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Papers

Clustering of risk factors and social class in childhood and adulthood in British women's heart and health study: cross sectional analysis

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Abstract

Objective To examine co-occurrence and clustering of risk factors used in the Framingham equation by social class in childhood and adult life.

Design Cross sectional study.

Setting 23 towns across England, Wales, and Scotland.

Participants 2936 women aged 60-79 years.

Main outcome measures Prevalence of risk factors (hypertension, obesity, smoking, left ventricular hypertrophy on electrocardiography, diabetes, and low concentration of high density cholesterol); ratios of observed to expected frequencies of clusters of risk factors.

Results Risk factors were more common in women from manual social classes in either childhood or adult life, and the co-occurrence of three or four of these risk factors was greater among more disadvantaged groups. Within the four socioeconomic groups, these risk factors occurred together more than would be expected from their individual frequency distributions, indicating that they were clustered. The extent of this clustering was similar in all four social class groups.

Conclusions Clustering of risk factors included in the Framingham risk function occurs in all social class groups, but the lack of social patterning makes it unlikely that clustering is an explanation of socioeconomic inequalities in cardiovascular disease. As the proportion of women with co-occurrence of risk factors is greatest in those from manual social class in childhood, this measure of socioeconomic position might prove useful in risk prediction.

Introduction

Measuring the co-occurrence of risk factors to predict risk of coronary heart disease among people without symptoms has gained in popularity with the production of risk factor scoring systems,[1 2] guidelines, and standards of care.[3–5] Early exploration of the multifactorial causes of coronary heart disease showed that risk factors tend to cluster together more than might be expected by the rules of probability.[6 7] For example, if 25% of a population smoke and 30% have hypertension and the two conditions are independent (that is, the occurrence of smoking is not predicted by the occurrence of hypertension), then it would be expected that the percentage who both smoke and are hypertensive would be 25% × 30%—that is, 7.5%. A greater co-occurrence of risk factors than that predicted from probability rules indicates clustering, which may imply an underlying common causal pathway.

Recent interest in clustering of risk factors has focused on the components of insulin resistance syndrome (hyperinsulinaemia, glucose intolerance, obesity, dyslipidaemia, and hypertension), which occur together more often than chance would dictate.[8] Socioeconomic position in childhood has strong effects on distributions of risk factors in adult life[9] and is important in determining components of the insulin resistance syndrome[10] and coronary heart disease,[9 11] leading us to hypothesise that socioeconomic position might be associated with differences in clustering of cardiovascular risk factors. Socioeconomic variation in risk of coronary heart disease may be explained by differential clustering of risk factors by socioeconomic position.[12] We therefore predicted that risk factors measured in adult life would cluster to a greater extent in populations with adverse socioeconomic position. This would have implications for the workload of primary care teams in deprived areas and would provide an explanation for the social inequalities in coronary heart disease that are only partly explained by adjustment for major risk factors. We explored the occurrence and clustering of risk factors for coronary heart disease in a representative sample of older women classified by socioeconomic position in childhood and in adult life.

Methods

Participants

The British women's heart and health study comprises women aged 60-79 years randomly selected from general practitioners' lists in 23 towns across England, Scotland, and Wales. Selection of towns, general practitioners, and participants was based on the methods used for the British regional heart study of men.[13] A total of 4286 women (60% of those invited) participated, and baseline data were collected between April 1999 and March 2001. Participants completed a questionnaire and attended a local health centre, where they were interviewed by a research nurse, were physically examined, and gave a blood sample. General practitioners' medical records were also reviewed for each participant, and details of diagnoses of cardiovascular disease, diabetes and cancer extracted. Full methodological details have been published previously.[14] We excluded participants with previous evidence of cardiovascular disease (doctor's diagnoses of coronary heart disease, stroke, peripheral vascular disease, angina) from the main analyses presented here.

Social class and risk factor measurements

We derived adult social class from the longest held occupation of the participant's husband for married women and her own for single women and childhood social class from the longest held

Table 1 Correlation matrix of continuously distributed risk factors used in analyses. Figures are correlation coefficients adjusted for age

	Blood pressure	HDLC	Body mass index	Blood glucose
Systolic blood pressure	1			
HDLC	-0.01* (–0.05 to 0.02)	1		
Body mass index	0.07 (0.02 to 0.11)	–0.28 (–0.31 to –0.24)	1	
Blood glucose	0.07 (0.03 to 0.12)	–0.12 (–0.15 to –0.09)	0.15 (0.11 to 0.19)	1

HDLC=high density lipoprotein cholesterol.
*P=0.52, all others P<0.01.

occupation of the participant's father. Social class in childhood and adulthood was categorised into non-manual (social classes I to III non-manual) and manual (III manual to V) according to the registrar general's occupational classification.[15]

We considered risk factors included in the Framingham risk equations (see box).[1] Blood samples were taken after women had fasted for six hours. We considered women to have hypertension if they had systolic blood pressure ≥ 160 mm Hg or diastolic blood pressure ≥ 95 mm Hg or were taking blood pressure medication.

