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Comparison of the associations of body mass index and measures of central adiposity and fat mass with coronary heart disease, diabetes, and all-cause mortality: a study using data from 4 UK cohorts[1–4]

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ABSTRACT

Background: Measures of regional adiposity have been proposed as alternatives to the measurement of body mass index (BMI) for identifying persons at risk of future disease.

Objective: The objective was to compare the magnitudes of association of BMI and alternative measurements of adiposity with coronary heart disease, diabetes, and cardiovascular disease risk factors and all-cause mortality.

Design: Data from 4 cohorts of adults [3937 women from the British Women's Heart and Health Study (BWHHS); 2367 and 1950 men from phases 1 and 3, respectively, of the Caerphilly Prospective Study (CaPS); 403 men and women from the Boyd Orr Study; and 789 men and women from the Maidstone-Dewsbury Study] were analyzed.

Results: The magnitudes of associations of BMI with incident coronary heart disease and cardiovascular disease risk factors were similar to those with measurements of central adiposity [waist circumference (WC), waist-hip ratio (WHR), or waist-height ratio (WHtR)] and more direct measurements of fat mass (bioimpedance/skinfold thickness). In CaPS (men only), there was no strong evidence of differences in the strengths of association with incident diabetes between BMI, WC, WHR, and WHtR (*P* for heterogeneity > 0.49 for all). In the BWHHS (women only), there was statistical evidence that WC [hazard ratio (HR): 2.35; 95% CI: 2.03, 2.73] and WHtR (HR: 2.29; 95% CI: 1.98, 2.66) were more strongly associated with diabetes than with BMI (HR: 1.80; 95% CI: 1.59, 2.04) (*P* for heterogeneity < 0.02 for both). Central adiposity measurements were positively associated with all-cause mortality, as was BMI, but only when those with a BMI (in kg/m^2) <22.5 were removed from the analyses.

Conclusion: No strong evidence supports replacing BMI in clinical or public health practice with other adiposity measures. *Am J Clin Nutr* 2010;91:547–56.

INTRODUCTION

Body mass index (BMI) has been routinely used in clinical and public health practice for decades to identify individuals and populations at risk of future cardiovascular disease and diabetes. However, in recent years, BMI has been criticized as a measure of risk because it reflects both fat and lean mass and because it does not identify fat distribution (1). There is a growing body of evidence suggesting that abdominal adiposity is a more important risk factor for cardiovascular and metabolic disease than is general adiposity (2). The mechanisms through which abdominal fat contributes to the risk of these diseases are not fully understood, although one of the components of abdominal fat—visceral adipose tissue, which is highly metabolically active—is believed to play a key role (3).

Several studies have recommended the use of anthropometric measures that capture abdominal adiposity, such as waist circumference (WC), waist-hip ratio (WHR), or waist-height ratio (WHtR) as alternatives to, or in addition to, BMI in assessing disease prediction in clinical practice and public health sur-

veillance (4–6). There are, however, concerns about the reliability of these measurements (7) because WC and hip circumference (HC) can differ depending on the precise site at which they are measured (8). Similarly, calls for more direct measurements of fat mass, such as by bioimpedance or the use of skinfold thicknesses, may be problematic in routine clinical and public health practice because of difficulties with accurate and reliable measurements (9–11). Height and weight (used to calculate BMI) can be reliably measured and there would need to be much stronger associations of measurements of central adiposity and fat mass, in comparison with BMI, for these to be proposed as preferred measurements in routine clinical and public health practice for identifying those at risk of future disease.

Results from published studies to date that have tried to compare different measurements of general and regional adiposity have not been consistent. BMI has been compared separately with different anthropometric measures, and different outcome measures have been assessed (4, 12–14).

We used data from 4 cohorts to compare the magnitude of associations of BMI with those of a range of alternative anthropometric measures in relation to incident coronary heart disease (CHD), diabetes, and all-cause mortality and a range of cardiovascular disease risk factors (arterial plaques, blood pressure, fasting glucose, insulin, and lipids). Our aim was to directly compare different measurements to address the question of whether measurements, such as WC or skinfold thickness, were sufficiently more strongly associated with disease outcomes to warrant using these, instead of BMI, in public health or clinical practice. By including a wider range of outcomes than used in previous studies, we will be able to provide a more complete answer to this question and address possible mechanisms underlying any differences.

SUBJECTS AND METHODS

Study populations

This study used data from the British Women's Heart and Health Study (BWHHS), the Caerphilly Prospective Study (CaPS), the Boyd Orr Study, and the Maidstone-Dewsbury Study. A brief summary of each study population is provided in **Table 1**. Ethical approval was obtained for each study as follows: for the BWHHS, Local- and Multi-Centre Research Ethics Committee approvals were obtained; for the Caerphilly Prospective Study, approval was obtained from the Mid-Glamorgan Research Ethics Committee; for the Boyd Orr follow-up study, ethical approval was obtained from the Multicentre Research Ethics Committee for Scotland; and for the Maidstone-Dewsbury Study, ethical approval was obtained from relevant local Research Ethics Committees.

BWHHS

Full details of the sample selection and data collection methods were described previously (15). Women ($n = 4286$) aged 60–79 y were randomly selected from general practice registers in 23 towns, chosen to be representative of the UK population.

Standing height was measured (without shoes) to the nearest millimeter, weight (in light clothing without shoes) to the nearest 0.1 kg, WC and hip circumference to the nearest millimeter, and blood pressure and fasting glucose, insulin, and lipids by using standard research protocols (*see* Online Supplemental Material under "Supplemental data" in the online issue) (15).

