Drug-Eluting Stents

Number: 0621

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

I. Aetna considers Food and Drug Administration (FDA)-approved everolimus-eluting stents, paclitaxel-eluting stents, sirolimus-eluting stents, and zotarolimus-eluting stents medically necessary for members with angina pectoris or silent ischemia and greater than 50 % stenosis of 1 or more coronary arteries.

II. Aetna considers FDA-approved drug-eluting stents medically necessary for the treatment of intra-coronary stent restenosis.

III. Aetna considers drug-eluting stents experimental and investigational for treatment of all other indications, including any of the following (not an all-inclusive list) because their effectiveness for these indications has not been established:

- Aorto-arteritis (also known as Takayasu arteritis); or
- Chronic kidney disease with multi-vessel disease; or
- Non-malignant gastric outlet obstruction; or
- Pancreato-biliary diseases such as bile duct obstruction

Policy History

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Review History

Definitions

Additional Information

Clinical Policy Bulletin Notes
(including their use in endoscopic retrograde cholangiopancreatography); or

- Stenotic lesions of non-coronary arteries (e.g., peripheral vascular disease*, renal artery stenosis); or
- Vein graft stenosis; or
- Venous stenosis associated with dialysis vascular access

IV. Aetna considers biodegradable (bioresorbable, bioabsorbable) polymer drug eluting stents experimental and investigational because their effectiveness has not been established.

V. Aetna considers antibody coated coronary stents experimental and investigational because their safety and effectiveness has not been established.

**Note:** The use of intravascular optical coherence tomography (coronary native vessel or graft) or catheter-based coronary vessel or graft spectroscopy (eg, infrared) during diagnostic evaluation and/or therapeutic intervention is considered integral to the primary procedure and not separately reimbursable.

* Aetna considers the Zilver PTX Drug-Eluting Peripheral Stent medically necessary for the primary treatment of femoropopliteal artery disease. See also **CPB 0785 - Peripheral Vascular Stents.**

**Background**

Drug-eluting coronary stents are placed during a percutaneous transluminal coronary angioplasty (PTCA), a procedure to dilate (widen) narrowed arteries of the heart. A catheter with a deflated balloon at its tip is inserted into a blood vessel in the arm or groin and advanced to the narrowed part of the coronary artery. The balloon is then inflated, pressing against the plaque and/or fatty materials and enlarging the inner diameter of the blood vessel so blood can flow more easily. The balloon is deflated and the catheter removed.
If a stent is to be placed, a stent delivery catheter is then threaded up into the affected area and a stent is left in place. Coronary stents are expandable metal mesh tubes that push against the walls of a coronary artery to keep it open. Due to problems with restenosis following the placement of these stents, drug-eluting stents were designed.

Drug-eluting stents are covered with a drug (eg, everolimus, sirolimus, zotarolimus or paclitaxel) that is slowly released to help prevent build-up of new tissue that grows in the artery, thereby preventing stenosis. Examples of US Food and Drug Administration (FDA) approved drug-eluting coronary stents may be found on the FDA website.

The use of stents has improved the results of percutaneous coronary re-vascularization. However, in-stent restenosis due to neointimal proliferation of connective tissue has been reported to occur in approximately 15 to 20 % of stent patients.

The macrolide anti-fungal agent sirolimus (rapamycin) has been shown to inhibit the proliferation of lymphocytes and smooth muscle cells and has been applied to the interior of balloon-expandable stents. The Rx Velocity consists of a stent coated with a mixture of synthetic polymers blended with sirolimus. The Rx Velocity is designed to release 80 % of the drug within 30 days after stent implantation. Only a small amount of the drug is required, and systemic side effects from the drug are avoided.

The FDA approved the stent based on a review of 2 clinical studies of safety and effectiveness of the sirolimus-eluting stent. In a multi-center, randomized, double-blind, controlled clinical trial conducted in the United States (the SIRIUS study), 1,058 patients were randomly assigned to receive either the sirolimus-eluting stent or an uncoated stainless steel stent. Patients in the SIRIUS study had blockages of 15 mm to 30 mm long in arteries that were 2.5 mm to 3.5 mm wide.

Results were similar for both types of stents in the weeks immediately following the procedure, but after 9 months the patients who received the drug-eluting stent had a significantly
lower rate of repeat procedures than patients who received the uncoated stent (4.2% versus 16.8%). In addition, patients treated with the drug-eluting stent had a re-stenosis rate of 8.9%, compared to 36.3% of patients with the uncoated stent. The combined occurrence of repeat angioplasty, bypass surgery, myocardial infarction and death was 8.8% for drug-eluting stent patients and 21% for the uncoated stent patients. The types of adverse events seen with the drug-eluting stent were similar to those that occurred with the uncoated stent.

The FDA's approval of the sirolimus-eluting stent was also based on the results of a non-U.S. multi-center, randomized, double-blind, controlled clinical trial (the RAVEL study) comparing sirolimus-eluting stents with standard uncoated stents in 238 adults with stable or unstable angina pectoris or silent ischemia and single coronary lesions amenable to stenting. Lesions had to be between 2.5 mm and 3.5 mm in diameter, such that they could be covered by an 18 mm stent. Patients with complex coronary lesions, such as those containing substantial calcium or thrombus, were excluded from the study.

The investigators reported that use of a sirolimus-eluting stent resulted in the virtual elimination of angiographic evidence of neointimal hyperplasia and re-stenosis and greatly reduced the need for repeated re-vascularization procedures. At 6 months after stent placement, there was significantly less in-stent late luminal loss (a measure of neointimal proliferation) in patients receiving sirolimus-eluting stents than in patients receiving standard, uncoated stents. None of the patients receiving sirolimus-eluting stents had restenosis of 50% or more of the luminal diameter, compared to 26.6% of patients receiving standard stents. Within 1 year following stent placement, percutaneous re-vascularization had been performed in 22.9% of recipients of standard, uncoated stents, and in none of the recipients of sirolimus-eluting stents. The investigators concluded that angina patients who received sirolimus-eluting stents had no angiographic evidence of late luminal loss or in-stent restenosis at 6 months after sirolimus-eluting stent placement and a very low rate of cardiovascular events within the year following stenting.
The safety and effectiveness of the Cypher stent in smaller diameter arteries or for longer blockage that required more than 2 stents was not studied in either trial. Also, the safety and effectiveness have not been studied in patients who are having a heart attack, patients who had previous intravascular radiation treatment, or patients who had their blockage in a bypass graft.

The FDA-approved labeling of the sirolimus-eluting stent warns that patients who are allergic to sirolimus or to stainless steel should not receive a Cypher stent. Caution is also recommended for people who have had recent cardiac surgery and for women who may be pregnant or who are nursing.

The FDA is requiring the manufacturer of the sirolimus-eluting stent to conduct a 2,000-patient post-approval study and continue to evaluate patients from ongoing clinical trials to assess the long-term safety and effectiveness of the sirolimus-eluting stent and to look for rare adverse events that may result from the use of this product.

The FDA has approved the paclitaxel-eluting stents (Taxus Express Paclitaxel-Eluting Coronary Stent System, Boston Scientific Corporation) for improving luminal diameter for the treatment of de novo lesions less than 28 mm in length in native coronary arteries greater than or equal to 2.5 to less than or equal to 3.75 mm in diameter. Paclitaxel (Taxol) is similar to sirolimus in that it has been shown to inhibit proliferation of connective tissues and smooth muscle.

Stone et al (2004) reported on the results of the Taxus-IV trial, a multi-center prospective, randomized, double-blind controlled clinical trial of a paclitaxel-eluting stent in 1,314 patients with angina or provokable ischemia who were receiving a stent in a single, previously untreated lesion in a native coronary artery. Patients in the Taxus-IV trial had vessel diameters between 2.5 and 3.75 mm, and had lesions between 10 to 28 mm in length that could be covered by a single stent. Patients with lesions of the left main coronary artery were excluded. Patients were randomly assigned to receive either a bare-metal stent (BMS) or a paclitaxel-eluting stent (PES). At 9 months follow-up, the rate of
target vessel re-vascularization due to ischemia was 12 % in patients who received the BMS, and 4.7 % in patients who received the PES (relative risk [RR] 0.39 (95 % confidence interval [CI]: 0.16 to 0.43). The rate of angiographic restenosis was 26.6 % in patients who received the BMS, and 7.9 % in patients who received the PES (RR 0.30 (95 % CI: 0.19 to 0.46). The rates of adverse events were similar between patients receiving the PES and the BMS.

The safety and effectiveness of the Taxus Express stent in smaller diameter arteries or for longer blockage that required more than 2 stents has not been studied. Also, the safety and effectiveness have not been studied in patients who are having a myocardial infarction, patients who had previous intravascular brachytherapy, or patients who had stenosis of a bypass graft.

The FDA-approved labeling of the PES warns that patients who are allergic to paclitaxel or to stainless steel should not receive a Taxus Express stent. Caution is also recommended for people who have had recent cardiac surgery and for women who may be pregnant or who are nursing.

The FDA is requiring the manufacturer of the PES to conduct a 2,000 patient post-approval study and continue to evaluate patients from ongoing clinical trials to assess the long-term safety and effectiveness of the PES and to look for rare adverse events that may result from the use of this product.

Use of certain drug-eluting stents may be contraindicated in individuals with known hypersensitivity to:

- Everolimus, paclitaxel, sirolimus, zotarolimus or structurally-related compounds (eg, polymethacrylates or polyolefin copolymers); or
- Materials used to make up the device or structurally-related compounds (eg, acrylic, cobalt, chromium, fluoropolymers, nickel, platinum, stainless steel, tungsten); or
- The polymer, its individual components or structurally-related compounds
Coronary artery stenting, regardless of stent type, is contraindicated for use in:

- Individuals who cannot receive recommended antiplatelet and/or anticoagulant therapy; or
- Individuals judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the stent or delivery device.

In a randomized controlled trial (n = 57), Duda et al (2005) examined the safety and effectiveness of the sirolimus-eluting S.M.A.R.T. Nitinol Self-expanding Stent by comparison with a bare stent in superficial femoral artery (SFA) obstructions. These investigators concluded that although there is a trend for greater efficacy in the sirolimus-eluting stent group, there were no statistically significant differences in any of the variables.

In a recent review on advances in the medical and surgical treatment of aorto-arteritis (also known as Takayasu arteritis), an inflammatory vascular disorder that produces arterial stenoses and aneurysms primarily involving the thoraco-abdominal aorta and its branches and the pulmonary arteries, Liang and Hoffman (2005) stated that new drugs that target intimal hyperplasia, as well as drug-eluting stents, deserve to be studied for possible utility as adjuncts to present treatments.

Dzavik (2005) stated that bifurcation lesions have been recognized as one of the most important challenges facing interventional cardiologists since the start of percutaneous coronary intervention (PCI). The potential of peri-procedural occlusion of the side branch (SB) was found to be significant, resulting in early attempts at protecting the SB with a 2nd guide wire and kissing balloon inflation in order to minimize this risk, and thus improve the procedural and short-term success of the procedure. The advent of stenting significantly improved the safety of the procedure, although, SB success continued to be a challenge. A variety of single- as well as double-stenting techniques were developed that improved the safety and short-term results of PCI involving SB. Long-term success, however, continued to elude, as a consequence of an increased need for
target lesion revascularization (TLR) and higher major adverse cardiac event (MACE) rates following PCI of bifurcation lesions. The introduction of drug-eluting stents appears to have brought bifurcation PCI to a new level of long-term efficacy. Specialty bifurcation stents have been developed to provide easy access to the SB, however, these have to date had little impact on practice and have not been adopted widely. New techniques such as crush stenting and its several permutations, and simultaneous kissing stenting developed specifically for drug-eluting stents have been developed. Debate continues as to which the most effective technique is. True randomized comparisons are, however, lacking. It is likely that all of the currently utilized techniques have a place in interventional cardiologists’ quiver, and that each is appropriate in a particular anatomical scenario. Nonetheless, well-designed randomized studies assessing the various bifurcation techniques especially in complex bifurcation lesions are needed. Moreover, Iakovou et al (2005) reported that the cumulative incidence of stent thrombosis 9 months after successful drug-eluting stent implantation in consecutive “real-world” patients was substantially higher than the rate reported in clinical trials. Premature anti-platelet therapy discontinuation, renal failure, bifurcation lesions, diabetes, and low ejection fraction were identified as predictors of thrombotic events.

Shammas and Dippel (2005) stated that peripheral vascular disease (PVD) is very prevalent in the United States. Patients with PVD have a heightened inflammatory state and are at high-risk of death from acute cardiovascular problems rather than from progression of PVD. Modifiable risk factors for PVD include smoking, hypertension, diabetes, hyperlipidemia, elevated high sensitivity C-reactive protein, obesity, and the metabolic syndrome. Symptomatic treatment of claudication includes smoking cessation, exercise, cilostazol, statins, and revascularization with percutaneous or surgical therapy. Anti-thrombotic therapy with aspirin or clopidogrel is important to reduce cardiovascular events but does not affect symptoms of claudication. Patients with rest limb ischemia or ulceration should be re-vascularized to minimize the chance of limb loss. Percutaneous re-vascularization is not without significant complications, however, and future research needs to focus on
inflammation, thrombosis, and restenosis in the PVD patient. Furthermore, new devices that tackle difficult lesions, drug-eluting stents, and pharmacological agents that reduce global atherosclerosis are on the horizon, and are likely to become critical components in the management of the PVD patient.

