Socio-economic position over the life course and all-cause, and circulatory diseases mortality at age 50-87 years: results from a Swedish birth cohort

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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 complete citation for the final journal article is:

- Mishra, GD; Chiesa, F; Goodman, A; de Stavola, B; Koupil, I; (2013) Socio-economic position over the life course and all-cause, and circulatory diseases mortality at age 50-87 years: results from a Swedish birth cohort. European journal of epidemiology, 28 (2). pp. 139-147.
- DOI: 10.1007/s10654-013-9777-z

Abstract

Both child and adult socio-economic position (SEP) predict adult mortality, but little is known about the variation in the impact of SEP across the life course. The Uppsala Birth Cohort Study is a representative birth cohort born 1915-1929 in Uppsala, Sweden. For the 5138 males and 5069 females alive in 1980, SEP was available at birth; in adulthood (age 31-45); and in later life (age 51-65). Follow-up for mortality (all-cause, and circulatory disease) was from 1980 to 2002. To test which life course model best described the association between SEP and mortality, we compared the fit of a series of nested Cox proportional hazards regression models (representing either the critical, accumulation or sensitive period models) with a fully saturated model. For all-cause mortality in both genders, the sensitive period model best described the influence of SEP across the life course with a heightened effect in later adult life (males: Hazard Ratio (95% confidence interval) for advantaged SEP: 0.89 (0.81-0.97) at birth, 0.90 (0.81-0.98) in adulthood, 0.74 (0.67-0.82) in later life; females: 0.87 (0.78-0.98), 0.95 (0.86-1.06), 0.73 (0.64-0.83)). The effect of SEP on circulatory diseases mortality in males was cumulative (HR: 0.84 (0.80-0.87) per unit time in advantaged SEP). For circulatory disease mortality among females, a sensitive period model was selected due to SEP in later adult life (HR: 0.64 (0.52-0.80)). These findings suggest that reducing inequality throughout the life course might reduce all-cause and circulatory disease mortality.

Introduction

The relationship over the life course between socioeconomic position (SEP) and mortality is of considerable interest in terms of health and social policy development. Numerous studies have demonstrated that SEP at various stages in life predicts adult both all-cause and circulatory disease mortality risk [1-5]. From a life course perspective, it is of interest to know whether there are differential effects on mortality risk from SEP at different stages in the life course, and various theoretical models have been proposed to describe how risk factors such as SEP may operate.[6]. In a critical period model, SEP would have an exclusive effect at some specific, limited time windows in the life course (e.g. childhood SEP has an effect but adult SEP does not) [7]. In the widely accepted definition of the accumulation model, SEP at separate stages of the life course influences the rates of mortality equally, leading to an accumulation of effects. A sensitive period model refers to settings where an exposure has a stronger effect at one time period than at other times (e.g. both childhood and adult SEP have independent effects, but the effect of SEP in childhood is greater). Sensitive periods are likely to be more common in behavioural development, whereas critical periods may be more evident for chronic disease risk associated with developmental mechanisms in biological subsystems [7]. Delineating the relative importance of childhood SEP and later adult SEP is relevant for the appropriate timing of public health interventions and of policy measures to reduce the impact of SEP on mortality rates.

A systematic review of models of life course socioeconomic factors recommended that multiple life course models should be tested in the same life course study [5]. To our knowledge only one study has compared different life course models (critical period, accumulation) on predicting premature cardiovascular and all-cause mortality [8]. It found a similar level of support for each model, perhaps reflecting the recognised difficulty of disentangling the effects of the different life course models [9]. Recently, we described a model selection approach to delineate the different life course hypotheses, given the assumption of no measurement error in the exposure or in the measured confounders, and no unmeasured confounding. We recommended comparing a set of nested models – each corresponding to a life course hypothesis – to an all-inclusive (saturated) model [10]. This approach is most applicable wherever cohort studies have exposure variables that have been collected over at least two time points.

