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Life-course socioeconomic disadvantage and lung function: a multicohort study of 70 496 individuals

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AUTHORS CONTRIBUTION

VR, SF and SS conceived the study. VR wrote the first and successive drafts of the manuscript. CM, VR and CC modelled and analysed the data. AL, AS, GG, MG, MZ, MK, PV, PVo, HB collected the data. All authors revised the manuscript for important intellectual content.

SUMMARY

This multicohort study of 70496 individuals from four European countries show that life-course socioeconomic disadvantage is associated with a lower lung function and is an important predictor of years of lung function loss during adulthood and older ages.

ABSTRACT

Background: Lung function is an important predictor of health and a marker of physical functioning at older ages. This study aimed to quantify the years of lung function lost according to disadvantaged socioeconomic conditions across life-course.

Methods: This multicohort study used harmonised individual-level data from six European cohorts with information on life-course socioeconomic disadvantage and lung function assessed by FEV_1 and FVC. 70496 participants (51% women) aged 18-93 years were included. Socioeconomic disadvantage was measured in early life (low paternal occupational position), early adulthood (low educational level), and adulthood (low occupational position). Risk factors for poor lung function (e.g., smoking, obesity, sedentary behaviour, cardiovascular and respiratory diseases) were included as potential mediators. The years of lung function lost due to socioeconomic disadvantage were computed at each life stage.

Results: Socioeconomic disadvantage during life-course was associated with a lower FEV_1. By age 45, individuals experiencing disadvantaged socioeconomic conditions had lost 4 to 5 years of healthy lung function vs their more advantaged counterparts (low educational level: -4.36 [95% CI -7.33;-2.37] for men and -5.14 [-10.32; -2.71] for women; low occupational position: -5.62 [-7.98;-4.90] for men and -4.32 [-13.31;-2.27] for women), after accounting for the risk factors for lung function. By ages 65 and 85, the years lung function lost due to socioeconomic disadvantage decreased by 2 to 4 years, depending on the socioeconomic indicator. Sensitivity analysis using FVC yielded similar results to those using FEV_1.

Conclusion: Life-course socioeconomic disadvantage is associated with lower lung function and predicts a significant number of years of lung function loss in adulthood and older ages.

Keywords: Socioeconomic disadvantage; Lung function; Life-course epidemiology; Adulthood; Older ages

INTRODUCTION

Lung function is a significant predictor of health and an important marker of physical functioning at older ages[1, 2]. Evidence from three large cohort studies showed that individuals with low lung function in early adulthood had a higher incidence of respiratory, cardiovascular, and metabolic diseases; a higher number of comorbidities; and higher premature mortality by all causes[3].

Exposure to socioeconomic disadvantage in childhood or adulthood is associated with reduced lung function and a higher prevalence of respiratory diseases during adulthood and older ages[4-8]. However, less is known about the effects of socioeconomic disadvantage on lung function at each stage of the life-course[8-10] or the extent to which exposure to socioeconomic disadvantage reduces life-years of healthy lung function. It also remains unclear whether socioeconomic disadvantage is directly associated with reduced lung function or has an indirect impact, via other risk factors[11, 12]. For example, individuals from disadvantaged socioeconomic conditions have a higher prevalence of early respiratory tract infections, preterm birth, and poor nutrition[13]; risk behaviours such as smoking and physical inactivity[14, 15]; and more exposure to indoor and outdoor pollution[16] and damaging occupational conditions[17], which also contribute to reduced lung function[18, 19].

Prior evidence showed that socioeconomic conditions over the life-course may help to predict outcomes of mobility, disability, and functioning[20-22], but the extent to which disadvantaged socioeconomic conditions may affect lung function still needs to be understood. Lung function could potentially be considered a summary measure of overall functioning at older ages because of its links with cognitive and physical functioning[1, 2]. It is, therefore, of critical importance to identify its risk factors from a life-course perspective.

In this study, we aimed to quantify the years of lung function lost according to socioeconomic disadvantage at three distinct stages, childhood, early adulthood, and adulthood, by sequentially controlling for time-ordered socioeconomic status and risk factors for poor lung function. We also aimed to establish the life stages in which disadvantaged conditions may have more adverse effects on lung function by analysing harmonised individual-level data from six European cohort studies.

METHODS

Study design and participants

This study is part of the European Commission’s Horizon 2020 consortium, the Lifepath project. Details about the project are available elsewhere[23]. In the present analysis, we included six studies, including five population-based cohorts (the COLAUS|PSYCOLAUS, CONSTANCES, ELSA, EPIPORTO, and NCDS) and one occupational-based cohort (the WHITEHALL II) from four European countries (United Kingdom, France, Switzerland, and Portugal). Detailed information on each cohort study is available in text S1 in the supplementary material.

Our analyses included 70 496 men and women aged 18 to 93 years with complete information on exposure (socioeconomic status measured by paternal occupational position, participant educational level, and participant occupational position) and outcome (lung function measured by spirometry).

Data on lung function were collected between 2002 and 2017 across the cohort studies included. Detailed information on lung function measurements is available in table S1 in the supplementary material. The relevant local or national ethics committees approved each study, and all participants gave written informed consent to participate.

Life-course socioeconomic disadvantage

Life-course socioeconomic disadvantage was assessed with multiple indicators at three life stages: childhood with low paternal occupational position, early adulthood with low participant educational level, and adulthood with low occupational position. The fathers' occupational position was chosen as a better surrogate of household socioeconomic conditions than mothers' occupational position because prior evidence showed that the effects of fathers' occupational position on individuals' health exceeds that of mothers'[24]. Meanwhile, participants' own occupation may be a good indicator of social networks, work-based stress, control, and autonomy[25]. Education reflects the material, intellectual resources of the family of origin, having the potential to capture the long-term influences of circumstances in both early life and young adulthood on adult health[25].

Both paternal occupational position and participant occupational position were retrospectively assessed using information on the last known occupational title at study enrolment and were predefined and harmonised between the study cohorts[20]. The European Socioeconomic Classification (ESEC) system[26], which includes nine categories, was used to code participants' paternal occupational position and their own occupational position. The tenth category included people who never worked or were unemployed long-term, and these people were excluded from the analysis. ESEC occupational classes 1 to 3 were considered high professions (including higher-level professionals and managers, higher-level clerical, services, and sales workers); ESEC classes 4 to 6 as intermediate professions (including small employers and self-employed, farmers, lower-level supervisors, and technicians); and ESEC classes 7 to 9 as low professions (including lower-level clerical, services, and sales workers; skilled workers; and semiskilled and unskilled workers). Participants' educational level was measured as completed years of schooling, categorised as high (including tertiary education or postsecondary); intermediate (higher secondary school); and low (including primary or lower secondary school).

Lung function

Lung function was assessed with spirometry performed according to American Thoracic Society (ATS) and European Respiratory Society (ERS) criteria[27]. In all cohorts, at least three reproducible and acceptable forced manoeuvres were performed; the highest technically satisfactory readings of forced expiratory volume in the first second (FEV_1) and forced vital capacity (FVC) in millilitres (mL) were collected. A single measure of FEV_1 and FVC were analysed from one wave of each cohort included (COLAUS – wave 2, 2014-2017; CONSTANCES - wave 1, 2012-2017; ELSA - wave 6, 2012-2013; EPIPORTO – wave 2, 2014-2015; NCDS – wave 8, 2002-2003; WHITEHALL II – wave11, 2012-2013). To harmonise spirometry values and allow comparisons between the cohorts, some exclusion criteria to FEV_1 and FVC were also defined[27]. Thus, participants with incomplete information, whose tests ended in the first second, or with a volume in the first second higher than the total volume were excluded from the analysis. Further details on the spirometry procedures and exclusions are available in Table S1 in the supplementary material. All the FEV_1 and FVC values used in the analyses were age- and height-adjusted and stratified by sex using the statistical method described here. Analyses were not stratified by race/ethnicity because almost all participants were white (99.3%).

Sociodemographic information, health risk factors, and disease history

Sex, age, and marital status were self-reported, and marital status was further categorised as married or living in common law vs single, divorced, or widow.

Health risk factors, such as body mass index (BMI), smoking, and sedentary behaviour, which are known to be associated with both socioeconomic disadvantage and lung function, were considered as covariates. Risk factor measurements that were closest to the lung function assessment were used. If data were unavailable at the same wave, we completed information from the preceding evaluation. Height and weight were measured using standard procedures. BMI was then calculated as weight (in kilograms, kg) divided by height (in square meters, m^2) and categorised as underweight (<18.5 kg/m^2), normal weight (18.5 to <25 kg/m^2), overweight (25 to <30 kg/m^2), or obese (≥30 kg/m^2), according to World Health Organization classification. Self-reported smoking was categorised as smokers, former smokers (ie, participants who had not smoked for at least six months), or never smokers. Smoking intensity was collected as the number of cigarettes per day (continuous variable) and further categorised in 1-19 and 20 or more cigarettes per day for all cohorts, excepting for NCDS which did not have this information available. Although physical activity was measured with different questions in each study, a dichotomised variable indicating the presence or absence of sedentary behaviour was harmonised. In all cohorts, the prevalence of cardiovascular disease was ascertained by using a harmonised variable referring to the medical diagnosis or self-reported diagnosis of angina and/or heart attack and/or coronary artery disease and/or myocardial infarction, with the exception of WHITEHALL II (information on stroke and coronary heart disease) and NCDS (information on medicines for cardiovascular disease). The prevalence of respiratory disease was ascertained using the prevalence of self-reported asthma, chronic bronchitis, emphysema, or chronic lung disease for all cohorts with the exception of ELSA, in which respiratory diseases were medically diagnosed. The NCDS only had information on medicines for respiratory disease.

Statistical analysis

Analyses were performed separately for men and women and all analyses accounted for cohort effects.

Association between socioeconomic disadvantage and lung function

Generalized linear models were used to investigate the relationship between socioeconomic disadvantage and lung function using FEV_1. The minimally adjusted model was adjusted for age and height. The fully adjusted model assessing paternal occupational position as exposure was adjusted for age, height, health risk factors (smoking, sedentary behaviour, and BMI), and history of disease (respiratory and cardiovascular). The fully adjusted model assessing educational level as exposure was adjusted for age, height, paternal occupational position, health risk factors, and history of disease. The fully adjusted model assessing occupational position as exposure was adjusted for age, height, paternal occupational position, educational level, health risk factors, and history of disease. These analyses allow us to evaluate the total effect of socioeconomic disadvantage on lung function and the variables included in fully adjusted models were considered mediators in the association of socioeconomic disadvantage with lung function, since they stand in the midst of the causal chain from socioeconomic disadvantage to lung function. Therefore, as we assessed total effects rather than direct effects, we did not perform mediation analysis and adjustments were sequentially performed considering the chronology of events over the life-course.

