

Associations of body shape index (ABSI) and hip index with liver, metabolic, and inflammatory biomarkers in the UK Biobank cohort

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Supplementary Methods

Definition of covariates

The following variables were defined as previously described [ref. 10]: age at enrolment (continuous scale, 5 years increment), region of the assessment centre (London, North-West, North-East, Yorkshire and Humber, West Midlands, East Midlands, South-East, South-West, Wales, Scotland), weight change during the last year preceding enrolment (weight loss, stable weight, weight gain), smoking status (never smoked, former occasional smoker, former regular smoker, current smoker), alcohol consumption (≤ 3 times/month, ≤ 4 times/week, daily), physical activity (less active, moderately active, very active), prevalent and incident cancers, and deaths (used for exclusions), and in women, hormone replacement therapy (HRT) use (never, past, current), and age at the last live birth (no live births, <30 years, ≥ 30 years). Missing values were assigned the sex-specific median category for the study dataset as follows: weight change (stable weight), smoking status (former occasional smoker), alcohol consumption (≤ 4 times/week), physical activity (moderately active), HRT use (never use), age at the last live birth (<30 years).

Fasting time was based on Field [74-0.0] “*Fasting time*” and was used on a continuous scale for the adjustment of partial correlations and categorised for the adjustment of multivariable linear models, with three categories defined as follows: 0-2 hours, 3-4 hours, 5 or more hours. Samples with unknown fasting time were assigned the sex-specific median value (3 hours for both sexes), or category (3-4 hours).

Time of blood collection was extracted from Field [3166-0.0] “*Time blood sample collected*”, calculating time in decimal hours as: $(\text{Hours} * 3600 + \text{Minutes} * 60 + \text{Seconds}) / 3600$. This variable was used on a continuous scale for the adjustment of partial correlations and was categorised for the adjustment of multivariable linear models, with three categories defined as follows: Morning (≥ 8 to <12 o'clock, first at 8:25), Afternoon (≥ 12 to <16 o'clock), Evening (≥ 16 o'clock, last at 21:05). Unknown times of blood collection were assigned the sex-specific median value (14.371 for women, 14.533 for men) or category (Afternoon).

Townsend deprivation index was based on Field [189-0.0] “*Townsend deprivation index at recruitment*” and was used as an indicator of socioeconomic status on a continuous scale for the adjustment of partial correlations and as terciles for the adjustment of multivariable linear models. Missing values were replaced with the sex-specific median value (-2.374 for women, -2.344 for men) and then terciles were defined with the following study-specific boundaries: -3.291 and -1.046 for women; -3.285 and -0.955 for men.

Diabetes status at enrolment was based on Field [2443-0.0] “*Diabetes diagnosed by doctor*”, Question: “*Has a doctor ever told you that you have diabetes?*”, Answer: 1 “*Yes*” (for category Yes), or answer 0 “*No*” (for category No), considering Answer -1 “*Do not know*” and -3 “*Prefer not to answer*” as missing information. We further re-defined women with gestational diabetes only, answering 1 “*Yes*” to Field [4041-0.0] “*Gestational diabetes only*”, Question: “*Did you only have diabetes during pregnancy?*” into category No with respect to diabetes status at enrolment. We also re-classified to category Yes participants with self-reported diabetes: codes: 1220 “*diabetes*”, 1222 “*type 1 diabetes*”, or 1223 “*type 2 diabetes*” in Fields [20002-0.0/33] “*Non-cancer illness code, self-reported*”. We additionally re-classified as category Yes participants with self-reported insulin use, in men from Fields [6177-0.0/2] “*Medication for cholesterol, blood pressure or diabetes*”, Question “*Do you regularly take any of the following medications? (you can select more than one answer)*”, Answer 3 “*Insulin*”, and in women from Field [6153-0/3] “*Medication for cholesterol, blood pressure, diabetes, or take exogenous hormones*”, Answer 3 “*Insulin*”. Last, we re-classified as category Yes participants with self-reported antidiabetic drugs from Fields [20003-0/47] “*Treatment/medication code2*” (see list of medication codes in Supplementary Table S1). It was not possible to discriminate between type 1 and type 2 diabetes based on the available information. Participants with missing values were assigned the median sex-specific category (No).

Lipid lowering drugs use was based on Fields [6153-0.0/3] in women and Fields [6177-0.0/2]. Participants providing Answer 1 “*Cholesterol lowering medication*” were assigned to category Yes and those providing answer -7 “*None of the above*”, or only answers 2 “*Blood pressure medication*”, or 3 “*Insulin*”, or in women 4 “*Hormone replacement therapy*”, or 5 “*Oral contraceptive pill or minipill*” were assigned to category No. We then re-classified to category Yes participants with self-reported lipid-lowering drugs from Fields [20003-0/47] “*Treatment/medication code2*” (see list of medication codes in Supplementary Table S1, including fibrates as well as statins). Participants with missing values were assigned the median sex-specific category (No).

Anti-hypertensive drugs use was based on Fields [6153-0.0/3] in women and Fields [6177-0.0/2]. Participants providing Answer 2 “*Blood pressure medication*” were assigned to category Yes and those providing answer -7 “*None of the above*”, or only answers 1 “*Cholesterol lowering medication*”, or 3 “*Insulin*”, or in women 4 “*Hormone replacement therapy*”, or 5 “*Oral contraceptive pill or minipill*” were assigned to category No. For the remaining participants, this information was considered missing and for them we used the sex-specific median category (No).

Nonsteroidal anti-inflammatory drugs (NSAID) use (Aspirin & Ibuprofen) was based, as in [ref. 14], on Fields [6154-0.1/5] “*Medication for pain relief, constipation, heartburn*”; Question: “*Do you regularly take any of the following? (You can select more than one answer)*”; Answer 1: “*Aspirin*” OR Answer 2: “*Ibuprofen*” for category Yes (n=51,941 in the final study dataset). Category No was defined as any of the following Answers: 3 “*Paracetamol*”, 4 “*Ranitidine*”, 5 “*Omeprazole*”, 6 “*Laxatives*” OR -7 “*None of the above*”. We then re-classified to category Yes participants with

self-reported NSAID use from Fields [20003-0/47] "Treatment/ medication code2" (see list of medication codes in Supplementary Table S1) (further n=1689). Participants with missing values were assigned the median sex-specific category (No).

Paracetamol use was based on Fields [6154-0.1/5] "*Medication for pain relief, constipation, heartburn*", Answer 3 "*Paracetamol*" for category Yes (n=53,652 in the final study dataset). Category No was defined as any of the following Answers: 1 "*Aspirin*", 2 "*Ibuprofen*", 4 "*Ranitidine*", 5 "*Omeprazole*", 6 "*Laxatives*" OR -7 "*None of the above*". We then re-classified to category Yes participants with self-reported paracetamol use from Fields [20003-0/47] "Treatment/ medication code2" (see list of medication codes in Supplementary Table S1) (further n=767). Participants with missing values were assigned the median sex-specific category (No).

Oophorectomy (bilateral) was used to define menopausal status and was based on Field: [2834-0.0] "*Bilateral oophorectomy (both ovaries removed)*"; Question: "*Have you had BOTH ovaries removed?*"; Answer 1: "Yes" OR an answer to Fields [20004-0.0/31] "*Operation code (self-reported operation)*" including code: 1355 "*bilateral oophorectomy*".

Hysterectomy was used to define menopausal status and was based on Field: [3591-0.0] "*Ever had hysterectomy (womb removed)*"; Question: "*Have you had a hysterectomy (womb removed)?*"; Answer 1: "Yes" OR an answer to Fields [20004-0.0/31] "*Operation code (self-reported operation)*" including codes: 1357 "*hysterectomy*", 1358 "*hysterectomy with oophorectomy*", or 1359 "*hysterectomy with cervical sparing*".

Menopausal status (MP) was defined in three categories: Post-menopausal were classified women with bilateral oophorectomy OR with self-reported post-menopausal status from Field [2724-0.0] "*Had menopause*"; Question: "*Have you had your menopause (periods stopped)?*"; Answer 1: "Yes"; Pre-menopausal were classified women who had not been defined as post-menopausal above AND had reported pre-menopausal status with Answer 0: "No" to Field [2724-0.0] AND had not reported hysterectomy; Undetermined or missing included the remaining women.

Oral contraceptives use was determined for women based on Field [2784-0.0] "*Ever taken oral contraceptive pill*"; Question: "*Have you ever taken the contraceptive pill? (include the 'mini-pill')*" as follows: Current use – Answer 1: "Yes" AND Answer -11: "*Still taking the pill*" in Field [2804-0.0] "*Age when last used oral contraceptive pill*" Question: "*How old were you when you last used the contraceptive pill?*"; Past use – Answer 1: "Yes" in Field [2784-0.0] with any other answer (not -11) or missing in Field [2804-0.0]; Never use – Answer 0: "No" in Field [2784-0.0]. We further re-classified to category Current use women providing Answer 5 "*Oral contraceptive pill or minipill*" to Fields [6153-0.0/3]. Women with missing information for oral contraceptive use following the above assignments were assigned the median category (Past use).

Supplementary Table S1 Categories of self-reported medications

Code	Name	Code	Name
Part A: Included in the study and used for adjustment			
Nonsteroidal anti-inflammatory drugs (NSAID)			
1140856412	norgesic tablet	1140882268	aspirin+codeine 300mg/8mg tablet
1140861806	aspirin 75mg tablet	1140882392	aspirin+codeine
1140864860	nu-seals aspirin 75mg e/c tablet	1140910496	propionic acid-ibuprofen
1140868226	aspirin	1141153134	anadin ibuprofen 200mg tablet
1140868282	aspirin+methocarbamol 325mg/400mg tablet	1141157412	ibuprofen product
1140871310	ibuprofen	1141163138	aspirin+papaveretum 500mg/7.71mg dispersible tablet
1140871462	naproxen	1141164044	isosorbide mononitrate+aspirin
1140872040	aspirin+metoclopramide 325mg/5mg effervescent tablet	1141167844	dipyridamole+aspirin
1140878030	ibuprofen+codeine phosphate	1141184546	ibuprofen+pseudoephedrine hydrochloride
1140881612	naproxen+misoprostol	1141187776	nurofen 200mg tablet
1140882108	aspirin+cyclizine hydrochloride 500mg/25mg tablet	1141194296	lemsip flu 12hr
1140882190	aspirin+glycine 500mg/133mg dispersible tablet		ibuprofen+pseudoephedrine capsule
Paracetamol containing medicines			
1140868240	paracetamol product	1140928954	paracetamol+diphenhydramine hydrochloride 500mg/25mg tablet
1140868274	paracetamol+chlormezanone 450mg/100mg tablet	1141156856	paracetamol+domperidone 500mg/10mg tablet
1140868278	paracetamol+pentazocine 500mg/15mg tablet	1141163764	paracetamol+prometh hcl 120mg/1.5mg/5ml colour free s/f susp
1140868322	paracetamol+methionine 500mg/250mg tablet	1141169026	paracetamol+diphenhydramine hcl 120/12.5mg/5ml s/f oral soln
1140872044	paracetamol+metoclopramide 500mg/5mg tablet	1141185058	mandanol infant paracetamol 120mg/5ml oral suspension
1140882266	paracetamol+sodium salicylate 150mg/100mg tablet	1141185060	mandanol 6+ paracetamol 250mg/5ml oral suspension
1140882394	paracetamol + codeine	1141188500	paracetamol+pseudoephedrine hydrochloride
1140882396	paracetamol+dihydrocodeine tartrate	1141188516	anadin paracetamol 500mg tablet
1140884404	paracetamol+caffeine	1141188780	six plus parapaed paracetamol 250mg/5ml s/f oral suspension
1140884408	paracetamol+dextropropoxyphene	1141188784	junior parapaed paracetamol 120mg/5ml s/f oral suspension
1140926016	paracetamol+methionine 500mg/100mg tablet	2038460150	paracetamol
Part B: Excluded from the study			
Antidiabetic drugs			
1140857494	glibornuride	1140874724	daonil 5mg tablet
1140857496	glutril 25mg tablet	1140874726	semi-daonil 2.5mg tablet
1140857500	glymidine	1140874728	euglucon 2.5mg tablet
1140857502	gondafon 500mg tablet	1140874732	malix 2.5mg tablet
1140857506	pramidex 500mg tablet	1140874736	diabetamide 2.5mg tablet
1140874646	glipizide	1140874744	gliclazide
1140874650	glibenese 5mg tablet	1140874746	diamicron 80mg tablet
1140874652	minodiab 2.5mg tablet	1140883066	insulin product
1140874664	tolazamide	1140884600	metformin
1140874666	tolanase 100mg tablet	1141152590	glimepiride
1140874674	tolbutamide	1141153254	troglitazone
1140874678	glyconon 500mg tablet	1141153262	romozin 200mg tablet
1140874680	rastinon 500mg tablet	1141156984	amaryl 1mg tablet
1140874686	glucophage 500mg tablet	1141171646	pioglitazone
1140874690	orabet 500mg tablet	1141171652	actos 15mg tablet
1140874706	chlorpropamide	1141177600	rosiglitazone
1140874712	diabinese 100mg tablet	1141177606	avandia 4mg tablet
1140874716	glymese 250mg tablet	1141189090	rosiglitazone 1mg / metformin 500mg tablet
1140874718	glibenclamide	1141189094	avandamet 1mg / 500mg tablet

Code	Name	Code	Name
Lipid lowering drugs			
1140861848	colestid 5g/sachet granules	1140861954	fenofibrate
1140861856	gemfibrozil	1140861958	simvastatin
1140861858	lipid 300 capsule	1140861970	lipostat 10mg tablet
1140861866	nicofuranose	1140862026	ciprofibrate
1140861868	nicotinic acid product	1140862028	modalim 100mg tablet
1140861876	probucol	1140888590	colestipol
1140861878	lurselle 250mg tablet	1140888594	fluvastatin
1140861892	acipimox	1140888648	pravastatin
1140861894	olbetam 250mg capsule	1140910632	eptastatin
1140861922	lipid lowering drug	1140910652	synvinolin
1140861924	bezafibrate	1140910654	velastatin
1140861926	bezalip 200mg tablet	1141146234	atorvastatin
1140861928	bezalip-mono 400mg m/r tablet	1141157260	bezafibrate product
1140861936	questran 4g/sachet powder	1141157262	gemfibrozil product
1140861942	cholestyramine+aspartame 4g/sachet powder	1141192410	rosuvastatin
1140861944	clofibrate	1141192414	crestor 10mg tablet
1140861946	atromid-s 500mg capsule		
Glucocorticoids			
1140857532	cortelan 25mg tablet	1140874896	hydrocortisone
1140857534	oradexon 500micrograms tablet	1140874930	prednisolone
1140865840	predfoam 20mg enema	1140874936	deltacortril enteric 2.5mg e/c tablet
1140868364	prednisone	1140874940	deltastab 1mg tablet
1140868370	decortisyl 5mg tablet	1140874944	precortisyl 1mg tablet
1140868426	triamcinolone	1140874950	prednesol 5mg tablet
1140868434	ledercort 2mg tablet	1140874954	hydrocortistab 20mg tablet
1140874790	betamethasone	1140874956	hydrocortone 10mg tablet
1140874792	betnelan 500mcg tablet	1140874976	methylprednisolone
1140874794	betnesol 500mcg soluble tablet	1140874978	medrone 2mg tablet
1140874810	cortistab 5mg tablet	1140884704	cortisone product
1140874814	cortisyl 25mg tablet	1141157402	prednisolone product
1140874816	dexamethasone	1141173346	cortisone
1140874822	decadron 500micrograms tablet		

Coding 4 in UK Biobank.

Supplementary Table S2 Biomarker availability

	Field Value	Field QC	Min	Max	Low	Reportable	High	Available
MEN								
Liver function tests								
Bilirubin T	30840-0.0	30846-0.0	1.43	130.76	8	115,870 (100)	0	115,878 (95.1)
Bilirubin D	30660-0.0	30666-0.0	1.00	47.56	8126	107,807 (93.0)	0	115,933 (95.1)
ALP	30610-0.0	30616-0.0	15.0	1039.7	12	116,386 (100)	3	116,401 (95.5)
GGT	30730-0.0	30736-0.0	5.80	1101.0	3	116,334 (100)	16	116,353 (95.5)
AST	30650-0.0	30656-0.0	3.30	571.5	2	115,910 (100)	1	115,913 (95.1)
ALT	30620-0.0	30626-0.0	3.18	416.49	7	116,300 (100)	4	116,311 (95.4)
Metabolic biomarkers								
HDL-C	30760-0.0	30766-0.0	0.347	4.186	3	107,421 (100)	0	107,424 (88.1)
ApoA1	30630-0.0	30636-0.0	0.420	2.499	4	107,275 (99.9)	98	107,377 (88.1)
LDL-C	30780-0.0	30786-0.0	0.266	8.992	2	116,141 (100)	0	116,143 (95.3)
ApoB	30640-0.0	30646-0.0	0.401	2.00	152	115,620 (99.8)	68	115,840 (95.0)
Triglycerides	30870-0.0	30876-0.0	0.233	11.278	2	116,272 (100)	50	116,324 (95.4)
HbA1c	30750-0.0	30756-0.0	15.40	266.3	56	115,971 (100)	0	116,027 (95.2)
Glucose	30740-0.0	30746-0.0	1.542	36.813	2	107,344 (100)	0	107,346 (88.1)
Inflammatory biomarkers								
Lymphocytes	30120-0.0	-	0.05	75.5	3	118,462 (100)	0	118,465 (97.2)
Monocytes	30130-0.0	-	0.01	10.22	16	118,449 (100)	0	118,465 (97.2)
Neutrophils	30140-0.0	-	0.02	25.42	1	118,464 (100)	0	118,465 (97.2)
CRP	30710-0.0	30716-0.0	0.08	79.96	25	116,122 (99.9)	55	116,202 (95.3)
WOMEN								
Liver function tests								
Bilirubin T	30840-0.0	30846-0.0	1.08	77.96	1	128,818 (100)	0	128,819 (95.0)
Bilirubin D	30660-0.0	30666-0.0	1.00	25.96	28071	100,866 (78.2)	0	128,937 (95.1)
ALP	30610-0.0	30616-0.0	10.1	1119.9	11	129,369 (100)	0	129,380 (95.4)
GGT	30730-0.0	30736-0.0	5.00	1132.7	6	129,311 (100)	5	129,322 (95.4)
AST	30650-0.0	30656-0.0	4.10	947.2	2	128,902 (100)	1	128,905 (95.1)
ALT	30620-0.0	30626-0.0	3.01	469.94	18	129,350 (100)	5	129,373 (95.4)
Metabolic biomarkers								
HDL-C	30760-0.0	30766-0.0	0.228	4.401	1	117,436 (100)	0	117,437 (86.6)
ApoA1	30630-0.0	30636-0.0	0.672	2.5	3	116,589 (99.5)	576	117,168 (86.4)
LDL-C	30780-0.0	30786-0.0	0.803	9.554	1	129,157 (100)	0	129,158 (95.3)
ApoB	30640-0.0	30646-0.0	0.400	2.0	196	128,943 (99.8)	111	129,250 (95.3)
Triglycerides	30870-0.0	30876-0.0	0.252	11.227	1	129,289 (100)	4	129,294 (95.4)
HbA1c	30750-0.0	30756-0.0	15.40	127.7	47	128,745 (100)	0	128,792 (95.0)
Glucose	30740-0.0	30746-0.0	1.798	24.045	1	117,357 (100)	0	117,358 (86.6)
Inflammatory biomarkers								
Lymphocytes	30120-0.0	-	0.01	79.99	2	131,147 (100)	0	131,149 (96.7)
Monocytes	30130-0.0	-	0.01	12.26	56	131,093 (100)	0	131,149 (96.7)
Neutrophils	30140-0.0	-	0.01	18.30	1	131,148 (100)	0	131,149 (96.7)
CRP	30710-0.0	30716-0.0	0.08	79.95	48	129,149 (99.9)	52	129,249 (95.3)

ALP – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **AST** – aspartate aminotransferase; **Bilirubin D** – direct bilirubin; **Bilirubin T** – total bilirubin; **CRP** – C-reactive protein; **HbA1c** – glycated haemoglobin; **HDL-C** – high-density-lipoprotein cholesterol; **LDL-C** – low-density-lipoprotein cholesterol.

Field QC – biomarker reportability field; **Field Value** – biomarker value field; **Min** – lowest detected value; **Max** – highest detected value; **Low** – number of participants with attempted measurements but with levels below the limit of detection (percentage from total attempted measurements per

sex); **Reported** – number of participants with reported values (percentage from total attempted measurements per sex); **High** – number of participants with attempted measurements above the upper limit of detection (percentage from total attempted measurements per sex); **Available** – number of participants with attempted measurements, comprising reported values and imputation of missing low and high levels (percentage from total in the study dataset per sex). Note that the study dataset included participants with available measurements (low, reported, or high) for at least one of the examined biomarkers.

Reportability codes:

1: “*Reportable at assay and after aliquot correction, if attempted*” – values used as provided.

