

PCIにおける近年の進歩 心臓から全身へ

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中村正人

虚血性心疾患の診断学、治療学

- 両者ともに低侵襲が大きなテーマ
- **診断**
 - 造影検査がgold standard
 - 冠動脈CTの進歩
- **治療(血行再建)**
 - 冠動脈バイパス術がgold standard
 - カテーテル治療の進歩
- アテローム血栓症の概念と治療

今昔の冠動脈造影の比較



診断から治療へ大きく進展

1960年代

冠動脈造影が施行される

1970年代

CABGが導入、左室造影が同時に施行される

1980年代

冠動脈形成術 (PCI)
再灌流療法が確立

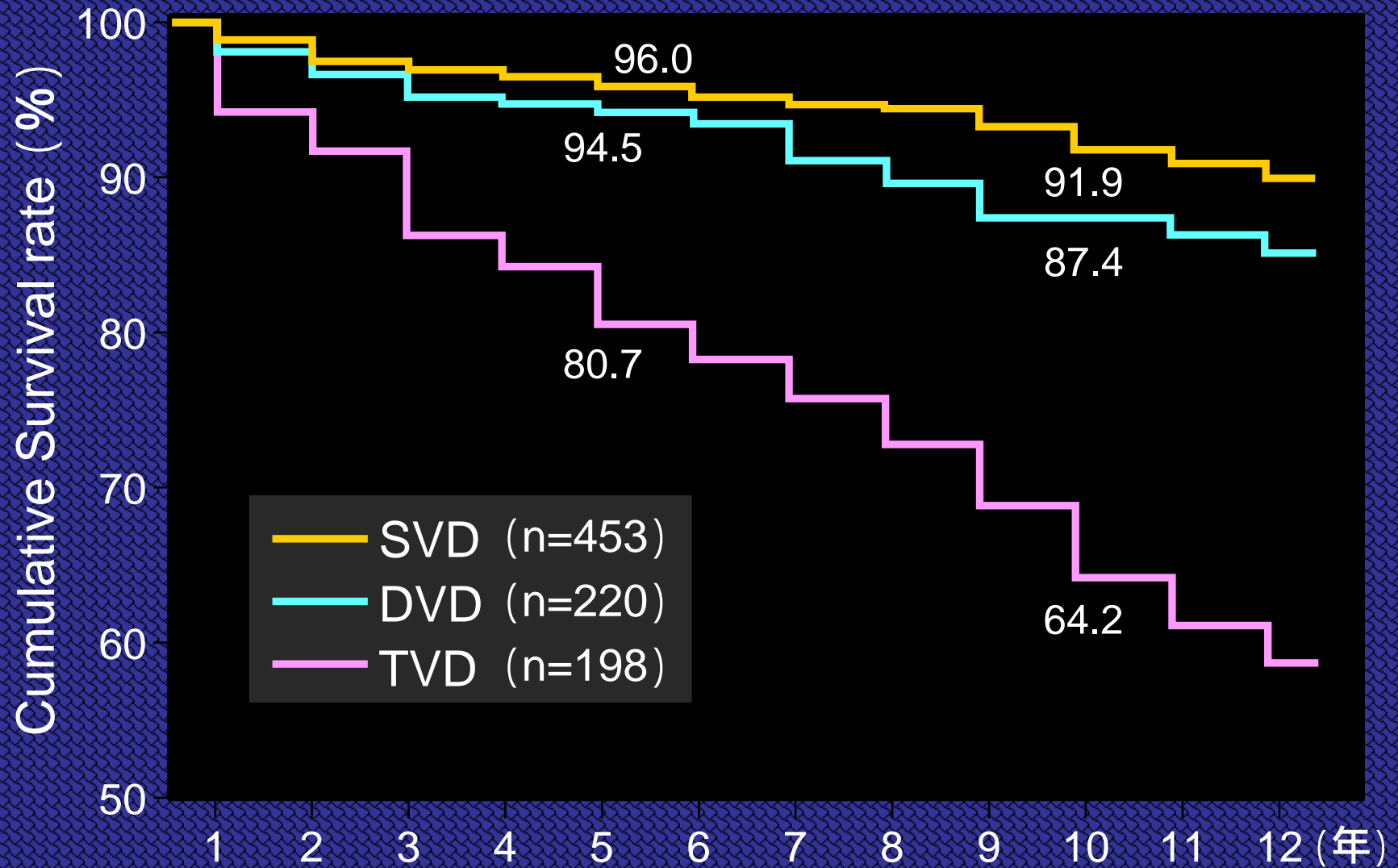
1990年代

New deviceが登場; 定量的評価が要求される

2000年代

DES 時代

罹患枝数別の累積生存曲線



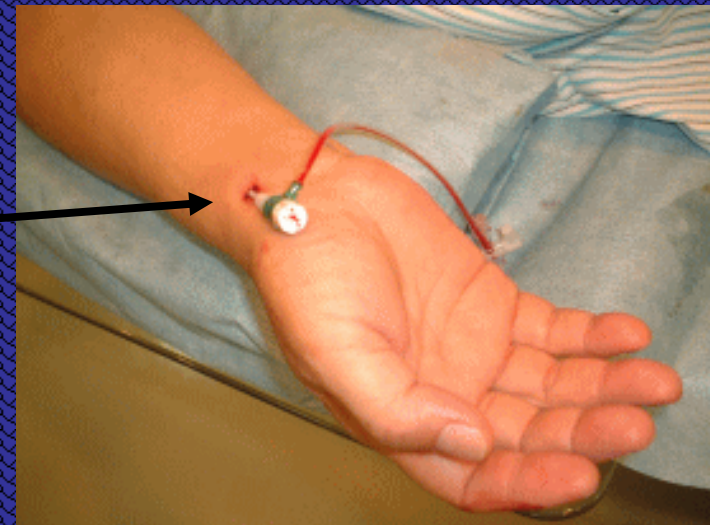
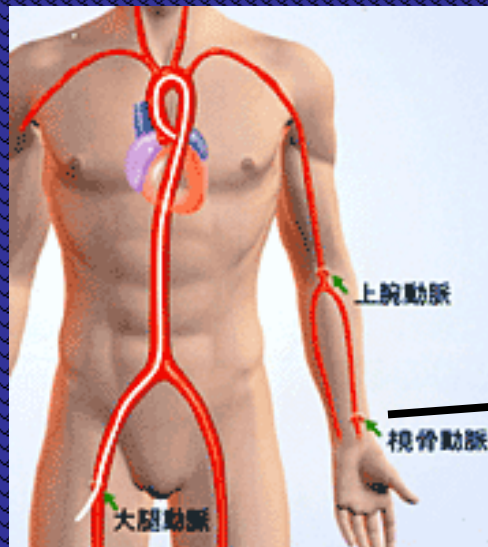
S Nishiyama et al: Jpn Heart J 1993 34 539-550

冠動脈造影

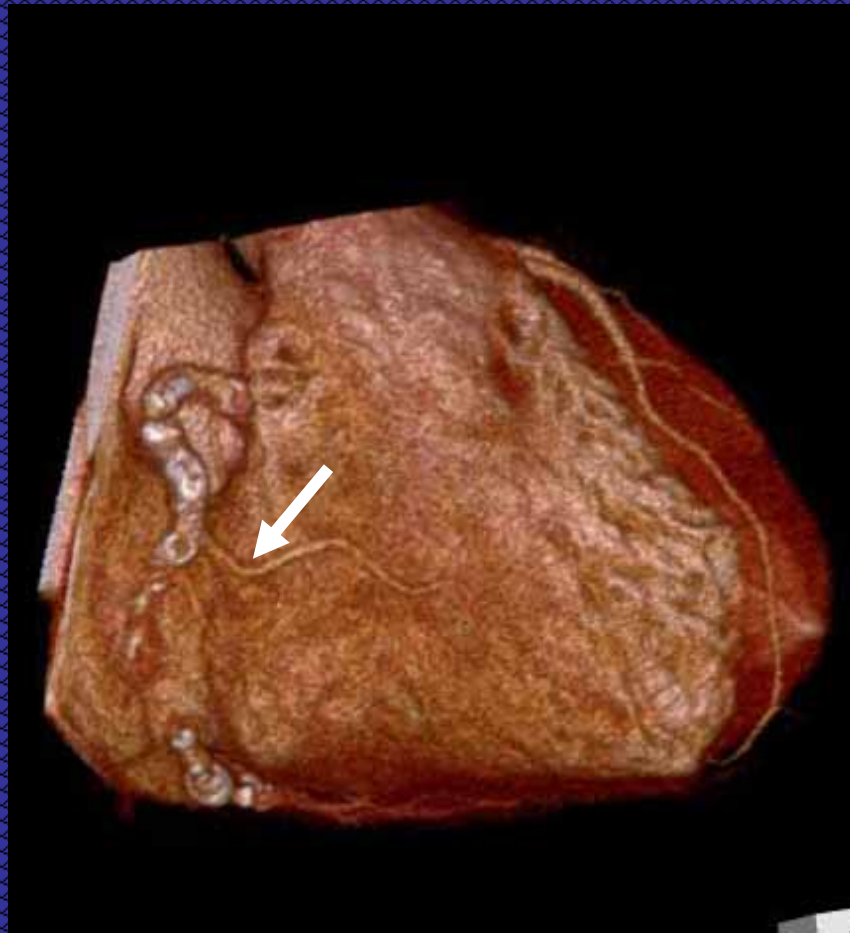
虚血性心疾患診断におけるgold standard

- 低侵襲への歩み
 - カテーテルの細径化
 - 大腿動脈から橈骨動脈

- 低侵襲
- 止血が容易
- 安静時間が短い
- 尿道バルーンが不要
- 血腫の合併が少ない



造影検査とCTの比較



1977 **Balloon Angioplasty**

1980

Directional Atherectomy

Laser Angioplasty

Rotational Atherectomy

Stents

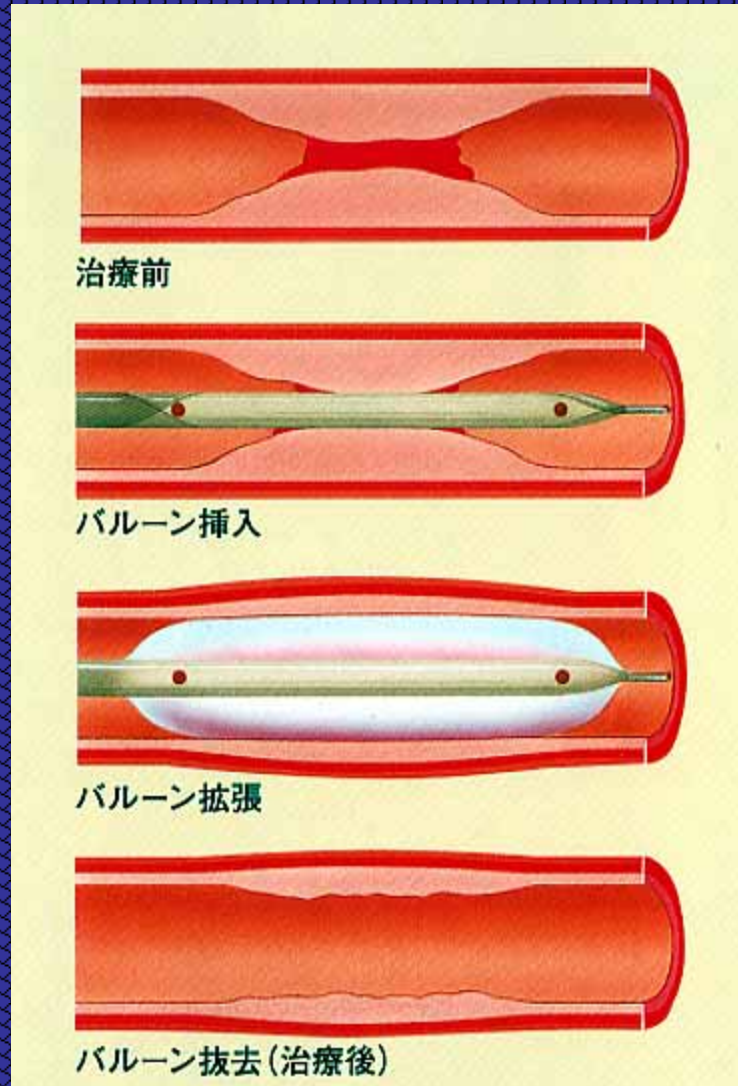
1990

2000

2,000,000 procedures



バルーン拡張術



問題点(限界)

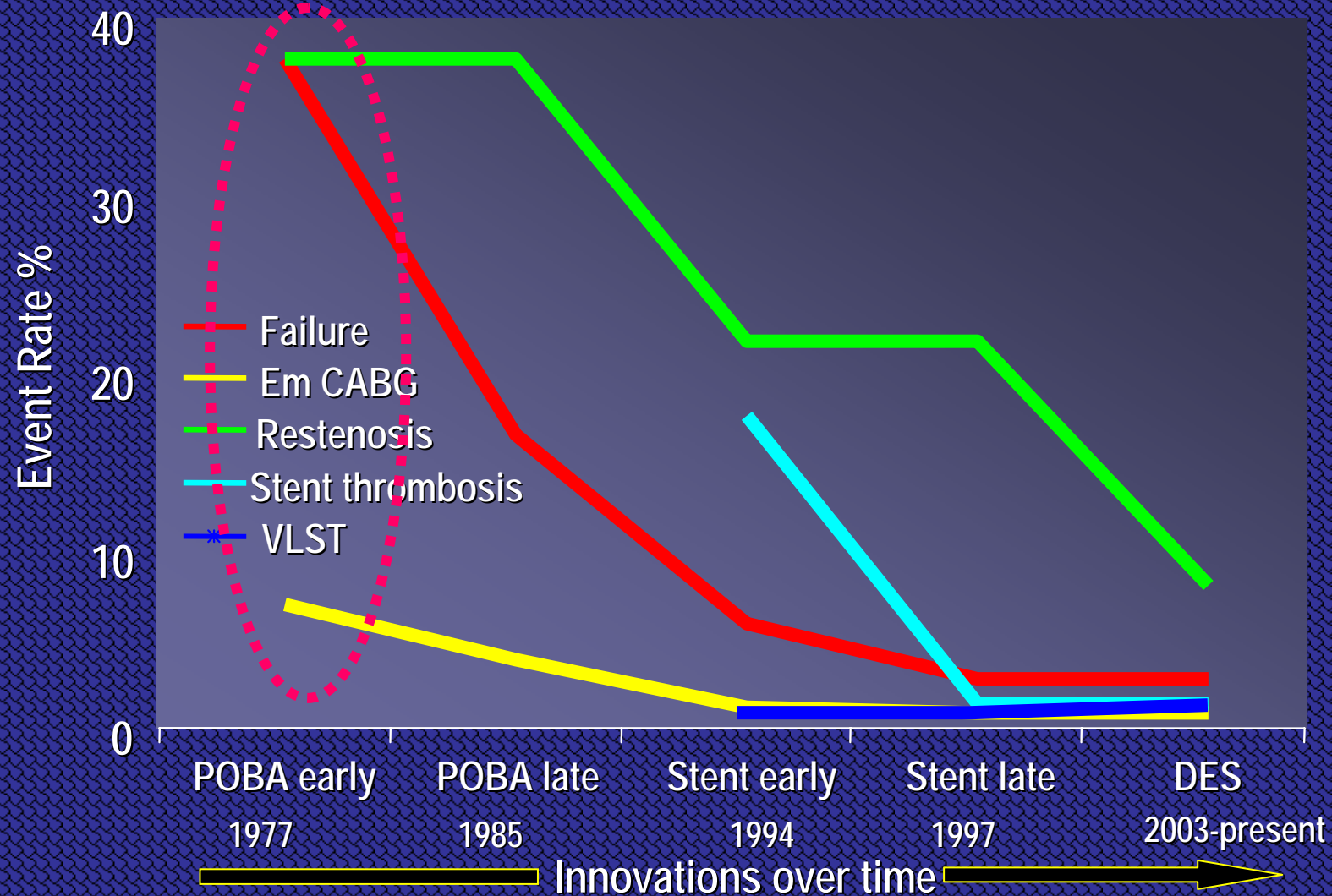
拡張困難な病変の存在
不成功

急性冠閉塞からの確実な離脱
緊急バイパス術

再狭窄

再PCI/バイパス術

Evolution of PCI (Percutaneous Coronary Intervention)



