# Effects of IVUS-Guided versus Angiography-Guided New-Generation Drug-Eluting Stent Implantation: Meta-analysis with Individual Patient-Level Data from 2,345 Randomized Patients


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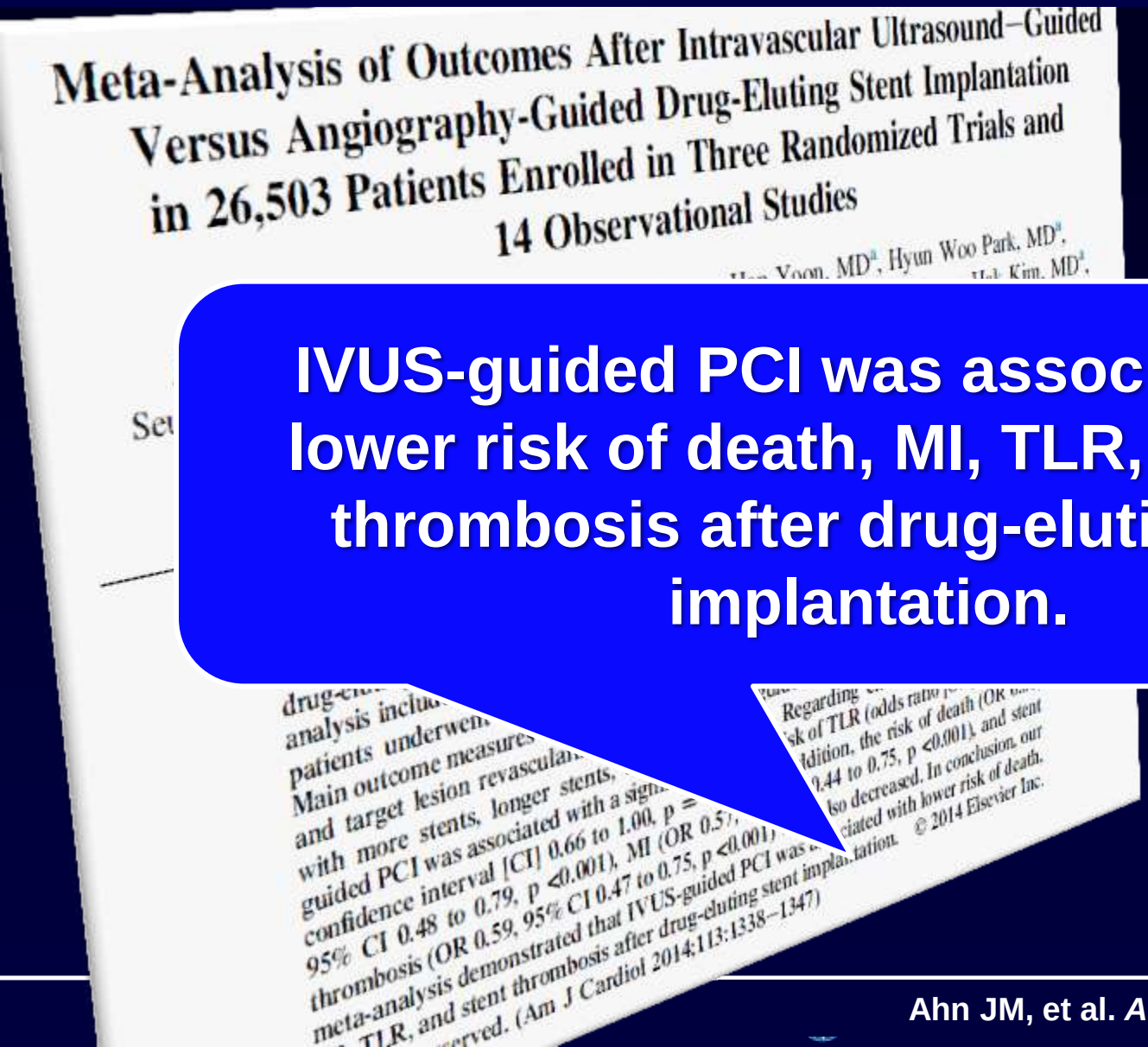
Shin DH, Hong SJ, Hong MK (corresponding author). JACC Intv 2016:9; 2232-9

# Previous Meta-analyses

**Study-level meta-analysis in all study**

| Author | Year | | Total number of patients analyzed | Included studies |
|---|---|---|---|---|
| Zhang Y | 2012 | EuroIntervention | 19,619 patients | 1 randomized trial<br>10 observational studies |
| Klersy C | 2013 | Int J Cardiol | 18,707 patients | 3 randomized trials<br>9 observational studies |
| Jang JS | 2014 | JACC Cardiovasc Interv | 24,893 patients | 3 randomized trials<br>12 observational studies |
| Ahn JM | 2014 | Am J Cardiol | 26,503 patients | 3 randomized trials<br>14 observational studies |

