

ICSS Safety results

- The following slides were presented to the ICSS Investigators Meeting on 22/05/09 and most of them were also presented at the European Stroke Conference on 27/05/09
- They are NOT for PUBLICATION in any form prior to a formal publication of the results to be submitted to the Lancet

ICSS Safety results

**Safety results of the International Carotid Stenting Study (ICSS):  
Early outcome of patients randomised between carotid stenting and endarterectomy for symptomatic carotid stenosis**

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ICSS Safety results

**International Carotid Stenting Study (ICSS, CAVATAS 2)**

- A multicentre open randomised trial with independent neurological assessment of outcome events blinded to allocated treatment
- Aims: To determine the risks and long term benefits of carotid artery stenting in comparison to carotid endarterectomy in patients with symptomatic carotid artery stenosis

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**International Carotid Stenting Study Main Inclusion Criteria**

- Extracranial internal carotid artery stenosis (>50% measured using NASCET equivalent)
  - Exclusion: Pseudo-occlusion ('string sign')
- Management discussed at multidisciplinary meeting
- Patient and lesion suitable for both treatments
- Recent, relevant symptoms
- Age > 40 years (no upper limit)
- Suitable consenting patients then randomised between stenting and endarterectomy

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**International Carotid Stenting Study Treatment protocol**

- Stenting
  - Stents and protection devices approved by TSC
  - Several devices approved for use in the trial
  - Protection devices recommended at discretion of interventionists: not mandatory
  - Aspirin plus clopidogrel prior to stenting
- Carotid endarterectomy
  - Local or general anaesthesia

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**International Carotid Stenting Study: Investigator requirements**

- Attend approved carotid stenting course
- Centres submitted CVs & audited outcome data
- Enrolled as **experienced** centre
  - > 50 carotid operations, > 10 cases/ year
  - > 50 stents anywhere, > 10 carotid stents and audit data & CV accepted by credentialing committee
- Enrolled as **supervised** centre if insufficient cases
  - Treatment of randomised patients then supervised by an approved experienced interventionist
  - Promoted to experienced centre after 20 cases randomised with satisfactory results

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### Principle research questions

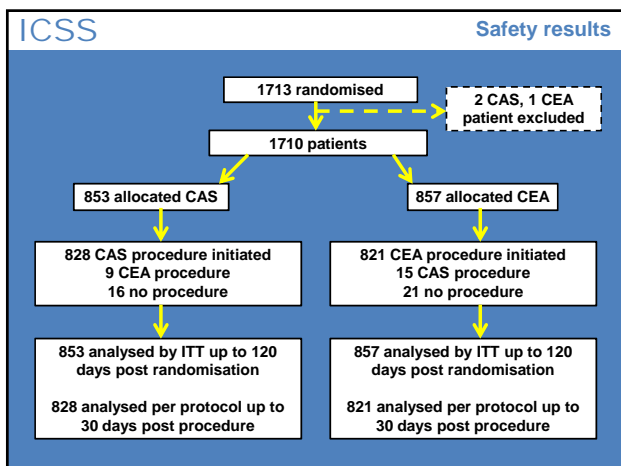
- Primary long term outcome measure
  - Long term survival free of disabling stroke
  - Awaits completion of longer term follow up
- Primary Safety measure
  - 30 day rate of stroke, myocardial infarction or death
  - Data to be presented at ESC, Stockholm

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### Recruitment

- Recruitment started May 2002
- Completed on target October 2008
- 50 centres, 15 countries; total patients 1713

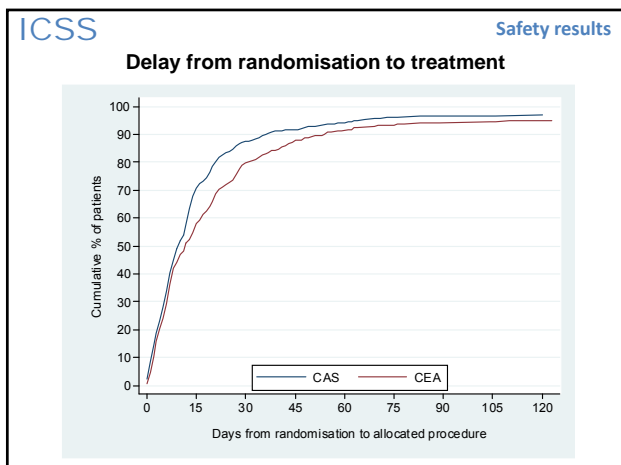
UK	505	Netherlands	475
Australia	226	Sweden	127
Switzerland	122	Spain	51
New Zealand	40	Belgium	37
Canada	34	Finland	33
Poland	19	Norway	16
Slovenia	12	Germany	9
	Ireland	5	



