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The Predictive Value of Different Measures of Obesity for Incident Cardiovascular Events and Mortality

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Context: To date, it is unclear which measure of obesity is the most appropriate for risk stratification.

Objective: The aim of the study was to compare the associations of various measures of obesity with incident cardiovascular events and mortality.

Design and Setting: We analyzed two German cohort studies, the DETECT study and SHIP, including primary care and general population.

Participants: A total of 6355 (mean follow-up, 3.3 yr) and 4297 (mean follow-up, 8.5 yr) individuals participated in DETECT and SHIP, respectively.

Interventions: We measured body mass index (BMI), waist circumference (WC), waist-to-height ratio (WHtR), and waist-to-hip ratio (WHR) and assessed cardiovascular and all-cause mortality and the composite endpoint of incident stroke, myocardial infarction, or cardiovascular death.

Results: In both studies, we found a positive association of the composite endpoint with WHtR but not with BMI. There was no heterogeneity among studies. The relative risks in the highest versus the lowest sex- and age-specific quartile of WHtR, WC, WHR, and BMI after adjustment for multiple confounders were as follows in the pooled data: cardiovascular mortality, 2.75 (95% confidence interval, 1.31–5.77), 1.74 (0.84–3.6), 1.71 (0.91–3.22), and 0.74 (0.35–1.57), respectively; all-cause mortality, 1.86 (1.25–2.76), 1.62 (1.22–2.38), 1.36 (0.93–1.69), and 0.77 (0.53–1.13), respectively; and composite endpoint, 2.16 (1.39–3.35), 1.59 (1.04–2.44), 1.49 (1.07–2.07), and 0.57 (0.37–0.89), respectively. Separate analyses of sex and age groups yielded comparable results. Receiver operating characteristics analysis yielded the highest areas under the curve for WHtR for predicting these endpoints.

Conclusions: WHtR represents the best predictor of cardiovascular risk and mortality, followed by WC and WHR. Our results discourage the use of the BMI. **(*J Clin Endocrinol Metab* 95: 0000–0000, 2010)**

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Abbreviations: AUC, Area under the curve; BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; HC, hip circumference; HDL, high-density lipoprotein; ROC, receiver operating characteristic; RR, relative risk; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio.

Obesity is an increasing problem worldwide. It is a major risk factor for the development of chronic diseases and mortality (1–4). However, large-scale studies have shown that increased body mass index (BMI; weight in kilograms divided by the square of height in meters) was not associated with increased mortality. In fact, overweight subjects (BMI, 25–29.9 kg/m^2) survive longer than normal-weight subjects, and only persons with severe obesity, defined as BMI of at least 35 kg/m^2, are at increased risk of early death (5–9). Several studies pointed to a superior role of measures of abdominal obesity over BMI in predicting cardiovascular risk (4, 10–22).

BMI does not distinguish between overweight due to muscle or fat accumulation. Moreover, visceral rather than sc fat accumulation is associated with increased secretion of free fatty acids, hyperinsulinemia, insulin resistance, hypertension, and dyslipidemia (23, 24).

In summary, there is agreement that abdominal obesity is a better indicator of cardiovascular risk and mortality than BMI. However, the studies available to date still give no conclusive answer as to which anthropometric parameter best predicts cardiovascular events and mortality. Large prospective studies comparing objective measures of obesity are still lacking. Thus, the World Health Organization still recommends BMI as a universal criterion of overweight and obesity, although the additional use of waist circumference (WC) or waist-to-hip ratio (WHR) is encouraged (2). In general practice, BMI is still used as the main criterion to prompt behavioral, medical, or surgical interventions against obesity.

In this study, we compared different anthropometric measures of obesity with respect to their value to predict adverse cardiovascular events, cardiovascular mortality, and overall mortality in two German prospective large-scale studies, the nationwide Diabetes Cardiovascular Risk Evaluation: Targets and Essential Data for Commitment of Treatment study (DETECT) and the Study of Health in Pomerania (SHIP).

Subjects and Methods

The DETECT study

Subjects

The design of the DETECT study has been described elsewhere (25). In brief, 7519 subjects attending a primary care practice in Germany during a specified half day in September 2003 were included. The study conformed to the principles of the Declaration of Helsinki and was approved by the local ethics committee. All subjects gave written informed consent. Mortality and incident events were recorded from the treating physicians during a follow-up visit between September 2007 and February 2008. Ethnicity was not recorded but, being representative of the German population, the participants were mainly of Caucasian ethnicity [1.2% inhabitants of African or Southeast-Asian origin (Statistisches Bundesamt 2009)].

Of the 7519 subjects, 554 were excluded because of missing anthropometric data. Of the remaining 6965 subjects, 610 were excluded due to loss to follow-up. Thus, valid data with all anthropometric measures and follow-up for mortality and cardiovascular events were available in 6355 subjects. Mean follow-up was 3.3 yr.

Instruments and measures

Information on age, sex, sociodemographic characteristics, and medical histories were assessed by standardized interviews by the primary care physicians. Physicians were advised to measure weight, height, blood pressure, WC (measured midway between the lower rib margin and the iliac crest in the horizontal plane), and hip circumference (HC) according to written, standardized instructions given in a manual (18).

Fasting or nonfasting blood samples were collected and shipped by courier at room temperature within 24 h to the central laboratory. Upon arrival in the central laboratory, the samples were centrifuged immediately, and serum and plasma were stored at −20 C until further processing.

SHIP

Subjects

SHIP is a longitudinal population-based cohort study in the northeast of Germany on 4310 subjects sampled in 12 age strata of equal size (26, 27). The study conformed to the principles of the Declaration of Helsinki and was approved by the local ethics committee. All subjects gave written informed consent. SHIP only included subjects of Caucasian origin.

Mortality was tracked by death registers. Incident diseases were defined by self-report as recorded during the 5-year follow-up in the SHIP study center.

Of 4310 subjects, 13 were excluded due to missing anthropometric data and no subjects were excluded due to loss to follow-up for mortality. Valid data including anthropometric measures on vital status and incident cardiovascular events were available in 4297 subjects and in 3293 subjects, respectively. The mean duration of follow-up for mortality and cardiovascular events was 8.5 and 5.2 yr, respectively.

Instruments and measures

Information on age, sex, sociodemographic characteristics, and medical histories was assessed by standardized interviews by computer-aided standardized interviews.

Study nurses measured weight, height, blood pressure, WC, and HC according to written, standardized instructions given in a manual (26, 27). Nonfasting blood samples were taken between 0700 and 1600 h and analyzed immediately.

Predictors and covariates

In total, we studied 10,652 subjects with a mean follow-up of 5.3 yr for mortality (n = 641,632 subject years). For incident cardiovascular events, we excluded patients with preexisting stroke or myocardial infarction, and mean follow-up was 4.0 yr. Thus, we studied 9,057 subjects for cardiovascular events (n = 529,348 subject years).

The following anthropometric parameters were calculated: BMI, WHR (WC divided by HC), and waist-to-height ratio (WHtR; WC divided by measured height in centimeters).

For both studies, we defined covariables as follows: liver disease–physician- or self-reported diagnosis of liver disease or aspartate-amino-transferase or alanine-amino-transferase more than three times the upper limit of reference (135 and 129 U/liter, respectively); kidney failure–estimated glomerular filtration rate, using the Cockroft-Gault formula, of less than 30 ml/min; lack of physical activity–self-reported physical activity of less than 2 h/wk; diabetes mellitus–fasting blood glucose level of at least 126 mg/dl, nonfasting blood glucose of at least 200 mg/dl, intake of oral antidiabetic drugs or insulin, or known from history; metabolic syndrome–presence of at least three of the following conditions: serum triglycerides of at least 150 mg/dl, high-density lipoprotein (HDL) less than 40 mg/dl in men and less than 50 mg/dl in women, measured blood pressure of at least 130/85 mm Hg, fasting blood glucose of at least 110 mg/dl or nonfasting glucose of at least 140 mg/dl, or diabetes as defined above (28); hypertension–systolic blood pressure of at least 140 mm Hg or diastolic blood pressure of at least 90 mm Hg or use of blood pressure-lowering medication; dyslipidemia–levels of total cholesterol greater than 240 mg/dl, low-density lipoprotein cholesterol greater than 160 mg/dl, or HDL cholesterol less than 40 mg/d, or use of lipid-lowering medication (28); coronary artery disease (CAD), stroke, and cancer–physician's diagnosis; smoking status–self-reported former, never, or current smoking.

