Safety and Effectiveness of Drug-Eluting and Bare-Metal Stents for Patients With Off- and On-Label Indications

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Objectives
Our main objective was to evaluate the longer-term safety and efficacy of drug-eluting stents (DES) in off-label indications as compared with bare-metal stents (BMS).

Background
DES are frequently implanted in patients with off-label indications. However, the longer-term safety and effectiveness of DES among patients with off-label indications are not well understood.

Methods
Propensity score matching analysis was performed in a population-based cohort that included 6,944 off-label and 9,126 on-label patients who received percutaneous coronary interventions (PCIs) in Ontario, Canada, between December 1, 2003, and March 31, 2006. Off-label indications were defined on the basis of clinical and procedural characteristics.

Results
For patients with off-label indications, rates of repeat target vessel revascularization at 3 years were significantly lower among patients treated with DES compared with those treated with BMS (11.6% vs. 15.3%, p < 0.001). Myocardial infarction rates were not significantly different between patients treated with DES and BMS (p = 0.52). Mortality rates were significantly lower among off-label patients treated with DES compared with BMS at 3 years of follow-up (6.9% vs. 10.5%, p < 0.001). For patients with on-label indications, the use of DES was associated with significantly lower rates of target vessel revascularization, but composite rates of myocardial infarction or death were not significantly different from BMS.

Conclusions
For patients with off-label indications, DES implantation was associated with lower target vessel revascularization without an associated increase in longer-term risk of myocardial infarction or death compared with BMS. (J Am Coll Cardiol 2009;53:1773–82) © 2009 by the American College of Cardiology Foundation

Drug-eluting stents (DES) have been demonstrated to be highly effective in reducing the need for future coronary revascularization (1–3). Although some early reports have suggested that patients receiving DES may have higher rates of stent thrombosis, myocardial infarction, or even death (4–8), subsequent evaluations have confirmed the safety of DES for patients with “on-label” indications, namely patient subsets that have been enrolled by trials with procedure indications approved by the Food and Drug Administration (FDA) (9–11). In contrast, DES use in patients with off-label indications, generally defined as clinical or procedural characteristics that have not been approved by the FDA, is associated with substantially higher risk of adverse outcomes as compared with on-label use of DES (12,13). Although a recent study by Marroquin et al. (14) suggests that the outcomes associated with off-label use of DES did not differ significantly with bare-metal stents (BMS) at 1 year, residual concerns persist due to the possibility that adverse outcomes associated with DES may not be apparent until after a year (7). Furthermore, the study compared a contemporary DES cohort with a historical cohort of patients treated with BMS, raising the possibility that the
outcomes of the contemporary DES group might have benefited from improvement in drug therapy and angioplasty procedure techniques (14).

Since DES are commonly implanted among patients with off-label indications, addressing this knowledge gap could have a substantial impact on the practice of interventional cardiology. The availability of a large population-based percutaneous coronary intervention (PCI) database with linkages to ongoing administrative data afforded a unique opportunity to compare patients with off-label indications treated with DES and BMS in a concurrent time frame with longer-term follow-up. Accordingly, the main objective of our study was to evaluate the longer-term safety and effectiveness of DES versus BMS in patients with off-label indications.

Methods

Data sources. The Ontario PCI database has been previously described (15). Briefly, the Cardiac Care Network (CCN) of Ontario maintains a prospective clinical registry of all patients undergoing cardiac catheterization, PCI, and coronary artery bypass grafting surgery in Ontario, Canada. Nurse coordinators at each cardiac invasive center gather data on demographics, clinical characteristics, procedure characteristics, and relevant comorbid conditions. Since 2003, mandatory fields have included the number of stents, characteristics of each stent, and location of stent placement (15). For the study, the CCN database was linked to the Canadian Institute for Health Information hospital discharge abstract database to identify additional comorbid conditions, the Ontario Diabetes Database to confirm diabetes status, and Statistics Canada Census data to determine socioeconomic status. Linkages with these various administrative databases were performed using unique encrypted patient identifiers to protect patient confidentiality.

This study was approved by the Research Ethics Board at the Sunnybrook Health Sciences Center. The need for informed patient consent was waived, as the CCN database is a prescribed registry under Ontario’s health information privacy legislation.