2: “*Reportable at assay but not reportable after any corrections (too low)*” – see code 4.

3: “*Reportable at assay but not reportable after any corrections (too high)*” – see code 5.

4: “*Not reportable at assay (too low)*” – values were replaced with half the lowest detected level for all except direct bilirubin, which was imputed with quantile regression imputation of left-censored data (QRILC) (**imputeLCMD** v2.0 package in R), following log-transformation.

5: “*Not reportable at assay (too high)*” – replaced with the highest detected value.

Biomarker values for participants without attempted measurements were considered missing and these participants were excluded from the analysis of the corresponding biomarker.

Supplementary Table S3 Characteristics of study participants by sex and body shape phenotypes

	MEN					WOMEN				
	Overall	Pear	Slim	Wide	Apple	Overall	Pear	Slim	Wide	Apple
Cohort size: n (% per sex)	121,879	32,736 (26.9)	37,383 (30.7)	32,504 (26.7)	19,256 (15.8)	135,559	35,985 (26.5)	31,054 (22.9)	39,632 (29.2)	28,888 (21.3)
Anthropometry: mean (SD)										
Height (cm)	176.5 (6.7)	176.5 (6.7)	176.1 (6.6)	176.9 (6.8)	176.7 (6.7)	163.1 (6.2)	163.0 (6.2)	163.0 (6.2)	162.9 (6.3)	163.5 (6.1)
Weight (kg)	84.6 (13)	83.5 (13.1)	84.4 (12.4)	84.8 (13.6)	86.2 (12.9)	69.8 (12.4)	68.4 (12.3)	68.6 (11.6)	70.6 (13.2)	71.7 (11.8)
Waist circumference (cm)	94.8 (10.2)	91.3 (9.3)	91.2 (8.8)	99.4 (9.9)	100.1 (9.3)	82.5 (11.1)	77.3 (9.1)	77.0 (8.6)	87.5 (11.2)	88.0 (9.8)
Hip circumference (cm)	102.7 (6.8)	104.3 (6.5)	99.7 (5.9)	105.4 (6.8)	101.0 (5.9)	102.2 (9.1)	103.7 (9.0)	97.9 (7.7)	105.5 (9.7)	100.2 (7.5)
Waist-to-hip ratio	0.92 (0.06)	0.87 (0.05)	0.91 (0.05)	0.94 (0.05)	0.99 (0.05)	0.81 (0.07)	0.74 (0.04)	0.79 (0.04)	0.83 (0.05)	0.88 (0.05)
BMI category: n (%)										
Normal weight: BMI $\geq$ 18.5 to <25	36,310 (29.8)	11,164 (34.1)	10,187 (27.3)	10,316 (31.7)	4643 (24.1)	61,755 (45.6)	18,681 (51.9)	15,355 (49.4)	17,127 (43.2)	10,592 (36.7)
Overweight: BMI $\geq$ 25 to <30	62,024 (50.9)	15,912 (48.6)	20,029 (53.6)	15,760 (48.5)	10,323 (53.6)	49,574 (36.6)	11,813 (32.8)	11,255 (36.2)	14,007 (35.3)	12,499 (43.3)
Obese: BMI $\geq$ 30 to <45	23,545 (19.3)	5660 (17.3)	7167 (19.2)	6428 (19.8)	4290 (22.3)	24,230 (17.9)	5491 (15.3)	4444 (14.3)	8498 (21.4)	5797 (20.1)
Weight change, last year: n (%)										
Lost weight	15,788 (13.0)	4452 (13.6)	5483 (14.7)	3524 (10.8)	2329 (12.1)	18,929 (14.0)	4585 (12.7)	4845 (15.6)	5115 (12.9)	4384 (15.2)
Stable weight	77,851 (63.9)	21,547 (65.8)	23,919 (64.0)	20,671 (63.6)	11,714 (60.8)	71,542 (52.8)	19,726 (54.8)	16,788 (54.1)	20,508 (51.7)	14,520 (50.3)
Gained weight	26,017 (21.3)	6227 (19.0)	7358 (19.7)	7627 (23.5)	4805 (25.0)	42,870 (31.6)	11,108 (30.9)	8957 (28.8)	13,288 (33.5)	9517 (32.9)
Missing	2223 (1.8)	510 (1.6)	623 (1.7)	682 (2.1)	408 (2.1)	2218 (1.6)	566 (1.6)	464 (1.5)	721 (1.8)	467 (1.6)
Smoking status: n (%)										
Never smoked	45,279 (37.2)	13,193 (40.3)	14,479 (38.7)	11,328 (34.9)	6279 (32.6)	60,518 (44.6)	17,547 (48.8)	14,010 (45.1)	17,404 (43.9)	11,557 (40.0)
Former occasional smoker	33,394 (27.4)	9814 (30.0)	10,163 (27.2)	8796 (27.1)	4621 (24.0)	38,740 (28.6)	10,549 (29.3)	8843 (28.5)	11,433 (28.8)	7915 (27.4)
Former regular smoker	27,727 (22.7)	6385 (19.5)	7936 (21.2)	8193 (25.2)	5213 (27.1)	24,374 (18.0)	5616 (15.6)	5376 (17.3)	7333 (18.5)	6049 (20.9)
Current smoker	15,161 (12.4)	3272 (10.0)	4698 (12.6)	4096 (12.6)	3095 (16.1)	11,567 (8.5)	2186 (6.1)	2759 (8.9)	3350 (8.5)	3272 (11.3)
Missing	318 (0.3)	72 (0.2)	107 (0.3)	91 (0.3)	48 (0.2)	360 (0.3)	87 (0.2)	66 (0.2)	112 (0.3)	95 (0.3)
Alcohol intake: n (%)										
Up to three times a month	23,157 (19.0)	6095 (18.6)	7111 (19.0)	6169 (19.0)	3782 (19.6)	43,504 (32.1)	11,581 (32.2)	9694 (31.2)	13,127 (33.1)	9102 (31.5)
Up to four times a week	67,421 (55.3)	18,647 (57.0)	21,733 (58.1)	17,098 (52.6)	9943 (51.6)	68,478 (50.5)	18,592 (51.7)	16,223 (52.2)	19,356 (48.8)	14,307 (49.5)
Daily	31,228 (25.6)	7974 (24.4)	8521 (22.8)	9217 (28.4)	5516 (28.6)	23,507 (17.3)	5798 (16.1)	5122 (16.5)	7125 (18.0)	5462 (18.9)
Missing	73 (0.1)	20 (0.1)	18 (0.0)	20 (0.1)	15 (0.1)	70 (0.1)	14 (0.0)	15 (0.0)	24 (0.1)	17 (0.1)
Physical activity: n (%)										
Inactive	16,443 (13.5)	3685 (11.3)	3908 (10.5)	5692 (17.5)	3158 (16.4)	21,081 (15.6)	5387 (15.0)	4083 (13.1)	7009 (17.7)	4602 (15.9)
Moderately active	52,282 (42.9)	13,427 (41.0)	14,470 (38.7)	15,530 (47.8)	8855 (46.0)	69,967 (51.6)	18,480 (51.4)	15,145 (48.8)	21,275 (53.7)	15,067 (52.2)
Active	52,892 (43.4)	15,576 (47.6)	18,932 (50.6)	11,194 (34.4)	7190 (37.3)	44,150 (32.6)	12,050 (33.5)	11,769 (37.9)	11,198 (28.3)	9133 (31.6)
Missing	262 (0.2)	48 (0.1)	73 (0.2)	88 (0.3)	53 (0.3)	361 (0.3)	68 (0.2)	57 (0.2)	150 (0.4)	86 (0.3)
Townsend index										
Mean (SD)	-1.55 (2.96)	-1.71 (2.87)	-1.51 (2.98)	-1.55 (2.97)	-1.32 (3.07)	-1.63 (2.86)	-1.80 (2.75)	-1.67 (2.87)	-1.56 (2.88)	-1.47 (2.95)
Missing: n (%)	150 (0.1)	49 (0.1)	48 (0.1)	31 (0.1)	22 (0.1)	151 (0.1)	38 (0.1)	41 (0.1)	41 (0.1)	31 (0.1)
Time of sample collection: n (%)										
Morning: $\geq$ 8 am to <12 am	33,871 (27.8)	9716 (29.7)	10,763 (28.8)	8430 (25.9)	4962 (25.8)	34,783 (25.7)	10,012 (27.8)	8326 (26.8)	9375 (23.7)	7070 (24.5)
Afternoon: $\geq$ 12 am to <4 pm	44,251 (36.3)	11,495 (35.1)	13,055 (34.9)	12,512 (38.5)	7189 (37.3)	56,067 (41.4)	14,681 (40.8)	12,163 (39.2)	17,216 (43.4)	12,007 (41.6)
Evening: $\geq$ 4 pm to $\leq$ 8:15 pm	43,656 (35.8)	11,488 (35.1)	13,547 (36.2)	11,531 (35.5)	7090 (36.8)	44,558 (32.9)	11,254 (31.3)	10,545 (34.0)	12,978 (32.7)	9781 (33.9)
Missing	101 (0.1)	37 (0.1)	18 (<0.0)	31 (0.1)	15 (0.1)	151 (0.1)	38 (0.1)	20 (0.1)	63 (0.2)	30 (0.1)

	MEN					WOMEN				
	Overall	Pear	Slim	Wide	Apple	Overall	Pear	Slim	Wide	Apple
Fasting time: n (%)										
0-2 hours	33,771 (27.7)	9319 (28.5)	10,750 (28.8)	8512 (26.2)	5190 (27.0)	36,840 (27.2)	9918 (27.6)	8795 (28.3)	10320 (26.0)	7807 (27.0)
3-4 hours	59,352 (48.7)	15,801 (48.3)	17,945 (48.0)	16,222 (49.9)	9384 (48.7)	70,446 (52.0)	18,721 (52.0)	15,904 (51.2)	20,822 (52.5)	14,999 (51.9)
≥5 hours	28,754 (23.6)	7615 (23.3)	8687 (23.2)	7770 (23.9)	4682 (24.3)	28,268 (20.9)	7343 (20.4)	6354 (20.5)	8490 (21.4)	6081 (21.1)
Missing	2	1	1	-	-	5	3	1	-	1
NSAID: n (%)										
No	97,571 (80.1)	26,599 (81.3)	29,804 (79.7)	25,957 (79.9)	15,211 (79.0)	104,066 (76.8)	27,618 (76.7)	23,843 (76.8)	30,458 (76.9)	22,147 (76.7)
Yes	23,126 (19.0)	5878 (18.0)	7218 (19.3)	6220 (19.1)	3810 (19.8)	30,504 (22.5)	8124 (22.6)	6990 (22.5)	8853 (22.3)	6537 (22.6)
Missing	1182 (1.0)	259 (0.8)	361 (1.0)	327 (1.0)	235 (1.2)	989 (0.7)	243 (0.7)	221 (0.7)	321 (0.8)	204 (0.7)
Paracetamol: n (%)										
No	100,676 (82.6)	27,541 (84.1)	31,028 (83)	26,570 (81.7)	15,537 (80.7)	100,142 (73.9)	26,878 (74.7)	23,193 (74.7)	28,859 (72.8)	21,212 (73.4)
Yes	20,009 (16.4)	4935 (15.1)	5992 (16)	5604 (17.2)	3478 (18.1)	34,410 (25.4)	8858 (24.6)	7640 (24.6)	10444 (26.4)	7468 (25.9)
Missing	1194 (1.0)	260 (0.8)	363 (1.0)	330 (1.0)	241 (1.3)	1007 (0.7)	249 (0.7)	221 (0.7)	329 (0.8)	208 (0.7)
Assessment region: n (%)										
London	13,950 (11.4)	3706 (11.3)	4277 (11.4)	3612 (11.1)	2355 (12.2)	16,469 (12.1)	4172 (11.6)	3650 (11.8)	4833 (12.2)	3814 (13.2)
North-West	18,273 (15.0)	4579 (14.0)	7105 (19.0)	3660 (11.3)	2929 (15.2)	18,974 (14.0)	4580 (12.7)	5578 (18.0)	4498 (11.3)	4318 (14.9)
North-East	14,557 (11.9)	3714 (11.3)	5368 (14.4)	3387 (10.4)	2088 (10.8)	16,136 (11.9)	4343 (12.1)	3934 (12.7)	4307 (10.9)	3552 (12.3)
Yorkshire and Humber	18,609 (15.3)	4804 (14.7)	5180 (13.9)	5337 (16.4)	3288 (17.1)	21,084 (15.6)	5990 (16.6)	4339 (14.0)	6340 (16.0)	4415 (15.3)
West Midlands	11,114 (9.1)	2343 (7.2)	3763 (10.1)	3111 (9.6)	1897 (9.9)	10,928 (8.1)	2351 (6.5)	3094 (10.0)	3168 (8.0)	2315 (8.0)
East Midlands	8549 (7.0)	2598 (7.9)	1841 (4.9)	2711 (8.3)	1399 (7.3)	9738 (7.2)	2911 (8.1)	1188 (3.8)	3397 (8.6)	2242 (7.8)
South-East	11,411 (9.4)	3616 (11.0)	1682 (4.5)	4474 (13.8)	1639 (8.5)	12,840 (9.5)	3823 (10.6)	1469 (4.7)	5189 (13.1)	2359 (8.2)
South-West	11,254 (9.2)	3417 (10.4)	3235 (8.7)	2876 (8.8)	1726 (9.0)	13,050 (9.6)	3582 (10.0)	3168 (10.2)	3602 (9.1)	2698 (9.3)
Wales	5122 (4.2)	1394 (4.3)	1449 (3.9)	1492 (4.6)	787 (4.1)	5651 (4.2)	1352 (3.8)	1271 (4.1)	1872 (4.7)	1156 (4.0)
Scotland	9040 (7.4)	2565 (7.8)	3483 (9.3)	1844 (5.7)	1148 (6.0)	10,689 (7.9)	2881 (8.0)	3363 (10.8)	2426 (6.1)	2019 (7.0)
Menopausal status: n (%)										
Pre-menopausal						40,814 (30.1)	12,269 (34.1)	11,380 (36.6)	9381 (23.7)	7784 (26.9)
Post-menopausal						81,551 (60.2)	20,234 (56.2)	16,659 (53.6)	26,458 (66.8)	18,200 (63.0)
Undetermined or missing						13,194 (9.7)	3482 (9.7)	3015 (9.7)	3793 (9.6)	2904 (10.1)
HRT use: n (%)										
Never						96,512 (71.2)	26,684 (74.2)	23,453 (75.5)	26,508 (66.9)	19,867 (68.8)
Past						38,714 (28.6)	9224 (25.6)	7528 (24.2)	13,019 (32.8)	8943 (31.0)
Missing						333 (0.2)	77 (0.2)	73 (0.2)	105 (0.3)	78 (0.3)
OC use: n (%)										
Never						21,519 (15.9)	5491 (15.3)	4459 (14.4)	7003 (17.7)	4566 (15.8)
Past						113,782 (83.9)	30,422 (84.5)	26,545 (85.5)	32,544 (82.1)	24,271 (84.0)
Missing						258 (0.2)	72 (0.2)	50 (0.2)	85 (0.2)	51 (0.2)
Age at the last live birth: n (%)										
No live births						25,650 (18.9)	7504 (20.9)	6336 (20.4)	7047 (17.8)	4763 (16.5)
< 30 years						48,308 (35.6)	12,479 (34.7)	10,710 (34.5)	14,442 (36.4)	10,677 (37.0)
≥ 30 years						61,349 (45.3)	15,960 (44.4)	13,961 (45.0)	18,047 (45.5)	13,381 (46.3)
Missing						252 (0.2)	42 (0.1)	47 (0.2)	96 (0.2)	67 (0.2)

ABSI – a body shape index (cut-offs ≥ 80 for men, ≥ 73 for women); **Apple** – large-ABSI-small-HI; **BMI** – body mass index; **HRT** – hormone replacement therapy; **HI** – hip index (cut-offs ≥ 49 for men, ≥ 64 for women); **NSAID** – nonsteroidal anti-inflammatory drugs; **OC** – oral contraceptives; **Pear** – small-ABSI-large-HI; **SD** – standard deviation; **Slim** – small-ABSI-small-HI; **Wide** – large-ABSI-large-HI; **n (%)** – number (percentage from total per column).

Supplementary Table S4 Linear and non-linear associations of biomarkers with body size and body shape indices (continuous)

		MEN				WOMEN			
		Count	BMI	ABSI	HI	Count	BMI	ABSI	HI
			(per one SD)	(per one SD)	(per one SD)		(per one SD)	(per one SD)	(per one SD)
Liver function tests									
Bilirubin total	LIN	115,878	-0.06 (-0.07 to -0.06)**	-0.06 (-0.06 to -0.05)**	0.02 (0.01 to 0.02)**	128,819	-0.11 (-0.11 to -0.10)**	-0.06 (-0.06 to -0.05)**	0.01 (0.01 to 0.02)*
	SB1		-0.05 (-0.07 to -0.03)**	-0.06 (-0.08 to -0.05)**	0.03 (0.02 to 0.04)*		-0.19 (-0.21 to -0.17)**	-0.09 (-0.10 to -0.08)**	0.01 (0.00 to 0.02)
	SB2		-0.01 (-0.03 to 0.00)	0.01 (-0.01 to 0.02)	-0.02 (-0.03 to 0.00)		0.09 (0.07 to 0.10)**	0.04 (0.03 to 0.06)**	0.00 (-0.01 to 0.02)
p non-linearity			0.106	0.464	0.020		1*10⁻²¹	2*10⁻⁷	0.547
Bilirubin direct	LIN	115,933	-0.07 (-0.07 to -0.06)**	-0.06 (-0.07 to -0.06)**	0.03 (0.03 to 0.04)**	128,937	-0.10 (-0.11 to -0.10)**	-0.08 (-0.08 to -0.07)**	0.03 (0.03 to 0.04)**
	SB1		-0.14 (-0.15 to -0.12)**	-0.09 (-0.11 to -0.08)**	0.03 (0.02 to 0.05)**		-0.24 (-0.26 to -0.22)**	-0.13 (-0.14 to -0.11)**	0.02 (0.01 to 0.04)
	SB2		0.08 (0.06 to 0.09)**	0.04 (0.03 to 0.06)**	0.00 (-0.02 to 0.01)		0.15 (0.13 to 0.16)**	0.06 (0.05 to 0.08)**	0.01 (0.00 to 0.03)
p non-linearity			3*10⁻¹⁹	4*10⁻⁷	0.901		2*10⁻⁶⁰	4*10⁻¹⁵	0.070
ALP	LIN	116,401	0.06 (0.05 to 0.07)**	0.09 (0.08 to 0.10)**	-0.02 (-0.03 to -0.01)**	129,380	0.17 (0.17 to 0.18)**	0.08 (0.07 to 0.08)**	0.01 (0.00 to 0.01)
	SB1		0.07 (0.05 to 0.08)**	0.07 (0.06 to 0.09)**	-0.04 (-0.05 to -0.02)**		0.25 (0.24 to 0.27)**	0.09 (0.07 to 0.10)**	0.00 (-0.01 to 0.01)
	SB2		-0.01 (-0.02 to 0.01)	0.02 (0.01 to 0.04)	0.02 (0.01 to 0.04)		-0.08 (-0.10 to -0.07)**	-0.01 (-0.03 to 0.00)	0.01 (0.00 to 0.02)
p non-linearity			0.382	0.006	0.003		5*10⁻²⁴	0.053	0.155
GGT	LIN	116,353	0.26 (0.25 to 0.26)**	0.12 (0.11 to 0.12)**	-0.07 (-0.08 to -0.06)**	129,322	0.22 (0.21 to 0.22)**	0.12 (0.11 to 0.12)**	-0.06 (-0.07 to -0.06)**
	SB1		0.38 (0.36 to 0.40)**	0.13 (0.11 to 0.14)**	-0.06 (-0.07 to -0.04)**		0.13 (0.11 to 0.15)**	0.14 (0.13 to 0.15)**	-0.09 (-0.10 to -0.07)**
	SB2		-0.14 (-0.15 to -0.12)**	-0.01 (-0.03 to 0.00)	-0.02 (-0.03 to 0.00)		0.09 (0.08 to 0.11)**	-0.03 (-0.04 to -0.01)	0.03 (0.02 to 0.05)*
p non-linearity			2*10⁻⁶⁰	0.168	0.021		4*10⁻²⁷	4*10⁻⁴	9*10⁻⁶
AST	LIN	115,913	0.15 (0.15 to 0.16)**	0.02 (0.01 to 0.02)**	-0.04 (-0.04 to -0.03)**	128,905	0.04 (0.03 to 0.04)**	0.04 (0.04 to 0.05)**	-0.04 (-0.05 to -0.03)**
	SB1		0.10 (0.08 to 0.12)**	-0.02 (-0.03 to -0.01)	-0.03 (-0.04 to -0.02)*		-0.12 (-0.14 to -0.10)**	0.02 (0.01 to 0.04)	-0.06 (-0.07 to -0.05)**
	SB2		0.06 (0.04 to 0.08)**	0.05 (0.03 to 0.06)**	-0.01 (-0.02 to 0.01)		0.17 (0.15 to 0.18)**	0.02 (0.01 to 0.04)	0.03 (0.01 to 0.04)
p non-linearity			2*10⁻¹¹	2*10⁻⁸	0.318		5*10⁻⁷⁵	0.002	1*10⁻⁴
ALT	LIN	116,311	0.33 (0.33 to 0.34)**	0.10 (0.09 to 0.10)**	-0.08 (-0.09 to -0.08)**	129,373	0.23 (0.22 to 0.23)**	0.12 (0.11 to 0.13)**	-0.08 (-0.09 to -0.08)**
	SB1		0.46 (0.44 to 0.47)**	0.13 (0.12 to 0.14)**	-0.06 (-0.07 to -0.04)**		0.18 (0.16 to 0.20)**	0.15 (0.14 to 0.17)**	-0.10 (-0.11 to -0.09)**
	SB2		-0.14 (-0.16 to -0.13)**	-0.04 (-0.06 to -0.03)**	-0.03 (-0.05 to -0.02)*		0.05 (0.03 to 0.07)**	-0.04 (-0.05 to -0.02)**	0.02 (0.01 to 0.03)
p non-linearity			7*10⁻⁷⁰	1*10⁻⁷	2*10⁻⁶		1*10⁻⁸	6*10⁻⁷	0.007
Metabolic biomarkers									
HDL-C	LIN	107,424	-0.30 (-0.31 to -0.30)**	-0.08 (-0.09 to -0.07)**	0.08 (0.08 to 0.09)**	117,437	-0.30 (-0.30 to -0.29)**	-0.16 (-0.16 to -0.15)**	0.11 (0.11 to 0.12)**
	SB1		-0.53 (-0.55 to -0.52)**	-0.14 (-0.16 to -0.13)**	0.06 (0.05 to 0.07)**		-0.43 (-0.45 to -0.41)**	-0.23 (-0.24 to -0.21)**	0.11 (0.10 to 0.12)**
	SB2		0.26 (0.24 to 0.28)**	0.09 (0.07 to 0.10)**	0.03 (0.02 to 0.05)*		0.14 (0.12 to 0.15)**	0.09 (0.07 to 0.10)**	0.01 (0.00 to 0.02)
p non-linearity			3*10⁻²¹⁶	4*10⁻²⁶	3*10⁻⁵		4*10⁻⁵⁸	9*10⁻³¹	0.118

