

1 **Table 1: Baseline characteristics of individuals with, and without, clinically-**
 2 **apparent cardiovascular disease, by frailty status.**
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	Free of clinically-apparent cardiovascular disease (n=1096)				Has clinically-apparent cardiovascular disease (n=303)			
	Robust (n=341)	Pre-frail (n=603)	Frail (n=152)	p for trend*	Robust (n=53)	Pre-frail (n=168)	Frail (n=82)	p for trend*
Age (years)	77 (3.6)	78 (4.5)	81 (5.3)	<0.0001	78 (4.4)	78 (4.1)	80 (5.4)	0.003
Manual occupation	146 (43%)	263 (44%)	73 (48%)	0.37	25 (47%)	74 (44%)	46 (56%)	0.20
Never smoked	153 (45%)	239 (40%)	47 (31%)	0.04	16 (30%)	57 (34%)	21 (26%)	0.50
Long-term ex-smoker	164 (48%)	316 (52%)	92 (61%)		34 (64%)	98 (58%)	56 (68%)	
Recent ex-smoker	13 (4%)	26 (4%)	9 (6%)		3 (6%)	6 (4%)	2 (2%)	
Current smoker	11 (3%)	22 (4%)	4 (3%)		0	7 (4%)	3 (4%)	
Physical measurements								
Systolic blood pressure (mmHg)	148 (18)	147 (18)	143 (20)	0.07	145 (19)	141 (20)	136 (23)	0.01
Diastolic blood pressure (mmHg)	78 (11)	77 (11)	75 (12)	0.10	75 (11)	73 (11)	69 (12)	0.001
BMI <20 kg/m ²	3 (0.9%)	13 (2%)	6 (4%)	0.007	0	3 (2%)	6 (7%)	0.01
BMI 20-24.9 kg/m ²	118 (35%)	162 (27%)	41 (27%)		17 (32%)	36 (21%)	16 (20%)	
BMI 25-29.9 kg/m ²	174 (51%)	311 (52%)	76 (50%)		28 (53%)	92 (55%)	38 (46%)	
BMI ≥ 30 kg/m ²	46 (13%)	117 (19%)	29 (19%)		9 (15%)	37 (22%)	22 (27%)	
Comorbidities								
Mild cognitive impairment	119 (35%)	246 (41%)	75 (49%)	0.005	20 (38%)	69 (41%)	36 (44%)	0.14
Severe cognitive impairment	25 (7%)	44 (7%)	14 (9%)		5 (9%)	17 (10%)	14 (17%)	
Diabetes mellitus	42 (12%)	83 (14%)	36 (24%)	0.007	10 (19%)	34 (20%)	21 (26%)	0.30
eGFR	77 (14)	74 (18)	69 (20)	<0.0001	73 (16)	68 (20)	65 (19)	0.05
Peripheral vascular disease	2 (0.6%)	24 (4%)	7 (5%)	0.006	2 (4%)	8 (5%)	10 (12%)	0.03
Prior myocardial infarction	-	-	-		37 (70%)	114 (68%)	50 (61%)	0.24
Heart failure	-	-	-		9 (17%)	37 (22%)	34 (41%)	0.0005
Prior stroke	-	-	-		14 (26%)	49 (29%)	27 (33%)	0.40
Total number of comorbidities (not including MI, HF or stroke)								
Zero or one	140 (41%)	198 (33%)	23 (15%)	<0.0001	20 (38%)	35 (21%)	8 (10%)	<0.0001
Two, three or four	174 (51%)	321 (56%)	80 (53%)		31 (58%)	98 (58%)	45 (55%)	
Five or more	27 (8%)	84 (14%)	49 (32%)		2 (4%)	35 (21%)	29 (35%)	
Taking five or more regular medications	71 (21%)	191 (32%)	73 (48%)	<0.0001	29 (55%)	112 (67%)	61 (74%)	0.02
Inflammatory biomarkers								
CRP (mg/L)	1.0 (0.5-2.0)	1.4 (0.7-3.1)	1.9 (0.7-5.1)	<0.0001†	0.8 (0.3-1.9)	1.5 (0.7-3.0)	2.0 (0.7-5.2)	0.0002†
IL-6 (pg/mL)	2.3 (1.5-3.4)	3.1 (1.9-4.6)	3.9 (2.2-6.2)	<0.0001†	2.7 (1.6-4.1)	3.2 (1.8-4.7)	4.6 (2.5-7.2)	<0.0001†
Coagulation biomarkers								
tPA (ng/mL)	8.3 (6.1-11)	9.1 (6.7-12)	10.0 (7.5-13)	<0.0001†	8.6 (6.6-10.8)	9.5 (7.0-12.5)	9.1 (6.4-12.8)	0.36†
D-dimer (ng/mL)	198 (140-270)	233 (158-314)	263 (165-412)	<0.0001†	248 (143-337)	239 (144-326)	306 (218-434)	0.03†
Endothelial biomarkers								
vWF (IU/dL)	107 (79-133)	119 (91-143)	131 (101-177)	<0.0001†	120 (88-142)	127 (91-177)	144 (100-227)	0.11†

Cardiac biomarkers								
hs-cTnT (pg/mL)	8.4 (6.1-13)	10.5 (7.2-15)	15.0 (9.1-23)	<0.0001†	10 (6.5-16.4)	11 (7.2-16.4)	20 (12.8-32.5)	<0.0001†
NT-proBNP (pg/mL)	87 (51-156)	123 (64-244)	198 (97-492)	<0.0001†	227 (115-516)	196 (89-572)	479 (162-1700)	0.0001†
Imaging								
CIMT (mm)	0.79 (0.2)	0.80 (0.2)	0.83 (0.2)	0.001	-	-	-	-
cfPWV (m/s)	9.9 (1.7)	10.4 (1.6)	10.5 (1.6)	0.0002	-	-	-	-
DC (10 ⁻³ kPa)	13.1 (4.1)	12.1 (4.1)	11.0 (3.6)	<0.0001	-	-	-	-
ABPI <0.9	65 (20%)	142 (25%)	40 (32%)	0.007	-	-	-	-
ABPI >1.4	10 (3%)	10 (2%)	2 (2%)	0.20	-	-	-	-

- 1 Values are mean (SD) for normally-distributed continuous variables, n (%) for
- 2 categorical variables, and geometric mean (interquartile range) for non-normally
- 3 distributed continuous variables.
- 4 * "Trend" denotes *p* value for association with frailty status modelled as an ordinal
- 5 variable.
- 6 † Statistical comparisons made with variable natural log-transformed.
- 7 BMI= body mass index, eGFR= estimated glomerular filtration rate, CRP= C-reactive
- 8 protein, IL-6= interleukin-6, tPA= tissue plasminogen activator, vWF= von Willebrand
- 9 factor, hs-cTnT= high-sensitivity cardiac troponin T, NT-proBNP= N-terminal B-type
- 10 natriuretic peptide, CIMT= carotid intima media thickness, cfPWV= carotid-femoral
- 11 pulse wave velocity, DC= carotid distensibility coefficient, ABPI= ankle brachial
- 12 pressure index

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