For the analyses concerned with incident disease outcomes, all women with prevalent disease at baseline were removed (*see* Online Supplemental Material under "Supplemental data" in the online issue for information on definition of prevalent disease). Incident CHD and diabetes were ascertained through biennial review of medical notes (date of latest record: 31 August 2007) and through routine death registrations (up until 31 May 2008). CHD was defined as physician diagnosis of myocardial infarction (MI) or angina or death from CHD (ICD10 codes I20–I25, I51.6); diabetes was defined as a new physician diagnosis of diabetes (there were no deaths from diabetes that were not previously identified in the medical records).

Information on covariates [social class, smoking (never, ex, current: 1–9, 10–19, 20–29, or >29 cigarettes/d), and exercise

TABLE 1
Details of the study populations

Study	Year of data collection	n	Age range	Female	Study participants
			y	%	
British Women's Heart and Health Study	1999–2001	4286	60–79	100	Women randomly selected from general practice registers in 23 towns representative of the UK population
Caerphilly Prospective Study					
Phase 1	1979–1983	2512	45–59	0	89% sample of all men of this age from the electoral register and general practice lists in Caerphilly and adjoining villages
Phase 2	1984–1988	2398	47–67	0	Follow-up of phase 1 men and an additional 447 men of the same age living in the study area (reconstructed cohort: 2959)
Phase 3	1989–1993	2154	52–72	0	Follow-up of men from phase 2
Boyd Orr follow-up study	2002–2003	405	63–82	54	65-y follow-up of children from the Carnegie Survey of Diet and Health originally living in 16 urban and rural districts in Britain in 1937–1939
Maidstone-Dewsbury Study	1996	792	56–77	53	Male participants of the British Regional Heart Study from the towns of Maidstone and Dewsbury along with females of the same age range selected from the same general practitioner practices

(<2, 2–3, or >3 h/wk)] was collected at interview or by questionnaire by using a modified version of the EPIC (European Prospective Investigation into Cancer and Nutrition) physical activity questionnaire (16).

Caerphilly Prospective Study

The Caerphilly Prospective Study comprises 2512 men—89% of all men aged between 45 and 59 y at baseline data collection (1979–1983) living in Caerphilly and adjoining villages (17). The men have been followed an additional 4 times. During phase 2, an additional 447 men of the same age group living in the same area entered the study for the first time. This is known as the "reconstructed cohort," and there were 2959 subjects available for mortality and CHD analyses.

Because different anthropometric measures were taken at the different phases of data collection, men from phase 1 and men from phase 3 were considered as separate cohorts for the purposes of analysis. Full details of the methods used at each phase were published elsewhere (17). Standing height, weight, WC and hip circumference, skinfold thicknesses, blood pressure, and fasting glucose, insulin, and lipids were all measured by using standard research procedures (17) (see Online Supplemental Material under "Supplemental data" in the online issue).

For the analyses concerned with incident disease outcomes, all men with prevalent disease at baseline were removed (see Online Supplemental Material under "Supplemental data" in the online issue for information on definition of prevalent disease). Incident CHD was defined as acute MI (satisfying WHO criteria) or death from heart disease (ICD 9 codes: 410–414, ICD 10 codes: I20-25, I51.6). Nonfatal MI was ascertained up until 28 February 2007 through a variety of sources: 1) detailed searches of medical notes, following self-report of CHD by men attending follow-up; 2) self-reported questionnaire data; or 3) hospital episode statistics (ICD 10 codes I21-23). Incident diabetes was ascertained from self report of diagnosis at phases 2, 3, 4, and 5 (for phase 1 analysis) and at phases 4 or 5 (for phase 3 analysis). Deaths from CHD up to 31 July 2008 were obtained from the National Health Service central registry.

Information on social class (at phases 1 and 2) and smoking (never, ex, and current smoker of pipe or cigar, and 1–14, 15–24, or ≥25 cigarettes/d) (at phases 1 and 3) were collected by questionnaire. Physical activity data for phase 3 men (categorized into tertiles of daily leisure-time energy expenditure) was estimated from information collected at phase 2 by using the Minnesota Leisure Time Physical Activity Questionnaire (18).

Boyd Orr Study

Between 1937 and 1939, 4999 children (aged 0–19 y) from 16 centers across the United Kingdom took part in the Carnegie Survey of Diet and Health. In 2002, 2563 surviving members of the original cohort were found to be alive and living in England and Scotland (19). All 732 of these 2563 participants living in or around 4 centers with appropriate clinics (London, Aberdeen, Dundee, and Wisbech) were invited to take part in a detailed clinical assessment in 2002, and 405 (55%) attended the assessment.

A detailed description of the data collection methods is provided elsewhere (19, 20). Standing height, weight, WC, hip and

thigh circumferences, fat mass, blood pressure, and fasting glucose, insulin, and lipids were all assessed by using standard research procedures (see Online Supplemental Material under "Supplemental data" in the online issue).

Ultrasound, using an Advanced Technology Laboratories high-definition imaging 3000 duplex system (Advanced Technology Laboratories, Signal Hill, CA), of the carotid and femoral arteries was used to assess the presence of arterial plaques. A full description of the methods and variables derived was described previously (21). The scans were undertaken by a single ultrasonographer, supervised by the same ultrasonographer who performed the scans in Maidstone-Dewsbury (see below). Information on smoking (current, ex, and never), a validated exercise score (never to mild or infrequent, infrequent or moderate, frequent or moderate, and frequent or vigorous), and social class were collected via self-completed questionnaire.

