Attribution of Adverse Events Following Coronary Stent Placement Identified Using Administrative Claims Data

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Background—More than 600,000 coronary stents are implanted during percutaneous coronary interventions (PCIs) annually in the United States. Because no real-world surveillance system exists to monitor their long-term safety, claims data are often used for this purpose. The extent to which adverse events identified with claims data can be reasonably attributed to a specific medical device is uncertain.

Methods and Results—We used deterministic matching to link the NCDR (National Cardiovascular Data Registry) CathPCI Registry to Medicare fee-for-service claims for patients aged ≥65 years who underwent PCI with drug-eluting stents (DESs) between July 1, 2009 and December 31, 2013. We identified subsequent PCIs within 1 year of the index procedure in Medicare claims as potential safety events. We linked these subsequent PCIs back to the NCDR CathPCI Registry to ascertain how often the revascularization could be reasonably attributed to the same coronary artery as the index PCI (ie, target vessel revascularization). Of 415,306 DES placements in 368,194 patients, 33,174 repeat PCIs were identified in Medicare claims within 1 year. Of these, 28,632 (86.3%) could be linked back to the NCDR CathPCI Registry; 16,942 (51.1% of repeat PCIs) were target vessel revascularizations. Of these, 8,544 (50.4%) were within a previously placed DES: 7,652 for in-stent restenosis and 1,341 for stent thrombosis. Of 16,176 patients with a claim for acute myocardial infarction in the follow-up period, 4,446 (27.5%) were attributed to the same coronary artery in which the DES was implanted during the index PCI (ie, target vessel myocardial infarction). Of 24,288 patients whose death was identified in claims data, 278 (1.1%) were attributed to the same coronary artery in which the DES was implanted during the index PCI.

Conclusions—Most repeat PCIs following DES stent implantation identified in longitudinal claims data could be linked to real-world registry data, but only half could be reasonably attributed to the same coronary artery as the index procedure. Attribution among those with acute myocardial infarction or who died was even less frequent. Safety signals identified using claims data alone will require more in-depth examination to accurately assess stent safety. (J Am Heart Assoc. 2020;9:e013606. DOI: 10.1161/JAHA.119.013606.)

Key Words: drug-eluting stent • percutaneous coronary intervention • real-world data • registry • surveillance

In recent years, the US Food and Drug Administration has increasingly shifted toward a life-cycle regulatory approach for medical devices, allowing the agency more flexibility in premarket clinical trial requirements with greater reliance on longitudinal postmarket surveillance to confirm and continue to reassess safety and effectiveness. The recent creation of the

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Accompanying Tables S1 and S2 and Figure S1 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013606

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Clinical Perspective

What Is New?

- Claims data are often used for postmarket surveillance of coronary stents.
- The extent to which adverse events (repeat percutaneous coronary intervention, myocardial infarction, and death) identified with claims data can be attributed to a previously placed stent is uncertain.
- By linking Medicare claims with a national registry of percutaneous coronary interventions, we found that only half of repeat percutaneous coronary interventions, one-fourth of myocardial infarctions, and 1% of deaths identified with claims data within 1 year after index percutaneous coronary intervention could be attributed to a previously placed coronary drug-eluting stent.

What Are the Clinical Implications?

- Although real-world data sources, such as claims, are increasingly important for longitudinal postmarket surveillance of medical devices, including coronary stents, claims data alone may be insufficient to ascertain stent safety and may only serve as a signal for further evaluation.
- Postmarket surveillance would be strengthened with complementary data sources, in addition to claims, to evaluate stent safety.

National Evaluation System for health Technology is intended to promote the use of real-world evidence to support medical device regulatory evaluations, and the US Food and Drug Administration recently released a Guidance Document about how real-world evidence can support medical device regulatory decision making. An important and frequently used source of data for these purposes is administrative claims, which are billing data collected by health plans that include basic demographic and clinical information, as well as longitudinal information on clinical encounters, as long as patients have continuous coverage with the same health plan aggregating the claims. Although their ubiquity makes claims data attractive, they have important limitations, not unlike other real-world evidence sources. These data are not principally designed to support research; lack detailed clinical information; and may not include all of the diagnoses or procedures performed during a hospitalization or clinic visit. With respect to safety surveillance, claims data have been used with the hope that relevant outcomes can be identified from claims and be reasonably attributed to medical device performance. For claims data to be useful for this purpose, it is critical to know whether adverse events identified using claims data can be reasonably attributed to the medical device in question.

Coronary stents play a key role in the revascularization of patients with coronary artery disease. In 2014, over 667,000 percutaneous coronary interventions (PCIs), >90% of which include stent placement, were recorded in the National Cardiovascular Data Registry (NCDR) CathPCI Registry, which includes >90% of PCI-capable hospitals in the United States. However, important safety concerns pertaining to coronary stents have been discovered since their original approval, including late-stent thrombosis among drug-eluting stents (DESs), higher thrombosis and myocardial infarction (MI) risk associated with bioresorbable vascular scaffolds, and in-stent restenosis, a progressive narrowing from vascular remodeling and neointimal hyperplasia. Despite these concerns, coronary stent surveillance has been challenging because there is no established surveillance system and it is unknown how often the clinical sequelae of these safety-related adverse events that can be identified in claims data, such as need for repeat coronary revascularization, can be reasonably attributed to a previously placed stent.

Coronary stents thus offer a unique opportunity to better understand the utility of claims data to characterize medical-device–related adverse events because they are commonly implanted and existing data sources containing detailed information on coronary stent implantations have been linked to administrative claims. Specifically, the NCDR CathPCI Registry includes detailed patient, clinical, and procedural information—including coronary artery–level data—for patients receiving PCI. Claims data from this study can inform our ability to determine whether they are related to previous coronary stent placement.

Accordingly, we sought to assess the extent to which a repeat PCI identified using claims data could be reasonably attributed to the same coronary artery in which a coronary stent was first implanted (ie, target vessel revascularization [TVR]). We focused on TVR because it is an end point frequently used to assess coronary stent safety postimplantation. We did this by identifying index DES placements from the NCDR CathPCI Registry, characterizing incidence of safety-related adverse events during 1 year of patient follow-up using Medicare fee-for-service (FFS) claims data and then linking those patients who experienced safety-related adverse events in claims back to the NCDR CathPCI Registry. We also sought to understand what characteristics are associated with greater attribution of a repeat PCI to the artery that had previously received a stent, given that those factors could help target surveillance efforts.

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Methods
This study was approved by the Yale University Human Investigation Committee; informed consent for the purpose of this project was not required. The study was approved by the NCDR and the CathPCI Research & Publications Committee reviewed the final manuscript before submission, but had no role in the design, conduct, or reporting of the study. Requests to access the CathPCI data that were used for this study can be sent to the American College of Cardiology’s NCDR at ncdr@acc.org; https://cvquality.acc.org/NCDR-Home registries/hospital registries/cathpci registry.

Data Sources
The CathPCI Registry, an initiative sponsored by the American College of Cardiology Foundation and the Society for Cardiovascular Angiography and Interventions, is the largest PCI registry in the United States, used in >90% of PCI-capable hospitals9 and has been described previously.13,14 Data on patient demographics, comorbidities, episode of care, and procedural data are included from hospitalization during which PCI is performed. A data quality program ensures reliable and consistent data.15 All data elements are recorded by trained abstractors and electronically forwarded to a secure data server. Institutions had to meet NCDR quality criteria for reporting to be included. We identified longitudinal outcomes in inpatient and outpatient institutional claims for Medicare FFS beneficiaries using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. These data sets contain claims for inpatient admissions and outpatient care, including procedures for Medicare FFS patients. Additionally, we used 2009–2014 Medicare Beneficiary Summary Files to obtain FFS enrollment and the postdischarge vital status of each beneficiary. We linked Medicare inpatient and outpatient institutional claims to the NCDR CathPCI Registry using deterministic matching on Social Security number, date of birth, and sex.

Study Population
We identified all patients aged ≥65 years who underwent a DES implantation from July 1, 2009 and December 31, 2013, were linked to CMS claims data, and who were continuously enrolled in FFS Part A and B for 1 year following the index procedure or until the date of death if they died within the year after the procedure (Figure 1). Patients aged ≥65 years who cannot be linked to CMS claims data are likely enrolled in the Medicare Advantage program.16 We excluded patients who received both a bare-metal stent and a DES, multiple DESs at 1 visit in different coronary arteries, or a single DES that crossed >1 of the 4 major epicardial coronary arteries (left main, left anterior descending, left circumflex, and right coronary artery) because attribution to a single stent in a single vessel would be more challenging. We included patients who received multiple DESs at 1 visit within the same coronary artery as a single implant.

