Stent thrombosis, major bleeding and antiplatelet therapy in the e-SELECT registry

1 year follow up of 15,000 patients treated with Sirolimus eluting CYPHER Select plus stent

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On behalf of the e-SELECT investigators

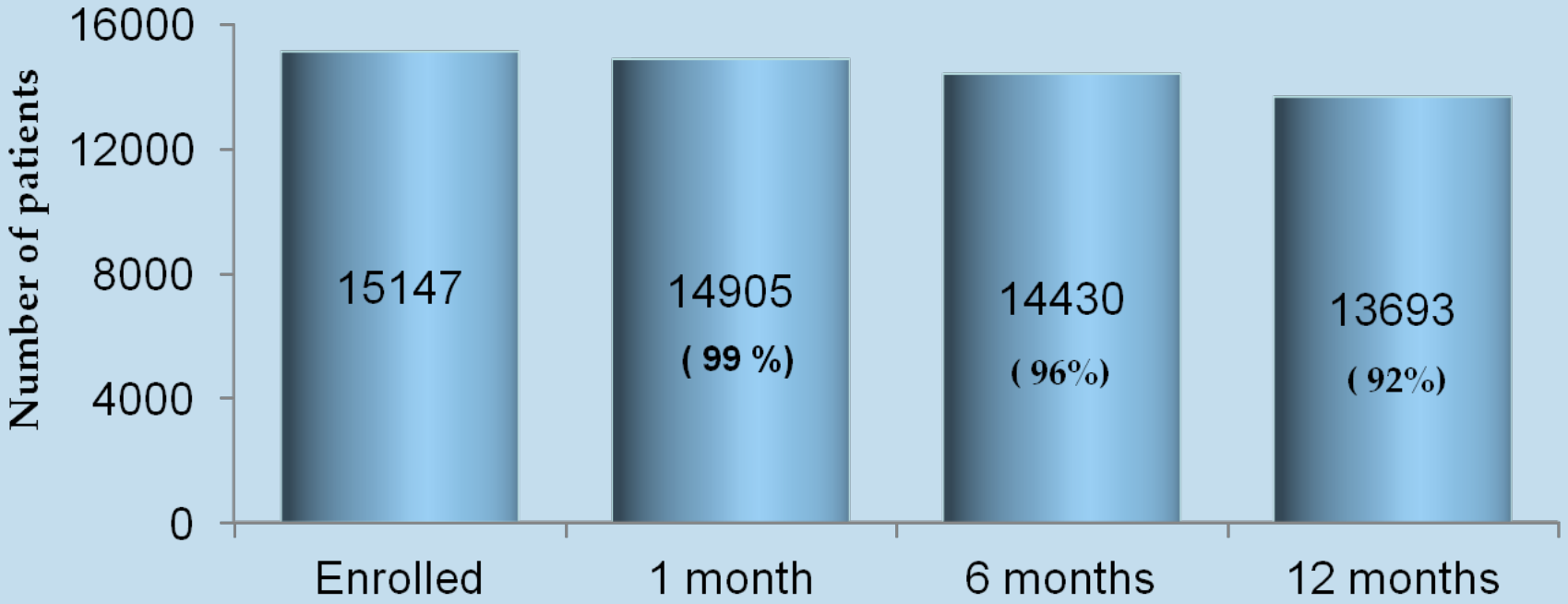
e-SELECT registry design

Design	Multicenter, prospective, observational registry (Clinicaltrials.gov:NCT00438919)
Enrollment	Consecutive patients treated with only CYPHER Select®/CYPHER Select Plus® Sirolimus-eluting stents at index procedure
Patients	15,147 (enrollment completed 30 April, 2008)
Sites	320 sites worldwide from 56 countries (outside US and Japan)
Follow Up	1 month, 6 months, 12 months
Incl./excl. criteria	All-comers
Steering Committee	P. Urban (Chair), A. Abizaid, A. Banning, A. Bartorelli, V. Dzavik, S.G. Ellis, R. Gao, D.Holmes, M.H. Jeong, V. Legrand, F. Neumann, C. Spaulding, S. Worthley
CEC	C. Naber, E. Barbato, L. Jensen, A. Chieffo, V.S. Srinivas, K. Sano
Database	KIKA medical, Nancy
Data analysis	Cardialysis, Rotterdam
Monitoring	Covance [20% = 3000 randomized patients]
Sponsor	Cordis, Johnson & Johnson

Timelines

Enrollment

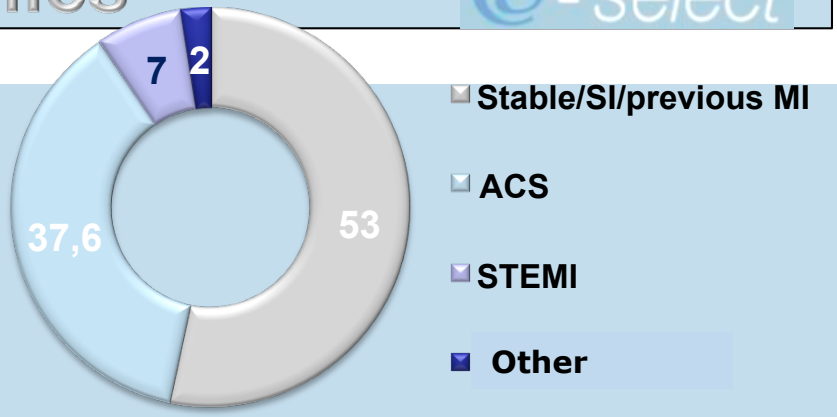
1 year FU



FOLLOW UP VISIT

Baseline demographics

n =15,147 patients



	Stable	ACS	STEMI	ALL
Age	62.3 ± 10.5	62.4 ± 11.2	58.8± 11.9	62.1 ± 10.8
BMI ≥30	24.9%	24.1%	20.9%	24.4%
Diabetes	30.2%	31.6%	26.2%	30.4%
Creatinine>177 umol/l	2.7%	2.8%	1.0%	2.6%
Charlson index ≥3	9.9%	11.2%	7.6%	10.3%
on AVK	2.2%	1.8%	0.8%	2.0%
Prior PCI or CABG	43.3%	41.8%	12%	41.2%
LVEF <30%	1.7%	2.0%	3.1%	1.9%

