Risk factors for intracranial haemorrhage in ischaemic stroke patients treated with rtPA

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Stroke thrombolysis with rtPA

increases odds of ICH by 4 times

causes 27 extra fatal ICH per 1000 treated

non-fatal, large ICHs ↑ death & disability

Risk factors for post rtPA ICH

inform thresholds for licensed treatment

influence rtPA treatment in clinical practice

Research questions

In an unbiased samples of studies:

1. What are the summary effect sizes of baseline patient factors on post rtPA ICH?

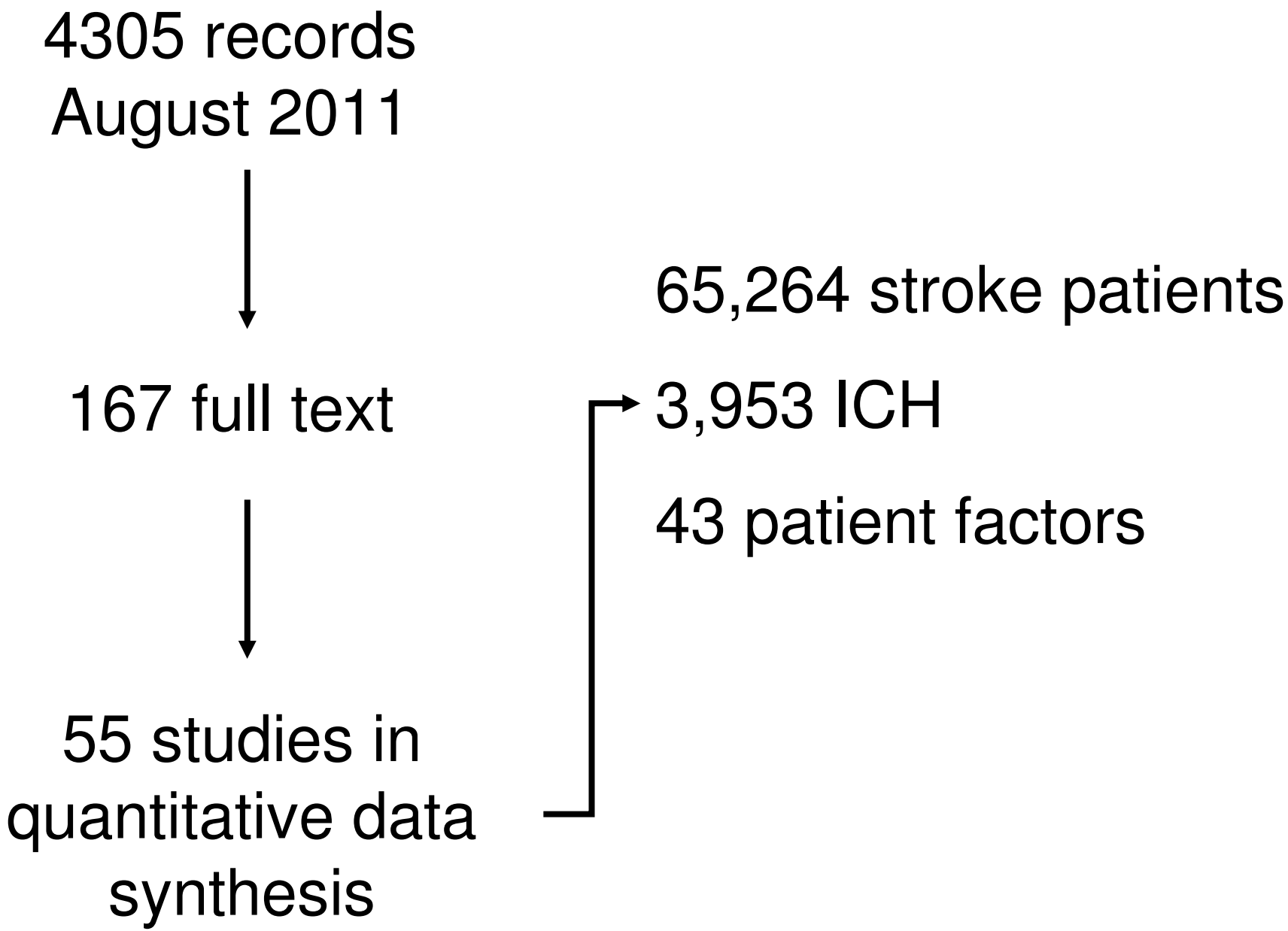
2. Do aspects of study design modify these effect sizes?

Systematic search for studies

- iv rtPA treated ischaemic stroke patients
- patients factors measured before rtPA
- primary not pooling studies
- at least 10 symptomatic or parenchymal ICHs <10 days post treatment

