IARC HANDBOOKS

ABSENCE OF EXCESS BODY FATNESS

VOLUME 16

This publication represents the views and expert opinions of an IARC Working Group on the Evaluation of Cancer-Preventive Interventions, which met in Lyon, 5–12 April 2016

LYON, FRANCE - 2018

IARC HANDBOOKS OF CANCER PREVENTION

International Agency for Research on Cancer

World Health Organization

2.2 Cancer-preventive effects by organ site

2.2.1 Cancer of the colorectum

Colorectal cancer (CRC) accounts for about 10% of all cancer diagnoses and 8.5% of all cancer deaths worldwide (Ferlay et al., 2013). CRC is more common in high-income countries than in low- and middle-income countries and is more prevalent in men than in women. It is well established that the risk of CRC changes within one generation after migration from low-incidence areas to high-incidence areas and thus has a strong environmental component. Cancers of the colon and of the rectum, although similar in many ways, have important differences in their risk factor profiles. Cancers of the rectum seem to be less associated with dietary factors and more associated with consumption of alcohol (particularly beer). Cancers of the colon arise most often from colorectal adenomas, and cancers in the proximal colon tend to have a worse prognosis than cancers in the distal colon.

In 2001, the Working Group of the *IARC Handbook* on weight control and physical activity (IARC, 2002) concluded that there was *sufficient evidence* for a cancer-preventive effect of avoidance of weight gain for cancer of the colon. The 2007 World Cancer Research Fund (WCRF) review concluded that there was convincing evidence that both body fatness and waist circumference were associated with increased risk of CRC (WCRF/AICR, 2007). The 2007 conclusions were reaffirmed in 2011 (WCRF/AICR, 2011). Results from studies published since 2001 are summarized here and in Table 2.2.1a, Table 2.2.1b, and Table 2.2.1c.

(a) Cohort studies

A total of 39 cohort studies have been published since 2001 (excluding analyses that were later updated and analyses based on fewer than 100 incident cases). Table 2.2.1a summarizes their results for body mass index (BMI) at baseline, with comments on findings according to other measures of body fatness, such as weight change over the life-course and waist circumference.

(i) Body mass index

Although findings vary across studies, there is a general observation of a positive association between BMI and colon cancer risk across most studies, and a much weaker (but still positive) association between BMI and rectal cancer risk. In the studies that included both colon cancer and rectal cancer, the association with BMI for colon cancer was almost always either stronger or of the same magnitude as that for rectal cancer. For both colon cancer and rectal cancer, the association with BMI is stronger in men than in women. The association between BMI and colon cancer is approximately linear with increasing BMI levels. In a meta-analysis of prospective studies (Table 2.2.1c), the relative risk per 5 kg/m^2 increase in BMI was estimated to be 1.24 in men and 1.09 in women for colon cancer, and 1.09 in men and 1.02 in women for rectal cancer (all $P < 0.05$, except for rectal cancer in women, with $P = 0.26$) (Renehan et al., 2008). Another meta-analysis reported a relative risk of CRC for obesity relative to normal weight of 1.53 (95% confidence interval [CI], 1.44–1.62) in men and 1.25 (95% CI, 1.14–1.37) in women, and an overall increase in CRC risk of 18% (95% CI, 14–21%) per 5 kg/m^2 increase in BMI (Ning et al., 2010). The most recent meta-analysis of CRC, by Ma et al. (2013), based on 43 cohorts, estimated the relative risk for obesity relative to normal weight to be 1.33 (95% CI, 1.25–1.42).

In women, an interaction between use of hormone replacement therapy (HRT) and the BMI–CRC association has not been found consistently in the identified cohort studies that have investigated this (Lin et al., 2004; Adams et al., 2007; Wang et al., 2007; Aleksandrova et al., 2013; Kabat et al., 2015). There is not a consistent

set of evidence pointing to a differential of the BMI association for proximal versus distal colon subsites (Lin et al., 2004; Larsson et al., 2006; Bassett et al., 2010; Laake et al., 2010; Oxentenko et al., 2010; Hughes et al., 2011; Matsuo et al., 2012; Kitahara et al., 2013). BMI is also associated with risk of colorectal adenomas (Keum et al., 2015). The BMI–CRC association is observed consistently in diverse parts of the world (Renehan et al., 2008; Ma et al., 2013).

Several investigators have assessed the association between BMI at different ages or weight gain over the life-course and later colon cancer risk and/or rectal cancer risk. BMI at earlier ages seems to also be related to colon cancer risk (see Section 2.3), but BMI closer to the time of diagnosis is more consistently and strongly associated with risk than is BMI earlier in life (Bassett et al., 2010; Hughes et al., 2011). Weight gain since age 18 years has been found to be associated with colon cancer risk in several studies (Thygesen et al., 2008; Bassett et al., 2010; Renehan et al., 2012), but it is difficult to separate the effects of long-term weight gain from those of the resultant excess adiposity.

(ii) Waist circumference

Several cohorts have included measurements of waist circumference. Waist circumference at baseline is about as strongly associated with risk as is BMI in those studies that used identical quantile cut-off points for both measures (Table 2.2.1a). The meta-analysis of CRC and waist circumference by Ma et al. (2013), based on 13 prospective cohort studies, estimated the relative risk for the highest versus lowest categories of waist circumference across studies to be 1.46 (95% CI, 1.33–1.60), and no heterogeneity among studies was found ($P = 0.323$).

(b) Case–control studies

Since 2002, a total of 11 case–control studies, in Australia, Canada, China, Europe, the Republic of Korea, Thailand, and the USA, have reported on the association of BMI with CRC risk (Table 2.2.1b). In most of the studies, BMI was calculated from body height and self-reported body weight for a recent period before cancer diagnosis; in some of the studies, body weight was measured after diagnosis. Most studies showed an increase in risk of cancers of both the colon and the rectum with increasing BMI, and in some studies the association of BMI with risk was stronger for colon cancer than for rectal cancer. Some, but not all, studies showed more pronounced BMI-associated increases in risk in men than in women, although globally the evidence indicated increases in risk in both sexes. A meta-analysis of 12 case–control studies (Ning et al., 2010) found a relative risk of 1.23 for colon and rectal cancers combined, per 5 kg/m^2 increase in BMI.

The frequent observation of stronger associations of BMI with colon cancer risk in men than in women has led to the hypothesis that high blood levels of estrogens might confer protection against colon cancer. To address this issue, a few studies provided results in women stratified by estrogen status (determined by menopausal status and use of HRT). In a study in Germany in postmenopausal women only, a stratified analysis by users and non-users of postmenopausal HRT showed a strong association between BMI and CRC risk in the non-users only (odds ratio [OR], 3.30; 95% CI, 1.25–8.72 for BMI ≥ 30 kg/m^2 compared with BMI < 23 kg/m^2, based on 31 cases in the highest BMI category) and no association in the ever-users (OR, 0.89; 95% CI, 0.29–2.75) (Hoffmeister et al., 2007). These findings were opposite to those from a previous large study in the USA, which showed an increase in colon cancer risk only in estrogen-positive women (i.e. women who were premenopausal or who were users of postmenopausal HRT; OR, 2.38; 95% CI, 1.50–3.77 for BMI > 30 kg/m^2 compared with BMI < 23 kg/m^2, based on 77 cases in the highest BMI category) compared with no association in estrogen-negative women (i.e. women

who were postmenopausal and were non-users of HRT; OR, 1.02; 95% CI, 0.71–1.46 for BMI > 30 kg/m^2 compared with BMI < 23 kg/m^2, based on 134 cases in the highest BMI category) (Slattery et al., 2003). Another study, conducted in Shanghai, China, in a relatively lean population, showed a direct association of BMI with colon cancer risk in premenopausal women (OR, 2.9; 95% CI, 1.7–8.6 for BMI > 23.6 kg/m^2 compared with BMI < 19.0 kg/m^2, based on 62 cases in the highest BMI category) and an inverse association in postmenopausal women (OR, 0.6; 95% CI, 0.3–0.9 for BMI > 23.6 kg/m^2 compared with BMI < 19.0 kg/m^2, based on 50 cases in the highest BMI category) (Hou et al., 2006). A fourth study, in Canada, found an absence of association both in "estrogen-positive" women and in "estrogen-negative" women (Campbell et al., 2007).

With regard to molecular tumour subtypes, Campbell et al. (2010) showed a BMI-associated increase in risk for tumours that have a microsatellite-stable phenotype (recent BMI, OR per 5 kg/m^2 increase, 1.38; 95% CI, 1.24–1.54), whereas no association was observed for tumours characterized by microsatellite instability (OR, 1.05; 95% CI, 0.84–1.31) (see Section 4.2.3c).

(c) Mendelian randomization studies

Two recent studies have applied Mendelian randomization to assess the association between BMI and CRC risk (Table 2.2.1d). In the first study, Thrift et al. (2015) used a genetic risk score (GRS) derived from 77 single nucleotide polymorphisms (SNPs) associated with higher BMI, identified by the Genetic Investigation of Anthropometric Traits (GIANT) consortium, which involved more than 300 000 individuals of European descent. In their analysis, higher BMI was associated with an increased risk of CRC (GRS-related OR per 5 kg/m^2 increase in BMI, 1.50; 95% CI, 1.13–2.01). The point estimate obtained using the Mendelian randomization approach was greater in magnitude than the point estimate obtained from conventional covariate-adjusted analysis (minimally adjusted OR per 5 kg/m^2 increase in BMI, 1.18; 95% CI, 1.15–1.22); however, the 95% confidence intervals overlapped and they were not statistically significantly different from one another ($P_{difference}$ = 0.10). In addition, there was a positive association between BMI and CRC risk in women (GRS-related OR per 5 kg/m^2 increase in BMI, 1.82; 95% CI, 1.26–2.61), and this estimate was much greater than that obtained from conventional observational analyses (OR, 1.14; 95% CI, 1.10–1.18; $P_{difference}$ = 0.01); although there was no strong evidence from Mendelian randomization analyses for an association in men (GRS-related OR per 5 kg/m^2 increase in BMI, 1.18 (95% CI, 0.73–1.92), the results were in the same direction as in the observational results in the same sample ($P_{difference}$ = 0.70). [This discrepancy between the sexes may be due to sex-specific residual confounding or measurement error in observational analyses. Alternatively, the distribution of body fat, rather than total body fatness (reflected by BMI), may be a more important predictor of CRC risk for men than for women.]

In the second study, Gao et al. used 15 SNPs reliably associated with childhood BMI (Felix et al., 2016) and 77 SNPs reliably associated with adult BMI (Locke et al., 2015) as Mendelian randomization instruments and assessed their association with CRC risk (Gao et al., 2016). Mendelian randomization analyses showed an 8% increase in risk of CRC with each increase of 1 kg/m^2 in adult BMI [assuming that a standard deviation was equivalent to 4.5 kg/m^2]. There was no evidence of an association with childhood BMI.