The Uppsala Birth Cohort Study (UBCoS) is a large-scale Swedish study that has already provided further evidence that adult morbidity and mortality is increased by socio-economic adversity in both childhood and adulthood [11-13]. However, no previous studies have tested the nature of these relationships in the same study, or provided a systematic evaluation of which life course model best describes the association. This paper, therefore, uses UBCoS to investigate whether the effect of SEP upon all-cause and circulatory disease mortality accumulates over the life course or if SEP is more important at some stages of life than at others. In so doing, we demonstrate both a novel methodological approach for life course epidemiology and also address a substantive question of considerable interest for policy makers and health practitioners.

Materials and Methods

The Uppsala Birth Cohort Study consists of all 14,192 live births at the Uppsala University Hospital, Sweden between 1915-1929. This cohort was representative of Sweden as a whole in terms of infant mortality and subsequent fertility [14]. Archived obstetric records provided detailed information on various birth and socio-demographic characteristics, including parental occupation. 13,811 (97%) cohort members were successfully traced through parish records, and 12,168 survived and remained in Sweden long enough to receive a personal identity number in 1947 [11]. These personal numbers were then used to link subjects to census data from 1960 onwards and to routine registers for hospitalisation, emigration and death up to 2002. In this paper we focus on the 11,290

cohort members still alive and in Sweden in 1980, at which point they were aged 50-65. Of these, we excluded 1083 (9.6%) who were missing SEP data for at least one point in the life course (see below), giving a total study population of 5138 men and 5069 women.

Socio-economic position over the life course
This study utilises data on social class at three time points: at birth, in adulthood (age 30-45), and in later life (age 50-65). Social class at birth was based on the father's occupation, or for an unmarried mother, on her own occupation. Social class at ages 30-45 (based of occupation of head of household) and 50-65 (based on own occupation) were obtained from the 1960 and 1980 census respectively. We used the Swedish socio-economic classification (SEI) [15] of occupation for coding of SEP at all ages. In order to create comparable SEP groups across the life course, occupational social class was dichotomised into disadvantaged and advantaged (as detailed in the Online Resource 1). This also had the advantage of limiting the number of alternative life course trajectories to 8, whereas three categories over three time points would have given 27 trajectories.

Cause-specific mortality
Circulatory disease mortality was defined according to the International Classification of Diseases (Circulatory diseases, ICD8 and ICD9: 390-459; ICD10: I00-I99), and was limited to deaths where one of the above diagnoses was the main cause of death.

Statistical methods

Cox proportional hazards models were used, with age as the time scale, to estimate all-cause and circulatory disease mortality rates by life course SEP. The results from the latter are to be interpreted conditionally on surviving from all other causes. Follow-up started on January 1, 1980 and continued until date of death, first emigration or December 31st 2002. All models were stratified by sex and adjusted for birth year (categorised as 1915-1919, 1920-1924, and 1925-1929) as no evidence was found for interactions between SEP and birth year.

To test which life course model provided the best fit to the mortality data, we compared a fully saturated model with a series of nested Cox proportional hazard models, representing either the critical period, accumulation, or sensitive period models [10] as well as a 'no effects' model (see Online Resource 2). The accumulation hypothesis is usually tested by summing the number of times that an individual has had an adverse SEP across the life span to form an overall score, which is then used as the exposure in regression models for health outcomes. This method assumes that the effect of SEP at each time point is the same. By contrast, the sensitive period model allows the effects of SEP to vary across the life course, which can be modelled by simultaneously including all SEP indicators in the model. We compared nested and saturated model 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 mortality. If different, non-nested life course models provided similar fit to the fully saturated model, we selected the one with the lowest Akaike's information criterion (AIC). Similar findings were obtained when fitting models for the cumulative incidence function of circulatory disease mortality [16] (in order to deal with competing causes of death).

Results

Of the cohort members who were alive at the 1980 census, 3885 (38%) died during the 22-years follow-up period, including 2344 males (46% of all males, mean age 72 years) and 1541 females (30% of all females, mean age 73 years). Circulatory disease was recorded as the main cause of death in 48% of male deaths and 40% of female deaths (Table 1). Disadvantaged SEP at any stage of the life course was associated with a higher crude mortality rate, and an even larger differential was seen when comparing those who were disadvantaged at all stages with those who were advantaged at all stages (e.g. 29.6 vs. 16.6 deaths per thousand in men for all-cause mortality: 17.1 vs. 10.7 in women: see Table 2).

