

# Spirometry for patients in hospital and one month after admission with an acute exacerbation of COPD

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**Aim:** To assess whether spirometry done in hospital during an admission for an acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is clinically useful for long-term management.

**Methods:** Patients admitted to hospital with a clinical diagnosis of AECOPD had spirometry post-bronchodilator at discharge and approximately 4 weeks later.

**Results:** Spirometry was achieved in less than half of those considered to have AECOPD. Of 49 patients who had spirometry on both occasions, 41 met the GOLD criteria for COPD at discharge and 39 of these met the criteria at 1 month. For the 41, spirometry was not statistically different between discharge and 1 month but often crossed arbitrary boundaries for classification of severity based on FEV<sub>1</sub>. The eight who did not meet GOLD criteria at discharge were either misclassified due to comorbidities that reduce FVC, or they did not have COPD as a cause of their hospital admission.

**Conclusion:** Spirometry done in hospital at the time of AECOP is useful in patients with a high pre-test probability of moderate-to-severe COPD. Small changes in spirometry at 1 month could place them up or down one grade of severity. Spirometry at discharge may be useful to detect those who warrant further investigation.

**Keywords:** classification of COPD, spirometry, acute exacerbation of COPD, primary care, cohort study

## Introduction

The diagnosis of chronic obstructive pulmonary disease (COPD) is based on clinical features and spirometry.<sup>1</sup> Spirometry is required in the assessment of severity which determines guideline treatment recommendations. It is also valuable to predict risk of death<sup>2</sup> and readmission to hospital.<sup>3</sup> In patients admitted to our hospital with an acute exacerbation of COPD (AECOPD), often spirometry appears to never have been done prior to admission, and is seldom done during admission. Primary care clinicians and patients need a confirmed diagnosis and severity classification to support management decisions. There are often practical barriers to spirometry in the community,<sup>4</sup> whereas it may be readily accessible while patients are in hospital, with trained staff available to administer and interpret the test. However, Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines state that spirometry should be done “when the patient is clinically stable and free from respiratory tract infection”.<sup>1</sup> The guideline injunction is based on concern that spirometry at this time might lead to false positive diagnosis or overestimation of severity. We wanted to explore the validity of this concern.

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There are only limited data available on the reproducibility of spirometry when comparing tests completed around the time of an AECOPD with tests done after resolution of the acute episode.<sup>4-7</sup> White and colleagues found that pre- and post-bronchodilator spirometry measurements were 'stable' between day 5 and day 28 on patients after initiating treatment for AECOPD.<sup>4</sup> However, patients in this study were diagnosed and treated in primary care, and mostly had mild-to-moderate COPD – post bronchodilator Forced Expiratory Volume in 1 second ( $FEV_1$ ) was around 60% of predicted. Similarly, Herpel and colleagues found relatively little change in spirometry in clinically stable patients with a wider range of COPD severity, but reported only pre-bronchodilator measurements.<sup>5</sup> However, most patients in hospital with AECOPD are given frequent salbutamol or another short-acting bronchodilator, making valid pre-bronchodilator measurement difficult to achieve and raising concerns that to do so might interfere with therapy.

Donohue<sup>6</sup> reported that the minimally clinical important difference (MCID) in  $FEV_1$  is not definitively known, although major trials have used figures ranging from 45 to 180 mL. Most studies use pre-bronchodilator tests, and a pre-bronchodilator  $FEV_1$  improvement of about 100 mL correlates with other important clinical outcomes. The author also noted that change in  $FEV_1$  can be practically useful only if it exceeds the bounds of measurement error, ie, mean change score for the group  $\pm 2SD$ ; any smaller change would be indistinguishable from measurement error.

We therefore sought, in our patient population, to assess whether post-bronchodilation spirometry done in hospital just prior to discharge following a clinical diagnosis of AECOPD produces measurements which are *not clinically different* to measurements made 1 month later.