Statistical analyses

We did analyses in each cohort and in both cohorts pooled, stratified according to study cohort, sex, and age (≤65 yr and >65 yr). The homogeneity of associations between measures of obesity and outcome between both cohorts was tested by a χ^2 test of homogeneity. We divided subjects into quartiles of the different anthropometric parameters. We performed all analyses with sex- and age-specific quartiles (using 10-yr strata). For the separate analyses of study cohorts, we used sex-, age-, and cohort-specific quartiles (using 10-yr strata) of each cohort. The quantitative anthropometric parameters were additionally analyzed by estimating the relative risk (RR) of 1 SD increase for the respective outcome.

We calculated the RRs for the following endpoints: overall mortality, cardiovascular mortality, and composite endpoint of incident stroke, myocardial infarction, or cardiovascular death. The RRs were estimated by Poisson regression models with robust estimation of error variances (29, 30). We adjusted for potential confounders selected by clinical association or known correlation. The regression models for the estimation of RR were adjusted for: M1, time of follow-up (crude analyses); M2, time of follow-up, age, sex, and cohort; M3, time of follow-up, age, sex, cohort, educational status, professional status, marital status, smoking status, physical activity, kidney failure, cancer, and liver disease; and M4, all parameters + BMI for measures of abdominal obesity or WHtR for BMI. We modeled missing values in sociodemographic variables (proportion < 0.5%) by a nonresponse category. The model fit of the Poisson regression models was assessed by the Link test of Pregibon. The hypothesis of correctly specified predictor variables could not be rejected for all models at the 5% significance level. Generally, 95% confidence intervals (CIs) were estimated, and statistical inference is based on a significance level of 5%. For a mediator analysis, we then additionally adjusted M3 and M4 for cardiovascular diseases and cardiovascular risk factors alone or in different combinations. Finally, the area under the curve (AUC) was estimated by receiver operating characteristics (ROC) to evaluate the strength of the association of anthropometric parameters and outcome variables. ROC analysis was performed for both crude anthropometric parameters and sex- and age-specific percentiles of anthropometric parameters. Differences between AUCs were tested with a nonparametrical test (31). In a further step, we estimated cutoff levels for the sex- and age-specific percentiles of the different anthropometric parameters by calculating that point on the curve where the sum of sensitivity and specificity was highest.

All statistical analyses were conducted with the software package STATA 10.1 (Stata Corp., College Station, TX).

Results

Baseline characteristics

Table 1 summarizes the baseline characteristics of both study populations. Participants in DETECT were older and had higher anthropometric indices of abdominal obesity than participants in SHIP but showed no difference in BMI.

The Pearson correlation coefficients of WHtR with WC, WHR, HC, and BMI were 0.94, 0.61, 0.70, and 0.81, respectively. The Pearson correlation coefficients of BMI with WC, WHR, and HC were 0.77, 0.31, and 0.78, respectively.

For all anthropometric parameters, the age- and sex-specific interquartile ranges showed a tendency to increase with age (Supplemental Table 1 published on The Endocrine Society's Journals Online web site at http://jcem.endojournals.org). The interquartile ranges after exclusion of subjects with previous myocardial infarction or stroke for assessment of the composite endpoint were not different from the total sample. Therefore, we used the same interquartile ranges for all endpoints studied here. For all parameters, subjects in the 4th quartile had a lower educational level, were less often employed, smoked less often, and had higher prevalence of diabetes, hypertension, dyslipidemia, metabolic syndrome, CAD, kidney diseases, and liver diseases. Subjects in the 4th quartile of WHtR, WC, HC, and BMI were more often physically inactive (Supplemental Table 2).

Regression analyses

During the study follow-up, in DETECT and SHIP we observed 244 and 376 deaths, 69 and 112 cardiovascular deaths, and 194 and 131 composite endpoints of incident stroke, myocardial infarction, or cardiovascular death, respectively. There was no indication of heterogeneity of RRs between cohorts for any anthropometric parameter or endpoint (χ^2 test for homogeneity; P values ranging from 0.10 to 0.97 among all anthropometric parameters and endpoints). Therefore, we did an analysis of both separate cohorts and pooled data.

TABLE 1. Subject characteristics of the study sample

	Total	DETECT	SHIP
n	10,652	6,355	4,297
Age, mean (SD)	54.8 (15.6)	58.1 (14.1)	49.8 (16.4)
18–44 yr	3,002 (28.2%)	1,276 (20.1%)	1,726 (40.2%)
45–65 yr	4,551 (42.7%)	2,884 (45.4%)	1,667 (38.8%)
66+ yr	3,099 (29.1%)	2,195 (34.5%)	904 (21.0%)
Females	5,956 (55.9%)	3,771 (59.3%)	2,185 (50.9%)
Anthropometric parameters, mean (SD)			
WHtR	0.55 (0.08)	0.56 (0.08)	0.53 (0.08)
WC	92.7 (14.6)	94.9 (14.7)	89.3 (13.9)
WHR	0.89 (0.10)	0.91 (0.11)	0.87 (0.09)
HC	104.2 (11.5)	105.1 (12.5)	102.9 (9.8)
BMI	27.2 (4.8)	27.2 (4.8)	27.3 (4.7)
Educational status			
<10 school years	4,470 (42.8%)	2,765 (44.7%)	1,705 (40.0%)
10 school years	3,413 (32.7%)	1,551 (25.1%)	1,862 (43.7%)
>10 school years	2,567 (24.6%)	1,868 (30.2%)	699 (16.4%)
Family status			
Married	7,231 (68.5%)	4,435 (70.7%)	2,796 (65.3%)
Single	1,376 (13.0%)	571 (9.1%)	805 (18.8%)
Divorced/widowed	1,946 (18.4%)	1,265 (20.2%)	681 (15.9%)
Professional status			
Employed	4,540 (43.2%)	2,475 (39.4%)	2,065 (48.7%)
Unemployed/homemaker	1,610 (15.3%)	896 (14.3%)	714 (16.8%)
Retired	4,364 (41.5%)	2,904 (46.3%)	1,460 (34.4%)
Smoking status			
Smoker	4,958 (47.5%)	3,425 (55.5%)	1,533 (35.8%)
Ex-smoker	2,961 (28.3%)	1,511 (24.5%)	1,450 (33.9%)
Non-smoker	2,528 (24.2%)	1,233 (20.0%)	1,295 (30.3%)
Physical inactivity	5,058 (49.8%)	1,846 (31.4%)	3,212 (75.1%)
GFR, mean (SD)	66.1 (17.0)	57.1 (11.3)	79.5 (15.1)
Kidney failure (GFR < 30)	66 (0.6%)	56 (0.9%)	10 (0.2%)
Cancer	280 (2.6%)	228 (3.6%)	52 (1.2%)
Liver disease	372 (3.5%)	346 (5.4%)	26 (0.6%)
Diabetes mellitus	1,518 (14.3%)	1,158 (18.2%)	360 (8.4%)
CAD	1,045 (9.8%)	899 (14.2%)	146 (3.4%)
Stroke	219 (2.1%)	122 (1.9%)	97 (2.3%)
Hypertension	5,882 (55.3%)	3,918 (61.7%)	1,964 (45.8%)
Dyslipidemia	4,999 (47.0%)	3,052 (48.0%)	1,947 (45.5%)
Metabolic syndrome	4,752 (44.6%)	2,954 (46.5%)	1,798 (41.8%)

Data are expressed as number (percent) unless otherwise designated. Physical inactivity, physical activity for less than 2 h/wk. GFR, glomerular filtration rate: creatinin^-1.154 * age^-0.203 for male and creatinin^-1.154 * age^-0.203 * 0.742 for female. Metabolic syndrome, presence of two or more of the following risk factors: triglycerides of at least 150 mg/dl, blood pressure of at least 130/85 mm Hg, HDL cholesterol below 40 mg/dl in men and below 50 mg/dl in women, and fasting glucose of at least 110 mg/dl or nonfasting glucose of at least 140 mg/dl.

Figure 1 displays the RR for the three endpoints in different quartiles of the anthropometric parameters, compared with the lowest quartile after adjustment for time of follow-up, age, sex, cohort (if applicable), educational status, professional status, marital status, smoking status, physical activity, kidney failure, cancer, liver disease, and BMI/WHtR as appropriate in each cohort and pooled data.

In both DETECT and SHIP, there was a linear increase of RR with WHtR and the composite endpoints with significant differences in the 4th quartile. In SHIP, there were also significant findings for WHtR and the other endpoints. There was similar although not significant tendency in DETECT. The other measures of abdominal obesity pointed in the same direction. However, BMI showed a negative association with the composite endpoint.

