

ORIGINAL ARTICLE

Body fat percentage, body mass index and waist-to-hip ratio as predictors of mortality and cardiovascular disease

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ABSTRACT

Objective To study the utility of body fat percentage in predicting health outcomes when other obesity indices are considered.

Methods We conducted a prospective cohort study to evaluate the independent utility of body fat percentage and other obesity indices in predicting mortality and cardiovascular disease (CVD).

Results We prospectively followed 15 062 European Prospective Investigation into Cancer (EPIC)-Norfolk participants who attended a health examination during 1997–2000 for all-cause mortality and incidence of CVD up to end of December 2011 and end of March 2009, respectively. During the follow-up, 2420 died and 4665 had incident CVD. After exclusion of prior stroke, myocardial infarction and cancer and adjusting for potential confounders, body mass index (BMI) and waist-to-hip ratio (WHR), the HR of mortality for men were 0.86 (0.68 to 1.09), 0.81 (0.61 to 1.07) and 0.76 (0.55 to 1.05) and for women were 0.91 (0.70 to 1.17), 0.75 (0.55 to 1.02) and 0.87 (0.61 to 1.23) for second, third and fourth quartile compared with the first (bottom) quartile of body fat percentage. The respective HRs for incident CVD were 0.99 (0.83 to 1.19), 0.85 (0.69 to 1.04) and 0.81 (0.64 to 1.03) for men and 0.98 (0.82 to 1.17), 0.89 (0.73 to 1.10) and 1.02 (0.81 to 1.29) for women. In contrast, higher BMI and WHR were associated with an increased risk of both outcomes and WHR appeared to have the best predictive value among three indices.

Conclusions Once BMI and WHR are taken into account, fat percentage does not add to prediction of mortality or CVD in middle-aged and older-aged adults.

INTRODUCTION

Obesity is linked to poor health outcomes; it is one of the major modifiable risk factors for cardiovascular disease (CVD), which is the leading cause of mortality and morbidity worldwide.¹ Obesity is usually defined using body mass index (BMI >30 kg/m² as obese),¹ but BMI does not differentiate between fat mass and fat free mass or represent the pattern of fat distribution.

While there is evidence to support the relationships between truncal obesity and visceral fat in predicting mortality and CVD,^{2,3} there is a paucity of evidence about the value of body fat percentage when other obesity indices are also considered. Body fat percentage measured using impedance is increasingly advocated as a better measure of

obesity, but there are few data as to whether body fat percentage may predict mortality or CVD when either measured on its own or after taking into account other indices of obesity such as BMI or waist-to-hip ratio (WHR).

Several studies have evaluated the prognostic value of body fat percentage and found that higher body fat percentage is associated with better survival.^{4–7} However, these studies have been conducted in specific cohort such as patients with heart failure⁴ and coronary heart disease (CHD)^{5–7} and not in a general population.

In this study, we examined the relationships between BMI, WHR and body fat percentage and all-cause mortality and incidence of CVD in a general population of middle-aged and older-aged men and women.

METHODS

Participants

Participants were from the European Prospective Investigation into Cancer (EPIC)-Norfolk prospective population study, which recruited men and women aged between 40 and 79 years from general practice age-sex registers at the study baseline during 1993–1997 in Norfolk, UK. The detailed recruitment method and study protocol of EPIC-Norfolk have been described previously.⁸

Briefly, all eligible community dwelling adults from 35 participating general practices were invited to participate. A total of 25 639 participants (99.6% White British) attended a baseline health examination. They provided written consent to participate in the study, and the Norwich Local Research Ethics Committee approved the study. Three years after the first health check, all participants were invited back for a second health check (1997–2000) in which measurements performed at the baseline health check were repeated with additional inclusion of percentage body fat using impedance. The participants completed a second follow-up health questionnaire.

Measurements

Trained nurses examined individuals at the second clinic visit. In addition to the basic anthropometric measures used in the first health examination, resistance was assessed by using the TBF-531 Body Fat Monitor Scale (Tokyo, Japan), a validated impedance technique. Impedance measurements were used to calculate the fat mass using published



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equations,⁹ and the body fat percentage was the fat mass expressed as a percentage of the body weight.

The description of data collection methods for other participant variables including weight, BMI, WHR, serum total cholesterol, education status, occupational social class, physical activity, smoking status, alcohol consumption and prevalent illness is described in the online supplementary data.

