Improving brain health in patients by reducing risk factors for stroke

AIMS

This fellowship aimed to find out whether lowering the blood pressure, higher cholesterol and glucose lowers the risk of dementia. This is important, because in Scotland there are about 1 million people with higher blood pressure, 2 million with high cholesterol and 317,000 people with diabetes. The fellowship used the following methods:

- Following up people in randomised controlled trials of stroke prevention treatments.
- Using genetic databases to identify people at risk.
- Developing the use of routinely collected healthcare data for dementia prevention trials.

KEY FINDINGS

- Following up large scale randomised trials led to the following findings:
  - In the first Asymptomatic Carotid Surgery Trial (ACST-1), long term follow up demonstrated that although operating on narrowing of an artery in the neck (carotid artery) reduces the risk of stroke, it did not reduce the risk of dementia. However, dementia risk was high in people with narrowing of the carotid artery.
  - In the Anglo-Scandinavian Cardiovascular Outcomes Trial (ASCOT), although atorvastatin and amlodipine reduced the risk of stroke, these medicines did not reduce the risk of dementia. However, dementia risk was high in people with high blood pressure in this study
  - In the UK Prospective Diabetes Study (UKPDS), although lowering blood pressure or better controlling diabetes reduced the risk of all complications of diabetes, they did not show that they reduce the risk of dementia. However, dementia risk was high in people with diabetes in this study.
- People with stroke had the memory and understanding of someone 15 years older, with greater effect with more severe stroke.
- Genetic markers of some proteins were associated with better thinking speed in mid-life
- The computer programs we developed can read the text of brain scan reports accurately and quickly.

CHIEF SCIENTIST OFFICE

WHAT DID THE STUDY INVOLVE?

- People who had taken part in randomised trials of treatments to reduce the risk of heart attack and stroke were followed up into routine electronic health records. We found out who had been admitted to hospital with dementia. I collaborated with trials in Oxford, London and Canada.
- The project PhD student examined problems with thinking and memory after stroke, measured with pen and paper tests. We used a dataset of people who had taken part in large international randomised trials.
- With a post-doctoral student funded by the fellowship, we examined the genetic effect of different proteins relevant to blood vessel diseases on speed of thinking, dementia and stroke.
- With colleagues in informatics, we developed a way to read brain imaging reports using a technique called natural language programming. Scans that showed stroke or damage to blood vessels was of particular interest. We could read hundreds of thousands of reports that would not otherwise have been possible.
- People who had taken part in large randomised trials, and who had been affected by dementia were consulted before beginning these research projects.

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

The results of two of the studies following up participants in large randomized controlled studies are summarized below. None of the studies showed that reduction of blood pressure, diabetes, or cholesterol in midlife reduce later risk of dementia.