Table 2.2.1a Cohort studies of measures of body fatness and cancer of the colorectum

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Terry et al. (2001) Women in Swedish mammography programme (ages 40–76 yr) Sweden 1987–1998	61 463 Women Incidence	Colon	BMI < 22 22–24.2 24.2–26.7 > 26.7 [P_{trend}]	291 total	 1.0 1.05 (0.72–1.51) 1.09 (0.77–1.56) 1.21 (0.86–1.70) [0.25]	Age, education level, alcohol consumption, diet	Stronger risk within the women in age group 40–54 yr (P_{trend} = 0.06)
	61 463 Women Incidence	Rectum	BMI < 22 22–24.2 24.2–26.7 > 26.7 [P_{trend}]	159 total	 1.0 0.92 (0.56–1.54) 1.14 (0.71–1.83) 1.32 (0.83–2.08) [0.13]	Age, education level, alcohol consumption, diet	
Terry et al. (2002) Women in Canadian mammography programme (ages 40–59 yr) Canada 1980–1993	89 835 Women Incidence	Colon and rectum	BMI < 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	527 total	 1.0 1.03 (0.84–1.26) 1.08 (0.82–1.41) [0.57]	Age, smoking, education level, physical activity, OC use, HRT use, parity	Association stronger in premenopausal ages than postmenopausal ages ($P_{interaction}$ = 0.01)
Calle et al. (2003) Population-based cohort USA 1982–1998	404 576 Men Mortality	Colon and rectum	BMI 18.5–24.9 25–29.9 30–34.9 35–39.9 [P_{trend}]	 1292 1811 337 54	 1.00 1.20 (1.12–1.30) 1.47 (1.30–1.66) 1.84 (1.39–2.41) [< 0.001]	Age, education level, smoking, physical activity, alcohol consumption, marital status, race, aspirin use, fat intake, vegetable intake	
	495 477 Women Mortality		BMI 18.5–24.9 25–29.9 30–34.9 35–39.9 ≥ 40 [P_{trend}]	 1706 906 312 67 21	 1.00 1.10 (1.01–1.19) 1.33 (1.17–1.51) 1.36 (1.06–1.74) 1.46 (0.94–2.24) [< 0.001]	Additionally adjusted for HRT use	

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Lin et al. (2004) Women's Health Study USA 1993–2002	39 876 Women Incidence	Colon and rectum	BMI < 23 23–24.9 25–26.9 27–29.9 ≥ 30 [P_{trend}]	 44 45 31 40 42	 1.0 1.45 (0.96–2.20) 1.28 (0.81–2.04) 1.72 (1.12–2.66) 1.67 (1.08–2.59) [0.018]	Age, study group, family history, history polyps, physical activity, smoking, aspirin use, consumption of red meat, alcohol consumption, HRT use	Stronger association with proximal colon. Similar findings by HRT status in never-users of HRT. Proximal and distal subsites similar
MacInnis et al. (2004) Population-based cohort Australia 1990–2003	16 556 Men Incidence	Colon	BMI < 24.8 24.8–26.9 27–29.2 ≥ 29.2 [P_{trend}]	 26 37 39 51	 1.0 1.3 (0.8–2.2) 1.4 (0.8–2.3) 1.7 (1.1–2.8) [0.02]	Age, education level, country of birth	
	16 556 Men Incidence		WC < 87 87–93 93–99.3 ≥ 99.3 [P_{trend}]	 22 19 48 64	 1.0 10.8 (0.4–1.4) 1.7 (1.0–2.8) 2.1 (1.3–3.5) [< 0.001]	Age, education level, country of birth	
Moore et al. (2004) Framingham Study cohort USA 1948–1999	3764 Men and women aged 30–54 yr at baseline Incidence	Colon	BMI 18.5–24.9 25–29.9 ≥ 30	 67 69 21	 1.0 1.3 (0.91–1.8) 1.5 (0.92–2.5)	Age, sex, education level, height, alcohol consumption, smoking, physical activity	
			WC Small Medium Large Extra large	 17 61 46 33	 1.0 1.1 (0.66–2.0) 1.6 (0.91–2.9) 2.0 (1.1–3.7)	Age, sex, education level, height, alcohol consumption, smoking, physical activity	Additional adjustment for BMI has no effect on estimates

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Moore et al. (2004) (cont.)	3802 Men and women aged 55–79 yr at baseline Incidence	Colon	BMI 18.5–24.9 25–29.9 ≥ 30	 39 79 31	 1.0 1.8 (1.2–2.6) 2.4 (1.5–3.9)	Age, sex, education level, height, alcohol consumption, smoking, physical activity	Associations more evident in men than in women, and stronger in the proximal site
			WC Small Medium Large Extra large	 11 53 47 38	 1.0 1.4 (0.74–2.7) 2.1 (1.1–4.0) 2.6 (1.3–5.2)	Age, sex, education level, height, alcohol consumption, smoking, physical activity	Adjustment for BMI has no effect on estimates
Samanic et al. (2004) United States Veterans cohort USA 1969–1996	4 500 700 Men Incidence	Colon	Obesity Non-obese Obese Non-obese Obese	 White men: 16 704 1420 Black men: 3830 262	 1.00 1.47 (1.39–1.55) 1.00 1.45 (1.28–1.64)	Age, calendar year	Obesity defined as discharge diagnosis of obesity: ICD-8: 277; ICD-9: 278.0 No significant differences in risk observed between White and Black veterans
	4 500 700 Men Incidence	Rectum	Obesity Non-obese Obese Non-obese Obese	 White men: 9849 719 Black men: 1773 93	 1.00 1.23 (1.14–1.33) 1.00 1.11 (0.90–1.37)	Age, calendar year	No significant differences in risk observed between White and Black veterans
Wei et al. (2004) Nurses' Health Study USA 1976–2000	46 632 Men Incidence	Colon	BMI < 23 23–24.9 25–29.9 ≥ 30 [P_{trend}]	 57 119 225 51	 1.0 1.33 (0.97–1.83) 1.54 (1.15–2.07) 1.85 (1.26–2.72) [0.001]	Age, family history, physical activity, smoking, diet, screening history. alcohol consumption, height	

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Wei et al. (2004) (cont.)	87 733 Women Incidence		BMI < 23 23–24.9 25–29.9 ≥ 30 [P_{trend}]	 210 141 207 113 	 1.0 1.10 (0.88–1.36) 1.11 (0.91–1.35) 1.28 (1.10–1.62) [0.05]		
	46 632 Men Incidence	Rectum	BMI < 23 23–24.9 25–29.9 ≥ 30 [P_{trend}]	 24 42 55 11 	 1.0 1.16 (0.70–1.94) 0.93 (0.57–1.53) 1.03 (0.49–2.14) [0.70]	Age, family history, physical activity, smoking, diet, screening history, alcohol consumption, height	
	87 733 Women Incidence		BMI < 23 23–24.9 25–29.9 ≥ 30 [P_{trend}]	 56 46 68 34 	 1.0 1.37 (0.92–2.02) 1.40 (0.98–2.01) 1.56 (1.01–2.42) [0.04]		
Engeland et al. (2005) Population-based cohort Norway 1963–2001	963 709 Men Incidence	Colon and rectum	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 90 11 432 9953 1512 	 0.84 (0.68–1.03) 1.0 1.15 (1.12–1.18) 1.40 (1.32–1.48) [< 0.001]	Age at BMI measurement, birth cohort	Relationships similar for colon vs rectum
	1 038 010 Women Incidence		BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 298 11 136 8780 3916 	 1.04 (0.93–1.17) 1.0 1.02 (0.99–1.05) 1.06 (1.02–1.10) [0.01]	Age at BMI measurement, birth cohort	Relationships similar for colon vs rectum. In women, associations stronger for colon
Kuriyama et al. (2005) Population-based prospective cohort Japan 1984–1992	12 485 Men Incidence	Colon and rectum	BMI < 18.5–24.9 25–27.5 27.5–29.9 ≥ 30 [P_{trend}]	 114 25 11 5 	 1.00 1.04 (0.67–1.60) 1.58 (0.85–2.94) 1.78 (0.73–4.38) [0.3710]	Age, smoking, alcohol consumption, diet, health insurance	

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Kuriyama et al. (2005) (cont.)	15 052 Women Incidence		BMI < 18.5–24.9 25–27.5 27.5–29.9 ≥ 30 [P_{trend}]	 73 22 11 9	 1.00 1.11 (0.69–1.80) 1.28 (0.68–2.43) 2.06 (1.03–4.13) [0.06]		
Oh et al. (2005) Civil servants and private school workers cohort Republic of Korea 1992–2001	781 283 Men Incidence	Colon (excluding rectosigmoid)	BMI < 18.5 18.5–22.9 23.0–24.9 25.0–26.7 27.0–29.9 ≥ 30 [P_{trend}]	 14 359 316 190 63 11	 1.00 (0.62–1.63) 1.00 1.24 (1.07–1.43) 1.33 (1.13–1.57) 1.07 (0.83–1.38) 1.92 (1.15–3.22) [0.001]	Age, smoking, alcohol consumption, physical activity, family history, residence area	
	781 283 Men Incidence	Rectosigmoid	BMI < 18.5 18.5–22.9 23.0–24.9 25.0–26.7 27.0–29.9 ≥ 30 [P_{trend}]	 20 606 480 326 117 14	 0.64 (0.36–1.13) 1.00 1.06 (0.92–1.22) 1.29 (1.10–1.52) 1.15 (0.91–1.46) 1.08 (0.56–2.10) [0.003]	Age, smoking, alcohol consumption, physical activity, family history, residence area	
Rapp et al. (2005) VHM&PP (population-based cohort) Austria 1985–2002	67 447 Men Incidence	Colon	BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}]	 86 128 39 7	 1.00 1.14 (0.86–1.50) 1.56 (1.06–2.30) 2.48 (1.15–5.39) [0.005]	Age, smoking status, occupational group	
	78 484 Women Incidence		BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}]	 122 106 35 8	 1.00 1.13 (0.86–1.47) 1.11 (0.76–1.62) 0.88 (0.43–1.81) [0.73]	Age, smoking status, occupational group	

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Rapp et al. (2005) (cont.)	67 447 Men Incidence	Rectum	BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}]	 45 69 24 – 	 1.00 1.20 (0.82–1.75) 1.66 (1.01–2.73) – [0.05]	Age, smoking status, occupational group	All obese categories were merged (from BMI 30 kg/m^2 onwards) to ensure at least 5 cases
	78 484 Women Incidence		BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}]	 68 48 12 5 	 1.00 0.90 (0.62–1.31) 0.66 (0.36–1.23) 0.96 (0.38–2.39) [0.32]	Age, smoking status, occupational group	
Bowers et al. (2006) ATBC cohort Finland 1985–2002	29 133 Men Incidence	Colon	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	 2 77 98 50	 1.47 (0.36–5.98) 1.00 1.07 (0.79–1.44) 1.78 (1.25–2.55)	Age, number of cigarettes smoked per day, total cholesterol, height, type 2 diabetes	Cohort of smokers
	29 133 Men Incidence	Rectum	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	 1 61 87 34	 0.96 (0.13–6.96) 1.0 1.18 (0.85–1.64) 1.51 (0.99–2.29)		
	29 133 Men Incidence	Colon and rectum	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	 3 138 185 84	 1.25 (0.40–3.93) 1.0 1.12 (0.90–1.39) 1.66 (1.27–2.18)		
Larsson et al. (2006) Population-based cohort Sweden 1997–2005	45 906 Men Incidence	Colon	BMI < 23 23–24.9 25–26.9 27–29.9 ≥ 30 [P_{trend}]	 47 72 65 61 39 	 1.00 1.11 (0.77–1.61) 1.07 (0.73–1.56) 1.15 (0.78–1.70) 1.60 (1.03–2.48) [0.08]	Age, education level, family history, diabetes, smoking, aspirin use, physical activity	Proximal and distal subsites similar. WC also positively associated