## Methods

### Participants

Patients were eligible if they were admitted to an adult medical ward at a large teaching hospital in New Zealand (Middlemore Hospital) with a diagnosis of AECOPD. We note that there is no universally accepted definition of AECOPD but accept the criteria of the Canadian Thoracic Society which specifies a worsening of COPD symptoms leading to increased use of medications.<sup>7,8</sup> Patients were excluded if they were discharged after-hours or over weekends or public holidays, or if they had a condition making technically adequate spirometry impossible, such as a stroke or dementia. Patients were recruited from September 2008

to March 2009. The study was approved by the Northern X Regional Ethics Committee, ref NTX/07/11/123.

### Spirometry

Spirometry was performed on a Microlab spirometer and Spida 5 software (both from Micro Medical Ltd, Rochester, Kent, UK). These use NHANES III data for predicted values<sup>9</sup> with a 10% correction factor for Polynesian people.<sup>10</sup> We used 'Caucasian' values for European and 'Polynesian' values for Maori and Pacific Island patients. The device was calibrated weekly. Testing was done by two registered nurses who were trained and certified to local standards which align with American Thoracic Society/European Respiratory Society standards.<sup>11</sup> All spirometry was done post-bronchodilation. The protocol called for spirometry on the day of discharge and at home 30 days after discharge.

If a patient cannot produce a satisfactory Force Vital Capacity (FVC, defined as expiration for 6 seconds or plateau on the volume-time curve), the  $FEV_1/FVC$  ratio can be spuriously high due to an invalid FVC. This ratio may also be raised due to comorbidities limiting FVC. In this case the protocol called for the spirometry to be reviewed by a respiratory physician (HR) looking for other features of COPD, in particular for a mid-expiratory concavity.

Analyses were based on detecting a statistically significant change in  $FEV_1$  (see power calculations), a change sufficient to alter severity grading according to the GOLD criteria<sup>1</sup> or a change that exceeded 100 mL or 150 mL (representing the MCID).<sup>6</sup>

### Power calculations

To determine whether spirometry was 'stable' over 1 month, we needed sufficient patients to allow us to detect the smallest clinically important change.

We assumed mean  $FEV_1$  at discharge as 1.5 L (SD 0.42); and that within-patient variation is 0.106 L (SD 0.10) (based on data from Herpel et al).<sup>5</sup> The small standard deviation of the difference in repeated measures implies that the correlation between the measurements within-patient is relatively large. A series of power calculations were made. Using a correlation of 0.75, power of 90%, and a significance of 1%, we would need a sample size of 63 to detect a difference of 150 mL between two measures, or 36 to detect a difference of 200 mL.

### Statistical analysis

We used Stata software for statistical analysis (v 10.1; StataCorp, College Station, TX). Means are compared by paired *t*-test. Statistical significance is cited at  $P < 0.05$ .

## Results

Numbers at each stage of the recruitment process are given in Figure 1. Consent to join the study was given by 54, however four were excluded as unlikely to have COPD after review of all patient records by a respiratory physician (HR) who was blind to the study spirometry results. One had a history of childhood asthma and was a lifelong non-smoker. One had severe left sided heart failure, a 10 pack-year history of smoking, and normal spirometry in 2006. One had a 20 pack-year history of smoking, stopping in 1975, normal spirometry in 2007, and a CT scan in 2009 that showed no evidence of COPD. One had normal spirometry in October 2009. One further patient declined the 1-month spirometry due to illness at the time, leaving data on 49 patients at both discharge and 1 month. All 49 patients fitted the phenotype of COPD, with slowly progressive shortness of breath and cough and sputum production, onset in middle age, with a prolonged history of cigarette smoking, and having excluded asthma as the primary diagnosis. They all had a clinical diagnosis of COPD accepted by a senior clinician and met the criteria for AECOPD. The median number of admissions to hospital in the previous 2 years, including the index admission, and for reasons that included COPD, was 3.5 with a range of 1 to 22.

Median time from admission to ‘discharge’ spirometry was 4 days (inter-quartile range 2 to 7). Median length of stay

in hospital was 6 days (inter-quartile range 4 to 11). Counting from ‘discharge’ spirometry, data from the ‘1-month’ check was collected at a mean of 34.3 days (SD 6.3). Three patients were readmitted to hospital within 2 weeks of discharge, so we used their baseline spirometry collected at the end of the first admission, but counted days after discharge from their second discharge.

