**Thorax Online First, published on August 16, 2007 as 10.1136/thx.2007.080572**



# Validation of FEV6 in the elderly: correlates of performance and repeatability

Vincenzo Bellia[1], Claudio Sorino[1], Filippo Catalano[1], Giuseppe Augugliaro[1], Nicola Scichilone[1], Riccardo Pistelli[2], Claudio Pedone[3], Raffaele Antonelli-Incalzi[4].

[1]Dipartimento di Medicina, Pneumologia, Fisiologia e Nutrizione Umana, Università di Palermo, Palermo, Italy
[2]Università Cattolica del Sacro Cuore, Roma, Italy
[3]Fisiopatologia Respiratoria, Università Campus Bio-Medico, Roma, Italy

[4]Geriatria, Università Campus Bio-Medico, Roma, Italy

**Corresponding author:**
Vincenzo Bellia, MD
Università di Palermo, DIMPEFINU
via Trabucco 180
90146 Palermo, Italy
Tel.+39916802652
Fax +39916891857
E-mail: v.bellia@unipa.it
2nd E-mail: belliav@infcom.it

**Keywords**
Spirometry
Forced Expiratory Volume
Respiratory Function Tests
Aged
Lung Diseases, Obstructive

# Abstract

Forced expiratory volume in six seconds (FEV6) has been proposed as a more easily measurable parameter than forced vital capacity (FVC) to diagnose airway disease using spirometry. We aimed to estimate FEV6 repeatability, to identify correlates of a good quality FEV6 and of volumetric differences between FEV6 and FVC in elderly patients.

We examined 1531 subjects aged 65-100 yrs enrolled in the Sa.R.A project (cross-sectional, multicenter, non interventional study). FEV6 was measured on volume-time curves that achieved both a satisfactory start of test and end of test. Correlates of FEV6 achievement were assessed by logistic regression.

FEV6 and FVC were obtained in respectively 82.9%, and 56.9% of spirometries with acceptable start of test. Female sex, older age, lower educational level, depression, cognitive impairment and lung restriction independently affected the achievement of FEV6. A good repeatability (difference between the best two values <150ml) was found in 91.9% of tests for FEV6 and in 86% for FVC; the corresponding figures in obstructed patients were 94% and 78.4%. Both FEV6 and FVC repeatability were affected by male sex and lower education. Finally, male sex, airway obstruction and smoking habit were independently associated with greater volumetric differences between FEV6 and FVC.

In elderly patients, FEV6 is more easily achievable and more reproducible than FVC, although in this population still 1 out 6 patients could not achieve it.


# Introduction

Spirometry is the most frequently performed respiratory function test and has a primary diagnostic role in the elderly, since many factors (co-morbidity, blunted sensitivity to dyspnea, polipharmacy) variously confound or conceal the clinical expression of respiratory disorders in this age group (1, 2). However, performing a reliable spirometry involves strict patient collaboration to satisfy current guidelines for acceptability and repeatability (3). A vigorous physical effort and, occasionally, the prolongation of expiration for up to 20 seconds are needed to obtain the complete lung emptying and, thus, to measure forced vital capacity (FVC). Unfortunately, elderly subjects or patients with severe respiratory diseases quite frequently cannot afford such an effort (4, 5). For this reason, there is an increasing interest in more easily measurable spirometric parameters that could replace FVC in the elderly. Among these parameters, Forced Expiratory Volume in six seconds (FEV6) has been proven to be able to predict lung function decline in adult smokers (6), and to be a reliable surrogate for FVC in the spirometric diagnosis of airway obstruction and restriction (7-12). Recently, reference equations and lower limits of normality for FEV6 and for $FEV_1$/FEV6 have been produced in selected populations (13-16). However, to date no study has focused on the factors related to a good quality FEV6 and to the correlates of volumetric differences between FEV6 and FVC in elderly patients.

On this basis, we analysed the spirometric findings obtained in the Italian multicenter SA.R.A. (SAlute Respiratoria nell'Anziano, Respiratory Health in the Elderly) study to identify factors that influence the achievement of an acceptable FEV6 and to assess FEV6 repeatability. We also purposed to quantify the differences between the best FEV6 and FVC, as well as between the best FEV1/FEV6 and FEV1/FVC, and to search for inherent explanatory factors.

# Methods

Analysed data derive from a sample of 1971 subjects aged 65-100 years enrolled in the SA.R.A. multicenter case-control study. Details on the recruitment criteria, studied population and diagnostic procedures are available elsewhere (1).

Spirometry was not obtained in 101 subjects because of early interruption of expiration, physical impairment, inability to understand the instructions, lack of collaboration and refusal. Therefore, 1870 spirometries were obtained and retained for analysis. Briefly, the sample included 1054 (56.4%) subjects with a normal spirometry (429 healthy and 625 with non respiratory diseases), 509 subjects (27.2%) with an obstructive and 307 (16.4%) with a restrictive pattern (for criteria see below).

Spirometries were performed according to the guidelines of the American Thoracic Society (ATS) (17); a rigorous quality control program was implemented throughout the study: the results have been published elsewhere (1). Spirometric flow-volume curves were considered acceptable if they had Extrapolated Volume (VEXT) <5% of the FVC or 0.150 L (start-of-test criterion), and a Forced Expiratory Time (FET) ≥6 seconds or an obvious plateau in the volume-time curve (end-of-test criterion), in absence of cough, glottis closure or other significant interruptions of the manoeuvre. According to recommendations by ATS (17), we did not exclude curves which did not satisfy the repeatability criteria, in order to avoid the exclusion of data in which an abnormal lung function causes a greater coefficient of variation than in normal subjects. There are different proposed surrogate measures of FVC, such as the FVC6 (maximum volume exhaled at any time during the first six seconds) (13) or the FEV6 (volume forcefully exhaled at exactly six seconds after back-extrapolated time zero). We chose the latter because it is the measure proposed by the ATS and the European Respiratory Society (ERS) (3) and has been shown to be a reliable surrogate of the FVC (7-12). Figure 1 shows examples of valid sessions for the measurement of FVC6, FEV6, and FVC. FEV1 and FEV6 were measured on all acceptable curves. FVC was measured only on curves with an end-expiratory plateau ≥1 second, i. e. of an end expiratory phase ≥1 second with a volume change lower than the minimal detectable volume of 0.026 L (18).

We defined airways obstruction as FEV1/FVC below the lower limit of normal (LLN: mean - 1.645*SD) of SA.R.A. study reference population (19), restriction as FVC below LLN with normal or increased FEV1/FVC (18). Severity of airways obstruction was evaluated on the basis of FEV1 expressed in % of predicted (3): mild (≥70%), moderate (60–69%), moderately severe (50–59%), severe (35–49%), very severe (<35%) (Figure 2).

The following data possibly affecting the quality of measurements were collected: social-demographic characteristics (sex, age, instruction level), smoking habit, spirometric index of airway obstruction (FEV1 and FVC as percent of predicted), anthropometric characteristics (body mass index: BMI, waist/hip ratio, occiput-wall distance), mood state (15-item Geriatric Depression Scale: GDS (20)), cognitive function (Mini Mental State Examination: MMSE (21)), physical performance (Barthel's index (22), 6 Minutes Walking Test: 6MWT (23)).