Outcomes and Definitions
We aimed to characterize the proportion of repeat PCIs within 1 year of index DES implantation that represented TVR. We chose to focus first on TVR, instead of target lesion revascularization, because lesion information may be inconsistently reported, particularly for patients who receive multiple procedures from multiple providers.

We first identified subsequent PCIs in CMS claims in the year after an index PCI using ICD-9-CM procedure codes or Current Procedural Terminology codes (see Table S1 for ICD-9-CM/CPT codes). We subsequently linked these claims back to the CathPCI Registry to determine which vessel was revascularized. For all analyses, we defined TVR as an unstaged repeat PCI performed in the same vessel treated during the index PCI. Branch vessels were all collapsed to the primary epicardial coronary artery because our analysis was conducted at the vessel level (eg, diagonal vessels were considered part of the left anterior descending system and obtuse marginals were considered part of the left circumflex system). We considered a repeat PCI staged if it occurred within 60 days of the index PCI given that ≤25% of staged PCIs occur >1 month after index PCI,17 and did not have a primary discharge diagnosis code of myocardial infarction (MI) or any other diagnostic code suggesting a procedural complication. We still followed patients identified as having a staged PCI after 60 days for subsequent revascularization, MI, or death within 1 year of the index procedure.

Among those identified as TVR, we also examined whether the repeat PCI was performed on a specific lesion that had been previously stented with a DES and, if so, we categorized it as attributable to either in-stent restenosis or stent thrombosis. We also characterized MI and death in the year following the index PCI.18 Although many causes of MI or death are not likely stent related, we still examined both because these are the most important clinical events that can be secondary to stent-related complications, and these are the types of adverse events commonly used by regulators to ascertain medical product safety. We identified MI using ICD-9-CM primary discharge diagnosis codes during a subsequent hospitalization. We obtained dates of death from the master summary beneficiary file.

For patients for whom repeat revascularization and MI events were identified from Medicare claims, we further sought to understand whether baseline patient demographic, clinical, and procedural characteristics were associated with
successful attribution to the same coronary artery in which a DES had been previously placed.

**Patient, Clinical, and Procedural Characteristics of Interest**

We identified multiple patient, clinical, or procedural characteristics of interest (Table 1). These included patient demographics, cardiovascular history, and other relevant clinical history. We also included procedural and hospital characteristics from the episode of care associated with the original PCI and stent implantation, as well as characteristics of the coronary artery in which the stent was implanted. If 2 DESs were placed in the same artery, their lengths were added, ignoring potential overlap between stents. Among previously treated lesions, we determined whether previous PCI included a stent and, if so, whether the index procedure was performed for in-stent restenosis or in-stent thrombosis.

**Statistical Analysis**

We estimated the proportion of patients for whom potential stent-related safety events (TVR, MI, and death) identified from Medicare claims could be attributed to the same coronary artery in which a DES had been previously placed, overall and stratified by the individual safety end points: TVR, MI, and death. For patients with multiple safety events identified after stent implantation, we analyzed events separately. We performed a sensitivity analysis for patients without a history of previous PCI. We used $\chi^2$ tests for categorical variables and Wilcoxon or $t$ tests for continuous variables. We considered comparisons significant at $P<0.05$. 

**Figure 1.** Flow diagram of included drug-eluting stent placements. BMS indicates bare-metal stent; CMS, Centers for Medicare and Medicaid Services; DES, drug-eluting stent; FFS, fee-for-service; PCI, percutaneous coronary intervention; SSN, Social Security number.
### Table 1. Patient, Procedural, and Vessel Characteristics

|                        | No.  | %     |
|------------------------|------|-------|
| N procedures           | 415  | 306   |
| **Demographics**       |      |       |
| Age, y, mean (SD)      | 74.23| 6.56  |
| Sex: female            | 158  | 38.06 |
| Race                   |      |       |
| White                  | 381  | 91.87 |
| Black                  | 21   | 5.11  |
| Asian                  | 602  | 1.45  |
| Other                  | 651  | 1.57  |
| Hispanic or Latino ethnicity | 14 | 3.51 |
| **Cardiovascular history** | | |
| Previous MI            | 127  | 30.62 |
| Previous HF            | 60   | 14.61 |
| Previous valve surgery/procedure | 798 | 1.92 |
| Cerebrovascular disease | 67   | 16.38 |
| Peripheral arterial disease | 66 | 16.00 |
| NYHA class (among those with HF in previous 2 wk) | | |
| I                      | 4674 | 10.22 |
| II                     | 13   | 30.06 |
| III                    | 17   | 38.15 |
| IV                     | 996  | 21.57 |
| Cardiomyopathy or left ventricular systolic dysfunction | 47 | 11.36 |
| Cardiogenic shock w/in 24 h | 46 | 1.12 |
| Cardiac arrest w/in 24 h | 43 | 1.04 |
| **Other clinical history** | | |
| Current/recent smoker (w/in 1 y) | 53 | 12.82 |
| Hypertension           | 363  | 87.44 |
| Dyslipidemia           | 347  | 83.68 |
| Currently on dialysis  | 959  | 2.31  |
| Chronic lung disease   | 73   | 17.60 |
| Diabetes mellitus      | 157  | 38.00 |
| **Procedure characteristics** | | |
| CAD presentation       |      |       |
| No symptoms, no angina | 37   | 9.00  |
| Symptoms unlikely to be ischemic | 12 | 3.05 |
| Stable angina          | 79   | 19.07 |
| Unstable angina        | 176  | 42.60 |
| NSTEMI                  | 70   | 16.98 |
| STEMI or equivalent    | 38   | 9.31  |
| Previous PCI           | 190  | 45.87 |
| Previous CABG          | 98   | 23.64 |

### Table 1. Continued

|                        | No.  | %     |
|------------------------|------|-------|
| **Diagnostic Cath status** | | |
| Elective               | 177  | 50.68 |
| Urgent                 | 129  | 36.93 |
| Emergency              | 42   | 12.25 |
| Salvage                | 472  | 0.14  |
| **Procedure year**     |      |       |
| 2009                   | 43   | 10.42 |
| 2010                   | 100  | 24.09 |
| 2011                   | 89   | 21.49 |
| 2012                   | 91   | 21.93 |
| 2013                   | 91   | 22.06 |
| **PCI status**         |      |       |
| Elective               | 208  | 50.22 |
| Urgent                 | 162  | 39.10 |
| Emergency              | 43   | 10.54 |
| Salvage                | 611  | 0.15  |
| **IABP**               | 5240 | 1.26  |
| Other mechanical ventricular support | 138 | 0.33 |
| **Multivessel disease** | 208 | 50.17 |
| **Vessel characteristics** | | |
| No. of stents placed, median (IQR) | 1.00 | (1.00–2.00) |
| Sum of stent diameter, median (IQR) | 3.00 | (2.75–5.00) |
| Sum of stent length, median (IQR) | 22.00 | (15.00–33.00) |
| **Stent length categorized** | | |
| Short (≤16 mm)         | 141  | 34.02 |
| Medium (>16–28 mm)     | 146  | 35.28 |
| Long (>28 mm)          | 127  | 30.70 |
| Mean vessel stenosis before Tx, median (IQR) | 90.00 | (80.00–95.00) |
| **Preprocedure TIMI flow** | | |
| TIMI—0                 | 37   | 9.17  |
| TIMI—1                 | 32   | 7.92  |
| TIMI—2                 | 82   | 20.00 |
| TIMI—3                 | 260  | 62.92 |
| **Previously treated lesion** | | |
| Previously treated lesion | 50 | 12.21 |
| Among previously treated lesions | | |
| Previously treated lesion time frame | | |
| <1 mo                  | 1994 | 3.94  |
| 1 to 5 mo              | 5668 | 11.21 |
| 6 to 12 mo             | 6370 | 12.60 |
| 1 to 2 y               | 7209 | 14.26 |
| >2 y                   | 2565 | 50.16 |
For analyses examining whether baseline patient demographic, clinical, and procedural characteristics were associated with successful attribution, we did not correct for multiple comparisons because these analyses were considered exploratory.

### Results

#### Study Cohort

Between July 1, 2009 and December 31, 2013, 919,636 patients aged ≥65 years identified in the CathPCI Registry received a total 1,208,454 DES placements during 1,056,056 PCI procedures (Figure 1). We excluded 27,085 DES placements for left main bifurcation lesions, 17,077 multivessel PCIs with inability to identify which vessel received the DES, and 278,747 in which multiple DESs were implanted into >1 coronary artery. Next, we excluded 251,951 DES placements in patients who could not be linked to CMS data for longitudinal follow-up (this includes patients enrolled in Medicare Advantage plans, Medicaid plans, other state-sponsoring plans, or employer-based insurance), 611 without CMS FFS information, and 217,677 who did not have continuous Part A and B FFS enrollment for 1 year post-PCI. Our final sample of NCDR-Medicare FFS-linked data included 415,306 index DES placements in 368,194 patients at 1,380 hospitals.

