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Parental height in relation to offspring coronary heart disease: examining transgenerational influences on health using the west of Scotland Midspan Family Study

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Background Adult height is known to be inversely related to coronary heart disease (CHD) risk. We sought to investigate the transgenerational influence of parental height on offspring's CHD risk.

Methods Parents took part in a cardiorespiratory disease survey in two Scottish towns during the 1970s, in which their physical stature was measured. In 1996, their offspring were invited to participate in a similar survey, which included an electrocardiogram recording and risk factor assessment.

Results A total of 2306 natural offspring aged 30–59 years from 1456 couples were subsequently flagged for notification of mortality and followed for CHD-related hospitalizations. Taller paternal and/or maternal height was associated with socio-economic advantage, heavier birthweight and increased high-density lipoprotein cholesterol in offspring. Increased height in fathers, but more strongly in mothers (risk ratio for 1 SD change in maternal height = 0.85; 95% confidence interval: 0.76 to 0.95), was associated with a lower risk of offspring CHD, adjusting for age, sex, other parental height and CHD risk factors.

Conclusion There is evidence of an association between taller parental, particularly maternal, height and lower offspring CHD risk. This may reflect an influence of early maternal growth on the intrauterine environment provided for her offspring.

Keywords Coronary heart disease, mortality, intergenerational, height

Introduction

There has been recent renewed interest in the early life origins of chronic disease.[1] Given the paucity of studies with extended follow-up of well-characterized cohorts of young persons, investigators have instead used adult markers of early life exposures—most commonly height.[2,3] Although under a considerable degree of genetic control, height captures environmental exposures in pre-adult life,[3] such as illness,[2,3] living conditions,[4,5] nutrition[5] and, possibly, psychosocial stress.[2,5] The advantage of using height as a marker of early life insults is that it ceases to change in early adulthood and is relatively stable across the adult life course. A series of studies has shown that adult height is inversely associated with future coronary heart disease (CHD) risk.[2,6–9] This relationship appears to hold after adjustment for candidate confounding variables, which include socio-economic position and cigarette smoking.[8]

A natural progression of the line of enquiry is to explore the transgenerational influence of pre-adult environment on offspring health, particularly their CHD risk.[10] Evidence from animal studies indicates that health traits induced by environmental insults during early development may be transmitted to subsequent generations.[11] The hypothesis that poor development leads to detrimental effects on cardiovascular disease risk across generations in humans is supported by limited evidence.[12] A nutrition-linked mechanism influencing cardiovascular mortality through the male line has been suggested.[13] In the few previous studies, taller parental height has been associated with lower systolic and diastolic blood pressure,[14–16] triglycerides[17] and body mass index (BMI)[14] and higher birthweight[17] and high-density lipoprotein (HDL) cholesterol,[17] in offspring. Additionally, socio-economic position, by which height is strongly patterned, appears to influence CHD risk across up to three generations.[18] Therefore, there is a strong *prima facie* case for an inverse relation between parental height and clinical CHD in the offspring. However, to our knowledge, the association has not been examined in any detail.

We used the Scottish Midspan Family Study to test the hypotheses of association of taller parental height with lower risk of offspring CHD and with lower prevalence of related risk factors. In doing so, we controlled for potential confounders—including socio-economic factors, mediating offspring CHD risk factors and the well-established parent–offspring height correlation.[4,19] Comparing the magnitude of the association of the height of each parent with offspring CHD risk is of value: similar effects of maternal and paternal height on offspring CHD may suggest that associations were generated by factors just as likely to be transmitted from either parent to offspring (e.g. nuclear genetic variation and socio-economic position); by contrast, a stronger maternal height–offspring CHD gradient may specifically implicate maternal characteristics, such as the influence of intrauterine milieu,[20–22] or stronger maternal–offspring than paternal–offspring associations for aspects such as behavioural factors.[23]

