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ABSENCE OF EXCESS BODY FATNESS

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2.2.7 Cancer of the pancreas

Cancer of the pancreas is the seventh leading cause of cancer death worldwide (Ferlay et al., 2015). Even in developed countries, few individuals diagnosed with pancreatic cancer survive more than 5 years (Sirri et al., 2016). Pancreatic cancer incidence and mortality rates have been increasing both in the USA (Kohler et al., 2015) and in western Europe (Bosetti et al., 2013), despite declines in cigarette smoking, an established risk factor for pancreatic cancer. It has been suggested that these increases may be at least partly attributable to increases in the prevalence of obesity (Ma & Jemal, 2013). Notably, type 2 diabetes mellitus, which is caused by obesity, is also an established risk factor for pancreatic cancer, and the incidence of diabetes is also increasing.

The great majority (> 85%) of pancreatic tumours are ductal adenocarcinomas and derive from the exocrine component of the pancreas. Other pancreatic tumours are a more heterogeneous collection of different tumour types and include, among others, acinar cell carcinoma of the pancreas (about 5% of exocrine pancreatic cancers), cystadenocarcinomas, adenosquamous carcinomas, pancreatic mucinous cystic neoplasms, and pancreatic neuroendocrine (islet cell) tumours (1–2% of all pancreatic cancers).

In 2001, the Working Group of the *IARC Handbook* on weight control and physical activity (IARC, 2002) concluded that the evidence of an association between avoidance of weight gain and pancreatic cancer was *inadequate*. Because of the high case fatality of pancreatic cancer, results from studies of pancreatic cancer incidence and mortality can be considered comparable. Results from individual cohort studies with more than 100 cases of pancreatic cancer (Table 2.2.7a), from case–control studies (Table 2.2.7b), and from meta-analyses or pooled analyses (Table 2.2.7c) are summarized in this section.

(a)   Cohort studies

Since 2000, more than 30 individual cohort studies including pooled analyses have reported on the associations of excess body fatness with pancreatic cancer incidence or mortality (Table 2.2.7a). In addition, seven meta-analyses of cohort studies have been published since then (Table 2.2.7c).

BMI, usually ascertained at study enrolment at or after middle age, was by far the most common measure of excess body weight examined in these cohort studies. In a comprehensive meta-analysis by the WCRF Continuous Update Project that included 23 cohort studies of pancreatic cancer incidence and more than 9500 incident cases of pancreatic cancer, the summary relative risk for a continuous 5 kg/m^2 increase in BMI was 1.10 (95% CI, 1.07–1.14), with similar results in men and in women (WCRF/AICR, 2012). Other meta-analyses or pooled cohort studies, all with considerable overlap in study populations, have reported similar results per 5 kg/m^2 increase in BMI (Larsson et al., 2007; Renehan et al., 2008; Genkinger et al., 2011, 2015).

The largest study that presented categorical BMI results was an analysis that included nearly 6000 pancreatic cancer deaths in White men and women in the Cancer Prevention Study II (Arnold et al., 2009). In that analysis, obesity (i.e. BMI ≥ 30 kg/m^2) was associated on average with a 40% higher risk of pancreatic cancer mortality compared with normal BMI (18.5– < 25 kg/m^2), and results were similar in men and in women separately. [No associations were found in Black men and women, but the sample size was very small compared with the group of White men and women.]

Relatively few large studies of BMI and pancreatic cancer have been conducted in populations that were not predominantly of European descent. Relative risks from the largest study in

African Americans, a pooled analysis of seven cohorts (Bethea et al., 2014), and from a study in the Republic of Korea with 1860 cases (Jee et al., 2008), the largest in an Asian population, appear consistent with those observed in meta-analyses of populations of Caucasians. However, BMI was not associated with risk of pancreatic cancer in a pooled analysis of the Asia Cohort Consortium (Lin et al., 2013b).

Some evidence suggests that the association between BMI and pancreatic cancer may differ by smoking status. In the large NIH-AARP cohort, there was a statistically significant interaction between BMI and smoking status, with a positive association between BMI and risk of pancreatic cancer in never-smokers and in former smokers but not in current smokers (Stolzenberg-Solomon et al., 2013). Similarly, increased BMI was associated with higher risk of pancreatic cancer in never-smokers and in former smokers in other studies, although these interactions were not statistically significant (Genkinger et al., 2011; Aune et al., 2012).

A limited number of individual cohort studies have examined the association between BMI in early adulthood, usually defined as age 18–21 years, and pancreatic cancer incidence or mortality (Patel et al., 2005; Lin, et al., 2007; Verhage et al., 2007; Stolzenberg-Solomon et al., 2013), with mixed results. [These studies calculated BMI in early adulthood based on weight in young adulthood recalled by participants who were middle-aged or older.]

The largest analysis of BMI in early adulthood, as well as BMI change after early adulthood in relation to pancreatic cancer mortality, is a pooled analysis including more than 3000 pancreatic cancer deaths from 14 cohorts (Genkinger et al., 2015). In that pooled analysis, an increase of 5 kg/m^2 in BMI in early adulthood was associated with a relative risk of 1.18 (95% CI, 1.11–1.25), and BMI change after early adulthood was also significantly associated with increased

risk (RR per 5 kg/m^2 increase, 1.05, 95% CI, 1.01–1.10).

Several other individual cohort studies examined associations of change in weight (Samanic et al., 2006, Lin et al., 2007, Luo et al., 2008, Johansen et al., 2009) or change in BMI (Verhage et al., 2007) with risk of pancreatic cancer. None of these studies reported statistically significant associations, except for a study in Sweden that found higher risk in a small group of men with a weight increase of 15% or more in 6 years (Samanic et al., 2006) and another study that reported significant positive associations in a small group of men with a BMI increase of 8 kg/m^2 or more since age 20 years (Verhage et al., 2007).

Several individual cohort studies have examined associations of waist circumference with risk of pancreatic cancer (Larsson et al., 2005; Berrington de González et al., 2006; Luo et al., 2008; Stolzenberg-Solomon et al., 2008). In the WCRF meta-analysis, the relative risk per 10 cm increase in waist circumference was 1.11 (95% CI, 1.05–1.18) (WCRF/AICR, 2012). In addition, waist circumference was examined in a large pooled analysis of pancreatic cancer mortality including data from 11 cohort studies (Genkinger et al., 2015); a higher waist circumference was associated with increased risk of pancreatic cancer mortality (RR per 10 cm increase, 1.07; 95% CI, 1.00–1.14), and no differences in risk were observed between men and women.

(b)   Case–control studies

A total of 15 independent case–control studies, conducted in Canada, China, Europe, Japan, North Africa (Egypt), and the USA, reported on the association of BMI with cancer of the pancreas (Table 2.2.7b). In all studies, the assessment of BMI was based on self-reported height and usual body weight or body weight during a relatively recent time frame before cancer diagnosis. In a few studies, additional self-reports were also obtained for body weight

up to 20 years before cancer diagnosis, or body weight at various pre-specified ages in the more distant past. In all but two studies (Pezzilli et al., 2005; Lo et al., 2007), the estimated association of BMI with risk of pancreatic cancer was adjusted for smoking, as well as for various other potential confounding factors.

For usual BMI before disease onset, 7 of the 14 studies reported statistically significant increases in risk, either overall or in sex-stratified analyses (Silverman et al., 1998; Hanley et al., 2001; Eberle et al., 2005; Anderson et al., 2009; Li et al., 2009; Halfdanarson et al., 2014; Zheng et al., 2016).

Of the remaining studies, the majority showed odds ratios above 1.0. In studies presenting sex-stratified analyses, positive associations with BMI appeared to be somewhat stronger and more often significant for men than for women (Hanley et al., 2001; Silverman, 2001; Eberle et al., 2005; Fryzek et al. 2005; Li et al., 2009).

