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Body Weight, Fat Distribution and Colorectal Cancer Risk: A Report from Cohort Studies of 134 255 Chinese Men and Women

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Abstract

OBJECTIVE—To evaluate the association of body size and fat distribution with risk of colorectal cancer (CRC) in Chinese men and women.

DESIGN—Population-based, prospective cohort study.

SUBJECTS—The analysis included 134 255 Chinese adults enrolled in the Shanghai Women's Health Study and the Shanghai Men's Health Study, with an average follow-up of 11.0 and 5.5 years, respectively.

MEASUREMENTS—Waist circumference (WC), body mass index (BMI) and waist-to-hip ratio (WHR) were measured by trained interviewers at baseline. Multivariable Cox models were used to calculate adjusted hazard ratios (HRs) for incident CRC.

RESULTS—A total of 935 incident CRC cases were identified. Both measures of general adiposity (measured by BMI) and central adiposity (measured by WHR and WC) were significantly associated with increased risk of colon cancer in men but not in women. Multivariable adjusted HRs for colon cancer in men in the highest compared with the lowest quintiles were 2.15 (95% CI: 1.35-3.43; *P* for trend = 0.0006) for BMI, 1.97 (95% CI: 1.19-3.24; *P* for trend = 0.0004) for WHR and 2.00 (95% CI: 1.21-3.29; *P* for trend = 0.0002) for WC. The BMI-associated risk was attenuated in analyses stratified by WHR, while the WHR-associated risk remained significant in the high BMI stratum (HR for comparison of extreme tertiles of WHR: 3.38, 95% CI: 1.47-7.75; *P* for trend = 0.0002). None of these anthropometric measures were significantly associated with rectal cancer.

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CONFLICT OF INTEREST

None of the authors had any financial conflicts of interest to declare.

CONCLUSION—Obesity, particularly central obesity, was associated with increased risk of colon cancer in men.

Keywords

Obesity; colorectal cancer; cohort study

INTRODUCTION

In 2008, it was estimated that about 1.24 million people were diagnosed with colorectal cancer (CRC) worldwide, accounting for 9.8% of all cancer incidence.(1) In urban Shanghai, China, the incidence rate of colon cancer over the past 3 decades has doubled in both men and women, while the increase in rectal cancer incidence has been much smaller (approximately 9%).(2, 3) Accompanying the rise of colon cancer is a parallel increase in the prevalence of obesity in this population.(4)

The International Agency for Research into Cancer has recently classified CRC as an obesity-related cancer (5) and the World Cancer Research Fund also considers evidence for greater body fatness as a cause of CRC to be convincing.(6) However, several recent systematic reviews and meta-analyses have shown significant heterogeneity in the body fatness and CRC association by sex. The association for men is generally stronger and more consistent than that for women.(7-11) The mechanisms underlying this sex difference, although not well understood, are thought to be related to sex steroid hormone exposures.(12) Moreover, although both general and central obesity have been associated with CRC risk, measures of central adiposity such as waist-to-hip ratio (WHR) and waist circumference (WC), have been shown to be better predictors of CRC risk in prospective cohort studies.(13-17) Most previous studies were conducted in Western societies, where overweight and obesity is highly prevalent,(16, 18-22) and were based on self-reported anthropometric measurements. Data from relatively lean populations and, more importantly, from studies with directly measured anthropometric variables are clearly needed to further our understanding of the association between obesity and CRC risk.

In the present analysis, we evaluated the association between measures of general and central adiposity and CRC risk in two large prospective cohorts - the Shanghai Women's Health Study (SWHS) and the Shanghai Men's Health Study (SMHS), both conducted in relatively lean Chinese populations with anthropometric measurements administered by trained interviewers at baseline.

MATERIALS AND METHODS

Study population

The SWHS and the SMHS are both population-based, prospective cohort studies conducted in urban Shanghai, China. Previous publications have described the designs and methods in detail for the SWHS (23) and the SMHS.(24) Briefly, the SWHS recruited 74 941 women aged 40-70 years from 1997 to 2000, with a participation rate of 92.33%.(23) The SMHS recruited 61 491 men aged 40-74 years from 2002 to 2006, with a participation rate of

73.99%.(24) For both cohorts, trained interviewers administered in-person interviews at baseline, using a structured questionnaire, to collect information on demographic characteristics, diet, physical activity, personal habits, family cancer history, reproductive history and hormone use (for the SWHS only) and other characteristics. Both studies were approved by the Institutional Review Boards of the Shanghai Cancer Institute and Vanderbilt University, and all participants provided written informed consent before the in-person interview.

