The approved use of Actual DES in complex subgroups: Diabetics, ISR, Bifurcation

Dr.J.Belardi

Courtesy of Medtronic

Conflicto de Intereses

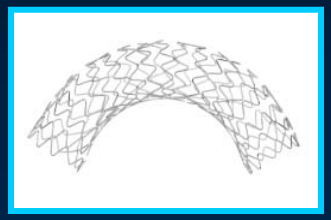
- Consultor Medtronic
- Consultor Eli Lilly

Resolute Integrity™ DES

System Components

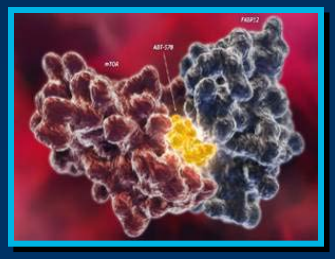
Established Components

- Integrity™ cobalt alloy stent



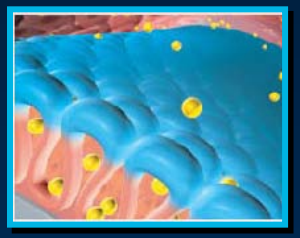
- MicroTrac™ delivery system

- Zotarolimus antiproliferative drug

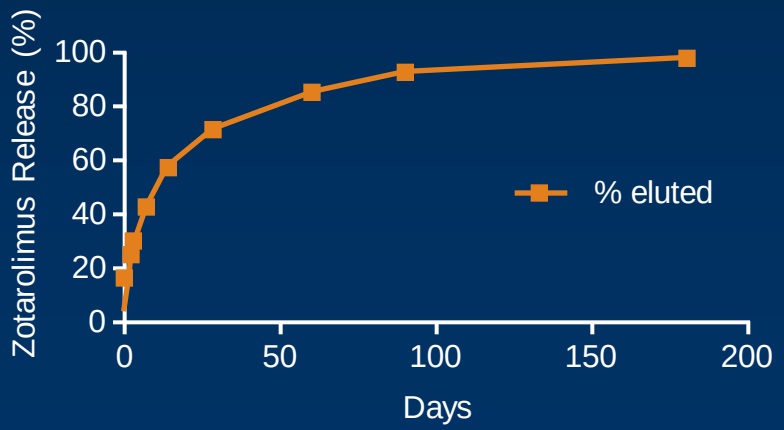


Unique Polymer Technology

- BioLinx™ polymer is a unique blend of three polymers to control drug release, support biocompatibility and enhance elution rate



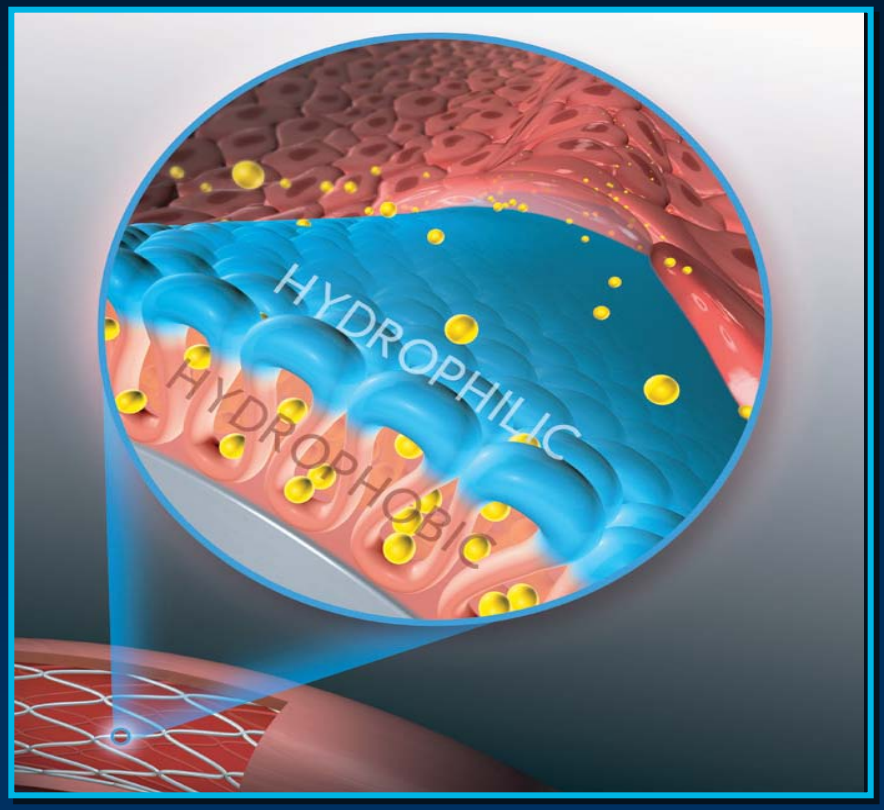
- Drug-release kinetics: complete elution by 180 days



Udipi K, et al. *EuroIntervention.* 2007; 3:137-9
Meredith IT, et al. *J Am Coll Cardiol Intv*. 2009; 2:977-85
Meredith IT, et al. *EuroIntervention*. 2007; 3:50-53

Resolute™ ZES Polymer

BioLinx™: a Polymer Specifically Designed for DES



Components of a safe polymer:

- **Mimics the body's chemistry**
- **Complete drug elution**
- **Compatible with stent delivery**

BioLinx polymer system design:

- **Extended drug elution**
- **Low inflammation[1]**
- **Minimal thrombotic risk[2]**
- **Rapid and functional endothelial healing[1]**

A biostable polymer that applies the basics of membrane structure will provide extended drug elution over time while maintaining biocompatibility

[1] In porcine models. [2] Based on test data on file at Medtronic, Inc.
Preclinical results may not be indicative of clinical performance of DES

Complex Subgroups

DIABETES

RESOLUTE Pooled Diabetics

Background

- Patients with diabetes have significantly higher event rates because of:
  - Endothelial dysfunction
  - Impaired platelet function
  - Altered coagulation / fibrinolysis
  - Increased smooth muscle cell proliferation
- Current data on performance in patients with diabetes is predominantly on standard risk patients
- Patient level data from 5 RESOLUTE clinical trials were pooled together to evaluate the clinical outcomes of patients with diabetes. Results were analyzed for both standard risk and all diabetic patient cohorts including the more complex patients that are traditionally seen to date.

RESOLUTE Pooled Diabetic Analysis

Diabetic Patient Populations

RESOLUTE	139
RESOLUTE AC	1140
RESOLUTE Int	2349
RESOLUTE US	1402
RESOLUTE Japan	100

5130 Resolute population

Total diabetic patient population
N = 1535

Matched cohort diabetic population
N = 878 (standard risk)

Standard risk patient cohort pre-specified for FDA indication

Matched cohort is all enrolled diabetic subjects excluding subjects with bifurcation, saphenous vein graft (SVG), ISR, AMI (≥2 hours), left ventricular ejection fraction (LVEF) <30%, an unprotected left main lesion, ≥3 vessels, renal impairment (creatinine ≥ 140μmol/L), total lesion length pervessel >27 mm, ≥2 lesions per vessel, lesion with thrombus, or lesion with total occlusion.

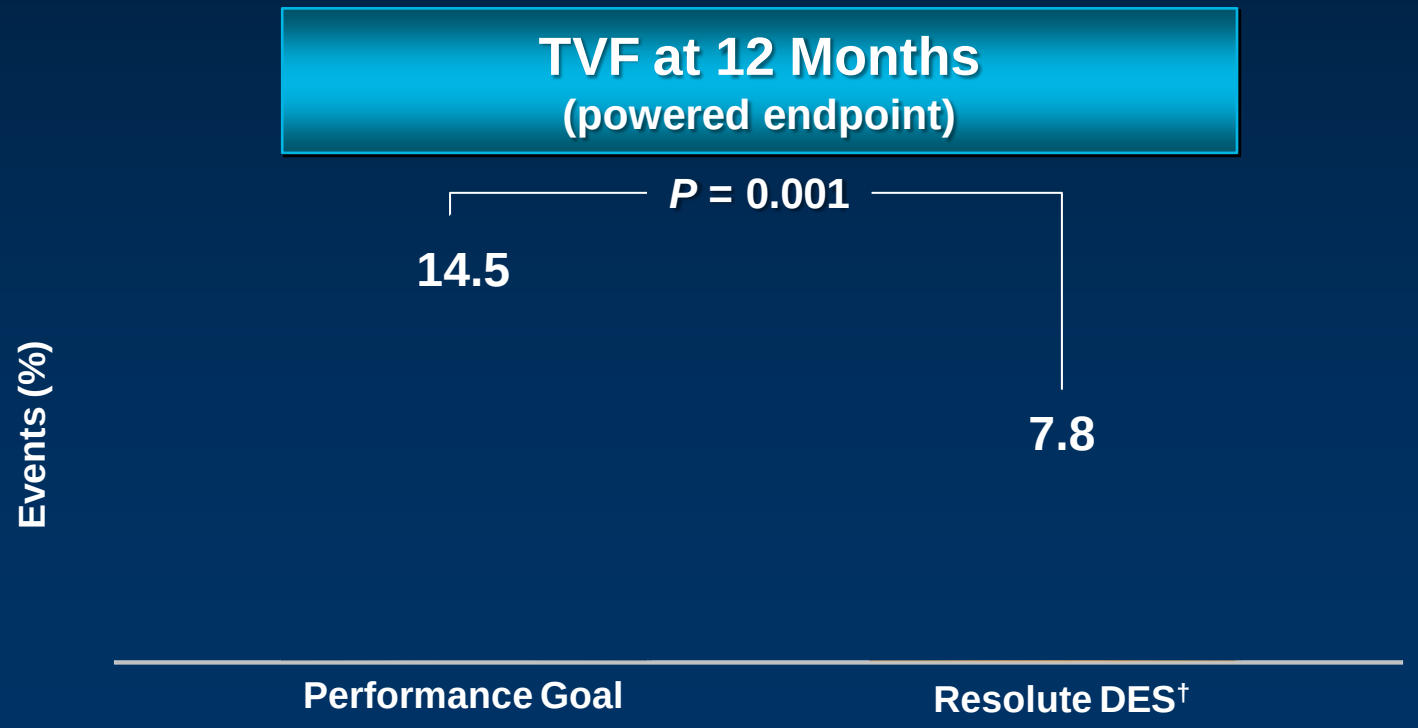
RESOLUTE Pooled Diabetic Analysis

FDA Indication

Prespecified diabetes analysis designed with FDA for diabetes indication

Performance goal prespecified based on meta-analysis: DIABETES, RAVEL DM, SIRIUS DM, TAXUS IV, SCORPIUS, ENDEAVOR Pooled DM.

Standard risk patient population from Pooled RESOLUTE matched to performance goal patient population



TVF: target vessel failure (cardiac death, TV-MI, and clinically driven TVR)
†RESOLUTE matched cohort diabetes pooled analysis (N = 878).

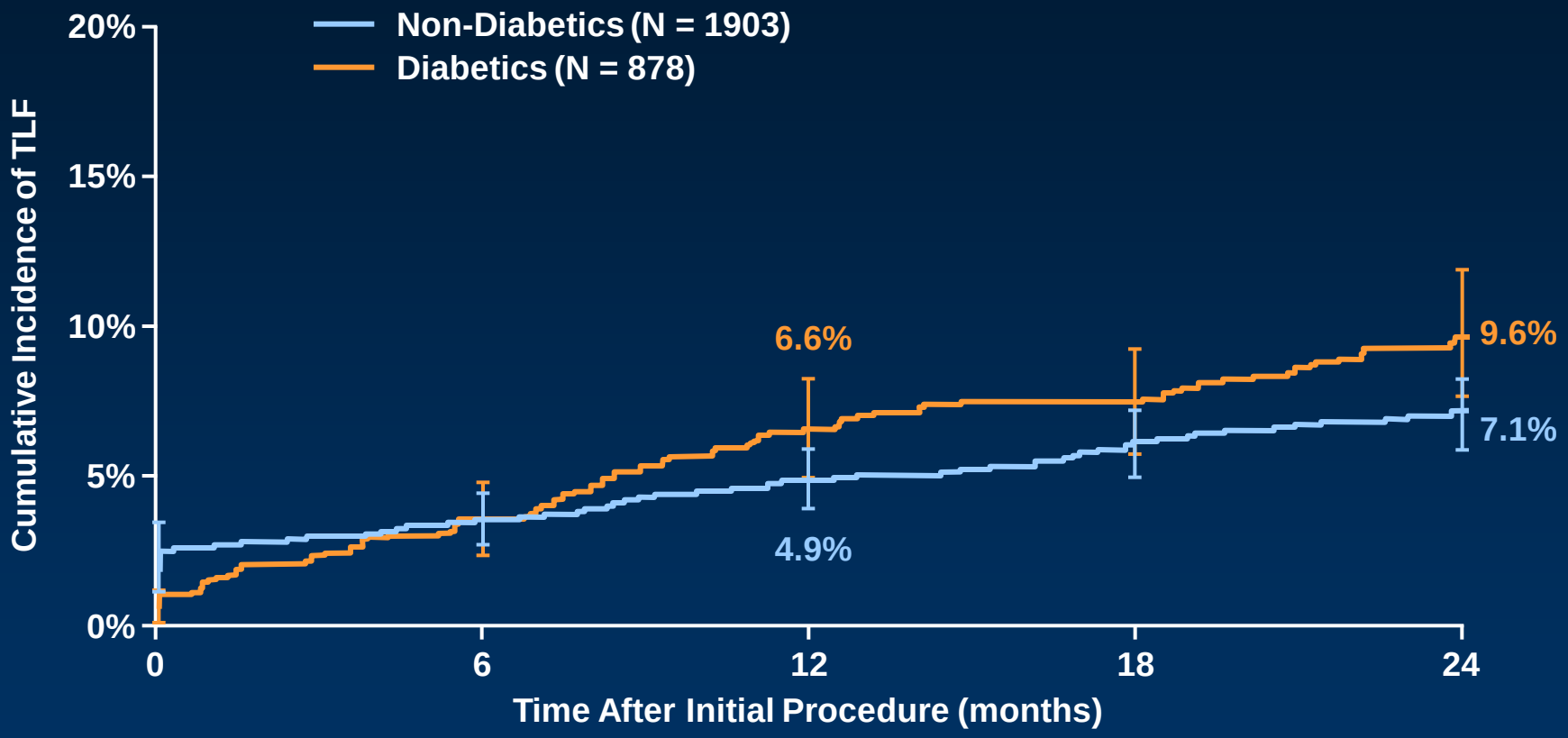
RESOLUTE Pooled Diabetic Analysis

Baseline Characteristics – Standard Risk Patients

%	*Non-Diabetics N = 1903*	*Diabetics N = 878*
Age (yr)	63.5± 10.8	65.2 ± 10.2
Male	74.3	66.4
Diabetes mellitus	0	100.0
IDDM	0	28.5
Hypertension	73.1	87.6
Hyperlipidemia	76.0	86.2
Current smoker	22.1	18.2
Family history	42.2	37.8
Prior MI	25.5	24.9
Prior PCI	29.5	34.6
Prior CABG	7.4	10.5
Clinical status:		
Stable angina	45.5	46.2
Unstable angina	31.3	28.9
Myocardial infarction	6.6	5.4

