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Combined association of general and central obesity with incidence and mortality of cancers in 22 sites

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28	Abbreviations
29	BMI: Body mass index
30	WC: Waist circumference
31	HR: Hazard Ratio
32	CI: Confidence Interval
33	UK: United Kingdom
34	WCRF: World Cancer Research Fund
35	P _{adj} : P value adjusted
36	

ABSTRACT

Background: Body mass index (BMI) and waist circumference (WC) are measures of general obesity and central obesity, respectively, and both have been shown to be associated with cancer. However, there is insufficient evidence of their combined association with the risk of cancer.

Objective: This study aimed to investigate the associations between combinations of BMI and WC and cancer at 22 sites.

Design: 386,101 (54.5% women) UK Biobank participants aged from 37 to 73 years were included. The outcomes were incidence and mortality from cancer at 22 sites. Participants were categorized as normal weight (BMI 18.5-24.9 kg/m²) or overweight (including obese, BMI≥25 kg/m²), and normal WC or centrally obese (WC ≥94 cm for men and ≥80 cm for women). Four mutually exclusive groups were derived: (1) normal weight without central obesity, (2) normal weight with central obesity, (3) overweight without central obesity, and (4) overweight with central obesity. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals.

Results: The mean follow-up period was 8.8 years. Compared with participants with normal weight and WC, men who were overweight and centrally obese had higher cancer incidence risk at three sites (stomach (HR: 1.75, 95% CI, 1.33, 2.32, $p_{adj}=0.002$), kidney (HR: 1.45, 95% CI, 1.17, 1.81, $p_{adj}=0.016$), and colorectal (HR: 1.31, 95%CI, 1.17, 1.47, $p_{adj}<0.001$ cancer). Similar associations were found at four sites in women (endometrial (HR: 2.48, 95% CI, 2.06, 2.98, $p_{adj}<0.001$), uterine (HR: 2.23, 95%CI, 1.89, 2.64, $p_{adj}<0.001$), kidney (HR: 1.84, 95% CI, 1.37, 2.46, $p_{adj}=0.001$) and breast (HR: 1.24, 95%CI, 1.16, 1.32, $p_{adj}<0.001$) and all-cause cancer (HR: 1.07, 95%CI, 1.03, 1.10, $p_{adj}=0.003$). Only endometrial cancer mortality (HR: 3.28, 95% CI, 1.77, 6.07, $p_{adj}=0.004$) was significantly associated with being overweight and centrally obese. For colorectal, kidney and stomach cancer, the associations were stronger for central obesity than for general obesity.

Conclusions: The combination of obesity and central obesity was associated with a higher risk at several cancer sites and some associations were sex-specific.

KEYWORDS: Body mass index, waist circumference, cancer, obesity, sex.

INTRODUCTION

Body mass index (BMI) is the most commonly used indicator of adiposity and has been shown to be a strong risk factor for several non-communicable diseases (1). However, whilst BMI is a measure of general obesity, it does not provide any information on body fat distribution (1). This is important as body fat distribution, particularly accumulation of fat in central depots, has been shown to be a risk factor for several non-communicable diseases independent of general obesity. For example, waist circumference (WC), a measure of central obesity, has been demonstrated to be a stronger predictor of cardiometabolic risk than BMI (2-5). These studies indicate the potential utility of using WC, in addition to BMI, in clinical practice for cardio-metabolic risk assessment (5).

Obesity and central obesity are not only associated with cardiometabolic disease but also with certain cancers. Most of the evidence regarding adiposity and cancer comes from studies that have considered BMI and WC separately (4, 6-8). Bhaskaran et al. (6), found an association with BMI with 17, out of 22, cancer sites in a cohort study of 5.24 million UK adults. BMI has been associated with many cancers including: colorectal, postmenopausal breast, esophageal, pancreatic, liver, endometrial, kidney, oral, stomach, gallbladder, ovarian, advanced prostate, and cervical cancer (9-12). However, Barberio et al.(4) in a recent study, highlighted that WC could be a better predictor than BMI. High BMI and high WC were associated with high risk of all-cancer. Adjustment for WC attenuated the effect size of BMI, especially among women. Existing evidence on adiposity and cancer has considered BMI and WC separately, or studied only all-cause cancer in a selective population (4, 6-8, 13). It should also be noted that the association between adiposity and cancer could vary by sex (8, 14).

Sun et al, showed that women with normal weight and central adiposity had higher risk of cancer mortality (13). However, this analysis was restricted to women and used World Health Organization cut-offs, rather than the current cut-off recommendation for central adiposity based on cancer risk (12). Consistent with the evidence for cardiovascular disease, where BMI and WC provide complementary information for risk stratification (4, 6), we hypothesized that people with higher BMI and WC had higher risk of cancer compared with people having only one adiposity marker, and even more so compared with people having normal BMI and WC. To test this hypothesis, we used data from the UK Biobank prospective cohort study and investigated the associations of different combinations of BMI and WC with cancer at 22 sites.

METHODS

Subjects and Data sources

Between 2006 and 2010 UK Biobank recruited over 502,000 participants (53.4% women) aged from 37 to 73 years. Participants attended one of 22 assessment centers across England, Scotland, and Wales where they completed a self-administered, touch-screen questionnaire and face-to-face interview (15). Our analyses excluded participants who reported prevalent cancer at baseline (n=41,437), and people who were underweight (n=2,122). In addition, 72,832 individuals were excluded due to missing exposure or covariate data. The study population comprised the remaining 386,101 (76.8%) participants.

Study outcomes and exposure

The outcomes for this study were cancer incidence and mortality; overall and at 22 sites. The date and cause of death were obtained from death certificates held by the National Health Service Information Centre (England and Wales) and the National Health Service Central Register Scotland (Scotland). Dates and causes of hospital admission were obtained from the Health Episode Statistics (England and Wales) and Scottish Morbidity Records (Scotland). Detailed information about the record linkage procedures can be found at <http://content.digital.nhs.uk/services>. Incident cancer was defined as the first record of the cancer of interest, at hospitalization or death. At the time of analysis, mortality data were available up to 01 June 2020. Mortality analyses were, therefore, censored at this date or date of death, whichever occurred earlier. Hospital admission data were available until 31 March 2017 for Scotland and Wales and until 01 June 2020 for England. Therefore, analyses of incident cancers were censored at these dates, or the date of first hospitalization for, or death from, the cancer of interest, whichever occurred earlier.

The International Classification of Diseases, 10th revision (ICD-10) was used to define the following 24 cancers: all-cause (C00-C97, D37, D48), oral (C00-C14), esophageal (C15), stomach (C16), colorectal (C18, C19, and C20), liver (C22), gallbladder (C23), pancreatic (C25), lung (C34), malignant melanoma (C43), breast (C50), uterine (C53-C55), endometrial (C54), cervical (C53), ovarian (C56), prostate (C61), testicular (C62), kidney (C64-C65), bladder (C67), brain (C71), thyroid (C73), and lymphatic and hematopoietic tissue (C81-C96) cancers, and non-Hodgkin lymphoma (C82-C85), multiple myeloma (C90), and leukemia (C91-C95). Of these, 17 cancer sites were studied for both men and women; two

were specific to men (testicular and prostate) and five to women (breast, endometrial, uterine, cervical and ovarian).

Body mass index and waist circumference categories

Height was measured to the nearest centimeter, using a Seca 202 stadiometer, and body weight to the nearest 0.1 kg, using a Tania BC-418 body composition analyzer. Body mass index (BMI) was calculated as weight divided by height², and the World Health Organization's criteria were used to derive the following categories: underweight (<18.5 kg/m²), normal weight (18.5 to <25 kg/m²), overweight (25 to <30 kg/m²), obese (>30 kg/m²) (16). The natural indent was used to measure waist circumference (or umbilicus if not visible). In accordance with the latest recommendation from the WCRF, the following cut-off values for central obesity were used: ≥94 cm for men and ≥80 cm for women (12). For the purpose of this study, the following category combinations were derived: (1) normal weight without central obesity (BMI 18.5-24.9 kg/m²; WC <88 cm for women and <94 cm for men), (2) normal weight with central obesity (BMI 18.5-24.9 kg/m²; WC ≥80 cm for women and ≥94 cm for men), (3) overweight without central obesity (BMI 25.0-29.9 kg/m²; WC <88 cm for women and <94 cm for men), (4) overweight with central obesity (BMI 25.0-29.9 kg/m²; WC ≥80 cm for women and ≥94 cm for men), (5) obese without central obesity (BMI ≥30.0 kg/m²; WC <88 cm for women and <94 cm for men), and (6) obese with central obesity (BMI ≥30.0 kg/m²; WC ≥80 for women and ≥94 for men). Due to insufficient numbers in category 5 (n=1,145), categories 3 with 5 were combined, as were categories 4 and 6.

Covariates

Sociodemographic factors (age, sex, educational qualifications and ethnicity) were self-reported at the baseline assessment using a touch screen questionnaire. Townsend area deprivation index was derived from the postcode of residence using aggregated data on unemployment, car and homeownership, and household overcrowding (17). Past and current physician-diagnosed medical conditions were self-reported at baseline and used to derive a multimorbidity count of the following: stroke, angina, heart attack, hypertension, cancer, diabetes, hypertension, chronic obstructive pulmonary disease, or longstanding illness (18). A diet score representing cumulative dietary risk factors was derived from ten foods items (processed meat, red meat, oily fish, milk type, spread type, cereal intake, salt added to food, water, and fruit and vegetables). The score ranged from 0 to 9, with each point representing one dietary risk factor (19). Level of physical activity level over a typical week was

self-reported using the International Physical Activity Questionnaire and presented as MET-mins per week (20). Time spent on sedentary behaviors included watching television and leisure-time computer use. Smoking was self-reported and categorized into never, ex- and current smokers. The other covariates were specific to women, including menopausal status, hormone replacement therapy, ages at menarche, first and last birth, and number live births, and were self-reported at baseline using the touch screen questionnaire. Further details of these measurements are contained in the UK Biobank protocol (<http://www.ukbiobank.ac.uk>).

