# Comparison of the Efficacy and Safety of *Z*otarolimus-*E*luting Stent versus *S*irolimus-Eluting Stent and Pacli*T*axel-Eluting Stent for Coronary Lesions:

# The ZEST Trial

## Featuring the First Presentation of the ZEST 2-Year Results

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on behalf of the ZEST trial

# ZEST Trial – Disclosure Information

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- CardioVascular Research Foundation (CVRF), Seoul, Korea
- Korea Health 21 R&D Project, Ministry of Health and Welfare, Korea (0412-CR02-0704-0001) &
- Medtronic Vascular

# ZEST: Study Algorithm

All Comer requiring PCI with DES for coronary lesions
in 19 Centers of Korea
(Total 2,645 patients)

Randomize 1:1:1
stratified by 1) Sites, 2) Diabetes, 3) Long lesions (≥ 28 mm)

**ENDEAVOR®**
**(N=883)**

**CYPER Select®**
**(N=878)**

**TAXUS Liberte™**
**(N=884)**

Clinical follow-up at 12 months
Angiographic follow-up at 9 months

# Enrollment Criteria

## Major Inclusion Criteria

- Significant CAD (≥ 50% stenosis), amenable to stent-assisted PCI
- Stable angina or ACS (unstable angina, NSTEMI)
- No limitations on the number of lesions or vessels or on the length of the lesions, reflecting routine clinical practice.

## Major Exclusion Criteria

- STEMI requiring primary PCI
- Severe LV dysfunction (EF < 25%) or cardiogenic shock
- Left main disease
- In-stent restenosis of DES
- Termini illness
- Participation in another coronary-device study.

# Study Endpoints

## Primary end point

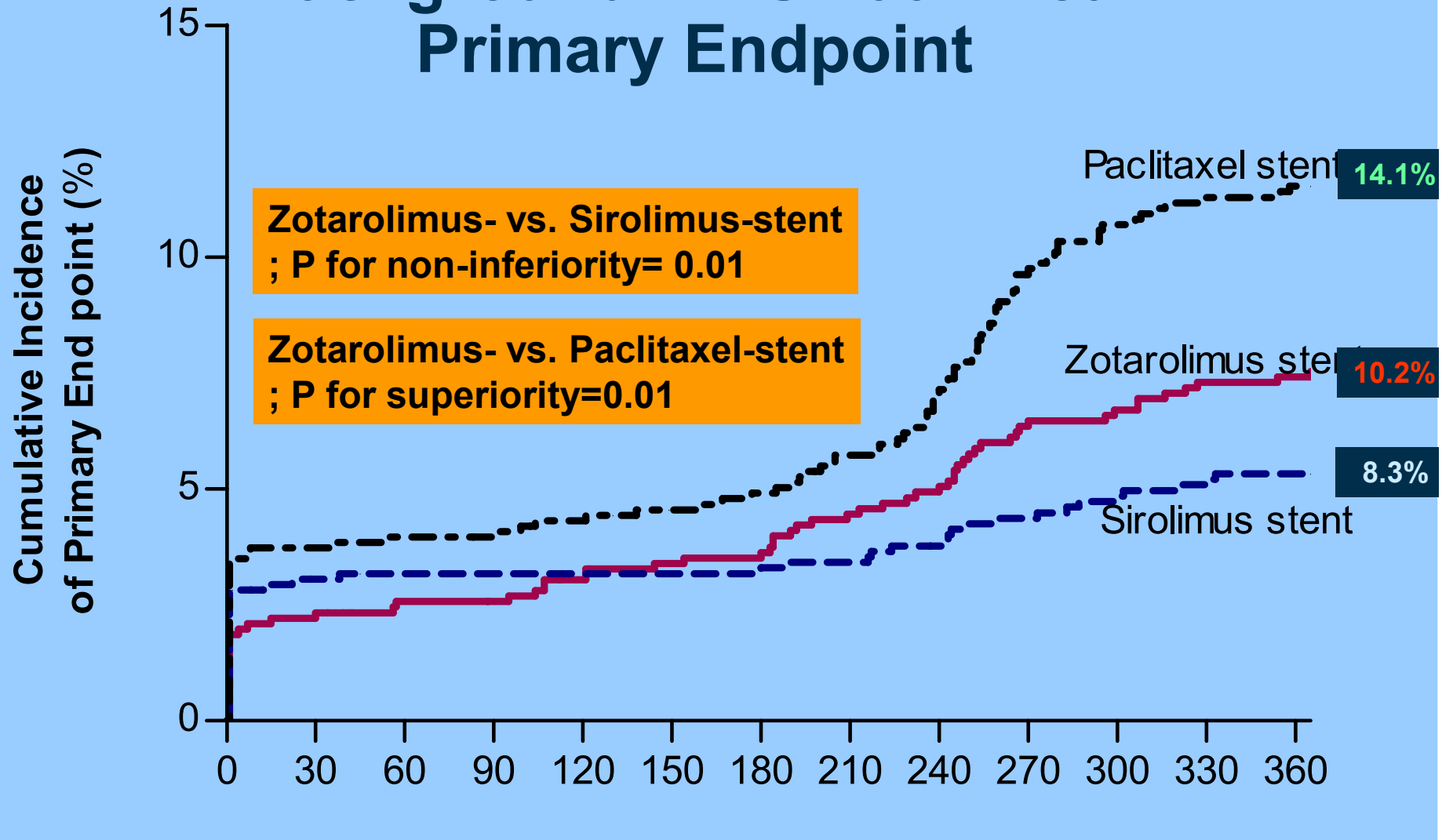
- The composite clinical outcome of
  - Death from any cause
  - Myocardial infarction (MI)
  - Ischemia-driven target-vessel revascularization (TVR)

  at 12 months after the index procedure.

## Secondary end point

- Individual components of the primary outcome.
- Composite of death or MI.
- Ischemia-driven target-lesion revascularization (TLR).
- Stent thrombosis by the ARC definition.
- In-stent and in-segment late loss and binary restenosis at 9 months angiography.

