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Anthropometric measures of body fat and obesity-related cancer risk: sex-specific differences in Framingham Offspring Study adults

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Abstract

Background/Objective: Obesity has been associated with risk of developing certain cancers. A limited number of studies have examined effects of various anthropometric measures of body composition on cancer risk. The aim of this study was to estimate the sex-specific effects of various anthropometric measures on risk of obesity-related cancers (ObCa).

Subjects/Methods: Data on body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), and hip circumference (HC) among 3,818 45–69 year-olds in the Framingham Offspring Study were included. Cox proportional hazards models were used to estimate adjusted risks of 16 obesity-related cancers, with the most common being postmenopausal breast, endometrial, and colon cancers.

Results: Obesity as measured by BMI in both men and women was a predictor of ObCa; those in the highest quintile (Q5) of BMI (≥30.3 in women; >31.1 kg/m^2 in men) had more than twice the risk of ObCa (HR=2.07; 95% CI: 1.06–4.07 (women) and HR=2.25; 95% CI: 1.08–4.69 (men)). Waist-related measures (WC, WHtR) were stronger predictors of ObCa in men than in women and HC confounded the relations between waist size and cancer risk. After adjusting for HC, men in Q5 of WC had more than a three-fold increased risk of ObCa (HR:=3.22; 95% CI: 1.39–7.45). Comparable effects in women were weak and non-statistically significant. Results were similar for WHtR. Finally, a J-shaped relation was found between HC and ObCa after adjusting for WC among men but not in women.

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Conclusion: These results suggest that obesity as measured by BMI is a predictor of obesity-related cancer risk in men and women. These results suggest that waist and hip circumference measures are inter-related and confound the independent effects of each measure. Among men, a large waist size and a small hip size are independent predictors of cancer risk.

Introduction

Obesity and overweight are strong risk factors for certain types of cancers,[1] with some evidence that the types of cancer associated with excess adiposity may be sex-specific. A systematic review and meta-analysis of prospective studies by Renehan et al. concluded that a 5 kg/m^2 increase in body mass index (BMI) in men led to moderately large increased risks (24–52% increased risks) for esophageal adenocarcinoma, thyroid cancer, colon, and renal cancers while weaker effects were found for rectal cancer and malignant melanoma.[2] In women, the effects (34–59% increased risks) of a 5 kg/m^2 increase in BMI were largest for endometrial, gallbladder, esophageal adenocarcinoma, and renal cancers; weaker effects in women were found for colon, pancreatic, thyroid, and postmenopausal breast cancers.

Some evidence suggests that waist circumference (WC) may be more strongly associated than BMI with colorectal, postmenopausal breast, endometrial, and pancreatic cancers.[1,3] Few studies to date have compared the associations between different anthropometric measures of body fat and obesity-related cancers in men and women separately. Hip circumference (HC), a surrogate for the level of protective gluteofemoral depots, has been used in studies investigating the role of body fat distribution and type 2 diabetes, cardiovascular disease (CVD), and coronary heart disease (CHD) as well as total mortality.[4–6] Less attention has been given to HC and cancer risk, so evaluating its effect could help to clarify the role of body fat distribution as a risk factor for obesity-related cancers in men and women. Since women tend to have larger hips relative to waist size than men, HC may inform the understanding of sex-specific cancer risk attributable to the location of excess body fat.

The objective of this study is to evaluate the sex-specific effects of anthropometric measures of body fat and fat distribution (BMI, WC, waist-to-height ratio (WHtR), and HC) on overall risk of obesity-related cancers in the long-term Framingham Offspring Study.

SUBJECTS AND METHODS

Study Population

The Framingham Offspring Study (FOS) is a prospective study of 5124 subjects who were offspring of the original Framingham Heart Study participants. The FOS began in 1971. Exams 1 through 8 were conducted during the following respective time periods: 1971–1975, 1979–1983,1983–1987,1987–1991,1991–1995,1995–1998, 1998–2001, and 2005–2008. At each examination visit, data on the following variables were collected: anthropometry, urinalysis, blood chemistries, blood pressure, medical history, and lifestyle habits. Subjects were also asked to report any diseases or conditions that had occurred since their last visit. The FOS data set is publicly available through BioLINCC at the National Institutes of Health (https://biolincc.nhlbi.nih.gov/studies/framoffspring/). These analyses

were approved by the Institutional Review Board at Boston University Medical Center. Informed consent was obtained from all subjects in the Framingham Offspring Study.

