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SPECIAL THEME: LIFECOURSE AND SOCIAL EPIDEMIOLOGY

Lifecourse influences on health among British adults: Effects of region of residence in childhood and adulthood

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Background It has been suggested that early life exposures are important determinants of geographical variations in adult diseases. We examined inter-regional migrants in Britain to evaluate the relative importance of early and recent exposures for adult cardiorespiratory risk factors, mental ill-health and sensory function.

Methods A total of 9023 persons born throughout England, Scotland and Wales during 1 week in 1958 were followed periodically through childhood into adulthood. At 44–45 years, height, body mass index (BMI), blood pressure (BP), glycosylated haemoglobin, total and high-density lipoprotein (HDL) cholesterol, triglycerides, fibrinogen, total immunoglobulin E (IgE), one-second forced expiratory volume (FEV1), hearing threshold at 4 kHz, visual impairment, symptoms of depression and anxiety, and chronic widespread pain were measured. Analysis of migration between 12 regions included 3125 cohort members who were examined in a region different to their birthplace.

Results Height, BMI, diastolic BP (DBP), FEV1, log-transformed IgE and hearing threshold varied by region among non-migrants (each $P < 0.05$). Among inter-regional migrants, the spatial associations with current region, independent of

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birthplace, followed closely the geographical pattern shown among non-migrants for BMI, DBP and FEV1 (each $P < 0.001$). In contrast, of the 15 outcomes, only adult height was related to region of birth, after adjustment for region of examination ($P = 0.002$)

Conclusions Although individual disease risk is predicted by early life factors, early exposures do not explain regional variations in cardiovascular and respiratory risk factors among middle-aged adults in Britain. Geographical inequalities in cardiorespiratory health are more strongly related to factors associated with region of examination that influence obesity, BP and ventilatory function.

Keywords Birth cohort, health inequalities, geographical variation, migration

Introduction

In an influential series of papers in the mid-1980s, Barker and Osmond noted that geographical variations in mortality from ischaemic heart disease[1], stroke[2] and chronic bronchitis[3] within England and Wales during 1968–78 were correlated with the spatial patterns of infant and maternal mortality five decades earlier. They hypothesised that these ecological associations arose from 'programming' of cardio-respiratory risk in pre-natal or early post-natal life, stimulating two decades of research into lifecourse epidemiology.[4] An alternative explanation is that these geographical correlations arise from ecological confounding, due to historical continuities in the variations of social and environmental conditions across Britain.[5]

Studies of migrants can help to distinguish between these alternative explanations. If geographical variations in mortality risk are determined to a substantial degree early in life (or by genetic factors), then the patterns of death, cardiorespiratory disease and associated risk factors should be related more closely to place of birth than to place of current residence, whereas birthplace would be less influential if recent social circumstances, environmental exposures or medical care were the main contributors to geographical variations in disease risk and mortality.

There have been no migrant studies within the UK for cardiovascular risk factors other than blood pressure (BP),[6] or for other common diseases and risk indicators. In this article, we report migration analyses of cardiorespiratory risk factors, sensory function and mental health that were ascertained during biomedical examination of a national British birth cohort in early middle age. In an extension of the statistical methods applied earlier to case-control data,[7] we use the measurements on non-migrants to score each geographical region, for use in a quantitative assessment of the independent effects of birthplace and current area of residence among inter-regional migrants. This complements the companion paper that analyses socio-economic inequalities in disease risk by social position in childhood and adulthood.[8]

Methods

Subjects and measurements

The British 1958 birth cohort (also known as the National Child Development Study) is a longitudinal study of persons born in England, Scotland and Wales during 1 week in March 1958 who were originally recruited for the Perinatal Mortality Survey.[9] The cohort was followed up at ages 7, 11 and 16 years by parental interviews and examinations conducted by school medical officers, and at ages 16, 23, 33 and 42 years by means of interviews with participants. Immigrants of the same dates of birth were identified at ages 7, 11 and 16, and followed into adulthood, but adult immigrants (after age 16) have not been included.

All cohort members who were still in contact with the cohort study team, and at age 42, had not required a proxy interview (e.g. due to learning disability), were invited to participate in a clinical examination in their home at the age of 44–45 years. The home visits were carried out from September 2002 to March 2004 by a team of 122 trained nurses from the National Centre for Social Research, who conduct the annual Health Surveys of England and Scotland. Visits occurred in every region in each month of fieldwork. From a target sample of 12 069 persons, 9377 (78%) cohort members were visited (Figure 1), of whom 9023 were born in England, Scotland and Wales.

