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Intergenerational educational trajectories and premature mortality from chronic diseases: A registry population-based study

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A B S T R A C T

The tracking of educational gradients in mortality across generations could create a long shadow of social inequality, but it remains understudied. We aimed to assess whether intergenerational educational trajectories shape inequalities in early premature mortality from chronic diseases. The study included 544 743 participants of the Swiss National Cohort, a registry population-based study. Individuals were born 1971–1980 and aged 10–19 at the start of the study (1990). Mortality follow-up was until 2018. Educational trajectories were High–High (reference), High–Low, Low–High, Low–Low, corresponding to the sequence of parental-individual attained education. Examined deaths were related to cardiovascular diseases (CVD), cancers, and substance use. Sex-specific inequalities in mortality were quantified via standardized cumulative risk differences/ratios between age 20 and 45. We triangulated findings with a negative outcome control. For women, inequalities were negligible. For men, while inequalities in cancers deaths were negligible, inequalities in CVD mortality were associated to low individual education regardless of parental education. Excess CVD deaths for Low–High were negligible while High–Low provided 234 (95% confidence intervals: 100 to 391) and Low–Low 185 (115 to 251) additional CVD deaths per 100 000 men compared to High–High. That corresponded to risk ratios of 2.7 (1.6 to 4.5) and 2.3 (1.6 to 3.4), respectively. Gradients in substance use mortality were observed only when education changed across parent-offspring. Excess substance use deaths for Low–Low were negligible while High–Low provided 225 (88 to 341) additional and Low–High 80 (23 to 151) fewer substance use deaths per 100 000 men compared to High–High. That corresponded to risk ratios of 1.8 (1.3 to 2.5) and 0.7 (0.5 to 0.9), respectively. Inequalities in premature mortality were driven by individual education and by parental education for some chronic diseases. This could justify the development of intergenerational prevention strategies.

1. Introduction

Higher premature mortality rates have been consistently observed in individuals with a lower educational attainment compared to those with a higher education across Western societies (Hummer & Hernandez, 2013; Korda et al., 2020; Mackenbach et al., 2016). According to the theory of fundamental causes of inequalities in health and mortality (Phelan et al., 2010), education provides material and non-material resources encompassing accrued knowledge, healthy behaviours, higher job market return, and beneficial social relations, which all act on health in a protective way. Additionally, the putative causal effect of education on mortality has been corroborated by natural experiments leveraging compulsory schooling laws, and by experimental and twin studies (Galama et al., 2018; Hamad et al., 2018). Notably, a review of all these studies (Galama et al., 2018) points to some differences by context and sex, suggesting that men experience larger educational inequalities in health than women.

While the relationship between individual education and premature mortality has been extensively documented, little is known about how intergenerational educational trajectories, that is the sequence of both parental and individual attained education, may impact mortality. In fact, socialization theory predicts that health-related behaviours, social norms and beliefs are transmitted across generations whilst being also influenced by the schooling environment (Singh-Manoux & Marmot, 2005). Thus, the familial environment may contribute to the amount of cultural and social capital a person has access to, and eventually to social inequalities in health (Abel, 2008). This hypothesis is particularly relevant for inequalities in chronic diseases (CDs), as substantial experimental evidence supports their life course origin (Baird et al., 2017). Consequently, by assessing the effect of both parental and individual educational exposure via intergenerational trajectories we may expand our knowledge about the processes underlying educational inequalities

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in mortality related to CDs and inform public health actions. In fact, while the education attained by an individual is partly affected by that of their parents (Bukodi & Goldthorpe, 2012), various social theories endow different predictions of how these two educational exposures may impact health. A theory of cumulative advantage or resource multiplication predicts that both parental and individual education drive inequalities (Willson et al., 2007); a theory of resource substitution predicts that only individual education drives inequalities (Ross & Mirowsky, 2011); and finally a theory of social mobility predicts that only the direction of change – upward or downward – across the two matters (Erikson & Goldthorpe, 1992). Disentangling these alternative models with empirical data is important for public health, as each theory provides a set of different entry points – identification of groups at higher risk or prioritization of family and/or institution related educational exposure – for informing actions to reduce educational inequalities in premature mortality due to CDs.

Three studies, two from Finland and one from Belgium, have explicitly investigated the parental/individual educational inequalities in premature mortality related to CDs (De Grande et al., 2015; Elo et al., 2014; Martikainen et al., 2020). Despite the heterogeneity in the examined CDs and birth cohorts, overall these studies broadly supported the resource substitution theory, with some exception. Specifically, Elo et al. (Elo et al., 2014) reported that among Finns born before 1950, inequalities in cardiovascular-related deaths were consistent with the resource multiplication theory. To corroborate these findings, more research is needed in other contexts, that is in other countries and birth periods, while discerning among different categories of CDs. The study from De Grande et al. (De Grande et al., 2015) included Belgian young adults born after 1971 and examined only one category of CDs-related mortality, that is cancer.

In this study, we aimed to utilize population-based multi-generational registry data to assess the role of parental and individual educational attainment in driving inequalities in mortality due to specific categories of chronic diseases among contemporary Swiss young adult men and women. Importantly, mortality of young adults may help to identify early-life risk factors to intervene upon for delaying or reducing the burden of mortality in older life, to which chronic diseases as cancers and cardiovascular diseases are the largest contributors (Baird et al., 2017; Stringhini et al., 2017). We implemented a counterfactual-based framework to assess inequalities and ran a negative outcome control to triangulate findings (Sanderson et al., 2018).

2. Methods

2.1. Data source

Data were from the Swiss National Cohort, a population-based study built with sociodemographic data collected at 1990 and 2000 censuses that were linked to mortality, live birth and emigration registries through a combination of deterministic and probabilistic methods (see Supplementary Material) (Bopp et al., 2009).

2.2. Target, study and analytic populations

The target population corresponded to Swiss residents born between 1971 and 1980. The study population included all adolescents aged 10–19 – thus born 1971–1980 – living in Switzerland at the 1990 census, and who survived or did not leave the country until the age of 20 years (N = 695 972, see Supplementary Fig. S1). This cut-off age was chosen in order to follow-up individuals until a minimal age required for the attainment of a high level education (see next paragraph). Mortality follow-up was from December 4th, 1990 (census date) up to December 31st, 2018 when participants were aged 38–47. The analytic sample (N = 544 743–78% of the study population) was derived by excluding individuals for whom parental education was unknown (N = 51 222), and records from the 1990 and 2000 censuses could not be linked (N = 100 007).