The study by Fryzek et al. (2005) in the USA showed inverse associations of current BMI (at diagnosis) and cancer of the pancreas and no association with BMI 5 years before interview. However, analyses based on recalled BMI 20 years before interview showed a statistically significant direct association with risk of pancreatic cancer, although in men only. In a similar type of analysis, a case–control study in the Czech Republic and Slovakia (Urayama et al., 2011) also showed a statistically significant association of pancreatic cancer with recalled BMI at age 20 years and at age 40 years, but not with BMI 2 years before interview (OR, 0.98; 95% CI, 0.85–1.13).

In two studies, associations of BMI with risk of pancreatic cancer were estimated separately for never-smokers and ever-smokers.

In the USA, Fryzek et al. (2005) reported a statistically significant and up to 3.3-fold increase in risk of pancreatic cancer (95% CI, 1.2–9.2) only in never-smokers in the highest category of BMI compared with those with low BMI, and no relationship was found in smokers.

A second study, also in the USA (Li et al., 2009), reported a positive association of BMI with risk of pancreatic cancer both in ever-smokers (OR per 5 kg/m^2 increase, 1.75; 95% CI, 1.37–2.22) and in never-smokers (OR, 1.46; 95% CI, 1.16–1.84).

One case–control study in the USA (with 309 cases and 602 controls) specifically addressed the association of BMI with pancreatic neuroendocrine tumours, a rare pancreatic cancer tumour, and observed an increased risk in individuals who were obese (BMI ≥ 30 kg/m^2) compared with those with a lower BMI (OR, 1.65; 95% CI, 1.11–2.45) (Halfdanarson et al., 2014).

Table 2.2.7a Cohort studies of measures of body fatness and cancer of the pancreas

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Friedman & van den Eeden (1993) Nested case–control study within Kaiser Permanente USA 1964–1988	450 cases, 2687 controls Men and women Incidence	Pancreas	BMI, per 1 kg/m² increase Weight, per 5 kg	450	1.02 (1.00–1.04) 1.06 (1.01–1.11)	Age, cigarette smoking, race	
Gapstur et al. (2000) Chicago Heart Association Detection Project in Industry Cohort USA 1967–1995	20 475 Men Mortality 15 183 Women Mortality	Pancreas ICD-8: 157	BMI < 24.129 24.129–26.292 26.293–28.630 ≥ 28.631 BMI < 20.978 20.978–23.240 23.241–26.156 ≥ 26.157	10 21 23 42 9 6 16 12	1.00 1.76 (0.83–3.74) 1.68 (0.80–3.53) 3.04 (1.52–6.08) 1.00 0.48 (0.17–1.26) 1.09 (0.47–2.51) 0.73 (0.30–1.80)	Age Age	
Isaksson et al. (2002) Swedish Twin Registry Sweden 1969–1997	21 884 Men and women Incidence	Pancreas	BMI < 18.5 18.5–24.99 25–30 > 30	5 84 70 4	2.30 (0.93–5.71) 1.00 1.36 (0.99–1.88) 0.56 (0.20–1.52)	Age, sex, smoking	No associations were observed for adult weight gain (in kg)
Samanic et al. (2004) United States Veterans cohort USA 1969–1996	4 500 700 Men Incidence	Pancreas ICD-9: 157	Obesity Non-obese Obese Non-obese Obese	White men: 5483 391 Black men: 1638 83	 1.00 1.20 (1.07–1.33) 1.00 1.07 (0.86–1.34)	Age, calendar year	Obesity defined as discharge diagnosis of obesity: ICD-8: 277; ICD-9: 278.0

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Batty et al. (2005) Whitehall Study United Kingdom 1967–2002	18 403 Men Mortality	Pancreas ICD-8/9: 157 ICD-10: C25	BMI 18.5–24.9 25.0–29.9 ≥ 30 [P_{trend}]	75 69 3	1.00 1.18 (0.83–1.68) 0.58 (0.18–1.91) [0.80]	Age, employment grade, physical activity, smoking, marital status, prevalent disease, weight loss in past year, BP medication, height, skinfold thickness, systolic BP, plasma cholesterol, glucose intolerance, diabetes	
Larsson et al. (2005) Swedish Mammography Cohort (SMC) Sweden 1987–2004 Cohort of Swedish Men (COSM) Sweden 1997–2004	83 053 Men and women Incidence	Pancreas ICD-9: 157, excluding 157.4	BMI < 20 20–24.9 25–29.9 ≥ 30 [P_{trend}] WC (cm), quartiles (sex-specific) Men: Women: < 90 < 76 90–94 76–81 95–101 82–89 ≥ 102 ≥ 90 [P_{trend}]	5 50 54 19 16 20 34 36	0.96 (0.38–2.46) 1.00 1.25 (0.84–1.86) 1.81 (1.04–3.15) [0.04] 1.00 1.15 (0.59–2.25) 1.59 (0.87–2.93) 1.72 (0.93–3.20) [0.05]	Age, education level, physical activity, smoking, alcohol consumption, sex	In stratified analyses, stronger associations with BMI in men than in women

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Patel et al. (2005) Cancer Prevention Study II (CPS II) Nutrition Cohort 1992–1999	145 627 Men and women Incidence and mortality	Pancreas ICD-9: 157.0–157.9 ICD-10: C25.0–25.9	BMI at baseline < 25 25–29.9 ≥ 30 [P_{trend}] BMI at age 18 yr < 21 21–22.9 ≥ 23 [P_{trend}] Adult weight change (kg) < −2.27 −2.27 to 4.54 4.55–9.07 9.08–13.61 ≥ 13.62 [P_{trend}]	50 33 22 59 25 17 4 20 18 21 38	1.00 1.03 (0.76–1.38) 2.08 (1.48–2.93) [0.0001] 1.00 1.07 (0.77–1.49) 1.33 (0.95–1.85) [0.11] 1.74 (0.94–3.22) 1.00 1.12 (0.70–1.79) 0.97 (0.60–1.58) 0.96 (0.61–1.52) [0.16]	Age, smoking, years since quitting smoking, education level, family history of pancreatic cancer, gall bladder disease, diabetes, height, energy intake, physical activity	In stratified analyses, association with BMI at baseline was stronger in men than in women
Sinner et al. (2005) Iowa Women's Health Study USA 1986–2001	28 002 Women Incidence	Pancreas ICD-10: C25	BMI < 25 25–29.9 ≥ 30	84 72 53	1.00 0.94 (0.69–1.29) 1.14 (0.81–1.62)	Age, smoking status, multivitamin use	
Berrington de González et al. (2006) EPIC cohort 10 European countries 1991–2004	438 405 Men and women Incidence	Pancreas	BMI < 20 20–22.9 23–24.9 25–26.9 27–29.9 30–34.9 ≥ 35 per 5 kg/m² [P_{trend}]	9 48 85 71 43 50 13	0.67 (0.33–1.37) 1.00 0.99 (0.69–1.41) 0.82 (0.56–1.19) 0.76 (0.50–1.16) 1.16 (0.77–1.76) 1.19 (0.64–2.23) 1.09 (0.95–1.24) [0.24]	Sex, smoking, diabetes Weight and WC estimates also adjusted for height	