Maidstone-Dewsbury Study

The Maidstone-Dewsbury Study (performed in 1996) comprised the male participants (n = 425) of the British Regional Heart Study (22) from the towns of Maidstone-Dewsbury and a random sample of women (n = 367) of a similar age (56–77 y) selected from the same general practice registers in these towns (23).

Standing height, weight, WC, hip and thigh circumferences, fat mass, blood pressure, and fasting glucose, insulin, and lipids were all assessed by using standard research procedures (23) (see Supplementary Table 5 under "Supplemental data" in the online issue).

The presence of carotid or femoral arterial plaques was assessed by ultrasound using an Advanced Technology Laboratories high-definition imaging 3000 triplex system. A detailed description of the methods used was published previously (23). Information on smoking (never, ex, and current: 1–9, 10–19, 20–29, or >29 cigarettes/d), social class, and exercise (<2, 2–3, or >3 h/wk of running, cycling, or swimming) was collected via self-administered questionnaire.

Statistics

The central to peripheral skinfold (CP) ratio (in CaPS phase 1) was calculated as the ratio of central (subscapular + abdominal) to peripheral (biceps + triceps) skinfold-thickness measures. Fat mass index (in the Boyd Orr Study) was calculated as fat mass (kg)/height squared (m^2). Age- and sex-standardized z scores were calculated for each anthropometric measure within each cohort to allow comparison between the different anthropometric measurements. Pearson's correlation coefficients were used to examine the relation between anthropometric measures.

Because of skewed distributions, blood triglycerides, glucose, and insulin were $\log_e$ transformed in all data sets. Associations with continuously measured outcomes were investigated by using multivariable linear regression, and multivariable logistic regression was used to investigate associations with arterial plaque prevalence.

Cox proportional hazards regression models, with age as the time variable, were used to assess the relation between anthropometric measures and all-cause mortality, fatal and nonfatal

incident CHD (in BWHHS and CaPS), and incident diabetes (in BWHHS). Proportionality assumptions were assessed by cumulative hazard function (Nelson Aalen) plots, and Weibull survival analysis was conducted when assumptions were violated. Because the use of Weibull survival analysis made little difference to the hazard ratios, only hazard ratios from Cox regression are presented. In CaPS, logistic regression was used to assess associations between measures of adiposity and incident diabetes because dates of diagnosis for diabetes were not available.

To limit the possible effect of reverse causality, individuals with baseline disease were excluded (for CHD: $n = 719$ from the BWHHS, $n = 144$ from CaPS phase 1, and $n = 333$ from CaPS phase 3; for diabetes: $n = 407$ from the BWHHS, $n = 47$ from the CaPS phase 1, and $n = 173$ from the CaPS phase 3). Therefore the eligible cohorts for these analyses (ie, after removal of prevalent disease) were as follows: BWHHS (4286 for all-cause mortality, 3567 for CHD, and 3879 for diabetes), CaPS phase 1 (2512 for all-cause mortality, 2368 for CHD, and 2465 for diabetes), and CaPS phase 3 (2553 for all-cause mortality, 2220 for CHD, and 2380 for diabetes). In addition, all survival analyses were repeated, with exclusion of the first year of follow-up time in the BWHHS and the first 2 y in CaPS. The shorter exclusion time in the BWHHS reflects the shorter follow-up period and smaller number of disease events in this study than in CaPS. Because BMI has a nonlinear (J-shaped) association with all-cause mortality, we repeated the analyses after removing participants with a BMI (in kg/m^2) < 22.5.

Regression analyses were adjusted for smoking, exercise (not available in CaPS phase 1), and socioeconomic class (all treated as categorical indicator variables) and were based on subjects with complete anthropometric and covariate data.

We a priori decided to consider the appropriateness of pooling results from individual studies for binary outcomes (incident CHD, diabetes, all-cause mortality, and arterial plaques) to increase the precision of estimates. For the 2 studies with arterial plaque outcomes, we were satisfied that these were sufficiently similar for this to be reasonable and therefore present pooled estimates as our main results (separate results are available from the authors). For CHD, diabetes, and all-cause mortality outcomes, which were available in the BWHHS and CaPS phase 3, the 2 studies had important population differences. The BWHHS

TABLE 2
Pearson's correlation coefficients between age- and sex-standardized z scores of anthropometric measures[1]

Study	BMI	WC	WHR	WHtR	HC	Fat mass	WT	Biceps	Triceps	Sub	Abd	CP
BWHHS ($n = 3937$)												
BMI	1											
WC	0.85	1										
WHR	0.38	0.72	1									
WHtR	0.87	0.96	0.72	1								
HC	0.90	0.81	0.2	0.77	1							
CaPS												
Phase 3 ($n = 1950$)												
BMI	1											
WC	0.89	1										
WHR	0.58	0.80	1									
WHtR	0.90	0.94	0.82	1								
HC	0.86	0.82	0.32	0.71	1							
Phase 1 ($n = 2367$)												
BMI	1											
Biceps	0.58							1				
Triceps	0.56							0.63	1			
Subscapular	0.71							0.59	0.58	1		
Abdominal	0.66							0.48	0.48	0.67	1	
CP ratio	0.23							−0.22	−0.31	0.33	0.54	1
Boyd Orr ($n = 403$)												
BMI	1											
WC	0.88	1										
WHR	0.60	0.82	1									
WHtR	0.90	0.95	0.82	1								
HC	0.83	0.78	0.33	0.7	1							
Fat mass	0.92	0.83	0.62	0.90	0.73	1						
WT	0.44	0.68	0.80	0.69	0.29	0.48	1					
Maidstone-Dewsbury ($n = 789$)												
BMI	1											
WC	0.84	1										
WHR	0.49	0.76	1									
WHtR	0.87	0.95	0.76	1								
HC	0.83	0.83	0.29	0.74	1							

[1] WC, waist circumference; WHR, waist-hip ratio; WHtR, waist-height ratio; HC, hip circumference; CP, central to peripheral skinfold ratio; WT, waist-thigh ratio; Sub, subscapular; Abd, abdominal; CaPS, Caerphilly Prospective Study; BWHHS, British Women's Heart and Health Study. $P < 0.001$ for all coefficients.

