

TCT 2006 ⊕ Washington DC

***Contemporary Outcome in
Carotid Stenting (and CEA)***
**Predictive Variables and Risk
Benefit Considerations**

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***Statistics - the only science
that enables different experts
using the same figures
to draw different conclusions***

Evan Esar (1899-1995)

Evidence for treating ...

- **symptomatic patients**
- **asymptomatic patients**
- **the 'high-risk' patient**

The International CEA Trials

ECST	surgical risk (%)	medical risk (%)	ARR (%)	NNT (%)	CVE prevented per 1000 CEAs
<30%	9.8 at 5y	3.9 at 5y	-5.9		
30-49%	10.2 at 5y	8.2 at 5y	-2.0		
50-69%	15.0 at 5y	12.1 at 5y	-2.9		
70-99%	10.5 at 5y	19.0 at 5y	+8.5	12	83 at 5y

NASCET	surgical risk (%)	medical risk (%)	ARR (%)	NNT (%)	CVE prevented per 1000 CEAs
30-49%	14.9 at 5y	18.7 at 5y	+3.8		
50-69%	15.7 at 3y	22.2 at 3y	+6.5	15	67 at 3y
70-99%	8.9 at 3y	28.3 at 3y	+19.4	5	200 at 3y

The International CEA Trials

ECST	surgical	medical	ARR	NNT	CVE prevented
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2 different methods for measuring stenosis

+

2 different definitions for operative stroke

+

2 different methods of describing risk

=

many different interpretations of results!

50-69%	15.7 at 3y	22.2 at 3y	+6.5	15	67 at 3y
70-99%	8.9 at 3y	28.3 at 3y	+19.4	5	200 at 3y

CETC

Carotid Endarterectomy Trialists Collaboration

- combined ALL of the data from ECST, NASCET & VA
- 5,893 patients in database
- 33,000 patient years follow-up
- all angiograms reanalysed using NASCET method

CETC

ipsilateral stroke at 5 years including operative risk

stenosis	CEA	BMT	ARR	NNT	CVE/1000
<30%	12.05%	9.78%	-2.2%	-	-
30-49%	14.78%	18.06%	3.2%	31	32
50-69%	13.61%	18.18%	4.6%	21	46
70-99%	10.36%	26.24%	15.9%	6	159
near occlusion	16.82%	15.15%	-1.7%	-	-

CETC

Ipsilateral stroke at 5 years including operative risk

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AHA Guidelines 2006

For patients with TIA or ischemic stroke within the last six months and ipsilateral severe (70-99%) stenosis, CEA *by a surgeon with a peri-operative morbidity/mortality of <6%* is recommended.

(Class I, Evidence level A)

AHA Guidelines 2006

For patients with TIA or ischaemic stroke within the last six months and ipsilateral severe (70-99%) stenosis, CEA *by a surgeon with a peri-operative morbidity/mortality of <6%* is recommended.

(Class I, Evidence Level A)

For patients with TIA or ischaemic stroke within the last six months and ipsilateral moderate (50-69%) stenosis, CEA is recommended, depending on patient specific factors such as age, gender, co-morbidity and severity of initial symptom.

(Class I, Evidence Level A)

CETC

Ipsilateral stroke at 5 years including operative risk

stenosis	CEA	BMT	ARR	NNT	CVE/1000
<30%	12.05%	9.78%	-2.2%	-	-
50-69%	13.61%	18.18%	4.6%	21	46
70-99%	10.36%	26.24%	15.9%	6	59
near occlusion	16.82%	15.15%	-1.7%		

954 unnecessary procedures

Take-home Messages

The assumption that all patients have the same risk/benefit is flawed

achieving maximum benefit: -incremental stenosis

- age
- rapid intervention
- gender
- plaque morphology
- contralateral occlusion
- operative risk

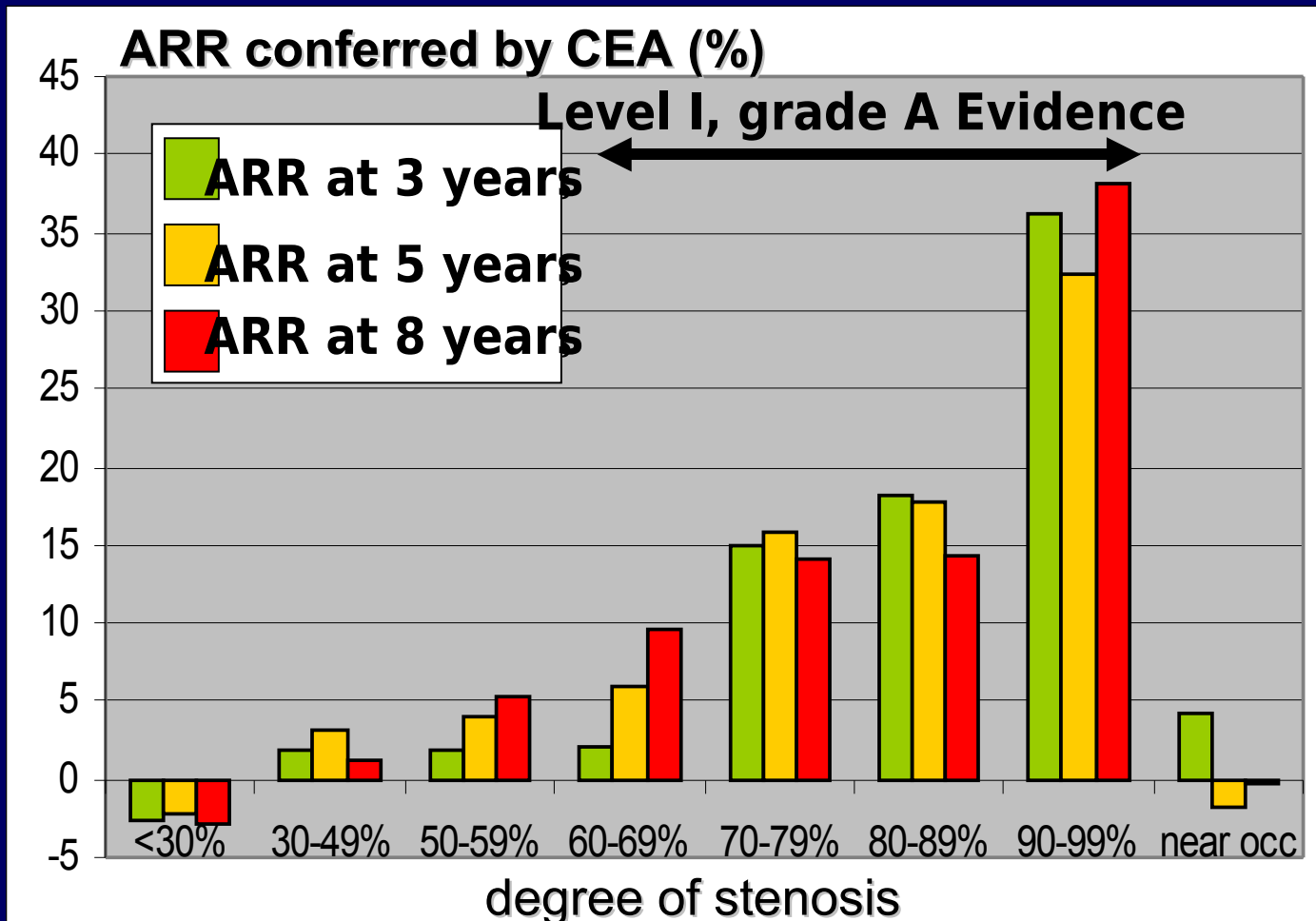
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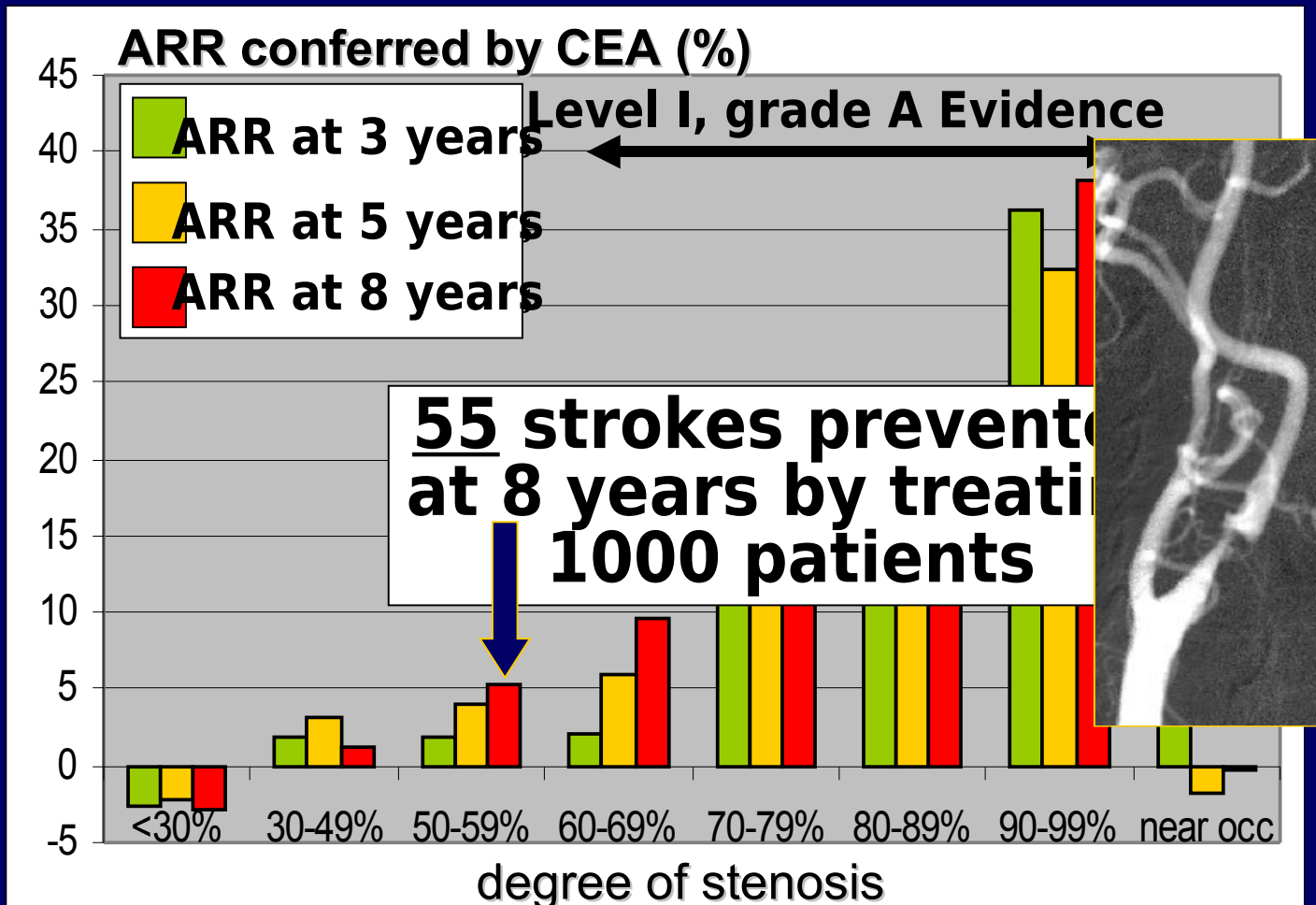
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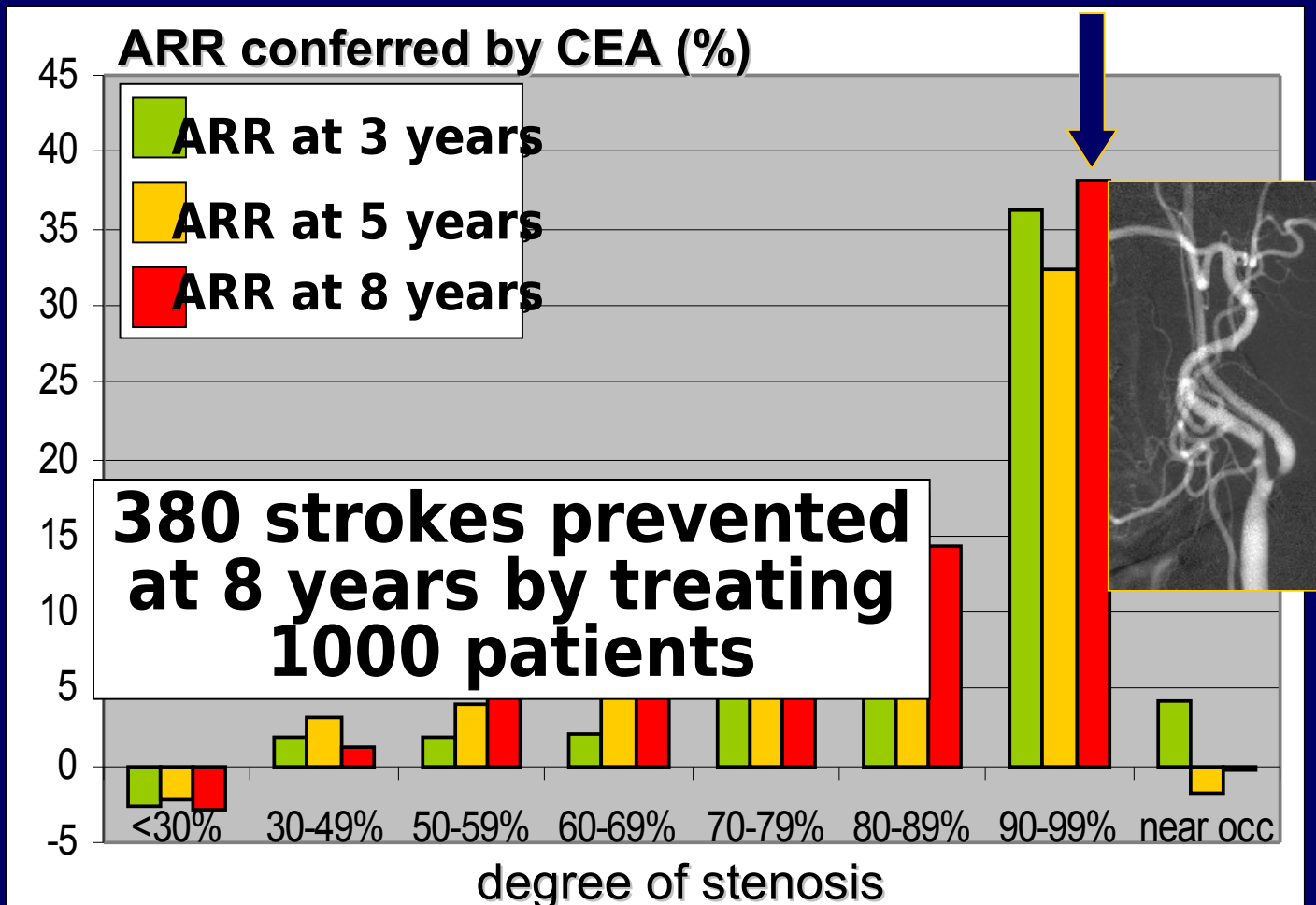
Incremental Stenosis