Materials and methods

Study participants

Between 1972 and 1976, 7049 men and 8353 women (including 4064 married couples) aged 45–64 years residing in the towns of Renfrew and Paisley in the west of Scotland took part in one of the 'Midspan' prospective cohort studies, with an 80% response level.[24,25] A range of data were gathered, including measured height and self-reported occupational social class. In 1993/94, locally resident offspring of the married couples were traced via the first-generation study participants or the death certificate informant where both participants had died. In total, 3202 offspring aged 30–59 years were invited to participate in a cardiorespiratory survey (the Midspan Family Study). This led to completion of a questionnaire and participation in a medical examination in 1996 by 2338 offspring (1477 families), representing a 73% response from invited offspring (84% for families).[26]

Parental and offspring measurements

Parental height without shoes was measured to the nearest centimetre during the original cross-sectional study.[27] Occupational social class of the parents was based on the Registrar General's 1966 classification scheme[28] and that of the offspring on the 1990 system.[29] Women's own occupation was used unless they were housewives and/or did not give a previous occupation, in which case their husbands' or fathers' job title was used. Area-level socio-economic position was scored using the postcode sector-based Carstairs index of material deprivation;[30] data were grouped in quintiles, with deprived areas defined as the highest scoring 20%. Offspring study members reported their years of full-time education.[31] Enquiries were also made about their smoking history. Offspring respondents estimated daily consumption of beer, wine and spirits (and similar drinks) during the previous week, and data were converted to total units (10 ml: ~8 g of ethanol).[32] Subjects gave informed consent, and local research ethics committees approved the study protocol. Offspring height was measured in stocking feet to the nearest millimetre using a Holtain stadiometer after participants had inhaled and stretched to their maximum stature. Weight to the nearest 0.1 kg was measured using Seca digital scales (Hamburg, Germany) without shoes and wearing indoor clothes. BMI was computed using the standard formula [weight (kg)/height $(m)^2$]. Waist circumference measurements were taken under clothing. Birthweight was available from hospital records for 676 participants;[33]

for a further 1192 participants, birthweight was self-reported;[34] with some evidence of bias relative to hospital records, correction was made to address misclassification.[34] Three readings of systolic and diastolic blood pressure were made on the left arm using an automated Dinamap 8100 instrument while the participant was seated.[35] The average of the last two of these measurements was used in the analyses. Values for total and HDL plasma cholesterol, blood glucose, fibrinogen[36] and white blood count were ascertained from assayed non-fasting venous blood samples.[7] Forced expiratory volume in 1 s (FEV_1; in litres) was measured using a Fleisch pneumotachograph connected to Spirotrac III software (Vitalograph, UK).

Ascertainment of CHD

Participants were 'flagged' for notification of mortality until embarkation from the UK (four individuals who were alive and CHD free before emigration, with median 5.8 years of follow-up) or the end of 2006, with the General Register Office in Scotland. CHD deaths and events were categorized according to the International Classification of Disease (ICD version 9, 410–414 and 429.2; ICD version 10, I200–I259). Electronic linkage to hospital discharges via the Scottish Morbidity Record scheme (~90% accurate and 99% complete)[37] was used to retrieve details of all CHD hospital discharges to the end of 2006.

Prevalent CHD at the time of survey was based on three criteria:[38] angina, defined as definite or possible grades I or II from the Rose Angina Questionnaire;[39] possible myocardial infarction, based on severe chest pain lasting for half an hour or more[38] and electrocardiogram (recorded as part of the clinical examination) evidence of myocardial ischaemia, based on Minnesota codings 1.1–1.3 (definite, probable or possible myocardial infarction), 4.1–4.4 and 5.1–5.3 (definite, probable or possible myocardial ischaemia) and 7.1 (left bundle branch block).[40] Electrocardiograms were recorded on a Siemens 440 digital electrocardiograph and the waveforms analysed by computer software that automatically provided the Minnesota codes (reviewed in a dedicated laboratory).[41,42]

Statistical methods

After excluding 2 offspring who refused record linkage consent and 30 offspring who were adopted/step-children, the analytical sample comprised 1024 male and 1282 female offspring from 1456 families. Baseline characteristics of parents and offspring according to parental height were modelled using logistic regression with correction to obtain risk ratios (RRs) and accompanying confidence intervals (CIs)[43] (for categorical variables) and multiple linear regression (for continuous variables).