Case ascertainment

All participants were flagged for death at the Office of National Statistics. Participants were also linked to National Health Service (NHS) hospital information system so that admission anywhere in the UK was notified to EPIC-Norfolk. They were also linked to ENCORE (East Norfolk Commission Record) for admission episodes. Mortality and incident CVD were identified from the death certificates (Office of National Statistics) or hospital discharge code International Classification of Diseases (ICD) 9, 401–448 or ICD 10, I10–I79 for CVD incidence. These ascertainment methods of EPIC-Norfolk have been previously validated using hospital records for incident stroke cases.¹⁰

The follow-up time started at baseline for this study (date of second health check) and ended at the censor date defined as date of the event (date of death or incident CVD) or end of March 2009 for CVD events and end of December 2011 for mortality outcome. Incident CVD was defined as ischaemic heart disease (myocardial infarction, coronary artery disease) and stroke.

Statistical analysis

Statistical analyses were carried out using STATA V10.0 (Texas, USA). The outcomes of interest were all-cause mortality and the incident cardiovascular event (CVD). The predictor variables were different obesity measures, BMI, WHR and body fat percentage. We performed Cox-proportional hazards models to determine the associations between quartiles of obesity indices and the subsequent risk of all-cause mortality and incident CVD using the bottom quartile as the reference category; for meaningful comparison, the HRs were presented by quartiles of these indices rather than change in one unit. Sex-specific analyses were conducted using sex-specific quartile cut-off points for individual indices. Participants with missing data were excluded from analyses.

Multivariate adjustments were made to examine how far the association between these obesity indices and the risk of mortality and CVD might be explained by other known lifestyle, socioeconomic and cardiovascular risk factors. Stepwise adjustments were constructed to compare directly these three indicators of obesity. We adjusted for age in model A, age, smoking status, alcohol use, physical activity, social class and education level in model B, additionally adjusted for blood pressure, cholesterol level, diabetes, stroke, myocardial infarction and cancer in model C, additionally adjusting all obesity indices model D and model E was constructed as per model D after exclusion of prevalent stroke, myocardial infarction and cancer at time of second health check. As blood pressure, cholesterol levels are intermediate risk factors on the pathway from body fat to the mortality and CV outcomes, we constructed model F by removing these two parameters from model E. Finally, as waist circumference used in isolation is an index of total adiposity,¹¹ we repeated the model E for both outcomes using waist circumference rather than WHR in the model (model G) for fat % and BMI analyses.

We further examined the combined effect of these indices (BMI and body fat %, WHR and body fat %, and WHR and BMI) by constructing fully adjusted Cox-proportional hazard

models (as in model E) using tertiles values. Participants who were in tertiles 1 for both indices examined were entered into the model as the reference category for both outcomes.

Sensitivity analysis

We assessed for interactions between smoking status and measures of adiposity as well as interactions between age and measures of adiposity. We also conducted additional sensitivity analysis considering high and low body fat percentage (men <75th centile vs >75th centile and women <65th centile vs >65th centile).

RESULTS

Of 15 786 EPIC-Norfolk participants who attended the second health check, 15 545 had their body fat percentage measured. Of them, 15 062 (6505 men and 8557 women) were eligible to be included in the study, after excluding participants with any missing values for BMI and WHR measured at the second health check. The mean follow-up was 11.7 years (total person-years=176 350 years) for all-cause mortality and 8.2 years (total person-years=123 746 years) for incident CVD. During the follow-up, there were a total of 2420 people who died and 5665 had incident CVD.

Table 1 shows the sex-specific sample characteristics and crude rates of outcomes over the respective follow-up periods. Both BMI and WHR values were significantly higher in men, but women had significantly higher percentage of body fat. Outcomes evaluated were also significantly higher for men compared with women (death 21% vs 13%, CVD 37% vs 27%).

Tables 2 and 3 show the adjusted Cox-proportional HRs and corresponding 95% CI for the risk of death and CVD during study follow-up by sex-specific quartiles of BMI, WHR and body fat percentage, respectively. Quartile 1 represents the lowest (bottom), and the quartile 4 represents the highest (top) quartiles.

There was no consistent relationship between body fat percentage and both mortality and CVD. A somewhat U-shaped relationship was observed between body fat percentage and mortality in women for the same level of adjustment. Among women, higher WHR was associated with the highest HRs for both outcomes. Similarly for men, higher WHR was associated with the highest HRs for mortality but higher BMI was associated with a higher HR for risk of CVD.

The sensitivity analyses after excluding those with prevalent myocardial infarction (MI), stroke and cancer at the time of second health check (model E) did not alter the results materially for WHR, and body fat percentage. Substituting waist circumference in place of WHR in the model (model G) did not alter the results. However, removing intermediate risk factors (blood pressure and cholesterol) from the covariates (model F) did show a significant reduction in the risk of mortality in men with higher total body fat percentage.

The HRs for mortality and cardiovascular events based on the tertiles of BMI, WHR and body fat percentage are shown in the appendix (see online supplementary figures S1–S4).