Study sample. We identified a cohort of patients who received PCI in Ontario from December 1, 2003, to March 31, 2006, which included an additional year of PCI patients compared to our previous cohort (15). This time frame was chosen to allow at least 1 year of follow-up to examine longer-term outcomes. From this initial cohort, we excluded patients who had both DES and BMS during the index PCI, patients with severe comorbidities (e.g., dementia, metastatic cancer, severe liver disease) because of competing risks of death, and patients who had an invalid Ontario health card number because we could not determine their longer-term outcomes. Patients who had missing information on important prognostic factors such as socioeconomic status (n = 1,027), Canadian Cardiovascular Society angina classification (n = 622 for missing, n = 1,579 for unknown), and stent type (n = 822) were also excluded because of our inability to use their propensity scores for matching.

Definitions. The off-label cohort was defined using both clinical and procedural characteristics. For clinical characteristics, we considered off-label indications as patients who presented with cardiogenic shock. We also considered PCI on the same day as hospitalization for myocardial infarction as an off-label indication. For procedural characteristics, we considered off-label indications as patients who had multivessel stenting; stent location in the left main artery, in a restenotic lesion, or in the bypass graft; total stent length >33 mm; or stent diameter (sirolimus-eluting stent <2.5 or >3.5 mm, paclitaxel-eluting stent <2.5 or >3.75 mm, BMS <2.5 or >3.5 mm) (16,17).

Because previous studies varied in their definitions of off-label indications (12–14), we also created an additional off-label cohort to examine the robustness of our results. We reanalyzed our data defining a more restrictive off-label cohort using only procedure characteristics (stent location, stent length, and stent size) similar to previous studies (12–14). Our results did not change materially compared with the original definition.

Outcomes. The primary effectiveness outcome of our study was repeat target vessel revascularization. The primary safety outcomes were myocardial infarction and all-cause mortality. Target vessel revascularization was determined using information from the CCN database; myocardial infarction was assessed using the Canadian Institute for Health Information hospital discharge abstract database (International Classification of Diseases, 10th Revision, disease codes: I21 and I22) (18); and mortality was determined from the Ontario Registered Persons Database. These outcomes were assessed through March 31, 2007, with complete follow-up data for each outcome.

Statistical analysis. Propensity score matching analysis was used to account for potential confounding and selection biases (15,19,20). The predicted probability of DES use was calculated by fitting a logistic regression model using all of the clinically relevant variables shown in Table 1. A greedy, nearest neighbor 1:1 matching algorithm was used to match subjects based on the logit of the propensity score with calipers width of 0.2 standard deviations of the logit of the propensity score (19,20). Standardized differences of the mean <0.1 were taken to indicate good balance in the matched sample (19,20). Patients were used only in 1 propensity score-matched pair, and those without a suitable match were excluded from the analysis.

We first stratified our study sample according to off- and on-label indications and subsequently performed propensity matching within each subgroup. Matching within each
<table>
<thead>
<tr>
<th>Patients, n</th>
<th>On-Label Use</th>
<th>Baseline Characteristics of the Propensity Matched Study Cohort*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS DES</td>
<td>BMS DES</td>
<td>BMS DES</td>
</tr>
<tr>
<td>4,563</td>
<td>4,563</td>
<td>3,472</td>
</tr>
</tbody>
</table>

Demographics

- **Mean age (yrs) ± SD**
  - 65–74: 62.3 ± 11.9 (BMS), 62.0 ± 11.5 (DES), 63.2 ± 12.3 (BMS), 63.2 ± 11.8 (DES)
  - 75–84: 1,178 (25.8%), 1,216 (26.6%), 899 (25.9%), 924 (26.6%)
  - 85 or older: 3,472 (99.6%), 3,472 (99.6%)

- **Sex**
  - Male: 3,155 (69.1%), 3,183 (69.8%), 2,491 (71.7%), 2,484 (71.5%)

Admission characteristics

- **Recent AMI (same day as PCI)**: 0, 0, 824 (23.7%), 812 (23.4%)
- **Recent AMI (days 1 to 7)**: 1,074 (23.5%), 1,082 (23.7%), 567 (16.3%), 585 (16.8%)
- **Recent AMI (days 7 to 30)**: 305 (6.7%), 306 (6.7%), 213 (6.1%), 220 (6.3%)
- **No prior AMI**: 3,184 (69.8%), 3,175 (69.6%), 1,868 (53.8%), 1,855 (53.4%)