In preliminary analyses, parental height revealed similar relationships with prevalent CHD, hospitalization and deaths from CHD (results not shown); these outcomes were therefore combined into analyses of 'any CHD'. Corrected logistic regression analyses were used to compute risk ratios[43] and account for the clustering of offspring within families was made using robust variance estimates.[44] The majority of variables had no or few missing data, although three variables had >10% missing (Table 1). With at least one data item missing for 925 (41%) offspring, we used multiple imputation with 41 imputed data sets based on the chained equations procedure[45] using all the variables in Table 1.

Given there was no strong evidence that effect estimates for mother's and father's height in relation to offspring CHD differed in sons or daughters ($P > 0.05$ for all height by sex interactions), all data were combined and gender adjusted. Model 1, in which we controlled for parental age, offspring age and sex, was the basic model. In Model 2, we also adjusted for all indicators of socio-economic position in parent and offspring and a range of CHD risk factors (following individual examination). In Models 3 and 4, we additionally adjusted for the height of the other parent, simultaneously enabling assessment of the difference in strength of parental effects using z-tests; Model 4 additionally included offspring height to account for parent–offspring height correlations. Here, P-values were obtained based on the difference between the mutually adjusted parental effects values relative to the pooled variance. Associations for all-cause mortality (73 deaths) and non-cardiovascular mortality (54 deaths) were also examined. All analyses were conducted in STATA (Version 9.1; College Station, Texas, USA).

Results

As anticipated, the height of fathers was greater than that of mothers, and the height of their male offspring was greater than that of the female offspring (Table 1). A quarter of offspring were current smokers, and an average of 12.3 units of alcohol were consumed per week.

Unsurprisingly, offspring height correlated with the height of both the father ($\rho = 0.34$; $P < 0.001$) and the mother ($\rho = 0.39$; $P < 0.001$). As expected, taller fathers, as well as their offspring, were less likely to be from lower socio-economic groups (Table 2). Taller men also tended to produce offspring with lower BMI in adulthood but who were more likely to smoke. Paternal stature was associated with elevated levels of HDL cholesterol, lower levels of fibrinogen and greater FEV_1 in the offspring, although associations for the latter two were attenuated after adjustment.

Taller mothers were more likely to be from a higher socio-economic background and have taller and heavier offspring. Both total plasma and HDL cholesterol were lower, and FEV_1 and birthweight were greater in

Table 1 Characteristics of parents (1972–76) and offspring (1996) in the Midspan Family Study in Renfrew and Paisley in Scotland ($n = 2306$)

Characteristics		*n* missing
Parental characteristics		
Manual occupational social class (father)[a], *n* (%)	1590 (69.0)	0
Fathers' age (years)[b], mean (SD)	54.8 (4.9)	0
Mothers' age (years)[b], mean (SD)	52.6 (4.8)	0
Fathers' height (cm)[c], mean (SD)	169.6 (6.5)	3
Mothers' height (cm)[c], mean (SD)	157.9 (5.6)	1
Offspring characteristics		
Males, *n* (%)	1024 (44.4)	0
Manual occupational social class[a], *n* (%)	721 (31.3)	0
Deprived area of residence, *n* (%)	761 (33.1)	5
Duration of education (years), mean (SD)	12.2 (2.8)	4
Current cigarette smoking, *n* (%)	583 (25.3)	0
Age at interview (years), mean (SD)	45.0 (6.2)	0
Height (cm), mean (SD)	167.4 (9.2)[d]	1
Birthweight (kg), mean (SD)	3.6 (0.5)	457
Alcohol consumption (units/week), mean(SD)	12.3 (15.3)	0
BMI (kg/m^2), mean (SD)	26.2 (4.6)	17
Waist circumference (cm), mean (SD)	86.1 (13.3)	19
Systolic blood pressure (mmHg), mean (SD)	127.2 (15.9)	25
Diastolic blood pressure (mmHg), mean (SD)	74.6 (11.2)	25
Total plasma cholesterol (mmol/l), mean (SD)	5.3 (1.0)	72
HDL cholesterol (mmol/l), mean (SD)	1.4 (0.4)	368
Non-fasting blood glucose (mmol/l), mean (SD)	5.3 (1.6)	67
Fibrinogen (g/l), mean (SD)	3.2 (0.8)	92
White blood cell count ($\times 10^9$/l), mean (SD)	6.2 (1.8)	251
FEV_1 (l), mean (SD)	3.1 (0.7)	77