Lung function and age

A generalised additive mixed model using a mgvc 4 algorithm was used to estimate FEV_1, with age and height as fixed-effect predictors and cohort as a random effect at the intercept and age slope. We computed 95% CIs from the uncertainty of the estimated smoothing function. The lung function decline by year was also estimated for each age group: 18-24; 25-44; 45-64; 65 or older. The age groups were based on the lung function periods of growth and decline. From 18 to 25 years of age, lung function might slightly increase until the maximal lung function attainment. From 25 to 45 years of age the maximal lung function has already been attained and individuals are in the plateau phase when merely small fluctuations in lung function indices occur. After this period, they enter in the decline phase during adulthood, characterised by a smooth decrease in lung function over time. After 65 years of old, the decline phase is more accentuated due to the physiological ageing of the lungs.

Years of lung function lost

The number of years of lung function lost was computed from the mixed-model predictions of FEV_1 along with age. The mixed model of FEV_1 included a random cohort effect at the intercept and age slope. Fixed effects included age, age squared (age^2), height, and the socioeconomic factor under study in the minimally adjusted models. The fully adjusted models included age, age^2, height, the socioeconomic indicators as previously described, smoking, sedentary behaviour, BMI, respiratory and cardiovascular disease, and an interaction term between age and socioeconomic factor. The structure of the models was determined through likelihood ratio tests. Confidence intervals for years of lung function lost were determined through 5000 bootstrap samples, applying a model-based parametric bootstrap method. For all examined factors, we computed the years of lung function lost associated with the exposure by predicting the chronological age of the unexposed group (high socioeconomic status) equivalent to the FEV_1 at age 45, 65, or 85 years in the exposed group (intermediate or low socioeconomic status). This method allows years of lung function lost by a given age to be retrospectively calculated, as opposed to the classic years of life lost prospectively calculated.

Supplementary analyses

As supplementary analyses, we repeated the generalized linear models and computed the number of years of lung function lost using the FVC. Moreover, because smoking is one of the main predictors of reduced lung function, we repeated the linear regression analyses on the association of socioeconomic disadvantage and FEV_1, stratifying results by smoking status. We also stratified results by smoking intensity (number of cigarettes per day) using a subsample of our data (n=14 403), since we did not have this information for all participants. Finally, we performed a multiple imputation model using chained equations to check whether results were similar using the total sample (n=96 600) in contrast to using only participants with complete exposure and outcome information (n= 70 496). This technique allows imputing missing information for several variables at a time through an iterative process (the chained equations). Fifteen completed data sets were generated, and results were combined to produce estimates with standard errors that should correctly reflect the variability of data. We imputed data for the exposure (the three socioeconomic indicators) and covariates (smoking, sedentary behaviour, and BMI, respiratory and cardiovascular disease. The outcome measure was not imputed. Analyses were performed using STATA (Version 15.0, StataCorp, College Station, TX) and R® (R Foundation).

RESULTS

Of 96 600 eligible participants from the six cohort studies, 70 496 participants were included in this study (Figure S1). We found statistically significant differences between included and excluded participants, with those included being older (48.8 vs 47.8 years, $p<0.001$) and more likely to have high educational level (52.2% vs 38.4%, $p<0.001$) and high occupational position (31.7% vs 25.9%, $p<0.001$) (Table S2). The mean (SD) age of included participants was 48.8 (12.4) years and 50.5% were women (Table 1). The mean (SD) FEV_1 values were 3501.9 (524.1) and 2788.1 (511.5) mL and FVC values were 4446.8 (626.1) and 3480.4 (602.5) mL in men and women, respectively. Most participants had a low paternal occupational position (43.7%), a high own educational level (52.2%), and an intermediate own occupational position (35.3%). About half of the participants were never smokers (45.9%) and presented normal weight (52.4%). The prevalence of sedentary behaviour was 26.4%, of cardiovascular disease was 3.6%, and of respiratory disease was 13.3% (Table 1). Detailed information on the characteristics of participants by sex and cohort is available in the supplementary material (Table S3).

Figure 1 shows the age-related decline in FEV_1 in both men and women using the GAMM model. An increased decline with age was observed, more accentuated among men than women.

Participants with intermediate or low paternal occupational position, own educational level, and own occupational position had a lower FEV_1 vs higher socioeconomic counterparts (minimally adjusted models) (Table 2). In fully adjusted models, these associations attenuated but remained significant considering paternal occupational position (men, intermediate: -147.3 mL [95% CI -163.0; -131.6]; low: -167.4 mL [-182.8; -152.0] and women, intermediate: -153.1 mL [95% CI -167.9; -138.4]; low-175.4 mL [-190.0; -160.8]) and own educational level (men, intermediate: -164.6 mL [-177.5; -151.7]; low: -210.6 mL [-226.5; -194.7] and women, intermediate: -208.6 [-221.3; -196.0]; low: -333.6 mL [-348.6; -318.6]) (Table 2). Sensitivity analysis using FVC yielded similar results to those using FEV_1 (Table S4).

Figures 2, 3, and 4 show the years of lost function by ages 45, 65, and 85 according to intermediate or low socioeconomic conditions using the three socioeconomic indicators. By age 45, compared with individuals with high socioeconomic status, the years lung function lost were -4.36 (95% CI -7.33; -2.37) and -5.14 (-10.32; -2.71) in men and women, respectively, of low educational level and -5.62 (-7.98; -4.90) and -4.32 (-13.31; -2.27) in men and women, respectively, of low occupational position (Figure 2, fully adjusted models). These findings suggest a difference of 4 to 5 years in lost lung function, meaning that, overall, a 45-year-old man or woman who experienced socioeconomic disadvantage had the same lung function as a 49- to 50-year-old man or woman who had experienced more favourable socioeconomic conditions, independently of the socioeconomic indicator used. By age 65, the years of lost function due to disadvantaged socioeconomic conditions diminished in men and women, respectively, to -2.78 (-4.37; -1.64) and -1.40 (-2.53; -0,.45) for low educational level and to -4.30 (-5.35; -3.37) and -4.32 (-13.31; -2.27) for low occupational position (Figure 3, fully adjusted models). By age 85, a reduction in the years of lost function was also observed, compared with by age 45. This reduction was more pronounced among women, with differences observed only for low occupational position (-1.29 [-2.55; -0.44]), while in men differences were observed for low educational level (-1.85 [-3.86; -0.49]) and low occupational position (-3.52 [-4.53; -2.39]) (Figure 4, fully adjusted models). The sensitivity analysis computing the years of lung function lost using FVC by ages 45, 65, and 85 years showed similar trends, with a slightly higher magnitude of differences between individuals with low vs high socioeconomic status (Table S5 in the supplementary material).

The association of socioeconomic disadvantage with lung function were independent of smoking status, since they were also observed in participants who never smoked (Table S6 in the supplementary material). Yet, the greater number of cigarettes smoked per day the lower FEV_1 among low socioeconomic status participants (Table S7 in the supplementary material). The sensitivity analysis using the total sample yielded results similar to those found in our main analyses (Table S8).

DISCUSSION

In this multicohort study using individual-level data of 70 496 individuals from six European cohort studies, socioeconomic disadvantage from childhood to adulthood was associated with lower lung function and predicts a significant number of years of lung function loss during adulthood and older ages. By age 45, 4 to 5 years of healthy lung function was lost in both men and women according to socioeconomic disadvantage. These associations remained after controlling for health risk factors for respiratory health, including smoking, sedentary behaviour, obesity, and cardiovascular and respiratory disease.

We also found that socioeconomic differences diminished with age but did not disappear. A difference of 2 to 3 years of healthy lung function was observed at the age of 85 between low vs high socioeconomic groups, depending on the socioeconomic indicator. These findings suggest a narrowing of the socioeconomic gradient in respiratory health at older ages, which is in line with evidence showing that in relative terms social inequalities in health tend to narrow with advancing age[28]. Previous studies[5, 28] suggest that selective mortality may be the key mechanism to explain this effect. Thus, we could hypothesize that the narrowing of social inequalities at 65 and 85 years of age may be due to the earlier death of individuals in more disadvantaged socioeconomic conditions, leaving relatively robust high socioeconomic status survivors and reducing the gap between the more advantaged and disadvantaged groups in mortality[5, 28]. We observed that participants who reached older ages and were included in the 85-years analyses were more likely to have a higher educational level, which in part support this theory.

Another known explanation is the "universality of biological frailty" hypothesis[29], in which morbidity becomes compressed among more advantaged groups until late in life and hence inequalities are reduced at older ages. This pattern of narrowing of health inequalities has mainly been observed in cross-sectional studies, which rely on comparing individuals at different ages[30], whereas longitudinal studies primarily report a widening in the social gradient in health with advancing age, as a result of the accumulated effects of social disadvantage over time[31, 32]. The only previous study that we found specifically on social inequalities and lung function presented cross-sectional evidence that socioeconomic disparities in lung function increase with age, especially for men[33]. In contrast, the study by Benzeval and colleagues[30] using longitudinal data from three European cohort studies found that inequalities are more pronounced at middle age and then narrow after the age of 65, which is in line with our observations. The effects of narrowing or widening of health inequalities may be complicated by cohort effects because differences may widen with age but increase with younger cohorts, producing an artefactual appearance of convergence if age is modelled without adjustment for cohort[34]. Nevertheless, in our study, all analyses accounted for cohort effects to minimise this artefact. Moreover, we performed regression analyses separately for each cohort study and then conducted a meta-analysis of the lung function differences using the three socioeconomic indicators (data not shown), which yielded similar results to those presented in Table 2. Thus, the weight of evidence seems to suggest that inequalities in health tend to be more evident at middle age and then narrow at older ages[28, 30, 31, 35], supporting our findings.

We also observed that the narrowing of the socioeconomic gradient in lung function was more pronounced among women than men. This could be explained by sex differences in life expectancy because women tend to live longer than men [36], and naturally will be more susceptible to the narrowing of the social gradient. Yet, other studies on socioeconomic inequalities on lung function suggested that both boys and men[37, 38] are more sensitive to socioeconomic inequalities in health. Indeed, a systematic review aimed at disentangling women's apparent relative immunity to the socioeconomic gradient in health concluded that the gradient appears stronger for men than for women for all health outcomes, except cardiovascular disease [39]. More studies are needed to clarify whether there are sex differences in survival bias or men are indeed more susceptible to socioeconomic inequalities affecting their health.

We found that early-life socioeconomic disadvantage (ie, measured in childhood and early adulthood) was associated with lower lung function, independent of adult life disadvantage, health risk factors (smoking, sedentary behaviour, and BMI), and cardiovascular and respiratory diseases. These findings agree with previous literature suggesting that some exposures at a specific period in the life-course, namely at early ages when lungs are growing, may influence the anatomical structure and physiological function of the lungs and will eventually result in disease[40, 41]. In addition, the effects of adult life disadvantage on lung function seemed to be almost fully explained by the socioeconomic conditions that individuals were exposed to during early ages, namely their fathers' paternal occupational position and the educational level attained in early adulthood. These findings support the hypothesis that early life may be particularly important, having the potential to shape and influence the life-course socioeconomic trajectories of individuals during adulthood and then influence later respiratory health outcomes[42]. In our study, we used occupational position as the single indicator of disadvantaged socioeconomic conditions in early life. Other important factors, and in particular material disadvantage, housing conditions or overcrowding in early life, could not be examined as this information was not available widely across cohorts. Given the strong influence of those factors on lung function [43, 44], our results for years of functioning lost due to disadvantaged socioeconomic conditions may be underestimated. Yet, the results of this study using an individual level indicator as paternal occupational position agree with some studies [43, 44] looking at the association of material socioeconomic disadvantage in early-life (measured with housing quality, overcrowding, residential area deprivation in addition to paternal occupational position) and lung function in adulthood and older ages.

