

Thrombolysis in Stroke

Where we are at King's

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Stroke epidemiology in UK

- Every year approximately 130,000 people in England have a stroke
- Stroke is the third largest cause of death in England
 - 11 per cent of deaths in England are as a result of stroke
- 20–30 per cent of people who have a stroke die within a month
- 25 per cent of strokes occur in people under the age of 65
- Stroke is the single largest cause of adult disability
 - 300,000 people in England live with moderate to severe disability as a result of stroke
- Ethnic minorities are at higher risk of stroke

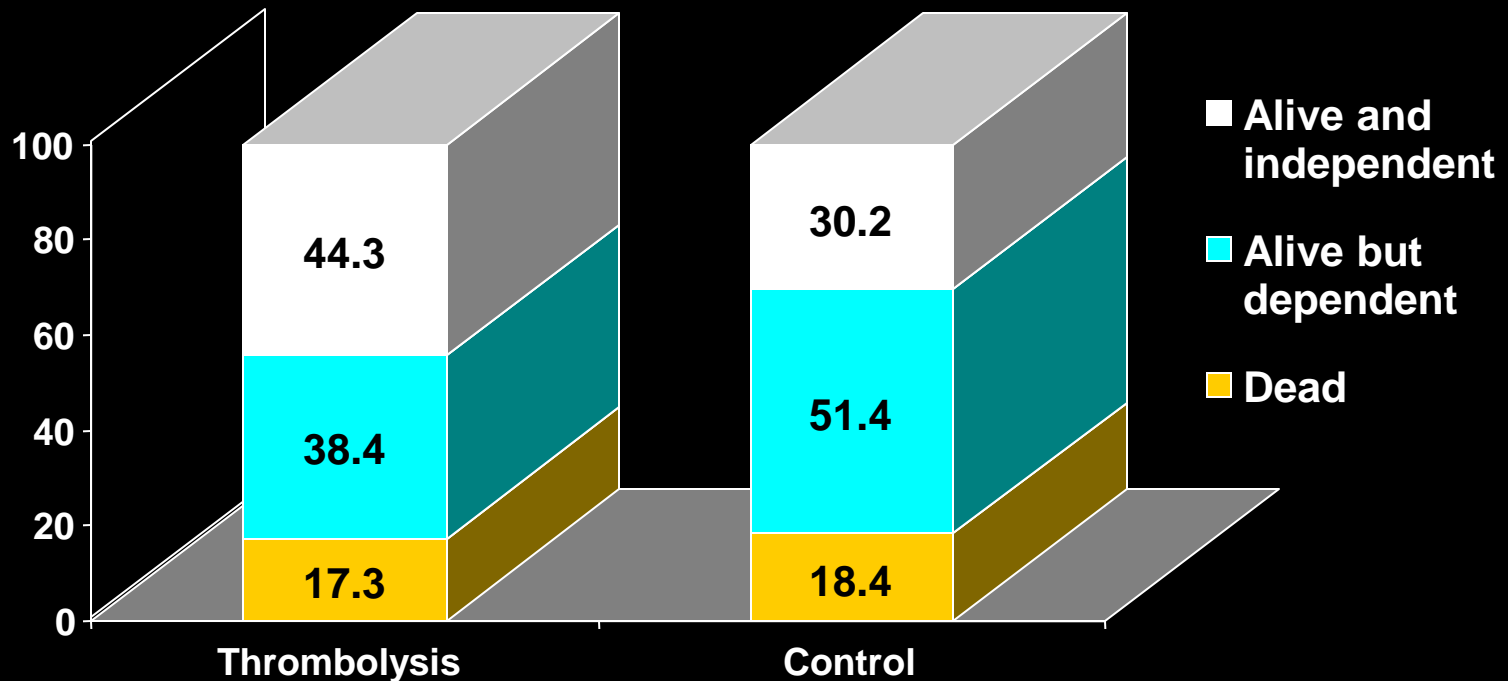
Not so long ago.....

- Stroke is a non-acute condition
- Hospitalisation for nursing, therapy or social needs (1988)
- Diagnosis clinically clear, CT scan required in less than 5%, a rate $>10\%$ needs justification (1994)
- Little acute care can do, emphasis on rehabilitation (1997)

But things have changed.....

