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Education and adult cause-specific mortality—examining the impact of family factors shared by 871 367 Norwegian siblings

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Objective To estimate the impact family factors shared by siblings has on the association between length of education and cause-specific mortality in adulthood.

Methods The study population ($n = 871\,367$) was all Norwegians born 1940–59 having one or more sibling within the cohort and alive in 1990. Length of education was obtained in 1990. Follow-up of deaths was from 1991 to 2008 when participants were aged 32–68 years.

Results Sixty-five per cent of participants had one or more siblings who had completed a different number of years of formal education. A one-category difference in education was associated with a 30% increase in the hazard rate of death by all causes among men in the cohort analysis and 23% in within siblings analysis, and in women, increases were 22% and 14%, respectively. For cardiovascular disease, increases were 36% and 25% in men and 51% and 36% in women. For lung cancer, they were 48% and 29% in men and 53% and 22% in women. External causes and alcohol-related causes in men were generally similar in both analyses.

Conclusions This study suggests that at least some of the educational inequalities in all-cause, cardiovascular disease and lung cancer, external and alcohol-related mortality are explained by factors shared by siblings.

Keywords education, mortality, siblings, family

Introduction

There is ample evidence showing that socio-economically disadvantaged individuals have worse health than advantaged individuals.[1] These health differentials are generally not confined to marginalized groups of society but are found across the whole gradient. A number of studies have found that more deprived childhood socio-economic circumstances are related to increased risk of adult mortality, even for younger generations who have not experienced a similar degree of hardship compared with the poorer members of society in previous generations.[2,3]

In Norway, there is evidence that survival inequalities related to educational attainment are widening,[4] but the mechanisms underlying these associations are

unclear. Children of parents with disadvantaged socio-economic circumstances tend to complete fewer years of education and have lower attainment; thus, the association of education with mortality may be a simple reflection of the established association of disadvantaged childhood socioeconomic position (SEP) with increased all-cause and cause-specific mortality.[5] Parenting practice and parental behaviours, such as smoking and excessive alcohol consumption, might influence health behaviours in children, as may educational attainment itself, and these may mediate the observed association of education/childhood SEP with adult mortality.[6–9]

One method that could be used to unpick some of these mechanisms is a within sibling comparison study.[10] Full siblings share a number of characteristics, such as parental/childhood SEP, housing conditions, neighbourhoods, access to schooling and family patterns of health-related behaviour. Thus, by comparing within siblings associations of education with mortality with the same associations between unrelated individuals, it is possible to investigate whether these associations are explained by shared parental and family characteristics. An attenuation in effect between education and mortality would provide evidence for that. Siblings also share on average 50% of their germ line genetic variation; therefore, this design will also control for some contribution of shared genetic variation to the association. In this study, we compared the association between length of education and cause-specific mortality in adulthood between unrelated individuals and within siblings to assess the impact of early life family environment on educational inequalities in adult cause-specific mortality.

Methods

Population

The population included all Norwegians born in the period 1 January 1940 to 31 December 1959 who participated in the 1960 census and survived to 1991 ($n = 1\,238\,650$). In 1963, all Norwegians were given a personal identity number that was applied to the 1960 census. Family information was recorded for families, with young children giving almost full inter-generational linkage for those born after 1952 and partial linkage for those born before. In this study, we have only included participants born after 1952 or those born earlier for whom family and household numbers were given in 1960. By using information on number of children in the household and oldest woman and man in the household, it was possible to identify mothers and fathers among those born after 1940, with negligible degree of misclassification in cases where the two methods could be compared.[11] The chance of being included drops gradually for older cohorts from ~100% among those born after 1952 to ~80% among those born in 1940. After exclusion of those with no information on education ($n = 47\,384$), those with no parental linkage ($n = 95\,851$) and those in sibling groups of one ($n = 224\,048$), this study included 871 367 individuals in 337 627 sibling groups.

Exposure

Education was defined as the longest time spent in formal education by 1990, derived from the educational register collected by Statistics Norway. As the youngest participants turned 30 years old in 1990, educational length at this age will represent complete education for most participants. Length of education was categorized into the following five ordered aged groups: 7–9 years (representing completion of primary school education only), 10–11 years (middle school), 12 years (secondary school), 12–16 years (college) and >16 years (usually indicating completion of a university degree).