		MEN				WOMEN			
		Count	BMI	ABSI	HI	Count	BMI	ABSI	HI
			(per one SD)	(per one SD)	(per one SD)		(per one SD)	(per one SD)	(per one SD)
Metabolic biomarkers (continued)									
ApoA1	LIN	107,377	-0.23 (-0.24 to -0.22)**	-0.05 (-0.06 to -0.05)**	0.05 (0.05 to 0.06)**	117,168	-0.22 (-0.23 to -0.22)**	-0.09 (-0.10 to -0.09)**	0.08 (0.07 to 0.08)**
	SB1		-0.42 (-0.44 to -0.41)**	-0.10 (-0.11 to -0.09)**	0.03 (0.02 to 0.05)**		-0.36 (-0.38 to -0.34)**	-0.14 (-0.15 to -0.12)**	0.07 (0.06 to 0.08)**
	SB2		0.21 (0.20 to 0.23)**	0.07 (0.05 to 0.08)**	0.03 (0.01 to 0.04)		0.14 (0.12 to 0.16)**	0.05 (0.04 to 0.07)**	0.01 (0.00 to 0.03)
p non-linearity			3*10 ⁻¹⁴²	5*10 ⁻¹⁶	3*10 ⁻⁴		2*10 ⁻⁵⁸	2*10 ⁻¹¹	0.057
LDL-C	LIN	116,143	0.12 (0.12 to 0.13)**	0.06 (0.06 to 0.07)**	-0.04 (-0.05 to -0.04)**	129,158	0.14 (0.14 to 0.15)**	0.11 (0.11 to 0.12)**	-0.08 (-0.08 to -0.07)**
	SB1		0.42 (0.41 to 0.44)**	0.13 (0.12 to 0.14)**	0.00 (-0.01 to 0.01)		0.39 (0.38 to 0.41)**	0.18 (0.17 to 0.19)**	-0.05 (-0.06 to -0.04)**
	SB2		-0.34 (-0.35 to -0.32)**	-0.09 (-0.11 to -0.07)**	-0.06 (-0.07 to -0.04)**		-0.26 (-0.28 to -0.25)**	-0.09 (-0.10 to -0.07)**	-0.04 (-0.05 to -0.02)**
p non-linearity			<1*10 ⁻³¹⁷	3*10 ⁻²⁶	3*10 ⁻¹³		2*10 ⁻²¹⁶	3*10 ⁻³¹	2*10 ⁻⁷
ApoB	LIN	115,840	0.17 (0.16 to 0.17)**	0.07 (0.07 to 0.08)**	-0.06 (-0.06 to -0.05)**	129,250	0.17 (0.16 to 0.17)**	0.13 (0.12 to 0.13)**	-0.09 (-0.09 to -0.08)**
	SB1		0.46 (0.44 to 0.48)**	0.14 (0.13 to 0.15)**	-0.01 (-0.03 to 0.00)		0.40 (0.38 to 0.41)**	0.20 (0.18 to 0.21)**	-0.07 (-0.08 to -0.06)**
	SB2		-0.33 (-0.35 to -0.31)**	-0.09 (-0.11 to -0.07)**	-0.06 (-0.07 to -0.04)**		-0.24 (-0.26 to -0.22)**	-0.09 (-0.10 to -0.07)**	-0.03 (-0.04 to -0.01)*
p non-linearity			1*10 ⁻³¹⁷	2*10 ⁻²⁶	6*10 ⁻¹⁴		1*10 ⁻¹⁷⁸	2*10 ⁻²⁹	5*10 ⁻⁵
Triglycerides	LIN	116,324	0.31 (0.30 to 0.32)**	0.13 (0.12 to 0.13)**	-0.11 (-0.12 to -0.11)**	129,294	0.30 (0.29 to 0.30)**	0.22 (0.22 to 0.23)**	-0.14 (-0.15 to -0.14)**
	SB1		0.60 (0.59 to 0.62)**	0.20 (0.19 to 0.21)**	-0.08 (-0.09 to -0.07)**		0.47 (0.46 to 0.49)**	0.32 (0.31 to 0.33)**	-0.14 (-0.15 to -0.13)**
	SB2		-0.33 (-0.35 to -0.31)**	-0.10 (-0.12 to -0.08)**	-0.05 (-0.06 to -0.03)**		-0.19 (-0.20 to -0.17)**	-0.12 (-0.13 to -0.11)**	0.00 (-0.02 to 0.01)
p non-linearity			1*10 ⁻³¹⁷	3*10 ⁻³⁶	2*10 ⁻¹⁰		4*10 ⁻¹²²	6*10 ⁻⁶⁴	0.672
HbA1c	LIN	116,027	0.15 (0.14 to 0.15)**	0.05 (0.04 to 0.05)**	-0.03 (-0.04 to -0.03)**	128,792	0.13 (0.13 to 0.14)**	0.07 (0.07 to 0.08)**	-0.05 (-0.05 to -0.04)**
	SB1		0.01 (0.00 to 0.03)	0.03 (0.01 to 0.04)*	-0.05 (-0.07 to -0.04)**		-0.02 (-0.04 to 0.00)	0.10 (0.09 to 0.12)**	-0.05 (-0.06 to -0.04)**
	SB2		0.15 (0.13 to 0.17)**	0.03 (0.01 to 0.04)	0.03 (0.01 to 0.04)		0.16 (0.14 to 0.17)**	-0.04 (-0.05 to -0.02)**	0.00 (-0.01 to 0.02)
p non-linearity			4*10 ⁻⁶⁶	0.001	2*10 ⁻⁴		1*10 ⁻⁷⁴	3*10 ⁻⁷	0.687
Glucose	LIN	107,346	0.12 (0.11 to 0.12)**	0.03 (0.03 to 0.04)**	-0.04 (-0.04 to -0.03)**	117,358	0.11 (0.11 to 0.12)**	0.04 (0.03 to 0.04)**	-0.05 (-0.05 to -0.04)**
	SB1		0.07 (0.06 to 0.09)**	0.01 (-0.01 to 0.02)	-0.04 (-0.05 to -0.03)**		0.08 (0.06 to 0.10)**	0.03 (0.02 to 0.05)*	-0.05 (-0.06 to -0.04)**
	SB2		0.05 (0.03 to 0.06)**	0.03 (0.01 to 0.05)	0.00 (-0.01 to 0.02)		0.03 (0.01 to 0.05)	0.00 (-0.01 to 0.02)	0.00 (-0.01 to 0.02)
p non-linearity			3*10 ⁻⁷	7*10 ⁻⁴	0.849		5*10 ⁻⁴	0.782	0.580
Inflammatory biomarkers									
Lymphocytes	LIN	118,465	0.17 (0.16 to 0.17)**	0.03 (0.03 to 0.04)**	-0.02 (-0.03 to -0.02)**	131,149	0.13 (0.13 to 0.14)**	0.05 (0.05 to 0.06)**	-0.04 (-0.04 to -0.03)**
	SB1		0.24 (0.22 to 0.25)**	0.05 (0.04 to 0.06)**	-0.01 (-0.02 to 0.00)		0.20 (0.19 to 0.22)**	0.07 (0.06 to 0.09)**	-0.04 (-0.05 to -0.02)**
	SB2		-0.08 (-0.10 to -0.06)**	-0.02 (-0.04 to -0.01)	-0.02 (-0.03 to 0.00)		-0.07 (-0.09 to -0.06)**	-0.03 (-0.04 to -0.01)	0.00 (-0.02 to 0.01)
p non-linearity			7*10 ⁻²²	0.006	0.039		1*10 ⁻¹⁷	2*10 ⁻⁴	0.566

		MEN				WOMEN			
		Count	BMI	ABSI	HI	Count	BMI	ABSI	HI
			(per one SD)	(per one SD)	(per one SD)		(per one SD)	(per one SD)	(per one SD)
Inflammatory biomarkers (continued)									
Monocytes	LIN	118,465	0.12 (0.12 to 0.13)**	0.06 (0.06 to 0.07)**	-0.03 (-0.03 to -0.02)**	131,149	0.07 (0.07 to 0.08)**	0.04 (0.03 to 0.04)**	-0.01 (-0.01 to 0.00)
	SB1		0.11 (0.09 to 0.13)**	0.06 (0.05 to 0.08)**	-0.02 (-0.03 to -0.01)		0.07 (0.05 to 0.09)**	0.04 (0.02 to 0.05)**	-0.02 (-0.03 to -0.01)
	SB2		0.01 (-0.01 to 0.03)	0.00 (-0.02 to 0.01)	-0.01 (-0.02 to 0.01)		0.00 (-0.01 to 0.02)	0.00 (-0.01 to 0.02)	0.01 (0.00 to 0.03)
p non-linearity			0.170	0.874	0.336		0.586	0.912	0.109
Neutrophils	LIN	118,465	0.09 (0.08 to 0.09)**	0.09 (0.08 to 0.09)**	-0.03 (-0.03 to -0.02)**	131,149	0.12 (0.12 to 0.13)**	0.06 (0.06 to 0.07)**	0.00 (-0.01 to 0.00)
	SB1		0.05 (0.03 to 0.06)**	0.08 (0.06 to 0.09)**	-0.03 (-0.05 to -0.02)**		0.08 (0.06 to 0.09)**	0.08 (0.06 to 0.09)**	-0.02 (-0.03 to -0.01)
	SB2		0.04 (0.03 to 0.06)**	0.02 (0.00 to 0.03)	0.01 (-0.01 to 0.02)		0.05 (0.03 to 0.07)**	-0.02 (-0.03 to 0.00)	0.02 (0.00 to 0.03)
p non-linearity			4*10⁻⁷	0.057	0.250		5*10⁻⁹	0.022	0.013
CRP	LIN	116,202	0.33 (0.32 to 0.33)**	0.14 (0.13 to 0.14)**	-0.04 (-0.05 to -0.04)**	129,249	0.47 (0.46 to 0.47)**	0.11 (0.11 to 0.12)**	-0.02 (-0.02 to -0.01)**
	SB1		0.43 (0.42 to 0.45)**	0.13 (0.12 to 0.14)**	-0.06 (-0.07 to -0.05)**		0.57 (0.55 to 0.58)**	0.14 (0.12 to 0.15)**	-0.03 (-0.04 to -0.02)**
	SB2		-0.12 (-0.13 to -0.10)**	0.01 (-0.01 to 0.02)	0.02 (0.01 to 0.04)		-0.10 (-0.12 to -0.09)**	-0.03 (-0.05 to -0.02)*	0.02 (0.00 to 0.03)
p non-linearity			5*10⁻⁴⁸	0.417	0.001		1*10⁻⁴⁰	9*10⁻⁶	0.013

ABSI – a body shape index; **ALP** – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **AST** – aspartate aminotransferase; **BMI** – body mass index; **Count** – number of participants with available biomarker measurements; **CRP** – C-reactive protein; **GGT** – gamma-glutamyltransferase; **HbA1c** – haemoglobin A1c (glycated haemoglobin); **HDL-C** – high-density lipoprotein cholesterol; **HI** – hip index; **LDL-C** – low-density lipoprotein cholesterol; **SD** – standard deviation; **SB1, SB2** – first and second spline base.

LIN – estimates for SD difference (95% confidence interval) were obtained from multivariable linear regression models with each biomarker on a continuous scale (sex-specific z-scores, following log-transformation) as an outcome variable and BMI+ABSI+HI on a continuous scale (sex-specific z-scores) as independent variables (Figure 1); **SB1+SB2** – estimates for SD difference (95% confidence interval) were obtained from multivariable linear regression models as in LIN, but replacing one of BMI, ABSI, or HI with restricted cubic splines (knots at -2, 0, and 2) and retaining the other two anthropometric indices on a linear scale. All models were additionally adjusted for height, age at enrolment, weight change within the last year preceding enrolment, smoking status, alcohol consumption, physical activity, Townsend deprivation index, region of the assessment centre, time of blood collection, fasting time, use of nonsteroidal anti-inflammatory drugs, paracetamol use, and in women also menopausal status, oral contraceptives use, hormone replacement therapy use, and age at the last live birth. Covariates are defined in Supplementary Methods.

* – $p < 0.0001$ from Wald test for the individual term; ** – $p < 1 \times 10^{-6}$

p non-linearity – p-value from a likelihood ratio test comparing a fully adjusted linear model (LIN) nested within the corresponding fully adjusted model including restricted cubic splines for one of the anthropometric indices (SB1+SB2) (p non-linearity < 0.0001 are shown in bold).

Supplementary Table S5 Associations of biomarkers with body shape phenotypes (categorical)

		Bilirubin direct		ALP		GGT		AST		ALT	
		Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)
MEN											
ALL	Pear	31,181	reference	31,285	reference	31,272	reference	31,175	reference	31,275	reference
	Slim	35,575	-0.05 (-0.06 to -0.03)**	35,738	0.02 (0.00 to 0.03)	35,722	0.09 (0.07 to 0.10)**	35,571	0.05 (0.04 to 0.07)**	35,693	0.11 (0.09 to 0.12)**
	Wide	30,911	-0.09 (-0.11 to -0.08)**	31,035	0.13 (0.12 to 0.15)**	31,022	0.16 (0.14 to 0.17)**	30,909	0.02 (0.01 to 0.04)	31,017	0.13 (0.12 to 0.15)**
	Apple	18,266	-0.13 (-0.15 to -0.11)**	18,343	0.16 (0.14 to 0.17)**	18,337	0.26 (0.24 to 0.27)**	18,258	0.07 (0.06 to 0.09)**	18,326	0.24 (0.22 to 0.25)**
p body shape		4*10 ⁻⁵¹		2*10 ⁻¹⁰³		1*10 ⁻²⁰⁰		4*10 ⁻¹⁸		4*10 ⁻¹⁷¹	
NW	Pear	10,654	reference	10,677	reference	10,674	reference	10,651	reference	10,681	reference
	Slim	9,658	-0.06 (-0.09 to -0.03)*	9,708	0.00 (-0.02 to 0.03)	9,703	0.06 (0.03 to 0.09)*	9,663	0.04 (0.01 to 0.07)	9,703	0.08 (0.05 to 0.10)**
	Wide	9,815	-0.15 (-0.18 to -0.13)**	9,850	0.16 (0.14 to 0.19)**	9,848	0.18 (0.15 to 0.21)**	9,820	0.01 (-0.02 to 0.03)	9,852	0.14 (0.12 to 0.17)**
	Apple	4,390	-0.22 (-0.26 to -0.19)**	4,406	0.19 (0.15 to 0.22)**	4,404	0.31 (0.27 to 0.34)**	4,389	0.05 (0.02 to 0.09)	4,403	0.24 (0.20 to 0.27)**
OW	Pear	15,156	-0.14 (-0.16 to -0.12)**	15,209	0.09 (0.06 to 0.11)**	15,200	0.34 (0.32 to 0.37)**	15,157	0.13 (0.10 to 0.15)**	15,200	0.41 (0.39 to 0.43)**
	Slim	19,107	-0.20 (-0.22 to -0.18)**	19,169	0.12 (0.10 to 0.15)**	19,162	0.45 (0.43 to 0.47)**	19,102	0.18 (0.16 to 0.21)**	19,150	0.53 (0.51 to 0.56)**
	Wide	15,005	-0.22 (-0.25 to -0.20)**	15,062	0.22 (0.19 to 0.24)**	15,050	0.52 (0.49 to 0.54)**	14,996	0.16 (0.13 to 0.18)**	15,050	0.57 (0.54 to 0.59)**
	Apple	9,818	-0.27 (-0.29 to -0.24)**	9,854	0.26 (0.23 to 0.28)**	9,853	0.61 (0.59 to 0.64)**	9,813	0.21 (0.18 to 0.24)**	9,848	0.67 (0.65 to 0.70)**
OB	Pear	5,371	-0.27 (-0.30 to -0.24)**	5,399	0.21 (0.18 to 0.24)**	5,398	0.76 (0.73 to 0.79)**	5,367	0.40 (0.37 to 0.43)**	5,394	0.92 (0.89 to 0.95)**
	Slim	6,810	-0.25 (-0.28 to -0.22)**	6,861	0.19 (0.16 to 0.22)**	6,857	0.83 (0.80 to 0.86)**	6,806	0.45 (0.42 to 0.48)**	6,840	1.02 (1.00 to 1.05)**
	Wide	6,091	-0.28 (-0.31 to -0.24)**	6,123	0.29 (0.26 to 0.32)**	6,124	0.83 (0.80 to 0.86)**	6,093	0.42 (0.39 to 0.46)**	6,115	0.98 (0.95 to 1.01)**
	Apple	4,058	-0.27 (-0.31 to -0.24)**	4,083	0.29 (0.26 to 0.33)**	4,080	0.91 (0.88 to 0.95)**	4,056	0.48 (0.45 to 0.52)**	4,075	1.10 (1.06 to 1.13)**
p interaction		8*10 ⁻¹⁷		1*10 ⁻⁵		8*10 ⁻¹⁴		0.785		7*10 ⁻⁹	
WOMEN											
ALL	Pear	34,257	reference	34,390	reference	34,369	reference	34,260	reference	34,389	reference
	Slim	29,522	-0.05 (-0.07 to -0.04)**	29,635	-0.04 (-0.05 to -0.02)**	29,622	0.07 (0.05 to 0.08)**	29,515	0.06 (0.04 to 0.07)**	29,636	0.10 (0.08 to 0.11)**
	Wide	37,685	-0.13 (-0.15 to -0.12)**	37,794	0.11 (0.09 to 0.12)**	37,778	0.16 (0.15 to 0.17)**	37,680	0.05 (0.03 to 0.06)**	37,797	0.16 (0.15 to 0.18)**
	Apple	27,473	-0.17 (-0.19 to -0.16)**	27,561	0.10 (0.09 to 0.12)**	27,553	0.29 (0.27 to 0.30)**	27,450	0.13 (0.12 to 0.15)**	27,551	0.32 (0.31 to 0.34)**
p body shape		8*10 ⁻¹³¹		3*10 ⁻¹³¹		<1*10 ⁻³¹⁷		5*10 ⁻⁶³		<1*10 ⁻³¹⁷	
NW	Pear	17,825	reference	17,895	reference	17,885	reference	17,824	reference	17,894	reference
	Slim	14,592	-0.04 (-0.06 to -0.02)	14,648	-0.03 (-0.05 to -0.02)	14,638	0.03 (0.01 to 0.05)	14,592	0.06 (0.04 to 0.08)**	14,648	0.07 (0.05 to 0.09)**
	Wide	16,268	-0.15 (-0.17 to -0.13)**	16,320	0.11 (0.09 to 0.13)**	16,314	0.09 (0.07 to 0.11)**	16,275	0.01 (-0.01 to 0.03)	16,324	0.10 (0.08 to 0.12)**
	Apple	10,085	-0.20 (-0.22 to -0.18)**	10,119	0.13 (0.10 to 0.15)**	10,114	0.17 (0.15 to 0.19)**	10,080	0.05 (0.03 to 0.07)*	10,115	0.20 (0.18 to 0.22)**
OW	Pear	11,222	-0.16 (-0.18 to -0.14)**	11,266	0.18 (0.16 to 0.20)**	11,258	0.10 (0.08 to 0.12)**	11,227	-0.05 (-0.08 to -0.03)*	11,266	0.14 (0.12 to 0.16)**
	Slim	10,706	-0.23 (-0.25 to -0.21)**	10,747	0.17 (0.14 to 0.19)**	10,746	0.20 (0.17 to 0.22)**	10,701	0.00 (-0.03 to 0.02)	10,749	0.25 (0.23 to 0.27)**
	Wide	13,328	-0.30 (-0.32 to -0.28)**	13,372	0.32 (0.30 to 0.34)**	13,364	0.33 (0.31 to 0.35)**	13,326	0.02 (0.00 to 0.04)	13,369	0.36 (0.34 to 0.38)**
	Apple	11,891	-0.33 (-0.36 to -0.31)**	11,920	0.31 (0.29 to 0.33)**	11,919	0.47 (0.45 to 0.49)**	11,879	0.10 (0.08 to 0.13)**	11,918	0.54 (0.52 to 0.56)**
OB	Pear	5,210	-0.28 (-0.31 to -0.25)**	5,229	0.51 (0.48 to 0.54)**	5,226	0.47 (0.44 to 0.50)**	5,209	0.04 (0.01 to 0.07)	5,229	0.49 (0.46 to 0.52)**
	Slim	4,224	-0.35 (-0.39 to -0.32)**	4,240	0.43 (0.40 to 0.46)**	4,238	0.61 (0.58 to 0.64)**	4,222	0.12 (0.09 to 0.15)**	4,239	0.67 (0.63 to 0.70)**
	Wide	8,089	-0.36 (-0.39 to -0.34)**	8,102	0.53 (0.51 to 0.55)**	8,100	0.70 (0.67 to 0.72)**	8,079	0.16 (0.13 to 0.19)**	8,104	0.73 (0.70 to 0.75)**
	Apple	5,497	-0.39 (-0.42 to -0.36)**	5,522	0.49 (0.47 to 0.52)**	5,520	0.86 (0.83 to 0.88)**	5,491	0.32 (0.29 to 0.35)**	5,518	0.93 (0.90 to 0.96)**
p interaction		2*10 ⁻⁸		3*10 ⁻¹³		5*10 ⁻⁴¹		4*10 ⁻²⁹		2*10 ⁻⁴³	

