

2.2.11 Cancer of the endometrium

Cancer of the endometrium is the sixth most common cancer diagnosis in women ([WCRF/AICR, 2013](#)). Known risk factors for endometrial cancer include exogenous estrogens, as delivered in menopausal estrogen replacement therapies unopposed with progesterone, and diabetes. Tobacco smoking is associated with reduced risk, by mechanisms that are not well understood. There are two subtypes of endometrial cancer: type 1, which is most common (accounting for about 80–90% of endometrial cancer), and type 2, which is more lethal but much less common (about 10–20%).

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 endometrium. The 2007 WCRF review concluded that there was convincing evidence of a positive association between body fatness and risk of endometrial cancer ([WCRF/AICR, 2007](#)), and this was later reaffirmed ([WCRF/AICR, 2013](#)).

(a) Cohort studies

The scientific evidence since 2000 includes 20 publications from cohort studies (excluding analyses that were later updated and analyses based on fewer than 100 incident cases). [Table 2.2.11a](#) presents those findings by BMI at baseline, with comments on findings according to smoking status, use of HRT, weight change over the life-course, and waist circumference.

In general, findings are very consistent across studies, showing a strongly positive association between BMI and endometrial cancer risk. All of the 20 cohort studies showed a statistically significant positive association. There is an approximately linear pattern of increasing risk with increasing BMI. The relative risk per 5 kg/m²

has been estimated to be 1.6–1.9 ([Renehan et al., 2008](#); [Yang et al., 2012](#); [Bhaskaran et al., 2014](#)).

Among those studies that distinguished endometrial cancers by type ([Björge et al., 2007](#); [McCullough et al., 2008](#); [Yang et al., 2013](#)), all studies showed positive associations with BMI for both type 1 and type 2, with a stronger association for type 1 cancers.

The association between BMI and endometrial cancer risk was much stronger in never-users of HRT than in ever-users ([McCullough et al., 2008](#); [Canchola et al., 2010](#)); in a meta-analysis of 24 studies ([Crosbie et al., 2010](#)), the relative risk per 5 kg/m² was 1.18 in ever-users compared with 1.90 in never-users.

In the two studies that reported differences by smoking status, there was no difference in the association of BMI with endometrial cancer risk between smokers and never-smokers ([Reeves et al., 2007](#); [Bhaskaran et al., 2014](#)).

In those studies that included measurements of waist circumference and hip circumference ([Conroy et al., 2009](#); [Canchola et al., 2010](#); [Reeves et al., 2011](#); [Kabat et al., 2015](#)), waist circumference and waist-to-hip ratio were less strongly associated with risk than was BMI.

In those studies that examined the association between BMI at different ages and subsequent risk of endometrial cancer ([Jonsson et al., 2003](#); [Chang et al., 2007](#); [McCullough et al., 2008](#); [Canchola et al., 2010](#); [Park et al., 2010](#); [Yang et al., 2012](#)), BMI at earlier times in life was generally more weakly related or was not related to risk of endometrial cancer, compared with BMI at baseline.

(b) Case-control studies

A total of 30 case-control studies have been published since 2000 on the association between BMI at diagnosis and endometrial cancer risk, including 21 population-based studies and 9 hospital-based studies ([Table 2.2.11b](#)). Studies were conducted in the USA ($n = 10$), Australia,

Canada, China, the Czech Republic, Israel, Italy, Japan, Mexico, Puerto Rico, the Republic of Korea, Switzerland, and the United Kingdom. In most of the studies, a statistically significant increased risk of endometrial cancer was observed in overweight and obese women compared with normal-weight women.

Among the case–control studies that evaluated BMI measured or recalled at different ages ([Xu et al., 2006](#); [Lucenteforte et al., 2007](#); [Thomas et al., 2009](#); [Dal Maso et al., 2011](#); [Hosono et al., 2011](#); [Lu et al., 2011](#); [Nagle et al., 2013](#)), an increased risk of endometrial cancer was also observed; the BMI measured or recalled closer to the date of diagnosis was usually related to the highest risk.

Six studies reported associations between waist circumference and endometrial cancer risk, showing a 2–5-fold increase in risk for women in the highest category of waist circumference versus the lowest.

(c) *Pooled analyses and meta-analyses*

Several recent pooled analyses and meta-analyses have been published on the association between BMI and endometrial cancer risk ([Dobbins et al., 2013](#); [Felix et al., 2013](#); [Setiawan et al., 2013](#); [Cote et al., 2015](#); [Jenabi & Poorolajal, 2015](#); [Table 2.2.11c](#)).

