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***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)

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## Evidence for treating ...

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

# The International CEA Trials

| <b>ECST</b> | surgical<br>risk (%) | medical<br>risk (%) | ARR<br>(%) | NNT<br>(%) | CVE prevented<br>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                       |

| <b>NASCET</b> | surgical<br>risk (%) | medical<br>risk (%) | ARR<br>(%) | NNT<br>(%) | CVE prevented<br>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

**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

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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

# Take-home Messages

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

**achieving maximum benefit:** -incremental stenosis

-age

-rapid intervention

-gender

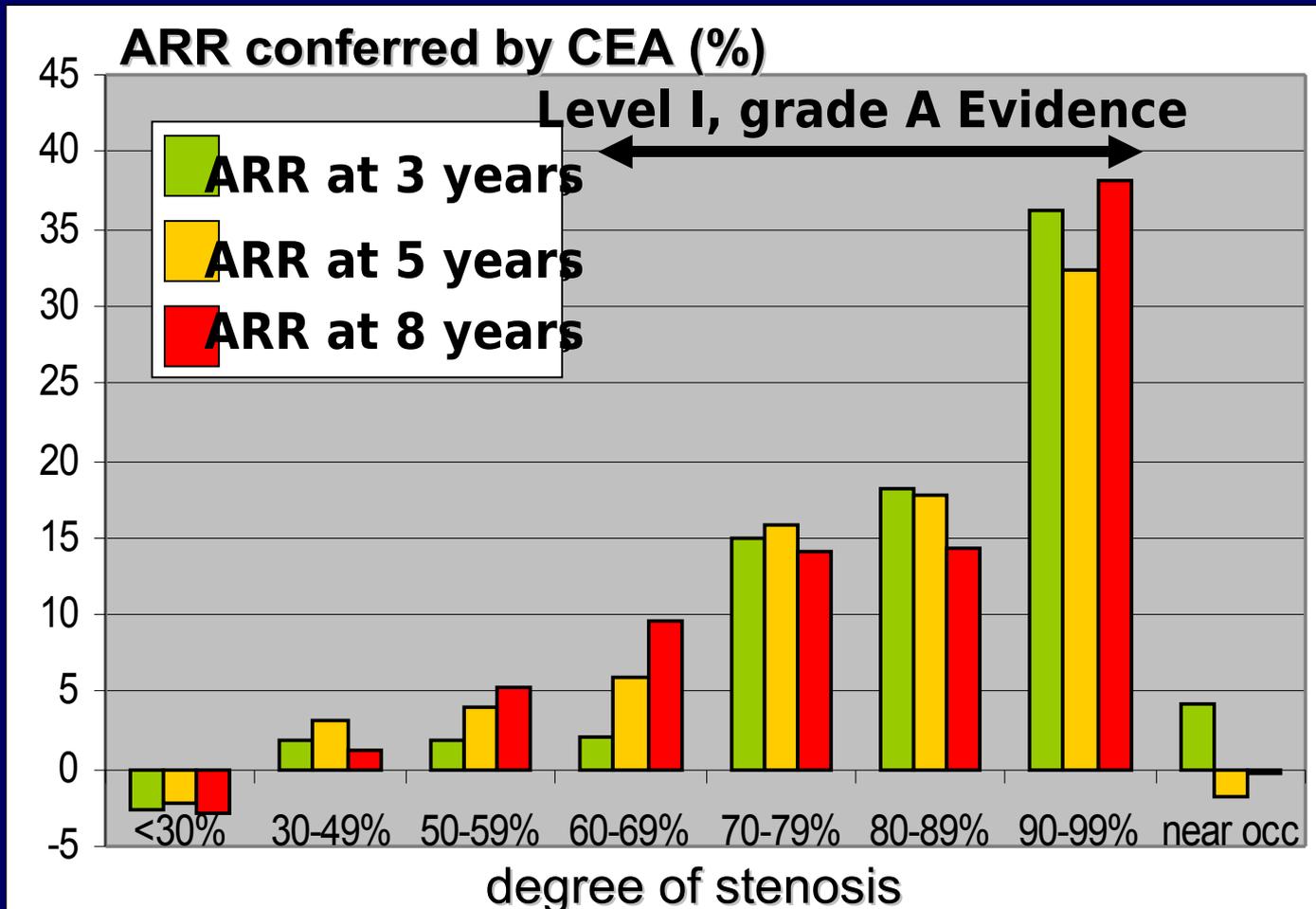
-plaque morphology

-contralateral

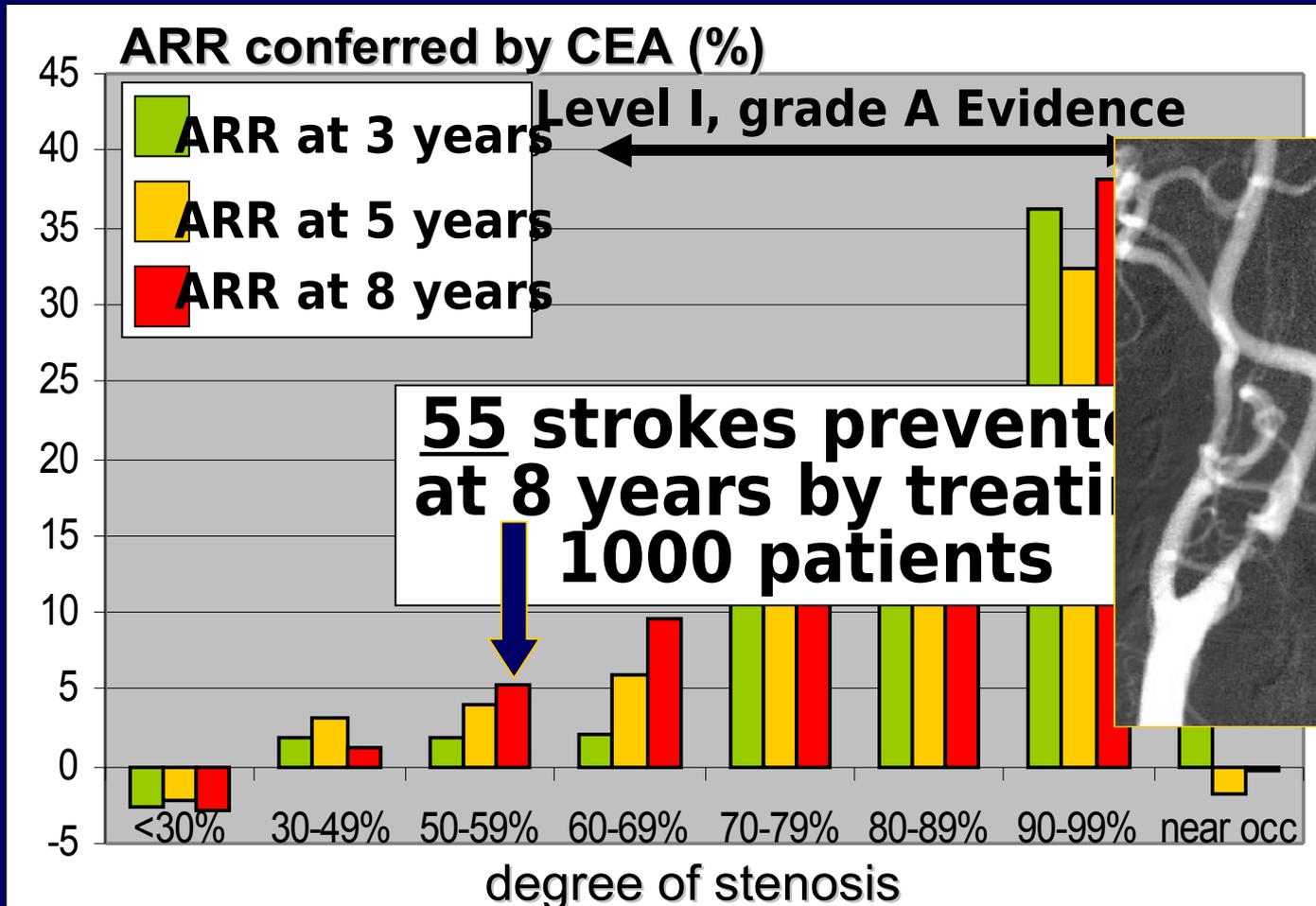
occlusion

-operative risk

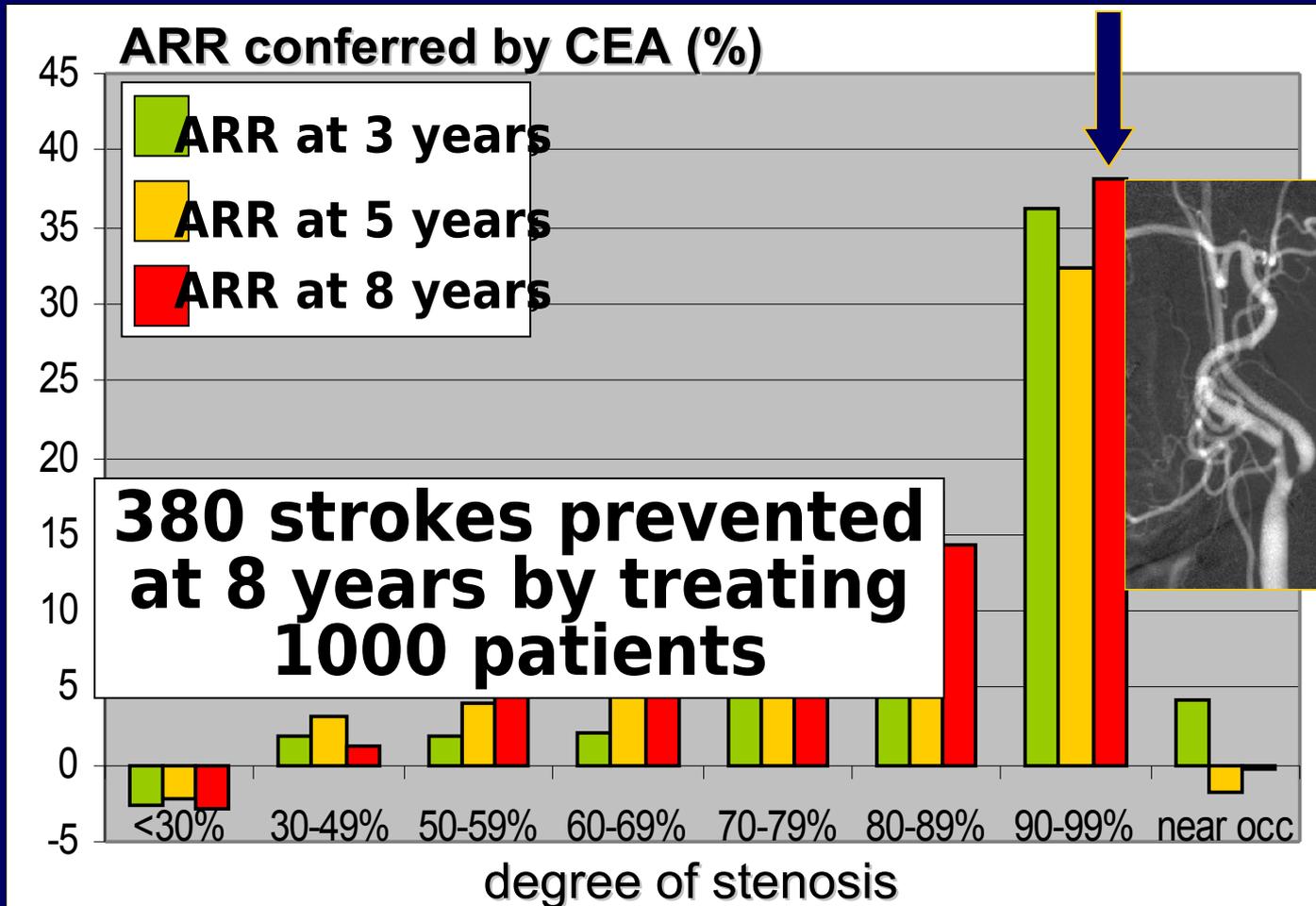
# Incremental Stenosis



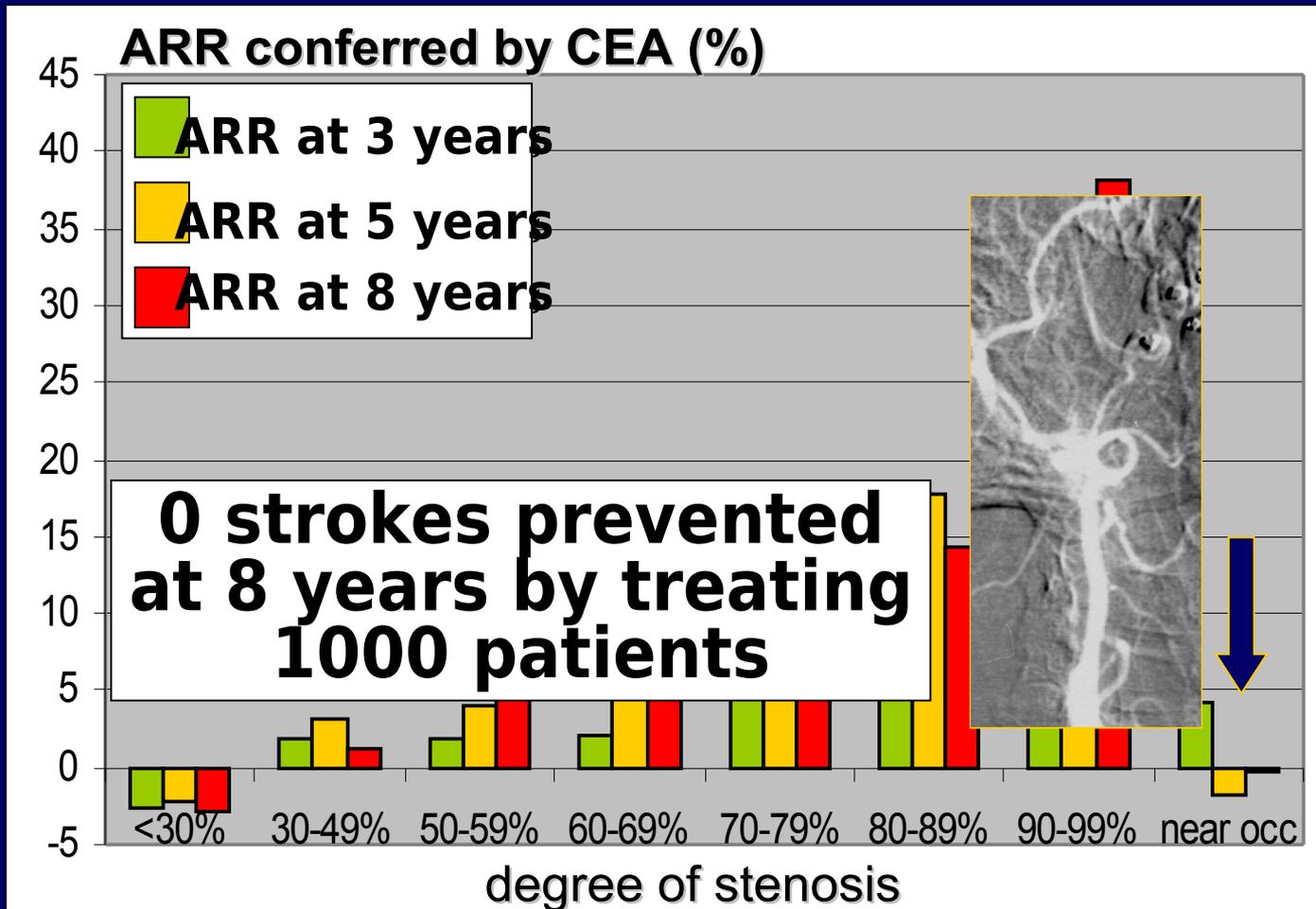
# Incremental Stenosis



# Incremental Stenosis



# Incremental Stenosis



# Conclusion

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

