Longitudinal decline in lung function: a community-based cohort study in Korea

Ah Young Leem, Boram Park, Young Sam Kim, Joon Chang, Sungho Won & Ji Ye Jung

Progressive decline in lung function is the hallmark of chronic obstructive pulmonary disease (COPD). We aimed to assess the rate of decline in forced expiratory volume in 1 second (FEV₁) in patients from a community cohort database in Korea. 5,865 subjects aged 40–69 years from the Ansung-Ansan cohort database I–III (2001–2006) were included in this study. We assessed the annual rate of decline in FEV₁ over time in relation to smoking status, patient sex, and presence or absence of pre-bronchodilator airflow limitation using a generalized additive mixed model. The mean follow-up duration was 3.8 years. The annual mean decline in FEV₁ in the entire cohort was significantly more rapid for men than women (31.3 mL vs 27.0 mL, \( P = 0.003 \)). Among men without pre-bronchodilator airflow limitation, annual mean declines in FEV₁ were 31.5, 35.5, and 40.1 mL for never smokers, former smokers (\( P = 0.09 \) vs. never smokers), and current smokers (\( P < 0.001 \) vs. never smokers), respectively; and 23.4, 19.7, and 33.9 mL, respectively, for men with pre-bronchodilator airflow limitation. Thus, among Korean males, smoking accelerates lung function decline over time whereas smoking cessation slows the rate of FEV₁ decline regardless of pre-bronchodilator airflow limitation. This underscores the importance of smoking cessation in Koreans.

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity, mortality, and increased medical expenses worldwide. Currently, COPD is the fourth leading cause of death and is predicted to become the third leading cause of death by 2030. Fletcher and Peto reported that exposure to tobacco smoke accelerates the age-related decline in lung function as assessed by the forced expiratory volume in 1 second (FEV₁), leading to clinical disease. Since then, several population studies have supported this causal link, and therapeutic clinical trials have targeted reductions in the rapid decline in FEV₁. However, observed declines in FEV₁ in these trials and in observational cohorts of patients with COPD have been variable, particularly among patients with severe airflow limitation.

Cigarette smoking is the most important risk factor for acceleration of lung function decline. Lung damage in smokers is characterized by inflammation and airway remodelling leading to airflow limitation and destruction of the lung parenchyma. The underlying lung characteristics may vary; moreover, smokers differ in their susceptibility to emphysema or bronchitis. The strongest and most consistent detrimental effect from smoking has been found in current smokers and has been shown to decrease over time after smoking cessation.

However, COPD results from a complex interaction between genes and the environment. Cigarette smoking is the leading environmental risk factor for COPD, but <50% heavy smokers develop COPD during their lifetimes. Genetic factors, age, sex, and exposure to particles are also risk factors. Furthermore, any factor that affects lung growth has the potential to increase an individual’s risk of developing COPD. In previous studies, the birth weight and FEV₁ in adulthood were positively associated, and factors in early life seem to be as important as heavy smoking for the prediction of lung function in adult life.

A progressive decline in lung function has been considered the hallmark of COPD. It is also possible that a normal decline in FEV₁ could lead to COPD. A recent study by Lange et al. analysed three different longitudinal cohorts and reported that approximately 50% of patients developed COPD because of an accelerated decline in FEV₁ over time, while the other 50% developed COPD because of abnormal lung development and growth.

1 Division of Pulmonary, Department of Internal Medicine, Institute of Chest Disease, Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea. 2 Department of Epidemiology and Biostatistics, School of Public Health, Seoul National University, Seoul, Korea. Ah Young Leem and Boram Park contributed equally.

Correspondence and requests for materials should be addressed to S.W. (email: sunghow@gmail.com) or J.Y.J. (email: STOPYES@yuhs.ac)
Relatively few studies evaluating the decline in lung function in healthy subjects have been reported in Asia. Therefore, the present study aimed to evaluate the rate of decline in FEV₁ in patients selected from a community cohort database in Korea.

