CONTROVERSIES & UPDATES IN VASCULAR SURGERY
JANUARY 22-24 2015
MARRIOTT RIVE GAUCHE & CONFERENCE CENTER PARIS, FRANCE

Asymptomatic carotid stenosis: do we have new data?

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Disclosure

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I have no potential conflicts of interest to report:

Interventions for Carotid Stenosis

- Long-term evidence is of most importance

… and this is changing

1.Prior symptoms or brain infarcts may identify higher-risk patients with ‘asymptomatic’ carotid stenosis

ACST-1

3120 patients without *recent ipsilateral* symptoms from tight carotid artery stenosis

Medical treatment alone	vs	Medical Treatment + early operation (CEA)

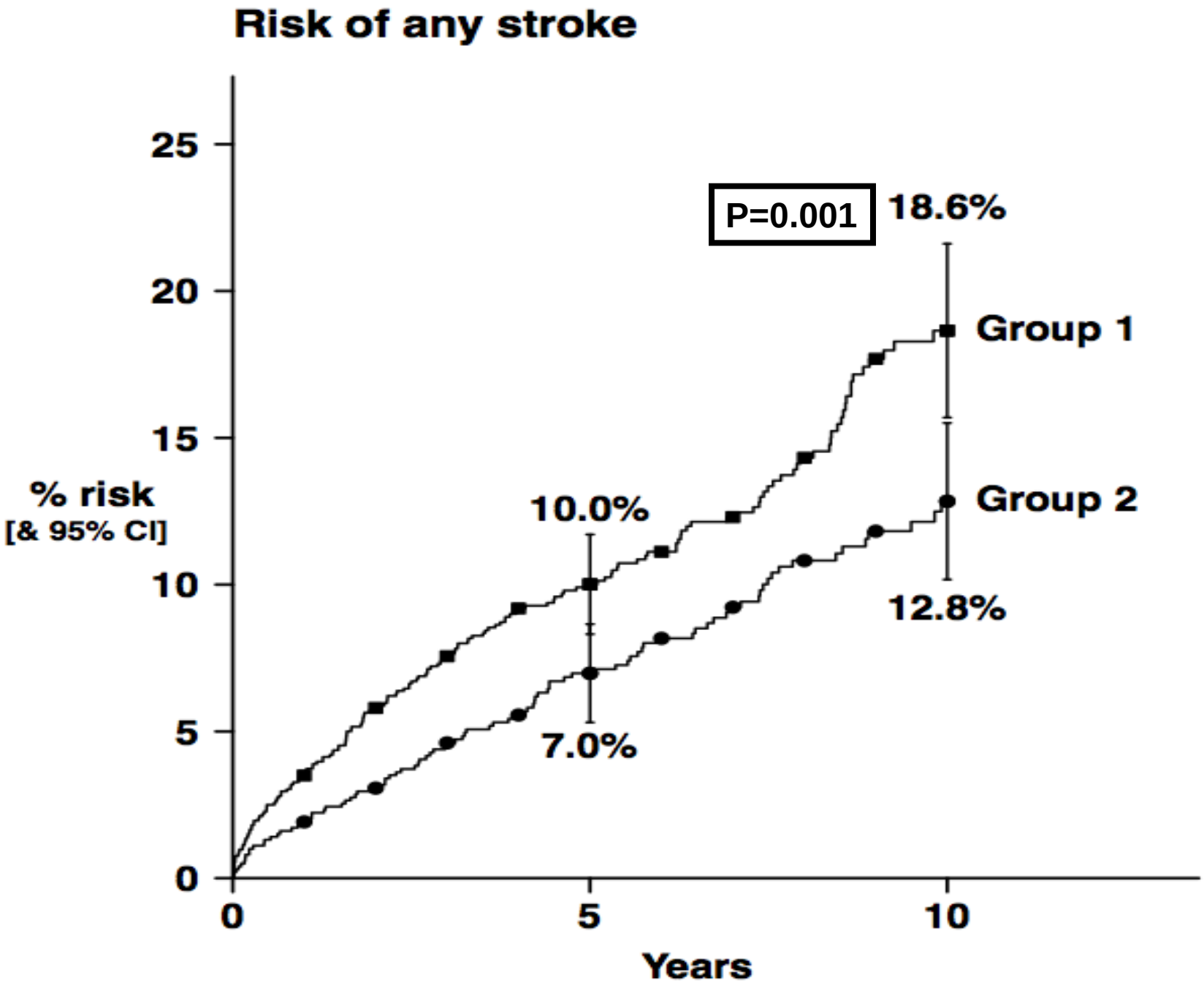
But, many stenoses were only found because unrelated symptoms prompted investigation…

