

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Pischon T, Boeing H, Hoffmann K, et al. General and abdominal adiposity and risk of death in Europe. *N Engl J Med* 2008;359:2105-20.

Online supplement

Pischon et al.: General and Abdominal Adiposity and Risk of Death in Europe

Appendix 1: Correction of Participants' Body Weight and Waist and Hip circumference

Each participant's body weight and waist and hip circumference was corrected to reduce heterogeneity due to protocol differences in clothing worn during measurement. For subjects who were normally dressed and without shoes, 1.5 kg for weight and 2.0 cm for circumferences were subtracted from the original measurement, while for subjects in light clothing without shoes 1 kg was subtracted from weight. For part of the Oxford (UK) cohort, linear regression models were used to predict sex- and age-specific values from subjects with both measured and self-reported body measures (1-3).

References

1. Haftenberger M, Lahmann PH, Panico S, et al. Overweight, obesity and fat distribution in 50- to 64-year-old participants in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Public Health Nutr* 2002;5(6B):1147-62.
2. Spencer EA, Appleby PN, Davey GK, Key TJ. Validity of self-reported height and weight in 4808 EPIC-Oxford participants. *Public Health Nutr* 2002;5(4):561-5.
3. Spencer EA, Roddam AW, Key TJ. Accuracy of self-reported waist and hip measurements in 4492 EPIC-Oxford participants. *Public Health Nutr* 2004;7(6):723-7.

Supplementary Table 1: Cohort characteristics and number of deaths in men and women by country in EPIC

Country	Cohort Size, n		Mean age, y		Mean follow-up, y		Person-years		Deaths, n	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
France	0	19,589	-	52.8	-	12.9	0	252,059	0	348
Italy	13,648	30,150	50.1	50.6	9.1	9.2	123,870	278,191	370	516
Spain	14,787	24,455	50.7	48.3	10.9	10.8	160,440	263,902	675	430
UK	21,365	50,828	52.4	47.5	9.2	9.4	196,404	476,282	1543	1673
The Netherlands	9511	25,919	42.9	50.7	10.6	9.8	100,401	254,314	326	820
Greece	10,025	14,722	52.3	53.1	7.0	7.3	70,262	107,340	686	426
Germany	20,453	27,366	52.2	49.0	8.3	8.3	169,798	227,811	868	425
Sweden	9521	13,798	58.7	57.2	11.4	11.4	108,515	157,289	1196	845
Denmark	25,042	28,208	56.5	56.7	9.9	10.1	248,112	285,181	2141	1435
Total	124,352	235,035	52.5	51.0	9.5	9.8	1,177,801	2,302,430	7805	6918

Supplementary Table 2: Characteristics of study participants by BMI*

	BMI								
	<18.5	18.5-<21.0	21.0-<23.5	23.5-<25.0	25.0-<26.5	26.5-<28.0	28.0-<30.0	30.0-<35.0	≥35.0
Men	496	4783	18,495	19,819	22,608	19,734	18,799	16,899	2719
Age, years, mean	49.9	48.1	50.4	52.1	52.8	53.3	53.5	53.7	53.6
Alcohol consumption, g/d, mean	21.9	19.8	21.1	21.6	22.6	23.7	24.1	25.8	27.1
Smoking status†, %									
Never smoker	25.1	34.3	34.9	33.2	32.1	29.2	28.6	27.2	26.7
Past smoker	20.6	23.0	30.3	34.7	36.8	39.5	40.2	41.0	40.4
Current smoker	53.8	41.7	33.5	30.7	29.5	29.8	29.9	30.4	31.6
Weight, kg, mean	54.6	62.7	69.7	74.8	78.8	82.8	87.2	94.9	112.4
Height, cm, mean	175.7	176.2	175.9	175.4	174.8	174.2	173.5	172.7	172.5
Waist circumference, cm, mean	74.2	79.2	84.7	89.0	92.5	96.1	100.2	106.9	120.0
Hip circumference, cm, mean	87.6	91.4	94.8	97.5	99.6	101.6	104.1	108.4	117.9
Waist-hip-ratio, mean	0.85	0.87	0.89	0.91	0.93	0.95	0.96	0.99	1.02
Education†, %									
No school degree or primary school	23.1	21.9	20.8	23.9	26.7	31.5	36.8	42.8	46.2
Technical/professional school	24.4	24.8	24.4	24.9	25.8	25.6	25.2	23.4	23.0
Secondary school or university degree	48.7	49.4	51.3	48.2	44.4	40.1	35.2	30.9	27.4
Physical activity†, %									
Inactive	14.9	19.5	20.5	20.6	20.9	20.6	20.4	20.3	21.1
Moderately inactive	31.9	29.7	28.4	28.0	28.1	28.2	28.4	28.5	30.9
Moderately active	40.2	35.8	35.0	34.8	35.0	35.1	35.2	36.0	35.2
Active	10.0	12.3	13.5	13.9	13.5	13.7	13.7	13.5	11.7

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	BMI								
	<18.5	18.5-<21.0	21.0-<23.5	23.5-<25.0	25.0-<26.5	26.5-<28.0	28.0-<30.0	30.0-<35.0	≥35.0
Women	4108	28,614	57,938	34,925	29,333	22,876	21,764	26,290	9187
Age, years, mean	45.5	46.1	49.0	51.3	52.3	53.2	53.9	54.1	53.6
Alcohol consumption, g/d, mean	8.6	10.0	9.9	9.3	8.7	8.0	7.2	6.2	4.6
Smoking status†, %									
Never smoker	51.3	52.9	53.2	53.4	54.6	57.1	59.8	63.0	65.0
Past smoker	19.4	22.6	24.2	24.4	23.6	21.9	20.6	18.9	19.5
Current smoker	28.1	22.9	21.3	21.0	20.6	19.8	18.5	16.9	14.5
Weight, kg, mean	47.2	53.6	59.3	63.8	67.2	70.7	74.4	81.4	97.0
Height, cm, mean	163.2	163.4	162.9	162.2	161.5	161.0	160.2	159.4	158.6
Waist circumference, cm, mean	64.8	68.7	73.2	77.3	80.6	84.0	87.7	94.1	105.7
Hip circumference, cm, mean	87.0	91.4	95.6	98.9	101.5	104.1	106.9	112.2	124.0
Waist-hip-ratio, mean	0.75	0.75	0.77	0.78	0.80	0.81	0.82	0.84	0.85
Education†, %									
No school degree or primary school	13.6	14.0	18.2	24.5	30.5	35.4	41.3	47.7	51.2
Technical/professional school	21.5	23.7	25.9	26.1	25.5	24.8	22.6	21.1	20.3
Secondary school or university degree	60.0	57.2	50.7	44.5	39.2	35.1	31.4	26.1	22.4
Physical activity†, %									
Inactive	18.5	19.2	18.1	16.6	15.2	13.9	12.4	11.3	11.1
Moderately inactive	41.9	37.1	33.9	31.5	29.3	28.5	27.1	26.1	25.8
Moderately active	31.9	34.7	37.7	41.1	44.2	47.0	49.5	51.7	53.1
Active	6.6	7.7	8.7	9.0	9.5	8.7	9.3	9.4	8.5

*All values except age and number of subjects are standardized to the sex-specific age distribution of the study population using 5-year categories

†Numbers do not sum up to 100% due to missing values

Supplementary Table 3: Relative risk of death according to quintiles of waist-hip-ratio in men and women in the European Prospective Investigation into Cancer and Nutrition (EPIC)

