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# Clinical Outcomes With Drug-Eluting and Bare-Metal Stents in Patients With ST-Segment Elevation Myocardial Infarction

## Evidence From a Comprehensive Network Meta-Analysis

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**Objectives** The authors investigated the relative safety and efficacy of different drug-eluting stents (DES) and bare metal stents (BMS) in patients with ST-segment elevation myocardial infarction (STEMI) using a network meta-analysis.

**Background** The relative safety of DES and BMS in patients with STEMI continues to be debated, and whether advances have been made in this regard with second-generation DES is unknown.

**Methods** Randomized controlled trials comparing currently U.S. approved DES or DES with BMS in patients with STEMI were searched using MEDLINE, EMBASE, and Cochrane databases. Information on study design, inclusion and exclusion criteria, sample characteristics, and clinical outcomes was extracted.

**Results** Twenty-two trials including 12,453 randomized patients were analyzed. At 1-year follow-up, cobalt-chromium everolimus eluting stents (CoCr-EES) were associated with significantly lower rates of cardiac death or myocardial infarction (MI) and stent thrombosis (ST) than BMS. Differences in ST were apparent as early as 30 days and were maintained for 2 years. CoCr-EES were also associated with significantly lower rates of 1-year ST than paclitaxel-eluting stents (PES). Sirolimus-eluting stents (SES) were also associated with significantly lower rates of 1-year cardiac death/myocardial infarction than BMS. CoCr-EES, PES, and SES, but not zotarolimus-eluting stents, had significantly lower rates of 1-year target vessel revascularization (TVR) than BMS, with SES also showing lower rates of TVR than PES.

**Conclusions** In patients with STEMI, steady improvements in outcomes have been realized with the evolution from BMS to first-generation and now second-generation DES, with the most favorable safety and efficacy profile thus far demonstrated with CoCr-EES. (J Am Coll Cardiol 2013;62:496–504) © 2013 by the American College of Cardiology Foundation

Primary percutaneous coronary intervention (PCI) performed by an experienced team and in a timely fashion is the treatment of choice for patients with ST-segment elevation acute myocardial infarction (STEMI) (1). The introduction of bare-metal stents (BMS) has provided additional benefit compared to balloon angioplasty by reducing the risk of recurrent ischemia and

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restenosis (2), and drug-eluting stents (DES) have further improved clinical outcomes by further reducing restenosis and target vessel revascularizations (TVR) (3). However, concern has been raised over the ongoing propensity for very late stent thrombosis (StThr) of first-generation sirolimus-eluting stents (SES; Cypher, Cordis Corp., Miami Lakes, Florida) and paclitaxel-eluting stents (PES) (Taxus, Boston Scientific, Natick, Massachusetts) (4,5). This concern is particularly relevant for patients with STEMI, who, compared to patients with stable coronary artery disease, have greater rates of ST due to heightened platelet activation and the presence of thrombus (6,7).

To overcome the safety concerns with first-generation DES, newer devices have been developed that use novel stent materials, designs, and delivery systems with enhanced biocompatible polymers, and new antiproliferative agents compared to their predecessors. However, studies performed so far comparing second-generation DES with first-generation DES or BMS in patients with STEMI have not been powered to detect significant differences in the occurrence of death, MI, or ST (8,9). Moreover, previous meta-analyses have compared pooled PES and SES versus BMS, thus leaving undetermined whether there are stent-related differences between these two devices or whether second-generation DES have improved outcomes compared to first-generation DES (or BMS) (10,11).

Network meta-analyses and mixed treated comparisons are novel research methods capable of comparing different treatments using a common reference treatment, and their role in clinical research has been established (12). Accordingly, we performed an updated contemporary, comprehensive network meta-analysis to investigate whether there are major differences in safety and efficacy among first-generation DES, second-generation DES, and BMS in patients with STEMI undergoing primary PCI.