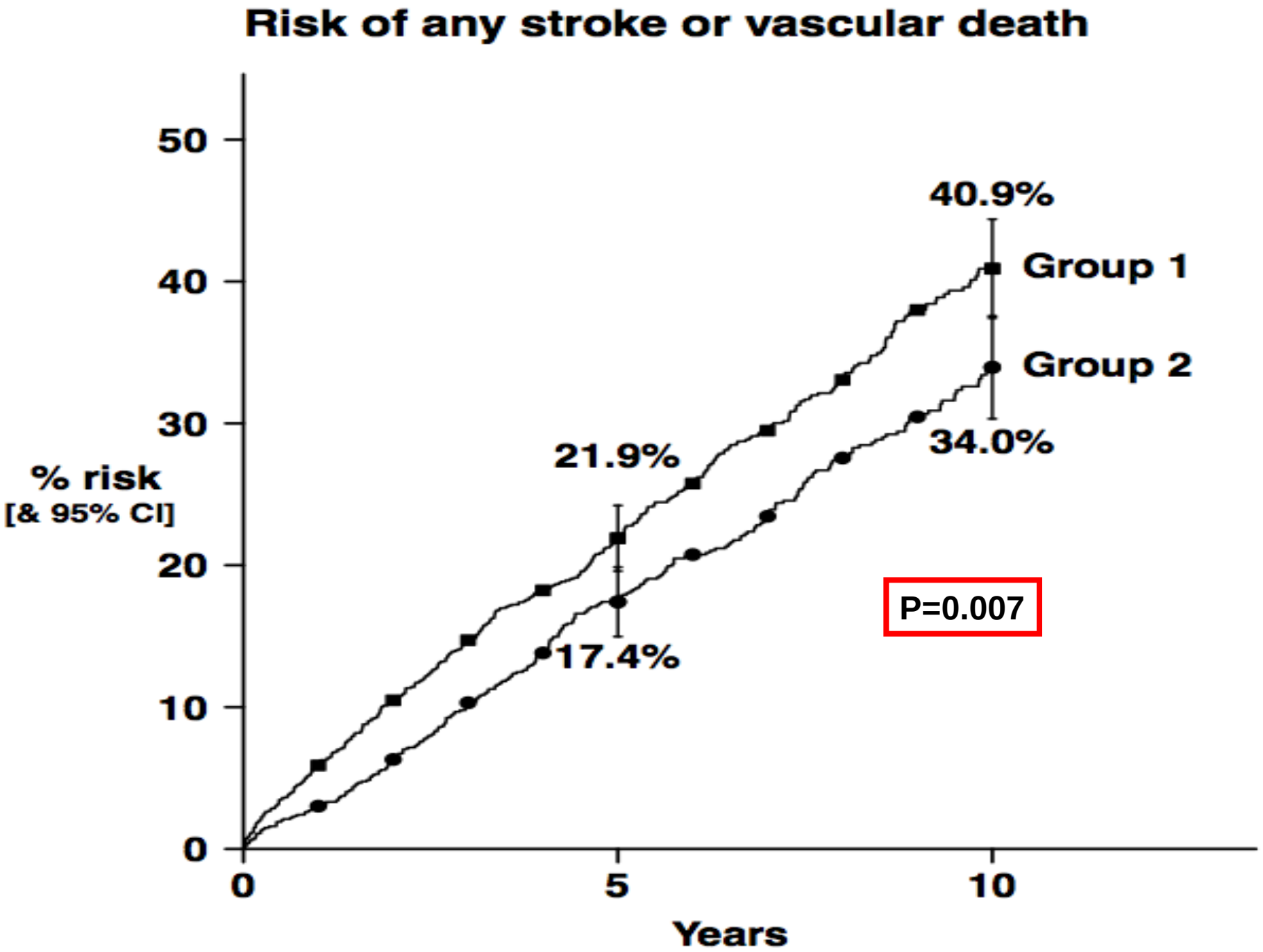
‘Asymptomatic’ - a misnomer?
– many of the patients in ACST-1 had previous stroke-type symptoms or CT brain infarcts

Group 1 (n=1331) – definite symptoms/infarcts

Group 2 (n=1002) – definitely none

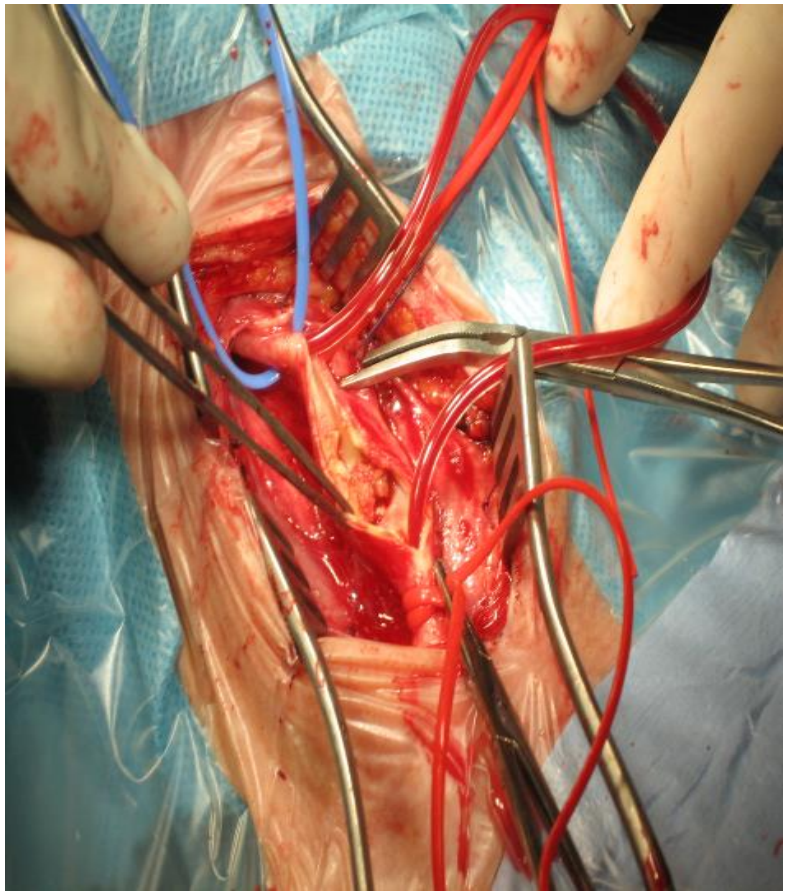
Excluded patients (n=787) had no imaging (this was not compulsory) or answered ‘uncertain’ to the question about symptoms