Men and women ages 45–69 years were included at the first exam at which they met the age criteria and had all available measures needed for the final statistical models. Subjects were excluded for the following reasons: (a) did not attend exam visits after exam 3 (n=712) for BMI analyses or after exam 4 (n=807) for waist-related analyses, (b) less than age 45 (n=199) or older than age 70 (n=146) at baseline, (c) missing anthropometric measures (n=67), (d) missing covariates (n=42), or (e) prevalent cancer at baseline (n=140). Analyses evaluating the association of BMI and cancer risk started at exam 3 and included 3,818 subjects. Analyses for WC, WHtR, and HC effects on cancer risk began at exam 4 included 3,723 individuals.

Exposure Variables

Height and weight were measured at each visit using a standard beam balance.[7] Visit-specific BMI for each subject was calculated by dividing the visit-specific weight measurement (in kilograms) by mean adult height (meters, squared) using all measures taken between 21 and 60 years of age. WC, HC, and WHtR were used as anthropometric indicators of fat distribution. WC and HC were measured starting at exam 4. Missing values for WC or HC at exam 4 were replaced with available exam 5 measures whenever the subject's change in weight between exams 3 and 5 did not exceed 10 pounds. WC was measured in a horizontal plane at the level of the umbilicus with the subject standing upright. WHtR was calculated by dividing WC by height.

Outcome Variables

Obesity-related cancer outcomes have been selected based on previously-published studies and include the following: female reproductive (post-menopausal breast, uterine/endometrial, and ovarian), colon, rectal, stomach, liver, gallbladder, pancreatic, kidney, thyroid, esophageal adenocarcinoma, leukemia, non-Hodgkin's lymphoma and multiple myeloma.[2,8,9] Some recent evidence also suggests that excess body fat is associated with liver, ovarian, and gastric cancer; therefore, we included these cancer types in our analyses.[10–14] Cases of cancer arising from the uterine cervix were excluded due to its strong association with human papilloma virus. Post-menopausal breast cancers excluded tumors in the skin of the breast and carcinoma in situ. There were a total of 299 obesity-related cancer cases for the BMI analyses and 267 cases for waist and hip-related analyses. The most common cancer type for women was post-menopausal breast cancer while the most common type for men was colon cancer.

For colorectal cancer, tumors in the proximal colon, distal colon, and rectum were included. Proximal colon cancer includes cancer in the cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure. Distal colon cancer includes cancer in the descending and sigmoid colon. Appendiceal carcinomas were excluded. Diagnoses were confirmed from pathology, laboratory, and clinical records; date of diagnosis was taken from available pathology reports. When the date of diagnosis was not available or when the diagnosis occurred before the confirmatory pathological test was completed, the diagnosis date was

accepted from these other records, as has been previously described in Framingham.[15] All self-reported cancer cases were confirmed by outside medical and pathological records. Cancer cases were coded using the World Health Organization's International Classification of Diseases for Oncology.[16]

Potential Confounding

Potential confounders that were evaluated and included in the final multivariable models were as follows: age (years), sex, cigarettes per day, grams of alcohol per week, average adult height (inches), education (less than high school, high school graduate, some college, or college graduate), and a physical activity index created by summing self-reported moderate and vigorous activity, where each type of activity was weighted by estimates of oxygen consumption from previous studies.[17] Factors that altered the final hazard ratios (HRs) by more than 5% were retained in the final models. To isolate the effects of overall body fat and central body fat, BMI, WC, and HC were also treated as potential confounders when appropriate. The final WC and WHtR predictive models controlled for BMI and/or HC while final models for BMI and cancer risk included WC and HC (in men) as covariates. Other potential confounders that were explored but not used in the final multivariable models (since they had no confounding effect on the HRs) included energy-adjusted intakes of macronutrients and micronutrients (e.g., fiber, iron, soy, dairy, processed meats), pack-years of smoking, prevalent alcohol use disorders, and prevalent CVD.

Separate analyses evaluated whether prevalent CVD might constitute a competing risk among obese subjects, since premature death from CVD might limit the opportunity for development of obesity-related cancer. CVD events included cerebrovascular disease, coronary heart disease, and congestive heart failure. The addition of time-dependent CVD status did not alter the effect, and thus not included in the final models.

