The Total IN.PACT™ Drug-Coated Balloon Pooled Analyses: Imaging and Propensity-Matched Cohorts

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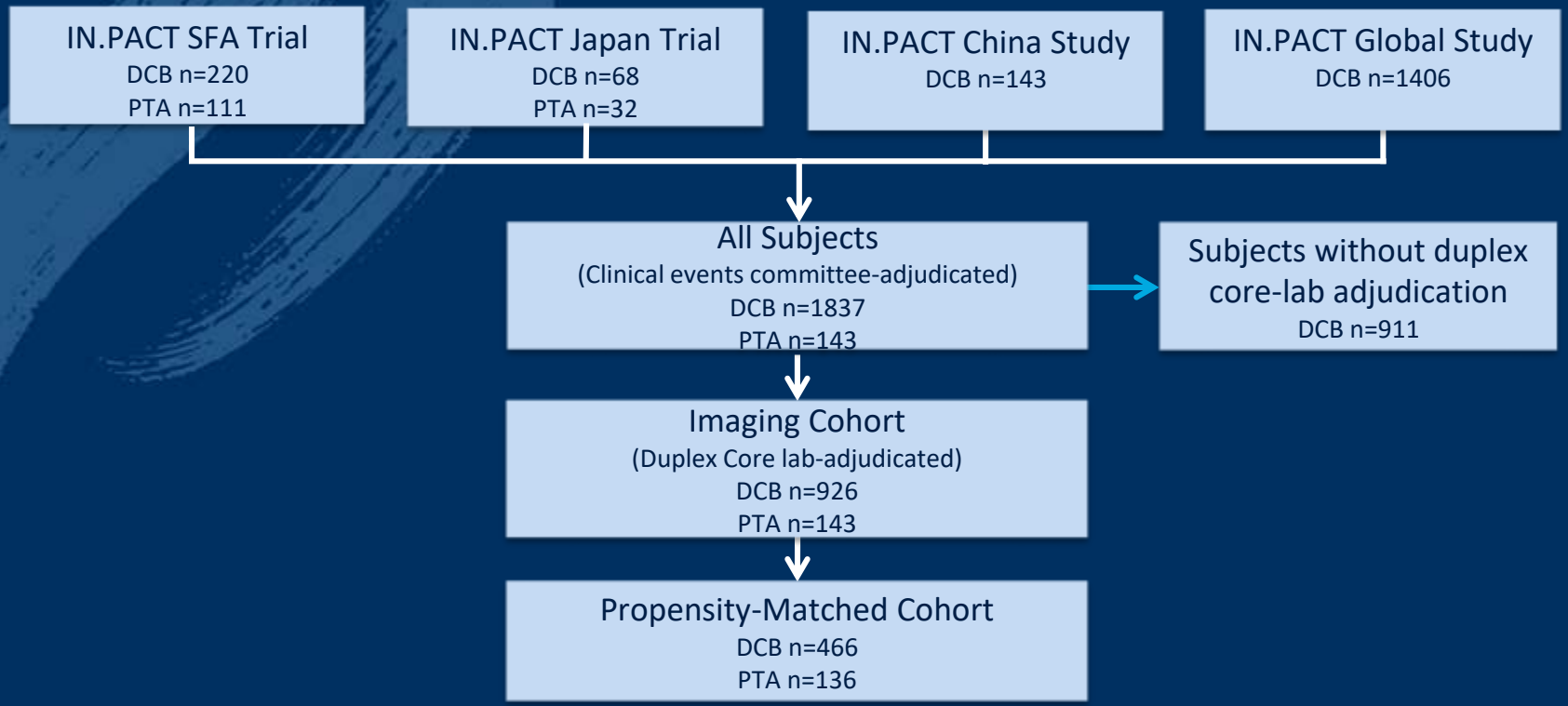
Disclosures
John R. Laird

- Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
Consulting Fees/Honoraria	Boston Scientific, Medtronic, Abbott, Bard/Becton Dicksenson Peripheral Intervention, Philips
Scientific Advisory board/stock options	Reflow Medical, Endoluminal Sciences, Syntervention, PQ Bypass, Eximo Medical, Shockwave Medical, NexGen

