Cardiovascular risk factors in British children from towns with widely differing adult cardiovascular mortality

Peter H Whincup, Derek G Cook, Fiona Adshead, Stephanie Taylor, Olia Papacosta, Mary Walker, Valerie Wilson

Abstract

Objective—To examine whether cardiovascular risk factors differ in children from towns in England and Wales with widely differing adult cardiovascular death rates.

Design—School based survey conducted during 1994 in 10 towns, five with exceptionally high adult cardiovascular mortality (standardised mortality ratio 131–143) and five with exceptionally low adult cardiovascular mortality (64–75). Towns were surveyed in high-low pairs.

Subjects—3415 white children aged 8–11 years with physical measurements (response rate 75%), including 1287 with blood samples (response rate 64%), of whom 515 had blood samples taken 30 minutes after a glucose load.

Results—Children in towns with high cardiovascular mortality were on average shorter than those in towns with low mortality (mean difference 1.2 cm; 95% confidence interval 0.3 to 2.1 cm; $P = 0.02$) and had a higher ponderal index (0.34 kg/m^3 ; 0.16 to 0.52 kg/m^3 ; $P = 0.006$). Mean systolic pressure was higher in high mortality towns, particularly after adjustment for height (2.0 mm Hg ; 0.8 to 3.2 mm Hg ; $P = 0.009$). Mean waist:hip ratio, total cholesterol concentration, and 30 minute post-load glucose measurements were similar in high and low mortality towns. The differences in height and blood pressure between high and low mortality towns were unaffected by standardisation for birth weight.

Conclusions—The differences in height, ponderal index, and blood pressure between towns with high and low cardiovascular mortality, if persistent, may have important future public health implications. Their independence of birth weight suggests that the childhood environment rather than the intrauterine environment is involved in their development.

Introduction

The geographic variation in mortality from cardiovascular disease across Great Britain, with the lowest rates in the south east and the highest in south Wales, northern England, and Scotland, is well described¹ but poorly understood.² Earlier attempts to account for these variations emphasised differences in patterns of adult smoking and blood pressure.³ Several ecological studies, however, have now examined the possibility that geographic variations in cardiovascular risk might have their origins in childhood or earlier. Strong geographical associations between infant mortality and adult cardiovascular mortality many years later have been described,^{4–5} but studies examining the geographical relations between childhood blood pressure and adult cardiovascular mortality have yielded conflicting results.^{6–7} Nevertheless, consistent relations have also been observed in individuals between size at birth (particularly birth weight) and several factors that are markers of cardiovascular risk in adult life, including blood pressure,⁸ glucose tolerance,⁹ serum lipid concentrations,¹⁰ and central obesity¹¹; in the case of blood

pressure and glucose tolerance, these relations have been described in children of 10 years or under.^{12–14}

We have examined the extent to which cardiovascular risk factors differ in 8–11 year old children from areas of England and Wales with exceptionally high and exceptionally low adult cardiovascular mortality. Where variations in risk factors were apparent we examined the extent to which birth weight (the marker of size at birth most consistently related to cardiovascular risk factors¹⁵) can account for these variations.

Subjects and methods

SAMPLING PROCEDURES

The study design was based on an earlier investigation of cardiovascular risk factors in 5–7 year old children in 1990.⁷ Ten population centres (50 000 to 100 000 people) in England and Wales were included, selected on the basis of adult cardiovascular mortality (England and Wales, 1979–83, for men and women aged 35–64 years) to include the five centres with the lowest adult cardiovascular mortality (Esher, Leatherhead, Bath, Chelmsford, Tunbridge Wells) and the five with the highest (Wigan, Rochdale, Burnley, Port Talbot, Rhondda) (fig 1). Table 1 summarises the standardised mortality ratios for cardiovascular disease in the study towns (varying by a factor of two between towns with high and low mortality). In each town the 10 junior schools corresponding to the stratified random sample of 10 infant schools included in the earlier study were identified. Within each school 50 children were invited to take part. These included children who had taken part in the earlier study (30 on average) supplemented by a random sample of children (20 on average) from the same classes.