# Previous Meta-analyses


Meta-Analysis of Outcomes After Intravascular Ultrasound–Guided Versus Angiography-Guided Drug-Eluting Stent Implantation in 26,503 Patients Enrolled in Three Randomized Trials and 14 Observational Studies

Hyun Woo Park, MD

**IVUS-guided PCI was associated with lower risk of death, MI, TLR, and stent thrombosis after drug-eluting stent implantation.**

Ahn JM, et al. *Am J Cardiol.* 2014;113:1338-1347

# Previous meta-analysis

| | Author | Year | # of Patients | Stent Type |
|---|---|---|---|---|
| 3 Randomized | Jakabcin et al. | 2010 | **210** | All first-generation DES |
| | Chieffo et al. | 2013 | **284** | All first-generation DES |
| | Kim et al. | 2013 | **543** | All second-generation DES |
| 14 Observational | Agostoni | 2005 | **58** | All first-generation DES |
| | Roy et al. | 2008 | **1768** | All first-generation DES |
| | Park et al. | 2009 | **290** | ation DES |
| | Yoon et al | 2013 | **1574** | Both first- and second-DES |
| | Witzenbichler et al. | 2012 | **8583** | Both first- and second-DES |

**The proportion of second-generation DES was <45% of overall DES-treated patients.**

**→ The published data evaluating the clinical usefulness of IVUS guidance in exclusively second-generation DES implantation are quite limited**



Ahn JM, et al. *Am J Cardiol.* 2014;113:1338-1347

# Recent Meta-analyses

## Outcomes with IVUS -guided stent implantation: A meta-analysis of 7 randomized trials in the DES era

**Table 1. Baseline Characteristics of the Included Studies**

| Characteristic | IVUS-XPL[14] | CTO-IVUS[15] | AIR-CTO[16] | Tan et al[26] | Kim et al[27] | AVIO[28] | HOME DES IVUS[29] |
|---|---|---|---|---|---|---|---|
| Year | 2015 | 2015 | 2015 | 2015 | 2013 | 2013 | 2010 |
| Patients, n | 700/700 | 201/201 | 115/115 | 61/62 | 269/274 | 142/142 | 105/105 |
| Clinical presentation | | | | | | | |
| Stable angina, % | 51/51 | 100/100 | 71/76 | 30/34 | 53/51 | 70/64 | 38/40 |
| Unstable angina, % | 35/32 | 0/0 | 9/10 | 70/66 | 38/39 | 30/26 | 43/39† |
| ST-elevation MI, % | 14/17 | 0/0 | 20/15‡ | 0/0 | 9/10 | 0/0 | 29/21 |
| LVEF, % | 63/62 | 57/57 | 55/56 | 55/53 | 55/54 | 55/56 | NR |
| Follow-up duration, mo | 12 | 12 | 24 | 24 | 12 | 24 | 18 |

**Data with both first- and second-generation DES**

**Systemic review, not patient level analysis**

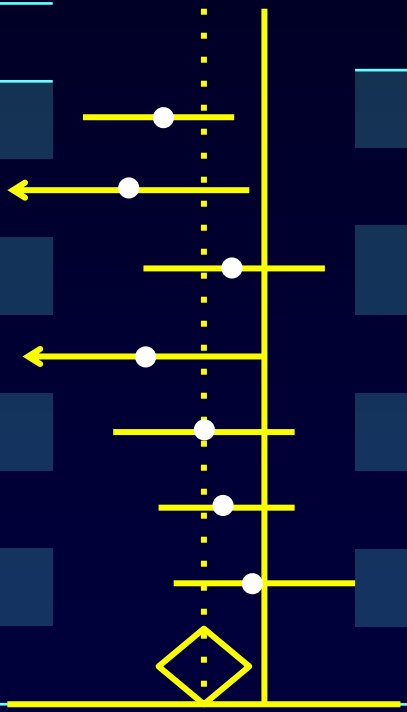
Elgendy IY, et al. *Circ Cardiovasc Interv* 2016;9:e003700

# Meta-analysis of 7 randomized trials: IVUS vs. angio -guided (first and next-generation) DES implantation

Event: cardiac death, MI, TLR

Study-level meta-analysis

| Study | Year | OR | Events: IVUS | Events: Angio |
|---|---|---|---|---|
| IVUS-XPL | 2015 | 0.49 | 19/700 | 39/700 |
| CTO-IVUS | 2015 | 0.37 | 5/201 | 14/201 |
| AIR-CTO | 2015 | 0.82 | 25/115 | 29/115 |
| Tan et al | 2015 | 0.42 | 8/61 | 17/62 |
| Kim (RESET) | 2013 | 0.60 | 12/269 | 20/274 |
| AVIO | 2013 | 0.67 | 24/142 | 33/142 |
| HOME DES IVUS | 2010 | 0.91 | 11/105 | 12/105 |
| Overall | | 0.60 | 104/1593 | 164/1599 |

