# Ethnic- and Sex-free Formulae for Detection of Airway Obstruction

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***Rationale:*** **Spirometric detection of airway obstruction in adults requires separate predictive formulae for each ethnicity and sex for percentage of $FEV_1/FVC$ (%$FEV_1/FVC$) and percentage of $FEV_3/FVC$ (%$FEV_3/FVC$), the major measurements for defining airway obstruction.**

***Objectives:*** **To eliminate the need for multiple formulae for black, Latin, and white men and women by developing single formulae with less variance than current formulae for %$FEV_1/FVC$ and %$FEV_3/FVC$.**

***Methods:*** **Data from nearly 6,000 healthy never-smokers 20.0–79.9 yr of age in the Third National Health and Nutrition Examination Survey were reevaluated mathematically and graphically based on the preliminary hypothesis that predictive normal $FEV_1/FVC$ and $FEV_3/FVC$ ratios could be calculated from the age and FVC alone, without considering ethnicity, sex, or height. Current and new formulae were evaluated, first considering the population as consisting of 36 equally weighted subgroups (6 decades $\times$ 3 ethnicities $\times$ 2 sexes) and then weighting each individual equally.**

***Measurements and Results:*** **For each year of age, the slope of %$FEV_1/FVC$ versus FVC approximated $-1.8$%/l/yr; the slope of %$FEV_3/FVC$ versus FVC approximated $-0.8$%/l/yr. After trial and error iterations, the optimal formulae were %$FEV_1/FVC = 98.8 - 0.25 \times$ years $- 1.79 \times$ FVC and %$FEV_3/FVC = 105.4 - 0.20 \times$ years $- 0.75 \times$ FVC.**

***Conclusions*:** **These two new predicting formulae for %$FEV_1/FVC$ and %$FEV_3/FVC$, which require only age and FVC as variables, approximate actual values closer than previously published separate formulae for each ethnicity and sex. With 95% confidence limits, they should allow better discrimination between normality and airway obstruction in adults of at least these three ethnicities.**

**Keywords:** $FEV_1$; $FEV_3$; FVC; reference values; spirometry

Percentage of $FEV_1/FVC$ (%$FEV_1/FVC$) and percentage of $FEV_3/FVC$ (%$FEV_3/FVC$), but not midexpiratory phase forced expiratory flow ($FEF_{25–75\%}$), are useful in discriminating airway obstruction from normality (1). Hankinson and colleagues (2) derived ethnic- and sex-specific formulae for FVC, $FEV_1$, $FEV_1/FVC$, and other spirometric measurements for black, Latin, and white male and female never-smokers in the Third National Health and Nutrition Examination Survey (NHANES-III) (3). Despite considering height, weight, sitting height, and body mass index in their models and their use of logarithmic, square root, and high-order polynomial equations, they found it necessary to present different formulae for men and women for each ethnicity (six groups in all) (2). Other studies using the same equipment and techniques to concurrently examine two or more ethnic groups have also shown higher values for %$FEV_1/FVC$ in blacks than whites and for women than men of similar age, sex, and height (4–7).

The $FEV_1/FVC$ has long been accepted as the dominant measure of airway obstruction, although its specific cut-off values have been in dispute (8, 9). Hankinson and colleagues (2) did not report statistical significance of height in their $FEV_1/FVC$ formulae. However, their polynomial predicting equations to calculate mean normal FVC and $FEV_1$ values and the raw NHANES-III data (3) disclose lower $FEV_1/FVC$ ratios in taller, identically aged subjects in each of the six adult groups. More recently, it was found that $FEV_3/FVC$, or the equivalent data expressed as $1 - FEV_3/FVC$, which tends to measure lung units with longer time constants, and the $FEV_1/FVC$ normally decline in almost a perfect linear fashion from age 20 to 80 yr (1). Also, in the NHANES-III, never-smokers and white men and women tended to be taller and to have larger FVCs than similarly aged blacks and Latins, who tended to have higher $FEV_1/FVC$ and $FEV_3/FVC$ ratios.

Reviewing these findings, we postulated that only age and the absolute FVC were dominant factors in determining normal $FEV_1/FVC$ and $FEV_3/FVC$ ratios and that these two factors, rather than the factors of age, height, sex, and ethnicity, might adequately predict mean and normal limits for $FEV_1/FVC$ and $FEV_3/FVC$. We further suspected that the changes in these ratios due to age and FVC changes would be subtractive, not divisive or multiplicative.