RESOLUTE Pooled Diabetic Analysis

Standard Risk Pts – Target Lesion Failure to 2 Years

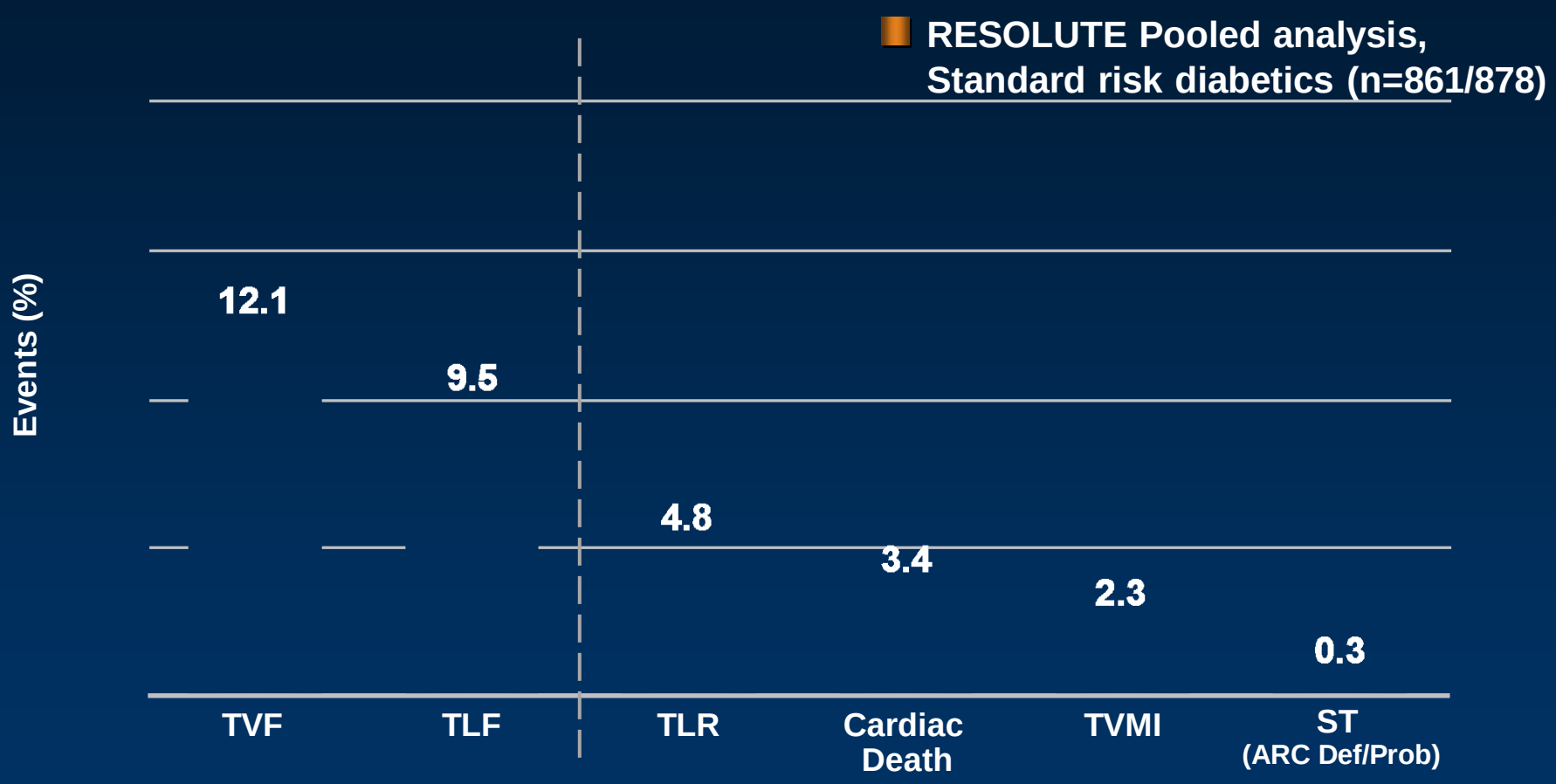


No. at risk					
Non-Diabetics	1903	1870	1816	1763	1714
Diabetics	878	873	839	800	785

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE Pooled Diabetic Analysis

Standard Risk Pts – Clinical Outcomes at 24 Months



TLR is ischemia driven.

RESOLUTE Pooled Diabetic Analysis

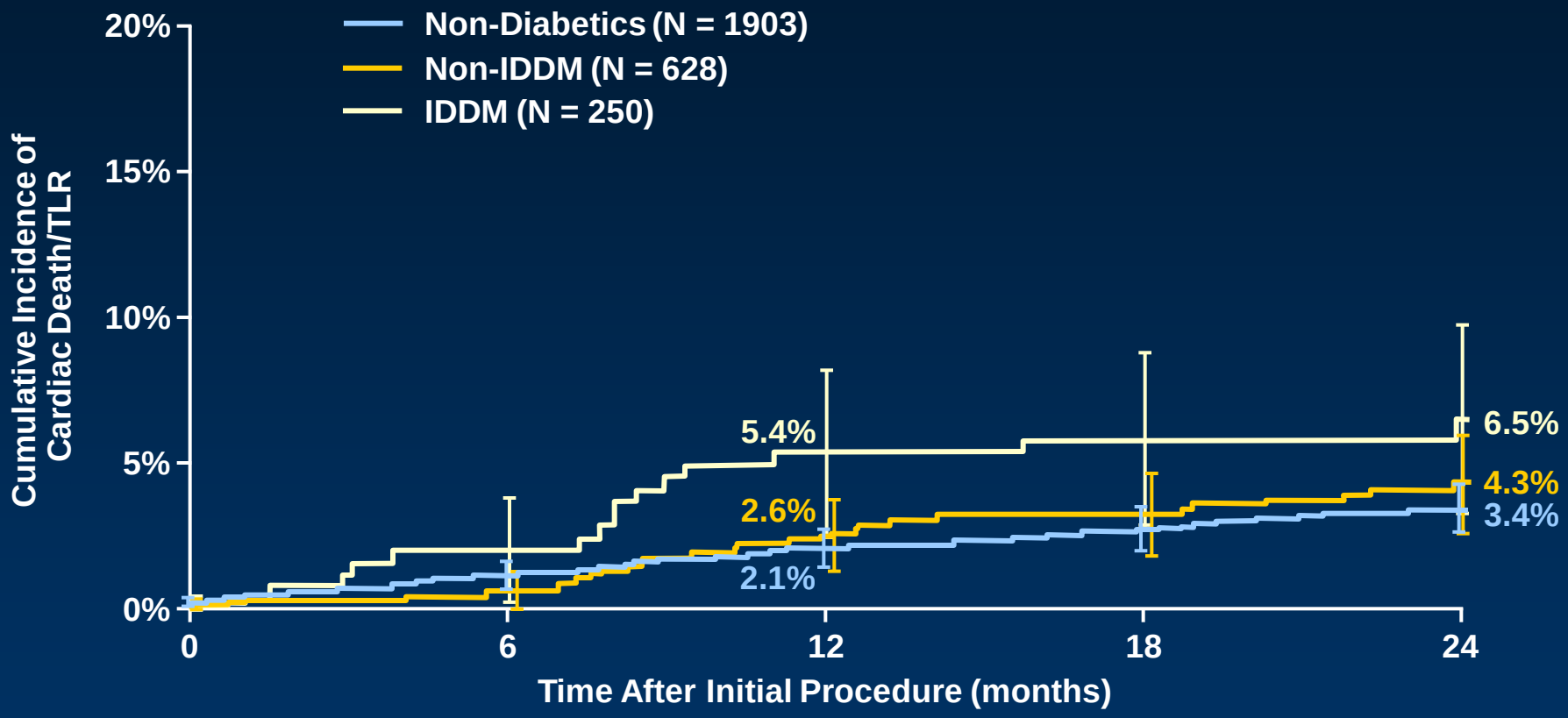
Baseline Characteristics – Standard Risk Patients

%	*Non-Diabetics N = 1903*	*Non-IDDM N = 628*	*IDDM N = 250*
Age (yr)	63.5± 10.8	65.5 ± 10.3*	64.6 ± 10.0
Male	74.3	70.4	56.4**
Diabetes mellitus	0	100.0*	100.0
IDDM	0	0	100.0**
Hypertension	73.1	86.0*	91.6**
Hyperlipidemia	76.0	86.0*	86.8
Current smoker	22.1	18.6	17.2
Family history	42.2	37.6	38.4
Prior MI	25.5	25.7	22.9
Prior PCI	29.5	33.9*	36.4
Prior CABG	7.4	11.1*	8.8
Clinical status:		*	
Stable angina	45.5	46.8	44.8
Unstable angina	31.3	28.5	30.0
Myocardial infarction	6.6	4.3	8.0

*p-value <0.05 Non-IDDM vs. Non-Diabetics
** p-value <0.05 IDDM vs Non-IDDM

RESOLUTE Pooled Diabetic Analysis

Standard Risk Pts – Target Lesion Revascularization to 2 Years

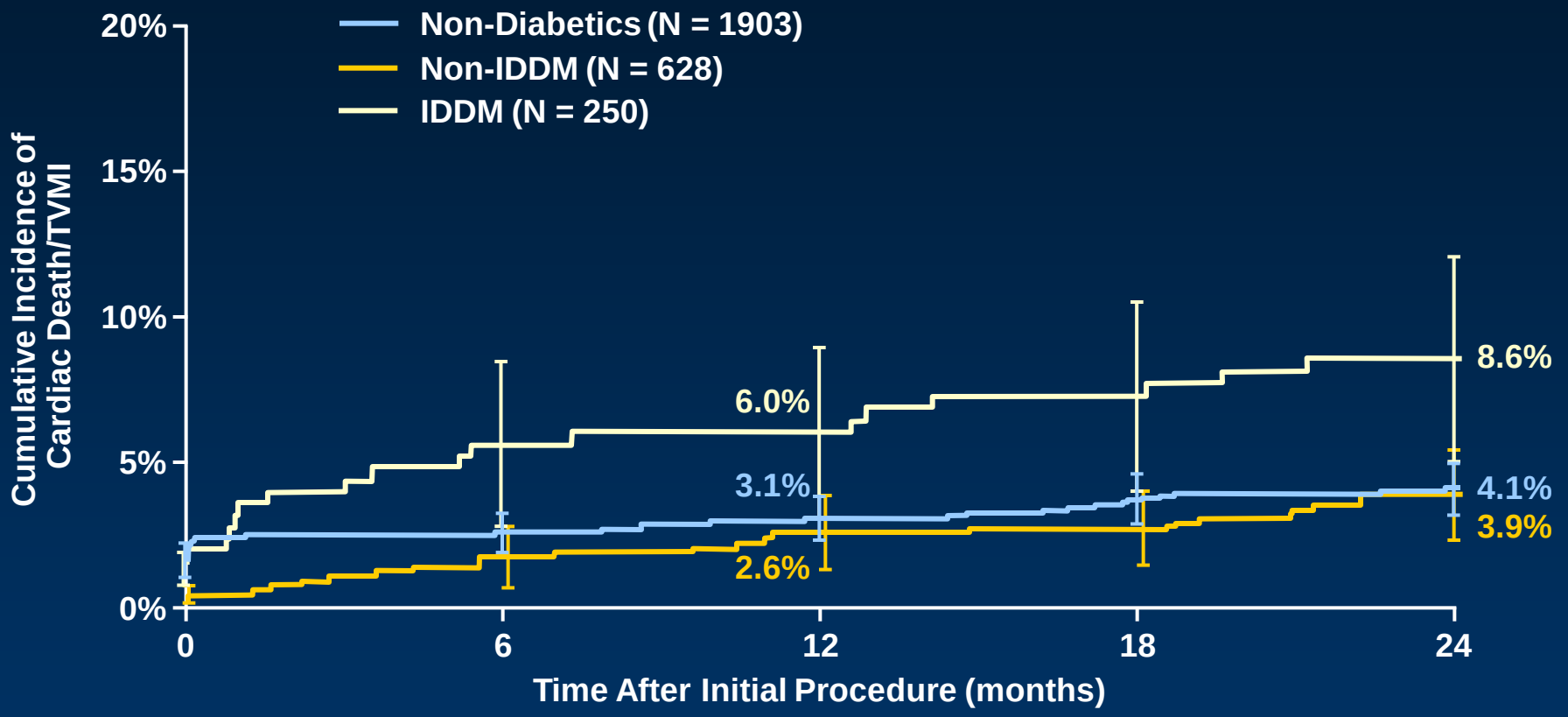


No. at risk					
Non-Diabetics	1903	1900	1859	1809	1763
Non-IDDM	628	627	614	589	579
IDDM	250	250	236	222	216

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE Pooled Diabetic Analysis

Standard Risk Pts – Cardiac Death/TVMI to 2 Years

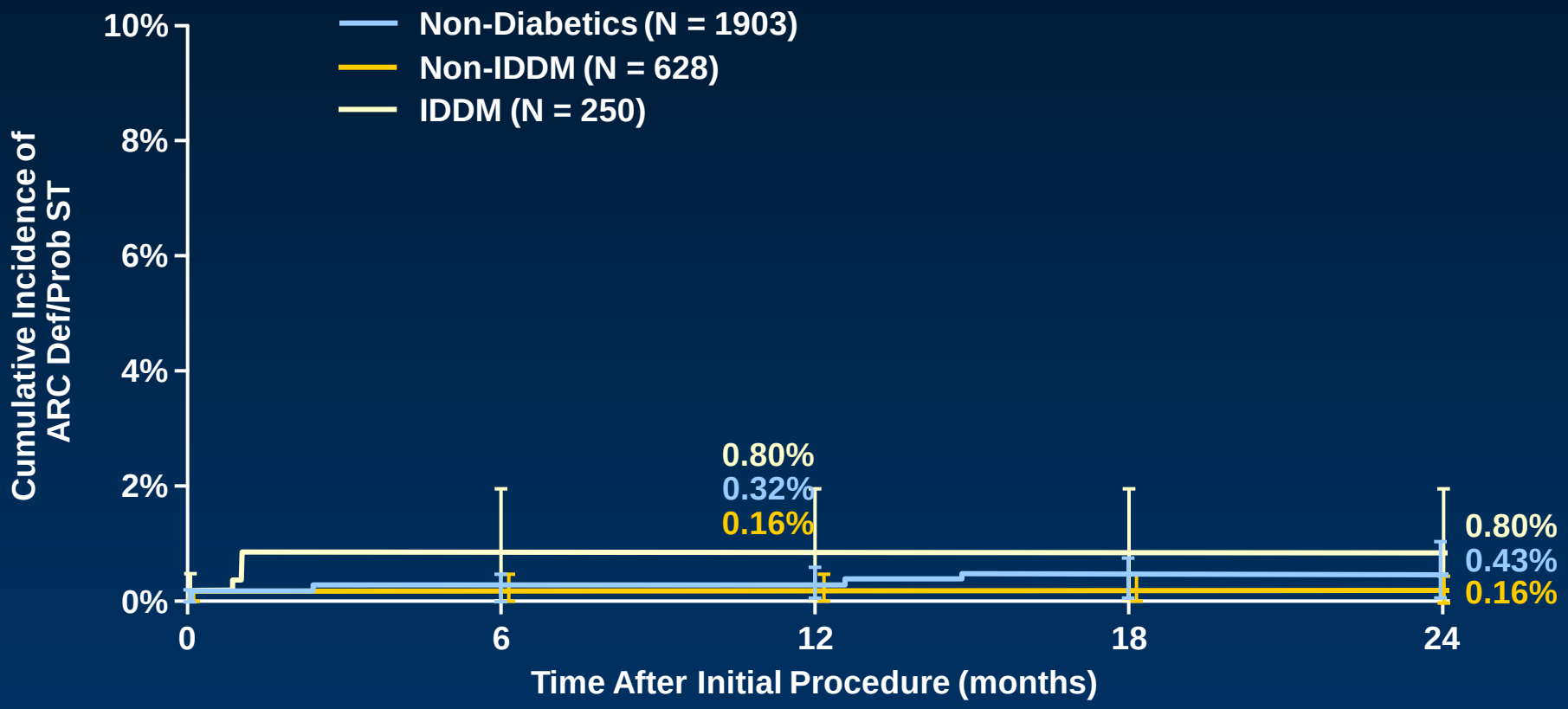


No. at risk					
Non-Diabetics	1903	1872	1833	1796	1757
Non-IDDM	628	626	613	599	593
IDDM	250	248	232	227	222

