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## Comparison of smoking reduction with improvement of social conditions in early life

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1 **Title page**

2 **Comparison of smoking reduction with improvement of social**  
3 **conditions in early life: simulation in a British cohort**

4

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24 **Word count** : 3623 words (abstract = 253, main text = 3370)

25

## 1 **Key Messages**

- 2       • Health care evaluation models and simulations can help to assess and  
3       prioritize preventive policies in different age groups, and assess their potential  
4       impacts on social inequalities
- 5       • Using data from the 1958 National Child Development Study British birth  
6       cohort and a potential outcome approach, simulations showed that a  
7       counterfactual scenario with reduced adverse childhood experience (ACE) and  
8       higher education was associated with a decrease in premature mortality
- 9       • Mortality in a counterfactual scenario with reduced ACE and higher education  
10      was close to the mortality in a counterfactual scenario with reduced smoking in  
11      adulthood
- 12      • Counterfactual scenarios with reduced ACE, higher education or reduced  
13      smoking were associated with larger decreases in mortality among individuals  
14      whose parents had a low educational level, suggesting that strengthening  
15      interventions in early deprived environments could reduce social inequalities

16

17

18

## 1 **Abstract**

2 **Background.** Health care evaluation models can be useful to assign different levels  
3 of priority to interventions or policies targeting different age groups or different  
4 determinants of health. We aimed to assess early mortality in counterfactual  
5 scenarios implying reduced adverse childhood experience (ACE) and/or improved  
6 educational attainment (childhood and early life characteristics), compared to a  
7 counterfactual scenario implying reduced smoking in adulthood.

8 **Methods.** We used data from the 1958 National Child Development Study British  
9 birth cohort, which initially included 18 558 subjects. Applying a potential outcome  
10 approach, scenarios were simulated to estimate the expected mortality between age  
11 16 and 55 under a counterfactual decrease by half of the observed level of exposure  
12 to (i) ACE, (ii) low educational attainment (at age 22), (iii) ACE and low educational  
13 attainment (a combined exposure), (iv) smoking at age 33. Estimations were  
14 obtained using g-computation, separately for men and women. Analyses were further  
15 stratified according to the parental level of education to assess social inequalities.

16 **Results.** The study population included 12 164 members. The estimated decrease in  
17 mortality in the counterfactual scenarios with reduced ACE and improved educational  
18 attainment was close to the decreased mortality in the counterfactual scenario with  
19 reduced smoking, showing a relative difference in mortality of respectively -7.2%  
20 (95%CI = [-12.2% to 1.2%]) versus -7.0% [-13.1% to +1.2%] for women, and -9.9%  
21 [-15.6% to -6.2%] versus -12.3% [-17.0% to -5.9%] for men.

22 **Conclusion.** Our results highlight the potential value of targeting early social  
23 characteristics such as ACE and education, compared to well-recognized  
24 interventions on smoking.

1

2 **Keywords:**

3 Decision Support Techniques; Health Policy; Social Determinants of Health;

4 Education; Adverse Childhood Experiences; Smoking;

## 1 **Introduction**

2 A growing body of literature is advocating for policies and public health interventions  
3 to reduce health inequalities and the related incidence of chronic diseases.[1-3] Tools  
4 such as health-care evaluation models can be useful to inform and support policy  
5 makers to prioritize decisions. These models are “analytic methodologies that  
6 account for events over time and across populations, based on data drawn from  
7 primary and/or secondary sources, and whose purpose is to estimate the effects of  
8 an intervention on valued health consequences and costs”.[4] Using these tools,  
9 several competing health policies could be modelled and compared.

10 A large body of evidence emphasizes the importance of the early years of life in  
11 constructing health in adulthood. The socio-economic environment during pregnancy  
12 as well as the socio-economic position (SEP) of the parents have been shown to  
13 predict various health outcomes.[5-8] Educational attainment in young adulthood is a  
14 predictor of both future SEP and future health behaviors, such as smoking.[9,10]

15 Assessing the priority of early life interventions compared to interventions in  
16 adulthood using experimental designs would require extremely difficult and costly  
17 long-term studies. Therefore, quantification of long term results using models and  
18 simulations might be a valuable approach to assign different levels of priority to  
19 interventions and policies targeting different age groups or different determinants of  
20 health. Microsimulation models have been developed and used by suppliers of health  
21 insurances, health care services and governments to guide their choices.[11]  
22 Weinstein et al. pointed out that the quality of these models depends on (i) a relevant  
23 causal structure, consistent with theory, (ii) relevant data and (iii) models  
24 validation.[4]

1 Various methods have been applied. For example, Lhachimi et al. identified several  
2 quantitative methods in health impact assessment enabling to model changes in risk  
3 factors and their effects on health, in different real-life populations.[12] Briggs et al.  
4 presented a taxonomy of modeling methods to assess public health interventions,  
5 outlining decision trees, comparative risk assessment, Markov models, system  
6 dynamic models, discrete event simulations, and agent-based models, as well as the  
7 use of multistate lifetables and microsimulations.[13] In order to estimate the potential  
8 impact of social policies, several simulation approaches have been developed for  
9 various health questions: impact of cancer screening, transmission of infectious  
10 diseases, and effect of diagnosis and treatment of chronic diseases.[14]

