

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/m² 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/m² 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/m² 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/m² compared with BMI < 23 kg/m², 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/m² compared with BMI < 23 kg/m², 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/m² compared with BMI < 23 kg/m², 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/m² compared with BMI < 19.0 kg/m², 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/m² compared with BMI < 19.0 kg/m², 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/m² 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/m² 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/m² 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 ($P_{\text{difference}} = 0.10$). In addition, there was a positive association between BMI and CRC risk in women (GRS-related OR per 5 kg/m² 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; $P_{\text{difference}} = 0.01$); although there was no strong evidence from Mendelian randomization analyses for an association in men (GRS-related OR per 5 kg/m² 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 ($P_{\text{difference}} = 0.70$). [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/m² in adult BMI [assuming that a standard deviation was equivalent to 4.5 kg/m²]. 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 [<i>P</i> _{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 (<i>P</i> _{trend} = 0.06)
	61 463 Women Incidence	Rectum	BMI < 22 22–24.2 24.2–26.7 > 26.7 [<i>P</i> _{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 [<i>P</i> _{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 (<i>P</i> _{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 [<i>P</i> _{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 Additionally adjusted for HRT use	
	495 477 Women Mortality		BMI 18.5–24.9 25–29.9 30–34.9 35–39.9 ≥ 40 [<i>P</i> _{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]		

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 [<i>P</i> _{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 [<i>P</i> _{trend}] WC < 87 87–93 93–99.3 ≥ 99.3 [<i>P</i> _{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	
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 WC Small Medium Large Extra large	67 69 21 17 61 46 33	1.0 1.3 (0.91–1.8) 1.5 (0.92–2.5) 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 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	White men: 16 704 1420	1.00 1.47 (1.39–1.55)	Age, calendar year	Obesity defined as discharge diagnosis of obesity: ICD-8: 277; ICD-9: 278.0
			Non-obese Obese	Black men: 3830 262	1.00 1.45 (1.28–1.64)		No significant differences in risk observed between White and Black veterans
	4 500 700 Men Incidence	Rectum	Obesity Non-obese Obese	White men: 9849 719	1.00 1.23 (1.14–1.33)	Age, calendar year	No significant differences in risk observed between White and Black veterans
			Non-obese Obese	Black men: 1773 93	1.00 1.11 (0.90–1.37)		
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	Rectum	BMI									
			< 23	210	1.0							
			23–24.9	141	1.10 (0.88–1.36)							
			25–29.9	207	1.11 (0.91–1.35)							
					≥ 30	113	1.28 (1.10–1.62)					
					[<i>P</i> _{trend}]		[0.05]					
	46 632 Men Incidence		BMI					Age, family history, physical activity, smoking, diet, screening history, alcohol consumption, height				
			< 23	24	1.0							
			23–24.9	42	1.16 (0.70–1.94)							
			25–29.9	55	0.93 (0.57–1.53)							
					≥ 30	11	1.03 (0.49–2.14)					
					[<i>P</i> _{trend}]		[0.70]					
87 733 Women Incidence	BMI											
	< 23	56	1.0									
	23–24.9	46	1.37 (0.92–2.02)									
	25–29.9	68	1.40 (0.98–2.01)									
			≥ 30	34	1.56 (1.01–2.42)							
			[<i>P</i> _{trend}]		[0.04]							
Engeland et al. (2005) Population-based cohort Norway 1963–2001	963 709 Men Incidence	Colon and rectum	BMI			Age at BMI measurement, birth cohort	Relationships similar for colon vs rectum					
			< 18.5	90	0.84 (0.68–1.03)							
			18.5–24.9	11 432	1.0							
			25–29.9	9953	1.15 (1.12–1.18)							
					≥ 30			1512	1.40 (1.32–1.48)			
					[<i>P</i> _{trend}]				[< 0.001]			
	1 038 010 Women Incidence		BMI						Age at BMI measurement, birth cohort	Relationships similar for colon vs rectum. In women, associations stronger for colon		
			< 18.5	298	1.04 (0.93–1.17)							
			18.5–24.9	11 136	1.0							
			25–29.9	8780	1.02 (0.99–1.05)							
					≥ 30			3916			1.06 (1.02–1.10)	
					[<i>P</i> _{trend}]						[0.01]	
Kuriyama et al. (2005) Population-based prospective cohort Japan 1984–1992	12 485 Men Incidence	Colon and rectum	BMI			Age, smoking, alcohol consumption, diet, health insurance						
			< 18.5–24.9	114	1.00							
			25–27.5	25	1.04 (0.67–1.60)							
			27.5–29.9	11	1.58 (0.85–2.94)							
			≥ 30	5	1.78 (0.73–4.38)							
			[<i>P</i> _{trend}]		[0.3710]							