ニューデバイス時代



閉じたところ



広がったところ



アテレクトミー療法



●ロータブレーター

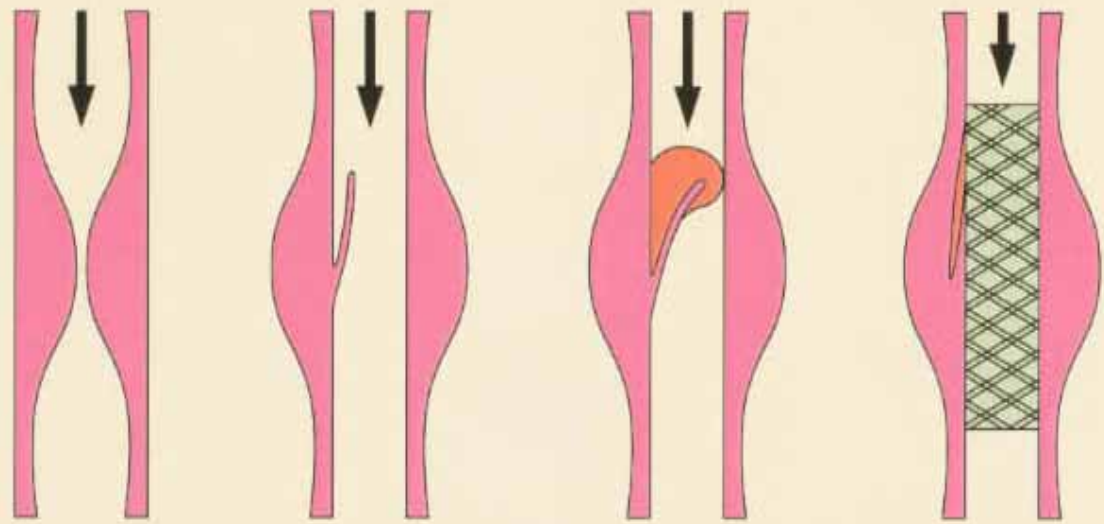
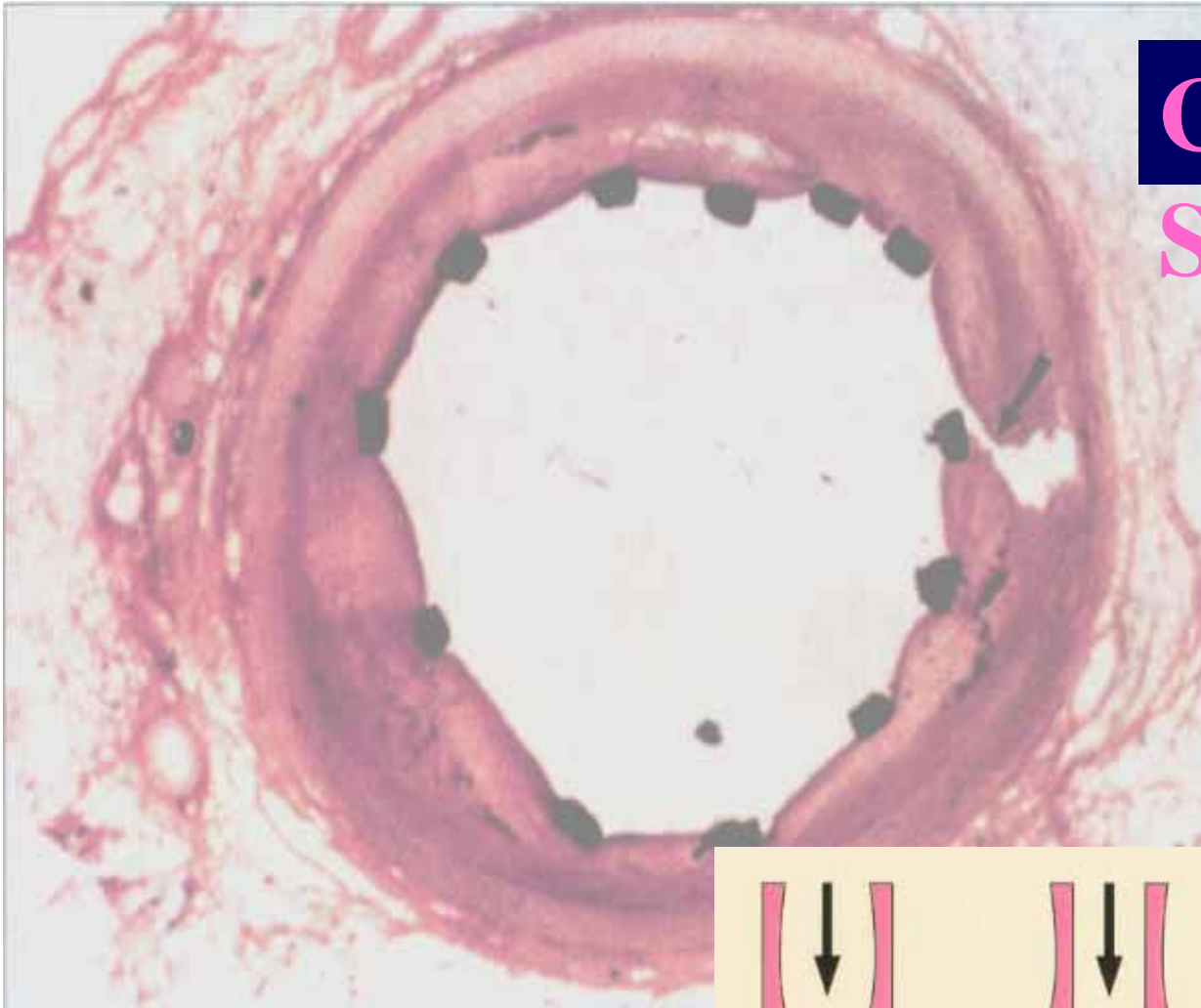
ダイヤモンドが先端についたドリルで狭窄部分を広げます。



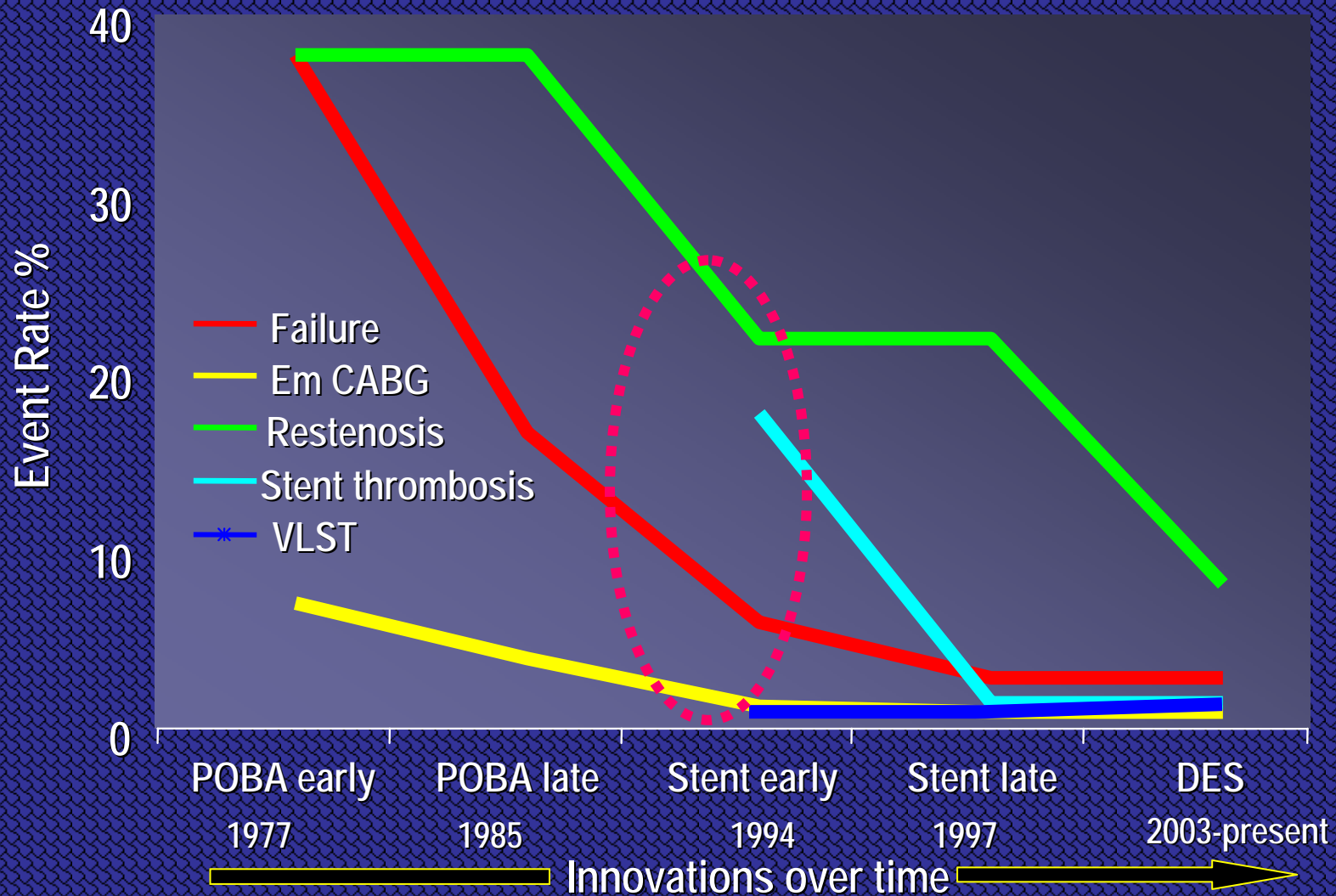
●DCA

血管内の詰まった部分を削り取って、血流を確保します。

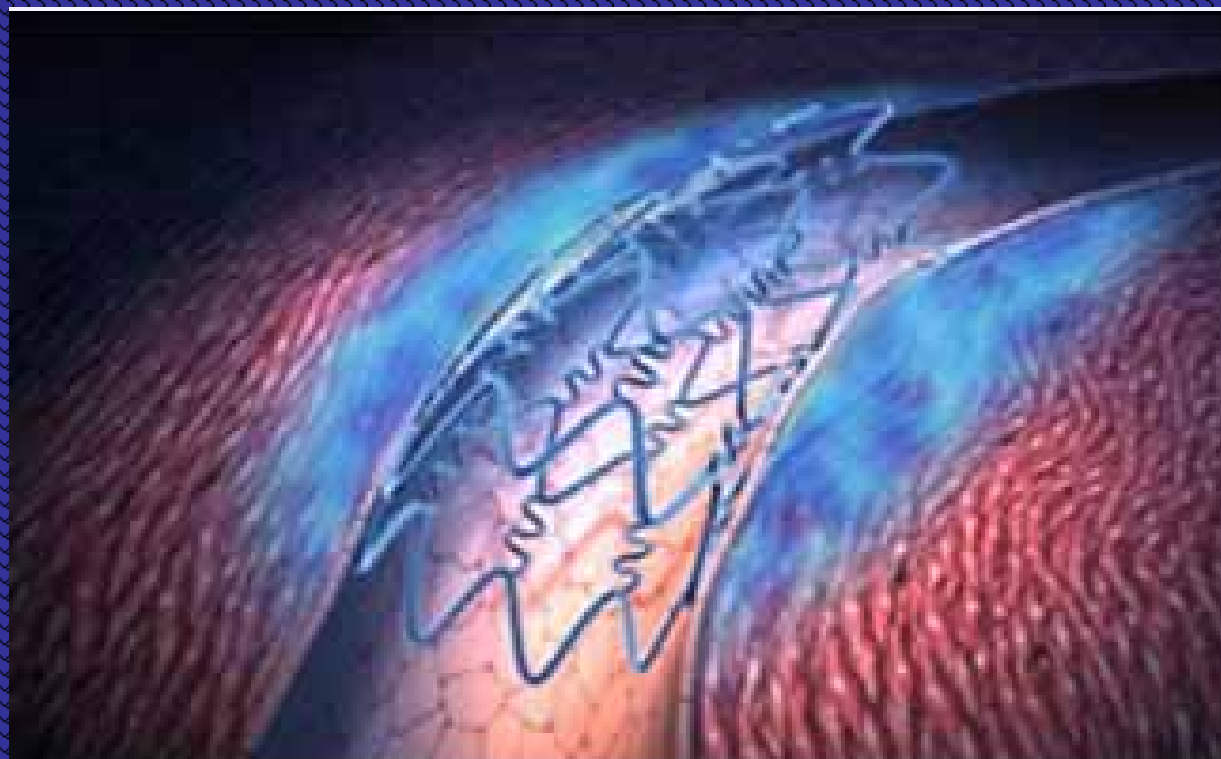
Coronary Stents



Evolution of PCI (Percutaneous Coronary Intervention)



薬剤溶出型ステント



血管内に植え込まれた薬剤溶出性ステント（模式図）
徐々に血管壁内に薬剤が溶出してゆくことにより再狭窄を予防する

DES時代



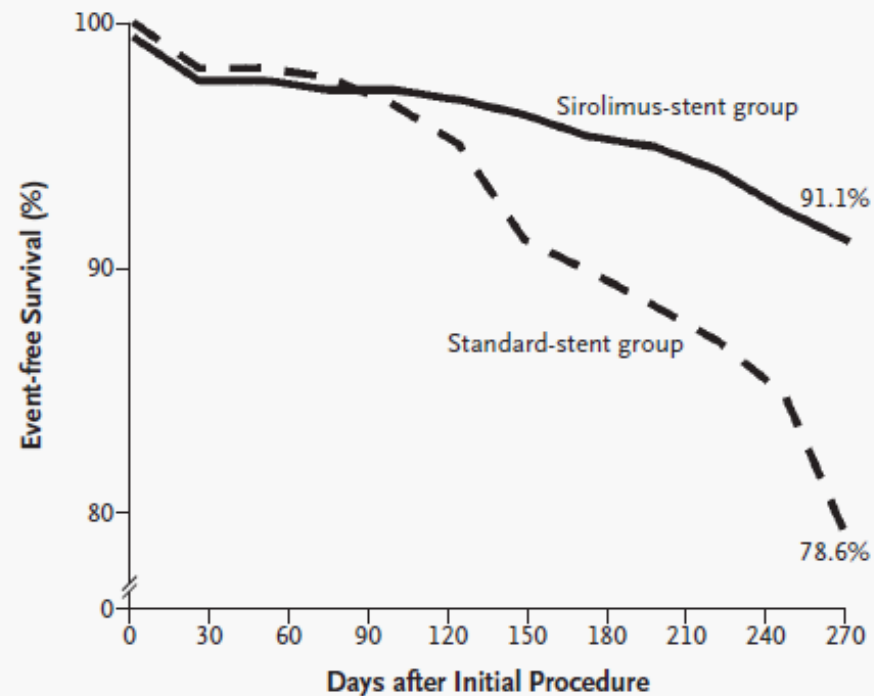
SES

PES



Sirolimus-Eluting Stents versus Standard Stents in Patients with Stenosis in a Native Coronary Artery

Jeffrey W. Moses, M.D., Martin B. Leon, M.D., Jeffrey J. Popma, M.D., Peter J. Fitzgerald, M.D., Ph.D., David R. Holmes, M.D., Charles O'Shaughnessy, M.D., Ronald P. Caputo, M.D., Dean J. Kereiakes, M.D., David O. Williams, M.D., Paul S. Teirstein, M.D., Judith L. Jaeger, B.A., and Richard E. Kuntz, M.D., for the SIRIUS Investigators*

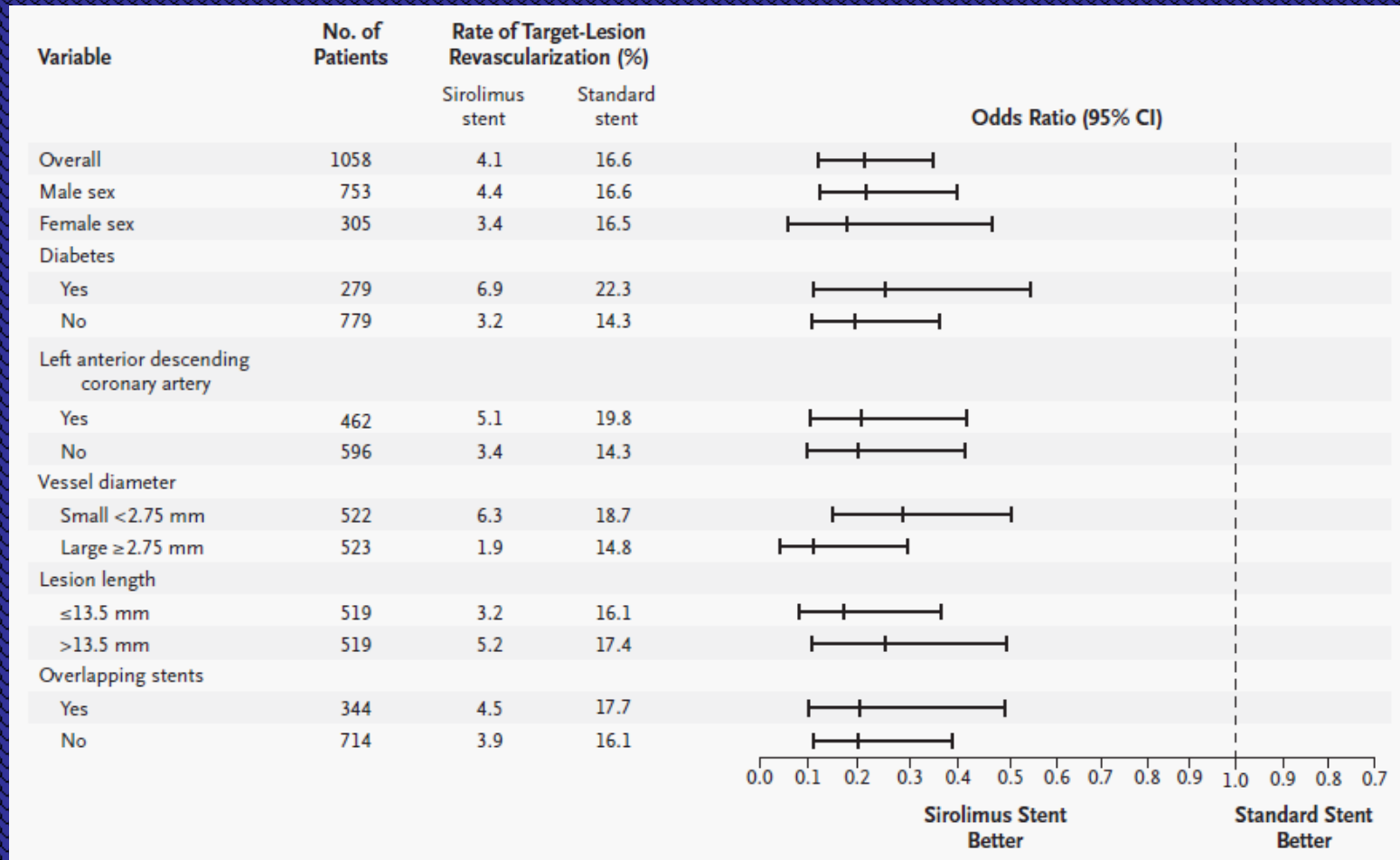


No. at Risk

Sirolimus stent	533	529	527	524	520	515	509	505	493	477
Standard stent	525	523	521	514	506	481	474	465	451	436

