

Imperial College
London



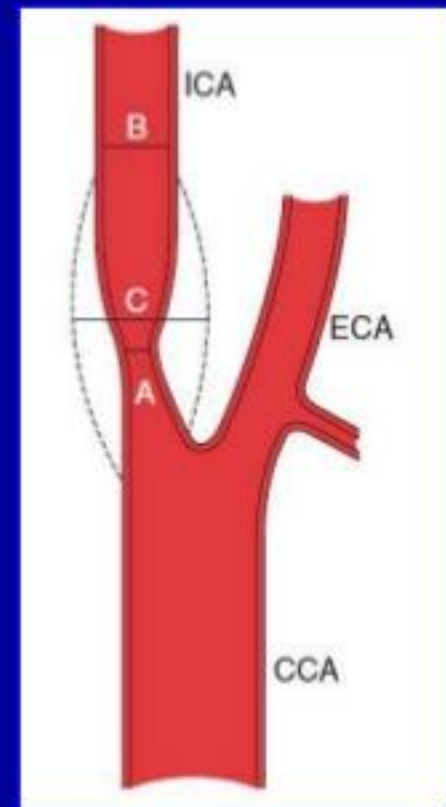
Should we operate a<70% symptomatic stenosis?

Professor Alun H Davies
Imperial College,
London

CRITERIA ICA stenosis on angiogram

Diameter reduction

* NASCET $(B - A / B) \times 100$	** ECST $(C - A / C) \times 100$
30%	65%
40%	70%
50%	75%
60%	80%
70%	85%
80%	91%
90%	97%



