# Spirometric reference values for healthy adults in the Mazandaran province of Iran*, **

## Valores de referência para espirometria em adultos saudáveis na província de Mazandaran, Irã

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## Abstract

**Objective:** One of the major issues in the use of spirometry is the evaluation of the values obtained in comparison with standardized reference values. Such reference values should be determined by studying populations similar to the population in which they are intended to be used. Considering the anthropometric differences among races and the effect of regional issues, such as climate and air quality, it is recommended that these standards be set and used regionally. The objective of this study was to measure the spirometric values in residents of the Mazandaran province in Iran, as well as to determine which standardized reference values most closely correlate with the values obtained and to devise predictive equations for the target population. **Methods:** This was a cross-sectional study of 1,499 volunteers, from whom demographic and anthropometric data were collected. After having been instructed in the correct procedure, each volunteer underwent spirometry. From each volunteer, we obtained three spirometry curves that met the acceptability criteria established by the American Thoracic Society. The test with the highest values of $FEV_1$ and FVC was employed in the analysis. **Results:** We observed significant correlations between the measured values and the reference values, for both genders. The strongest correlations were with the European Respiratory Society reference values and with the 18-20 year age bracket. The predictive equations devised were based on the regression coefficients obtained and the demographic data collected. **Conclusions:** Our results show that the European Respiratory Society standard is the most appropriate standard for use in the population studied.

**Keywords:** Spirometry/statistics & numerical data; Climate effects; Reference values; Iran.

## Resumo

**Objetivo:** Um dos maiores problemas no uso da espirometria é a avaliação dos valores obtidos em comparação a valores de referência padronizados. Tais valores de referência devem ser determinados pelo estudo de populações semelhantes àquelas que se deseja utilizar. Considerando as diferenças antropométricas entre raças e o efeito de variáveis regionais, como clima e qualidade do ar, recomenda-se que esses padrões sejam definidos e utilizados regionalmente. O objetivo deste estudo foi medir os valores espirométricos em residentes da província de Mazandaran, no Irã; determinar quais valores de referência padronizados se correlacionam de forma mais próxima aos valores obtidos; e produzir equações preditivas para a população alvo. **Métodos:** Estudo transversal com 1.499 voluntários, dos quais dados demográficos e antropométricos foram coletados. Após terem sido instruídos quanto ao procedimento adequado, cada voluntário foi submetido à espirometria, sendo obtidas três curvas espirométricas de acordo com os critérios de aceitabilidade da *American Thoracic Society*. O teste com os maiores valores de $VEF_1$ e CVF foram utilizados na análise. **Resultados:** Houve correlações significativas entre os valores medidos e os valores de referência em ambos os gêneros. As correlações mais fortes ocorreram com os valores de referência da *European Respiratory Society* e com a faixa etária de 18-20 anos. As equações preditivas produzidas basearam-se nos coeficientes de regressão obtidos e nos dados demográficos coletados. **Conclusões:** Nossos resultados mostram que os valores de referência da *European Respiratory Society* são os mais apropriados para a população estudada.

**Descritores:** Espirometria/ estatística & dados numéricos; Efeitos do clima; Valores de referência; Irã (geográfico).

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## Introduction

Spirometry is one of the best methods of assessing lung function. It is also used in the diagnosis and follow-up of many pulmonary diseases, as well as providing evidence for use in court cases regarding legal compensation for pulmonary impairment.[1-3] One of the foundations of the use of spirometry is the comparison between the values obtained from an individual and those that are considered the reference (predicted) values. Reference values are based on various factors, including age, gender, height, weight, and race.[1-3] It has been suggested that numerous other factors, such as the type of climate, influence these values and should therefore also be considered.[2,3]

There are significant differences among reference values, depending on the formulas employed. To be generalizable, these values must be obtained by studying representative samples of the general population.[2] It has been recommended that these standards be set by governments.[1] It is currently accepted that referral centers should devise reference values by studying samples of healthy individuals within their region.[2] A study involving 41 male medical students between 23 and 26 years of age, conducted in 1994 in the city of Zanjan, Iran, showed that the mean FVC in the studied population was 90% of the predicted value.[4] Another study, involving 423 children and adolescents, was conducted in 2000 in the city of Isfahan, Iran[5] The authors showed that there is difference between the most widely used reference values and those obtained for the general population of Iran.[5] A study conducted in Spain by Castellsagué et al. in 1998 demonstrated differences among ethnicities in terms of lung volumes.[6] Gore et al. found that the most widely used reference values were applicable to Whites in Australia.[7] In a study conducted by our group in 2006 in the city of Sari, Iran, we found that the spirometric values (FVC, $FEV_1$, and $FEF_{25-75\%}$) for healthy adults (≥ 18 years of age) were more similar to the European Respiratory Society (ERS) standard than to other standards.[8] Common mathematical formulas used for calculating standard spirometric indices are typically based on values obtained for small samples of healthy individuals in Europe or the United States, and those values are then generalized to the population of the world at large, disregarding the fact there are anthropometric differences among races and environmental differences among regions.