SIRIUS trial

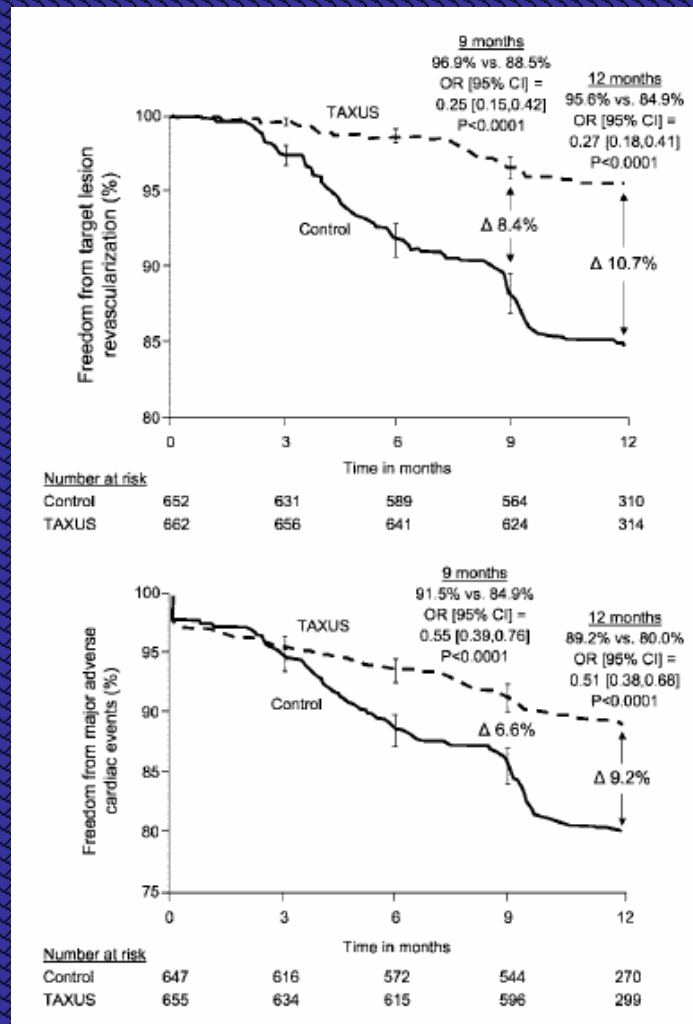
様々な病変形態で有効性が示された



One-Year Clinical Results With the Slow-Release, Polymer-Based, Paclitaxel-Eluting TAXUS Stent

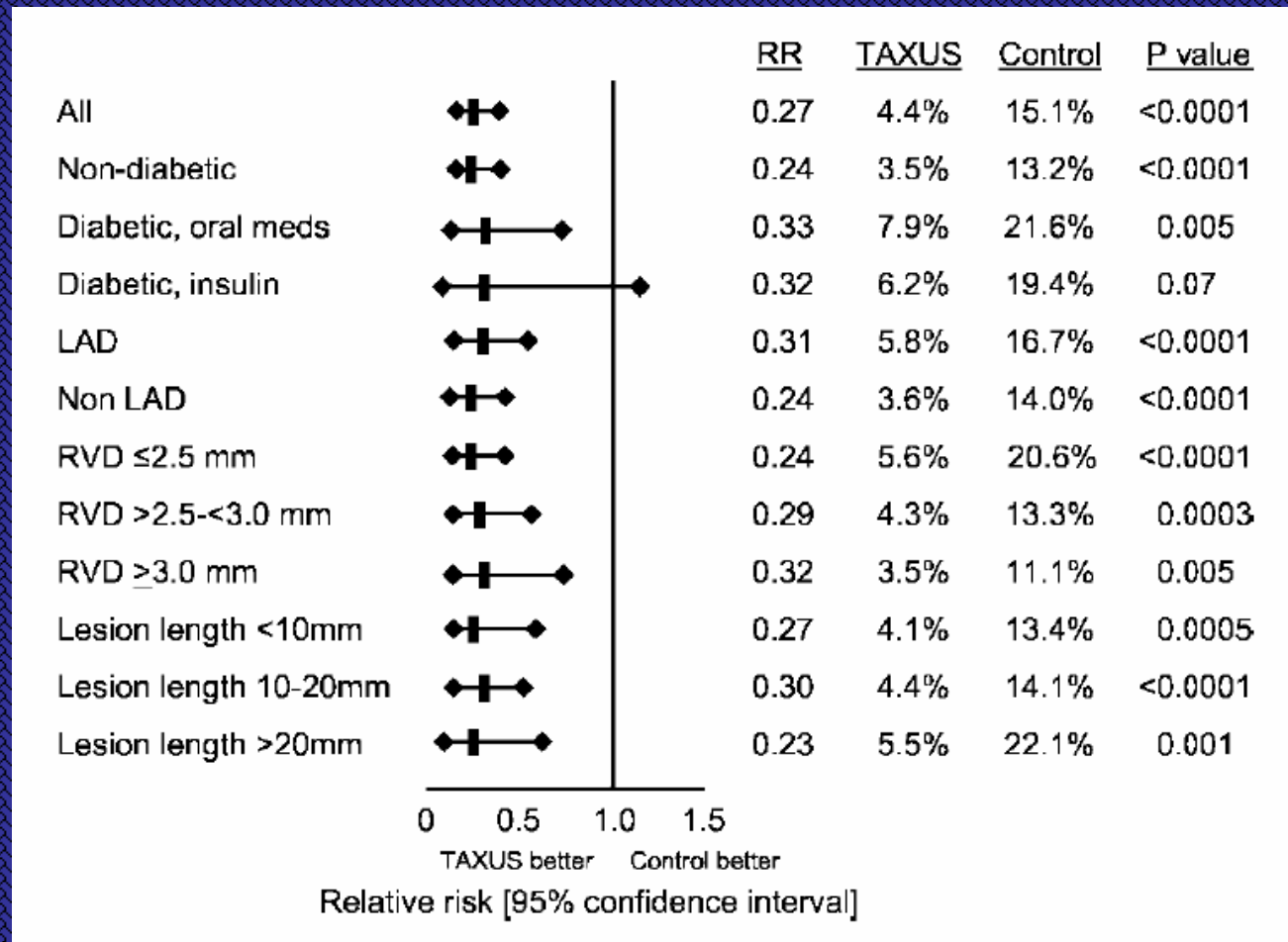
The TAXUS-IV Trial

Gregg W. Stone, MD; Stephen G. Ellis, MD; David A. Cox, MD; James Hermiller, MD; Charles O'Shaughnessy, MD; James Tift Mann, MD; Mark Turco, MD; Ronald Caputo, MD; Patrick Bergin, MD; Joel Greenberg, MD; Jeffrey J. Popma, MD; Mary E. Russell, MD; for the TAXUS-IV Investigators*

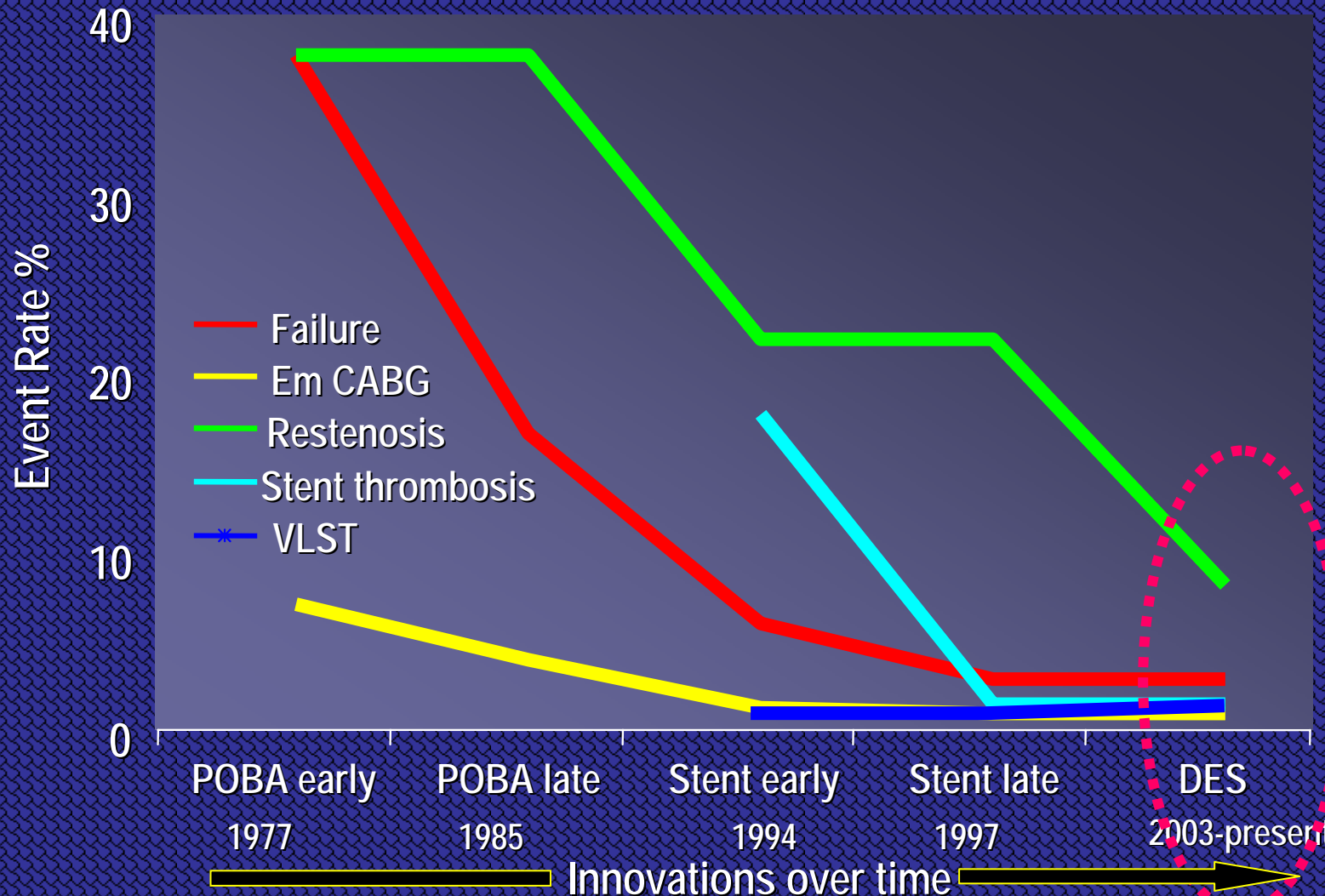


TAXUS trial

様々な病変において有効性が示された



Evolution of PCI (Percutaneous Coronary Intervention)