2.3. Causal model, exposure, outcome and covariates

The causal model underlying our study is represented in Fig. 1. We designed it to focus on inequalities in CD-specific premature mortality (outcome) driven by trajectories of intergenerational educational attainment (exposure). In the model, the inequalities correspond to the total effect of the exposure on the outcome. The exposure is explicitly assumed to act via two underlying pathways, representing the portions of the total effect mediated or not by competing causes of deaths (Young et al., 2020). The effect via competing causes of deaths is present because individuals who died of causes other than CDs cannot die of CDs. The (controlled) direct effect, that is the effect not mediated by competing causes of deaths, represents the effect of the exposure when deaths due to causes other than CDs are removed. The estimation of the latter requires the strong and potentially unrealistic assumption of a counterfactual elimination of competing deaths. For example, the estimation of the direct effect of the exposure on cancer-related deaths would require the ability to run a study where participants can die only due to cancer during the follow-up, which is implausible or unrealistic. For this reason, in our analyses we focused on estimating total effects.

Parental and individual highest educational achievement were self-reported by parents at 1990 census and by participants at 2000 census (when they were aged 20–29), respectively. Answers were categorized as 'Low' for any degree lower than high-school or second vocational training and 'High' otherwise (see Supplementary Material and Supplementary Table 1). The Swiss education system is hierarchically differentiated such that access to high education is mostly channelled by selective institutional tracks. Consequently, after completion of compulsory schooling most individuals follow either a basic vocational training or a higher education track (Burger, 2021). Finally, participants were classified into four intergenerational trajectories: High–High (high parental and individual education), High–Low (high parental and low individual education), Low–High (low parental and high individual education), and Low–Low (low parental and individual education).

We grouped CDs-related deaths into three categories: CVD, Cancer and Substance use (alcohol and drugs). They corresponded to those with the highest prevalence (Supplementary Tables 2–5). ICD codes of underlying causes of death were mapped into these three categories following a classification by Martinez et al. (Martinez et al., 2020) ICD–10 garbage codes (16%, see Supplementary Tables 3–5) were re-assigned to the selected CD categories or any other cause via a

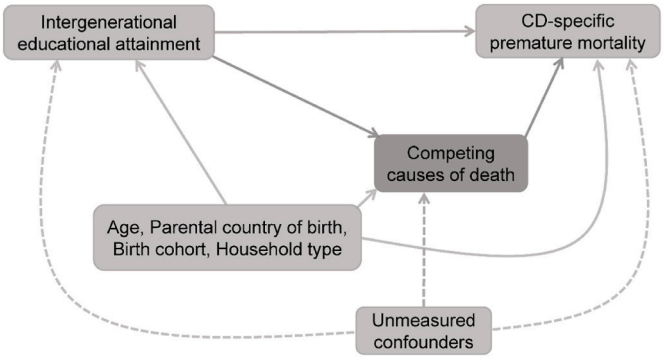

Fig. 1. Causal model. Trajectory of intergenerational educational attainment represents the exposure and CD-specific premature mortality (e.g. cardiovascular diseases) the outcome. Measured potential time-invariant confounders are age, parental country of birth, birth cohort, and type of household in adolescence. Unmeasured confounders are with dashed arrows. Measured potential time-varying mediators are competing causes of death (e.g. all deaths but those due to cardiovascular diseases). For the sake of simplicity, censoring due to loss at follow-up is not drawn.

data-driven predictive model (see Supplementary Material).

Potential confounders were participant's age, sex, birth cohort, household type during adolescence, and parental country of birth (see Table 1).

Table 1
Baseline characteristics of the analytic sample. Household characteristics in adolescence were retrieved from the 1990 census. Parental education is operationalized as the highest between mother and father education. Country of birth of parents is CH whenever at least one parent was born in Switzerland, EU whenever at least one parent was born in a European country but none in Switzerland, and Other for all remaining cases. Individual highest attained education was retrieved from the 2000 census.

	Total N = 544 743	Men N = 283 761 (52%)	Women N = 260 982 (48%)
Household characteristics in adolescence			
Type			
Couple with children	488 919 (90%)	255 212 (90%)	233 707 (90%)
Single parent with children	55 824 (10%)	28 549 (10%)	27 275 (10%)
Highest education of parents			
High	165 720 (30%)	84 966 (30%)	80 754 (31%)
Low	379 023 (70%)	198 795 (70%)	180 228 (69%)
Country of birth of parents			
CH	429 589 (79%)	223 445 (79%)	206 144 (79%)
EU	78 584 (14%)	40 745 (14%)	37 839 (14%)
Other	36 570 (7%)	19 571 (7%)	16 999 (7%)
Individual characteristics			
Birth cohort			
1971–1975	242 761 (45%)	127 009 (45%)	115 752 (44%)
1976–1980	301 982 (55%)	156 752 (55%)	145 230 (56%)
Highest attained education			
High	170 831 (31%)	88 806 (31%)	82 025 (31.4%)
Low	348 973 (64%)	181 179 (64%)	167 794 (64.3%)
Missing	24 939 (5%)	13 776 (5%)	11 163 (4.3%)
Educational trajectory			
High–High	83 560 (15%)	42 765 (15%)	40 795 (15.6%)
High–Low	75 489 (14%)	38 599 (14%)	36 890 (14.1%)
Low–High	87 271 (16%)	46 041 (16%)	41 230 (15.8%)
Low–Low	273 484 (50%)	142 580 (50%)	130 904 (50.2%)
Missing	24 939 (5%)	13 776 (5%)	11 163 (4.3%)
Mortality			
All-cause	7877 (1.4%)	5625 (2.0%)	2252 (0.9%)
CVD	697 (0.1%)	467 (0.2%)	230 (0.1%)
Cancer	1275 (0.2%)	685 (0.2%)	590 (0.2%)
Substance use	874 (0.2%)	711 (0.3%)	163 (0.1%)
Other causes	5031 (0.9%)	3762 (1.3%)	1269 (0.5%)
Follow-up time [years], mean (standard deviation)	23.7 (7.7)	23.8 (7.6)	23.6 (7.8)
Follow-up number of person-years [100 000]	130	68	62
Crude mortality rate [number of deaths per 100 000 person-years]	61	83	37

