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Tweet: "Drug eluting stents not associated with increased mortality compared with bare metal stents in peripheral arterial interventions among CMS patients"

Abbreviations:
ALI, acute limb ischemia
BMS, bare metal stent
CLI, critical limb ischemia
CMS, Centers for Medicare and Medicaid Services (CMS)
CI, confidence interval
DES, drug-eluting stent
HR, hazard ratio
IQR, interquartile range
PAD, peripheral artery disease

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Drug-eluting stents (DES) are important additions to the armamentarium of devices used for peripheral artery revascularization, associated with decreased rates of restenosis and target vessel revascularization (1-3). A recent meta-analysis found an association between peripheral paclitaxel-coated devices and increased long-term mortality (4). These findings have not been replicated in other data sources with extended follow-up.

Patients admitted with a principal diagnosis of peripheral artery disease (PAD) (5) in the U.S. Centers for Medicare and Medicaid Services (CMS) fee-for-service Medicare Provider Analysis and Review files were identified using ICD-9-CM codes. The study started 12/1/2012, corresponding to the approval of the first peripheral DES (Zilver PTX, Cook Medical, Bloomington, Indiana), and continued through 9/30/15. ICD-9-PCS codes were used to identify peripheral DES (00.55) and bare-metal stent (BMS) (39.90) placement. For patients with repeated procedures, only the first procedure was included. Comorbidities were ascertained using index diagnosis codes and from all hospitalizations within 12 months of the procedure. Temporal trends of BMS and DES use were plotted over quarterly time periods. The cumulative incidence of death through 12/31/16 was calculated using Kaplan-Meier methods, and log-rank tests were used to evaluate for differences between groups. Multivariable Cox regression was used to calculate hazard ratios (HR), adjusted for age, sex, and comorbiditie s(5). Sub-group analyses were performed among patients with critical limb ischemia (CLI) and acute limb ischemia (ALI). P-values <0.05 were considered significant.

Among 51,456 patients who underwent peripheral stenting, the average age was 72.8±10.5 years, 54.2% were male, 59.7% had CLI, 7.1% had ALI, and 39.3% were diabetic. Median follow-up was 2.0 years (IQR 1.2-3.0 years; longest 4.1 years). During the study, there was a gradual uptake in peripheral DES use (Figure 1A). Patients treated with DES versus BMS

had similar mortality through 4.1 years (51.7% for DES versus 50.1% for BMS; log-rank p-value=0.16), and this relationship persisted after stratification by CLI (Figure 1B). There was no association between stent type and mortality after multivariable adjustment (HR for DES versus BMS: 0.98; 95%CI 0.93-1.03; p=0.53). In addition, there was no adjusted relationship between stent type and death among patients with CLI (HR: 0.97; 95%CI 0.92-1.03; p=0.32) or ALI (HR: 0.99; 95%CI 0.81-1.21; p=0.95).

In this study of CMS beneficiaries admitted for peripheral artery revascularization, we observed a gradual uptake of DES use and found no difference in mortality between DES and BMS through the end of follow-up. This finding remained after multivariable adjustment, and among patients with CLI or ALI.

Peripheral artery revascularization has been challenged by high rates of restenosis and need for re-intervention. The first DES indicated for femoropopliteal artery revascularization, the paclitaxel-eluting Zilver PTX, was approved in November 2012 after demonstrating improved patency at 12 months compared with balloon angioplasty and BMS (3). Follow-up data through 5 years (1,2) have shown persistent efficacy over these other devices, supporting their routine use.

However, the long-term safety of these devices has not been well-established, mainly due to their limited duration on the market. A recent meta-analysis of randomized trials has raised concern regarding a possible association with long-term mortality (4). In particular, this meta-analysis found that DES use corresponded with an 87% increased odds of all-cause death at 5 years (4). Due to the significant implications of these findings and the increasing use of peripheral DES, investigation of this relationship in other data sources is needed urgently, thus motivating this analysis.

This analysis is limited by an inability to localize the lesion of interest, possible misclassification due to use of claims codes, lack of data on outpatient procedures and drug-coated balloons (no ICD-9-PCS code), the potential influence of unmeasured confounding, and the inability to determine specific causes of death. In addition, this CMS population was older and had more comorbidities, including CLI, compared with the Katsanos et al. meta-analysis (4).

In summary, we found no evidence of increased long-term mortality following peripheral artery revascularization with DES compared with BMS among CMS beneficiaries, suggesting the safety of these devices in routine practice.