Board Member VIVA Physicians

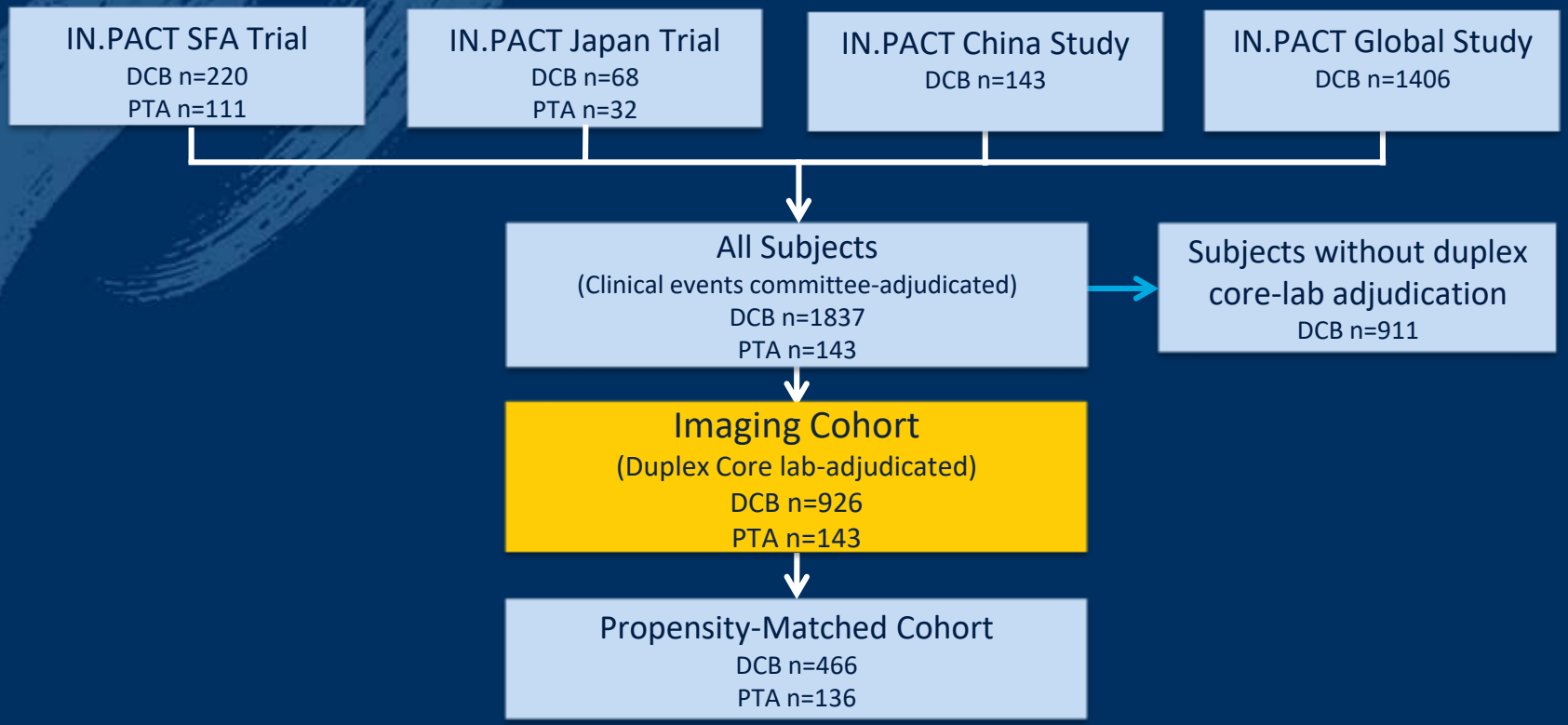
Total IN.PACT Pooled Analysis Initiative



Total IN.PACT Pooled Analysis Initiative

- Diverse population across 147 sites and 28 countries
- Gain insights into outcomes across a broad spectrum of patient and lesion types
- Offer an independent data analysis (Baim Institute for Clinical Research formerly known as HCRI)

Total IN.PACT Imaging Analysis



Baseline Clinical Characteristics

Total IN.PACT 12-month Baseline	Imaging Cohort		
	DCB (N=926 Subjects)	PTA (N=143 Subjects)	P-value
Age	68.6 ± 9.7	69.4 ± 9.0	0.338
Male	68.5%	70.6%	0.629
Hypertension	83.9%	88.1%	0.216
Hyperlipidemia	69.5%	81.1%	0.004
Diabetes	40.4%	50.3%	0.029
Active Smoker	37.2%	35.0%	0.642
Previous Peripheral Revascularization	50.8%	52.4%	0.720
Below-the-knee Disease of Target Leg	47.4%	49.0%	0.787
Rutherford Category			0.039
2 3 4 5	35.2% 55.0% 8.0% 1.8%	42.7% 51.7% 4.9% 0.7%	
ABI/TBI*(mmHg)	0.68 ± 0.22	0.74 ± 0.18	<0.001

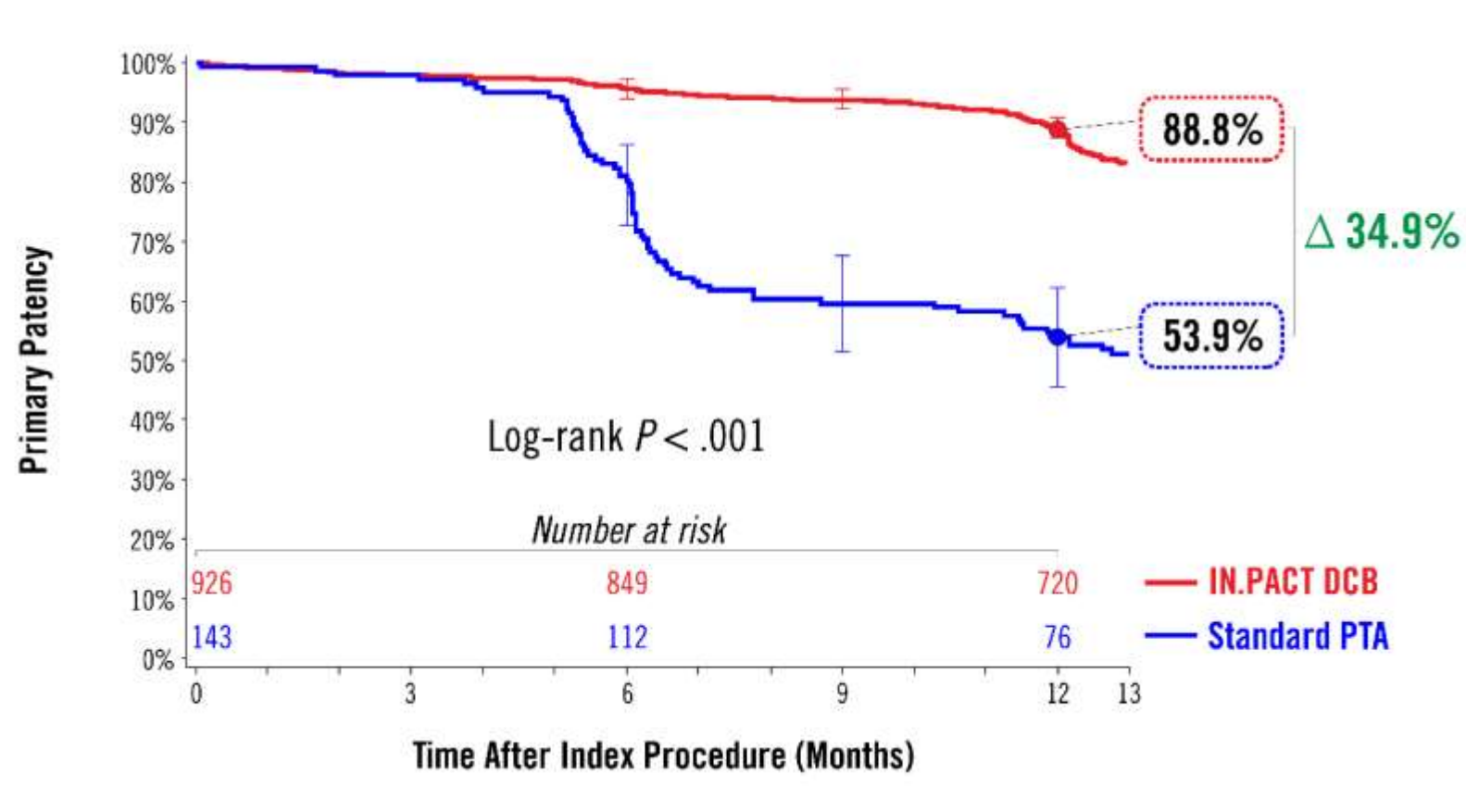
*TBI allowed / used in case of incompressible vessels in IN.PACT SFA II phase