11 Based on the literature, we assume that policies during childhood could produce a  
12 large impact, directly on health and indirectly through health behaviors by multiple  
13 causal chains along the lifecourse. Using a potential outcome approach and  
14 individual data from a cohort, we aimed to provide information quantifying the  
15 potential impact of policies in childhood and early life, compared to policies applied  
16 later in adulthood, and thus help prioritize prevention policies among different age  
17 groups. More precisely, we compared a counterfactual scenario combining reduced  
18 adverse childhood experiences (ACE) and improved education to a counterfactual  
19 scenario with reduced smoking in adulthood (a classic health behavior targeted in  
20 public health policies).

21 One additional objective was to assess social inequalities in health and particularly to  
22 quantify the results when targeting populations of lower socio-economic position. This  
23 approach would allow exploring the effectiveness of proportionate universalism.[15]

24

## 25 **Methods**

1 We used data from the 1958 National Child Development Study (NCDS) which  
2 included all births during one week in 1958 (n=18 558) in Great Britain.[16-19]  
3 Subsequent data collections were carried out on cohort members aged 7, 11, 16, 23,  
4 33, 42, 46, 50 and 55. The NCDS has been described in detail elsewhere.[20]  
5 Information was collected on economic, medical, developmental and social aspects  
6 of their lives.

7 ACE was measured from data collected between 7 and 16 years old. We therefore  
8 included members who were alive at 16 years old. We excluded members with one  
9 or more missing sweep between birth and 16 years old to avoid creating the ACE  
10 measure from extensive missing information.

11 We aimed to simulate counterfactual scenarios with the following features:

12 1) The model relies on an explicit causal framework (working causal model) which  
13 could be applied to other cohorts. The conceptual model was simple, using adverse  
14 childhood experience, educational level in early adulthood, and smoking at 33 years  
15 of age as exposures of interest (Figure 1).

16 2) The approach includes socio-economic and behavior variables of interest as well  
17 as other relevant variables (confounding factors: social position, different health  
18 behaviors, context variables, health status and measurements, etc.) in the causal  
19 structural framework.

20 3) Counterfactual scenarios are defined by a change in the distribution of the  
21 exposure of interest. This approach is referred to as “stochastic interventions” in the  
22 literature.[21]

23 4) Results are also estimated after stratification on early socio-economic position  
24 (parental educational level), in order to assess social inequalities.

25 (Figure 1 here)



1

2 **Variables**

3 The outcome (Y) was mortality before 55 years of age. All deaths up to 31st  
4 December 2013 (before 55 years old) have been collected and systematically  
5 ascertained through a variety of sources, including death certificates supplied by the  
6 National Health Service Central Register.[20,22]

7 Exposures of interest: Counterfactual scenarios were simulated for various  
8 exposures of interest at 2 different life periods.

9 1) In early life, which should affect mortality mostly indirectly through a set of social,  
10 psychosocial and behavioral (including smoking) pathways:

11 - "Adverse childhood experience" (ACE), defined as: "intra-familial events or  
12 conditions causing chronic stress responses in the child's immediate  
13 environment, including notions of maltreatment and deviation from societal  
14 norms, where possible to be distinguished from conditions in the  
15 socioeconomic and material environment".[23] The concept of ACEs arose in  
16 the late 1990s with the "ACEs' study", which showed a dose-response  
17 relationship between adverse events and conditions in childhood and causes  
18 of death.[24] Kelly-Irving et al. recently reviewed the emergence of the ACEs  
19 framework in the field of social epidemiology, epidemiological evidences and  
20 limitations of the concept.[25]

21 - Member's educational level at age 22 (a proxy of adolescents and young  
22 adults socio-economic position).

23 2) In adulthood, exposure to smoking at age 33, which should affect mortality more  
24 directly, through cancers and cardiovascular diseases.

1 Counterfactual scenarios were firstly simulated separately for each exposure of  
 2 interest, a change in the joint distribution was then considered for the combined  
 3 exposure to ACE and educational level.

4 Confounders (denoted  $L$ ): other variables depicted in Figure 1 were considered as  
 5 potential confounders.

6 Exposures and confounders are fully described in Table 1. The set of confounders ( $L$ )  
 7 taken into account in each analysis depends on the exposure under study: every  
 8 variable preceding the exposure under study in the causal model is included in the  
 9 set  $L$ .

10 (Table 1 here)

11

## 12 **Statistical methods**

### 13 ***Estimated parameters in the counterfactual scenarios under study***

14 The expected mortality before 55 years old has been estimated in the following  
 15 counterfactual scenarios, in which we halved the exposure: (i) to ACE, (ii) to a low  
 16 educational attainment, (iii) to ACE and to a low educational attainment (a combined  
 17 exposure focusing on children and adolescents), and (iv) to smoking at 33 years old.  
 18 Counterfactual changes in the exposure distributions were applied among members  
 19 alive at the time of the exposure of interest at each step.