Owens et al (2011) stated that the endovascular management of symptomatic atherosclerotic SFA disease is challenging and requires consideration of unique anatomical, hemodynamic, and biomechanical factors. The current armamentarium of balloon catheters and flexible nitinol BMS have limited long-term effectiveness due to intimal hyperplasia resulting in re-stenosis. Unfortunately, the remarkably low re-stenosis rates achieved with drug-eluting stents (DES) placed in the coronary vasculature has not been replicated in the femoral artery. The reason for this is multi-factorial including delivery platforms, drug and dosage selection and trial design flaws. Currently, however, there are several novel therapies and delivery platforms in the development pipeline that have exhibited biologic effectiveness in pre-clinical and early clinical trials. While these offer promise in improving outcomes following lower extremity intervention, caution is warranted until the safety of these new technologies can be ensured.

Henry et al (2005) stated that percutaneous angioplasty and stent placement seem a useful technique for the treatment of vertebro-basilar insufficiency. This technique appears safe and effective for alleviating symptoms and improving blood flow to the cerebral circulation, with a low complications rate and good long-term results. However, this procedure needs experienced interventionists to choose the stent and have appropriate placement of the stent in the ostium of the vertebral artery (VA). The tortuosity of the VA may be technically challenging. The new coronary stents seem to be well-suited to treat atherosclerotic lesions of the origin and of the proximal VA. A large variability of restenosis risk has been reported. Drug-eluting stents may be the solution. The authors stated that prospective, randomized trials are needed to ascertain the clinical effectiveness of VA stenting in stroke prevention, its durability, and to define more clearly its indications.
Vermeersch and Agostoni (2005) noted that the percutaneous treatment of patients with obstructive atherosclerotic disease in degenerated coronary saphenous vein bypass grafts still remains one of the great challenges in interventional cardiology. These researchers discussed the actual evidence-based knowledge for the percutaneous management of this lesion subset, focusing in particular on the devices that are actually considered the "gold standard" for this treatment: BMS and distal protection devices. They commented on the negative results of the randomized trials regarding the promising polytetrafluoroethylene-covered stent-grafts, and offered insights into the currently available evidence for the use of DES in saphenous vein grafts. The authors stated that these devices are potentially the key promise for the long-term successful sealing of vein graft disease; however, clear and definitive data from controlled studies are needed.

Kolluri et al (2006) noted that renal artery stenosis (RAS) is a progressive manifestation of atherosclerosis. It is associated with hypertension and progressive renal failure. Non-invasive testing includes renal artery duplex, computed tomographic angiography and magnetic resonance angiography. Percutaneous transluminal renal angioplasty and stenting (PTRAS) is indicated for significant atherosclerotic RAS while percutaneous transluminal renal angioplasty is indicated for fibromuscular dysplasias associated with the proper clinical indications. PTRAS is associated with a high technical success rate and an acceptable adverse event and restenosis rate. Moreover, PTRAS appears to improve control of hypertension and renal preservation. All patients should be followed clinically and with periodic duplex ultrasonography. Restenosis is treated with repeat angioplasty and occasionally stenting. Current and future areas of investigation will involve distal protection and DES.

At the 2006 European Society/World Congress of Cardiology, results of 3 studies suggested that DES may lead to an increased risk of death and cardiac events compared with BMS. One study suggested an increase in death and Q-wave myocardial infarction (MI) in subjects receiving a sirolimus-eluting stent, while the other indicated that this type of DES might increase non-cardiac mortality.
In the first study, Camenzind and associates performed a meta-analysis on randomized clinical studies comparing 1st-generation DES with BMS. Sirolimus-eluting stent trials entailed the RAVEL, SIRIUS, E-SIRIUS, and C-SIRIUS, and included 878 patients fitted with the novel stent and 870 who received BMS. The PES trials entailed TAXUS II, IV, V, and VI, and included information on 1,685 patients fitted with this stent and 1,675 who received BMS. The pooled incidence of death and Q-wave MI combined, analyzed from within the program by time points of follow-up, was significantly higher with the sirolimus-eluting stent than the BMS at 3 years, at 6 % versus 4 %, representing a 33 % relative increase in risk. In PES trials, the incidence of the combined endpoint at 3 years was 3.5 % with the DES compared with 3.1 % for the BMS. Pooling the latest follow-up data from each trial program revealed that the incidence all-cause death or MI was 2.4 % higher with the sirolimus-eluting stent than the BMS (6.3 % versus 3.9 %) and 0.3 % higher for PES than the BMS (2.6 % versus 2.3 %). Further analysis indicated that the rate of total mortality and Q-wave MI combined was a significant 38 % higher with the sirolimus-eluting stent versus the BMS (p = 0.03), while there was a trend towards a 16 % higher incidence with the PES. These researchers warned against indiscriminate use of 1st-generation DES and said that use of BMS may still be maintained, while awaiting safer 2nd-generation DES.

In the second study, Nordmann et al conducted a meta-analysis of randomized controlled trials that compared sirolimus-eluting stents and PES with BMS in their effect on total, cardiac, and non-cardiac mortality using last follow-up data. They found that although there was a trend to benefits with the DES for reducing total mortality at 1 year compared with BMS, there was a trend to increased mortality in years 2, 3, and 4 of follow-up. Furthermore, at 2 and 3 years’ follow-up, there was increased non-cardiac mortality (cancer, lung disease, and stroke) with the sirolimus-eluting stent versus the BMS (odds ratio = 2.74 and 2.04, respectively), the majority of which related to cancer. These investigators concluded that preliminary evidence suggests that sirolimus-eluting stents but not PES may lead to increased non-cardiac mortality. Follow-up and assessment of cause-specific deaths in patients receiving DES are mandatory to determine the
A third study tracked stent thrombosis rates in 8,000-plus patients enrolled in studies in Holland and Switzerland. Wenaweser reported that over 3 years, the cumulative rate of thrombosis was 2.9 %, but what was disturbing was that the rate was linear -- starting at 1.2 % at 30 days (similar to BMS) and then 0.6 % each year thereafter. Unlike BMS, thrombosis did not seem to wane with time, but continued to increase at the same rate, confirming concerns that DES suppress cell growth too much in some individuals, opening the door to thrombosis, which have serious consequences.

In the light of ongoing concerns over the safety of DES, the Society for Cardiovascular Angiography and Interventions (SCAI) has issued guidelines for use of the devices (Hodgson et al, 2007). The guidelines advise physicians to ensure that patients meet published guidelines' criteria for percutaneous coronary intervention before implantation of any stent. The guidelines also recommend that the physician decide on an individual-patient basis whether a DES, BMS, or surgical revascularization is most appropriate; discuss the risks and benefits with the patient; and document it in the medical record. The guidelines recommend that providers know which patients (those with diabetes, renal failure, etc.) and lesions (complex, long, small-diameter, etc.) carry high-risk for thrombosis with DES. Ideally, physicians should assess patients' likelihood of long-term compliance with dual antiplatelet therapy before implantation. Continuation for 1 year is strongly recommended in patients not at high risk for bleeding, and continuation beyond 1 year should be considered in patients at higher risk for stent thrombosis.

Tu and colleagues (2007) stated that the placement of DES decreases the frequency of repeat re-vascularization procedures in patients undergoing PCI in randomized clinical trials. However, there is uncertainty about the effectiveness of DES, and increasing concern about their safety, in routine clinical practice. From the Cardiac Care Network of Ontario's population-based clinical registry of all patients undergoing PCI in Ontario, Canada, these investigators identified a well-balanced cohort of 3,751
pairs of patients, matched on the basis of propensity score, who received either BMS alone or DES alone during an index PCI procedure between December 1, 2003, and March 31, 2005. The primary outcomes of the study were the rates of target-vessel re-vascularization, MI, and death. The 2-year rate of target-vessel re-vascularization was significantly lower among patients who received DES than among those who received BMS (7.4 % versus 10.7 %, p < 0.001). Drug-eluting stents were associated with significant reductions in the rate of target-vessel re-vascularization among patients with 2 or 3 risk factors for re-stenosis (i.e., presence of diabetes, small vessels [less than 3 mm in diameter], and long lesions [greater than or equal to 20 mm]) but not among lower-risk patients. The 3-year mortality rate was significantly higher in the BMS group than in the DES group (7.8 % versus 5.5 %, p < 0.001), whereas the 2-year rate of MI was similar in the 2 groups (5.2 % and 5.7 %, respectively; p = 0.95). The authors concluded that DES are effective in reducing the need for target-vessel re-vascularization in patients at highest risk for re-stenosis, without a significantly increased rate of death or MI.

In a meta-analysis, Stettler et al (2007) compared the safety and effectiveness of 2 DES (sirolimus-eluting stent and PES) and BMS. These investigators searched relevant sources from inception to March, 2007, and contacted investigators and manufacturers to identify randomized controlled trials in patients with coronary artery disease that compared DES with BMS, or that compared sirolimus-eluting stents head-to-head with PES. Safety outcomes included mortality, MI, and definite stent thrombosis; the effectiveness outcome was target lesion re-vascularization. These researchers included 38 trials (18,023 patients) with a follow-up of up to 4 years. Trialists and manufacturers provided additional data on clinical outcomes for 29 trials. A network meta-analysis with a mixed-treatment comparison method to combine direct within-trial comparisons between stents with indirect evidence from other trials while maintaining randomization was performed. Mortality was similar in the 3 groups: hazard ratios (HR) were 1.00 (95 % CI: 0.82 to 1.25) for sirolimus-eluting versus BMS, 1.03 (0.84 to 1.22) for PES versus BMS, and 0.96 (0.83 to 1.24) for sirolimus-eluting versus PES. Sirolimus-eluting stents
were associated with the lowest risk of MI (HR 0.81, 95 % CI: 0.66 to 0.97, p = 0.030 versus BMS; 0.83, 0.71 to 1.00, p = 0.045 versus PES). There were no significant differences in the risk of definite stent thrombosis (0 days to 4 years). However, the risk of late definite stent thrombosis (greater than 30 days) was increased with PES (HR 2.11, 95 % CI: 1.19 to 4.23, p = 0.017 versus BMS; 1.85, 1.02 to 3.85, p = 0.041 versus sirolimus-eluting stents). The reduction in target lesion re-vascularization seen with DES compared with BMS was more pronounced with sirolimus-eluting stents than with PES (0.70, 0.56 to 0.84; p = 0.0021). The authors concluded that the risks of mortality associated with DES and BMS are similar. Sirolimus-eluting stents seem to be clinically better than BMS and PES.

In a meta-analysis, Schomig et al (2007) made a synthesis of the available evidence on the relative safety and effectiveness of 2 DES: (i) sirolimus-eluting stents (SES) and (ii) PES in patients with coronary artery disease. A total of 16 randomized trials of SES versus PES with a total number of 8,695 patients were included in this analysis. A full set of individual outcome data from 5,562 patients was also available. Mean follow-up period ranged from 9 to 37 months. The primary effectiveness end point was the need for re-intervention (target lesion re-vasculization). The primary safety end point was stent thrombosis. Secondary end points were death and recurrent MI. No significant heterogeneity was found across trials. Compared with PES, SES significantly reduced the risk of re-intervention (HR 0.74; 95 % CI: 0.63 to 0.87, p < 0.001) and stent thrombosis (HR 0.66; 95 % CI: 0.46 to 0.94, p = 0.02) without significantly impacting on the risk of death (HR 0.92; 95 % CI: 0.74 to 1.13, p = 0.43) or MI (HR 0.84; 95 % CI: 0.69 to 1.03, p = 0.10). The authors concluded that SES are superior to PES in terms of a significant reduction of the risk of re-intervention and stent thrombosis. The risk of death was not significantly different between the 2 DES, but there was a trend toward a higher risk of MI with PES, especially after the first year from the procedure. The observation that SES are superior to PES is in agreement with the analysis from Gurm et al (2008) who reported that patients treated with SES appear to have a significantly lower risk of re-stenosis and need for target vessel re-vascularization compared with those treated with PES.
The National Institute for Health and Clinical Excellence's (NICE, 2008) recommended the use of DES for the treatment of coronary artery disease only if the target artery to be treated has less than a 3-mm caliber or the lesion is longer than 15 mm, and the price difference between DES and BMS is no more than 300 pounds sterling.