## METHODS

### Subjects

Data exclusively from NHANES-III, obtained from multiple United States' sites with informed consent, which respected privacy, was used. Spirometric data, which complied with optimal 1994 American Thoracic Society (ATS) standards (10), obtained on a disc from the National Center for Health Statistics (3), included 5,907 never-smoking women and men 20.0–79.9 yr of age without known heart, lung, or neuromuscular disease who had been classified as African-American (black), Mexican-American (Latin), or Caucasian (white).

### Statistical Methods

Subjects were grouped by ethnicity and sex into six groups for every year or decade of age for calculation of mean values for age, FVC, %$FEV_1/FVC$, and slope and intercept of the values of %$FEV_1/FVC$ versus FVC for each age group. Using individuals of both sexes and all ethnicities of that age together, slopes, intercepts, and correlation coefficients of %$FEV_1/FVC$ versus FVC and versus height were separately calculated for each year of age and decade from 20 through 79. These yearly values of mean %$FEV_1/FVC$ ($y$ axis) were plotted against FVC ($x$ axis) using discriminating symbols for each of the six groups. On review of individual data, we found that 28 of the 5,907 participants had %$FEV_1/FVC$ versus FVC values that were 3.6 or more SD below ($n = 24$) or 3.6 or more SD above ($n = 4$) mean values for their age and FVC, so that each had less than 1 chance in 6,000 of being within normal limits (11). Data from these 28 subjects were eliminated; further analyses used the remaining 5,879 subjects.

After graphing mean %$FEV_1/FVC$ versus mean FVC values by year and decade, it was evident that age and FVC were arithmetically, not exponentially or multiplicatively, related to %$FEV_1/FVC$. Therefore,

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TABLE 1. NUMBER OF NEVER-SMOKERS BY DECADE, ETHNICITY, AND SEX

| Decade | Black Women | Latin Women | White Women | Black Men | Latin Men | White Men | Totals |
|---|---|---|---|---|---|---|---|
| Three | 371 (−1) | 428 (−1) | 223 | 289 (−5) | 304 | 181 | 1,796 (−7) |
| Four | 306 (−2) | 312 | 274 (−2) | 145 (−1) | 165 | 177 | 1,379 (−5) |
| Five | 191 | 200 (−1) | 209 | 91 (−1) | 95 | 113 | 899 (−2) |
| Six | 98 (−1) | 85 | 221 (−1) | 33 | 46 | 83 | 566 (−2) |
| Seven | 103 | 160 (−2) | 201 | 51 | 71 (−1) | 119 | 705 (−3) |
| Eight | 78 (−2) | 58 (−2) | 293 (−4) | 24 | 18 (−1) | 91 | 562 (−9) |
| Totals | 1,147 (−6) | 1,241 (−6) | 1,422 (−7) | 633 (−7) | 699 (−2) | 764 | 5,907 (−28) |

The numbers in parentheses are subjects removed from the final analyses because each deviated from mean values of $\%FEV_1/FVC$ of their age and FVC by more than 3.6 SD.