Anthropometry

Anthropometric measurements, including weight, circumferences of waist and hips and standing and sitting heights, were taken at baseline by trained interviewers who were retired medical professionals.(25) Each participant wore light clothing during the measurement. All measurements were taken twice with tolerance limits of 1 kg for weight measurement and 1 cm for measurements of height and circumferences of the waist and hips. If the measurements were greater than the tolerance limits, a third measurement was taken. The average of the two closest measurements was used in the analysis. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

In the SWHS, information on self-reported weight and height at age 20 years for all participants and weight at age 50 years for women aged over 50 years at baseline were collected; in the SMHS, self-reported weight at age 20 and 40 years were obtained. In the present study, weight change was defined as the difference between weight at baseline and the recalled weight at age 20. BMI at age 20 was calculated using recalled weight and recalled height. BMI at age 50 for women and at age 40 for men were calculated using recalled weight and measured height at baseline.

Case identification

Incident CRC cases were identified through a combination of annual record linkage with the Shanghai Cancer Registry and the Shanghai Vital Statistics databases and active follow-up surveys conducted every 2-3 years. For the SWHS, the in-person follow-up rates were 99.8% for the first (2000–2002), 98.7% for the second (2002–2004), 96.7% for the third (2004–2007) and 92.0% for the fourth (2007-2011) surveys. For the SMHS, the in-person follow-up response rates were 97.6% for the first (2004–2008) and 93.6% for the second (2008-2011) surveys. For the incident cancer cases identified through record linkages, all possible matches were verified by home visits. Medical charts from the diagnostic hospital were reviewed for diagnosis confirmation. The present study included all incident CRC cases diagnosed between the date of baseline enrollment and December 31, 2009.

Statistical analysis

For the present analyses, we excluded individuals with a prior history of cancer (SWHS, n=1 579; SMHS, n=0, as having a history of cancer was part of the exclusion criteria for participation in the SMHS); self-reported cases whose diagnosis of cancer could not be confirmed (SWHS, n=265, including 12 CRC cases; SMHS, n=174, including 7 CRC cases) and individuals who reported implausible total energy intake (<500 or >3 500 kcal/d in the

SWHS [n=125]; <500 or >4 500 kcal/d in the SMHS [n=34]). The resulting cohort populations used in this analysis consist of 72 972 women and 61 283 men (134 255 adults).

A Cox regression model was used, with age as the time scale, to compute hazard ratios (HR) and 95% confidence intervals (CI) of developing CRC associated with anthropometric measurements and to adjust for potential confounders. Entry time was defined as age at enrollment and exit time was defined as age at CRC diagnosis or censoring (either December 31, 2009 or date of death), whichever came first. All anthropometric measurements were categorized into quintiles based on distributions of these measurements in each entire cohort, with the lowest quintile serving as the reference, and also analyzed as continuous variables to evaluate linear trends.

Potential confounding variables chosen based on *a priori* considerations (26) included age at baseline (continuous), education (4 categories: elementary school or less, junior high, high school and professional education or above), income (3 categories: low, middle and high), cigarette use (yes or no, for the SWHS only), pack-years of cigarette use (continuous, for the SMHS only), tea consumption (yes or no), alcohol consumption (yes or no), physical activity (measured by metabolic equivalent task hours per week per year, continuous), family history of CRC (yes or no), menopausal status (yes or no, for the SWHS only) and intakes (continuous) of total energy, red meat, fruits and vegetables. Associations of colon and rectal cancers with most of these covariates, such as age, education, household income, family history of CRC, tea consumption, cigarette smoking, intake of fruits and vegetables, were statistically significant or of borderline significance in this study (data not shown). Since diabetes is likely an intermediate condition in the causal pathway between obesity and colon cancer, we did not include this variable in the primary model. To address the potential influence of pre-diagnosed disease on the risk estimates, we conducted sensitivity analyses by excluding the first year of observation and CRC cases diagnosed during the same time period. All analyses were conducted using SAS, version 9.2, software (SAS Institute, Inc., Cary, North Carolina). All statistical tests were based on two-sided probability.