Standing height was measured to the nearest millimetre using a Leicester portable stadiometer placed on a hard floor. Weight was measured to the nearest 0.1 kg in light clothing with shoes removed. Where it was not possible to obtain an accurate measurement, or consent was not provided, self-reported weight ($n = 100$) or height ($n = 84$) was recorded. Body mass index (BMI) was calculated as kg/m^2 excluding two participants who were pregnant at the time of interview.

BP and pulse rate were measured three times in the seated position after a period of 5 min rest, using the Omron 705CP automated sphygmomanometer (Omron, Tokyo, Japan), with a large cuff for subjects with a mid-upper arm circumference of $\geqslant$32 cm. The mean BP was determined for readings that the nurse considered to be reliable.

Spirometry was performed in the standing position without noseclips, using Vitalograph Micro spirometers, checked daily for calibration drift. At least three blows were recorded, and up to five were performed if the best-test variation [assessed by the sum of one-second forced expiratory volume (FEV1) and forced vital capacity] was $>5\%$. In the analysis, all readings with a best-test variation $>10\%$ were excluded. FEV1 measurements were adjusted for height and gender, using separate linear regression models for males and females. Values with standardized residuals greater than $+3$ SD units were excluded from subsequent analyses.

Venous blood samples were obtained without prior fasting, and posted to a central laboratory. Glycosylated haemoglobin (HbA1c) was assayed by ion exchange high performance liquid

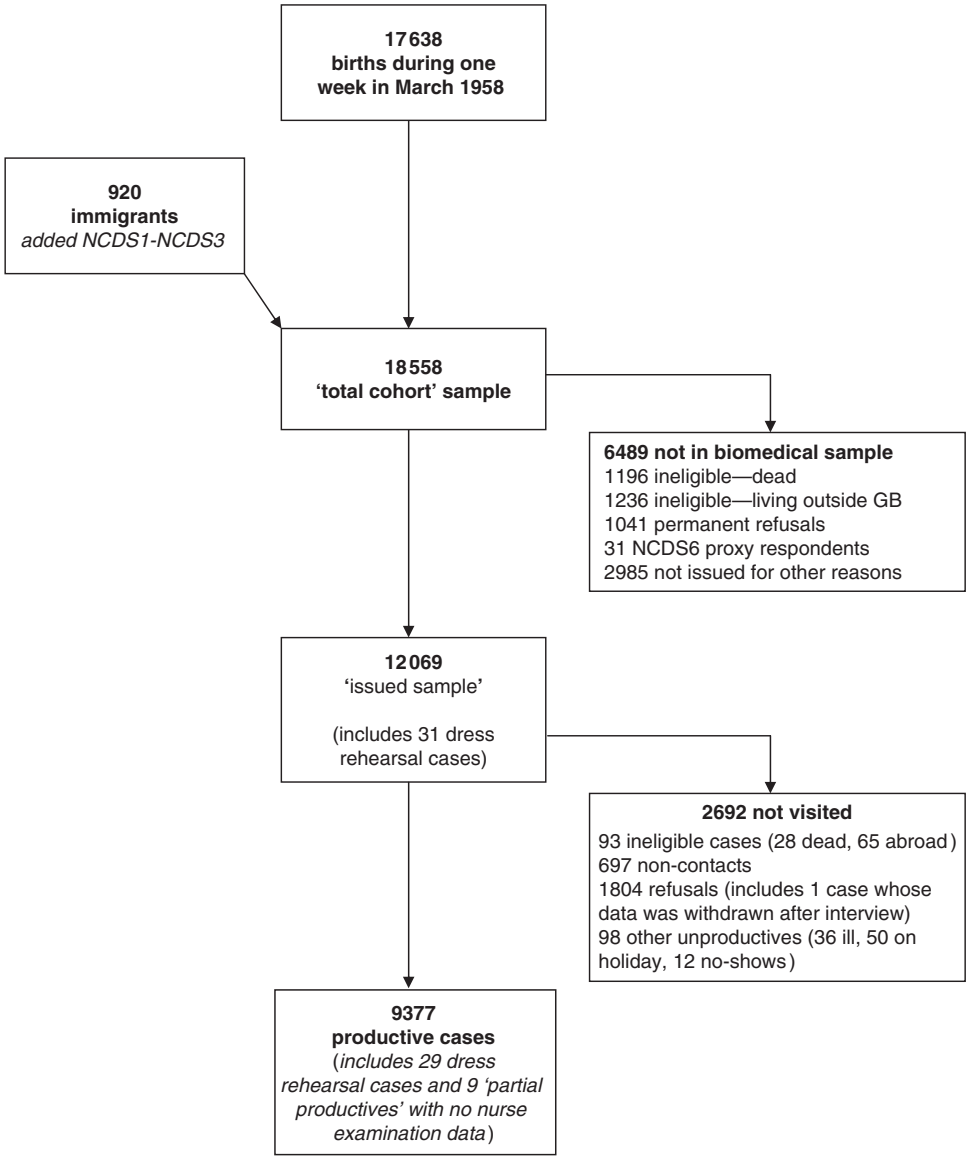

Figure 1 Flow diagram defining the issued sample and outcomes for the biomedical survey

chromatography on whole blood. Triglycerides, total and high-density lipoprotein (HDL) cholesterol were measured by autoanlyser. Fibrinogen was assayed by the Clauss method on citrated plasma samples (MDA 180 coagulometer, Biomerieux, Basingstoke, UK). Total circulating immunoglobulin E (IgE) was measured using the HYTEC enzyme immunoassay; values > 2000 were recoded to 2000 and zero values to 0.5.