Further analysis considering interaction between smoking status and measures of adiposity did not show any significant interaction except for male ex-smoker and WHR. Stratified analysis for men by smoking status examining quartiles of WHR and outcome in fully adjusted model showed significant increased risk of mortality in male ex-smokers with highest WHR quartiles compared with the bottom quartile. Further analysis considering interactions of age category (≥ 65 and <65 years) and measures of adiposity, the significant interactions

Table 1 Sample characteristics 15 062 men and women of EPIC-Norfolk at the study baseline (1997–2000) and the study outcomes (mortality and incident CVD) at follow-up

	Men N=6505	Women N=8557	p Value
Mean age* (years)	62.7 (9.1)	61.4 (9.0)	<0.0001
Body fat (%)	23.5 (6.1)	39.8 (9.1)	<0.0001
BMI (kg/m ²)	26.9 (3.3)	26.5 (4.3)	<0.0001
WHR	0.93 (0.06)	0.79 (0.06)	<0.0001
Smoking			<0.0001
Current	620 (10)	793 (9)	
Ex-smoker	3485 (54)	2663 (31)	
Never smoked	2354 (36)	5028 (59)	
Alcohol consumption (units/week)	10.0 (12)	5.0 (6)	<0.0001
Physical activity			<0.0001
Inactive	1762 (27.1)	2253 (26.3)	
Moderately inactive	1628 (25.0)	2786 (32.6)	
Moderately active	1626 (25.0)	2057 (24.0)	
Active	1489 (22.9)	1461 (17.1)	
Social class			<0.0001
I	528 (8)	579 (7)	
II	2640 (41)	3133 (39)	
III non-manual	805 (13)	1663 (20)	
III manual	1479 (23)	1689 (20)	
IV	801 (13)	1038 (12)	
V	152 (2)	294 (4)	
Missing	100 (2)	161 (2)	
Education level			<0.0001
No qualification	1769 (27)	3209 (38)	
O-level	579 (9)	1055 (12)	
A-level	3064 (47)	3210 (38)	
Degree or higher	1091 (17)	1078 (13)	
Mean systolic BP (mm Hg)	136.5 (17.6) N=6493	133.4 (18.4) N=8541	<0.0001
Mean cholesterol (mmol/L)	5.9 (1.1) N=6181	6.2 (1.2) N=7988	<0.0001
Diabetes	262 (4.0)	197 (2.3)	<0.0001
Prevalent stroke	192 (3.0)	108 (1.3)	<0.0001
Prevalent MI	254 (3.9)	120 (1.4)	<0.0001
Prevalent cancer	333 (5.1)	726 (8.5)	<0.0001
Outcome			
Death	1354 (21)	1066 (13)	<0.0001
Incident CVD	2383 (37)	2282 (27)	<0.0001

Values presented are mean (SD) for continuous and number (%) for categorical data.

*Age at the time of the second health check.

BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer; WHR, waist-to-hip ratio.

were observed in men for both outcomes and only significant interactions for risk of CVD in women. Sensitivity analyses stratified by sex-specific high and low body fat percentage showed no significant differences for both sexes for both outcomes (see online supplementary table S1).

DISCUSSION

We found no evidence that higher fat percentage as measured using body impedance techniques in middle and older age is associated with increased risk of mortality and CVD. Though not significant, if anything, the apparent trend was towards an inverse relationship particularly for mortality and CVD for men and a U-shaped relationship for women. In contrast, WHR was strongly and independently related to mortality and CVD

incidence in both men and women even after adjusting for life-style behaviours, social class, education, diabetes, systolic blood pressure, cholesterol and other obesity indices, BMI and body fat percentage. BMI also appeared to predict incidence of CVD in model independently of both WHR and body fat percentage though less consistently than WHR.

Traditionally, BMI has been widely used in health assessment as a proxy measure of adiposity in predicting cardiovascular and metabolic disease risk. There are clear advantages of using BMI; it is convenient to measure and the relationship with CVD is well established in many studies worldwide.^{12–15} In addition, the link between obesity and adverse outcomes is not without controversy as there is a well-known obesity paradox where there is better survival and fewer cardiovascular events in patients with chronic disease with elevated BMI compared with non-obese controls.¹⁶ Since BMI encompasses both fat and lean mass including muscle and skeletal mass, fat percent has been increasingly suggested to be preferred as an indicator of body fat. However, there are a few studies that have been able to compare directly fat percent measures and other adiposity measures in the same individuals for prediction of future health outcomes. Studies that examined the body fat percentage to date mainly focused on the diagnostic value of body fat distribution and body fat,¹⁷ determining the healthy body fat percentage using BMI as gold standard,¹⁷ developing equations to predict percentage body fat,¹⁸ and differences in the relationship between body fat percentage and BMI in different ethnic groups.^{19–20}

