Obesity and overweight in relation to disease-specific mortality in men with and without existing coronary heart disease in London: The original Whitehall study

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Abstract

Background: The few reports of the association of obesity and/or overweight with total and cardiovascular disease mortality in persons with existing coronary heart disease (CHD) reveal inconsistent findings. We sought to examine these relationships in both men with and without prevalent CHD in a prospective cohort study.

Methods: In the Whitehall study of London-based male government employees, 18,403 middle-age men were followed up for a maximum of 35 years having participated in a medical examination in the late 1960s in which weight, height, CHD status, and a range of other social, physiological and behavioural characteristics were measured.

Results: In age-adjusted analyses of men with baseline CHD there was a modest elevated risk in the overweight relative to normal weight groups for all-cause mortality (hazards ratio [95% CI]: 1.10 [1.00, 1.20]) and coronary heart disease mortality (1.28 [1.11, 1.47]), but not for stroke mortality (1.01 [0.73, 1.40]). Mortality rates were similarly raised in the obese group. While these slopes were markedly steeper in men who were apparently CHD-free at study induction, the difference in the gradients according to baseline CHD status did not attain statistical significance at conventional levels (p-value for interaction: $\geq$0.24). There was some attenuation of the weight–mortality relationships when potential mediating and confounding factors were added to the multivariable models in both men with and without a prior history of CHD.

Conclusions: Avoidance of obesity and overweight in adult life in both men with and without CHD may reduce their later risk of total and coronary heart disease mortality.

Introduction

In England,[1] as in other industrialised societies,[2] the decline in case fatality associated with acute coronary syndromes – seemingly attributable to advances in treatment – has led to an increased prevalence of coronary heart disease (CHD). In comparison with their disease-free counterparts, persons with existing CHD experience elevated rates of total mortality, recurrent CHD, and stroke.[3] There is therefore a need to identify risk factors for these health outcomes in individuals with prevalent CHD.

In large scale prospective cohort studies of individuals who are apparently healthy at study induction, obesity and overweight are established risk factors for total mortality,[4] CHD[5] and probably stroke.[6] In order to simplify data interpretation in studies in which CHD is the outcome of interest, investigators generally, although not always,[7;8] either exclude from their analyses persons with existing CHD at study induction[9;10] or make statistical adjustment for CHD status.[11] As a consequence, much less is understood about the influence, if any, of adiposity on these outcomes in individuals with a history of CHD.

We located five studies[12-16] with longer term follow-up (defined as ≥ one year) which had reported on the relation of obesity and/or overweight (as indexed by body mass index) with total mortality, cardiovascular disease, CHD and/or stroke (table 1) in persons with prevalent CHD. For all-cause mortality, findings are inconsistent with inverse,[14] 'U'-shaped,[12] and reverse 'J'-shaped[13;15;16] relations observed with adiposity. Results for weight and re-infarction are similarly discrepant such that positive,[12] null[14] and J-shaped[15] associations have been found. While only one study has examined the influence of adiposity on stroke risk in CHD patients,[15] effect estimates for the apparent null relation were not reported. This discordance in findings across studies may be attributable, at least in part, to limited statistical power in some studies owing to a low number of cases; variability in the definition of obesity and overweight across reports, so complicating comparison; and a failure in some studies to adjust for potentially important covariates in the weight–mortality relation, particularly socioeconomic position.[17]

Extended mortality surveillance of the Whitehall study cohort affords us the opportunity to address these issues of data paucity and methodological shortcomings. Taking place in the late 1960s, over eighteen thousand middle-aged London-based government employees participated in a medical examination in which CHD status, body mass index, and a range of covariate data were assessed.[18] For the purposes of comparison, in the present analyses we present the obesity–mortality gradients separately in men with and without baseline CHD.

