Supplemental Material: Cardiometabolic Health Outcomes Associated With Discordant Visceral and Liver Fat Phenotypes: The Dallas Heart Study

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Supplemental Methods

Methods: Definitions of CVD and CHD in UK Biobank

Data used to create the definitions included: ICD-10 codes and corresponding dates from the inpatient hospital data - both primary and secondary diagnoses were used, OPCS-4 codes and corresponding dates from the inpatient hospital data - both main and secondary operation were used, ICD-10 codes for cause of death from the death register data - both primary and contributory causes of death were used, self-reported non-cancer illness codes (field 20002 in UK Biobank) - codes reported at any of the following visits were used: 0) Initial assessment visit (2006-2010), 1) First repeat assessment visit (2012-13), 2) Imaging visit (2014+). CVD cases were identified using the following ICD-10 codes and OPCS-4 codes. For the OPCS-4 codes, all subcategories of the codes were used (for example, L31 includes the codes L311, L312, L313, L314, L318, and L319).

Category	Type of code	Code	Meaning
Myocardial infarction	ICD-10	I210	I21.0 Acute transmural myocardial infarction of anterior wall
Myocardial infarction	ICD-10	I211	I21.1 Acute transmural myocardial infarction of inferior wall
Myocardial infarction	ICD-10	I212	I21.2 Acute transmural myocardial infarction of other sites
Myocardial infarction	ICD-10	I213	I21.3 Acute transmural myocardial infarction of unspecified site
Myocardial infarction	ICD-10	I214	I21.4 Acute subendocardial myocardial infarction
Myocardial infarction	ICD-10	I219	I21.9 Acute myocardial infarction, unspecified
Myocardial infarction	ICD-10	I220	I22.0 Subsequent myocardial infarction of anterior wall
Myocardial infarction	ICD-10	I221	I22.1 Subsequent myocardial infarction of inferior wall
Myocardial infarction	ICD-10	I228	I22.8 Subsequent myocardial infarction of other sites
Myocardial infarction	ICD-10	I229	I22.9 Subsequent myocardial infarction of unspecified site
Unstable angina hospitalization	ICD-10	I200	I20.0 Unstable angina
Percutaneous coronary intervention	OPCS-4	K49	K49 Transluminal balloon angioplasty of coronary artery
Percutaneous coronary intervention	OPCS-4	K50	K50 Other therapeutic transluminal operations on coronary artery
Coronary artery bypass graft surgery	OPCS-4	K40	K40 Saphenous vein graft replacement of coronary artery
Coronary artery bypass graft surgery	OPCS-4	K45	K45 Connection of thoracic artery to coronary artery
Coronary artery bypass graft surgery	OPCS-4	K46	K46 Other bypass of coronary artery
Ischemic stroke (cerebrovascular accident)	ICD-10	I630	I63.0 Cerebral infarction due to thrombosis of precerebral arteries
Ischemic stroke (cerebrovascular accident)	ICD-10	I631	I63.1 Cerebral infarction due to embolism of precerebral arteries

Ischemic stroke (cerebrovascular accident)	ICD-10	I632	I63.2 Cerebral infarction due to unspecified occlusion or stenosis of precerebral arteries
Ischemic stroke (cerebrovascular accident)	ICD-10	I633	I63.3 Cerebral infarction due to thrombosis of cerebral arteries
Ischemic stroke (cerebrovascular accident)	ICD-10	I634	I63.4 Cerebral infarction due to embolism of cerebral arteries
Ischemic stroke (cerebrovascular accident)	ICD-10	I635	I63.5 Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries
Ischemic stroke (cerebrovascular accident)	ICD-10	I636	I63.6 Cerebral infarction due to cerebral venous thrombosis, nonpyogenic
Ischemic stroke (cerebrovascular accident)	ICD-10	I638	I63.8 Other cerebral infarction
Ischemic stroke (cerebrovascular accident)	ICD-10	I639	I63.9 Cerebral infarction, unspecified
Transient ischemic attack	ICD-10	I650	I65.0 Occlusion and stenosis of vertebral artery
Transient ischemic attack	ICD-10	I651	I65.1 Occlusion and stenosis of basilar artery
Transient ischemic attack	ICD-10	I652	I65.2 Occlusion and stenosis of carotid artery
Transient ischemic attack	ICD-10	I653	I65.3 Occlusion and stenosis of multiple and bilateral precerebral arteries
Transient ischemic attack	ICD-10	I658	I65.8 Occlusion and stenosis of other precerebral artery
Transient ischemic attack	ICD-10	I659	I65.9 Occlusion and stenosis of unspecified precerebral artery
Transient ischemic attack	ICD-10	I660	I66.0 Occlusion and stenosis of middle cerebral artery
Transient ischemic attack	ICD-10	I661	I66.1 Occlusion and stenosis of anterior cerebral artery
Transient ischemic attack	ICD-10	I662	I66.2 Occlusion and stenosis of posterior cerebral artery
Transient ischemic attack	ICD-10	I663	I66.3 Occlusion and stenosis of cerebellar arteries
Transient ischemic attack	ICD-10	I664	I66.4 Occlusion and stenosis of multiple and bilateral cerebral arteries
Transient ischemic attack	ICD-10	I668	I66.8 Occlusion and stenosis of other cerebral artery
Transient ischemic attack	ICD-10	I669	I66.9 Occlusion and stenosis of unspecified cerebral artery
Cerebrovascular revascularization procedure	OPCS-4	L29	L29 Reconstruction of carotid artery
Cerebrovascular revascularization procedure	OPCS-4	L30	L30 Other open operations on carotid artery
Cerebrovascular revascularization procedure	OPCS-4	L31	L31 Transluminal operations on carotid artery
Cerebrovascular revascularization procedure	OPCS-4	L33	L33 Operations on aneurysm of cerebral artery
Cerebrovascular revascularization procedure	OPCS-4	L34	L34 Other open operations on cerebral artery
Cerebrovascular revascularization procedure	OPCS-4	L35	L35 Transluminal operations on cerebral artery