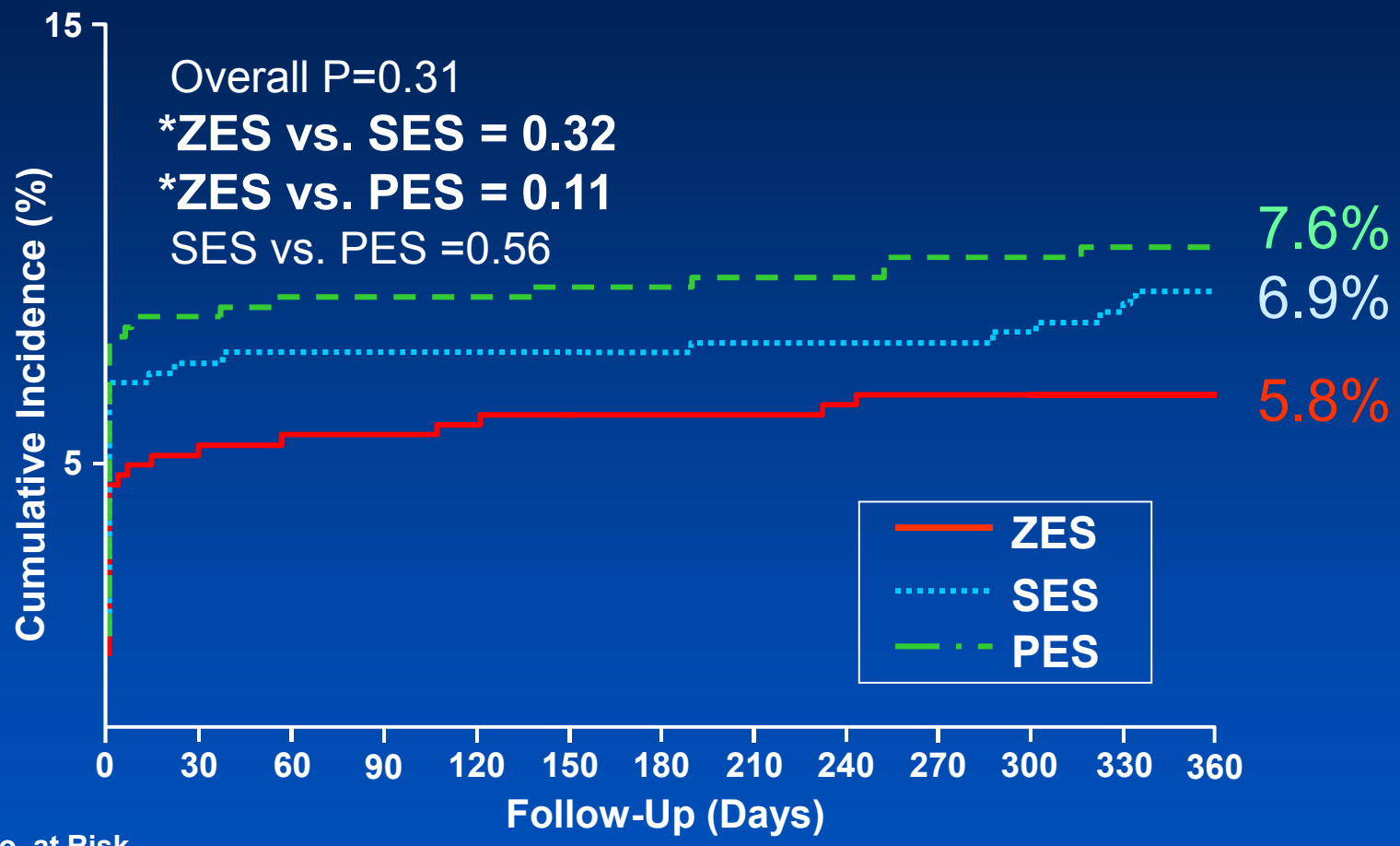
# Background: ZEST at 1-Year Primary Endpoint




| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Zotarolimus stent | 883 | 827 | 816 | 790 | 782 |
| Sirolimus stent | 878 | 816 | 813 | 802 | 792 |
| Paclitaxel stent | 884 | 821 | 808 | 763 | 745 |

[Final-acceptance and In-Press; JACC2010]

# Death or MI at 12 month




**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 828 | 824 | 820 | 820 |
| SES | 878 | 817 | 814 | 811 | 804 |
| PES | 884 | 821 | 815 | 808 | 803 |

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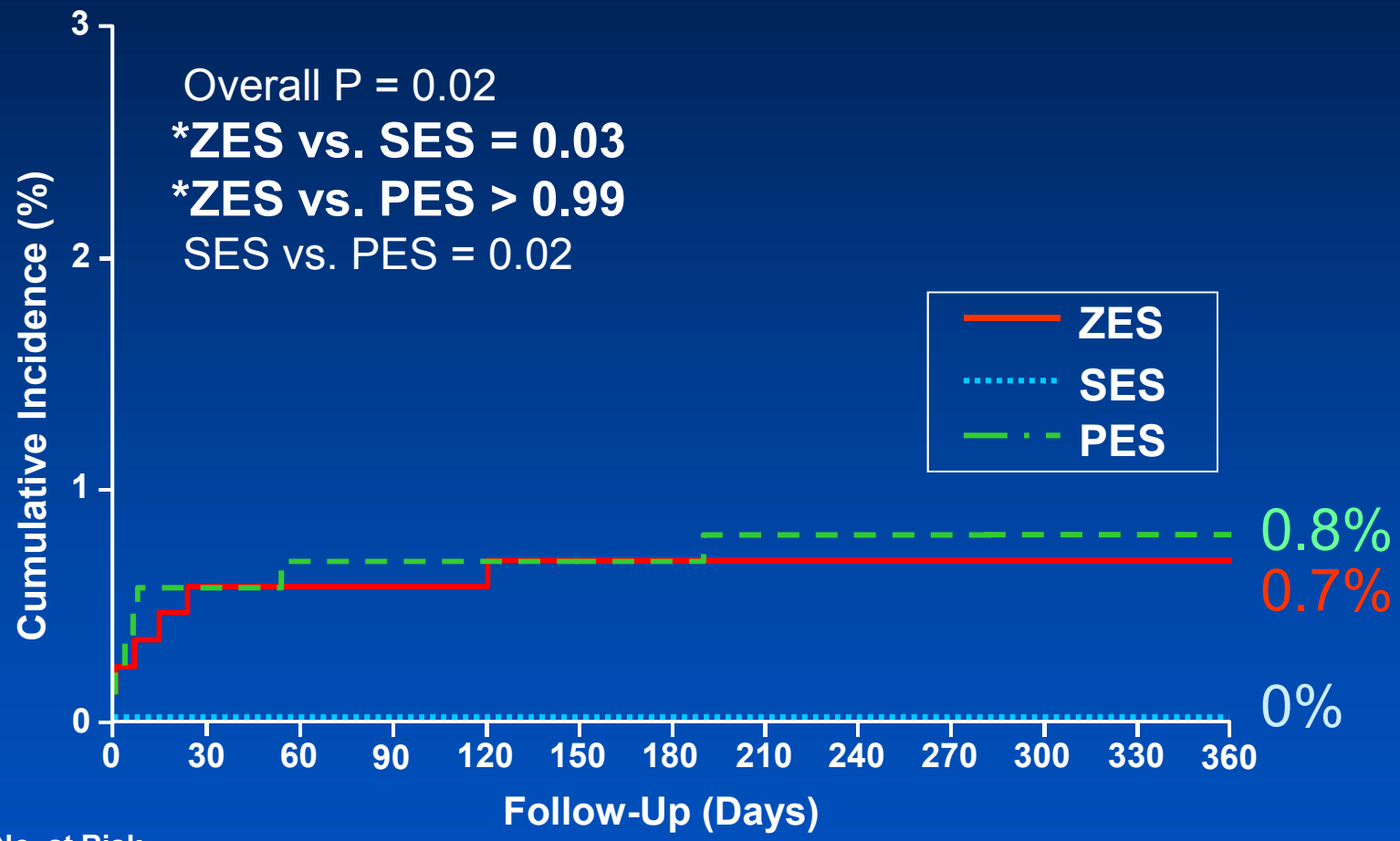
# Stent thrombosis at 12 month

## : ARC Definite or Probable Criteria




| No. at Risk | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 869 | 866 | 861 | 861 |
| SES | 878 | 869 | 867 | 863 | 857 |
| PES | 884 | 875 | 868 | 859 | 853 |