- Introduction of IV thrombolysis
- Major developments in diagnosis and imaging
- Establishment of stroke as a speciality
- HfL, SLCSN and HASU development
- At King's alignment of stroke in regional neuroscience centre

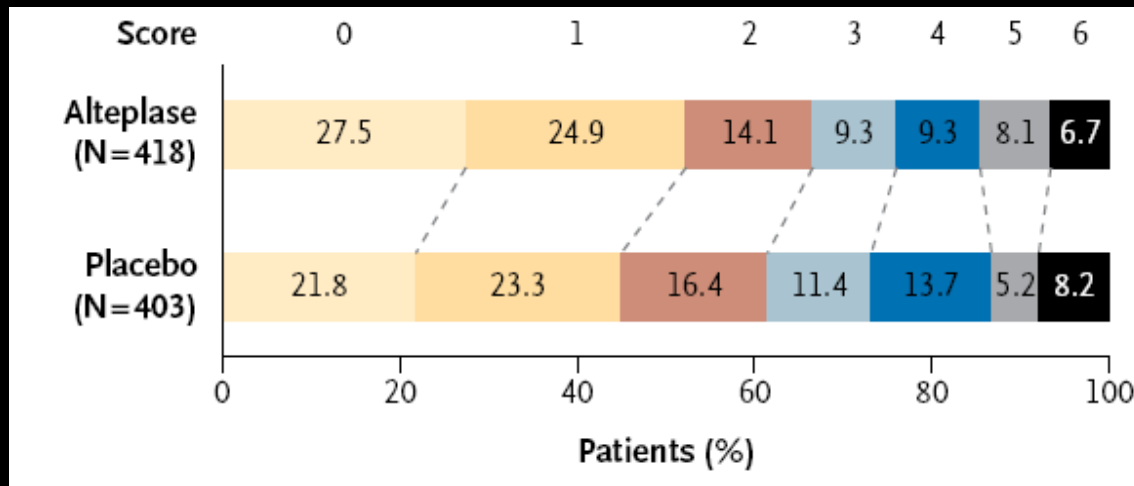
Thrombolysis in 3 hours



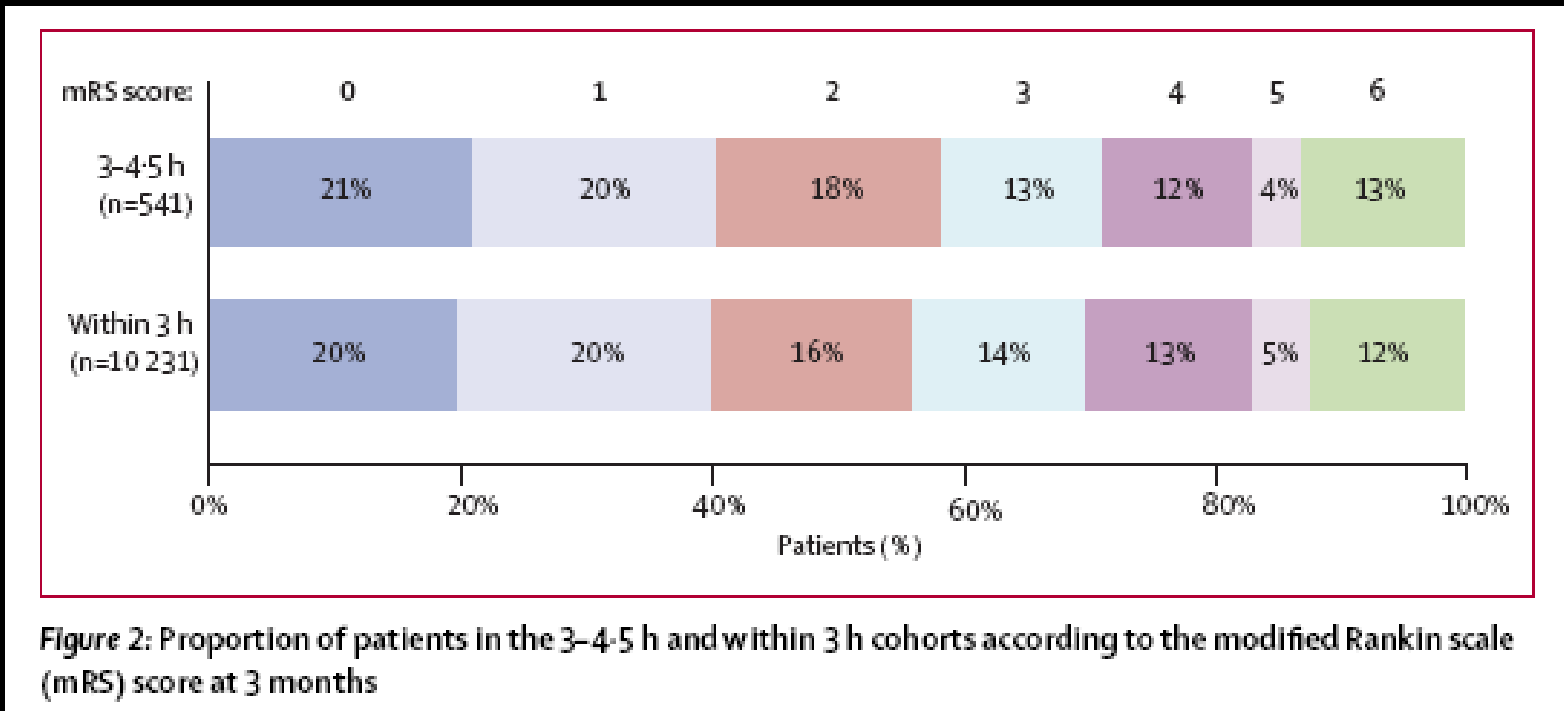
Differences/1000: 141 extra alive and independent (P<0.01)
1 out of every 7 patients treated has a better outcome (NNT=7)