Baseline Lesion/Procedural Characteristics

Total IN.PACT	Imaging Cohort		
	DCB (N=1054 Lesions)	PTA (N=143 Lesions)	P-value
Lesion Characteristics			
Lesion Type			
De Novo	75.5%	95.8%	<0.001
Restenotic (non-stented)	6.2%	4.2%	0.451
In-stent restenosis	18.3%	0%	-
Lesion Length (cm)	15.56 ± 10.35	8.83 ± 5.31	<0.001
Calcification	61.6%	56.6%	0.274
Occluded Lesion (100% stenosis)	45.4%	18.6%	<0.001
Procedural Characteristics			
Provisional Stent	19.4%	10.5%	0.008

Total IN.PACT Imaging Cohort

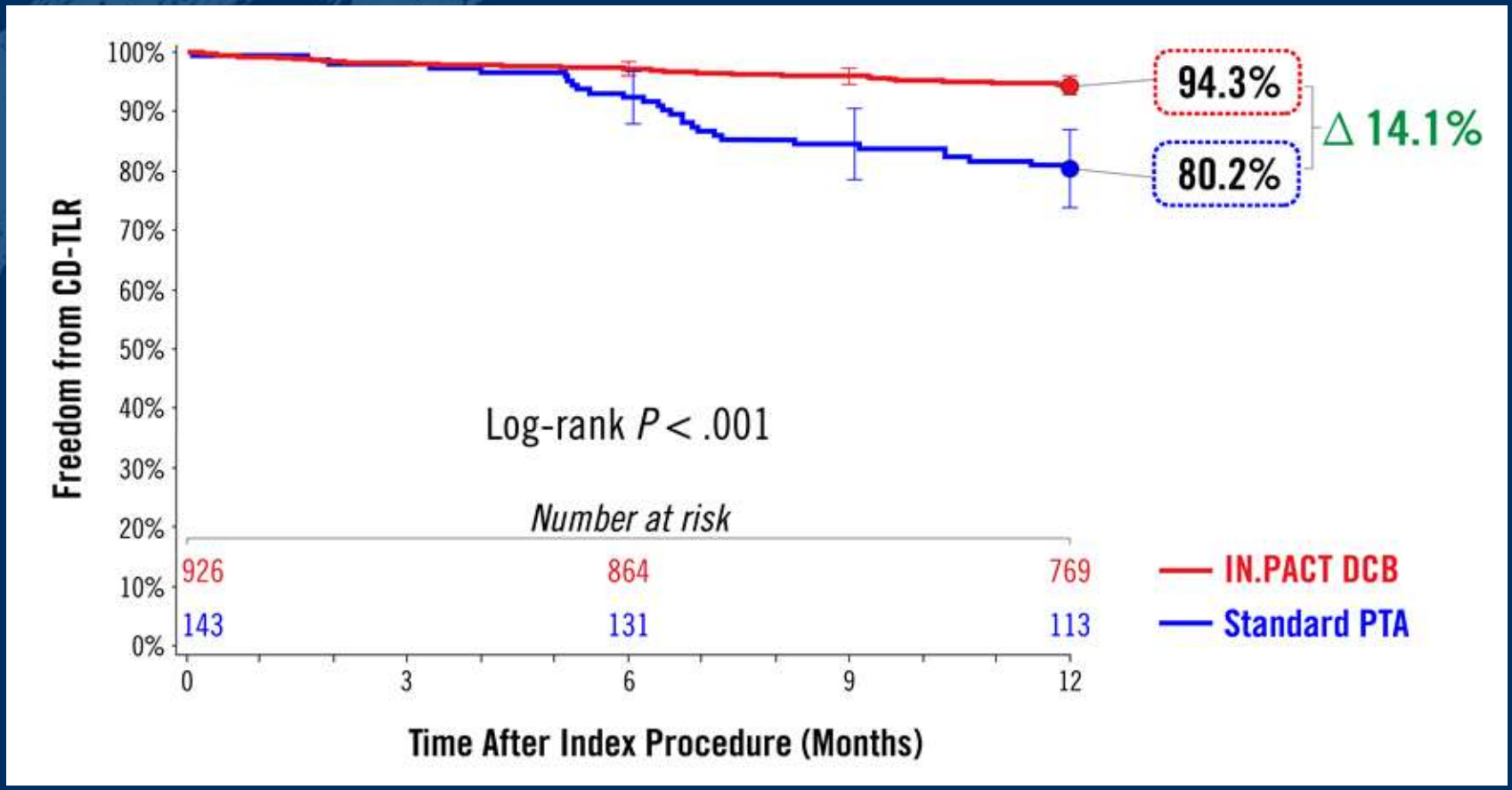
Primary Patency through 12 Months*



*Duplex Core lab- and CEC-adjudicated

Total IN.PACT Imaging Cohort

Secondary Outcome: Freedom from CD-TLR through 12 Months*



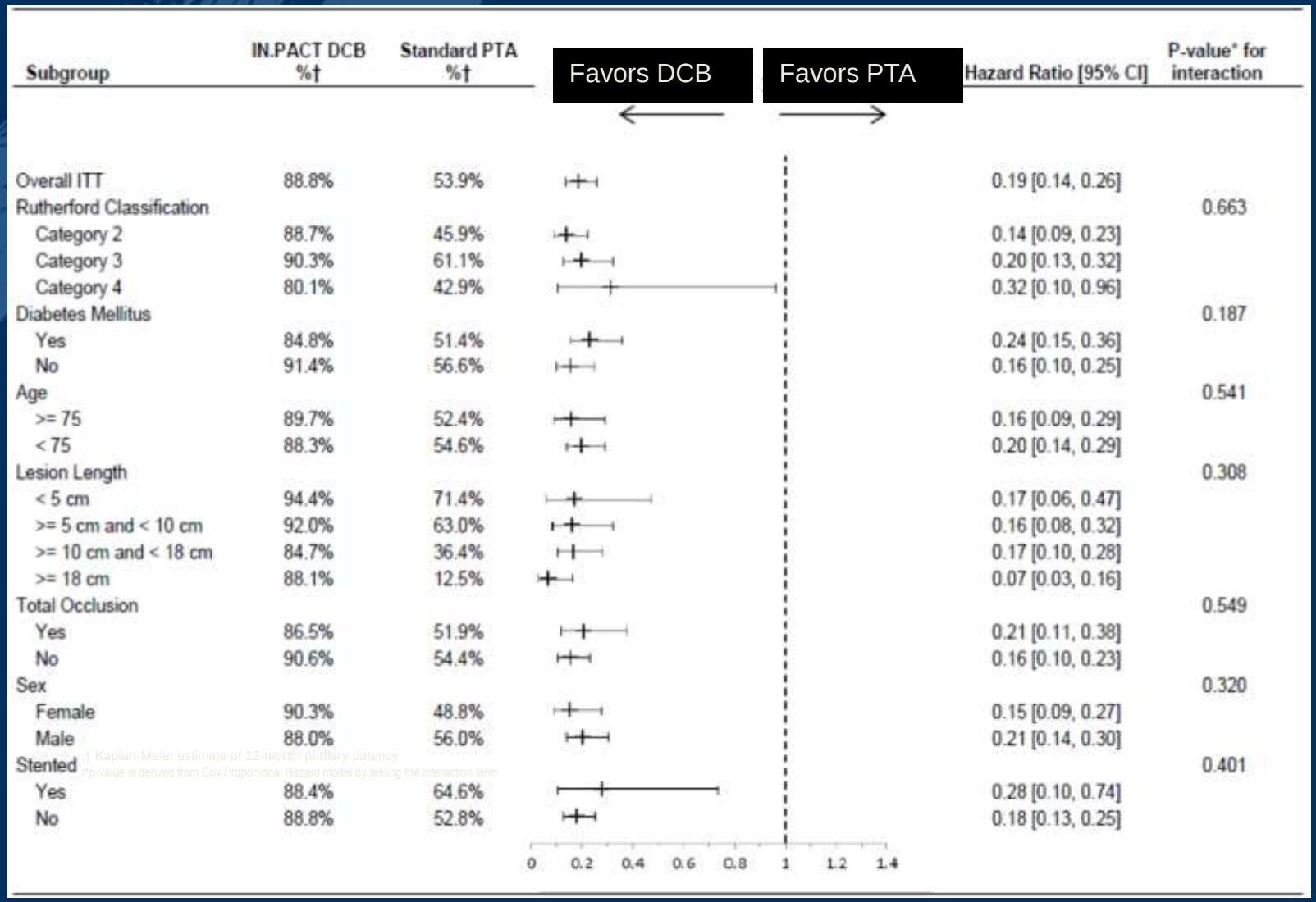
*Independent clinical events committee-adjudicated

Total IN.PACT Safety Outcomes

Total IN.PACT 12-month	Imaging Cohort		
Safety	**DCB (N=926 Subjects)**	**PTA (N=143 Subjects)**	**P-value**
Clinically-driven TLR[1]	5.8%	19.9%	<0.001
Any TLR	6.2%	19.9%	<0.001
Primary Safety Endpoint[2]	94.1%	78.0%	<0.001
Device- or procedure- related death (30 days)	0.1%	0%	1.000
Major Adverse Events[3]	9.0%	22.7%	<0.001
All-cause death	2.6%	0.0%	0.061
Major Target Limb Amputation	0%	0%	-
Clinically-driven TVR[4]	6.4%	22.0%	<0.001
Thrombosis	2.4%	2.8%	0.767

1. Clinically-driven TLR defined as any re-intervention within the target lesion(s) due to symptoms or drop of ABI ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI
2. Primary Safety Endpoint is a composite of freedom from device- and procedure-related mortality through 30 days, freedom from major target limb amputation and TVR within 12 months post-index procedure
3. Major adverse events is defined as all-cause mortality, clinically-driven TVR, major target limb amputation, thrombosis at the target lesion site
4. Clinically-driven TVR is defined as any re-intervention within the target vessel due to symptoms or drop of ABI of ≥ 20% or > 0.15 when compared to post-index procedure baseline ABI

