SUPPLEMENTAL MATERIAL

Data S1.

Systematic literature review

Search terms used on PubMed and Embase (up to 18th October 2019):
("muscle mass" or "skeletal muscle" or “sarcopenia” or "fat mass" or "body fat" or "body composition" or "fat free mass" or "lean mass" or "adiposity") AND ("mortality" or "death" or "survival" or "cardiovascular disease" or "CVD" or "stroke" or "coronary heart disease" or "congestive heart failure")
Studies were excluded if they were done in patients or ill people (including but not limited to hospitalised, intensive care or dialysis patients, those with cancer, diabetes, COPD, CKD, dementia, HIV), done in children or adolescents, investigating a diet or exercise intervention, done in animals, molecular, cellular-level studies, or genetic studies. Only findings from prospective cohort studies published after 2000 with more than 600 participants are presented below.

Table S1. Summary of search findings.

Exposure	Outcome	Sex	Number of associations identified in studies			
			Null	Negative	Positive	U or J-shaped
Muscle mass	All-cause mortality	Combined men and women	7	8	3	
		Men only	10	7	1	3
		Women only	10	9	1	2
Muscle mass	CVD	Combined men and women	2	2	2	
		Men only	7	2	1	
		Women only	5	2	1	
Fat mass	All-cause mortality	Combined men and women	7	2	3	
		Men only	12	4	17	5
		Women only	13	10	19	3
Fat mass	CVD	Combined men and women	2	1	10	3
		Men only	11	2	16	
		Women only	12		13	
Low muscle, high fat	All-cause mortality	Combined men and women			1	
		Men only	2		2	
		Women only	2		1	
High Muscle, low fat	All-cause mortality	Combined men and women		1		
		Men only				
		Women only				
Low Muscle, high fat	CVD	Combined men and women			1	
		Men only	1			
		Women only	1			
High muscle, low fat	CVD	Combined men and women		1		
		Men only				
		Women only				

Each association assessed in the studies is counted distinctly (i.e. the number of associations exceeds the number of studies identified since some studies analysed more than one exposure/outcome combination). 'Muscle mass' includes studies that assessed measurements of lean mass from techniques such as bioimpedance analysis (BIA), dual energy x-ray absorptiometry (DEXA), mid upper arm circumference and calf circumference (it does not include studies of muscle quality such as grip strength). 'Fat mass' includes studies that assessed measurement of adiposity such as fat mass as determine by BIA or DEXA, percentage body fat, waist circumference, waist to hip ratio. Studies of BMI or body fat distribution indices are not included.

Table S2. Systematic literature review.

Reference		Study name (date of recruitment)	Study participants (location, N, age)	Body composition measurement	Exposure definition/coding	Outcome	Shape of association
68	Abramowitz, et al. (2018)	NHANES (1999-2004)	USA, n=11687 aged >20 yrs	DEXA (Appendicular skeletal muscle mass)	Low muscle defined as ASMI <5.45kg/m^2 (women) or <7.26kg/m^2 (men) [2,3]	All-cause mortality	BMI and mortality: U (low muscle group), 0 (preserved muscle group) ASMI and mortality (men and women combined): -
69	Allison, et al. (2002)	NHANES I & II	USA, n=10169 men aged 25-75yrs	Skinfolds (indicator of fat mass), upper arm circumference (fat free mass indicator), BMI	Modelled continuously	All-cause mortality	BMI and all-cause mortality: U (men) Fat free mass and mortality: linear - (men) Fat mass and mortality: linear + (men)
70	Andersen, et al. (2015)	Shanghai Men's Health Study and Shanghai Women's Health Study (1996-2000)	China, n=116442 aged 40-74yrs	Waist to hip ratio	Quintiles of WHR	All-cause and CVD mortality	WHR and mortality: linear + (men) WHR and mortality: linear + (women) WHR and CVD mortality: linear + (men) WHR and CVD mortality: linear + (women)
71	Atkins, et al. (2014)	NHANES (1999-2004)	USA, n=11687 aged >20yrs	Waist circumference, midupper arm circumference, triceps skinfold thickness	4 groups created: Optimal (MAMC >25.9cm and WC ≤102cm), sarcopenic (MAMC ≤25.9cm and WC ≤102cm), sarcopenic obese (MAMC ≤25.9cm and WC>102cm), obese (WC >102cm and MAMC >25.9cm)	All-cause mortality, CVD mortality, CVD events	Sarcopenia and mortality: 0 (men) Sarcopenia and mortality: + (women) Sarcopenia and CVD: 0 (men) Sarcopenia and CVD: + (women)
72	Bachettini et al. (2019)	n/a	Brazil, n=1291 aged >=60 years	Using the European Working Group on Sarcopenia in Older People (EWGSOP) definitions of sarcopenia	Sarcopenia, binary	All-cause mortality	Severe sarcopenia and mortality: + (men and women combined) Other sarcopenia and mortality: 0 (men and women combined)
73	Balogun, et al. (2017)	Tasmanian Older Adult Cohort study	Tasmania, n=1099 aged >50yrs	DEXA (Appendicular lean mass), lower limb strength	Calculated ALM/height^2 [2], ALM/BMI [1], ALM/weight*100 [12] from DEXA. Measured grip, lower-limb muscle, and upper-limb muscle strength and/or quality. Low muscle mass or function defined as participants in the lowest 20% of the sex-specific distribution for each measurement	Mortality, falls, fracture	Muscle strength or quality and mortality (men and women combined): 0 Low appendicular lean mass/BMI and mortality (men and women combined): + Low appendicular lean mass/height^2 and mortality (men and women combined): 0 Low appendicular lean mass/weight and mortality (men and women combined): 0
74	Batsis, et al. (2014)	NHANES III (1988-1994)	USA, n=4652 aged >60years	BIA (skeletal muscle index, % body fat)	4 definitions used: Normal if SMI ⩾10.76kg/m^2 (men) >6.76kg/m^2 (women); Class I sarcopenia if SMI 8.51–10.75 (men) 5.76–6.75 (women); Class II sarcopenia: ⩽8.50 kg/m2 ⩽5.75 [17]. Obesity defined as body fat >27% (men) >38% (women) [3]	All-cause mortality	Sarcopenia only and mortality: 0 (men) Sarcopenia only and mortality: + (women) Sarcopenic obese and mortality: 0 (men) Sarcopenic obese and mortality: 0 (women) Obese only and mortality: 0 (men) Obese only and mortality: 0 (women)
45	Batsis, et al. (2017)	NHAHES (1999-2004)	USA, n=4984 aged >60 yrs	DEXA (Appendicular lean mass), waist circumference, BMI	Low lean mass defined as: ALM <19.75kg (men) <15.02kg (women) [1] or ALM:BMI <0.789 (men), <0.512 (women). Obesity defined as body fat >25% (men) >35% (women) [9].	All-cause and CVD mortality	Low lean mass and mortality: + (men) Low lean mass and mortality: 0 (women) Low lean mass and CVD: + (men) Low lean mass and CVD: 0 (women) Low lean mass with obesity and mortality: + (men) Low lean mass with obesity and mortality: 0 (women) Low lean mass with obesity and CVD : 0 (men) Low lean mass with obesity and CVD : 0 (women) Obesity (body fat %) and mortality: - (men)

							Obesity (body fat %) and mortality: - (women) Obesity (body fat %) and CVD: 0 (men) Obesity (body fat %) and CVD: 0 (women)
75	Bea, et al. (2015)	Women's Health Initiative (1993-1998)	USA, n=10525 postmenopausal women aged 50-79yrs	DEXA (total body fat %, lean body mass %), BMI	Quintiles of each exposure	All-cause mortality	Fat mass and mortality (women aged 50-59): linear + Fat mass and mortality (women aged >70): linear - Lean mass and mortality (women aged 50-59): linear – Lean mass and mortality (women aged >70): linear +
76	Bigaard, et al (2004)	Diet, Cancer and Health study (1993-1997)	Denmark, n=51053 aged 50-64yrs	BIA (fat free mass index, body fat mass index)	Modelled continuously using linear splines, and relative risks estimated per 10% increase in waist circumference and per kg/m^2 increase in body fat mass index and fat free mass index Results stratified into high and low range corresponding to cut-offs at the 40th and 60th percentiles	All-cause mortality	Fat mass and mortality: J (men) Fat mass and mortality: J (women) Fat free mass and mortality: reverse J (men) Fat free mass and mortality: reverse J (women) WC and mortality: linear + (men) WC and mortality: linear + (women)
77	Bigaard, et al. (2005)	Diet, Cancer and Health (1993-1997)	Denmark, n=57058 adults	BIA (body fat mass index, fat free mass index), waist circumference	Modelled continuously using linear splines	All-cause mortality	Body fat mass index and all-cause mortality: J (men) Body fat mass index and all-cause mortality: J (women) Fat free mass index and mortality: reverse J (men) Fat free mass index and mortality: reverse J (women)
78	Boloukat, et al. (2018)	Tehran Lipid and Glucose Study	Iran, n=4631 aged >40yrs	BMI, waist circumference, waist-to-height ratio, WHR	Modelled continuously per 1 unit increase in each exposure	CHD or stroke incidence	WC and CVD: 0 (men) WC and CVD: 0 (women) WHR and CVD: 0 (men) WHR and CVD: 0 (women) Waist-to-height ratio and CVD: 0 (men) Waist-to-height ratio and CVD: 0 (women)
43	Brown, et al. (2016)	NHANES (1988-1994)	USA, n=4425 aged >60 yrs	BIA (skeletal muscle index), gait speed	Sarcopenia defined as low gait speed (<0.8m/s) and SMI <10.76 (men), <6.75 (women)	All-cause and CVD mortality	Sarcopenia and mortality: + (men) Sarcopenia and mortality: + (women) Sarcopenia and CVD: 0 (men) Sarcopenia and CVD: + (women)
79	Brown, et al. (2017)	NHANES III (1988-1994)	USA, n=1487 aged >65 yrs	BIA (Appendicular lean mass)	Modelled continuously per 1 SD of ALM	All-cause mortality	Appendicular lean mass and mortality: - linear (men) Appendicular lean mass and mortality: - linear (women)
44	Cesari, et al (2009)	InChianti study (1998-2000)	Italy, n=934 aged >65yrs	Peripheral quantitative computerised tomography (muscle density, muscle area, fat area)	Modelled continuously per 1 SD increase of each exposure	All-cause mortality	Muscle area and mortality (men and women combined): 0 Fat area and mortality (men and women combined): 0
80	Chen, et al. (2018)	China Kadoorie Biobank (2004-2008)	China, n=489301 aged 30-79yrs	BMI, body fat %, waist circumference	7 groups for each exposure, and BMI per 5kg/m^2, % body fat per 10%, waist circumference per 1 SD	Ischaemic and haemorrhagic stroke incidence	BMI and stroke/haemorrhage (men and women combined): + linear WC and stroke/haemorrhage (men and women combined): + linear Body fat % and stroke/haemorrhage (men and women combined): + linear
81	Chen et al. (2019)	Women's Health Initiative	USA, n=2,683 postmenopausal women with normal BMI	DEXA - % whole body and regional fat quartiles, fat mass index (dividing total or regional fat mass in kg by height squared)	Quartiles	CVD	Whole body fat mass and mortality: 0 (women) Leg fat and mortality: - (women) trunk fat and mortality: + (women)
82	Cheung, et al. (2016)	NHANES (1999-2004)	USA, n=2841 aged >65yrs	DEXA (Appendicular lean mass)	Calculated ALM, ALM/BMI, ALM/H^2 from DEXA. Sarcopenia defined using cut-points for each measure (given in their supplementary index).	All-cause mortality	Low appendicular lean mass and mortality: + (men and women combined)
83	Chin, et al (2013)	KNHANES (2008-2012)	South Korea, n=1578 aged >65yrs	DEXA (Appendicular skeletal muscle mass)	Sarcopenia defined as ASM/weight <1 SD below the gender-specific mean of a reference group aged 20-39 years. Equates to <32.2% men, <25.6% women.	CVD incidence	Sarcopenic and CVD (men and women combined): +