In the pooled data, WHtR showed the highest RR in the 4th quartile for all three endpoints. BMI was inversely associated with the composite endpoint. The RRs in the highest quartile *vs.* the lowest quartile of WHtR, WC, WHR, and BMI after full adjustment (model 4) were as follows: cardiovascular mortality, 2.75 (95% CI, 1.31–5.77), 1.74 (0.84–3.6), 1.71 (0.91–3.22), and 0.74 (0.35–1.57), respectively; all-cause mortality, 1.86 (1.25–2.76), 1.62 (1.22–2.38), 1.36 (0.93–1.69), and 0.77 (0.53–1.13), respectively; and composite endpoint, 2.16 (1.39–3.35), 1.59 (1.04–2.44), 1.49 (1.07–2.07), and 0.57 (0.37–0.89), respectively. The results were similar after exclusion of diabetic subjects (data not shown). The associations pointed in the same direction when

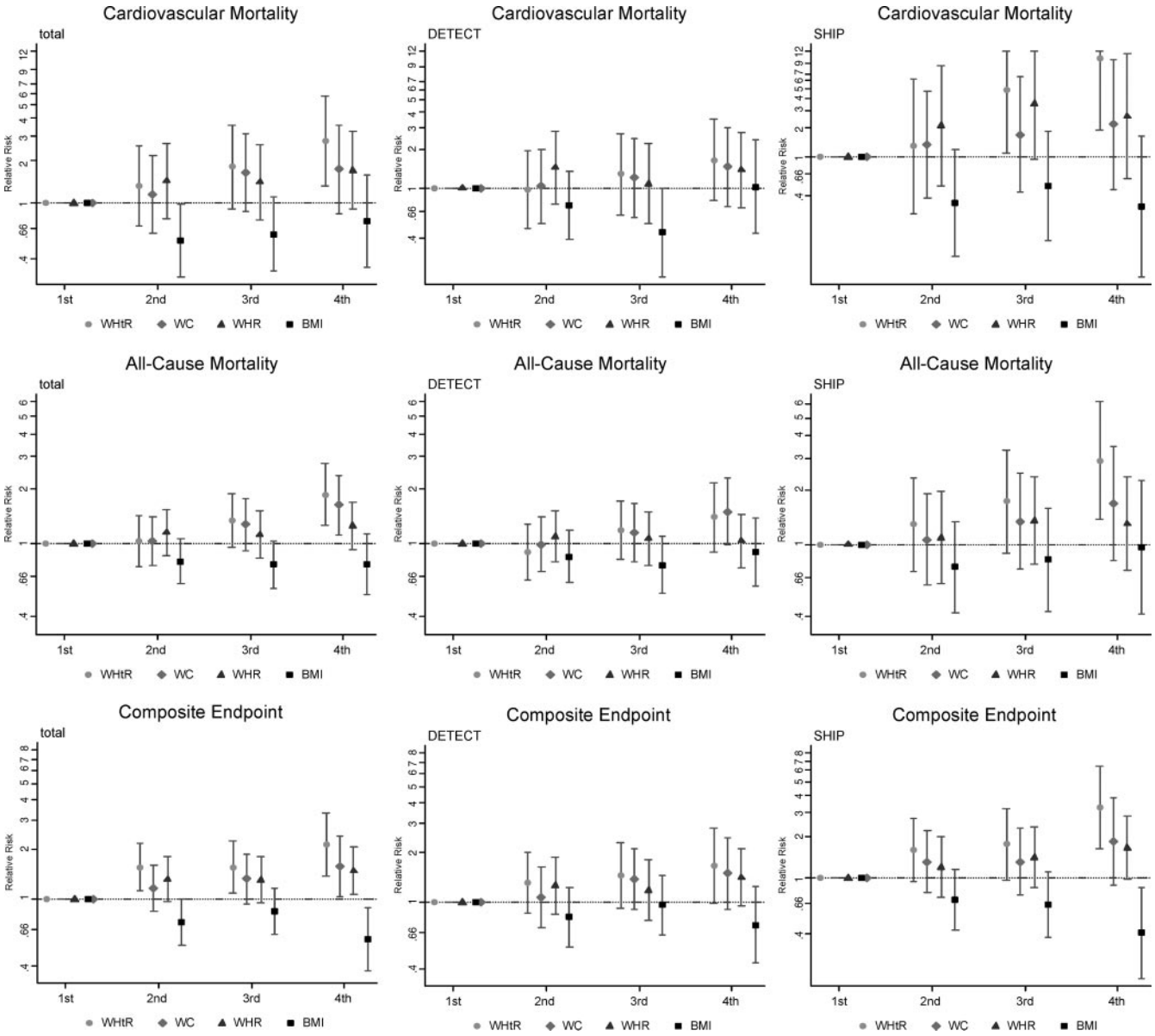

FIG. 1. RR for follow-up events in quartiles of anthropometric parameters by study cohort, adjusted for time of follow-up, age, sex, cohort (if applicable), educational status, professional status, marital status, smoking status, physical activity, kidney failure, cancer, liver disease, and BMI (for measures of abdominal obesity) or WHtR (for BMI).

we used an increase of 1 SD of each anthropometric parameter as shown in Fig. 2.

In women, both WHtR and WC showed significant associations for all endpoints. In men, there were significant positive associations of WHtR and of WHR with the composite endpoint and an inverse association of BMI with the composite endpoint (Supplemental Fig. 1). In subjects older than 65 yr, WHtR was significantly associated with all endpoints, whereas in subjects aged up to 65 yr, WHtR was significantly associated with all cardiovascular mortality and the composite endpoint (Supplemental Fig. 2).

Adjustment for different confounders caused little change of effect measures (Supplemental Fig. 3). Additional adjustment for BMI or WHtR had opposite effects on the RR of WHtR and BMI, respectively. Analyses of WHtR in strata of BMI less than 25, 25–29.9, and 30 kg/m^2 or greater revealed a tendency for increasing RR of mortality within the BMI strata of less than 25 and 25–29.9 kg/m^2 but no clear effect in subjects with a BMI of 30 kg/m^2 or greater (data not shown).

In a further step, we assessed the possible influence of potential mediators. We calculated the RR for an increase of WHtR or BMI of 1 SD and then additionally adjusted for potential mediators. Inclusion of different variables either alone or in combination had little effect on the association of WHtR and BMI with incident endpoints (Supplemental Table 3).

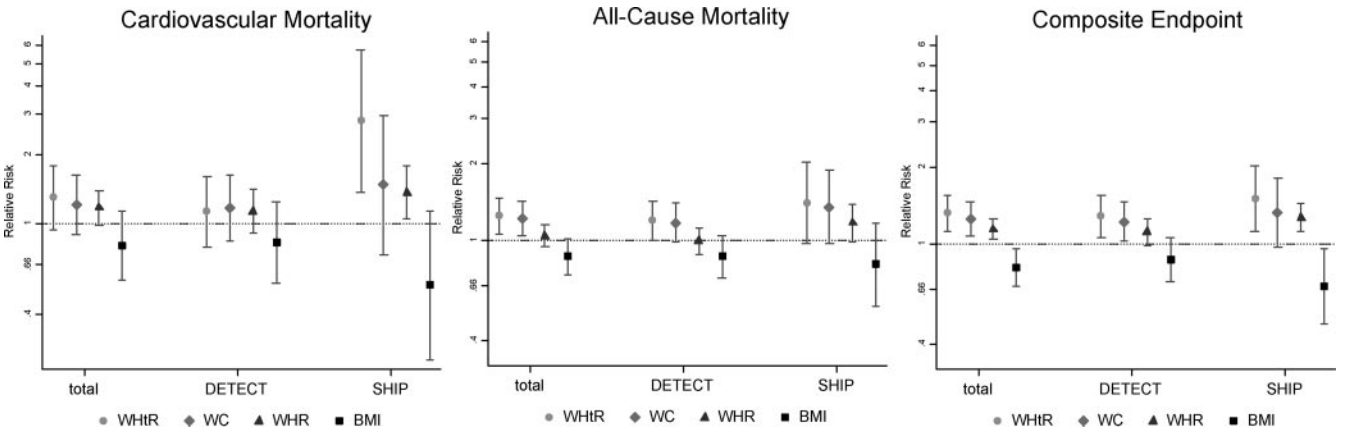

FIG. 2. RR for follow-up events for an increase of 1 SD of each respective anthropometric parameter by study cohort, adjusted for time of follow-up, age, sex, cohort (if applicable), educational status, professional status, marital status, smoking status, physical activity, kidney failure, cancer, liver disease, and BMI (for measures of abdominal obesity) or WHtR (for BMI).