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### Baseline data at randomisation

	Surgery (CEA)	Stenting (CAS)
Total Patients	857	853
Mean age (SD)	70.1 (9.1)	70.2 (9.1)
Male (%)	71	70
Female (%)	29	30
Hypertensive (%)	69	69
Mean BP (Sys/dia )	146/79	147/79
Cardiac Failure (%)	5	3
Angina (%)	9	10
NIDDM (%)	17	16
Insulin dependent Di (% Diabetes)	5	6
Atrial Fibrillation (%)	7	7
Previous MI (%)	18	18
N Current Smoker (%)	23	24
N Ex-smoker (%)	49	48
Cholesterol (mmol/L)	4.9	4.9
Treated hyperlipidaemia (%)	66	61
Stenosis (ipsilateral)		
50-69% (%)	9	11
70-99% (%)	91	89



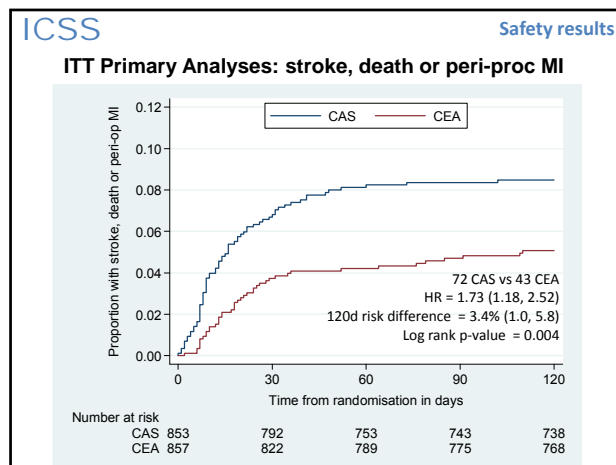
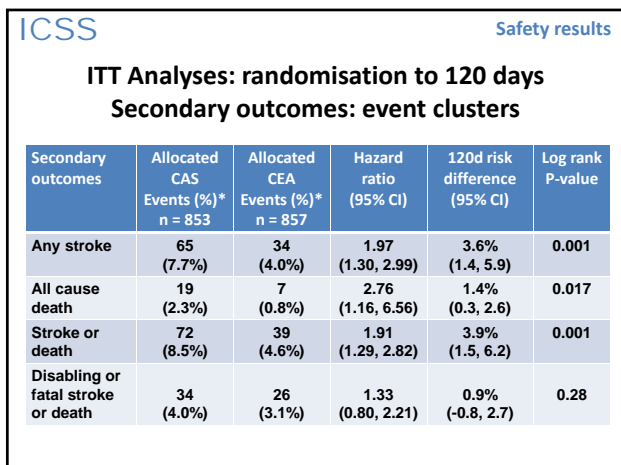
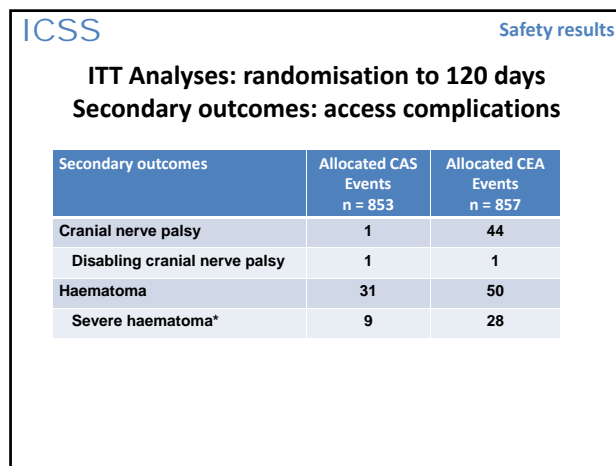
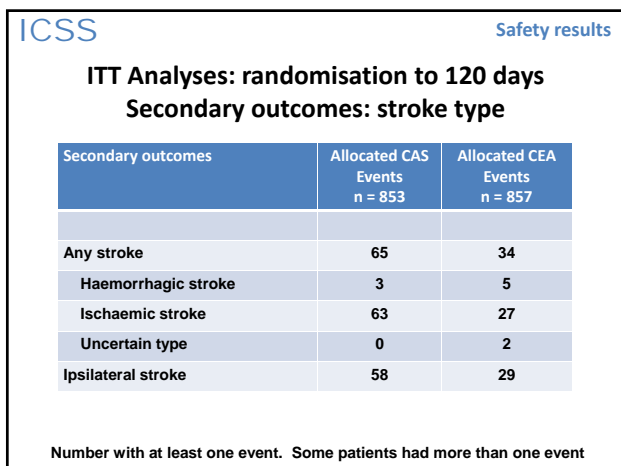
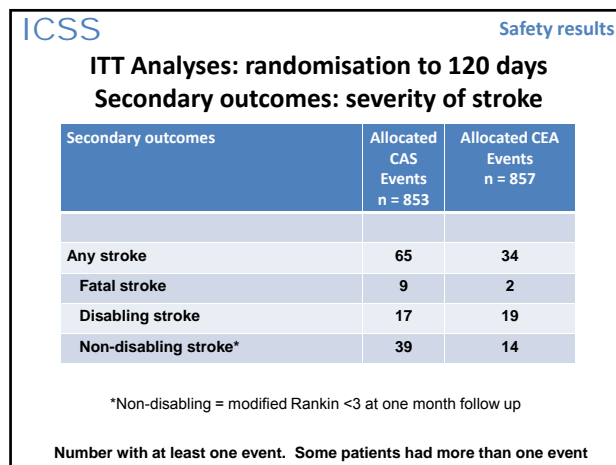
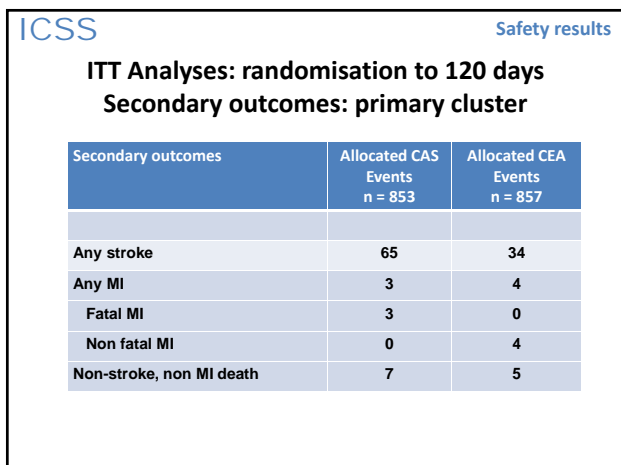
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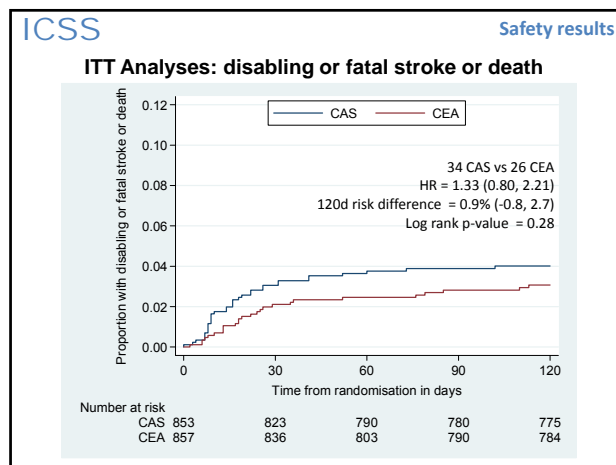
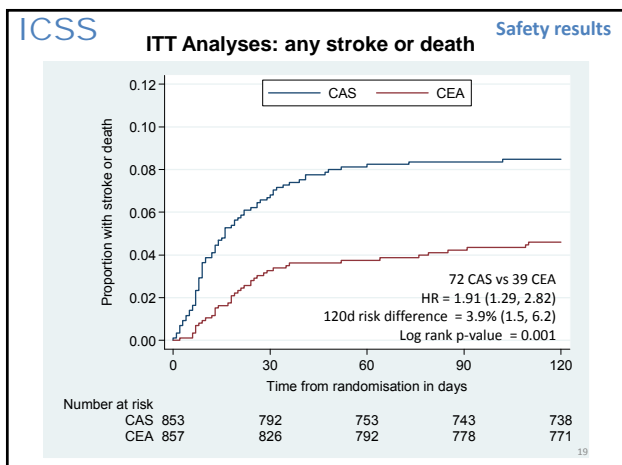
### ITT Analyses: randomisation to 120 days