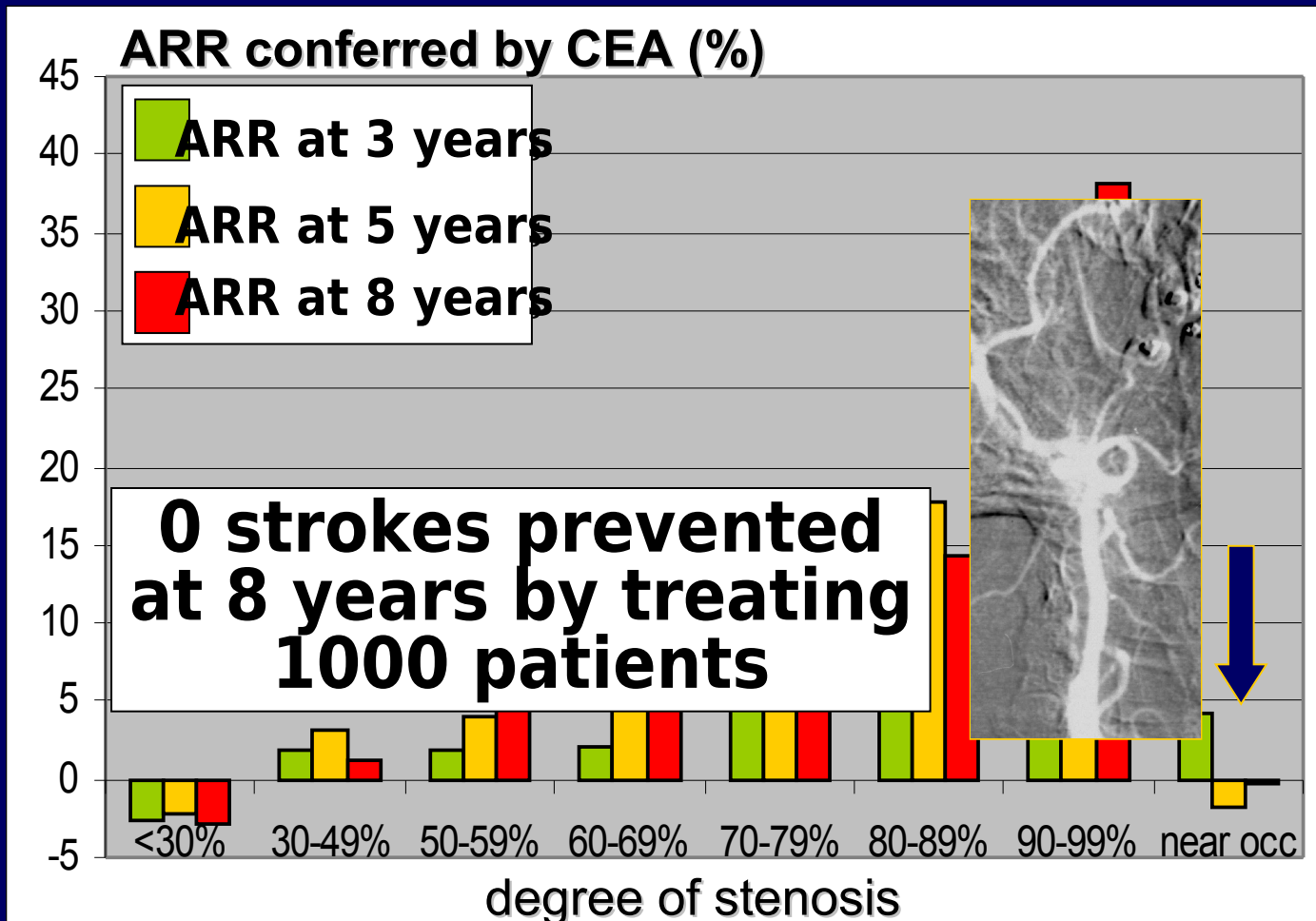
Incremental Stenosis



Incremental Stenosis



Incremental Stenosis



Conclusion

You cannot treat symptomatic patients with '50-99% stenoses' as being a homogenous group of equal risk.