Risk of any stroke
25
20
15
10
5
0
% risk
[& 95% CI]
P=0.001
18.6%
Group 1
10.0%
Group 2
12.8%
7.0%
0
5
10
Years


Risk of any stroke or vascular death
50
40
30
20
10
0
% risk
[& 95% CI]
40.9%
Group 1
Group 2
34.0%
21.9%
17.4%
P=0.007
0
5
10
Years

2. ICSS - long-term evidence …changing the future for CAS

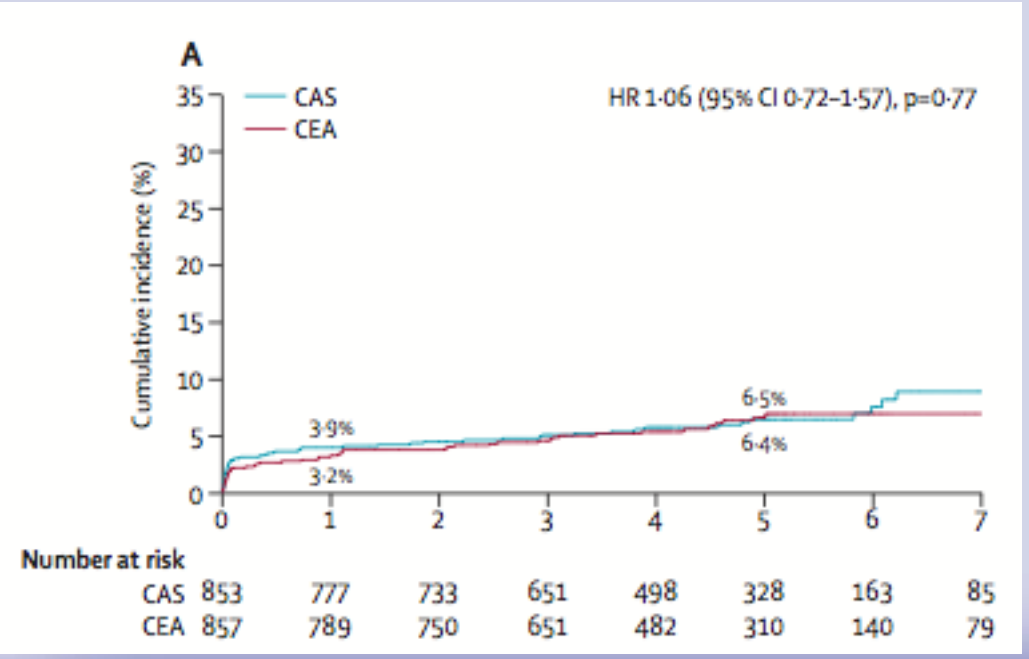
But why operate if stenting works as well or better?