Fig 1—Ten towns study: geographical distribution of study towns

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BMJ 1996;313:79–84

SURVEY PROCEDURES

Ethical approval was obtained from the British Paediatric Association Ethics Advisory Committee and from all relevant local research ethics committees. All measurements were made between April and November 1994. The 10 towns were visited in five pairs (table 1). Each pair included one low mortality and one high mortality town and was surveyed within three weeks. The surveys in each town were conducted during a one week period. Two schools were visited each day, each by a specially trained field team consisting of two nurses (who carried out physical measurements) and a doctor (who carried out blood sampling). Each nurse carried out about one quarter of the physical measurements in each town. Informed written parental consent was sought in all cases; parents were asked to obtain their child's agreement before agreeing. The younger 30 children in each school were asked to have physical measurements alone, while the older 20 children were also asked to provide a blood sample and to have measurements of waist and hip circumference.

Physical measurements—Children were examined after five minutes' rest. They were dressed in light clothing without shoes. Height was measured to the last complete millimetre with a portable stadiometer (CMS, Camden). Weight was measured to the last complete 0.1 kg with a digital electronic weighing scale (Soehnle). Ponderal index (weight/height³) was independent of age and height in this study population and was used as an index of weight for height. Blood pressure was measured with the child seated and the arm supported at chest level. Two blood pressure measurements were made one minute apart in the right arm by using the Dinamap 1846SX oscillometric blood pressure recorder (Critikon, United States).^{16 17} All measurements were made with the small adult cuff size (cuff bladder dimensions 22 cm x 10 cm), thereby ensuring that the minimum cuff bladder width to arm circumference ratio of 40% recommended by the American Heart Association¹⁸ was met for 89% of the study population. Room temperature was measured at the time of blood pressure measurement with an RS electronic thermometer. Ethnic group was assessed on the basis of the child's appearance into five main groupings (white, Afro-Caribbean, Asian, Oriental, other). Waist circumference was measured at the end of normal expiration at the mid-point between the iliac crest and the lower edge of the ribs in the mid-axillary line, with the child standing with feet 15 cm apart. Hip circumference was measured at the point of maximum circumference over the buttocks.

Blood sampling—Blood samples were taken after an overnight fast, after physical measurements were completed, and at least 45 minutes after the administration of local anaesthetic skin cream (EMLA). All children were offered breakfast after the procedure. In half the children samples were collected directly after the fast, and in half samples were taken 30 minutes after ingestion of a standard glucose load (1.75 g/kg). Blood samples were centrifuged, separated, and frozen at -20°C within eight hours of collection. All analyses were carried out in a central laboratory (department of clinical biochemistry, St George's Hospital Medical School). Plasma glucose concentration (fluoride oxalate sample) was analysed by using the Glucose-Technicon Axon system (method No SM4-2143F90). Glucose results presented in this paper are based only on children with post-load measurements. Total serum cholesterol concentration was measured with the Technicon Dax system (method No SM4-1139M90). Total cholesterol results have been presented for all subjects as values did not vary systematically between fasting and non-fasting subjects.

Parental questionnaire—A questionnaire with reply paid postage was forwarded to parents on the day of the survey. Parents were asked to provide information on the child's general health and weight at birth and on their occupation(s), which was coded in accordance with the registrar general's 1980 coding manual. Two reminders were sent when appropriate. The validity of birth weights was checked in 1575 children born in hospitals in the study towns, subject to maternal consent. Close overall agreement was observed between maternal recall and birth record data, with more than 94% of recalled birth weights within 200 g of the birth record birth weight (mean (SD) difference 1 (120) g).