Total IN.PACT Imaging: Subgroup Analysis



Subgroup	IN.PACT DCB %†	Standard PTA %†	Hazard Ratio [95% CI]	P-value* for interaction
Overall ITT	88.8%	53.9%	0.19 [0.14, 0.26]	
Rutherford Classification				0.663
Category 2	88.7%	45.9%	0.14 [0.09, 0.23]	
Category 3	90.3%	61.1%	0.20 [0.13, 0.32]	
Category 4	80.1%	42.9%	0.32 [0.10, 0.96]	
Diabetes Mellitus				0.187
Yes	84.8%	51.4%	0.24 [0.15, 0.36]	
No	91.4%	56.6%	0.16 [0.10, 0.25]	
Age				0.541
>= 75	89.7%	52.4%	0.16 [0.09, 0.29]	
< 75	88.3%	54.6%	0.20 [0.14, 0.29]	
Lesion Length				0.308
< 5 cm	94.4%	71.4%	0.17 [0.06, 0.47]	
>= 5 cm and < 10 cm	92.0%	63.0%	0.16 [0.08, 0.32]	
>= 10 cm and < 18 cm	84.7%	36.4%	0.17 [0.10, 0.28]	
>= 18 cm	88.1%	12.5%	0.07 [0.03, 0.16]	
Total Occlusion				0.549
Yes	86.5%	51.9%	0.21 [0.11, 0.38]	
No	90.6%	54.4%	0.16 [0.10, 0.23]	
Sex				0.320
Female	90.3%	48.8%	0.15 [0.09, 0.27]	
Male	88.0%	56.0%	0.21 [0.14, 0.30]	
Stented				0.401
Yes	88.4%	64.6%	0.28 [0.10, 0.74]	
No	88.8%	52.8%	0.18 [0.13, 0.25]	

† Kaplan-Meier estimate of 12-month primary patency
*p-value is derived from Cox Proportional Hazard model by testing the interaction term

Predictors of Loss of Patency

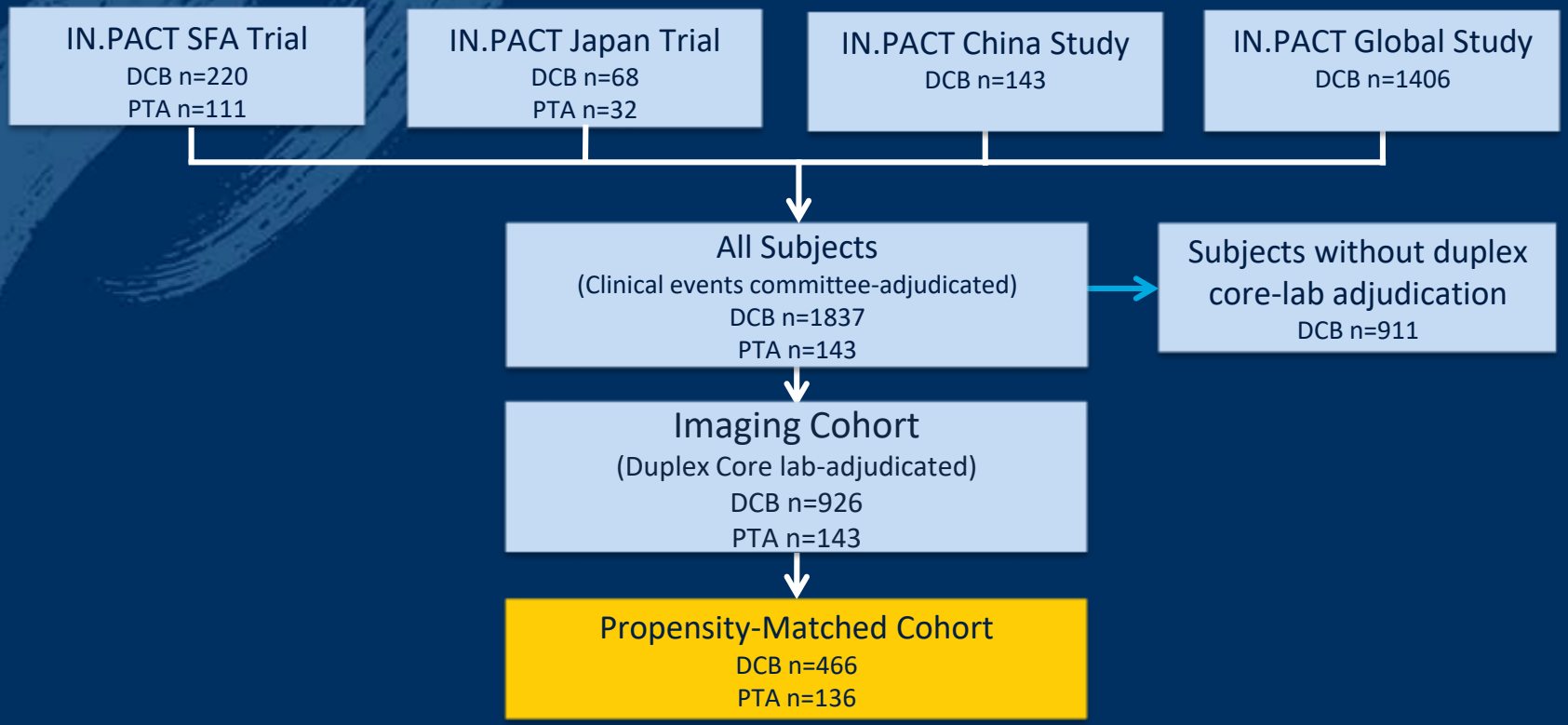
Overall Imaging Analysis

- DCB
  - Diabetes mellitus
  - Rutherford category 4 versus 2-3
  - Previous revascularization of popliteal artery
  - Pre-procedure % diameter stenosis
  - Age
- PTA
  - Lesion length* ($p<0.001$)
  - Previous revascularization on iliac artery

While lesion length was a strong predictor of patency failure for PTA, lesion length did not emerge as a predictor of loss of patency for IN.PACT™ Admiral™ DCB.

