Carotid Stenting 2012

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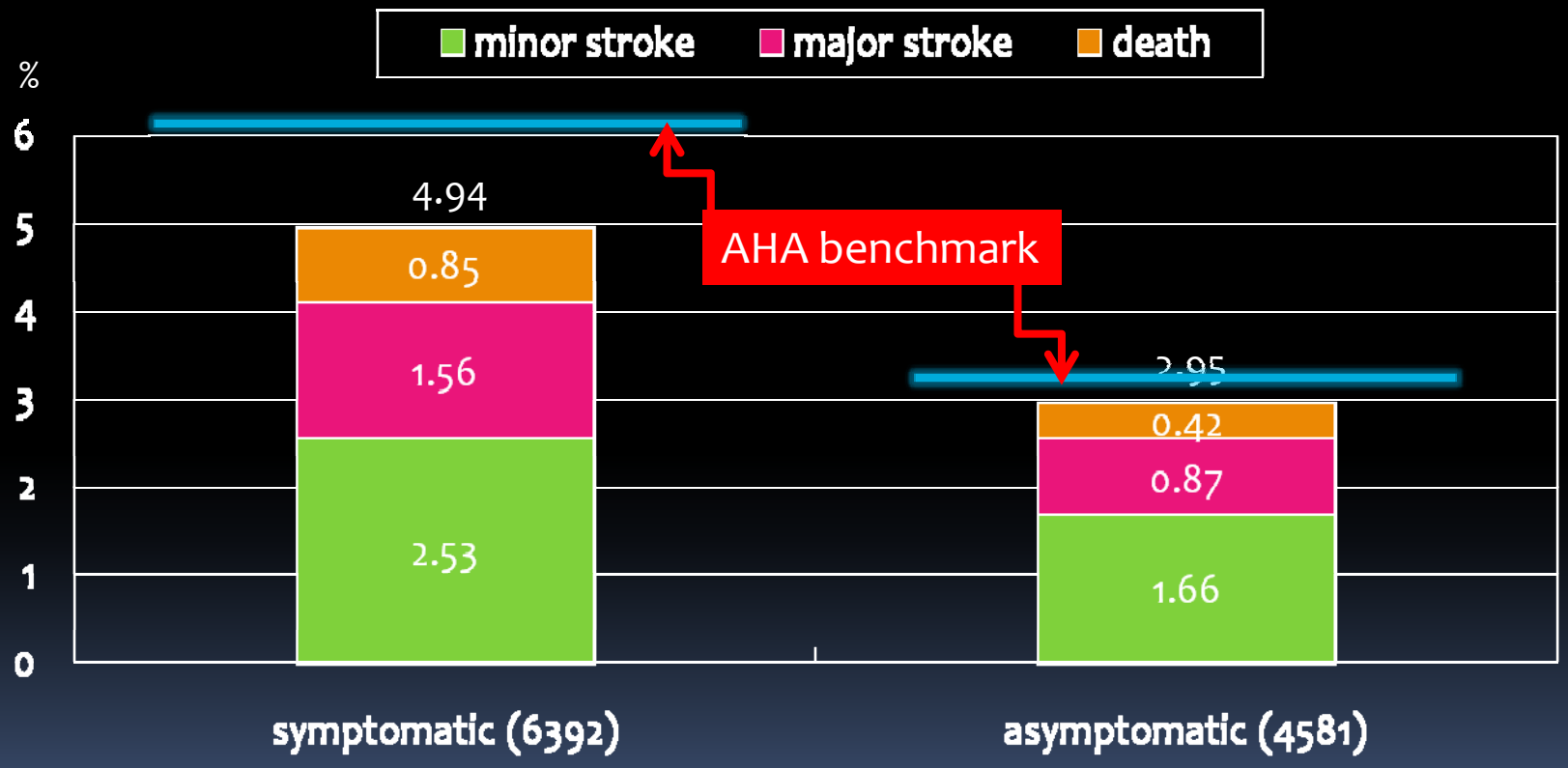
The long and winding road for CS

- Ever since its introduction, carotid artery stenting (CS) has been challenged by surgeons
- Numerous registries and a few high- quality trials have demonstrated the value of CS, especially for high surgical risk patients undergoing arotid endarterectomy (CE)