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# Take-home Messages

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stenosis

-age

-rapid intervention

-gender

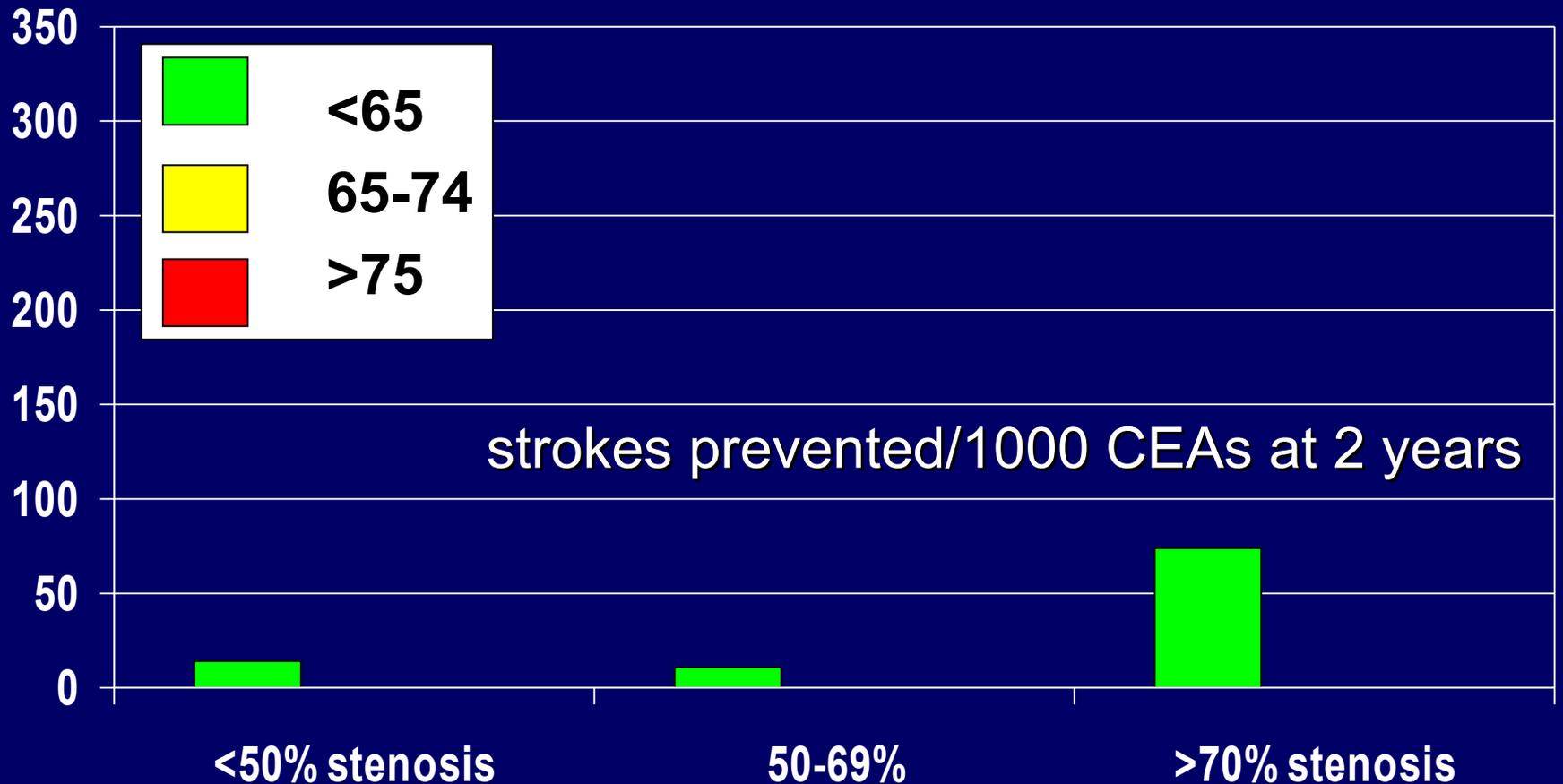
-plaque morphology

-contralateral

occlusion

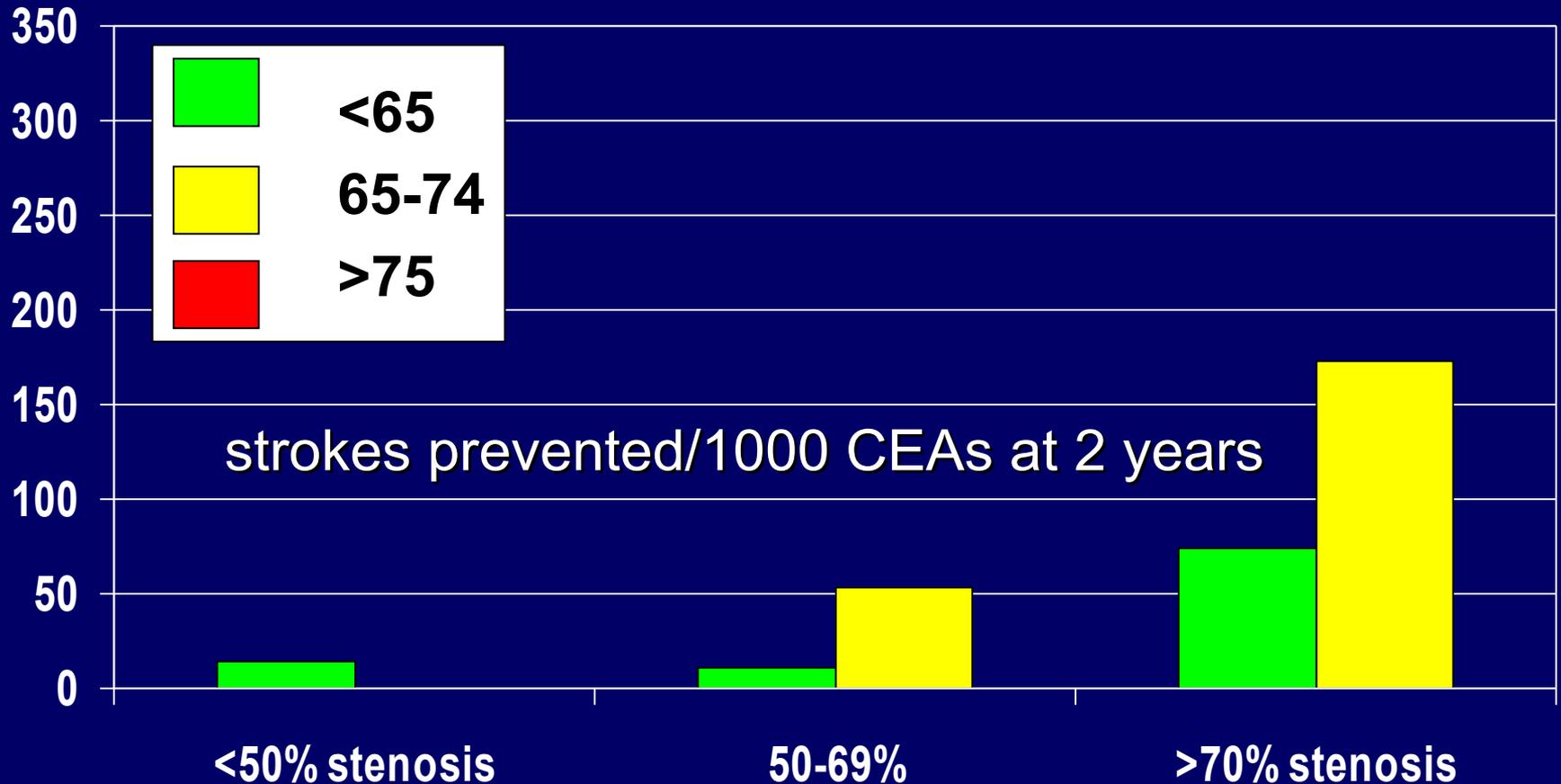
-operative risk

# Effect of Age on Benefit from CEA



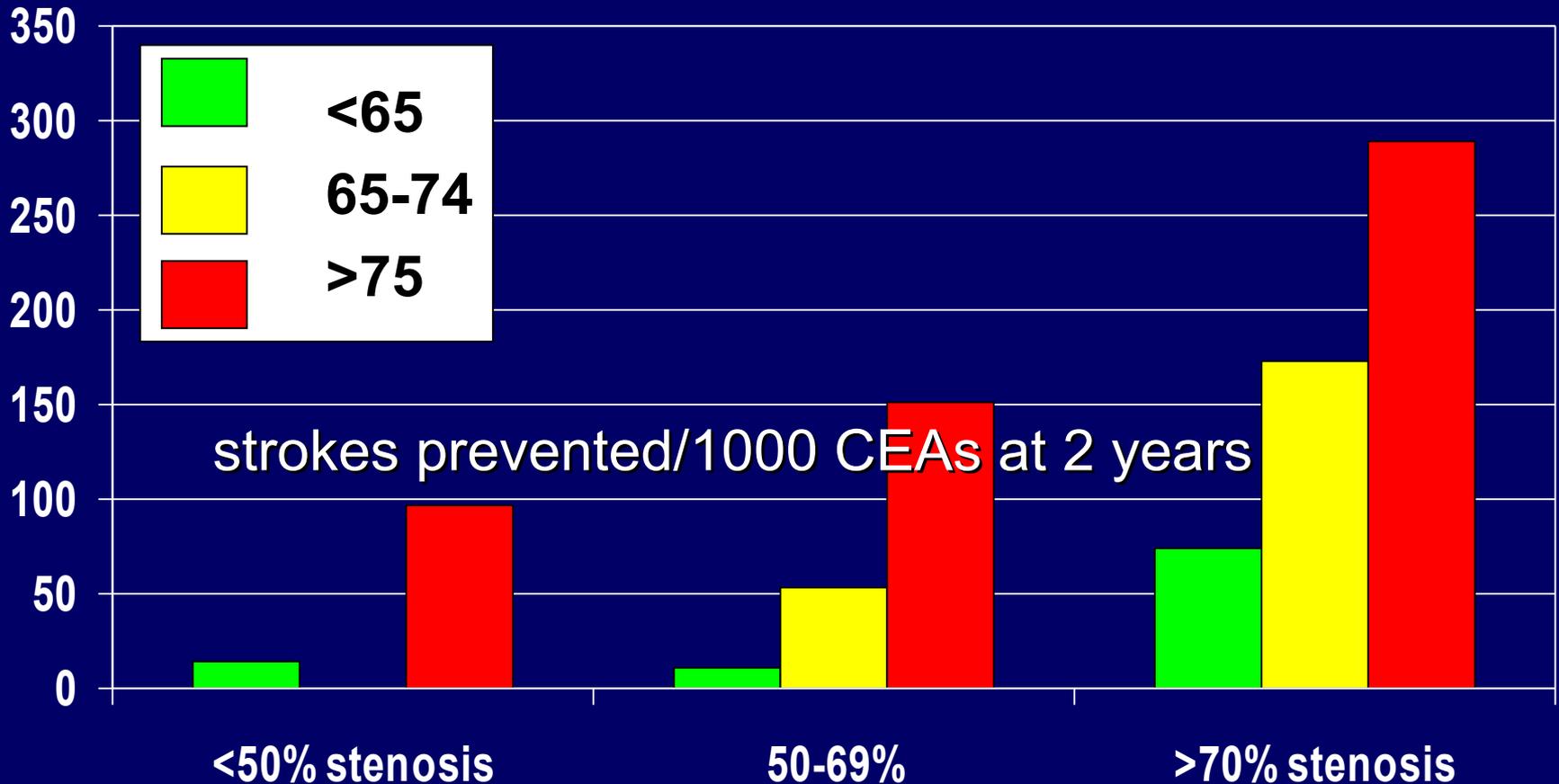
adapted from NASCET 2001

# Effect of Age on Benefit from CEA



adapted from NASCET 2001

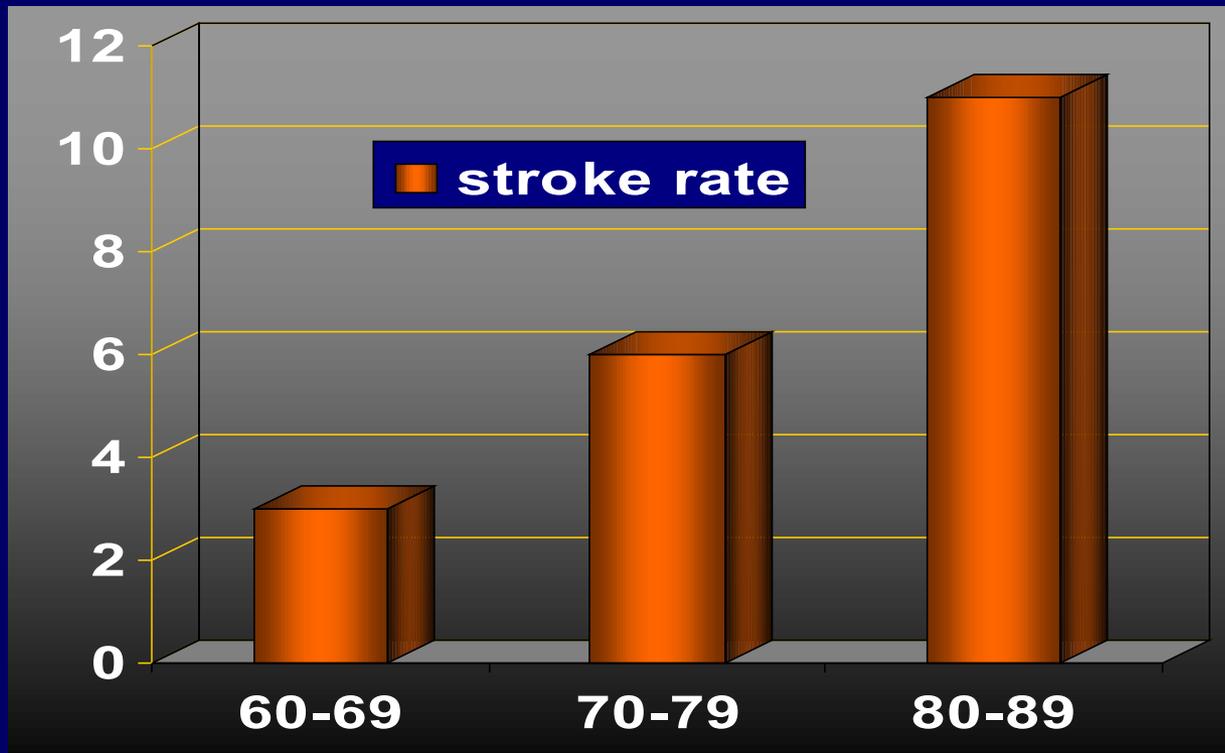
# Effect of Age on Benefit from CEA



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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# Take-home Messages

