The effect of early-life and adult socioeconomic position on development of lifestyle-related diseases.

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Abstract

Background: Early-life socioeconomic position is associated with lifestyle-related diseases in adulthood. However, evidence is lacking on the extent to which adult socioeconomic position mediates this association.

Methods: Time to either chronic obstructive pulmonary disease(COPD), cardiovascular disease or diabetes were assessed in the Danish population born between 1961-1971 (n=793,674) from age 30 until 2015. Early-life position was assessed in 1981 (by parental) and again at age 30 (own) by four markers; income, occupation, education – divided into high, middle, low – and a combined score for all markers. Using a counterfactual approach, we estimated the total effect of early-life position on disease onset and the degree to which adult position mediated this effect.

Results: Results of the time-to-event analysis showed a gradient of all early-life markers on the risk of developing all lifestyle-related diseases. Most markedly, comparing those in the lowest to the highest educational position, the hazard of COPD was 130% higher for women (hazard ratio= 2.30[95%confidence interval=2.20-2.41]) and 114% higher for men (2.14 [2.05-2.25]). 67%[63%-70%] of the effect of educational position was mediated through adult position for COPD, 55% for cardiovascular disease and 50% for diabetes. For the combined score 44%,29% and 33%, respectively, was mediated.

Conclusion: About one tenth to two-thirds of the effect of early-life position is mediated by the position attained in adulthood. The degree mediated depend on the outcome investigated, gender and the social position marker used. Alternative pathways from early-life position to adult health may play a key role in developing more effective behavioural changing policies.

Keywords: social inequality, mediation, early-life, childhood, lifecourse

Introduction

By 2030, cardiovascular disease, diabetes and chronic obstructive pulmonary disease are estimated to account for around a third of the global projection of all-cause mortality (1). These diseases have all been shown to be heavily socially patterned and are consistently documented to be associated with socioeconomic position (SEP) throughout the life course (2–8).

Several scholars have stressed the need for more studies investigating the mechanisms through which early-life socioeconomic position influences adult health (9–11). While studies have demonstrated that adult SEP partly mediates early-life SEP (6,8,12–14), more studies are needed to assess the magnitude of the mediating effect (13). More precise knowledge on the magnitude of the mediating effect can enable a better understanding of the social aetiology of lifestyle-related diseases. A few previous studies have attempted to quantify the degree of the mediating effect of adult SEP on health (12,e.g. 15). However, issues of using self-reported and retrospectively assessed SEP markers that differs in early-life and adulthood (14–16), small sample sizes and dichotomous measures of SEP markers (12,17) stresses the need for additional studies. Moreover, in traditionel models, interpreting the change in ratios between a model with and without the proposed mediator as evidence of mediation (as in i.e. ,15) does not produce an accurate estimate of the mediating effect (18–20).

In addition to modelling issues, previous studies typically used one of either employment, occupation or income as a marker of SEP (8,21). However, these markers are not interchangeable with each other. Educational level, income and occupation reflect distinct aspects of an individual's position in the social hierarchy. This position in part determines the degree of access to specific resources; knowledge, monetary, or prestige that can be used to improve health as well as the

more general social and cultural circumstances in which one is embedded. Thus, it is not possible to discern which type of resource that might be best targeted for a specific disease and knowledge on the combined effect of having access to a broader range of resources (22).

In this study, we investigate the extent to which the effect of early-life socioeconomic position on onset of either cardiovascular disease, COPD or diabetes, respectively, are mediated by the position attained in adulthood. Recent methodological developments have made it possible to model longitudinal data while assessing both direct and indirect effects as well as the degree mediated using a counterfactual approach. Such an approach has been shown to be more mathematically consistent and to produce unbiased estimates of the degree of formal mediation in survival models (18,23).

In line with recent studies (8,14,16), our study addresses the concerns raised in this introduction. We add to existing work in several ways. 1) We use data from an entire Danish national cohort, 2) we use several different markers of socioeconomic position measured during the two life stages investigated in this study, 3) we assess the same markers in early-life and adulthood, 4) both the outcomes and the markers of SEP are objectively assessed via the Danish National Registers and 5) we utilize recent methodological developments to gain a more precise estimate of both the total effect of early-life SEP on onset of adult lifestyle related diseases and the precise degree to which the SEP attained in adulthood mediates this association.