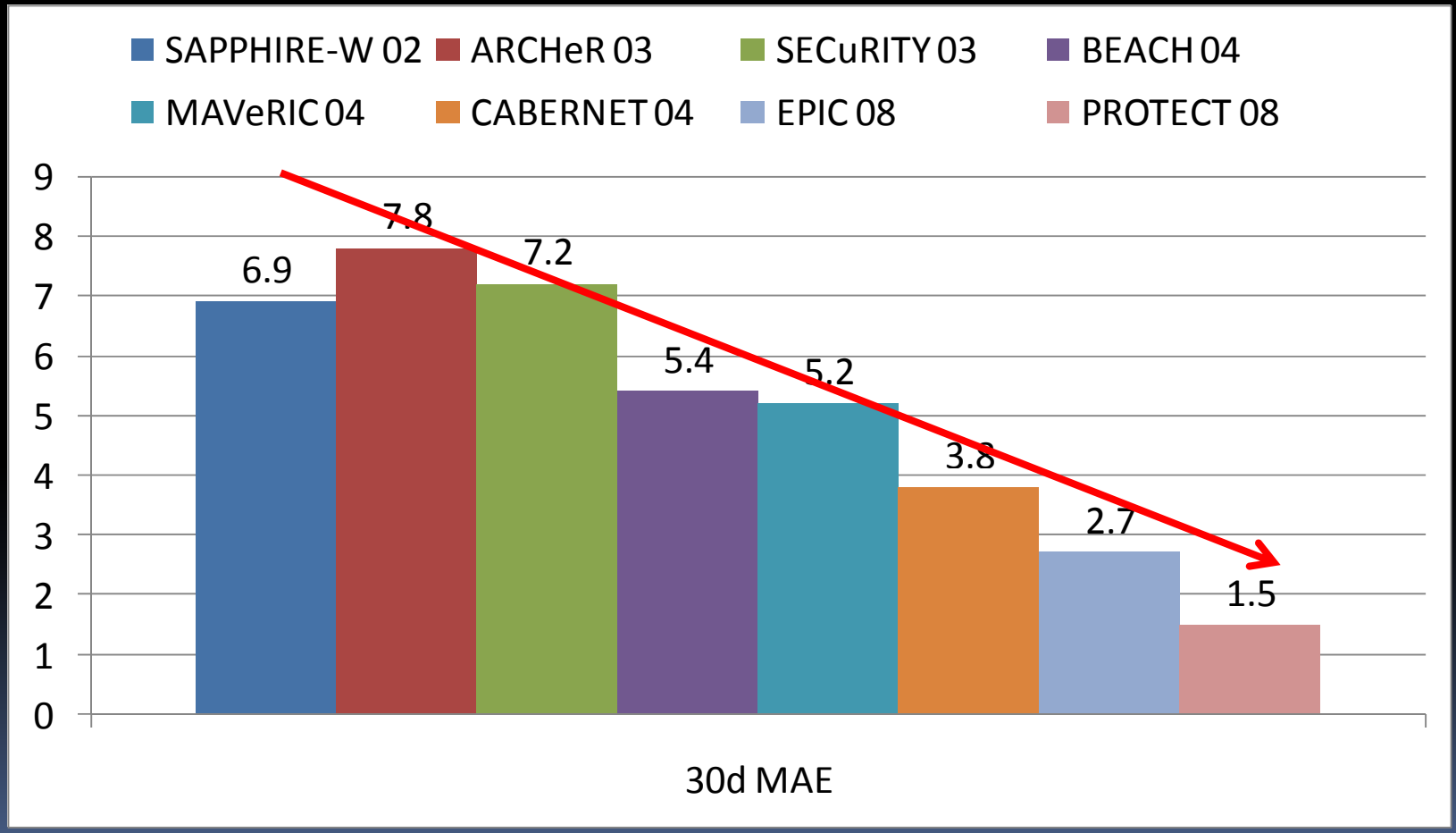
- But believe me, you will still hear surgeons asking for more trials

Global CS experience (30d events)



Wholey et al. CCI 2003

MAE in high surgical risk CS registries



CE vs. CS registries

- CaRESS: Prospective comparative cohorts

Zairns et al, J Endovasc Ther 2009;16:397

No difference at all

- REAC… …ensity-matched registries

CS vs CE	Death/stroke	Stroke/TIA	Death/MI/stroke	Death	Stroke
RR @2y	0.85	1.20	0.72	0.63	1.48
95% CI	0.57-1.26	0.73-1.96	0.51-1.01	0.40-1.00	0.79-2.80

Banglore et al, Circulation 2010;122:1091

"Latest" registries

- CAPTURE 2:
  - 3388 <80y asym pts in 180 US sites (459 operators)
  - 2/3 sites without any 30d death/stroke
  - Operator with >72 cases/y 30d death/stroke <3%

Gray et al. J Am Coll Cardiol Intv. 2011;4:235

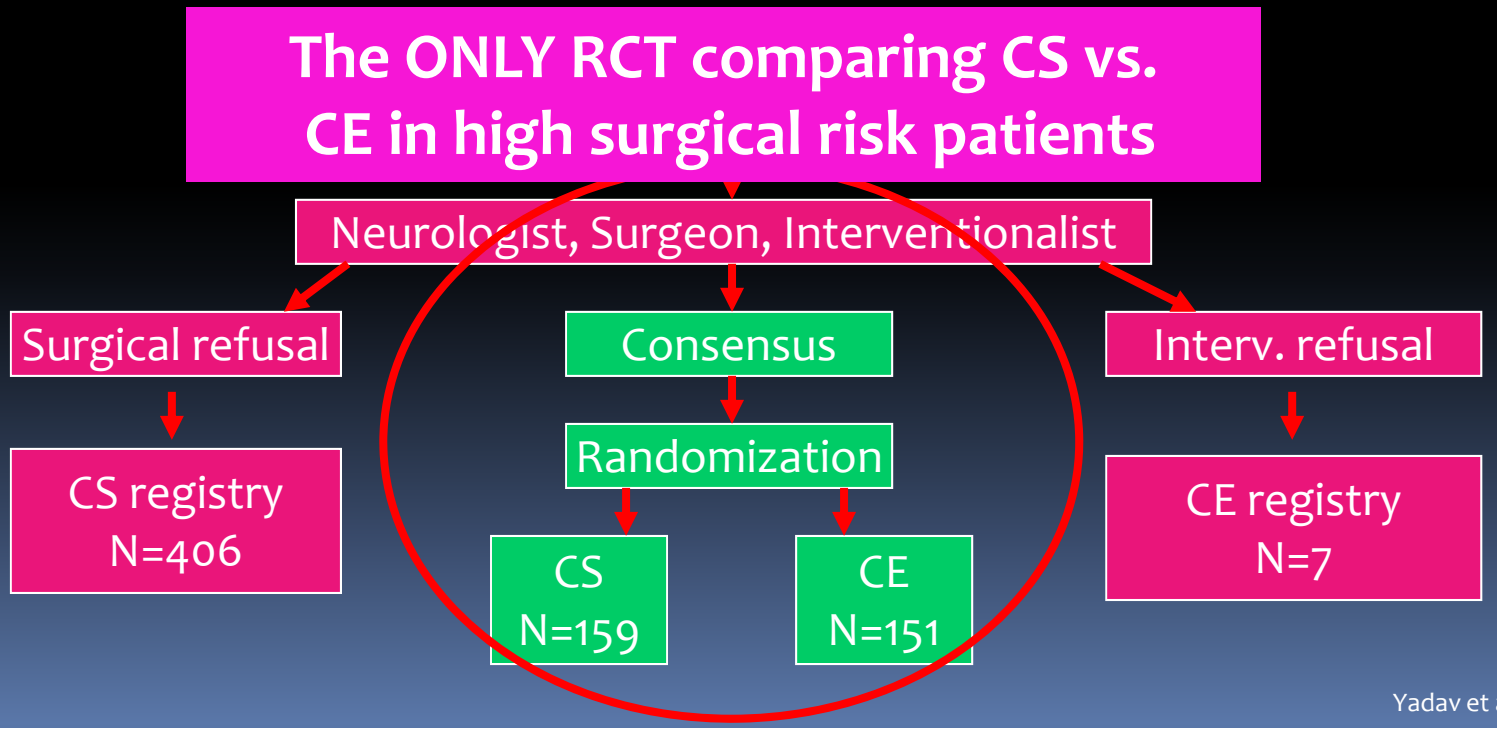
- Long term stroke prevention vs. CE:

	CS (1084)	CE (1118)	P
30d death/stroke	2.8%	2.0%	0.27
30d death/stroke + 5y ipsi stroke	3.7%	4.7%	0.4

De Rango et al. J Am Coll Cardiol. 2011;57:664

SAPPHIRE design

- RCT and parallel registries in high risk patients
- Primary end point: (30d D/S/MI+1y ipsi. S+1y D)
- Non-inferiority hypothesis



Yadav et al. NEJM 2004

30d results

	CS (n=159)	CE (n=151)	P
Death	1 (0.6)	3(2.0)	0.29
Stroke	5 (3.1)	5 (3.3)	0.94
major ipsi	0	2 (1.3)	0.15
major non-ipsi	1 (0.6)	1 (0.7)	0.97
minor ipsi	4 (2.5)	1 (0.7)	0.20
minor non-ipsi	1(0.6)	1 (0.7)	0.97
MI	3 (1.9)	10 (6.6)	0.04
Q	0	2 (1.3)	0.15
Non-Q	3 (1.9)	8 (5.3)	0.11
D/S/MI	7 (4.4)	15 (9.9)	0.06
Major vascular complication	2 (1.3)	1 (0.7)	0.60

Yadav et al. NEJM 2004

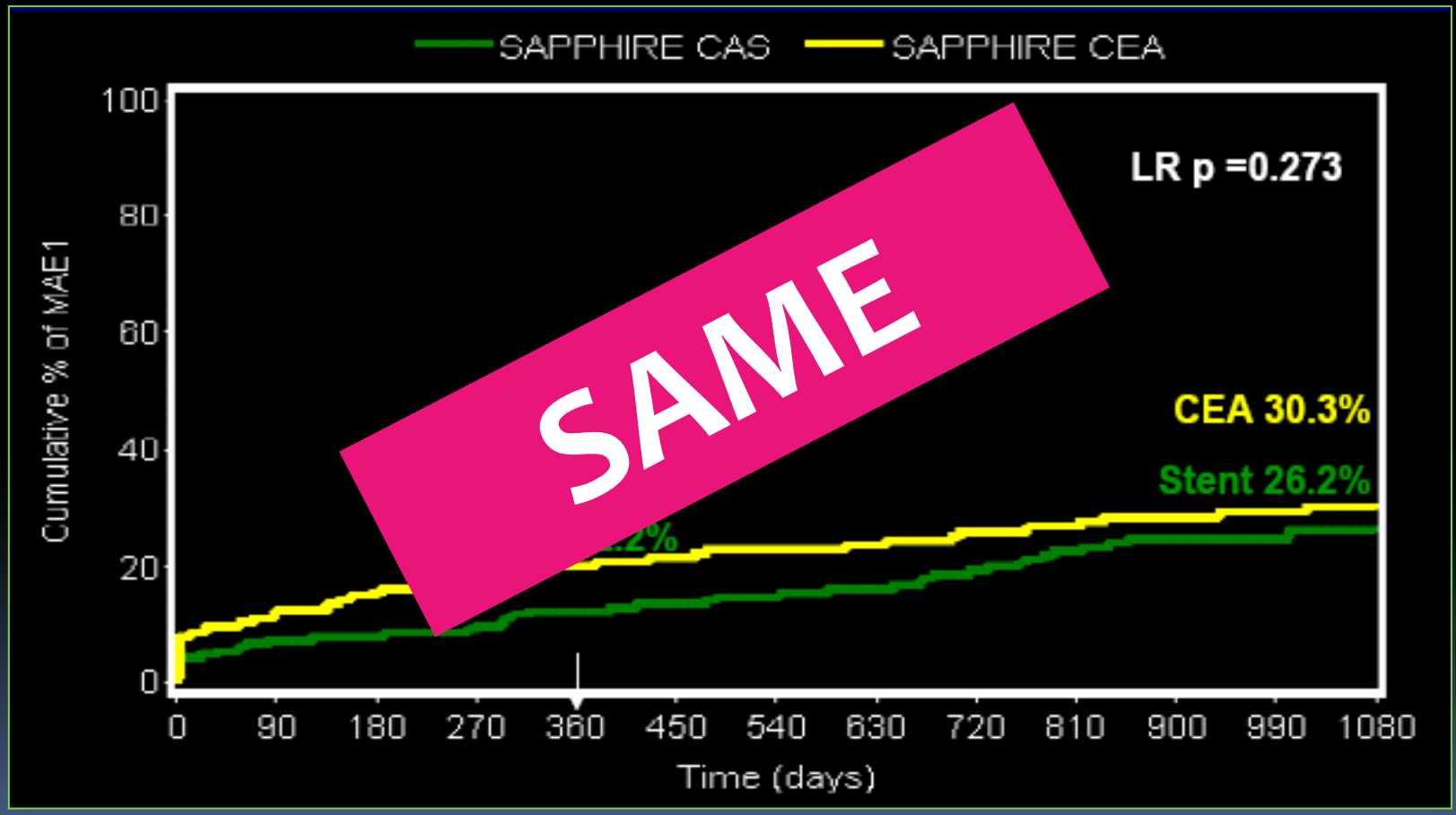
1y results

	CS (n=159)	CE (n=151)	P
