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

- Educational level and lung function –

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Abstract

Background

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 so far findings have been inconclusive.

Methods

To investigate the relation between educational level, Forced Expiratory Volume in 1 second (FEV_1), and decline of FEV_1 over time, linear mixed effects models were fitted to baseline and 10-year follow-up data from the Doetinchem Cohort Study. The study population (26-66 yrs at baseline) consisted of 2679 men and 3026 women 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 reference class.

Results

Low educational level was associated with a higher prevalence of smoking and with a lower smoking-adjusted FEV_1 at baseline (men: -148 ml, women: -47 ml). In women, low educational level was associated with a faster FEV_1 decline (3 ml/yr, age- and height-adjusted), which was not explained by smoking. In men, no differences in rates of decline between educational levels were observed.

Conclusions

FEV_1 decline was faster in less educated women, independent of smoking. In men, FEV_1 decline did not differ between educational levels.

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Introduction

The impact of Chronic Obstructive Pulmonary Disease (COPD), in terms of morbidity, mortality and health care costs, is expected to grow substantially over the next 20 years, 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) And several cross-sectional studies have reported an association between low socioeconomic status and reduced levels of the Forced Expiratory Volume in 1 second (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 men than women.(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 of lung function with age is seen especially in smokers (2, 11). As smoking is more prevalent among those with a 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 on 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 men and not in women.(13) Another study in men observed that low educational level was associated with rapid decline in FEV_1 in the never smokers only.(14)

In this paper we investigate the longitudinal association between baseline educational level (as proxy of socioeconomic status) and the rate of FEV_1 decline during 10 years of follow-up using data of the Doetinchem Cohort Study on 2679 men and 3026 women aged 26-66 years at baseline. We furthermore report on the educational gradient in baseline FEV_1.

Subjects and methods

Study population

A detailed description of the prospective Doetinchem Cohort Study has been published previously.(15) Initially, 12.405 inhabitants aged 20-59 years of Doetinchem, a town in a rural area of the Netherlands, participated in the 'Monitoring Project on Cardiovascular Disease Risk Factors' between 1987 and 1991 (first examination round). A total of 7769 of these participants were re-invited between 1993 and 1997 (participation rate 79%). For the third and fourth round, all persons *invited* for the previous round were re-invited with exception of those who died or emigrated during follow-up or who actively refused to participate in the previous round. The participation rate was 75% (of 6579) in 1998-2002 and 79% (of 4925) in 2003-2006. Participation rates at round 2 to 4 were comparable in men and women, but were clearly lower in those with a low (men: 60-67%, women: 59-73%) than those with a high (men: 85-87%, women: 85-89%) level of education (for definition of educational level, see Methods).

Since pulmonary function was only measured from 1994 onwards, in this paper we refer to the second round as the baseline examination. The numbers of persons who performed a pulmonary function test in round 2 to 4 were 4916, 4836 and 3874, respectively. Pulmonary function data were not yet available for 2007 at the time of analysis. About 95% of all performed measurements were technically acceptable and reproducible (valid FEV_1 value). The study population consisted of persons with a valid FEV_1 value in all three rounds (n=2282), persons with a valid FEV_1 value in two of the three rounds (n=2335) and persons with a valid FEV_1 value in one of the three rounds (n=1426). Excluded from the analysis were 817 records, because of pregnancy at that moment or missing values for educational level or main covariates. The final study population consisted of 2679 men (5760 records) and 3026 women (6365 records).

Methods

Information on demographic variables, presence of chronic diseases and risk factors including diet were collected using standardized questionnaires at baseline and follow-up.(15) Dietary intake data for 2003 to 2006 were not available when this paper 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, Germany). Participants were measured in a sitting position while wearing a nose clip. At least three technically acceptable manoeuvres for measuring the FEV_1 had to be achieved, of which two had to be reproducible according to ERS criteria.(16) The maximum value of the reproducible manoeuvres was used in the analysis. Spirometry was performed pre-bronchodilator only.