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories		Exposed cases	Relative risk (95% CI)	Covariates	Comments
Berrington de González et al. (2006) (cont.)			Weight (kg), quartiles (sex-specific)					
			Men:	Women:				
			< 73	< 58	66	1.00		
			73–79	58–63	65	0.90 (0.63–1.28)		
			80–87	64–71	85	1.02(0.73–1.44)		
			≥ 88	≥ 72	103	1.14 (0.82–1.61)		
			per 5 kg			1.05 (0.99–1.10)		
			$[P_{trend}]$			[0.06]		
			WC (cm), quartiles (sex-specific)					
			Men:	Women:				
			< 88	< 73	51	1.00		
			88–93	73–78	59	0.96 (0.65–1.41)		
			94–100	79–87	79	1.05(0.72–1.53)		
			≥ 101	≥ 88	91	1.33 (0.93–1.92)		
			per 10 cm			1.24 (1.04–1.48)		
			$[P_{trend}]$			[0.03]		
Samanic et al. (2006) Swedish Construction Worker Cohort Sweden 1958–1999	362 552 (107 815 in weight change analysis) Men Incidence	Pancreas ICD-7: 157	BMI				Attained age, calendar year, smoking	
			18.5–24.9		352	1.00		
			25–29.9		289	0.95 (0.82–1.12)		
			≥ 30		57	1.16 (0.87–1.53)		
			$[P_{trend}]$			[> 0.5]		
			6-yr weight change					
			−4% to +4.9%		86	1.00		
			5–9.9%		41	1.45 (1.00–2.11)		
			10–14.9%		13	1.53 (0.85–2.77)		
			≥ 15%		7	2.67 (1.22–5.84)		
			$[P_{trend}]$			[> 0.5]		

Table 2.2.7a   (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Lin et al. (2007) JACC cohort Japan 1988–2003	43 579 Men Mortality	Pancreas ICD-10: C25	BMI at baseline < 20 20–22.4 22.5–24.9 25–27.4 27.5–29.9 ≥ 30 [P_{trend}]	46 71 57 26 6 1	1.12 (0.76–1.63) 1.00 0.94 (0.66–1.34) 1.02 (0.65–1.62) 0.62 (0.23–1.70) 0.58 (0.08–4.16) [0.47]	Age, smoking, diabetes, gall bladder disease	
			BMI at age 20 yr < 20 20–22.4 22.5–24.9 25–27.4 27.5–29.9 ≥ 30 [P_{trend}]	27 45 45 21 6 4	1.39 (0.86–2.24) 1.00 1.13 (0.75–1.71) 1.54 (0.92–2.58) 1.65 (0.70–3.86) 3.51 (1.26–9.78) [0.01]		
			Weight change (kg) < −5 −5 to < 0 0 > 0–4.9 ≥ 5	45 22 47 12 21	1.63 (1.05–2.53) 1.39 (0.82–2.33) 1.00 1.11 (0.58–2.12) 0.85 (0.49–1.47)		
	59 107 Women Mortality	Pancreas ICD-10: C25	BMI at baseline < 20 20–22.4 22.5–24.9 25–27.4 27.5–29.9 ≥ 30 [P_{trend}]	33 50 62 30 16 4	1.15 (0.74–1.80) 1.00 1.33 (0.91–1.95) 1.21 (0.77–1.92) 1.57 (0.86–2.86) 1.04 (0.37–2.89) [0.28]	Age, smoking, diabetes, gall bladder disease	

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Lin et al. (2007) (cont.)			BMI at age 20 yr				
			< 20	25	0.81 (0.50–1.31)		
			20–22.4	51	1.00		
			22.5–24.9	48	1.08 (0.73–1.61)		
			25–27.4	15	0.69 (0.39–1.23)		
			27.5–29.9	3	0.46 (0.14–1.48)		
			≥ 30	1	0.43 (0.06–3.15)		
			[P_{trend}]		[0.09]		
			Weight change (kg)				
			< −5	14	0.41 (0.22–0.74)		
			−5 to < 0	14	0.61 (0.34–1.11)		
			0	59	1.00		
			> 0–4.9	13	0.70 (0.38–1.28)		
			≥ 5	43	0.93 (0.60–1.45)		
Luo et al. (2007) Japan Public Health Center Prospective Study Japan 1990–2003	47 499 Men Incidence	Pancreas ICD-10: C25	BMI 14–20.9 21–24.9 25–40 [P_{trend}]	37 69 22	1.4 (0.8–2.5) 1.0 0.7 (0.4–1.1) [0.01]	Smoking, diabetes, physical activity, study area, age, alcohol use, history of cholelithiasis	
	52 161 Women Incidence		BMI 14–20.9 21–24.9 25–40 [P_{trend}]	14 49 33	0.7 (0.4–1.3) 1.0 1.1 (0.7–1.6) [0.3]		
Máchová et al. (2007) National Cancer Registry, nested case–control study Czech Republic 1987–2002	17 110 Men Incidence	Pancreas ICD-10: C25	BMI 18.5–24.9 25–29.9 ≥ 30	114 total	1.00 1.24 (0.74–2.07) 1.81 (0.98–3.31)	Age, smoking, hypertension, height	Nested case–control study, reporting odds ratios
	20 856 Women Incidence		BMI 18.5–24.9 25–29.9 ≥ 30	80 total	1.00 0.68 (0.37–1.26) 0.95 (0.50–1.79)		

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Nöthlings et al. (2007) Multiethnic Cohort Study USA 1993–2002	77 255 Men Incidence	Pancreas ICD-10: C25.0–25.3, C25.7–25.9	BMI < 25 25–29.9 ≥ 30 [P_{trend}]	110 89 38	1.00 0.99 (0.74–1.33) 1.51 (1.02–2.26) [0.085]	Ethnicity, smoking, family history of pancreatic cancer, diabetes, age, energy intake, intake of red meat, intake of processed meat, physical activity	
	90 175 Women Incidence		BMI < 25 25–29.9 ≥ 30 [P_{trend}]	52 62 62 61	1 0.80 (0.59–1.09) 0.65 (0.43–0.99) [0.031]		
Verhage et al. (2007) Netherlands Cohort Study on Diet and Cancer The Netherlands 1986–1999	2366 Men Incidence	Pancreas ICD-10: C25	BMI at baseline < 23 23–24.9 25–26.9 27–29.9 ≥ 30 [P_{trend}] per 1 kg/m² BMI at age 20 yr < 20 20–20.9 21–22.9 ≥ 23 [P_{trend}] per 1 kg/m² BMI change since age 20 yr < 0 0–3.9 4–7.9 ≥ 8 [P_{trend}] per 1 kg/m²	44 67 50 39 20 35 26 60 52 14 84 60 15	1.10 (0.72–1.69) 1.00 0.93 (0.61–1.39) 1.17 (0.75–1.81) 2.69 (1.47–4.92) [0.141] 1.05 (0.99–1.12) 1.00 0.80 (0.46–1.40) 0.99 (0.62–1.59) 1.07 (0.67–1.73) [0.56] 1.03 (0.96–1.10) 0.99 (0.53–1.85) 1.00 1.34 (0.90–1.99) 2.21 (1.09–4.49) [0.052] 1.07 (0.99–1.15)	Age, smoking, diabetes, hypertension	When restricting to microscopically confirmed exocrine pancreatic cancer, significant positive associations were found with increased BMI and weight at baseline, and with BMI change since age 20 yr