Statistical Analysis

Each anthropometric measure (BMI, WC, WHtR, and HC) was classified into sex-specific quintiles (Q1-Q5) to optimize statistical power and allow for comparison between measures. The effects of each measures on obesity-related cancer risk were evaluated using Cox proportional hazards models. Follow-up time was calculated within quintiles of body fat as the time from the anthropometry measurement to the first of the following outcomes: obesity-related cancer occurrence, death, loss to follow up, or end of exam visit 8. Cancer incidence was calculated by dividing the number of obesity-related cancers by the total person-time in each category of body fat. Mean follow-up time following BMI measurement was 15.1 years and for waist and hip-related exposures was 13.4 years. Q2 was used as the referent category for all analyses. The proportional hazards assumption was tested in all multivariable Cox models and no violations were found. As a result of an apparent J-shaped relation between measures of anthropometry measures and cancer risk, the second quintile was used as the referent category for all analyses.

To eliminate the possibility that the effects could be biased as a result of an excess of preclinical cancers occurring among the leaner subjects, separate analyses were performed with follow-up time starting 3 years and 6 years after the time of the baseline body fat

measurement. As this had no impact on the results, all analyses presented here include follow-up time starting at the time of the anthropometry measure.

Finally, to compare the impact of different measures of body fat on the risk of obesity-related cancer, the attributable risk (AR) was calculated within each quintile of BMI, WC, WHtR, and HC.

Results

Baseline characteristics of the study population of 45–69 year olds according to category of BMI are shown in Table 1. Mean alcohol intake in men was similar across BMI categories but women with a lower BMI had slightly higher alcohol intakes. Men smoked more than women but smoking was inversely associated with BMI in both sexes. The prevalences of dyslipidemia, HBP, and diabetes or impaired fasting glucose increased linearly with increasing BMI.

The risk of obesity-related cancers among men and women associated with sex-specific quintiles of four different anthropometric measures of body fat are shown in Tables 2–4.

Table 2 includes three multivariable models – the first is the standard baseline model (including age, height, education, cigarettes smoked per day, alcohol intake, and physical activity) and the second adds WC to the models while the third adds HC to the model 1. In the baseline model, there was no statistically significant adverse effect of higher BMI levels among men. However, women in quintile 4 (Q4) vs. Q2 had an approximately 60% increased risk of developing an obesity-related cancer while women in Q5 nearly a 75% increased risk. The adverse effects of obesity were strengthened among men, particularly after controlling for HC (HR: 2.25; 95% CI: 1.08, 4.69 for Q5 vs. Q2) and among women after controlling for WC (HR: 2.07; 95% CI: 1.06, 4.07). The addition of WC and HC to these models in some cases leads to a reduction in the precision around the estimated effects (e.g., controlling for WC in models for women). While the shape of the relation between BMI and obesity-related cancer risk was slightly J-shaped, there were no statistically significant increased risks in Q1 (vs. Q2). Obesity-related cancer risks associated with standard cutoff values for BMI (<25, 25-<30, ≥30 kg/m^2) can be found in Supplemental Table 1. There, we found that the increased risk of cancer among men was associated with obesity (BMI >30 kg/m^2) while the increased risk among women was elevated for those who were either overweight or obese.

In Table 3, men in the highest quintile of WC had more than a two-fold increased risk of obesity-related cancer (HR: 2.25; 95%CI: 1.19, 2.23 for Q5 vs. Q2). After adjusting for BMI, and especially for HC, the HRs for a larger WC in men were strengthened. In the baseline model, WC among women was more weakly associated with cancer risk and these effect estimates were substantially attenuated by controlling for either BMI or HC. Additional analyses using absolute cutoff values for waist size among men and women can be found in Supplemental Table 2. In table 3, for both men and women, the results for WHtR analyses are similar to those for WC. Those in the lowest WHtR quintile (Q1) had higher

obesity-related cancer rates than those in Q2. Once again, adjusting for HC strengthened the effects of this waist-related measure among men but attenuated it among women.

Table 4 examines the direct effect of HC on risk of obesity-related cancer. Of note, men with the smallest HC (Q1) had more than a two-fold increased risk of obesity-related cancers compared with those in Q2. This was not the case for women. Adjusting for WC further strengthened the adverse effects of a small HC while attenuating the effects of a larger HC.