Methods

In the Whitehall study, data were collected on 18,403 non-industrial London-based male government employees aged from 40 to 64 years when examined between September 1967 and January 1970, representing a 74% response. This involved the completion of a study questionnaire and participation in a medical examination, both of which have been described in detail elsewhere.[18] In brief, the questionnaire included enquiries regarding civil service employment grade (an indicator of socio-economic position), smoking habits, chronic bronchitis, marital status, physical activity, unexplained weight loss in the preceding year, physician-

diagnosed heart problems or high blood pressure, the use of drug therapy for high blood pressure, and family history of CHD (one third of subjects only). Forced expiratory volume in one second (FEV_1) adjusted for height,[19] fasting plasma cholesterol, post challenge two hour blood glucose and blood pressure were determined using standardised protocols.

Ascertainment of obesity and overweight

Height was measured with the subject wearing shoes and standing with his back to a measuring rod; readings were taken to the nearest ½ in. (approximately 12.7 mm) below.[18] Weight was recorded with the participant wearing shoes but with jacket removed; readings were taken to the nearest ½ lb (227g).[18] Following conversion from imperial to metric units, body mass index (BMI) (weight [kg] divided by height squared [m^2]) was computed. Using this index of adiposity, we defined normal weight (18.5–<25.0 kg/m^2), overweight (25.0–29.99 kg/m^2) and obesity (≥ 30.0 kg/m^2) according to criteria advanced by the World Health Organisation.[20] We excluded 3 men with missing data for height and weight and a further 220 men in the underweight category (<18.5 kg/m^2) because there were too few subjects with CHD (N=47) to facilitate meaningful analyses. Using these classifications, we,[21] and others,[22;23] have recently reported on the link between weight and organ-specific cancers.

Ascertainment of CHD

For the purpose of these analyses, the presence of CHD was defined on the basis of a resting electrocardiogram (ECG) and/or self-report.[24] The ECG was regarded as positive for CHD if Q/QS items (codes 1.1-3), ST/T items (codes 4.1-4 or 5.1-3) or left bundle branch block (code 7.1) were present. All traces were double coded by trained technicians[25] according to the Minnesota system[26] with adjudication by a physician if dispute arose. Self-reported CHD was defined as a positive response to the Rose angina questionnaire[27] or a report of severe pain across the front of the chest lasting for half an hour or more. These various assessments of existing CHD, approved by the World Health organisation,[26;28] have been shown to be strongly predictive of CHD mortality in the present cohort.[29] CHD status was unknown on 162 men who were excluded from all analyses.

Ascertainment of mortality

The records of study participants were traced and flagged using the procedures of the National Health Service Central Registry (NHSCR) until 31st December 2002. Among decedents, 91.6% of death certificates were coded according to the eighth revision of the International Classification of Diseases (ICD),[30] 7.0% according to the ninth revision[31] and 1.4% according to the tenth revision.[32] Deaths were classified as CHD (ICD8/9: 410-414; ICD10: I20-I25), stroke (ICD8/9: 430-438; ICD10: I60-I69), cardiovascular disease (ICD8/9: 390-458; ICD10: I00-I99) or non-cardiovascular disease (all other deaths with specified cause).

Data manipulation and statistical analyses

In the present study, existing disease at study entry was defined as a positive response to enquiries regarding a range of health conditions: intermittent claudication, physician-diagnosed heart problems or high blood pressure (one question), dyspnoea, and bronchitis. Further, men with diabetes comprised those who gave a positive response to the questionnaire enquiry: "are you, or have you been, diabetic?", or those who had blood glucose level two hours after the glucose load of ≥11.1 mmol/l (≥200 mg/100ml). A blood glucose of 5.4 to 11.0 mmol/l (96 to 199 mg/100ml) was used to designate participants with impaired glucose tolerance (IGT), with all