A large meta-analysis of 20 case–control studies reported a relative risk of 1.43 (95% CI, 1.30–1.56) for overweight and of 3.33 (95% CI, 2.87–3.79) for obese women compared with normal-weight women ([Jenabi & Poorolajal, 2015](#)). In a pooled analysis of 7 cohort studies and 14 case–control studies, the risk of endometrial cancer was similar for obese Black and White women compared with their normal-weight counterparts ([Cote et al., 2015](#)).

A recent pooled analysis of 10 cohort studies and 14 case–control studies explored the heterogeneity of the association between BMI and endometrial cancer risk according to tumour types ([Setiawan et al., 2013](#)). They reported stronger associations among type 1 (RR per

2 kg/m², 1.20; 95% CI, 1.19–1.21) compared with type 2 tumours (RR, 1.12; 95% CI, 1.09–1.14) and among endometrioid grade 1 and 2 compared with endometrioid grade 3. The heterogeneity was present when cohort studies and case–control studies were considered separately, or when registry-based studies were compared with those where cases were further ascertained through pathology reports.

(d) *Mendelian randomization studies*

[Nead et al. \(2015\)](#) applied Mendelian randomization to assess the association of markers of metabolic disease, including BMI, with risk of endometrial cancer using 32 genetic variants as instrumental variables for BMI ([Speliotes et al., 2010](#)). Mendelian randomization analyses showed that each increase of 1 standard deviation in BMI was associated with a significant increase in risk of endometrial cancer (OR, 3.86; 95% CI, 2.24–6.64) ([Table 2.2.11d](#)).

Table 2.2.11a Cohort studies of measures of body fatness and cancer of the endometrium

Reference Cohort Location Follow-up period	Total number of subjects Incidence/ mortality	Subtype	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Calle et al. (2003) Population-based cohort USA 1982–1998	495 477 Mortality		BMI 18.5–24.9 25–29.9 30–34.9 35–39.9 ≥ 40 [<i>P</i> _{trend}]	333 225 105 25 16	1.00 1.50 (1.26–1.78) 2.53 (2.02–3.18) 2.77 (1.83–4.18) 6.25 (3.75–10.42) [< 0.001]	Age, education level, smoking, physical activity, alcohol consumption, marital status, aspirin use, fat intake, vegetable intake, HRT use	
Jonsson et al. (2003) Swedish Twin Registry Sweden 1969–1997	14 131 Incidence		BMI < 18.49 18.5–24.99 25–29.99 ≥ 30	1 69 46 21	0.4 (0.1–3.1) 1.0 1.3 (0.9–1.9) 3.2 (2.0–5.2)	Age	Recalled BMI at ages 25 yr and 40 yr gave RR for BMI ≥ 25.0 vs < 25.0 of 1.9 (1.2–3.0) and 2.0 (0.9–4.4), respectively
Rapp et al. (2005) Population-based cohort Austria 1985–2002	78 484 Incidence		BMI 18.5–24.9 25.0–29.9 30–34.9 ≥ 35 [<i>P</i> _{trend}]	63 59 33 20	1.0 1.29 (0.90–1.86) 2.13 (1.38–3.27) 3.93 (2.35–6.56) [< 0.001]	Age, smoking, occupation	
Lukanova et al. (2006) Population-based cohort Sweden 1994–2004	35 362 Incidence		BMI 18.5–24.9 25–29.9 ≥ 30 [<i>P</i> _{trend}]	42 41 35	1.0 1.45 (0.93–2.24) 2.93 (1.85–4.61) [0.0001]	Age, tobacco use	
Bjorge et al. (2007) Norwegian health surveys Norway 1963–2003	1 million Incidence	Type 1	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [<i>P</i> _{trend}]	82 2960 2361 1761	0.90 (0.72–1.12) 1.00 1.39 (1.32–1.47) 2.72 (2.56–2.90) [< 0.001]	Age, birth cohort	Similar association for BMI at ages 20–49 yr and 50–74 yr
		Type 2	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [<i>P</i> _{trend}]	4 366 369 253	0.42 (0.16–1.13) 1.00 1.26 (1.09–1.46) 1.94 (1.64–2.30) [< 0.001]	Age, birth cohort	Similar association for BMI at ages 20–49 yr and 50–74 yr