TABLE 3
Association of anthropometric measures with all-cause mortality, incident coronary heart disease (CHD), and incident diabetes in the British Women's Heart and Health Study[1]

	Age-adjusted			All adjusted[3]		
	HR[2]	95% CI	P	HR[2]	95% CI	P
Incident CHD (n = 3160; 309 events)						
BMI	1.12	(1.00, 1.25)	0.05	1.09	(0.98, 1.23)	0.12
WC	1.21	(1.08, 1.34)	0.001	1.17	(1.04, 1.31)	0.007
WHR	1.22	(1.10, 1.36)	<0.001	1.17	(1.05, 1.30)	0.006
WHtR	1.23	(1.10, 1.37)	<0.001	1.18	(1.05, 1.32)	0.004
HC	1.10	(0.98, 1.23)	0.10	1.09	(0.97, 1.22)	0.15
Incident diabetes (n = 3413; 140 events)						
BMI	1.80	(1.60, 2.03)	<0.001	1.80	(1.59, 2.04)	<0.001
WC	2.37	(2.05, 2.73)	<0.001	2.35	(2.03, 2.73)	<0.001
WHR	2.05	(1.79, 2.36)	<0.001	2.01	(1.74, 2.33)	<0.001
WHtR	2.28	(1.98, 2.63)	<0.001	2.29	(1.98, 2.66)	<0.001
HC	1.76	(1.55, 2.00)	<0.001	1.73	(1.52, 1.97)	<0.001
All-cause mortality (n = 3778; 486 events)						
BMI	0.98	(0.90, 1.08)	0.73	0.97	(0.89, 1.07)	0.54
WC	1.12	(1.03, 1.23)	0.009	1.09	(0.99, 1.19)	0.08
WHR	1.22	(1.11, 1.33)	<0.001	1.15	(1.05, 1.26)	0.002
WHtR	1.15	(1.05, 1.25)	0.002	1.10	(1.01, 1.20)	0.04
HC	0.99	(0.90, 1.08)	0.78	0.99	(0.90, 1.08)	0.75

[1] WC, waist circumference; WHR, waist-hip ratio; WHtR, waist-height ratio; HC, hip circumference; HR, hazard ratio.
[2] From Cox regression; represents risk per 1-SD increase in each anthropometric measure.
[3] Adjusted for age, socioeconomic class, smoking, and exercise.

is a study of women only (age range: 60–79 y), and CaPS is a study of men only (age range: 52–72 y). Adjusted point estimates from the individual studies were pooled by using the "metan" command in STATA. In the main analyses, we present both the results for each study separately and also for the pooled analyses. In all pooled analyses, we tested for heterogeneity using the I^2 statistic. Random-effects models were used when heterogeneity (I^2 statistic) was >50%. To pool diabetes outcomes we determined odds ratios (from logistic regression analyses) in the BWHHS and combined these with the odds ratios from CaPS. All analyses were conducted by using STATA 10 (StataCorp LP, College Station, TX)

TABLE 4
Association of anthropometric measures with all-cause mortality, incident coronary heart disease (CHD), and incident diabetes in phase 3 of the Caerphilly Prospective Study[1]

	Age-adjusted				All adjusted[4]			
	HR[2]	OR[3]	95% CI	P	HR[2]	OR[3]	95% CI	P
Incident CHD (n = 1758; 317 events)								
BMI	1.11	—	(0.99, 1.24)	0.07	1.15	—	(1.03, 1.28)	0.02
WC	1.13	—	(1.01, 1.26)	0.03	1.15	—	(1.03, 1.29)	0.01
WHR	1.15	—	(1.03, 1.28)	0.02	1.14	—	(1.02, 1.27)	0.03
WHtR	1.17	—	(1.04, 1.31)	0.01	1.19	—	(1.06, 1.33)	0.003
HC	1.05	—	(0.94, 1.17)	0.42	1.09	—	(0.97, 1.22)	0.14
Incident diabetes (n = 1806; 124 events)								
BMI	—	1.79	(1.50, 2.13)	<0.001	—	1.80	(1.51, 2.15)	<0.001
WC	—	1.95	(1.62, 2.35)	<0.001	—	1.98	(1.64, 2.40)	<0.001
WHR	—	1.89	(1.57, 2.28)	<0.001	—	1.95	(1.60, 2.36)	<0.001
WHtR	—	1.95	(1.62, 2.34)	<0.001	—	1.99	(1.65, 2.41)	<0.001
HC	—	1.52	(1.29, 1.80)	<0.001	—	1.51	(1.27, 1.80)	<0.001
All-cause mortality (n = 1920; 855 events)								
BMI	0.94	—	(0.87, 1.01)	0.08	0.99	—	(0.92, 1.06)	0.8
WC	1.02	—	(0.95, 1.09)	0.6	1.06	—	(0.99, 1.13)	0.12
WHR	1.08	—	(1.01, 1.16)	0.03	1.08	—	(1.01, 1.16)	0.03
WHtR	1.04	—	(0.97, 1.11)	0.29	1.07	—	(1.00, 1.15)	0.07
HC	0.94	—	(0.88, 1.01)	0.09	1.00	—	(0.93, 1.07)	1.0

[1] WC, waist circumference; WHR, waist-hip ratio; WHtR, waist-height ratio; HC, hip circumference; HR, hazard ratio; OR, odds ratio.
[2] From Cox regression; represents risk per 1-SD increase in each anthropometric measure.
[3] From logistic regression; represents odds per 1-SD increase in anthropometric measure.
[4] Adjusted for age, socioeconomic class, smoking, and exercise.

