

LSHTM Research Online

Heshmati, Amy; Mishra, Gita; Goodman, Anna; Koupil, Ilona; (2019) Socioeconomic position at four time points across the life course and all-cause mortality: updated results from The Uppsala Birth Cohort Multigenerational Study. Longitudinal and life course studies. ISSN 1757-9597 https://researchonline.lshtm.ac.uk/id/eprint/4653490 (In Press)

Downloaded from: http://researchonline.lshtm.ac.uk/4653490/

DOI:

Usage Guidelines:

Please refer to usage guidelines at https://researchonline.lshtm.ac.uk/policies.html or alternatively contact researchonline@lshtm.ac.uk.

Available under license: http://creativecommons.org/licenses/by-nc-nd/2.5/

https://researchonline.lshtm.ac.uk

Socio-Economic Position At Four Time Points Across The Life Course And All-Cause Mortality: Updated Results From The Uppsala Birth Cohort Multigenerational Study

Amy Heshmati¹, Gita D Mishra², Anna Goodman¹³, Ilona Koupil¹⁴

1 Department of Public Health Sciences, Stockholm University and Centre for Health Equity Studies (CHESS), Stockholm University/Karolinska Institutet, Sweden

2 School of Public Health, University of Queensland, Brisbane, Australia

3 Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, UK

4 Department of Public Health Sciences, Karolinska Institutet, Stockholm, Sweden

Corresponding author: Amy Heshmati, Department of Public Health Sciences, Stockholm University and Centre for Health Equity Studies (CHESS), Stockholm University/Karolinska Institutet, Sveavägen 160, 10 691 Stockholm, SWEDEN. amy.heshmati@su.se

Note: this is a personal version, created by Anna Goodman, of the text of the accepted journal article. It reflects all changes made in the peer review process, but does not incorporate any minor modifications made at the proof stage. The' in press' citation for the journal article is as follows]:

Heshmati, A., G. Mishra, A. Goodman and I. Koupil (In press). "Socioeconomic position at four time points across the life course and all-cause mortality: updated results from The Uppsala Birth Cohort Multigenerational Study." <u>Longitudinal and Life Course Studies</u>

Copyright © and Moral Rights for this paper are retained by the individual authors and/or other copyright owners

<u>Abstract</u>

Socioeconomic position (SEP) is associated with all-cause mortality across all stages of the life course; however, it is valuable to distinguish at what time periods SEP has the most influence on mortality. Our aim was to investigate whether the effect of SEP on allcause mortality accumulates over the life course or if some periods of the life course are more important. Our study population were from the Uppsala Birth Cohort Multigenerational Study, born 1915-1929 at Uppsala University Hospital, Sweden. We followed 3,951 men and 3,601 women who had SEP available at birth, during childhood (at age ten), in adulthood (ages 30-45) and in later life (ages (50-65) from 15 September 1980 until emigration, death, or until 31 December 2010. We compared a set of nested Cox proportional regression models, each corresponding to a specific life course model (critical, sensitive and accumulation models), to a fully saturated model, to ascertain which model best describes the relationship between SEP and mortality. Analyses were stratified by gender. For both men and women the effect of SEP across the life course on all-cause mortality is best described by the sensitive period model, whereby being advantaged in later life (ages 50-65 years) provides the largest protective effect. However, the linear accumulation model also provided a good fit of the data for women suggesting that as improvements in SEP at any stage of the life course corresponds to a decrease in all-cause mortality.

Key Words: Life course, Mortality, Social Class, Socioeconomic position, Sweden

Introduction

Research has demonstrated that socioeconomic position (SEP) is associated with allcause mortality across all stages of the life course (Galobardes, Lynch, & Smith, 2008; Huisman, Read, Towriss, Deeg, & Grundy, 2013; Padyab, Malmberg, Norberg, & Blomstedt, 2013; Vathesatogkit, Batty, & Woodward, 2014). However, it is valuable to distinguish at what time periods SEP has the most influence on mortality.

Several theoretical life course models have been proposed: the *critical period* model, the sensitive period model and the accumulation model (Ben-Shlomo & Kuh, 2002; Kuh, Ben-Shlomo, Lynch, Hallqvist, & Power, 2003) all of which may be relevant for understanding of when and how socioeconomic inequalities in health arise. The *critical period* is a specific period where an exposure has an effect on health in later life. This effect may be adverse or protective, and outside this period, the exposure has no excess effect on health. For example, SEP would only have an effect on mortality at a specific window, such as early childhood. The sensitive period model is similar to the critical period model; an exposure will have a stronger effect during a certain time, but outside of this period, the association will be weaker than during the sensitive period. In contrast to the critical period model, in the sensitive period model there is possibility to modify or reverse the effects outside the sensitive period (Ben-Shlomo, Mishra, & Kuh, 2014; Kuh et al., 2003). For example, both childhood and adult SEP have independent effects on mortality, but the effect in childhood is greater. The accumulation model is when the exposure gradually accumulates over the life course affecting health in later life. With respect to SEP mortality, SEP at separate stages of the life course influences the rates of mortality equally leading to an accumulation of effects.

A structural approach to modelling the effects of binary exposure variables over the life course has been proposed to compare different life course models (Mishra et al., 2009). A previous study investigating the relationship between SEP at various stages across the life course and mortality have compared a set of nested models, each corresponding to a theoretical life course model, to an all-inclusive fully saturated model (Mishra, Chiesa, Goodman, De Stavola, & Koupil, 2013) and thus providing a systematic approach in

testing multiple life course models simultaneously. This structural approach of analysis has been applied to many other studies (Kroger, Fritzell, & Hoffmann, 2016; Murray et al., 2015; Murray et al., 2016; Smith et al., 2015).

Using data from the Uppsala Birth Cohort Multigenerational Study (UBCoS Multigen), we expand and update Mishra et al's (2013) study to investigate whether the effect of SEP on all-cause mortality in old age accumulates over the life course or if some periods of the life course are more important than others. We extend on this previous study by a) including an additional eight years of follow-up and b) looking at SEP over four time points – at birth, during childhood (at age ten), in adulthood (ages 30-45) and in later life (ages 50-65).

The possibility to classify SEP at two distinct time points during early life remains the most original feature of our study. Health in later life is influenced by early life social conditions in what Hayward and Gorman (2004) have coined 'the long arm of childhood'. The first years of life are regarded as a critical period during which health trajectories are determined by interactions of environmental, biological and genetic factors (Maggi, Irwin, Siddiqi, & Hertzman, 2010). Neurobiological development in early childhood (Hertzman, 2012; Maggi et al., 2010), gene regulation (Borghol et al., 2012) and developmental plasticity (Lea, Tung, Archie, & Alberts, 2017; Michels, 2017) are all plausible mechanisms for how early social environments 'gets under the skin' and changes biological and developmental processes (Hertzman, 2012). Empirical studies of developmental origins of health and disease attempt to identify the sensitive and critical periods in early life, but have mostly focussed on monitoring growth and nutritional statues (Barker, Osmond, Kajantie, & Eriksson, 2009), and studies on social mobility during childhood and health in later life are just emerging in the literature (Heshmati, Chaparro, Goodman, & Koupil, 2017). Thus, this study fills an important gap within life course research.