ECASS-III (tPA in 3-4.5 hrs)

End Point	Intention-to-Treat Population			
	Alteplase Group (N=418) <i>no. (%)</i>	Placebo Group (N=403) <i>no. (%)</i>	Odds Ratio (95% CI)	P Value
Primary end point				
mRS score of 0 or 1 — unadjusted analysis	219 (52.4)	182 (45.2)	1.34 (1.02–1.76)	0.04†
mRS score of 0 or 1 — adjusted analysis‡	—	—	1.42 (1.02–1.98)	0.04§
Prespecified safety end points				
Any ICH	113 (27.0)	71 (17.6)	1.73 (1.24–2.42)	0.001

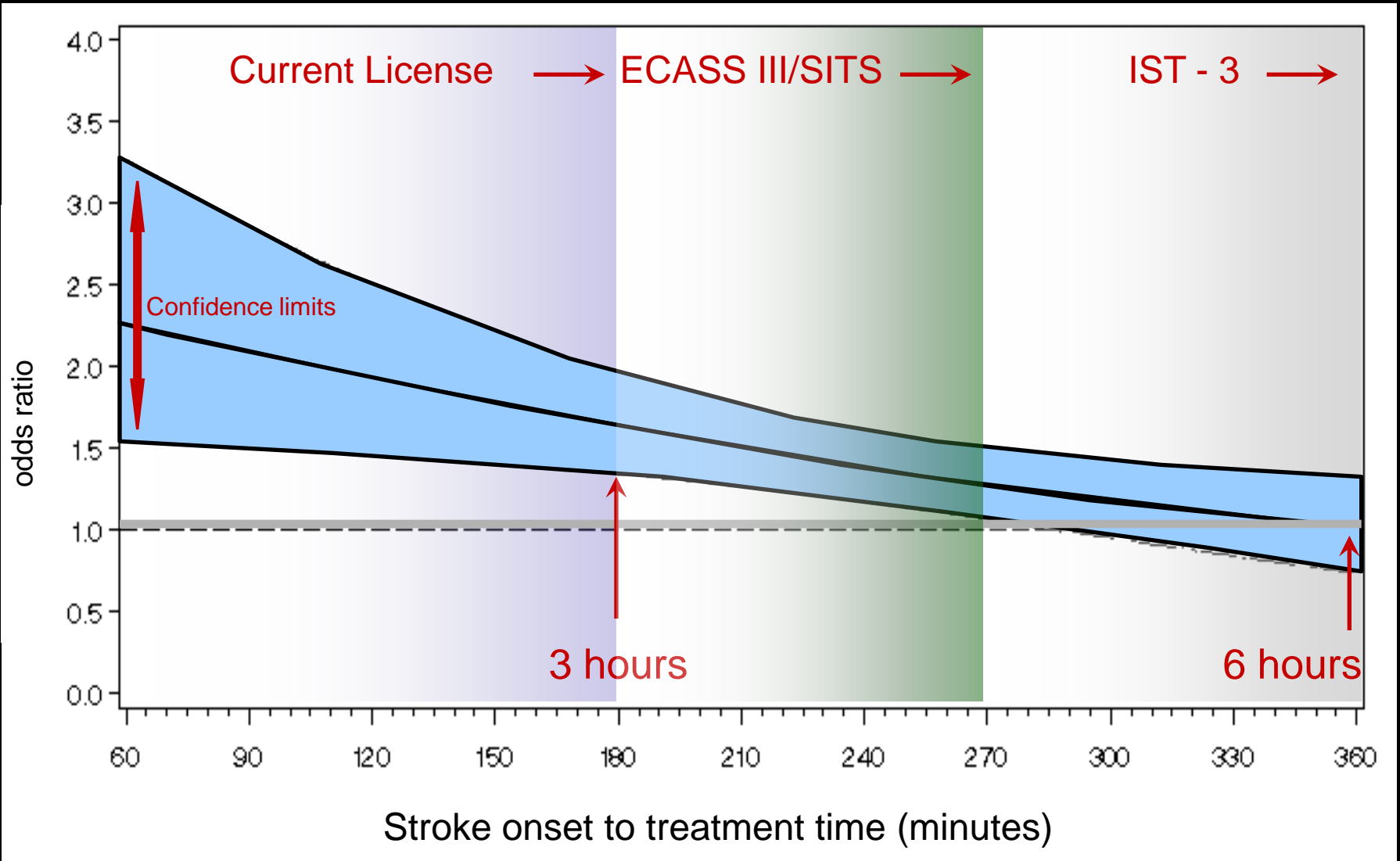


SITS : 3-4.5 h v 0-3h



No significant difference in independence: 58% vs 56.3% OR 1.04; p=0.42
or mortality: 12.7% vs 12.2% OR 1.02; p=0.72

