

### 2.2.20 Haematopoietic malignancies of lymphoid origin

Haematopoietic malignancies are a heterogeneous group of cancers that arise from the blood, the bone marrow, and lymphoid tissue, and the cells of origin are either lymphoid or myeloid. Historically, haematopoietic cancers were grouped into five major categories: Hodgkin lymphoma, non-Hodgkin lymphoma (NHL), multiple myeloma (also referred to as plasma cell myeloma), acute leukaemia, and chronic leukaemia. However, these historical groupings do not reflect the current understanding of etiology and pathogenesis or current clinical practice. In 2001, the World Health Organization (WHO) introduced a new classification system (Jaffe et al., 2001), which was subsequently updated (Swerdlow et al., 2008) and is considered the reference standard for classification of these malignancies. The WHO classification has been adopted worldwide, and the terminology has been incorporated into the third edition of the International Classification of Diseases for Oncology (ICD-O-3) (WHO, 2013).

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 cancers of the haematopoietic system (e.g. NHL, multiple myeloma) was *inadequate*. In the current review are included epidemiological studies of BMI, weight, or waist circumference at baseline in relation to risk of the more common types of haematopoietic malignancies for which the body of evidence was substantial enough to review. These include Hodgkin lymphoma, NHL, B-cell lymphoma overall, chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, multiple myeloma, T-cell lymphoma, leukaemia overall, acute myeloid leukaemia (AML), and chronic myeloid

leukaemia (CML). Also included are findings from prospective studies with at least 50 cases for any specific subtype, meta-analyses or pooled analyses from prospective and case-control studies, and findings from case-control studies with at least 50 cases that were not included in a meta-analysis or pooled analysis. For malignancies for which there was evidence suggesting a relationship between BMI or weight at baseline and risk, the Working Group also weighed into their evaluation studies that assessed weight change and weight during young adulthood in relation to risk. Not all studies separated the haematopoietic cancers according to the current WHO classification system. Therefore, findings are presented about relationships between BMI and both individual haematological cancers and groups of cancers.

Table 2.2.20a and Table 2.2.20b (both web only, available at: <http://publications.iarc.fr/570>) present data for cohort and case-control studies, respectively, for subsites with *inadequate* evidence; Table 2.2.20c and Table 2.2.20d present the corresponding studies for subsites with *sufficient* or *limited* evidence.

#### (a) Hodgkin lymphoma

There are at least four individual prospective studies and one meta-analysis of BMI at baseline in relation to incidence of Hodgkin lymphoma (Table 2.2.20a, web only, available at: <http://publications.iarc.fr/570>). Results from three prospective studies in men (i.e. the United States Veterans cohort, the NIH-AARP cohort, and the Swedish Construction Worker cohort) showed increased risks (Samanic et al., 2004, 2006; Lim et al., 2007), none of which were statistically significant, whereas a Norwegian cohort study found a positive association in women but not in men (Engeland et al., 2007). [Most studies had limited statistical power, particularly at the high end of the BMI categories.] However, in the meta-analysis of five studies, obesity was

associated with a statistically significant 41% higher risk of Hodgkin lymphoma compared with normal BMI ([Larsson & Wolk, 2011](#)).

Only three case-control studies with at least 50 cases have evaluated the relationship between BMI and risk of Hodgkin lymphoma (Table 2.2.20b, web only, available at: <http://publications.iarc.fr/570>). The largest study, including 618 cases from the Scandinavian Lymphoma Etiology Study and 3187 population controls, did not find a relationship between BMI and risk of Hodgkin lymphoma in individuals younger or older than 45 years, assessed separately because of the bimodal distribution of the disease ([Chang et al., 2005](#)). A second large study, including 567 cases and 697 controls, also did not find a relationship between BMI and risk of Hodgkin lymphoma in subgroups defined by sex and age ([Li et al., 2013](#)). However, a smaller study of 216 cases and 216 matched controls, which considered BMI 5 years before cancer diagnosis, found an increased risk of Hodgkin lymphoma with BMI  $\geq 30$  kg/m<sup>2</sup> compared with normal BMI in men, but not in women ([Willett & Roman, 2006](#)).

#### (b) *Non-Hodgkin lymphoma*

There are at least 21 individual prospective studies and 4 meta-analyses or pooled analyses of BMI and/or weight at baseline in relation to NHL (Table 2.2.20a, web only, available at: <http://publications.iarc.fr/570>). There were no associations of either BMI or weight with NHL incidence or mortality in 12 individual prospective studies ([Samanic et al., 2004, 2006](#); [Fujino et al., 2007](#); [Maskarinec et al., 2008](#); [Song et al., 2008](#); [Andreotti et al., 2010](#); [De Roos et al., 2010](#); [Kanda et al., 2010](#); [Hemminki et al., 2011](#); [Kabat et al., 2012](#); [Bertrand et al., 2013](#); [Bhaskaran et al., 2014](#)). The other nine studies found positive associations in men and/or women ([Calle et al., 2003](#); [Oh et al., 2005](#); [Rapp et al., 2005](#); [Chiu et al., 2006](#); [Engeland et al., 2007](#); [Lim et al., 2007](#); [Reeves et al., 2007](#); [Troy et al., 2010](#); [Chu et al., 2011](#)).

Three meta-analyses showed a positive association between BMI and NHL incidence and/or mortality ([Larsson & Wolk, 2007a, 2011](#); [Renehan et al., 2008](#)), whereas one pooled analysis found no association ([Whitlock, et al., 2009](#)). [The inconsistent evidence from individual prospective studies and meta-analyses may be due to the variation in histological subtypes included in a classification of NHL.]

No association between waist circumference and NHL incidence was seen in the Women's Health Initiative in the USA ([Kabat et al., 2012](#)). However, in a cohort in Taiwan, China, high abdominal obesity (waist circumference  $\geq 90$  cm in men and  $\geq 80$  cm in women) was associated with an 86% higher risk of fatal NHL compared with lower waist circumference ([Chu et al., 2011](#)).

A total of 11 hospital-based or population-based case-control studies have evaluated the relationship between BMI and risk of any NHL (Table 2.2.20b, web only, available at: <http://publications.iarc.fr/570>). A meta-analysis of six of these reports published in 2004 and 2005 ([Pan et al., 2004](#); [Skibola et al., 2004](#); [Bosetti et al., 2005](#); [Cerhan et al., 2005](#); [Chang et al., 2005](#); [Willett et al., 2005](#)) reported a relative risk of NHL of 1.22 (95% CI, 1.00–1.50) in individuals with BMI  $\geq 30$  kg/m<sup>2</sup> ([Larsson & Wolk, 2007a](#)). A subsequent pooled analysis from the InterLymph Consortium included data from 10 000 cases of NHL and 16 000 controls drawn from 18 case-control studies identified through the International Lymphoma Epidemiology Consortium ([Willett et al., 2008](#)). That study did not find a relationship between BMI and risk of NHL, with a relative risk of NHL of 0.84 (95% CI, 0.72–0.99) in individuals with BMI of 30–39.9 kg/m<sup>2</sup> and a relative risk of 0.63 (95% CI, 0.40–0.99) in those with BMI  $\geq 40$  kg/m<sup>2</sup>.

#### (c) *B-cell lymphoma*

The association between excess body fatness and the incidence of B-cell lymphoma was examined in three individual prospective

studies (Table 2.2.20a, web only, available at: <http://publications.iarc.fr/570>) [notably, under the current classification, this includes all B-cell malignancies previously included under NHL]. Although no association was found with BMI and/or weight in men or in women in the EPIC cohort ([Britton et al., 2008](#)), there were statistically significant positive trends with weight in the California Teachers Study ([Lu et al., 2009](#)) and with BMI in the Cancer Prevention Study II Nutrition Cohort ([Patel et al., 2013](#)).

In the one study that assessed waist circumference, there was no association with the incidence of B-cell lymphoma in either men or women ([Britton et al., 2008](#)).

