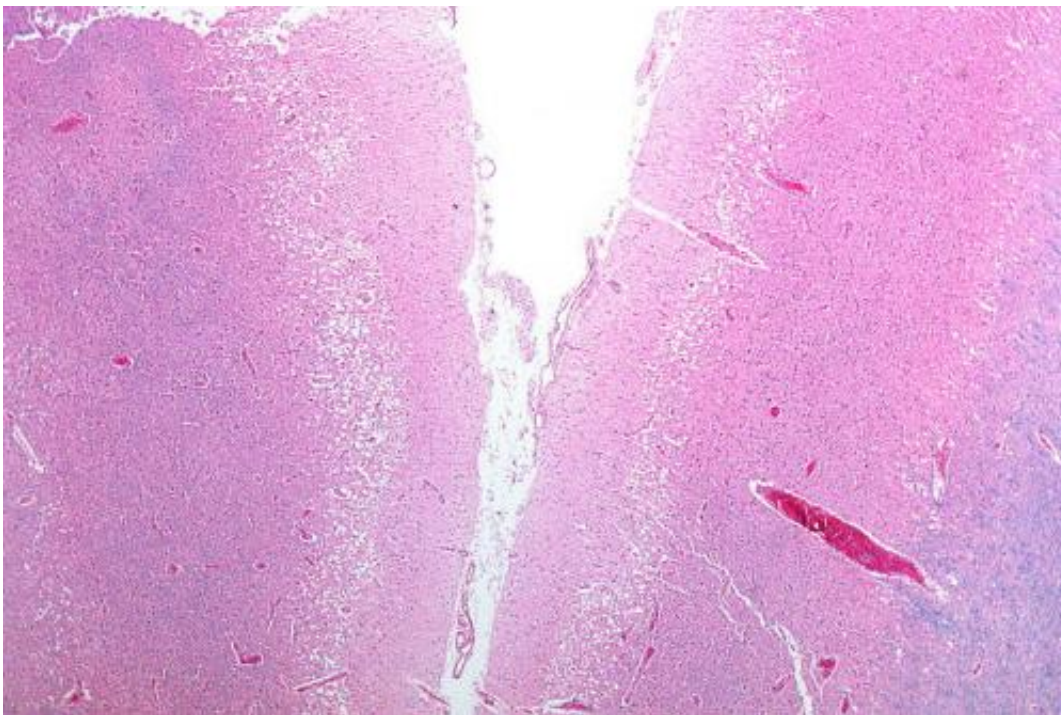


# Meta-analysis shows that alteplase given promptly after stroke reduces long-term disability

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Micrograph showing cortical pseudolaminar necrosis, a finding seen in strokes on medical imaging and at autopsy. H&E-LFB stain. Credit: Nephron/Wikipedia

Many more stroke patients could benefit from thrombolytic treatment (the use of drugs to break up or dissolve blood clots), but it needs to be administered as quickly as possible after the first signs of illness, according to new findings from the largest meta-analysis to date

investigating the clot-busting drug alteplase. The study, which involved more than 6700 stroke patients, is published in *The Lancet*.

The [emergency treatment](#) with alteplase markedly improves the chances of a good outcome when administered within 4-5 hours of onset of symptoms but, although still worthwhile, its benefit diminishes the later it is given.

The findings show just how important it is for people with acute ischaemic [stroke](#) (in which blood flow to an area of the brain is blocked or reduced) to be identified quickly and treated by specialist staff in order to reduce the subsequent degree of disability.

"Our results show that alteplase [treatment](#) is a very effective means of limiting the degree of disability in [stroke patients](#)", said study co-author and senior statistician Dr Jonathan Emberson, from the Clinical Trial Service Unit at the University of Oxford in the UK.

Dr Emberson and colleagues conducted a meta-analysis of individual patient data from all the major trials of alteplase for treatment of acute ischaemic stroke. Analysis of data from nine randomised trials involving 6756 [patients](#) (1729 older than 80 years of age) showed that alteplase treatment significantly increased the odds of a good stroke outcome (no significant disability 3–6 months after stroke), with faster treatment offering the best chance of recovery.

The odds of a good stroke outcome were 75% greater for patients given alteplase within 3 hours of initial [stroke symptoms](#), compared with those who did not receive the drug; for those given the drug between 3 and 4-5 hours post-stroke there was a 26% increased chance of a good outcome; while for those with a delay of more than 4-5 hours in receiving treatment, there was just a 15%, not statistically significant, increase in the chance of a good recovery.

According to Dr Emberson, "Although alteplase increased the risk of death from intracranial haemorrhage by about 2% within the first few days after stroke, by a few months survivors treated with alteplase were less likely to be disabled than those not receiving such treatment. Indeed, alteplase increased the proportion who avoided disability altogether by about 10% for patients treated within 3 hours and 5% for those treated between 3 and 4-5 hours."

According to Kennedy Lees, study co-author and Professor of Cerebrovascular Medicine at the University of Glasgow, UK, "What this shows is that we are up against the clock when treating ischaemic stroke. Every minute counts. People need to be identified quickly and systems need to be in place to get them scanned, diagnosed accurately, and then treated within minutes to hours."

Importantly, the benefits of alteplase were observed in all patient groups studied, including those aged 80 or over and those with severe strokes. Richard Lindley, Professor of Geriatric Medicine at the University of Sydney, and a study co-author added, "These results demonstrate that upper age limits in clinical trials can inadvertently lead to the elderly being excluded from an effective treatment. These new results tell us that the elderly should be treated with the same urgency as younger patients."

Study co-author Peter Sandercock, Professor of Neurology, University of Edinburgh said, "I cannot over-emphasise how useful these analyses are—they provide the type of clear information that patients and their families need when weighing the benefits and risks of this important treatment."

Writing in a linked Comment, Michael Hill and Shelagh Coutts from the Hotchkiss Brain Institute and Department of Clinical Neurosciences, Calgary, Canada, point out that, "The data render obsolete the European

licensing label for alteplase—which excludes patients older than 80 years and those with severe stroke. The finding of a small benefit of treatment up to 4-5 h from onset makes the advice of the US Food and Drug Administration and Health Canada to not treat patients after 3 h from onset similarly outdated."

They add, "The question now is not whether we can extend the window for treatment. Rather, how do we get everyone treated faster and how do we dispel preconceived notions about not treating older patients or those with milder strokes?... Audits show that patients with ischaemic stroke are offered thrombolysis too rarely or, if they are offered it, too slowly. Quick treatment requires efficient processes and a team approach. Pre-hospital systems to identify patients and bring them to the appropriate hospitals, emergency department swarming, rapid simple imaging, and use of telemedicine must be harnessed to reduce times to treatment. Strategies to do so will vary by region but it is simply unacceptable not to achieve very fast treatment times."

**More information:** *The Lancet*, [www.thelancet.com/journals/lan...](http://www.thelancet.com/journals/lan...)  
[http://www.thelancet.com/journals/lan... \(14\)60584-5/abstract](http://www.thelancet.com/journals/lan...)

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