

Spirometric Reference Values from a Sample of the General U.S. Population

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Spirometric reference values for Caucasians, African-Americans, and Mexican-Americans 8 to 80 yr of age were developed from 7,429 asymptomatic, lifelong nonsmoking participants in the third National Health and Nutrition Examination Survey (NHANES III). Spirometry examinations followed the 1987 American Thoracic Society recommendations, and the quality of the data was continuously monitored and maintained. Caucasian subjects had higher mean FVC and FEV₁ values than did Mexican-American and African-American subjects across the entire age range. However, Caucasian and Mexican-American subjects had similar FVC and FEV₁ values with respect to height, and African-American subjects had lower values. These differences may be partially due to differences in body build: observed Mexican-Americans were shorter than Caucasian subjects of the same age, and African-Americans on average have a smaller trunk:leg ratio than do Caucasians. Reference values and lower limits of normal were derived using a piecewise polynomial model with age and height as predictors. These reference values encompass a wide age range for three race/ethnic groups and should prove useful for diagnostic and research purposes. Hankinson JL, Odenclantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population.

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The third National Health and Nutrition Examination Survey (NHANES III) was conducted from 1988 to 1994, and it comprised a random sample of the U.S. population living in households. The sample was selected from households in 81 counties across the United States, and included an oversampling of African-American and Mexican-American populations. Pulmonary function data (spirometry) were collected on 20,627 survey participants 8 yr of age and older. Because data were collected in a standardized manner for all survey participants, valid comparisons among different race/ethnic groups were possible. This analysis of the NHANES III spirometry data was conducted to develop reference equations to describe normal pulmonary function for three major race/ethnic groups: Caucasians, African-Americans, and Mexican-Americans.

Many studies have published lung function reference values for a variety of race/ethnic groups and age ranges. Hsu and colleagues (1) described ventilatory function in children and young adults 7 to 20 yr of age in the same three race/ethnic groups surveyed in NHANES III. Schwartz and colleagues (2) generated predictive equations based on data collected on African-American and Caucasian participants 6 to 24 yr of age in the NHANES II survey. Recent work by Wang and colleagues (3, 4) studied pulmonary function in African-American and

Caucasian children between 6 and 18 yr of age. Both Knudson and coworkers (5) and Crapo and colleagues (6) studied Caucasian adults exclusively; in a separate study Crapo and coworkers (7) looked at the lung function of healthy Hispanic Americans. Similarly, Coultas and colleagues (8) developed spirometric prediction equations for a group of Hispanic children and adults in New Mexico. In a recent reference value study, Glindmeyer and colleagues (9) compared Caucasian and African-American men and women 18 to 65 yr of age. However, no recent study has collected pulmonary measurements for both sexes across an extensive range of ages for Caucasians, African-Americans, and Mexican-Americans.

One significant aspect of NHANES III was the use of equipment and procedures that met the 1987 American Thoracic Society's (ATS) spirometry recommendations (10), and featured automated quality assessment during test performance. To maintain the highest level of technician performance, a quality control center continuously reviewed the data and provided quality control reports and follow-up training as appropriate. In 1994, as NHANES III was completing data collection, the ATS revised its 1987 spirometry recommendations (11), which included changes in both the extrapolated volume and the reproducibility criteria. In addition the NHANES III spirometry protocol called for each participant to perform a minimum of five maneuvers, which differed from the three acceptable maneuvers recommended by the ATS (10, 11). To make findings from NHANES III useful to future investigations utilizing the 1994 ATS recommendations, the raw data were also reanalyzed to follow the 1994 ATS recommendations, and the impact of using a minimum of five versus three maneuvers was investigated.

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TABLE 1
NUMBER OF ADULT SUBJECTS EXCLUDED USING EXCLUSION CRITERIA

| Adults 17 yr of Age and Older (n = 16,484)* | Number Excluded | Number Remaining |
|-------------------------------------------------------------------------|-----------------|------------------|
| Spirometry judged "unusable" (< 2 acceptable curves) | 277 | 16,207 |
| Adults 90 yr of age and older (actual age was unavailable) | 68 | 16,139 |
| Race/ethnicity coded as "Other" | 636 | 15,503 |
| Cigarette smokers (Question R1.) | 7,667 | 7,836 |
| Cigar and/or pipe smokers (Questions R23. and R26.) | 313 | 7,523 |
| Smoked cigarettes, cigars, and/or pipes during the 5 d prior to exam | 408 | 7,115 |
| MD diagnosis of asthma (Question C1.e.) | 454 | 6,661 |
| MD diagnosis of chronic bronchitis (Question C1.f.) | 181 | 6,480 |
| MD diagnosis of emphysema (Question C1.g.) | 15 | 6,465 |
| MD diagnosis of lung cancer (Question C1.o.) | 0 | 6,465 |
| Whistling and/or wheezing in chest in last 12 mo (Question L6.) | 419 | 6,046 |
| Whistling and/or wheezing in chest, apart from colds (Question L10.) | 112 | 5,934 |
| Persistent cough (Question L1.) | 158 | 5,776 |
| Persistent phlegm production (Question L3.) | 125 | 5,651 |
| Moderate shortness of breath (Question L5.) | 848 | 4,803 |
| Adults older than 80 yr of age (too few observations in minority cells) | 169 | 4,634 |

* Total number of participants with pulmonary function measures.

METHODS

Spirometry was performed in 20,627 survey participants (16,484 adults and 4,143 youths) as part of NHANES III. The NHANES III is the most recent in a series of studies designed to assess the health and nutrition status of adults and children in the United States through interviews and direct physical examinations. The sample design of the NHANES III is a stratified multistage probability sample of the U.S. population. The survey was conducted by the National Center for Health Statistics (NCHS) beginning in 1988 and continuing until 1994. Detailed description of the survey design and data collection methodology have been published by NCHS (12, 13). The participants (for children a proxy—ideally a parent or guardian) also completed a detailed administered questionnaire that gathered information on sex, race, ethnicity, health, and limited occupational history. Body measurements were also taken, including standing height, weight, and sitting height. Standing height was measured without shoes with the subject's back to a vertical backboard. Both heels were placed together, touching the base of the vertical board.