Results

Baseline characteristics. Of the initial 8,842 participants in the Ansung-Ansan cohort, 7,111 (80.4%) underwent at least two pulmonary function tests and were included in this study. Valid data for the smoking history were available for 5,865 of the 7,111 subjects, revealing 3,979 never smokers, 686 former smokers, and 1,200 current smokers (Fig. 1). The mean (standard deviation) follow-up duration was 3.8 (0.7) years. Table 1 shows the distribution of subjects in the different groups stratified by sex, lung function, and the smoking status.

Table 1. Distribution of subjects in different groups categorized by sex, lung function, and smoking status. Abbreviations: OLD, obstructive lung disease.

Rate of decline in FEV₁ in healthy never smokers. Figure 2 shows the decline in FEV₁ with age in male and female never smokers without obstructive lung disease (OLD). Men exhibited higher absolute FEV₁ values than did women at all time points. The annual rate of decline was significantly more rapid for male healthy never smokers (31.3 mL; 95% confidence interval [CI], 28.5–34.1) than for their female counterparts (27.0 mL; 95% CI, 25.9–28.1; \( P = 0.003 \)).

Effect of smoking on the decline in lung function. Figure 3 compares the decline in FEV₁ among male healthy never smokers, former smokers with and without OLD, and current smokers with and without OLD. The baseline characteristics of the subjects are shown in Supplementary Table 1. The annual rate of decline in FEV₁ was the fastest for current smokers (36.9 mL; 95% CI, 32.5–41.5; \( P = 0.023 \)) than for healthy never smokers (31.8 mL; 95% CI, 28.4–34.1). It also tended to be more rapid for current smokers (32.0 mL; 95% CI, 25.2–38.8) than for healthy never smokers (27.2 mL; 95% CI, 26.2–28.2; \( P = 0.165 \)).
| Characteristics       | Men (n = 2,376) | Women (n = 3,489) |
|-----------------------|-----------------|-------------------|
| Age, years            | 51.0 ± 8.4      | 52.3 ± 8.8        |
| Height, cm            | 167.1 ± 5.7     | 154.0 ± 5.5       |
| Weight, kg            | 68.3 ± 9.4      | 59.1 ± 8.3        |
| BMI, kg/m²            | 24.4 ± 2.8      | 24.9 ± 3.2        |

**Smoking status**

- Never smoker: 557 (23.4) Men, 3,422 (98.1) Women
- Former smoker: 681 (28.7) Men, 5 (0.1) Women
- Current smoker: 1,138 (47.9) Men, 62 (1.8) Women

**Lung function**

- FEV₁, L: 3.4 ± 0.6 Men, 2.5 ± 0.5 Women
- FEV₁, % of the predicted value: 107.0 ± 15.1 Men, 117.0 ± 17.3 Women
- FVC, L: 4.3 ± 0.7 Men, 3.1 ± 0.6 Women
- FVC, % of predicted value: 102.6 ± 13.2 Men, 107.5 ± 14.8 Women
- FEV₁/FVC ratio, %: 78.4 ± 7.9 Men, 81.7 ± 6.4 Women

**Follow-up duration**

- 2 years: 383 (16.1) Men, 486 (13.9) Women
- 4 years: 1,993 (83.9) Men, 3,003 (86.1) Women

Table 2. Baseline characteristics of patients in the Ansung-Ansan cohort who had valid smoking history data (n = 5,865). Notes: Data are presented as numbers (%) or means ± standard deviations. Abbreviations: BMI, body mass index; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

![Image](https://example.com/image.png)

**Figure 2.** Comparison of the annual mean decline in FEV₁ for healthy male (n = 521) and female (n = 3,297) never smokers. The annual mean decline in FEV₁ is 31.3 mL (95% CI, 28.5–34.1) for men and 27.0 mL (95% CI, 25.9–28.1) for women (P = 0.003). Abbreviations: CI, confidence interval; FEV₁, forced expiratory volume in 1 second.

