Spirometric Reference Values for the 6-s FVC Maneuver

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Spirometric Reference Values for the 6-s FVC Maneuver*

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Study objectives: **The guidelines of the National Lung Health Education Program for COPD screening proposed a shorter FVC maneuver (forced expiratory volume at 6 s of exhalation [FEV_6]). Although reference values for FEV_6 are available from the third National Health and Nutrition Examination Survey, forced expiratory flow between 25% and 75% of FVC ($FEF_{25–75\%}$) reference values for the shorter 6-s maneuver are not available and are needed. In particular, calculation of largest observed volume during the first 6 s of an FVC maneuver (FVC_6), from a shortened FVC maneuver, is necessary because the $FEF_{25–75\%}$ measurement is based on a percentage of FVC or, for a shorter maneuver, FVC_6.**

Design: **We reanalyzed the raw volume-time curves from the third National Health and Nutrition Examination Survey to calculate FVC_6, forced expiratory volume at 0.5 s of exhalation, forced expiratory volume at 3 s of exhalation, ratio of the FEV_1 to largest observed volume during the first 6 s of an FVC maneuver expressed as a percentage ($FEV_1/FEV_6\%$), and forced expiratory flow between 25% and 75% of the largest observed volume during the first 6 s of an FVC maneuver ($FEF_{25–75\%6}$) in addition to the previously reported values for FEV_1, FEV_6, and $FEV_1/FEV_6\%$.**

Patients or participants: **Using the same normal, asymptomatic, nonsmoking reference population from a previous study, reference values for these parameters were derived from best values.**

Results: **A total of 2,261 white, 2,564 African-American, and 2,666 Mexican-American subjects aged 8 to 80 years were included in the analysis. Fifty-four subjects from the previous study were not included due to missing raw volume-time curves.**

Conclusions: **These reference values, utilizing the FVC_6, provide investigators with the means of evaluating the relative merits of using the shorter FVC maneuver as a surrogate for the traditional FVC. They are needed particularly for calculating $FEF_{25–75\%}$, as statistically significant differences were observed between the $FEF_{25–75\%}$ and $FEF_{25–75\%6}$.** ***(CHEST 2003; 124:1805–1811)***

Key words: FEV_1; forced expiratory volume at 6 s of exhalation; FVC; reference values; spirometry

Abbreviations: $FEF_{25–75\%}$ = forced expiratory flow between 25% and 75% of FVC; $FEF_{25–75\%6}$ = forced expiratory flow between 25% and 75% of the largest observed volume during the first 6 s of an FVC maneuver; $FEV_{0.5}$ = forced expiratory volume at 0.5 s of exhalation; $FEV_1/FEV_6\%$ = ratio of the FEV_1 to forced expiratory volume at 6 s of exhalation expressed as a percentage; $FEV_1/FVC_6\%$ = ratio of the FEV_1 to largest observed volume during the first 6 s of an FVC maneuver expressed as a percentage; FEV_3 = forced expiratory volume at 3 s of exhalation; FEV_6 = forced expiratory volume at 6 s of exhalation; FVC_6 = largest observed volume during the first 6 s of an FVC maneuver; Ht^2_{LLN} = height-squared coefficient for lower limit of normal; Ht^2_{PRD} = height-squared coefficient for predicted value; $Intercept_{PRD}$ = intercept of predicted; $Intercept_{LLN}$ = intercept of lower limit of normal; LLN = lower limit of normal

The National Lung Health Education Program screening guidelines for COPD[1] proposed using a shortened, 6-second FVC maneuver (forced expiratory volume at 6 s of exhalation [FEV_6]) for "office" spirometry. The shorter FVC maneuver may prove to have the same utility, with less subject effort, in terms of identifying subjects with obstructive or restrictive lung disease patterns. It also provides a more explicit end of test, making it easier for spirometry software to identify end of test. In addition, several less expensive, flow-type spirometers are available that may be able to accurately measure FEV_1 and largest observed volume during the first 6 s of an FVC maneuver (FVC_6), but have difficulties accurately measuring FVC from maneuvers with long exhalation times due to zero flow errors. The 6-s volume can be calculated in two ways: the FVC_6 and the FEV_6. Time zero is calculated using back-extrapolation for both methods. These two methods produce similar results, but sometimes FEV_6 is slightly smaller than FVC_6 because the