After an explanation of the test procedure, each subject attempted to perform at least five FVC maneuvers, with an additional goal of meeting the ATS acceptability and reproducibility criteria. Forced exhaled volumes were measured using a dry rolling-seal spirometer. The spirometer used a digital shaft encoder to measure volume with a volume resolution of 2.6 ml and a sampling interval of 10 ms. All of the digital volume-time curves were saved on digital tape (as much as 20 s

of exhalation), allowing recalculation of all parameters and test performance with regard to ATS acceptability and reproducibility criteria. The spirometry system has been independently tested (14) and found to exceed the ATS spirometry equipment recommendations.

During the performance of the FVC maneuver, real-time displays of flow-volume and volume-time curves were provided to the technicians with an indication of when 6 s of exhalation had been achieved. At the completion of each maneuver, a display was provided of all the flow-volume curves, the FVC, FEV₁, PEF, and expiratory time, and the percentage difference between each value of FVC, FEV₁, and PEF and the corresponding largest value. The computer also determined whether the last maneuver was unacceptable (cough, excessive extrapolated volume, and late peak flow) and whether additional maneuvers were needed to meet the ATS acceptability and reproducibility criteria. The technicians were instructed to obtain a minimum of five maneuvers and a maximum of eight, ensuring that the subject produced the highest possible peak flows, and that maximum exhalation continued for at least 6 s and until there was a plateau in the volume-time curve: no change in volume (40 ml) for at least 2 s. For Spanish-speaking subjects, a Spanish-speaking technician administered the test or an interpreter was provided. The test was performed in the standing position and noseclips were worn unless there was a valid reason these conditions could not be met.

A more detailed description of the study and spirometry procedures is available (13) and a more detailed description of the results of

TABLE 2
NUMBER OF YOUNG SUBJECTS EXCLUDED USING EXCLUSION CRITERIA

| Subjects | Number Excluded | Number Remaining |
|--------------------------------------------------------------------------------------------|-----------------|------------------|
| Youths 8 to 16 yr of age, n = 4,143* | | |
| Spirometry judged "unusable" (< 2 acceptable curves) | 40 | 4,103 |
| Race/ethnicity coded as "Other" | 186 | 3,917 |
| Cigarette smokers (Questions B1. and B3.) | 239 | 3,678 |
| Smoked cigarettes, cigars, and/or pipes during 5 d prior to exam (Questions B11. and B27.) | 98 | 3,580 |
| MD diagnosis of asthma (Question E1.g.) | 324 | 3,256 |
| MD diagnosis of chronic bronchitis (Question E1.h.) | 86 | 3,170 |
| Whistling and/or wheezing in chest in last 12 mo (Question G8.) | 280 | 2,890 |
| Whistling and/or wheezing in chest, apart from colds (Question G12.) | 52 | 2,838 |
| Youths 12 yr of age and older, n = 1,298 | | |
| Persistent cough (Question G2.) | 22 | 2,816 |
| Persistent phlegm production (Question G4.) | 10 | 2,806 |
| Youths younger than 12 yr of age, n = 1,540 | | |
| Reported constant "problems" with coughing in the preceding 12 mo (Questions G6. and G7.) | 10 | 2,796 |
| Youth with measured height > 10 cm lower than all other observations | 1 | 2,795 |

* Total number of participants with pulmonary function measures.

TABLE 3
AGE DISTRIBUTION OF THE SELECTED REFERENCE POPULATION

| | Age (yr) | | | | | | | | | | | | Total (n) |
|------------------------|----------|----|-------|----|-------|----|-------|----|-------|----|-------|----|--------------|
| | 8-13 | | 14-20 | | 21-35 | | 36-50 | | 51-65 | | 66-80 | | |
| | n | % | n | % | n | % | n | % | n | % | n | % | |
| Male subjects | | | | | | | | | | | | | |
| Caucasian | 268 | 30 | 154 | 17 | 192 | 21 | 124 | 14 | 70 | 8 | 90 | 10 | 898 |
| African-American | 351 | 34 | 254 | 25 | 251 | 24 | 109 | 11 | 35 | 3 | 27 | 3 | 1,027 |
| Mexican-American | 386 | 35 | 224 | 20 | 306 | 27 | 111 | 10 | 57 | 5 | 32 | 3 | 1,116 |
| Female subjects | | | | | | | | | | | | | |
| Caucasian | 284 | 21 | 172 | 12 | 260 | 19 | 239 | 17 | 192 | 14 | 236 | 17 | 1,383 |
| African-American | 393 | 27 | 316 | 21 | 382 | 26 | 219 | 15 | 100 | 7 | 71 | 5 | 1,481 |
| Mexican-American | 381 | 25 | 270 | 18 | 444 | 29 | 225 | 15 | 117 | 8 | 86 | 6 | 1,523 |

applying the ATS acceptability and reproducibility criteria in this study has been reported by Hankinson and Bang (15).

Quality control of the spirometry data was conducted by the National Institute for Occupational Safety and Health (NIOSH), Morgantown, West Virginia, which served as the quality control center. In addition to formal initial training of at least 1 wk and a pilot study of 820 subjects (data not included), the technicians were continuously monitored during the entire study by a senior quality control technician who periodically traveled to the field to observe and provide additional instructions. At the completion of each study location (approximately 300 subjects per location), a quality control report evaluating each technician's performance was used to determine whether additional training or monitoring was warranted. In addition, the raw flow-volume and volume-time curves were reviewed by a senior technician and the subject's performance was graded. Those subjects whose performance was judged to be unacceptable by two senior technicians (less than two acceptable curves) were excluded from this analysis.

In 1994, the ATS approved a new statement on spirometry (11) that changed the reproducibility criteria to a constant 200 ml and the extrapolated volume lower limit from 100 to 150 ml. The ATS also recommended that three acceptable and reproducible maneuvers be performed, in contrast to the minimum of five maneuvers used in the NHANES III data collection protocol. To determine the impact of strictly following the 1994 ATS spirometry recommendations, the raw volume-time curves were reanalyzed to provide new values of FVC, FEV₁, etc., which would have been obtained if the 1994 ATS recommendations had been in place during the NHANES III survey period. Specifically, each raw volume-time curve was reprocessed in the order

that it was obtained (including unacceptable maneuvers). When the 1994 ATS minimum criteria were met (three acceptable maneuvers with a reproducible FVC and FEV₁), no additional curves were used in the recalculation of this new set of spirometric parameters. In addition, when all curves were used, the 1994 acceptability and reproducibility criteria were used.

For use in the development of reference values, only asymptomatic, lifelong nonsmoking subjects with at least two acceptable maneuvers were included in our analysis. Applying these criteria eliminated 13,198 of the 20,627 study participants who performed spirometry, leaving 7,429 subjects (see Tables 1 and 2).