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Larsson et al. (2006) (cont.)	45 906 Men Incidence	Rectum	BMI < 23 23–24.9 25–26.9 27–29.9 ≥ 30 [P_{trend}]	 25 39 49 46 21	 1.00 1.08 (0.65–1.80) 1.35 (0.83–2.19) 1.53 (0.93–2.51) 1.44 (0.79–2.61) [0.06]	Age, education level, family history, diabetes, smoking, aspirin use, physical activity	
	45 906 Men Incidence	Colon and rectum	WC < 88 88–92 93–97 98–103 ≥ 104 [P_{trend}]	 47 67 95 96 102	 1.00 1.06 (0.73–1.55) 1.32 (0.92–1.88) 1.37 (0.96–1.96) 1.29 (0.90–1.85) [0.03]	Age, education level, family history, diabetes, smoking, aspirin use, physical activity	
Lukanova et al. (2006) Population-based cohort Sweden 1985–2003	33 424 Men Incidence	Colon and rectum	BMI < 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 45 69 22	 1.0 1.17 (0.80–1.71) 1.61 (0.95–2.65) [0.08]	Age, calendar year, smoking	Association with obesity significant only when excluding cases diagnosed within 1 yr of recruitment
	35 362 Women Incidence		BMI < 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 43 39 26	 1.0 1.27 (0.82–1.97) 2.01 (1.22–3.27) [0.005]	Age, calendar year, smoking	
MacInnis et al. (2006a) Melbourne Collaborative Cohort Study Australia 1990–2003	24 072 Women Incidence	Colon	BMI, tertiles T1 (< 25) T2 (25–29) T3 (≥ 30) [P_{trend}]	212 total	 1.0 0.8 (0.6–1.1) 1.0 (0.7–1.4) [0.59]	Age, education level, country of birth, HRT use	No differences between proximal and distal, or by disease stage (early vs late)
			WC, tertiles T1 (< 75) T2 (75–79) T3 (≥ 80) [P_{trend}]	212 total	 1.0 1.4 (1.0–1.9) 1.4 (1.0–1.9) [0.02]	Age, education level, country of birth, HRT use	No differences between proximal and distal, or by disease stage (early vs late)

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
MacInnis et al. (2006b) Population-based cohort Australia 1990–2003	16 867 Men Incidence	Rectum	BMI, tertiles			Age, country of birth, SES, height	Similar results in women (n = 24 247), no sex interaction
			< 25	24	1.0		
			25–29.9	86	1.7 (1.1–2.7)		
			≥ 30	24	1.3 (0.8–2.4)		
			[P_{trend}]		[0.48]		
			WC			Age, country of birth	Similar results in women (n = 24 247), no sex interaction
			< 94	57	1.0		
			94–101.9	43	1.3 (0.9–1.9)		
			≥ 102	34	1.4 (0.9–2.2)		
			[P_{trend}]		[0.11]		
Pischon et al. (2006) EPIC cohort Europe 1992–2003	129 731 Men Incidence	Colon	BMI			Age, centre, smoking, education level, alcohol consumption, physical activity, diet	
			< 23.6	64	1.0		
			23.6–25.3	85	1.18 (0.85–1.63)		
			25.4–27	74	1.00 (0.71–1.41)		
			27.1–29.3	88	1.19 (0.85–1.66)		
			≥ 29.4	110	1.55 (1.12–2.15)		
			[P_{trend}]		[0.006]		
			WC			Age, centre, smoking, education level, alcohol consumption, physical activity, diet, height	
			< 86	63	1.00		
			86–91.8	57	0.73 (0.50–1.04)		
			91.9–96.5	78	0.97 (0.69–1.36)		
			96.6–102.9	95	1.10 (0.79–1.53)		
			≥ 103	125	1.39 (1.01–1.93)		
			[P_{trend}]		[0.001]		

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Pischon et al. (2006) (cont.)	238 546 Women Incidence	Colon	BMI < 23.6 23.6–25.3 25.4–27 27.1–29.3 ≥ 29.4 [P_{trend}]	 87 96 120 137 135 123 	 1.0 0.92 (0.68–1.23) 1.02 (0.77–1.35) 1.09 (0.83–1.45) 1.06 (0.79–1.42) [0.40]	Age, centre, smoking, education level, alcohol consumption, physical activity, diet	
			WC < 70.2 70.2–75.8 75.9–80.9 81–88.9 ≥ 89 [P_{trend}]	 62 91 125 135 149 	 1.0 1.10 (0.80–1.52) 1.23 (0.90–1.68) 1.25 (0.91–1.70) 1.48 (1.08–2.03) [0.008]	Age, centre, smoking, education level, alcohol consumption, physical activity, diet, height	
	129 731 Men Incidence	Rectum	BMI < 23.6 23.6–25.3 25.4–27 27.1–29.3 ≥ 29.4 [P_{trend}]	 52 52 58 69 64 	 1.0 0.88 (0.60–1.30) 0.96 (0.66–1.40) 1.11 (0.77–1.62) 1.05 (0.72–1.55) [0.47]	Age, centre, smoking, education level, alcohol consumption, physical activity, diet	WC, null association
	238 546 Women Incidence		BMI < 23.6 23.6–25.3 25.4–27 27.1–29.3 ≥ 29.4 [P_{trend}]	 47 44 72 63 65 	 1.0 0.78 (0.51–1.18) 1.14 (0.78–1.66) 0.95 (0.64–1.41) 1.06 (0.71–1.58) [0.51]	Age, centre, smoking, education level, alcohol consumption, physical activity, diet	WC, null association
Samanic et al. (2006) Swedish Construction Worker Cohort Sweden 1971–1999	362 552 Men Incidence	Colon	BMI 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 763 842 190 	 1.00 1.24 (1.12–1.37) 1.74 (1.48–2.04) [< 0.001]	Age, year, smoking status	

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Samanic et al. (2006) (cont.)	362 552 Men Incidence	Rectum	BMI 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 626 610 126	 1.00 1.08 (0.96–1.21) 1.36 (1.13–1.66) [< 0.01]	Age, year, smoking status	
Adams et al. (2007) NIH-AARP cohort USA 1995–2000	307 708 Men Incidence	Colon	BMI 18.5–22.9 23–24.9 25–27.4 27.5–29.9 30–32.5 32.5–34.9 35–39.9 ≥ 40 [P_{trend}]	 136 260 479 367 219 110 76 29	 1.0 1.11 (0.90–1.37) 1.22 (1.01–1.48) 1.44 (1.18–1.76) 1.53 (1.23–1.90) 1.57 (1.22–2.03) 1.71 (1.29–2.27) 2.39 (1.59–3.58) [< 0.0005]	Age, alcohol consumption, smoking, supplemental calcium intake, consumption of red meat	
	209 436 Women Incidence		BMI 18.5–22.9 23–24.9 25–27.4 27.5–29.9 30–32.5 32.5–34.9 35–39.9 ≥ 40 [P_{trend}]	 151 141 172 106 77 42 52 28	 1.0 1.20 (0.95–1.51) 1.29 (1.03–1.60) 1.31 (1.01–1.68) 1.28 (0.97–1.69) 1.13 (0.80–1.60) 1.46 (1.06–2.02) 1.49 (0.98–2.25) [0.02]	Additionally adjusted for HRT use	Similar findings by HRT status
	307 708 Men Incidence	Rectum	BMI 18.5–22.9 23–24.9 25–27.4 27.5–29.9 30–32.5 32.5–34.9 ≥ 35 [P_{trend}]	 74 101 218 135 74 42 33	 1.0 0.78 (0.58–1.06) 1.01 (0.77–1.31) 0.96 (0.72–1.28) 0.94 (0.68–1.30) 1.10 (0.75–1.61) 1.0 (0.68–1.58) [0.31]	Age, alcohol consumption, smoking, supplemental calcium intake, consumption of red meat	

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Adams et al. (2007) (cont.)	209 436 Women Incidence		BMI 18.5–22.9 23–24.9 25–27.4 27.5–29.9 30–32.5 32.5–34.9 ≥ 35 [P_{trend}]	 60 49 60 37 26 14 32	 1.0 1.05 (0.72–1.53) 1.13 (0.79–1.63) 1.16 (0.76–1.76) 1.09 (0.68–1.75) 0.95 (0.52–1.71) 1.44 (0.92–2.25) [0.20]	Additionally adjusted for HRT use	Similar findings by HRT status
Driver et al. (2007) Physicians' Health Study USA 1982–2004	22 071 Men Incidence	Colon and rectum	BMI < 25 25–29.9 ≥ 30 [P_{trend}]	 190 171 20	 1.0 1.26 (1.05–1.52) 1.62 (1.09–2.42) [P_{trend}]	Age, smoking, alcohol consumption, diabetes, exercise	
Fujino et al. (2007) JACC cohort Japan 1988–1997	46 465 Men Incidence	Colon	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	 12 155 36 1	 0.86 (0.48–1.57) 1.0 1.14 (0.79–1.65) 0.54 (0.07–3.90)	Age, study area	Weight at age 20 yr also positively associated with risk
	64 327 Women Incidence		BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	 14 128 42 8	 0.98 (0.56–1.71) 1.0 1.09 (0.77–1.56) 1.94 (0.94–3.98)	Age, study area	Weight at age 20 yr also positively associated with risk
	46 465 Men Incidence	Rectum	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	 6 128 21 2	 0.57 (0.25–1.30) 1.0 0.78 (0.49–1.24) 1.27 (0.31–5.17)	Age, study area	Weight at age 20 yr also positively associated with risk
	64 321 Women Incidence		BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	 2 58 19 2	 0.36 (0.08–1.48) 1.0 1.04 (0.62–1.76) 1.00 (0.24–4.12)	Age, study area	

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Lundqvist et al. (2007) Twin cohorts Sweden and Finland 1961–2004	24 821 older twins (mean baseline age, 56 yr) 10 804 men and 14 017 women Incidence	Colon and rectum	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 7 274 196 36	 1.0 (0.5–2.1) 1.0 1.1 (0.9–1.3) 1.3 (0.9–1.8) [0.12]	Smoking, sex, country, physical activity, education level, diabetes	No association with rectal cancer
	43 328 younger twins (mean baseline age, 30 yr) 20 992 men and 22 336 women Incidence		BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 4 146 47 7	 0.6 (0.2–1.7) 1.0 1.0 (0.7–1.4) 1.1 (0.5–2.5) [0.53]	Smoking, physical activity, education level, diabetes	No association with rectal cancer
Reeves et al. (2007) Population-based cohort United Kingdom 1996–2001	1.2 million Women Incidence	Colon and rectum	BMI < 22.5 22.5–24.9 25.0–27.4 27.5–29.9 ≥ 30 per 10 kg/m²	 789 1034 913 555 717	 1.02 (0.95–1.10) 1.00 1.04 (0.97–1.11) 1.01 (0.93–1.10) 1.01 (0.94–1.09) 1.00 (0.92–1.08)	Age, region, SES, reproductive history, smoking, alcohol consumption, physical activity, time since menopause, HRT use	
Wang et al. (2007) Cancer Prevention Study II (CPS II) Nutrition Cohort USA 1992–2003	73 842 Women	Colon and rectum	BMI < 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 399 274 141	 1.0 1.08 (0.93–1.27) 1.19 (0.97–1.45) [0.04]	Age, education level, endoscopy history, baseline HRT use, NSAID use, multivitamin use, smoking, physical activity, diabetes	Cohort of postmenopausal women Similar findings by HRT status (never, former, current use)
Song et al. (2008) Korean medical insurance cohort Republic of Korea 1994–2003	107 481 Women Incidence	Colon (above rectosigmoid junction)	BMI < 18.5 18.5–20.9 21–22.9 23.0–24.9 25.0–26.9 27.0–29.9 ≥ 30 [risk per 1 kg/m²]	 11 46 86 141 129 64 32	 0.94 (0.37–2.39) 1.03 (0.63–1.70) 1.00 1.69 (1.17–2.44) 1.73 (1.18–2.53) 1.21 (0.77–1.90) 2.43 (1.40–4.23) [1.05 (1.02–1.09)]	Age, height, smoking, alcohol consumption, exercise, pay level at study entry	Cohort of postmenopausal women (age 40–64 yr) Results presented are those after excluding patients diagnosed within the first 5 yr of follow-up