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stenosis

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-gender

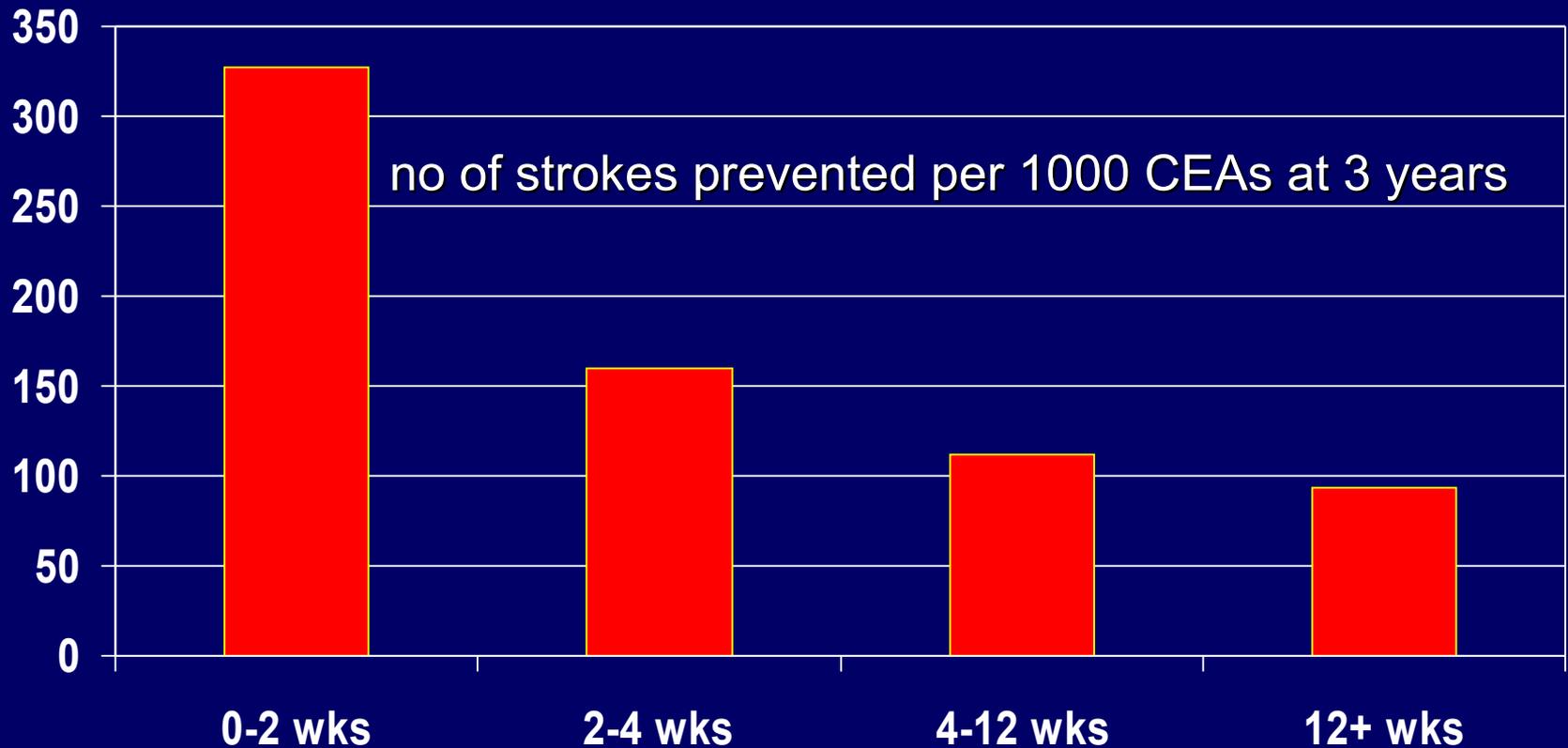
-plaque morphology

-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.*

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# Take-home Messages

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stenosis

-age

-rapid intervention

-gender

-plaque morphology

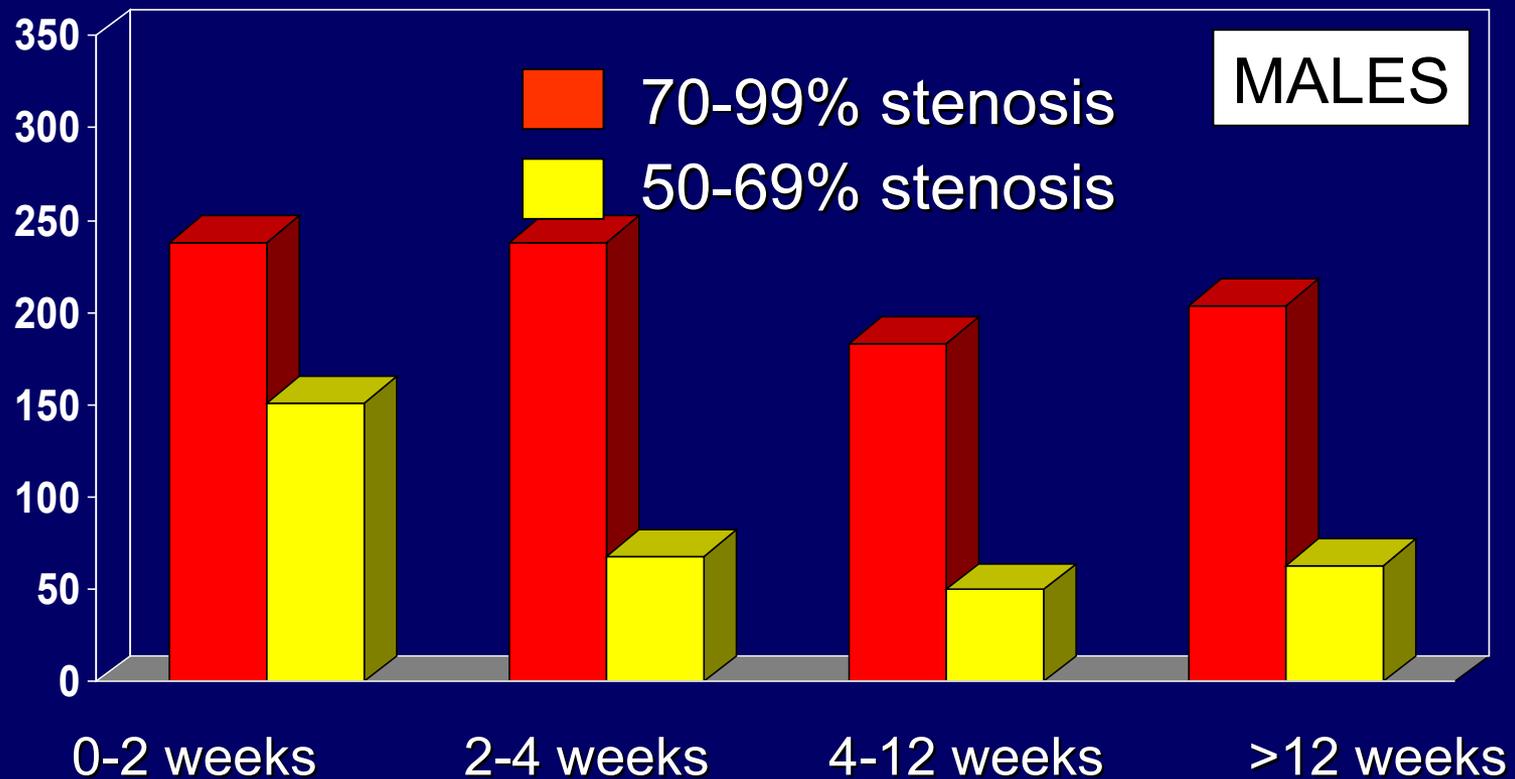
-contralateral

occlusion

-operative risk

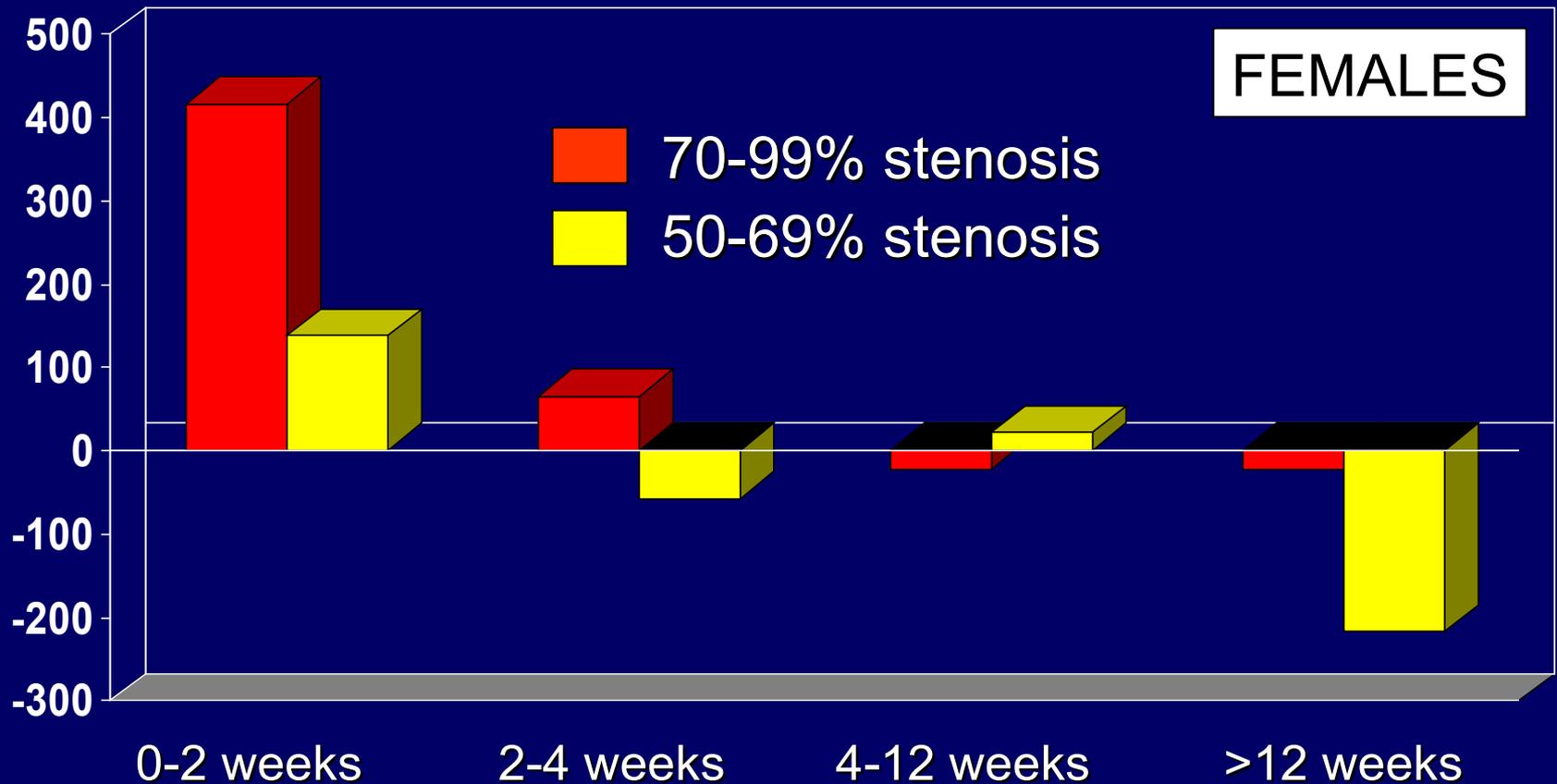