In the figures, the mean values of largest FEV₁ and FEV₁/FVC% (averaged over 2-yr age or 2-cm height intervals) were plotted using the Axum plotting software (MathSoft, Cambridge, MA). Similarly for the comparison with other reference values studies, the mean values of age and height (averaged over 2-yr age increments) were used in the appropriate reference equation to calculate the values, as a function of age. For example, the mean height and mean age for the group of subjects 20 and 21 years of age were used in the reference equations to calculate their corresponding age-group predicted FEV₁.

Statistical analyses were performed using SAS 6.12 for Windows. Assumptions of distributional normality were tested using the Shapiro-Wilk test. Reference equations and equations to calculate the lower limit of normal (LLN) criteria were developed using the SAS procedures PROC REG and PROC UNIVARIATE as well as graphic procedures for analysis of the distribution of residuals. Independent variables considered for inclusion in the models were age, standing height, weight, sitting height, and body mass index. The form

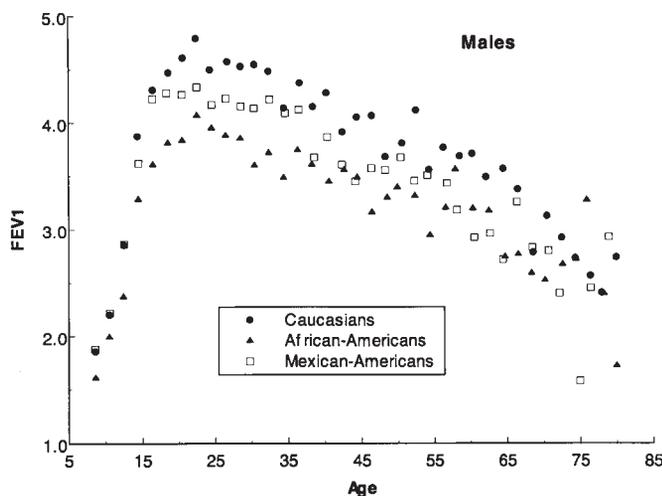


Figure 1. Mean FEV₁ versus age (2-yr increments) for male subjects.

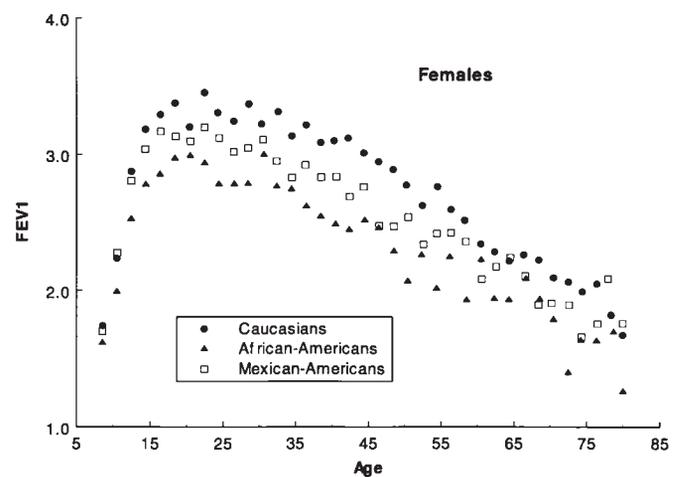


Figure 2. Mean FEV₁ versus age (2-yr increments) for female subjects.

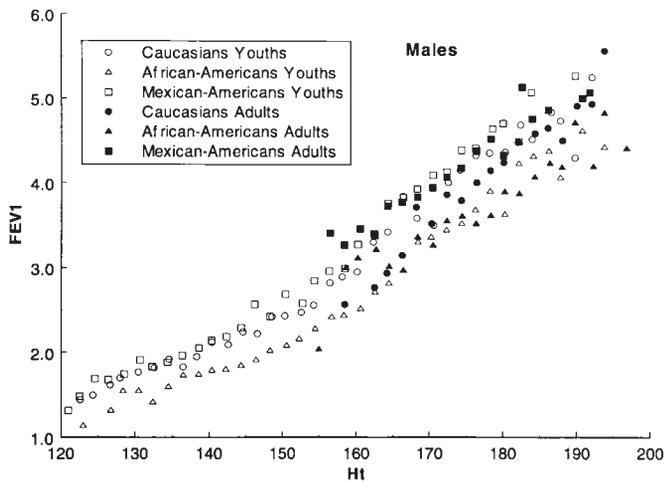


Figure 3. Mean FEV₁ versus height (2-cm increments) for youth and adult male subjects.

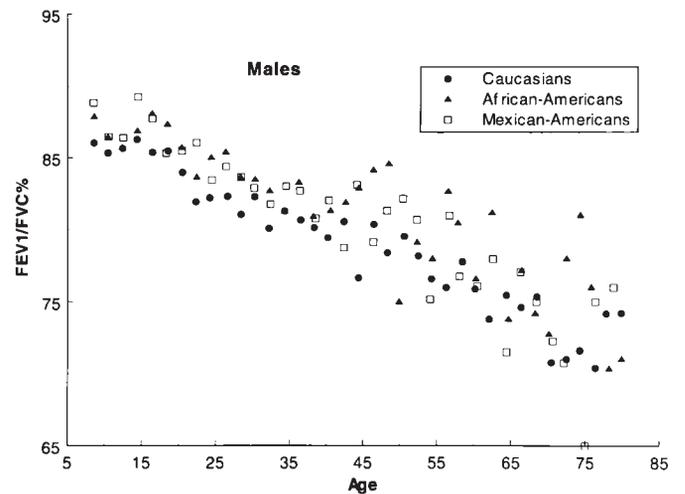


Figure 5. Mean FEV₁/FVC% versus age (2-yr increments) for male subjects.

of the model and choice of independent variables were based on a combination of statistical significance, fraction of explained variability (R^2), and other considerations related to simplicity, ease of use, reliability, and, to a lesser degree, compatibility with methods used by other investigators. One further objective was to develop equations that included the entire age range of 8 to 80 yr and were free of any discontinuities over the age and height ranges of the reference population.

Because other models did not appear to offer significant statistical advantages over a lower-order polynomial, the lower-order polynomial model was chosen because of its ease of use and the success other investigators have had using this model in their reference equations. However, for age, a single lower-order polynomial was not fully adequate, and piecewise polynomials with one or more change points were considered. Methods to locate change points included a combination of graphic analysis to determine the approximate location and R^2 to refine the graphic estimation. Graphic methods included the plotting of averages, and the examination of higher-order polynomial models for the location of extrema.