Ethics

All participants provided written informed consent before enrolment in the study, which was conducted in accordance with the Declaration of Helsinki. The study was approved by the NHS National Research Ethics Service (Ref: 11/NW/0382).

Statistical analyses

Descriptive characteristics were presented as means with standard deviations (SD) for quantitative variables and percentages for categorical variables. The results were reported as hazard ratios (HR) and their 95% confidence intervals (95% CI). The proportional hazard assumption was checked based on Schoenfeld residuals. Age violated the assumption, and this was addressed by treating age as an ordinal variable, which produced largely similar results. Firstly, to investigate differences in cancer risk between BMI and WC, ratios of hazard ratios were estimated for the obesity (binary variable) x WC (continuous variable) interaction terms using Cox models. Secondly, Cox proportional hazard models with follow-up time as the time-dependent variable were used to investigate associations of combined categories of BMI and WC with incidence (fatal and not fatal) and mortality for 24 cancer sites and all-cause cancer. Individuals with normal weight and normal WC were the reference group.

All analyses were conducted for both sexes, as well as women and men separately, and adjusted for age (ordinal variable), sex, deprivation, ethnicity, education, multimorbidity, smoking, alcohol consumption, diet risk score, physical activity and discretionary sedentary time. The association of combined categories of BMI and WC with lung, oral and esophageal cancers were restricted to never smokers only because these cancers are strongly influenced by smoking. For analyses specific to women, we also conducted subgroup analyses by pre and postmenopausal status. These subgroup analyses were conducted because of potential moderations menopausal status. To minimize potential

reverse causation, all analyses excluded participants who had cancer events within two years of follow-up. Sensitivity analyses were conducted excluding participants with comorbidities at baseline (study population 144,311) and non-white participants (study population=366,450). Due to reduced statistical power, the sensitivity analyses were not sex-specific, and results were not reported for combined BMI/WC categories with fewer than 5 events. Finally, in order to avoid inflated type-I errors, all p-values were corrected for multiple testing using Holm's method (21), which performs similarly to Bonferroni's method while retaining higher statistical power (22). The multiple testing corrected p-values are denoted as P_{adj} .

All analyses were performed using R version 3.6.2. A two-sided P-value <0.05 was considered statistically significant.

RESULTS

Characteristics of the study population

Of the 24 cancers studied, cervical and gallbladder cancers did not have sufficient events and were removed, resulting in 22 cancer sites. The median follow-up period was 8.8 years [IQR 8.6-9.9] for incidence and 9.3 years [IQR 8.6-9.9] for mortality. Over the follow-up period, 42,189 people developed cancer, and 9,826 died from cancer. Table 1 and Supplementary Table 1 present the characteristics of the study population at baseline. In summary, the study sample contained more women and had a mean age of 56.2 years; 55.6% of participants were never smokers and 37.4% did not have multimorbidity. Among women, 31.1%, were normal weight without central obesity. Compared with this sub-group, overweight women with central obesity, were 2.3 years older and had a similar proportion of never smokers. Among men, 22.5% had normal weight and no central obesity, and 56.8% were overweight with central obesity.

Cancer risk by combined categories of body mass index and waist circumference

There were no interactions found between general and central obesity after correcting for multiple testing ratios of HRs and interaction p-values as shown in Supplementary Table 2.

Compared with men who had normal weight and WC, men who were overweight and centrally obese had a higher risk of incidence of cancer at three sites: stomach (HR: 1.75, 95% CI, 1.33, 2.32), kidney (HR: 1.45, 95% CI, 1.17, 1.81), and colorectal (HR: 1.31, 95% CI, 1.17, 1.47) cancer. Overweight men

who were not centrally obese were not at higher risk of any incident cancers (Table 2). The associations with kidney (HR: 1.75, 95% CI, 1.14, 2.71) and colorectal (HR: 1.27, 95% CI, 1.02, 1.58) cancer mortality had a similar magnitude of association but became non-significant after adjusting for multiple testing. Overweight men who were not centrally obese had a higher risk of brain cancer mortality (HR: 1.79, 95% CI, 1.25, 2.75) compared with people with normal BMI and WC (Supplementary Table 3).

The results for women are presented in Table 3. Women who were overweight and centrally obese were at higher risk of cancer incidence overall (HR: 1.07, 95% CI, 1.03, 1.10) and at four sites (endometrial, uterine, kidney and breast cancer) compared with women with normal BMI and WC. The hazard ratio was greatest for endometrial cancer (HR: 2.48, 95% CI, 2.06, 2.98) followed by uterine (HR: 2.23, 95% CI, 1.89, 2.64), then kidney (HR: 1.84, 95% CI, 1.37, 2.46) and finally breast (HR: 1.24, 95% CI, 1.16, 1.32) cancer. Interestingly, women with normal weight and central obesity were also at higher risk of breast cancer (HR: 1.21, 95% CI, 1.10, 1.33) compared with those with normal BMI and WC. No other associations were significant for other categories and cancers (Table 3). For mortality, only endometrial cancer was significantly associated with women being overweight and centrally overweight or obese (HR: 3.28, 95% CI, 1.77, 6.07) (Supplementary Table 4).

People who were either overweight or obese people as well as having central obesity were at higher risk of endometrial, uterine, kidney, colorectal, breast and all-cause cancers while those who were obese and centrally obese were also at increased risk of stomach and liver cancer (Supplementary Table 5)

Sensitivity analyses

The associations among women differed by menopausal status (Table 4). Among premenopausal women, the association with breast cancer was stronger in those who had normal weight and central obesity whereas, among postmenopausal women, the association was stronger in those who were both overweight and centrally obese ($P_{\text{interaction}}=0.02$). For endometrial and uterine cancers, the associations were generally stronger among postmenopausal women even though the interactions were not significant.

When participants with baseline morbidity were excluded, being overweight with central obesity was associated with endometrial, uterine, breast and all-cause cancer (Supplementary Table 6). Finally,

when the analyses were restricted to only those with white ethnicity, the results were largely similar to the main findings (Supplementary Table 7).

DISCUSSION

This study provided novel evidence regarding the risk of cancer associated with different combinations of general and central adiposity. Overweight people with central obesity had higher risk of developing cancer at several sites. People with both general and central obesity had higher risk of six cancers than people with only one type of obesity, and even higher risk than those with neither. Some of the associations differed between men and women and, among the latter, the associations with breast cancer were moderated by menopausal status.

Our findings corroborated previous evidence, including the WCRF Obesity and Cancer 2018 Report, and meta-analysis of prospective cohort studies, which supported the association between BMI and cancer at several sites (8, 23, 24). In our study, adiposity (assessed using BMI and WC) was associated with a higher risk of kidney, colorectal, postmenopausal breast, endometrial and uterine cancers. Our findings were also consistent with recent Mendelian randomization (MR) studies that suggested high BMI may be causally related to several site-specific cancers (10, 25-27). Furthermore, our epidemiological evidence of associations with other cancers, such as stomach cancer, is supported by previous MR studies (10, 28).

There is convincing evidence (29) that adiposity is associated with an increased risk of colorectal cancer, derived mainly through BMI measured in prospective cohorts (28-31) and in MR studies (10, 26, 32). However, this association is stronger in men than women (14). Different hypotheses have been proposed for these sex differences. It has been suggested that, adult weight gain in men may be a more important risk factor for colorectal cancer (33), whereas early life obesity in women may be more important (34). One plausible mechanism behind these associations may be hormonal differences which warrants further investigation (35).

We found that the association between general adiposity combined with central adiposity and higher risk of breast cancer was mainly driven by postmenopausal women. This is consistent with previous evidence from prospective cohort studies that have shown an association between BMI and postmenopausal breast cancer (8, 27, 36). Sun Y et al. showed, using data from the Women's Health Initiative, that postmenopausal women who had normal weight but central obesity had a similar risk of

all-cause cancer incidence and mortality as women who were overweight (13). In our study this association were stronger in premenopausal women but not for postmenopausal and only for breast cancer (Table 4).

People who were overweight but not centrally obese had a higher risk of brain cancer mortality. This was consistent with a previous metaanalysis showing an association between BMI and brain cancer (23). Previous meta-analyses showed an inverse association between obesity and lung cancer overall (37, 38), but a positive association among never smokers (39). Our analyses were restricted to never smokers because of anticipation of effect modification and the strong risk of a negative association in current and former smokers being due to reverse causation.

The mechanism underlying the association between adiposity and cancer could be related to adiposity induced inflammation (40, 41), and the resultant increase in circulating adipokines, cytokines, and chemokines (42). These create a tumor microenvironment, which is critical in the initiation and progression of cancer (40). Adiposity may also generate systemic metabolic dysregulation - increased insulin, dyslipidemia, glycemia, oxidative stress, and insulin growth factor-1 (40, 41, 43) - which have been associated with cancer, especially the latter (44-47). Central adiposity appears to have an important role in this association. Barberio et al. (4) reported a stronger association for WC than BMI even though BMI was still a significant predictor of cancer (8). Therefore, both measures should contribute to the prediction of several cancers. BMI and WC are easily and cheaply measured, even in clinical practice, and use of both in combination may enhance the prediction of cancer.

Limitations

This study is not free from limitations. UK Biobank is not representative of the general population in terms of lifestyle and therefore, we should be cautious in generalizing summary statistics (48). However, relative risks can be generalized and were consistent with a more representative population cohort (49). Measurements were collected from all participants, by trained staff rather than self-report, but only on one occasion. However, it is unlikely that anthropometric measurements will have changed markedly over a mean follow-up period of 9 years. Among over 20,000 UK Biobank participants who had longitudinal BMI measurements, the intra-correlation coefficients for BMI were 92.6% (95% CI 92.4%-92.8%) and 89.8% (95% CI 89.6%-90.0%) for 4.4- and 8.5-years follow-up respectively. Reverse causation is a potential limitation of cohort studies. However, to minimize this risk, we performed

landmark analyses excluding all participants with prevalent cancer or cancer diagnosed within the first 2-years of follow up. We did not have sufficient statistical power to conduct subgroup analyses for non-white people, which may have different association patterns. Moreover, recent evidence from MR studies has reported causal links between BMI and several cancer sites, consistent with our results, and Barberio et al. showed that WC was a stronger predictor, which we also reported for some cancer sites (4, 10). Last, but not least, causality cannot be confirmed in any observational study and residual confounding may occur because of the omission of some covariates, such as the dosage of smoking.