Take-home Messages

The assumption that all patients have the same risk/benefit is flawed

achieving maximum benefit: -incremental
stenosis

-age

-rapid intervention

-gender

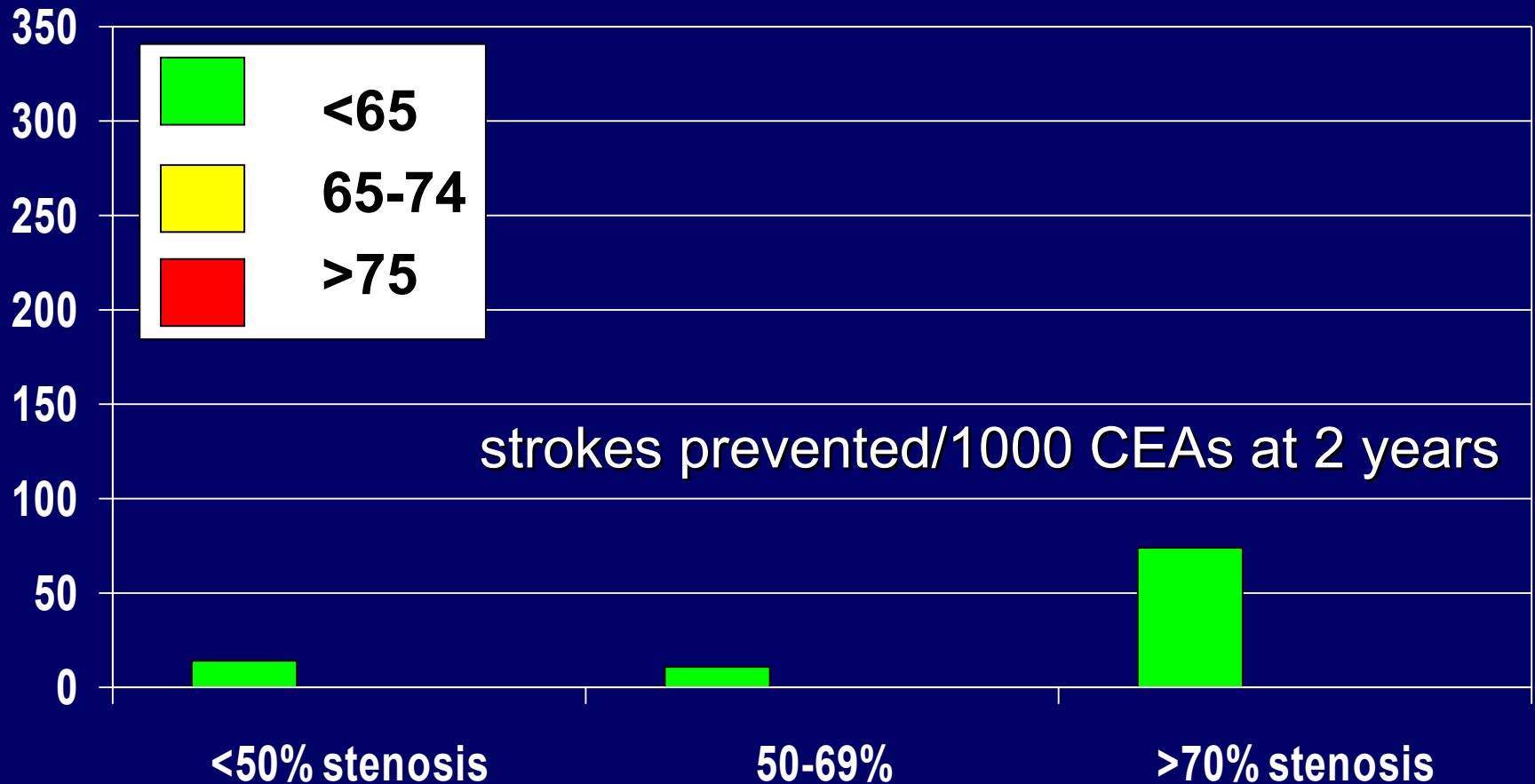
-plaque morphology

-contralateral

occlusion

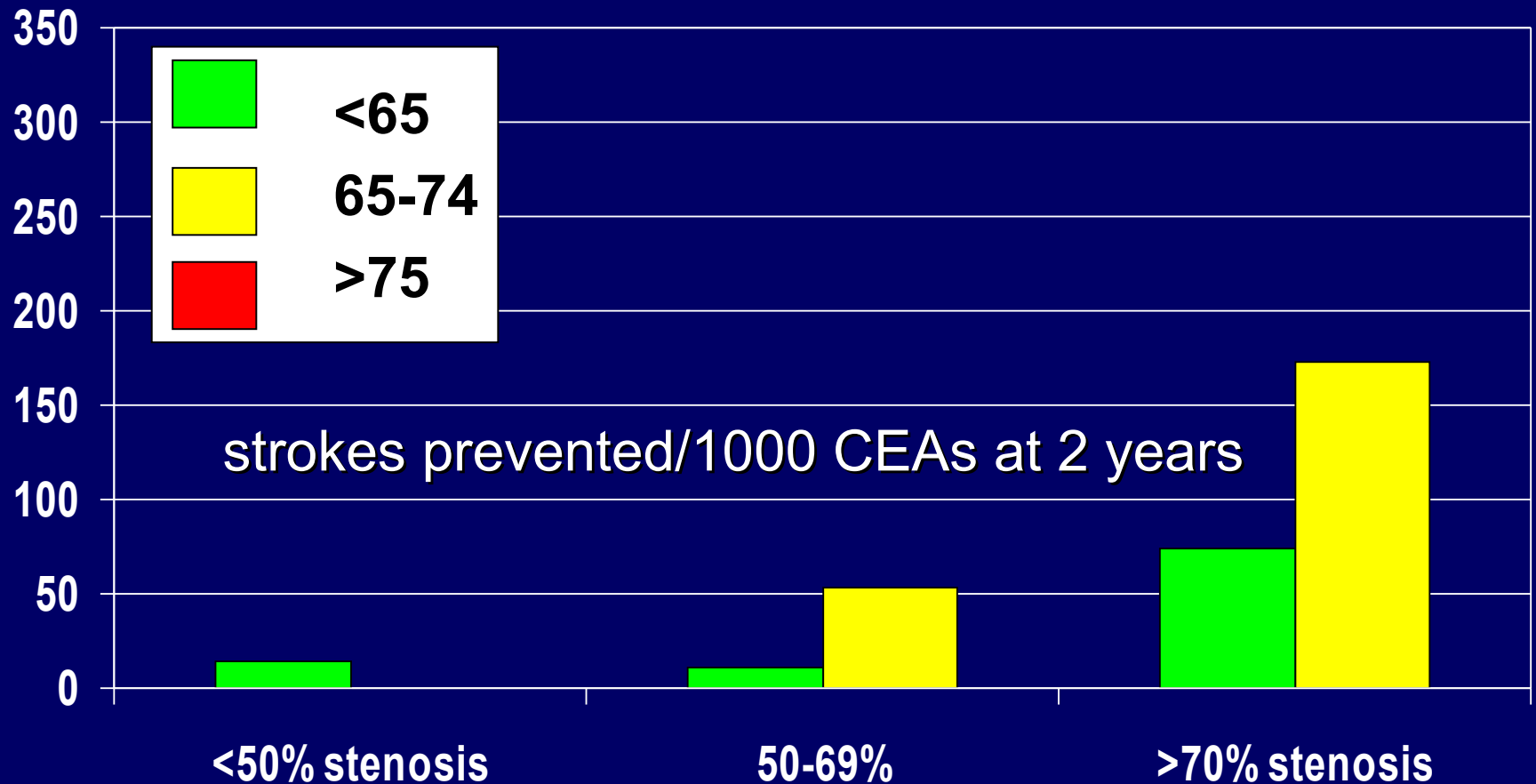
-operative risk

Effect of Age on Benefit from CEA



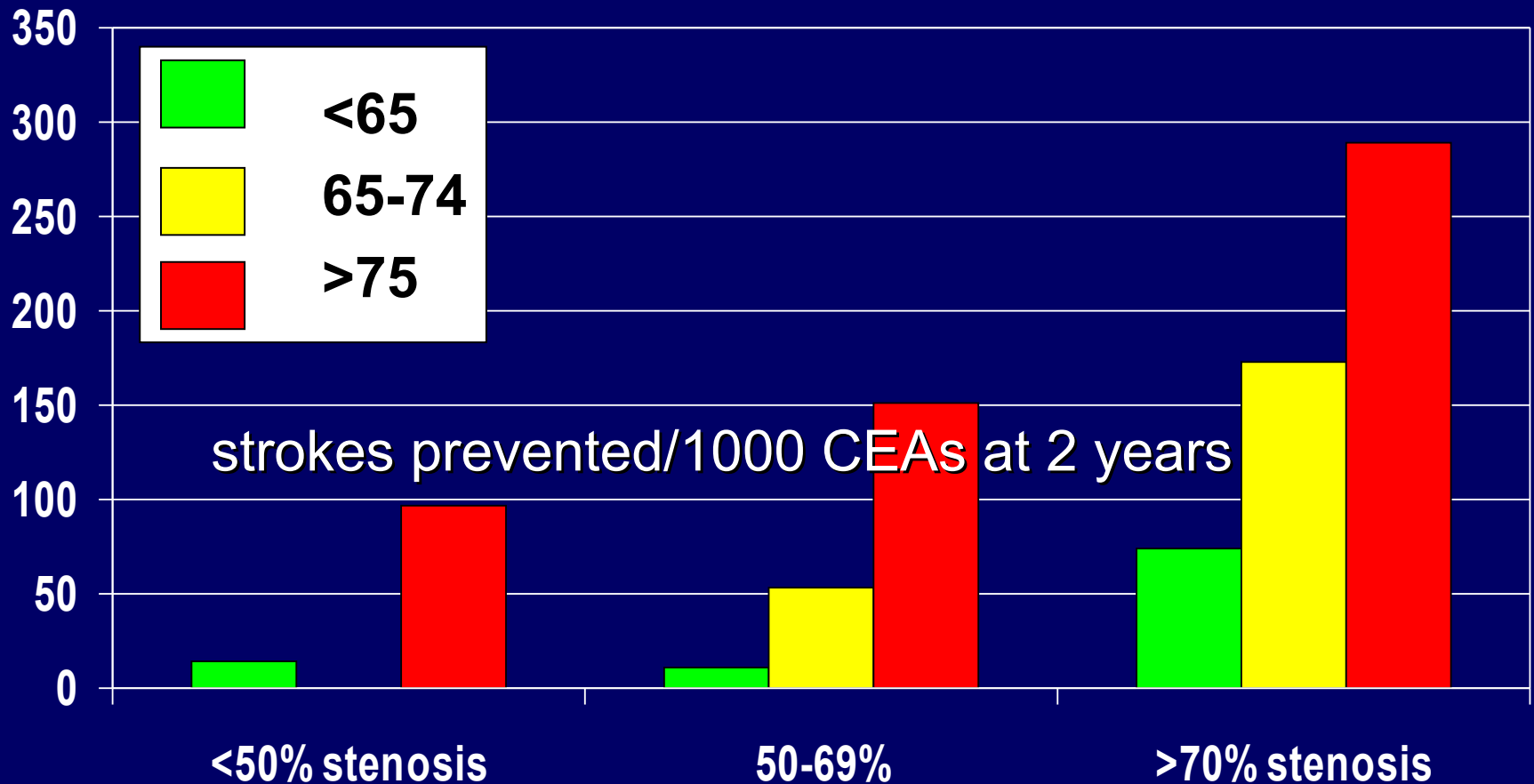
adapted from NASCET 2001

Effect of Age on Benefit from CEA



adapted from NASCET 2001

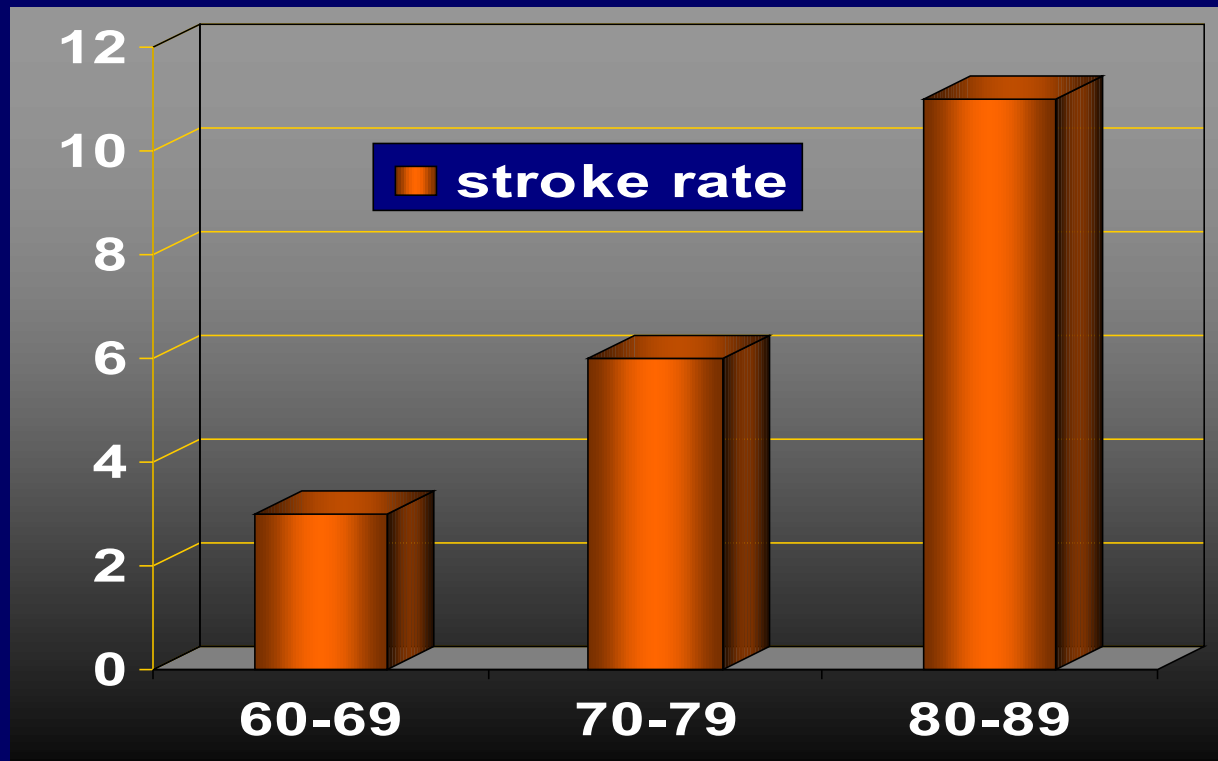
Effect of Age on Benefit from CEA



adapted from NASCET 2001

Effect of Age on Benefit from CAS

Stroke rates increase with age



adapted from ProCAS, Lennox Hill etc.

Conclusion

The general feeling that elderly patients do not gain significant benefit because of an increased procedural risk is unsustainable.