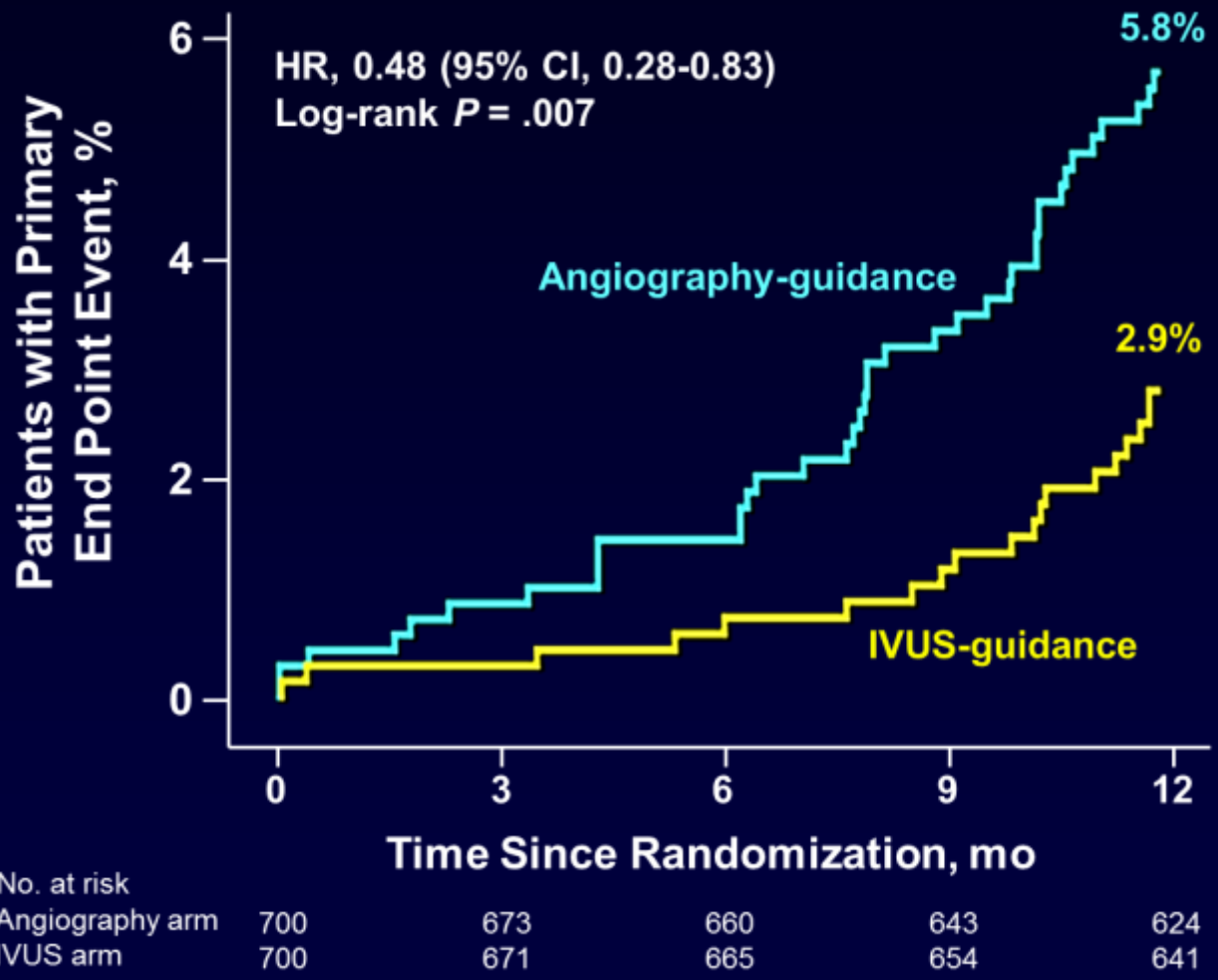


IVUS better Angio better

Islam Y. Elgendy et al. *Circ Cardiovasc Interv*. 2016;9:e003700

# IVUS-XPL: Randomized Trial

## MACE: Cardiac death, MI, or TLR




Hong SJ, Kim BK, Hong MK (corresponding author). JAMA 2015:314:2155-63

# IVUS-XPL: Randomized Trial

| | IVUS-guidance (n=700) | Angiography-guidance (n=700) | Hazard ratio (95% CI) | Log-Rank *P* value |
|---|---|---|---|---|
| **Primary End Point** | | | | |
| MACE | 19 (2.9%) | 39 (5.8%) | 0.48 (0.28–0.83) | .007 |
| **Secondary End Point** | | | | |
| Cardiac death | 3 (0.4%) | 5 (0.7%) | 0.60 (0.14-2.52) | .48 |
| Target lesion related MI | 0 | 1 (0.1%) | - | .32 |
| Ischemia-driven TLR | 17 (2.5%) | 33 (5.0%) | 0.51 (0.28-0.91) | .02 |