*P-value < 0.001

Total IN.PACT Propensity-Matched Analysis



Baseline Clinical Characteristics

Total IN.PACT 12-month Baseline	Propensity-Matched		
	DCB (N=466 Subjects)	PTA (N=136 Subjects)	P-value
Age	68.6 ± 4.9	69.3 ± 9.2	0.358
Male	70.3%	70.6%	0.882
Hypertension	86.2%	88.2%	0.428
Hyperlipidemia	75.3%	80.9%	0.095
Diabetes	46.2%	48.5%	0.531
Active Smoker	35.5%	36.0%	0.874
Previous Peripheral Revascularization	43.8%	51.5%	0.047
Below-the-knee Disease of Target Leg	45.8%	47.8%	0.675
Rutherford Category			0.508
2	43.0%	44.1%	
3	50.9%	50.7%	
4	6.1%	5.1%	
5	0.0%	0.0%	
ABI/TBI*(mmHg)	0.73 ± 0.12	0.75 ± 0.17	0.290

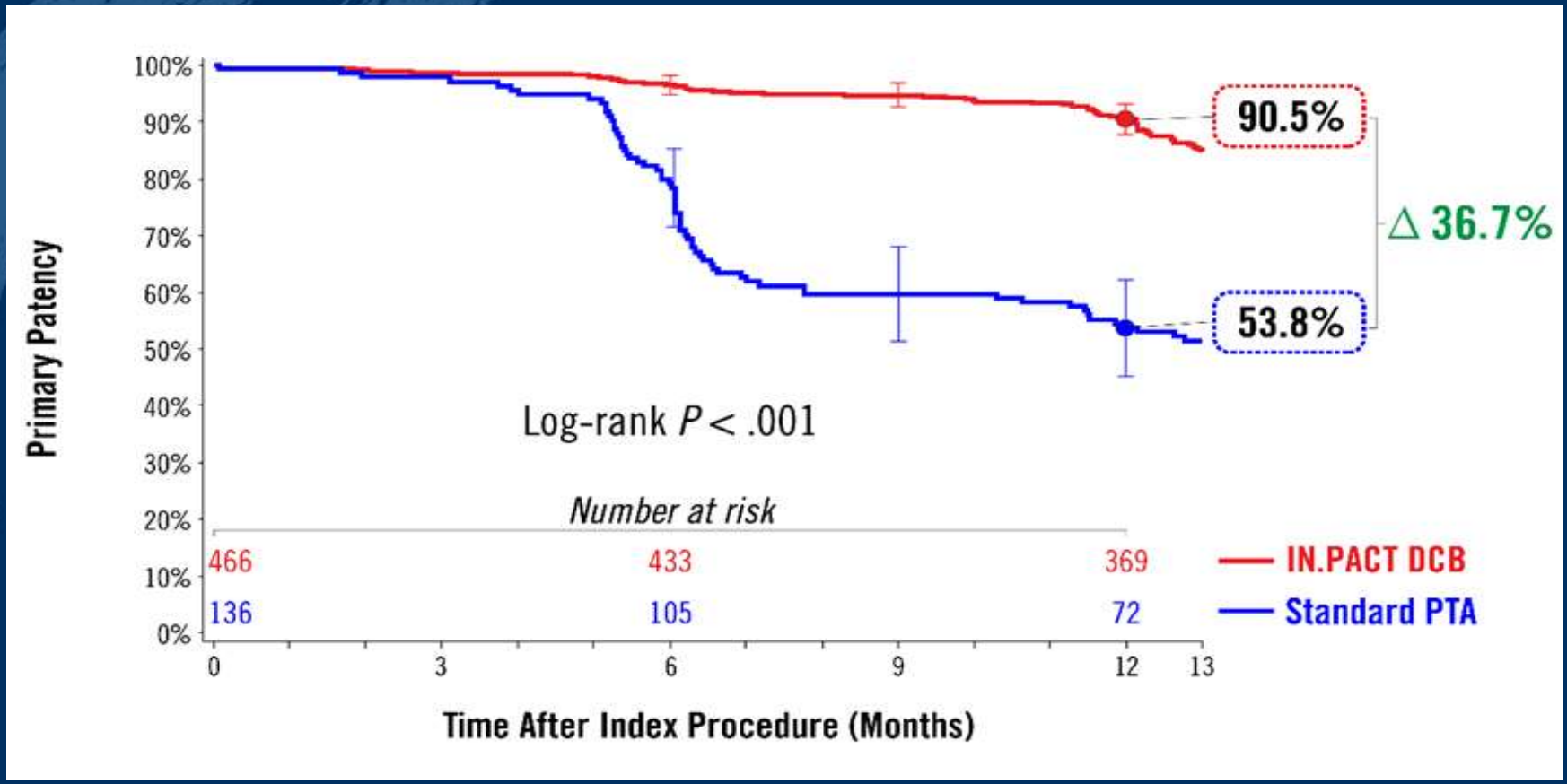
*TBI allowed / used in case of incompressible vessels in IN.PACT SFA II phase