We estimated FEV6 and FVC repeatability by calculating the difference between the two highest values of the index obtained from each subject. A minority of subjects with a difference > 1000 ml were considered outliers and not included in the analysis (N=10 for FEV6 and N=18 for FVC). We also expressed repeatability using mean differences and 95% agreement limits, according to the Bland and Altman method (24). The analysis of intraindividual FEV6 repeatability was carried out in subjects with at least two valid FEV6 (VEXT <150 ml and FET ≥6 seconds; n=1345). FEV6 repeatability was compared with the repeatability of FVC calculated in a subset of 1135 subjects with two or more valid FVC (VEXT <150 ml and plateau ≥1 second).

Differences between groups were analysed using Pearson's $\chi^2$ for dichotomous variables and Student's *t* test or Mann-Whitney test for continuous variables, as appropriate. For the identification of independent correlates of our outcomes, we used multivariable logistic analysis or linear regression. Variables entered in the models were chosen on the basis of univariable analysis results. Independent variables were considered statistically significant if the Odds Ratio (OR) was different from 1 and if the 95% confidence interval (CI) did not include 1.

All the analyses were performed using Epi Info (CDC, Atlanta, Georgia and WHO, Geneva, Switzerland) and Stata (Stata Corporation, College Station TX) software packages.

# Results

**FEV6 achievement**

Among the 1870 subjects who performed spirometry, 1531 (81.9%) obtained a VEXT < 150 ml in at least three curves, and 1485 (79.4%) obtained a FET ≥6 seconds in at least three curves. Among the 1531 subjects with VEXT <150 ml in at least three curves, 1269 (82.9%) obtained a FET of 6 seconds or more in at least three curves, 871 (56.9%) attained a plateau of end expiration ≥1 second in at least three curves (Figure 3).

The main demographic and clinical characteristics of 1531 subjects with a positive start-of-test criterion are presented in Table 1. Most of the subjects had lower educational level and were former or current smokers. Nutritional status, as reflected by BMI, was on average good. Mood depression, corresponding to a GDS score greater than 5, was found in 20% of men and 36.5% of women, while cognitive impairment affected about one participant out of seven.

The mean FEV1% was 86.5% ($5^{th}$ and $95^{th}$ percentiles = 37.3 and 126.6 respectively), while the mean FEV1/FVC% was 64.2% for males ($5^{th}$ and $95^{th}$ percentiles = 34.6 and 89.1 respectively), and 74.4% for females ($5^{th}$ and $95^{th}$ percentiles = 52.9 and 89.1 respectively). Obstructed subjects for the most part were males, and obstruction was severe or very severe in over 40% of them.

Table 2 compares the characteristics of people who could or could not achieve a valid FEV6. Older people and those with a lower educational level, a restrictive respiratory pattern and physical or neuropsychological impairment were less likely to achieve a valid FEV6. According to results from multivariable logistic model, female sex, older age, lower educational level, depression, cognitive impairment, and restrictive spirometric pattern were all independently and negatively correlated with the achievement of a valid FEV6 (Table 3).

**Intraindividual FEV6 and FVC repeatability**

The mean difference between the two best values of FEV6 was 62 ± 84 ml, (coefficients of variation of 1.35%); spirometries with a difference between the two best values of FEV6 lower than 150 ml were 1236, corresponding to 91.9%. In the subset having two or more measurable FVCs, the mean difference between the two best values of FVC was 72 ± 87 ml (coefficients of variation of 1.21%), while spirometries with a difference between the two best values of FVC lower than 150 ml were 976, corresponding to 86% of the total. Repeatability of FEV6 was high even in subjects with airway obstruction (<150 ml in 94% of tests), whereas FVC repeatability in the same group decreased (78.4%). Table 4 shows the mean differences between the two best FEV6 and FVC along with 95% agreement limits and centiles distribution stratified by gender.

Several factors were associated with poor FEV6 repeatability in the univariable analyses (Table 5). Only male sex (OR = 1.04; 95% CI = 1.11-2.68), and lower educational level (OR= 1.76; 95% CI = 1.08-2.85) remained associated with lack of repeatability of FEV6 in a multivariable model corrected for age, cognitive function, Barthel index and 6-Minute Walking Test.

**Differences between the largest FVC and FEV6, between FEV1/FEV6 and FEV1/FVC, and correlates of differences.**

Among the 871 spirometries characterized by three acceptable curves and a plateau ≥1 second in at least three curves, the mean difference between FVC and FEV6 was 182 ± 171 ml (range 0-1279 ml). The mean difference between FEV1/FEV6 and FEV1/FVC was 4.14 ± 3.10% (range 0-17%). As expected, the difference between FVC and FEV6 increases as the absolute values of FVC increases (Figure 4). In a linear multivariable regression, male sex, airway obstruction, and smoking habit emerged as independent correlates of a higher difference between FVC and FEV6 and between the best FEV1/FEV6 and FEV1/FVC ($p < 0.001$). FVC - FEV6 difference was 0 in 23 subjects, whereas it exceeded 1000 ml in 5 subjects, all characterized by a rather severe obstruction (mean FEV1/FVC: 35.2%, SD: 9%). The positive relationship between FVC - FEV6 difference and the degree of airway obstruction is confirmed by the significant correlation shown in Figure 5.

# Discussion

The findings of our study indicate that in elderly subjects FEV6 is more easily achieved and more reproducible than FVC. The potential implication of this results are evident, since FEV6 was obtained in more than 80% of spirometries with acceptable start-of-test, whereas a reliable FVC could be measured in less than 60% of spirometries.

To our knowledge, this is the first study that also addressed the factors that influenced the achievement and the repeatability of FEV6 in the elderly. Factors that negatively affected the attainment of an expiration of at least 6 seconds, which is the only end of test requirement for FEV6, were female sex, older age, lower educational level, depression, cognitive impairment, and a restrictive spirometric pattern. The mechanism through which age affects the achievement of FEV6 is unclear. In older subjects airway closure occurs at lung volumes above FRC, impairing the FEV6 manoeuvre. In fact, some studies have demonstrated that the decline in lung function accelerates in more advanced ages (25-29). Our results support this explanation: among people aged 77 years or older (corresponding to the 75th percentile of age distribution), 75% of participants achieved an acceptable FEV6 vs. 83% in the entire sample (data not shown). However, since even the most accurate multivariable analysis could miss important explanatory variables, older age might also be considered a “summary index” of conditions hampering the achievement of FEV6.

The collaboration of the patient is an essential requirement for a reliable test: cognitive impairment is a well recognized negative correlate of the achievement of FEV6 (1, 30-32). Conversely, depressed mood has never been previously recognized as negative correlate of the achievement of any spirometric measure. Lack of motivation to perform the spirometric manoeuvre might underlie the negative relationship between depression and achievement of FEV6. The fact that less educated subjects achieved FEV6 less frequently than the more educated ones probably reflects education-related differences in the ability to understand and to perform the spirometric manoeuvre.

Patients with a restrictive functional pattern had difficulties in performing a measurable FEV6 manoeuvre. In 64 out of 272 restricted patients the FVC manoeuvre lasted less than 6 seconds. It is conceivable that restricted patients have less air to expire and, thus, need less time to do it. Furthermore, restrictive lung diseases are frequently associated with increased lung stiffness which could make the expiration explosive and therefore shorter. Our sample included only patients with mild to moderate restrictive respiratory pattern, and it is conceivable that a greater proportion of patients will not achieve a FET ≥6 seconds and a measurable FEV6 in samples including severely restricted patients. Our findings are indirectly supported by the observation of Vanderwoorde et al. that FEV6 had lesser sensitivity to a diagnosis of restrictive pattern than to a diagnosis of an obstructive one (8).