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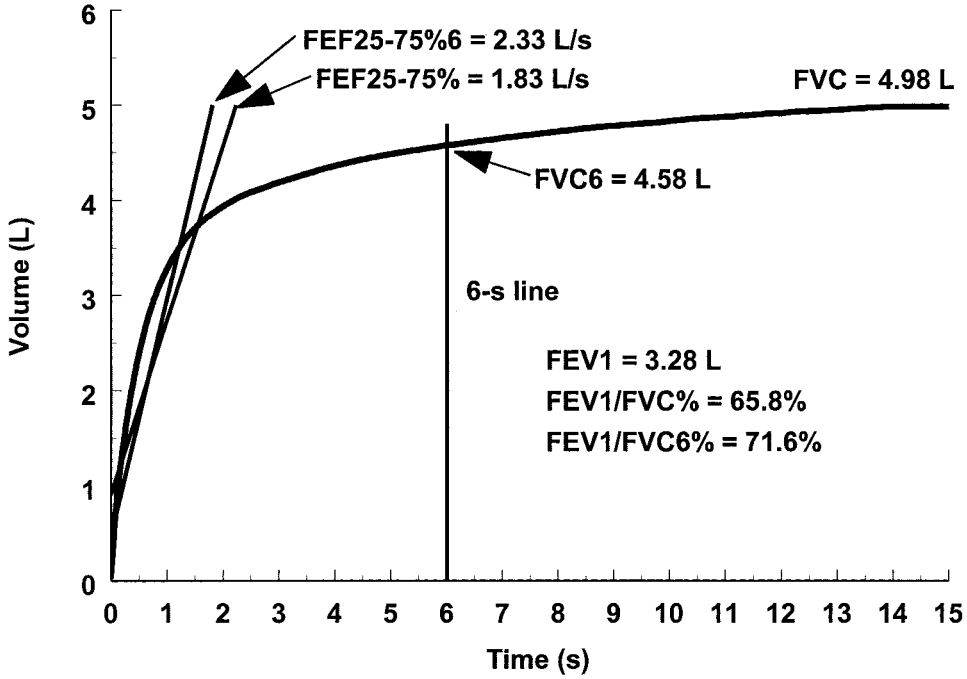

FIGURE 1. Sample volume-time curve illustrating differences between FVC- and FVC_6-derived parameters.

volume-time curve slightly decreases immediately before the 6-s point where the FEV_6 is measured. The differences between FVC and FVC_6 are illustrated in Figure 1.

Although reference values for FEV_6 are available from the third National Health and Nutrition Examination Survey, reference values for forced expiratory flow between 25% and 75% of FVC ($FEF_{25–75\%}$) using the shorter 6-s maneuver, FVC_6, forced expiratory volume at 0.5 s of exhalation ($FEV_{0.5}$), and ratio of the FEV_1 to largest observed volume during the first 6 s of an FVC maneuver expressed as a percentage ($FEV_1/FVC_6\%$) are not available. It is more appropriate to measure and report FVC_6 than FEV_6 because FEV_6 is sometimes less than FVC_6. For this reason, the $FEF_{25–75\%}$ should be based on FVC or FVC_6, and be labeled as $FEF_{25–75\%}$ and forced expiratory flow between 25% and 75% of the largest observed volume during the first 6 s of an FVC maneuver ($FEF_{25–75\%6}$), respectively.

At least a portion of the variability in $FEF_{25–75\%}$ is associated with FVC measurement, and using a truncated curve may reduce the within and between-subject variability of $FEF_{25–75\%}$. This may be particularly true for older individuals and those with airways obstruction, where expiratory maneuvers typically exceed 6 s and FVC gradually increases with expiratory times up to 20 s.

In Figure 1, a subject with mild airways obstruction exhaled for 15 s. The FVC in this example is 4.98 L, and the $FEF_{25–75\%}$ is 1.83 L/s. If the curve is truncated at 6 s (vertical 6-s line), the resulting FVC_6 would be 4.58 L. When the new FVC_6 is used in the calculation of the $FEF_{25–75\%}$, the new line is steeper because 25% and 75% of the FVC_6 is smaller than 25% and 75% of the FVC. The resulting $FEF_{25–75\%6}$ is 2.33 L/s or approximately 500 mL/s higher than the initial $FEF_{25–75\%}$. In addition, the $FEV_1/FVC_6\%$ is 71.6% higher than the FEV_1/FVC ratio of 65.8%, a difference of 5.8%.

