# Choosing the Better $GLI_{2012}$ Equation in South African Population Groups

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**Author contributions**

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To the editor:

Spirometry is an effective and widely available technique to measure lung function. Correct interpretation of spirometry is imperative when utilized to diagnose and manage lung pathology. The Global Lung Initiative 2012 ($GLI_{2012}$) provide robust and representative reference equations for lung function in four ethnic groups; however, the $GLI_{2012}$ are limited in data from African populations and 'Black' equations in $GLI_{2012}$ were solely derived using data from African-Americans. For populations lacking reference range equations and for individuals of mixed ethnic origin, the $GLI_{2012}$ taskforce provided a composite 'Other' equation.(1)

The Pan African Thoracic Society is reluctant to endorse the use of the $GLI_{2012}$ 'Other' or 'Black' equations in Africa without evidence of their applicability in African populations.(2) In this study we aimed to collect spirometry data in healthy South Africans to determine if the 'Black' or 'Other' $GLI_{2012}$ reference equations were a good fit, or whether new reference equations are required. We hypothesized that the $GLI_{2012}$ 'Black' reference equations will not fit black South African adults and children. Some of the results of this study have been previously reported in the form abstracts(3–5).

In this cross-sectional population-based study healthy children and adults between the age of 5 and 95 years were recruited from two provinces in South Africa: KwaZulu-Natal and the Western Cape. South Africa has a population of over 57 million people who belong to four major ethnic groups: Black-African (80.9%), Mixed-Ethnicity (8.8%), Caucasian (7.8%) and Indian/Asian (2.5%).(6) In line with $GLI_{2012}$ recommendations, we recruited a representative sample of at least 300 participants for each ethnic population.(7) Participants were recruited between 01 August 2017 and 31 July 2018.

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Anthropometric measurements were obtained and spirometry was performed as per international recommendations. Spirometry data were converted to *z*-scores using the $GLI_{2012}$ Desktop Software for Large Datasets (version 1.3.4 Build 3, 7 April 2013) and summarised by ethnic group. A good fit was determined if the average z-score was not statistically or physiologically different from an average z-score of zero (standard deviation of 1). A difference of more than 0.5 z-scores from zero was considered to be clinically significant as it represents a difference greater than sampling variability.(7)

A total of 4223 participants were recruited; of these 546 (13%) were excluded. Exclusions included those who were acutely unwell or had a previous diagnosis of respiratory, cardiac or neuromuscular disease. Past and current smokers were also excluded as per GLI methodology and the American Thoracic Society (ATS) recommendations.(8) Tests with missing data, failing quality control, or with z-scores greater than +/-5 were excluded. Demographic characteristics of the final cohort (3676 participants) are included in Table 1. Observed z-scores from Black-African participants (n=2116) showed that the $GLI_{2012}$ 'Other' had the best fit for this group [Figure 1; mean z-score ± standard deviation (SD) of 0.13 ± 1.28 for $FEV_1$, 0.13 ± 1.32 for FVC and -0.01 ± 0.87 for $FEV_1$/FVC].

The 'Other' equations were also the best fit for the Mixed-Ethnicity group (n=693) [Figure 1; mean z-scores 0.22 ± 1.44 ($FEV_1$), 0.24 ± 1.56 (FVC) and -0.02 ± 0.85 ($FEV_1$/FVC)]. The 'Northeast-Asian' equations had a similar average z-score but had much wider variability. The Caucasian participants (n=343) demonstrated a good fit with the $GLI_{2012}$ 'Caucasian' equation [Figure 1; mean z-score 0.21 ± 1.22 ($FEV_1$), 0.19 ± 1.24 (FVC) and 0.02 ± 0.91 ($FEV_1$/FVC)]. Participants of Asian ancestry (n=524) demonstrated a good fit to the 'Southeast-Asian' and 'Black' equation. [Figure 1; Southeast-Asian mean z-scores -0.18±

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1.03 ($FEV_1$), -0.13 ± 1.09 (FVC) and -0.1± 0.93 ($FEV_1$/FVC) and Black equation mean z-scores 0.15 ± 1.03 ($FEV_1$), 0.04 ±1.07 (FVC) and 0.23 ±0.87 ($FEV_1$/FVC)]. Across all ethnic groups, the $FEV_1$/FVC ratio z-scores were close to zero (Figure 1).