RESULTS

The mean age (s.d.) at baseline was 52.5 years (9.1) in the SWHS and 55.4 (9.7) in the SMHS. For women, the means for BMI and WHR were 24.0 (3.4) and 0.81 (0.05), respectively; for men, the means for BMI and WHR were 23.7 (3.1) and 0.90 (0.06), respectively. Baseline characteristics of these two study populations according to quintiles of BMI and WHR are presented in Table 1. In general, both women and men with a higher BMI or WHR were older and were more likely to have a prior history of diabetes and higher intake of total energy. Cigarette use was associated with lower BMI for men but higher WHR for both men and women. Women with a higher BMI or WHR were also more likely to participate in exercise; in contrast, their male counterparts were less likely to engage in exercise.

A total of 935 incident CRC cases were identified. In the SWHS, 622 incident CRC cases were identified during an average follow-up of 11.0 years, including 382 cases of colon cancer and 240 cases of rectal cancer. In the SMHS, 313 incident CRC cases were identified

during an average follow-up of 5.5 years, including 180 cases of colon cancer and 133 cases of rectal cancer. Overall, among women, neither BMI nor WHR were associated with risk of colon cancer, rectal cancer or both cancers combined (Table 2). Compared with women in the lowest quintile of BMI at baseline, women in the highest quintile had a multivariable HR for CRC of 1.08 (95% CI: 0.82-1.43; P for trend=0.75). For WHR, the corresponding HR was 1.01 (95% CI: 0.79-1.31; P for trend=0.65). Similar results were also observed for other anthropometric measurements, including BMI at age 20, BMI at age 50, baseline waist circumference and weight gain since age 20 and when BMI at baseline was categorized according to WHO criteria.

However, among men, positive associations between obesity-related measurements and risk of colon cancer were observed (Table 3). Multivariable HRs for the comparison of extreme quintiles were 2.15 (95% CI: 1.35-3.43), 1.97 (95% CI: 1.19 - 3.24) and 2.00 (95% CI: 1.21 - 3.29), respectively, for BMI, WHR and WC. Tests for linear trend were highly significant (P for trend<0.001 for all). Similar results were observed when BMI at baseline was categorized according to WHO criteria. A positive association was also found for BMI at age 40 (corresponding HR = 2.01, 95% CI: 1.24-3.24, P for trend = 0.0005). The multivariable HR for per s.d. increase (3.1 kg/m²) in BMI was 1.30 (95% CI: 1.12-1.50, P = 0.004); the HR for per s.d. increase (0.06) in WHR was 1.33 (95% CI: 1.15-1.54, P =0.0002); and the HR for per s.d. increase (8.7 cm) in WC was 1.32 (95% CI: 1.14-1.52, P =0.0002) (data not shown in tables). The sex-differences in BMI- and WHR-associated risk estimates for colon cancer were statistically significant (P for heterogeneity = 0.04 and 0.006, respectively, derived from the fully adjusted model with a multiplicative interaction term of gender and obesity) and of borderline significance for WC (P for heterogeneity = 0.07). In contrast, none of the anthropometric measurements studied were statistically associated with risk of rectal cancer in men, although the P for heterogeneity in BMI-, WHR-, and WC-associated risk of colon versus rectal cancer were statistically insignificant.

BMI and WHR were moderately correlated (Pearson r = 0.57). Further analysis showed that the BMI-associated risk in men was attenuated in analyses stratified by WHR, whereas the positive association between WHR and colon cancer risk remained significant for the high BMI stratum (HR for comparison of extreme tertiles of WHR: 3.38, 95% CI: 1.47-7.75; P for trend =0.0002) (Table 4).

We found no evidence that associations of BMI, WHR or WC and CRC risk varied significantly by age at baseline or age at menopause (for the SWHS only), nor did the associations significantly differ by lifestyle factors such as physical activity or intake of fruits and vegetables (data not shown). We also conducted analyses excluding the first year of follow-up and CRC cases that occurred within that time period (36 in the SWHS and 47 in the SMHS). Results were similar to those observed for the entire study population (data not shown). Additional sensitivity analyses stratified by the follow-up period of the SWHS (the first 5.5 years versus the second 5.5 years) were conducted. There were no differences in the associations of CRC and anthropometric measurements by number of follow-up years (data not shown).

DISCUSSION

Although CRC has been classified as an obesity-related cancer,(5) significant heterogeneity in the obesity and CRC association by cancer site and sex was suggested in this analysis of two large prospective cohort studies in China. We found that high BMI, WHR and WC were associated with increased risk of colon cancer in men but not in women. None of these anthropometric measurements were significantly associated with risk of rectal cancer. It is worth noting that unlike previous studies, most of which were conducted in Western populations, our study was conducted in a generally lean population of Chinese women and men, with a mean BMI of 24.0 kg/m².