In Iran, there is a lack of regional and even national spirometric standards, as well as a lack of comprehensive studies on the subject. Therefore, the objective of this study was to determine whether the spirometric values in our population are similar to any of the standard reference values, as well as to use the values obtained in order to devise predictive equations specifically for use in the population of Iran.

## Methods

This was a cross-sectional study of healthy adults (≥ 18 years of age) residing in the Mazandaran province of Iran. Volunteers were randomly recruited from urban and rural health centers in every city in the province. The study was approved by the Institutional Review Board and Research Ethics Committee of the Mazandaran University of Medical Sciences. All volunteers gave written informed consent.

Assuming a sample composed of both genders and distributed throughout four age brackets, we calculated the appropriate sample size by using information obtained from previous studies of FVC and $FEV_1$, together with the following formula:

$$N = 7 = 0/S\,\alpha = 0.05\ d = ./1$$

where S is the standard deviation, $\alpha$ is the probability threshold, and d is the effect size. Using these calculations, we estimated the sample size required to be 1,500 individuals.

For the individuals selected, we collected demographic data (age and gender) using a questionnaire and anthropometric data (height and weight) through direct measurement with the appropriate tools (scale and stadiometer). Those data were entered into the computer program provided with the self-calibrating spirometer employed (Spirolab Π, Medical International Research, Rome, Italy). After each volunteer had been instructed in the correct procedure, the spirometry tests were conducted with the individual in a standing position. From each volunteer, we obtained three spirometry curves that met the acceptability criteria established by the American Thoracic Society. The test with the highest values of FVC and $FEV_1$ was used in the analysis.[9,10]

**Table 1 -** Demographic, anthropometric, and spirometric characteristics of adult residents of the Mazandaran province in Iran, by gender.

| Characteristic | Males | Females | Total |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | Mean ± SD |
| Age (years) | 36.02 ± 10.49 | 35.44 ± 10.19 | 35.76 ± 10.35 |
| Height (cm) | 172.15 ± 7.09 | 158.78 ± 6.18 | 165.87 ± 9.44 |
| Weight (kg) | 77.72 ± 12.53 | 69.89 ± 12.78 | 74.05 ± 13.23 |
| FVC (L) | 4.59 ± 0.73 | 3.22 ± 0.54 | 3.94 ± 0.94 |
| $FEV_1$ (L) | 3.90 ± 0.63 | 2.80 ± 0.49 | 3.38 ± 0.79 |
| $FEF_{25-75\%}$ (L) | 4.46 ± 1.00 | 3.43 ± 0.86 | 3.98 ± 1.10 |

We applied the following exclusion criteria: having upper or lower respiratory symptoms; having dyspnea; being a smoker or former smoker; being a passive smoker; having been exposed to occupational hazards such as dust and irritating gases; using beta blockers; having heart disease, musculoskeletal disorders, or any other disabling chest disease; being unable or unwilling to participate in the study; and producing spirometry curves that did not meet the acceptability criteria. It is notable that 39 individuals were excluded because they were uncooperative or produced unacceptable spirometry curves.

The values obtained for our sample were compared with the reference values established by the ERS, the Intermountain Thoracic Society (ITS), the European Community for Coal and Steel (ECCS), Knudson, and Morris.[2] Using the values obtained, we also devised predictive equations specifically for use in the population of Iran.

The statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA). Differences between means were determined with paired t-tests, correlations were identified with Pearson's correlation coefficient, and the prediction model was constructed by regression analysis.

## Results

We evaluated 1,499 individuals (795 males and 704 females), all between 18 and 60 years of age. We found that the mean spirometric values were higher in males than in females (Table 1). As expected, spirometric values showed a strong positive correlation with height (Table 2). The correlation between spirometric values and weight was weaker but still significant for certain parameters. As was also expected, there was an inverse correlation between age and spirometric values.