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	73	1.00		
			25–27.5	22	1.11 (0.69–1.80)		
			27.5–29.9	11	1.28 (0.68–2.43)		
			≥ 30 [<i>P</i> _{trend}]	9	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				Age, smoking, alcohol consumption, physical activity, family history, residence area
			< 18.5	14	1.00 (0.62–1.63)		
			18.5–22.9	359	1.00		
			23.0–24.9	316	1.24 (1.07–1.43)		
			25.0–26.7	190	1.33 (1.13–1.57)		
			27.0–29.9	63	1.07 (0.83–1.38)		
	781 283 Men Incidence	Rectosigmoid	BMI				Age, smoking, alcohol consumption, physical activity, family history, residence area
			< 18.5	20	0.64 (0.36–1.13)		
			18.5–22.9	606	1.00		
			23.0–24.9	480	1.06 (0.92–1.22)		
			25.0–26.7	326	1.29 (1.10–1.52)		
27.0–29.9	117	1.15 (0.91–1.46)					
≥ 30 [<i>P</i> _{trend}]	14	1.08 (0.56–2.10) [0.003]					
Rapp et al. (2005) VHM&PP (population-based cohort) Austria 1985–2002	67 447 Men Incidence	Colon	BMI				Age, smoking status, occupational group
			18.5–24.9	86	1.00		
			25–29.9	128	1.14 (0.86–1.50)		
			30–34.9	39	1.56 (1.06–2.30)		
			≥ 35 [<i>P</i> _{trend}]	7	2.48 (1.15–5.39) [0.005]		
	78 484 Women Incidence		BMI				Age, smoking status, occupational group
			18.5–24.9	122	1.00		
			25–29.9	106	1.13 (0.86–1.47)		
			30–34.9	35	1.11 (0.76–1.62)		
≥ 35 [<i>P</i> _{trend}]	8	0.88 (0.43–1.81) [0.73]					