(d) *Subtypes of B-cell lymphoma*

(i) *Chronic lymphocytic leukaemia/small lymphocytic lymphoma*

Most of the individual prospective studies (Table 2.2.20a, web only, available at: <http://publications.iarc.fr/570>) found no associations of BMI and/or weight at baseline with the incidence of CLL or CLL/SLL ([Ross et al., 2004](#); [Samanic et al., 2006](#); [Engeland et al., 2007](#); [Lim et al., 2007](#); [Lu et al., 2009](#); [Pylypchuk et al., 2009](#); [Kabat et al., 2012](#); [Bertrand et al., 2013](#); [Patel et al., 2013](#); [Saber Hosnijeh et al., 2013](#)). However, in the United States Veterans study, the largest individual prospective study, the risk of CLL was 30% higher in obese White men and 72% higher in obese Black men compared with non-obese men ([Samanic et al., 2004](#)). In the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial in the USA, baseline weight, but not BMI, was positively associated with risk ( $P_{\text{trend}} < 0.215$ ) ([Troy et al., 2010](#)). Although an earlier meta-analysis of three cohort studies suggested a 25% higher risk of CLL for obesity versus normal weight ([Larsson & Wolk, 2008](#)), an updated meta-analysis of six prospective studies found no association between BMI as a continuous measure and incidence of CLL/SLL ([Larsson & Wolk, 2011](#)).

No association between waist circumference and CLL/SLL incidence was found in the three studies that examined this relationship ([Ross et al., 2004](#); [Kabat et al., 2012](#); [Saber Hosnijeh et al., 2013](#)).

Five case-control studies with at least 50 cases assessed the relationship between BMI and risk of CLL/SLL (Table 2.2.20b, web only, available at: <http://publications.iarc.fr/570>) and found no association between BMI and CLL/SLL risk ([Chang et al., 2005](#); [Pan et al., 2005](#); [Morton et al., 2008](#); [Chen et al., 2011](#); [Kelly et al., 2012](#)).

(ii) *Diffuse large B-cell lymphoma*

Associations of baseline BMI and/or weight with risk of DLBCL have been examined in at least nine individual prospective studies and two meta-analyses (Table 2.2.20c). Most individual prospective studies found no evidence of an association ([Lim et al., 2007](#); [Britton et al., 2008](#); [Maskarinec et al., 2008](#); [Lu et al., 2009](#); [Pylypchuk et al., 2009](#); [Kabat et al., 2012](#); [Bertrand et al., 2013](#)). However, two large studies in the USA did report statistically significant trends between baseline weight ([Troy et al., 2010](#)) or BMI ([Patel et al., 2013](#)) and DLBCL incidence. Both meta-analyses also showed statistically significant positive associations. One meta-analysis reported a relative risk per 5 kg/m<sup>2</sup> increase of 1.13 (95% CI, 1.02–1.26) ([Larsson & Wolk, 2011](#)). In the other meta-analysis, both overweight and obesity in men and women were associated with increased risk ([Castillo et al., 2014](#)).

Six individual studies assessed the association between BMI or weight in early adulthood and incidence of DLBCL. In the two large studies in the USA, there were statistically significant positive associations of weight at age 20 years ( $P_{\text{trend}} = 0.013$ ) ([Troy et al., 2010](#)) and of young adult BMI in men and women combined ( $P_{\text{trend}} = 0.02$ ) ([Bertrand et al., 2013](#)) with risk of DLBCL. However, in none of the four other studies was BMI and/or body weight at age 18 years ([Lu et al., 2009](#); [Patel et al., 2013](#)), at

age 20 years (Pylypchuk et al., 2009), or at age 21 years (Maskarinec et al., 2008) associated with DLBCL incidence. Similarly, adult weight gain was not associated with risk of DLBCL in any of the studies that examined this association (Maskarinec et al., 2008; Troy et al., 2010; Patel et al., 2013).

In the EPIC cohort, there was a 2-fold (RR, 2.03; 95% CI, 0.96–4.28) higher incidence of DLBCL for waist circumference  $\geq 102$  cm versus  $< 102$  cm in men (based on only 21 cases in the group with high waist circumference), and no association in women (Britton et al., 2008). Similarly, there was no association between waist circumference and risk of DLBCL in the Women's Health Initiative in the USA (Kabat et al., 2012).

A pooled analysis of 19 case–control studies from the InterLymph Consortium of 4667 cases of DLBCL and 22 639 controls found a significant positive association between risk of DLBCL and young adult BMI, but not usual adult BMI (Cerhan et al., 2014). A case–control study from the National Enhanced Cancer Surveillance System in Canada, including 419 cases of DLBCL, found an odds ratio for individuals with BMI  $\geq 30$  kg/m<sup>2</sup> of 1.35 (95% CI, 0.99–1.83) (Pan et al., 2005). Another case–control study, by Chen et al., (2011), including 245 cases of DLBCL, did not find a relationship between BMI and risk of DLBCL (Table 2.2.20d).

### (iii) Follicular lymphoma

None of the nine individual prospective studies (Lim et al., 2007; Britton et al., 2008; Maskarinec et al., 2008; Lu et al., 2009; Pylypchuk et al., 2009; Troy et al., 2010; Kabat et al., 2012; Bertrand et al., 2013; Patel et al., 2013) or the one meta-analysis (Larsson & Wolk, 2011) showed any evidence of an association between BMI and/or weight and the incidence of follicular lymphoma (Table 2.2.20a, web only, available at: <http://publications.iarc.fr/570>).

Waist circumference was also not associated with the incidence of follicular lymphoma in

the two studies that examined this relationship (Britton et al., 2008; Kabat et al., 2012).

The largest study evaluating the association between BMI and follicular lymphoma (Table 2.2.20b, web only, available at: <http://publications.iarc.fr/570>) was a pooled analysis of 3530 cases and 22 639 population controls from 19 case–control studies in the InterLymph Consortium, which found no relationship between BMI and risk of follicular lymphoma (Linnet et al., 2014). Two additional case–control studies not included in the pooled analysis also found no association between adult BMI and risk of follicular lymphoma (Pan et al., 2005; Chen et al., 2011).

Therefore, the relationship between BMI and risk of NHL varies by subtype, with a positive association seen in some studies limited to the risk of DLBCL, but not in studies assessing the risk of any NHL or of follicular lymphoma.

### (e) Multiple myeloma

In the individual prospective studies that examined the association of baseline BMI and/or weight with multiple myeloma incidence or mortality (Table 2.2.20c), most found positive associations for at least one measure of excess body fatness at baseline (Calle et al., 2003; Samanic et al., 2004; Blair et al., 2005; Birmann et al., 2007; Engeland et al., 2007; Fujino et al., 2007; Reeves et al., 2007; Troy et al., 2010; Hofmann et al., 2013). In particular, a positive association was observed in the largest studies. In the United States Veterans cohort of more than 4 million men, the risk of multiple myeloma was 22% higher in obese White men and 26% higher in obese Black men compared with non-obese men (Samanic et al., 2004). Similarly, the Million Women Study in the United Kingdom found positive associations between BMI and multiple myeloma incidence and mortality (31% and 56% increase, respectively, per 10 kg/m<sup>2</sup>) (Reeves et al., 2007). In a Norwegian cohort study of more than 2 million men and women whose height and weight were measured at baseline in 1963, there



were statistically significant dose-related positive associations between BMI and risk of multiple myeloma in men (RR, 1.14 for overweight and 1.28 for obesity vs normal BMI;  $P_{\text{trend}} < 0.001$ ) and in women (RR, 1.12 for overweight, 1.23 for grade I, 1.42 for grade II, and 1.57 for grade III obesity vs normal BMI;  $P_{\text{trend}} < 0.001$ ) (Engeland et al., 2007). One study found an inverse association (Samanic et al., 2006), and several studies found no association (Oh et al., 2005; Fernberg et al., 2007; Pylypchuk et al., 2009; De Roos et al., 2010; Lu et al., 2010; Kanda et al., 2010; Patel et al., 2013; Bhaskaran et al., 2014).