* NASCET: North American Symptomatic Carotid Endarterectomy Trial

** ECST: European Carotid Surgery Trial

Time from event and benefit

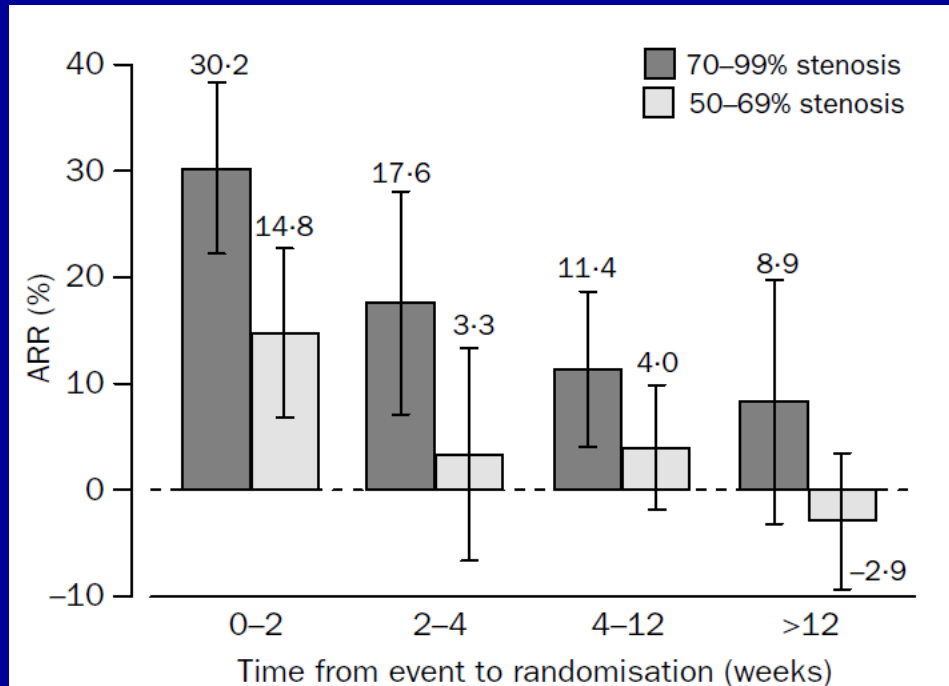


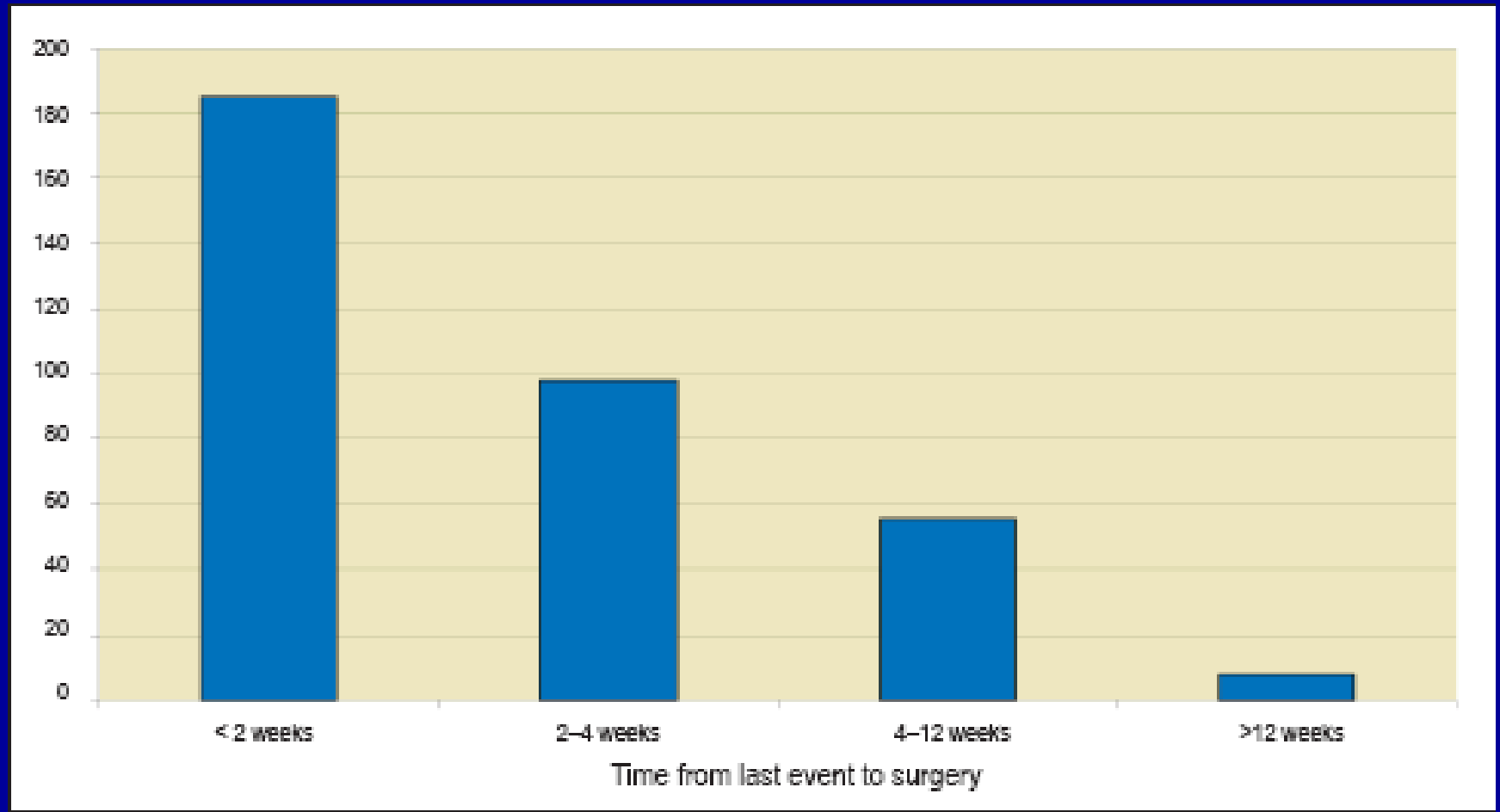
Figure 5: **Absolute reduction with surgery in the 5-year cumulative risk of ipsilateral carotid ischaemic stroke and any stroke or death within 30 days after trial surgery in patients with 50-69% stenosis and $\geq 70\%$ stenosis without near-occlusion stratified by the time from last symptomatic event to randomisation**

Numbers above bars indicate actual absolute risk reduction. Vertical bars are 95% CIs.

Rothwell et al., Lancet, 2004

Number of strokes saved at 5 years

Per 1000 CEAs in 50-99% stenosis

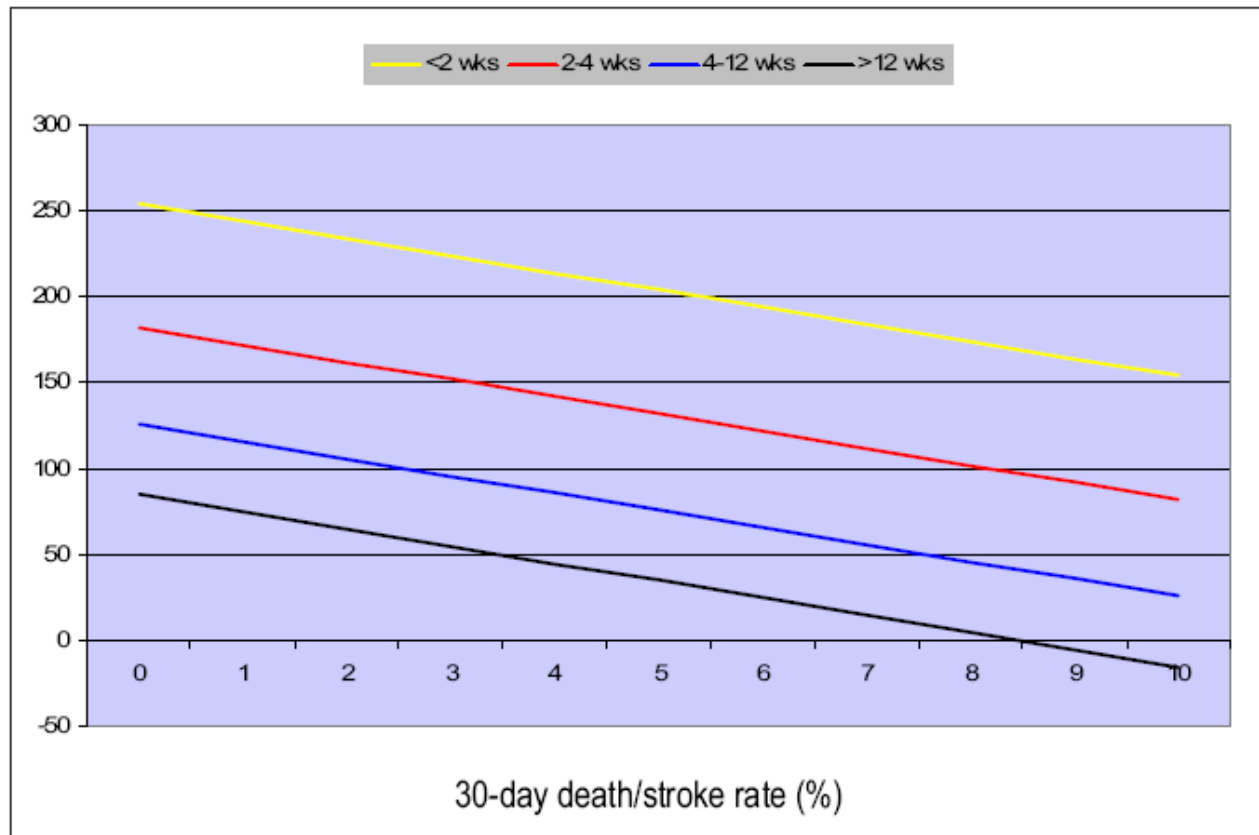


Time is brain!