They have the most to gain!

But CAS must keep the 6% limit!!!

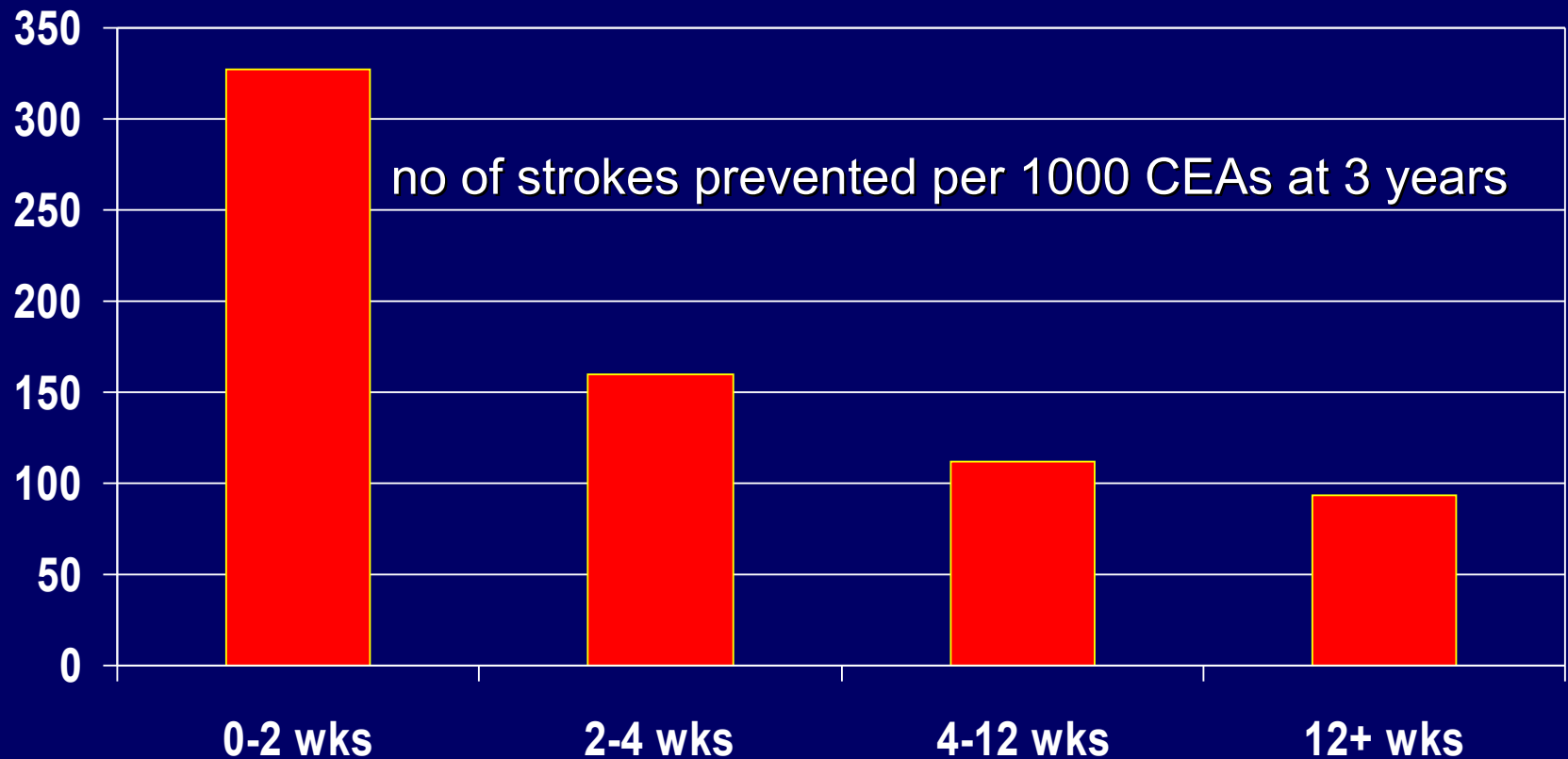
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achieving maximum benefit: -incremental
stenosis

- age
- rapid intervention
- gender
- plaque morphology
- contralateral
occlusion
- operative risk

Rapid Tx of Symptomatic Patients



time from last event to randomisation

adapted from Rothwell 2004

Conclusion

*Every third stroke is a second stroke!
ICA stenosis should be treated as early
as reasonably possible, regardless of
the invasive method used.*

Take-home Messages

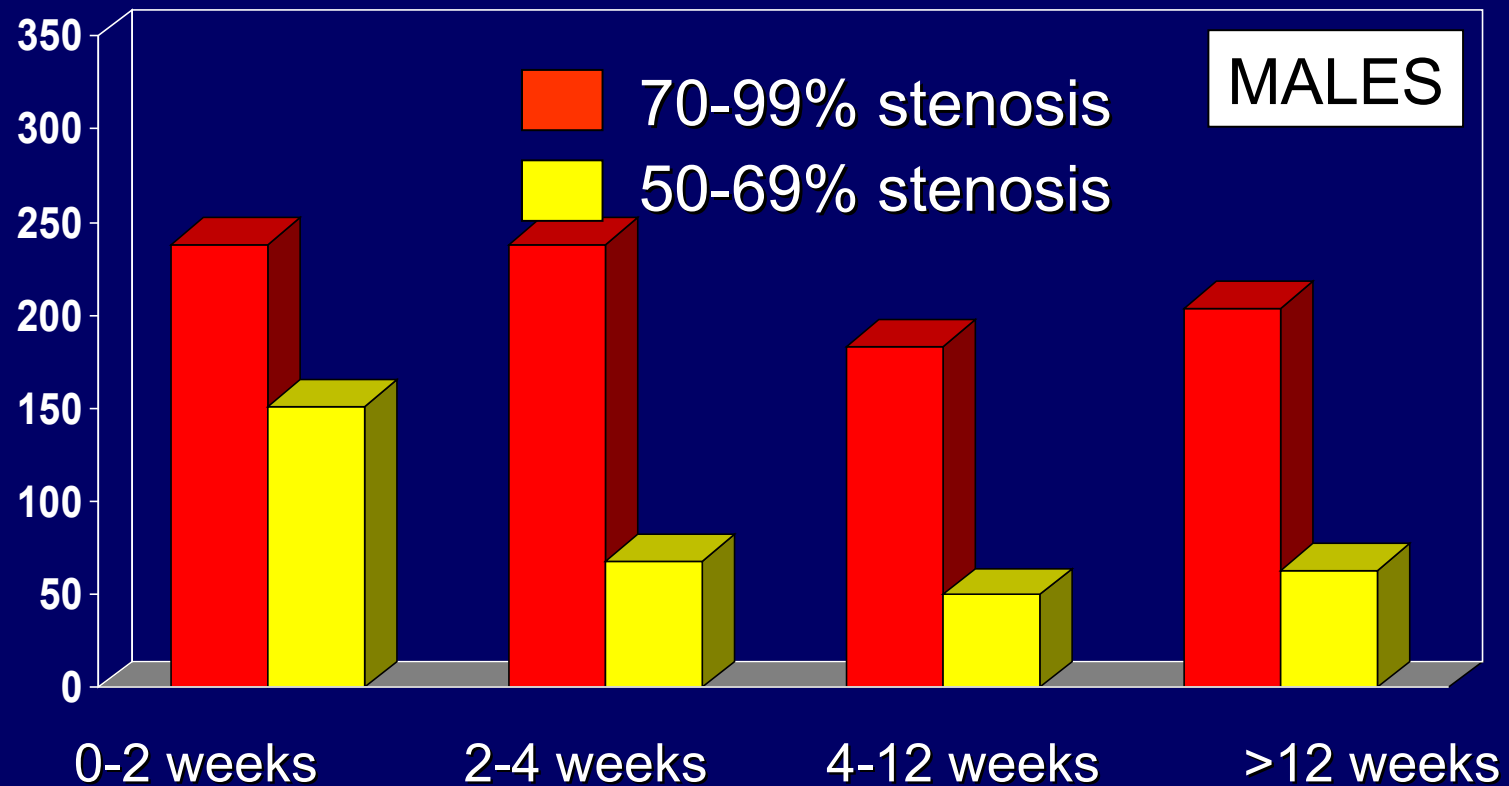
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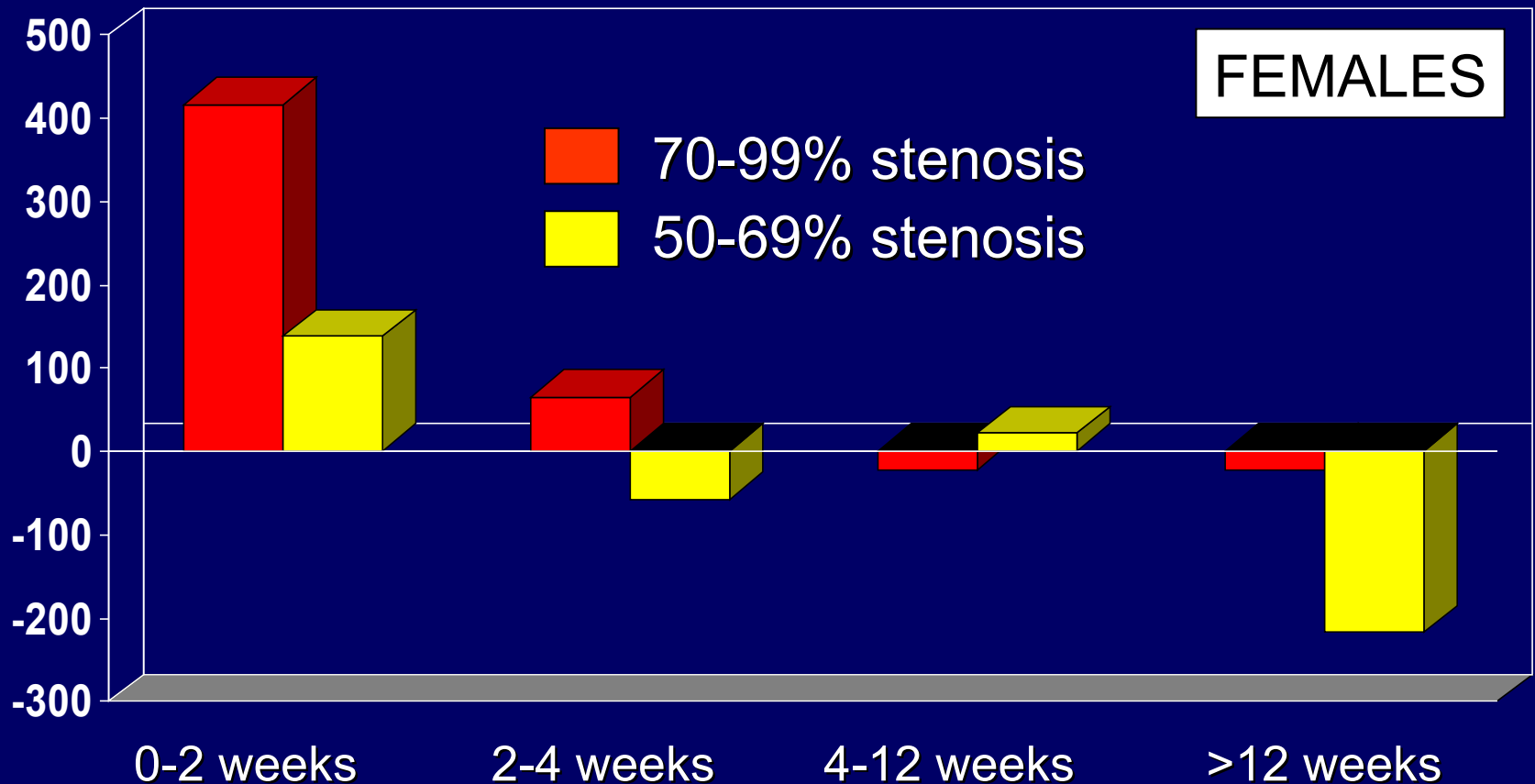
Gender, Delay & Stenosis Severity