Women achieved FEV6 less frequently than men. This could be explained by the fact that women tend to have lower levels of FVC in comparison to age-matched men. Smaller lungs could more easily complete emptying in less than 6 seconds and therefore women are more likely to achieve an adequate plateau, thus allowing for FVC to be measured, even if the manoeuvre is interrupted before a FEV6 can be measured. Actually, in the SA.R.A. population, 24.2% of women with FET less than 6 seconds had a plateau, as opposed to 9.1% of males ($p<0.001$). At any rate, our results indicate that even FEV6 might not be a suitable surrogate of FVC in elderly women and in people with a restrictive pattern. A possible solution to the problem could be re-defining FEV6 as the largest volume exhaled anytime during the first six seconds i.e. the above-mentioned FVC6 (13): the latter could be obtained in a larger number of subjects, including mainly women and patients with spirometric restriction.

Confirming data by Swanney et al. (7), FEV6 was more reproducible than FVC. Both FEV6 and FVC repeatability were affected by male sex and lower education. Since males have larger volumes than females, and because FEV6 is obviously lesser than FVC, it seems logical that FVC and FEV6 should have different criteria for reproducibility and these should also be gender-specific. To express reproducibility as percent of the best value instead of using the cut off point of 150 ml could be a possible solution.

In our study, the mean difference between the best FEV6 and FVC was 182 ml, while Demir et al (33) reported a mean difference of 95 ± 121 ml in 5114 adult patients (age 49.95 ± 15.48 years), and Enright et al (6) found that, on average, the FEV6 was 112 ml smaller than the FVC in adult smokers. A potential source of this discrepancy could be our choice of calculating FVC only when a 1 second plateau was reached, thus excluding curves in which FVC could be underestimated because of an early interruption of expiration. The possibility that the observed differences could be linked to different male/female ratios between study samples can also be excluded: indeed, the proportion of females was 53.7% in our sample and 53.6% in the Demir’s study. In the Enright’s sample females amounted to 37.5% only; however, given that the FVC-FEV6 difference is higher in males, the greater fraction of males in the Enright’s sample is expected to increase and not to decrease such difference.

On the other hand, the severity of airway obstruction was directly related to the difference between FVC and FEV6. In fact, the expiration time is on average proportional to the severity of airway obstruction and, thus, the proportion of FVC expired in the first 6 seconds is expected to decrease in parallel with FEV1. Interestingly, all subjects having a FVC-FEV6 difference above one litre were among the most obstructed. Demir et al (33) also noticed a higher difference between FVC and FEV6 in patients with airway obstruction. Similarly, Enright et al (6) found that the difference between the two spirometric indexes was on average 6-9% larger in smokers with more severe airway obstruction. In comparison with previous studies (6, 33), our sample consisted of subjects with less severe airway obstruction (average FEV1 %: 86.5), whereas Demir reported a mean FEV1% predicted of 72.9 +/- 24.4%, and Enright of 74.8 +/- 9.5% in males, 74.9 +/- 9.3% in females. Thus, our study emphasizes the inverse relationship between FEV1% and FVC - FEV6 by confirming it in a less obstructed population.

We found that, in addition to airway obstruction, male sex and smoking habit were positive correlates of the FVC - FEV6 difference. The greater lung volumes and, then, expiration times of males and the smoke-related risk of airway disease in smokers are likely explanations to these findings.

This study has some limitations. First, we defined restriction according to spirometric evidence, but only the measurement of total lung capacity can provide a definitive diagnosis (34). However, this limitation would impact more on a study assessing the diagnostic accuracy of FEV6 than on our study, which aimed at identifying factors associated with the achievement of a satisfactory FEV6. Second, in our study FVC was considered reliable only if the subject reached a plateau ≥1 second. This criterion is very restrictive and excludes the operator’s option considered a possible alternative by the ATS/ERS statements (3). At any rate, it seems an acceptable choice for the sake of standardization, since in a multicenter study it would not have been possible to evaluate the subjective terms of judgement adopted by individual operators. Third, we cannot exclude that in selected cases we might have observed glottis closure and not a true plateau. Finally, a high proportion of our COPD patient had severe or very severe obstruction (over 40% of them has predicted FEV1 below 50%). Indeed, we identified airways obstruction, as it has been suggested (18, 35, 36), using the LLN of FEV1/FVC of our reference population of elderly people (19), which was lower than the classic 70%, thus reducing the proportion of people with mild obstruction.

In conclusion, in elderly patients FEV6 can be a valid alternative to FVC in the identification of airway obstruction because the spirometric manoeuvre is easy to perform, and it satisfies the criteria for repeatability and diagnostic accuracy. However, very old, poorly educated and cognitively impaired subjects, women, and patients with a restrictive respiratory pattern have more difficulty in achieving a satisfactory FEV6. Thus, the measurement of FEV6 represents an important step forward with regard to FVC, although this index may not be the ideal surrogate of FVC for very old and frail subjects.

Supported by research funds of DIMPEFINU, Università di Palermo

## Figure legends

**Figure 1**
Volume-time curves of valid sessions for the measurement of FVC6, FEV6 and FVC (see methods for definitions).

**Figure 2**
Severity of airways obstruction on the basis of FEV1 % predicted among subjects with FEV1/FVC < LLN.

**Figure 3**
Pathway used for the selection of tests.

**Figure 4**
Relationship between FVC - FEV6 and FVC.

**Figure 5**
Relationship between FVC - FEV6 and FEV1/FVC.

**Table 1 –** *Main characteristics of the sample**

| | | males | females |
|---|---|---|---|
| **Number of subjects** | | 785 | 746 |
| **Age, (years)** | m | 73.85 | 73.53 |
| | sd | 6.46 | 6.24 |
| | range | 65 - 100 | 65 - 98 |
| **Instruction Level** | ≤ 5 years | 463 (59.0%) | 498 (66.8%) |
| | > 5 years | 322 (41.0%) | 248 (33.2%) |
| **Smoking habit** | NS | 542 (72.7%) | 136 (17.3%) |
| | CS | 80 (10.7%) | 121 (15.4%) |
| | FS | 124 (16.6%) | 528 (67.3%) |
| **GDS** | ≤ 5 | 628 (80.0%) | 474 (63.5%) |
| | > 5 | 157 (20.0%) | 272 (36.5%) |
| **MMSE** | ≤ 23 | 103 (13.1%) | 125 (16.8%) |
| | > 23 | 682 (86.9%) | 621 (83.2%) |
| **BMI (Kg/m$^2$)** | m | 26.2 | 26.7 |
| | sd | 3.8 | 5.2 |
| | range | 15.3 – 38.6 | 15.4 – 41.1 |
| | obesity rate (BMI >30) | 118 (15.0%) | 167 (22.4%) |
| **Spirometric pattern** | obstructive | 388 (25.3%) | |
| | restrictive | 272 (17.8%) | |
| | normal | 871 (56.9%) | |

**subjects who performed spirometries with a satisfactory start of test (VEXT < 150 ml)*

*Definition of abbreviations*:
GDS = 15-item Geriatric Depression Scale, MMSE = Mini Mental State Examination
NS = non smokers, CS = current smokers, FS = former smokers