Consideration was given to developing a single equation for all three race/ethnic groups (Caucasian, African-American, and Mexican-American). Models were tested to determine whether any substantial improvement resulted from including information on race/

ethnicity, and, if so, whether such improvement represented a constant difference or whether there were departures from parallelism as a function of the independent variables. The bases for assessing the effect of race/ethnicity included formal hypothesis testing, changes in R^2 , and differences between the predicted values for different models relative to the magnitude of either predicted value and relative to the standard deviation over the range of the predictors.

The effect of transforming the pulmonary function parameters prior to modeling was examined. Transformations considered included logarithmic, square root, and dividing the pulmonary function parameter by the square of height. Aspects explored included improvement in the R^2 and the standard error of the prediction, changes in the distribution of the residuals and the homogeneity of the variance over the predictors, and changes in the effect of including race/ethnicity information. Variance homogeneity was tested by linear and quadratic regression models of the absolute values of the residuals, which are less sensitive to outliers. Prior to distribution examination, residuals were normalized on the basis of inhomogeneity models.

RESULTS

The largest number of NHANES III subjects were excluded from the reference population because of a history of smoking

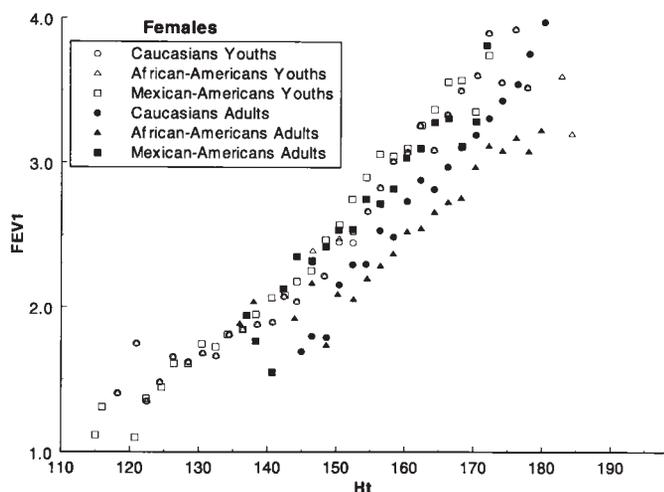


Figure 4. Mean FEV₁ versus height (2-cm increments) for youth and adult female subjects.

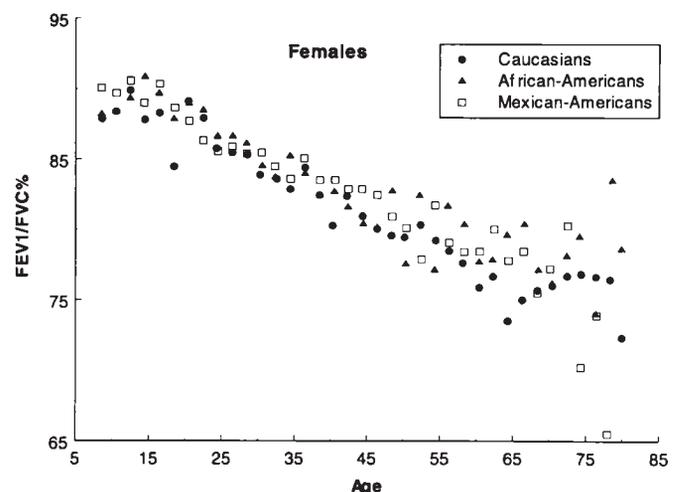


Figure 6. Mean FEV₁/FVC% versus age (2-yr increments) for female subjects.

TABLE 4
PREDICTION AND LOWER LIMIT OF NORMAL EQUATIONS FOR
SPIROMETRIC PARAMETERS FOR MALE SUBJECTS*

| Male Subjects | Intercept | Age | Age ² | Ht _{PRD} (cm) ² | Ht _{LLN} (cm) ² | R ² |
|---------------------------------|-----------|----------|------------------|-------------------------------------|-------------------------------------|----------------|
| Caucasian < 20 yr of age | | | | | | |
| FEV ₁ | -0.7453 | -0.04106 | 0.004477 | 0.00014098 | 0.00011607 | 0.8510 |
| FEV ₆ | -0.3119 | -0.18612 | 0.009717 | 0.00018188 | 0.00015323 | 0.8692 |
| FVC | -0.2584 | -0.20415 | 0.010133 | 0.00018642 | 0.00015695 | 0.8668 |
| PEF | -0.5962 | -0.12357 | 0.013135 | 0.00024962 | 0.00017635 | 0.7808 |
| FEF ₂₅₋₇₅ | -1.0863 | 0.13939 | | 0.00010345 | 0.00005294 | 0.5601 |
| Caucasian ≥ 20 yr of age | | | | | | |
| FEV ₁ | 0.5536 | -0.01303 | -0.000172 | 0.00014098 | 0.00011607 | 0.8510 |
| FEV ₆ | 0.1102 | -0.00842 | -0.000223 | 0.00018188 | 0.00015323 | 0.8692 |
| FVC | -0.1933 | 0.00064 | -0.000269 | 0.00018642 | 0.00015695 | 0.8668 |
| PEF | 1.0523 | 0.08272 | -0.001301 | 0.00024962 | 0.00017635 | 0.7808 |
| FEF ₂₅₋₇₅ | 2.7006 | -0.04995 | | 0.00010345 | 0.00005294 | 0.5601 |
| African-American < 20 yr of age | | | | | | |
| FEV ₁ | -0.7048 | -0.05711 | 0.004316 | 0.00013194 | 0.00010561 | 0.8080 |
| FEV ₆ | -0.5525 | -0.14107 | 0.007241 | 0.00016429 | 0.00013499 | 0.8297 |
| FVC | -0.4971 | -0.15497 | 0.007701 | 0.00016643 | 0.00013670 | 0.8303 |
| PEF | -0.2684 | -0.28016 | 0.018202 | 0.00027333 | 0.00018938 | 0.7299 |
| FEF ₂₅₋₇₅ | -1.1627 | 0.12314 | | 0.00010461 | 0.00004819 | 0.4724 |
| African-American ≥ 20 yr of age | | | | | | |
| FEV ₁ | 0.3411 | -0.02309 | | 0.00013194 | 0.00010561 | 0.8080 |
| FEV ₆ | -0.0547 | -0.02114 | | 0.00016429 | 0.00013499 | 0.8297 |
| FVC | -0.1517 | -0.01821 | | 0.00016643 | 0.00013670 | 0.8303 |
| PEF | 2.2257 | -0.04082 | | 0.00027333 | 0.00018938 | 0.7299 |
| FEF ₂₅₋₇₅ | 2.1477 | -0.04238 | | 0.00010461 | 0.00004819 | 0.4724 |
| Mexican-American < 20 yr of age | | | | | | |
| FEV ₁ | -0.8218 | -0.04248 | 0.004291 | 0.00015104 | 0.00012670 | 0.8536 |
| FEV ₆ | -0.6646 | -0.11270 | 0.007306 | 0.00017840 | 0.00015029 | 0.8657 |
| FVC | -0.7571 | -0.09520 | 0.006619 | 0.00017823 | 0.00014947 | 0.8641 |
| PEF | -0.9537 | -0.19602 | 0.014497 | 0.00030243 | 0.00021833 | 0.7530 |
| FEF ₂₅₋₇₅ | -1.3592 | 0.10529 | | 0.00014473 | 0.00009020 | 0.5482 |
| Mexican-American ≥ 20 yr of age | | | | | | |
| FEV ₁ | 0.6306 | -0.02928 | | 0.00015104 | 0.00012670 | 0.8536 |
| FEV ₆ | 0.5757 | -0.02860 | | 0.00017840 | 0.00015029 | 0.8657 |
| FVC | 0.2376 | -0.00891 | -0.000182 | 0.00017823 | 0.00014947 | 0.8641 |
| PEF | 0.0870 | 0.06580 | -0.001195 | 0.00030243 | 0.00021833 | 0.7530 |
| FEF ₂₅₋₇₅ | 1.7503 | -0.05018 | | 0.00014473 | 0.00009020 | 0.5482 |