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

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

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 (<i>n</i> = 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)		
			[<i>P</i> _{trend}]		[0.48]		
			WC				
< 94	57	1.0	Age, country of birth	Similar results in women (<i>n</i> = 24 247), no sex interaction			
94–101.9	43	1.3 (0.9–1.9)					
≥ 102	34	1.4 (0.9–2.2)					
[<i>P</i> _{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)		
			[<i>P</i> _{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)					
[<i>P</i> _{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				Age, centre, smoking, education level, alcohol consumption, physical activity, diet	
			< 23.6	87	1.0			
			23.6–25.3	96	0.92 (0.68–1.23)			
			25.4–27	120	1.02 (0.77–1.35)			
			27.1–29.3	137	1.09 (0.83–1.45)			
			≥ 29.4	135 123	1.06 (0.79–1.42)			
	[<i>P</i> _{trend}]		[0.40]					
			WC				Age, centre, smoking, education level, alcohol consumption, physical activity, diet, height	
	< 70.2	62	1.0					
	70.2–75.8	91	1.10 (0.80–1.52)					
	75.9–80.9	125	1.23 (0.90–1.68)					
	81–88.9	135	1.25 (0.91–1.70)					
≥ 89	149	1.48 (1.08–2.03)						
[<i>P</i> _{trend}]		[0.008]						
129 731 Men Incidence	Rectum	BMI				Age, centre, smoking, education level, alcohol consumption, physical activity, diet	WC, null association	
		< 23.6	52	1.0				
		23.6–25.3	52	0.88 (0.60–1.30)				
		25.4–27	58	0.96 (0.66–1.40)				
		27.1–29.3	69	1.11 (0.77–1.62)				
		≥ 29.4	64	1.05 (0.72–1.55)				
[<i>P</i> _{trend}]		[0.47]						
238 546 Women Incidence	Colon	BMI				Age, centre, smoking, education level, alcohol consumption, physical activity, diet	WC, null association	
		< 23.6	47	1.0				
		23.6–25.3	44	0.78 (0.51–1.18)				
		25.4–27	72	1.14 (0.78–1.66)				
		27.1–29.3	63	0.95 (0.64–1.41)				
		≥ 29.4	65	1.06 (0.71–1.58)				
[<i>P</i> _{trend}]		[0.51]						
Samanic et al. (2006) Swedish Construction Worker Cohort Sweden 1971–1999	362 552 Men Incidence	Colon	BMI			Age, year, smoking status		
			18.5–24.9	763	1.00			
			25–29.9	842	1.24 (1.12–1.37)			
			≥ 30	190	1.74 (1.48–2.04)			
[<i>P</i> _{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	
Samanic et al. (2006) (cont.)	362 552	Rectum	BMI			Age, year, smoking status		
	Men		18.5–24.9	626	1.00			
	Incidence		25–29.9	610	1.08 (0.96–1.21)			
			≥ 30	126	1.36 (1.13–1.66)			
			[<i>P</i> _{trend}]		[< 0.01]			
Adams et al. (2007) NIH-AARP cohort USA 1995–2000	307 708	Colon	BMI			Age, alcohol consumption, smoking, supplemental calcium intake, consumption of red meat		
	Men		18.5–22.9	136	1.0			
	Incidence		23–24.9	260	1.11 (0.90–1.37)			
			25–27.4	479	1.22 (1.01–1.48)			
			27.5–29.9	367	1.44 (1.18–1.76)			
			30–32.5	219	1.53 (1.23–1.90)			
			32.5–34.9	110	1.57 (1.22–2.03)			
			35–39.9	76	1.71 (1.29–2.27)			
			≥ 40	29	2.39 (1.59–3.58)			
			[<i>P</i> _{trend}]		[< 0.0005]			
	209 436	Rectum	BMI			Age, alcohol consumption, smoking, supplemental calcium intake, consumption of red meat	Additionally adjusted for HRT use	Similar findings by HRT status
	Women		18.5–22.9	151	1.0			
	Incidence		23–24.9	141	1.20 (0.95–1.51)			
25–27.4			172	1.29 (1.03–1.60)				
27.5–29.9			106	1.31 (1.01–1.68)				
30–32.5		77	1.28 (0.97–1.69)					
			32.5–34.9	42	1.13 (0.80–1.60)			
			35–39.9	52	1.46 (1.06–2.02)			
			≥ 40	28	1.49 (0.98–2.25)			
			[<i>P</i> _{trend}]		[0.02]			
307 708	Rectum	BMI			Age, alcohol consumption, smoking, supplemental calcium intake, consumption of red meat			
Men		18.5–22.9	74	1.0				
Incidence		23–24.9	101	0.78 (0.58–1.06)				
		25–27.4	218	1.01 (0.77–1.31)				
		27.5–29.9	135	0.96 (0.72–1.28)				
		30–32.5	74	0.94 (0.68–1.30)				
		32.5–34.9	42	1.10 (0.75–1.61)				
			≥ 35	33	1.0 (0.68–1.58)			
			[<i>P</i> _{trend}]		[0.31]			