remaining men were termed normoglycaemic.[19;33] Persons who, according to the questionnaire enquiry, had declared themselves to be diabetic did not undergo a blood glucose test. Using these data on diabetes, we created three covariates: one each to indicate the presence of diabetes or IGT, and another (continuous) variable for blood glucose level in normoglycaemics in which persons with diabetes or IGT were denoted zero. Similarly, smoking status was grouped into four categories (never, ex-smoker, current pipe or cigar smoker, current cigarette smoker) together with additional adjustment for the number of cigarettes smoked per day in current smokers. An indicator variable for whether or not the study participant had any first degree relatives (parents, siblings or children) with heart disease was also created. Finally, during the baseline study, the physical activity enquiries on the questionnaire were modified. Levels of this behaviour were therefore determined from either an item about travel activity[34] (administered to approximately the first two-thirds of study participants) or from leisure activities[35] (administered to the remainder). Analyses of the weight–mortality relation indicated that there was no confounding effect due to questionnaire type.

The vital status of 17,868 men (99% of those available for analysis) was ascertained; 16,996 (95.1%) of these had full baseline data. In analyses of baseline characteristics according to presence of CHD at study induction and also level of obesity and overweight, the prevalence of the baseline characteristics were adjusted for age (5 year age groups) by the direct standardisation method. Differences and trends in proportions were tested for statistical significance using the Mantel-Haenszel test. For continuous variables, least squares means were used to present the age-adjusted means and tests for differences between the CHD groups and trends across obesity, overweight and normal weight groups were computed by fitting a CHD group term and a linear trend term respectively.

Hazard ratios and accompanying confidence intervals were computed for the relation of obesity and overweight with each mortality outcome using Cox's proportional hazards regression model[36] with follow-up period as the time scale. These models were initially adjusted for age and then for other potential covariates. P-values for trends in effect estimates across the weight categories were also calculated. For the purposes of statistical adjustment, age, plasma cholesterol, height-adjusted FEV_1,[19] systolic and diastolic blood pressure and blood glucose in normoglycaemics were fitted as continuous variables; while unexplained weight loss in the last year (2 levels), employment grade (5), marital status (4), blood pressure-lowering medication (2), physical activity (6) and disease at study entry (2) were fitted categorically. All statistical analyses were conducted using SAS computer software (SAS Institute Inc., 1989).

Results

In table 2 the baseline characteristics of men with and without prevalent CHD at study induction are presented. As expected, men with CHD had less favourable characteristics. Thus, they were older, had higher cholesterol and blood pressure levels and poorer lung function than their disease-free co-workers. Men with CHD were also more likely to be physically inactive, smoke cigarettes, be without a partner, and reported having experienced unintentional weight loss in the preceding year, although differences according to CHD status was not substantial. They were also more likely to carry a morbid load other than CHD as evidenced by the increased prevalence of blood pressure-lowering medication use and IGT.

In table 3 we present the relation (age-adjusted) of obesity and overweight with baseline characteristics in men with and without CHD. Men with obesity and overweight comprised 4.2% (N=711 men) and 41.5% (N=7048 men) of the analytical sample, respectively. In general, unfavourable levels of most characteristics were apparent in the higher weight categories in both men with and without CHD at induction. The morbid load of overweight and obese men – according to disease at entry, glucose intolerance and diabetes – was generally raised in comparison to their normal weight colleagues. In comparison to the obese, leaner men were also younger, had lower plasma cholesterol and blood pressure levels, were more active, and were less likely to be employed in a low grade job. By contrast, there was a reduced prevalence of smokers in the overweight and obese men. The relations of obesity and overweight to five mortality endpoints in men with and without baseline CHD are depicted in table 4. A total of 10,845 men (64%) had died (8886 without baseline CHD; 1959 with baseline CHD) during a maximum of 35 years follow-up. Following age-adjustment in men with CHD, a modest elevated risk in the overweight groups relative to the normal weight was apparent for all-cause (1.10; 1.00,1.20), cardiovascular disease (1.27; 1.13, 1.43) and CHD mortality (1.28; 1.11, 1.47), but not for non-cardiovascular disease (0.88; 0.77, 1.02) or stroke (1.01; 0.73, 1.40). The number of cases in the stroke analyses was low, however. In general, in men with CHD, the point estimates were similar in the obese and overweight groups. Hazard ratios for these outcomes were similar in men with obesity.