Statistical analysis

We classified women into four socioeconomic groups: childhood non-manual/adult non-manual, childhood manual/adult non-manual, childhood non-manual/adult manual, childhood manual/adult manual. The prevalence of each risk factor (95% confidence intervals) was tabulated for each of the four groups with adjustment for age and town effects. We produced an age adjusted Pearson's partial correlation matrix for each of the continually distributed risk factors. We derived expected frequencies of co-occurrence of risk factors from none through to six risk factors by combining probabilities, assuming a binomial distribution and independence between them. Observed to expected ratios were estimated for all participants and separately for each of the four socioeconomic groups; in these analyses the expected frequencies were those predicted given the prevalences of risk factor within each socioeconomic group and indicate clustering when observed:expected ratios are high for no risk factors, low for a single risk factor, and high for three or more factors. We repeated analyses in women with existing coronary heart disease. To test the significance of the overall distribution of expected and observed counts within each social class group, we calculated χ^2 statistics with 3 degrees of freedom. In analyses we used robust standard errors, taking into account possible non-independence between women from the same towns, to estimate confidence intervals.

Measured risk factors

- Total cholesterol and high density lipoprotein cholesterol concentrations (measured on frozen serum samples with Hitachi 747 analyser (Roche Diagnostics) and standard reagents)
- Blood pressure (measured with Dinamap 1846SX vital signs monitor, mean of two seated readings)
- Height (without shoes, recorded to nearest mm with Harpenden stadiometer)
- Weight (measured in light clothing without shoes to nearest 0.1 kg with Soenhle portable scales)
- Obesity (body mass index (BMI) > 30 kg/m^2)
- Smoking (current (including those who reported giving up within six months of attending for baseline examination) *v* a combined group of former or never smokers)
- Low concentration of high density lipoprotein cholesterol (≤ 0.9 mmol/l)
- Diabetes (diagnosed by doctor or fasting glucose concentration ≥ 7 mmol/l)
- Left ventricular hypertrophy (on electrocardiographic evidence of definite/probable Minnesota codes)

Results

Of the 4286 participants, 2936 provided data on both childhood and adult social class and had no diagnosis of myocardial infarction, angina, stroke, or peripheral vascular disease at baseline survey. A total of 822 women reported that they had cardiovascular diseases diagnosed by a doctor. Women with data on adult and childhood social class tended to be slightly younger (68.8 *v* 69.4 years, P < 0.01), to smoke less (10.5 *v* 17.3% current smokers, P < 0.01), and to be slightly less obese (BMI 26.0 *v* 29.5 kg/m^2, P = 0.07), but other risk factors did not vary between those with and without relevant data.

The partial correlation coefficients adjusted for age between risk factors, while mostly significant, were not particularly high (see table 1). There were weak correlations between systolic blood pressure and the other variables, with the strongest correlation being between body mass index and high density lipoprotein cholesterol.

Of the 2936 women, 42.4% (1245) were classified as manual social class in both childhood and adulthood, 33.4% (980) were manual in childhood and non-manual in adult life, 16.8% (493) were non-manual at both times, and the remaining 7.4% (218) were non-manual in childhood and manual in adulthood. Table 2 shows the distribution of risk factors for all participants and for the four social class groups. Smoking was more common among those who were in a manual class compared with a non-manual class at both times. Similar patterns were seen for obesity, diabetes, and left ventricular hypertrophy, although significant differences between social class groups were apparent only for smoking and obesity. Low concentrations of high density lipoprotein cholesterol were more common in those classified as childhood manual and adult manual. Hypertension showed a similar prevalence in all groups, but was lower in women in non-manual classes at both times. In general, those with manual social class at either childhood or adulthood had more risk factors than those who were non-manual at both times.

Table 3 shows the expected and observed frequencies of the number of risk factors experienced, broken down by social class groups and for the whole sample. None of the participants had five or six risk factors. In women in non-manual classes at both times, 47.7% had no risk factors compared with 31.6% of those in manual social classes at both times. More women with manual social class in childhood had three or four risk factors (childhood manual/adulthood non-manual 7.2%; childhood manual/adulthood manual 7.3%). Within all four socioeconomic groups risk factors for cardiovascular disease clustered, with a greater than expected number of women with no risk factors in all four groups, a lower than expected number with just one isolated risk factor, and a greater than expected number with three and four risk factors in all four groups. The pattern of clustering was similar in all four social class groups, strongly suggesting that there is

Table 2 Prevalence (95% confidence interval) of each risk factor, adjusted for age, by social class group among women with no evidence of cardiovascular disease