#### Patient and Procedural Characteristics

Mean age of patients undergoing PCI in our cohort was 74.2 years, 38.1% were female, and 91.9% were white (Table 1). Furthermore, 30.6% of patients had a history of previous MI, 45.9% previous PCI, and 23.6% previous coronary artery bypass graft. Unstable angina was coronary artery disease presentation in 42.6%, non–ST-segment–elevation myocardial infarction in 17.0%, and ST-segment–elevation myocardial infarction (STEMI) in 9.3%. At the index PCI, a median of 1 stent was placed (interquartile range, 1–2), with median stent length of 22 mm (interquartile range, 15–33). Twelve percent of lesions had been previously treated, half of which occurred >2 years before the index PCI; of these previously treated lesions, 92.2% were for in-stent restenosis and 9.8% for in-stent thrombosis.

Of the 415,306 DES placements in 368,194 patients, 61,409 (14.8%) were found to have had any adverse event identified within CMS claims data within 1 year: repeat PCI, MI, or death. Of these, 28,607 (46.6%) were successfully linked back to NCDR CathPCI Registry data because the patients underwent coronary angiography and/or PCI, 28,453 (85.8%) included data on coronary anatomy, and 16,942 (51.1%) were attributed to the same coronary artery treated during the index PCI (i.e., TVR). Of these, 9954 (58.8%) could be identified as having been inserted within a previously placed stent; of these, 1410 were previously placed bare metal stents and 8544 (50.4%) were previously placed DESs. Among the latter, 7652 were TVRs for in-stent restenosis and 1341 for stent thrombosis. Overall results of the proportion of

#### Adverse Events Linked from CMS Claims to the NCDR CathPCI Registry

**Target vessel revascularization**

Of the 415,306 DES placements in 368,194 patients, 33,174 (8.0%) were followed by repeat PCIs identified in CMS claims data (not considered staged PCIs) within 1 year (Figure 1). Of these, 28,632 (86.3%) were successfully linked back to NCDR CathPCI Registry data because the patient received diagnostic coronary angiography and/or PCI, 28,453 (85.8%) included data on coronary anatomy, and 16,942 (51.1%) were attributed to the same coronary artery treated during the index PCI (i.e., TVR). Of the 16,942 TVRs, 9954 (58.8%) could be identified as having been inserted within a previously placed stent; of these, 1410 were previously placed bare metal stents and 8544 (50.4%) were previously placed DESs. Among the latter, 7652 were TVRs for in-stent restenosis and 1341 for stent thrombosis.
patients with TVR were consistent in a sensitivity analysis of patients without a history of previous PCI (Figure S1).

**Myocardial infarction**

Of the 415,306 DES placements in 368,194 patients, 16,176 (3.9%) were followed by acute MIs identified in CMS claims data within 1 year (Figure 2). Of these, 8,693 (53.7%) were successfully linked to NCDR CathPCI Registry data because the patient received diagnostic coronary angiography and/or PCI, 6,856 (42.4%) included data on coronary anatomy from PCI, and 4,446 (27.5%) were attributed to the same coronary artery in which the stent was implanted during the index PCI (ie, target vessel MI), and 2410 could not be attributed to that same coronary artery. In total, of the 6856 DES placements that were followed by acute MI identified in CMS claims data with NCDR CathPCI data available on coronary anatomy from PCI, 278 (71.3%) were attributed to the same coronary artery in which the stent was implanted during the index PCI.

**Death**

Of the 415,306 DES placements in 368,194 patients, 24,288 (5.8%) were followed by patient death identified in CMS claims data within 1 year. Of these, 4,666 (1.9%) could be successfully linked to NCDR CathPCI Registry data because the patient received diagnostic coronary angiography and/or PCI, 390 (1.6%) included data on coronary anatomy from PCI, and 278 (1.1%) were attributed to the same coronary artery in which the DES was implanted during the index PCI, and 112 could not be attributed to that same coronary artery. In total, of the 390 DES placements that were followed by patient death identified in CMS claims data with NCDR CathPCI data available on coronary anatomy from PCI, 278 (71.3%) were attributed to the same coronary artery in which the stent was implanted during the index PCI.

**Association Between Index PCI Characteristics and Attribution of Repeat PCI or MI**

In exploratory analyses, several patient and procedural characteristics were associated with higher rates of successful attribution of a repeat PCI or MI identified from claims data to the same coronary artery as the originally placed DES, including previous MI, previous PCI before index stent placement, and previous coronary artery bypass grafting (Tables 2 and 3). Time from index to repeat PCI was also significantly associated with attribution: PCIs and MIs identified before 30 or >90 days after index PCI were more...
Table 2. Association of Patient, Procedural, Vessel, and Hospital Characteristics With Attribution of Repeat PCI Events to Index Vessel

|                         | Overall       | Not Attributed | Attributed     | P Value |
|-------------------------|---------------|----------------|----------------|---------|
|                         | No. | %   | No. | %   | No. | %   |         |
| N procedures            | 33  | 174 | 16  | 232 | 48.93 | 16  | 942 | 51.07 |
| Demographics            |     |     |     |     |       |     |     |       |
| Age, y, mean (SD)       | 73.86 | 6.36 | 73.95 | 49.33 | 73.77 | 50.67 | 0.265 |
| Sex: female             | 12  | 234 | 36.88 | 6035 | 49.33 | 6199 | 51.07 | 0.265 |
| Race                    |     |     |     |     |       |     |     |       |
| White                   | 30  | 225 | 91.11 | 14  | 752 | 48.81 | 15  | 473 | 51.19 |
| Black                   | 1915 | 5.77 | 924 | 48.25 | 991 | 51.75 |       |       |
| Asian                   | 495 | 1.49 | 277 | 55.96 | 218 | 44.04 |       |       |
| Other                   | 539 | 1.62 | 279 | 51.76 | 260 | 48.24 |       |       |
| Cardiovascular history  |     |     |     |     |       |     |     |       |
| Previous MI             | 12  | 701 | 38.30 | 5854 | 46.09 | 6847 | 53.91 | <0.001 |
| Previous HF             | 5803 | 17.50 | 2733 | 47.10 | 3070 | 52.90 | 0.002 |
| Cerebrovascular disease | 6662 | 20.09 | 3115 | 46.76 | 3547 | 53.24 | <0.001 |
| Peripheral arterial disease | 6909 | 20.83 | 3101 | 44.88 | 3808 | 55.12 | <0.001 |
| NYHA class (among those with HF in past 2 wk) |     |     |     |     |       |     |     | 0.545 |
| I                       | 396 | 10.66 | 197 | 49.75 | 199 | 50.25 |       |       |
| II                      | 1132 | 30.48 | 567 | 50.09 | 565 | 49.91 |       |       |
| III                     | 1415 | 38.10 | 670 | 47.35 | 745 | 52.65 |       |       |
| IV                      | 771 | 20.76 | 372 | 48.25 | 399 | 51.75 |       |       |
| Cardiomyopathy or left ventricular systolic dysfunction | 3969 | 11.97 | 1893 | 47.69 | 2076 | 52.31 | 0.097 |
| Other clinical history  |     |     |     |     |       |     |     |       |
| Current/recent smoker (w/in 1 y) | 3781 | 11.40 | 1972 | 52.16 | 1809 | 47.84 | <0.001 |
| Hypertension            | 30  | 198 | 91.06 | 14  | 671 | 48.58 | 15  | 527 | 51.42 | <0.001 |
| Dyslipidemia            | 28  | 999 | 87.49 | 13  | 969 | 48.17 | 15  | 030 | 51.83 | <0.001 |
| Chronic lung disease    | 5954 | 17.95 | 2874 | 48.27 | 3080 | 51.73 | 0.261 |
| Diabetes mellitus       | 15  | 585 | 46.99 | 7308 | 46.89 | 8277 | 53.11 | <0.001 |
| Procedure characteristics|     |     |     |     |       |     |     |       |
| CAD presentation        |     |     |     |     |       |     |     | <0.001 |
| No symptoms, no angina  | 2205 | 6.65 | 1198 | 54.33 | 1007 | 45.67 |       |       |
| Stable angina           | 6021 | 18.15 | 3055 | 50.74 | 2966 | 49.26 |       |       |
| Unstable angina         | 15  | 874 | 47.86 | 7434 | 46.83 | 8440 | 53.17 |       |       |
| STEMI                   | 5955 | 17.96 | 2847 | 47.81 | 3108 | 52.19 |       |       |
| STEMI or equivalent     | 2396 | 7.22 | 1324 | 55.26 | 1072 | 44.74 |       |       |
| Previous PCI            | 20  | 071 | 60.51 | 9130 | 45.49 | 10  | 941 | 54.51 | <0.001 |
| Previous CABG           | 12  | 096 | 36.47 | 5091 | 42.09 | 7005 | 57.91 | <0.001 |
| Diagnostic Cath status  |     |     |     |     |       |     |     | <0.001 |
| Elective                | 13  | 771 | 49.09 | 6723 | 48.82 | 7048 | 51.18 |       |       |
| Urgent                  | 11  | 399 | 40.64 | 5276 | 46.28 | 6123 | 53.72 |       |       |

