Invited Commentary

Invited Commentary: On Population Subgroups, Mathematics, and Interventions

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New sex-specific equations, each with race/ethnic-specific intercept, for predicted lung function illustrate a methodological point, that complex differences between groups may not imply interactions with other predictors, such as age and height. The new equations find that race/ethnic identity does not interact with either age or height in the prediction equations, although there are race/ethnic-specific offsets. Further study is warranted of the effect of possible small race/ethnic interactions on disease classification. Additional study of repeated measures of lung function is warranted, given that the new equations were developed in cross-sectional designs. Predicting lung function is more than a methodological exercise. Predicted values are important in disease diagnosis and monitoring. It is suggested that measurement and tracking of lung function throughout young adulthood could be used to provide an early warning of potential long-term lung function losses to encourage improvement of risky behaviors including smoking and failure to maintain normal body weight in the general population.

Abbreviations: FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

In this issue of the Journal, Kiefer et al. (1) present new formulae for predicted lung function in adults of given age, sex, race/ethnicity, and height. The base population for prediction was nonsmokers, free of respiratory disease. Persons aged 23 years (by which time most people have achieved peak lung function (2, 3)) through 80 years are included. Race/ethnic- and sex-specific predictions (4) have been used clinically, as part of the output of spirometric devices, and in epidemiologic research.

Given the large physiologic differences between men and women and also among race/ethnic groups, it seems to make sense that separate prediction equations should be developed (4). Although the updated predictions differed by sex and had race/ethnic-specific intercepts, the major point (1) was that the age and height coefficients in the new equations were not race/ethnic specific.

There is a tendency in epidemiology to assume that groups that are very different should be dealt with separately in analysis. Thus, we often do sex-specific analysis and elaborate on ways in which men and women differ. A difference (1) between men and women in predicting forced vital capacity (FVC), for example, was that the coefficient for age² was −0.2083 in women vs. −0.2476 in men. To get some idea of the implications of these coefficients on the shape of the FVC curve over age, we may multiply the coefficients by different age² values and see that, for fixed height and ethnicity, FVC in women is predicted to decrease 333 mL between the ages of 30 and 50 years, while that in men is predicted to decrease 396 mL, an additional loss of 63 mL over 20 years in men over women. Between the ages of 50 and 70 years, both predicted decreases are larger, 500 mL in women versus 594 mL in men, and the “gender gap” has increased to 94 mL. Thus, the expanding lung function difference between men and women is expressed in different coefficients for age².

Similarly, the different race/ethnic groups have patterns of lung function that differ from each other in certain ways. The point that Kiefer et al. (1) make is that, unlike the situation with sex, it is not necessary for an excellent representation of the patterns for the age and height coefficients to differ between race/ethnic groups. Thus, the FVC in African Americans was estimated to be 596 mL lower than
that in whites, among females, and 831 mL lower among males. This difference, however, was not judged to expand or contract depending on age or height. Small differences in FVC patterns were seen according to race/ethnicity, but these differences were tiny and were omitted from the final equations. The authors showed elegantly that the race/ethnic interactions and the Mexican-American main effects could be ignored without changing judgments about FVC in the different groups. Similar methodological conclusions were drawn for forced expiratory volume in 1 second (FEV₁) and for the FEV₁/FVC ratio.

The equations presented (1) are very complex, involving curvature in both age and height, sex specificity, and offsets for African Americans. Different patterns may be expressed by the same coefficients when there is curvature, for example, if one race/ethnic group has a starting value different from that of another group. Yet, certain features are held in common among the different groups, and outstanding predictions are achievable without race/ethnic specificity of the age and height coefficients. This methodological point is general in epidemiology: Groups may differ greatly in many respects and yet retain some common features in the fitting of statistical patterns. When a single equation can be used to fit a variety of patterns, the full sample size may be retained in variance estimation, and the precision of the analysis and the power in hypothesis testing are improved.

One area of inquiry in which omission of subtle race/ethnic differences may matter is in defining disease states on the basis of being below a cutoff point in FVC, FEV₁, or the FEV₁/FVC ratio (5). Small differences in the middle of the distribution of lung function can result in larger differences in the tails, for example, in defining the percentage of persons with airway obstruction or chronic obstructive pulmonary disease. This aspect of prediction was not considered by Kiefer et al. (1).

Further analyses of lung function prediction in other data sets among adults would also be helpful. Examination of repeated lung function measures across age would constitute a better test of the proposition that the rate of decline of lung function with age does not vary by race/ethnicity. The question of race/ethnicity itself is tricky; members of a given gene pool may differ greatly across geographic areas, for example, African Americans versus Africans in Africa, or Mexican Americans versus Mexicans in Mexico. Although these groups may have similar ancestry, geography-specific environment and cultural practices differ and may interact with the genetic configuration. In addition, as noted by Kiefer et al. (1), the increase in mixed-race persons blurs race/ethnic distinctions.

The prediction of lung function is a topic of more than methodological interest. Predicted lung function is invaluable in diagnosing devastating diseases of the lungs and the heart (5, 6). However, of equal importance is the association of lung function with future cardiovascular disease. Hole et al. observed a strong relation of FEV₁ with cardiovascular mortality. They observed, “The addition of FEV₁ for middle aged patients would provide an important indicator of subsequent general health as well as a means for deciding who might be most appropriate for receiving advice on risk factor modification aimed at reducing cardiorespiratory mortality” (7, p. 715).

However, some pulmonologists, discussing the above statement with the first author, have said that the data connecting lung function and cardiovascular disease are impressive, but they are at a loss regarding what treatment might be prescribed for a nonspecific condition of loss of lung function within its normal range. A suggestion would be to measure lung function as part of the general medical examination every few years starting in young adulthood. There are distinctly different patterns in which the lung function peak occurs and decline begins (3). It makes sense to bring attainment of a lower peak lung function or more rapid than average decline in lung function to the attention of patients. Among other things, cigarette smoking and obesity could be addressed in conjunction with the observation of the pattern of lung function change. Quitting smoking and reduced adiposity might attenuate that decline (3, 8). At minimum, a high rate of decline of lung function is a marker of increased long-term cardiorespiratory risk and might motivate general healthful lifestyle changes in young adults. Thus, there are several reasons for expanded use of spirometry in medicine and public health; having simple and accurate predictions of lung function for a given age, sex, race/ethnicity, and height is valuable in any such endeavor.

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REFERENCES