2.4. Inferential framework

We examined estimates of three total effects comparing the intergenerational trajectories High–Low, Low–High, and Low–Low with the High–High trajectory (reference). By doing so, we are able to disentangle among the three competing social theories and identify the role of parental and individual education in driving inequalities (Howe et al., 2016). In fact, if we observe non-negligible estimates for all three effects, this indicates that both parental and individual education drive inequalities in mortality (cf. resource multiplication theory). Conversely, if we observe non-negligible estimates associated to having a low individual education regardless of parental education, that is when having both a High–Low and a Low–Low trajectory, while we observe negligible estimates for having a Low–High trajectory, this indicates that individual education is the key driver of inequalities (cf. resource substitution theory). Finally, if we observe non-negligible estimates for having a Low–High or a High–Low trajectory, while Low–Low vs High–High is negligible, this indicates that the direction of change in achieved education or educational mobility across the parent-offspring drives inequalities (cf. social mobility theory).

The internal validity of the effect estimates relies on a set of assumptions: consistency, positivity, no residual confounding, no measurement error of exposure/outcome/confounders, and correct specification of the statistical estimation model (Westreich, 2020).

To strengthen our inference with respect to the no residual confounding assumption, we compared effects on the primary outcomes (chosen CD categories) with those on a negative outcome, that is non-avertable causes of death (Martinez et al., 2020) (see Supplementary Material). By hypothesizing that non-avertable deaths are not related to education and they share the same confounders of the exposure/primary outcomes relation, we expected the estimates of effects on non-avertable causes of death to be a measure of the potential residual confounding bias in the estimated effects on the primary outcomes. Thus, only inequalities in CD-specific mortality that were markedly larger than those in non-avertable causes of death were considered non-negligible (Sanderson et al., 2018). Conversely, inequalities in CD-specific mortality were considered negligible when they were comparable with those for the negative outcome.

2.5. Statistical and sensitivity analyses

Total effects were measured via marginal risk differences and ratios between age 20 and 45. The cumulative risk of dying of a specific CD due to a certain educational trajectory was computed as the predicted proportion of decedents from that CD based on the counterfactual scenario of every study participants having that educational trajectory and not being lost during follow-up. In practice, risks were estimated via the weighted Aalen-Johansen cumulative incidence function of cause-specific mortality with age as time-scale and four competing causes of death – the three CD categories and all remaining deaths. Risks related to all premature deaths were estimated via the complement of the weighted Kaplan-Meier survival probabilities. Weights were the product of stabilized inverse probability weights (IPWs) to account for measured confounders and potential non-random loss during follow-up (Cole & Hernán, 2008). Details about the IPWs models' specification are in Supplementary Material. Overall, weights had mean of one and maximum values not larger than six, indicating positivity held (Cole & Hernán, 2008).

Analyses were run separately for men and women, as previous studies have shown larger educational inequalities in men than in women (Galama et al., 2018).

Confidence intervals (CI) were generated via percentiles of 1000 bootstrap draws with replacement. Within each bootstrapped sample, the effect estimates were the average of 30 multiply imputed data sets for individual education (see Supplementary Material).

We assessed the sensitivity to potential violations of the assumption

of no IPWs model specification by incrementally truncating weights (Cole & Hernán, 2008), and to potential selection bias in the analytic sample by considering missingness of 100 007 individuals lost at 1990 census via IPWs (see Supplementary Material). Finally, to corroborate a putative effect of change in achieved education across the parent-offspring, we additionally estimated the contrasts High–Low vs (Low–Low and High–High) and Low–High vs (Low–Low and High–High), whereby each specific mobile trajectory is compared to all possible non-mobile trajectories. The contrasts in main analyses cannot disambiguate the putative effect of mobility itself from the effect of parental (origin) or individual (destination) education (van der Waal et al., 2017), because they compare whole educational trajectories. For example, a non-negligible estimate of High–Low vs High–High could be due to an effect of the downward mobility and/or of the low level of individual education.

3. Results

3.1. Characteristics of the analytic population

Characteristics of the analytic sample for all participants and separately for men and women are reported in Table 1. There were slightly more men (52%) than women. Most participants lived with both parents (90%) during adolescence, and had parents born in Switzerland (80%). While 50% of participants had low parental and low individual education, 14%/16% had a High–Low/Low–High educational trajectory. A high education was achieved by nearly half of participants with high educated parents, and by one out of four participants with low educated parents. Over a mean follow-up time of approximately 24 years, 7877 deaths occurred with a higher prevalence in men (N = 5625) than in women (N = 2252). While cancer-related deaths were similar in men and women (N = 685 and 590, 0.2% of participants), men had a higher number of deaths in all remaining death categories.

3.2. Intergenerational educational inequalities in all premature deaths

Mortality risks for men and women are reported in Table 2. The risk of premature mortality related to a High–High trajectory (reference risk) was higher in men than in women. Furthermore, having a High–Low or a Low–Low trajectory provided additional deaths that were larger for men than for women. Specifically, having a High–Low provided 854 (95% CI: 538 to 1172) additional deaths per 100 000 men, while having a Low–Low provided 451 (95% CI: 228 to 663) additional deaths per 100 000 men. For women, this corresponded to 320 (95% CI: 112 to 538) and 130 (95% CI: 28 to 279) additional deaths per 100 000 persons, respectively. Having a Low–High trajectory provided a small amount of fewer deaths for both men and women.

Table 2
Risk in the reference educational trajectory High–High and risk differences per 100 000 persons (95% confidence intervals) per category of death between age 20 and 45 for men and women. Risks were standardized by age, parental country of birth, household type, and birth cohort. Risk differences represent the total effect of exposure levels on death categories.