Outcomes

Follow-up of deaths was from 1991 to 2008 (i.e. when participants were aged 32–68 years). In addition to all-cause mortality, we examined education in relation to four specific causes of death that we believed to be associated with education through different mechanisms: cardiovascular disease (CVD) (International Classification of Disease (ICD-10): I00–I99), lung cancer (ICD-10: C32–C34), alcohol-related cause (ICD-10: F10, K70, K73–K74), external causes (ICD-10: V01–Y89).

Analysis and statistical methods

Cox proportional hazards regression model, with age as underlying time, was used. Time (years of age) at risk was counted from 1991 onwards. Individuals who did not die during follow-up were censored at their age at the end of follow-up (31 December 2008). In the cohort analyses, we used sandwich estimator corrected standard errors to take account of familial clustering. In the cohort analyses, familial clustering was treated as a nuisance, and the cohort analyses should produce results that should be similar to those found in studies of unrelated individuals. In the cohort analyses, the model has the form: $\lambda(t,z) = \lambda_0(t)e^{B_k Z_k}$, where λ denotes the hazard, which varies as a function of time t, and a vector of independent variables z. $\lambda_0(t)$ is the non-parametric baseline hazard, and B_k the log(hazard ratio) associated with a one-unit difference in the variable Z_k. For the within siblings analyses, we used the stratified Cox regression model of Holt and Prentice.[12] This model is given by: $\lambda(t,z) = \lambda_0(t)e^{B_k Z_k}$, where the hazard λ_i in the ith sibling group depends on a sibling groups-specific baseline hazard λ_{0i}. The proportional hazards assumption was examined by first plotting the scaled Schoenfeld residual against age, supplemented by a global test of a zero slope in the association between age and the scaled Schoenfeld residuals.

Results

Of the 1 238 650 individuals born from 1940 through 1959 having survived to 1991, 10% had missing identity of mothers, and 18% had no sibling within the cohort and were excluded from further analyses (Table 1). Those born in 1940 or 1960 were more likely to be excluded because of not having a sibling in the cohort than those born in the years between. As expected, from knowledge of the record linkage process (see Methods), individuals born before 1952 were more likely to be excluded because they lacked parental identity.

Sixty-five per cent of individuals had one or more sibling who had completed a different amount of education (Table 2). In the cohort analyses of all-cause mortality, a strong and pronounced educational gradient was observed in men and women (Figure 1 and Table 3). The point estimates and corresponding 95% confidence intervals (CI) are given in Table 3. Within siblings, the educational gradient with all-cause mortality was weaker than that seen in the cohort analysis (Figure 1 and Table 3). Graphically, this can be seen in Figure 1 by observing that the slope between any two points (not just adjacent points) is shallower in the within siblings analysis than in the cohort analyses. However, even in within-sibling groups, the less educated sibling was more likely to die during follow-up than the more educated sibling(s) on average. In the cohort analyses, every incremental step down the educational categories was associated with an increase in hazard ratio to 1.30 (95% CI: 1.29–1.32) in men. Within siblings, this was 1.23 (1.21–1.24). In women, the corresponding values were 1.22 (1.20–1.24) and 1.14 (1.12–1.16).

In the cohort analyses of cause-specific mortality, the steepest educational gradients were observed for lung cancer in men, CVD in women and alcohol-related causes in both sexes (Figure 1 and Table 3). A one-category difference in education was associated with a hazard rate of 1.36 for CVD in men and in the cohort analysis and 1.25 in the within siblings analysis; and in women 1.51 and 1.36, respectively. For lung cancer, these values were 1.48 and 1.29 in men and 1.53 and 1.22 in women. For alcohol-related causes, they were 1.57 and 1.40 in men and 1.77 and 1.64 in women, and for external causes, they were 1.39 and 1.28 in men and 1.25 and 1.19 in women. For external-related causes, the attenuation seemed mostly among those in lowest educational categories. As with all-cause mortality, education—cause-specific mortality gradients existed for all specific causes within siblings and in the cohort as a whole (i.e. representing associations between unrelated individuals).

Discussion

In this study, increasing mortality was found with decreasing length of education. This association was weakened when the analyses were examined within siblings. This suggests that the educational gradient in mortality is in part explained by early life characteristics that are similar for siblings. Interestingly, the difference between the within-sibling and whole cohort analyses differed by cause of mortality, being most marked for lung cancer with relative risk reduction of 40% in men and 60% in women and for CVD, 31% in men and 29% in women. For external causes, the attenuation was mostly seen among those in the lowest educational categories. These differences suggest that the importance of early life family characteristics in explaining the association between education and mortality in adulthood varies somewhat according to the cause of mortality.