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Song et al. (2008) (cont.)	107 481 Women Incidence	Rectum (below rectosigmoid junction)	BMI < 18.5 18.5–20.9 21–22.9 23.0–24.9 25.0–26.9 27.0–29.9 ≥ 30 [risk per 1 kg/m^2]	 10 69 110 140 102 85 20	 1.00 (0.43–2.33) 1.06 (0.67–1.67) 1.00 1.26 (0.88–1.81) 0.94 (0.63–1.40) 1.62 (1.10–2.38) 1.13 (0.57–2.24) [1.03 (0.99–1.06)]	Age, height, smoking, alcohol consumption, exercise, pay level at study entry	
Thygesen et al. (2008) Health Professionals Follow-Up Study USA 1986–2004	46 349 Men Incidence	Colon	BMI < 20 20.1–22.5 22.6–25 25.1–30 30.1–35 > 35	 9 50 205 341 75 13	 1.69 (0.83–3.44) 1.0 1.40 (1.03–1.92) 1.64 (1.21–2.22) 2.29 (1.58–3.31) 2.29 (1.23–4.26)	Age, physical activity, alcohol consumption, diet, smoking, aspirin use, family history, prior screening. All confounders were lagged 2 yr	Weight gain since age 21 yr positively associated with risk. The association became stronger when 2–4 yr of lag time for weight change was allowed
Wang et al. (2008) Cancer Prevention Study II (CPS II) Nutrition Cohort USA 1997–2005	44 068 Men Incidence	Colon	BMI < 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}] WC < 95 95–105 105–120 ≥ 120 [P_{trend}]	 143 179 64 16 165 195 157 29 	 1.0 0.93 (0.75–1.17) 1.34 (0.99–1.82) 1.93 (1.14–3.28) [0.01] 1.0 0.95 (0.77–1.17) 1.21 (0.96–1.52) 1.68 (1.12–2.53) [< 0.006]	Height, education level, physical activity, smoking, alcohol consumption, NSAID use, multivitamin use, screening history	

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Wang et al. (2008) (cont.)	51 083 Women Incidence	Colon	BMI < 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}]	 156 97 44 17	 1.0 0.92 (0.71–1.19) 1.25 (0.88–1.76) 1.40 (0.84–2.36) [0.18]	Height, education level, physical activity, smoking, alcohol consumption, NSAID use, multivitamin use, screening history, HRT use	
			WC < 85 85–95 95–110 ≥ 110 [P_{trend}]	 158 109 104 36	 1.0 1.01 (0.79–1.29) 1.27 (0.98–1.64) 1.75 (1.20–2.54) [0.003]	Height, education level, physical activity, smoking, alcohol consumption, NSAID use, multivitamin use, screening history, HRT use	
	44 068 Men Incidence	Rectum	BMI < 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}]	 50 63 23 6	 1.0 0.80 (0.55–1.16) 1.01 (0.61–1.68) 1.38 (0.58–3.28) [0.70]	Height, education level, physical activity, smoking, alcohol consumption, NSAID use, multivitamin use, screening history; for women, also adjusted for HRT use	WC, also null association
	51 083 Women Incidence		BMI < 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}]	 37 31 19 6	 1.0 1.34 (0.82–2.17) 2.62 (1.48–4.66) 2.67 (1.09–6.54) [0.001]		Similar association with WC
Andreotti et al. (2010) Agricultural workers USA 1993–2005	39 628 Men Incidence	Colon	BMI < 18.5 18.5–24.9 25.0–29.9 30–34.9 ≥ 35 per 1 kg/m^2	 1 44 112 58 15	 – 1.0 1.26 (0.86–1.86) 1.88 (1.23–2.91) 2.03 (1.05–3.93) 1.05 (1.02–1.09)	Race, education level, family history of colon cancer	

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Andreotti et al. (2010) (cont.)	28 319 Women Incidence		BMI < 18.5 18.5–24.9 25.0–29.9 30–34.9 ≥ 35 per 1 kg/m^2 [P_{trend}]	 1 40 49 19 4 	 – 1.0 1.48 (0.97–2.26) 1.36 (0.79–2.36) – 1.00 (0.96–1.04) [0.92]		
	39 628 Men Incidence	Rectum	BMI < 18.5 18.5–24.9 25.0–29.9 30–34.9 ≥ 35 per 1 kg/m^2 [P_{trend}]	 0 23 53 16 10 	 – 1.0 0.96 (0.51–1.82) 0.60 (0.24–1.50) 3.21 (1.34–7.71) 1.06 (1.00–1.12) [0.06]	Additionally adjusted for meat consumption	Results in women not presented due to too few incident cases
Bassett et al. (2010) Population-based cohort Australia 1990–2007	16 188 Men Incidence	Colon	BMI < 23 23–24.9 25.0–29.9 ≥ 30 [P_{trend}]	 13 38 160 66 	 0.60 (0.32–1.13) 1.0 1.31 (0.91–1.87) 1.51 (1.00–2.28) [< 0.01]	Place of birth, education level, diet, smoking, alcohol consumption	BMI at age 18 yr, null association. Positive association with weight gain since age 18 yr. Association stronger for proximal colon
	23 438 Women Incidence		BMI < 23 23–24.9 25.0–29.9 ≥ 30 [P_{trend}]	 64 59 102 67 	 0.95 (0.67–1.36) 1.0 0.84 (0.61–1.17) 1.00 (0.70–1.44) [0.90]		BMI at age 18 yr, null association. Weight gain since age 18 yr, also null association

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Laake et al. (2010) Population-based cohort Norway 1974–2005	38 822 Men Incidence	Colon	BMI < 18.5–22.9 23–24.9 25–27.4 27.5–29.9 ≥ 30 [P_{trend}]	 695 112 140 75 54	 1.0 1.16 (0.86–1.56) 1.19 (0.89–1.60) 1.20 (0.86–1.68) 1.80 (1.25–2.59) [0.004]	Age, physical activity, height, energy intake, smoking, education level, county	Association stronger for distal colon than proximal
	37 357 Women Incidence		BMI < 18.5–22.9 23–24.9 25–27.4 27.5–29.9 ≥ 30 [P_{trend}]	 115 95 81 57 71	 1.0 1.05 (0.80–1.38) 1.03 (0.77–1.38) 1.27 (0.92–1.76) 1.48 (1.09–2.02) [0.01]	Age, physical activity, height, energy intake, smoking, education level, county	Association stronger for distal colon
Oxentenko et al. (2010) Iowa Women's Health Study USA 1986–2005	36 941 Women Incidence after age 55 yr	Colon and rectum	BMI < 18.5 18.5–24.9 25–29.9 30–34.9 35–39.9 ≥ 40 [P_{trend}]	 19 495 548 272 93 37	 1.62 (0.98–2.66) 1.0 1.12 (0.99–1.28) 1.31 (1.12–1.54) 1.32 (1.03–1.68) 1.56 (1.10–2.22) [< 0.001]	Age, HRT use, OC use, smoking, physical activity, diabetes, alcohol consumption, diet, calcium intake, folate intake, vitamin E intake	Proximal and distal subsites similar. Association stronger for distal site
			WC, quartiles Q1 Q2 Q3 Q4 [P_{trend}]	 292 351 431 390	 1.0 1.18 (1.00–1.39) 1.34 (1.14–1.576) 1.32 (1.11–1.56) [< 0.001]	Age, HRT use, OC use, smoking, physical activity, diabetes, alcohol consumption, diet, calcium intake, folate intake, vitamin E intake	Proximal and distal subsites similar

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Parr et al. (2010) Pooled analysis of 39 cohort studies Asia, Australia, and New Zealand 1961–1999, median follow-up 4 yr	424 519 Men and women Incidence	Colon	BMI < 12–18.4 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	429 total	 0.63 (0.26–1.56) 1.0 1.13 (0.94–1.36) 1.50 (1.13–1.99) [0.02]	Age, sex, tobacco use	Stronger positive association in obese men
	424 519 Men and women Mortality	Rectum	BMI < 12–18.4 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	233 total	 0.86 (0.37–2.02) 1.0 1.44 (1.11–1.86) 1.68 (1.06–2.67) [0.03]	Age, sex, tobacco use	
Hughes et al. (2011) Population-based cohort The Netherlands 1986–2002	58 297 Men Incidence	Colon and rectum	BMI, quintiles Q1 Q2 Q3 Q4 Q5 [P_{trend}]	 232 238 240 247 254	 1.0 0.95 (0.74–1.24) 0.99 (0.77–1.28) 1.05 (0.81–1.36) 1.25 (0.96–1.62) [0.08]	Age, diet, occupation, physical activity, education level, family history, alcohol consumption, smoking	Rectal cancer not associated with BMI. Proximal and distal sites similar. Stronger associations with distal sites, P_{trend} significant. BMI at age 20 yr weakly associated
	62 573 Women Incidence		BMI, quintiles Q1 Q2 Q3 Q4 Q5 [P_{trend}]	 228 211 223 222 222	 1.0 0.88 (0.69–1.13) 0.94 (0.73–1.20) 0.91 (0.71–1.16) 0.97 (0.76–1.24) [0.90]	Age, diet, occupation, physical activity, education level, family history, alcohol consumption, smoking	BMI at age 20 yr, null association Rectal cancer also not associated with BMI

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Odegaard et al. (2011) Singapore Chinese Health Study cohort Shanghai, China 1993–2007	51 251 Men and women Incidence	Colon	BMI < 18.5 18.5–21.4 21.5–24.4 24.5–27.4 ≥ 27.5 [P_{trend}]	 51 162 181 123 79	 1.23 (0.90–1.68) 1.17 (0.95–1.45) 1.0 1.12 (0.89–1.43) 1.48 (1.13–1.92) [0.44]	Age, sex, year enrolment, dialect, education level, diabetes, family history, smoking, alcohol consumption, diet, physical activity, sleep duration	Significant U-shaped quadratic association (P_{trend} = 0.014). Stronger association in older subjects (> 65 yr) and non-smokers
	51 251 Men and women Incidence	Rectum	BMI < 18.5 18.5–21.4 21.5–24.4 24.5–27.4 ≥ 27.5 [P_{trend}]	 25 111 137 76 35	 0.77 (0.50–1.19) 1.04 (0.81–1.34) 1.0 0.95 (0.71–1.25) 0.93 (0.64–1.36) [0.92]	Age, sex, year of enrolment, dialect, education level, diabetes, family history, smoking, alcohol consumption, diet, physical activity, sleep duration	
Matsuo et al. (2012) 8 population-based cohorts (pooled) Japan 1984–2006	157 927 Men Incidence	Colon	BMI < 19 19–20.9 21–22.9 23–24.9 25–26.9 27–29.9 ≥ 30 [P_{trend}]	 98 317 473 512 319 168 32	 0.91 (0.70–1.17) 1.0 (0.85–1.16) 0.87 (0.75–1.00) 1.0 1.17 (1.01–1.36) 1.31 (1.09–1.58) 1.47 (0.99–2.18) [< 0.001]	Age, area, smoking, alcohol consumption, diet, physical activity	Association stronger for proximal colon
	183 457 Women Incidence		BMI < 19 19–20.9 21–22.9 23–24.9 25–26.9 27–29.9 ≥ 30 [P_{trend}]	 76 215 330 512 217 136 48	 0.71 (0.52–0.97) 0.87 (0.71–1.07) 1.00 (0.84–1.19) 1.0 1.21 (1.02–1.44) 1.11 (0.88–1.39) 1.18 (0.83–1.68) [0.003]	Age, area, smoking, alcohol consumption, diet, physical activity	Association stronger for proximal colon