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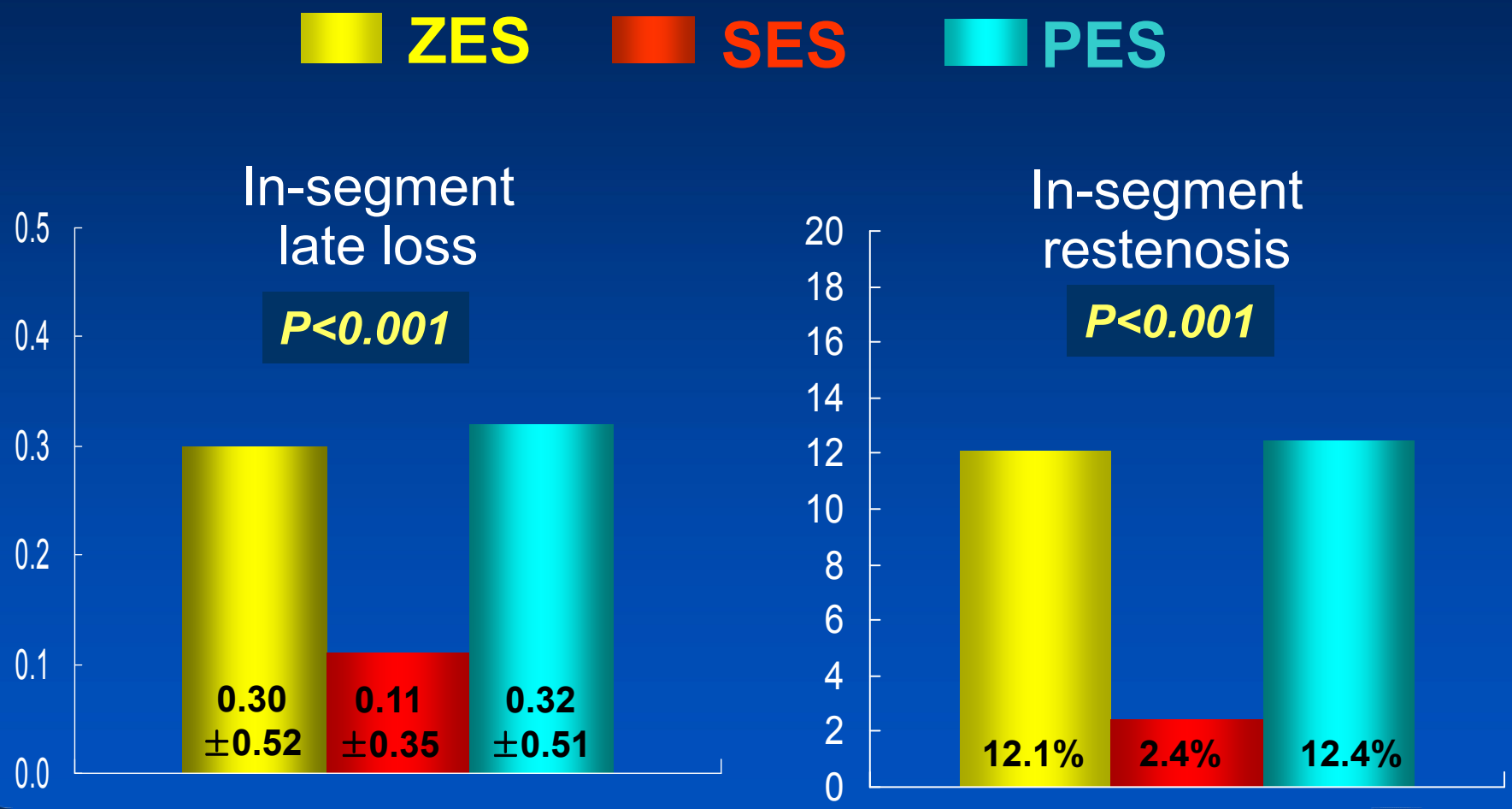
# Background: ZEST at 1-Year Angiographic Outcomes

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# Background: ZEST at 1 Year

- In this large-scale, practical RCT, the zotarolimus-eluting stent compared to the sirolimus-eluting and the paclitaxel-eluting stent resulted in:
  - ZES was noninferior to SES and was superior to PES in the composite endpoint of death, MI, and ischemia-driven TVR at 12 months.
  - Rate of death or MI at 1-year was similar among the 3 groups.
  - SES is associated with lowest angiographic restenosis, with lowest need for TLR, and with the lowest risk of stent thrombosis among the tested 3 type of DES.
- **Two-year clinical outcomes have not yet been reported**

# Baseline Characteristics

| Patients | ZES (n=883) | SES (n=878) | PES (n=884) | P value |
|---|---|---|---|---|
| Age (yr) | 62±9 | 62±10 | 62±10 | 0.80 |
| Male sex | 586 (66) | 591 (67) | 582 (66) | 0.80 |
| Body mass index | 25±3 | 25±3 | 25±3 | 0.88 |
| Diabetes mellitus | | | | |
| Any diabetes | 268 (30) | 247 (28) | 245 (28) | 0.42 |
| Requiring insulin | 32 (4) | 33 (4) | 36 (4) | 0.88 |
| Hypertension | 552 (63) | 517 (59) | 540 (61) | 0.29 |
| Hyperlipidemia | 466 (53) | 451 (51) | 446 (51) | 0.62 |
| Current smoker | 236 (27) | 256 (29) | 243 (28) | 0.51 |
| Family history of CAD | 48 (5) | 44 (5) | 52 (6) | 0.72 |

n (%)

# Baseline Characteristics

| Patients | ZES (n=883) | SES (n=878) | PES (n=884) | P value |
|---|---|---|---|---|
| Previous PCI | 75 (9) | 82 (9) | 83 (9) | 0.76 |
| Previous CABG | 6 (1) | 6 (1) | 5 (1) | 0.94 |
| Previous MI | 30 (3) | 39 (4) | 41 (5) | 0.37 |
| Previous CHF | 9 (1) | 4 (1) | 7 (1) | 0.39 |
| Chronic lung disease | 13 (2) | 8 (1) | 26 (3) | 0.004 |
| Cerebrovascular disease | 65 (7) | 55 (6) | 53 (6) | 0.47 |
| Peripheral vascular disease | 15 (2) | 21 (2) | 17 (2) | 0.57 |
| Renal insufficiency | 7 (1) | 7 (1) | 6 (1) | 0.95 |
| Multi-vessel disease | 414 (47) | 430 (49) | 410 (46) | 0.51 |
| Ejection fraction (%) | 61±8 | 61±8 | 61±8 | 0.59 |

n (%)

# Baseline Characteristics

| Patients | ZES (n=883) | SES (n=878) | PES (n=884) | P value |
|---|---|---|---|---|
| Clinical indication (%) | | | | 0.73 |
| Silent ischemia | 48 (5) | 44 (5) | 56 (6) | |
| Chronic stable angina | 348 (39) | 343 (39) | 343 (39) | |
| Unstable angina | 410 (46) | 424 (48) | 403 (46) | |
| NSTEMI | 77 (9) | 67 (8) | 82 (9) | |
| Electrocardiographic findings | | | | 0.99 |
| Sinus rhythm | 850 (96) | 849 (97) | 854 (97) | |
| Atrial fibrillation | 21 (2) | 18 (2) | 17 (2) | |
| Other | 12 (1) | 11 (1) | 13 (1) | |

n (%)

# Lesion Characteristics

| Lesions | ZES (n=1190) | SES (n=1218) | PES (n=1205) | P value |
|---|---|---|---|---|
| Location | | | | 0.39 |
| LAD | 622 (52) | 645 (53) | 611 (51) | |
| LCX | 252 (21) | 225 (19) | 253 (21) | |
| RCA | 316 (27) | 348 (29) | 340 (28) | |
| Coronary graft | 0 | 0 | 1 (0.1) | |
| ACC-AHA B2 or C type | 858 (72) | 921 (76) | 895 (74) | 0.14 |
| Total occlusion | 68 (6) | 76 (6) | 96 (8) | 0.07 |
| Thrombus-containing | 32 (3) | 37 (3) | 38 (3) | 0.78 |
| Bifurcation lesion | 181 (15) | 151 (12) | 168 (14) | 0.14 |
| Ostial lesion | 85 (7) | 72 (6) | 82 (7) | 0.45 |
| Restenotic lesion | 5 (0.4) | 12 (1) | 13 (1) | 0.16 |

n (%)

