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Does educational level influence lung function decline (Doetinchem Cohort Study)?

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ABSTRACT: Low socioeconomic status is associated with reduced lung function in adults. In addition, there are indications that lung function decline with age is accelerated in low socioeconomic groups, but, to date, findings have been inconclusive.

In order to investigate the relation between educational level, forced expiratory volume in 1 s (FEV_1) and decline in FEV_1 over time, linear mixed-effects models were fitted to baseline and 10-yr-follow-up data from the Doetinchem Cohort Study. The study population (26–66 yrs at baseline) consisted of 2,679 males and 3,026 females with an FEV_1 measurement in at least one of the three rounds of follow-up and information on relevant covariables. High educational level was used as the reference class.

Low educational level was associated with a higher prevalence of smoking and with a lower smoking-adjusted FEV_1 at baseline (-148 mL in males and -47 mL in females). In females, low educational level was associated with a faster FEV_1 decline (3.4 $mL \cdot yr^{-1}$, age- and height-adjusted), which was not explained by smoking. In males, no differences in rates of decline between educational levels were observed.

FEV_1 decline was faster in less-educated females, independent of smoking. In males, FEV_1 decline did not differ between educational levels.

KEYWORDS: **Education, lung function, sex, smoking, socioeconomic status**

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The impact of chronic obstructive pulmonary disease (COPD), in terms of morbidity, mortality and healthcare costs, is expected to grow substantially until ~2030, mainly due to ageing of the global population [1]. Impaired lung function is a hallmark of COPD [2]. It is also a risk factor for mortality from a wide range of other diseases, including cardiovascular disease and cancer [3, 4].

There is an intriguing, but still insufficiently explored, relation between lung function and socioeconomic status. Low socioeconomic status is associated with a higher risk of COPD [5]. Several cross-sectional studies have reported an association between low socioeconomic status and reduced forced expiratory volume in 1 s (FEV_1) or forced vital capacity (FVC) in adults, independent of smoking status [6–10]. In some studies, a larger socioeconomic gradient was observed in males than in females [6, 8, 9].

Reduced lung function in adults may result from suboptimal development of lung function during childhood and adolescence, or from accelerated lung function decline with age [11]. A more rapid decline in lung function with age is especially seen in smokers [2, 11]. As smoking is more prevalent among those of low socioeconomic status [6, 9, 12], it is likely that accelerated lung function decline with age is associated with low socioeconomic status. In addition, socioeconomic status might have an effect upon lung function decline independent of smoking. One of the few studies reporting on this subject observed that low educational level was associated with a faster FEV_1 decline in males but not in females [13]. Another study in males observed that low educational level was associated with rapid decline in FEV_1 in never-smokers alone [14].

In the present article, the longitudinal association between baseline educational level (as a proxy of socioeconomic status) and the rate of FEV_1 decline was investigated during 10 yrs of follow-up using data from the Doetinchem Cohort Study on 2,679 males and 3,026 females aged 26–66 yrs at baseline. Furthermore, the educational gradient in baseline FEV_1 is reported on.

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SUBJECTS AND METHODS

Study population

A detailed description of the prospective Doetinchem Cohort Study has been published previously [15]. Initially, 12,405 inhabitants of Doetinchem, a town in a rural area of the Netherlands, aged 20–59 yrs participated in the Monitoring Project on Cardiovascular Disease Risk Factors between 1987 and 1991 (first examination round). A total of 7,769 of these participants were reinvited between 1993 and 1997 (79% participation rate). For the third and fourth rounds, all persons invited for the previous round were invited again, with the exception of those who had died or emigrated during follow-up or who had actively refused to participate in the previous round. The participation rate was 75% (of 6,579) in 1998–2002 and 79% (of 4,925) in 2003–2006. Participation rates in rounds 2–4 were comparable in males and females, but were clearly lower in those with a low (60–67% in males and 59–73% in females) than those with a high level of education (85–87% in males and 85–89% in females) (for definition of educational level, see Methods section).