**Abbreviations and Acronyms**

**BMS** = bare-metal stent(s)
**CoCr-EES** = cobalt-chromium everolimus-eluting stent(s)
**DES** = drug-eluting stent(s)
**PES** = paclitaxel-eluting stent(s)
**PCI** = percutaneous coronary intervention
**PC-ZES** = phosphorylcholine-based zotarolimus-eluting stent(s)
**PRISMA** = Preferred Reporting Items for Systematic Reviews and Meta-analyses
**RCT** = randomized controlled trial
**SES** = sirolimus-eluting stent(s)
**StThr** = stent thrombosis
**STEMI** = ST-segment elevation acute myocardial infarction
**TVR** = target vessel revascularizations

## Methods

**Objectives, definitions, and study design.** In this network meta-analysis we compared the safety and efficacy of U.S. Food and Drug Administration (FDA)-approved DES and BMS in patients with STEMI. We restricted our analyses to FDA-approved DES as these are the devices with the widest use in the setting of STEMI. Thus, the DES studied in the present report were SES, PES (both Express and Liberté platforms), cobalt-chromium everolimus-eluting stents (CoCr-EES) (Xience, Abbott Vascular, Santa Clara, California), and phosphorylcholine-based zotarolimus-eluting stents (PC-ZES) (Endeavor, Medtronic, Santa Rosa, California).

As fewer studies with data at 2 years compared to 1 year have been reported for second-generation DES, we specified that the primary analyses for the present report be performed at 1-year follow-up. Safety endpoints included death, cardiac death, MI, death or MI, cardiac death or MI, and definite or definite/probable ST according to Academic Research Consortium (ARC) criteria. ST was further stratified as early (≤30 days) and late (31 days to 1 year). The efficacy endpoint was TVR.

The present review was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statements (13).

**Data source and study selection.** We searched for randomized controlled trials (RCTs) relevant to this meta-analysis in MEDLINE, PubMed, Cochrane Collaboration database, Embase, TCTMD.com, Clinical Trials.gov, Clinical Trials Results.org, and CardioSource.com, and in abstracts and presentations from major cardiovascular meetings using the keywords ST-segment elevation myocardial infarction, drug-eluting stent, everolimus-eluting stent, paclitaxel-eluting stent, sirolimus-eluting stent, zotarolimus-eluting stent, and bare metal stent. RCTs comparing 2 or 3 different DES or DES with BMS were identified and included in the meta-analysis. Two investigators (T.P. and D.D.R.) independently reviewed the titles, abstracts, and studies to determine whether they met inclusion criteria. Conflicts between reviewers were resolved by consensus. No language, publication date, or publication status restrictions were imposed. The most updated or most inclusive data for

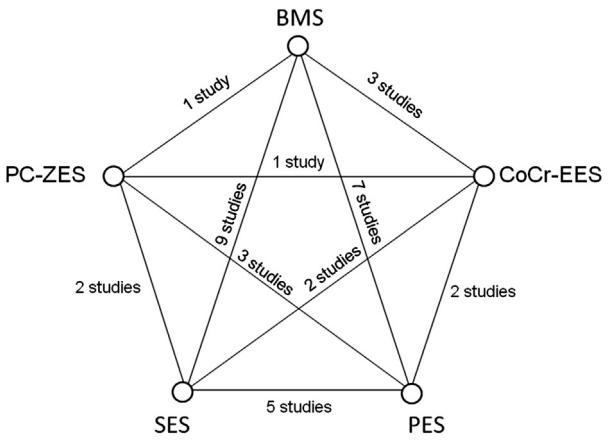


**Figure 1** Evidence Network Among Stents Included in the Meta-Analysis

CoCr-EES = cobalt-chromium everolimus-eluting stent(s); PES = paclitaxel-eluting stent(s); SES = sirolimus-eluting stent(s); BMS = bare-metal stent(s); PC-ZES = phosphorylcholine polymer-based zotarolimus-eluting stent(s).