# Lesion Characteristics

| Lesions | ZES (n=1190) | SES (n=1218) | PES (n=1205) | P value |
|---|---|---|---|---|
| Calcification | | | | 0.76 |
| None or mild | 1129 (95) | 1145 (94) | 1132 (94) | |
| Moderate | 40 (3) | 43 (4) | 46 (4) | |
| Severe | 21 (2) | 30 (3) | 27 (2) | |
| Lesion length | | | | 0.09 |
| <10 mm | 73 (6) | 71 (6) | 61 (5) | |
| 10-20 mm | 466 (39) | 444 (37) | 504 (42) | |
| >20 mm | 651 (55) | 703 (58) | 640 (53) | |

n (%)

# Procedural Characteristics

| Lesions | ZES (n=1190) | SES (n=1218) | PES (n=1205) | P value |
|---|---|---|---|---|
| No. of stents per lesion | 1.2±0.4 | 1.2±0.4 | 1.2±0.4 | 0.35 |
| No. of stents per patient | 1.6±0.9 | 1.6±0.9 | 1.6±0.9 | 0.92 |
| Length of stents per lesion | 27.9±13.1 | 28.9±13.5 | 28.9±14.3 | 0.12 |
| Length of stents per patients | 39.7±26.8 | 38.3±24.3 | 38.9±25.2 | 0.45 |
| Maximal stent diameter | 3.4±0.7 | 3.4±0.7 | 3.5±0.6 | 0.03 |
| Maximal pressure | 16.3±4.2 | 16.3±4.1 | 16.2±4.2 | 0.95 |
| Direct stenting | 84 (7) | 109 (9) | 89 (7) | 0.24 |
| Use of IVUS | 488 (41) | 514 (42) | 491 (41) | 0.62 |
| Use of glycoprotein IIb-IIIa inhibitors | 19 (2) | 15 (2) | 14 (2) | 0.64 |

n (%)

# Clinical Events During 24 Months of Follow-Up

# ZEST Patient Flow

All Comer requiring PCI with DES for coronary lesions
(**Total 2,645 patients, 3613 lesions**)

**Randomization**

| ENDEAVOR® (N=883) | CYPER select® (N=878) | TAXUS Liberte™ (N=884) |
|---|---|---|

**1-Year Clinical (N=2,603; 98.4%)**

| ENDEAVOR® (N=870; 98.5%) | CYPER select® (N=864; 98.4%) | TAXUS Liberte™ (N=869;98.3%) |
|---|---|---|

**2-Year Clinical (N=2,552; 96.5%)**

| ENDEAVOR® (N=853, 96.6%) | CYPER select® (N=847, 96.5%) | TAXUS Liberte™ (N=852, 96.4%) |
|---|---|---|

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*F/U window ±30 days

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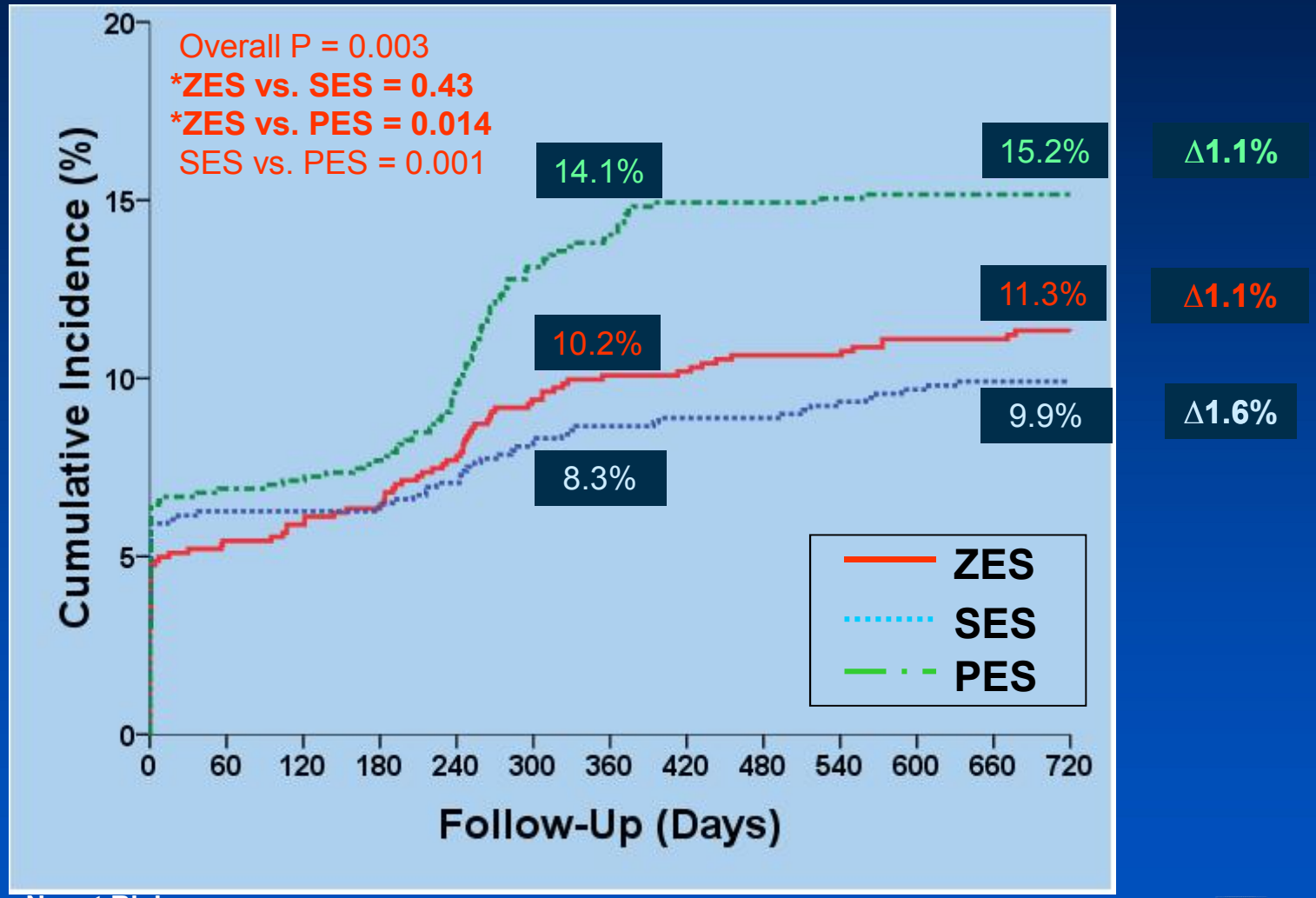
# Primary End Point at 24 month

## : Death, MI, Ischemia-driven TVR




**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 826 | 794 | 788 | 622 |
| SES | 878 | 821 | 802 | 795 | 621 |
| PES | 884 | 816 | 760 | 748 | 573 |