The attributable proportions for obesity-related cancers among those in each category of BMI, WC, WHtR, or HC are shown in Supplemental Table 3. Men in Q5 of WC and WHTR had the highest obesity-related cancer rates, and about 55% of obesity-related cancers among men with WC or WHTR in Q5 can be attributed to being in that highest quintile. Women in Q5 of BMI and the WHtR had the highest obesity-related cancer rates; 43% of these cancers among women in Q5 of BMI are estimated to be attributable to the high BMI.

Discussion

In this analysis of 45–69 year old men and women in the Framingham Offspring Study, there was a tendency for those in highest categories of BMI to have higher risks for obesity-related cancers. For both men and women, those in the highest quintile of BMI had more than twice the risk of obesity-related cancer. It was interesting to note that for men cancer risk began to rise only with a BMI of approximately 28 kg/m^2 and higher. It is possible that for these active middle-aged men, a BMI between 25 and 28 kg/m^2 reflects higher concentrations of lean mass rather than an excess of adiposity.

Waist-related measures of body fat, including WC and WHtR were much larger predictors of cancer risk for men than for women. Hip size was also an important factor among men in two ways—first, adjustment for HC in men strengthened the adverse impact of waist-related measures on risk of obesity-related cancers and second, men with the smallest hip sizes (adjusting for waist size) had much higher risks of obesity-related cancer. These analyses also suggest that HC is an important confounder of the relationship between body fat measures and cancer risk in men but not women.

Our results suggest that central body fat as measured by WC (or WHtR) may be a stronger risk factor for obesity-related cancer for men than it is for women. In these analyses, colon cancer was the predominant obesity-related cancer in men and since previous analyses have shown WC to be a stronger risk factor for colon cancer than BMI, it is not surprising that waist-related measures conveyed larger risk in men than in women.[18] The increased risks of obesity-related cancers were very similar for WC and WHtR. Since the two measures are strongly correlated (r=0.93) and the predictive values were similar, the results suggest that WHtR is not a superior measure. The relation between waist and hip-related measures and cancer risk was approximately J-shaped for men. We explored the possibility that reverse causality might be responsible for the excess cancer risk among the leanest subjects, first by excluding those with prevalent diabetes, alcoholism, and other chronic diseases. We also explored the impact of excluding all cancer cases occurring within 6 years of the measurement of body fat. None of these exploratory analyses explained the higher cancer

rates in the leanest subjects. Finally, we stratified by smoking and found that the excess cancer risk among those in the lowest quintiles of body fat was not different for smokers and non-smokers (even after accounting for past smoking and amount smoked). Confounding by unknown or unmeasured factors cannot be ruled out.

These analyses support existing published epidemiologic data showing that obesity is an important risk factor for a cluster of cancers. In this study, a set of pre-defined obesity-related cancers identified from published literature were included.[1,2,19] These results also support earlier studies examining the effects of obesity on incident obesity-related cancer in the original Framingham Heart Study cohort.[20] In that study, we found a 1.9 – 2.0-fold increased risk of obesity-related cancers among overweight and obese men. In the younger cohort Health Professional Follow-up Study (HPFS), obese men (BMI ≥30 kg/m^2) were also found to have a 90% increased risk of obesity-related cancers (colorectal, pancreatic, and esophageal cancers) while overweight men (BMI between 25–29.9 kg/m^2) had only 24–36% increased risk.[21] Our study is also in accordance with results from the Million Women Study which found higher risks of many individual obesity-related cancers in obese women but not among women with a BMI of 22.5–24.9 kg/m^2.[22] Notably, they found no association between BMI and colorectal cancer. In previous Framingham analyses, WC was a stronger risk factor for colon cancer than BMI among men; in addition, obesity-related effects were weaker in women than men.[18] Since BMI has been linked with colon cancer in a number of earlier studies, it is possible that the absence of an effect in the Million Women Study could be attributable to widespread colon cancer screening programs (with concurrent removal of colon polyps) in recent years. It is also possible that obese individuals may be targeted for more intense screening and removal of pre-cancerous adenomas.