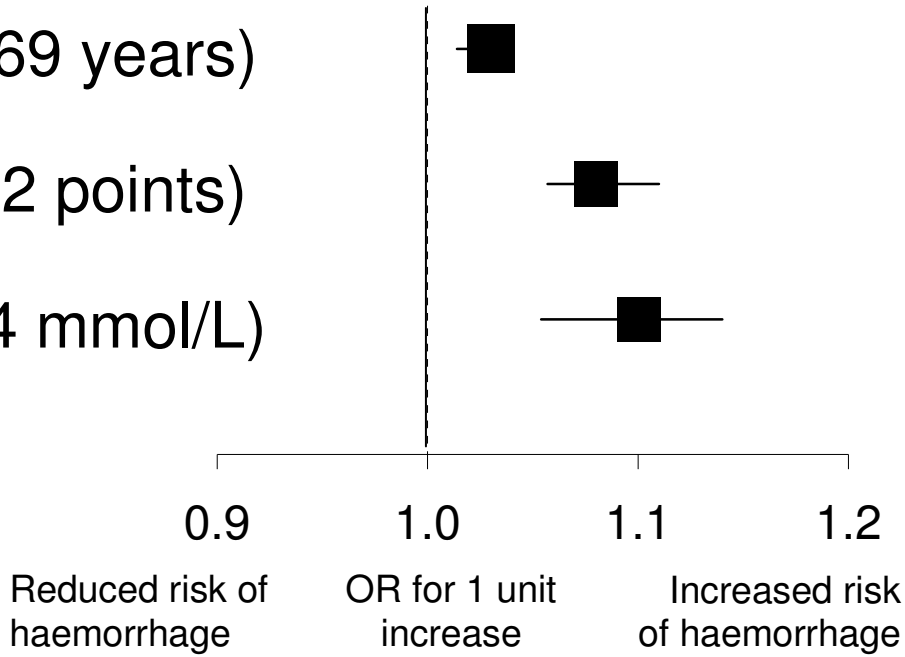
3 reviewers recorded or calculated

- effect sizes
- definition of intracranial haemorrhage
- study type and adjustment for confounders


4305 records
August 2011
167 full text
55 studies in
quantitative data
synthesis
65,264 stroke patients
3,953 ICH
43 patient factors

>10 studies had consistent effects sizes for age, glucose & NIHSS

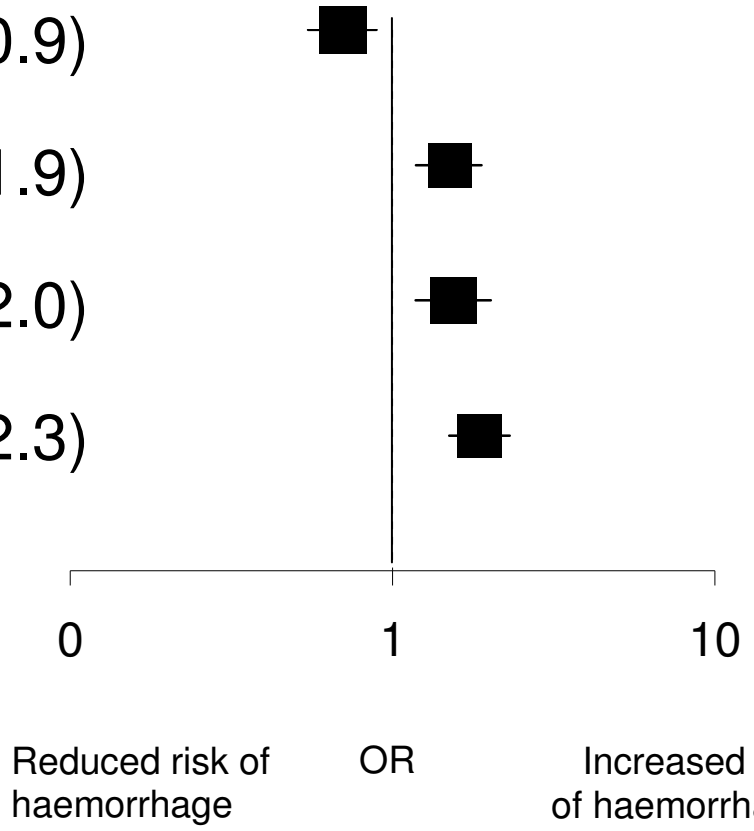
	2 x odds of ICH interval (95% CI)*	
Age	23 years	(17 to 69 years)
NIHSS	9 points	(7 to 12 points)
Glucose	7 mmol/L	(5 to 14 mmol/L)



*assume log-linear relationship with ICH

>10 studies had consistent effect sizes for smoking, diabetes, prior hypertension and AF

	Summary OR (95% CI)
Smoking	0·7 (0.6 to 0.9)
Prior hypertension	1·5 (1.2 to 1.9)
Diabetes	1·5 (1.2 to 2.0)
AF	1·9 (1.5 to 2.3)



Post rtPA ICH definitions

		Radiological definition	
		Any intracranial haemorrhage	Parenchymal haemorrhage
Clinical definition	Any deterioration	*NINDS-S (n=26)*	*ECASS-1 (n=9)* *
	Significant deterioration	*ECASS-3 (n=12)*	*SITS-MOST (n=8)*

* No clinical deterioration necessary

Summary proportion of rtPA ICH by ICH definition

		Radiological definition	
		Any intracranial haemorrhage	Parenchymal haemorrhage
Clinical definition	Any deterioration	*5%*	*12%*
	Significant deterioration	*7%*	*4%*

Summary proportion of rtPA ICH by ICH definition

		Radiological definition	
		Any intracranial haemorrhage	Parenchymal haemorrhage
Clinical definition	Any deterioration	*5%*	*12%*
	Significant deterioration	***7%***	*4%*

Most consistent estimate across studies (least statistical heterogeneity)

Effect of study design on effect sizes

Between study differences in effect sizes of

age, smoking, NIHSS, diabetes, prior hypertension, glucose, AF, CT visible brain lesion, or use of prior antiplatelets

….were not explained by

- ICH definition in studies
- Observational cohort vs clinical trial
- Adjustment for confounding factors in final models

There was no statistical evidence of small study bias

Conclusions

Individual factors measured before an infusion of rtPA have only a modest predictive power for subsequent ICH

Study design (particularly ICH definition) did not change the effect sizes of baseline factors to a significant degree