Charlson index of comorbidities

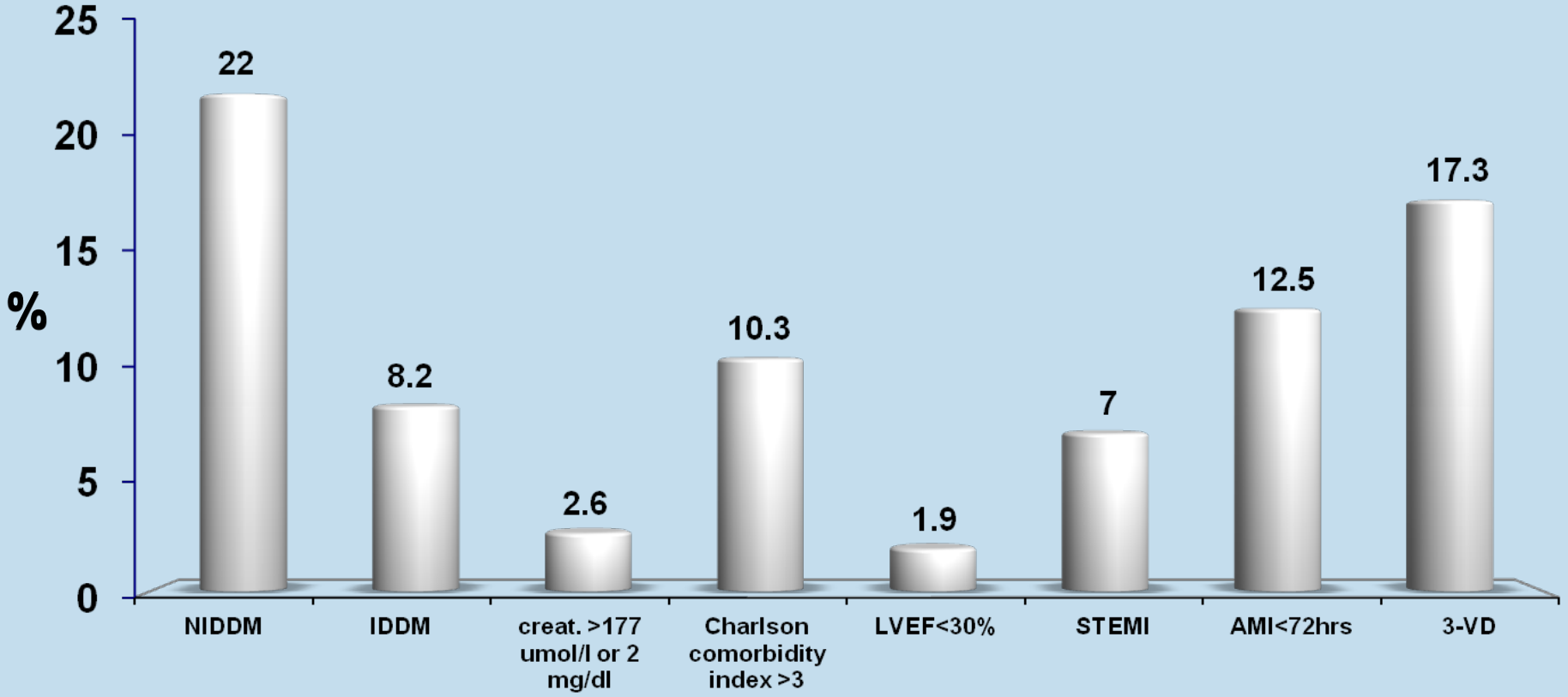
Mean Charlson Score 1.1 ± 1.3

	Points	Nb	%
Prior myocardial infarction	1	4854	32.1%
Congestive heart failure	1	630	4.2%
Peripheral vascular disease	1	941	6.2%
Prior CVA	1	643	4.2%
Hemiplegia	2	35	0.2%
Dementia	1	31	0.2%
Chronic obstructive lung disease	1	597	3.9%
Peptic ulcer	1	423	2.8%
Diabetes (without microvascular damage)	1	3987	26.4%
Diabetes (with microvascular damage)	2	590	3.9%
Moderate to severe liver disease	3	28	0.2%
Moderate to severe renal disease	2	370	2.5%
Malignancy	2	323	2.1%
Metastatic malignancy	6	13	0.1%
AIDS (stage C)	6	4	0.0%