Baseline Lesion/Procedural Characteristics

Total IN.PACT	Propensity-Matched		
	DCB (N=466 Lesions)	PTA (N=136 Lesions)	P-value
Lesion Characteristics			
Lesion Type			
De Novo	95.2%	95.6%	0.804
Restenotic (non-stented)	4.8%	4.4%	0.904
ISR	0%	0%	-
Lesion Length (cm)	10.46 ± 3.54	8.94 ± 5.32	0.002
Calcification	57.9%	56.5%	0.595
Occluded Lesion (100% stenosis)	30.9%	19.6%	0.001
Procedural Characteristics			
Provisional Stent	9.9%	11.0%	0.971

Total IN.PACT Propensity-Matched Cohort

Primary Outcome through 12 Months*



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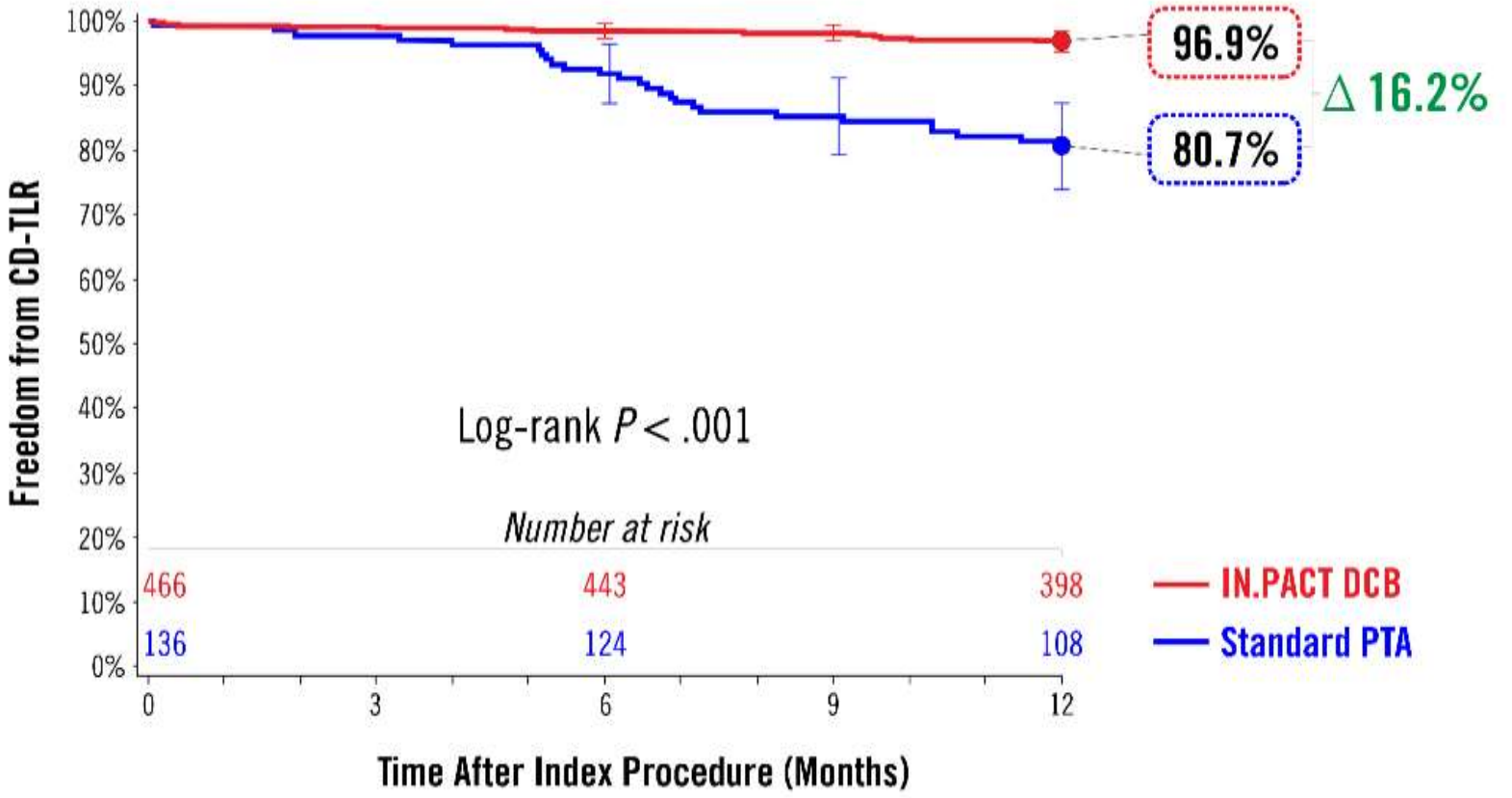
Total IN.PACT Propensity-Matched Cohort