Continued
Table 2. Continued

|                      | Overall | Not Attributed | Attributed | P Value |
|----------------------|---------|----------------|------------|---------|
|                      | No.     | %              | No.        | %       | No.     | %       |         |
| Emergency            | 2871    | 10.23          | 1537       | 53.54   | 1334    | 46.46   |         |
| Salvage              | 11      | 0.04           | 9          | 81.82   | 2       | 18.18   |         |
| Procedure year       |         |                |            |         |         |         | 0.335 |
| 2009                 | 3712    | 11.19          | 1826       | 49.19   | 1886    | 50.81   |         |
| 2010                 | 8046    | 24.25          | 3895       | 48.41   | 4151    | 51.59   |         |
| 2011                 | 7010    | 21.13          | 3378       | 48.19   | 3632    | 51.81   |         |
| 2012                 | 7243    | 21.83          | 3578       | 49.40   | 3665    | 50.60   |         |
| 2013                 | 7163    | 21.59          | 3555       | 49.63   | 3608    | 50.37   |         |
| PCI status           |         |                |            |         |         | <0.001  |         |
| Elective             | 16 137  | 48.66          | 8003       | 49.59   | 8134    | 50.41   |         |
| Urgent               | 14 055  | 42.38          | 6629       | 47.16   | 7426    | 52.84   |         |
| Emergency            | 2944    | 8.88           | 1578       | 53.60   | 1366    | 46.40   |         |
| Salvage              | 25      | 0.08           | 18         | 72.00   | 7       | 28.00   |         |
| Multivessel disease  | 21 553  | 64.97          | 11 002     | 51.05   | 10 551  | 48.95   | <0.001 |
| Repeat PCI           |         |                |            |         |         | <0.001  |         |
| Time from index to repeat PCI |       |                |            |         |         |         |         |
| ≤30 d                | 2248    | 6.78           | 1021       | 45.42   | 1227    | 54.58   |         |
| 31 to 90 d           | 4943    | 14.90          | 3090       | 62.51   | 1853    | 37.49   |         |
| >90 d                | 25 983  | 78.32          | 12 121     | 46.65   | 13 862  | 53.35   |         |
| Vessel characteristics|         |                |            |         |         |         |         |
| No. of stents placed, median (IQR) | 1.00  | (1.00–2.00) | 1.00       | 1.00    | 1.00    | <0.001  |         |
| Sum of stent diameter, median (IQR) | 3.00  | (2.50–3.50) | 3.00       | 3.00    | 3.00    | 0.472   |         |
| Sum of stent length, median (IQR) | 23.00 | (15.00–36.00) | 23.00  | 23.00  |         | <0.001  |         |
| Stent length categorized |        |                |            |         |         | <0.001  |         |
| Short (≤16 mm)       | 10 128  | 30.56          | 5034       | 49.70   | 5094    | 50.30   |         |
| Medium (>16–28 mm)   | 11 218  | 33.85          | 5690       | 50.72   | 5528    | 49.28   |         |
| Long (>28 mm)        | 11 790  | 35.58          | 5488       | 46.55   | 6302    | 53.45   |         |
| Mean vessel stenosis before Tx, median (IQR) | 90.00 | (80.00–95.00) | 90.00 |         | 90.00   | 0.009   |         |
| Previously treated lesion | 6720 | 20.26          | 2414       | 35.92   | 4306    | 64.08   | <0.001 |
| Among previously treated lesions |         |                |            |         |         |         |         |
| Previously treated lesion time frame |         |                |            |         |         | <0.001  |         |
| <1 mo                | 258     | 3.85           | 105        | 40.70   | 153     | 59.30   |         |
| 1 to 5 mo            | 1073    | 16.00          | 338        | 31.50   | 735     | 68.50   |         |
| 6 to 12 mo           | 1077    | 16.06          | 338        | 31.38   | 739     | 68.62   |         |
| 1 to 2 y             | 1046    | 15.60          | 363        | 34.70   | 683     | 65.30   |         |
| >2 y                 | 2679    | 39.94          | 1038       | 38.75   | 1641    | 61.25   |         |
| Time unknown         | 574     | 8.56           | 224        | 39.02   | 350     | 60.98   |         |
| Treated with stent   | 6295    | 93.76          | 2229       | 35.41   | 4066    | 64.59   | 0.001   |
| In-stent restenosis  | 5875    | 93.42          | 2062       | 35.10   | 3813    | 64.90   | 0.040   |
| In-stent thrombosis  | 538     | 8.56           | 220        | 40.89   | 318     | 59.11   | 0.005   |

Continued
frequently attributed compared with PCIs between 31 and 90 days (repeat PCI: 54.6% for <30 days versus 37.5% between 31 and 90 days versus 53.4% >90 days after index PCI; P<0.001). Total length of stent(s) placed at index PCI >28 mm was associated with greater attribution compared with shorter total stent lengths (repeat PCI: 53.5% for >28 mm versus 50.3% for ≤16 mm and 49.3% for >16–28 mm; P<0.001).

**Discussion**

Only half of all PCIs performed in the year after patients received a DES placement could be reasonably attributable to the same coronary artery as the index procedure, and even fewer were attributed to the same lesion as a previously placed stent. MIs and deaths can be reasonably attributable to a previously placed stent even less frequently. Whereas exploratory analyses showed that some patient and procedural characteristics were associated with higher rates of attribution, including the timing of when the event was observed, these findings suggest that using claims data alone for surveillance may be insufficient to ascertain stent safety. Rather, postmarket surveillance efforts would likely be strengthened by the use of complementary data sources, in addition to claims, when evaluating medical device safety.

Although real-world data sources, such as claims and registries, are increasingly important for postmarket surveillance of medical devices,

Table 2. Continued

| Overall | Not Attributed | Attributed | P Value |
|---------|---------------|------------|---------|
| No.     | %             | No.        | %       | No.     | %       |
| Lesion in graft |               |            |         |         |         |
| Not in graft | 27 675        | 83.46      | 14 066  | 50.83   | 13 609  | 49.17   | <0.001 |
| Vein    | 5106          | 15.40      | 1998    | 39.13   | 3108    | 60.87   |         |
| LIMA graft | 253           | 0.76       | 105     | 41.50   | 148     | 58.50   |         |
| Other artery | 124           | 0.37       | 58      | 46.77   | 66      | 53.23   |         |
| Lesion complexity |            |            |         |         |         |         | <0.001 |
| Non-high/non-C | 13 558        | 40.89      | 6805    | 50.19   | 6753    | 49.81   |         |
| High/C  | 19 600        | 59.11      | 9418    | 48.05   | 10 182  | 51.95   |         |
| Maximum lesion length, median (IQR) |     |            |         |         |         |         | <0.001 |
| Thrombus present | 3004          | 9.06       | 1546    | 51.46   | 1458    | 48.54   | 0.004   |
| Bifurcation lesion | 4082          | 12.31      | 1905    | 46.67   | 2177    | 53.33   | 0.002   |

Hospital characteristics

| Hospital location | Overall | Not Attributed | Attributed | P Value |
|------------------|---------|---------------|------------|---------|
| Rural            | 4293    | 12.94         | 2165       | 50.43   | 2128    | 49.57   | 0.006   |
| Suburban         | 10 140  | 30.57         | 5036       | 49.66   | 5104    | 50.34   |         |
| Urban            | 18 741  | 56.49         | 9031       | 48.19   | 9710    | 51.81   |         |
| Profit type      |         |               |            |         |         |         | 0.828   |
| Government       | 409     | 1.23          | 195        | 47.68   | 214     | 52.32   |         |
| Private/community| 29 092  | 87.70         | 14 249     | 48.98   | 14 843  | 51.02   |         |
| University       | 3673    | 11.07         | 1788       | 48.68   | 1885    | 51.32   |         |
| Teaching Hospital| 15 537  | 46.83         | 7448       | 47.94   | 8089    | 52.06   | <0.001  |
| PCI count, median (IQR) | 850.00       | (500–1347) | 835.00   | 864.50  |         | <0.001  |