Charlson et al., *J Chronic Dis* 1987; 40:373-83

Patients: clinical subsets

n =15,147 patients

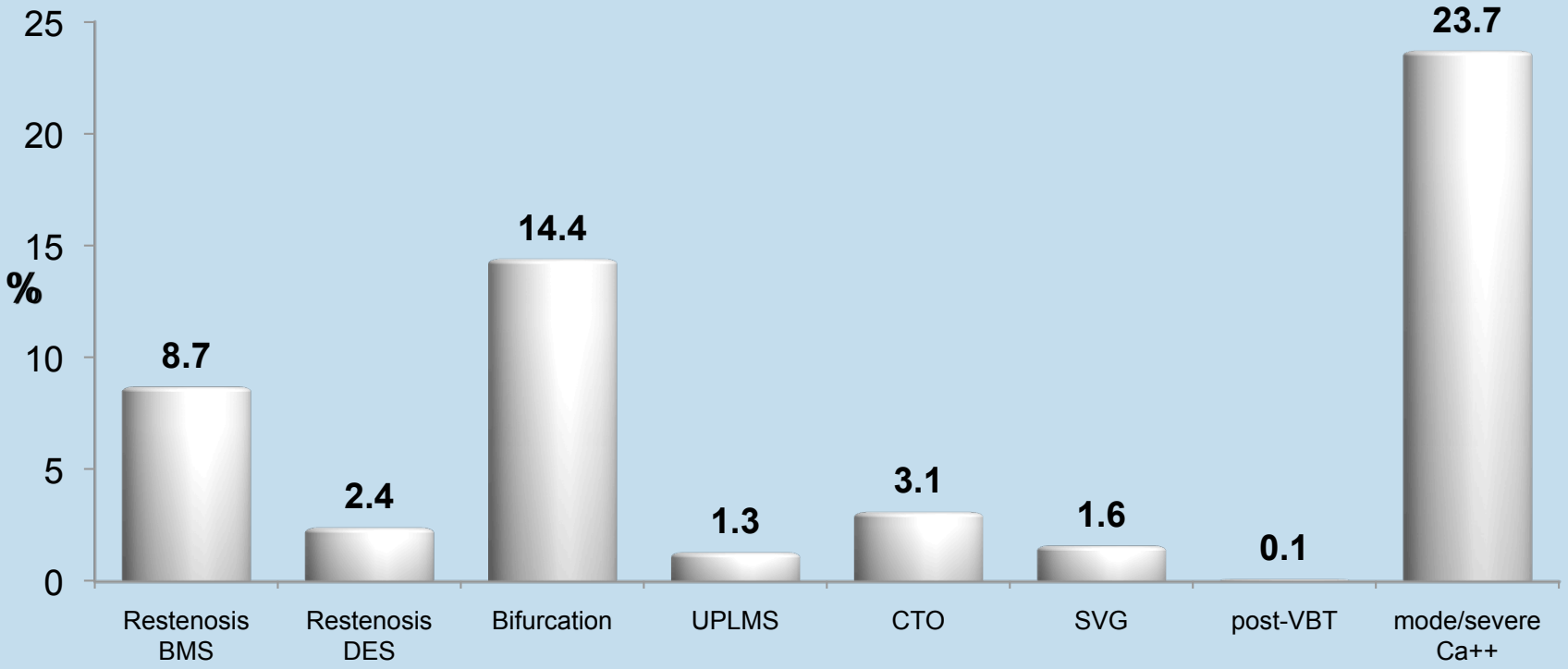


n =	3339	1238	351	1546	246	1062	1891	2627

Angiographic subsets

n =19,988 lesions (1.3 ± 0.6 lesions/patient)

RVD (on-site visual estimate, mm)	2.9 ± 0.4
Lesion length (on-site visual estimate, mm)	20.2 ± 11.6

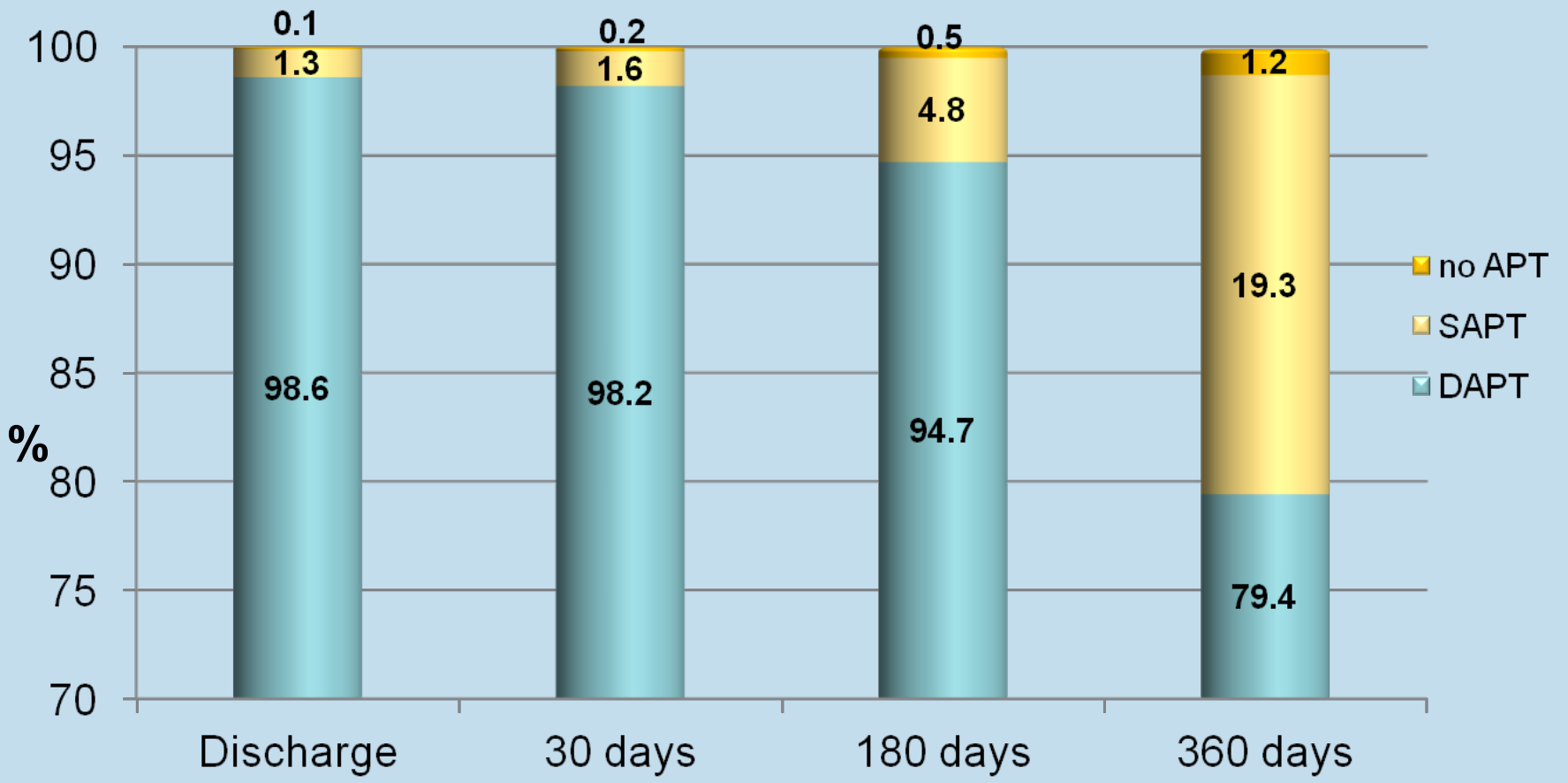


n =	1707	474	2831	253	617	317	9	4202

Procedure characteristics

Multi-vessel procedure	16.1%
Multi-lesion procedure	25.9%
Direct stenting (% lesions)	35.7%
Pressure deployment (atm)	15.5 ± 3.3
Post-dilation (% lesions / atm)	36.1/17.1±4.3
IVUS used (% procedures)	3.7%
RVD (on-site visual estimate, mm)	2.9 ± 0.5
Lesion length (on-site visual estimate, mm)	20.2 ± 11.6
Nominal stent diam/ref diam	1.1 ± 0.2
Total stent length/lesion length	1.4 ± 1.0
Total stent length per patient (mm)	33.5 ± 21.0
Total stent length per lesion (mm)	25.3 ± 13.2
Multiple SES per procedure	38.6%
Procedures with overlapping stents	14.7%