#### Primary short-term outcome

Primary outcome	Allocated CAS Events (%)* n = 853	Allocated CEA Events (%)* n = 857	Hazard ratio (95% CI)	120d risk difference (95% CI)	Log rank P-value
Stroke, death or peri-proc MI	72 (8.5%)	43 (5.1%)	1.73 (1.18, 2.52)	3.4% (1.0, 5.8)	<b>0.004</b>

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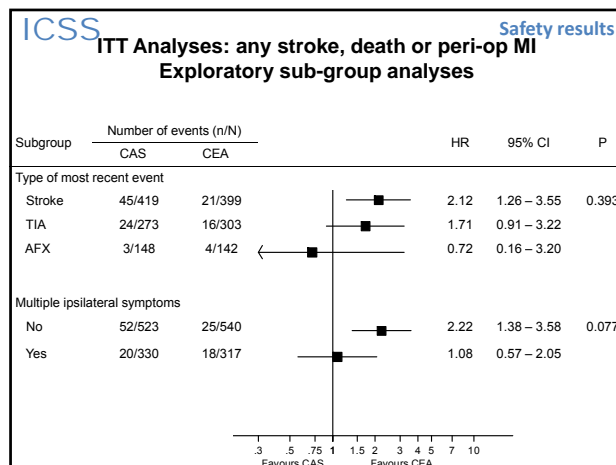
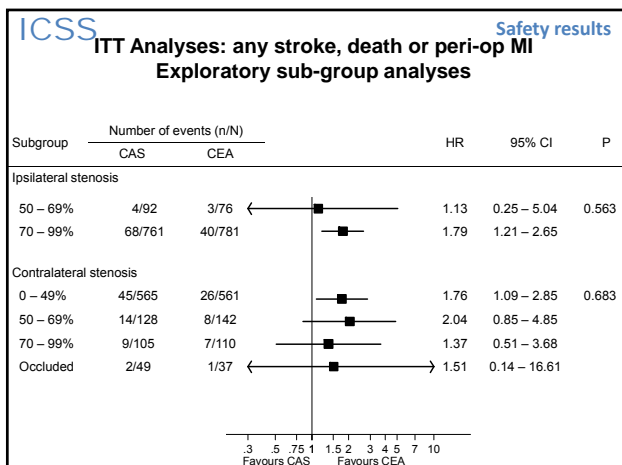
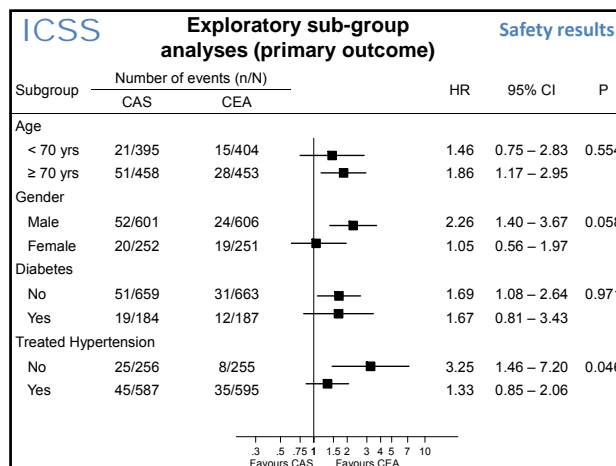