	All causes	CVD	Cancer	Substance use
MEN				
High–High	2322 (2148 to 2513)	142 (97 to 197)	313 (241 to 400)	266 (208 to 342)
High–Low vs High–High	854 (538 to 1172)	234 (100 to 391)	69 (−60 to 180)	225 (88 to 341)
Low–High vs High–High	−187 (−407 to 58)	43 (−23 to 110)	70 (−37 to 173)	−80 (−151 to −23)
Low–Low vs High–High	451 (228 to 663)	185 (115 to 251)	43 (−55 to 130)	72 (−18 to 143)
WOMEN				
High–High	1141 (1020 to 1274)	106 (65 to 149)	339 (270 to 431)	60 (33 to 94)
High–Low vs High–High	320 (112 to 538)	44 (−18 to 121)	77 (−63 to 199)	55 (0 to 113)
Low–High vs High–High	−174 (−349 to −13)	−24 (−74 to 25)	−31 (−152 to 64)	−18 (−50 to 14)
Low–Low vs High–High	130 (−28 to 279)	32 (−22 to 87)	25 (−73 to 106)	28 (−12 to 65)

3.3. Intergenerational educational inequalities in CD-related premature deaths

Mortality risks for men and women are reported in Figs. 2 and 3, respectively, Table 2 and Supplementary Table 6. For men the inequalities in the examined CD-related deaths explained a substantial proportion of the inequalities in all premature deaths. Risks of CVD mortality related to a High–High trajectory were similar across sex, however excess deaths associated to the other trajectories were larger for men than for women. Furthermore, while the reference risk of Cancer mortality was higher than that of CVD mortality, inequalities in Cancer deaths were smaller than those in CVD deaths. Finally, the reference risk of Substance use mortality was larger for men than for women, and so the inequalities.

3.3.1. Inequalities in CVD

For men, the reference risk of dying from CVD between age 20 and 45 corresponded to 142 deaths (95% CI: 97 to 197) per 100 000 persons. Having a High–Low trajectory provided 234 (95% CI: 100 to 391) additional CVD deaths per 100 000 persons, while having a Low–Low trajectory provided 185 (95% CI: 115 to 251) additional CVD deaths per 100 000 persons. That corresponded to risk ratios of 2.7 and 2.3, respectively (Supplementary Table 7). Notably, these risk differences were markedly larger than those for non-avertable deaths (Table 3). Conversely, having a Low–High trajectory provided smaller excess CVD deaths that were comparable with those for the negative outcome. Taken together, these findings indicate that for men individual education drives inequalities in CVD deaths.

For women, the reference risk of dying from CVD between age 20 and 45 corresponded to 106 deaths (95% CI: 65 to 149) per 100 000 persons. All effects on CVD deaths were of smaller size than those for men and comparable with those on the negative outcome. Taken together, this indicates that for women intergenerational educational inequalities in CVD mortality are negligible.

3.3.2. Inequalities in cancer

The reference risk of dying from Cancer between age 20 and 45 corresponded to 313 deaths (95% CI: 241 to 400) per 100 000 men and 339 deaths (95% CI: 270 to 431) per 100 000 women. All effects on Cancer were smaller than those on CVD and were comparable with those on the negative outcome. Taken together, this indicates that intergenerational educational inequalities in Cancer mortality are negligible for men and women.

3.3.3. Inequalities in Substance use

For men, the reference risk of dying from Substance use between age 20 and 45 corresponded to 266 deaths (95% CI: 208 to 342) per 100 000 persons. Having a High–Low trajectory provided 225 (95% CI: 88 to 341) additional Substance use deaths per 100 000 persons, corresponding to a risk ratio of 1.8. Notably, this risk difference was larger than that for non-avertable deaths. Having a Low–High trajectory corresponded to 80 (95% CI: 23 to 151) fewer Substance use deaths per 100 000 persons, corresponding to a risk ratio of 0.7. This risk difference was not compatible with that for non-avertable deaths as the latter suggested residual confounding in the opposite direction. Finally, having a Low–Low trajectory provided smaller excess Substance use deaths that were also comparable with that for the negative outcome. Taken together, this indicates that for men the direction of change between parental and individual education drives inequalities in Substance use deaths.