Table 1. All-cause and cause-specific mortality information during the follow up period of 1980 to 2002 for males (*n* 5138) and females (*n* 5069) born 1915-1929 who were alive in 1980*

	All		Males		Females	
Cause of death	n (%)	Incidence rate per 1000 person-years (95% CI)	n (%)	Incidence rate per 1000 person-years (95% CI)	n (%)	Incidence rate per 1000 person-years (95% CI)
All-cause mortality	3885 (38.1)	19.4 (18.8, 20.0)	2344 (45.6)	24.3 (23.4, 25.3)	1541 (30.4)	14.8 (14.1, 15.6)
Circulatory diseases	1742 (17.1)	8.7 (8.3, 9.1)	1124 (21.9)	11.7 (11.0, 12.4)	618 (12.2)	5.9 (5.5, 6.4)
Ischaemic heart disease	1024 (10.0)	5.1 (4.8, 5.4)	724 (14.1)	7.5 (7.0, 8.1)	300 (5.9)	2.9 (2.6, 3.2)
Cerebrovascular disease	314 (3.1)	1.6 (1.4, 1.8)	173 (3.4)	1.8 (1.5, 2.1)	141 (2.8)	1.4 (1.1, 1.6)
Respiratory diseases	240 (2.4)	1.2 (1.1, 1.4)	138 (2.7)	1.4 (1.2, 1.7)	102 (2.0)	1.0 (0.8, 1.2)

*Participants with had not emigrated, and with complete information on socio-economic position at birth, at age 30-45 (1960), and at age 50-65 (1980)

Table 2. All-case and cause-specific mortality in 1980-2002 by socio-economic positions through life in males (*n* 5138) and females (*n* 5069) born 1915-1929.

			Males mortality			Females mortality	
Method of describing socio economic position (SEP)			*Total n*	All-cause *n* (rate per 1000)	Circulatory disease *n* (rate per 1000)	*Total n*	All-cause *n* (rate per 1000)	Circulatory disease *n* (rate per1000)
Time period individually:								
SEP at birth								
Disadvantaged (0)			3365	1609 (25.9)	805 (12.9)	3434	1090 (15.6)	424 (6.1)
Advantaged (1)			1773	735 (21.5)	319 (9.3)	1635	451 (13.3)	194 (5.7)
SEP at age 30-45 years								
Disadvantaged (0)			2874	1408 (26.6)	689 (13.0)	2059	655 (15.6)	277 (6.6)
Advantaged (1)			2264	936 (21.5)	435 (10.0)	3010	886 (14.3)	341 (5.5)
SEP at age 50-65 years								
Disadvantaged (0)			3118	1614 (28.7)	774 (13.8)	3646	1233 (16.7)	512 (6.9)
Advantaged (1)			2020	730 (18.2)	350 (8.7)	1423	308 (10.2)	106 (3.5)
SEP trajectories across three time period:								
Birth	age 30-45	age50-65						
0	0	0	1694	895 (29.6)	446 (14.8)	1319	455 (17.1)	181 (6.8)
1	0	0	662	314 (25.2)	136 (10.9)	493	148 (14.6)	72 (7.1)
0	1	0	493	271 (31.3)	134 (15.5)	1252	448 (17.9)	180 (7.2)
0	1	1	352	137 (19.9)	78 (11.3)	179	41 (11.0)	20 (5.4)
1	1	0	269	134 (27.4)	58 (11.9)	582	182 (15.1)	79 (6.6)
1	0	1	166	62 (18.9)	29 (8.8)	68	11 (7.4)	4 (2.7)
0	1	1	826	306 (18.6)	147 (8.9)	684	146 (10.0)	43 (2.9)
1	1	1	676	225 (16.6)	96 (7.1)	492	110 (10.7)	39 (3.8)
Accumulation score: number of times 'advantaged')†								
0			1694	895 (29.6)	446 (14.8)	1319	455 (17.1)	181 (6.8)
1			1507	722 (25.8)	348 (12.4)	1924	637 (16.4)	272 (7.0)
2			1261	502 (20.4)	234 (9.5)	1334	339 (12.0)	126 (4.5)
3			676	225 (16.6)	96 (7.1)	492	110 (10.7)	39 (3.8)