Pfisterer et al (2009) evaluated the long-term benefit-risk ratio of DES versus BMS relative to stent size. All 826 consecutive BASKET (BAsel Stent Kosten-Effektivitäts Trial) patients randomized 2:1 to DES versus BMS were followed after 3 years. Data were analyzed separately for patients with small stents (less than 3.0 mm vessel/less than 4.0 mm bypass grafts, n = 268) versus only large stents (greater than or equal to 3.0 mm native vessels, n = 558). Clinical events were related to stent thrombosis. Three-year clinical target vessel revascularization (TVR) rates remained borderline reduced after DES [9.9 versus 13.9 % (BMS), p = 0.07], particularly in patients with small stents (10.7 versus 19.8 %, p = 0.03; large stents: 9.5 versus 11.5 %, p = 0.44). Cardiac death/MI rates (12.7 versus 10.0 %, p = 0.30) were similar, however, death/MI beyond 6 months was higher after DES [9.1 versus 3.8 % BMS, p = 0.009], mainly due to increased late death/MI in patients with large stents (9.7 versus 3.1 %, p = 0.006). The results paralleled findings for stent thrombosis. The authors concluded that the clinical benefit of DES was maintained at no overall increased risk of death or death/MI up to 3 years. However, death/MI rates were increased in DES versus BMS patients beyond 6 months, especially in patients with large stents, paralleling findings for stent thrombosis. Thus, stent size appears to influence the 3-year benefit-risk ratio after DES implantation.

Kirtane and colleagues (2009) performed a meta-analysis of DES studies to estimate the relative impact of DES versus BMS on safety and efficacy end points, particularly for non-FDA-labeled indications. Comparative DES versus BMS studies published or presented through February 2008 with greater than or equal to 100 total patients and reporting mortality data with cumulative follow-up of greater than or equal to 1 year were identified. Data were abstracted from studies comparing DES with BMS; original source data were used when available. Data from 9,470 patients
in 22 randomized controlled trials (RCTs) and from 182,901 patients in 34 observational studies were included. Observational and RCT data were analyzed separately. In RCTs, DES (compared with BMS) were associated with no detectable differences in overall mortality (HR, 0.97; 95% CI: 0.81 to 1.15; p = 0.72) or MI (HR, 0.95; 95% CI: 0.79 to 1.13; p = 0.54), with a significant 55% reduction in target vessel re-vascularization (HR, 0.45; 95% CI: 0.37 to 0.54; p < 0.0001); point estimates were slightly lower in off-label compared with on-label analyses. In observational studies, DES were associated with significant reductions in mortality (HR, 0.78; 95% CI: 0.71 to 0.86), MI (HR, 0.87; 95% CI: 0.78 to 0.97), and TVR (HR, 0.54; 95% CI: 0.48 to 0.61) compared with BMS. The authors concluded that in RCTs, no significant differences were observed in the long-term rates of death or MI after DES or BMS use for either off-label or on-label indications. In real-world non-randomized observational studies with greater numbers of patients but the admitted potential for selection bias and residual confounding, DES use was associated with reduced death and MI. Both RCTs and observational studies demonstrated marked and comparable reductions in target vessel re-vascularization with DES compared with BMS. These data in aggregate suggested that DES are safe and efficacious in both on-label and off-label use, but highlighted differences between RCT and observational data comparing DES and BMS.

In a systematic review and meta-analysis, Brar et al (2009) compared outcomes by stent type for death, MI, TVR, and stent thrombosis in RCTs of ST-segment elevation myocardial infarction (STEMI). A secondary analysis was performed among registry studies. These investigators searched Medline, Embase, the Cochrane Library, and Internet sources for articles comparing outcomes between DES and BMS among patients with STEMI between January 2000 and October 2008. Randomized controlled trials and registries including patients 18 years of age and older receiving a DES or BMS were included. These researchers extracted variables related to the study design, setting, participants, and clinical end points. A total of 13 RCTs were identified (n = 7,352). Compared with BMS, DES significantly reduced TVR (relative risk [RR]: 0.44; 95% CI: 0.35 to 0.55), without increasing death (RR: 0.89; 95% CI: 0.70 to 1.14),
MI (RR: 0.82; 95 % CI: 0.64 to 1.05), or stent thrombosis (RR: 0.97; 95 % CI: 0.73 to 1.28). These observations were durable over 2 years. Among 18 registries (n = 26,521), DES significantly reduced TVR (RR: 0.54; 95 % CI: 0.40 to 0.74) without an increase in MI (RR: 0.87, 95 % CI: 0.62 to 1.23). Death was significantly lower in the DES group within 1 year of the index PCI, but there were no differences within 2 years (p = 0.45). The authors concluded that the use of DES appears safe and efficacious in RCTs and registries of patients with STEMI. The DES significantly reduce TVR compared with BMS, without an increase in death, MI, or stent thrombosis within 2 years of the index procedure.

Trikalinos and associates (2009) noted that over the past 2 decades, percutaneous transluminal balloon coronary angioplasty (PTCA), BMS, and DES succeeded each other as catheter-based treatments for coronary artery disease. These researchers carried out a systematic overview of RCTs comparing these interventions with each other and with medical therapy in patients with non-acute coronary artery disease. They searched Medline for trials contrasting at least 2 of the 4 interventions (PTCA, BMS, DES, and medical therapy). Eligible outcomes were death, MI, coronary artery bypass grafting, TLR/TVR, and any re-vascularisation. Random effects meta-analyses summarized head-to-head (direct) comparisons, and network meta-analyses integrated direct and indirect evidence. A total of 61 eligible trials (25,388 patients) investigated 4 of 6 possible comparisons between the 4 interventions; no trials directly compared DES with medical therapy or PTCA. In all direct or indirect comparisons, succeeding advancements in PCI did not produce detectable improvements in deaths or MI. The RR for indirect comparisons between DES and medical therapy was 0.96 (95 % CI: 0.60 to 1.52) for death and 1.15 (0.73 to 1.82) for MI. By contrast, these investigators recorded sequential significant reductions in target lesion or vessel re-vascularisation with BMS compared with PTCA (RR 0.68 [0.60 to 0.77]) and with DES compared with BMS (0.44 [0.35 to 0.56]). The RR for the indirect comparison between DES and PTCA for TLR/TVR was 0.30 (0.17 to 0.51). The authors concluded that sequential innovations in the catheter-based treatment of non-acute coronary artery disease showed no evidence of an effect on death or MI when compared with
medical therapy. These results lend support to present recommendations to optimize medical therapy as an initial management strategy in patients with this disease.

Biondi-Zoccai et al (2008) conducted a systematic review of basic science and clinical evidence on the Xience V everolimus-eluting stents (EES), by thoroughly searching PubMed and online databases (updated September 2007). They also compared the clinical results of Xience V versus PES (Taxus) and SES (Cypher) by means of direct and indirect comparison meta-analysis. A total of 3 clinical studies has been retrieved focusing on Xience V, however both most recent and important trials were still unpublished. The first trial compared Xience V versus BMS, whereas the other 2 RCTs compared Xience V versus Taxus. Direct meta-analysis of Xience V versus Taxus showed that Xience V was significantly superior to Taxus in preventing binary angiographic re-stenosis and TVR (p < 0.05 for both). Indirect comparison between Xience V and Cypher, exploiting a recent 16-trial large meta-analysis, showed that Xience V was at least as effective as Cypher in preventing TVR (p = 0.12). The authors concluded that EES (Xience V) appear as a major breakthrough in coronary interventions, and superior efficacy has already been demonstrated in comparison to PES (Taxus). Data available to date also suggested that Xience V is at least as effective as SES (Cypher). Whether long-term results and direct comparison to Cypher will also be favorable remains to be established by future clinical trials.

Stone and colleagues (2009) reported the 2-year clinical follow-up data of EES in the treatment of patients with de novo native coronary artery lesions (SPIRIT) III trial. A total of 1,002 patients with up to 2 de novo native coronary artery lesions (reference vessel diameter, 2.5 to 3.75 mm; lesion length less than or equal to 28 mm) were randomized 2:1 to EES versus PES. Anti-platelet therapy consisted of aspirin indefinitely and a thienopyridine for greater than or equal to 6 months. Between 1 and 2 years, patients treated with EES compared with PES tended to have fewer episodes of protocol-defined stent thrombosis (0.2 % versus 1.0 %; p = 0.10) and MI (0.5 % versus 1.7 %; p = 0.12), with similar rates of cardiac death (0.3 % versus 0.3 %; p = 1.0) and
TVR (2.9 % versus 3.0 %; p = 1.0). As a result, at the completion of the 2-year follow-up, treatment with EES compared with PES resulted in a significant 32 % reduction in target vessel failure (10.7 % versus 15.4 %; HR, 0.68; 95 % CI: 0.48 to 0.98; p = 0.04) and a 45 % reduction in major adverse cardiac events (cardiac death, MI, or target lesion revascularization; 7.3 % versus 12.8 %; hazard ratio, 0.55; 95 % CI: 0.36 to 0.83; p = 0.004). Among the 360 patients who discontinued clopidogrel or ticlopidine after 6 months, stent thrombosis subsequently developed in 0.4 % of EES patients versus 2.6 % of PES patients (p = 0.10). The authors concluded that patients treated with EES rather than PES experienced significantly improved event-free survival at a 2-year follow-up in the SPIRIT III trial, with continued divergence of the hazard curves for target vessel failure and major adverse cardiac events between 1 and 2 years evident. The encouraging trends toward fewer stent thrombosis episodes after 6 months in EES-treated patients who discontinued a thienopyridine and after 1 year in all patients treated with EES rather than PES deserve further study.

Chevalier and associates (2008) compared zotarolimus-eluting stents (ZES) with PES in a randomized trial of percutaneous intervention for de novo coronary artery stenosis. The primary end point was defined as non-inferiority of in-segment late lumen loss after 9 months. A total of 29 investigative sites in Europe, Australia, as well as New Zealand enrolled 401 patients, 396 of whom received a study stent. After 9 months, late lumen loss was significantly greater in the ZoMaxx group (in-stent 0.67 +/- 0.57 mm versus 0.45 +/- 0.48 mm; p < 0.001; in-segment 0.43 +/- 0.60 mm versus 0.25 +/- 0.45 mm; p = 0.003), resulting in significantly higher rates of greater than 50 % angiographic restenosis (in-stent 12.9 % versus 5.7 %; p = 0.03; in-segment 16.5 % versus 6.9 %; p = 0.007). The upper bound of the 95 % CI on the difference in in-segment late lumen loss between the 2 treatment groups (0.27 mm) exceeded the 0.25 mm value pre-specified for non-inferiority. There were no significant differences between ZoMaxx and Taxus-treated groups with respect to TVR (8.0 % versus 4.1 %; p = 0.14), major adverse cardiac events (12.6 % versus 9.6 %; p = 0.43), or stent thrombosis (0.5 % in both groups). The authors concluded that after 9 months, ZES showed
less neointimal inhibition than PES, as shown by higher in-stent late loss and re-stenosis by qualitative coronary angiography.

Waseda and colleagues (2009) compared the vessel response between ZES and PES using intra-vascular ultrasound (IVUS). Data were obtained from patients with serial (baseline and 8-months follow-up) IVUS analysis available (n = 198). Volumetric analysis was performed for vessel, lumen, plaque, stent, and neointima. Cross-sectional narrowing (given as percentage) was defined as neointimal area divided by stent area. Neointima-free frame ratio was calculated as the number of frames without IVUS-detectable neointima divided by the total number of frames within the stent. Subsegment analysis was performed at every matched 1-mm subsegment throughout the stent. At follow-up, the ZES group showed significantly greater percentage of neointimal obstruction (16.6 +/- 12.0 % versus 9.9 +/- 8.9 %, p < 0.01) and maximum cross-sectional narrowing (31.8 +/- 16.1 % versus 25.2 +/- 14.9 %, p < 0.01) with smaller minimum lumen area than the PES group did. However, the incidence of maximum cross-sectional narrowing greater than 50 % was similar in the 2 groups. Neointima-free frame ratio was significantly lower in the ZES group. In overall analysis, whereas the PES group showed positive remodeling during follow-up (13.7 +/- 4.2 mm(3)/mm to 14.3 +/- 4.3 mm(3)/mm), the ZES group showed no significant difference (12.7 +/- 3.6 mm(3)/mm to 12.9 +/- 3.5 mm(3)/mm). In subsegment analysis, significant focal positive vessel remodeling was observed in 5 % of ZES and 25 % of PES cases (p < 0.05). The authors concluded that there were different global and focal vessel responses for ZES and PES. Both DES showed a similar incidence of lesions with severe narrowing despite ZES having a moderate increase in neointimal hyperplasia compared with neointimal hyperplasia in PES. There was a relatively lower neointima-free frame ratio in ZES, suggesting a greater extent of neointimal coverage.

The Endeavor ZES from Medtronic received FDA approval on February 1, 2008, while Xience V EES from Abbott Vascular was approved by FDA on July 2, 2008 (Doostzadeh et al, 2010).