Strokes prevented/1000 CEAs at 5 years



Gender, Delay & Stenosis Severity

Strokes prevented/1000 CEAs at 5 years



Conclusion

It is an uncomfortable observation that unless women with moderate stenoses receive treatment within a month of symptoms, they gain little benefit but face all the risks. They should not be considered 'high-risk'

Take-home Messages

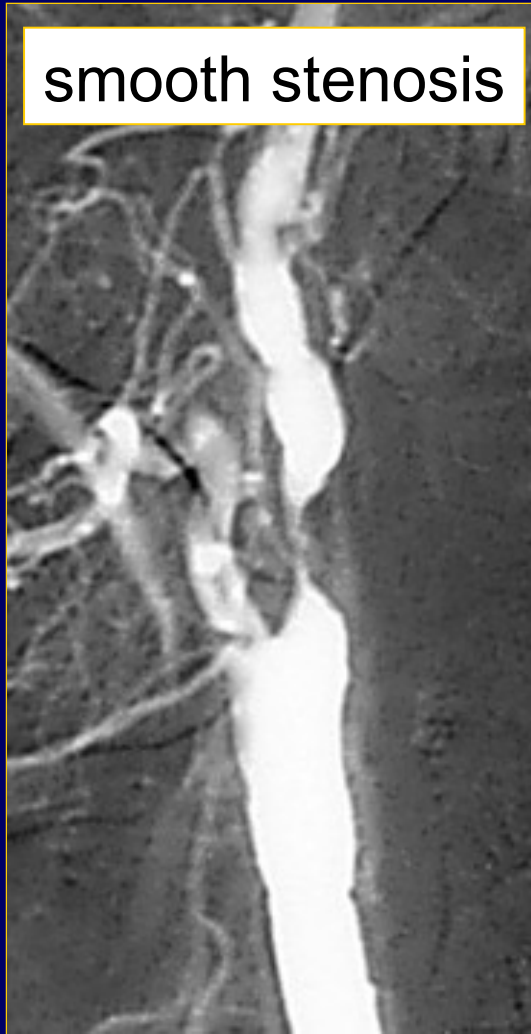
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- contralateral
occlusion
- operative risk

Influence of Plaque Morphology

smooth stenosis

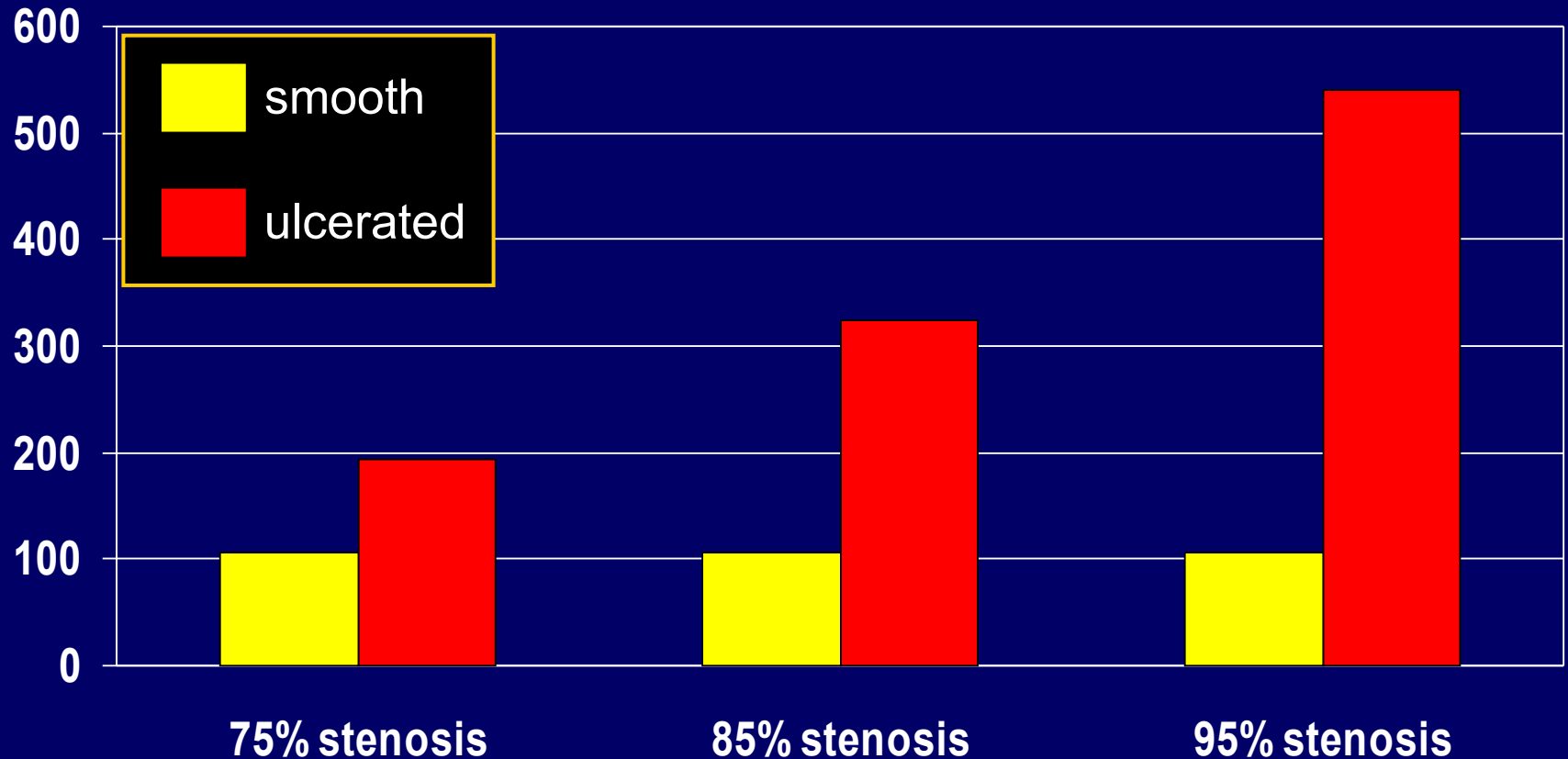


ulcerated stenosis



A confers benefit in ulcerated stenosis

ipsilateral strokes prevented/1000 CEAs at 2 years



adapted from NASCET 1994

Conclusion

There has been much debate about the merits of studying plaque morphology. A simple assessment of whether the surface is irregular or smooth could have immense predictive benefit.