Several meta-analyses or pooled analyses of excess body fatness in relation to multiple myeloma incidence and/or mortality have been conducted (Larsson & Wolk, 2007b; Renehan et al., 2008; Parr et al., 2010; Wallin & Larsson, 2011; Teras et al., 2014). No association between BMI and multiple myeloma mortality was found in the Asia-Pacific Cohort Study Collaboration (Parr et al., 2010). However, in the meta-analysis by Wallin & Larsson (2011), which included studies worldwide, overweight and obesity were associated with a statistically significantly increased risk of multiple myeloma incidence (RR, 1.12 for overweight and 1.21 for obesity, based on 15 studies) and mortality (RR, 1.15 for overweight and 1.54 for obesity, based on 5 studies). The two earlier meta-analyses (Larsson & Wolk, 2007b; Renehan et al., 2008) found statistically significant positive associations of a similar magnitude. Consistent with these findings, in a pooled analysis of data from 20 prospective studies (Teras et al., 2014), there was a statistically significant positive association between BMI and multiple myeloma mortality (RR per 5 kg/m<sup>2</sup> increase in BMI, 1.09).

Given the observed associations between baseline BMI and risk of multiple myeloma, associations with young adult BMI and with BMI change were also examined. Several studies found no association between young adult BMI and risk of multiple myeloma (Fujino et al., 2007;

Pylypchuk et al., 2009; De Roos et al., 2010; Lu et al., 2010; Patel et al., 2013), whereas in two large studies young adult BMI was positively associated with risk (Troy et al., 2010; Hofmann et al., 2013). In the large pooled analysis by Teras et al. (2014) there was a statistically significant positive association between increasing levels of young adult BMI (beginning in the overweight category) and multiple myeloma mortality, although there was no association for change in BMI during adulthood.

High waist circumference was associated with increased multiple myeloma incidence in one prospective study of postmenopausal women (Blair et al., 2005), but not in two other studies (Britton et al., 2008; Lu et al., 2010). In the large pooled analysis by Teras et al. (2014), there was a statistically significant positive association between waist circumference and multiple myeloma mortality in men and women combined (RR per 5 cm increase, 1.06).

Five case-control studies have evaluated the relationship between BMI and the risk of multiple myeloma, four of which were included in a meta-analysis (Larsson & Wolk, 2007b; Table 2.2.20d). An increased risk of multiple myeloma was reported in individuals who were overweight (RR, 1.43; 95% CI, 1.23–1.68) and those who were obese (RR, 1.82; 95% CI, 1.47–2.26). One additional study reported no significant association (Wang et al., 2013).

#### (f) *T-cell lymphoma*

In the Cancer Prevention Study II Nutrition Cohort (Table 2.2.20a, web only, available at: <http://publications.iarc.fr/570>), there was a positive association between BMI and the incidence of T-cell lymphoma ( $P_{\text{trend}} = 0.013$ ) (Patel et al., 2013). However, in two European cohort studies there was no association (Lukanova et al., 2006; Lim et al., 2007). In the Cancer Prevention Study II Nutrition Cohort, BMI at age 18 years was not associated with the incidence of T-cell lymphoma (Patel et al., 2013).

**Table 2.2.20c Cohort studies of measures of body fatness and haematopoietic malignancies of lymphoid origin with sufficient or limited evidence**

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<i>Diffuse large B-cell lymphoma</i>							
<a href="#">Lim et al. (2007)</a> NIH-AARP cohort USA 1995–2003	473 984 Men and women Incidence	DLBCL ICD-O-2: 9680–9684, 9688, 9710–9712, 9715	BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [ <i>P</i> <sub>trend</sub> ]	119 141 61 21	1.00 0.92 (0.72–1.18) 1.10 (0.81–1.51) 1.17 (0.73–1.88) [0.42]	Age, ethnicity, education level, alcohol intake, cigarette smoking, height, physical activity	
<a href="#">Britton et al. (2008)</a> EPIC cohort 10 European countries 1993–1998	141 425 Men Incidence	DLBCL	BMI < 25 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ] Weight (kg) < 72.7 72.7–79.8 79.9–87.7 ≥ 87.8 [ <i>P</i> <sub>trend</sub> ] WC (cm) < 102 ≥ 102	24 37 10  19 13 20 19  44 21	1.00 0.83 (0.39–1.76) 0.94 (0.56–1.59) [0.63]  1.00 0.59 (0.29–1.20) 0.90 (0.46–1.74) 0.86 (0.42–1.77) [1.00]  1.00 2.03 (0.96–4.28)	Age, study centre	Also examined height, hip circumference, and waist-to-hip ratio
	230 558 Women Incidence	DLBCL	BMI < 25 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ]	30 31 12	1.00 1.27 (0.63–2.55) 1.54 (0.92–2.57) [0.28]	Age, study centre	Also examined height, hip circumference, and waist-to-hip ratio

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Britton et al. (2008)</a> (cont.)			Weight (kg) < 72.7 72.7–79.8 79.9–87.7 ≥ 87.8 [ <i>P</i> <sub>trend</sub> ]	14 12 21 26	1.00 0.78 (0.35–1.69) 1.32 (0.66–2.68) 1.62 (0.81–3.25) [0.06]		
			WC (cm) < 88 ≥ 88	47 21	1.00 0.88 (0.42–1.85)		
<a href="#">Maskarinec et al. (2008)</a> Multiethnic Cohort 1993–2002	87 079 Men Incidence	DLBCL ICD-O-3: 9675, 9680, 9684	BMI at baseline < 22.5 22.5–24.9 25.0–29.9 ≥ 30.0 [ <i>P</i> <sub>trend</sub> ] BMI at age 21 yr < 18.5 18.5–24.9 25.0–29.9 ≥ 30.0 [ <i>P</i> <sub>trend</sub> ] Weight (lb) at baseline < 152.0 152.0–170.0 170.1–192.0 > 192.0 [ <i>P</i> <sub>trend</sub> ] Weight (lb) at age 21 yr < 130.0 130.0–145.0 145.1–165.0 > 165.0 [ <i>P</i> <sub>trend</sub> ]	23 44 60 23  14 105 17 5  47 37 32 35  43 34 38 27	0.65 (0.35–1.21) 1.00 0.90 (0.56–1.43) 0.78 (0.40–1.52) [0.69] 0.56 (0.27–1.15) 1.00 0.78 (0.41–1.48) 1.03 (0.36–2.91) [0.51] 1.00 1.97 (1.16–3.36) 1.36 (0.75–2.49) 1.87 (0.95–3.68) [0.12] 1.00 0.87 (0.50–1.53) 1.24 (0.64–2.41) 1.26 (0.63–2.50) [0.33]	Age, ethnicity, education level, alcohol consumption	

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments	
<a href="#">Maskarinec et al. (2008)</a> (cont.)		DLBCL ICD-O-3: 9675, 9680, 9684	Annual weight change (lb)					
			0 or loss	32	1.00			
			≤ 1	89	1.07 (0.62–1.86)			
			> 1	31	1.14 (0.56–2.34)			
			[ <i>P</i> <sub>trend</sub> ]		[0.69]			
			BMI at baseline					Age, ethnicity, education
			< 22.5	27	1.41 (0.66–3.00)			level, alcohol
			22.5–24.9	30	1.00			consumption, age
			25.0–29.9	43	1.06 (0.58–1.96)			at first birth
			≥ 30.0	28	1.45 (0.75–2.82)			
			[ <i>P</i> <sub>trend</sub> ]		[0.80]			
			BMI at age 21 yr					
			< 18.5	16	1.02 (0.50–2.10)			
			18.5–24.9	91	1.00			
			25.0–29.9	11	1.08 (0.50–2.33)			
			≥ 30.0	4	0.94 (0.25–3.55)			
			[ <i>P</i> <sub>trend</sub> ]		[1.00]			
			Weight (lb) at baseline					
			< 125.0	26	1.00			
			125.0–143.0	38	0.74 (0.40–1.38)			
			143.1–167.0	35	1.35 (0.67–2.75)			
			> 167.0	30	1.20 (0.57–2.52)			
			[ <i>P</i> <sub>trend</sub> ]		[0.40]			
Weight (lb) at age 21 yr								
< 105.0	22	1.00						
105.0–118.0	34	0.70 (0.35–1.41)						
118.1–127.0	34	0.97 (0.48–1.96)						
> 127.0	33	1.10 (0.53–2.29)						
[ <i>P</i> <sub>trend</sub> ]		[0.44]						
Annual weight change (lb)								
0 or loss	19	1.00						
≤ 1	85	0.56 (0.21–1.55)						
> 1	28	0.93 (0.34–2.54)						
[ <i>P</i> <sub>trend</sub> ]		[0.85]						



Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Lu et al. (2009)</a> California Teachers Study USA 1995–2007	121 216 Women Incidence	DLBCL	BMI at baseline < 20 20–24.9 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ] BMI at age 18 yr < 19.5 19.5–20.7 20.8–22.4 > 22.4 [ <i>P</i> <sub>trend</sub> ] Weight (kg) at baseline < 56.7 56.7– < 63.5 63.5– < 73.0 ≥ 73.0 [ <i>P</i> <sub>trend</sub> ] Weight (kg) at age 18 yr < 52.6 52.6– < 57.2 57.2– < 61.7 ≥ 61.7 [ <i>P</i> <sub>trend</sub> ]	17 64 41 26	1.42 (0.83–2.42) 1.00 1.07 (0.72–1.59) 1.37 (0.86–2.16) [0.50] 0.98 (0.62–1.56) 1.00 0.90 (0.56–1.45) 1.23 (0.79–1.92) [0.30] 1.24 (0.76–2.03) 1.00 0.90 (0.57–1.43) 1.08 (0.68–1.72) [0.81] 0.88 (0.54–1.41) 1.00 1.16 (0.72–1.84) 1.23 (0.79–1.92) [0.19]	Weight, height, age at menarche, and physical activity	Also included results for height and physical activity
<a href="#">Pylypchuk et al. (2009)</a> Netherlands Cohort Study on Diet and Cancer The Netherlands 1986–1999	5000 Men and women Incidence	DLBCL ICD-O-3: 9675, 9680, 9684	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ] per 4 kg/m <sup>2</sup>	3 112 101 8	1.91 (0.58–6.30) 1.00 1.16 (0.88–1.53) 0.62 (0.30–1.30) [0.77] 0.92 (0.77–1.10)	Age, sex	Case-cohort design

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Pylypchuk et al. (2009)</a> (cont.)			BMI at age 20 yr < 20 20–21.4 21.5–22.9 23–24.9 ≥ 25 [P <sub>trend</sub> ]	39 43 41 43 16	0.96 (0.61–1.50) 1.00 0.99 (0.64–1.54) 1.35 (0.88–2.10) 1.29 (0.71–2.35) [0.12]		
<a href="#">Troy et al. (2010)</a> PLCO Trial USA 1993–2006	142 982 Men and women Incidence	DLBCL	BMI at baseline < 18.5 18.5–24.9 25–29.9 ≥ 30 [P <sub>trend</sub> ] BMI at age 20 yr < 18.5 18.5–24.9 25–29.9 ≥ 30 [P <sub>trend</sub> ] Weight change (kg) per 10 yr Loss Gain 0–2 Gain 2.1–4 Gain 4.1–6 Gain ≥ 6 [P <sub>trend</sub> ] Weight (kg) at baseline, quartiles (sex-specific) Men: < 77.4 77.4–85.5 85.6–95.5 > 95.5 [P <sub>trend</sub> ] Women: < 61.5 61.5–70.0 70.1–80.0 > 80.0	4 58 87 63 17 157 35 1 10 53 66 46 37 51 46 54 63	– 1.00 1.07 (0.76–1.50) 1.58 (1.10–2.27) [0.056] 1.22 (0.74–2.02) 1.00 1.19 (0.82–1.73) – [0.230] 0.70 (0.35–1.39) 1.00 1.13 (0.78–1.63) 1.32 (0.88–1.97) 1.41 (0.91–2.18) [0.114] 1.00 1.05 (0.71–1.57) 1.18 (0.81–1.74) 1.63 (1.12–2.37) [< 0.01]	Age, race/ ethnicity, education level	

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Troy et al. (2010)</a> (cont.)			Weight (kg) at age 20 yr, quartiles (sex-specific) Men: < 64.2 64.2–72.7 72.8–79.5 > 79.5 [P <sub>trend</sub> ]	Women: < 51.9 51.9–54.5 54.6–59.1 > 59.1	40 1.00 41 1.26 (0.81–1.95) 66 1.46 (0.98–2.17) 65 1.67 (1.12–2.50) [0.013]		
<a href="#">Larsson &amp; Wolk (2011)</a> Meta-analysis Multiple locations 1999–2010	6 studies Men and women Incidence	DLBCL	BMI per 5 kg/m <sup>2</sup>		NR 1.13 (1.02–1.26)		
<a href="#">Kabat et al. (2012)</a> Women's Health Initiative USA 1993–2009	158 975 Women Incidence	DLBCL ICD-O-3: 9678–9680, 9684	BMI at baseline < 25 25– < 30 30– < 35 ≥ 35 [P <sub>trend</sub> ] Weight (kg) at baseline < 62.0 62.0– < 70.4 70.4– < 81.6 ≥ 81.6 [P <sub>trend</sub> ] WC (cm) at baseline < 76.1 76.1– < 84.6 84.6– < 95.0 > 95.0 [P <sub>trend</sub> ]	99 115 55 33 73 79 80 70 70 80 68 84	1.00 1.23 (0.93–1.62) 1.11 (0.78–1.58) 1.30 (0.85–1.99) [0.25] 1.00 1.09 (0.78–1.51) 1.11 (0.79–1.56) 1.05 (0.72–1.52) [0.77] 1.00 1.13 (0.82–1.58) 1.02 (0.72–1.44) 1.28 (0.91–1.81) [0.25]	Age, smoking, alcohol consumption, education level, ethnicity, physical activity, energy intake, substudy	Also included estimates for height, hip circumference, waist-to-hip ratio, and weight/BMI at ages 18 yr, 35 yr, and 50 yr

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Bertrand et al. (2013)</a> Nurses' Health Study and Health Professionals Follow-up Study USA 1976–2008	163 184 Men and women Incidence	DLBCL	Adult BMI per 5 kg/m <sup>2</sup> [ <i>P</i> <sub>trend</sub> ]	[261]	1.10 (0.91–1.33) [0.31]	Age, height, smoking, physical activity, race	
			Young adult BMI per 5 kg/m <sup>2</sup> [ <i>P</i> <sub>trend</sub> ]	[241]	1.29 (1.05–1.57) [0.02]		
	46 390 Men Incidence	DLBCL	Adult BMI 15–22.9	11	1.00	Age, height, smoking, physical activity, race	
			23–24.9	25	1.57 (0.75–3.28)		
			25–26.9	23	1.58 (0.75–3.34)		
			27–29.9	17	1.65 (0.75–3.64)		
			30–45	10	2.18 (0.88–5.40)		
			per 5 kg/m <sup>2</sup> [ <i>P</i> <sub>trend</sub> ]		1.30 (0.92–1.82) [0.14]		
			Young adult BMI 15–18.4	4	1.36 (0.46–4.02)		
			18.5–22.9	40	1.00		
23–24.9	19	0.94 (0.54–1.64)					
25–29.9	17	1.16 (0.65–2.08)					
116 794 Women Incidence	DLBCL	30–45	4	2.70 (0.93–7.86)			
		per 5 kg/m <sup>2</sup> [ <i>P</i> <sub>trend</sub> ]		1.29 (0.89–1.88) [0.18]			
		Adult BMI 15–22.9	60	1.00	Age, height, smoking, physical activity, race		
		23–24.9	38	0.97 (0.64–1.46)			
		25–26.9	31	1.06 (0.69–1.65)			
		27–29.9	23	0.85 (0.52–1.38)			
		30–45	33	1.36 (0.88–2.10)			
		per 5 kg/m <sup>2</sup> [ <i>P</i> <sub>trend</sub> ]		1.04 (0.88–1.23) [0.65]			