Methods

Using the unique personal identifier in the Danish Civil Registration System (24,25), we identified all Danish citizens born between 1961-1971. The unique identifier for each study participant was used to retrieve information from different Danish longitudinal registers. Each participant was then linked with their registered mother and/or father. Via the Danish registries, a link to at least the mother is available for nearly everybody born after 1960 (26). Using information from the Integrated Database for Labour Market Research (IDA) (27) and the Population's Education Register (28), we obtained information on occupational position, educational level and yearly adjusted annual income of the parents in 1981 and for the study participants in the year in which they turned 30 years old. From the Cause-of-Death register and The Danish National Prescription Registry, we found all citizens who were diagnosed with COPD, cardiovascular disease or diabetes using the International Classification Codes (ICD10 and 8) of disease and the Anatomic Therapeutic Chemical (ATC) code (See Table S1 in the supplementary materials for the specific codes for each outcome).

Study sample

871,753 Danish citizens born in 1961-1971 were identified in the Danish national registers. After removing those who died before their 30th birthday (baseline) and those with missing values on at least one of early-life or adult SEP markers, 91% of the original study cohort remained (n=793,674) (Figure 1). The eligible study sample was followed from age 30 until first onset of (1) COPD; (2) cardiovascular disease or (3); diabetes or study end at the 31st of December 2015. Similarly to Nandi et al. (29), we defined three separate samples excluding prevalent cases of each outcome at

baseline. The three samples comprised of 788,747 diabetes-free, 792,768 COPD-free and 792,675 cardiovascular disease-free participants.

< Insert Figure 1 about here >

Markers of socioeconomic position

Information on socioeconomic position in early-life for all study participants was measured in 1981 by parental position. For the educational and occupational marker, the parent with the highest level was chosen as the marker of early-life SEP. Income was calculated as the combined income of the registered parents. Information on adulthood SEP was measured by the participants' income, occupation and educational level at age 30 (from 1991-2002).

Educational levels

Educational level was classified into three categories according to the International Standard Classification of Education (ISCED) (30). The highest educational group consisted of those with a bachelor's degree or higher (ISCED levels: Bachelor or equivalent, master or equivalent or doctoral or equivalent), the middle group of those with high school or equivalent (ISCED levels: Upper secondary and short cycle tertiary) and the lowest group consisted of those whose highest completed education was secondary school or lower (ISCED levels: Primary and lower secondary).

Occupational levels

Information on occupational position was obtained from the IDA database. Similar to Andersen et al. (31) occupational group was divided into three groups similar to the British Registrar General's Classification I-V. The highest occupational group was similar to occupational group 1-3 (non-manual groups: managers and salaried employees), the middle occupational group was similar to

occupational groups 4-5 (manual groups: skilled and unskilled workers), and the low occupational group consisted of unemployed and those outside the labour force.

Income levels

Information on annual income was obtained from the IDA database. We used yearly adjusted annual income to allow for comparison of income over time. Income was then divided it into three groups based on tertiles – the high earners 33.3%, the middle 33.3% and the lowest 33.3%.

Number of high socioeconomic positions

Finally, we created a composite measure of SEP to investigate whether belonging to high positions on all three markers were more protective than merely investigating one measure (32). We combined the three markers into the most advantaged (high on all three markers), the middle group (mixed combinations of the three markers) and most disadvantaged (low on all three markers).

Sociodemographic confounders

Similar to Nandi et al. (29) all models were adjusted for birth year (1961-1971) and ethnicity (Danish origin or other).