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Verhage et al. (2007) (cont.)			Weight at baseline (kg)				
			< 65	74	1.00		
			65–69	47	1.16 (0.76–1.76)		
			70–74	46	1.13 (0.75–1.70)		
			75–79	21	0.92 (0.53–1.59)		
			≥ 80	36	1.55 (0.99–2.45)		
			[P_{trend}]		[0.18]		
			continuous per kg		1.01 (0.99–1.03)		
	2438 Women Incidence	Pancreas ICD-10: C25	BMI at baseline			Age, smoking, diabetes, hypertension	When restricting to microscopically confirmed exocrine pancreatic cancer, significant positive associations were found with increased weight at baseline and with BMI change since age 20 yr. A significant P_{trend} was also observed with increased BMI at baseline
			< 23	46	1.02 (0.66–1.58)		
			23–24.9	45	1.00		
			25–26.9	55	1.69 (1.11–2.58)		
			27–29.9	38	1.41 (0.89–2.25)		
			≥ 30	19	1.31 (0.74–2.31)		
			[P_{trend}]		[0.052]		
			per 1 kg/m^2		1.04 (1.00–1.08)		
			BMI at age 20 yr				
			< 20	65	1.00		
			20–20.9	27	0.93 (0.58–1.51)		
			21–22.9	42	0.69 (0.46–1.04)		
			≥ 23	52	0.97 (0.66–1.44)		
			[P_{trend}]		[0.535]		
			per 1 kg/m^2		1.02 (0.95–1.09)		
			BMI change since age 20 yr				
			< 0	15	0.67 (0.37–1.21)		
			0–3.9	76	1.00		
			4–7.9	63	1.08 (0.75–1.55)		
			≥ 8	31	1.72 (1.11–2.67)		
			[P_{trend}]	185	[0.004]		
			per 1 kg/m^2		1.05 (1.01–1.10)		

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Verhage et al. (2007) (cont.)			Weight at baseline (kg) < 65 65–69 70–74 75–79 ≥ 80 [P_{trend}] continuous per kg	59 42 39 31 39	1.00 1.23 (0.81–1.88) 1.30 (0.84–1.99) 1.58 (0.99–2.52) 1.64 (1.07–2.52) [0.010] 1.02 (1.01–1.03)		
Jee et al. (2008) National Health Insurance Corporation Republic of Korea 1992–2006	770 556 Men Incidence	Pancreas	BMI < 20.0 20.0–22.9 23.0–24.9 25.0–29.9 ≥ 30.0 [P_{trend}]	199 678 524 442 17	0.87 (0.71–1.08) 1.01 (0.87–1.16) 1.00 1.06 (0.90–1.24) 1.34 (0.75–2.38) [0.1139]	Age, smoking	
	423 273 Women Incidence		BMI < 20.0 20.0–22.9 23.0–24.9 25.0–29.9 ≥ 30.0 [P_{trend}]	80 246 178 253 34	0.88 (0.62–1.24) 1.09 (0.84–1.40) 1.00 1.35 (1.05–1.74) 1.80 (1.14–2.86) [0.0014]	Age, smoking	
Luo et al. (2008) Women's Health Initiative USA 1993–2005	138 503 Women Incidence	Pancreas	BMI < 22.0 22.0–24.9 25.0–29.9 30.0–34.9 ≥ 35.0 [P_{trend}]	25 62 84 56 24	0.8 (0.5–1.2) 1.0 0.9 (0.6–1.2) 1.1 (0.7–1.5) 0.8 (0.5–1.3) [0.9]	Age, treatment assignments, cigarette smoking, diabetes	Study of postmenopausal women

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Luo et al. (2008) (cont.)			WC (cm), quintiles (range, median)				
			35.0–74.5, 70.5	41	1.0		
			74.6–81.0, 78.0	50	1.1 (0.7–1.7)		
			81.1–88.0, 85.0	46	1.0 (0.7–1.6)		
			88.1–97.4, 92.4	63	1.4 (0.9–2.0)		
			97.5–194.2, 105.0	51	1.1 (0.7–1.6)		
			$[P_{trend}]$		[0.6]		
			per 10 cm		1.05 (0.95–1.15)		
			Type of weight change:				
			Stable weight	85	1.0		
			Steady gain in weight	77	0.9 (0.6–1.2)		
			Lost weight and kept it off	5	0.6 (0.3–1.5)		
			Weight up and down (> 10 lb)	83	0.9 (0.7–1.2)		
Stolzenberg-Solomon et al. (2008) NIH-AARP cohort USA 1995–2000	293 562 Men Incidence	Pancreatic adenocarcinoma ICD-10: C25.0–25.9 Excludes endocrine tumours	BMI			Age, smoking, race, energy intake, energy-adjusted total fat intake, diabetes; for WC, also adjusted for BMI	
			18.5– < 25.0	110	1.00		
			25.0–29.9	227	1.22 (0.97–1.54)		
			30.0–34.9	66	1.09 (0.80–1.48)		
			≥ 35.0	26	1.61 (1.05–2.49)		
			$[P_{trend}]$		[0.07]		
			WC (cm)				
			< 88.9	40	1.00		
			88.9–93.3	35	1.00 (0.62–1.61)		
			93.3–98.4	39	0.81 (0.49–1.32)		
			98.4–106	46	0.96 (0.58–1.58)		
			≥ 106	52	0.95 (0.54–1.67)		
			$[P_{trend}]$		[0.91]		

Table 2.2.7a   (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Stolzenberg-Solomon et al. (2008) (cont.)	201 473 Women Incidence		BMI 18.5– < 25.0 25.0–29.9 30.0–34.9 35.0 [P_{trend}] WC (cm) < 74.9 74.9–83.2 83.2–92.1 ≥ 92.1 [P_{trend}]	84 84 38 19 14 24 28 34	1.00 1.33 (0.98–1.81) 1.40 (0.95–2.07) 1.29 (0.78–2.16) [0.09] 1.00 1.74 (0.89–3.41) 1.88 (0.92–3.85) 2.53 (1.13–5.65) [0.04]	Age, smoking, race, energy intake, energy-adjusted total fat intake, diabetes; for WC, also adjusted for BMI	
Arnold et al. (2009) Cancer Prevention Study II (CPS II) USA 1984–2004	48 525 Black men and women Mortality 17 602 Black men Mortality 30 923 Black women Mortality 1 011 864 White men and women Mortality	Pancreas ICD-9: 157	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	2 122 136 80 0 45 65 33 2 77 71 47 86 2644 2351 690	0.44 (0.11–1.77) 1.00 0.89 (0.70–1.40) 1.06 (0.80–1.42) – 1.00 1.02 (0.69–1.49) 1.66 (1.05–2.63) 0.60 (0.15, 2.44) 1.00 0.82 (0.59–1.14) 0.82 (0.56–1.18) 0.93 (0.75–1.16) 1.00 1.15 (1.08–1.22) 1.40 (1.28–1.52)	Age, diabetes, family history of pancreatic cancer, cholecystectomy, smoking status; analysis for men and women also adjusted for sex	

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Arnold et al. (2009) (cont.)	444 351 White men Mortality		BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	19 1080 1479 336	0.83 (0.53–1.31) 1.00 1.11 (1.02–1.20) 1.42 (1.25–1.60)		
	567 513 White women Mortality		BMI < 18.5 18.5–24.9 25–29.9 ≥ 30	67 1564 872 354	0.97 (0.76–1.24) 1.00 1.20 (1.10–1.30) 1.37 (1.22–1.54)		
Johansen et al. (2009) Malmö Preventive Project Sweden 1974–2004	33 325 Men and women Incidence	Pancreas ICD-7: 157 ICD-10: C25	BMI < 20 20–24.9 25–29.9 ≥ 30 continuous Weight gain > 10 kg No Yes Missing	10 101 54 18 118 52 13	0.84 (0.44–1.61) 1.00 0.83 (0.60–1.16) 1.38 (0.83–2.28) 1.04 (0.995–1.08) 1.00 1.07 (0.77–1.48) 0.65 (0.34–1.27)	Age, sex, smoking, alcohol consumption	
Meinhold et al. (2009) ATBC subcohort of non-diabetics Finland 1985–2004	27 035 Men Incidence	Pancreas ICD-9: 157, excluding 157.4	BMI, quartiles Q1 Q2 Q3 Q4 continuous [P_{trend}]	117 139 41 8	1.00 0.97 (0.76–1.24) 1.03 (0.72–1.47) 1.42 (0.69–2.93) 1.01 (0.94–1.08) [0.80]	Age, smoking, energy intake, diabetes mellitus (self-reported)	
Stevens et al. (2009) Million Women Study USA 1996–2006	1.29 million Women Incidence	Pancreas ICD-10: C25	BMI < 22.5 22–24.9 25–27.4 27.5–29.9 30–32.4 ≥ 32.5	246 311 260 188 119 152	RR (floating SE) 1.02 (0.07) 1.00 (0.06) 0.99 (0.06) 1.17 (0.09) 1.27 (0.12) 1.42 (0.12)	Age, region, SES, smoking, height	