		Adulthood non-manual		Adulthood manual			
	All participants	Childhood non-manual	Childhood manual	Childhood non-manual	Childhood manual	χ^2 df=3	P value*
Smoking, current	10.3 (8.9 to 11.9)	7.2 (5.4 to 9.6)	9.9 (8.0 to 12.2)	7.2 (4.6 to 11.3)	12.6 (10.1 to 15.5)	13.8	0.003
Hypertension (≥160 or ≥90 mm Hg or on medication)	44.9 (42.7 to 47.1)	38.2 (33.8 to 42.7)	46.7 (43.5 to 50)	45.3 (38.8 to 51.9)	45.6 (42.4 to 48.9)	5.0	0.173
Low HDLC ≤0.9 mmol/l	2.4 (1.7 to 3.6)	2.4 (1.3 to 4.5)	2.2 (1.4 to 3.5)	1 (0.1 to 6.7)	2.9 (1.9 to 4.4)	2.9	0.406
Obese (BMI >30 kg/m^2)	24.3 (22.1 to 26.6)	15.2 (12.6 to 18.3)	24 (20.6 to 27.6)	23.2 (18.5 to 28.7)	28.6 (25.9 to 31.4)	24.5	<0.001
Diabetes (diagnosed or fasting glucose ≥7 mmol/l)	7.5 (6.7 to 8.3)	4.9 (3.3 to 7.2)	8.1 (6.3 to 10.3)	6 (3.7 to 9.5)	8.3 (6.9 to 9.9)	6.7	0.083
LVH (Minnesota code definite/probable)	8.2 (7.3 to 9.3)	7.3 (5.1 to 10.3)	8.2 (6.4 to 10.5)	7.2 (4.1 to 12.4)	8.7 (7.5 to 10)	1.0	0.790

HDLC=high density lipoprotein cholesterol, LVH=left ventricular hypertrophy.
*For difference between social class groups.

no difference in clustering between them. In all cases but the smallest social class group (child non-manual, adult manual) χ^2 values were large and highly unlikely to be due to chance.

We also looked at clustering in women with cardiovascular disease, who we had excluded from the analyses reported above. We found a similar pattern of clustering, with more women than expected with no risk factors (O:E ratio 122.7) and three or more risk factors (O:E ratio 124.6), and fewer than expected with one or two risk factors (O:E ratios 90.7 and 92.5, respectively). Not surprisingly, the proportion with three or more risk factors was higher (13.1%) in this group than those in the main analyses. Inclusion of these women in the main analysis (see table 3) did not materially alter the pattern of clustering by social class.

Discussion

People who are obese, smoke, and have hypertension and hypercholesterolaemia might be considered common high risk stereotypic patients who require multiple risk factor intervention. While it may seem self evident that such risk factors cluster in individuals, we have shown that the occurrence of such clustering is uncommon, with only 4-7% of older women exposed to three or more risk factors. We had hypothesised that clustering would have been more marked in women who had experienced greater social disadvantage throughout their lives, as exposures in early life may set in train adverse risk factor profiles with a similar underlying pathophysiological process resulting in clustering of risk factors in adult life. Although risk factors were more common in women from manual social classes in either childhood or adult life, they showed broadly similar patterns of clustering in all four social class groups. Thus, our main hypothesis was not supported.

Clustering of risk factors

Correlation between risk factors does not mean that they are clustered. The appropriate analysis is to compare the expected with the observed distribution of risk factors, assuming that the risk factors are statistically independent of each other. Our analysis has simplified the underlying nature of the data, which include both normally and binomially distributed risk factors, by dichotomising the continuous variables and then modeling all risk factors as binary. The threshold used to define high risk may influence the degree of clustering found, as shown in an earlier study in which higher thresholds (90th centile) were associated with greater clustering.[6] We used thresholds previously determined by their clinical utility in risk scoring, and, despite these being considerably lower than the 90th centile, clustering was still evident. Among women with diagnosed cardiovascular disease we found a similar pattern of clustering of risk factors.

Clustering and occurrence of cardiovascular disease

The importance of clustering is that the associations with cardiovascular disease tend to be greater than expected.[6] Recent findings from the large study on atherosclerosis risk in communities have shown that of the 57 combinations of six components of insulin resistance syndrome, those with all six components have the largest excess carotid artery intimal-medial thickness, and these associations are synergistic.[16]

Socioeconomic position, risk factors, and coronary heart disease

Co-occurrence in childhood of risk factors for coronary heart disease tends to continue into adult life,[17 18] and the associations between them and childhood and adult social class have been examined in several studies.[9] Behavioural risk factors such as exercise and smoking correlate with adult social class,[19] whereas

Table 3 Expected (Exp) and observed (Obs) frequencies (%) of clusters of risk factors by social class group among women with no evidence of cardiovascular disease.