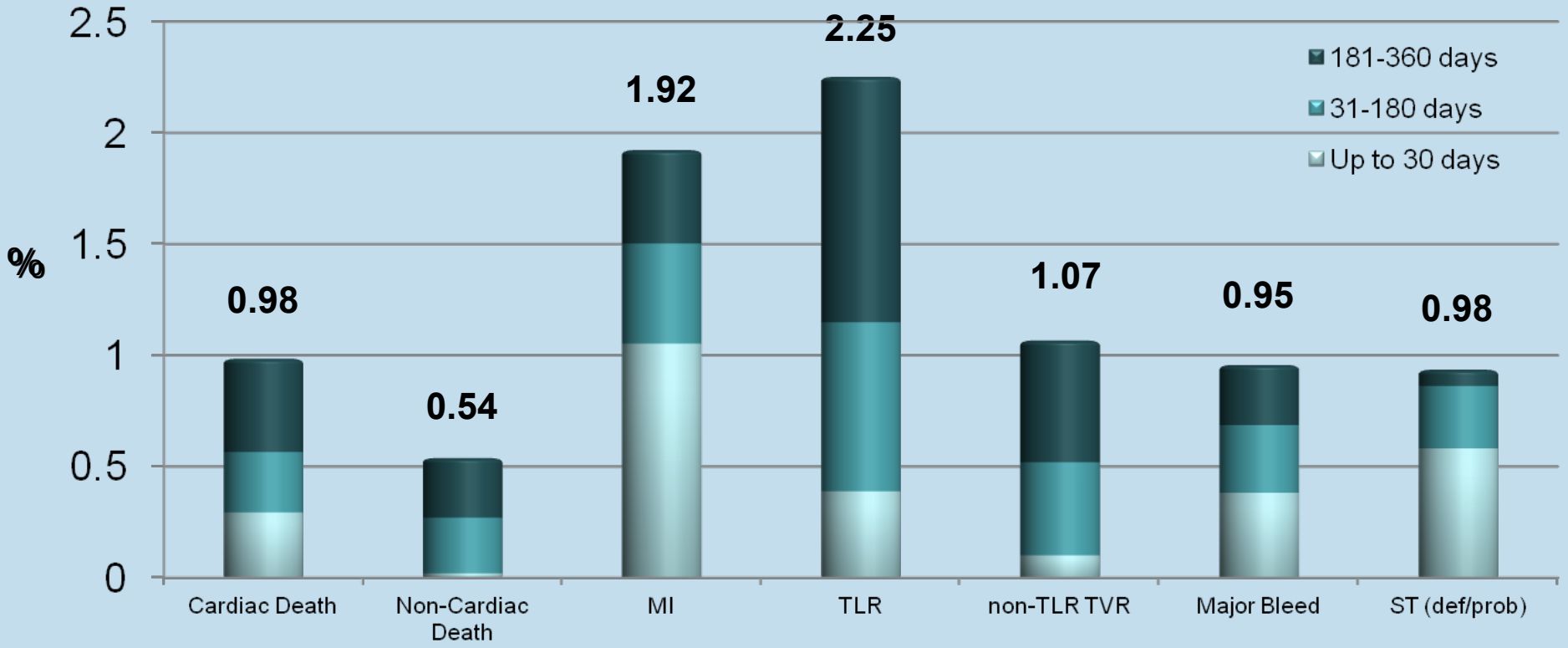
Antiplatelet Regimen



2% of patients were discharged on AVK
1,9% were taking AVK at 30 days, 2.2 % at 180 days, and 2.4 % at 360 days.