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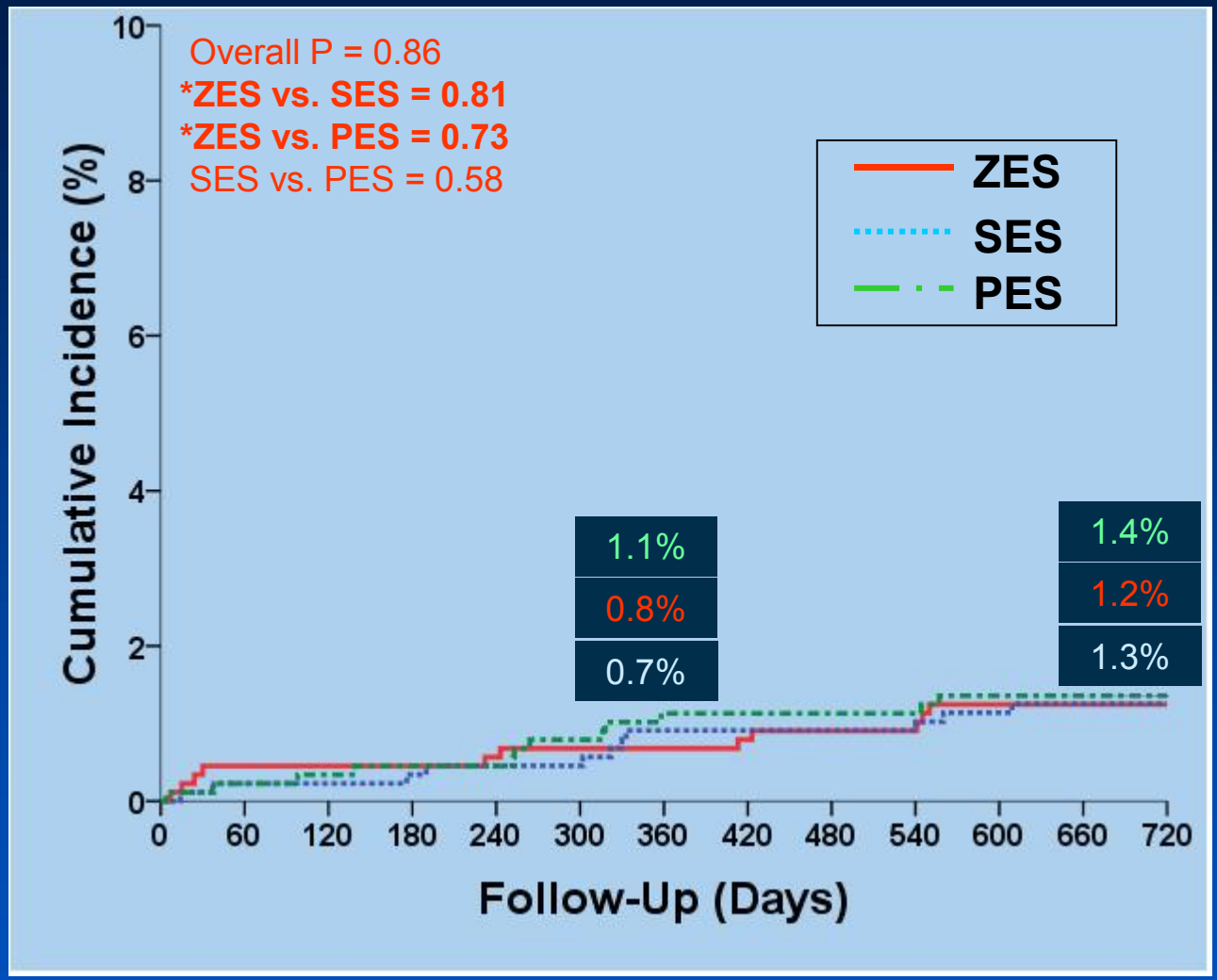
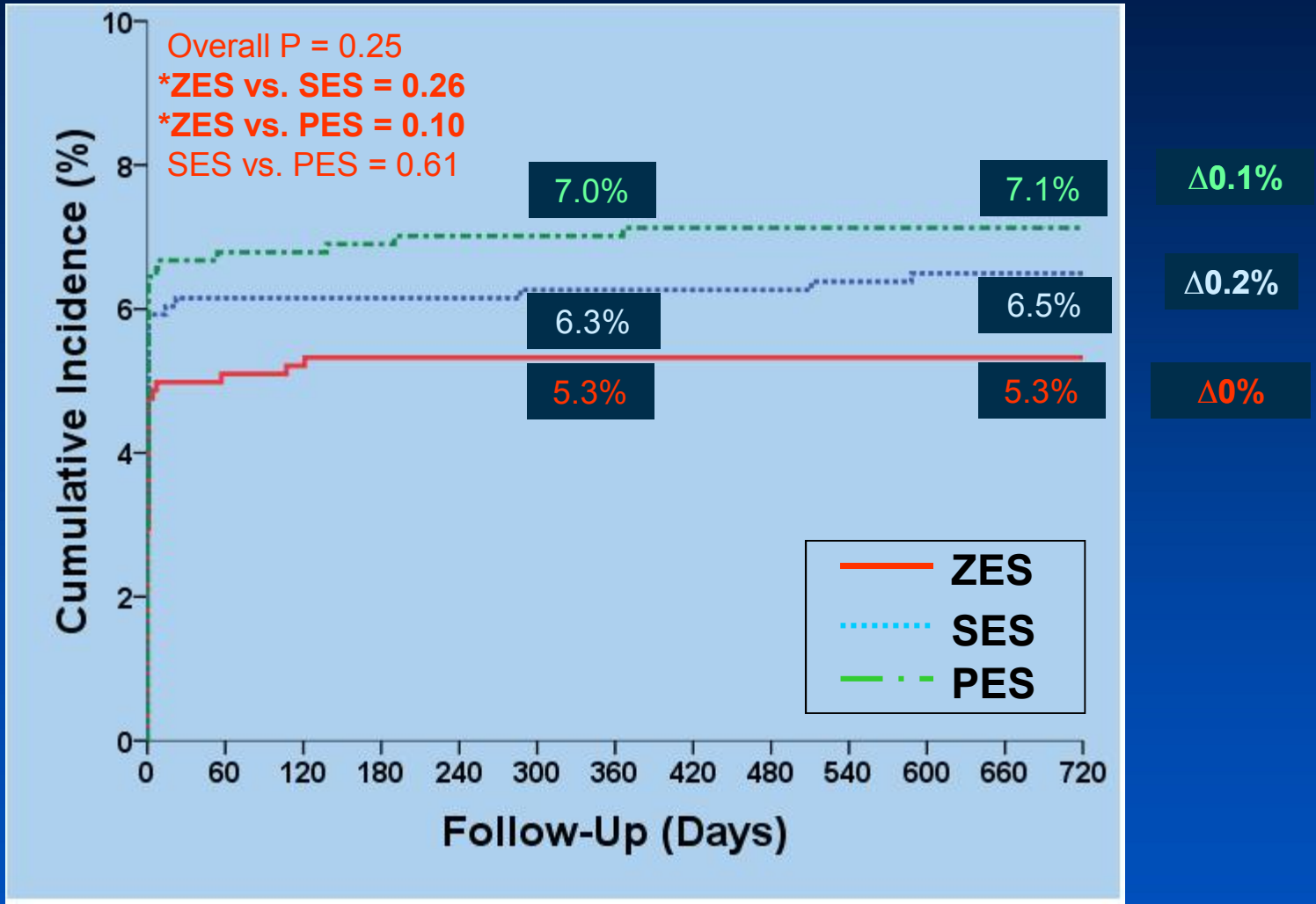
# Death at 24 month




**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 879 | 877 | 874 | 684 |
| SES | 878 | 875 | 870 | 868 | 674 |
| PES | 884 | 880 | 874 | 870 | 664 |