CONCLUSION

Our findings provide evidence that combining information on general obesity, based on BMI, with central obesity, based on WC, identifies people at higher risk of several cancers. Their combination could provide a useful marker for targeting cancer prevention in clinical practice.

Patients consent: Not required

Data availability: Data is available upon request from UK Biobank (www.ukbiobank.ac.uk)

Authors' contributions: Study conception and design: SPS, JPP, CCM and FH. Data analysis: SPS and CCM. Interpretation of results: SPS, FH. JPP and CCM. Original draft preparation: SPS, CCM and FH. Review, editing and approval of manuscript: all authors (SPS, FPR, JB, SG, JPP, CCM and FH).

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Table 1: Characteristics by BMI and WC categories and sex.

	Women				Men			
	Normal weight (18.5 – 24.9 kg/m ²)		Overweight (≥25 kg/m ²)		Normal weight (18.5 – 24.9 kg/m ²)		Overweight (≥25 kg/m ²)	
	Without central obesity	With central obesity	Without central obesity	With central obesity	Without central obesity	With central obesity	Without central obesity	With central obesity
N (%)	65,396 (31.1)	17,958 (8.5)	15,954 (7.6)	110,951 (52.85)	39,588 (22.5)	4,360 (2.5)	32,013 (18.2)	99,881 (56.8)
Age, Mean (SD)	54.6 (8.13)	56.9 (7.91)	55.2 (8.10)	56.9 (7.83)	55.6 (8.41)	58.4 (7.81)	55.1 (8.44)	57.2 (7.99)
Townsend deprivation index								
Lower deprivation	24,400 (37.3%)	6,325 (35.2%)	5,920 (37.1%)	34,846 (31.4%)	13,827 (34.9%)	1,489 (34.2%)	11,471 (35.8%)	33,565 (33.6%)
Middle	22,587 (34.5%)	6,185 (34.4%)	5,530 (34.7%)	37,358 (33.7%)	12,776 (32.3%)	1,493 (34.2%)	10,882 (34.0%)	33,230 (33.3%)
Higher deprivation	18,409 (28.2%)	5,448 (30.3%)	4,504 (28.2%)	38,748 (34.9%)	12,985 (32.8%)	1,378 (31.6%)	9,660 (30.2%)	33,086 (33.1%)
Height (m), Mean (SD)	1.63 (0.0618)	1.65 (0.0622)	1.60 (0.0599)	1.62 (0.0624)	1.76 (0.0681)	1.80 (0.0673)	1.74 (0.0645)	1.76 (0.0674)
Weight (kg), Mean (SD)	59.5 (5.71)	64.7 (5.32)	67.8 (5.54)	80.2 (12.8)	71.6 (6.77)	78.5 (6.14)	80.3 (6.50)	94.0 (12.8)
Waist circumference (cm) , Mean (SD)	72.4 (4.33)	83.5 (3.46)	76.1 (2.72)	93.2 (10.1)	84.7 (5.23)	96.2 (2.34)	89.4 (3.27)	104 (8.79)
Body Mass index (kg/m ²) Mean (SD)	22.4 (1.56)	23.7 (1.03)	26.4 (1.23)	30.5 (4.54)	23.1 (1.40)	24.2 (0.757)	26.7 (1.30)	30.3 (3.72)
Smoking								
Never	41,4329 (63.4%)	10,330 (57.5%)	10,223 (64.1%)	64,897 (58.5%)	22,597 (57.1%)	2,088 (47.9%)	17,648 (55.1%)	45,570 (45.6%)
Previous	18,487 (28.3%)	5,903 (32.9%)	46,69 (29.3%)	36,914 (33.3%)	11,596 (29.3%)	1,565 (35.9%)	10,997 (34.4%)	43,270 (43.3%)
Current	5,480 (8.4%)	1,725 (9.6%)	1,062 (6.7%)	9,140 (8.2%)	5,396 (13.6%)	707 (16.2%)	3,368 (10.5%)	11,041 (11.1%)
Alcohol intake								
Daily or almost daily	12,633 (19.3%)	3,818 (21.3%)	2,226 (14.0%)	14,912 (13.4%)	10,543 (26.6%)	1,350 (31.0%)	7,512 (23.5%)	24,787 (24.8%)
3-4 times a week	16,051 (24.5%)	4,240 (23.6%)	3,525 (22.1%)	20,458 (18.4%)	10,633 (26.9%)	1,116 (25.6%)	9,191 (28.7%)	26,134 (26.2%)
Once or twice a week	17,175 (26.3%)	4,604 (25.6%)	4,641 (29.1%)	28,892 (26.0%)	9,798 (24.7%)	1,002 (23.0%)	8,859 (27.7%)	2,6531 (26.6%)
1-3 times a month	7,586 (11.6%)	1,942 (10.8%)	2,146 (13.5%)	15,868 (14.3%)	3,364 (8.5%)	313 (7.2%)	2,781 (8.7%)	9,201 (9.2%)
Special occasions only	7,185 (11.0%)	2,005 (11.2%)	2,125 (13.3%)	19,275 (17.4%)	2,712 (6.9%)	280 (6.4%)	2,013 (6.3%)	7,171 (7.2%)
Never	4,766 (7.3%)	1,349 (7.5%)	1,291 (8.1%)	11,547 (10.4%)	2,539 (6.4%)	299 (6.9%)	1,657 (5.2%)	6,058 (6.1%)
Sedentary time (hours/day), Mean (SD)	4.25 (1.84)	4.49 (1.89)	4.64 (1.88)	4.99 (2.08)	4.79 (2.23)	5.21 (2.31)	5.28 (2.28)	5.86 (2.50)
Physical activity (MET-min/day, Mean (SD)	1.52 (1.33)	1.63 (1.50)	1.58 (1.40)	1.93 (1.82)	1.66 (1.42)	1.87 (1.73)	1.64 (1.35)	1.95 (1.73)
Diet score, Mean (SD)	4.85 (1.55)	4.72 (1.54)	4.81 (1.52)	4.58 (1.54)	4.27 (1.68)	4.03 (1.63)	4.23 (1.62)	3.92 (1.58)
Baseline diabetes								
No	64,873 (99.2%)	17,633 (98.2%)	15,783 (98.9%)	105,047 (94.7%)	38,553 (97.4%)	4,124 (94.6%)	30,912 (96.6%)	90,299 (90.4%)
Yes	523 (0.8%)	325 (1.8%)	171 (1.1%)	5904 (5.3%)	1035 (2.6%)	236 (5.4%)	1101 (3.4%)	9582 (9.6%)
Baseline hypertension								
No	57,675 (88.2%)	14,699 (81.9%)	13,337 (83.6%)	76,338 (68.8%)	33,248 (84.0%)	3,298 (75.6%)	24,647 (77.0%)	62,114 (62.2%)
Yes	7723 (11.8%)	3259 (18.1%)	2617 (16.4%)	34617 (31.2%)	6341 (16.0%)	1062 (24.4%)	7366 (23.0%)	37772 (37.8%)
Baseline CVD								
No	56,510 (86.4%)	14,287 (79.6%)	12,950 (81.2%)	73,109 (65.9%)	31,844 (80.4%)	3,100 (71.1%)	23,440 (73.2%)	57,513 (57.6%)
Yes	8,816 (13.5%)	3,643 (20.3%)	2,983 (18.7%)	37,655 (33.9%)	7,694 (19.4%)	1,252 (28.7%)	8,537 (26.7%)	42,255 (42.3%)
Missing	72 (0.1%)	28 (0.2%)	21 (0.1%)	191 (0.2%)	51 (0.1%)	8 (0.2%)	36 (0.1%)	118 (0.1%)
Baseline longstanding illness								
No	51,481 (78.7%)	13,195 (73.5%)	12,188 (76.4%)	70,756 (63.8%)	28,768 (72.7%)	2,727 (62.5%)	23,167 (72.4%)	5,9761 (59.8%)
Yes	12,773 (19.5%)	43,93 (24.5%)	3,476 (21.8%)	37,259 (33.6%)	10,159 (25.7%)	1,560 (35.8%)	8,322 (26.0%)	38,125 (38.2%)
Missing	1,142 (1.7%)	370 (2.1%)	290 (1.8%)	2,936 (2.6%)	661 (1.7%)	73 (1.7%)	524 (1.6%)	1,995 (2.0%)
Baseline multimorbidity								
no illness	31,831 (48.7%)	7,268 (40.5%)	6,873 (43.1%)	32,729 (29.5%)	19,275 (48.7%)	1,586 (36.4%)	14,334 (44.8%)	30,414 (30.5%)
1+ illness	33,565 (51.3%)	10,690 (59.5%)	9,081 (56.9%)	78,222 (70.5%)	20,313 (51.3%)	2,774 (63.6%)	17,679 (55.2%)	69,467 (69.5%)

Data are presented as number of participants and their percentage (%) unless otherwise specified. Data available for 386,101.

Table 2: Association of BMI and WC categories with cancer incidence in men.

