Spirometry Reference Values for Navajo Children Ages 6–14 Years

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Summary. Spirometry is the most important tool in diagnosing pulmonary disease and is the most frequently performed pulmonary function test. Since respiratory disease is the single greatest cause for morbidity and mortality on the Navajo Nation, the purpose of this study was to create new age and race-specific pulmonary nomograms for Navajo children. Five hundred fifty-eight healthy children, ages 6–14 years, attending Navajo Nation elementary schools in Arizona, were asked to perform spirometry to develop population-specific and tribe-specific nomograms for forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), and FEV1 Ratio (FEV1/FVC). Spirometry tests from 284 girls and 274 boys met American Thoracic Society quality control standards. Lung function values, except for FEV1/FVC, all increased with height. The lower limit of the normal range for FEV1/FVC was 80%. The spirometry reference equations from the healthy boys and girls were developed. Height and the natural log of height were significant predictors of FEV1, FVC, and $FEF_{25-75\%}$ in the gender-specific models. The resulting population-specific spirometry reference equations should be used when testing Navajo children ages 6–14 years. However, the use of the NHANES III spirometry reference equations for Caucasian children may not result in significant misclassification in clinical settings providing that a maximal effort is given by the Navajo child being tested. **Pediatr Pulmonol. 2009; 44:489–496.** © 2009 Wiley-Liss, Inc.

Key words: **pulmonary function tests; forced vital capacity; forced expiratory volume; reference equations; American Indians; Native Americans; Navajo children; pulmonary nomogram.**

INTRODUCTION

It is well understood that race is a significant determinant of lung function.[1,2] Anthropomorphic differences such as sitting height, standing height, and weight vary significantly between ethnic groups. When anthropometric characteristics are genetically tightly conserved across an ethnic population, it weakens the power of that nomogram to predict and estimate pulmonary function volumes of another ethnic group. Thus it has been widely accepted that nomograms should be race-specific.[3–8]

Significant differences in pulmonary function have been reported in adults comparing the measured outcomes for volumes and capacities between African-Americans, Caucasians,[5,9] Native Americans,[5,8] Inuits,[10] and between African and subcontinent Indian adults.[7] A number of studies have reported pulmonary function for children <19 years.[3,4,6,11,12] Of these, two studies have reported spirometric values for Native American children–Navajo adolescents,[3] and the Warm Springs Indian children.[11]

Spirometry is the most important tool in screening for pulmonary disease and is the most frequently performed pulmonary function test. The American Thoracic Society (ATS) recommends that spirometry reference equations from the third National Health and Nutrition Examination Study (NHANES III) be used whenever possible.

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However, NHANES III studies did not include American Indians or children under the age of 8 years, an unfortunate and significant oversight.[13] Moreover, previous spirometry studies of Native American children did not include children from the large population of Navajo in Arizona[11] or did not include children under the age of 14 years.[3] Therefore, the purpose of this study was to measure spirometry in Navajo Native American children ages 6–14 years and to derive the tribe-specific reference values to be used in clinical practice.

MATERIALS AND METHODS

Recruitment

The research protocol for this study was reviewed and approved by the Institutional Review Board for Human Subjects of the Navajo Nation and Northern Arizona University before any data was collected. Additionally, the Navajo Health Department, Navajo Community Health Boards, the Navajo School Boards, the Navajo Community and School Districts, the Principals of Navajo Schools, and Navajo parent–teacher groups at the various elementary schools all approved the study prior to testing.

Elementary school principals in Navajo Nation school districts in Arizona were contacted and agreed to send letters about the study to the parent(s)/guardian(s) of all enrolled students between the ages of 6 and 14 years. Each student who was ultimately tested and included in the statistical analysis of this study had to have parents and paternal and maternal grandparents of pure Navajo descent. Children who had parents or grandparents from other tribes or ethnic backgrounds were excluded from the final population (N = 558) and statistical analysis of this study. This population of 558 children approximately constituted a 5% sample of all Navajo children in the elementary schools of the Navajo Nation.

Assent was obtained from all students whose parent(s)/guardian(s) consented to their participation in the study. The Principal Investigator and one research assistant were trained in the correct procedures for pulmonary function testing. Other coworkers were involved in conducting the medical questionnaire interviews for all students in either the Navajo language or in English.

Standing height was measured to the nearest centimeter (cm) in stocking feet rounding up when $\geq$0.5 cm according to standard procedures with the participant standing erect with the head in the Frankfort plane and the back against the vertical wall mounted stadiometer. Sitting height was measured to the nearest cm rounding up when $\geq$0.5 cm according to standard procedures with the child sitting erect on a high-backed wooden chair that had a metric measurement on the back rest of the chair. Weight was measured using a double beam adjustable balance that was zeroed before body weights were determined. Auscultation of lung fields was performed to detect adventitious sounds such as wheezing, rhonchi, or crackles. A short respiratory questionnaire was interviewer administered either in the Navajo or English language depending on the language literacy of the child. Questions included histories of lung disease, thoracic surgery, medication use, the use of tobacco products, the use of ceremonial tobacco, home heating fuels, farm animal or pet presence, and allergens or dust exposures.