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE Pooled Diabetic Analysis

Standard Risk Pts – ARC Def/Prob Stent Thrombosis to 2 Years



No. at risk					
Non-Diabetics	1903	1902	1876	1842	1806
Non-IDDM	628	627	617	604	598
IDDM	250	250	240	234	229

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE Pooled Diabetic Analysis

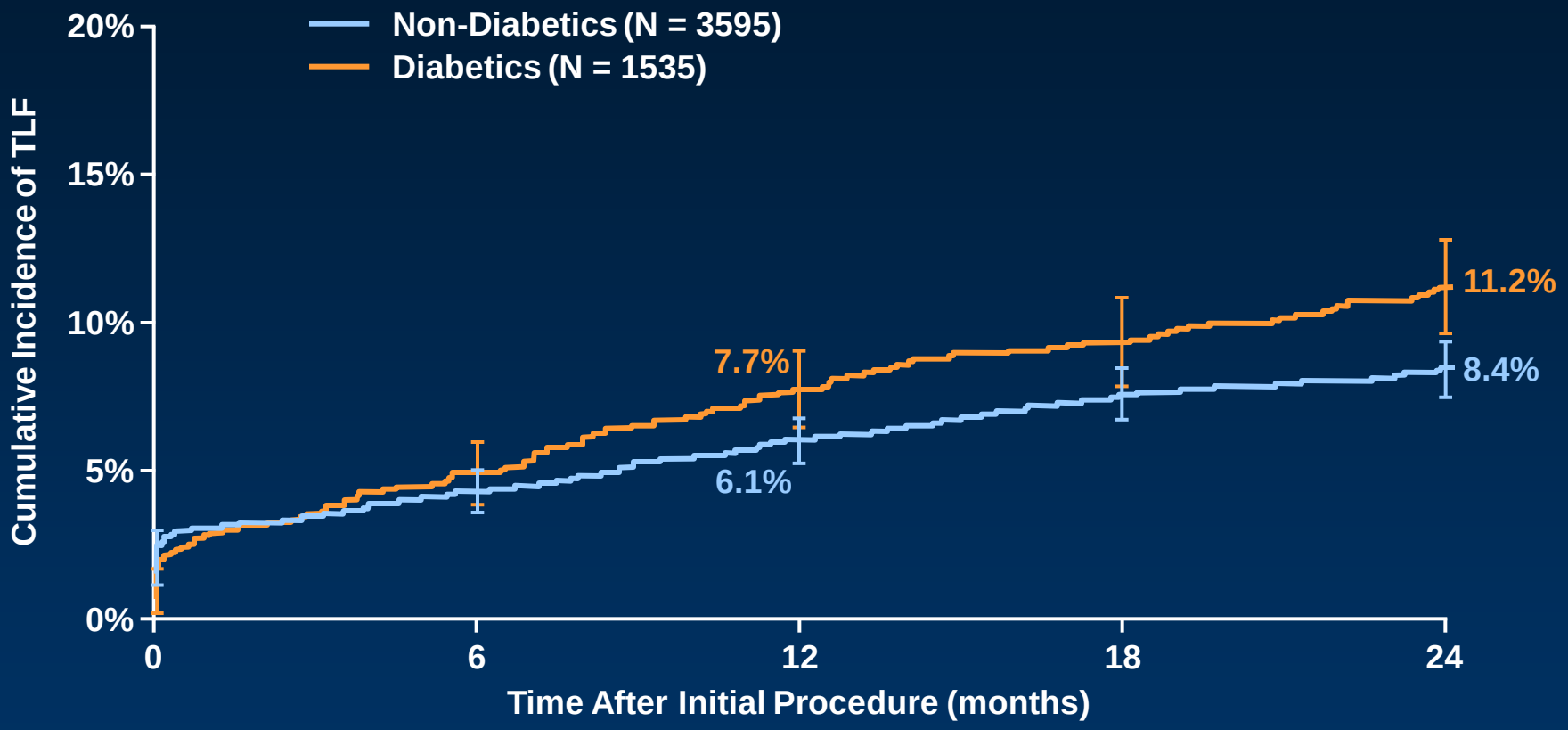
Baseline Characteristics

%	*Standard Risk Diabetics N = 878*	*All Diabetics N = 1535*
Age (yr)	65.2 ± 10.2	65.6 ± 10.2
Male	66.4	68.1
Diabetes mellitus	100.0	100.0
IDDM	28.5	29.6
Prior MI	24.9	27.6
Prior PCI	34.6	34.5
Reason for Revascularization:		
Stable angina	46.2	39.7
Unstable angina	28.9	26.8
Myocardial infarction	5.4	18.1
LAD	44.8	46.8
RVD (mm)	2.7 ± 0.5	2.7 ± 0.5
Lesions per patient	1.1 ± 0.4	1.3 ± 0.6
Stent length per patient	22.5 ± 11.3	28.5 ± 18.8
Complex patients*	0	42.8

* Complex patient definition: bifurcation, bypass grafts, ISR, AMI <72 hr, LVEF <30%, unprotected LM, >2 vessels stented, renal insufficiency or failure (creatinine >140 µmol/L), lesion length >27 mm, >1 lesion per vessel, lesion with thrombus or TO (preprocedure TIMI = 0).

RESOLUTE Pooled Diabetic Analysis

All Patients – Target Lesion Failure to 2 Years

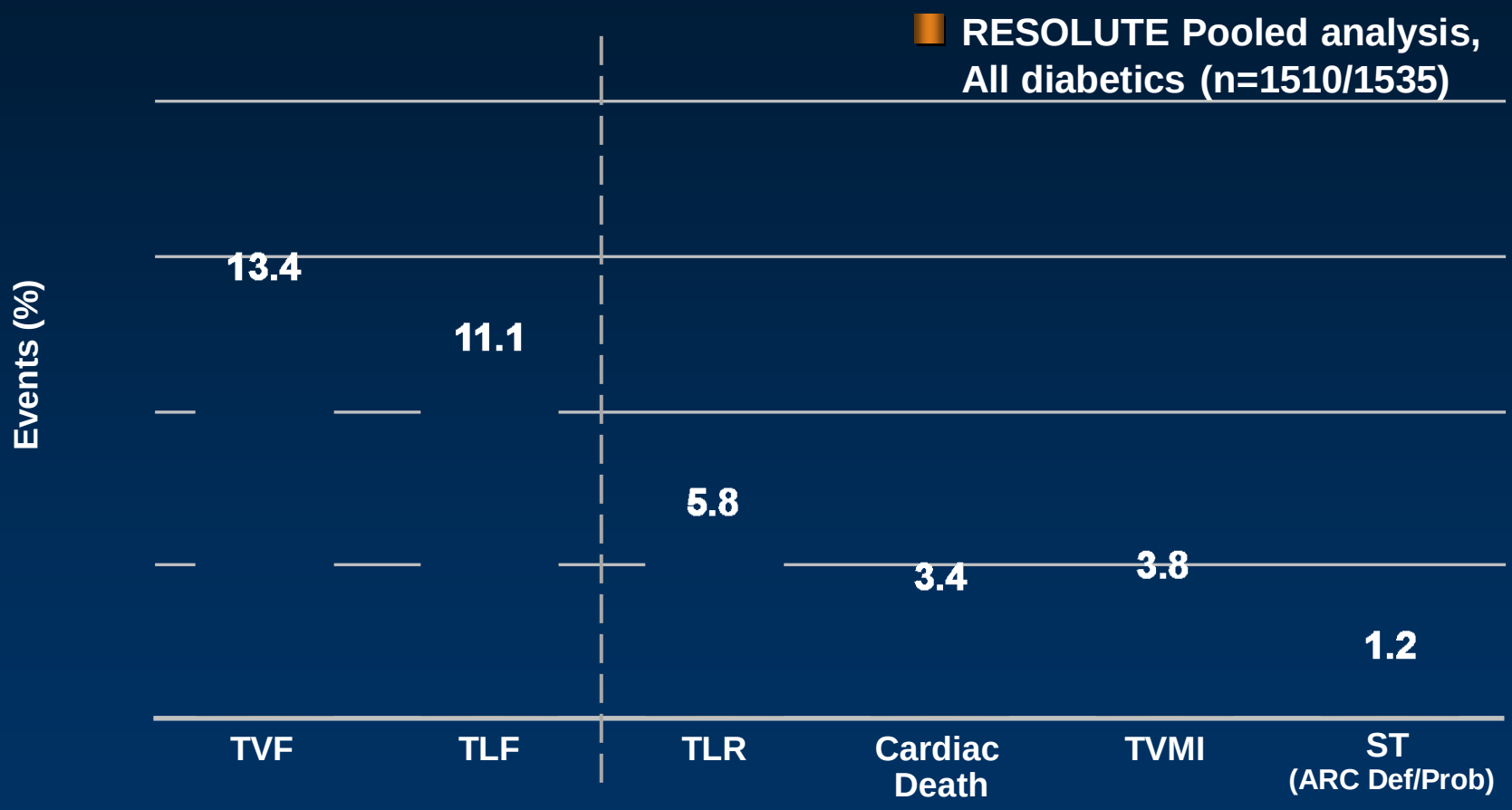


No. at risk					
Non-Diabetics	3595	3540	3399	3301	3198
Diabetics	1535	1518	1447	1386	1345

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE Pooled Diabetic Analysis

All Diabetic Patients – Clinical Outcomes at 24 Months



TLR is ischemia driven.

RESOLUTE Pooled Diabetic Analysis

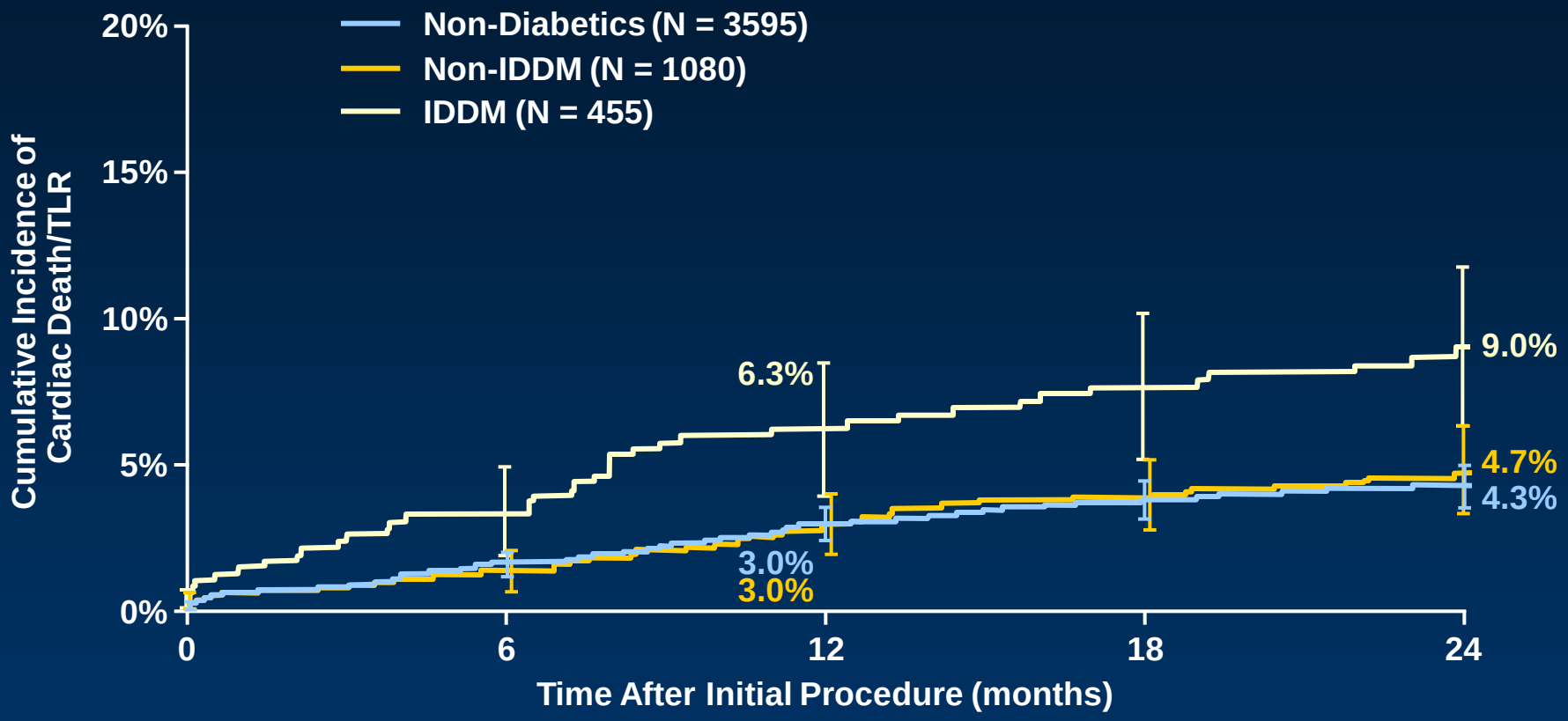
Baseline Characteristics – All Patients

%	*Non-Diabetics N = 3595*	*Non-IDDM N = 1080*	*IDDM N = 455*
Age (yr)	63.1 ± 11.2	65.8 ± 10.2*	65.2 ± 10.1
Male	77.8	71.9*	59.3**
Diabetes mellitus	0	100.0*	100.0
IDDM	0	0	100.0**
Hypertension	67.8	84.6*	90.3**
Hyperlipidemia	67.7	80.0*	81.8
Current smoker	26.0	19.7*	14.7**
Family history	38.1	34.0*	37.6
Prior MI	25.9	26.7	29.8
Prior PCI	29.3	32.7*	38.9**
Prior CABG	7.4	11.2*	11.2
Clinical status:		*	
Stable angina	38.0	40.2	38.5
Unstable angina	25.5	26.2	28.1
Myocardial infarction	24.3	17.8	18.9