Table 3 shows the mean values of FVC, $FEV_1$, and $FEF_{25-75\%}$ obtained in our sample. As can be seen in Table 4, the values obtained correlated significantly with all of the established reference values, regardless of gender ($p < 0.001$ for all). Among the male volunteers, the mean FVC did not differ significantly from the Knudson reference value ($p = 0.193$, $T = -1.302$); and the mean $FEF_{25-75\%}$ did not differ significantly from the ERS reference value ($p < 0.961$, $T = 0.049$). Among the female volunteers, the mean FVC did not differ significantly from the ERS reference value ($p = 0.783$, $T = 0.275$); the mean $FEV_1$ did not differ significantly from the ERS or Knudson reference values ($p = 0.733$, $T = 0.341$ and $p = 0.169$, $T = 1.38$, respectively); and the mean $FEF_{25-75\%}$ did not differ significantly from the ITS or Morris reference values ($p = 0.33$, $T = -2.138$ and $p = 0.431$, $T= -0.788$, respectively). We also found that the values obtained for FVC correlated significantly with the established reference values across all age brackets (Table 5).

On the basis of the regression coefficient values obtained and the demographic data

**Table 2 -** Correlation coefficients for the parameters measured in adult residents of the Mazandaran province in Iran, by age, height, weight, and gender.

| Parameter | FVC | | $FEV_1$ | | $FEF_{25-75\%}$ | |
|---|---|---|---|---|---|---|
| | Male | Female | Male | Female | Male | Female |
| Age | −0.553** | −0.577** | −0.588** | −0.602** | −0.356** | −0.423** |
| Height | 0.665** | 0.576** | 0.595** | 0.509** | 0.253** | 0.244** |
| Weight | 0.172** | 0.047 | 0.153** | 0.01 | 0.108** | 0.007 |

**Table 3 -** Values obtained for adult residents of the Mazandaran province in Iran, together with the corresponding international standards.

| Parameter | Measured | ERS | ITS | Morris | Knudson |
|---|---|---|---|---|---|
| | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD |
| FVC (L) | 3.94 ± 0.94 | 3.96 ± 0.86 | 4.20 ± 0.87 | 3.98 ± 0.88 | 4.18 ± 0.84 |
| $FEV_1$ (L) | 3.38 ± 0.79 | 3.36 ± 0.99 | 3.52 ± 0.68 | 3.35 ± 0.73 | 3.52 ± 0.67 |
| $FEF_{25-75\%}$ (L) | 3.97 ± 1.10 | 4.09 ± 0.58 | 3.88 ± 0.63 | 3.72 ± 0.71 | 3.95 ± 0.62 |

ERS: European Respiratory Society; and ITS: Intermountain Thoracic Society.

collected, we devised the following predictive equations:

For males

$$FVC = 5.6H \times 10^{-2} - 2.5A \times 10^{-2} - W \times 10^{-3} - 4.067$$

$$FEV_1 = 3.9H \times 10^{-2} - 2.6A \times 10^{-2} - 1.94$$

$$FEF_{25-75\%} = 1.6H \times 10^{-2} - 3.2A \times 10^{-2} + 7W \times 10^{-3} + 2.306$$

For females

$$FVC = 3.7H \times 10^{-2} - 2.5A \times 10^{-2} + 3W \times 10^{-3} - 2.034$$

$$FEV_1 = 2.8H \times 10^{-2} - 2.5A \times 10^{-2} - 3W \times 10^{-3} - 0.942$$

$$FEF_{25-75\%} = 1.6H \times 10^{-2} - 3.5A \times 10^{-2} - 6W \times 10^{-3} + 1.774$$

where $H$ is height (in cm), $A$ is age (in years), and $W$ is weight.

As can be seen in Table 5, the mean FVC was most similar to the ERS standard, for both genders. However, the mean $FEV_1$ was most similar to the ERS standard in males and to the ITS standard in females. The mean $FEF_{25-75\%}$ was most similar to the ERS standard in males and to the Knudson standard in females.

## Discussion

In our sample, the mean spirometric indices were higher in males than in females. This can be attributed, in part, to the influence that height has on these parameters.

A study conducted in 1997 by Pan et al.[11] showed that, in the local population of Taiwan, the mean FVC and $FEV_1$, adjusted for age and height, were lower than the standard reference values established for White populations. The authors found that age and height both had a significant influence on spirometric parameters. The results of the present study also show that spirometric indices decrease in parallel with increasing age. We obtained the highest values for the 18-20 year age bracket, a finding that differs slightly from those of an earlier study conducted by our group,[8] in which the highest values were obtained for the 20-30 year age bracket.

In a study conducted in England and involving 6,053 healthy individuals (16-75 years of age), FVC, $FEV_1$, and the $FEV_1$/FVC ratio were found to be considerably higher than the ERS reference values.[12] However, in the present study, as well as in our earlier study,[8] the mean FVC was lower than the ERS reference value. In addition, we found that the mean $FEV_1$, although higher than the ERS and Knudson reference values, was lower than the ITS and Morris reference values. Furthermore, in our sample, the mean $FEF_{25-75\%}$ was lower than the ERS reference value but higher than other standards. A multicenter study involving 12,900 subjects (20-44 years of age) in 14 European countries compared the measured FVC and $FEV_1$ with the ERS reference values and found that the ERS reference values were noticeably lower than the overall mean.[13] Nevertheless, the results of the present study show that the ERS reference values are noticeably higher than the mean values obtained among residents of the Mazandaran province in Iran.