Take-home Messages

The assumption that all patients have the same risk/benefit is flawed

achieving maximum benefit: -incremental
stenosis

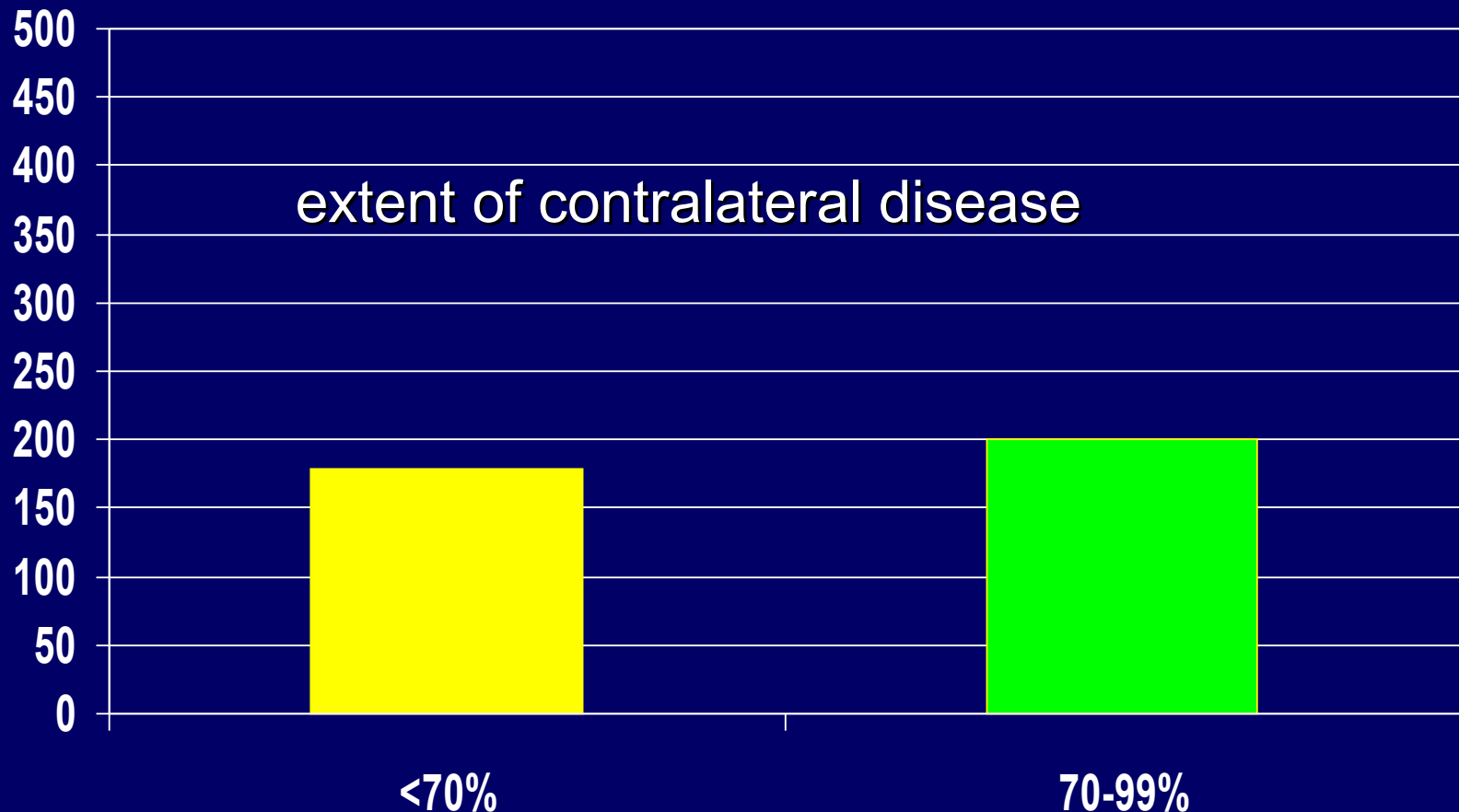
- age
- rapid intervention
- gender
- plaque morphology
- contralateral ICA
occlusion
- operative risk

Stenosis & Contralateral Occlusion



Effect of Contralateral Disease

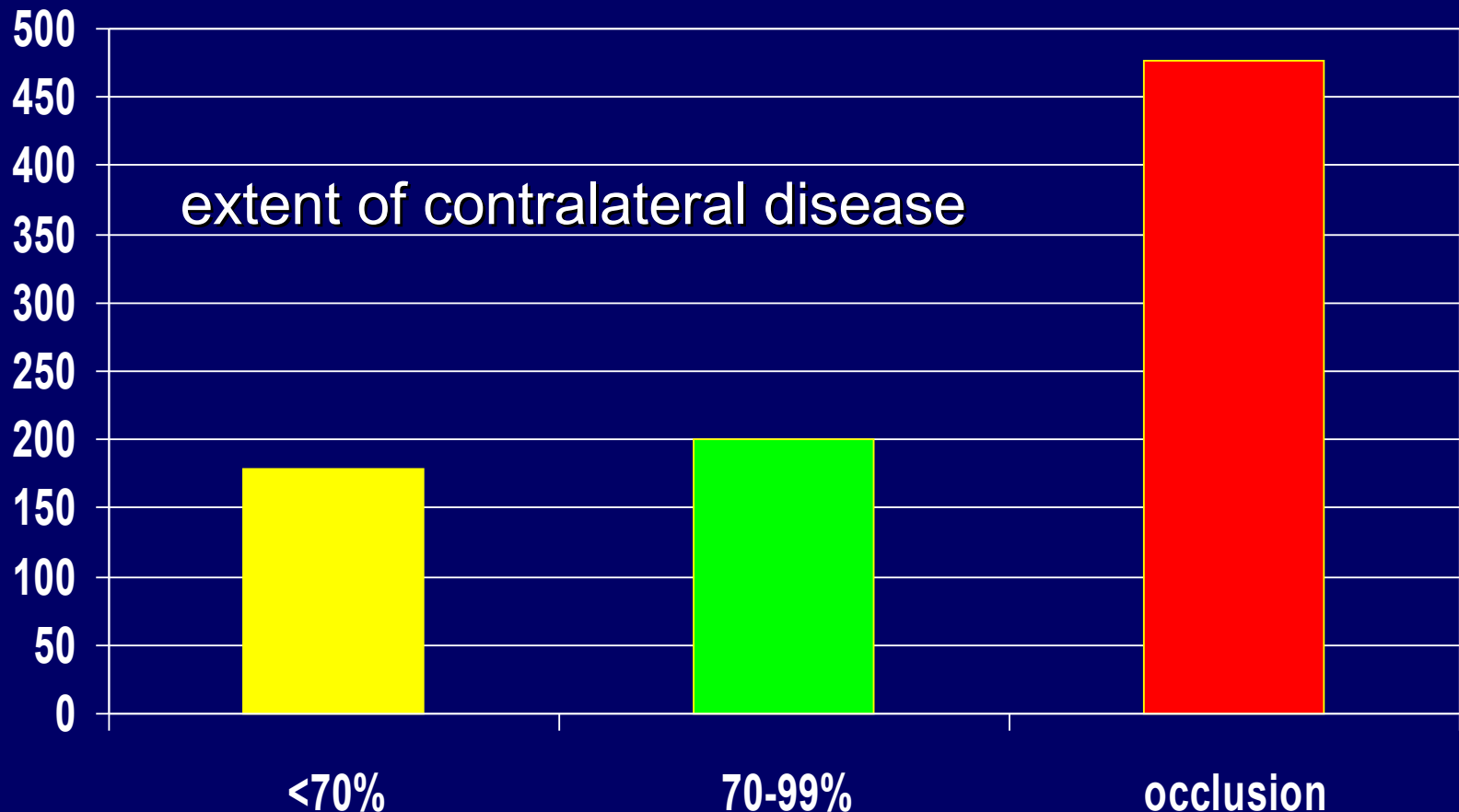
No of ipsilateral strokes prevented per 1000 CEAs at 2 years



NASCET 1995

Effect of Contralateral Disease

No of ipsilateral strokes prevented per 1000 CEAs at 2 years



NASCET 1995

Conclusion

In parallel with plaque irregularity, the presence of contralateral occlusion is the single biggest predictor of benefit from intervention. NASCET stroke risk of 14.7% much higher than with CAS (~5%)!

Take-home Messages

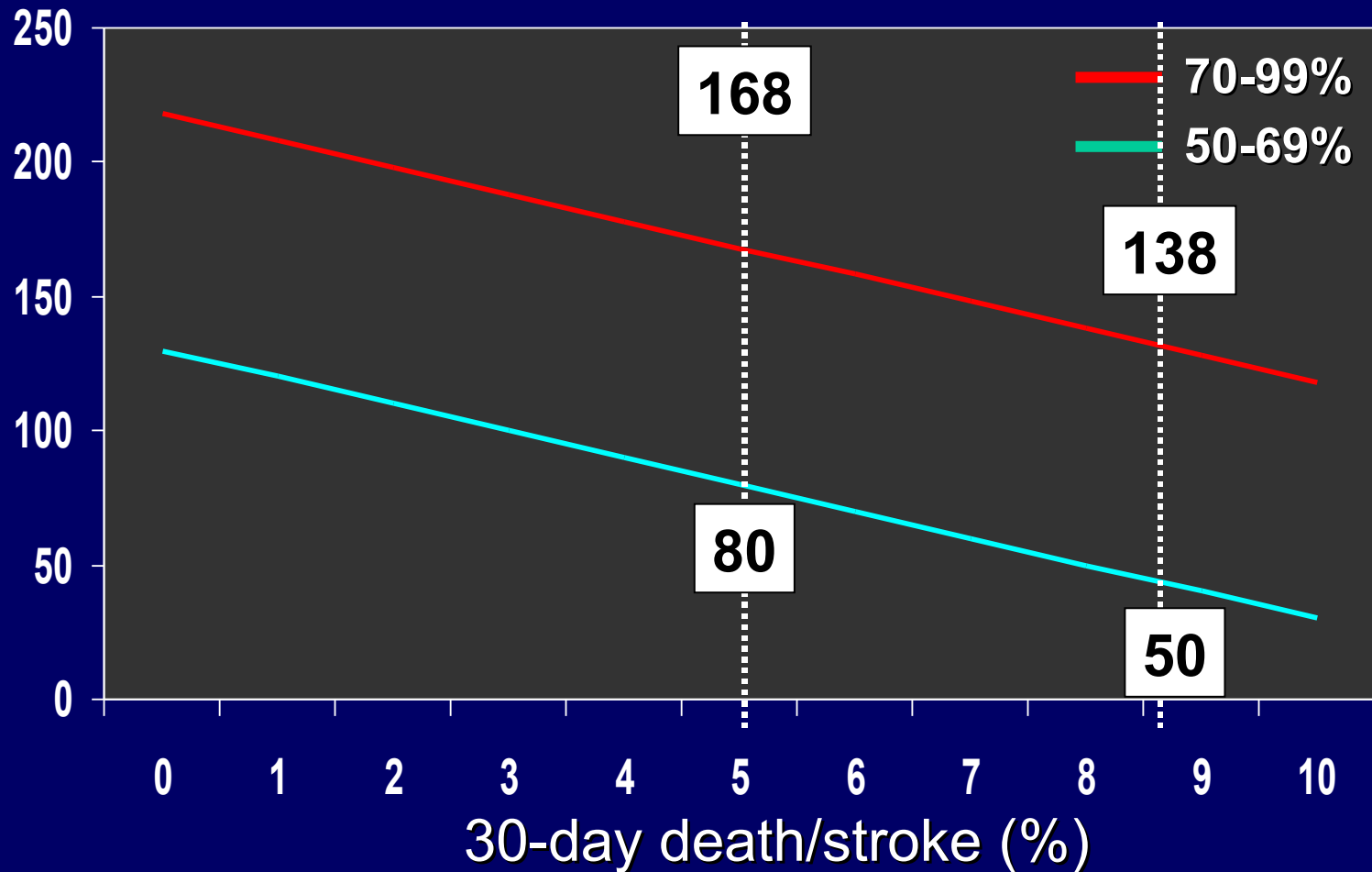
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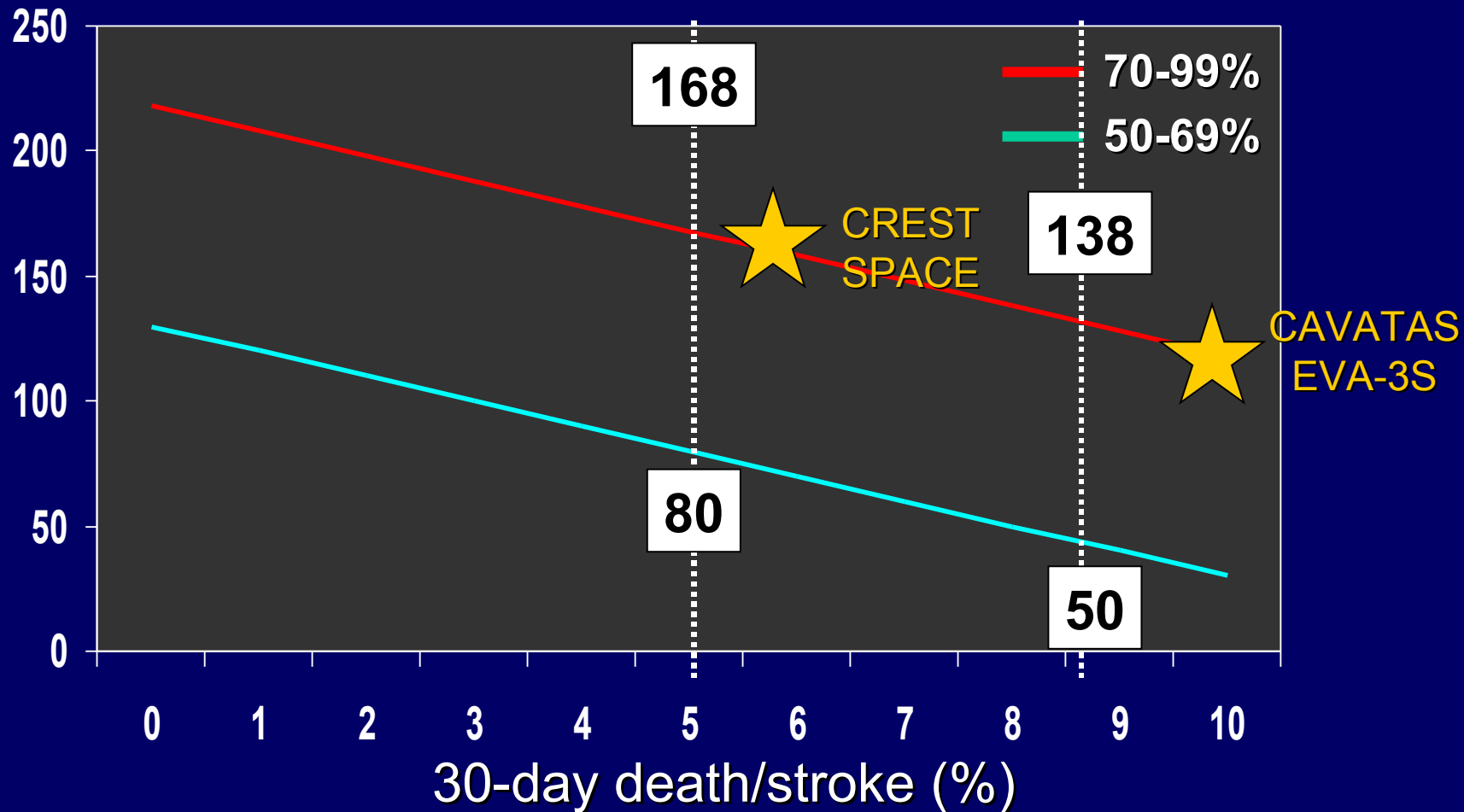
Effect of 30-d Risk on Outcome