# Gender, Delay & Stenosis Severity

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

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

**achieving maximum benefit:** -incremental  
stenosis

-age

-rapid intervention

-gender

-plaque morphology

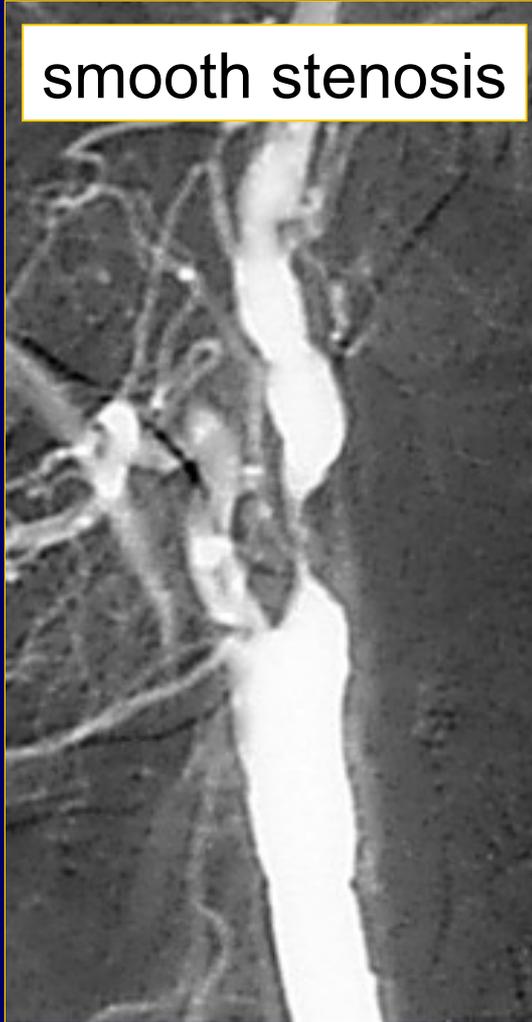
-contralateral

occlusion

-operative risk

# Influence of Plaque Morphology

smooth stenosis

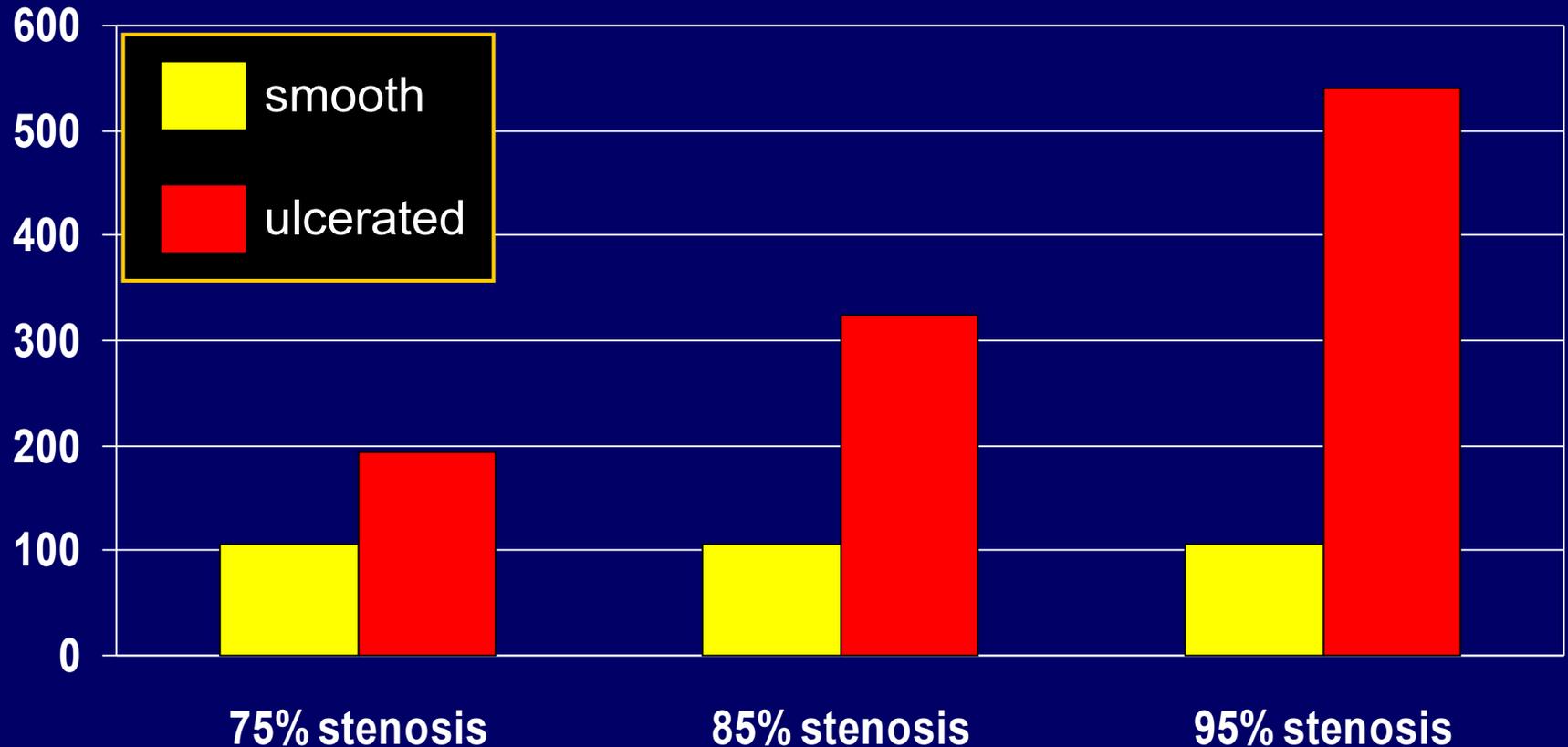


ulcerated stenosis



# 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.*

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# 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