* Ht_{PRD} coefficient is used for prediction equation and Ht_{LLN} is used (replaces Ht_{PRD}) for the lower limit of normal equation. Lung function parameter = b₀ + b₁ * age + b₂ * age² + b₃ * height².

(Tables 1 and 2). The age distributions by sex and race/ethnic groups of the reference population is shown in Table 3.

The mean FEV₁ values versus age for each of the three race/ethnic groups are shown in Figure 1 (males) and Figure 2 (females). For both males (Figure 1) and females (Figure 2), Caucasian subjects had higher mean FVC (not shown) and FEV₁ values than did Mexican-American subjects across the entire age range. African-American males and females had lower mean FVC (not shown) and FEV₁ values than did both the Caucasian and the Mexican-American subjects. The mean values of FEV₁ versus height for adults and youths are shown in Figure 3 (males) and Figure 4 (females). Caucasian and Mexican-American height groups had similar FVC (not shown) and FEV₁ values. However, with the exception of female youths, African-Americans had lower values of mean FEV₁ for all heights when compared with Caucasian and Mexican-American subjects. The lower FEV₁ values for Mexican-Americans compared with Caucasian values seen in Figures 1 and 2 and not present in Figures 3 and 4, where the FEV₁ is slightly higher for Mexican-Americans, are most likely due to the lower mean heights for all Mexican-American age groups in Figures 1 and 2 (p < 0.0001).

In contrast to the difference between race/ethnic groups observed for FVC and FEV₁, Figures 5 and 6 show relatively small, but statistically significant, differences in the FEV₁/

FVC% between the three groups: Caucasian values are slightly lower than African-American and Mexican-American values.

In developing the regression model, age was found to be a necessary independent variable for all pulmonary function parameters. Height and weight were similar in terms of improving the R², with little improvement when both are used in the model, height being chosen as the preferred measure. Body mass index offered improvements similar to weight. The addition of sitting height to a model where standing height is already present offered little improvement if the three race/ethnic groups are modeled with separate equations. Sitting height can to some degree account for between-race differences, but a common equation that includes sitting height is not as accurate as separate race/ethnic equations that do not include sitting height. Therefore, only age and height were used in the reference equations for FVC, FEV₁, FEV₆, PEF, and FEF₂₅₋₇₅.

Because of the change in pulmonary function values with age—a sharp rise in adolescence followed by a gradual decline—the effect of age is not easily modeled with a single polynomial. Therefore, piecewise polynomials with a single change point were used in the reference equations for FVC, FEV₁, FEV₆, PEF, and FEF₂₅₋₇₅. Although higher-order polynomials, the most obvious alternative, were used as an exploratory tool, higher-order terms were not statistically significant