[a]III manual, IV and V.
[b]Age at Renfrew/Paisley interview, 1972–76.
[c]Height at Renfrew/Paisley interview, 1972–76.
[d]Height of male offspring: mean = 175.0 cm and SD = 6.5 cm; height of female offspring: mean = 161.3 cm and SD = 5.9 cm.

offspring of taller mothers. These associations generally held after multiple adjustment, including that for height of the other parent (Model 3) and offspring height (Model 4). The large change in the magnitude of the sex effect from Model 3 to Model 4 is as expected because adjusting for height has a dramatic impact on the associations with a strongly height-related characteristic such as sex (Model 4). Differential effects of paternal and maternal height were seen for birthweight, BMI, waist circumference, smoking and HDL cholesterol in the adult offspring.

A total of 481 (20.9%) of the 2306 offspring had either a CHD event (13 deaths and 69 hospitalizations) or prevalent CHD at time of survey (399 cases). In analyses adjusted for age (parent and offspring) and offspring sex, there was a suggestion of a weak inverse association between paternal height and any offspring CHD, such that taller men had offspring with somewhat lower risk (Table 3). This relationship was attenuated when various markers of socio-economic position and CHD risk factors in the offspring were added to the multivariable model (Model 2). There was a stronger relation between maternal height and offspring CHD risk. A dose–response effect was also apparent across the stature groups ($P_{trend} = 0.039$ for Model 2). These effects were unchanged after adjustment for a range of covariates, which included socio-economic position and CHD risk factors. Mutual adjustment for height

Table 2 Relation of 1 SD increase (95% CIs) in paternal and maternal height with their own characteristics (measured in 1972–76) and offspring characteristics (measured in 1996) in the Midspan Family Study in Renfrew and Paisley in Scotland ($n = 2306$)