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Bertrand et al. (2013)</a> (cont.)			Young adult BMI 15–18.4 18.5–22.9 23–24.9 25–29.9 30–45 per 5 kg/m <sup>2</sup> [P <sub>trend</sub> ]	14 104 18 17 4	0.71 (0.40–1.24) 1.00 0.99 (0.60–1.64) 1.26 (0.75–2.11) 1.39 (0.51–3.81) 1.28 (1.01–1.63) [0.04]		
<a href="#">Patel et al. (2013)</a> Cancer Prevention Study II Nutrition Cohort USA 1992–2007	152 423 Men and women Incidence	DLBCL	BMI at baseline < 18.5 18.5– < 25 25– < 30 ≥ 30 [P <sub>trend</sub> ] BMI at age 18 yr < 18.5 18.5– < 22.5 22.5– < 25 25– < 30 ≥ 30 [P <sub>trend</sub> ] Adult weight change (lb) Loss > 5 Loss 5 to gain 20 Gain 21–40 Gain 41–60 Gain > 60 [P <sub>trend</sub> ]	1 159 199 85  52 245 88 44 7  11 147 142 83 52	0.28 (0.04–1.97) 1.00 1.30 (1.05–1.61) 1.62 (1.23–2.12) [0.0001] 0.86 (0.64–1.17) 1.00 1.07 (0.83–1.38) 1.01 (0.72–1.42) 1.30 (0.60–2.80) [0.32] 0.60 (0.32–1.10) 1.00 0.97 (0.77–1.22) 0.97 (0.74–1.28) 1.11 (0.80–1.54) [0.25]	Age, sex, family history of haematopoietic cancer, education level, smoking status, physical activity, alcohol consumption	



**Table 2.2.20c (continued)**

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Castillo et al. (2014)</a> Meta-analysis of 10 cohorts, 6 case-control	NR Men and women Incidence NR Men Incidence NR Women Incidence	DLBCL  DLBCL  DLBCL	BMI Overweight Obese BMI Overweight Obese BMI Overweight Obese		1.14 (1.04–1.24) 1.29 (1.16–1.43)  1.27 (1.09–1.47) 1.40 (1.00–1.95)  1.22 (1.07–1.38) 1.34 (1.16–1.54)		
<i>Multiple myeloma</i>							
<a href="#">Calle et al. (2003)</a> Cancer Prevention Study II USA 1982–1998	495 477 Women Mortality  404 576 Men Mortality	Multiple myeloma	BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [ <i>P</i> <sub>trend</sub> ] BMI 18.5–24.9 25–29.9 30–34.9 ≥ 35 [ <i>P</i> <sub>trend</sub> ]	341 187 72 20  259 368 70 11	1.00 1.12 (0.93–1.34) 1.47 (1.13–1.91) 1.44 (0.91–2.28) [0.004]  1.00 1.18 (1.01–1.39) 1.44 (1.10–1.89) 1.71 (0.93–3.14) [0.002]	Age, race, education level, smoking, physical activity, alcohol consumption, marital status, aspirin use, fat and vegetable consumption	
<a href="#">Samanic et al. (2004)</a> United States Veterans cohort USA 1969–1996	4 500 700 Men Incidence	Multiple myeloma ICD-9: 203	Obesity  Non-obese Obese  Non-obese Obese	White men: 2817 204  Black men: 1509 89	1.00 1.22 (1.05–1.40)  1.00 1.26 (1.02–1.56)	Age, calendar year	Obesity defined as discharge diagnosis of obesity: ICD-8: 277; ICD-9: 278.0
<a href="#">Blair et al. (2005)</a> Iowa Women’s Health Study USA 1986–2001	37 083 Women Incidence	Multiple myeloma	BMI 18.5–24.9 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ]	30 37 28	1.0 1.3 (0.78–2.0) 1.5 (0.92–2.6) [0.10]	Age	Also included analyses of height, waist-to-hip ratio, and hip circumference

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Blair et al. (2005)</a> (cont.)			Weight (lb) < 138 138–160 ≥ 161 [ <i>P</i> <sub>trend</sub> ]	19 40 36	1.0 2.0 (1.1–3.4) 1.9 (1.1–3.4) [0.04]		
			WC (in) < 31.75 31.76–36.25 ≥ 36.26 [ <i>P</i> <sub>trend</sub> ]	19 37 39	1.0 1.9 (1.1–3.2) 2.0 (1.1–3.5) [0.02]		
<a href="#">Oh et al. (2005)</a> Korea National Health Insurance Corporation Republic of Korea 1992–2001	781 283 Men Incidence	Multiple myeloma	BMI < 18.5 18.5–22.9 23–24.9 25–26.9 27–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ]	2 36 45 14 6 0	1.19 (0.29–4.96) 1.00 1.72 (1.11–2.68) 0.96 (0.51–1.77) 0.98 (0.30–3.32) – [0.61]	Age, smoking, alcohol intake, physical activity, family history of cancer, urban/ rural residence	
<a href="#">Samanic et al. (2006)</a> Swedish Construction Worker Cohort Sweden 1958–1999	362 552 Men Incidence	Multiple myeloma ICD-7: 203	BMI 18.5–24.9 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ]	231 201 20	1.00 0.96 (0.79–1.16) 0.58 (0.37–0.93) [0.06]	Attained age, calendar year, smoking	
<a href="#">Birmann et al. (2007)</a> Nurses' Health Study and Health Professionals Follow-up Study combined USA 1980–2002	136 623 Men and women Incidence	Multiple myeloma	BMI < 22 22–24.9 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ]	28 64 84 39	1.0 1.2 (0.8–1.9) 1.3 (0.9–2.0) 1.5 (0.9–2.5) [0.11]	Age, sex, physical activity, cohort	

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Birmann et al. (2007)</a> (cont.) Nurses' Health Study  Health Professionals Follow-up Study	89 663 Women Incidence	Plasma cell myeloma	BMI			Age, physical activity	
			< 22	21	1.0		
			22–24.9	32	1.1 (0.7–2.0)		
			25–29.9	53	1.6 (1.0–2.7)		
	46 960 Men Incidence		≥ 30	23	1.2 (0.7–2.2)		
			[ <i>P</i> <sub>trend</sub> ]		[0.43]		
			BMI				Age, physical activity
			< 22	7	1.0		
22–24.9	32	1.3 (0.5–2.9)					
25–29.9	31	1.0 (0.4–2.2)					
<a href="#">Engeland et al. (2007)</a> Norwegian cohort Norway 1963–2001  1 038 010 Women Incidence	963 709 Men Incidence	Multiple myeloma	BMI			Age, birth cohort	
			< 18.5	11	0.69 (0.38–1.25)		
			18.5–24.9	1596	1.00		
			25–29.9	1417	1.14 (1.06–1.22)		
			≥ 30	209	1.28 (1.10–1.47)		
			[ <i>P</i> <sub>trend</sub> ]		[< 0.001]		
	1 038 010 Women Incidence		BMI				Attained age, snuff use, daily tobacco smoking
			< 18.5	24	0.85 (0.57–1.27)		
			18.5–24.9	1161	1.00		
			25–29.9	1125	1.12 (1.03–1.22)		
			30–34.9	436	1.23 (1.10–1.38)		
			35–39.9	110	1.42 (1.17–1.74)		
<a href="#">Fernberg et al. (2007)</a> Swedish construction workers Sweden 1971–2004	336 381 Men Incidence	≥ 40	26	1.57 (1.06–2.31)			
		[ <i>P</i> <sub>trend</sub> ]		[< 0.001]			
		BMI			Attained age, snuff use, daily tobacco smoking		
		18.5–25	256	1.00			
25.1–30	236	1.04 (0.86–1.24)					
> 30	27	0.70 (0.46–1.06)					

