Interactions of platelets with obesity in relation to lung cancer risk in the UK Biobank cohort

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Supplementary Methods

Selection of non-smoking covariates

Non-smoking covariates were selected *a priori*, based on previous reports for associations with platelet parameters and lung cancer risk, as explained below. The adjustment for drug use aimed to account for exogenous influences on metabolic and inflammatory conditions, thrombosis, and liver fat accumulation and function, which can affect platelet parameters and platelet activity.

Alcohol consumption can contribute to liver fat accumulation and fibrosis [68] and the inverse association of platelet count (PLT) with body mass index (BMI), which we have previously described for UK Biobank men, was strongest for daily alcohol consumption [10]. At the same time, lower lung cancer risk has been described in light and moderate drinkers compared to non-drinkers among never smokers [69]. PLT and platelet aggregation increase after strenuous physical exercise [70], but there is evidence that higher long term physical activity is associated with lower lung cancer risk [71]. Low socioeconomic status (proxied in our study by Townsend deprivation index) is associated with less healthy lifestyle and higher lung cancer risk [72]. Patients with type 2 diabetes mellitus or impaired fasting glucose have higher PLT, higher mean platelet volume (MPV), wider platelet distribution width (PDW) [73] and, at least for women, higher lung cancer risk [74]. We have adjusted for use of antihypertensive drugs, as indicative of consistent, clinically diagnosed hypertension. Systolic and diastolic blood pressure are associated positively with PLT and PDW [75], and systolic blood pressure is also associated positively with lung cancer risk [76]. Lipid-lowering drugs, specifically statins, can reduce liver fat accumulation and the risk of developing non-alcoholic fatty liver disease (NAFLD) [77]. Paracetamol has substantial hepatotoxicity [78] and regular paracetamol use has been associated with higher lung cancer risk [79]. Platelets are key participants in immuno-inflammation [34], and their function is likely to be affected by nonsteroidal anti-inflammatory drugs (NSAID), antiaggregants, and anticoagulants. Blood samples in UK Biobank were collected throughout the day irrespective of fasting status and we have included adjustment for time of blood collection, to account for diurnal variations in platelet parameters [80], and for fasting time, to account for post-prandial changes [81]. We have stratified the models by menopausal status in women, because the positive association of BMI with PLT, that we have previously described for UK Biobank women, was weaker in post-menopausal compared to premenopausal women [10]. We have also stratified by use of hormone replacement therapy (HRT) because sex-steroids are likely to contribute to differences between women and men and between pre-menopausal and post-menopausal women and HRT has been associated with lower lung cancer risk [82]. Last, we have included as covariate weight change within the year preceding recruitment, to account for recent BMI dynamics.

Rationale for including BMI and height in the same model

BMI (Quételet index) has been developed as an index of relative weight to evaluate weight independent of height, so BMI is designed to be uncorrelated with height. The power coefficient for

height in the formula for BMI has been established empirically, based on data collected in the 19th century, and indicates that weight increases proportionally to the square of height [83]. As BMI is based on a model which was fitted in a 19th century dataset, this may not be calibrated well in contemporary datasets. Indeed, in UK Biobank, BMI is correlated weakly inversely with height (correlation coefficients -0.06 for men and -0.11 for women [17]). Including height as an adjustment variable in the model aims to account for the weak residual correlation of BMI with height, and thus to ensure that BMI truly reflects associations independent of height, as intended.

We have previously shown that such adjustment approach is able to compensate for residual correlations in relation to another allometric index, hip index [17]. In analogy to BMI, hip index has been created to evaluate hip circumference independent of BMI and height using data from the National Health and Nutrition Examination Survey (NHANES) [84]. However, although hip index calculated with power coefficients based on NHANES (HI_{NHANES}), i.e. it is calibrated in NHANES and thus is uncorrelated with BMI and height in NHANES, it was substantially inversely correlated with BMI in UK Biobank men (corelation coefficient -0.31 [17]). Nevertheless, estimates for cancer risk obtained from models adjusting HI_{NHANES} for BMI and height showed no material difference to risk estimates for hip index calculated with power coefficients based on UK Biobank (HI_{UKB}), which was uncorrelated with BMI and height in UK Biobank because it was re-calibrated in the UK Biobank dataset [17].