Forty-one patients met GOLD criteria for COPD at discharge and 39 of these met the criteria at 1 month. The two who no longer met GOLD criteria had FEV<sub>1</sub>/FVC of 0.56 and 0.67 at discharge and 0.70 and 0.71 at 1 month, respectively (GOLD criteria specifies <0.70). Their FEV<sub>1</sub> percentages predicted were 26 and 23 at discharge and 49 and 45 at 1 month, respectively. Their FEV<sub>1</sub> decreased from discharge to 1 month by 60 mL and 130 mL, respectively. One of the patients who did not meet GOLD criteria at discharge did so at 1 month (FEV<sub>1</sub>/FVC 0.70 and 0.68, FEV<sub>1</sub> percent predicted 51 and 46, respectively).

For the 41 patients meeting GOLD criteria at discharge, mean patient age was 67.8 (SD 10.9) years, there were 15 women, and the ethnic breakdown was 15 European, 15 Maori, and 11 Pacific Island. Table 1 shows their spirometry and severity classification at discharge and at 1 month. Spirometry change was not statistically significant. Apart from the two patients who no longer met GOLD COPD

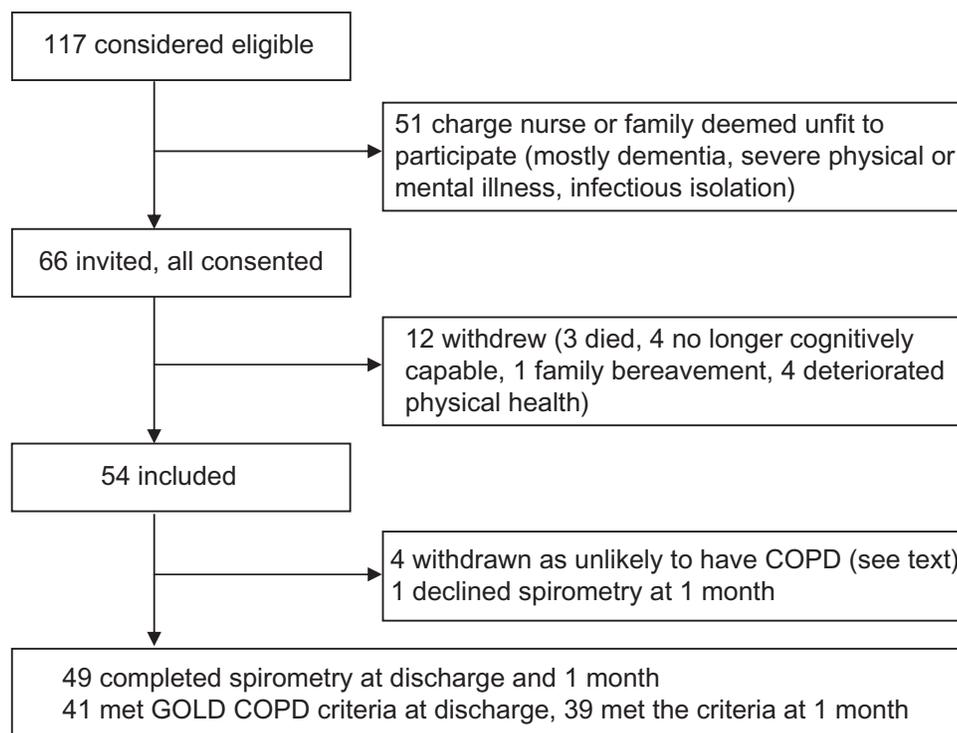


Figure 1 Patient numbers in study.

**Table 1** Patients with COPD according to GOLD spirometry criteria at hospital discharge

	Discharge	1 month	P value
FEV <sub>1</sub>	1.04 (0.51)	1.08 (0.48)	0.26
FVC	2.09 (0.89)	2.18 (0.81)	0.12
FEV <sub>1</sub> /FVC	0.50 (0.11)	0.50 (0.12)	1.00
FEV <sub>1</sub> % predicted	38.7 (14.4)	40.6 (14.3)	0.18
<b>Classification (FEV<sub>1</sub> % predicted)</b>			
Moderate (50 to <80)	10		
Mild		0	
Moderate		8	
Severe		2	
Severe (30 to <50)	18		
Moderate		4	
Severe		11	
Very severe		2	
Very severe (<30)	13		
Severe		6	
Very severe		6	

**Notes:** Spirometry measures and GOLD severity classification at discharge and at 1 month. Results are mean (SD) or counts. N = 41. One 'severe' and one 'very severe' patient at discharge no longer met GOLD criteria at 1 month (see text).