Statistical analysis

Time zero (baseline) for all time-to-event analyses was set at the 30th birthday for each participant. The SEP markers of socioeconomic position in childhood and adulthood, as well as birth year and ethnicity were summarized at baseline separately for men and women. All analyses were performed separately for each of the investigated outcomes (COPD, cardiovascular disease, diabetes). We estimated natural direct and indirect effects partitioning the total effect of each

early-life SEP marker on COPD, diabetes and cardiovascular disease, respectively, according to mediation through adult SEP (23). This entailed using a Cox-regression model for the hazard rate of the outcome as the natural effect model with time zero as the participants' 30th birthday.

We report the hazard ratio (HR) with 95% confidence intervals (95% CI) for total, natural direct and natural indirect effects of the early-life SEP markers on the rate of COPD, diabetes or cardiovascular disease. Results for the different SEP markers are obtained in separate analyses. The percent (%) mediated through adult SEP was calculated as the ratio between the natural indirect and the total effect for each SEP marker. To assess evidence of a formal mediating effect, 95% confidence intervals (95% CI) for the mediated effect were estimated using 1000 bootstrap samples, for details see Lange et al. (33). The same bootstrap procedure was used to compute 95% CI for the total and direct effect. The data from the different Danish registries was combined using the statistical program SAS. Subsequent data management, and all statistical analyses were performed in R (34).

Similar to Jahn et al. (35), we stratified the analysis by gender to investigate potential gender differences in the association between SEP and lifestyle-related outcome adjusted for birth year and ethnicity. To investigate robustness of the results, we performed sensitivity analyses with the study samples stratified by birth year and with outcome artificially censored after 14 years for all study participants. Lastly, to check the robustness of combining SEP markers, we assessed whether two different approaches of combining the SEP three markers would change the results. We performed an additional analyses were we counted i) the number of high positions in the three markers and ii) the number of low positions in the three markers (both ranging from 3-0).

Results

During follow-up 20,561 participants experienced onset of cardiovascular disease, 33,805 had onset of diabetes and 10,075 onset of COPD. Study characteristics of the eligible study population (n=793,674) are shown in Table 1. Both men and women had grown up under similar SEP levels across education, income levels, occupational position and combined SEP positions. The majority had grown up under a middle early-life SEP marked by both education, income and occupational position. 10% of the study population had grown up in the most advantaged group who had the highest position on the three markers and 11.5% in families with the lowest positions on all three markers. At age 30, more women than men had a bachelor's degree or higher (22.4% vs 15.9%), but fewer women had high occupational positions (16.1%vs. 18.6%) and high-income levels (19.1% vs 47.9%). More men compared to women belonged to the most advantaged group in adulthood (7.9% vs. 5%).

< Insert Table 1 about here >

Figure 2 shows the total effect of educational SEP in early-life on the hazard of developing COPD, diabetes or cardiovascular disease and the proportion mediated by adult educational SEP. The results for SEP measured by income and occupation were similar but with smaller effect sizes (results can be found in Figure S2 and S3 in the supplementary materials). For both men and women, the total association between early-life educational SEP was strongest for COPD, and there was a clear increase in risk as SEP got lower for all outcomes. For COPD, there was an estimated 62% increase in hazard for women and 67% increase for men who had grown up in families with a middle educational SEP compared to those who had high educational SEP. For those in the lowest SEP, the total increase in hazard was 130% for women and 114% for men

compared to those in high SEP. About two-thirds of this association were mediated through adult SEP for women (middle: 67%, low vs high: 68%) and 54% and 66% for men. For both diabetes and cardiovascular disease, the effects were less pronounced and the degree of the total effect of early-life SEP mediated through adult SEP was around half for both men and women.

< Insert Figure 2 about here >

Looking at the combined score in early-life, we observe a substantial social gradient (Figure 3). The study participants who had grown up in the most advantaged SEP families with high positions in all three markers; education, income and occupation, had the lowest hazard of developing any of the three diseases. The effects were largest for COPD for both men and women. For women, the effect sizes were similar for diabetes and cardiovascular disease. For men, the effects sizes were higher for diabetes than for cardiovascular disease. This result was robust for different ways of combining the three SEP markers (results can be found in Figure S4 in the supplementary materials).