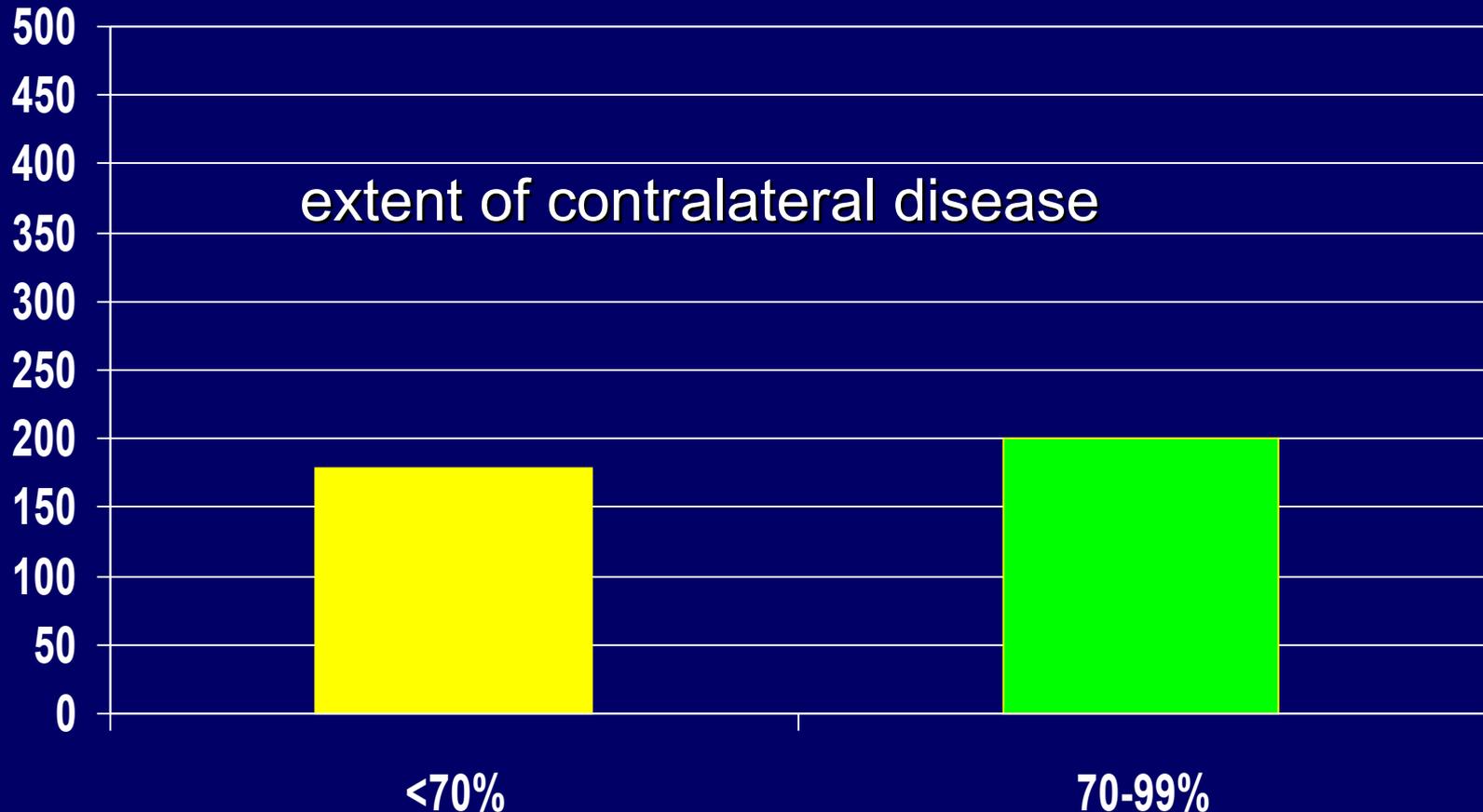
-operative risk

# Stenosis & Contralateral Occlusion



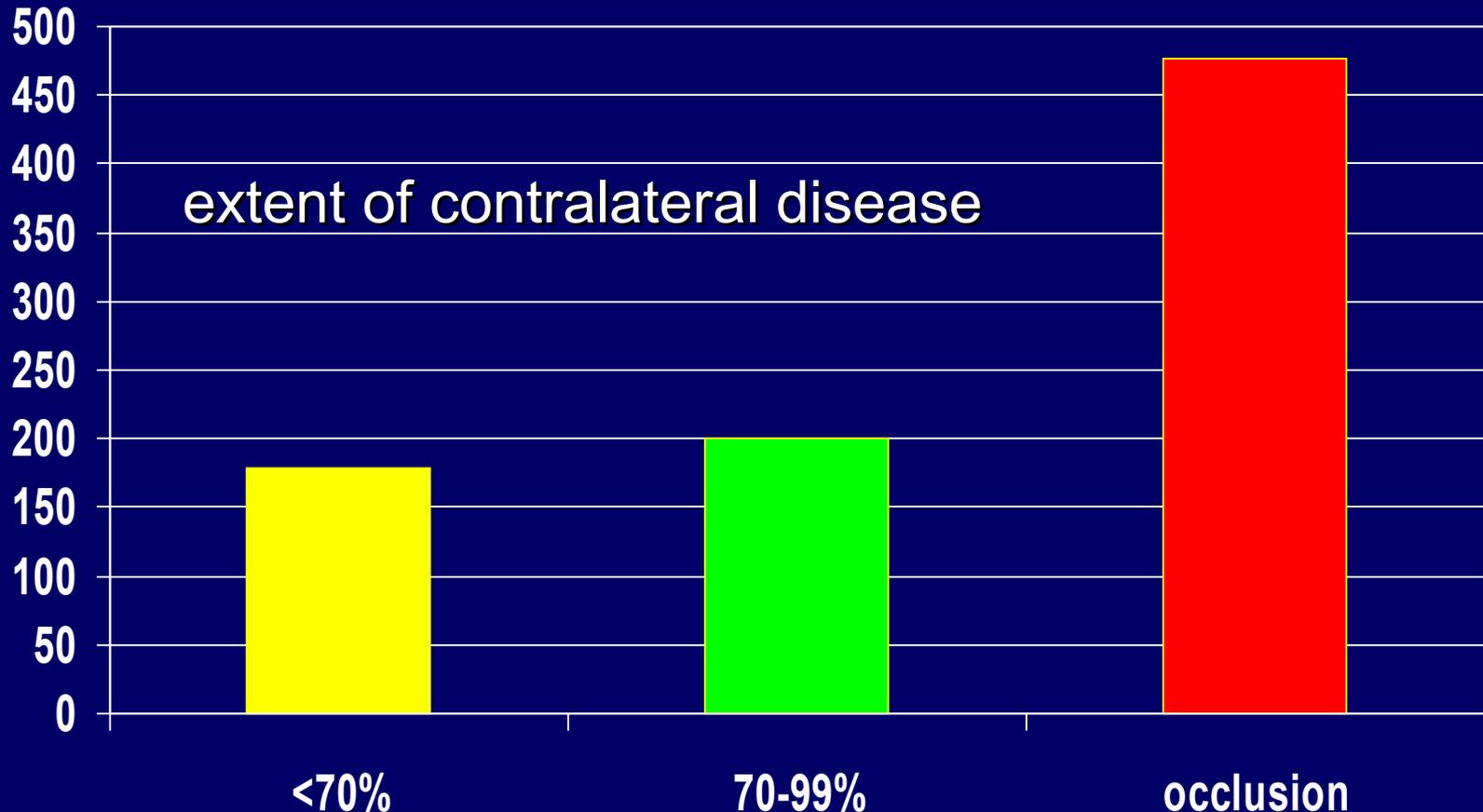
# Effect of Contralateral Disease

No of ipsilateral strokes prevented per 1000 CEAs at 2 years



# Effect of Contralateral Disease

No of ipsilateral strokes prevented per 1000 CEAs at 2 years



# 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%)!*

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# Take-home Messages