Cancer site	Normal weight (18.5 – 24.9 kg/m ²)					Overweight (≥25 kg/m ²)					
	Without central obesity		With central obesity			Without central obesity			With central obesity		
	Total/Event	HR	Total/Event	HR (95% CI)	P adj	Total/Event	HR (95% CI)	P adj	Total/Event	HR (95% CI)	P adj
All-cause	38,893/4,411	1.00 (Ref.)	4,251/663	1.11 (1.02; 1.20)	0.306	31,562/3,496	1.02 (0.97; 1.06)	1.000	97,898/13,478	1.05 (1.02; 1.09)	0.051
Bladder	39,550/235	1.00 (Ref.)	4,352/28	0.79 (0.54; 1.17)	1.000	31,991/192	1.06 (0.87; 1.28)	1.000	99,744/825	1.13 (0.97; 1.31)	1.000
Brain	39,570/65	1.00 (Ref.)	4,359/12	1.53 (0.82; 2.83)	1.000	32,004/77	1.54 (1.11; 2.15)	0.208	99,846/187	1.12 (0.84; 1.50)	1.000
Colorectal	39,517/378	1.00 (Ref.)	4,348/49	0.94 (0.70; 1.27)	1.000	31,967/296	1.02 (0.87; 1.18)	1.000	99,619/1,410	1.31 (1.17; 1.47)	<0.001
Kidney	39,573/102	1.00 (Ref.)	4,358/19	1.31 (0.80; 2.13)	1.000	32,001/83	1.03 (0.77; 1.38)	1.000	99,826/464	1.45 (1.17; 1.81)	0.016
Leukemia	39,568/115	1.00 (Ref.)	4,359/13	0.83 (0.46; 1.47)	1.000	32,006/90	1.02 (0.78; 1.35)	1.000	99,840/386	1.20 (0.97; 1.48)	1.000
Liver	39,581/49	1.00 (Ref.)	4,360/8	1.01 (0.48; 2.13)	1.000	32,008/33	0.87 (0.56; 1.35)	1.000	99,858/277	1.51 (1.11; 2.06)	0.139
Lung	22,589/38	1.00 (Ref.)	2,086/3	0.64 (0.20; 2.09)	1.000	17,645/32	1.13 (0.70; 1.81)	1.000	45,559/93	0.99 (0.67; 1.47)	1.000
Lymphatic	39,530/335	1.00 (Ref.)	4,356/49	1.08 (0.80; 1.46)	1.000	31,980/264	1.03 (0.87; 1.21)	1.000	99,744/1,086	1.16 (1.02; 1.31)	0.342
Melanoma	39,562/158	1.00 (Ref.)	4,356/19	0.96 (0.60; 1.55)	1.000	31,997/146	1.18 (0.94; 1.48)	1.000	99,813/549	1.32 (1.10; 1.58)	0.051
Multiple Myeloma	39,578/72	1.00 (Ref.)	4,360/8	0.84 (0.41; 1.75)	1.000	32,004/64	1.17 (0.83; 1.64)	1.000	99,851/226	1.18 (0.90; 1.56)	1.000
Non-Hodgkin	39,562/162	1.00 (Ref.)	4,358/27	1.23 (0.82; 1.85)	1.000	31,997/124	1.00 (0.79; 1.26)	1.000	99,815/484	1.06 (0.88; 1.27)	1.000
Esophagus	22,594/27	1.00 (Ref.)	2,086/2	0.62 (0.15; 2.62)	1.000	17,646/21	1.04 (0.59; 1.85)	1.000	45,552/106	1.60 (1.03; 2.48)	0.466
Oral	22,591/36	1.00 (Ref.)	2,088/6	1.58 (0.66; 3.76)	1.000	17,642/31	1.09 (0.67; 1.77)	1.000	45,557/78	0.90 (0.60; 1.37)	1.000
Pancreas	39,580/99	1.00 (Ref.)	4,360/15	1.04 (0.60; 1.79)	1.000	32,008/80	1.03 (0.77; 1.39)	1.000	99,840/362	1.17 (0.93; 1.47)	1.000
Stomach	39,578/61	1.00 (Ref.)	4,358/14	1.59 (0.89; 2.84)	1.000	32,003/60	1.27 (0.89; 1.81)	1.000	99,834/327	1.75 (1.33; 2.32)	0.002
Thyroid	39,583/11	1.00 (Ref.)	4,360/2	1.55 (0.34; 7.01)	1.000	32,013/16	1.83 (0.85; 3.96)	1.000	99,874/41	1.36 (0.68; 2.69)	1.000
Prostate	39,429/1,319	1.00 (Ref.)	4,331/205	1.16 (1.00; 1.35)	0.910	31,901/1,079	1.07 (0.98; 1.16)	1.000	99,448/3,679	1.02 (0.95; 1.09)	1.000
Testis	39,585/13	1.00 (Ref.)	4,360/1	0.78 (0.10; 6.01)	1.000	32,008/14	1.33 (0.62; 2.83)	1.000	99,876/36	1.18 (0.61; 2.27)	1.000

Data are presented in hazard ratio with 95% confidence intervals. The reference group was men with normal BMI and normal WC. Analyses were adjusted for age, education, deprivation, ethnicity, comorbidity, diet score, smoking, sedentary behavior and physical activity. Central obesity (≥94 cm men). Significant results in bold.

Table 3: Association of BMI and WC categories with cancer incidence in women.

Cancer site	Normal weight (18.5 – 24.9 kg/m ²)					Overweight (≥25 kg/m ²)					
	Without central obesity		With central obesity			Without central obesity			With central obesity		
	Total/Event	HR	Total/Event	HR (95% CI)	P adj	Total/Event	HR (95% CI)	P adj	Total/Event	HR (95% CI)	P adj
All-cause	64,473/5,547	1.00 (Ref.)	17,654/1,816	1.05 (1.00; 1.11)	1.000	15,729/1,330	0.96 (0.90; 1.01)	1.000	109,065/11,448	1.07 (1.03; 1.10)	0.003
Bladder	65,381/103	1.00 (Ref.)	17,954/29	0.81 (0.53; 1.22)	1.000	15,948/31	1.16 (0.78; 1.74)	1.000	110,912/245	1.06 (0.83; 1.35)	1.000
Brain	65,386/61	1.00 (Ref.)	17,955/28	1.49 (0.95; 2.33)	1.000	15,954/23	1.50 (0.92; 2.42)	1.000	110,928/145	1.24 (0.90; 1.69)	1.000
Colorectal	65,328/444	1.00 (Ref.)	17,933/154	1.08 (0.90; 1.30)	1.000	15,933/117	1.05 (0.85; 1.28)	1.000	110,800/1,015	1.15 (1.02; 1.29)	0.363
Kidney	65,388/59	1.00 (Ref.)	17,954/30	1.52 (0.98; 2.37)	1.000	15,950/25	1.60 (1.00; 2.55)	1.000	110,916/248	1.84 (1.37; 2.46)	0.001
Leukemia	65,380/104	1.00 (Ref.)	17,958/36	1.03 (0.70; 1.51)	1.000	15,952/22	0.81 (0.51; 1.29)	1.000	110,929/241	1.07 (0.84; 1.36)	1.000
Liver	65,386/57	1.00 (Ref.)	17,955/20	1.03 (0.62; 1.72)	1.000	15,953/11	0.73 (0.38; 1.39)	1.000	110,939/153	1.14 (0.83; 1.56)	1.000
Lung	41,420/77	1.00 (Ref.)	10,327/29	1.27 (0.82; 1.94)	1.000	10,220/25	1.24 (0.79; 1.96)	1.000	64,881/158	1.06 (0.79; 1.40)	1.000
Lymphatic	65,340/375	1.00 (Ref.)	17,943/115	0.94 (0.76; 1.16)	1.000	15,947/80	0.83 (0.65; 1.05)	1.000	110,860/818	1.03 (0.91; 1.17)	1.000
Melanoma	65,351/266	1.00 (Ref.)	17,949/69	0.91 (0.70; 1.19)	1.000	15,941/61	0.92 (0.70; 1.22)	1.000	110,884/420	0.92 (0.78; 1.08)	1.000
Multiple Myeloma	65,386/74	1.00 (Ref.)	17,954/19	0.80 (0.48; 1.32)	1.000	15,953/17	0.90 (0.53; 1.53)	1.000	110,938/190	1.23 (0.92; 1.62)	1.000
Non-Hodgkin	65,366/187	1.00 (Ref.)	17,948/54	0.90 (0.66; 1.22)	1.000	15,950/41	0.85 (0.61; 1.19)	1.000	110,894/388	1.00 (0.83; 1.20)	1.000
Esophagus	41,424/29	1.00 (Ref.)	10,329/7	0.79 (0.35; 1.81)	1.000	10,223/5	0.63 (0.24; 1.63)	1.000	64,893/68	1.12 (0.71; 1.77)	1.000
Oral	41,424/40	1.00 (Ref.)	10,330/7	0.67 (0.30; 1.50)	1.000	10,222/9	0.92 (0.45; 1.90)	1.000	64,892/54	0.85 (0.55; 1.30)	1.000
Pancreas	65,383/110	1.00 (Ref.)	17,957/30	0.79 (0.53; 1.18)	1.000	15,951/35	1.25 (0.85; 1.82)	1.000	110,917/265	1.10 (0.87; 1.39)	1.000
Stomach	65,390/50	1.00 (Ref.)	17,955/14	0.82 (0.45; 1.48)	1.000	15,953/12	0.91 (0.48; 1.71)	1.000	110,939/122	1.00 (0.71; 1.41)	1.000
Thyroid	65,387/46	1.00 (Ref.)	17,954/11	0.85 (0.44; 1.64)	1.000	15,950/5	0.43 (0.17; 1.08)	1.000	110,932/117	1.29 (0.90; 1.84)	1.000
Breast	65,087/1,598	1.00 (Ref.)	17,861/552	1.21 (1.10; 1.33)	0.003	15,866/392	1.01 (0.91; 1.13)	1.000	110,324/3,409	1.24 (1.16; 1.32)	<0.001
Endometrium	65,376/147	1.00 (Ref.)	17,945/55	1.25 (0.92; 1.70)	1.000	15,947/58	1.60 (1.18; 2.16)	0.061	110,848/685	2.48 (2.06; 2.98)	<0.001
Ovary	65,358/226	1.00 (Ref.)	17,945/55	0.79 (0.58; 1.06)	1.000	15,945/48	0.84 (0.61; 1.14)	1.000	110,879/436	0.99 (0.84; 1.18)	1.000
Uterine	65,368/180	1.00 (Ref.)	17,941/56	1.05 (0.78; 1.41)	1.000	15,946/64	1.44 (1.08; 1.91)	0.279	110,829/750	2.23 (1.89; 2.64)	<0.001

Data are presented in hazard ratio with 95% confidence intervals. The reference group was women with normal BMI and normal WC. Analyses were adjusted for age, education, deprivation, ethnicity, comorbidity, diet score, smoking, sedentary behavior and physical activity. Central obesity (≥80 cm women). Significant results in bold.

