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Socioeconomic status and telomere length: the West of Scotland Primary Prevention Study

Running title: Socioeconomic status and telomere length

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Abstract

Background. It has been hypothesised that socio-economically deprived people age more rapidly than their more advantaged counterparts and this is manifested in shorter telomeres. However, in the very few studies conducted, substantial uncertainty exists regarding this relationship.

Methods. In the present investigation, 1542 men in the West of Scotland Primary Prevention Study responded to a series of enquiries about their socioeconomic position (educational attainment, employment status, area-based deprivation), had their physical stature measured (a proxy for of early life social circumstances), and provided a blood specimen from which Leucocyte DNA was extracted and telomere length ascertained.

Results. There was no strong evidence that any marker of these four socioeconomic position was robustly related to telomere length. The only exception was employment status: men who reported being out of work had significantly shorter telomere than those who were employed (p-value: 0.001).

Conclusion. In this cross-sectional study – the largest to date to examine the relationship – we found little evidence of an association between socioeconomic status and telomere length.

Introduction

A series of studies spanning several decades have shown that low socioeconomic status (SES) – typically indexed by education, occupational social class, income, neighbourhood deprivation, and physical stature – is related to elevated rates of a range of chronic diseases including cardiovascular disease (CVD) and selected cancers.[1, 2] Investigators have attempted to understand how socioeconomic disadvantage “gets under the skin” to give rise to this elevated disease risk. Access to resources (e.g., education and income), physical exposures in the living and working environment (e.g., housing conditions), health-related behaviours (e.g., tobacco smoking and diet), and psychological characteristics (e.g., IQ, personality disposition, psychosocial stress) appear to explain some, although by no means all, of the socioeconomic gradient.[1] Another mechanistic possibility is that, as CVD and cancer are, in part, ageing-related diseases, socioeconomic disadvantage increases mortality risk by accelerating the ageing process.

Telomere dynamics (length, attrition) capture biological ageing above and beyond chronological age, such that shorter telomeres represent increased biological senescence. Given the afore described socioeconomic variations in age-related chronic disease, and the recent observation that shorter telomere length is related to CVD risk,[3-5] one would anticipate that socioeconomic adversity would lead to reduced telomere length. However, in only three previous studies examining this relation of which we are aware, the evidence is inconclusive with positive[6] and null associations reported.[7, 8] Notably, the only positive finding of a relation between socioeconomic disadvantage and telomere length was in the largest conducted to date – a cross-sectional analyses of 1552 female twins.[6]

In the present analysis we used the West of Scotland Primary Prevention Study (WOSCOPS),[4] a population-based intervention for the prevention of coronary heart disease (CHD) of very similar size to the afore-described twin study. While we have previously reported on the predictive value of a series of physiological and behavioural variables for telomere length in this cohort,[4] this is the first analysis examining the impact, if any, of socioeconomic factors on this biological marker of the ageing process. In capturing socioeconomic data at the level of the individual *and* geographical area, we provide a comprehensive evaluation of the relation of social disadvantage with telomere length.

Methods

The WOSCOPS has been described in detail elsewhere.[9] In brief, following population-based screening, 6595 men aged 45–64 years, with no prior history of myocardial infarction, were classified as being at high risk of CHD based on an unfavourable lipid profile. The men were then randomly assigned to receive pravastatin or placebo and followed up for an average of 4.9 years. The present analyses are based on the analytical sample of a case-control study nested within this prospective trial[4] in which men who developed CHD during follow-up (cases) were matched for age and smoking status with two CHD-free controls.

Leucocyte DNA, extracted from blood obtained at recruitment and suitable for telomere length analysis, was available for 484 cases and 1058 controls. The measurement of leukocytes telomere length, which involved a quantitative PCR-based technique that compares telomere repeat sequence copy number to single-copy gene (36b4) copy number in a given sample, has been comprehensively described.[4] We have previously

confirmed that this novel PCR assay, which is capable of high throughput, is highly reproducible.[4]

During interviews with trained research nurses, four indicators of socioeconomic position were ascertained at study induction: three at the level of the individual (education, employment status, and height) and one at the level of the neighbourhood ('Carstairs' index). Highest educational attainment was based on 4 categories (secondary school with leaving certificate [no graduation]; school leaving certificate [with graduation]; further education but no degree; university degree or similar). Employment status was categorised into four groups (unemployed, retired, invalid, employed). Height, directly measured using a standard protocol, was used as a proxy for of early life socio-economic position,[10] such that shorter persons generally originate from more impoverished backgrounds.[11-14] The Carstairs' index is a continuously scored variable, comprising four variables at postcode sector level that were judged to represent socio-economic disadvantage in the population (lack of car ownership, Registrar General's social class classification of IV or V, overcrowded households and male unemployment). Higher scores denote greater deprivation. Following a series of standard enquiries, study members also reported their alcohol intake, cigarette habit, and existing illness.[9]

We used linear regression to quantify the relation of each indicator of socioeconomic position with telomere length in which the latter was log-transformed to have an approximated normal distribution. With no evidence that the development of CHD modified the socioeconomic position--telomere length relation, data from cases and controls were pooled and adjustment made for case/control status. We first examined the association between each of our markers of socioeconomic position and covariates with

telomere length in bivariate analyses, after which we controlled for all non-SES variables in the model.