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Matsuo et al. (2012) (cont.)	157 927 Men Incidence	Rectum	BMI < 19 19–20.9 21–22.9 23–24.9 25–26.9 27–29.9 ≥ 30 [P_{trend}]	 59 179 325 284 158 80 26	 0.91 (0.65–1.27) 0.98 (0.80–1.21) 1.12 (0.94–1.33) 1.0 1.12 (0.91–1.37) 1.20 (0.91–1.58) 1.57 (0.97–2.53) [0.20]	Age, area, smoking, alcohol consumption, diet, physical activity	
	183 457 Women Incidence		BMI < 19 19–20.9 21–22.9 23–24.9 25–26.9 27–29.9 ≥ 30 [P_{trend}]	 53 97 147 284 80 54 20	 1.44 (0.99–2.08) 1.12 (0.84–1.50) 1.05 (0.81–1.35) 1.0 0.88 (0.64–1.20) 0.99 (0.70–1.39) 1.39 (0.81–2.39) [0.785]	Age, area, smoking, alcohol consumption, diet, physical activity	
Park et al. (2012) EPIC-Norfolk study cohort England 1993–2006	11 166 Men Incidence	Colon and rectum	BMI < 23.9 23.9–25.5 25.5–26.9 27–28.8 ≥ 28.9 [P_{trend}]	 67 41 30 32 27	 1.00 0.75 (0.50–1.12) 0.74 (0.48–1.14) 0.90 (0.58–1.38) 0.97 (0.61–1.54) [0.85]	Age, sex, smoking, alcohol consumption, education level, exercise, family history, diet	WC, also null association
	13 078 Women Incidence		BMI < 23.9 23.9–25.5 25.5–26.9 27–28.8 ≥ 28.9 [P_{trend}]	 34 31 44 21 30	 1.00 1.20 (0.72–1.98) 1.87 (1.17–2.99) 1.10 (0.62–1.93) 1.97 (1.18–3.30) [0.02]	Age, sex, smoking, alcohol consumption, education level, exercise, family history, diet	WC, null association

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Park et al. (2012) (cont.)	13 078 Women Incidence		WC < 73 73–78 78–83.3 83.4–90.4 ≥ 90.5 [P_{trend}]	 20 22 30 41 47	 1.00 0.86 (0.46–1.62) 1.16 (0.65–2.06) 1.52 (0.88–2.62) 1.65 (0.97–2.86) [0.001]	Age, sex, smoking, alcohol consumption, education level, exercise, family history, diet	
Renehan et al. (2012) NIH-AARP cohort USA 1995–2006	168 294 Men Incidence	Colon	BMI < 18.5 18.5–21.9 22.0–22.9 23.0–24.9 25.0–27.4 27.5–29.9 30.0–32.4 32.5–34.9 ≥ 35 [P_{trend}]	 6 98 93 349 600 438 249 124 113	 0.89 (0.39–2.02) 1.0 0.91 (0.68–1.22) 1.01 (0.80–1.27) 1.07 (0.86–1.34) 1.26 (1.01–1.58) 1.29 (1.01–1.64) 1.33 (1.01–1.75) 1.53 (1.16–2.03) [< 0.0001]	Age, race, education level, physical activity, smoking, alcohol consumption	BMI at ages 18, 35, and 50 yr shows similar associations as baseline BMI (mean baseline age, 62.8 yr)
	105 385 Women Incidence		BMI < 18.5 18.5–21.9 22.0–22.9 23.0–24.9 25.0–27.4 27.5–29.9 30.0–32.4 32.5–34.9 ≥ 35 [P_{trend}]	 14 148 68 176 207 127 82 54 86	 1.33 (0.76–2.30) 1.0 1.00 (0.75–1.34) 1.08 (0.87–1.35) 1.11 (0.89–1.38) 1.15 (0.90–1.47) 1.00 (0.76–1.32) 1.07 (0.78–1.48) 1.23 (0.93–1.64) [0.20]	Age, race, education level, physical activity, smoking, alcohol consumption, HRT use	BMI at ages 35 yr and 50 yr shows similar associations as baseline BMI, but BMI at age 18 yr null association

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Renehan et al. (2012) (cont.)	168 294 Men Incidence	Rectum	BMI < 18.5 18.5–21.9 22.0–22.9 23.0–24.9 25.0–27.4 27.5–29.9 30.0–32.4 32.5–34.9 ≥ 35 [P_{trend}]	 4 37 45 150 215 149 78 44 40	 1.63 (0.58–4.59) 1.0 1.22 (0.78–1.91) 1.20 (0.82–1.74) 1.06 (0.74–1.53) 1.15 (0.79–1.67) 0.99 (0.65–1.49) 1.22 (0.77–1.92) 1.43 (0.90–2.28) [0.51]	Age, race, education level, physical activity, smoking, alcohol consumption	BMI at ages 18, 35, and 50 yr shows similar associations as baseline BMI (mean baseline age, 62.8 yr)
	105 385 Women Incidence		BMI < 18.5 18.5–21.9 22.0–22.9 23.0–24.9 25.0–27.4 27.5–29.9 30.0–32.4 32.5–34.9 ≥ 35 [P_{trend}]	 6 43 22 50 64 32 20 20 25	 1.94 (0.82–4.58) 1.0 1.15 (0.68–1.93) 1.07 (0.71–1.63) 1.21 (0.82–1.81) 1.01 (0.63–1.61) 0.85 (0.49–1.47) 1.45 (0.84–2.51) 1.28 (0.76–2.16) [0.45]	Age, race, education level, physical activity, smoking, alcohol consumption, HRT use	BMI at ages 18, 35, and 50 yr also null association

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Aleksandrova et al. (2013) EPIC cohort (6 centres) Europe 1992–2010	74 091 Men Incidence	Colon	Weight change from age 20 yr			Age, weight at age 20 yr, smoking, education level, alcohol consumption, physical activity, consumption of red meat, fish and shellfish intake, intake of fruits and vegetables, fibre intake	
			Loss	37	0.84 (0.43–1.64)		
			Stable	67	1.0		
			2–5 kg gain	65	1.20 (0.67–2.14)		
			5–10 kg gain	122	0.97 (0.58–1.63)		
			10–15 kg gain	127	0.88 (0.53–1.48)		
			15–20 kg gain	114	1.09 (0.65–1.84)		
			≥ 20 kg gain	165	1.31 (0.78–2.19)		
			[P_{trend}]		[0.13]		
	127 605 Women Incidence		Weight change from age 20 yr				Similar findings by HRT status
			Loss	70	0.97 (0.56–1.68)		
			Stable	66	1.0		
			2–5 kg gain	87	1.34 (0.81–2.23)		
			5–10 kg gain	158	1.07 (0.68–1.69)		
			10–15 kg gain	139	1.05 (0.65–1.69)		
			15–20 kg gain	112	1.36 (0.83–2.23)		
			≥ 20 kg gain	141	1.49 (0.92–2.42)		
			[P_{trend}]		[0.05]		
	74 091 Men Incidence	Rectum	Weight change from age 20 yr				
			Loss	31	1.15 (0.53–2.49)		
			Stable	45	1.0		
			2–5 kg gain	48	0.64 (0.30–1.35)		
			5–10 kg gain	107	1.37 (0.74–2.52)		
			10–15 kg gain	103	1.28 (0.69–2.35)		
			15–20 kg gain	72	1.22 (0.65–2.30)		
			≥ 20 kg gain	91	1.36 (0.73–2.52)		
			[P_{trend}]		[0.16]		
	127 605 Women Incidence		Weight change from age 20 yr				
			Loss	32	1.77 (0.84–3.76)		
			Stable	39	1.0		
			2–5 kg gain	50	2.15 (1.12–4.11)		
			5–10 kg gain	84	1.34 (0.78–2.31)		
			10–15 kg gain	88	1.65 (0.93–2.93)		
			15–20 kg gain	53	1.82 (0.94–3.51)		
			≥ 20 kg gain	71	1.45 (0.79–2.66)		
			[P_{trend}]		[0.96]		

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Kitahara et al. (2013) PLCO trial subjects (screening arm) USA 1993–2001	36 912 Men Incidence	Colon and rectum	BMI < 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 128 270 148	 1.0 1.19 (0.96–1.48) 1.48 (1.16–1.89) [0.002]	Age, study centre, screening history, race/ethnicity, tobacco use, HRT use	Proximal, distal, and rectal associations with BMI all similar, but only proximal significant
	37 562 Women Incidence		BMI < 18.5–24.9 25–29.9 ≥ 30 [P_{trend}]	 156 154 106	 1.0 1.07 (0.86–1.34) 1.03 (0.80–1.33) [0.74]	Age, study centre, screening history, race/ethnicity, tobacco use, HRT use	All subsites null for BMI associations
Bhaskaran et al. (2014) Health system clinical database United Kingdom 1987–2012	5 243 978 Men and women Incidence	Colon	per 5 kg/m^2	13 465	1.10 (1.07–1.13)	Age, sex, year, diabetes, alcohol consumption, smoking, SES	Similar association in never-smokers. Significant sex interaction above 22 kg/m^2 (stronger association in men)
	5 243 978 Men and women Incidence	Rectum	per 5 kg/m^2	6123	1.04 (1.00–1.08)		Similar association in never-smokers

Table 2.2.1a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Kabat et al. (2015) Women's Health Initiative cohort USA 1992–2013	143 901 Women Incidence	Colon and rectum	BMI, quintiles Q1 Q2 Q3 Q4 Q5 [P_{trend}]	1908 total	 1.0 1.18 (1.01–1.38) 1.15 (0.98–1.38) 1.27 (1.09–1.48) 1.44 (1.23–1.68) [< 0.0001]	Age, alcohol consumption, smoking, physical activity, age at menarche, age at first birth, parity, HRT use, family history, ethnicity, education level, aspirin use, diabetes, treatment allocation	Associations stronger in ever-users of HRT Similar findings by HRT status
			WC, quintiles Q1 Q2 Q3 Q4 Q5 [P_{trend}]	1908 total	 1.0 1.49 (1.26–1.75) 1.36 (1.15–1.61) 1.67 (1.41–1.96) 1.90 (1.61–2.25) [< 0.0001]		

ATBC, Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; BMI, body mass index (in kg/m^2); CI, confidence interval; CRC, colorectal cancer; EPIC, European Prospective Investigation into Cancer and Nutrition; HRT, hormone replacement therapy; JACC, Japan Collaborative Cohort Study for Evaluation of Cancer Risk; NIH-AARP, National Institutes of Health–AARP Diet and Health Study; NSAID, non-steroidal anti-inflammatory drug; OC, oral contraceptive; PLCO, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; SES, socioeconomic status; VHM&PP, Vorarlberg Health Monitoring and Prevention Program; WC, waist circumference (in cm); yr, year or years

Table 2.2.1b Case–control studies of measures of body fatness and cancer of the colorectum