Naylor 2007

Benefit of Urgent Treatment

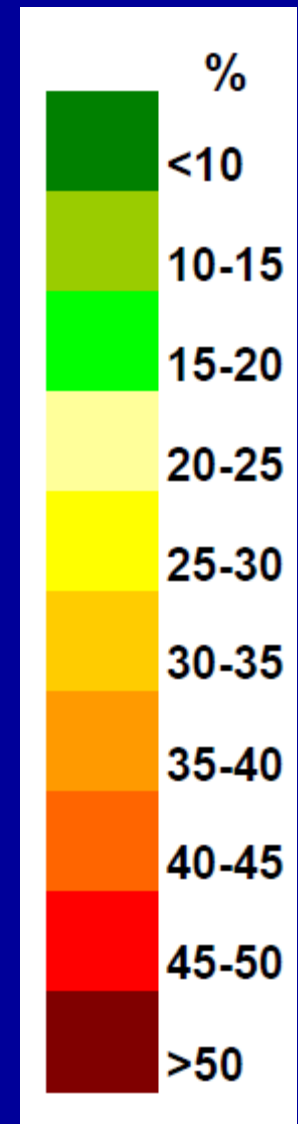
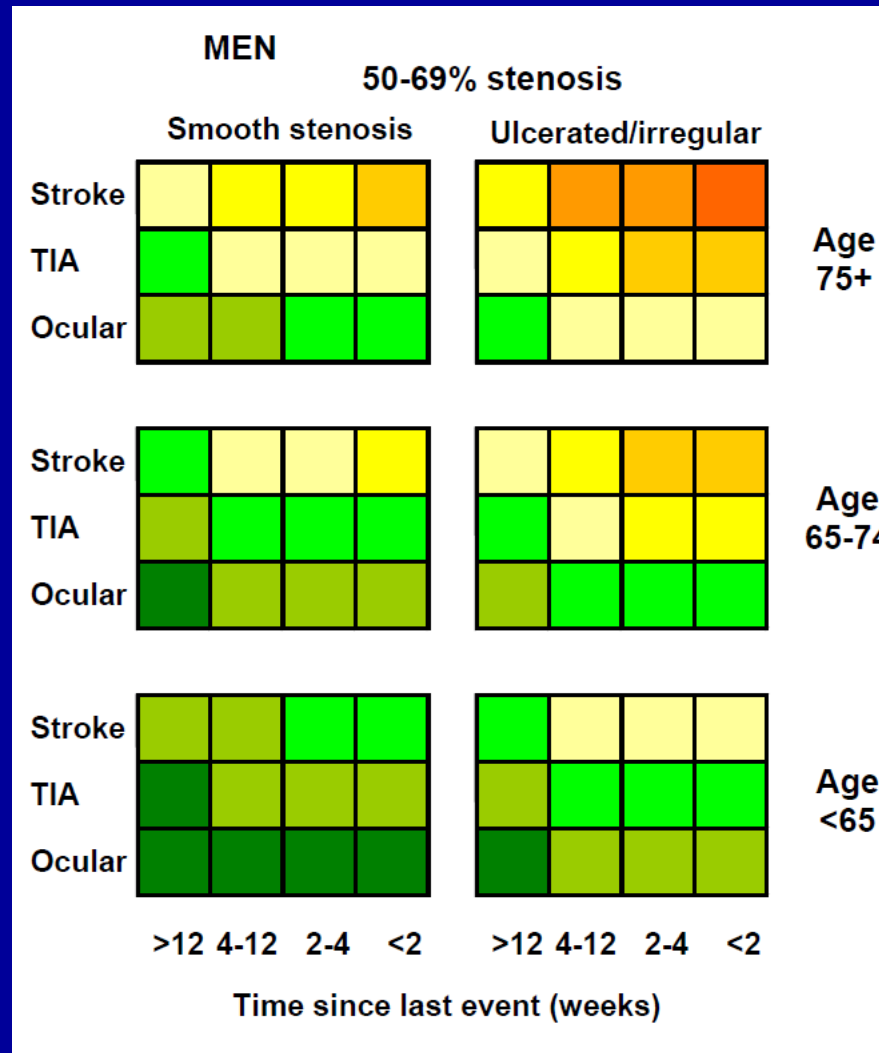
Figure 4: Strokes prevented per 1000 CEAs at five years stratified for:
(i) delay from last event to surgery and (ii) 30-day death/stroke risk (recalculated from CETC).¹⁰