					Sarcopenic obesity if both sarcopenic and obese BMI		
84	Chuang, et al. (2014)	Elderly Nutrition and Health Survey (1999-2000)	Taiwan, n=1512 aged >65yrs	BIA (skeletal muscle mass index), BMI, waist circumference	Low/high risk groups defined as ASMI <11.45kg/m^2 (men) 8.51kg/m^2 (women) based off quartiles	All-cause mortality	Low skeletal muscle index and mortality: 0 (men) Low skeletal muscle index and mortality: + (women) Low skeletal muscle index and CVD: 0 (men) Low skeletal muscle index and CVD: + (women)
85	Chuang, et al. (2016)	Elderly Nutrition and Health Survey	Taiwan, n=1485 aged >65 yrs	BIA (skeletal muscle mass index)	Sarcopenia defined as SMMI men <11.45, women <8.51 [14] Sarcopenic obesity defined as being sarcopenic and having a high triglyceride (>150mg/dL) and high waist circumference (>90cm men, >80cm women)	All-cause and CVD mortality	Abdominal obesity and mortality: 0 (men and women combined) Abdominal obesity and CVD: 0 (men and women combined) Sarcopenic and mortality: 0 (men and women combined) Sarcopenic and CVD: 0 (men and women combined) Sarcopenic obesity and mortality: + (men and women combined) Sarcopenic obesity and CVD: + (men and women combined)
86	de Almeida Roediger, et al. (2019)	SABE (2000-2010)	Brazil, n=1504 aged >60yrs	BMI, waist circumference, wait-to-hip ratio skinfold, mid-upper arm circumference, calf circumference, arm muscle area	All exposures analysed as binary variables as either high vs low or adequate vs inadequate.	All-cause mortality	WC and mortality: 0 (men and women combined) WHR and mortality: 0 (men and women combined) MAMC (muscle) and mortality: - (men and women combined) Calf circumference (muscle) and mortality: - (men and women combined)
87	de Santana et al. (2019)	n/a	Brazil, n=839 aged >=65yrs	DEXA (total fat, appendicular lean mass)	Low lean mass, presence of visceral adipose issue	CVD mortality, all cause morality	Low muscle and CVD mortality: + (men and women combined) Low muscle and mortality: + (men and women combined) Fat mass and CVD mortality: + (men and women combined) Fat mass and mortality: + (men and women combined)
88	Dolan, et al. (2007)	Study of Osteoporotic Fractures	USA, n=8029 women aged >65	BIA (lean mass, fat mass, % body fat), BMI, waist girth	Quintiles of each exposure	All-cause mortality	Fat mass and mortality (women): U Lean mass and mortality (women): 0 BMI and mortality (women): U
89	Dong et al (2018)	NHANES III (1988-1994)	USA, n=16415) aged 18-89yrs	BIA (body fat %), WHR	Body fat % and WHR modelled continuously using cubic splines at 4 knots. Also created 9 groups to assess joint associations	All-cause mortality	Body fat % and mortality: U (men) Body fat % and mortality : U (women) WHR and mortality: U (men) WHR and mortality: + linear (women)
90	Gale, et al. (2007)	n/a	UK, n=800 aged >65yrs	Skinfolds (fat mass, fat free mass), BMI, grip strength	Modelled continuously per 1 SD increase in each exposure	All-cause and CVD mortality	Body fat % and CVD: 0 (men) Body fat % and CVD: 0 (women) Body fat % and mortality: 0 (men) Body fat % and mortality: 0 (women) MAMC (muscle) and CVD: 0 (men) MAMC (muscle) and CVD: 0 (women) Fat free mass and CVD: 0 (men) Fat free mass and CVD: 0 (women) MAMC (muscle) and mortality: 0 (men) MAMC (muscle) and mortality: 0 (women) Fat free mass and mortality: 0 (men) Fat free mass and mortality: 0 (women) Grip strength and CVD: + (men) Grip strength and CVD: 0 (women) Grip strength and mortality: + (men) Grip strength and mortality: 0 (women)
91	Gillum, et al. (2001)	NHANES I (1992)	USA, n=6936 aged 45-74yrs	BMI, Subscapular skinfold (SSF), subscapular to triceps skinfold thickness ratio (SFR)	Each exposure modelled in quartiles and results stratified by race, sex and smoking status	Stroke incidence	Trunk obesity and stroke: weak U (white men ex-smokers) Trunk obesity and stroke: 0 (women) Overall obesity and stroke: U (white men ex-smokers) Overall obesity and stroke: 0 (women)
92	Gnatiuc et al. (2019)	Mexico City cohort study	Mexico, n=159,755 aged 35 to <75	BMI, waist-to-hip ratio, waist circumference	Continuously	all-cause mortality	BMI and mortality: J (men and women cobined) WHR and mortality: + (men and women combined)

							WC and mortality: + (men and women combined)
93	Graf, et al. (2015)	n/a	Switzerland, n=3181 aged >65yrs	BIA (fat mass index, fat free mass index)	Quartiles of FMI and FFMI	All-cause mortality	Fat free mass index and mortality: 0 (women) Fat free mass index and mortality: - (men) Fat mass index and mortality: 0 (men) Fat mass index and mortality: 0 (women)
94	Han, et al. (2010)	Korean Longitudinal Study on Health and Aging	South Korea, n=877 aged >65yrs	BIA (lean mass, fat mass, fat percentage, lean mass index), BMI, waist circumference	3 groups for each exposure: <25th percentile, 25-75th percentile, >75th percentile	All-cause mortality	Lean mass and mortality: - (men and women combined) Fat mass and mortality: 0 (men and women combined)
95	Heitmann, et al. (2000)	n/a	Sweden, n=787 men aged 60yrs	Whole body potassium counter (lean body mass and fat mass calculated)	Quintiles, fractional polynomials	All-cause mortality	Fat free mass and mortality: reverse J (men) Fat mass and mortality: J (men) BMI and mortality: U (men)
96	Hirani, et al. (2017)	Concord Health and Aging in Men Project (2005-2013)	Australia, n=1666 men aged >70yrs	DEXA (Appendicular lean mass, fat %)	Low lean mass defined as ALM:BMI ratio <0.789 [6], Obesity defined as fat % > 30% [7]. 4 groups created: neither obese nor low muscle, obese only, low muscle only, sarcopenic obesity	Frailty, disability, institutionalisation and mortality	Obesity and mortality (men): 0 Low muscle and mortality (men): 0 Sarcopenic obesity and mortality (men): 0
97	Hotchkiss, et al. (2013)	Scottish Health Survey	Scotland, n=9329 aged 18-86yrs	BMI, Waist circumference, waist to hip ratio	Quartiles of WC and WHR. BMI groups (WHO classification)	All-cause mortality, CVD incidence and mortality	Adiposity and incident CHD: + (men) Adiposity and incident CHD: + (women) Adiposity and mortality: + (men) Adiposity and mortality: + (women) Adiposity and CHD mortality: 0 (men) Adiposity and CHD mortality: 0 (women)
98	Howell, et al. (2018)	NHANES III and NHANES (1999-2010)	USA, n=5849 Mexican Americans aged >20yrs	BIA (lean mass, fat mass, body fat %), waist circumference, waist-to-height ratio, skinfolds	Modelled continuously: BMI per 5kg/m^2, WC per 5cm, Waist to height ratioper 0.5, skinfolds per 5mm, % body fat per 5%, lean mass per 5kg, fat mass per 5kg	All-cause and CVD mortality	Fat mass and CVD mortality: - (men) Fat mass and CVD mortality: + (women) Fat mass and mortality: 0 (men) Fat mass and mortality: + (women) Lean mass and CVD mortality: 0 (men) Lean mass and CVD mortality: + (women) Lean mass and mortality: 0 (men) Lean mass and mortality: - (women)
9	Iliodromiti, et al. (2018)	UK Biobank (2006-2010)	UK, n=296535 aged 40-69yrs	BMI, waist-circumference, waist-to-hip ratio, BIA (body fat %)	All exposures treated as continuous variables (BMI 22kg/m^2 was referent value)	CVD incidence	BMI and CVD: J (men and women combined) WC and CVD: + linear (men and women combined) WHR and CVD: + linear (men and women combined) Body fat % and CVD: + linear (men and women combined)
99	Kahn, et al. (2012)	NHANES III (1988-1994)	USA, n=11437 aged 18-64 yrs	BMI, waist circumference, waist-to-hip ratio, waist-to-height ratio	Modelled continuously per 1 SD increase in each exposure and also in quartiles	All-cause mortality	WC and all-cause mortality: + (men) WC and all-cause mortality: + (women) WHR and all-cause mortality: + (men) WHR and all-cause mortality: + (women) Waist-to-height ratio and all-cause mortality: + (men) Waist-to-height ratio and all-cause mortality: + (women)
100	Katzmarzyk, et al. (2002)	Canada Fitness Survey	Canada, n=10323 aged 20-69yrs	Waist circumference, skinfolds principal component of skinfold residuals (indicates subcutaneous adipose tissue distribution)	Modelled each exposure continuously using polynomial models	All-cause mortality	WC and all-cause mortality: J (men) WC and all-cause mortality: linear + (women) Skinfolds (adiposity) and mortality: J (men), Skinfolds (adiposity) and mortality: linear + (women) BMI and mortality: J (men) BMI and mortality: linear + (women)
101	Kim, et al. (2017)	UK Biobank (2006-2010)	UK, n=403199 aged 40-69 yrs	Grip strength, BMI, waist circumference, % body fat	Per 5kg increase in GS, quintiles of GS within BMI/%body fat/waist circumference categories	All-cause and CVD mortality	Grip strength and all-cause mortality: linear – (men) Grip strength and all-cause mortality: linear – (women) Grip strength and CVD mortality: linear – (men) Grip strength and CVD mortality: linear – (women)

102	Kizer, et al. (2011)	Cardiovascular Health Study	USA, n=3754 aged 65-100yrs	BIA (fat free mass, fat mass) BMI, waist circumference, waist to hip ratio, waist to height ratio	Quintiles	Ischemic stroke incidence, CHD	Fat mass and stroke or CHD: 0 (men) Fat mass and stroke or CHD: 0 (women) Fat free mass and stroke or CHD: 0 (men) Fat free mass and stroke or CHD: 0 (women) WC and stroke: 0 (men) WC and stroke: 0 (women) WHR and stroke: 0 WC and CHD: + WHR and CHD: +
103	Kouvari et al. (2019)	ATTICA and GREECS	Greece, n=10428	Lean mass index and fat mass index created through total body lean and fat mass (indirectly calculated through population formals based on body weight, height, waist circumference) divided by height squared	Tertiles	CVD	Fat mass and CVD: + (men) Fat mass and CVD: + (women) Lean mass and CVD: U (men) Lean mass and CVD: U (women)
54	Lee et al (2018)	Health Professionals Follow-up Study (1987-2012)	USA, n=38006 men aged 40-75 years	Derived predicted lean body mass and fat mass using equations developed by NHANES and based on age, race, height, weight, waist circumference	Quintiles of predicted lean body mass and fat mass	All-cause and cause-specific (CVD, cancer, respiratory, other) mortality	BMI & all-cause mortality: J (men) Fat mass & all-cause mortality: linear (men) Lean mass & all-cause mortality: U (men) Fat & CVD: linear (men) Lean body mass & CVD: weak U (men) BMI & CVD: U (men)
104	Lee, et al. (2012)	n/a	China, n=3978 aged >65yrs	DEXA (body fat %), waist circumference, waist to hip ratio, relative abdominal fat (abdominal fat/whole body fat)	Quintiles	All-cause and CVD mortality	All-cause mortality and % body fat: - (men) All-cause mortality and % body fat: 0 (women) All-cause mortality and waist circumference: 0 (men) All-cause mortality and waist circumference: 0 (women) All-cause mortality and WHR: 0 (men) All-cause mortality and WHR: 0 (women) CVD mortality and WC: 0 (men) CVD mortality and WC: 0 (women) CVD mortality and % body fat: 0 (men) CVD mortality and % body fat: 0 (women) CVD mortality and WHR: 0 (men) CVD mortality and WHR: 0 (women)
105	Levitan, et al. (2009)	Swedish Mammography Cohort and the Cohort of Swedish Men	Sweden, n=80360 aged 45-79yrs	BMI, waist circumference, waist to hip ratio, waist to height ratio	Continuously (per 1 IQR increase in each exposure)	Heart failure hospitalisation or mortality	WC and CVD: linear + (men) WC and CVD: linear + (women) WHR and CVD: + (men) WHR and CVD: 0 (women) Waist-to-height ratio and CVD: + linear (men) Waist-to-height ratio and CVD: + linear (women)
106	Li, et al. (2018)	NHANES (1999-2002)	USA, n=4449 aged >50 yrs	DEXA (Appendicular lean mass)	Low muscle mass defined as appendicular lean mass (ALM) <19.75kg (M) or <15.02kg (F) and ALM/BMI <0.512 (M) and <0.789kg (F). Based on FNISH Sarcopenia Project definition [1]. Low muscle strength	All-cause mortality	Low muscle alone and mortality: 0 (men and women combined) Low muscle with low strength and mortality: + (men and women combined)
107	Myint, et al. (2014)	EPIC-Norfolk (1997-2000)	UK, n=15062 aged 40-79yrs	BIA (body fat %)	Quartiles of body fat %	All-cause mortality and CVD incidence	Body fat % and mortality: 0 (men) Body fat % and mortality: 0 (women) Body fat % and CVD: 0 (men) Body fat % and CVD: 0 (women)

108	Nalini et al. (2019)	Golestan Cohort Study	Iran, n=50,045 aged 40-75	BMI, waist circumference, waist to hip ratio, waist to height ratio	Quintiles	All cause and CVD mortality	BMI and all-cause mortality: 0 (men) BMI and all-cause mortality: 0 (women) BMI and CVD mortality: + (men) BMI and CVD mortality: + (women) Waist to height ratioand mortality: + (men) Waist to height ratioand mortality: + (women) Waist to height ratioand CVD mortality: + (men) Waist to height ratioand CVD mortality: + (women) WC and mortality: 0 (men) WC and mortality 0 (women) WC and CVD mortality: + (men) WC and CVD mortality: + (women) WHR and mortality: + (men) WHR And mortality: + (women) WHR and CVD mortality: + (men) WHR and CVD mortality: + (women)
109	Newman, et al. (2006)	Health, Aging and Body Composition study	USA, n=29292 aged 70-79yrs	DEXA (leg and arm lean mass), CT scan (thigh muscle area), knee extension strength	Per 1 SD increase	All-cause mortality	Arm or leg lean mass and mortality: 0 (men and women combined) Grip strength and mortality: + (men and women combined)
110	Ofstad et al (2019)	HUNT 2	Norway, n=61,016	BMI, WC, WHR, estimated total body fat (based on the YMCA's gender specific formulas), ABSI	Quartiles	CVD mortality	Body fat (estimated) and CVD mortality: + (men) Body fat (estimated) and CVD mortality: + (women) WC and CVD mortality: + (men) WC and CVD mortality: + (women) BMI and CVD mortality: +
48	Ortega, et al. (2016)	Aerobics Centre Longitudinal Study (1979-2003)	USA, n=60335 aged >20 years	BMI, body fat % determined by hydrostatic weighing or skinfold measurements, fat mass index, fat free mass index, fat free mass	For each exposure: very low <5th percentile, low 5-15th percentile, middle 15th-85th percentile, high 85-95th percentile, very high >95th	CVD mortality	BMI and CVD: + linear (men and women combined) Body fat % and CVD: J (men and women combined) Fat mass index and CVD: J (men and women combined) Fat free mass and CVD: 0 (men and women combined) Fat free mass index and CVD: + (men and women combined)
111	Otsuka, et al (2018)	Longitudinal Study of Aging (1997-2013)	Japan, n=1978 aged 40-79 yrs	DEXA (Appendicular lean mass excluding bones [4])	ALM/leg length, ALM/height, ALM/height^2, ALM/weight*100, ALM/BMI*10	All-cause mortality or disability	Lean mass and mortality: 0 (men) Lean mass and mortality: 0 (women)
112	Padwal, et al. (2016)	Population Health Research Data Repository	Canada, n=54420 aged >40yrs (91% women)	DEXA (body fat %), BMI	Quintiles of BMI and body fat %. Fully adjusted models included both BMI and body fat %	All-cause mortality	BMI and mortality: U (men) BMI and mortality: U (women) Body fat % and mortality: J (men) Body fat % and mortality: reverse J (women)
113	Park, et al. (2014)	KNHANES (2008-2012)	South Korea, n=7208 aged >50yrs	DEXA (ASM, SMI)	SMI normal >32% (men) >25.4% (women), class I sarcopenia 29-32% (men) 22.8-25.4% (women), class II sarcopenia <29% (men) <22.8% (women) - corresponded to 1 and 2 SDs below gender-specific means of younger population [18]	CVD incidence	Sarcopenia and CVD (men): + Sarcopenia and CVD (women): 0
114	Park, et al. (2018)	Korean National Health Insurance Cohort (2008-2013)	South Korea, n=465,629 adults	Weight-adjusted-waist index, waist circumference (WC), BMI, waist-to-height	10 groups of each index	All-cause and CVD mortality	BMI and all-cause mortality: U (men and women combined) WC and all-cause mortality: U (men and women combined) WHR and all-cause mortality: U (men and women combined)