MATERIALS AND METHODS

Raw spirograms from the third National Health and Nutrition Examination Survey used in the derivation of previous reference values[2,3] were reanalyzed by truncating all maneuvers after 6 s of exhalation. Time zero was calculated using back-extrapolation. FVC_6, $FEV_{0.5}$, FEV_1, forced expiratory volume at 3 s of

Table 1—*Subjects by Age, Gender, and Race

Variables	Race (n = 7,375)		
	White	African American	Mexican American
Male subjects	896	1,023	1,112
< 20 yr old	414 (46.21)	585 (57.18)	576 (51.80)
≥ 20 yr old	482 (53.79)	438 (42.82)	536 (48.20)
Female subjects	1,365	1,474	1,505
< 18 yr old	400 (29.30)	583 (39.55)	562 (37.34)
≥ 18 yr old	965 (70.70)	891 (60.45)	943 (62.66)

*Data are presented as No. or No. (%).

Table 2—*Spirometry Coefficients for Prediction and LLN Equations for Male Subjects

Parameters	Intercept	Age	Age^2	Ht^2_{PRD}	Ht^2_{LLN}	R^2
White < 20 yr of age						
$FEF_{25-75\%6}$	− 1.174	0.12900		0.0001148	0.00006172	0.549
$FEV_{0.5}$	− 0.542	0.00294	0.0022700	0.0000962	0.00007519	0.813
FEV_1	− 0.783	− 0.03800	0.0043350	0.0001420	0.00011714	0.851
FEV_3	− 0.462	− 0.15200	0.0086100	0.0001758	0.00014784	0.867
FEV_6	− 0.317	− 0.18500	0.0096410	0.0001819	0.00015310	0.868
FVC_6	− 0.318	− 0.18400	0.0096150	0.0001817	0.00015289	0.867
White ≥ 20 yr of age						
$FEF_{25-75\%6}$	2.193	− 0.04000		0.0001148	0.00006172	0.549
$FEV_{0.5}$	0.354	0.00950	− 0.0002997	0.0000962	0.00007517	0.813
FEV_1	0.513	− 0.01300	− 0.0001740	0.0001420	0.00011714	0.851
FEV_3	0.403	− 0.02000	− 0.0001365	0.0001758	0.00014784	0.867
FEV_6	0.077	− 0.00717	− 0.0002353	0.0001819	0.00015310	0.868
FVC_6	0.089	− 0.00735	− 0.0002339	0.0001817	0.00015289	0.867
Whites all ages						
$FEV_1/FEV_6\%$	87.36%†	− 0.139			78.30%‡	0.213
$FEV_1/FVC_6\%$	87.27%†	− 0.137			78.26%‡	0.211
African American < 20 yr of age						
$FEF_{25-75\%6}$	− 1.129	0.1250		0.0001049	0.00004605	0.478
$FEV_{0.5}$	− 0.457	− 0.0280	0.0030570	0.0000934	0.00007101	0.772
FEV_1	− 0.613	− 0.0710	0.0048850	0.0001314	0.00010528	0.809
FEV_3	− 0.575	− 0.1290	0.0069270	0.0001593	0.00013085	0.829
FEV_6	− 0.463	− 0.1540	0.0077730	0.0001638	0.00013468	0.831
FVC_6	− 0.455	− 0.1550	0.0077830	0.0001638	0.00013467	0.830
African American ≥ 20 yr of age						
$FEF_{25-75\%6}$	2.099	− 0.0370		0.0001049	0.00004605	0.478
$FEV_{0.5}$	0.486	− 0.0130	− 0.0000451	0.0000934	0.00007101	0.772
FEV_1	0.514	− 0.0320	0.0000969	0.0001314	0.00010528	0.809
FEV_3	0.252	− 0.0350	0.0001177	0.0001593	0.00013085	0.829
FEV_6	0.086	− 0.0280	0.0000729	0.0001638	0.00013468	0.831
FVC_6	0.090	− 0.0280	0.0000737	0.0001638	0.00013467	0.830
African American all ages						
$FEV_1/FEV_6\%$	88.72%†	− 0.128			78.83%‡	0.090
$FEV_1/FVC_6\%$	88.58%†	− 0.125			78.70%‡	0.086
Mexican American < 20 yr of age						
$FEF_{25-75\%6}$	− 1.340	0.1120		0.0001421	0.00008473	0.549
$FEV_{0.5}$	− 0.539	− 0.0140	0.0029170	0.0001046	0.00008315	0.819
FEV_1	− 0.950	− 0.0220	0.0036140	0.0001501	0.00012573	0.856
FEV_3	− 0.944	− 0.0640	0.0054870	0.0001751	0.00014811	0.868
FEV_6	− 0.821	− 0.0890	0.0064240	0.0001783	0.00015043	0.869
FVC_6	− 0.815	− 0.0890	0.0064290	0.0001784	0.00015056	0.869
Mexican American ≥ 20 yr of age						
$FEF_{25-75\%6}$	1.681	− 0.0390		0.0001421	0.00008473	0.549
$FEV_{0.5}$	0.509	− 0.0046	− 0.0001732	0.0001046	0.00008315	0.819
FEV_1	0.567	− 0.0250	− 0.0000451	0.0001501	0.00012573	0.856
FEV_3	0.537	− 0.0280	− 0.0000394	0.0001751	0.00014811	0.868
FEV_6	0.401	− 0.0190	− 0.0001022	0.0001783	0.00015043	0.869
FVC_6	0.399	− 0.0190	− 0.0001032	0.0001784	0.00015056	0.869
Mexican American all ages						
$FEV_1/FEV_6\%$	89.22%†	− 0.150			80.52%‡	0.159
$FEV_1/FVC_6\%$	89.09%†	− 0.147			80.42%‡	0.156