Other pathways should also be considered. For instance, cigarette smoking is a primary predictor of low lung function and is more prevalent among disadvantaged socioeconomic groups[45]. Thus, it may explain the social gradient in lung function[5]. Nevertheless, our findings showed that after accounting for smoking status, the effects of socioeconomic disadvantage on lung function attenuated but remained significant, suggesting that these effects were independent of smoking status. We also performed a sensitivity analysis stratifying results by smoking, which showed that the effects of socioeconomic disadvantage on lung function were significant among never smokers, former smokers, and current smokers. This suggests that although smoking is an important factor for lung function in our study, it is not the determinant factor because participants of low socioeconomic status who never smoked also had reduced lung function, as previously described[5, 12]. We also observed that the greater number of cigarettes smoked per day the lower FEV_1 among low socioeconomic status participants, reinforcing the smoking intensity dose-effect on lung function. Yet, more detailed information on smoking would strengthen our results because we were not able to characterise passive exposure to smoking during early life or smoking intensity for all participants, factors that have been previously associated with reduced lung function[46, 47]. Obesity and the presence of sedentary behaviour may also be important for the social patterning of lung function, but the results of this study were independent of these factors, as shown in other studies[5, 8]. Thus, acting on socioeconomic conditions from early ages onwards[48] might have positive effects on lung function but also on the health-risk factors for lung function over the life-course, namely smoking, obesity and sedentary behaviour.

The strongest association between socioeconomic disadvantage and lower lung function were observed by educational level. Prior studies[5, 49] sought to explain this association by adjusting for smoking status, physical activity, and body composition; however, as in our study, the effects of educational level in lung function seem largely independent of these factors. This evidence suggests that a low educational level may be an important and consistent upstream risk factor for low lung function, but further research is needed to disentangle the precise mechanism(s) underlying this association. Thus, enhancing populations' educational level might help to improve respiratory health, but this hypothesis warrants further investigation. On the other hand, the individuals' occupational position was the indicator associated with a higher number of years of lung function lost, mainly in men, which makes sense since occupational position during adulthood will determine retirement pension at older ages.

The effects of socioeconomic disadvantage were observed on both FEV_1 and FVC indicators, yet the magnitude of the effects on FVC were slightly stronger than on FEV_1. FVC largely reflects lung volume, while FEV_1 is influenced by both airways flow obstruction and lung volume[6]. With advancing age even healthy participants show a reduction in lung volume and as our sample includes a large percentage of older adults, this might explain the slightly higher number of years of lung function lost associated to FVC. In addition, the differences between low vs high socioeconomic groups were in the range of 140-380 mL, which are higher that the values proposed (100–140 mL) as minimal clinically important differences by the American Thoracic and European Respiratory Societies[50]. A difference higher than 100mL in FEV_1 might be considered clinically relevant based on clinical anchoring to endpoints such as exacerbations, perception of dyspnoea, and lung function decline[51]. Thus, our findings suggest that socioeconomic disadvantage since early ages might translate in clinically relevant consequences for respiratory health over the life-course.

Strengths and limitations

The strengths of this study are the use of harmonised individual-level data from six cohort studies with information on socioeconomic indicators in different stages of the life-course. In addition, the FEV_1 and

FVC are reliable and robust health indicators to characterise lung function, with broader use in clinical and research fields, associated with several health outcomes[3].

Some limitations should also be considered. The harmonisation process requires standardising variables across cohorts, meaning that some cohort specificities may have been smoothed out or lost. The cohorts participating in the LIFEPATH consortium were from high-income countries so our results might not be generalizable to other populations. Health-risk factors (smoking, BMI, sedentary behaviour) were self-reported, and thus subject to some degree of measurement error and social desirability. However, due to the longitudinal nature of the cohorts included, we were able to complete and compare information on lifestyle factors with information from the preceding evaluations, reducing missing data and improving the reliability and validity of information. Other factors, such as early-life respiratory tract infections, poor nutrition, pollution levels, low housing conditions and damaging occupational exposures might contribute to explain the relationship between life-course socioeconomic disadvantage and lung function but we did not have that information for all included cohorts. These factors deserve to be explored by further studies. Cardiovascular disease was characterised using information on major cardiovascular disease (including angina and/or heart attack and/or coronary artery disease and/or myocardial infarction), which may lead to some degree of underestimation since mild cardiovascular disease, such as arterial hypertension, some type of arrhythmias, cardiomyopathies, could not be considered. The use of chronological age to compare years of lung function between the socioeconomic groups might not directly reflect the individuals' functional and health characteristics, since such characteristics vary extensively by individuals. However, other more precise measure of biological age or functional capacity were not available for all the included cohorts. Our approach that uses chronological age to calculate differences in lung function at the ages of 45, 65 and 85 years remains a simple and direct way to compare individuals of the same age, translating in a clear message for health policy implications. The cohort studies included were subject to attrition and we had some differential exclusions, as previously described. For instance, individuals of disadvantaged socioeconomic status tend to die earlier, when compared with those from high socioeconomic status. Yet, the results of our sensitivity analysis using the total sample (Table S8) showed that we might have underestimated the effects and, if those participants were included, the associations would be even more evident, mainly at 45 years of age. In addition, we cannot exclude the possibility of reverse causality because poorer lung function in early ages may have prevented participants' educational attainment, with potential implications in occupational position. There is likely to be unmeasured confounding, measurement error, and heterogeneity across cohorts regarding the socioeconomic variables. Also, as lung age was calculated retrospectively some misclassification might occur in fully adjusted models which considered predictors beyond age and height that can vary over the life-course (smoking, sedentary behaviour, BMI, respiratory and cardiovascular disease). Because our analyses relied on cross-sectional data, we cannot totally exclude reverse causality and thus infer a causal relationship between socioeconomic disadvantage and respiratory health. However, socioeconomic conditions in early life preceded respiratory health assessment, and our estimates indicate a potential effect of socioeconomic disadvantage on lung function at adulthood and older ages.

CONCLUSION

This study shows that socioeconomic disadvantage is associated with lower lung function across the life-course and predicts a significant number of years of lung function loss in adulthood and older ages. Social inequalities in lung function are particularly wide in middle age and seem to narrow with ageing. These findings suggest that actions to improve respiratory health over the life-course should consider the negative effects of adverse socioeconomic conditions from early ages onwards.

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Table 1: Characteristics of the participants included by sex (n=70 496).

	Men (n=34 843)	**Women** (n=35 653)	**Total** (n=70 496)
DEMOGRAPHICS, ANTHROPOMETRICS			
Age, mean (SD), y	49.2 (12.2)	48.4 (12.5)	48.8 (12.4)
Age groups, n (%), y			
18-44	11 242 (32.3)	12 569 (35.3)	23 881 (33.8)
45-64	19 055 (54.7)	18 825 (52.8)	37 880 (53.7)
65 or older	4546 (13.0)	4259 (11.9)	8805 (12.5)
Race/ethnicity			
White	34 527 (99.2)	35 396 (99.3)	69 923 (99.3)
Non-white	289 (0.8)	237 (0.7)	526 (0.7)
Height, mean (SD), cm	175.9 (6.8)	162.7 (6.4)	169.1 (9.2)
Weight, mean (SD), kg	80.5 (13.2)	65.7 (13.9)	73.0 (15.5)
LUNG FUNCTION, mean (SD), mL			
FEV_1	3501.9 (524.1)	2788.1 (511.5)	3140.9 (628.9)
FVC	4446.8 (626.1)	3480.4 (602.5)	3958.1 (781.5)
SOCIOECONOMIC STATUS, n (%)			
Paternal occupational position (ESEC class)			
High (1-3)	6285 (18.0)	6989 (19.6)	13 274 (18.8)
Intermediate (4-6)	12 899 (37.0)	13 515 (37.9)	26 414 (37.5)
Low (7-9)	15 659 (44.9)	15 149 (42.5)	30 808 (43.7)
Participants' educational level			
High (tertiary school)	17 345 (49.8)	19 446 (54.5)	36 791 (52.2)
Intermediate (higher secondary school)	10 945 (31.4)	9448 (26.5)	20 393 (28.9)
Low (primary/lower secondary school)	6553 (18.8)	6759 (19.0)	13 312 (18.9)
Participants' occupational position (ESEC class)			
High (1-3)	14 072 (40.4)	8269 (23.2)	22 341 (31.7)
Intermediate (4-6)	10 986 (31.5)	13 875 (38.9)	24 861 (35.3)
Low (7-9)	9785 (28.1)	13 509 (37.9)	23 294 (33.0)
HEALTH RISK FACTORS, n (%)			
Smoking			
Never	13 994 (41.4)	17 395 (50.4)	31 389 (45.9)
Former	13 635 (40.3)	10 836 (31.4)	24 471 (35.8)
Current	6172 (18.3)	6297 (18.2)	12 469 (18.2)
Sedentary behavior (yes)	8919 (26.5)	9069 (26.3)	17 988 (26.4)
BMI			
Under/normal weight	15 065 (43.4)	21 732 (61.2)	36 707 (52.4)
Overweight/obese	19 621 (56.6)	13 773 (38.8)	33 394 (47.6)
DISEASE HISTORY, n (%)			
Cardiovascular disease	1681 (4.8)	831 (2.3)	2512 (3.6)
Respiratory disease	4668 (13.5)	4703 (13.2)	9371 (13.3)

Legend: ESEC, European Socioeconomic Classification; FEV_1: forced expiratory volume in the first-second age and height-adjusted; FVC: forced vital capacity age and height-adjusted; BMI: body mass index; mL: millilitres.

Table 2: Serially adjusted association of life-course socioeconomic disadvantage with lung function by sex.

	FEV$_1$ differences, B (95%CI), mL			
	MEN		WOMEN	
	Minimally adjusted model[1]	Fully adjusted model[2]	Minimally adjusted model[1]	Fully adjusted model[2]
Paternal occupational position				
High	Reference	Reference	Reference	Reference
Intermediate	**-175.8 (-191.5; -160.2)**	**-147.3 (-163.0; -131.6)**	**-177.0 (-191.6; -162.4)**	**-153.1 (-167.9; -138.4)**
Low	**-206.3 (-221.5; -191.2)**	**-167.4 (-182.8; -152.0)**	**-215.1 (-229.4; -200.8)**	**-175.4 (-190.0; -160.8)**
Participants' educational level				
High	Reference	Reference		
Intermediate	**-214.6 (-226.8; -202.4)**	**-164.6 (-177.5; -151.7)**	**-241.7 (-253.7; -229.8)**	**-208.6 (-221.3; -196.0)**
Low	**-273.7 (-288.2; -259.2)**	**-210.6 (-226.5; -194.7)**	**-381.7 (-395.2; -368.2)**	**-333.6 (-348.6; -318.6)**
Participants' occupational position				
High	Reference	Reference		
Intermediate	**-83.0 (-96.5; -69.6)**	-3.6 (-17.1; 9.9)	**-127.7 (-141.5; -113.9)**	**33.3 (17.7; 48.9)**
Low	**-96.4 (-109.4; -83.3)**	**60.3 (44.8; 75.9)**	**-171.3 (-185.2; -157.5)**	**-28.4 (-42.3; -14.5)**

Legend: FEV$_1$: forced expiratory volume in the first second; B: beta-coefficient of linear regression models; CI: confidence interval; In bold statistically significant values.