†higher scores indicate higher number of times in advantaged socio-economic position. Disadvantaged socio-economic position denoted by 0 and advantaged socio-economic position denoted by 1.

Table 3 shows the estimated hazard ratios obtained from fitting Cox regression models to all-cause mortality, and to circulatory diseases mortality among males by the different life course SEP models. For all-cause mortality in males (shown in columns 5 and 6), there was strong evidence for an inferior fit for all three critical period models ($p \leq 0.01$ for all three log likelihood ratio comparisons) compared with the saturated model, which allowed a unique estimate for each SEP trajectory. This indicates that focussing on only one time period lost important information about the effect of SEP on mortality, and thus a critical period model could not adequately describe the data. By contrast, summing SEP across the three time periods into a combined accumulation score resulted in models that were not significantly worse than the saturated model. While the accumulation model gave adequate fit to the data, a better fit – as judged by the log likelihood and lower Akaike information criterion (AIC) – was provided by the sensitive period model. The latter allowed advantaged SEP to have different effects at different ages, with advantaged SEP at 50-65 years showing the larger protective effect (hazard ratio 0.64, 95%CI 0.67 to 0.82 versus 0.89, 95%CI 0.81, 0.97, for SEP at birth, and versus 0.90, 95%CI 0.81, 0.98, for SEP at 30-45 years). Thus the model best describing the effect of SEP across the life course upon male all-cause mortality was a sensitive period model in which SEP at all time points was important, but where there was a particularly large effect of SEP in late adult life, conditional on the effects at other ages.

Similarly for circulatory disease mortality among males (Table 3) the critical period model showed a poor fit to the data compared with the saturated model. The accumulation and sensitive period models both provided better descriptions of the data, but lower AIC for the accumulation models suggests that the effects of SEP can be treated as equivalent across different stages of the life course.

Estimated hazard ratios for all-cause mortality among females by the different life course SEP models (Table 4) indicate similar- but not identical- findings to those for males. The critical model for exposure at 50-65 years and the sensitive period models provided as adequate fits to the data to the saturated model and lower AIC than other model specifications, both pointing to the largest effect of SEP as being in late life (age 50-65). Similar results were found for circulatory disease mortality.

Table 3: Hazard ratios (95% confidence intervals) for mortality during the follow-up period of 1998-2002 in males, for alternative life course socio-economic position models (n = 5138)