Adjusting for HC in these analyses strengthened the effect of WHtR and WC in men but attenuated the effects in women. We controlled for HC here since a larger HC has been used as a surrogate measure for a larger fat distribution around the gluteofemoral area. Fat in the gluteofemoral depot has been shown to be protective against cardiometabolic risk and inversely associated with levels of inflammatory cytokines which have been associated with carcinogenesis.[23] In the current analyses, it is possible that the attenuation of the effects of WC and WHtR in women when HC was added to the model was a result of higher correlations between HC and waist measures in women (r=0.79 and r=0.75, for WC and WHtR, respectively) than in men (r=0.72 and r=0.69, respectively).

One unique contribution of these results is the finding in men that a lower HC was a strong risk factor for obesity-related cancer. The few studies that have examined the association of HC, and specific incident cancers have found increased risk of higher HC and postmenopausal breast cancer[9,24,25], thyroid and colon cancer in men[26,27] and, recently, endometrial cancer[28,29]. None of these studies adjusted for WC. However, several studies have concluded that HC is inversely associated with cardiovascular disease or diabetes risk after controlling for WC.[6,30] The current results support the idea that the phenotype characterized by a larger WC and a smaller HC may be an important risk factor for obesity-related cancer risk among men.

Relative to HC alone, it has been more common for WC and HC to be treated as a ratio, which is a more complex measure. Since WC and HC have each been independently associated with some chronic diseases and with opposing effects (a larger WC being a risk factor and larger HC generally protective), controlling one for the other may yield a less cumbersome interpretation than when using their ratio. Therefore, in contrast to previous studies, this was our approach.

The mechanism by which obesity promotes cancer risk may be linked with the role of adipose tissue in the promotion of chronic, low-grade inflammation.[31] Excess adiposity increases insulin and estrogen levels as well as other pro-inflammatory factors influencing immune function and creating a tumor-promoting microenvironment.[32,33,34] Within the central body fat compartment, visceral fat (which constitutes about 15% of total fat mass [35,36] is generally considered to be more metabolically active and pro-inflammatory relative to abdominal subcutaneous fat, which is greater in volume.[37] Both have been shown to be associated with cardiometabolic risk.[37,38,39] In this study, BMI, WHtR, and WC were all strongly associated with obesity-related cancer in men, especially after adjusting for HC. Since men more readily distribute excess body fat in the abdominal and visceral regions, this may lead to higher obesity-related cancer risks in men than in women, particularly for these anthropometric measures of central body fat. In women, BMI (especially when controlling for WC) was more strongly associated with obesity-related cancer than were waist-related measures, perhaps suggesting that overall body mass is an important risk factor in women than is fat distribution.

Important strengths of this study include its prospective design and the carefully-collected and updated ascertainment of incident cancers. Another important strength of this study is the standardized assessment of the anthropometric measures of body fat every four years compared with some studies that have relied on self-report.

There are also some limitations to this study. First of all, there is no direct measure of visceral adiposity and WC and HC were not measured at every exam. The small number of identified obesity-related cancer cases also limited the statistical power for these analyses. Despite these limitations, our findings contribute to the understanding of sex-specific differences in the role of body fat in the development of obesity-related cancers.

In sum, BMI was a reasonable predictor of obesity-related cancer risk in both men and women. Specifically, cancer risk among women increased with a BMI of approximately 26 kg/m^2 and higher and among men, of 28 kg/m^2 and higher Waist and hip circumference measures were important markers of obesity-related cancer risk, particularly in men. Those men with a larger WC and smaller HC were at higher risk for developing obesity-related cancers. Future studies of the impact of waist size or BMI on cancer risk should control for HC in the multivariable models.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Baseline subject characteristics according to standard BMI categories