*p-value <0.05 Non-IDDM vs. Non-Diabetics
** p-value <0.05 IDDM vs Non-IDDM

RESOLUTE Pooled Diabetic Analysis

All Patients – Target Lesion Revascularization to 2 Years

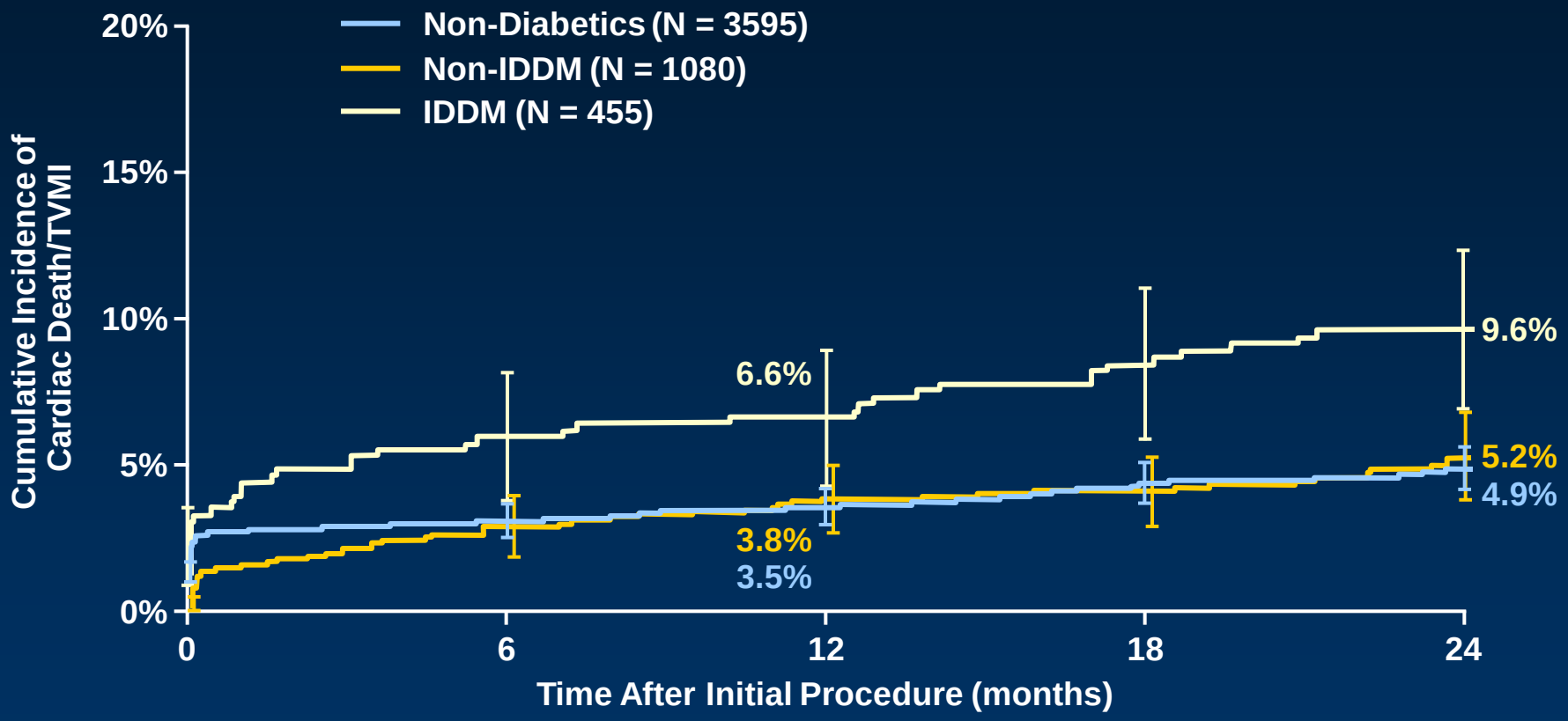


No. at risk					
Non-Diabetics	3595	3589	3479	3385	3285
Non-IDDM	1080	1078	1046	1007	985
IDDM	455	454	428	409	389

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE Pooled Diabetic Analysis

All Patients – Cardiac Death/TVMI to 2 Years

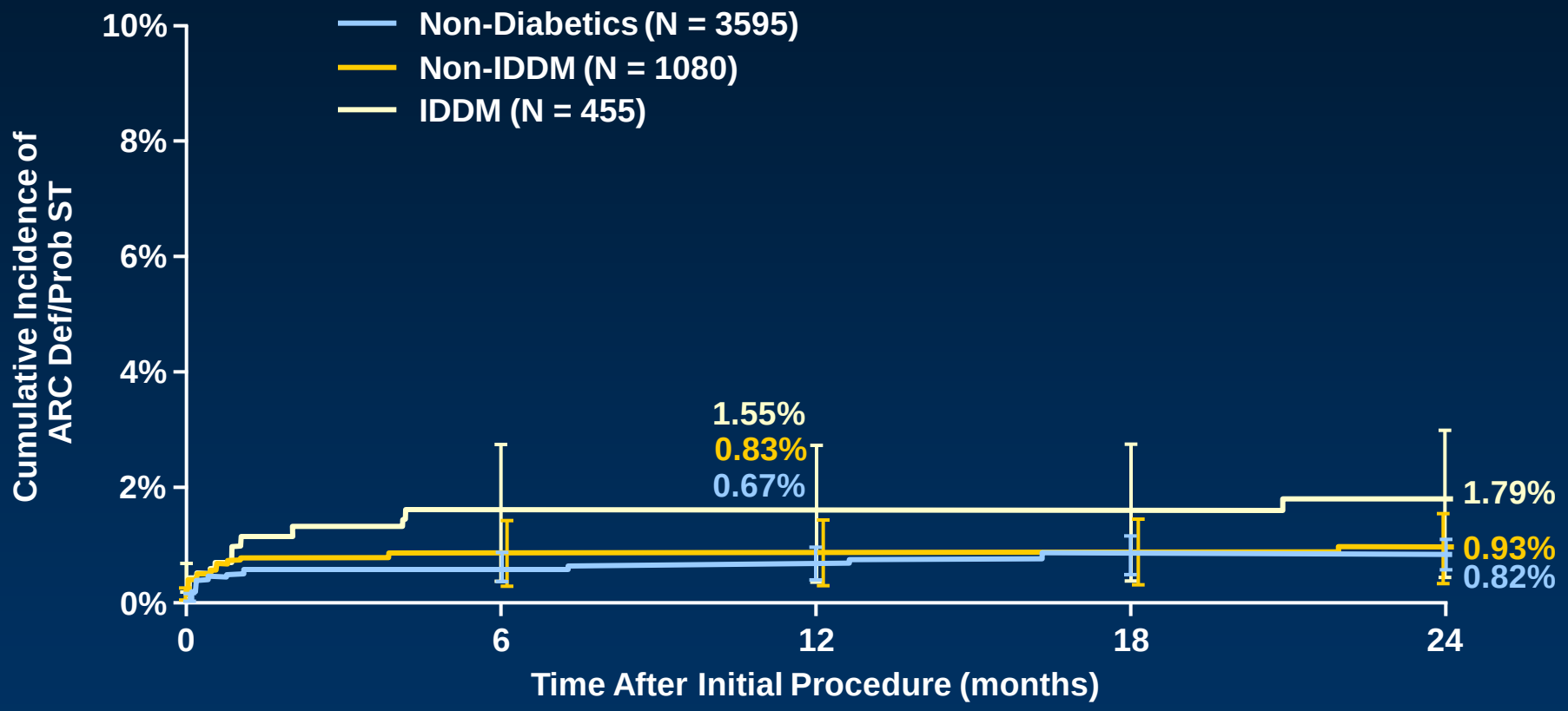


No. at risk					
Non-Diabetics	3595	3543	3442	3387	3306
Non-IDDM	1080	1075	1041	1017	1005
IDDM	455	445	423	416	400

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE Pooled Diabetic Analysis

All Patients – ARC Def/Prob Stent Thrombosis to 2 Years



No. at risk					
Non-Diabetics	3595	3590	3522	3471	3396
Non-IDDM	1080	1078	1054	1032	1020
IDDM	455	454	437	431	417

Error bars indicate a point-wise two-sided 95% confidence interval (±1.96*SE). Standard Error based on the Greenwood Formula.

RESOLUTE Pooled Diabetic Analysis

Conclusions

- The Resolute Zotarolimus-eluting stent is safe and effective in patients with diabetes mellitus.
- Long-term clinical data of patients with non-insulin treated diabetes are equivalent to patients without diabetes.
- Patients with insulin-treated diabetes remain a higher-risk subset and coronary artery bypass surgery should be strongly considered as an alternative revascularization strategy in these patients.

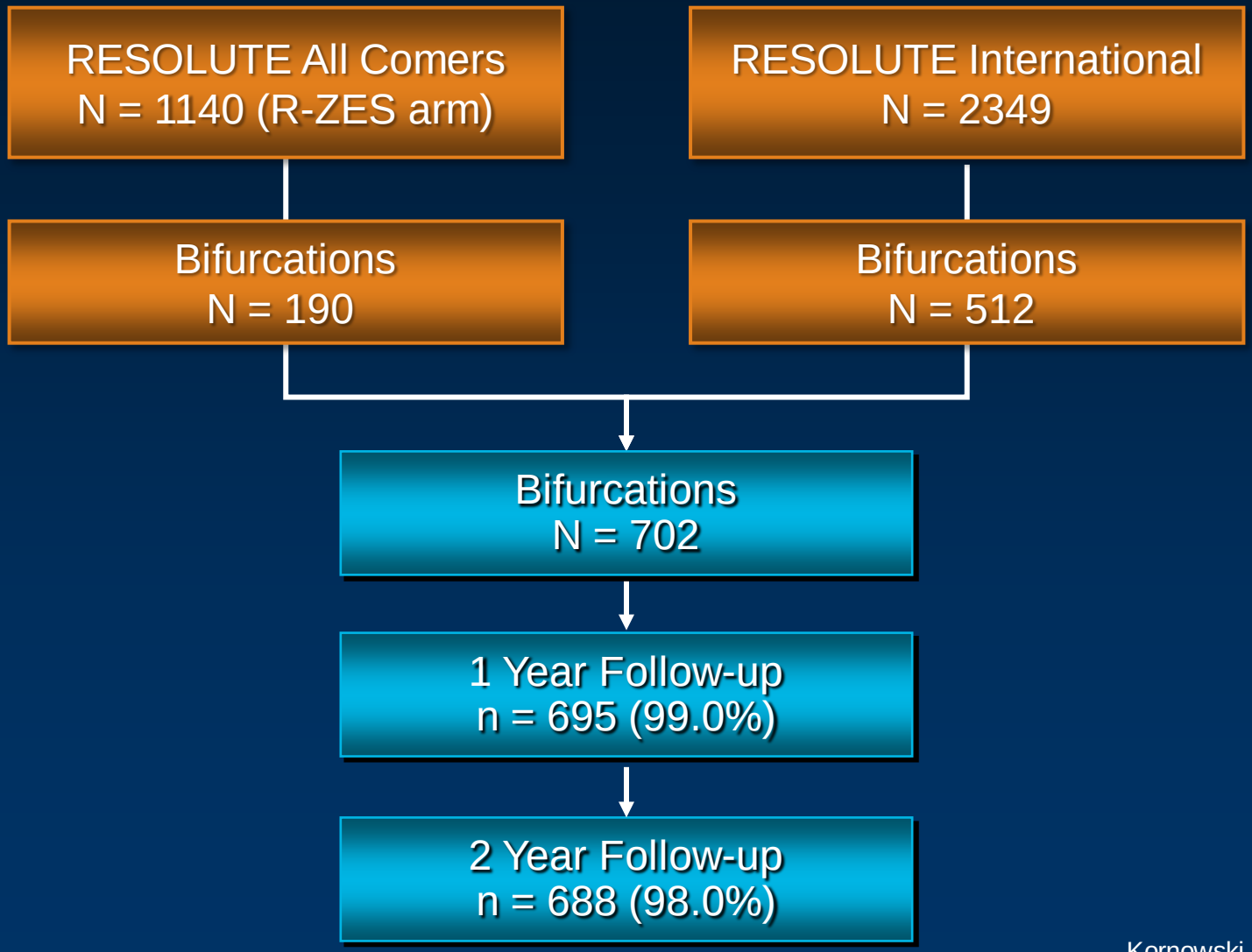
Complex Subgroups

DIABETES

BIFURCATIONS

RESOLUTE Pooled – Bifurcation Subset

Patient Flowchart



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RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for bifurcation subset analysis.

RESOLUTE Pooled – Bifurcation Subset

Lesion Characteristics

%	*N = 702 patients, 1087 lesions*
Lesion location	
LAD	**64.8**
LCX	**33.5**
RCA	**21.9**
Left main	**6.4**
De novo	**97.3**
B2/C	**73.2**
Thrombus (angiographically visible)	**9.4**
Total occlusions (TIMI 0)	**10.9**

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for bifurcation subset analysis.

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RESOLUTE Bifurcation Subset

*Medina Classification**

(1,1,1)
29.4%

(1,1,0)
8.4%

(1,0,1)
3.7%

(0,1,1)
7.1%

(1,0,0)
4.1%

(0,1,0)
9.1%

(0,0,1)
3.0%

*Medina classification only available in RESOLUTE All Comers (R-AC) trial; n = 296 lesions
RESOLUTE All Comers was not specifically designed or powered for bifurcation subset analysis.

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RESOLUTE Pooled – Bifurcation Subset

Procedure Characteristics II

%	*N = 702 patients, 1087 lesions*
Double guidewires	63.9
Main vessel stented	98.0
Side branch stenting	19.1
Bifurcation technique	
Culotte	5.4
Mini-crush\Crush	25.9
T	38.8
Simultaneous Kissing Stent	7.5
V	9.5
Other	12.9
Kissing balloon post-dilatation (R-INT only)	78.4

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for bifurcation subset analysis

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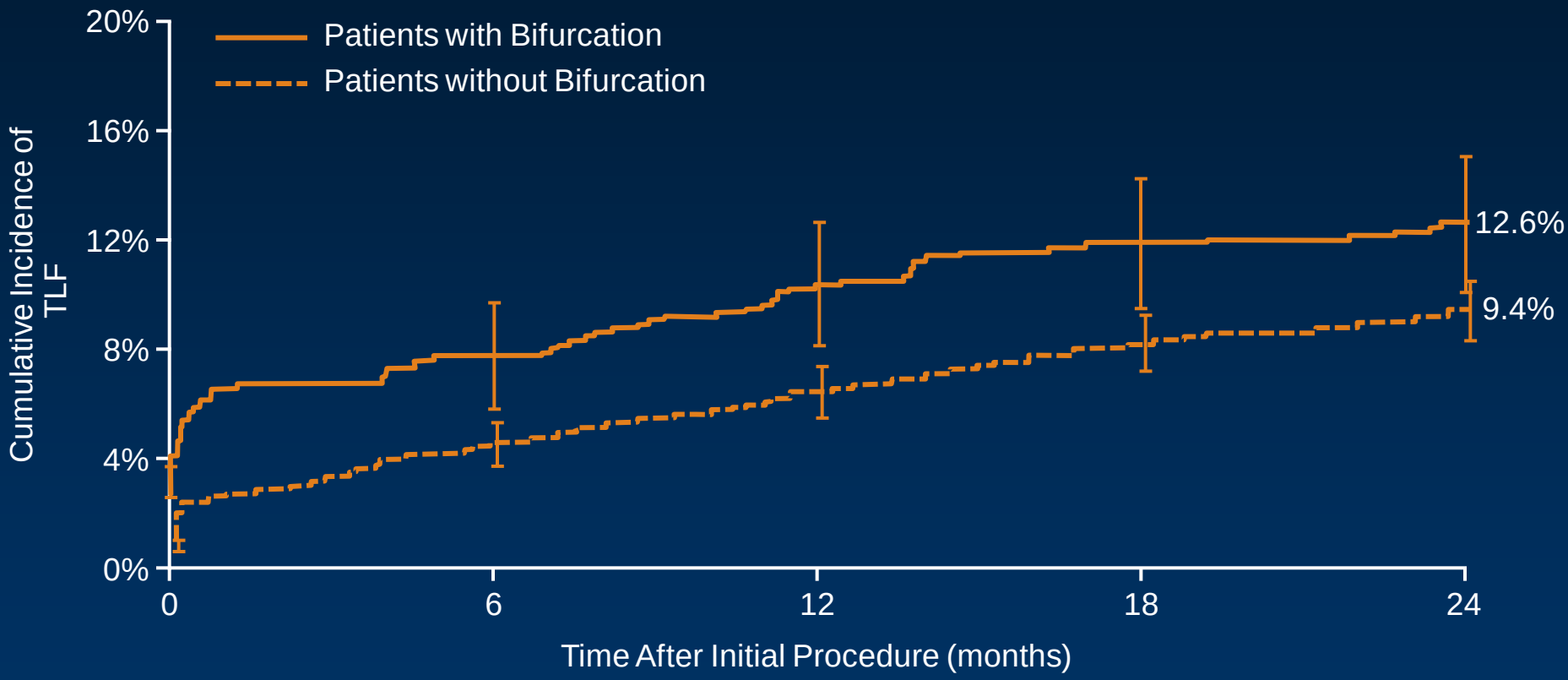
RESOLUTE Pooled – Bifurcation Subset

Target Lesion Failure (Cardiac Death, TV-MI, TLR) to 2 Years



Patients at risk

Bifur	**702**	**683**	**637**	**614**	**596**
%CI	**2.6%**	**7.7%**	**10.3%**	**11.8%**	**12.6%**
No Bifur	**2773**	**2745**	**2622**	**2547**	**2458**
%CI	**1.0%**	**4.5%**	**6.4%**	**8.2%**	**9.4%**

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for bifurcation subset analysis.