Outcome of thrombolysis and time of onset



European and US Guidelines

- European Stroke Organisation Intravenous rtPA (0.9 mg/kg body weight, maximum 90 mg), with 10% of the dose given as a bolus followed by a 60-minute infusion, is recommended within 4.5 hours of onset of ischaemic stroke (**Class I, Level A**).
- American Stroke Association to issue this new advisory, giving tPA a **class 1, Level B** recommendation for use in the 3-to-4.5-hour window

KCH 0-3 h v 3-6 h

	0-3 h n=129 (63%)	3-6 h n=76 (37%)	p
Baseline characteristics			
Age (y, mean±SD)	71±15	69±16	0.34
Male	68 (53%)	39 (51%)	0.85
Diabetes	23 (18%)	14 (18%)	0.92
Baseline blood pressure (mmHg, mean±SD)			
systolic	145±21	145±21	0.84
diastolic	79±14	77±16	0.45
Baseline glucose (mmol/l, mean±SD)	7.0±2.8	7.7±4.2	0.19
Baseline NIHSS (median±IQR)	14±9	11±11	0.029
Outcome at 24 hours			
Significantly better: NIHSS 0 or ≥4 decrease	76 (61%)	42 (57%)	0.57
Significantly worse: NIHSS ≥4 increase or death	10 (8%)	6 (8%)	0.98
Symptomatic intracerebral hemorrhage	3 (2%)	1 (1%)	0.61
Outcome at 3 months			
modified Rankin score 0-2	60 (48%)	38 (52%)	0.58
modified Rankin score 3-5	33 (26%)	23 (32%)	0.44
Dead	17 (14%)	9 (12%)	0.80