			All-cause mortality		Circulatory disease mortality	
Model type	Variables in model	Level (0= Disadv 1= Adv)	Hazard ratio (95% CI)	Model fit & comparison to saturated model†	Hazard ratio (95% CI)	Model fit & comparison to saturated model†
Saturated model[a] (1 model)	Trajectory across three time points	0,0,0 1,0,0 0,1,0 0,0,1 1,1,0 1,0,1 0,1,1 1,1,1	1 0.87 (0.77, 0.99) 0.92 (0.80, 1.06) 0.76 (0.64, 0.91) 0.83 (0.69, 1.00) 0.78 (0.60, 1.01) 0.66 (0.58, 0.75) 0.57 (0.49, 0.66)	LL= -18365; p-value not applicable; AIC= 36749	1 0.76 (0.63, 0.92) 0.90 (0.74, 1.09) 0.89 (0.70, 1.14) 0.72 (0.54, 0.94) 0.76 (0.52, 1.10) 0.65 (0.54, 0.78) 0.50 (0.40, 0.62)	LL= -8805; p-value not applicable; AIC= 17629
Critical period models[b] (3 models)	SEP at birth	0 1	1 0.84 (0.77, 0.91)	LL= -18401; p<0.001; AIC= 36807	1 0.73 (0.64, 0.84)	LL= -8822; p<0.001; AIC= 17651
	SEP at 30-45 years	0 1	1 0.77 (0.71, 0.83)	LL= -18388; p<0.001; AIC= 36782	1 0.73 (0.65, 0.82)	LL= -8820; p<0.001; AIC= 17646
	SEP at 50-65 years	0 1	1 0.69 (0.63, 0.76)	LL= -18374; p= 0.01; AIC= 36754	1 0.71 (0.62, 0.80)	LL= -8819; p<0.001; AIC= 17644
Accumulation model[c] (1 model)	No. times 'advantaged', categorical	0 times 1 times 2 times 3 times	1 0.87 (0.78, 0.95) 0.72 (0.64, 0.80) 0.57 (0.50, 0.66)	LL= -18370; p= 0.07; AIC= 36749	1 0.84 (0.73, 0.97) 0.68 (0.58, 0.79) 0.50 (0.40, 0.62)	LL= -8807; p= 0.56; AIC= 17624
	No. times 'advantaged', linear††		0.84 (0.80, 0.87)	LL= -18370; p= 0.16; AIC= 36746	0.81 (0.76, 0.85)	LL= -8807; p= 0.69; AIC= 17621
Sensitive period model[d] (1 model)	SEP at birth	0 1	1 0.89 (0.81, 0.97)	LL= -18367; p= 0.63; AIC= 36744	1 0.77 (0.68, 0.88)	LL= -8807; p= 0.51; AIC= 17624
	SEP at 30-45 years	0 1	1 0.90 (0.81, 0.98)		1 0.84 (0.73, 0.96)	
	SEP at 50-65 years	0 1	1 0.74 (0.67, 0.82)		1 0.80 (0.69, 0.92)	
Empty model[e] (1 model)	[SEP not entered		-	LL=-18408 ; p<0.001 ; AIC= 36820	-	LL=-8834; p<0.001; AIC=17672

Model summary: [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 no. times 'advantaged': i.e. assume all time periods important, with interchangeable effect sizes; [d] All time periods as main effects in a single model; i.e. 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. † Column presents log likelihood (LL); p-value compared to saturated model (first model shown) and AIC value. †† p-value for test for departure from linearity: all-cause= 0.68; circulatory diseases= 0.62. All models adjust for year of birth. The proportional hazards test was met for circulatory disease mortality (p-value for global test of Schoenfeld's residuals 0.522). For total mortality, the proportional hazard assumption was met after the addition of an interaction term between year of birth category and the 10-year age band (p-value for global test of Schoenfeld's residuals was 0.314)

Table 4: Hazard ratios (95% confidence intervals) for mortality during the follow-up period of 1998-2002 in females, for alternative life course socio-economic position models (n = 5069)