**Table 2** - *Characteristics of participants who did or did not achieve FEV6.*

| | without 3FEV6 | with 3FEV6 | significance |
|---|---|---|---|
| **Total** (1531 subjects) | 262 (17.1%) | 1269 (82.9%) | |
| | | | |
| **Age, yr** m +/- sd | 76.4 +/- 7.4 | 73.2 +/- 6.0 | P < 0.001 |
| **Respiratory function** | | | |
| Obstructed (388) | 46 (17.5%) | 342 (26.9%) | P < 0.01 |
| Normal (871) | 144 (55.0%) | 727 (57.3%) | |
| Restricted (272) | 72 (27.5%) | 200 (15.8%) | |
| **Smoking habit** | | | |
| Non smokers (679) | 146 (55.7%) | 533 (42.0%) | P < 0.001 |
| Current or former smokers (852) | 115 (44.3%) | 737 (58.0%) | |
| **Sex** | | | |
| Female (746) | 154 (58.8%) | 592 (46.6%) | P < 0.001 |
| Male (785) | 108 (41.2%) | 677 (53.4%) | |
| **Spirometric parameters** | | | |
| FEV1 (% of predicted) m +/- sd | 87.5 +/- 27.5 | 86.3 +/- 26.8 | P = 0.505 |
| FVC (% of predicted) m +/- sd | 82.5 +/- 21.4 | 92.3 +/- 19.5 | P < 0.001 |
| FEV1/FVC m +/- sd | 77.4 +/- 13.9 | 7.8 +/- 13.9 | P < 0.001 |
| **Educational level** | | | |
| ≤ 5 years (961) | 203 (77.5%) | 758 (59.7%) | P < 0.001 |
| > 5 years (570) | 59 (22.5%) | 511 (40.3%) | |
| **Geriatric Depression Scale** m +/- sd | 5.0 +/- 3.7 | 3.7 +/- 3.3 | P < 0.001 |
| **Mini Mental Status Examination** m +/- s | 25.3 +/- 4.1 | 27.2 +/- 3.2 | P < 0.001 |
| **Barthel score** m +/- sd | 91.7 +/- 10.7 | 94.1 +/- 6.8 | P < 0.001 |
| **6-Minute Walking Test** (m) m +/- sd | 282 +/- 138 | 333 +/- 123 | P < 0.001 |
| **Body Mass Index** ($kg/m^2$) m +/- sd | 26.3 +/- 5.0 | 26.6 +/- 4.5 | P = 0.166 |
| **Waist-hip ratio** m +/- sd | 0.95 +/- 0.1 | 0.94 +/- 0.1 | P = 0.612 |
| **Occiput-wall distance** (cm) m +/- sd | 5.6 +/- 4.6 | 5.8 +/- 4.5 | P = 0.376 |

**Table 3** - *Factors negatively influencing FEV6 achievement. Multivariable logistic analysis on 1531 subjects with a satisfactory start of test.*

| | Odds ratio | P value | 95% confidence interval |
|---|---|---|---|
| **Older age (for 5 year)** | 1.42 | < 0.001 | 1.25 – 1.59 |
| **Female sex** | 1.58 | 0.022 | 1.08 – 2.31 |
| **Lower education** * | 1.77 | 0.001 | 1.25 – 2.51 |
| **Depression** † | 1.54 | 0.045 | 1.12 – 2.13 |
| **Cognitive impairment** ‡ | 1.61 | 0.009 | 1.09 - 2.37 |
| **Spirometric restriction** § | 1.98 | < 0.001 | 1.37 – 2.86 |

Also corrected by smoking habit, Barthel index and 6-Minute Walking Test,

* Lower education: ≤ 5 years

† Depression: GDS > 5

‡Cognitive impairment: MMSE < 24

§ Spirometric restriction: FVC < LLN and FEV1/FVC ≥ LLN

**Table 4 -** *Characteristics of FEV6 and FVC repeatability*

| | | mean | 95% agreement limits | percentiles | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 5th | 10th | 25th | 50th | 75th | 90th | 95th |
| ***FEV6 repeatability*** *(ml)* | Males | 68.5 | -126.0 – 262.0 | 3 | 6 | 18 | 40 | 80 | 146 | 205 |
| | Females | 55.8 | -79.4 – 191.0 | 3 | 6 | 15 | 35 | 71 | 118 | 159 |
| ***FVC repeatability*** *(ml)* | Males | 96.2 | -254.6 – 447.0 | 3 | 9 | 24 | 60 | 125 | 200 | 271 |
| | Females | 69.4 | -315.7 – 454.5 | 3 | 6 | 19 | 42 | 80 | 139 | 182 |

Mean (SD) FEV6: 3016 (777) ml for males, 2341 (560) ml in females
Mean (SD) FVC: 3187 (611) ml for males, 2323 (812) ml in females

**Table 5 -** *Characteristics of participants with and without a* ***FEV6 repeatability*** *< 150 ml*

| | ***FEV6 repeatability ≥ 150 ml*** | ***FEV6 repeatability < 150 ml*** | **significance** |
|---|---|---|---|
| **Total** (1345 subjects) | 109 (8.1%) | 1236 (91.9%) | |
| | | | |
| **Age, yr** m +/- sd | 74.8 +/- 6.2 | 73.1 +/- 6.0 | P = 0.004 |
| **Respiratory function** | | | |
| Obstructed (352) | 21 (19.3%) | 331 (26.8%) | P = 0.150 |
| Restricted (222) | 23 (21.1%) | 199 (16.1%) | |
| Normal (771) | 65 (59.6%) | 706 (57.1%) | |
| **Smoking habit** | | | |
| Non smokers (568) | 44 (40.4%) | 524 (42.4%) | P = 0.591 |
| Current or former smokers (777) | 65 (59.6%) | 712 (57.6%) | |
| **Sex** | | | |
| Female (631) | 40 (36.7%) | 591 (47.8%) | P = 0.026 |
| Male (714) | 69 (63.3%) | 645 (52.2%) | |
| **Spirometric parameters** | | | |
| FEV1 (% of predicted) m +/- sd | 86.9 +/- 26.5 | 88.1 +/- 26.7 | P = 0.770 |
| FVC (% of predicted) m +/- sd | 88.9 +/- 18.4 | 92.0 +/- 19.6 | P = 0.107 |
| FEV1/FVC m +/- sd | 69.9 +/- 14.7 | 67.9 +/- 13.7 | P = 0.104 |
| **Educational level** | | | |
| ≤ 5 years (821) | 82 (75.2%) | 739 (59.8%) | P = 0.001 |
| > 5 years (524) | 27 (24.8%) | 497 (40.2%) | |
| **Geriatric Depression Scale** m +/- sd | 4.1 +/- 3.6 | 3.7 +/- 3.3 | P = 0.301 |
| **Mini Mental Status Examination** m +/- sd | 25.9 +/- 4.4 | 27.2 +/- 3.1 | P < 0.001 |
| **Barthel score** m +/- sd | 91.6 +/- 13.1 | 94.1 +/- 6.6 | P = 0.001 |
| **6-Minute Walking Test** (m) m +/- sd | 304.4 +/- 130.1 | 334.5 +/- 122.9 | P = 0.020 |
| **Body Mass Index** ($kg/m^2$) m +/- sd | 25.9 +/- 3.8 | 26.6 +/- 4.3 | P = 0.086 |
| **Waist-hip ratio** m +/- sd | 1.01 +/- 0.10 | 1.00 +/- 0.05 | P = 0.208 |
| **Occiput-wall distance** (cm) m +/- sd | 5.9 +/- 4.2 | 5.7 +/- 4.5 | P = 0.659 |

## References


1. Bellia V., R. Pistelli, F. Catalano, et al. Quality control of spirometry in the elderly. The SA.R.A. study. SAlute Respiration nell'Anziano = Respiratory Health in the Elderly. *Am J Respir Crit Care Med* 2000;161:1094-100.