Adipose tissue is an endocrine organ responsible for the secretion of the adipokines that play a role in energy balance, inflammation, insulin sensitivity and angiogenesis.(27)

Accumulation of adipose tissue, visceral adiposity in particular, confers an excess risk of insulin resistance.(28) Both insulin and insulin-like growth factor 1 are important determinants of cell proliferation and apoptosis and thus may promote carcinogenesis.(29, 30) Markers of insulin resistance have been associated with elevated risk of CRC.(31)

Excess secretion of cytokines from adipose tissues can induce a chronic pro-inflammatory response, (32) possibly promoting colorectal carcinogenesis.(33)

BMI, a measure of general adiposity, has been used as the primary measure of body fatness in most previous cohort studies of CRC.(13-22, 34, 35) A positive association between BMI and CRC risk has been found in many, but not all, previous studies.(14-22, 35) In our study, men in the highest quintile of BMI had an over 2-fold increase in risk of colon cancer compared with the lowest quintile. An important limitation of BMI in measurement of overall body fatness is that this measure is unable to distinguish fat mass and non-fat mass, in particular among elderly people. On the other hand, WHR and WC, measures of central adiposity, are less affected by loss of muscle mass during aging and represent a measure of adiposity that takes into account of the accumulation of abdominal fat.(36) Among middle-aged and elderly adults, accumulation of visceral fat is a stronger determinant of insulin resistance and hyperinsulinemia than general fat.(37, 38) Previous epidemiological studies have shown that CRC risk is more strongly related to WC or WHR than to BMI, although results are not entirely consistent.(13-16) In the present study, both measures for overall obesity (BMI) and central obesity (WHR or WC) were positively associated with colon cancer risk in men. However, the BMI-associated risk among men was attenuated and not statistically significant in analyses stratified by WHR, whereas the positive association between WHR and colon cancer risk remained significant in the high BMI stratum.

Our finding of a positive association between obesity and CRC risk in men but not in women is generally in agreement with previous observations.(13, 15-18, 20, 21, 34, 35) As summarized in a meta-analysis of prospective observational studies,(39) the elevated risk of CRC with increasing BMI is more pronounced in men than in women. The association of obesity with CRC in women is complicated by estrogen exposure. On the one hand, adipose tissue is the primary source of endogenous estrogen production among postmenopausal women.(40) Estrogen supplement use among postmenopausal women has been associated with reduced risk of CRC.(15) On the other hand, accumulation of adipose tissue results in

insulin resistance and inflammation, which is positively related to CRC risk. It has been suggested that menopausal status (21) and hormonal replacement therapy (HRT) (15, 41) may modify the association of body fatness and CRC. However, we found no association of obesity measurements with CRC risk in either pre- or postmenopausal women. Only about 2% of SWHS participants reported having ever used HRT, (23) which hindered our assessment of potential effect modification by HRT. We can only speculate that among these relatively lean Chinese women, detrimental effects related to adipose tissue could be offset by its estrogenic effect. This hypothesis needs further evaluation.

We found that the association of adiposity with CRC differed by anatomic site. WHR and BMI were positively associated with risk of colon cancer but not rectal cancer, which is consistent with most previous reports,(14-16, 18, 39) suggesting that this risk factor does not contribute equally to colon and rectal cancers. The potential mechanisms driving this observation need further research.

Several limitations of our study should be considered when interpreting the results. Pre-clinical disease could influence weight and thus anthropometrics. However, sensitivity analyses conducted by excluding CRC cases occurring in the first year of follow-up showed no material changes in the risk estimates for CRC. In addition, despite having carefully adjusted for a range of potential confounding variables, including known risk factors for CRC and other lifestyle factors, we could not completely rule out the possibility of residual confounding due to unmeasured or inaccurately measured covariates. Changes in weight during the course of follow-up are likely. Failure to take weight change into consideration could attenuate the estimated association between obesity measurements and CRC risk, particularly in the SWHS. However, we did not find that the association of CRC risk and anthropometric measurements significantly differed by number of follow-up years in a stratified analysis in the SWHS. On the other hand, the short interval between anthropometric measurements and CRC events in the SMHS may have reduced the effect of fluctuations in body weight and fat distribution over time on the disease association. However, this raises another concern about the effect of subclinical illness on the results. In a sensitivity analysis, we omitted the first year of follow-up and excluded events occurring during the same time period from the analysis to minimize the potential bias. These exclusions did not significantly alter the results in either cohort.