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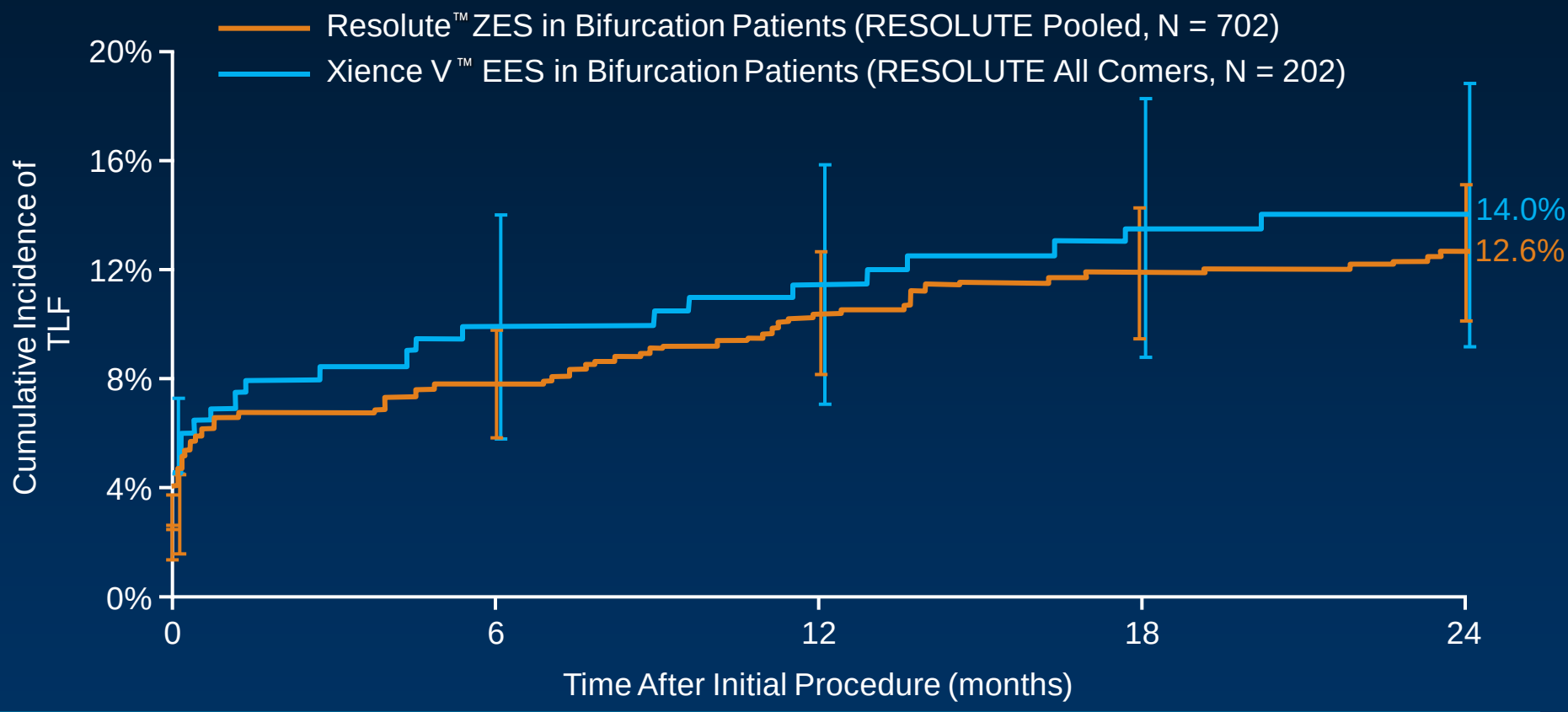
RESOLUTE Pooled – Bifurcation Subset

Perspective: TLF to 2 Years – Comparison to Xience V EES (R-AC)



Patients at risk					
R-ZES	702	683	637	614	596
%CI	2.6%	7.7%	10.3%	11.8%	12.6%
EES	202	193	181	176	170
%CI	4.5%	9.9%	11.4%	13.5%	14.0%

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for bifurcation subset analysis.

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RESOLUTE Pooled – Bifurcation Subset

Conclusion

In the pooled dataset with Resolute™ DES in bifurcation lesions we observed:

- **Excellent technical/angiographic success rate with 19.1% need for SB stenting in the treated cohort.**
- **Sustainable clinical efficacy out to two years, with very low rates of TLR (6.1%) and a favorable TLF rate of 12.6%.**
- **Sustained safety with low stent thrombosis (2.3%, mostly early) up to two years.**
- **Thus, the Resolute DES platform is a viable treatment option for bifurcation lesion management.**

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for bifurcation subset analysis.

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Complex Subgroups

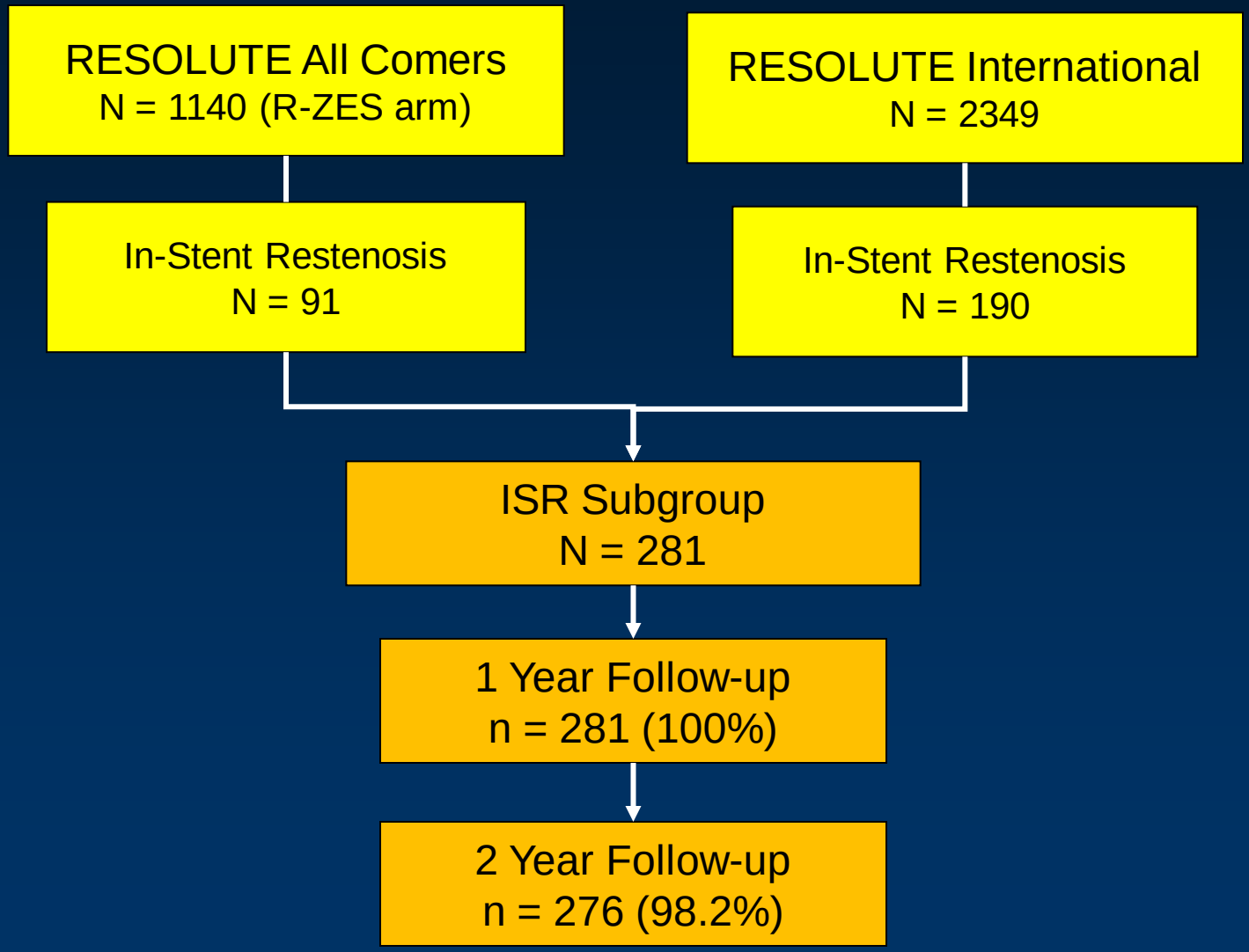
DIABETES

BIFURCATIONS

IN STENT RESTENOSIS

RESOLUTE Pooled – ISR Subgroup

Patient Flowchart



RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis.

Richardt G. PCR 2012

RESOLUTE Pooled – ISR Subgroup

Baseline Characteristics

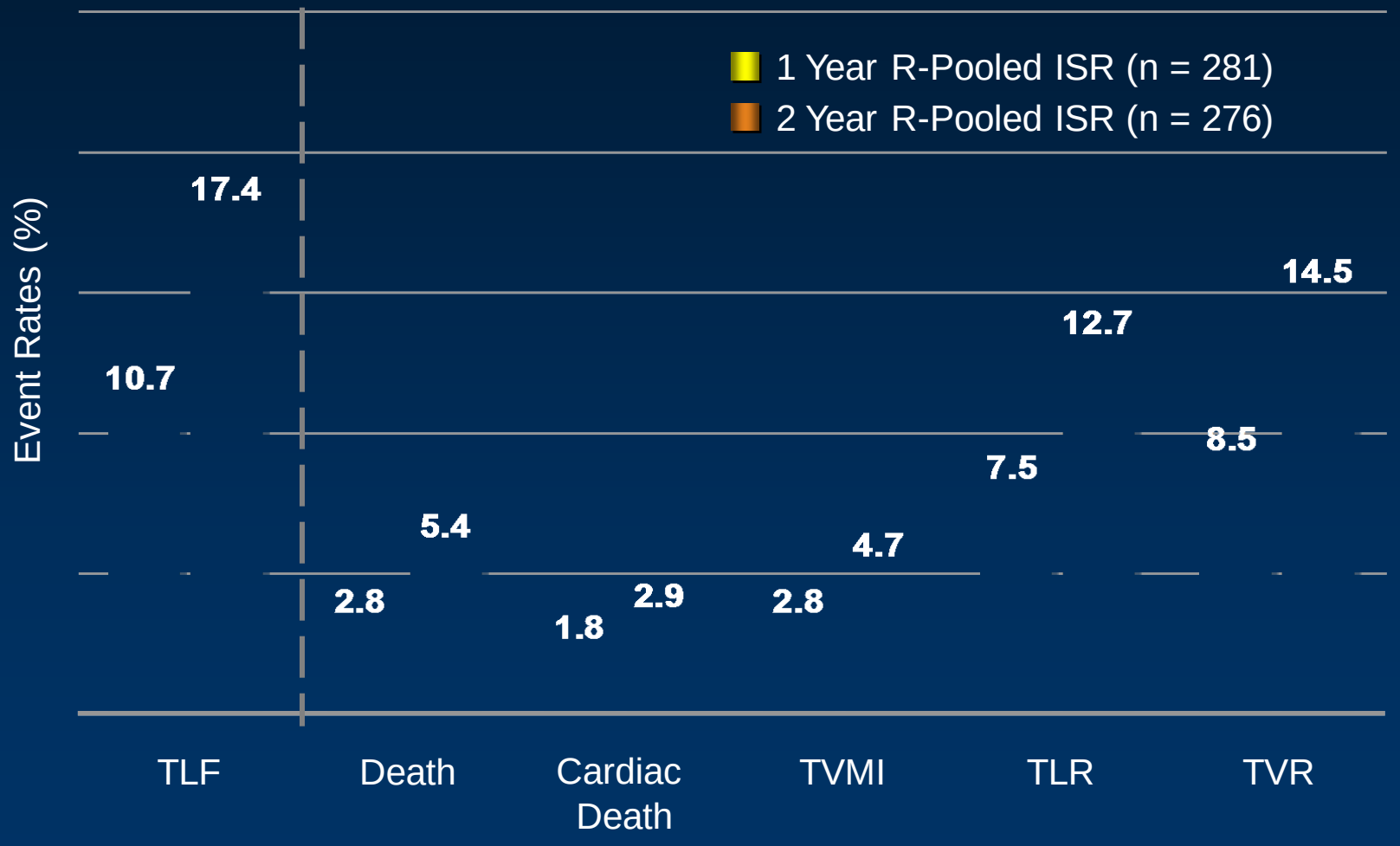
%	ISR N = 281	No ISR N = 3194	P
Age (yr)	65.3 ± 10.5	63.6 ± 11.1	0.015
Male	77.6	77.4	0.94
Diabetes mellitus	31.0	27.9	0.27
IDDM	12.1	8.4	0.034
Hypertension	79.0	68.0	<0.001
Hyperlipidemia	81.1	62.4	<0.001
Current smoker	14.6	25.8	<0.001
Family history of CAD	36.2	32.0	0.20
Prior MI	53.9	25.3	<0.001
Prior PCI	98.6	24.4	<0.001
Prior CABG	12.5	8.5	0.026
Cardiac status:			<0.001
Stable angina	42.7	35.4	
Unstable angina	30.6	23.4	
Myocardial infarction	16.7	32.6	

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis.

Richardt G. PCR 2012

RESOLUTE Pooled – ISR Subgroup

Clinical Outcomes at 1 & 2 Years



TLF (Target Lesion Failure) is defined as cardiac death, TVMI, or clinically driven TLR. RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis. Note previous reported data on patients with ISR: TAXUS V-ISR TVR at 9 months: 10.5%, ISAR-DESIRE TVR at 1 year: SES 8%, PES 19%, PEP-CAD II trial TLR at 1 year for PES:15.4%.