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Stevens et al. (2009) (cont.)	1.29 million Women Mortality		BMI < 22.5 22–24.9 25–27.4 27.5–29.9 30–32.4 ≥ 32.5	334 400 347 227 139 188	RR (floating SE) 1.08 (0.06) 1.00 (0.05) 1.03 (0.05) 1.09 (0.07) 1.14 (0.10) 1.36 (0.10)	Age, region, SES, smoking, height	
Whitlock et al. (2009) Pooled analysis of 57 cohort studies Europe, Japan, and USA Follow-up varied by cohort	894 576 Men and women Mortality	Pancreas ICD-9: 157	BMI, per 5 kg/m^2 For BMI 15–25 For BMI 25–50 For BMI 15–50	470 520	0.87 (0.65–1.17) 1.04 (0.86–1.25) 1.07 (0.97–1.19)	Study, sex, age, baseline smoking	
Arslan et al. (2010) Pancreatic Cancer Cohort Consortium (PanScan) pooled analysis, nested case–control Follow-up varies by cohort	2170 (men: 1059; women: 1111) Incidence	Pancreas	BMI < 18.5 ≥ 18.5– < 25.0 ≥ 25– < 30 ≥ 30– < 35 ≥ 35 [P_{trend}]	19 759 868 325 124	0.84 (0.44–1.59) 1.00 1.15 (1.00–1.33) 1.13 (0.93–1.37) 1.26 (0.93–1.71) [0.047]	Cohort, age, sex, anthropometry source, smoking, diabetes history	Non-significant positive associations were observed with WC (P_{trend} = 0.09)
Jiao et al. (2010) Pooled analysis of 7 cohort studies Follow-up varies by cohort	943 759 Men and women Incidence	Pancreatic adenocarcinoma ICD-10: C25 excluding C25.4 ICD-8/9: 157 excluding 157.4	BMI 16.5–18.4 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}] per 5 kg/m^2	17 855 1109 381 92	0.89 (0.55–1.44) 1.00 1.13 (1.03–1.23) 1.19 (1.05–1.35) 1.19 (0.96–1.48) [0.001] 1.08 (1.03–1.14)	Age, sex, cohort, smoking	

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Jiao et al. (2010) (cont.)	458 070 Men Incidence		BMI 16.5–18.4 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}] per 5 kg/m^2	7 465 793 240 43	0.88 (0.42–1.86) 1.00 1.11 (0.99–1.25) 1.11 (0.95–1.30) 1.34 (0.98–1.84) [0.03] 1.05 (0.98–1.12)		
	485 689 Women Incidence		BMI 16.5–18.4 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}] per 5 kg/m^2	10 390 316 141 49	0.91 (0.48–1.70) 1.00 1.15 (0.99–1.34) 1.34 (1.11–1.64) 1.09 (0.81–1.47) [0.01] 1.12 (1.05–1.19)		
Parr et al. (2010) Pooled analysis of 39 cohort studies Asia, Australia, and New Zealand 1961–1999, median follow-up 4 yr	326 387 Men and women Mortality	Pancreas ICD-9: 157 ICD-10: C25	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 per 5 kg/m^2 [P_{trend}]	11 114 65 90 21	0.71 (0.38–1.31) 1.00 (0.86–1.16) 0.93 (0.75–1.15) 0.75 (0.48–1.18) 0.93 (0.78–1.11) [0.24]	Age, sex, smoking	
Genkinger et al. (2011) Pooling project of prospective studies of diet and cancer (14 cohort studies)	Women: 531 755 Men: 314 585 Incidence and mortality	Pancreas	BMI at baseline < 21 21–22.9 23–24.9 25–29.9 ≥ 30 [P_{trend}] per 5 kg/m^2	All: 196 290 457 847 345	1.16 (0.96–1.40) 1.00 1.07 (0.92–1.25) 1.18 (1.03–1.36) 1.47 (1.23–1.75) [< 0.001] 1.14 (1.07–1.21)	Smoking, diabetes, alcohol consumption, energy intake, age, baseline year	No statistically significant interaction by sex was found for BMI at baseline, BMI in early adulthood, or BMI change

Table 2.2.7a   (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Genkinger et al. (2011) (cont.)	Women: 531 755 Men: 314 585 Incidence and mortality	Pancreas	BMI at baseline < 21 21–22.9 23–24.9 25–29.9 ≥ 30 $[P_{trend}]$ per 5 kg/m^2	Women: 148 177 221 378 192	1.15 (0.92–1.44) 1.00 1.08 (0.88–1.32) 1.29 (1.04–1.61) 1.46 (1.17–1.80) [0.002] 1.13 (1.06–1.21)		
			BMI at baseline < 21 21–22.9 23–24.9 25–29.9 ≥ 30 $[P_{trend}]$ per 5 kg/m^2	Men: 48 113 236 469 153	1.19 (0.85–1.68) 1.00 1.07 (0.85–1.34) 1.09 (0.88–1.34) 1.50 (1.07–2.11) [0.06] 1.14 (1.01–1.29)		
			BMI in early adulthood < 18.5 18.5–20.9 21–22.9 23–24.9 ≥ 25 $[P_{trend}]$ per 5 kg/m^2	All: 163 519 426 276 214	0.95 (0.79–1.15) 0.99 (0.87–1.13) 1.00 1.09 (0.92–1.29) 1.21 (1.01–1.45) [0.03] 1.20 (1.10–1.30)		
			BMI in early adulthood < 18.5 18.5–20.9 21–22.9 23–24.9 ≥ 25 $[P_{trend}]$ per 5 kg/m^2	Women: 121 351 239 113 94	0.92 (0.70–1.21) 0.96 (0.81–1.14) 1.00 0.98 (0.78–1.24) 1.16 (0.90–1.50) [0.18] 1.14 (1.02–1.28)		

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Genkinger et al. (2011) (cont.)	Women: 531 755 Men: 314 585 Incidence and mortality	Pancreas	BMI in early adulthood < 18.5 18.5–20.9 21–22.9 23–24.9 ≥ 25 [P_{trend}] per 5 kg/m^2 BMI change < −2 −2 to +2 2–5 5–10 > 10 [P_{trend}]	Men: 42 168 187 163 120 All: 79 391 493 491 144	1.02 (0.72–1.45) 1.03 (0.78–1.35) 1.00 1.19 (0.87–1.62) 1.21 (0.88–1.68) [0.06] 1.27 (1.12–1.44) 1.44 (1.13–1.85) 1 0.98 (0.85–1.12) 1.13 (0.98–1.30) 1.40 (1.13–1.72) [0.04]		
Klein et al. (2013) Pancreatic Cancer Cohort Consortium (PanScan)	3349 Men and women Incidence	Pancreas	BMI < 18.5 18.5–24.9 25–30 > 30	NR	0.91 (0.54–1.53) 1.00 1.08 (0.96–1.22) 1.26 (1.09–1.45)	Sex, age, study	
Lin et al. (2013b) Pooled analysis of 16 cohort studies from Asia Cohort Consortium Follow-up varies by cohort	799 542 Men and women Mortality	Pancreas	BMI < 18.5 18.5–19.9 20–22.4 22.5–24.9 25–27.4 27.5–29.9 ≥ 30	All: 116 130 432 454 232 89 36	1.04 (0.84–1.30) 0.82 (0.67–1.00) 0.91 (0.80–1.05) 1.00 0.95 (0.80–1.11) 1.01 (0.80–1.29) 0.96 (0.67–1.37)	Age, sex, cohort, smoking, type 2 diabetes	No associations were observed when results were stratified by Asian region (i.e. East Asia vs South Asia)