20 For an exposure of interest (denoted  $A$ ), the target causal parameters were defined  
 21 as differences ( $\Psi_{dif}$ ) and relative differences ( $\Psi_{rel}$ ) between the mortality under the  
 22 observed level of exposure to  $A$  and the mortality had the level of exposure to  $A$  been  
 23 halved:

24  $\Psi_{dif} = \mathbb{E}(Y_{P_\delta}) - \mathbb{E}(Y_{A=obs})$  and  $\Psi_{rel} = \frac{\mathbb{E}(Y_{P_\delta}) - \mathbb{E}(Y_{A=obs})}{\mathbb{E}(Y_{A=obs})}$ , where  $\mathbb{E}(Y_{A=obs})$  denotes the

25 expected potential outcome (mortality before 55 years old) under the observed level

1 of exposure and  $\mathbb{E}(Y_{P_\delta})$  is the expected potential outcome, had the level of exposure  
 2 been divided by  $\delta = 2$  in the study population.

3 Under the randomization assumption (no residual confounding given  $L$ ) and the  
 4 consistency assumption ( $A = a$  implies that the potential outcome  $Y_a$  is equal to the  
 5 observed value  $Y$ ),  $\mathbb{E}(Y_{A=obs})$  was estimated from the observed mean  $\mathbb{E}(Y)$ , and  $\mathbb{E}$   
 6 ( $Y_{P_\delta}$ ) was estimated using g-computation.[21] Logistic regressions were used to  
 7 estimate conditional expectations of the outcome, denoted  $\bar{Q}(A,L) = P(Y = 1|A,L)$ ,  
 8 and treatment mechanism  $g(L) = P(A = 1|L)$ . From the estimated  $\hat{Q}(A,L)$  functions,  
 9 we predicted mean probabilities of death for each member  $i$  under the counterfactual  
 10 exposure  $A = 1$  or  $A = 0$  (denoted  $\hat{Q}(1,L)_i$  and  $\hat{Q}(0,L)_i$ ). The counterfactual scenario  
 11 was defined as dividing by  $\delta = 2$  the treatment mechanism  $P_\delta(L) = \frac{g(L)}{\delta}$ . In  
 12 counterfactual scenarios the mean mortality  $\mathbb{E}(Y_{P_\delta})$  can be written using the g-  
 13 formula:[21]

$$14 \quad \mathbb{E}(Y_{P_\delta}) = \sum_{l \in L} [\bar{Q}(1,L=l) \times P_\delta(L=l) + \bar{Q}(0,L=l) \times [1 - P_\delta(L=l)]] \times P(L=l),$$

15 which was estimated by direct standardization

$$16 \quad \hat{\mathbb{E}}(Y_{P_\delta}) = \frac{1}{n} \sum_{i=1}^n [\hat{Q}(1,L=l) \times \hat{P}_\delta(L=l) + \hat{Q}(0,L=l) \times [1 - \hat{P}_\delta(L=l)]].$$

17 In counterfactual scenarios changing the joint exposure to ACE and educational  
 18 level, a reduced exposure to ACE has a first indirect effect on the level of exposure to  
 19 a low educational level, which is then reinforced in the joint exposure, when reducing  
 20 the level of exposure to low educational level. Computational details are given in the  
 21 supplementary online document. Statistical analyses were computed using Stata SE  
 22 v14 and R v3.4 with the Stremr package to estimate the expected potential  
 23 outcomes.[26]

1 Estimations were computed separately for men and women. In order to study social  
2 inequalities defined by the early childhood socioeconomic environment, analyses  
3 were also performed with and without stratification on parental level of education.  
4 Multiple imputation using chained equations has been applied for missing data and  
5 the 95% CI were estimated by bootstrapping.[27,28]

6

## 7 **Results**

8 In the 1958 NCDS cohort, 17,685 members were alive at 16 years old. We excluded  
9 5521 members who had at least one missing sweep between birth and 16 years old.  
10 The study population included 12,164 members.

11 Variables at baseline, 23 years old, 33 years old and deaths during follow-up are  
12 described in Table 2. After multiple imputation, parents had a limited education for  
13 65.4% of men and 64.1% of women; high ACE was observed among 12.0% of men  
14 and 9.5% of women; 31.4% of men and 34.8% of women did not pass O levels; and  
15 33.2% of men and 32.5% of women were smokers at 33 years old. We studied  
16 counterfactual interventions that would halve these prevalences. In the selected  
17 population, 271 men (4.4%) and 168 (2.9%) women died before 55 years old.