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 [<i>P</i> _{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 [<i>P</i> _{trend}]	190 171 20	1.0 1.26 (1.05–1.52) 1.62 (1.09–2.42) [<i>P</i> _{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)	24 821 older twins (mean baseline age, 56 yr)	Colon and rectum	BMI < 18.5	7	1.0 (0.5–2.1)	Smoking, sex, country, physical activity, education level, diabetes	No association with rectal cancer
Twin cohorts	56 yr	18.5–24.9	274	1.0			
Sweden and Finland 1961–2004	10 804 men and 14 017 women	25–29.9	196	1.1 (0.9–1.3)			
Incidence		≥ 30	36	1.3 (0.9–1.8) [0.12]			
	43 328 younger twins (mean baseline age, 30 yr)		BMI < 18.5	4	0.6 (0.2–1.7)	Smoking, physical activity, education level, diabetes	No association with rectal cancer
	30 yr	18.5–24.9	146	1.0			
	20 992 men and 22 336 women	25–29.9	47	1.0 (0.7–1.4)			
Incidence		≥ 30	7	1.1 (0.5–2.5) [0.53]			
Reeves et al. (2007)	1.2 million Women	Colon and rectum	BMI < 22.5	789	1.02 (0.95–1.10)	Age, region, SES, reproductive history, smoking, alcohol consumption, physical activity, time since menopause, HRT use	
Population-based cohort	Incidence	22.5–24.9	1034	1.00			
United Kingdom 1996–2001		25.0–27.4	913	1.04 (0.97–1.11)			
		27.5–29.9	555	1.01 (0.93–1.10)			
		≥ 30	717	1.01 (0.94–1.09) 1.00 (0.92–1.08)			
Wang et al. (2007)	73 842 Women	Colon and rectum	BMI < 18.5–24.9	399	1.0	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)
Cancer Prevention Study II (CPS II)		25–29.9	274	1.08 (0.93–1.27)			
Nutrition Cohort USA		≥ 30	141	1.19 (0.97–1.45) [0.04]			
1992–2003		[<i>P</i> _{trend}]					
Song et al. (2008)	107 481 Women	Colon (above rectosigmoid junction)	BMI < 18.5	11	0.94 (0.37–2.39)	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
Korean medical insurance cohort	Incidence	18.5–20.9	46	1.03 (0.63–1.70)			
Republic of Korea 1994–2003		21–22.9	86	1.00			
		23.0–24.9	141	1.69 (1.17–2.44)			
		25.0–26.9	129	1.73 (1.18–2.53)			
		27.0–29.9	64	1.21 (0.77–1.90)			
		≥ 30	32	2.43 (1.40–4.23) [1.05 (1.02–1.09)]			
		[risk per 1 kg/m ²]					

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 [<i>P</i> _{trend}] WC < 95 95–105 105–120 ≥ 120 [<i>P</i> _{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			Height, education level, physical activity, smoking, alcohol consumption, NSAID use, multivitamin use, screening history, HRT use	
			< 18.5–24.9	156	1.0		
			25–29.9	97	0.92 (0.71–1.19)		
			30–34.9	44	1.25 (0.88–1.76)		
			≥ 35	17	1.40 (0.84–2.36)		
			[<i>P</i> _{trend}]		[0.18]		
	44 068 Men Incidence	Rectum	WC			Height, education level, physical activity, smoking, alcohol consumption, NSAID use, multivitamin use, screening history, HRT use	WC, also null association
			< 85	158	1.0		
			85–95	109	1.01 (0.79–1.29)		
			95–110	104	1.27 (0.98–1.64)		
			≥ 110	36	1.75 (1.20–2.54)		
			[<i>P</i> _{trend}]		[0.003]		
51 083 Women Incidence	Colon	BMI			Height, education level, physical activity, smoking, alcohol consumption, NSAID use, multivitamin use, screening history; for women, also adjusted for HRT use	Similar association with WC	
		< 18.5–24.9	37	1.0			
		25–29.9	31	1.34 (0.82–2.17)			
		30–34.9	19	2.62 (1.48–4.66)			
		≥ 35	6	2.67 (1.09–6.54)			
		[<i>P</i> _{trend}]		[0.001]			
Andreotti et al. (2010) Agricultural workers USA 1993–2005	39 628 Men Incidence	Colon	BMI			Race, education level, family history of colon cancer	
			< 18.5	1	–		
			18.5–24.9	44	1.0		
			25.0–29.9	112	1.26 (0.86–1.86)		
			30–34.9	58	1.88 (1.23–2.91)		
			≥ 35	15	2.03 (1.05–3.93)		
per 1 kg/m ²		1.05 (1.02–1.09)					