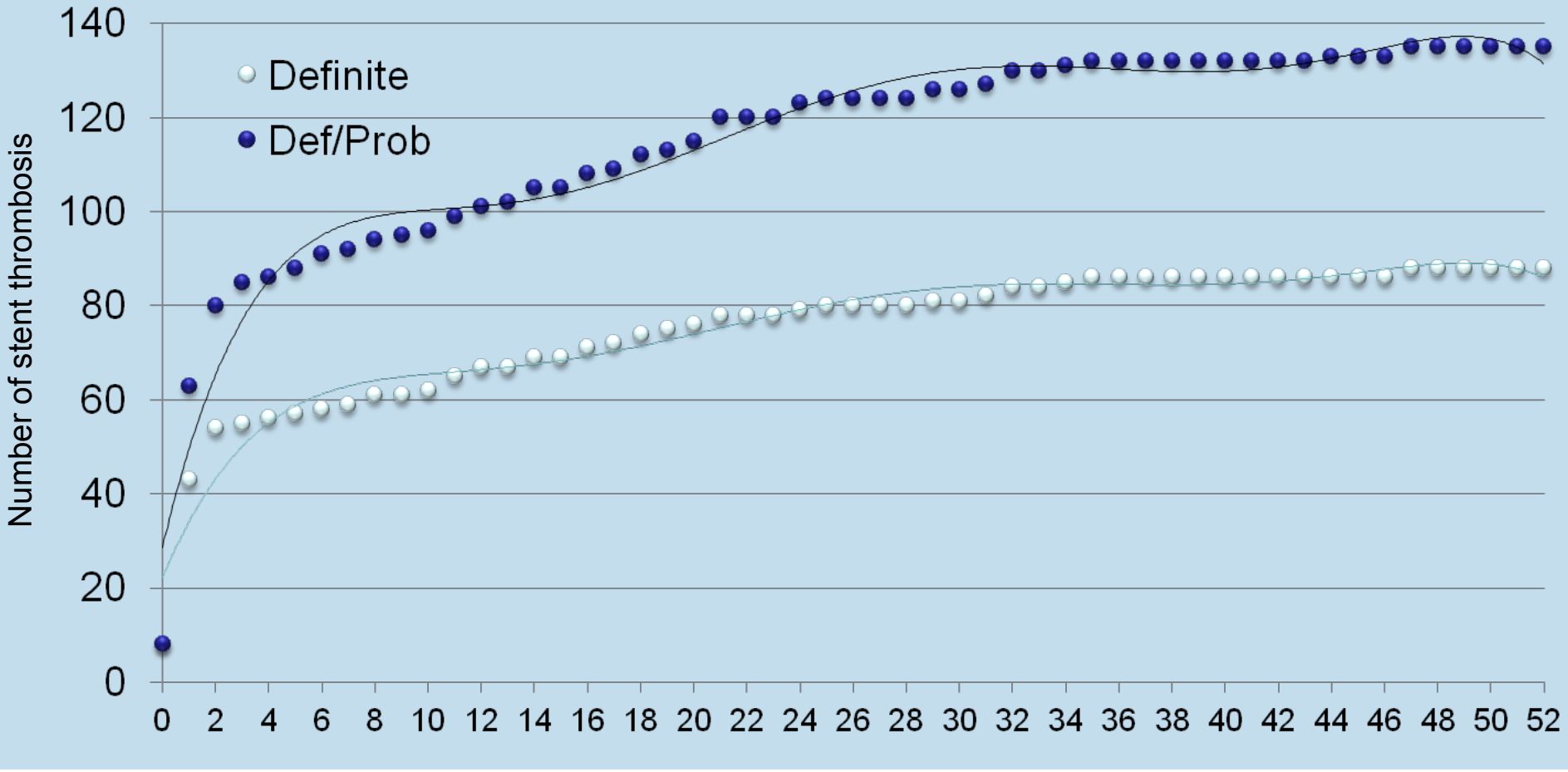
Adverse Events

CEC-adjudicated events

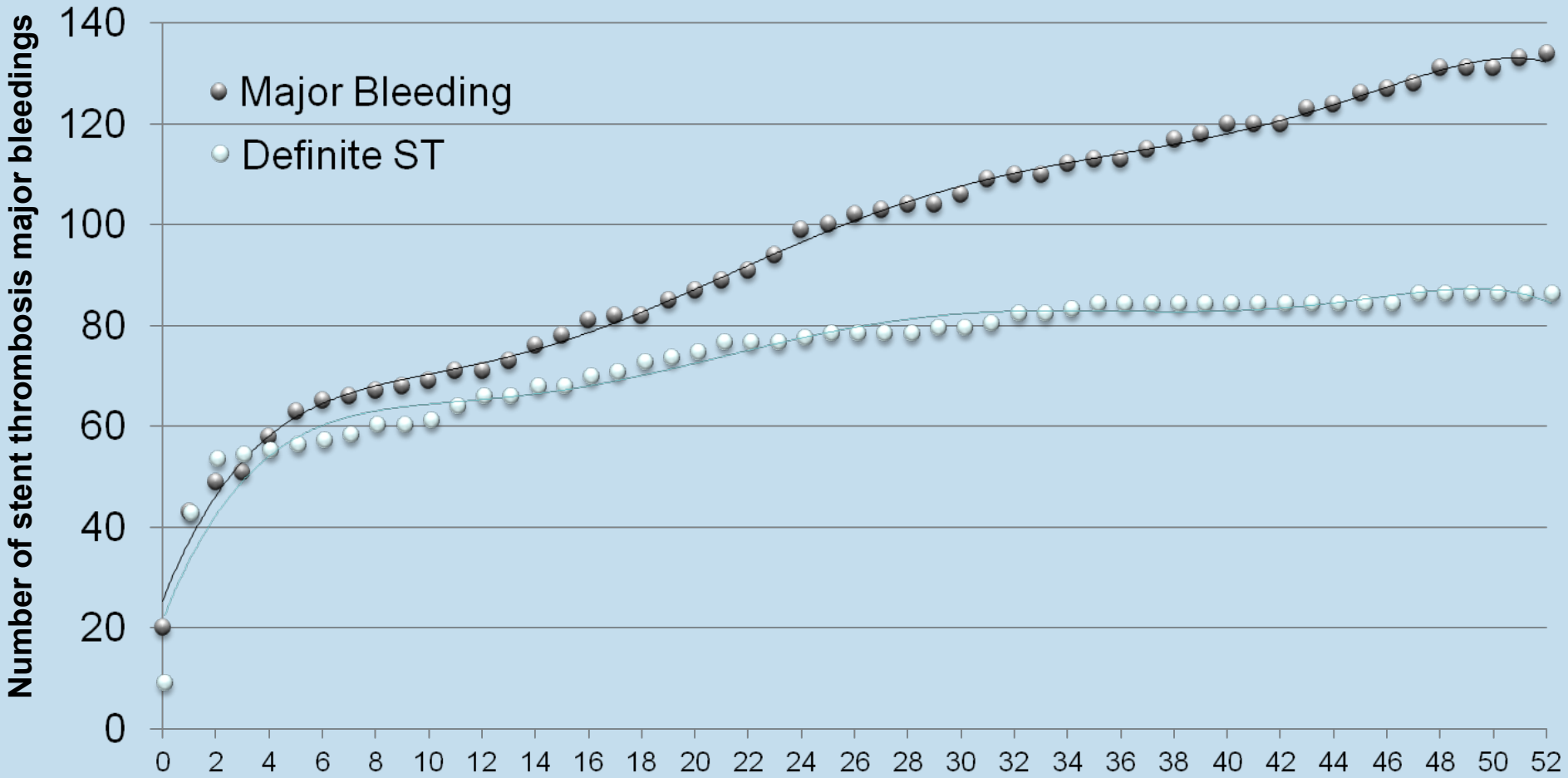


Timing of stent thrombosis

87 (64%) ST (def+prob) occur