RESULTS

Representativeness

Details of representativeness of the participants included in the analyses presented for each study are provided elsewhere (*see* Online Supplemental Material under "Supplemental data" in the online issue).

Correlations between anthropometric measures

Correlations between anthropometric variables are shown in **Table 2**. In all cohorts, BMI correlated strongly with WC, WHtR, and HC (>0.8 for all coefficients). More modest correlations were observed between BMI and WHR (0.38–0.60). WC and WHtR were very highly correlated in all data sets ($r >$ 0.94). Correlations between BMI and individual skinfold-thickness measures in phase 1 of the CaPS ranged from 0.71 (with subscapular) to 0.56 (triceps). Only a weak correlation was observed between BMI and the CP skinfold ratio (0.23). In Boyd Orr, BMI correlated very strongly with the fat mass index ($r =$ 0.92) and moderately with the waist-thigh (WT) ratio ($r = 0.60$).

Associations with cardiovascular disease risk factors

Associations of metabolic and cardiovascular disease risk factors (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, systolic blood pressure, diastolic blood pressure, fasting glucose, and fasting insulin) with BMI and other anthropometric measures are shown elsewhere (*see* Supplementary Tables 1–5 under "Supplemental data" in the online issue).

Across the 4 cohorts, all anthropometric measures were positively associated with plasma triglycerides, systolic blood pressure, and diastolic blood pressure and were negatively associated with HDL cholesterol. Fasting glucose and insulin (only available in the BWHHS, CaPS, and Boyd Orr) were positively associated with all anthropometric measures. There was only weak evidence of positive associations between each anthropometric measurement and LDL cholesterol.

The magnitudes of associations of BMI, WHR, WHtR, and WC were similar with all of these cardiovascular disease risk factors in all 4 cohorts. HC was less strongly associated with triglycerides and insulin than were the other anthropometric measurements. The strength of associations of BMI and individual skinfold-thickness measures in CaPS phase 1 with these risk factors were generally of a similar magnitude, although the associations of CP ratio with systolic blood pressure, insulin, and triglycerides appeared to be weaker than equivalent associations between BMI and the association of triceps with total cholesterol was weaker than that of BMI with this outcome.

Associations with incident CHD, diabetes, and all-cause mortality

The results for the associations of each anthropometric measurement with incident CHD, diabetes, and all-cause mortality in the BWHHS, CaPS phase 3, and CaPS phase 1 are shown in **Tables 3, 4,** and **5**, respectively. The results are further summarized in **Figure 1**. Additional results, including numbers of cases and median years of follow-up for each outcome, are

TABLE 5
Association of anthropometric measures with all-cause mortality, incident coronary heart disease (CHD), and incident diabetes in phase 1 of the Caerphilly Prospective Study[1]

	Age-adjusted				All adjusted[4]			
	HR[2]	OR[3]	95% CI	P	HR[2]	OR[3]	95% CI	P
Incident CHD (*n* = 2181; 511 events)								
BMI	1.21	—	(1.11, 1.32)	<0.001	1.30	—	(1.19, 1.41)	<0.001
Biceps	1.13	—	(1.05, 1.23)	0.002	1.19	—	(1.10, 1.29)	<0.001
Triceps	1.10	—	(1.01, 1.20)	0.03	1.13	—	(1.04, 1.23)	0.003
Subscapular	1.17	—	(1.08, 1.27)	<0.001	1.25	—	(1.15, 1.35)	<0.001
Abdominal	1.09	—	(1.00, 1.18)	0.06	1.14	—	(1.05, 1.25)	0.002
CP ratio	1.03	—	(0.95, 1.13)	0.44	1.06	—	(0.97, 1.15)	0.21
Incident diabetes (*n* = 2265; 205 events)								
BMI	—	1.96	(1.70, 2.26)	<0.001	—	1.98	(1.71, 2.28)	<0.001
Biceps	—	1.60	(1.42, 1.81)	<0.001	—	1.61	(1.42, 1.82)	<0.001
Triceps	—	1.50	(1.32, 1.70)	<0.001	—	1.50	(1.32, 1.70)	<0.001
Subscapular	—	1.91	(1.68, 2.17)	<0.001	—	1.93	(1.69, 2.20)	<0.001
Abdominal	—	1.74	(1.52, 1.99)	<0.001	—	1.74	(1.52, 2.00)	<0.001
CP ratio	—	1.23	(1.07, 1.40)	0.002	—	1.22	(1.06, 1.39)	0.004
All-cause mortality (*n* = 2304; 1228 events)								
BMI	0.95	—	(0.89, 1.01)	0.07	1.01	—	(0.95, 1.08)	0.70
Biceps	1.01	—	(0.95, 1.07)	0.84	1.06	—	(1.00, 1.12)	0.06
Triceps	1.00	—	(0.95, 1.06)	0.91	1.04	—	(0.98, 1.10)	0.2
Subscapular	0.95	—	(0.89, 1.01)	0.08	1.02	—	(0.96, 1.08)	0.61
Abdominal	0.93	—	(0.88, 0.99)	0.02	0.99	—	(0.93, 1.05)	0.66
CP ratio	0.91	—	(0.86, 0.96)	0.001	0.94	—	(0.88, 0.99)	0.03