Table 2.2.11a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Incidence/mortality	Subtype	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Chang et al. (2007) NIH-AARP cohort USA 1995–2000	103 882 Incidence		BMI < 25 25–29.9 ≥ 30 [<i>P</i> _{trend}]	200 181 296	1.0 1.31 (1.07–1.61) 3.03 (2.50–3.68) [< 0.0001]	Age, physical activity, diabetes, HRT use, age at menarche, parity, age at menopause, OC use, smoking, race	BMI at ages 18 yr, 35 yr, and 50 yr not associated with risk
Friberg et al. (2007) Swedish mammography cohort Sweden 1987–2003	36 773 Incidence		BMI < 30 ≥ 30	154 43	1.0 2.49 (1.77–3.51)	Age, physical activity	Women without diabetes
Lundqvist et al. (2007) Twin cohort studies Sweden and Finland 1961–2004	14 017 older twins (mean baseline age, 56 yr) Incidence		BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 per 1 kg/m ² [<i>P</i> _{trend}]	1 92 57 30	0.3 (0.1–2.5) 1.0 1.2 (0.8–1.6) 3.2 (2.1–4.8) 1.11 (1.06–1.15) [< 0.0001]	Smoking, physical activity, education level, diabetes	
Reeves et al. (2007) Population-based cohort United Kingdom 1996–2001	1.2 million Incidence		BMI < 22.5 22.5–24.9 25.0–27.4 27.5–29.9 ≥ 30 per 10 kg/m ²	340 524 516 366 911	0.84 (0.75–0.93) 1.00 1.21 (1.11–1.32) 1.43 (1.29–1.58) 2.73 (2.55–2.92) 2.89 (2.62–3.18)	Age, region, SES, reproductive history, smoking, alcohol consumption, physical activity, HRT use	Association similar in never-smokers
Lindemann et al. (2008) HUNT cohort Norway 1984–2002	36 761 Incidence		BMI < 20 20–24 25–29 30–34 35–39 ≥ 40 [<i>P</i> _{trend}]	4 64 90 32 23 9	0.53 (0.19–1.47) 1.00 1.74 (1.25–2.43) 1.66 (1.06–2.59) 4.28 (2.58–7.09) 6.36 (3.08–13.16) [< 0.0001]	Age, physical activity, hypertension, alcohol consumption	Similar associations for women aged < 55 yr and aged ≥ 55 yr

Table 2.2.11a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Incidence/ mortality	Subtype	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
McCullough et al. (2008) Cancer Prevention Study II (CPS II) USA 1992–2003	33 436 Incidence		BMI < 22.5 22.5–24.9 25–29.9 30–34.9 ≥ 35 [<i>P</i> _{trend}]	54 53 91 76 44	0.92 (0.63–1.34) 1.00 1.40 (0.99–1.96) 3.27 (2.29–4.67) 4.70 (3.12–7.07) [< 0.0001]	Age, age at menarche, age at menopause, parity, HRT use, smoking, exercise, OC use	Stronger association for never- vs ever- users of HRT. Stronger association for type 1 vs type 2 cancer; null association with BMI at age 18 yr
Song et al. (2008) Korean medical insurance cohort Republic of Korea 1994–2003	107 481 Incidence		BMI < 18.5 18.5–20.9 21–22.9 23.0–24.9 25.0–26.7 27.0–29.9 ≥ 30 per 1 kg/m ²	2 6 16 22 28 31 7	1.26 (0.29–5.51) 0.74 (0.29–1.90) 1.00 1.20 (0.62–2.32) 1.61 (0.84–3.09) 2.70 (1.42–5.13) 2.95 (1.20–7.24) 1.13 (1.07–1.20)	Age, smoking, alcohol consumption, exercise	
Conroy et al. (2009) Women's Health Study USA 1992–2007	19 917 Incidence		BMI < 22.5 22.5–24.9 25–29.9 ≥ 30 [<i>P</i> _{trend}]	57 50 68 89	1.00 0.97 (0.65–1.44) 1.09 (0.75–1.58) 2.49 (1.73–3.59) [< 0.0001]	Age, physical activity, smoking, alcohol consumption, diet, parity, HRT use	Weaker association with WC
Epstein et al. (2009) Lund cohort Sweden 1990–2007	17 822 Incidence		BMI < 25 25–29.9 ≥ 30	45 41 36	1.0 1.4 (0.9–2.2) 3.5 (2.2–5.4)	Age	
Canchola et al. (2010) California Teachers Study Cohort USA 1995–2006	28 418 never-users of HRT Incidence		BMI < 25 25–29.9 ≥ 30 [<i>P</i> _{trend}] per 1 kg/m ²	34 26 48	1.0 1.2 (0.74–2.1) 3.5 (2.2–5.5) [< 0.001] 1.07 (1.04–1.09)	Age, parity, age at first pregnancy, physical activity, OC use	Much weaker association among HRT users. Similar risk for recalled BMI at age 18 yr; association also observed with WC