Strengths and limitations

The main strengths of this study are its large sample size, population coverage and ability to examine the impact of early life environment in within siblings analyses, with adequate statistical power. Collecting information on potential confounders and mediators of this association and then accounting for these in the analyses would be a more appropriate approach. Such an approach would have the additional advantage that it could dissect the possible role of specific early life characteristics and also take account of potential adult mediators. However, we are unaware of any cohort that has all potential confounders and mediators. Furthermore, prospective cohorts with such data are more likely to be affected by selection bias (i.e. different associations in those who remain through follow-up and collection of time-varying covariables) than our population register study. Educational attainment was recorded in adulthood when most would have finished their education, and the follow-up of deaths was recorded through adulthood to a maximum of age 63 years. Deaths before 65 years in Western populations are generally considered premature; hence, our results refer to associations of education with premature mortality, and it is possible that with longer follow-up into older ages our findings might differ. Although we have matched siblings on the basis of having the same mother and father, we do not know whether any parents separated during early life, and if they did so, whether this affected discordancy in educational attainment among siblings or the amount of early life that each sibling spent together. For this generation, growing up in a divorced family was uncommon, e.g. the rate of divorce was constant from 1940 to 1970 at 4 per 1000 marriages. Since then the rate has increased to 12 per 1000 marriages.[13] For those finishing primary education before 1967, when compulsory education was increased from 7 to 9 years, some were classified in this category even if they had less. This could have underestimated effects in the lowest educational group.

Table 1 Characteristics of the population of all Norwegians born 1940–60 who survived until 1990 stratified by those who were included or excluded (either because of not having a sibling or having missing information on parents or other data) from our study

Characteristics of the population	Included ($n = 871\,367$)	Excluded	
		No siblings in the cohort ($n = 224\,048$)	Missing information on parental status or other data ($n = 95\,851$)
Year of birth	*n* (%)	*n* (%)	*n* (%)
1940–45	170 166 (20)	65 022 (29)	53 706 (49)
1946–50	235 315 (27)	49 896 (22)	17 098 (19)
1951–55	248 384 (28)	34 958 (16)	12 461 (16)
1956–60	217 502 (25)	74 172 (33)	12 586 (17)
Education, in years[a]			
7–9	111 775 (13)	30 725 (14)	15 212 (16)
10–11	102 057 (12)	28 243 (12)	10 251 (11)
12	203 427 (23)	56 221 (25)	18 556 (19)
12–16	270 815 (31)	68 218 (31)	24 221 (25)
>16	183 293 (21)	40 641 (18)	27 611 (29)
Sex			
Male	451 617 (52)	117 364 (52)	39 883 (42)
Female	419 750 (48)	106 684 (48)	55 968 (58)
Mortality			
Alive in 2009	826 125 (95)	209 816 (94)	88 671 (93)
Died 1991–2008	45 242 (05)	14 232 (07)	7180 (07)
Siblings			
One	–	224 048	–
Two	390 962 (45)	–	–
Three	264 819 (30)	–	–
Four	127 996 (15)	–	–
Five or more	87 590 (10)	–	–

[a]Missing education data ($n = 47\,384$) by group was as follows: 2% among the included, 2% among those with no siblings and 20% among those with missing information on parental status.

Assumptions in the sibling design

In the sibling analysis, only siblings who are discordant for education contribute to the estimation of the parameters for education. It might also be that familial causes of discordance in education can impact on the shared baseline hazard. For example, the risk of death for individuals with high education may be higher if these individuals originate from a sibling group with discordant educations than if originating from a sibling group where all siblings had high educations. The association between education of interest and the baseline hazard is the motivation behind the use of the fixed effect models rather than shared frailty models, where independence between the frailty and independent variables are assumed. In families where all siblings have the same level of education, sibling comparisons no longer contribute with information compared with the cohort analysis. This could potentially introduce bias in the comparison. We examined this by estimating all-cause mortality when we restricted the data to only include groups with educationally discordant siblings. This gave essentially similar results.