Culture change at King's

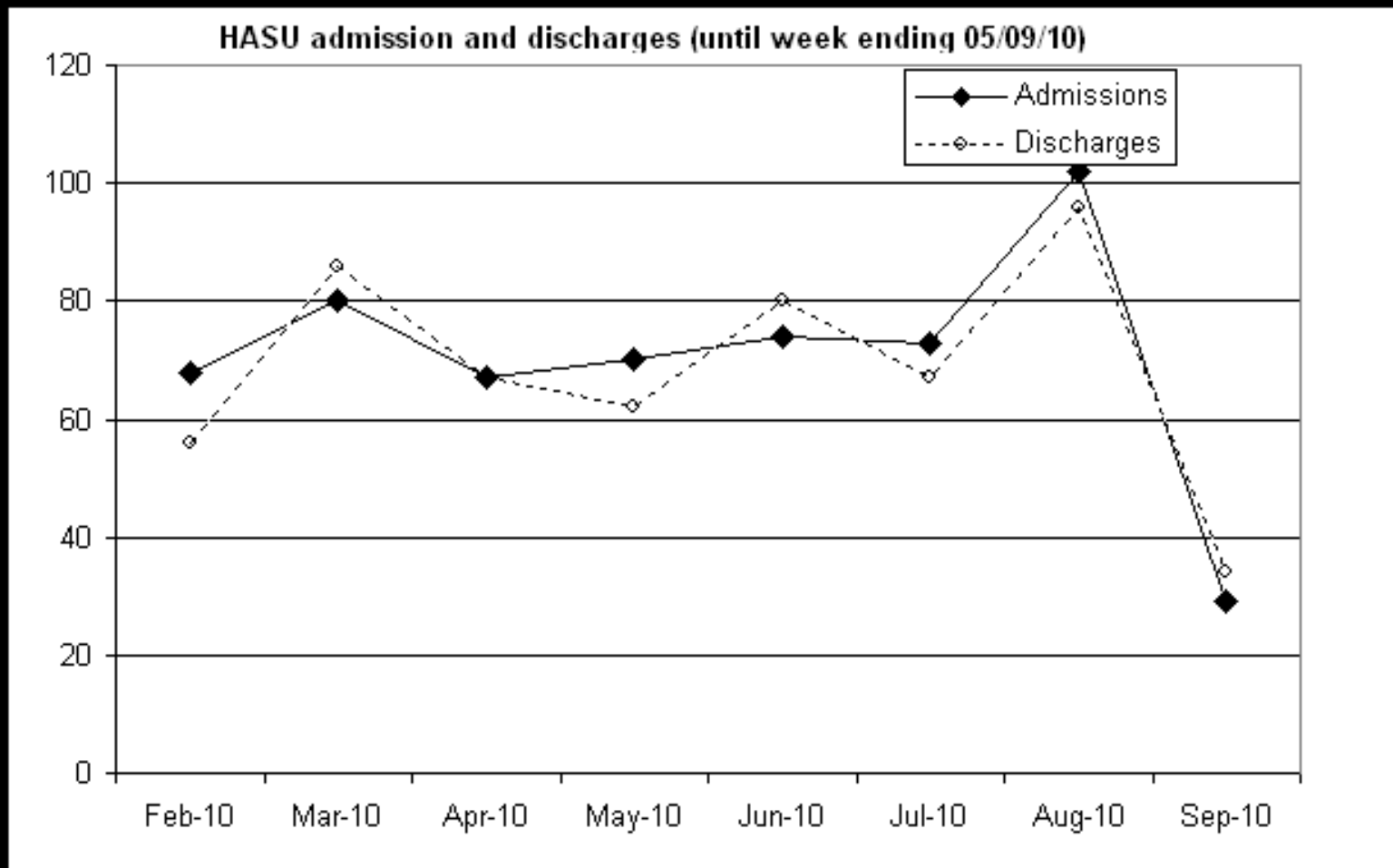
- FROM

- What reason can we find for not giving thrombolysis?

- TO

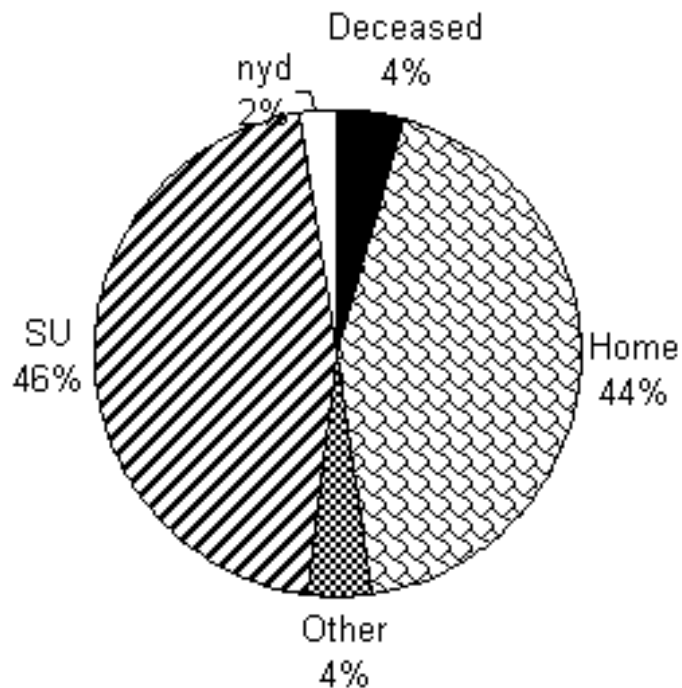
- Why shouldn't we give thrombolysis?
- Individualised risk/benefit assessment in cases outside of guidelines.