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Fujino et al. (2007)</a> Japan Collaborative Cohort Study Japan NR	NR Men Mortality	Multiple myeloma	BMI < 18.5 18.5–24 25–29 ≥ 30 Weight (kg) < 55 55–62 ≥ 63 Weight (kg) at age 20 yr < 55 55–60 ≥ 61	3 36 5 0 12 20 15 25 12 10	0.96 (0.29–3.16) 1.00 0.70 (0.27–1.80) N.A. 1.00 1.51 (0.73–3.11) 1.41 (0.64–3.12) 1.00 0.91 (0.38–2.14) 0.98 (0.40–2.42)	Age, area of study	[No information provided on follow-up or number of people in study]
	NR Women Mortality	Multiple myeloma	BMI < 18.5 18.5–24 25–29 ≥ 30 Weight (kg) < 49 49–54 ≥ 55 Weight (kg) at age 20 yr < 47 47–52 ≥ 53	2 31 7 4 18 12 17 24 9 11	0.59 (0.14–2.48) 1.00 0.77 (0.34–1.77) 4.34 (1.51–12.5) 1.00 0.93 (0.44–1.96) 1.17 (0.59–2.33) 1.00 0.76 (0.32–1.81) 0.87 (0.38–1.97)	Age, area of study	[No information provided on follow-up or number of people in study]
<a href="#">Larsson &amp; Wolk (2007b)</a> Meta-analysis Multiple locations 1994–2007	9 cohort studies Men and women Incidence	Multiple myeloma	BMI per 5 kg/m <sup>2</sup>	6987 total	1.11 (1.03–1.19)		

**Table 2.2.20c (continued)**

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Larsson &amp; Wolk (2007b)</a> (cont.)	9 cohort studies Men and women Mortality		BMI per 5 kg/m <sup>2</sup>	1492 total	1.19 (1.12–1.28)		
	9 cohort studies Men and women Incidence and mortality		BMI Normal Overweight Obese per 5 kg/m <sup>2</sup>	8479 total	1.00 1.12 (1.07–1.18) 1.27 (1.15–1.41) 1.14 (1.09–1.20)		Similar values for BMI per 5 kg/m <sup>2</sup> for men and women separately
<a href="#">Reeves et al. (2007)</a> Million Women Study United Kingdom 1996–2005	1 222 630 Women Incidence	Multiple myeloma ICD-10: C90	BMI < 22.5	76	0.80 (0.64–1.00)	Age, geographical region, SES, reproductive history, smoking status, alcohol intake, physical activity	
			22.5–24.9	127	1.00 (0.84–1.19)		
			25–27.4	118	1.11 (0.92–1.32)		
			27.5–29.9	73	1.11 (0.88–1.40)		
			≥ 30	97	1.16 (0.95–1.42)		
			per 10 kg/m <sup>2</sup>				1.31 (1.04–1.65)
	1 222 630 Women Mortality		BMI < 22.5	46	0.99 (0.74–1.32)		
			22.5–24.9	63	1.00 (0.78–1.28)		
			25–27.4	68	1.26 (0.99–1.59)		
			27.5–29.9	38	1.13 (0.82–1.55)		
			≥ 30	69	1.63 (1.28–2.08)		
			per 10 kg/m <sup>2</sup>		1.56 (1.15–2.10)		
<a href="#">Britton et al. (2008)</a> EPIC cohort 10 European countries 1993–1998	141 425 Men Incidence	Multiple myeloma	BMI < 25	43	1.00	Age, study centre	Also examined height, hip circumference, and waist-to-hip ratio; analyses by weight and WC gave similar results
			25–29.9	72	1.33 (0.79–2.23)		
			≥ 30	24	1.17 (0.80–1.72)		
			[P <sub>trend</sub> ]		[0.26]		
	230 558 Women Incidence	Multiple myeloma	BMI < 25	59	1.00	Age, study centre	Also examined height, hip circumference, and waist-to-hip ratio; analyses by weight and WC gave similar results
	25–29.9		49	0.93 (0.55–1.56)			
	≥ 30		21	1.06 (0.72–1.58)			
	[P <sub>trend</sub> ]			[0.89]			

Absence of excess body fatness



Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Renehan et al. (2008)</a> Meta-analysis Multiple locations 1966–2007	7 studies Men Incidence 6 studies Women Incidence	Multiple myeloma	BMI per 5 kg/m <sup>2</sup>		1.11 (1.05–1.18)		
<a href="#">Pylypchuk et al. (2009)</a> Netherlands Cohort Study on Diet and Cancer The Netherlands 1986–1999	5000 Men and women Incidence	Multiple myeloma ICD-O-3: 9731, 9732, 9734	BMI < 25 25–29.9 ≥ 30 [P <sub>trend</sub> ] per 4 kg/m <sup>2</sup>	135 126 18	1.00 1.23 (0.95–1.58) 1.13 (0.68–1.88) [0.17] 1.13 (0.97–1.31)	Age, sex	Case-cohort design Similar results for BMI at age 20 yr
<a href="#">De Roos et al. (2010)</a> Women's Health Initiative USA 1994–2008	81 219 Women Incidence	Multiple myeloma	BMI at enrolment < 25 25–29.9 30–34.9 ≥ 35 [P <sub>trend</sub> ]	39 35 10 7	1.00 1.03 (0.65–1.63) 0.66 (0.33–1.33) 0.83 (0.37–1.87) [0.37]	Age, minority race, education level, region of the USA, smoking	Similar results for BMI at age 18 yr, age 35 yr, and age 50 yr
<a href="#">Kanda et al. (2010)</a> Japanese men and women Japan 1992–2006	94 547 Men and women Incidence	Plasma cell myeloma ICD-O-3: 9731, 9732	BMI < 18.5 18.5–22.9 23.0–24.9 25–29.9 ≥ 30 per 1 kg/m <sup>2</sup> Weight (kg), quartiles (sex-specific) Men:           Women: 30–57           27–49 58–63           50–53 64–69           54–59 70–115          60–98 per 5 kg	2 33 29 22 2 22 21 25 20	0.56 (0.13–2.36) 0.70 (0.42–1.15) 1.00 0.79 (0.45–1.38) 0.76 (0.18–3.20) 1.01 (0.95–1.09) 1.00 1.05 (0.57–1.93) 1.35 (0.74–2.46) 1.14 (0.59–2.21) 1.06 (0.93–1.22)	Age, sex, study area, pack-years of smoking, alcohol consumption	Also included estimates for height Similar results for weight at baseline and at age 20 yr

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Lu et al. (2010)</a> California Teachers Study USA 1995–2007	121 216 Women Incidence	Multiple myeloma	BMI at baseline < 20 20–24.9 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ] Weight (lb) at baseline < 131 131–154 ≥ 155 [ <i>P</i> <sub>trend</sub> ]	9 55 28 14  38 36 32	0.92 (0.45–1.86) 1.00 0.83 (0.53–1.31) 0.86 (0.48–1.55) [0.55] 1.00 0.85 (0.54–1.36) 0.71 (0.43–1.16) [0.18]	Height, race	Also included estimates for hip circumference, waist-to-hip ratio, waist-to-height ratio, and height Similar results for BMI at age 18 yr, for weight at age 18 yr, and for WC
<a href="#">Parr et al. (2010)</a> Asia-Pacific Cohort Studies Collaboration 1961–1999 Average follow- up 4 yr	326 387 Men and women Mortality	Myeloma ICD-9: 203 ICD-10: C90	BMI < 18.5 18.5–24.9 25–29.9 ≥ 30 per 5 kg/m <sup>2</sup> [ <i>P</i> <sub>trend</sub> ]	3 12 19 25 10	1.94 (0.57–6.68) 1.00 (0.70–1.43) 0.87 (0.54–1.41) 1.20 (0.59–2.43) 1.05 (0.73–1.50) [0.78]	Age, sex, smoking	
<a href="#">Troy et al. (2010)</a> PLCO Trial USA 1993–2006	142 982 Men and women Incidence	Plasma cell myeloma	BMI at baseline < 18.5 18.5–24.9 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ] BMI at age 20 yr < 18.5 18.5–24.9 25–29.9 ≥ 30 [ <i>P</i> <sub>trend</sub> ]	2 57 112 66  12 173 41 12	– 1.00 1.45 (1.05–2.01) 1.69 (1.18–2.41) [< 0.01] 0.71 (0.40–1.29) 1.00 1.33 (0.94–1.88) 3.08 (1.71–5.54) [< 0.001]	Age, race/ ethnicity, education level	