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	Rectum	BMI					
			< 18.5	1	–			
			18.5–24.9	40	1.0			
			25.0–29.9	49	1.48 (0.97–2.26)			
			30–34.9	19	1.36 (0.79–2.36)			
	≥ 35		4	–				
	39 628 Men Incidence		per 1 kg/m ² [<i>P</i> _{trend}]	1.00 (0.96–1.04) [0.92]				
			BMI					
			< 18.5	0	–			
			18.5–24.9	23	1.0			
25.0–29.9		53	0.96 (0.51–1.82)					
Bassett et al. (2010) Population-based cohort Australia 1990–2007	16 188 Men Incidence	Colon	BMI			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	13	0.60 (0.32–1.13)			
			23–24.9	38	1.0			
			25.0–29.9	160	1.31 (0.91–1.87)			
			≥ 30	66	1.51 (1.00–2.28)			
	23 438 Women Incidence		[<i>P</i> _{trend}]	[< 0.01]				
			BMI					
			< 23	64	0.95 (0.67–1.36)			
			23–24.9	59	1.0			
			25.0–29.9	102	0.84 (0.61–1.17)			
	≥ 30	67	1.00 (0.70–1.44)					
	[<i>P</i> _{trend}]	[0.90]						

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 [<i>P</i> _{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 [<i>P</i> _{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 [<i>P</i> _{trend}] WC, quartiles Q1 Q2 Q3 Q4 [<i>P</i> _{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
				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)	424 519	Colon	BMI	429 total		Age, sex, tobacco use	Stronger positive association in obese men	
Pooled analysis of 39 cohort studies	Men and women Incidence		< 12–18.4		0.63 (0.26–1.56)			
Asia, Australia, and New Zealand			18.5–24.9		1.0			
1961–1999, median follow-up 4 yr			25–29.9		1.13 (0.94–1.36)			
	424 519	Rectum	BMI	233 total		Age, sex, tobacco use		
	Men and women Mortality		< 12–18.4		0.86 (0.37–2.02)			
			18.5–24.9		1.0			
			25–29.9		1.44 (1.11–1.86)			
			≥ 30		1.50 (1.13–1.99)			
			[<i>P</i> _{trend}]		[0.02]			
Hughes et al. (2011)	58 297	Colon and rectum	BMI, quintiles			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, <i>P</i> _{trend} significant. BMI at age 20 yr weakly associated	
Population-based cohort	Men Incidence		Q1	232	1.0			
The Netherlands 1986–2002			Q2	238	0.95 (0.74–1.24)			
			Q3	240	0.99 (0.77–1.28)			
			Q4	247	1.05 (0.81–1.36)			
			Q5	254	1.25 (0.96–1.62)			
			[<i>P</i> _{trend}]		[0.08]			
	62 573		BMI, quintiles			Age, diet, occupation, physical activity, education level, family history, alcohol consumption, smoking		BMI at age 20 yr, null association
	Women Incidence		Q1	228	1.0			Rectal cancer also not associated with BMI
			Q2	211	0.88 (0.69–1.13)			
			Q3	223	0.94 (0.73–1.20)			
			Q4	222	0.91 (0.71–1.16)			
			Q5	222	0.97 (0.76–1.24)			
			[<i>P</i> _{trend}]		[0.90]			