Moreover, there are only a few studies that examined the relationship of body fat percentage on specific health outcomes. Davison *et al* showed that women in the highest quintile of the percentage body fat (based on waist circumference, triceps skin-fold thickness and sex) and with BMI ≥ 30 kg/m² were two times more likely to report functional limitations than women in the comparison group with similar findings in men using NHANES III data.²¹ Hara *et al* reported an interesting finding that there appeared to be difference in the effect of body fat (as measured by DEXA) between leg and trunk; they found that while trunk fat has a pro-atherosclerotic effect, leg fat has a negative correlation with coronary atherosclerosis.²² A Swiss study showed that obesity defined by body fat percentage (assessed using bioelectrical impedance analysis) is more related with 10-year risk of fatal CVD compared with other markers of obesity, BMI, waist circumference and WHR, using SCORE risk.²³ However, the correlation of CVD risk with body fat was modest; *r* values were 0.31 for men and only 0.18 for women.²³ Pajunen *et al*²⁴ recently showed that body fat percentage (assessed by near-infrared interactance device) predicts cardiovascular (CVD) and CHD events in a prospective population-based survey (FINRISK'92 survey). They also found that the body fat lost its predictive power in a fully adjusted model in women. They concluded that it did not provide any additional predictive power over and above the simpler measures, such as BMI or WHR. Our findings also suggest that body fat percentage used on its own as an indicator of adiposity does not appear to relate consistently to future mortality and CVD risk in a middle-aged and older-aged population.

Our study has several advantages over the existing literature. We have a large sample size compared with several other studies, we have a long follow-up (11.7 years for all-cause mortality and 8.2 years for incident CVD), which allows us to capture the adequate number of events (2420 died and 4665 had incident CVD) and we are able to compare directly three different measures of adiposity and their crude and independent

Table 2 Adjusted HRs for mortality and cardiovascular disease incidence among men in EPIC-Norfolk (1997/2000–2009/2011) by quartile categories of obesity indices