ROC analyses

To compare the predictive values of the anthropometric measures, we performed ROC analyzes and calculated the respective areas under the ROC curves (AUC) for prediction of cardiovascular endpoints as shown in Table 2. The AUC is a measure of the degree of separation between exposed and nonexposed subjects by a specific test. An AUC of 1 indicates perfect separation between affected and nonaffected subjects, and an AUC of 0.5 indicates no discriminative value of the test used.

Using absolute values of the anthropometric measures, WHtR showed the highest AUC for all endpoints (0.648, 0.679, and 0.630 for all-cause mortality, cardiovascular mortality, and the composite endpoint, respectively), and the AUC of WHtR was significantly higher than the AUCs of all other anthropometric parameters. We then analyzed the AUCs by using sex- and age-specific percentiles (using 10-yr strata of age) of the different anthropometric parameters to eliminate confounding effects of sex and age. In this analysis, WHtR also showed the highest AUC for all endpoints (0.531, 0.562, and 0.547 for all-cause mortality, cardiovascular mortality, and the composite endpoint, respectively). These differences were significant in most cases. The estimated cutoff levels ranged between the 25th and 74th percentiles for the respective anthropometric parameters and endpoints. Supplemental Table 1 displays the corresponding cutoffs for the respective sex and age

TABLE 2. ROC analyses for prediction of endpoints by absolute values of anthropometric measures and age- and sex-specific percentiles of anthropometric measures

	Absolute values			Age- and sex-specific percentiles					
	AUC	95% CI	*P* value[a]	AUC	95% CI	*P* value[a]	Cutoff percentile[b]	Sens	Spec
All-cause mortality									
WHtR	0.648	0.63–0.67	(ref)	0.531	0.51–0.56	(ref)	74	33.6	73.8
WC	0.626	0.61–0.65	0.000	0.508	0.48–0.53	0.000	53	49.8	53.1
WHR	0.630	0.61–0.65	0.074	0.512	0.49–0.53	0.041	28	76.8	27.6
HC	0.571	0.55–0.59	0.000	0.506	0.48–0.53	0.004	30	71.9	29.8
BMI	0.573	0.55–0.60	0.000	0.528	0.50–0.55	0.685	25	52.1	55.1
Cardiovascular mortality									
WHtR	0.679	0.65–0.71	(ref)	0.562	0.52–0.60	(ref)	74	38.7	73.6
WC	0.651	0.62–0.68	0.001	0.530	0.49–0.57	0.000	51	56.4	51.9
WHR	0.655	0.62–0.69	0.186	0.537	0.50–0.58	0.180	48	59.1	47.8
HC	0.582	0.54–0.62	0.000	0.516	0.48–0.56	0.008	30	75.1	29.8
BMI	0.588	0.55–0.63	0.000	0.542	0.50–0.59	0.154	76	37.0	75.2
Composite endpoint									
WHtR	0.630	0.60–0.66	(ref)	0.547	0.52–0.58	(ref)	37	70.8	36.8
WC	0.622	0.59–0.65	0.153	0.535	0.50–0.57	0.019	58	47.7	58.4
WHR	0.616	0.59–0.65	0.317	0.535	0.50–0.57	0.370	25	82.5	24.3
HC	0.569	0.54–0.60	0.000	0.523	0.49–0.55	0.045	49	56.0	49.4
BMI	0.565	0.53–0.59	0.000	0.525	0.49–0.56	0.023	46	60.0	45.8

ref, Reference; Sens, sensitivity; Spec, specificity.

[a] *P* value for test of equality of AUC with reference WHtR.

[b] Cutoff estimated by age group- and sex-specific percentiles.

groups derived by these percentiles. For all anthropometric parameters, the cutoffs increased with age.

Discussion

Our study shows that measures of abdominal obesity including WHtR, WC, and WHR predict death, cardiovascular death, and cardiovascular events clearly better than BMI. In the ROC analysis, the AUCs of WHtR were significantly larger than the AUCs of the other anthropometric parameters. This suggests that WHtR is the best indicator of future cardiovascular risk and overall mortality among different measures of abdominal obesity. Although cardiovascular risk conditions at baseline accumulated among obese subjects, mediator analysis showed little or no effect modification by these baseline conditions. This indicates that incident cardiovascular events were not relevantly mediated by other baseline cardiovascular diseases and risk factors.

In light of the growing epidemic of obesity, it is increasingly important to identify patients that are at particularly high risk of obesity-related morbidity and mortality. To date, BMI is still used as a standard measure of obesity (2). In general practice, BMI is still used as the main criterion to prompt behavioral, medical, or surgical interventions against obesity.

Our data showed that increased BMI was related neither to more cardiovascular endpoints nor to higher all-cause mortality. Rather, BMI showed a U-shaped association with cardiovascular mortality and a negative association with the composite endpoint of fatal and nonfatal cardiovascular events.

Although this seems surprising, this is partially in line with other findings. A meta-analysis on mortality in patients with heart disease also demonstrated a protective effect of increased BMI on mortality (9), and large cohort studies indicated a U-shaped association of BMI with decreased mortality in overweight, compared with normal-weight subjects (5–8). However, in these studies, either overall or cardiovascular mortality was increased in subjects with very high BMI. In our study, the lower boundary of the 4th quartile for BMI ranged between 26 and 30 kg/m^2, depending on age and sex. Therefore, our study did not allow discriminating between higher degrees of obesity as assessed by BMI. This is probably the reason why we did not find increased mortality in subjects with the highest BMI in our study. The reason for the negative association of BMI with incident cardiovascular events is not clear. Again, we do not know whether this association would persist in persons with very high BMI.

Generally, additional adjustment of measures of abdominal obesity or of BMI for BMI or WHtR, respectively, had opposite effects on the association with all endpoints. This is surprising because BMI and WHtR were highly intercorrelated. BMI neither takes the distribution of fat into account nor distinguishes between the accumulation of lean or fat mass. In addition, BMI is less sensitive to changes in lifestyle patterns than measures of abdominal obesity because reduction of calorie intake and increased physical activity causes reduction of body fat paralleled by an increase in muscle mass. This results in marked changes in measures of abdominal obesity but no change or little change in BMI (32). It appears that these factors play a major role in cardiovascular risk. These results confirm the findings of other studies that show that high BMI is not associated with adverse outcomes after cardiac events (9, 33).

Our finding that WHtR was the best prospective indicator of cardiovascular risk confirms the findings of several cross-sectional studies that have shown that WHtR best indicates the presence of cardiovascular risk factors (13–15, 17, 18, 20). This is also in line with prospective studies (12, 21). However, these studies were based either on small sample sizes (12) or on self-reported measures and displayed only small differences between measures (21). Self-reporting of anthropometric measures is subject to systematic error and can be particularly biased by age, sex, weight, smoking status, and socioeconomic status (34, 35).

Two recent large prospective studies (4, 22) demonstrated the importance of abdominal obesity for risk of death but did not compare different measures of abdominal obesity. Moreover, Zhang *et al.* (22) also used self-reported measures of obesity.

Apart from BMI, suggestions for cutoffs have also been given for WC, WHR, and WHtR, although the database has been rather poor to date. The American Heart Association recommended 102 cm for men and 88 cm for women as cutoff levels for WC, and 0.95 for men and 0.88 for women as cutoff levels for WHR (36). More recently, a general cutoff of 0.5 has been suggested for WHtR (37). The estimated cutoff levels we found imply that it seems reasonable to use age-dependent cutoffs for risk assessment. Having found similar levels in the respective age groups for WHtR and BMI, our findings confirm that for WHtR and BMI probably, identical cutoffs can be used both in men and women.

Our study has several limitations. Although we studied more than 10,000 subjects, the number of endpoints analyzed was rather small. Due to size restriction, our study did not allow distinguishing effects of small subgroups, such as those with extreme obesity. Although our study gave a rough estimate of cutoff levels for cardiovascular risk, the sensitivities and specificities we found were, in part, rather low. Further studies are needed to confirm our results and to calculate precise cutoffs for different subgroups.

We included subjects from two different cohorts, a nationwide cohort in the primary care setting and a regional population-based sample, both in Germany. Although we have tried to minimize study bias by adjusting for study cohorts, we cannot rule out a remaining bias. Potential sources of bias include differences in populations, in the prevalence and reporting of diseases, in data quality, and in the number of persons lost to follow-up. On the other hand, the fact that we found similar effects in both cohorts and no heterogeneity between cohorts indicates that the results are independent of study cohorts.

The subjects studied here were mainly Caucasian, middle-European subjects. We do not know whether these results are generalizable to other ethnicities and races. We only assessed cardiovascular risks and overall mortality. Conclusions on other obesity-associated health risks, such as orthopedic or psychological complications or cancer prevalence, are not possible.

