

Off Label Use of DES. (First Generation DES).

**A. Pichard,
L. Satler, K. Kent, R. Waksman,
W. Suddath, N. Bernardo, H. Sievert,
S. Epstein, N. Weissman,
A. Fuisz, G. Weigold, J. Lindsay, L Miller.**

**Washington Hospital Center
Washington, D.C.**

Off-Label Use



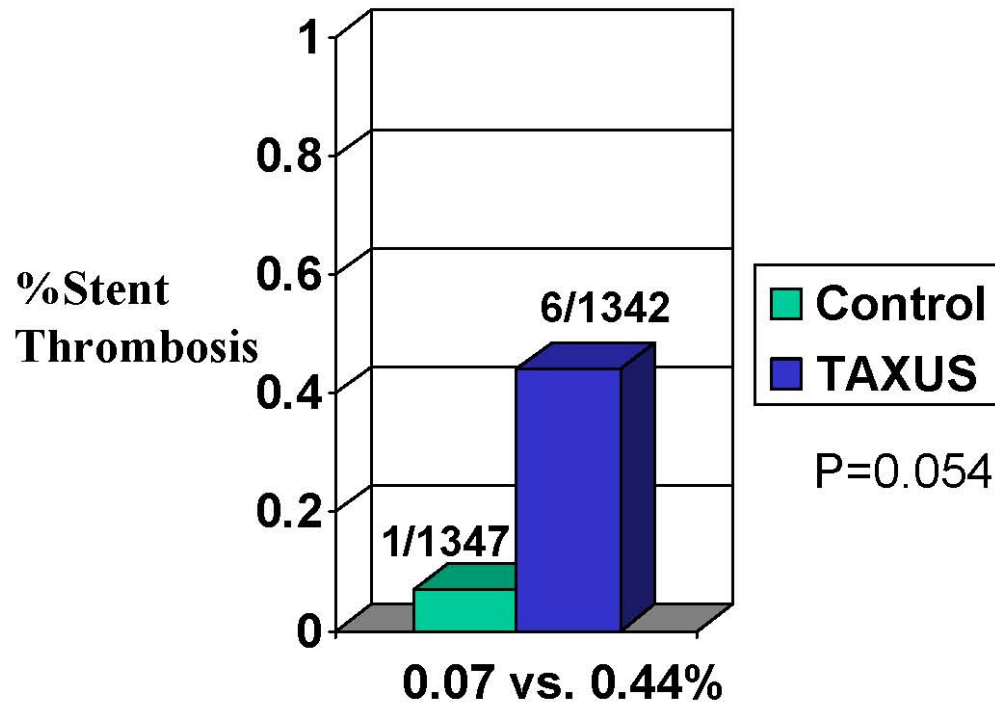
- **Use of a medical product for other than originally approved.**
- **Use not explicitly included in product labeling.**

“On Label Use”

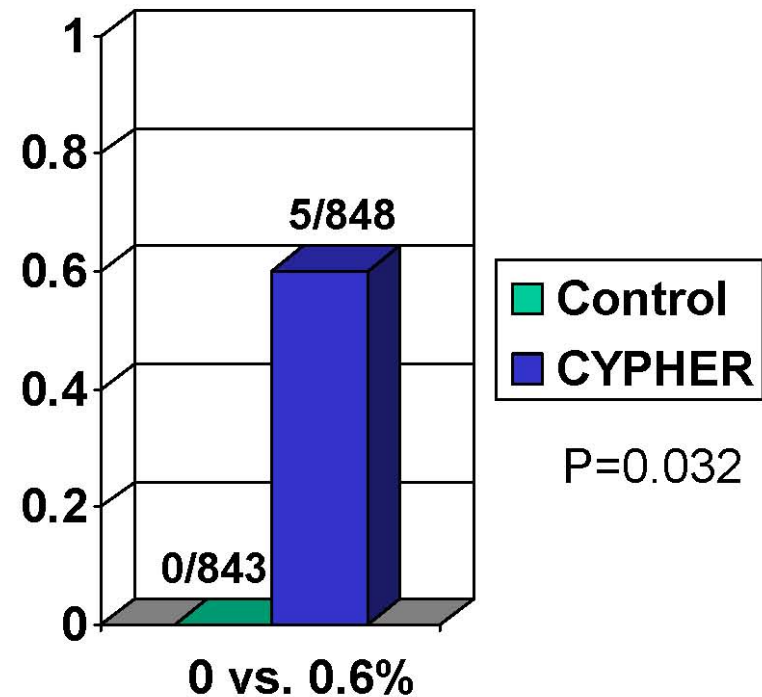
- **Single lesion**
- **De novo lesion**
- **Native coronary**
- **Patients with stable CAD only.**
- **Cypher: 2.5-3.5 mm vessel, <30 mm long.**
- **Taxus: 2.5-3.75 mm vessel, <28 mm long.**
- **Endeavor: 2.5-3.5 mm vessel, <28 mm long.**

Late DES Thrombosis On-Label Use Per Protocol Definitions

TAXUS I, II-SR, IV, V



RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS



Stent Thrombosis >1 Year Post-Implant Pooled
RCT's



U.S. Food and Drug Administration

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH



Conclusions. On Label Use

- **Both approved DES are associated with a small increase in thrombosis compared to metal stent that emerges 1 yearpost stent impalntation.**
- **Increase in stent thrombosis was not associated with an increase in Death or MI vs. BMS.**
- **The concerns of DES Thrombosis do not outweigh the benefits of DES vs BMS, when DES is used within the limits of their approved indications for use**

Off Label Use

- **Vessel size: Cypher < 2.5 mm or > 3.5mm,
Taxus <2.5mm or >3.75mm.**
- **Unstable syndromes, all MI's.**
- **Bifurcation**
- **CTO**
- **Ostial lesions**
- **Long lesions (> 28 or 30 mm).**
- **Bypass grafts.**
- **In-stent restenosis lesions.**
- **Multiple lesions or multiple vessels.**
- **Left main coronary artery.**

FDA Panel Discourages Off-Label Use of Drug-Eluting Stents

Continuing Antiplatelet Therapy Emphasized

BY WAYNE KUZNAR

GAITHERSBURG, Md—After off-label, and some estimate this

2 days of testimony, uncertainty hung over an advisory panel hearing to examine the safety of drug-eluting stents (DESs). DESs were deemed to pose an additional risk to patients used for simple stent placement, called on-label use, compared with bare-metal stents.