CVEs prevented at 5 years per 1000 patients



Effect of 30-d Risk on Outcome

CVEs prevented at 5 years per 1000 patients



Conclusion

*No surgeon or interventionist can justify offering treatment on the basis of the International Trials if his procedural risks are out of accepted guidelines.
Personal audit is mandatory.*

Evidence for treating ...

- **symptomatic patients**
- **asymptomatic patients**
- **the 'high-risk' patient**

ACAS & ACST Findings

	5 year stroke risk surgery	BMT	ARR	RRR	NNT	CVE/ 1000
ACAS (n=1662)	5.1%	11.0%	5.9%	54%	17	59

Criticisms of ACAS

- ❖ disabling/fatal stroke not reduced
- ❖ ACAS observed no significant benefit in women
- ❖ patients had to live 5 years to gain benefit
- ❖ stroke reduction only achieved in year five
- ❖ concerns over surgeon selection
- ❖ no association between stenosis severity & stroke risk
- ❖ no association between bilateral disease & stroke risk

ACAS & ACST Findings

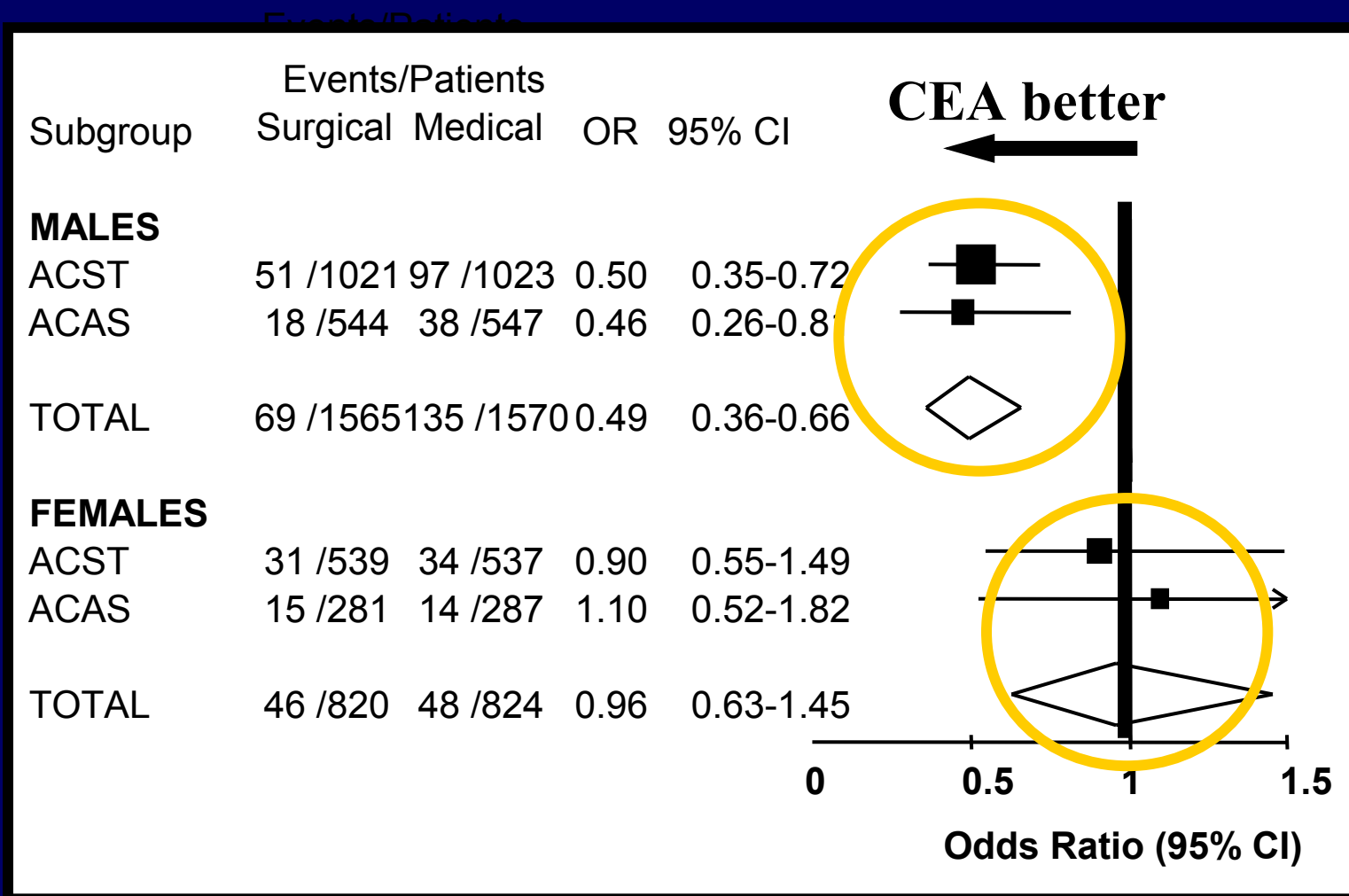
	5 year stroke risk surgery	BMT	ARR	RRR	NNT	CVE/ 1000
ACAS (n=1662)	5.1%	11.0%	5.9%	54%	17	59
ACST (n=3120)	6.4%	11.8%	5.4%	46%	19	53

ACAS, 1995 ACST, 2004

Principle Messages from ACST

- ❖ maximum benefit in patients aged <75 years
- ❖ no evidence of benefit in patients aged >75 yrs
- ❖ 'apparent' benefit for men *and* women
- ❖ 50% reduction in disabling/fatal stroke

Benefit in Women?



Benefit in Women?

You cannot ignore the obvious fact that women gained less benefit from intervention than men.

Treatment should probably be reserved for women aged <70 years with no significant co-morbidity.

Asymptomatic females could never be considered 'high-risk'

Evidence for treating ...

- symptomatic patients
- asymptomatic patients
- the 'high-risk' patient

Evidence for treating ...