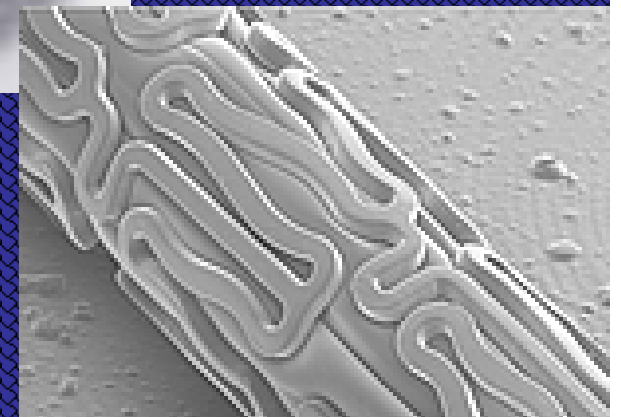
代表的なDES



第一世代



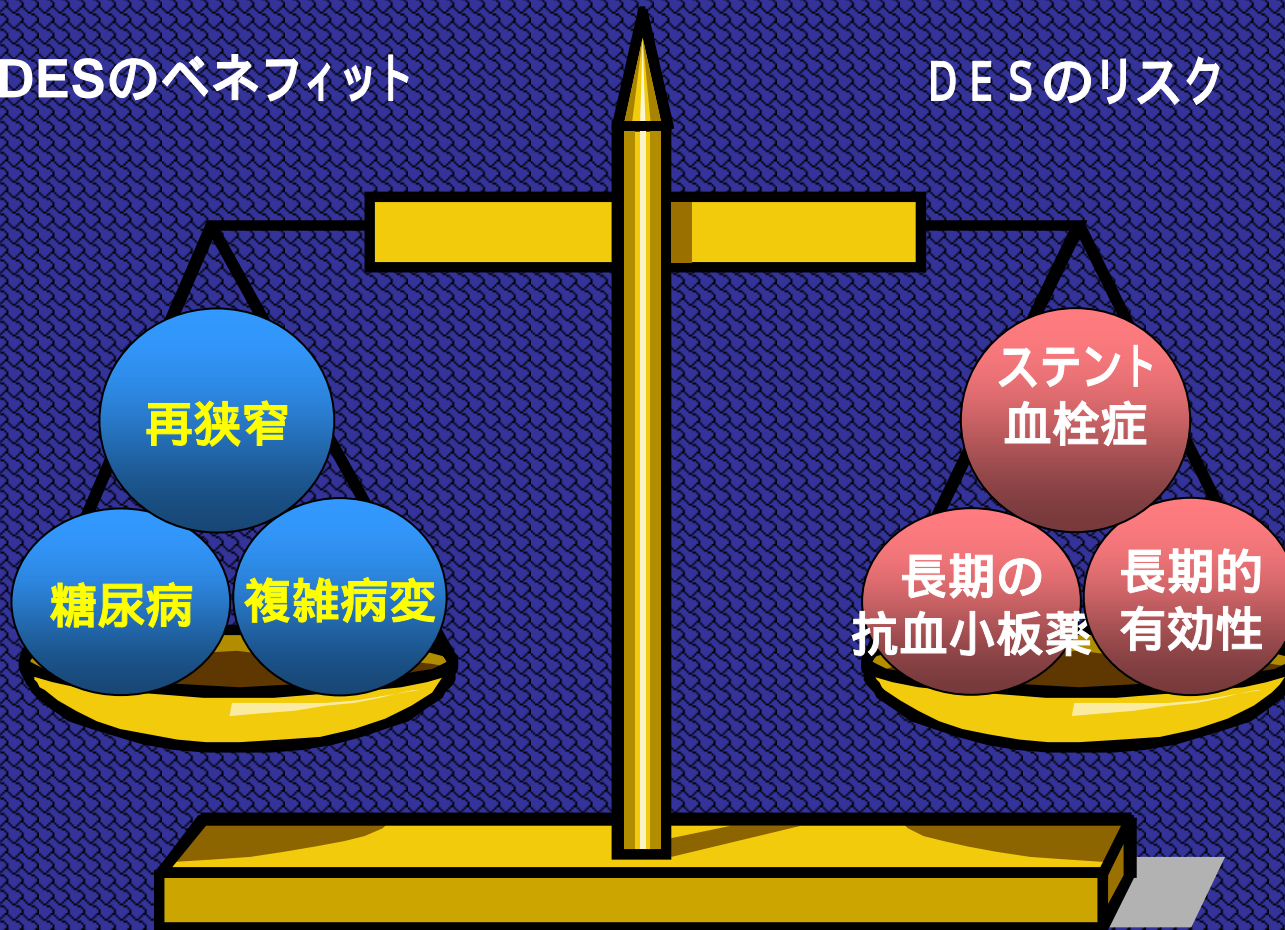
第二世代



DES or BMS

DESのベネフィット

DESのリスク

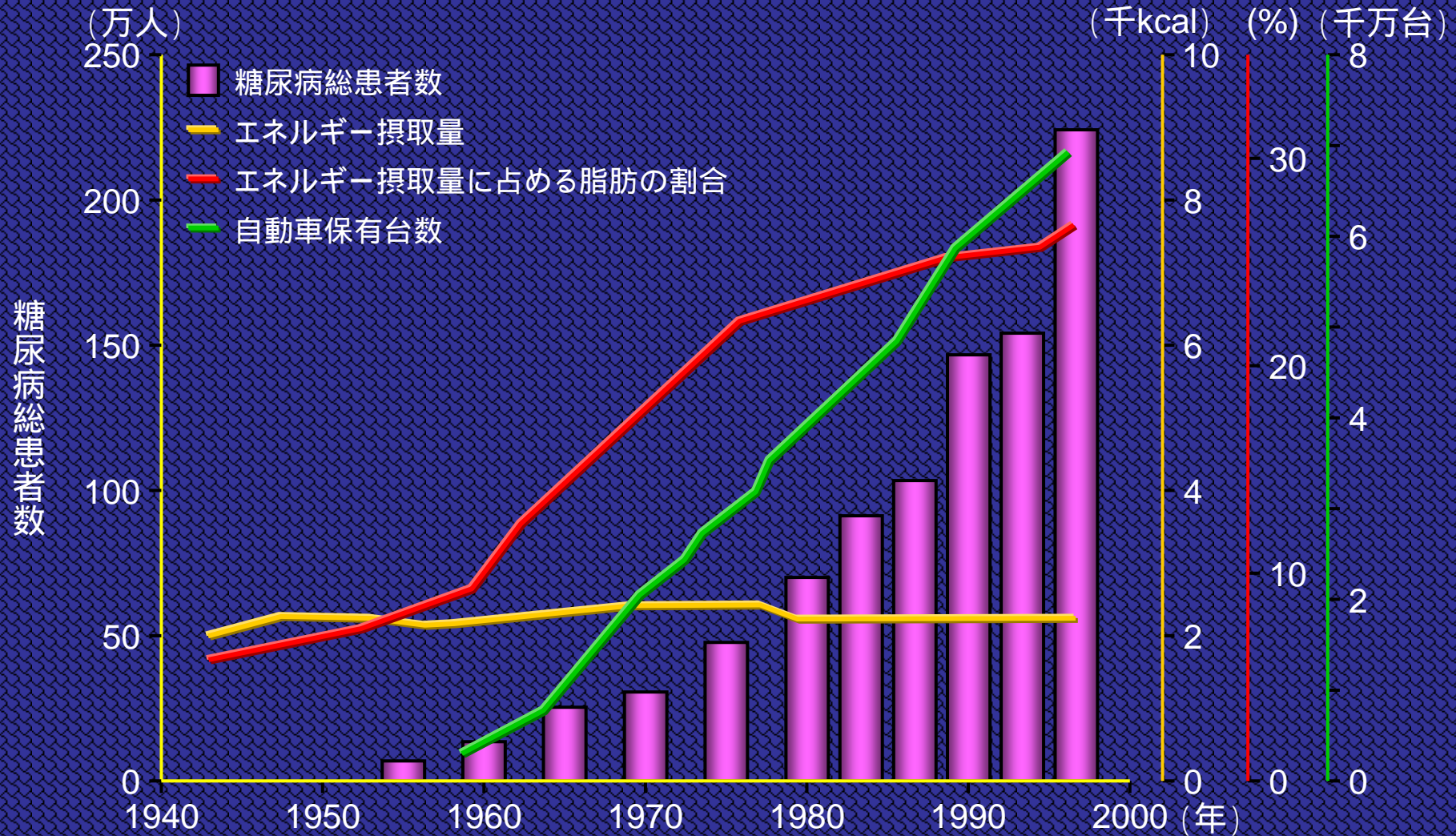


全世界の糖尿病患者数

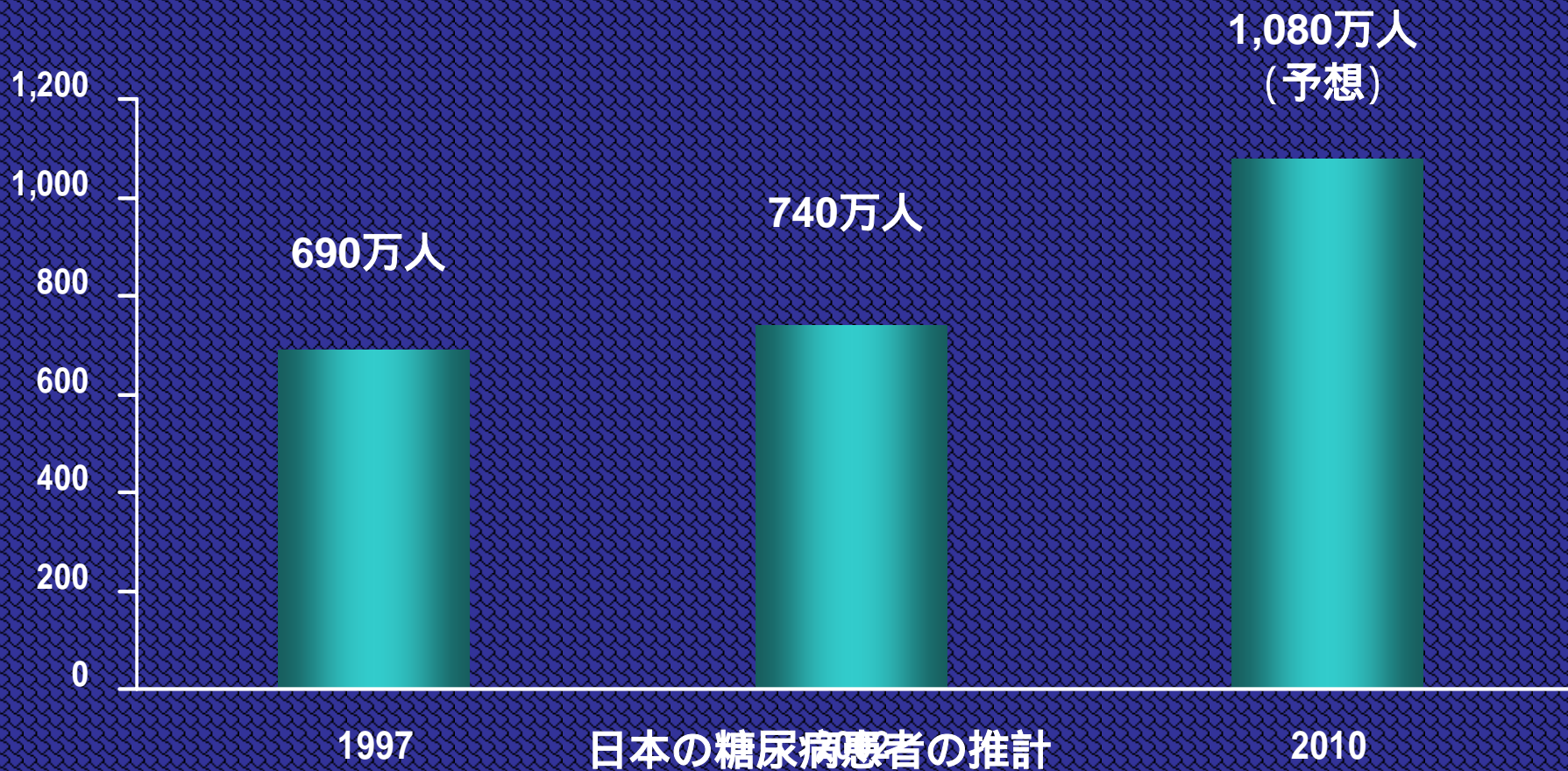


Rank	Country	2000 Diabetics	2030 <i>(millions)</i>
1	India	31.7	79.4
2	China	20.8	42.3
3	USA	17.7	30.3
4	Indonesia	8.4	21.3
5	Japan	6.8	8.9

日本では食生活の欧米化にともない、 糖尿病患者が増加している



日本の糖尿病患者の推計



Source: 厚生労働省 糖尿病実態調査、
岡山明: 糖尿病有病率のBMIによる寄与とBMI変化による推計、健康日本21糖尿病分科会、1999



2006年12月20日
国連で「糖尿病の全世界的脅威を認知する
決議」が加盟192カ国の全会一致で可決した
世界で10秒に1人の命を奪う糖尿病

2007年11月14日
世界糖尿病デー (WHO)

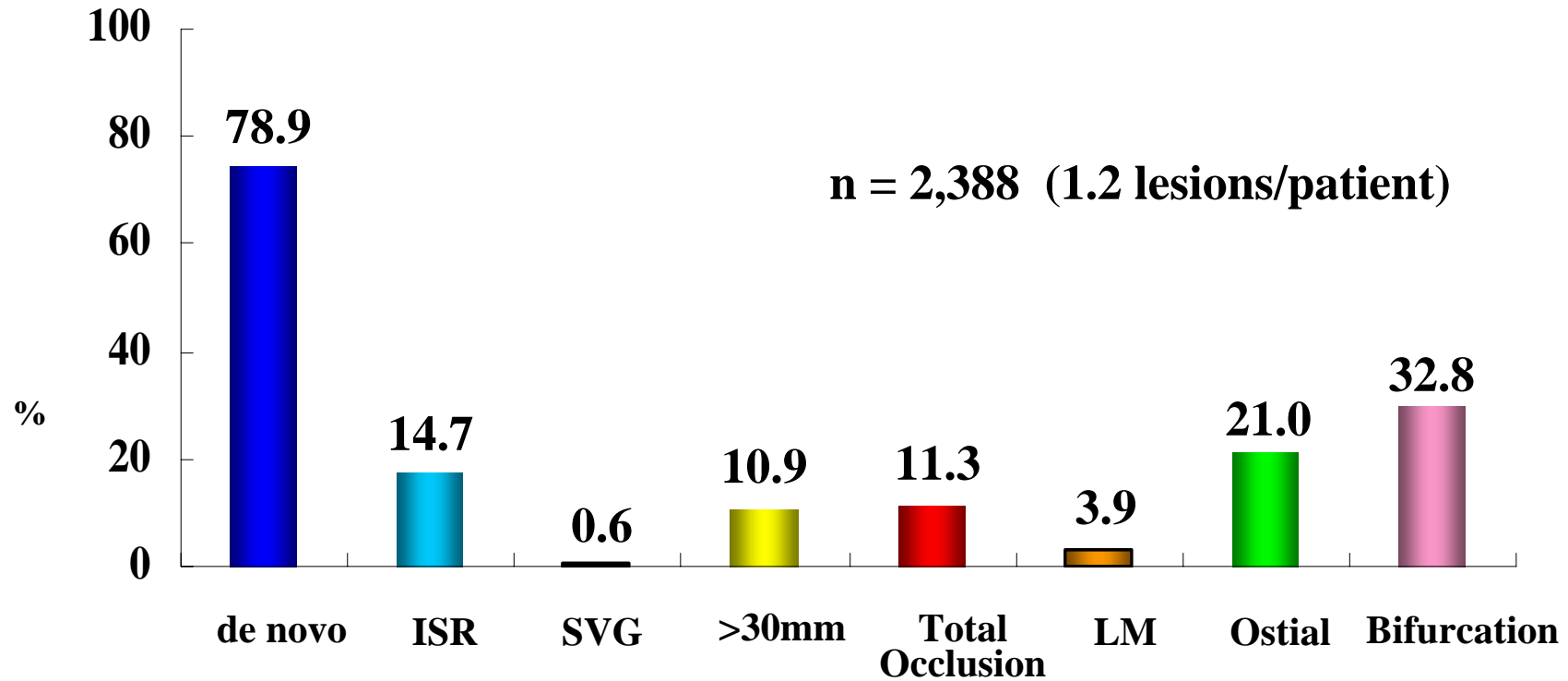


“Unite for Diabetes”
糖尿病との戦いの為に団結せよ



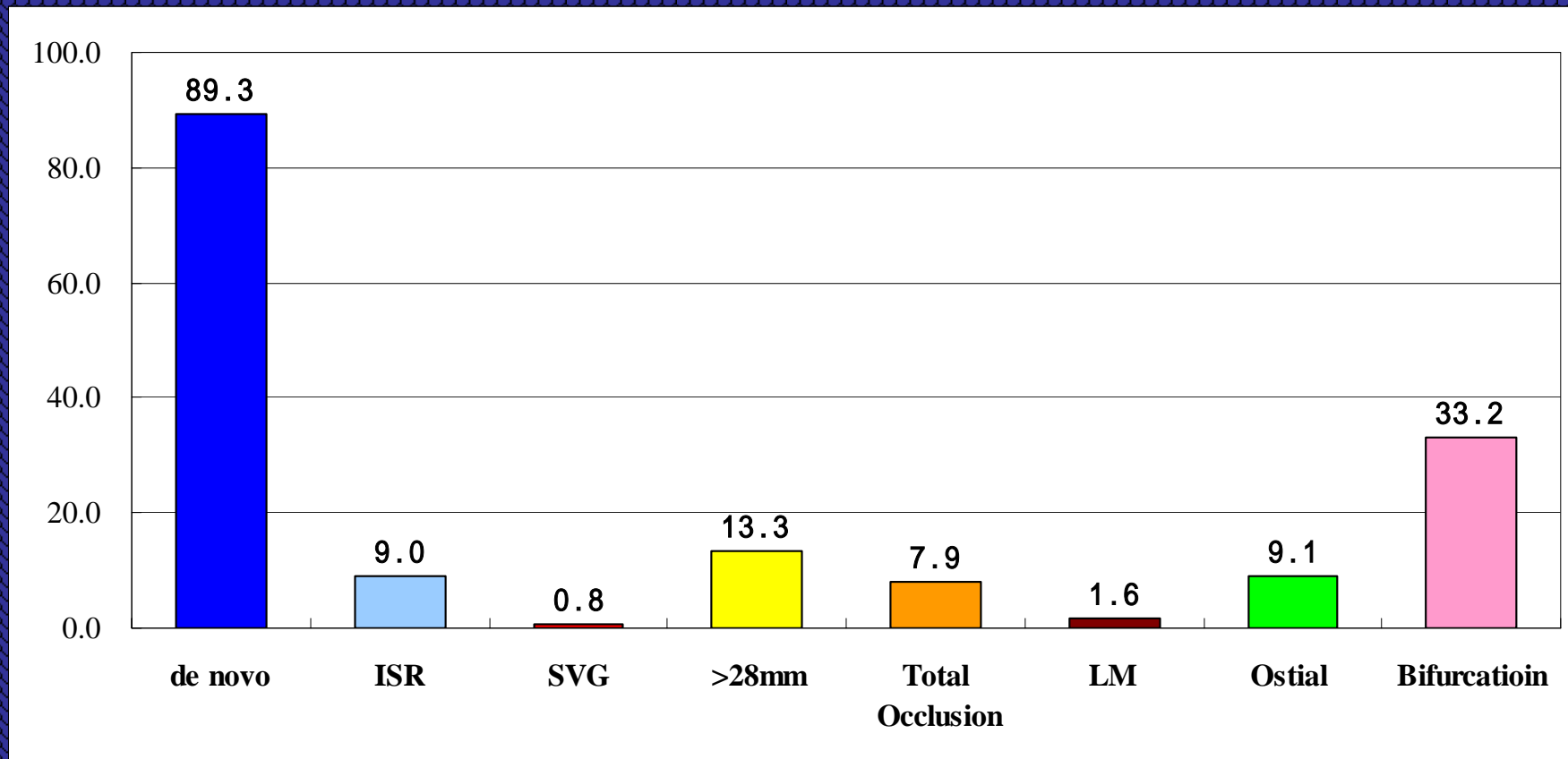
糖尿病患者の為に我々、循環器医師も立ち向かう必要性が高まっている？

Lesions Treated in Cypher PMS



	de novo	ISR	SVG	>30mm	Total Occlusion	LM	Ostial	Bifurcation
1st Year (n=1,184)	74.7	17.3	0.8	10.6	10.7	3.6	20.9	30.0
2nd Year (n=1,204)	83.0	12.0 ↓	0.5	11.1	11.8	4.1	21.2	↑ 35.6
P-Value 0.003		<0.001		N.S.	N.S.	N.S.	N.S.	