| Stent thrombosis | 2 (0.3%) | 2 (0.3%) | 1.00 (0.14-7.10) | 1.00 |
| Acute | 1 (0.1%) | 1 (0.1%) | - | - |
| Sub-acute | 1 (0.1%) | 0 | - | - |
| Late | 0 | 1 (0.1%) | - | - |

Hong SJ, Kim BK, Hong MK (corresponding author). JAMA 2015 :314:2155-63

# From the IVUS-XPL Trial

- Can IVUS reduce **only TLR**?
- Can IVUS improve **HARD CLINICAL OUTCOMES** such as cardiac death, MI, or stent thrombosis?
- Is there **patient-level** meta-analysis with **second-generation DES alone**?

# AIM

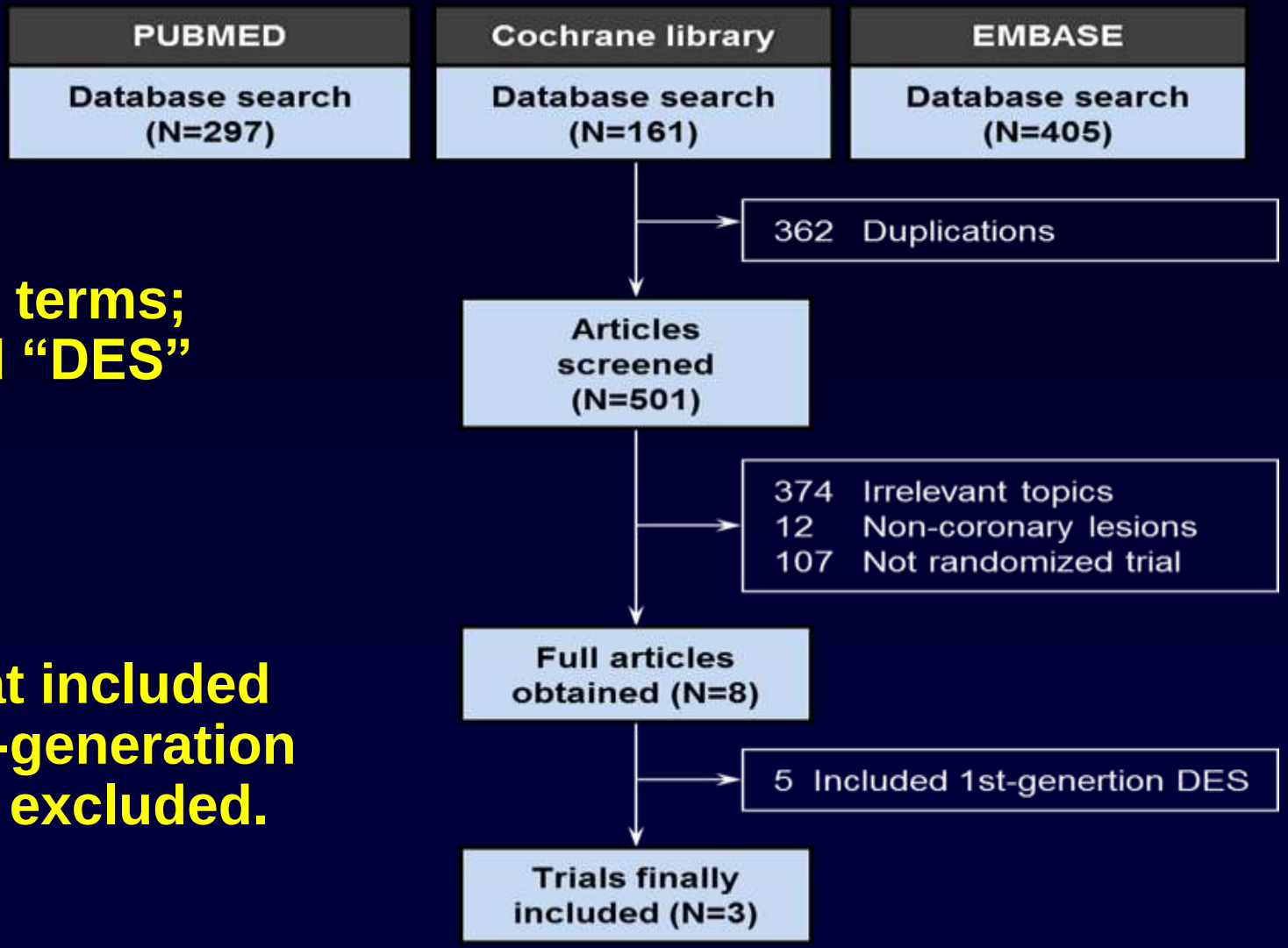
- To evaluate whether IVUS guidance improves hard clinical endpoints in new-generation DES-treated patients using a meta-analysis of individual patient-level randomized trial data.