Pure tone audiometry was performed in the home by air conduction in both ears, with test tones at 1 kHz and 4 kHz according to the British Society of Audiology's recommended procedure.[10] MA25 portable audiometers with TDH 49 earphones in audiocups were used, calibrated to British Standard BS EN ISO 389–1 (2000). We used hearing level at 4 kHz in the better ear, if hearing at 1 kHz was better than 30 dB. Distance visual acuity in each eye was measured using the 3 m Keeler crowded logarithm of the minimum angle of resolution (LogMAR) test booklet with distance correction (glasses or contact lenses) if prescribed for distance vision, and pinhole. Vision impairment was defined as logMAR > 0.2 (~6/12 or worse) in the better eye.

Symptoms of depression and anxiety in the previous week were measured by the revised Clinical Interview Schedule[11] administered by the nurse. Participants who reported two or more items for either the depressive ideas or anxiety symptom modules were classified as high scorers for the respective symptom.

Chronic widespread pain, ascertained by self-completed questionnaire including a manikin (shaded by participants), was defined, as proposed by the American College of Rheumatology in their classification of fibromyalgia,[12] as pain occurring for longer than 3 months: both above and below the waist; on both the left and right sides of the body; and in the axial skeleton (upper spine, low back or sternum).

Table 1 Distribution of all participants and non-migrants by region of birth, and migrants according to their place of birth and place of examination (with column percentages in parentheses)

		Original cohort	Examined 2002–04	Non-migrants	Migrants classified by:	
Region	**Counties (as defined in 1958)**	Place of birth	Place of birth	Place of birth	Place of birth	Place of examination
Northwestern	Cheshire, Lancashire, Isle of Man	2304 (12.4)	1130 (12.1)	801 (13.5)	329 (10.5)	174 (5.6)
Northern	Cumberland, Durham, Northumberland, Westmoreland, Yorkshire North Riding	1257 (6.8)	655 (7.0)	481 (8.2)	174 (5.6)	114 (3.6)
E and W Ridings	Yorkshire East and West Ridings	1491 (8.0)	770 (8.2)	533 (9.0)	237 (7.6)	154 (4.9)
North Midlands	Derbyshire, Leicestershire, Lincolnshire, Northamptonshire, Nottinghamshire, Rutland	1273 (6.9)	687 (7.3)	480 (8.1)	207 (6.6)	272 (8.7)
Eastern	Bedfordshire, Cambridgeshire, Essex, Hertfordshire, Huntingdonshire, Norfolk, Suffolk East and West	1224 (6.6)	695 (7.4)	441 (7.5)	254 (8.1)	484 (15.5)
Greater London	As defined in 1965	2640 (14.2)	1284 (13.7)	443 (7.5)	841 (26.9)	219 (7.0)
Southeastern (not London)	Kent, Surrey, Sussex East and West	919 (5.0)	474 (5.1)	296 (5.0)	178 (5.7)	460 (14.7)
Southern	Berkshire, Buckinghamshire, Dorset, Hampshire, Isle of Wight, Oxfordshire	1000 (5.4)	547 (5.8)	317 (5.4)	230 (7.4)	459 (14.7)
Southwestern	Channel Islands, Cornwall, Devon, Gloucestershire, Somerset, Wiltshire	985 (5.3)	521 (5.6)	378 (6.4)	143 (4.6)	384 (12.3)
Midlands	Herefordshire, Shropshire, Staffordshire, Warwickshire, Worcestershire	1653 (8.9)	846 (9.0)	608 (10.3)	238 (7.6)	197 (6.3)
Wales	All Welsh counties	915 (4.9)	483 (5.2)	369 (6.3)	114 (3.6)	118 (3.8)
Scotland	All Scottish counties including Inner and Outer Hebrides, Orkney and Shetland	2004 (10.8)	931 (9.9)	751 (12.7)	180 (5.8)	90 (2.9)
Elsewhere	Northern Ireland and countries outside the UK	893 (4.8)	354 (3.8)			(Excluded from this analysis)
TOTAL		18558 (100)	9377 (100)	5898 (100)	3125 (100)	3125 (100)

Socio-economic position in childhood is based on father's occupation recorded in 1958, (or at the age 7 years if data were unavailable at birth; $n = 422$). Adult socio-economic position is based on the participant's current or most recent occupation at age 42 (or 33 if data were unavailable at 42; $n = 1558$). Occupation was categorized using the Registrar General's Classification into six classes: professional (I), managerial/technical (II), other non-manual (IIInm), skilled manual (IIIm), partly skilled (IV) and unskilled manual (V); those with no male head of household in childhood were grouped with class V.