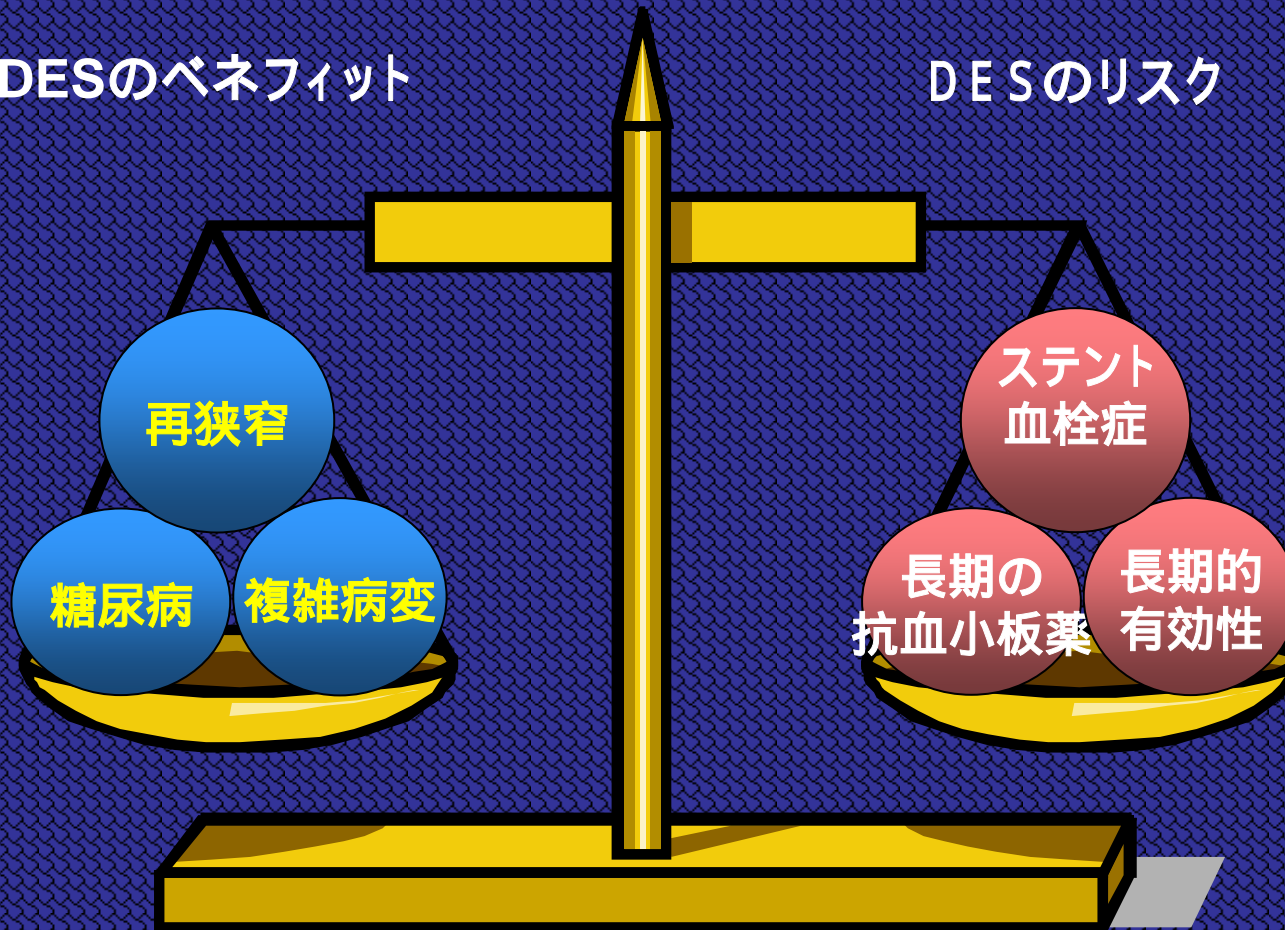
Lesion Treated in TAXUS PMS



DES or BMS

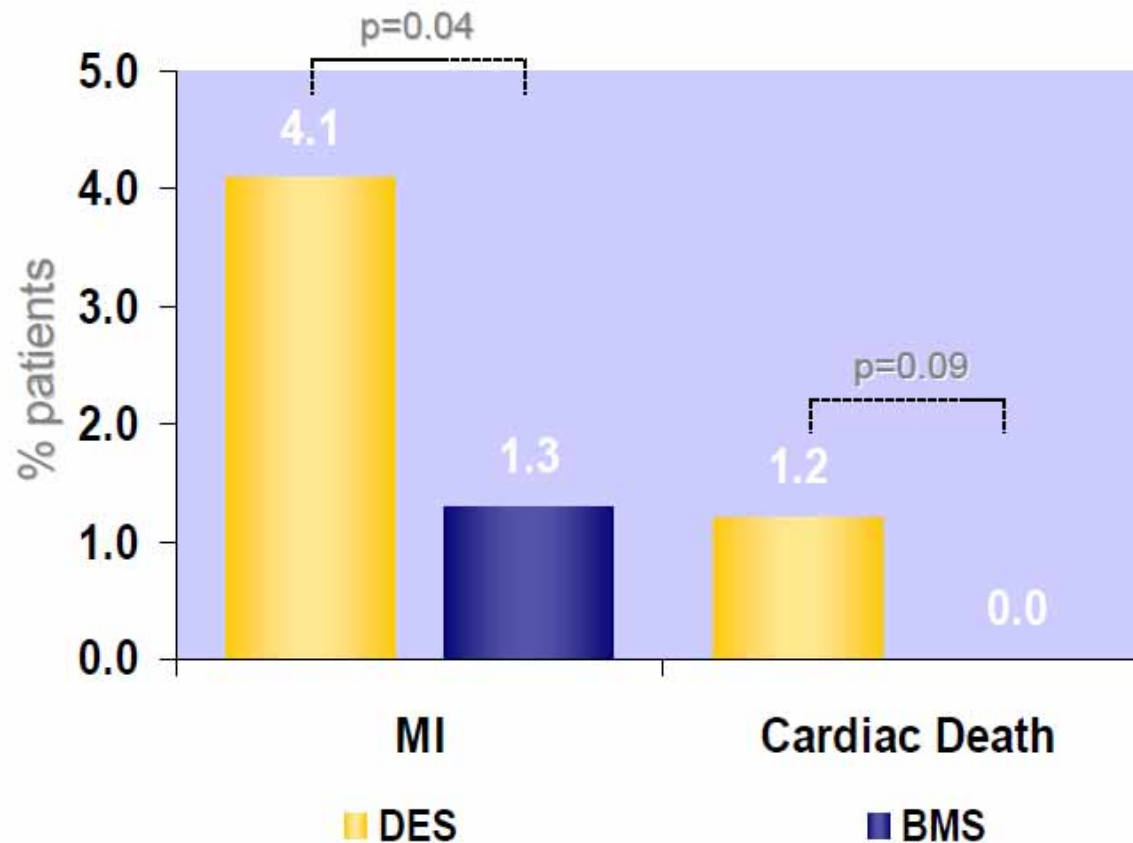
DESのベネフィット

DESのリスク



BASKET-LATE Trial

Components of primary composite endpoint:
nonfatal MI/cardiac death (%)



- Non-fatal MI was higher in the DES group compared with the BMS group (4.1% vs. 1.3%, $p=0.04$).
- Also, cardiac death trended higher in the DES group than in the BMS group (1.2% vs. 0%, $p=0.09$).

JAPANESE SUMMARY ; ARCの定義

- **Definite** :急性冠症候群としての臨床像があり、且つ、造影あるいは剖検による血栓が確認されたもの。
- **Probable** :標的病変の灌流域の心筋梗塞で他の責任病変が同定されないもの(アンジオ確認なし)、あるいは、30日以内の説明のできない死亡。
- **Possible** :30日以降の説明のできない死亡。

危惧された問題点

- Off label病変はステント血栓症のリスクが高いのではないかと？
- 抗血小板薬の適切な服薬期間は？

Ontario PCI Registry

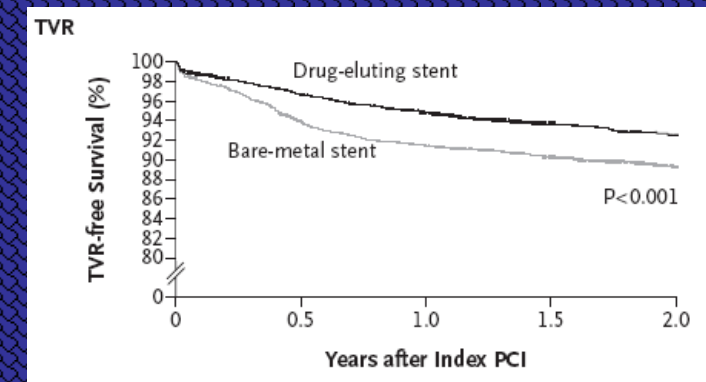
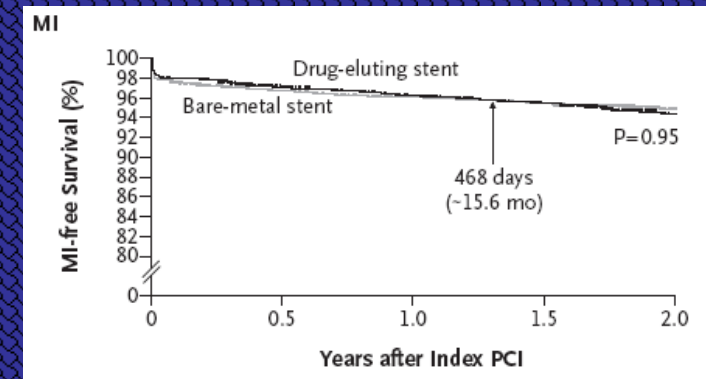
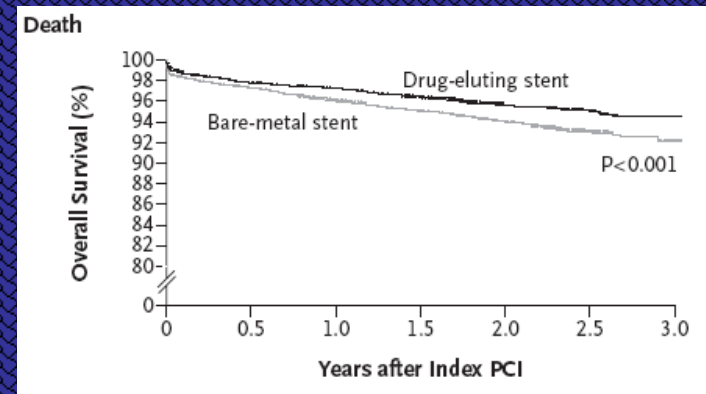
2 and 3-year Clinical Results

From 18,314 PCI at 12 centers in Ontario

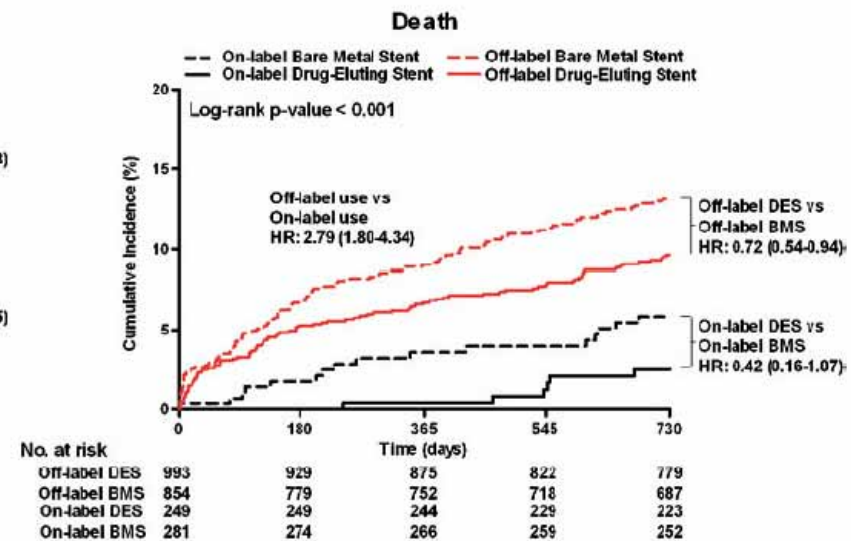
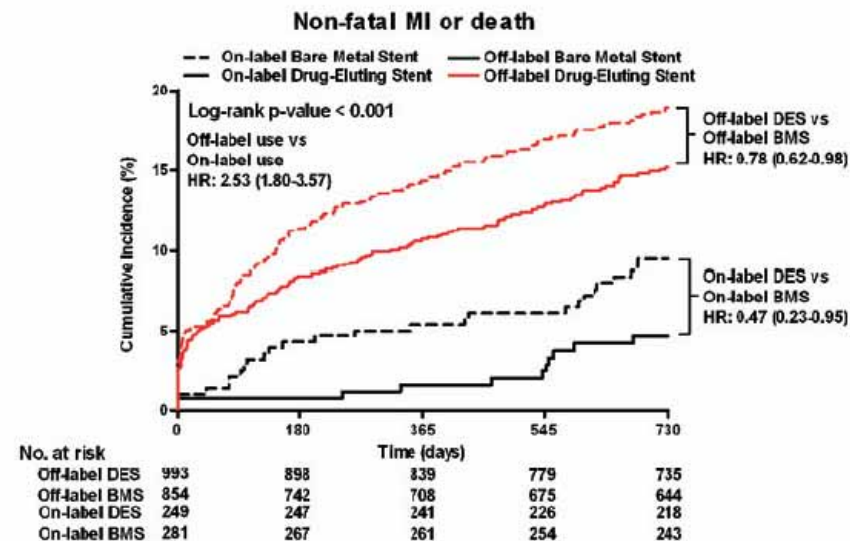
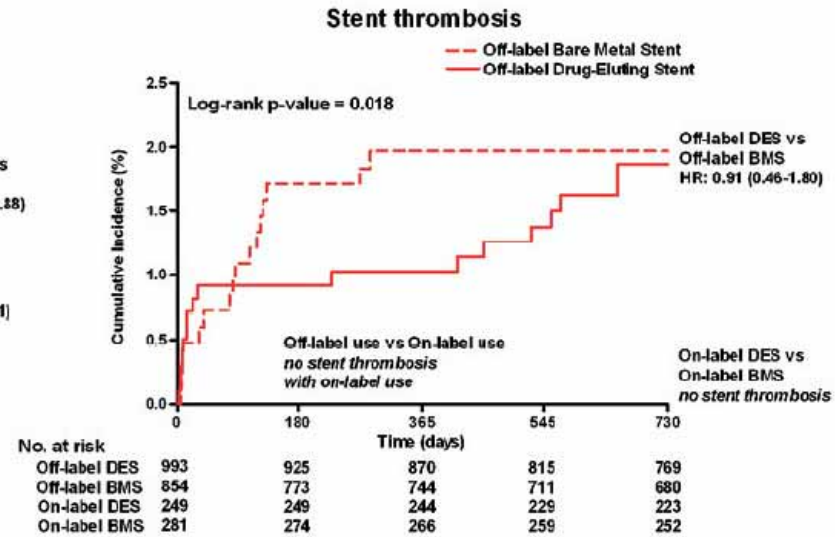
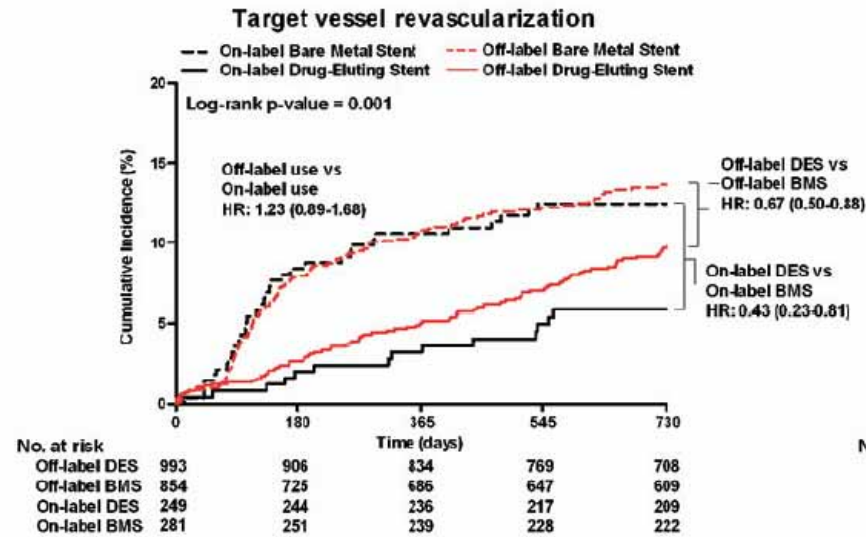
- Treated December 2003 and March 2005
 - 3,751 DES cases (38% of PCI, 82.9% TAXUS Stent)
 - 3,751 propensity-matched BMS patients
- Received 1 year of ASA + Plavix
- Follow-up out to 3 years

	BMS	DES (OR)	p-value
• Death	7.8	5.5 (0.7)	0.001
• MI (2 yr)	5.2	5.7 (1.1)	0.95
• TVR (2 yr)	10.7	7.4 (0.69)	0.001
• small (< 3mm)	all 3 (0.38 [17.6 - 7.2%])* any 2 (0.34-0.66 [12 - 6%])* any 1 (0.78-0.82 [8 - 6%])		
• long (>20 mm)			
• DM			

*p < 0.05



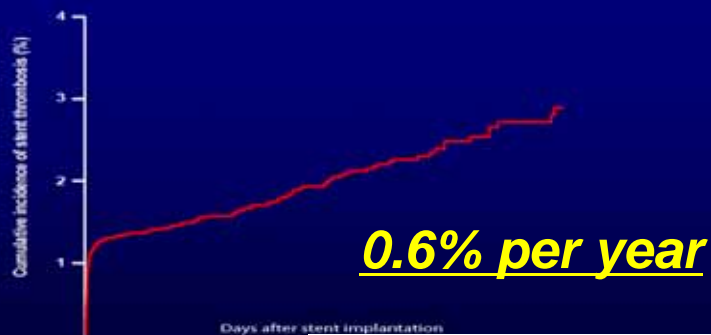
K-M plots of cumulative event up to 2 Years for “on-” and “off”-label BMS and DES



Stent Thrombosis: Trend in foreign countries

Bern/Rotterdam

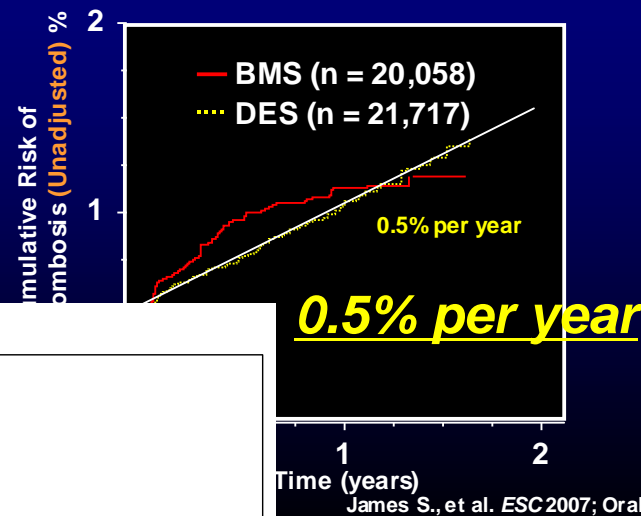
Cumulative Incidence of Stent Thrombosis in Patients with SES or PES