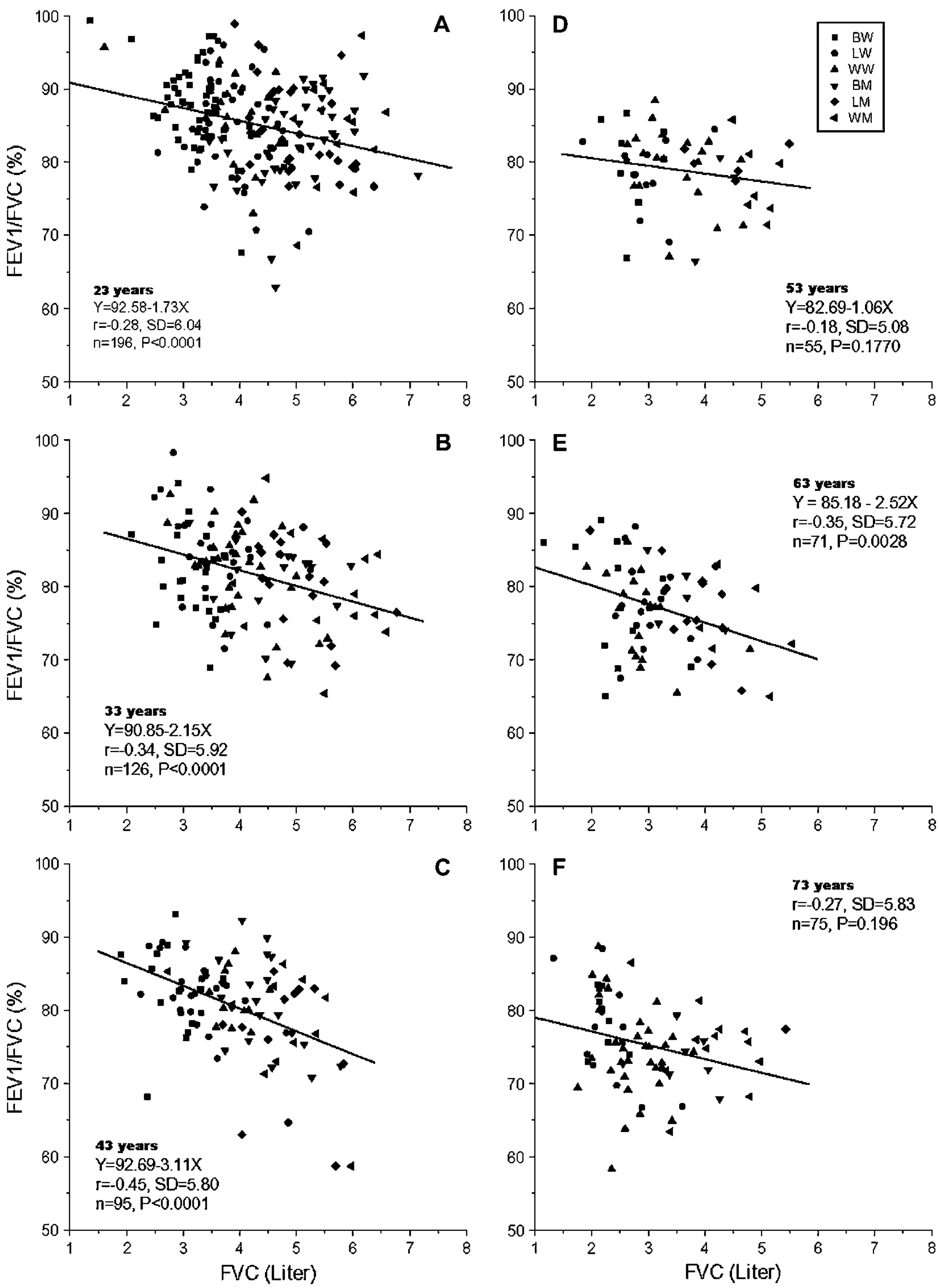


*Figure 1.* Individual data of $\%FEV_1/FVC$ ratios versus FVC with regression equations at 23, 33, 43, 53, 63, and 73 yr of age. BW = black women; LW = Latin women; WW = white women; BM = black men; LM = Latin men; WM = white men. *Regression lines* identify mean slopes (change in $\%FEV_1/FVC$ per change in liters of FVC) for each age group.