| FEV₁ decline (ml/yr) | P-value |
|----------------------|---------|
| Men                  | 31.3 (28.5 – 34.1) | 0.003 |
| Women                | 27.0 (25.9 – 28.1)  |       |

*Data were presented as mean and 95% confidence intervals
are shown in Supplementary Table 2. Figure 4A compares the decline in FEV₁ among male healthy never smokers, healthy former smokers, and healthy current smokers. The annual rate of decline in FEV₁ was the fastest for healthy current smokers (40.1 mL; 95% CI, 37.0–42.2; \( P < 0.001 \) vs. healthy never smokers; \( P = 0.025 \) vs. healthy former smokers), while it was statistically indistinguishable between healthy former smokers (35.5 mL; 95% CI, 33.2–37.8 mL) and healthy never smokers (\( P = 0.098 \)).

Figure 4B compares the decline in FEV₁ among male healthy never smokers, former smokers with OLD, and current smokers with OLD. The annual rate of decline in FEV₁ was significantly more rapid for current smokers with OLD (33.9 mL; 95% CI, 30.2–37.6 mL) than for former smokers with OLD (19.7 mL; 95% CI, 15.1–24.3; \( P = 0.009 \)), while there was no significant difference between healthy current smokers and current smokers with OLD (Fig. 4C).

**Discussion**

In the present study, the annual decline in lung function was estimated for a population-based cohort in Korea. Healthy men and those with OLD who were current smokers showed a significantly increased rate of decline in FEV₁ than did their former smoker counterparts. The rate of decline in FEV₁ was similar between former smokers and never smokers among men without OLD and between male healthy current smokers and male current smokers with OLD.

Studies of the decline in lung function in population-based cohorts have been previously reported\(^{25,26}\). The mean decline in FEV₁ in healthy never smokers in our study was similar to that in the European Community.
We found annual mean FEV₁ declines of 31.8 mL for men and 27.2 mL for women, while the ECRHS reported respective decreases of 32 mL and 24 mL. Although the participants in our study were older than those in the ECRHS, they were taller on average. The average annual decline in FEV₁ in current smokers in our study was consistent with that in the Swiss Study on Air Pollution and Lung Diseases in Adults, where the annual mean decline in FEV₁ was 43.8 mL for male current smokers and 34.7 mL for their female counterparts (43.7 mL for men and 32.0 mL for women in our study). Omori et al. reported similar declines in FEV₁ in the Japanese male population stratified by age and the smoking status.

Several previous reports have analysed the relationship between declining lung function and smoking status in healthy subjects. Fletcher and Peto considered that the rate of decline in FEV₁ would normalize after smoking cessation at any age. Many studies have reported beneficial effects of smoking cessation on lung function decline. Faller and Peto considered that the rate of decline in FEV₁ would normalize after smoking cessation at any age. Many studies have reported beneficial effects of smoking cessation on lung function decline. We found that the rate of decline in FEV₁ in men was not different between healthy never smokers and healthy former smokers. In the study by Kohansal et al., smoking cessation had a beneficial effect at any age, although it was more pronounced in earlier quitters. The rate of decline in FEV₁ in both men and women who smoked but quit before the age of 30 years was similar to that in healthy never smokers.