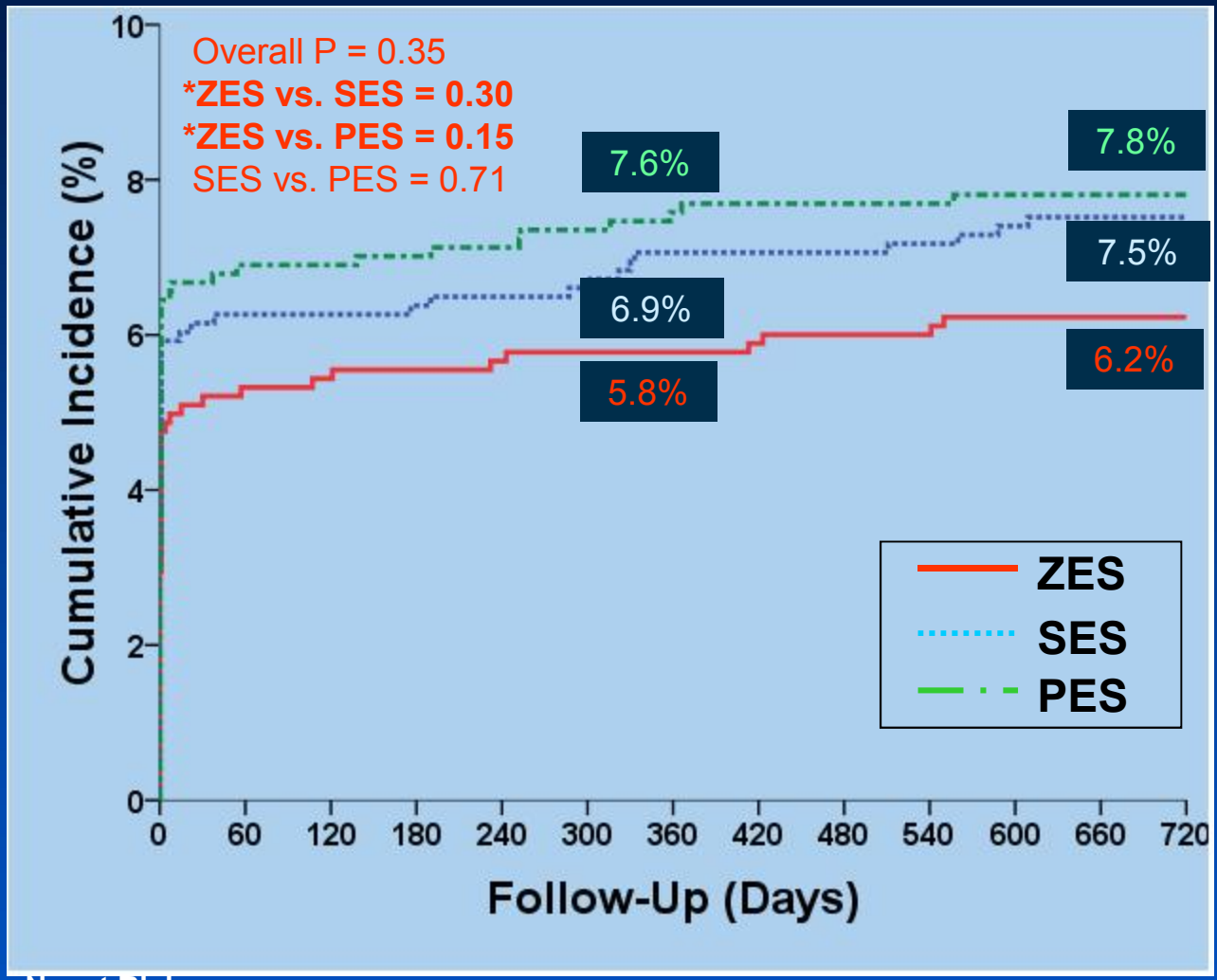
# MI at 24 month




**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 834 | 832 | 829 | 651 |
| SES | 878 | 822 | 817 | 815 | 634 |
| PES | 884 | 822 | 817 | 812 | 623 |

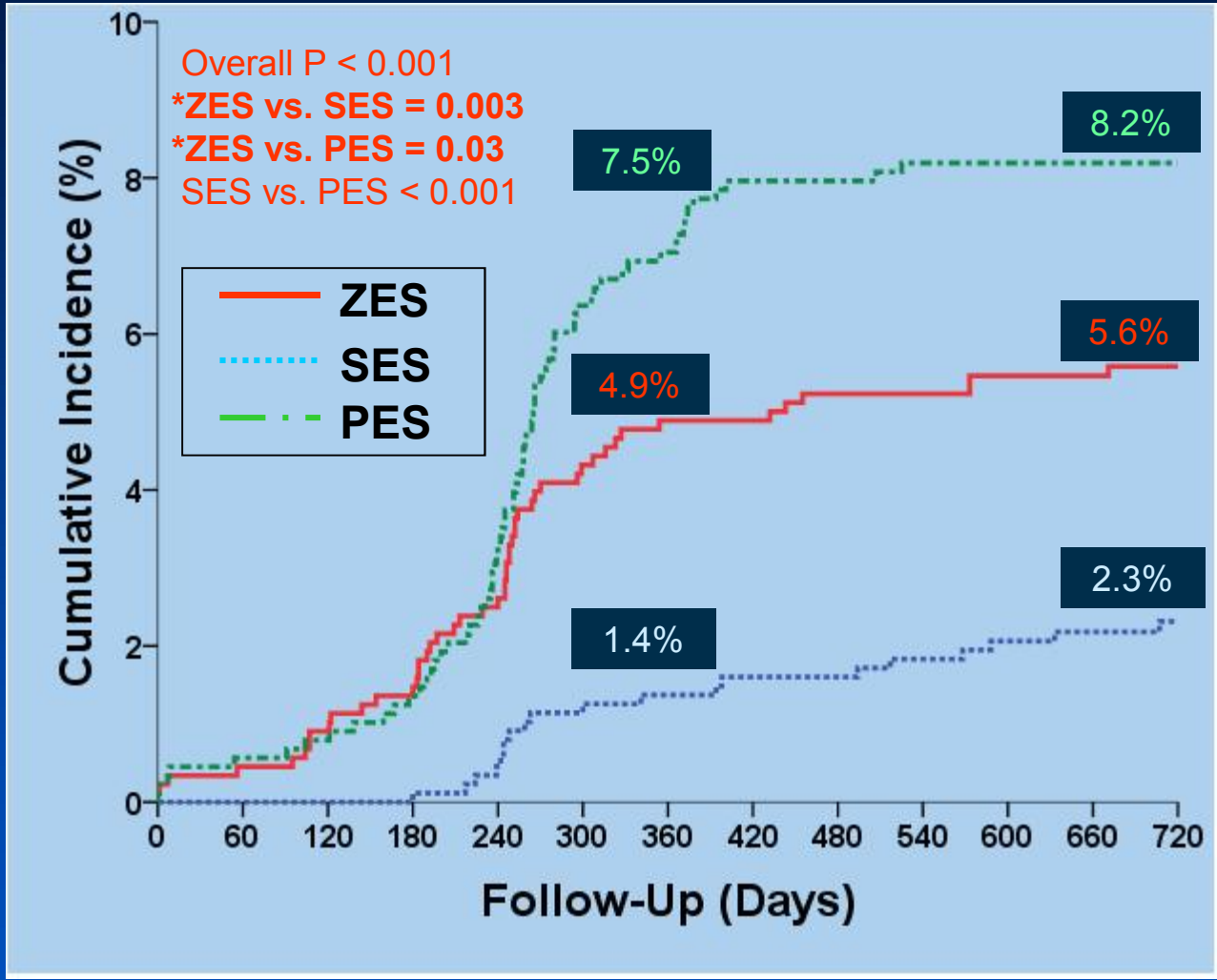
# Death or MI at 24 month




**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 834 | 832 | 829 | 651 |
| SES | 878 | 822 | 816 | 814 | 632 |
| PES | 884 | 822 | 817 | 812 | 624 |