Methods

Sample

The study participants were from the first generation of UBCoS Multigen (http://www.chess.su.se/ubcosmg/). The cohort consists of 14,192 live births born at Uppsala University Hospital, Sweden between 1915 and 1929 (Koupil, 2007), and is considered representative of the Swedish population during this time (Goodman & Koupil, 2009). Parish records were able to trace 97% of the cohort (n=13,811) until routine registers became available in the 1960s. Our sample was restricted to those who were still alive and living in Sweden on the 15 September 1980 (n=11,336). The sample was further restricted to account for missing data on SEP; we excluded 210 individuals at birth, 2478 individuals at age 10, 265 individuals in adulthood and 831 individuals in later life. The final analytical sample comprised of 3951 men and 3601 women who had SEP recorded at all four time points over the life course. The Regional Ethics Committee in Stockholm approved the study.

Variables

Our SEP variables were social class at four time points over the life course: at birth, during childhood (at age ten), in adulthood (ages 30-45) and in later life (ages (50-65). Social class at birth and at age ten was based on father's occupation or mother's occupation if she was not married. Social class at birth was primarily obtained from obstetric records (n=7135; 94%), but also derived from data collected within five years of the child's birth using a sibling's obstetric records or from Census 1930. Social class at age ten was predominately taken from archived school records for the child's third year of primary school (n=6844; 90.6%); it was also possible to assign family social class within five years of age ten based on birth or school records of a sibling (n=198; 2.6%) or from Census 1930 (n=510; 6.8%). Social class at ages 30-45 was obtained from Census 1960 and was based on the occupation of the head of the household. Social class at ages 50-65 was obtained from Census 1980 and was based on the highest occupation of either

the individual or their cohabiting partner. We used the Swedish socio-economic classification (SEI) of occupation for coding SEP (Statistics Sweden).

In order to create comparable SEP groups across the life course and based on the categorisation that Mishra et al (2013) employed, social class was dichotomised at each time period.. SEP at birth was categorised into *advantaged* which included higher and intermediate non-manual, entrepreneurs and farmers, and lower non-manual social classes; or *disadvantaged*, which were those from skilled manual, unskilled manual or unemployed social classes. House sons or daughters were also included in the disadvantaged category. They were single men or women who were living with their families at the birth of their child. SEP at age ten had the same categorisation as SEP at birth except house sons and daughters were not included. SEP at age 30-45 (in 1960) was classified into advantaged, which included professionals (e.g. doctors, lawyers etc), academics, entrepreneurs, business managers and office employees (e.g. supervisors, technicians, office and trade personnel); or *disadvantaged*, which included employees in the agriculture, service industry or military, students and others who were neither employed or studying. SEP at age 50-65 (in 1980) was grouped into *advantaged*, which included entrepreneurs, farmers, professionals, academics, lower to higher employees; or disadvantaged which included skilled manual workers, unskilled manual workers, retirees, housework, students and part-time employees. Social class was coded as *missing* for those who were recorded as having retired and who were 62 years of age or over, because it was relatively common (>30%) to have retired by this age, and also the category is relatively heterogeneous as it does not take into account prior social class. Social class was coded as *disadvantaged* for those who are not working and were under 62 years of age.

Adjustment variables were marital status in 1960 and in 1980 to take into account family dissolution, whereby socioeconomic position in adulthood is likely to reflect the woman's own occupation if not married; and highest level of educational attainment to consider life-style and health related behaviours. Marital status was divided into four categories: married; separated/divorced; single; and widowed. Highest level of educational attainment recorded at age 21+ was grouped into three categories: low (compulsory

education ≤ 10 years); medium; (senior high school ≤ 3 years) and high (any tertiary study) education. Data on marital status was available from Censuses 1960 and 1980, and information on education was available from Censuses 1960 and 1980 and the Education Register.

All-cause mortality data was obtained from the Causes of Death Register and date of emigration was obtained from the Total Population database (Ludvigsson et al., 2016).

Statistical Methods

We used STATA v14 to fit Cox proportional hazard models with age at the time scale to estimate all-cause mortality in old age. Follow-up began on the 15 September 1980 (the date of the 1980 Census when the final measure for social class was taken) and continued until date of death, emigration, or until the 31 December 2010. All analyses were stratified by gender, and were adjusted for birth year in order to control for possible cohort effects; birth years were divided into three groups (1915-1919, 1920-1924 and 1925-1929).

To assess which life course model gave the best fit to the data, we compared a fully saturated model with a series of nested Cox proportional hazard models, denoting either zathe critical period, sensitive period or accumulation models as well as the 'no effects' model (for a more detailed description please see (Mishra et al., 2013)). In the critical period model, SEP at each period is modelled individually, while the sensitive period model allows the effects of SEP to vary across the life course, which can be modelled by simultaneously including all SEP variables in the model. The accumulation model was assessed by adding the number of times an individual was advantaged across their life course to form an overall score, which was then used as the exposure. This model assumes that the effect of SEP at each period is the same. Nested and saturated models were compared using likelihood ratio tests, with large p values (p<0.10) indicating that the more parsimonious, nested model provided an adequate description of the relationship between SEP and all-cause mortality. If different, non-nested life course models provided similar fit to the fully saturated model, the model with the lowest Akaike's Information Criterion (AIC) was selected.

Results

Our study population only included individuals with complete data; from the eligible sample who were alive and living in Sweden on the 15 September 1980 (n=11,336), only 67% (n=7552) had SEP at all four-time points. When comparing our study population (n=7552) to those excluded from analysis (n=3784), women were under-represented (53% excluded vs. 48% study population), as were those born between 1915 and 1919 (36% excluded vs. 20% study population), and individuals from disadvantaged SEP at birth (68% excluded vs. 66% study population) and at ages 30-45 (47% excluded vs. 43% study population).

Table S1 compares the study population to those who have emigrated or died between 1960 and 1979 (see Supplementary material). Individuals who had emigrated or died were more likely to be born between 1915 and 1919, disadvantaged at age 10 and in 1960, have low education, be separated/divorced or single, and male.

Among our study population, 4771 (63%) had died by the end of follow-up period on the 31 December 2010, this included 2800 men (mean age 75.8 years; 71% of all men) and 1971 women (mean age 78.0 years; 55% of all women).

Table 1 presents the descriptive statistics and rates per 1000 for all-cause mortality in old age stratified by gender. Individuals who were disadvantaged at any period had higher rates of all-cause mortality compared with those who were advantaged, and this variance increased when comparing the rates from those who were always disadvantaged and always advantaged. All-cause mortality rates were greater in men regardless of SEP. Social mobility during childhood was relatively static and no statistically significant differences between the genders was observed (p=0.08); 53% of men and women were consistently disadvantaged during childhood (that is, disadvantaged borth at birth and at age 10), whilst approximately 30% were stable advantaged in childhood. Only 5% and

12% of individuals experienced downward and upward mobility during childhood, respectively.

Table 1. Descriptive statistics and rates per 1000 for all-cause mortality from 15 September 1980 to 31 December 2010 by socio-economic position (SEP) over the life course among individuals born in Uppsala, Sweden between 1915-1929; stratified by gender (males n=3951; females n=3601).