CABG indicates coronary artery bypass graft; CAD, coronary artery disease; Cath, catheterization; HF, heart failure; IQR, interquartile range; LIMA, left internal mammary artery; MI, myocardial infarction; NSTEMI, non–ST-segment–elevation myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; Tx, treatment.
Table 3. Patient, Procedural, Vessel, and Hospital Characteristics of PCIs With Attributed AMI Events

|                               | Overall | Not Attributed | Attributed | P Value |
|-------------------------------|---------|----------------|------------|---------|
|                               | No. %   | No. Row %      | No.        | Row %   |
| N procedures                  | 16 176  | 11 730 72.51   | 4446 27.49 |         |
| Demographics                  |         |                |            |         |
| Age, y, mean (SD)             | 74.91   | 75.10 74.39    |            | <0.001  |
| Sex: female                   | 6549 40.49 | 4770 72.84 | 1779 27.16 | 0.451   |
| Race                          |         |                |            | 0.364   |
| White                         | 14 386 88.93 | 10 427 72.48 | 3959 27.52 |         |
| Black                         | 1219 7.54  | 872 71.53      | 347 28.47  |         |
| Asian                         | 280 1.73  | 210 75.00      | 70 25.00   |         |
| Other                         | 291 1.80  | 221 75.95      | 70 24.05   |         |
| Cardiovascular history        |         |                |            |         |
| Previous MI                   | 7199 44.52 | 5059 70.27 | 2140 29.73 | <0.001  |
| Previous HF                   | 4108 25.41 | 3039 73.98 | 1069 26.02 | 0.015   |
| Cerebrovascular disease       | 3784 23.41 | 2712 71.67 | 1072 28.33 | 0.183   |
| Peripheral arterial disease   | 4012 24.82 | 2867 71.46 | 1145 28.54 | 0.086   |
| NYHA class (among those with HF in past 2 wk) | 0.640 |
| I                             | 248 8.50  | 180 72.58      | 68 27.42   |         |
| II                            | 766 26.24 | 587 76.63      | 179 23.37  |         |
| III                           | 1170 40.08 | 882 75.38 | 288 24.62  |         |
| IV                            | 735 25.18 | 554 75.37      | 181 24.63  |         |
| Cardiomyopathy or left ventricular systolic dysfunction | 2671 16.52 | 1955 73.19 | 716 26.81 | 0.389   |
| Other clinical history        |         |                |            |         |
| Current/recent smoker (w/in 1 y) | 2312 14.30 | 1688 73.01 | 624 26.99 | 0.563   |
| Hypertension                  | 14 749 91.21 | 10 641 72.15 | 4108 27.85 | <0.001  |
| Dyslipidemia                  | 13 746 85.06 | 9860 71.73 | 3886 28.27 | <0.001  |
| Chronic lung disease          | 3556 22.00 | 2623 73.76      | 933 26.24  | 0.002   |
| Diabetes mellitus             | 8446 52.22 | 6012 71.18      | 2434 28.82 | 0.060   |
| Procedure characteristics     |         |                |            |         |
| CAD presentation              |         |                |            | <0.001  |
| No symptoms, no angina        | 944 5.84  | 696 73.73      | 248 26.27  |         |
| Stable angina                 | 1860 11.50 | 1345 72.31 | 515 27.69  |         |
| Unstable angina               | 6068 37.52 | 4194 69.12 | 1874 30.88 |         |
| NSTEMI                         | 5126 31.70 | 3794 74.01 | 1332 25.99 |         |
| STEMI or equivalent            | 1911 11.82 | 1511 79.07 | 400 20.93  |         |
| Previous PCI                  | 9153 56.60 | 6339 69.26 | 2814 30.74 | <0.001  |
| Previous CABG                 | 6035 37.32 | 4137 68.55 | 1898 31.45 | <0.001  |
| Diagnostic Cath status        |         |                |            | <0.001  |
| Elective                      | 4563 33.33 | 3146 68.95 | 1417 31.05 |         |
| Urgent                        | 6973 50.93 | 5051 72.44 | 1922 27.56 |         |
| Emergency                     | 2148 15.69 | 1662 77.37 | 486 22.63  |         |

Continued
Table 3. Continued

| Overall | Not Attributed | Attributed | P Value |
|---------|---------------|------------|---------|
|         | No. | %     | No. | Row % | No. | Row %   |         |
| Salvage | 7   | 0.05  | 6   | 85.71 | 1   | 14.29   |         |
| Procedure year |       |         |       |       |       |         | 0.149   |
| 2009    | 1543 | 9.54   | 1130 | 73.23 | 413  | 26.77   |         |
| 2010    | 3562 | 22.02  | 2622 | 73.61 | 940  | 26.39   |         |
| 2011    | 3449 | 21.32  | 2472 | 71.67 | 977  | 28.33   |         |
| 2012    | 3739 | 23.11  | 2733 | 73.09 | 1006 | 26.91   |         |
| 2013    | 3883 | 24.00  | 2773 | 71.41 | 1110 | 28.59   |         |
| PCI status <0.001 |     |         |       |       |       |         |         |
| Elective | 5484 | 33.92  | 3855 | 70.30 | 1629 | 29.70   |         |
| Urgent | 8434 | 52.16  | 6126 | 72.63 | 2308 | 27.37   |         |
| Emergency | 2231 | 13.80  | 1728 | 77.45 | 503  | 22.55   |         |
| Salvage | 20  | 0.12   | 16  | 80.00 | 4    | 20.00   |         |
| Multivessel disease | 10 733 | 66.35  | 7729 | 72.01 | 3004 | 27.99   | 0.044   |
| Repeat PCI <0.001 |     |         |       |       |       |         |         |
| Time from index to repeat PCI |       |         |       |       |       |         |         |
| ≤30 d | 3537 | 21.87  | 2741 | 77.50 | 796  | 22.50   |         |
| 31 to 90 d | 3013 | 18.63  | 2410 | 79.99 | 603  | 20.01   |         |
| >90 d | 9626 | 59.51  | 6579 | 68.35 | 3047 | 31.65   |         |
| Vessel characteristics <0.001 |     |         |       |       |       |         |         |
| No. of stents placed, median (IQR) | 1.00 | (1.00–2.00) | 1.00 | 1.00 | <0.001 |         |
| Sum of stent diameter, median (IQR) | 3.00 | (2.75–5.50) | 3.00 | 3.50 | <0.001 |         |
| Sum of stent length, median (IQR) | 23.00 | (15.00–36.00) | 23.00 | 24.00 | <0.001 |         |
| Stent length categorized <0.001 |     |         |       |       |       |         |         |
| Short (≤16 mm) | 5038 | 31.17  | 3747 | 74.37 | 1291 | 25.63   |         |
| Medium (>16–28 mm) | 5486 | 33.94  | 4026 | 73.39 | 1460 | 26.61   |         |
| Long (>28 mm) | 5640 | 34.89  | 3946 | 69.96 | 1694 | 30.04   |         |
| Mean vessel stenosis before Tx, median (IQR) | 90.00 | (80.00–95.00) | 90.00 | 90.00 | 0.104  |         |
| Previously treated lesion | 3027 | 18.72  | 1923 | 63.53 | 1104 | 36.47   | <0.001  |
| Among previously treated lesions |       |         |       |       |       |         |         |
| Previously treated lesion time frame |       |         |       |       |       |         | 0.009   |
| <1 mo | 142  | 4.70   | 99  | 69.72 | 43   | 30.28   |         |
| 1 to 5 mo | 529  | 17.50  | 314 | 59.36 | 215  | 40.64   |         |
| 6 to 12 mo | 457  | 15.12  | 286 | 62.58 | 171  | 37.42   |         |
| 1 to 2 y | 408  | 13.50  | 259 | 63.48 | 149  | 36.52   |         |
| >2 y | 1209 | 39.99  | 802 | 66.34 | 407  | 33.66   |         |
| Time unknown | 278  | 9.20   | 159 | 57.19 | 119  | 42.81   |         |
| Treated with stent | 2828 | 93.49  | 1793 | 63.40 | 1035 | 36.60   | 0.657   |
| In-stent restenosis | 2607 | 92.25  | 1649 | 63.25 | 958  | 36.75   | 0.546   |
| In-stent thrombosis | 326  | 11.55  | 213 | 65.34 | 113  | 34.66   | 0.434   |
| Lesion in graft <0.001 |     |         |       |       |       |         |         |

Continued
leverage real-world data for surveillance.\textsuperscript{19} Claims are ubiquitous and longitudinal, but lack the granularity of registries. Registries are a key data source for surveillance. The Medical Device Epidemiology Network is focused on creation of coordinated registry networks for several device types, including cardiovascular devices, to provide evidence across a device’s total product life cycle.\textsuperscript{20} However, registries often do not include longitudinal follow-up data (such as the CathPCI Registry),\textsuperscript{21} and thus claims data are often used. Claims data have been shown to be concordant between physician-adjudication and administrative claims for some events such as mortality and heart failure hospitalization.\textsuperscript{22} These real-world data sources differ from clinical trials for stents, where specific stent-related outcomes (such as stent thrombosis or in-stent restenosis) or outcomes specific to the vessel that had received PCI (such as TVR) are ascertained and independently adjudicated to determine whether they meet criteria for standardized definitions.\textsuperscript{18} However, costs, complexity, and duration make performing clinical trials infeasible to generate evidence in some circumstances\textsuperscript{23}; therefore, real-world data sources will continue to be increasingly leveraged to provide evidence of benefits and risks of therapies,\textsuperscript{21} and we need to understand how to use claims and registries to refine estimates of device safety. Furthermore, some rare adverse events may never be detected in clinical trials, given that trials include fewer patients than when devices are used in real-world clinical practice as well as shorter follow-up durations for devices—which may be implanted lifelong.