Participant Preparation

The forced vital capacity (FVC) maneuver was both explained and demonstrated prior to testing. Participants were standing during spirometric testing. At the end of every FVC maneuver, acceptability and reproducibility checks were applied, quality control messages displayed, and the best three previous flow-volume curves from the test sessions were displayed. The FVC maneuver was repeated until at least three acceptable and two reproducible FVC maneuvers were obtained, in accordance with the 1994 ATS recommendations.[14] Other measures of pulmonary function that were of interest in this study were forced expiratory volume in 1 sec (FEV1), the ratio of FEV1/FVC (FEV1%), and forced expiratory flow 25–75% ($FEF_{25-75\%}$).

Instruments

An automated flow-sensing spirometer was used (Survey Tachometer, Ferraris Respiratory, 901 Front Street, Louisville, CO 80027). The performance of this spirometry system was validated by third-party testing and found to meet ATS standards.[14] Calibration checks using a 3.00 L syringe were performed before testing began at an elementary school, or when the spirometer was moved to another testing site or whenever more than 3 hr had elapsed from the beginning of testing. Calibration checks were performed to ensure better than 3% volume accuracy. Time zero of each maneuver was determined using the back-extrapolation technique. Measurements from the three acceptable FVC maneuvers with the highest sum of FVC plus FEV1 were stored by the spirometry system. The largest FEV1 and the largest FVC from the acceptable FVC maneuvers were reported.

Statistical Analysis

Data from participants with upper respiratory infections, a history of chronic lung disease, or suboptimal quality spirometry were excluded from the analyses. After stratification by gender, descriptive statistics were determined for the primary outcome variables of FVC, FEV1, FEV1/FVC, $FEF_{25-75\%}$. The independent predictors of these variables were determined using both linear and nonlinear regression models. Independent variables

TABLE 1— Anthropometric Data and Mean (5th–95th Confidence Interval) Pulmonary Function Results

	Boys	Girls
Anthropometric		
Height standing (cm)	136 (116–160)	136 (116–156)
Height sitting (cm)	72.5 (63.5–83.8)	72.6 (63.5–82.6)
Sitting standing^{-1}	0.53 (0.50–0.56)	0.53 (0.50–0.56)
Weight (kg)	36.5 (21.3–62.6)	36.9 (22.0–60.7)
BMI (m/kg^2)	19.2 (15.1–27.3)	19.4 (15.1–27.6)
Pulmonary function		
FVC (L)	2.60 (1.57–3.95)	2.42 (1.50–3.54)
FEV1 (L)	2.24 (1.42–3.48)	2.15 (1.36–3.16)
FEV1/FVC (%)	86.8 (78.5–95.3)	88.9 (80.3–95.9)
$FEF_{25-75\%}$ (L/sec)	2.67 (1.65–4.15)	2.74 (1.67–4.18)

TABLE 2— Reference Equations for Spirometry for Navajo Girls (n = 284) and Navajo Boys (n = 274)

	Predicted value	LLN	R^2
Girls			
FVC	42.0 + 0.133 Ht–11.7 lnHt	–0.42	0.83
FEV1	40.8 + 0.122 Ht–11.2 lnHt	–0.32	0.82
$FEF_{25-75\%}$	54.3 + 0.150 Ht–14.6 lnHt	–1.01	0.48
Boys			
FVC	52.3 + 0.157 Ht–14.5 lnHt	–0.38	0.89
FEV1	50.8 + 0.143 Ht–13.9 lnHt	–0.35	0.86
$FEF_{25-75\%}$	70.3 + 0.176 Ht–18.7 lnHt	–0.92	0.50

Ht, standing height in centimeters; lnHt, natural log of height (cm). LLN = subtract this value for the lower limit of the normal range (5th percentile).

considered included age, weight, standing height, sitting height, body mass index as well as their square, and natural logarithm values. To define the lower limit of the normal ranges (LLNs), the fifth percentiles were determined. Stata version 8 was used for the analyses. The predicted values of FEV1/FVC were compared using Bonferroni *t*-tests.

RESULTS

Anthropometric and spirometry data of the healthy group and the entire cohort are given in Table 1. Spirometry results from 11 girls and 9 boys were excluded due to suboptimal spirometry quality (<3 acceptable maneuvers obtained). Spirometry results from 8 girls and 5 boys were excluded since they had a documented history of asthma or chronic respiratory symptoms. None of the children tested reported a history of using standard American smoking or chewing tobacco. Even though the smoking of a plant called ''Mountain Tobacco'' was used by the adult population in tribal ceremonies, none of the children reported use of this plant.