STATISTICAL METHODS

All analyses were carried out with the SAS statistical package.¹⁹ The units in the main analyses were towns, although adjustments were made by using individual data and standard linear regression techniques. Town mean values were adjusted throughout for age, sex, and (physical measurements only) observer, although these adjustments had no important effect on the differences observed. In addition, blood pressure measurements were adjusted for the effects of venepuncture and room temperature and blood glucose measurements for small differences in timing of blood samples (27 to 33 minutes), made on a minute by minute basis. Age, height, birth weight, and room temperature were fitted as continuous variables; sex, observer, venepuncture, and timing of blood samples as categorical variables. Comparisons of high and low mortality towns were carried out on a paired basis by applying paired *t* tests on 4df where necessary. This analysis took variations within as well as between towns in each factor into account. Paired analyses were used to minimise the effects of measurement drift, seasonal factors, and the change in average age, particularly between the first six and the last four towns (measured before and after the summer holidays, respectively). All differences have been presented as high mortality town minus low mortality town.

Results

In all, 3728 subjects took part in the study (75% response rate), including 1408 children who provided a blood sample (64% response rate). The present report is based on 3415 white children (1769 boys, 1646 girls), of whom 1287 provided blood samples. Of these, 515 were taken 30 minutes (27-33 minutes) after a full glucose load. Overall, questionnaires with information on birth weight were available for 2899 of these subjects.

Table 1—Cardiovascular mortality, infant mortality, and prevalence of low birth weight in 10 study towns

Area	Survey pair	Standardised mortality ratio for cardiovascular disease*	Infant mortality 1000/year† (No of deaths)	Prevalence (%) of low birth weight <2500 g† (No of births)
Low mortality:				
Esher	1	64	7.2 (46)	6.3 (6469)
Chelmsford	2	71	8.2 (90)	5.7 (11 050)
Leatherhead	3	70	7.1 (34)	6.1 (4819)
Bath	4	75	9.0 (123)	6.3 (13 794)
Tunbridge Wells	5	71	7.7 (49)	6.2 (6373)
Mean		70	7.8	6.1
High mortality:				
Wigan	1	140	8.4 (105)	7.3 (12 537)
Port Talbot	2	143	5.0 (22)	5.7 (4421)
Burnley	3	131	14.9 (150)	7.9 (10 356)
Rochdale	4	136	10.8 (103)	8.4 (9662)
Rhondda	5	138	10.7 (34)	9.2 (5421)
Mean		138	10.0	7.7

*Based on deaths in men and women aged 35-64 years in England and Wales 1979-83.

†Based on years 1983-5. Source: OPCS Monitor (DH3 series).

Table 2—Physical measurements* made in towns with high and low cardiovascular mortality: all children. All values are means (SE)