		Mal			Fema	
			ause mortality			ause mortality
	Total	Cases	Rate per 1000 (95% CI)	Total	Cases	Rate per 1000 (95% CI)
SEP at birth						
Disadvantaged	2542	1861	35.2 (33.6-36.8)	2409	1345	22.8 (21.6-24.0
Advantaged	1409	939	30.2 (28.3-32.2)	1192	626	21.0 (19.4-22.7
SEP at age 10						
Disadvantaged	2256	1669	35.8 (34.1-37.6)	2148	1196	22.8 (21.5-24.1
Advantaged	1695	1131	30.2 (28.5-32.0)	1453	775	21.3 (19.9-22.9
SEP at age 30-45 years						
Disadvantaged	1867	1378	35.8 (33.9-37.7)	1365	786	23.8 (22.2-25.5
Advantaged	2084	1422	31.2 (29.7-32.9)	2236	1185	21.3 (20.1-22.5
SEP at age 50-65 year						
Disadvantaged	1516	1185	39.9 (37.7-42.3)	1567	951	25.6 (24.0-27.3
Advantaged	2435	1615	29.7 (28.3-31.2)	2034	1020	19.7 (18.6-21.0
SEP trajectories ^a						
0,0,0,0	720	587	42.8 (39.5-46.4)	560	341	26.2 (23.6-29.1
1,0,0,0	60	45	35.9 (26.8-48.1)	39	25	25.9 (17.5-38.4
0,1,0,0	157	110	33.3 (27.6-40.1)	146	88	24.5 (19.9-30.2
0,0,1,0	196	155	42.5 (36.3-49.8)	352	215	25.9 (22.7-29.6
0,0,0,1	428	299	32.8 (29.3-36.8)	266	142	21.4 (18.1-25.2
1,1,0,0	214	153	33.7 (28.8-39.5)	188	110	24.3 (20.2-29.3
1,0,1,0	17	12	31.8 (18.1-56.1)	34	19	22.2 (14.2-34.9
1,0,0,1	36	29	42.0 (29.2-60.4)	18	10	21.2 (11.4-39.4
0,1,1,0	55	47	43.2 (32.4-57.5)	67	46	28.7 (21.5-38.3
0,1,0,1	83	54	27.3 (20.9-35.6)	51	21	15.7 (10.2-24.0
0,0,1,1	710	481	30.4 (27.8-33.3)	800	408	20.1 (18.2-22.1
1,1,1,0	97	76	42.8 (34.1-53.5)	181	107	24.8 (20.5-30.0
1,1,0,1	169	101	25.7 (21.2-31.2)	97	49	19.3 (14.6-25.6
1,0,1,1	89	61	30.7 (23.8-39.4)	79	36	18.2 (13.1-25.2
0,1,1,1	193	128	29.9 (25.1-35.5)	167	84	19.8 (16.0-24.6
1,1,1,1	727	462	27.9 (25.4-30.6)	556	270	19.1 (16.9-21.5
Accumulation score ^b						
0	720	587	42.8 (39.5-46.4)	560	341	26.2 (23.6-29.1
1	841	609	35.2 (32.5-38.1)	803	470	24.1 (22.0-26.4
2	1115	776	31.7 (29.5-34.0)	1158	614	21.1 (19.5-22.8
3	548	366	30.5 (27.6-33.8)	524	276	21.1 (18.8-23.8
4	727	462	27.9 (25.5-30.6)	556	270	19.1 (16.9-21.5
SEP trajectories during ch	ildhood					
0,0	2054	1522	36.0 (34.2-37.9)	1978	1106	22.9 (21.6-24.3
1,0	202	147	34.1 (29.0-40.1)	170	90	21.1 (17.2-25.9
0,1	488	339	31.8 (28.6-35.4)	431	239	22.2 (19.5-25.2
1,1	1207	792	29.6 (27.6-31.7)	1022	536	21.0 (19.3-22.8
Marital status 1960						
Married	3239	2277	32.7 (31.4-34.1)	3026	1613	21.5 (20.4-22.5

Separated/divorced Single	164 535	136 376	44.3 (37.4-52.4) 33.6 (30.4-37.2)	201 339	135 204	28.9 (24.4-34.2) 25.0 (21.8-28.6)
Widowed	13	11	44.8 (24.8-81.0)	35	19	22.9 (14.6-36.0)
Marital status in 1980						
Married	3142	2175	31.9 (30.6-33.3)	2623	1382	21.2 (20.1-22.3)
Separated/divorced	376	279	37.1 (33.0-41.7)	397	222	22.8 (20.0-26.0)
Single	347	275	40.9 (36.3-46.0)	248	158	26.6 (22.8-31.1)
Widowed	86	71	45.1 (35.8-56.9)	333	209	26.3 (23.0-30.1)
Education						
Low	2219	1660	36.5 (34.8-38.3)	2257	1301	23.8 (22.5-25.1)
Medium	1216	825	30.9 (28.9-33.1)	1025	528	20.5 (18.8-22.3)
High	516	315	26.5 (23.7-29.6)	319	142	17.2 (14.6-20.3)

^a Disadvantaged socio-economic position is denoted by 0; advantaged socio-economic position is denoted by 1

^b Number of times advantaged

Table 2 displays the hazard ratios from fitting Cox proportional models to all-cause mortality in old age by the different life course SEP models. The saturated model shows the 16 SEP trajectories across four time points, that is at birth, age 10, in 1960 (aged 31-45) and in 1980 (aged 51-65). For both men and women, those who were advantaged across three or four time points over the life course had lower risk of all-cause mortality compared to individuals who were always disadvantaged. This trend can also be observed in both the categorical and linear accumulation models. The critical period model presents the independent relationship of SEP at each time point with mortality.

Model type	Variables in model	Level	Males (n=3,951)		Females (n=3,601)	
		0=Disadvantaged; 1= Advantaged	HR (95%CI)	Model fit and comparison to the saturated model ^f	HR (95%CI)	Model fit and comparison to the saturated model
Saturated model ^a	Trajectory across four	0,0,0,0	1	LL=-21,036;	1	LL=-14,765;
(1 model)	time points	1,0,0,0	0.84 (0.62-1.14)	p-value not	1.03 (0.69-1.55)	p value not
		0,1,0,0	0.73 (0.60-0.90)	applicable;	0.89 (0.71-1.13)	applicable;
		0,0,1,0	0.96 (0.81-1.15)	AIC=42,107	0.89 (0.75-1.05)	AIC=29,564
		0,0,0,1	0.84 (0.73-0.97)		0.85 (0.70-1.03)	
		1,1,0,0	0.80 (0.67-0.96)		0.91 (0.73-1.13)	
		1,0,1,0	0.66 (0.37-1.17)		0.82 (0.52-1.30)	
		1,0,0,1	1.07 (0.74-1.56)		0.67 (0.35-1.25)	
		0,1,1,0	1.00 (0.74-1.35)		0.92 (0.68-1.25)	
		0,1,0,1	0.66 (0.50-0.87)		0.64 (0.41-1.00)	
		0,0,1,1	0.71 (0.63-0.80)		0.75 (0.65-0.86)	
		1,1,1,0	0.95 (0.74-1.20)		0.80 (0.64-1.00)	
		1,1,0,1	0.63 (0.51-0.77)		0.69 (0.51-0.93)	
		1,0,1,1	0.68 (0.52-0.88)		0.69 (0.49-0.98)	
		0,1,1,1	0.67 (0.56-0.82)		0.69 (0.55-0.88)	
		1,1,1,1	0.63 (0.56-0.72)		0.68 (0.58-0.79)	
Critical period models ^b (4	SEP at birth	0	1	LL=-21,070;	1	LL=-14,781;
models)		1	0.84 (0.78-0.91)	p<0.001; AIC=42,146	0.89 (0.81-0.98)	p=0.004 AIC 29,568
	SEP at 10 years	0	1	LL=-21,066;	1	LL=-14,781
		1	0.82 (0.76-0.88)	p<0.001; AIC=42,138	0.89 (0.81-0.97)	p=0.004; AIC=29,568
	SEP at 30-45 years	0	1	LL=-21,068;	1	LL=-14,777
	•	1	0.83 (0.77-0.90)	p<0.001;	0.84 (0.76-0.92)	; p=0.054
				AIC=42,142		AIC=29,559
	SEP at 50-65 years	0	1	LL=-21,055;	1	LL=-14,771
		1	0.76 (0.70-0.82)	p<0.001;	0.79 (0.72-0.86)	p=0.664; AIC=29,547

