EUROPEAN RESPIRATORY JOURNAL
EDITORIAL
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Addressing the effect of ancestry on lung volume

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Shareable abstract (@ERSpublications)
Current spirometry reference values are dependent on geographic ancestry due to differences in body structure affecting the relationship between height and lung volume. New indices are needed to develop reference values which are independent of ancestry. https://bit.ly/3P9YCJ0

Cite this article as: Graham BL, Miller MR, Thompson BR. Addressing the effect of ancestry on lung volume. *Eur Respir J* 2022; 59: 2200882 [DOI: 10.1183/13993003.00882-2022].

Received: 27 April 2022
Accepted: 28 April 2022

Provision of healthcare should not be influenced by ethnicity, skin colour or ancestry. To avoid discrimination, all healthcare practices and procedures should be systematically examined for possible influence by racism. The interpretation of spirometry is a case in point. Predicted normal values for spirometry are based on the sex, age, height and geographic ancestry of the individual. Some argue that including geographic ancestry leads to systemic racism [1, 2].

Racism in spirometry dates from Cartwright [3] in 1851 observing that “the expansibility of the lungs is considerably less in the black than the white race of similar size, age and habit”, and “the deficiency … may be safely estimated at 20 per cent”. Cartwright inappropriately interpreted this as supporting his racist assertion that African slaves consume less oxygen than Europeans, which was a physical advantage for working in cotton fields, thus rationalising African slavery. The differences in lung volumes between people of African and European ancestry were not disputed, but Cartwright’s interpretation has cast racist overtones on predicting lung volumes based on ancestry. An expert panel developing 1978 standards for spirometry surveillance of exposure to cotton dust [4, 5] recommended a reduction of 15% as a “correction factor” for predicting African–American lung volumes to avoid “inadvertently fostering discrimination [against them] in hiring practices.” Conversely, applying a “correction factor” for people of African ancestry could diminish eligibility for compensation for occupationally induced lung function impairment. As Kaminsky [6] noted, there can be both positive and negative consequences.

The term “race correction” is itself racist and is no longer used. Large studies of healthy people, notably the National Health and Nutrition Examination Survey (NHANES III) [7], developed separate prediction equations for people who self-identified as “white, black or Hispanic”, eliminating the use of a correction factor. The Global Lung Function Initiative (GLI) prediction equations [8] continued this approach, predicting values separately for “Caucasians” (European ancestry), African–Americans, North East Asians and South East Asians. For the same age, sex and height the predicted normal lung volumes for someone of African ancestry are lower than that for someone of European ancestry. Braun *et al.* [9] claimed that Cartwright’s racist interpretation of spirometry continues today because of the use of different predicted values for people of African ancestry. Braun *et al.* [9] suggest that the differences between people of European and African ancestry are due to socioeconomic and environmental factors, but notes that “the specific details of how social class and race influence lung function physiologically, however, remains to be determined.”

Why are differences in spirometric volumes for people of different ancestry still evident today? The two competing explanations are 1) that it is primarily due to a long legacy of racial prejudice through poorer socio-economic status, education and nutrition, to mention a few causes, and 2) that it is primarily due to intrinsic differences in body structure. Socio-economic deprivation can lead to lower lung function [10], but its effect was found to be small (<10%) in relation to the effect of anthropomorphic differences (50%) [11] and accounted for ⩽3% of differences in lung volumes amongst a Chinese population [12]. Furthermore, Inuit people have larger lungs than predicted for people of European ancestry [13, 14] and yet they experience socio-economic deprivation when compared to Canadians of European ancestry [15]. A study of central African schoolchildren found that the GLI African ancestry predicted lung volumes worked well for healthy children but malnourished children had z-scores reduced by about 0.5 [16], suggesting that the lower predicted values for healthy people of African ancestry were not due to socio-economic deprivation.

The effects of anthropomorphic differences appear to be dominant. Standing height, which is used to predict lung volume, is a summation of leg, spine and head length, with only spine length linked to lung volume. People with proportionally longer legs have smaller lung volumes than people of the same height with proportionally shorter legs. The difference in the ratio of leg length to overall height between African and European groups is significant [17–19]. Substituting sitting height for standing height was found to reduce spirometric differences by close to 40% [11]. Including sitting height as a predictor, or its ratio to standing height, may help but in children only reduced the observed differences by just over 10% [20] and in adults only accounted for about 1% of the variance in forced expiratory volume in 1 s (FEV_1) [21]. People indigenous to equatorial African regions have proportionally longer arms and legs to facilitate body cooling in a hot climate, complying with Allen's rule for all homeothermic species [22, 23]. Conversely, people indigenous to cold climates, such as the polar regions (*e.g.* Inuit) or at altitude, have proportionally shorter limbs to preserve body heat. Genome-wide analysis of body proportion found that differences in the ratio of sitting height to total height between people of African and European ancestry are heritable [18]. Since the relationship between standing height and lung volume differs between these groups, separate prediction equations for each group are needed to minimise the variable contribution of height to lung volumes.

GLI combined all the available spirometric data to develop universal predicted values for all groups, which eliminates ancestral categories (the GLI 'Other' category) [8], but the universal application of this would be at the cost of expanded confidence intervals and failure to provide the most accurate prediction available for lung volumes. There would be a tendency for lung disorders to be under-diagnosed in individuals of European ancestry and over-diagnosed in individuals of African ancestry. Assuming that the same height coefficient can be used for different body types diminishes precision: one size does not fit all.