For women, the reference risk of dying from Substance use between

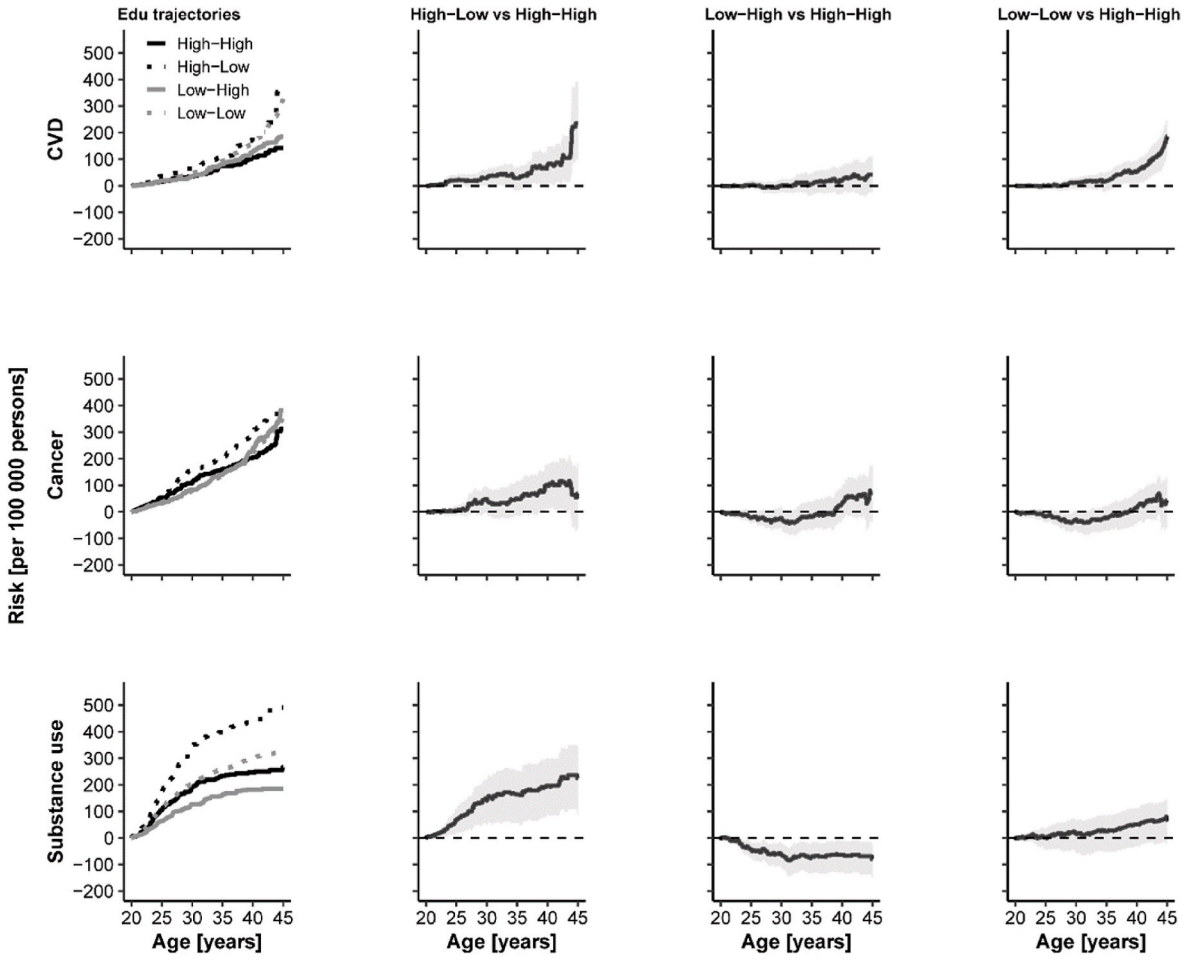

Fig. 2. Mortality risks for men. For each category of death (rows: CVD, Cancer, Substance use), the weighted cumulative incidence or risk per 100 000 persons between age 20 and 45 is reported for the four intergenerational educational trajectories (first column from left). Additionally, inequalities as risk differences are reported from the second to the fourth column (High–Low, Low–High, and Low–Low with respect to High–High). 95% confidence intervals are rendered with a grey ribbon while the risk difference point estimate is represented by a black line. Risks were standardized by age, parental country of birth, household type, and birth cohort. Risk differences represent the total effect of exposure levels on death categories.

age 20 and 45 corresponded to 60 deaths (95% CI: 33 to 94) per 100 000 persons. All effects were smaller than those for men and comparable with the effects on the negative outcome. Taken together, this indicates that for women intergenerational educational inequalities in Substance use mortality are negligible.

3.4. Sensitivity analyses

Inequalities were similar to those reported in main analyses when truncating weights (Supplementary Figs. 2–5), indicating negligible bias from the potential miss-specification of the IPWs models. Inequalities were also similar when considering participants lost at baseline via IPWs (Supplementary Figs. 6–7), indicating negligible selection bias in the analytic population. Compared to non-mobile trajectories having a High–Low trajectory corresponded to 159 (95% CI: 66 to 270) additional Substance use deaths per 100 000 men, and having a Low–High trajectory provided 122 (95% CI: 75 to 186) fewer Substance use deaths per 100 000 men. This corroborated the finding described in main analyses that the direction of change between parental and individual education contributed to drive inequalities in Substance use deaths for men.

4. Discussion

4.1. Main findings

We quantified inequalities in specific categories of CD-related premature mortality due to intergenerational educational trajectories among contemporary Swiss young adults between age 20 and 45. For women, inequalities were negligible. For men, inequalities in Cancer mortality were negligible, while substantive in CVD and Substance use deaths. Specifically, there were excess CVD deaths when having a low individual education regardless of parental education, indicating those inequalities were driven by individual education or the resource substitution model held. Inequalities in Substance use mortality were observed only when education changed across parent-offspring, indicating the social mobility model held.

4.2. Comparison with other studies

This is one of few studies to examine inequalities in sex- and cause-specific premature mortality by intergenerational educational trajectories among young adults. Compared to two previous studies ran in Finnish and Belgian participants (De Grande et al., 2015; Elo et al., 2014), we were able to examine inequalities in CVD and Substance use deaths. In fact, the Finnish study examined two categories of deaths: one encompassing alcohol-related, accidental and violent causes of death,