	Waist-hip-ratio quintile					P _{trend} *	P _{interaction} †
	1	2	3	4	5		
	Men						
Waist-hip-ratio	<0.89	0.89-<0.92	0.92-<0.95	0.95-<0.99	≥0.99		
Number of deaths	969	1202	1445	1702	2394		
Crude relative risk‡	1	0.99 (0.91-1.08)	1.11 (1.03-1.21)	1.23 (1.13-1.33)	1.66 (1.53-1.79)	<0.0001	
Multivariable adjusted RR§							
without BMI	1	1.01 (0.92-1.10)	1.07 (0.98-1.16)	1.15 (1.06-1.24)	1.44 (1.33-1.56)	<0.0001	
with BMI	1	1.15 (1.05-1.26)	1.26 (1.16-1.38)	1.36 (1.24-1.49)	1.68 (1.53-1.84)	<0.0001	
	Multivariable adjusted relative risks in subgroups§						
BMI tertiles							0.01
<24.9	1	1.12 (1.00-1.26)	1.21 (1.07-1.37)	1.32 (1.16-1.51)	1.86 (1.58-2.19)	<0.0001	
24.9-<27.7	1	1.25 (1.03-1.51)	1.44 (1.19-1.73)	1.55 (1.29-1.87)	1.80 (1.48-2.17)	<0.0001	
≥27.7	1	1.00 (0.74-1.35)	0.94 (0.71-1.26)	1.00 (0.76-1.33)	1.28 (0.97-1.69)	<0.0001	
Smoking status¶							0.79
Never smoker	1	1.05 (0.87-1.28)	1.20 (0.98-1.46)	1.30 (1.06-1.59)	1.68 (1.36-2.07)	<0.0001	
Former smoker	1	1.13 (0.96-1.31)	1.25 (1.07-1.46)	1.36 (1.17-1.59)	1.77 (1.51-2.07)	<0.0001	
Current smoker	1	1.19 (1.04-1.37)	1.36 (1.19-1.57)	1.48 (1.28-1.70)	1.85 (1.60-2.15)	<0.0001	
Age category							0.66
<55 years	1	1.17 (0.99-1.38)	1.31 (1.10-1.55)	1.45 (1.22-1.72)	1.93 (1.61-2.32)	<0.0001	
55-65 years	1	1.12 (0.98-1.29)	1.27 (1.11-1.45)	1.34 (1.17-1.53)	1.56 (1.35-1.79)	<0.0001	
≥65 years	1	1.16 (0.98-1.38)	1.19 (1.00-1.41)	1.29 (1.08-1.53)	1.60 (1.34-1.91)	<0.0001	
Follow-up 							0.68
≤5 years	1	1.12 (0.97-1.30)	1.22 (1.06-1.42)	1.33 (1.15-1.55)	1.55 (1.33-1.81)	<0.0001	
>5 years	1	1.17 (1.05-1.31)	1.29 (1.15-1.44)	1.37 (1.23-1.54)	1.75 (1.55-1.97)	<0.0001	

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	Waist-hip-ratio quintile					P _{trend} *	P _{interaction} †	
	1	2	3	4	5			
Cause of death							0.002	
Cancer	1	1.17 (1.01-1.37)	1.30 (1.12-1.52)	1.36 (1.16-1.59)	1.54 (1.31-1.82)	<0.0001		
Circulatory	1	1.05 (0.88-1.24)	1.01 (0.85-1.21)	1.17 (0.98-1.39)	1.33 (1.11-1.60)	0.0002		
Respiratory	1	1.71 (1.11-2.65)	1.69 (1.08-2.65)	2.35 (1.52-3.65)	3.32 (2.12-5.21)	<0.0001		
Other	1	1.20 (0.96-1.50)	1.50 (1.20-1.87)	1.58 (1.25-1.98)	2.07 (1.63-2.62)	<0.0001		
		Women						
Waist-hip-ratio	<0.73	0.73-<0.77	0.77-<0.80	0.80-<0.85	≥0.85			
Number of deaths	782	1077	1271	1548	2185			
Crude relative risk‡	1	1.09 (0.99-1.19)	1.12 (1.02-1.22)	1.25 (1.15-1.37)	1.63 (1.49-1.78)	<0.0001		
Multivariable adjusted RR§								
without BMI	1	1.06 (0.97-1.16)	1.07 (0.97-1.17)	1.16 (1.06-1.27)	1.45 (1.33-1.58)	<0.0001		
with BMI	1	1.09 (0.99-1.20)	1.12 (1.02-1.22)	1.23 (1.12-1.34)	1.51 (1.37-1.66)	<0.0001		
		Multivariable adjusted relative risks in subgroups§						
BMI tertiles							0.05	
<23.0	1	1.08 (0.94-1.23)	1.16 (1.00-1.33)	1.35 (1.16-1.57)	1.69 (1.42-2.02)	<0.0001		
23.0-<26.6	1	1.00 (0.86-1.18)	0.98 (0.84-1.14)	1.03 (0.88-1.20)	1.36 (1.16-1.60)	<0.0001		
≥26.6	1	1.21 (0.94-1.56)	1.21 (0.96-1.53)	1.32 (1.05-1.65)	1.60 (1.28-1.99)	<0.0001		
Smoking status¶							0.57	
Never smoker	1	1.05 (0.92-1.20)	1.04 (0.91-1.20)	1.14 (0.99-1.31)	1.38 (1.21-1.59)	<0.0001		
Former smoker	1	1.06 (0.88-1.27)	1.03 (0.85-1.24)	1.11 (0.92-1.34)	1.46 (1.21-1.77)	<0.0001		
Current smoker	1	1.22 (1.01-1.46)	1.37 (1.15-1.65)	1.61 (1.35-1.93)	2.02 (1.68-2.42)	<0.0001		

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	Waist-hip-ratio quintile					P _{trend} *	P _{interaction} †
	1	2	3	4	5		
Age category							0.62
<55 years	1	1.19 (1.03-1.38)	1.09 (0.93-1.27)	1.18 (1.01-1.39)	1.48 (1.25-1.75)	<0.0001	
55-65 years	1	0.97 (0.84-1.13)	1.08 (0.94-1.24)	1.20 (1.04-1.38)	1.45 (1.26-1.67)	<0.0001	
≥65 years	1	1.15 (0.92-1.44)	1.20 (0.97-1.49)	1.29 (1.05-1.59)	1.63 (1.32-2.00)	<0.0001	
Follow-up ‡							0.20
≤5 years	1	1.13 (0.95-1.34)	1.16 (0.98-1.38)	1.21 (1.02-1.43)	1.67 (1.41-1.98)	<0.0001	
>5 years	1	1.07 (0.96-1.20)	1.10 (0.98-1.22)	1.23 (1.10-1.38)	1.43 (1.28-1.60)	<0.0001	
Cause of death							0.0001
Cancer	1	1.03 (0.90-1.18)	1.04 (0.91-1.19)	1.09 (0.95-1.25)	1.23 (1.07-1.42)	0.001	
Circulatory	1	1.04 (0.82-1.33)	1.15 (0.92-1.45)	1.28 (1.02-1.61)	1.72 (1.37-2.16)	<0.0001	
Respiratory	1	1.81 (1.01-3.24)	2.13 (1.21-3.73)	2.18 (1.24-3.83)	3.30 (1.88-5.78)	<0.0001	
Other	1	1.35 (1.05-1.73)	1.29 (1.00-1.66)	1.44 (1.12-1.86)	2.07 (1.61-2.67)	<0.0001	

*p-value for trend based on median waist-hip-ratio within quintiles

†p-value for the likelihood ratio test of comparing the model with interaction terms between waist-hip-ratio and the stratification variable to the model without these interaction terms (8 degrees of freedom each for BMI, smoking, age, and cause of death, 4 degrees of freedom each for preexisting disease and length of follow-up); for cause of death and length of follow-up the data augmentation method described by Lunn and McNeil was used (see statistical methods for details)