Results from the remaining 284 girls and 274 boys were analyzed. Spirometry results from 33 girls and 48 boys who reported recent upper respiratory infections were retained in the data set because they no longer had symptoms, their lungs were clear to auscultation and this variable was not significant when added to any of the models under analysis.

The spirometry reference equations from the healthy boys and girls are given in Table 2. Height and the natural log of height were significant predictors of FEV1, FVC, and $FEF_{25\%-75\%}$ in the gender-specific models. Different from the findings of other studies [3,6,11,13] the relationship between height and the dependent variables was more linear, with a correlation coefficient of $r \geq 0.9$ for all relations between height and each of the other dependent variables. Although age and body mass index and height squared were statistically significant predictors in most of the models, the overall variance explained by the models improved <2% in each case, making the addition of these variables in this age range unnecessary.

The total amount of variance explained by the demographic variables in the models predicting the FEV1/FVC was <5%, so the predicted value is the same as the mean value in Table 1 and the lower LLN is the same as the 5th percentile in Table 1. Also, comparisons of the predicted FEV1/FVC values for all of the children included in the data set are presented in Tables 3a (males)

TABLE 3a— Comparison of the Predicted FEV1/FVC Values for the Study's Males Using the Current and NHANES II Equations

Age (years)	Navajo FEV1/FVC	Caucasian FEV1/FVC	Mexican-American FEV1/FVC	African-American FEV1/FVC
All (n = 274)	0.988 ± 0.052	0.845 ± 0.035*	0.870 ± 0.009*	0.862 ± 0.024*
6 (n = 26)	1.075 ± 0.030	0.767 ± 0.002*	0.849 ± 0.001*	0.810 ± 0.003*
7 (n = 36)	1.037 ± 0.022	0.809 ± 0.006*	0.861 ± 0.002*	0.839 ± 0.006*
8 (n = 51)	1.012 ± 0.025	0.840 ± 0.012*	0.870 ± 0.003*	0.860 ± 0.010*
9 (n = 42)	0.980 ± 0.025	0.854 ± 0.014*	0.873 ± 0.003*	0.868 ± 0.011*
10 (n = 46)	0.969 ± 0.022	0.872 ± 0.015*	0.877 ± 0.004*	0.880 ± 0.012*
11 (n = 27)	0.948 ± 0.019	0.875 ± 0.015*	0.877 ± 0.003*	0.881 ± 0.012*
12–14 (n = 46)	0.921 ± 0.022	0.871 ± 0.015*	0.875 ± 0.004*	0.877 ± 0.012*

Values are mean ± standard deviation.
*Indicates a value significantly different ($P < 0.0005$) from its corresponding value using the Navajo prediction equation.

TABLE 3b— Comparison of the Predicted FEV1/FVC Values for the Study's Females Using the Current and NHANES II Equations

Age (years)	Navajo FEV1/FVC	Caucasian FEV1/FVC	Mexican-American FEV1/FVC	African-American FEV1/FVC
All (n = 284)	0.912 ± 0.016	0.897 ± 0.022*	0.911 ± 0.018*	0.806 ± 0.054*
6 (n = 28)	0.941 ± 0.011	0.930 ± 0.019*	0.946 ± 0.012*	0.696 ± 0.011*
7 (n = 40)	0.927 ± 0.013	0.913 ± 0.022*	0.928 ± 0.012*	0.747 ± 0.008*
8 (n = 55)	0.917 ± 0.008	0.903 ± 0.014*	0.917 ± 0.007*	0.785 ± 0.001*
9 (n = 34)	0.909 ± 0.007	0.894 ± 0.014*	0.908 ± 0.006*	0.815 ± 0.002*
10 (n = 56)	0.903 ± 0.006	0.887 ± 0.013*	0.901 ± 0.005*	0.838 ± 0.005*
11 (n = 42)	0.898 ± 0.005	0.880 ± 0.012*	0.895 ± 0.005*	0.856 ± 0.007*
12–14 (n = 29)	0.895 ± 0.003	0.878 ± 0.009*	0.891 ± 0.003*	0.881 ± 0.015*

Values are mean ± standard deviation.
*Indicates a value significantly different ($P < 0.0005$) from its corresponding value using the Navajo prediction equation.

and 3b (females). To compare the accuracy of the current FEV1/FVC equations, FEV1/FVC values predicted by the use of the NHANES III equations are also included in Tables 3a and 3b. Since the NHANES III equations use age as a significant component of the equations, the data are subdivided into the different ages used in deriving the current equations. As shown in Tables 3a and 3b, the use of the NHANES III prediction equations yield significantly lower FEV1/FVC values across all of the ages tested.