Machan (2006) reviewed the use of DES outside the coronary
artery. The majority of research and clinical data on DES are from their use in coronary artery atherosclerosis; however, these devices can be used outside the coronary circulation in both vascular and non-vascular structures. In non-coronary arteries the principal indication for DES is the same as in the coronary circulation, prevention of re-stenosis. Human experience has been essentially limited to trials or compassionate use; 2 small controlled studies and a number of small observational single-center reports have been published, and there are trials in progress. To date, the data have not been as compelling as in the coronary circulation. The physical characteristics of each vascular bed such as external compressive forces, blood flow rates, wall thickness relative to lumen size, as well as vessel wall composition differ significantly from the coronary circulation and each presents unique challenges to local drug delivery. Outside the vascular bed, the principal expected use is the prevention of tissue ingrowth following stent insertion in tubular structures such as the trachea, esophagus or bile ducts. The authors concluded that considerable further study of DES is needed in each anatomical region to determine the ideal stent/drug combination and clinical appropriateness.

Lee (2009) noted that in unresectable malignant bile duct obstruction, endoscopic stent insertion is the treatment of choice. However, the current stent allows only mechanical palliation of the obstruction, and has no anti-tumor effect. Currently, in the vascular field, the DES is very highly favored. The requirements for a DES in a non-vascular tract, such as the bile duct, are far different from those of a DES to be used in the vascular tract. The non-vascular DES must suppress tumor proliferation and mucosal hyperplasia. For example, the non-vascular stent might be covered with a membrane that gradually releases a chemo-agent. Currently, there is not much experience with DES in the bile duct. Nevertheless, these researchers are continuously testing many anti-tumor agents in animal and human studies. The authors concluded that they expect and hope DES will work effectively for tumor cells in diverse ways and, more importantly, will prolong stent patency and the patients' survival periods. However, considerable investigation and a clinical study of DES will be required to achieve these goals.
In a meta-analysis, Joyal et al (2010) compared DES to BMS for the treatment of vein graft stenosis. PubMed and the Cochrane clinical trials database were systematically searched to identify all RCTs and observational studies examining DES for vein graft stenosis published in English between 2003 and 2009. Inclusion criteria included follow-up duration greater than or equal to 6 months. Data were stratified by study design and pooled using random effects models. A total of 20 studies were found to meet inclusion criteria; 18 studies were observational and 2 were RCTs. In observational studies, DES were associated with a reduction in MACE (odds ratio [OR] 0.50, 95 % CI: 0.35 to 0.72), death (OR 0.69, 95 % CI: 0.53 to 0.91), TVR (OR 0.54, 95 % CI: 0.37 to 0.79), and TLR (OR 0.54, 95 % CI: 0.37 to 0.78). The incidence of MI was similar between groups. In the RCTs, pooled results were inconclusive because of small sample sizes. The authors concluded that although data from observational studies suggest that the use of DES for vein graft stenosis has favorable effects on MACE, death, TVR, and TLR, these data should be interpreted with caution due to their observational nature. Corresponding RCT data are inconclusive. There remains a need for large multi-center RCTs to address the safety and effectiveness of DES for vein graft stenosis.

Nakagawa (2011) stated that the effectiveness of the use of DES in the treatment of STEMI, a representative condition of acute coronary syndrome, is still unknown. In this article, data of registry, randomized, and meta-analyses studies were reviewed. Drug eluting stents showed a consistent trend toward decreasing the risk of repeat re-vascularization without increasing the incidence of death, recurrent MI, and stent thrombosis as compared to BMS. The findings concerning the use of DES in patients with STEMI are: (i) its short-term effect of reducing the re-stenosis and repeat re-vascularization rates is evident; (ii) no randomized studies have demonstrated the usefulness of DES in the prevention of death and recurrent MI; (iii) no randomized or meta-analyses studies have shown results sufficient to eliminate long-term safety concerns; and most importantly, and (iv) there are no data clearly indicating safety concerns.

Palmerini et al (2012) compared the risk of thrombosis between
BMS and DES. For this network meta-analysis, RCTs comparing different DES, or DES with BMS currently approved in the United States were identified through Medline, Embase, Cochrane databases, and proceedings of international meetings. Information about study design, inclusion and exclusion criteria, sample characteristics, and clinical outcomes was extracted. A total of 49 trials including 50,844 patients randomly assigned to treatment groups were analysed. One-year definite stent thrombosis was significantly lower with cobalt-chromium everolimus eluting stents (CoCr-EES) than with BMS (odds ratio [OR] 0.23, 95 % CI: 0.13 to 0.41). The significant difference in stent thrombosis between CoCr-EES and BMS was evident as early as 30 days (OR 0.21, 95 % CI: 0.11 to 0.42) and was also significant between 31 days and 1 year (OR 0.27, 95 % CI: 0.08 to 0.74). CoCr-EES were also associated with significantly lower rates of 1-year definite stent thrombosis compared with paclitaxel-eluting stents (OR 0.28, 95 % CI: 0.16 to 0.48), permanent polymer-based sirolimus-eluting stents (OR 0.41, 95 % CI: 0.24 to 0.70), phosphorylcholine-based zotarolimus-eluting stents (OR 0.21, 95 % CI: 0.10 to 0.44), and Resolute zotarolimus-eluting stents (OR 0.14, 95 % CI: 0.03 to 0.44). At 2-year follow-up, CoCr-EES were still associated with significantly lower rates of definite stent thrombosis than were BMS (OR 0.35, 95 % CI: 0.17 to 0.69) and paclitaxel-eluting stents (OR 0.34, 95 % CI: 0.19 to 0.62). No other DES had lower definite thrombosis rates compared with BMS at 2-year follow-up. The authors concluded that in RCTs completed to date, CoCr-EES has the lowest rate of stent thrombosis within 2 years of implantation. The finding that CoCr-EES also reduced stent thrombosis compared with BMS, if confirmed in future RCTs, represents a paradigm shift.

De Luca and colleagues (2012) performed a meta-analysis using individual patient data to evaluate the long-term safety and effectiveness of DES compared with BMS in patients undergoing primary PCI for STEMI. Formal searches of electronic databases (MEDLINE and CENTRAL) and scientific session presentations from January 2000 to June 2011 were carried out. These investigators examined all completed randomized trials of DES for STEMI. Individual patient data were obtained from 11 of 13 trials identified, including a total of 6,298 patients (3,980 [63.2 %]
randomized to DES [99 % sirolimus-eluting or paclitaxel-eluting stents] and 2,318 [36.8 %] randomized to BMS). At long-term follow-up (mean [SD], 1,201 [440] days), DES implantation significantly reduced the occurrence of TVR (12.7 % versus 20.1 %; hazard ratio [95 % CI], 0.57 [0.50 to 0.66]; p < 0.001, p value for heterogeneity, 0.20), without any significant difference in terms of mortality, re-infarction, and stent thrombosis. However, DES implantation was associated with an increased risk of very late stent thrombosis and re-infarction. The authors concluded that the present pooled patient-level meta-analysis demonstrated that among patients with STEMI undergoing primary PCI, sirolimus-eluting and paclitaxel-eluting stents compared with BMS are associated with a significant reduction in TVR at long-term follow-up. Although there were no differences in cumulative mortality, re-infarction, or stent thrombosis, the incidence of very late re-infarction and stent thrombosis was increased with these DES.

Werner et al (2012) presented the 5-year angiographical and clinical results of a retrospective registry assessing the performance of sirolimus-eluting stents (SES) in the treatment of infra-popliteal atherosclerotic disease. From 2004 to 2009, a total of 158 patients (95 men; mean age of 71.9 years) with chronic lower limb ischemia (Rutherford categories 3 to 6) underwent primary SES placement in focal infra-popliteal lesions. The angiographical endpoint was patency, defined as freedom from in-stent stenosis (ISS) greater than 50 %. Clinical endpoints were death, amputation, and bypass surgery. Results were correlated with patient and lesion characteristics and cumulative outcomes were assessed with Kaplan-Meier analysis. Technical success was achieved in all cases. The primary patency rates were 97.0 % after 6 months, 87.0 % after 12 months, and 83.8 % at 60 months. In-stent stenosis was predominantly observed in the first year after stent placement. Female gender was associated with a higher rate of ISS. During clinical follow-up of 144 (91 %) patients over a mean 31.1 +/- 20.3 months, there were 27 (18.8 %) deaths, 4 (2.8 %) amputations, and no bypass surgery. Clinical status improved in 92 % of the patients with critical limb ischemia (CLI) and 77 % of the patients suffering from claudication (p = 0.022). The authors concluded that treatment of focal infra-popliteal
lesions with SES showed encouraging long-term angiographical results in this registry. Clinical improvement was evident, but more pronounced in CLI patients than in patients suffering from claudication. They stated that further studies are needed to evaluate the potential clinical benefit of SES as compared to balloon angioplasty or BMS in the treatment of infra-popliteal lesions.

Athappan and Ponniah (2009) stated that studies on percutaneous transluminal cardiac angioplasty (PTCA) in patients with end stage renal disease (ESRD) on hemodialysis (HD) have suggested high rates of procedural complications and re-stenosis. Bare metal stent PCI has significantly reduced re-stenosis and subsequent TLR in these patients, although not to the level of non-hemodialysis (NH) controls. The introduction of DES has dramatically reduced re-stenosis rates compared with BMS in patients with various clinical and angiographic characteristics, however their impact on patients with ESRD on dialysis is unclear due to consistent exclusion of this population from major trials. The purpose of this study was therefore to compare the outcomes of PCI with DES and BMS when used for ESRD patients on HD, by meta-analytical techniques. Comparative studies published between January 2002 and January 2009 of DES versus BMS in ESRD patients on dialysis were identified using an electronic search and reviewed using a random effects model. The primary endpoints of this study were the hard endpoints of mortality, MI and TLR. A secondary endpoint of this analysis was late luminal loss. In-hospital mortality and MI were also assessed. Heterogeneity was assessed using Cochrane Q and I(2) statistics. A total of 5 reports comprising 641 patients (279 DES, and 362 BMS) were included in the analysis. All the studies were non-randomized comparisons between DES and BMS. The length of follow-up was in the range between 9 and 12 months. In-hospital clinical outcomes were similar between the 2 groups. At follow-up there was a trend towards lower TLR (OR 0.50, CI: 0.27 to 0.93, p = 0.011 I(2) = 48 %) and decreased late luminal loss (weighted mean difference [WMD] -0.34, CI: -0.58 to 0.10, p = 0.09, I(2) = 58 %) in patients undergoing PCI with implantation of DES. There was no difference in the rates of all-cause mortality (OR 0.66, CI: 0.40 to 1.08, p = 0.070, I(2) = 0 %), and MI (OR 1.35,
The authors concluded that in ESRD patients on HD undergoing PCI, DES are safe and reduce repeat revascularizations. Moreover, they noted that the limited number of patients as well as the limited quality of primary studies included need careful interpretation of these results. They stated that further well-designed, large RCTs are needed to establish the strategy of management in ESRD patients undergoing PCI.

The potential superiority of DES over BMS in reducing TLR or TVR in patients with ESRD on HD has not been established. Small studies comparing DES to BMS in this population have yielded inconclusive results mainly due to the small sample size. Abdel-Latif et al (2010) examined the total weight of evidence regarding the use of DES and BMS in patients with ESRD. These investigators searched MEDLINE, EMBASE, Science Citation Index, CINAHL, and the Cochrane CENTRAL database of controlled clinical trials (December 2009) for controlled trials comparing DES to BMS in ESRD patients. They conducted a fixed-effects meta-analysis across 7 eligible studies (n = 869 patients). Compared with BMS-treated patients, DES-treated patients had significantly lower TLR/TVR (OR 0.55 CI: 0.39 to 0.79) and major adverse cardiac events (MACE) (OR 0.54; CI: 0.40 to 0.73). The absolute risk reduction (ARR) with DES in TLR/TVR was -0.09 (CI: -0.14 to -0.04; NNT 11) and in MACE was -0.13 (CI: -0.19 to -0.07; NNT 8). A trend towards lower incidence of all-cause mortality was also noted with DES (OR 0.68; CI: 0.45 to 1.01). No significant differences were noted between the 2 groups in the relative or absolute risk of MI. The authors concluded that the use of DES in patients with ESRD is safe and yields significant reduction in the risk of TLR/TVR and MACE. Moreover, they stated that larger RCTs are needed to confirm the results of this meta-analysis and establish the appropriate stent choice in this high-risk population.

Otsuka et al (2011) stated that long-term outcomes after SES implantation in HD patients have remained controversial. These researchers investigated the impact of HD on outcomes after SES implantation. They analyzed the data on 2,050 patients who underwent SES implantation in a multi-center prospective registry in Japan. Three-year clinical outcomes were compared between
the HD group (n = 106) and the NH group (n = 1,944). At the 3-year clinical follow-up, the rates of unadjusted cardiac mortality (HD: 16.3 versus NH: 2.3 %) and TLR (HD: 19.4 versus NH: 6.6 %) were significantly higher in the HD group than the NH group (p < 0.001). Although HD group had a numerically higher stent thrombosis rate, the difference in stent thrombosis between the 2 groups (HD: 2.0 versus NH: 0.7 %) did not reach statistical significance. Using Cox's proportional-hazard models with propensity score adjustment for baseline differences, the HD group had higher risks of TLR [HD: 16.3 versus NH: 6.1 %; HR, 2.83; 95 % CI: 1.62 to 4.93, p = 0.0003] and cardiac death (HD: 12.3 versus NH: 2.3 %; HR, 5.51; 95 % CI: 2.58 to 11.78, p < 0.0001). The consistent results of analyses, whether unadjusted or adjusted for other baseline clinical and procedural differences, identify HD as an independent risk factor for cardiac death and TLR. The authors concluded that PCI with SES in HD patients has a higher incidence of repeat revascularization and mortality compared with those in NH patients. Moreover, HD appears to be strongly associated with mortality and repeat revascularization even after SES implantation.