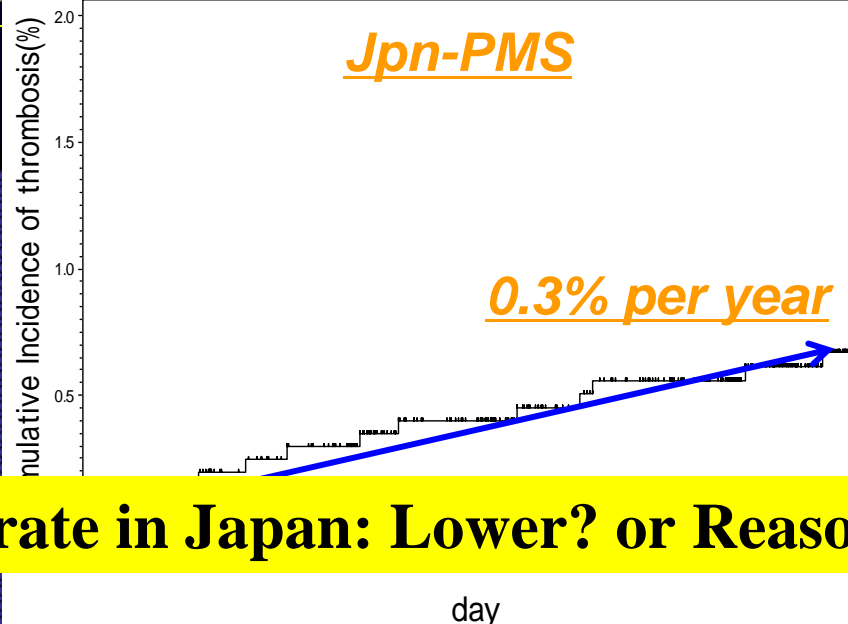
Days after PCI	9	30	365
Cumulative Incidence (%)	1.1	1.2	1.7
Cumulative Events (n)	79	90	116
Patients at Risk (n)	7173	7041	5549

SCAAR

SCAAR: Stent Thrombosis (Unadjusted) in Total Cohort (n = 41,775)

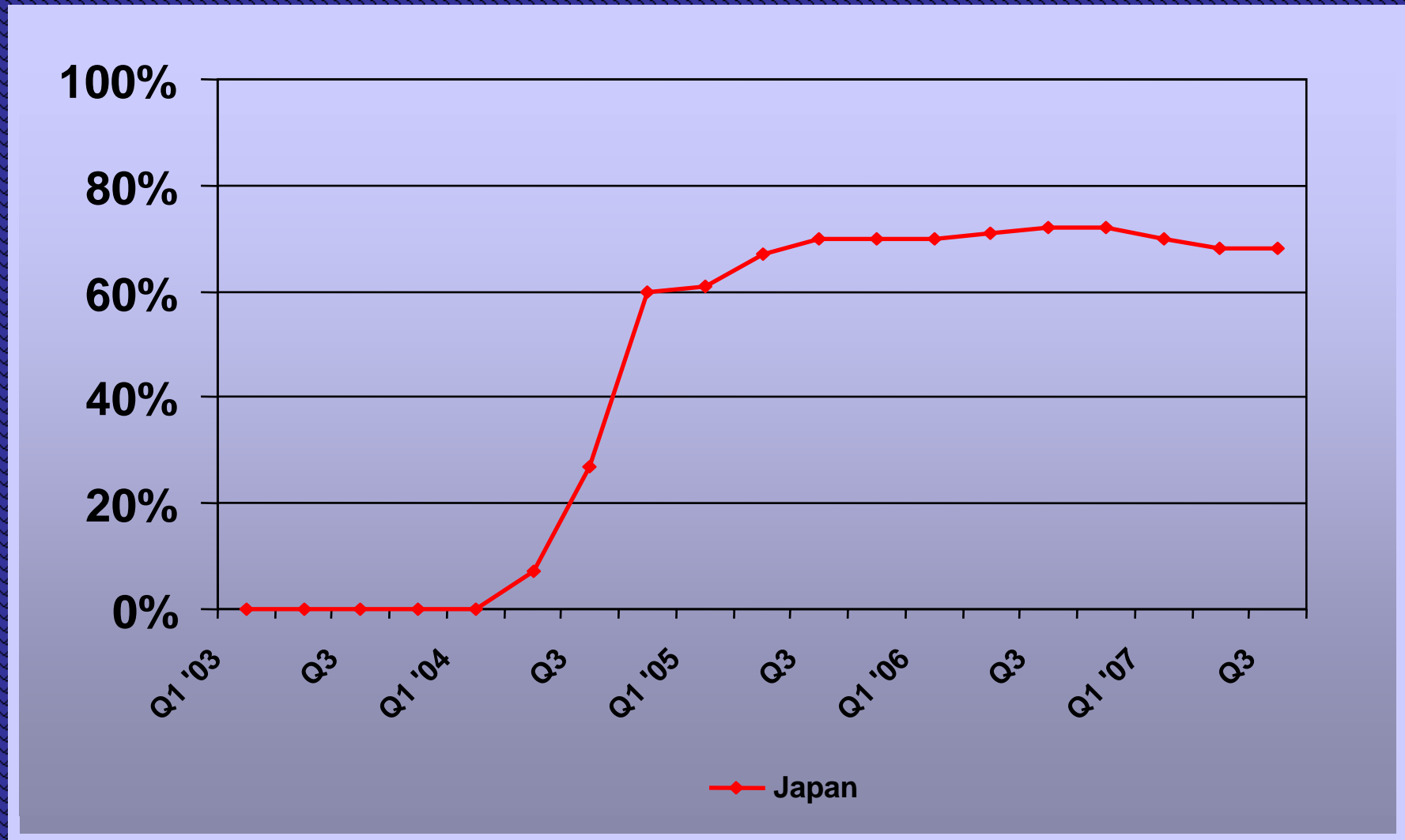


Jpn-PMS



ST rate in Japan: Lower? or Reasonable?

The trend of DES use

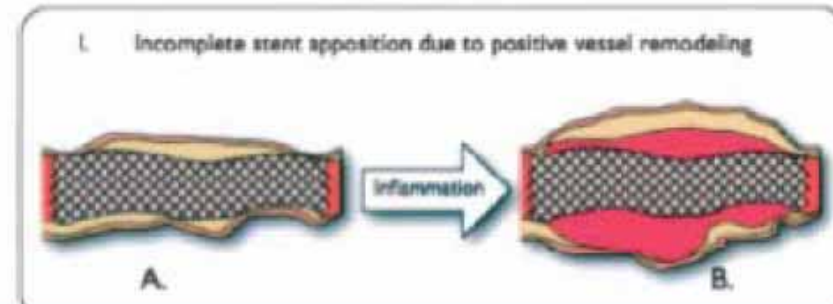


BMS選択例

- 長期に抗血小板薬服薬不可能
- 服薬のcompliance不良例
- BMSで成績が期待できる症例
- DES留置が困難例
- AMI
 - 出血性合併症のリスクに関して不明
 - 救命が重要で、再狭窄の防止はsecondary
 - Mal appositionのリスクが高い

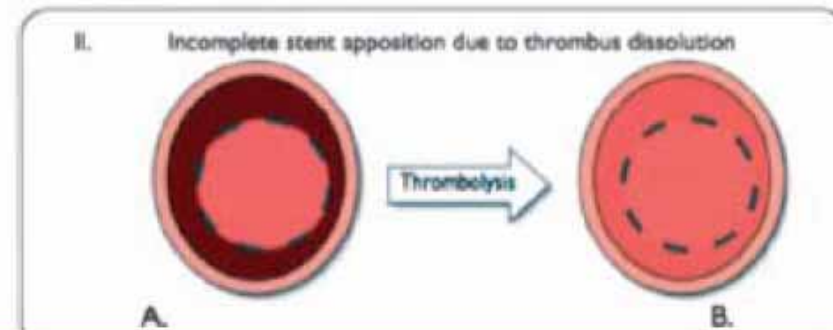
Mechanisms of Incomplete Apposition

POSITIVE REMODELING

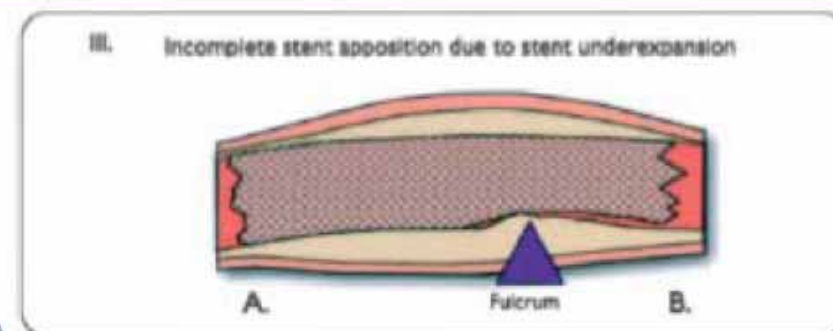


THROMBUS DISSOLUTION

- ✓ AMI cases more frequent with thrombotic lesions



STENT UNDEREXPANSION

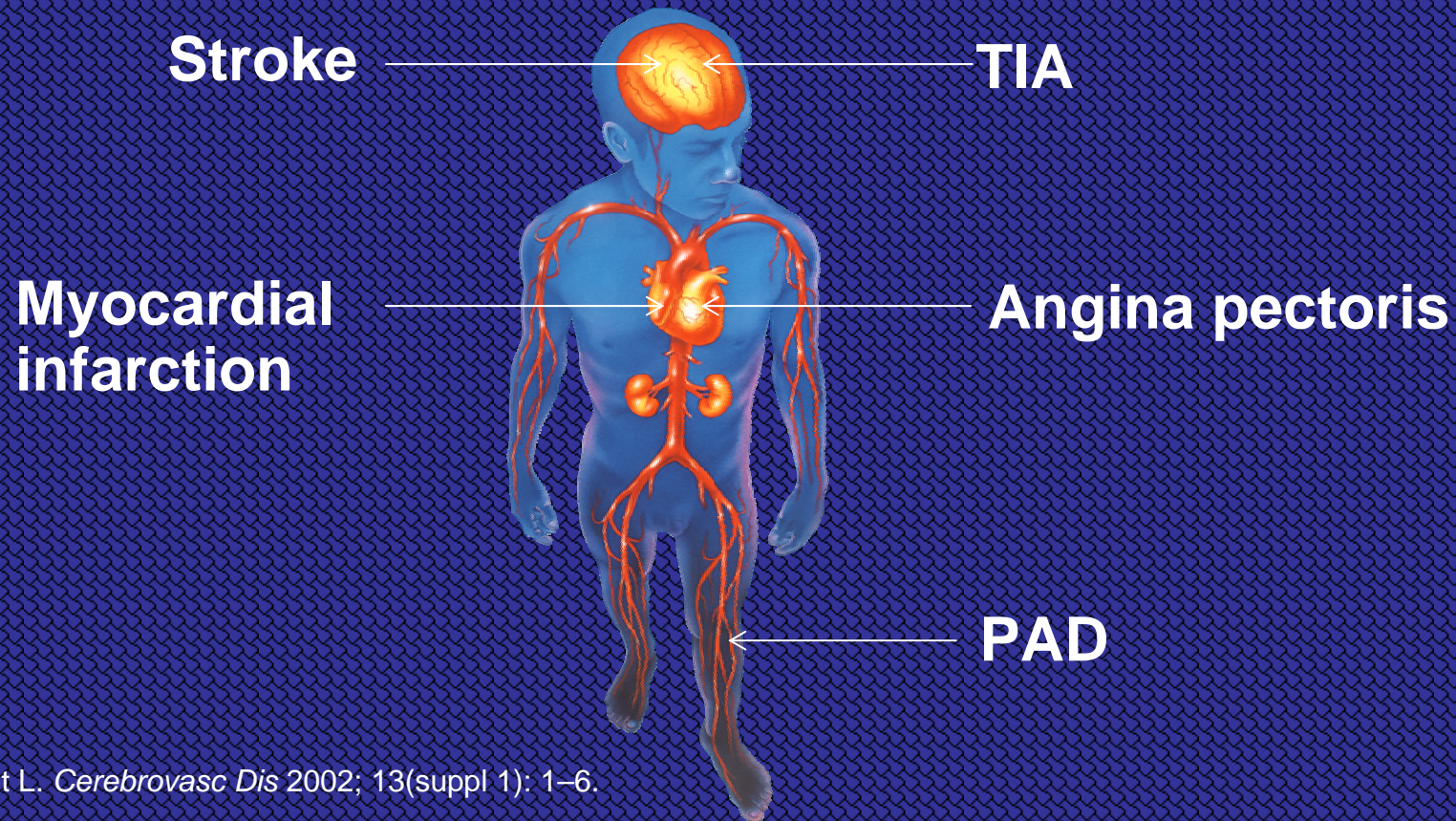


虚血性心疾患の診断学、治療学

- 両者ともに低侵襲が大きなテーマ
- 診断
 - 造影検査がgold standard
 - 冠動脈CTの進歩
- 治療(血行再建)
 - 冠動脈バイパス術がgold standard
 - カテーテル治療の進歩
- アテローム血栓症の概念と治療

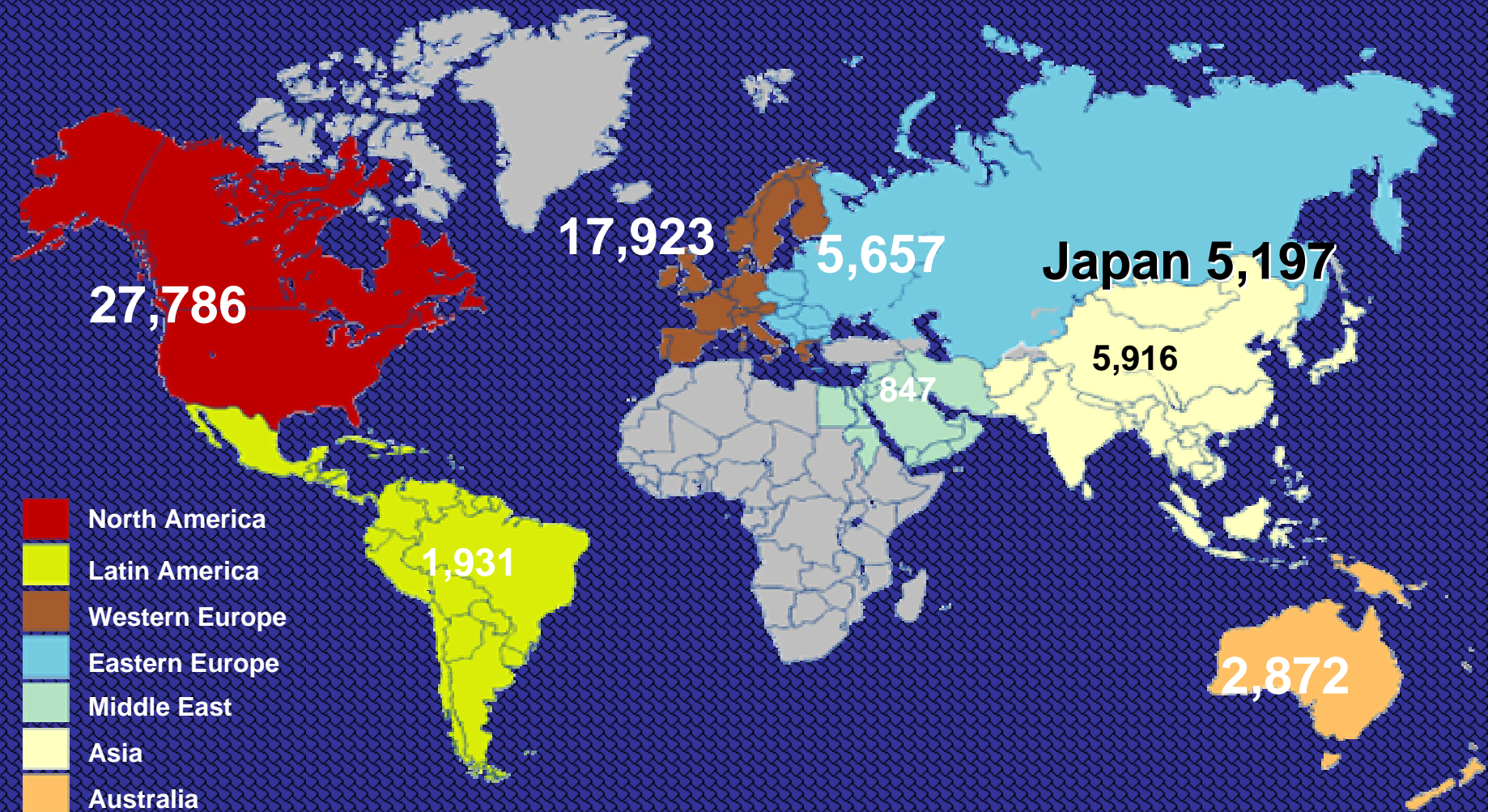
Atherothrombosis is polyvascular disease

