An evaluation of spirometric reference equations for detecting obstructive airway disease in South African children: A cohort study

T L Mkhize,[1] MB ChB; **L B Zurba,**[2] Dipl Nurs, PGDip Bus Leadership;
R Masekela,[1,3] MB BCh, MMed (Paed), Dip Allerg (SA), Cert Pulmonol (SA) Paed, PhD

[1] *Department of Paediatrics and Child Health, College of Health Sciences, School of Clinical Medicine, University of KwaZulu-Natal, Durban, South Africa*
[2] *Education for Health Africa, Durban, South Africa*
[3] *Africa Health Research Institute, Durban, South Africa*

Corresponding author: *R Masekela (masekelar@ukzn.ac.za)*

Background. Accurate diagnosis of obstructive lung disease in paediatric populations depends on the use of spirometry reference equations that reflect the regional and ethnic diversity of the population studied.
Objectives. To evaluate the diagnostic variability between the Global Lung Initiative 2012 (GLI_{2012}) and Polgar reference equations in a multi-ethnic cohort of South African (SA) children.
Methods. This retrospective cohort study analysed spirometry data from 171 children, aged 6 - 18 years, attending a paediatric pulmonology clinic in Durban, SA, from January 2012 to December 2021. Key spirometry parameters (forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC) and FEV_1/FVC ratio) were calculated using both the GLI_{2012} and Polgar reference equations. Diagnostic outcomes across ethnic groups were compared to assess the variability and potential diagnostic implications of each reference standard.
Results. Comparison of spirometry outcomes using the GLI_{2012} and Polgar reference equations revealed diagnostic variability across ethnic groups. GLI_{2012} identified a higher rate of obstructive lung disease, with abnormality rates of 24.6% among white children, 0.6% among black African children and 2.3% among Asian children, compared with Polgar, which reported rates of 23.9%, 0% and 1.6%, respectively. There was a statistically significant difference in FEV_1/FVC ratios before and after administration of a bronchodilator between the two reference equations (mean (standard deviation) pre-bronchodilator FEV_1/FVC ratio 0.86 (0.06) for both equations; post-bronchodilator ratio 0.88 (0.09) for GLI_{2012} and 0.85 (0.09) for Polgar (p=0.023)). There was no statistically significant difference in the proportion of children diagnosed with obstructive lung disease by age or ethnicity when comparing GLI_{2012} with Polgar.
Conclusion. This study underscores the diagnostic variability that arises from using global spirometry reference equations in a multi-ethnic paediatric population, particularly in SA. Future studies should include a more diverse ethnic representation to enhance data relevance.

Keywords. Spirometry, paediatric, obstructive airway disease, lung function, reference equations, ethnicity.

Afr J Thoracic Crit Care Med 2025;31(4):e3189. https://doi.org/10.7196/AJTCCM.2025.v31i4.3189

Study synopsis
What the study adds. This study reveals significant variability in rates of paediatric obstructive lung disease across ethnic groups in South Africa, emphasising discrepancies between the Global Lung Initiative 2012 and Polgar reference equations. It underscores the limitations of non-region-specific lung function standards, which may result in misclassification and inconsistent diagnoses in diverse populations.
Implications of the findings. Developing African-specific reference standards is crucial for accurate diagnosis and effective clinical interventions. Future longitudinal studies should track lung function growth across ethnic and socioeconomic groups, offering deeper insights and enhancing diagnostic precision. Expanding research to include more diverse ethnic representation will strengthen the applicability of findings and support equitable healthcare for paediatric respiratory conditions across the continent.