‡Crude relative risk calculated using Cox proportional hazard regression using age as the underlying time variable and stratified by center and age at recruitment

§Multivariable adjusted models were based on the crude model with additional adjustment for smoking (never, former with quit≥10y, former with quit<10y, former with time since quit unknown, current with <15 cig/d, current with 15-24 cig/d, current with ≥25 cig/d, current with number of cig unknown, and missing); education (no school degree, primary school degree, technical or professional school degree, secondary school degree, university degree, and missing); alcohol consumption (nondrinker, 0.1-4.9 g/d, 5.0-14.9 g/d, 15.0-29.9 g/d, and ≥30 g/d), activity (inactive, moderately inactive, moderately active, active, and missing), height (quintiles), and BMI (<18.5, 18.5-<21.0, 21.0-<23.5, 23.5-<25.0, 25.0-<26.5, 26.5-<28.0, 28.0-<30.0, 30.0-<35.0, ≥35.0)

¶Relative risks in strata of smoking status are not adjusted for smoking status

|| Follow-up ≤ 5 years indicates that follow-up time of all participants was censored after 5 years (i.e., only death occurring during the first 5 years are considered). Follow-up > 5 years indicates that person-time and incident events from the first 5 years of follow-up were excluded (i.e., that analysis includes only those deaths that occurred after more than 5 years of follow-up)

Supplementary Table 4: Measures of calibration, discrimination, and reclassification for different multivariable adjusted models to predict 5-year risk of death*

	Model with BMI	Model with BMI and waist circumference	Model with BMI and waist-hip-ratio
Men			
Nagelkerke's R^2 †, %	15.52	15.70	15.68
Hosmer-Lemeshow statistic‡			
χ^2	11.91	14.18	10.09
p-value	0.155	0.077	0.259
C-statistic§	0.7948	0.7961¶	0.7964¶,
Net reclassification index**	-	0.00487 (p=0.41)	0.00042 (p=0.95)
Integrated discrimination index††	-	0.00095 (p<0.0001)	0.00075 (p=0.004)
Women			
Nagelkerke's R^2 †, %	12.77	12.94	13.02
Hosmer-Lemeshow statistic‡			
χ^2	2.46	4.946	4.485
p-value	0.963	0.763	0.811
C-statistic§	0.7977	0.7990¶	0.7995¶,
Net reclassification index**	-	0.00674 (p=0.30)	0.02271 (p=0.004)
Integrated discrimination index††	-	0.00075 (p<0.0001)	0.00099 (p<0.0001)

*The multivariable logistic model includes age (5-year categories), center, smoking (never, former with quit \geq 10y, former with quit<10y, former with time since quit unknown, current with <15 cig/d, current with 15-24 cig/d, current with \geq 25 cig/d, current with number of cig unknown, and missing); education (no school degree, primary school degree, technical or professional school degree, secondary school degree, university degree, and missing); alcohol consumption (nondrinker, 0.1-4.9 g/d, 5.0-14.9 g/d, 15.0-29.9 g/d, and \geq 30 g/d), activity (inactive, moderately inactive, moderately active, active, and missing), height (quintiles), and BMI (<18.5, 18.5-<21.0, 21.0-<23.5, 23.5-<25.0, 25.0-<26.5, 26.5-<28.0, 28.0-<30.0, 30.0-<35.0, \geq 35.0)

When using quintiles for BMI, models including either BMI or waist circumference or waist-hip-ratio showed equal discrimination (c-statistic for each model 0.793; p>0.05), while for women, the c-statistic of models including waist circumference (0.798) or waist-hip-ratio (0.799) was significantly higher than that with BMI (0.797; p<0.05 for comparisons with circumference measures).

†Nagelkerke's R^2 is a measure of the fraction of the -2 log likelihood explained by the predictors, analogous to the percentage of variance explained in a linear model, ranging from 0% to 100% (1).

‡The Hosmer-Lemeshow statistic is a measure of model calibration, comparing predicted and observed probabilities of death based on deciles of predicted risk. Smaller χ^2 values and larger p-values indicate better calibration. P-values <0.05 indicate significant lack of fit (2).

§ The c-statistic is a measure of discrimination, reflecting the probability the model assigns a higher risk to those who died within 5 years than to those who did not. The c-statistic ranges from 0.5 (no discriminative ability) to 1.0 (perfect discrimination) (3).

¶ $p < 0.05$ versus model without waist circumference or waist-hip-ratio

|| $p > 0.05$ versus model with waist circumference

** The net reclassification index quantifies the improvement in risk classification (based on the pre-defined risk categories used in Table 4 and Supplementary Table 4) when waist circumference or waist-hip-ratio are added to the model including BMI. It is the sum of differences in proportions of participants moving up minus the proportion moving down for participants who developed events, and the proportion of participants moving down minus the proportion moving up for participants who did not develop events (4). Clearly, this index depends on the choice of risk categories.

†† The integrated discrimination index does not depend on the choice of risk categories and quantifies jointly the overall improvement in sensitivity and specificity. It is calculated as the difference between the integrated difference in sensitivities and the integrated difference in 'one minus specificities' (4).

Supplementary Table 5: Expected and observed 5-year risk of death using the multivariable adjusted model with and without waist-hip-ratio*

Men	5-year risk by model with BMI	5-year risk by model with BMI and WHR				Total reclassified
		<2.5%	2.5%-<5.0%	5.0%-<7.5%	≥7.5%	
<2.5%						
Total participants, n	86,036	1833	0	0		
Participants classified in each stratum by the model with BMI and WHR, %	97.91	2.09	0.00	0.00		2.09
Observed 5-year risk, %	0.90	2.89	-	-		
2.5%-<5.0%						
Total participants, n	2045	17,252	1000	0		
Participants classified in each stratum by the model with BMI and WHR, %	10.08	85.00	4.93	0		15.01
Observed 5-year risk, %	2.49	3.52	4.30	.		
5.0%-<7.5%						
Total participants, n	0	929	4964	574		
Participants classified in each stratum by the model with BMI and WHR, %	0	14.37	76.76	8.88		23.25
Observed 5-year risk, %	-	5.06	6.89	8.19		
≥7.5%						
Total participants, n	0	0	568	5637		
Participants classified in each stratum by the model with BMI and WHR, %	0	0	9.15	80.85		9.15
Observed 5-year risk, %	-	-	8.27	14.17		

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Women 5 year-risk by model with BMI	5-year risk by model with BMI and WHR				Total reclassified
	<1.25%	1.25%-<2.50%	2.50%-<3.75%	≥3.75%	
<1.25%					
Total participants, n	178,984	4057	0	0	
Participants classified in each stratum by the model with BMI and WHR, %	97.78	2.22	0.00	0.00	2.22
Observed 5-year risk, %	0.41	1.33	-	-	
1.25%-2.50%					
Total participants, n	3826	24,529	2077	0	
Participants classified in each stratum by the model with BMI and WHR, %	12.57	80.60	6.83	0.00	19.40
Observed 5-year risk, %	1.28	1.70	2.55	-	
2.50%-<3.75%					
Total participants, n	0	1982	6199	1227	
Participants classified in each stratum by the model with BMI and WHR, %	0	21.07	65.89	13.04	34.11
Observed 5-year risk, %	-	1.56	2.73	5.30	
≥3.75%					
Total participants, n	0	0	1225	7977	
Participants classified in each stratum by the model with BMI and WHR, %	0.00	0.00	13.31	86.69	13.31
Observed 5-year risk, %	-	-	3.27	7.06	

