RESEARCH REPORT

Skinfold thickness, body mass index, and fatal coronary heart disease: 30 year follow up of the Northwick Park heart study

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Study objective: To examine the effect of baseline body mass index (BMI) and skinfold thickness (ST) on fatal coronary heart disease (CHD) and all cause mortality after 30 years of follow up.

Design: Prospective cohort study.

Setting: Northwick Park heart study (NPHS) designed to investigate the role of haemostatic variables on CHD.

Participants: 1511 men and 691 women enrolled in NPHS aged 40 to 64 years at entry.

Main results: Baseline BMI (kg/m^2) and forearm, triceps, subscapular, and suprailiac skinfolds ST (mm) were measured. Cox regression was used to calculate hazard ratios for fatal CHD and total mortality for each standard deviation unit increase in obesity adjusting for age, smoking status, total cholesterol, systolic blood pressure, fibrinogen, and factor VII activity. Subjects experienced 250 fatal CHDs and 819 all cause deaths over 30 years (median: 26 years; IQR: 22–28 years). Among men, only BMI ($\text{RR}=1.29$, $95\%\text{CI}=1.12$ to 1.49) significantly increased the risk of fatal CHD. Among women, BMI ($\text{RR}=1.48$, $95\%\text{CI}=1.07$ to 2.06), as well as, subscapular ($\text{RR}=1.65$, $95\%\text{CI}=1.19$ to 2.30), forearm ($\text{RR}=1.46$, $95\%\text{CI}=1.08$ to 1.97), and triceps ($\text{RR}=1.63$, $95\%\text{CI}=1.12$ to 2.39) skinfolds were predictive of fatal CHD. None of the estimates for all cause mortality were significant except for subscapular skinfold in women ($\text{RR}=1.20$, $95\%\text{CI}=1.02$ to 1.42). There was no evidence of interaction between obesity and sex for fatal CHD or all cause death. The effect of obesity on fatal CHD or all cause deaths does not seem to be mediated substantially by cholesterol, systolic blood pressure, or haemostatic variables.

Conclusions: BMI is an important risk factor for fatal CHD where its prognostic significance remains after up to 30 years of follow up.

Obesity is a known risk factor for coronary heart disease (CHD) and death resulting from CHD.¹ Body mass index (BMI) has been commonly used as an index of obesity in epidemiological research because of its wide availability and high correlation with percentage body fat.² Since the discovery that centrally distributed body fat is an important risk factor for CHD events, skinfold thickness, and waist to hip ratio have also been used as a measure of central obesity.³

The Northwick Park heart study (NPHS) was started in 1972 to study the role of haemostatic variables in the development of CHD.⁴ An earlier paper⁵ published in 1989 examined the role of haemostatic variables and the association of skinfold thickness at four sites, BMI, and other cardiovascular risk factors with CHD events. Because of the limited number of events among women and in ethnic minorities, the paper only reported data from white men, aged 40 to 64 years at entry with up to six years of follow up ($n=1511$). BMI was more strongly predictive than the skinfold measures considered: for each standard deviation unit (3 kg/m^2) increase in BMI, there was a 44% increase in relative risk for fatal or non-fatal CHD. Furthermore, there was a persistent association between BMI and fatal or non-fatal CHD even when other known risk factors, such as blood pressure, cholesterol, and haemostatic variables, were taken into account. Consistent with the hypothesis that central obesity increases the risk of CHD events, subscapular skinfold was found to be closely associated with CHD related death; for each 7 mm increase in skinfold thickness, there was a 25% increase in fatal or non-fatal CHD.

To further examine the relation between obesity, haemostatic variables, and fatal outcomes over a longer period, we present in this report results of the NPHS that now include up to 30 years of follow up of the original cohort of 1511 men, as well as previously unreported results for 691 women who were recruited at the same time as the men.

METHODS

The NPHS is a prospective cohort study designed to investigate the role of haemostatic variables on the risk of acute thrombotic events associated with CHD.⁴ Details of the NPHS are reported elsewhere.⁶ Briefly, a total of 3452 subjects (2413 men, 1039 women) were recruited between 1972 and 1978 from three occupational groups in north west London (a food processing factory, post office and communications staff, and local government staff). The overall response rate among potential participants was about 80%.