TABLE 5
PREDICTION AND LOWER LIMIT OF NORMAL EQUATIONS FOR
SPIROMETRIC PARAMETERS FOR FEMALE SUBJECTS*

| Female Subjects | Intercept | Age | Age ² | Ht _{PRD} (cm) ² | Ht _{LLN} (cm) ² | R ² |
|---------------------------------|-----------|----------|------------------|-------------------------------------|-------------------------------------|----------------|
| Caucasian < 18 yr of age | | | | | | |
| FEV ₁ | -0.8710 | 0.06537 | | 0.00011496 | 0.00009283 | 0.7494 |
| FEV ₆ | -1.1925 | 0.06544 | | 0.00014395 | 0.00011827 | 0.7457 |
| FVC | -1.2082 | 0.05916 | | 0.00014815 | 0.00012198 | 0.7344 |
| PEF | -3.6181 | 0.60644 | -0.016846 | 0.00018623 | 0.00012148 | 0.5559 |
| FEF ₂₅₋₇₅ | -2.5284 | 0.52490 | -0.015309 | 0.00006982 | 0.00002302 | 0.5005 |
| Caucasian ≥ 18 yr of age | | | | | | |
| FEV ₁ | 0.4333 | -0.00361 | -0.000194 | 0.00011496 | 0.00009283 | 0.7494 |
| FEV ₆ | -0.1373 | 0.01317 | -0.000352 | 0.00014395 | 0.00011827 | 0.7457 |
| FVC | -0.3560 | 0.01870 | -0.000382 | 0.00014815 | 0.00012198 | 0.7344 |
| PEF | 0.9267 | 0.06929 | -0.001031 | 0.00018623 | 0.00012148 | 0.5559 |
| FEF ₂₅₋₇₅ | 2.3670 | -0.01904 | -0.000200 | 0.00006982 | 0.00002302 | 0.5005 |
| African-American < 18 yr of age | | | | | | |
| FEV ₁ | -0.9630 | 0.05799 | | 0.00010846 | 0.00008546 | 0.6687 |
| FEV ₆ | -0.6370 | -0.04243 | 0.003508 | 0.00013497 | 0.00010848 | 0.6615 |
| FVC | -0.6166 | -0.04687 | 0.003602 | 0.00013606 | 0.00010916 | 0.6536 |
| PEF | -1.2398 | 0.16375 | | 0.00019746 | 0.00012160 | 0.4736 |
| FEF ₂₅₋₇₅ | -2.5379 | 0.43755 | -0.012154 | 0.00008572 | 0.00003380 | 0.3787 |
| African-American ≥ 18 yr of age | | | | | | |
| FEV ₁ | 0.3433 | -0.01283 | -0.000097 | 0.00010846 | 0.00008546 | 0.6687 |
| FEV ₆ | -0.1981 | 0.00047 | -0.000230 | 0.00013497 | 0.00010848 | 0.6615 |
| FVC | -0.3039 | 0.00536 | -0.000265 | 0.00013606 | 0.00010916 | 0.6536 |
| PEF | 1.3597 | 0.03458 | -0.000847 | 0.00019746 | 0.00012160 | 0.4736 |
| FEF ₂₅₋₇₅ | 2.0828 | -0.03793 | | 0.00008572 | 0.00003380 | 0.3787 |
| Mexican-American < 18 yr of age | | | | | | |
| FEV ₁ | -0.9641 | 0.06490 | | 0.00012154 | 0.00009890 | 0.7268 |
| FEV ₆ | -1.2410 | 0.07625 | | 0.00014106 | 0.00011480 | 0.7208 |
| FVC | -1.2507 | 0.07501 | | 0.00014246 | 0.00011570 | 0.7103 |
| PEF | -3.2549 | 0.47495 | -0.013193 | 0.00022203 | 0.00014611 | 0.4669 |
| FEF ₂₅₋₇₅ | -2.1825 | 0.42451 | -0.012415 | 0.00009610 | 0.00004594 | 0.4305 |
| Mexican-American ≥ 18 yr of age | | | | | | |
| FEV ₁ | 0.4529 | -0.01178 | -0.000113 | 0.00012154 | 0.00009890 | 0.7268 |
| FEV ₆ | 0.2033 | 0.00020 | -0.000232 | 0.00014106 | 0.00011480 | 0.7208 |
| FVC | 0.1210 | 0.00307 | -0.000237 | 0.00014246 | 0.00011570 | 0.7103 |
| PEF | 0.2401 | 0.06174 | -0.001023 | 0.00022203 | 0.00014611 | 0.4669 |
| FEF ₂₅₋₇₅ | 1.7456 | -0.01195 | -0.000291 | 0.00009610 | 0.00004594 | 0.4305 |

* Ht_{PRD} coefficient is used for prediction equation and Ht_{LLN} is used (replaces Ht_{PRD}) for the lower limit of normal equation. Lung function parameter = b₀ + b₁ * age + b₂ * age² + b₃ * height².

and their inclusion did not improve the R². Plots of lung function versus age using higher-order polynomials in age and outcomes from using different change points suggested that the best change point for males was between 19 and 23 yr of age and for females between 17 and 21 yr of age. On the basis of the R² values over these intervals, it was concluded that 20 yr was the best change point for males and 18 yr for females.

The residuals for FVC, FEV₁, FEV₆, PEF, and FEF₂₅₋₇₅ were all inhomogeneous in variance with respect to height², and as a consequence, the standard error of the estimate (SEE) for these variables was modeled as: SEE = b₁ * height². The normed residuals corresponding to these models do not differ significantly from the Gaussian in the case of FVC, FEV₁, FEV₆, and PEF, as determined by the Shapiro-Wilk test. The normed residuals of the FEF₂₅₋₇₅ showed some indication of right skewing. Transformation (square root and logarithmic) prior to modeling did reduce the skewness in the FEF₂₅₋₇₅. Transformations were not needed for FVC, FEV₁, FEV₆, and PEF; the LLN of the population was computed for these lung function parameters as predicted - 1.645 * SEE. Because the FEF₂₅₋₇₅ had a skewed distribution, the LLN for that parameter is based on the observed lower fifth percentile.

The general form of the reference equations shown in the tables is:

TABLE 6
PREDICTION AND LOWER LIMIT OF NORMAL
EQUATIONS FOR FEV₁/FEV₆% AND FEV₁/FVC%
FOR MALE AND FEMALE SUBJECTS*

| | Intercept _{PRD} | Age | Intercept _{LLN} | R ² |
|--------------------------------------|--------------------------|---------|--------------------------|----------------|
| Male subjects | | | | |
| Caucasian | | | | |
| FEV ₁ /FEV ₆ % | 87.340 | -0.1382 | 78.372 | 0.2151 |
| FEV ₁ /FVC% | 88.066 | -0.2066 | 78.388 | 0.3448 |
| African-American | | | | |
| FEV ₁ /FEV ₆ % | 88.841 | -0.1305 | 78.979 | 0.0937 |
| FEV ₁ /FVC% | 89.239 | -0.1828 | 78.822 | 0.1538 |
| Mexican-American | | | | |
| FEV ₁ /FEV ₆ % | 89.388 | -0.1534 | 80.810 | 0.1711 |
| FEV ₁ /FVC% | 90.024 | -0.2186 | 80.925 | 0.2713 |
| Female subjects | | | | |
| Caucasian | | | | |
| FEV ₁ /FEV ₆ % | 90.107 | -0.1563 | 81.307 | 0.3048 |
| FEV ₁ /FVC% | 90.809 | -0.2125 | 81.015 | 0.3955 |
| African-American | | | | |
| FEV ₁ /FEV ₆ % | 91.229 | -0.1558 | 81.396 | 0.1693 |
| FEV ₁ /FVC% | 91.655 | -0.2039 | 80.978 | 0.2284 |
| Mexican-American | | | | |
| FEV ₁ /FEV ₆ % | 91.664 | -0.1670 | 83.034 | 0.2449 |
| FEV ₁ /FVC% | 92.360 | -0.2248 | 83.044 | 0.3352 |

* Intercept_{PRD} is used for prediction equation and Intercept_{LLN} is used (replaces Intercept_{PRD}) for the lower limit of normal equation. Lung function parameter = b₀ + b₁ * age.