In summary, our finding from these two large prospective studies confirms a positive association between obesity and colon cancer in men. Furthermore, our study suggests that central obesity plays a more important role in colon carcinogenesis than does general obesity. Potential differences in the obesity and colorectal cancer association by sex and anatomic site (colon versus rectum) warrant further investigation.

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Table 1
Baseline characteristics by BMI and WHR quintile in SWHS and SMHS1

Variable	Quintile category ²					P
	Q1	Q2	Q3	Q4	Q5	
	BMI					
N	14 429	14 568	14 650	14 685	14 617	
	Women					
	Men					
Age (years) ³	50.1±8.7	50.7±8.6	52.0±8.8	53.8±8.9	56.0±8.9	<0.0001
	Women					
	Men					
Total energy intake (kcal day ⁻¹) ⁴	1 631.3±3.3	1 656.3±3.3	1 673.1±3.2	1 689.0±3.2	1 718.9±3.3	<0.0001
	Women					
	Men					
Physical activity ^{4,5}	103.7±0.4	105.2±0.4	107.1±0.4	107.9±0.4	108.8±0.4	<0.0001
	Women					
	Men					
Education, high school and above (%)	48.6	46.8	42.9	38.5	30.5	<0.0001
	Women					
	Men					
Ever smoke (%)	3.5	2.3	2.4	2.6	3.3	0.8
	Women					
	Men					
Ever drink (%)	2.2	2.4	2.3	2.4	2.1	0.7
	Women					
	Men					
Diabetes (%)	3.3	3.8	4.0	4.6	5.9	<0.0001
	Women					
	Men					
Family history of colorectal cancer (%)	4.3	6.3	6.8	6.3	7.5	<0.0001
	Women					
	Men					
	1.9	2.2	2.2	2.2	2.0	0.001
	Women					
	Men					
	13 754	10 358	16 420	14 668	17 751	
N						
	Women					
	Men					
Age (years) ³	49.3±8.0	50.2±8.3	51.6±8.6	53.2±9.0	56.6±9.1	<0.0001
	Women					
	Men					
Total energy intake (kcal day ⁻¹) ⁴	1 661.0±3.4	1 662.9±3.9	1 669.4±3.1	1 680.2±3.2	1 689.0±3.0	<0.0001
	Women					
	Men					
Physical activity ^{4,5}	106.2±0.4	104.7±0.4	106.6±0.4	107.5±0.4	107.2±0.4	<0.0001
	Women					
	Men					

Variable	Quintile category ²					P	
	Q1	Q2	Q3	Q4	Q5		
	Men	62.1±0.3	60.9±0.3	60.2±0.3	59.4±0.3	56.4±0.3	<0.0001
Education, high school and above (%)	Women	48.9	46.7	43.3	39.2	32.8	<0.0001
	Men	58.2	60.9	61.2	60.3	58.1	0.3
Ever smoke (%)	Women	2.8	2.4	2.4	2.5	3.4	0.0001
	Men	69.4	67.9	68.1	69.4	73.1	<0.0001
Ever drink (%)	Women	2.1	2.1	2.2	2.4	2.3	0.02
	Men	30.1	32.0	33.3	35.0	37.2	<0.0001
Diabetes (%)	Women	1.8	2.6	3.4	4.3	7.2	<0.0001
	Men	3.6	5.2	6.2	6.6	9.6	<0.0001
Family history of colorectal cancer (%)	Women	2.2	2.2	2.2	2.3	2.2	1.0
	Men	2.1	2.1	2.1	2.1	2.2	0.4

¹ All variables (except age) were standardized to the age distribution at baseline. The general linear model for continuous variables and Cochran-Mantel-Haenszel statistics for categorical variables were used.

² Quintile cutoffs for BMI: 21.10, 22.88, 24.55 and 26.70 in the SWHS; 21.13, 22.93, 24.43, and 26.19 in the SMHS. Quintile cutoffs for WHR: 0.77, 0.78, 0.81, and 0.84 in the SWHS; 0.85, 0.88, 0.90, and 0.94 in the SMHS.

³ Values are mean±s.d.

⁴ Values are mean±s.e.

⁵ Measured by metabolic equivalent task hours per week per year (MET-h.wk⁻¹.y⁻¹).