AIC=42,115

Accumulation model ^c (1 model)	No. times 'advantaged', categorical	0 times 1 time 2 times 3 times 4 times	$1 \\ 0.85 (0.76-0.95) \\ 0.75 (0.67-0.83) \\ 0.70 (0.62-0.80) \\ 0.63 (0.56-0.72)$	LL=-21,048; p=0.02; AIC=42,108	1 0.88 (0.77-1.01) 0.78 (0.68-0.89) 0.73 (0.62-0.86) 0.68 (0.58-0.79)	LL=-14,769, p=0.745; AIC=29,550
	No. times 'advantaged', linear ^g		0.89 (0.87-0.92)	LL=-21,049; p=0.034; AIC=42,104	0.91 (0.87-0.94)	LL=-14,769; p=0.864; AIC=29,544
Sensitive period model ^d (1 model)	SEP at birth SEP at 10 years	0 1 0 1	1 0.97 (0.88-1.07) 1 0.87 (0.79-0.95)	LL=-21,044; p=0.137; AIC=42,101	1 0.96 (0.85-1.09) 1 0.93 (0.82-1.04)	LL=-14,766; p=0.998; AIC=29,544
	SEP at 30-45 years SEP at 50-65 years	0 1 0 1	1 0.95 (0.87-1.04) 1 0.80 (0.73-0.87)		1 0.91 (0.83-1.00) 1 0.82 (0.75-0.91)	
Empty model ^e (1 model)	SEP not entered			LL=-21,080; p<0.001; AIC=42,164		LL=-14,784; p<0.001; AIC=29,572

^a Each possible trajectory assumed unique and estimated separately: the fully saturated model

^bEach time period as main effect in three separate models; i.e. each model assumes only one time period important

^c Summed score of number of times 'advantaged': i.e. assume all time periods important, with interchangeable effect sizes

^d All time periods as main effects in a single model; assume all time periods important, with effect sizes that may differ

^e Model not entering SEP at all; *LL* log likelihood; *AIC* Akaike information criterion; *SEP* socio-economic position; *Disadv* disadvantaged SEP; *Adv* advantaged SEP

^fColumn presents log likelihood (LL); p value compared to saturated model (first model shown) and AIC value

^g p value for test for departure from linearity: males=0.51; females= 0.84

for departure from linearity: males=0.51; females= 0.84

Among men an inferior fit was observed for all four critical period models (p<0.001 for all log likelihood ratio comparisons) when compared with the saturated model which has estimates for 16 SEP trajectories (Table 2). This suggests that including only one time point lost valuable information about the effect of SEP on mortality; hence, a critical period model could not adequately describe the data. Moreover, adding SEP across four time points in a combined accumulation score also provided a poor fit to the data (p<0.05 for all log likelihood ratio comparisons). The sensitive period models offered an adequate fit (p>0.10 for log likelihood ratio comparison). This model showed that SEP had differing effects at different periods; being advantaged at age 10 appears to be more protective than at birth, though the effect of advantage at birth was not statistically significant; however, having advantaged SEP at 50-65 years provided the largest protective effect for all-cause mortality. Therefore, the sensitive period model best described the effect of SEP across the life course on all-cause mortality in men.

The estimates for all-cause mortality by specific life course SEP models among women differed somewhat to the results we found in men. The critical period model for exposure at 50-65 years, the accumulation model and the sensitive period model all gave adequate fits to the data to the saturated model. However, the linear accumulation model and the sensitive period models provided superior fits – they have lower AIC than the other models, suggesting that as SEP increases there is a corresponding decrease in all-cause mortality among women, but also that the largest protective effect is at age 50-65 years. In contrast to the sensitive period model in males, there was no difference between SEP at birth and age 10 in their effect on all-cause mortality among women.

Tables S2 and S3 show the hazard ratios from fitting Cox proportional models to all-cause mortality in old age by the different life course SEP models adjusted for marital status in 1960 and 1980, respectively (see Supplementary material). For both men and women the hazard ratios for all-cause mortality did not alter appreciably, and the sensitive period model still provided the best fit to the data for men. The linear accumulation models and the sensitive period models still provided the best fit for the data among women; however, the linear accumulation model had a slightly lower AIC suggesting that this model is marginally superior to sensitive period model.

Furthermore, across all the life course models, the hazard ratios for all-cause mortality attenuated somewhat after adjustment with highest level of educational attainment for both men and women (Table S4). Again, the sensitive period model provided the best fit for the data among men. Among women, the critical period model for exposure at 50-65 years, the linear accumulation model and the sensitive period model all gave adequate fits to the data. However, the linear accumulation model provided a marginally superior fit due to the model having the lowest AIC.

Discussion

Summary of findings

Our results suggest that for both men and women the effect of SEP across the life course on allcause mortality in old age is best described by the sensitive period model, whereby being advantaged in later life (ages 50-65 years) provides the largest protective effect. However, the linear accumulation model also provided a good fit of the data for women suggesting that as SEP increases there is a corresponding decrease in all-cause mortality.

Methodological considerations

The core strength of this study was the quality and unique features of data from UBCoS Multigen Study; this study is a large, well-established, historical longitudinal cohort with excellent completeness of follow-up and allowed us to observe individuals across their life course (Koupil, 2007). With an extended period of follow-up, we were able to measure mortality up to age 81-95 years. Moreover, we have been able to extend on a previous study (Mishra et al., 2013) by including SEP at age 10 and address the potential effects of social mobility in childhood.

The study does have some limitations. Our study population only included individuals with complete data. When comparing our study population to those excluded from analysis, there appears to be a selection bias such that women and individuals born between 1915 and 1919

were under-represented. This is likely because we excluded those who were 62 years and older and retired in 1980. There was also an under-representation towards those from disadvantaged SEP at birth and at age 30-45 years. However, we do not believe this will have compromised the internal validity of the study because there were sufficient numbers in both advantaged and disadvantaged groups to study the associations between SEP and all-cause mortality.

The time points for SEP to analyse the theoretical life course models was directed by the availability of data from UBCoS Multigen and Censuses 1960 and 1980. Consequently, age varied by up to 15 years for the 1960 and 1980 measurement points, and only SEP at birth and at age 10 years were distinct time points where one could evaluate possible critical and sensitive periods. In addition, the accumulation model does not indicate the precise length of exposure of advantaged or disadvantaged SEP as the length of exposure is unknown between the measurements. Moreover, inconsistencies in measuring SEP between men and women in adulthood may have implications for interpreting the different findings across gender. It is more likely that men's own occupation has been used to classify their SEP in mid adulthood and one may expect the association with mortality to be stronger. On the other hand, being a house-wife was still relatively common in the older generations of the women from our study and the use of the head of household's occupation in this group may be a good measure of the social conditions in the family. In the analyses where we adjusted for marital status in 1960 and in 1980, there was little variation in the effect on all-cause mortality, and there was only slight changes concerning the best model fit among men.