In the present study, the rate of decline in FEV₁ in current smokers with OLD was similar to that in healthy never smokers and healthy current smokers. In a population-based cohort from three cities in Latin America, the annual mean post-bronchodilator decline in FEV₁ was 27 mL for patients with COPD at baseline and 36 mL for those without COPD. A more rapid decline was associated with older age, higher baseline lung function, and smoking at baseline. A greater decline in FEV₁ in men and patients with better lung function suggests that the decline is proportional to lung size. In a study by Ware et al., the annual rate of decline was greater for elderly nonsmokers (12.9 mL at the age of 25 vs. 58.2 mL at the age of 75 years).
Several studies evaluating the decline in lung function in Korean patients with COPD have been published\(^{36,37}\). Kim et al. reported that the adjusted annual rate of decline in the post-bronchodilator \(FEV_1\) was 28.3 mL, with no significant difference in the rate of decline in lung function among groups stratified according to the 2014 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines (\(-34.4 \pm 7.9\) [group A], \(-26.2 \pm 9.4\) [group B], \(-22.7 \pm 16.0\) [group C], and \(-24.0 \pm 8.7\) mL/year [group D])\(^{36}\). The decline that we report in healthy never smokers was more rapid than that in former smokers with OLD, and slower than that in current smokers with OLD. This discrepancy may be attributable to baseline \(FEV_1\) differences between the two studies; the airflow limitation in smokers with OLD in the present study was milder than that in the GOLD A group in the study by Kim et al. Small number of former smokers with OLD might not represent real lung function decline of former smokers with OLD. However, in the group of former smoker with OLD, absolute \(FEV_1\) at 40 years was lower than in the group of healthy never smoker. Therefore, the amount of decline of \(FEV_1\) might be less in the group of former smoker with OLD because healthy never smokers have more to lose than former smokers with OLD in early stage. In another study, the annual post-bronchodilator \(FEV_1\) declined more rapidly in older patients with COPD (25.0 mL for patients older than 67 years vs. 13.0 mL for younger patients)\(^{37}\). However, the rate of decline in lung function in the healthy population in Korea has not been reported. We investigated the effect of smoking and smoking cessation on the normal decline in lung function over time in a large cohort of both men and women, including healthy never smokers.

Our study has some strengths and potential limitations. The main strengths include its prospective design and the inclusion of spirometric measurements for a large population-based cohort including both rural and urban communities. However, the study duration was relatively short. Given that half the subjects were aged 40–49 years, they would have still been younger than 55 years after a mean follow-up period of 3.8 years. However, the Ansung-Ansan cohort study is ongoing, and we hope to analyse the data further with a longer follow-up period. Moreover, we used pre-bronchodilator spirometric values rather than post-bronchodilator values; accordingly, we used OLD for patient stratification instead of COPD. In addition, data concerning smoking cessation were purely based on a questionnaire, with no objective confirmation using a biological method. Self-reporting of the smoking status may be biased by societal factors, because women are less likely to report their smoking status because of the fear of stigma. Moreover, the duration of smoking in pack-years, and the mean number of years since smoking cessation could not be analysed because of the lack of data. Furthermore, because of the lack of information such as birth weight, we could not evaluate the impact of lung underdevelopment on lung function. Moreover, the number of women in all groups except for the healthy never smoker group was very small. Because the analysis of these groups might result in very unreliable estimates, only healthy never smokers were analysed. Finally, we could not exclude the participants with a restrictive pattern on spirometry.

In conclusion, the present study demonstrated the rate of decline in lung function over time in a large community-based Korean cohort. The findings suggest that continued smoking accelerates the decline in lung function, regardless of the presence of OLD. This underscores the importance of smoking cessation in the Korean population.

**Methods**

**Study populations.** The ongoing Ansung-Ansan cohort study was initiated in 2001 and supported from the National Genome Research Institute (Korea Centers for Disease Control and Prevention). It is a part of the Korean Genome and Epidemiology Study, which is based on a series of large community-based epidemiological surveys investigating chronic disease in Koreans. Further information on the study design and protocols have been published previously\(^{38,39}\).

From Ansung-Ansan cohort I (2001–2002), 8,842 subjects aged 40–69 years with valid lung function measurements and no previous history of asthma, bronchiectasis, or lung destruction, were included. Follow-up examinations and surveys are performed biennially (Fig. 1). We analysed data from a baseline survey and two subsequent biennial surveys (I–III: 2001–2006). Of the 8,842 subjects in the Ansung-Ansan cohort I, 7,111 who underwent pulmonary function testing ≥2 times during surveys I–III were used as the study population in the present research. Valid data concerning the smoking history were available for 5,865 of the 7,111 subjects.

The Korea Centers for Disease Control and Prevention obtained written informed consent from all participants on collection of the data, and the Institutional Review Board of Severance Hospital approved the present study protocol (4-2016-0458). All methods were performed in accordance with the approved protocol and with the relevant guidelines and regulations.