Death	11 (7.0)	19 (12.9)	0.08
Stroke	9 (5.8)	11 (7.7)	0.52
major ipsi	0	5 (3.5)	0.02
major non-ipsi	1 (0.6)	1 (0.7)	0.97
minor ipsi	6 (3.8)	3 (2.2)	0.37
minor non-ipsi	3 (2.0)	3 (2.1)	0.89
MI	4 (2.5)	12 (8.1)	0.03
Cranial nerve palsy	0	8 (5.3)	0.003
TVR	1 (0.7)	6 (4.6)	0.04
30d D/S+1y ipsi S+1y neuro D	8 (5.1)	11 (7.5)	0.40
30d D/S/MI+1y ipsi S+1y neuro D	19 (12)	30 (20.1)	0.048

Primary end point non-inferiority p=0.004

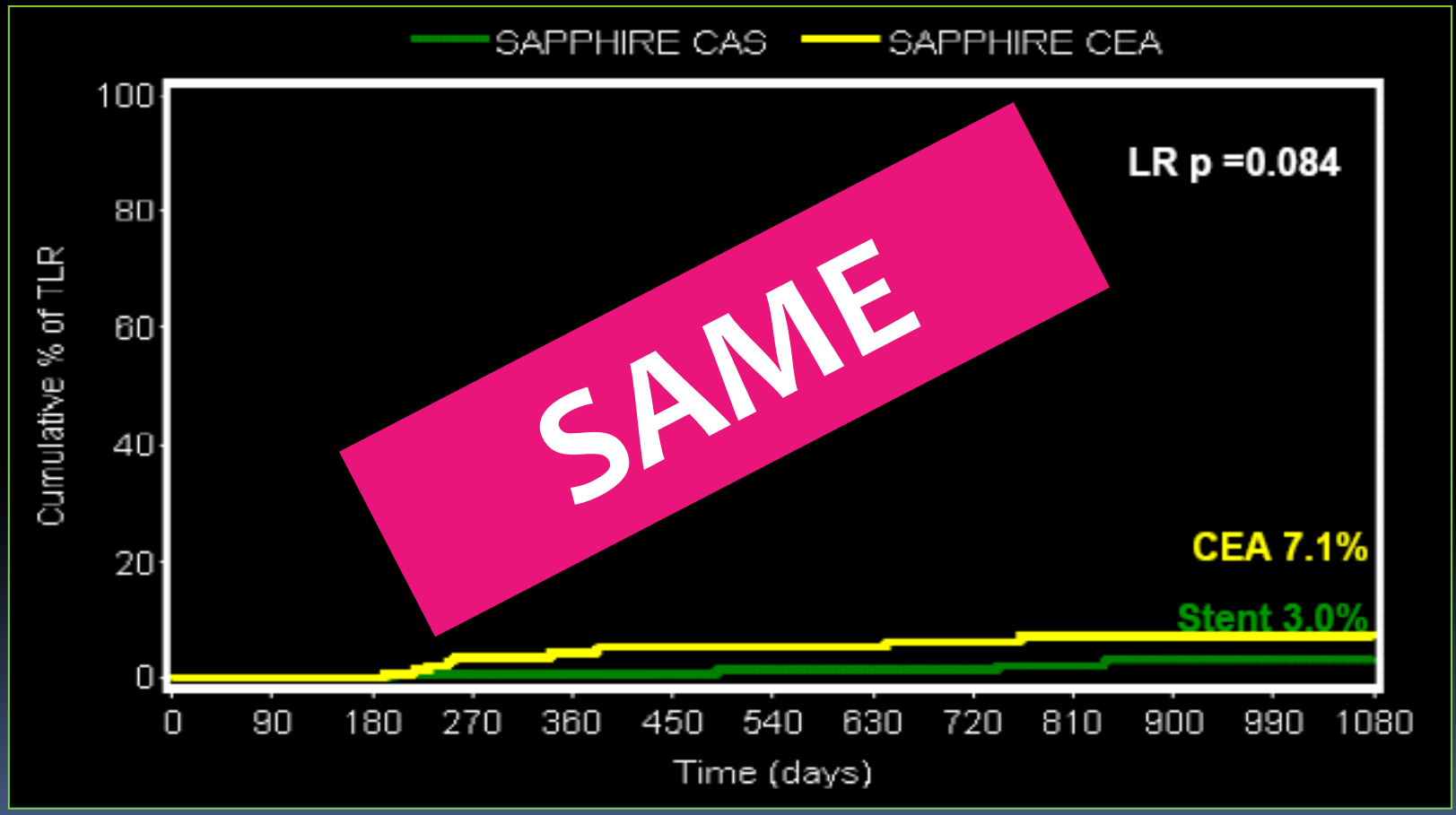
Yadav et al. NEJM 2004

3y MAE



Gurm et al. NEJM 2008

3y TLR



Gurm et al. NEJM 2008

What SAPPHIRE tells us

- In high surgical risk patients (up to 70% of the real-world cases) CS and CE are equivalent in stroke and neurological death prevention at 3y
- But CE does results in more MI and cranial nerve palsy, which are not insignificant