			All-cause mortality		Circulatory disease mortality	
Model type	Variables in model	Level (0= Disadv 1= Adv)	Hazard ratio (95% CI)	Model fit & comparison to saturated model†	Hazard ratio (95% CI)	Model fit & comparison to saturated model†
Saturated model[a] (1 model)	Trajectory across three time points	0,0,0 1,0,0 0,1,0 0,0,1 1,1,0 1,0,1 0,1,1 1,1,1	1 0.85 (0.71,1.03) 0.95 (0.83,1.08) 0.73 (0.53,1.01) 0.79 (0.67,0.94) 0.48 (0.26,0.87) 0.64 (0.53,0.78) 0.68 (0.55,0.83)	LL= -12139; p-value not applicable; AIC= 24297	1 1.04 (0.79, 1.37) 0.93 (0.76, 1.15) 0.93 (0.59, 1.48) 0.84 (0.65, 1.10) 0.45 (0.17, 1.20) 0.49 (0.35, 0.69) 0.62 (0.44, 0.87)	LL= -4811; p-value not applicable; AIC= 9640
Critical period models[b] (3 models)	SEP at birth	0 1	1 0.85 (0.76, 0.95)	LL= -12155; p<0.001; AIC= 24317	1 0.94 (0.78, 1.12)	LL= -4826; p<0.001; AIC= 9658
	SEP at 30-45 years	0 1	1 0.88 (0.79, 0.97)	LL= -12151; p<0.001; AIC= 24317	1 0.79 (0.67, 0.92)	LL= -4822; p<0.001; AIC= 9650
	SEP at 50-65 years	0 1	1 0.71 (0.62, 0.80)	LL= -12145; p= 0.11; AIC= 24295	1 0.61 (0.50, 0.76)	LL= -4815; p= 0.25; AIC= 9636
Accumulation model[c] (1 model)	No. times 'advantaged', categorical	0 times 1 times 2 times 3 times	1 0.91 (0.80, 1.02) 0.71 (0.62, 0.82) 0.68 (0.55, 0.84)	LL= -12144; p= 0.07; AIC= 24298	1 0.96 (0.79, 1.16) 0.66 (0.53, 0.83) 0.62 (0.44, 0.88)	LL= -4816; p= 0.05; AIC= 9642
	No. times 'advantaged', linear††		0.86 (0.81, 0.91)	LL= -12145; p= 0.08; AIC= 24296	0.83 (0.76, 0.91)	LL= -4818; p= 0.04; AIC= 9642
Sensitive period model[d] (1 model)	SEP at birth	0 1	1 0.87 (0.78, 0.98)	LL= -12141; p= 0.49; AIC= 24292	1 0.98 (0.83, 1.17)	LL= -4813; p= 0.31; AIC= 9637
	SEP at 30-45 years	0 1	1 0.95 (0.86, 1.06)		1 0.87 (0.73, 1.02)	
	SEP at 50-65 years	0 1	1 0.73 (0.64, 0.83)		1 0.64 (0.52, 0.80)	
Empty model[e] (1 model)	[SEP not entered		-	LL= -12160; p<0.001 ; AIC=24323	-	LL=-4826; p<0.001; AIC=9656

Model summary: [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 no. times 'advantaged': i.e. assume all time periods important, with interchangeable effect sizes; [d] All time periods as main effects in a single model; i.e. 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. † Column presents log likelihood (LL); p-value compared to saturated model (first model shown) and AIC value. †† p-value for test for departure from linearity: all-cause= 0.68; circulatory diseases= 0.62. All models adjust for year of birth. The proportional hazards test was met for circulatory disease mortality (p-value for global test of Schoenfeld's residuals 0.522). For total mortality, the proportional hazard assumption was met after the addition of an interaction term between year of birth category and the 10-year age band (p-value for global test of Schoenfeld's residuals was 0.314).

Discussion

We have used a systematic approach to identify the life course model that best fits the data for all-cause mortality (occurring over the age of 50-65 years) and within that, one major cause of mortality: circulatory diseases. Findings from our cohort of Swedish men and women born 1915-1929 indicate that for both males and females the effect of SEP across the life course on all-cause mortality in old age is best described by the sensitive period model, whereby SEP in later adult life was found to have the strongest effect when SEP at all ages were mutually adjusted. For males an accumulation model best explained the effect of SEP on circulatory disease mortality (conditionally on surviving other causes of death): the total exposure to adverse SEP is what matters rather than when the exposure occurred. In contrast for circulatory disease among females, it was not possible to distinguish statistically between the sensitive period model and the critical period model, but both highlighted the importance of SEP in late adult life.

Interpretation and comparisons with other studies

Like many other studies, we have found that both childhood and adulthood SEP contributed to all-cause mortality in males [1-2, 17-20], and females [3, 19, 21-23]. Beyond this, a direct comparison with previous studies is difficult, however, as there are a number of issues that pertain to SEP data measurement, methodology and possibly also the specific context of Sweden during the periods when our cohort members went through different stages of their life course. The males and females in this study were born from 1915 to 1929 in Uppsala and followed for mortality from age 50-65 onwards, using prospectively collected SEP data. By contrast most previous studies have focused on younger cohorts [4, 18, 21, 23-26], were restricted to males [1, 25-27]; usually used only two time points for SEP measurement [1, 4, 18-19, 22-23, 26]; and often used retrospective (recalled) SEP at birth or lacked birth SEP altogether [1, 4, 17-19, 25-26]. Comparison with other studies is further hindered as their analyses have not been explicitly framed in terms of life course models, but instead have implicitly tested sensitive period models by mutually adjusting for SEP at the various time points. Rather than implicitly assuming a model *a priori*, our findings arise out of a systematic approach to testing for the model with the best fit to the data within a life course framework.