Educational level was used as an indicator of socioeconomic status and was categorized into: low (intermediate secondary education or less), intermediate (intermediate vocational or higher secondary education) and high (higher vocational or university education). Five categories for smoking status were defined: current smoker (smoking cigarettes: with filter, without filter or unknown), former smoker, never smoker. Pack years of cigarette smoking were calculated as the product of the number of years smoked and the average number of cigarettes smoked per day, 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 divided by height squared (kg/m^2). Physical activity was categorized into 4 levels based on the number of hours per week spent on moderate or intense activity (1=≤0.5, 2=0.5-3.5, 3=≥3.5 with <2 hrs/wk intense activity, 4=≥3.5 with ≥2 hrs/wk intense activity).(17)

Statistical analyses

All analyses were performed using the SAS statistical package (version 9.1, Cary, USA), and for men and women separately. Linear mixed effects models for the analysis of repeated measures were used (proc MIXED; estimation by restricted ML) to study baseline educational level in relation to baseline FEV_1 and in relation to FEV_1 decline during follow-up. This statistical method takes into account that repeated measurements in the same individual are not independent. It furthermore allows individuals to have unequal numbers of observations. Only persons with a valid FEV_1 value in at least two rounds contribute to the estimation of the FEV_1 decline. The random effects portion of the model consisted of a random intercept only. Specification of a random slope as well 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 as covariates baseline values of: age, age squared, height and height squared. To estimate age-related decline in FEV_1, we included time of follow-up and an interaction term of baseline age with time. Time of follow-up was modelled as years (0, 5, 10 yrs) from the baseline examination of pulmonary function. The interaction term of baseline age with time was included to allow the decline in lung function to vary with baseline age (stronger decline in older subjects). Baseline age was centred at 45 years, and the regression coefficient for time therefore represents the average decline in FEV_1 for a 45-year-old person.

Subsequently, baseline educational level was entered into this model as a main effect on baseline FEV_1. 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 (the reference). 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 number of pack years at baseline as well as smoking status and the number of cigarettes smoked as time-dependent variables. That is, at each round, smoking status and the number of cigarettes smoked were updated. 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 men (Table 1) and women (Table 2). At the baseline examination of pulmonary function, complete data on age, height, pulmonary function and lifestyle factors including smoking were available for 2104 men and 2325 women. Baseline educational level was low in 45%, intermediate in 32% and high in 23% of the men. In women, 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 effect models, the age-related decline in FEV_1 over 10-yrs of follow-up was estimated to be 30 ml/yr (95%CI=29 to 32) in men and 24 ml/yr (95%CI=23 to 25) in women. 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/yr (95%CI=0.4 to 0.7) faster in men and 0.4 ml/yr (95%CI=0.3 to 0.5) faster in women.

Educational level

Low educational level was associated with a lower baseline FEV_1 level. Compared to those with a high educational level, baseline FEV_1 was 221 ml lower in men (Table 3) and 75 ml lower in women (Table 4) with the lowest level of education. Adjustment for smoking attenuated the educational gradient in baseline FEV_1 to 148 ml in men and 47 ml in women (Tables 3 and 4). These results were not altered in a relevant way by additional adjustment for baseline values of physical activity, weight or intake of fruits, vegetables, whole grain products or alcohol (data not shown).

In men, baseline educational level was not associated with the rate of FEV_1 decline during follow-up (Table 3). Women with a low educational level had a 3.4 ml/yr faster FEV_1 decline than highly educated women. An intermediate level of education in women was associated with a 2.0 ml/yr 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 at each round or baseline intake of fruits, vegetables, whole grain products or alcohol (data not shown).

The effect of low (vs. high) educational level on FEV_1 decline was stronger in younger women (interaction with age (yrs): $p<0.01$). Low educational level was associated with a 7.3 ml/yr (95%CI= 2.8 to 11.8) faster FEV_1 decline in women up to age 40 (lower tertile for age) and with a 3.8 ml/yr (95%CI=-0.2 to 7.9) faster FEV_1 decline in women aged 40-50 years (middle tertile). In the eldest women, no statistically significant association was observed (low vs. high: 2.4 ml/yr *slower* FEV_1 decline, 95%CI = -2.5 to 7.2). This interaction with age remained unchanged after adjustment for smoking (baseline 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 started out with a lower baseline FEV_1 compared to never smokers. FEV_1 decline during follow-up was 11 ml/yr faster in currently smoking men and 7 ml/yr faster in currently smoking women compared to never smoking men and women 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 ànd baseline smoking status in men and women. In all strata for educational level a statistically significant effect of smoking was observed, except for women with a high educational level. In never smoking men, FEV_1 decline tended to be slower in those with a low vs. those with a high level of education (23.6 vs. 28.1 ml/yr). In all other strata for smoking status in men and women, observed rates of decline were either comparable across educational levels or faster in the less educated (Table 6).