In conclusion, our findings show that BMI is not appropriate for prediction of mortality and cardiovascular risk. Therefore, it is not useful as an indicator of the main health complications associated with obesity. This strongly indicates that BMI alone should no longer be used as a universal measure of obesity in the decision making for risk stratification and weight-loss strategies.

Although WHtR, WC, and WHR predict these health risks, WHtR is the best predictor of cardiovascular risk. Moreover, a fixed cutoff point for WC irrespective of height might underestimate the relative amount of abdominal fat in short subjects and overestimate it in tall subjects (38), and WHR is more complicated to measure than WHtR. This makes WHtR an ideal candidate and a simple tool for assessing obesity-associated risk. A cutoff level of 0.5 for subjects aged up to 40 yr and of 0.6 for subjects aged 50 yr or older seems to give a reasonable assessment of future risk of death and cardiovascular events. For the age group between 40 and 50 yr, the cutoff levels lie somewhere between 0.5 and 0.6.

However, these are rather rough estimates and further prospective studies are needed to confirm our results, to establish more precise cutoff levels, and to test generalizability to other populations and other obesity-associated risks.

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Supplemental figure 1

Relative Risk for follow-up events in quartiles of anthropometric parameters by sex, adjusted for time of follow-up, age, sex (if applicable), cohort, educational status, professional status, marital status, smoking status, physical activity, kidney failure, cancer, liver disease, and BMI (for measures of abdominal obesity) or WHtR (for BMI).

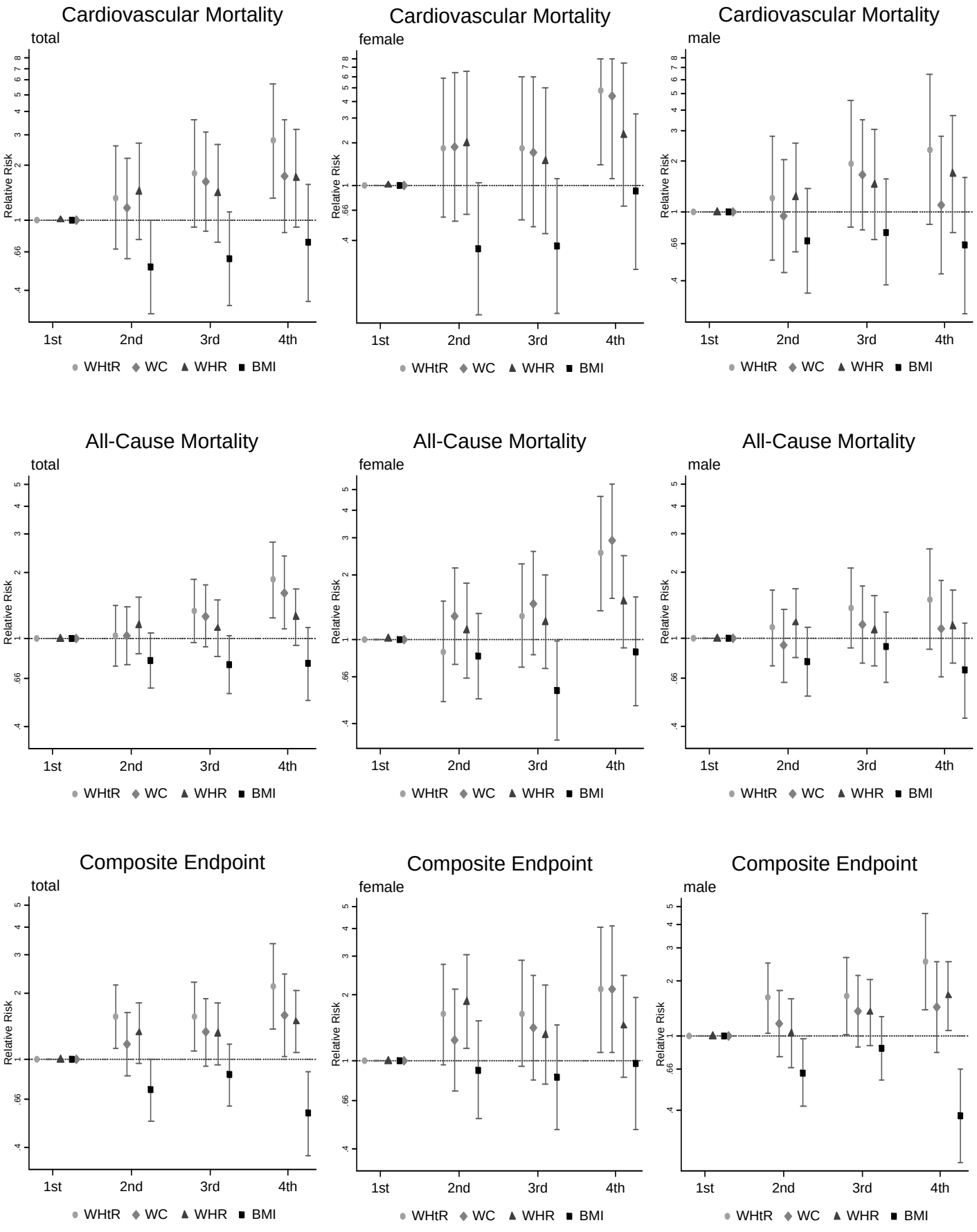
Supplemental figure 1

Relative Risk for Follow-up events in quartiles of anthropometric parameters by age group, adjusted for time of follow-up, age (if applicable), sex, cohort, educational status, professional status, marital status, smoking status, physical activity, kidney failure, cancer, liver disease, and BMI (for measures of abdominal obesity) or WHtR (for BMI). Please note that error bars have been truncated for age group up to 65 years and cardiovascular mortality.