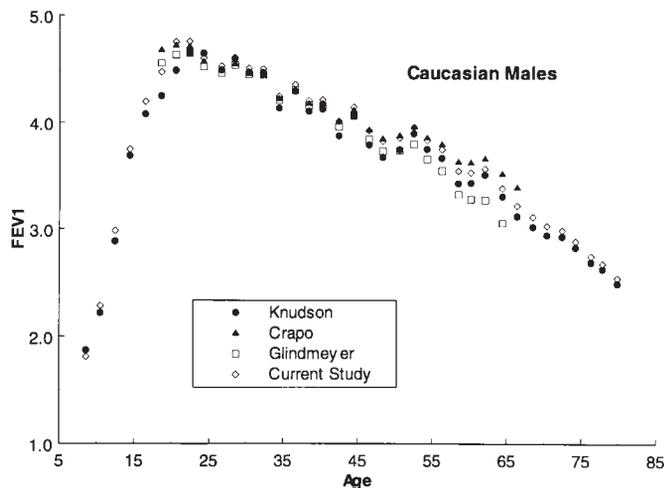


Figure 7. Predicted FEV₁ versus age for Caucasian male subjects using equations from Knudson (5), Crapo (6), Glindmeyer (9), and current study.

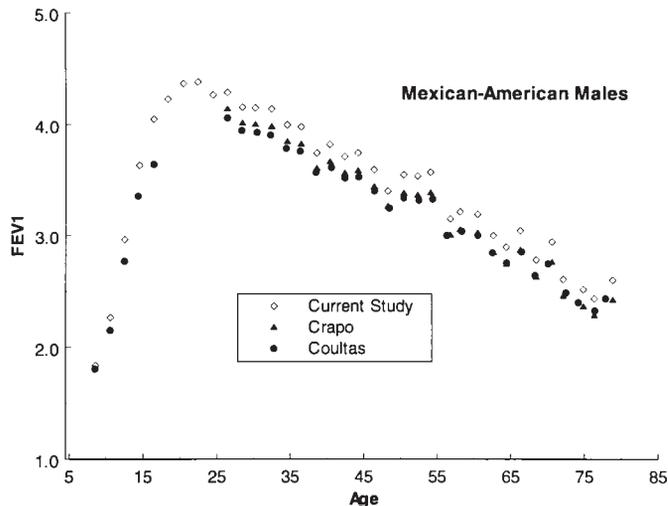


Figure 9. Predicted FEV₁ versus age for Mexican-American male subjects using equations from Crapo (7), Coultas (8), and current study.

$$\text{lung function parameter} = b_0 + b_1 * \text{age} + b_2 * \text{age}^2 + b_3 * \text{height}^2. \quad (1)$$

The Ht_{PRD} coefficient (b_3 or coefficient, which is multiplied by height squared) in Tables 4 and 5 is used in the prediction equation, and the Ht_{LLN} coefficient (b_3) is used in place of the Ht_{PRD} when calculating the LLN rather than subtracting a constant value from the predicted value.

The reference equations for the FEV₁/FVC% and FEV₁/FEV₆% for males and females by race/ethnic group are shown in Table 6. The Intercept_{PRD} term in Table 6 is used in the prediction equation, and the Intercept_{LLN} term replaces the Intercept_{PRD} when calculating the LLN. The FEV₁/FEV₆% is provided as a potential surrogate for the FEV₁/FVC% as a measure that does not require a prolonged exhalation. Only age is needed in the model, which has the general form:

$$\text{lung function parameter} = b_0 + b_1 * \text{age}. \quad (2)$$

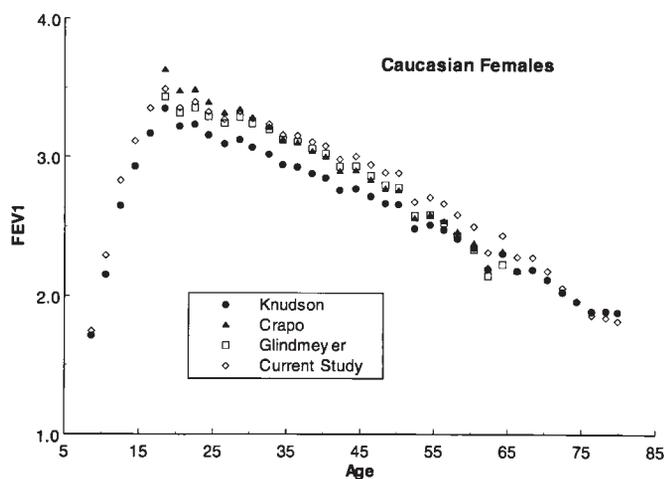


Figure 8. Predicted FEV₁ versus age for Caucasian female subjects using equations from Knudson (5), Crapo (6), Glindmeyer (9), and current study.

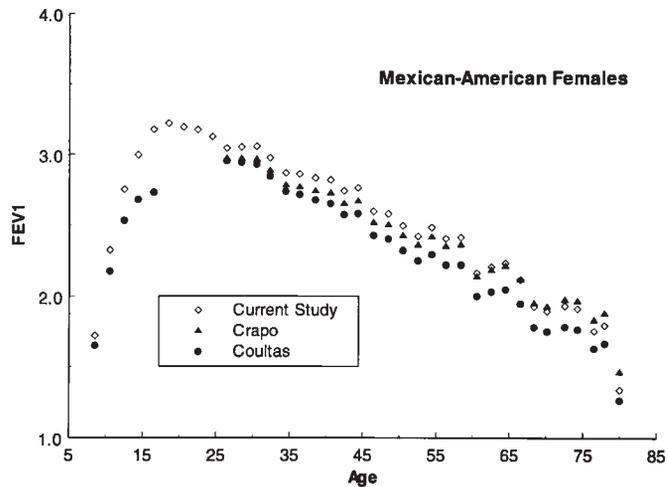


Figure 10. Predicted FEV₁ versus age for Mexican-American female subjects using equations from Crapo (7), Coultas (8), and current study.

In a separate analysis, reference equations using the minimum number of curves needed to meet the 1994 ATS recommendations (three acceptable curves with a reproducible test) (ATS-min) were calculated. Averaged over all the subjects, the mean differences between the FVC and FEV₁ using all the curves compared with ATS-min were 62.5 and 52 ml, respectively. We observed these differences to be approximately the same for all ages and heights.

A comparison of the reference equations from this study with those of other studies of Caucasian subjects—Crapo and colleagues (6), Knudson and coworkers (5), and Glindmeyer and colleagues (9)—are shown in Figure 7 (males) and Figure 8 (females). The reference values from the present study appear to be similar or slightly higher than those from other studies.