Table 2.2.11a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Incidence/ mortality	Subtype	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Dossus et al. (2010) EPIC cohort Europe 1992–2003	370 000 Incidence		BMI < 25 25–29.9 ≥ 30 [<i>P</i> _{trend}]	81 82 61	1.0 1.23 (0.82–1.84) 2.02 (1.26–3.23) [0.005]	Age, centre	
Park et al. (2010) Multiethnic Cohort USA (California, Hawaii) 1993–2004	50 376 women aged 45–75 yr, from 5 racial/ ethnic populations		BMI at baseline < 25 25– < 30 ≥ 30 [<i>P</i> _{trend}]	175 119 169	1.00 1.36 (1.06–1.75) 3.54 (2.70–4.63) [< 0.001]	Age, ethnicity, education level, age at menarche, menopausal status, age at menopause, HRT use, OC use, parity, smoking history, diabetes, hypertension	Results available for BMI at age 21 yr, BMI change since age 21 yr, weight at baseline, and weight at age 21 yr
Reeves et al. (2011) Women's Health Initiative USA 1993–NR	86 937 Incidence		BMI < 25 25–29.9 ≥ 30 [<i>P</i> _{trend}]	264 207 334	1.0 0.84 (0.67–1.05) 1.68 (1.33–2.13) [0.0001]	Age, race, education level, smoking, physical activity, intake of fruits and vegetables, diabetes, dietary fat, fibre intake	WHR more weakly associated, and association disappears with BMI adjustment
Ollberding et al. (2012) Multiethnic Cohort USA 1993–2007	46 027 Incidence		BMI < 25 25–29.9 ≥ 30 [<i>P</i> _{trend}]	489 total	1.00 1.38 (1.09–1.74) 2.68 (2.10–3.42) [< 0.01]	Age, race, ethnicity, hypertension, diabetes, smoking, HRT use, OC use, parity	
Yang et al. (2012) Million Women Study United Kingdom 1996–2009	249 791 Incidence		BMI < 22.5 22.5–27.4 27.5–32.4 32.5–34.9 ≥ 35 per 5 kg/m ²	139 465 390 158 258	1.00 1.40 (1.27–1.53) 2.63 (2.39–2.91) 5.07 (4.33–5.93) 7.72 (6.79–8.77) 1.87 (1.77–1.96)	Age, region, height, age at menarche, age at menopause, parity, HRT use, alcohol consumption, smoking, exercise	(Update of study by Reeves et al., 2007) Body size and BMI at ages 10 yr and 20 yr less associated than BMI at baseline
Yang et al. (2013) NIH-AARP cohort USA 1995–2006	114 409 Incidence	Type 1	BMI < 30 ≥ 30	708 570	1.00 2.93 (2.62–3.28)	Age, OC use, HRT use, parity, age at menarche, menopausal status, race, smoking	Most women postmenopausal at time of study entry

Table 2.2.11a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Incidence/ mortality	Subtype	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Yang et al. (2013) (cont.)		Type 2	BMI < 30 ≥ 30	86 47	1.00 1.83 (1.27–2.63)	Age, OC use, HRT use, parity, menarche, menopause, race, smoking	
Bhaskaran et al. (2014) Health system clinical database United Kingdom 1987–2012	5.24 million Incidence		BMI per 5 kg/m ²	2758	1.62 (1.56–1.69)	Age, sex, year, diabetes, alcohol consumption, smoking, SES	Similar association in never-smokers
Kabat et al. (2015) Women's Health Initiative cohort USA 1992–2013	143 901 Incidence		BMI, quintiles Q1 Q2 Q3 Q4 Q5 [P _{trend}]	1157 total	1.0 0.93 (0.76–1.14) 1.08 (0.89–1.32) 1.29 (1.06–1.58) 2.32 (1.93–2.80) [< 0.0001]	Age, alcohol consumption, smoking, parity, HRT use, OC use, ethnicity, education	Similar association with WC

BMI, body mass index (in kg/m²); CI, confidence interval; EPIC, European Prospective Investigation into Cancer and Nutrition; HRT, hormone replacement therapy; NIH-AARP, National Institutes of Health–AARP Diet and Health Study; NR, not reported; OC, oral contraceptive; RR, relative risk; SES, socioeconomic status; WC, waist circumference; WHR, waist-to-hip ratio; yr, year or years

Table 2.2.11b Case-control studies of measures of body fatness and cancer of the endometrium