But when used off-label, as for bifurcation lesions, multiple stenoses, the benefit ratio of DESs was not

at least 60% of DESs are used

When DES are used Off-label, they are associated with increased risk of stent thrombosis, myocardial infarction and death, compared with on-label use.

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Conclusions. Off Label Use

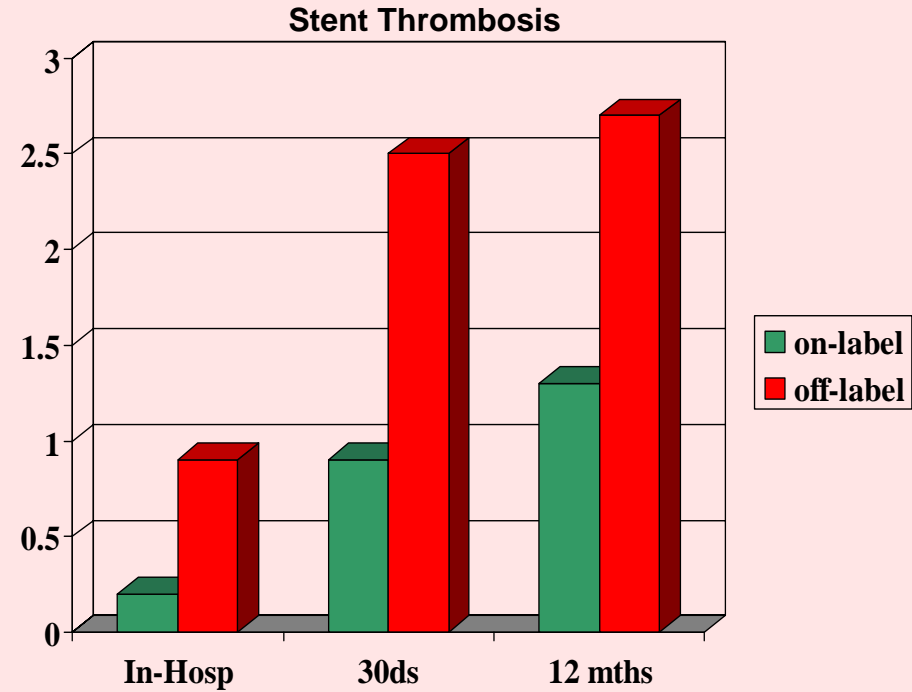
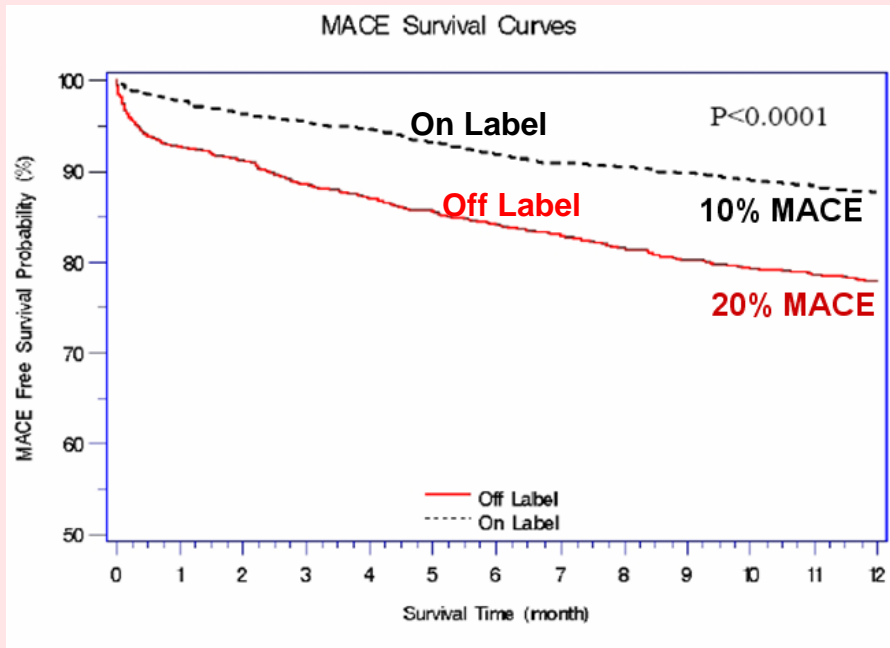
- **With more complex lesions there is an expected increase risk in adverse events, for both DES and BMS.**
- **Data on Off label use of DES are limited and further studies are needed to determine optimal treatment for patients with complex lesions.**

Off Label Data

On Label - Off Label use of DES.

Washington Hospital Center. Roy et al. AJC 2008; 101:293-9

3138 pts consecutive patients with DES (4656 lesions)