Spirometry plays a crucial role in diagnosing, managing and monitoring respiratory diseases in paediatric populations. It serves as a non-invasive, objective tool for assessing lung function, particularly in conditions such as asthma, chronic obstructive pulmonary disease and other obstructive airway diseases.[1] Accurate spirometry interpretation depends on reference equations that account for age, sex, height and ethnicity of the individual being tested.[2] Inaccurate reference standards can lead to misdiagnoses, resulting in inappropriate treatment strategies that may worsen patient outcomes.[3]

The Global Lung Initiative 2012 (GLI_{2012}) spirometry reference equations are widely used internationally and were developed using a large multi-ethnic dataset that included data from >74 000 healthy individuals from various regions of the world.[2] However, the applicability of these equations to African populations has been questioned owing to the under-representation of African data in the GLI dataset. Specifically, only 4.8% of the GLI_{2012} dataset is derived from African populations, predominantly from the North African region, which may not accurately represent the lung function of individuals in sub-Saharan Africa.[4]

Research indicates that lung function varies significantly across different ethnic groups owing to genetic, environmental and socioeconomic determinants.[5] For example, studies have shown that black African children generally have lower lung volumes compared with their white counterparts when using the same spirometry reference standards.[6] This discrepancy is likely to be particularly pronounced in children from sub-Saharan Africa, where environmental factors such as indoor air pollution, malnutrition and recurrent respiratory infections are prevalent.[7]

The reliance on non-African reference equations in African settings has been a subject of ongoing debate. Studies suggest that using non-African reference standards may lead to both overdiagnosis and underdiagnosis of obstructive lung disease in African populations.[8] For instance, a study conducted in Nigeria using the GLI_{2012} reference equation found that a significant proportion of children were misclassified as having abnormal lung function, which could lead to unnecessary treatment or the overlooking of serious conditions.[9]

In South Africa (SA), where the burden of both infectious and non-infectious respiratory diseases is particularly high, the country's diverse population, which includes a mixture of ethnic groups such as black African, white, Indian and mixed-ethnicity individuals, further complicates the application of universal reference equations.[10] A study including people 3 - 95 years of age in SA found that local black African children had a better fit to GLI_{2012}-Other when using the GLI_{2012} reference equation.[11] However, this study was limited in the proportion of individuals of European descent.

In 2022, the GLI made new recommendations for the use of a race-neutral equation, GLI_{2022}, which could be universally used in all populations.[12] Since this recommendation, many studies have assessed, largely in adult populations, the population-level differences in the interpretation of lung function.[13,14] Using a multi-ethnic approach may have both positive and negative consequences for individual patients, including eligibility for jobs, benefits, medications and life-saving procedures. For black African individuals, the proportion who would be classified as having abnormal lung function would increase on average by 0.6 *z*-scores and ~8% if using percentage predicted values.[2]

Given the critical role of spirometry in managing paediatric respiratory diseases, there is an urgent need for research that evaluates the applicability of existing reference equations in African populations and explores the development of new, regionally appropriate standards. The present study aimed to address this gap by comparing the diagnostic outcomes of obstructive lung disease in SA children using two different spirometry reference equations. Additionally, we assessed whether ethnicity influences the proportion of children diagnosed with obstructive lung disease.

Methods

Study design

This was a retrospective descriptive cohort analytical study.

Study population

The study population consisted of children aged 6 - 18 years who underwent spirometry testing at a private pulmonology clinic in Durban, KwaZulu-Natal Province, SA, over a 9-year period from 1 January 2012 to 31 December 2021. This clinic serves a diverse population, including children of various ethnic backgrounds, namely black African, white, Indian and mixed ethnicity.

Children were included if they had complete, reliable and reproducible spirometry tests. Children with incomplete spirometry records or those unable to perform at least three acceptable and two reproducible manoeuvres (per American Thoracic Society and European Respiratory Society guidelines) were excluded.[13]

Spirometry data collection and reference equations

Spirometry data were collected using the KoKo SX 1000 spirometer (Ferraris, USA). Daily calibration was performed according to the manufacturer's instructions, and all tests were performed by an experienced respiratory nurse trained in paediatric spirometry. The parameters recorded were forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC) and the FEV_1/FVC ratio.

Reference equations used in the analysis

The spirometry parameters were analysed using two reference equations, GLI_{2012} and Polgar, each derived from distinct demographic datasets. We analysed the data using two reference equations only because of the study population we recruited. The GLI_{2012} reference equation was derived from a pool of >74 000 individuals aged 3 - 95 years across multiple ethnicities globally.[8] The proportion of children aged <18 years in this dataset was ~24%. Only 1.7% of the dataset comprised individuals identified as African or African American, highlighting the under-representation of these groups.[2] The Polgar reference equation was derived from 400 European and North American children aged 6 - 18 years, with no Africans included in the dataset.[15] This reference equation is used in some pulmonary function laboratories in SA that have paediatric patients. For the interpretation of the GLI_{2012} reference equation, GLI-White was used for the white children, GLI-Black for black African children, and GLI-SE Asian for Asian children.