Peripheral arterial disease revascularization procedure	OPCS-4	L16	L16 Extra-anatomic bypass of aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L18	L18 Emergency replacement of aneurysmal segment of aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L19	L19 Other replacement of aneurysmal segment of aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L20	L20 Other emergency bypass of segment of aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L21	L21 Other bypass of segment of aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L22	L22 Attention to prosthesis of aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L23	L23 Plastic repair of aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L25	L25 Other open operations on aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L26	L26 Transluminal operations on aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L27	L27 Transluminal insertion of stent graft for aneurysmal segment of aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L28	L28 Transluminal operations on aneurysmal segment of aorta
Peripheral arterial disease revascularization procedure	OPCS-4	L50	L50 Other emergency bypass of iliac artery
Peripheral arterial disease revascularization procedure	OPCS-4	L51	L51 Other bypass of iliac artery
Peripheral arterial disease revascularization procedure	OPCS-4	L52	L52 Reconstruction of iliac artery
Peripheral arterial disease revascularization procedure	OPCS-4	L53	L53 Other open operations on iliac artery
Peripheral arterial disease revascularization procedure	OPCS-4	L54	L54 Transluminal operations on iliac artery
Peripheral arterial disease revascularization procedure	OPCS-4	L56	L56 Emergency replacement of aneurysmal femoral artery
Peripheral arterial disease revascularization procedure	OPCS-4	L57	L57 Other replacement of aneurysmal femoral artery
Peripheral arterial disease revascularization procedure	OPCS-4	L58	L58 Other emergency bypass of femoral artery
Peripheral arterial disease revascularization procedure	OPCS-4	L59	L59 Other bypass of femoral artery
Peripheral arterial disease revascularization procedure	OPCS-4	L60	L60 Reconstruction of femoral artery
Peripheral arterial disease revascularization procedure	OPCS-4	L62	L62 Other open operations on femoral artery
Peripheral arterial disease revascularization procedure	OPCS-4	L63	L63 Transluminal operations on femoral artery
Heart failure (systolic or diastolic) hospitalization	ICD-10	I501	I50.1 Left ventricular failure
Heart failure (systolic or diastolic) hospitalization	ICD-10	I509	I50.9 Heart failure, unspecified

Atrial fibrillation hospitalization	ICD-10	I480	I48.0 Paroxysmal atrial fibrillation
Atrial fibrillation hospitalization	ICD-10	I481	I48.1 Persistent atrial fibrillation
Atrial fibrillation hospitalization	ICD-10	I482	I48.2 Chronic atrial fibrillation
Atrial fibrillation hospitalization	ICD-10	I489	I48.9 Atrial fibrillation and atrial flutter, unspecified

The following variables were created:

- cvd_pre = 1 if the subject had any of the ICD-10 or OPCS-4 codes with a corresponding date less than its scanning date. Otherwise cvd_pre = 0.
- cvd_post = 1 if the subject had any of the ICD-10 or OPCS-4 codes with a corresponding date greater or equal than its scanning date. Otherwise cvd_post = 0.

The following self-reported non-cancer illness codes were used to exclude controls:

1066 - heart/cardiac problem
1067 - peripheral vascular disease
1068 - venous thromboembolic disease
1493 - other venous/lymphatic disease
Controls were excluded as follows: If a subject had both cvd_pre = 0 and cvd_post = 0, and, in addition, reported any of the codes above, then both cvd_pre and cvd_post were set to missing values.

Supplemental Table 1. Median cutoffs used for high visceral adipose tissue (VAT) and high liver fat (LF) in the Dallas Heart Study and UK Biobank

	Dallas Heart Study	UK Biobank
VAT (kg)		
Male		4.73
Black	6.52	--
Non-Black	6.95	--
Female		2.35
Black	3.89	--
Non-Black	5.16	--
LF (%)		
Male		3.21
Hispanic	3.63	--
Non-Hispanic	3.20	--
Female		2.45
Hispanic	4.16	--
Non-Hispanic	3.23	--

Supplemental Table 2. Baseline characteristics of the Dallas Heart Study population stratified by normal/abnormal visceral adipose tissue