In this large, representative sample of the South African population, we found that the $GLI_{2012}$ 'Caucasian' fit the Caucasian population well. For the Indian population, both Black and the Southeast-Asian equations demonstrated a good fit. As the South East Asian data reflects the ethnic background of the Indian population best, we determined that South East Asian showed the best fit, but that a larger dataset would be useful to confirm this. The $GLI_{2012}$ 'Other' equations fit the Black-African and Mixed-Ethnicity populations well. In South Africa, the black population largely represents a mixture of Bantu and Khoi-San ancestry. As these genetic groups predominate in wider Southern Africa, it may be appropriate to extrapolate our conclusions to the Southern African region.

However, previous studies investigating the use of $GLI_{2012}$ equations in Africa are relatively scarce and have provided conflicting results from cohorts in different regions of Africa. (9–12). We previously found that there is wide regional variability in lung function in Africa, and that no single $GLI_{2012}$ equation can be used for the African continent.(13)

Ethnicity may be an important determinant of optimal lung function; it can also be confounded by different environmental and socioeconomic exposures that affect lung development and health. We note that in our study population, the majority lived in brick housing and had access to electricity which may not be representative of other parts of Southern Africa. Some caution may therefore need to be applied in extrapolating our study results to the populations of different envirnonmental and socioeconomic backgrounds. Further studies across Africa would help to determine best practices for each region/population.

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The GLI2012 'Black' equation was derived entirely from African-American subjects from the United States' datasets and it may be that this population is genetically closer to those in Central and West Africa. It is likely that individuals living in the United States experience a different nutritional and socio-economic environment to those living in South Africa, and this may lead to further disparity in their lung function. We recommend that GLI should re-label the $GLI_{2012}$ 'Black' equations to reflect the population from which the data was derived (i.e. African-American).

Despite including a wide range of participants (5 to 95 years), our study was limited by few participants over the age of 50 years. As the health outcomes in South Africa continue to improve, further data in older individuals will be necessary to confirm validity. Further, smoking habits were self-reported and we did not screen for human immunodeficiency virus infection. The strengths of this study are the large sample size, standardized equipment and measurement protocols and data quality control.

Conclusion: The findings of this study will help to inform clinical practice in South Africa.

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Figure 1. Distribution of z-scores of $FEV_1$, FVC and $FEV_1$/FVC for Black African, Caucasian, Indian and Mixed Ethnicity individuals using the $GLI_{2012}$ reference equations. The equations that resulted in the closest fit to a mean z-score of zero, and a standard deviation of one were selected as best fit.

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Table 1. Characteristics of the study population (KwaZulu-Natal and Western Cape province, South Africa). Children and young adults (<25 years) constituted 55% of the population.