“When carotid endarterectomy is not feasible in high-risk patients and carotid stenting is, patients should undergo stenting regardless of the medical risk”

Alhaddad

AHA Guidelines

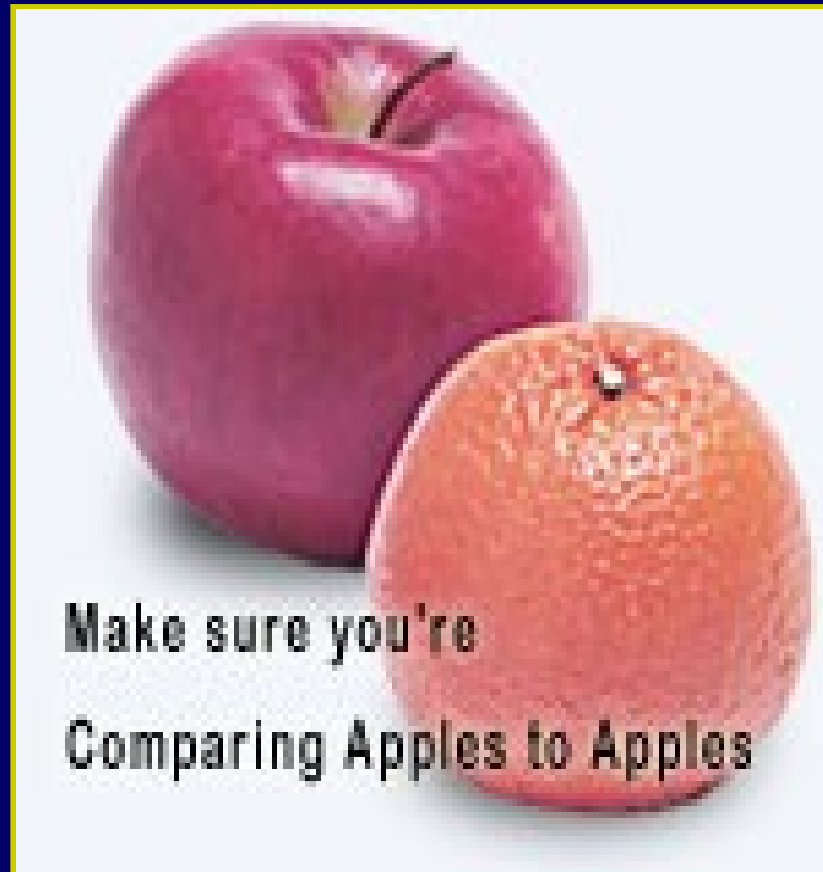
Among patients with a severe ($>70\%$) symptomatic stenosis in whom the stenosis is difficult to access surgically, major medical conditions are present, or other specific circumstances exist (e.g. radiation arteritis, recurrent stenosis), CAS is not inferior to CEA and may be considered, provided CAS is performed with established peri-procedural risks of 4-6%.

Class IIa, Evidence Level B

Opinion or Evidence?

“Registries of carotid stenting in patients at high risk for CEA are consistent with the SAPPHERE trial. Patients who have serious co-morbid medical or anatomical conditions that increase the risk from an open surgical approach or general anaesthesia should be primary candidates for carotid stenting”

***Do we have enough data
to make this recommendation?***



Make sure you're
Comparing Apples to Apples

SAPPHIRE

723 'high risk' patients considered for inclusion

general criteria: symptomatic + stenosis >50%
asymptomatic + stenosis >80%

'high-risk' criteria - significant cardiac disease
- severe pulmonary disease
- contralateral occlusion
- contralateral RLN palsy
- previous neck surgery
- radiation arteritis
- recurrent stenosis
- age >80 years

Some Interventions are Obviously High-risk





'High-risk' for what, exactly?

high risk plaque
symptomatic

high risk patient
cardiac disease
pulmonary disease
>80 years

high risk procedure
contralat occlusion
rec laryngeal N palsy
PMH neck surgery
radiation arteritis
recurrent stenosis

'High-risk' for what, exactly?

<u>high risk plaque</u> symptomatic 	<u>high risk patient</u> cardiac disease pulmonary disease >80 years 	<u>high risk procedure</u> contralat occlusion rec laryngeal N palsy PMH neck surgery radiation arteritis recurrent stenosis
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It is difficult, based on evidence, to place 'asymptomatic' patients within any of these categories

Unexplained Paradoxes

Based on evidence, will CAS prevent stroke?

	symptomatic	asymptomatic
aged >75 years	+++	0
with plaque irregularity	+++	0
incremental stenosis	+++	0
with contralateral occlusion	+++	0

based on data from ECST, NASCET, ACAS, ACST, SPACE, and SAPPHIRE

SAPPHIRE

71% of the randomised patients were

asymptomatic

in whom:

30 day death/stroke

following angioplasty = 5.8%

following surgery = 6.1%

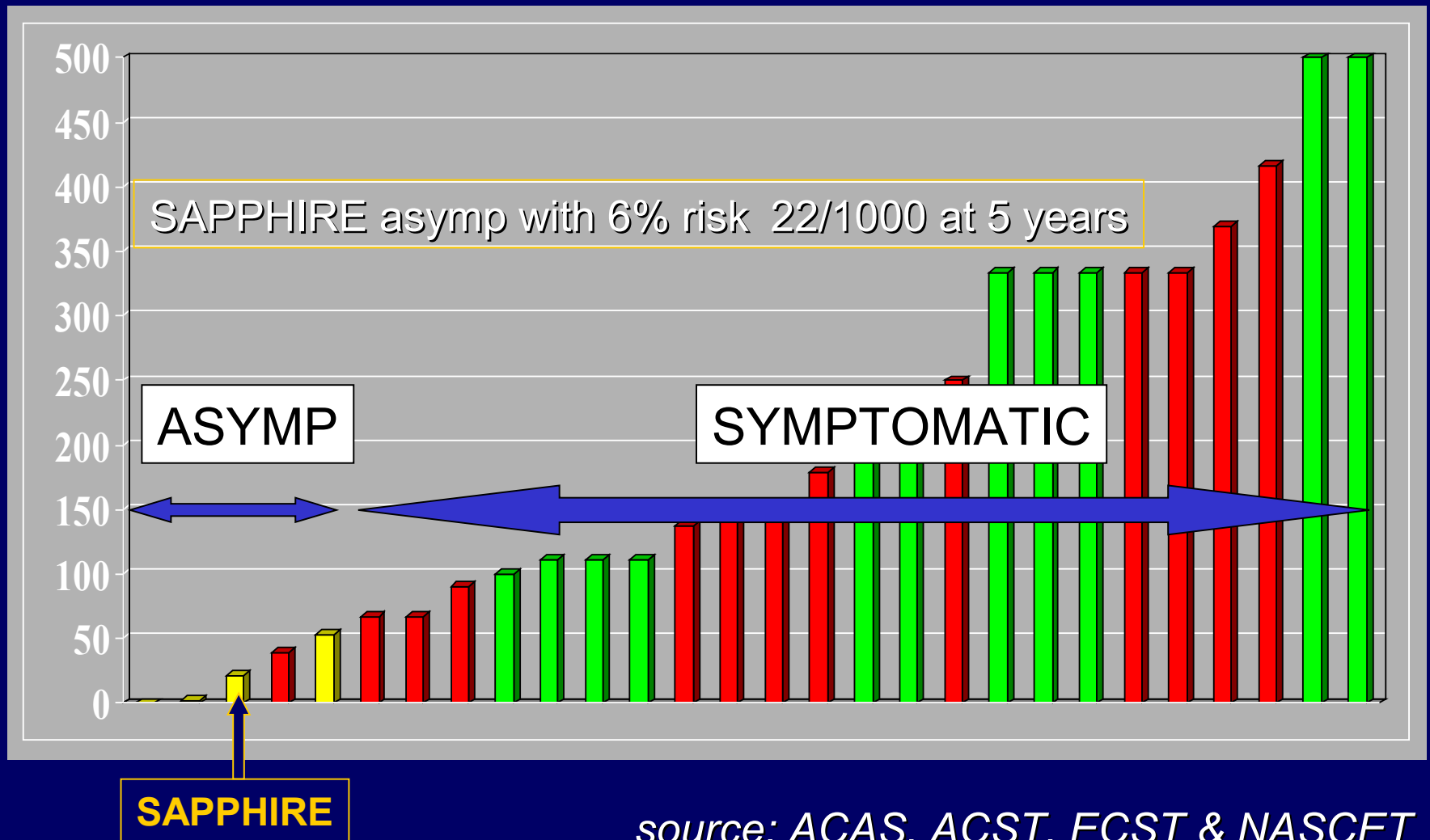
Conclusions from SAPPHERE

So, a trial where 70%+ were asymptomatic and in whom there was a 6% procedural risk and in whom you will

never

confer any long term benefit in stroke prevention has been used to develop guidelines for all high-risk patients i.e. including all the symptomatic ones!

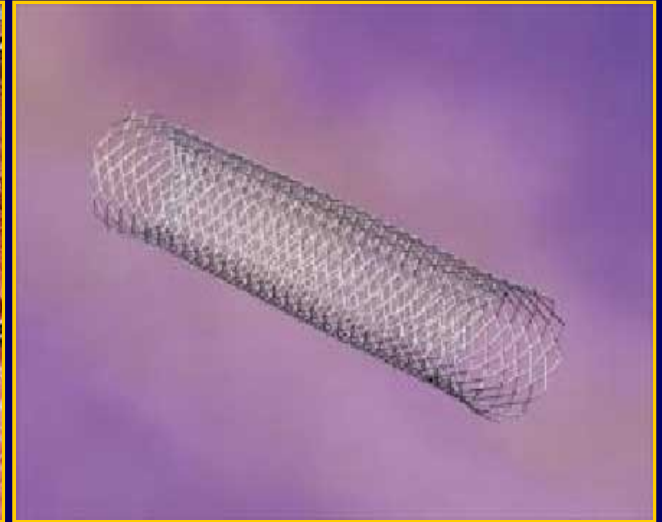
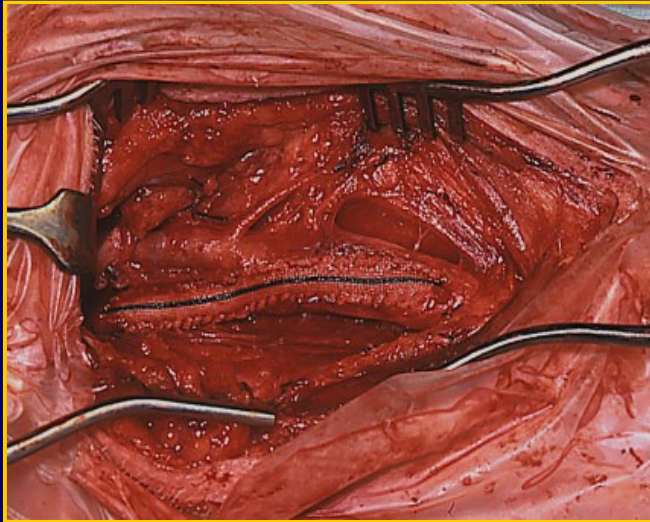
Strokes Prevented per 1000 CEAs



“high relative risk/benefit group”

<i>patient subgroup</i>	CVE prevented per 1000 CEAs
SAPPHIRE asymp with 6% risk	22 at 5y
symp, 70-99% aged >75 years	333 at 2y
symp, 70-99% with high co-morbidity	333 at 2y
symp, 70-99% recurrent TIAs for >6 mths	333 at 2y
symp, 70-99% with operations <2 weeks	333 at 3y
symp, 80-99% with intracranial disease	333 at 3y
symp, 90-99% with no string sign	370 at 3y
symp, 70-99%, with contralateral occlusion	500 at 2y
symp, 90-99% with plaque ulceration	500 at 2y

What in whom?



We have still a lot of unanswered questions

Parting message.....

Irrespective of any debate about which asymptomatic patient should be treated, whether CEA or CAS is safer, how and by whom CAS should be performed, ALL pale into insignificance compared with the effect of delay in treating symptomatic patients with severe carotid artery disease.