18 (Table 2 here)

19 Results in the counterfactual scenarios under study are shown in Table 3 for the  
20 whole population of men and women. The estimated relative difference in mortality  
21 characterizing a counterfactual improvement of member's educational level was  
22 -7.20% [-13.24%; -3.03%] among men and -4.43% [-8.97%; +2.40%] among women.  
23 In women, the estimated effect of a combined counterfactual exposure decreasing  
24 ACE and improving educational level was about the same as in the counterfactual

1 scenario reducing smoking in adulthood: the relative difference was -7.19% (95% CI  
2 = [-12.24%; +1.18%]) versus -7.01% [-13.08%; +1.17%]. In men, the estimated  
3 effect of the combined counterfactual exposure in childhood was slightly smaller than  
4 the estimated effect of a counterfactual decrease on smoking, with relative  
5 differences of -9.95% [-15.60%; -6.24%] versus -12.29% [-16.95%; -5.91%].

6 (Table 3 here)

7 Results stratified by the educational level of the parents are shown in Table 4. In  
8 counterfactual scenarios with reduced smoking exposure, the estimated effect was  
9 larger among men whose parents had low educational level. An opposite trend was  
10 estimated for women. In counterfactual scenarios combining a reduced ACE and  
11 improved educational attainment, the estimated relative effects were larger among  
12 men and women whose parents had low educational level: -12.14% [-18.62%;  
13 -6.26%] versus -4.84% [-10.49%; -0.82%] in men and -8.90% [-15.93%; -0.07%]  
14 versus -3.28% [-10.82%; +4.70%] in women (tables 3). In Figure S1 (supplementary  
15 document), the estimated absolute decrease in mortality in the counterfactual  
16 scenarios combining change on ACE and education, or on smoking, was slightly  
17 larger among people whose parents had low educational level (except for the  
18 intervention on smoking among women).

19 (Table 4 here)

20

## 21 **Discussion**

### 22 ***Main findings***

1 Our results suggest that promoting policies and interventions in early life that would  
2 decrease ACE and improve education could reduce premature mortality, with an  
3 effect close to the effect achieved by interventions that would reduce smoking in  
4 adulthood. In the stratified analyses, counterfactual scenarios with reduced ACE,  
5 higher educational level or reduced smoking were associated with stronger effects  
6 among individuals whose parents had a low educational level (except for smoking  
7 among women), suggesting that strengthening policies in early deprived  
8 environments could reduce social inequalities, in accordance with proportionate  
9 universalism.

#### 10 ***Strengths and limitations***

11 Considering the prevalence of the exposures of interest is essential to interpret the  
12 results: by definition, the estimated impact of stochastic counterfactual exposures  
13 depends on both the observed prevalence and the relative risk related to the  
14 exposure. For example, stronger impacts could be expected in counterfactual  
15 scenarios in which the exposure to low educational level was decreased by half (from  
16 approximately 33% to 16.5%) compared to scenarios in which the exposure to ACE  
17 was decreased by half (from approximately 11% to 5.5%).

18 Some limitations relate to measurement issues and definition of the exposures of  
19 interest. Measurement errors are probably much smaller for smoking than for ACE  
20 which is less clearly defined and difficult to quantify. In this respect, non-differential  
21 measurement errors can result in underestimation of the potential impact of  
22 interventions. Moreover, the consistency assumption is questionable for several  
23 exposures of interest, making it more difficult to shape interventions or policies that  
24 would achieve a given level of exposure. This assumption “entails that the exposure  
25 is defined with enough specificity that different variants of the exposure do not have

1 different effects on the outcome”. [29] The concepts behind educational level and the  
2 mechanisms involved are multidimensional: do we care about literacy, self-esteem,  
3 self-efficacy, confidence in the future, or material means to go to college and  
4 university? Mixing the content of education can violate the consistency assumption  
5 and induce misclassification of subjects. Similarly, the conceptual components of  
6 ACE have been debated and are subject to historical and geographic variations. [25]  
7 The variable ambiguity in the definition of each exposure makes them difficult to  
8 compare. However, it is noteworthy that studies estimating the effect of compulsory  
9 school laws as natural experiments, for which interventions are more specifically  
10 defined, showed results consistent with ours, suggesting that increased educational  
11 attainment reduces mortality, potentially through a decrease in smoking and  
12 obesity. [30] Regarding intervention strategies to address ACEs, concerns have been  
13 raised about the inappropriate use of the ACE score as a screening tool at the  
14 individual level. [25,31] Larkin et al. gave examples of strategies based on public  
15 health and social science research. They recommended the development of  
16 integrated and multidisciplinary service structures to support parents and families, at  
17 the level of the community. [32] Interventions should focus on structural changes (e.g.  
18 economic support for families, social norms, quality child care, early life education,  
19 parenting skills) in order to avoid individual deterministic interpretations and  
20 stigmatization of families and children. [25] Overall, effective social work activities  
21 targeting the social environment during childhood could lead to societal cost-savings,  
22 which should be assessed in collaboration with economists. [32]

23 Other simulation methods, such as Markov-based modeling or agent-based models,  
24 can be more versatile to combine data from multiple sources in complex longitudinal  
25 structures. [13,33] But they also rely on a larger number of unverifiable assumptions.