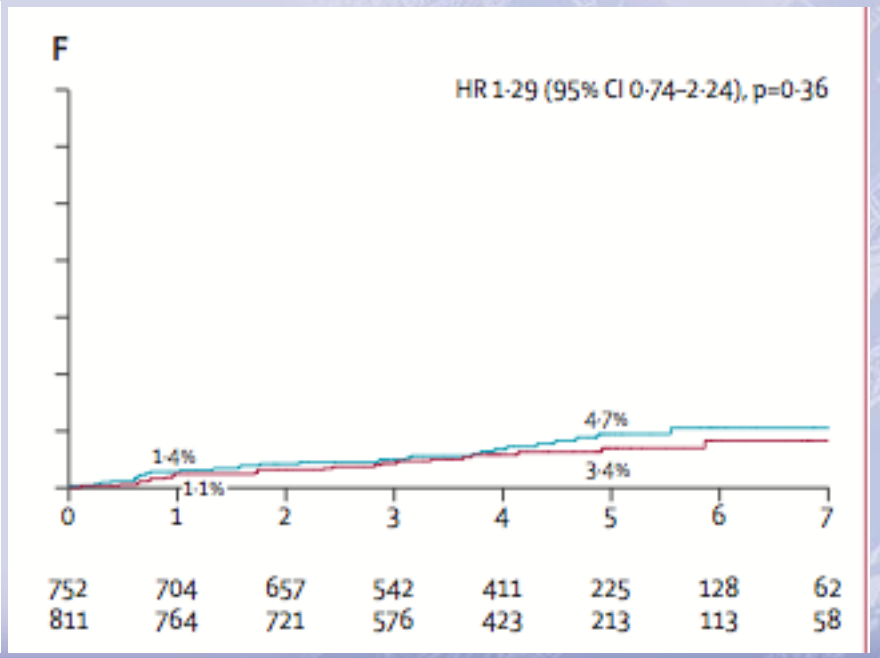
ICSS 4 year follow up

post-procedure

fatal/ disabling stroke



ipsilateral stroke



ICSS 4 year follow up (*Lancet, Oct 2014)*

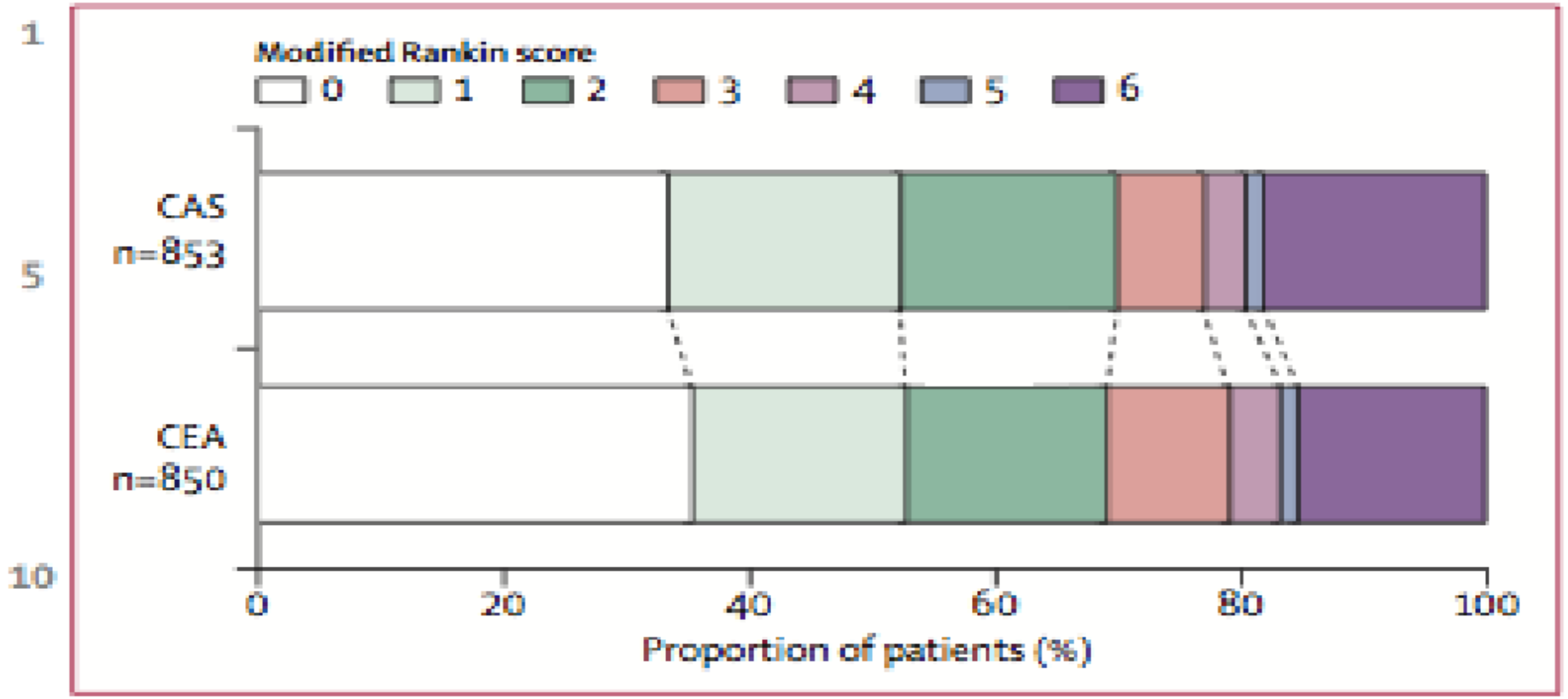


Figure 3: Functional ability measured by the modified Rankin Scale at the end of follow-up*

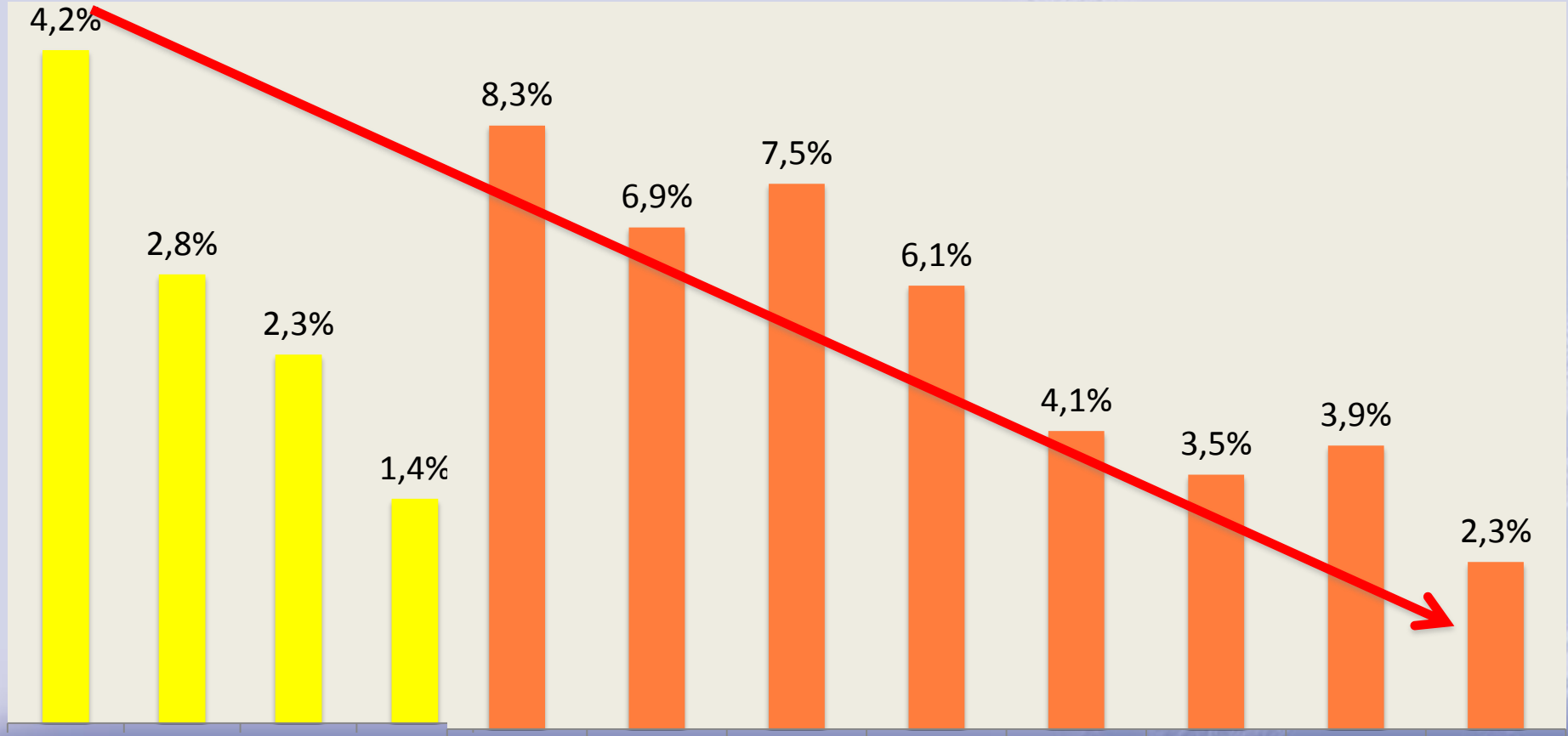
ICSS 4 yr follow up, 1700 symptomatic patients *Lancet (14th Oct 2014)*