Statistical analysis

Regression analyses were performed using STATA version 9.1 (STATA Corporation, Texas, USA). Continuous outcome measures were log-transformed if necessary to normalize their distribution (HDL cholesterol, triglycerides, fibrinogen, total IgE and hearing threshold).

For all measurements in the field, probability plots of the means by nurse and by instrument were inspected for outliers. This identified outlying hearing data from one nurse which was excluded from subsequent analyses.

Place of birth and place of residence at examination were both coded to the regional boundaries prevailing in 1958 with Greater London (as defined in 1965) further distinguished. Twelve regions were thus defined (Table 1). Migrants were identified as those whose birth region differed from their region at examination, no account being taken of intervening moves. The regional distribution of each outcome was assessed for the non-migrants and migrants separately.

In contrast to variables such as socio-economic position, where there is a conventional ranking imposed on the classification, the ranking of regions is not defined *a priori*. We, therefore, used the non-migrant data to generate quantitative scores for each region. For each outcome, this score variable was calculated as the mean value among non-migrants born in that region (for quantitative outcomes) or the logodds

among non-migrants born in that region (for dichotomous outcomes). The regional score was then introduced as an explanatory variable in models based only on inter-regional migrants, assigned, in turn, to the region of birth and to the region of examination. This is an efficient method of evaluating early (place of birth) and later (place of examination) effects, because it allows more epidemiologically focused and statistically powerful (1df) trend tests to be applied to the migrant data, rather than drawing conclusions based solely on (11df) tests of heterogeneity across regions of birth or examination.

In modelling the data for migrants, we first fitted a linear regression model including birth region and current region simultaneously, both as categorical variables. *F*-tests for heterogeneity for region in 1958 and 2002–04 (each on 11df) were used as an overall estimate of the independent effects of region of birth and adulthood on each continuous outcome. A similar approach was adopted for binary outcome measures using logistic regression, where the likelihood ratio test (on 11df) was used to test for the independent effects of region at birth and in adulthood.

Two models were then fitted for each outcome in migrants only. The first model included current region (as 12 categories) and the score variable assigned to region of birth. In this model, the parameter estimate and associated (1df) significance test for the score variable evaluates the extent to which geographical variations in each outcome among migrants are determined by their region of birth, independent of region of examination. If region of birth totally explained the geographical variation, then the expected value of the regression coefficient for the score variable would be 1.0. For illustration, persons born in regions where the population is generally taller would be expected to be taller as adults regardless of their region of residence in adulthood. As shown in Table 2, adult height is associated with region of birth independent of region of examination ($P = 0.002$, 1df), but the regression coefficient for the score variable differs both from zero and from unity (0.55, 95%CI 0.20 – 0.91), indicating some influence of later place of residence in addition to the birthplace effect, plausibly due to geographical mobility during childhood.

The second model included region of birth (as 12 categories) and the score variable assigned to region of examination. In this model, the score variable evaluates the extent to which geographical variations in each outcome among migrants are determined by their region of examination, independent of region of birth. If region of examination totally explained the geographical variation, then the expected value of the regression coefficient for the score variable would be 1.0. As shown in Table 2, adult BMI is associated with region of examination independent of region of birth ($P = 0.001$, 1df), and the regression coefficient for the score variable (0.93, 95%CI 0.36 –1.50) is very close to unity. This implies a dominant effect of current place of residence, independent of region of residence early in life. This is represented visually by the superimposed regression line in the lower left-hand portion of Figure 1, relating BMI in migrants to the mean BMI of non-migrants in their region of birth.

All regression models in migrants included adjustment for gender. Regression models were further elaborated by adjusting for socio-economic position in childhood and adulthood as categorical variables. Where the predominant influence was region of examination, possible artifacts arising from observer, instrument or laboratory batch were evaluated by random effects modelling.

Results

Table 1 shows the distribution of all 18 558 original cohort members and the 9377 participants in the biomedical survey, by region of birth. The proportion of the full cohort who were examined in 2002–04 varied by birthplace from 46.5% in Scotland to 56.7% in Eastern England, but the resulting regional distribution for participants was similar to that for the full cohort (Table 1).