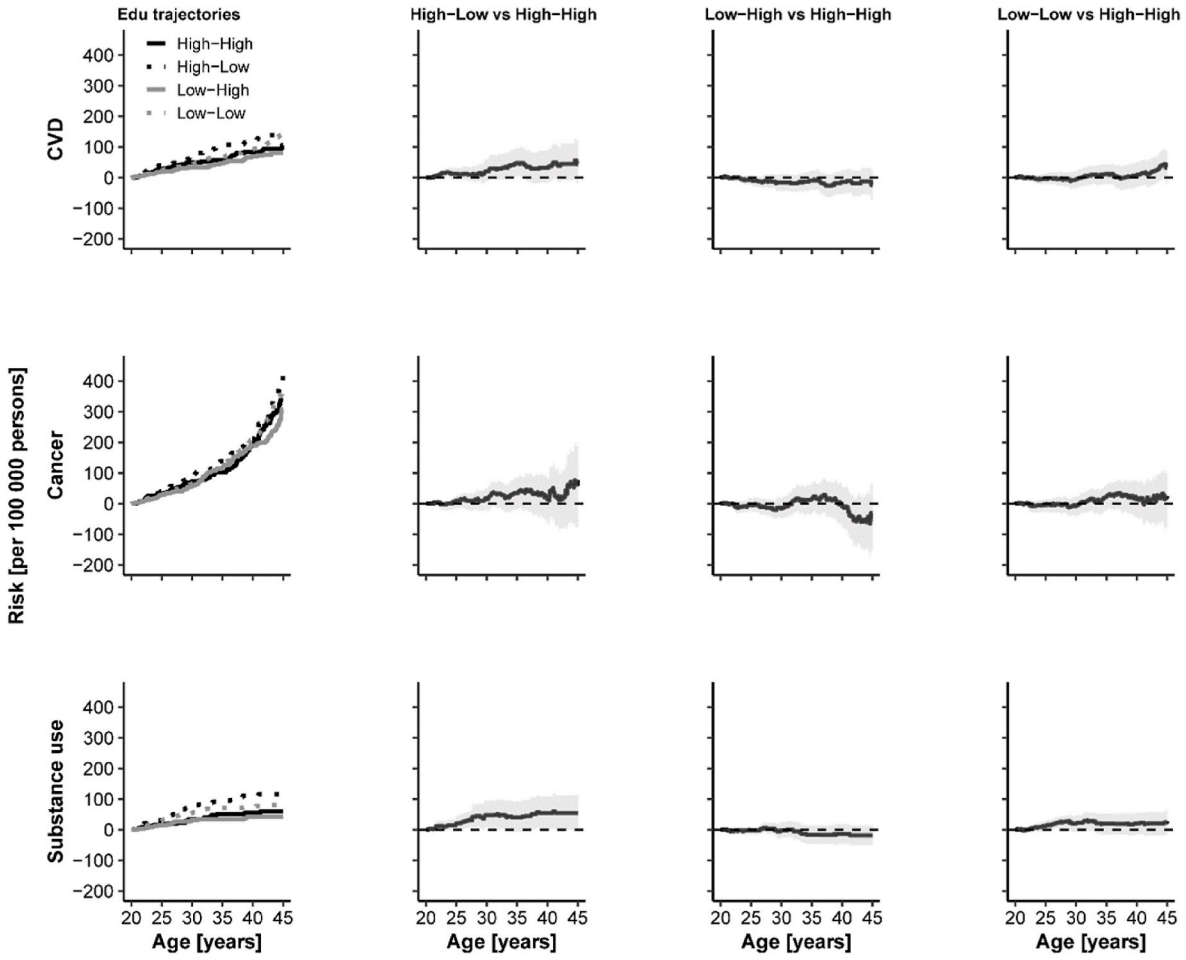

Fig. 3. Mortality risks for women. For each category of death (rows: CVD, Cancer, Substance use), the weighted cumulative incidence or risk per 100 000 persons between age 20 and 45 is reported for the four intergenerational educational trajectories (first column from left). Additionally, inequalities as risk differences are reported from the second to the fourth column (High–Low, Low–High, and Low–Low with respect to High–High). 95% confidence intervals are rendered with a grey ribbon while the risk difference point estimate is represented by a black line. Risks were standardized by age, parental country of birth, household type, and birth cohort. Risk differences represent the total effect of exposure levels on death categories.

Table 3
Negative outcome control. Risk difference per 100 000 persons (95% confidence intervals) between age 25 and 45 is reported per category of death (rows) and effect (columns). The cumulative risk was calculated for participants surviving until age 25, because among them deaths occurred only after 1994 and as such were recorded via ICD–10 codes. In fact, the categorization into non-avertable deaths provided by Martinez et al.(Martinez et al., 2020) is based on ICD–10 codes. Risks were standardized by age, parental country of birth, household type, and birth cohort. Risk differences represent the total effect of exposure levels on death categories.

	High–Low vs High–High	Low–High vs High–High	Low–Low vs High–High
MEN			
CVD	213 (86 to 354)	39 (−24 to 99)	186 (122 to 245)
Non-avertable	89 (−15 to 210)	68 (−16 to 147)	66 (2 to 131)
Cancer	61 (−53 to 171)	93 (−24 to 202)	59 (−33 to 148)
Non-avertable	89 (−15 to 210)	68 (−16 to 147)	66 (2 to 131)
Substance use	153 (62 to 248)	−32 (−90 to 21)	72 (7 to 133)
Non-avertable	89 (−15 to 210)	68 (−16 to 147)	66 (2 to 131)
WOMEN			
CVD	33 (−25 to 94)	−15 (−62 to 30)	36 (−11 to 78)
Non-avertable	74 (−19 to 175)	−41 (−110 to 26)	33 (−38 to 99)
Cancer	61 (−60 to 185)	−31 (−135 to 80)	26 (−68 to 108)
Non-avertable	74 (−19 to 175)	−41 (−110 to 26)	33 (−38 to 99)
Substance use	35 (−8 to 84)	−12 (−46 to 14)	16 (−17 to 47)
Non-avertable	74 (−19 to 175)	−41 (−110 to 26)	33 (−38 to 99)

and one including all other causes; while the Belgian study examined suicide, road accidents, other violent deaths, cancers, and other diseases. The latter described substantive inequalities in Cancer deaths for both men and women. Compared to our findings of negligible inequalities in Cancer mortality, this may point to country-related differences in cancer screening, access to medical care or lifestyle behaviours that should deserve further examination. Additionally, the Belgian study reported substantive inequalities in deaths related to other diseases encompassing CVD, alcohol and drug use, which might be consistent with the inequalities in CVD and Substance use deaths observed in our study. However, the Belgian study supported the resource substitution model for those inequalities, while our findings supported the social mobility model for inequalities in Substance use deaths and the theory of resource substitution only for inequalities in CVDs. This difference with the Belgian study could be explained by the fact that we were able to examine specifically those two categories of death, and to triangulate findings with a negative control outcome.

Previous empirical evidence has suggested a differential impact of social characteristics by sex and cause of death. Our observed sex differences in the educational gradient in premature mortality are in line with previous reports (Galama et al., 2018; Mackenbach et al., 2016). Among the possible explanations for these sex differences are that men with low education are more likely to engage in unhealthy lifestyle behaviors than women with low education (Ross et al., 2012), or that men with low education are more likely to be unemployed than their

female counterparts (van Hedel et al., 2018). In terms of differential impact by cause of death, our finding for CVD, Cancer and Substance use deaths in men differs with that from a study in Finns born before 1950 (Elo et al., 2014). Therein both parental and individual education were reported to contribute to inequalities in CVD mortality. Conversely, our results indicated that individual education only drives excess in CVD deaths. This is in agreement with the resource substitution model, whereby parental education is only indirectly associated with premature CVD mortality via individual education. By providing resources necessary for the educational success of their offspring, highly educated parents therefore may influence the premature mortality risk of their children (Mirowsky & Ross, 2003). Indeed, in our study population the likelihood of achieving a high education was twofold in individual having high educated parents compared to those having low educated parents. The Finnish study reported non-negligible educational inequalities in lung cancer mortality, while in our study the inequalities in all cancers were negligible. This could be explained by the fact that educational inequalities in Cancer may be type-dependent, or they may appear later in life, for example after age 50. In support of the latter, the Finnish study examined participants aged 35–72 years, and a study across European populations during the 2000s reported that inequalities in breast cancer mortality were negligible for women younger than 50 years of age (Gadeyne et al., 2017). Finally, the Finnish study described negligible associations for both parental and individual education with alcohol-related deaths, while we observed substantive inequalities driven by the direction of change in intergenerational education. Context encompassing country (Finland vs Switzerland) and birth cohort (<1950 vs 1970s), the implemented inferential framework and statistical methods for assessing inequalities may explain this difference. Potential mechanisms underlying the empirical evidence for the social mobility model in our study encompass the loss/gain of social networks (Lundberg, 1991), and the stress/psychological benefit arising from acquiring a social environment different from the parental one (Gugushvili et al., 2019). Additionally, health selection could explain the excess/fewer substance use deaths when having a downward/upward educational mobility (Mackenbach, 2012; Simons et al., 2013).