during the first month after stent implantation

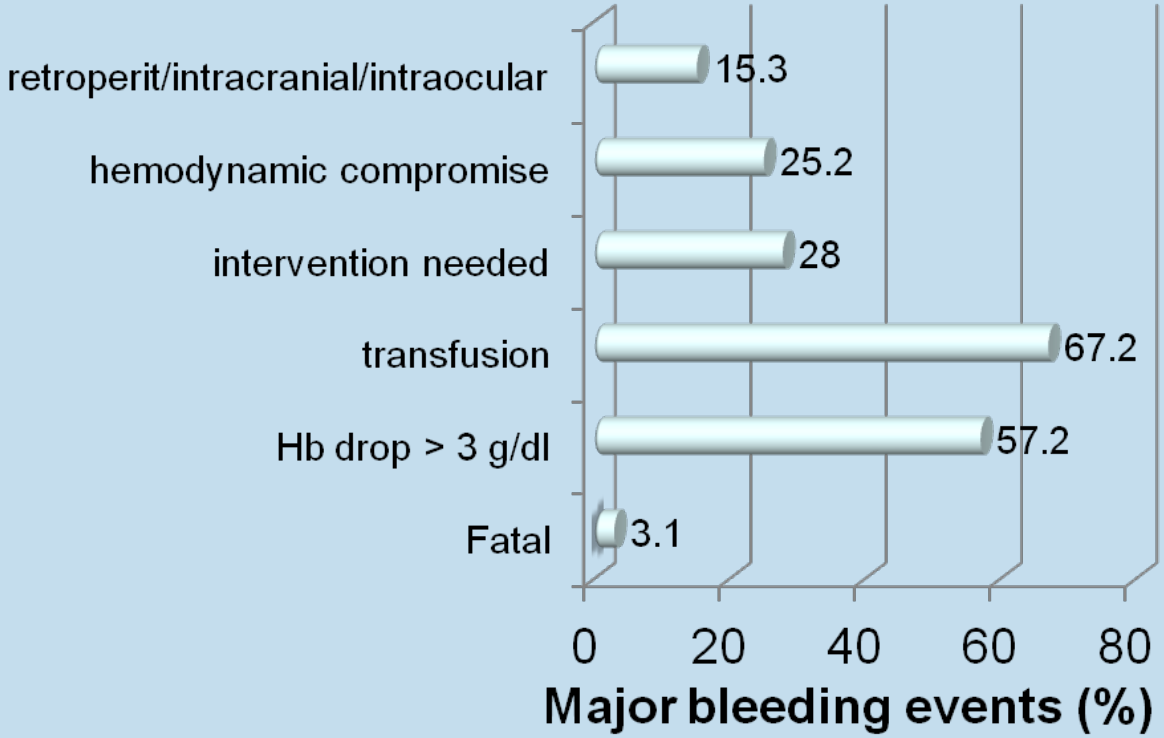


Timing of ST and MB



Major bleeding at 360 days

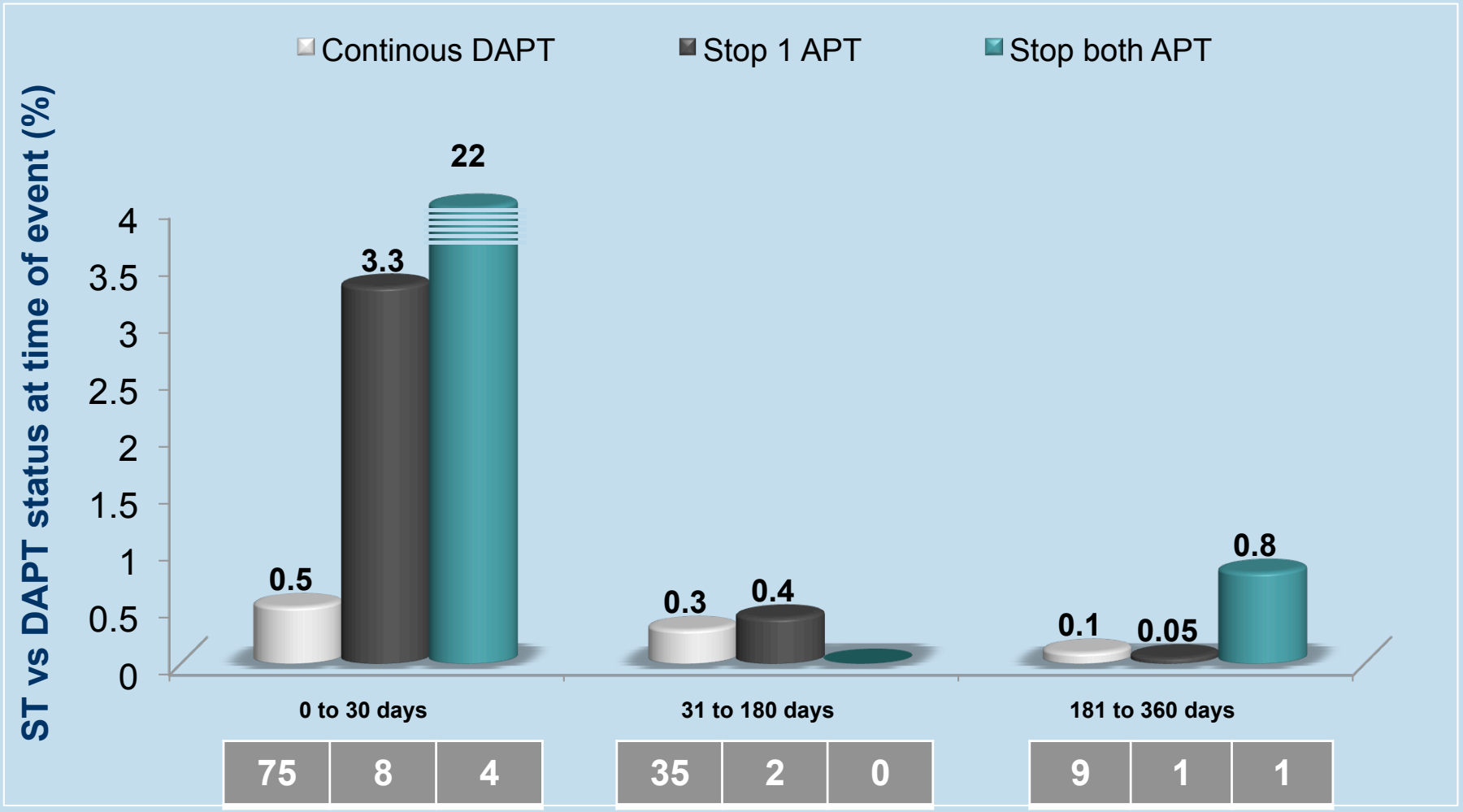