*The multivariable logistic model includes age (5-year categories), center, smoking (never, former with quit≥10y, former with quit<10y, former with time since quit unknown, current with <15 cig/d, current with 15-24 cig/d, current with ≥25 cig/d, current with number of cig unknown, and missing); education (no school degree, primary school degree, technical or professional school degree, secondary school degree, university degree,

and missing); alcohol consumption (nondrinker, 0.1-4.9 g/d, 5.0-14.9 g/d, 15.0-29.9 g/d, and ≥ 30 g/d), activity (inactive, moderately inactive, moderately active, active, and missing), height (quintiles), and BMI (<18.5 , $18.5-<21.0$, $21.0-<23.5$, $23.5-<25.0$, $25.0-<26.5$, $26.5-<28.0$, $28.0-<30.0$, $30.0-<35.0$, ≥ 35.0)

Supplementary Table 6: Relative risk of death from major causes according to BMI in men and women in the European Prospective Investigation into Cancer and Nutrition (EPIC)*

	BMI								P _{LRT} †	
	<18.5	18.5-<21.0	21.0-<23.5	23.5-<25.0	25.0-<26.5	26.5-<28.0	28.0-<30.0	30.0-<35.0		≥35.0
Men										
Cause of death										
Ischemic heart disease	1.17 (0.54-2.56)	1.10 (0.77-1.57)	1.02 (0.80-1.31)	1.00	1.11 (0.89-1.40)	1.13 (0.89-1.43)	1.50 (1.20-1.88)	1.72 (1.37-2.16)	2.64 (1.86-3.73)	<0.0001
Cerebrovascular disease	1.41 (0.49-4.12)	1.39 (0.78-2.46)	0.90 (0.58-1.39)	1.00	0.99 (0.66-1.49)	1.14 (0.76-1.70)	0.88 (0.58-1.36)	1.27 (0.84-1.92)	1.86 (0.97-3.58)	0.30
Colorectal cancer	‡	1.64 (0.74-3.67)	1.83 (1.10-3.05)	1.00	1.22 (0.73-2.04)	1.95 (1.21-3.16)	2.13 (1.32-3.44)	2.66 (1.65-4.29)	2.55 (1.17-5.57)	0.002
Lung cancer	1.52 (0.70-3.32)	1.29 (0.91-1.83)	0.74 (0.56-0.98)	1.00	0.72 (0.55-0.94)	0.63 (0.48-0.83)	0.56 (0.42-0.75)	0.55 (0.41-0.74)	0.56 (0.31-1.00)	<0.0001
Prostate cancer	0.52 (0.07-4.14)	1.11 (0.52-2.37)	0.95 (0.57-1.58)	1.00	0.97 (0.60-1.57)	0.96 (0.58-1.60)	0.93 (0.55-1.59)	1.07 (0.62-1.85)	2.04 (0.83-4.99)	0.88
Women										
Cause of death										
Ischemic heart disease	1.02 (0.44-2.39)	0.88 (0.55-1.40)	1.02 (0.72-1.44)	1.00	1.26 (0.87-1.81)	1.27 (0.87-1.86)	1.58 (1.10-2.28)	1.44 (1.00-2.07)	3.28 (2.20-4.89)	<0.0001
Cerebrovascular disease	1.02 (0.44-2.38)	1.16 (0.78-1.73)	1.18 (0.86-1.62)	1.00	0.94 (0.65-1.36)	1.00 (0.68-1.45)	1.06 (0.73-1.54)	0.97 (0.67-1.40)	1.40 (0.88-2.24)	0.76
Breast cancer	1.11 (0.47-2.60)	0.87 (0.56-1.35)	0.79 (0.55-1.13)	1.00	1.12 (0.76-1.66)	1.38 (0.93-2.06)	1.62 (1.09-2.40)	1.55 (1.05-2.28)	1.79 (1.07-2.99)	0.002
Colorectal cancer	0.52 (0.16-1.65)	0.88 (0.57-1.36)	0.64 (0.45-0.91)	1.00	0.60 (0.40-0.91)	0.75 (0.49-1.13)	1.02 (0.69-1.51)	0.64 (0.41-0.98)	1.14 (0.67-1.94)	0.03
Lung cancer	0.71 (0.29-1.79)	1.51 (1.04-2.19)	1.23 (0.90-1.70)	1.00	0.93 (0.64-1.36)	0.95 (0.64-1.41)	0.91 (0.60-1.32)	0.86 (0.56-1.32)	0.83 (0.42-1.64)	0.09

*Multivariable adjusted relative risks calculated using Cox proportional hazard regression using age as the underlying time variable and stratified by center and age at recruitment with additional adjustment for smoking (never, former with quit ≥10y, former with quit <10y, former with time since quit unknown, current with <15 cig/d, current with 15-24 cig/d, current with ≥25 cig/d, current with number of cig unknown, and missing); education (no school degree, primary school degree, technical or professional school degree, secondary school degree, university degree, and missing); alcohol consumption (nondrinker, 0.1-4.9 g/d, 5.0-14.9 g/d, 15.0-29.9 g/d, and ≥30 g/d), activity (inactive, moderately inactive, moderately active, active, and missing), and height (quintiles). All covariates were entered using dummy coding into the models.

†p-value for the likelihood ratio test of comparing the model with BMI categories to the model without BMI categories with 8 degrees of freedom

‡not estimable because the number of incident cases was too low in this category

Supplementary Table 7: Relative risk of death from major causes according to quintiles of waist circumference in men and women in the European Prospective Investigation into Cancer and Nutrition (EPIC)

	Waist circumference quintile					P _{trend} †
	1	2	3	4	5	
Men						
Waist, cm	<86.0	86.0-<91.5	91.5-<96.5	96.5-<102.7	≥102.7	
Ischemic heart disease	1	1.32 (1.02-1.70)	1.35 (1.02-1.80)	1.63 (1.19-2.22)	1.68 (1.18-2.39)	0.008
Cerebrovascular disease	1	1.10 (0.71-1.70)	1.09 (0.67-1.79)	1.47 (0.86-2.49)	1.38 (0.74-2.58)	0.26
Colorectal cancer	1	1.17 (0.69-1.98)	1.26 (0.70-2.25)	1.34 (0.71-2.54)	1.90 (0.94-3.84)	0.04
Lung cancer	1	1.20 (0.88-1.65)	1.78 (1.27-2.49)	2.04 (1.38-3.00)	2.92 (1.87-4.57)	<0.0001
Prostate cancer	1	1.34 (0.77-2.35)	1.26 (0.66-2.42)	1.93 (0.96-3.89)	3.02 (1.36-6.72)	0.004
Women						
Waist, cm	<70.1	70.1-<75.6	75.6-<81.0	81.0-<89.0	≥89.0	
Ischemic heart disease	1	1.32 (0.86-2.03)	1.15 (0.73-1.83)	1.46 (0.89-2.39)	2.16 (1.26-3.70)	0.001
Cerebrovascular disease	1	1.14 (0.77-1.70)	1.09 (0.71-1.68)	1.64 (1.03-2.60)	2.05 (1.21-3.47)	0.002
Breast cancer	1	1.11 (0.75-1.64)	0.79 (0.50-1.25)	0.95 (0.58-1.56)	1.08 (0.61-1.91)	0.67
Colorectal cancer	1	1.02 (0.66-1.58)	0.89 (0.55-1.45)	0.97 (0.56-1.66)	1.00 (0.53-1.88)	0.95
Lung cancer	1	1.09 (0.76-1.55)	1.10 (0.74-1.63)	1.21 (0.77-1.90)	1.47 (0.86-2.51)	0.15