Shin DH, Hong SJ, Hong MK (corresponding author). JACC Intv 2016:9; 2232-9

# Study Selection

**The search terms; "IVUS" and "DES"**

**Studies that included use of first-generation DESs were excluded.**




Shin DH, Hong SJ, Hong MK (corresponding author). JACC Intv 2016:9; 2232-9

# Endpoints and Definitions

- **Primary endpoint:**

  **MACE of hard clinical endpoint, defined as a composite of cardiac death, myocardial infarction, and stent thrombosis.**

# Results: 3 RCTs with 2,345 Patients

| Trials (Year) | No. of patients | | Lesion characteristics | Primary endpoint |
|---|---|---|---|---|
| | IVUS-group | Angio-group | | |
| RESET-IVUS (2013) | 269 | 274 | Long lesions | MACE (Composite of cardiac death, MI, TVR, or stent thrombosis) |
| CTO-IVUS (2014) | 201 | 201 | CTO | Cardiac death |
| IVUS-XPL (2015) | 700 | 700 | Long lesions | MACE (Composite of cardiac death, target-lesion related MI, and ischemia-driven TLR) |
| | 1170 | 1175 | | |

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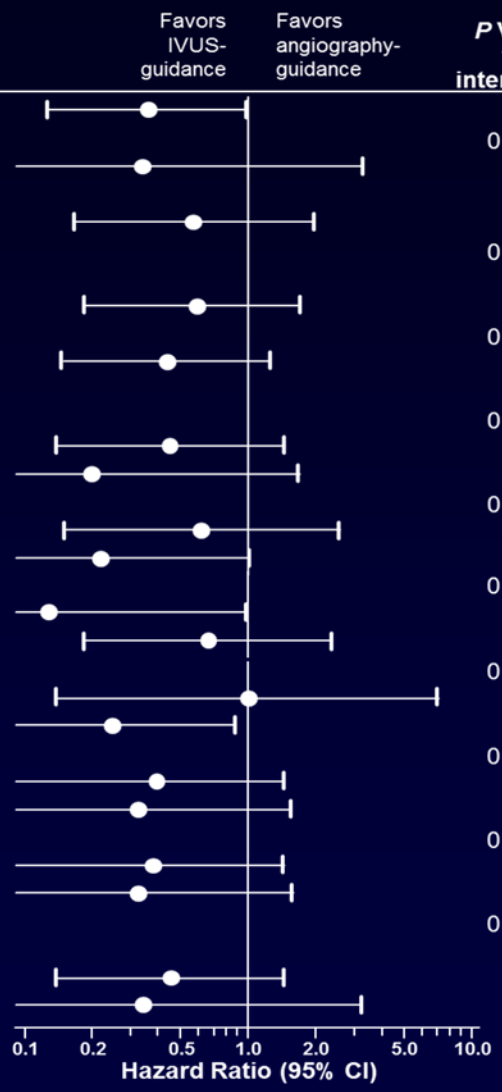
# Randomized patient characteristics, individual data

| Variables | IVUS guidance (n=1170) | Angiography guidance (n=1175) | *p* value |
|---|---|---|---|
| Age (year) | 62.9 ± 9.6 | 63.5 ± 9.4 | 0.142 |
| Male | 822 (70.3) | 793 (67.5) | 0.161 |
| Clinical presentation | | | 0.396 |
| Stable angina | 702 (60.0) | 698 (59.4) | |
| Unstable angina | 344 (29.4) | 332 (28.3) | |
| Acute myocardial infarction | 124 (10.6) | 145 (12.3) | |
| Diabetic mellitus | 405 (34.6) | 406 (34.6) | > 0.99 |
| Hypertension | 745 (63.7) | 750 (63.8) | 0.972 |
| Dyslipidemia | 636 (65.6) | 623 (64.0) | 0.21 |
| Prior PCI | 107 (11.9) | 101 (11.2) | 0.712 |
| No. of diseased vessels | | | |
| 1 | 383 (32.7) | 389 (33.1) | |
| 2 | 415 (35.5) | 427 (36.3) | |
| 3 | 372 (31.8) | 359 (30.6) | |
| Stent type | | | 0.994 |
| Biolimus-eluting stent | 101 (8.6) | 100 (8.5) | |
| Everolimus-eluting stent | 834 (71.3) | 838 (71.3) | |
| Zotarolimus-eluting stent | 235 (20.1) | 237 (20.2) | |
| Number of stents per lesion | 1.7 ± 0.9 | 1.7 ± 0.8 | 0.544 |
| Total stent length (mm) | 43.5 (33, 60) | 42 (33, 56) | 0.382 |
| Multivessel PCI | 323 (27.6) | 314 (26.7) | 0.631 |