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Troy et al. (2010)</a> (cont.)			Weight change (kg) per 10 yr				
			Loss	16	1.00 (0.56–1.78)		
			Gain 0–2	52	1.00		
			Gain 2.1–4	78	1.40 (0.98–2.00)		
			Gain 4.1–6	51	1.48 (1.00–2.20)		
			Gain > 6	42	1.55 (1.02–2.36)		
			[ <i>P</i> <sub>trend</sub> ]		[0.216]		
<a href="#">Wallin &amp; Larsson (2011)</a> Meta-analysis Multiple locations	15 studies Men and women Incidence	Multiple myeloma ICD-O-3: 9732/3	BMI Overweight Obesity per 5 kg/m <sup>2</sup>	NR	1.12 (1.07–1.18) 1.21 (1.08–1.35) 1.12 (1.08–1.16)		
	5 studies Men and women Mortality	Multiple myeloma ICD-O-3: 9732/3	BMI Overweight Obesity per 5 kg/m <sup>2</sup>	NR	1.15 (1.05–1.27) 1.54 (1.35–1.76) 1.21 (1.13–1.30)		
<a href="#">Hofmann et al. (2013)</a> NIH-AARP cohort USA 1995–1996	305 618 Men and women Incidence	Multiple myeloma ICD-O-3: 9732	BMI at baseline < 18.5 18.5–22.49 22.5–24.9 25–29.9 30–34.9 ≥ 35 [ <i>P</i> <sub>trend</sub> ] BMI at age 50 yr < 18.5 18.5–22.49 22.5–24.9 25–29.9 30–34.9 ≥ 35 [ <i>P</i> <sub>trend</sub> ]	1 53 99 207 82 34  3 73 129 193 45 18	0.30 (0.04–2.17) 1.0 1.02 (0.73–1.43) 1.09 (0.80–1.48) 1.26 (0.89–1.78) 1.55 (1.01–2.39) [0.008]  0.78 (0.25–2.49) 1.00 1.14 (0.85–1.52) 1.16 (0.88–1.54) 1.23 (0.84–1.80) 1.77 (1.05–2.99) [0.04]	Age, sex, race	Analyses also for women and men separately

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Hofmann et al. (2013)</a> (cont.)			BMI at age 35 yr < 18.5 18.5–22.49 22.5–24.9 25–29.9 30–34.9 ≥ 35 [ <i>P</i> <sub>trend</sub> ]	7 136 159 131 22 8	0.77 (0.36–1.66) 1.00 1.42 (1.12–1.79) 1.27 (0.99–1.63) 1.41 (0.89–2.22) 2.53 (1.24–5.18) [0.004]		
			BMI at age 18 yr < 18.5 18.5–22.49 22.5–24.9 ≥ 25 [ <i>P</i> <sub>trend</sub> ]	55 237 86 64	0.93 (0.69–1.25) 1.00 1.12 (0.88–1.44) 1.38 (1.04–1.82) [0.015]		
<a href="#">Patel et al. (2013)</a> Cancer Prevention Study II Nutrition Cohort USA 1992–2007	152 423 Men and women Incidence	Multiple myeloma	BMI at baseline < 18.5 18.5– < 25 25– < 30 ≥ 30 [ <i>P</i> <sub>trend</sub> ]	1 144 149 58	0.32 (0.04–2.30) 1.00 1.00 (0.79–1.26) 1.17 (0.86–1.60) [0.25]	Age, sex, family history of haematopoietic cancer, education level, smoking status, physical activity, alcohol consumption	
			BMI at age 18 yr < 18.5 18.5– < 22.5 22.5– < 25 25– < 30 ≥ 30 [ <i>P</i> <sub>trend</sub> ]	44 197 66 31 7	0.89 (0.64–1.24) 1.00 1.01 (0.75–1.34) 0.92 (0.61–1.37) 1.77 (0.82–3.84) [0.37]		

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Patel et al. (2013)</a> (cont.)			Adult weight change (lb) Loss > 5 Loss 5 to gain 20 Gain 21–40 Gain 41–60 Gain > 60 [P <sub>trend</sub> ]	10 105 133 68 28	0.77 (0.40–1.47) 1.00 1.25 (0.96–1.61) 1.08 (0.79–1.47) 0.81 (0.53–1.24) [0.85]		
<a href="#">Bhaskaran et al. (2014)</a> Clinical Practice Research Datalink United Kingdom 1987–2012	5 243 978 Men and women Incidence	Multiple myeloma ICD-10: C90	BMI per 5 kg/m <sup>2</sup> [P <sub>trend</sub> ]	2969	1.03 (0.98–1.09) [0.15]	Age, sex, diabetes, smoking, alcohol consumption, SES, calendar year	
<a href="#">Teras et al. (2014)</a> Pooled analysis of 20 cohorts Multiple locations 1970–2002	1 564 218 Men and women Mortality	Multiple myeloma ICD-9: 203; ICD-10: C90	BMI at baseline 15.0–18.4 18.5–20.9 21.0–22.9 23.0–24.9 25.0–27.4 27.5–29.9 30.0–34.9 ≥ 35 per 5 kg/m <sup>2</sup> Young adult BMI 15.0–18.4 18.5–20.9 21.0–22.9 23.0–24.9 25.0–27.4 27.5–29.9 ≥ 30.0 per 5 kg/m <sup>2</sup>	15 85 171 302 351 215 178 71 121 319 275 160 92 31 26	1.21 (0.71–2.06) 1.02 (0.79–1.32) 1.00 1.22 (1.01–1.47) 1.15 (0.95–1.38) 1.24 (1.01–1.52) 1.23 (0.99–1.52) 1.52 (1.15–2.02) 1.09 (1.03–1.16) 0.99 (0.80–1.23) 0.91 (0.78–1.07) 1.00 1.04 (0.85–1.26) 1.11 (0.87–1.40) 1.49 (1.03–2.16) 1.82 (1.22–2.73) 1.22 (1.09–1.35)	Race, sex, education level, marital status, alcohol consumption, physical activity, smoking	



**Table 2.2.20c (continued)**

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Teras et al. (2014)</a> (cont.)			BMI gain				
			≤ -2.5	34	1.12 (0.77-1.64)		
			-2.5 to < 0	67	0.84 (0.64-1.10)		
			0-2.5	221	1.00		
			2.5-4.9	266	1.04 (0.87-1.24)		
			5.0-7.4	220	1.17 (0.96-1.41)		
			7.5-9.9	113	1.10 (0.87-1.38)		
			≥ 10	103	1.17 (0.92-1.50)		
			per 1 kg/m <sup>2</sup>		1.06 (0.98-1.14)		
	647 478		WC (cm), quartiles (sex-specific)				
	Men and women		Men: Women:				
	Mortality		< 90 < 70	112	1.00	Race, sex, education level, marital status, alcohol consumption, physical activity, smoking	Also provided estimates for waist- to-hip ratio and height
			90-99 70-79	216	1.28 (1.01-1.62)		
			100-109 80-89	153	1.32 (1.02-1.71)		
			≥ 110 ≥ 90	108	1.47 (1.10-1.96)		
			per 5 cm		1.06 (1.02-1.10)		
	656 771		BMI at baseline				
	Men		15.0-18.4	1	-	Race, education level, marital status, alcohol consumption, physical activity, smoking	Also provided estimates for waist- to-hip ratio and height
	Mortality		18.5-20.9	17	0.97 (0.57-1.67)		
			21.0-22.9	63	1.00		
			23.0-24.9	176	1.37 (1.03-1.83)		
			25.0-27.4	219	1.20 (0.90-1.59)		
			27.5-29.0	130	1.29 (0.95-1.75)		
			30.0-34.9	93	1.28 (0.93-1.78)		
			≥ 35	24	1.48 (0.91-2.38)		
			per 5 kg/m <sup>2</sup>		1.11 (1.00-1.22)		
			Young adult BMI				
			15.0-18.4	40	0.85 (0.60-1.21)		
			18.5-20.9	136	0.91 (0.73-1.15)		
			21.0-22.9	155	1.00		
			23.0-24.9	92	0.88 (0.68-1.14)		
			25.0-27.4	62	1.00 (0.74-1.34)		
			27.5-29.0	21	1.47 (0.93-2.32)		
			≥ 30.0	10	1.36 (0.72-2.59)		
			per 5 kg/m <sup>2</sup>		1.15 (0.98-1.35)		