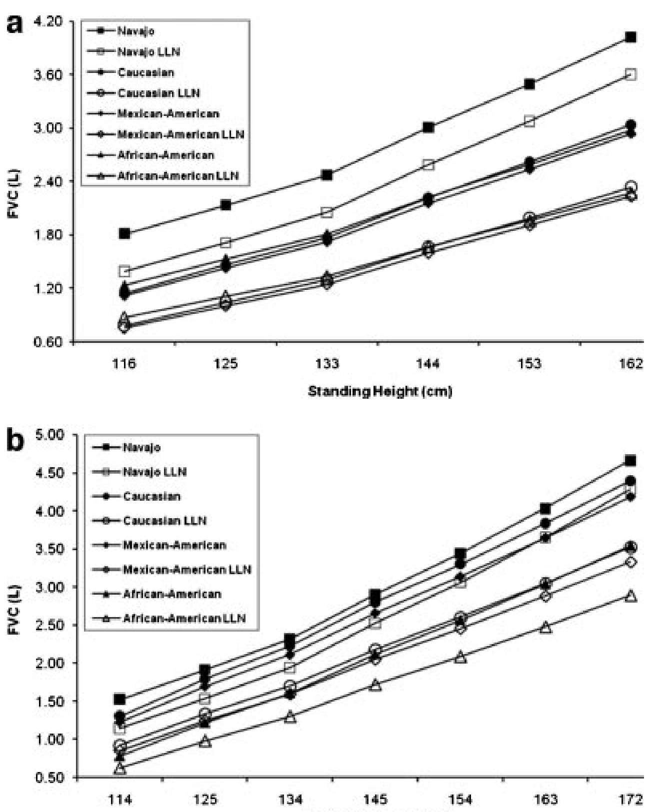

Fig. 1. a: The expected FVC values for 6-year-old Navajo, Caucasian, Mexican-American, and African-American females. b: The expected FVC values for 6-year-old Navajo, Caucasian, Mexican-American, and African-American males. Values were calculated using either the NHANES III equations (Caucasian, Mexican-American, and African-American) or the equations in Table 2 (Navajo).

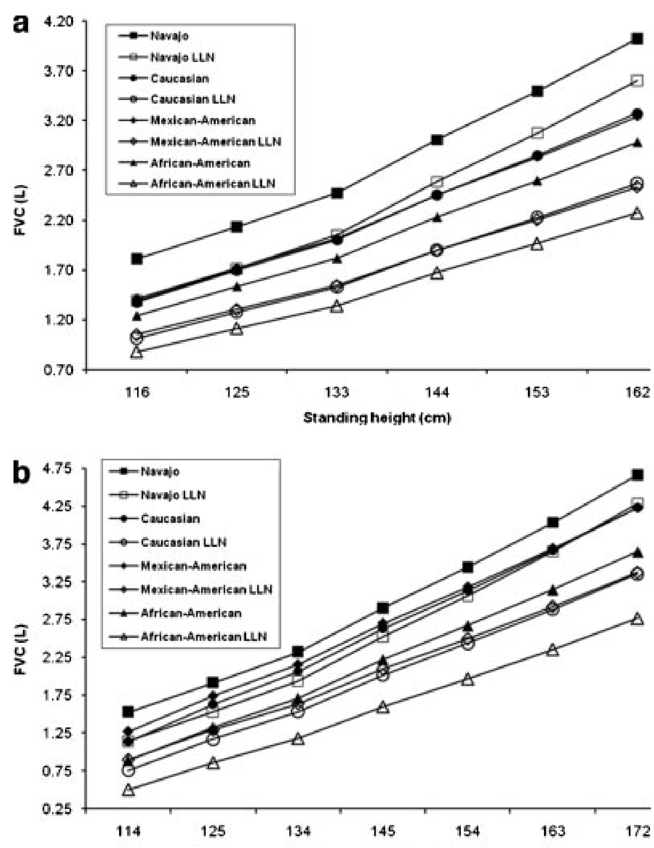

Fig. 2. a: The expected FVC values for 10-year-old Navajo, Caucasian, Mexican-American, and African-American females. b: The expected FVC values for 10-year-old Navajo, Caucasian, Mexican-American, and African-American males. Values were calculated using either the NHANES III equations (Caucasian, Mexican-American, and African-American) or the equations in Table 2 (Navajo).