In men with no evidence of baseline CHD, there was a positive association between weight and each outcome in an age-adjusted analysis. The magnitude of these relations was typically higher than in analyses featuring men with baseline CHD. The elevated risk was largely evident in obese men for all-causes ($HR_{\text{obese cf. normal weight}}$; 95% CI: 1.53; 1.39, 1.69), stroke (1.64; 1.17, 2.28), and non-cardiovascular disease (1.24; 1.08, 1.44), while for cardiovascular disease and CHD there was a suggestion of an incremental effect across the weight categories. On comparing gradients across mortality outcomes according to baseline CHD status, these differences did not reach statistical significance at conventional levels in any of the analyses (P for interaction$\geq$ 0.24). In both men with and without CHD, with the exception of non-cardiovascular disease, the relation of each endpoint with weight was partially attenuated following adjustment for covariates. In general, control for potential mediating variables (e.g., systolic and diastolic blood pressure and plasma cholesterol) rather than potential confounding variables (e.g., employment grade and physical activity) was responsible for this attenuation.

Our definition of CHD comprised both positive responses to items on the Rose questionnaire and ECG measurement. That the former is self-reported raises concerns about validity. We therefore examined the effect on our results, if any, of confining our analyses to men with only positive findings for the latter. A similar pattern of association was seen to that apparent when the all-inclusive definition was used. Given that some men in the normal weight group may have experienced weight loss because of existing medical conditions other than CHD, we first re-computed our analyses after dropping deaths occurring within the first 10 years of mortality surveillance. In so doing we reasoned that persons with serious illness would have died during this time frame. We hypothesised that this approach would have the effect of lowering the mortality rate in the normal weight group and therefore strengthen the overall positive relationship between weight and mortality. In addition, we fitted interaction terms for the BMI

categories with the logarithm of the follow-up time, expecting the positive weight–mortality relation to increase in magnitude with follow-up time. Both these hypotheses were supported in men with and without CHD at study induction, although the interaction terms were only statistically significant at conventional levels ($p \leq 0.05$) for the overweight category in men without baseline CHD for all-cause and non-cardiovascular disease mortality (data not shown).

Discussion

The main finding of the present study of men with baseline CHD was an elevated rate of all-cause, cardiovascular disease, and CHD mortality in the overweight and obese groups. There was, however, no apparent relation between weight and stroke risk, although the number of cases was low in this analysis. As expected, in men who were apparently CHD-free at study induction, obesity and overweight were positively related to each of these endpoints. While the gradients were somewhat steeper in this group, they were not significantly different to those apparent in men with baseline CHD.

Comparison with other studies

The elevated rates of total mortality,[4] and CHD,[5] and probably stroke[6] in overweight or obese men without prevalent CHD are generally consistent across large scale prospective studies and accord with the findings herein. By observing attenuation in these associations following adjustment for mediating variables but not confounding variables, we found support for the suggestion[5] that some of the weight–mortality effect may be ascribed to the relation of increased weight with other risk indices for mortality such as raised blood pressure and plasma cholesterol levels. We were, however, unable to examine the suggestion made recently that the influence of obesity and overweight on mortality risk may also be partially mediated via other health indices such as hyperinsulinemia and hyperleptinemia.[37]

In persons with a history of CHD, studies of the relation of weight and the mortality outcomes reported herein are, as discussed, rather discrepant (table 1). While we found a positive BMI-total mortality gradient, Ness et al. reported an reverse 'J'-shaped relation,[16] which has been replicated elsewhere.[13] Similarly, a positive overweight/obesity–CHD gradient has been observed in some,[12] but not all,[14] studies. In the only report to examine the link between BMI and stroke in men with ischaemic heart disease,[15] there was little evidence of an effect, supporting the results of the present analyses. That we found that obesity/overweight was a predictor of CHD but not stroke mortality in men with prevalent CHD could indicate differences in the functions of coronary and cerebral arteries.