Then the surgeons strike back

- EVA-3S Mas et al. NEJM 2006
  - Sx >60% average surgical risk, stopped at 527 cases
  - 30d D/S rate significantly higher in CS (9.6% vs. 3.9%, p=0.01) and "unethical to continue"
- SPACE SPACE collaborative group Lancet 2006
  - Sx >50% average surgical risk, stopped at 1200 cases
  - "Absence of further funding and futility to continue"
  - 30d D/S rates similar (6.81% CS vs. 6.34% CE, p=0.09)
  - "CS was not proven to be non-inferior to CE"

ICSS (interim analysis)

- 1713 average surgical risk symptomatic patients randomized, EPD not mandatory
- Primary endpoints: death/disabling stroke @3y

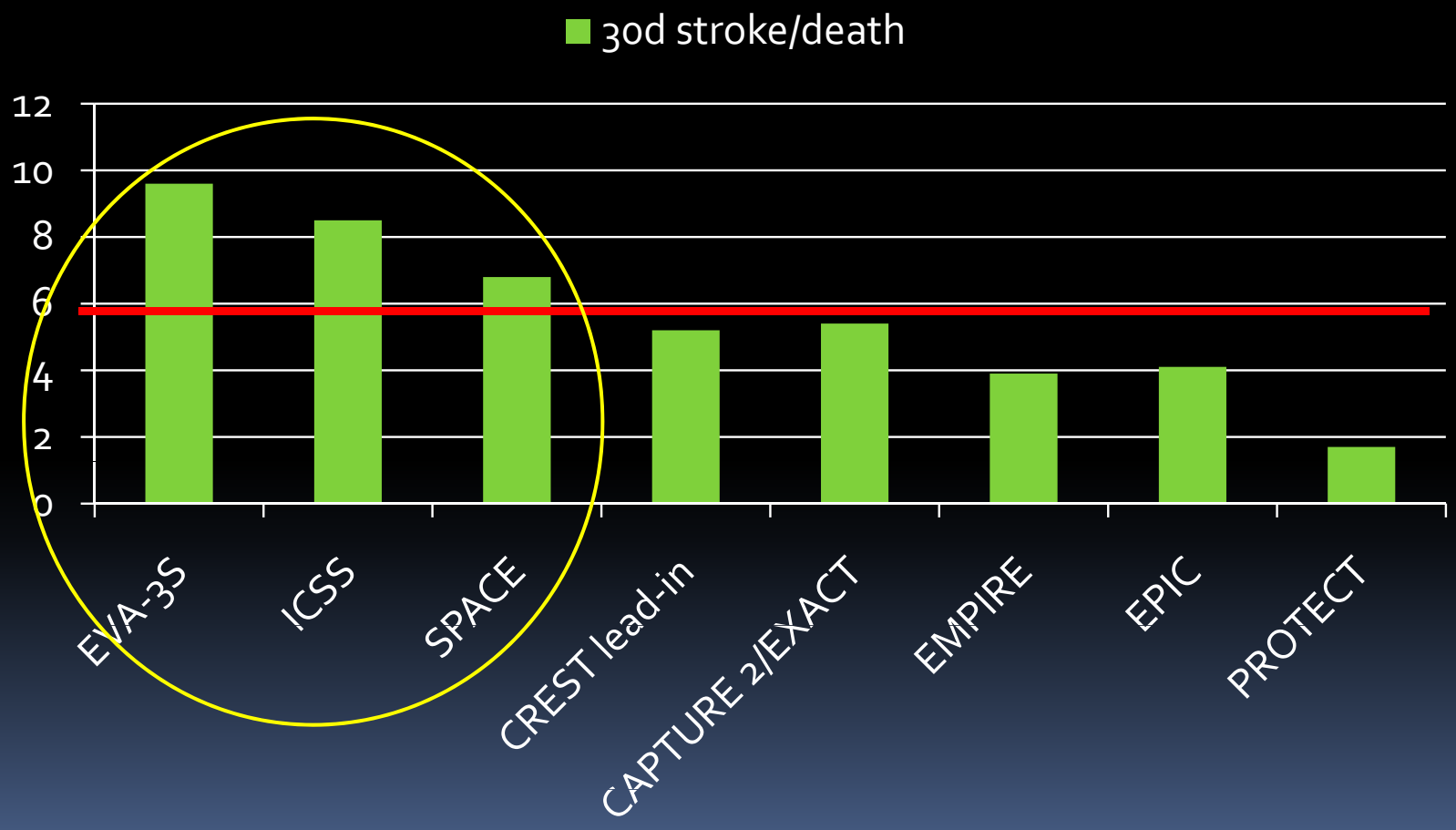
	CS (855)	CE (858)	P
120d death/disabling stroke	4%	3.2%	0.34
death/stroke/MI	8.5%	5.2%	0.006
death	2.3%	0.8%	0.017
Any stroke	7.7%	4.1%	0.002
cranial nerve palsy	0.1%	5.2%	<0.0001
severe hematoma	1.1%	3.3%	0.0007