Table 3. Continued

| Attribution of Adverse Events to Coronary Stents | Dhruva et al |

| Table 3. Continued | Overall | No. | % | Not Attributed | No. | Row % | Attributed | No. | Row % | P Value |
|---------------------|---------|-----|---|---------------|-----|------|------------|-----|------|---------|
| Not in graft        |         | 13 257 | 81.98 | 9807 | 73.98 | 3450 | 26.02 |
| Vein                |         | 2725 | 16.85 | 1796 | 65.91 | 929 | 34.09 |
| LIMA graft          |         | 119 | 0.74 | 72 | 60.50 | 47 | 39.50 |
| Other artery        |         | 70 | 0.43 | 51 | 72.86 | 19 | 27.14 |
| Lesion complexity   |         |     |     |     |       |     |       |
| Non-high/non-C      |         | 6397 | 39.58 | 4741 | 74.11 | 1656 | 25.89 |
| High/C              |         | 9764 | 60.42 | 6977 | 71.46 | 2787 | 28.54 |
| Maximum lesion length, median (IQR) | 18.00 | (12.00–26.00) | 18.00 | 18.00 | <0.001 |
| Thrombus present    |         | 2011 | 12.45 | 1523 | 75.73 | 488 | 24.27 |
| Bifurcation lesion  |         | 2022 | 12.51 | 1428 | 70.62 | 594 | 29.38 |
| Hospital location   |         |     |     |     |       |     |       |
| Rural               | 2402 | 14.85 | 1796 | 74.77 | 606 | 25.23 |
| Suburban            | 4798 | 29.66 | 3473 | 73.83 | 1325 | 27.62 |
| Urban               | 8976 | 55.49 | 6461 | 71.98 | 2515 | 28.02 |
| Profit type         |         |     |     |     |       |     |       |
| Government          | 165 | 1.02 | 117 | 70.91 | 48 | 29.09 |
| Private/community   | 14 031 | 86.74 | 10 153 | 72.36 | 3878 | 27.64 |
| University          | 1980 | 12.24 | 1460 | 73.74 | 520 | 26.26 |
| Teaching Hospital   | 8090 | 50.01 | 5898 | 72.90 | 2192 | 27.10 |
| PCI count, median (IQR) | 800.00 | (476–1300) | 795.00 | 803.00 | 0.011 |

AMI indicates acute myocardial infarction; CABG, coronary artery bypass graft; CAD, coronary artery disease; Cath, catheterization; HF, heart failure; IQR, interquartile range; LIMA, left internal mammary artery; MI, myocardial infarction; NSTEMI, non-ST-segment–elevation myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STEMI, ST-segment–elevation myocardial infarction; Tx, treatment.
end-point adjudication, the kappa statistic was 0.76 for acute MI identified in International Classification of Diseases, Ninth Revision (ICD-9) claims.26 Second, they lack granular detail about PCI location. International Classification of Diseases, Tenth Revision (ICD-10) codes came into use in the United States from October 2015 and include 5 times as many diagnoses and 18 times as many procedures as the previously used ICD-9 codes, including greater detail about the number of sites in which stents are placed, stent restenosis, stent thrombosis, and stent fracture. However, ICD-10 codes still do not provide information about which coronary artery receives PCI.27 The possible exception is STEMI, for which ICD-10 codes detail the level of the culprit coronary artery which, presumably, would receive intervention. However, 50% of patients with STEMI have multivessel disease,28 and other coronary arteries may also receive stent placement during primary PCI for STEMI based on guideline recommendations.29 This means that although the utility of claims data identified in our study may improve with the transition to ICD-10, the extent of improvement requires further study. Third, claims data are currently available in finalized form only after a ≈2-year delay; to be used more effectively, they will also need to be made available more quickly. Fourth, and most critically for identifying stents of a specific manufacturer or model, claims data do not include unique device identifiers for medical devices. Unique device identifiers are barcodes that contain information about a device manufacturer, model, description, and other characteristics.30,31 If unique device identifiers become included into claims data, specific stents and other implanted medical devices could be tracked longitudinally for surveillance purposes.32

Although linking claims to the CathPCI Registry helps understand whether repeat PCI is TVR, this approach is still insufficient to comprehensively understand the multiple clinical factors that determine stent safety. Patient, physician, and hospital characteristics are associated with usage of certain stents and adverse events; this means that risk standardization is necessary for surveillance. However, the lack of detailed clinical data when using administrative claims as the longitudinal data source makes this inadequate at the patient level. For example, patient adherence to thienopyridines declines within 1 year, thus increasing the risk of stent thrombosis.33 Therefore, surveillance of DES using real-world data could be made more robust through combination with additional data sources such as electronic health records, pharmacy claims data, and patient-reported data.

Whereas mortality is arguably the most important clinical end point for DES safety, not unexpectedly, we could only determine that ≈1% of deaths identified in claims could be reasonably attributed to a complication within the same coronary artery in which the index PCI was performed. Because CathPCI Registry data are available for patients with documented PCI and sometimes diagnostic coronary angiography, we cannot ascertain the reason for death identified in claims for the vast majority of patients because these patients died outside of the hospital or even when hospitalized and did not receive coronary angiography and/or PCI. Some of these deaths could have been stent-related, such as stent thrombosis leading to acute MI and sudden cardiac death. When patients had a documented repeat PCI but died, 71.4% were in the same coronary artery as was initially stented. As with death, there is incomplete attribution of MIs to previously placed stents, such as patients who experienced an MI and did not receive medical care, did not receive diagnostic coronary angiography, or did not receive PCI. Real-world safety evaluations will often use death and MI as end points, given their clinical significance and the ease with which they can be ascertained from nationally representative claims data, but will also lack the capacity for adjudication as is done in clinical trials. Therefore, our finding that only a small proportion represent adverse events that can be attributable to previously placed stents means that these claims-based end points can only serve as a signal that must be further evaluated and refined with complementary data sources.

Our findings may be considered in the context of several limitations. First, we excluded patients receiving multivessel PCI, which is performed in a substantial minority of cases. When multiple coronary arteries receive PCI, attribution of stent-related safety events will be more difficult. Second, we excluded patients with repeat procedures within 60 days unless they had an MI code or complication code. Although we presumed that most of these patients were receiving staged PCI,17 we still may have missed some stent-related complications, particularly if a repeat PCI occurred within the same coronary artery as the index PCI. Third, we did not include in-hospital stent-related adverse events, which are nearly always stent thrombosis. Claims data preclude distinguishing index from repeat PCI within a given hospitalization. Fourth, we did not examine coronary artery bypass grafting in longitudinal follow-up, which may infrequently be a reason for revascularization after a stent-related adverse event. Fifth, we did not examine patients longitudinally in the NCDR CathPCI Registry and then attempt to locate a corresponding CMS claim. Sixth, although the CathPCI Registry captures granular information on the coronary segment in which a device is used, these data are inconsistently reported and unlikely to be reliable. For that reason, we instead focused on the less-granular TVR, making our estimates a “better” case scenario for attribution of adverse events to a previously placed stent.

Seventh, we did not evaluate adverse events occurring because of operator-level variation in performance of PCI. Finally, our findings are applicable only to coronary stents, given that a comprehensive national registry exists to capture
PCI and the expected adverse events can be captured within claims data.

In conclusion, by linking longitudinal claims data to a comprehensive national registry of PCIs multiple times, we found that approximately half of repeat PCIs within 1 year occur in the same coronary artery as the initial PCI with DES placement, indicating a DES-related adverse event. MI and death, although more clinically important, could be attributed much less often to the same coronary artery as the index PCI. These findings suggest that using claims data for surveillance of DESs, even when linked to a national PCI registry, may be insufficient. As momentum grows to leverage real-world data for medical device surveillance, these limitations will need to be surmounted through novel strategies to bring together complementary data sources to inform a robust postmarket surveillance system.