Dementia

HR 0.94 (95% CI: 0.82, 1.07), p=0.323

Dementia

HR 0.98 (95% CI 0.75–1.28); $p = .89$
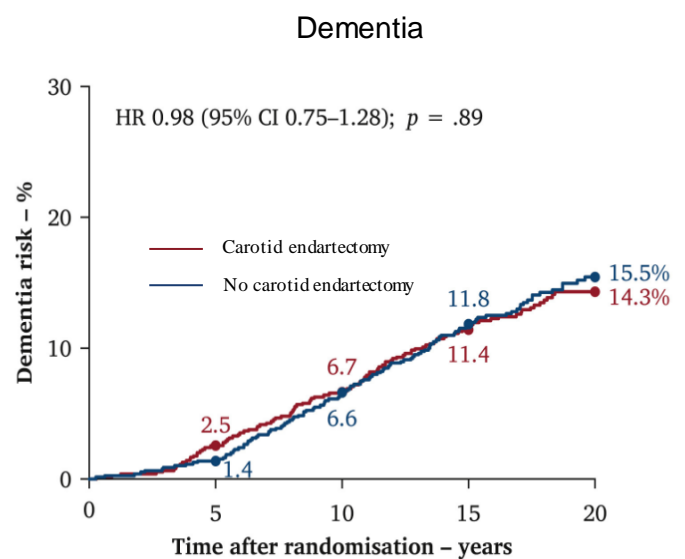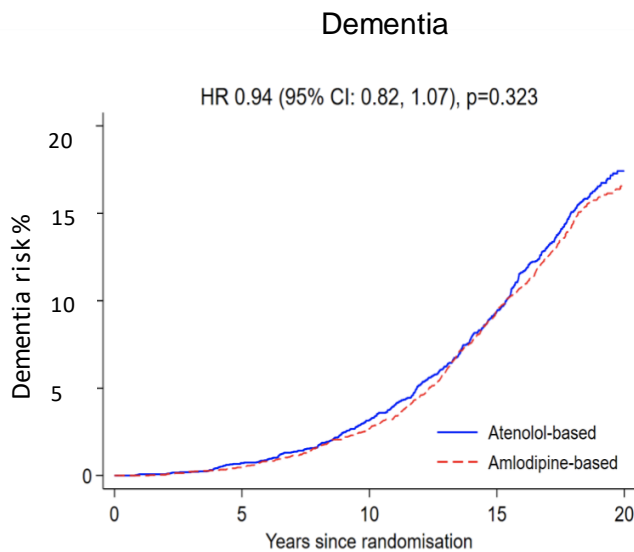
The ASCOT study randomly allocated 8,580 people in the UK with high blood pressure to one of two blood pressure lowering drugs, atenolol or amlodipine. Of these, 4,505 were randomly allocated to atorvastatin or placebo.

Over 20 years, atorvastatin did not reduce the incidence of dementia. The effect of 5 years of amlodipine was to reduce incidence of stroke by 18% (95% confidence interval (CI) 7 to 28%). There was considerable uncertainty for dementia (6% reduction, 95%CI: +7% to – 18%)

The ACST-1 study randomly allocated 1,601 people with asymptomatic narrowing of the carotid artery in the UK and Sweden to either surgery to remove the narrowing, or no surgery.

Over 20 years, surgery had no statistically significant effect on the incidence of dementia (2% reduction, 95%CI: +28% to -25%), but did not exclude a reduction or increase of dementia of about 25%.

WHAT IMPACT COULD THE FINDINGS HAVE?

- **Patients:** for people with risk factors for stroke, we can be confident that lowering blood pressure or cholesterol reduces the risk of stroke, and treating diabetes reduces diabetic complications in the long term. However, whether these treatments reduce dementia to an important degree is not certain.

- **Policy:** no change is needed to current treatment policies. However, it is very important that the Chief Scientist Office continue to advocate to reduce the administrative burden and delay to data access for researchers. On of the studies took up to 5 years to get governance approval.

- **Practice:** clinicians should be aware that the beneficial effects of early treatment of risk factors for stroke accrue over many years.

HOW WILL THE OUTCOMES BE DISSEMINATED?

I have disseminated the findings to professional groups at the European Stroke Conference, the European Society of Vascular Surgeons, and the European Association for the Study of Diabetes. I have published our findings in academic journals and more manuscripts are in preparation. I have shared this work with patient and public networks through the Stroke Association, the Alzheimer's Association, and Health Data Research UK.

The next steps are to
- To leverage our natural language processing algorithms to invite people for trials of treatments (collaboration with Tufts University, US). An application to CSO Response Mode Funding Scheme is in progress. This application has a PPI work-package,
- To ensure our natural language processing algorithm data is available to as many researchers as possible (collaboration with electronic Data Research and Innovation Service funded by the Alzheimer's Disease Data Initiative).

CONCLUSIONS

- It is unlikely that better control of vascular risk factors will lead to a big reduction in the risk of dementia, although will reduce the risk of stroke.

- Imaginative use of data collected by the NHS could reduce costs and speed up studies by epidemiologists and clinicians, but streamlining of access processes are needed.

RESEARCH TEAM & CONTACT

Dr William Whiteley

Centre for Clinical Brain Sciences, University of Edinburgh

william.whiteley@ed.ac.uk

@edinburghstroke