Secondary Outcome: Freedom from CD-TLR through 12 months*



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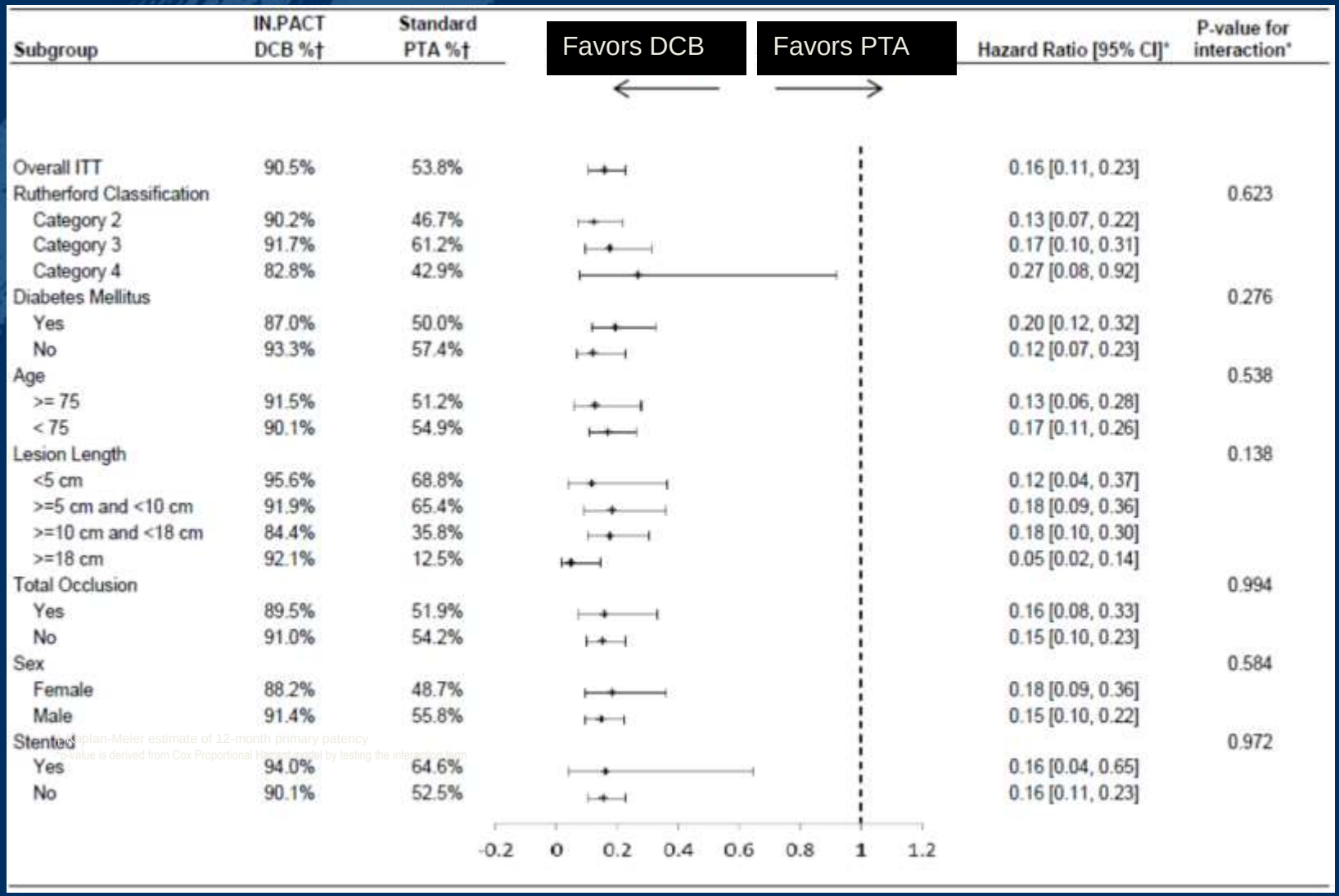
Total IN.PACT Propensity-Matched: Subgroup Analysis



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Overall ITT	90.5%	53.8%	0.16 [0.11, 0.23]	
Rutherford Classification				0.623
Category 2	90.2%	46.7%	0.13 [0.07, 0.22]	
Category 3	91.7%	61.2%	0.17 [0.10, 0.31]	
Category 4	82.8%	42.9%	0.27 [0.08, 0.92]	
Diabetes Mellitus				0.276
Yes	87.0%	50.0%	0.20 [0.12, 0.32]	
No	93.3%	57.4%	0.12 [0.07, 0.23]	
Age				0.538
>= 75	91.5%	51.2%	0.13 [0.06, 0.28]	
< 75	90.1%	54.9%	0.17 [0.11, 0.26]	
Lesion Length				0.138
<5 cm	95.6%	68.8%	0.12 [0.04, 0.37]	
>=5 cm and <10 cm	91.9%	65.4%	0.18 [0.09, 0.36]	
>=10 cm and <18 cm	84.4%	35.8%	0.18 [0.10, 0.30]	
>=18 cm	92.1%	12.5%	0.05 [0.02, 0.14]	
Total Occlusion				0.994
Yes	89.5%	51.9%	0.16 [0.08, 0.33]	
No	91.0%	54.2%	0.15 [0.10, 0.23]	
Sex				0.584
Female	88.2%	48.7%	0.18 [0.09, 0.36]	
Male	91.4%	55.8%	0.15 [0.10, 0.22]	
Stented				0.972
Yes	94.0%	64.6%	0.16 [0.04, 0.65]	
No	90.1%	52.5%	0.16 [0.11, 0.23]	

† Kaplan-Meier estimate of 12-month primary patency
* P-value is derived from Cox Proportional Hazard model by testing the interaction term

Statistical Predictors of Loss of Patency Propensity-Matched Cohort

Propensity-Matched Analysis

- **DCB**
  - **Diabetes mellitus**
  - **Previous revascularization on common femoral artery**
  - **Restenotic vs de novo lesion**
  - **Pre-procedure % diameter stenosis**
- **PTA**
  - **Lesion length*** ($p<0.001$)
  - **Previous revascularization on iliac artery**

Conclusions

- The largest, multi-ethnic, pooled, independently-adjudicated drug-coated balloon (DCB) series to date, The IN.PACT™ Admiral™ DCB demonstrated superior patency and freedom from CD-TLR over PTA through 12 months in both the imaging and propensity-matched analyses.

- The IN.PACT™ Admiral™ DCB continues to demonstrate a superior safety profile compared to PTA.

- Furthermore, in multiple subgroup analyses, the IN.PACT™ Admiral™ DCB consistently remained superior to PTA for primary patency and freedom from CD-TLR.

Thank You

The Total IN.PACT™ Drug-Coated Balloon Pooled Analyses: Imaging and Propensity-Matched Cohorts

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