CEA vs CAS…

- ‘equivalent long-term disability’
- ‘quality of life is similar (after CAS) compared with endarterectomy’

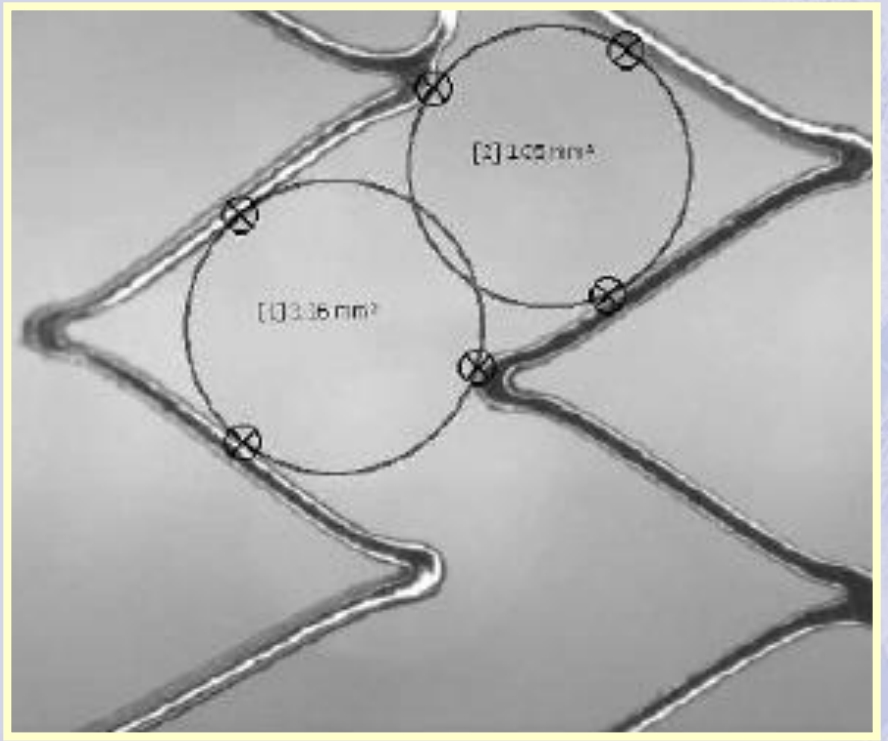
3. Better procedural outcomes for CEA and CAS

Procedural hazards of CEA and CAS are falling in recent trials and registries

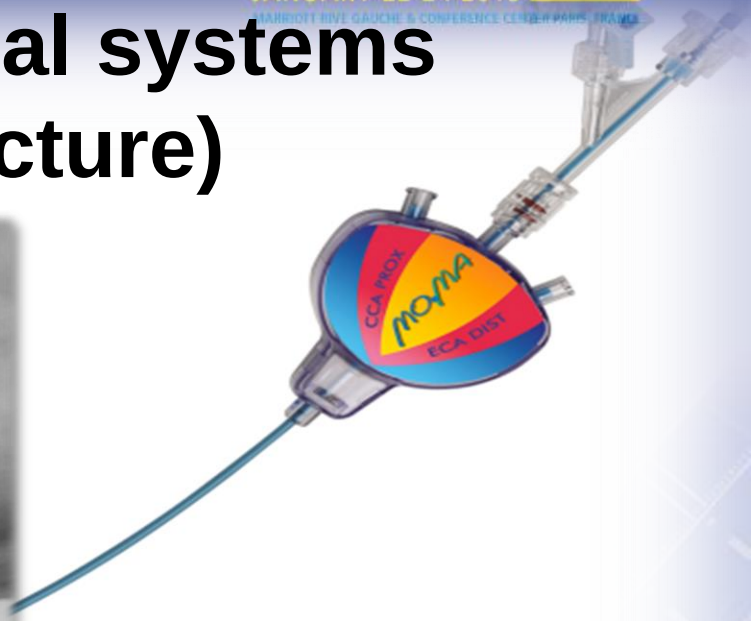


Open cell vs closed-cell stent design

Closed–cell safer?