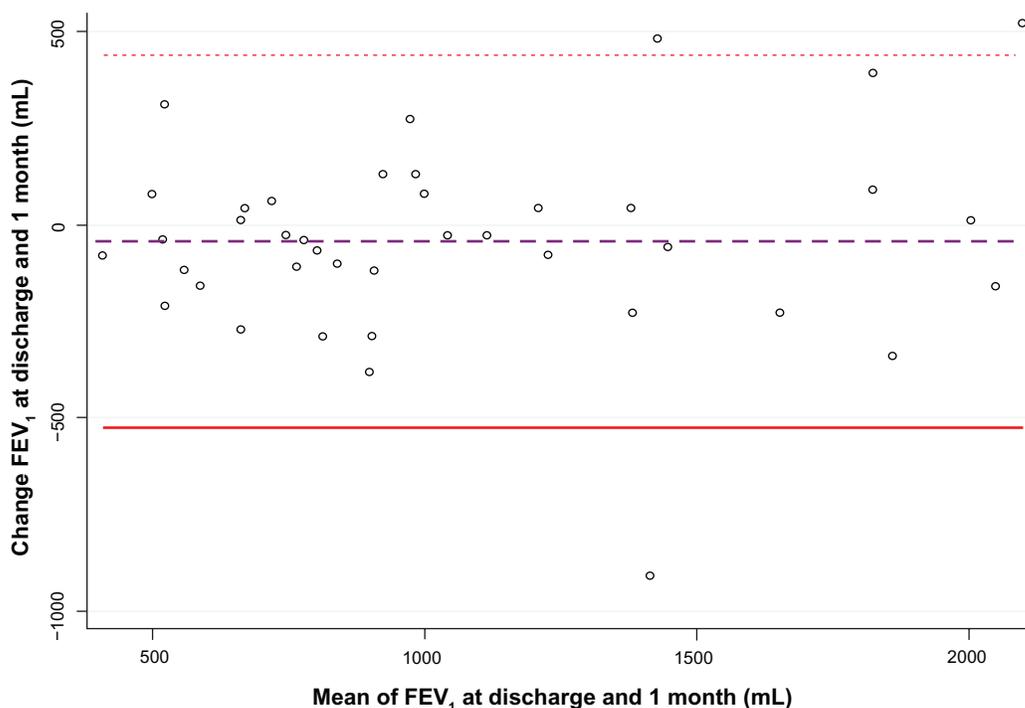
criteria, no patient moved more than one severity grade up or down. Following discharge, five patients decreased FEV<sub>1</sub> by more than 200 mL, five patients decreased by more than 150 mL, and seven decreased by more than 100 mL; 15 increased by more than 100 mL, 11 increased by more than

150 mL, and nine increased by more than 200 mL. Individual changes for each of the 41 patients meeting GOLD criteria at discharge are shown in Figure 2. This figure shows that smaller or larger changes in FEV<sub>1</sub> seem to occur regardless of mean value (which is an approximation of baseline or underlying value for each patient).

For the eight patients who failed to meet GOLD spirometry criteria for COPD at discharge, mean age was 65.1 (SD 8.7), five were women, and the ethnic breakdown was one European, five Maori, and two Pacific Islanders. At 1 month they all had a FEV<sub>1</sub>/FVC ratio of 0.7 or greater.

### Discussion

Between discharge and follow up at 1 month, post-bronchodilator spirometry did not significantly change and no patient moved more than one GOLD COPD severity grade up or down. Absolute changes were typically short of the MICD. These results were the same whether we considered all the patients who were clinically diagnosed as having AECOPD, those who met GOLD criteria for COPD at discharge, or those who met the criteria at 1 month. We interpret these results to mean that spirometry done 4 days after admission is clinically stable over the following month.