1 Some authors pointed out the advantage in inferring results from real-world data  
2 rather than relying too heavily on simulated mathematical models of reality.[34,35]  
3 Using individual data and observed joint distributions from actual cohorts as in our  
4 analysis, can strengthen the internal validity of the results. Such approaches can be  
5 based on explicit statements about the causal assumptions to estimate the effects of  
6 counterfactual interventions.[36] They can also be used in a lifecourse perspective for  
7 time varying exposures, integrating baseline and time varying confounders.[37]

8 Some limitations and constraints also arise from using cohorts. Potentially important  
9 confounders might be missing, especially for early exposures (for example, variables  
10 characterizing the child's socioeconomic environment and health).  
11 Representativeness of cohorts can be limited by the sample selection. The variables  
12 collected and the availability of outcomes of interest might also be limited. In the 1958  
13 NCDS cohort, the sample is representative of a British population born in 1958, but  
14 due to the historical delay, the causal relationships and the intensity of the relations  
15 might be different nowadays. Moreover, it was not possible to study mortality after 55  
16 years old. The proportion of low educational attainment or smoking has decreased  
17 during the last decades, which probably results in an overestimation of our estimates.  
18 As an example for comparison, Blakely et al. simulated the expected health benefit  
19 from an ongoing tobacco tax increase scenario, taking into account the expected  
20 decrease in smoking between 2011 and 2061 in the "no intervention" scenario. They  
21 estimated a much smaller decrease in mortality than in our estimates (relative  
22 differences in mortality ranging from -0.11% to -2.22%, depending on sex, age, and  
23 ethnicity).[38] Regarding the limitation related to the maximum length of follow-up,  
24 several studies showed a moderate association between ACEs and disease  
25 occurring later in life (cancers, heart disease, respiratory disease).[39] An interesting



1 perspective would be to study whether decreasing the exposure to ACEs can have a  
2 sustained effect beyond the age of 60. This would require cohorts with older  
3 participants or waiting for future evaluations in the 1958 NCDS cohort.

4 The fundamental cause of health inequalities as stated by Link and Phelan might be  
5 another theoretical limitation: social factors embody access to a large set of  
6 resources (money, knowledge, prestige, power ...), affecting diseases through  
7 multiple mechanisms, thus making individual-based interventions focusing on a  
8 single resource ineffective.[40] Under this theory, systems models should be much  
9 more complex than our simple models, integrating larger sets of resources, context  
10 and their possible interactions. Arnold et al discuss the differences between directed  
11 acyclic graphs (DAG)-informed regression modeling, microsimulation and agent-  
12 based modeling, in the current paradigm of causal inference in epidemiology.[33] Our  
13 method is closer to DAG-inform regression modeling, while agent-based models  
14 might be more appropriate to explore how social phenomena emerge in complex  
15 systems, by agent-to-agent or agent-environment interactions. More specifically, El-  
16 Sayed et al. described how agent-based modeling and social network analysis can  
17 be used for a better integration of social interactions operating at the macro- and the  
18 micro-scale.[41] Applications can be found in the literature, for example to explore the  
19 role of economic segregation on healthy eating, or to study marginalization of  
20 minorities induced by the evolution of smoking behaviors, but their number is still  
21 limited.[42,43]

22 The predictive validity of simulation models beyond the context and timeframe of the  
23 data under study is particularly difficult to assess, as future events are not available  
24 at the time the model is developed.[4,35] Providing realistic estimations to fuel the  
25 political and social debate is thus particularly challenging. External validity of these

1 approaches will have to be evaluated, comparing results from different cohorts, or  
2 trying to validate estimations based on external data.

3 Other simulation studies have been carried out to assess health policies targeting  
4 tobacco use and health disparities. For example, Over et al. showed health gains  
5 with a reimbursement of cessation support or a tax increase scenario in groups of  
6 various socioeconomic status (SES).[44] But while health outcomes appeared to be  
7 improved in the lowest SES group, the expected benefits were greater in higher SES  
8 groups and both simulated policies were not associated with a reduction in  
9 socioeconomic differences. Moreover, the lowest SES group has the most  
10 unfavorable incremental cost-effectiveness ratio.[44] On the other hand, Blakely et al  
11 showed how tobacco taxes could reduce mortality and health inequalities measured  
12 by ethnicity.[38]

13 In the literature, randomized intervention on schooling to improve access to early  
14 education or quality of schooling showed improvement of health outcomes.[45]  
15 Based on several European populations, some authors showed on the contrary that  
16 larger proportions of educated populations could be associated with a decreased life  
17 expectancy and larger inequalities.[46] Comparisons of simulation results between  
18 different cohorts and designs should be interpreted with caution: different results  
19 could be true and informative, related to different contexts or different populations, or  
20 they could reflect unstable or uncertain results.

21 A key question is to describe and integrate relevant information about the context,  
22 which is essential both in the implementation phase of an intervention and in the  
23 interpretation of the results with possible effect modifications. Some researchers  
24 differentiate between the fixed theoretical aspects of interventions (“key functions”)  
25 and their variable form according to the context.[47,48] Some formal tools have also

1 been recently developed to clarify and assess when and how transportability is  
2 feasible.[49]

### 3 **Conclusion**

4 Our results based on simulations highlight the potential value of early interventions  
5 targeting ACE and education, compared to more traditional and well-recognized  
6 interventions on smoking. These models and their methodological development may  
7 contribute to transfer knowledge from research to policy and help decision making.