< Insert Figure 3 about here >

Discussion

In this study, we have investigated the association between early-life SEP and the development of three lifestyle-related health outcomes: cardiovascular disease, COPD and diabetes from age 30 and until 31th of December 2015. All markers of SEP were associated with an increase in the risk of developing the three diseases as the SEP position got lower, with a clear social gradient in the effect sizes. The effect sizes was highest with education as the SEP marker and COPD as the outcome. Additional adverse effects was observed for participants who had grown up in low SEP conditions on all three markers.

Our results are largely consistent with previous literature on health outcomes showing that socioeconomic adversity in both early-life and adulthood are important for the development of diseases (6,8,12,29,36) as well as evidence for both the chains of risk hypothesis were adverse conditions in early-life heighten the risk for adverse conditions in adulthood which in turn heightens the risk for ill health and the sensitive period life course model (37). However, our study adds to the current literature by investigating an entire population cohort, by using objectively measured markers of SEP from national registers and investigating the combined effect of belonging to a high position in the social hierarchy when assessed by both income, educational and occupational positions while focusing on potential gender differences. Similar to our study, Cheval et al. (8) showed attenuated but still significant associations between early-life SEP and peak expiratory flow, which in part reflect COPD, and Nandi et al (29) showed similar evidence for diabetes and cardiovascular disease . Using a time-to-event counterfactual approach, our analyses showed more specifically evidence of a formal mediation for all outcomes and SEP markers. Our study demonstrated that the degree mediated by adult position varies depending on

the outcome investigated (68%(65%-71%) for COPD, 51%(49%-54%) for diabetes and 50%(47%-53%) for cardiovascular disease) but not by gender even though the total effect varied slightly depending on gender. In the study by Savelieva et al. (12) they found evidence of 33% mediation in cardiovascular health by a combined SEP score of education, income, occupational status and occupational stability. This was similar to our study which gave evidence of a formal mediation of 33% for men(28%-39%) and 29%(24%-35%) for women when focusing on ICD diagnoses of cardiovascular disease. That is, a substantial direct effect remained that could not be accounted for by adult SEP for all three lifestyle-related outcomes. Early-life is often highlighted as a sensitive period for exposures to social and physical determinants of lifestyle-related diseases in adulthood (37). An potential explanation for the remaining direct effect may be the biological and social embedding within adverse childhood conditions that is above and beyond those of influences through adult SEP attainment. Pathways from childhood socioeconomic adversity to adult health includes the early influences on the individual's health-related behaviour (38), attitudes and resilience to adversity (13) and a risk of increased allostatic load (9). The results from this study thus stress the need to investigate other factors such as the physiologic and social embodiment of early-life SEP, behaviours, and risk factors established in early life which may serve as important mediators of early-life socioeconomic disadvantage above that of adult SEP attainment. Further to asses potential interactive effects between SEP at different life stages and risk factors. An important addition of our study to the current literature is the demonstration of how differences in the degree mediated depend on outcome. A potential explanation of this result may be that while all diseases investigated are lifestyle-related they differ in which important risk factors are anchored more or less in childhood. For example the higher degree of mediation by adult SEP for COPD may be due to smoking being a greater risk factor and is highly influenced by adult SEP (15) while

allostatic load and eating habits are greater risk factors for diabetes and cardiovascular diseases and are at the same time more anchored in early-life (9). Thus in terms of policy, our study may indicate that no one size fits all apply for when to best intervene in the life course. Instead, this may depend on the specific health outcome of interest. For example learned stress responses, allostatic load and eating habits may be much harder to change in adulthood compared to e.g. smoking habits.

This study has several key strengths. We used data from an entire national cohort with a long and almost complete follow-up period. We included the most commonly used SEP markers from the Danish national registers measured in both early-life and adulthood which further negated the issues of using retrospectively assessed SEP and potential self-reporting bias typical in studies of SEP and health. We investigated three lifestyle-related diseases for which similar estimates were found.