**Figure 2** Difference between FEV<sub>1</sub> at 1 month and FEV<sub>1</sub> at discharge from hospital for each patient. Central line is observed average agreement. Upper and lower lines are 95% limits of agreement.

**Note:** N = 41.

Of 41 patients who met GOLD COPD criteria at discharge, only two did not meet the criteria at 1 month. In this group of patients it seems that false positive diagnosis from doing spirometry close to an acute exacerbation is not a clinical problem.

Although many patients crossed guideline classification boundaries of severity, with implications for guideline-based management decisions, we note that these boundaries are arbitrary points on a continuum. The GOLD guidelines state that they provide a “simple classification” “for educational reasons” using cut points “that have not been clinically validated”.<sup>1</sup> Changes that shift patients across such boundaries may reflect noise of measurement more than real airways change, which supports the need for clinical judgment when applying guidelines to individual patients.

Study strengths include testing patients from our own population, which has a unique ethnic mix. Limitations include a relatively small study size. Prior power calculations indicated that our 41 participants gave sufficient power to detect a change in FEV<sub>1</sub> of 200 mL. The assumed standard deviation of samples proved correct. The assumed correlation 0.75 between FEV<sub>1</sub> at baseline and 1 month proved well short of the correlation 0.88 in our real sample (indicating greater ‘stability’ or ‘lack of change’ than we had anticipated). Consistent with this was the mean change of 40 mL in our patients which was lower than the lowest MCID reported in the literature (45 mL) and well short of the more commonly used figures of 100 or 150 mL.<sup>6</sup> For three patients, we used discharge spirometry from one admission, but repeat testing was carried out 1 month after second admission shortly after the first. We would expect clinically that spirometry at the end of the first admission was either similar to, or worse than, spirometry at the end of the second admission – if the latter, then measurements for these patients would overestimate the change from discharge to 1 month. We note that less than half of those admitted with COPD were deemed fit for spirometry which may have introduced some selection bias into our study. We do not know whether those who did participate were more or less ‘stable’ in their spirometry than those who did not participate.

It is possible that our patients’ spirometry might have continued to improve past 1 month. However, Parker et al followed 20 patients for 60 days after an AECOPD and, while their patients took a mean of 41 days to symptomatic recovery, their FEV<sub>1</sub> was back to baseline within about 14 days.<sup>7</sup> This implies that FEV<sub>1</sub> is measuring a process that is associated with, rather than central to, the pathophysiology of COPD. Indeed, Fabbri and Rabe suggest that COPD

should no longer be considered a disease only of the lungs, but a chronic systemic inflammatory syndrome.<sup>12</sup> A similar point was made by Celli et al who noted that the BODE index recognizes systemic manifestations not reflected in FEV<sub>1</sub>.<sup>2</sup>

Eight patients had been admitted to hospital with a clinical diagnosis of AECOPD, but failed to meet GOLD spirometry criteria at discharge, in each case due to FEV<sub>1</sub>/FVC being 0.70 or greater. Percent predicted FEF<sub>25–75</sub> (age adjusted) in these patients ranged from 12% to 73% and in each case the flow loop had a concave shape. Clinically it was considered that their FEV<sub>1</sub>/FVC may have been ‘artificially’ elevated due to a low FVC that was consistent in each case with known comorbidities, particularly obesity or congestive heart failure.

Our 41 patients with COPD at discharge had a mean of three comorbidities, including some with comorbidities that may decrease FVC (especially heart failure and obesity) and therefore raise the FEV<sub>1</sub>/FVC ratio or may reduce airway caliber (especially obesity) and therefore decrease FEV<sub>1</sub>/FVC ratio. Others have commented on the high rate of false negative spirometry in patients who undoubtedly clinically have COPD.<sup>13</sup> There has also been criticism of the use of 0.7 as the cut point for FEV<sub>1</sub>/FVC ratio rather than using the lower limit of normal of an age predicted ratio;<sup>14,15</sup> the problem of reduced lung volume with age was specifically noted in the GOLD guidelines.<sup>1</sup> Our patients who did not meet COPD spirometry criteria at either time may have had mixed lung disease but should not be thereby denied COPD management. Such patients need more formal physiological assessment including lung volumes and diffusion capacity for carbon monoxide.

