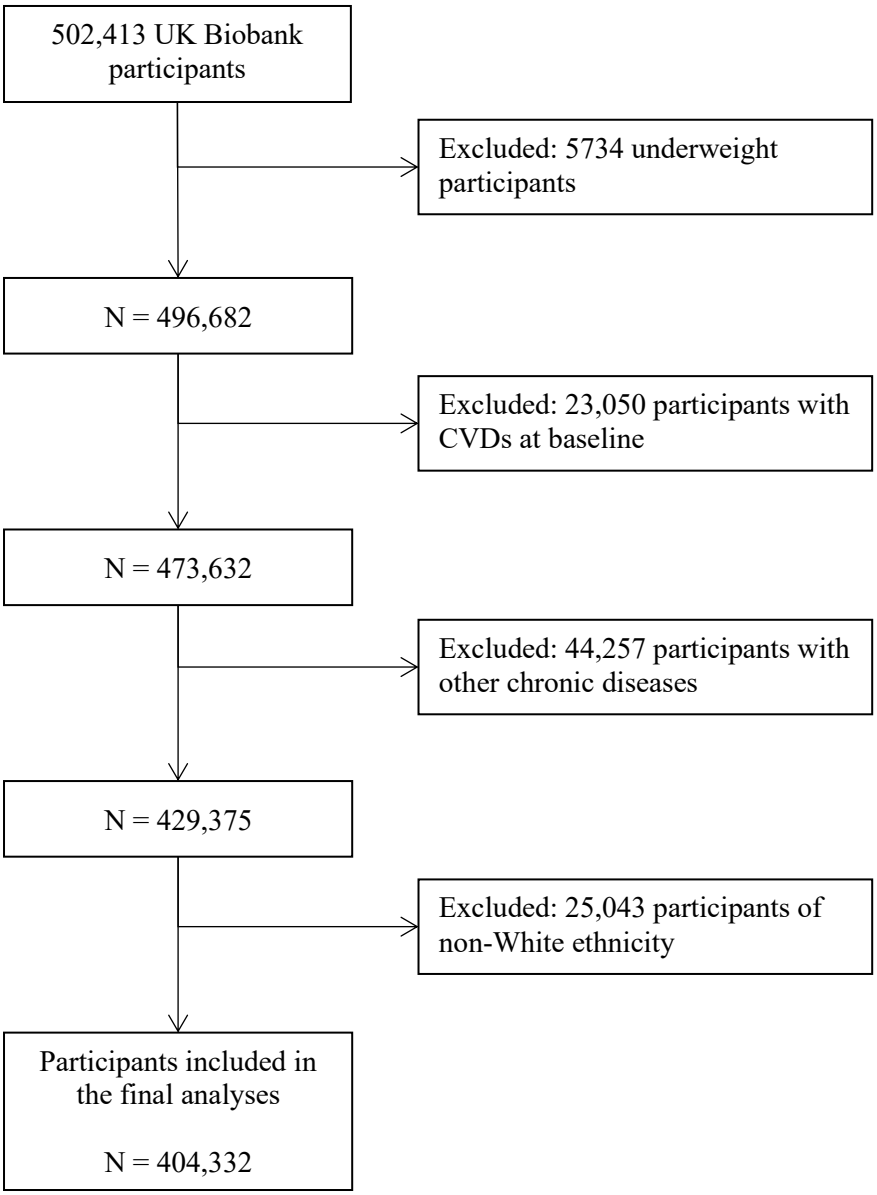
Supplementary Materials

Supplementary Figure 1 Participants flowchart



Supplementary Table 1. Participant characteristics by central obesity

Characteristics	Without central obesity	With central obesity
Total *N*	269,463 (66.64%)	134,785 (33.34%)
Age, years, mean (SD)	55.41 (8.15)	57.75 (7.62)
Sex		
Female	156,202 (57.97%)	64,817 (48.09%)
male	113,261(42.03%)	69,968 (51.91%)
Deprivation index, mean (SD)	-1.66 (2.88)	-1.22 (3.08)
Physical activity, MET min/week, mean (SD)	2576.12 (2264.09)	2334.36 (2195.67)
TV viewing (hours), mean (SD)	2.58 (1.46)	3.09 (1.63)
Diet type		
Vegetarians	4,369 (1.62%)	1,248 (0.93%)
Fish eaters	6,780 (2.52%)	1,773 (1.32%)
Fish & poultry eaters	3,033 (1.13%)	862 (0.64%)
Meat-eaters	230,735 (85.63%)	115,802 (85.92%)
Others	24,546 (9.11%)	15,100 (11.20%)
Smoking status		
Never	158,132 (59.1)	65,654 (48.5)
Previous	84,489 (31.6)	53,844 (39.7)
Current	24,839 (9.3)	15,988 (11.8)
Alcohol consumption, units/week, mean (SD)	15.97 (17.27)	19.06 (21.80)
BMI, kg/m^2, mean (SD)	25.96 (3.99)	30.13 (4.72)
Lipids		
LDL-c, mmol/L, mean (SD)	3.58 (0.83)	3.65 (0.90)
Triglycerides, mmol/L, mean (SD)	1.54 (0.88)	2.14 (1.17)
Lp(a), nmol/L, mean (SD)	49.48 (59.86)	48.88 (60.05)
ApoB, g/L, mean (SD)	1.03 (0.23)	1.07 (0.25)
Blood pressure		
SBP, mmHg, mean (SD)	135.88 (18.47)	141.90 (18.01)
DBP, mmHg, mean (SD)	81.20 (9.95)	84.79 (9.87)
Metabolic markers		
HbA1c, mmol/L, mean (SD)	34.78 (4.91)	37.44 (7.95)
Glucose, mmol/L mean (SD)	4.98 (0.91)	5.31 (1.51)
Liver function markers		
ALT, U/L, mean (SD)	21.48 (12.69)	27.58 (16.69)