				Adulthood non-manual						Adulthood manual					
No of risk factors*	All participants (n=2626)			Childhood non-manual (n=451)			Childhood manual (n=888)			Childhood non-manual (n=187)			Childhood manual (n=1100)		
	Exp	Obs	O:E	Exp	Obs	O:E	Exp	Obs	O:E	Exp	Obs	O:E	Exp	Obs	O:E
0	30.9	36.1	116.9	41.2	47.7	115.6	30.0	35.5	118.3	33.5	38.0	113.2	27.5	31.6	114.8
1	44.8	38.1	85.1	43.3	33.5	77.3	45.2	38.2	84.5	45.7	40.6	88.9	44.1	39.5	89.5
2	20.2	19.3	95.6	13.5	14.9	110.1	20.6	19.1	93.0	17.9	16.6	92.8	22.9	21.7	94.9
3 or 4	4.2	6.5	156.7	1.9	4.0	205.7	4.2	7.2	170.3	2.9	4.8	167.7	5.5	7.3	132.0
χ^2, df=3	85.5, P<0.0001			25.0, P<0.0001			38.0, P<0.0001			4.8, P=0.12			18.9, P<0.002		

*No women had either five or six risk factors, those with three or four risk factors were combined because of small numbers.

obesity seems to be more consistently associated with childhood social class.[20] Childhood social class also seems to be linked with other risk factors involved in insulin resistance syndrome.[21] Evidence linking childhood socioeconomic position to coronary heart disease in adult life independently of adult socioeconomic position suggests that such associations are not necessarily mediated through lifelong disadvantage.[22–26] However, adjustment for adult socioeconomic position may result in attenuation of any childhood effect[27] and might be interpreted as indicating that current rather than lifetime disadvantage is of greater relevance. It is more plausible to consider that the accumulation of socioeconomic disadvantage begins in childhood[28] and is moulded by the prevailing social and economic context through which individuals live.[29] Our failure to find greater clustering in disadvantaged women probably reflects the complex relations between risk factors and socioeconomic position and the risk factors selected for examination.

Study limitations

Our response rate (60%) was moderate but consistent with other large epidemiological surveys, including the health survey for England, in which participants were visited in their own homes.[30] Distributions of cardiovascular risk factors in women in our study are similar to those for older women in the health survey for England. The social class distribution of the women in our study is similar to that found in the 1991 census (52% in manual social class in our study *v* 55% older adults in the 1991 census). Responders were younger and less likely to have diabetes and stroke but had similar prevalences of coronary heart disease and cancer to non-responders. Our cohort may therefore have been healthier, but this would bias the associations observed only if they were in a different direction or markedly different in the non-responders, which seems unlikely.

Women without social class data were more likely to have fathers or husbands, or both, who were long term unemployed, and they were more likely to smoke. If we had included them the degree of clustering observed might have been increased, making our estimates conservative. Finally, most of the women examined were of white ethnic background (99.6%) and possibly risk factors may cluster in socially determined patterns more in men and ethnic minority groups than in white British women. Replication of these analyses in men and in ethnic minority groups would be of interest.

Implications

Clustering of risk factors—in distinction to the co-occurrence of risk factors—implies that they are not independent of each other and may therefore reflect an underlying causal or pathogenetic mechanism. The clustering we observed was similar in each social class group and, unlike the clustering observed in insulin resistance syndrome,[8] does not seem to be particularly associated with causal mechanisms operating in childhood. Clustering of risk factors may be of relevance in explaining observed variations in risk for coronary heart disease. If clustering is more pronounced in geographically or socially defined groups and clusters of risk factors operate synergistically—that is, with greater than additive effect— to increase risk for coronary heart disease, then much of any "unexplained" variation may be explained by risk factor clustering. However, the lack of any social class patterning of clustering observed here suggests that, for these risk factors at least, this is not a plausible explanation for social inequalities in women's risk for coronary heart disease.

Simply including socioeconomic position into risk factor scoring systems would be an effective means of identifying population subgroups in whom co-occurrence of risk factors is more likely to occur and in whom need for treatment is greater.

What is already known on this topic

Manual childhood social class, independently of adult social class, is associated with increased risk of coronary heart disease

Risk factors for coronary heart disease tend to cluster—that is they co-occur more commonly than independence would predict—and have synergistic effects in increasing risk

The co-occurrence of risk factors is now widely used to predict individual risk of coronary heart disease by means of risk factor scoring methods

What this study adds

The magnitude of co-occurrence of three or more risk factors included in the Framingham equation is more common among women in manual childhood social classes, and upward social mobility does not reduce this exposure level

Risk factors in the Framingham equation cluster, with more women than expected exposed to none or three or four risk factors and a fewer exposed to a single risk factor; clustering of three or more risk factors is not common

Clustering is not socially patterned and cannot explain social inequalities in risk for coronary heart disease

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