	Q1	Q2	Q3	Q4	p Value*
<i>All-cause mortality</i>					
<i>Fat % quartile</i>					
Model A 1354/6505	1.00	0.91 (0.78 to 1.06)	0.89 (0.77 to 1.03)	1.02 (0.88 to 1.19)	0.75
Model B 1255/6197	1.00	0.89 (0.76 to 1.04)	0.84 (0.72 to 0.99)	0.97 (0.83 to 1.14)	0.73
Model C 1101/5582	1.00	0.90 (0.76 to 1.07)	0.93 (0.79 to 1.10)	1.00 (0.85 to 1.19)	0.96
Model D 1101/5582	1.00	0.85 (0.69 to 1.05)	0.82 (0.64 to 1.05)	0.79 (0.60 to 1.05)	0.10
Model E 854/4987	1.00	0.86 (0.68 to 1.09)	0.81 (0.61 to 1.07)	0.76 (0.55 to 1.05)	0.09
Model F 960/5502	1.00	0.81 (0.65 to 1.01)	0.66 (0.50 to 0.85)	0.64 (0.48 to 0.87)	0.004
Model G 854/4987	1.00	0.90 (0.71 to 1.12)	1.07 (0.84 to 1.36)	1.27 (0.95 to 1.70)	0.11
<i>WHR quartile</i>					
Model A 1354/6505	1.00	0.94 (0.79 to 1.10)	1.00 (0.85 to 1.18)	1.20 (1.03 to 1.40)	0.02
Model B 1255/6197	1.00	0.93 (0.78 to 1.10)	1.00 (0.85 to 1.18)	1.16 (0.99 to 1.36)	0.07
Model C 1101/5582	1.00	0.87 (0.73 to 1.05)	0.98 (0.82 to 1.17)	1.14 (0.96 to 1.35)	0.14
Model D 1101/5582	1.00	0.90 (0.74 to 1.09)	1.02 (0.84 to 1.24)	1.17 (0.97 to 1.43)	0.11
Model E 854/4987	1.00	0.97 (0.78 to 1.20)	1.10 (0.89 to 1.37)	1.28 (1.03 to 1.59)	0.03
Model F 960/5502	1.00	0.97 (0.80 to 1.19)	1.10 (0.90 to 1.35)	1.29 (1.05 to 1.59)	0.01
No model G	–	–	–	–	–
<i>BMI quartile</i>					
Model A 1354/6505	1.00	0.95 (0.81 to 1.11)	0.91 (0.78 to 1.06)	1.12 (0.97 to 1.30)	0.13
Model B 1255/6197	1.00	0.92 (0.79 to 1.08)	0.94 (0.80 to 1.11)	1.09 (0.93 to 1.27)	0.28
Model C 1101/5582	1.00	0.96 (0.81 to 1.14)	0.95 (0.80 to 1.13)	1.10 (0.93 to 1.30)	0.27
Model D 1101/5582	1.00	1.05 (0.85 to 1.29)	1.06 (0.82 to 1.35)	1.21 (0.91 to 1.60)	0.19
Model E 854/4987	1.00	1.01 (0.80 to 1.29)	0.97 (0.73 to 1.29)	1.16 (0.84 to 1.60)	0.37
Model F 960/5502	1.00	1.04 (0.83 to 1.30)	1.14 (0.87 to 1.48)	1.31 (0.97 to 1.76)	0.07
Model G 854/4987	–	0.88 (0.68 to 1.12)	0.98 (0.74 to 1.31)	1.14 (0.82 to 1.60)	0.44
<i>Cardiovascular disease incidence</i>					
<i>Fat % quartile</i>					
Model A 2383/6505	1.00	1.19 (1.06 to 1.34)	1.19 (1.06 to 1.34)	1.43 (1.28 to 1.61)	<0.0001
Model B 2242/6197	1.00	1.17 (1.04 to 1.32)	1.15 (1.02 to 1.29)	1.37 (1.22 to 1.54)	<0.0001
Model C 1977/5582	1.00	1.11 (0.98 to 1.27)	1.12 (0.98 to 1.27)	1.17 (1.03 to 1.33)	0.02
Model D 1977/5582	1.00	1.06 (0.93 to 1.21)	1.05 (0.91 to 1.20)	1.08 (0.93 to 1.24)	0.32
Model E 1605/4987	1.00	0.99 (0.83 to 1.19)	0.85 (0.69 to 1.04)	0.81 (0.64 to 1.03)	0.09
Model F 1802/5502	1.00	0.99 (0.83 to 1.17)	0.79 (0.64 to 0.96)	0.81 (0.65 to 1.01)	0.06
Model G 1605/4987	1.00	0.91 (0.76 to 1.10)	0.92 (0.74 to 1.16)	1.06 (0.80 to 1.40)	0.68
<i>WHR quartile</i>					
Model A 2383/6505	1.00	1.21 (1.07 to 1.37)	1.33 (1.18 to 1.51)	1.52 (1.35 to 1.71)	<0.0001
Model B 2242/6197	1.00	1.21 (1.07 to 1.38)	1.30 (1.15 to 1.48)	1.48 (1.31 to 1.67)	<0.0001
Model C 1977/5582	1.00	1.19 (1.05 to 1.38)	1.20 (1.05 to 1.38)	1.26 (1.10 to 1.43)	0.001
Model D 1977/5582	1.00	1.16 (1.01 to 1.34)	1.16 (1.00 to 1.34)	1.17 (1.01 to 1.36)	0.04
Model E 1605/4987	1.00	1.14 (0.97 to 1.33)	1.14 (0.98 to 1.34)	1.22 (1.04 to 1.44)	0.02
Model F 1802/5502	1.00	1.15 (1.00 to 1.34)	1.17 (1.01 to 1.37)	1.34 (1.14 to 1.56)	<0.0001
No model G	–	–	–	–	–
<i>BMI quartile</i>					
Model A 2383/6505	1.00	1.10 (0.97 to 1.24)	1.28 (1.14 to 1.44)	1.55 (1.39 to 1.74)	<0.0001
Model B 2242/6197	1.00	1.08 (0.96 to 1.23)	1.31 (1.16 to 1.48)	1.51 (1.34 to 1.70)	<0.0001
Model C 1977/5582	1.00	1.02 (0.89 to 1.16)	1.21 (1.06 to 1.38)	1.24 (1.09 to 1.41)	0.001
Model D 1977/5582	1.00	1.01 (0.86 to 1.19)	1.27 (1.05 to 1.53)	1.36 (1.09 to 1.69)	0.01
Model E 1605/4987	1.00	1.03 (0.86 to 1.24)	1.32 (1.07 to 1.63)	1.39 (1.09 to 1.76)	0.01
Model F 1802/5502	1.00	1.09 (0.92 to 1.29)	1.45 (1.19 to 1.77)	1.59 (1.27 to 2.00)	<0.0001
Model G 1605/4987	1.00	0.96 (0.80 to 1.15)	1.05 (0.85 to 1.29)	1.26 (0.99 to 1.62)	<0.0001

Q1 represents quartile 1 (bottom quartile) and Q4 represents quartile 4 (top quartile). The cut-off points for quartiles of BMI are 24.6, 26.6 and 28.8 for men, for WHR are 0.89, 0.93 and 0.96 for men, and for body fat % are 19.5, 23 and 27 for men.

We used forward stepwise adjustments to evaluate the potential effect of confounders using models A to G as follows:

Model A: age.

Model B: age, smoking status, alcohol consumption, physical activity, social class, education.

Model C: age, smoking status, alcohol consumption, physical activity, social class, education, BP, cholesterol, diabetes, prior stroke, prior MI, prior cancer.