Reference Study location Period	Total number of cases Total number of controls Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
McCann et al. (2000)	232	BMI			Age
USA	639	< 27.5	112	1.0	
1986–1991	Population	≥ 27.5	120	2.6 (1.9–3.6)	
Salazar-Martínez et al. (2000)	85	BMI			Age, an ovulatory index, smoking, physical activity, menopausal status, hypertension, diabetes
Mexico	668	< 25	21	1.0	
1995–1997	Population	25–30	28	1.1 (0.61–2.1)	
		> 30	35	2.2 (1.2–4.2)	
Benshushan et al. (2001, 2002)	128	BMI			
Israel	255	< 27	49	1.00	
1989–1992	Population	≥ 27	79	2.47 [1.51–4.06]	
Newcomer et al. (2001)	740	BMI			Age
USA	2372	< 22.55	97	1.0	
1991–1994	Population	22.55–25.34	120	1.2 (0.9–1.7)	
		25.35–29.14	150	1.6 (1.2–2.1)	
		≥ 29.15	293	3.0 (2.3–3.9)	
McElroy et al. (2002)	148	BMI			Age
USA	659	< 22.7	13	1.00	
1991–1994	Population	22.7–25.5	18	1.52 (0.80–2.88)	
		25.6–29.0	20	1.60 (0.84–3.03)	
		≥ 29.1	45	3.72 (2.10–6.57)	
Augustin et al. (2003)	410	BMI			Age, study centre, education level, history of diabetes and hypertension, HRT use, total energy intake
Italy and Switzerland	753	< 20	33	1.0	
1988–1998	Hospital	20–25	162	1.2 (0.8–2.0)	
		25– < 30	131	1.3 (0.8–2.2)	
		≥ 30	84	2.2 (1.2–3.8)	
Dal Maso et al. (2004)	87	BMI			Age, education level
Italy	132	< 25	20	1.00	
1999–2002	Hospital	25–29	34	1.80 (0.90–3.59)	
		≥ 30	33	5.87 (2.58–13.38)	

Table 2.2.11b (continued)

Reference Study location Period	Total number of cases Total number of controls Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
Xu et al. (2005, 2006) China 1997–2001	832 846 Population	BMI, quartiles Recent BMI > 25.69 vs < 21.03 BMI at age 20 yr > 21.09 vs < 17.63 BMI at age 30 yr > 22.43 vs < 18.81 BMI at age 40 yr > 24.00 vs < 19.83 BMI at age 50 yr > 25.30 vs < 20.83 BMI at age 60 yr > 25.97 vs < 21.48	302 205 226 269 217 122	3.3 (2.4–4.5) 1.3 (1.0–1.8) 1.5 (1.1–2.0) 2.0 (1.5–2.8) 2.5 (1.7–3.6) 2.9 (1.7–4.9)	Age, education level, years of menstruation, OC use, number of pregnancies, menopausal status, family history of cancer; for recent BMI, additionally adjusted for BMI at age 20 yr
Xu et al. (2005) China 1997–2001	832 846 Population	WC (cm) ≤ 73 74–79 80–86 > 86	102 157 215 357	1.0 1.9 (1.4–2.7) 2.6 (1.9–3.6) 4.7 (3.4–6.4)	Age, education level, years of menstruation, number of pregnancies, BMI
Okamura et al. (2006) Japan 1998–2000	155 96 Hospital	BMI < 20.04 20.04–21.63 21.64–23.92 ≥ 23.93	36 27 45 47	1.00 0.47 (0.22–0.99) 1.24 (0.58–2.67) 1.92 (0.86–4.30)	Age
Trentham-Dietz et al. (2006) USA 1991–1994	740 2342 Population	BMI 14.5–22.6 22.6–25.4 25.5–29.2 29.1–82.4	100 123 153 313	1.00 1.19 (0.88–1.61) 1.62 (1.21–2.18) 3.20 (2.42–4.24)	Age, age at menarche, parity, menopausal status, age at menopause, smoking, HRT use, recent physical activity, diabetes
Weiss et al. (2006) USA 1985–1991, 1994–1995, 1997–1999	1304 1779 Population	BMI < 30.0 30.0–34.9 ≥ 35.0	Low tumour aggressiveness: 374 57 65	1.0 1.6 (1.2–2.3) 5.1 (3.5–7.4)	HRT use, age, county of residence, reference year Tumours with moderate or high aggressiveness gave very similar results

Table 2.2.11b (continued)