Duarte et al.[14] evaluated FVC and $FEV_1$ in a sample composed of 643 White individuals in Brazil. The authors evaluated the values obtained

**Table 4 -** Correlation coefficients of the values obtained for adult residents of the Mazandaran province in Iran, in comparison with international standards, by gender.

| Parameter | ERS | | ITS | | Knudson | | Morris | |
|---|---|---|---|---|---|---|---|---|
| | Male | Female | Male | Female | Male | Female | Male | Female |
| FVC (L) | 0.748 | 0.720 | 0.735 | 0.717 | 0.730 | 0.694 | 0.700 | 0.697 |
| $FEV_1$ (L) | 0.723 | 0.683 | 0.711 | 0.696 | 0.706 | 0.683 | 0.684 | 0.616 |
| $FEF_{25-75\%}$ (L) | 0.371 | 0.417 | 0.355 | 0.435 | 0.364 | 0.458 | 0.366 | 0.440 |

ERS: European Respiratory Society; and ITS: Intermountain Thoracic Society.

**Table 5 -** Correlation coefficients of the FVC values obtained for adult residents of the Mazandaran province in Iran, in comparison with international standards, by age and gender.

| Age bracket | ERS | | ITS | | Knudson | | Morris | |
|---|---|---|---|---|---|---|---|---|
| | Male | Female | Male | Female | Male | Female | Male | Female |
| <20 | 0.744** | 0.395** | 0.649** | 0.377** | 0.715** | 0.416** | 0.649** | 0.315** |
| 20-30 | 0.636** | 0.568** | 0.635** | 0.509** | 0.598** | 0.484** | 0.577** | 0.484** |
| 30-40 | 0.562** | 0.585** | 0.560** | 0.610** | 0.591** | 0.546** | 0.524** | 0.585** |
| >40 | 0.675** | 0.616** | 0.666** | 0.647** | 0.658** | 0.635** | 0.662** | 0.641** |

ERS: European Respiratory Society; and ITS: Intermountain Thoracic Society.

in comparison with the current (2006) Brazilian standards, as well as in comparison with those established by Knudson and by the ECCS. They showed that the values obtained were most similar to the 2006 Brazilian standards, whereas they differed significantly from the Knudson and ECCS standards, which effectively invalidated the use of those standards in Brazil.[14] However, the values obtained in the present study did not differ significantly from the predicted values established by the ECCS. In another study conducted in Brazil in 2004,[15] the values of $FEV_1$ and FVC were found to exceed those obtained 12 years prior (in 1992), a difference that could be attributable to technical factors.

In 2000, Golshan & Nematbakhsh conducted a study in the city of Isfahan.[16] The authors suggested that the lung volume reference values recommended for American and Europeans are appropriate for use in adults in Isfahan, despite the fact that estimated lung volumes were slightly higher in the last group. In an earlier study conducted in Brazil, spirometric values were obtained in 1,070 individuals.[17] The authors showed that the mean FVC obtained for females was 4% lower than the Knudson standard, leading to a higher rate of diagnosis of restrictive disorders in females, whereas there was no significant difference for males. They also found that mean $FEV_1$ was higher than the Knudson standard for both genders, increasing the sensitivity of $FEV_1$ for the diagnosis of obstructive lung disorders, although there was no significant difference in terms of the mean $FEF_{25-75\%}$.[17]

The results of the present study show that all of the parameters measured correlated significantly with all of the standards evaluated, regardless of gender ($p < 0.001$ for all). A study of 41 male students (23-26 years of age) at Zanjan University showed that the mean FVC in the studied population was 90% of the predicted value.[4] Sharifian et al.[18] evaluated 1,589 residents of the Kurdistan province in Iran and showed that the mean FVC obtained was lower than the reference value, whereas the mean $FEV_1$ was comparable. In the present study, mean values were > 99% of the ERS reference values, > 93% of the Knudson reference values, and > 98% of the ITS reference values. The predictive equations we have devised make it clear that the values obtained for FVC were most similar to the ERS reference values, for both genders, whereas those obtained for $FEV_1$ were most similar to the ERS reference values in males and to the ITS reference values in females. The mean $FEF_{25-75\%}$ correlated most strongly with the ERS reference values in males and with the Knudson reference values in females.

On the basis of our results, taken together with those of previous studies, we can recommended the use of our predictive equations in all spirometry tests conducted in the region under study.

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