Definition of covariates

The following variables were defined as previously described in [17]: age at recruitment (5-year categories for stratification of survival models), 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 within the year preceding recruitment (weight loss, stable weight, weight gain), alcohol consumption (≤3 times/month, ≤4 times/week, daily), physical activity (less active, moderately active, very active), Townsend deprivation index (sex-specific quintile cut-offs: -3.985, -2.870, -1.487, 1.088 for men; -3.979, -2.865, -1.532, 0.925 for women). HRT use (never, former, current) was defined as previously described in [ref. 24], taking into account self-reported current medication (listed in Supplementary Table S1 of [24]) The following variables were defined as previously described in [25]: menopausal status (pre-menopausal (excluding women with hysterectomy), post-menopausal (including women with bilateral oophorectomy), unknown); fasting time (0-2 hours, 3-4 hours, ≥5 hours); time of blood collection (morning <12:00, afternoon 12:00 to <16:00, evening ≥16:00 o'clock); diabetes status (yes/no); antihypertensive drugs (yes/no) (see further details in Supplementary Methods of [25] and lists of medications in Supplementary Table S1 of [25]). Lipid lowering drugs use (yes/no) was also defined as in [ref. 25], but additionally reclassifying as "Yes" based on the following codes from Fields [20003-0.0…47] "*Treatment/medication code*" (1140865576 cholestyramine; 1140909780 colestyramine; 1141157416 cholestyramine product). Paracetamol use (yes/no) was also defined as in [25], but additionally reclassifying as "Yes" based on the following code from Fields [20003-

0.0…47] "*Treatment/medication code*" (1140871968 isometheptene mucate+paracetamol 65mg/325mg capsule). Missing values were assigned the median sex-specific category as follows: weight change (stable weight), alcohol consumption (≤4 times/week), physical activity (moderately active), Townsend deprivation index (third quintile), HRT use (never), fasting time (3-4 hours), time of blood collection (afternoon); diabetes status (no); antihypertensive drugs (no); lipid-lowering drugs (no); paracetamol (no).

Family history of cancer was defined using three sets of fields as in [17]: Fields [20107-0.0/9] "*Illness of father*", Fields [20110-0.0/10] "*Illness of mother*", and Fields [20111-0.0/11] "*Illness of siblings*". Category "Breast/prostate/bowel" was based on Answers: 5 "Breast cancer", OR 13 "Prostate cancer", OR 4 "Bowel cancer", to any of the three sets of fields. Category "Lung cancer" was based on Answer: 3 "Lung cancer" to any of the three sets of fields. Category "No cancer" included all remaining participants.

Smoking status (used for cross-classification and stratification) was defined with three categories as follows: Category "Current smoker" – was based on Field [1239-0.0] "*Current tobacco smoking*"; Question: "*Do you smoke tobacco now?*"; Answer 1: "Yes, on most or all days" OR Answer 2: "Only occasionally"; Category "Former smoker" – was based on Field [1249-0.0] "*Past tobacco smoking*"; Question: "*In the past, how often have you smoked tobacco?*"; Answer 1: "Smoked on most or all days" OR Answer 2: "Smoked occasionally", when the answer to Filed [1239-0.0] was not 1 or 2; Category "Never smoker" – was based on Field [1249-0.0] Answer 3: "Just tried once or twice" OR Answer 4: "I have never smoked", when the answer to [Filed 1239-0.0] was not 1 or 2. Missing values were assigned the median sex-specific category "Never smoked" for women and "Former smoker" for men.

Smoking status and intensity (used for adjustment) was defined using smoking status as follows: Category "Never smoked" was divided based on Field [1249-0.0] in two categories: "Never smoked" – based on Answer 4: "I have never smoked" and "Just tried" – based on Answer 3: "Just tried once or twice"; Category "Former smoker" was divided in four categories: "Former occasional" – based on Field [1249-0.0] Answer 2: "Only occasionally"; "Former regular: quit≥20 years"; "Former regular: quit ≥10 years"; and "Former regular: quit <10 years" – based on time since quit calculated as the difference between Field [2897-0.0] "Age stopped smoking" and age at recruitment; Category "Current smoker" was divided in three groups: "Current occasional" – based on Field [1239-0.0] Answer 2: "Only occasionally"; "Current regular: ≤10 cigarettes" and "Current regular: >10 cigarettes" – based on the number of cigarettes per day from Field [3456-0.0] "Number of cigarettes currently smoked daily (current cigarette smokers)"; Question: "In the past, how often have you smoked tobacco?". Missing values were assigned the median sex-specific category per smoking status: "Never smoked" for both sexes; "Former regular: quit ≥20 years" for both sexes; "Current regular: ≤10 cigarettes" for women and "Current regular: >10 cigarettes" for men.