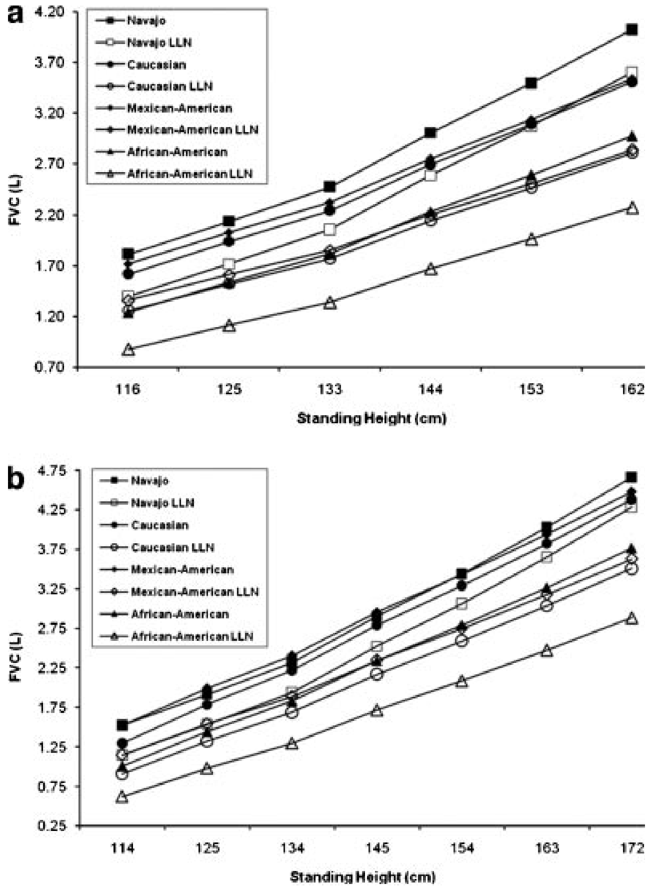

Fig. 3. a: The expected FVC values for 14-year-old Navajo, Caucasian, Mexican-American, and African-American females. b: The expected FVC values for 14-year-old Navajo, Caucasian, Mexican-American, and African-American males. Values were calculated using either the NHANES III equations (Caucasian, Mexican-American, and African-American) or the equations in Table 2 (Navajo).

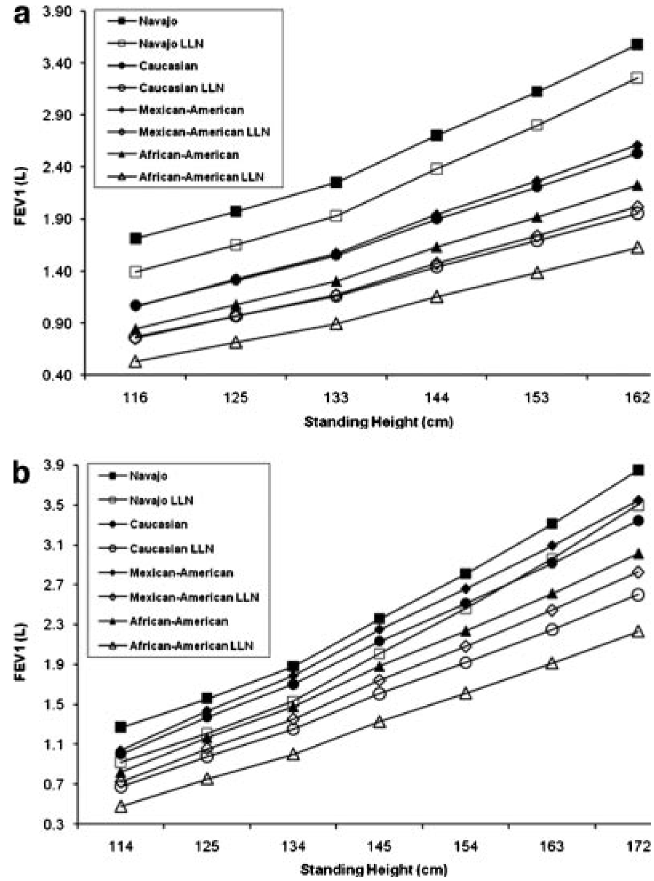

Fig. 4. a: The expected FEV1 values for 6-year-old Navajo, Caucasian, Mexican-American, and African-American females. b: The expected FEV1 values for 6-year-old Navajo, Caucasian, Mexican-American, and African-American males. Values were calculated using either the NHANES III equations (Caucasian, Mexican-American, and African-American) or the equations in Table 2 (Navajo).

To compare the accuracy of the current equations, Comparisons using the predicted values derived in this study with those of the NHANES III Caucasian, Mexican-American, and African-American children are presented in Figures 1–9. Again, since the NHANES III calculations incorporate both age and height, comparisons are depicted for three different ages. To reduce the number of graphs, we include comparisons for only the upper, lower and middle ages of the current database (14, 6, and 10, respectively).

DISCUSSION

These results expand the age range of our previous study of spirometry in healthy Navajo adolescents[3] incorporating the life span between 6 and 18 years of age. The current results for children whose age overlaps our previous study are very similar, providing external validation of the results.