[1] CP ratio, central to peripheral skinfold ratio; HR, hazard ratio; OR, odds ratio.
[2] From Cox regression; represents risk per 1-SD increase in each anthropometric measure.
[3] From logistic regression; represents odds per 1-SD increase in anthropometric measure.
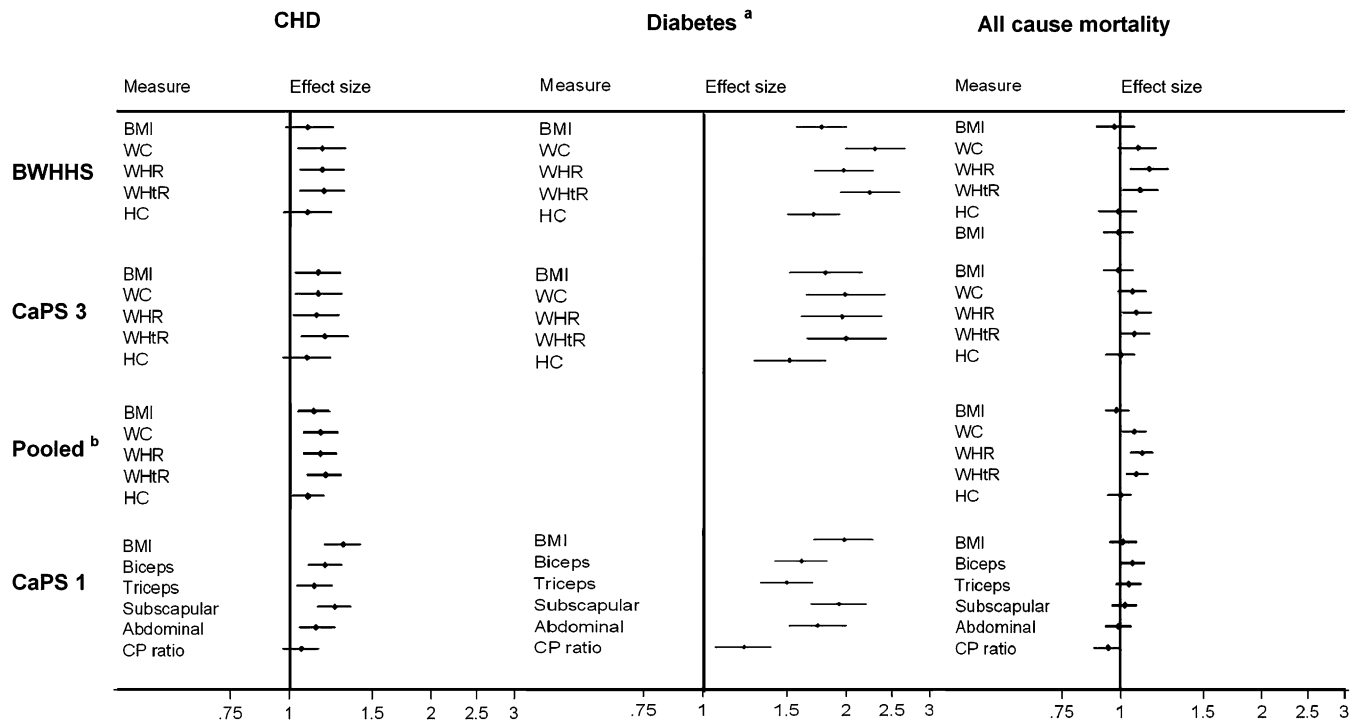[4] Adjusted for age, socioeconomic class, smoking, and exercise.

FIGURE 1. Associations of anthropometric measures with coronary heart disease (CHD), diabetes, and all-cause mortality. Points represent effect sizes, and bars represent 95% CIs. [a]All effect sizes are hazard ratios from Cox regression, other than diabetes results from phases 1 and 3 of the Caerphilly Prospective Study (CaPS 1 and CaPS 3), which are odds ratios from logistic regression. [b]Pooled estimates from the British Women's Heart and Health Study (BWHHS) and CaPS 3. WC, waist circumference; WHR, waist-hip ratio; WHtR, waist-height ratio; HC, hip circumference; CP ratio, central to peripheral skinfold ratio.

shown elsewhere (*see* Supplementary Table 6 under "Supplemental data" in the online issue) as are the results of pooled analyses (*see* Supplementary Tables 7 and 8 under "Supplemental data" in the online issue).

Because CaPS phase 1 had different measurements of adiposity (skinfold thickness but no circumferences) from the BWHHS and CaPS, the results from this study were not pooled with those from BWHHS or CaPS phase 3 for any outcomes. There was no strong statistical evidence for between-study differences in pooled analyses of BWHHS and CaPS phase 3 ($I^2 \leq 13.5\%$, $P \geq 0.28$) for any association analyses with incident CHD or all-cause mortality. There was some statistical evidence of heterogeneity between the 2 studies for the associations of WC, WHtR, and HC with diabetes (I^2 values all $>50\%$), but for other measurements there was no evidence of heterogeneity between the 2 studies.