				ratio (WHR), a body shape index (ABSI)			Weight-adjusted-waist index and all-cause mortality: U (men and women combined) ABSI and all-cause mortality: U (men and women combined) Weight-adjusted-waist index and CVD mortality: linear + (men and women combined) A Body Shape Index and CVD mortality: linear + (men and women combined) BMI and CVD: inverse J (men and women combined) WC and CVD: inverse J (men and women combined) WHR and CVD: inverse J (men and women combined)
115	Reis, et al. (2009)	NHANES III (1988-1994)	USA, n=12,228 aged 30-102ys	Waist-to-thigh ratio, waist-to-hip ratio, waist circumference, BMI	BMI categories, quintiles of WC, WHR and waist-to-thigh ratio	All-cause mortality	WHR and mortality: linear + (men) WHR and mortality: 0 (women) Waist-to-height ratio and mortality: + linear (men) Waist-to-height ratio and mortality: + (women) BMI and mortality: U (men) BMI and mortality: U (women) WC and mortality: J (women) WC and mortality: J (men)
116	Reis, et al. (2009)	NHANES III (1988-1994)	USA, n=5,780 aged 30-64yrs	BMI, waist circumference, waist to hip ratio, waist to thigh ratio	Quartiles of each exposure, results stratified by sex and race (white/black)	All-cause mortality	BMI and all-cause mortality: 0 (men) BMI and all-cause mortality: 0 (women) WHR and all-cause mortality: linear + (women) WHR and all-cause mortality: 0 (men) Waist-to-thigh ratio and all-cause mortality: linear + (men) Waist-to-thigh ratio and all-cause mortality: linear + (women) WC and all-cause mortality: 0 (men) WC and all-cause mortality: 0 (women)
117	Rexrode, et al. (2001)	Physicians Health Study	USA, n=16,164 men aged 40-84yrs	Waist circumference, waist to hip ratio, BMI	Quintiles of each exposure	CHD	WC and CVD: linear + (men) WHR and CVD: + linear (men) BMI and CVD: + linear (men)
118	Sim et al (2019)	Perth Longitudinal Study in Aging women	Australia, n=903 older women	DEXA (appendicular lean mass), BMI, grip strength, timed up and go	Various definitions of sarcopenia. Foundation of National Institues of Health (FNIH), European Working Group on Sarcopenia in Older People (EWGSOP), and the adapted FNIH (AUS-POPF) using Australian population-specific cut points (<2 standard deviation below mean of young healthy)	All cause mortality	Lean mass and mortality: 0 (women)
119	Simpson, et al. (2007)	Melbourne Collaborative Cohort Study	Australia, n=41313 aged 27-75yrs	BIA (fat mass, body fat %), BMI, waist circumference, waist to hip ratio	Quintiles	All-cause mortality	BMI and all-cause mortality: U (men) BMI and all-cause mortality: U (women) WC and all-cause mortality: linear + (men) WC and all-cause mortality: linear + (women) WHR and all-cause mortality: linear + (men) WHR and all-cause mortality: linear + (women) Fat mass and all-cause mortality: linear + (men) Fat mass and all-cause mortality: 0 (women) Body fat % and all-cause mortality: linear + (men) Body fat % and all-cause mortality: 0 (women)
46	Spahilari, et al. (2016)	Cardiovascular Health Study	USA, n=1355 aged >65yrs	DEXA (Total, appendicular lean and fat mass)	ALM, fat mass and lean principal components modelled linearly. Fat principal components modelled in quartiles	All-cause, CVD and non-CVD mortality	Appendicular lean mass and CVD: linear – (men and women combined) Appendicular lean mass and mortality: linear - (men and women combined) Fat mass and CVD: linear - (men and women combined) Fat mass and mortality: linear - (men and women combined)

47	Srikanthan, et al. (2014)	NHANES III (1988-1994)	USA, n=3659 men aged >55 and women aged >65yrs	BIA (SMI), non-muscle index (BMI - SMI)	Quartiles of SMI	All-cause mortality	Skeletal muscle index and mortality: weak – (men and women combined)
120	Srikanthan, et al. (2016)	NHANES (1999-2004)	USA, n=6541 aged >20yrs	DEXA (Appendicular skeletal muscle mass index, trunk fat mass index)	4 groups: Low muscle/low fat (ASMI<median, TRFI<median), Low muscle/high fat (ASMI<median, TRFI>=median), High muscle/low fat (ASMI>=median, TRFI<median), high muscle. High fat (ASMI>=median, TRFI>=median)	All-cause and CVD mortality	High muscle/low fat and CVD: - (men and women combined) High muscle/low fat and mortality: - (men and women combined) All other body composition groups and mortality: 0 (men and women combined) All other body composition group and CVD: 0 (men and women combined)
121	Stefan, et al. (2008)	Cooper Centre Longitudinal study (1970-2005)	USA, n=11335 women	BMI, skinfolds (% body fat), waist circumference, waist to height ratio, waist to hip ratio	Categorised as high or normal for each exposure. Cut-offs: Body fat 30%, Waist to hip ratio 0.75, waist to height ratio 0.5	All-cause mortality	Body fat % and all-cause mortality (women): 0 WC and all-cause mortality (women): 0 WHR and all-cause mortality (women): 0 Waist-to-height ratio and all-cause mortality (women): 0 BMI and all-cause mortality (women): 0
122	Sui, et al. (2007)	Aerobics Centre Longitudinal Study (1979-2001)	USA, n=2603 aged >60yrs	Hydrostatic weighing or skinfolds (% body fat, fat mass, fat free mass), waist circumference, BMI	BMI categories, WC categorised as abdominal obese if >88cm (men) or >102cm (women), % Body fat % categorised as obese if >25% (men), >30% (women), quintiles of FFM	All-cause mortality	WC and all-cause mortality: 0 (men and women combined) Body fat % and all-cause mortality: 0 (men and women combined) Fat free mass and all-cause mortality: + (men and women combined)
123	Tanne, et al. (2005)	Israeli Ischemic Heart Disease project	Israel, n=9151 men aged >23 ys	BMI, Subscapular skinfold (SSF), subscapular to triceps skinfold thickness ratio (SFR)	Exposures analysed per 1 SD increase	Stroke and CHD mortality	Trunk obesity and CVD mortality (men): 0 Body fat distribution and CHD (men): + linear Body fat distribution and stroke (men): 0
124	The DECODE Study Group (2008)	DECODE study	Europe, n=15521 aged 30-89yrs	Waist circumference	Abdominal obesity defined as waist circumference >94cm (men) or >80cm (women)	CVD mortality	WC and CVD mortality (men and women combined): 0
125	Thomson, et al. (2016)	Women's Health Initiative Observational Study	USA, n=77505 women	BMI, a body shape index, body adiposity index	Quintiles of ABSI and WC, BMI groups	All-cause mortality	A Body Shape Index and CVD: linear + (women) BMI and CVD: U (women) Body adiposity index and CVD: U (women)
126	Toss, et al. (2012)	n/a	Sweden, n=921 aged >65yrs	DEXA (fat and lean mass)	Assessed continuously per kg	All-cause mortality	Lean mass and mortality: linear - (men) Lean mass and mortality: linear - (women) Fat mass and mortality: linear - (women) Fat mass and mortality: 0 (men)
127	Van Aller et al (2018)	NHANES (1999-2004)	USA, n=3577 aged >=50yrs	DEXA	Body composition phenotype (4 categories based on having low adiposity or high adiposity and low muscle mass or high muscle mass), Trunk FM/ASM ratio, Fat mass/fat free mass ratio. Then defined sarcopenic obese from cut-offs at various percentiles for each of these measures	All cause mortality	Sarcopenic obesity and mortality: + (men) aged 50 - 70 yr Sarcopenic obesity and mortality: + (women) aged 50 - 70 yr Sarcopenic obesity and mortality: 0 (men) aged > 70 yr Sarcopenic obesity and mortality: 0 (women) aged >70 yr
128	Wang, et al. (2013)	Kailuan study	China, n=94733 aged 18-98yrs	BMI, waist circumference, waist-to-hip ratio, waist-to-height ratio	Quintiles	Total stroke, ischemic stroke, haemorrhagic stroke	WC and total stroke: + linear (men and women combined) WHR and total stroke: + linear (men and women combined) Waist-to-height ratio and total stroke: + linear (men and women combined)
129	Wannamethee, et al. (2007)	British Regional Heart Study (1998-2000)	UK, n=4107 men aged 60-79	Mid-upper arm circumference, mid arm muscle circumference, BMI, BIA (Fat mass index, fat free mass index)	Quartiles of each exposure	All-cause mortality	Fat mass and mortality: 0 (men) Fat free mass and mortality: 0 (men) MAMC (muscle) and mortality: - linear (men)

130	Wannamethee, et al. (2014)	British Regional Heart Study (1998-2000)	UK, n=4046 men aged 60-79yrs	Mid-upper arm circumference, mid arm muscle circumference, BMI	Tertiles of MAMC, and results stratified by prior CVD condition (none, coronary heart disease, heart failure)	All-cause mortality	MAMC (muscle) and CHD (men): linear - MAMC (muscle) and heart failure (men): 0
131	Yang, et al. (2019)	n/a	China, n=329 aged >=70yrs from 4 nursing homes	SARC-F and SARC-CalF questionnaires to screen for sarcopenia.	Score of >= 4 (SARC-F) or >=11 (SARC-CalF) indicate sarcopenia	All-cause mortality	Sarcopenia and mortality: + (men and women combined)
132	Yuki, et al. (2017)	Longitudinal Study of Aging (1997-2013)	Japan, n=700 aged 65-79yrs	DEXA (skeletal muscle mass index), grip strength, gait speed	Low muscle mass defined as SMI <7.0 (men), <5.4 (women) [15]. Low grip strength defined as <26kg (men) <18kg (women) [15]. Low gait speed defined as <0.8m/s [15]. Sarcopenia if low SMI and one of low grip strength or low gait speed	All-cause mortality	Sarcopenia and mortality: + (men) Sarcopenia and mortality: 0 (women)
133	Zaslavsky, et al. (2017)	Women's Health Initiative Observational Study (1993-1998)	USA, n=876 frail women aged >65	DEXA (Appendicular, central and total lean and fat mass)	Quartiles of each measurement	All-cause mortality	Lean mass & mortality: 0 (women) Fat mass & mortality: linear - (women)
134	Zhang, et al. (2007)	Shanghai Women's Health Study (1996-2000)	China, n=72773 women aged 40-70yrs	Waist to hip ratio	Quintiles	All-cause and CVD mortality	WHR and mortality: linear + (women) WHR and CVD mortality: linear + (women)
135	Zhu, et al. (2003)	NHANES I & II	USA, n=13369 women aged 25-75yrs	Skinfolds (fat mass, fat free mass)	All exposures analysed as continuous	All-cause mortality	BMI and mortality (women): U Fat free mass and mortality (women): linear - Fat mass and mortality (women): linear -
136	Zong, et al. (2016)	NHANES (1996-2006)	USA, n=9471 aged >20yrs	DEXA (body fat % for whole-body, trunk, leg)	Quartiles of each measure of FM%	All-cause and CVD mortality	Body fat % and CVD: U (men and women combined) Body fat % and all-cause mortality: U (men and women combined)

Acronyms: ABSI: A body shape index; ASMI: Appendicular skeletal muscle mass index (appendicular skeletal muscle mass, kg/height^2, m^2); BAI: Body adiposity index; BIA: bioimpedance analysis; BFMI: Body fat mass index (= fat mass index); BMI: Body mass index (body mass, kg/ height^2, m^2); DEXA: Dual energy x-ray absorptiometry; FFM: Fat free mass; FFMI: Fat free mass index (fat free mass, kg/ height^2, m^2); FM: Fat mass; FMI: Fat mass index (fat mass, kg/ height^2, m^2); GS: Grip strength; KNHANES: Korea National Health and Nutrition Examination Survey; NHANES: National Health and Nutrition Examination Survey; SMI: Skeletal muscle mass index (Skeletal muscle mass of whole body, kg/height^2, m^2)

Table S3. Derivation of variables used in analysis from the UK Biobank questionnaire and interviews.

