**Application number/Title:** 34763- Genetic analyses of age-of-onset in cerebral small vessel disease

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**Keywords provided by the Applicant PI to describe the research project:**
age-of-onset, cerebral-small-vessel-disease, epidemiology, genetics, heritability

**Application Lay Summary:**
Cerebral small vessel disease is a common disease contributes greatly to death and disability in people aged 60 years and older and can cause stroke, depression, and cognitive decline. Many risk factors, both genetic and environmental, may contribute to the development of this disease. Therefore, developing effective prevention strategies and treatments is challenging. We propose to study the genetic contributions to this condition which will help us identify who may be at risk of developing this disease earlier in life and develop new ways to prevent and treat cerebral small vessel disease.

Over one year, we will use genetic and clinical data from the UK biobank to study cerebral small vessel disease related conditions, including ischemic and hemorrhagic stroke, late life depression and cognitive decline.

Our first aim is to determine the heritability of age-of-onset of the cerebral small vessel disease related stroke, late life depression and cognitive decline.

Our second aim is to determine the proportion of genetic contribution that is shared by these conditions and the mutations that contribute jointly to accelerate their development.

Our third aim is to use the identified genetic risk factors to develop a prediction tool for cerebral small vessel disease related conditions.

Our fourth aim is to identify non-genetic clinical factors, such as brain imaging and laboratory factors, that modify the genetic effects of this disease.
Our study is unique because of its focus not just on the development of cerebral small vessel disease, but on genetic factors that contribute to earlier onset of this disease and related conditions such as stroke, depression, and cognitive decline. It is our hope that the results generated from this project will help develop new ways to promote brain health in the elderly population, with the goal of preserving brain functions that are crucial for the well-being of older people.