Among the weaknesses of this study we count the use of only one time-point measurement of early-life SEP. The use of early-life SEP markers measured at one single time point has been argued to be a weak proxy for the SEP spanning the entire early-life period (39), and more studies are needed to investigate whether changes in SEP across early-life are important considerations within public health. However, using multiple markers of SEP in both early-life and adulthood seems to provide a better representation of the complex multifactorial phenomenon that SEP is and may more fully account for its mediating effects (9). Only participants who had been officially diagnosed with one of the three diseases were included, and if the risk of non-diagnoses diseases is socially skewed, it may impact the validity of the results. In the measure of income, we only assessed the participants' annual tax-reported income without taking potential partner's income

into account as well as material assets. Thus, this measure may be a crude proxy of the material SEP circumstances. Importantly, we did not include factors that may confound the association between adult SES and lifestyle-related diseases such as lifestyle and childhood health status which may have biased the results (19). However, the study by Nandi et al. included both lifestyle and childhood health while obtaining similar results for heart disease and diabetes. However, it is possible that the estimates may be attenuated is they were to be included in the model. Such confounders would include current smoking, body mass index and alcohol consumption (29). Further studies should investigate whether the results can be replicated in other countries.

Adverse SEP status in childhood is related to lifestyle-related diseases in adulthood. The increased risk extends beyond the SEP status in later adulthood. This stresses that early socioeconomic interventions for children in low SEP status may be important for lowering the risk of adult life-style related diseases.

Conflicts of interest

None declared.

Funding

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Key points

- Socioeconomic position in both early-life and adulthood are important determinants of lifestyle-related diseases in adulthood.
- About one tenth to two-thirds of the influence of early-life position was mediated by the position attained in adulthood.

- The degree mediated depended both on the outcome investigated and the social position marker.
- Early-life is a sensitive period for exposures to social and physical determinants of lifestyle-related diseases in adulthood that is only partly mediated by the socioeconomic attained in adulthood.
- Research on alternative pathways from early-life to adult health may play a key role in developing more effective behavioural changing policies.

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Tables

Table 1. Socio-demographic characteristics of the eligible study population (n=793,674)

Variable	Men (n=405,064)	Women (n=388,610)	Total (n=793,674)
Year of birth			
1961	35632 (8.8%)	33962 (8.7%)	69594 (8.8%)
1962	33628 (8.3%)	32421 (8.3%)	66049 (8.3%)
1963	33956 (8.4%)	32219 (8.3%)	66175 (8.3%)
1964	35433 (8.7%)	33500 (8.6%)	68933 (8.7%)
1965	38216 (9.4%)	36809 (9.5%)	75025 (9.5%)
1966	41361 (10.2%)	39724 (10.2%)	81085 (10.2%)
1967	39919 (9.9%)	38301 (9.9%)	78220 (9.9%)
1968	38941 (9.6%)	37146 (9.6%)	76087 (9.6%)
1969	37963 (9.4%)	36705 (9.4%)	74668 (9.4%)
1970	35522 (8.8%)	34415 (8.9%)	69937 (8.8%)
1971	34493 (8.5%)	33408 (8.6%)	67901 (8.6%)
Ethnicity			
Danish	400921 (99.0%)	385344 (99.2%)	786265 (99.1%)
Other	4143 (1.0%)	3266 (0.8%) *	7409 (0.9%)
SEP in early-life by:			
Education			

High	72373 (17.9%)	68743 (17.7%)		141116 (17.8%)
Middle	183464 (45.3%)	175732 (45.2%)		359196 (45.3%)
Low	149227 (36.8%)	144135 (37.1%)	*	293362 (37.0%)
Occupation				
High	138463 (34.2%)	131322 (33.8%)		269785 (34.0%)
Middle	176634 (43.6%)	170665 (43.9%)		347299 (43.8%)
Low	89967 (22.2%)	86623 (22.3%)	*	176590 (22.2%)
Income				
High	133667 (33.0%)	129371 (33.3%)		263038 (33.1%)
Middle	137043 (33.8%)	131163 (33.8%)		268206 (33.8%)
Low	134354 (33.2%)	128076 (33.0%)	*	262430 (33.1%)
Combined SEP positions				
Most advantaged	40464 (10.0%)	38761 (10.0%)		79225 (10.0%)