# Subgroup Analysis for MACE

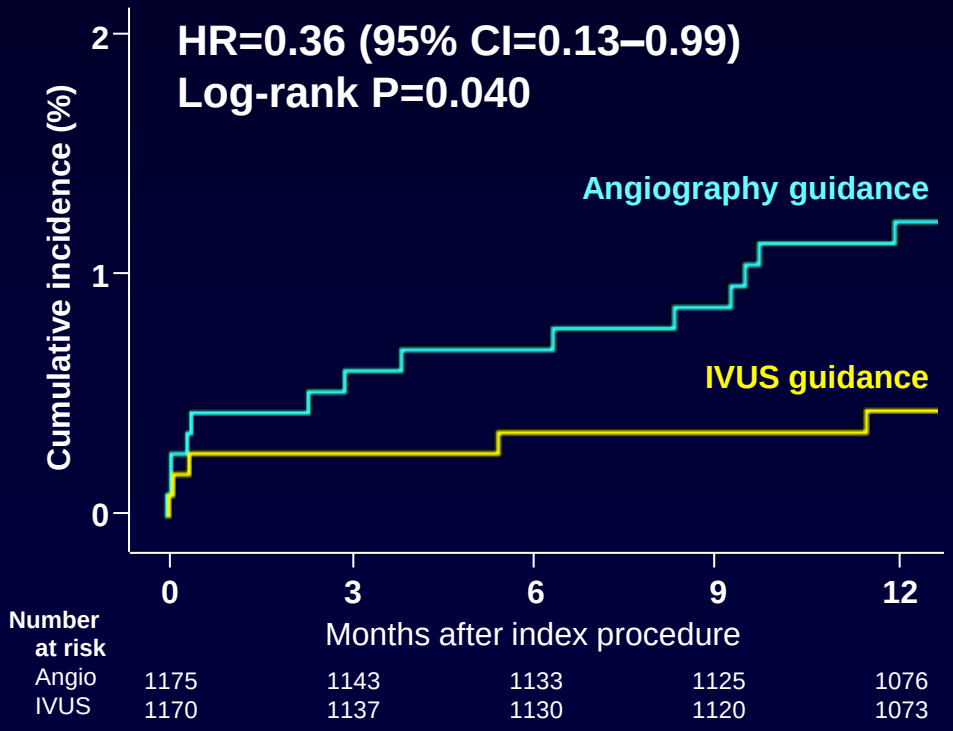
| | IVUS-guidance | | Angiography-guidance | | Hazard Ratio (95% CI) | *P* Value for interaction |
|---|---|---|---|---|---|---|
| | No. of events | No. of patients | No. of events | No. of patients | | |
| **All patients** | **5** | **1170** | **14** | **1175** | **0.36 (0.13–0.99)** | |
| **Study** | | | | | | 0.195 |
| RESET IVUS | 1 | 269 | 3 | 274 | 0.34 (0.04–3.25) | |
| CTO IVUS | 0 | 201 | 4 | 201 | – | |
| IVUS XPL | 4 | 700 | 7 | 700 | 0.57 (0.17–1.96) | |
| **Age** | | | | | | 0.075 |
| <65 years | 0 | 600 | 5 | 587 | – | |
| ≥65 years | 5 | 570 | 9 | 588 | 0.58 (0.19–1.72) | |
| **Sex** | | | | | | 0.924 |
| Male | 5 | 822 | 11 | 793 | 0.44 (0.15–1.26) | |
| Female | 0 | 348 | 3 | 382 | – | |
| **Hypertension** | | | | | | 0.514 |
| Yes | 4 | 745 | 9 | 750 | 0.45 (0.14–1.46) | |
| No | 1 | 425 | 5 | 425 | 0.20 (0.02–1.70) | |
| **Diabetes mellitus** | | | | | | 0.339 |
| Yes | 3 | 405 | 5 | 406 | 0.61 (0.15–2.56) | |
| No | 2 | 765 | 9 | 769 | 0.22 (0.05–1.02) | |
| **Clinical presentation** | | | | | | 0.175 |
| Stable angina | 1 | 702 | 8 | 698 | 0.13 (0.02–1.00) | |
| Acute coronary syndrome | 4 | 468 | 6 | 477 | 0.67 (0.19–2.39) | |
| **Multivessel PCI** | | | | | | 0.241 |
| Yes | 2 | 323 | 2 | 314 | 1.00 (0.14–7.10) | |
| No | 3 | 847 | 12 | 861 | 0.25 (0.07–0.89) | |
| **Number of stents** | | | | | | 0.846 |
| <1 | 3 | 754 | 8 | 778 | 0.39 (0.10–1.46) | |
| ≥2 | 2 | 416 | 6 | 397 | 0.32 (0.06–1.57) | |
| **Stent length** | | | | | | 0.863 |
| <43 mm (median value) | 3 | 801 | 8 | 817 | 0.38 (0.10–1.45) | |
| ≥43 mm | 2 | 369 | 6 | 358 | 0.32 (0.07–1.59) | |
| **Type of drug-eluting stent** | | | | | | 0.630 |
| Biolimus-eluting stent | 0 | 101 | 2 | 100 | – | |
| Everolimus-eluting stent | 4 | 834 | 9 | 838 | 0.45 (0.14–1.45) | |
| Zotarolimus-eluting stent | 1 | 235 | 3 | 237 | 0.34 (0.04–3.23) | |