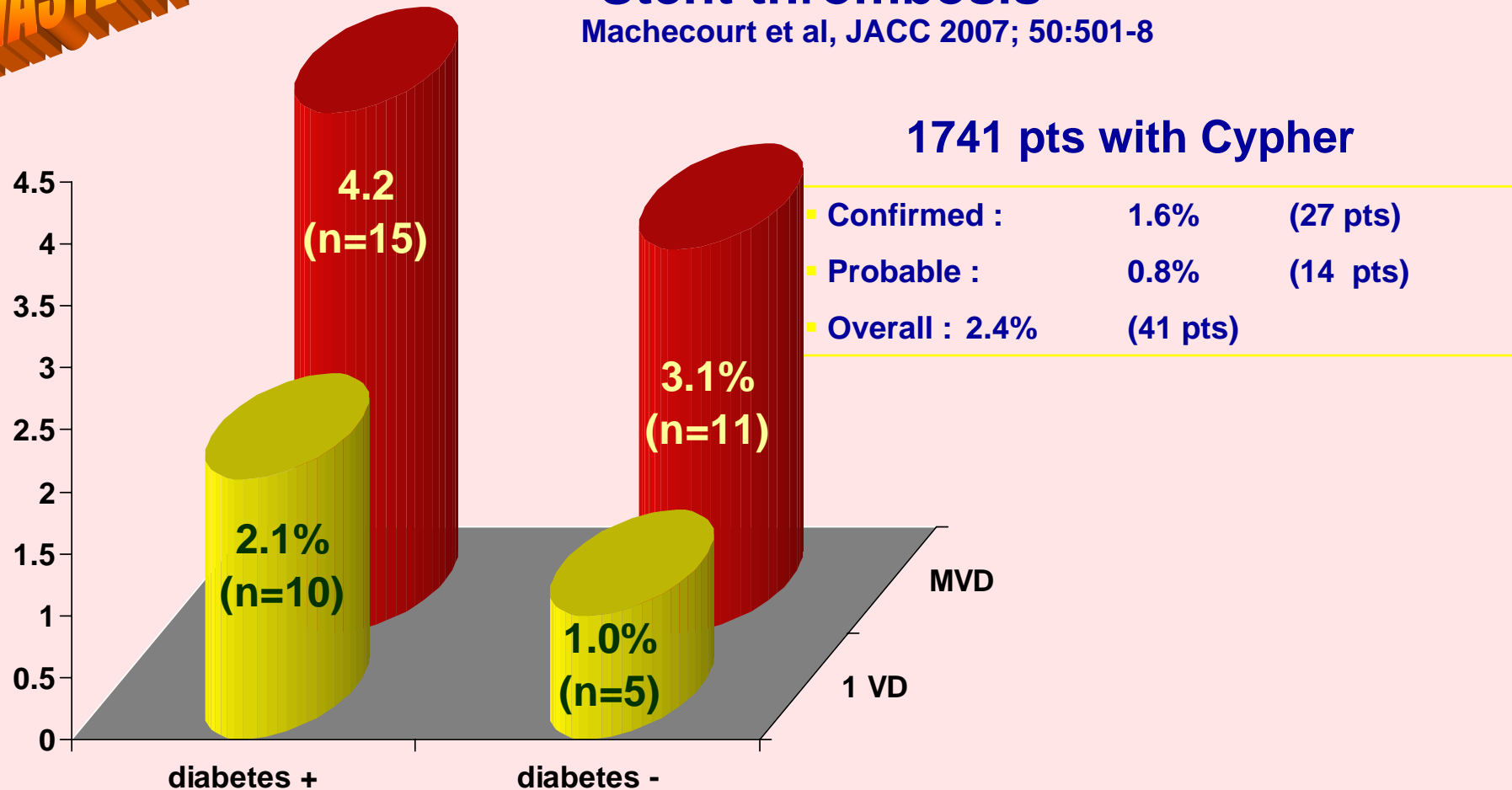
On Label 1773 patients (2228 lesions)
Off Label 1365 patients (2428 lesions)



Stent thrombosis

Machecourt et al, JACC 2007; 50:501-8

1741 pts with Cypher



Confirmed :	1.6%	(27 pts)
Probable :	0.8%	(14 pts)
Overall :	2.4%	(41 pts)