Newer FLOW-reversal systems and direct puncture)



Reduce emboli, early results now comparable to CEA

3. CREST 2, ACT 1, SPACE 2: update

The CREST-2/SPACE-2 Research question

For asymptomatic patients with stenosis which ***might require*** intervention:

Which is generally better
(in addition to good medical treatment)? :

Intervention or

Medical treatment alone

SPACE-2

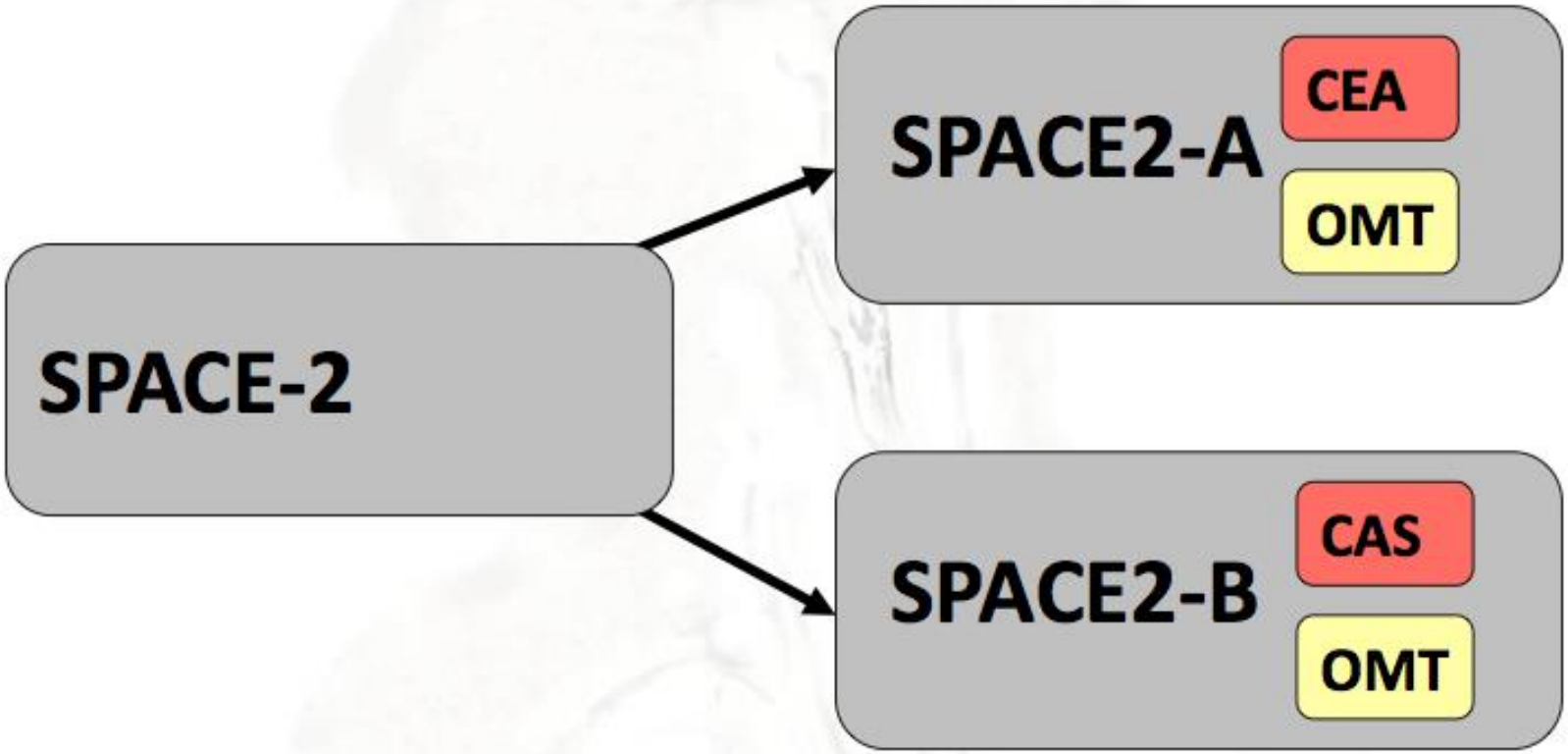
Stent-protected Angioplasty in Asymptomatic Carotid Artery Stenosis vs. Endarterectomy