Covariate	Categories used in analysis	UK Biobank variable used (question ID) and source
Body composition variables (exposures)		
Appendicular skeletal muscle mass (aSMM)	Quintiles of the residuals from the model of aSMM regressed on height	Arm predicted mass (left) (UKBBID: 23126) ‡, arm predicted mass (right) (UKBBID: 23122) ‡, leg predicted mass (left) (UKBBID: 23118)‡, leg predicted mass (right) (UKBBID: 23114). Height (UKBBID: 12144) ‡.
Fat mass (FM)	Quintiles	Whole body fat mass (UKBBID: 23100)‡
Body composition groups	1. Low aSMM / low FM 2. Low aSMM / moderate FM 3. Low aSMM / high FM 4. Moderate aSMM / low FM 5. Moderate aSMM / moderate FM 6. Moderate aSMM / high FM 7. High aSMM / low FM 8. High aSMM / moderate FM 9. High aSMM / high FM	Tertiles of aSMM within tertiles of FM derived from: arm predicted mass (left) (UKBBID: 23126) ‡, arm predicted mass (right) (UKBBID: 23122) ‡, leg predicted mass (left) (UKBBID: 23118)‡, leg predicted mass (right) (UKBBID: 23114), Whole body fat mass (UKBBID: 23100)‡, Height (UKBBID: 12144) ‡. Low aSMM, residuals of aSMM regressed on height: -10.82 - ≤-0.97 (men), -5.88 - ≤ -0.57 (women) Moderate aSMM: residuals of aSMM regressed on height: -0.97- ≤ 0.85 (men), -0.57 - ≤ 0.45 (women) High aSMM: residuals of aSMM regressed on height: 0.85 - ≤ 14.50 (men), 0.46 - ≤ 11.99 (women) Low FM, kg: 5.0 - ≤ 18.1 (men), 5.0 - ≤ 21.4 (women) Moderate FM: 18.2 - ≤ 24.1 (men), 21.5 - ≤ 28.8 (women) High FM: 24.2 - ≤ 98.6 (men), 28.9 - ≤ 109.8 (women)
BMI	Continuous (kg/m^2)	Body mass index (UKBBID: 21001)‡
Waist circumference	Continuous (cm)	Waist circumference (UKBBID: 48)‡
Grip strength	Continuous (kg)	Hand grip strength (left) (UKBBID: 46)‡, Hand grip strength (right) (UKBBID: 47)‡
Sociodemographic characteristics		
Sex	Men Women	Sex (UKBBID: 31)*
Education	Higher degree (college or university degree, or professional qualifications) Any school degree (A levels, AS levels, O levels, GCSEs or CSEs) Vocational qualifications (NVQ, HND or HNC) Other (none of the above qualifications)	Qualifications (UKBBID: 6138)†
Townsend index	Quintiles (high index indicates most deprivation)	Townsend index (UKBBID: 189)*
Lifestyle factors		
Smoking status	Never Current Previous	Smoking status (UKBBID: 20116)†
Alcohol intake	None Occasional (<1 unit/week) Moderate (1-14 units/week) Heavy (>14 units/week)	Alcohol intake frequency (UKBBID: 1558)† Depending on the participants' response, they were asked how much they consumed per week or month of the following alcoholic drinks:

		Red wine (UKBBID: 4407, 1568)†; champagne and white wine (UKBBID: 4418, 1578)†; beer and cider (UKBBID: 4429, 1588)†; spirits (UKBBID: 4440, 1598)†; fortified wine (UKBBID: 4451, 1608)†; other (UKBBID: 4462, 5364)†.
Saturated fat score	None Low Medium High Unknown	Beef intake (UKBBID: 1369)†, cheese intake (UKBBID: 1408)†, pork intake (UKBBID: 1389)†, lamb intake (UKBBID: 1379)†, processed meat intake (UKBBID: 1349), spread type (UKBBID: 1428)† The amount of each food eaten per week was totalled, then split into groups based off tertiles (with 'none' subsequently separated from the low category).
Fruit and vegetable score	None Low Medium High Unknown	Fresh fruit intake (UKBBID: 1309)†, raw vegetable intake (UKBBID: 1299)†, cooked vegetable intake (UKBBID: 1289). The amount of each food eaten per week was totalled, then split into groups based off tertiles (with 'none' subsequently separated from the low category).
Oily fish score	Unknown None Low Medium High	Oily fish intake (UKBBID: 1329)† The amount of oily fish per week was split into groups based off tertiles (with 'none' subsequently separated from the low category).
Physical activity (IPAQ MET scores)	Low Moderate High	Number of days/week of vigorous physical activity 10+ minutes (UKBBID: 904)†; Duration of vigorous activity (UKBBID: 914)† Number of days/week of moderate physical activity 10+ minutes (UKBBID: 884)†; Duration of moderate activity (UKBBID: 894)† Number of days/week walked 10+ minutes (UKBBID: 864)†; Duration of walks (UKBBID: 874)†
Medical history		
Type 2 diabetes	No Yes (if diagnosed by doctor or taking insulin for diabetes)	Diabetes diagnosed by doctor (UKBBID: 2443)† Medication for cholesterol, blood pressure or diabetes (men) (UKBBID: 6177)†; Medication for cholesterol, blood pressure, diabetes, or take exogenous hormones (women) (UKBBID: 6153)†
Hypertension	No Yes (if diagnosed by doctor, had an SBP >140mmHg, DBP >90mmHg or taking medication for blood pressure)	Vascular/heart problems diagnosed by doctor (high blood pressure is one response) (UKBBID: 6150)† Systolic blood pressure, automated reading / manual reading (UKBBID: 4080 / 93)‡ Diastolic blood pressure, automated reading / manual reading (UKBBID: 4079 / 94)‡ Medication for cholesterol, blood pressure or diabetes (men) (UKBBID: 6177)†; Medication for cholesterol, blood pressure, diabetes, or take exogenous hormones (women) (UKBBID: 6153)†
Cholesterol	No Yes (if taking cholesterol-lowering medication)	Medication for cholesterol, blood pressure or diabetes (men) (UKBBID: 6177)†; Medication for cholesterol, blood pressure, diabetes, or take exogenous hormones (women) (UKBBID: 6153)†; blood lipids (UKBBID: 30690,30760,30870)
Prior cancer	No Yes (if cancer had been previously diagnosed by a doctor)	Cancer diagnosed by doctor (UKBBID: 2453)†
Menopause	No Yes (if responded to questions saying they have experienced the menopause)	Had menopause (women only) (UKBBID 2724)†

*Recruitment questions
†Touchscreen questions
‡Physical measurements

Table S4. Baseline characteristics of the study population according to appendicular skeletal muscle mass and fat mass quintiles.

	Men appendicular skeletal muscle mass (aSMM) quintiles, range (kg)					Men fat mass (FM) quintiles, range (kg)					Total
	13.5 - ≤ 24.0	24.1 - ≤ 26.0	26.1 - ≤ 27.6	27.7 - ≤ 30.0	30.1 - ≤ 54.5	5.0 - ≤ 15.7	15.8 - ≤ 19.4	19.5 - ≤ 22.9	23.0 - ≤ 27.5	27.6 - ≤ 98.6	
Age at recruitment, mean (SD)	61.0 (6.4)	58.2 (7.4)	56.0 (7.8)	54.0 (7.9)	51.7 (7.8)	54.9 (8.3)	56.0 (8.2)	56.5 (8.1)	56.7 (8.0)	56.9 (7.8)	56.2 (8.1)
aSMM (kg), mean (SD)	24.6 (2.9)	25.9 (2.8)	26.9 (2.9)	28.1 (3.0)	30.5 (3.6)	24.6 (2.7)	25.7 (2.7)	26.7 (2.7)	28.0 (2.8)	31.0 (3.6)	27.2 (3.7)
FM (kg), mean (SD)	22.4 (7.1)	21.6 (7.2)	21.4 (7.4)	21.5 (7.8)	22.2 (9.2)	12.4 (2.4)	17.5 (1.1)	21.0 (1.0)	24.9 (1.3)	33.6 (6.2)	21.8 (7.8)
Body mass index (BMI), mean (SD)	26.0 (3.5)	26.8 (3.5)	27.4 (3.6)	28.2 (3.8)	29.7 (4.4)	23.3 (1.8)	25.6 (1.6)	27.1 (1.6)	29.0 (1.8)	33.1 (3.5)	27.6 (4.0)
Weight (kg), mean (SD)	81.1 (12.1)	83.0 (12.1)	84.9 (12.4)	87.3 (13.0)	92.6 (15.1)	71.7 (7.0)	78.7 (6.3)	84.0 (6.2)	90.3 (6.5)	104.3 (11.8)	85.8 (13.6)
Height (cm), mean (SD)	176.6 (6.7)	175.9 (6.7)	175.8 (6.7)	176.0 (6.7)	176.6 (6.7)	175.3 (6.8)	175.5 (6.6)	176.0 (6.5)	176.6 (6.6)	177.6 (6.7)	176.2 (6.7)
Higher education, n (%)	12740 (39.7)	13085 (40.7)	13140 (40.9)	13096 (40.7)	12645 (39.3)	13909 (43.1)	13669 (42.1)	12987 (40.6)	12406 (38.8)	11735 (36.7)	64706 (40.2)
Current smokers, n (%)	3714 (11.6)	3431 (10.7)	3573 (11.1)	3563 (11.1)	3724 (11.6)	4366 (13.5)	3600 (11.1)	3368 (10.5)	3385 (10.6)	3286 (10.3)	18005 (11.2)
Low fruit and vegetable intake, n (%)	14779 (46.0)	14122 (43.9)	13977 (43.5)	13996 (43.5)	13367 (41.6)	13624 (42.2)	13909 (42.8)	14191 (44.3)	14168 (44.3)	14349 (44.8)	70241 (43.7)
High saturated intake, n (%)	11706 (36.4)	11786 (36.6)	11647 (36.2)	11637 (36.2)	11778 (36.6)	10457 (32.4)	11354 (34.9)	11699 (36.6)	12111 (37.9)	12933 (40.4)	58554 (36.4)
Low oily fish intake, n (%)	10919 (34.0)	11292 (35.1)	11342 (35.3)	11807 (36.7)	11988 (37.3)	11197 (34.7)	11452 (35.2)	11518 (36.0)	11520 (36.0)	11661 (36.4)	57348 (35.7)
Heavy drinkers, n (%)	19948 (62.1)	19885 (61.8)	19841 (61.7)	19608 (61.0)	18666 (58.1)	17562 (54.4)	19859 (61.1)	20297 (63.4)	20535 (64.2)	19695 (61.5)	97948 (60.9)
Low physical activity, n (%)	7247 (22.6)	6670 (20.7)	6300 (19.6)	5901 (18.3)	5518 (17.2)	4580 (14.2)	5351 (16.5)	6030 (18.8)	6918 (21.6)	8757 (27.4)	31636 (19.7)
Hypertension, n (%)	20146 (62.7)	18878 (58.7)	18102 (56.3)	17362 (54.0)	17370 (54.0)	12683 (39.3)	16508 (50.8)	18523 (57.9)	20600 (64.4)	23544 (73.5)	91858 (57.1)
Type 2 diabetes, n (%)	1300 (4.1)	1250 (3.9)	1156 (3.6)	1191 (3.7)	1408 (4.4)	388 (1.2)	666 (2.1)	906 (2.8)	1462 (4.6)	2883 (9.0)	6305 (3.9)
Cancer history (>5 years ago), n (%)	1176 (3.7)	927 (2.9)	816 (2.5)	662 (2.1)	652 (2.0)	780 (2.4)	836 (2.6)	856 (2.7)	872 (2.7)	889 (2.8)	4233 (2.6)
Cholesterol medication, n (%)	6204 (19.5)	5171 (16.2)	4646 (14.6)	4145 (13.0)	3842 (12.0)	2175 (6.8)	3807 (11.8)	4664 (14.7)	5922 (18.6)	7440 (23.4)	24008 (15.0)
	Women appendicular skeletal muscle mass (aSMM) quintiles, range (kg)					**Women fat mass (FM) quintiles, range (kg)**					**Total**
	10.3 - ≤ 16.5	16.6 - ≤ 17.5	17.6 - ≤ 18.6	18.6 - ≤ 19.9	20.0 - ≤ 39.2	5.0 - ≤ 18.5	18.6 - ≤ 22.8	22.9 - ≤ 27.1	27.2 - ≤ 33.3	33.4 - ≤ 109.8	
Age at recruitment, mean (SD)	58.9 (7.0)	57.1 (7.6)	55.8 (7.9)	54.6 (8.0)	53.2 (8.1)	54.1 (8.1)	55.7 (8.0)	56.6 (7.9)	57.0 (7.7)	56.4 (7.8)	55.9 (8.0)
aSMM (kg), mean (SD)	17.0 (1.7)	17.5 (1.7)	18.0 (1.8)	18.7 (1.9)	20.3 (2.5)	16.6 (1.5)	17.3 (1.4)	17.9 (1.4)	18.8 (1.5)	21.1 (2.3)	18.3 (2.3)
FM (kg), mean (SD)	27.7 (8.5)	26.0 (8.4)	25.5 (8.8)	25.3 (9.5)	27.0 (11.9)	15.2 (2.6)	20.7 (1.2)	24.9 (1.3)	29.9 (1.7)	41.1 (7.4)	26.3 (9.6)
Body mass index (BMI), mean (SD)	25.9 (4.2)	26.0 (4.2)	26.3 (4.4)	26.8 (4.8)	28.5 (6.0)	21.6 (1.7)	24.0 (1.5)	25.9 (1.7)	28.3 (2.0)	33.9 (4.3)	26.7 (4.9)
Weight (kg), mean (SD)	69.1 (11.6)	68.8 (11.6)	69.4 (12.1)	70.8 (12.9)	75.9 (16.3)	56.4 (4.7)	63.2 (3.7)	68.5 (3.7)	75.3 (4.2)	90.9 (11.1)	70.8 (13.3)
Height (cm), mean (SD)	163.4 (6.2)	162.6 (6.1)	162.5 (6.2)	162.6 (6.2)	163.3 (6.2)	161.6 (6.1)	162.5 (6.1)	162.9 (6.1)	163.3 (6.1)	164.0 (6.2)	162.9 (6.2)
Higher education, n (%)	14330 (36.6)	15246 (38.9)	16033 (40.9)	16513 (42.2)	17056 (43.6)	18112 (45.5)	16503 (42.6)	15834 (39.8)	14520 (37.7)	14209 (36.4)	79178 (40.4)
Current smokers, n (%)	3039 (7.8)	3164 (8.1)	3231 (8.2)	3258 (8.3)	3377 (8.6)	3792 (9.5)	3166 (8.2)	3151 (7.9)	3062 (8.0)	2898 (7.4)	16069 (8.2)
Low fruit and vegetable intake, n (%)	12608 (32.2)	12333 (31.5)	11874 (30.3)	11521 (29.4)	10910 (27.9)	12125 (30.5)	11518 (29.7)	11756 (29.6)	11613 (30.2)	12234 (31.3)	59246 (30.3)
High saturated intake, n (%)	11699 (29.9)	11407 (29.1)	11252 (28.7)	11485 (29.3)	11212 (28.6)	10415 (26.2)	10824 (27.9)	11615 (29.2)	11762 (30.6)	12439 (31.9)	57055 (29.1)
Low oily fish intake, n (%)	12200 (31.2)	12678 (32.4)	12619 (32.2)	13034 (33.3)	13137 (33.6)	12971 (32.6)	12521 (32.3)	12669 (31.8)	12425 (32.3)	13082 (33.5)	63668 (32.5)
Heavy drinkers, n (%)	12955 (33.1)	12840 (32.8)	13025 (33.2)	13134 (33.5)	12318 (31.5)	13562 (34.1)	13654 (35.2)	13525 (34.0)	12561 (32.6)	10970 (28.1)	64272 (32.8)
Low physical activity, n (%)	10117 (25.8)	8974 (22.9)	8431 (21.5)	7986 (20.4)	7837 (20.0)	6398 (16.1)	7114 (18.4)	8288 (20.8)	9385 (24.4)	12160 (31.1)	43345 (22.1)
Hypertension, n (%)	19371 (49.5)	17669 (45.1)	16440 (42.0)	15877 (40.5)	16330 (41.7)	11345 (28.5)	14192 (36.6)	17091 (43.0)	19293 (50.1)	23766 (60.9)	85687 (43.8)
Type 2 diabetes, n (%)	635 (1.6)	673 (1.7)	669 (1.7)	805 (2.1)	1250 (3.2)	239 (0.6)	363 (0.9)	524 (1.3)	860 (2.2)	2046 (5.3)	4032 (2.1)
Cancer history (>5 years ago), n (%)	2540 (6.5)	2298 (5.9)	2010 (5.1)	1933 (4.9)	1845 (4.7)	1912 (4.8)	2052 (5.3)	2278 (5.7)	2214 (5.8)	2170 (5.6)	10626 (5.4)
Cholesterol medication, n (%)	4294 (11.0)	3605 (9.3)	3163 (8.1)	3015 (7.8)	3080 (7.9)	1536 (3.9)	2350 (6.1)	3349 (8.5)	4201 (11.0)	5721 (14.8)	17157 (8.8)
Post-menopausal, n (%)	28352 (72.4)	25700 (65.6)	23352 (59.6)	21067 (53.8)	17594 (44.9)	21266 (53.5)	22970 (59.3)	24686 (62.1)	24170 (62.8)	22973 (58.8)	116065 (59.3)