| | Black African (n=2116) | Caucasian (n=343) | Mixed Ethnicity (n=693) | Indian (n=524) | Total (n=3676) |
|---|---|---|---|---|---|
| Sex - Female | 1200 (56.6%) | 153 (44.6%) | 404 (58.3%) | 326 (62.2%) | 2083 (56.7%) |
| Age | | | | | |
| < 25 years | 1128 (53.3%) | 212 (61.8%) | 440 (63.5%) | 243 (46.4%) | 2023 (55.0%) |
| >25 years | 988 (46.7%) | 131 (38.2%) | 253 (36.5%) | 281 (53.6%) | 1653 (45.0%) |
| Weight for age Z-score | 0.04 (±0.41) | 0.10 (±0.66) | 0.09 (±0.47) | 0.12 (±0.56) | 0.07 (±0.48) |
| Height for age Z-score | -0.27 (±0.84) | 0.08 (±0.87) | -0.40 (±1.12) | -0.25 (±0.95) | -0.26 (±0.92) |
| BMI for age Z-score | 0.99 (±1.28) | 0.71 (±1.15) | 0.90 (±1.034) | 1.01 (±1.28) | 0.95 (±1.29) |
| Cormic index | 0.51 (±0.03) | 0.52 (±0.04) | 0.50 (±0.03) | 0.52 (±0.03) | 0.51 (±0.03) |
| Stunting* | 110 (5.2%) | 5 (1.5%) | 64 (9.2%) | 37 (7.1%) | 216 (5.9%) |
| Province | | | | | |
| KwaZulu-Natal | 1260 (59.6%) | 236 (68.8%) | 306 (44.2%) | 517 (98.7%) | 2319 (63.1%) |
| Western Cape | 856 (40.4%) | 107 (31.2%) | 387 (55.8%) | 7 (1.3%) | 1357 (36.9%) |
| Living region | | | | | |
| Rural | 1020 (48.2%) | 11 (3.2%) | 192 (27.7%) | 0 (0.0%) | 1223 (33.3%) |
| Urban | 1096 (51.8%) | 332 (96.8%) | 501 (72.3%) | 524 (100.0%) | 2453 (66.7%) |
| Housing Type† | | | | | |
| Temporary | 136 (6.4%) | 1 (0.3%) | 10 (1.5%) | 1 (0.2%) | 148 (4.0%) |
| Wooden | 17 (0.8%) | 0 (0.0%) | 16 (2.3%) | 5 (1.0%) | 38 (1.0%) |
| Brick | 1891 (89.5%) | 338 (98.5%) | 658 (95.1%) | 510 (97.8%) | 3397 (92.6%) |
| Other | 68 (3.2%) | 4 (1.2%) | 8 (1.2%) | 5 (1.0%) | 85 (2.3%) |
| Household size† | | | | | |
| 1 - 3 people | 248 (11.8%) | 94 (27.4%) | 102 (14.7%) | 90 (17.2%) | 534 (14.6%) |
| 4 - 5 people | 881 (42.0%) | 210 (61.2%) | 368 (53.1%) | 284 (54.3%) | 1743 (47.6%) |
| 6 or more people | 970 (46.2%) | 39 (11.4%) | 223 (32.2%) | 149 (28.5%) | 1381 (37.8%) |
| Access to electricity | 2058 (97.4%) | 341 (99.4%) | 687 (99.1%) | 520 (99.6%) | 3606 (98.2%) |
| Heating/lighting fuel | | | | | |
| Wood | 139 (6.6%) | 1 (0.3%) | 4 (0.6%) | 1 (0.2%) | 145 (4.0%) |
| Paraffin | 11 (0.5) | 0 (0.0%) | 2 (0.3%) | 0 (0.0%) | 13 (0.4%) |
| Gas | 75 (3.6%) | 37 (10.8%) | 16 (2.3%) | 14 (2.7%) | 142 (3.9%) |
| Electricity | 1967 (93.1%) | 325 (94.8%) | 680 (98.1%) | 514 (98.1%) | 3486 (94.9%) |
| Cooking Fuel | | | | | |
| Electricity | 1988 (94.0%) | 319 (93.0%) | 682 (98.4%) | 516 (98.5%) | 3505 (95.3%) |
| Coal | 6 (0.3%) | 2 (0.6%) | 1 (0.1%) | 0 (0.0%) | 9 (0.3%) |
| Wood | 169 (8.0%) | 1 (0.3%) | 0 (0.0%) | 0 (0.0%) | 170 (4.6%) |
| Paraffin/gas | 26 (1.2%) | 30 (8.8%) | 7 (1.0%) | 12 (2.3%) | 75 (2.1%) |

*Stunting defined as Height-for-age Z-score <-2, †Missing data
Mean (±standard deviation) reported for continuous variables.