Table 2.2.20c (continued)

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Teras et al. (2014)</a> (cont.)			BMI gain				
			≤ -2.5	11	1.04 (0.55–1.97)		
			-2.5 to < 0	33	0.96 (0.65–1.42)		
			0–2.5	117	1.00		
			2.5–4.9	147	1.04 (0.81–1.33)		
			5.0–7.4	108	1.05 (0.80–1.38)		
			7.5–9.9	60	1.18 (0.85–1.64)		
			≥ 10	40	1.20 (0.82–1.76)		
			per 1 kg/m <sup>2</sup>		1.07 (0.94–1.21)		
			WC (cm)				
			< 90	62	1.00		
			90–99	144	1.25 (0.93–1.69)		
			100–109	83	1.26 (0.90–1.77)		
			≥ 110	38	1.38 (0.91–2.08)		
			per 5 cm		1.06 (1.01–1.12)		
	907 447 Women Mortality		BMI at baseline			Race, education level, marital status, alcohol consumption, physical activity, smoking	Also provided estimates for waist- to-hip ratio and height
			15.0–18.4	14	1.39 (0.79–2.43)		
			18.5–20.9	68	1.01 (0.75–1.38)		
			21.0–22.9	108	1.00		
			23.0–24.9	126	1.08 (0.83–1.39)		
			25.0–27.4	132	1.11 (0.86–1.44)		
			27.5–29.0	85	1.20 (0.90–1.60)		
			30.0–34.9	85	1.18 (0.89–1.58)		
			≥ 35	47	1.51 (1.06–2.15)		
			per 5 kg/m <sup>2</sup>		1.07 (0.99–1.16)		
			Young adult BMI				
			15.0–18.4	81	1.11 (0.84–1.47)		
			18.5–20.9	183	0.94 (0.75–1.19)		
			21.0–22.9	120	1.00		
			23.0–24.9	68	1.31 (0.97–1.76)		
			25.0–27.4	30	1.28 (0.86–1.91)		
			27.5–29.0	10	1.42 (0.75–2.71)		
			≥ 30.0	16	2.32 (1.37–3.92)		
			per 5 kg/m <sup>2</sup>		1.27 (1.10–1.47)		

**Table 2.2.20c (continued)**

Reference Cohort Location Follow-up period	Total number of subjects Sex Incidence/ mortality	Organ site (ICD code)	Exposure categories	Exposed cases	Relative risk (95% CI)	Covariates	Comments
<a href="#">Teras et al. (2014)</a> (cont.)			BMI gain				
			≤ -2.5	23	1.16 (0.72–1.89)		
			-2.5 to < 0	34	0.75 (0.51–1.10)		
			0–2.5	104	1.00		
			2.5–4.9	119	1.02 (0.78–1.33)		
			5.0–7.4	112	1.28 (0.98–1.68)		
			7.5–9.9	53	1.00 (0.71–1.40)		
			≥ 10	63	1.12 (0.81–1.56)		
			per 1 kg/m <sup>2</sup>		1.04 (0.95–1.15)		
			WC (cm)				
			< 70	50	1.00		
			70–79	72	1.32 (0.90–1.94)		
			80–89	70	1.42 (0.94–2.13)		
			≥ 90	70	1.54 (1.00–2.36)		
			per 5 cm		1.05 (1.00–1.11)		

BMI, body mass index (in kg/m<sup>2</sup>); CI, confidence interval; DLBCL, diffuse large B-cell lymphoma; EPIC, European Prospective Investigation into Cancer and Nutrition; ICD, International Classification of Diseases; ICD-O, International Classification of Diseases for Oncology; NIH-AARP, National Institutes of Health–AARP Diet and Health Study; NR, not reported; PLCO Trial, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; RR, relative risk; SES, socioeconomic status; WC, waist circumference; yr, year or years

**Table 2.2.20d Case-control studies of measures of body fatness and haematopoietic malignancies of lymphoid origin with sufficient or limited evidence**

Reference Study location Period	Total number of cases Total number of controls Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding
<i>Diffuse large B-cell lymphoma</i>					
<a href="#">Pan et al. (2005)</a> Canada 1994–1997	419 from National Enhanced Cancer Surveillance System 3106 Population	Adult BMI 2 yr before interview/diagnosis 18.5– < 25 25– < 30 ≥ 30 [ <i>P</i> <sub>trend</sub> ]	162 184 69	1.00 1.37 (1.09–1.73) 1.35 (0.99–1.83) [0.015]	Age, province, sex, education level, pack-years of smoking, alcohol consumption, exposure to some chemicals, occupational exposures, physical activity, energy intake
<a href="#">Chen et al. (2011)</a> USA 1996–2000	245 868 Population	Usual adult BMI assessed via interview < 25 25–30 > 30	77 56 28	1.0 1.5 (1.0–2.2) 1.1 (0.7–1.8)	Age, race, total energy intake
<a href="#">Cerhan et al. (2014)</a> Pooled analysis from InterLymph Consortium of 19 case- control studies Europe, Japan, North America	4667 22 639	Young adult BMI 15– < 18.5 18.5– < 22.5 22.5– < 25 25– < 30 30–50 [ <i>P</i> <sub>trend</sub> ] Usual adult BMI 15– < 18.5 18.5– < 22.5 22.5– < 25 25– < 30 30– < 35 35–50 [ <i>P</i> <sub>trend</sub> ]	64 517 276 226 54 33 722 850 1310 419 175	0.93 (0.69–1.24) 1.00 1.11 (0.93–1.31) 1.47 (1.22–1.77) 1.58 (1.12–2.23) [0.002] 0.58 (0.39–0.85) 1.00 0.91 (0.81–1.03) 0.93 (0.83–1.04) 0.95 (0.82–1.10) 1.06 (0.86–1.30) [0.042]	
<i>Multiple myeloma</i>					
<a href="#">Larsson &amp; Wolk (2007b)</a> Meta-analysis of 4 case- control studies Studies published in 1994–2007	1166 total 8247 total	BMI ≤ 25 25–29.9 ≥ 30		1.00 1.43 (1.23–1.68) 1.82 (1.47–2.26)	Note: the reference category was ≤ 25 in all but 3 studies

**Table 2.2.20d (continued)**

Reference Study location Period	Total number of cases Total number of controls Source of controls	Exposure categories	Exposed cases	Relative risk (95% CI)	Adjustment for confounding
<a href="#">Wang et al. (2013)</a> USA 1985–1992	278 from Los Angeles County Multiple Myeloma Case–Control Study 278 Population	Self-reported BMI 1 yr before cancer diagnosis or at time of interview			Sex, age ± 5 yr, race
		< 25	All: 116	1.00	
		25–29.9	98	0.75 (0.51–1.10)	
		30–34.9	43	0.98 (0.59–1.62)	
		≥ 35	21	1.86 (0.84–4.14)	
			Men:		
		< 25	58	1.00	
		25–29.9	65	0.85 (0.52–1.39)	
		30–34.9	19	0.96 (0.46–2.01)	
		≥ 35	8	1.80 (0.51–6.30)	
			Women:		
		< 25	58	1.00	
		25–29.9	33	0.62 (0.34–1.17)	
		30–34.9	24	0.92 (0.45–1.88)	
		≥ 35	11	1.56 (0.55–4.40)	

BMI, body mass index (in kg/m<sup>2</sup>); CI, confidence interval; yr, year or years

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