Since pulmonary function was only measured from 1994 onwards, in the present article, the second round is referred to as the baseline examination. The numbers of persons who underwent a pulmonary function test in rounds 2–4 were 4,916, 4,836 and 3,874, respectively. Pulmonary function data were not yet available for 2007 at the time of the present analysis. Approximately 95% of all measurements performed were technically acceptable and reproducible (valid FEV_1). The study population consisted of persons with a valid FEV_1 in all three rounds (n=2,282), persons with a valid FEV_1 in two of the three rounds (n=2,335) and persons with a valid FEV_1 in one of the three rounds (n=1,426). Records (n=817) were excluded from the analysis because of pregnancy at that time or missing data for educational level or the main covariates. The final study population consisted of 2,679 males (5,760 records) and 3,026 females (6,365 records).

Methods

Information on demographic variables, presence of chronic diseases and risk factors, including diet, were collected using standardised questionnaires at baseline and follow-up [15]. Dietary intake data for 2003–2006 were not available at the time the present article was written. The physical examination included measurement of pulmonary function, weight and height.

Pulmonary function measurements were performed by trained paramedics using a heated pneumotachometer (Jaeger, Hochberg, Germany). Measurements were made with the participants in a sitting position while wearing a nose clip. At least three technically acceptable FEV_1 manoeuvres had to be achieved, of which two had to be reproducible according to European Respiratory Society criteria [16]. The maximum value of the reproducible manoeuvres was used in the analysis. Only pre-bronchodilator spirometry was performed.

Educational level was used as an indicator of socioeconomic status and was categorised into: low (intermediate secondary education or less), intermediate (intermediate vocational or higher secondary education), and high (higher vocational or university education). Five categories of smoking status were defined: current smoker (smoking cigarettes: with filter, without filter, and unknown), former smoker, and never-smoker. Cumulative cigarette smoking (in pack-years) was calculated as the product of the number of years smoked and the mean number of cigarettes smoked daily, divided by 20. The presence of COPD symptoms was defined as one or more of the following symptoms: chronic cough, chronic phlegm, or breathlessness when walking on level ground with people of the same age. Body mass index (BMI) was calculated as weight (in kilograms) divided by height (in metres) squared. Physical activity was categorised into four levels based on the number of hours per week spent on moderate or intense activity (1: $\leqslant 0.5\ h \cdot week^{-1}$, 2: $0.5–3.5\ h \cdot week^{-1}$, 3: $\geqslant 3.5\ h \cdot week^{-1}$ with $<2\ h \cdot week^{-1}$ of intense activity, and 4: $\geqslant 3.5\ h \cdot week^{-1}$ with $\geqslant 2\ h \cdot week^{-1}$ of intense activity) [17].

Statistical analyses

All analyses were performed using the SAS statistical package (version 9.1; SAS Institute, Cary, NC, USA), and for males and females separately. Linear mixed-effects models for the analysis of repeated measures (PROC MIXED; estimation by restricted maximum likelihood) were used to study baseline educational level in relation to baseline FEV_1 and to FEV_1 decline during follow-up. This statistical method takes into account the fact that repeated measurements in the same individual are not independent. It, furthermore, permits individuals to have unequal numbers of observations. Only persons with a valid FEV_1 in at least two rounds contributed to the estimation of FEV_1 decline. The random-effects portion of the model consisted only of a random intercept. Specification of a random slope also did not alter the results in a relevant way, and these data are not presented.

In order to properly adjust for age and height, the mixed-effects models contained baseline values of age, age squared, height and height squared as covariates. In order to estimate age-related decline in FEV_1, time of follow-up and an interaction term of baseline age with time were included. Time of follow-up was modelled in years (0, 5 and 10) from the baseline examination of pulmonary function. The interaction term of baseline age with time was included to permit the decline in lung function to vary with baseline age (stronger decline in older subjects). Baseline age was centred at 45 yrs, and the regression coefficient for time, therefore, represents the mean decline in FEV_1 for a 45-yr-old person.

Subsequently, baseline educational level was entered into this model as a main effect on baseline FEV_1. In order to investigate differences in lung function decline during follow-up between levels of baseline education, an interaction term of education with time was included. In this model containing an interaction term with time, the regression coefficient for time represents the FEV_1 decline in the participants with the highest level of education (reference class). Similar models were used to study the effect of baseline smoking status on baseline FEV_1 and on FEV_1 decline.