Lancet 2010;375(9719):985–97

BUT EVA-3S/SPACE/ICSS…

- Are all incomplete studies!!
- In-experienced (even tutored) interventionists allowed, and tutored case counted
  - 1.7 CS/site/year and 5% emergent conversion to CE in EVA-3S
  - 2 sites produced 5 (out of their 11 cases) of the 17 major strokes in ICSS
- Allow CS without embolic protection
- In fact, SPACE tells us "it is futile to prove any difference between CS and CE"

European "outliers"



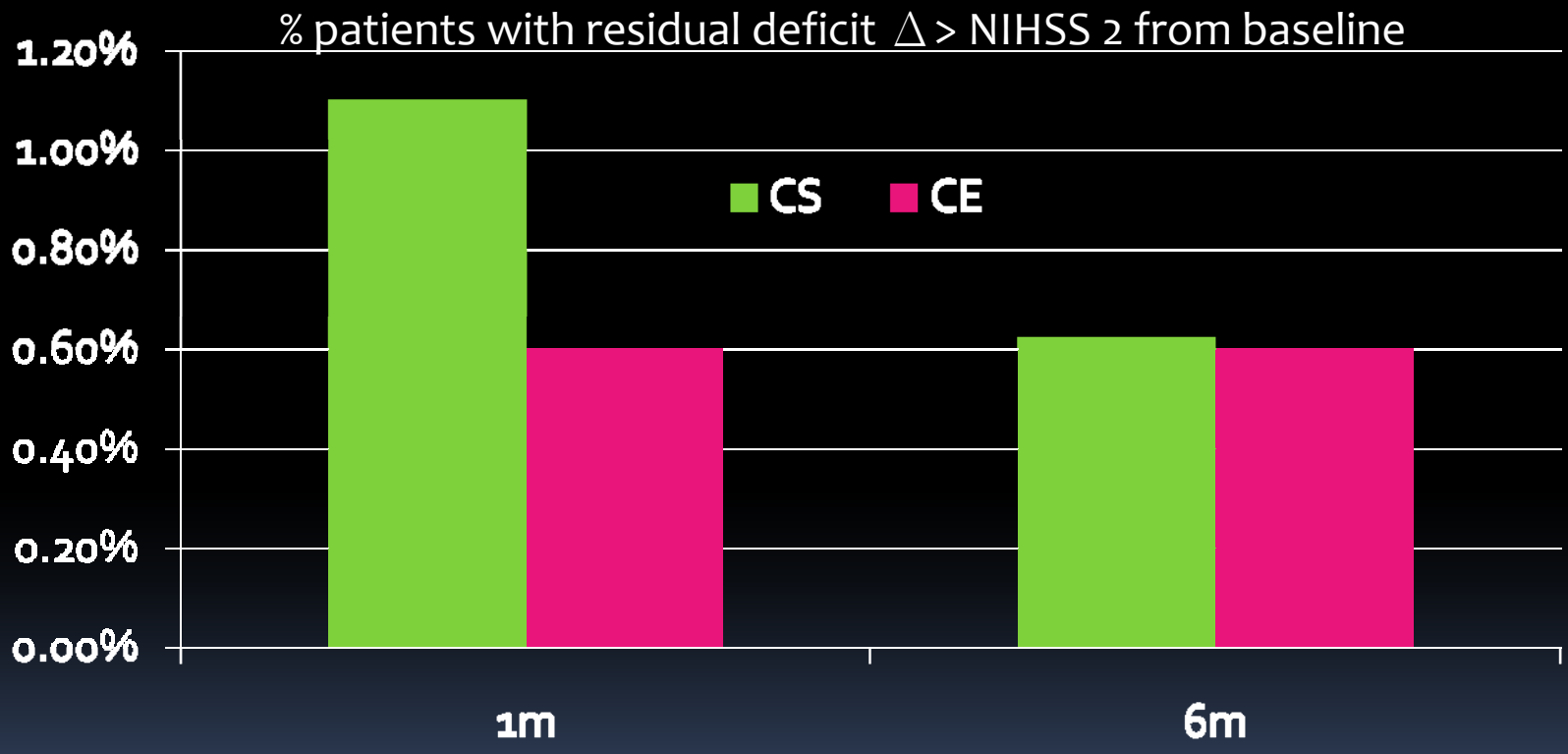
CREST: The largest complete CS vs. CE RCT

- 2502 average surgical risk patients randomized with EPD mandatory

	CS (1262)	CE (1240)	P
1° endpoint: death/stroke/MI a@4y	7.2%	6.8%	0.51
Peri-procedural death	0.7%	0.3%	0.18
79% are minor	4.1%	2.3%	0.01
Major stroke	0.9%	0.6%	0.52
MI	1.1%	2.3%	0.03
Ipsi-stroke post-4y	2.0%	2.4%	0.85