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Boutron-Ruault et al. (2001) France (Burgundy) Period NR	CRC: Men: 109 Women: 62 Population	BMI, quintiles (sex-specific) Men: Women: < 22.9 < 20.3 23–24.4 20.4–22.6 25–25.9 22.7–23.9 26–28.7 24–26.1 > 28.7 > 26.1 [P_{trend}]	 29 45 23 40 34	 1.0 1.7 (0.9–3.0) 0.8 (0.4–1.6) 1.4 (0.8–2.6) 1.1 (0.6–2.1) [0.92]	Age	
Slattery et al. (2003) USA (Northern California, Utah, Minnesota) 1991–1994	Colon cancer: Men: 1095 Women: 1286 Population	BMI < 23 23–24 25–27 28–30 > 30 BMI < 23 23–24 25–27 28–30 > 30 BMI in estrogen-positive women < 23 23–24 25–27 28–30 > 30 BMI in estrogen-negative women < 23 23–24 25–27 28–30 > 30	Men: 56 119 320 305 295 Women: 144 146 224 152 211 56 60 59 49 77 88 86 165 103 134	 1.00 0.06 (0.64–1.44) 1.13 (0.79–1.63) 1.54 (1.06–2.23) 1.88 (1.29–2.74) 1.00 1.22 (0.90–1.65) 1.27 (0.96–1.67) 1.30 (0.96–1.76) 1.45 (1.09–1.92) 1.00 1.28 (0.81–2.02) 1.09 (0.69–1.73) 1.56 (0.95–2.56) 2.38 (1.50–3.77) 1.00 1.21 (0.80–1.82) 1.28 (0.90–1.82) 1.10 (0.75–1.62) 1.02 (0.71–1.46)	Age	Additional adjustment for dietary factors, NSAID use, physical activity level, and family history of CRC did not significantly alter associations

Table 2.2.1b (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Pan et al. (2004) Canada (eight Canadian provinces), NECSS study 1994–1997	Colon cancer: Men: 959 Women: 768 Population	BMI Men: < 25 25– < 30 ≥ 30 [P_{trend}] Women: < 25 25– < 30 ≥ 30 [P_{trend}]	 NR NR 	 1.00 1.54 (1.27–1.86) 2.16 (1.68–2.78) [< 0.0001] 1.00 1.22 (0.98–1.52) 1.77 (1.35–2.32) [< 0.0001]	5-yr age group, province, education level, smoking, alcohol consumption, total energy intake, diet, recreational physical activity Women only: menopausal status, number of live births, age at menarche, age at end of first pregnancy	
	Rectal cancer: Men: 858 Women: 589 Population	Men: < 25 25– < 30 ≥ 30 [P_{trend}] Women: < 25 25– < 30 ≥ 30 [P_{trend}]	NR NR 	1.00 1.41 (1.15–1.71) 1.75 (1.35–2.28) [0.0001] 1.00 1.28 (1.02–1.61) 1.50 (1.11–2.02) [0.0045]		
Chung et al. (2006) Republic of Korea 2002–2004	CRC: 105 Hospital	BMI < 22.9 23.0–24.9 ≥ 25.0	 37 32 36	 1.0 1.4 (0.6–3.3) 2.3 (0.9–5.8)	Age, sex, glucose, triglycerides, cholesterol	
Hou et al. (2006) China (Shanghai) 1990–1993	Colon cancer: Men: 461 Women: 465 Population	BMI, quintiles < 19.2 19.2–20.3 20.4–21.3 21.4–22.8 > 22.8 [P_{trend}]	Men: 80 85 68 109 119	 1.0 1.0 (0.7–1.4) 1.0 (0.7–1.4) 1.2 (0.9–1.8) 1.7 (1.1–2.4) [0.005]	Age, education level, family income, marital status, total energy intake, diet Women only: number of pregnancies, years of menstruation	In women, a significant interaction was observed by menopausal status ($P_{interaction}$ = 0.03)

Table 2.2.1b (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Hou et al. (2006) (cont.)		BMI, quintiles	Women:			
		< 19	86	1.0		
		19.1–20.5	91	1.2 (0.8–1.7)		
		20.6–21.9	80	0.9 (0.6–1.3)		
		22.0–23.6	92	1.1 (0.8–1.7)		
		> 23.6	116	1.4 (1.0–2.1)		
		[P_{trend}]		[0.08]		
		BMI in premenopausal women				
		< 19	15	1.0		
		19.1–20.5	19	1.2 (0.6–2.8)		
		20.6–21.9	20	1.2 (0.3–3.1)		
		22.0–23.6	24	1.3 (0.6–3.2)		
		> 23.6	62	2.9 (1.7–8.6)		
		[P_{trend}]		[0.01]		
		BMI in postmenopausal women				
		< 19	66	1.0		
		19.1–20.5	72	1.1 (0.6–1.5)		
		20.6–21.9	58	0.8 (0.5–1.2)		
		22.0–23.6	71	0.8 (0.6–1.4)		
		> 23.6	50	0.6 (0.3–0.9)		
		[P_{trend}]		[0.03]		
Campbell et al. (2007) Canada (Ontario and Newfoundland) 1997–2003	CRC: Men: 1292 Women: 1404 Population	BMI	Men:		Age, education level, consumption of red meat, physical activity, province of residence, CRC screening endoscopy, history of high cholesterol/ triglycerides Women only: menopausal status, use of postmenopausal HRT	Associations were moderately stronger for colon than rectum. Significant associations with weight gain since age 20 yr were observed in men only (≥ 20 kg vs reference 1–5 kg)
		18.5–24.99	298	1.0		
		25–29.99	627	1.29 (1.07–1.56)		
		≥ 30	322	1.80 (1.43–2.27)		
		BMI	Women:			
		18.5–24.99	616	1.0		
		25–29.99	443	0.99 (0.83–1.20)		
		≥ 30	260	0.94 (0.75–1.18)		
		BMI in estrogen-positive women				
		18.5–24.99	260	1.0		
		25–29.99	148	0.89 (0.66–1.21)		
		≥ 30	80	0.67 (0.45–0.98)		

Table 2.2.1b (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Campbell et al. (2007) (cont.)		BMI in estrogen-negative women				
		18.5–24.99	356	1.0		
		25–29.99	295	1.08 (0.85–1.37)		
		≥ 30	180	1.05 (0.79–1.40)		
Hoffmeister et al. (2007) Germany 2003–2004	CRC: Women: 208 Population	BMI			Age, county of residence, history of rheumatic disease, hyperlipidaemia, former health check-up, former colorectal endoscopy, smoking, alcohol consumption, regular NSAID use, use of statins, OC use	Cohort of postmenopausal women
		< 23	51	1.00		
		23– < 25	39	0.80 (0.42–1.53)		
		25– < 27	25	0.78 (0.39–1.58)		
		27– < 30	46	1.71 (0.89–3.31)		
		≥ 30	40	1.82 (0.92–3.62)		
		[P_{trend}]		[0.02]		
		BMI in never-users of HRT				
		< 23	24	1.00		
		23– < 25	31	1.31 (0.55–3.12)		
		25– < 27	18	1.60 (0.58–4.44)		
		27– < 30	33	2.76 (1.07–7.12)		
		≥ 30	31	3.30 (1.25–8.72)		
		[P_{trend}]		[0.01]		
		BMI in ever-users of HRT				
		< 23	27	1.00		
		23– < 25	8	0.49 (0.16–1.48)		
		25– < 27	7	0.36 (0.11–1.13)		
		27– < 30	13	1.18 (0.40–3.48)		
		≥ 30	9	0.89 (0.29–2.75)		
		[P_{trend}]		[0.96]		
Sriamporn et al. (2007) North-eastern Thailand 2002–2006	CRC: 253 Hospital	BMI			Age, sex, place of residence	
		< 25	34	1		
		≥ 25		0.5 (0.3–0.8)		
		[P_{trend}]		[< 0.5]		

Table 2.2.1b (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Campbell et al. (2010) Canada (Ontario and Newfoundland) 1997–2003	CRC: Men: 877 Women: 917 Sibling controls	BMI			Age, endoscopy screening, smoking Women only: postmenopausal HRT use	Only microsatellite stable tumours showed increased risk at higher BMI
			Women:			
		< 18.5	24	1.77 (0.91–3.45)		
		18.5–24.99	404	1.00		
		25–29.99	252	1.00 (0.80–1.25)		
		≥ 30	212	1.34 (1.03–1.75)		
		per 5 kg/m²		1.20 (1.10–1.32)		
		[P_{trend}]		[< 0.001]		
			Men:			
		< 18.5	2	0.51 (0.09–2.89)		
		18.5–24.99	223	1.00		
		25–29.99	408	1.33 (1.06–1.68)		
		≥ 30	222	1.79 (1.33–2.40)		
		per 5 kg/m²		1.30 (1.15–1.47)		
		[P_{trend}]		[< 0.001]		
		Adult weight change				
			Women:			
		Loss	94	0.70 (0.049–1.00)		
		0–5 kg gain	158	1.00		
		6–10 kg gain	155	0.88 (0.64–1.20)		
		11–20 kg gain	249	0.93 (0.70–1.23)		
		≥ 21 kg gain	229	1.08 (0.80–1.47)		
		per 5 kg		1.06 (1.01–1.12)		
		[P_{trend}]		[< 0.01]		
			Men:			
		Loss	104	1.40 (0.95–2.06)		
		0–5 kg gain	93	1.00		
		6–10 kg gain	143	1.47 (1.05–2.07)		
		11–20 kg gain	257	1.72 (1.25–2.36)		
		≥ 21 kg gain	233	2.23 (1.58–3.14)		
		per 5 kg		1.08 (1.03–1.14)		
		[P_{trend}]		[0.003]		

Table 2.2.1b (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Choe et al. (2013) Republic of Korea (Seoul) 2004–2008	CRC: 153 (stage I) Hospital	BMI, quartiles Q1 Q2 Q3 Q4	NR	 1.0 0.81 (0.48–1.38) 1.32 (0.80–2.19) 1.58 (0.95–2.63)	Current smoking status, alcohol consumption	No significant associations were observed when comparing CRC risk vs colorectal adenoma (554 cases in total) across quartiles of BMI
Boyle et al. (2014) Australia 2005–2007	CRC: 918 Population	BMI at age 20 yr Normal Overweight Obese [P_{trend}]	NR	 1.00 1.25 (0.92–1.71) 0.89 (0.44–1.77) [0.401]	Age group, sex, SES, energy intake, lifetime vigorous recreational physical activity, alcohol consumption, tobacco use, diabetes	No differences in associations were observed with BMI at age 40 yr

BMI, body mass index (in kg/m^2); CI, confidence interval; CRC, colorectal cancer; HRT, hormone replacement therapy; NECSS, National Enhanced Cancer Surveillance System; NR, not reported; NSAID, non-steroidal anti-inflammatory drug; OC, oral contraceptive; SES, socioeconomic status; yr, year or years

Table 2.2.1c Meta-analyses of measures of body fatness and cancer of the colorectum