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Lin et al. (2013b) (cont.)			BMI < 18.5 18.5–19.9 20–22.4 22.5–24.9 25–27.4 27.5–29.9 ≥ 30	Women: 53 59 174 213 129 52 28	0.89 (0.64–1.24) 0.85 (0.63–1.15) 0.78 (0.63–0.96) 1.00 1.01 (0.81–1.27) 1.02 (0.74–1.39) 1.09 (0.72–1.65		
			BMI < 18.5 18.5–19.9 20–22.4 22.5–24.9 25–27.4 27.5–29.9 ≥ 30	Men: 63 71 258 241 103 37 8	1.20 (0.90–1.61) 0.80 (0.61–1.05) 1.03 (0.86–1.24) 1.00 0.87 (0.69–1.10) 0.99 (0.69–1.42) 0.64 (0.30–1.35)		
Stolzenberg-Solomon et al. (2013) NIH-AARP cohort USA 1995–2006	501 698 Men and women Incidence	Pancreatic adenocarcinoma ICD-10: C25.0–25.9	BMI at age 18 yr < 18.5 18.5–22.4 22.5–24.9 25–27.4 ≥ 27.5 [P_{trend}] BMI at age 35 yr < 18.5 18.5–22.4 22.5–24.9 25–29.9 ≥ 30 [P_{trend}]	188 652 216 91 59 34 405 350 346 71	1.08 (0.92–1.27) 1.00 1.07 (0.92–1.25) 1.11 (0.89–1.39) 1.56 (1.19–2.03) [0.005] 1.04 (0.73–1.48) 1.00 1.08 (0.94–1.25) 1.22 (1.05–1.41) 1.37 (1.06–1.79) [0.001]	Smoking, total fat consumption, energy intake, sex	

Table 2.2.7a   (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Stolzenberg-Solomon et al. (2013) (cont.)			BMI at age 50 yr				
			< 18.5	27	1.26 (0.85–1.85)		
			18.5–24.9	532	1.00		
			25–29.9	499	1.13 (1.00–1.29)		
			≥ 30	148	1.22 (1.02–1.47)		
			[P_{trend}]		[0.01]		
			BMI at age > 50 yr				
			< 18.5	25	1.18 (0.79–1.75)		
			18.5–24.9	689	1.00		
			25–29.9	934	1.09 (0.98–1.20)		
			30–34.9	340	1.14 (1.00–1.30)		
			≥ 35	134	1.29 (1.07–1.55)		
			[P_{trend}]		[0.01]		
Bhaskaran et al. (2014) Clinical Practice Research Datalink United Kingdom 1987–2012	5 243 978 Men and women Incidence	Pancreas ICD-10: C25	BMI, per 5 kg/m²	3851 total	1.05 (1.00–1.10)	Age, diabetes, smoking, alcohol consumption, SES, calendar year, sex	A 11% significant risk was observed when restricting to non-smokers only
Bethea et al. (2014) Pooled study of African Americans (7 cohorts) USA Follow-up times differ across cohorts (at least 5 yr)	239 597 Men and women Mortality NR Men Mortality	Pancreas ICD-10: C25 ICD-9: 157	BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}] BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}]	187 270 128 60 68 123 45 10	1.00 1.08 (0.90–1.31) 1.25 (0.99–1.57) 1.31 (0.97–1.77) [0.03] 1.00 1.15 (0.85–1.55) 1.36 (0.93–2.00) 1.14 (0.58–2.24) [0.20]	Age, smoking, education level, marital status, alcohol consumption, physical activity; analysis for men and women also adjusted for sex	

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Bethea et al. (2014) (cont.)	NR Women Mortality		BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [P_{trend}]	119 147 83 50	1.00 1.03 (0.80–1.31) 1.16 (0.87–1.55) 1.34 (0.95–1.89) [0.08]		
Untawale et al. (2014) Singapore Chinese Health Study China 1993–2011	51 251 Men and women Incidence	Pancreas	BMI < 18.5 18.5–21.4 21.5–24.4 24.5–27.4 ≥ 27.5 [P_{trend}]	23 55 53 47 16	1.89 (1.15–3.09) 1.34 (0.92–1.96) 1.00 1.46 (0.99–2.17) 1.02 (0.58–1.79) [0.08]	Age, sex, enrolment year, dialect, education level, diabetes, smoking history, alcohol consumption, diet, physical activity, sleep duration, energy intake	
Genkinger et al. (2015) National Cancer Institute BMI and Mortality Cohort Consortium (pooled analysis of 20 cohort studies) Follow-up varies by cohort	1 564 218 for BMI at baseline 1 096 492 for BMI in early adulthood 647 478 for WC Men and women Mortality	Pancreas ICD-9: 157 ICD-10: C25	BMI at baseline 15–18.4 18.5–21 21–22.9 23–24.9 25–27.4 27.5–29.9 30–34.9 35– < 60 continuous	51 296 574 908 1134 653 617 212	1.10 (0.83–1.47) 1.01 (0.87–1.16) 1.00 1.12 (1.01–1.24) 1.14 (1.03–1.26) 1.14 (1.01–1.27) 1.27 (1.13–1.43) 1.34 (1.14–1.57) 1.09 (1.05–1.12)	Age, race, education level, marital status, alcohol consumption, physical activity, smoking status	The positive association of WC with increased risk of pancreatic cancer mortality remained significant when additionally adjusting for BMI No differences between men and women in associations with BMI at baseline and in early adulthood, or with WC Stronger positive associations of pancreatic cancer risk with BMI change in women than in men

Table 2.2.7a (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site or cancer type (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
Genkinger et al. (2015) (cont.)			BMI in early adulthood				
			15–18.4	376	1.01 (0.89–1.14)		
			18.5–21	1036	0.98 (0.89–1.08)		
			21–22.9	814	1.00		
			23–24.9	510	1.13 (1.01–1.26)		
			25–27.4	331	1.36 (1.20–1.55)		
			27.5–29.9	93	1.48 (1.20–1.84)		
			30–39.9	61	1.43 (1.11–1.85)		
			per 5 kg/m^2		1.18 (1.11–1.25)		
			BMI change				
			< −2.5	117	1.24 (1.01–1.53)		
			−2.5 to 0	269	1.12 (0.97–1.29)		
			0–2.4	658	1.00		
			2.5–4.9	828	1.07 (0.97–1.19)		
			5–7.4	640	1.11 (0.99–1.24)		
			7.5–9.9	357	1.11 (0.98–1.27)		
			≥ 10	354	1.28 (1.12–1.47)		
			per 5 kg/m^2		1.05 (1.01–1.10)		
			WC (cm), quartiles (sex-specific)				
			Men: Women:				
			< 90 < 70	385	1.00		
			90–99 70–79	660	1.11 (0.98–1.27)		
			110–109 80–89	531	1.26 (1.10–1.45)		
			≥ 110 ≥ 90	371	1.31 (1.12–1.54)		
			per 10 cm		1.09 (1.04–1.13)		
			[P_{trend}]		[< 0.0001]		
Meyer et al. (2015) Swiss cohort study Switzerland 1977–2008	35 703 Men and women Mortality	Pancreas ICD-8: 157 ICD-10: C25	BMI < 25 25–29.9 ≥ 30	127 total	1.00 1.20 (0.81–1.78) 1.60 (0.93–2.75)	Sex, age, survey, alcohol consumption, physical activity, civil status, years of education, nationality, diet	