*Multivariable adjusted relative risks calculated using Cox proportional hazard regression using age as the underlying time variable and stratified by center and age at recruitment with additional adjustment for smoking (never, former with quit≥10y, former with quit<10y, former with time since quit unknown, current with <15 cig/d, current with 15-24 cig/d, current with ≥25 cig/d, current with number of cig unknown, and missing); education (no school degree, primary school degree, technical or professional school degree, secondary school degree, university degree, and missing); alcohol consumption (nondrinker, 0.1-4.9 g/d, 5.0-14.9 g/d, 15.0-29.9 g/d, and ≥30 g/d), activity (inactive, moderately inactive, moderately active, active, and missing), height (quintiles), and BMI (<18.5, 18.5-<21.0, 21.0-<23.5, 23.5-<25.0, 25.0-<26.5, 26.5-<28.0, 28.0-<30.0, 30.0-<35.0, ≥35.0)

†p-value for trend based on median waist circumference within quintiles

Supplementary Table 8: Relative risk of death from major causes according to quintiles of waist-hip-ratio in men and women in the European Prospective Investigation into Cancer and Nutrition (EPIC)

	Waist-hip-ratio quintile					P _{trend} *
	1	2	3	4	5	
	Men					
Waist-hip-ratio	<0.89	0.89-<0.92	0.92-<0.95	0.95-<0.99	≥0.99	
Ischemic heart disease	1	0.84 (0.67-1.06)	0.85 (0.67-1.08)	1.04 (0.82-1.31)	1.08 (0.85-1.38)	0.12
Cerebrovascular disease	1	1.24 (0.82-1.88)	1.08 (0.70-1.66)	1.04 (0.67-1.62)	1.24 (0.79-1.96)	0.54
Colorectal cancer	1	1.51 (0.91-2.51)	1.52 (0.91-2.56)	1.84 (1.10-3.09)	2.15 (1.27-3.66)	0.004
Lung cancer	1	1.13 (0.82-1.56)	1.41 (1.04-1.92)	1.50 (1.10-2.06)	1.76 (1.27-2.46)	0.0002
Prostate cancer	1	1.33 (0.76-2.33)	1.81 (1.06-3.11)	1.10 (0.60-2.02)	1.94 (1.07-3.52)	0.06
	Women					
Waist-hip-ratio	<0.73	0.73-<0.77	0.77-<0.80	0.80-<0.85	≥0.85	
Ischemic heart disease	1	0.99 (0.65-1.52)	0.96 (0.63-1.44)	1.31 (0.88-1.94)	1.56 (1.05-1.94)	0.0006
Cerebrovascular disease	1	1.33 (0.87-2.05)	1.57 (1.04-2.36)	1.64 (1.09-2.47)	1.96 (1.30-2.97)	0.0009
Breast cancer	1	0.83 (0.59-1.17)	0.80 (0.57-1.14)	0.78 (0.54-1.11)	0.99 (0.69-1.41)	0.89
Colorectal cancer	1	0.99 (0.65-1.49)	1.13 (0.76-1.68)	1.00 (0.66-1.52)	1.18 (0.77-1.81)	0.43
Lung cancer	1	1.32 (0.88-1.96)	1.55 (1.05-2.29)	1.46 (0.97-2.18)	2.06 (1.37-3.09)	0.0004

*Multivariable adjusted relative risks calculated using Cox proportional hazard regression using age as the underlying time variable and stratified by center and age at recruitment with additional adjustment for smoking (never, former with quit \geq 10y, former with quit $<$ 10y, former with time since quit unknown, current with $<$ 15 cig/d, current with 15-24 cig/d, current with \geq 25 cig/d, current with number of cig unknown, and missing); education (no school degree, primary school degree, technical or professional school degree, secondary school degree, university degree, and missing); alcohol consumption (nondrinker, 0.1-4.9 g/d, 5.0-14.9 g/d, 15.0-29.9 g/d, and \geq 30 g/d), activity (inactive, moderately inactive, moderately active, active, and missing), height (quintiles), and BMI ($<$ 18.5, 18.5- $<$ 21.0, 21.0- $<$ 23.5, 23.5- $<$ 25.0, 25.0- $<$ 26.5, 26.5- $<$ 28.0, 28.0- $<$ 30.0, 30.0- $<$ 35.0, \geq 35.0)

†p-value for trend based on median waist-hip-ratio within quintiles

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Supplementary Figure 1

Label:

Multivariable adjusted relative risk of death in men (Panels A) and women (Panel B) according to BMI categories (18.5-<25.0; 25.0-<30.0; \geq 30.0) and quintiles of waist-hip-ratio.

Footnote:

Symbols indicate relative risks and error bars indicate 95%-confidence intervals. The reference category represents participants in the middle category of BMI and the bottom quintile of waist-hip-ratio. Age was used as the underlying time variable in the regression models with stratification by center and age at recruitment and additional adjustment for smoking, education, alcohol consumption, physical activity, and height.

Supplementary Figure 2

Label:

Multivariable adjusted relative risk of death in men (Panels A, B and C) and women (Panels D, E and F) who never smoked according to BMI (Panels A and D), waist circumference (Panels B and E) and waist-hip-ratio (Panels C and F) in EPIC.

Footnote:

Solid lines indicate relative risks and dashed lines indicate 95%-confidence intervals derived from restricted cubic spline regression with knots placed at the 5th, 25th, 75th, and 95th percentile of the sex-specific distribution of each anthropometric variable. The reference point for BMI is the midpoint of the reference group (23.5-<25.0) from categorical analysis. The reference points for waist circumference and waist-hip-ratio are the sex-specific medians of these variables. The graphic displays are truncated at the 1st and 99th percentiles. Age was used as the underlying time variable in the regression models with stratification by center and age at recruitment and additional adjustment for smoking, education, alcohol consumption, physical activity, and height.

Supplementary Figure 3

Label:

Multivariable adjusted relative risk of death in men (Panels A and B) and women (Panels C and D) who never smoked according to waist circumference (Panels A and C) and waist-hip-ratio (Panels B and D) after adjustment for BMI in EPIC.

Footnote:

Solid lines indicate relative risks and dashed lines indicate 95%-confidence intervals derived from restricted cubic spline regression with knots placed at the 5th, 25th, 75th, and 95th percentile of the sex-specific distribution of each anthropometric variable. The reference points for waist circumference and waist-hip-ratio are the sex-specific medians of these variables. The graphic displays are truncated at the 1st and 99th percentiles. Age was used as the underlying time variable in the regression models with stratification by center and age at recruitment and additional adjustment for smoking, education, alcohol consumption, physical activity, height, and BMI.

Supplementary Figure 4

Label:

Multivariable adjusted relative risk of death in men (Panels A and B) and women (Panels C and D) who never smoked according to tertiles of BMI and quintiles of waist circumference (Panels A and C) or waist-hip-ratio (Panels B and D), respectively.

Footnote:

Note that the scale of the y-axis differs from the other figures. Symbols indicate relative risks and error bars indicate 95%-confidence intervals. The reference category represents participants in the middle tertile of BMI and the bottom quintile of waist circumference or waist-hip-ratio, respectively. Age was used as the underlying time variable in the regression models with stratification by center and age at recruitment and additional adjustment for smoking, education, alcohol consumption, physical activity, and height.

*The upper boundary of the 95%-confidence intervals for the relative risk of men in the lowest tertile of BMI and the highest quintile of waist circumference was 13.27.