	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	*P*-value[e]
Paternal height[f]					
Parental characteristics					
Manual occupational social class (father)[g]	0.70 (0.63 to 0.79)	0.73 (0.65 to 0.82)	0.75 (0.66 to 0.85)	0.71 (0.62 to 0.81)	–
Age (years)[h]	−0.58 (−0.84 to −0.31)	−0.62 (−0.89 to −0.35)	−0.67 (−0.96 to −0.38)	−0.85 (−1.16 to −0.55)	–
Offspring characteristics					
Males	0.97 (0.91 to 1.04)	0.99 (0.92 to 1.07)	1.01 (0.92 to 1.09)	2.29 (1.98 to 2.60)	–
Manual occupational social class[g]	0.86 (0.79 to 0.94)	0.97 (0.89 to 1.06)	0.96 (0.87 to 1.06)	1.02 (0.92 to 1.13)	–
Deprived area of residence	0.88 (0.82 to 0.95)	0.92 (0.85 to 0.99)	0.93 (0.86 to 1.01)	0.95 (0.87 to 1.03)	–
Duration of education (years)	0.30 (0.17 to 0.42)	0.09 (−0.02 to 0.20)	0.01 (−0.10 to 0.12)	0.03 (−0.10 to 0.15)	–
Current cigarette smoking	1.02 (0.94 to 1.11)	1.09 (1.00 to 1.19)	1.13 (1.03 to 1.24)	1.13 (1.02 to 1.25)	–
Age at interview (years)	0.09 (−0.02 to 0.37)	0.19 (−0.10 to 0.47)	0.33 (0.03 to 0.64)	0.56 (0.23 to 0.89)	–
Height (cm)	3.10 (2.85 to 3.35)	3.05 (2.80 to 3.30)	2.06 (1.81 to 2.30)	2.06 (1.81 to 2.30)	–
Birthweight (kg)	0.04 (0.01 to 0.07)	0.04 (−0.01 to 0.07)	0.01 (−0.02 to 0.04)	−0.02 (−0.06 to 0.01)	–
Alcohol consumption (units/week)	−0.07 (−0.63 to 0.50)	0.03 (−0.54 to 0.60)	0.09 (−0.52 to 0.70)	−0.09 (−0.78 to 0.60)	–
BMI (kg/m^2)	−0.37 (−0.56 to −0.17)	−0.32 (−0.53 to −0.12)	−0.39 (−0.62 to −0.17)	−0.30 (−0.54 to −0.06)	–
Waist circumference (cm)	0.07 (−0.43 to 0.57)	0.20 (−0.31 to 0.71)	−0.35 (−0.90 to 0.20)	−0.79 (−1.39 to −0.20)	–
Systolic blood pressure (mmHg)	−0.02 (−0.67 to 0.64)	0.10 (−0.58 to 0.79)	0.02 (−0.73 to 0.77)	0.26 (−0.51 to 1.04)	–
Diastolic blood pressure (mmHg)	−0.13 (−0.61 to 0.35)	−0.09 (−0.59 to 0.41)	−0.14 (−0.68 to 0.40)	−0.08 (−0.64 to 0.49)	–
Total plasma cholesterol (mmol/l)	−0.05 (−0.09 to 0.00)	−0.05 (−0.09 to −0.01)	−0.02 (−0.07 to 0.03)	0.02 (−0.03 to 0.06)	–
HDL cholesterol (mmol/l)	0.02 (0.00 to 0.04)	0.01 (0.00 to 0.03)	0.03 (0.01 to 0.05)	0.03 (0.01 to 0.05)	–
Non-fasting blood glucose (mmol/l)	−0.05 (−0.11 to 0.01)	−0.07 (−0.13 to −0.01)	−0.08 (−0.14 to −0.01)	−0.07 (−0.15 to 0.00)	–
Fibrinogen (g/l)	−0.06 (−0.09 to −0.03)	−0.02 (−0.05 to 0.02)	−0.04 (−0.07 to 0.00)	−0.02 (−0.06 to 0.02)	–
White blood cell count ($\times 10^9/l$)	−0.02 (−0.10 to 0.06)	0.00 (−0.08 to 0.08)	0.02 (−0.08 to 0.11)	0.03 (−0.06 to 0.13)	–
FEV_1 (l)	0.12 (0.10 to 0.15)	0.11 (0.08 to 0.13)	0.07 (0.05 to 0.10)	0.00 (−0.03 to 0.02)	–
Maternal height[f]					
Parental characteristics					
Manual occupational social class (father)[g]	0.82 (0.72 to 0.93)	0.84 (0.75 to 0.94)	0.94 (0.83 to 1.06)	0.89 (0.78 to 1.02)	0.01
Age (years)[h]	−0.51 (−0.74, 0.28)	−0.55 (−0.78 to 0.32)	−0.52 (−0.79 to 0.26)	−0.72 (−1.00 to −0.44)	<0.01
Offspring characteristics					
Males	0.94 (0.87 to 1.01)	0.97 (0.89 to 1.05)	0.97 (0.88 to 1.05)	2.56 (2.20 to 2.94)	0.57
Manual occupational social class[g]	0.89 (0.82 to 0.97)	1.02 (0.93 to 1.11)	1.03 (0.94 to 1.14)	1.12 (1.01 to 1.25)	0.25

(continued)