**Spirometry.** Lung function was assessed using spirometry (VMAX2130, SensorMedics Corporation, Yorba, CA, USA) at baseline and the first and second follow-up visits. Spirometry was performed according to American Thoracic Society/European Respiratory Society guidelines\(^{40}\).

**Definition.** Individuals who declared that they had never smoked before the study were considered never smokers, those who declared that they had smoked but stopped before the study were considered former smokers, and those who reported active smoking during the study period were considered current smokers. OLD was defined by a pre-bronchodilator \(FEV_1/\text{forced vital capacity ratio of}<0.7\). Individuals without OLD were considered healthy subjects.

**Statistical analysis.** We stratified participants into groups according to the smoking status (never smoker, former smoker, and current smoker) at cohort inception and the presence or absence of OLD. Subjects who did not respond to the questionnaires for the smoking history were excluded, while those with consistent reporting of the smoking history were included and categorized into never, former, and current smokers. Subjects whose smoking status changed from current smoker to former smoker during the study period were categorized as
former smokers. We then determined the rate of decline in FEV₁ over time according to the smoking status, sex, and OLD status in subjects for whom two or more spirometry measurements were available.

The FEV₁ values measured at each assessment were analysed using linear mixed models. We included age, sex, the body mass index, height, the smoking status, and the interaction of age and smoking as covariates. The model for all subjects i at time point j was as follows:

$$FEV_{i,j} = \beta_0 + \beta_1 \text{age}_i + \beta_2 \text{sex}_i + \beta_3 \text{BMI}_i + \beta_4 \text{smoking status}_i + \beta_5 \text{smoking status}_i \cdot \text{sex}_i + b_i + e_{ij},$$

where $$(e_{ij}, \ldots, e_{ij}) \sim MVN(0, \Sigma), \ b_i \sim iid \ MVN(0, \sigma^2)$$

while the model for female or male sex was as follows:

$$FEV_{i,j} = \beta_0 + \beta_1 \text{age}_i + \beta_2 \text{BMI}_i + \beta_3 \text{smoking status}_i + \beta_4 \text{smoking status}_i \cdot \text{sex}_i + b_i + e_{ij},$$

where $$(e_{ij}, \ldots, e_{ij}) \sim MVN(0, \Sigma), \ b_i \sim iid \ MVN(0, \sigma^2).$$

Generalized additive mixed models were used to determine the best fit for the decline in FEV₁ over time, and all figures were generated from these models. All statistical analyses were performed using R version 3.4.3 (R Foundation for Statistical Computing, Vienna, Austria). For the linear mixed models and the generalized linear mixed models, the “nlme” and “mgcv” packages, respectively, were used.