*If the coefficient is blank, it is not used in the equation.

†$Intercept_{PRD}$.

‡$Intercept_{LLN}$.

inhalation (FEV_3), forced expiratory volume at 6 s of exhalation (FEV_6), $FEF_{25-75\%6}$, ratio of the FEV_1 to forced expiratory volume at 6 s of exhalation expressed as a percentage ($FEV_1/FEV_6\%$), and $FEV_1/FVC_6\%$ were then calculated from the truncated raw volume-time curves. As in the previous reference value study,[2,3] only asymptomatic, nonsmoking subjects with at least two acceptable maneuvers based on American Thoracic Society[4] standards were included in the study. As recommended by the American Thoracic Society,[4] the largest observed FVC_6, $FEV_{0.5}$, FEV_1, FEV_3, and FEV_6 from acceptable curves were reported for each subject. The $FEF_{25-75\%6}$ was selected from the maneuver with the largest sum of FVC_6 plus FEV_1. The $FEV_1/FVC_6\%$ and $FEV_1/FEV_6\%$ were obtained using the largest FEV_1, FEV_6, and FVC_6,

Table 3—*Spirometry Coefficients for Prediction and LLN Equations for Female Subjects

Parameters	Intercept	Age	Age^2	Ht^2_{PRD}	Ht^2_{LLN}	R^2
White < 18 yr of age						
$FEF_{25–75\%6}$	− 0.156	0.10200		0.0000874	0.00003916	0.454
$FEV_{0.5}$	− 0.945	0.14200	− 0.0035070	0.0000763	0.00005856	0.700
FEV_1	− 1.205	0.12500	− 0.0021930	0.0001131	0.00009185	0.765
FEV_3	− 0.839	0.01300	0.0020520	0.0001407	0.00011668	0.771
FEV_6	− 0.751	− 0.01200	0.0027370	0.0001464	0.00012151	0.758
FVC_6	− 0.745	− 0.01200	0.0027500	0.0001465	0.00012161	0.758
White ≥ 18 yr of age						
$FEF_{25–75\%6}$	2.292	− 0.03400		0.0000874	0.00003916	0.454
$FEV_{0.5}$	0.366	0.01100	− 0.0002679	0.0000763	0.00005856	0.700
FEV_1	0.410	− 0.00069	− 0.0002225	0.0001131	0.00009185	0.765
FEV_3	0.085	0.00340	− 0.0002776	0.0001407	0.00011668	0.771
FEV_6	− 0.187	0.01200	− 0.0003453	0.0001464	0.00012151	0.758
FVC_6	− 0.184	0.01200	− 0.0003449	0.0001465	0.00012161	0.758
White all ages						
FEV_1/FEV_6%	90.19%†	− 0.15900			81.47%‡	0.315
FEV_1/FVC_6%	90.08%†	− 0.15800			81.39%‡	0.313
African American < 18 yr of age						
$FEF_{25–75\%6}$	− 0.566	0.10300		0.0000944	0.00004068	0.355
$FEV_{0.5}$	− 0.740	0.07500	− 0.0008657	0.0000763	0.00005657	0.617
FEV_1	− 0.954	0.05300	0.0001981	0.0001088	0.00008611	0.677
FEV_3	− 0.751	− 0.01800	0.0027240	0.0001307	0.00010540	0.679
FEV_6	− 0.684	− 0.03500	0.0032630	0.0001344	0.00010837	0.670