Charytan et al (2011) examined the long-term clinical outcomes following DES or BMS placement in patients with severely reduced glomerular filtration rate (GFR). All adults with chronic kidney disease (CKD) and severely decreased GFR (GFR; serum creatinine greater than 2.0 mg/dL or dialysis dependence) undergoing PCI with stent placement between April 1, 2003, and September 30, 2005, at all acute-care nonfederal hospitals in Massachusetts were included in this analysis. Patients were classified as DES-treated if all stents were drug eluting and BMS-treated if all stents were bare metal. Patients treated with both types of stents were excluded from the primary analysis. 2-year crude mortality risk differences (drug-eluting - bare-metal stents) were determined from vital statistics records, and risk-adjusted mortality, MI, and revascularization differences were estimated using propensity score matching of patients with severely reduced GFR based on clinical and procedural information collected at the index admission. A total of 1,749 patients with severely reduced GFR (24 % dialysis dependent) were treated with DES (n = 1,256) or BMS (n = 493) during the study. Overall
2-year mortality was 32.8 % (unadjusted DES versus BMS; 30.1 % versus 39.8 %; p < 0.001). After propensity score matching 431 patients with a DES to 431 patients with a BMS, 2-year risk-adjusted mortality, MI, and TVR rates were 39.4 % versus 37.4 % (risk difference, 2.1 %; 95 % CI: -4.3 to 8.5; p = 0.5), 16.0 % versus 19.0 % (risk difference, -3.0 %; 95 % CI: -8.2 to 2.1; p = 0.3), and 13.0 % versus 17.6 % (risk difference, -4.6 %; 95 % CI: -9.5 to 0.3; p = 0.06). The authors concluded that in patients with severely decreased GFR, treatment with DES was associated with a modest decrease in TVR not reaching statistical significance and was not associated with a difference in risk-adjusted rates of mortality or MI at 2 years compared with BMS.

Green et al (2011) examined the safety and effectiveness of DES in patients with CKD not on renal replacement therapy. Patients were drawn from the National Heart, Lung, and Blood Institute Dynamic Registry and were stratified by renal function based on estimated GFR. Of the 4,157 participants, 1,108 had CKD ("low GFR" less than 60 ml/min/1.73 m²), whereas 3,049 patients had normal renal function ("normal GFR" greater than or equal to 60 ml/min/1.73 m²). For each stratum of renal function, these investigators compared risk of death, MI, or repeat revascularization between subjects who received DES and BMS at the index procedure. Patients with low GFR had higher 1-year rates of death and MI and a decreased rate of repeat revascularization compared to patients with normal GFR. Use of DES was associated with a decreased need for repeat revascularization in the normal-GFR group (adjusted HR 0.63, 95 % CI: 0.50 to 0.79, p <0.001) but not in the low-GFR group (HR 0.69, 95 % CI: 0.45 to 1.06, p = 0.09). Risks of death and MI were not different between the 2 stents in either patient population. The authors concluded that the presence of CKD predicted poor outcomes after PCI with high rates of mortality regardless of stent type. Moreover, the effect of DES in decreasing repeat revascularization appeared to be attenuated in these patients.

Also, an UpToDate review on “Use of stents for venous stenosis associated with dialysis vascular access” (Beathard, 2013) states that “Although not yet evaluated clinically for dialysis vascular access, there is preliminary evidence in animals that sirolimus-
eluting stents may provide short-term effectiveness in animal model arteriovenous grafts”.

McLoughlin and Byrne (2008) stated that self-expanding metal stents (SEMS) play an important role in the management of patients with malignant obstructing lesions in the gastrointestinal tract. Traditionally, they have been used for palliation in malignant gastric outlet and colonic obstruction as well as esophageal malignancy. The development of the polyflex stent, which is a removable self-expanding plastic stent, allows temporary stent insertion for benign esophageal disease and possibly for patients undergoing neoadjuvant chemotherapy prior to esophagectomy. Potential complications of SEMS insertion include perforation, tumor overgrowth or ingrowth, and stent migration. Newer stents are being developed with the aim of increasing technical and clinical success rates, while reducing complication rates. Other areas of development include biodegradable stents for benign disease and radioactive or drug-eluting stents for malignant disease. It is hoped that, in the future, newer stents will improve our management of these difficult conditions and, possibly, provide prognostic as well as symptomatic benefit in the setting of malignant obstruction.

Katsanos et al (2010) noted that minimally invasive image-guided insertion of SEMS in the upper gastrointestinal tract is the current treatment of choice for palliation of malignant esophageal or gastro-duodenal outlet obstructions. These investigators presented a concise review of contemporary stenting practice of the upper gastrointestinal tract, and the procedures in terms of appropriate patient evaluation, indications, and contraindications for treatment were analyzed, along with available stent designs, procedural steps, clinical outcomes, inadvertent complications, and future technology. Latest developments include biodegradable polymeric stents for benign disease and radioactive or drug-eluting stents for malignant obstructions.

Bioabsorbable Polymer Stents:

Bioabsorbable drug-eluting stents (DES) refers to the incomplete breakdown of material which may be partially digested and
remain indefinitely in local tissue. Stent material and polymer may be bioabsorbable. The majority of currently approved DES have a durable polymer, which remains permanently on the stent after the drug is eluted. The polymer itself may result in vascular inflammation or delay endothelialization and healing, therefore contributing to the risk of stent thrombosis. The premise of the bioabsorbable polymer stent is that with the polymer being completely biodegradable, it removes the potential stimulus for chronic inflammation, and the patient is essentially left with a bare-metal stent (Cutlip and Abbott, 2017).

Ma and colleagues (2012) stated that “Although some non-biodegradable polymer-coated DES claimed to be safe long-term, there remains caution regarding the inflammatory response. Thus, biodegradable polymers are being considered and investigated to store and deliver drugs. The most commonly used polymers now are poly(lactic acid) (PLA), poly(glycolic acid) and their copolymer, poly(lactic-co-glycolic acid) (PLGA), which can be fully degraded and metabolized by the body. A multitude of biodegradable polymer-coated stents are currently in clinical trials. For example, the Sparrow™ NiTi stent system (Surmodics Inc., Eden Prairie, MN, USA) employs SynBiosys™ biodegradable polymer PLGA to elute sirolimus; the CE-approved Biomatrix® stent (Biosensors International, Singapore), which was licensed to Terumo Corporation (Tokyo, Japan) with a new brand name (Nobori®) in May 2007, releases a sirolimus analogue, biolimus A9, from PLA coated on 316L stainless steel stent platform; both Excel® (JW Medical Systems, China) and Cura™ (OrbusNeich Medical, Inc., FL, USA) are PLA and sirolimus-coated stainless steel stents; Conor Medstent™ stent (Conor Medsystems, CA, USA) uses PLGA while Infinnium™ stent (Sahajanand Medical Technologies, India) utilizes PLA to elute paclitaxel. In spite of many promising preliminary results, the development of biodegradable polymers in DES is still a challenge”.

The Australian Safety and Efficacy Register of New Interventional Procedures – Surgical’s assessment on “Biodegradable stents” (ASERNIP-S, 2013) considers biodegradable polymer drug eluting stents to be investigational. The authors stated that this assessment of biodegradable polymer stents for coronary artery
disease (CAD) was based on a meta-analysis of 10 RCTs, a large RCT and a single-arm registry with 5 years of data. The most rigorous evidence, a recent meta-analysis, found no significant benefit of biodegradable stents for CAD with respect to death, MI or late ST, although benefits were found in rates of TLR and late lumen loss (LLL). The authors postulated that the lack of demonstrated benefit could have been due to heterogeneity among studies for the TLR and LLL outcomes, and variation in types of non-biodegradable DES employed (with most being 1st versus 2nd generation DES). As such, the findings of this meta-analysis cannot be highly weighted. Ideally, future studies should compare stents that utilize the same metal scaffold and anti-proliferative drug, with the only difference being the presence of a durable versus biodegradable polymer, so that the true safety and effectiveness of biodegradable polymer DES can be determined.

Ye and colleagues (2013) noted that DES with biodegradable polymers (BP) have been developed to address the risk of thrombosis associated with 1st-generation DES. These researchers determined the safety and effectiveness of BP biolimus-eluting stents (BP-BES) versus durable polymer (conventional) DES (DP-DES). Systematic database searches of MEDLINE (1950 to June 2013), EMBASE (1966 to June 2013), the Cochrane Central Register of Controlled Trials (Issue 6 of 12, June 2013), and a review of related literature were conducted. All RCTs comparing BP-BES versus DP-DES were included. A total of 8 RCTs investigating 11,015 patients undergoing PCI were included in the meta-analysis. The risk of major adverse cardiac events did not differ significantly between the patients treated with the BP-BES and the DP-DES (RR, 0.970; 95 % CI: 0.848 to 1.111; p = 0.662). However, BP-BES was associated with reduced risk of very late ST compared with the DP-DES, while the risk of early or late ST was similar (RR for early or late ST, 1.167; 95 % CI: 0.755 to 1.802; p = 0.487; RR 0.273; 95 % CI: 0.115 to 0.652; p = 0.003; p for interaction = 0.003). The authors concluded that in this meta-analysis of RCTs, treatments with BP-BES did not significantly reduce the risk of major adverse cardiac events, but demonstrated a significantly lower risk of very late ST when compared to DP-DES. They stated that this conclusion requires
confirmation by further studies with long-term follow-up.

Palmerini and associates (2014) examined the relative safety and effectiveness of bioabsorbable polymer-based BES versus DP-DES and DP-BMS by means of a network meta-analysis. Randomized controlled trials comparing bioabsorbable polymer-BES versus currently U.S.-approved DES or BMS were searched through MEDLINE, EMBASE, and Cochrane databases. Information on study design, inclusion and exclusion criteria, sample characteristics, and clinical outcomes was extracted. Data from 89 trials including 85,490 patients were analyzed. At 1-year follow-up, bioabsorbable polymer-BES were associated with lower rates of cardiac death/MI, MI, and TVR than BMS and lower rates of TVR than fast-release zotarolimus-eluting stents. The bioabsorbable polymer-BES had similar rates of cardiac death/MI, MI, and TVR compared with other 2nd-generation DP-DES but higher rates of 1-year ST than cobalt-chromium everolimus-eluting stents (CoCr-EES). The bioabsorbable polymer-BES were associated with improved late outcomes compared with BMS and paclitaxel-eluting stents, considering the latest follow-up data available, with non-significantly different outcomes compared with other DP-DES although higher rates of definite ST compared with CoCr-EES. The authors concluded that in this large-scale network meta-analysis, bioabsorbable polymer-BES were associated with superior clinical outcomes compared with BMS and 1st-generation DES and similar rates of cardiac death/MI, MI, and TVR compared with 2nd-generation DP-DES but higher rates of definite ST than CoCr-EES.

Zhang (2014) noted that delayed re-endothelialization may be the pathophysiological cause of ST. Biodegradable polymer DES (BP-DES) may reduce the risk of ST. These investigators evaluated the risk of ST in patients treated with BP-DES. Studies were retrieved from the PubMed, Cochrane Library, and EMBASE online databases. A total of 12 studies (15,155 patients) with long-term follow-up (greater than or equal to 12 months) were included. Compared with DP-DES, BP-DES did not significantly decrease the risk of definite and probable ST (RR, 0.89; 95 % CI: 0.68 to 1.18; \( p = 0.425 \)) and definite ST (RR, 0.92; 95 % CI: 0.66 to 1.30; \( p = 0.648 \)). Furthermore, there was no difference in the risk of late ST
(RR, 1.17; 95% CI: 0.39 to 3.53; p = 0.780). However, the rate of early ST was slightly higher in the BP-DES group (RR, 1.60; 95% CI: 0.94 to 2.73; p = 0.084) than in the DP-DES group. A significant reduction in very late ST (greater than 12 months) was evident with the BP-DES group (RR, 0.27; 95% CI: 0.10 to 0.68; p = 0.006). Subgroup analysis showed that there was no difference in the rate of definite and probable ST between the BP-DES and 1st- or 2nd-generation DES groups. The authors concluded that biodegradable polymer stents were associated with a significantly lower risk of very late ST. However, there was no difference in the risk of definite and probable ST between the 2 groups.

