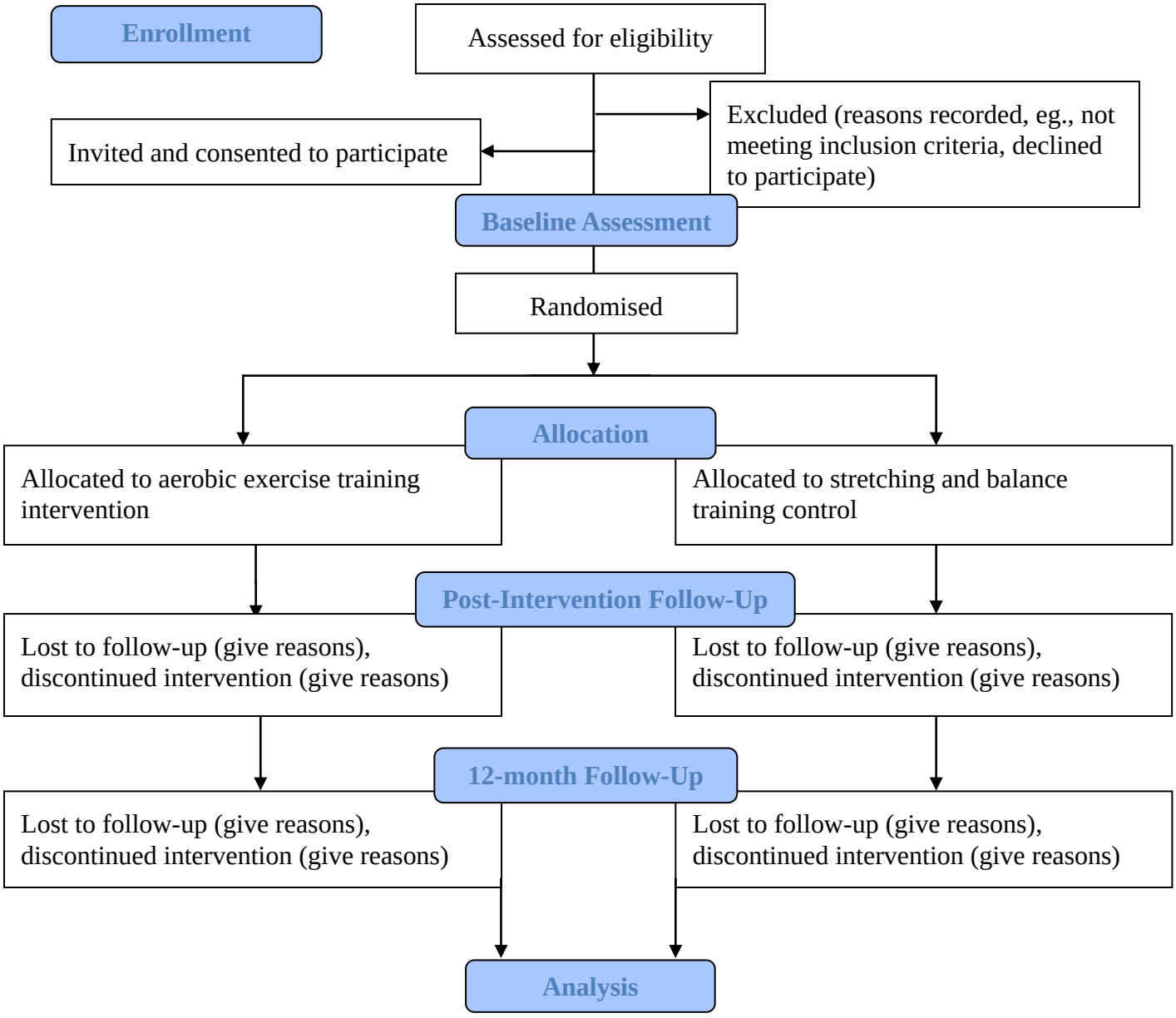

Supplementary Figure 1. PISCES study flow diagram.