In the regression analysis, age was used as underlying time and was adjusted for. However, year of birth could also play a role, as there could be secular trends in the outcome that could also be related to education. Directly modelling the influence of birth year in this data set is hampered by the fact that the range of birth year is strongly restricted, especially for those aged <45 or >55 years in the follow-up period. For those aged 45–55 years, we modelled an interaction term that suggested a relative advantage in survival of individuals with long educations was greater the later the birth year. Also, a strong influence on birth year would be detected as deviations from proportional hazards, precisely because of the association between age of death and birth year. Our analysis did not detect any of this, although the power to test this is limited because of the restricted

Table 2 Differences in length of education among siblings according to sibship size in 871 367 Norwegians in 337 627 sibling groups

Difference in education, in years	All ($n = 855\,096$ pairs)	Two siblings ($n = 195\,024$ pairs)	Three siblings ($n = 264\,463$ pairs)	Four siblings ($n = 191\,512$ pairs)	Five or more siblings ($n = 204\,097$ pairs)
	n (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Both > 16	32 626 (4)	10 176 (5)	11 877 (5)	6716 (4)	3857 (2)
>16 vs 12–16	41 184 (5)	12 683 (7)	14 809 (6)	8301 (4)	5391 (3)
>16 vs 12	42 831 (5)	12 111 (6)	14 880 (6)	9072 (5)	6768 (3)
>16 vs 10–11	36 876 (4)	9572 (5)	12 204 (5)	8079 (4)	7021 (3)
>16 vs 7–9	10 810 (1)	2365 (1)	3122 (1)	2455 (1)	2868 (1)
Both 12–16	18 106 (2)	5446 (3)	6315 (2)	3748 (2)	2597 (1)
12–16 vs 12	45 882 (5)	12 888 (7)	15 844 (6)	9623 (5)	7527 (4)
12–16 vs 10–11	45 132 (5)	11 303 (6)	15 078 (6)	9792 (5)	8959 (4)
12–16 vs 7–9	15 021 (2)	3100 (2)	4506 (2)	3441 (2)	3974 (2)
Both 12	52 199 (6)	13 938 (7)	16 776 (6)	11 153 (6)	10 332 (5)
12 vs 10–11	126 910 (15)	30 268 (16)	40 696 (15)	27 843 (15)	28 103 (14)
12 vs 7–9	65 583 (8)	12 171 (6)	18 337 (7)	15 351 (8)	19 724 (10)
Both 10–11	100 414 (12)	22 621 (12)	31 348 (12)	22 861 (12)	23 584 (12)
10–11 vs 7–9	125 842 (15)	22 559 (12)	35 200 (13)	29 971 (16)	38 112 (19)
Both 7–9	95 680 (11)	13 823 (7)	23 471 (9)	23 106 (12)	35 280 (17)

age range where this can be formally tested. Another problem with modelling birth year is that it greatly reduces power. If analysis is stratified according to birth year, this breaks up many of the sibling groups and renders them uninformative for the effect of education. Standard errors of most parameter estimates increased by about a factor of 1.5–2 by including an interaction term between birth year and education. This means that our analyses are averaging somewhat heterogeneous effects. Future research should investigate this issue specifically, because rather than seeing this merely as a technical problem, the degree to which life course influences are stable across birth cohorts is a substantial research issue in itself because these may be context specific.[3,14,15]

Siblings share the same parents, but they may not share the same environment. A fundamental distinction has been drawn between 'stable' and 'dynamic' family context.[16] Birth order and age difference are not equally shared between siblings. And as the number of siblings may change, the material resources and socio-economic position of the family may also change. In a sensitivity analysis, we included number of siblings and birth order as covariates, but these had little impact on the estimates.

Many phenotypes in childhood later show substantial within-sibling differences.[17,18] Inter-individual estimates of heritable, shared and non-shared environmental effects in twin studies come from subtracting the heritable and shared components from the total variance and the non-shared part being the remaining variance.[19] The differences between siblings not belonging to the heritable but to the non-shared component, could originate from child-specific differences in parental treatment in the family that siblings do not share, as have been shown in studies on child development.[20,21] A more general discussion of biases in heritability estimates is available elsewhere.[19] For outcomes in adulthood, the non-shared differences could be a result of stochastic processes that as individuals grow older make siblings increasingly less similar.[22] Our sibling approach is a way of adjusting for many characteristics that are assumed to be picking up stable aspects of the family context and are shared (identical or similar) by siblings.