The classification of SEP into a binary variable is necessary in order to apply the SEP trajectory method without losing power because the number of strata becomes unmanageable. It is, however, a simplistic way of representing SEP that does not allow for the assessment of potential social gradients.

Furthermore, using a structured modelling approach to determine the best theoretical life course model for the data has not been without criticism. (Hardy & Tilling, 2016) have commentated that choosing a model based on p-values is not perfect, because there may be cases where more than one model fits the fully saturated model. We found this was the case for our findings among

women whereby both the linear accumulation model and the sensitive period models provided superior fits based on the AIC. However, in their recent review of life course epidemiology, (Ben-Shlomo, Cooper, & Kuh, 2016) have stated that the critical and sensitive period models should be seen as a subset of the accumulation model rather than as separate models when using the same exposure over the life course. Their rationale was that an exposure's effect over the life course does not add up simply, but varies in the strength of effect. This is not in contradiction with the structured modelling approach where both the critical period model and sensitive period model could be seen as a special case of the accumulation model.

Lastly, a small proportion of our study population had retired. Retirees were included in our study if were under 62 years of age and categorised as disadvantaged. If retirees had been excluded from the study then we believe there would have been a somewhat stronger effect for SEP at age 50-65 years. It is also possible that some of the decrease in SEP noted among the study subjects during adulthood might be due to their deteriorated health.

Comparison with other studies

This study is an update of a previous study (Mishra et al., 2013). Mishra et al (2013) used three measures of SEP over the life course – at birth, in adulthood (30-45 years) and in later life (50-65 years), we extended on this by including SEP at age 10 and by following the study population for a further eight years (81-95 years). Despite the additional SEP measurement at school age and a longer follow-up, our current findings confirm the conclusions from the previous study. In both studies, the sensitive period model best described the association between SEP over the life course and all-cause mortality for both men and women. In the earlier study, the critical period at 50-65 years also provided adequate fit in women reinforcing that SEP in later life had the largest effect on all-cause mortality.

In this paper, we have selected our models based on the goodness of fit of the hypothesised model with the saturated model. In the event that it was difficult to judge which was the best model to select, Smith et al (2015) proposed a new method using least absolute shrinkage. In our analysis, conclusions concerning which life course model fitted the data best are based on the AIC and log likelihood value.

Our study found that both men and women who were disadvantaged in childhood, whether that was at birth and/or at age ten, had increased risk of all-cause mortality in older age. These results add to the increasing body of literature which shows that individuals from lower socio-economic backgrounds during childhood have increased risk of mortality in later life (Galobardes, Lynch, & Smith, 2008).

A Swedish population registered based study (Padyab et al., 2013) explored the relationship between SEP over the life course and mortality; however, this study only focused on midlife (measured SEP at age 30, 40 and 50 years). The authors found that being disadvantaged at all time points had a significantly negative impact on mortality as did accumulative disadvantage during midlife.

Our results support that an individual's social background over the life course, including during early childhood does affect their risk of all-cause mortality in later life even after adjustment for educational attainment. The all-cause mortality rates were greater in men compared to women regardless of their SEP, consistent with a generally shorter life expectancy in men compared to women (Statistics Sweden, 2016; OECD 2017). Our measure of SEP was occupational status, which usually is indicative of income level and educational attainment. Higher income levels allows individuals to have access to more resources, such as quality food and housing in neighbourhoods that are more desirable. Higher educational attainment is not only a mechanism in which an individual can improve their life chances by being able to obtain better job prospects and thus income, but also have enhanced health capital whereby they adopt healthier lifestyles and behaviours (Kuh et al, 2004). Furthermore, having higher education enables those individuals access appropriate healthcare (OECD, 2017) even in countries like Sweden that have a universal healthcare system.

Conclusion

For both men and women the effect of SEP across the life course on all-cause mortality in old age is best described by the sensitive period model, whereby being advantaged in later life (ages 50-65 years) provides the largest protective effect. However, the linear accumulation model also

provided a good fit of the data for women suggesting that as improvements in SEP at any stage of the life course corresponds to a decrease in all-cause mortality.

Conflict of interest

The authors declare that there are no conflicts of interest.

Acknowledgements

This work was supported by funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 635316 (ATHLOS project) and by grants from the Swedish Research Council (Vetenskapsrådet): Methods in register-based research in life course and social epidemiology (project number 2013-5104); and the Swedish Research Council for Health, Working Life and Welfare (Forte): Social mobility and health among Swedish men and women born 1915-2010: life course and intergenerational effects across the twentieth century (project number 2013-1084). Research visits to Sweden by GM were funded by Forte (project No 2013-1850).

References

- Barker, D. J., Osmond, C., Kajantie, E., & Eriksson, J. G. (2009). Growth and chronic disease: findings in the Helsinki Birth Cohort. Ann Hum Biol, 36(5), 445-458. doi:10.1080/03014460902980295
- Ben-Shlomo, Y., Cooper, R., & Kuh, D. (2016). The last two decades of life course epidemiology, and its relevance for research on ageing. *Int J Epidemiol*, 45(4), 973-988. doi:10.1093/ije/dyw096
- Ben-Shlomo, Y., & Kuh, D. (2002). A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. *Int J Epidemiol,* 31(2), 285-293.

- Ben-Shlomo, Y., Mishra, G., & Kuh, D. (2014). Life Coure Epidemiology. In W. Ahrens & I. Pigeot (Eds.), *Handbook of Epidemiology* (pp. 1521-1549). New York: Springer Science+Business Media.
- Borghol, N., Suderman, M., McArdle, W., Racine, A., Hallett, M., Pembrey, M., . . . Szyf, M. (2012). Associations with early-life socio-economic position in adult DNA methylation. *Int J Epidemiol*, *41*(1), 62-74. doi:10.1093/ije/dyr147
- Galobardes, B., Lynch, J. W., & Smith, G. D. (2008). Is the association between childhood socioeconomic circumstances and cause-specific mortality established? Update of a systematic review. *J Epidemiol Community Health*, 62(5), 387-390. doi:10.1136/jech.2007.065508
- Goodman, A., & Koupil, I. (2009). Social and biological determinants of reproductive success in Swedish males and females born 1915–1929. *Evolution and Human Behavior*, 30(5), 329-341. doi:10.1016/j.evolhumbehav.2009.03.007
- Hardy, R., & Tilling, K. (2016). Commentary: The use and misuse of life course models. *Int J Epidemiol*, 45(4), 1003-1005. doi:10.1093/ije/dyw101
- Hayward, M. D., & Gorman, B. K. (2004). The long arm of childhood: the influence of earlylife social conditions on men's mortality. Demography, 41(1), 87–107.
- Hertzman, C. (2012). Putting the concept of biological embedding in historical perspective. *Proc Natl Acad Sci U S A, 109 Suppl 2,* 17160-17167. doi:10.1073/pnas.1202203109
- Heshmati, A., Chaparro, M. P., Goodman, A., & Koupil, I. (2017). Early life characteristics, social mobility during childhood and risk of stroke in later life: findings from a Swedish cohort. *Scand J Public Health*, 45(4), 419-427. doi:10.1177/1403494817696600
- Huisman, M., Read, S., Towriss, C. A., Deeg, D. J., & Grundy, E. (2013). Socioeconomic inequalities in mortality rates in old age in the World Health Organization Europe region. *Epidemiol Rev, 35*, 84-97. doi:10.1093/epirev/mxs010
- Koupil, I. (2007). The Uppsala studies on developmental origins of health and disease. J Intern Med, 261(5), 426-436. doi:10.1111/j.1365-2796.2007.01799.x
- Kroger, H., Fritzell, J., & Hoffmann, R. (2016). The Association of Levels of and Decline in Grip Strength in Old Age with Trajectories of Life Course Occupational Position. *PLoS One*, *11*(5), e0155954. doi:10.1371/journal.pone.0155954