The difference between spirometry values predicted using the GLI European ancestry equations and GLI African ancestry equations is eliminated if the height used in the equations is adjusted to account for the difference in trunk to leg length ratio between people of African and European ancestry. Figure 1 shows that if the height used in the GLI European ancestry equations is reduced by 6.5%, the predicted FVC is within 1% of the FVC predicted by the GLI equation for African ancestry. This was found to be the case

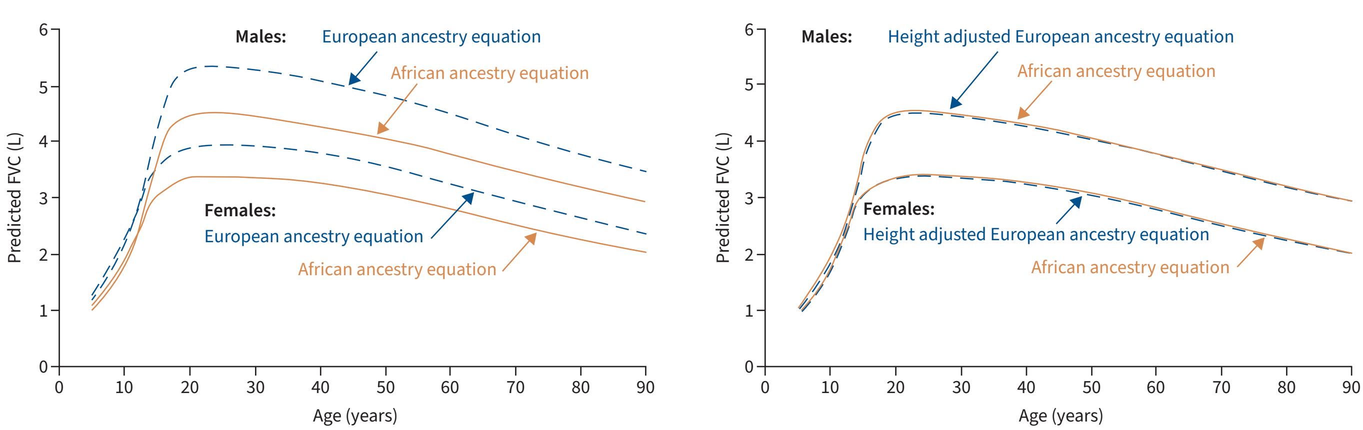

FIGURE 1 Forced vital capacity (FVC) predicted for males (adult height 175 cm; upper lines) and females (adult height 165 cm; lower lines) using Global Lung Function Initiative (GLI) equations [8] for European ancestry (dashed blue lines) and African ancestry (solid orange lines). In the right panel, the height used in the European ancestry equations has been reduced by 6.5% to account for the difference in trunk to height ratios between the two groups, demonstrating that height alone accounts for the difference in GLI predicted lung volumes. This applies to all ages and all heights, and to forced expiratory volume in 1 s as well as FVC.

independent of age, height or sex, and also applied to FEV_1. Similar results were found using NHANES III equations. Equally, the African ancestry equations could be used for people of European ancestry with the converse height adjustment. This suggests that one set of equations can be used for both people of European ancestry and people of African ancestry if a better estimate of trunk length is used in place of standing height. The ratio of arm span to standing height is about 6% to 7% higher in people of African compared to European ancestry [24]. It may be possible that using a variable such as (height squared)/(arm span) could provide prediction equations that are independent of European ancestry, African ancestry or mixed ancestry.

Is there a difference between distinguishing groups by geographic ancestry and distinguishing groups by what is commonly, but inappropriately, termed "race"? Changing the terminology does not change the groups defined by the words. Geographic ancestry posits that differences between groups result from geographical influences over tens of thousands of years [22, 23]. While geographic ancestry provides more accurate predictions of lung volume, it does not make any such distinction less susceptible to racial prejudice and systemic racism in healthcare. There is a need to predict spirometric measures without requiring individuals to either self-identify their ancestry or to be classified into particular ethnic or geographic ancestral categories. DNA analysis can estimate the contribution of ancestry in an individual to help improve their lung volume prediction [21, 25], which may be especially helpful with migration leading to mixed ancestry. However, there are logistical and ethical concerns regarding the acquisition, storage and broad use of DNA information.

New indices of body size that can be easily and reliably measured and correlate strongly with lung volume irrespective of an individual's ancestry are needed to replace height alone in order to develop globally applicable, high precision predicted lung volumes. This will require considerable time and funding. Until then, using ancestry-specific lung volume prediction equations, such as offered by GLI [8], generally provides the most accurate prediction of lung volumes. Continued vigilance remains essential so that identification of a person's ancestry does not incur subsequent prejudice, discrimination or injustice.

Conflict of interest: B.L. Graham reports personal fees for lectures from MGC Diagnostics Corporation and Vyaire Medical, personal fees for lectures and education course development from the Lung Association of Saskatchewan, personal fees for consultancy from Chiesi Farmaceutici S.p.A., and a patent use agreement from Hans Rudolph Inc, outside the submitted work; and has a patent calibration syringe device pending. M.R. Miller and B.R. Thompson have nothing to disclose.

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