HASU Admissions at King's

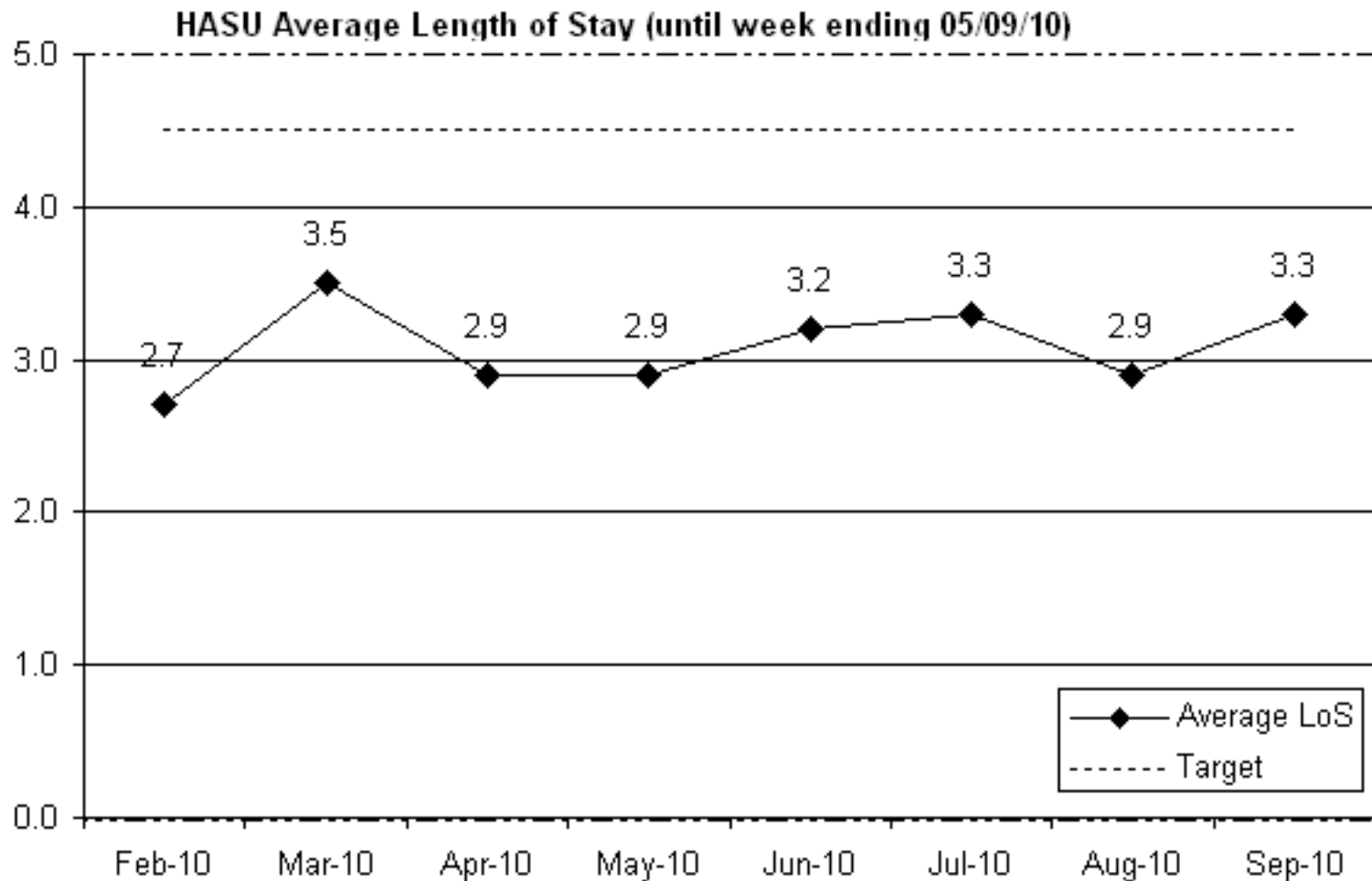


Outcome of HASU admissions

HASU admissions by outcome since 01/02/10



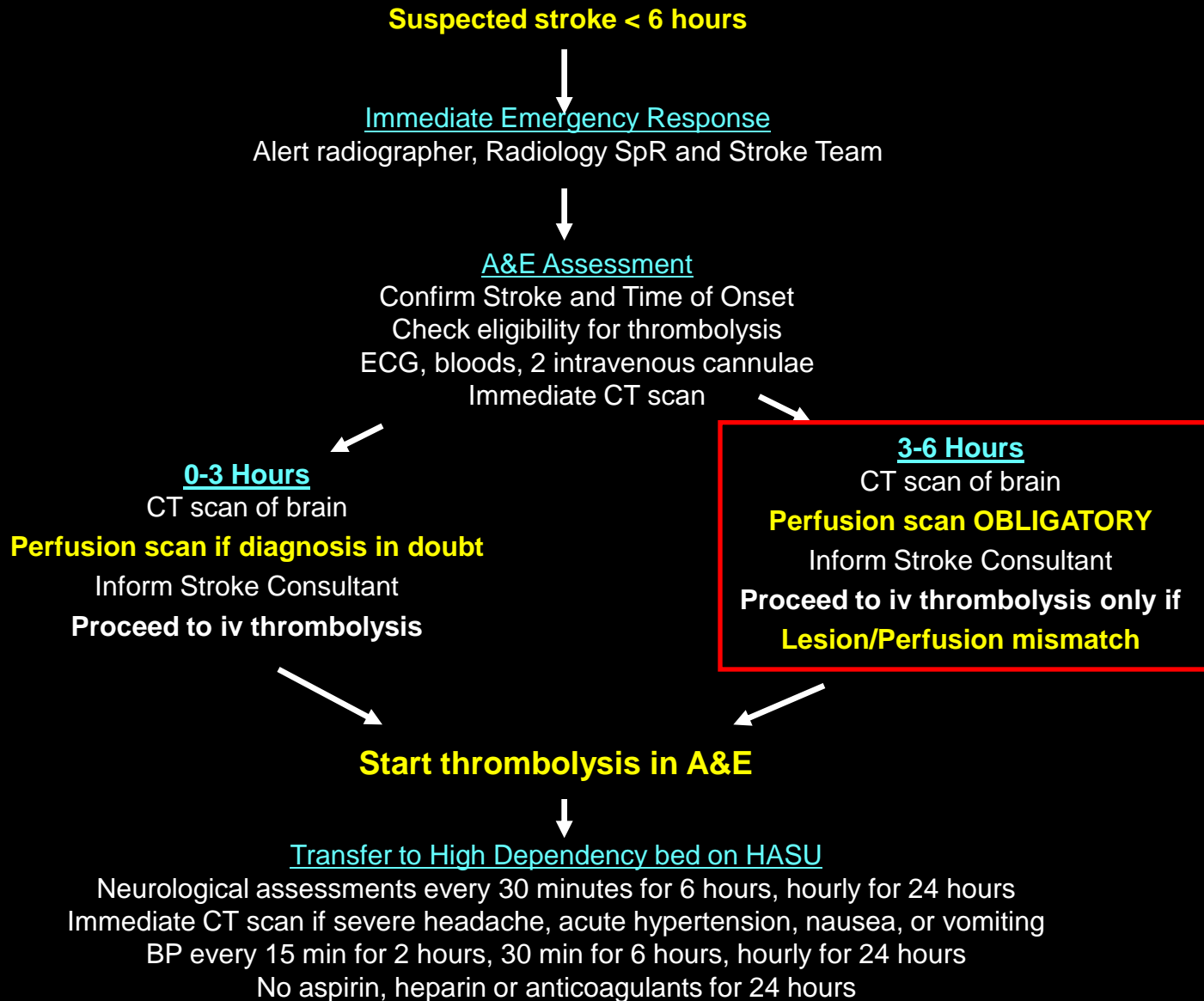
LOS on HASU at King's



One month snapshot (June 2010)