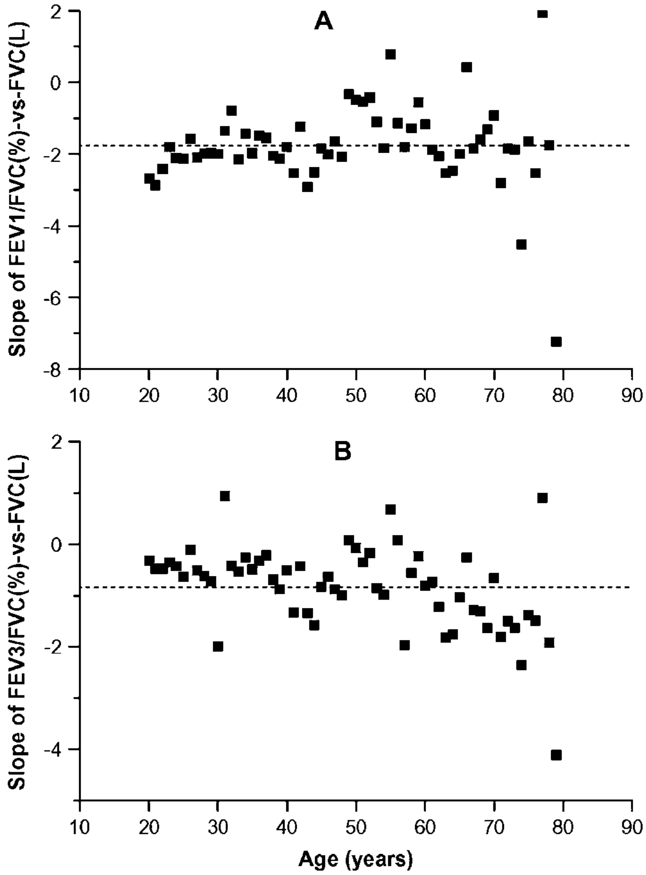


***Figure 2.*** (A) Slopes of change in $\%FEV_1/FVC$ per change in liters of FVC for each year from 20 to 79 yr of age. Mean ± SD slope = −1.78 ± 1.19%/L. (B) Yearly slopes of change in $\%FEV_3/FVC/\Delta$ in liters of FVC for each year from 20 to 79 yr of age. Mean ± SD slope = −0.84 ± 0.82%/L. Over age 73 yr, the smaller number of participants may account for higher variability. Each mean slope (*dashed line*) differs from zero by $p < 0.0001$.

mean and deviations between the actual and predicted values using the initial formula $\%FEV_1/FVC = 100 - 0.25 \times yr - 2.0 \times FVC$ (in liters) and the mean values for each of the 36 groups (6 sex-ethnicity groups × 6 decades = 36) were calculated.

We used mean $\%FEV_1/FVC$ values of each of 36 groups, equally weighted, and a successive iterative process to reduce the absolute differences between actual group means and successive single formula predicted values to a minimum. This required approximately 30 successive changes to one or more of the three factors (constant, age constant, or FVC constant). The second iterative process used each of 5,879 individuals, equally weighted, with approximately 10 successive changes to one or more factors, to reduce the absolute differences between

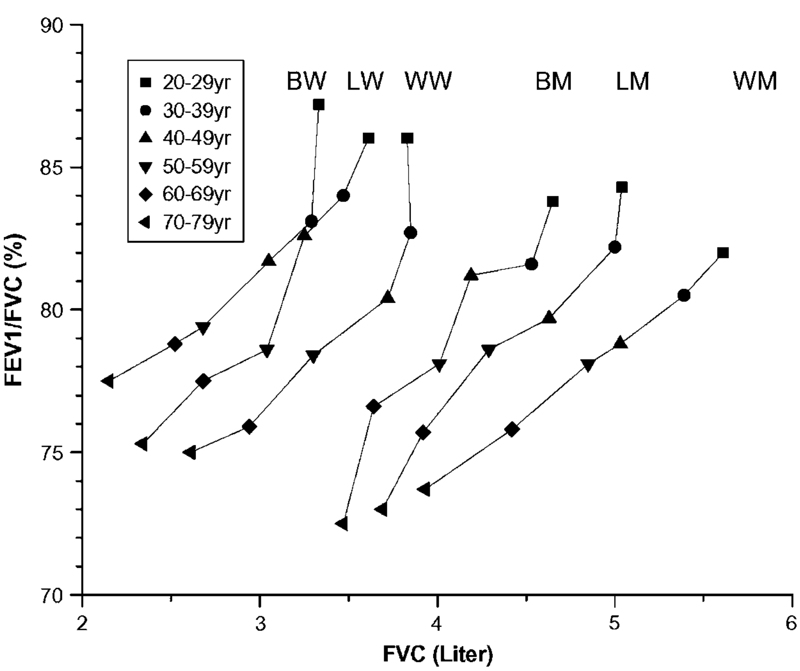


***Figure 3.*** Changes by decade in mean $\%FEV_1/FVC$ and mean FVC for groups, which from *left* to *right* are: black women (BW), Latin women (LW), white women (WW), black men (BM), Latin men (LM), and white men (WM). *Lines* connect each group. There are fewer participants (average of 40) in each of the three older black and Latin men's groups.