Table 4: Association BMI and WC categories breast, endometrial, ovary and uterine cancer by menopausal status

			Premenopausal			Postmenopausal			P interaction
	General obesity	Central obesity	Total/Event	HR 95% CI	P value	Total/Event	HR 95% CI	P value	
Breast	Normal weight	No	12,087/261	1.00 (Ref.)		24,846/614	1.00 (Ref.)		0.020
		Yes	2,408/75	1.42 (1.10; 1.84)	0.007	8,379/244	1.15 (0.99; 1.33)	0.067	
	Overweight and obese	No	2,664/63	1.12 (0.85; 1.48)	0.419	6,459/161	1.03 (0.87; 1.23)	0.742	
		Yes	13,584/318	1.12 (0.94; 1.33)	0.189	49,545/1,600	1.32 (1.20; 1.46)	<0.001	
Endometrial	Normal weight	No	12,128/18	1.00 (Ref.)		24,960/71	1.00 (Ref.)		0.105
		Yes	2,417/5	1.26 (0.46; 3.41)	0.651	8,422/27	1.10 (0.70; 1.71)	0.687	
	Overweight and obese	No	2,673/5	1.17 (0.43; 3.18)	0.753	6,494/33	1.73 (1.14; 2.62)	0.010	
		Yes	13,622/41	1.57 (0.87; 2.81)	0.133	49,803/381	2.46 (1.89; 3.19)	<0.001	
Ovary	Normal weight	No	12,126/16	1.00 (Ref.)		24,956/103	1.00 (Ref.)		0.105
		Yes	2,417/3	0.83 (0.24; 2.89)	0.769	8,421/29	0.79 (0.52; 1.19)	0.255	
	Overweight and obese	No	2,674/4	1.10 (0.36; 3.30)	0.871	6,490/30	1.08 (0.72; 1.63)	0.706	
		Yes	13,626/34	1.68 (0.90; 3.16)	0.104	49,821/215	0.98 (0.76; 1.25)	0.840	
Uterine	Normal weight	No	12,124/21	1.00 (Ref.)		24,957/84	1.00 (Ref.)		0.248
		Yes	2,415/5	1.09 (0.41; 2.91)	0.858	8,421/27	0.93 (0.60; 1.43)	0.728	
	Overweight and obese	No	2,673/5	1.05 (0.39; 2.80)	0.923	6,493/34	1.50 (1.01; 2.24)	0.046	
		Yes	13,620/52	1.77 (1.04; 3.03)	0.036	49,796/415	2.27 (1.78; 2.89)	<0.001	

Data are presented in hazard ratio with 95% confidence intervals. Cox proportional hazard were done. The reference group was women with normal BMI and normal WC. Analyses were adjusted for age, education, deprivation, ethnicity, comorbidity, diet score, smoking, sedentary behavior, physical activity, age menarche, first and last live birth and hormonal replacement. Normal weight (BMI 18.5 – 24.9 kg/m²), Overweight (BMI ≥25 kg/m²), Central obesity (≥80 women). Significant results in bold.

Supplementary Materials

Combined association of general and central obesity with incidence and mortality of cancers in 22 sites

Parra-Soto S et al.

Supplementary Table 1: Characteristic by sex

	Women	Men	Overall
n	210,259 (54.5%)	175,842 (45.5%)	386,101
Age			
Mean (SD)	56.1 (8.03)	56.5 (8.22)	56.2 (8.12)
Townsend deprivation index			
Lower	71,491 (34.0%)	60,352 (34.3%)	131,843 (34.1%)
Middle	71,660 (34.1%)	58,381 (33.2%)	130,041 (33.7%)
Higher	67,108 (31.9%)	57,109 (32.5%)	124,217 (32.2%)
Height (m)			
Mean (SD)	1.63 (0.0629)	1.76 (0.0682)	1.69 (0.0928)
Weight (Kg)			
Mean (SD)	71.5 (13.9)	86.1 (14.2)	78.2 (15.8)
Waist (cm)			
Mean (SD)	84.6 (12.3)	96.9 (11.2)	90.2 (13.3)
Body Mass index (kg/m2)			
Mean (SD)	27.1 (5.09)	27.9 (4.19)	27.4 (4.72)
Smoking			
Never	126,882 (60.3%)	87,904 (50.0%)	214,786 (55.6%)
Previous	65,976 (31.4%)	67,431 (38.3%)	13,3407 (34.6%)
Current	17,407 (8.3%)	20,513 (11.7%)	37,920 (9.8%)
Alcohol intake			
Daily or almost daily	33,589 (16.0%)	44,192 (25.1%)	77,781 (20.1%)
3-4 times a week	44,274 (21.1%)	47,074 (26.8%)	91,348 (23.7%)
Once or twice a week	55,312 (26.3%)	46,190 (26.3%)	101,502 (26.3%)
1-3 times a month	27,542 (13.1%)	15,659 (8.9%)	43,201 (11.2%)
Special occasions only	30,589 (14.5%)	12,176 (6.9%)	42,765 (11.1%)
Never	18,953 (9.0%)	10,551 (6.0%)	29,504 (7.6%)
Sedentary time, Mean (SD)	4.69 (2.00)	5.50 (2.44)	5.06 (2.25)
Physical activity, Mean (SD)	1.75 (1.64)	1.83 (1.61)	1.79 (1.62)
Diet score, Mean (SD)	4.69 (1.55)	4.06 (1.62)	4.40 (1.61)
Diabetes diagnostic			
No	203,336 (96.7%)	163,888 (93.2%)	367,224 (95.1%)
Yes	6,923 (3.3%)	11,954 (6.8%)	18,877 (4.9%)
Longstanding illness			
No	147,620 (70.2%)	114,423 (65.1%)	262,043 (67.9%)
Yes	57,901 (27.5%)	58,166 (33.1%)	116,067 (30.1%)
Missing	4,738 (2.3%)	3,253 (1.8%)	7,991 (2.1%)
Multimorbidity			
no illness	78,701 (37.4%)	65,609 (37.3%)	14,4310 (37.4%)
1+ illness	131558 (62.6%)	110233 (62.7%)	241791 (62.6%)

Data are presented as number of participants and their percentage (%) unless otherwise specified. Data available for 386,101.

Supplementary Table 2: Interaction Body mass index obese with waist circumference

Cancer sites	Incident Cancer				Cancer mortality		
	Total	Events	RHR 95% CI	P adj	Deaths	RHR 95% CI	P adj
All-cause	379525	42189	1.00 (1.00; 1.00)	1.000	9826	1.00 (1.00; 1.01)	1.000
Bladder	385832	1688	1.00 (0.99; 1.01)	1.000	267	1.00 (0.97; 1.02)	1.000
Brain	386002	598	0.99 (0.97; 1.00)	1.000	499	0.98 (0.96; 1.00)	0.380
Colorectal	385445	3863	1.00 (1.00; 1.01)	1.000	1020	1.01 (1.00; 1.02)	1.000
Kidney	385966	1030	0.99 (0.98; 1.01)	1.000	282	0.98 (0.96; 1.00)	1.000
Leukemia	385992	1007	1.00 (0.99; 1.01)	1.000	354	0.99 (0.97; 1.02)	1.000
Liver	386040	608	1.02 (1.00; 1.03)	0.447	383	1.02 (1.00; 1.04)	0.327
Lung	214727	455	1.00 (0.98; 1.02)	1.000	217	1.01 (0.98; 1.04)	1.000
Lymphatic	385700	3122	1.00 (0.99; 1.01)	1.000	926	1.00 (0.98; 1.01)	1.000
Melanoma	385853	1688	1.00 (0.99; 1.01)	1.000	159	1.00 (0.97; 1.04)	1.000
Multiple Myeloma	386024	670	0.99 (0.97; 1.01)	1.000	187	1.00 (0.97; 1.03)	1.000
Non-Hodgkin	385890	1467	1.00 (0.99; 1.02)	1.000	364	0.99 (0.97; 1.01)	1.000
Esophagus	214747	265	1.01 (0.98; 1.03)	1.000	139	1.02 (0.99; 1.05)	1.000
Oral	214746	261	1.02 (0.99; 1.05)	1.000	41	1.01 (0.95; 1.08)	1.000
Pancreas	385996	996	1.00 (0.99; 1.02)	1.000	802	1.01 (0.99; 1.02)	1.000
Stomach	386010	660	1.00 (0.99; 1.02)	1.000	268	1.02 (1.00; 1.05)	1.000
Thyroid	386053	249	0.99 (0.96; 1.01)	1.000	15	0.93 (0.83; 1.05)	1.000
Prostate	175109	6282	0.99 (0.99; 1.00)	1.000	552	0.98 (0.96; 1.01)	1.000
Testis	175829	64	0.96 (0.89; 1.03)	1.000	0	NA	
Breast	209138	5951	0.99 (0.98; 1.00)	0.015	426	1.00 (0.98; 1.02)	1.000
Ovary	210127	765	1.00 (0.99; 1.02)	1.000	341	1.03 (1.01; 1.06)	0.327
Uterine	210084	1050	1.01 (1.00; 1.03)	0.875	171	1.01 (0.98; 1.04)	1.000
Endometrium	210116	945	1.01 (1.00; 1.02)	1.000	112	0.99 (0.96; 1.03)	1.000

Data are presented in ratio hazard ratio with 95% confidence intervals. Analyses were adjusted for age, education, deprivation, ethnicity, comorbidity, diet score, smoking, sedentary behavior and physical activity. Body mass index as binary variable (BMI <30 and ≥ 30 kg/m²) and waist circumference as continuous variable.

Supplementary Table 3: Association BMI and WC categories with cancer mortality in men.