- Monthly multi-disciplinary audit of stroke calls
- 71 Stroke admissions in June 2010
- 52 Patients seen within six hours
- 25 Patients thrombolysed, all within 4.5 hours, 3 within 3 to 4.5 hrs, 22 within 3 hrs.
- 35% of patients with stroke received thrombolysis

THROMBOLYSIS PATHWAY AT KING'S



Challenges in thrombolysis

- Delays in presentation
- Patient selection
 - Greater safety
 - Extension of time window
- Increased effectiveness
 - Recanalisation
 - Clinical outcome

**Suspect a stroke?
Act FAST. Call 999.**

**F
A
S
T**

F **Facial weakness**

Can the person smile? Has their mouth or eye drooped?

A **Arm weakness**

Can the person raise both arms?

S **Speech problems**

Can the person speak clearly and understand what you say?

T **Test these symptoms**

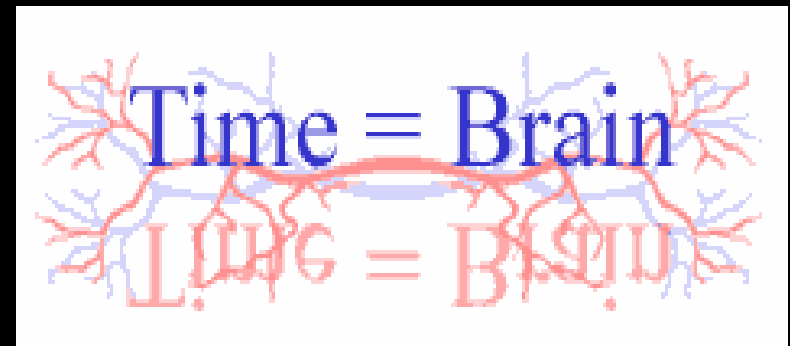
Stroke is a medical emergency.

By calling 999 early treatment can be given which can prevent further brain damage.

Stroke helpline 0845 3033 100 www.stroke.org.uk



London Ambulance Service



Stroke Networks

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Patient selection.....the problem

- Clinical: 25% patients not AIS
- CT scans are insensitive
 - Exclude haemorrhage, large infarcts
 - No “positive” information
- MRI
 - Not universally available, time consuming
 - Acute v old lesions (unless DWI)
 - No information on “at risk” brain

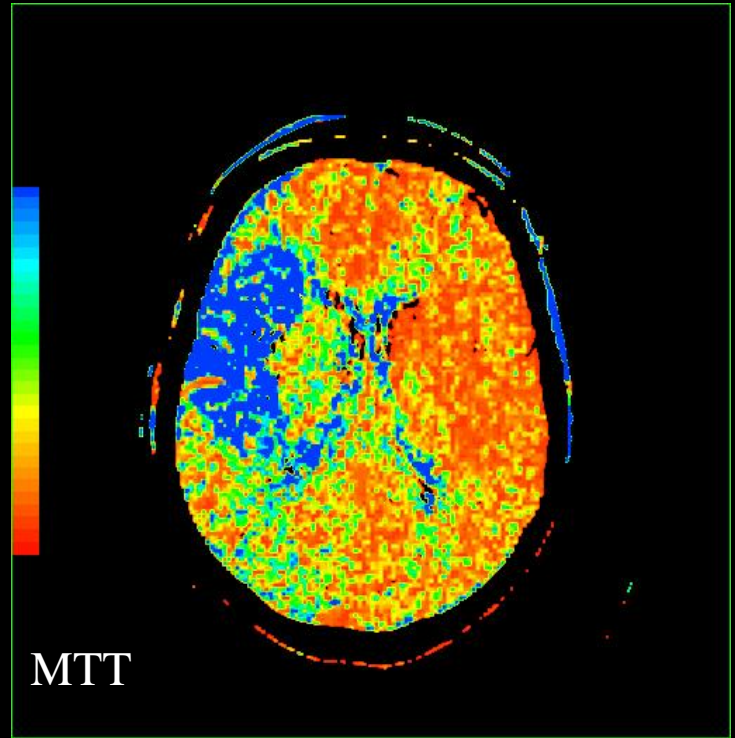
Seeing the problem

Perfusion imaging in AIS:

- Predicts subsequent infarct expansion
- Represents at-risk but salvageable tissue
- Identifies patients with the greatest potential to benefit
- Present in 50-75% patients at 6 hours