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-age

-rapid intervention

-gender

-plaque morphology

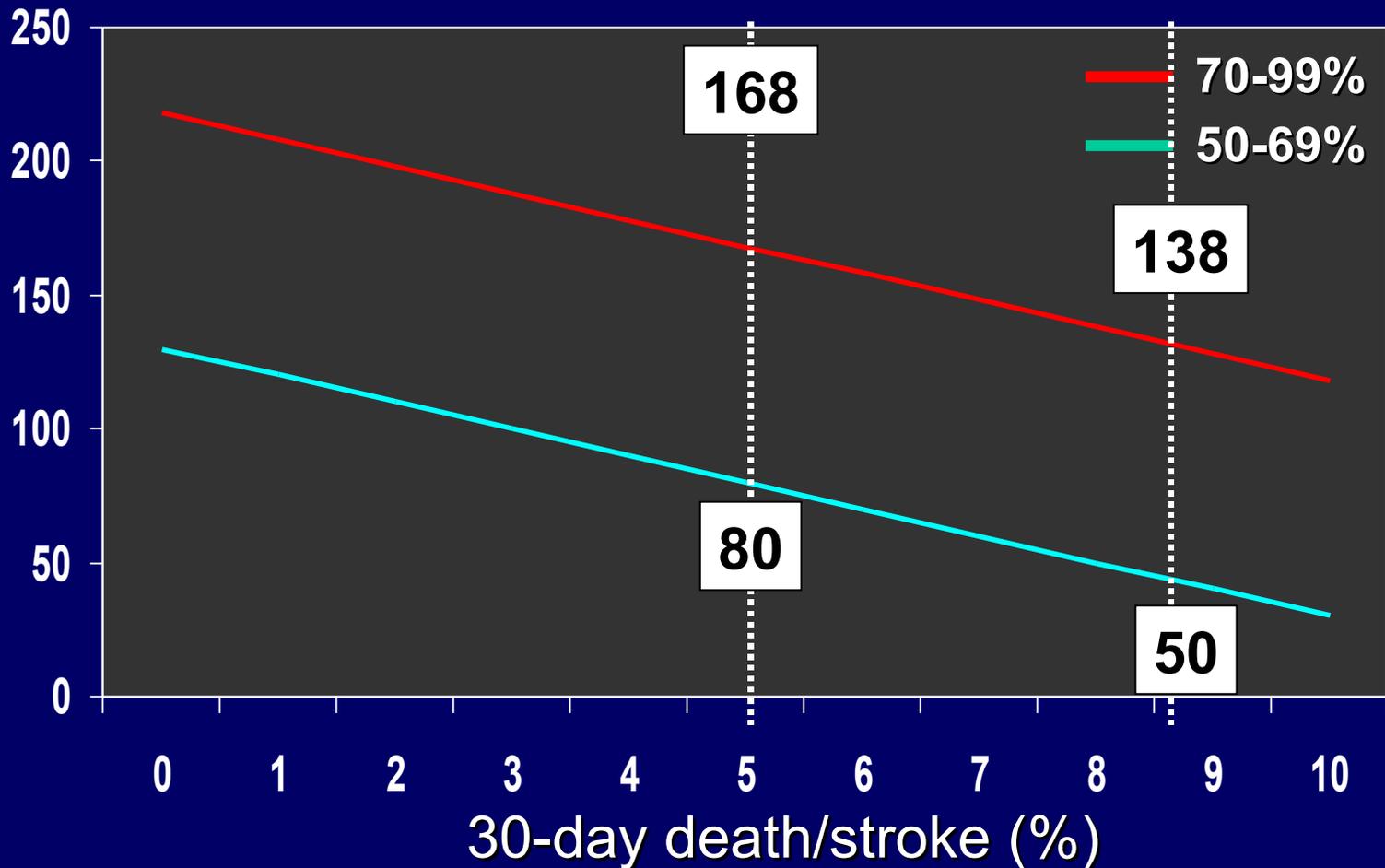
-contralateral

occlusion

-operative risk

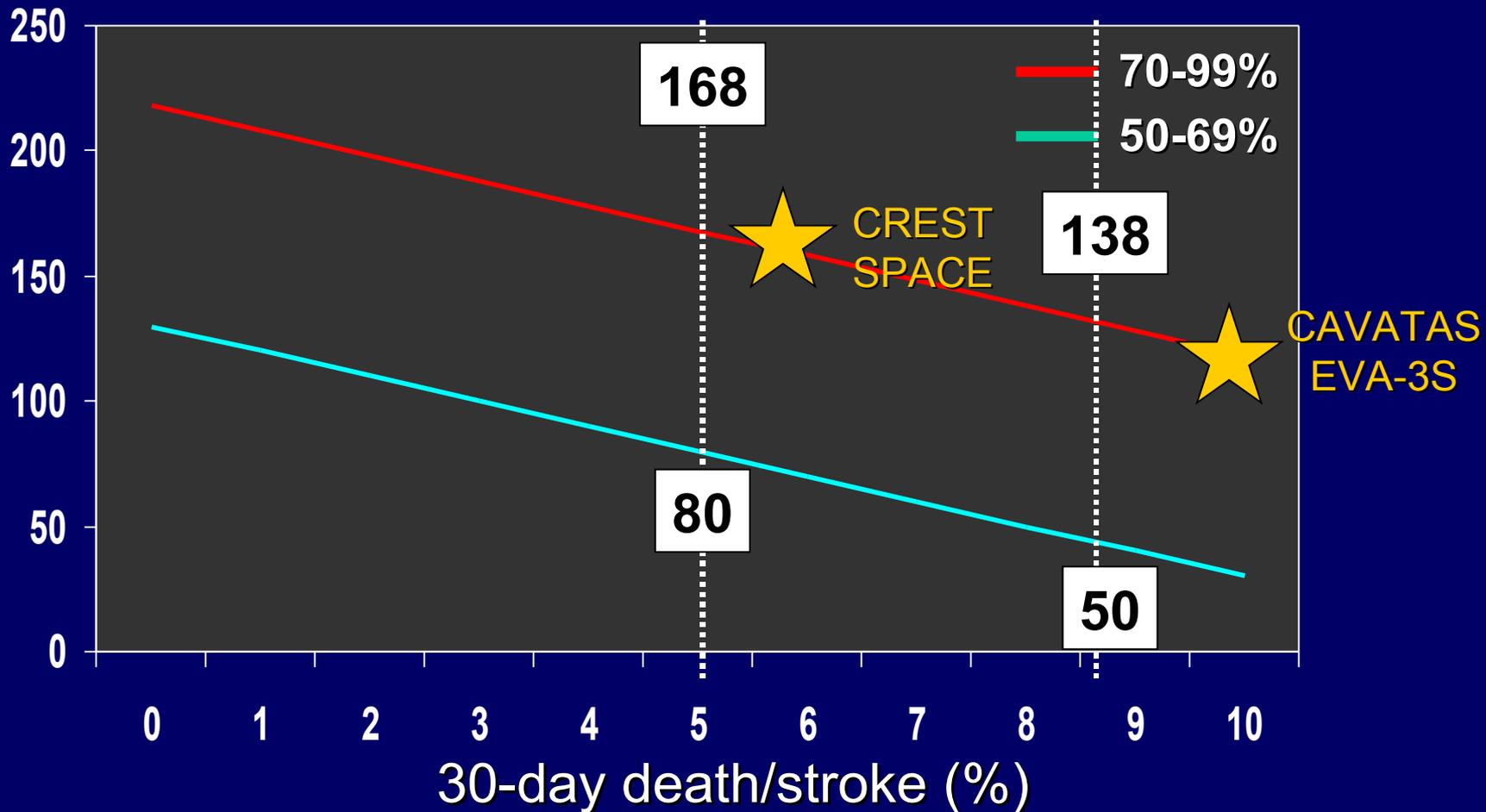
# Effect of 30-d Risk on Outcome

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.*

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## Evidence for treating ...