Given the relatively small population size of Navajo living in the United States and specifically on the Navajo Reservation, we could not hope to achieve the large numbers of study participants from population-based studies of Caucasian children in the United States[13] and Europe.[15] However, our sample represents ~5% of Navajo children ages 6–14 years and is large enough over this age range to provide stable reference values. Moreover, it should be noted that in the NHANES III study, the number of children used between the ages of 8 and 14 ranged from 268 to 393 for the six different subcategories (race, sex)[13] making the number of children used in this study similar to the NHANES numbers. However, in our study, the number of children tested (N = 128: 66 females; 62 males) under the age of 8 years constituted 23% of the size of the cohort. This important data characterizes the pulmonary function

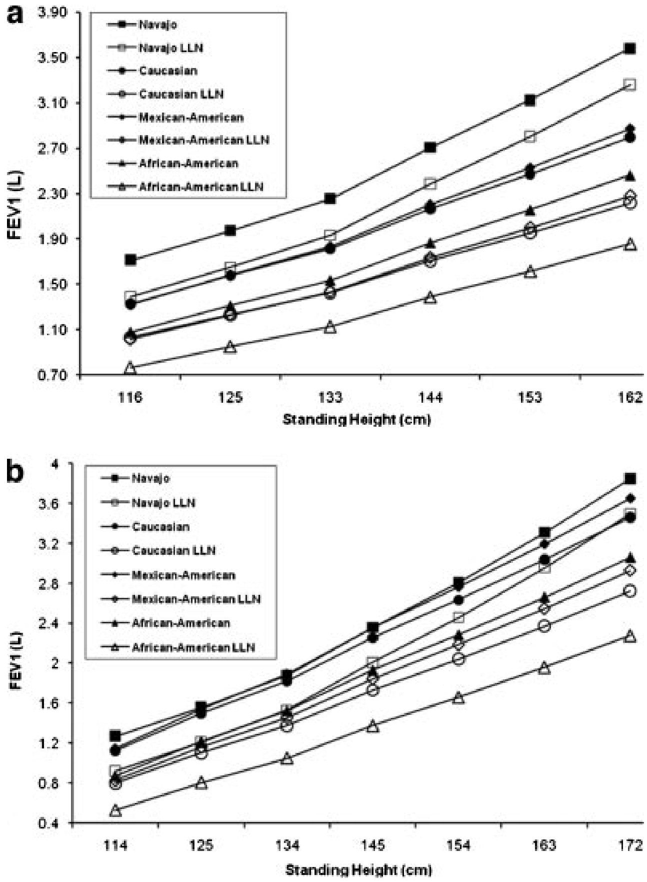

Fig. 5. a: The expected FEV1 values for 10-year-old Navajo, Caucasian, Mexican-American, and African-American females. b: The expected FEV1 values for 10-year-old Navajo, Caucasian, Mexican-American, and African-American males. Values were calculated using either the NHANES III equations (Caucasian, Mexican-American, and African-American) or the equations in Table 2 (Navajo).

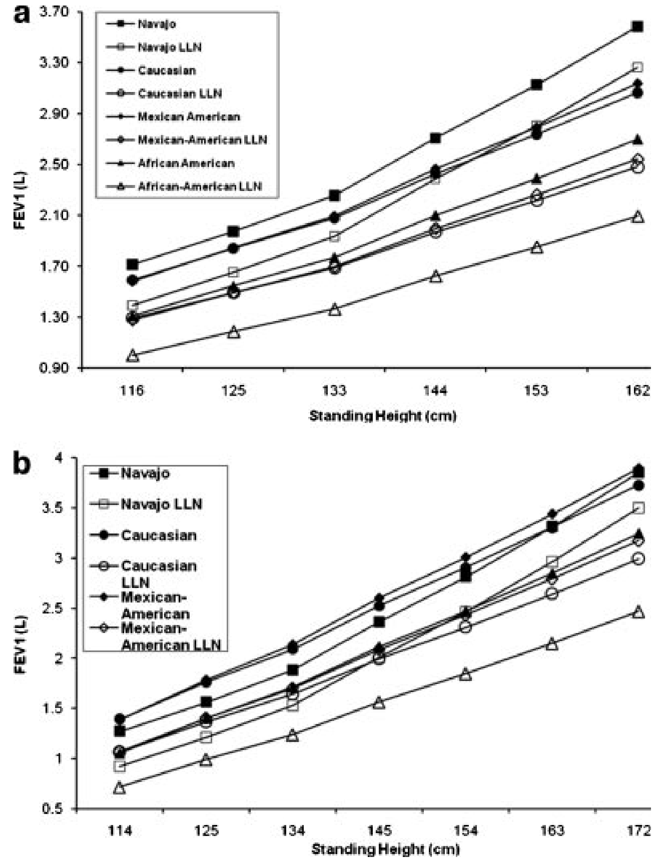

Fig. 6. a: The expected FEV1 values for 14-year-old Navajo, Caucasian, Mexican-American, and African-American females. b: The expected FEV1 values for 14-year-old Navajo, Caucasian, Mexican-American, and African-American males. Values were calculated using either the NHANES III equations (Caucasian, Mexican-American, and African-American) or the equations in Table 2 (Navajo).

values in the age ranges not tested in children from the NHANES III database. As in those studies,[13,15] we also found that the FVC and FEV1 increased with increasing age and height and for a given age and height, the values from girls were slightly lower than those for boys. We also found that an exponential function of height in the models explained slightly more variance and reduced the residual scatter when compared to linear models. When using separate models for boys and girls, age and height are highly co-linear, so that either one substitutes for the other in the models, and the age $\times$ height interaction terms were not significant.