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Attribution of Adverse Events to Coronary Stents

Dhruva et al

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Table S1. ICD-9 CM/CPT codes used to identify longitudinal outcomes in inpatient and outpatient institutional claims for Medicare fee-for-service beneficiaries.

| Outcome                      | Source   | Code   | Definition                                                                 |
|------------------------------|----------|--------|---------------------------------------------------------------------------|
| Repeat percutaneous coronary intervention (PCI) | ICD-9 SG | 00.66  | Percutaneous transluminal coronary angioplasty [PTCA]                      |
|                              | ICD-9 SG | 36.06  | Insertion of non-drug-eluting coronary artery stent(s)                    |
|                              | ICD-9 SG | 36.07  | Insertion of drug-eluting coronary artery stent(s)                        |
|                              | ICD-9 SG | 36.09  | Other removal of coronary artery obstruction                              |
|                              | CPT      | 92920  | PTCA                                                                      |
|                              | CPT      | 92921  | PTCA; each additional branch of a major coronary artery                   |
|                              | CPT      | 92924  | Percutaneous transluminal coronary atherectomy with angioplasty           |
|                              | CPT      | 92925  | Percutaneous transluminal coronary atherectomy, with coronary angioplasty when performed; each additional branch of a major coronary artery |
|                              | CPT      | 92928  | Percutaneous trans catheter insertion of stent with coronary angioplasty |
|                              | CPT      | 92929  | Percutaneous trans catheter insertion of stent with coronary angioplasty |
|                              | CPT      | 92933  | Percutaneous transluminal coronary atherectomy, with intracoronary stent, with coronary angioplasty when performed; single major coronary artery or branch |
|                              | CPT      | 92934  | Percutaneous transluminal coronary atherectomy with angioplasty and insertion of stent |
CPT 92937  Percutaneous transluminal revascularization of coronary artery with atherectomy and insertion of stent

CPT 92938  Percutaneous transluminal revascularization of coronary artery bypass graft with angioplasty and insertion of stent

CPT 92941  Percutaneous transluminal revascularization of coronary artery bypass graft with atherectomy, angioplasty and insertion of stent

CPT 92943  Percutaneous transluminal revascularization of coronary artery bypass graft with atherectomy, angioplasty and insertion of stent

CPT 92944  Percutaneous transluminal revascularization of coronary artery bypass graft with atherectomy, angioplasty and insertion of stent

CPT 92980  Transcatheter placement of an intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel

CPT 92981  Transcatheter placement of an intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; each additional vessel

CPT 92982  Percutaneous transluminal coronary balloon angioplasty, single vessel

CPT 92984  Percutaneous transluminal coronary balloon angioplasty, each additional vessel

CPT 92995  Percutaneous transluminal coronary atherectomy, by mechanical or other method, with or without balloon angioplasty; single vessel
CPT 92996  Percutaneous transluminal coronary atherectomy, by mechanical or other method, with or without balloon angioplasty; each additional vessel

CPT C9600  Percutaneous transcatheater placement of drug-eluting intracoronary stent(s), with coronary angioplasty when performed; single major coronary artery or branch

CPT C9601  Percutaneous transcatheater placement of drug-eluting intracoronary stent(s), with coronary angioplasty when performed; each additional branch of a major coronary artery (list separately in addition to code for primary procedure)

CPT C9602  Percutaneous transluminal coronary atherectomy, with drug-eluting intracoronary stent, with coronary angioplasty when performed; single major coronary artery or branch

CPT C9603  Percutaneous transluminal coronary atherectomy, with drug-eluting intracoronary stent, with coronary angioplasty when performed; each additional branch of a major coronary artery (list separately in addition to code for primary procedure)

CPT C9604  Percutaneous transluminal revascularization of or through coronary artery bypass graft (internal mammary, free arterial, venous), any combination of drug-eluting intracoronary stent, atherectomy and angioplasty, including distal protection when performed; single vessel

CPT C9605  Percutaneous transluminal revascularization of or through coronary artery bypass graft (internal mammary, free arterial,
venous), any combination of drug-eluting intracoronary stent, atherectomy and angioplasty, including distal protection when performed; each additional branch subtended by the bypass graft (list separately in addition to code for primary procedure)

CPT C9606 Percutaneous transluminal revascularization of acute total/subtotal occlusion during acute myocardial infarction, coronary artery or coronary artery bypass graft, any combination of drug-eluting intracoronary stent, atherectomy and angioplasty, including aspiration thrombectomy when performed, single vessel

CPT C9607 Percutaneous transluminal revascularization of chronic total occlusion, coronary artery, coronary artery branch, or coronary artery bypass graft, any combination of drug-eluting intracoronary stent, atherectomy and angioplasty; single vessel

CPT C9608 Percutaneous transluminal revascularization of chronic total occlusion, coronary artery, coronary artery branch, or coronary artery bypass graft, any combination of drug-eluting intracoronary stent, atherectomy and angioplasty; each additional coronary artery, coronary artery branch, or bypass graft (list separately in addition to code for primary procedure)

CPT G0290 Transcatheter placement of a drug-eluting intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; single vessel
| CPT      | G0291 | Transcatheter placement of a drug-eluting intracoronary stent(s), percutaneous, with or without other therapeutic intervention, any method; each additional vessel |
|----------|-------|---------------------------------------------------------------------------------|
| Acute myocardial infarctions (AMIs) | ICD-9 DX | 410.01 | AMI of anterolateral wall, initial episode of care |
|          | ICD-9 DX | 410.11 | AMI of other anterior wall, initial episode of care |
|          | ICD-9 DX | 410.21 | AMI of inferolateral wall, initial episode of care |
|          | ICD-9 DX | 410.31 | AMI of inferoposterior wall, initial episode of care |
|          | ICD-9 DX | 410.41 | AMI of other inferior wall, initial episode of care |
|          | ICD-9 DX | 410.51 | AMI of other lateral wall, initial episode of care |
|          | ICD-9 DX | 410.61 | True posterior wall infarction, initial episode of care |
|          | ICD-9 DX | 410.71 | Subendocardial infarction, initial episode of care |
|          | ICD-9 DX | 410.81 | AMI of other specified sites, initial episode of care |
|          | ICD-9 DX | 410.91 | AMI of unspecified site, initial episode of care |
Table S2. Characteristics of procedures with adverse events within one year identified in Medicare claims data linked and not linked to National Cardiovascular Data Registry.