From our analyses, 354 participants born in Northern Ireland or outside the UK were excluded, leaving 9023 (4487 men, 4536 women) participants born in England, Scotland or Wales, of whom 3125 (1534 men, 1591 women) were examined in a region different to their region of birth. About one-quarter of these migrants moved from Greater London, mainly to the surrounding Eastern, Southeastern and Southern regions of England (Table 1).

Among the 5898 non-migrants, there was unadjusted regional variation in height, BMI, diastolic BP (DBP), FEV1, total IgE and hearing thresholds but not in levels of total or HDL cholesterol, glycosylated haemoglobin, triglycerides or fibrinogen. Visual acuity, anxiety, depression and chronic widespread pain did not show heterogeneity by region (Table 2).

Among the 3125 inter-regional migrants, 11df tests for heterogeneity showed independent effects of current region for BMI, DBP, FEV1, triglycerides and anxiety after adjustment for birth region and gender; and birth region for adult height after adjustment for current region and gender (Table 2).

When the average values for non-migrants were used to score each region of examination, there were positive trends ($P < 0.001$, 1df) for BMI, DBP and FEV1, suggesting that the association of these cardiorespiratory risk factors with current region (independent of birth region and gender) follows the geographical pattern found in non-migrants (Figure 2). These trends persisted after adjustment for social position in childhood and adulthood ($P < 0.002$, 1df). After further adjustment for potential confounders, including observer and instrument effects and factors given in Table 3, the associations for place of current residence remained for DBP ($P < 0.0001$), BMI ($P = 0.002$) and FEV1 ($P = 0.02$). The current region variation in triglycerides was not so clearly related to the average value in non-migrants ($P = 0.08$ after adjustment). The corresponding graphical presentations for each health outcome appear in the web supplement as Figure 3W and supporting data as Table 4W.

For anxiety symptoms, there was evidence of heterogeneity among the migrants in relation to current region ($P = 0.02$, 11df), and a trend ($P = 0.02$, 1df) in relation to current region, scored by the average values for non-migrants. In contrast, height showed a trend for birth region (independent of current region and gender, $P = 0.002$) that persisted after additional adjustment for childhood and adulthood social class ($P = 0.003$). For two outcomes, a weak correlation was observed between birth region effect and non-migrant score: this relationship was positive for triglycerides ($P = 0.06$) but

Table 2 Regional heterogeneity in biomedical outcomes among non-migrants and migrants, and association of outcomes in migrants with scores derived from regional mean values in non-migrants[a]

Risk factor or condition	Non-migrants	Migrants	
		Region of birth	Region at examination
Adult height (cm)			
P-value for heterogeneity (11df)	0.0001	0.05	0.46
P-value for score parameter (1df)		0.002	0.42
Coefficient (95%CI) for score		0.55 (0.20, 0.91)	−0.16 (−0.54, 0.23)
BMI (kg/m^2)			
P-value for heterogeneity (11df)	0.0003	0.34	0.03
P-value for score parameter (1df)		0.50	0.001
Coefficient (95%CI) for score		0.19 (−0.36, 0.73)	0.93 (0.36, 1.50)
DBP (mmHg)			
P-value for heterogeneity (11df)	0.02	0.34	<0.001
P-value for score parameter (1df)		0.55	<0.001
Coefficient (95%CI) for score		0.15 (−0.34, 0.65)	1.35 (0.86, 1.84)
FEV1 adjusted for height (ml)			
P-value for heterogeneity (11df)	0.02	0.53	0.007
P-value for score parameter (1df)		0.29	0.001
Coefficient (95%CI) for score		−0.35 (−0.88, 0.18)	0.90 (0.42, 1.39)
HbA1c (% total)			
P-value for heterogeneity (11df)	0.91	0.97	0.11
P-value for score parameter (1df)		0.97	0.20
Coefficient (95%CI) for score		0.02 (−1.05, 1.09)	0.64 (−0.34, 1.62)
Total cholesterol (mmol/l)			
P-value for heterogeneity (11df)	0.08	0.48	0.64
P-value for score parameter (1df)		0.30	0.07
Coefficient (95%CI) for score		−0.35 (−1.00, 0.31)	0.56 (−0.04, 1.15)
HDL cholesterol (mmol/l)			
P-value for heterogeneity (11df)	0.13	0.45	0.13
P-value for score parameter (1df)		0.76	0.12
Coefficient (95%CI) for score		0.12 (−0.63, 0.86)	0.53 (−0.13, 1.20)
Triglyceride(mmol/l)			
P-value for heterogeneity (11df)	0.12	0.71	0.008
P-value for score parameter (1df)		0.06	0.09
Coefficient (95%CI) for score		0.60 (−0.02, 1.22)	0.58 (−0.09, 1.26)
Fibrinogen (g/L)			
P-value for heterogeneity (11df)	0.19	0.08	0.97
P-value for score parameter (1df)		0.30	0.52
Coefficient (95%CI) for score		0.42 (−0.37, 1.22)	−0.23 (−0.94, 0.48)
Total IgE (kU/L)			
P-value for heterogeneity (11df)	0.006	0.62	0.45
P-value for score parameter (1df)		0.06	0.10
Coefficient (95%CI) for score		−0.37 (−0.75, 0.02)	0.36 (−0.07, 0.79)
Hearing threshold at 4 kHz (dB)			
P-value for heterogeneity (11df)	0.03	0.06	0.08
P-value for score parameter (1df)		0.47	0.22
Coefficient (95%CI) for score		−0.17 (−0.62, 0.28)	0.38 (−0.22, 0.98)
Visual impairment (%)			
P-value for heterogeneity (11df)	0.14	0.67	0.43
P-value for score parameter (1df)		0.16	0.94