2. Battaglia S., M. C. Sandrini, F. Catalano, et al. Effects of aging on sensation of dyspnea and health-related quality of life in elderly asthmatics. *Aging Clin Exp Res* 2005;17(4):287-92.

3. Miller M. R., J. Hankinson, V. Brusasco, et al. Standardisation of spirometry. *Eur Respir J* 2005;26(2):319-38.

4. Kelley A., E. Garshick, E. R. Gross, et al. Spirometry testing standards in spinal cord injury. *Chest* 2003;123(3):725-30.

5. Stoller J. K., A. S. Buist, B. Burrows, et al. Quality control of spirometry testing in the registry for patients with severe alpha1-antitrypsin deficiency. alpha1-Antitrypsin Deficiency Registry Study Group. *Chest* 1997;111(4):899-909.

6. Enright R. L., J. E. Connett, and W. C. Bailey. The FEV1/FEV6 predicts lung function decline in adult smokers. *Respir Med* 2002;96(6):444-9.

7. Swanney M. P., R. L. Jensen, D. A. Crichton, et al. FEV(6) is an acceptable surrogate for FVC in the spirometric diagnosis of airway obstruction and restriction. *Am J Respir Crit Care Med* 2000;162:917-9.

8. Vandevoorde J., S. Verbanck, D. Schuermans, et al. FEV1/FEV6 and FEV6 as an alternative for FEV1/FVC and FVC in the spirometric detection of airway obstruction and restriction. *Chest* 2005;127(5):1560-4.

9. Akpinar-Elci M., K. B. Fedan, and P. L. Enright. FEV6 as a surrogate for FVC in detecting airways obstruction and restriction in the workplace. *Eur Respir J* 2006;27(2):374-7.

10. Hansen J. E., X. G. Sun, and K. Wasserman. Should forced expiratory volume in six seconds replace forced vital capacity to detect airway obstruction? *Eur Respir J* 2006;27(6):1244-50.

11. Pedersen O. F. FEV6: a shortcut in spirometry? *Eur Respir J* 2006;27(2):245-7.

12. Jensen R.L., R.O. Crapo, P. Enright, et al. A statistical rationale for the use of Forced Expired Volume in 6s. *Chest* 2006;130;1650-1656

13. Hankinson J. L., R. O. Crapo, and R. L. Jensen. Spirometric reference values for the 6-s FVC maneuver. *Chest* 2003;124(5):1805-11.

14. Garcia-Rio F., J. M. Pino, A. Dorgham, et al. Spirometric reference equations for European females and males aged 65-85 yrs. *Eur Respir J* 2004;24(3):397-405.

15. Vandevoorde J., S. Verbanck, D. Schuermans, et al. Obstructive and restrictive spirometric patterns: fixed cut-offs for FEV1/FEV6 and FEV6. *Eur Respir J* 2006;27(2):378-83.

16. Swanney M. P., L. E. Beckert, C. M. Frampton, et al. Validity of the American Thoracic Society and other spirometric algorithms using FVC and forced expiratory volume at 6 s for predicting a reduced total lung capacity. *Chest* 2004;126(6):1861-6.

17. 1995. Standardization of Spirometry, 1994 Update. American Thoracic Society. *Am J Respir Crit Care Med* 152(3):1107-36.

18. Pellegrino R., G. Viegi, V. Brusasco, et al. Interpretative strategies for lung function tests. *Eur Respir J* 2005;26(5):948-68.

19. Pistelli R., V. Bellia, F. Catalano, et al. Spirometry reference values for women and men aged 65-85 living in southern Europe: the effect of health outcomes. *Respiration* 2003 70(5):484-9.

20. Brink T.L., J.A. Yesavage, O. Lum, 1982. Screening tests for geriatric depression. Clinical Gerontologist Vol. 1, no. 1, pp. 37-43. 1982.

21. Folstein M. F., S. E. Folstein, and P. R. McHugh. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;2(3):189-98.

22. Mahoney F. I., and D. W. Barthel. Functional Evaluation: The Barthel Index. *Md State Med J* 1965;14:61-5.

23. Guyatt G. H., M. J. Sullivan, P. J. Thompson, et al. The 6-minute walk: a new measure of exercise capacity in patients with chronic heart failure. *Can Med Assoc J* 1985;132(8):919-23.

24. Bland, J. M., D. G. Altman. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*, 1986; i: 307-310

25. Glindmeyer H. W., J. J. Lefante, C. McColloster, et al. Blue-collar normative spirometric values for Caucasian and African-American men and women aged 18 to 65. *Am J Respir Crit Care Med* 1995;151:412-22.

26. Burrows B., M. D. Lebowitz, A. E. Camilli, et al. Longitudinal changes in forced expiratory volume in one second in adults. Methodologic considerations and findings in healthy nonsmokers. *Am Rev Respir Dis* 1986 ;133(6):974-80.

27. Brandli O., C. Schindler, N. Kunzli, et al. Lung function in healthy never smoking adults: reference values and lower limits of normal of a Swiss population. *Thorax* 1996;51(3):277-83.

28. Dockery D. W., J. H. Ware, B. G. Ferris, et al. Distribution of forced expiratory volume in one second and forced vital capacity in healthy, white, adult never-smokers in six U.S. cities. *Am Rev Respir Dis* 1985;131(4):511-20.

29. Ware J. H., D. W. Dockery, T. A. Louis, et al. Speizer. Longitudinal and cross-sectional estimates of pulmonary function decline in never-smoking adults. *Am J Epidemiol* 1990;132(4):685-700.

30. Pezzoli L., G. Giardini, S. Consonni, et al. Quality of spirometric performance in older people. *Age Ageing* 2003;32(1):43-6.

31. Milne J. S., and J. Williamson. Respiratory function tests in older people. *Clin Sci* 1972;42(3):371-81.

32. Sherman C. B., D. Kern, E. R. Richardson, et al. Cognitive function and spirometry performance in the elderly. *Am Rev Respir Dis* 1993;148(1):123-6.

33. Demir T., H. D. Ikitimur, N. Koc, et al. The role of FEV6 in the detection of airway obstruction. *Respir Med* 2005;99(1):103-6.

34. Aaron S. D., R. E. Dales, and P. Cardinal. How accurate is spirometry at predicting restrictive pulmonary impairment? *Chest* 1999;115(3):869-73.