χ^2 test for trend: p<0.05 for all characteristics across the aSMM and FM quintiles. All characteristics were determined at the baseline assessment clinic through touch-screen questionnaires, interviews and/or physical measurements. Higher education: college or university degree or professional qualifications. Low physical activity: <600 metabolic equivalent (MET)-minutes per week[32] . Heavy alcohol drinker: >14 units of alcohol a week)[137]. Hypertension: systolic blood pressure >140mmHg, diastolic blood pressure >90mmHg, was diagnosed by a doctor or were taking medication to lower blood pressure. Diabetes and cholesterol: taking medication for these conditions or diagnosed by a doctor. Cancer history: diagnosed with cancer >5 years ago (those with more recent cancer had been excluded). Low fruit and vegetable intake: the lowest consumption tertile (< 21 portions per week). High saturated fat: the highest saturated fat tertile, based off portions per week of beef, lamb, pork and whether they consumed animal or plant-based spreads. Low oily fish: lowest consumption tertile (< 1 portion per week).

Table S5. Baseline characteristics of the study population according to body composition groups.

Men	Low Muscle / Low Fat	Med Muscle / Low Fat	High Muscle / Low Fat	Low Muscle / Med Fat	Med Muscle / Med Fat	High Muscle / Med Fat	Low Muscle / High Fat	Med Muscle / High Fat	High Muscle / High Fat
Age at recruitment, mean (SD)	59.0 (7.3)	55.1 (8.0)	51.7 (8.0)	60.3 (6.7)	56.3 (7.7)	52.6 (8.0)	60.7 (6.5)	56.7 (7.6)	53.2 (7.8)
Appendicular skeletal muscle (kg), mean (SD)	22.9 (2.1)	24.9 (1.9)	27.1 (2.3)	24.5 (1.9)	26.6 (1.8)	29.1 (2.2)	27.3 (2.6)	29.6 (2.5)	32.7 (3.3)
Fat mass (kg), mean (SD)	14.6 (2.8)	14.3 (2.8)	13.8 (3.1)	21.0 (1.7)	21.0 (1.7)	21.0 (1.7)	29.8 (5.5)	30.0 (5.8)	31.3 (7.2)
Body mass index (BMI), mean (SD)	22.8 (1.6)	24.1 (1.6)	25.4 (1.8)	25.7 (1.3)	27.2 (1.2)	28.6 (1.4)	29.7 (2.8)	31.4 (2.9)	33.5 (3.6)
Weight, mean (SD)	70.3 (6.3)	74.0 (6.3)	78.3 (7.0)	79.7 (5.3)	83.8 (5.1)	88.8 (5.9)	93.6 (9.7)	98.4 (10.0)	105.4 (12.3)
Height, mean (SD)	175.4 (6.8)	175.1 (6.7)	175.5 (6.7)	176.1 (6.6)	175.7 (6.5)	176.2 (6.6)	177.4 (6.6)	177.0 (6.6)	177.3 (6.7)
Higher education, n (%)	7753 (42.8)	7814 (43.2)	7626 (42.1)	7240 (41.0)	7309 (41.3)	6949 (39.3)	6488 (36.4)	6760 (37.9)	6767 (38.0)
Current smokers, n (%)	2406 (13.3)	2139 (11.8)	2285 (12.6)	1850 (10.5)	1882 (10.6)	1951 (11.0)	1768 (9.9)	1823 (10.2)	1901 (10.7)
Low fruit and vegetable intake, n (%)	8143 (45.0)	7708 (42.6)	7199 (39.8)	7903 (44.7)	7827 (44.3)	7593 (42.9)	8095 (45.5)	7900 (44.3)	7873 (44.2)
High saturated intake, n (%)	6078 (33.6)	6014 (33.2)	6006 (33.2)	6423 (36.4)	6406 (36.2)	6510 (36.8)	6978 (39.2)	7064 (39.6)	7075 (39.7)
Low oily fish intake, n (%)	6141 (33.9)	6302 (34.8)	6510 (36.0)	5948 (33.7)	6296 (35.6)	6698 (37.9)	6280 (35.3)	6539 (36.7)	6634 (37.2)
Heavy drinkers, n (%)	10276 (56.8)	10373 (57.3)	10233 (56.5)	11242 (63.6)	11271 (63.7)	10997 (62.2)	11508 (64.7)	11370 (63.8)	10498 (58.9)
Low physical activity, n (%)	3250 (18.0)	2669 (14.7)	2204 (12.2)	3657 (20.7)	3413 (19.3)	2993 (16.9)	4695 (26.4)	4475 (25.1)	4280 (24.0)
Hypertension, n (%)	8641 (47.7)	7727 (42.7)	7208 (39.8)	10898 (61.7)	10187 (57.6)	9600 (54.3)	12947 (72.7)	12437 (69.8)	12213 (68.6)
Diabetes, n (%)	298 (1.6)	245 (1.4)	274 (1.5)	558 (3.2)	505 (2.9)	500 (2.8)	1233 (6.9)	1245 (7.0)	1447 (8.2)
Cholesterol medication, n (%)	1930 (10.7)	1505 (8.4)	1195 (6.7)	3179 (18.1)	2527 (14.4)	2093 (11.9)	4515 (25.5)	3723 (21.0)	3341 (18.9)
Cancer diagnosed by doctor (>5 years ago), n (%)	573 (3.2)	407 (2.3)	373 (2.1)	591 (3.3)	480 (2.7)	340 (1.9)	651 (3.7)	468 (2.6)	350 (2.0)
Women	**Low Muscle / Low Fat**	**Med Muscle / Low Fat**	**High Muscle / Low Fat**	**Low Muscle / Med Fat**	**Med Muscle / Med Fat**	**High Muscle / Med Fat**	**Low Muscle / High Fat**	**Med Muscle / High Fat**	**High Muscle / High Fat**
Age at recruitment, mean (SD)	57.1 (7.7)	54.6 (8.0)	52.2 (7.9)	58.7 (7.1)	56.6 (7.8)	54.4 (8.1)	58.7 (7.1)	56.5 (7.7)	54.7 (8.0)
Appendicular skeletal muscle (kg), mean (SD)	15.7 (1.0)	16.7 (1.0)	18.0 (1.3)	16.7 (1.0)	17.8 (0.9)	19.2 (1.2)	18.7 (1.5)	20.0 (1.5)	22.1 (2.3)
Fat mass (kg), mean (SD)	17.8 (2.8)	17.1 (3.1)	16.4 (3.4)	25.1 (2.1)	24.9 (2.1)	24.9 (2.1)	36.1 (6.7)	36.3 (6.9)	38.8 (8.8)
Body mass index (BMI), mean (SD)	21.8 (1.7)	22.5 (1.8)	23.1 (1.9)	24.9 (1.6)	25.9 (1.6)	26.9 (1.8)	30.0 (3.5)	31.5 (3.7)	34.0 (4.7)
Weight, mean (SD)	56.8 (4.4)	58.6 (4.8)	60.9 (5.3)	66.1 (3.6)	68.4 (3.6)	71.5 (4.0)	80.9 (9.2)	84.0 (9.5)	90.9 (12.6)
Height, mean (SD)	161.6 (6.2)	161.6 (6.1)	162.5 (6.1)	163.1 (6.1)	162.6 (6.1)	163.1 (6.2)	164.2 (6.2)	163.5 (6.1)	163.6 (6.2)
Higher education, n (%)	9086 (41.3)	9855 (44.8)	10384 (47.2)	8069 (37.2)	8681 (39.9)	9277 (42.7)	7548 (35.0)	7976 (37.0)	8302 (38.5)
Current smokers, n (%)	1977 (9.0)	1946 (8.8)	2027 (9.2)	1652 (7.6)	1721 (7.9)	1795 (8.3)	1596 (7.4)	1618 (7.5)	1737 (8.1)
Low fruit and vegetable intake, n (%)	7248 (33.0)	6664 (30.3)	6047 (27.5)	6700 (30.9)	6491 (29.9)	6072 (28.0)	6863 (31.8)	6737 (31.2)	6424 (29.8)
High saturated intake, n (%)	5875 (26.7)	5960 (27.1)	5867 (26.7)	6416 (29.5)	6303 (29.0)	6340 (29.2)	6864 (31.8)	6720 (31.2)	6710 (31.1)
Low oily fish intake, n (%)	6984 (31.8)	7159 (32.5)	7342 (33.4)	6680 (30.8)	6845 (31.5)	7228 (33.3)	6969 (32.3)	7150 (33.1)	7311 (33.9)
Heavy drinkers, n (%)	7167 (32.6)	7649 (34.8)	7893 (35.9)	7415 (34.1)	7400 (34.0)	7428 (34.2)	6840 (31.7)	6542 (30.3)	5752 (26.7)
Low physical activity, n (%)	4468 (20.3)	3679 (16.7)	2965 (13.5)	4922 (22.7)	4536 (20.9)	4116 (19.0)	6478 (30.0)	6130 (28.4)	6051 (28.1)
Hypertension, n (%)	7938 (36.1)	6817 (31.0)	5918 (26.9)	9983 (46.0)	9342 (43.0)	8681 (40.0)	12572 (58.3)	11981 (55.5)	12455 (57.8)
Diabetes, n (%)	155 (0.7)	138 (0.6)	175 (0.8)	247 (1.1)	285 (1.3)	362 (1.7)	626 (2.9)	786 (3.7)	1258 (5.9)
Cholesterol medication, n (%)	1357 (6.2)	979 (4.5)	695 (3.2)	2057 (9.5)	1829 (8.5)	1607 (7.5)	3079 (14.4)	2720 (12.7)	2834 (13.3)
Cancer diagnosed by doctor (>5 years ago) , n (%)	1270 (5.8)	1077 (4.9)	932 (4.2)	1433 (6.6)	1173 (5.4)	1092 (5.0)	1358 (6.3)	1175 (5.5)	1116 (5.2)
Menopause, n (%)	14788 (67.3)	12378 (56.3)	9432 (42.9)	15674 (72.2)	13585 (62.5)	11126 (51.2)	15109 (70.1)	13077 (60.6)	10896 (50.6)

All characteristics were determined at the baseline assessment clinic through touch-screen questionnaires, interviews and/or physical measurements. Higher education: has a college or university degree or professional qualifications. Low physical activity: <600 metabolic equivalent (MET)-minutes per week[32]. Heavy alcohol drinker: drinking >14 units of alcohol a week[137]). Hypertension: if participants had a systolic blood pressure >140mmHg, diastolic blood pressure >90mmHg, had been diagnosed by a doctor or were taking medication to lower blood pressure. Diabetes and high cholesterol: participants were taking medication for these conditions or diagnosed by a doctor. Cancer history: diagnosed with cancer >5 years ago (those with more recent cancer had been excluded). Low fruit and vegetable intake: the lowest consumption tertile (< 21 portions per week). High saturated fat: the highest saturated fat tertile, based off portions per week of beef, lamb, pork and whether they consumed animal or plant-based spreads. Low oily fish: lowest consumption tertile (< 1 portion per week).

