Which reference set for spirometry?

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Interpretation of spirometry typically requires comparison of the patient’s measured values (FVC, FEV1, FEV1/FVC ratio) with expected values. For many years, pulmonary function laboratories have had to choose which set of reference or predicted equations should be used. The choice was often made based on comparison of the equipment/techniques and the sample population tested in the normative study to those of the laboratory. Recently, the American Thoracic Society and European Respiratory Society (ATS/ERS) published recommendations regarding selection of reference values, including those for spirometry. For pulmonary function laboratories in the United States, the NHANES III study was suggested as the most appropriate for spirometry predicteds in Caucasians, African-Americans and Mexican Americans.

The NHANES III (National Health and Nutrition Examination Survey) reference equations were published in 1999. There are many reasons a lab might consider switching to the NHANES III reference set; let’s consider a few of them:

1. NHANES III used equipment and techniques that met or exceeded the ATS guidelines. The data was collected from 1989-1994 and complied with the 1987 ATS recommendations for spirometry (both equipment and testing procedures). The data was re-analyzed to comply with the revised 1994 ATS recommendations as well. The use of standardized equipment and procedures makes this data set very appealing to laboratories also trying to comply with ATS/ERS recommendations.

[ILLUSTRATION OMITTED]
2. NHANES III tested a large population of healthy, non-smoking subjects. Over twenty thousand subjects were tested; after applying strict exclusion criteria, 7429 subjects were used in the data set. This normal population included approximately equal numbers of subjects from the three ethnic groups mentioned above.

3. The sample population spanned the ages of 8 to 80 years. NHANES III included children, adolescents, and adults across a large age range. An advantage of this design is that there are no 'holes' in predicted set, as sometimes occurs when different authors are selected to provide normal values for children, adolescents, and adults. Additionally, the NHANES III regression equations were modeled to provide reasonable estimates of spirometric values in the transition from adolescent to adult lung function. Separate regression coefficients are provided for males and females in each ethnic group, with separate age breakpoints (adolescent vs. adult) for males and females.

4. NHANES III included the most commonly used spirometric parameters. Regression coefficients are provided for FVC, FEV1, FEV1/FVC, FEF25%-75%, and PEF (peak expiratory flow). In addition to providing coefficients for the normal values, statistically sound coefficients for the lower limit of normal (LLN) are included. Use of the LLN for interpretation of spirometry has also been recommended by the joint ATS/ERS standardization guideline.

5. NHANES III predicted values compare favorably with previously published studies. Predicted values from NHANES III tend to be slightly higher than the values from older studies for each of the ethnic groups described. One exception to this finding is the predicted values for FEF25%-75% which tend to be slightly lower, at least in comparison to some older studies. The small differences between this study and previously published data may be due to the rigorous adherence to acceptability and repeatability criteria during testing, and to the fact that five acceptable curves were obtained instead of the ATS recommended three curves.

6. NHANES III predicted values confirmed the 12 to 15% difference in lung volumes between Caucasians and African-Americans. As shown in other studies, the FEV1 and FVC in African-Americans are smaller than in Caucasians of similar height,
while the FEV1/FVC% is the same. Some PFT laboratories apply a 'correction factor' to Caucasian-derived predicted values to make them appropriate for other races (0.85 to 0.88 for African-Americans). The NHANES III data indicate that this is a reasonable approximation, but provide separate regressions that better account for the differences across various ages and heights in African-Americans.

7. Besides the usual spirometric parameters, the NHANES III reference set provides expected values for the FEV6 and FEV1/FEV6 ratio. The FEV6 has been suggested as a surrogate for measurement of the FVC. Using the FEV6 in place of the FVC for simple spirometry avoids many issues related to prolonged expiration, both in normal subjects and in patients who have obstructive lung disease. The FEV6, and the FEV1/FEV6 ratio, are recommended by the National Lung Health Education Program (NLHEP) for spirometers designed for use in physicians' offices or in primary care practices.

Pulmonary function laboratories considering changing reference sets need to carefully consider whether the new equations adequately describe normal subjects tested in their community. Previously, the ATS suggested comparing 20-40 healthy subjects using different sets of equations to evaluate the applicability of a particular reference set. Such a small sample may not be able to detect real differences between the predicted set and the local population. However, many PFT labs have databases that are large enough to select a subset of apparently healthy subjects and compare these individuals using different reference equations. This can be done fairly easily because most spirometry software permits the user to select among predicted sets. Even if this type of comparison is impractical, pulmonary function laboratories and others performing spirometry should look carefully at the robustness of the NHANES III reference set.

Changing reference sets for spirometry includes additional concerns for the PFT laboratory. Predicted values calculated using separate regression coefficients for different ethnic groups obviates the need to apply 'correction' factors. For spirometry software that provides this capability, the correction (i.e. adjustment) factor should be set to 1.00, or turned off, which ever is appropriate. Because NHANES III provides predicteds for only Caucasians, African-Americans, and Mexican
Americans, correction factors for other ethnic groups may still be appropriate. Race-appropriate corrections should be applied to FVC and FEV1, but not to the FEV1/FVC ratio.

In PFT laboratories that also perform lung volumes, another question arises when race-specific equations (i.e. NHANES III) are used for spirometry. If the predicted slow vital capacity (SVC) is forced to the same value as the predicted FVC, what should be done for predicted lung volumes? In this situation, correction based on race for TLC, FRC and RV may be appropriate. The ATS/ERS guideline suggests correction factors of 0.88 for TLC and FRC, and 0.93 for RV, in African-American and Asian American subjects. In order to accomplish this, race-correction needs to be turned on for lung volumes, even though it is turned off for spirometry. As in the case of spirometric variables, only the TLC, FRC and RV need to be corrected; RV/TLC is not corrected.

Changing reference sets can be confusing for both pulmonary function laboratory personnel and for the end-users of the data (referring physicians). Spirometer manufacturers should provide software that supports modifications to the reference equations, along with the addition of new regressions as they become available. For complicated reference sets with tables of coefficients (as in the NHANES III set), vendors should include appropriate software to implement the equations. In all cases, final reports should include name references to the predicted sets used for specific tests (spirometry, lung volumes, DLCO, etc.) so that anyone using the data for interpretation can determine the source of the 'normal' values. When changing reference sets, it is a good idea for the PFT lab to specify that different predicted values are being used. Labs that adopt a new reference set should include a statement detailing the change and its effective date on all reports. This statement will allow clinicians to make sense of percent predicted values in patients who may have had serial tests in the same lab using different regression equations.

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