N Engl J Med 2010;363(1):11–23

Minor peri-stroke recovers

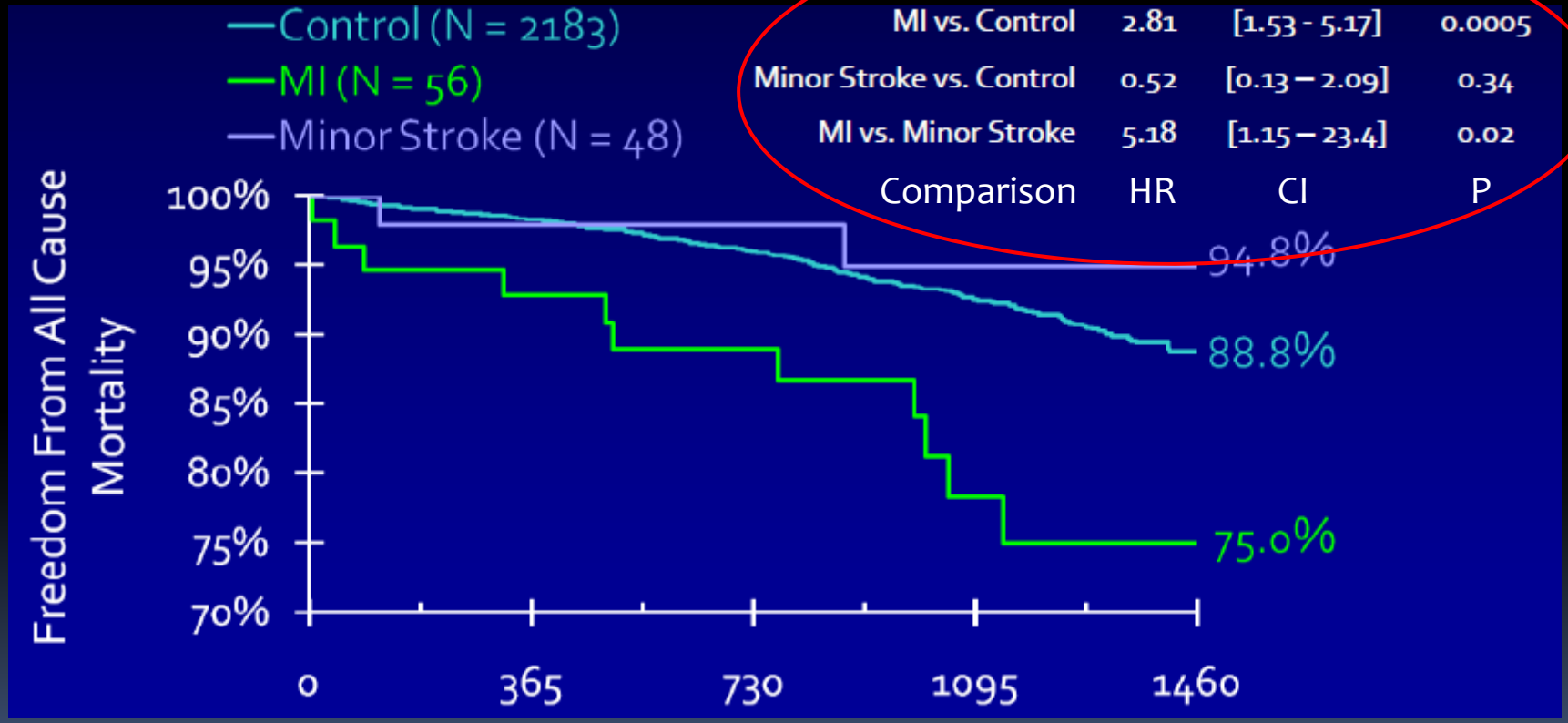


Most peri-stroke in CS are minor, and by 6m the neurological status are equivalent to CE