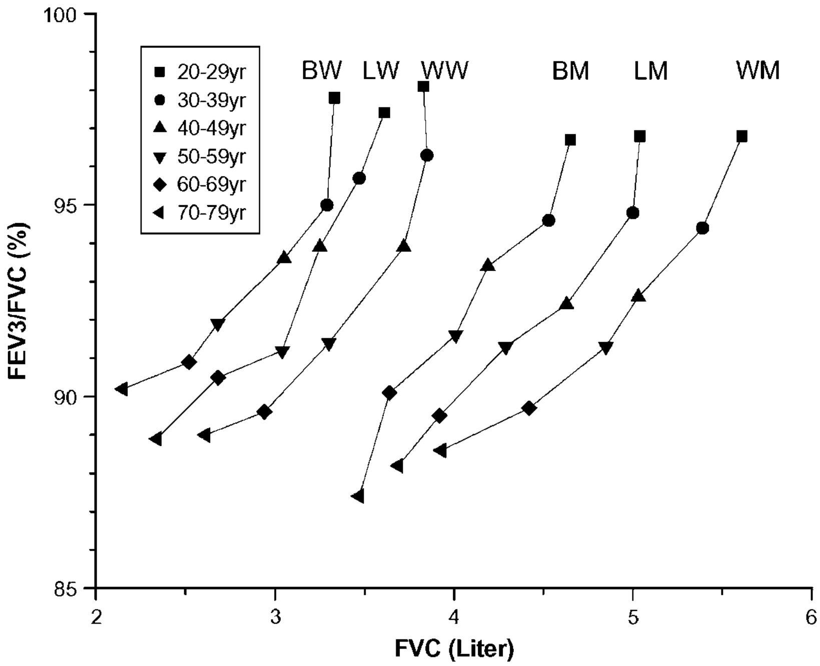


*Figure 4.* Changes by decade in mean %$FEV_3$/FVC and mean FVC for six groups, which from left to right are: black women (BW), Latin women (LW), white women (WW), black men (BM), Latin men (LM), and white men (WM). Lines connect each group. There are fewer participants (average of 40) in each of the three older black and Latin men's groups.

individual and successive single formulae predicted values to a minimum. The final iterative process used minor modifications to obtain a compromise single formula with slightly higher differences than the group or individual formula but lower differences than the combination of the 12 and 6 prior ethnic-, sex-, height-, and age-specific previously derived formulae (1, 2).

A final formula that best minimized absolute differences between actual and predicted %$FEV_3$/FVC versus FVC for each of the 36 groups and the 5,879 individuals was derived and compared with the six older %$FEV_3$/FVC formulae (1). Correlation coefficients and paired *t* tests at a level of $p \leq 0.05$ were considered significant (11).

## RESULTS

The final analyses included 1,141 black women, 1,235 Latin women, 1,415 white women, 626 black men, 697 Latin men, and 764 white men 20.0–79.9 yr of age. From Decades 3–8, there were, respectively, 1,789, 1,374, 897, 564, 702, and 553 subjects, resulting in relative underrepresentation of men and older subjects (Table 1). Mean FVC stabilized from ages 20–34 and then declined progressively, and the mean %$FEV_1$/FVC progressively decreased from age 20. Figure 1 shows the individual values from all six groups with appropriate slopes of %$FEV_1$/FVC versus FVC for the fourth year of each decade. Figure 2A illustrates the 60 mean annual slopes of %$FEV_1$/FVC versus FVC from 20–79 yr, with annual mean ± SD values of $-1.78 \pm 1.19$%/L. Despite higher variability over age 74 when groups were small and mean FVC values were below 2.7 L, slopes for each year from 40–60 yr of age collectively differed significantly ($p < 0.0001$) from zero ($r = -0.258$). These correlation coefficients also were more significant ($p < 0.0001$) than the annual correlation coefficients for %$FEV_1$/FVC versus height ($r = -0.172$). Thus, for all the subjects of a given age, regardless of ethnicity or sex, the %$FEV_1$/FVC was nearly 2% higher if FVC was 1 L smaller.

Although the 36 decade-ethnic-sex groups differed considerably in number of subjects, we weighted each group similarly and plotted mean values of %$FEV_1$/FVC versus FVC for each in Figure 3. Figure 4 shows similar values for %$FEV_3$/FVC. Mean ± SD annual slopes of %$FEV_3$/FVC versus FVC (Figure 2B) for 60 yr were $-0.84 \pm 0.82$, significantly different from zero ($p < 0.0001$).