Data and statistical analysis

All spirometry data was collected using the KoKo spirometry software. Patient identifiers were removed from the dataset prior to analysis to maintain anonymity.

The primary analysis involved comparing the proportion of children diagnosed with obstructive lung disease across the two reference equations. Obstructive lung disease was defined as an FEV_1/FVC ratio <70% and an FEV_1 <80% of the predicted value.[2,16]

Statistical tests included paired *t*-tests that compared the means of spirometry parameters between different reference equations in the same individuals. Analysis of variance was used to assess differences in diagnostic outcomes across the two reference equations, while χ^2 tests determined the associations between ethnicity and the proportion of children diagnosed with obstructive lung disease.

Ethical approval for the study was obtained from the KwaZulu-Natal Department of Health (17 May 2022, ref. no. NHRD Ref KZ_202205_003) and the University of KwaZulu-Natal Biomedical Research Ethics Committee (ref. no. BREC/00003899/2022).

Results

Population demographics and baseline characteristics

A total of 171 children aged 6 - 18 years were studied, with a mean (standard deviation (SD)) age of 11.7 (3.3) years. Of the children, 106 (61.9%) were male, and 65 (38.1%) were female (Table 1). The cohort was predominantly white (*n*=139; 81.3%), with smaller proportions of black African (*n*=10; 5.8%) and Asian (*n*=22; 12.9%) children. Mean weight and height were 39.0 (15.7) kg (range 16.1 - 95.6 kg) and 143.0 (17.9) cm (range 110.0 - 189.0 cm), respectively. There were statistically significant differences between the sexes for weight (*p*=0.014) and height (*p*=0.046).

Proportion of children diagnosed with obstruction across reference equations

When analysing the proportion of children diagnosed with obstructive lung disease, comparisons between the GLI_{2012} and Polgar reference equations showed minor differences. Using the GLI_{2012} reference equation, the mean (SD) pre-bronchodilator FEV_1 was 2.36 (0.78) L, while the Polgar reference equation yielded a slightly lower mean of 2.32 (0.77) (*p*=0.032) (Fig. 1). Post-bronchodilator FEV_1 values were comparable between the GLI_{2012} and Polgar reference equations, with a mean of 2.33 (0.80) L for both, and the difference was not statistically significant (*p*=0.075). The mean pre-bronchodilator FEV_1/FVC ratio was 0.86 (0.06) for both GLI_{2012} and Polgar, while post-bronchodilator FEV_1/FVC ratios again indicated a slight increase for GLI_{2012}, with a mean of 0.88 (0.09) compared with 0.85 (0.09) for Polgar (*p*=0.023). Post-bronchodilator FVC values were identical across the GLI_{2012} and Polgar reference equations, with a mean of 2.66 (0.99) L.

Ethnic group differences in diagnosed obstructive lung disease

Abnormal spirometry patterns as determined by GLI_{2012} and Polgar varied across ethnic groups. According to the GLI_{2012} reference equation, 24.6% of white children (*n*=42) had obstructive lung disease (95% confidence interval (CI) 18.0 - 31.2), with early obstructive impairment in 20 children (11.7%) (95% CI 7.0 - 16.4) (Fig. 2). Among Black children, only 1 case of obstructive disease was identified (0.6%; 95% CI 0.0 - 1.8), with early obstructive impairment in 3 children (1.8%; 95% CI 0.0 - 3.8). Among Asian children, obstructive disease was present in 4 (2.3%; 95% CI 0.0 - 4.5), with early obstructive impairment in another 4 (2.3%; 95% CI 0.0 - 4.5). Using the Polgar reference equation, reported rates of obstructive disease were 23.9%, 0% and 1.6%, respectively.