4.3. Limitations and strengths

Our findings might be subject to selection bias due to individuals lost at baseline. However, a sensitivity analysis suggested that this bias is negligible. There could also be selection bias because we conditioned on survival until age 20. For instance, a simulation study reported that selective survival could lead to underestimation of the effect of education on cognitive function in old age (Mayeda et al., 2018). Thus, our findings may not generalize to the target population.

Another potential limitation is information bias due to probabilistic linkage, misclassification of cause-specific mortality and self-report of attained education. The bias due to misclassification related to probabilistic linkage is likely small and may have led to an underestimation of the risk differences (Schmidlin et al., 2013). We mitigated the potential misclassification of mortality causes due to garbage codes by reassigning them using a data-driven predictive method with a misclassification rate of approximately 10%. Finally, we note that misclassification of parental education was not affected by recall bias since educational attainment was reported by the parents themselves and not by their offspring later in life as in most retrospective studies of mortality at older ages.

Our observational study might be subject to potential residual confounding, and to detect it we implemented a negative control. However, we did not attempt to calibrate the estimated effects on the primary outcomes as residual measurement errors in the exposure, primary and negative outcomes do not allow to precisely adjust for unobserved confounding (Sanderson et al., 2018).

Finally, we may have potential violations of the consistency assumption underlying the estimation of effects. We operationalized education through degree completed without differentiating between duration and quality of education, attributes that could be both associated with cause-specific mortality and potential targets of intervention (Rehkopf et al., 2016).

Major strengths of our study include the large size of the analytic population and the ability to triangulate findings with a negative control outcome. The large sample size allowed to study sex- and category-specific CD-related premature mortality in young adulthood, despite low event rates in that age range. Additionally, we adopted a causal framework with transparent identifying assumptions to estimate marginal effects via risk difference/ratio. This is in contrast with previous studies, where conditional hazard ratios were estimated. The latter are known to provide potentially biased effect estimates due to both non-collapsibility and implicit selection bias of the hazard ratio (Daniel et al., 2021; Young et al., 2020).

4.4. Conclusions

We have provided empirical evidence that intergenerational educational inequalities in premature mortality are present and differ by sex and cause of death among contemporary Swiss young adults. Our findings support that a person's low education is a key contributor to these inequalities. Thus, they support the importance of achieving a high education and of interventions on both human agency and institutional structure facilitating it, including those providing non-standard pathways to high education in hierarchically differentiated schooling systems as the Swiss one. Additionally, our results for inequalities in premature deaths indicate that they are driven by different educational exposures encompassing the familial and schooling environments, and point to cause-specific high-risk groups of premature mortality. Their identification for Substance use deaths may inform prioritization of intergenerational prevention strategies focusing on high-risk individuals identified by their intergenerational educational trajectory. Overall, designing prevention strategies based on our study findings could reduce educational inequalities in premature mortality and ultimately the burden of chronic disease-related deaths across the life course and across generations.

Ethics approval

Not needed since data were deidentified from public registries.

Author contributions

Daniela Anker: Software, Validation, Formal analysis, Data Curation, Writing – Original Draft, Visualization. **Stéphane Cullati**: Writing – Review & Editing. **Naja Hulvej Rod**: Writing – Review & Editing. **Arnaud Chiolero**: Resources, Writing – Review & Editing. **Cristian Carmeli**: Conceptualization, Methodology, Software, Validation, Formal analysis, Data Curation, Writing – Original Draft, Visualization, Supervision, Project administration.

Data statement

Individual data from different data sets were used for the construction of the SNC. All these data are the property of the Swiss Federal Statistical Office (SFSO) and can only be made available by legal agreements with the SFSO. This also applies to derivatives such as the analysis files used for this study. However, after approval of the SNC Scientific Board, a specific SNC module contract with the SFSO would allow researchers to receive analysis files for replication of the analysis. Data requests should be sent to Prof. Milo Puhan (chairman of the SNC Scientific Board, miloalan.puhan@uzh.ch).

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None.

Declaration of competing interest

We declare no conflict of interest.

Data availability

See Data statement reported in the cover page

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ssmph.2022.101282.

References

Abel, T. (2008). Cultural capital and social inequality in health. *Journal of Epidemiology & Community Health, 62*, e13.

Baird, J., Jacob, C., Barker, M., Fall, C. H., Hanson, M., Harvey, N. C., et al. (2017). *Developmental origins of health and disease: A lifecourse approach to the prevention of non-communicable diseases* (Vol. 5). Basel): Healthcare.

Bopp, M., Spoerri, A., Zwahlen, M., Gutzwiller, F., Paccaud, F., Braun-Fahrländer, C., et al. (2009). Cohort profile: The Swiss national cohort–a longitudinal study of 6.8 million people. *International Journal of Epidemiology, 38*, 379–384.

Bukodi, E., & Goldthorpe, J. H. (2012). Decomposing 'social origins': The effects of parents' class, status, and education on the educational attainment of their children. *European Sociological Review, 29*, 1024–1039.

Burger, K. (2021). Human agency in educational trajectories: Evidence from a stratified system. *European Sociological Review, 37*, 952–971.

Cole, S. R., & Hernán, M. A. (2008). Constructing inverse probability weights for marginal structural models. *American Journal of Epidemiology, 168*, 656–664.

Daniel, R., Zhang, J., & Farewell, D. (2021). Making apples from oranges: Comparing noncollapsible effect estimators and their standard errors after adjustment for different covariate sets. *Biometrical Journal, 63*, 528–557.

De Grande, H., Vandenheede, H., & Deboosere, P. (2015). Educational inequalities in the transition to adulthood in Belgium: The impact of intergenerational mobility on young-adult mortality in 2001-2009. *PLoS One, 10*, Article e0142104.

Elo, I. T., Martikainen, P., & Myrskylä, M. (2014). Socioeconomic status across the life course and all-cause and cause-specific mortality in Finland. *Social Science & Medicine, 119*, 198–206.

Erikson, R., & Goldthorpe, J. H. (1992). *The constant flux: A study of class mobility in industrial societies*. Clarendon Press.