		HDL-C		ApoA1		LDL-C		ApoB		Triglycerides	
		Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)
MEN											
ALL	Pear	28,891	reference	28,870	reference	31,236	reference	31,177	reference	31,264	reference
	Slim	32,954	-0.11 (-0.13 to -0.10)**	32,945	-0.08 (-0.09 to -0.06)**	35,645	0.07 (0.05 to 0.08)**	35,536	0.09 (0.08 to 0.11)**	35,710	0.16 (0.14 to 0.17)**
	Wide	28,627	-0.11 (-0.13 to -0.10)**	28,615	-0.07 (-0.09 to -0.06)**	30,967	0.09 (0.08 to 0.11)**	30,900	0.11 (0.09 to 0.12)**	31,018	0.17 (0.16 to 0.19)**
	Apple	16,952	-0.21 (-0.23 to -0.19)**	16,947	-0.14 (-0.15 to -0.12)**	18,295	0.12 (0.10 to 0.14)**	18,227	0.16 (0.14 to 0.18)**	18,332	0.32 (0.30 to 0.34)**
p body shape		8*10 ⁻¹³¹		3*10 ⁻⁵³		6*10 ⁻⁴⁷		4*10 ⁻⁷⁷		1*10 ⁻³⁰³	
NW	Pear	9,809	reference	9,799	reference	10,663	reference	10,665	reference	10,672	reference
	Slim	8,933	-0.09 (-0.12 to -0.07)**	8,924	-0.06 (-0.09 to -0.04)*	9,685	0.08 (0.05 to 0.11)**	9,689	0.10 (0.07 to 0.12)**	9,701	0.12 (0.09 to 0.14)**
	Wide	9,012	-0.17 (-0.19 to -0.14)**	9,000	-0.12 (-0.14 to -0.09)**	9,830	0.18 (0.15 to 0.21)**	9,835	0.19 (0.16 to 0.21)**	9,844	0.26 (0.24 to 0.29)**
	Apple	4,061	-0.29 (-0.32 to -0.25)**	4,061	-0.21 (-0.24 to -0.17)**	4,398	0.24 (0.21 to 0.28)**	4,396	0.28 (0.25 to 0.31)**	4,403	0.43 (0.39 to 0.46)**
OW	Pear	14,066	-0.46 (-0.49 to -0.44)**	14,055	-0.37 (-0.39 to -0.34)**	15,184	0.34 (0.32 to 0.36)**	15,157	0.38 (0.35 to 0.40)**	15,194	0.52 (0.49 to 0.54)**
	Slim	17,647	-0.58 (-0.61 to -0.56)**	17,643	-0.44 (-0.47 to -0.42)**	19,125	0.40 (0.38 to 0.43)**	19,070	0.47 (0.45 to 0.49)**	19,154	0.69 (0.67 to 0.71)**
	Wide	13,880	-0.57 (-0.60 to -0.55)**	13,879	-0.44 (-0.46 to -0.41)**	15,026	0.43 (0.41 to 0.46)**	14,990	0.48 (0.46 to 0.51)**	15,055	0.69 (0.67 to 0.72)**
	Apple	9,097	-0.67 (-0.70 to -0.64)**	9,085	-0.49 (-0.52 to -0.46)**	9,833	0.45 (0.42 to 0.47)**	9,791	0.53 (0.50 to 0.56)**	9,850	0.84 (0.81 to 0.87)**
OB	Pear	5,016	-0.85 (-0.88 to -0.82)**	5,016	-0.65 (-0.68 to -0.62)**	5,389	0.45 (0.42 to 0.48)**	5,355	0.56 (0.53 to 0.60)**	5,398	0.94 (0.91 to 0.97)**
	Slim	6,374	-0.97 (-1.00 to -0.94)**	6,378	-0.74 (-0.76 to -0.71)**	6,835	0.47 (0.44 to 0.50)**	6,777	0.61 (0.58 to 0.64)**	6,855	1.08 (1.05 to 1.11)**
	Wide	5,735	-0.88 (-0.91 to -0.85)**	5,736	-0.65 (-0.68 to -0.62)**	6,111	0.40 (0.37 to 0.43)**	6,075	0.52 (0.49 to 0.56)**	6,119	0.94 (0.91 to 0.97)**
	Apple	3,794	-0.98 (-1.01 to -0.94)**	3,801	-0.72 (-0.76 to -0.69)**	4,064	0.44 (0.41 to 0.48)**	4,040	0.59 (0.55 to 0.62)**	4,079	1.10 (1.07 to 1.13)**
p interaction		1*10 ⁻¹⁹		2*10 ⁻¹³		7*10 ⁻³²		2*10 ⁻³²		2*10 ⁻⁶²	
WOMEN											
ALL	Pear	31,245	reference	31,166	reference	34,340	reference	34,372	reference	34,364	reference
	Slim	26,893	-0.15 (-0.16 to -0.13)**	26,830	-0.10 (-0.11 to -0.08)**	29,581	0.09 (0.08 to 0.11)**	29,617	0.11 (0.09 to 0.12)**	29,621	0.17 (0.16 to 0.19)**
	Wide	34,269	-0.23 (-0.24 to -0.22)**	34,187	-0.14 (-0.15 to -0.12)**	37,720	0.17 (0.15 to 0.18)**	37,755	0.19 (0.17 to 0.20)**	37,763	0.33 (0.31 to 0.34)**
	Apple	25,030	-0.44 (-0.45 to -0.42)**	24,985	-0.28 (-0.29 to -0.26)**	27,517	0.30 (0.28 to 0.31)**	27,506	0.34 (0.33 to 0.36)**	27,546	0.58 (0.56 to 0.59)**
p body shape		<1*10 ⁻³¹⁷		2*10 ⁻²⁷⁸		<1*10 ⁻³¹⁷		<1*10 ⁻³¹⁷		<1*10 ⁻³¹⁷	
NW	Pear	16,273	reference	16,215	reference	17,867	reference	17,888	reference	17,874	reference
	Slim	13,259	-0.12 (-0.14 to -0.09)**	13,214	-0.08 (-0.10 to -0.06)**	14,615	0.06 (0.04 to 0.08)**	14,644	0.07 (0.05 to 0.09)**	14,640	0.11 (0.09 to 0.13)**
	Wide	14,763	-0.22 (-0.24 to -0.20)**	14,711	-0.14 (-0.16 to -0.12)**	16,289	0.16 (0.14 to 0.18)**	16,310	0.18 (0.16 to 0.20)**	16,312	0.30 (0.28 to 0.32)**
	Apple	9,166	-0.39 (-0.41 to -0.37)**	9,142	-0.25 (-0.27 to -0.22)**	10,097	0.29 (0.27 to 0.31)**	10,104	0.32 (0.30 to 0.34)**	10,116	0.51 (0.48 to 0.53)**
OW	Pear	10,200	-0.31 (-0.33 to -0.29)**	10,183	-0.26 (-0.29 to -0.24)**	11,249	0.20 (0.18 to 0.23)**	11,258	0.22 (0.19 to 0.24)**	11,262	0.28 (0.26 to 0.30)**
	Slim	9,763	-0.50 (-0.52 to -0.48)**	9,749	-0.38 (-0.41 to -0.36)**	10,737	0.33 (0.31 to 0.35)**	10,741	0.36 (0.34 to 0.38)**	10,743	0.52 (0.50 to 0.54)**
	Wide	12,157	-0.56 (-0.59 to -0.54)**	12,135	-0.41 (-0.43 to -0.38)**	13,342	0.41 (0.39 to 0.43)**	13,355	0.44 (0.42 to 0.46)**	13,353	0.67 (0.65 to 0.69)**
	Apple	10,824	-0.82 (-0.84 to -0.80)**	10,804	-0.59 (-0.61 to -0.56)**	11,910	0.53 (0.51 to 0.55)**	11,891	0.60 (0.58 to 0.62)**	11,913	0.97 (0.95 to 0.99)**
OB	Pear	4,772	-0.72 (-0.75 to -0.69)**	4,768	-0.55 (-0.58 to -0.52)**	5,224	0.34 (0.31 to 0.37)**	5,226	0.39 (0.36 to 0.42)**	5,228	0.70 (0.67 to 0.72)**
	Slim	3,871	-0.89 (-0.92 to -0.86)**	3,867	-0.65 (-0.69 to -0.62)**	4,229	0.48 (0.45 to 0.51)**	4,232	0.55 (0.52 to 0.58)**	4,238	0.95 (0.92 to 0.98)**
	Wide	7,349	-0.94 (-0.97 to -0.92)**	7,341	-0.67 (-0.70 to -0.65)**	8,089	0.46 (0.44 to 0.49)**	8,090	0.55 (0.53 to 0.57)**	8,098	1.01 (0.98 to 1.03)**
	Apple	5,040	-1.11 (-1.14 to -1.08)**	5,039	-0.79 (-0.82 to -0.76)**	5,510	0.61 (0.58 to 0.63)**	5,511	0.71 (0.69 to 0.74)**	5,517	1.23 (1.20 to 1.26)**
p interaction		2*10 ⁻¹⁴		3*10 ⁻⁶		4*10 ⁻¹¹		5*10 ⁻¹⁰		2*10 ⁻⁴⁰	

HbA1c				Glucose		Lymphocytes		Neutrophils		CRP	
		Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)	Count	SD _{diff} (95% CI)
MEN											
ALL	Pear	31,151	reference	28,864	reference	31,875	reference	31,875	reference	31,250	reference
	Slim	35,677	0.05 (0.03 to 0.06)**	32,931	0.07 (0.05 to 0.08)**	36,365	0.02 (0.01 to 0.04)	36,365	0.02 (0.01 to 0.04)	35,653	0.04 (0.03 to 0.06)**
	Wide	30,914	0.06 (0.05 to 0.08)**	28,608	0.04 (0.02 to 0.06)*	31,530	0.05 (0.03 to 0.06)**	31,530	0.12 (0.11 to 0.14)**	30,987	0.20 (0.18 to 0.21)**
	Apple	18,285	0.13 (0.11 to 0.15)**	16,943	0.11 (0.09 to 0.13)**	18,695	0.08 (0.06 to 0.09)**	18,695	0.16 (0.14 to 0.18)**	18,312	0.25 (0.23 to 0.27)**
p _{body shape}		4*10 ⁻⁴⁶		5*10 ⁻³¹		2*10 ⁻¹⁸		2*10 ⁻¹⁰³		6*10 ⁻²⁶⁴	
NW	Pear	10,641	reference	9,800	reference	10,866	reference	10,866	reference	10,671	reference
	Slim	9,708	0.04 (0.01 to 0.07)	8,923	0.04 (0.02 to 0.07)	9,900	0.02 (-0.01 to 0.05)	9,900	0.03 (0.01 to 0.06)	9,694	0.08 (0.06 to 0.11)**
	Wide	9,790	0.01 (-0.01 to 0.04)	9,004	0.02 (-0.01 to 0.05)	10,013	0.05 (0.02 to 0.07)	10,013	0.13 (0.11 to 0.16)**	9,836	0.25 (0.22 to 0.28)**
	Apple	4,428	0.08 (0.05 to 0.11)*	4,058	0.10 (0.06 to 0.13)**	4,508	0.09 (0.06 to 0.12)**	4,508	0.19 (0.16 to 0.23)**	4,400	0.35 (0.32 to 0.39)**
OW	Pear	15,141	0.07 (0.05 to 0.09)**	14,050	0.10 (0.08 to 0.13)**	15,526	0.21 (0.19 to 0.23)**	15,526	0.10 (0.08 to 0.12)**	15,188	0.47 (0.45 to 0.49)**
	Slim	19,135	0.12 (0.09 to 0.14)**	17,640	0.17 (0.15 to 0.20)**	19,512	0.24 (0.22 to 0.26)**	19,512	0.12 (0.10 to 0.14)**	19,126	0.51 (0.48 to 0.53)**
	Wide	15,024	0.14 (0.11 to 0.16)**	13,870	0.13 (0.11 to 0.16)**	15,286	0.26 (0.24 to 0.28)**	15,286	0.21 (0.19 to 0.24)**	15,043	0.65 (0.63 to 0.67)**
	Apple	9,804	0.20 (0.18 to 0.23)**	9,087	0.19 (0.17 to 0.22)**	10,032	0.29 (0.27 to 0.32)**	10,032	0.25 (0.22 to 0.28)**	9,841	0.71 (0.69 to 0.74)**
OB	Pear	5,369	0.32 (0.29 to 0.35)**	5,014	0.25 (0.21 to 0.28)**	5,483	0.45 (0.42 to 0.48)**	5,483	0.24 (0.21 to 0.27)**	5,391	0.95 (0.92 to 0.98)**
	Slim	6,834	0.38 (0.35 to 0.41)**	6,368	0.34 (0.31 to 0.37)**	6,953	0.46 (0.43 to 0.49)**	6,953	0.25 (0.22 to 0.28)**	6,833	0.94 (0.91 to 0.96)**
	Wide	6,100	0.45 (0.42 to 0.48)**	5,734	0.35 (0.31 to 0.38)**	6,231	0.50 (0.47 to 0.53)**	6,231	0.36 (0.33 to 0.39)**	6,108	1.09 (1.06 to 1.11)**
	Apple	4,053	0.52 (0.49 to 0.56)**	3,798	0.43 (0.40 to 0.47)**	4,155	0.50 (0.46 to 0.53)**	4,155	0.37 (0.34 to 0.41)**	4,071	1.07 (1.04 to 1.11)**
p _{interaction}		7*10 ⁻⁸		0.002		0.499		0.337		2*10 ⁻¹⁷	
WOMEN											
ALL	Pear	34,173	reference	31,227	reference	34,850	reference	34,850	reference	34,355	reference
	Slim	29,549	0.06 (0.05 to 0.08)**	26,871	0.05 (0.04 to 0.07)**	30,083	0.04 (0.03 to 0.06)**	30,083	-0.01 (-0.02 to 0.01)	29,612	-0.01 (-0.02 to 0.01)
	Wide	37,607	0.10 (0.09 to 0.11)**	34,244	0.05 (0.03 to 0.06)**	38,267	0.07 (0.05 to 0.08)**	38,267	0.10 (0.08 to 0.11)**	37,761	0.17 (0.15 to 0.18)**
	Apple	27,463	0.19 (0.18 to 0.21)**	25,016	0.13 (0.11 to 0.15)**	27,949	0.14 (0.13 to 0.16)**	27,949	0.10 (0.08 to 0.11)**	27,521	0.20 (0.19 to 0.22)**
p _{body shape}		2*10 ⁻¹⁴⁷		4*10 ⁻⁵³		7*10 ⁻⁷⁹		3*10 ⁻⁷⁷		1*10 ⁻³¹³	
NW	Pear	17,695	reference	16,262	reference	18,091	reference	18,091	reference	17,873	reference
	Slim	14,576	0.04 (0.02 to 0.06)	13,253	0.04 (0.01 to 0.06)	14,897	0.02 (0.00 to 0.04)	14,897	-0.02 (-0.04 to 0.00)	14,638	-0.01 (-0.03 to 0.01)
	Wide	16,276	0.05 (0.03 to 0.07)*	14,751	0.04 (0.01 to 0.06)	16,574	0.04 (0.02 to 0.06)*	16,574	0.10 (0.08 to 0.12)**	16,306	0.15 (0.13 to 0.17)**
	Apple	10,088	0.12 (0.10 to 0.14)**	9,163	0.11 (0.08 to 0.13)**	10,277	0.10 (0.08 to 0.12)**	10,277	0.08 (0.06 to 0.11)**	10,105	0.20 (0.18 to 0.22)**
OW	Pear	11,271	0.03 (0.01 to 0.05)	10,194	0.07 (0.05 to 0.10)**	11,457	0.11 (0.08 to 0.13)**	11,457	0.08 (0.06 to 0.11)**	11,257	0.47 (0.45 to 0.49)**
	Slim	10,729	0.10 (0.08 to 0.12)**	9,748	0.15 (0.12 to 0.17)**	10,895	0.17 (0.15 to 0.19)**	10,895	0.09 (0.07 to 0.11)**	10,742	0.48 (0.46 to 0.50)**
	Wide	13,273	0.15 (0.13 to 0.17)**	12,152	0.13 (0.11 to 0.15)**	13,536	0.21 (0.19 to 0.23)**	13,536	0.19 (0.17 to 0.21)**	13,361	0.67 (0.65 to 0.69)**
	Apple	11,875	0.25 (0.23 to 0.28)**	10,816	0.23 (0.21 to 0.26)**	12,085	0.30 (0.28 to 0.32)**	12,085	0.21 (0.19 to 0.23)**	11,904	0.72 (0.70 to 0.74)**
OB	Pear	5,207	0.22 (0.20 to 0.25)**	4,771	0.25 (0.22 to 0.28)**	5,302	0.30 (0.27 to 0.33)**	5,302	0.31 (0.28 to 0.34)**	5,225	1.18 (1.16 to 1.21)**
	Slim	4,244	0.33 (0.30 to 0.36)**	3,870	0.31 (0.27 to 0.34)**	4,291	0.37 (0.34 to 0.40)**	4,291	0.31 (0.28 to 0.34)**	4,232	1.16 (1.13 to 1.18)**
	Wide	8,058	0.43 (0.41 to 0.46)**	7,341	0.32 (0.30 to 0.35)**	8,157	0.37 (0.34 to 0.39)**	8,157	0.40 (0.37 to 0.42)**	8,094	1.32 (1.30 to 1.34)**
	Apple	5,500	0.54 (0.51 to 0.56)**	5,037	0.38 (0.35 to 0.41)**	5,587	0.44 (0.41 to 0.47)**	5,587	0.38 (0.35 to 0.41)**	5,512	1.29 (1.27 to 1.32)**
p _{interaction}		6*10 ⁻²⁴		0.035		2*10 ⁻⁶		0.025		5*10 ⁻¹¹	

ABSI – a body shape index (cut-offs ≥ 80 for men, ≥ 73 for women); **ALP** – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **Apple** – large-ABSI-small-HI; **AST** – aspartate aminotransferase; **BMI** – body mass index; **Count** – number of participants with available biomarker measurements per category; **CRP** – C-reactive protein; **GGT** – gamma-glutamyltransferase; **HbA1c** – haemoglobin A1c (glycated haemoglobin); **HDL-C** – high-density lipoprotein cholesterol; **HI** – hip index (cut-offs ≥ 49 for men, ≥ 64 for women); **LDL-C** – low-density lipoprotein cholesterol; **NW** – normal weight ($\text{BMI} \geq 18.5$ to $< 25 \text{ kg/m}^2$); **OB** – obese ($\text{BMI} \geq 30$ to $< 45 \text{ kg/m}^2$); **OW** – overweight ($\text{BMI} \geq 25$ to $< 30 \text{ kg/m}^2$); **Pear** – small-ABSI-large-HI; **Slim** – small-ABSI-small-HI; **Wide** – large-ABSI-large-HI.