Subjects underwent standardised interviews by trained nurses who collected information on the demographic characteristics of participants and cardiovascular risk factors including cigarette smoking. Fibrinogen, factor VII, and cholesterol were assayed using previously described methods.⁴ Blood pressure measurements were obtained using a standard sphygmomanometer before and after venipuncture, and the mean of the two readings was used as the final

Abbreviations: NPHS, Northwick Park heart study; BMI, body mass index; ST, skinfold thickness; CHD, coronary heart disease; TAR, trunk to arm skinfold ratio

Table 1 Measures of obesity at baseline by fatal CHD, all cause mortality and sex

	Men				Women			
	Fatal CHD		All cause mortality		Fatal CHD		All cause mortality	
Obesity measure	Yes (n = 216)	No (n = 1295)	Yes (n = 641)	No (n = 870)	Yes (n = 34)	No (n = 657)	Yes (n = 178)	No (n = 513)
BMI (kg/m ²)	26.4 (3.0)	25.4 (2.9)	25.6 (3.1)	25.5 (2.9)	26.0 (4.1)	24.7 (3.5)	25.5 (3.8)	24.6 (3.4)
Forearm (mm)	6.1 (2.0)	5.9 (2.2)	5.8 (2.0)	6.0 (2.3)	9.8 (4.5)	8.5 (3.4)	9.0 (3.8)	8.4 (3.4)
Triceps (mm)	10.3 (4.0)	9.8 (3.8)	9.7 (3.8)	10.0 (3.9)	21.2 (6.9)	19.7 (6.5)	20.3 (6.5)	19.6 (6.6)
Subscapular (mm)	18.3 (6.8)	16.4 (6.3)	16.8 (6.7)	16.7 (6.2)	19.8 (10.5)	17.1 (7.9)	18.4 (8.8)	16.8 (7.7)
Suprailiac (mm)	14.2 (7.0)	13.1 (6.5)	12.7 (6.4)	13.7 (6.6)	16.5 (8.5)	16.2 (8.4)	17.1 (9.3)	15.9 (8.0)
TAR	2.02 (0.64)	1.9 (0.6)	1.93 (0.61)	1.93 (0.57)	1.17 (0.40)	1.20 (0.45)	1.22 (0.45)	1.19 (0.45)

Mean (standard deviation) reported for each obesity measure. Trunk to arm skinfold ratio (TAR) defined as (subscapular + suprailiac)/(triceps + forearm).

measure. Information on history of CHD was gathered through physician interview.

Skinfold thickness was measured at four sites—forearm, triceps, subscapular, and suprailiac—using Holtain skinfold callipers while the patient was standing.⁷ For each skinfold measure, a skinfold of about 1.5 cm in depth was picked up between the thumb and forefinger and the calliper jaws applied. Triceps skinfold was measured halfway between the inferior border of the coracoid process and the tip of the olecranon process. The forearm skinfold was picked up on the lateral aspect of the forearm at the midpoint of the radius. The subscapular skinfold was measured at a 45° angle to the vertical parallel to the medial edge of the scapula and just above the iliac crest in the mid-axillary line. Weight and height were measured on a Stephen's beam balance that included a height attachment while the subject was wearing light clothing. BMI (kg/m²) was calculated using height and weight measured at baseline.² An index of central obesity, trunk to arm skinfold ratio (TAR), was calculated by dividing the sum of the subscapular and suprailiac skinfolds by the sum of the triceps and forearm skinfolds. Correlations between the skinfold measures used in the NPHS have been reported previously.⁷

Because of the limited number of fatal CHD events among ethnic minorities enrolled in the NPHS cohort, as well as subjects under the age of 40, we restricted our analysis to white men and women aged 40 to 64 years at entry. Follow up for death attributable to CHD was performed through the NHS Central Registry as previously described.⁴ We have only considered the occurrence of fatal CHD because data on non-fatal episodes ended in 1984. Subjects with a known history of CHD at entry to the study were excluded. Follow up for fatal outcomes was assessed through May 2003. In total, data from 1511 men and 691 women were included in the analysis.