Model D: age, smoking status, alcohol consumption, physical activity, social class, education, BP, cholesterol, diabetes, prior stroke, prior MI, prior cancer, fat%, WHR, BMI.

Model E: age, smoking status, alcohol consumption, physical activity, social class, education, BP, cholesterol, diabetes, prior stroke, prior MI, prior cancer, fat%, WHR, BMI with exclusion of prior stroke, prior MI, prior cancer.

Model F: as in model E after excluding BP and cholesterol from the model.

Model G: as in model E using quartiles of waist circumference rather than WHR (therefore models are constructed only for fat % and BMI analyses).

*p Values are difference between bottom and top quartiles. Any missing values were excluded in the individual model.

BMI, body mass index; BP, blood pressure; EPIC, European Prospective Investigation into Cancer; WHR, waist-to-hip ratio.

Table 3 Adjusted HRs of mortality and CVD incidence outcome among women of EPIC-Norfolk (1997/2000–2009/2011) by quartile categories of obesity indices

	Q1	Q2	Q3	Q4	p Value*
<i>All-cause mortality</i>					
<i>Fat % quartile</i>					
Model A 1066/8577	1.00	0.87 (0.73 to 1.03)	0.81 (0.68 to 0.96)	1.05 (0.89 to 1.23)	0.59
Model B 976/7999	1.00	0.87 (0.73 to 1.03)	0.81 (0.68 to 0.97)	0.98 (0.83 to 1.17)	0.83
Model C 822/6962	1.00	0.86 (0.71 to 1.05)	0.81 (0.66 to 0.99)	0.97 (0.80 to 1.18)	0.77
Model D 822/6962	1.00	0.85 (0.68 to 1.07)	0.78 (0.60 to 1.02)	0.91 (0.67 to 1.23)	0.53
Model E 650/6247	1.00	0.91 (0.70 to 1.17)	0.75 (0.55 to 1.02)	0.87 (0.61 to 1.23)	0.43
Model F 763/7146	1.00	0.86 (0.68 to 1.09)	0.70 (0.53 to 0.93)	0.80 (0.58 to 1.09)	0.16
Model G 650/6247	1.00	1.21 (0.91 to 1.60)	0.89 (0.61 to 1.29)	1.08 (0.68 to 1.72)	0.74
<i>WHR quartile</i>					
Model A 1066/8577	1.00	1.11 (0.91 to 1.37)	1.11 (0.91 to 1.36)	1.44 (1.20 to 1.74)	<0.0001
Model B 976/7999	1.00	1.11 (0.90 to 1.37)	1.07 (0.87 to 1.31)	1.33 (1.10 to 1.62)	0.004
Model C 822/6962	1.00	1.07 (0.85 to 1.33)	1.06 (0.85 to 1.33)	1.32 (1.07 to 1.63)	0.01
Model D 822/6962	1.00	1.11 (0.88 to 1.39)	1.14 (0.90 to 1.43)	1.42 (1.14 to 1.78)	0.002
Model E 650/6247	1.00	1.17 (0.91 to 1.50)	1.11 (0.86 to 1.44)	1.47 (1.14 to 1.89)	0.003
Model F 763/7146	1.00	1.18 (0.93 to 1.49)	1.09 (0.86 to 1.38)	1.40 (1.11 to 1.77)	<0.0001
No model G	–	–	–	–	–
<i>BMI quartile</i>					
Model A 1066/8577	1.00	0.84 (0.71 to 1.01)	0.87 (0.73 to 1.03)	1.06 (0.73 to 1.25)	0.53
Model B 976/7999	1.00	0.87 (0.72 to 1.05)	0.88 (0.73 to 1.05)	1.02 (0.86 to 1.22)	0.82
Model C 822/6962	1.00	0.91 (0.74 to 1.11)	0.87 (0.72 to 1.06)	0.97 (0.80 to 1.19)	0.80
Model D 822/6962	1.00	0.96 (0.76 to 1.22)	0.93 (0.70 to 1.22)	0.96 (0.70 to 1.32)	0.80
Model E 650/6247	1.00	1.00 (0.77 to 1.29)	0.94 (0.68 to 1.28)	1.00 (0.70 to 1.43)	0.99
Model F 763/7146	1.00	1.03 (0.81 to 1.31)	1.03 (0.77 to 1.37)	1.17 (0.84 to 1.52)	0.35
Model G 650/6247	1.00	1.22 (0.93 to 1.60)	0.91 (0.65 to 1.27)	1.12 (0.75 to 1.66)	0.59
<i>CVD incidence</i>					
<i>Fat % quartile</i>					
Model A 2282/8557	1.00	1.07 (0.95 to 1.22)	1.20 (1.07 to 1.36)	1.60 (1.42 to 1.79)	<0.0001
Model B 2096/7999	1.00	1.05 (0.92 to 1.19)	1.14 (1.00 to 1.29)	1.46 (1.29 to 1.65)	<0.0001
Model C 1802/6962	1.00	0.99 (0.86 to 1.10)	1.08 (0.94 to 1.24)	1.32 (1.15 to 1.50)	<0.0001
Model D 1802/6962	1.00	0.95 (0.83 to 1.10)	1.00 (0.87 to 1.15)	1.19 (1.04 to 1.37)	0.01
Model E 1541/6247	1.00	0.98 (0.82 to 1.17)	0.89 (0.73 to 1.10)	1.02 (0.81 to 1.29)	0.84
Model F 1782/7146	1.00	0.98 (0.83 to 1.16)	0.89 (0.73 to 1.08)	1.00 (0.81 to 1.24)	0.98
Model G 1541/6247	1.00	1.04 (0.86 to 1.27)	1.27 (1.00 to 1.62)	1.41 (1.04 to 1.91)	0.03
<i>WHR quartile</i>					
Model A 2282/8557	1.00	1.21 (1.05 to 1.39)	1.38 (1.20 to 1.57)	1.71 (1.59 to 2.06)	<0.0001
Model B 2096/7999	1.00	1.18 (1.02 to 1.36)	1.29 (1.12 to 1.48)	1.66 (1.45 to 1.90)	<0.0001
Model C 1802/6962	1.00	1.12 (0.96 to 1.30)	1.20 (1.03 to 1.39)	1.46 (1.27 to 1.69)	<0.0001
Model D 1802/6962	1.00	1.11 (0.95 to 1.30)	1.16 (0.99 to 1.35)	1.36 (1.16 to 1.58)	<0.0001
Model E 1541/6247	1.00	1.14 (0.97 to 1.35)	1.17 (1.00 to 1.38)	1.30 (1.10 to 1.54)	0.002
Model F 1782/7146	1.00	1.19 (1.02 to 1.39)	1.21 (1.04 to 1.41)	1.39 (1.19 to 1.62)	<0.0001
No model G	–	–	–	–	–
<i>BMI quartile</i>					
Model A 2282/8557	1.00	1.04 (0.92 to 1.19)	1.24 (1.09 to 1.40)	1.72 (1.53 to 1.94)	<0.0001
Model B 2096/7999	1.00	1.03 (0.90 to 1.18)	1.15 (1.01 to 1.31)	1.58 (1.40 to 1.80)	<0.0001
Model C 1802/6962	1.00	0.96 (0.82 to 1.11)	1.08 (0.94 to 1.25)	1.39 (1.21 to 1.60)	<0.0001
Model D 1802/6962	1.00	0.96 (0.81 to 1.14)	1.05 (0.87 to 1.28)	1.28 (1.04 to 1.59)	0.02
Model E 1541/6247	1.00	0.94 (0.78 to 1.13)	1.03 (0.83 to 1.27)	1.23 (0.97 to 1.56)	0.08
Model F 1782/7146	1.00	1.00 (0.85 to 1.19)	1.10 (0.90 to 1.33)	1.38 (1.11 to 1.72)	0.004
Model G 1541/6247	1.00	1.02 (0.85 to 1.23)	1.27 (1.02 to 1.57)	1.47 (1.14 to 1.90)	0.003