Despite a lack of studies with similar methodology, strong accumulative effect of SEP on circulatory disease mortality identified among males in UBCoS appears consistent with findings from other studies. These show both childhood and adulthood SEP to be associated with cardiovascular disease mortality in males, though only one has used a summed score to test explicitly for an accumulation model [1, 17]. A large census based study of inhabitants of Oslo used a summed relative index of inequality for housing conditions over three decades and showed that those males and females who spent most of their lives in deprived social conditions were at greatest risk of premature mortality from coronary heart diseases [17]. Our findings for females from the UBCoS cohort also identified the accumulative effects on circulatory disease mortality, but strongly highlighted the importance of SEP in late adult life. This is consistent with a study of females born 1945-1959 from data in the Swedish Work and Mortality Database [23], where it was found that the effect of adult social class was stronger than childhood social class on mortality risk from cardiovascular disease mortality. Nevertheless, it should be noted that the relationship between SEP in later life and all-cause mortality may partly reflect reverse causation whereby declining health at this time adversely impacts SEP. It is also likely that with these age cohorts, much of the effects due to differences in SEP are likely to be mediated by smoking behaviours.

Methodological considerations

There are a number of additional limitations and strengths in this study that need to be considered when interpreting our findings. First, all-cause mortality gives an overall picture of health effect

(survival) but more cause-specific analyses may provide more clues regarding specific mechanisms. It is both possible and plausible that different life course models are relevant for specific types of circulatory disease.

Other key issues relate to the determination and definition of SEP through life. Our choice of time points for SEP that could be analysed as potential sensitive or critical periods were driven by data availability in the UBCoS; and for the 1960 and 1980 measurement points the age of our participants varied by up to 15 years. This makes 'birth' the only tightly defined measurement point as a potential critical period. It also means that the identification of the accumulation model here does not refer to the exact length of exposure to advantaged or disadvantaged SEP as the duration of exposure is unknown between measurements. There is also potential for misclassification of SEP due to differences in whether the father's occupation, the occupation of head of the household or the adult person's own occupation is used to assign the occupation-based social class. This may particularly affect women [28] and may therefore have exaggerated the observed effect of SEP in late adulthood in females.

In addition, classifying SEP into a binary variable of advantaged or disadvantaged, is a very simplified approach, and prevented us from examining any potential gradient of effects across the social spectrum. However including more levels would have greatly increased the number of possible SEP trajectories through life, with a corresponding decline in the number of participants (and especially number of events) in each. Last, in 1980 mean age of retirement in Sweden was 64 years among males and 63 years in females, meaning a small proportion of the sample (then aged 50-65) had by then taken recent age-retirement [29]. Pensioners were not excluded from the analysis, but were classified as disadvantaged; if they had been excluded then we would expect the results to show a slightly stronger effect for SEP for late adult life.

In spite of these limitations, there are relatively few large-scale studies that are able to investigate the effect of prospectively collected SEP across the life course on mortality rates in both males and females in this older generation. Our straightforward approach provides a systematic way to select without *a priori* assumptions from three life course models (critical, accumulation, and sensitive) the one that best explains the associations with mortality, in terms of being the simplest model that captures the most information. Future work needs to examine specific types of mortality that are shared across both genders as well as those that are sex specific, such as breast cancer, and the impact of social mobility on mortality rates.