Wang and colleagues (2014) stated that BP-DES represent a promising strategy to improve the delayed healing and hypersensitive reaction in the vessel. However, the safety and effectiveness of BP-DES versus permanent polymer DES (PP-DES) are less well-defined. In a meta-analysis, these researchers compared the total, short (less than 30 days), mid (30 days to 1 year) and long (greater than 1 year) term outcomes of BP-DES versus PP-DES. PubMed, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for RCTs to compare any of approved BP- and PP-DES. Effectiveness end-points were TLR and in-stent late loss (ISLL). Safety end-points were death, MI, and composite of definite and probable ST. The meta-analysis included 19 RCTs (n = 18,395) with interesting results. As compared with DES, there was a significantly reduced very late ST (OR [95% CI]: 0.42 [0.24 to 0.77], p = 0.852) and ISLL (OR [95% CI]: -0.07 [-0.12 to 0.02], p = 0.000) in BP-DES patients. However, there were no differences between BP-DES and PP-DES for other safety and effectiveness outcomes, except that the stratified analysis showed a significant decreased TLR with BP-DES as compared to paclitaxel-eluting stent (OR [95% CI]: 0.41 [0.20 to 0.81], p = 0.457). The authors concluded that BP-DES are more effective in reducing very late ST and ISLL, as well as comparable to PP-DES with regard to death, TLR and MI. Moreover, they stated that further large RCTs with long-term follow-up are needed to better define the relative merits of BP-DES.

Kwong and Yu (2014) systematically reviewed the latest randomized evidence on the safety and effectiveness of BP-DES as
compared to DP-DES. MEDLINE, Embase, and the Cochrane database were searched in August 2013 for eligible RCTs comparing BP-DES with DP-DES. Clinical outcomes of interest were mortality, MI, TLR, TVR, and ST. A total of 20 RCTs randomizing 20,021 participants were included, of whom 11,045 were allocated to BP-DES and 8,976 to DP-DES. Treatment of BP-DES was not associated with a significant reduction of any of the clinical outcomes (all-cause mortality, OR: 0.94, 95 % CI: 0.80 to 1.10, p = 0.42; cardiovascular mortality, OR: 0.97, 95 % CI: 0.79 to 1.19, p = 0.74; MI, OR: 1.07, 95 % CI: 0.91 to 1.26, p = 0.41; TLR, OR: 0.87, 95 % CI: 0.69 to 1.08, p = 0.20; TVR, OR: 1.05, 95 % CI: 0.85 to 1.28, p = 0.67; definite/probable ST, OR: 0.80, 95 % CI: 0.59 to 1.07, p = 0.14). The authors concluded that current randomized data indicate that clinical safety and effectiveness profiles of BP-DES are comparable to those of DP-DES. Moreover, they stated that findings from large-scale studies with rigorous methodology and long follow-up duration are needed.

Niu and co-workers (2014) compared the short- and long-term outcomes and the ST risk in patients treated with BP-DES versus PP-DES. These investigators searched Medline, Embase, Web of science, CENTRAL databases, and conference proceedings/abstracts for RCTs comparing BP-DES with PP-DES. The primary end-point was to compare the risks of overall and different temporal categories definite/probable ST. Other clinical outcomes were TLR, MI, and all-cause death in short-term (less than or equal to 1 year) and long-term follow-up. The meta-analyses were performed by computing ORs with 95 % CIs using a random-effects model. A total of 19 RCTs including 20,229 patients were analyzed. Overall, BP-DES significantly decreased the risks of very late definite/probable ST (OR 0.33; 95 % CI: 0.16 to 0.70), and TLR in long-term follow-up (OR 0.70; 95 % CI: 0.52 to 0.95) compared with PP-DES. There were no significant differences between the groups regarding MI incidence and mortality during both short- and long-term follow-up period. In stratified analyses, the long-term superiority of BP-DES was only maintained by using 1st-generation DES as the comparators. The authors concluded that the present meta-analysis indicated that BP-DES were more effective than PP-DES at reducing the risks of very late ST and long-term TLR, but it could vary by
heterogeneities in the use of PP-DES comparators. Moreover, they stated that additional rigorous RCTs with longer follow-up periods are needed to verify these very promising long-term endpoints.

Pilgrim et al (2014) compared the safety and effectiveness of a novel, ultrathin strut cobalt-chromium stent releasing sirolimus from a biodegradable polymer with a thin strut durable polymer everolimus-eluting stent. These researchers performed a randomized, single-blind, non-inferiority trial with minimum exclusion criteria at 9 hospitals in Switzerland. They randomly assigned (1:1) patients aged 18 years or older with chronic stable CAD or acute coronary syndromes undergoing PCI to treatment with biodegradable polymer sirolimus-eluting stents or durable polymer everolimus-eluting stents. Randomization was via a central web-based system and stratified by center and presence of ST segment elevation MI. Patients and outcome assessors were masked to treatment allocation, but treating physicians were not. The primary end-point, target lesion failure, was a composite of cardiac death, target vessel MI, and clinically-indicated target lesion re-vascularization at 12 months. A margin of 3.5 % was defined for non-inferiority of the biodegradable polymer sirolimus-eluting stent compared with the durable polymer everolimus-eluting stent. Analysis was by intention-to-treat. Between February 24, 2012, and May 22, 2013, these investigators randomly assigned 2,119 patients with 3,139 lesions to treatment with sirolimus-eluting stents (1,063 patients, 1,594 lesions) or everolimus-eluting stents (1,056 patients, 1,545 lesions). A total of 407 (19 %) patients presented with ST-segment elevation MI. Target lesion failure with biodegradable polymer sirolimus-eluting stents (69 cases; 6.5 %) was non-inferior to durable polymer everolimus-eluting stents (70 cases; 6.6 %) at 12 months (absolute risk difference -0.14 %, upper limit of 1-sided 95 % CI: 1.97 %, p for non-inferiority < 0.0004). No significant differences were noted in rates of definite stent thrombosis (9 [0.9 %] versus 4 [0.4 %], rate ratio [RR] 2.26, 95 % CI: 0.70 to 7.33, p = 0.16). In pre-specified stratified analyses of the primary endpoint, biodegradable polymer sirolimus-eluting stents were associated with improved outcome compared with durable polymer everolimus-eluting stents in the subgroup of
patients with ST-segment elevation myocardial infarction (7 [3.3 %] versus 17 [8.7 %], RR 0.38, 95 % CI: 0.16 to 0.91, p = 0.024, p for interaction = 0.014). The authors concluded that in a patient population with minimum exclusion criteria and high adherence to dual anti-platelet therapy, biodegradable polymer sirolimus-eluting stents were non-inferior to durable polymer everolimus-eluting stents for the combined safety and effectiveness outcome target lesion failure at 12 months. Moreover, they stated that the noted benefit in the subgroup of patients with ST-segment elevation myocardial infarction needs further study.

In a meta-analysis, Lv and colleagues (2015) evaluated the safety and effectiveness of BP-DESs. PubMed, Science Direct, China National Knowledge Infrastructure, and Chongqing VIP databases were searched for RCTs comparing the safety and effectiveness of BP-DESs versus DP-DESs. Effectiveness included the prevalence of TLR, TVR, and LLL, and safety of these stents at the end of follow-up for the selected research studies were compared. A total of 16 qualified original studies that addressed a total of 22,211 patients were included in this meta-analysis. In regard to effectiveness, no statistically significant difference in TLR (OR = 0.94, p = 0.30) or TVR (OR 1.01, p = 0.86) was observed between patients treated with BP-DESs and those with DP-DESs. However, there were significant differences in in-stent LLL (WMD = -0.07, p = 0.005) and in-segment LLL (WMD = -0.03, p = 0.05) between patients treated with BP-DESs and with DP-DESs. In terms of safety, there was no significant difference in overall mortality (OR 0.97, p = 0.67), cardiac death (OR 0.99, p = 0.90), early stent thrombosis (ST) and late ST (OR 0.94, p = 0.76; OR 0.96, p = 0.73), or MI (OR 0.99, p = 0.88) between patients treated with BP-DESs and with DP-DESs. However, there was a statistically significant difference in very late ST (OR 0.69, p = 0.007) between these 2 groups. In addition, the general trend of the rates of TVR and TLR of BP-DESs groups was lower than DP-DESs groups after a 1-year follow-up. The authors concluded that BP-DESs are safe, efficient, and exhibit superior performance to DP-DESs with respect to reducing the occurrence of very late ST and LLL. The general trend of the rates of TVR and TLR of BP-DESs groups was lower than DP-DESs groups after a 1-year follow-up. Moreover, these investigators stated that the follow-up periods of the studies examined in this
investigation ranged from 6 to 48 months. To incorporate additional clinical studies with long follow-up times into meta-analyses of this topic and thereby obtain more stable and reliable conclusions, it is necessary to conduct additional large-scale rigorous RCTs with lengthy follow-up durations. Furthermore, they noted that this meta-analysis exhibited the following limitations: (i) the included studies did not have identical follow-up periods; instead, the range of follow-up durations was relatively broad (between 6 and 48 months), and (ii) the limitations of the meta-analytical approach are well known and documented; thus, the safety and effectiveness of various types of stents was not specifically identified.

Gao and colleagues (2015) evaluated the safety and effectiveness of the novel abluminal groove-filled biodegradable polymer-coated sirolimus-eluting FIREHAWK stent (MicroPort Medical, Shanghai, China) in a large cohort of patients. Trials on the FIREHAWK stent allowing targeted sirolimus release were not individually powered to reliably estimate low-frequency safety end-points such as stent thrombosis (ST) or to examine long-term safety and effectiveness. Additionally, the China FDA requires an objective performance criterion (OPC) study for new drug-eluting stents. The primary end-point, target lesion failure (TLF), was defined as the composite of cardiac death, target vessel MI, or clinically indicated TLR at 12 months. Patient-level data from 1,007 patients with de-novo native coronary lesions exclusively treated with the FIREHAWK stent in the TARGET serial studies (I and II) were prospectively collected, pooled and analyzed throughout a 2-year follow-up. The 12-month rate of TLF in 1,003 patients (follow-up rate of 99.6 %) was 3.9 % (upper 95 % CI: 5.3 %), which was significantly lower than the performance goal of 9.0 % (p < 0.0001). The 24-month rates of TLF, PoCE (a composite of all-cause death, all MI, or any re-vascularization), and ARC definite or probable ST were 4.6 %, 7.8 % and 0.1 %, respectively. In subgroup analysis, long lesion (greater than or equal to 30 mm) was an independent predictor of TLF within 2 years (HR: 2.44; 95 % CI: 1.32 to 4.53, p < 0.01). The authors concluded that this pooled, patient-level analysis indicated that the FIREHAWK stent exhibits a promising 2-year safety and effectiveness profile.
Zhu and colleagues (2015) noted that durable polymer SES (DP-SES) are associated with a low risk of stent thrombosis; BP-DES were designed to reduce these risks. However, their benefits are still variable. These investigators undertook a meta-analysis of randomized trials identified by systematic searches of Medline, Embase, and the Cochrane Database. A total of 11 studies (9,676 patients) with a mean follow-up of 22.6 months were included. Overall, compared with DP-SES, BP-DES significantly lowered the rate of definite or probable stent thrombosis (RR, 0.73; 95% CI: 0.55 to 0.97; p = 0.03; I(2) = 0.0 %) due to a decreased risk of very late stent thrombosis (RR, 0.26; 95% CI: 0.11 to 0.63; p = 0.00; I(2) = 0.0 %). However, BP-DES were associated with a comparable rate of early and late stent thrombosis. Meanwhile, BP-DES were associated with a broadly equivalent risk of TVR (RR, 0.90; 95% CI: 0.78 to 1.03; p = 0.13; I(2) = 0.0 %), cardiac death (RR, 0.89; 95% CI: 0.72 to 1.09; p = 0.24; I(2) = 0.0 %), MI (RR, 1.03; 95% CI: 0.84 to 1.26; p = 0.79; I(2) = 0.0 %), and MACE (RR, 0.91; 95% CI: 0.83 to 1.0; p = 0.08; I(2) = 0.0 %). Furthermore, angiographic data showed that in-stent and in-segment late luminal loss were similar between the 2 groups. The authors concluded that compared with DP-SES, BP-DES were associated with a lower rate of very late stent thrombosis and an equivalent risk of MACE. Moreover, they stated that larger randomized studies are needed to confirm this finding.

Kereiakis et al (2015) performed a multi-center, randomized controlled trial for regulatory approval to determine noninferiority of the Synergy stent to the durable polymer Promus Element Plus everolimus-eluting stent. Patients (n = 1,684) scheduled to undergo PCI for non-ST-segment-elevation acute coronary syndrome or stable CAD were randomized to receive either the Synergy stent or the Promus Element Plus stent. The primary end-point of 12-month target lesion failure was observed in 6.7 % of Synergy and 6.5 % Promus Element Plus treated subjects by intention-to-treat (p = 0.83 for difference; p = 0.0005 for non-inferiority), and 6.4 % in both the groups by per-protocol analysis (p = 0.0003 for non-inferiority). Clinically indicated revascularization of the target lesion or definite/probable ST were observed in 2.6 % versus 1.7 % (p = 0.21) and 0.4 % versus 0.6 % (p = 0.50) of Synergy versus Promus
Element Plus-treated subjects, respectively. The authors concluded that, in this randomized trial, the Synergy bioabsorbable polymer everolimus-eluting stent was non-inferior to the Promus Element Plus everolimus-eluting stent with respect to 1-year target lesion failure. The investigators stated that these data support the relative safety and efficacy of Synergy in a broad range of patients undergoing PCI.