FVC_6	− 0.691	− 0.03400	0.0032160	0.0001346	0.00010856	0.669
African American ≥ 18 yr of age						
$FEF_{25–75\%6}$	1.907	− 0.03500		0.0000944	0.00004068	0.355
$FEV_{0.5}$	0.430	− 0.00322	− 0.0001459	0.0000763	0.00005657	0.617
FEV_1	0.338	− 0.01300	− 0.0000943	0.0001088	0.00008611	0.677
FEV_3	− 0.011	− 0.00655	− 0.0001726	0.0001307	0.00010540	0.679
FEV_6	− 0.192	0.00080	− 0.0002330	0.0001344	0.00010837	0.670
FVC_6	− 0.184	0.00015	− 0.0002237	0.0001346	0.00010851	0.669
African American all ages						
FEV_1/FEV_6%	91.19%†	− 0.15600			81.17%‡	0.165
FEV_1/FVC_6%	91.14%†	− 0.15900			81.14%‡	0.169
Mexican American < 18 yr of age						
$FEF_{25–75\%6}$	− 0.284	0.08400		0.0001114	0.00005840	0.374
$FEV_{0.5}$	− 0.933	0.12500	− 0.0028200	0.0000832	0.00006368	0.650
FEV_1	− 1.356	0.14000	− 0.0026930	0.0001175	0.00009485	0.723
FEV_3	− 1.230	0.08400	− 0.0002572	0.0001370	0.00011160	0.728
FEV_6	− 1.139	0.06100	0.0005522	0.0001407	0.00011451	0.719
FVC_6	− 1.146	0.06300	0.0004865	0.0001407	0.00011453	0.719
Mexican American ≥ 18 yr of age						
$FEF_{25–75\%6}$	1.802	− 0.03200		0.0001114	0.00005840	0.374
$FEV_{0.5}$	0.369	0.00560	− 0.0002291	0.0000832	0.00006368	0.650
FEV_1	0.486	− 0.00864	− 0.0001445	0.0001175	0.00009485	0.723
FEV_3	0.364	− 0.00611	− 0.0001826	0.0001370	0.00011160	0.728
FEV_6	0.222	− 0.00018	− 0.0002257	0.0001407	0.00011451	0.719
FVC_6	0.225	− 0.00035	− 0.0002240	0.0001407	0.00011453	0.719
Mexican American all ages						
FEV_1/FEV_6%	91.71%†	− 0.17000			83.07%‡	0.248
FEV_1/FVC_6%	91.57%†	− 0.16800			82.95%‡	0.245

*If the coefficient is blank, it is not used in the equation.
†$Intercept_{PRD}$.
‡$Intercept_{LLN}$.

regardless of the acceptable curve on which they occurred. Statistical analyses were performed using Mathcad 2000 (MathSoft; Cambridge, MA). Based on results from the previous reference values study[2] (same population used in this reanalysis), the general form of the reference equations for FVC_6, $FEV_{0.5}$, FEV_1, FEV_3, FEV_6, and $FEF_{25–75\%6}$ is as follows:

Equation 1, lung function parameter

$$= b_0 + b_1 \times age + b_2 \times age^2 + b_3 \times height^2$$

Separate equations were derived for male subjects < 20 years old and ≥ 20 years old. For women, separate equations were used for subjects < 18 years old and ≥ 18 years old, consistent