db+ 3% vs. db- 1.7% p=.07

Ins+ DM 3.7% vs. db- 1.7% p=.001

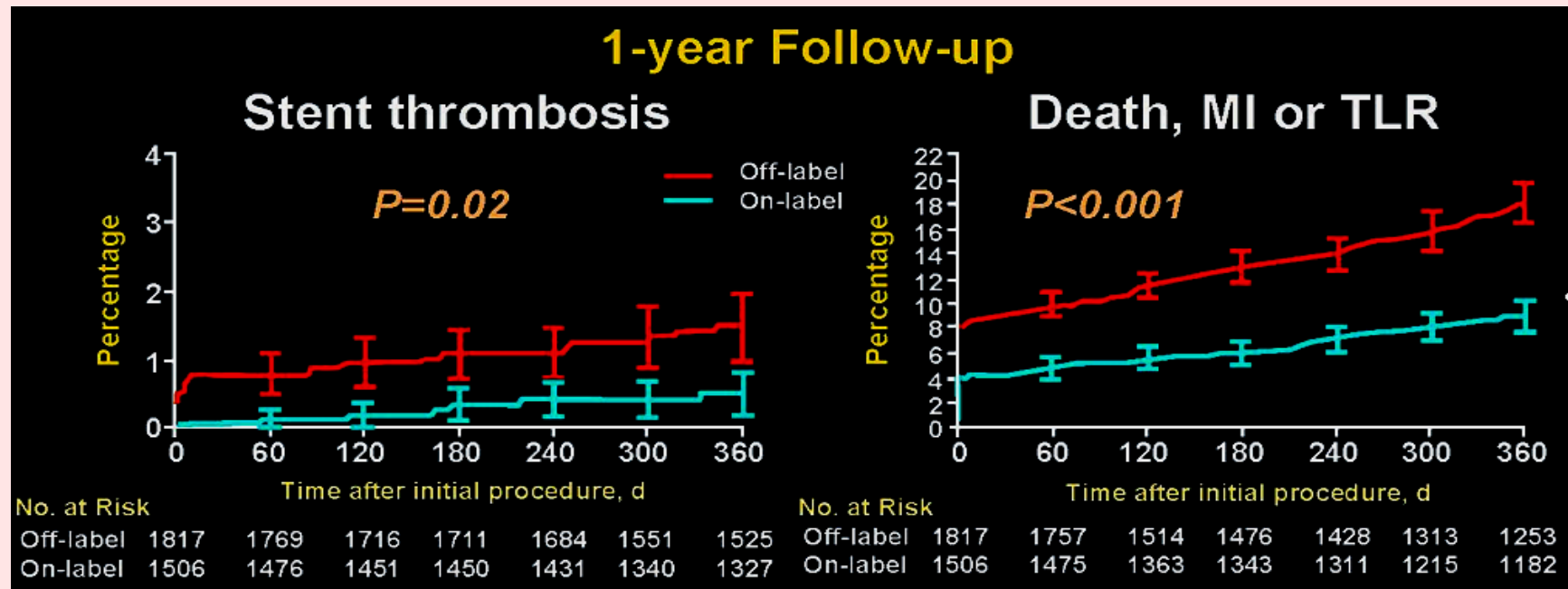
XVD 3.7% vs. 1VD 1.5% p<004

Off Label Use

Win et al. EVENT Registry. JAMA 2007;297:2001-9

3323 patients

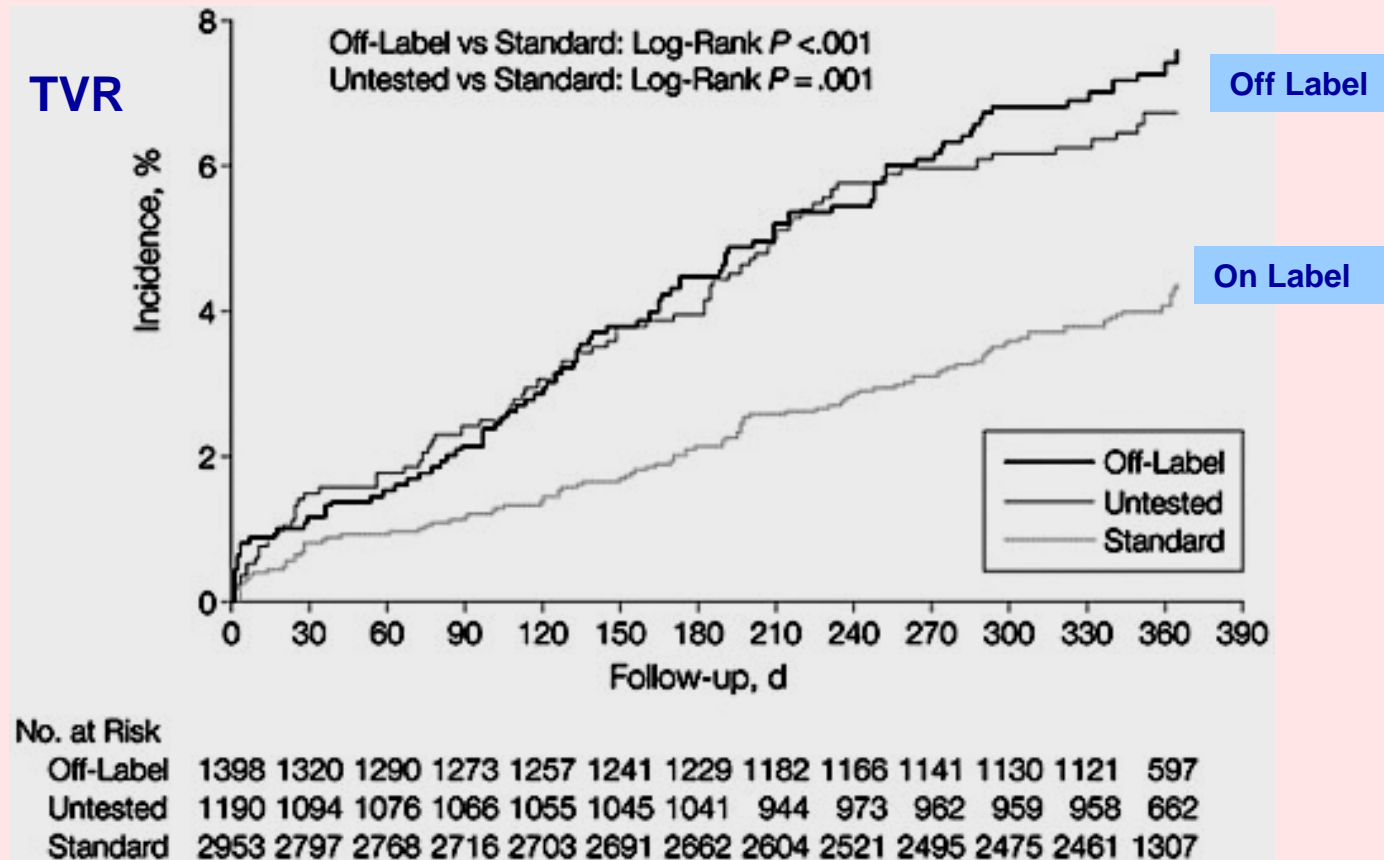
1-year Follow-up



There was no evidence of interaction between label status and concurrent dual antiplatelet therapy status, nor between 6-month dual antiplatelet therapy status for any of the outcomes at 6 or 12 months.