Cardiogenic shock

- 0, 0, 95 (2.7%), 80 (2.3%)

Cardiac risk factors and comorbidities

- **Hypertension**: 1,779 (39.0%), 1,776 (38.9%), 1,354 (39.0%), 1,409 (40.6%)
- **Diabetes**: 1,406 (30.8%), 1,426 (31.3%), 1,122 (32.3%), 1,116 (32.1%)
- **Prior coronary artery bypass grafting**: 261 (5.7%), 263 (5.8%), 50 (1.4%), 50 (1.4%)
- **Prior PCI**: 286 (6.3%), 280 (6.1%), 220 (6.3%), 246 (7.1%)
- **Prior stroke or transient ischemic attack**: 117 (2.6%), 123 (2.7%), 118 (3.4%), 112 (3.2%)
- **Chronic obstructive pulmonary disease**: 217 (4.8%), 206 (4.5%), 168 (4.8%), 155 (4.5%)
- **Heart failure**: 216 (4.7%), 213 (4.7%), 210 (6.0%), 188 (5.4%)
- **Peripheral vascular disease**: 271 (5.9%), 257 (5.6%), 260 (7.5%), 255 (7.3%)
- **Cancer**: 50 (1.1%), 43 (0.9%), 33 (1.0%), 33 (1.0%)
- **Hemodialysis**: 42 (0.9%), 43 (1.2%), 43 (1.2%), 42 (1.2%)

Socioeconomic status

- **I**: 865 (19.0%), 885 (19.4%), 670 (19.3%), 642 (18.5%)
- **II**: 930 (20.4%), 950 (20.8%), 692 (19.9%), 728 (21.0%)
- **III**: 945 (20.7%), 931 (20.4%), 705 (20.3%), 710 (20.4%)
- **IV**: 932 (20.4%), 921 (20.2%), 705 (20.3%), 680 (19.6%)

Procedural characteristics

- **Stent location**
  - Left main: 0, 0, 108 (3.1%), 116 (3.3%)
  - Left anterior descending: 2,188 (48.0%), 2,176 (47.7%), 1,622 (46.7%), 1,601 (46.1%)
  - Left circumflex: 1,052 (23.1%), 1,063 (23.3%), 1,131 (32.6%), 1,083 (31.2%)
  - Right coronary artery: 1,323 (29.0%), 1,324 (29.0%), 1,341 (38.6%), 1,346 (38.6%)
  - Bypass graft (vein or arterial graft): 0, 0, 301 (8.7%), 294 (8.5%)
  - Multiple vessel stenting: 0, 0, 986 (28.4%), 933 (26.9%)
  - Stent for restenosis: 0, 0, 55 (1.6%), 76 (2.2%)

- **Stent characteristics, mean ± SD**
  - No. of stented vessels: 1.00 ± 0.00, 1.00 ± 0.00, 1.30 ± 0.50, 1.28 ± 0.48
  - No. of stents: 1.11 ± 0.32, 1.11 ± 0.32, 2.01 ± 1.00, 2.00 ± 0.98
  - Stent diameter: 2.94 ± 0.32, 2.94 ± 0.33, 2.86 ± 0.46, 2.87 ± 0.41
  - Stent length: 19.0 ± 6.1, 19.0 ± 6.2, 36.8 ± 21.0, 36.7 ± 18.6

All values are presented as n (%) unless otherwise specified. *Off-label indications include cardiogenic shock; percutaneous coronary intervention (PCI) same day as acute myocardial infarction (AMI); multivessel stenting; stent location in the left main artery, in a restenotic lesion, or in the bypass graft; total stent length >33 mm; or stent diameter (sirolimus-eluting stent <2.5 or >3.5 mm, paclitaxel-eluting stent <2.5 or >3.75 mm, bare-metal stent [BMS] <2.5 or >3.5 mm). CCS = Canadian Cardiovascular Society; DES = drug-eluting stent.
subgroup allowed the creation of a matched sample of DES and BMS patients within each subgroup who had a similar distribution of demographics, clinical, and procedure characteristics. However, the characteristics across the off- and on-label indications were not matched, and outcomes should not be compared across these subgroups (19,20). The distribution of categorical variables, distribution of continuous variables, and survival curves were compared using appropriate statistical methods for matched data. We reported p values that compared the Kaplan-Meier survival curves for each outcome over the entire follow-up period. Due to the matched-pair nature of our data, calculating p values comparing outcomes at specific points in time was not possible (19,20).