SD_{diff} (95% CI) – estimates for standard deviation difference (95% confidence interval) were obtained from multivariable linear regression models including each biomarker on a continuous scale (sex-specific z-scores, following log-transformation) as an outcome variable and the following two combinations as independent variables: an ABSI-by-HI cross-classification and BMI categories (for ALL, reference “pear”), or an BMI-by-ABSI-by-HI cross-classification (for NW, OW, and OB, reference “pear”-NW). All models were adjusted for height, age at enrolment, weight change within the last year preceding enrolment, smoking status, alcohol consumption, physical activity, Townsend deprivation index, region of the assessment centre, time of blood collection, fasting time, use of nonsteroidal anti-inflammatory drugs, paracetamol use, and in women also menopausal status, oral contraceptives use, hormone replacement therapy use, and age at the last live birth. Covariates are defined in Supplementary Methods.

p_{body shape} (for ALL) – was obtained from a likelihood ratio test comparing a model including only BMI categories and covariates with a model additionally including an ABSI-by-HI cross-classification (evaluates the significance of body-shape overall) (**p_{body shape} < 0.0001** are shown in bold).

p_{interaction} (for NW, OW, and OB) – was obtained from a likelihood ratio test comparing the additive model including the ABSI-by-HI cross-classification, BMI categories, and covariates with the interaction model including the BMI-by-ABSI-by-HI cross-classification and covariates (evaluates heterogeneity by BMI) (**p_{interaction} < 0.0001** are shown in bold).

* – $p < 0.0001$ from Wald test for the individual term; ** – $p < 1 \times 10^{-6}$

Supplementary Table S6 Biomarker boundaries

	Unit	LL count	LL cut-off	2.5 th centile	Median	97.5 th centile	UL cut-off	UL count
MEN								
Bilirubin total	μmol/L	12	2	5.03	9.15	24.0	50	58
ALP	U/L	12	15	48.1	77.8	127.7	300	45
GGT	U/L	3	5	14.2	31.0	135.1	1000	24
AST	U/L	7	8	17.3	25.8	48.2	250	23
ALT	U/L	7	3	11.4	23.2	62.9	250	19
HDL-C	mmol/L	4	0.4	0.83	1.27	2.02	3.5	10
ApoA1	g/L	17	0.7	1.07	1.42	1.96	2.6	0
LDL-C	mmol/L	121	1.5	2.34	3.71	5.37	7.5	12
ApoB	g/L	152	0.4	0.67	1.07	1.57	2.1	0
Triglycerides	mmol/L	16	0.3	0.64	1.66	4.96	11	56
HbA1c	mmol/mol	56	15	27.3	34.4	42.2	100	42
Glucose	mmol/L	3	2	3.78	4.89	6.46	25	9
Lymphocytes	*10 ⁹ /L	14	0.2	0.97	1.80	3.15	10	28
Neutrophils	*10 ⁹ /L	44	0.3	2.1	3.90	7.29	15	9
CRP	mg/L	25	0.08	0.2	1.15	10.9	80	0
WOMEN								
Bilirubin total	μmol/L	4	2	4.17	7.34	18.6	50	9
ALP	U/L	13	15	45.1	80.2	137.3	300	49
GGT	U/L	6	5	10.4	19.7	92.3	1000	7
AST	U/L	14	8	15.2	22.5	39.6	250	16
ALT	U/L	18	3	8.72	16.8	44.7	250	24
HDL-C	mmol/L	2	0.4	1.02	1.60	2.46	3.5	19
ApoA1	g/L	5	0.7	1.20	1.63	2.26	2.6	0
LDL-C	mmol/L	95	1.5	2.28	3.68	5.55	7.5	21
ApoB	g/L	196	0.4	0.64	1.04	1.58	2.1	0
Triglycerides	mmol/L	7	0.3	0.57	1.25	3.52	11	6
HbA1c	mmol/mol	47	15	27.6	34.6	41.8	100	25
Glucose	mmol/L	2	2	3.88	4.88	6.45	25	0
Lymphocytes	*10 ⁹ /L	18	0.2	1.04	1.90	3.30	10	21
Neutrophils	*10 ⁹ /L	51	0.3	2.09	3.90	7.14	15	6
CRP	mg/L	48	0.08	0.19	1.13	10.9	80	0

ALP – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **AST** – aspartate aminotransferase; **CRP** – C-reactive protein; **GGT** – gamma-glutamyltransferase; **HbA1c** – haemoglobin A1c (glycated haemoglobin); **HDL-C** – high-density lipoprotein cholesterol; **LDL-C** – low-density lipoprotein cholesterol.

Values shown were used for exclusion of participants with extreme biomarker measurements in Figure 4 as follows:

LL cut-off – lower limit cut-off, used for exclusion of extremely low values; **LL count** – number of excluded participants with extremely low values; **UL cut-off** – upper limit cut-off, used for exclusion of extremely high values; **UL count** – number of excluded participants with extremely high values.

2.5th centile & 97.5th centile are marked in Figure 4.

Supplementary Table S7 Associations of biomarkers with body size and body shape indices: subgroups according to biomarker levels

				BMI		ABSI		HI	
	Cut-off		Count	SD _{diff} (95% CI)	p-value	SD _{diff} (95% CI)	p-value	SD _{diff} (95% CI)	p-value
MEN									
AST	70	Below	115,201	0.146 (0.141 to 0.152)**	<1*10 ⁻³¹⁷	0.008 (0.002 to 0.013)	0.009	-0.032 (-0.038 to -0.027)**	5*10 ⁻³¹
		Above	712	-0.180 (-0.274 to -0.086)	2*10⁻⁴	0.021 (-0.087 to 0.129)	0.707	-0.002 (-0.105 to 0.100)	0.963
ALT	10	Below	1421	-0.021 (-0.053 to 0.012)	0.207	0.001 (-0.028 to 0.029)	0.966	0.010 (-0.017 to 0.038)	0.464
		Above	114,890	0.322 (0.317 to 0.327)**	<1*10 ⁻³¹⁷	0.095 (0.090 to 0.101)**	3*10 ⁻²⁴⁸	-0.080 (-0.085 to -0.075)**	5*10 ⁻¹⁹³
ALT	70	Below	114,354	0.307 (0.302 to 0.312)**	<1*10 ⁻³¹⁷	0.088 (0.082 to 0.093)**	1*10 ⁻²²⁶	-0.074 (-0.079 to -0.069)**	7*10 ⁻¹⁸⁰
		Above	1957	-0.057 (-0.083 to -0.031)*	2*10⁻⁵	-0.005 (-0.036 to 0.025)	0.738	-0.002 (-0.030 to 0.026)	0.900
HDL-C	1.8	Below	100,063	-0.237 (-0.242 to -0.232)**	<1*10 ⁻³¹⁷	-0.066 (-0.072 to -0.061)**	3*10 ⁻¹²⁷	0.067 (0.062 to 0.072)**	6*10 ⁻¹⁴⁵
		Above	7361	-0.080 (-0.093 to -0.066)**	2*10 ⁻³⁰	0.021 (0.010 to 0.031)*	9*10⁻⁵	-0.003 (-0.013 to 0.008)	0.629
ApoA1	1.8	Below	100,397	-0.177 (-0.182 to -0.172)**	<1*10 ⁻³¹⁷	-0.049 (-0.055 to -0.044)**	3*10 ⁻⁷⁰	0.048 (0.042 to 0.053)**	2*10 ⁻⁷²
		Above	6980	-0.061 (-0.075 to -0.046)**	1*10 ⁻¹⁶	0.025 (0.014 to 0.037)*	2*10⁻⁵	-0.005 (-0.016 to 0.007)	0.421
HbA1c	30	Below	11,114	0.006 (-0.015 to 0.026)	0.591	-0.039 (-0.059 to -0.019)	1*10⁻⁴	0.012 (-0.007 to 0.031)	0.222
		Above	104,913	0.133 (0.128 to 0.137)**	<1*10 ⁻³¹⁷	0.050 (0.045 to 0.055)**	7*10 ⁻⁸⁰	-0.032 (-0.037 to -0.027)**	4*10 ⁻³⁶
HbA1c	48	Below	115,188	0.114 (0.109 to 0.120)**	<1*10 ⁻³¹⁷	0.032 (0.026 to 0.037)**	2*10 ⁻²⁹	-0.024 (-0.029 to -0.018)**	2*10 ⁻¹⁸
		Above	839	-0.153 (-0.267 to -0.038)	0.009	0.202 (0.057 to 0.348)	0.006	-0.099 (-0.218 to 0.019)	0.101
Neutrophils	2.0	Below	2125	-0.070 (-0.144 to 0.003)	0.061	-0.110 (-0.176 to -0.043)	0.001	0.034 (-0.030 to 0.098)	0.294
		Above	116,340	0.074 (0.069 to 0.079)**	1*10 ⁻¹⁷³	0.084 (0.079 to 0.089)**	8*10 ⁻²⁰³	-0.027 (-0.032 to -0.022)**	2*10 ⁻²⁴
Neutrophils	7.5	Below	115,981	0.089 (0.084 to 0.095)**	1*10 ⁻²²⁶	0.081 (0.076 to 0.087)**	3*10 ⁻¹⁷²	-0.026 (-0.031 to -0.021)**	8*10 ⁻²¹
		Above	2484	-0.012 (-0.027 to 0.002)	0.095	0.005 (-0.011 to 0.021)	0.558	0.006 (-0.010 to 0.022)	0.455
CRP	8.0	Below	111,698	0.322 (0.317 to 0.327)**	<1*10 ⁻³¹⁷	0.124 (0.119 to 0.129)**	<1*10 ⁻³¹⁷	-0.042 (-0.047 to -0.037)**	1*10 ⁻⁶⁵
		Above	4504	-0.051 (-0.064 to -0.038)**	1*10⁻¹⁴	-0.023 (-0.039 to -0.007)	0.005	-0.008 (-0.023 to 0.007)	0.280
WOMEN									
ALP	35	Below	476	-0.040 (-0.172 to 0.091)	0.545	0.008 (-0.104 to 0.120)	0.891	0.010 (-0.103 to 0.124)	0.859
		Above	128,904	0.169 (0.164 to 0.174)**	<1*10 ⁻³¹⁷	0.075 (0.070 to 0.080)**	6*10 ⁻²⁰³	0.008 (0.004 to 0.013)	6*10 ⁻⁴
AST	70	Below	128,476	0.032 (0.027 to 0.038)**	3*10 ⁻³³	0.037 (0.032 to 0.042)**	1*10 ⁻⁴⁵	-0.036 (-0.041 to -0.031)**	8*10 ⁻⁴⁵
		Above	429	-0.095 (-0.239 to 0.049)	0.195	0.073 (-0.084 to 0.229)	0.361	0.053 (-0.095 to 0.202)	0.482
ALT	10	Below	7314	-0.009 (-0.022 to 0.005)	0.206	0.002 (-0.009 to 0.014)	0.690	0.009 (-0.003 to 0.020)	0.146
		Above	122,059	0.209 (0.204 to 0.214)**	<1*10 ⁻³¹⁷	0.109 (0.104 to 0.115)**	<1*10 ⁻³¹⁷	-0.077 (-0.082 to -0.072)**	5*10 ⁻²⁰⁴
ALT	70	Below	128,587	0.219 (0.214 to 0.224)**	<1*10 ⁻³¹⁷	0.112 (0.107 to 0.117)**	<1*10 ⁻³¹⁷	-0.077 (-0.082 to -0.072)**	4*10 ⁻²⁰⁴
		Above	786	-0.020 (-0.083 to 0.042)	0.520	-0.067 (-0.132 to -0.002)	0.042	-0.003 (-0.063 to 0.056)	0.914

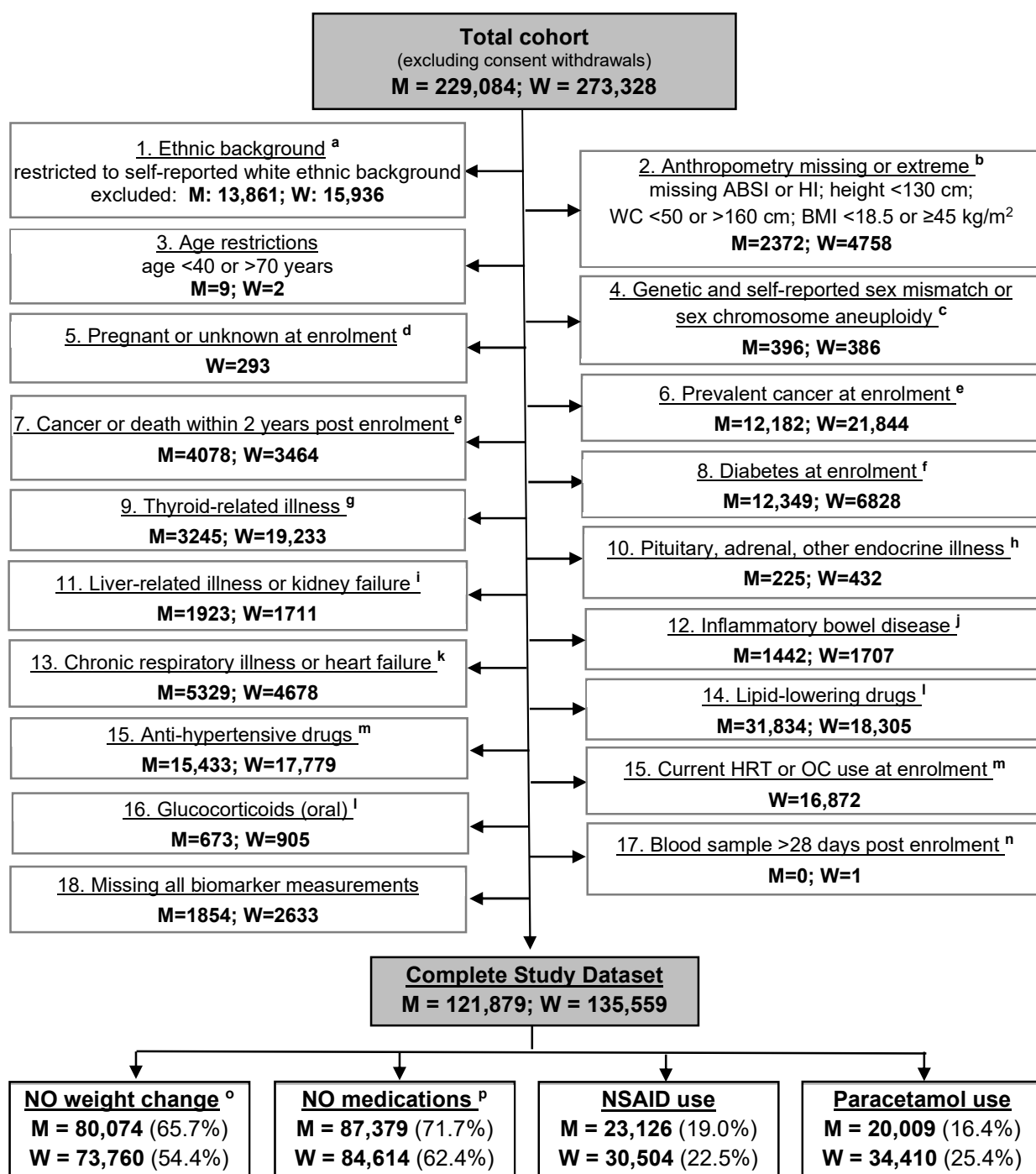
				BMI		ABSI		HI	
	Cut-off		Count	SD _{diff} (95% CI)	p-value	SD _{diff} (95% CI)	p-value	SD _{diff} (95% CI)	p-value
WOMEN (continued)									
HbA1c	48	Below	128,377	0.114 (0.109 to 0.119)**	<1*10 ⁻³¹⁷	0.062 (0.057 to 0.067)**	7*10 ⁻¹³¹	-0.044 (-0.049 to -0.039)**	4*10 ⁻⁶⁸
		Above	415	-0.171 (-0.345 to 0.003)	0.054	0.185 (-0.031 to 0.400)	0.093	-0.005 (-0.182 to 0.172)	0.954
Neutrophils	2.0	Below	2398	-0.190 (-0.268 to -0.112)*	2*10⁻⁶	-0.092 (-0.153 to -0.031)	0.003	0.034 (-0.027 to 0.096)	0.268
		Above	128,751	0.115 (0.110 to 0.120)**	<1*10 ⁻³¹⁷	0.057 (0.053 to 0.062)**	7*10 ⁻¹²¹	-0.007 (-0.012 to -0.002)	0.003
Neutrophils	7.5	Below	128,809	0.121 (0.115 to 0.126)**	<1*10 ⁻³¹⁷	0.057 (0.052 to 0.062)**	1*10 ⁻¹⁰⁵	-0.002 (-0.007 to 0.003)	0.463
		Above	2340	-0.013 (-0.027 to 0.001)	0.064	0.016 (0.001 to 0.031)	0.035	-0.013 (-0.027 to 0.001)	0.068
CRP	8.0	Below	123,801	0.428 (0.424 to 0.433)**	<1*10 ⁻³¹⁷	0.099 (0.095 to 0.103)**	<1*10 ⁻³¹⁷	-0.017 (-0.022 to -0.013)**	1*10 ⁻¹⁵
		Above	5448	-0.060 (-0.070 to -0.050)**	2*10⁻³²	0.003 (-0.009 to 0.015)	0.649	0.011 (0.000 to 0.021)	0.056

ABSI – a body shape index; **ALP** – alkaline phosphatase (U/L); **ALT** – alanine aminotransferase (U/L); **ApoA1** – apolipoprotein A1 (g/L); **AST** – aspartate aminotransferase (U/L); **BMI** – body mass index; **Count** – number of participants with available biomarker measurements per subgroup; **CRP** – C-reactive protein (mg/L); **HbA1c** – haemoglobin A1c (glycated haemoglobin, mmol/mol); **HDL-C** – high-density lipoprotein cholesterol (mmol/L); **HI** – hip index; **Neutrophils** (*10⁹/L).

Cut-off – see units above; **Below** – biomarker levels < cut-off; **Above** – biomarker levels ≥ cut-off.

SD_{diff} (95% CI) – estimates for standard deviation difference (95% confidence interval) for each biomarker, per one SD increment of the corresponding anthropometric index, were obtained from multivariable linear regression models with each biomarker on a continuous scale (sex-specific z-scores, following log-transformation) as an outcome variable and BMI, ABSI, and HI on a continuous scale (sex-specific z-scores) as independent variables. All models were adjusted for height, age at enrolment, weight change within the last year preceding enrolment, smoking status, alcohol consumption, physical activity, Townsend deprivation index, region of the assessment centre, time of blood collection, fasting time, use of nonsteroidal anti-inflammatory drugs, paracetamol use, and in women also menopausal status, oral contraceptives use, hormone replacement therapy use, and age at the last live birth. Covariates are defined in Supplementary Methods.

* – p<0.0001 from Wald test for the individual term; ** – p<1*10⁻⁶ (biomarkers with opposite direction of the association in the two groups and p<0.0002 for the small tail-end group are shown in bold).



Supplementary Figure S1 Flow diagram of UK Biobank participants in the study

ABSI – a body shape index; **BMI** – body mass index; **HI** – hip index; **HRT** – hormone replacement therapy; **M** – number of men; **NSAID** – nonsteroidal anti-inflammatory drugs; **OC** – oral contraceptives; **W** – number of women; **WC** – waist circumference.

The exclusion criteria were applied sequentially in the displayed order, such that each excluded individual was counted only once. Specific fields used to define the exclusions are listed below:

^a – Field [21000-0.0] “*Ethnic background*”; in the study were retained participants with codes: 1 “*White*”, 1001 “*British*”, 1002 “*Irish*”, 1003 “*Any other white background*”.