On-Off Label DES

Beohar, Williams et al. (Discover Registry) JAMA 2007;297:1992-2000



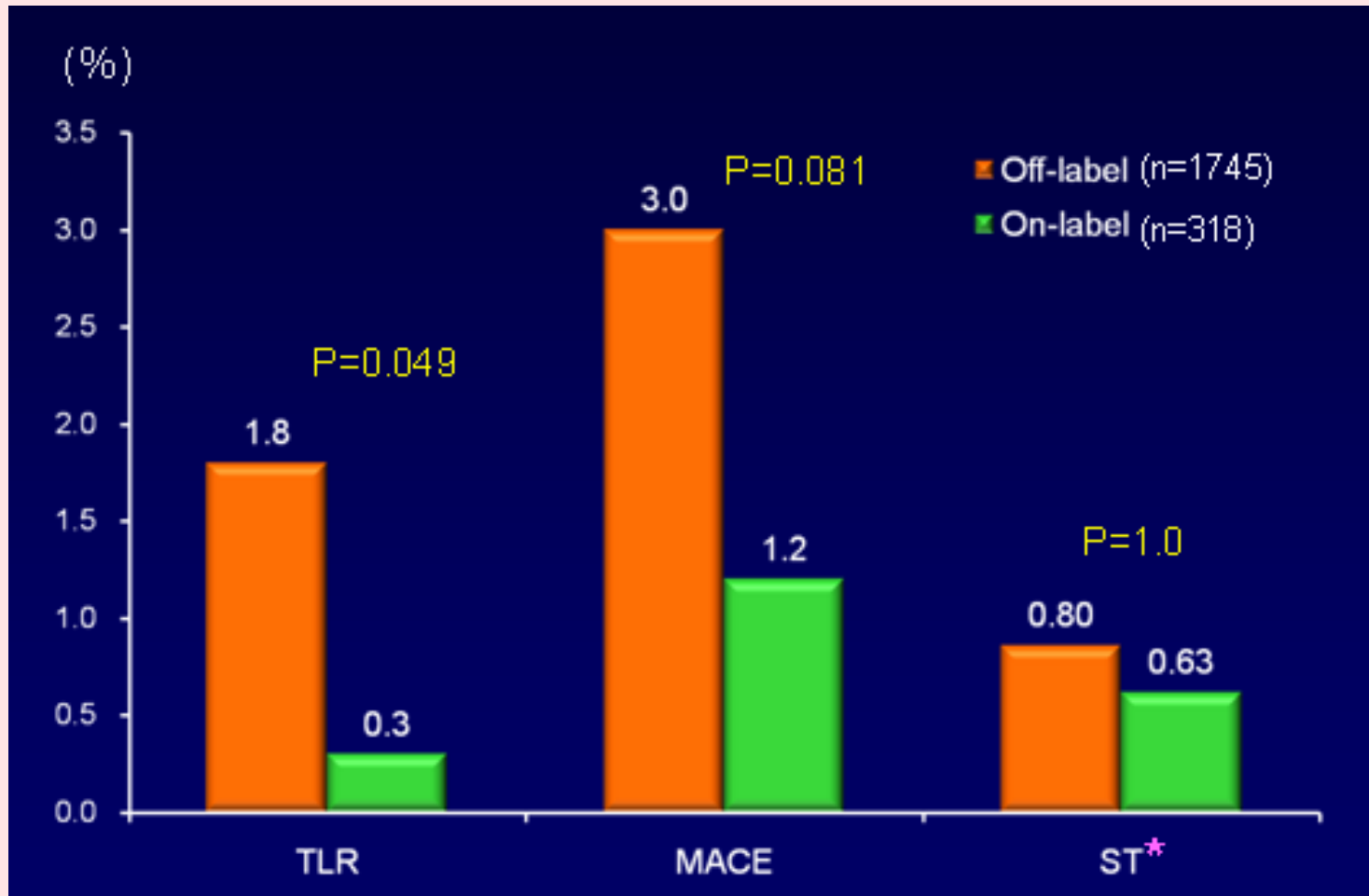
Untested: LM, ostial, bifurcation, CTO.

Off label: RS, bypass graft, long lesions, vessel size < 2.5 or > 3.5 mm.

Standard: on label

On Label vs. Off Label DES.

CREATE Registry. Han et al. ACC2008

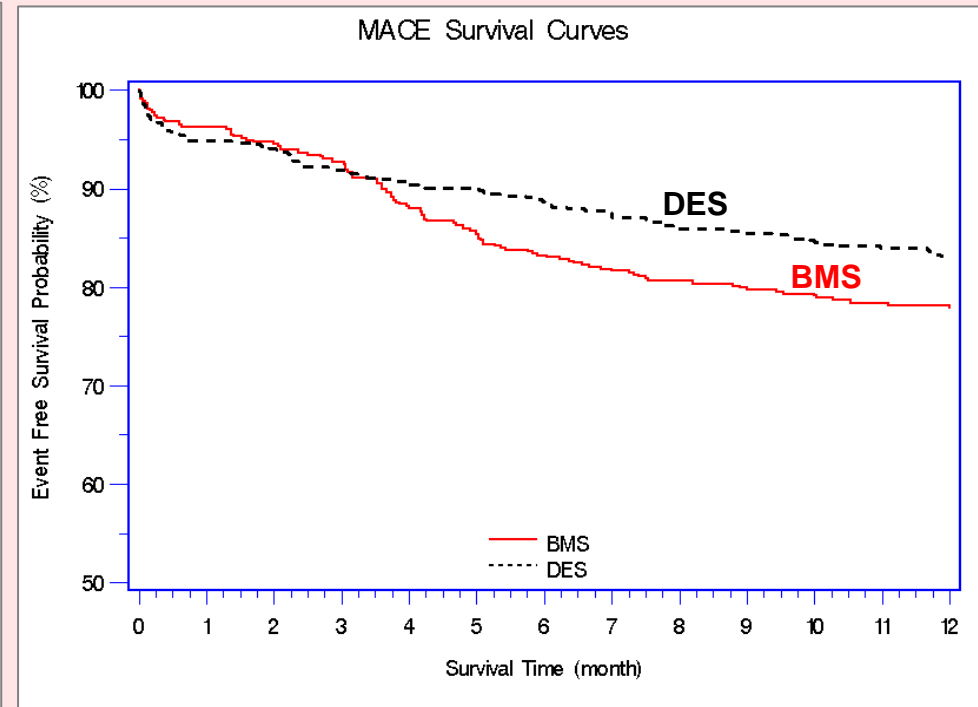
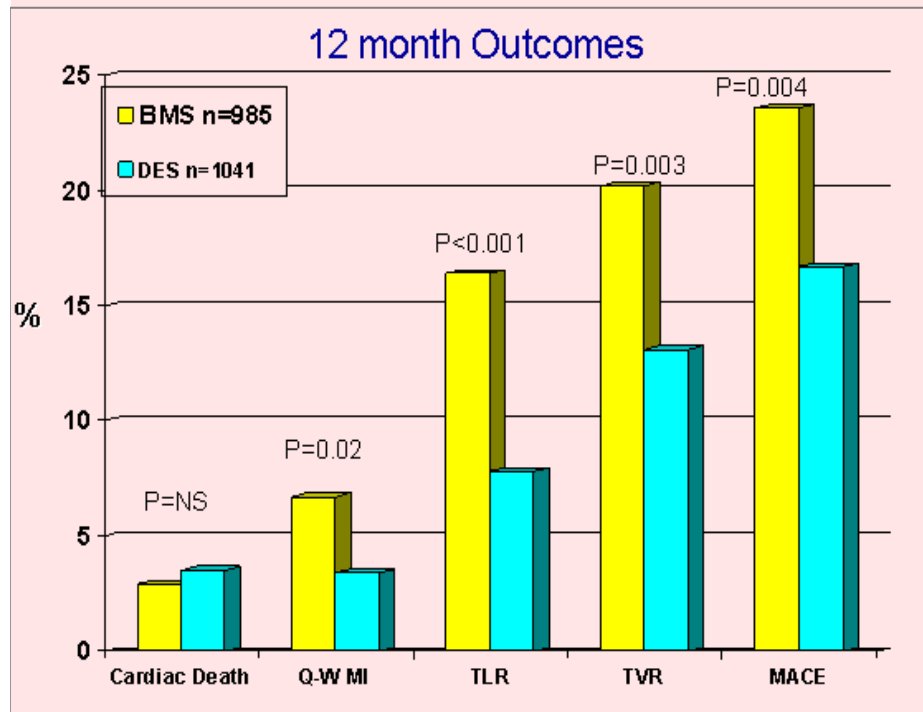