Results

In table 1 we present the associations of the four indicators of socioeconomic position, and each covariates, with telomere length. As we have previously reported,[4] older men and those who developed CHD had, on average, shorter telomere length than those in the younger age groups and those who were CHD-free at follow-up, respectively. In unadjusted analyses, there was no strong evidence that any marker of socioeconomic position had an influence on telomere length. The only exception was employment status: men who reported being out of work had significantly shorter telomere than those who were employed. In analyses in which we adjusted for potential covariates (age, smoking, BMI, alcohol intake, existing illness, statin treatment and case/control status), the impact of unemployment on telomere length remained. Additionally, retired men appeared to have a longer telomere length than the employed although this was of borderline statistical significance.

Discussion

In the present study there was little evidence of a relationship between socio-economic disadvantage and telomere length: of the four indicators of socio-economic status utilising individual and area-based indices, there was a suggestion that only unemployed men had a significantly shorter telomere length than the employed; comparison of other employment classifications revealed no such differences. Whilst the effect for unemployed relative to the employed may be genuine, as one of several comparisons necessarily conducted in the course of these analyses, it is more likely to have occurred

Table 1: Regression coefficients (95% confidence interval) for the association of markers of socio-economic status with telomere length in WOSCOPS (n=1542)

	Unadjusted	Lower 95%CI	Upper 95%CI	P-value	Multiply- adjusted	Lower 95%CI	Upper 95%CI	P-value
Height (m)	0.221	-0.152	0.594	0.246	0.103	-0.276	0.482	0.595
Carstairs score	-0.004	-0.012	0.003	0.222	-0.005	-0.012	0.003	0.21
Employment status:								
• Unemployed vs employed	-0.117	-0.189	-0.046	0.001	-0.099	-0.171	-0.027	0.007
• Retired vs employed	0.009	-0.066	0.085	0.805	0.079	-0.003	0.162	0.06
• Invalid vs employed	0.042	-0.061	0.144	0.427	0.077	-0.028	0.182	0.152
Educational attainment	-0.002	-0.03	0.026	0.877	-0.006	-0.035	0.023	0.676
Age (per 2 yr increase)	-0.017	-0.027	-0.007	0.001				
Cigarette smoking	0.035	-0.015	0.085	0.174				
BMI (kg/m²)	-0.001	-0.009	0.007	0.794				
Alcohol intake (units per week)	0.003	-0.064	0.07	0.929				
Existing illness	-0.003	-0.067	0.061	0.934				
Statin treatment	0.015	-0.035	0.066	0.547				
Case/control	-0.055	-0.109	-0.001	0.045				

Body mass index (BMI) was computed using the standard formulae (weight[kg]/height²[m²]. Height, educational attainment, and Carstairs deprivation score were treated as continuous (ordinal) variables. For height and educational attainment, the regression coefficient summarises a unit increase (higher socioeconomic status) in relation to telomere length; for the Carstairs index, the unit increase reflects increasing deprivation. For age, the regression coefficient summarises a 2 yr. increase in relation to telomere length. Other covariates were dichotomised: smoking (current smoker vs. non/former), alcohol intake (alcohol consumption ≥ 20 units per week vs. less), existing illness (diabetes/hypertension vs. neither), statin treatment (yes vs. no), and case/control (CHD vs. CHD-free). Multiple-adjustment is adjustment for age, smoking, BMI, alcohol intake, existing illness, statin treatment, and case/control status, but not the SES variables.

by chance. Further, in the UK, ‘unemployment’ represents a heterogeneous group of individuals: whilst it will comprise people in poverty, it will also include those who are not seeking work because they are independently financially secure. This therefore complicates data interpretation. Of the three previous studies in this field,[6-8] in only one, an analysis of female twins,[6] did occupational social class reveal any association with telomere length. In cross-sectional analyses in which a six category scale of this index was collapsed into two groups[6] – manual and non-manual – women in the former occupations had markedly shorter telomere lengths than those in the latter. However, in analyses which the authors utilised the full range of social class categories, there was no evidence of a relationship; nor were the other socioeconomic measures – income and education – associated with telomere length.

The strengths of this study lie in its size and its population-based sampling. It is not, however, without its shortcomings such as the absence of measurement of other recognised socio-economic indicators -- income, occupational social class, housing tenure, and household amenities -- and its focus on men, although we are not aware of any biologically or socially plausible explanation for a differential socio-economic status-telomere length association according to gender.

In conclusion, the balance of evidence to date does not provide clear evidence of a SES-telomere length gradient; further examination may be justified. Ideally, these would utilise a prospective cohort design.

Box. What this paper adds

What is already known on this subject?

- It has been hypothesised that socio-economically deprived people age more rapidly than their more advantaged counterparts, and this is manifested in shorter telomeres.
- In the very few studies conducted, substantial uncertainty exists regarding this relationship.

What does this study add?

- In this cross-sectional study – the largest to date to examine the relationship – we found little evidence of an association between socioeconomic status and telomere length.

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