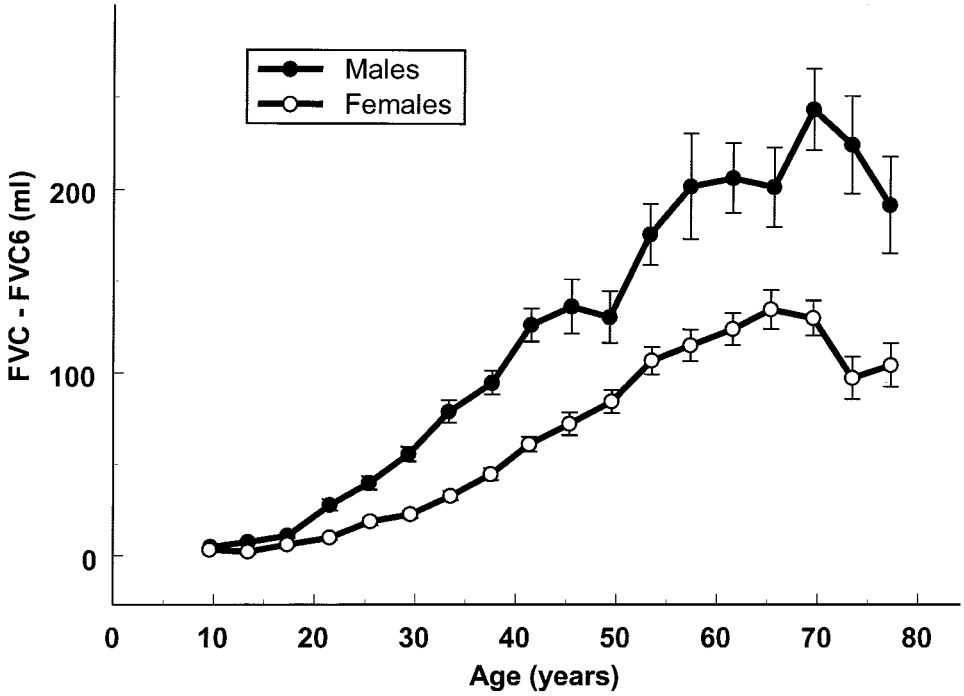

FIGURE 2. Differences between FVC and FVC_6 vs age for male and female subjects.

with the previous study.[2] The equations on either side of the age break points were constrained to intercept at 18 years and 20 years of age to prevent a discontinuity.

The lower limit of normal (LLN) for the population was computed for lung function parameters as predicted (1.645 × standard error of the estimate), with an additional adjustment for a slight change in the standard error of the estimate for different heights. For the computation of the LLN, the height-squared coefficient for the predicted value coefficient (Ht^2PRD), used for calculation of predicted values, is replaced by the height-squared coefficient for LLN (Ht^2LLN). Specifically, in equation 1, b_3 is Ht^2PRD for calculating predicted values and Ht^2LLN for calculating the LLN.

The general form for calculating predicted FEV_1/FEV_6% and FEV_1/FVC_6% is as follows:

$$\text{Equation 2, lung function parameter} = b_0 + b_1 \times \text{age}$$

The LLN for FEV_1/FEV_6% and FEV_1/FVC_6% is calculated by replacing the b_0 or intercept coefficient in equation 2 (intercept of predicted [InterceptPRD] vs intercept of LLN [InterceptLLN]).

RESULTS

Table 1 shows the number of adult and youth subjects by age, gender, and race groups for the selected reference population. This distribution is approximately the same as in the previous reference value study,[2] as only those subjects without raw volume-time curves were excluded.