- Kuh, D., Ben-Shlomo, Y., Lynch, J., Hallqvist, J., & Power, C. (2003). Life course epidemiology. *J Epidemiol Community Health*, 57(10), 778-783.
- Kuh, D., Power, C., Blane, D., & Bartley, M (2004). Socioeconomic pathways between childhood and adult health. In: Kuh D & Ben-Shlomo Y (eds). A Life Course Approach to Chronic Disease Epidemiology, pp. 371-395. Oxford University Press. Oxford
- Lea, A. J., Tung, J., Archie, E. A., & Alberts, S. C. (2017). Developmental plasticity: Bridging research in evolution and human health. *Evol Med Public Health*, 2017(1), 162-175. doi:10.1093/emph/eox019
- Ludvigsson, J. F., Almqvist, C., Bonamy, A. K., Ljung, R., Michaelsson, K., Neovius, M., . .
 Ye, W. (2016). Registers of the Swedish total population and their use in medical research. *Eur J Epidemiol*, *31*(2), 125-136. doi:10.1007/s10654-016-0117-y
- Maggi, S., Irwin, L. J., Siddiqi, A., & Hertzman, C. (2010). The social determinants of early child development: an overview. *J Paediatr Child Health*, 46(11), 627-635. doi:10.1111/j.1440-1754.2010.01817.x
- Michels, K. B. (2017). Developmental plasticity: Friend or foe? *Evol Med Public Health*, 2017(1), 183-184. doi:10.1093/emph/eox022
- Mishra, G., Nitsch, D., Black, S., De Stavola, B., Kuh, D., & Hardy, R. (2009). A structured approach to modelling the effects of binary exposure variables over the life course. *Int J Epidemiol*, 38(2), 528-537. doi:10.1093/ije/dyn229
- Mishra, G. D., Chiesa, F., Goodman, A., De Stavola, B., & Koupil, I. (2013). Socioeconomic position over the life course and all-cause, and circulatory diseases mortality at age 50-87 years: results from a Swedish birth cohort. *Eur J Epidemiol*, 28(2), 139-147. doi:10.1007/s10654-013-9777-z
- Murray, E. T., Hardy, R., Hughes, A., Wills, A., Sattar, N., Deanfield, J., . . . Whincup, P. (2015). Overweight across the life course and adipokines, inflammatory and endothelial markers at age 60-64 years: evidence from the 1946 birth cohort. *Int J Obes (Lond), 39*(6), 1010-1018. doi:10.1038/ijo.2015.19
- Murray, E. T., Jones, R., Thomas, C., Ghosh, A. K., Sattar, N., Deanfield, J., . . . Whincup, P. (2016). Life Course Socioeconomic Position: Associations with Cardiac Structure and Function at Age 60-64 Years in the 1946 British Birth Cohort. *PLoS One*, *11*(3), e0152691. doi:10.1371/journal.pone.0152691

- OECD (2017), "Life expectancy by sex and education level", in Health at a Glance 2017: OECD Indicators, OECD Publishing, Paris. doi: https://doi.org/10.1787/health_glance-2017-7-en
- Padyab, M., Malmberg, G., Norberg, M., & Blomstedt, Y. (2013). Life course socioeconomic position and mortality: a population register-based study from Sweden. *Scand J Public Health*, *41*(8), 785-791. doi:10.1177/1403494813493366
- Smith, A. D., Heron, J., Mishra, G., Gilthorpe, M. S., Ben-Shlomo, Y., & Tilling, K. (2015). Model Selection of the Effect of Binary Exposures over the Life Course. *Epidemiology*, 26(5), 719-726. doi:10.1097/EDE.00000000000348
- Statistics Sweden. Meddelanden I samordningsfrågor [Report on co-ordination issues] 5.
 Stockholm: Statistics Sweden; 1989Statistics Sweden, Life expectancy in Sweden 2011–2015. Life tables at national and county level. Örebro: Statistics Sweden; 2016
- Vathesatogkit, P., Batty, G. D., & Woodward, M. (2014). Socioeconomic disadvantage and disease-specific mortality in Asia: systematic review with meta-analysis of population-based cohort studies. *J Epidemiol Community Health*, 68(4), 375-383. doi:10.1136/jech-2013-203053

SUPPLEMENTARY MATERIAL

Table S1: Comparing the study population (n=7552) to those who have died or emigrated between 1960 and 1979 (n=917).

	Emigrated or died	1960-79		Study population		
	Ν	%	Ν	%		
SEP at birth						
Disadvantaged	612	68.2	4951	65.6	0.11	
Advantaged	285	31.8	2601	34.4		
Missing	20					
SEP at age 10						
Disadvantaged	473	62.7	4404	58.3	0.02	
Advantaged	282	37.4	3148	41.7		
Missing	162					
SEP in 1960 (aged 30-45)						
Disadvantaged	435	50.5	3232	42.8	< 0.001	
Advantaged	427	49.5	4320	57.2		
Missing	55					
Birth cohort						
1915-1919	346	37.7	1488	19.7	< 0.001	
1920-1924	321	35.0	2991	39.6		
1925-1929	250	27.3	3073	40.7		
Gender						
Men	588	64.1	3951	52.3	< 0.001	
Women	329	35.9	3601	47.7		
Marital status in 1960						
Married	626	72.5	6265	83.0	< 0.001	
Separated/divorced	92	10.7	365	4.8		
Single	138	16.0	874	11.6		
Widowed	7	0.8	48	0.6		
Education						
Low	667	76.5	4476	59.3	< 0.001	
Medium	151	17.3	2241	29.7		
High	54	6.2	835	11.1		
Missing	45	0.2				