- ^b – anthropometric measurements were obtained from Fields [48-0.0] “*Waist circumference*”, Field [49-0.0] “*Hip circumference*”, Field [50-0.0] “*Standing height*” and Field [21002-0.0] “*Weight*”.
- ^c – excluded were participants with code 1 for Field [22019-0.0] “*Sex chromosome aneuploidy*” OR with a mismatch between Field [22001-0.0] “*Genetic sex*” and Field [34-0.0] “*Sex (self-reported)*”.
- ^d – Field [3140-0.0] “*Pregnant*”; Answer: 1 “Yes”, OR Answer 2: “Unsure”, OR Missing.
- ^e – prevalent and incident cancer cases and deaths were ascertained according to our previous publication [ref. 10].
- ^f – definition based on a combination of self-reported diabetes status (see Supplementary Methods) and antidiabetic drug use (see list in Supplementary Table S1).
- ^g – exclusions comprised thyroid-related non-cancer illness self-reported at enrolment from Fields [20002-0.0...33] “*Non-cancer illness code, self-reported*”, including the following codes (as listed in UK Biobank Coding 6):

1224	thyroid problem (not cancer)
1225	hyperthyroidism/thyrotoxicosis
1226	hypothyroidism/myxoedema
1228	thyroid radioablation therapy
1428	thyroiditis
1522	grave's disease
1610	thyroid goitre

Note from UK Biobank: *If the participant was uncertain of the type of illness they had had, then they described it to the interviewer (a trained nurse) who attempted to place it within the coding tree. If the illness could not be located in the coding tree, then the interviewer entered a free-text description of it. These free-text descriptions were subsequently examined by a doctor and, where possible, matched to entries in the coding tree. Free-text descriptions which could not be matched with very high probability have been marked as "unclassifiable".*

- ^h – exclusions comprised pituitary, adrenal, and other endocrine non-cancer illness self-reported at enrolment (as in ^g) with codes:
- | | |
|------|--|
| 1232 | disorder of adrenal gland |
| 1233 | adrenal tumour |
| 1234 | adrenocortical insufficiency/addison's disease |
| 1235 | hyperaldosteronism/conn's syndrome |
| 1236 | phaeochromocytoma |
| 1237 | disorder of pituitary gland |
| 1238 | pituitary adenoma/tumour |
| 1239 | cushings syndrome |
| 1429 | acromegaly |
| 1430 | hypopituitarism |
| 1431 | hyperprolactinaemia |
| 1432 | carcinoid syndrome/tumour |
| 1682 | benign insulinoma |

ⁱ – exclusions comprised liver-related non-cancer illness and kidney failure self-reported at enrolment (as in ^g) with codes:

- 1136 liver/biliary/pancreas problem
- 1155 hepatitis
- 1156 infective/viral hepatitis
- 1157 non-infective hepatitis
- 1158 liver failure/cirrhosis
- 1159 bile duct disease
- 1160 bile duct obstruction/ascending cholangitis
- 1192 renal/kidney failure
- 1193 renal failure requiring dialysis
- 1194 renal failure not requiring dialysis
- 1475 sclerosing cholangitis
- 1506 primary biliary cirrhosis
- 1507 haemochromatosis
- 1508 jaundice (unknown cause)
- 1578 hepatitis a, 1579 hepatitis b, 1580 hepatitis c, 1581 hepatitis d, 1582 hepatitis e
- 1604 alcoholic liver disease / alcoholic cirrhosis

^j – exclusions comprised inflammatory bowel disease (non-cancer illness) self-reported at enrolment (as in ^g) with codes:

- 1461 inflammatory bowel disease
- 1462 crohns disease
- 1463 ulcerative colitis

^k – exclusions comprised chronic respiratory non-cancer illness or heart failure self-reported at enrolment (as in ^g) with codes:

- 1076 heart failure/pulmonary odema
- 1112 chronic obstructive airways disease/copd
- 1113 emphysema/chronic bronchitis
- 1114 bronchiectasis
- 1115 interstitial lung disease
- 1120 asbestosis
- 1121 pulmonary fibrosis
- 1122 fibrosing alveolitis/unspecified alveolitis
- 1124 respiratory failure
- 1126 spontaneous pneumothorax/recurrent pneumothorax
- 1412 bronchitis
- 1472 emphysema
- 1496 alpha-1 antitrypsin deficiency

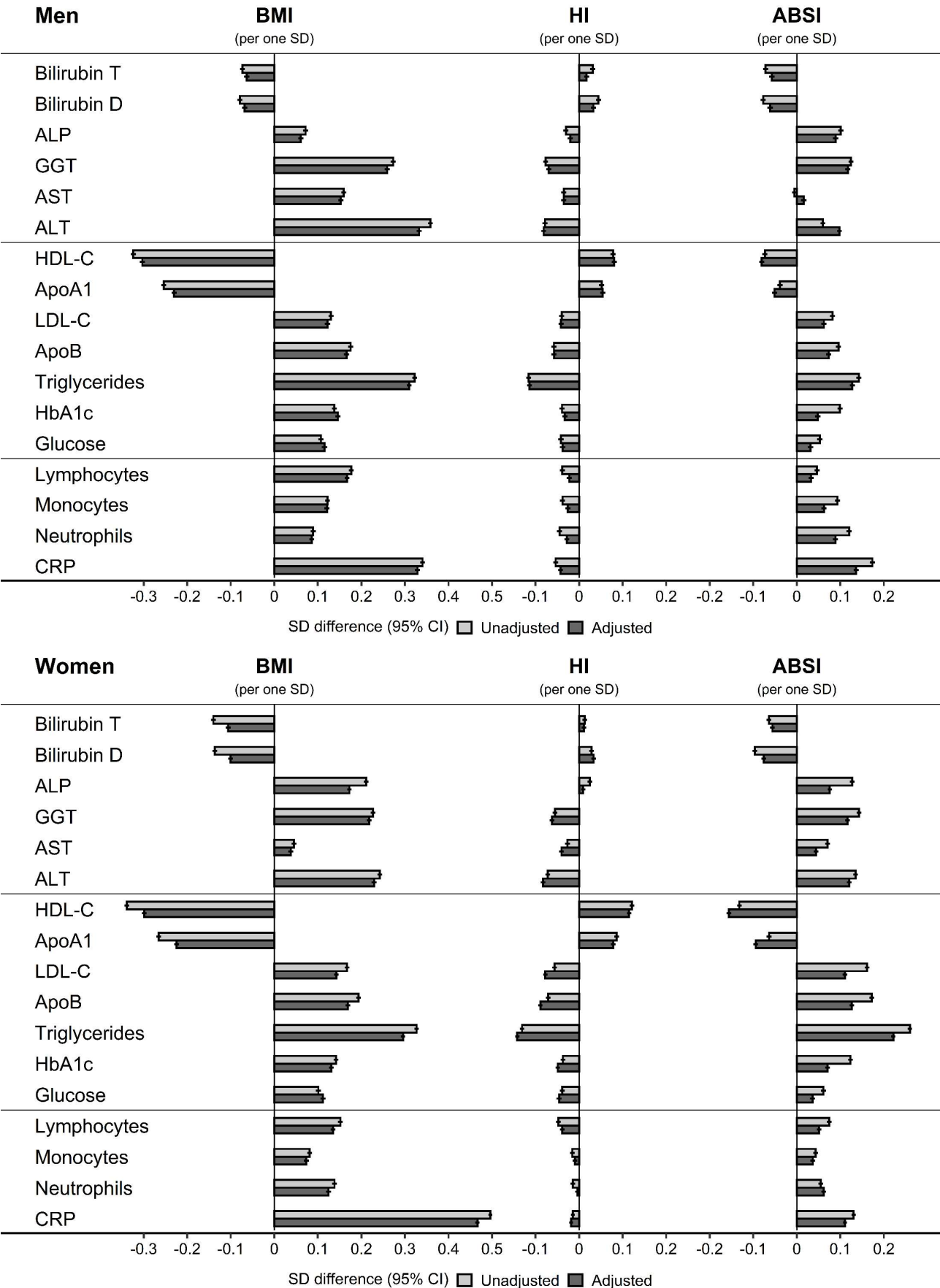
^l – see list of lipid-lowering drugs or glucocorticoids for exclusion in Supplementary Table S1.

^m – see definition of HRT, OC, and anti-hypertensive drugs use in Supplementary Methods.

ⁿ – calculated as the difference between the date of blood sample collection extracted from Field [3166-0.0] "*Time blood sample collected*" and the date of the baseline visit (at enrolment) Field [53-0.0] "*Date of attending assessment centre*".

^o – excluding participants with weight loss or weight gain within the last year preceding enrolment (self-reported in Field [2306-0.0] "*Weight change compared with 1 year ago*").

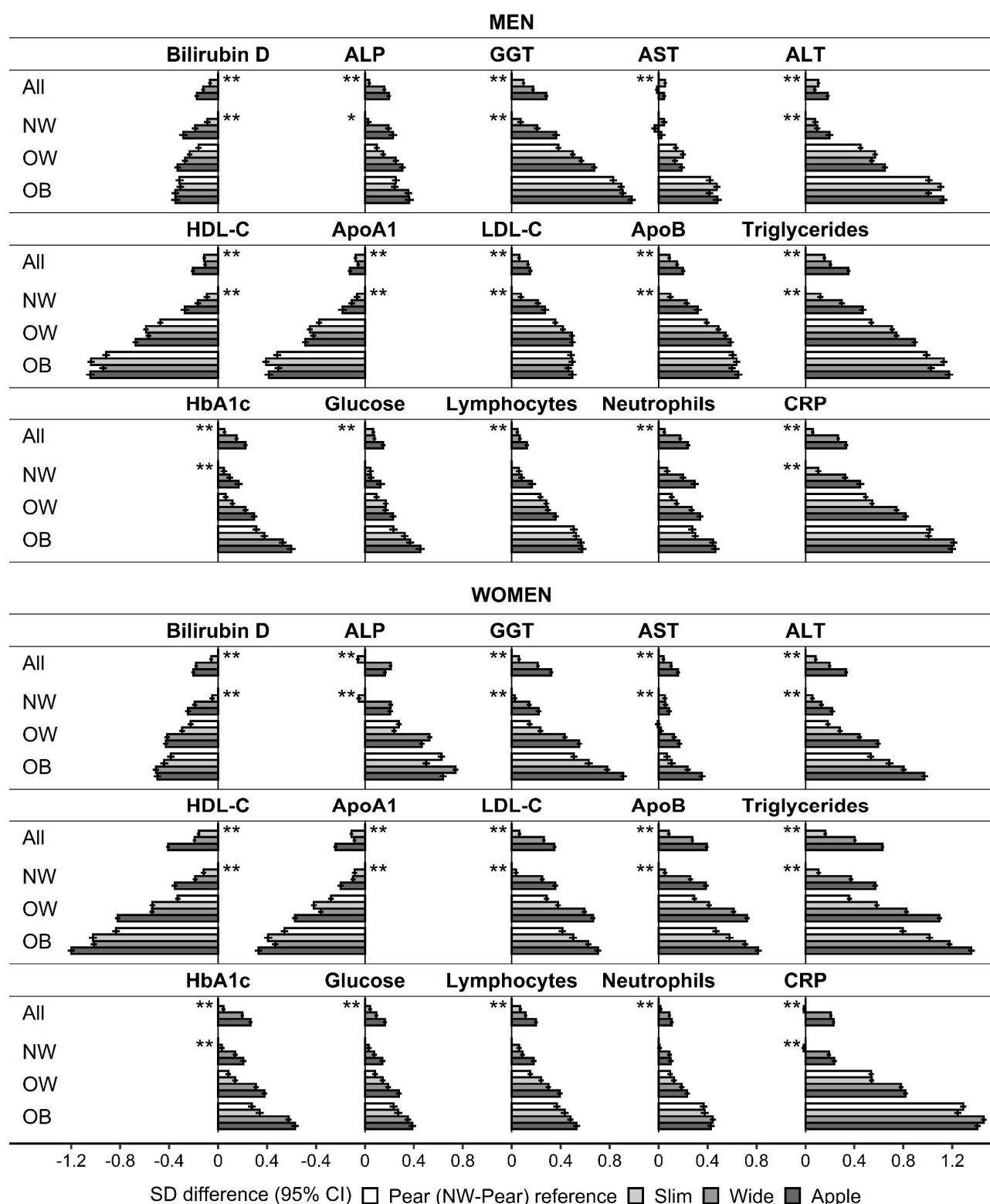
^p – excluding participants with NSAID or paracetamol use.



Supplementary Figure S2 Associations of biomarkers with body size and body shape indices (continuous, unadjusted)

ABSI – a body shape index; **ALP** – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **AST** – aspartate aminotransferase; **Bilirubin D** – direct bilirubin; **Bilirubin T** – total bilirubin; **BMI** – body mass index; **CRP** – C-reactive protein; **GGT** – gamma-glutamyltransferase; **HbA1c** – haemoglobin A1c (glycated haemoglobin); **HDL-C** – high-density lipoprotein cholesterol; **HI** – hip index; **LDL-C** – low-density lipoprotein cholesterol; **SD** – standard deviation.

SD difference (95% CI) – unadjusted estimates for standard deviation difference (95% confidence interval) were obtained from multivariable linear regression models including each biomarker on a continuous scale (sex-specific z-scores, following log-transformation) as an outcome variable and BMI, ABSI, and HI on a continuous scale (sex-specific z-scores) as independent variables without any covariates. Adjusted models are included for comparison (estimates and covariates correspond to Figure 1). Adjustment variables included height, age at enrolment, weight change within the last year preceding enrolment, smoking status, alcohol consumption, physical activity, Townsend deprivation index, region of the assessment centre, time of blood collection, fasting time, nonsteroidal anti-inflammatory drug use, paracetamol use, and in women also menopausal status, oral contraceptives use, hormone replacement therapy use, and age at the last live birth.



Supplementary Figure S3 Associations of biomarkers with body shape phenotypes (categorical, unadjusted)

ABSI – a body shape index (cut-offs ≥ 80 for men, ≥ 73 for women); **ALP** – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **Apple** – large-ABSI-small-HI; **AST** – aspartate aminotransferase; **Bilirubin D** – direct bilirubin; **BMI** – body mass index; **CRP** – C-reactive protein; **GGT** – gamma-glutamyltransferase; **HbA1c** – haemoglobin

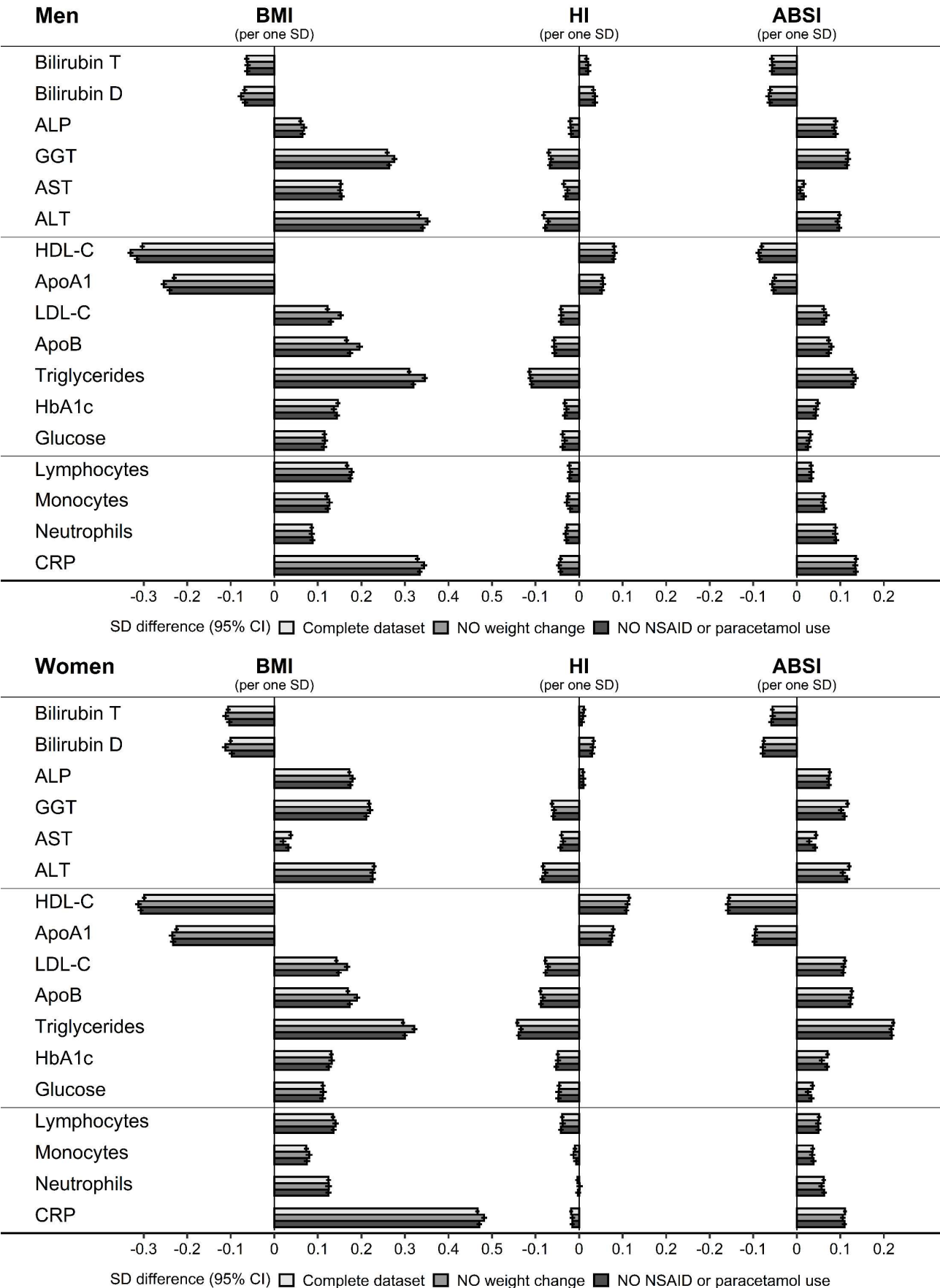
A1c (glycated haemoglobin); **HDL-C** – high-density lipoprotein cholesterol; **HI** – hip index (cut-offs ≥ 49 for men, ≥ 64 for women); **LDL-C** – low-density lipoprotein cholesterol; **NW** – normal weight ($\text{BMI} \geq 18.5$ to $< 25 \text{ kg/m}^2$); **OB** – obese ($\text{BMI} \geq 30$ to $< 45 \text{ kg/m}^2$); **OW** – overweight ($\text{BMI} \geq 25$ to $< 30 \text{ kg/m}^2$); **Pear** – small-ABSI-large-HI; **Slim** – small-ABSI-small-HI; **Wide** – large-ABSI-large-HI.

SD difference (95% CI) – estimates for standard deviation difference (95% confidence interval) were obtained from multivariable linear regression models including each biomarker on a continuous scale (sex-specific z-scores, following log-transformation) as an outcome variable and the following two combinations as independent variables: an ABSI-by-HI cross-classification and BMI categories (for ALL, reference “pear”), or an BMI-by-ABSI-by-HI cross-classification (for NW, OW, and OB, reference “pear”-NW). There was no further adjustment for covariates.

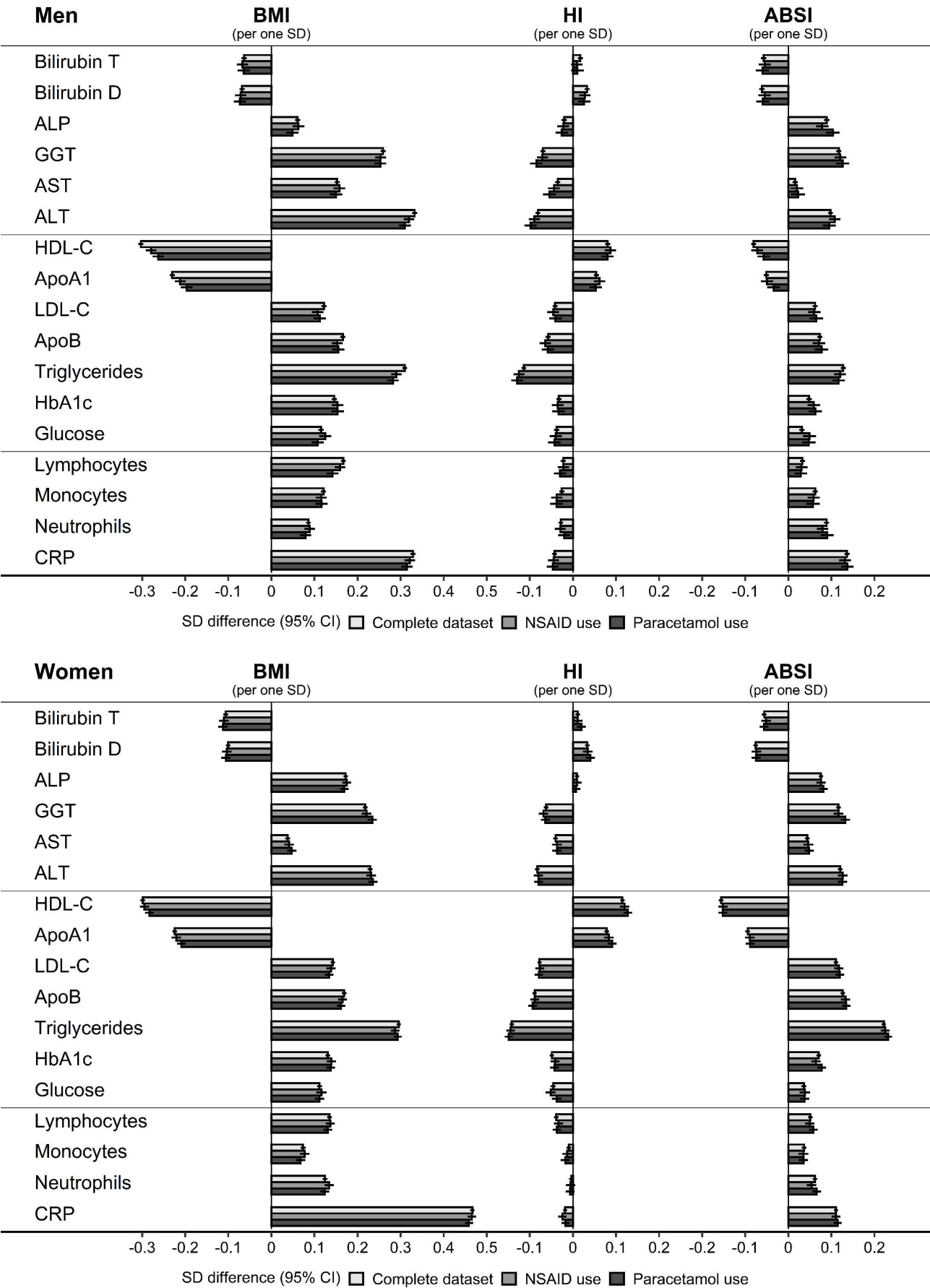
p_{body shape} (for ALL) – was obtained from a likelihood ratio test comparing a model including only BMI categories with a model additionally including an ABSI-by-HI cross-classification (evaluates the significance of body-shape overall).

p_{interaction} (for NW, OW, and OB) – was obtained from a likelihood ratio test comparing the additive model including the ABSI-by-HI cross-classification, BMI categories with the interaction model including the BMI-by-ABSI-by-HI cross-classification (evaluates heterogeneity by BMI).