Middle	318399 (78.6%)	305135 (78.5%)		623534 (78.6%)
Most disadvantaged	46201 (11.4%)	44714 (11.5%)		90915 (11.5%)
SEP in adulthood by:				
Education				
High	64231 (15.9%)	87166 (22.4%)		151397 (19.1%)
Middle	236189 (58.3%)	205714 (52.9%)		441903 (55.7%)
Low	104644 (25.8%)	95730 (24.6%)	**	200374 (25.2%)
Occupation				
High	75458 (18.6%)	62420 (16.1%)		137878 (17.4%)
Middle	264262 (65.2%)	241837 (62.2%)		506099 (63.8%)
Low	65344 (16.1%)	84353 (21.7%)	**	149697 (18.9%)
Income				
High	194104 (47.9%)	74240 (19.1%)		268344 (33.8%)
Middle	109610 (27.1%)	157897 (40.6%)		267507 (33.7%)

Low	101350 (25.0%)	156473 (40.3%)	**	257823 (32.5%)
Combined SEP positions				
Most advantaged	32059 (7.9%)	19376 (5.0%)		51435 (6.5%)
Middle	345434 (85.3%)	331421 (85.3%)		676855 (85.3%)
Most disadvantaged	27571 (6.8%)	37813 9.7%)	**	65384 (8.2%)

*< 0.05, **<0.0001

Figure legends

Figure 1. Flowchart of study population

Figure 2. Total effect (HR and 95%CI) of educational position in early-life on COPD, diabetes and cardiovascular disease, respectively, and the proportion (%) mediated by educational position in adulthood for Danish women (top) and men (bottom) born between 1961-1971

Figure 3. Total effect (HR and 95%CI) of degree of advantaged position in early-life on COPD, diabetes and cardiovascular disease, respectively, and the proportion (%) mediated by number of degree of advantaged position in adulthood for Danish women (top) and men (bottom) born between 1961-1971

Figures

Figure 1.

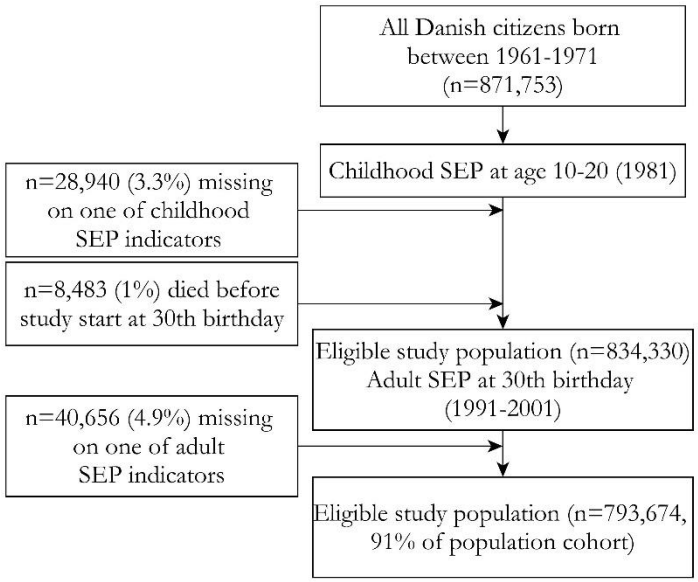


Figure 2.