Reference Study location Period	Total number of cases Total number of controls Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
Lucenteforte et al. (2007) Italy and Switzerland 1988–2006	777 1550 Hospital	BMI at diagnosis < 30 ≥ 30 BMI at age 30–39 yr < 25 ≥ 25	555 218 532 215	1.0 2.4 (1.9–3.1) 1.0 1.6 (1.3–2.0)	Age, history of diabetes, physical activity, history of hypertension, year of interview, study centre, education level, parity, menopausal status, OC use, HRT use
Máchová et al. (2007) Czech Republic 1987–2002	87 20 776 Population	BMI < 25 ≥ 25– < 30 ≥ 30	NR	1.00 1.84 (0.95–3.57) 3.25 (1.65–6.37)	Age, smoking, hypertension, height
Niwa et al. (2007) Japan 2001–2004	110 220 Hospital	BMI < 25.0 ≥ 25.0	75 35	1.00 2.35 (1.32–4.17)	
Wen et al. (2008) China 1997–2003	1046 1035 Population	BMI < 20.92 20.93–22.68 22.69–24.32 24.33–26.47 > 26.47 WC (cm) < 71 72–76 77–80 81–87 > 87	104 128 190 214 408 71 141 168 282 382	1.1 (0.9–1.5) 1.0 (0.9–1.1) 1.0 1.0 (0.9–1.2) 1.1 (0.8–1.5) 0.5 (0.3–0.6) 0.7 (0.6–0.8) 1.0 1.5 (1.3–1.7) 2.3 (1.7–3.1)	Age at menarche, menopausal status, total years of menstruation, OC use, cancer history in first-degree relatives, and BMI (for WC) or WC (for BMI)
Fortuny et al. (2009) USA 2001–2005	469 467 Population	BMI < 25 25– < 30 30– < 35 ≥ 35	118 127 80 142	1.0 1.6 (1.1–2.2) 2.0 (1.4–3.0) 7.6 (4.8–11.8)	Age
Thomas et al. (2009) USA 1980–1982	421 3159 Population	Adult BMI < 25.0 25.0–29.9 30.0–34.9 ≥ 35.0	LMP < 45 yr: 59 26 23 30	1.0 2.9 (1.7–4.8) 6.0 (3.3–10.7) 21.7 (11.3–41.7)	Age, race, education level, OC use, parity, use of estrogen therapy, menopausal status, history of high blood pressure

Table 2.2.11b (continued)

Reference Study location Period	Total number of cases Total number of controls Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
Thomas et al. (2009) (cont.)		Adult BMI < 25.0 25.0–29.9 30.0–34.9 ≥ 35.0	LMP ≥ 45 yr: 168 60 31 24	1.0 1.5 (1.0–2.1) 2.3 (1.4–3.6) 3.7 (2.0–6.6)	Weaker associations with BMI at age 18 yr vs adult BMI for both LMP < 45 yr and LMP ≥ 45 yr
Tong et al. (2009) Republic of Korea 1998–2006	125 302 Hospital	BMI < 23 23–25 ≥ 25	30 34 61	1.0 1.19 (0.62–2.29) 2.65 (1.44–4.89)	Age
Chandran et al. (2010) USA 2001–2005	424 398 Population	BMI < 25 25–29.9 30–34.9 ≥ 35	105 121 68 123	1.00 1.93 (1.36–2.75) 2.02 (1.32–3.08) 8.47 (5.16–13.89)	Age
Charneco et al. (2010) Puerto Rico 2004–2007	74 88 Hospital	BMI ≤ 24.9 25.0–29.9 ≥ 30 BMI < 30 ≥ 30	6 25 43 31 43	1.00 4.44 (1.60–12.26) 9.85 (3.61–26.87) 1.00 4.11 (1.76–9.93)	Crude Age, education level, employment status, poultry consumption, OC use, diabetes, hypertension
John et al. (2010) USA 1996–1999	472 443 Population	BMI < 25 25–29.9 ≥ 30	176 135 184	1.00 0.92 (0.67–1.26) 1.93 (1.39–2.68)	Age, race/ethnicity
Zhang et al. (2010) China 2004–2008	942 1721 Population	BMI 18.5–24.9 25.0–29.9 ≥ 30.0	571 284 80	1.00 1.51 (1.26–1.81) 6.15 (3.98–9.51)	
Dal Maso et al. (2011) Italy 1992–2006	454 908 Hospital	BMI ≥ 30: BMI at baseline BMI at age 30 yr BMI at age 50 yr BMI, 5 kg/m ² increase WC (cm) ≥ 96 vs < 84	168 29 96 189 127	4.08 (2.90–5.74) 1.78 (1.01–3.14) 3.37 (2.26–5.04) 1.89 (1.65–2.17) 2.68 (1.78–4.03)	Age, study centre, calendar period of interview, years of education, smoking habits, age at menarche, age at menopause, parity, OC use, HRT use