Continued

Table 2 Continued

Risk factor or condition	Non-migrants	Migrants	
		Region of birth	Region at examination
Coefficient (95%CI) for score		−0.34 (−0.79, 0.11)	0.02 (−0.36, 0.39)
Depressive symptoms (%)			
P value for heterogeneity (11df)	0.36	0.62	0.52
P value for score parameter (1df)		0.24	0.23
Coefficient (95%CI) for score		0.48 (−0.33, 1.30)	0.49 (−0.30, 1.27)
Anxiety symptoms (%)			
P value for heterogeneity (11df)	0.61	0.99	0.02
P value for score parameter (1df)		0.56	0.02
Coefficient (95%CI) for score		−0.24 (−1.05, 0.56)	1.26 (0.22, 2.31)
Chronic widespread pain (%)			
P value for heterogeneity (11df)	0.29	0.10	0.54
P value for score parameter (1df)		0.37	0.58
Coefficient (95%CI) for score		−0.40 (−1.27, 0.47)	−0.20 (−0.90, 0.51)

[a]Means in migrants by region of birth are adjusted for current region and gender. Means in migrants by region at examination are adjusted for region of birth and gender. FEV1 is additionally adjusted for height throughout. Non-migrants analyses are based on 4849–5890 subjects; migrant analyses are based on 2561–3118 subjects.

negative for log-transformed IgE ($P = 0.06$). Given the lack of overall heterogeneity for these risk factors in relation to birthplace (Table 2), these results may be type 1 errors.

A comparison between migrants and non-migrants showed migrants to be taller and to have lower levels of BMI, DBP, HbA1c, HDL cholesterol, triglycerides, fibrinogen, hearing loss, and a lower prevalence of depressive symptoms. These effects were attenuated after adjustment for all potential confounders (listed in Table 3), but persisted ($P < 0.05$) for height, BMI, HDL cholesterol and triglycerides. In general, differences between migrants and non-migrants are considerably smaller than the regional variations in these outcomes.

Discussion

The 'early origins' hypothesis was stimulated by *ecological* (area-based) correlations,[1–3] but it has been investigated mainly by studies of *individuals*.[4] Our migrant study provides the most comprehensive test, to date, of the importance of early life factors as determinants of the geographical variations in risk of common diseases and risk factors for premature death in British adults. Our results generally implicate region of current residence as much more important than region of birth, particularly for BMI, BP and ventilatory function. However, the effect of region of current residence on ventilatory function was attenuated in analyses stratified by gender. None of the other outcomes exhibited this attenuation in gender stratified analyses. Some important risk factors, including cholesterol, glucose intolerance and fibrinogen, as well as indicators of sensory function and mental ill-health, showed little evidence of regional inequalities. Adult height provides a counter example, and as expected is influenced by region of residence early in life.

Few studies of disease risk among migrants within the UK have been reported. Among a representative 1% sample, enumerated in 1939 and at census in 1971, regional variations in mortality from ischaemic heart disease and stroke were related to both place of enumeration in 1939 and place of residence in 1971.[7] Among men followed for 22 years in the British Regional Heart Study, zone of examination was more strongly associated with incident ischaemic heart disease (fatal and non-fatal) than was zone of birth, even after adjusting for major risk factors.[13] BP levels in the same study were also influenced primarily by zone of examination rather than zone of birth,[6] consistent with our results and also with studies of international migrants.[14] We are not aware of previous migrant studies of other cardiovascular risk factors or the other outcomes we tested.

We found evidence of a more favourable cardiovascular risk profile among migrants, which is consistent with the lower levels of cardiovascular mortality among inter-regional migrants in Britain.[7] However, not all measurements showed this pattern: interesting exceptions being total cholesterol, total IgE and anxiety symptoms. This suggests that it may be unwise to make generalized assumptions about 'healthy migrant' effects.

