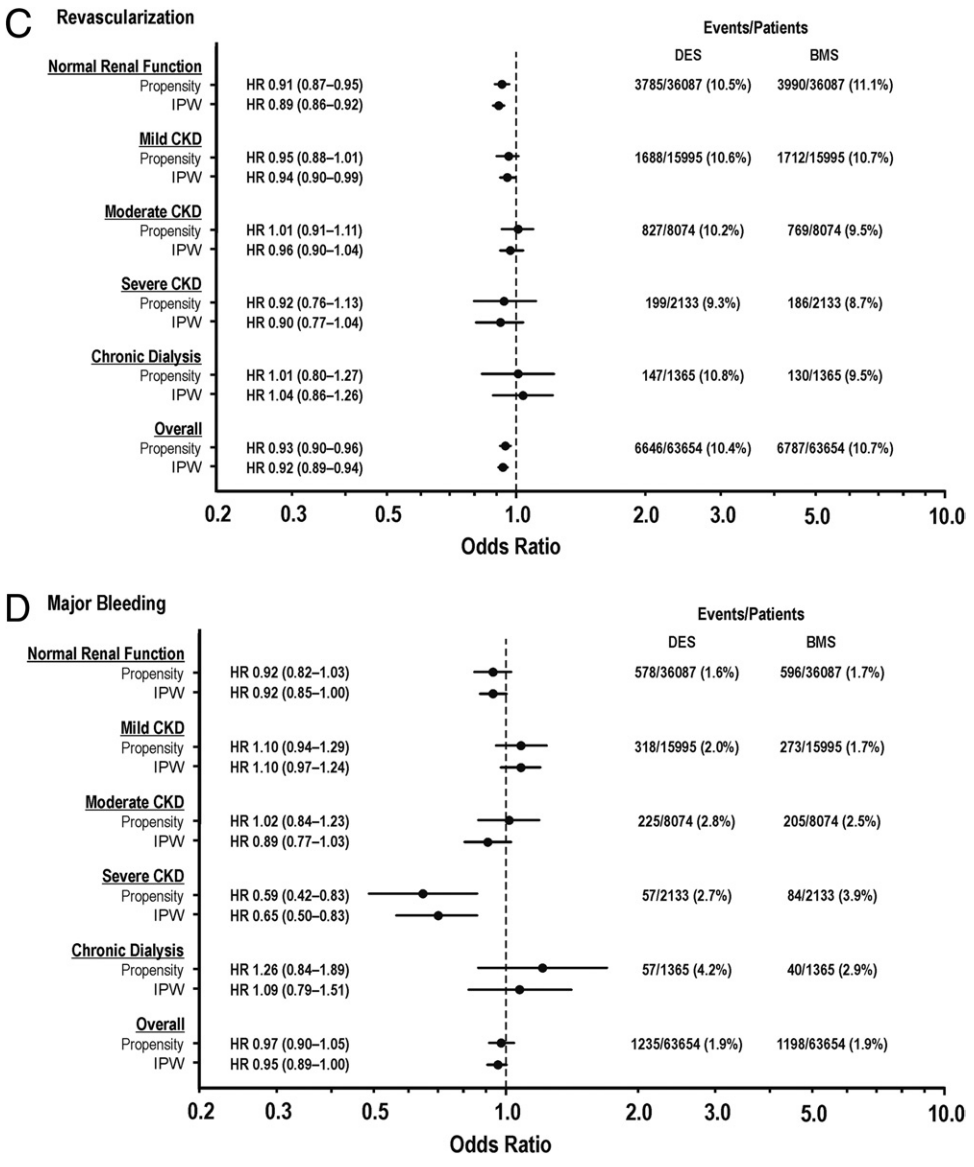

Figure 4 Continued

mild, moderate, or severe CKD as well as dialysis patients is associated with a lower absolute and adjusted mortality than patients who receive BMS. Similar benefits are also seen in the 30-month MI endpoint except that an associated decrease in MI is not seen in the long-term dialysis subgroup. These data support the use of DES in patients with CKD, and there does not appear to be any signal of harm in any CKD subgroup including dialysis patients. Although a mortality benefit has not been demonstrated among RCTs, this limitation could reflect limited follow-up, the enrollment of only low-risk patients with low event rates, or a relatively small number of patients. Alternatively, our mortality data could represent residual unmeasured confounding by indication where BMS placement is a surrogate for sicker patients that persists despite the adjustment of many variables and multiple sensitivity analyses that support our primary findings.

Because our follow-up was linked to the Medicare administrative data files, it is not possible to determine target vessel revascularization or stent thrombosis through ICD-9 coding. However, we were able to detect general repeat revascularization procedures (PCI or coronary artery bypass graft surgery) and found that DES use was associated with decreased revascularization in patients with normal renal function but not in patients with CKD. Small studies have shown an association between DES and lower restenosis and total lesion revascularization rates in patients with mildly impaired renal function, whereas others have not shown any

benefit of DES compared with BMS in patients with CKD (19,41–43).

Study limitations. There are several important considerations when interpreting the results of this study. First, patients and hospitals participating in the NCDR may not be representative of all U.S. practice and represent only patients older than the age of 65. However, the CathPCI registry represents more than 1,000 hospitals across the United States and thus captures a significant portion of PCIs nationally. Second, our linked dataset does not have data on medication during the longitudinal follow-up period. Therefore, we could not directly assess the influence of dual-antiplatelet therapy on our findings, which is likely a critical effect modifier of DES outcomes. Third, as in all observational studies, unmeasured confounders that could influence the receipt of a BMS instead of a DES must be considered. However, multiple sensitivity analyses performed in our study and the sentinel NCDR-linked Medicare cohort looking at the overall DES cohort compared with BMS cohort yielded similar results (24). Fourth, although mortality after stenting was very high in severe CKD and dialysis, it is unclear what the survival would have been without revascularization. The lack of an appropriate comparator arm (medically treated coronary artery disease patients only) makes inferences about the effectiveness of PCI versus medical therapy incomplete.

Conclusions

In a large national cohort study of Medicare beneficiaries undergoing PCIs, we found that >40% of older patients undergoing PCIs have CKD. A strong, independent graded association between increasing severity of CKD and increasing cardiovascular events was observed. Patients with normal renal function and most subgroups of CKD who received a DES had significantly lower mortality rates throughout 30 months of follow-up. The benefits of DES with regard to MI, revascularization, and major bleeding were present in most, but not all, subgroups. In the absence of a definitive large RCT, this is the largest registry study to date that suggests that DES appear to be safe in older patients with varying levels of CKD undergoing PCIs.

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Key Words: comparative effectiveness research ■ drug-eluting stent(s) ■ renal insufficiency.

APPENDIX

For supplemental tables and material, please see the online version of this article.