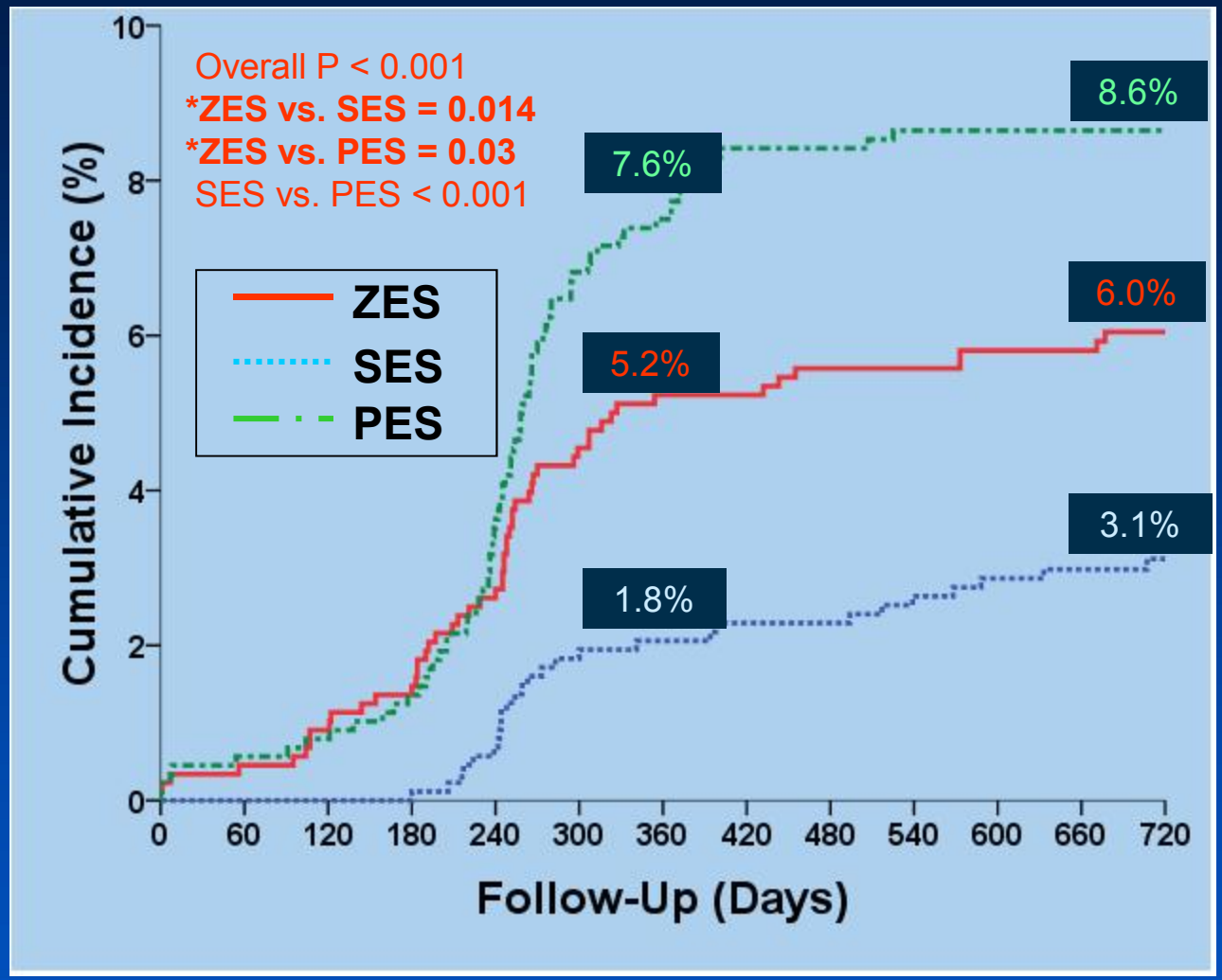
# Ischemia-Driven TLR at 24 month




**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 867 | 835 | 829 | 653 |
| SES | 878 | 874 | 859 | 853 | 665 |
| PES | 884 | 869 | 813 | 800 | 611 |

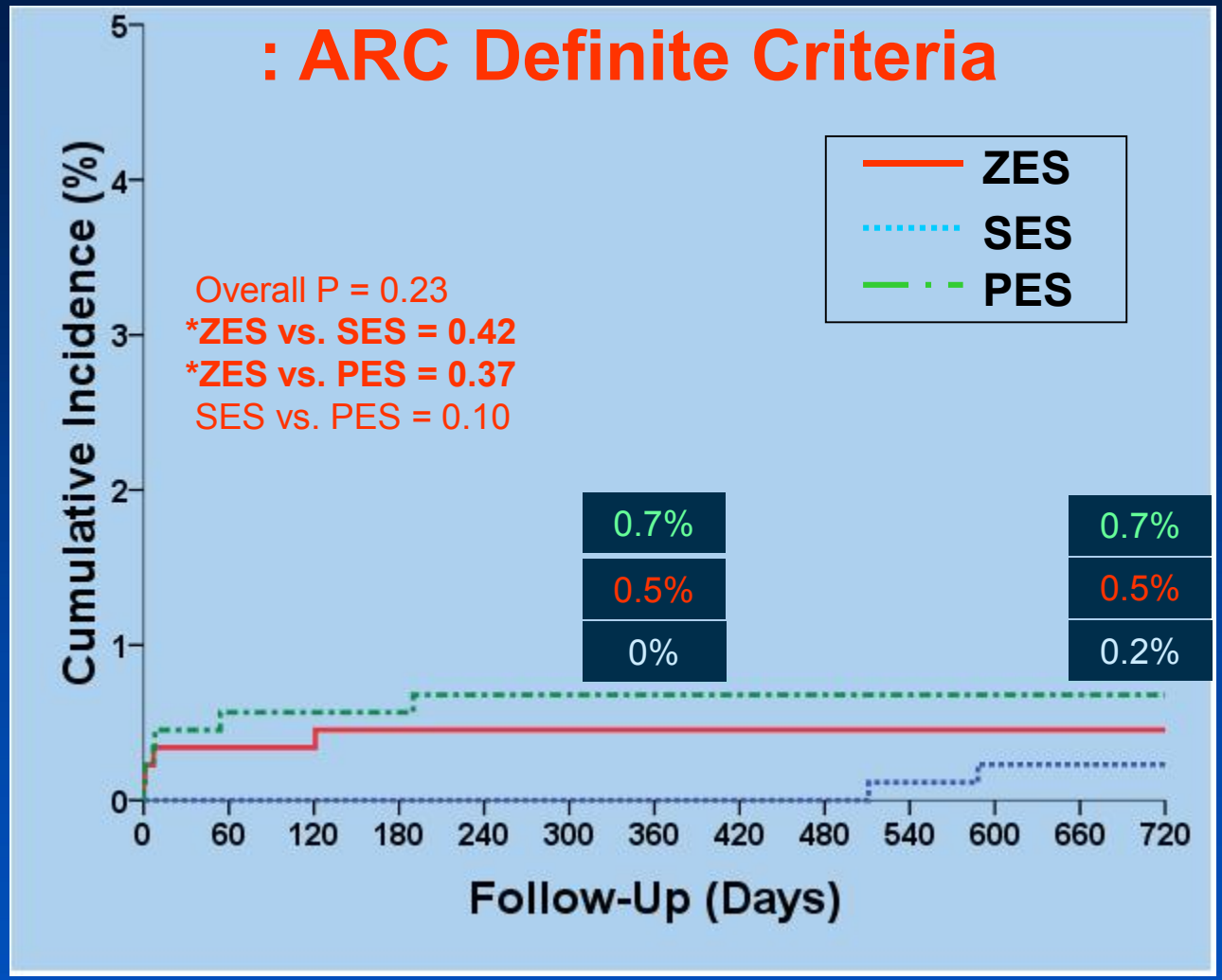
# Ischemia-Driven TVR at 24 month




**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 867 | 832 | 826 | 650 |
| SES | 878 | 874 | 853 | 846 | 659 |
| PES | 884 | 869 | 809 | 796 | 608 |