Supplementary Figure 5

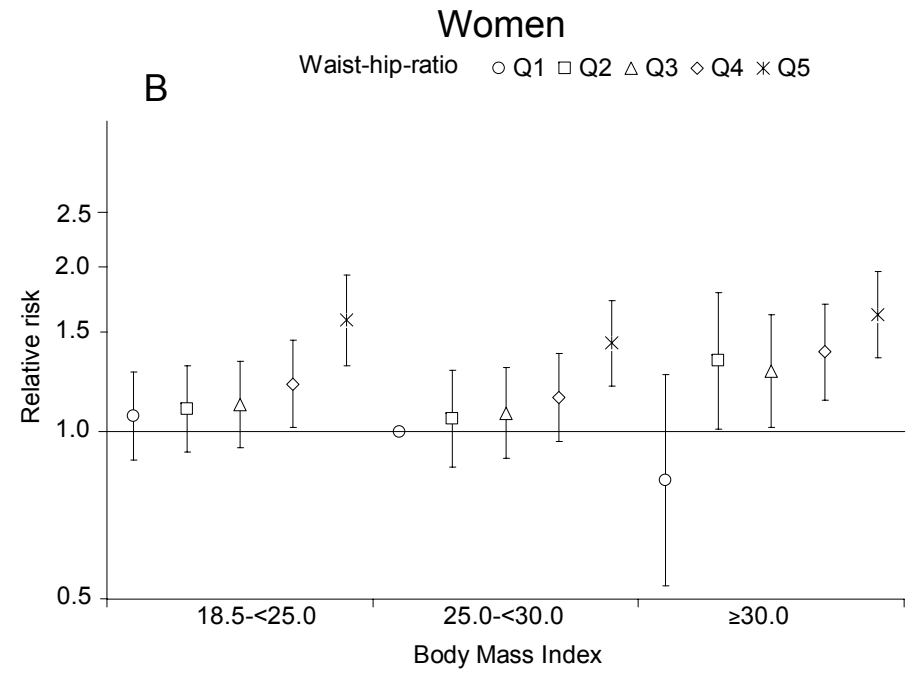
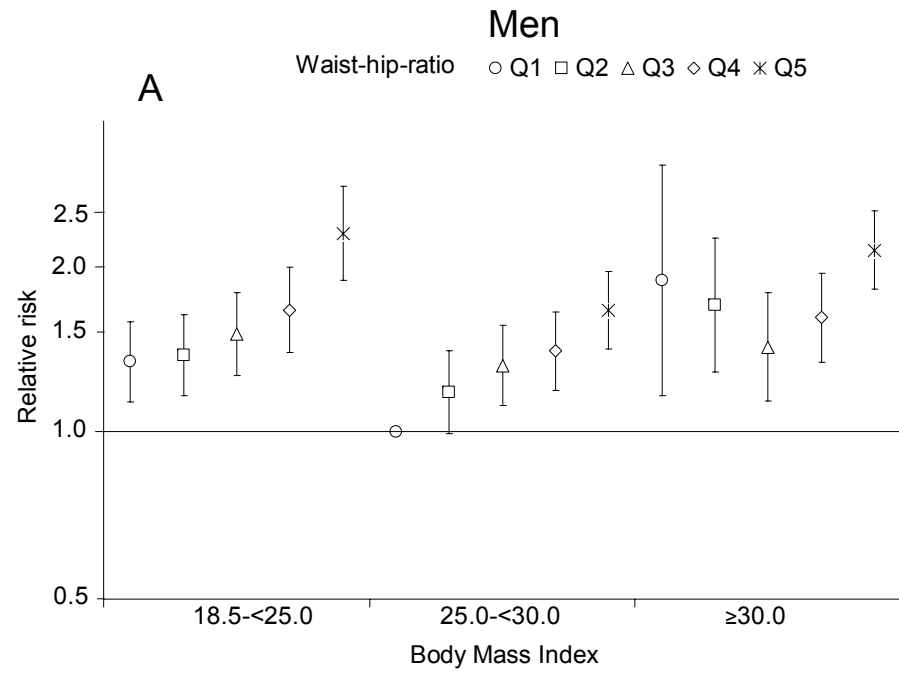
Label:

Cause-specific multivariable adjusted relative risk of death in men (Panels A, B and C) and women (Panels D, E and F) according to BMI (Panels A and D), waist circumference (Panels B and E) and waist-hip-ratio (Panels C and F) in EPIC.

Footnote:

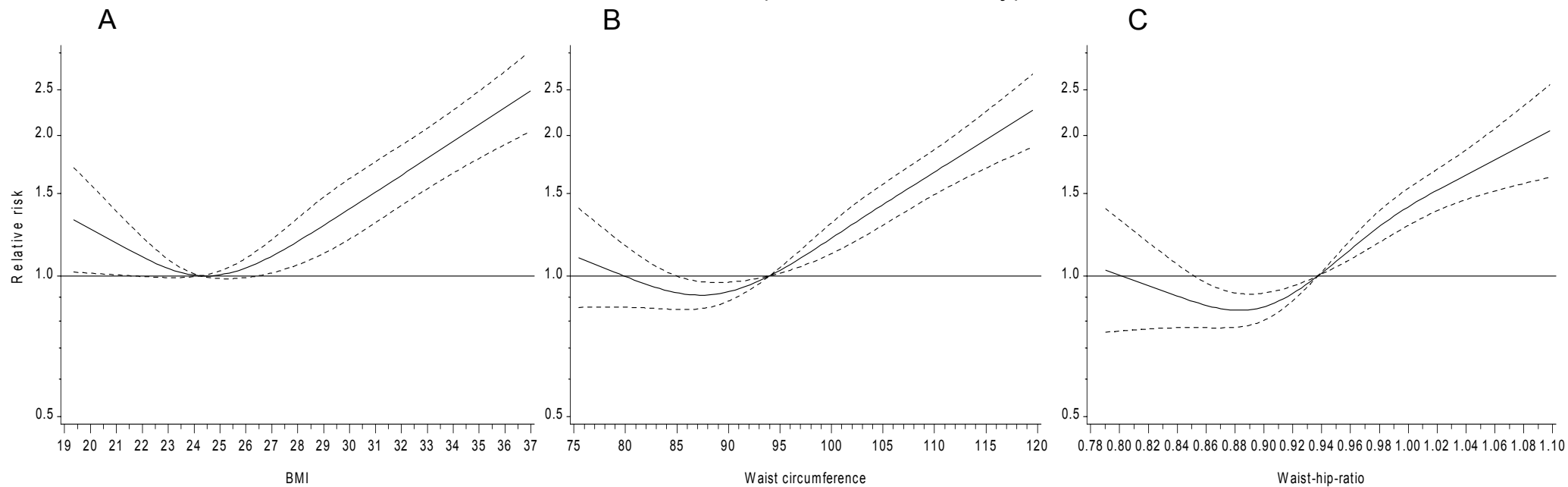
Lines indicate relative risks of death according to the underlying causes as indicated, derived from restricted cubic spline regression with knots placed at the 5th, 25th, 75th, and 95th percentile of the sex-specific distribution of each anthropometric variable. The reference point for BMI is the midpoint of the reference group (23.5-<25.0) from categorical analysis. The reference points for waist circumference and waist-hip-ratio are the sex-specific medians of these variables. The graphic displays are truncated at the 1st and 99th percentiles. Age was used as the underlying time variable in the regression models with stratification by center and age at recruitment and additional adjustment for smoking, education, alcohol consumption, activity, and height. Models for waist circumference and waist-hip-ratio were additionally adjusted for BMI.