Town	No of children	Age (years)	Height (cm)	Weight (kg)	Ponderal index (kg/m ³)	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	Heart rate/min
All	3415	10.45 (0.01)	141.0 (0.1)	35.9 (0.1)	12.70 (0.03)	112.4 (0.2)	65.5 (0.1)	81.4 (0.2)
Low cardiovascular mortality:								
Esher	299	10.59 (0.04)	141.5 (0.4)	35.9 (0.4)	12.61 (0.11)	109.6 (0.6)	63.9 (0.4)	83.1 (0.7)
Chelmsford	364	10.62 (0.03)	141.2 (0.3)	35.1 (0.4)	12.43 (0.10)	111.3 (0.6)	65.7 (0.4)	80.2 (0.6)
Leatherhead	292	10.81 (0.04)	141.5 (0.4)	35.0 (0.4)	12.29 (0.11)	109.2 (0.6)	63.6 (0.4)	80.6 (0.7)
Bath	333	10.27 (0.03)	141.9 (0.3)	35.7 (0.4)	12.41 (0.10)	112.7 (0.6)	65.4 (0.4)	81.9 (0.6)
Tunbridge Wells	440	10.19 (0.03)	141.8 (0.3)	36.9 (0.4)	12.83 (0.09)	114.7 (0.5)	66.4 (0.3)	82.5 (0.5)
High cardiovascular mortality:								
Wigan	380	10.65 (0.03)	140.2 (0.3)	35.4 (0.4)	12.76 (0.10)	112.2 (0.6)	65.0 (0.4)	80.2 (0.6)
Port Talbot	342	10.55 (0.04)	141.2 (0.3)	36.8 (0.4)	12.96 (0.10)	113.9 (0.6)	66.4 (0.4)	81.4 (0.6)
Burnley	321	10.61 (0.03)	140.1 (0.3)	35.0 (0.4)	12.61 (0.11)	110.9 (0.6)	65.1 (0.4)	79.1 (0.6)
Rochdale	226	10.08 (0.04)	140.2 (0.4)	35.2 (0.5)	12.69 (0.13)	113.0 (0.7)	66.3 (0.5)	81.4 (0.8)
Rhondda	418	10.19 (0.03)	140.2 (0.3)	36.9 (0.4)	13.26 (0.09)	114.9 (0.5)	66.3 (0.3)	83.9 (0.6)
Mean (SE) difference (high – low)		–0.08 (0.05)	–1.2 (0.3)	0.1 (0.4)	0.34 (0.06)	1.5 (0.5)	0.8 (0.3)	–0.5 (0.6)
95% Confidence interval		–0.22 to 0.06	–0.3 to –2.1	–1.0 to 1.3	0.16 to 0.52	0.0 to 2.9	0.1 to 1.6	–2.7 to 1.8
P value		0.19	0.02	0.75	0.006	0.05	0.04	0.6

*Physical measurements adjusted for age, sex, observer, and effect of venepuncture and room temperature (blood pressure only).

Table 3—Measurements* made in high and low cardiovascular mortality towns: older children only. All values are means (SE)

Town	No of children	Age (years)	Waist:hip ratio	Total cholesterol (mmol/l)	Glucose test	
					No of children	Post-load glucose (mmol/l)
All	1287	10.99 (0.01)	0.798 (0.002)	4.66 (0.02)	515	7.0 (0.06)
Low cardiovascular mortality:						
Esher	113	11.12 (0.03)	0.797 (0.005)	4.65 (0.07)	39	6.6 (0.2)
Chelmsford	132	11.21 (0.03)	0.793 (0.005)	4.61 (0.07)	50	7.1 (0.2)
Leatherhead	119	11.39 (0.03)	0.786 (0.005)	4.64 (0.07)	55	7.5 (0.2)
Bath	138	10.63 (0.03)	0.801 (0.005)	4.74 (0.07)	62	7.0 (0.2)
Tunbridge Wells	164	10.71 (0.02)	0.801 (0.004)	4.65 (0.06)	60	7.3 (0.2)
High cardiovascular mortality:						
Wigan	143	11.19 (0.03)	0.798 (0.004)	4.64 (0.07)	54	6.9 (0.2)
Port Talbot	118	11.24 (0.03)	0.802 (0.005)	4.59 (0.07)	45	7.0 (0.2)
Burnley	123	11.10 (0.03)	0.797 (0.005)	4.63 (0.07)	48	6.9 (0.2)
Rochdale	94	10.57 (0.03)	0.791 (0.006)	4.76 (0.08)	43	6.8 (0.2)
Rhondda	143	10.76 (0.03)	0.805 (0.004)	4.70 (0.06)	59	7.1 (0.2)
Mean (SE) difference (high-low)		–0.04 (0.07)	0.003 (0.004)	0.01 (0.01)		–0.2 (0.1)
95% Confidence interval		–0.22 to 0.14	–0.007 to 0.014	–0.03 to 0.04		–0.6 to 0.2
P value		0.58	0.46	0.67		0.33

*All measurements adjusted for age, sex, and observer (waist:hip ratio only).