Alternative explanations

Confounding, bias, and chance may plausibly explain the associations reported herein. We incorporated a wide range of social, behavioural, and physiological variables into our statistical models so minimising confounding as a likely explanation. The loss to follow-up in this cohort study was low, so also reducing concerns regarding selection bias. In the present analyses we necessarily conducted a large number of statistical tests (there were a total of 5 mortality outcomes in men with and without prevalent CHD). It is therefore conceivable that some of the present results could have arisen by chance alone. While we explored the effect of reverse causality due to both measured and unmeasured disease, given that the weight–mortality

gradients were all positive, rather than inverse, this would not have accounted for such associations.

Study strengths and limitations

The strengths of the present study include its size; its prospective design; the measurement of a range of covariate data including socio-economic position; and the definition of obesity and overweight which matches WHO criteria.[20] This study is not, however, without its weaknesses. The assessment of obesity/overweight was based on BMI, a widely used index of overall adiposity but one that does not provide an indication of fat distribution. Although skinfold thickness was measured in the Whitehall study participants, readings were only taken at the triceps, so rendering the data of little practical use. The cardiovascular disease outcomes reported herein were based on mortality surveillance. Thus, our results reflect the combined effect of weight on survival and incidence. It is unclear if a differential association by endpoint definition might exist as we do not have data on non-fatal events with which to make such a comparison.

In conclusion, the present study found support for an elevated risk of mortality from all-cause, cardiovascular disease, CHD and stroke in obese/overweight men who were CHD-free at study induction. With the exception of stroke mortality, similar patterns of association were apparent in men with existing CHD. Becoming overweight or obese in middle-aged men with or without CHD should be avoided.

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Contributions

David Batty generated the idea for this paper and wrote the first draft on which all authors commented. Elizabeth Breeze and Martin Shipley updated the mortality data. Martin Shipley conducted all data analyses, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1. Studies examining the relation of obesity and overweight with longer term mortality, recurrent CHD and stroke in persons with existing CHD

Study name[reference number]	**Study description**	**Outcome**	**Main findings**
Physicians' Health Study[13]	5010 men (age not reported) with self-reported CHD or stroke. BMI categorised into 4 groups.	913 deaths comprising 703 cardiovascular disease deaths after mean of 5 yr. surveillance.	Reverse 'J'-shaped relation of BMI groups with total and cardiovascular disease mortality.
Group Health Cooperative[15]	2677 men and women aged 30 to 79 yr. with a hospital admission for myocardial infarction (MI). BMI categorised into quintiles.	431 deaths; 445 reinfarctions (fatal and non-fatal); 124 strokes (fatal or non-fatal) after mean of 3.4 yr. surveillance.	Relation of BMI with CHD was 'J'-shaped; null with stroke (estimates not reported); and reverse 'J'-shaped with total mortality.
Diet and Reinfarction Trial[16]	2033 men (age not reported) with a hospital discharge record for MI. BMI categorised into quartiles.	1083 deaths comprising 739 CHD deaths after up to 17 yr surveillance.	Reverse 'J'-shaped relation of BMI with total and CHD mortality
Group Health Cooperative[12]	691 women aged 66.2 yr. (mean) with a hospital discharge record for MI. BMI categorised into 'thin', 'normal weight', 'overweight' and 'obese'.	166 deaths & 127 reinfarctions (fatal and non-fatal) after up to 13 yr surveillance.	BMI positively related to re-infarction. BMI-total mortality association 'U'-shaped.
San Diego and Vancover study[14]	1760 men and women (age & sex-distribution reported) with a hospital admission for acute MI. BMI categorised into 'normal weight', 'overweight' and 'underweight'.	Mortality and re-infarction after 12 months (numbers not reported).	Relation of BMI categories inverse for mortality and null for re-infarction.

Note: all studies utilise a cohort design; assessment of obesity and overweight is based on BMI; follow-up is at least 1 year post study recruitment.