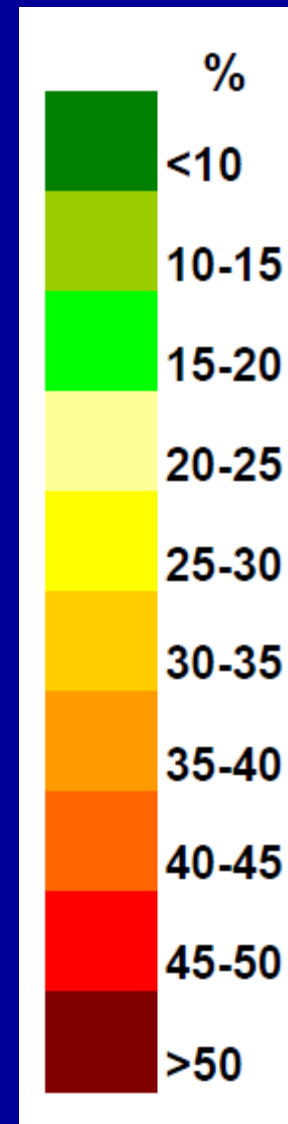
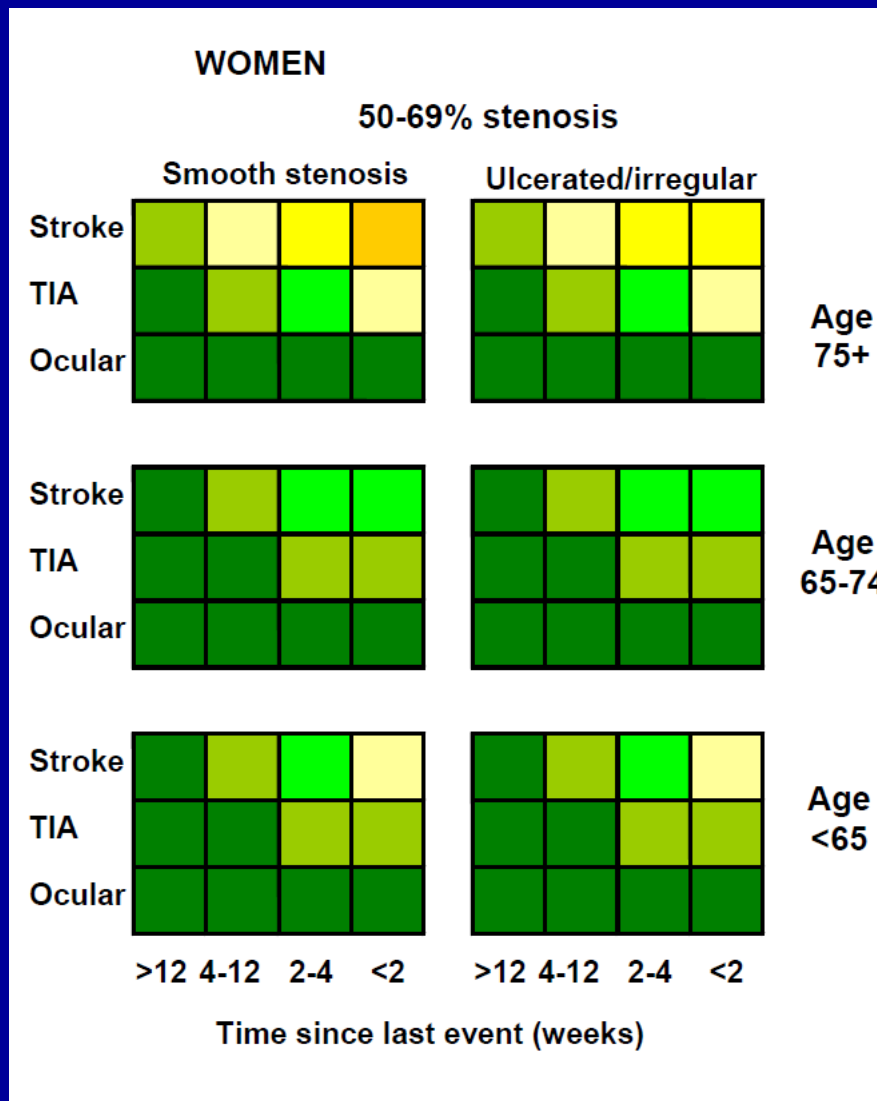
Time is brain!

Naylor 2007

5 year stroke risk



5 year stroke risk



Time is brain!