Model type	Variables in model	Level	Males (n=3,951)		Females (n=3,601)	
		0=Disadvantaged; 1= Advantaged	HR (95%CI)	Model fit and comparison to the saturated model ^f	HR (95%CI)	Model fit and comparison to the saturated model
Saturated model ^a	Trajectory across	0,0,0,0	1	LL=-21,025; p-	1	LL=-14,755;
(1 model)	four time points	1,0,0,0	0.86 (0.64-1.17)	value not	1.06 (0.70-1.59)	p value not
		0,1,0,0	0.72 (0.59-0.88)	applicable;	0.91 (0.72-1.15)	applicable;
		0,0,1,0	0.98 (0.82-1.17)	AIC=42,091	0.90 (0.76-1.07)	AIC=29,550
		0,0,0,1	0.87 (0.76-1.00)		0.87 (0.72-1.06)	
		1,1,0,0	0.80 (0.67-0.95)		0.91 (0.73-1.13)	
		1,0,1,0	0.63 (0.35-1.12)		0.84 (0.53-1.33)	
		1,0,0,1	1.10 (0.76-1.60)		0.68 (0.36-1.28)	
		0,1,1,0	1.02 (0.76-1.38)		0.94 (0.69-1.28)	
		0,1,0,1	0.67 (0.50-0.88)		0.65 (0.42-1.01)	
		0,0,1,1	0.73 (0.65-0.83)		0.76 (0.66-0.88)	
		1,1,1,0	0.94 (0.74-1.19)		0.81 (0.65-1.01)	
		1,1,0,1	0.63 (0.51-0.78)		0.70 (0.52-0.95)	
		1,0,1,1	0.70 (0.53-0.91)		0.71 (0.50-1.00)	
		0,1,1,1	0.69 (0.57-0.84)		0.72 (0.57-0.91)	
		1,1,1,1	0.65 (0.58-0.74)		0.68 (0.58-0.80)	
Critical period	SEP at birth	0	1	LL=-21,056;	1	LL=-14,770
models ^b (4 models)		1	0.84 (0.78-0.91)	p<0.001; AIC=42,123	0.88 (0.80-0.97)	p=0.010; AIC 29,551
	SEP at 10 years	0	1	LL=-21,051;	1	LL=-14,770
		1	0.81 (0.75-0.88)	p<0.001; AIC=42,113	0.89 (0.81-0.97)	p=0.009 AIC=29,551
	SEP at 30-45 years	0	1	LL=-21,056;	1	LL=-14,766
	5	1	0.85 (0.79-0.91)	p<0.001; AIC=42,124	0.84 (0.77-0.92)	p=0.066 AIC=29,545
	SEP at 50-65 years	0	1	LL=-21,045;	1	LL=-14,761
		1	0.78 (0.72-0.84)	p<0.001; AIC=42,102	0.80(0.73-0.87)	p=0.664 AIC=29,533
Accumulation	No. times	0 times	1	LL=-21,037;	1	LL=-14,758

Table S2. Hazard ratios (95%CI) for mortality from 15 September 1980-31 December 2010 by different course SEP models (n=7,552) adjusted for marital status(1960)

model ^c (1 model)	'advantaged', categorical	1 time 2 times 3 times 4 times	0.86 (0.77-0.97) 0.76 (0.68-0.85) 0.71 (0.63-0.81) 0.65 (0.58-0.74)	p=0.02; AIC=42,092	$\begin{array}{c} 0.90 \; (0.78 \text{-} 1.04) \\ 0.79 \; (0.70 \text{-} 0.91) \\ 0.75 \; (0.64 \text{-} 0.88) \\ 0.68 \; (0.58 \text{-} 0.80) \end{array}$	p=0.812; AIC=29,535
	No. times 'advantaged', linear ^g		0.90 (0.87-0.93)	LL=-21,038; p=0.039; AIC=42,087	0.91 (0.88-0.94)	LL=-14,759; p=0.920; AIC=29,529
Sensitive period	SEP at birth	0	1	LL=-21,034;	1	LL=-14,756;
model ^d (1 model)	SEP at 10 years	1 0	0.97 (0.87-1.07) 1	p=0.09; AIC=42,086	0.95 (0.84-1.08) 1	p=0.997; AIC=29,530
		1	0.86 (0.78-0.95)		0.93 (0.83-1.05)	
	SEP at 30-45 years	0	1		1	
		1	0.96 (0.88-1.05)		0.92 (0.83-1.01)	
	SEP at 50-65 years	0	1		1	
		1	0.82 (0.75-0.89)		0.83 (0.75-0.91)	
Empty model ^e (1	SEP not entered			LL=-21,065;		LL=-14,773;
model)				p<0.001;		p=0.002;
				AIC=42,141		AIC=29,556

^a Each possible trajectory assumed unique and estimated separately: the fully saturated model

^b Each time period as main effect in three separate models; i.e. each model assumes only one time period important

^c Summed score of number of times 'advantaged': i.e. assume all time periods important, with interchangeable effect sizes

^d All time periods as main effects in a single model; assume all time periods important, with effect sizes that may differ

^e Model not entering SEP at all; *LL* log likelihood; *AIC* Akaike information criterion; *SEP* socio-economic position; *Disadv* disadvantaged SEP; *Adv* advantaged SEP

^fColumn presents log likelihood (LL); *p* value compared to saturated model (first model shown) and AIC value

^g p value for test for departure from linearity: males=0.51; females= 0.84

l ratios (95%CI) for morta	lity from 15 S	September 1980-31 December 2010	0 by different course SEP models (n=7,552) adjusted for marital	status
Variables in model	Loval	Males $(n-3.051)$	Famalas (n-3.601)	

Model type	Variables in model	Level	Males (n=3,951)		Females (n=3,601)	
		0=Disadvantaged; 1= Advantaged	HR (95%CI)	Model fit and comparison to the saturated model ^f	HR (95%CI)	Model fit and comparison to the saturated model
Saturated model ^a	Trajectory across	0,0,0,0	1	LL=-21,017;	1	LL=-14,760
(1 model)	four time points	1,0,0,0	0.87 (0.64-1.18)	p-value not	1.04 (0.69-1.56)	<i>p</i> value no
	-	0,1,0,0	0.73 (0.59-0.90)	applicable;	0.90 (0.71-1.13)	applicable
		0,0,1,0	1.00 (0.84-1.20)	AIC=42,074	0.89 (0.75-1.06)	AIC=29,560
		0,0,0,1	0.89 (0.78-1.03)		0.87 (0.71-1.06)	
		1,1,0,0	0.79 (0.66-0.94)		0.90 (0.72-1.11)	
		1,0,1,0	0.67 (0.38-1.18)		0.82 (0.52-1.30)	
		1,0,0,1	1.12 (0.77-1.63)		0.67 (0.35-1.25)	
		0,1,1,0	1.02 (0.76-1.37)		0.92 (0.68-1.25)	
		0,1,0,1	0.69 (0.52-0.91)		0.66 (0.43-1.03)	
		0,0,1,1	0.75 (0.66-0.84)		0.76 (0.66-0.88)	
		1,1,1,0	0.94 (0.74-1.19)		0.79 (0.64-0.99)	
		1,1,0,1	0.66 (0.53-0.81)		0.70 (0.52-0.94)	
		1,0,1,1	0.72 (0.55-0.94)		0.71 (0.50-1.00)	
		0,1,1,1	0.70 (0.58-0.85)		0.71 (0.56-0.90)	
		1,1,1,1	0.66 (0.58-0.75)		0.68 (0.58-0.79)	
Critical period	SEP at birth	0	1	LL=-21,045;	1	LL=-14,774
models ^b (4 models)		1	0.84 (0.78-0.91)	p<0.001; AIC=42,102	0.88 (0.80-0.96)	p=0.012 AIC 29,561
	SEP at 10 years	0	1	LL=-21,039;	1	LL=-14,774
		1	0.81 (0.75-0.87)	p<0.001;	0.88 (0.81-0.97)	p=0.011
				AIC=42,091		AIC=29,56
S	SEP at 30-45 years	0	1	LL=-21,045;	1	LL=-14,771
		1	0.85 (0.79-0.92)	p<0.001;	0.84 (0.77-0.92)	p=0.092
				AIC=42,103		AIC=29,55
	SEP at 50-65 years	0	1	LL=-21,037;	1	LL=-14,766
		1	0.79 (0.73-0.85)	p<0.001;	0.80 (0.73-0.87)	p=0.573
				AIC=42,086		AIC=29,544