Table 2 Continued

	Model 1[a]	Model 2[b]	Model 3[c]	Model 4[d]	*P*-value[e]
Deprived area of residence	0.90 (0.83 to 0.98)	0.94 (0.86 to 1.02)	0.97 (0.88 to 1.06)	0.99 (0.90 to 1.09)	0.47
Duration of education (years)	0.38 (0.24 to 0.53)	0.21 (0.09 to 0.32)	0.21 (0.08 to 0.34)	0.23 (0.05 to 0.38)	0.08
Current cigarette smoking	0.91 (0.84 to 0.99)	0.95 (0.87 to 1.04)	0.91 (0.82 to 1.00)	0.90 (0.81 to 1.00)	<0.01
Age at interview (years)	−0.02 (−0.25 to 0.22)	0.11 (−0.14 to 0.35)	0.12 (−0.15 to 0.40)	0.39 (0.09 to 0.68)	<0.01
Height (cm)	3.33 (3.06 to 3.59)	3.28 (3.02 to 3.54)	2.47 (2.22 to 2.73)	2.47 (2.22 to 2.73)	0.06
Birthweight (kg)	0.08 (0.05 to 0.11)	0.08 (0.05 to 0.11)	0.08 (0.04 to 0.11)	0.04 (0.00 to 0.07)	0.03
Alcohol consumption (units/week)	−0.20 (−0.89 to 0.49)	−0.10 (−0.83 to 0.64)	−0.13 (−0.92 to 0.66)	−0.34 (−1.23 to 0.54)	0.63
BMI (kg/m^2)	−0.04 (−0.26 to 0.17)	0.01 (−0.20 to 0.22)	0.17 (−0.06 to 0.40)	0.28 (0.04 to 0.53)	<0.01
Waist circumference (cm)	1.03 (0.49 to 1.57)	1.19 (0.65 to 1.73)	1.34 (0.75 to 1.93)	0.80 (0.17 to 1.44)	<0.01
Systolic blood pressure (mmHg)	0.07 (−0.57 to 0.72)	0.21 (−0.45 to 0.88)	0.20 (−0.52 to 0.93)	0.50 (−0.31 to 1.31)	0.68
Diastolic blood pressure (mmHg)	−0.02 (−0.50 to 0.47)	0.03 (−0.46 to 0.51)	0.08 (−0.44 to 0.60)	0.15 (−0.40 to 0.70)	0.49
Total plasma cholesterol (mmol/l)	−0.08 (−0.12 to −0.03)	−0.08 (−0.13 to −0.04)	−0.07 (−0.12 to −0.02)	−0.03 (−0.08 to 0.02)	0.24
HDL cholesterol (mmol/l)	−0.01 (−0.03 to 0.01)	−0.02 (−0.03 to 0.00)	−0.03 (−0.05 to −0.01)	−0.02 (−0.05 to 0.00)	<0.01
Non-fasting blood glucose (mmol/l)	−0.00 (−0.06 to 0.06)	−0.01 (−0.08 to 0.05)	0.02 (−0.05 to 0.09)	0.02 (−0.05 to 0.09)	0.09
Fibrinogen (g/l)	−0.04 (−0.07 to 0.01)	−0.02 (−0.05 to 0.01)	−0.01 (−0.04 to 0.03)	0.01 (−0.02 to 0.05)	0.17
White blood cell count ($\times 10^9$/l)	−0.05 (−0.13 to 0.02)	−0.04 (−0.12 to 0.04)	−0.05 (−0.14 to 0.04)	−0.03 (−0.13 to 0.07)	0.45
FEV_1 (l)	0.13 (0.10 to 0.15)	0.11 (0.09 to 0.14)	0.08 (0.06 to 0.11)	−0.01 (−0.03 to 0.02)	0.74

[a]Model 1: Adjusted for father's or mother's age, offspring age at interview and offspring sex (where these covariates were the outcome of interest, the covariate was dropped from the model).
[b]Model 2: Adjustment as in Model 1 plus parental and offspring socio-economic position (where these covariates were the outcome of interest, the covariate was dropped from the model).
[c]Model 3: Adjustment as in Model 2 plus mutual adjustment for parental height; values are estimates (95% CIs) of RRs for categorical variables and regression coefficients for continuous variables.
[d]Model 4: Adjustment as in Model 3 plus adjustment for offspring height (where offspring height was the outcome of interest, it was dropped from the model); values are estimates (95% CIs) of RRs for categorical variables and regression coefficients for continuous variables.
[e]*z*-test of difference between maternal and paternal height effects in Model 4.
[f]Height of father (SD = 6.5 cm) or mother (SD = 5.6 cm) at Renfrew/Paisley interview 1972–76.
[g]III manual, IV and V combined, with I, II and III non-manual combined as the reference category.
[h]Age of father or mother at Renfrew/Paisley interview 1972–76.