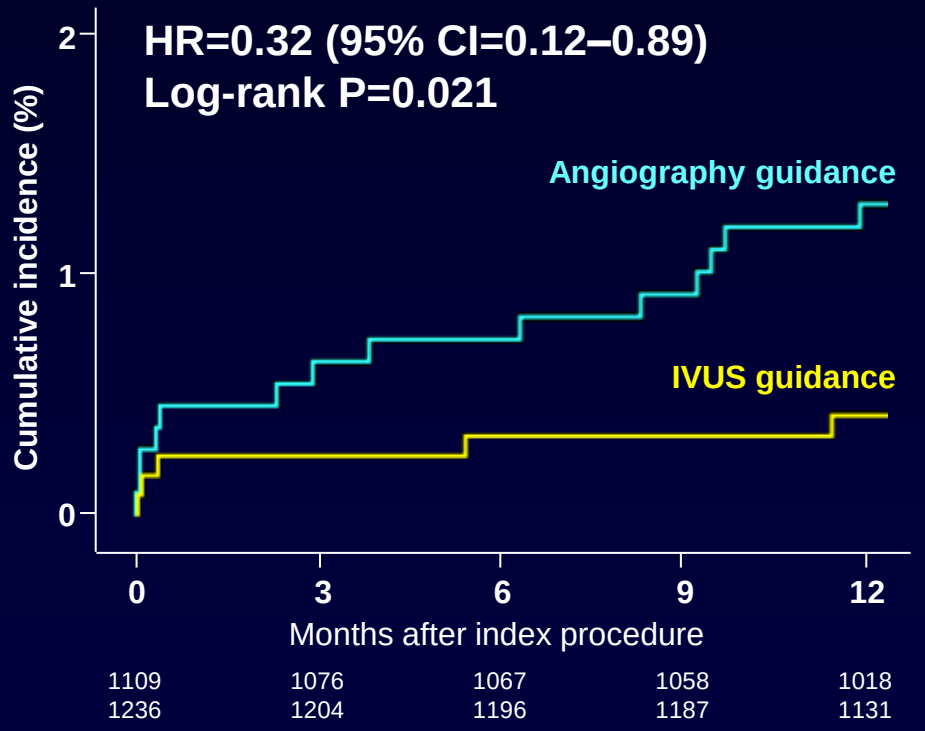
# Primary Endpoint: MACE

## MACE (cardiac death, MI, or stent thrombosis)

### Intention-to treat analysis




### Per-protocol analysis

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# Stent optimization by IVUS

| Trial (Year) | IVUS-criteria for stent optimization | % of patients meeting the criteria |
|---|---|---|
| RESET-IVUS (2013) | • Minimal CSA ≥ CSA at distal reference segments | 49% (126/256) |
| CTO-IVUS (2014) | • Minimal stent area ≥distal reference lumen area<br>• Stent area at CTO ≥5 $mm^2$ as far as vessel area permits<br>• Complete stent apposition | 60% (117/196) |
| IVUS-XPL (2015) | • Minimal CSA ≥ CSA at distal reference segments | 54% (363/678) |
| Overall | | 54% (606/1130) |