Accumulation	No. times	0 times	1	LL=-21,027;	1	LL=-14,763;
model ^c	'advantaged',	1 time	0.88 (0.79-0.99)	p=0.03;	0.89 (0.78-1.03)	p=0.884;
(1 model)	categorical	2 times	0.77 (0.69-0.86)	AIC=42,073	0.79 (0.69-0.90)	AIC=29,544
	-	3 times	0.73 (0.64-0.83)		0.74 (0.63-0.86)	
		4 times	0.66 (0.58-0.75)		0.68 (0.58-0.79)	
	No. times		0.90 (0.88-0.93)	LL=-21,038;	0.91 (0.87-0.94)	LL=-14,763;
	'advantaged',			p=0.070;		p=0.954;
	linear ^g			AIC=42,068		AIC=29,539
Sensitive period	SEP at birth	0	1	LL=-21,025;	1	LL=-14,761;
model ^d (1 model)		1	0.97 (0.88-1.08)	p=0.112;	0.95 (0.84-1.08)	p=0.998;
	SEP at 10 years	0	1	AIC=42,069	1	AIC=29,540
	-	1	0.85 (0.77-0.94)		0.93 (0.82-1.04)	
	SEP at 30-45 years	0	1		1	
	-	1	0.96 (0.88-1.04)		0.91 (0.82-1.00)	
	SEP at 50-65 years	0	1		1	
	•	1	0.83 (0.76-0.91)		0.84 (0.76-0.92)	
Empty model ^e (1	SEP not entered			LL=-21,054;		LL=-14,778;
model)				p<0.001;		p=0.002
				AIC=42,119		AIC=29,566

^a Each possible trajectory assumed unique and estimated separately: the fully saturated model

^b Each time period as main effect in three separate models; i.e. each model assumes only one time period important

^c Summed score of number of times 'advantaged': i.e. assume all time periods important, with interchangeable effect sizes

^d All time periods as main effects in a single model; assume all time periods important, with effect sizes that may differ

^e Model not entering SEP at all; *LL* log likelihood; *AIC* Akaike information criterion; *SEP* socio-economic position; *Disadv* disadvantaged SEP; *Adv* advantaged SEP

^fColumn presents log likelihood (LL); *p* value compared to saturated model (first model shown) and AIC value

^g p value for test for departure from linearity: males=0.51; females= 0.84

Model type	Variables in	Level	Males (n=3,951)		Females (n=3,601)	
	model	0=Disadvantaged; 1= Advantaged	HR (95%CI)	Model fit and comparison to the saturated model ^f	HR (95%CI)	Model fit and comparison to the saturated model
Saturated model ^a	Trajectory across	0,0,0,0	1	LL=-21,029;	1	LL=-14,762
(1 model)	four time points	1,0,0,0	0.84 (0.62-1.13)	p-value not	1.04 (0.69-1.56)	p value no
		0,1,0,0	0.73 (0.59-0.89)	applicable;	0.89 (0.70-1.12)	applicable
		0,0,1,0	0.98 (0.82-1.18)	AIC=42,095	0.90 (0.75-1.06)	AIC=29,562
		0,0,0,1	0.88 (0.76-1.01)		0.87 (0.71-1.06)	
		1,1,0,0	0.80 (0.67-0.96)		0.91 (0.73-1.13)	
		1,0,1,0	0.69 (0.39-1.23)		0.83 (0.52-1.31)	
		1,0,0,1	1.12 (0.77-1.63)		0.69 (0.37-1.30)	
		0,1,1,0	1.00 (0.74-1.35)		0.93 (0.68-1.26)	
		0,1,0,1	0.67 (0.51-0.89)		0.65 (0.42-1.01)	
		0,0,1,1	0.77 (0.67-0.87)		0.78 (0.67-0.90)	
		1,1,1,0	0.97 (0.76-1.23)		0.82 (0.66-1.02)	
		1,1,0,1	0.66 (0.53-0.82)		0.72 (0.53-0.97)	
		1,0,1,1	0.73 (0.56-0.95)		0.74 (0.52-1.04)	
		0,1,1,1	0.71 (0.59-0.87)		0.73 (0.57-0.92)	
		1,1,1,1	0.69 (0.61-0.79)		0.72 (0.61-0.85)	
Critical period	SEP at birth	0	1	LL=-21,052;	1	LL=-14,773
models ^b (4 models)		1	0.87 (0.80-0.94)	p<0.001;	0.92 (0.83-1.01)	p=0.077
				AIC=42,114		AIC 29,556
	SEP at 10 years	0	1	LL=-21,047;	1	LL=-14,773
		1	0.83 (0.77-0.90)	p=0.001;	0.91 (0.83-1.00)	p=0.10
				AIC=42,103		AIC=29,555
	SEP at 30-45 years	0	1	LL=-21,054;	1	LL=-14,771
	-	1	0.89 (0.83-0.97)	p<0.001; AIC=42,118	0.87 (0.79-0.96)	p=0.257 AIC=29,551
	SEP at 50-65 years	0	1	LL=-21,046;	1	LL=-14,766
	years	1	0.81 (0.75-0.88)	p=0.002; AIC=42,101	0.82 (0.75-0.90)	p=0.851; AIC=29,543

Table S4. Hazard ratios (95%CI) for mortality from 15 September 1980-31 December 2010 by different course SEP models (n=7,552) adjusted for education

Accumulation model ^c (1 model)	No. times 'advantaged', categorical	0 times 1 time 2 times 3 times 4 times	$1 \\ 0.87 (0.77-0.97) \\ 0.79 (0.70-0.88) \\ 0.74 (0.65-0.85) \\ 0.69 (0.61-0.79)$	LL=-21,039; p=0.038; AIC=42,094	1 0.89 (0.78-1.03) 0.80 (0.70-0.92) 0.76 (0.65-0.90) 0.72 (0.61-0.86)	LL=-14,765. p=0.883; AIC=29,546
	No. times 'advantaged', linear ^g		0.91 (0.89-0.94)	LL=-21,040; p=0.071; AIC=42,090	0.92 (0.89-0.96)	LL=-14,766; p=0.941; AIC=29,541
Sensitive period model ^d (1 model)	SEP at birth	0	1	LL=-21,037; p=0.157; AIC=42,089	1	LL=-14,763; p=0.997; AIC=29,543
		1	0.98 (0.89-1.09)		0.98 (0.86-1.11)	
	SEP at 10 years	0	1		1	
		1	0.86 (0.78-0.95)		0.93 (0.82-1.04)	
	SEP at 30-45 years	0	1		1	
		1	0.98 (0.90-1.07)		0.93 (0.84-1.02)	
	SEP at 50-65 years	0	1		1	
		1	0.84 (0.77-0.92)		0.85 (0.77-0.94)	
Empty model ^e (1 model)	SEP not entered			LL=-21,058; p<0.001; AIC=42,124		LL=-14,775; p=0.048; AIC=29,557

^a Each possible trajectory assumed unique and estimated separately: the fully saturated model

^b Each time period as main effect in three separate models; i.e. each model assumes only one time period important

^c Summed score of number of times 'advantaged': i.e. assume all time periods important, with interchangeable effect sizes

^d All time periods as main effects in a single model; assume all time periods important, with effect sizes that may differ

^e Model not entering SEP at all; *LL* log likelihood; *AIC* Akaike information criterion; *SEP* socio-economic position; *Disadv* disadvantaged SEP; *Adv* advantaged SEP

^fColumn presents log likelihood (LL); *p* value compared to saturated model (first model shown) and AIC value

^g p value for test for departure from linearity: males=0.51; females= 0.84

SEP at 4 time points