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

# ACAS & ACST Findings

|                  | 5 year stroke risk |       |      |     |     |              |
|------------------|--------------------|-------|------|-----|-----|--------------|
|                  | surgery            | BMT   | ARR  | RRR | NNT | CVE/<br>1000 |
| ACAS<br>(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

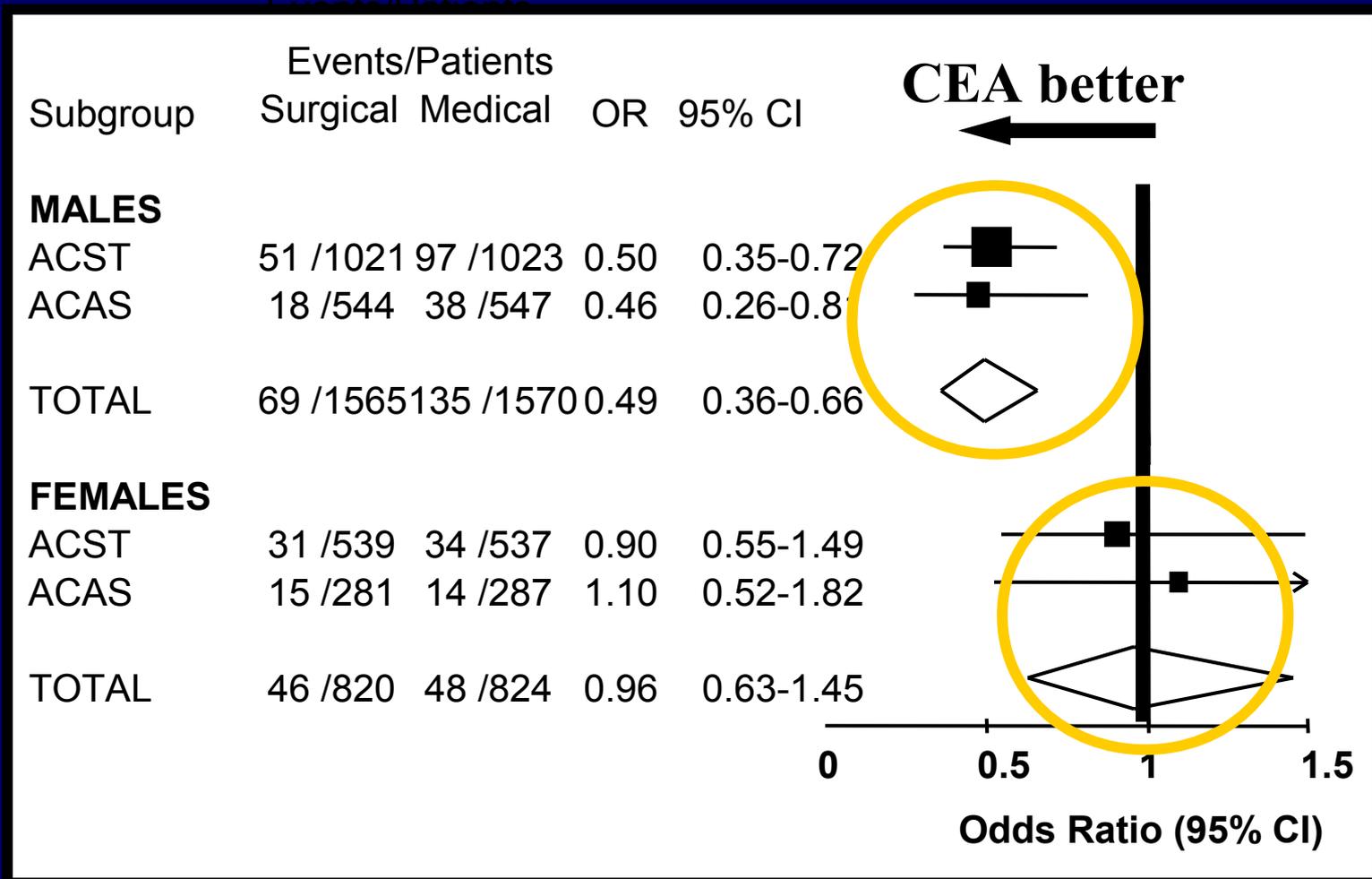
|                  | 5 year stroke risk<br>surgery | BMT   | ARR  | RRR | NNT | CVE/<br>1000 |
|------------------|-------------------------------|-------|------|-----|-----|--------------|
| ACAS<br>(n=1662) | 5.1%                          | 11.0% | 5.9% | 54% | 17  | 59           |
| ACST<br>(n=3120) | 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'*

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## Evidence for treating ...

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

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## 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

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# AHA Guidelines

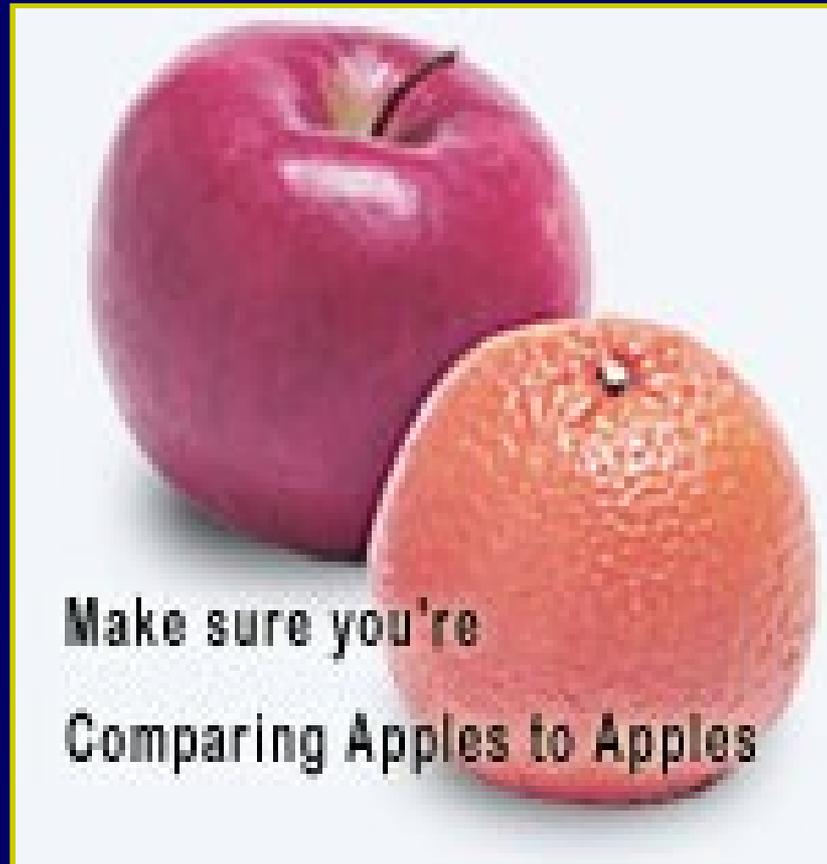
Among patients with a severe (>70%) symptomatic stenosis in whom the stenosis is difficult to access surgically, major medical conditions are present, or other specific circumstances exist (e.g. radiation arteritis, recurrent stenosis), CAS is not inferior to CEA and may be considered, provided CAS is 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?***



# 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><br>symptomatic | <u>high risk patient</u><br>cardiac disease<br>pulmonary disease<br>>80 years | <u>high risk procedure</u><br>contralat occlusion<br>rec laryngeal N palsy<br>PMH neck surgery<br>radiation arteritis<br>recurrent stenosis |
|--|---|---|

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 SAPHIRE

# 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!

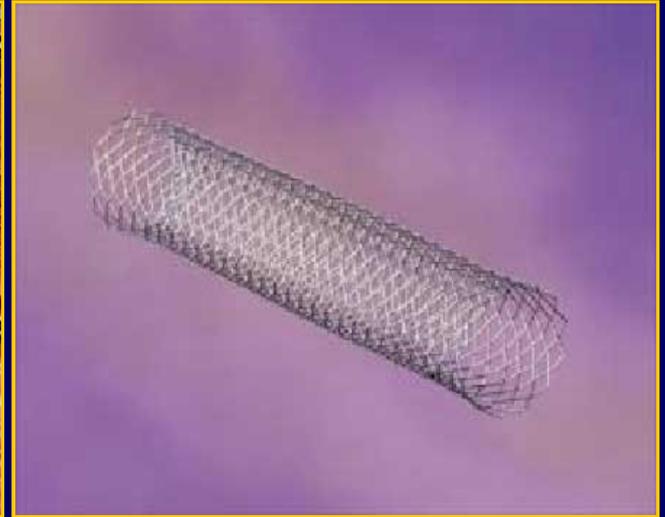
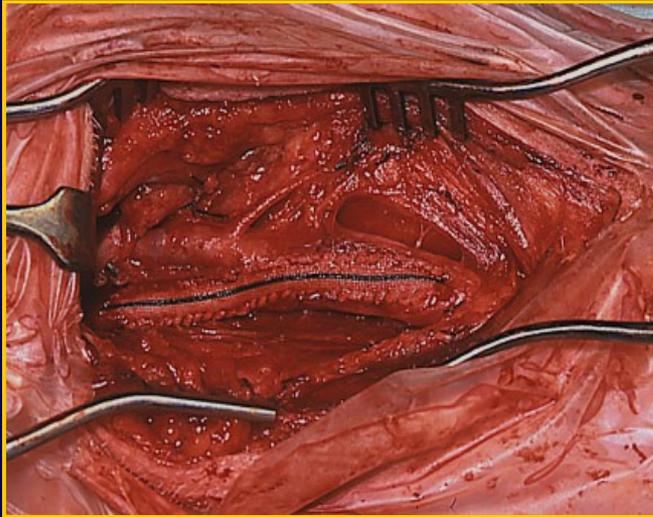
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# “high relative risk/benefit group”

| <i>patient subgroup</i>                    | CVE prevented<br>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.