Adjustments for smoking were performed by inclusion in the model of the smoking history in pack-years at baseline, as well as smoking status and the number of cigarettes smoked as time-dependent variables. That is, in each round, smoking status and the number of cigarettes smoked were updated.

TABLE 1 Characteristics of the study population at baseline and forced expiratory volume in 1 s (FEV_1) in the three rounds by educational level#: males

	Educational level		
	High (ref)	Intermediate	Low
Subjects at baseline n	491	672	941
Age yrs	46.8±9.2	43.3±10.0***	47.5±9.7
Height m	1.81±0.07	1.80±0.07	1.78±0.07***
Smoking¶ %			
Current smokers	18.7	29.3	41.3
Former smokers	41.1	38.2	38.6
Never-smokers	40.1	32.4	20.1
Smoking history pack-yrs			
Current smokers	18.5±12.2	17.1±12.5	22.6±14.5**
Former smokers	14.0±14.3	14.7±15.1	17.5±16.3*
Lifestyle %			
Overweight+	46.6	54.6**	61.5***
Physical activity (intense)§	25.3	22.2	14.3***
Intake			
Fruit/veg $g \cdot day^{-1 f}$	290±6.4	256±5.5***	260±4.6***
Wholegrain $g \cdot day^{-1 f}$	87±3.6	61±3.1***	54±2.6***
Alcohol (1–3 $gl \cdot day^{-1}$) %	39.2	36.6	30.1***
FEV_1 mL##			
Round 2: 1994–1997¶¶	4157±25	4042±22***	3935±18***
Round 3: 1998–2002++	3958±23	3855±21**	3776±18***
Round 4: 2003–2006§§	3861±26	3755±24**	3688±21***

Data are presented as mean±SD except for intake and FEV_1 which are presented as mean±SEM, unless otherwise stated. ref: reference; gl: glass. #: low: intermediate secondary education or less; intermediate: intermediate vocational or higher secondary education; and high: higher vocational or university education; ¶: association between smoking status and educational level of $p<0.0001$ (Chi-squared test); +: body mass index $>25\ kg \cdot m^{-2}$; §: $\geqslant 3.5\ h \cdot week^{-1}$ of moderate or intense activity, of which $\geqslant 2\ h \cdot week^{-1}$ is intense activity; f: adjusted for total energy intake; ##: adjusted for age, age squared, height and height squared; ¶¶: baseline examination of pulmonary function; ++: n=974, 687 and 560; §§: n=723, 566 and 468. *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$ *versus* reference class.

TABLE 2 Characteristics of the study population at baseline and forced expiratory volume in 1 s (FEV_1) in the three rounds by educational level#: females

	Educational level		
	High (ref)	Intermediate	Low
Subjects at baseline n	351	542	1432
Age yrs	44.4±8.5	41.2±9.6***	47.3±9.8***
Height m	1.68±0.06	1.68±0.06	1.65±0.06***
Smoking¶ %			
Current smokers	24.8	31.2	35.4
Former smokers	39.0	32.3	30.5
Never-smokers	36.2	36.5	34.2
Smoking history pack-yrs			
Current smokers	13.4±10.3	13.4±9.2	17.3±10.3**
Former smokers	8.4±8.8	7.2±7.3	10.5±13.0
Lifestyle %			
Overweight+	29.1	32.7	51.8***
Physical activity (intense)§	15.7	11.8	6.8***
Intake			
Fruit/veg $g \cdot day^{-1 f}$	343±7.3	319±5.9*	291±3.6***
Wholegrain $g \cdot day^{-1 f}$	70±2.9	53±2.3***	43±1.4***
Alcohol (1–3 $gl \cdot day^{-1}$) %	24.7	22.9	19.0*
FEV_1 mL##			
Round 2: 1994–1997¶¶	3086±21	3050±17	2990±10***
Round 3: 1998–2002++	2957±18	2929±16	2889±10**
Round 4: 2003–2006§§	2887±20	2840±18	2785±12***