Statistical analysis

For each obesity measure, Cox regression was used to calculate the relative risk of fatal CHD and all cause mortality occurring up to 30 years of follow up. When proportionality of the hazard function was assessed by including the obesity measures as a time dependent term in the Cox models, it was

found to be satisfactory for all six obesity measures. To evaluate the individual contribution of each covariate on the relative risk estimates, covariates were added sequentially: age, smoking status, total cholesterol, systolic blood pressure (SBP), fibrinogen, and factor VII activity.

In most analyses, BMI and skinfold measures were analysed in fourths to avoid assumptions of linearity. BMI was represented in fourths of its distribution, rather than through the widely used World Health Organisation defined cut off points for obesity, because of the comparatively small number of events in subjects with BMI less than 18 kg/m² or greater than 30 kg/m². Where BMI and skinfold thickness measures are represented as continuous variables, the coefficients of interest can be interpreted as the change in relative risk associated with one standard deviation unit of the exposure. Possible interaction between sex and each measure of obesity was assessed based on an a priori basis.⁸ All statistical analyses were performed using Stata (version 8.2, College Station, TX, USA).

RESULTS

A total of 1511 men and 691 women were followed for up to 30 years from baseline (median 26 years; IQR 22 years–28 years). The average BMI was 25.5 kg/m² (SD 3.0 kg/m²) in men and 24.8 kg/m² (SD 3.5 kg/m²) in women. Men experienced 216 fatal CHD events and 641 all cause deaths, while women experienced 34 fatal CHD events and 178 all cause deaths. The crude mortality rate for fatal CHD was 6.3 per 1000 person years in men and 2.0 per 1000 person years in women. The all cause mortality rate was 18.6 per 1000 person years in men and 10.3 per 1000 person years in women.

We found that cases of fatal CHD consistently had higher rates of obesity compared with non-cases, with the exception of TAR in women (table 1). Differences in obesity measures between cases and non-cases for all cause mortality were less consistent than those for fatal CHD.

Crude and adjusted relative risk estimates for fatal CHD are shown in table 2, where each obesity measure is represented as a continuous variable. Among the obesity measures considered, BMI was the only measure significantly pre-

Table 2A Effect of adding covariates to the relative risk of fatal CHD for each standardised unit of obesity measure in men

Model	Variable added	BMI	Forearm	Triceps	Subscapular	Suprailiac	TAR
1	Unadjusted	1.36 (1.20,1.54)	1.10 (0.97,1.25)	1.11 (0.98,1.26)	1.28 (1.13,1.44)	1.14 (1.01,1.29)	1.16 (1.02,1.31)
2	Model 1 + age	1.36 (1.19,1.54)	1.11 (0.97,1.25)	1.14 (1.01,1.30)	1.24 (1.10,1.41)	1.18 (1.04,1.33)	1.14 (1.01,1.29)
3	Model 2 + smoking	1.39 (1.22,1.57)	1.12 (0.99,1.27)	1.16 (1.02,1.32)	1.26 (1.12,1.43)	1.23 (1.08,1.39)	1.16 (1.03,1.31)
4	Model 3 + cholesterol	1.39 (1.22,1.59)	1.11 (0.98,1.27)	1.13 (0.98,1.30)	1.24 (1.09,1.41)	1.23 (1.08,1.40)	1.16 (1.03,1.31)
5	Model 4 + SBP	1.32 (1.15,1.51)	1.06 (0.93,1.21)	1.09 (0.95,1.25)	1.17 (1.02,1.33)	1.15 (1.01,1.32)	1.11 (0.98,1.26)
6	Model 5 + fibrinogen	1.30 (1.13,1.49)	1.05 (0.91,1.20)	1.09 (0.94,1.26)	1.15 (1.00,1.31)	1.14 (0.99,1.31)	1.10 (0.97,1.24)
7	Model 6 + factor VII	1.29 (1.12,1.49)	1.04 (0.91,1.20)	1.10 (0.95,1.26)	1.15 (1.00,1.32)	1.15 (1.00,1.31)	1.10 (0.97,1.24)

Trunk to arm skinfold ratio (TAR) defined as (subscapular + suprailiac) / (triceps + forearm), SBP = systolic blood pressure. Men: 1 SD unit = Forearm (2.2 mm), triceps (3.9 mm), subscapular (6.4 mm), suprailiac (6.6 mm), BMI (3.0 kg/m²), TAR (0.60).