	Normal VAT (n=1616)	Abnormal VAT (n=448)	*p*-value
Age, median (IQR)	44 (36,52)	47 (40, 54)	<.001
Female, No. (%)	1022 (63.2)	91 (20.3)	<.001
Race, No. (%)			
White	465 (28.8)	200 (44.6)	<.001
Black	838 (51.9)	138 (30.8)	<.001
Hispanic	281 (17.4)	97 (21.7)	.04
Other	32 (2.0)	13 (2.9)	.24
Weight, median (IQR)- kg	78 (67.1, 90.3)	98 (88, 110.7)	<.001
Height, median (IQR)- cm	166.4 (159, 172.3)	172.7 (165.1, 180.3)	<.001
Body Mass Index, median (IQR)- kg/m^2	27.9 (24.5, 32.4)	32.7 (29.8, 36.6)	<.001
Waist Circumference, median (IQR)- cm	93 (84.5, 102)	110 (103, 118.5)	<.001
VAT, median (IQR)- kg	1.8 (1.3, 2.3)	3.4 (3.1, 3.8)	<.001
LF, median (IQR)- %	3.04 (1.84, 5.12)	7.21 (4.01, 12.53)	<.001
DEXA			
Fat mass, median (IQR)- kg[a]	24 (17.6, 32.1)	28.5 (23.8, 36.7)	<.001
Lean mass, median (IQR)- kg[a]	51.5 (43.5, 60.3)	65.7 (58.1, 72.7)	<.001
Lower body fat, median (IQR)- kg[a]	8.8 (6.1, 11.9)	8.6 (6.7, 11.3)	.99
Truncal fat, median (IQR)- kg[a]	11.4 (8.1, 15.6)	16.0 (13.0, 19.6)	<.001
Diabetes Mellitus, No. (%)[b]	148 (9.2)	83 (18.5)	<.001
Hypercholesterolemia, No. (%)	202 (12.5)	77 (17.2)	.01
Low High-density lipoprotein cholesterol, No. (%)	636 (39.4)	235 (52.5)	<.001
Metabolic Syndrome, No. (%)	465 (28.8)	269 (60.0)	<.001
Current Smoker, No. (%)[c]	414 (25.7)	101 (22.6)	.18
Prior Cardiovascular disease, No. (%)	100 (6.2)	36 (8.0)	.16
Physical Activity, median (IQR)- MET min/week[d]	133 (0, 544)	133 (0, 540)	.63

Abnormal VAT is defined as 2.87 kg, or >= 95th percentile of population without hypertension, dyslipidemia, high triglycerides, obesity, T2DM, or CVD.[a]n = 2022, [b]n = 2063, [c]n = 2059, [d]n = 1918

Supplemental Table 3. Baseline characteristics of the Dallas Heart Study population stratified by normal/abnormal liver fat

	Normal LF	Abnormal LF	*p*-value
Age, median (IQR)	44 (36, 53)	46 (38, 53)	.01
Female, No. (%)	807 (56.7)	306 (47.7)	<.001
Race, No. (%)			
White	449 (31.6)	216 (33.7)	.33
Black	750 (52.7)	226 (35.3)	<.001
Hispanic	204 (14.3)	174 (27.2)	<.001
Other	20 (1.4)	25 (3.9)	<.001
Weight, median (IQR)- kg	78 (66.9, 90.7)	92.5 (79.8, 106)	<.001
Height, median (IQR)- cm	167.6 (160.0,175.3)	167.6 (160.0, 175.3)	.84
Body Mass Index, median (IQR)- kg/m^2	27.6 (24.3, 31.7)	32.6 (28.9, 36.6)	<.001
Waist Circumference, median (IQR)- cm	93 (84, 102.5)	106 (97, 116)	<.001
VAT, median (IQR)- kg	1.8 (1.3, 2.4)	2.7 (2.2, 3.4)	<.001
LF, median (IQR)- %	2.60 (1.67, 3.71)	9.85 (7.22, 15.04)	<.001
DEXA			
Fat mass, median (IQR)- kg[a]	23.3 (17.1, 30.6)	29.6 (23.7, 38.2)	<.001
Lean mass, median (IQR)- kg[a]	52.4 (43.8, 61.7)	58.8 (49.9, 67.9)	<.001
Lower body fat, median (IQR)- kg[a]	8.6 (6.0, 11.5)	9.4 (6.9, 12.5)	<.001
Truncal fat, median (IQR)- kg[a]	11.1 (7.9, 14.9)	15.8 (12.5, 19.7)	<.001
Diabetes Mellitus, No. (%)[b]	103 (7.2)	128 (20)	<.001
Hypercholesterolemia, No. (%)	167 (11.7)	112 (17.5)	<.001
Low High-density lipoprotein cholesterol, No. (%)	521 (36.6)	350 (54.6)	<.001
Metabolic Syndrome, No. (%)	359 (25.2)	375 (58.5)	<.001
Current Smoker, No. (%)[c]	374 (26.4)	141 (22)	.03
Prior Cardiovascular disease, No. (%)	88 (6.2)	48 (7.5)	.27
Physical Activity, median (IQR)- MET min/week[d]	159 (0, 630)	109 (0, 495)	.03

Abnormal LF is defined as ≥5.5%. [a]n = 2022, [b]n = 2063, [c]n = 2059, [d]n = 1918

Supplemental Table 4. Association of visceral adipose tissue (VAT) and liver fat (LF) with prevalent cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) in the Dallas Heart Study

	Prevalent CVD		Prevalent T2DM	
	HR (95% CI)	***p*-value**	**Odds Ratio (95% CI)**	***p*-value**
Model 1				
VAT	1.44 (1.26 - 1.63)	<.001	1.58 (1.37 - 1.81)	<.001
LF	0.99 (0.97- 1.02)	.63	1.32 (1.17 - 1.49)	<.001
Model 2				
VAT	1.21 (1.06 - 1.40)	.007	1.24 (1.06-1.45)	.01
LF	1.00 (0.98 - 1.03)	.95	1.33 (1.17 - 1.50)	<.001
Model 3				
VAT	0.95 (0.79 - 1.15)	.60	1.30 (1.05 - 1.62)	.02
LF	1.02 (0.99 - 1.05)	.09	1.34 (1.17 - 1.56)	<.001

HR calculated for incident CVD and OR calculated for incident T2DM.
Model 1 is unadjusted
Model 2 is adjusted for age and BMI
Model 3 is adjusted for Model 2 + sex, race/ethnicity, smoking, hypercholesterolemia, hypertension, physical activity, postmenopausal status (women only), and family history of CVD or T2DM