Explanations of the findings

From a causal inference perspective, the sibling design has the advantage of potentially eliminating confounding factors equally shared by siblings. Apart from the 50% genetic similarities siblings share throughout life, their shared environment is likely to decrease in influence with age. The sibling design will consequently be most useful for testing causality on early life factors where family confounding may be important.[23] Length of education is considered to

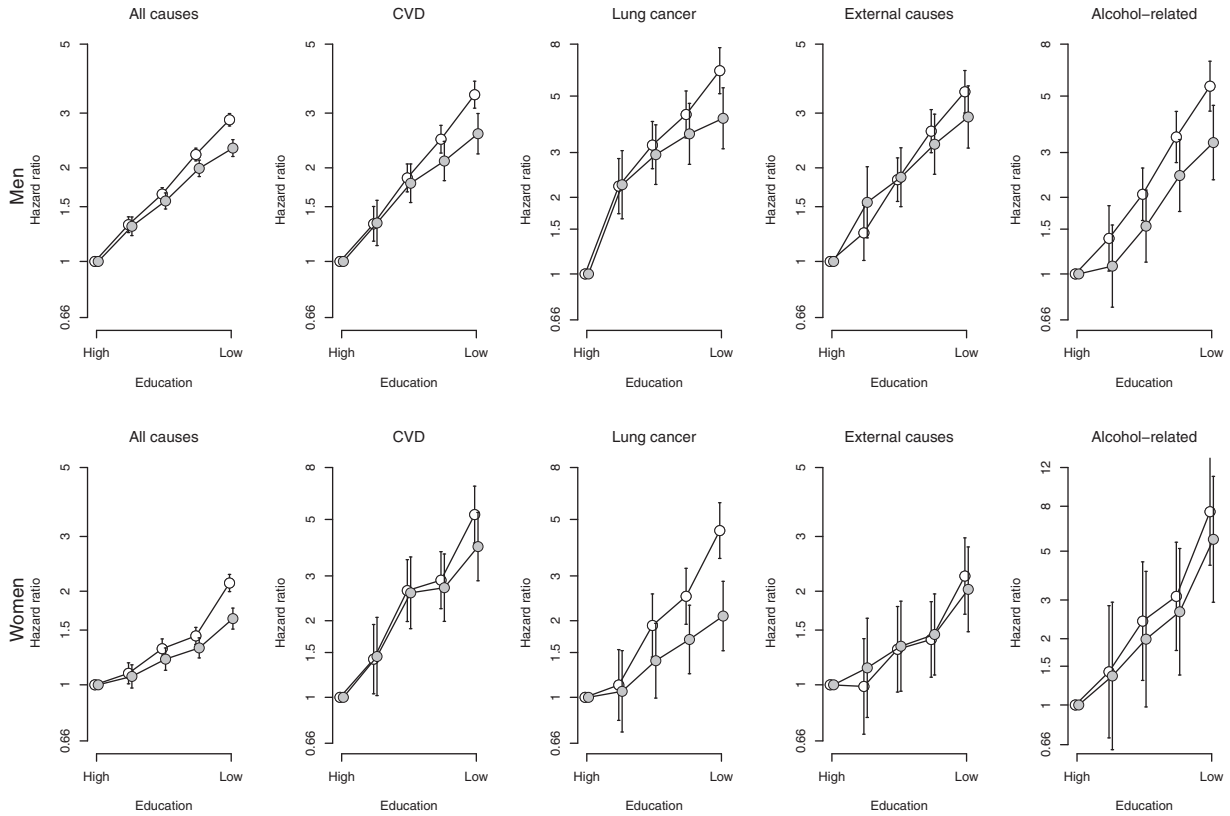

Figure 1 All-cause and cause-specific mortality in relation to education in 871 367 Norwegians in 337 627 sibling groups. White circles represent associations from the cohort analyses, grey circles represent associations from the within-sibling analyses

reflect early life environment more than occupational class and income because it often does not change through adulthood.[24]

Premature mortality because of CVD has been linked to a number of risk factors through the life course, including intrauterine growth retardation, rapid growth in infancy, childhood cognitive development, childhood overweight/obesity and their associated cardiometabolic risk factors and tracking of these into adulthood[25] and access to preventive and curative medical services later in the disease process.[26] Recent studies have shown that traditional risk factors, such as smoking, physical inactivity, cholesterol and hypertension, are likely to explain more of socioeconomic inequalities in all-cause and cardiovascular mortality than previously anticipated, especially when these are measured several times during the life course, and inequalities are expressed in absolute rather than relative terms.[15,27] Thus, for CVDs, our study provides further evidence supporting the notion that early life and family factors play a role in addition to the traditional risk factors in adulthood.