134 major bleeding events = 1.0 %



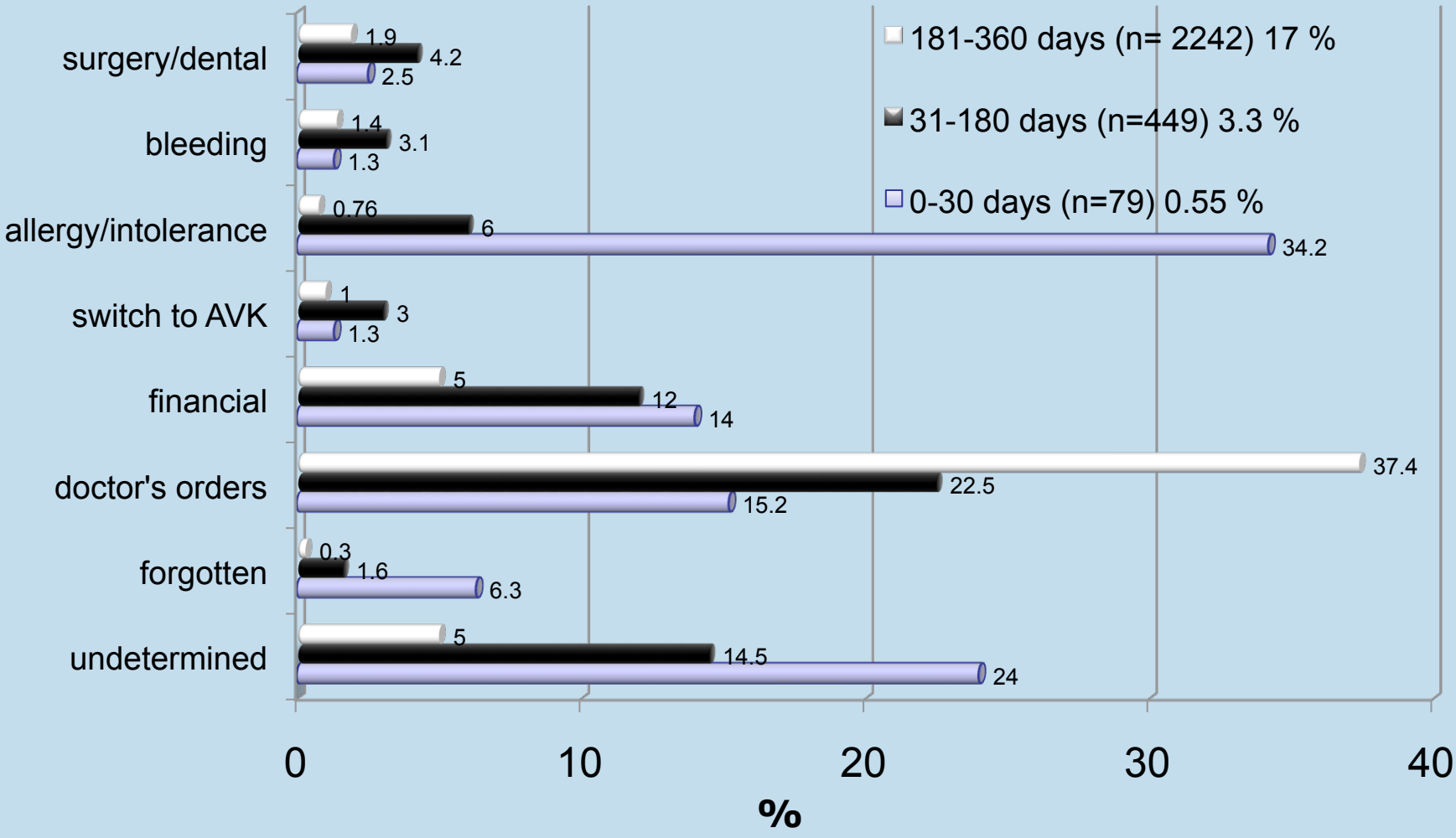
For patients on treatment:
32 % stopped aspirin
30 % stopped thienopyridine
63 % stopped AVK