Sensitivity analyses were performed on the unmatched cohort of patients who met study eligibility using multivariable Cox proportional hazards regression adjusting for clinically relevant characteristics listed in Table 1. Subgroup analyses of patients with myocardial infarction (same day as PCI), multiple vessel stenting, and diabetes were also performed using regression techniques.

SAS version 9.1 (SAS Institute, Cary, North Carolina) was used for statistical analyses. A 2-sided p value of ≤0.05 was considered statistically significant in the comparison of outcomes.

Results

Study sample. After inclusion and exclusion criteria were applied, our cohort included 14,916 patients who had on-label indications and 14,088 patients who had at least 1 off-label indication. After applying propensity score matching and excluding patients without a suitable match, our main analysis included 4,563 matched pairs of patients (n = 9,126) with on-label indications and 3,472 matched pairs of patients (n = 6,944) with off-label indications.

In the off-label group, the mean age was 63 years, 32% had diabetes, and 23% had an acute myocardial infarction on the same day as the index PCI (Table 1). Stents were placed most commonly (46%) in the left anterior descending artery, mean stent length was 37 mm, and mean stent diameter was 2.9 mm.

All demographics, clinical, and procedural characteristics were well balanced in the matched pairs of DES and BMS patients. None of the admission or procedure characteristics had standardized difference of the means exceeding 0.1.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Clinical Outcomes After Index PCI Among On- and Off-Label Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcomes</strong></td>
<td><strong>On-Label Use</strong></td>
</tr>
<tr>
<td></td>
<td>BMS (n = 4,563)</td>
</tr>
<tr>
<td>Target vessel revascularization (%)</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>4.2</td>
</tr>
<tr>
<td>1 yr</td>
<td>6.7</td>
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<tr>
<td>1.5 yrs</td>
<td>7.9</td>
</tr>
<tr>
<td>2 yrs</td>
<td>8.8</td>
</tr>
<tr>
<td>2.5 yrs</td>
<td>9.4</td>
</tr>
<tr>
<td>3 yrs</td>
<td>10.3</td>
</tr>
<tr>
<td>Myocardial infarction (%)</td>
<td>0.43</td>
</tr>
<tr>
<td>6 months</td>
<td>1.1</td>
</tr>
<tr>
<td>1 yr</td>
<td>1.7</td>
</tr>
<tr>
<td>1.5 yrs</td>
<td>2.4</td>
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<tr>
<td>2 yrs</td>
<td>3.0</td>
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<tr>
<td>2.5 yrs</td>
<td>3.5</td>
</tr>
<tr>
<td>3 yrs</td>
<td>3.9</td>
</tr>
<tr>
<td>Death (%)</td>
<td>0.0075</td>
</tr>
<tr>
<td>6 months</td>
<td>2.0</td>
</tr>
<tr>
<td>1 yr</td>
<td>2.9</td>
</tr>
<tr>
<td>1.5 yrs</td>
<td>3.7</td>
</tr>
<tr>
<td>2 yrs</td>
<td>4.8</td>
</tr>
<tr>
<td>2.5 yrs</td>
<td>5.7</td>
</tr>
<tr>
<td>3 yrs</td>
<td>6.6</td>
</tr>
<tr>
<td>Myocardial infarction or death (%)</td>
<td>0.089</td>
</tr>
<tr>
<td>6 months</td>
<td>3.0</td>
</tr>
<tr>
<td>1 yr</td>
<td>4.4</td>
</tr>
<tr>
<td>1.5 yrs</td>
<td>5.8</td>
</tr>
<tr>
<td>2 yrs</td>
<td>7.4</td>
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<tr>
<td>2.5 yrs</td>
<td>8.5</td>
</tr>
<tr>
<td>3 yrs</td>
<td>9.7</td>
</tr>
</tbody>
</table>

*Outcome rates were derived from paired Kaplan-Meier curves; †p values were calculated by comparing the paired Kaplan-Meier curves. Abbreviations as in Table 1.
indicating the creation of a well-balanced propensity matched cohort for the off-label group (Table 1). Similarly, patients with on-label indications were also well matched between the DES and BMS groups in terms of demographics, admission characteristics, and clinical characteristics after propensity score matching (Table 1).