For the never smoking men with a high educational level, who had a relatively fast FEV_1 decline, baseline characteristics were as expected: a healthy lifestyle (low BMI, high fruit and whole grain intake and 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 to assess potential selection bias. Men and women contributing to the main analyses on educational differences in FEV_1 decline (i.e. those with at least two valid FEV_1 values) more frequently had a high level of education. Furthermore, in this group, the prevalence of smoking at round 2 was lower and age was somewhat lower (approximately 2 yrs). These differences in smoking prevalence and age with the rest of the cohort, however, were equally observed in those with a low and those with a high educational level in both sexes. Men and women with a valid FEV_1 value at round 4, compared to “drop-outs”, had a relatively high baseline level of the FEV_1 and the FEV_1 decline between round 2 and 3 was relatively fast for all educational levels. This difference in FEV_1 decline tended to be somewhat more pronounced in men and women with a high level of education.

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

In line with tradition, educational gradients in lung function are given age- and height-adjusted throughout the paper. 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 men and from 131 to 75 ml in women.

For the FVC results were generally similar to those presented for the FEV_1, while for the FEV_1/FVC no associations with educational level were observed in men or women (data not shown).

Discussion

In our large cohort of Dutch adults, a more rapid decline of FEV_1 was observed in women with a low educational level compared to those with a high educational level (a 3 ml/yr faster decline). This difference was not seen in men, and it was independent of smoking. Baseline FEV_1 was lower in those with a low level of educational, even after adjustment for smoking, with a larger educational gradient in men (-148 ml) than in women (-47 ml).

Smoking at baseline was observed more frequently in men and women with a low educational level and was associated with a faster rate of decline of FEV_1 in both men (11 ml/yr faster) and women (7 ml/yr faster). Given the relation between smoking and lung function decline(2, 11), and the evidence that smoking is more common in lower socioeconomic status(6, 9, 12), a faster decline in FEV_1 would be expected in men and women with a low educational level. However, we observed an educational gradient in FEV_1 decline in women only. Although the observed difference in FEV_1 decline between women with a low vs. those with a high educational level (± 3 ml/yr) appears modest, it is substantial relative to the observed effect of smoking (= 7 ml/yr). The additional loss during 10 years of follow-up in the women with a low educational level (3 X 10 = 30 ml), is comparable to ±1 year of age-related FEV_1 decline (= 24 ml/yr in women in this cohort).

Our findings on the effect of baseline smoking status on FEV_1 decline are consistent with other studies.(18-22) Also 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 women was not explained by smoking. Extensive adjustments for smoking (i.e. baseline 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. Also other factors associated with socioeconomic status, i.e. level of physical activity, body weight and dietary factors, did not affect the observed differences in FEV_1 decline between women with a low and those with a high level of education.

In almost all categories of smoking status in men and women, 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 men who had never smoked at baseline, however, FEV_1 decline tended to be slower in those with a low educational level. The high proportion of never smokers among men with a high level of education (± 40%) may (partly) explain the absence of an educational gradient in FEV_1 decline in men. Additional analyses showed that other characteristics of the never smoking men with a 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.

The observed effect of education on FEV_1 decline in women varied by age. No association was observed in women over 50 years (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 women with a low (vs. high) educational level who were former smokers at baseline (results not shown). The data seem to suggest that among women who started smoking in the 1960s and 1970s (and quit since then), those with a low educational level had a slower than expected rate of FEV_1 decline. Why is unclear. We can, therefore, not exclude the possibility that the observed interaction is a chance finding.