Table 2
Hazard ratios (HR) and 95% confidence intervals (CI) of colorectal cancer associated with anthropometric measurements in women, the Shanghai Women's Health Study (1997 – 2009)¹

	Colorectal cancer			Colon cancer			Rectal cancer		
	Person years	No. of cases	HR ² 95% CI	No. of cases	HR ² 95% CI	No. of cases	HR ² 95% CI	No. of cases	HR ² 95% CI
BMI at baseline, kg/m ² , n=72 949									
<21.10	159 042	85	1.00	52	1.00	33	1.00	33	1.00
21.10-22.88	161 165	116	1.27 0.96-1.68	63	1.10 0.76-1.58	53	1.55 1.00-2.39	53	1.55 1.00-2.39
22.89-24.55	161 608	129	1.27 0.97-1.68	88	1.36 0.96-1.92	41	1.11 0.70-1.76	41	1.11 0.70-1.76
24.56-26.70	161 146	150	1.31 1.00-1.72	92	1.23 0.87-1.74	58	1.44 0.93-2.23	58	1.44 0.93-2.23
26.71	158 939	141	1.08 0.82-1.43	86	1.00 0.70-1.43	55	1.22 0.78-1.90	55	1.22 0.78-1.90
<i>P</i> for trend			0.75		0.97		0.64		0.64
BMI at baseline, kg/m ² , n=72 949									
<25	520 838	362	1.00	222	1.00	140	1.00	140	1.00
25-29.99	240 835	222	1.02 0.86-1.21	138	0.99 0.79-1.23	84	1.07 0.81-1.41	84	1.07 0.81-1.41
30	40 226	37	0.89 0.63-1.25	21	0.78 0.50-1.23	16	1.07 0.63-1.81	16	1.07 0.63-1.81
<i>P</i> for trend			0.73		0.43		0.66		0.66
BMI at age 20, kg/m ² , n=62 236									
<17.54	137 763	83	1.00	50	1.00	33	1.00	33	1.00
17.54-18.72	134 841	89	1.03 0.77-1.39	53	1.01 0.69-1.49	36	1.06 0.66-1.71	36	1.06 0.66-1.71
18.73-19.99	141 323	109	1.17 0.88-1.55	69	1.21 0.84-1.74	40	1.10 0.69-1.74	40	1.10 0.69-1.74
20.00-21.62	136 215	94	0.99 0.73-1.33	62	1.06 0.73-1.55	32	0.87 0.53-1.42	32	0.87 0.53-1.42
21.63	138 789	107	1.08 0.81-1.44	64	1.06 0.73-1.54	43	1.11 0.70-1.75	43	1.11 0.70-1.75
<i>P</i> for trend			0.77		0.75		0.96		0.96
BMI at age 50, kg/m ² , n=33 169									
<20.70	72 814	76	1.00	49	1.00	27	1.00	27	1.00
20.70-22.45	72 561	96	1.29 0.95-1.74	60	1.24 0.85-1.82	36	1.37 0.83-2.25	36	1.37 0.83-2.25
22.46-24.11	72 553	76	1.04 0.75-1.43	50	1.06 0.71-1.57	26	1.00 0.58-1.72	26	1.00 0.58-1.72
24.12-26.21	72 263	99	1.33 0.99-1.80	67	1.40 0.96-2.02	32	1.22 0.73-2.04	32	1.22 0.73-2.04
26.22	71 175	89	1.19 0.87-1.63	56	1.18 0.80-1.74	33	1.2 0.72-2.03	33	1.2 0.72-2.03

	Colorectal cancer			Colon cancer			Rectal cancer		
	Person years	No. of cases	HR ² 95% CI	No. of cases	HR ² 95% CI	No. of cases	HR ² 95% CI	No. of cases	HR ² 95% CI
<i>P</i> for trend			0.29		0.31		0.70		
WHR, n=72 951									
<0.77	152 133	92	1.00	53	1.00	39	1.00		
0.77-0.78	114 519	60	0.81	37	0.85	23	0.75		0.45-1.26
0.79-0.81	181 223	144	1.08	92	1.15	52	0.98		0.65-1.49
0.82-0.84	161 491	126	0.95	81	1.00	45	0.88		0.57-1.36
0.85	192 549	199	1.01	118	0.96	81	1.11		0.74-1.66
<i>P</i> for trend			0.65		0.92		0.40		
WC, cm, n=72 962									
<70	131 037	60	1.00	33	1.00	27	1.00		
70-74	177 641	108	1.21	64	1.27	44	1.13		0.70-1.82
75-79	171 313	148	1.46	91	1.55	57	1.36		0.86-2.17
80-84	153 372	124	1.15	78	1.21	46	1.07		0.66-1.75
85	168 677	182	1.26	116	1.34	66	1.17		0.73-1.88
<i>P</i> for trend			0.43		0.46		0.73		
Weight gain since age 20, kg, n=65 440									
<2.5	140 530	90	1.00	58	1.00	32	1.00		
2.5-7.9	146 339	113	1.31	67	1.21	46	1.50		0.95-2.36
8.0-11.9	136 116	84	1.06	57	1.11	27	0.96		0.58-1.61
12.0-16.9	143 611	114	1.31	71	1.25	43	1.43		0.90-2.26
17.0	156 350	123	1.16	68	0.96	55	1.54		0.99-2.39
<i>P</i> for trend			0.39		0.83		0.11		