* – $p < 0.0001$; ** – $p < 1 \times 10^{-6}$



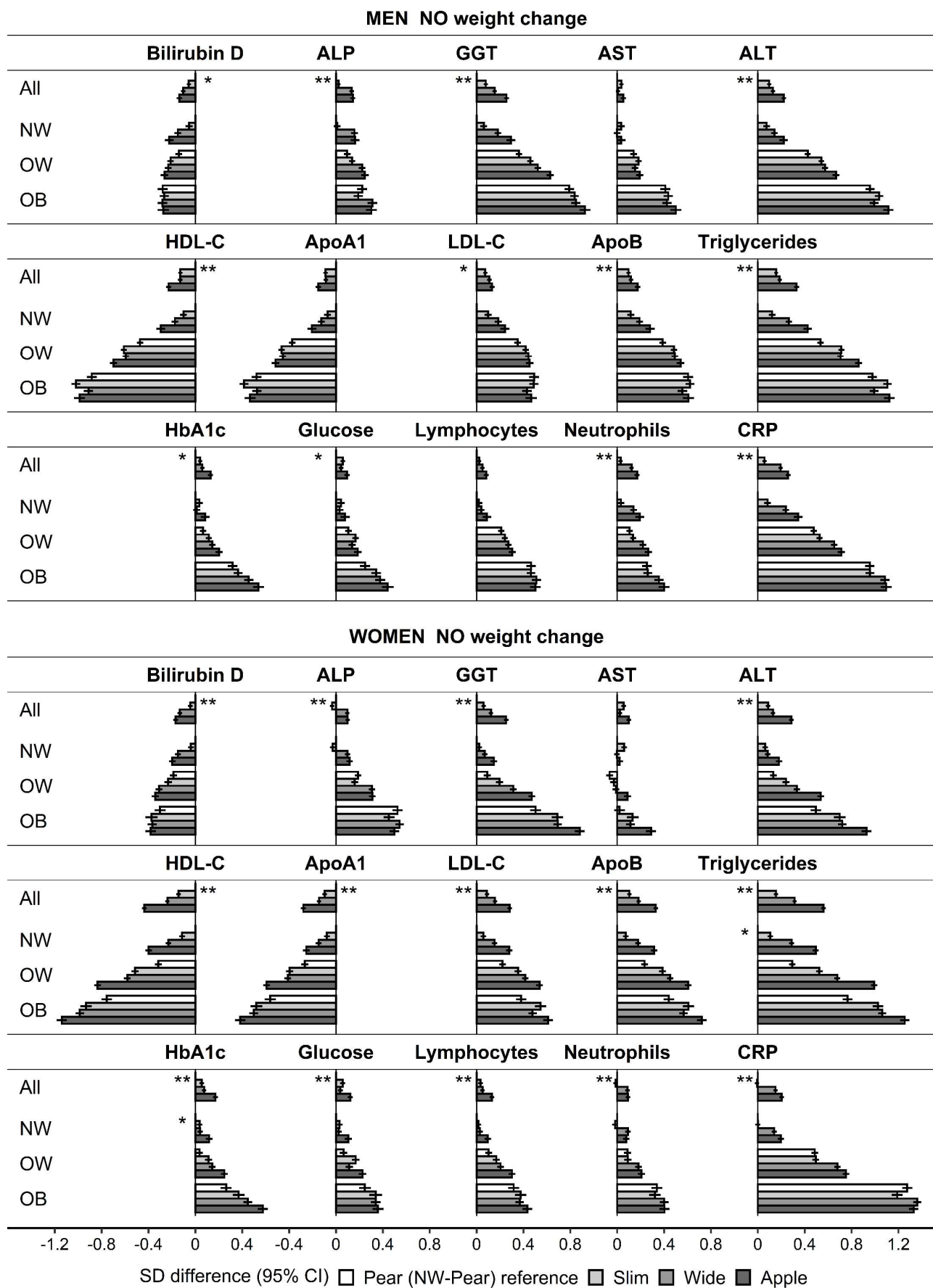
Supplementary Figure S4A Associations of biomarkers with body size and body shape indices: excluding weight loss or medication use



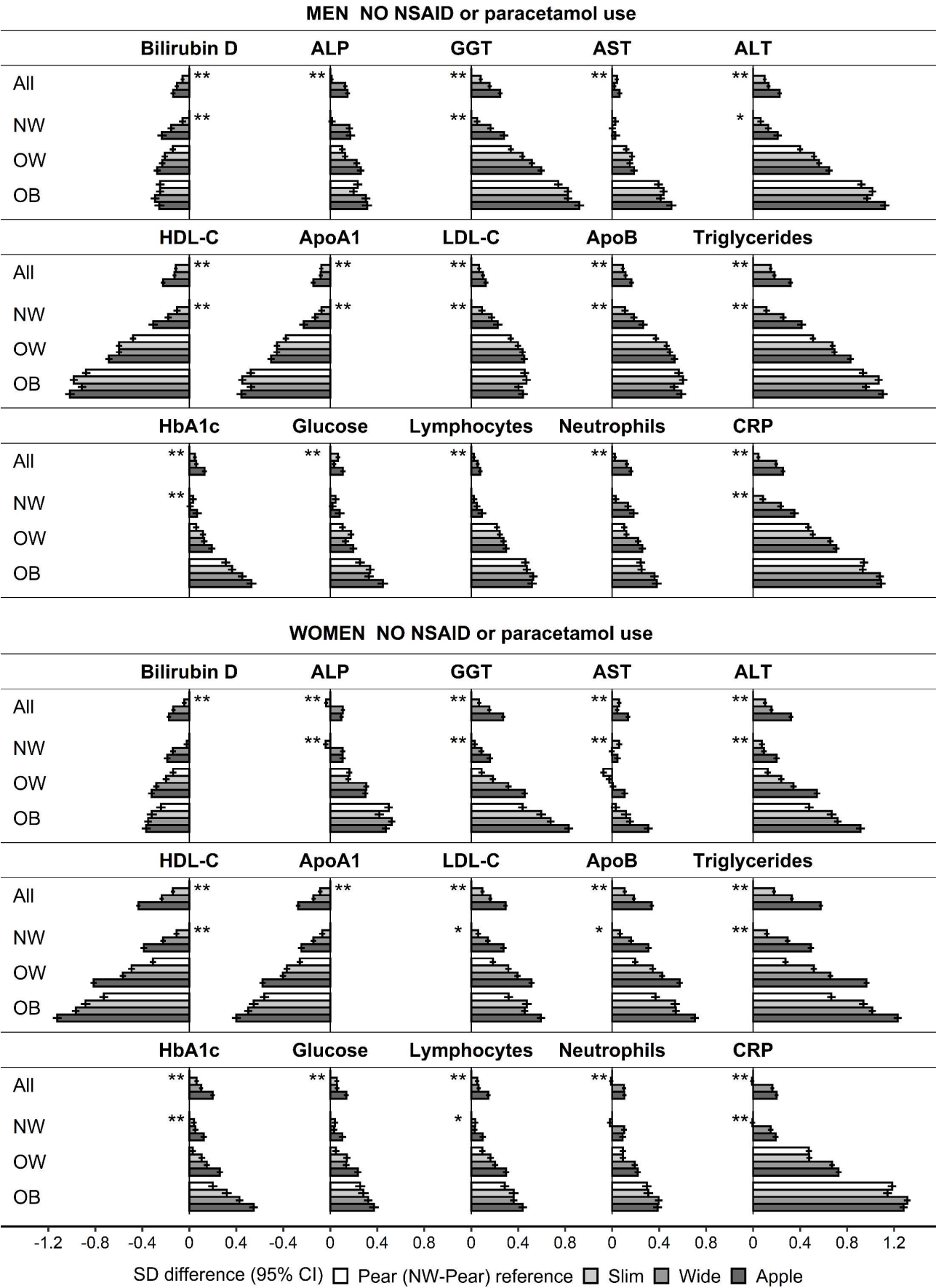
Supplementary Figure S4B Associations of biomarkers with body size and body shape indices: subgroups with medication use

ABSI – a body shape index; **ALP** – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **AST** – aspartate aminotransferase; **Bilirubin D** – direct bilirubin; **Bilirubin T** – total bilirubin; **BMI** – body mass index; **CRP** – C-reactive protein; **GGT** – gamma-glutamyltransferase; **HbA1c** – haemoglobin A1c (glycated haemoglobin); **HDL-C** – high-density lipoprotein cholesterol; **HI** – hip index; **LDL-C** – low-density lipoprotein cholesterol; **NSAID** – nonsteroidal anti-inflammatory drugs; **SD** – standard deviation; **NO weight change** – no weight loss or weight gain within the last year preceding enrolment (self-reported).

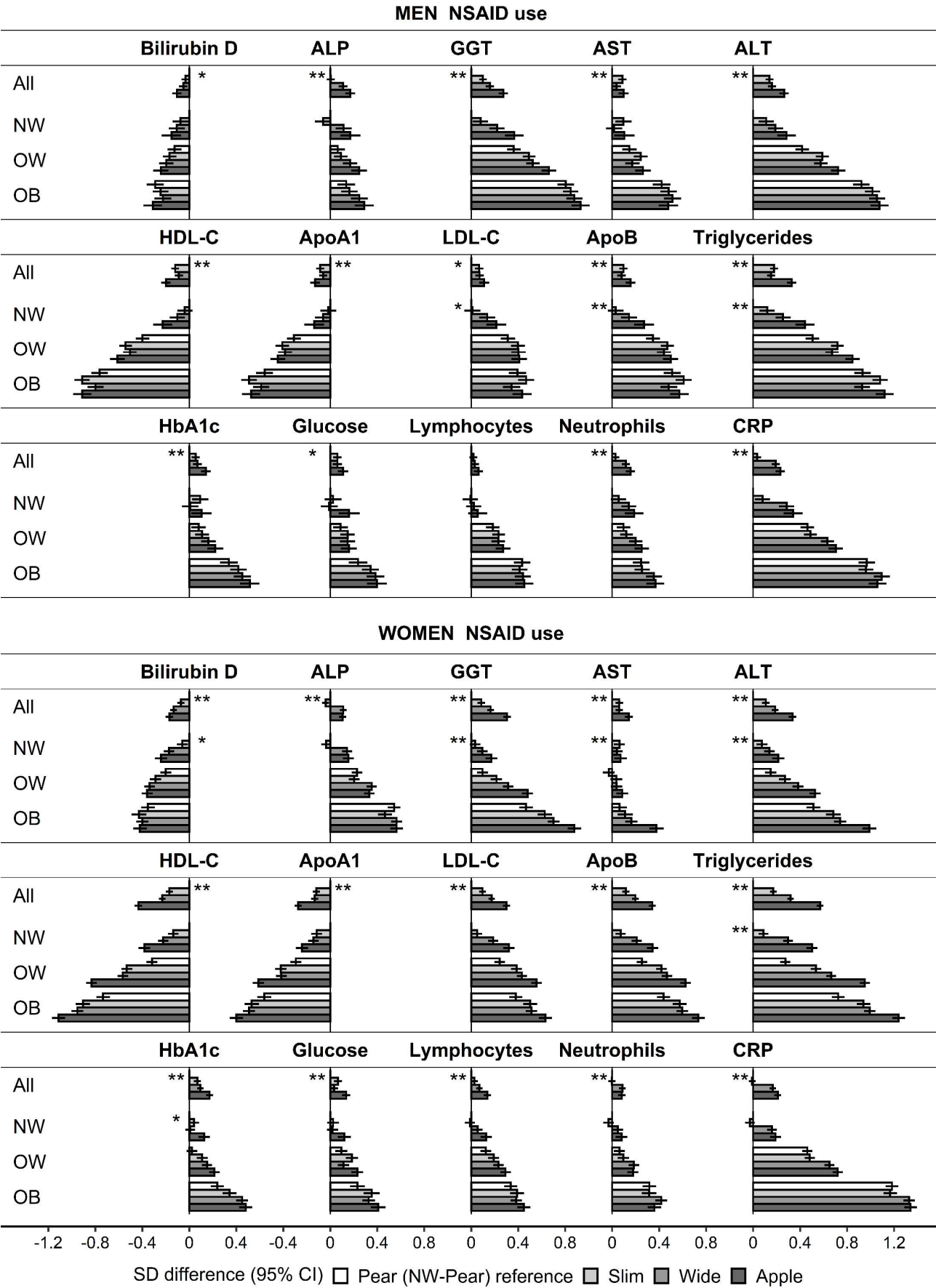
SD difference (95% CI) – estimates for standard deviation difference (95% confidence interval) were obtained from multivariable linear regression models including each biomarker on a continuous scale (sex-specific z-scores, following log-transformation) as an outcome variable and BMI, ABSI, and HI on a continuous scale (sex-specific z-scores) as independent variables. All models were adjusted for height, age at enrolment, weight change within the last year preceding enrolment (except for the subgroup with no weight change), smoking status, alcohol consumption, physical activity, Townsend deprivation index, region of the assessment centre, time of blood collection, fasting time, NSAID use (for the subgroups with no weight change and paracetamol use), paracetamol use (for the subgroups with no weight change and NSAID use), and in women also menopausal status, oral contraceptives use, hormone replacement therapy use, and age at the last live birth. Covariates are defined in Supplementary Methods. Participant counts per subgroup are shown in Supplementary Figure S1 and by subgroup and body shape phenotype in Table 1.



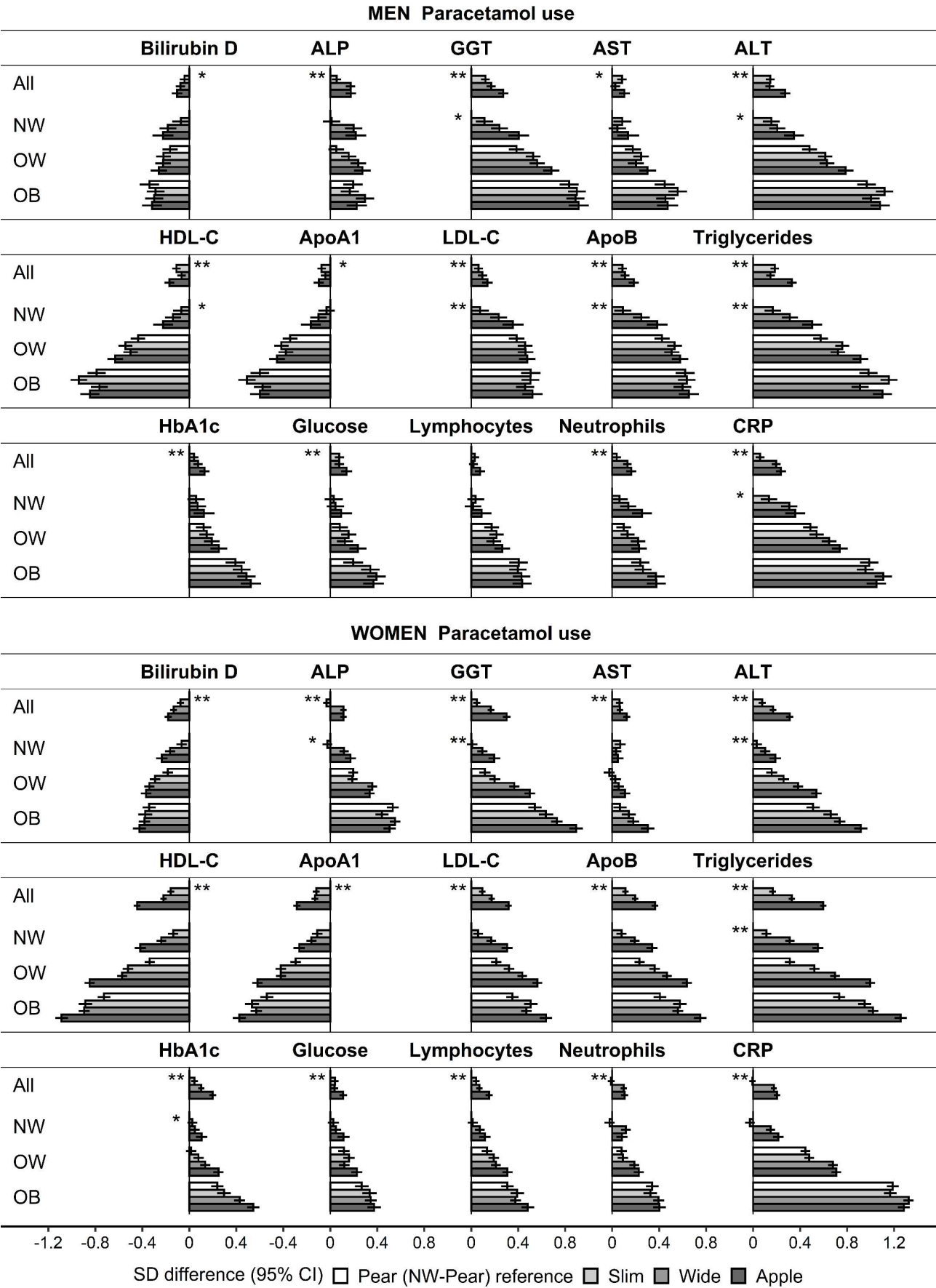
Supplementary Figure S5A Associations of biomarkers with body shape phenotypes: subgroup without recent weight change



Supplementary Figure S5B Associations of biomarkers with body shape phenotypes: subgroup without NSAID or paracetamol use



Supplementary Figure S5C Associations of biomarkers with body shape phenotypes: subgroup with NSAID use



Supplementary Figure S5D Associations of biomarkers with body shape phenotypes: subgroup with paracetamol use

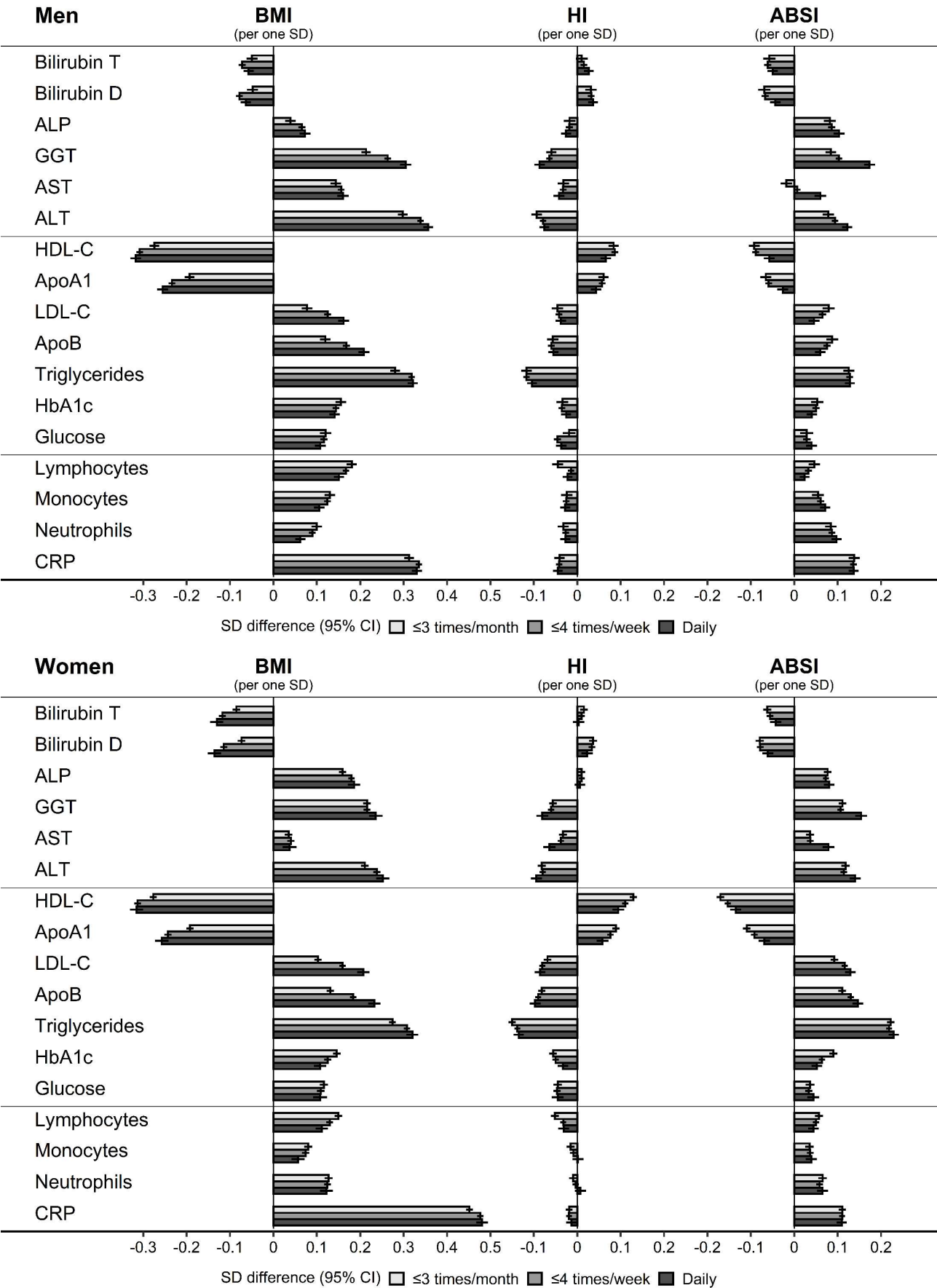
ABSI – a body shape index (cut-offs ≥ 80 for men, ≥ 73 for women); **ALP** – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **Apple** – large-ABSI-small-HI; **AST** – aspartate aminotransferase; **Bilirubin D** – direct bilirubin; **BMI** – body mass index; **CRP** – C-reactive protein; **GGT** – gamma-glutamyltransferase; **HbA1c** – haemoglobin A1c (glycated haemoglobin); **HDL-C** – high-density lipoprotein cholesterol; **HI** – hip index (cut-offs ≥ 49 for men, ≥ 64 for women); **LDL-C** – low-density lipoprotein cholesterol; **NSAID** – nonsteroidal anti-inflammatory drugs; **NW** – normal weight ($\text{BMI} \geq 18.5$ to $< 25 \text{ kg/m}^2$); **OB** – obese ($\text{BMI} \geq 30$ to $< 45 \text{ kg/m}^2$); **OW** – overweight ($\text{BMI} \geq 25$ to $< 30 \text{ kg/m}^2$); **Pear** – small-ABSI-large-HI; **Slim** – small-ABSI-small-HI; **NO weight change** – no weight loss or weight gain within the last year preceding enrolment (self-reported); **Wide** – large-ABSI-large-HI.