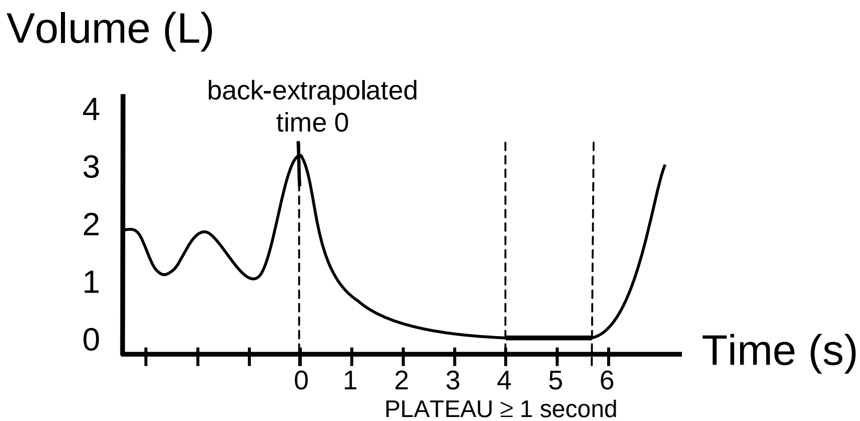
35. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Executive summary December 2006.

36. Hardie J.A., A.S. Buist, W.M. Vollmer, et al. Risk of over-diagnosis of COPD in asymptomatic elderly never-smokers. Eur Respir J 2002; 20:1117–1122.

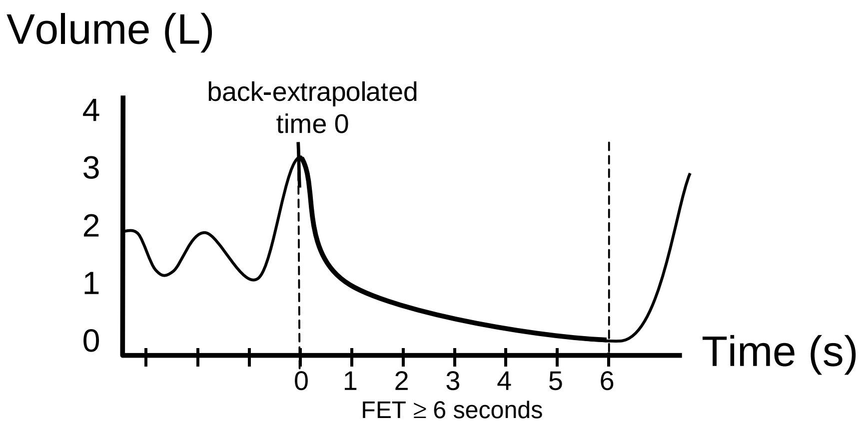
## Appendix: The SARA Study Group

*Coordinators:* V. Bellia (Palermo), F. Rengo (Napoli). *Scientific Committee Members:* R. Antonelli Incalzi (Taranto), V. Grassi (Brescia), S. Maggi (Padua), G. Masotti (Florence), G. Melillo (Naples), D. Olivieri (Parma), M. Palleschi (Rome), R. Pistelli (Rome), M. Trabucchi (Rome), S. Zuccaro (Rome).

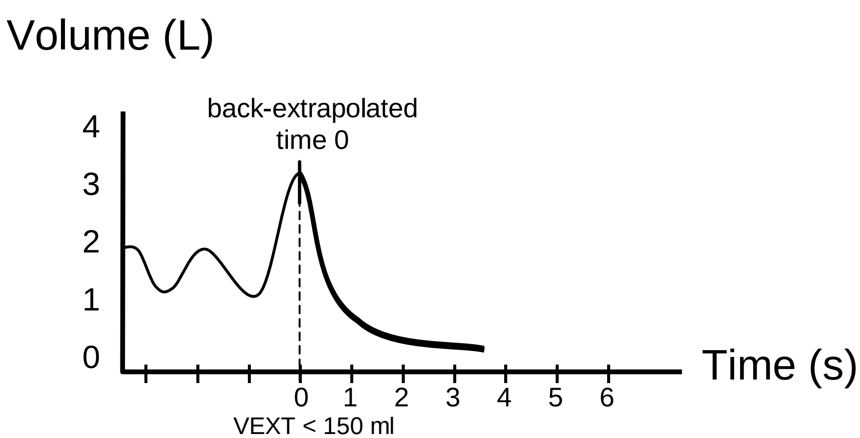
*List of participating centers, principal investigator and associated investigators (the latter in brackets):* (1) Div. Medicina I, Osp. Geriatrici INRCA, Ancona. D.L. Consales (D. Lo Nardo, P. Paggi). (2) Div. Geriatria, Osp. Civile, Asti. F. Goria (P. Fea, G. Iraldi, R. Corradi). (3) Catt. Geront. e Geriatria, Policlinico Universitario, Bari. A. Capurso (R. Flora, S. Torres, G. Venezia, M. Mesto). (4) V Div. Geriatria, Osp. Malpighi, Bologna. S. Semeraro (L. Bellotti, A. Tansella). (5) I Div. Med. Generale, Osp. Civile, Brescia. V. Grassi (S. Cossi, G. Guerini, C. Fantoni, M. De Martinis, L. Pini). (6) Clinica Pneumologica, Fondazione 'E. Maugeri', Telese (BN). G. Melillo (R. Battiloro, C. Gaudiosi, S. De Angelis). (7) Ist. Med. Int. e Geriatria, Osp. Cannizzaro, Catania. L. Motta (I. Alessandria, S. Savia). (8) Ist. Geront. e Geriat., Osp. Ponte Nuovo, Univ. of Florence. G. Masotti (M. Chiarlone, S. Zacchei). (9) Div. Geriatria, Osp. Morgagni, Forli`. V. Pedone (D. Angelini, D. Cilla). (10) Div. Geriatria, Osp. Galliera, Genova. E. Palummeri (M. Agretti, P. Costelli, D. Torriglia). (11) G.ppo Ricerca Geriatrica, Osp. Richiedei, Gussago (BS). M. Trabucchi (P. Barbisoni, F. Guerini, P. Ranieri). (12) Div. Geriatria, Osp. Generale, L'Aquila. F. Caione (D. Caione, M. La Chiara). (13) I Div. Geriatria, Osp. San Gerardo, Monza. G. Galetti (A. Cantatore, D. Casarotti, G. Anni). (14) Catt. Gerontologia e Geriatria, Univ. Federico II, Napoli. F. Rengo (F. Cacciatore, A.I. Pisacreta, C. Calabrese). (15) Ist. Med. Int., Osp. Geriatrico, Padova. G. Enzi (P. Dalla Montà, S. Peruzza, P. Albanese, F. Tiozzo). (16) Ist. Mal. App. Resp., Osp. Rasori, Parma. D. Olivieri (V. Bocchino, A. Comel, N. Barbarito). (17) Ist. Geront. e Geriatria, Policlin. Monteluce, Perugia. U. Senin (F. Arnone, L. Camilli, S. Peretti). (18) Div. Geriatria, Osp. Israelitico, Roma. S.M. Zuccaro (M. Marchetti,L. Palleschi). (19) Div. Geriatria, Osp. Gen. Addolorata, Roma. M. Palleschi (C. Cieri, F. Vetta). (20) Ist. Med. Int. e Geriatria, Polic. Gemelli, Roma. P.U. Carbonin (F. Pagano, P. Ranieri). (21) Ist. Sem. Med. e Geriatria, Pol. Le Scotte, Siena. S. Forconi (G. Abate, G. Marotta, E. Pagni). (22) Fond. San Raffaele, Cittadella della Carità, Taranto. R. Antonelli-Incalzi (C. Imperiale, C. Spada). (23) Catt. Geront. e Geriatria, Osp. Maggiore, Milano. C. Vergani (G. Giardini, M.C. Sandrini, I. Dallera). (24) Catt. Mal. App. Resp., Osp. V. Cervello, Palermo. V. Bellia (F. Catalano, N. Scichilone, S. Battaglia). *Coordinating Center:* Istituto di Medicina Generale e Pneumologia, Catt. Mal. App. Respiratorio, Università degli Studi di Palermo.