Supplemental Table 5. Associations of visceral adipose tissue (VAT) and liver fat (LF) with biomarkers of cardiometabolic risk in the Dallas Heart Study

	High VAT / High LF			High VAT / Low LF			Low VAT / High LF		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
LDL-C (mg/dL)	0.11*	0.08*	0.09*	0.10*	0.08*	0.09*	0.05	0.04	0.04
LDL small (nm)	0.68*	0.51*	0.48*	0.48*	0.35*	0.34*	0.36*	0.31*	0.28*
Total Cholesterol (mg/dL)	0.06*	0.07*	0.07*	0.04*	0.04*	0.04*	0.05*	0.05*	0.05*
LDL large (nm)	-0.41*	-0.42*	-0.38*	-0.17*	-0.18*	-0.17*	-0.24*	-0.25*	-0.23*
LDL med small (nm)	0.66*	0.50*	0.46*	0.44*	0.31*	0.30*	0.33*	0.28*	0.25*
LDL very small (nm)	0.69*	0.51*	0.48*	0.50*	0.36*	0.35*	0.35*	0.29*	0.27*
LDL size (nm)	-0.03*	-0.03*	-0.03*	-0.02*	-0.02*	-0.02*	-0.02*	-0.02*	-0.02*
VLDL small (nm)	0.22*	0.18*	0.18*	0.23*	0.20*	0.18*	-0.02	-0.04	-0.03
VLDL medium (nm)	0.49*	0.54*	0.50*	0.39*	0.42*	0.42*	0.38*	0.40*	0.38*
VLDL size (nm)	0.094*	0.10*	0.08*	-0.02	-0.01	-0.02	0.04*	0.04*	0.03*
HDL small (nm)	0.13*	0.12*	0.13*	0.09*	0.08*	0.08*	0.09*	0.08*	0.08*
HDL size (nm)	-0.04*	-0.03*	-0.03*	-0.03*	-0.02*	-0.02*	-0.02*	-0.02*	-0.01*
Triglycerides (mg/dL)	0.48*	0.47*	0.42*	0.19*	0.18*	0.18*	0.29*	0.29*	0.26*
VLDL large (nm)	0.91*	0.91*	0.84*	0.33*	0.32*	0.31*	0.60*	0.60*	0.56*

HDL-C (mg/dL)	-0.19*	-0.14*	-0.12*	-0.14*	-0.10*	-0.10*	-0.09*	-0.07*	-0.06*
HDL large (nm)	-0.47*	-0.38*	-0.33*	-0.28*	-0.22*	-0.20*	-0.23*	-0.20*	-0.18*
MPO (ng/mL)	0.10*	0.05	0.06	0.09*	0.06	0.06	0.01	-0.002	-0.001
PGRPs (ng/mL)	0.13*	0.08*	0.07*	0.12*	0.08*	0.08*	-0.001	-0.02	-0.03
Adiponectin(ng/mL)	-0.45*	-0.35*	-0.31*	-0.26*	-0.19*	-0.19*	-0.29*	-0.26*	-0.25*
Leptin (µg/L)	1.15*	0.43*	0.37*	0.89*	0.34*	0.33*	0.52*	0.30*	0.28*
Glucose (mg/dL)	0.12*	0.08*	0.02	0.05*	0.02	0.01	0.06*	0.05*	0.02
Fructosamine (µU/mL)	-0.02*	0.006	-0.01	-0.03*	-0.01	-0.01	0.006	0.02	0.005
Insulin (µU/mL)	0.91*	0.60*	0.35*	0.47*	0.24*	0.21*	0.37*	0.28*	0.20*
HOMA-IR (units)	1.0*	0.68*	0.37*	0.53*	0.27*	0.22*	0.42*	0.32*	0.22*
Caspase-3 (ng/mL)	0.05	0.05	0.02	-0.05	-0.48	-0.05	0.03	0.03	0.02
Uric Acid (mg/mL)	0.20*	0.13*	0.12*	0.11*	0.06*	0.06*	0.11*	0.09*	0.09*
CAC (Agatston Unit)	0.46*	0.18	0.08	0.20	0.004	-0.03	0.16	0.06	0.03
AWT (mm)	0.09*	0.09*	0.07*	0.05*	0.05*	0.04	0.03	0.03	0.03
APB (%)	0.24*	0.47*	0.34*	-0.13	0.05	0.001	0.11	0.17	0.13
eGFR (ml/min/1.73 m2)	-0.01	-0.003	-0.009	-0.02	-0.01	-0.01	-0.003	-0.0002	0.002
Cystatin C (mg/L)	0.07*	0.01	0.007	0.06*	0.01	0.01	-0.001	-0.02	-0.02
D-Dimer (ng/mL)	0.05	-0.01	-0.02	0.14*	0.09	0.08	0.03	0.01	-0.0003