Supplementary Table 1. Neuropsychological test battery and assessment of mood and quality of life.[9]

Cognitive Domain	Task/Questionnaire
Processing speed	Detection Task - Computerised Cogstate Battery
	Trail-Making-Test Part A
	Digit-Symbol Coding Task
Attention	Identification Task - Computerised Cogstate Battery
	Cancellation Task
Working memory	One-Back Task - Computerised Cogstate Battery
	Digit Span Task
Memory	Hopkins Verbal Learning Task
	Rey Complex Figure Task - Delayed Recall
Executive function	Trail-Making-Test Part B
	Rey Complex Figure Task - Copy Organisational Score
	Clock Drawing Test - Organisational Score
Language	Verbal Fluency Task
	Controlled Oral Word Association Test
	Boston Naming Test
	Token Test
Visuospatial function	Rey Complex Figure Task - Copy
Mood/Quality of Life	
Depression	Patient Health Questionnaire-9
Anxiety	Generalised Anxiety Disorder-7
Fatigue	Fatigue Assessment Scale
Quality of life	Assessment of Quality of Life Scale

Supplementary Information: Exploratory outcomes

Recurrent stroke: Intercurrent macro- and micro-infarction will be diagnosed by two neurologists on inspection of FLAIR, MPRAGE and T2 images for stroke greater than 10 days old. DWI images will be inspected for recent stroke within 10 days. These will be manually traced and masked for future analyses. The presence of recurrent stroke (clinical or silent) will be dichotomised as a binary variable in the analysis (i.e. recurrence: yes/no).

Blood pressure: 24-hour ambulatory BP monitoring and a 15-minute electrocardiograph-based HR variability assessment will be performed. Circadian BP pattern classification is based on the percentage decline in night-time BP compared with daytime BP. The normal ranges of ambulatory BP are defined as follows: daytime BP <135/85 mm Hg, night-time BP <120/75 mm Hg, 24-hour BP <130/80 mm Hg. Statistical analysis will be performed using BP as a continuous variable (i.e. BP averaged over a 24 hour period).

Blood biomarkers - BDNF and HbA1c: A 27 ml sample of whole venous blood at each assessment timepoint will be drawn. Of the whole sample, 9 ml will be collected in a plain tube, allowed to clot for at least 20 minutes at room temperature, and then centrifuged to isolate the serum. The serum will be divided into 4 x 1 ml tubes for storage at -80°C until assayed. The remaining 18 ml will be collected in lithium heparin/EDTA tubes, stored on ice, and centrifuged within 15 minutes to separate the plasma. Plasma will be aliquoted into 8 x 1 ml tubes and stored at -80°C until assayed. It is intended that blood samples will be collected within the same time period at every participant visit in an attempt to account for any biomarker circadian variation. The samples will be then split in two and placed into two separate, locked freezers to ensure a second sample is potentially available for back-up analyses.

APOE ε4 genotyping: The APOE ε4 genotype in our study population will be collected to determine the association between APOE ε4 status stroke, dementia and the effect on exercise training. Two 5 ml vacutainer tubes of venous blood will be taken at one of the assessment time-points for genetic analysis. One sample will be used for APOE ε4 genotyping and the second will be retained for further exploratory genetic analyses by the study investigators. Genomic DNA

(50 ng) will be extracted using the Genomic-tip 20G (Qiagen, Hilden, Germany) and the APOE ε4 region of interest will be amplified with specific primers (Invitrogen, Carlsbad, CA). The resulting DNA fragment will be sequenced with BDV3.1 (Applied Biosystems, Foster City, CA) using the APOE-forward primer on an ABI 3130-xl genetic analyser. APOE ε4 status (present, absent) will be dichotomised as a binary variable in the analysis.

Analysis plan for exploratory outcomes

Exploratory analysis of the relationship between CRF and PA and ambulatory BP, recurrent stroke, pre-specified growth factors (i.e. BDNF and HbA1c) and APOE ε4 will be analysed using appropriate repeated measures regression models. Appropriate statistical analysis for comparison of parametric and non-parametric distributions (as appropriate) will also be conducted.