A three-arm Clinical Trial

Reiff T et al., Int J Stroke (2009); 4: 294-9

Design Modification

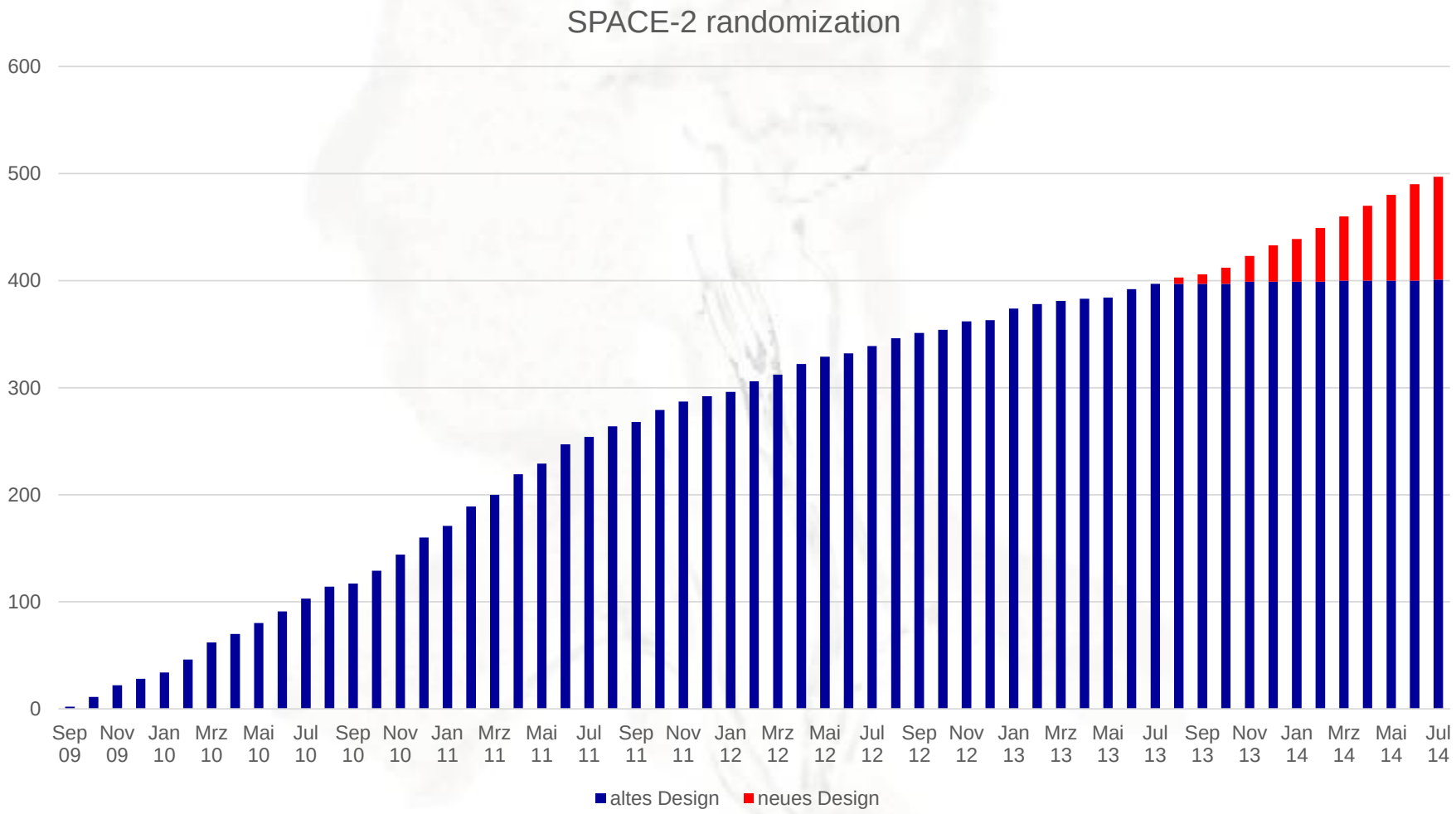
SPACE-2



Reiff T et al., Int J Stroke (2014); 9: E12-3
www.space-2.de

Randomization (Jul 2014)

SPACE-2



SPACE-2

Early termination of the study

- Even after modification / simplification of the protocol, recruitment rate did not increase as expected (wished)
- Based on this observation funding was stopped by the German research foundation (DFG)
- One of the main-problems are enormous numbers of patients treated outside the trial
- Maybe also because of economic reasons
  - OMT: ~ 0€
  - CEA/CAS: ~ 6000€

SPACE-2

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- Based on this observation funding was stopped by the German research foundation (DFG)
- One of the main-problems are enormous numbers of patients treated outside the trial
- Maybe also because of economic reasons
- Discussion (with the DFG) about continuation of the Follow-Up-examinations are ongoing
- Participation in ACST-2 or ECST-2 left to the discretion of the centers, but supported – in general – by the SC

4. ACST-2 the current status

the ACST-2 research question..

For asymptomatic patients with tight stenosis requiring intervention:

Which procedure is generally better
(in addition to good medical treatment)? :

carotid surgery (CEA)
or
carotid stenting (CAS)?

***Consider for* ACST-2:** when procedure clearly thought necessary by physician and patient

Randomise if:

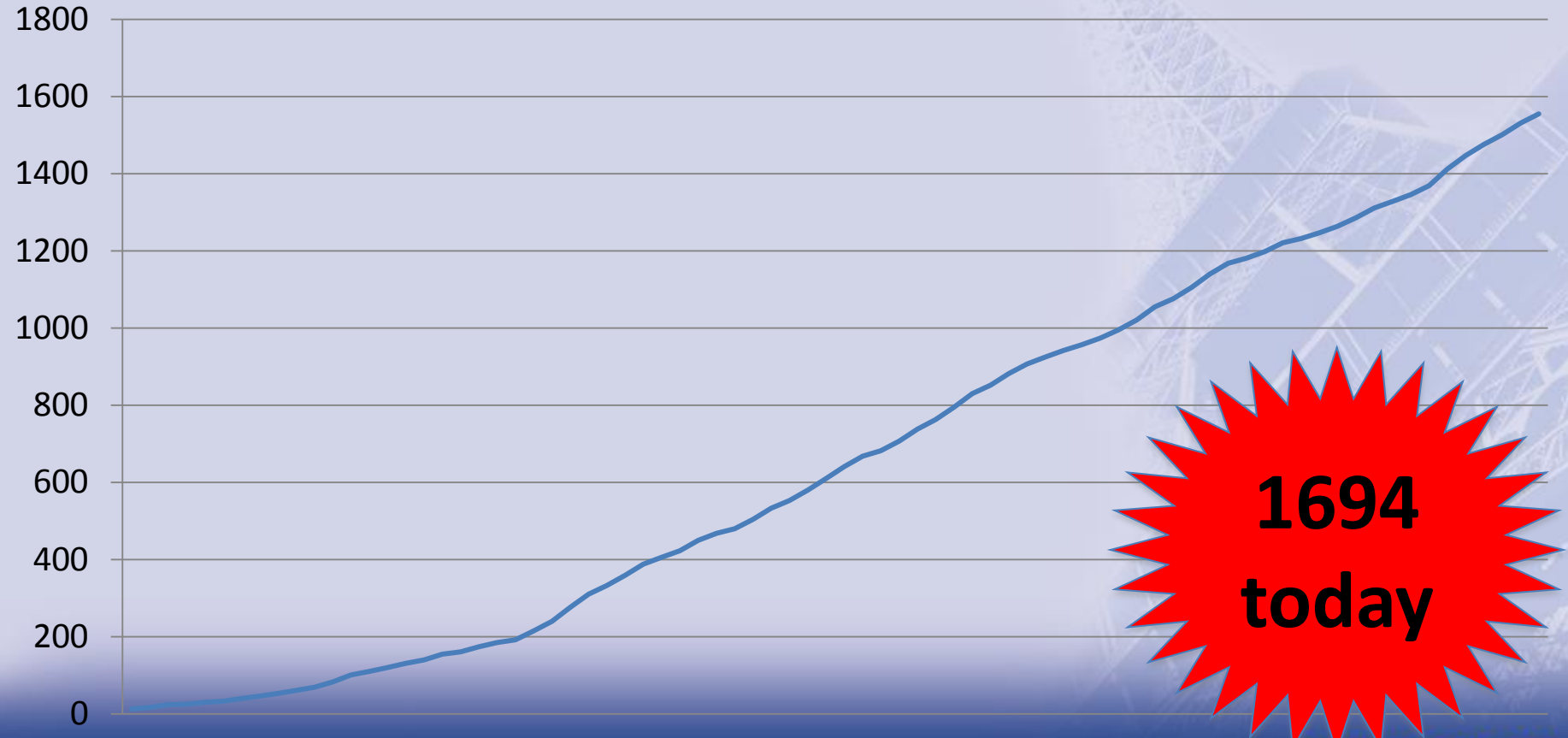
arch imaging confirms suitable for *both* procedures

ACST-2: Overview

- First patient randomised: 2008
- Some patients are now in their 7th year of follow up
- 113 Centres in 28 countries

ACST-2 Recruitment - almost 1700 patients

Target 3600 by end of 2019



ACST-2: Experienced collaborators

207 centre/operators' experience to 2014:

(73 do both procedures)

	CEA	CAS
Total procedures	118,287	45,693
Experience (median) in Years [range]	17 [2-44]	11 [2-26]
Procedures/operator (median) [range]	346 [21-7350]	150 [4-3326]

ACST-2

Sex, Age, Co-morbidities:

Men	70%
Mean age	**72 years**
Ischaemic heart disease	36%
Diabetic	**30%**
Renal impairment	6%

* **ACST-1: mean age 68, diabetes 20%**

ACST-2

Stroke risk factors:

Atrial Fibrillation	6%
Age >75 yrs	**39%**
Previous stroke symptoms or infarct	**43%**

ACST-1: 20% >75 yrs, 41% previous symptoms or infarct

ACST-2 - Stents and CPDs (all CE-marked)

Stent	CP Device	Type
Boston Wallstent	Emboshield	Filter
Cordis Precise	Filterwire	Filter
Ev3 Protégé® RX	Mo.Ma	Prox occ
Cristallo Ideale	Spider	Filter
Abbott RX Acculink	AngioGuard	Filter
Abbott Xact	Accunet	Filter
Boston Adapt	Gore Flow Reversal	Prox occ
Optimed Sinus Carotid RX	Twin One	Dist balloon

ACST-2: Drug therapy at entry and at 2013 follow up

85% lipid-lowering, now 88%

88% anti-hypertensive, now 90%

99% anti-thrombotic, still 99%

Drug names/ dose recorded each year directly from patient
Anti-thrombotic = Anti-platelet or anti-coagulant, includes patients on more than1 Anti-platelet agent

ACST-2: Open vs Endovascular treatment

Blinded procedural outcomes for >1000 patients

Interventional fatal or disabling stroke **1.0%**

Lower than for CEA in **ACST-1: 1.7%**

- Prior symptoms or brain infarcts may identify higher-risk patients with ‘asymptomatic’ carotid stenosis
- ACST-1 had many patients with these ‘higher-risk’ characteristics
- ACST-2 may have an even higher risk population; older patients, 50% more have diabetes, and more than 40% had prior symptoms or brain infarcts
- To reduce their long-term stroke risk effectively, consider them for ACST-2

5. Future best evidence will come from ACST-2, SPACE 2, ACT1, CREST-2, ECST-2 - all the Large Trials collaborating….

We will then be able to determine the impact of:

- current medical treatment (mostly more statins)
- greater operator experience (especially with CAS)
- newer devices and techniques
- on older, but often fitter patients

ACST-2
A very European Trial
– Join us and create the future evidence!

www.acst.org.uk