|                              | Procedures with AE not linked to NCDR with coronary artery info | Procedures with AE linked to NCDR with coronary artery info from PCI |
|------------------------------|-----------------------------------------------------------------|------------------------------------------------------------------|
| N Procedures                 | 61,409                                                          | 32,802                                                          | 28,607                                                          | 46.58                                                          |
| Demographics                 |                                                                  |                                                                  |                                                                  |
| Age - Mean (SD)              | 75.14                                                           | 76.24                                                           | 73.88                                                           | 6.91                                                           | 7.17                                                           | 6.36                                                           |
| Sex: Female                  | 23,408                                                          | 12,909                                                          | 10,499                                                          | 38.12                                                          | 39.35                                                          | 36.70                                                          |
| Race                         |                                                                  |                                                                  |                                                                  |
| White                        | 55,660                                                          | 29,554                                                          | 26,106                                                          | 90.64                                                          | 90.10                                                          | 91.26                                                          |
| Black                        | 3,849                                                           | 2,203                                                           | 1,646                                                           | 6.27                                                           | 6.72                                                           | 5.75                                                           |
| Asian                        | 906                                                             | 486                                                             | 420                                                             | 1.48                                                           | 1.48                                                           | 1.47                                                           |
| Other                        | 994                                                             | 559                                                             | 435                                                             | 1.62                                                           | 1.70                                                           | 1.52                                                           |
| Hispanic or Latino Ethnicity | 2,413                                                           | 1,376                                                           | 1,037                                                           | 3.94                                                           | 4.20                                                           | 3.63                                                           |
| Cardiovascular History       |                                                                  |                                                                  |                                                                  |
| Prior MI                     | 24,096                                                          | 13,027                                                          | 11,069                                                          | 39.26                                                          | 39.73                                                          | 38.71                                                          |
| Prior Heart Failure          | 15,438                                                          | 10,435                                                          | 5,003                                                           | 25.15                                                          | 31.83                                                          | 17.50                                                          |
| Prior Valve Surgery/Procedure| 1,719                                                           | 1,038                                                           | 681                                                             | 2.80                                                           | 3.17                                                           | 2.38                                                           |
| Cerebrovascular Disease      | 13,758                                                          | 7,997                                                           | 5,761                                                           | 22.42                                                          | 24.39                                                          | 20.15                                                          |
| Peripheral Arterial Disease  | 14,417                                                          | 8,396                                                           | 6,021                                                           | 23.49                                                          | 25.61                                                          | 21.05                                                          |
| Category                                      | Count | Percentage |
|----------------------------------------------|-------|------------|
| NYHA Class (among those with HF in prior 2 weeks) |       |            |
| Class I                                      | 850   | 7.54       |
| Class II                                     | 2,900 | 25.71      |
| Class III                                    | 4,522 | 40.09      |
| Class IV                                     | 3,007 | 26.66      |
| Cardiomyopathy or Left                       |       |            |
| Ventricular Systolic Dysfunction             | 10,475| 17.06      |
| Cardiogenic Shock w/in 24 Hrs                | 941   | 1.53       |
| Cardiac Arrest w/in 24 Hrs                   | 724   | 1.18       |
| Other Clinical History                       |       |            |
| Current/Recent Smoker (w/in 1 year)          | 8,122 | 13.23      |
| Hypertension                                 | 55,484| 90.39      |
| Dyslipidemia                                 | 51,773| 84.39      |
| Currently on Dialysis                        | 3,936 | 6.42       |
| Chronic Lung Disease                         | 14,920| 24.31      |
| Diabetes Mellitus                            | 29,303| 47.73      |
| Procedure Characteristics                    |       |            |
| CAD Presentation                             |       |            |
| No symptom, no angina                        | 4,620 | 7.52       |
| Symptom unlikely to be                       |       |            |
| ischemic                                     | 1,564 | 2.55       |
| Stable angina                                | 9,363 | 15.25      |
| Unstable angina                              | 25,962| 42.29      |
| Category                                      | 2009       | 2010       | 2011       | 2012       | 2013       |
|-----------------------------------------------|------------|------------|------------|------------|------------|
| Non-STEMI                                     | 14,044     | 8,905      | 5,139      | 17.97      | 12.87      |
| ST-Elevation MI (STEMI) or equivalent         | 5,844      | 3,797      | 2,047      | 7.16       | 6.83       |
| Prior PCI                                     | 33,562     | 16,163     | 17,399     | 60.83      |            |
| Prior CABG                                    | 20,638     | 10,074     | 10,564     | 36.93      |            |
| Diagnostic Cath Status                        |            |            |            |            |            |
| Elective                                      | 21,599     | 9,693      | 11,906     | 48.98      |            |
| Urgent                                        | 22,921     | 12,989     | 9,932      | 40.86      |            |
| Emergency                                     | 6,753      | 4,293      | 2,460      | 10.12      |            |
| Salvage                                       | 58         | 49         | 9          | 0.04       |            |
| Procedure Year                                |            |            |            |            |            |
| 2009                                          | 6,439      | 3,181      | 3,258      | 11.39      |            |
| 2010                                          | 14,567     | 7,618      | 6,949      | 24.29      |            |
| 2011                                          | 12,902     | 6,895      | 6,007      | 21.00      |            |
| 2012                                          | 13,662     | 7,413      | 6,249      | 21.84      |            |
| 2013                                          | 13,839     | 7,695      | 6,144      | 21.48      |            |
| PCI Status                                    |            |            |            |            |            |
| Elective                                      | 26,001     | 12,118     | 13,883     | 48.55      |            |
| Urgent                                        | 28,315     | 16,140     | 12,175     | 42.58      |            |
| Emergency                                     | 6,970      | 4,452      | 2,518      | 8.81       |            |
| Salvage                                       | 92         | 73         | 19         | 0.07       |            |
| IABP                                          | 1,136      | 864        | 272        | 0.95       |            |
| Other Mechanical Ventricular Support          |            |            |            |            |            |
| Support                                       | 335        | 245        | 90         | 0.31       |
### Vessel Characteristics

|                           | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) |
|---------------------------|--------------|--------------|--------------|--------------|--------------|
| # of Stents Placed        | 1.00 (1.00-2.00) | 1.00 (1.00-2.00) | 1.00 (1.00-2.00) | 1.00 (1.00-2.00) | 1.00 (1.00-2.00) |
| Sum of Stent Diameter     | 3.00 (2.75-5.00) | 3.00 (2.75-5.00) | 3.00 (2.75-5.00) | 3.00 (2.75-5.00) | 3.00 (2.75-5.00) |
| Sum of Stent Length Median| 22.00 (15.00-33.00) | 22.00 (15.00-33.00) | 22.00 (15.00-32.00) | 22.00 (15.00-32.00) | 22.00 (15.00-32.00) |

### Stent Length Categorized

| Category                  | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) |
|---------------------------|--------------|--------------|--------------|--------------|--------------|
| Small (16mm or less)      | 141,135      | 34.02        | 141,135      | 34.02        | 141,135      | 34.02        |
| Medium (>16mm - 28mm)     | 146,361      | 35.28        | 146,361      | 35.28        | 146,361      | 35.28        |
| Large (> 28mm)            | 127,332      | 30.70        | 127,332      | 30.70        | 127,332      | 30.70        |

### Mean Vessel Stenosis Prior to Tx

| Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) |
|--------------|--------------|--------------|--------------|--------------|--------------|
| (80.00-95.00)| (80.00-95.00)| (80.00-95.00)| (80.00-95.00)| (80.00-95.00)| (80.00-95.00)|

### Pre-Procedure TIMI Flow

| TIMI Flow | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) |
|-----------|--------------|--------------|--------------|--------------|--------------|
| TIMI - 0  | 37,967       | 9.17         | 37,967       | 9.17         | 37,967       | 9.17         |
| TIMI - 1  | 32,786       | 7.92         | 32,786       | 7.92         | 32,786       | 7.92         |
| TIMI - 2  | 82,852       | 20.00        | 82,852       | 20.00        | 82,852       | 20.00        |
| TIMI - 3  | 260,598      | 62.92        | 260,598      | 62.92        | 260,598      | 62.92        |

### Previously Treated Lesion

| Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) |
|--------------|--------------|--------------|--------------|--------------|--------------|
| 50,666       | 12.21        | 50,666       | 12.21        | 50,666       | 12.21        |

### Among previously Treated Lesions:

| Previously Treated Lesion Timeframe | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) | Median (IQR) |
|------------------------------------|--------------|--------------|--------------|--------------|--------------|
| < 1 month                          | 1,994        | 3.94         | 1,994        | 3.94         | 1,994        | 3.94         |
| 1-5 months                         | 5,668        | 11.21        | 5,668        | 11.21        | 5,668        | 11.21        |
| Time            | Treated with Stent | In-stent Restenosis | In-stent Thrombosis | Lesion in Graft | Lesion Complexity |
|-----------------|--------------------|---------------------|---------------------|-----------------|-------------------|
| 6-12 months     | 6,370              | 6,370               | 6,370               | 377,850         | 190,068           |
| 1-2 years       | 7,209              | 7,209               | 7,209               | 34,644          | 224,936           |
| >2 years        | 25,365             | 25,365              | 25,365              | 1,854           |                   |
| Time unknown    | 3,959              | 3,959               | 3,959               | 795             |                   |

| Lesion Complexity | Maximum Lesion Length - Median (IQR), mm | Thrombus Present | Bifurcation Lesion |
|-------------------|----------------------------------------|------------------|-------------------|
| Non-High/Non-C    | (12.00-24.00)                          | 41,432           | 50,592            |
| High/C            | (12.00-24.00)                          | 41,432           | 50,592            |

NCDR: National Cardiovascular Data Registry
PCI: Percutaneous Coronary Intervention
CABG: Coronary Artery Bypass Graft

CAD: Coronary Artery Disease

HF: Heart Failure

Hrs: Hours

IABP: Intra-Aortic Balloon Pump

LIMA: Left Internal Mammary Artery

MI: Myocardial Infarction

NYHA: New York Heart Association

STEMI: ST-Elevation MI

TIMI: Thrombolysis In Myocardial Infarction

Tx: Treatment
Figure S1. Attribution of adverse events identified in Medicare claims data after index drug-eluting stent placement in patients 65 years and older, 2009-2013 who did not have a history of prior percutaneous coronary intervention.

| AEs within 1 year in Medicare claims data | 27,831 | 13,099 | 7,017 | 12,480 |
| AEs within 1 year in Medicare claims data linked to NCDR | 11,908 (42.8%) | 11,214 (85.6%) | 3,317 (47.3%) | 190 (1.5%) |
| AEs within 1 year in Medicare claims data linked to NCDR with coronary artery info from PCI | 11,205 (40.3%) | 11,153 (85.1%) | 2,611 (37.2%) | 160 (1.3%) |
| AEs within 1 year in Medicare claims data linked to NCDR with coronary artery info with repeat PCI occurring within same coronary artery | 6,040 (21.7%) | 6,000 (45.8%) | 1,631 (23.2%) | 112 (0.9%) |
| Repeat PCI in area of previously placed drug-eluting stent due to: | | Restenosis 2,433 | Thrombosis 550 |

AEs, adverse events; MI, myocardial infarction; NCDR, National Cardiovascular Data Registry; PCI, percutaneous coronary intervention.