Table S6. Partial correlation coefficients between appendicular skeletal muscle mass, fat mass and height, adjusted for age at recruitment.

Men	**aSMM**	**FM**	**Height**
aSMM	-	0.7132	0.5185
FM	0.7132	-	0.1375
Height	0.5185	0.1375	-
Women	**aSMM**	**FM**	**Height**
aSMM	-	0.7771	0.4403
FM	0.7771	-	0.1544
Height	0.4403	0.1544	-

Table S7. CVD sequential model adjustment.

Hazard ratios of CVD associated with appendicular skeletal muscle mass (aSMM) and fat mass (FM)

	Quintile	No. events	Age and height adjusted	+ Socio-demographics*	+ Lifestyle factors†	+ Medical history‡	+ Mutual adjustment for ASM or FM
Appendicular skeletal muscle mass (aSMM)							
Men	1	4373	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
	2	3715	0.99 (0.95 - 1.03)	1.00 (0.96 - 1.04)	1.01 (0.97 - 1.06)	1.01 (0.97 - 1.06)	1.02 (0.97 - 1.06)
	3	3385	1.03 (0.98 - 1.08)	1.04 (1.00 - 1.09)	1.06 (1.01 - 1.11)	1.06 (1.01 - 1.11)	1.07 (1.02 - 1.12)
	4	3055	1.07 (1.02 - 1.12)	1.08 (1.03 - 1.14)	1.11 (1.06 - 1.16)	1.10 (1.05 - 1.15)	1.10 (1.05 - 1.16)
	5	2971	1.25 (1.19 - 1.31)	1.26 (1.20 - 1.32)	1.29 (1.23 - 1.35)	1.27 (1.21 - 1.33)	1.25 (1.19 - 1.31)
	Non-linearity p-value		p<0.001	p<0.001	p<0.001	p<0.001	0.014
		χ^2	103	106	120	106	87
Women	1	2617	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
	2	2182	0.92 (0.87 - 0.97)	0.93 (0.88 - 0.98)	0.93 (0.88 - 0.99)	0.93 (0.88 - 0.98)	0.95 (0.90 - 1.01)
	3	1848	0.85 (0.80 - 0.91)	0.87 (0.82 - 0.92)	0.87 (0.82 - 0.93)	0.87 (0.82 - 0.92)	0.89 (0.84 - 0.95)
	4	1753	0.89 (0.83 - 0.94)	0.90 (0.85 - 0.96)	0.91 (0.86 - 0.97)	0.90 (0.85 - 0.96)	0.92 (0.87 - 0.98)
	5	1885	1.08 (1.02 - 1.15)	1.09 (1.03 - 1.16)	1.09 (1.03 - 1.16)	1.06 (1.00 - 1.13)	1.03 (0.97 - 1.09)
	Non-linearity p-value		p<0.001	p<0.001	p<0.001	p<0.001	p<0.001
		χ^2	69	63	59	51	26
Fat mass (FM)							
Men	1	2565	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
	2	3097	1.14 (1.08 - 1.20)	1.14 (1.08 - 1.20)	1.15 (1.09 - 1.21)	1.14 (1.09 - 1.21)	1.16 (1.10 - 1.22)
	3	3393	1.25 (1.19 - 1.31)	1.24 (1.18 - 1.31)	1.25 (1.19 - 1.32)	1.24 (1.18 - 1.31)	1.26 (1.20 - 1.33)
	4	3835	1.42 (1.35 - 1.49)	1.40 (1.33 - 1.47)	1.40 (1.33 - 1.48)	1.38 (1.31 - 1.45)	1.40 (1.33 - 1.47)
	5	4609	1.76 (1.68 - 1.85)	1.71 (1.63 - 1.79)	1.71 (1.62 - 1.79)	1.65 (1.57 - 1.73)	1.65 (1.57 - 1.73)
	Non-linearity p-value		p<0.001	0.002	0.005	0.024	0.081
		χ^2	654	571	638	455	453
Women	1	1313	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
	2	1653	1.16 (1.08 - 1.25)	1.15 (1.07 - 1.24)	1.16 (1.08 - 1.25)	1.16 (1.08 - 1.24)	1.16 (1.08 - 1.25)
	3	2037	1.32 (1.23 - 1.42)	1.30 (1.21 - 1.39)	1.31 (1.22 - 1.40)	1.30 (1.21 - 1.39)	1.31 (1.22 - 1.40)
	4	2357	1.56 (1.46 - 1.67)	1.51 (1.41 - 1.62)	1.51 (1.41 - 1.62)	1.49 (1.39 - 1.59)	1.50 (1.40 - 1.61)
	5	2925	2.07 (1.94 - 2.21)	1.97 (1.84 - 2.10)	1.95 (1.82 - 2.08)	1.88 (1.76 - 2.01)	1.88 (1.76 - 2.01)
	Non-linearity p-value		p<0.001	p<0.001	0.003	0.016	0.038
		χ^2	639	540	491	430	429

Test for non-linearity across quintiles conducted using LRTs with 4df (p<0.05 indicates significant departure from linearity). Adjusted hazard ratios (HR) and 95% confidence intervals (CI) obtained using Cox proportional hazard regression. Age at risk adjusted for by using age during study as the underlying timescale for Cox regression. Height adjusted for by inclusion as continuous variable for FM and by regression out of variation due to height for ASM. *Sociodemographic characteristics: Townsend index of deprivation, education. †Lifestyle factors: smoking status, alcohol intake, physical activity, oily fish intake, fruit and vegetable intake, saturated fat intake. ‡Medical history: diabetes, cancer history, menopause (women). χ^2 values were calculated from likelihood ratio tests to estimate the improvement in model fit.

Table S8. Mortality sequential model adjustment.

Hazard ratios of all-cause mortality associated with appendicular skeletal muscle mass (aSMM) and fat mass (FM)

	Quintile	No. events	Age and height adjusted	+ Socio-demographics*	+ Lifestyle factors†	+ Medical history‡	+ Mutual adjustment for ASM or FM
Appendicular skeletal muscle mass (aSMM)							
Men	1	2706	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
	2	2013	0.94 (0.88 - 0.99)	0.95 (0.90 - 1.01)	0.97 (0.92 - 1.03)	0.97 (0.92 - 1.03)	0.98 (0.92 - 1.04)
	3	1673	0.94 (0.88 - 1.00)	0.96 (0.90 - 1.02)	0.99 (0.93 - 1.05)	0.99 (0.93 - 1.05)	0.99 (0.93 - 1.06)
	4	1378	0.94 (0.88 - 1.00)	0.96 (0.89 - 1.02)	1.00 (0.93 - 1.07)	0.99 (0.93 - 1.06)	1.00 (0.93 - 1.06)
	5	1312	1.12 (1.05 - 1.20)	1.13 (1.06 - 1.21)	1.19 (1.11 - 1.27)	1.17 (1.09 - 1.25)	1.16 (1.08 - 1.24)
	Non-linearity p-value		p<0.001	p<0.001	p<0.001	p<0.001	0.002
		χ^2	33	30	34	29	25
Women	1	1732	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
	2	1391	0.91 (0.85 - 0.98)	0.92 (0.86 - 0.99)	0.93 (0.86 - 0.99)	0.92 (0.86 - 0.99)	0.93 (0.87 - 1.00)
	3	1255	0.92 (0.86 - 0.99)	0.93 (0.87 - 1.00)	0.94 (0.87 - 1.01)	0.94 (0.88 - 1.01)	0.95 (0.89 - 1.03)
	4	1176	0.96 (0.89 - 1.03)	0.97 (0.90 - 1.04)	0.98 (0.91 - 1.06)	0.98 (0.91 - 1.06)	0.99 (0.92 - 1.07)
	5	1208	1.11 (1.03 - 1.20)	1.11 (1.03 - 1.20)	1.13 (1.05 - 1.22)	1.12 (1.03 - 1.20)	1.11 (1.03 - 1.19)
	Non-linearity p-value		p<0.001	p<0.001	p<0.001	p<0.001	0.003
		χ^2	31	28	29	26	21
Fat mass (FM)							
Men	1	1573	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
	2	1542	0.89 (0.83 - 0.95)	0.89 (0.83 - 0.95)	0.90 (0.84 - 0.96)	0.89 (0.83 - 0.96)	0.90 (0.84 - 0.96)
	3	1727	0.97 (0.91 - 1.04)	0.96 (0.90 - 1.03)	0.97 (0.91 - 1.04)	0.96 (0.90 - 1.03)	0.97 (0.90 - 1.04)
	4	1870	1.05 (0.98 - 1.12)	1.02 (0.96 - 1.1)	1.02 (0.95 - 1.09)	1.00 (0.94 - 1.07)	1.01 (0.94 - 1.08)
	5	2370	1.35 (1.27 - 1.44)	1.28 (1.2 - 1.37)	1.27 (1.19 - 1.35)	1.22 (1.14 - 1.31)	1.22 (1.14 - 1.31)
	Non-linearity p-value		p<0.001	p<0.001	p<0.001	p<0.001	p<0.001
		χ^2	198	145	126	101	98
Women	1	1126	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
	2	1228	0.97 (0.90 - 1.06)	0.97 (0.89 - 1.05)	0.98 (0.90 - 1.06)	0.98 (0.90 - 1.06)	0.99 (0.91 - 1.07)
	3	1321	0.95 (0.87 - 1.03)	0.94 (0.86 - 1.01)	0.94 (0.86 - 1.02)	0.93 (0.86 - 1.01)	0.94 (0.87 - 1.02)
	4	1414	1.02 (0.94 - 1.10)	0.99 (0.92 - 1.08)	0.98 (0.91 - 1.07)	0.98 (0.90 - 1.06)	0.99 (0.92 - 1.08)
	5	1673	1.27 (1.18 - 1.37)	1.21 (1.12 - 1.31)	1.18 (1.09 - 1.28)	1.16 (1.07 - 1.26)	1.17 (1.08 - 1.26)
	Non-linearity p-value		p<0.001	p<0.001	p<0.001	p<0.001	p<0.001
		χ^2	82	62	47	41	37

Test for non-linearity across quintiles conducted using LRTs with 4df (p<0.05 indicates significant departure from linearity). Adjusted hazard ratios (HR) and 95% confidence intervals (CI) obtained using Cox proportional hazard regression. Age at risk adjusted for by using age during study as the underlying timescale for Cox regression. Height adjusted for by inclusion as continuous variable for FM and by regression out of variation due to height for ASM. *Sociodemographic characteristics: Townsend index of deprivation, education. †Lifestyle factors: smoking status, alcohol intake, physical activity, oily fish intake, fruit and vegetable intake, saturated fat intake. ‡Medical history: diabetes, cancer history, menopause (women). χ^2 values were calculated from likelihood ratio tests to estimate the improvement in model fit.

Table S9. CVD sensitivity analyses.

Hazard ratios of CVD associated with appendicular skeletal muscle mass (aSMM) and fat mass (FM)

	Quintile	Remove first 2 years of follow up		Remove outliers		Remove participants with BMI > 35	
		No. events	HR (95% CI)	No. events	HR (95% CI)	No. events	HR (95% CI)
Appendicular skeletal muscle mass (aSMM)							
Men	1	3804	1 (reference)	4316	1 (reference)	4283	1 (reference)
	2	3250	1.06 (1.01 - 1.11)	3715	1.02 (0.97 - 1.06)	3614	1.03 (0.98 - 1.08)
	3	2939	1.12 (1.06 - 1.17)	3385	1.07 (1.02 - 1.12)	3198	1.07 (1.02 - 1.12)
	4	2666	1.19 (1.13 - 1.25)	3055	1.1 0(1.05 - 1.16)	2800	1.11 (1.06 - 1.17)
	5	2597	1.37 (1.30 - 1.44)	2819	1.23 (1.17 - 1.29)	2448	1.25 (1.18 - 1.31)
Non-linearity p-value			0.038		0.057		0.046
Women	1	2327	1 (reference)	2582	1 (reference)	2505	1 (reference)
	2	1947	0.97 (0.91 - 1.03)	2182	0.95 (0.90 - 1.01)	2075	0.96 (0.90 - 1.01)
	3	1667	0.93 (0.87 - 0.99)	1848	0.89 (0.84 - 0.95)	1699	0.88 (0.83 - 0.94)
	4	1570	0.96 (0.90 - 1.02)	1753	0.92 (0.87 - 0.98)	1555	0.92 (0.86 - 0.98)
	5	1681	1.08 (1.01 - 1.15)	1682	1.01 (0.95 - 1.07)	1375	1.01 (0.94 - 1.08)
Non-linearity p-value			p<0.001		p<0.001		p<0.001
Fat Mass (FM)							
Men	1	2293	1 (reference)	2565	1 (reference)	2565	1 (reference)
	2	2701	1.13 (1.07 - 1.19)	3097	1.16 (1.1 - 1.22)	3097	1.16 (1.10 - 1.22)
	3	2907	1.20 (1.14 - 1.27)	3393	1.26 (1.19 - 1.32)	3393	1.26 (1.19 - 1.32)
	4	3341	1.36 (1.28 - 1.43)	3835	1.40 (1.33 - 1.47)	3828	1.40 (1.33 - 1.47)
	5	4014	1.60 (1.51 - 1.68)	3994	1.62 (1.54 - 1.71)	3460	1.61 (1.53 - 1.70)
Non-linearity p-value			0.038		0.211		0.286
Women	1	1173	1 (reference)	1313	1 (reference)	1313	1 (reference)
	2	1487	1.16 (1.07 - 1.25)	1653	1.16 (1.08 - 1.25)	1652	1.15 (1.07 - 1.24)
	3	1806	1.27 (1.18 - 1.37)	2037	1.30 (1.21 - 1.40)	2037	1.29 (1.21 - 1.39)
	4	2118	1.48 (1.37 - 1.59)	2357	1.50 (1.40 - 1.60)	2351	1.49 (1.39 - 1.59)
	5	2608	1.84 (1.71 - 1.98)	2493	1.82 (1.70 - 1.96)	1856	1.76 (1.63 - 1.89)
Non-linearity p-value			0.026		0.230		0.681

Test for non-linearity across quintiles conducted using LRTs with 4df ($p<0.05$ indicates significant departure from linearity). Adjusted hazard ratios (HR) and 95% confidence intervals (CI) obtained using Cox proportional hazard regression. Adjusted for age at risk, Townsend index of deprivation, education, smoking status, alcohol intake, physical activity, oily fish intake, fruit and vegetable intake, saturated fat intake, diabetes, cancer history, menopause (women), and mutually adjusted for FM and ASM. Height is adjusted for by inclusion as continuous variable for FM and by regression out of variation due to height for ASM. For the analysis without outliers, the top and bottom 25% of values were removed.