Gender

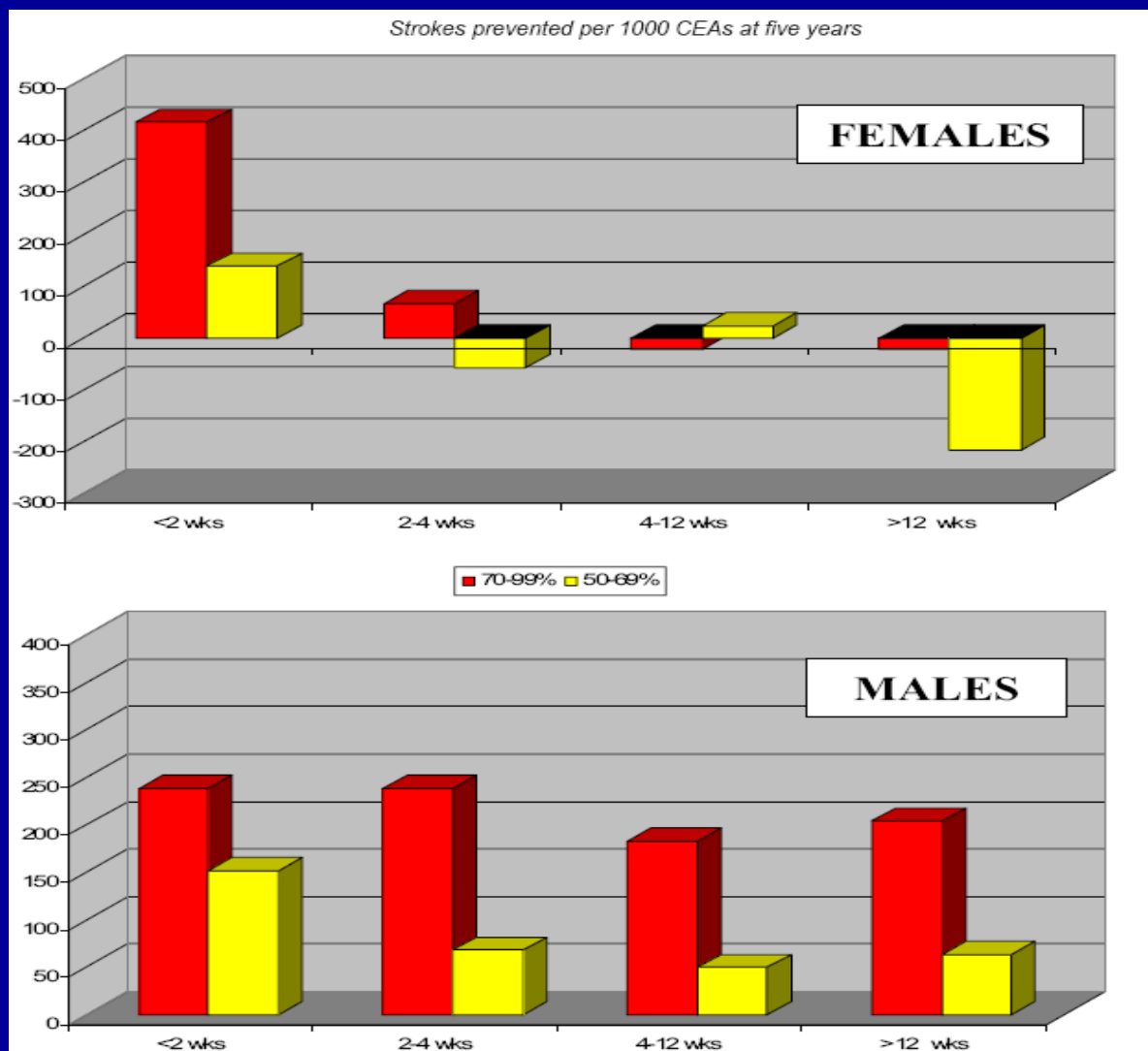


Figure 2: Effect of gender and timing from event to CEA on prevention of late stroke relative to degree of stenosis (recalculated from CETC).¹⁰

Naylor,
2007



SIGN

Scottish Intercollegiate Guidelines Network



4.3.1 CAROTID IMAGING IN PATIENTS WITH CAROTID TERRITORY TIA OR STROKE AND/OR RETINAL EVENT

A good quality meta-analysis showed that the most cost-effective diagnostic strategies for carotid stenosis are those that offer surgery to a larger proportion of patients quickly after the warning TIA/minor stroke.⁵⁶ The benefit of performing carotid endarterectomy (CEA) diminishes with time from the event (see section 1.1), reinforcing the need for early assessment. The nearer to the time of stroke/TIA, the less important the actual degree of stenosis is in predicting benefit from CEA.

The time of highest risk for recurrence of stroke/TIA is in the first hours or days after the primary warning event as stroke related to carotid bifurcation disease relates to stability of the plaque. TIA carries at least as high a risk of subsequent disabling stroke as minor stroke and its investigation and treatment should be treated with equivalent urgency. Cost-effectiveness modelling shows the best strategy is to offer surgery to a larger proportion of patients earlier than is currently the case in Scotland.⁵⁶

1+

- “The benefit of performing CEA diminishes with time from the event... The nearer to the time of stroke/TIA, the less important the actual degree of stenosis is in predicting benefit from CEA.”



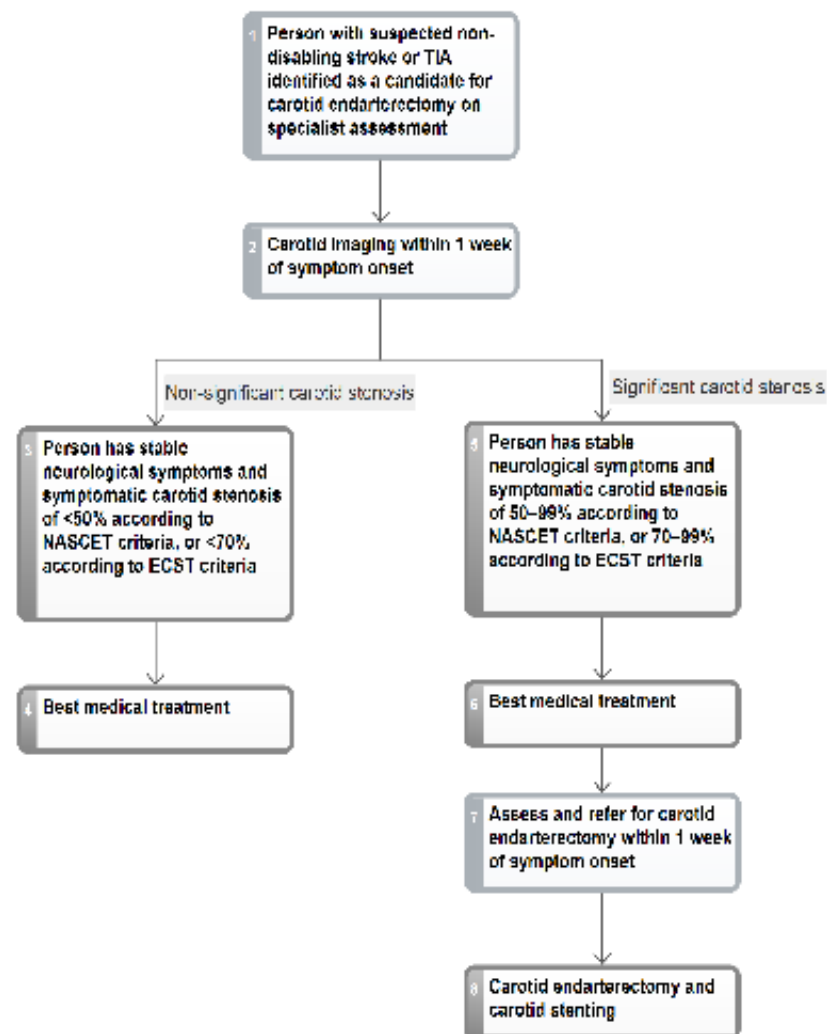
Royal College
of Physicians

National clinical guideline for stroke

People with an acute non-disabling stroke with stable neurological symptoms or with a TIA who have symptomatic carotid stenosis of 50–99% according to the NASCET criteria should:

- be assessed and referred for carotid endarterectomy to be performed within 1 week of onset of symptoms
- receive best medical treatment (control of blood pressure, antiplatelet agents, cholesterol lowering through diet and drugs, and lifestyle advice including smoking cessation).

- NASCET 50-69%
- CEA within one week



2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/ SAIP/SCAI/SIR/SNIS/SVM/SVS Guideline on the Management of Patients With Extracranial Carotid and Vertebral Artery Disease

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American Stroke Association, American Association of Neuroscience Nurses, American Association of Neurological Surgeons, American College of Radiology, American Society of Neuroradiology, Congress of Neurological Surgeons, Society of Atherosclerosis Imaging and Prevention, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of NeuroInterventional Surgery, Society for Vascular Medicine, and Society for Vascular Surgery

Developed in Collaboration With the American Academy of Neurology and Society of Cardiovascular Computed Tomography

7.1. Recommendations for Selection of Patients for Carotid Revascularization*

CLASS I

1. Patients at average or low surgical risk who experience nondisabling ischemic stroke[†] or transient cerebral ischemic symptoms, including hemispheric events or amaurosis fugax, within 6 months (symptomatic patients) should undergo CEA if the diameter of the lumen of the ipsilateral internal carotid artery is reduced more than 70%[‡] as documented by noninvasive imaging (20,83) (*Level of Evidence: A*) or more than 50% as documented by catheter angiography (20,70,83,359) (*Level of Evidence: B*) and the anticipated rate of perioperative stroke or mortality is less than 6%.

2. CAS is indicated as an alternative to CEA for symptomatic patients at average or low risk of complications as compared with endovascular intervention when the diameter of the lumen of the ipsilateral internal carotid artery is reduced by more than 70% as documented by noninvasive imaging or more than 50% as documented by catheter angiography and the anticipated rate of periprocedural stroke or mortality is less than 6% (360). (*Level of Evidence: B*)
3. Selection of asymptomatic patients for carotid revascularization should be guided by an assessment of comorbid conditions, life expectancy, and other individual factors and should include a thorough discussion of the risks and benefits of the procedure with an understanding of patient preferences. (*Level of Evidence: C*)

CLASS IIa

1. It is reasonable to perform CEA in asymptomatic patients who have more than 70% stenosis of the internal carotid artery if the risk of perioperative stroke, MI, and death is low (74,76,359,361–363). (*Level of Evidence: A*)

2. It is reasonable to choose CEA over CAS when revascularization is indicated in older patients, particularly when arterial pathoanatomy is unfavorable for endovascular intervention (360,364–368). (*Level of Evidence: B*)
3. It is reasonable to choose CAS over CEA when revascularization is indicated in patients with neck anatomy unfavorable for arterial

Do
Symptoms 6/12
Nascet 50 -69%

established (360). (*Level of Evidence: B*)

2. In symptomatic or asymptomatic patients at high risk of complications for carotid revascularization by either CEA or CAS because of comorbidities,[§] the effectiveness of revascularization versus medical therapy alone is not well established (35,361,362,366, 369–372,375,376). (*Level of Evidence: B*)

1. Except in extraordinary circumstances, carotid revascularization by either CEA or CAS is not recommended when atherosclerosis narrows the lumen by less than 50% (35,70,74,369,377). (Level of Evidence: A)

2. Carotid revascularization is not recommended for patients with chronic total occlusion of the targeted carotid artery. (Level of Evidence: C)

3. Carotid revascularization is not recommended for patients with severe disability¹ caused by cerebral ischemia and no preservation of useful function. (Level of Evidence: C)

7.3.5.1. RECOMMENDATIONS FOR MANAGEMENT OF PATIENTS UNDERGOING CAROTID ARTERY STENTING

CLASS I

1. Before and for a minimum of 30 days after CAS, dual-antiplatelet therapy with aspirin (81 to 325 mg daily) plus clopidogrel (75 mg daily) is recommended. For patients intolerant of clopidogrel, ticlo-

pidine (90 mg daily) is recommended. (Level of Evidence: C)

2. For patients with carotid stenosis, treatment with aspirin (81 to 325 mg daily) plus clopidogrel (75 mg daily) is recommended. (Level of Evidence: C)

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31. For patients with carotid stenosis, treatment with aspirin (81 to 325 mg daily) plus clopidogrel (75 mg daily) is recommended. (Level of Evidence: C)

32. For patients with carotid stenosis, treatment with aspirin (81 to 325 mg daily) plus clopidogrel (75 mg daily) is recommended. (Level of Evidence: C)

Do not do if
< 50% stenosis

7.5. Durability of Carotid Revascularization

7.5.1. Recommendations for Management of Patients Experiencing Restenosis After Carotid Artery Stenting

CLASS IIa

1. In patients with symptomatic cerebral ischemia and recurrent carotid stenosis due to intimal hyperplasia or atherosclerosis, it is reasonable to repeat CEA or perform CAS using the same criteria as recommended for initial revascularization (see Sections 7.5.2 and 7.5.3). (Level of Evidence: C)