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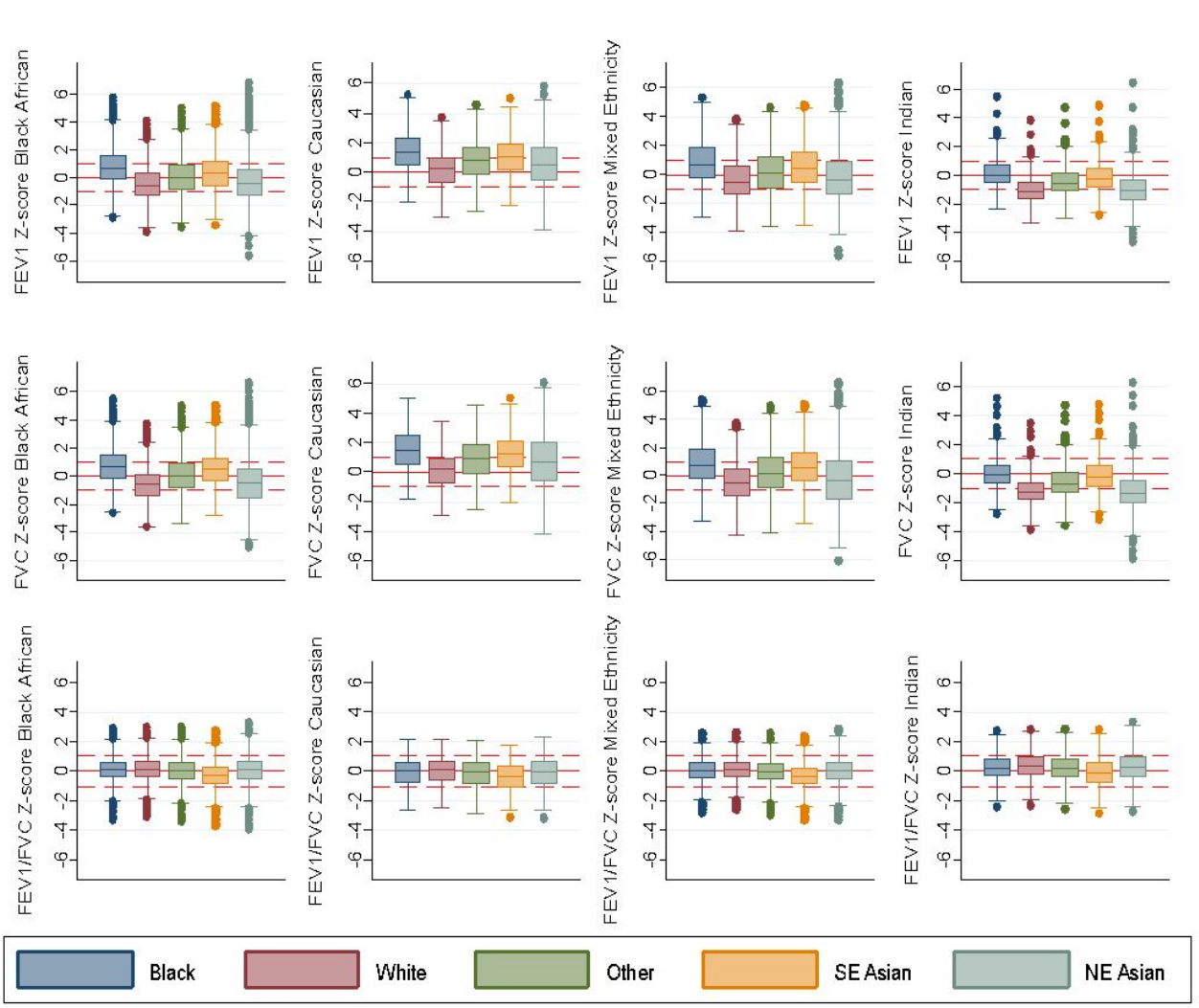


Figure 1. Distribution of z-scores of $FEV_1$, FVC and $FEV_1$/FVC for Black African, Caucasian, Mixed Ethnicity and Indian individuals using the $GLI_{2012}$ reference equations ('Black', 'White', 'Other', 'SE Asian' and 'NE Asian'). The equations that resulted in the closest fit to a mean z-score of zero, and a standard deviation of one were selected as best fit.

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