ATBC, Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; BMI, body mass index (in kg/m^2); BP, blood pressure; CI, confidence interval; EPIC, European Prospective Investigation into Cancer and Nutrition; ICD, International Classification of Diseases; JACC, Japan Collaborative Cohort Study for Evaluation of Cancer Risk; NIH-AARP, National Institutes of Health–AARP Diet and Health Study; NR, not reported; SE, standard error; SES, socioeconomic status; WC, waist circumference; yr, year or years

Table 2.2.7b Case–control studies of measures of body fatness and cancer of the pancreas

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Bueno de Mesquita et al. (1990) The Netherlands 1984–1988	Men: 89 Women: 79 Population	BMI 2 yr before diagnosis < 23 > 27.9 [P_{trend}] BMI 2 yr before diagnosis < 21.6 > 28.7 [P_{trend}]	Men: 20 20 Women: 15 12	1.00 0.88 (0.40–1.90) [> 0.50] 1.00 1.10 (0.46–2.80) [> 0.90]	10-yr age group, response status, total smoking	
Ghadirian et al. (1991) Canada 1984–1988	179 Population	BMI < 21.1 > 26.5	42 40	1.00 0.88 (0.42–1.80)	Age, sex, response status, cigarette smoking	
Ji et al. (1996) China 1990–1993	Men: 255 Women: 183 Population	BMI < 19.4 > 22.5 [P_{trend}] BMI < 19.4 > 23.2 [P_{trend}]	Men: 72 59 Women: 43 54	1.0 1.40 (0.91–2.10) [0.14] 1.00 1.50 (0.85–2.50) [0.57]	Age, income, smoking, physical activity, response status, diabetes, vitamin C, total energy In women only: green tea drinking	
Hanley et al. (2001) Canada (7 Canadian provinces) 1994–1997	312 Population	BMI 2 yr before interview < 23.7 23.7– < 25.8 25.8– < 28.3 ≥ 28.3 [P_{trend}]	Men: 31 44 40 57	1.0 1.79 (1.01–3.19) 1.36 (0.74–2.49) 1.90 (1.08–3.35) [0.03]	Age, province, percentage weight change, energy intake, composite index of physical activity	Men who reported a 2.9% or greater decrease in weight from their maximum lifetime weight were at significantly reduced risk of pancreatic cancer
		BMI 2 yr before interview < 22.1 22.1– < 24.5 24.5– < 27.4 ≥ 27.4 [P_{trend}]	Women: 32 22 34 51	1.0 0.64 (0.35–1.18) 0.78 (0.44–1.40) 1.21 (0.70–2.06) [0.39]	Age, province, energy intake, age at first menstruation, cigarette smoking	Women who reported a 12.5% or greater decrease in weight from their maximum lifetime weight were at significantly reduced risk of pancreatic cancer

Table 2.2.7b (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Silverman (2001) USA (Atlanta, Detroit, New Jersey) 1986–1989	Men: 218 Women: 213 Population	BMI 17.35–23.13 23.17–25.07 25.09–27.18 ≥ 27.2 [P_{trend}] BMI 20.49–27.54 27.56–30.25 30.30–34.21 ≥ 34.43 [P_{trend}]	Men: 51 39 55 73 Women: 40 54 57 62	1.0 0.8 (0.5–1.3) 1.1 (0.7–1.7) 1.5 (1.0–2.3) [0.019] 1.0 1.4 (0.9–2.3) 1.5 (0.9–2.4) 1.5 (0.9–2.5) [0.129]	Age at diagnosis/interview, race, area, diabetes mellitus, gall bladder disease, cigarette smoking, alcohol consumption, income (men), marital status (women), energy intake from food	An interaction was observed between BMI and total energy intake in relation to pancreatic cancer risk; those with high BMI and high energy intake were at 60% increased risk.
Eberle et al. (2005) USA 1995–1999	Men: 291 Women: 241 Population	Adult BMI < 23.1 23.1– < 25.1 25.1– < 27.1 ≥ 27.1 [P_{trend}] Adult BMI < 21.5 21.5– < 23.4 23.4– < 25.8 ≥ 25.8 [P_{trend}] BMI at age 25 yr < 20.9 20.9– < 22.8 22.8– < 24.7 ≥ 24.7 [P_{trend}] BMI at age 25 yr < 19.7 19.7– < 21.0 21.0– < 22.5 ≥ 22.5 [P_{trend}]	Men: 48 70 75 95 Women: 67 51 62 61 Men: 44 76 79 91 Women: 54 50 64 72	1.0 1.6 (1.04–2.5) 1.6 (1.1–2.5) 2.1 (1.4–3.2) [0.0007] 1.0 0.72 (0.47–1.1) 0.86 (0.58–1.3) 0.91 (0.61–1.4) [NS] 1.0 1.7 (1.1–2.6) 1.8 (1.2–2.8) 2.0 (1.4–3.1) [0.001] 1.0 0.88 (0.57–1.4) 1.2 (0.77–1.7) 1.3 (0.84–1.9) [0.13]	Age, cigarette smoking only for usual BMI in men	

Table 2.2.7b (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Fryzek et al. (2005) USA (South-eastern Michigan) 1996–1999	Men: 119 Women: 112 Population	Current BMI, quartiles			Age, sex, race, county group, smoking, relative with pancreatic cancer, income, medical history of diabetes	
		Q1: ≤ 24.4	33	1.0		
		Q2: 24.5–27.3	59	0.4 (0.3–0.7)		
		Q3: 27.4–31.5	22	0.2 (0.1–0.3)		
		Q4: 31.5–67.8	17	0.1 (0.0–0.2)		
		$[P_{trend}]$		[< 0.0001]		
		BMI 5 yr before interview, quartiles				
		Q1: ≤ 24.1	46	1.0		
		Q2: 24.2–26.5	56	1.1 (0.6–1.8)		
		Q3: 26.6–30.3	68	1.3 (0.8–2.2)		
		Q4: 30.4–68.5	61	1.0 (0.6–1.8)		
		$[P_{trend}]$		[0.77]		
		BMI 20 yr before interview, quartiles				
		All:				
		Q1: 0.0–22.2	43	1.0		
		Q2: 22.3–24.4	48	1.1 (0.6–1.9)		
		Q3: 24.5–27.4	71	1.6 (0.9–2.6)		
		Q4: 27.5–43.0	69	1.4 (0.8–2.5)		
		$[P_{trend}]$		[0.15]		
		Men:				
		Q1: 0.0–22.2	8	1.0		
		Q2: 22.3–24.4	25	1.6 (0.6–4.1)		
		Q3: 24.5–27.4	43	2.6 (1.0–6.4)		
		Q4: 27.5–43.0	43	2.4 (1.0–6.2)		
		$[P_{trend}]$		[0.048]		
		Women:				
		Q1: 0.0–22.2	35	1.0		
		Q2: 22.3–24.4	23	1.2 (0.6–2.5)		
		Q3: 24.5–27.4	28	1.5 (0.7–3.0)		
		Q4: 27.5–43.0	26	1.4 (0.7–3.0)		
		$[P_{trend}]$		[0.37]		