Over the past two decades, ample evidence has accumulated that individual risk of disease is predicted by measures of growth and health in the first few years of life.[4] What is much less clear is the extent to which these *individual-level* associations explain the level of disease risk in different *populations*.[15] The companion paper[8] shows that for many of the outcomes studied, adult health is related to social inequalities in childhood after adjustment for adult social position. Comparing that article with this one, three features are noteworthy.

First, outcomes that show social inequalities do not necessarily vary by region, even among non-migrants. Secondly, all outcomes that were independently related to region of examination (obesity, BP and lung function) were also

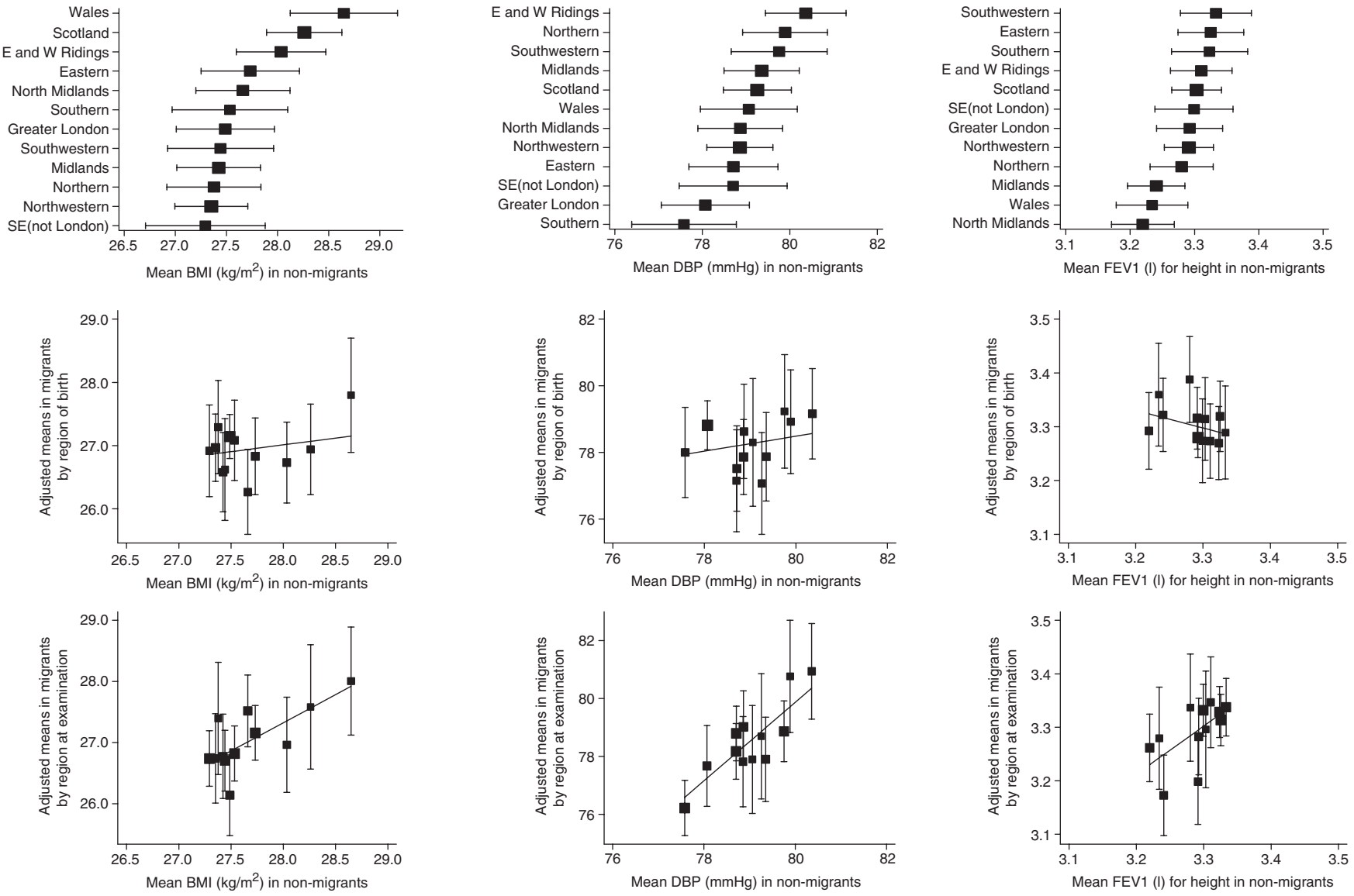

Figure 2 Regional variation in body mass index, diastolic blood pressure and one-second forced expiratory volume in non-migrants, and in migrants classified by region of birth, and region of examination