Antiaggregant / Anticoagulant use was based 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" for category "Yes". Category "No" was defined as any of the following Answers: 2 "Ibuprofen", 3 "Paracetamol", 4 "Ranitidine", 5 "Omeprazole", 6 "Laxatives" OR -7 "None of the above", and information for the remaining participants was considered missing. We re-classified to category "Yes" participants with self-reported antiaggregant use in Fields [20003-0/47] "Treatment/ medication code" with the following codes (UK Biobank Coding 4):

1140856412	norgesic tablet
1140861776	antiplatelet drug
1140861778	dipyridamole
1140861780	persantin 25mg tablet
1140861790	cerebrovase 25mg tablet
1140861800	platet 100mg effervescent tablet
1140861804	angettes 75mg tablet
1140861806	aspirin 75mg tablet
1140861808	disprin cv 100mg m/r tablet
1140864860	nu-seals aspirin 75mg e/c tablet
1140868226	aspirin
1140868258	aspav dispersible tablet
1140868282	aspirin+methocarbamol 325mg/400mg tablet
1140872040	aspirin+metoclopramide 325mg/5mg effervescent tablet
1140882108	aspirin+cyclizine hydrochloride 500mg/25mg tablet
1140882190	aspirin+glycine 500mg/133mg dispersible tablet
1140882268	aspirin+codeine 300mg/8mg tablet
1140882392	aspirin+codeine
1140909772	acetylsalicylic acid
1140909890	sulfinpyrazone
1140911756	askit powder
1141163138	aspirin+papaveretum 500mg/7.71mg dispersible tablet
1141164044	isosorbide mononitrate+aspirin
1141167844	dipyridamole+aspirin
1141167848	asasantin retard m/r capsule
1141168318	clopidogrel
1141168322	plavix 75mg tablet

We additionally reclassified to category "Yes" participants with self-reported anticoagulant use in Fields [20003-0/47] with the following codes:

1140861506	calciparine 5000iu/0.2ml prefilled syringe
1140861568	minihep calcium 5000iu/0.2ml injection
1140861574	uniparin-ca 5000iu/0.2ml prefilled syringe
1140861578	monoparin-ca 5000iu/0.2ml injection
1140861584	fragmin 10,000iu/1ml injection
1140861588	enoxaparin
1140861594	clexane 20mg/0.2ml prefilled syringe
1140861602	innohep 5000iu/0.5ml injection amp
1140861604	logiparin 2500iu/0.21ml prefilled syringe
1140861696	nicoumalone
1140861698	sinthrome 1mg tablet
1140861702	phenindione
1140861704	dindevan 10mg tablet
1140864956	subcutaneous heparin
1140877958	heparinoid+salicylic acid 0.2%/2% cream
1140877960	heparinoid+salicylic acid 0.2%/2% gel

1140881842	heparin
1140888204	dalteparin
1140888206	tinzaparin
1140888266	warfarin
1140909770	acenocoumarol
1140910832	sodium warfarin
1140926360	alphaparin 3000iu/0.3ml prefilled syringe
1140926444	certoparin
1141171364	reviparin
1141171374	clivarine 1432iu/0.25ml prefilled syringe
1141189054	bemiparin

Missing values were assigned the median sex-specific category "No" for both sexes.

Nonsteroidal anti-inflammatory drugs (NSAID) use was based 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 2: "Ibuprofen" for category "Yes". Category "No" was defined as any of the following Answers: 1 "Aspirin", 3 "Paracetamol", 4 "Ranitidine", 5 "Omeprazole", 6 "Laxatives" OR -7 "None of the above", and information for the remaining participants was considered missing. We re-classified to category "Yes" participants with self-reported NSAID use in Fields [20003-0.0…47] "*Treatment/medication code*" for the following codes (UK Biobank Coding 4):