[1] The minimally adjusted model was adjusted for age and height.

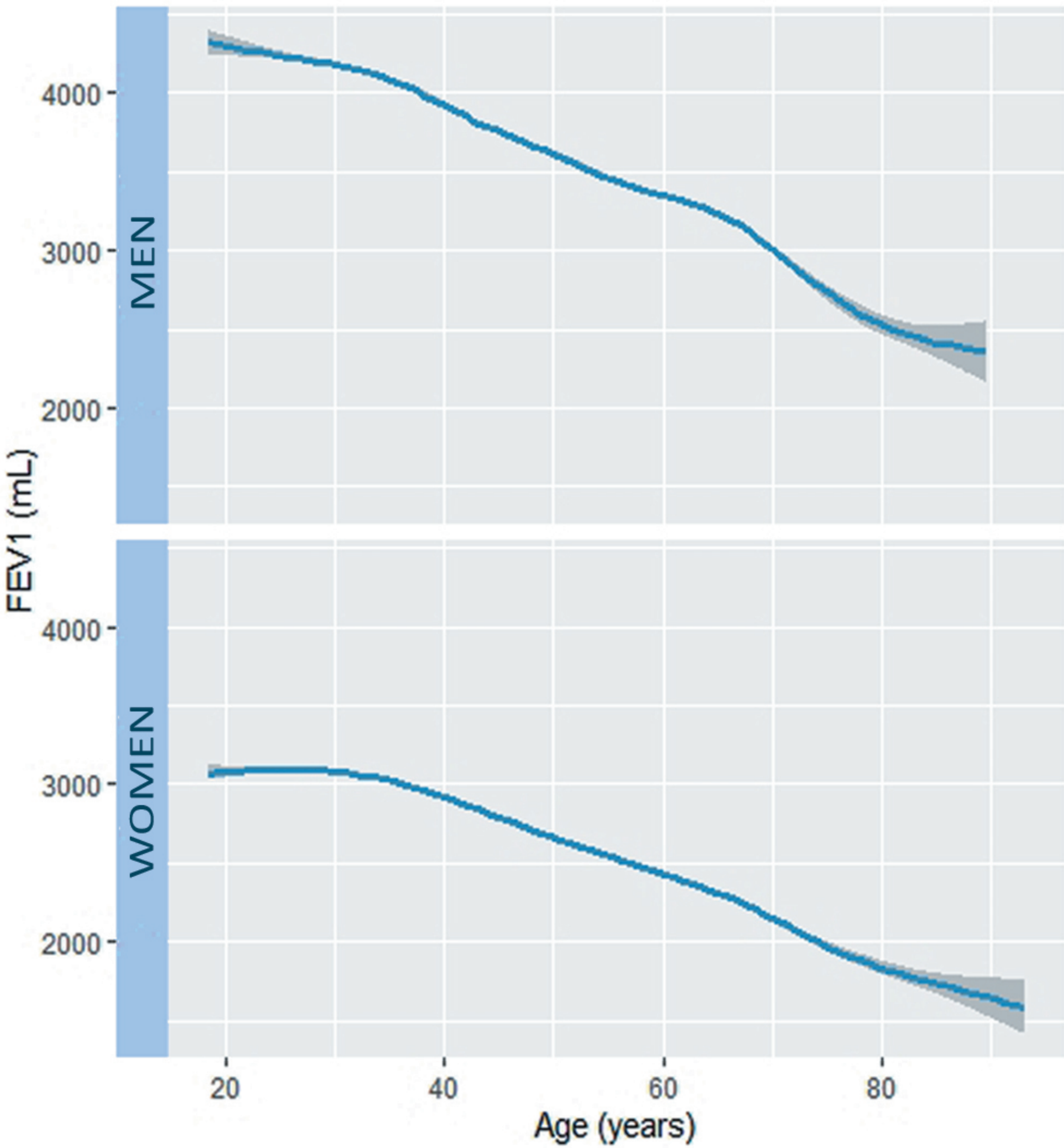
[2] The fully adjusted model assessing paternal occupational position as exposure was adjusted for age, height, health risk factors (smoking, sedentary behavior, and body mass index), and history of disease (respiratory and cardiovascular); the fully adjusted model assessing educational level as exposure was adjusted for age, height, paternal occupational position, health risk factors, and history of disease; and the fully adjusted model assessing occupational position as exposure was adjusted for age, height, paternal occupational position, educational level, health risk factors, and history of disease.

Figure 1: Age- and height-adjusted forced expiratory volume in the first second (FEV_1) as a function of age in men and women, along with lung function decline by year for the different age groups, using cross-sectional data.

Figure 2: Years of function lost (YFL) by age 45 due to intermediate or low socioeconomic conditions, based on cross-sectional data. The reference categories were high paternal occupational position, high educational level, and high occupational position. (1) The minimally adjusted model was adjusted for age and height. (2) The fully adjusted model assessing paternal occupational position as exposure was adjusted for age, height, health risk factors (smoking, sedentary behaviour, and body mass index), and history of disease (respiratory and cardiovascular). (2) The fully adjusted model assessing educational level as exposure was adjusted for age, height, paternal occupational position, health risk factors, and history of disease. (2) The fully adjusted model assessing occupational position as exposure was adjusted for age, height, paternal occupational position, educational level, health risk factors, and history of disease.

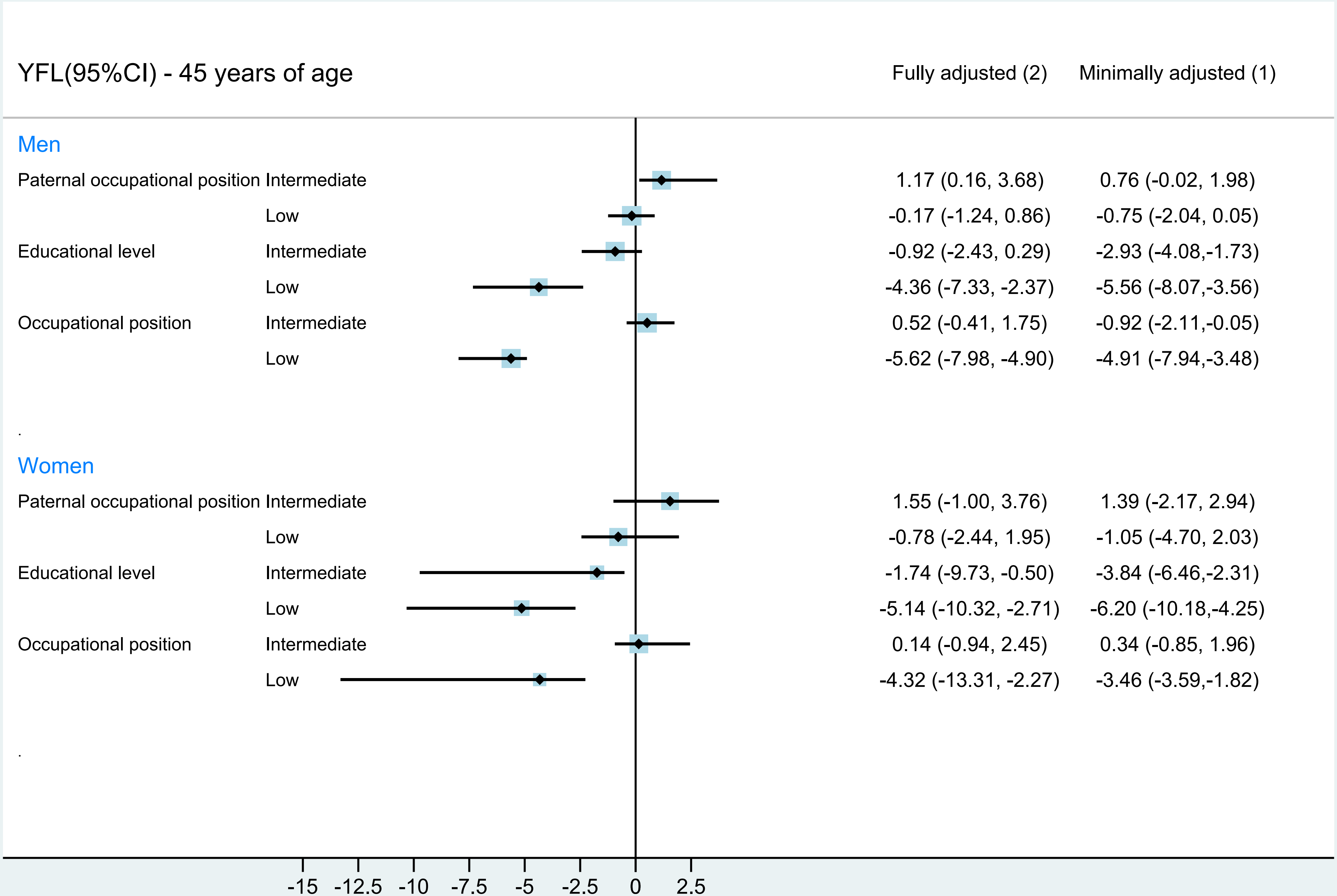
Figure 3: Years of function lost (YFL) by age 65 due to intermediate or low socioeconomic conditions, based on cross-sectional data. The reference categories were high paternal occupational position, high educational level, and high occupational position. (1) The minimally adjusted model was adjusted for age and height. (2) The fully adjusted model assessing paternal occupational position as exposure was adjusted for age, height, health risk factors (smoking, sedentary behaviour, and body mass index), and history of disease (respiratory and cardiovascular). (2) The fully adjusted model assessing educational level as exposure was adjusted for age, height, paternal occupational position, health risk factors, and history of disease. (2) The fully adjusted model assessing occupational position as exposure was adjusted for age, height, paternal occupational position, educational level, health risk factors, and history of disease.