As in the European study,[15] the FEV1/FVC (FEV1%) in our study did not significantly vary by age, height, or gender. In the NHANES III study, the FEV1% predicted value and LLN also did not vary significantly by race or age (for children), so we recommend that a fixed value for the LLN (80%) be used to define airflow limitation (airways obstruction) for Navajo children. For determining a restrictive type of lung function impairment, the LLN for the FVC may be set as either the fifth percentile (as given in Table 2) or a percentage of the predicted value (about 83%). Note that both submaximal inhalation efforts and submaximal exhalation time will falsely decrease the measured FVC. Differences in FEV1 or FVC of $<$0.20 L and differences in $FEF_{25-75\%}$ and peak flow of $<$15% are within the ''noise of measurement'' (the within subject coefficient of variation) for children,[16] therefore, we suggest that differences within these ranges are not clinically significant.

In general, when comparing our predicted values with those of the NHANES III Caucasian, Mexican-American, and African-American children, the Navajo children appear to have spirometry values greater than those that would be predicted for children of other races. This difference is most visible between Navajos and African-Americans where the expected values of the African-Americans mainly fall below the Navajo LLN. This is

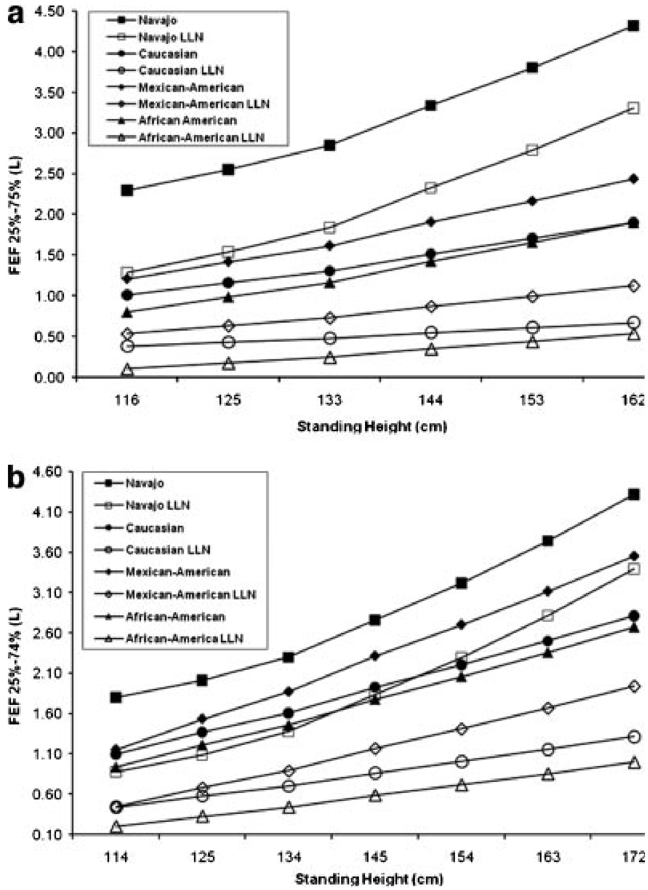

Fig. 7. a: The expected $FEF_{25-75\%}$ values for 6-year-old Navajo, Caucasian, Mexican-American, and African-American females. b: The expected $FEF_{25-75\%}$ values for 6-year-old Navajo, Caucasian, Mexican-American, and African-American males. Values were calculated using either the NHANES III equations (Caucasian, Mexican-American, and African-American) or the equations in Table 2 (Navajo).