Table 2B Effect of adding covariates to the relative risk of fatal CHD for each standardised unit of obesity measure in women

Model	Variable added	BMI	Forearm	Triceps	Subscapular	Suprailiac	TAR
1	Unadjusted	1.35 (1.02,1.79)	1.36 (1.04,1.79)	1.25 (0.91,1.70)	1.32 (1.00,1.75)	1.05 (0.75,1.46)	0.94 (0.66,1.34)
2	Model 1 + age	1.28 (0.96,1.70)	1.35 (1.02,1.78)	1.20 (0.87,1.64)	1.31 (0.99,1.74)	1.01 (0.72,1.42)	0.93 (0.67,1.30)
3	Model 2 + smoking	1.29 (0.98,1.70)	1.37 (1.04,1.80)	1.22 (0.90,1.65)	1.35 (1.03,1.79)	1.07 (0.76,1.50)	0.97 (0.70,1.34)
4	Model 3 + cholesterol	1.45 (1.07,1.96)	1.51 (1.14,2.00)	1.49 (1.08,2.06)	1.54 (1.14,2.08)	1.22 (0.84,1.78)	0.96 (0.67,1.36)
5	Model 4 + SBP	1.37 (1.00,1.86)	1.40 (1.04,1.87)	1.37 (0.99,1.89)	1.46 (1.07,2.00)	1.12 (0.76,1.64)	0.90 (0.64,1.27)
6	Model 5 + fibrinogen	1.56 (1.14,2.14)	1.52 (1.14,2.04)	1.70 (1.17,2.47)	1.68 (1.22,2.32)	1.31 (0.88,1.94)	0.95 (0.67,1.33)
7	Model 6 + factor VII	1.48 (1.07,2.06)	1.46 (1.08,1.97)	1.63 (1.12,2.39)	1.65 (1.19,2.30)	1.23 (0.81,1.87)	0.92 (0.65,1.30)

Trunk to arm skinfold ratio (TAR) defined as (subscapular + suprailiac)/(triceps + forearm)

SBP = systolic blood pressure. Women: 1 SD unit = forearm (3.5 mm), triceps (6.4 mm), subscapular (8.1 mm), suprailiac (8.4 mm), BMI (3.5 kg/m²), TAR (0.45).

dictive of fatal CHD in men (table 2A): for each standard deviation increase in BMI (3 kg/m²), there was a 29% increase in risk for fatal CHD ($p < 0.01$). Subscapular skinfold and suprailiac skinfold were only marginally significant. Among women (table 2B), there was a 48% increase in risk for fatal CHD for each standard deviation increase in BMI ($p = 0.03$). The relative risk for forearm skinfold ($p = 0.02$) was comparable to that for BMI, while the estimates for subscapular skinfold ($p < 0.01$) and triceps skinfold ($p = 0.01$) were slightly higher.

Table 2 also shows the influence of sequentially adding covariates to the relative risk estimates for fatal CHD. In both men and women, the estimates derived from the fully adjusted model (model 7) were not noticeably different from those of the crude model (model 1). Moreover, the addition of haemostatic variables had little effect on the relative risk estimates, suggesting that the effect of obesity on fatal CHD is not mediated through the haemostatic system to an appreciable extent. Covariate adjustment seems to have a larger influence on the relative risk estimates in women; however, this may be attributable to the comparatively small number of women who experienced a fatal CHD event.

Further examination of BMI shows that men in the highest fourth of BMI had an 83% greater risk of fatal CHD compared with those in the lowest fourth ($p < 0.01$) (table 3); those in the highest fourth of suprailiac skinfold distributions had also experienced a significant increase in risk ($p < 0.05$). Women in the highest quartile of BMI had over a fivefold increase in risk ($p = 0.03$); both forearm ($p = 0.03$) and triceps skinfolds ($p = 0.02$) were also predictive of fatal CHD. Despite these apparent sex differences, however, there was insufficient statistical evidence of interaction between sex and obesity for fatal CHD.