8

1 **Titles of Figures and Tables.**

2 Figure 1. Directed acyclic graph of the working causal model

3

4 Table 1. Description of variables

5

6 Table 2. Description of the variables at baseline, 23 years old, 33 years old and  
7 deaths before 55 years old

8

9 Table 3. Absolute and relative effects on mortality of changing the level of exposure  
10 to adverse childhood experience (ACE), member's educational level, smoking, and  
11 the joint exposure to ACE and member's educational level

12

13 Table 4. Absolute and relative effects on mortality in counterfactual scenarios among  
14 Men or Women, stratified by the educational level of their parents

15

16

## 1 **Ethics approval**

2 Multicentre Research Ethics Committee (MREC) approval has been sought for NCDS  
3 follow-ups from 2000 on (London MREC in 2000, South East MREC in 2002, London  
4 MREC in 2008, London-Central in 2013). The 1958 and 1965 follow-ups pre-dated  
5 the establishment of ethics committees, the 1969, 1974, 1981 and 1991 follow-ups  
6 came before the establishment of the MREC system. Internal ethical reviews were  
7 undertaken for these surveys. In 1958, consent to participate in surveys was gained  
8 by respondents agreeing to be interviewed or respondents returning the completed  
9 questionnaire to the study team. Involvement in subsequent surveys adopted the  
10 same approach. NCDS sought informed parental consent for the 7-year (1965), 11-  
11 year (1969) and 16-year (1974) surveys. A detailed review of the ethical practices  
12 throughout NCDS is available here:

13 [https://cls.ucl.ac.uk/wp-content/uploads/2017/07/NCDS-Ethical-review-and-Consent-](https://cls.ucl.ac.uk/wp-content/uploads/2017/07/NCDS-Ethical-review-and-Consent-2014.pdf)  
14 [2014.pdf](https://cls.ucl.ac.uk/wp-content/uploads/2017/07/NCDS-Ethical-review-and-Consent-2014.pdf)

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## 18 **Data availability**

19 NCDS data are open access datasets available to non-profit research  
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11 **Conflict of interest**

12 None declared.

13

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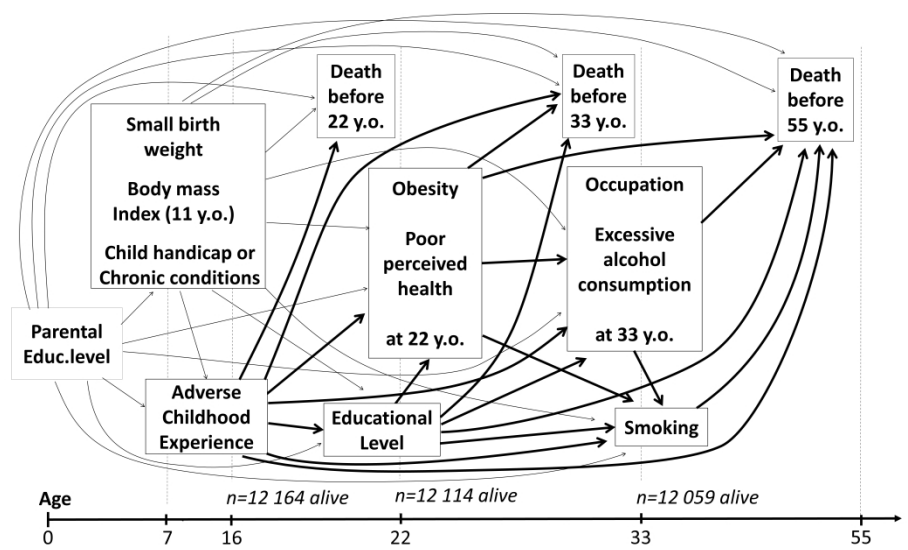


Figure 1

677x381mm (300 x 300 DPI)

Table 1. Description of variables

<b>Variable</b>	<b>Type</b>	<b>Categories and description</b>
Adverse childhood experience (ACE)	Exposure of interest	<p>ACEs were constructed from six dimensions of adversity using data collected prospectively between age 7 and 16:</p> <ol style="list-style-type: none"> <li>1. child in care;</li> <li>2. physical neglect indicated by a child's teacher;</li> <li>3. living in a household where a family member was in prison or on probation;</li> <li>4. parental separation;</li> <li>5. living in a household which has contact with mental health services;</li> <li>6. a family member has alcohol abuse problem.</li> </ol> <p><i>High</i> = exposure to 2 or more ACE dimensions;  <i>Low</i> = exposure to 0 or 1 ACE dimension</p>
Member's educational level at age 22	Exposure of interest	<p><i>High</i> = passed O-levels;</p> <p><i>Low</i> = less than O-levels</p>
Smoking at age 33	Exposure of interest	<p><i>Yes</i> = Member reported smoking at the time of sweep 5 (age 33);</p> <p><i>No</i> = Member reported not smoking or less than 1 cigarette/day at the time of sweep 5 (age 33)</p>
Parental educational level	Confounder	<p><i>High</i> = stayed at school after the minimum leaving age</p> <p><i>Low</i> = did not stay at school after the minimum leaving age</p>
Small birth weight	Confounder	<p><i>Yes</i> = Birth weight &lt; 1 standard deviation or gestational age &lt; 28 weeks</p> <p><i>No</i> = Birth weight ≥ 1 standard deviation and gestational age ≥ 28 weeks</p>