HL Kao

CREST PMA analysis mandated by FDA

But MI does matter

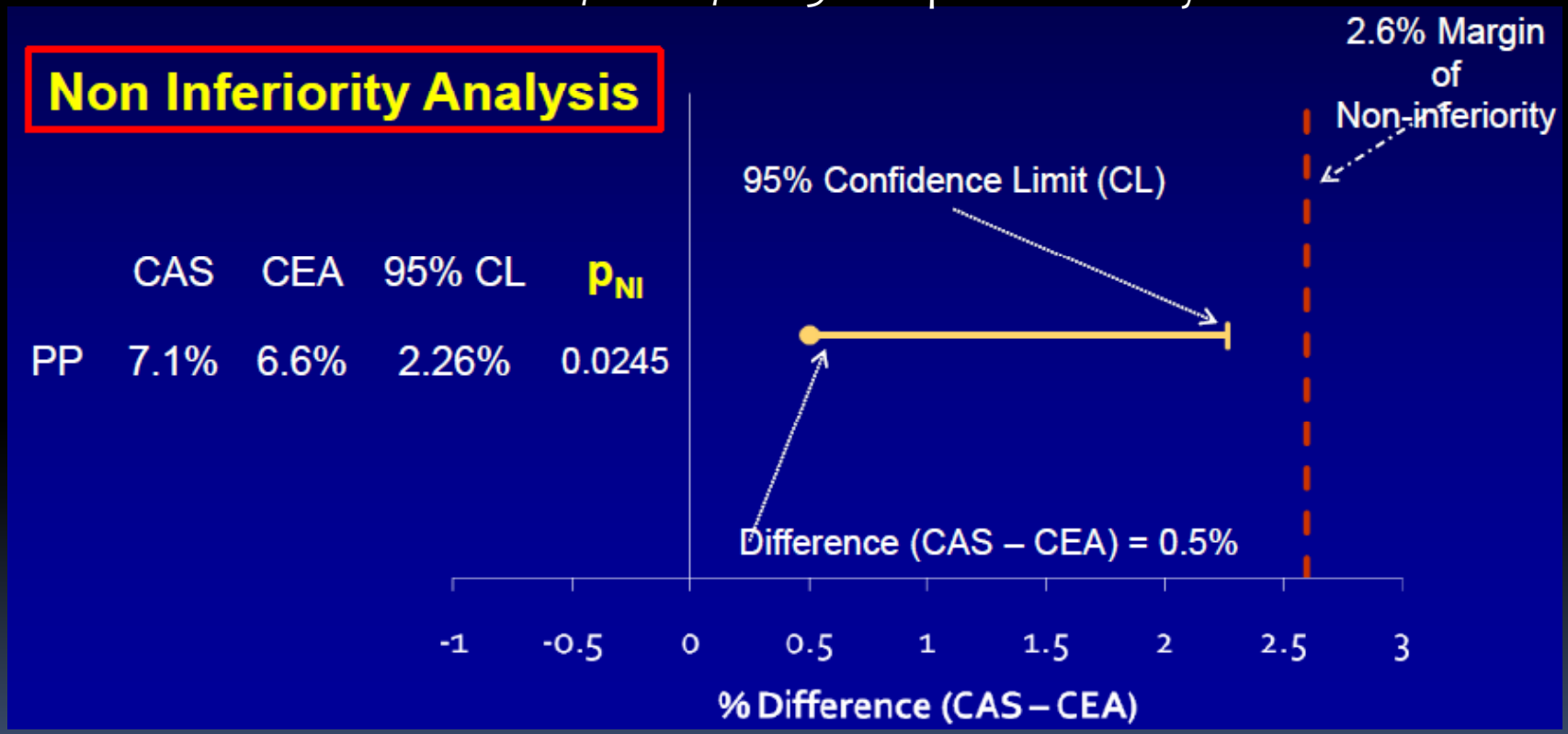


Comparison	HR	CI	P
MI vs. Control	2.81	[1.53 - 5.17]	0.0005
Minor Stroke vs. Control	0.52	[0.13 – 2.09]	0.34
MI vs. Minor Stroke	5.18	[1.15 – 23.4]	0.02

Peri-procedural MI leads to higher mortality, but stroke doesn't

CS is at least non-inferior to CE

All death/stroke/MI <30d + ipsi stroke at 1y



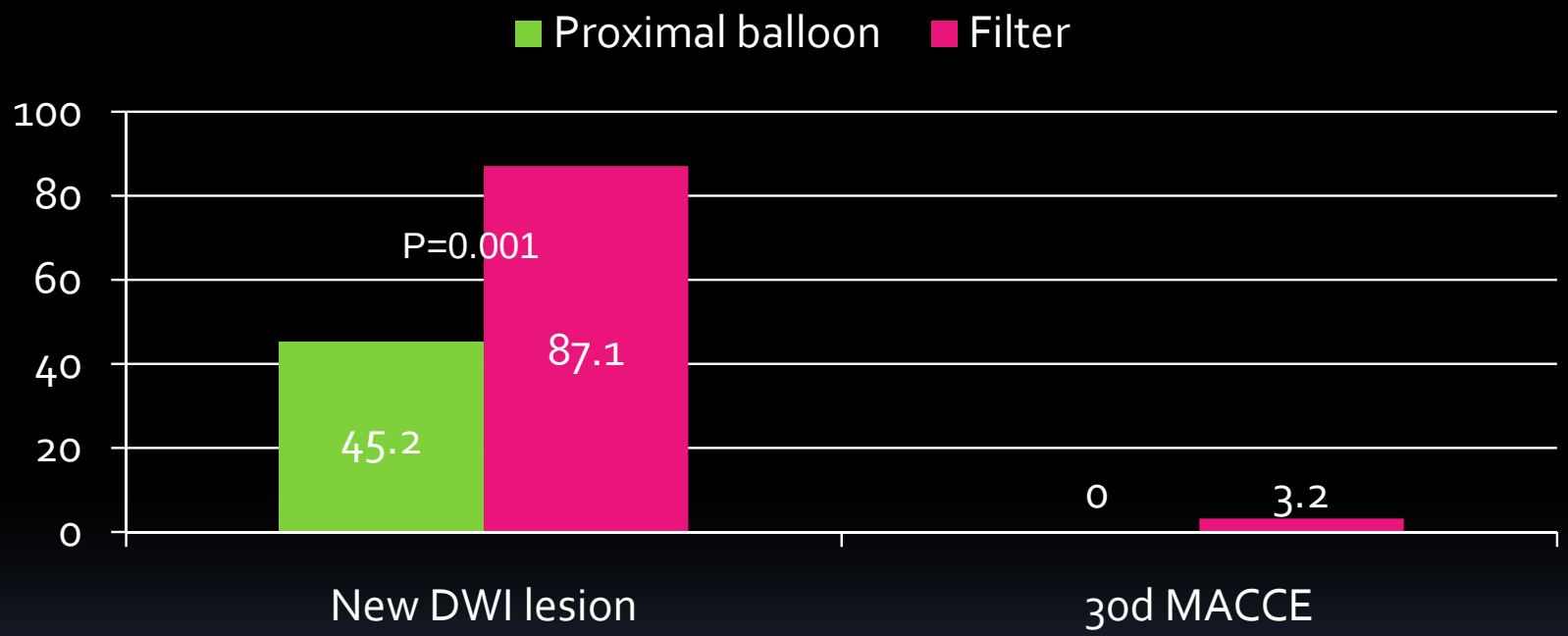
CREST PMA analysis mandated by FDA

My understanding after all these…

- High surgical risk patients: CS ≥ CE
- Low/average surgical risk patients: CS ≒ CE, (or best medical treatment?)
  - More minor stroke associated with CS, but
  - More MI associated with CE
- Experience is a crucial factor
- Remember, CS doesn't have to be better than CE, equivalence is enough!!
- And don't forget patient preference!!

Be honest, which one do you like?

How to prevent embolism in CS



- PROFI trial: 62 CS randomized
- Number (median 0 [0-4] vs.2 [0-13], p=0.0001) and volume (0 [0-0.84] vs. 0.47 [0-0.84], p=0.0001) of new lesions significantly less in proximal group

Bijuklic K et al. JACC 2012;59(15):1383

Conclusions

- Adequately designed/executed studies showed
  - CS and CE are equivalent in average surgical risk patients, and
  - CS is better than CE in high surgical risk patients, which is the majority in real-world
- Operator experience and essential equipment are important for CS, as well as for CE or everything else in medicine

洞察力

Do we really need more data to find the truth?