Table 3 RRs (95% CIs) for the relation of paternal and maternal height (measured in 1972–76) with CHD in the offspring (determined in 1996–2006) in the Midspan Family Study in Renfrew and Paisley in Scotland ($n = 2306$)

	Height (cm)	Total $n = 2306$	Events $n = 481$	Model 1[a] RR (95% CI)	Model 2[b] RR (95% CI)	Model 3[c] RR (95% CI)	Model 4[d] RR (95% CI)
Paternal height	Tertile 1 (148–167)	846	194	1.00 (reference)	(1.00)	1.00	1.00
	Tertile 2 (168–172)	723	148	0.90 (0.73 to 1.11)	0.96 (0.77 to 1.18)	0.99 (0.79 to 1.23)	0.98 (0.78 to 1.22)
	Tertile 3 (173–200)	737	139	0.83 (0.66 to 1.04)	0.95 (0.75 to 1.20)	1.05 (0.82 to 1.32)	1.02 (0.79 to 1.30)
P-value (trend)				0.106	0.678	0.737	0.895
1 SD (6.5 cm) increase		2306	481	0.93 (0.85 to 1.03)	0.99 (0.89 to 1.09)	1.04 (0.93 to 1.16)	1.03 (0.92 to 1.15)
Maternal height	Tertile 1 (139–155)	780	186	1.00 (reference)	1.00	1.00	1.00
	Tertile 2 (156–160)	842	181	0.90 (0.73 to 1.11)	0.92 (0.73 to 1.14)	0.91 (0.73 to 1.14)	0.90 (0.71 to 1.13)
	Tertile 3 (161–177)	683	114	0.70 (0.54 to 0.90)	0.75 (0.57 to 0.98)	0.74 (0.56 to 0.97)	0.72 (0.53 to 0.96)
P-value (trend)				0.006	0.039	0.034	0.029
1 SD (5.6 cm) increase		2306	481	0.88 (0.79 to 0.97)	0.88 (0.79 to 0.97)	0.87 (0.78 to 0.96)	0.85 (0.76 to 0.95)

[a]Model 1: adjusted by father's or mother's age, offspring age at interview and offspring sex.
[b]Model 2: Model 1 plus adjustment for own social class, father's social class (Registrar General's standard six groupings for both), area deprivation, years of education, cigarette smoking status, alcohol/week, BMI, waist circumference, birthweight, systolic blood pressure, diastolic blood pressure, total cholesterol, HDL cholesterol, random glucose, fibrinogen, white blood cell count and FEV_1.
[c]Model 3: Model 2 plus mutual adjustment for parental height.
[d]Model 4: Model 3 plus adjustment for offspring height.

of the other parent also did not impact substantially on these effect estimates. A statistical comparison of the relative strength of each parent's height as a predictor of offspring CHD confirmed that maternal height had a greater influence [per standard deviation (SD) change] than paternal height ($P = 0.034$). When additionally adjusting for offspring height, effect estimates were effectively unchanged (Model 4).

In analyses in which offspring all-cause mortality and non-cardiovascular mortality were the outcome, there were weak inverse relationships with fathers' and mothers' physical stature (results not shown). Finally, analyses were repeated on the subset of study members with no missing data ($n = 1356$), and, again, results were found to be similar to those reported here.

Discussion

In keeping with previous studies,[4,14,17] we found that paternal and/or maternal height was associated with offspring socio-economic advantage,[4] birthweight[14,46] and HDL cholesterol,[17] with more favourable levels of these risk factors apparent in those born to taller parents. We also found hitherto unexamined associations for greater parental height with lower levels of fibrinogen and superior lung function in the offspring. There was a relation between greater parental height (particularly maternal—robust to adjustment for a range of social and biological measures) and offspring CHD, but no clear association when either total mortality or non-cardiovascular mortality was the outcome.

We are not aware of other studies that have examined the association of the height of each parent with adult offspring CHD risk factors and events as comprehensively. A study focusing on childhood growth and CHD among women found mothers' heights were unrelated to the occurrence of CHD in their daughters, but there were no data on the fathers.[47] In a recent Indian study, taller maternal, but not paternal, height was associated with lower infant and childhood mortality.[48]