Reference	Total number of studies Total number of cases	Organ site	Exposure categories	Relative risk (95% CI)	Adjustment for confounding
Moghaddam et al. (2007)	31 studies (23 cohort studies, 8 case–control studies) 70 906 cases (49% women)	Colon and rectum	BMI ≥ 30 vs < 25	1.35 (1.24–1.46)	Age (all studies) and other factors (not in all studies): sex, diabetes, smoking, alcohol consumption, hypertension, hypercholesterolaemia, medication, race, family history, physical activity, diet, education level, SES, pregnancy (for women), menstruation (for women), study centre
	8 cohort studies N/A	Colon and rectum	WC Highest vs lowest category	1.50 (1.35–1.67)	
Renehan et al. (2008)	22 prospective studies in men 22 440 incident cases	Colon	BMI per 5 kg/m² increase	1.24 (1.20–1.28)	Age (all studies) and other factors (not in all studies): family history, inflammatory bowel disease, Western diet, increased weight, alcohol consumption, previous CRC, medical conditions (e.g. type 2 diabetes, acromegaly), intake of fruits and vegetables, fat intake, vitamin D and calcium intake, physical activity, aspirin use, HRT use
	19 prospective studies in women 20 975 incident cases	Colon	BMI per 5 kg/m² increase	1.09 (1.05–1.12)	
	18 prospective studies in men 14 894 incident cases	Rectum	BMI per 5 kg/m² increase	1.09 (1.06–1.12)	Age (all studies) and other factors (not in all studies): family history, inflammatory bowel disease, Western diet, increased weight, alcohol consumption, previous CRC, medical conditions (e.g. type 2 diabetes, acromegaly), intake of fruits and vegetables, fat intake, vitamin D and calcium intake, physical activity, aspirin use, HRT use
	14 prospective studies in women 9052 incident cases	Rectum	BMI per 5 kg/m² increase	1.02 (1.00–1.05)	
Ning et al. (2010)	51 studies (39 prospective and 12 retrospective) 93 812 cases	Colon and rectum	BMI per 5 kg/m² increase	1.18 (1.14–1.21)	Cancer site, sex, menopausal status (for women), directly measured BMI or self-reported BMI, and adjustment for physical activity
Ma et al. (2013)	41 prospective studies 85 935 cases	Colon and rectum	BMI ≥ 30 vs < 25	1.33 (1.25–1.42)	Age (36 studies), smoking (32 studies), physical activity (23 studies), alcohol consumption (23 studies). Fewer adjusted for energy intake (9 studies), NSAID/aspirin use (8 studies), folate intake (7 studies), calcium intake (6 studies), diabetes (6 studies)
	13 prospective studies 6546 cases	Colon and rectum	WC Highest vs lowest category	1.46 (1.33–1.60)	

BMI, body mass index (in kg/m²); CI, confidence interval; CRC, colorectal cancer; HRT, hormone replacement therapy; N/A, not applicable; NSAID, non-steroidal anti-inflammatory drug; SES, socioeconomic status; WC, waist circumference

Table 2.2.1d Mendelian randomization studies of measures of body fatness and cancer of the colorectum

Reference Study	Characteristics of study population	Sample size	Exposure (unit)	Odds ratio (95% CI)	Adjustment for confounding	Comments
Thrift et al. (2015) Genetics and Epidemiology of Colorectal Cancer Consortium (GECCO)	11 studies of individuals of European descent (6 cohort and 5 case–control)	20 512 (10 226 cases and 10 286 controls)	Weighted genetic risk score representing an increase of 5 kg/m^2 in BMI	All: 1.50 (1.13–2.01) Men: 1.18 (0.73–1.92) Women: 1.82 (1.26–2.61)	Study, and the top three principal components of ancestry	
Gao et al. (2016) Genetic Associations and Mechanisms in Oncology (GAME-ON) Consortium	6 studies of individuals of European ancestry	9931 (5100 cases and 4831 controls)	Increase of 1 SD in genetically predicted childhood BMI or adult BMI	Childhood BMI: 1.20 (0.90–1.59) Adult BMI: 1.39 (1.06–1.82)	N/A	Waist-to-hip ratio, null association: 1.29 (0.75–2.22)

BMI, body mass index (in kg/m^2); CI, confidence interval; N/A, not applicable; SD, standard deviation

References

Adams KF, Leitzmann MF, Albanes D, Kipnis V, Mouw T, Hollenbeck A, et al. (2007). Body mass and colorectal cancer risk in the NIH-AARP cohort. *Am J Epidemiol*, 166(1):36–45. doi:10.1093/aje/kwm049 PMID:17449892

Aleksandrova K, Pischon T, Buijsse B, May AM, Peeters PH, Bueno-de-Mesquita HB, et al. (2013). Adult weight change and risk of colorectal cancer in the European Prospective Investigation into Cancer and Nutrition. *Eur J Cancer*, 49(16):3526–36. doi:10.1016/j.ejca.2013.06.021 PMID:23867126

Andreotti G, Hou L, Beane Freeman LE, Mahajan R, Koutros S, Coble J, et al. (2010). Body mass index, agricultural pesticide use, and cancer incidence in the Agricultural Health Study cohort. *Cancer Causes Control*, 21(11):1759–75. doi:10.1007/s10552-010-9603-9 PMID:20730623

Bassett JK, Severi G, English DR, Baglietto L, Krishnan K, Hopper JL, et al. (2010). Body size, weight change, and risk of colon cancer. *Cancer Epidemiol Biomarkers Prev*, 19(11):2978–86. doi:10.1158/1055-9965.EPI-10-0543 PMID:20870733

Bhaskaran K, Douglas I, Forbes H, dos-Santos-Silva I, Leon DA, Smeeth L (2014). Body-mass index and risk of 22 specific cancers: a population-based cohort study of 5.24 million UK adults. *Lancet*, 384(9945):755–65. doi:10.1016/S0140-6736(14)60892-8 PMID:25129328

Boutron-Ruault MC, Senesse P, Méance S, Belghiti C, Faivre J (2001). Energy intake, body mass index, physical activity, and the colorectal adenoma-carcinoma sequence. *Nutr Cancer*, 39(1):50–7. doi:10.1207/S15327914nc391_7 PMID:11588902

Bowers K, Albanes D, Limburg P, Pietinen P, Taylor PR, Virtamo J, et al. (2006). A prospective study of anthropometric and clinical measurements associated with insulin resistance syndrome and colorectal cancer in male smokers. *Am J Epidemiol*, 164(7):652–64. doi:10.1093/aje/kwj253 PMID:16877536

Boyle T, Fritschi L, Tabatabaei SM, Ringwald K, Heyworth JS (2014). Smoking, alcohol, diabetes, obesity, socioeconomic status, and the risk of colorectal cancer in a population-based case-control study. *Cancer Causes Control*, 25(12):1659–68. doi:10.1007/s10552-014-0470-7 PMID:25301194

Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ (2003). Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *N Engl J Med*, 348(17):1625–38. doi:10.1056/NEJMoa021423 PMID:12711737

Campbell PT, Cotterchio M, Dicks E, Parfrey P, Gallinger S, McLaughlin JR (2007). Excess body weight and colorectal cancer risk in Canada: associations in subgroups of clinically defined familial risk of cancer. *Cancer Epidemiol Biomarkers Prev*, 16(9):1735–44. doi:10.1158/1055-9965.EPI-06-1059 PMID:17855691

Campbell PT, Jacobs ET, Ulrich CM, Figueiredo JC, Poynter JN, McLaughlin JR, et al.; Colon Cancer Family Registry (2010). Case-control study of overweight, obesity, and colorectal cancer risk, overall and by tumor microsatellite instability status. *J Natl Cancer Inst*, 102(6):391–400. doi:10.1093/jnci/djq011 PMID:20208017

Choe EK, Kim D, Kim HJ, Park KJ (2013). Association of visceral obesity and early colorectal neoplasia. *World J Gastroenterol*, 19(45):8349–56. doi:10.3748/wjg.v19.i45.8349 PMID:24363527

Chung YW, Han DS, Park YK, Son BK, Paik CH, Lee HL, et al. (2006). Association of obesity, serum glucose and lipids with the risk of advanced colorectal adenoma and cancer: a case-control study in Korea. *Dig Liver Dis*, 38(9):668–72. doi:10.1016/j.dld.2006.05.014 PMID:16790371

Driver JA, Gaziano JM, Gelber RP, Lee IM, Buring JE, Kurth T (2007). Development of a risk score for colorectal cancer in men. *Am J Med*, 120(3):257–63. doi:10.1016/j.amjmed.2006.05.055 PMID:17349449

Engeland A, Tretli S, Austad G, Bjørge T (2005). Height and body mass index in relation to colorectal and gallbladder cancer in two million Norwegian men and women. *Cancer Causes Control*, 16(8):987–96. doi:10.1007/s10552-005-3638-3 PMID:16132807

Felix JF, Bradfield JP, Monnereau C, van der Valk RJ, Stergiakouli E, Chesi A, et al.; Bone Mineral Density in Childhood Study (BMDCS); Early Genetics and Lifecourse Epidemiology (EAGLE) consortium; Early Growth Genetics (EGG) Consortium; Bone Mineral Density in Childhood Study BMDCS (2016). Genome-wide association analysis identifies three new susceptibility loci for childhood body mass index. *Hum Mol Genet*, 25(2):389–403. doi:10.1093/hmg/ddv472 PMID:26604143

Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. (2013). GLOBOCAN 2012 v1.0, cancer incidence and mortality worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer. Available from: http://globocan.iarc.fr.

Fujino Y; Japan Collaborative Cohort Study for Evaluation of Cancer (2007). Anthropometry, development history and mortality in the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC). *Asian Pac J Cancer Prev*, 8(Suppl):105–12. PMID:18260709

Gao C, Patel CJ, Michailidou K, Peters U, Gong J, Schildkraut J, et al.; Colorectal Transdisciplinary Study (CORECT); Discovery, Biology and Risk of Inherited Variants in Breast Cancer (DRIVE); Elucidating Loci Involved in Prostate Cancer Susceptibility (ELLIPSE); Follow-up of Ovarian Cancer Genetic Association and Interaction Studies (FOCI); and Transdisciplinary

Research in Cancer of the Lung (TRICL) (2016). Mendelian randomization study of adiposity-related traits and risk of breast, ovarian, prostate, lung and colorectal cancer. *Int J Epidemiol*, 45(3):896–908. doi:10.1093/ije/dyw129 PMID:27427428

Hoffmeister M, Raum E, Winter J, Chang-Claude J, Brenner H (2007). Hormone replacement therapy, body mass, and the risk of colorectal cancer among postmenopausal women from Germany. *Br J Cancer*, 97(11):1486–92. doi:10.1038/sj.bjc.6604066 PMID:17987040

Hou L, Ji BT, Blair A, Dai Q, Gao YT, Potter JD, et al. (2006). Body mass index and colon cancer risk in Chinese people: menopause as an effect modifier. *Eur J Cancer*, 42(1):84–90. doi:10.1016/j.ejca.2005.09.014 PMID:16321519

Hughes LAE, Simons CCJM, van den Brandt PA, Goldbohm RA, van Engeland M, Weijenberg MP (2011). Body size and colorectal cancer risk after 16.3 years of follow-up: an analysis from the Netherlands Cohort Study. *Am J Epidemiol*, 174(10):1127–39. doi:10.1093/aje/kwr247 PMID:21984660

IARC (2002). Weight control and physical activity. Lyon, France: IARC Press (IARC Handbooks of Cancer Prevention, Vol. 6). Available from: http://publications.iarc.fr/376.