Table 2 summarises the average measurements made in all children, in children in each study town, and the paired differences between high and low mortality towns. Children in high mortality towns were on average more than 1 cm shorter and had a higher ponderal index than children in low mortality towns. Children in Rhondda had an exceptionally high mean ponderal index. These differences were similar in boys and girls and were little affected by adjustment for social class (data not presented). The use of a modified ponderal index with stable variance across childhood²⁰ had no important effect on this finding. Mean blood pressures were higher in high mortality towns, with differences at the margin of significance; there were no important differences in heart rate. Height is a strong determinant of blood pressure, independent of age, both in this study and others.^{21 22} Adjustment for height accentuated the mean difference in blood pressure between high and low mortality towns both for systolic pressure (mean difference 2.0 mm Hg; 95% confidence interval 0.8 to 3.2 mm Hg; $P = 0.009$) and for diastolic pressure (mean difference 1.0 mm Hg; 0.2 to 1.7; $P = 0.02$). These differences were similar in boys and girls. Further adjustment for ponderal index reduced but did not abolish the differences in blood pressure,

both for systolic pressure (1.3 mm Hg; 0.1 to 2.4; $P = 0.04$) and for diastolic pressure (0.8 mm Hg; 0.0 to 1.5; $P = 0.05$).

Table 3 gives data on waist:hip ratios, total cholesterol concentrations, and post-load glucose measurements in the older children. The differences in all of these measurements between high and low mortality towns were small and not significant; 95% confidence intervals excluded high-low differences of more than 0.014 in waist:hip ratio, 0.04 mmol/l in total cholesterol, and 0.2 mmol/l in post-load blood glucose.

EFFECT OF ADJUSTMENT FOR BIRTH WEIGHT ON DIFFERENCES IN HEIGHT, PONDERAL INDEX, AND BLOOD PRESSURE

The two groups of towns examined in this study differed not only in their adult cardiovascular mortality but also in their infant mortality and prevalence of low birth weight, both of which were higher in the towns with high cardiovascular mortality at the time these children were born (table 1). Within the white study population there were corresponding differences between high and low mortality towns in the prevalence of low birth weight (mean difference 2.3%; $P = 0.07$) and in mean

Table 4—Differences in height, ponderal index, and blood pressure in children from towns with high and low mortality: effect of adjustment for birth weight

Measure and adjustment for birth weight	Mean (95% confidence interval)	P value
Height (cm):		
Not adjusted	1.0 (0.2 to 1.8)	0.03
Adjusted	0.9 (0.1 to 1.7)	0.04
Ponderal index (kg/m ³):		
Not adjusted	0.35 (0.14 to 0.57)	0.01
Adjusted	0.37 (0.14 to 0.59)	0.01
Systolic pressure (mm Hg) (height standardised):		
Not adjusted	1.5 (0.1 to 2.9)	0.04
Adjusted	1.5 (0.0 to 2.9)	0.05

Based on 2899 subjects with data on birth weight. All analyses are adjusted for age, sex, observer, and effect of venepuncture and room temperature (blood pressure only).

birth weight (40 g; $P = 0.04$). As birth weight is related to childhood height ($r = 0.16$), ponderal index ($r = 0.10$), and blood pressure standardised for height ($r = -0.07$) in individual children with birthweight data ($n = 2899$), it is important to consider whether birth weight might explain the differences observed between high and low mortality towns in height, ponderal index, and blood pressure. The effects of adjustment for birth weight on these differences were therefore examined in the 2899 subjects with data on birth weight (table 4). In this population, adjustment for birth weight produced only slight attenuation of the differences in height and in blood pressure standardised for height, while the differences in ponderal index became more distinct.