Table 2.2.11b (continued)

Reference Study location Period	Total number of cases Total number of controls Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
Delahanty et al. (2011) China 1996–2005	832 2049 Population	BMI < 21.7 21.7–24.5 > 24.5			Age, income, education level
			14.0% 28.3% 57.7%	1.00 1.68 (1.30–2.18) 3.13 (2.44–4.01)	
Friedenreich et al. (2011) Canada 2002–2006	515 962 Population	WC (cm) ≥ 88	343	2.32 (1.82–2.96)	Reference WC not reported Age
Hosono et al. (2011) Japan 2001–2005	222 2162 Hospital	BMI at baseline < 25 ≥ 25 BMI at age 20 yr < 25 ≥ 25 BMI change from age 20 yr to enrolment ≤ 0 0–3 > 3			Age, smoking, alcohol consumption, regular exercise, age at menarche, duration of menstruation, parity, diabetes history, history of OC use, history of HRT use
			152 65 196 17 57 73 82	1.00 2.22 (1.59–3.09) 1.00 2.30 (1.29–4.11) 1.00 1.26 (0.86–1.84) 1.48 (0.95–2.29)	
Lu et al. (2011) USA 2004–2009	668 674 Population	BMI > 30 vs < 25: current 5 yr in the past at age 20s at age 30s at age 40s at age 50s at age 60s			Age, ethnic group, education level, pregnancy, family history of cancer, estrogen use, OC use, smoking, alcohol consumption
			354 321 60 106 150 156 67	4.76 (3.50–6.49) 4.22 (3.05–5.84) 1.96 (1.16–3.29) 2.19 (1.46–3.28) 3.84 (2.62–5.61) 5.44 (3.62–8.17) 4.09 (2.32–7.21)	
Rosato et al. (2011) Italy 1992–2006	454 798 Hospital	BMI ≤ 30 > 30 WC (cm) < 80 vs ≥ 80 ≤ 88 vs > 88			Age, study centre, year of interview, education level, age at menarche, parity, menopausal status, OC use, HRT use
			312 142 266 195	1.00 3.83 (2.74–5.36) 1.62 (1.00–2.62) 1.90 (1.34–2.71)	
Friedenreich et al. (2012) Canada 2002–2006	541 961 Population	BMI per 1 kg/m ² increase		1.10 (1.08–1.12)	Same study/data set as Friedenreich et al. (2011) Adjusted for age

Table 2.2.11b (continued)

Reference Study location Period	Total number of cases Total number of controls Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates Comments
Amankwah et al. (2013) Canada 2002–2006	524 1032 Population	BMI < 25 25– < 30 ≥ 30 [<i>P</i> _{trend}] WC (cm) > 96.0 vs ≤ 76.5	87 124 256 220	1.00 1.26 (0.91–1.73) 2.81 (2.06–3.84) [< 0.001] 4.21 (2.90–6.10)	Age, residence type (rural or urban), age at menarche, menopausal status/ hormone use, parity/age at first pregnancy, hypertension
Becker et al. (2013) United Kingdom 1995–2012	2554 15 324 Population	BMI < 25 25–29.9 30–59.9	560 560 877	1.00 1.49 (1.32–1.68) 3.18 (2.82–3.57)	Crude estimates
King et al. (2013) USA 2001–2005	424 398 Population	BMI < 25 25–29.9 30–34.9 ≥ 35	105 121 68 123	1.00 1.93 (1.36–2.75) 2.02 (1.32–3.08) 8.47 (5.16–13.89)	Age
Nagle et al. (2013) Australia 2005–2007	1398 1538 Population	Recent BMI ≥ 40 vs < 25 Maximum BMI ≥ 40 vs < 25 BMI at age 20 yr ≥ 30 vs < 25 BMI change from age 20 yr Always overweight vs always normal Change from maximum to recent BMI Always ≥ 30 vs always < 25	192 257 72 203 203 637	7.98 (5.41–11.77) 6.62 (4.72–9.29) 0.75 (0.43–1.33) 3.60 (2.62–4.95) 3.60 (2.62–4.95) 3.71 (2.96–4.67)	Age, age at menarche, parity, duration of OC use, HRT use ≥ 3 months, smoking status, diabetes

BMI, body mass index (in kg/m²); CI, confidence interval; HRT, hormone replacement therapy; LMP, last menstrual period; NR, not reported; OC, oral contraceptive; WC, waist circumference; yr, year or years