**Target vessel revascularization.** Overall, DES use was associated with a reduction in target vessel revascularization after the index PCI. Among patients with off-label indications, target vessel revascularization rates were 11.6% for patients who received a DES and 15.3% for those who received a BMS at 3-year follow-up (p < 0.001) (Table 2, Fig. 1A). A significant reduction in the rates of target vessel revascularization was also observed for on-label patients treated with DES, although the absolute rate of reduction was slightly smaller (absolute difference of 2.3%; 10.3% in the BMS group vs. 8.0% in the DES group) at 3-year follow-up (Table 2, Fig. 1B).

**Myocardial infarction and death.** For patients with off-label indications, the median follow-up duration for myocardial infarction and death was 2 years, and 11% had a follow-up period of more than 3 years. The rate of myocardial infarction during the study period did not differ significantly between the DES and the BMS groups for patients with off-label indications (p = 0.52) (Fig. 2A). However, myocardial infarction rates of pa-
patients treated with DES and BMS appeared to diverge after 18 months; the rate was 1.6% higher in the DES group by 3 years of follow-up. The use of DES was associated with significantly lower rates of death (3-year rates: 6.9% for DES, 10.5% for BMS, \( p < 0.001 \)) and the composite end point of myocardial infarction or death (3-year rates: 12.6% for DES, 14.7% for BMS, \( p = 0.002 \)) (Table 2, Figs. 3A and 4A).

For patients with on-label indications, the rate of death was also significantly lower among patients who received a DES compared with those who received a BMS (3-year rates: 5.2% for DES, 6.6% for BMS, \( p = 0.008 \)) (Table 2, Fig. 3B). However, rates of myocardial infarction or the combined rates of myocardial infarction or death did not differ significantly among patients who were treated with DES as compared with patients treated with BMS (\( p = 0.43 \) for myocardial infarction, \( p = 0.089 \) for myocardial infarction or death) (Table 2, Figs. 2B and 4B).

**Sensitivity analysis.** Results of the sensitivity analysis using multivariate proportional hazard models of the unmatched sample of 29,002 patients were similar to those of the propensity score-matched cohort in which DES were associated with a significant reduction in death and target vessel revascularization without an associated increased risk of myocardial infarction (Table 3). When DES and BMS were compared in subgroups, DES were associated with a significant reduction in death compared with BMS (Table 3).

**Discussion**

We conducted a comprehensive evaluation of the safety and efficacy of DES among patients with off-label indications,
and determined longer-term outcomes with virtually 100% follow-up. Using liberal definitions to create an off-label cohort that included clinical and procedural characteristics, we found that DES were effective in reducing the need for target vessel revascularization without observing an increased risk of myocardial infarction. More importantly, patients with off-label indications receiving DES had lower mortality rates when compared with patients receiving BMS. These findings were robust under different definitions of off-label indications. Our results should alleviate recent concerns and may lend support to the contemporary practice in implanting DES among patients with off-label indications. DES are frequently implanted among patients with off-label indications and therefore, early studies demonstrating a higher risk of adverse outcome associated with DES brought significant concerns in clinical practice (12,13). We found that approximately one-half of all patients who received DES had at least 1 off-label indication. This estimate is consistent with the proportions reported in the National Heart, Lung, and Blood Institute Dynamic Registry (48.7%), the Evaluation of Drug Eluting Stents and

![Figure 3 Mortality in Off-Label Patients](image-url)

Death in the propensity score-matched cohort comparing DES and BMS for patients with (A) off-label and (B) on-label indications. Abbreviations as in Figure 1.
Ischemic Events Registry (54.7%), and the D.E.S.Cover Registry (47%) (12–14).

The main finding of the paper was the observation that mortality rates were lower among patients with off-label indications treated with DES compared with BMS. Survival curves among patients with off-label indications continued to slowly diverge over time, favoring fewer deaths among patients treated with DES, which may support the potential beneficial impact of DES on mortality at longer term in parallel with its ability to reduce repeat revascularization (21). Although randomized trials have not been able to demonstrate an impact of DES on mortality, the finding of lower mortality rates associated with DES is concordant with a growing body of literature that has suggested that DES may lower mortality compared with BMS (15,22–24).