| | |
|---|---|
| VEXT | < 150 ml |
| FET | ≥ 6 seconds |
| PLATEAU | ≥ 1 second |
| Mesurable: FEV1, FVC6, FEV6, FVC | |

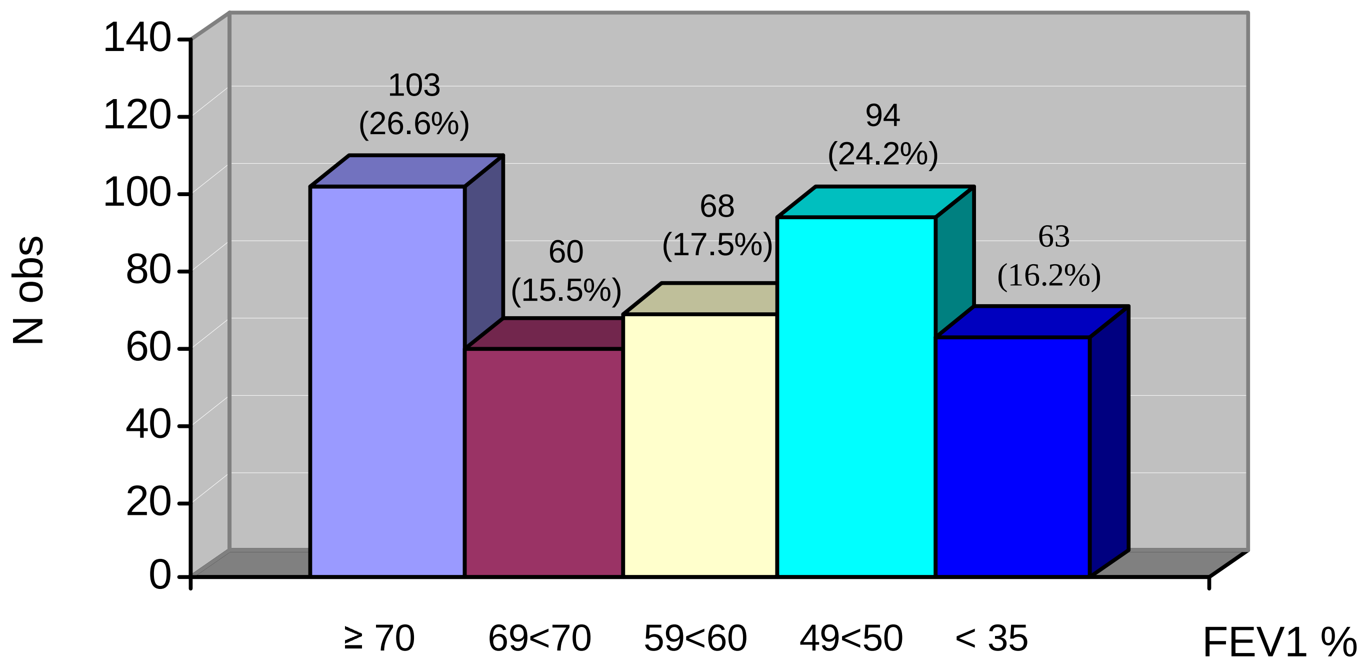



| | |
|---|---|
| VEXT | < 150 ml |
| FET | ≥ 6 seconds |
| PLATEAU | Any |
| Mesurable: FEV1, FVC6, FEV6 | |




| | |
|---|---|
| VEXT | < 150 ml |
| FET | ≥ 2 seconds |
| PLATEAU | Any |
| Mesurable: FEV1, FVC6 | |

Figure 1



140
120
100
80
60
40
20
0
N obs
103
(26.6%)
60
(15.5%)
68
(17.5%)
94
(24.2%)
63
(16.2%)
≥ 70
69<70
59<60
49<50
< 35
FEV1 %


Figure 2

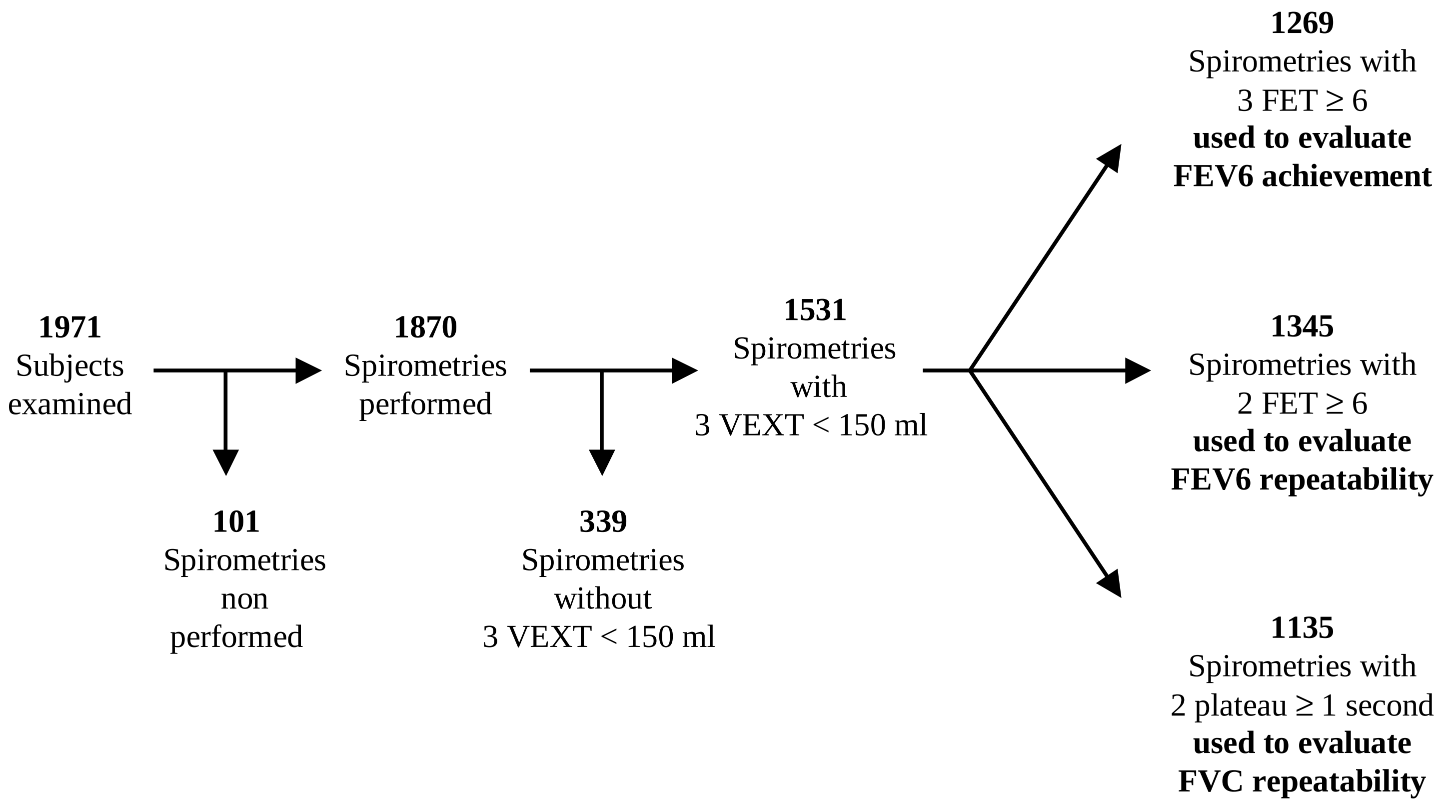

1971
Subjects examined
101
Spirometries non performed
1870
Spirometries performed
339
Spirometries without 3 VEXT < 150 ml
1531
Spirometries with 3 VEXT < 150 ml
1269
Spirometries with 3 FET ≥ 6
used to evaluate FEV6 achievement
1345
Spirometries with 2 FET ≥ 6
used to evaluate FEV6 repeatability
1135
Spirometries with 2 plateau ≥ 1 second
used to evaluate FVC repeatability