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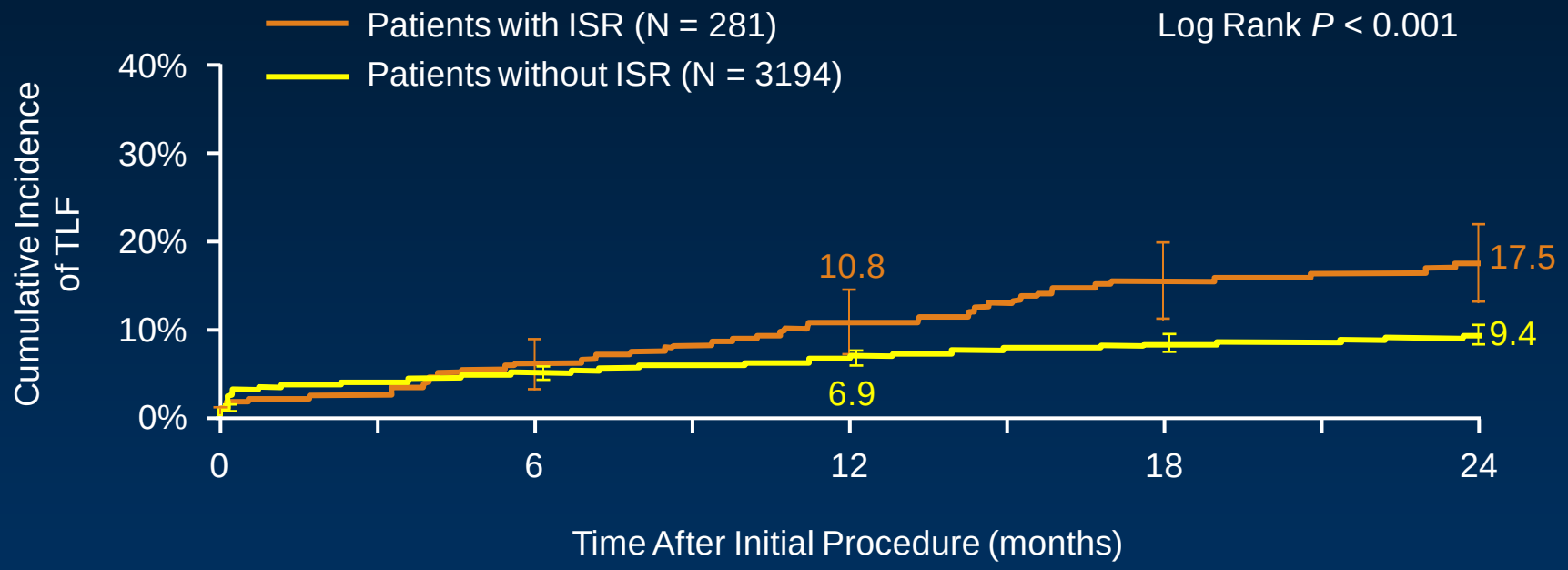
RESOLUTE Pooled – ISR Subgroup

Target Lesion Failure (TLF) to 2 Years



Pts at risk					
ISR	**281**	**280**	**262**	**248**	**231**
% CI	**0.36**	**6.1**	**10.8**	**15.5**	**17.5**
No-ISR	**3194**	**3148**	**2997**	**2913**	**2823**
% CI	**1.4**	**5.1**	**6.9**	**8.4**	**9.4**

TLF is defined as cardiac death, TVMI, or clinically driven TLR. RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis. Note previous reported data on patients with ISR: PEP-CAD II trial TLR at 1 year for PES:15.4%.

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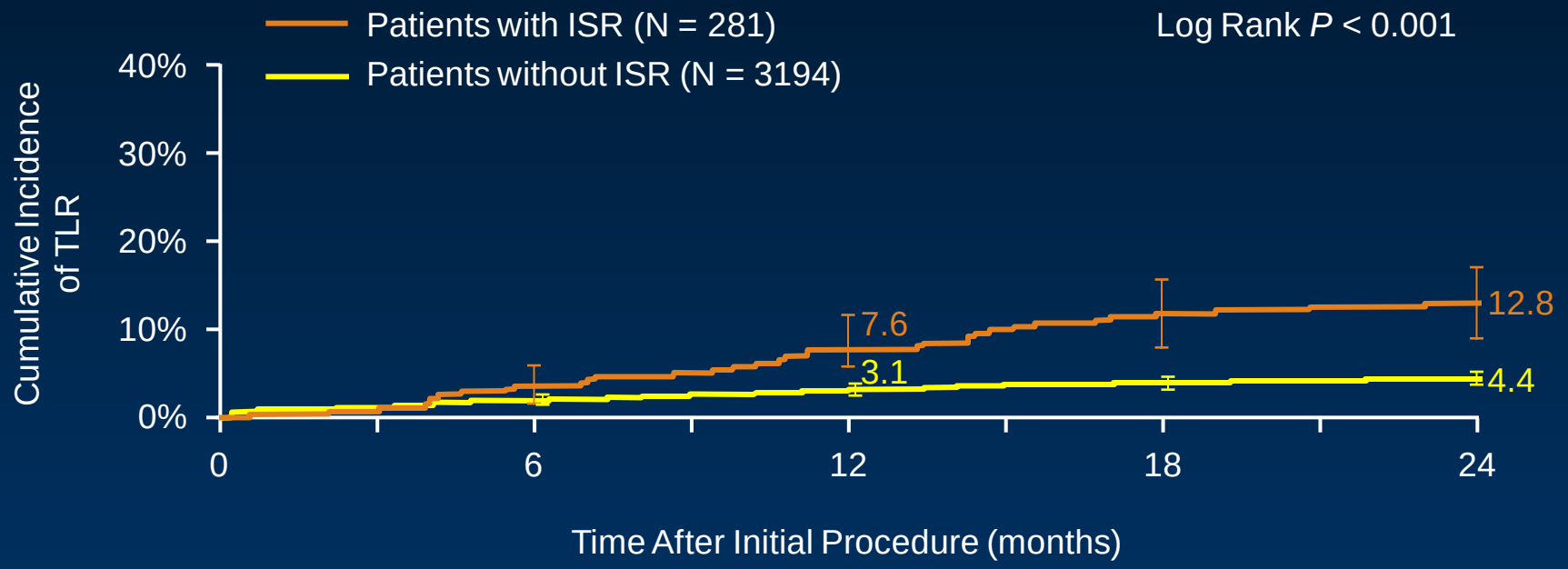
RESOLUTE Pooled – ISR Subgroup

Target Lesion Revascularization to 2 Years



Pts at risk					
ISR	**281**	**281**	**267**	**253**	**237**
% CI	**0.0**	**3.6**	**7.6**	**11.7**	**12.8**
No-ISR	**3194**	**3188**	**3072**	**2994**	**2903**
% CI	**0.1**	**1.9**	**3.1**	**3.9**	**4.4**

TLR is clinically driven. RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis.
Note previous reported data on patients with ISR: PEP-CAD II trial TLR at 1 year for PES:15.4%.

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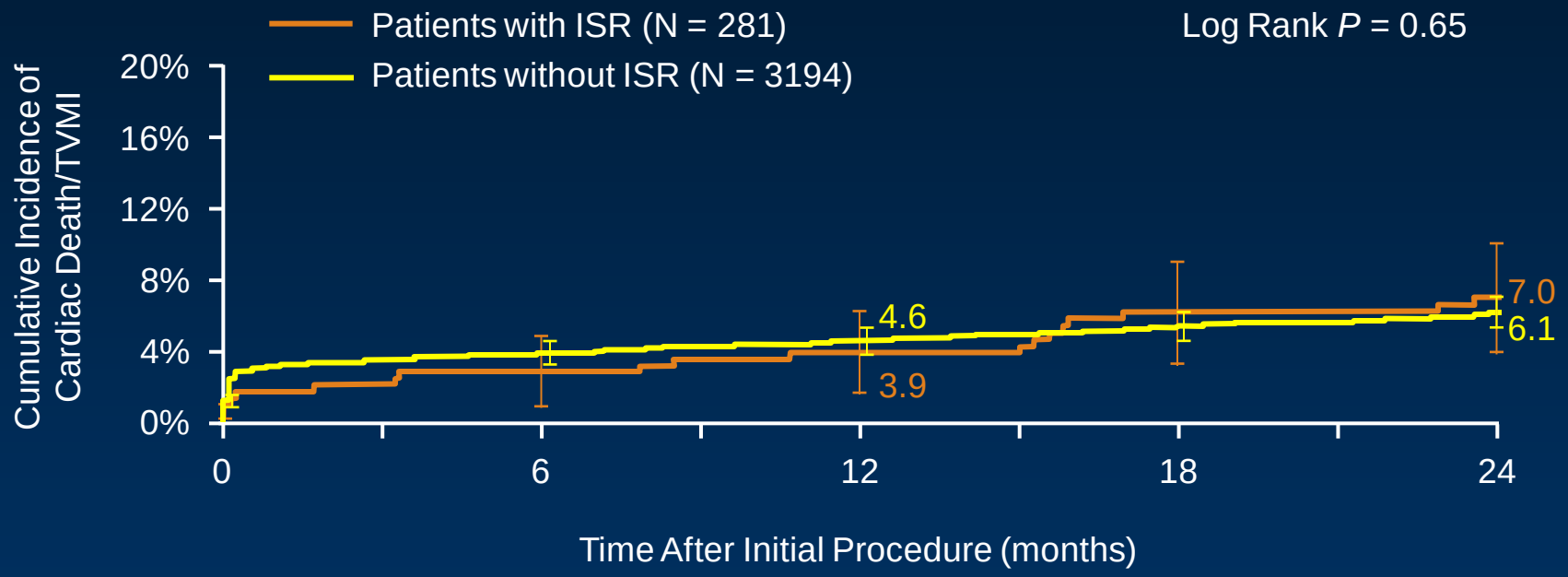
RESOLUTE Pooled – ISR Subgroup

Cardiac Death & Target Vessel MI to 2 Years



Pts at risk					
ISR	**281**	**280**	**271**	**267**	**257**
% CI	**0.4**	**2.9**	**3.9**	**6.1**	**7.0**
No-ISR	**3194**	**3150**	**3034**	**2984**	**2912**
% CI	**1.3**	**3.9**	**4.6**	**5.4**	**6.1**

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis.

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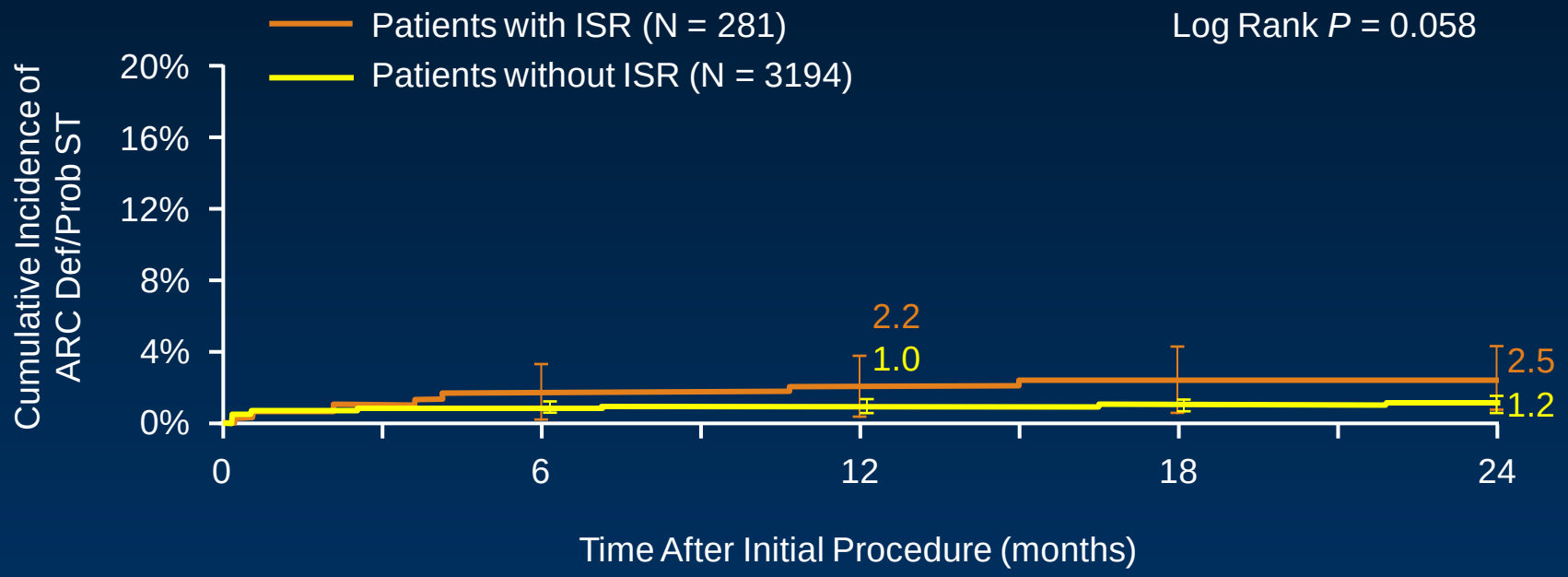
ARC Def/Prob Stent Thrombosis to 2 Years



Pts at risk					
ISR	**281**	**281**	**274**	**270**	**264**
% CI	**0.0**	**1.8**	**2.2**	**2.5**	**2.5**
No-ISR	**3194**	**3186**	**3109**	**3065**	**2995**
% CI	**0.2**	**0.9**	**1.0**	**1.1**	**1.2**

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis.

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RESOLUTE Pooled – ISR Subgroup

Conclusions

- **This is one of largest datasets on patients with ISR from 2 prospective trials that were designed with consistent definitions, adjudication methods and data collection.**
- **PCI of ISR with Resolute™ ZES was safe with no excess of ST, cardiac death or TV-MI observed out to 2 years.**
- **Compared to non-ISR patients, the TLF rate nearly doubled in patients with ISR, mainly driven by a higher TLR rate. Consequently, ISR was the strongest independent predictor for TLF in the total population.**

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis.