Body mass index (BMI) at age 11	Confounder	4-level variable, based on the quartiles of the BMI distribution in the cohort
Presence of handicap or severe conditions during childhood	Confounder	Yes = the parents or the member declared congenital conditions, disabilities, chronic respiratory or circulatory conditions, sensory impairment, or special schooling between 7 and 16 years old (sweeps 1 to 3) No = the parents and the member did not declare any of the above condition
Obesity at age 22	Confounder	Yes = BMI > 30 kg/m <sup>2</sup> ; No = BMI ≤ 30 kg/m <sup>2</sup>
Poor perceived health at age 22	Confounder	Yes = description of own health as “fair” or “poor” No = description of own health as “good” or “excellent”
Occupation at age 33	Confounder	Using the 1991 Registrar General’s (RGs) social class <i>Manual</i> = “Skilled manual” or “Partly skilled” or “Unskilled” <i>Non-manual</i> = “Professional” or “Managerial\tech” or “Skilled non-manual” <i>Other</i> = “Not applicable”
Excessive alcohol consumption at age 33	Confounder	Yes = men (respectively women) drinking more than 21 (respectively 14) units/week No = men (respectively women) drinking less than 21 (respectively 14) units/week



Table 2. Description of the variables at baseline, 23 years old, 33 years old and deaths before 55 years old

	Among men, n=6240			Among women, n=5924		
	n	%*	%**	n	%*	%**
<b>Parental education level (missing : n = 2 [0.03%] &amp; n = 4 [0.07%] )</b>						
short	4079	65.4%	65.4%	3796	64.1%	64.1%
long	2159	34.6%	34.6%	2124	35.9%	35.9%
<b>Small birth weight (missing : n = 838 [13.4%] and n = 797 [13.5%] )</b>						
no	4626	85.6%	85.5%	4381	85.4%	84.9%
yes	776	14.4%	14.6%	746	14.6%	15.1%
<b>Body mass index (11 years old) (missing : n =1017 [16.3%] and n = 907 [15.3%] )</b>						
9.6-15. kg/m <sup>2</sup>	1333	25.5%	25.9%	1243	24.8%	24.6%
15.8-17.0 kg/m <sup>2</sup>	1419	27.2%	26.8%	1137	22.7%	22.9%
17.0-18.5 kg/m <sup>2</sup>	1342	25.7%	25.4%	1208	24.1%	24.3%
18.5-37,8 kg/m <sup>2</sup>	1129	21.6%	21.9%	1429	28.5%	28.2%
<b>Handicap/sever conditions during childhood (missing : n = 0 [0.0%] and n = 0 [0.0%] )</b>						
no	4228	67.8%	-	4237	71.5%	-
yes	2012	32.2%	-	1687	28.5%	-
<b>Adverse childhood experience (missing : n = 3086 [49.5%] and n = 2876 [48.6%] )</b>						
0-1	2876	91.2%	88.0%	2835	93.0%	90.5%
2 to 6	278	8.8%	12.0%	213	7.0%	9.5%
<b>Death between 16 and 23 years old</b>						
no	6206	99.5%	-	5908	99.7%	-
yes	34	0.5%	-	16	0.3%	-

Table 2 (continued)

<b>Sweep t = 4, 23 years old</b> <b>(n alive = 12 114)</b>	Among men, n=6206			Among women, n=5908		
	n	%*	%**	n	%*	%**
<b><i>Educational level (missing : n = 1334 [21.5%] and n = 1012 [17.1%])</i></b>						
less than O levels	1475	30.3%	31.4%	1675	34.2%	34.8%
passed O levels	3397	69.7%	68.6%	3221	65.8%	65.2%
<b><i>Obesity (missing : n = 1434 [23.1%] and n = 1099 [18.6%])</i></b>						
non	4668	97.8%	97.7%	4660	96.9%	96.8%
yes	104	2.2%	2.3%	149	3.1%	3.2%
<b><i>Poor perceived health (missing : n = 1339 [21.6%] and n = 1015 [17.2%])</i></b>						
good/excellent	4476	92.0%	91.8%	4386	89.6%	89.4%
fair/poor	391	8.0%	8.2%	507	10.4%	10.6%
<b><i>Death between between 23 and 33 years old</i></b>						
no	6167	99.4%	-	5892	99.7%	-
yes	39	0.6%	-	16	0.3%	-

Table 2 (continued)