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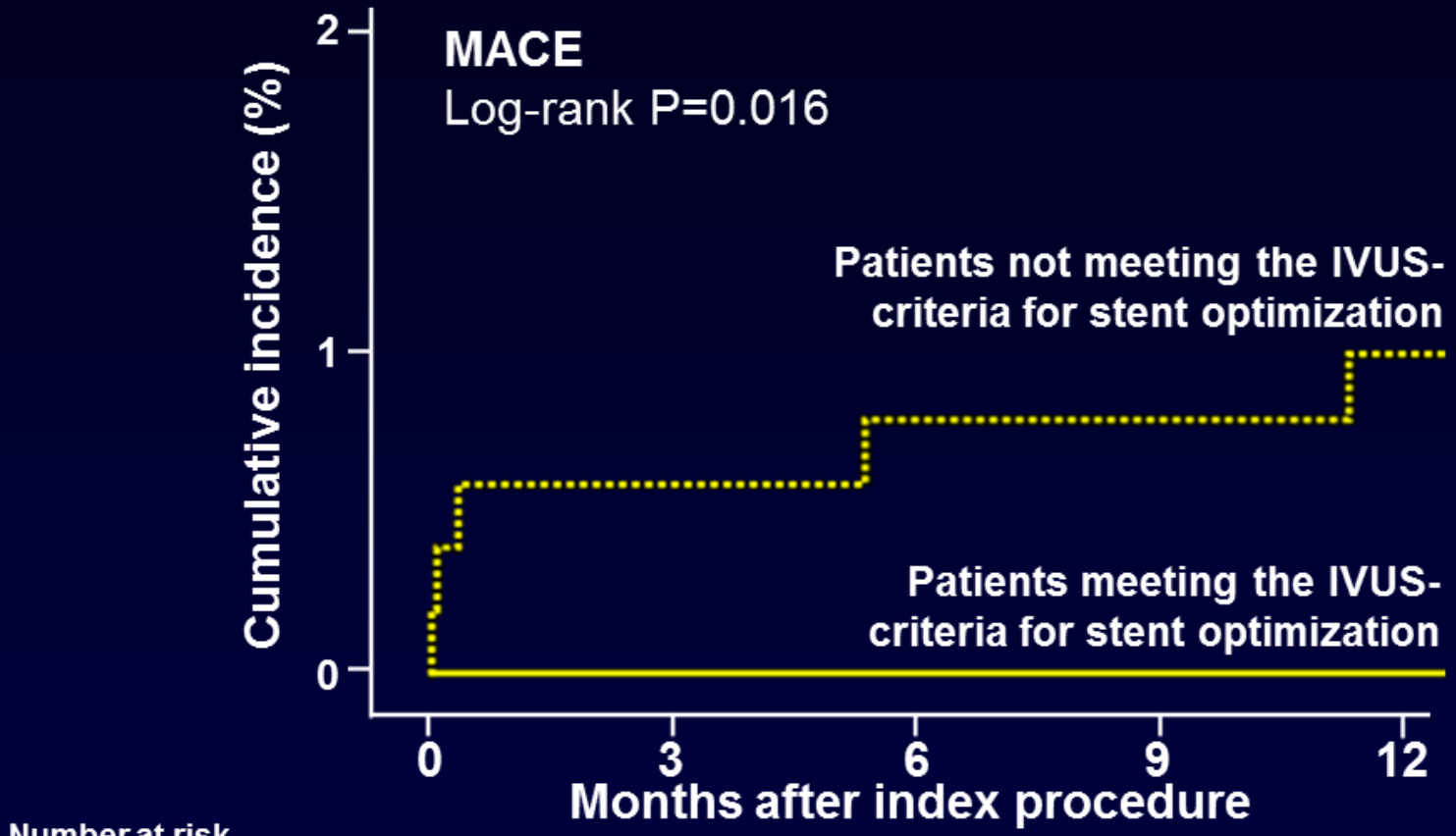
# Stent optimization by IVUS

**MACE (cardiac death, MI, or stent thrombosis)**




**Number at risk**

| | | | | | |
|---|---|---|---|---|---|
| Not meeting the criteria | 524 | 506 | 505 | 504 | 483 |
| Meeting the criteria | 606 | 592 | 586 | 578 | 564 |

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# Summary

1. Compared with angiography-guidance, IVUS-guidance for complex lesions was associated with a relative risk reduction of 64% for hard end points of MACE (the composite of cardiac death, MI and stent thrombosis at 1 year).
2. Fifty-four percent of patients met the IVUS-criteria for stent optimization.
3. MACE was significantly lower in the patients who met the IVUS-criteria vs. those who did not meet the IVUS-criteria.

# Conclusions

- **Compared with angiography guidance, IVUS-guided new-generation DES implantation was associated with favorable outcome, the composite of cardiac death, myocardial infarction, or stent thrombosis.**