<u>SCAF/17/01 - Preventing dementia by targeting risk factors for cerebrovascular</u> <u>disease</u>

About 40% of people with dementia have problems with the small brain blood vessels that contribute in partly or wholly to their dementia. People with higher levels of blood pressure, LDL cholesterol or diabetes ('vascular risk factors') in their middle years have a higher risk of dementia. This may because these risk factors lead to symptomatic or asymptomatic strokes, due to damage the small brain blood vessels, or an effect on brain damage due to Alzheimer's disease.

If we could show that lowering vascular risk factors reduced the risk of dementia this would be important for public health. To show this, the best study design would be a 'randomised controlled trial'. The trial would randomly allocate one group of patients to lowering of vascular risk factors, and a second group to a placebo or control treatment. Because dementia takes a long time to develop, both groups would need to be followed for ten to twenty years to see which group had the lowest dementia risk.

In this fellowship, I will use a cost-effective method to replicate this best study design. Randomised trials of vascular risk lowering were performed ten to twenty years ago, but they measured the risk of dementia with only five years follow up - not long enough to show any difference in risk. I will extend the length of follow up of these trials for ten or twenty years, and find out which trial participants develop dementia with national health records in UK, Sweden and Canada. The result of this work will be to determine whether lowering vascular risk factors (like blood pressure, cholesterol and diabetes) in the middle years lowers the risk of dementia. This will be important for public health, and has implications on who should be treated and at what age.

Damage to the small blood vessels can be detected on brain scans. These findings are called 'cerebral small vessel disease', and might identify those patients who are at highest risk of dementia due to vascular risk factors. In order to test treatments in patients with 'cerebral small vessel disease' it is important to be able to identify them. On promising source of data are reports of brain scans performed in routine clinical practice. I have developed a method to identify these patients using reports of brain scans across the whole country. In this study, I will measure the risk these patients have of dementia, stroke and death in the long term. This method will make it possible to identify patients with cerebral small vessel disease for new large clinical studies at low cost.