For all cause mortality, none of the adjusted relative risk estimates were significant except for subscapular skinfold thickness among women, who experienced a 20% increase in total mortality with each 8 mm increase in subscapular skinfold thickness ($p = 0.03$). In addition, repeat analysis

using death attributable to any cardiovascular disease as an outcome yielded similar results to those for fatal CHD (results not shown).

DISCUSSION

The NPHS is the longest running prospective cohort study of haemostatic variables in the UK, if not worldwide, and has thus accumulated a sufficiently large number of CHD deaths to permit analyses over a long period of time. The most striking finding of our analyses is the long term—up to 30 years—over which initial measures of obesity predict death from CHD, which was established for both women, as well as for men. In this study, BMI was shown to be a strong predictor of fatal CHD in both men and women; forearm skinfold, triceps skinfold, and subscapular skinfold were also predictive in women. These findings are consistent with an earlier NPHS report⁷ showing BMI and skinfold measures to be strongly predictive of non-fatal and fatal CHD. However, our analyses have been limited only to fatal events as data on non-fatal outcomes were not ascertained after 1984 when they were published as part of the main findings⁴ of NPHS. The effect of obesity on fatal CHD does not seem to be substantially mediated by blood pressure, cholesterol, or the haemostatic factors measured in this study although these variables are moderately associated with obesity.⁴

What this paper adds

- Obesity is an important risk factor for fatal CHD where its prognostic significance remains after 30 years of follow up.
- The effect of obesity on fatal CHD does not seem to be substantially mediated by blood pressure, cholesterol, or the haemostatic factors measured in this study.

Table 3 Relative risk of fatal CHD by fourths of obesity

	Fourth of obesity	BMI	Forearm	Triceps	Subscapular	Suprailiac	TAR
Men	1st	1.00	1.00	1.00	1.00	1.00	1.00
	2nd	1.02 (0.63,1.65)	1.62 (1.05,2.49)	1.06 (0.70,1.62)	1.31 (0.84,2.03)	1.42 (0.94,2.15)	0.74 (0.48,1.13)
	3rd	1.48 (0.95,2.31)	1.40 (0.89,2.20)	1.25 (0.84,1.87)	1.19 (0.76,1.86)	1.14 (0.73,1.78)	0.91 (0.60,1.37)
	4th	1.83 (1.19,2.82)	1.54 (0.99,2.41)	1.02 (0.66,1.57)	1.45 (0.94,2.24)	1.55 (1.01,2.37)	1.27 (0.86,1.87)
Women	1st	1.00	1.00	1.00	1.00	1.00	1.00
	2nd	1.67 (0.30,9.34)	2.22 (0.55,8.89)	2.91 (0.59,14.53)	2.06 (0.50,8.42)	0.49 (0.12,2.02)	0.44 (0.13,1.55)
	3rd	3.15 (0.63,15.68)	1.83 (0.43,7.73)	3.44 (0.70,16.95)	2.18 (0.54,8.79)	0.74 (0.22,2.55)	0.84 (0.30,2.40)
	4th	5.44 (1.13,26.15)	4.37 (1.20,15.93)	6.07 (1.29,28.49)	3.82 (0.96,15.21)	1.88 (0.64,5.54)	0.83 (0.29,2.39)

Cox regression model adjusted for age, current smoking, cholesterol, systolic blood pressure, fibrinogen, and factor VII activity. Trunk to arm skinfold ratio (TAR) defined as (subscapular + suprailiac)/(triceps + forearm). Quartiles for men: BMI (23.7 kg/m², 25.4 kg/m², 27.2 kg/m²); forearm (4.3 mm, 5.6 mm, 7.0 mm); triceps (7.2 mm, 9.2 mm, 11.6 mm); subscapular (12.0 mm, 15.8 mm, 20.2 mm); TAR (1.5, 1.8, 2.3). Quartiles for women: BMI (22.3 kg/m², 24.3 kg/m², 26.5 kg/m²); forearm (6.0 mm, 8.0 mm, 10.6 mm); triceps (15.0 mm, 19.2 mm, 23.6 mm); subscapular (11.2 mm, 15.2 mm, 21.4 mm); TAR (1.1, 1.4, 5.2).