Guidelines state that spirometry should be performed when the patient is “stable and free from respiratory infection”.<sup>1</sup> Apart from the fact that these patients are probably never free of respiratory infection, this restriction appears unnecessary, and in our own area this may be a barrier to enrolment in the community chronic care management program. Our patients living in South Auckland often experience difficulties in accessing community services (due to cost, language barriers, travel, or taking time off work), and may therefore miss the opportunity for spirometry. Others have noted that it can be difficult to achieve spirometry in community general practice.<sup>4</sup>

The study suggests that, in patients with a high pre-test probability of COPD, spirometry at the time of discharge from hospital during an AECOPD can be used to confirm the diagnosis and to make an initial judgment about severity. However, for about one-fifth of our patients, the diagnosis of

COPD was cast in doubt by the spirometry results at 1 month, suggesting that they would warrant further investigation to confirm COPD or an alternative or additional diagnosis for their clinical symptoms. It would be helpful to have universally agreed criteria for grading severity – others have noted that some criteria may correlate better than others with outcomes.<sup>16</sup>

## Acknowledgments

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## Disclosure

The authors report no conflicts of interest in this work.

## References

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Bethesda, MD: Global Initiative for Chronic Obstructive Lung Disease (GOLD); 2010. Available at: [http://www.goldcopd.org/uploads/users/files/GOLDReport\\_April112011.pdf](http://www.goldcopd.org/uploads/users/files/GOLDReport_April112011.pdf). Accessed on September 20, 2011.
2. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med*. 2004;350(10):1005–1012.
3. Celli BR, Barnes PJ. Exacerbations of COPD. *Eur Respir J*. 2007;29(6):1224–1238.
4. White AJ, O'Brien C, Hill SL, Stockley RA. Exacerbations of COPD diagnosed in primary care: changes in spirometry and relationship to symptoms. *COPD*. 2005;2(4):419–425.
5. Herpel LB, Kanner RE, Lee SM, et al. Variability of spirometry in chronic obstructive pulmonary disease: results from two clinical trials. *Am J Respir Crit Care Med*. 2006;173(10):1106–1113.
6. Donohue JF. Minimal clinically important differences in COPD lung function. *COPD*. 2005;2(1):111–124.
7. Parker CM, Voduc N, Aaron SD, Webb KA, O'Donnell DE. Physiological changes during symptom recovery from moderate exacerbations of COPD. *Eur Respir J*. 2005;26(3):420–428.
8. O'Donnell DE, Aaron SD, Bourbeau J, et al. Canadian Thoracic Society recommendations for management of chronic obstructive respiratory disease – 2003. *Can Respir J*. 2003;10 Suppl A:11A–65A.
9. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general US population. *Am J Respir Crit Care Med*. 1999;159(1):179–187.
10. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl*. 1993;16:5–40.
11. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *Eur Respir J*. 2005;26(2):319–338.
12. Fabbri LM, Rabe KF. From COPD to chronic systemic inflammatory syndrome? *Lancet*. 2007;370(9589):797–799.
13. Fabbri LM. Single disease versus patient oriented guidelines for chronic respiratory diseases. *Postgraduate Course 25. Pulmonary Rehabilitation – From Science to Implementation*. San Diego, CA: American Thoracic Society; 2009.
14. Levy M, Quanjer P, Booker R, Cooper BG, Holmes S, Small I; General Practice Airways Group. Diagnostic spirometry in primary care. Proposed standards for general practice compliant with American Thoracic Society and European Respiratory Society recommendations. *Prim Care Respir J*. 2009;18(3):130–147.
15. Fragoso C, Concato J, McAvay G, et al. The Ratio of FEV<sub>1</sub> to FVC as a basis for establishing chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2010;181(5):446–451.
16. Tsoumakidou M, Tzanakis N, Voulgaraki O, et al. Is there any correlation between the ATS, BTS, ERS and GOLD COPD's severity scales and the frequency of hospital admissions? *Respir Med*. 2004;98(2):178–183.

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