¹ All anthropometric measurements were categorized into quintiles, except for BMI at baseline, for which categories were defined by both quintile cutoffs and WHO criteria.

² Multivariable HRs were adjusted for age at baseline, education, income, cigarette use, alcohol consumption, tea consumption, physical activity, family history of colorectal cancer, menopausal status and intakes of total energy, red meat, fruits and vegetables.

Table 3
Hazard ratios (HR) and 95% confidence intervals (CI) of colorectal cancer associated with anthropometric measurements in men, the Shanghai Men's Health Study (2002-2009)¹

	Person years	No. of cases	Colorectal cancer			Colon cancer			Rectal cancer		
			HR ²	95%CI	No. of cases	HR ²	95% CI	No. of cases	HR ²	95% CI	
BMI at baseline, kg/m ² , n=61 248											
<21.13	66 812	47	1.00		25	1.00		22	1.00		
21.14-22.93	67 482	58	1.18	0.80-1.73	30	1.14	0.67-1.94	28	1.22	0.70-2.14	
22.94-24.43	67 328	54	1.06	0.72-1.58	29	1.06	0.62-1.82	25	1.07	0.60-1.90	
24.44-26.19	67 168	61	1.20	0.82-1.76	33	1.21	0.72-2.04	28	1.18	0.67-2.07	
26.20	67 040	93	1.71	1.20-2.44	63	2.15	1.35-3.43	30	1.20	0.69-2.10	
<i>P</i> for trend			0.003			0.0006			0.61		
BMI at baseline, kg/m ² , n=61 248											
<25	224 834	185	1.00		96	1.00		89	1.00		
25-29.99	102 540	114	1.25	0.99-1.58	77	1.61	1.19-2.18	37	0.85	0.57-1.24	
30	8 457	14	1.74	1.01-3.01	7	1.66	0.77-3.59	7	1.84	0.85-3.99	
<i>P</i> for trend			0.014			0.0021			0.88		
BMI at age 20, kg/m ² , n=52 894											
<17.93	57 266	41	1.00		21	1.00		20	1.00		
17.93-19.02	59 105	41	0.96	0.62-1.48	25	1.14	0.64-2.04	16	0.77	0.40-1.49	
19.03-19.89	57 163	47	1.08	0.71-1.64	23	1.02	0.57-1.85	24	1.14	0.63-2.06	
19.90-21.00	57 129	55	1.19	0.79-1.79	35	1.46	0.85-2.51	20	0.91	0.49-1.69	
21.01	60 376	65	1.21	0.81-1.79	39	1.38	0.81-2.36	26	1.02	0.57-1.84	
<i>P</i> for trend			0.19			0.14			0.78		
BMI at age 40, kg/m ² , n=57 130											
<20.05	63 206	53	1.00		28	1.00		25	1.00		
20.05-21.46	61 390	47	0.93	0.62-1.37	25	0.94	0.55-1.61	22	0.91	0.51-1.62	
21.47-22.81	63 685	45	0.88	0.59-1.30	26	0.96	0.56-1.64	19	0.78	0.43-1.41	
22.82-24.50	63 542	63	1.32	0.91-1.91	38	1.53	0.94-2.50	25	1.09	0.62-1.90	
24.51	62 559	69	1.61	1.12-2.31	44	2.01	1.24-3.24	25	1.18	0.67-2.07	