Cancer site	Normal weight (18.5 – 24.9 kg/m ²)					Overweight (≥25 kg/m ²)					
	Without central obesity		With central obesity			Without central obesity			With central obesity		
	Event	HR	Event	HR (95% CI)	P adj	Event	HR (95% CI)	P adj	Event	HR (95% CI)	P adj
All-cause	39,505/1,032	1.00 (Ref.)	4,346/172	1.11 (0.94; 1.30)	1.000	31,977/738	0.92 (0.84; 1.01)	1.000	99,635/3,604	1.09 (1.02; 1.17)	0.258
Bladder	39,585/46	1.00 (Ref.)	4,360/6	0.83 (0.36; 1.96)	1.000	32,013/17	0.48 (0.28; 0.84)	0.173	99,880/139	0.94 (0.67; 1.33)	1.000
Brain	39,577/51	1.00 (Ref.)	4,359/11	1.77 (0.92; 3.40)	1.000	32,010/71	1.79 (1.25; 2.57)	0.029	99,862/159	1.19 (0.86; 1.65)	1.000
Colorectal	39,581/110	1.00 (Ref.)	4,360/10	0.67 (0.35; 1.29)	1.000	32,012/78	0.91 (0.68; 1.22)	1.000	99,858/394	1.27 (1.02; 1.58)	0.497
Kidney	39,585/25	1.00 (Ref.)	4,360/3	0.80 (0.24; 2.64)	1.000	32,011/23	1.16 (0.66; 2.05)	1.000	99,876/145	1.75 (1.14; 2.71)	0.203
Leukemia	39,586/39	1.00 (Ref.)	4,360/6	1.00 (0.42; 2.36)	1.000	32,013/33	1.06 (0.67; 1.69)	1.000	99,869/154	1.22 (0.85; 1.75)	1.000
Liver	39,584/35	1.00 (Ref.)	4,360/5	0.88 (0.34; 2.24)	1.000	32,013/17	0.61 (0.34; 1.09)	1.000	99,871/177	1.31 (0.90; 1.89)	1.000
Lung	22,596/25	1.00 (Ref.)	2,087/2	0.63 (0.15; 2.66)	1.000	17,647/13	0.67 (0.34; 1.32)	1.000	45,566/47	0.76 (0.46; 1.26)	1.000
Lymphatic	39,580/106	1.00 (Ref.)	4,359/14	0.89 (0.51; 1.55)	1.000	32,009/81	0.99 (0.74; 1.33)	1.000	99,856/357	1.11 (0.89; 1.38)	1.000
Melanoma	39,586/20	1.00 (Ref.)	4,360/2	0.78 (0.18; 3.34)	1.000	32,013/18	1.14 (0.60; 2.17)	1.000	99,878/57	1.05 (0.62; 1.78)	1.000
Multiple Myeloma	39,587/25	1.00 (Ref.)	4,360/2	0.60 (0.14; 2.52)	1.000	32,012/11	0.62 (0.31; 1.27)	1.000	99,877/67	1.13 (0.70; 1.82)	1.000
Non-Hodgkin	39,583/41	1.00 (Ref.)	4,359/6	0.98 (0.42; 2.32)	1.000	32,010/37	1.18 (0.76; 1.84)	1.000	99,874/124	0.97 (0.67; 1.39)	1.000
Esophagus	22,596/13	1.00 (Ref.)	2,088/2	1.23 (0.28; 5.46)	1.000	17,648/8	0.80 (0.33; 1.95)	1.000	45,567/63	1.80 (0.97; 3.35)	0.918
Oral	22,597/7	1.00 (Ref.)	2,088/1	1.33 (0.16; 10.89)	1.000	17,648/5	0.89 (0.28; 2.82)	1.000	45,569/15	0.77 (0.30; 1.99)	1.000
Pancreas	39,583/79	1.00 (Ref.)	4,360/11	0.97 (0.51; 1.82)	1.000	32,009/58	0.92 (0.66; 1.30)	1.000	99,851/299	1.20 (0.93; 1.54)	1.000
Prostate	39,585/114	1.00 (Ref.)	4,359/18	1.07 (0.65; 1.75)	1.000	32,012/73	0.85 (0.63; 1.14)	1.000	99,872/347	1.05 (0.84; 1.30)	1.000
Stomach	39,584/30	1.00 (Ref.)	4,360/2	0.47 (0.11; 1.95)	1.000	32,009/24	1.04 (0.61; 1.79)	1.000	99,871/124	1.34 (0.89; 2.02)	1.000

Data are presented in hazard ratio with 95% confidence intervals. The reference group was people with normal BMI and normal WC. Analyses were adjusted for age, education, deprivation, ethnicity, comorbidity, diet score, sedentary behavior and physical activity. Central obesity (≥94 cm men). Significant results in red.

Supplementary Table 4: Association BMI and WC categories with cancer mortality in women

Cancer site	Normal weight (18.5 – 24.9 kg/m ²)					Overweight (≥25 kg/m ²)					
	Without central obesity		With central obesity			Without central obesity			With central obesity		
	Event	HR	Event	HR (95% CI)	P adj	Event	HR (95% CI)	P adj	Event	HR (95% CI)	P adj
All-cause	65,341/1,106	1.00 (Ref.)	17,926/352	0.93 (0.83; 1.05)	1.000	15,943/267	0.93 (0.82; 1.07)	1.000	110,809/2,555	1.02 (0.95; 1.10)	1.000
Bladder	65,396/7	1.00 (Ref.)	17,958/4	1.60 (0.47; 5.50)	1.000	15,952/5	2.77 (0.88; 8.76)	1.000	110,948/43	2.47 (1.09; 5.61)	0.601
Colorectal	65,392/114	1.00 (Ref.)	17,956/42	1.13 (0.79; 1.61)	1.000	15,953/28	0.97 (0.64; 1.47)	1.000	110,942/244	1.04 (0.82; 1.31)	1.000
Kidney	65,394/15	1.00 (Ref.)	17,957/9	1.71 (0.75; 3.91)	1.000	15,953/6	1.47 (0.57; 3.81)	1.000	110,947/56	1.53 (0.85; 2.76)	1.000
Leukemia	65,391/29	1.00 (Ref.)	17,958/7	0.70 (0.31; 1.60)	1.000	15,954/6	0.80 (0.33; 1.92)	1.000	110,944/80	1.25 (0.80; 1.95)	1.000
Liver	65,392/33	1.00 (Ref.)	17,955/15	1.31 (0.71; 2.42)	1.000	15,953/7	0.78 (0.34; 1.77)	1.000	110,945/94	1.15 (0.76; 1.74)	1.000
Lung	41,427/41	1.00 (Ref.)	10,329/10	0.85 (0.43; 1.70)	1.000	10,223/12	1.17 (0.61; 2.23)	1.000	64,893/67	0.97 (0.65; 1.46)	1.000
Lymphatic	65,389/91	1.00 (Ref.)	17,956/28	0.90 (0.59; 1.38)	1.000	15,954/14	0.59 (0.33; 1.03)	1.000	110,940/235	1.16 (0.90; 1.50)	1.000
Melanoma	65,396/22	1.00 (Ref.)	17,958/2	0.30 (0.07; 1.27)	1.000	15,953/7	1.25 (0.53; 2.93)	1.000	110,951/31	0.76 (0.43; 1.35)	1.000
Multiple Myeloma	65,396/17	1.00 (Ref.)	17,957/6	1.02 (0.40; 2.59)	1.000	15,954/6	1.39 (0.55; 3.54)	1.000	110,950/53	1.41 (0.80; 2.49)	1.000
Non-Hodgkin	65,395/41	1.00 (Ref.)	17,957/14	1.03 (0.56; 1.89)	1.000	15,954/1	0.09 (0.01; 0.66)	0.410	110,948/100	1.10 (0.75; 1.61)	1.000
Esophagus	41,429/16	1.00 (Ref.)	10,330/5	0.96 (0.35; 2.63)	1.000	10,223/1	0.22 (0.03; 1.68)	1.000	64,896/31	0.82 (0.43; 1.56)	1.000
Oral	41,428/5	1.00 (Ref.)	10,330/1	0.72 (0.08; 6.22)	1.000	10,223/0	0.00 (0.00; 0.00)	1.000	64,897/7	0.78 (0.23; 2.62)	1.000
Pancreas	65,390/89	1.00 (Ref.)	17,958/25	0.80 (0.51; 1.25)	1.000	15,953/30	1.28 (0.85; 1.94)	1.000	110,933/211	1.04 (0.80; 1.35)	1.000
Stomach	65,394/23	1.00 (Ref.)	17,958/8	1.07 (0.48; 2.40)	1.000	15,954/4	0.65 (0.22; 1.89)	1.000	110,947/53	1.03 (0.62; 1.71)	1.000
Thyroid	65,395/1	1.00 (Ref.)	17,958/0	0.00 (0.00; 0.00)	1.000	15,954/0	0.00 (0.00; 0.00)	1.000	110,949/5	1.58 (0.17; 14.52)	1.000
Breast	65,395/123	1.00 (Ref.)	17,956/37	1.02 (0.70; 1.47)	1.000	15,953/24	0.79 (0.51; 1.22)	1.000	110,944/242	1.04 (0.83; 1.31)	1.000
Endometrium	65,396/12	1.00 (Ref.)	17,958/8	1.97 (0.80; 4.83)	1.000	15,954/5	1.59 (0.56; 4.52)	1.000	110,949/87	3.28 (1.77; 6.07)	0.004
Ovary	65,394/115	1.00 (Ref.)	17,958/17	0.46 (0.28; 0.77)	0.069	15,954/25	0.85 (0.55; 1.31)	1.000	110,942/184	0.80 (0.62; 1.02)	1.000
Uterine	65,396/29	1.00 (Ref.)	17,957/13	1.37 (0.71; 2.64)	1.000	15,953/9	1.19 (0.56; 2.53)	1.000	110,948/120	1.91 (1.25; 2.90)	0.055

Data are presented in hazard ratio with 95% confidence intervals. The reference group was people with normal BMI and normal WC. Analyses were adjusted for age, education,

deprivation, ethnicity, comorbidity, diet score, sedentary behavior and physical activity. Central obesity (≥80 cm women). Significant results in red.