Table S10. CVD mediation analyses.

Hazard ratios of CVD associated with appendicular skeletal muscle mass (aSMM) and fat mass (FM)

	Quintile	No. events	Adjust for BMI	Adjust for hypertension	Adjust for cholesterol
Appendicular skeletal muscle mass (aSMM)					
Men	1	2861	1 (reference)	1 (reference)	1 (reference)
	2	2457	0.96 (0.92 - 1.01)	1.02 (0.98 - 1.07)	1.03 (0.99 - 1.08)
	3	2209	0.97 (0.93 - 1.02)	1.06 (1.02 - 1.11)	1.08 (1.03 - 1.14)
	4	2004	0.98 (0.93 - 1.03)	1.10 (1.05 - 1.16)	1.14 (1.09 - 1.20)
	5	1907	1.04 (0.99 - 1.10)	1.23 (1.17 - 1.29)	1.28 (1.21 - 1.35)
	Non-linearity p-value		0.015	0.031	0.123
	Main model χ^2		106	87	74
	Adjusted model χ^2		12	79	92
	% Change		87%	9%	20%
Women	1	2617	1 (reference)	1 (reference)	1 (reference)
	2	2182	0.92 (0.87 - 0.97)	0.95 (0.90 - 1.01)	0.93 (0.88 - 0.99)
	3	1848	0.84 (0.79 - 0.89)	0.90 (0.84 - 0.95)	0.87 (0.82 - 0.93)
	4	1753	0.84 (0.79 - 0.90)	0.92 (0.87 - 0.98)	0.94 (0.88 - 1.00)
	5	1885	0.90 (0.85 - 0.96)	1.02 (0.96 - 1.09)	1.04 (0.98 - 1.11)
	Non-linearity p-value		p<0.001	p<0.001	p<0.001
	Main model χ^2		51	26	29
	Adjusted model χ^2		43	23	30
	% Change		17%	12%	3%
Fat mass (FM)					
Men	1	2565	1 (reference)	1 (reference)	1 (reference)
	2	3097	1.05 (0.99 - 1.10)	1.12 (1.06 - 1.18)	1.09 (1.03 - 1.15)
	3	3393	1.06 (1.00 - 1.12)	1.19 (1.13 - 1.25)	1.15 (1.09 - 1.22)
	4	3835	1.09 (1.03 - 1.16)	1.29 (1.22 - 1.36)	1.27 (1.20 - 1.34)
	5	4609	1.10 (1.01 - 1.19)	1.48 (1.41 - 1.56)	1.49 (1.41 - 1.58)
	Non-linearity p-value		0.726	0.102	0.009
	Main model χ^2		455	453	398
	Adjusted model χ^2		8	274	252
	% Change		98%	40%	37%
Women	1	1313	1 (reference)	1 (reference)	1 (reference)
	2	1653	1.07 (0.99 - 1.16)	1.12 (1.05 - 1.21)	1.13 (1.05 - 1.23)
	3	2037	1.13 (1.05 - 1.22)	1.23 (1.15 - 1.32)	1.25 (1.16 - 1.35)
	4	2357	1.21 (1.11 - 1.32)	1.37 (1.28 - 1.47)	1.40 (1.30 - 1.52)
	5	2925	1.29 (1.15 - 1.46)	1.64 (1.54 - 1.76)	1.73 (1.60 - 1.87)
	Non-linearity p-value		0.991	0.119	0.047
	Main model χ^2		430	429	398
	Adjusted model χ^2		20	258	259
	% Change		95%	40%	35%

Adjusted hazard ratios (HR) and 95% confidence intervals (CI) obtained using Cox proportional hazard regression. Adjusted for age at risk, Townsend index of deprivation, education, smoking status, alcohol intake, physical activity, oily fish intake, fruit and vegetable intake, saturated fat intake, diabetes, cancer history, menopause (women), and mutually adjusted for FM and ASM ASM (except for the model adjusted for BMI). Height is adjusted for by inclusion as continuous variable for FM and by regression out of variation due to height for ASM. Test for non-linearity across quintiles conducted using LRTs with 4df (p<0.05 indicates significant departure from linearity). The χ^2 values were calculated from likelihood ratio tests to estimate the improvement in model fit.

Table S11. Mortality sensitivity analyses.

Hazard ratios of all-cause mortality associated with appendicular skeletal muscle mass (aSMM) and fat mass (FM)

	Quintile	Remove first 2 years of follow up		Remove outliers		Remove participants with BMI > 35	
		No. events	HR (95% CI)	No. events	HR (95% CI)	No. events	HR (95% CI)
Appendicular skeletal muscle mass (aSMM)							
Men	1	2532	1 (reference)	2660	1 (reference)	2648	1 (reference)
	2	1897	1.00 (0.94 - 1.06)	2013	0.98 (0.92 - 1.04)	1941	0.98 (0.92 - 1.04)
	3	1566	1.02 (0.96 - 1.09)	1673	0.99 (0.93 - 1.06)	1568	0.98 (0.92 - 1.05)
	4	1283	1.03 (0.97 - 1.11)	1378	1.00 (0.93 - 1.07)	1259	0.99 (0.93 - 1.06)
	5	1219	1.22 (1.14 - 1.31)	1263	1.16 (1.08 - 1.24)	1076	1.13 (1.05 - 1.22)
Non-linearity p-value			0.004		0.002		0.011
Women	1	1647	1 (reference)	1712	1 (reference)	1663	1 (reference)
	2	1307	0.93 (0.86 – 1.00)	1391	0.93 (0.87 – 1.00)	1327	0.93 (0.86 - 1.00)
	3	1183	0.96 (0.89 - 1.03)	1255	0.95 (0.89 - 1.03)	1159	0.93 (0.86 - 1.00)
	4	1119	1.01 (0.93 - 1.09)	1176	0.99 (0.92 - 1.07)	1072	0.98 (0.90 - 1.05)
	5	1148	1.13 (1.05 - 1.22)	1093	1.09 (1.01 - 1.18)	932	1.06 (0.98 - 1.15)
Non-linearity p-value			0.001		0.008		0.006
Fat Mass (FM)							
Men	1	1468	1 (reference)	1573	1 (reference)	1573	1 (reference)
	2	1451	0.90 (0.84 - 0.97)	1542	0.90 (0.83 - 0.96)	1542	0.89 (0.83 - 0.96)
	3	1620	0.97 (0.90 - 1.04)	1727	0.97 (0.90 - 1.04)	1727	0.97 (0.90 - 1.03)
	4	1742	1.00 (0.93 - 1.07)	1870	1.01 (0.94 - 1.08)	1869	1.00 (0.94 - 1.07)
	5	2216	1.22 (1.14 - 1.30)	2039	1.19 (1.11 - 1.27)	1781	1.17 (1.09 - 1.25)
Non-linearity p-value			p<0.001		p<0.001		p<0.001
Women	1	1058	1 (reference)	1126	1 (reference)	1126	1 (reference)
	2	1162	0.99 (0.91 - 1.07)	1228	0.98 (0.90 - 1.06)	1228	0.98 (0.90 - 1.06)
	3	1244	0.94 (0.86 - 1.02)	1321	0.94 (0.87 - 1.02)	1321	0.93 (0.86 - 1.01)
	4	1336	0.99 (0.91 - 1.07)	1414	0.99 (0.91 - 1.07)	1409	0.98 (0.90 - 1.06)
	5	1604	1.18 (1.09 - 1.28)	1422	1.12 (1.03 - 1.22)	1069	1.08 (0.99 - 1.17)
Non-linearity p-value			p<0.001		0.001		0.018

Adjusted hazard ratios (HR) and 95% confidence intervals (CI) obtained using Cox proportional hazard regression. Adjusted for age at risk, Townsend index of deprivation, education, smoking status, alcohol intake, physical activity, oily fish intake, fruit and vegetable intake, saturated fat intake, diabetes, cancer history, menopause (women), and mutually adjusted for FM and ASM. Height is adjusted for by inclusion as continuous variable for FM and by regression out of variation due to height for ASM. Test for non-linearity across quintiles conducted using LRTs with 4df (p<0.05 indicates significant departure from linearity). For the analysis without outliers, the top and bottom 25% of values were removed.

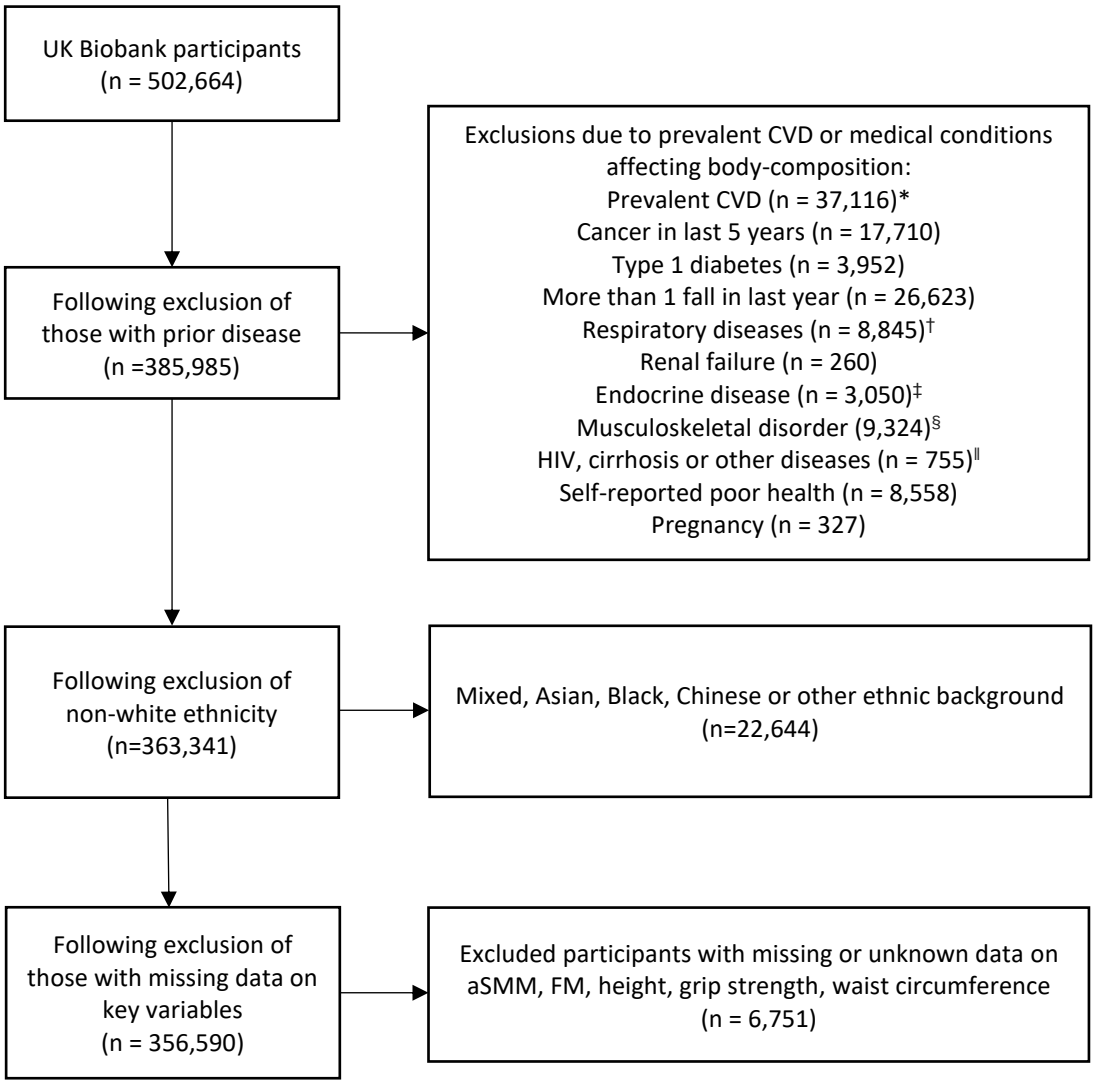
Table S12. Mortality mediation analyses.