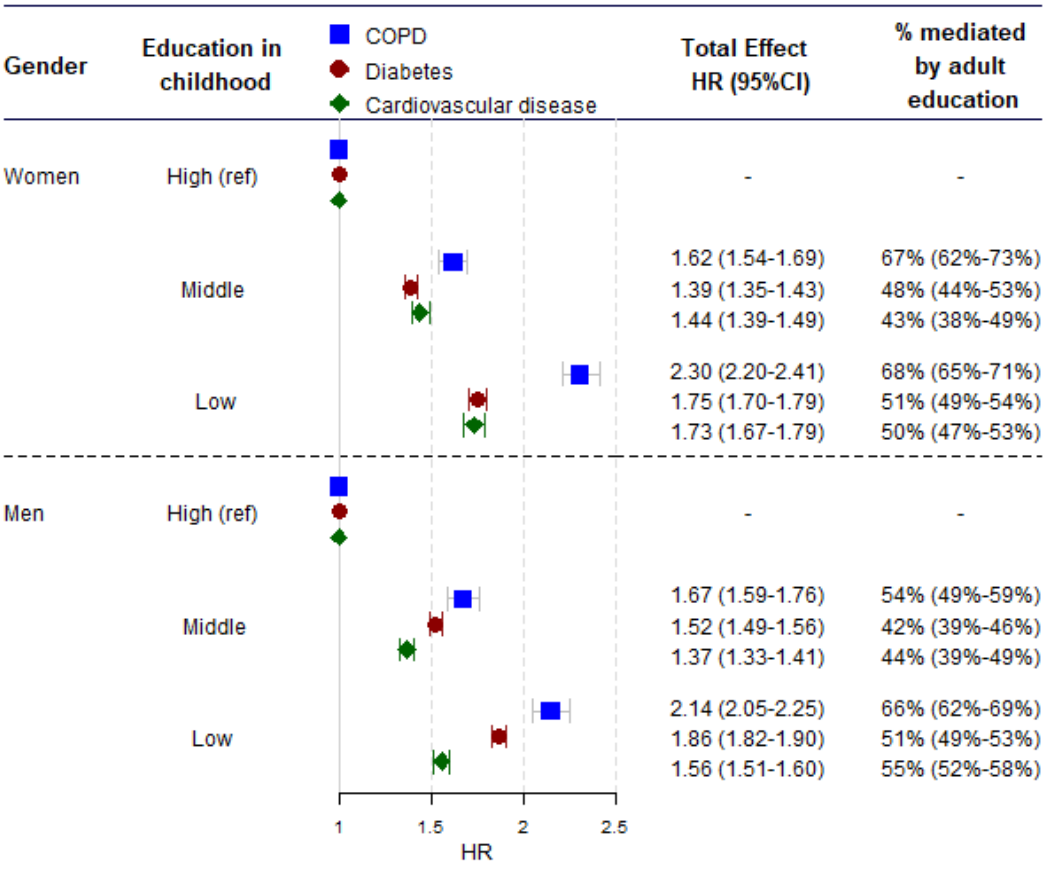
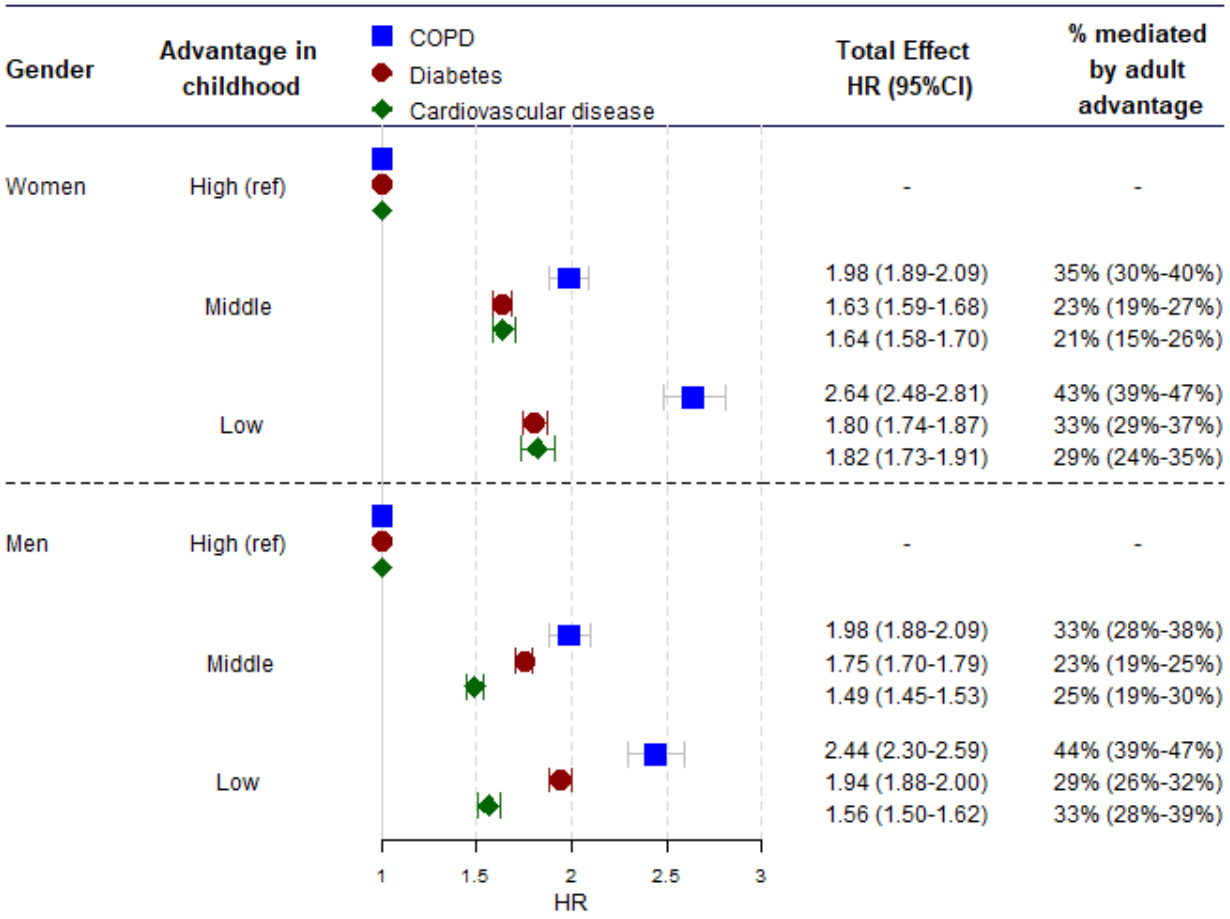