Table 2.2.11c Pooled analyses and meta-analyses of measures of body fatness and cancer of the endometrium

Reference	Number and type of studies	Population size and type	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustments Comments
Crosbie et al. (2010)	Meta-analysis of 24 studies published 1966–2009	17 710 cases	BMI 27 32 37 42 per 5 kg/m ²		1.22 (1.19–1.24) 2.09 (1.94–2.26) 4.36 (3.75–5.10) 9.11 (7.26–11.51) 1.60 (1.52–1.68)	$P_{\text{heterogeneity}} = 0.215$
Dobbins et al. (2013)	Meta-analysis of 16 cohort and case–control studies		Obese vs normal-weight		1.85 (1.30–2.65)	$P_{\text{heterogeneity}} = 0.00001$
Felix et al. (2013)	Pooled analysis of 13 studies (E2C2)	8096 cases (primarily endometrioid endometrial carcinomas) and 28 829 controls	BMI < 25 25–30 ≥ 30 [P_{trend}]	2675 2246 2479	1.00 1.37 (1.28–1.46) 3.03 (2.82–3.26) [0.0001]	Age, race, age at menarche, parity, menopausal status, menopausal estrogen plus progestin, menopausal estrogen use, OC use, smoking status, history of diabetes, site
Setiawan et al. (2013)	Pooled analysis of 10 cohort studies and 14 case–control studies in China, Europe, and North America (E2C2)	14 069 cases and 35 312 controls	BMI 18– < 25 25– < 30 30– < 35 35– < 40 ≥ 40 [P_{trend}] BMI 18– < 25 25– < 30 30– < 35 35– < 40 ≥ 40 [P_{trend}]	Type 1: 4602 3718 2294 1247 992 Type 2: 330 253 159 65 47	1.00 1.45 (1.37–1.53) 2.52 (2.35–2.69) 4.45 (4.05–4.89) 7.14 (6.33–8.06) [< 0.0001] 1.00 1.16 (0.98–1.38) 1.73 (1.40–2.12) 2.15 (1.60–2.88) 3.11 (2.19–4.44) [< 0.0001]	Age, study, race/ethnicity, age at menarche, parity, OC use, menopausal status, menopausal HRT use, smoking status
Cote et al. (2015)	Pooled analysis of 7 cohort studies and 4 case–control studies	2011 Black women (516 cases and 1495 controls) 19 297 White women (5693 cases and 13 604 controls)	BMI 18.5–24.9 25–29.9 ≥ 30 BMI 18.5–24.9 25–29.9 ≥ 30	Black women: 76 129 300 White women: 1950 1541 2107	1.00 1.37 (0.97–1.94) 2.93 (2.11–4.07) 1.00 1.43 (1.32–1.56) 2.99 (2.74–3.26)	Age, smoking, OC use, diabetes, study site, age at menarche, parity as a continuous variable

Table 2.2.11c (continued)

Reference	Number and type of studies	Population size and type	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustments Comments
Jenabi & Poorolajal (2015)	Meta-analysis of 20 cohort studies	32 281 242 participants total	BMI		1.00	$P_{\text{heterogeneity}}$: Overweight: $P = 0.001$ Obesity: $P = 0.001$
			Normal		1.34 (1.20–1.48)	
			Overweight		2.54 (2.27–2.81)	
	Meta-analysis of 20 case-control studies		BMI		1.00	$P_{\text{heterogeneity}}$: Overweight: $P = 0.017$ Obesity: $P = 0.001$
			Normal		1.43 (1.30–1.56)	
			Overweight		3.33 (2.87–3.79)	
		Obese				

BMI, body mass index (in kg/m²); CI, confidence interval; E2C2, Epidemiology of Endometrial Cancer Consortium; OC, oral contraceptive; yr, year or years

Table 2.2.11d Mendelian randomization studies of measures of body fatness and cancer of the endometrium

Reference	Characteristics of study population	Sample size	Exposure	Outcome	Odds ratio (95% CI) with each SD increase in exposure
Nead et al. (2015)	Cases were from the Australian National Endometrial Cancer Study (ANECS) or the Studies of Epidemiology and Risk Factors in Cancer Heredity study (SEARCH), United Kingdom Control participants were from the Wellcome Trust Case Control Consortium (WTCCC), and Australian control participants were from parents of twins in the Brisbane Adolescent Twin Study and from the Hunter Community Study	9560 (1287 cases and 8273 controls)	BMI	Endometrial cancer	3.86 (2.24–6.64)

BMI, body mass index (in kg/m²); CI, confidence interval; SD, standard deviation; yr, year or years

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