	Person years	Colorectal cancer			Colon cancer			Rectal cancer		
		No. of cases	HR ²	95%CI	No. of cases	HR ²	95% CI	No. of cases	HR ²	95% CI
<i>P</i> for trend			0.002			0.0005				0.45
WHR, n=61 217										
<0.85	55 577	38	1.00		21	1.00		17	1.00	
0.85-0.88	74 530	52	1.00	0.66-1.52	27	0.94	0.53-1.67	25	1.07	0.58-1.98
0.89-0.90	51 955	41	1.14	0.74-1.78	23	1.17	0.65-2.12	18	1.11	0.57-2.15
0.91-0.94	85 306	91	1.51	1.03-2.21	49	1.49	0.89-2.49	42	1.53	0.87-2.70
0.95	68 301	91	1.65	1.12-2.41	60	1.97	1.19-3.24	31	1.24	0.69-2.26
<i>P</i> for trend			0.0004			0.0004				0.20
WC, cm, n=61 240										
<78	65 104	47	1.00		21	1.00		26	1.00	
78-82	61 822	38	0.82	0.53-1.26	19	0.91	0.49-1.70	19	0.74	0.41-1.34
83-86	65 073	53	1.04	0.70-1.54	30	1.31	0.75-2.30	23	0.82	0.47-1.44
87-91	70 828	80	1.38	0.96-1.98	48	1.84	1.10-3.08	32	1.01	0.60-1.70
92	72 966	95	1.38	0.97-1.97	62	2.00	1.21-3.29	33	0.88	0.52-1.49
<i>P</i> for trend			0.004			0.0002				0.95
Weight gain since age 20, kg, n=54 049										
<3.7	58 773	55	1.00		28	1.00		27	1.00	
3.7-9.4	59 616	43	0.83	0.56-1.24	24	0.92	0.53-1.59	19	0.75	0.41-1.34
9.5-13.9	56 205	45	0.99	0.67-1.470	22	0.96	0.55-1.68	23	1.02	0.58-1.78
14.0-19.4	61 868	54	1.11	0.76-1.62	36	1.48	0.90-2.43	18	0.73	0.40-1.34
19.5	60 936	62	1.33	0.92-1.92	37	1.60	0.97-2.64	25	1.06	0.61-1.83
<i>P</i> for trend			0.05			0.01				0.90

¹ All anthropometric measurements were categorized into quintiles, except for BMI at baseline, for which categories were defined by both quintile cutoffs and WHO criteria.

² Multivariable HRs were adjusted for age at baseline, education, income, pack-years of cigarette use, tea consumption, alcohol consumption, physical activity, family history of colorectal cancer and intakes of total energy, red meat, fruits and vegetables.

Table 4
Stratified analysis of BMI, WHR and colorectal cancer risk, the Shanghai Men's Health Study (2002-2009)

	Colorectal cancer				Rectal Cancer					
	Person years	No. of cases	HR ¹	95%CI	No. of cases	HR ¹	95%CI	No. of cases	HR ¹	95%CI
WHR 0.90 (median), n=32 908										
BMI Tertile ²	89 162	65	1.00		33	1.00		32	1.00	
Tertile 2	60 134	41	0.9	0.60-1.34	20	0.85	0.48-1.51	21	0.95	0.54-1.65
Tertile 3	32 963	25	0.89	0.55-1.44	18	1.34	0.74-2.44	7	0.45	0.19-1.09
P for trend			0.57			0.47			0.11	
WHR>0.90, n=28 340										
BMI Tertile ²	22 555	21	1.00		11	1.00		10	1.00	
Tertile 2	52 043	54	1.07	0.64-1.77	30	1.09	0.55-2.19	24	1.03	0.49-2.16
Tertile 3	78 974	107	1.33	0.83-2.14	68	1.57	0.83-2.99	39	1.04	0.52-2.11
P for trend			0.13			0.07			0.9	
BMI >23.67 (median), n=30 713										
WHR Tertile ²	82 733	60	1.00		32	1.00		28	1.00	
Tertile 2	50 871	37	0.94	0.62-1.42	22	1.02	0.58-1.78	15	0.86	0.46-1.61
Tertile 3	34 828	33	1.13	0.74-1.73	16	1.03	0.57-1.89	17	1.24	0.68-2.28
P for trend			0.66			0.92			0.58	
BMI>23.67, n=30 504										
WHR Tertile ²	23 668	12	1.00		6	1.00		6	1.00	
Tertile 2	49 744	43	1.62	0.85-3.09	23	1.69	0.68-4.21	20	1.53	0.61-3.83
Tertile 3	93 825	128	2.59	1.43-4.69	81	3.38	1.47-7.75	47	1.81	0.77-4.26
P for trend			0.0001			0.0002			0.16	

¹ Multivariable HRs were adjusted for age at baseline, education, income, pack-years of cigarette use, tea consumption, alcohol consumption, physical activity, family history of colorectal cancer and intakes of total energy, red meat, fruits and vegetables.

² Tertile cutoffs for BMI: 22.41 and 24.98; and tertile cutoffs for WHR: 0.88 and 0.92.