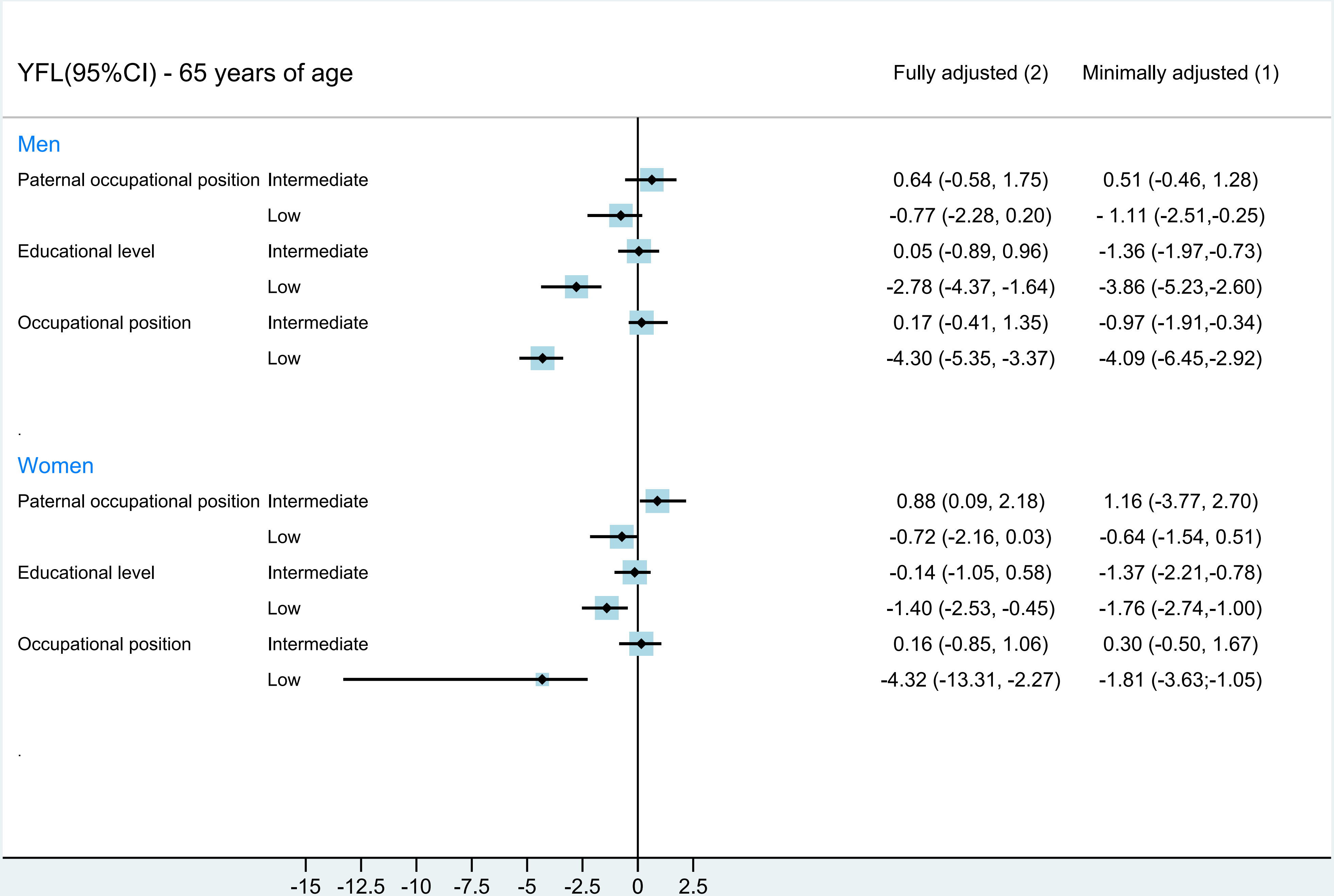
Figure 4: Years of function lost (YFL) by age 85 due to intermediate or low socioeconomic conditions, based on cross-sectional data. The reference categories were high paternal occupational position, high educational level, and high occupational position. (1) The minimally adjusted model was adjusted for age and height. (2) The fully adjusted model assessing paternal occupational position as exposure was adjusted for age, height, health risk factors (smoking, sedentary behaviour, and body mass index), and history of disease (respiratory and cardiovascular). (2) The fully adjusted model assessing educational level as exposure was adjusted for age, height, paternal occupational position, health risk factors, and history of disease. (2) The fully adjusted model assessing occupational position as exposure was adjusted for age, height, paternal occupational position, educational level, health risk factors, and history of disease.



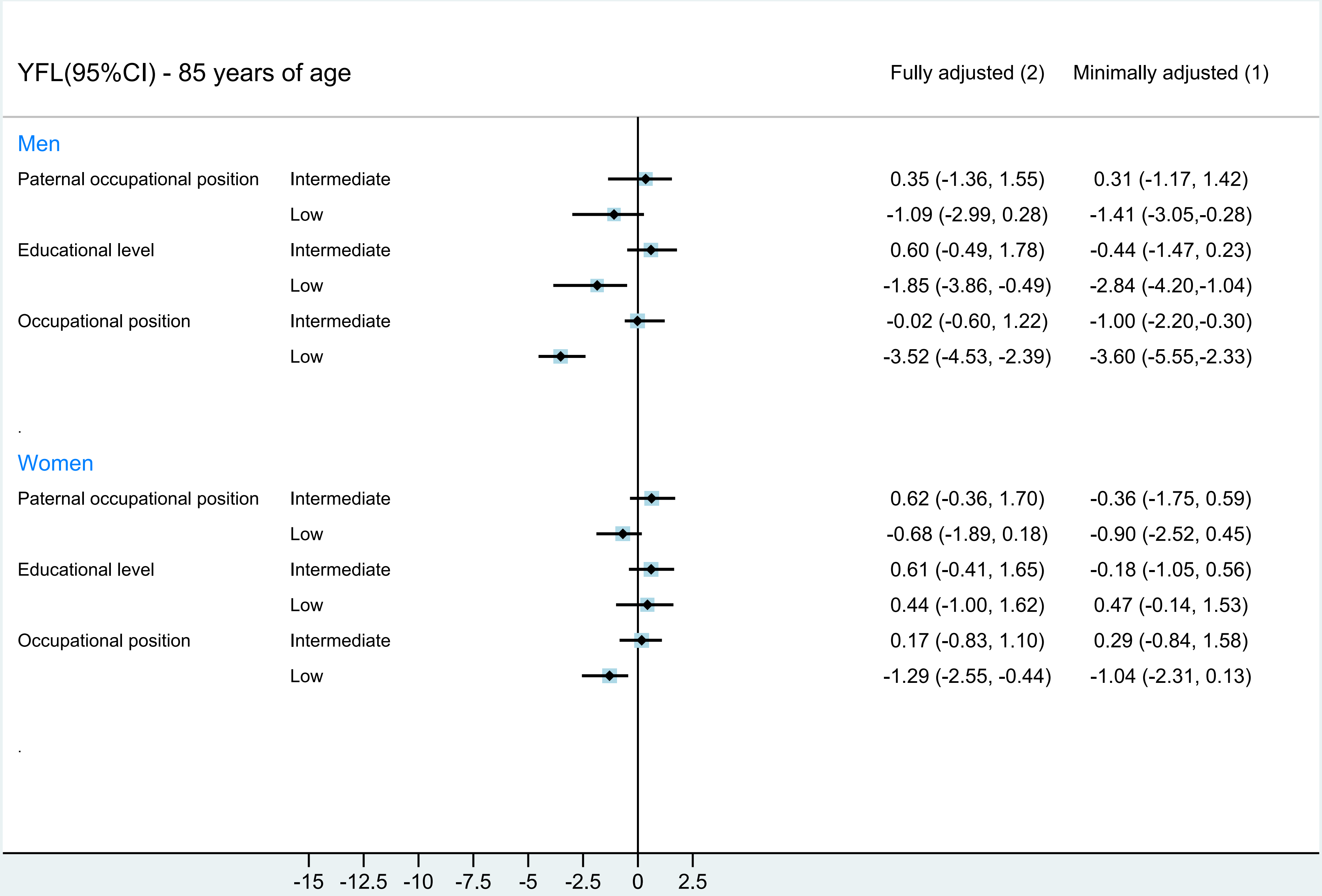
MEN	Age groups, y	Decline/year, mL mean (SD)
	18-24	-11.6 (2.4)
	25-44	-25.1 (11.1)
	45-64	-25.4 (6.8)
	65 or older	-36.2 (17.3)

WOMEN	Age groups, y	Decline/year, mL mean (SD)
	18-24	2.8 (1.0)
	25-44	-15.1 (9.7)
	45-64	-24.2 (6.0)
	65 or older	-27.2 (8.6)


YFL(95%CI) - 45 years of age
Fully adjusted (2)
Minimally adjusted (1)
Men
Paternal occupational position
Intermediate
1.17 (0.16, 3.68)
0.76 (-0.02, 1.98)
Low
-0.17 (-1.24, 0.86)
-0.75 (-2.04, 0.05)
Educational level
Intermediate
-0.92 (-2.43, 0.29)
-2.93 (-4.08,-1.73)
Low
-4.36 (-7.33, -2.37)
-5.56 (-8.07,-3.56)
Occupational position
Intermediate
0.52 (-0.41, 1.75)
-0.92 (-2.11,-0.05)
Low
-5.62 (-7.98, -4.90)
-4.91 (-7.94,-3.48)
Women
Paternal occupational position
Intermediate
1.55 (-1.00, 3.76)
1.39 (-2.17, 2.94)
Low
-0.78 (-2.44, 1.95)
-1.05 (-4.70, 2.03)
Educational level
Intermediate
-1.74 (-9.73, -0.50)
-3.84 (-6.46,-2.31)
Low
-5.14 (-10.32, -2.71)
-6.20 (-10.18,-4.25)
Occupational position
Intermediate
0.14 (-0.94, 2.45)
0.34 (-0.85, 1.96)
Low
-4.32 (-13.31, -2.27)
-3.46 (-3.59,-1.82)
-15
-12.5
-10
-7.5
-5
-2.5
0
2.5



YFL(95%CI) - 65 years of age
Fully adjusted (2)
Minimally adjusted (1)
Men
Paternal occupational position Intermediate
0.64 (-0.58, 1.75)
0.51 (-0.46, 1.28)
Low
-0.77 (-2.28, 0.20)
- 1.11 (-2.51,-0.25)
Educational level Intermediate
0.05 (-0.89, 0.96)
-1.36 (-1.97,-0.73)
Low
-2.78 (-4.37, -1.64)
-3.86 (-5.23,-2.60)
Occupational position Intermediate
0.17 (-0.41, 1.35)
-0.97 (-1.91,-0.34)
Low
-4.30 (-5.35, -3.37)
-4.09 (-6.45,-2.92)
Women
Paternal occupational position Intermediate
0.88 (0.09, 2.18)
1.16 (-3.77, 2.70)
Low
-0.72 (-2.16, 0.03)
-0.64 (-1.54, 0.51)
Educational level Intermediate
-0.14 (-1.05, 0.58)
-1.37 (-2.21,-0.78)
Low
-1.40 (-2.53, -0.45)
-1.76 (-2.74,-1.00)
Occupational position Intermediate
0.16 (-0.85, 1.06)
0.30 (-0.50, 1.67)
Low
-4.32 (-13.31, -2.27)
-1.81 (-3.63;-1.05)
-15
-12.5
-10
-7.5
-5
-2.5
0
2.5


YFL(95%CI) - 85 years of age
Fully adjusted (2)
Minimally adjusted (1)
Men
Paternal occupational position
Intermediate
0.35 (-1.36, 1.55)
0.31 (-1.17, 1.42)
Low
-1.09 (-2.99, 0.28)
-1.41 (-3.05,-0.28)
Educational level
Intermediate
0.60 (-0.49, 1.78)
-0.44 (-1.47, 0.23)
Low
-1.85 (-3.86, -0.49)
-2.84 (-4.20,-1.04)
Occupational position
Intermediate
-0.02 (-0.60, 1.22)
-1.00 (-2.20,-0.30)
Low
-3.52 (-4.53, -2.39)
-3.60 (-5.55,-2.33)
Women
Paternal occupational position
Intermediate
0.62 (-0.36, 1.70)
-0.36 (-1.75, 0.59)
Low
-0.68 (-1.89, 0.18)
-0.90 (-2.52, 0.45)
Educational level
Intermediate
0.61 (-0.41, 1.65)
-0.18 (-1.05, 0.56)
Low
0.44 (-1.00, 1.62)
0.47 (-0.14, 1.53)
Occupational position
Intermediate
0.17 (-0.83, 1.10)
0.29 (-0.84, 1.58)
Low
-1.29 (-2.55, -0.44)
-1.04 (-2.31, 0.13)
-15
-12.5
-10
-7.5
-5
-2.5
0
2.5

Supplementary material

Text S1: Details on study design and participants of the cohorts included in analysis.