With one exception, all anthropometric measurements were positively associated with CHD in the BWHHS, CaPS phase 3, and CaPS phase 1 studies and in the pooled analyses for measurements based on WC or hip circumference and BMI from the BWHHS and CaPS phase 3. The one exception was the null association of CP ratio with incident CHD in CaPS phase 1. Within BWHHS and CaPS phase 3, the magnitudes of associations of different anthropometric measurements with incident CHD appeared similar, and there was no statistical evidence that they differed from each other ($P > 0.3$ for all). In all 3 studies, all anthropometric measurements were positively associated with incident diabetes and these associations were stronger than those seen for incident CHD. In BWHHS there was statistical evidence that the associations of WC and WHtR with diabetes

were stronger than the association of BMI with diabetes ($P < 0.02$ for both); however, no evidence of differences in associations between WHR and BMI was observed ($P = 0.26$). Point estimates for all measurements looked similar, with each being associated with an approximate doubling of risk. In CaPS phase 3, there was no evidence that the associations of any of the measures of central adiposity with incident diabetes differed from that of BMI ($P > 0.44$).

Measurements of central adiposity based on WC were positively associated with all-cause mortality in both the BWHHS and CaPS phase 3, but BMI was not associated with all-cause mortality in either of these studies or in CaPS phase 1 (or in pooled estimates), and none of the individual skinfold-thickness measurements in CaPS phase 1 were associated with all-cause mortality. When the analyses were repeated with those with BMI < 22.5 removed, BMI was positively associated with all-cause mortality in the BWHHS and CaPS phase 1, with no strong evidence that the associations differed between BMI and measures of central adiposity (**Table 6**). For all of these prospective associations, the findings remained essentially unchanged when early years of follow-up were excluded.

Associations with arterial plaque

In the Boyd Orr Study, 289 of 331 (87.3%) subjects had at least one arterial (carotid or femoral) plaque, 211 of 331 (63.8%) had a carotid plaque, and 253 of 330 had a femoral plaque (76.7%). In the Maidstone-Dewsbury Study, 516 of 674 (76.6%) subjects had at least one carotid or femoral plaque, 380 of 674 (56.4%) had a carotid plaque, and 426 of 673 (63.3%) had

TABLE 6
Adjusted associations of anthropometric measures with all-cause mortality in subjects with a BMI (in kg/m^2) ≥ 22.5[1]

	HR[2]	95% CI	P
BWHHS (*n* = 3308; 395 events)			
BMI	1.11	(1.01, 1.22)	0.02
WC	1.25	(1.14, 1.37)	<0.001
WHR	1.22	(1.10, 1.34)	<0.001
WHtR	1.26	(1.14, 1.38)	<0.001
HC	1.14	(1.04, 1.25)	<0.001
CaPS phase 3 (*n* = 1722; 747 events)			
BMI	1.03	(0.95, 1.10)	0.50
WC	1.10	(1.02, 1.18)	0.01
WHR	1.14	(1.06, 1.22)	0.001
WHtR	1.12	(1.04, 1.20)	0.004
HC	1.02	(0.95, 1.10)	0.61
CaPS phase 1 (*n* = 1985; 1022 events)			
BMI	1.10	(1.03, 1.17)	0.004
Biceps	1.09	(1.02, 1.15)	0.008
Triceps	1.08	(1.02, 1.15)	0.01
Subscapular	1.07	(1.01, 1.14)	0.02
Abdominal	1.04	(0.98, 1.11)	0.22
CP ratio	0.97	(0.91, 1.03)	0.28

[1] CaPS, Caerphilly Prospective Study; BWHHS, British Women's Heart and Health Study; CP ratio, central to peripheral skinfold ratio; HR, hazard ratio; WC, waist circumference; WHR, waist-hip ratio; WHtR, waist-height ratio; HC, hip circumference.

[2] From Cox regression; represents risk per 1-SD increase in each anthropometric measure. Adjusted for age, socioeconomic class, smoking, and exercise in the BWHHS and CaPS phase 3; adjusted for age, socioeconomic class, and smoking in CaPS phase 1.

TABLE 7
Pooled adjusted odds ratios (ORs) for associations between anthropometric measures and presence of arterial plaque from the Boyd Orr and Maidstone-Dewsbury studies[1]

	OR[2]	95% CI	P
Any plaque			
BMI	0.96	(0.81, 1.15)	0.67
WC	1.07	(0.90, 1.28)	0.44
WHR	1.21	(1.01, 1.45)	0.035
WHtR	1.12	(0.94, 1.33)	0.22
HC	0.93	(0.79, 1.11)	0.43
Femoral plaque			
BMI	0.94	(0.81, 1.09)	0.39
WC	1.01	(0.87, 1.17)	0.87
WHR	1.09	(0.93, 1.27)	0.28
WHtR	1.05	(0.90, 1.23)	0.51
HC	0.94	(0.81, 1.09)	0.39
Carotid plaque			
BMI[3]	1.09	(0.87, 1.36)	0.42
WC	1.14	(1.00, 1.31)	0.058
WHR	1.25	(1.09, 1.44)	0.001
WHtR	1.19	(1.03, 1.37)	0.016
HC	1.04	(0.90, 1.19)	0.63

[1] WC, waist circumference; WHR, waist-hip ratio; WHtR, waist-height ratio; HC, hip circumference.

[2] From logistic regression; represents the odds per 1-SD increase in anthropometric measure. Adjusted for age, sex, smoking, social class, and exercise.

[3] Combined by using a random-effects method because of evidence of heterogeneity ($I^2 > 50\%$); all other results in table were combined by using a fixed-effects method.

a femoral plaque. In the pooled analysis (**Table 7**), measurements of central adiposity, but not of BMI, were positively associated with carotid plaques. However, there was no strong evidence of differences between estimates for any of the anthropometric measures in their association with carotid plaque ($P \geq 0.08$ for all). There was little evidence that any of the measures of adiposity were associated with femoral plaque.