Gadeyne, S., Menvielle, G., Kulhanova, I., Bopp, M., Deboosere, P., Eikemo, T. A., et al. (2017). The turn of the gradient? Educational differences in breast cancer mortality in 18 European populations during the 2000s. *International Journal of Cancer, 141*, 33–44.

Galama, T., Lleras-Muney, A., & Kippersluis, H.v. (2018). *The effect of education on health and mortality: A review of experimental and quasi-experimental evidence*. Oxford University Press.

Gugushvili, A., Zhao, Y., & Bukodi, E. (2019). Falling from grace' and 'rising from rags': Intergenerational educational mobility and depressive symptoms. *Social Science & Medicine, 222*, 294–304.

Hamad, R., Elser, H., Tran, D. C., Rehkopf, D. H., & Goodman, S. N. (2018). How and why studies disagree about the effects of education on health: A systematic review and meta-analysis of studies of compulsory schooling laws. *Social Science & Medicine, 212*, 168–178.

van Hedel, K., van Lenthe, F. J., Oude Groeniger, J., & Mackenbach, J. P. (2018). What's the difference? A gender perspective on understanding educational inequalities in all-cause and cause-specific mortality. *BMC Public Health, 18*, 1105.

Howe, L. D., Smith, A. D., Macdonald-Wallis, C., Anderson, E. L., Galobardes, B., Lawlor, D. A., et al. (2016). Relationship between mediation analysis and the structured life course approach. *International Journal of Epidemiology, 45*, 1280–1294.

Hummer, R. A., & Hernandez, E. M. (2013). The effect of educational attainment on adult mortality in the United States. *Population Bulletin, 68*, 1–16.

Korda, R. J., Biddle, N., Lynch, J., Eynstone-Hinkins, J., Soga, K., Banks, E., et al. (2020). Education inequalities in adult all-cause mortality: First national data for Australia using linked census and mortality data. *International Journal of Epidemiology, 49*, 511–518.

Lundberg, O. (1991). Causal explanations for class inequality in health–an empirical analysis. *Social Science & Medicine, 32*, 385–393.

Mackenbach, J. P. (2012). The persistence of health inequalities in modern welfare states: The explanation of a paradox. *Social Science & Medicine, 75*, 761–769.

Mackenbach, J. P., Kulhánová, I., Artnik, B., Bopp, M., Borrell, C., Clemens, T., et al. (2016). Changes in mortality inequalities over two decades: Register based study of European countries. *BMJ, 353*, i1732.

Martikainen, P., Elo, I., Tarkiainen, L., Mikkonen, J., Myrskylä, M., & Moustgaard, H. (2020). The changing contribution of childhood social characteristics to mortality: A comparison of Finnish cohorts born in 1936-50 and 1961-75. *International Journal of Epidemiology, 49*, 896–907.

Martinez, R., Lloyd-Sherlock, P., Soliz, P., Ebrahim, S., Vega, E., Ordunez, P., et al. (2020). Trends in premature avertable mortality from non-communicable diseases for 195 countries and territories, 1990-2017: A population-based study. *Lancet Global Health, 8*, e511–e523.

Mayeda, E. R., Filshtein, T. J., Tripodis, Y., Glymour, M. M., & Gross, A. L. (2018). Does selective survival before study enrolment attenuate estimated effects of education on rate of cognitive decline in older adults? A simulation approach for quantifying survival bias in life course epidemiology. *International Journal of Epidemiology, 47*, 1507–1517.

Mirowsky, J., & Ross, C. (2003). *Education, social status, and health*. New York: Aldine de Gruyter.

Phelan, J. C., Link, B. G., & Tehranifar, P. (2010). Social conditions as fundamental causes of health inequalities: Theory, evidence, and policy implications. *Journal of Health and Social Behavior, 51*(Suppl), S28–S40.

Rehkopf, D. H., Glymour, M. M., & Osypuk, T. L. (2016). The consistency assumption for causal inference in social epidemiology: When a rose is not a rose. *Current Epidemiology Reports, 3*, 63–71.

Ross, C. E., Masters, R. K., & Hummer, R. A. (2012). Education and the gender gaps in health and mortality. *Demography, 49*, 1157–1183.

Ross, C. E., & Mirowsky, J. (2011). The interaction of personal and parental education on health. *Social Science & Medicine, 72*, 591–599.

Sanderson, E., Macdonald-Wallis, C., & Davey Smith, G. (2018). Negative control exposure studies in the presence of measurement error: Implications for attempted effect estimate calibration. *International Journal of Epidemiology, 47*, 587–596.

Schmidlin, K., Clough-Gorr, K. M., Spoerri, A., Egger, M., Zwahlen, M., & Cohort, S. N. (2013). Impact of unlinked deaths and coding changes on mortality trends in the Swiss National Cohort. *BMC Medical Informatics and Decision Making, 13*, 1.

Simons, A. M., Groffen, D. A., & Bosma, H. (2013). Socio-economic inequalities in all-cause mortality in europe: An exploration of the role of heightened social mobility. *The European Journal of Public Health, 23*, 1010–1012.

Singh-Manoux, A., & Marmot, M. (2005). Role of socialization in explaining social inequalities in health. *Social Science & Medicine, 60*, 2129–2133.

Stringhini, S., Carmeli, C., Jokela, M., Avendaño, M., Muennig, P., Guida, F., et al. (2017). Socioeconomic status and the 25 × 25 risk factors as determinants of premature mortality: A multicohort study and meta-analysis of 1·7 million men and women. *Lancet, 389*, 1229–1237.

van der Waal, J., Daenekindt, S., & de Koster, W. (2017). Statistical challenges in modelling the health consequences of social mobility: The need for diagonal reference models. *International Journal of Public Health, 62*, 1029–1037.

Westreich, D. (2020). *Epidemiology by design: A causal approach to the health sciences*. New York: Oxford University Press.

Willson, A. E., Shuey, K. M., & Elder, G. H., Jr. (2007). Cumulative advantage processes as mechanisms of inequality in life course health. *American Journal of Sociology, 112*, 1886–1924.

Young, J. G., Stensrud, M. J., Tchetgen Tchetgen, E. J., & Hernán, M. A. (2020). A causal framework for classical statistical estimands in failure-time settings with competing events. *Statistics in Medicine, 39*, 1199–1236.