Discussion

In this study we compared the cardiovascular risk profiles of children living in towns with exceptionally high and exceptionally low adult cardiovascular mortality. Children in high mortality towns were on average shorter and had a higher mean ponderal index and higher mean blood pressures (particularly after height standardisation). Waist:hip ratio, total cholesterol concentration, and post-load glucose measurements were, however, similar in high and low mortality towns. Strengths of the survey design were, firstly, the pairing of towns at the extremes of the distribution of adult cardiovascular mortality, both in measurement and analysis, to limit the effect of measurement drift and seasonal effects on high-low comparisons; and, secondly, the use of a stratified sampling method designed to include representative samples of children attending state primary schools within each study town.²³ The exclusion of children attending independent schools (more important in low mortality towns) and the limited response to blood sampling (although consistent with other recent studies in children²⁴), however, may have reduced the range of social circumstances represented in the study population. The effect of these exclusions is probably the underestimation of differences between high and low mortality areas in factors which show a strong social class gradient—height and ponderal index in the present study. The effect on the results reported of exclusion of children from ethnic minority groups (particularly Asian children in Burnley and Rochdale) was small.

OTHER STUDIES

When compared with the results of other recent British studies,²⁵⁻²⁷ the average heights, weights, and total cholesterol concentrations were similar. However, even if we allow for the systematic overestimation of systolic pressure by the Dinamap 1846 instrument,¹⁸ both

systolic and diastolic pressures are higher than those observed in 10 year olds in the Brompton study (based in Farnborough, Kent).²⁶ The extent to which these differences reflect differences in methodology or the different geographical and social composition of the study populations remains uncertain. The observation that children in high cardiovascular mortality areas are shorter than those in low mortality areas is consistent with the findings of our earlier study in 5-7 year olds⁷ and the 1970 British birth survey at 10 years.²⁸ The geographical variation in ponderal index is consistent with recent findings in adults; the particularly high mean ponderal indices observed in South Wales (particularly Rhondda) in the present study are consistent with our findings in earlier surveys.^{7, 23} While the presence of higher mean blood pressures in areas of high cardiovascular mortality would be consistent with earlier studies in adults,^{3, 29} three earlier geographical studies have failed to observe consistent relations between childhood blood pressure and adult cardiovascular mortality.^{6, 7, 28} Two of those studies, however, were consistent with the present one in observing that average blood pressures in Surrey towns (Guildford, Esher, Leatherhead) were particularly low, despite the measurements being conducted at different times of year.^{6, 7}

The absence of variation in total cholesterol concentrations between areas with high and low cardiovascular mortality is consistent with the findings of adult surveys—notably, the British regional heart study³ and the health surveys for England.³⁰ The total cholesterol concentrations in children in this study, although comparable with those observed in other British studies,²⁷ may be high by international standards, an issue of considerable potential public health importance.

IMPLICATIONS FOR FUTURE DEVELOPMENT OF CARDIOVASCULAR RISK

Current evidence suggests that the direct effect of social circumstances in childhood on adult cardiovascular risk is likely to be small.^{31, 32} The shorter stature, higher ponderal index, and higher mean blood pressures observed in the children in high mortality towns, however, all carry potentially adverse consequences if maintained, or amplified, during passage into adult life.³³⁻³⁵ The extent to which this will occur depends on the experience of this particular cohort and is therefore difficult to predict accurately. The differences in height observed could be a reflection of differences in the timing of growth as well as differences in its velocity. The differences in height in children in these towns, however, were already clearly established at 5-7 years⁷ and are similar at 8-11 years in girls and boys (despite their differences in physical maturation at this age). Moreover, there are differences of a similar pattern in the average reported paternal and maternal heights of this study population. These observations suggest that short term differences in the timing of growth are not responsible for the height differences observed and that they are likely to persist in the longer term. The natural history of the differences in blood pressure will depend to some extent on the natural history of the differences in ponderal index and height. If the differences in ponderal index between high and low mortality areas become more distinct the differences in blood pressure are likely to increase. The increase in differences in blood pressure after adjustment for height suggests that, when differences in physical maturity are taken into account, average blood pressures are higher in high mortality towns. Although height is strongly related to blood pressure in children,^{22, 23} its relation with blood pressure in adult life is weak.³⁴ Whether the differences in blood pressure per se, or the differences in blood pressure standardised for height, will provide a better