sCD40L (ng/mL)	-0.09*	-0.13*	-0.17*	-0.09*	-0.12*	-0.13*	0.003	-0.008	-0.02
sESAM (ng/mL)	0.04	-0.001	-0.02	0.04	0.003	-.0005	-0.006	-0.02	-0.03
sVCAM (ng/mL)	-0.03	-0.03	-0.04	-0.06	-0.06	-0.07	0.04	0.04	0.03
sICAM (ng/mL)	-0.04	-0.04	-0.07	-0.06	-0.07	-0.08	0.03	0.03	0.02
hs-CRP (mg/L)	0.93*	0.35*	0.32*	0.69*	0.26*	0.25*	0.45*	0.27*	0.26*
PG (ng/mL)	0.09*	0.16*	0.16*	0.04	0.1*	0.1*	0.04	0.06	0.06
MCP-1 (pg/mL)	0.0008	-0.02	-0.05	0.01	-0.004	-0.01	-0.007	-0.02	-0.03
MMP-9 (ng/mL)	0.19*	0.16*	0.14*	0.06	0.04	0.45	-0.04	-0.05	-0.04
CCL11 (pg/mL)	-0.04	0.07	0.05	-0.16	-0.07	-0.07	-0.09	-0.06	-0.08
CXCL1 (ng/mL)	0.013	0.007	0.01	0.02	0.01	0.01	0.008	0.007	0.007
CXCL2 (ng/mL)	-0.02	-0.02	-0.01	-0.02	-0.02	-0.02	-0.02	-0.02	-0.01
LTβR (ng/mL)	0.04*	0.02	0.006	0.06*	0.04	0.04	-0.01	-0.02	-0.02
GDF-15 (ng/mL)	-0.03	0.01	0.01	-0.04	-0.01	-0.007	-0.04	-0.02	-0.02
sRAGE (ng/mL)	-0.09*	-0.03	-0.03	-0.06*	-0.01	-0.02	-0.06*	-0.04	-0.04
hs-cTnT (ng/mL)	0.12*	0.10*	0.10*	0.11*	0.10	0.10	0.13*	0.13*	0.12*
BNP (pg/mL)	-0.17*	-0.19	-0.14	0.08	0.06	0.07	-0.20*	-0.21*	-0.19*
Pro-BNP (pg/mL)	-0.37*	-0.37*	-0.29*	-0.03	-0.04	-0.01	-0.22*	-0.23*	-0.21*
TNFR1A (ng/mL)	0.18*	0.08	0.08	0.13*	0.05	0.06	-0.02	-0.04	-0.05

*P<0.05. Abbreviations: APB, aortic plaque burden; AWT, aortic wall thickness; BNP, B-type natriuretic peptide; CAC, coronary artery calcium; CCL11, chemokine (c-c motif) ligand 11; CXCL1, chemokine (c-x-c motif) 1; CXCL2, chemokine (cx-c motif) 2; eGFR, estimated glomerular filtration rate; GDF-15, growth differentiation factor-15; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; hs-cTnT, highly sensitive cardiac troponin T; HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; LTβR, lymphotoxin β receptor; MCP-1, monocyte chemoattractant protein-1; MMP-9, matrix metallopeptidase-9; MPO, myeloperoxidase; OPG, osteoprotegerin; PG, peptidoglycan, PGLYRP-1, peptidoglycan recognition protein-1; Pro BNP, Pro-B-type natriuretic peptide; sCD40L, soluble CD40 Ligand; sESAM, soluble endothelial cell-

selective molecule; sICAM, soluble intracellular adhesion molecule; sRAGE, soluble receptor for advanced glycation end products; sVCAM, soluble vascular cell adhesion molecule; TNFR1A, tumor necrosis factor alpha-1 receptor

Supplemental Table 6. Baseline characteristics of the study population free from prevalent cardiovascular disease or type 2 diabetes mellitus in the Dallas Heart Study

Characteristic	High VAT – High LF (n=609)	High VAT – Low LF (n=257)	Low VAT – High LF (n=257)	Low VAT – Low LF (n=608)	*p*-value
Age, median (IQR)	48 (36-53)	46 (38-53)	41 (34-49)	40 (34-48)	<.001
Female, No. (%)	331 (54.35)	140 (54.47)	140 (54.47)	331 (54.44)	>.99
Race, No. (%)					
White	235 (38.59)	71 (27.63)	91 (35.41)	212 (34.87)	.02
Black	245 (40.23)	137 (53.31)	111 (43.19)	271 (44.57)	.01
Hispanic	116 (19.05)	48 (18.68)	44 (17.12)	112 (18.42)	.92
Weight, median (IQR), kg	93.44 (82.33-106.82)	86.18 (75.3-100.24)	75.75 (66.86-85.20)	69.45 (61.96-80.15)	<.001
BMI, median (IQR), kg/m^2	32.67 (29.41-36.85)	30.26 (27.42-34.21)	27.25 (24.89-30.38)	24.95 (22.47-27.50)	<.001
Waist circumference, median (IQR), cm	106 (99-114.5)	100 (94-108)	91.5 (85-98)	85.5 (78-92.5)	<.001
VAT, median (IQR), kg	2.76 (2.23-3.30)	2.38 (1.98-2.89)	1.56 (1.3-2.07)	1.36 (1.03-1.66)	<.001
Ectopic Liver Fat, median (IQR), %	6.98 (4.59-11.30)	2.33 (1.66 -2.84)	4.77 (3.90-7.47)	1.85 (1.20 -2.57)	<.001
Hypercholesterolemia, No. (%)	94 (15.44)	32 (12.45)	30 (11.67)	39 (6.41)	<.001
Low HDL, No. (%)	323 (53.04)	119 (46.30)	100 (38.91)	165 (27.14)	<.001
Metabolic Syndrome, No. (%)	319 (52.38)	82 (31.91)	57 (22.18)	42 (6.91)	<.001
Smoking, No. (%)[c]	132 (21.67)	58 (22.66)	52 (20.31)	168 (27.72)	.03
Hypertension, No. (%)[a]	227 (37.71)	84 (33.20)	60 (23.53)	96 (15.97)	<.001
HOMA-IR, median (IQR)[b]	4.15 (2.79-5.87)	2.86 (1.78-4.16)	2.42 (1.42-3.86)	1.56 (1.01-2.45)	<.001
ALT, median (IQR)	23 (16-30)	19 (15-28)	19 (14-29)	17 (13-24)	<.001