Hazard ratios of all-cause mortality associated with appendicular skeletal muscle mass (aSMM) and fat mass (FM)

	Quintile	No. events	Adjust for BMI	Adjust for hypertension	Adjust for cholesterol
Appendicular skeletal muscle mass (aSMM)					
Men	1	2706	1 (reference)	1 (reference)	1 (reference)
	2	2013	0.95 (0.89 - 1.01)	0.98 (0.92 - 1.04)	0.98 (0.92 - 1.05)
	3	1673	0.95 (0.89 - 1.01)	0.99 (0.93 - 1.05)	0.97 (0.91 - 1.04)
	4	1378	0.93 (0.87 - 1.00)	0.99 (0.93 - 1.06)	0.96 (0.89 - 1.03)
	5	1312	1.06 (0.98 - 1.14)	1.15 (1.07 - 1.23)	1.13 (1.05 - 1.22)
	Non-linearity p-value		0.001	0.002	0.001
	Main model χ^2		29	25	21
	Adjusted model χ^2		16	24	20
	% Change		45%	4%	5%
Women	1	1732	1 (reference)	1 (reference)	1 (reference)
	2	1391	0.92 (0.86 - 0.99)	0.93 (0.87 - 1.00)	0.93 (0.86 - 1.00)
	3	1255	0.93 (0.87 - 1.00)	0.95 (0.89 - 1.03)	0.95 (0.88 - 1.03)
	4	1176	0.96 (0.89 - 1.03)	0.99 (0.92 - 1.07)	0.99 (0.91 - 1.07)
	5	1208	1.06 (0.98 - 1.14)	1.10 (1.02 - 1.19)	1.10 (1.02 - 1.20)
	Non-linearity p-value		0.003	0.003	0.004
	Main model χ^2		26	21	21
	Adjusted model χ^2		16	20	19
	% Change		38%	5%	9%
Fat mass (FM)					
Men	1	1573	1 (reference)	1 (reference)	1 (reference)
	2	1542	0.86 (0.79 - 0.92)	0.88 (0.82 - 0.95)	0.90 (0.84 - 0.97)
	3	1727	0.90 (0.83 - 0.97)	0.94 (0.88 - 1.01)	0.98 (0.91 - 1.06)
	4	1870	0.90 (0.82 - 0.98)	0.97 (0.91 - 1.04)	1.01 (0.94 - 1.09)
	5	2370	1.01 (0.90 - 1.13)	1.17 (1.09 - 1.25)	1.24 (1.15 - 1.34)
	Non-linearity p-value		p<0.001	p<0.001	p<0.001
	Main model χ^2		101	98	88
	Adjusted model χ^2		36	81	87
	% Change		64%	17%	1%
Women	1	1126	1 (reference)	1 (reference)	1 (reference)
	2	1228	0.91 (0.84 - 0.99)	0.98 (0.90 - 1.06)	0.97 (0.89 - 1.06)
	3	1321	0.82 (0.75 - 0.90)	0.93 (0.86 - 1.01)	0.97 (0.89 - 1.06)
	4	1414	0.81 (0.73 - 0.90)	0.97 (0.90 - 1.06)	1.00 (0.91 - 1.09)
	5	1673	0.83 (0.71 - 0.96)	1.13 (1.05 - 1.23)	1.16 (1.06 - 1.27)
	Non-linearity p-value		0.033	p<0.001	0.003
	Main model χ^2		41	37	31
	Adjusted model χ^2		22	31	26
	% Change		46%	16%	16%

Adjusted hazard ratios (HR) and 95% confidence intervals (CI) obtained using Cox proportional hazard regression. Adjusted for age at risk, Townsend index of deprivation, education, smoking status, alcohol intake, physical activity, oily fish intake, fruit and vegetable intake, saturated fat intake, diabetes, cancer history, menopause (women), and mutually adjusted for FM and ASM (except for the model adjusted for BMI). Height is adjusted for by inclusion as continuous variable for FM and by regression out of variation due to height for ASM. Test for non-linearity across quintiles conducted using LRTs with 4df (p<0.05 indicates significant departure from linearity). The χ^2 values were calculated from likelihood ratio tests to estimate the improvement in model fi

Figure S1. Exclusions and selection of the study population included in the analysis from the UK Biobank.



*Prior CVD: follows the same definition and codes from HES reported in the manuscript as well as self-reported from verbal interviews and touchscreen questionnaire including instances of heart attack/myocardial infarction, heart failure, angina, heart failure, stroke, transient ischaemic attack, subdural haemorrhage, aortic aneurysm rupture, cerebral aneurysm, peripheral vascular disease, leg claudication, arterial embolism, .

†Respiratory diseases: chronic obstructive pulmonary disease, emphysema, chronic bronchitis, bronchiectasis (occurred anytime)

‡Endocrine diseases: Cushing's syndrome, hyperthyroidism (occurred anytime)

§Musculoskeletal diseases: motor neurone disease, osteoporosis, rheumatoid arthritis, fractures (occurred anytime)

‖HIV, cirrhosis or other disease: pancreatitis, encephalitis, meningitis, intracranial abscess, empyema, Stevens Johnson Syndrome and carcinoid syndrome/tumour (occurred in the last year); liver cirrhosis, HIV/AIDS (occurred anytime)

Figure S2. Splines.

Adjusted hazard ratios (HRs) of incident cardiovascular disease (CVD) and all-cause mortality associated with appendicular skeletal muscle mass (aSMM), whole body fat mass (FM) and body mass index (BMI) estimated using restricted cubic splines

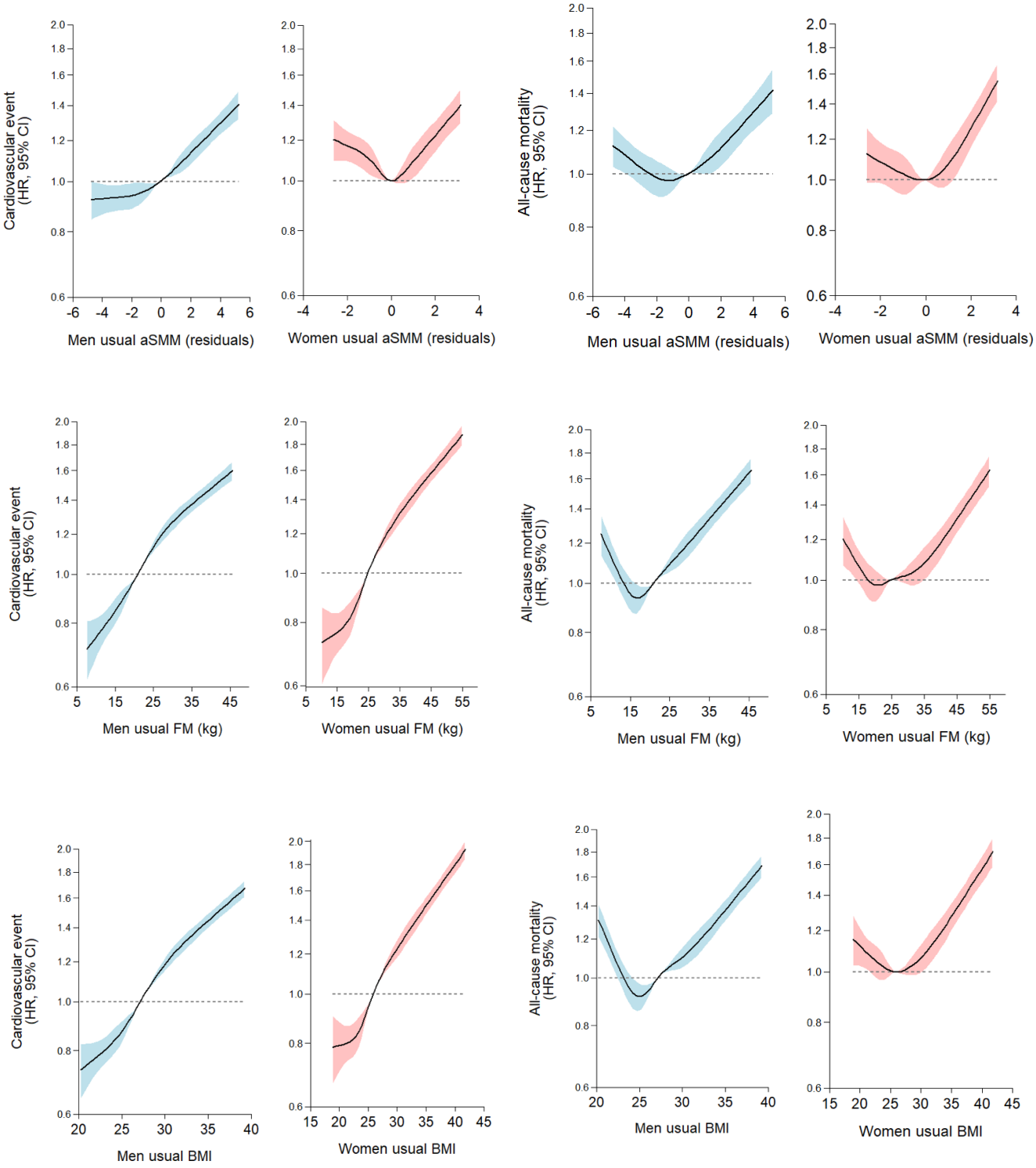
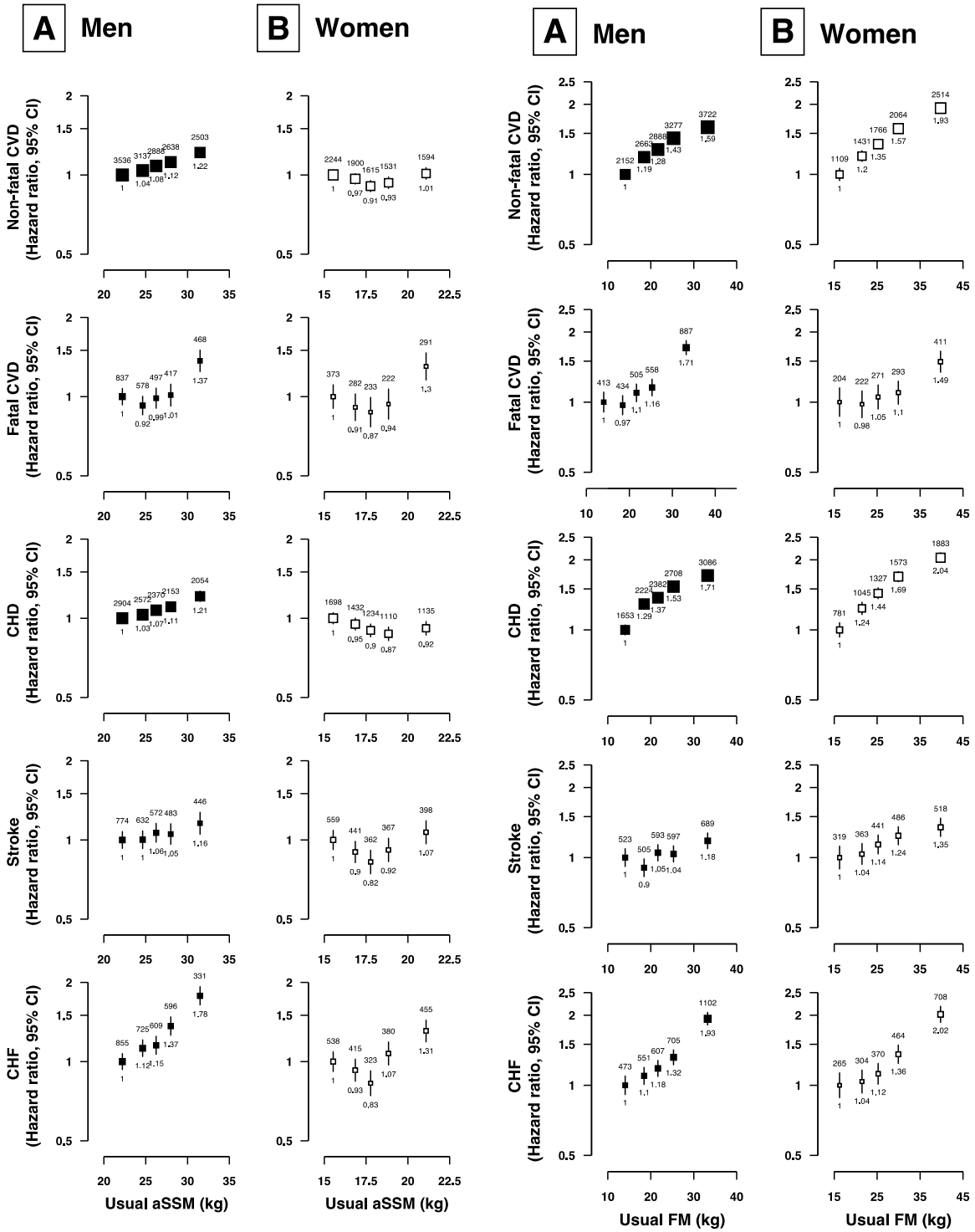


Figure S3. Associations with CVD subtypes.

Adjusted hazard ratios for the association between cardiovascular disease (CVD) subtypes (coronary heart disease, stroke and congestive heart failure) with i) appendicular skeletal muscle mass (aSMM) and ii) fat mass (FM)

i) Appendicular skeletal muscle mass ii) Fat mass



i A, adjusted hazard ratios for the association between CVD subtypes with aSSM in men. **i B**, adjusted hazard ratios for the association between CVD subtypes with aSSM in women. **ii A**, adjusted hazard ratios for the association between CVD subtypes with FM in men. **ii B**, adjusted hazard ratios for the association between CVD subtypes with FM in women

Adjusted hazard ratios (HR) and 95% group-specific confidence intervals (CI) obtained using floated absolute risk method of Cox proportional hazard regression. Adjusted for age at risk, Townsend index of deprivation, education, smoking status, alcohol intake, physical activity, oily fish intake, fruit and vegetable intake, saturated fat intake, diabetes, cancer history, menopause (women), and mutually adjusted for FM and ASM. Height is adjusted for by inclusion as continuous variable for FM and by regression out of variation due to height for ASM. HRs are plotted at the mean of the resurvey values for the baseline-defined quintiles ("usual" values) to correct for measurement error.