References

1. Mannino, D. M. et al. Economic Burden of COPD in the Presence of Comorbidities. Chest 148, 138–150 (2015).
2. Mannino, D. M. & Buist, A. S. Global burden of COPD: risk factors, prevalence, and future trends. Lancet 370, 765–773 (2007).
3. Pauwels, R. A. et al. Long-term treatment with inhaled budesonide in persons with mild chronic obstructive pulmonary disease who continue smoking. European Respiratory Society Study on Chronic Obstructive Pulmonary Disease. N Engl J Med 340, 1948–1953 (1999).
4. Fletcher, C. & Peto, R. The natural history of chronic airflow obstruction. Br Med J 1, 1645–1648 (1977).
5. Anthonisen, N. R., Matthay, R. A., Karpf, D. L., & King, J. B. The progression of chronic obstructive pulmonary disease: the ISOLDE trial. BMJ 320, 1297–1303 (2000).
6. Wise, R., Connett, J., Weimann, G., Scanlon, P. & Skews, M. Effect of inhaled tiotropium on the decline in pulmonary function in chronic obstructive pulmonary disease: the ISOLDE trial. Lancet 343, 1902–1909 (2000).
7. Decramer, M. et al. Effects of N-acetylcysteine on outcomes in chronic obstructive pulmonary disease (Bronchitis Randomized on NAC Cost-Utility Study, BRONCUS): a randomised placebo-controlled trial. Lancet 365, 1552–1560 (2005).
8. Antoniou, S. A. UPLIFT Study: the effects of long-term therapy with inhaled tiotropium in chronic obstructive pulmonary disease. Evaluation of: Tashkin DP, Celli BR, Senn S et al.: a 4-year trial of tiotropium in chronic obstructive pulmonary disease. N Engl J Med (2008) 359(15):1543–1554. Expert Opin Pharmacother 10, 719–722 (2009).
9. Decramer, M. et al. N-acetylcysteine on outcomes in chronic obstructive pulmonary disease (Bronchitis Randomized on NAC Cost-Utility Study, BRONCUS): a randomised placebo-controlled trial. Lancet 365, 1552–1560 (2005).
10. Fukushima, F. A. et al. Lung function decline in male heavy smokers relates to baseline airflow obstruction severity. Chest 142, 1530–1538 (2012).
11. Pauwels, R. A., Buist, A. S., Calverley, P. M., Jenkins, C. R. & Hur, S. S. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med 163, 1256–1276 (2001).
12. Amin, K., Ekberg-Jansson, A., Lofdahl, C. G. & Venge, P. Relationship between inflammatory cells and structural changes in the lungs of asymptomatic and never smokers: a biopsy study. Thorax 58, 135–142 (2003).
13. Costo Piqer, M. G. & Costo, M. G. Disease of the airways in chronic obstructive pulmonary disease. Eur Respir J 34, 41–49 (2001).
14. Clark, K. D. et al. Patterns of lung disease in a "normal" smoking population: are emphysema and airflow obstruction found together? Chest 120, 743–747 (2001).
15. Mannino, D. M. et al. Lung function decline in male heavy smokers relates to baseline airflow obstruction severity. Chest 142, 1530–1538 (2012).
16. Pauwels, R. A., Buist, A. S., Calverley, P. M., Jenkins, C. R. & Hur, S. S. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med 163, 1256–1276 (2001).
17. Amin, K., Ekberg-Jansson, A., Lofdahl, C. G. & Venge, P. Relationship between inflammatory cells and structural changes in the lungs of asymptomatic and never smokers: a biopsy study. Thorax 58, 135–142 (2003).
18. Costo Piqer, M. G. & Costo, M. G. Disease of the airways in chronic obstructive pulmonary disease. Eur Respir J 34, 41–49 (2001).
19. Clark, K. D. et al. Patterns of lung disease in a "normal" smoking population: are emphysema and airflow obstruction found together? Chest 120, 743–747 (2001).
20. Scanlon, P. D. et al. Smoking cessation in mild-to-moderate chronic obstructive pulmonary disease. The Lung Health Study. Am J Respir Crit Care Med 161, 381–390 (2000).
21. Rennergard, S. I. & Vestbo, J. COPD: the dangerous underestimate of 15%. Lancet 367, 1216–1219 (2006).
22. Global Management and Prevention of Chronic Obstructive Pulmonary Disease (GOLD). Global strategy for prevention, d. a. m. o. C. G., 2018 [Accessed 30 April 2018]. Available from, http://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf (2018).
23. Lawlor, D. A., Ebrahim, S. & Davey Smith, G. Association of birth weight with adult lung function: findings from the British Women’s Heart and Health Study and a meta-analysis. Thorax 60, 851–888 (2005).
24. Lange, P. et al. Lung-Function Trajectories Leading to Chronic Obstructive Pulmonary Disease. N Engl J Med 373, 111–122 (2015).