* ST=stent thrombosis

Off Label DES and BMS.

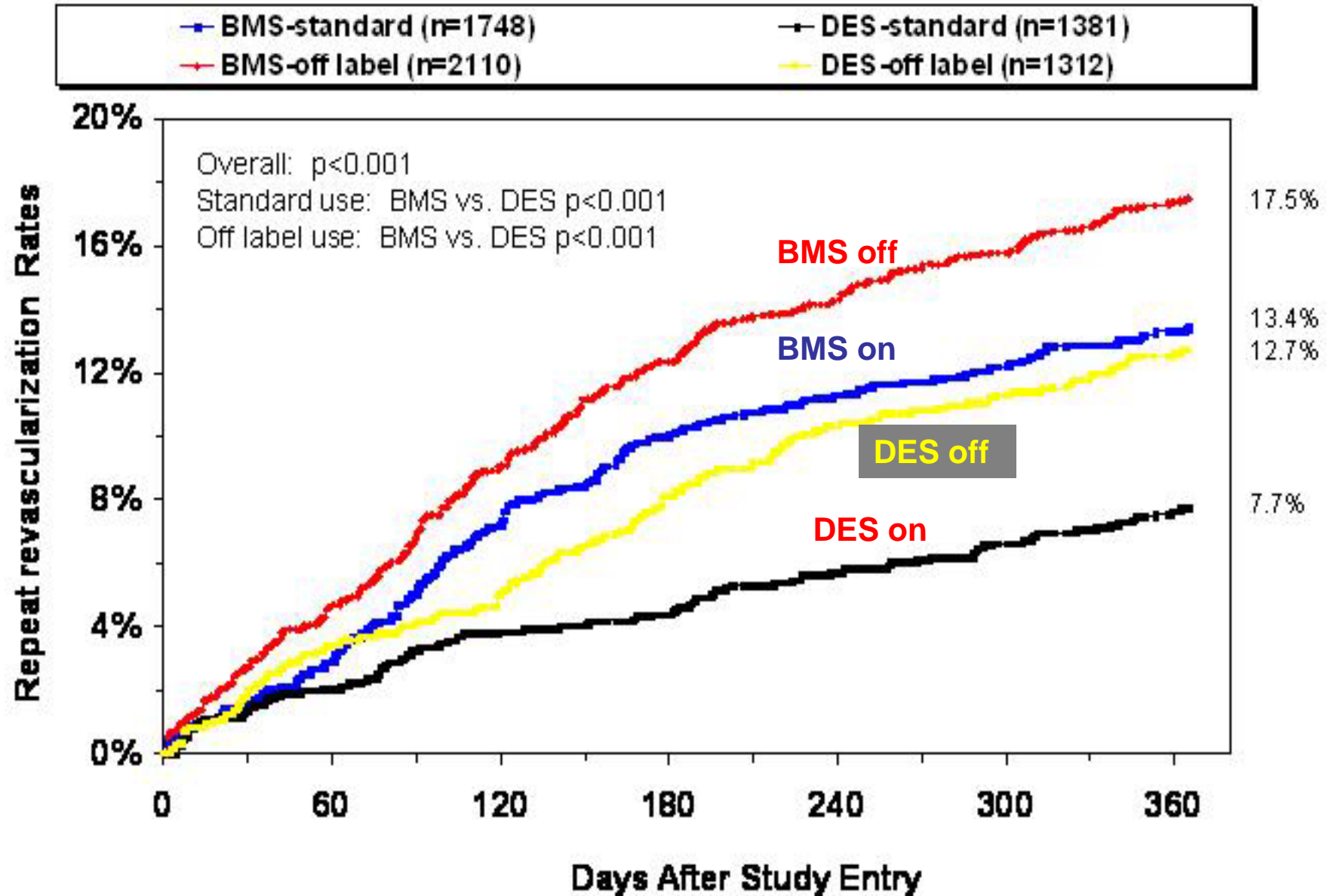
WHC. Roy et al. AJC 2008; 101: 293-9

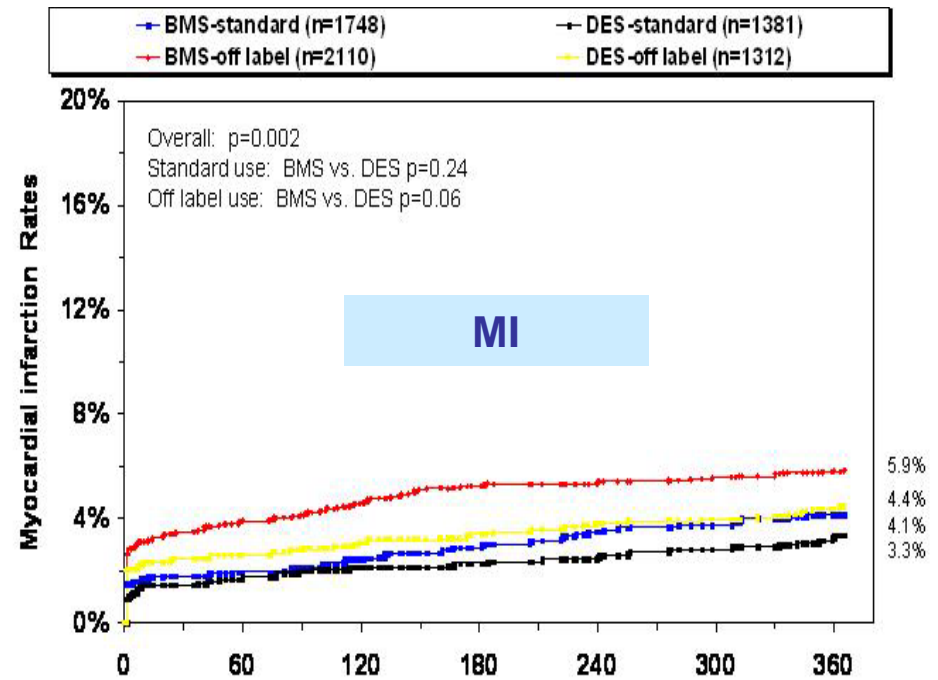
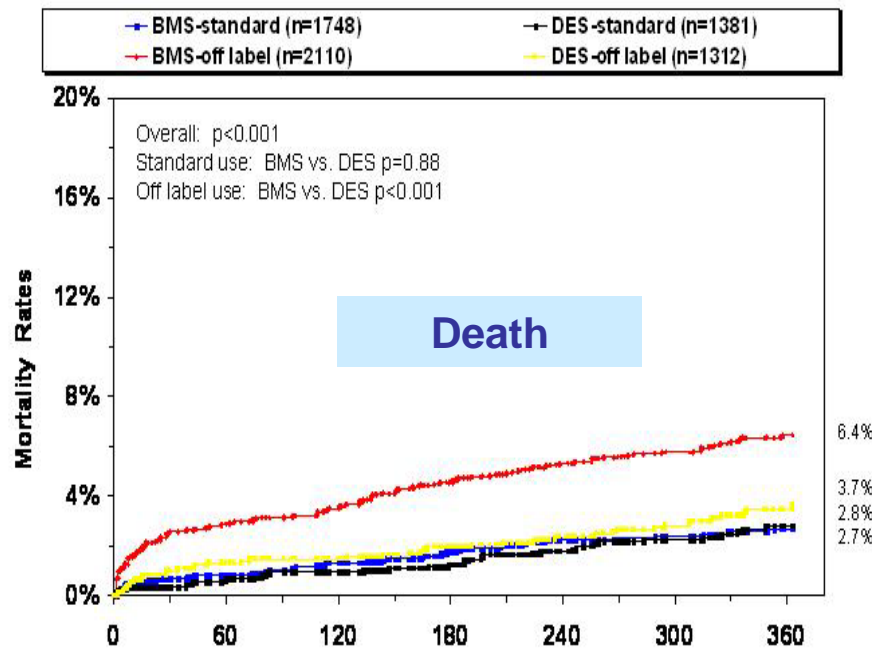