A comparison with other studies of Mexican-American subjects—Crapo and coworkers (7) and Coultas and colleagues (8)—are shown in Figure 9 (males) and Figure 10 (fe-

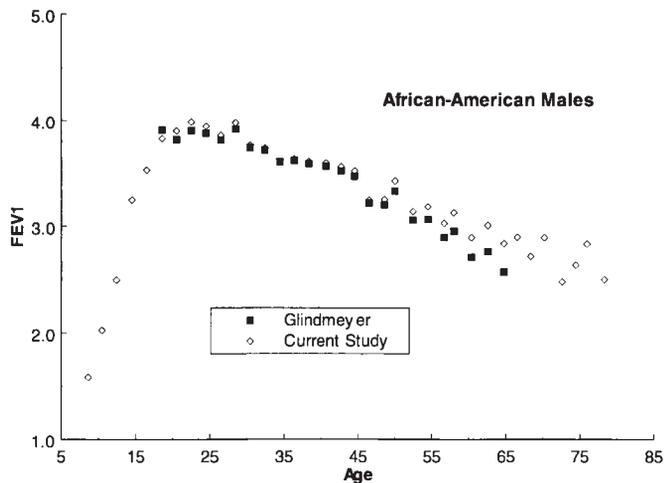


Figure 11. Predicted FEV₁ versus age for African-American male subjects using equations from Glindmeyer (9) and current study.

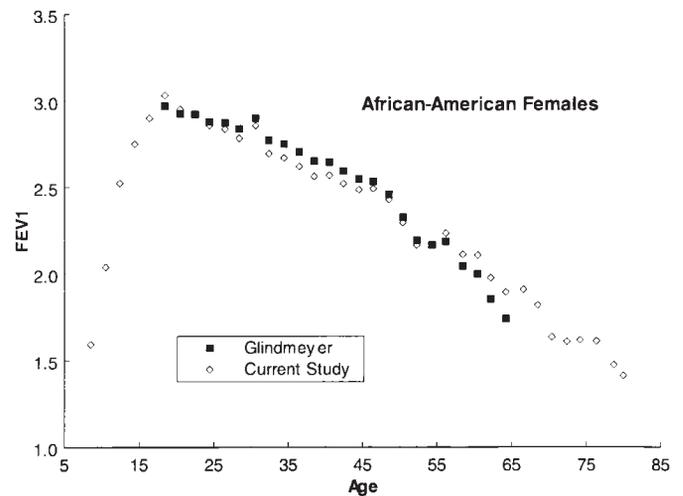


Figure 12. Predicted FEV₁ versus age for African-American female subjects using equations from Glindmeyer (9) and current study.

males). Similar to the comparison for Caucasian subjects, the reference values from the present study are similar or slightly higher than those from Crapo and Coultas. A comparison with a study by Glindmeyer and colleagues (9) of African-American subjects is presented in Figure 11 (males) and Figure 12 (females). Again, the reference values from the present study appear to be similar to those observed by Glindmeyer.

Similar results (not shown) were obtained for FVC comparisons with the exception that older subjects tended to have slightly higher values of FVC in the present study, especially when compared with the results of Glindmeyer and colleagues.

DISCUSSION

It can clearly be seen in Figures 1 and 2 that both male and female Mexican-Americans and African-Americans have lower FEV₁ values than do Caucasians for all age groups. However, only the African-Americans have lower FEV₁ values for the same height. The lower FEV₁ values observed for Mexican-Americans are attributable to the shorter heights observed in Mexican-Americans when compared with Caucasian subjects of similar age. This was confirmed when height was plotted as a function of age (not shown) and when heights were statistically compared. Although African-Americans have similar heights for a particular age, their FEV₁ values are lower than both Caucasians and Mexican-Americans. Other recent studies (9, 16) have also observed a lower FEV₁ in African-Americans, yet a similar FEV₁/FVC%. The ATS statement (17) also concluded that when compared with Caucasians of European descent, values for most other races usually show smaller static and dynamic lung volumes but similar or higher FEV₁/FVC%. They further suggested that these differences may be due to in part a difference in body build: African-Americans on average having a smaller trunk:leg ratio than do Caucasians.

Our data suggest that the practice of deriving African-American reference values by using an adjustment factor of approximately 12 to 15% applied to the Caucasian values does approximate the difference between the two groups. However, this correction factor was not optimal for all ages and heights observed in our study, and it could result in a 4% error for some ages and heights. In addition, the SEE was slightly greater in the African-American population, requiring a slightly different LLN cutoff than for Caucasian subjects.

The FVC and FEV₁ values in the present study are similar or slightly higher than those observed in other studies. The present study strictly followed the 1987 ATS test performance criteria during data collection and used a real-time computer to verify that an acceptable and reproducible test had been obtained. For elderly subjects, this often resulted in as many as eight maneuvers being obtained, typically with long exhalation times (greater than 10 s). The emphasis on quality control in NHANES III may explain the slightly larger values observed in the present study when compared with other studies, particularly in those subjects who typically have difficulty satisfying the ATS acceptability and reproducibility criteria.

Because many laboratories may strictly follow the ATS acceptability and reproducibility criteria in terms of the number of maneuvers performed, results from these laboratories may not be completely comparable to those obtained using the present study's five-curve minimum. Therefore, a separate analysis was conducted using only the data from the number of curves needed to meet the 1994 ATS acceptability and reproducibility criteria (ATS-min). When the ATS-min was used, slightly lower FVC and FEV₁ values were obtained; however, on average these differences were small.

The reference values for FEV₆ provided in this study are not widely available in the literature. The FEV₆ is a potential surrogate for the FVC in those situations where long exhalation times are impractical or unwarranted, particularly in elderly or severely obstructed subjects. In the severely or moderately obstructed subject, long exhalation times (greater than 6 s) may not be needed for diagnosis or to follow disease progression. However, the utility of the FEV₁/FEV₆% as a surrogate for the FEV₁/FVC% in detecting and monitoring airway obstruction remains to be fully investigated.

These reference equations were generated using data collected from three race/ethnic groups across a wide range of ages and geographic locations within the United States. The on-going quality control program ensured that the highest possible quality was maintained during data collection throughout the 6-yr survey; all equipment and procedures met the ATS recommendations for spirometry. The reference values calculated after strictly following the 1994 ATS acceptability and reproducibility criteria should prove especially useful for current and future diagnostic and research purposes.

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