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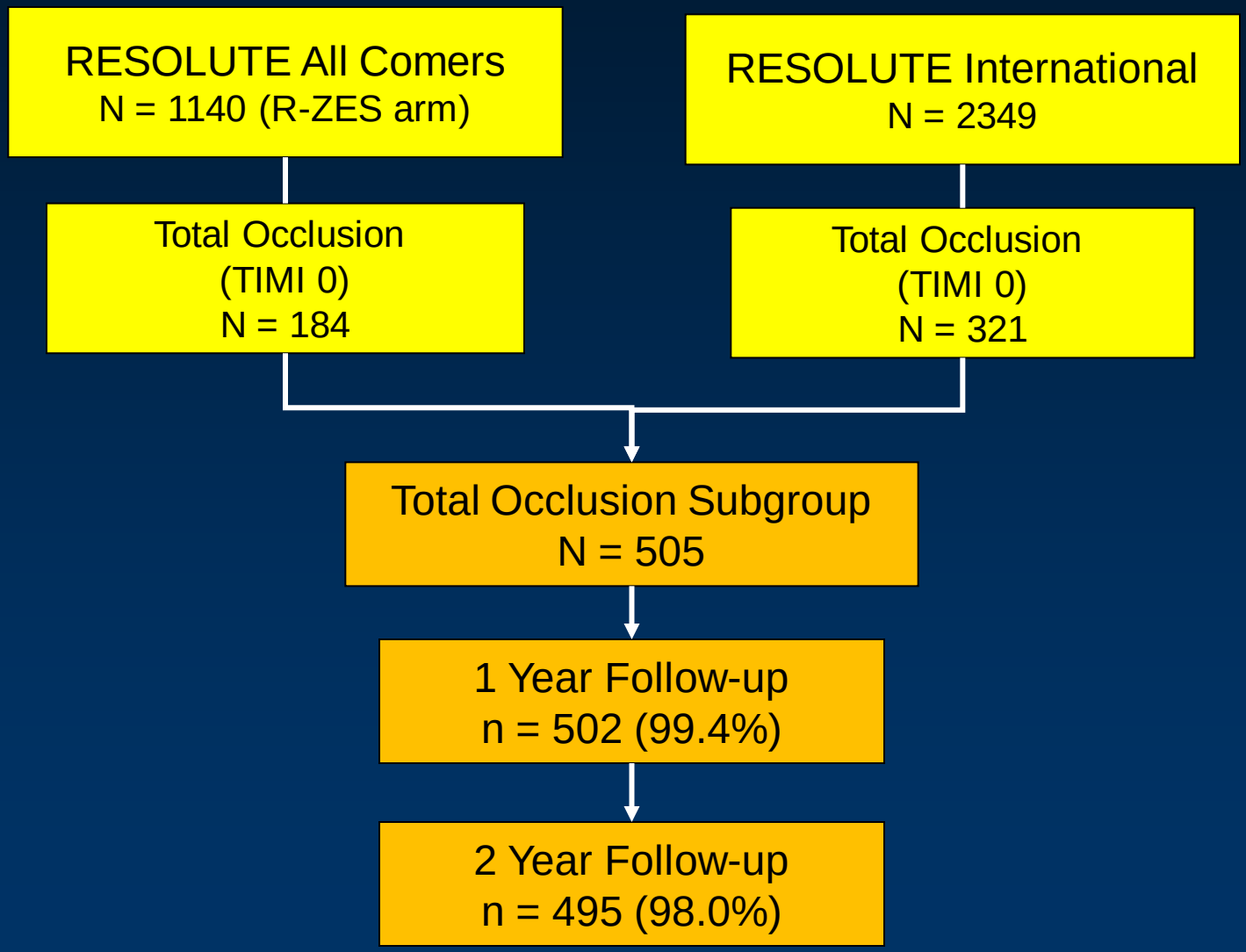
Muchas Gracias !!

RESOLUTE Pooled TO Subgroup

Patient Flowchart



RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for TO subset analysis.

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RESOLUTE Pooled TO Subgroup

Baseline Characteristics

%	*N = 505 pts*
Age (yr)	60.6 ± 11.3
Male	76.4
Diabetes mellitus	22.0
IDDM	7.3
Hypertension	60.8
Hyperlipidemia	55.6
Current smoker	37.4
Family history of CAD	34.5
Prior MI	22.9
Prior PCI	18.0
Prior CABG	4.0
Cardiac status:	
Stable angina	22.0
Unstable angina	10.3
Myocardial infarction	62.2

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for TO subset analysis.

Silber S. JIM 2012

RESOLUTE Pooled TO Subgroup

Lesion & Procedure Characteristics

	N = 505 pts
Lesion location (%)	
LAD	**47.3**
LCx	**27.1**
RCA	**49.9**
Left Main	**1.2**
B2/C lesion (%)	**83.9**
RVD* (mm)	**2.87 ± 0.48**
MLD* (mm)	**0.23 ± 0.44**
Diameter stenosis* (%)	**91.8 ± 15.6**
Lesions per patient (n)	**1.5 ± 0.8**
Stents per patient (n)	**2.0 ± 1.3**
Stent length per patient (mm)	**42.1 ± 28.3**
Direct stenting (%)	**26.2**

* For RESOLUTE International (R-INT) angiographic measurements are site reported.
RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for TO subset analysis.

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RESOLUTE Pooled TO Subgroup

Acute Success Rates

%	*N = 505 pts*
Lesion success **(the attainment of <50% residual stenosis of the target lesion using any percutaneous method)**	**98.6**
Device success **(the attainment of <50% residual stenosis of the target lesion using only the assigned device)**	**97.3**
Procedure success **(the attainment of <50% residual stenosis of the target lesion and no in-hospital MACE)**	**94.6**

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for TO subset analysis.

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RESOLUTE Pooled TO Subgroup

Clinical Outcomes to 2 Years

% (n)	*30 Days n = 502*	*1 Year n = 502*	*2 Year n = 495*
Death (all)	0.8	1.2	3.2
Cardiac	0.8	1.0	2.6
Target vessel MI (all)	2.0	2.4	2.6
Cardiac death + target vessel MI	2.8	3.4	5.3
ST def/prob	1.6	2.0	2.2
Early (0 – 30d)	1.6	1.6	1.6
LST (>30d – 1yr)	--	0.4	0.4
VLST (>1 yr)	--	--	0.2
TLR (clinically driven)	1.4	3.6	5.1
TVR (clinically driven)	1.8	4.2	5.9
TLF (cardiac death, target vessel MI, TLR)	3.8	6.2	9.3
TVF (cardiac death, target vessel MI, TVR)	4.0	6.6	9.9
MACE (death, MI, TLR, emergent CABG)	3.8	6.6	10.3

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for TO subset analysis.

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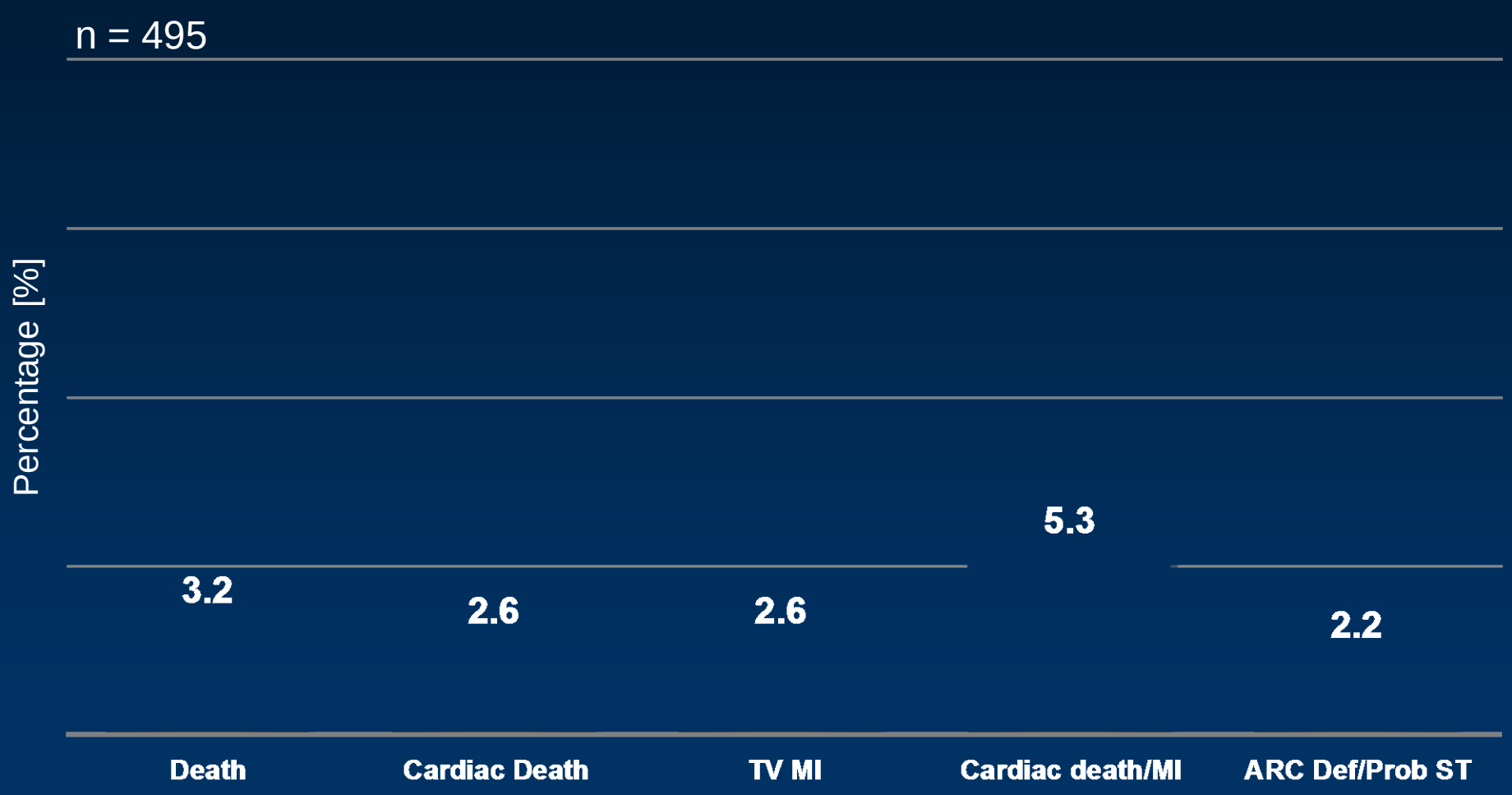
RESOLUTE Pooled TO Subgroup

Safety Outcomes to 2 Years



RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for TO subset analysis.

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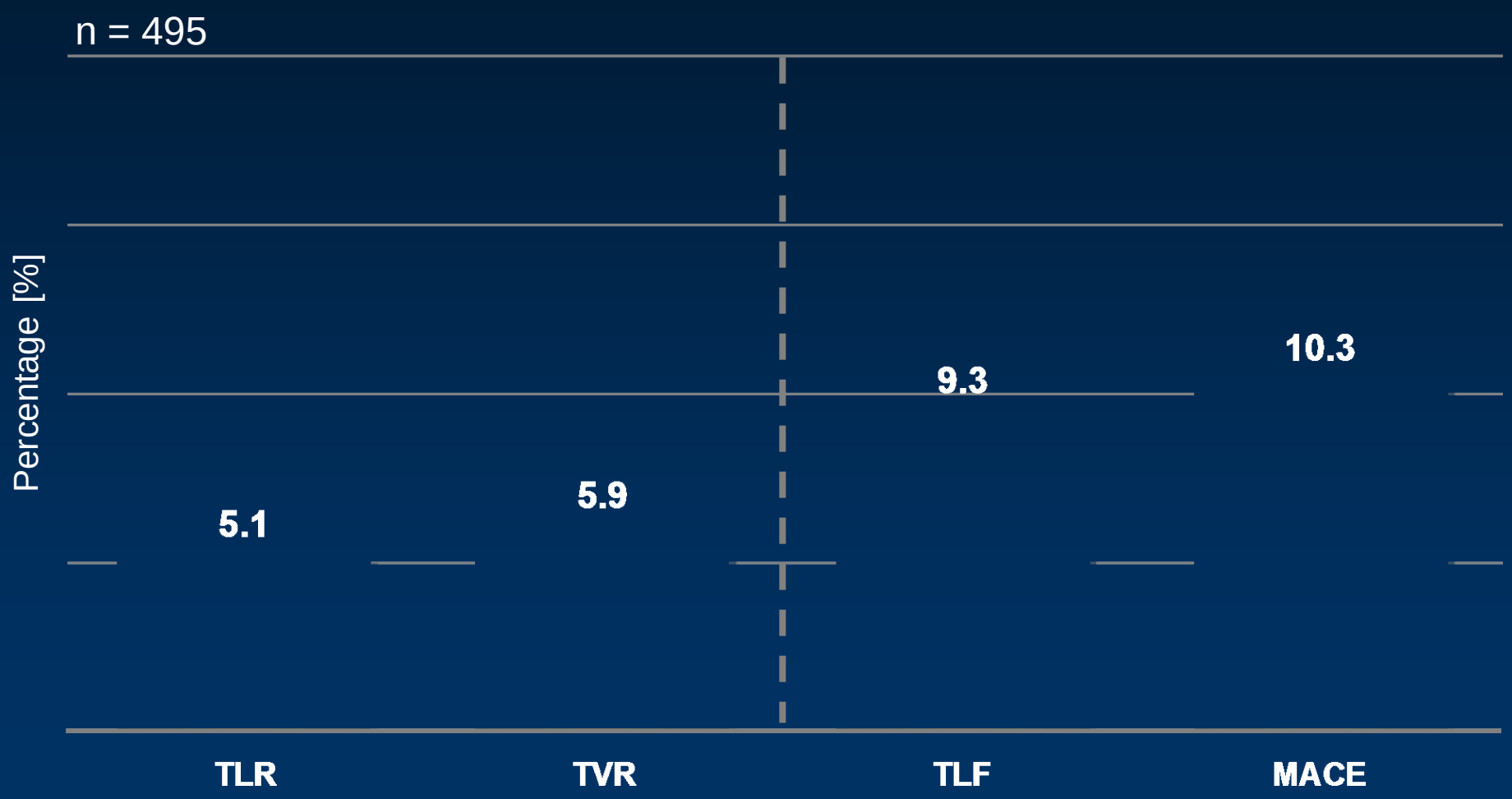
RESOLUTE Pooled TO Subgroup

Efficacy Outcomes to 2 Years



TLR is clinically driven. TLF (Target Lesion Failure) is defined as cardiac death, TVMI, or clinically driven TLR. MACE (Major Adverse Cardiac Event) is defined as death, MI, emergent CABG, or clinically driven TLR. RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for TO subset analysis.