1140868336	synflex 275mg tablet
1140871080	benorylate
1140871082	benoral 750mg tablet
1140871092	salsalate
1140871094	disalcid 500mg capsule
1140871100	azapropazone
1140871102	rheumox 300mg capsule
1140871168	voltarol 25mg e/c tablet
1140871174	voltarol 100mg suppository
1140871180	rhumalgan 25mg e/c tablet
1140871188	etodolac
1140871202	fenbufen
1140871206	lederfen 300mg tablet
1140871218	fenbuzip 300mg tablet
1140871226	fenoprofen
1140871228	fenopron 300mg tablet
1140871236	flurbiprofen
1140871238	froben 50mg tablet
1140871248	volraman 25mg e/c tablet
1140871256	valenac 25mg e/c tablet
1140871260	diclozip-25 e/c tablet
1140871266	arthrotec tablet
1140871274	isclofen 50mg e/c tablet
1140871276	flamrase 25mg e/c tablet
1140871282	diflunisal
1140871284	dolobid 250mg tablet
1140871310	ibuprofen
1140871320	arthrofen 200 tablet
1140871336	indomethacin
1140871344	artracin 25mg capsule
1140871564	rimoxyn 250mg tablet
1140871568	nycopren 250mg e/c tablet
1140871582	pirozip 10 capsule
1140871590	flamatrol 10mg capsule
1140871604	sulindac
1140871606	clinoril 100mg tablet
1140871614	tiaprofenic acid
1140871616	surgam 200mg tablet
1140871628	prosaid 250mg tablet
1140871638	napratec tablet combination pack
1140871654	phenylbutazone product
1140871660	butacote 100mg e/c tablet
1140871662	butazone 100mg tablet
1140871666	piroxicam
1140871672	feldene 10mg capsule
1140875336	nabumetone
1140875338	relifex 500mg tablet
1140875346	tenoxicam
1140875546	piroxicam 0.5% gel
1140875630	movelat cream
1140875632	movelat gel
1140875640	traxam gel
1140875642	ketoprofen 2.5% gel
1140877880	fepron 600mg tablet
1140878030	ibuprofen+codeine phosphate
1140878036	diclofenac sodium+misoprostol
1140881612	naproxen+misoprostol
1140883812	parfenac 5% cream
1140884488	diclofenac
1140884498	felbinac

1140871348	imbrilon 25mg capsule
1140871354	indocid 25mg capsule
1140871360	flexin-25 continus m/r tablet
1140871370	apsifen 200mg tablet
1140871374	brufen 200mg tablet
1140871386	ebufac 200mg tablet
1140871388	cuprofen 200mg tablet
1140871392	isisfen 400mg tablet
1140871394	fenbid 300mg spansule
1140871396	lidifen 200mg tablet
1140871402	codafen continus m/r tablet
1140871404	junifen 100mg/5ml s/f suspension
1140871406	motrin 200mg tablet
1140871408	ibumed 400mg tablet
1140871416	rimafen 200mg tablet
1140871430	rimacid 25mg capsule
1140871434	indomod 25mg m/r capsule
1140871442	indomax 25 capsule
1140871454	contraflam 250mg capsule
1140871462	naproxen
1140871468	laraflex 250mg tablet
1140871472	naprosyn 250mg tablet
1140871482	rheuflex-250 tablet
1140871484	valrox 250mg tablet
1140871490	pranoxen continus 375mg m/r tablet
1140871506	ketoprofen
1140871516	orudis 50mg capsule
1140871522	oruvail 100 m/r capsule
1140871528	ketovail 100mg m/r capsule
1140871532	ketonal 50mg capsule
1140871542	mefenamic acid
1140871546	ponstan 250mg capsule
1140871556	arthroxen 250mg tablet
1140910496	propionic acid-ibuprofen
1140910686	hydroxyphenylbutazone
1140911748	ibuprofen+menthol 5%/3% gel
1140911750	deep relief ibuprofen gel
1140911754	anadin tablet
1140925806	aceclofenac
1140925808	preservex 100mg tablet
1140926732	meloxicam
1141145722	slofenac sr 75mg m/r tablet
1141149110	cuprofen 5% gel
1141153134	anadin ibuprofen 200mg tablet
1141157412	ibuprofen product
1141157452	indomethacin product
1141164746	dexketoprofen
1141164750	keral 25mg tablet
1141165574	galprofen 100mg/5ml oral suspension
1141165754	librofem 200mg tablet
1141169526	piroxicam-beta-cyclodextrin
1141169530	brexidol 20mg tablet
1141182674	fenactol 25mg e/c tablet
1141182708	ipocol 400mg e/c tablet
1141182754	piroxicam-betadex
1141184156	lornoxicam
1141184162	xefo 4mg tablet
1141184290	vioxxacute 25mg tablet
1141184292	vioxxacute 50mg tablet
1141184546	ibuprofen+pseudoephedrine hydrochloride
1141187776	nurofen 200mg tablet
1141190952	cuprofen plus tablet
1141191742	calprofen 100mg/5ml s/f oral suspension
1141194296	lemsip flu 12hr ibuprofen+pseudoephedrine capsule
1141200748	care ibuprofen 10% gel