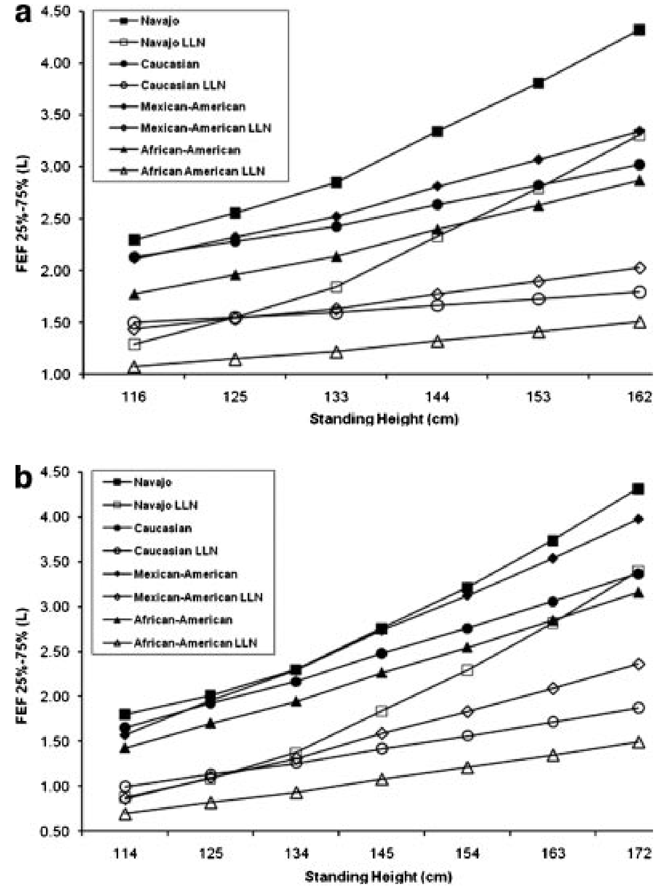

Fig. 8. a: The expected $FEF_{25-75\%}$ values for 10-year-old Navajo, Caucasian, Mexican-American, and African-American females. b: The expected $FEF_{25-75\%}$ values for 10-year-old Navajo, Caucasian, Mexican-American, and African-American males. Values were calculated using either the NHANES III equations (Caucasian, Mexican-American, and African-American) or the equations in Table 2 (Navajo).

especially visible amongst the females for all three of the spirometry values. The expected spirometry values for Caucasians and Mexican-Americans usually fall between the expected Navajo values and their corresponding LLN. As age and height increase, it appears that the differences between Navajos, Caucasians, and Mexican-Americans diminish, especially amongst the tall older males. Therefore, when our population-specific reference equations are not available when configuring a spirometer for clinical use, the NHANES III equations for Caucasian or Mexican-American male children might be chosen without a substantial increased risk in the misclassification rates for detecting airways obstruction and restrictive impairment. The use of either NHANES equation for female children will at the least give somewhat lower values and may increase the number of ‘‘false-positive’’ results. Notwithstanding the equation used, minimizing misclassification of spirometry results requires optimal coaching for maximal spirometry maneuvers.

Limitations of our study include the following: We used a flow-sensing spirometer, while many hospital-based pulmonary function laboratories use a volume-sensing spirometer. In theory, the FEV1 and FVC results could vary by up to 6% according to the choice of spirometer; however, we believe that most Indian Health Clinics will choose to purchase a flow-sensing spirometer due to the reduced risk of cross-contamination and lower cost.

In summary, we recommend that our new population-specific reference equations be used when testing Navajo children ages 6–14 years because these formulas were created from testing the population of interest. However, the use of the NHANES III equations for Caucasians may estimate the various lung capacities and volumes with the result that few diagnoses for obstructive or restrictive disease will be made. However, it will be necessary, in the clinical setting, to insure that the Navajo child is coached to give their maximal effort during the FVC maneuver if the NHANES III formulas are used.

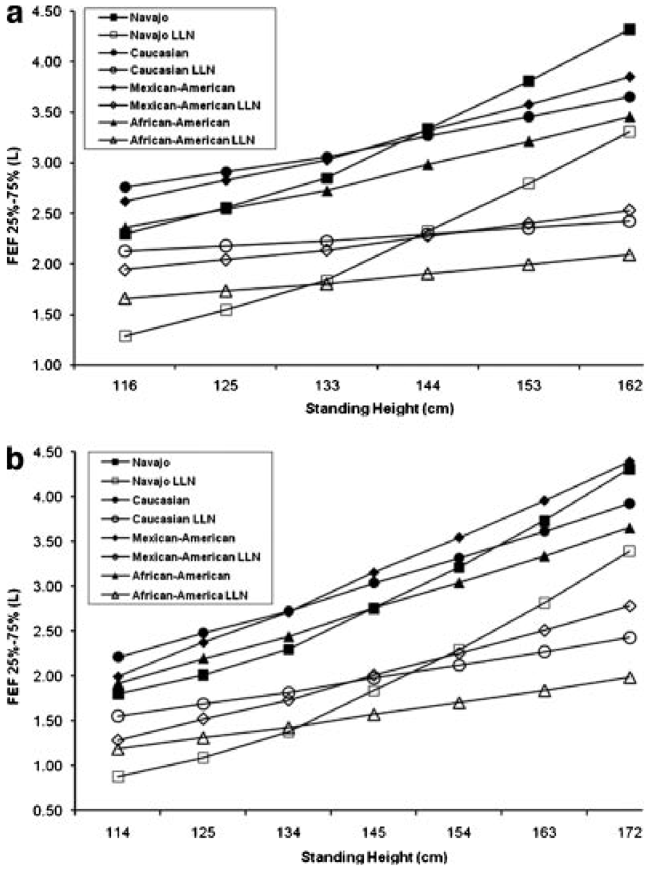

Fig. 9. a: The expected $FEF_{25-75\%}$ values for 14-year-old Navajo, Caucasian, Mexican-American, and African-American females. b: The expected $FEF_{25-75\%}$ values for 14-year-old Navajo, Caucasian, Mexican-American, and African-American males. Values were calculated using either the NHANES III equations (Caucasian, Mexican-American, and African-American) or the equations in Table 2 (Navajo).

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