While our results need to be confirmed in other studies, this is the first to identify systematically the impact of SEP, especially in late adult life, on all-cause mortality as being best explained by a sensitive period model for both genders. (4) The sensitive period model can accommodate many different scenarios for the effect of SEP. Thus this finding may be interpreted as evidence suggesting that reducing inequalities at this late stage in life can still be worthwhile, but it does not imply that addressing SEP inequalities at other stages, especially in early life, should be neglected. A similar result was found for the role of SEP and circulatory diseases among females, with the sensitive and critical period (for ages 50-65 years) models found to be similarly valid from a statistically perspective. However in the absence of a plausible biological explanation, the selection of the simpler critical period model is not justified and this finding instead serves to highlight the strength of influence of SEP in late adult life as captured by the sensitive period model. For males only the accumulation model was identified, whereby addressing SEP throughout the life course is beneficial for reducing risk of death due to circulatory disease in old age.

Conflicts of interest:

None

Source of funding:

Swedish Research Council and Swedish Council for Working Life and Social Research for funding this project.

Acknowledgments:

We are grateful to Rawya Mohsen, Bitte Modin and Reidar Österman for help with data management, and to Marit Gisselmann for her input into the classifications of socio economic position.

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Appendix 1

SEP at birth was categorised as: disadvantaged (unskilled manual worker in manufacture and service, skilled manual worker in manufacture and service, *house son or house daughter*); advantaged (lower non-manual I and II, intermediate non-manual, academic title, higher education student, higher non-manual, higher non-manual (large company), professionals, self-employed, farmers). Note that *house sons* or *house daughters* were single men or women living with their parents at the time of the birth of their child.

SEP at age 30-45 was categorised as: disadvantaged (self-employed without employees (except in the academic profession) or worker, student, other); advantaged (self employed with employees, self employed in academic profession, executive manager, employee (including chief technician, clerk), employee in service sector, military sector).

SEP at age 50-65 was classified as: disadvantaged (unskilled manual worker in manufacture and service, skilled manual worker in manufacture and service, self employed, farmer, unclassifiable employee, pensioner, housework, student, short term part-time worker); advantaged (lower employee I and II, intermediate employee, higher employee, self employed in academic profession).

Appendix 2

Equations for life course models including the constraints imposed on the fully saturated model to derive the life course model.

The full model (Saturated)
$\log h(t) = \alpha(t) + \beta_1 S_1 + \beta_2 S_2 + \beta_3 S_3 + \theta_{12} S_1 S_2 + \theta_{23} S_2 S_3 + \theta_{13} S_1 S_3 + \theta_{123} S_1 S_2 S_3$
where $h(t)$ refers to log hazard ratio function, $h_0(t)$ is the baseline hazard function with $\alpha(t) = \log h_0(t)$, and S_j are binary indicator of socio economic circumstances as time j, with j=1,2,3; $S_j = 0$ refers to disadvantaged SEP at time j while $S_j = 1$ refers to advantaged SEP at time j.

Early life Critical period model:
$\log h(t) = \alpha(t) + \beta_1 S_1$
constraints: $\beta_2 = \beta_3 = 0$; $\theta_{12} = \theta_{23} = \theta_{13} = \theta_{123} = 0$
and similarly for mid- and late- life with S_2 and S_3 replacing S_1 and β_2 and β_3 replacing β_1

Accumulation model: summed score
$\log h(t) = \alpha(t) + \beta \Sigma_j S_j$
constraints: $\beta_1 = \beta_2 = \beta_3 = \beta$; $\theta_{12} = \theta_{23} = \theta_{13} = \theta_{123} = 0$

Sensitive period model: mutually adjusted
$\log h(t) = \alpha(t) + \beta_1 S_1 + \beta_2 S_2 + \beta_3 S_3$
constraints: $\beta_1 \neq \beta_2 \neq \beta_3$; $\theta_{12} = \theta_{23} = \theta_{13} = \theta_{123} = 0$

where $h(t)$ refers to log hazard ratio function, is the baseline hazard function $\alpha(t) = \log h_0(t)$ and S_i are binary indicator of socio economic circumstances as time *i*, with i=1,2,3; S= 0 refers to disadvantaged SEP while S= 1 refers to advantaged SEP.