	Men			Women		
	BMI (kg/m^2)					
	18.5– <25	25– <30	≥30	18.5– <25	25– <30	≥30
Characteristics	n=401	n=969	n=446	n=968	n=632	n=402
	Mean (s.d.)			Mean (s.d.)		
BMI (kg/m^2)	23.3 (1.4)	27.4 (1.4)	33.4 (3.2)	22.4 (1.6)	27.1 (1.4)	35.2 (4.7)
Age (years)	52.3 (6.5)	52.2 (6.6)	51.4 (5.8)	51.1 (6.0)	52.2 (6.4)	52.6 (6.7)
WC (in.)	35.1 (2.5)	38.5 (2.4)	44.0 (3.7)	29.8 (3.0)	34.1 (3.3)	41.3 (5.0)
WHtR	0.51 (0.03)	0.56 (0.03)	0.64 (0.05)	0.47 (0.04)	0.54 (0.05)	0.65 (0.08)
HC (in.)	37.9 (1.8)	40.0 (1.9)	43.8 (3.0)	37.6 (2.2)	40.9 (2.4)	46.8 (4.3)
Height (in.)	69.3 (2.5)	68.9 (2.6)	69.0 (2.6)	63.8 (2.3)	63.4 (2.3)	63.4 (2.4)
Alcohol (g)	16.5 (19.9)	17.4 (22.1)	17.6 (25.2)	9.1 (13.1)	7.4 (12.9)	5.2 (10.1)
Cigarettes /day	7.6 (13.6)	6.0 (12.9)	5.8 (13.1)	5.1 (10.4)	5.5 (10.6)	4.2 (10.2)
Physical activity index	14.0 (9.9)	13.3 (9.0)	13.7 (10.3)	12.6 (7.3)	11.9 (8.0)	11.2 (7.1)
Glucose (mg/dL)	96.2 (22.5)	99.6 (24.6)	107.3 (33.5)	89.4 (12.4)	95.0 (22.1)	107.3 (38.4)
SBP (mmHg)	124.2 (17.0)	127.8 (16.1)	131.9 (15.1)	118.8 (16.8)	125.3 (17.5)	132.3 (18.2)
DBP (mmHg)	77.4 (9.8)	81.2 (9.1)	84.6 (8.8)	74.4 (9.3)	77.9 (9.4)	81.6 (9.8)
	Column Percent			Column Percent		
Education (> HS)	64.8%	66.1%	63.9%	61.5%	53.2%	48.0%
IFG or T2DM	30.4%	35.0%	50.7%	10.9%	24.4%	43.5%
T2DM	3.2%	5.7%	11.4%	1.1%	2.9%	12.2%
Dyslipidemia[a]	35.4%	54.2%	65.7%	26.8%	48.3%	67.4%
HBP[b]	27.2%	37.8%	57.6%	18.8%	29.9%	49.8%

BMI=body mass index, WC=waist circumference, WHtR=waist-to-height ratio, HC=hip circumference, SBP=systolic blood pressure, DBP=diastolic blood pressure, HS=high school, IFG=impaired fasting glucose (fasting glucose 100–125 mg/dL), T2DM=type 2 diabetes mellitus, HBP=high blood pressure

[a]Dyslipidemia = use of lipid-lowering medication, TG ≥150, or HDL <40 (men),<50 (women).

[b]High blood pressure identified using modified JNC-7 criteria.

Table 2.

Effect of adjusting for waist or hip circumferences on risk of obesity-related cancer according to quintiles of BMI

BMI Category	N	Range: BMI (kg/m^2)	Cases	I/1000 py	Model 1[a] HR (95%CI)	Model 2[b] HR (95%CI)	Model 3[c] HR (95%CI)
Men							
Quintile 1	375	18.53–24.83	24	4.22	1.08 (0.60–1.92)	1.11 (0.60–2.05)	1.04 (0.57–1.90)
Quintile 2 (Ref)	375	24.84–26.74	22	3.89	1.00	1.00	1.00
Quintile 3	377	26.75–28.35	20	3.38	0.87 (0.47–1.59)	0.84 (0.44–1.58)	0.87 (0.46–1.66)
Quintile 4	377	28.36–31.05	25	4.38	1.17 (0.66–2.08)	1.23 (0.65–2.31)	1.35 (0.72–2.51)
Quintile 5	376	31.06–52.98	29	5.33	1.55 (0.88–2.71)	1.81 (0.84–3.88)	2.25 (1.08–4.69)
Women							
Quintile 1	413	18.55–22.25	35	5.61	1.23 (0.75–2.02)	1.18 (0.70–1.97)	1.22 (0.73–2.04)
Quintile 2 (Ref)	412	22.26–24.25	29	4.56	1.00	1.00	1.00
Quintile 3	413	24.26–26.74	33	5.14	1.10 (0.67–1.82)	1.19 (0.71–1.99)	1.15 (0.69–1.93)
Quintile 4	414	26.75–30.33	45	7.30	1.59 (1.00–2.54)	1.80 (1.07–3.03)	1.67 (0.99–2.80)
Quintile 5	412	30.34–57.86	48	8.06	1.74 (1.09–2.77)	2.07 (1.06–4.07)	1.74 (0.88–3.43)

[a]Model 1: Adjusted for age, height, education, cigarettes/day, grams of alcohol intake, and physical activity.