Q1 represents quartile 1 (bottom quartile) and Q4 represents quartile 4 (top quartile). The cut-off points for quartiles of BMI are 23.5, 25.8 and 28.9 for women, for WHR are 0.74, 0.78 and 0.82 for women, and for body fat % are 33.5, 39 and 45 women.

We used forward stepwise adjustments to evaluate the potential effect of confounders using models A to G as follows:

Model A: age.

Model B: age, smoking status, alcohol consumption, physical activity, social class, education.

Model C: age, smoking status, alcohol consumption, physical activity, social class, education, BP, cholesterol, diabetes, prior stroke, prior MI, prior cancer.

Model D: age, smoking status, alcohol consumption, physical activity, social class, education, BP, cholesterol, diabetes, prior stroke, prior MI, prior cancer, fat%, WHR, BMI.

Model E: age, smoking status, alcohol consumption, physical activity, social class, education, BP, cholesterol, diabetes, prior stroke, prior MI, prior cancer, fat%, WHR, BMI with exclusion of prior stroke, prior MI, prior cancer.

Model F: as in model E after excluding BP and cholesterol from the model.

Model G: as in model E using quartiles of waist circumference rather than WHR (therefore models are constructed only for fat % and BMI analyses).

*p Values are difference between bottom and top quartiles. Any missing values were excluded in the individual model.