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. Kryzanowski et al.(13) observed no independent effect of education on the rate of FEV_1 decline during 13 years of follow-up. In their bivariate analyses, the rate of decline was slower in men with a high (vs. low) educational level, while no difference was observed in the women. Burchfiel et al.(14) studied educational attainment (< high school vs. other) and occupational status in relation to FEV_1 decline during 6 years of follow-up in men. In the main analyses, FEV_1 decline was categorised into rapid (≥60 ml/yr) vs. 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 only. This finding was, however, not confirmed when FEV_1 decline was modelled as a continuous variable (in ml/yr). In our study, FEV_1 decline tended to be *slower* in never smoking men with a low (vs. high) educational level in our study. Also in a few studies which used socioeconomic status as a covariate, crude effects on lung function decline were inconsistent.(19-21)

The level of the FEV_1 at baseline was consistently lower in those with a low educational level and in both sexes, also after adjustment for smoking. The observed educational gradient was larger in men than women, which is in line with most other studies reported in the literature(6, 8, 9). The earliest step of COPD may involve a suboptimal development of lung function during childhood and adolescence, leading to a lower achieved 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 our 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 with low socioeconomic status.

A limitation of this study is that lower educated people were under-represented in our cohort.(15) Men and women contributing to our main analyses were furthermore less likely to be a smoker at 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 with a low and those with a high educational level, which suggests that our main results may not be severely influenced by selection bias with regard to smoking or age. In the men and women with a valid FEV_1 value at round 4, FEV_1 decline between previous rounds was observed to be relatively fast for all educational levels and slightly more so in those with a high educational level. These observations on FEV_1 decline are somewhat in contrast with our 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 we have identified several sources of potential (selection) biases, it is hard to determine whether or to what extent these may have affected our estimates.

Strengths of this 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 our study.

Conclusion:

Women with a low educational level had a faster decline of FEV_1 over 10 years of follow-up than women with a high level of education, which was not explained by smoking (or other lifestyle factors associated with socioeconomic status). In men, the FEV_1 decline did not differ between educational levels. As expected, baseline FEV_1 was lower in the less educated, with a larger educational gradient in men than in women.

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Table 1: Characteristics of the study population at baseline and FEV_1 in the 3 rounds, according to educational level: men

		Educational level[1]		
		High (=ref)	Intermediate	Low
At baseline:		*n=491*	*n=672*	*n=941*
Age (years)		46.8 (9.2)	43.3 (10.0)***	47.5 (9.7)
Height (meters)	mean (SD)	1.81 (0.07)	1.80 (0.07)	1.78 (0.07)***
	mean (SD)			
Smoking:[2]				
Current smokers	%	18.7	29.3	41.3
Former smokers	%	41.1	38.2	38.6
Never smokers	%	40.1	32.4	20.1
Pack years:				
Current smokers	mean (SD)	18.5 (12.2)	17.1 (12.5)	22.6 (14.5)**
Former smokers	mean (SD)	14.0 (14.3)	14.7 (15.1)	17.5 (16.3)*
Lifestyle:				
Overweight (BMI >25 kg/m^2)	%	46.6	54.6**	61.5***
Physical activity (heavy)[3]	%	25.3	22.2	14.3***
Fruit and vegetable intake (g/day)[4]	mean (SE)	290 (6.4)	256 (5.5)***	260 (4.6)***
Whole grain intake (g/day)[4]	mean (SE)	87 (3.6)	61 (3.1)***	54 (2.6)***
Alcohol intake (1-3 glasses/day)	%	39.2	36.6	30.1***
Per round: FEV_1 (ml)[5]				
Round 2: 1994-1997[6]	mean (SE)	4157 (25)	4042 (22)***	3935 (18)***
Round 3: 1998-2002	mean (SE)[7]	3958 (23)	3855 (21)**	3776 (18)***
Round 4: 2003-2006	mean (SE)[8]	3861 (26)	3755 (24)**	3688 (21)***

[1] low= intermediate secondary education or less, intermediate= intermediate vocational or higher secondary education, high= higher vocational or university education
[2] association smoking status and educational level: CHISQ : $p<0.0001$
[3] ≥3.5 hrs/wk moderate or heavy activity, of which ≥2 hrs/wk heavy activity)
[4] adjusted for total energy intake
[5] adjusted for age, age squared, height and height squared
[6] baseline examination of pulmonary function
[7] n= 974, 687 and 560
[8] n= 723, 566 and 468

compared to reference: * $p<0.05$, ** $p<0.01$, *** $p<0.001$

Table 2: Characteristics of the study population at baseline and FEV_1 in the 3 rounds, according to educational level: women