The final optimal formula for %$FEV_1$/FVC, which minimized deviations of actual minus predicted values for the groups and individuals, was %$FEV_1$/FVC = 98.8 – 0.25 × yr – 1.79 × FVC (in liters). Because the values are symmetrically distributed about the mean, the lower-limit-of-normal values at the 95% confidence limits are 9.38% lower (1.645 × 5.70 = 9.38). The

**TABLE 2. MEAN ACTUAL – PREDICTED DEVIATIONS OF %$FEV_1$/FVC AND %$FEV_3$/FVC FOR NHANES-III ADULT NEVER-SMOKERS, GROUPED BY DECADE, ETHNICITY, AND SEX, USING SEVERAL FORMULAE**

| Formulae | Black Women | Latin Women | White Women | Black Men | Latin Men | White Men | Average |
|---|---|---|---|---|---|---|---|
| %$FEV_1$/FVC | | | | | | | |
| Hankinson and colleagues (2) (Tables 4 and 5) | +0.18 | −0.19 | +0.03 | −0.60 | −0.42 | +0.69 | −0.05 |
| Hankinson and colleagues (2) (Table 6; six formulae for %$FEV_1$/FVC) | −0.28 | −0.48 | −0.46 | −1.07 | −0.40 | +0.48 | −0.37 |
| Final: %$FEV_1$/FVC = 98.8 − 0.25 × yr – 1.79 × FVC | −0.06 | −0.19 | −0.53 | 0.00 | +0.29 | +0.62 | +0.02 |
| %$FEV_3$/FVC | | | | | | | |
| Hansen and colleagues (1) (Table 2; six formulae for %$FEV_3$/FVC) | +0.14 | −0.22 | −0.27 | −0.22 | −0.32 | +0.01 | −0.15 |
| Final: %$FEV_3$/FVC = 105.4 – 0.20 × yr – 0.75 × FVC | −0.13 | −0.30 | +0.13 | −0.12 | −0.08 | +0.42 | −0.01 |

*Definition of abbreviation*: NHANES-III = Third National Health and Nutrition Examination Survey.
Each value is mean actual – predicted deviation of each ethnic-sex group for six decades, equally weighted (values closest to zero are optimal).

**TABLE 3. MEAN DEVIATIONS AND SEM FOR ACTUAL – PREDICTED %$FEV_1$/FVC AND %$FEV_3$/FVC CALCULATED FOR EACH OF 5,879 NHANES-III NEVER-SMOKERS USING SEVERAL FORMULAE**

| Formulae | Mean Deviation, All Groups | SEM, by Group Black Women | Latin Women | White Women | Black Men | Latin Men | White Men | All |
|---|---|---|---|---|---|---|---|---|
| %$FEV_1$/FVC | | | | | | | | |
| Hankinson and colleagues (2) (Tables 4 and 5; 12 polynomial formulae for $FEV_1$ and FVC) | −0.03 | 6.13 | 5.67 | 5.85 | 6.28 | 5.52 | 5.85 | 5.88 |
| Hankinson and colleagues (2) (Table 6; six formulae for %$FEV_1$/FVC) | −0.35 | 6.20 | 5.61 | 5.89 | 6.31 | 5.46 | 5.87 | 5.89 |
| Final: %$FEV_1$/FVC = 98.8 − 0.25 × years – 1.79 × FVC | −0.02 | 5.97 | 5.47 | 5.71 | 6.13 | 5.25 | 5.68 | 5.70 |
| %$FEV_3$/FVC | | | | | | | | |
| Hansen and colleagues (1) (Table 2; six formulae for %$FEV_3$/FVC) | −0.09 | 3.48 | 2.99 | 3.65 | 3.21 | 2.78 | 3.28 | 3.23 |
| Final: %$FEV_3$/FVC = 105.4 – 0.20 × years − 0.75 × FVC | −0.07 | 3.43 | 2.95 | 3.59 | 3.19 | 2.72 | 3.25 | 3.19 |

For definition of abbreviation, *see* Table 2.
Each value is mean or SEM of actual – predicted deviation for all individuals in that group. Values closest to zero are optimal.

other final optimal formula was %$FEV_3$/FVC = 105.4 − 0.20 × yr – 0.79 × FVC (in liters) with 95% confidence limits 5.25% lower (1.645 × 3.19 = 5.25; Table 3). Tables 2 and 3 compare these new formulae with older formulae for six ethnic-sex groups and for 5,879 individuals. Better predictors result in lower deviations in actual – predicted values.