For lung cancer and alcohol-related causes, the attenuation in effect of education points to the influence of the uptake in adolescence and early adulthood of smoking and alcohol consumption.[29] Characteristics of one's family during childhood and adolescence (including poor relationships between parents and children, parental educational attainment and possibly parental substance misuse) seem to be the primary social factors associated with smoking and alcohol initiation. For external causes, attenuation in effect was only seen among those in the lower education strata, which is consistent with risk of accidental deaths being mostly driven by the socioeconomic environment in adulthood.[3]

The parameter estimates in the cohort and sibling models should not be interpreted literally as an assessment on the relative importance of childhood vs adulthood in causing educational inequalities in mortality for several reasons. First, the sibling design rests on an assumption of shared vulnerability, the validity of which is largely unknown.[29] We do not know how much of this construct could be the 50% of additive genetic influence that siblings have in common.[10] Genetics can only have a limited role, because the personal traits responsible for the length of education an individual achieves, such as cognitive ability or personality and later related to chronic disease, are complex traits that are probably determined by many genes.[30,31] It is not plausible that a complete set of genes associated with a particular

Table 3 All-cause and cause-specific mortality in relation to education in 871 367 in 337 627 sibling groups

		Hazard ratio of mortality (95% CI)			
		Men		Women	
Cause of death	**Education**	Cohort	Within siblings	Cohort	Within siblings
All-causes ($n = 45\ 242$)	7–9 years	2.86 (2.73–2.99)	2.32 (2.18–2.46)	2.13 (1.99–2.27)	1.63 (1.51–1.76)
	10–11 years	2.21 (2.11–2.31)	1.99 (1.87–2.12)	1.44 (1.35–1.53)	1.31 (1.22–1.42)
	12 years	1.65 (1.57–1.73)	1.56 (1.47–1.66)	1.31 (1.22–1.40)	1.21 (1.11–1.31)
	12–16 years	1.31 (1.24–1.39)	1.30 (1.21–1.39)	1.09 (1.01–1.18)	1.06 (0.98–1.16)
	>16 years	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
	Per one-step	1.30 (1.29–1.32)	1.23 (1.21–1.24)	1.22 (1.20–1.24)	1.14 (1.12–1.16)
	Rate[a]	364.89		218.98	
CVD ($n = 8539$)	7–9 years	3.44 (3.11–3.80)	2.58 (2.22–2.99)	5.23 (4.04–6.76)	3.91 (2.87–5.33)
	10–11 years	2.47 (2.23–2.74)	2.10 (1.82–2.43)	2.89 (2.23–3.74)	2.70 (1.99–3.66)
	12 years	1.86 (1.67–2.06)	1.78 (1.55–2.06)	2.63 (1.99–3.47)	2.57 (1.86–3.56)
	12–16 years	1.32 (1.16–1.50)	1.33 (1.12–1.57)	1.41 (1.03–1.93)	1.45 (1.02–2.06)
	>16 years	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
	Per one-step	1.36 (1.34–1.39)	1.25 (1.21–1.29)	1.51 (1.44–1.58)	1.36 (1.28–1.43)
	Rate[a]	84.44		24.75	
Lung cancer ($n = 4131$)	7–9 years	6.29 (5.11–7.75)	4.09 (3.10–5.39)	4.52 (3.51–5.82)	2.09 (1.52–2.86)
	10–11 years	4.23 (3.42–5.24)	3.55 (2.70–4.68)	2.49 (1.94–3.21)	1.69 (1.24–2.30)
	12 years	3.21 (2.59–3.97)	2.94 (2.25–3.85)	1.92 (1.44–2.55)	1.39 (0.99–1.95)
	12–16 years	2.21 (1.72–2.84)	2.24 (1.65–3.05)	1.12 (0.81–1.54)	1.06 (0.73–1.53)
	>16 years	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
	Per one–step	1.48 (1.43–1.53)	1.29 (1.23–1.35)	1.53 (1.46–1.61)	1.22 (1.15–1.29)
	Rate[a]	30.64		22.84	
Alcohol-related ($n = 2088$)	7–9 years	5.47 (4.36–6.85)	3.28 (2.34–4.60)	7.56 (4.32–13.23)	5.66 (2.93–10.94)
	10–11 years	3.45 (2.74–4.35)	2.44 (1.76–3.37)	3.12 (1.77–5.49)	2.65 (1.37–5.14)
	12 years	2.06 (1.62–2.61)	1.54 (1.11–2.14)	2.40 (1.29–4.47)	1.99 (0.98–4.05)
	12–16 years	1.38 (1.03–1.85)	1.07 (0.74–1.56)	1.42 (0.71–2.83)	1.35 (0.63–2.93)
	>16 years	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
	Per one-step	1.57 (1.51–1.64)	1.40 (1.31–1.50)	1.77 (1.60–1.96)	1.64 (1.43–1.88)
	Rate[a]	20.77		5.92	
External causes ($n = 3558$)	7–9 years	3.51 (3.00–4.11)	2.92 (2.32–3.67)	2.24 (1.69–2.97)	2.03 (1.48–2.78)
	10–11 years	2.62 (2.24–3.08)	2.38 (1.91–2.98)	1.40 (1.06–1.85)	1.45 (1.08–1.96)
	12 years	1.83 (1.56–2.15)	1.87 (1.50–2.32)	1.30 (0.95–1.79)	1.33 (0.95–1.86)
	12–16 years	1.24 (1.01–1.52)	1.55 (1.19–2.02)	0.99 (0.69–1.41)	1.13 (0.79–1.64)
	>16 years	1 (ref.)	1 (ref.)	1 (ref.)	1 (ref.)
	Per one-step	1.39 (1.34–1.43)	1.28 (1.22–1.34)	1.25 (1.17–1.33)	1.19 (1.11–1.28)
	Rate[a]	34.94		10.57	