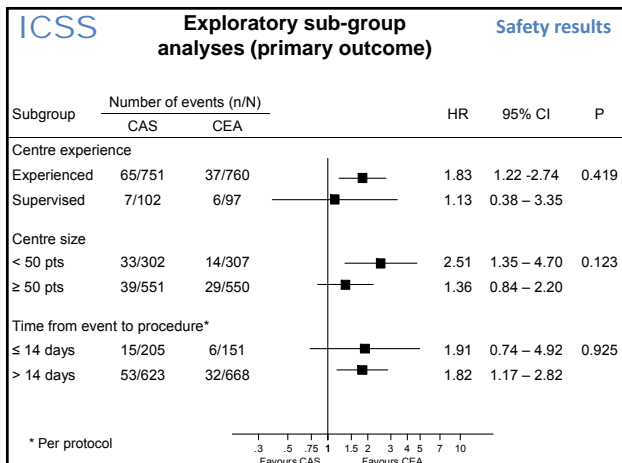


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**Per Protocol 30 day Procedural Risk Analyses:  
Restricted to allocated treatment initiated**

Primary outcome	CAS Events (%) n = 828	CEA Events (%) n = 821	Risk ratio (95% CI)	Risk difference (95% CI)	P-value
Stroke, death or MI	61 (7.4%)	33 (4.0%)	1.83 (1.21, 2.77)	3.3% (1.1, 5.6)	0.003
Any stroke	58 (7.0%)	27 (3.3%)	2.13 (1.36, 3.33)	3.7% (1.6, 5.8)	0.001
Stroke or death	61 (7.4%)	28 (3.4%)	2.16 (1.40, 3.34)	4.0% (1.8, 6.1)	<0.001
All cause death	11 (1.3%)	4 (0.5%)	2.73 (0.87, 8.53)	0.8% (-0.1, 1.8)	0.072
Disabling or fatal stroke or death	26 (3.1%)	18 (2.2%)	1.43 (0.79, 2.59)	0.9% (-0.6, 2.5)	0.23





**ICSS Safety results**

**ICSS-MRI substudy**  
**Lead investigator: Leo Bonati**

- 5 ICSS centres recruited patients into substudy
- MRI with vascular sequences performed in consecutive ICSS patients if consent obtained and no contra-indication to MRI
  - 1-7 days pre-procedure
  - 1-3 days post-procedure (early scan)
  - 3-6 weeks post-procedure (late scan)
- Scans analysed blind to treatment
  - **Primary outcome**
    - Early ischaemia: New abnormality on post-procedure DWI
  - **Secondary outcomes**
    - FLAIR abnormality on late MRI at site of early ischaemia

**ICSS MRI Substudy results Safety results**

	CAS (n=108)	CEA (n=92)	OR (95% CI)
<b>New ischaemia</b>	<b>50 (46.3%)</b>	<b>13 (14.1%)</b>	<b>5.24 (2.61-10.53)</b> p<0.001
<b>Events between treatment and early scan</b>			
No event	42	11	
TIA	0	0	
Stroke	8	2	
<b>FLAIR abnormal at site of early ischaemia on late scan</b>	<b>28 (32.2%)</b>	<b>6 (7.9%)</b>	<b>5.54 (2.15-14.29)</b> p<0.001



**ICSS Safety results**

**Summary and conclusions**

- **Strong evidence that CEA is safer than CAS in the primary ITT analysis (any stroke, death or perio-op MI, 8.5% v 5.1%, p=004)**
- **Twice as many strokes after CAS than after CEA in the per-protocol analysis (7.0% v 3.3%, p=0.001)**
- **Difference largely driven by non-disabling stroke**
- **Higher 30 day risk of any cranial nerve palsy and haematoma in CEA arm compared to CAS arm.**
- **Blinded MRI substudy supports the results of the main study and makes it unlikely that the difference is the result of bias**
- **Carotid endarterectomy is the treatment of choice for suitable patients with recently symptomatic carotid stenosis**

