

Final report summary:

Can lowering blood pressure and cholesterol after stroke prevent cognitive decline?

Prevention of Decline in Cognition After Stroke Trial (PODCAST):
a factorial randomised controlled trial of blood pressure and lipid
lowering

PROJECT CODE: TSA 2008-09

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Why did we fund this research?

A person's cognitive ability includes their ability to perceive, think, and remember things.

Problems with cognitive ability often occur after stroke, and for many patients these problems do not get worse. However, although little is known about the relationship between stroke and dementia, some research suggests that around one in three stroke survivors could go on to develop dementia within five years of their stroke¹.

As there are no known interventions which are known to delay or prevent dementia from happening, we need research into potential treatments.

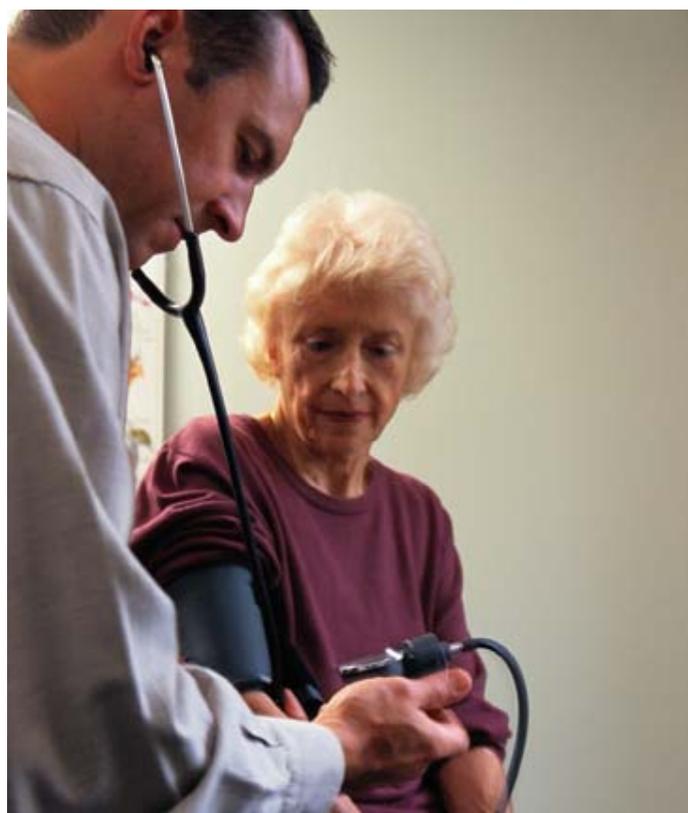
Research has shown that lowering blood pressure and cholesterol can reduce the chance of another stroke happening, known as recurrent stroke^{2,3}.

Early evidence also suggests that lowering blood pressure may reduce the chance of developing dementia after stroke^{4,5}, although there is no evidence which suggests that lowering cholesterol can reduce this risk.

Lowering blood pressure, or cholesterol levels below the standard guideline treatment levels is known as 'intensive' blood pressure, or cholesterol lowering therapy.

The main aim of the PODCAST trial was to determine if intensive blood pressure lowering therapy and/or 'intensive' cholesterol lowering therapy after stroke might reduce cognitive decline and dementia any more than moderate, standard guideline treatment levels⁶.

If definitive evidence were to be found, it could change the management of patients by health care professionals and have a significant impact upon the societal burden of dementia.



What did the researchers do?

Stroke patients without dementia were randomly allocated to receive treatment appropriate to reduce their blood pressure to either the standard-guideline level or receive more 'intensive' treatment to bring their blood pressure down to a level lower than the standard guideline (so bringing the systolic reading down to 125 rather than 140 to achieve blood pressure of 80/125, for example).

In addition, about 90% of these patients had a stroke caused by a clot (ischaemic stroke) and were also randomly allocated treatment to bring their cholesterol down to either the standard-guideline level (less than 3.0 mmol/L) or an 'intensive' level lower than the guideline level (1.4 rather than 3 mmol/L).

The PODCAST trial was designed to have two stages of recruitment and funding. This project was the first stage, designed to be a pilot, randomised controlled trial (RCT) which aimed to recruit 600 stroke patients from 30 UK sites over two years, and perform follow up studies for at least another year. This was funded jointly by the Stroke Association and Alzheimer's Society.

The aims were to see:

- how safe and tolerable the blood pressure and cholesterol treatments were to patients
- how feasible it was to achieve lowered targets of blood pressure and cholesterol
- how practical it was to recruit patients and sites to a large trial of this kind
- whether telephone and clinic assessment of cognitive ability could be completed satisfactorily.

If this first stage of PODCAST was successful, the aim was to seek further funding to proceed with the second stage of the trial.

What did the research find?

Due to some of the challenges encountered during the trial, PODCAST identified many design issues of relevance for similar trials in the future. For example, recruitment was limited due to a number of reasons.

Only 83 patients were recruited to the pilot stage of PODCAST from 19 UK sites between 7 October 2010 and 31 January 2014. Seventy-seven patients took part in both the blood pressure lowering, and cholesterol lowering arms of the study.

The main cause was the cost of the cholesterol lowering drugs used in the study, and the reluctance of NHS commissioning bodies to buy them. Delays and limitations to recruitment were also caused by the additional costs of treating patients who took part in the trial after their participation had finished.

Further limitations of PODCAST were that not all patients were seen in clinic for the final, assessment after two years (63 out of 83 seen), hence treatment may not have been given for long enough.

Analysis of the data from patients recruited to the trial showed no reduction in dementia, serious adverse events (SAEs), or deaths associated with either intensive blood pressure lowering, or intensive cholesterol lowering treatment. However, this is unsurprising. The low recruitment rate to the trial meant that this result may not be reliable and clinical benefits might have shown if sufficient numbers of patients were recruited.

Although the blood pressure lowering arm of PODCAST achieved its target levels, the cholesterol lowering arm of the trial did not. The study also showed that the intensive treatments are safe to use in patients after stroke.

Lessons from PODCAST, particularly with regard to recruitment to large trials of its kind, suggested new approaches were needed for research into cognitive problems and dementia after stroke.

The PODCAST study has informed a new research programme to address vascular dementia, the second most common form of dementia in the UK. The programme is jointly funded by the Stroke Association, the British Heart Foundation and Alzheimer's Society and launched in 2016.

Three studies from the programme were awarded in 2017 and can be found on our website: stroke.org.uk/research

A summary of the challenges encountered in PODCAST was published in the journal, *Trials*, in 2015⁷.

The final results of PODCAST were published in the journal, *PLOS One*, in 2017⁸.

What does this mean for stroke survivors?

PODCAST demonstrated the challenges encountered in large trials of its kind, and which would affect similar trials planning to recruit from the same population of stroke survivors.

It showed that new approaches were needed for research into cognitive problems and dementia after stroke. Lessons from PODCAST informed the planning of a vascular dementia research programme launched in 2016. The programme has been jointly funded by the Stroke Association, Alzheimer's Society, and the British Heart Foundation.

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