STEEPLE definition of major bleeding Montalescot G. at al, NEJM 2006;355:1006-17

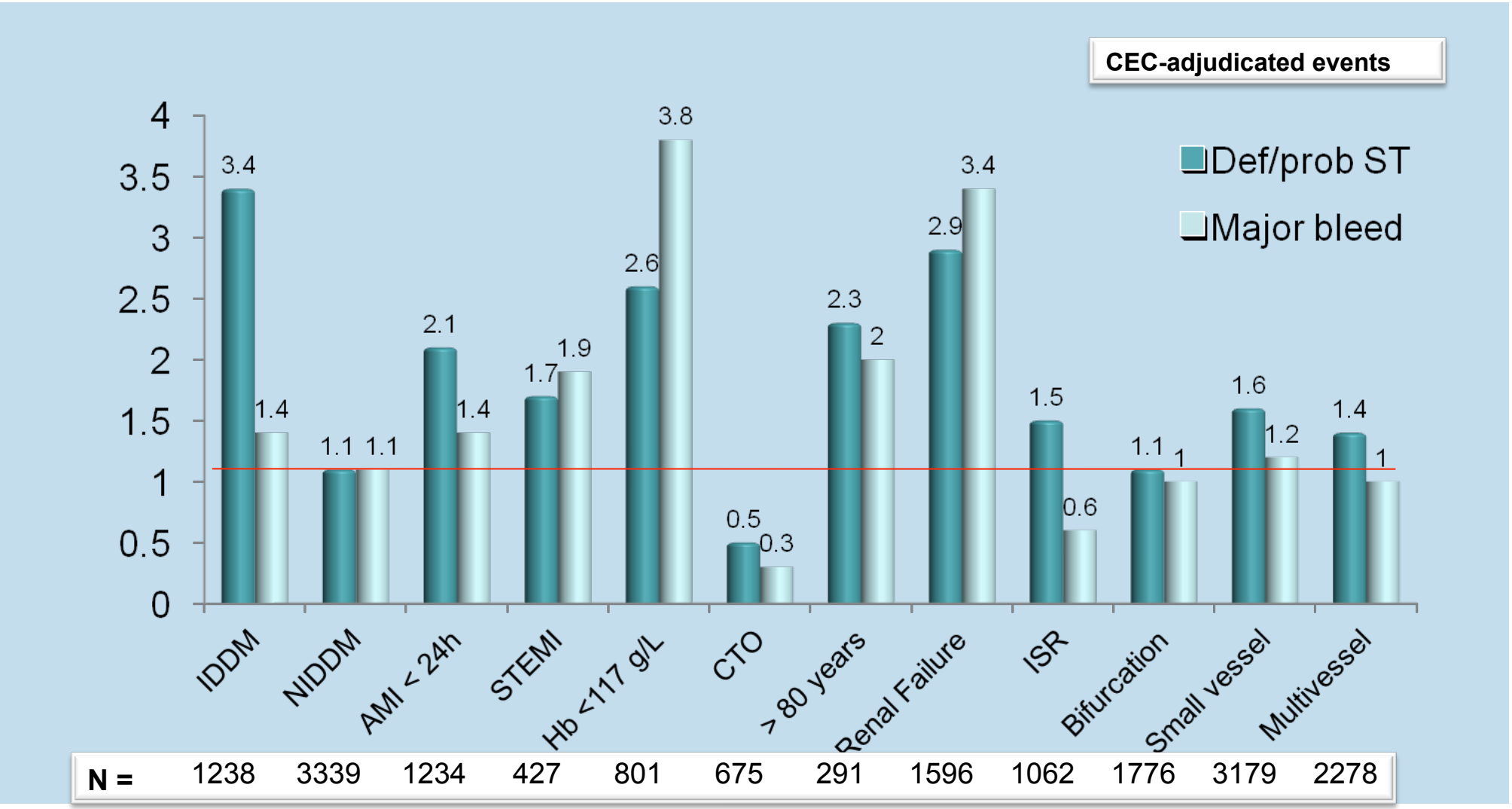
ST risk and DAPT compliance



Reasons for Clopidogrel discontinuation



ST and major bleeding at 360 days

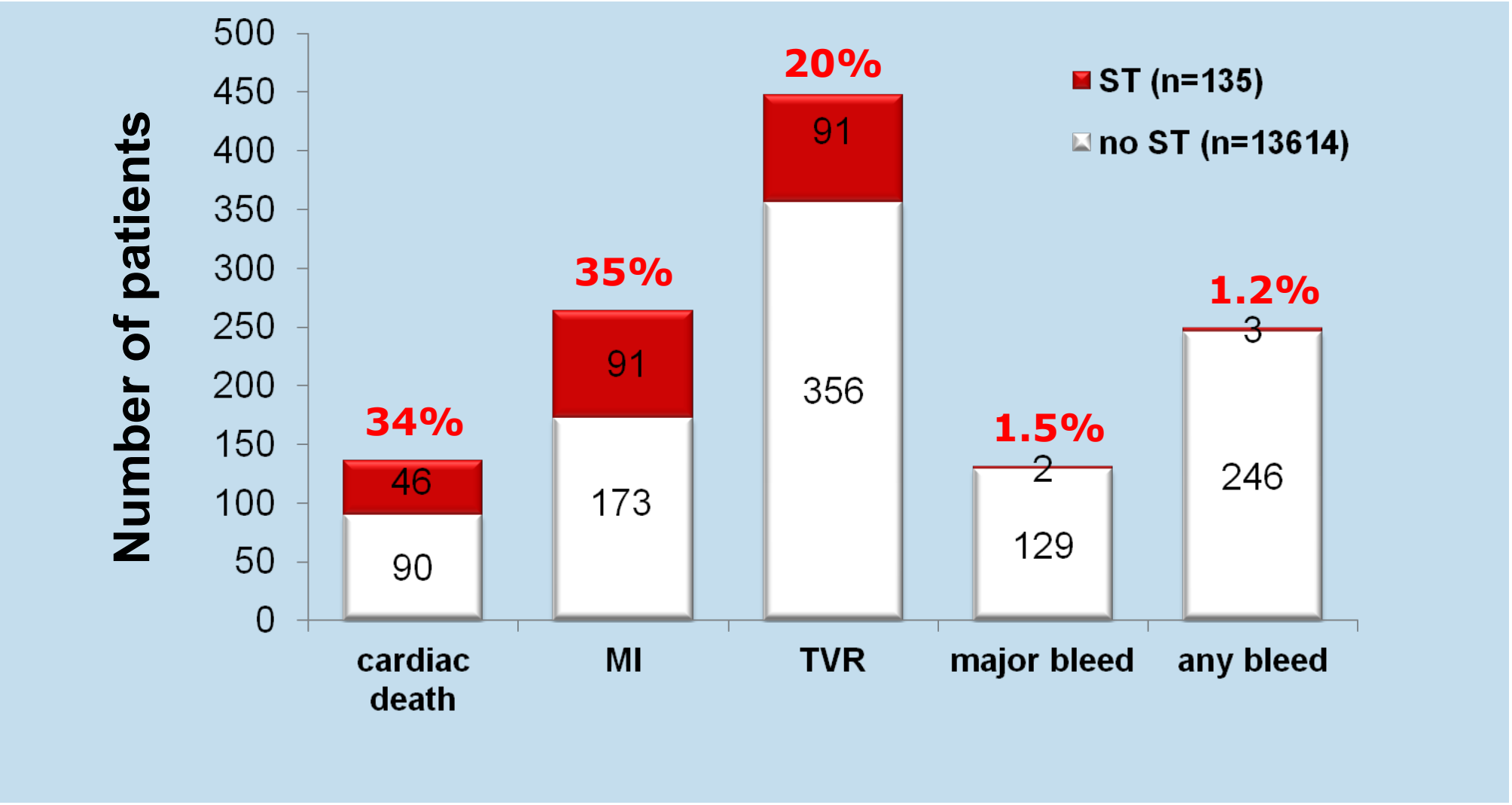


ST assocation with adverse events

	def/prob ST (135)	No def/prob ST (13,614)	Total (13,749)
34% Cardiac death	46	90	136
35% Myocardial Infarction	91	173	264
20% TVR	91	356	447
1.5% Major bleeding	2	129	131
1.2% Any bleeding	3	246	249

During entire FU (0-360 days)

ST association with main adverse events



Conclusions I

- ✓ **The e-SELECT registry is the first study to document the relative importance of both stent thrombosis and major bleeding in a large cohort of all-comer PCI patients treated with a DES. These patients demonstrate a low rate of ST and MB following successful implantation of one or several SES, together with excellent compliance with the current ESC PCI guidelines for anti-platelet therapy.**
- ✓ **Interrupting DAPT during the first 30 days is associated with a marked increase in the risk of ST. Beyond 180 days, stopping one APT drug in some patients appears safe, but the risk of stopping both APT drugs probably remains high.**

Conclusions II

- ✓ **Many of the predictors of ST are also predictors of major bleeding, yet individual patients only rarely suffer both complications during a one year follow-up period. It thus appears that patients are either « bleeders » or « clotters », but not both.**
- ✓ **In agreement with numerous registries and randomized trials, the majority of ST events occurs within the first 30 days, and their incidence became comparatively rare beyond the first 6 months. Conversely, the slope of the MB curve is quite steady, and shows no inflexion at 6 months.**
- ✓ **This begs the question of how necessary DAPT still is beyond the first 6 months after implantation of SES, since the persistent bleeding risk associated with prolonged DAPT must be weighed against the potential protection against ST.**