Data are presented as mean±SD, except for intake and FEV_1 which are presented as mean±SEM, unless otherwise stated. ref: reference; gl: glass. #: low: intermediate secondary education or less; intermediate: intermediate vocational or higher secondary education; and high: higher vocational or university education; ¶: association between smoking status and educational level of $p<0.001$ (Chi-squared test); +: body mass index $>25\ kg \cdot m^{-2}$; §: $\geqslant 3.5\ h \cdot week^{-1}$ of moderate or intense activity, of which $\geqslant 2\ h \cdot week^{-1}$ is intense activity; f: adjusted for total energy intake; ##: adjusted for age, age squared, height and height squared; ¶¶: baseline examination of pulmonary function; ++: n=1,460, 561 and 394; §§: n=1,070, 501 and 382. *: $p<0.05$; **: $p<0.01$; ***: $p<0.001$ *versus* reference class.

As a consequence, the coefficients of FEV_1 decline were also adjusted for change in smoking status and the number of cigarettes smoked during follow-up.

RESULTS

In all three rounds for which pulmonary data were available, FEV_1 showed a positive cross-sectional association with educational level in both males (table 1) and females (table 2). On baseline examination of pulmonary function, complete data on age, height, pulmonary function and lifestyle factors, including smoking, were available for 2,104 males and 2,325 females. The baseline educational level was low in 45%, intermediate in 32% and high in 23% of the males. In females, this was 62, 23 and 15%, respectively. Educational level was inversely associated with the prevalence of current smoking at baseline in both sexes (tables 1 and 2).

Using linear mixed-effects models, the age-related decline in FEV_1 over 10 yrs of follow-up was estimated to be 30 $mL \cdot yr^{-1}$ (95% CI 29–32 $mL \cdot yr^{-1}$) in males and 24 $mL \cdot yr^{-1}$ (95% CI 23–25 $mL \cdot yr^{-1}$) in females. The rate of FEV_1 decline was faster in older persons: per year higher baseline age, the rate of decline in FEV_1 was 0.5 $mL \cdot yr^{-1}$ (95% CI 0.4–0.7 $mL \cdot yr^{-1}$) faster in males and 0.4 $mL \cdot yr^{-1}$ (95% CI 0.3–0.5 $mL \cdot yr^{-1}$) faster in females.

Educational level

Low educational level was associated with a lower baseline FEV_1. Compared to those with a high educational level, baseline FEV_1 was 221 mL lower in males (table 3) and 75 mL lower in females (table 4) with the lowest level of education. Adjustment for smoking attenuated the educational gradient in baseline FEV_1 to 148 mL in males and 47 mL in females (tables 3 and 4). These results were not altered in a

TABLE 3 Baseline educational level# in relation to baseline forced expiratory volume in 1 s (FEV_1) and FEV_1 decline during follow-up in males¶ (linear mixed-effects model)

	Educational level		
	High	Intermediate	Low
Basic model+			
Baseline FEV_1 mL	Ref	-115 (-176– -55)	-221 (-277- -165)
FEV_1 decline mL·yr^{-1}	Ref^f	1.4 (-2.2-5.0)	1.4 (-2.0-4.9)
Smoking-adjusted model§			
Baseline FEV_1 mL	Ref	-80 (-139– -22)	-148 (-203– -93)
FEV_1 decline mL·yr^{-1}	Ref^f	1.3 (-2.3-5.0)	1.6 (-1.8-5.0)

Data are presented as β (95% confidence interval), where β (the longitudinal linear regression coefficient) is effectively an adjusted mean, and relative to reference class. #: low: intermediate secondary education or less; intermediate: intermediate vocational or higher secondary education; and high: higher vocational or university education; ¶: n=2,679 (5,760 records); +: including baseline age, age squared, height, height squared and interaction term of baseline age with time, with baseline age centred at 45 yrs; §: additionally adjusted for baseline smoking history in pack-years plus smoking status and number of cigarettes smoked per round, with smoking status in five categories: current smoker (smoking cigarettes: with filter, without filter, and unknown), former smoker, and never-smoker; ^{f}: rate of FEV_1 decline in the highly educated of 29.4 mL·yr^{-1} (95% CI 26.7–32.1 mL·yr^{-1}) in basic model, and 29.6 mL·yr^{-1} (95% CI 26.8–32.3 mL·yr^{-1}) in smoking-adjusted model.