We additionally reclassified to category “Yes” participants with self-reported aminosalicylates use in Fields [20003-0/47] with the following codes:

1140865578	mesalazine
1140865668	sulphasalazine
1140865670	salazopyrin 500mg tablet
1140879502	olsalazine
1140909702	sulfasalazine
1140909776	etamsylate
1140910598	5asa - mesalazine
1140910600	aminosalicylic acid
1140910678	azodisalicylic acid
1140910680	disodium azodisalicylic acid

Missing values were assigned the median sex-specific category “No” for both sexes.

Supplementary Table S1 Flow chart of study participants

	Exclusions	Total	Men	Women
	Total (excluding withdrawals up to the time of analysis):	502,369	229,068	273,301
1.	Ethnic background (restricted to self-reported white) [a]		13,862	15,935
2.	Anthropometric measurements missing or extreme [b]		2373	4758
3.	Genetic & self-reported sex mismatch or sex chromosome aneuploidy [a]		396	386
4.	Age restrictions (age <40 or >70 years)		9	2
5.	Pregnant or unknown at recruitment [a]		0	105
6.	Prevalent cancer at recruitment [a]		12,189	21,857
7.	Antihemorrhagic agents [c]		14	582
8.	Platelet parameters missing		7870	10,915
	Total excluded (%):	91,253 (18.2)	36,713 (16.0)	54,540 (20.0)
	Total included:	**411,116**	**192,355**	**218,761**

The exclusion criteria were applied sequentially in the displayed order, counting each excluded individual only once.

[a] – for UK Biobank Field names, definition of variables, and definition of prevalent cancer cases see Supplementary Methods in [17].

[b] – missing anthropometric measurements; height <130 cm; waist circumference <50 or >160 cm; body mass index (BMI) <18.5 or ≥45 kg/m^2. Field names for waist and hip circumferences, weight, and height are listed in Supplementary Methods of [17].

[c] – self-reported use of medications from Fields [20003-0/47] “Treatment/ medication code” with the following codes:

1140861766 ethamsylate
1140861832 tranexamic acid
1140861834 cyklokapron 500mg tablet

Supplementary Table S2 Characteristics of study participants

	MEN	WOMEN
Cohort	192,355	218,761
Anthropometry: mean (SD)		
Height: cm	175.9 (6.8)	162.6 (6.2)
Weight: kg	86.0 (13.7)	71.2 (13.1)
Waist circumference: cm	96.9 (11.0)	84.3 (12.0)
Hip circumference: cm	103.4 (7.2)	103.1 (9.7)
Weight change: n (%)		
Weight loss	27,864 (14.5)	33,178 (15.2)
Stable weight	118,401 (61.6)	111,439 (50.9)
Weight gain	42,842 (22.3)	70,714 (32.3)
Missing	3248 (1.7)	3430 (1.6)
Smoking status: n (%)		
Never smoked	65,799 (34.2)	95,457 (43.6)
Just tried	27,728 (14.4)	33,210 (15.2)
Former occasional	21,000 (10.9)	26,790 (12.2)
Former regular: quit ≥20 years	27,427 (14.3)	20,842 (9.5)
Former regular: quit ≥10 years	12,130 (6.3)	10,229 (4.7)
Former regular: quit <10 years	14,018 (7.3)	12,151 (5.6)
Former regular: quit missing	202 (0.1)	207 (0.1)
Current occasional	6517 (3.4)	4494 (2.1)
Current regular: ≤10 cigarettes/day	4521 (2.4)	6009 (2.7)
Current regular: >10 cigarettes/day	11,437 (5.9)	8556 (3.9)
Current regular: cigarettes/day missing	949 (0.5)	117 (0.1)
Missing	627 (0.3)	699 (0.3)
Alcohol consumption: n (%)		
≤3 times / month	39,056 (20.3)	76,439 (34.9)
≤4 times / week	102,751 (53.4)	105,400 (48.2)
Daily	50,399 (26.2)	36,791 (16.8)
Missing	149 (0.1)	131 (0.1)
Physical activity: n (%)		
Less active	29,222 (15.2)	36,442 (16.7)
Moderately active	86,138 (44.8)	114,041 (52.1)
Very active	76,376 (39.7)	67,498 (30.9)
Missing	619 (0.3)	780 (0.4)
Family history: n (%)		
No cancer	124,884 (64.9)	140,467 (64.2)
Breast, bowel, prostate	43,457 (22.6)	50,070 (22.9)
Lung cancer	24,014 (12.5)	28,224 (12.9)
Townsend index		
Median (IQR)	-2.27 (4.01)	-2.29 (3.85)
Missing: n (%)	236 (0.1)	246 (0.1)
Time of sample: n (%)		
<12:00	51,153 (26.6)	53,646 (24.5)
12:00 to <16:00	74,304 (38.6)	93,892 (42.9)
≥16:00	66,797 (34.7)	71,104 (32.5)
Missing	101 (0.1)	119 (0.1)
Fasting time: n (%)		
0-2 hours	50,276 (26.1)	57,135 (26.1)
3-4 hours	95,802 (49.8)	114,942 (52.5)
≥5 hours	46,274 (24.1)	46,678 (21.3)
Missing	3 (<0.1)	6 (<0.1)