None of the measures of obesity was associated with an increased risk of death from any cause (with the exception of subscapular skinfold thickness in women). This is in one sense not surprising given the heterogeneous disease categories that make up the definition of all cause mortality. On the other hand, all causes do of course include CHD as well as several cancers, particularly of the large bowel and, in women, of the breast and uterus, the risk of which may be increased with overweight and obesity.⁹ Weight loss will almost certainly have preceded the diagnosis of cancer or be associated with other wasting chronic diseases from which participants may have died, and this would tend to weaken any true association. Moreover, although weight loss may precede the diagnosis of cancer, it is not likely to be an important confounder over such a long follow up period. Misclassification of cause of death also has to be considered.

It has previously been suggested that fluctuations in weight (that is, intended loss through slimming and then an increase in weight) may be associated with an increased risk of CHD.¹⁰ Although follow up BMI measurement was available in the NPHS for most participants at six years, the analyses were not performed using these data because of the large variation in the timing of the second visit and because we felt that this interval was too long to assess the shorter term fluctuations that may be of more relevance.

Our findings are consistent with a recent paper published by Flegal and colleagues that examined the role of BMI on all cause mortality using pooled data from the US national health and nutrition examination surveys.¹¹ The investigators found no significant association between overweight (BMI 25 to 30 kg/m²) and moderate obesity (BMI 30 to 35 kg/m²) for long term, all cause mortality. When we reanalysed the NPHS data using these same categorisations of BMI and adjusted for available covariates, our results for all cause mortality were found to be similar (data not shown). However, the results for fatal CHD were consistent with those of the primary analysis in this report showing a significant relation with BMI.

Our findings for all cause mortality were also similar to those of the British regional heart study where investigators reported a U shaped relation between BMI and all cause mortality.¹² However, most of our relative risk estimates (as measured in fourths) failed to reach statistical significance, perhaps because of the smaller number of events included in the analysis relative to the British regional heart study.

Central obesity is associated with a higher risk of developing diabetes and impaired glucose tolerance,¹³ which are likely to be important contributors to the increased risk of fatal CHD. Recent evidence from the DECODE study¹⁴ shows that insulin resistance increases with age but the upward trend is partly attributable to increases in BMI with age. NPHS did not include waist circumference but it may be that TAR, the trunk to arm skinfold ratio, derived from skinfold on the trunk is a useful guide to the extent of central obesity.

Policy implications

- Early intervention to prevent obesity or promote long term weight loss in those who are already obese is likely to reduce long term burden of cardiovascular disease burden in the general population.
- This study reinforces the need to develop effective strategies for tackling weight gain to prevent plateauing or reversal of declining trends in CHD mortality by national, as well as, international trends towards increasing prevalence of obesity.

A limitation of this study was that the study population was formed using occupational groups, and we may, therefore, have excluded subjects with serious illnesses including morbid obesity, potentially leading to a slight underestimate of the impact of obesity on health outcomes. Another limitation was that we did not adjust for other known and potentially important confounding variables, such as socioeconomic status. We also did not have longitudinal data on the obesity measures to account for the effect of changes of weight on CHD over time.^{10–15} The generalisability of this study is limited given that few non-white participants were included in the study.

We found that BMI provides robust prediction of fatal CHD both in men and in women. The measurement of BMI is of course comparatively easy to make and the same clearly applies to waist-hip measurement. It seems probable that the latter would provide the same predictive value as BMI, in which case, the public health implication that a meaningful estimate of the risk of CHD death can be made for many years ahead and may well—although this would remain to be shown—provides additional motivation to those who are overweight or obese to lose weight and to maintain a more ideal weight indefinitely.

In conclusion, BMI is an important risk factor for fatal CHD where its prognostic significance remains after 30 years of follow up. Moreover, this association does not seem to be substantially mediated by cholesterol, SBP, or the haemostatic variables measured.

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CONTRIBUTORS

All authors were involved in the concept, planning, and design of this study, as well as, in the interpretation of results and writing of the final report. JK performed all statistical analyses. All authors gave approval of this version of the manuscript to be published and are responsible for the overall content of this study as guarantors.

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