1041 DES lesions matched with 985 BMS lesions. All Off Label



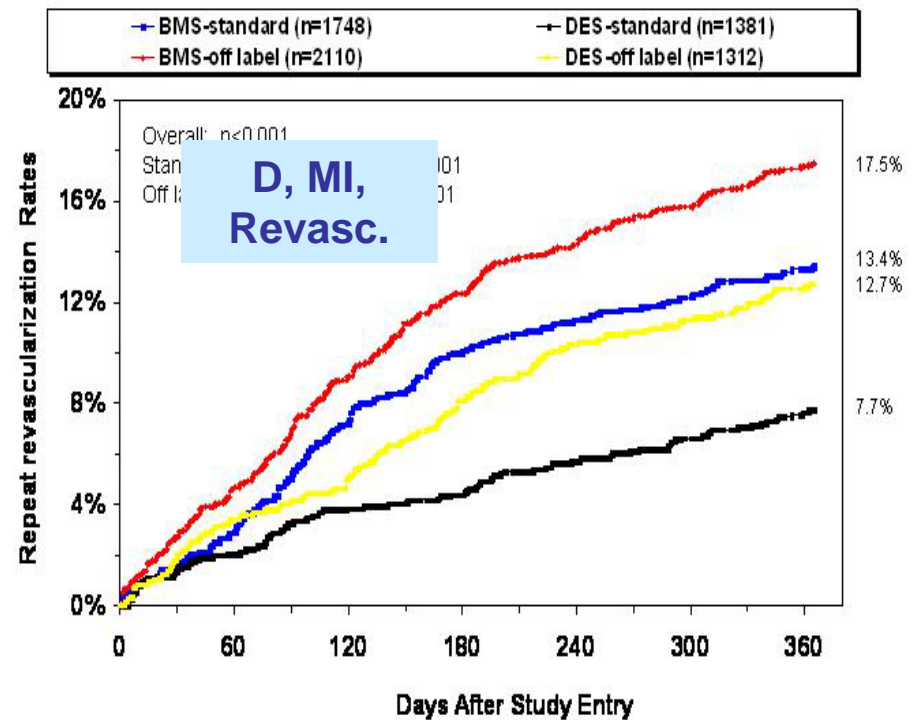
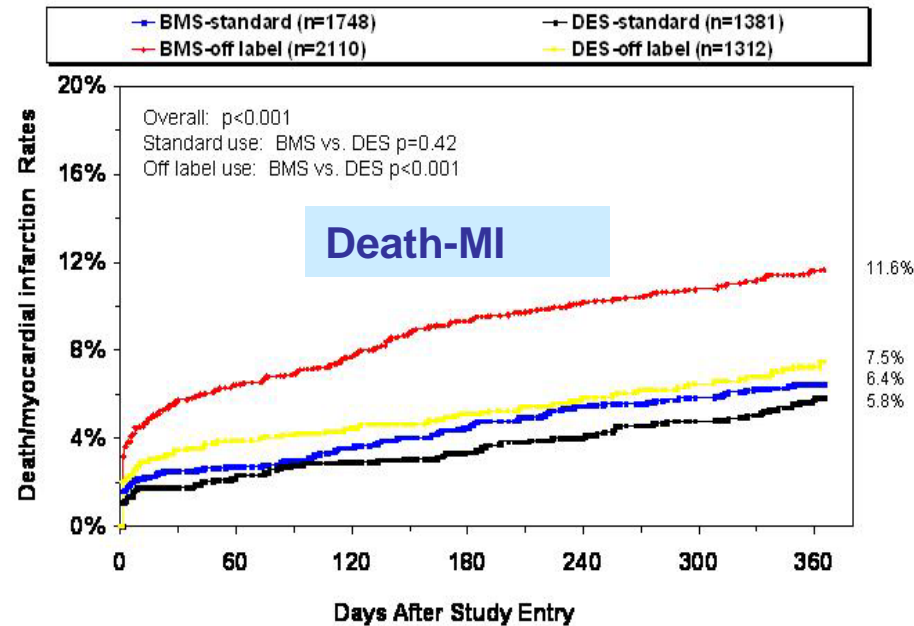
Off Label DES vs BMS