Table 2 (male subjects) and Table 3 (female subjects) show the results or the coefficients for the reference equations for FVC_6, $FEV_{0.5}$, FEV_1, FEV_3, FEV_6, FEV_1/FVC_6%, FEV_1/FEV_6%, and $FEF_{25–75\%6}$. A total of 2,261 white, 2,564 African-

Table 4—*Parameters for Male Subjects, Three Age Groups, and All Races Combined

Parameters	Age, yr		
	< 20 (n = 1,575)	20–40 (n = 928)	> 40 (n = 528)
FVC, L	3.22 (1.28)	4.93 (0.78)	4.34 (0.87)
FVC_6, L	3.21 (1.28)†	4.94 (0.77)†	4.17 (0.84)†
FVC − FVC_6, mL	7.3 (20.6)	54.8 (64.6)	175.0 (134.6)
$FEF_{25–75\%}$, L/s	3.17 (1.32)	4.39 (1.14)	3.12 (1.23)
$FEF_{25–75\%6}$, L/s	3.22 (1.33)	4.53 (1.13)	3.50 (1.20)
$FEF_{25–75\%}$ − $FEF_{25–75\%6}$, mL/s	− 53.1 (62.2)†	− 143.3 (125.4)†	− 280.0 (297.5)†
FEV_1/FVC%, %	86.1 (5.92)	83.2 (5.98)	77.6 (7.18)
FEV_1/FVC_6%, %	86.4 (5.77)	84.1 (5.53)	80.7 (5.88)
FEV_1/FVC% − FEV_1/FVC_6%, %	− 0.18 (0.60)†	− 0.89 (1.03)†	− 3.15 (2.28)†

*Data are presented as mean (SD).
†Statistically significant from zero and other age group means ($p < 0.01$).

Table 5—*Parameters for Female Subjects, Three Age Groups, and All Races Combined*

Parameters	Age, yr		
	< 20 (n = 1,725)	20–40 (n = 1,389)	> 40 (n = 1,320)
FVC, L	2.82 (0.77)	3.53 (0.56)	2.99 (0.66)
FVC_6, L	2.81 (0.77)	3.50 (0.56)	2.99 (0.65)
$FVC - FVC_6$, mL	3.9 (24.1)†	24.9 (38.4)†	99.8 (92.70)†
$FEF_{25–75\%}$, L/s	3.08 (0.69)	3.49 (0.90)	2.33 (0.95)
$FEF_{25–75\%6}$, L/s	3.13 (1.00)	3.58 (0.89)	2.60 (0.92)
$FEF_{25–75\%} - FEF_{25–75\%6}$, mL/s	− 48.5 (68.5)†	− 88.6 (89.3)†	− 264.1 (221.5)†
$FEV_1/FVC\%$, %	89.1 (5.96)	85.5 (5.92)	78.9 (6.96)
$FEV_1/FVC_6\%$, %	89.2 (5.76)	86.1 (5.56)	81.5 (5.69)
$FEV_1/FVC\% - FEV_1/FVC_6\%$, %	− 0.11% (0.70)†	− 0.60% (0.90)†	− 2.62% (2.43)†

*Data are presented as mean (SD).
†Statistically significant from zero and other age group means ($p < 0.01$).

American, and 2,666 Mexican-American subjects aged 8 to 80 years were included in the analysis. Of the 7,429 subjects included in the previous reference values study,[2] the raw volume-time curves of 54 subjects were not available due to curve storage problems. Although these few missing subjects resulted in only slightly different results for FEV_1, FEV_6, and $FEV_1/FEV_6\%$ than previously reported,[2] the revised coefficients for these parameters are presented in Tables 2, 3.

Figure 2 shows the differences between FVC and FVC_6 for male and female subjects vs age. The three racial groups were combined because the differences between FVC and FVC_6 between races were not statistically significant ($p > 0.05$); however, there was a small statistically significant difference between male and female subjects (mean, 52 mL and 42 mL, respectively; $p < 0.01$). The differences between FVC and FVC_6 increased with age.

Table 4 (male subjects) and Table 5 (female subjects) show the mean and SD for several parameters for three age groups. Since there were no differences between races, all races were combined for this analysis. Differences between $FVC - FVC_6$, $FEF_{25–75\%} - FEF_{25–75\%6}$, and $FEV_1/FVC\% - FEV_1/FVC_6\%$ were all statistically different from zero ($p < 0.01$) for all three age groups. There was also a statistically significant increase in the differences between the FVC- vs FVC_6-derived parameters with increased age (< 20 years vs 20 to 40 years, vs > 40 years).