TABLE 4 Baseline educational level# in relation to baseline forced expiratory volume in 1 s (FEV_1) and FEV_1 decline during follow-up in females¶ (linear mixed-effects model)

	Educational level		
	High	Intermediate	Low
Basic model+			
Baseline FEV_1 mL	Ref	-25 (-73– 23)	-75 (-117– -34)
FEV_1 decline mL·yr^{-1}	Ref^f	2.0 (-0.9–5.0)	3.4 (0.9–6.0)
Smoking-adjusted model§			
Baseline FEV_1 mL	Ref	-15 (-61– 31)	-47 (-87– -6)
FEV_1 decline mL·yr^{-1}	Ref^f	1.9 (-1.0–4.8)	3.3 (0.7–5.8)

Data are presented as β (95% confidence interval), where β (the longitudinal linear regression coefficient) is effectively an adjusted mean, and relative to reference class. #: low: intermediate secondary education or less; intermediate: intermediate vocational or higher secondary education; and high: higher vocational or university education; ¶: n=3,026 (6,365 records); +: including baseline age, age squared, height, height squared and interaction term of baseline age with time, with baseline age centred at 45 yrs; §: additionally adjusted for baseline smoking history in pack-years plus smoking status and number of cigarettes smoked per round, with smoking status in five categories: current smoker (smoking cigarettes: with filter, without filter, and unknown), former smoker, and never-smoker; ^{f}: rate of FEV_1 decline in the highly educated of 21.3 mL·yr^{-1} (95% CI 19.1–23.5 mL·yr^{-1}) in basic model, and 21.8 mL·yr^{-1} (95% CI 19.5–24.1 mL·yr^{-1}) in smoking-adjusted model.

relevant way by additional adjustment for baseline values of physical activity, weight or intake of fruits, vegetables, wholegrain products or alcohol (data not shown).

In males, baseline educational level was not associated with the rate of FEV_1 decline during follow-up (table 3). Females of low educational level showed a 3.4 mL·yr^{-1} faster FEV_1 decline than highly educated females. An intermediate level of education in females was associated with a 2.0 mL·yr^{-1} faster FEV_1 decline, a difference of borderline significance (table 4). The effect of educational level on FEV_1 decline was not relevantly altered by adjustment for smoking (tables 3 and 4) nor by additional adjustment for the level of physical activity or weight in each round, or baseline intake of fruits, vegetables, wholegrain products or alcohol (data not shown).

The effect of low (*versus* high) educational level on FEV_1 decline was stronger in younger females (interaction with age in years of $p<0.01$). Low educational level was associated with a 7.3 mL·yr^{-1} (95% CI 2.8–11.8 mL·yr^{-1}) faster FEV_1 decline in females aged up to 40 yrs (lower tertile for age) and with a 3.8 mL·yr^{-1} (95% CI -0.2–7.9 mL·yr^{-1}) faster FEV_1 decline in females aged 40–50 yrs (middle tertile). In the eldest females, no significant association was observed (low *versus* high: -2.4 mL·yr^{-1} FEV_1 decline; 95% CI -7.2–2.5 mL·yr^{-1}). This interaction with age remained unchanged after adjustment for smoking (baseline smoking in pack-years, and time-dependent smoking status and number of cigarettes smoked) or age of smoking debut.

Smoking status

Table 5 shows that current smokers had a lower baseline FEV_1 than never-smokers. FEV_1 decline during follow-up was 11.2 mL·yr^{-1} faster in currently smoking males and 7.0 mL·yr^{-1} faster in currently smoking females than in never-smoking males and females, respectively (table 5).

Educational level and smoking status

Table 6 gives the rate of FEV_1 decline during follow-up after stratification for baseline educational level and baseline smoking status in males and females. In all strata of educational level, a significant effect of smoking was observed, except for females of high educational level. In never-smoking males, FEV_1 decline tended to be slower in those with a low *versus* those with a high level of education (23.6 *versus* 28.1 mL·yr^{-1}). In all other strata of smoking status, in males and females, observed rates of decline were either comparable across educational levels or faster among the less educated (table 6).

