Application number/Title: 2532 - UK Biobank Stroke Study (UKBiSS): developing an in-depth understanding of the determinants of stroke and its subtypes

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Keywords provided by the Applicant PI to describe the research project:

Stroke, ischaemic, haemorrhagic, genetics, blood pressure

Application Lay Summary:

1a: Stroke is the second commonest case of death worldwide and a major global cause of severe disability. The three main pathological types (ischaemic stroke, intracerebral and subarachnoid haemorrhage) and their subtypes are likely to be caused by a combination of genetic and non-genetic lifestyle and environmental exposures, with individually modest effects and complex interactions. The aims of this proposal are to: 1) establish reliably the major lifestyle, environmental and genetic determinants of stroke and its pathological types and subtypes; 2) improve understanding of the different causal pathways for pathological types and subtypes of stroke.

1b: Substantial gaps remain in our knowledge of the genetic, lifestyle and environmental causes of stroke and its subtypes. We will study both established and potential new risk factors, determine differences in associations between subtypes, and shed new light on causal pathways through Mendelian randomization and mediation analyses. The resulting improved understanding of stroke mechanisms will enable better targeting of existing strategies for stroke

prevention and treatment and underpin the discovery of new interventions, benefiting both stroke patients and the wider public.

1c: We will look at how lifestyles (e.g., smoking, diet, physical activity, alcohol, etc.), biomarker levels (e.g., inflammation and coagulation markers, vitamin D, lipids), disease conditions (e.g., hypertension, diabetes, renal function, mental health, etc.), measured before people develop stroke, and genetic factors influence risk of developing stroke, both separately and combined. We also want to investigate how the shape and strength of these associations differ for different pathological types and subtypes of stroke.

1d: We'd like to request data on all participants in the cohort (approx. 503,000), from the baseline and repeat assessments, assayed biomarkers, genome-wide genotyping data, summary data from the accelerometry data collection, available multimodal imaging data (derived measures rather than raw data), and data from the web questionnaires (24-hour dietary questionnaire, including derived nutrient values, cognitive assessments, mental health). We also request linked health related data for all participants from available primary, secondary health care and death and cancer registries for identifying prevalent and incident stroke pathological types and subtypes and other major diseases (e.g., to enable competing risks analyses).