COLAUS|PSYCOLAUS. COLAUS|PSYCOLAUS is an ongoing prospective study assessing the clinical, biological, and genetic determinants of cardiovascular disease in the city of Lausanne, Switzerland, and the association of cardiovascular risk factors and diseases with mental disorders. The initial survey was conducted between 2003 and 2006 and included 6733 participants aged between 35 and 75 years; the first follow-up survey was conducted 5.5 years afterwards and included 5064 participants. In each survey, data on socioeconomic status, lifestyle, mental status, and cardiovascular risk factors are collected by questionnaire or clinical examination. https://www.colaus-psycolaus.ch/

CONSTANCES. The CONSTANCES cohort was established in late 2012. Supported by the French National Research Agency (ANR-11-INBS-0002), it was designed as a randomly selected sample of French adults aged 18 to 69 years at inception; at the end of 2019, 215 000 participants were included. At enrolment, the participants complete questionnaires collecting data on health, lifestyle, individual, familial, social, and occupational factors and life events and benefits from a comprehensive health examination. The follow-up includes a yearly self-administered questionnaire, a health examination every four years, and an annual linkage to social and health national databases (Zins et al, 2015). http://www.constances.fr/index_EN.php

ELSA. The English Longitudinal Study of Ageing (ELSA) is a panel study of a representative cohort of men and women living in England aged ≥50 years. It was designed as a sister study to the Health and Retirement Study in the USA and is multidisciplinary in orientation, involving the collection of economic, social, psychological, cognitive, health, biological, and genetic data. The study commenced in 2002, and the sample has been followed up every two years. Data are collected using computer-assisted personal interviews and self-completion questionnaires, with additional nurse visits for the assessment of biomarkers every 4 years. The original sample consisted of 11 391 members, ranging in age from 50 to 100 years. http://www.elsa-project.ac.uk/

EPIPORTO. The EPIPorto study was initiated in 1999 and recruited 2485 adult dwellers aged 18 years or older in the city of Porto, northwest of Portugal. Briefly, simple random digit dialing of landline telephones was used to select households. Most houses (>95%) had a landline telephone at the time of this procedure. A table of random numbers was used to define the last four digits that were specific to individual houses, assuming the local prefix codes to limit the universe to the city of Porto. Nonexisting numbers, those corresponding to fax numbers, or telephone numbers of nonindividual subscribers were ignored. The household was considered unreachable after at least four dialing attempts at different hours and including week and weekend days. Within each household, a permanent resident aged 18 years or older was selected using simple random sampling. The proportion of participation was 70%. A follow-up evaluation was conducted from 2005 to 2008 (participation rate=68% of the baseline sample) by trained interviewers using structured questionnaires and forms, following the same protocol for data collection as at baseline. In both evaluations, participants were invited to visit the Department at Medical School for an interview, which included a questionnaire on social, demographic, behavioural, and clinical data and a physical examination including blood collection. http://ispup.up.pt/research/research-structures/

NCDS. The National Child Development Study (NCDS) recruited 17 415 babies born in one week of 1958 (98.2% of all births that week) in Great Britain (England, Scotland, and Wales). Participants were surveyed at birth and ages 7, 11, 16, 23, 33, 42, 44/45, 46, and 50 years. Information was collected on economic, medical, developmental, and social aspects of participants' lives. At age 46/47 (the cut-off age of this study), a subsample of participants (n=11 881; 77.9% of the target) took part in a biomedical survey (Power & Elliott, 2006).
http://www.cls.ioe.ac.uk/page.aspx?&sitesectionid=724&sitesectiontitle=Welcome+to+the+1958+National+Child+Development+Study

WHITEHALL II. The Whitehall II study was established in 1985 to examine the socioeconomic gradient in health among 10 308 London-based civil servants (6895 men and 3413 women) aged 35 to 55 years. Baseline examination (phase 1) took place during 1985-1988, and involved a clinical examination and a self-administered questionnaire containing sections on demographic characteristics, health, lifestyle factors, work characteristics, social support, and life events. https://www.ucl.ac.uk/whitehallII

Table S1: Spirometry description and information on exclusions from the analysis.

Cohort Study **(Wave, year of test)**	**Test setup**	**N of participants who completed spirometry**	**N of participants with acceptable FEV_1 and FVC** ***Spirometry-related reasons for exclusion**	**N of participants included (with complete information in exposures and outcome)**
COLAUS|PSYCOLAUS (Wave 2, 2014-2017)	Spirometry was performed using SentrySuite Masterscreen PFT equipment (CareFusion, San Diego, USA), according to ATS/ERS recommendations [28], performing a minimum of three acceptable forced manoeuvres. The highest technically acceptable values of FEV_1 and FVC were analysed.	3359	3359	2313
CONSTANCES (Wave 1, 2012-2017)	Spirometry was performed according to ATS/ERS recommendations [28], performing a minimum of three acceptable forced manoeuvres. The highest technically acceptable values of FEV_1 and FVC were analysed.	70 694	70 211 *Incomplete information in FEV_1 or FVC (n=189) *End of test in first second, FEV_1=FVC (n=69) * FEV_1>FVC (n=225)	54 690
ELSA (Wave 6, 2012-2013)	Spirometry was performed using Vitalograph Escort portable spirometer, performing a minimum of three acceptable forced manoeuvres. The highest technically acceptable values of FEV_1 and FVC were analysed.	6875	6819 *Incomplete information in FEV_1 (n=10) *End of test in first second, FEV_1=FVC (n=9) *Sub-maximal effort, FEV_1 < 0.5L (n=24) * FEV_1>FVC (n=13)	2195
EPIPORTO (Wave 2, 2014-2015)	Spirometry was performed using SpiroLab II®, according to ATS/ERS recommendations [28], performing a minimum of three acceptable forced manoeuvres. The highest technically acceptable values of FEV_1 and FVC were analysed.	1496	1460 *End of test in first second, FEV_1=FVC (n=1) *Sub-maximal effort, FEV_1 < 0.5L (n=35)	1274
NCDS (Wave 8 2002-2003)	Spirometry was performed using a Vitalograph Micro hand-held spirometer, performing a minimum of three acceptable forced manoeuvres. The highest technically acceptable values of FEV_1 and FVC were analysed.	9089	9068 *Sub-maximal effort, FEV_1 and FVC < 0.5L (n=1) *End of test in first second, FEV_1=FVC (n=10) * FEV_1>FVC (n=10)	6666
WHITEHALL II (Wave 11, 2012-2013)	Spirometry was performed using a portable flow spirometer (MicroPlus Spirometer; Micro Medical Ltd., Kent, United Kingdom), according to ATS/ERS recommendations [28]. The largest FVC and FEV1 values from three manoeuvres were analysed.	5040	5028 *Sub-maximal effort, FEV_1 < 0.5L (n=2) *End of test in first second, FEV_1=FVC (n=10)	3358

Legend: ATS/ERS, American Thoracic Society/European Respiratory Society; FEV_1: forced expiratory volume in the first second; FVC: forced vital capacity age and height-adjusted; N: number; NA: not applicable.

Lifepath participants with spirometry measurements n=96 600					
COLAUS/PSYCOLAUS	**CONSTANCES**	**ELSA**	**EPIPORTO**	**NCDS**	**WHITEHALL II**
n=3359	n=70 694	n=6922	n=1496	n=9089	n=5040

Excluded from the analyses to harmonise spirometry[1] and with missing information in age and height n=4988					
COLAUS/PSYCOLAUS	**CONSTANCES**	**ELSA**	**EPIPORTO**	**NCDS**	**WHITEHALL II**
n=201	n=483	n=3906	n=174	n=34	n=190

Excluded from the analyses due to missing information in socioeconomic indicators[2] n=21 116					
COLAUS/PSYCOLAUS	**CONSTANCES**	**ELSA**	**EPIPORTO**	**NCDS**	**WHITEHALL II**
n=838	n=15 372	n=915	n=186	n=2282	n=1523

Included in the analyses n= 70 496					
COLAUS/PSYCOLAUS	**CONSTANCES**	**ELSA**	**EPIPORTO**	**NCDS**	**WHITEHALL II**
n=2313	n=54 690	n=2195	n=1274	n=6666	n=3358

Figure S1: Overview of the study flowchart.

[1]Reasons for exclusion were incomplete information for FEV_1 and FVC, tests which ended in the first second or with a volume in the first second higher than total volume.

[2]Included participants had complete information for the three socioeconomic indicators, ie, paternal occupational position, educational level, and occupational position.

Table S2: Comparison of included and excluded participants according to demographic and socioeconomic factors.

	Included	Excluded	p-value
Age, mean (SD), y	48.8 (12.4)	47.8 (15.0)	**<0.001**
Sex, n (%)			**<0.001**
Women	35 653 (50.6)	13 802 (54.6)	
Men	34 843 (49.4)	11 498 (45.4)	
Height, mean (SD), cm	169.1 (9.2)	168.0 (9.3)	**<0.001**
Socioeconomic indicators, n (%)			
Paternal occupational position			0.081
High	13 274 (18.8)	2041 (19.7)	
Intermediate	26 414 (37.5)	3810 (36.8)	
Low	30 808 (43.7)	4490 (43.5)	
Educational level			**<0.001**
High	36 791 (52.2)	7517 (38.4)	
Intermediate	20 393 (28.9)	6 705 (34.2)	
Low	13 312 (18.9)	5355 (27.4)	
Occupational position			**<0.001**
High	22 341 (31.7)	3393 (25.9)	
Intermediate	25 861 (35.3)	4899 (37.4)	
Low	23 294 (33.0)	4814 (36.7)	

Legend: In bold statistically significant values.

Table S3: Characteristics of participants included by sex and cohort (n=70 496).