NIH Dynamic Registry. Marroquin et al. NEJM 2008;358:342-50





One-year cumulative death/myocardial infarction by stent type & labeling indications



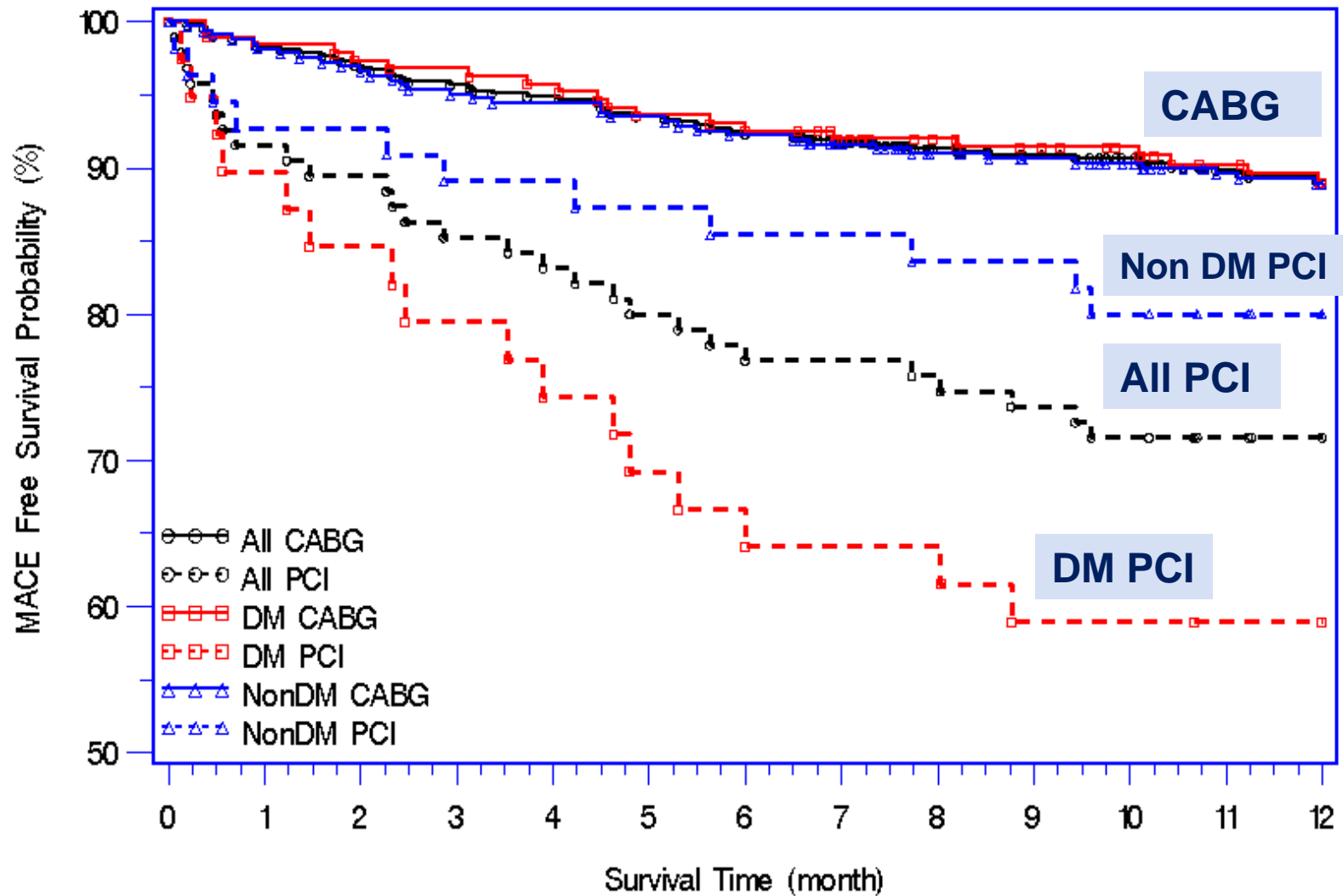
DES vs BMS Off Label Conclusion.

- DES offers the most benefit in Off Label lesions.**
- DES in Off Label lesions have more MACE than On Label.**

**Outcome of DES
in Patients with
Multiple Vessel Disease**

3 Vessel Disease. CABG vs PCI

WHC. Javaid et al. Circulation 2007; 116: I-200-6



- **For multiple off-label lesions (long, small, bifurc, etc.), specially in diabetics, DES is better than BMS but may not the best solution for the patient.**
- **Other alternatives to PCI need to be carefully considered, i.e., coronary surgery.**

Conclusions

- **DES is the best device available for the treatment of “off-label” lesions.**
- **DES is better than BMS in “off-label” lesions.**
- **The results of the Randomized Clinical Trials in “on-label” lesions cannot be applied to “off-label” lesions.**
- **PCI of “off-label” lesions can have significant MACE events on follow up.**
- **Solid clinical judgment required to decide best therapy in patients with “off-label” lesions.**