For the never-smoking male with a high educational level, who showed a relatively fast FEV_1 decline, baseline characteristics were as expected: a healthy lifestyle (low BMI, high fruit and wholegrain intake, and an average level of physical activity), a relatively high baseline FEV_1, and a low prevalence of COPD symptoms (data not shown).

Additional analyses

Additional analyses were performed in order to assess potential selection bias. Males and females contributing to

TABLE 5 Baseline smoking status in relation to baseline forced expiratory volume in 1 s (FEV_1) and FEV_1 decline during follow-up in males# and females¶ (linear mixed-effects model+)

	Smoking status		
	Never	Former	Current
Males			
Baseline FEV_1 mL	Ref	-58 (-112- -3)	-286 (-342- -230)
FEV_1 decline $mL \cdot yr^{-1}$	Ref§	2.1 (-1.2-5.5)	11.2 (7.7-14.8)
Females			
Baseline FEV_1 mL	Ref	13 (-20–47)	-155 (-190- -121)
FEV_1 decline $mL \cdot yr^{-1}$	Ref§	-0.5 (-2.6-1.7)	7.0 (4.7-9.2)

Data are presented as β (95% confidence interval), where β (the longitudinal linear regression coefficient) is effectively an adjusted mean, and relative to reference class. #: n=2,679 (5,760 records); ¶: n=3,026 (6,365 records); +: including baseline age, age squared, height, height squared and interaction term of baseline age with time, with baseline age centred at 45 yrs; §: rate of FEV_1 decline in never-smokers of 26.4 $mL \cdot yr^{-1}$ (95% CI 23.9–28.8 $mL \cdot yr^{-1}$) in males, and 22.0 $mL \cdot yr^{-1}$ (95% CI 20.5-23.5 $mL \cdot yr^{-1}$) in females.

the main analyses on educational differences in FEV_1 decline (*i.e.* those with at least two valid FEV_1 measurements) more frequently had a high level of education. Furthermore, in this group, the prevalence of smoking in round 2 was lower, and age was somewhat lower (~2 yrs). These differences from the rest of the cohort in smoking prevalence and age, however, were observed equally in those with a low and those with a high educational level in both sexes. Males and females with a valid FEV_1 in round 4, compared to drop-outs, had a relatively high baseline level of FEV_1, and the FEV_1 decline between rounds 2 and 3 was relatively fast for all educational levels. This difference in FEV_1 decline tended to be somewhat more pronounced in males and females with a high level of education.

Smoking history in pack-years was not used as a time-dependent variable in the main analyses, since it was not possible to calculate this parameter identically in all three rounds (due to the fact that questions regarding smoking behaviour were different in round 4). However, additional analyses showed that, after adjustment for smoking by inclusion of the best possible estimate of time-dependent smoking history in pack-years (*i.e.* calculated in a different way for round 4 than for rounds 2 and 3) and time-dependent smoking status in the models, the observed educational gradients in both FEV_1 and FEV_1 decline did not differ from those presented in tables 3 and 4.

In line with tradition, educational gradients in lung function are given adjusted for age and height throughout the present article. However, the effect of adjustment for height is interesting when studying socioeconomic gradients in adult FEV_1, since adult height has been suggested to be another biomarker for exposures influencing pre- and postnatal growth. Adjustment for height substantially reduced the observed educational gradient in baseline FEV_1 from 346 (only age-adjusted) to 221 mL (age- and height-adjusted) in males and from 131 to 75 mL in females.

FVC results were generally similar to those presented for FEV_1, whereas, for FEV_1/FVC, no associations with educational level were observed in males or females (data not shown).

DISCUSSION

In the present large cohort of Dutch adults, a more rapid decline in FEV_1 was observed in females of low educational level than in those of high educational level (3.4 $mL \cdot yr^{-1}$ faster). This difference was not seen in males, and was independent of smoking. Baseline FEV_1 was lower in those with a low level of education, even after adjustment for smoking, with a larger educational gradient in males (-148 mL) than in females (-47 mL).