	MEN	WOMEN
Diabetes: n (%)		
Yes	12,241 (6.4)	6567 (3.0)
Missing	521 (0.3)	384 (0.2)
Lipid-lowering drugs use: n (%)		
Yes	44,831 (23.3)	27,520 (12.6)
Missing	1459 (0.8)	819 (0.4)
Antihypertensive drugs use: n (%)		
Yes	46,109 (24.0)	36,804 (16.8)
Missing	1638 (0.9)	858 (0.4)
Antiaggregant/anticoagulant use: n (%) (#)		
Aspirin	36,558 (19.0) (91.1)	21,784 (10.0) (92.8)
Antiaggregant (other than aspirin)	895 (0.5) (2.2)	516 (0.2) (2.2)
Anticoagulant only	2685 (1.4) (6.7)	1170 (0.5) (5.0)
Missing	2046 (1.1)	1867 (0.9)
NSAID use: n (%)		
Yes	29,796 (15.5)	46,787 (21.4)
Missing	2023 (1.1)	1750 (0.8)
Paracetamol use: n (%)		
Yes	32,150 (16.7)	57,921 (26.5)
Missing	2159 (1.1)	1875 (0.9)
HRT use: n (%)		
Never		132,371 (60.5)
Past		66,692 (30.5)
Current		19,203 (8.8)
Missing		495 (0.2)
Menopause: n (%)		
Pre-menopausal		51,958 (23.8)
Post-menopausal		142,294 (65.0)
Unknown		24,509 (11.2)
Menopause-HRT-use: n (%)		
Pre-menopausal		51,958 (23.8)
Post/Unknown: Never		82,872 (37.9)
Post/Unknown: Past		65,756 (30.1)
Post/Unknown: Current		18,175 (8.3)
Age at recruitment: n (%)		
40 to <45 years	19,579 (10.2)	21,912 (10.0)
45 to <50 years	24,415 (12.7)	29,317 (13.4)
50 to <55 years	28,146 (14.6)	34,547 (15.8)
55 to <60 years	34,248 (17.8)	41,083 (18.8)
60 to <65 years	47,250 (24.6)	53,560 (24.5)
65 to 70 years	38,717 (20.1)	38,342 (17.5)
Region: n (%)		
London	22,043 (11.5)	26,127 (11.9)
North-West	30,310 (15.8)	32,993 (15.1)
North-East	23,689 (12.3)	26,882 (12.3)
Yorkshire Humber	29,319 (15.2)	33,382 (15.3)
West Midlands	17,904 (9.3)	17,886 (8.2)
East Midlands	13,358 (6.9)	15,174 (6.9)
South-East	16,857 (8.8)	20,188 (9.2)
South-West	16,755 (8.7)	201,53 (9.2)
Wales	8243 (4.3)	9331 (4.3)
Scotland	13,877 (7.2)	16,645 (7.6)

HRT – hormone replacement therapy; **IQR** – interquartile range; **n (%)** – number of participants (percentage from total per sex); **(#)** – percentage from total antiaggregant/anticoagulant users per sex; **NSAID** – non-steroidal anti-inflammatory drugs.

Comparisons between obesity categories and sexes were performed with unpaired-samples t-test for anthropometric measures, Wilcoxon rank sum (Mann-Whitney) test for Townsend deprivation index, and χ^2-test for categorical variables (after imputation). All differences were significant at $p<0.0001$, except missing Townsend deprivation index ($p>0.05$).

For definition of medications see **Supplementary Methods**.

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