Table 3 Differences between migrants and non-migrants adjusted for region of birth, region at examination and gender

Risk factor or condition	Total N	Number of Migrants	Absolute differences: migrants vs non-migrants (95% CI)	*P* value
Height (cm)	9008	3118	1.16 (0.85, 1.47)	<0.001
BMI (kg/m^2)	8994	3113	−0.72 (−0.96, −0.47)	<0.001
DBP (mmHg)	8944	3098	−0.51 (−1.02, −0.01)	0.05
FEV1 adjusted for height (l)	8191	2877	0.02 (−0.001, 0.05)	0.05
HbA1c (% total)	7633	2646	−0.05 (−0.09, −0.02)	0.002
Cholesterol (mmol/l)	7534	2599	−0.01 (−0.07, 0.04)	0.67
Hearing threshold at 4 kHz[a]	8454	2931	−0.04 (−0.05, −0.02)	<0.001
			Relative differences (%): migrants vs non-migrants	
HDL cholesterol (mmol/l)	7518	2598	3.4 (2.1, 4.7)	<0.001
Triglycerides (mmol/l)	7510	2591	−6.5 (−9.2, −3.6)	<0.001
Fibrinogen (g/l)	7410	2561	−2.0 (−3.1, −1.0)	<0.001
Total IgE (kU/l)	7420	2561	1.5 (−5.9, 9.5)	0.70
			Odds ratios: migrants vs non-migrants (95% CI)	
Prevalence of visual impairment	8971	3107	0.87 (0.61, 1.24)	0.43
Prevalence of depressive symptoms	8945	3096	0.81 (0.67, 0.98)	0.03
Prevalence of anxiety symptoms	8945	3096	1.00 (0.82, 1.21)	0.97
Prevalence of chronic widespread pain	8248	2858	0.88 (0.75, 1.03)	0.12

[a]Absolute differences based on natural log scale using transformation of log (hearing level—constant).

Additional adjustments: After adjustment for social economic position in childhood and adulthood and additional factors listed below, the difference between migrants and non-migrants were attenuated and remained statistically significant ($P < 0.05$) for height, BMI, HDL cholesterol and triglyceride only.

Height: nurse; BMI: Weight measured on hard floor/carpet, recent food consumption, nurse; BP: Medication for blood pressure reduction, recent food consumption, ambient air temperature, time of day, month of examination, nurse, instrument; FEV1: Height, use of inhalers within the last 24 hours, upper respiratory tract infection in the last 3 weeks, month of examination, nurse, instrument; HbA1c: Treatment for diabetes, month of examination, sample delay; Total cholesterol: delay in processing blood sample, month of examination, HDL Cholesterol: delay in processing blood sample, recent food consumption, time of day, month of examination; Triglycerides: delay in processing blood sample, recent food consumption, time of day, Fibrinogen and Total IgE: time of day, month of examination and laboratory batch; Hearing: background noise during test, nurse, instrument, Vision, anxiety; depression: nurse, Chronic widespread pain: no additional adjustments.

In all instances nurse, instrument and laboratory batch were fitted as random effects.

independently related to socio-economic position in adulthood, but the regional variations were independent of social position and vice versa. Thirdly, while all cardiovascular risk factors studied were related independently to childhood social class (along with hearing threshold, depression and chronic pain), there was no evidence of a strong influence of birthplace on any of these outcomes. This implies that different causal pathways and biological mechanisms underlie social and geographical distribution of disease risk in this cohort.

Conclusion

Our results suggest that early life factors, including genetic variation, do not explain, to any great extent, the regional variation in cardiovascular and respiratory risk factors, sensory function and mental ill-health among middle-aged adults in Britain. Geographical inequalities in cardiovascular health are more strongly related to factors associated with region of residence that influence obesity, and BP, but not circulating lipids or plasma fibrinogen. The correlations observed between adult mortality rates and past infant mortality rates at the population (area) level[1–3] are thus more likely to arise from historical continuities in lifestyle and environmental exposures[5], than from 'programming' of cardiorespiratory risk, as originally implied.

Ethical approval for the medical examination of the British 1958 Birth Cohort was obtained from South East MREC (ref: 01/1/44).

Supplementry material

Supplementry material can be foung at *IJE* online (http://ije.oxfordjournals.org).

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Conflicts of Interest: None to declare.

KEY MESSAGES

- Among a diverse range of biomedical outcomes measured in middle aged British adults, including the main cardiorespiratory risk factors, none apart from adult height are related to birthplace, independent of region of examination.
- Regional variations in BMI, BP and ventilatory function are related to region of residence in middle age, independent of birthplace, socio-economic and other potential confounding factors.
- These findings are not consistent with the predictions of the 'early origins' hypothesis for adult chronic disease.

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