Figure 3

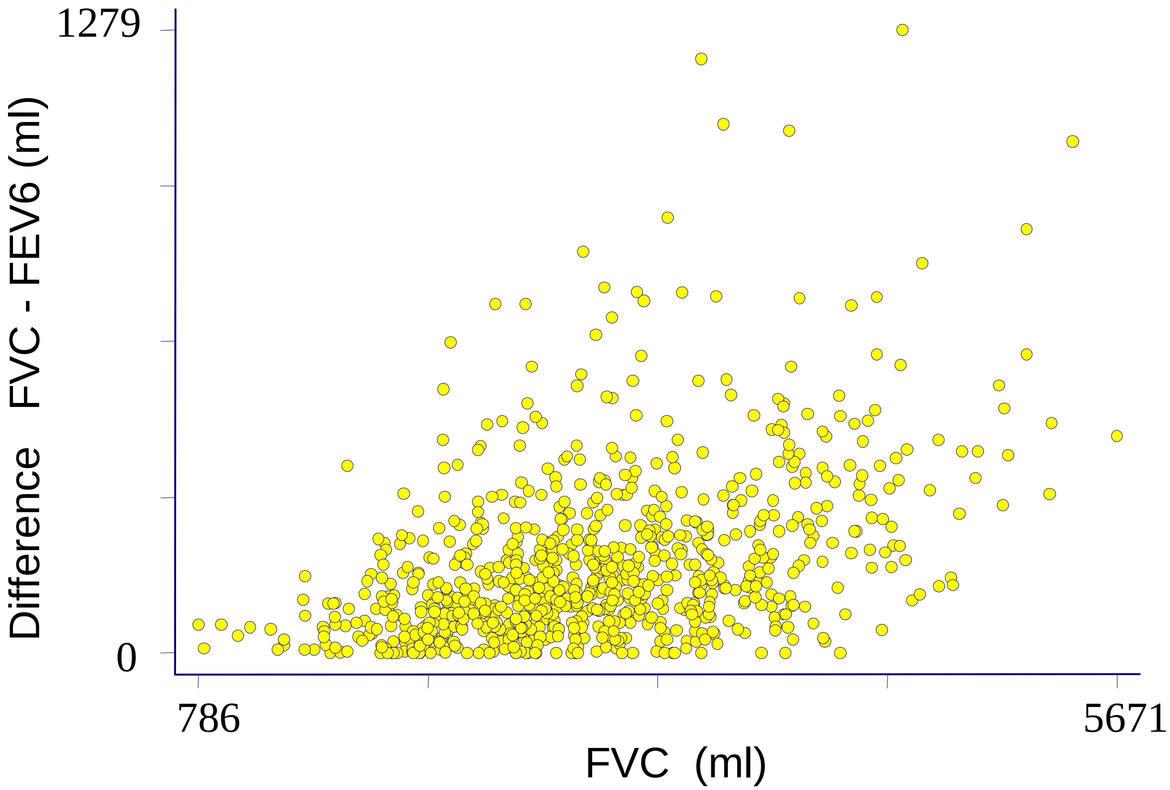



Figure 4

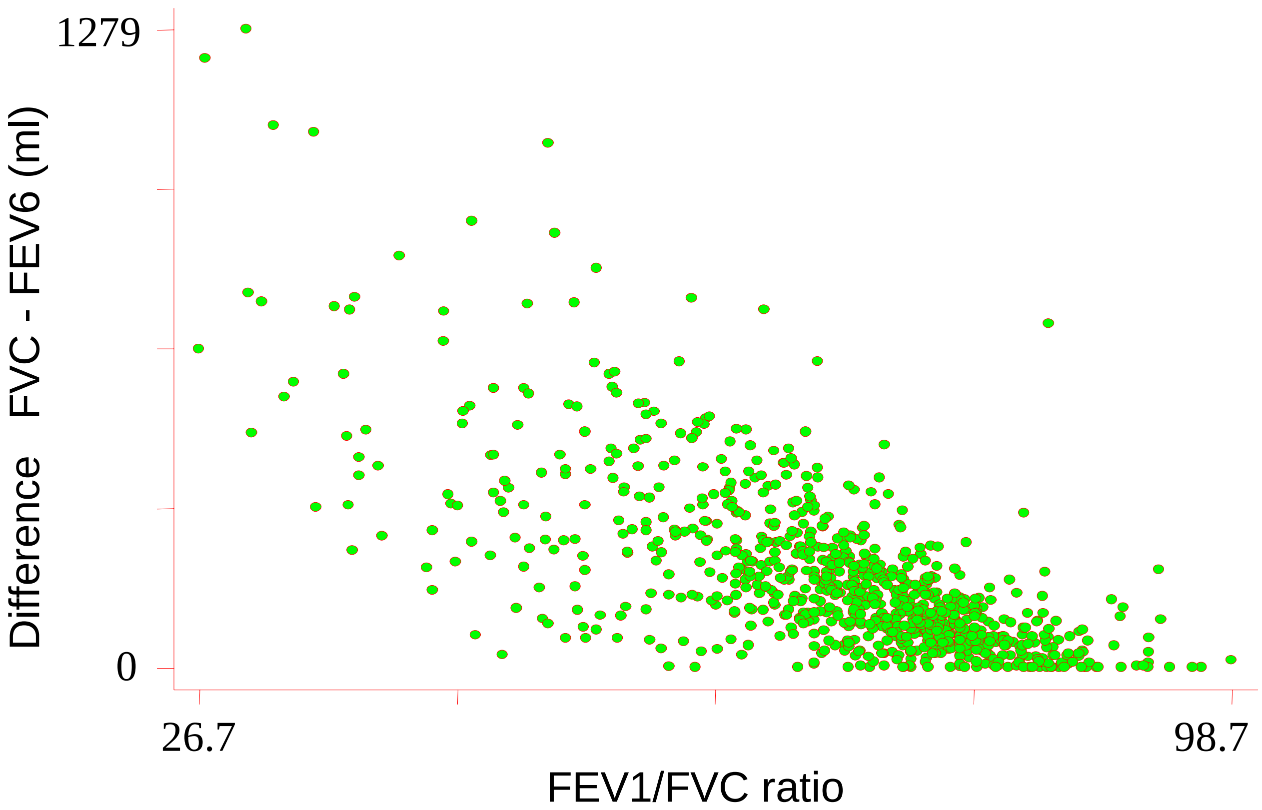



Figure 5