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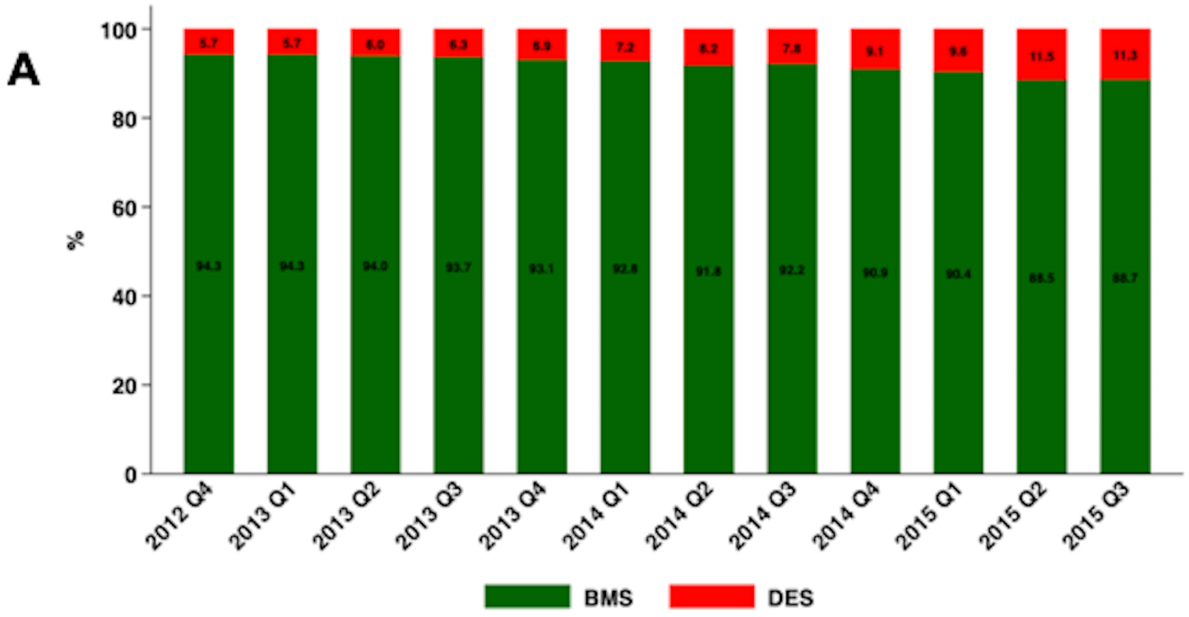
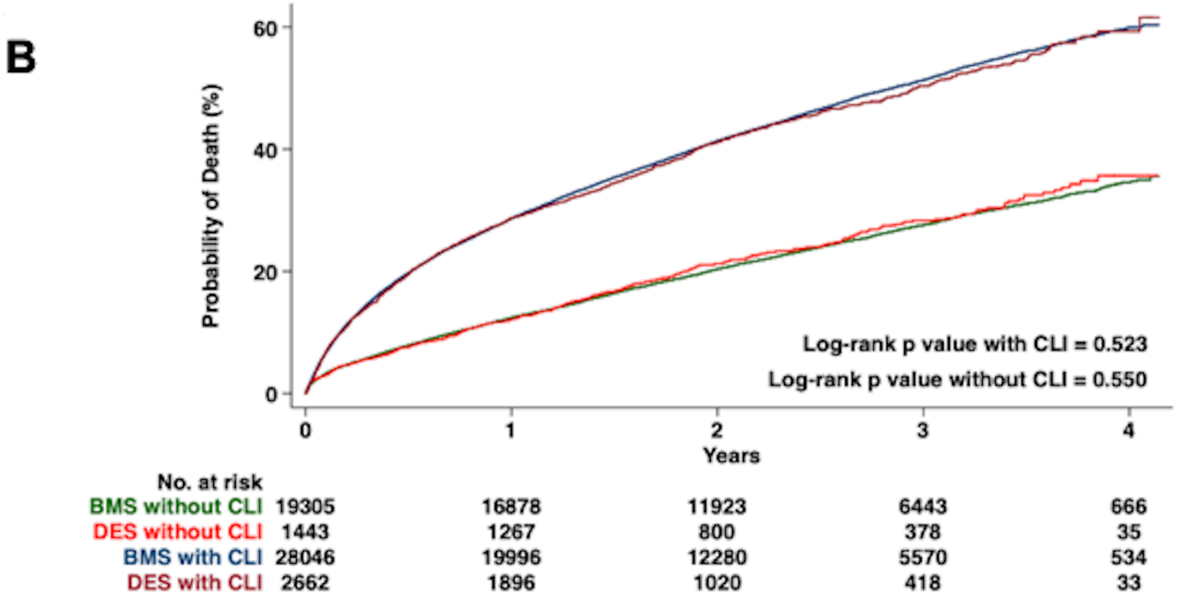
Figure: Temporal trends in use of DES for PAD(A) and long-term survival stratified by CLI diagnosis(B).





No. at risk					
BMS without CLI	19305	16878	11923	6443	666
DES without CLI	1443	1267	800	378	35
BMS with CLI	28046	19996	12280	5570	534
DES with CLI	2662	1896	1020	418	33