AST, median (IQR)	21 (18-26)	20 (17-26)	21 (18-27)	20 (17-24)	<.001
Family History – diabetes, No. (%)	255 (41.87)	88 (34.24)	78 (30.35)	197 (32.40)	<.001
Family History – CVD, No. (%)	513 (84.24)	213 (82.88)	201 (78.21)	469 (77.14)	.01
Physical activity[d]	114 (0-472)	124 (0-639)	156 (0-660)	239 (0-727)	<.001
Postmenopausal, No. (%)[e]	157 (25.86)	52 (20.23)	45 (17.51)	85 (14.07)	<.001
Aortic wall thickness, median (IQR)[f]	1.72 (1.55-1.89)	1.69 (1.51-1.85)	1.6 (1.44-1.78)	1.6 (1.44-1.74)	<.001

p-value is trend across all VAT/LF groups

[a] n=602, n=253, n=255, n=601 for high VAT-high LF, high VAT-low LF, low VAT-high LF, low VAT-low LF, respectively
[b] n=594, n=256, n=252, n=588 for high VAT-high LF, high VAT-low LF, low VAT-high LF, low VAT-low LF, respectively
[c] n=609, n=256, n=256, n=606 for high VAT-high LF, high VAT-low LF, low VAT-high LF, low VAT-low LF, respectively
[d] n=566, n=238, n=238, n=560 for high VAT-high LF, high VAT-low LF, low VAT-high LF, low VAT-low LF, respectively
[e] n=607, n=257, n=257, n=604 for high VAT-high LF, high VAT-low LF, low VAT-high LF, low VAT-low LF, respectively
[f] n=539, n=226, n=233, n=553 for high VAT-high LF, high VAT-low LF, low VAT-high LF, low VAT-low LF, respectively

Supplemental Table 7. Frequency of cardiovascular disease event types by body fat phenotype in the Dallas Heart Study

CVD Event	Phenotype			
	High VAT-High LF	**High VAT-Low LF**	**Low VAT-High LF**	**Low VAT-Low LF**
MI	16	8	2	5
CV Death	11	5	1	7
CABG	6	0	0	0
PCI	5	2	2	3
Stroke	7	7	3	6
Cerebrovascular Revascularization Event	0	1	2	2
PAR	0	1	0	1
CHF	8	4	2	3
TIA	4	1	1	0
Unstable Angina	0	0	1	1
Total	**57**	**29**	**14**	**28**

Abbreviations: MI, myocardial infarction. CABG, coronary artery bypass graft surgery. PCI, percutaneous coronary intervention. PAR, peripheral arterial revascularization procedure CHF, congestive heart failure. TIA, transient ischemic attack.

Supplemental Table 8. Associations of visceral adipose tissue (VAT) and liver fat (LF) as continuous markers with incident cardiovascular disease (CVD) and type 2 diabetes (T2DM) in the Dallas Heart Study

	Incident CVD		Incident T2DM	
	HR (95% CI)	***p*-value**	**Odds Ratio (95% CI)**	***p*-value**
VAT	1.24 (1.07 – 1.43)	.004	1.32 (1.06 – 1.64)	.01
LF	0.98 (0.84 – 1.14)	.76	1.28 (1.08 – 1.52)	.005
p-value for interaction		.19		.07

HR calculated for incident CVD and OR calculated for incident T2DM.
Model is adjusted for age and BMI.

Supplemental Table 9. Multivariable-adjusted associations of body fat phenotypes with incident cardiovascular disease and type 2 diabetes using additional covariates in the Dallas Heart Study