Clinical entity caused by the same pathological mechanism



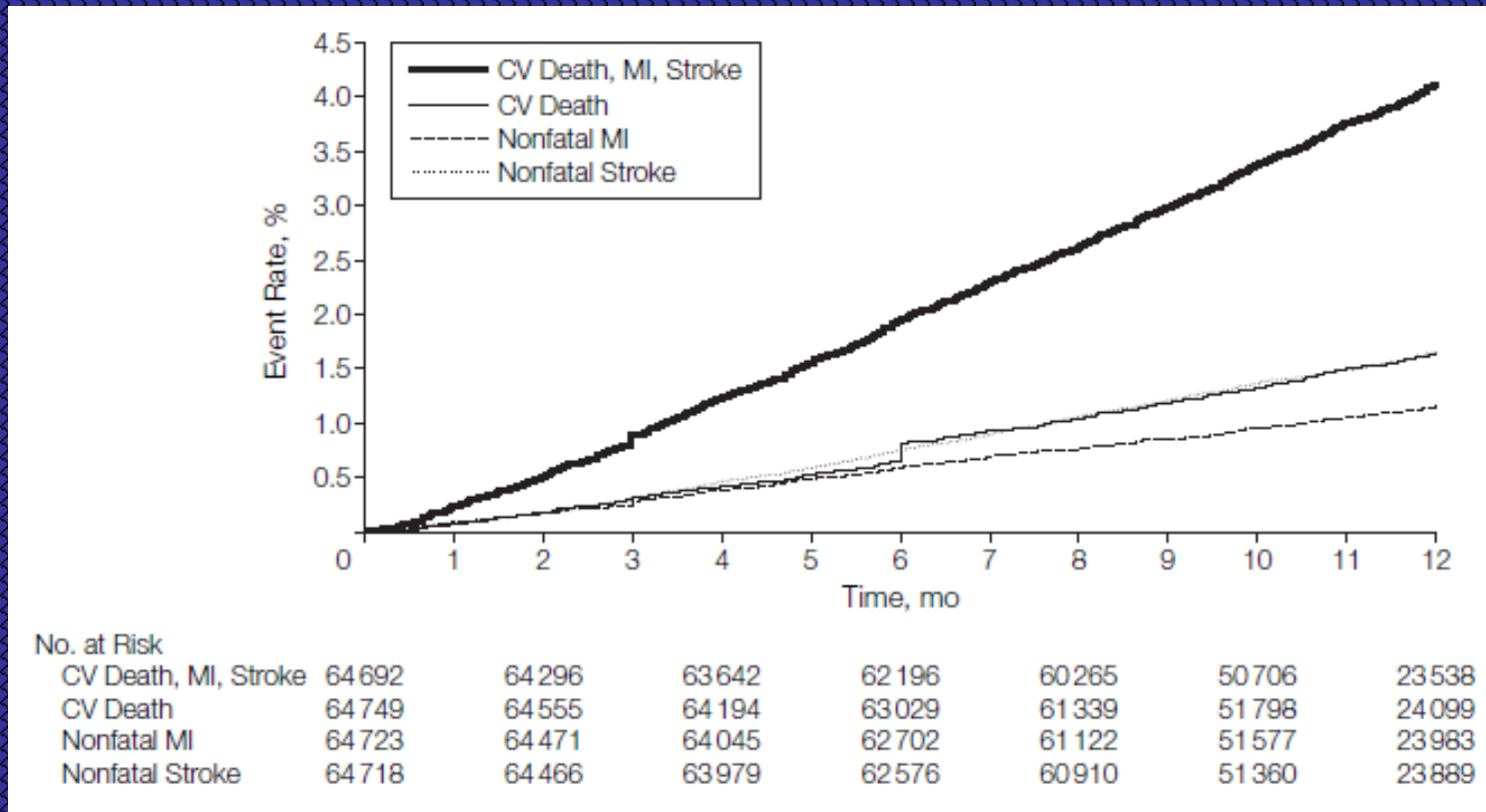
REACH-Registry; outpatients registry

Enrolled pts number; 68,129 patients in 5,580 sites* in 44 countries



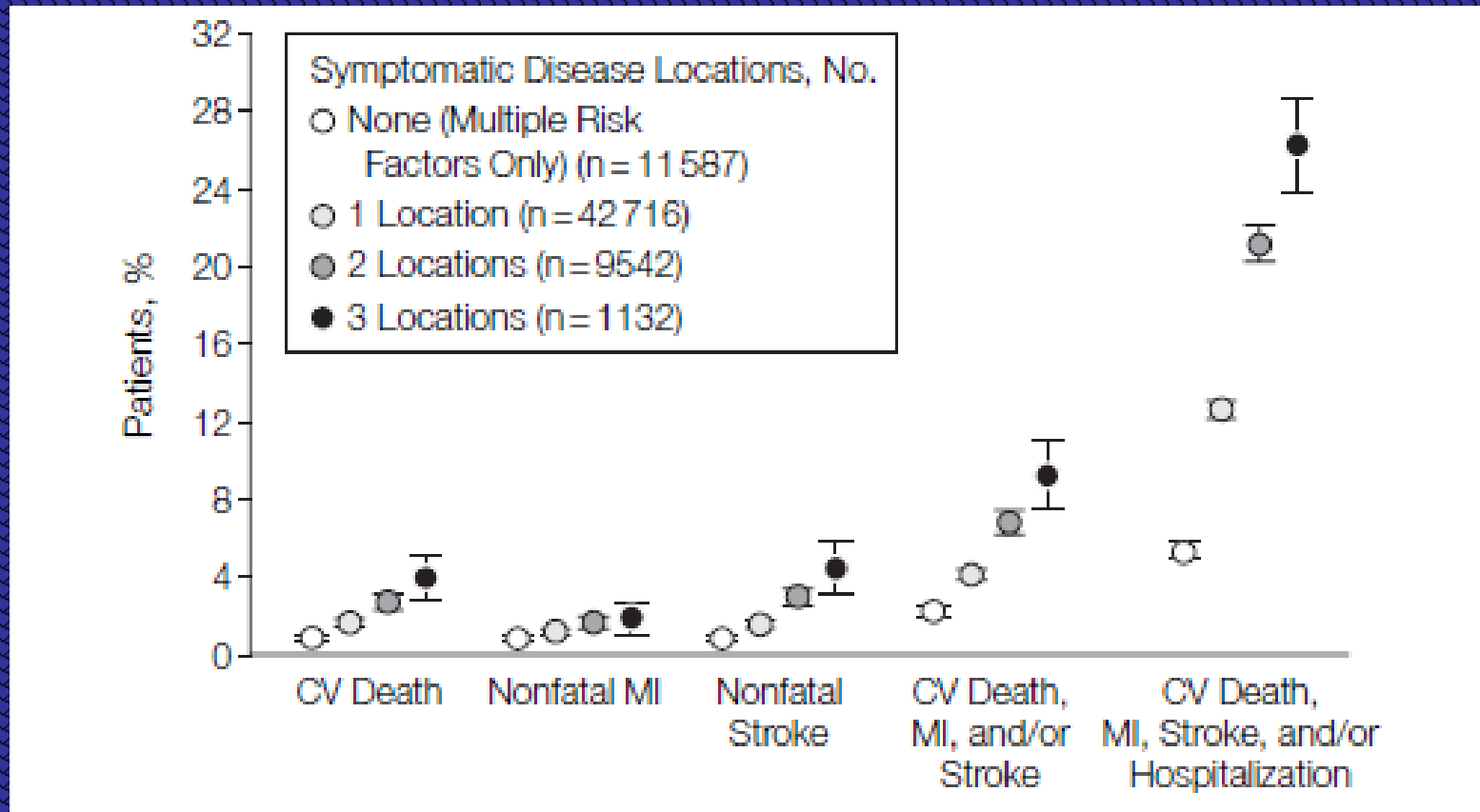
* up to 15 patients/site (up to 20 in the US)

Event curves from enrollment to 1yr



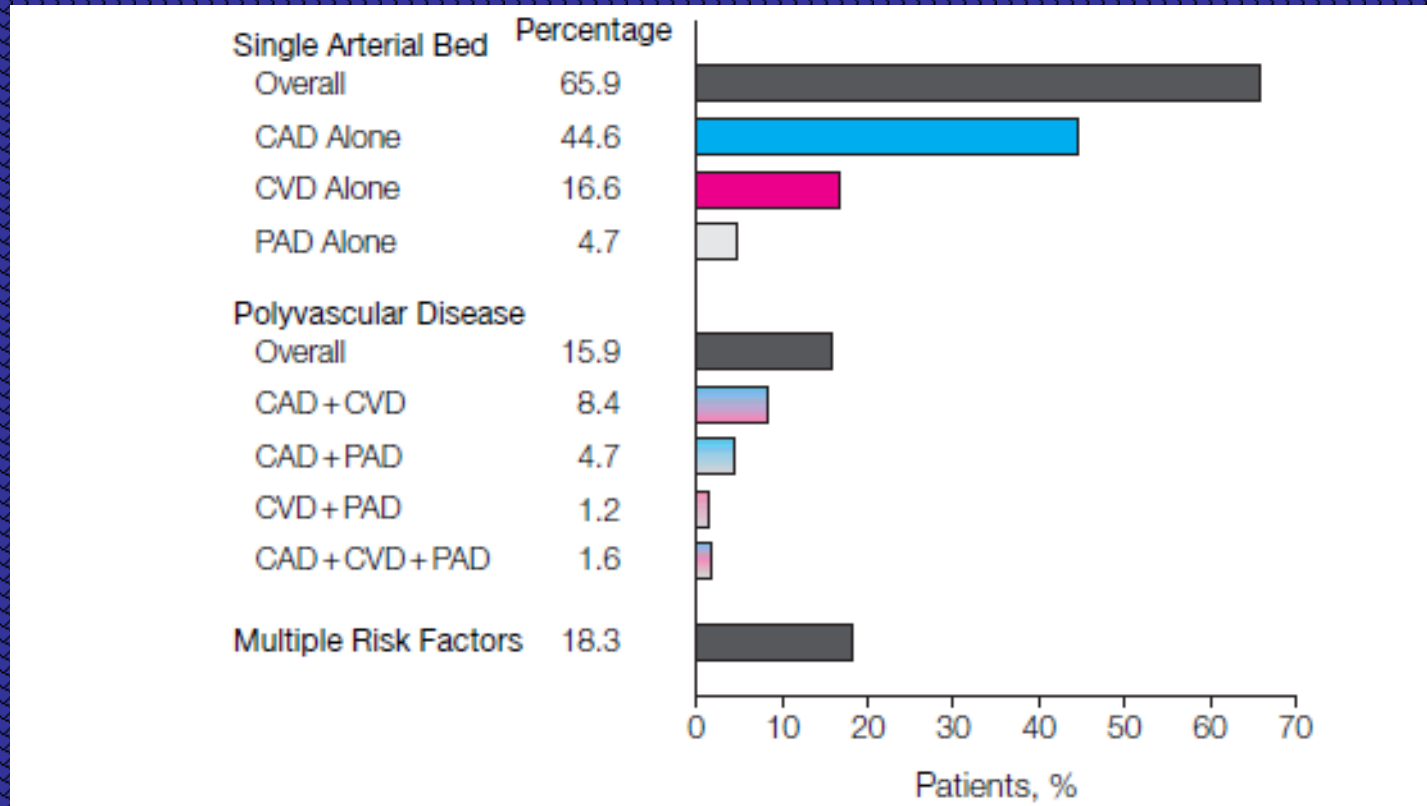
Event rate demonstrate linearity

CV event as a function of number of symptomatic disease



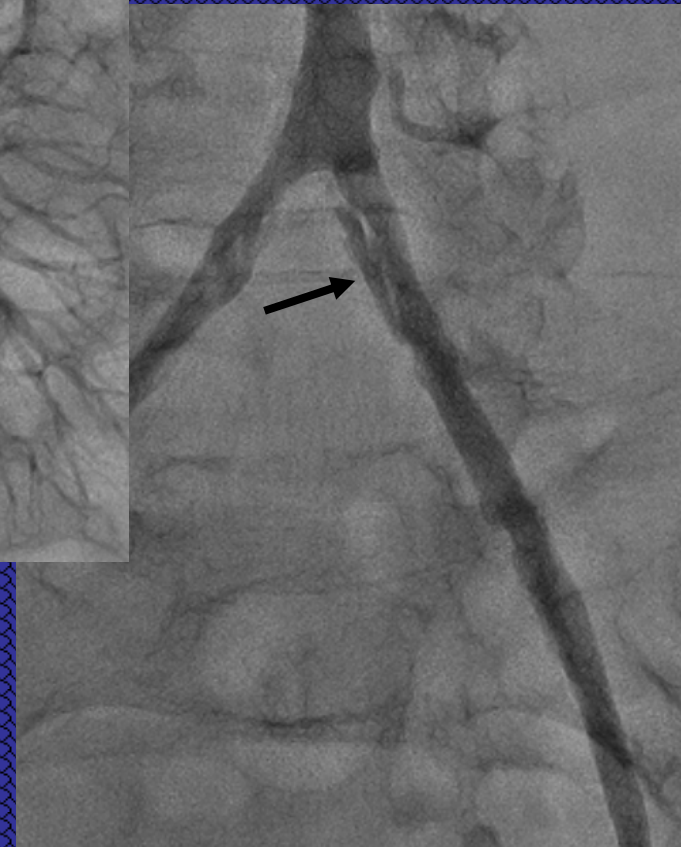
Event rates increased in stepwise fashion with the number of symptomatic vascular beds.

Prevalence of polyvascular disease

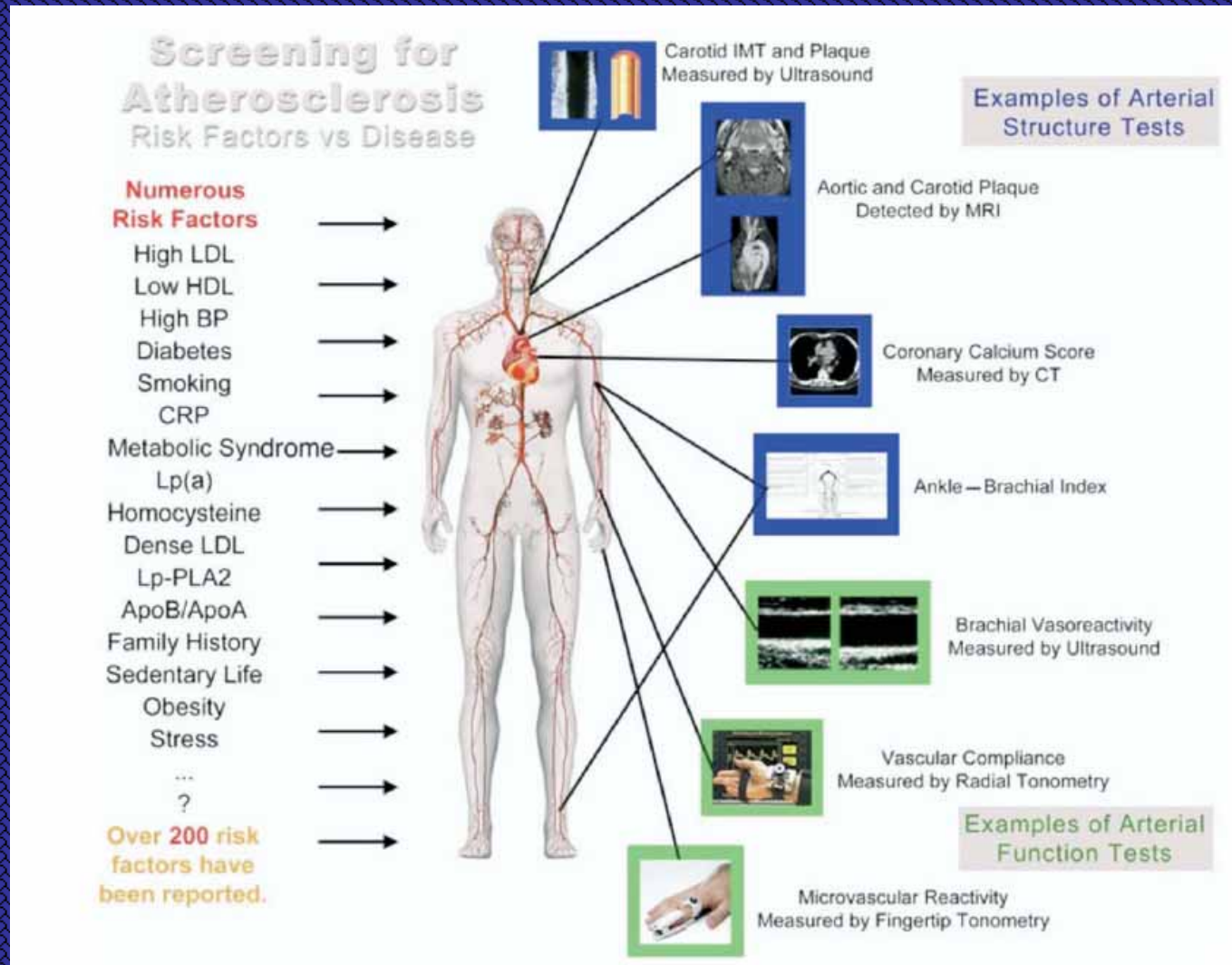


Of the patients with symptomatic atherosclerosis, a significant proportion had symptomatic polyvascular disease