		Educational level[1]		
		High (=ref)	Intermediate	Low
At baseline:		*n=351*	*n=542*	*n=1432*
Age (years)	mean (SD)	44.4 (8.5)	41.2 (9.6)***	47.3 (9.8)***
Height (meters)	mean (SD)	1.68 (0.06)	1.68 (0.06)	1.65 (0.06)***
Smoking:[2]				
Current smokers	%	24.8	31.2	35.4
Former smokers	%	39.0	32.3	30.5
Never smokers	%	36.2	36.5	34.2
Pack years:				
Current smokers	mean (SD)	13.4 (10.3)	13.4 (9.2)	17.3 (10.3)**
Former smokers	mean (SD)	8.4 (8.8)	7.2 (7.3)	10.5 (13.0)
Lifestyle:				
Overweight (BMI >25 kg/m^2)	%	29.1	32.7	51.8***
Physical activity (heavy)[3]	%	15.7	11.8	6.8***
Fruit and vegetable intake (g/day)[4]	mean (SE)	343 (7.3)	319 (5.9)*	291 (3.6)***
Whole grain intake (g/day)[4]	mean (SE)	70 (2.9)	53 (2.3)***	43 (1.4)***
Alcohol intake (1-3 glasses/day)	%	24.7	22.9	19.0*
Per round: FEV_1 (ml)[5]				
Round 2: 1994-1997[6]	mean (SE)	3086 (21)	3050 (17)	2990 (10)***
Round 3: 1998-2002	mean (SE)[7]	2957 (18)	2929 (16)	2889 (10)**
Round 4: 2003-2006	mean (SE)[8]	2887 (20)	2840 (18)	2785 (12)***

[1] low= intermediate secondary education or less, intermediate= intermediate vocational or higher secondary education, high= higher vocational or university education
[2] association smoking status and educational level: CHISQ: $p<0.001$
[3] ≥3.5 hrs/wk moderate or heavy activity, of which ≥2 hrs/wk heavy activity)
[4] adjusted for total energy intake
[5] adjusted for age, age squared, height and height squared
[6] baseline examination of pulmonary function
[7] n= 1460, 561 and 394
[8] n= 1070, 501 and 382

compared to reference: * $p<0.05$, ** $p<0.01$, *** $p<0.001$

Table 3: Baseline educational level[1] in relation to baseline FEV_1 and FEV_1 decline during follow-up in men[2] (linear mixed effect model)

		Educational level		
		High	Intermediate ß (95%CI)	Low ß (95%CI)
Basic model[3]	Baseline FEV_1 (ml)	ref	-115 (-176 to -55)	-221 (-277 to -165)
	FEV_1 decline (ml/yr)	ref[5]	-1.4 (-5.0 to 2.2)	-1.4 (-4.9 to 2.0)
Additionally adjusted for smoking[4]	Baseline FEV_1 (ml)	ref	-80 (-139 to -22)	-148 (-203 to -93)
	FEV_1 decline (ml/yr)	ref[5]	-1.3 (-5.0 to 2.3)	-1.6 (-5.0 to 1.8)

[1] low= intermediate secondary education or less, intermediate= intermediate vocational or higher secondary education, high= higher vocational or university education

[2] number of men/records: 2679 / 5760

[3] included in model: baseline age, age squared, height and height squared and interaction term of baseline age with time; baseline age centred at 45 years

[4] additionally adjusted for: baseline pack years plus smoking status and number of cigarettes smoked per round, with smoking status in 5 categories: current smoker (smoking cigarettes: with filter, without filter or unknown), former smoker, never smoker

[5] rate of FEV_1 decline in the high educated: basic model = -29.4 ml/yr (95%CI= -32.1 to -26.7), smoking-adjusted model = -29.6 ml/yr (95%CI= -32.3 to -26.8)

Table 4: Baseline educational level[1] in relation to baseline FEV_1 and FEV_1 decline during follow-up in women[2] (linear mixed effect model)