Discussion

These results provide reference values for a shorter or 6-s exhalation for use when a longer, more complete, FVC maneuver may not be warranted (*eg*, "office spirometry"). Reference values for the FVC_6, $FEV_{0.5}$, FEV_1, FEV_3, FEV_6, $FEF_{25–75\%6}$, $FEV_1/FEV_6\%$, and $FEV_1/FVC_6\%$ are provided. Although reference values for the FEV_1, FEV_6, and $FEV_1/FEV_6\%$ have been previously published,[2] values for FVC_6, $FEV_1/FVC_6\%$, $FEV_{0.5}$, FEV_3, and $FEF_{25–75\%6}$ were not previously available.

The increasing differences between the FVC- and FVC_6-derived parameters with age (Fig 2; Tables 4, 5) were expected. Older adult subjects require longer expiratory times to reach their FVC, and the impact of a shortened maneuver is greatest in these subjects. The statistically significant difference between $FEF_{25–75\%}$ and $FEF_{25–75\%6}$ for subjects > 40 years of age (280 mL/s for male and 264 mL/s for female subjects) demonstrates the need for separate reference equations for the shortened FVC_6 maneuver.

Swanney et al[5] studied the utility of shortened 6-s FVC maneuver in consecutive patients tested in a referral pulmonary laboratory. They found the reproducibility of FEV_6 was superior to that of FVC. In addition, FEV_6 was found to be a reliable alternative to FVC for diagnosing airway obstruction, and was reasonably comparable to FVC for the spirometric diagnosis of restriction. In a longitudinal study of adult smokers, Enright et al[6] found $FEV_1/FEV_6\%$ was nearly as strong an independent predictor of subsequent decline in lung function as $FEV_1/FVC\%$.

The reference values for additional spirometric parameters should allow other investigators to study the utility of the 6-s FVC maneuver. Specifically, classification results using FVC_6, $FEV_1/FVC_6\%$, and $FEF_{25–75\%6}$ can now be compared to those using a complete FVC maneuver.

We had hypothesized that reducing the variability in FVC would mean $FEF_{25–75\%6}$ would show less population variability than the $FEF_{25–75\%}$; but as can be seen in Tables 4, 5, there is essentially no difference in the SD of these two parameters. Although the LLN was slightly closer to the predicted due to slightly less variation within the population

(*eg*, for white male subjects, 58.1% vs 56.1% of predicted $FEF_{25–75\%6}$ and $FEF_{25–75\%}$, respectively), these differences were also small in this healthy population. In populations where long exhalations are required to reach FVC, with a correspondingly greater variability in FVC, this may not be the case. Additional research will be needed to determine if $FEF_{25–75\%6}$ variability is reduced, and its clinical utility improved, in such circumstances.

The youngest people in this study were 8 years old. As with any reference values study, the reference equations are not recommended for use beyond the age range used in deriving the equations. Use outside the test range is particularly problematic with reference equations that contain squared terms, such as those used in our analysis.

Appendix

Calculation of FVC_6 and $FEF_{25–75\%6}$ Predicted and LLN for a White Male Subject, 175 cm Tall and 30 Years of Age

From Table 2, the equation for FVC_6 is as follows:

predicted $FVC_6 = 0.089 - 0.00735 \times age - 0.0002339 \times age^2 + 0.0001817 \times Ht^2_{PRD}$

predicted $FVC_6 = 0.089 - (0.00735)(30) - (0.0002339)(30)(30) + (0.0001817)(175)(175) = 5.22$ L

LLN $FVC_6 = 0.089 - 0.00735 \times age - 0.0002339 \times age^2 + 0.00015289 \times Ht^2_{LLN}$

LLN $FVC_6 = 0.089 - (0.00735)(30) - (0.0002339)(30)(30) + (0.00015289)(175)(175) = 4.34$ L

From Table 2, the equation for $FEF_{25–75\%6}$ is as follows:

predicted $FEF_{25–75\%6} = 2.139 - 0.04 \times age + 0.0001148 \times Ht^2_{PRD}$

predicted $FEF_{25–75\%6} = 2.139 - (0.04)(30) + (0.0001148)(175)(175) = 4.45$ L/s

LLN $FEF_{25–75\%6} = 2.139 - 0.04 \times age + 0.0001148 \times Ht^2_{LLN}$

LLN $FEF_{25–75\%6} = 2.139 - (0.04)(30) + (0.00006172)(175)(175) = 2.83$ L/s

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