Silber S. JIM 2012

RESOLUTE Pooled – Bifurcation Subset

Clinical Outcomes at 1 and 2 Years

%	1 Year n = 695	2 Years n = 688
Death (all)	2.3	4.1
Cardiac death	1.6	2.6
Target vessel MI	5.9	6.4
Q Wave	1.3	1.6
Non Q wave	4.6	4.8
Cardiac death + target vessel MI	7.1	8.4
ARC Def/Prob ST (all)	2.0	2.3
Early (≤ 30 days)	2.0	2.0
Late (31-360 days)	0.1	0.1
Very Late (>360 days)	--	0.3
TLR	4.9	6.1
TVR	6.2	8.3
TLF (cardiac death, target vessel MI, TLR)	10.4	12.6
TVF (cardiac death, target vessel MI, TVR)	11.5	14.5
MACE (death, MI, TLR, emergent CABG)	11.4	14.4

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for bifurcation subset analysis

Kornowski R. PCR 2012

RESOLUTE Pooled – ISR Subgroup

Lesion & Procedure Characteristics

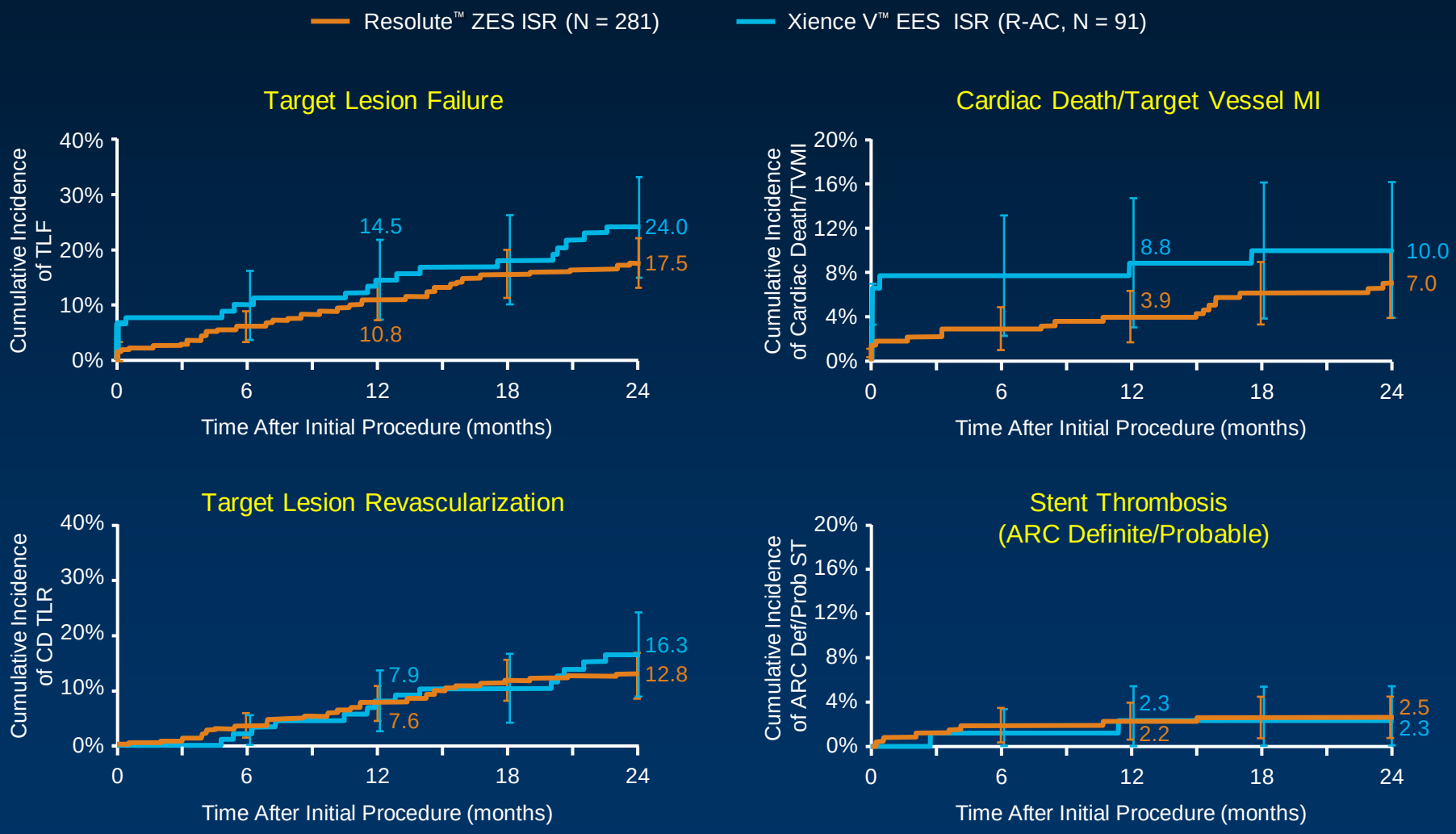
	ISR *N = 281 pts, 410 lesions*	*No ISR* *N = 3194 pts, 4614 lesions*	*P*
Lesion location (%)			
LAD	44.8	52.3	0.017
LCx	29.5	29.2	0.92
RCA	39.5	33.7	0.049
Left Main	2.1	2.5	0.68
SVG	4.3	1.6	0.001
LIMA	0.7	0.2	0.047
ISR after BMS (%)	70.8	NA	
ISR after DES (%)	26.0	NA	
Pre-procedure thrombus (%)	5.1	10.2	0.002
B2/C lesion (%)	59.7	64.4	0.07
RVD* (mm)	2.92 ± 0.56	2.84 ± 0.51	0.005
MLD* (mm)	0.69 ± 0.50	0.62 ± 0.49	0.005
Lesion length* (mm)	18.0 ± 12.9	16.6 ± 10.1	0.040
Pre-procedure % diameter stenosis*	75.5 ± 17.8	77.6 ± 17.6	0.022
Post-procedure % diameter stenosis*	10.7 ± 14.2	9.9 ± 13.9	0.22

* For RESOLUTE International (R-INT) angiographic measurements are site reported.
RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis.

Richardt G. PCR 2012

RESOLUTE Pooled – ISR Subgroup

Perspective: Comparison to Xience V EES in R-AC



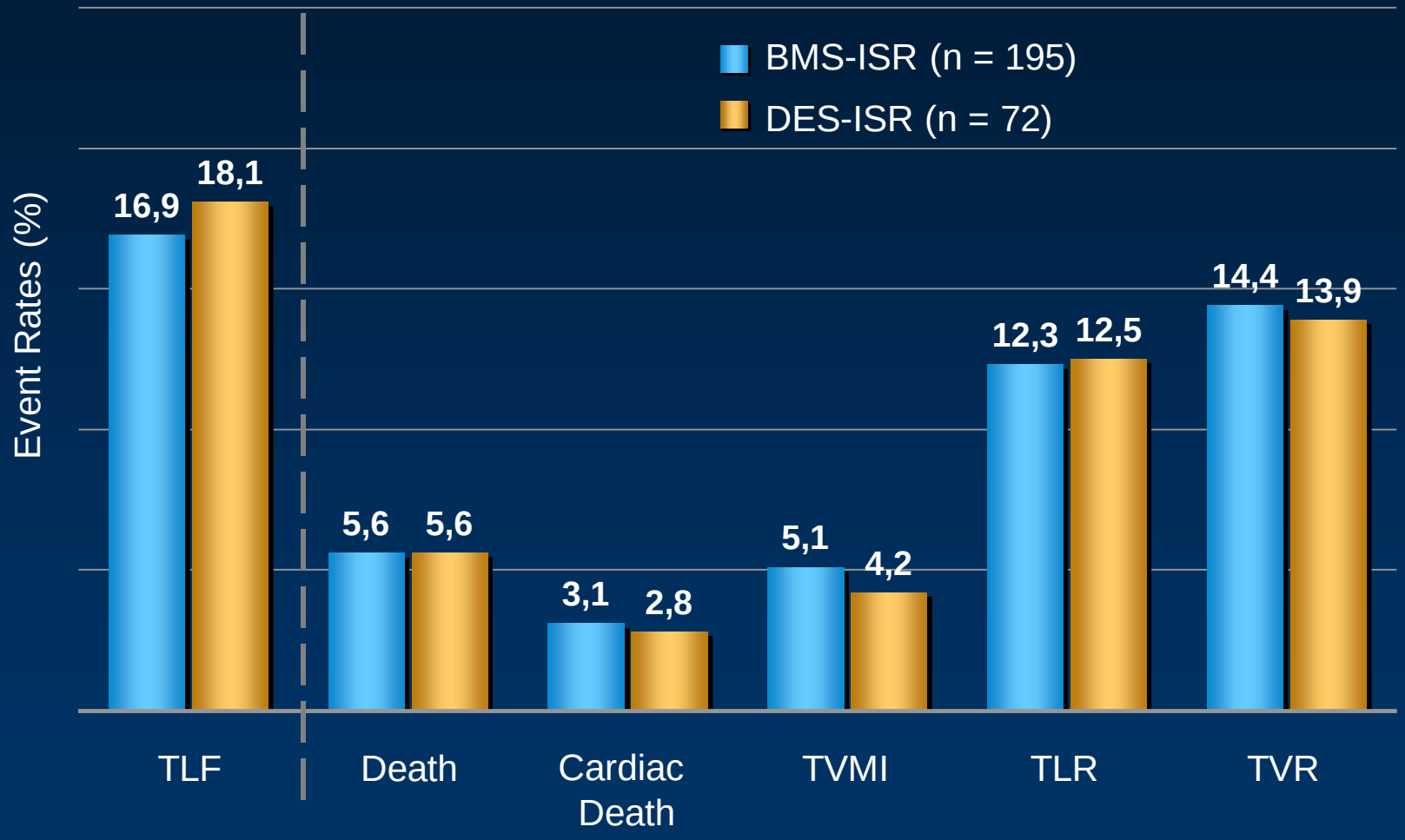
* R-ZES from RESOLUTE All-Comers + International trials

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis.

Richardt G. PCR 2012

RESOLUTE Pooled – ISR of BMS vs. DES

Clinical Outcomes at 2 Years

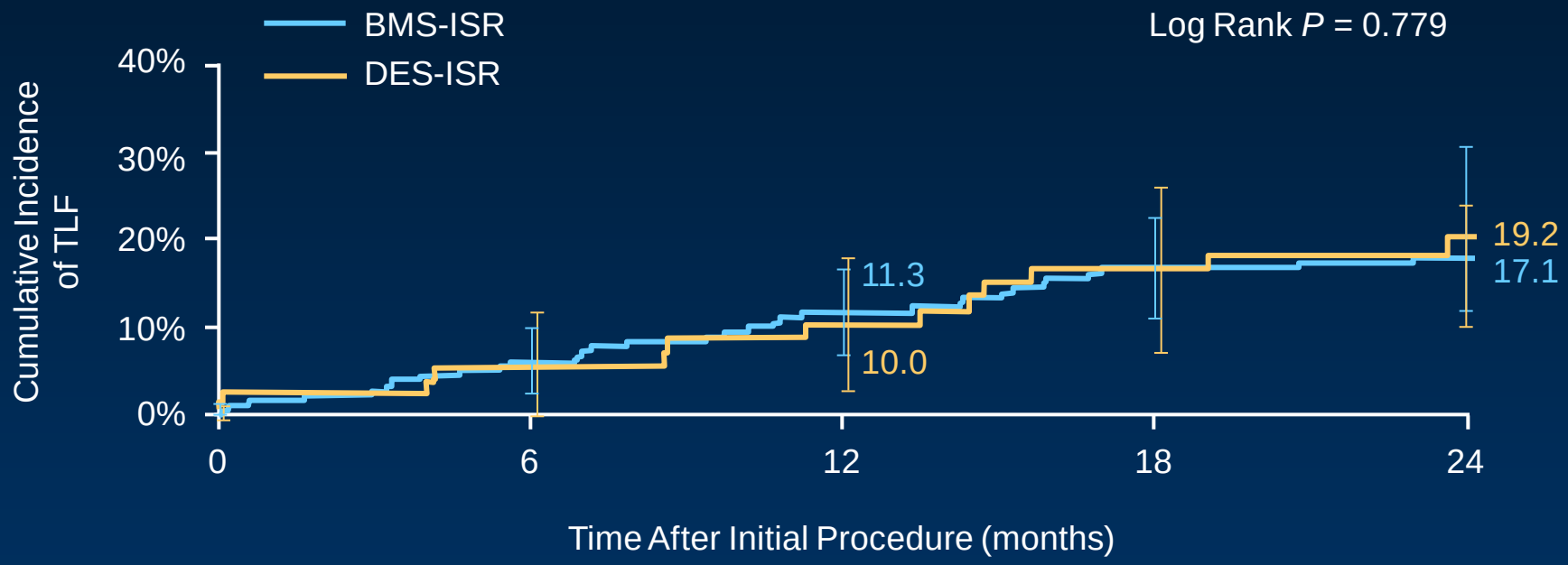


TLF (Target Lesion Failure) is defined as cardiac death, TVMI, or clinically driven TLR. RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis. Note, previously reported data on BMS-ISR: TAXUS V-ISR TVR at 9 months was 10.5% and on DES-ISR: ISAR-DESIRE II TLR at 1 year was SES 16.6%, PES 14.6%.

Richardt G. PCR 2012

RESOLUTE Pooled – ISR of BMS vs. DES

Target Lesion Failure (TLF) to 2 Years



Pts at risk					
BMS-ISR	**196**	**195**	**182**	**172**	**160**
% CI	**0.5**	**6.2**	**11.3**	**16.0**	**17.1**
DES-ISR	**70**	**70**	**66**	**62**	**57**
% CI	**0.0**	**5.7**	**10.0**	**15.9**	**19.2**

TLF (Target Lesion Failure) is defined as cardiac death, TVMI, or clinically driven TLR. RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis. Note, previously reported data on BMS-ISR: TAXUS V-ISR TVR at 9 months was 10.5% and on DES-ISR: ISAR-DESIRE II TLR at 1 year was SES 16.6%, PES 14.6%.

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RESOLUTE Pooled – ISR of BMS vs. DES

Data in Perspective at 12 Months

Trial	*Type of ISR*	*N*	*Device*	*TLR*	*TVR*
RESOLUTE Pooled	BMS-ISR	195	R-ZES	8.0%	9.0%
ISAR DESIRE[1]	BMS-ISR	100 100	SES PES		8% 19%
PEPCAD II[2]	BMS-ISR	66 65	DEB PES	6.3% 15.4%	
TAXUS V-ISR[3]	BMS-ISR	195	PES		10.5% (9M)
Steinberg et al.[4]	BMS-ISR	119	DES		10.3%
RESOLUTE Pooled	DES-ISR	73	R-ZES	5.5%	6.8%
ISAR DESIRE II[5]	DES-ISR	225 225	SES PES	16.6% 14.6%	
PEPCAD-DES[6]	DES-ISR	72	DEB	15.3% (6M)	
Steinberg et al.[4]	DES-ISR	119	DES		22.2%

[1] Kastrati A, et al. *JAMA*. 2005;293:165-71.
[2] Unverdorben M, et al. *Circulation*. 2009;119:2986-94.
[3] Koizumi T, et al. *Cardiovasc Revasc Med*. 2010;11:140-8.
[4] Steinberg D, et al. *Am J Cardiol* .2009;103:491-5.
[5] Mehilli J, et al. *J Am Coll Cardiol* . 2010;55:2710-6.
[6] Rittger H, et al. *J Am Coll Cardiol* .2012;59: 1377-82.

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for ISR subset analysis.

Richardt G. PCR 2012

RESOLUTE Pooled – Bifurcation Subset

Baseline Characteristics

%	*N = 702 patients*
Age (yr)	63.9 ± 11.1
Male	79.3
Diabetes mellitus	27.1
IDDM	7.7
Hypertension	68.9
Hyperlipidemia	64.4
Current smoker	23.9
Family history	33.4
Prior MI	27.7
Prior PCI	28.9
Prior CABG	6.6
Cardiac status:	
Stable angina	37.0
Unstable angina	23.9
Myocardial infarction (STEMI + NSTEMI)	31.2

RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for bifurcation subset analysis.

Kornowski R. PCR 2012

RESOLUTE Pooled – Bifurcation Subset

Procedure Characteristics I

%	*N = 702 patients, 1087 lesions*
Number of lesions treated per patient	1.55 ± 0.78
Number of stents per patient	2.0 ± 1.2
Total stent length per patient (mm)	37.4 ± 24.8
Lesion length* (mm)	17.1 ± 11.3
Reference Vessel Diameter* (mm)	2.86 ± 0.53
Minimum Lumen Diameter* (mm)	0.62 ± 0.50
Side Branch RVD* (R-INT only, mm)	2.2 ± 0.6 (n = 587)

*For RESOLUTE International (R-INT) angiographic measurements are site reported.
RESOLUTE All Comers and RESOLUTE International were not specifically designed or powered for bifurcation subset analysis

Kornowski R. PCR 2012