Smoking at baseline was observed more frequently in males and females of low educational level, and was associated with a faster rate of decline in FEV_1 in both males (11.2 $mL \cdot yr^{-1}$ faster) and females (7.0 $mL \cdot yr^{-1}$ faster). Given the relation between smoking and lung function decline [2, 11], and the evidence that smoking is more common in those of lower socioeconomic status [6, 9, 12], a faster decline in FEV_1 would be expected in males and females of low educational level. However, an educational gradient in FEV_1 decline was observed in females alone. Although the observed difference in FEV_1 decline between females of low and high educational level (~3 $mL \cdot yr^{-1}$) appears modest, it is substantial relative to the observed effect of smoking (7.0 $mL \cdot yr^{-1}$). The additional loss during 10 yrs of follow-up in the females of low educational level (30 mL) is comparable to ~1 yr of age-related FEV_1 decline (24 $mL \cdot yr^{-1}$ in females in the present cohort).

The present findings on the effect of baseline smoking status on FEV_1 decline are consistent with those of other studies [18–22]. In addition, within strata for educational level, the FEV_1 decline was always fastest in those smoking at baseline. Surprisingly, the educational gradient in FEV_1 decline observed in females was not explained by smoking. Extensive adjustments for smoking (*i.e.* baseline smoking history in pack-years plus smoking status and the number of cigarettes smoked per round) did not make any difference to the size of the observed effect. Other factors associated with socioeconomic status, *i.e.* level of physical activity, body weight and dietary factors, also did not affect the observed differences in FEV_1 decline between females with a low and with a high level of education.

In almost all categories of smoking status, in males and females, the FEV_1 decline was similar in those with a low and those with a high educational level, or faster in the less educated. In males who had never smoked at baseline, however, FEV_1 decline tended to be slower in those of low educational level. The high proportion of never-smokers among males with a high level of education (~40%) may (partly) explain the absence of an educational gradient in FEV_1 decline in males. Additional analyses showed that other characteristics of the never-smoking males of high educational level (high baseline FEV_1, low prevalence of COPD symptoms and relatively healthy lifestyle) do not provide an explanation for the faster FEV_1 decline observed in this subgroup.

TABLE 6 Forced expiratory volume in 1 s (FEV_1) decline during follow-up in males# and females¶ by baseline educational level (EL) and smoking status (linear mixed-effects model+)

Smoking status	FEV_1 decline $mL \cdot yr^{-1}$			
	High EL	Intermediate EL	Low EL	Low *versus* high EL
Males				
Current	35.8 (28.5-43.1)	39.8 (34.9-44.6)	37.4 (33.6-41.3)	1.5 (-6.3-9.3)
Former	27.6 (22.7-32.4)	28.8 (25.2-32.3)	28.8 (25.0-32.5)	1.3 (-4.0-6.7)
Never	28.1 (24.2-32.0)	26.2 (21.5-30.9)	23.6 (19.6-27.6)	-4.8 (-10.4-0.9)
Current *versus* never	8.2 (0.6-15.9)	11.1 (5.1-17.1)	14.1 (8.3-19.9)	
Females				
Current	24.6 (19.5-29.6)	29.2 (25.0-33.5)	29.7 (27.5-32.0)	5.5 (-0.1-11.1)
Former	21.7 (18.1-25.3)	20.4 (17.2-23.6)	21.7 (19.7-23.7)	-0.7 (-4.6-3.3)
Never	19.6 (16.0-23.2)	22.6 (19.2-26.0)	23.0 (21.0-25.1)	3.6 (-0.5-7.7)
Current *versus* never	4.7 (-1.3-10.6)	7.8 (3.2-12.5)	6.3 (3.4-9.2)	

Data are presented as β (95% confidence interval), where β (the longitudinal linear regression coefficient) is effectively an adjusted mean. #: n=2,679 (5,760 records); ¶: n=3,026 (6,365 records); +: including baseline age, age squared, height, height squared and interaction term of baseline age with time, with baseline age centred at 45 yrs.