Table 2.2.7b   (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Fryzek et al. (2005) (cont.)		BMI, ever-smokers				
		≤ 22.2	34	1.0		
		22.3–24.4	32	1.0 (0.5–1.8)		
		24.5–27.4	52	1.7 (0.9–3.1)		
		27.5–43.0	36	0.9 (0.5–1.8)		
		[P_{trend}]		[0.94]		
		BMI, never-smokers				
		≤ 22.2	9	1.0		
		22.3–24.4	16	1.6 (0.6–0.46)		
		24.5–27.4	19	1.5 (0.5–4.0)		
		27.5–43.0	33	3.3 (1.2–9.2)		
		[P_{trend}]		[0.014]		
Pezzilli et al. (2005) Italy	400 Hospital	BMI before diagnosis			Matched for sex, age (± 5 yr), social class, geographical region	
		< 23	110	1.01 (0.72–1.41)		
		23–29.9	246	1.00		
		≥ 30	44	0.96 (0.60–1.53)		
Lo et al. (2007) Egypt 2001–2004	194 Hospital	BMI 1 yr before			Age, sex, residence	
		< 27	99	1.0		
		27–31	59	1.4 (0.9–2.2)		
		≥ 32	28	1.5 (0.8–2.9)		
Anderson et al. (2009) Canada (Ontario) 2003–2007	422 Population	BMI 1 yr before			Age, education level, smoking status, family history of pancreatic cancer, weekly fruit servings, alcohol consumption, caffeinated beverages, allergies	
		< 25	148	1.00		
		25–29.9	183	1.77 (1.19–2.62)		
		≥ 30	83	3.51 (1.92–6.39)		

Table 2.2.7b (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Li et al. (2009) USA (Texas) 2004–2008	841 (men: 496; women: 282) Population (proxy controls)	Mean lifetime BMI, per 5 kg/m² increase	All: 841 Men: 496 Women: 345	1.55 (1.32–1.84) 1.80 (1.45–2.23) 1.32 (1.02–1.70)	Age, race, sex, smoking, alcohol consumption, history of diabetes, family history of cancer	Associations were somewhat stronger in ever-smokers than in never-smokers (1.75 vs 1.46) When stratifying BMI by age ranges, the greatest risk of pancreatic cancer was found at the ages of onset of overweight and/or obesity between 14–19 yr and 20–29 yr
Urayama et al. (2011) Czech Republic and Slovakia 2004–2009	574 Population	BMI at age 20 yr 18.5–21.1 21.2–22.8 22.9–24.5 > 24.5 per 5 kg/m² BMI at age 40 yr 18.5–23.0 23.1–24.8 24.9–27.3 > 27.3 per 5 kg/m² BMI 2 yr before interview 18.5–24.3 24.4–27.1 27.2–30.4 > 30.4 per 5 kg/m²	101 113 161 164 106 114 154 173 131 151 153 130	1.00 1.15 (0.79–1.69) 1.81 (1.24–2.63) 1.79 (1.23–2.61) 1.45 (1.15–1.84) 1.00 1.04 (0.72–1.52) 1.40 (0.97–2.03) 1.57 (1.09–2.27) 1.24 (1.04–1.47) 1.00 1.07 (0.75–1.52) 1.04 (0.73–1.47) 0.91 (0.63–1.30) 0.98 (0.85–1.13)	Centre, age at interview, sex, diabetes mellitus, chronic pancreatitis, smoking, alcohol consumption	
Lin et al. (2013a) Japan 2010–2012	360 (men: 145; women: 215) Hospital	BMI in the yr before study entry < 25 25.0–29.9 ≥ 30	278 64 16	1.00 0.96 (0.65–1.43) 1.21 (0.53–2.77)	Age, sex, history of diabetes, cigarette smoking	

Absence of excess body fatness

Table 2.2.7b (continued)

Reference Study location Period	Total number of cases Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding	Comments
Zheng et al. (2016) China 2011–2013	323 Population (family members of other inpatients)	Current BMI < 24.0 ≥ 24.0	 197 126	 1.00 1.77 (1.22–2.57)	Age, sex, race, residential areas, smoking, tea drinking, mental pressure, family history of pancreatic cancer, diabetes, gallstone, intake of pickles and vegetables	
Pancreatic neuroendocrine tumours						
Halfdanarson et al. (2014) USA (Mayo Clinic Rochester 2004–2011	309 Hospital	Current BMI < 30 ≥ 30	 141 61	 1.00 1.65 (1.11–2.45)		

BMI, body mass index (in kg/m²); CI, confidence interval; NS, not significant; yr, year or years

Table 2.2.7c Meta-analyses of measures of body fatness and cancer of the pancreas

Reference	Total number of studies Total number of cases	Exposure categories	Relative risk (95% CI)	Adjustment for confounding	Comments
Michaud et al. (2001)	2 cohort studies 350	BMI < 23 23–24.9 25.0–26.9 27.0–39.9 ≥ 30 [P_{trend}]	1.00 1.09 (0.79–1.49) 1.29 (0.92–1.80) 1.30 (0.91–1.87) 1.72 (1.19–2.48) [0.003]	Height, BMI at baseline, age, smoking, history of diabetes mellitus, cholecystectomy	
Berrington de Gonzalez et al. (2003)	6 case–control studies 8 cohort studies 6391	BMI, per 1 kg/m² increase	1.02 (1.01–1.03)	Age (all), smoking and diabetes (not all studies)	No differences were observed between men and women or when stratifying by study design (cohort vs case–control)
Larsson et al. (2007)	21 prospective studies (13 in men and 10 in women) 8062	BMI, per 5 kg/m² increase	All: 1.12 (1.06–1.17) Men: 1.16 (1.05–1.28) Women: 1.10 (1.02–1.19)	All studies adjusted for age, cigarette smoking; 13 studies also adjusted for diabetes	
Renehan et al. (2008)	12 prospective studies All studies: Men: 2390 Women: 2053 Studies with both sexes: Men: 839 Women: 778	BMI, per 5 kg/m² increase	Men: 1.07 (0.93–1.23) Women: 1.12 (1.03–1.23) Men: 1.07 (0.83–1.39) Women: 1.12 (0.95–1.33)	Method of BMI determination, extent of cancer site-specific risk factor adjustment, geographical region	When stratifying by region, the highest risk ratios were reported in North America (n = 2 studies)
Guh et al. (2009)	10 prospective studies (4 in men and 6 in women) NR	BMI Normal Overweight Obesity BMI Normal Overweight Obesity	Men: 1.00 1.28 (0.94–1.75) 2.29 (1.65–3.19) Women: 1.00 1.24 (0.98–1.56) 1.60 (1.17–2.20)		

Table 2.2.7c (continued)

Reference	Total number of studies Total number of cases	Exposure categories	Relative risk (95% CI)	Adjustment for confounding	Comments
Aune et al. (2012)	23 prospective studies 9504	BMI, per 5 kg/m² increase	All (23 studies): 1.10 (1.07–1.14) Men (14 studies): 1.13 (1.04–1.22) Women (15 studies): 1.10 (1.04–1.16) Never-smoker (5 studies): 1.11 (1.04–1.17) Ever-smoker (4 studies): 1.03 (0.95–1.10)		Non-linear association between BMI and pancreatic cancer risk, with the most pronounced increase in risk in those with BMI > 35
WCRF/AICR (2012)	23 cohort studies 9504	BMI, per 5 kg/m² increase	Incidence: 1.10 (1.07–1.14)	NR	No differences were observed between men and women. Some evidence for a non-linear dose–response with an increase in risk from BMI ≥ 25
		BMI, per 5 kg/m² increase	Mortality: 1.10 (1.02–1.19)		
	5 cohort studies 949	WC, per 10 cm increase	1.11 (1.05–1.18)	NR	
	4 cohort studies 900	BMI at age 20 yr, per 5 kg/m² increase	1.12 (0.97–1.29)	NR	

BMI, body mass index (in kg/m²); CI, confidence interval; NR, not reported; WC, waist circumference; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research; yr, year or years

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