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 [<i>P</i> _{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 (<i>P</i> _{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 [<i>P</i> _{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 [<i>P</i> _{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 [<i>P</i> _{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				Age, area, smoking, alcohol consumption, diet, physical activity	
			< 19	59	0.91 (0.65–1.27)			
			19–20.9	179	0.98 (0.80–1.21)			
			21–22.9	325	1.12 (0.94–1.33)			
			23–24.9	284	1.0			
			25–26.9	158	1.12 (0.91–1.37)			
			27–29.9	80	1.20 (0.91–1.58)			
	≥ 30	26	1.57 (0.97–2.53)					
			[<i>P</i> _{trend}]		[0.20]			
	183 457 Women Incidence	Rectum	BMI				Age, area, smoking, alcohol consumption, diet, physical activity	
			< 19	53	1.44 (0.99–2.08)			
			19–20.9	97	1.12 (0.84–1.50)			
			21–22.9	147	1.05 (0.81–1.35)			
			23–24.9	284	1.0			
25–26.9			80	0.88 (0.64–1.20)				
27–29.9			54	0.99 (0.70–1.39)				
≥ 30	20	1.39 (0.81–2.39)						
		[<i>P</i> _{trend}]		[0.785]				
Park et al. (2012) EPIC-Norfolk study cohort England 1993–2006	11 166 Men Incidence	Colon and rectum	BMI				Age, sex, smoking, alcohol consumption, education level, exercise, family history, diet	WC, also null association
			< 23.9	67	1.00			
			23.9–25.5	41	0.75 (0.50–1.12)			
			25.5–26.9	30	0.74 (0.48–1.14)			
			27–28.8	32	0.90 (0.58–1.38)			
			≥ 28.9	27	0.97 (0.61–1.54)			
					[<i>P</i> _{trend}]			
	13 078 Women Incidence	Colon and rectum	BMI				Age, sex, smoking, alcohol consumption, education level, exercise, family history, diet	WC, null association
			< 23.9	34	1.00			
			23.9–25.5	31	1.20 (0.72–1.98)			
			25.5–26.9	44	1.87 (1.17–2.99)			
			27–28.8	21	1.10 (0.62–1.93)			
			≥ 28.9	30	1.97 (1.18–3.30)			
					[<i>P</i> _{trend}]			

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			Age, sex, smoking, alcohol consumption, education level, exercise, family history, diet						
			< 73	20	1.00							
			73–78	22	0.86 (0.46–1.62)							
			78–83.3	30	1.16 (0.65–2.06)							
			83.4–90.4	41	1.52 (0.88–2.62)							
≥ 90.5	47	1.65 (0.97–2.86)										
			[<i>P</i> _{trend}]		[0.001]							
Renehan et al. (2012) NIH-AARP cohort USA 1995–2006	168 294 Men Incidence	Colon	BMI			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)					
			< 18.5	6	0.89 (0.39–2.02)							
			18.5–21.9	98	1.0							
			22.0–22.9	93	0.91 (0.68–1.22)							
			23.0–24.9	349	1.01 (0.80–1.27)							
			25.0–27.4	600	1.07 (0.86–1.34)							
			27.5–29.9	438	1.26 (1.01–1.58)							
			30.0–32.4	249	1.29 (1.01–1.64)							
			32.5–34.9	124	1.33 (1.01–1.75)							
			≥ 35	113	1.53 (1.16–2.03)							
								[<i>P</i> _{trend}]	[< 0.0001]			
			105 385 Women Incidence					BMI			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
								< 18.5	14	1.33 (0.76–2.30)		
18.5–21.9	148	1.0										
22.0–22.9	68	1.00 (0.75–1.34)										
23.0–24.9	176	1.08 (0.87–1.35)										
25.0–27.4	207	1.11 (0.89–1.38)										
27.5–29.9	127	1.15 (0.90–1.47)										
30.0–32.4	82	1.00 (0.76–1.32)										
32.5–34.9	54	1.07 (0.78–1.48)										
≥ 35	86	1.23 (0.93–1.64)										
			[<i>P</i> _{trend}]	[0.20]								

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				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)
			< 18.5	4	1.63 (0.58–4.59)			
			18.5–21.9	37	1.0			
			22.0–22.9	45	1.22 (0.78–1.91)			
			23.0–24.9	150	1.20 (0.82–1.74)			
			25.0–27.4	215	1.06 (0.74–1.53)			
			27.5–29.9	149	1.15 (0.79–1.67)			
	30.0–32.4	78	0.99 (0.65–1.49)					
	32.5–34.9	44	1.22 (0.77–1.92)					
	≥ 35	40	1.43 (0.90–2.28)					
			[P_{trend}]		[0.51]			
	105 385 Women Incidence	Rectum	BMI				Age, race, education level, physical activity, smoking, alcohol consumption, HRT use	BMI at ages 18, 35, and 50 yr also null association
			< 18.5	6	1.94 (0.82–4.58)			
			18.5–21.9	43	1.0			
22.0–22.9			22	1.15 (0.68–1.93)				
23.0–24.9			50	1.07 (0.71–1.63)				
25.0–27.4			64	1.21 (0.82–1.81)				
27.5–29.9			32	1.01 (0.63–1.61)				
30.0–32.4	20	0.85 (0.49–1.47)						
32.5–34.9	20	1.45 (0.84–2.51)						
≥ 35	25	1.28 (0.76–2.16)						
		[P_{trend}]		[0.45]				