In October 2015, the FDA approved the Boston Scientific Synergy Everolimus-Eluting Platinum Chromium Coronary Stent System. The Synergy stent is a thin-strut, platinum chromium metal alloy platform with an ultrathin bioabsorbable Poly(D,L-lactide-co-glycolide) abluminal everolimus-eluting polymer. The EVOLVE II study supported its noninferiority to other drug-eluting stents. “The EVOLVE II trial randomized 1684 patients with stable angina or non-ST segment elevation acute coronary syndrome to the SYNERGY stent or durable polymer platinum chromium EES. The primary end point of 12-month target lesion failure was observed in 6.7 percent of SYNERGY and 6.5 percent durable polymer EES-treated subjects (p = 0.83 for difference; p = 0.0005 for noninferiority). Clinically indicated target lesion revascularization or stent thrombosis were observed in 2.6 versus 1.7 percent (p = 0.21) and 0.4 versus 0.6 percent (p = 0.50) of SYNERGY versus PROMUS Element Plus-treated subjects, respectively” (Cutlip and Abbott, 2017). The bioabsorbable polymer is fully absorbed between three and four months. While existing DES devices reduce coronary restenosis, the polymer remains on the stent after the drug is delivered. Long-term exposure to the polymer may cause inflammation, which delays healing and has been associated with complications, including neoatherosclerosis and stent thrombosis. The Synergy Stent is designed for faster and sustained healing by eliminating long term polymer exposure.

**Bioresorbable Stents:**

Bioresorbable stents, or scaffolds, refers to stents and polymers that are fully biodegradable, a complete breakdown and removal of a material over time (Cutlip and Abbott, 2017).
An UpToDate review on “Coronary artery stent types in development” (Cutlip and Abbott, 2014) states that “The coronary stents currently available are permanent implants composed of a metallic alloy. Drug-eluting stents (DES) have additional durable polymer and anti-restenotic drug components. While bare metal stents (BMS) and DES have improved outcomes for patients, they have several limitations. The development of stent thrombosis after placement of BMS or DES and the residual rate of restenosis after DES are two reasons for the development of newer coronary artery stents. This topic will present studies of coronary artery stent types that show promise for reduction in rates of these adverse outcomes, including DES with bioresorbable polymers vascular scaffolds. The terms bioresorbable (also called biodegradeable) and bioabsorbable are used in this topic. Bioresorbable refers to the complete breakdown and removal of a material over time and often by a known mechanism. Bioabsorbable refers to incomplete breakdown; the material may be partially digested and remain indefinitely in local tissue. Stent material and polymer may be bioresorbable or bioabsorbable. Newer stent types are being developed to overcome some of the limitations of current stents, such as the development of stent thrombosis after placement of any intracoronary stent and the residual rate of restenosis after drug-eluting stent (DES). These newer stent types fall into three broad categories: stents with bioresorbable polymer; drug-eluting stents that are polymer free; or stents with a bioresorbable scaffold”.

Zhang and colleagues (2016) estimated the incidence of stent thrombosis after everolimus-eluting bioresorbable vascular scaffold (BVS) implantation and compared the safety and effectiveness of BVSs versus EESs in adults having PCI. Data sources included PubMed, Embase, Cochrane Central Register of Controlled Trials, conference proceedings, and relevant Web sites from inception through January 20, 2016. A total of 6 RCTs and 38 observational studies, each involving at least 40 patients with BVS implantation were included in this analysis. Two reviewers independently extracted study data and evaluated study risk of bias. The pooled incidence of definite or probable stent thrombosis after BVS implantation was 1.5 events per 100
patient-years (PYs) (95% CI: 1.2 to 2.0 events per 100 PYs) (126 events during 8,508 PYs). Six randomized trials that directly compared BVSs with EESs showed a non-statistically significant increased risk for stent thrombosis (OR, 2.05 [CI: 0.95 to 4.43]; p = 0.067) and MI (OR, 1.38 [CI: 0.98 to 1.95]; p = 0.064) with BVSs. The 6 observational studies that compared BVSs with EESs showed increased risk for stent thrombosis (OR, 2.32 [CI: 1.06 to 5.07]; p = 0.035) and MI (OR, 2.09 [CI: 1.23 to 3.55]; p = 0.007) with BVSs. The relative rates of all-cause and cardiac death, revascularization, and target lesion failure were similar for BVSs and EESs. The authors concluded that compared with EESs, BVSs did not eliminate and might increase risks for stent thrombosis and MI in adults having PCI. Moreover, they stated that results of large trials with long-term follow-up are needed to establish the safety or at least the non-inferiority of BVSs compared with EESs.

In an editorial that accompanied the afore-mentioned study by Zhang et al, Martin and Hasan (2016) stated that “although this is a major stride for BVS and the Absorb stent, the device is still in the early stage, and long-term post-marketing surveillance will be needed to ensure both safety and efficacy in broader populations”.

Mahmoud and associates (2017) stated that data regarding the long-term safety and effectiveness of everolimus-eluting BVS compared with EESs are limited. These researchers performed a meta-analysis to compare the long-term outcomes with both devices. Randomized trials reporting clinical outcomes beyond 1 year and comparing BVS with EESs were included. Summary estimates RRs were constructed. The primary efficacy outcome was target lesion failure, defined as CD, target vessel MI (TV-MI), and ischemia-driven TLR, and the primary safety outcome was definite or probable stent/scaffold thrombosis. A total of 6 trials with 5,392 patients were included (mean follow-up of 25 months); BVS had a higher rate of target lesion failure (RR, 1.33; 95% CI: 1.11 to 1.58) driven by the higher rates of TV-MI (RR, 1.65; 95% CI: 1.26 to 2.17) and TLR (RR, 1.39; 95% CI: 1.08 to 1.78). The risk of definite or probable stent/scaffold thrombosis (RR, 3.22; 95% CI: 1.89 to 5.49) and very late stent/scaffold thrombosis (greater than 1 year; RR, 4.78; 95% CI: 1.66 to 13.8)
was higher with BVS. The risk of CD and all-cause mortality was similar in both groups. The authors concluded that compared with EESs, BVS is associated with increased risk of target lesion failure driven by the increased rates of TV-MI and ischemia-driven TLR in these studies (mean follow-up of 25 months). The risk of definite or probable stent/scaffold thrombosis and very late stent/scaffold thrombosis appeared to be higher with BVS. They stated that further information from randomized trials is needed to assess clinical outcomes with BVS on complete resolution of the scaffold.

Nairooz and colleagues (2017) noted that data regarding long-term clinical outcomes with everolimus-eluting BVS versus 2nd-generation DES are scarce. These investigators searched online databases until October 2016 for studies comparing BVS versus DES reporting outcomes at 2-year follow-up. They performed a meta-analysis comparing BVS with DES across the spectrum of CAD. Random effects model OR was calculated for outcomes of interest including device-oriented composite events (DOCE; defined as composite of CD, TV-MI, and ischemia-driven TLR), all-cause mortality, definite ST, TV-MI and TLR. A total of 2,360 patients enrolled in 5 studies met inclusion criteria in this analysis. At 2-year follow-up, BVS was associated with higher rates of DOCE (6.9 % versus 4.5 %, OR = 1.53; 95 % CI: 1.06 to 2.23; p = 0.02), absolute risk increase (ARI) 2.4 %, relative risk increase (RRI) 53 %, TV-MI (4 % versus 1.8 %, OR = 1.94; 95 % CI: 1.02 to 3.67; p = 0.04), ARI 2.2 %, RRI 122 % and definite ST (2.1 % versus 0.6 %, OR = 3.39; 95 % CI: 1.46 to 7.88; p = 0.005), ARI 1.5 %, RRI 250 % compared with DES. No differences in all-cause mortality (OR = 0.86; 95 % CI: 0.26 to 2.81; p = 0.80) and TLR (OR = 1.44; 95 % CI: 0.81 to 2.54; p = 0.21) were observed between the 2 groups. The authors concluded that BVS may be associated with worse long-term clinical outcomes compared with DES. They stated that randomized clinical trials are needed to ascertain long-term safety and effectiveness of BVS and identify predictors of adverse events (AEs) with BVS compared with DES.

On March 18, 2017, the FDA informed health care providers treating patients with Absorb GT1 BVS that there is an increased rate of MACE observed in patients receiving the BVS, when
compared to patients treated with the approved metallic XIENCE DES. The FDA’s initial review of 2-year data from the BVS pivotal clinical study (the ABSORB III Trial) showed an 11 % rate of MACE (e.g., CD, heart attack, or the need for an additional procedure to re-open the treated heart vessel) in patients treated with the BVS at 2 years, compared with 7.9 % in patients treated with the already-approved Abbott Vascular’s metallic XIENCE DES (p = 0.03). This study also showed a 1.9 % rate of developing ST within the BVS versus 0.8 % within the XIENCE stent at 2 years. These observed higher MACE rates in BVS patients were more likely when the device was placed in small heart vessels. The FDA is working with Abbott Vascular, Inc. to conduct additional analyses to better understand the cause(s) of the higher cardiac event and device thrombosis rates in patients treated with BVS compared to the XIENCE stent. The FDA will continue to monitor the performance of the BVS in ongoing clinical studies and in reports submitted to FDA through MedWatch.

Cassese et al (2016) conducted a meta-analysis to assess the efficacy and safety of everolimus-eluting BVSs versus everolimus-eluting metallic stents in patients with ischaemic heart disease treated with percutaneous revascularisation. The authors searched Medline, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), scientific sessions abstracts, and relevant websites for randomized trials investigating everolimus-eluting BVSs versus everolimus-eluting metallic stents published or posted between Nov 30, 2006, and Oct 12, 2015. The primary efficacy outcome was TLR and the primary safety outcome was definite or probable stent (scaffold) thrombosis. Secondary outcomes were target lesion failure (the composite of cardiac death, target-vessel myocardial infarction, or ischaemia-driven target lesion revascularisation), myocardial infarction, death, and in-device late lumen loss. The authors derived ORs and weighted mean differences with 95 % CIs, and calculated the risk estimates for the main outcomes according to a random-effects model. The authors included 6 trials, comprising data for 3,738 patients randomized to receive PCI with either an everolimus-eluting BVS (n = 2,337) or an everolimus-eluting metallic stent (n = 1,401). Median follow-up was 12 months (IQR 9 to 12). Patients treated with BVSs had a
similar risk of TLR (OR 0.97 [95% CI: 0.66 to 1.43]; p = 0.87), target lesion failure (1.20 [0.90 to 1.60]; p = 0.21), MI (1.36 [0.98 to 1.89]; p = 0.06), and death (0.95 [0.45 to 2.00]; p = 0.89) as those treated with metallic stents. Patients treated with a BVS had a higher risk of definite or probable ST than those treated with a metallic stent (OR 1.99 [95% CI: 1.00 to 3.98]; p = 0.05), with the highest risk between 1 and 30 days after implantation (3.11 [1.24 to 7.82]; p = 0.02). Lesions treated with a BVS had greater in-device late lumen loss than those treated with a metallic stent (weighted mean difference 0.08 [95% CI 0.05 to 0.12]; p < 0.0001). The authors concluded that, compared with everolimus-eluting metallic stents, everolimus-eluting BVSs had similar rates of repeat revascularization at 1 year of follow-up, despite inferior mid-term angiographic performance. However, patients treated with a BVS had an increased risk of subacute ST. Studies with extended follow-up in a larger number of patients are needed to fully assess the long-term advantages of everolimus-eluting BVSs.

An accompanying editorial (Finn and Vermani, 2016) stated that "[t]he most striking and important findings [of Cassese and colleagues] concern the issue of stent thrombosis, which was more than twice as prevalent in patients with bioresorbable vascular scaffolds than in those with metallic stents. Many of the events occurred within the first 30 days despite optimal compliance with dual antiplatelet therapy. Although we are not informed as to the exact causes of thrombosis, the limitations of bioresorbable vascular scaffolds in terms of impaired endothelial cell coverage, and potential issues involving implantation techniques or scaffold integrity, are key issues to focus on to improve understanding of why relatively early thrombosis is increased. Perhaps equally important is whether at longer-term follow-up the apparent weaknesses of the bioresorbable vascular scaffold design, including prolonged degradation time and late inflammation with bulky struts, predispose the patient to late thrombotic events".