25. Omori, H., Nonami, Y. & Morimoto, Y. Effect of smoking on FEV decline in a cross-sectional and longitudinal study of a large cohort of Japanese males. Respir Med 10, 464–469 (2005).
26. Downs, S. H. et al. Accelerated decline in lung function in smoking women with airway obstruction: SAPALDIA 2 cohort study. Respir Res 6, 45 (2005).
27. Chinn, S. et al. Smoking cessation, lung function, and weight gain: a follow-up study. Lancet 365, 1629–1635; discussion 1600–1621 (2005).
28. Xu, X., Weiss, S. T., Rijcken, B. & Schouten, J. P. Smoking, changes in smoking habits, and rate of decline in FEV1: new insight into gender differences. Eur Respir J 17, 1056–1061 (1994).
29. Tagg, I. B., Segal, M. R., Speizer, F. E. & Weiss, S. T. The natural history of forced expiratory volumes. Effect of cigarette smoking and respiratory symptoms. Am Rev Respir Dis 138, 837–849 (1988).
30. Mannino, D. M. & Davis, K. J. Lung function decline and outcomes in an elderly population. Thorax 61, 472–477 (2006).
31. Mannino, D. M., Reichert, M. M. & Davis, K. J. Lung function decline and outcomes in an adult population. Am J Respir Crit Care Med 173, 985–990 (2006).
31. Kohansal, R. et al. The natural history of chronic airflow obstruction revisited: an analysis of the Framingham offspring cohort. *Am J Respir Crit Care Med* **180**, 3–10 (2009).
32. Perez-Padilla, R. et al. Lung function decline in subjects with and without COPD in a population-based cohort in Latin-America. *PLoS One* **12**, e0177032 (2017).
33. Thomsen, L. H. et al. Analysis of FEV1 decline in relatively healthy heavy smokers: implications of expressing changes in FEV1 in relative terms. *Copef* **11**, 96–104 (2014).
34. Camilli, A. E., Burrows, B., Knudson, R. J., Lyle, S. K. & Lebowitz, M. D. Longitudinal changes in forced expiratory volume in one second in adults. Effects of smoking and smoking cessation. *Am Rev Respir Dis* **135**, 794–799 (1987).
35. Ware, J. H. et al. Longitudinal and cross-sectional estimates of pulmonary function decline in never-smoking adults. *Am J Epidemiol* **132**, 685–700 (1990).
36. Kim, J. et al. Lung function decline rates according to GOLD group in patients with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* **10**, 1819–1827 (2015).
37. Kim, S. J. et al. Age-related annual decline of lung function in patients with COPD. *Int J Chron Obstruct Pulmon Dis* **11**, 51–60 (2016).
38. Leem, A. Y., Park, B., Kim, Y. S., Jung, J. Y. & Won, S. Incidence and risk of chronic obstructive pulmonary disease in a Korean community-based cohort. *Int J Chron Obstruct Pulmon Dis* **13**, 509–517 (2018).
39. Baik, I., Cho, N. H., Kim, S. H., Han, B. G. & Shin, C. Genome-wide association studies identify genetic loci related to alcohol consumption in Korean men. *Am J Clin Nutr* **93**, 809–816 (2011).
40. Miller, M. R. et al. Standardisation of spirometry. *Eur Respir J* **26**, 319–338 (2005).
41. Simon, N. W. *Generalized additive models: an introduction with R*. Boca Raton, FL: Chapman & Hall/CRC, 249–319 (2017).

**Acknowledgements**

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Education (2016R1D1A1B03933125). This research was also supported by a fund (code: 2014ER560600) from the Research of Korea Centers for Disease Control and Prevention and the Bio-Synergy Research Project of the Ministry of Science, ICT and Future Planning through the National Research Foundation (NRF-2017M3A9C4065964).

**Author Contributions**

Ah Young Leem contributed to the acquisition of data, analysis, and drafting of the article. Boram Park contributed to data analysis. Young Sam Kim and Joon Chang contributed to the study conception and design. Sungho Won contributed to data analysis and critical revision of the paper. Ji Ye Jung contributed to the study conception and design and critical revision of the paper. All authors take responsibility for all aspects of the work.

**Additional Information**

Supplementary information accompanies this paper at https://doi.org/10.1038/s41598-019-49598-9.

**Competing Interests:** The authors declare no competing interests.

**Publisher’s note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

© The Author(s) 2019