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	Similar findings by HRT status
			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)		
			[<i>P</i> _{trend}]		[0.13]		
	127 605 Women Incidence	Rectum	Weight change from age 20 yr				
			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)		
			[<i>P</i> _{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)			
		[<i>P</i> _{trend}]		[0.16]			
127 605 Women Incidence	Rectum	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)			
		[<i>P</i> _{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	Colon and rectum	BMI < 18.5–24.9	128	1.0	Age, study centre, screening history, race/ethnicity, tobacco use, HRT use	Proximal, distal, and rectal associations with BMI all similar, but only proximal significant
	Incidence		25–29.9	270	1.19 (0.96–1.48)		
			≥ 30	148	1.48 (1.16–1.89)		
			[<i>P</i> _{trend}]		[0.002]		
	37 562 Women		BMI < 18.5–24.9	156	1.0	Age, study centre, screening history, race/ethnicity, tobacco use, HRT use	All subsites null for BMI associations
	Incidence	25–29.9	154	1.07 (0.86–1.34)			
		≥ 30	106	1.03 (0.80–1.33)			
			[<i>P</i> _{trend}]		[0.74]		
Bhaskaran et al. (2014) Health system clinical database United Kingdom 1987–2012	5 243 978 Men and women	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)
	Incidence						
	5 243 978 Men and women	Rectum	per 5 kg/m ²	6123	1.04 (1.00–1.08)		Similar association in never-smokers
	Incidence						

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	1908 total	1.0	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	
			Q1		1.18 (1.01–1.38)			
			Q2		1.15 (0.98–1.38)			
			Q3		1.27 (1.09–1.48)			
			Q4		1.44 (1.23–1.68)			
			Q5		[< 0.0001]			
			[<i>P</i> _{trend}]					
			WC, quintiles	1908 total	1.0			Similar findings by HRT status
			Q1		1.49 (1.26–1.75)			
			Q2		1.36 (1.15–1.61)			
Q3		1.67 (1.41–1.96)						
Q4		1.90 (1.61–2.25)						
Q5		[< 0.0001]						
[<i>P</i> _{trend}]								

ATBC, Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; BMI, body mass index (in kg/m²); 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: < 22.9 23–24.4 25–25.9 26–28.7 > 28.7 [P _{trend}]	Women: < 20.3 20.4–22.6 22.7–23.9 24–26.1 > 26.1	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 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				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
		Men: < 25	NR	1.00		
		25– < 30		1.54 (1.27–1.86)		
		≥ 30		2.16 (1.68–2.78)		
		[<i>P</i> _{trend}]		< 0.0001		
		Women: < 25	NR	1.00		
25– < 30		1.22 (0.98–1.52)				
≥ 30		1.77 (1.35–2.32)				
[<i>P</i> _{trend}]		< 0.0001				
Rectal cancer: Men: 858 Women: 589 Population	Men: < 25	NR	1.00			
	25– < 30		1.41 (1.15–1.71)			
	≥ 30		1.75 (1.35–2.28)			
	[<i>P</i> _{trend}]		0.0001			
	Women: < 25	NR	1.00			
	25– < 30		1.28 (1.02–1.61)			
≥ 30		1.50 (1.11–2.02)				
[<i>P</i> _{trend}]		0.0045				
Chung et al. (2006) Republic of Korea 2002–2004	CRC: 105 Hospital	BMI			Age, sex, glucose, triglycerides, cholesterol	
		< 22.9	37	1.0		
		23.0–24.9	32	1.4 (0.6–3.3)		
≥ 25.0	36	2.3 (0.9–5.8)				
Hou et al. (2006) China (Shanghai) 1990–1993	Colon cancer: Men: 461 Women: 465 Population	BMI, quintiles	Men:		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 (<i>P</i> _{interaction} = 0.03)
		< 19.2	80	1.0		
		19.2–20.3	85	1.0 (0.7–1.4)		
		20.4–21.3	68	1.0 (0.7–1.4)		
		21.4–22.8	109	1.2 (0.9–1.8)		
		> 22.8	119	1.7 (1.1–2.4)		
[<i>P</i> _{trend}]		0.005				