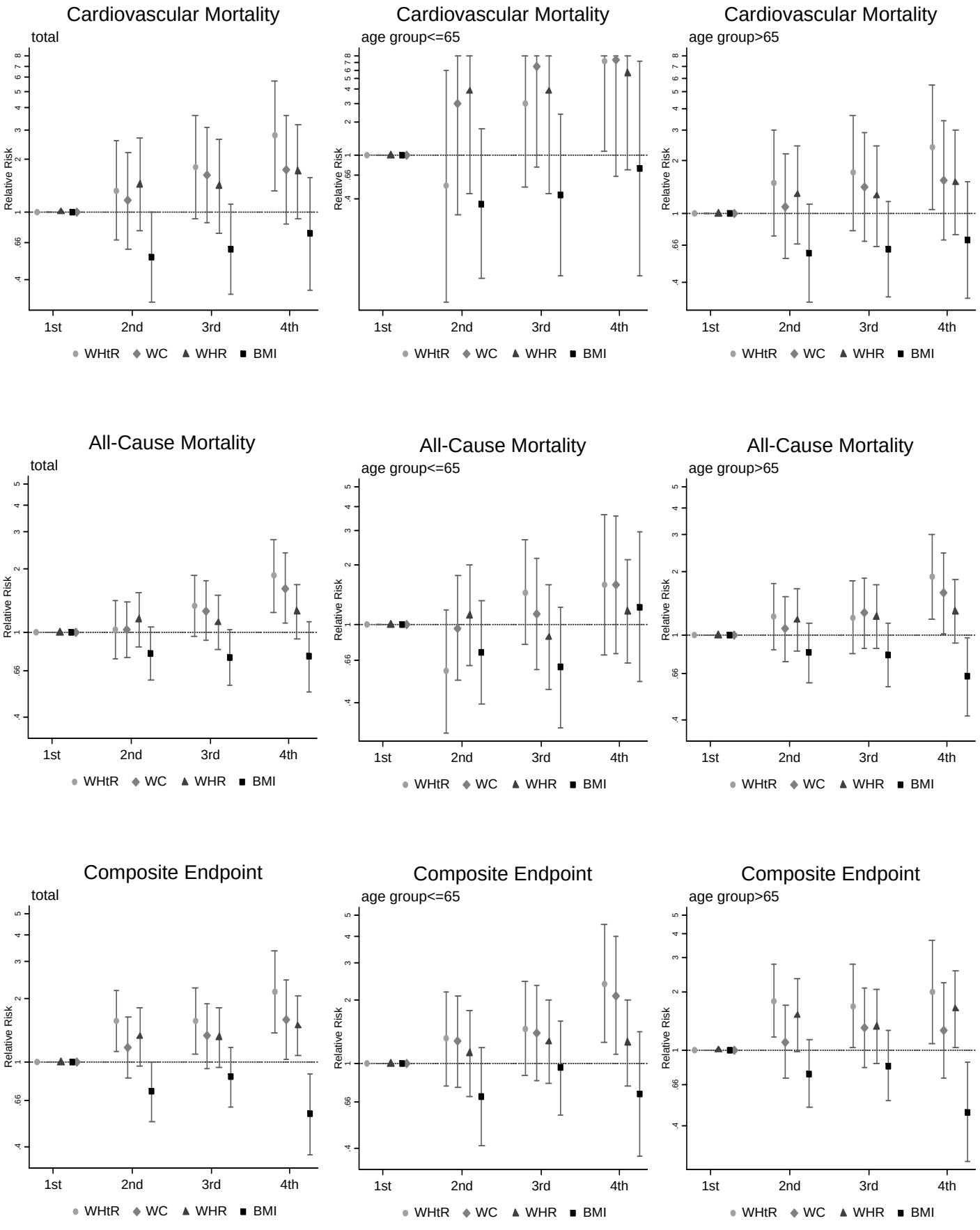
Supplemental figure 1

Relative Risk for follow-up events in quartiles of WHtR and BMI adjusted by MI) time of follow-up, (crude analyses); MII) time of follow-up, age, sex, and cohort; MIII) time of follow-up, age, sex, cohort, educational status, professional status, marital status, smoking status, physical activity, kidney failure, cancer, and liver disease; and MIV) all parameters + BMI (for measures of abdominal obesity) or WHtR (for BMI).

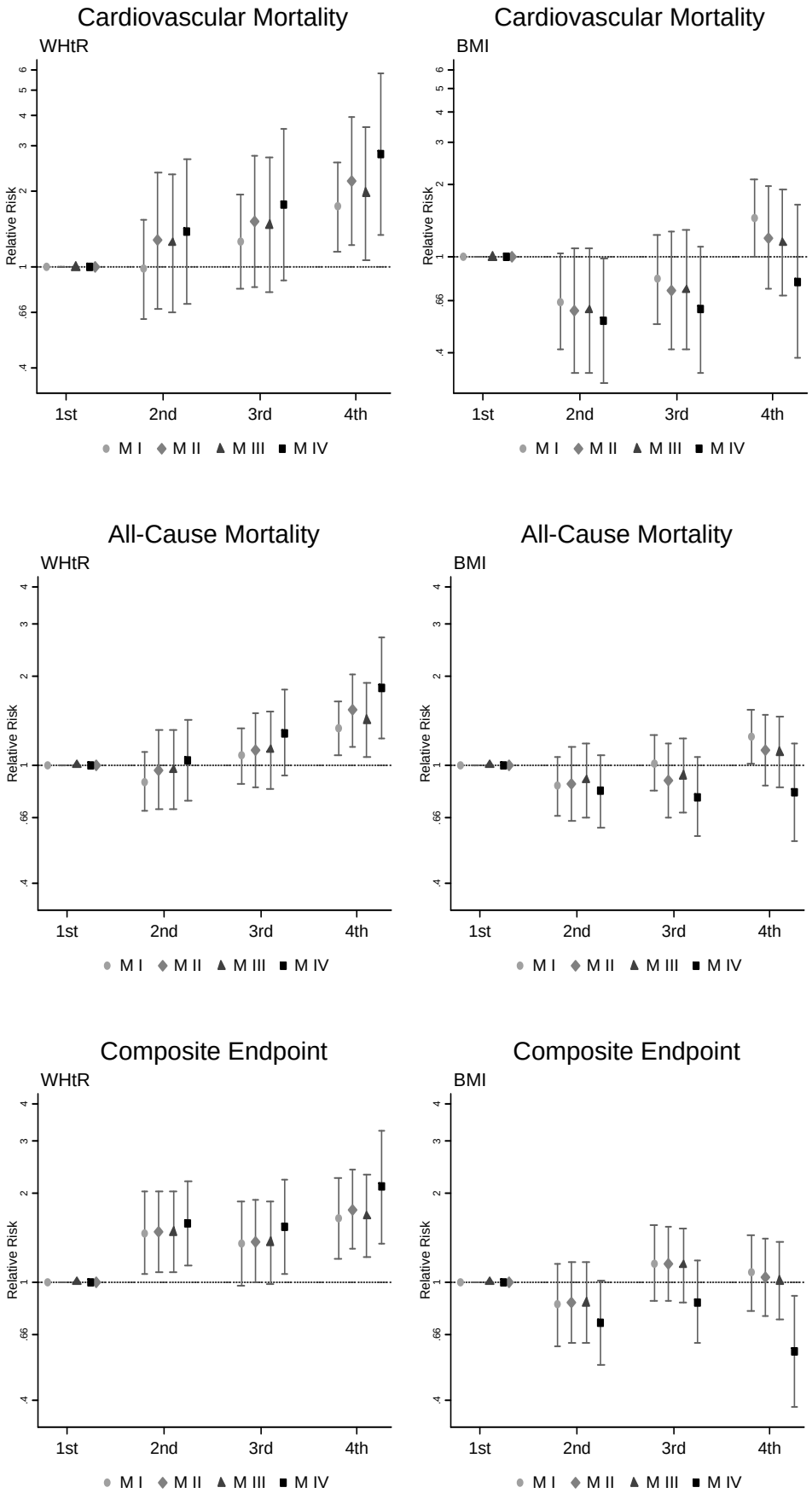
Supplemental figure 1



Supplemental figure 2



Supplemental figure 3



Supplemental table 1: Interquartile ranges of anthropometric parameters and estimated cutoffs