	MEN (n=26 876)						**WOMEN** (n=26 912)					
	COLAUS|PSYCOLAUS (n=1140)	**CONSTANCES** (n=26 238)	**ELSA** (n=1055)	**EPIPORTO** (n=518)	**NCDS** (n=3444)	**WHITEHALL II** (n=2448)	**COLAUS|PSYCOLAUS** (n=1173)	**CONSTANCES** (n=28 452)	**ELSA** (n=1140)	**EPIPORTO** (n=756)	**NCDS** (n=3222)	**WHITEHALL II** (n=910)
Baseline year	2003	2012	2002	1999/2003	1958	1985/1988	2003	2012	2002	1999/2003	1958	1985/1988
DEMOGRAPHICS, ANTHROPOMETRICS												
Age, mean (SD), y	54.5 (8.6)	48.5 (12.7)	70.5 (7.2)	57.9 (14.3)	45.7 (1.1)	48.9 (5.6)	54.5 (8.3)	47.4 (12.7)	70.4 (7.2)	57.1 (13.0)	45.8 (1.0)	49.2 (5.9)
Age groups, n (%)												
18-44	153 (13.4)	10 091 (38.5)	-	98 (18.9)	254 (7.4)	646 (26.4)	163 (13.9)	11 855 (41.7)	-	144 (19.0)	180 (5.6)	227 (24.9)
45-64	802 (70.4)	12 781 (48.7)	242 (22.9)	238 (45.9)	3190 (92.6)	1802 (73.6)	845 (72.0)	13 579 (47.7)	297 (26.1)	379 (50.1)	3042 (94.4)	683 (75.1)
65 or older	185 (16.2)	3366 (12.8)	813 (77.1)	182 (35.1)	-	-	165 (14.1)	3018 (10.6)	843 (73.9)	233 (30.8)	-	-
Height, mean (SD), cm	175.6 (7.2)	175.9 (6.7)	173.0 (6.9)	169.0 (7.0)	176.2 (6.6)	174.5 (6.8)	163.5 (6.6)	163.1 (6.3)	159.5 (6.4)	155.4 (5.9)	162.7 (6.1)	160.2 (6.5)
Weight, mean (SD), kg	82.1 (13.3)	79.3 (12.7)	84.1 (14.4)	76.0 (12.7)	86.4 (14.1)	81.0 (13.1)	66.6 (12.3)	64.5 (12.5)	71.1 (14.6)	67.7 (32.4)	71.0 (14.6)	69.4 (14.8)
LUNG FUNCTION, mean (SD), mL												
FEV_1	3384.6 (484.0)	3533.4 (523.2)	2843.3 (498.1)	2915.5 (601.3)	3629.1 (370.5)	3447.9 (434.2)	2701.1 (441.8)	2832.2 (500.1)	2085.9 (480.8)	2174.6 (538.5)	2865.2 (344.5)	2635.3 (430.8)
FVC	4345.7 (614.8)	4475.4 (620.3)	3771.0 (602.3)	3745.9 (699.0)	4614.6 (496.6)	4390.1 (563.1)	3428.5 (560.8)	3524.4 (587.1)	2753.7 (574.2)	2745.0 (621.3)	3591.2 (461.2)	3302.0 (553.9)
SOCIOECONOMIC STATUS, n (%)												
Paternal occupational position (ESEC class)												
High (1-3)	386 (33.9)	5249 (20.0)	103 (9.8)	77 (14.9)	223 (6.5)	247 (10.1)	368 (31.4)	6115 (21.5)	123 (10.8)	96 (12.7)	189 (5.9)	98 (10.8)
Intermediate (4-6)	430 (37.7)	10 578 (40.3)	396 (37.5)	112 (21.6)	565 (16.4)	818 (33.4)	462 (39.4)	11 642 (40.9)	464 (40.7)	165 (21.8)	516 (16.0)	266 (29.2)
Low (7-9)	324 (28.4)	10 411 (39.7)	556 (52.7)	329 (63.5)	2656 (77.1)	1383 (56.5)	343 (29.2)	10 695 (37.6)	553 (48.5)	495 (65.5)	2517 (78.1)	546 (60.0)
Participants' educational level												
High (tertiary school)	453 (39.7)	14 807 (56.4)	265 (25.1)	147 (28.4)	675 (19.6)	998 (40.8)	429 (36.6)	17 788 (62.5)	171 (15.0)	220 (29.1)	574 (17.8)	264 (29.0)
Intermediate (Higher secondary)	201 (17.6)	9465 (36.1)	315 (29.9)	82 (15.8)	140 (4.1)	742 (30.3)	186 (15.9)	8519 (29.9)	254 (22.3)	96 (12.7)	204 (6.3)	189 (20.8)
Low (Primary/ lower secondary)	486 (42.7)	1966 (7.5)	475 (45.0)	289 (55.8)	2629 (76.3)	708 (28.9)	558 (47.6)	2145 (7.5)	715 (62.7)	440 (58.2)	2444 (75.9)	457 (50.2)
Participants' occupational position (ESEC class)												
High (1-3)	319 (28.0)	10 533 (40.1)	254 (24.1)	124 (23.9)	1149 (33.4)	1693 (69.2)	115 (9.8)	7144 (25.1)	74 (6.5)	153 (20.2)	530 (16.4)	253 (27.8)
Intermediate (4-6)	432 (37.9)	7985 (30.4)	519 (49.2)	151 (29.2)	1242 (36.1)	657 (26.8)	396 (33.8)	10 302 (36.2)	696 (61.1)	130 (17.2)	1987 (61.7)	364 (40.0)
Low (7-9)	389 (34.1)	7720 (29.4)	282 (26.7)	243 (46.9)	1053 (30.5)	98 (4.0)	662 (56.4)	11 006 (38.7)	370 (32.5)	473 (62.6)	705 (21.9)	293 (32.2)
HEALTH RISK FACTORS, n (%)												
Smoking												
Never	437 (38.3)	10 413 (41.3)	305 (28.9)	152 (29.3)	1618 (47.0)	1069 (44.4)	520 (44.3)	13 749 (50.3)	501 (43.9)	543 (71.8)	1593 (49.5)	489 (55.5)
Former	457 (40.1)	10 065 (39.9)	616 (58.4)	228 (44.0)	1009 (29.3)	1260 (52.3)	403 (34.4)	8642 (31.6)	468 (41.1)	116 (15.4)	849 (26.4)	358 (40.6)
Current	246 (21.6)	4760 (18.9)	134 (12.7)	138 (26.6)	816 (23.7)	78 (3.3)	250 (21.3)	4966 (18.2)	171 (15.0)	97 (12.8)	779 (24.2)	34 (3.9)
Sedentary behavior (yes)	46 (4.7)	5932 (23.2)	237 (22.5)	380 (73.4)	1687 (54.1)	637 (26.1)	537 (51.5)	6227 (22.6)	328 (28.8)	582 (77.0)	1052 (35.3)[2]	343 (37.7)
BMI												
Under/normal weight	416 (36.5)	12 523 (48.0)	241 (22.8)	166 (32.0)	826 (24.0)	893 (36.5)	679 (57.9)	18 646 (65.9)	374 (32.9)	257 (34.0)	1411 (43.8)	365 (40.1)
Overweight/obese	724 (63.5)	13 560 (52.0)	814 (77.2)	352 (68.0)	2616 (76.0)	1555 (63.5)	494 (42.1)	9662 (34.1)	763 (67.1)	499 (66.0)	1810 (56.2)	545 (59.9)
DISEASE HISTORY, n (%)												
Cardiovascular disease	47 (4.1)	691 (2.6)	141 (13.4)	61 (11.8)	243 (7.1)	498 (20.3)	21 (1.8)	229 (0.8)	85 (7.5)	66 (8.7)	238 (7.4)	192 (21.1)
Respiratory disease	82 (7.2)	3749 (14.3)	143 (13.6)	48 (9.3)	238 (6.9)	408 (17.9)	109 (9.3)	3759 (13.2)	216 (18.9)	90 (11.9)	309 (9.6)	220 (26.0)

Legend: ESEC, European Socioeconomic Classification; FEV_1: forced expiratory volume in the first-second age and height-adjusted; FVC: forced vital capacity age and height-adjusted; BMI: body mass index; mL: millilitres.

Table S4: Serially adjusted association of life-course socioeconomic disadvantage with lung function by sex.

	FVC differences, B (95% CI), mL			
	MEN		WOMEN	
	Minimally adjusted model[1]	Fully adjusted model[2]	Minimally adjusted model[1]	Fully adjusted model[2]
Paternal occupational position				
High	Reference	Reference	Reference	Reference
Intermediate	**-197.1 (-215.7; -178.4)**	**-166.2 (-185.1; -147.3)**	**-200.0 (-217.2; -182.8)**	**-173.3 (-190.7; -155.9)**
Low	**-240.3 (-258.4; -222.1)**	**-198.5 (-217.1; -180.0)**	**-253.6 (-270.5; -236.8)**	**-208.7 (-226.0; -191.5)**
Participants' educational level				
High	Reference	Reference	Reference	Reference
Intermediate	**-245.8 (-260.5; -231.2)**	**-189.4 (-205.0; -173.8)**	**-274.3 (-288.5; -260.1)**	**-233.1 (-248.2; -218.0)**
Low	**-299.4 (-316.8; -282.0)**	**-227.0 (-246.2; -207.8)**	**-414.3 (-430.3; -398.3)**	**-351.6 (-369.4; -333.8)**
Participants' occupational position				
High	Reference	Reference	Reference	Reference
Intermediate	**-116.1 (-131.6; -100.5)**	-17.3 (-33.7; -1.0)	**-143.5 (-159.7; -127.2)**	**-35.9 (-52.4; -19.4)**
Low	**-131.2 (-147.3; -115.1)**	21.1 (2.3; 39.9)	**-220.9 (-237.2; -204.6)**	-0.5 (-19.0; 18.1)

Legend: FVC: forced vital capacity; B: beta-coefficient of linear regression models; CI: confidence interval; In bold statistically significant values.

[1] The minimally adjusted model was adjusted for age and height.

[2] The fully adjusted model assessing paternal occupational position as exposure was adjusted for age, height, health risk factors (smoking, sedentary behaviour, and body mass index), and history of disease (respiratory and cardiovascular); the fully adjusted model assessing educational level as exposure was adjusted for age, height, paternal occupational position, health risk factors, and history of disease; and the fully adjusted model assessing occupational position as exposure was adjusted for age, height, paternal occupational position, educational level, health risk factors, and history of disease.

Table S5: Years of lung function lost in FVC by ages 45, 65, and 85 years due to intermediate or low socioeconomic conditions.