## DISCUSSION

The new formulae (labeled as "Final" in Tables 2 and 3) show equal or lesser deviations from the mean and lower SEM for group and individual comparisons than the multiple ethnic-sex–specific formulae currently available. Because the new formulae are based solely on age and FVC and describe statistically valid narrower bands of normal for %$FEV_1$/FVC and %$FEV_3$/FVC for black, Latin, or white women and men, they should allow better discrimination between obstructive airway disease and normality (12) than the primary spirometric GOLD (Global Initiative for Chronic Obstructive Lung Disease) (9) criterion, which recommends a single absolute level of $FEV_1$/FVC of less than 70%.

The reasons for spirometric differences due to sex and ethnicity have been elusive and puzzling (2, 4–8). %$FEV_1$/FVC and %$FEV_3$/FVC can be related to changes with age (1). It seems to be a step forward to recognize that, using common equipment, technicians, and quality control, these ratios also relate to the size of the FVC, regardless of ethnicity and sex (Figure 1), at least in this never-smoking NHANES-III population. The slopes of %$FEV_1$/FVC and %$FEV_3$/FVC versus FVC differ significantly from zero (Figures 2A and 2B). That they are reasonably parallel in appearance and over a broad age range confirms their dependence on the FVC volume. As suggested by others (4, 7), there may be additional reasons for ethnic differences in $FEV_1$ and FVC in this diverse United States population, such as genetic, nutritional, environmental, socioeconomic, educational, fitness, or other unknown factors. However, in this population, FVC and age factors seem to dominate $FEV_1$/FVC and $FEV_3$/FVC. These ratios are far more useful and discriminating than the $FEF_{25–75}$, which has false positives in never-smokers and many false negatives in current smokers (1).

All cross-sectional studies include older survivors who may be healthier in the parameter measured than those who have not survived. So-called normal populations invariably contain some individuals with relevant disorders that alter lung function. In this series, we eliminated 28 individuals because each had less than a 1 in 6,000 chance of fitting within a normally distributed population (11). Some of these individuals may have had undiagnosed asthma, an acute or chronic infection, or significant neuromuscular, pulmonary, or cardiovascular disease. Perhaps an even larger number of individuals should have been excluded as not normal, further narrowing the variability, but this could have introduced an undesirable bias. Although the use of 95% confidence limits is somewhat arbitrary, it is traditional.

Total lung capacity (TLC) measurements were not available, but we can deduce from the studies of Crapo and colleagues (13) and Goldman and Becklake (14) that normal TLC values remain stable from age 30 onward. Thus, the $FEV_1$/TLC and $FEV_3$/TLC deteriorate even more than the $FEV_1$/FVC and $FEV_3$/FVC with age. To see if the findings from the current study could be more widely useful, it would have been advantageous to have individual data from other studies that concurrently included two or more ethnicities. The few other large spirometric studies (4–7) using the same equipment for populations of different ethnicities have demonstrated lower FVC and higher $FEV_1$/FVC values for black than white individuals of the same height and age. Reports with data from only one ethnicity at a time have less discriminatory value because differences in equipment and quality control cannot be excluded. The mean values of a recent Asian Indian series (15) from the United States, which followed current ATS standards, were considered but not used because only a single ethnicity was examined and because %$FEV_1$/FVC values for women were significantly lower than those for men of the same height and age, which is an unusual finding. Therefore, we encourage other investigators to ascertain if %$FEV_1$/FVC and %$FEV_3$/FVC values of two or more ethnicities do or do not fit into the pattern calculated from these new formulae.

In the formulae recommended, FVC is found on both sides of the equations, which is a cause for some concern. However, the interrelationships could also be expressed as $FEV_1$ = constant × FVC – constant × years × FVC – constant × FVC squared, which eliminates this concern but does not yield the most clinically useful result.

Clinically, because normality of $FEV_1$/FVC and $FEV_3$/FVC ratios depend on the FVC, this dependence might be helpful in assessing if elevated ratios are due to intrinsic lung disease with fibrosis and increased elastic recoil or to TLC and FVC reduction secondary to chest wall disease, cardiomegaly, pleural effusion, or other nonairway abnormalities. However, when ratios are low but within normal limits and the FVC is reduced, airway obstruction may be present.

***Conflict of Interest Statement*:** None of the authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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