GGT, U/L, mean (SD)	32.07 (35.00)	45.80 (52.41)
Kidney function markers		
ACR (urine), mg/mmol, mean (SD)	11.12 (50.73)	16.50 (75.33)
eGFR, ml/min, mean (SD)	95.31 (15.85)	87.34 (16.84)
Others		
CRP, mg/l, mean (SD)	2.11 (4.13)	3.38 (5.14)
HCT, L/L, mean (SD)	40.81 (3.45)	41.79 (3.53)

Numbers are n (%) unless otherwise specified. Some sub-categories, such as ethnicity, may not add up due to missing data. Abbreviations: ALT, alanine transaminase; ApoB, apolipoprotein B; BMI, body mass index; CRP, C-reactive protein; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; LDL-C, low-density lipoprotein-cholesterol; Lp(a), lipoprotein(a); SBP, systolic blood pressure; uACR, urine albumin to creatinine ratio.

Supplementary Table 2. Association between central obesity and biomarkers

	β (95% CI)
Lipids†	
LDL-c	0.17 (0.16, 0.17)
Triglycerides	0.49 (0.48, 0.50)
Lp(a)	-0.03 (-0.04, -0.02)
ApoB	0.24 (0.24, 0.25)
Blood pressure†	
SBP	0.15 (0.15, 0.16)
DBP	0.26 (0.25, 0.27)
Metabolic markers†	
HbA1c	0.31 (0.31, 0.32)
Liver function markers	
ALT	0.36 (0.36, 0.37)
GGT	0.24 (0.23, 0.25)
Kidney function markers	
uACR	0.07 (0.06, 0.07)
eGFR	-0.26 (-0.27, -0.26)
Others	
CRP	0.24 (0.23, 0.24)
HCT	0.14 (0.14, 0.15)

All biomarkers were standardised to sex-specific SD so that the beta coefficients are comparable.
All results are statistically significant ($P < 0.0001$)
All analyses adjusted for age, sex, ethnicity, deprivation, physical activity, sedentary behaviour, dietary intake, alcohol consumption, and smoking
†Medications for cholesterol, blood pressure and insulin were adjusted in the corresponding factors.