		Years of function lost (95% CI) in FVC			
		MEN		WOMEN	
At age 45 y		Minimally adjusted models[1]	Fully adjusted models[2]	Minimally adjusted models[1]	Fully adjusted models[2]
Paternal occupational position	Intermediate	0.87 (-0.46; 2.60)	**1.96 (0.52; 5.68)**	1.74 (-0.05; 3.95)	1.26 (-0.48; 3.21)
	Low	-0.70 (-2.37; 0.23)	0.46 (-0.70; 2.13)	**-4.99 (-7.32; -2.31)**	0.42 (-1.41; 3.72)
Educational level	Intermediate	**-3.21 (-4.44; -1.87)**	-0.47 (-2.24; 1.23)	**-7.18 (-9.86; -1.53)**	-3.43 (-8.05; 0.42)
	Low	**-6.29 (-9.21; -4.04)**	**-4.08 (-6.69; -2.13)**	**-8.45 (-10.53; -6.80)**	**-8.71 (-12.85; -4.35)**
Occupational position	Intermediate	-0.83 (-2.53; 0.38)	1.32 (-0.53; 4.30)	1.63 (-1.72; 3.04)	3.10 (-0.52; 6.32)
	Low	**-5.13 (-8.37; -3.62)**	**-5.24 (-8.34 ; -3.04)**	-2.30 (-4.30; 0.47)	-1.15 (-3.83; 0.41)
At age 65 y					
Paternal occupational position	Intermediate	-0.31 (-0.78; 1.14)	0.51 (-0.75; 1.53)	0.82 (-1.08; 2.39)	0.56 (-0.35; 1.54)
	Low	-0.79 (-2.16; 0.12)	-0.15 (-1.44; 0.85)	-1.62 (-3.11; 0.12)	-1.62 (-3.17; 0.28)
Educational level	Intermediate	**-1.46 (-2.18; -0.80)**	0.25 (-0.75; 1.20)	**-2.13 (-6.15; -1.12)**	-0.96 (-1.89; 3.09)
	Low	**-3.80 (-5.29; -2.64)**	**-2.23 (-3.71; -1.21)**	**-2.72 (-5.51; -1.64)**	-2.55 (-7.57; 3.45)
Occupational position	Intermediate	**-0.88 (-1.85; -0.23)**	0.48 (-0.93; 1.79)	-0.26 (-2.32; 0.88)	-0.87 (-2.71; 2.32)
	Low	**-3.74 (-5.62; -2.66)**	**-3.50 (-4.96; -2.17)**	-2.62 (-4.70; 0.40)	-3.41 (-5.22; 0.66)
At age 85 y					
Paternal occupational position	Intermediate	-0.07 (-1.57; 1.05)	-0.05 (-1.62; 1.24)	0.65 (-1.27; 1.51)	0.31 (-0.61; 1.51)
	Low	-0.84 (-2.41; 0.35)	-0.38 (-2.02; 0.91)	**-1.21 (-3.28; -0.30)**	**-1.40 (-2.86; -0.61)**
Educational level	Intermediate	-0.61 (-1.63; 0.07)	0.58 (-0.47; 1.64)	**-0.96 (-1.81; -0.34)**	-0.34 (-1.29; 0.55)
	Low	**-2.53 (-3.80; -0.78)**	**-1.36 (-3.18; -0.06)**	-0.88 (-1.50; 0.15)	-1.00 (-2.38; 0.22)
Occupational position	Intermediate	**-0.89 (-2.09; -0.21)**	0.14 (-1.43; 1.70)	-0.49 (-1.76; 0.84)	-0.88 (-1.95; 0.01)
	Low	**-3.05 (-4.74; -1.91)**	**-2.67 (-3.93; -1.36)**	**-1.97 (-3.34; -0.93)**	**-2.37 (-3.65; -1.46)**

Legend: FVC: forced vital capacity; The reference categories were high paternal occupational position, high education and high occupation; In bold statistically significant values.

[1] The minimally adjusted model was adjusted for age and height.

[2] The fully adjusted model assessing paternal occupational position as exposure was adjusted for age, height, health risk factors (smoking, sedentary behaviour, and body mass index), and history of disease (respiratory and cardiovascular). The fully adjusted model assessing educational level as exposure was adjusted for age, height, paternal occupational position, health risk factors, and history of disease. The fully adjusted model assessing occupational position as exposure was adjusted for age, height, paternal occupational position, educational level, health risk factors, and history of disease.

Table S6: Association of life-course socioeconomic disadvantage with lung function, stratified by smoking status and sex.

	FEV_1 differences, B (95% CI), mL		
	NEVER SMOKERS	FORMER SMOKERS	CURRENT SMOKERS
MEN			
Paternal occupational position			
High	Reference	Reference	Reference
Intermediate	**-175.2 (-199.5; -150.9)**	**-174.9 (-199.7; -150.2)**	**-146.8 (-183.1; -110.5)**
Low	**-209.1 (-232.7; -185.5)**	**-205.4 (-229.6; -181.2)**	**-185.5 (-220.1; -150.9)**
Participants' educational level			
High	Reference	Reference	Reference
Intermediate	**-248.1 (-267.7; -228.4)**	**-181.1 (-200.1; -162.1)**	**-158.9 (-187.2; -130.6)**
Low	**-291.1 (-314.5; -267.8)**	**-240.9 (-263.7; -218.1)**	**-280.1 (-311.8; -248.4)**
Participants' occupational position			
High	Reference	Reference	Reference
Intermediate	**-91.9 (-112.0; -71.8)**	**-95.7 (-115.8; -75.5)**	**-83.1 (-115.5; -50.7)**
Low	**-108.4 (-130.1; -86.7)**	**-95.0 (-116.5; -73.5)**	**-59.7 (-90.0; -29.4)**
WOMEN			
Paternal occupational position			
High	Reference	Reference	Reference
Intermediate	**-216.0 (-238.1; -193.8)**	**-146.5 (-171.3; -121.8)**	**-144.6 (-171.0; -118.2)**
Low	**-263.6 (-285.1; -241.9)**	**-169.6 (-194.1; -145.0)**	**-301.0 (-329.9; -272.2)**
Participants' educational level			
High	Reference	Reference	Reference
Intermediate	**-319.8 (-337.4; -302.1)**	**-181.0 (-201.9; -160.1)**	**-154.6 (-182.8; -126.4)**
Low	**-469.0 (-488.4; -449.5)**	**-296.3 (-320.6; -271.9)**	**-283.9 (-313.7; -254.1)**
Participants' occupational position			
High	Reference	Reference	Reference
Intermediate	**-153.8 (-174.1; -133.4)**	**-116.4 (-139.9; -93.0)**	**-69.5 (-101.4; -37.7)**
Low	**-255.5 (-276.1; -234.9)**	**-120.4 (-144.7; -96.2)**	**-61.8 (-92.4; -31.2)**

Legend: FEV_1: forced expiratory volume in the first-second; B: beta-coefficient of linear regression models age- and height-adjusted; CI: confidence interval; In bold statistically significant values.

Table S7: Association of life-course socioeconomic disadvantage with lung function, stratified by smoking intensity and sex.

FEV_1 differences (mL) – B (95%CI)[1]	**Smoking intensity**	
	1-20 cigarettes per day	≥21 cigarettes per day
MEN (n=6216)		
Paternal occupational position		
High	Reference	Reference
Intermediate	**-205.0 (-246.0; -163.9)**	**-111.0 (-186.0; -36.0)**
Low	**-244.7 (-285.3; -204.0)**	**-262.7 (-335.1; -190.3)**
Own educational level		
High	Reference	Reference
Intermediate	**-161.6 (-194.4; -128.8)**	**-176.1 (-232.2; -120.0)**
Low	**-369.6 (-410.5; -328.8)**	**-505.3 (-568.3; -442.2)**
Own occupational position		
High	Reference	Reference
Intermediate	**-72.2 (-108.6; -35.8)**	**-144.3 (-206.9; -81.7)**
Low	**-87.1 (-123.7; -50.4)**	**-199.6 (-262.3; -136.8)**
WOMEN (n=8187)		
Paternal occupational position		
High	Reference	Reference
Intermediate	**-132.4 (-163.1; -101.7)**	**-259.7 (-313.4; -205.9)**
Low	**-190.2 (-221.0; -159.3)**	**-477.5 (-548.7; -406.3)**
Own educational level		
High	Reference	Reference
Intermediate	**-191.5 (-217.3; -165.7)**	**-188.7 (-234.4; -142.9)**
Low	**-390.8 (-424.7; -356.9)**	**-411.4 (-494.8; -328.0)**
Own occupational position		
High	Reference	Reference
Intermediate	**-93.8 (-124.8; -62.8)**	**-115.0 (-180.4; -49.6)**
Low	**-97.2 (-127.6; -66.9)**	**-144.0 (-208.1; -79.9)**

Legend: FEV_1: forced expiratory volume in the first-second; B: beta-coefficient of linear regression models age- and height-adjusted; CI: confidence interval; In bold statistically significant values.

Table S8: Years of lung function lost in FEV_1 by ages 45, 65, and 85 years due to intermediate or low socioeconomic conditions using the total sample (n= 96 553).

		Years of function lost (95%CI) in FEV_1	
		Fully adjusted models[1]	
At age 45 y		MEN	WOMEN
Paternal occupational position	Intermediate	0.86 (-0.05; 2.48)	0.89 (-0.03; 2.02)
	Low	-0.66 (-1.58; 0.32)	**-1.39 (-2.61; -0.58)**
Educational level	Intermediate	**-1.86 (-3.51; -0.75)**	**-1.75 (-3.28; -0.67)**
	Low	**-5.00 (-7.93; -3.45)**	**-6.16 (-9.16; -4.18)**
Occupational position	Intermediate	-0.73 (-2.05; 0.05)	-0.21 (-1.78; 0.89)
	Low	**-6.30 (-9.79; -4.45)**	**-6.53 (-9.56; -4.45)**
At age 65 y			
Paternal occupational position	Intermediate	**0.77 (0.01; 1.85)**	**0.83 (0.12; 1.77)**
	Low	-0.69 (-1.55; 0.09)	-0.66 (-1.52; 0.12)
Educational level	Intermediate	-0.43 (-1.25; 0.48)	-0.25 (-1.23; 0.48)
	Low	**-3.09 (-4.36; -2.15)**	**-2.37 (-3.31; -1.55)**
Occupational position	Intermediate	0.12 (-0.60; 1.28)	0.67 (-0.36; 1.34)
	Low	**-4.16 (-5.63; -3.11)**	**-2.59 (-3.68; -1.95)**
At age 85 y			
Paternal occupational position	Intermediate	0.73 (-0.47; 1.99)	0.81 (-0.05; 1.71)
	Low	-0.70 (-1.85; 0.36)	-0.33 (-1.37; 0.60)
Educational level	Intermediate	0.37 (-0.40; 1.72)	0.47 (-0.45; 1.21)
	Low	**-2.00 (-3.05; -0.84)**	-0.46 (-1.30; 0.55)
Occupational position	Intermediate	0.60 (-0.19; 2.02)	1.09 (-0.04; 1.79)
	Low	**-2.91 (-4.03; -1.72)**	-0.56 (-1.64; 0.17)

Legend: FEV_1: forced expiratory volume in the first-second; The reference categories were high paternal occupational position, high educational level, and high occupational position.

[1]The fully adjusted model assessing paternal occupational position as exposure was adjusted for age, height, health risk factors (smoking, sedentary behaviour and BMI) and history of disease (respiratory and cardiovascular). The fully adjusted model assessing educational level as exposure was adjusted for age, height, paternal occupational position, health risk factors and history of disease. The fully adjusted model assessing occupational position as exposure was adjusted for age, height, paternal occupational position, educational level, health risk factors and history of disease.