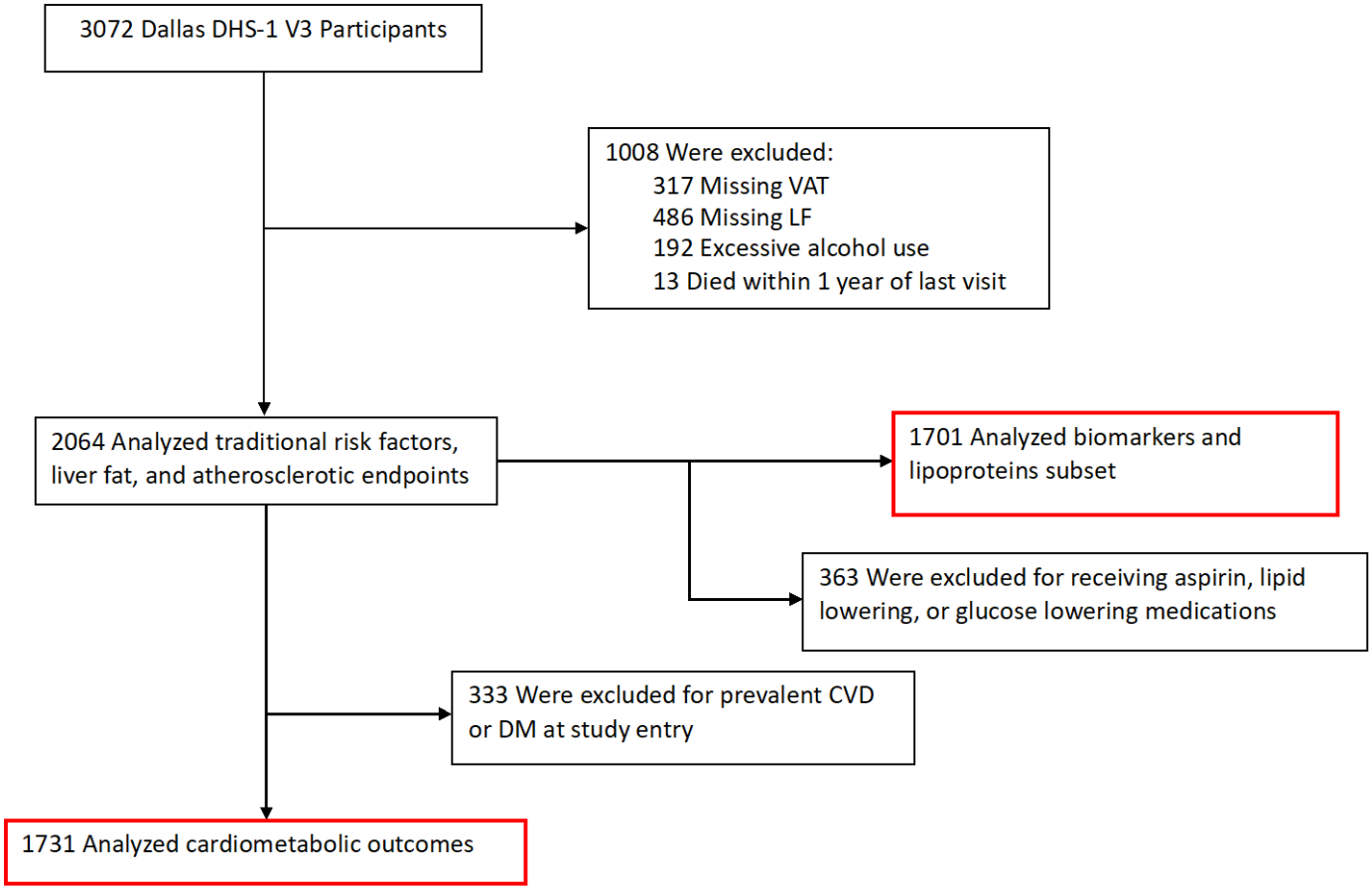
	Incident CVD		Incident T2DM	
	HR (95% CI)	***p*-value**	**Odds Ratio (95% CI)**	***p*-value**
Model 3				
High VAT-High LF	1.10 (0.62-1.98)	.73	5.52 (2.49-12.23)	<.001
High VAT-Low LF	1.31 (0.71-2.42)	.38	2.55 (1.01-6.45)	.04
Low VAT-High LF	1.16 (0.58-2.31)	.67	2.65 (1.05-6.72)	.04
Model 4				
High VAT – High LF	1.13 (0.63 – 2.02)	.69	4.29 (1.83 – 10.03)	<.001
High VAT – Low LF	1.29 (0.69 – 2.40)	.43	2.46 (0.94 – 6.43)	.07
Low VAT – High LF	1.22 (0.61 – 2.44)	.57	2.75 (1.05 – 7.19)	.04

HR calculated for incident CVD and OR calculated for incident T2DM. Referent group is low VAT-low LF.
Model 3 is adjusted for age, BMI, sex, race/ethnicity, smoking, hypercholesterolemia, hypertension, physical activity, postmenopausal status (women only), and family history of CVD or T2DM
Model 4 is adjusted for 3 + hs-CRP (CVD) or HOMA-IR (T2DM)

Supplemental Table 10. Baseline characteristics of the study population free from prevalent cardiovascular disease in the UK Biobank study