2. Reoperative CEA or CAS after initial revascularization is reasonable when duplex ultrasound and another confirmatory imaging method identify rapidly progressive restenosis that indicates a threat of complete occlusion. (Level of Evidence: C)

CLASS IIb

1. In asymptomatic patients who develop recurrent carotid stenosis due to intimal hyperplasia or atherosclerosis, reoperative CEA or CAS may be considered using the same criteria as recommended for initial revascularization. (Level of Evidence: C)

CLASS III: HARM

1. Reoperative CEA or CAS should not be performed in asymptomatic patients with less than 70% carotid stenosis that has remained stable over time. (Level of Evidence: C)

2. For patients with carotid stenosis, treatment with aspirin (81 to 325 mg daily) plus clopidogrel (75 mg daily) is recommended. (Level of Evidence: C)

ESVS Guidelines. Invasive Treatment for Carotid Stenosis: Indications, Techniques

C.D. Liapis ^{a,*}, Sir P.R.F. Bell ^b, D. Mikhailidis ^c, J. Sivenius ^d,
A. Nicolaides ^e, J. Fernandes e Fernandes ^f, G. Biasi ^g,
L. Norgren ^h, on behalf of the ESVS Guidelines Collaborators¹

Invasive treatment recommendation 1. Neurological symptomatology and degree of carotid stenosis

- The operative treatment of carotid disease is absolutely indicated in symptomatic patients with >70% (NASCET) stenosis [A] and probably with >50% (NASCET) stenosis [A]. The perioperative stroke/death rate should be <6%. CEA is contraindicated for symptomatic patients with less than 50% stenosis [A].
- CEA should be performed within 2 weeks of a patient's last symptoms [A].
- CEA can be recommended for asymptomatic men below 75 years with 70–99% stenosis if the risk associated with surgery is less than 3% [A].
- The benefit from CEA in asymptomatic women with carotid stenosis is significantly less than in men [A]. CEA should therefore be considered only in younger, fit women [A].

Invasive treatment recommendation 2. CAS in symptomatic patients

- The available level I evidence suggests that for symptomatic patients, surgery is currently the best option [A].
- Mid-term stroke prevention after successful CAS is similar to CEA [A].

- CAS should be offered to symptomatic patients, if they are at high risk for CEA, in high-volume centres with documented low peri-procedural stroke and death rates or inside an RCT [C].

Yes probably
50 - 69% stenosis

Critical issue

- The benefit from CAS in asymptomatic patients with carotid artery stenosis is still to be demonstrated.

ESVS Guidelines. Invasive Treatment for Carotid Stenosis: Indications, Techniques

C.D. Liapis^{a,*}, Sir P.R.F. Bell^b, D. Mikhailidis^c, J. Sivenius^d,
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- CEA should be performed within 2 weeks of a patient's last symptoms [A].
- CEA can be recommended for asymptomatic men between 60 and 75 years with 70–99% stenosis if the risk associated with surgery is less than 3% [A].
- The benefit from CEA in asymptomatic women with carotid stenosis is significantly less than in men [A]. CEA should therefore be considered only in younger, symptomatic women [A].

Invasive treatment recommendation 2. CAS in symptomatic patients

- The available level I evidence suggests that for symptomatic patients, surgery is currently the best option [A].
- Mid-term stroke prevention after successful CAS is similar to CEA [A].

- CAS should be offered to symptomatic patients, if they are at high risk for CEA, in high-volume centres with documented low peri-procedural stroke and death rates or inside an RCT [C].

No
< 50% stenosis

well-conducted clinical trials [C].

Critical issue

- The benefit from CAS in asymptomatic patients with carotid artery stenosis is still to be demonstrated.

THE 2nd EUROPEAN
ECST-2
CAROTID SURGERY TRIAL

Inclusion criteria

- 50-99% carotid stenosis with <3% annual stroke risk

Exclusion criteria

- >3% annual stroke risk
- Unfit for revascularisation

Randomized 1:1

Immediate revascularisation + BMT

BMT + optional delayed revascularisation
LDL <2mmol/L, BP <135/85mmHg

Follow-Up 5 – 10 years

1. Stroke or procedural death
2. Safety analysis of 320 MRIs at 2 years

The impact of thrombolysis



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of Physicians

National clinical guideline for stroke

- Thrombolysis should be administered to patients with ischaemic stroke presenting within 4.5-6 hours of onset of symptoms

High risk group of patients?

- Patients with stroke secondary to carotid atherosclerosis are considered higher risk of further events within a narrow time frame than patients with amaurosis fugax or TIA
- Therefore patients with symptomatic carotid atherosclerosis that receive thrombolysis may represent a high-risk group of patients
- No data available regarding the natural history of symptomatic 50-69% carotid stenosis post-thrombolysis

REVIEW

Safety of Carotid Intervention Following Thrombolysis in Acute Ischaemic Stroke

R. Mandavia^{*}, M.I. Qureshi, B. Dharmarajah, K. Head, A.H. Davies

Academic Section of Vascular Surgery, Imperial College London, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, UK

- Systematic review evaluating safety of 114 CEA procedures performed within 14 days of thrombolysis for acute ischaemic stroke
- Point estimate of 30-day stroke or death rate: 4.93% (95% CI 1.83 - 9.44).
- Represents strong recommendation with low quality evidence.