Study strengths and weaknesses

This study has several strengths, including direct height measurements for both parents, detailed assessment of CHD risk factors in the offspring and almost complete follow-up for hospitalizations and mortality experience. Further, all offspring were old enough to have achieved their full adult height, which is not always the case in two-generation studies. It is not, however, without its shortcomings. First, although we received death certificates for all study members throughout the UK, we could not gather hospital admission records for study members outside Scotland; however, these numbers are likely to be small. Second, although the response to both

surveys was high,[49] the target sample of offspring selected comprised only those who had remained resident in the vicinity of the original parent study. To examine whether non-participation of offspring would have any implications for the results herein, we compared the parental height and parental social class of offspring who participated with those who elected not to or who had migrated and found no evidence of marked differences ($P = 0.077$–0.497). At just >2300, the numbers of study members are reasonable but may not have yielded a sufficiently high number of CHD events to detect true effects. Height is a marker of environmental factors—many of which are socially patterned—operating during gestation and childhood[3] that we were unable to measure, and we only have data on social class in adulthood for the parental generation. Residual confounding from inaccurately measured socio-economic position may account for the observed associations between paternal height and offspring CHD. If present, this would also influence findings of associations for maternal height, but the stronger observed effects for the latter indicate potentially genuine maternal height–offspring CHD associations. CHD risk factors were accounted for by including them as covariates in regression models, although it is likely they are on the intermediate pathway between parental height and development of CHD and may require more sophisticated modelling.[50] However, results based on equivalent models excluding CHD risk factors yielded similar results, suggesting our approach has not led to meaningful distortion of estimates. Adjustment for birthweight alone had little impact on the estimates (data not shown). Finally, it is possible the associations between parental height and offspring CHD may have arisen because of confounding by genetic risk factors for premature CHD, whereby parents with CHD may have undergone illness-related shrinkage, and offspring of these shorter parents had a higher risk of CHD because of this genetic risk.[9] As CHD generally occurs earlier in men than women, one might expect that such confounding would be greater for paternal height–offspring CHD than maternal height–offspring CHD, but as this is contrary to our findings, such genetic risk factor confounding through a shrinkage effect is unlikely.

The differential effect for mothers' and fathers' stature in our data could indicate the existence of factors acting during the intrauterine period.[20,21] Given the differences we have found between maternal and paternal height in relation to BMI and waist circumference and the importance in metabolism of mitochondrial deoxyribonucleic acid—which is exclusively transmitted from mothers—this deoxyribonucleic acid is a possible candidate for stronger maternal effects. Alternatively, our findings may indicate that increased CHD risk in the offspring results from the enduring effect of poor maternal diet[21] or that maternal genes related to height could influence offspring outcomes through a purely mechanical effect on the intrauterine environment. With evidence of greater maternal than paternal influence on behavioural or other factors in the offspring,[23] this is also a possible explanation for our findings. As paternity was based on self-report, a non-causal explanation is that the occurrence of non-paternity led to an underestimation of the correlation of father–offspring characteristics; although within plausible ranges, this would have minor impact on the estimated relative risks.[51] It is somewhat surprising that adjustment for offspring height makes little difference to the strength of association between maternal height and offspring CHD. The simplest interpretation is that the maternal height effect on offspring CHD is not operating through pathway(s) that also influence offspring final height. We do not have the power to test this empirically, but it is possible there is an effect of parental height on offspring CHD that is qualitatively different, but complementary, to the effect of offspring height on offspring CHD. The association of parental height with alternative causes of death such as cancers remains to be explored.

Today, the possibility of transgenerational transmission of the detrimental effects of adverse conditions during gestation is particularly pertinent to populations of emerging economies. Countries such as India are transitioning between traditional (limited nutrition) and Western (abundant) lifestyles, with the accompanying hazardous combination of persistent low birthweight and relatively high subsequent adiposity in current generations.[52] Indeed, these nations are presently experiencing rising levels of CHD. Strategies that address sub-optimal maternal nutrition could be useful in the global containment of CHD in future generations.[12] In conclusion, in this first study of its kind, there was evidence of an association between offspring CHD and parental height—most strongly for mothers—suggesting possible intrauterine mechanisms.

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KEY MESSAGES

- In this study, taller parental height was associated with socio-economic advantage, greater birthweight, lower fibrinogen levels and elevated lung function in the offspring.
- Additionally, the offspring of taller parents (particularly mothers) were less likely to experience CHD.
- These findings suggest an influence of maternal growth on the intrauterine environment.
- Promotion of adequate maternal nutrition could reduce CHD risk.

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