Nevertheless, our study was not randomized and is subject to unmeasured confounding despite our rigorous attempt to balance our cohort on all available confounding variables.
Table 3
Clinical Outcomes Associated With the Use of DES in Patients With Off-Label Indications: Multivariate Cox Proportional Hazards Models*

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>All Off-Label Patients (n = 14,086)</th>
<th>Diabetic Patients (n = 4,513)</th>
<th>Multiple Vessel Stenting (n = 3,316)</th>
<th>Acute Myocardial Infarction (n = 3,364)†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>p Value</td>
<td>HR (95% CI)</td>
<td>p Value</td>
</tr>
<tr>
<td>Target vessel revascularization</td>
<td>0.65 (0.57–0.73)</td>
<td>&lt;0.001</td>
<td>0.54 (0.44–0.66)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.17 (0.97–1.41)</td>
<td>0.094</td>
<td>1.13 (0.85–1.49)</td>
<td>0.41</td>
</tr>
<tr>
<td>Death</td>
<td>0.56 (0.48–0.65)</td>
<td>&lt;0.001</td>
<td>0.56 (0.45–0.69)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Myocardial infarction or death</td>
<td>0.74 (0.66–0.84)</td>
<td>&lt;0.001</td>
<td>0.73 (0.59–0.84)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*See Table 1 and the Methods section for the definition of off-label indications. Each model was adjusted for variables as shown in Table 1. Hazard ratios (HRs) < 1 indicate a benefit associated with drug-eluting stents (DES). †Percutaneous coronary interventions on the same day as hospitalization for myocardial infarction.

We did not find an overall increased myocardial infarction rate associated with DES compared with BMS in the 3-year follow-up period. However, Kaplan-Meier curves of DES and BMS appeared to diverge over time, with possibly more myocardial infarction events occurring in the DES group after 18 months. Since information on stent thrombosis was not available in our database, we were unable to assess whether this trend was due to differences in rates of stent thrombosis associated with DES. Additional follow-up would be necessary to examine whether this trend continues to persist over time.

With regard to the efficacy of DES, we found that target vessel revascularization was significantly reduced compared with BMS among off- and on-label patients. Interestingly, a larger absolute reduction in target vessel revascularization was observed among patients in the off-label group as compared with the on-label group. These findings are consistent with the hypothesis that DES are more cost-effective when used in patients with higher risk of restenosis and also lend support to policies that recommend DES for patients with longer lesions and smaller vessels, analogous to our off-label group.

Study limitations. First, sirolimus-eluting stents are currently approved for de novo lesions in native coronary arteries no longer than 30 mm with reference vessel diameter of at least 2.5 to 3.5 mm (16), and paclitaxel-eluting stents for lesions no longer than 28 mm with a reference diameter of at least 2.5 to 3.75 mm (17). Since our data did not include specific lesion characteristics, we used stent size and length as surrogates for lesion length and vessel size to define our off-label cohort. Furthermore, we were unable to evaluate specific lesion subsets, such as ostial, bifurcation, or totally occluded arteries.

Second, a recent analysis by the Global Registry of Acute Coronary Events suggests that patients with ST-segment elevation myocardial infarction (STEMI) treated with DES had a significantly increased rate of death compared with BMS (25). We were unable to determine the safety of DES for STEMI specifically because this data element was not captured in our database, although several recent studies have suggested the safety of DES in STEMI patients in clinical practice (26,27). Third, we did not examine the impact of evidence-based medical therapy, such as thienopyridine, as a potential reason to explain the benefit associated with DES.

Finally, our study should be placed in the context of the PCI practice in Ontario, Canada. For example, Ontario has recommended a policy of 1-year clopidogrel coverage since 2003 for patients undergoing PCI where all patients over age 65 years are eligible to receive a 1-year supply of clopidogrel (15). Furthermore, the majority of younger patients have private insurance coverage for prescribed medications (15).

Conclusions

In summary, our study lends support to the contemporary practice of implanting DES for patients with off-label indications as we found that patients treated with DES had a lower risk of target vessel revascularization and mortality compared with those treated with BMS. These findings should be confirmed through large, randomized clinical trials evaluating patients with off-label indications.

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Key Words: drug-eluting stent • off-label indication • cardiovascular outcomes.