		women							men						
		1st Q	2nd Q	3rd Q	4th Q	cutoff ‡			1st Q	2nd Q	3rd Q	4th Q	cut-off ‡		
						all cause mortality	cardiovascular mortality	composite endpoint					all cause mortality	cardiovascular mortality	composite endpoint
WHtR	age 18-30	0.33 - 0.40	0.40 - 0.43	0.43 - 0.49	0.49 - 0.80	0.49	0.49	0.42	0.24 - 0.48	0.48 - 0.54	0.54 - 0.60	0.60 - 0.86	0.51	0.51	0.45
	age 31-40	0.37 - 0.43	0.43 - 0.47	0.47 - 0.51	0.51 - 0.70	0.52	0.52	0.45	0.36 - 0.53	0.53 - 0.57	0.57 - 0.61	0.61 - 0.86	0.55	0.55	0.50
	age 41-50	0.31 - 0.43	0.43 - 0.47	0.47 - 0.53	0.53 - 0.92	0.56	0.56	0.47	0.36 - 0.52	0.52 - 0.57	0.57 - 0.64	0.64 - 0.90	0.59	0.59	0.53
	age 51-60	0.38 - 0.48	0.48 - 0.52	0.52 - 0.56	0.56 - 0.83	0.60	0.60	0.51	0.34 - 0.55	0.55 - 0.59	0.59 - 0.63	0.63 - 0.90	0.61	0.61	0.55
	age 61-70	0.33 - 0.45	0.45 - 0.50	0.50 - 0.57	0.57 - 0.90	0.63	0.63	0.54	0.32 - 0.53	0.53 - 0.58	0.58 - 0.63	0.63 - 0.81	0.63	0.63	0.57
	age 70+	0.39 - 0.51	0.51 - 0.55	0.55 - 0.59	0.59 - 1.04	0.63	0.63	0.55	0.36 - 0.56	0.56 - 0.59	0.59 - 0.63	0.63 - 0.86	0.63	0.63	0.57
WC	age 18-30	54.5 - 67.0	67.1 - 72.5	72.8 - 82.4	82.5 - 127.0	73	73	79	40.0 - 79.0	79.2 - 87.5	87.6 - 99.0	99.1 - 144.0	85	84	86
	age 31-40	67.9 - 78.0	78.1 - 84.0	84.1 - 91.6	91.8 - 120.0	79	80	80	62.0 - 93.0	93.1 - 99.0	99.1 - 108.0	108.1 - 160.0	94	95	95
	age 41-50	52.0 - 71.5	71.8 - 78.0	78.1 - 88.0	88.2 - 145.0	84	84	82	57.0 - 84.3	84.5 - 93.0	93.1 - 103.0	103.2 - 146.0	98	98	100
	age 51-60	69.2 - 86.2	86.3 - 93.0	93.1 - 100.0	100.1 - 150.0	89	88	90	56.0 - 95.0	95.1 - 102.0	102.1 - 109.8	110.0 - 160.0	101	99	102
	age 61-70	50.5 - 75.0	75.1 - 83.0	83.2 - 93.6	94.0 - 150.0	94	96	96	51.0 - 84.0	84.2 - 92.0	92.2 - 100.0	100.5 - 128.0	102	102	102
	age 70+	62.0 - 91.2	91.3 - 97.3	97.5 - 105.1	105.2 - 170.0	93	95	95	61.0 - 95.0	95.1 - 101.0	101.1 - 109.0	109.2 - 148.0	102	102	103
WHR	age 18-30	0.62 - 0.73	0.73 - 0.77	0.77 - 0.81	0.81 - 1.36	0.74	0.76	0.73	0.37 - 0.79	0.79 - 0.84	0.84 - 0.88	0.88 - 1.73	0.83	0.86	0.82
	age 31-40	0.73 - 0.82	0.82 - 0.86	0.86 - 0.91	0.91 - 1.52	0.76	0.80	0.76	0.42 - 0.91	0.91 - 0.96	0.96 - 1.00	1.00 - 1.83	0.88	0.92	0.88
	age 41-50	0.58 - 0.76	0.76 - 0.80	0.80 - 0.85	0.85 - 1.41	0.78	0.82	0.78	0.62 - 0.81	0.81 - 0.86	0.86 - 0.90	0.90 - 1.70	0.92	0.95	0.91
	age 51-60	0.71 - 0.88	0.88 - 0.92	0.92 - 0.95	0.95 - 1.24	0.80	0.83	0.79	0.55 - 0.92	0.92 - 0.96	0.96 - 1.00	1.00 - 1.24	0.92	0.95	0.91
	age 61-70	0.43 - 0.78	0.78 - 0.82	0.82 - 0.87	0.87 - 1.80	0.82	0.85	0.81	0.48 - 0.82	0.82 - 0.85	0.85 - 0.90	0.90 - 1.65	0.93	0.96	0.92
	age 70+	0.66 - 0.91	0.91 - 0.95	0.95 - 0.99	0.99 - 1.95	0.82	0.85	0.82	0.49 - 0.92	0.92 - 0.96	0.96 - 1.00	1.00 - 1.34	0.92	0.95	0.92
HC	age 18-30	61.0 - 89.7	89.8 - 94.6	94.8 - 102.0	102.1 - 146.0	90	90	95	60.0 - 97.0	97.1 - 104.0	104.1 - 113.0	113.1 - 176.0	95	95	98
	age 31-40	50.0 - 94.0	94.1 - 98.5	98.6 - 103.0	103.2 - 129.0	93	93	98	58.0 - 99.0	99.1 - 104.0	104.1 - 110.0	110.4 - 172.0	97	97	98
	age 41-50	52.0 - 91.3	91.4 - 97.2	97.3 - 106.0	106.1 - 143.0	95	95	100	57.4 - 100.0	100.1 - 108.0	108.1 - 116.0	116.1 - 155.0	98	97	103
	age 51-60	70.0 - 96.2	96.4 - 101.5	101.6 - 107.0	107.4 - 146.5	98	98	104	81.4 - 100.2	100.3 - 105.5	105.6 - 111.5	111.8 - 165.0	98	100	103
	age 61-70	58.0 - 93.0	93.2 - 100.0	100.2 - 109.0	109.1 - 188.0	101	101	107	55.0 - 99.0	99.1 - 106.0	106.4 - 114.0	114.5 - 170.0	102	102	103
	age 70+	59.0 - 98.0	98.1 - 103.0	103.2 - 108.8	109.0 - 165.0	101	101	106	70.0 - 100.0	100.1 - 105.5	105.8 - 112.0	112.4 - 196.0	101	101	105
BMI	age 18-30	16.0 - 20.5	20.5 - 22.4	22.4 - 25.7	25.9 - 42.3	22.9	26.0	22.0	17.0 - 23.8	23.8 - 26.6	26.6 - 30.7	30.7 - 61.3	25.0	27.3	24.3
	age 31-40	17.9 - 22.5	22.5 - 24.5	24.6 - 27.2	27.2 - 39.6	24.2	27.3	23.3	17.0 - 25.3	25.3 - 27.6	27.6 - 30.6	30.6 - 56.8	26.8	28.9	25.9
	age 41-50	15.9 - 21.6	21.6 - 23.6	23.6 - 27.1	27.2 - 44.3	25.7	28.9	24.4	15.8 - 25.0	25.0 - 28.0	28.0 - 31.6	31.6 - 46.7	28.0	30.1	26.9
	age 51-60	18.3 - 24.2	24.3 - 26.2	26.3 - 28.9	28.9 - 47.9	27.4	30.8	26.2	17.5 - 25.6	25.6 - 28.1	28.1 - 30.6	30.6 - 52.3	28.1	30.6	27.2
	age 61-70	14.8 - 22.3	22.3 - 25.0	25.0 - 28.8	28.8 - 59.1	28.6	31.6	27.5	15.8 - 24.2	24.2 - 27.0	27.1 - 30.2	30.3 - 49.1	28.6	30.7	27.6
	age 70+	18.2 - 24.8	24.8 - 27.4	27.4 - 30.1	30.1 - 61.4	27.7	30.4	26.5	17.3 - 25.2	25.2 - 27.2	27.2 - 29.7	29.7 - 46.0	27.7	29.7	26.8

Q = quartile; WHtR = weight-to-height ratio; WC = waist circumference; WHR = waist-to-hip ratio; HC = hip cirumference; BMI = body mass index

‡ cutoff estimated by ROC analysis from age group- and sex-specific percentiles

Supplemental table 2: Distribution of sex, age, and potential confounders/mediators in quartiles of anthropometric parameters

	WHtR			WC			WHR			HC			BMI		
	1st Q %	4th Q %	p-value	1st Q %	4th Q %	p-value	1st Q %	4th Q %	p-value	1st Q %	4th Q %	p-value	1st Q %	4th Q %	p-value
age, mean(Sd)	54.4 (15.9)	55.0 (15.3)	0.172	54.6 (16.0)	54.9 (15.3)	0.554	54.4 (15.9)	55.0 (15.5)	0.229	54.7 (15.8)	54.8 (15.4)	0.740	54.6 (16.1)	54.8 (15.2)	0.795
female	56.4	55.5	0.504	56.3	55.7	0.658	56.4	56.2	0.870	55.7	56.3	0.658	56.4	55.9	0.726
educational status															
<10 school years	35.8	48.6		37.8	46.8		38.5	45.0		38.4	46.5		36.0	47.8	
10 school years	32.1	30.2	0.000	32.7	30.5	0.000	31.9	30.3	0.002	32.3	30.9	0.000	31.2	32.3	0.000
>10 school years	30.4	18.7	0.000	27.8	20.4	0.000	28.1	21.8	0.000	27.1	21.0	0.000	30.8	17.9	0.000
family status															
married	66.2	66.7		66.4	67.2		66.7	67.5		67.0	67.9		65.3	67.7	
single	14.0	13.5	0.598	13.3	13.8	0.783	14.1	12.6	0.129	12.7	14.0	0.340	14.7	13.4	0.115
divorced/ widowed	19.2	18.5	0.554	19.7	17.9	0.140	18.6	18.6	0.883	19.5	17.4	0.081	19.1	17.8	0.130
professional status															
employed	45.8	35.7		45.1	36.6		44.1	39.9		45.6	37.1		44.7	36.7	
unemployed/ homemaker	13.3	18.8	0.000	13.4	18.6	0.000	14.0	17.3	0.000	13.8	18.4	0.000	14.7	18.3	0.000
retired	39.8	43.9	0.000	40.3	43.1	0.000	40.7	41.2	0.062	39.3	43.1	0.000	39.4	43.4	0.000
smoking status															
smoker	47.3	44.2		47.2	45.2		49.2	44.4		46.1	46.8		47.1	44.8	
ex smoker	25.6	31.2	0.000	25.7	31.7	0.000	25.9	28.5	0.003	24.4	30.9	0.001	23.2	32.7	0.000
non smoker	25.5	22.7	0.487	25.6	21.2	0.039	23.6	24.8	0.024	27.6	20.6	0.000	27.7	20.9	0.001
physical inactivity	45.0	50.1	0.000	46.9	48.1	0.015	48.1	44.6	0.265	44.5	49.1	0.000	42.5	53.5	0.000
GFR; mean(Sd)	66.9 (17.1)	65.3 (17.6)	0.019	67.5 (17.2)	64.8 (17.4)	0.087	67.5 (16.7)	64.0 (17.3)	0.183	65.9 (17.6)	65.3 (16.8)	0.644	65.5 (17.3)	66.8 (17.4)	0.502
kidney failure (GFR<30)	0.5	1.0	0.001	0.6	1.0	0.000	0.6	0.9	0.000	0.7	0.8	0.189	0.6	0.7	0.005
cancer	2.6	2.5	0.819	2.6	2.5	0.918	2.5	3.2	0.112	2.6	2.5	0.887	2.8	2.3	0.245
liver disease	2.0	5.6	0.000	2.0	6.0	0.000	2.0	5.8	0.000	2.8	5.2	0.000	3.0	4.3	0.012
diabetes mellitus	7.5	23.5	0.000	8.1	23.9	0.000	9.9	20.5	0.000	8.9	22.6	0.000	8.3	22.4	0.000
CAD	8.1	11.8	0.000	8.3	11.7	0.000	8.9	11.3	0.005	8.9	11.4	0.003	9.0	10.4	0.099
stroke	1.6	2.7	0.006	2.0	2.7	0.080	2.1	2.2	0.627	1.9	2.3	0.282	1.7	2.3	0.120
hypertension	40.9	68.8	0.000	42.0	69.2	0.000	44.7	63.4	0.000	45.1	67.8	0.000	41.8	68.8	0.000
dyslipidemia	37.9	54.8	0.000	38.7	54.2	0.000	40.5	52.6	0.000	42.3	52.5	0.000	39.6	54.2	0.000
metabolic syndrome[1]	25.4	64.2	0.000	26.2	64.3	0.000	31.0	56.5	0.000	29.9	61.7	0.000	25.4	63.2	0.000