Urgent Carotid Surgery and Stenting May Be Safe After Systemic Thrombolysis for Stroke

Linn Koraen-Smith, MD; Thomas Troëng, MD, PhD; Martin Björck, MD, PhD;
Björn Kragsteman, MD, PhD; Carl-Magnus Wahlgren, MD, PhD;
on behalf of the Swedish Vascular Registry and the Riks-Stroke Collaboration

Stroke. 2014;45:776-780

- Retrospective review of registry data 2008 – 2012
- 30-day stroke and death rate for thrombolysis cohort 2.5%; for whole cohort was 3.3 %
- No significant difference in post-op bleeding rates requiring re-operation
- No correlation between time from thrombolysis to intervention and complications

Summary

- Current guidelines advocate CEA for patients with symptomatic 50-69% stenosis
- Benefit of CEA most marked with early intervention
- Hyper-acute patients receiving thrombolysis may represent a high-risk subgroup

Conclusion

- CEA advocated in 50-69% symptomatic stenosis, pending the outcome of the ECST-2 trial
- Are the thrombolysis group a different clinical entity?

Original article

Modelling the cost-effectiveness of asymptomatic carotid endarterectomy

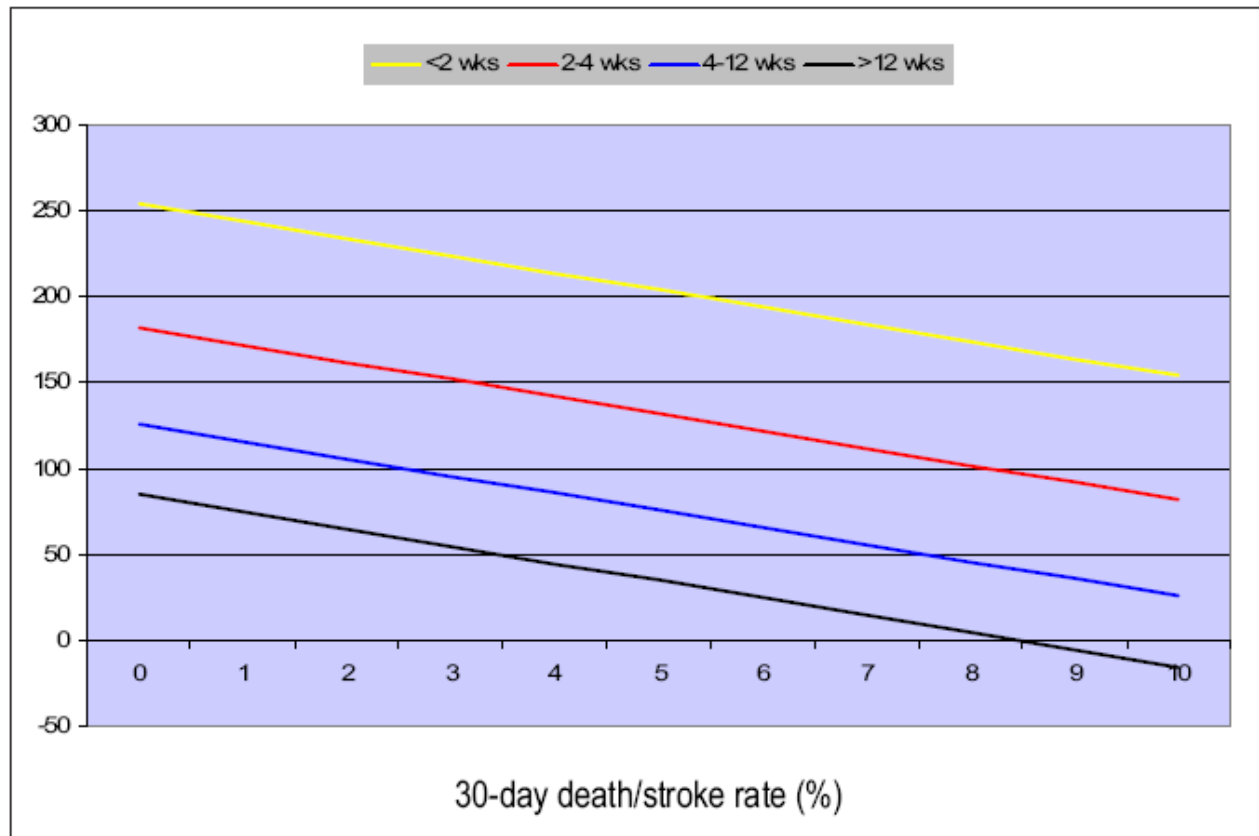
A. Thapar¹, L. Garcia Mochon³, D. Epstein², J. Shalhoub¹ and A. H. Davies¹

Stroke - Costs

- 4.4% of all NHS expenditure (1991)
- £1.36 billion cost to NHS
- 7.7 million lost working days
- £445 million in lost production (1991)

Benefit of Urgent Treatment

Figure 4: Strokes prevented per 1000 CEAs at five years stratified for:
(i) delay from last event to surgery and (ii) 30-day death/stroke risk (recalculated from CETC).¹⁰



Time is brain!

Naylor 2007

Safety of endovascular intervention post thrombolysis

Safety of Carotid Intervention Following Thrombolysis in Acute Ischaemic Stroke

R. Mandavila ^{*}, M.I. Qureshi, B. Dharmarajah, K. Head, A.H. Davies

Academic Section of Vascular Surgery, Imperial College London, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, UK

- Included 4 carotid angio only; no stroke/death

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on behalf of the Swedish Vascular Registry and the Riks-Stroke Collaboration

- Included 6 carotid stent patients; no stroke/death
- Insufficient data to conclude safety of stenting