Supplementary Table 5: Association of BMI (normal weight, overweight and obese) and WC categories with cancer mortality in men and women

Cancer site	Normal weight (18.5 – 24.9 kg/m ²)				Overweight (≥25 – 29.9 kg/m ²)				Obese (≥30 kg/m ²)	
	Without central obesity		With central obesity		Without central obesity		With central obesity		With central obesity	
	Event	HR	Event	HR (95% CI)	Event	HR (95% CI)	Event	HR (95% CI)	Event	HR (95% CI)
All-cause	104,931/338	1.00 (Ref.)	22,306/57	1.06 (1.01; 1.10)	47,021/216	0.99 (0.95; 1.02)	118,191/571	1.05 (1.02; 1.08)	92,465/499	1.06 (1.03; 1.09)
Bladder	104,956/126	1.00 (Ref.)	22,314/40	0.80 (0.60; 1.06)	47,042/96	1.05 (0.89; 1.25)	118,254/198	1.05 (0.92; 1.21)	92,520/134	1.21 (1.05; 1.40)
Brain	104,845/822	1.00 (Ref.)	22,281/203	1.47 (1.03; 2.11)	46,983/408	1.52 (1.16; 2.00)	118,039/1,357	1.22 (0.97; 1.54)	92,380/1,068	1.10 (0.85; 1.42)
Colorectal	104,980/13	1.00 (Ref.)	22,318/5	1.05 (0.90; 1.23)	47,047/2	1.01 (0.89; 1.14)	118,285/35	1.21 (1.11; 1.32)	92,540/38	1.27 (1.16; 1.40)
Kidney	104,948/219	1.00 (Ref.)	22,317/49	1.36 (0.99; 1.88)	47,040/112	1.11 (0.86; 1.43)	118,252/351	1.46 (1.21; 1.77)	92,517/276	1.80 (1.48; 2.18)
Leukemia	104,967/106	1.00 (Ref.)	22,315/28	0.98 (0.72; 1.34)	47,044/44	0.98 (0.77; 1.23)	118,274/191	1.12 (0.94; 1.33)	92,523/239	1.17 (0.97; 1.41)
Liver	64,009/115	1.00 (Ref.)	12,413/32	1.06 (0.70; 1.62)	27,327/57	0.78 (0.55; 1.11)	62,616/146	1.11 (0.87; 1.41)	47,824/105	1.58 (1.24; 2.01)
Lung	104,870/710	1.00 (Ref.)	22,299/164	1.15 (0.77; 1.70)	47,009/343	1.19 (0.86; 1.64)	118,161/1,043	1.06 (0.83; 1.36)	92,443/861	0.99 (0.74; 1.31)
Lymphatic	104,913/424	1.00 (Ref.)	22,305/88	0.99 (0.83; 1.17)	47,020/203	0.97 (0.85; 1.10)	118,212/553	1.06 (0.96; 1.17)	92,485/416	1.15 (1.03; 1.27)
Melanoma	104,964/146	1.00 (Ref.)	22,314/27	0.95 (0.75; 1.20)	47,039/80	1.01 (0.85; 1.19)	118,267/226	1.06 (0.93; 1.20)	92,522/190	1.11 (0.96; 1.28)
Multiple	104,928/349	1.00 (Ref.)	22,306/81	0.80 (0.53; 1.21)	47,029/165	1.11 (0.84; 1.47)	118,220/486	1.16 (0.93; 1.43)	92,489/386	1.30 (1.03; 1.63)
Myeloma										
Non-Hodgkin	64,018/56	1.00 (Ref.)	12,415/9	0.99 (0.78; 1.26)	27,331/26	0.96 (0.79; 1.16)	62,616/89	1.01 (0.88; 1.16)	47,829/85	1.04 (0.90; 1.22)
Esophagus	64,015/76	1.00 (Ref.)	12,418/13	0.80 (0.40; 1.63)	27,326/40	0.88 (0.55; 1.41)	62,618/76	1.24 (0.88; 1.75)	47,831/56	1.51 (1.05; 2.16)
Oral	104,963/209	1.00 (Ref.)	22,317/45	0.94 (0.52; 1.69)	47,041/114	1.02 (0.69; 1.51)	118,249/333	0.89 (0.64; 1.23)	92,508/294	0.83 (0.57; 1.20)
Pancreas	104,968/111	1.00 (Ref.)	22,313/28	0.86 (0.63; 1.20)	47,038/71	1.09 (0.87; 1.37)	118,257/219	1.08 (0.91; 1.29)	92,516/230	1.23 (1.02; 1.49)
Stomach	104,970/57	1.00 (Ref.)	22,314/13	1.18 (0.78; 1.79)	47,045/21	1.10 (0.82; 1.49)	118,274/80	1.28 (1.01; 1.61)	92,532/78	1.66 (1.31; 2.11)
Thyroid	104,931/338	1.00 (Ref.)	22,306/57	0.93 (0.51; 1.71)	47,021/216	1.01 (0.61; 1.67)	118,191/571	1.25 (0.88; 1.77)	92,465/499	1.41 (0.98; 2.03)
Prostate	39,429/1,1319	1.00 (Ref.)	4,331/205	1.16 (1.00; 1.34)	31,242/1,062	1.07 (0.98; 1.16)	55,724/2,260	1.07 (1.00; 1.15)	43,724/1,419	0.93 (0.86; 1.01)
Testis	39,585/13	1.00 (Ref.)	4,360/1	0.78 (0.10; 6.00)	31,348/14	1.35 (0.63; 2.89)	55,993/21	1.24 (0.61; 2.50)	43,883/15	1.09 (0.50; 2.38)
Breast	65,087/1598	1.00 (Ref.)	17,861/552	1.21 (1.10; 1.33)	15,610/388	1.02 (0.91; 1.14)	61,951/1,898	1.21 (1.13; 1.30)	48,373/1,511	1.27 (1.18; 1.37)
Endometrium	65,376/147	1.00 (Ref.)	17,945/55	1.26 (0.92; 1.72)	15,689/56	1.59 (1.17; 2.16)	62,260/260	1.72 (1.40; 2.12)	48,588/425	3.74 (3.07; 4.55)
Ovary	65,358/226	1.00 (Ref.)	17,945/55	0.79 (0.58; 1.06)	15,688/46	0.81 (0.59; 1.12)	62,263/244	0.98 (0.82; 1.18)	48,616/192	1.01 (0.82; 1.24)
Uterine	65,368/180	1.00 (Ref.)	17,941/56	1.05 (0.78; 1.42)	15,688/62	1.44 (1.07; 1.92)	62,249/292	1.59 (1.32; 1.92)	48,580/458	3.29 (2.74; 3.95)
Prostate	39,429/1,319	1.00 (Ref.)	4,331/205	1.16 (1.00; 1.34)	31,242/1,062	1.07 (0.98; 1.16)	55,724/2,260	1.07 (1.00; 1.15)	43,724/1,419	0.93 (0.86; 1.01)
Testis	39,585/13	1.00 (Ref.)	4,360/1	0.78 (0.10; 6.00)	31,348/14	1.35 (0.63; 2.89)	55,993/21	1.24 (0.61; 2.50)	43,883/15	1.09 (0.50; 2.38)

Data are presented in hazard ratio with 95% confidence intervals. The reference group was people with normal BMI and normal WC. Analyses were adjusted for age, education, deprivation, ethnicity, comorbidity, diet score, sedentary behavior and physical activity. Central obesity (≥ 94 cm Men, ≥ 80 cm women). Significant results in red.

Supplementary Table 6: Association BMI and WC categories with cancer incidence in men and women without comorbidities.