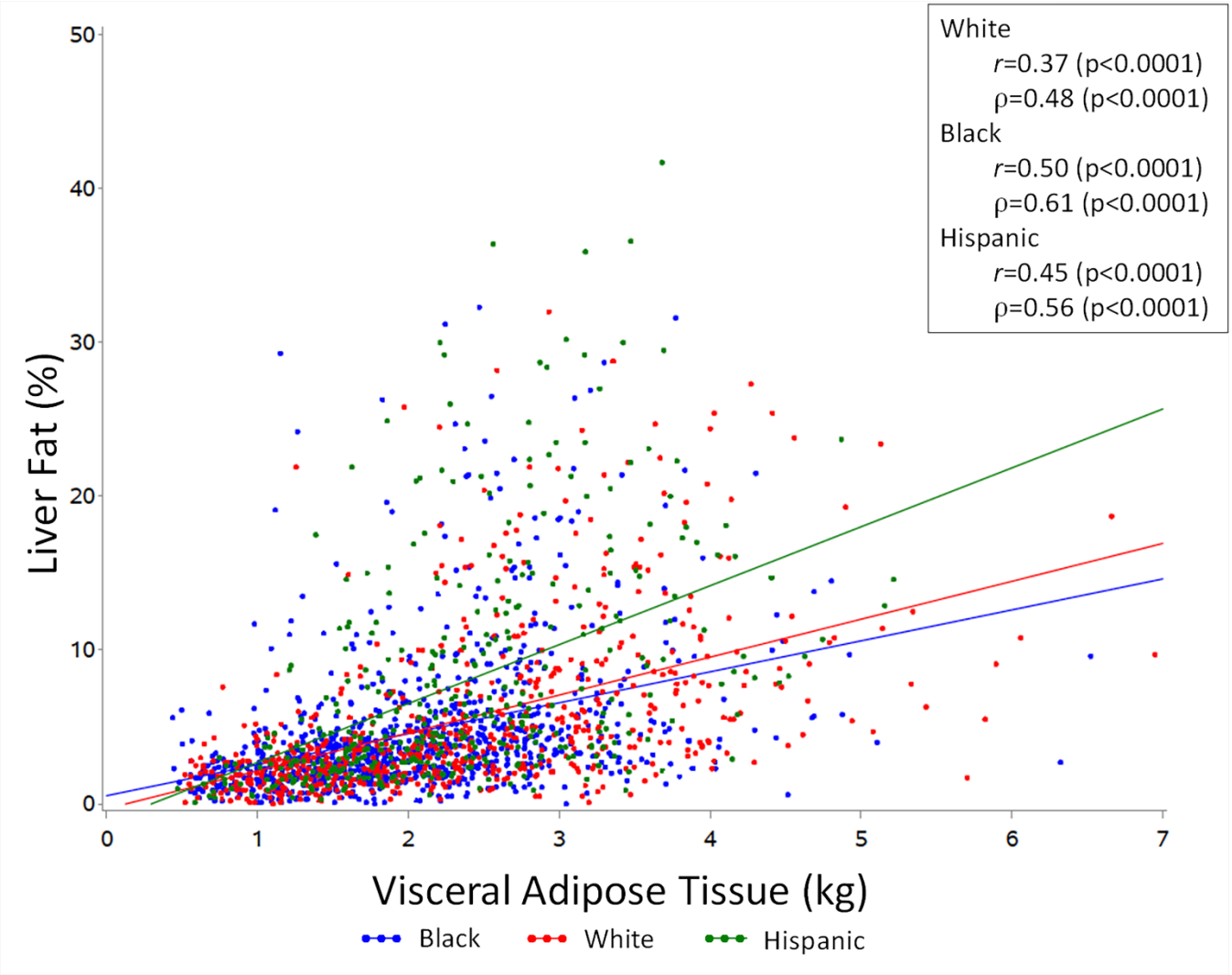
Characteristic	Overall (n=22354)	High VAT - High LF (n=7848)	High VAT - Low LF (n=2822)	Low VAT - High LF (n=2982)	Low VAT - Low LF (n=8702)	*p*-value
Age, median (IQR)	64 (57, 69)	64 (58, 69)	64 (58, 69)	64 (58, 69)	62 (56, 68)	<.001
Female, No. (%)	12067 (54.0)	4296 (54.7)	1540 (54.6)	1570 (52.6)	4661 (53.6)	.08
Race, No. (%) [White]	21743 (97.3)	7687 (97.9)	2771 (98.2)	2844 (95.4)	8441 (97.0)	<.001
Race, No. (%) [Black]	118 (0.5)	22 (0.3)	6 (0.2)	30 (1.0)	60 (0.7)	<.001
Race, No. (%) [Asian]	195 (0.9)	57 (0.7)	13 (0.5)	46 (1.5)	79 (0.9)	.04
Race, No. (%) [Chinese]	69 (0.3)	9 (0.1)	2 (0.1)	26 (0.9)	32 (0.4)	<.001
Race, No. (%) [Mixed]	90 (0.4)	26 (0.3)	9 (0.3)	13 (0.4)	42 (0.5)	.10
Weight, median (IQR)- kg	74.1 (64.7, 84.4)	83.0 (73.4, 93.5)	79.1 (70.5, 88.4)	69.0 (60.9, 77.7)	67.3 (59.8, 75.6)	<.001
Height, median (IQR)- cm	168.7 (162.2, 176.0)	168.3 (162.0, 176.0)	169.7 (163.0, 177.2)	168.0 (161.5, 175.0)	169.0 (162.5, 176.0)	.007
Body Mass Index, median (IQR)- kg/m2	25.7 (23.3, 28.6)	28.8 (26.6, 31.7)	27.2 (25.3, 29.3)	24.4 (22.6, 26.2)	23.5 (21.9, 25.2)	<.001
Waist Circumference, median (IQR)- cm	88.0 (79.0, 97.0)	88.0 (79.0, 97.0)	87.0 (79.0, 96.8)	88.0 (79.0, 97.0)	88.0 (79.0, 96.0)	.39
VAT, median (IQR)- L	3.2 (1.9, 4.9)	5.1 (3.6, 6.5)	4.2 (2.9, 5.6)	2.2 (1.6, 3.8)	1.8 (1.3, 2.8)	<.001
LF, median (IQR)- %	2.7 (1.8, 4.6)	5.4 (3.8, 9.1)	2.1 (1.7, 2.4)	3.6 (3.0, 4.7)	1.8 (1.4, 2.2)	<.001
Cholesterol Lowering Medication, No. (%)	9.9 (7.3, 13.0)	13.6 (11.5, 16.3)	11.9 (10.5, 13.8)	8.4 (6.9, 9.8)	7.1 (5.5, 8.7)	<.001
Current Smoker, No. (%)	9.6 (8.0, 12.1)	9.8 (8.3, 12.5)	9.7 (8.1, 12.2)	9.3 (7.8, 11.9)	9.4 (7.9, 11.8)	<.001

Supplemental Figure 1. Flow diagram of participant selection in the Dallas Heart Study



*Excessive alcohol consumption defined as >14 drinks/week or >4 drinks/day for men under age 65 or >7 drinks/week or >3 drinks/day for men over age 65 or women.

Supplemental Figure 2. Scatter plot of relationship between visceral adipose tissue and liver fat stratified by race/ethnicity in the Dallas Heart Study



Stratification of VAT (x-axis) and LF (y-axis) by ethnicity: White (red), Black (blue), and Hispanic (green). Pearson's *r* and Spearman's ρ correlation are reported for each ethnicity. Hispanic participants have higher LF per VAT, while White and Black participants have higher VAT per LF.