Key messages

- It has been suggested that cardiovascular risk may be strongly influenced by childhood or intra-uterine experience
- Development of cardiovascular risk factors in British children living in areas with widely different adult cardiovascular mortality has been little studied
- Children in areas of high mortality are on average shorter and have higher ponderal indices and higher blood pressures (particularly when height differences are taken into account) than those in areas of low mortality
- Total cholesterol concentration, waist:hip ratio, and post-load glucose/glucose tolerance are very similar in high and low mortality areas
- The differences in height, ponderal index, and blood pressure are independent of birth weight, suggesting that childhood rather than intrauterine factors may be important in their development

guide to adult blood pressure differences in this population remains uncertain.

It should be borne in mind that, in the development of overall cardiovascular risk, factors which cannot be quantified accurately at 8-11 years may also be important. For example, cigarette smoking, which is likely to become more prevalent in high mortality areas during adolescence,³⁶ may make the differences in risk profile between high and low mortality areas still more distinct during the second decade.

ORIGINS OF DIFFERENCES IN RISK FACTORS

Although the children in high mortality towns had a higher prevalence of low birth weight and lower mean birth weights, as others have found,³⁷ the differences in height, ponderal index, and blood pressure observed could not be accounted for by differences in birth weight. This suggests that factors operating in the childhood environment rather than the intrauterine environment are likely to be important in the development of these risk factor differences. The contribution of diet, physical activity, and social factors to the emergence of differences in risk factors needs to be explored in more detail; four of the five high mortality areas are among the most socially deprived boroughs in England and Wales.³⁸

It has been suggested that the "fetal origins hypothesis" plays an important part in geographical variation in cardiovascular risk within Britain.⁴⁵ The present study, examining variations in cardiovascular risk factors in children from towns at the extremes of the distribution of adult cardiovascular mortality, does not provide a definitive test of the contribution of intrauterine factors to geographical variation in cardiovascular risk. The more important question for the fetal origins hypothesis is whether cardiovascular risk factors in children differ between towns at the extremes of the distribution of infant mortality. The present study was not designed to cover this issue directly. It did, however, include towns with a threefold range in infant mortality (table 1), almost as wide as that for England and Wales as a whole (3.5-fold). At the town level, infant mortality, although strongly related to childhood height, does not show consistent relations with any of the other childhood cardiovascular risk factors reported here. This suggests that, whatever the importance of intrauterine influences on geographical variation in cardiovascular risk in the past, the case for their continuing importance has still to be proved.

We thank the schools, parents, and children who took part in the study; the members of our research team (Sally Gassor, Angela Murphy, Catherine Stuart, Louise Went); the directors of public health in Croydon and New River Health Authorities for allowing FA and ST to take part in the study; and Dr Azeem Majeed, Dr Ivan Perry, Jan Poloniecki. Biochemical analyses were performed by the department of clinical biochemistry at St George's Hospital (Professor Carol Seymour, Dr J A Nisbet).

Funding: Wellcome Trust (grant No 038976/Z/93/Z). MW was supported by the British Heart Foundation.

Conflict of interest: None.

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(Accepted 24 April 1995)

Dietary fat and risk of coronary heart disease in men: cohort follow up study in the United States

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Abstract

Objective—To examine the association between fat intake and the incidence of coronary heart disease in men of middle age and older.

Design—Cohort questionnaire study of men followed up for six years from 1986.

Setting—The health professionals follow up study in the United States.

Subjects—43 757 health professionals aged 40 to 75 years free of diagnosed cardiovascular disease or diabetes in 1986.

Main outcome measure—Incidence of acute myocardial infarction or coronary death.