Kabat GC, Xue X, Kamensky V, Lane D, Bea JW, Chen C, et al. (2015). Risk of breast, endometrial, colorectal, and renal cancers in postmenopausal women in association with a body shape index and other anthropometric measures. *Cancer Causes Control*, 26(2):219–29. doi:10.1007/s10552-014-0501-4 PMID:25430815

Keum N, Lee DH, Kim R, Greenwood DC, Giovannucci EL (2015). Visceral adiposity and colorectal adenomas: dose-response meta-analysis of observational studies. *Ann Oncol*, 26(6):1101–9. doi:10.1093/annonc/mdu563 PMID:25480876

Kitahara CM, Berndt SI, de González AB, Coleman HG, Schoen RE, Hayes RB, et al. (2013). Prospective investigation of body mass index, colorectal adenoma, and colorectal cancer in the prostate, lung, colorectal, and ovarian cancer screening trial. *J Clin Oncol*, 31(19):2450–9. doi:10.1200/JCO.2012.48.4691 PMID:23715565

Kuriyama S, Tsubono Y, Hozawa A, Shimazu T, Suzuki Y, Koizumi Y, et al. (2005). Obesity and risk of cancer in Japan. *Int J Cancer*, 113(1):148–57. doi:10.1002/ijc.20529 PMID:15386435

Laake I, Thune I, Selmer R, Tretli S, Slattery ML, Veierød MB (2010). A prospective study of body mass index, weight change, and risk of cancer in the proximal and distal colon. *Cancer Epidemiol Biomarkers Prev*, 19(6):1511–22. doi:10.1158/1055-9965.EPI-09-0813 PMID:20501754

Larsson SC, Rutegård J, Bergkvist L, Wolk A (2006). Physical activity, obesity, and risk of colon and rectal cancer in a cohort of Swedish men. *Eur J Cancer*, 42(15):2590–7. doi:10.1016/j.ejca.2006.04.015 PMID:16914307

Lin J, Zhang SM, Cook NR, Rexrode KM, Lee I-M, Buring JE (2004). Body mass index and risk of colorectal cancer in women (United States). *Cancer Causes Control*, 15(6):581–9. doi:10.1023/B:-CACO.0000036168.23351.f1 PMID:15280637

Locke AE, Kahali B, Berndt SI, Justice AE, Pers TH, Day FR, et al.; LifeLines Cohort Study; ADIPOGen Consortium; AGEN-BMI Working Group; CARDIOGRAMplusC4D Consortium; CKDGen Consortium; GLGC; ICBP; MAGIC Investigators; MuTHER Consortium; MIGen Consortium; PAGE Consortium; ReproGen Consortium; GENIE Consortium; International Endogene Consortium (2015). Genetic studies of body mass index yield new insights for obesity biology. *Nature*, 518(7538):197–206. doi:10.1038/nature14177 PMID:25673413

Lukanova A, Björ O, Kaaks R, Lenner P, Lindahl B, Hallmans G, et al. (2006). Body mass index and cancer: results from the Northern Sweden Health and Disease Cohort. *Int J Cancer*, 118(2):458–66. doi:10.1002/ijc.21354 PMID:16049963

Lundqvist E, Kaprio J, Verkasalo PK, Pukkala E, Koskenvuo M, Söderberg KC, et al. (2007). Co-twin control and cohort analyses of body mass index and height in relation to breast, prostate, ovarian, corpus uteri, colon and rectal cancer among Swedish and Finnish twins. *Int J Cancer*, 121(4):810–8. doi:10.1002/ijc.22746 PMID:17455257

Ma Y, Yang Y, Wang F, Zhang P, Shi C, Zou Y, et al. (2013). Obesity and risk of colorectal cancer: a systematic review of prospective studies. *PLoS One*, 8(1):e53916. doi:10.1371/journal.pone.0053916 PMID:23349764

MacInnis RJ, English DR, Haydon AM, Hopper JL, Gertig DM, Giles GG (2006b). Body size and composition and risk of rectal cancer (Australia). *Cancer Causes Control*, 17(10):1291–7. doi:10.1007/s10552-006-0074-y PMID:17111261

MacInnis RJ, English DR, Hopper JL, Gertig DM, Haydon AM, Giles GG (2006a). Body size and composition and colon cancer risk in women. *Int J Cancer*, 118(6):1496–500. doi:10.1002/ijc.21508 PMID:16187280

MacInnis RJ, English DR, Hopper JL, Haydon AM, Gertig DM, Giles GG (2004). Body size and composition and colon cancer risk in men. *Cancer Epidemiol Biomarkers Prev*, 13(4):553–9. PMID:15066919

Matsuo K, Mizoue T, Tanaka K, Tsuji I, Sugawara Y, Sasazuki S, et al.; Development and Evaluation of Cancer Prevention Strategies in Japan (2012). Association between body mass index and the colorectal cancer risk in Japan: pooled analysis of population-based cohort studies in Japan. *Ann Oncol*, 23(2):479–90. doi:10.1093/annonc/mdr143 PMID:21597097

Moghaddam AA, Woodward M, Huxley R (2007). Obesity and risk of colorectal cancer: a meta-analysis of 31 studies with 70,000 events. *Cancer Epidemiol Biomarkers Prev*, 16(12):2533–47. doi:10.1158/1055-9965.EPI-07-0708 PMID:18086756

Moore LL, Bradlee ML, Singer MR, Splansky GL, Proctor MH, Ellison RC, et al. (2004). BMI and waist circumference as predictors of lifetime colon cancer risk in Framingham Study adults. *Int J Obes Relat Metab Disord*, 28(4):559–67. doi:10.1038/sj.ijo.0802606 PMID:14770200

Ning Y, Wang L, Giovannucci EL (2010). A quantitative analysis of body mass index and colorectal cancer: findings from 56 observational studies. *Obes Rev*, 11(1):19–30. doi:10.1111/j.1467-789X.2009.00613.x PMID:19538439

Odegaard AO, Koh W-P, Yu MC, Yuan J-M (2011). Body mass index and risk of colorectal cancer in Chinese Singaporeans: the Singapore Chinese Health Study. *Cancer*, 117(16):3841–9. doi:10.1002/cncr.25936 PMID:21815135

Oh SW, Yoon YS, Shin SA (2005). Effects of excess weight on cancer incidences depending on cancer sites and histologic findings among men: Korea National Health Insurance Corporation Study. *J Clin Oncol*, 23(21):4742–54. doi:10.1200/JCO.2005.11.726 PMID:16034050

Oxentenko AS, Bardia A, Vierkant RA, Wang AH, Anderson KE, Campbell PT, et al. (2010). Body size and incident colorectal cancer: a prospective study of older women. *Cancer Prev Res (Phila)*, 3(12):1608–20. doi:10.1158/1940-6207.CAPR-10-0116 PMID:20719902

Pan SY, Johnson KC, Ugnat AM, Wen SW, Mao Y; Canadian Cancer Registries Epidemiology Research Group(2004). Association of obesity and cancer risk in Canada. *Am J Epidemiol*, 159(3):259–68. doi:10.1093/aje/kwh041 PMID:14742286

Park JY, Mitrou PN, Keogh RH, Luben RN, Wareham NJ, Khaw K-T (2012). Self-reported and measured anthropometric data and risk of colorectal cancer in the EPIC-Norfolk study. *Int J Obes*, 36(1):107–18. doi:10.1038/ijo.2011.61 PMID:21427695

Parr CL, Batty GD, Lam TH, Barzi F, Fang X, Ho SC, et al.; Asia-Pacific Cohort Studies Collaboration (2010). Body-mass index and cancer mortality in the Asia-Pacific Cohort Studies Collaboration: pooled analyses of 424,519 participants. *Lancet Oncol*, 11(8):741–52. doi:10.1016/S1470-2045(10)70141-8 PMID:20594911

Pischon T, Lahmann PH, Boeing H, Friedenreich C, Norat T, Tjønneland A, et al. (2006). Body size and risk of colon and rectal cancer in the European Prospective Investigation Into Cancer and Nutrition (EPIC). *J Natl Cancer Inst*, 98(13):920–31. doi:10.1093/jnci/djj246 PMID:16818856

Rapp K, Schroeder J, Klenk J, Stoehr S, Ulmer H, Concin H, et al. (2005). Obesity and incidence of cancer: a large cohort study of over 145,000 adults in Austria. *Br J Cancer*, 93(9):1062–7. doi:10.1038/sj.bjc.6602819 PMID:16234822

Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D; Million Women Study Collaboration (2007). Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *BMJ*, 335(7630):1134. doi:10.1136/bmj.39367.495995.AE PMID:17986716

Renehan AG, Flood A, Adams KF, Olden M, Hollenbeck AR, Cross AJ, et al. (2012). Body mass index at different adult ages, weight change, and colorectal cancer risk in the National Institutes of Health-AARP Cohort. *Am J Epidemiol*, 176(12):1130–40. doi:10.1093/aje/kws192 PMID:23186750

Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M (2008). Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *Lancet*, 371(9612):569–78. doi:10.1016/S0140-6736(08)60269-X PMID:18280327

Samanic C, Chow WH, Gridley G, Jarvholm B, Fraumeni JF Jr (2006). Relation of body mass index to cancer risk in 362,552 Swedish men. *Cancer Causes Control*, 17(7):901–9. doi:10.1007/s10552-006-0023-9 PMID:16841257

Samanic C, Gridley G, Chow W-H, Lubin J, Hoover RN, Fraumeni JF Jr (2004). Obesity and cancer risk among white and black United States veterans. *Cancer Causes Control*, 15(1):35–43. doi:10.1023/B:CACO.0000016573.79453.ba PMID:14970733

Slattery ML, Ballard-Barbash R, Edwards S, Caan BJ, Potter JD (2003). Body mass index and colon cancer: an evaluation of the modifying effects of estrogen (United States). *Cancer Causes Control*, 14(1):75–84. doi:10.1023/A:1022545017867 PMID:12708728

Song Y-M, Sung J, Ha M (2008). Obesity and risk of cancer in postmenopausal Korean women. *J Clin Oncol*, 26(20):3395–402. doi:10.1200/JCO.2007.15.7867 PMID:18612154

Sriamporn S, Wiangnon S, Suwanrungruang K, Rungsrikaji D, Sukprasert A, Thipsuntornsak N, et al. (2007). Risk factors for colorectal cancer in northeast Thailand: lifestyle related. *Asian Pac J Cancer Prev*, 8(4):573–7. PMID:18260731

Terry P, Giovannucci E, Bergkvist L, Holmberg L, Wolk A (2001). Body weight and colorectal cancer risk in a cohort of Swedish women: relation varies by age and cancer site. *Br J Cancer*, 85(3):346–9. doi:10.1054/bjoc.2001.1894 PMID:11487263

Terry PD, Miller AB, Rohan TE (2002). Obesity and colorectal cancer risk in women. *Gut*, 51(2):191–4. doi:10.1136/gut.51.2.191 PMID:12117878

Thrift AP, Gong J, Peters U, Chang-Claude J, Rudolph A, Slattery ML, et al. (2015). Mendelian randomization study of body mass index and colorectal cancer risk.

Cancer Epidemiol Biomarkers Prev, 24(7):1024–31. doi:10.1158/1055-9965.EPI-14-1309 PMID:25976416

Thygesen LC, Grønbaek M, Johansen C, Fuchs CS, Willett WC, Giovannucci E (2008). Prospective weight change and colon cancer risk in male US health professionals. *Int J Cancer*, 123(5):1160–5. doi:10.1002/ijc.23612 PMID:18546286

Wang Y, Jacobs EJ, Patel AV, Rodríguez C, McCullough ML, Thun MJ, et al. (2008). A prospective study of waist circumference and body mass index in relation to colorectal cancer incidence. *Cancer Causes Control*, 19(7):783–92. doi:10.1007/s10552-008-9141-x PMID:18322811

Wang Y, Jacobs EJ, Teras LR, Pavluck AL, Rodriguez C, Thun MJ, et al. (2007). Lack of evidence for effect modification by estrogen of association between body mass index and colorectal cancer risk among postmenopausal women. *Cancer Causes Control*, 18(8):793–9. doi:10.1007/s10552-007-9009-5 PMID:17619155

WCRF/AICR (2007). Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington (DC), USA: American Institute for Cancer Research. Available from: http://www.aicr.org/assets/docs/pdf/reports/Second_Expert_Report.pdf.

WCRF/AICR (2011). Continuous Update Project Report. Food, nutrition, physical activity, and the prevention of colorectal cancer. Washington (DC), USA: American Institute for Cancer Research. Available from: https://www.wcrf.org/sites/default/files/Colorectal-Cancer-2011-Report.pdf.

Wei EK, Giovannucci E, Wu K, Rosner B, Fuchs CS, Willett WC, et al. (2004). Comparison of risk factors for colon and rectal cancer. *Int J Cancer*, 108(3):433–42. doi:10.1002/ijc.11540 PMID:14648711