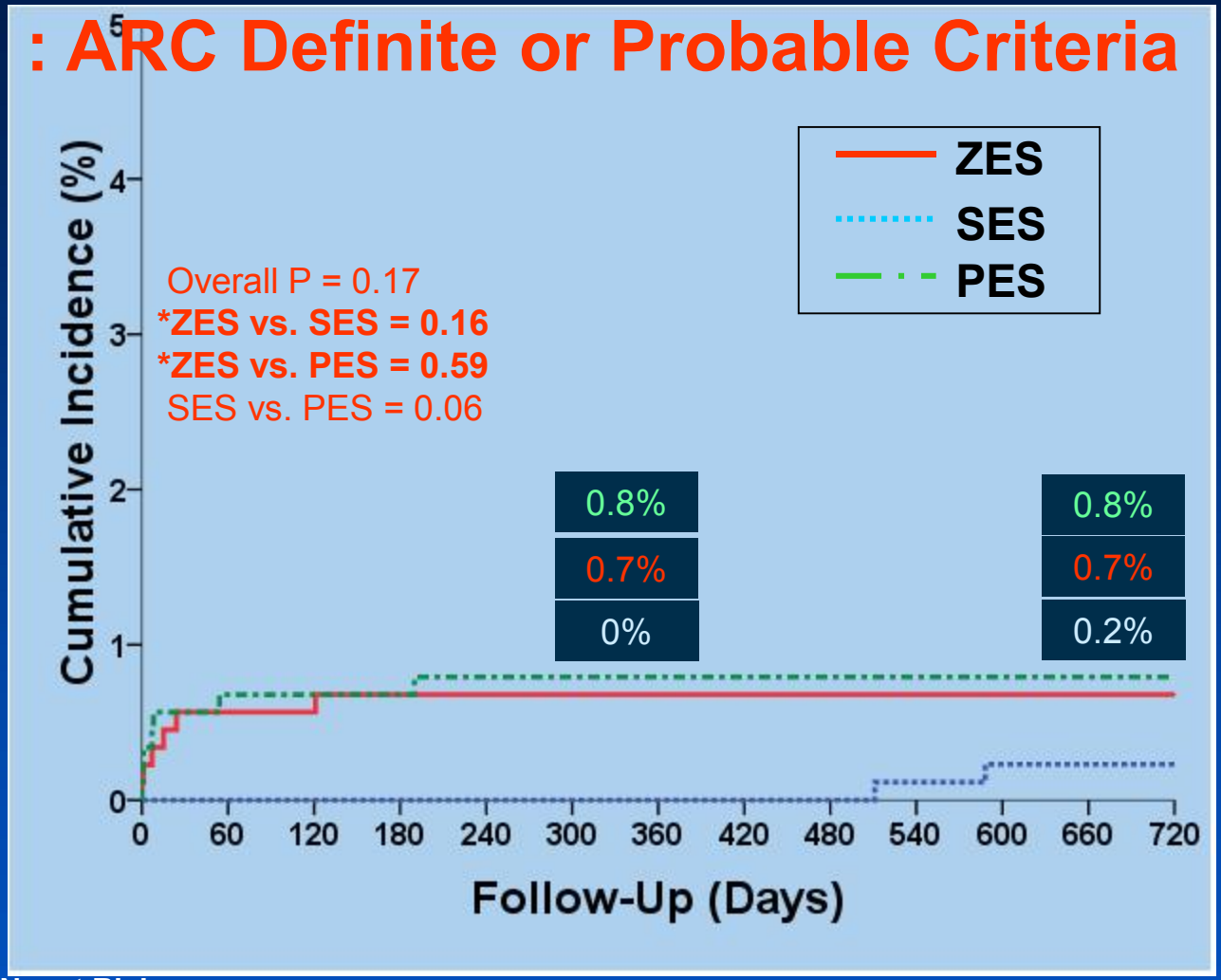
# Stent thrombosis at 24 month




**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 876 | 874 | 871 | 682 |
| SES | 878 | 895 | 870 | 869 | 673 |
| PES | 884 | 875 | 868 | 864 | 660 |

# Stent thrombosis at 24 month




**No. at Risk**

| | | | | | |
|---|---|---|---|---|---|
| ZES | 883 | 876 | 874 | 871 | 681 |
| SES | 878 | 895 | 870 | 869 | 673 |
| PES | 884 | 875 | 868 | 864 | 660 |

# Major Clinical Events at 24 Months

| | ZES (n=883) | SES (n=878) | PES (n=884) | P |
|---|---|---|---|---|
| Death | 11 (1.2) | 11 (1.3) | 12 (1.4) | 0.86 |
| Cardiac | 10 (1.1) | 7 (0.9) | 7 (0.9) | 0.82 |
| Noncardiac | 1 (0.1) | 4 (0.5) | 5 (0.6) | 0.50 |
| MI | 47 (5.3) | 57 (6.5) | 63 (7.1) | 0.25 |
| Q-wave | 6 (0.7) | 3 (0.3) | 5 (0.6) | 0.62 |
| Non-Q-wave | 41 (4.6) | 54 (6.2) | 58 (6.6) | 0.16 |
| Death or MI | 55 (6.2) | 66 (7.5) | 69 (7.8) | 0.35 |
| TLR | 49 (5.6) | 20 (2.3) | 71 (8.2) | <0.001 |
| TVR | 53 (6.0) | 27 (3.1) | 76 (8.6) | <0.001 |
| Primary end point* | 100 (11.3) | 87 (9.9) | 134 (15.2) | 0.003 |

*Primary end point: composite of death, MI, or ischemia-driven TVR

N (%)

# Stent Thrombosis at 24 Months

| | ZES (n=883) | SES (n=878) | PES (n=884) | P |
|---|---|---|---|---|
| **Type of ST** | | | | |
| Definite | 4 (0.5) | 2 (0.2) | 6 (0.7) | 0.23 |
| Definite or Probable | 6 (0.7) | 2 (0.2) | 7 (0.8) | 0.17 |
| **Timing of ST** | | | | |
| Definite or Probable | 6 (0.7) | 2 (0.2) | 7 (0.8) | 0.17 |
| Acute | 1 (0.1) | 0 | 1 (0.1) | 1.00 |
| Subacute | 4 (0.5) | 0 | 4 (0.5) | 0.14 |
| Late | 1 (0.1) | 2 (0.2) | 2 (0.2) | 0.9 |

# Conclusion: ZEST at 2 Year

- In this long-term follow-up of practical, large RCT, the zotarolimus-eluting stent compared to the sirolimus-eluting and the paclitaxel-eluting stent resulted in:
  - ZES resulted in similar rates of major adverse cardiac events compared with SES, and in fewer events compared with PES at 2 year, mainly due to the difference of repeat revascularization.
  - Rate of death, MI, or stent thrombosis at 2-year was similar among the 3 groups.
  - However, this trial was not powered for superiority for hard clinical endpoints, nor to assess low frequency event rates (death, MI, stent thrombosis).
  - Routine angiographic follow-up may have affected the results.


Thank You