	Normal weight (18.5 – 24.9 kg/m²)					Overweight (≥25 kg/m²)					
	Without central obesity		With central obesity			Without central obesity			With central obesity		
Cancer site	Event	HR	Event	HR (95% CI)	P adj	Event	HR (95% CI)	P adj	Event	HR (95% CI)	P adj
All-cause	50,463/4,216	1.00 (Ref.)	8,718/886	1.09 (1.02; 1.18)	0.353	20,967/1,756	0.98 (0.92; 1.03)	1.000	62,285/6,160	1.07 (1.03; 1.12)	0.018
Bladder	51,091/132	1.00 (Ref.)	8,850/19	0.85 (0.52; 1.38)	1.000	21,201/78	1.11 (0.84; 1.48)	1.000	63,111/216	1.02 (0.82; 1.28)	1.000
Brain	51,096/55	1.00 (Ref.)	8,852/17	1.90 (1.09; 3.29)	0.473	21,203/33	1.26 (0.81; 1.95)	1.000	63,130/112	1.50 (1.08; 2.09)	0.318
Colorectal	51,053/350	1.00 (Ref.)	8,843/66	0.97 (0.75; 1.27)	1.000	21,184/173	1.11 (0.93; 1.34)	1.000	63,054/598	1.20 (1.05; 1.37)	0.202
Kidney	51,099/66	1.00 (Ref.)	8,850/15	1.32 (0.75; 2.32)	1.000	21,204/33	1.01 (0.66; 1.54)	1.000	63,125/144	1.47 (1.09; 1.98)	0.246
Leukemia	51,093/91	1.00 (Ref.)	8,854/16	1.01 (0.59; 1.73)	1.000	21,203/41	0.90 (0.62; 1.31)	1.000	63,125/151	1.11 (0.85; 1.45)	1.000
Liver	51,098/39	1.00 (Ref.)	8,853/9	1.05 (0.50; 2.17)	1.000	21,205/12	0.72 (0.38; 1.39)	1.000	63,141/60	1.00 (0.66; 1.50)	1.000
Lung	32,725/51	1.00 (Ref.)	5,146/12	1.14 (0.61; 2.15)	1.000	13,067/19	1.04 (0.61; 1.78)	1.000	35,892/59	0.93 (0.63; 1.37)	1.000
Lymphatic	51,059/314	1.00 (Ref.)	8,847/55	0.96 (0.72; 1.28)	1.000	21,191/128	0.89 (0.72; 1.09)	1.000	63,091/452	1.01 (0.88; 1.18)	1.000
Melanoma	51,079/207	1.00 (Ref.)	8,848/30	0.83 (0.57; 1.22)	1.000	21,194/77	0.85 (0.65; 1.11)	1.000	63,107/269	1.01 (0.84; 1.22)	1.000
Multiple Myeloma	51,098/75	1.00 (Ref.)	8,853/11	0.85 (0.45; 1.61)	1.000	21,203/33	0.93 (0.61; 1.41)	1.000	63,135/94	0.91 (0.67; 1.24)	1.000
Non-Hodgkin	51,083/151	1.00 (Ref.)	8,849/27	0.95 (0.63; 1.44)	1.000	21,200/57	0.86 (0.63; 1.17)	1.000	63,116/211	1.00 (0.81; 1.24)	1.000
Esophagus	32,728/23	1.00 (Ref.)	5,146/4	1.07 (0.37; 3.14)	1.000	13,067/5	0.44 (0.17; 1.18)	1.000	35,895/33	1.07 (0.62; 1.85)	1.000
Oral	32,728/37	1.00 (Ref.)	5,148/6	1.04 (0.44; 2.49)	1.000	13,067/19	1.13 (0.64; 2.00)	1.000	35,892/37	0.80 (0.50; 1.28)	1.000
Pancreas	51,098/73	1.00 (Ref.)	8,854/13	0.90 (0.50; 1.63)	1.000	21,203/39	1.20 (0.81; 1.78)	1.000	63,129/128	1.19 (0.89; 1.60)	1.000
Stomach	51,100/40	1.00 (Ref.)	8,851/4	0.60 (0.21; 1.68)	1.000	21,205/25	1.18 (0.71; 1.95)	1.000	63,131/97	1.51 (1.04; 2.19)	0.582
Prostate	19,213/575	1.00 (Ref.)	1,582/68	1.14 (0.88; 1.47)	<0.0001	14,304/398	1.05 (1.92; 1.19)	0.490	30,328/954	1.03 (0.92; 1.114)	0.620
Testis	19,273/6	1.00 (Ref.)	1586/0	NA		14,330/5	1.06 (0.32; 3.05)	1.000	30,413/14	1.57 (0.59; 4.18)	1.000
Thyroid	51,100/22	1.00 (Ref.)	8,851/7	1.65 (0.70; 3.89)	1.000	21,206/7	0.96 (0.41; 2.29)	1.000	63,139/39	1.51 (0.88; 2.58)	1.000
Breast	31,690/771	1.00 (Ref.)	7,225/223	1.20 (1.03; 1.40)	0.019	6,828/166	1.00 (0.85; 1.19)	1.000	32,567/988	1.21 (1.10; 1.33)	<0.0001
Endometrium	31,821/64	1.00 (Ref.)	7,266/22	1.39 (0.86; 2.26)	0.258	6,871/26	1.88 (1.19; 2.98)	0.007	32,708/165	2.36 (1.76; 3.17)	<0.0001
Ovary	31,813/93	1.00 (Ref.)	7,263/26	1.08 (0.70; 1.67)	1.000	6,871/15	0.72 (0.41; 1.24)	0.229	32,710/128	1.19 (0.90; 1.57)	1.000
Uterine	31,818/80	1.00 (Ref.)	7,266/22	1.12 (0.70; 1.80)	1.000	6,871/31	1.79 (1.18; 2.72)	0.006	32,700/182	2.09 (1.59; 2.73)	<0.0001

Data are presented in hazard ratio with 95% confidence intervals. The reference group was people with normal BMI and normal WC. Analyses were adjusted for age, education,

deprivation, ethnicity, diet score, sedentary behavior and physical activity. Central obesity (≥94 cm Men, ≥80 cm women). Significant results in red.

Supplementary Table 7: Association of BMI and WC categories with cancer incidence in incidence in men and women of white ethnic background.

Cancer site	Normal weight (18.5 – 24.9 kg/m ²)					Overweight (≥25 kg/m ²)					
	Without central obesity		With central obesity			Without central obesity			With central obesity		
	Event	HR	Event	HR (95% CI)	P adj	Event	HR (95% CI)	P adj	Event	HR (95% CI)	P adj
All-cause	98,558/9686	1.00 (Ref.)	20,788/2406	1.06 (1.01; 1.11)	0.291	44,616/4662	0.98 (0.95; 1.01)	1.000	196,103/24193	1.05 (1.03; 1.08)	0.001
Bladder	100,076/331	1.00 (Ref.)	21,172/54	0.78 (0.58; 1.04)	1.000	45,242/217	1.05 (0.89; 1.25)	1.000	199,695/1037	1.10 (0.97; 1.25)	1.000
Brain	100,101/124	1.00 (Ref.)	21,180/40	1.51 (1.05; 2.16)	0.523	45,262/98	1.56 (1.19; 2.04)	0.280	199,811/323	1.16 (0.94; 1.44)	1.000
Colorectal	99,992/798	1.00 (Ref.)	21,151/195	1.05 (0.89; 1.23)	1.000	45,206/399	1.00 (0.88; 1.13)	1.000	199,463/2356	1.23 (1.13; 1.34)	<0.0001
Kidney	100,105/156	1.00 (Ref.)	21,178/46	1.32 (0.95; 1.83)	1.000	45,254/106	1.19 (0.93; 1.53)	1.000	199,781/692	1.59 (1.33; 1.90)	<0.0001
Leukemia	100,093/213	1.00 (Ref.)	21,183/47	0.97 (0.70; 1.33)	1.000	45,261/110	0.97 (0.77; 1.22)	1.000	199,806/605	1.13 (0.96; 1.33)	1.000
Liver	100,113/103	1.00 (Ref.)	21,181/27	1.05 (0.69; 1.61)	1.000	45,264/37	0.66 (0.45; 0.97)	0.679	199,836/418	1.30 (1.04; 1.63)	0.322
Lung	60,659/110	1.00 (Ref.)	11,569/29	1.11 (0.73; 1.67)	1.000	26,085/54	1.16 (0.83; 1.62)	1.000	102,669/229	1.00 (0.79; 1.27)	1.000
Lymphatic	100,017/685	1.00 (Ref.)	21,165/160	1.01 (0.85; 1.20)	1.000	45,233/328	0.94 (0.82; 1.08)	1.000	199,651/1836	1.09 (1.00; 1.20)	0.811
Melanoma	100,057/420	1.00 (Ref.)	21,171/88	0.96 (0.76; 1.21)	1.000	45,242/207	1.02 (0.86; 1.21)	1.000	199,734/964	1.08 (0.96; 1.22)	1.000
Multiple Myeloma	100,109/143	1.00 (Ref.)	21,180/27	0.83 (0.55; 1.25)	1.000	45,261/74	1.03 (0.78; 1.37)	1.000	199,829/387	1.15 (0.94; 1.40)	1.000
Non-Hodgkin	100,073/333	1.00 (Ref.)	21,172/79	1.02 (0.79; 1.30)	1.000	45,252/157	0.94 (0.78; 1.14)	1.000	199,751/854	1.05 (0.92; 1.20)	1.000
Esophagus	60,667/55	1.00 (Ref.)	11,571/9	0.82 (0.40; 1.66)	1.000	26,089/25	0.85 (0.53; 1.37)	1.000	102,671/169	1.33 (0.97; 1.82)	0.957
Oral	60,664/73	1.00 (Ref.)	11,574/12	0.92 (0.50; 1.71)	1.000	26,084/37	0.99 (0.66; 1.47)	1.000	102,676/125	0.87 (0.64; 1.18)	1.000
Pancreas	100,108/198	1.00 (Ref.)	21,183/43	0.88 (0.63; 1.22)	1.000	45,262/111	1.10 (0.87; 1.39)	1.000	199,796/606	1.17 (0.99; 1.38)	0.920
Stomach	100,112/107	1.00 (Ref.)	21,179/27	1.18 (0.77; 1.80)	1.000	45,259/66	1.04 (0.77; 1.42)	1.000	199,811/433	1.43 (1.15; 1.78)	0.022
Prostate	37,205/1257	1.00 (Ref.)	4,094/202	1.20 (1.04; 1.40)	0.106	29,966/1024	1.06 (0.98; 1.16)	0.144	95,109/3563	1.16 (1.08; 1.24)	<0.0001
Testis	37,347/12	1.00 (Ref.)	4,121/2	0.83 (0.18; 3.71)	1.000	29,966/13	2.28 (1.04; 5.02)	0.809	95,109/36	1.47 (0.75; 2.90)	1.000
Thyroid	100,115/53	1.00 (Ref.)	21,181/11	0.86 (0.45; 1.64)	1.000	45,267/20	1.01 (0.60; 1.71)	1.000	199,847/150	1.36 (0.98; 1.89)	0.920
Breast	62,475/1551	1.00 (Ref.)	16,971/527	1.19 (1.08; 1.32)	0.005	15,212/385	1.02 (0.91; 1.14)	0.737	103,727/3296	1.24 (1.17; 1.32)	0.015
Endometrium	62,758/142	1.00 (Ref.)	17,050/53	1.26 (0.91; 1.72)	0.152	15,292/56	1.59 (1.16; 2.16)	0.004	104,237/645	2.45 (2.03; 2.95)	<0.0001
Ovary	62,745/219	1.00 (Ref.)	17,051/52	0.78 (0.57; 1.05)	1.000	15,290/47	0.85 (0.62; 1.16)	0.305	104,265/417	1.01 (0.85; 1.20)	1.000
Uterine	62,750/173	1.00 (Ref.)	17,047/54	1.06 (0.78; 1.44)	0.649	15,291/61	1.42 (1.06; 1.90)	0.019	104,218/702	2.20 (1.85; 2.62)	<0.0001

Data are presented in hazard ratio with 95% confidence intervals. Cox proportional hazard were done. The reference group was men with normal BMI and normal WC. Analyses were adjusted for age, education, deprivation, ethnicity, comorbidity, diet score, smoking, sedentary behavior and physical activity. Central obesity (≥ 94 cm Men, ≥ 80 cm women). Significant results in red.