Table 2. Baseline characteristics[a] in men with and without prevalent CHD at baseline

	Without baseline CHD	With baseline CHD	P-value
Number (%)	14,400 (84.7)	2596 (15.3)	
	Mean (standard error)		
Age (yr.)	51.2 (0.1)	53.2 (0.1)	<0.001
Plasma cholesterol (mmol/l)	5.10 (0.01)	5.19 (0.02)	<0.001
FEV_1[b](l/sec)	3.16 (0.01)	3.04 (0.01)	<0.001
Systolic blood pressure (mmHg)	135.5 (0.2)	139.7 (0.4)	<0.001
Diastolic blood pressure (mmHg)	84.1 (0.1)	86.9 (0.3)	<0.001
Blood glucose[c] (mmol/l)	4.06 (0.01)	4.06 (0.01)	0.98
	Percent (standard error)		
Physically inactive	15.8 (0.3)	17.3 (0.8)	0.03
Unintentional weight loss in last yr	1.9 (0.1)	2.6 (0.3)	0.02
Current cigarette smoker	40.5 (0.4)	42.6 (1.0)	0.02
Low work grade	23.0 (0.3)	25.2 (0.8)	0.01
No partner	11.5 (0.3)	13.0 (0.7)	0.06
Disease at study entry[d]	6.6 (0.2)	25.0 (0.8)	<0.001
Blood pressure-lowering medication	1.1 (0.1)	4.1 (0.4)	<0.001
Glucose intolerance[c]	5.0 (0.2)	6.9 (0.5)	<0.001
Diabetic[d]	1.3 (0.1)	1.5 (0.2)	0.43
Family history of CHD[e]	12.7 (0.5)	16.3 (1.3)	0.003

[a]Adjusted for age (age is unadjusted)
[b]FEV_1 is forced expiratory volume in one second (adjusted for height)
[c]Data available for normoglycaemic men only
[d]See methods section for definition
[e]Assessed in a subset of 6287 men only.

Table 3. Obesity and overweight in relation to baseline characteristics[a]

	Without baseline CHD (N=14,400)					With baseline CHD (N=2596)			
	Normal weight	**Overweight**	**Obese**	**P-value for trend**		**Normal weight**	**Overweight**	**Obese**	**P-value for trend**
Number (%)	7901 (54.9)	5916 (41.1)	583 (4.0)			1336 (51.5)	1132 (43.6)	128 (4.9)	
Mean (standard error)									
Age (yr.)	50.8 (0.1)	51.7 (0.1)	52.1 (0.3)	<0.001		52.6 (0.2)	53.8 (0.2)	54.7 (0.5)	<0.001
Plasma cholesterol (mmol/l)	5.01 (0.01)	5.21 (0.02)	5.14 (0.05)	<0.001		5.14 (0.03)	5.24 (0.04)	5.25 (0.11)	0.06
FEV_1[b](l/sec)	3.15 (0.01)	3.17 (0.01)	3.10 (0.02)	0.19		3.00 (0.02)	3.08 (0.02)	3.09 (0.05)	<0.001
Systolic blood pressure (mmHg)	132.5 (0.2)	138.2 (0.3)	147.3 (0.8)	<0.001		136.1 (0.5)	142.3 (0.7)	155.6 (1.8)	<0.001
Diastolic blood pressure (mmHg)	132.5 (0.2)	138.2 (0.3)	147.3 (0.8)	<0.001		136.1 (0.5)	142.3 (0.7)	155.6 (1.8)	<0.001
Blood glucose[c](mmol/l)	4.06 (0.01)	4.07 (0.02)	4.11 (0.0.02)	0.03		4.06 (0.02)	4.06 (0.02)	4.10 (0.05)	0.72
Percent (standard error)									
Physically inactive	15.0 (0.4)	15.8 (0.5)	24.4 (1.8)	<0.001		16.4 (1.0)	17.8 (1.2)	19.2 (3.4)	0.18
Unintentional weight loss in last yr	2.9 (0.2)	0.9 (0.1)	0.0 (-)	<0.001		3.9 (0.5)	1.2 (0.4)	1.7 (1.2)	<0.001
Current cigarette smoker	43.5 (0.6)	37.2 (0.6)	36.7 (2.0)	<0.001		47.2 (37.7)	37.7 (1.5)	40.1 (5.4)	<0.001
Low work grade	22.9 (0.5)	22.6 (0.5)	29.2 (1.8)	0.08		25.2 (1.1)	24.3 (1.3)	32.9 (3.8)	0.46
No partner	12.2 (0.4)	10.4 (0.4)	14.1 (1.5)	0.09		13.5 (1.0)	12.0 (1.0)	13.7 (2.8)	0.73
Disease at study entry[d]	6.0 (0.3)	7.1 (0.3)	9.8 (1.2)	<0.001		24.4 (1.2)	25.1 (1.3)	28.7 (3.8)	0.31
Blood pressure-lowering medication	0.8 (0.1)	1.4 (0.2)	1.0 (0.4)	0.004		3.5 (0.5)	4.5 (0.6)	6.8 (2.1)	0.04
Glucose intolerance[d]	4.4 (0.2)	5.5 (0.3)	7.1 (1.0)	<0.001		6.1 (0.7)	7.2 (0.8)	11.2 (2.6)	0.02
Diabetic[d]	1.2 (0.1)	1.2 (0.1)	1.6 (0.5)	0.83		1.1 (0.3)	1.5 (0.4)	4.0 (1.6)	0.01
Family history of CHD[e]	12.1 (0.6)	13.7 (0.8)	10.8 (1.9)	0.40		15.8 (1.7)	17.1 (2.1)	12.5 (4.2)	0.91