[b]Model 2: model 1 plus WC

[c]Model 3: model 1 plus HC

Table 3.

Effect of waist circumference and waist-to-height ratio on risk of obesity-related cancer, after adjusting for hip circumference

	Waist Circumference			Waist-to-Height Ratio		
		Model 1[a]	Model 2[b]		Model 1[a]	Model 2[b]
WC Category	**WC (inches)**	**HR (95% CI)**	**HR (95% CI)**	**WHtRatio**	**HR[1] (95% CI)**	**HR[2] (95% CI)**
Men						
Quintile 1	28.0–35.9	1.60 (0.83, 3.09)	1.42 (0.72, 2.82)	0.401–0.517	1.73 (0.88, 3.39)	1.59 (0.79, 3.18)
Quintile 2 (Ref)	36.0–37.9	1.00	1.00	0.518–0.546	1.00	1.00
Quintile 3	38.0–39.7	0.80 (0.91, 1.90)	0.98 (0.47, 2.05)	0.547–0.574	1.11 (0.54, 2.28)	1.18 (0.57, 2.45)
Quintile 4	39.8–42.0	1.50 (0.78, 2.87)	1.76 (0.87, 3.53)	0.575–0.611	1.78 (0.91, 3.49)	2.01 (0.98, 4.11)
Quintile 5	42.1–59.8	2.25 (1.19, 2.23)	3.22 (1.39, 7.45)	0.612–0.858	2.24 (1.18, 4.25)	2.94 (1.27, 6.78)
Women						
Quintile 1	23.5–28.9	1.23 (0.75, 2.04)	1.31 (0.78, 2.19)	0.369–0.450	1.29 (0.78, 2.13)	1.36 (0.81, 2.29)
Quintile 2 (Ref)	29.0–31.0	1.00	1.00	0.451–0.491	1.00	1.00
Quintile 3	31.1–34.0	1.27 (0.77, 2.08)	1.21 (0.73, 2.01)	0.492–0.535	1.26 (0.75, 2.09)	1.20 (0.72, 2.02)
Quintile 4	34.1–37.9	1.53 (0.93, 2.52)	1.39 (0.81, 2.37)	0.536–0.594	1.25 (0.74, 2.10)	1.14 (0.66, 1.98)
Quintile 5	38.0–67.5	1.47 (0.90, 2.39)	1.17 (0.61, 2.27)	0.595–1.035	1.57 (0.95, 2.59)	1.25 (0.64, 2.46)

WC=waist circumference

[a]Model 1: Adjusted for age, height, education, cigarettes/day, grams of alcohol intake, and physical activity.

[b]Model 2: model 1 plus hip circumference.

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Table 4.

Effect of hip circumference on risk of obesity-related cancer adjusting for waist circumference

HC Quintiles	Range: HC (inches)	I/1000 py	Model 1[a] HR[1] (95% CI)	Model 2[b] HR[2] (95% CI)
Men				
Quintile 1	32.5–38.0	5.43	2.08 (1.05, 4.09)	2.45 (1.22, 4.94)
Quintile 2 (Ref)	38.1–39.4	2.94	1.00	1.00
Quintile 3	39.5–40.9	2.67	0.94 (0.42, 2.09)	0.83 (0.37, 1.87)
Quintile 4	41.0–42.9	5.13	1.80 (0.91, 3.57)	1.42 (0.68, 2.96)
Quintile 5	43.0–59.0	5.18	1.98 (0.98, 4.00)	1.17 (0.47, 2.94)
Women				
Quintile 1	31.5–36.9	5.46	1.12 (0.66, 1.90)	1.13 (0.66, 1.93)
Quintile 2 (Ref)	37.0–38.9	5.09	1.00	1.00
Quintile 3	39.0–40.9	6.19	1.23 (0.75, 2.02)	1.22 (0.74, 2.03)
Quintile 4	41.0–43.9	7.72	1.55 (0.96, 2.50)	1.52 (0.90, 2.57)
Quintile 5	44.0–65.5	7.01	1.42 (0.87, 2.32)	1.36 (0.69, 2.67)

HC=hip circumference

[a]Model 1: adjusts for age, height, education, cigarettes/day, grams of alcohol intake, and physical activity.

[b]Model 2: model 1 plus waist circumference