Supplementary Table 3. Association between central obesity and CVD by adjustment models

	ASCVD	HF
Baseline model	1.33 (1.29-1.37)	1.64 (1.57-1.71)
Additionally adjusted for:		
Lipids†	1.29 (1.25-1.33)	1.56 (1.50-1.63)
LDL-c	1.25 (1.21-1.30)	1.55 (1.48-1.62)
Triglycerides	1.31 (1.27-1.36)	1.55 (1.49-1.63)
Lp(a)	1.27 (1.23-1.31)	1.57 (1.50-1.64)
ApoB		
Blood pressure†	1.25 (1.21-1.29)	1.46 (1.40-1.53)
SBP	1.24 (1.20-1.28)	1.47 (1.41-1.54)
DBP		
Metabolic markers†	1.27 (1.23-1.31)	1.55 (1.49-1.63)
HbA1c		
Liver function markers	1.32 (1.28-1.37)	1.63 (1.56-1.70)
ALT	1.31 (1.27-1.36)	1.59 (1.53-1.67)
GGT		
Kidney function markers	1.33 (1.29-1.37)	1.63 (1.56-1.71)
uACR	1.25 (1.21-1.29)	1.44 (1.38-1.51)
eGFR		
Others	1.32 (1.27-1.36)	1.59 (1.52-1.66)
CRP	1.33 (1.29-1.38)	1.67 (1.60-1.74)
HCT	1.33 (1.29-1.37)	1.64 (1.57-1.71)

Numbers presented are HR (95% CI); all results are statistically significant ($P < 0.0001$)

All analyses adjusted for age, sex, ethnicity, deprivation, physical activity, sedentary behaviour, dietary intake, alcohol consumption, and smoking

†Medications for cholesterol, blood pressure and insulin were adjusted in the corresponding factors.

Supplementary Table 4. Mediators between central obesity and CVD

	ASCVD			HF		
	Natural indirect effect		Proportion mediated	Natural indirect effect		Proportion mediated
	HR (95% CI)	P-value	% (95% CI)	HR (95% CI)	P-value	% (95% CI)
Lipids†						
LDL-c	1.02 (1.02-1.03)	< 0.0001	9.3 (7.7, 11.1)	0.98 (0.98-0.99)	< 0.0001	-5.1 (-6.3, -3.6)
Triglycerides	1.04 (1.03-1.05)	< 0.0001	17.3 (13.5, 22.1)	1.00 (0.99-1.01)	0.92	0.4 (-3.1, 3.4)
Lp(a)	1.00 (1.00-1.00)	< 0.0001	-1.3 (-1.9, -0.9)	1.00 (1.00-1.00)	< 0.0001	-0.3 (-0.5, -0.1)
ApoB	1.04 (1.03-1.04)	< 0.0001	15.4 (12.8, 18.6)	0.98 (0.98-0.99)	< 0.0001	-4.7 (-6.7, -2.8)
Blood pressure†						
SBP	1.03 (1.03-1.03)	< 0.0001	13.9 (12.1, 16.6)	1.01 (1.01-1.02)	< 0.0001	4.3 (3.0, 5.4)
DBP	1.04 (1.03-1.04)	< 0.0001	16.0 (13.3, 19.1)	1.00 (1.00-1.01)	0.56	0.8 (-1.4, 2.9)
Metabolic markers†						
HbA1c	1.03 (1.03-1.04)	< 0.0001	13.5 (11.4, 16.6)	1.04 (1.03-1.05)	< 0.0001	9.2 (7.6, 11.9)
Liver function markers						
ALT	1.01 (1.00-1.02)	< 0.0001	3.9 (1.7, 6.6)	1.00 (0.99-1.01)	0.39	1.2 (-2.1, 3.7)
GGT	1.02 (1.01-1.02)	< 0.0001	6.7 (5.5, 8.1)	1.02 (1.02-1.03)	< 0.0001	5.5 (4.8, 6.4)
Kidney function markers						
uACR	1.00 (1.00-1.00)	< 0.0001	1.0 (0.7, 1.4)	1.00 (1.00-1.00)	< 0.0001	0.8 (0.6, 1.1)
eGFR	1.06 (1.06-1.07)	< 0.0001	24.5 (21.0, 27.9)	1.12 (1.11-1.13)	< 0.0001	27.3 (24.7, 29.7)
Others						
CRP	1.02 (1.01-1.02)	< 0.0001	6.9 (5.8, 8.3)	1.03 (1.03-1.03)	< 0.0001	6.9 (6.3, 7.7)
HCT	1.01 (1.00-1.01)	< 0.0001	2.2 (0.9, 3.6)	0.99 (0.98-0.99)	< 0.0001	-3.7 (-5.1, -2.4)

All analyses adjusted for age, sex, ethnicity, deprivation, physical activity, sedentary behaviour, dietary intake, alcohol consumption, and smoking

†Medications for cholesterol, blood pressure and insulin were adjusted in the corresponding factors