DISCUSSION

In this review, we focused on the specific issue of whether magnitudes of association of more direct measurements of fat mass or of regional adiposity are markedly stronger than those of BMI to address the question of whether these measurements should replace BMI in clinical practice or public health surveillance.

Overall, our results suggest that measurements of central adiposity or other regional measurements (skinfold thickness) of fat mass compared with BMI are not more strongly associated with incident CHD, carotid plaques, or a wide range of cardiovascular disease risk factors. In general, all measurements of adiposity were more strongly associated with diabetes than they were with CHD. We found some statistical evidence that measurements of central adiposity were more strongly associated with diabetes than was BMI in our cohort of women, but no evidence of such differences in our cohort of men. Associations with all-cause mortality were found only for measurements of central adiposity in the whole cohort. After the removal of participants with low BMI, however, we found linear associations of BMI with all-cause mortality.

Our findings with respect to CHD support those of several other prospective studies (including a previous analysis of incident CHD in CaPS phase 1 in men) (24–26). Some prospective studies have found evidence of stronger associations of abdominal adiposity measures with CHD than with BMI in women (27, 28) but not in men. These studies have generally been smaller than our study, particularly pertaining to our pooled results. A large, but prevalent (rather than prospective), case-control study found that WHR was more strongly associated with MI than with BMI in both men and women (adjusted hazard ratio, top compared with bottom quintile with both sexes combined: 1.12 for BMI and 1.75 for WHR) (5).

In BWWHS women, there was evidence to suggest that measures of central adiposity (WC and WHtR) were more strongly associated with diabetes risk than with BMI. It is possible that this may reflect ascertainment bias, with doctors being more likely to screen for diabetes in those women who are more centrally obese than other women. Some support for this is provided by the fact that, despite the stronger association of WC compared with BMI with future risk of diagnosis of diabetes in the BWHHS, the cross-sectional associations of different measurements of adiposity with fasting glucose and insulin (in the BWHHS, CaPS, and Boyd Orr) were all similar to one another. These findings are also consistent with similar cross-sectional analyses for fasting glucose and insulin in the British Regional Heart Study (14). There was some suggestive evidence that there were differences in the associations of waist measures (WC and WHtR) with diabetes between the BWHHS (all women) and CaPS (all men). It is possible that WC may be more strongly

associated with diabetes than with BMI in women but not in men. Other demographic and methodologic differences between the studies could explain the between-study difference, although we might then have anticipated similar differences between the studies for other outcomes. Given the fact that we used data from just 2 studies and made multiple comparisons in this review, the difference could have been due to chance. A recent meta-analysis of 32 studies found no overall difference between BMI, WC, and WHR in their association with incident diabetes (13) and showed no important differences between the sexes. However, the authors could only investigate heterogeneity in findings related to sex in a limited way because of the small numbers of studies in each group.

Recent findings from the prospective studies collaboration with >900,000 participants found positive linear associations of BMI from 22.5 with all-cause mortality, which are consistent with our findings (29). In the multicenter EPIC cohort study ($n \approx 360,000$ participants), BMI, WC, and WHR were all independently associated with all-cause mortality. The authors recommended the use of WC or WHR in addition to BMI for assessing risk of death; however, no direct comparisons of the magnitudes of associations between the different measures were made (4).

Our findings of slightly stronger associations of central adiposity measures with all-cause mortality might be explained by reverse causality, which is likely to affect BMI (because of general total-body muscle wasting and fat loss) more so than central adiposity (30). Whereas removal of the early years of follow-up should have reduced this effect, we may have had an insufficiently long follow-up to fully address this.

Study strengths and limitations

The strengths of this study were in the assessment of multiple outcomes and in the assessment of association in 4 independent studies. Information on all-cause mortality, CHD, and diabetes in CaPS and the BWHHS was prospectively ascertained for large numbers of men and women. In the Boyd Orr and Maidstone-Dewsbury studies, arterial plaque prevalence, an important preclinical measure of atherosclerosis (23), was assessed. One limitation of this review was that the populations under study were almost exclusively of European origin and were restricted to men and women older than 45 y. There were small amounts of missing data on covariables in 3 of the cohorts, with complete data available for 86–91% of the cohorts in the BWHHS, CaPS, and Maidstone-Dewsbury studies. We were unable to comment on more accurate measures for assessing general and visceral adiposity, such as computed tomography or magnetic resonance imaging. However, these methods are prohibitively expensive for widespread use in routine clinical or public health practice.

Implications and conclusions

On the basis of evidence from other studies regarding the poorer accuracy and reliability of measuring WC and hip circumference (7, 31, 32), we felt that associations of these with outcomes had to be considerably stronger than those of BMI for these to be proposed as alternatives in routine practice. We do not feel that this was shown in our results. Nonetheless, it is notable that BMI was not a stronger predictor of any outcomes than were

other measures, whereas measures of central adiposity had somewhat stronger associations with all-cause mortality and type 2 diabetes. Thus, further research regarding the role of centrally distributed adiposity, and indeed visceral adiposity, in disease outcomes is warranted.

An additional related question, which we have not attempted to address in this study, is whether measurements of regional adiposity would add value to the predictive ability of BMI in identifying those at risk of future cardiovascular disease. To assess this, one would need to show that BMI improves prediction (discrimination and reclassification of individuals) over and above established cardiovascular and type 2 diabetes risk factors and then further to demonstrate whether measures of regional adiposity improve prediction further. Future research with longer-term follow-up should be able to address this.

Currently, there does not appear to be strong evidence that measurements of waist or direct measurement of fat mass should replace BMI in routine public health surveillance or clinical practice.

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