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)		
		[<i>P</i> _{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)		
		[<i>P</i> _{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)		
		[<i>P</i> _{trend}]		[0.03]		
Campbell et al. (2007) Canada (Ontario and Newfoundland) 1997–2003	CRC: Men: 1292 Women: 1404 Population	BMI 18.5–24.99 25–29.99 ≥ 30	Men: 298 627 322	1.0 1.29 (1.07–1.56) 1.80 (1.43–2.27)	Age, education level, consumption of red meat, physical activity, province of residence, CRC screening	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)
		BMI 18.5–24.99 25–29.99 ≥ 30	Women: 616 443 260	1.0 0.99 (0.83–1.20) 0.94 (0.75–1.18)	endoscopy, history of high cholesterol/ triglycerides	
		BMI in estrogen-positive women			Women only: menopausal status, use of postmenopausal HRT	
		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 25–29.99 ≥ 30	356 295 180	1.0 1.08 (0.85–1.37) 1.05 (0.79–1.40)		
Hoffmeister et al. (2007) Germany 2003–2004	CRC: Women: 208 Population	BMI < 23 23– < 25 25– < 27 27– < 30 ≥ 30 [<i>P</i> _{trend}] BMI in never-users of HRT < 23 23– < 25 25– < 27 27– < 30 ≥ 30 [<i>P</i> _{trend}] BMI in ever-users of HRT < 23 23– < 25 25– < 27 27– < 30 ≥ 30 [<i>P</i> _{trend}]	51 39 25 46 40 24 31 18 33 31 27 8 7 13 9	1.00 0.80 (0.42–1.53) 0.78 (0.39–1.58) 1.71 (0.89–3.31) 1.82 (0.92–3.62) [0.02] 1.00 1.31 (0.55–3.12) 1.60 (0.58–4.44) 2.76 (1.07–7.12) 3.30 (1.25–8.72) [0.01] 1.00 0.49 (0.16–1.48) 0.36 (0.11–1.13) 1.18 (0.40–3.48) 0.89 (0.29–2.75) [0.96]	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
Sriamporn et al. (2007) North-eastern Thailand 2002–2006	CRC: 253 Hospital	BMI < 25 ≥ 25 [<i>P</i> _{trend}]	34	1 0.5 (0.3–0.8) [< 0.5]	Age, sex, place of residence	

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 < 18.5 18.5–24.99 25–29.99 ≥ 30 per 5 kg/m ² [P _{trend}]	Women: 24 404 252 212	1.77 (0.91–3.45) 1.00 1.00 (0.80–1.25) 1.34 (1.03–1.75) 1.20 (1.10–1.32) [< 0.001]	Age, endoscopy screening, smoking Women only: postmenopausal HRT use	Only microsatellite stable tumours showed increased risk at higher BMI
		< 18.5 18.5–24.99 25–29.99 ≥ 30 per 5 kg/m ² [P _{trend}]	Men: 2 223 408 222	0.51 (0.09–2.89) 1.00 1.33 (1.06–1.68) 1.79 (1.33–2.40) 1.30 (1.15–1.47) [< 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 [P _{trend}]		1.06 (1.01–1.12) [< 0.01]		
		Loss	Men: 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 [P _{trend}]		1.08 (1.03–1.14) [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 [<i>P</i> _{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/m²); 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/m ² 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/m ² increase	1.09 (1.05–1.12)	
	18 prospective studies in men 14 894 incident cases	Rectum	BMI per 5 kg/m ² increase	1.09 (1.06–1.12)	
	14 prospective studies in women 9052 incident cases	Rectum	BMI per 5 kg/m ² 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/m ² 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/m²); CI, confidence interval; N/A, not applicable; SD, standard deviation

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