**Associations between inflammation, cardiovascular biomarkers and incident frailty: the British Regional Heart Study**

**Supplementary methods**

**Socioeconomic class**

Socio-economic class was defined based on the longest-held occupation of participants at study entry (aged 40-59), using the Registrar General’s Social Class Classification. Three groups were defined: “non-manual” (class I, II, and III), “manual” (classes III, IV, and V), and “military” (employment with the Armed Forces).

**Tobacco usage**

Four groups of tobacco usage was defined: never-smokers, long term ex-smokers (stopped smoking 10 or more years prior), recent ex-smokers (stopped smoking less than 10 years prior), and current smokers.

**Multimorbidity**

As part of the baseline questionnaire, participants were asked if they had ever been told by a doctor that they had any of the following: cancer (at any site); anaemia; asthma; bronchitis; cataracts; chronic kidney disease; Crohn’s disease; depression; emphysema; gall bladder disease; gastric, peptic, or duodenal ulcers; glaucoma; gout; liver disease, cirrhosis or hepatitis; macular degeneration; osteoporosis; Parkinson’s disease; pneumonia; “prostate trouble”; shingles; ulcerative colitis; arthritis; a deep vein thrombosis and/or pulmonary embolus; and claudication.

The total number of reported comorbidities, plus any of: diabetes mellitus; atrial fibrillation; severe cognitive impairment; myocardial infarction; heart failure; and stroke (as defined elsewhere in Methods) were summed, without weighting, for each participant.

**Cognitive testing**

The TYM is a 10-task self-administered test that assesses orientation, copying, semantic knowledge, calculation, verbal fluency, similarities, naming, visuospatial abilities, and recall of a copied sentence. An 11th item measures the extent of help required from others, but all participants completed the TYM in a controlled setting without assistance and received the highest score for this task. Total TYM scores range between 0 to 50, with higher scores indicating better cognitive performance. Scores below 33 were defined as ‘severe cognitive impairment’, and scores between 33 and 45 (if older than 80 years) or 33 and 46 (if younger than 80 years of age) were defined as ‘mild cognitive impairment’.

**Physical examination**

Blood pressure was measured with an Omron sphygmomanometer twice in the right arm, with the subject seated and the arm supported. The mean of the two readings was used for analysis. With subjects in light clothing and without shoes, height was measured with a Harpenden stadiometer to the last complete 0.1 cm, and weight with a Tanita MA-418-BC body composition analyser (Tanita, Tokyo, Japan). Body mass index (BMI) was calculated as weight/(height)2 (kg/m2). Grip strength was measured using a Jamar Hydraulic Hand Dynamometer. Three measurements were taken with each hand, and the best of six used for analysis. Walking speed over 3 metres was recorded. Forced expiratory volume in 1s (FEV1) was measured using a Vitalograph Compact II instrument with subjects standing, without nose clips. FEV1 was standardised to the average study height, 1.71 m, using the formula: standardised FEV1=FEV1 × (1.71/height)2.

**Blood measurements**

Glucose was measured in a fluoride oxidase plasma sample and creatinine measured using enzymatic colorimetric assays. Total and high-density lipoprotein cholesterol were analysed using the methods of Nauck et al.(33); low-density lipoprotein cholesterol values were calculated using the Friedrickson-Friedwald equation. Estimated glomerular filtration rate (eGFR) was calculated using the MDRD equation.(34) Plasma interleukin-6 (IL-6) was measured using a high-sensitivity enzyme-linked immunosorbent assays (R&D systems, Oxon, UK). The lower limit of detection was 0.15pg/ml. High-sensitivity CRP was assayed by ultra-sensitive nephelometry (Dade Behring, Milton Keynes, UK). hs-TnT and NT-proBNP were measured by electrochemiluminescence immunoassay, performed on a Roche Elecsys 2010 automated platform (Roche Diagnostics, Burgess Hill, UK).