WW: 80 WL: 35



MTT

Current limitations:

- Limited neuroimaging facilities or support
- Controversy on best scanning modalities and protocols
- Cannot distinguish between tissue at risk and hypoperfused areas not destined to infarct
- Conflicting results from clinical studies

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Ultrasound-enhanced thrombolysis

- Combination of iv tPA in 3 hours with continuous transcranial ultrasound
 - Complete recanalisation 49% v 30%
 - Dramatic improvement 44% v 40%
 - ICH 3 v 3
- US enhanced thrombolysis with bubbles

Intra-arterial thrombolysis

- Benefits:

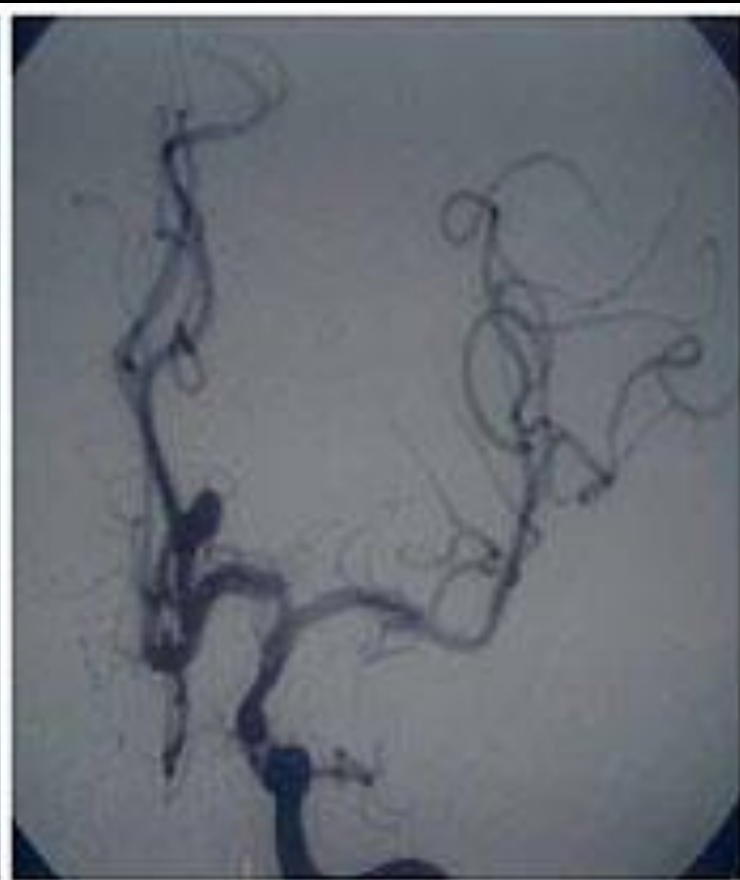
- Increased effectiveness
- Increased safety
- Longer time window

- Limitations

- Neuroradiology access
- Training and expertise
- Costs

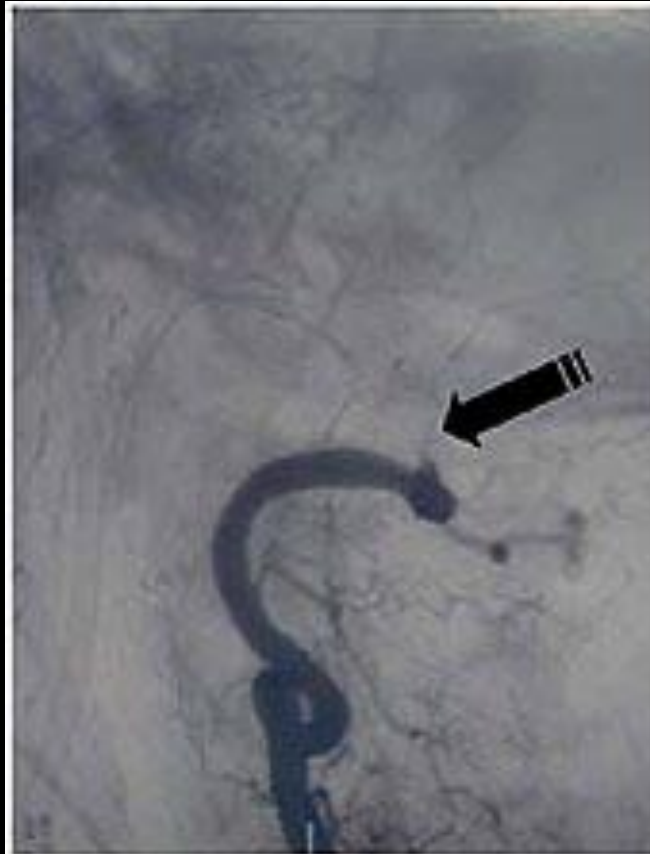


Before



After Intra-arterial Thrombolysis

Primary Angioplasty



Before



After Angioplasty and Stenting

Clot retrieval +/- angioplasty