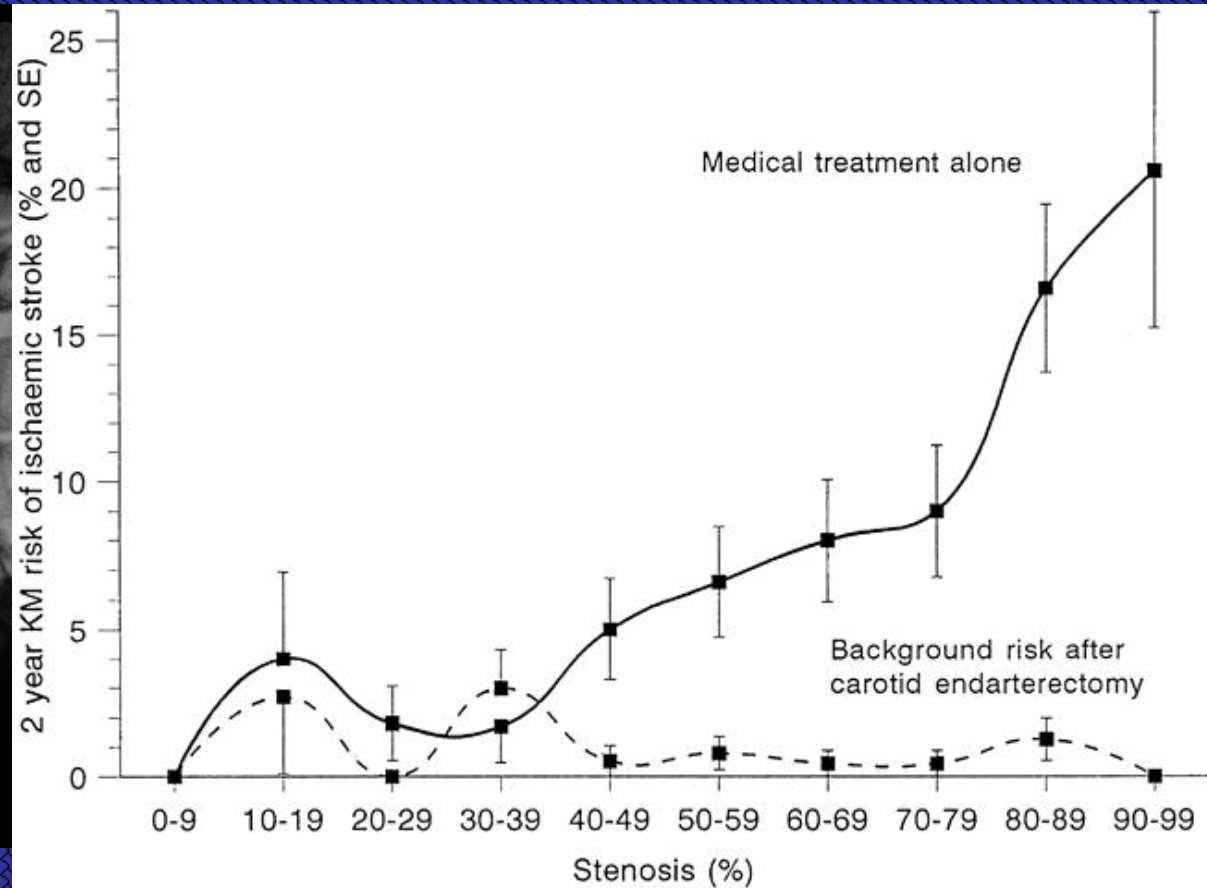
頸動脈と冠動脈に限らず 様々な血管における粥腫破綻



Assessment of advanced disease



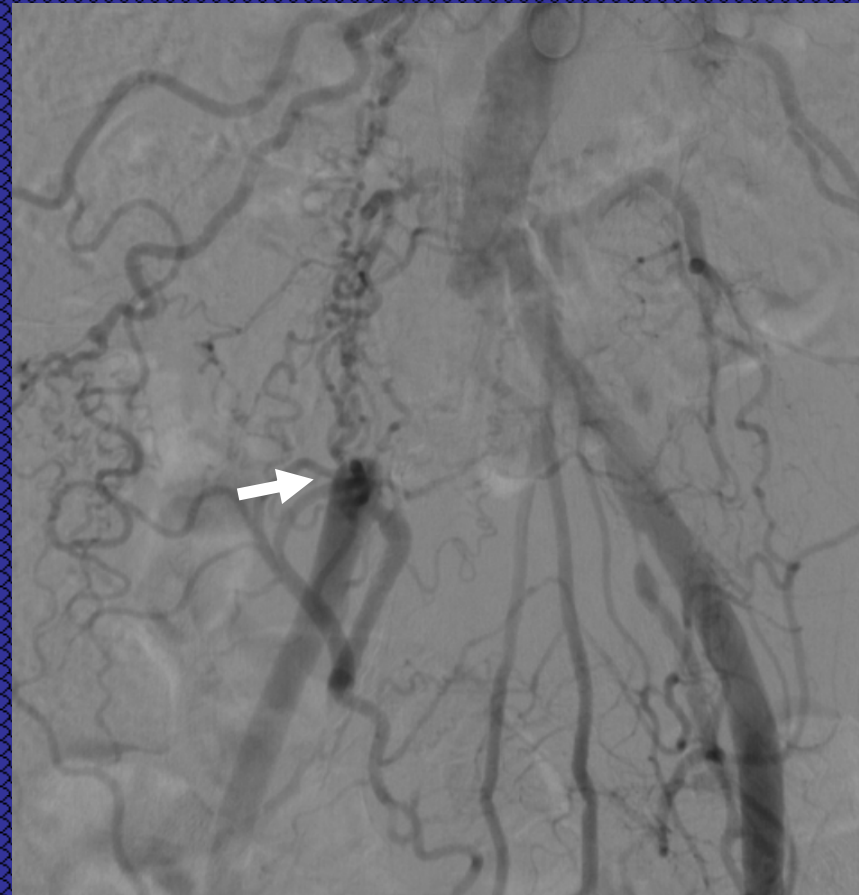
Carotid artery stenosis and Stroke



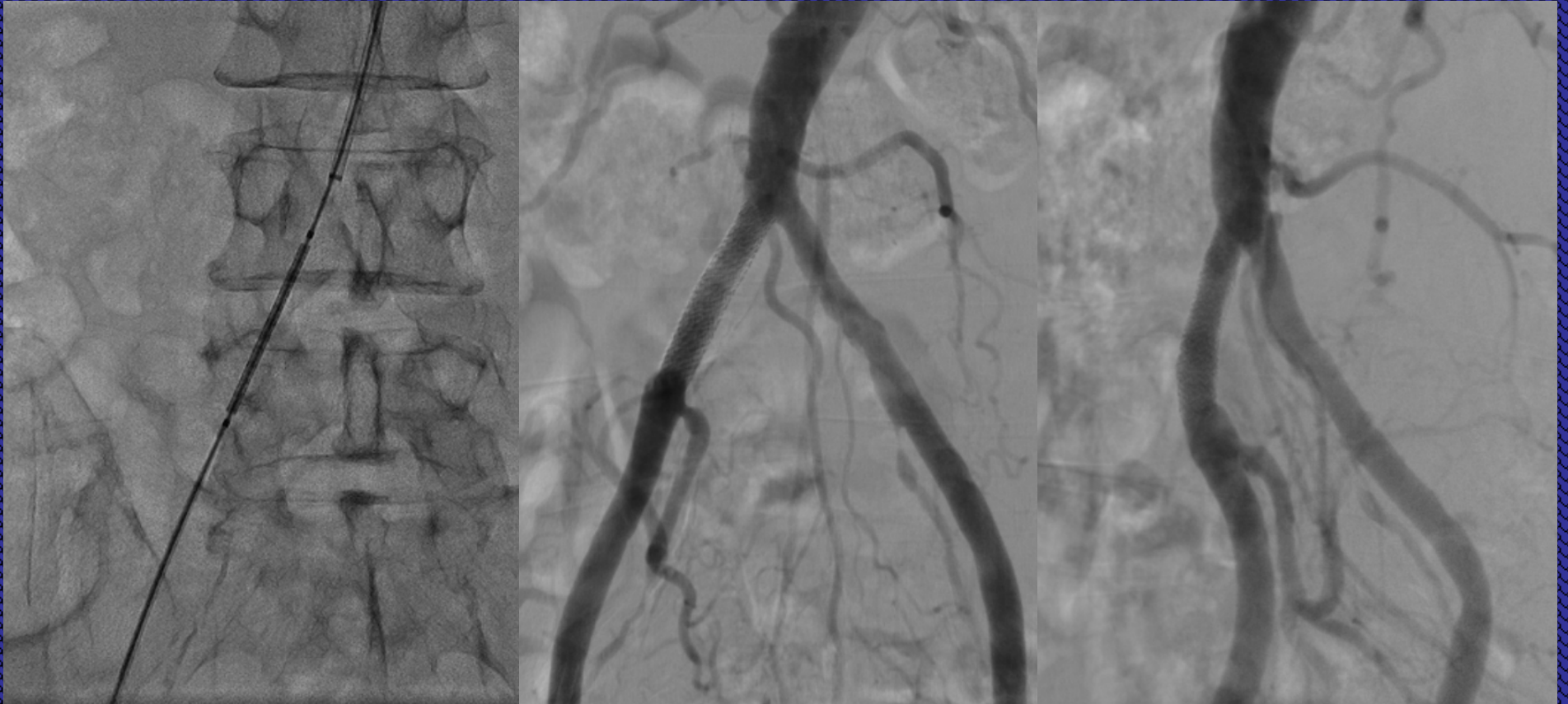
CAS



**GW selection is important, however,
back up support is more important**



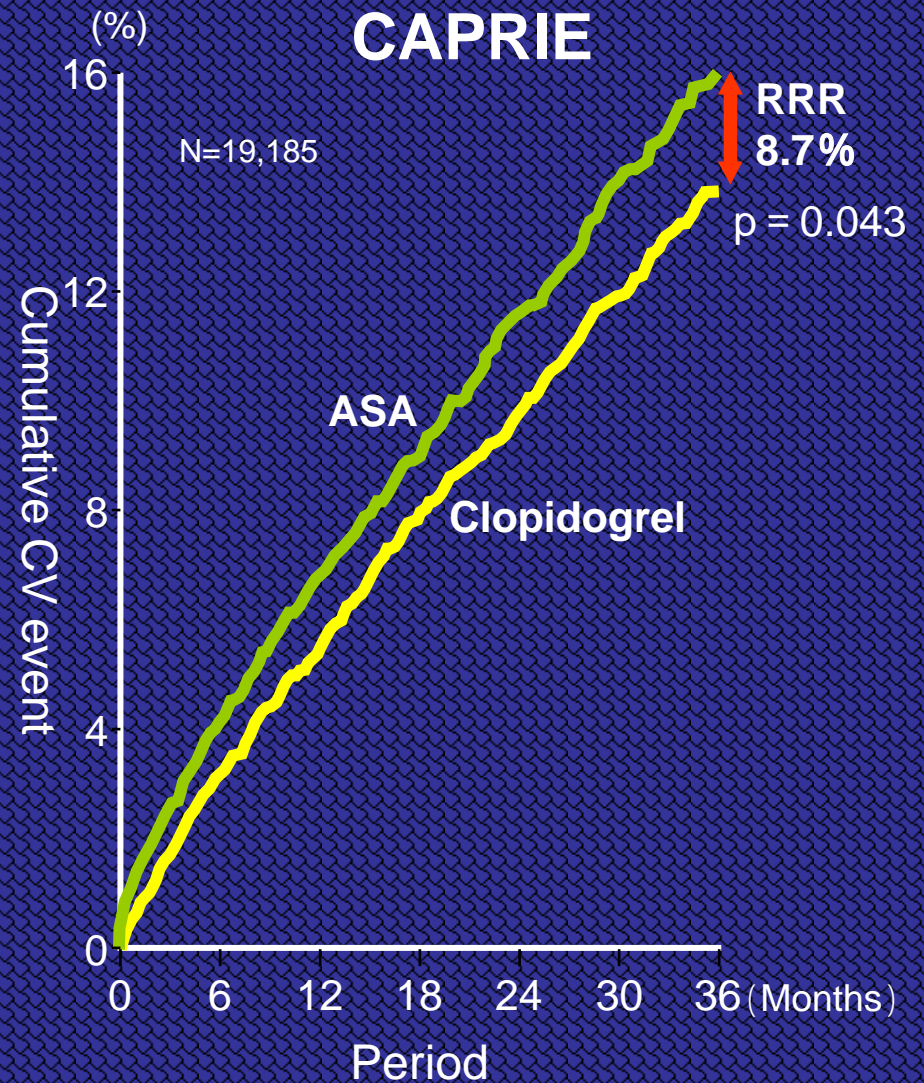
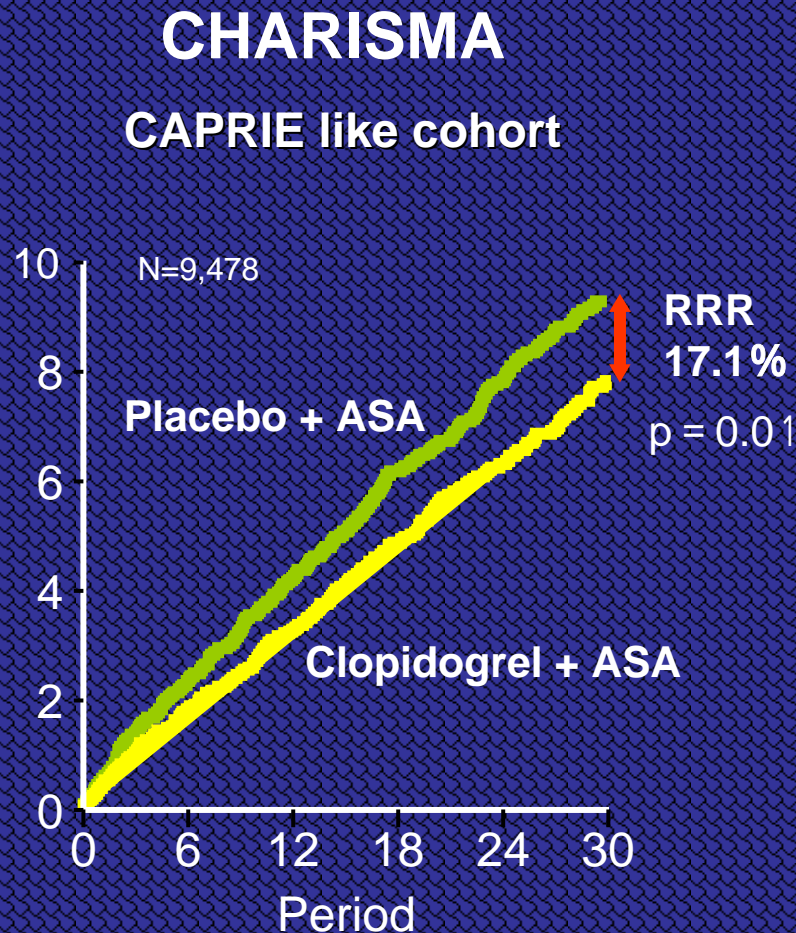
Final angiogram



薬物療法の進歩

Great progress of medical treatment

Event rate has decreased



CHARISMA

Medication use	Plavis+ASA (n = 7,802)	Placebo+ASA (n = 7,801)
ASA	7,775 (99.7)	7,777 (99.7)
Plavix and Placebo	7,750 (99.3)	7,760 (99.5)
Plavix (non blinded)	773 (9.9)	814 (10.4)
-bloker	4,292 (55.0)	4,344 (55.7)
ARB	1,990 (25.5)	2,020 (25.9)
Ramipril	1,387 (17.8)	1,424 (18.3)
ACEI	3,607 (46.2)	3,612 (46.3)
Statins	5,991 (76.8)	6,001 (76.9)
Lipid lowering agent	1,114 (14.3)	1,094 (14.0)
Antidiabetic agent	3,259 (41.8)	3,237 (41.5)

()%

CHARISMA · CAPRIE

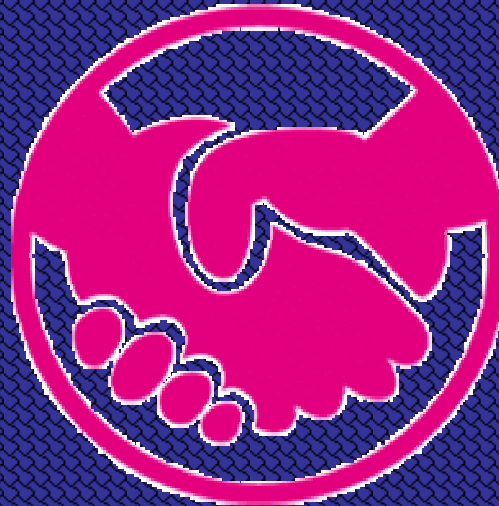
Medication use	Plavis+ASA (n = 7,802)	Placebo+ASA (n = 7,801)	CAPRIE (n=19,185)
ASA	7,775 (99.7)	7,777 (99.7)	
Plavix or placebo	7,750 (99.3)	7,760 (99.5)	-
Plavix (non-blinded)	773 (9.9)	814 (10.4)	
-blocker	4,292 (55.0)	4,344 (55.7)	39.6
ARB	1,990 (25.5)	2,020 (25.9)	-
ラミプリル	1,387 (17.8)	1,424 (18.3)	-
ACEI	3,607 (46.2)	3,612 (46.3)	29.8
Statins	5,991 (76.8)	6,001 (76.9)	25.5
Lipid lowering agent	1,114 (14.3)	1,094 (14.0)	
Anti diabetic agent	3,259 (41.8)	3,237 (41.5)	17.6

()%

Bhatt DL, et al: N Engl J Med 354, 1706-1717, 2006
Eur Heart J 1998;19 suppl 3

New diagram for IHD treatment

Optimal
PCI



Optimal
Medical
treatment