BMI, body mass index; BP, blood pressure; CVD, cardiovascular disease; EPIC, European Prospective Investigation into Cancer; WHR, waist-to-hip ratio.

relationships to endpoints. The UK NHS system allowed us to have complete follow-up (no lost to follow-up) for both outcomes examined. We are also able to include other covariates and compare findings in men and women. Some larger studies were based on men or women only¹³ or they did not include all obesity indices in the analyses.¹⁴

While older age is associated with progressive changes in total and regional fat distribution including a preferential increase in truncal obesity, in particular visceral fat, these changes cannot be detected by simple anthropometric measures alone and are influenced by gender, race or ethnicity, and physical activity patterns.²⁵ The distribution of fat is important as there is evidence to suggest that abdominal visceral fat is associated with higher cardiometabolic risk compared with subcutaneous adipose tissue.^{26–27} This may explain why the predictive value of body fat percent attenuated when adjusted for WHR, an obesity index that is particularly related to the body fat distribution. While body fat percentage appears to be associated with increased risk of CVD in unadjusted comparisons (using body fat percentage quartile), we found that body fat percent is not associated with mortality and CVD risk in middle and older age after taking into account socioeconomic and other known risk factors for CVD such as blood pressure and cholesterol levels.

Our finding that WHR is the anthropometric measure most strongly related to cardiovascular risk and all-cause mortality is supported by several studies. A Danish population-based study¹² and a combined evaluation of the Physician's Health Study and Women's Health Study¹³ found that WHR has the strongest associations with CVD compared with other anthropometric measures. A Swedish population-based study of over 26 000 participants found that increasing levels of WHR are associated with increased risk of cardiovascular events in women and men who had normal weight but not in men who were overweight or obese.¹⁴ However, a systematic review evaluated 25 studies of anthropometric measures (ie, BMI, waist circumference, WHR) and risk of mortality in older people and found inconsistent findings regarding the strongest predictor(s) of morbidity and mortality.¹⁵

Because smoking status is frequently a confounder in analyses examining the association between measures of adiposity and cardiovascular outcomes, we have performed stratified analysis by smoking status and the results were consistent.

Our study has limitations. Due to the requirement to provide detailed health and lifestyle information and to be able to attend a health examination, the response rate at the study baseline (1993–1997) was modest at ~40% in EPIC-Norfolk. This could introduce a healthy responder bias from the outset. Nevertheless, baseline characteristics of the study population are similar to other UK population samples except with a slightly lower prevalence of smokers.⁸ Moreover, truncation of distribution due to healthy responders is likely to attenuate the associations, but this should not affect the associations observed within the study participants; if anything, truncation of the distribution is likely to reduce power for any associations. There were only single measurements of body fat percentage and other covariates such as cholesterol, blood pressure, etc. Moreover, the blood sample taken was non-fasting sample and therefore less standardised for some of the parameters (eg, cholesterol level) compared with fasting blood sample. Nevertheless, random measurement error is likely only to attenuate any associations observed. We were unable to account for age-related changes such as change in height and sarcopenia, etc., occurring during follow-up. Several studies have suggested that fitness markedly alters the relationship between adiposity and prognosis.^{28–30} While we were not able to measure fitness, we were able to

adjust for habitual physical activity that included leisure and fitness activities. Another limitation was that a majority (99.6%) of participants were white Caucasian, so the results may not be generalisable to other, more ethnically diverse populations.

In particular, fat percentage was only indirectly measured using impedance and estimated using manufacturer algorithms. It may be that more direct assessments of body fat percentage through imaging, for example, MRI, or other methods such as dual X-ray absorptiometry may be able better to capture more accurately fat percentage. Nevertheless, impedance estimates are widely promoted as methods for assessment of body fat percentage.

In summary, our findings suggest that the total body fat percentage estimated using impedance is not significantly related to all-cause mortality and incidence of CVD in men and women after taking into account other obesity indices BMI and WHR. Among the three obesity indices examined, WHR appears to be a good prognostic indicator for both mortality and CVD outcome in middle and older age.

Key messages

What is known on this subject?

Measurement of total body fat has been recently promoted as an improved method for assessing obesity, but the evidence behind the utility of body fat percentage in predicting health outcomes such as mortality and cardiovascular disease incidence is lacking.

What might this study add?

Once body mass index (BMI) and waist-to-hip (WHR) are taken into account, fat percentage does not add to prediction of mortality or cardiovascular disease in middle-age and older-age adults.

How might this impact on clinical practice?

Among the obesity indicators: body fat percentage, BMI and WHR, clinicians should use WHR as a prognostic indicator because it best predicts both mortality and cardiovascular disease outcome in middle-age and older-age adults.

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Contributors PKM conceived the study and PKM and CSK analysed and prepared the draft manuscript with critical input from K-TK. RNL was responsible for data management. K-TK and NJW are EPIC-Norfolk Principal Investigators. All authors contributed in writing the paper.

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