The observed effect of education on FEV_1 decline in females varied with age. No association was observed in women aged >50 yrs (upper tertile of baseline age). The lack of association in this age group may be (largely) due to the finding that FEV_1 decline was slower in one subgroup, namely females of low (*versus* high) educational level who were former smokers at baseline (results not shown). The data seem to suggest that, among females who started smoking in the 1960s and 1970s (and have quit since then), those of low educational level showed a slower than expected rate of FEV_1 decline. Why is unclear. Therefore, the possibility that the observed interaction is a chance finding cannot be excluded.

Few studies have reported on socioeconomic differences in lung function decline with age in adults, and the results of the studies that have are inconclusive. KRZYZANOWSKI *et al.* [13] observed no independent effect of education on the rate of FEV_1 decline during 13 yrs of follow-up. In their bivariate analyses, the rate of decline was slower in males of high (*versus* low) educational level, whereas no difference was observed in the females. BURCHFIEL *et al.* [14] studied educational attainment (less than high school *versus* other) and occupational status in relation to FEV_1 decline during 6 yrs of follow-up in males. In the main analyses, FEV_1 decline was categorised into rapid ($\geqslant 60\ mL \cdot yr^{-1}$) *versus* other. Occupational status was not associated with rapid FEV_1 decline. An association between low educational attainment and rapid FEV_1 decline was observed among never-smokers alone. This finding was, however, not confirmed when FEV_1 decline was modelled as a continuous variable (in millilitres per year). In the present study, FEV_1 decline tended to be slower in never-smoking males of low (*versus* high) educational level. In addition, in a few studies which used socioeconomic status as a covariate, crude effects on lung function decline were inconsistent [19–21].

FEV_1 at baseline was consistently lower in those of low educational level of both sexes, including after adjustment for smoking. The observed educational gradient was larger in males than females, which is in line with most other studies reported in the literature [6, 8, 9]. The earliest step in COPD may involve suboptimal development of lung function during childhood and adolescence, leading to achievement of a lower maximum level in early adulthood [11]. Factors associated with socioeconomic status that may be involved are intrauterine lung development, childhood respiratory infections, housing conditions, passive smoking and diet [5]. Not only adult FEV_1 but also adult height has been suggested to be a biomarker for exposures influencing pre- and postnatal growth [23–25]. In the present study, adjustment for height substantially reduced the educational gradient in baseline FEV_1. This further supports a role for early life exposures as precursors of COPD later in life [26]. If true, the prevention of COPD could potentially start very early in life, and may specifically target families of low socioeconomic status.

A limitation of the current study is that lower educated people were under-represented in the present cohort [15]. Males and females contributing to the main analyses were, furthermore, less likely to be smokers in round 2 and relatively young compared to the rest of the cohort. However, these differences in smoking prevalence and age did not vary between those of low and high educational level, which suggests that the main results may not be severely influenced by selection bias with regard to smoking or age. In the males and females with a valid FEV_1 in round 4, FEV_1 decline between previous rounds was observed to be relatively fast at all educational levels and slightly more so in those of high educational level. These observations on FEV_1 decline are somewhat in contrast with the other findings on potential selection. It should further be noted that, with regard to the measurement of lung function, it cannot be excluded that errors of measurement or regression to the mean phenomena have influenced the results. Although several sources of potential (selection) biases have been identified, it is difficult to determine whether or to what extent these may have affected the present estimates.

The strengths of the present study are its prospective design and the fact that repeated measurements of pulmonary function were available for large numbers of persons. Besides detailed information on educational level and smoking behaviour, data were available for analysis on a range of other lifestyle factors. Educational level is widely used and accepted as a proxy for socioeconomic status [27]. It is often more strongly associated with health outcomes than income and occupation [28], which were not available in the present study.

In conclusion, females of low educational level showed a faster decline in FEV1 over 10 yrs of follow-up than females with a high level of education, which was not explained by smoking (or other lifestyle factors associated with socioeconomic status). In males, the FEV1 decline did not differ between educational levels. As expected, baseline FEV1 was lower in the less educated, with a larger educational gradient in males than in females.

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STATEMENT OF INTEREST
None declared.

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