Results—During follow up 734 coronary events were documented, including 505 non-fatal myocardial infarctions and 229 deaths. After age and several coronary risk factors were controlled for significant positive associations were observed between intake of saturated fat and risk of coronary disease. For men in the top versus the lowest fifth of saturated fat intake (median = 14.8% v 5.7% of energy) the multivariate relative risk for myocardial infarction was 1.22 (95% confidence interval 0.96 to 1.56) and for fatal coronary heart disease was 2.21 (1.38 to 3.54). After adjustment for intake of fibre the risks were 0.96 (0.73 to 1.27) and 1.72 (1.01 to 2.90), respectively. Positive associations between intake of cholesterol and risk of coronary heart disease were similarly attenuated after adjustment for fibre intake. Intake of linolenic acid was inversely associated with risk of myocardial infarction; this association became significant only after adjustment for non-dietary risk factors and was strengthened after adjustment for total fat intake (relative risk 0.41 for a 1% increase in energy, *P* for trend <0.01).

Conclusions—These data do not support the strong association between intake of saturated fat and risk of coronary heart disease suggested by international comparisons. They are compatible, however, with the hypotheses that saturated fat and cholesterol intakes affect the risk of coronary heart disease as predicted by their effects on blood cholesterol concentration. They also support a specific preventive effect of linolenic acid intake.

Introduction

International comparisons¹⁻⁴ and laboratory data⁵ suggest that diets high in saturated fat and cholesterol and low in polyunsaturated fat increase the risk of coronary heart disease. These diets increase blood cholesterol concentration,⁶⁻⁹ which is related to risk of coronary disease.¹⁰ The differences between countries, however, are far larger than one would predict based on effects of cholesterol concentrations. Results of prospective epidemiological investigations and ran-

domised trials have been inconsistent; small size or inadequate dietary assessment may explain most of the discrepancies.^{11 12} We therefore examined the association between dietary fat and cholesterol and risk of myocardial infarction in a large cohort of men in the United States.

Subjects and methods

POPULATION

The health professionals follow up study began in 1986 when 51 529 health professionals aged 40 to 75 years completed a 131 item food frequency questionnaire and provided information about medical history, risk factors for heart disease, and dietary changes during the past 10 years.¹³ Follow up questionnaires were sent in 1988, 1990, and 1992. We excluded from analysis 1595 men who did not satisfy the a priori criteria of daily energy intake between 3.34 and 17.56 MJ and fewer than 70 blanks out of 131 total listed food items. In addition, we excluded 6177 men with previous diagnosis of myocardial infarction, angina, coronary artery surgery, stroke, transient ischaemic attack, peripheral arterial disease, or diabetes. We followed the 43 757 eligible men for incidence of coronary disease during the subsequent six years. Over 94% returned follow up questionnaires in each two year follow up cycle. Participants not listed in the National Death Index who did not respond were assumed to be alive.

DIETARY ASSESSMENT

The 1986 questionnaire asked about average frequency of intake over the previous year of specified portions of 131 foods. We assessed its validity in a random sample of 127 men by comparing their calculated intake of fat with that reported during two diet records over one week taken about six months apart.¹⁴ The correlations between the two assessments of intake, adjusted for energy and corrected for within person variation in the diet records, were 0.75 for saturated fat, 0.76 for cholesterol, and 0.37 for linoleic acid. In addition, the calculated intakes of linoleic and *trans* unsaturated fatty acids were compared with their concentrations in adipose; the correlations between intake as a proportion of fat and the proportion in adipose were 0.48 for linoleic and 0.29 for *trans* fatty acids.¹⁵

CASES

As described elsewhere in detail,¹⁶ end points were fatal coronary disease (including sudden death) and non-fatal myocardial infarction occurring between the return of the baseline questionnaire and 31 January 1992. Participants reporting an incident of myocardial infarction on a follow up questionnaire were asked for permission to review medical records. Non-fatal myocardial infarction was confirmed by using World Health Organisation criteria: symptoms plus either

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BMJ 1996;313:84-90