SD difference (95% CI) – estimates for standard deviation difference (95% confidence interval) were obtained from multivariable linear regression models including each biomarker on a continuous scale (sex-specific z-scores, following log-transformation) as an outcome variable and the following two combinations as independent variables: an ABSI-by-HI cross-classification and BMI categories (for ALL, reference “pear”), or an BMI-by-ABSI-by-HI cross-classification (for NW, OW, and OB, reference “pear”-NW). All models were adjusted for height, age at enrolment, weight change within the last year preceding enrolment (except for the subgroup with no weight change), smoking status, alcohol consumption, physical activity, Townsend deprivation index, region of the assessment centre, time of blood collection, fasting time, NSAID use (for the subgroups with no weight change and paracetamol use), paracetamol use (for the subgroups with no weight change and NSAID use), and in women also menopausal status, oral contraceptives use, hormone replacement therapy use, and age at the last live birth. Covariates are defined in Supplementary Methods. Participant counts per subgroup are shown in Supplementary Figure S1 and by subgroup and body shape phenotype in Table 1.

p_{body shape} (for ALL) – was obtained from a likelihood ratio test comparing a model including only BMI categories and covariates with a model additionally including an ABSI-by-HI cross-classification (evaluates the significance of body-shape overall).

p_{interaction} (for NW, OW, and OB) – was obtained from a likelihood ratio test comparing the additive model including the ABSI-by-HI cross-classification, BMI categories, and covariates with the interaction model including the BMI-by-ABSI-by-HI cross-classification and covariates (evaluates heterogeneity by BMI).

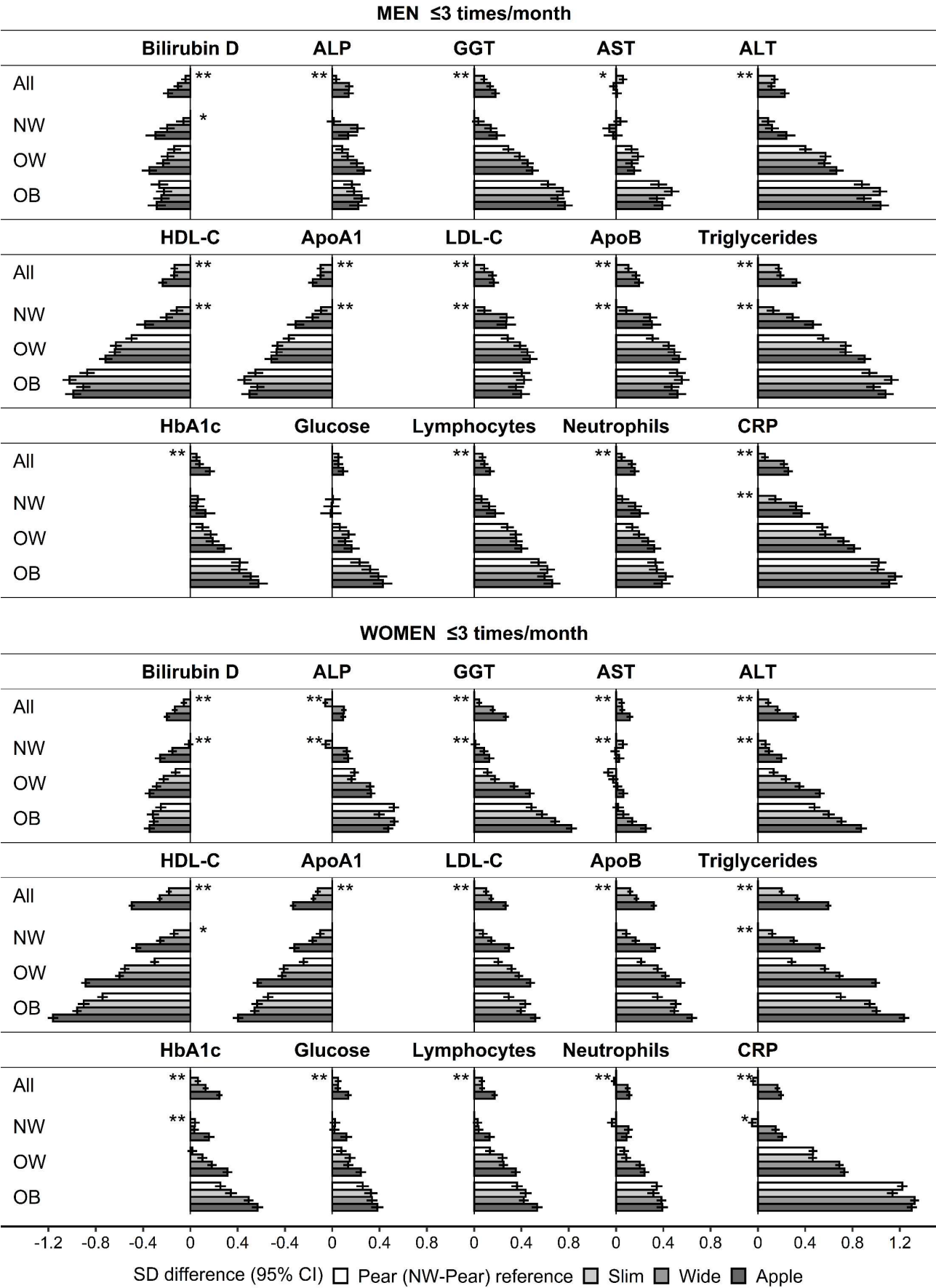
* – $p < 0.0001$; ** – $p < 1 \times 10^{-6}$



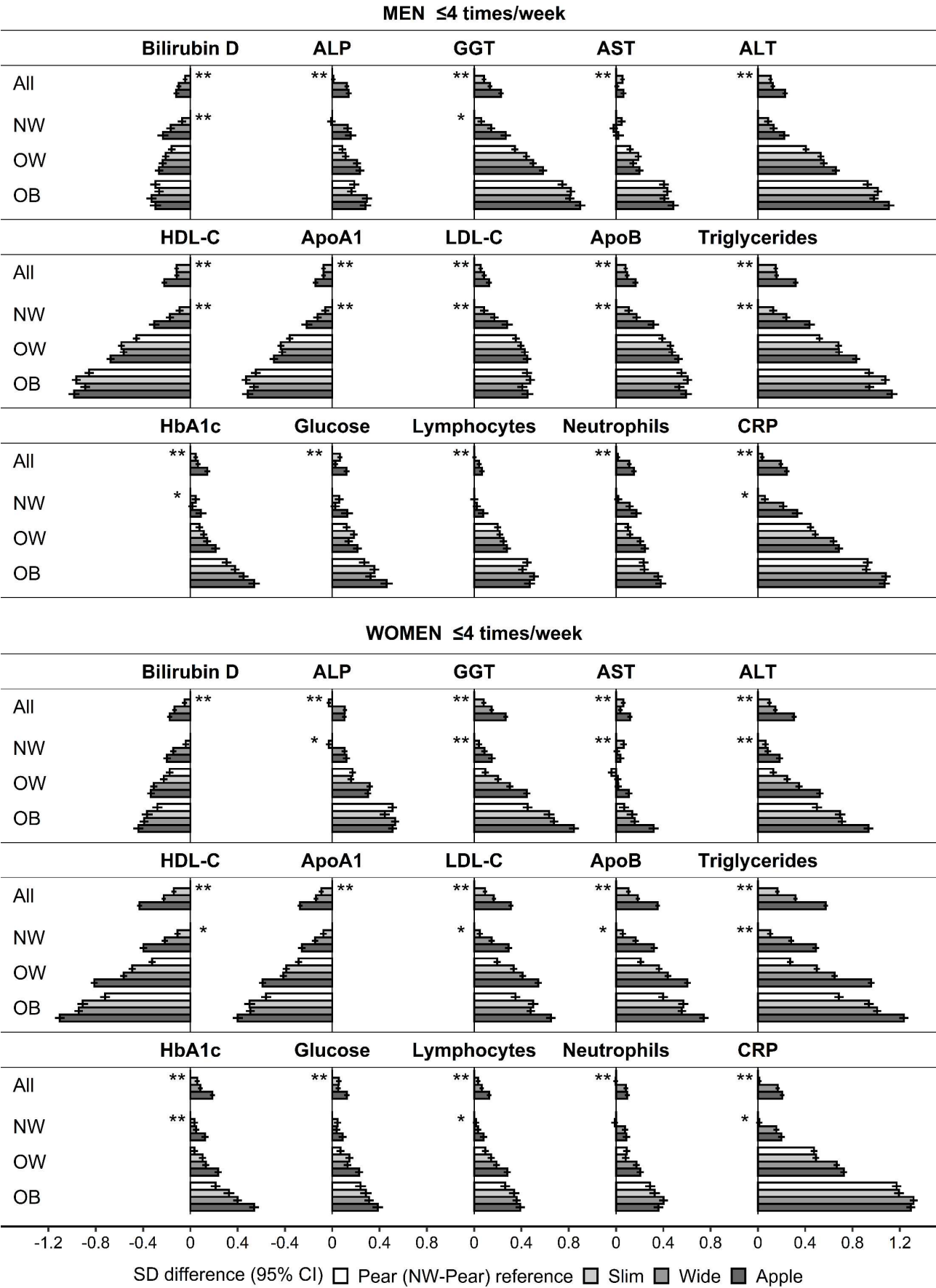
Supplementary Figure S6 Associations of biomarkers with body size and body shape indices: subgroups according to alcohol consumption

ABSI – a body shape index; **ALP** – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **AST** – aspartate aminotransferase; **Bilirubin D** – direct bilirubin; **Bilirubin T** – total bilirubin; **BMI** – body mass index; **CRP** – C-reactive protein; **GGT** – gamma-glutamyltransferase; **HbA1c** – haemoglobin A1c (glycated haemoglobin); **HDL-C** – high-density lipoprotein cholesterol; **HI** – hip index; **LDL-C** – low-density lipoprotein cholesterol; **SD** – standard deviation.

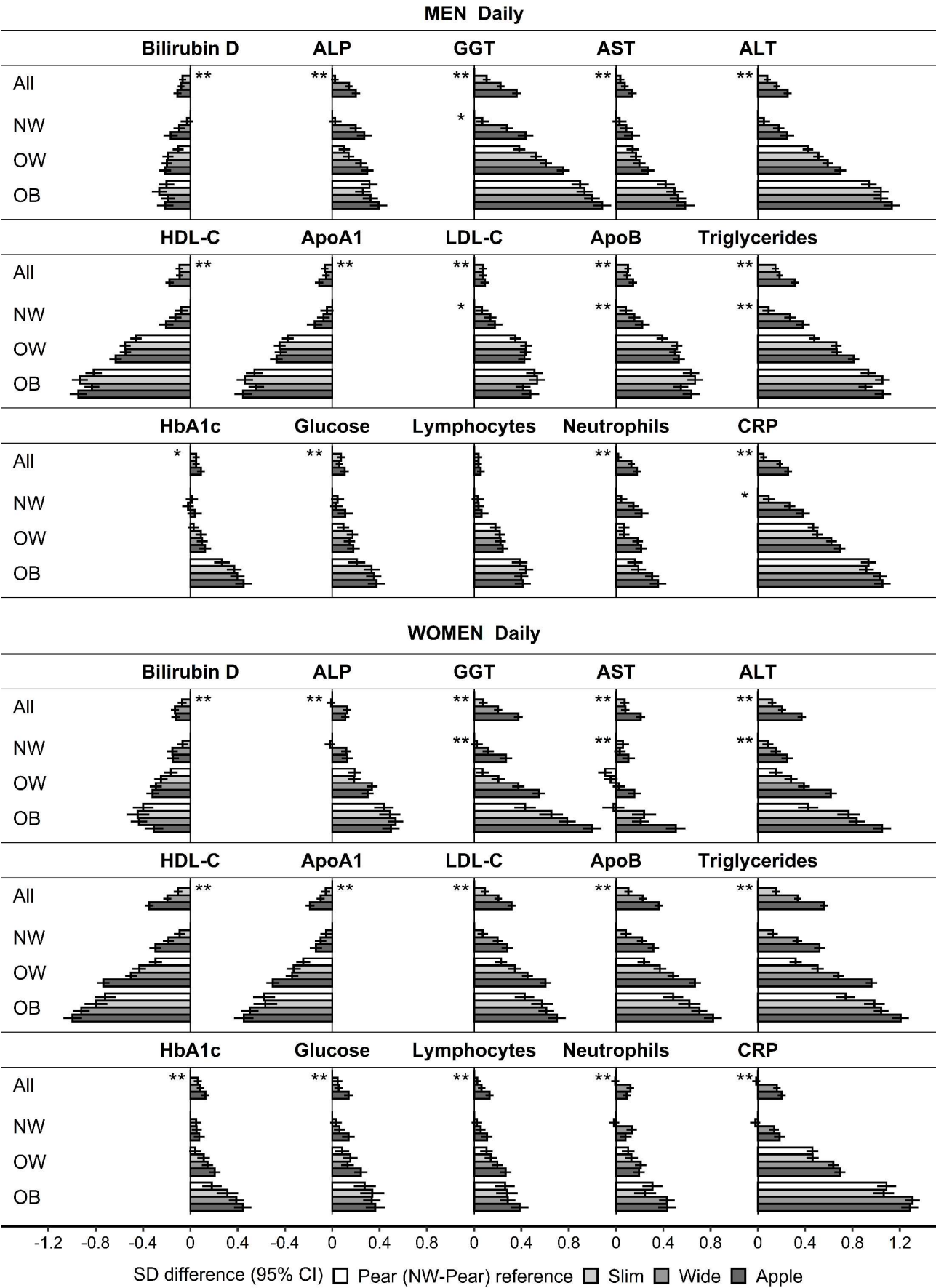
SD difference (95% CI) – estimates for standard deviation difference (95% confidence interval) were obtained from multivariable linear regression models including each biomarker on a continuous scale (sex-specific z-scores, following log-transformation) as an outcome variable and BMI, ABSI, and HI on a continuous scale (sex-specific z-scores) as independent variables. All models were adjusted for height, age at enrolment, weight change within the last year preceding enrolment, smoking status, physical activity, Townsend deprivation index, region of the assessment centre, time of blood collection, fasting time, NSAID use, paracetamol use, and in women also menopausal status, oral contraceptives use, hormone replacement therapy use, and age at the last live birth. Covariates are defined in Supplementary Methods.



Supplementary Figure S7A Associations of biomarkers with body shape phenotypes: up to 3 times a month alcohol consumption



Supplementary Figure S7B Associations of biomarkers with body shape phenotypes: up to four times a week alcohol consumption



Supplementary Figure S7C Associations of biomarkers with body shape phenotypes: daily alcohol consumption

ABSI – a body shape index (cut-offs ≥ 80 for men, ≥ 73 for women); **ALP** – alkaline phosphatase; **ALT** – alanine aminotransferase; **ApoA1** – apolipoprotein A1; **ApoB** – apolipoprotein B; **Apple** – large-ABSI-small-HI; **AST** – aspartate aminotransferase; **Bilirubin D** – direct bilirubin; **BMI** – body mass index; **CRP** – C-reactive protein; **GGT** – gamma-glutamyltransferase; **HbA1c** – haemoglobin A1c (glycated haemoglobin); **HDL-C** – high-density lipoprotein cholesterol; **HI** – hip index (cut-offs ≥ 49 for men, ≥ 64 for women); **LDL-C** – low-density lipoprotein cholesterol; **NSAID** – nonsteroidal anti-inflammatory drugs; **NW** – normal weight ($\text{BMI} \geq 18.5$ to $< 25 \text{ kg/m}^2$); **OB** – obese ($\text{BMI} \geq 30$ to $< 45 \text{ kg/m}^2$); **OW** – overweight ($\text{BMI} \geq 25$ to $< 30 \text{ kg/m}^2$); **Pear** – small-ABSI-large-HI; **Slim** – small-ABSI-small-HI; **Wide** – large-ABSI-large-HI.

SD difference (95% CI) – estimates for standard deviation difference (95% confidence interval) were obtained from multivariable linear regression models including each biomarker on a continuous scale (sex-specific z-scores, following log-transformation) as an outcome variable and the following two combinations as independent variables: an ABSI-by-HI cross-classification and BMI categories (for ALL, reference “pear”), or an BMI-by-ABSI-by-HI cross-classification (for NW, OW, and OB, reference “pear”-NW). All models were adjusted for height, age at enrolment, weight change within the last year preceding enrolment, smoking status, physical activity, Townsend deprivation index, region of the assessment centre, time of blood collection, fasting time, use of nonsteroidal anti-inflammatory drugs, paracetamol use, and in women also menopausal status, oral contraceptives use, hormone replacement therapy use, and age at the last live birth. Covariates are defined in Supplementary Methods. Participant counts per subgroup and body shape phenotype are shown in Supplementary Table S3 (missing values were assigned the sex-specific median category, ≤ 4 times/week for all).

p_{body shape} (for ALL) – was obtained from a likelihood ratio test comparing a model including only BMI categories and covariates with a model additionally including an ABSI-by-HI cross-classification (evaluates the significance of body-shape overall).

p_{interaction} (for NW, OW, and OB) – was obtained from a likelihood ratio test comparing the additive model including the ABSI-by-HI cross-classification, BMI categories, and covariates with the interaction model including the BMI-by-ABSI-by-HI cross-classification and covariates (evaluates heterogeneity by BMI).

* – $p < 0.0001$; ** – $p < 1 \times 10^{-6}$

References

The numbers of the cited references correspond to the main document.

10. Christakoudi, S., Tsilidis, K. K., Evangelou, E., Riboli, E. A Body Shape Index (ABSI), hip index and risk of cancer in the UK Biobank cohort. *Cancer Med* **10**, 5614-5628; 10.1002/CAM4.4097 (2021).
14. Christakoudi, S., Tsilidis, K. K., Evangelou, E. & Riboli, E. Association of body-shape phenotypes with imaging measures of body composition in the UK Biobank cohort: relevance to colon cancer risk. *BMC Cancer* **21**, 1160; 10.1186/s12885-021-08820-6 (2021).