Supplementary Figure 1

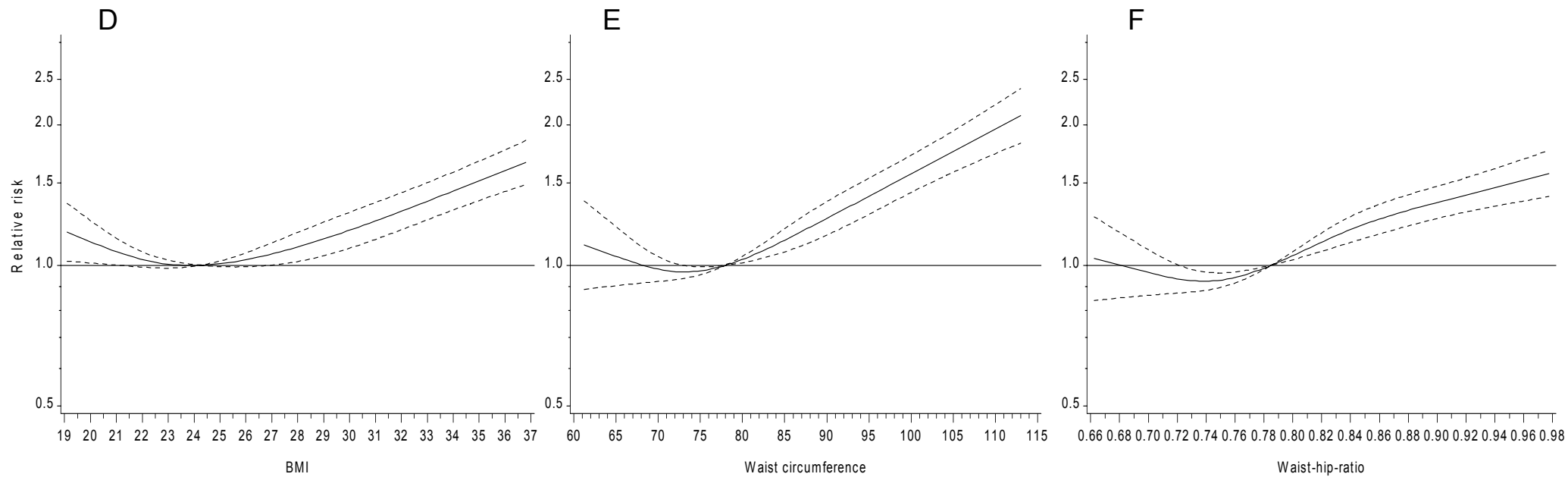


Supplementary Figure 2

Men (never smokers only)

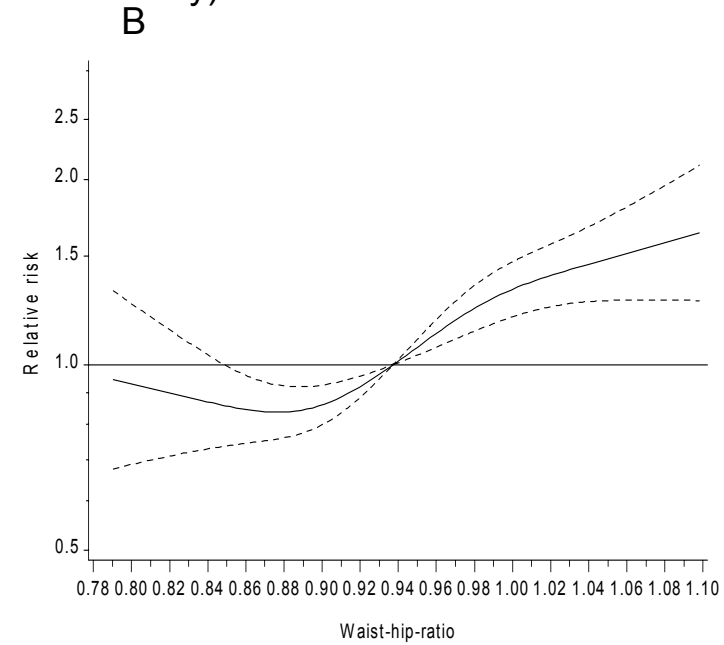
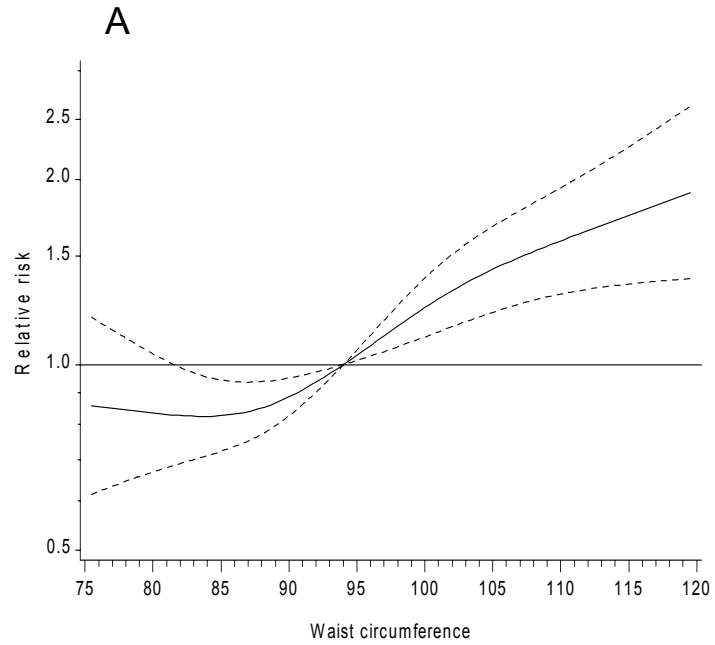


Women (never smokers only)

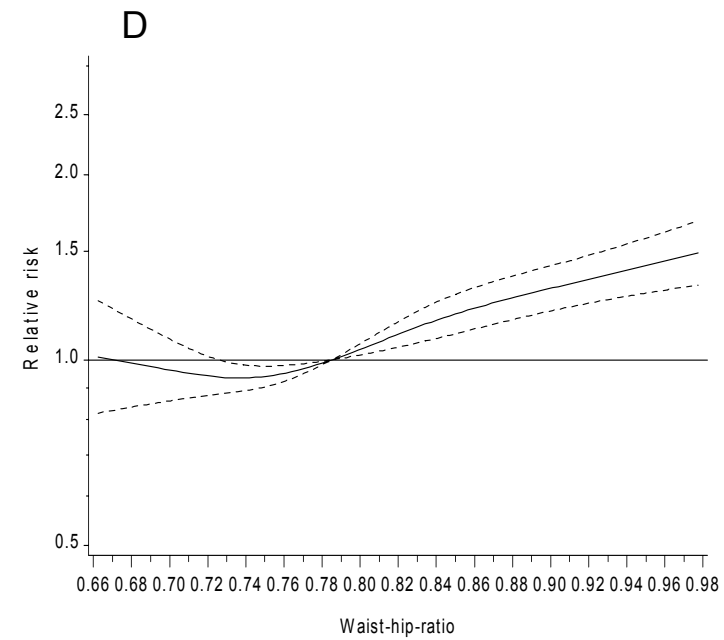
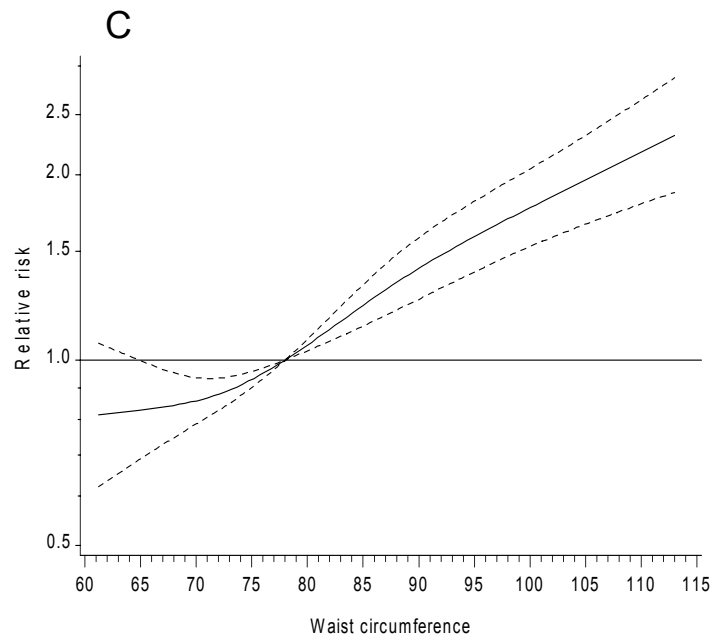