[a]Adjusted for age (age is unadjusted)
[b]FEV_1 is forced expiratory volume in one second (adjusted for height)
[c]Data available for normoglycaemic men only
[d]See methods section for definition
[e]Assessed in a subset of 6287 men only.

Table 4. Mortality rates and hazard ratios for selected mortality outcomes in relation to obesity and overweight in men with and without prevalent CHD at baseline in the original Whitehall study

Mortality outcome		Without baseline CHD (N=14,400)				With baseline CHD (N=2596)				
		Normal weight	Overweight	Obese	P–value for trend	Normal	Overweight	Obese	P for trend	P-value for interaction[e]
Numbers of subjects		7901	5916	583		1336	1132	128		
All causes	Number of deaths	4639	3807	440		955	895	109		
	Mortality rate[b] (age adjusted)	25.7	26.7	34.6		32.9	36.0	39.2		
	Hazard ratios (95% CI) – age adjusted	1.0 (ref)	1.06 (1.02, 1.11)	1.53 (1.39, 1.69)	<0.001	1.0 (ref)	1.10 (1.00, 1.20)	1.28 (1.05, 1.57)	0.005	0.95
	Hazard ratios (95% CI) – confounder adjusted[c]	1.0	1.08 (1.03, 1.13)	1.55 (1.41, 1.71)	<0.001	1.0	1.16 (1.05, 1.27)	1.32 (1.08, 1.62)	<0.001	0.31
	Hazard ratios (95% CI) – multiply adjusted[e]	1.0	1.00 (0.96, 1.04)	1.33 (1.20, 1.47)	0.004	1.0	1.10 (1.00, 1.21)	1.13 (0.92, 1.39)	0.05	0.24
CVD[f]	Number of deaths	2032	1839	241		517	562	62		
	Mortality rate (age adjusted)	11.3	12.9	19.4		17.9	22.5	22.2		
	Hazard ratios (95% CI) – age adjusted	1.0	1.17 (1.10, 1.24)	1.91 (1.67, 2.19)	<0.001	1.0	1.27 (1.13, 1.43)	1.31 (1.01, 1.71)	<0.001	0.78
	Hazard ratios (95% CI) – confounder adjusted[c]	1.0	1.18 (1.11, 1.26)	1.94 (1.70, 2.22)	<0.001	1.0	1.32 (1.17, 1.49)	1.35 (1.04, 1.77)	<0.001	0.83
	Hazard ratios (95% CI) – multiply adjusted[e]	1.0	1.03 (0.97, 1.10)	1.52 (1.32, 1.74)	<0.001	1.0	1.22 (1.08, 1.38)	1.08 (0.82, 1.42)	0.02	0.80
CHD	Number of deaths	1279	1183	159		361	394	45		
	Mortality rate (age adjusted)	7.0	8.3	10.2		12.4	15.7	16.3		
	Hazard ratios (95% CI) – age adjusted	1.0	1.20 (1.11, 1.30)	1.98 (1.68, 2.34)	<0.001	1.0	1.28 (1.11, 1.47)	1.34 (0.99, 1.84)	<0.001	0.67