		Educational level		
		High	Intermediate	Low
Basic model[3]	Baseline FEV_1 (ml)	ref	-25 (-73 to 23)	-75 (-117 to -34)
	FEV_1 decline (ml/yr)	ref[5]	-2.0 (-5.0 to 0.9)	-3.4 (-6.0 to -0.9)
Additionally adjusted for smoking[4]	Baseline FEV_1 (ml)	ref	-15 (-61 to 31)	-47 (-87 to -6)
	FEV_1 decline (ml/yr)	ref[5]	-1.9 (-4.8 to 1.0)	-3.3 (-5.8 to -0.7)

[1] low= intermediate secondary education or less, intermediate= intermediate vocational or higher secondary education, high= higher vocational or university education
[2] number of women/records: 3026 / 6365
[3] included in model: baseline age, age squared, height and height squared and interaction term of baseline age with time; baseline age centred at 45 years
[4] additionally adjusted for: baseline pack years plus smoking status and number of cigarettes smoked per round, with smoking status in 5 categories: current smoker (smoking cigarettes: with filter, without filter or unknown), former smoker, never smoker
[5] rate of FEV_1 decline in the high educated: basic model = -21.3 ml/yr (95%CI= -23.5 to -19.1), smoking-adjusted model = -21.8 ml/yr (95%CI= -24.1 to -19.5)

Table 5: Baseline smoking status in relation to baseline FEV_1 and FEV_1 decline during follow-up in men[1] and women[2] (linear mixed effect model)

		Smoking status		
		Never	Former	Current
Men[3]	Baseline FEV_1 (ml)	ref	-58 (-112 to -3)	-286 (-342 to -230)
	FEV_1 decline (ml/yr)	ref[4]	-2.1 (-5.5 to 1.2)	-11.2 (-14.8 to -7.7)
Women[3]	Baseline FEV_1 (ml)	ref	13 (-20 to 47)	-155 (-190 to -121)
	FEV_1 decline (ml/yr)	ref[4]	0.5 (-1.7 to 2.6)	-7.0 (-9.2 to -4.7)

[1] number of men/records: 2679 / 5760
[2] number of women/records: 3026 / 6365
[3] included in model: baseline age, age squared, height and height squared and interaction term of baseline age with time; baseline age centred at 45 years
[4] rate of FEV_1 decline in never smokers: men = -26.4 ml/yr (95%CI= -28.8 to -23.9), women = -22.0 ml/yr (95%CI= -23.5 to -20.5)

Table 6: FEV_1 decline during follow-up (ml/yr)[1] in men[2] and women[3] by baseline educational level and smoking status (linear mixed effect model)

	Baseline educational level			
Baseline smoking status	High ml/yr (95%CI)	Intermediate ml/yr (95%CI)	Low ml/yr (95%CI)	Low vs. High ml/yr (95%CI)
		Men		
Current	-35.8 (-43.1 to -28.5)	-39.8 (-44.6 to -34.9)	-37.4 (-41.3 to -33.6)	-1.5 (-9.3 to 6.3)
Former	-27.6 (-32.4 to -22.7)	-28.8 (-32.3 to -25.2)	-28.8 (-32.5 to -25.0)	-1.3 (-6.7 to 4.0)
Never	-28.1 (-32.0 to -24.2)	-26.2 (-30.9 to -21.5)	-23.6 (-27.6 to -19.6)	4.8 (-0.9 to 10.4)
Current vs. never	-8.2 (-15.9 to -0.6)	-11.1 (-17.1 to -5.1)	-14.1 (-19.9 to -8.3)	
		Women		
Current	-24.6 (-29.6 to -19.5)	-29.2 (-33.5 to -25.0)	-29.7 (-32.0 to -27.5)	-5.5 (-11.1 to 0.1)
Former	-21.7 (-25.3 to -18.1)	-20.4 (-23.6 to -17.2)	-21.7 (-23.7 to -19.7)	0.7 (-3.3 to 4.6)
Never	-19.6 (-23.2 to -16.0)	-22.6 (-26.0 to -19.2)	-23.0 (-25.1 to -21.0)	-3.6 (-7.7 to 0.5)
Current vs. never	-4.7 (-10.6 to 1.3)	-7.8 (-12.5 to -3.2)	-6.3 (-9.2 to -3.4)	

[1] included in model: baseline age, age squared, height and height squared and interaction term of baseline age with time; baseline age centred at 45 years

[2] number of men/records: 2679 / 5760
[3] number of women/records: 3026 / 6365