An assessment by the National Institute for Health and Care Excellence (2016) found: "The evidence suggests that the risks of death, myocardial infarction and target lesion failure are similar
for Absorb BVS, bare-metal stents and metallic drug-eluting stents at up to 12 months' follow-up. Stent thrombosis (definite or probable) was more frequent and medium-term in-device and in-segment lumen loss was greater with Absorb BVS than with some second-generation metallic drug-eluting stents. Key uncertainties around the evidence are about longer-term outcomes associated with the Absorb BVS compared with metallic drug-eluting stents. NICE interventional procedures guidance recommends that bioresorbable stent implantation should only be used with special arrangements for clinical governance, consent and audit or research”.

Polymer-Free Drug-Eluting Stents:

Navarese et al (2014) stated that the safety and effectiveness of polymer-free DESs in clinical practice is currently subject of debate; RCTs conducted so far provided conflicting results or were under-powered to definitively address this question. These investigators examined the safety and effectiveness profile of polymer-free versus DP-DES by a comprehensive meta-analysis of RCTs. MEDLINE, Google Scholar, EMBASE and Cochrane databases were searched for RCTs comparing polymer-free to DP-DES. Safety end-points at short-term (less than or equal to 1 year) and long-term follow-up (greater than 1 year) were: death, MI and stent thrombosis (ST); main effectiveness end-points were: TLR and TVR. A total of 8 RCTs including 6,178 patients were included. No significant differences in mortality were observed between polymer-free and DP-DESs at both short- and long-follow up (OR [95 % CI]: 0.79 [0.58 to 1.08], p = 0.14; and 1.80 [0.58 to 1.10], p = 0.17 respectively); polymer free and DP-DESs provided comparable short and long-term MI rates; at short-term: OR [95 % CI]: 1.13 [0.83 to 1.54], p = 0.44 and at long-term: OR [95 % CI]: 1.27 [0.87 to 1.85], p = 0.22. Similarly, these 2 different devices proved equally effective in regards to ST, TLR and TVR over the short and long follow-up period. The authors concluded that polymer-free DESs are as safe and effective as DP-DES; however, there is no evidence of any additional benefits provided by this new technology.

Antibody-Coated Stents:
Antibody coated stents are proposed to accelerate vessel healing, prevent thrombi and minimize restenosis. They purportedly eliminate the need for prolonged antiplatelet therapy post-implantation. Currently, antibody coated stents are not FDA approved.

An UpToDate review on “Coronary artery stent types in development” (Cutlip and Abbott, 2014) states that “A number of drug eluting stent models, including abciximab-coated, beta-estradiol, and dexamethasone stents, have been tested and not carried forward into regulatory approval clinical trials in the United States. The Combo stent combines sirolimus elution from an abluminal biodegradable polymer matrix with a CD34 antibody layer. The CD34 antibody is directed toward circulating endothelial progenitor cells with a goal of increasing the rate of cellular coverage and thus decreasing the rate of stent thrombosis. In the first-in-man trial, the Combo stent was noninferior to a paclitaxel-eluting stent for outcomes of nine-month angiographic in-stent late lumen loss and 12-month major adverse cardiovascular events”.

**Drug-Eluting Stents for the Treatment of Intra-Coronary Stent Restenosis:**

In a meta-analysis, Bajraktari and associates (2016) evaluated the safety and effectiveness of DEB compared with DES in patients with DES-ISR. These investigators carried out a systematic search and all randomized and observational studies that compared DEB with DES in patients with DES-ISR were included. The primary outcome measure- MACE-as well as individual events as TLR, ST, MI, CD and all-cause mortality, were analyzed. A total of 3 randomized and 4 observational studies were included (n = 2,052 patients); MACE (RR = 1.00, 95 % CI: 0.68 to 1.46, p = 0.99), TLR (RR = 1.15 [CI: 0.79 to 1.68], p = 0.44), ST (RR = 0.37 [0.10 to 1.34], p = 0.13), MI (RR = 0.97 [0.49 to 1.91], p = 0.93) and CD (RR = 0.73 [0.22 to 2.45], p = 0.61) were not different between patients treated with DEB and with DES. However, all-cause mortality was lower in patients treated with DEB (RR = 0.45 [0.23 to 0.87, p = 0.019) and in particular when compared to only 1st generation DES (RR 0.33 [0.15 to 0.74], p = 0.007). There was no
Goel and co-workers (2016) performed a meta-analysis of observational and randomized studies to compare the outcomes of management of DES-ISR using DES, DEB, or balloon angioplasty (BA). Eligible studies (25 single-arm and 13 comparative, including 4 randomized studies with a total of 7,474 patients with DES-ISR) were identified using Medline search and proceedings of international meetings. Outcomes studied included MACE, TLR, TVR, MI, ST, and mortality. Follow-up ranged from 0.5 to 3.5 years (mean of 1.4 years). The rate of TLR was significantly lower in the DES (OR 0.50, 95% CI: 0.36 to 0.69) and DEB (OR 0.31, 95% CI: 0.18 to 0.55) groups compared to BA. Similarly, TVR rate was significantly lower in the DES (OR 0.55, 95% CI: 0.39 to 0.77) and DEB (OR 0.32, 95% CI: 0.18 to 0.58) groups compared to BA. All other outcomes were similar between the DES/BA and DEB/BA comparisons; TLR was significantly lower in the DES group compared to BA for vessels less than or greater than 2.75 mm. The authors concluded that treatment of coronary DES-ISR with DES or DEB was associated with a reduction in the risk of TLR and TVR compared to BA alone. The relative risk reduction for TLR with DES was similar to DEB. They noted that DEBs have a potential role in the treatment of DES-ISR by avoiding placement of another layer of stent.

In a meta-analysis, Wang and colleagues (2017a) examined the effectiveness of DEB with DES in patients with ISR. Electronic databases were searched for RCTs and observational cohort studies that reported the clinical outcomes of using DEB comparing with DES implantation in patients with ISR. Clinical end-points such as MACE, MI, and CD were assessed. A total of 5 RCTs and 5 observational cohort studies with 962 patients in the DEB group and 908 patients in the DES group met inclusion criteria. There was no significant difference between DEB and DES in major clinical outcomes, such as MACE (OR 1.01; 95% CI: 0.64 to 1.58; p = 0.97; I² = 0%), all-cause death (OR 1.04; 95% CI: 0.54 to 1.98; p = 0.91; I² = 0%), CD (OR 1.44; 95% CI: 0.57 to 3.65; p = 0.44; I² = 0%), ST (OR 0.61; 95% CI: 0.16 to 2.33; p =
0.47; I² = 0 %), and MI (OR 1.02; 95 % CI: 0.53 to 1.94; p = 0.96; I² = 0 %); DEB was associated with a significant increase in TLR (OR 1.54; 95 % CI: 1.10 to 2.15; p = 0.01; I² = 57 %). The authors concluded that treatment of ISR using DEB led to comparable clinical outcomes with DES implantation.

Furthermore, an UpToDate review on “Intracoronary stent restenosis” (Levin and Cutlip, 2017) states that “Placement of a newer generation drug-eluting stent (DES), and in particular an everolimus-eluting stent, is the preferred treatment for patients with ISR, irrespective of whether the original stent was bare metal or drug-eluting. The various potential percutaneous coronary interventional (PCI) techniques of plain old balloon angioplasty, bare metal stenting, or older generation stenting, newer generation stenting, atherectomy, brachytherapy, and DEBs, have been compared in multiple studies ... The 2014 European Society of Cardiology/European Association for Cardio-Thoracic Surgery guideline on myocardial revascularization recommends either drug-eluting stent (DES) or drug-coated balloons for the treatment of intracoronary stent restenosis (ISR) (bare metal stents [BMS] or DES).”

Chronic Kidney Disease with Multi-Vessel Disease:

Wang and colleagues (2017b) noted that the optimal revascularization strategy of coronary artery bypass grafting (CABG) versus PCI with DES (PCI-DES) in patients with CKD and multi-vessel disease (MVD) remains unclear. In a meta-analysis, these researchers compared CABG and PCI-DES in these patients. PubMed, Embase and Cochrane Library electronic databases were searched from inception until June 2016. Studies that evaluated the comparative benefits of DES versus CABG in CKD patients with MVD were considered for inclusion. They pooled the ORs from individual studies and conducted heterogeneity, quality assessment and publication bias analyses. A total of 11 studies with 29,246 patients were included (17,928 DES patients; 11,318 CABG). Compared with CABG, pooled analysis of studies showed DES had higher long-term all-cause mortality (OR, 1.22; p < 0.00001), CD (OR, 1.29; p < 0.00001), MI (OR, 1.89; p = 0.02), repeat re-vascularization (OR, 3.47; p < 0.00001) and major
adverse cardiac and cerebrovascular events (MACCE) (OR, 2.00; p = 0.002), but lower short-term all-cause mortality (OR, 0.33; p < 0.00001) and cerebro-vascular accident (CVA) (OR, 0.64; p = 0.0001). Subgroup analysis restricted to patients with ESRD yielded similar results, but no significant differences were found regarding CVA and MACCE. The authors concluded that CABG for patients with CKD and MVD had advantages over PCI-DES in long-term all-cause mortality, MI, repeat re-vascularization and MACCE, but the substantial disadvantage in short-term mortality and CVA. They stated that future large RCTs are needed to confirm these findings.

<table>
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<tr>
<th>CPT Codes / HCPCS Codes / ICD-10 Codes</th>
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**Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":**

**Other CPT codes related to the CPB:**

<table>
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<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>0075T - 0076T</td>
<td>Transcatheter placement of extracranial vertebral artery stent(s), including radiologic supervision and interpretation, open or percutaneous</td>
</tr>
<tr>
<td>+0205T</td>
<td>Intravascular catheter-based coronary vessel or graft spectroscopy (eg, infrared) during diagnostic evaluation and/or therapeutic intervention including imaging supervision, interpretation, and report, each vessel (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>+0291T</td>
<td>Intravascular optical coherence tomography (coronary native vessel or graft) during diagnostic evaluation and/or therapeutic intervention, including imaging supervision, interpretation, and report; initial vessel (List separately in addition to primary procedure)</td>
</tr>
<tr>
<td>37236 - 37237</td>
<td>Transcatheter placement of an intravascular stent(s) (except lower extremity artery(s) for occlusive disease, cervical carotid, extracranial vertebral or intrathoracic carotid, intracranial, or coronary), open or percutaneous, including radiological supervision and interpretation and including all angioplasty within the same vessel, when performed</td>
</tr>
</tbody>
</table>
Transcatheter placement of an intravascular stent(s), open or percutaneous, including radiological supervision and interpretation and including angioplasty within the same vessel, when performed [vein]

Transcatheter placement of intravascular stent(s), intracranial (e.g., atherosclerotic stenosis), including balloon angioplasty, if performed

Percutaneous transcatheter placement of intracoronary stent(s), with coronary angioplasty when performed

Percutaneous transluminal coronary atherectomy, with intracoronary stent, with coronary angioplasty when performed

Percutaneous transluminal revascularization of or through coronary artery bypass graft (internal mammary, free arterial, venous), any combination of intracoronary stent, atherectomy and angioplasty, including distal protection when performed

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

Percutaneous transluminal revascularization of chronic total occlusion, coronary artery, coronary artery branch, or coronary artery bypass graft, any combination of intracoronary stent, atherectomy and angioplasty

**HCPCS codes covered if selection criteria are met:**

C1874 Stent, coated / covered, with delivery system [covered for (FDA)-approved everolimus, paclitaxel, sirolimus, and zotarolimus eluting stents only] [not covered for biodegradable (bioreosorbable, bioabsorbable) polymer drug eluting stents] [not covered for antibody-coated coronary stents]
C1875 Stent, coated / covered, without delivery system
[covered for (FDA)-approved everolimus, paclitaxel, sirolimus, and zotarolimus eluting stents only] [not covered for biodegradable (bioresorbable, bioabsorbable) polymer drug eluting stents] [not covered for antibody-coated coronary stents]

Other HCPCS codes related to the CPB:

C9600 - Percutaneous transcatheater placement of drug eluting intracoronary stent(s), with coronary angioplasty when performed
C9601
C9602 - Percutaneous transstiminal coronary atherectomy, with drug eluting intracoronary stent, with coronary angioplasty when performed
C9603
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
C9605
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
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
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)

**ICD-10 codes covered if selection criteria are met:**

I20.1 - I20.9  Angina pectoris
I25.10 - I25.9  Atherosclerotic heart disease of native coronary artery

**ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):**

I20.0  Unstable angina
I70.1 - I70.92  Atherosclerosis of renal artery and extremities
I77.1  Stricture of artery
K31.1  Adult hypertrophic pyloric stenosis
K80.00 - K87  Disorders of gallbladder, biliary tract and pancreas
M31.4  Aortic arch syndrome [Takayasu]
Q40.0  Congenital hypertrophic pyloric stenosis
T82.01x+ -  Complications of cardiac and vascular prosthetic devices, implants and grafts
T82.9xx+  

**The above policy is based on the following references:**


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AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0621 Drug-Eluting Stents

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania  revised 08/25/2017