	Hazard ratios (95% CI) – confounder adjusted[c]	1.0	1.21 (1.12, 1.31)	2.00 (1.70, 2.36)	<0.001	1.0	1.34 (1.16, 1.55)	1.40 (1.02, 1.92)	<0.001	0.99
	Hazard ratios (95% CI) – multiply adjusted[e]	1.0	1.07 (0.98, 1.16)	1.61 (1.36, 1.90)	<0.001	1.0	1.24 (1.07, 1.44)	1.13 (0.82, 1.56)	0.02	0.91
Stroke	Number of deaths	381	336	38		79	68	7		
	Mortality rate (age adjusted)	2.2	2.4	3.2		2.7	2.8	2.3		
	Hazard ratios (95% CI) – age adjusted	1.0	1.11 (0.96, 1.29)	1.64 (1.17, 2.28)	0.01	1.0	1.01 (0.73, 1.40)	1.06 (0.49, 2.31)	0.90	0.30
	Hazard ratios (95% CI) – confounder adjusted[c]	1.0	1.13 (0.97, 1.31)	1.70 (1.22, 2.39)	0.005	1.0	0.98 (0.70, 1.36)	1.06 (0.48, 2.30)	0.98	0.36
	Hazard ratios (95% CI) – multiply adjusted[e]	1.0	0.96 (0.83, 1.12)	1.25 (0.89, 1.76)	0.73	1.0	0.87 (0.62, 1.22)	0.78 (0.35, 1.73)	0.35	0.30
Non-CVD	Number of deaths	2590	1957	197		434	327	46		
	Mortality rate (age adjusted)	14.4	13.8	15.2		14.9	13.3	16.9		
	Hazard ratios (95% CI) – age adjusted	1.0	0.98 (0.92, 1.04)	1.24 (1.08, 1.44)	0.38	1.0	0.88 (0.77, 1.02)	1.26 (0.93, 1.70)	0.69	0.53
	Hazard ratios (95% CI) – confounder adjusted[c]	1.0	1.00 (0.94, 1.06)	1.27 (1.09, 1.46)	0.12	1.0	0.95 (0.82, 1.10)	1.29 (0.95, 1.75)	0.68	0.85
	Hazard ratios (95% CI) – multiply adjusted[e]	1.0	0.98 (0.92, 1.04)	1.19 (1.02, 1.38)	0.52	1.0	0.96 (0.82, 1.11)	1.23 (0.90, 1.69)	0.74	0.69

[a]Forty-one men with unknown cause of death have been excluded from the cause specific analyses

[b]Mortality rates are expressed per 1000 person-years

[c]Confounder adjusted model adjusted for the following: age, employment grade, physical activity, smoking habit, marital status, disease at entry and weight loss in the last year

[e]Multiply adjusted model adjusted for all potential confounding variables (as above) and the following: blood pressure-lowering medication, height-adjusted FEV_1, systolic blood pressure, diastolic blood pressure, plasma cholesterol, blood glucose (in normoglycaemics), glucose intolerance and diabetes status

[e]compares differences, if any, in the BMI–mortality slopes according to baseline CHD status

[f]cardiovascular disease