<b>Sweep t = 5, 33 years old</b> <b>(n alive = 12 059)</b>	Among men, n=6167			Among women, n=5892		
	n	%*	%**	n	%*	%**
<b><i>Occupation (missing : n = 1844 [29.9%] and n = 1385 [23.5%] )</i></b>						
manual	1999	46.2%	48.1%	1297	28.8%	29.6%
other	257	5.9%	6.0%	385	8.5%	8.9%
non manual	2067	47.8%	46.0%	2825	62.7%	61.5%
<b><i>Excessive alcohol consumption (missing : n = 1843 [29.9%] and n = 1390 [23.6%] )</i></b>						
no	3123	72.2%	72.1%	4123	91.6%	91.6%
yes	1201	27.8%	28.0%	379	8.4%	8.4%
<b><i>Smoking (missing : n = 1869 [30.3%] and n = 1405 [23.9%] )</i></b>						
no	2940	68.4%	66.8%	3073	68.5%	67.5%
yes	1358	31.6%	33.2%	1414	31.5%	32.5%
<b><i>Death before 55 years old</i></b>						
no	5896	95.6%		5724	97.1%	
yes	271	4.4%		168	2.9%	

\* percentages calculated among the observed values ;

\*\* average percentage after multiple imputation

Table 3. Absolute and relative effects on mortality of changing the level of exposure to adverse childhood experience (ACE), member's educational level, smoking, and the joint exposure to ACE and member's educational level

Counterfactual scenario	absolute difference		relative difference	
	mean	[95% CI]	mean	[95% CI]
Among men				
ACE $\geq$ 2	-0.22%	[-0.35% ; -0.08%]	-4.07%	[-6.34% ; -1.50%]
Member's low educational level	-0.36%	[-0.74% ; -0.17%]	-7.20%	[-13.24% ; -3.03%]
ACE $\geq$ 2 & low educational level	-0.55%	[-0.90% ; -0.36%]	-9.95%	[-15.60% ; -6.24%]
smoking	-0.54%	[-0.74% ; -0.26%]	-12.29%	[-16.95% ; -5.91%]
Among women				
ACE $\geq$ 2	-0.11%	[-0.21% ; -0.01%]	-3.40%	[-6.34% ; -0.26%]
Member's low educational level	-0.14%	[-0.27% ; +0.08%]	-4.43%	[-8.97% ; +2.40%]
ACE $\geq$ 2 & low educational level	-0.24%	[-0.42% ; +0.04%]	-7.19%	[-12.24% ; +1.18%]
smoking	-0.20%	[-0.38% ; +0.04%]	-7.01%	[-13.08% ; +1.17%]

ACE: adverse childhood experience; CI: confidence interval

Table 4. Absolute and relative effects on mortality in counterfactual scenarios among Men or Women, stratified by the educational level of their parents

Counterfactual scenario halving the level of...	absolute difference		relative difference	
	mean	[95% CI]	mean	[95% CI]
Low educational level of parents, among Men				
ACE $\geq$ 2	-0.31%	[-0.51% ; -0.08%]	-5.26%	[-8.17% ; -1.42%]
Member's low educational level	-0.45%	[-0.91% ; -0.20%]	-8.47%	[-15.51% ; -4.00%]
ACE $\geq$ 2 & low educational level	-0.72%	[-1.14% ; -0.39%]	-12.14%	[-18.62% ; -6.26%]
smoking	-0.67%	[-0.94% ; -0.35%]	-14.17%	[-19.48% ; -7.52%]
High educational level of parents, among Men				
ACE $\geq$ 2	-0.07%	[-0.28% ; +0.08%]	-1.41%	[-5.36% ; +1.50%]
Member's low educational level	-0.18%	[-0.39% ; +0.03%]	-4.13%	[-8.76% ; +0.69%]
ACE $\geq$ 2 & low educational level	-0.23%	[-0.50% ; -0.04%]	-4.84%	[-10.49% ; -0.82%]
smoking	-0.31%	[-0.55% ; -0.00%]	-8.26%	[14.06% ; -0.09%]
Low educational level of parents, among Women				
ACE $\geq$ 2	-0.14%	[-0.27% ; +0.03%]	-3.60%	[-6.96% ; +0.70%]
Member's low educational level	-0.22%	[-0.44% ; +0.08%]	-6.08%	[-12.02% ; +2.21%]
ACE $\geq$ 2 & low educational level	-0.35%	[-0.61% ; -0.00%]	-8.90%	[-15.93% ; -0.07%]
smoking	-0.17%	[-0.38% ; +0.11%]	-4.96%	[-11.41% ; +3.12%]
High educational level of parents, among Women				
ACE $\geq$ 2	-0.07%	[-0.20% ; +0.05%]	-2.88%	[-7.48% ; +2.17%]
Member's low educational level	-0.01%	[-0.23% ; +0.14%]	-0.50%	[-9.71% ; +6.86%]

ACE $\geq$ 2 & low educational level	-0.08% [-0.27% ; +0.12%]	-3.28%	[-10.82% ; +4.70%]
smoking	-0.22% [-0.40% ; +0.01%]	-11.43%	[-20.85% ; +0.68%]

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ACE: adverse childhood experience; CI: confidence interval