[a]Age adjusted mortality rate per 100 000 person-years.

personality profile or level of intelligence are transmitted intact from parent to child, because the relevant genes are located on different chromosomes and will become reassorted during meiosis. And, if some genotypes become concentrated in populations of low or high socio-economic position, social mobility will lead to dilution within a few generations, unless social mobility is affected by the associated phenotypes.

Secondly, regression models with adjustment for sibling similarities and lifestyle risk factors pooled into one analytical framework may conflate the

multilevel nature of what causes population health and inequalities during the life course. For example, lung cancer is substantially influenced by lifetime smoking trajectories in adulthood,[32] and the initiation of smoking behaviour usually takes place in adolescence.[28] If the data was available, we could have included a variable 'pack years of smoking' into our models and explained the gradient further. However, this single level analytical approach will not give a full understanding of what causes inequalities in lung cancer and other smoking related outcomes. A large body of evidence suggests determinants are found at multiple levels and stages through the life course from initiation and continuation of smoking, smoking policies and the carcinogenic effect of tobacco smoke on lung tissue. A division between proximal and distal factors in epidemiology and public health research and practice has been criticized because it cleaves levels of causation and may obscure the intermingling of specific exposures from the ecological and social environment.[33] And related to this study, readers could misinterpret the comparatively modest attenuation in the within sibling analysis effects as evidence for downstream or proximal causes (like individual level smoking behaviour) being more important than upstream or distal causes (like socio-economic environment in childhood shared by siblings influencing smoking initiation).

Finally, it has been argued that even if many studies of twins and siblings find small proportions of inter-individual variation in child and adult outcomes that may be part of the shared environment in childhood, these may still account for a large proportion of cases at population level.[23,34] This is because the often much larger non-shared variation may result from random or stochastic events that individuals experience during the life course, and these may not constitute realistic targets for intervention. This point is not directly transferable to educational inequalities because inequalities in adult mortality do not have the same interpretation as the inter-individual differences within a twin-research approach. The processes leading to educational inequalities in adult mortality are not stochastic in the same sense.[35] Future studies would benefit from investigating and comparing within sibling analysis of outcomes like body mass index at several time points through adult life to understand better the enduring impact early life family factors may have on both later inter-individual variation and inequalities.

Conclusions

This study suggests that at least some of the educational inequalities in all-cause, CVD and lung cancer, external and alcohol-related mortality are explained by factors shared by siblings.

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Ø.N., D.A.H., D.A.L. and L.M. contributed in the conception of the study. Ø.N. and L.M. designed the study. Ø.N. and L.M. analysed the data. Ø.N. drafted the article and D.A.H., D.A.L. and L.M. revised it critically for intellectual content. All authors have approved the final version. The reporting of this study has been in accordance with the checklist in the STROBE statement for cohort studies. The study has been approved by Regional Ethics Committee for medical research (REK Sør-Øst) 2010/260.

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Commentary: Education and mortality inequalities in Norway

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