Gender
Education in childhood
COPD
Diabetes
Cardiovascular disease
Total Effect HR (95%CI)
% mediated by adult education
Women
High (ref)
-
-
Middle
1.62 (1.54-1.69)
67% (62%-73%)
1.39 (1.35-1.43)
48% (44%-53%)
1.44 (1.39-1.49)
43% (38%-49%)
Low
2.30 (2.20-2.41)
68% (65%-71%)
1.75 (1.70-1.79)
51% (49%-54%)
1.73 (1.67-1.79)
50% (47%-53%)
Men
High (ref)
-
-
Middle
1.67 (1.59-1.76)
54% (49%-59%)
1.52 (1.49-1.56)
42% (39%-46%)
1.37 (1.33-1.41)
44% (39%-49%)
Low
2.14 (2.05-2.25)
66% (62%-69%)
1.86 (1.82-1.90)
51% (49%-53%)
1.56 (1.51-1.60)
55% (52%-58%)
1
1.5
2
2.5
HR

Figure 3.


Gender
Advantage in childhood
COPD
Diabetes
Cardiovascular disease
Total Effect HR (95%CI)
% mediated by adult advantage
Women
High (ref)
-
-
Middle
1.98 (1.89-2.09)
35% (30%-40%)
1.63 (1.59-1.68)
23% (19%-27%)
1.64 (1.58-1.70)
21% (15%-26%)
Low
2.64 (2.48-2.81)
43% (39%-47%)
1.80 (1.74-1.87)
33% (29%-37%)
1.82 (1.73-1.91)
29% (24%-35%)
Men
High (ref)
-
-
Middle
1.98 (1.88-2.09)
33% (28%-38%)
1.75 (1.70-1.79)
23% (19%-25%)
1.49 (1.45-1.53)
25% (19%-30%)
Low
2.44 (2.30-2.59)
44% (39%-47%)
1.94 (1.88-2.00)
29% (26%-32%)
1.56 (1.50-1.62)
33% (28%-39%)
1
1.5
2
2.5
3
HR