Supplementary Figure 3

Men (never smokers only)

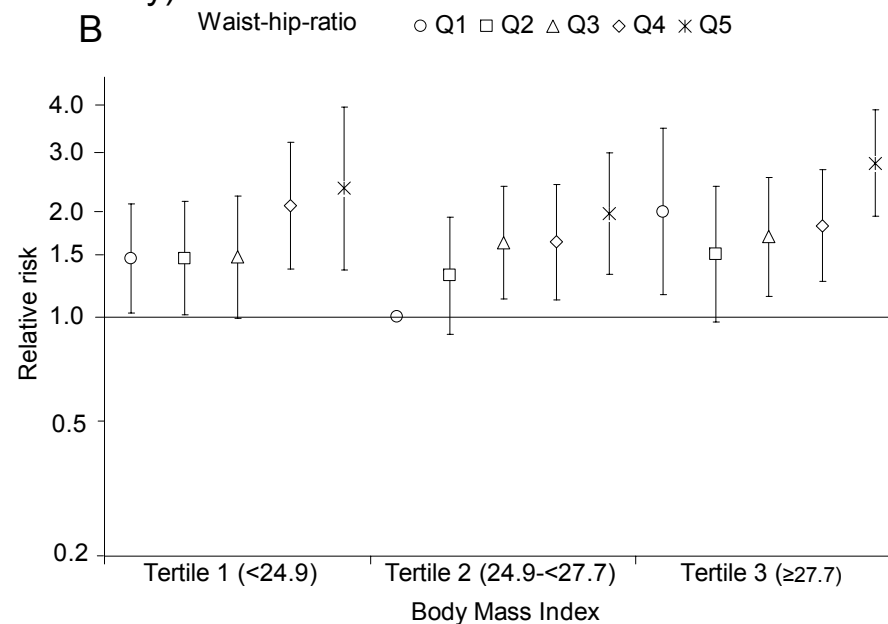
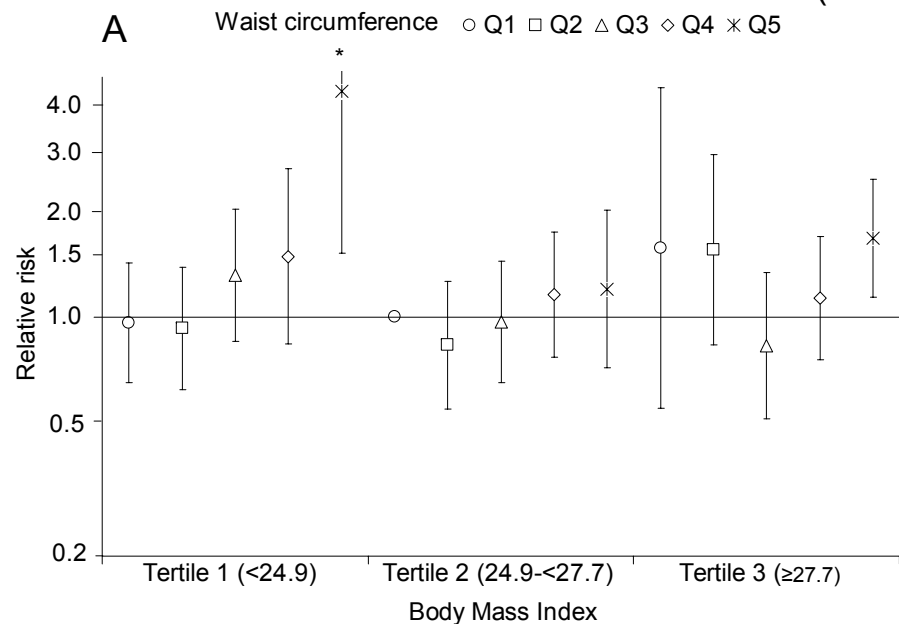


Women (never smokers only)

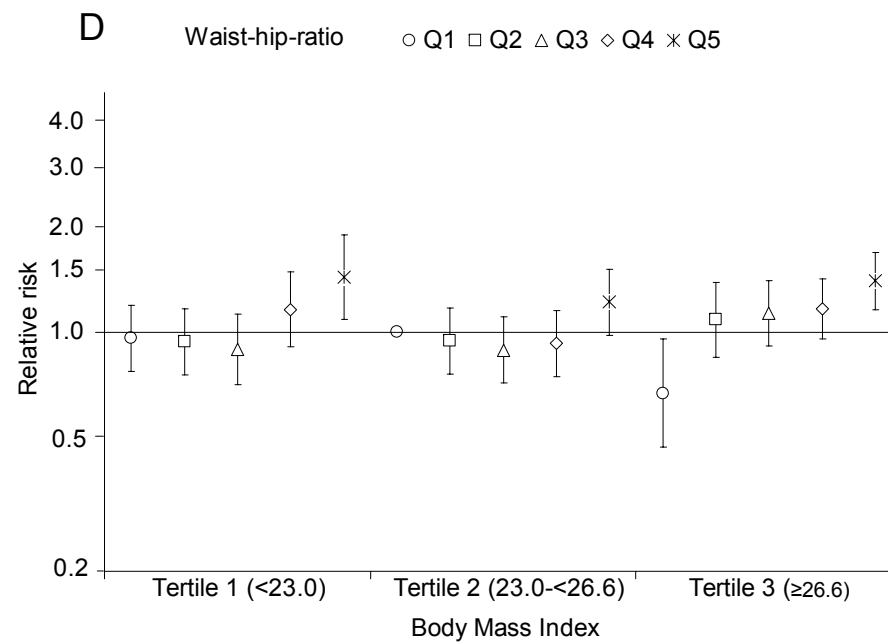
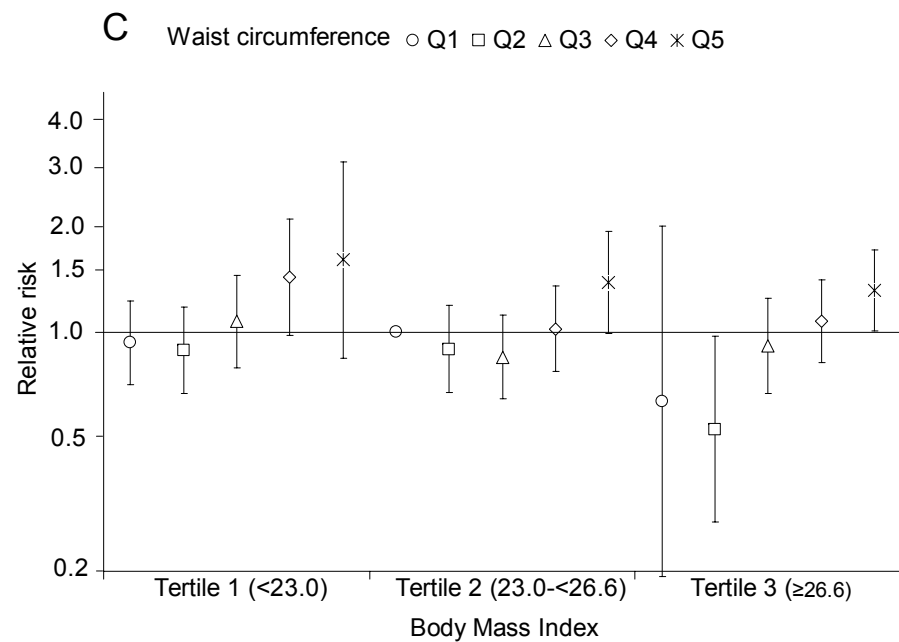


Supplementary Figure 4

Men (never smokers only)



Women (never smokers only)



Supplementary Figure 5