Q = quartile

[1] presence of two or more of the following risk factors: triglycerides ≥150 mg/dl or intake of fibrates or nicotinic acid, blood pressure ≥130/85 mmHg or hypertension as defined above, HDL cholesterol <40 mg/dl in men and <50 mg/l in women or intake of f

Supplemental table 3: Relative risks of endpoints for a 1 standard deviation (SD) increase of anthropometric parameters after additional adjustment for potential mediators.

	Cardiovascular Mortality				All-Cause Mortality				Composite Endpoint‡			
	WHtR		BMI		WHtR		BMI		WHtR		BMI	
	RR†	95%CI	RR†	95%CI	RR†	95%CI	RR†	95%CI	RR†	95%CI	RR†	95%CI
M1	**1.18***	1.04 - 1.33	1.12	0.98 - 1.28	**1.09***	1.01 - 1.17	1.08	1.00 - 1.16	**1.14***	1.04 - 1.25	1.07	0.97 - 1.18
M2	**1.23***	1.03 - 1.47	1.09	0.89 - 1.33	**1.16***	1.05 - 1.28	1.05	0.95 - 1.17	**1.18***	1.07 - 1.29	1.06	0.96 - 1.17
M3	1.16	0.97 - 1.40	1.04	0.85 - 1.29	**1.12***	1.01 - 1.24	1.04	0.94 - 1.15	**1.16***	1.05 - 1.27	1.05	0.95 - 1.16
M4	1.30	0.94 - 1.78	0.80	0.57 - 1.13	**1.24***	1.06 - 1.46	0.86	0.73 - 1.01	**1.32***	1.12 - 1.55	**0.81***	0.68 - 0.96
M3 + systolic blood pressure	**1.20***	1.00 - 1.44	1.08	0.88 - 1.32	**1.13***	1.02 - 1.25	1.05	0.94 - 1.16	**1.14***	1.03 - 1.25	1.03	0.93 - 1.15
M3 + diastolic blood pressure	1.16	0.96 - 1.40	1.04	0.84 - 1.29	1.10	1.00 - 1.22	1.02	0.92 - 1.14	**1.15***	1.04 - 1.26	1.04	0.94 - 1.15
M3 + fasting plasma glucose	1.09	0.90 - 1.31	0.98	0.78 - 1.22	1.08	0.98 - 1.20	1.00	0.90 - 1.12	**1.11***	1.01 - 1.23	1.00	0.90 - 1.12
M3 + triglyceride	1.14	0.95 - 1.37	1.03	0.83 - 1.27	**1.12***	1.01 - 1.23	1.03	0.93 - 1.15	**1.15***	1.04 - 1.27	1.04	0.94 - 1.15
M3 + LDL cholesterol	1.16	0.97 - 1.40	1.04	0.85 - 1.28	**1.12***	1.02 - 1.24	1.04	0.94 - 1.15	**1.15***	1.05 - 1.27	1.05	0.95 - 1.17
M3 + HDL cholesterol	1.15	0.95 - 1.38	1.03	0.83 - 1.27	**1.11***	1.01 - 1.23	1.03	0.92 - 1.14	**1.15***	1.04 - 1.27	1.04	0.93 - 1.15
M3 + total cholesterol	1.16	0.97 - 1.40	1.05	0.85 - 1.29	**1.12***	1.01 - 1.24	1.04	0.93 - 1.15	**1.15***	1.05 - 1.27	1.05	0.95 - 1.17
M3 + diabetes mellitus	1.12	0.93 - 1.35	1.00	0.81 - 1.24	1.10	0.99 - 1.21	1.01	0.91 - 1.13	**1.13***	1.02 - 1.24	1.02	0.92 - 1.14
M3 + CHD	1.19	0.98 - 1.43	1.06	0.86 - 1.31	**1.12***	1.01 - 1.24	1.04	0.94 - 1.16	**1.16***	1.05 - 1.28	1.05	0.95 - 1.16
M3 + stroke	1.16	0.96 - 1.40	1.04	0.85 - 1.28	**1.12***	1.01 - 1.24	1.04	0.93 - 1.15	**1.16***	1.05 - 1.27	1.05	0.95 - 1.16
M3 + dyslipidemia	1.16	0.97 - 1.40	1.05	0.85 - 1.29	**1.12***	1.01 - 1.24	1.04	0.93 - 1.15	**1.15***	1.04 - 1.26	1.04	0.94 - 1.16
M3 + metabolic syndrome	1.14	0.94 - 1.37	1.01	0.81 - 1.26	1.10	0.99 - 1.22	1.02	0.91 - 1.13	**1.13***	1.02 - 1.25	1.02	0.92 - 1.14
M3 + metabolic syndrome, CHD, stroke	1.16	0.96 - 1.41	1.03	0.82 - 1.29	1.11	0.99 - 1.23	1.02	0.91 - 1.14	**1.14***	1.03 - 1.26	1.02	0.92 - 1.14
M4 + metabolic syndrome	1.28	0.93 - 1.75	0.79	0.55 - 1.11	**1.23***	1.05 - 1.45	0.85	0.72 - 1.00	**1.30***	1.10 - 1.53	**0.80***	0.67 - 0.95
M4 + metabolic syndrome, CHD, stroke	1.32	0.96 - 1.81	0.79	0.55 - 1.12	**1.24***	1.05 - 1.46	0.85	0.72 - 1.00	**1.32***	1.12 - 1.55	**0.79***	0.67 - 0.94
M3 + FPG, HDL, LDL, BP	1.11	0.92 - 1.33	1.00	0.80 - 1.24	1.09	0.99 - 1.21	1.01	0.90 - 1.12	1.09	0.98 - 1.21	0.98	0.88 - 1.10
M3 + FPG, HDL, LDL, BP, CHD, stroke	1.13	0.94 - 1.37	1.01	0.81 - 1.27	1.10	0.99 - 1.22	1.01	0.91 - 1.13	1.10	0.99 - 1.22	0.99	0.88 - 1.11
M4 + FPG, HDL, LDL, BP	1.26	0.92 - 1.73	0.79	0.56 - 1.10	**1.24***	1.05 - 1.45	**0.84***	0.72 - 0.99	**1.28***	1.09 - 1.51	**0.78***	0.66 - 0.93
M4 + FPG, HDL, LDL, BP, CHD, stroke	1.30	0.95 - 1.79	0.79	0.56 - 1.11	**1.24***	1.06 - 1.46	**0.84***	0.72 - 1.00	**1.30***	1.10 - 1.53	**0.78***	0.66 - 0.93

* 1Sd WHtR: 0.09 (female), 0.07 (male); 1 Sd BMI: 5.2 (female), 4.1 (male)
† RR = relative risk for 1 Sd increase of antropometric parameter for the respective outcome; estimated by a poisson regression with robust error variances
‡Composite Endpoint: cardivascular mortality or incident myocardial infarction or incident stroke in patients
M1: unadjusted
M2: adjusted for age, gender, follow-up interval and sample
M3: adjusted for age, gender, follow-up interval, sample, educational status, profesional status, marital status, smoking status, physical activity, GFR, cancer and liver disease
M4: adjusted for age, gender, follow-up interval, sample, educational status, profesional status, marital status, smoking status, physical activity, GFR, cancer, liver disease and BMI (WHtR in case of BMI)