Effect of reference equation on ethnic variability in diagnosed abnormalities

When examining the influence of reference equations on the proportion of spirometry abnormalities by ethnicity, no statistically significant difference was found between diagnoses made using the GLI_{2012} v. Polgar equations (6.4% difference; 95% CI –13.3 - 25.5; *p*=0.5371) (Fig. 3). White children had consistently higher rates of diagnosed abnormalities than the other two groups irrespective of the reference equation used, which may suggest that both reference equations similarly affect diagnostic outcomes across different ethnic groups. However, the interpretation of these figures is limited by the smaller numbers of children in the black African and Asian groups.

Differences in outcomes by age group

Further analysis examined diagnostic outcomes by age group to assess whether age influenced the diagnosis of obstructive disease when applying different reference equations. Children were grouped into age categories 6 - 10 years, 11 - 14 years and 15 - 18 years and analysed for differences in the proportions of diagnosed abnormalities. The GLI_{2012} equation indicated a slightly higher prevalence of obstruction in the younger age groups (6 - 10 years 30.1%, 11 - 14 years 27.4%, and 15 - 18 years 24.5%), while the Polgar equation showed relatively consistent but slightly lower proportions across the age groups (6 - 10 years 22.3%, 11 - 14 years 21.8%, and 15 - 18 years 19.6%) (Fig. 4), although no statistically significant differences were noted between age groups (*p*=0.441).

Table 1. Baseline characteristics of the study population by ethnic group (*N*=171)

Characteristic	White, *n* (%)*	Black, *n* (%)*	Asian, *n* (%)*	Overall, *n* (%)*
Sample size	139 (81.3)	10 (5.8)	22 (12.9)	171 (100)
Age (years), mean (SD)	11.7 (3.3)	11.2 (3.1)	11.5 (3.5)	11.7 (3.28)
Male	84 (79.2)	6 (5.7)	16 (15.1)	106 (61.9)
Female	55 (84.6)	4 (6.2)	6 (9.2)	65 (38.1)
Weight (kg), mean (SD)	39.0 (15.7)	35.2 (14.8)	37.1 (15.0)	39.0 (15.7)
Height (cm), mean (SD)	143 (17.9)	140 (16.5)	141 (17.3)	143 (17.9)
Spirometry findings†				
Normal	74 (43.3)	6 (3.5)	13 (7.6)	93 (54.4)
Obstructive disease	42 (24.6)	1 (0.6)	4 (2.3)	47 (27.5)
Early obstructive impairment	20 (11.7)	3 (1.8)	4 (2.3)	27 (15.8)
Mild restrictive ventilatory defect	1 (0.6)	0	1 (0.6)	2 (1.2)
Moderate restrictive ventilatory defect	2 (1.2)	0	0	2 (1.2)

SD = standard deviation.
*Except where otherwise indicated.
†Interpretation based on GLI_{2012} reference equation.

Discussion

In the present study, we found that when comparing the commonly used GLI_{2012} and Polgar reference equations the proportion of children diagnosed with obstructive airway disease was higher using GLI_{2012} v. Polgar, especially in white children, and the GLI_{2012} equation may potentially overestimate airway obstruction in our cohort of SA children, most of whom were white. While GLI_{2012} may potentially overestimate abnormalities, Polgar may underestimate them. The implications of such misclassification are significant: a higher abnormality rate identified by GLI_{2012} could lead to unnecessary treatment, while Polgar's conservative outcomes might delay necessary interventions. This pattern is similar to findings of Ndukwu *et al.*[8] in West Africa, who found differences in diagnostic findings depending on reference equations used to classify disease.

Unsurprisingly, we also found that in black African children there were higher rates of abnormalities using GLI_{2012} corrected for ethnicity (GLI-Black) compared with Polgar. As the Polgar reference equation is from an exclusively white cohort of children, previous studies have found differences in lung function when comparing black African with white cohorts. In contrast to previous studies, white children in the present study exhibited the highest rates of obstructive disease, but the present study is limited by a greater representation from the white population. It is interesting to note that these differences still exist when comparing the present study with the previous study in SA, where healthy children were mostly recruited from government schools, which mainly serve a lower socioeconomic group.[11]

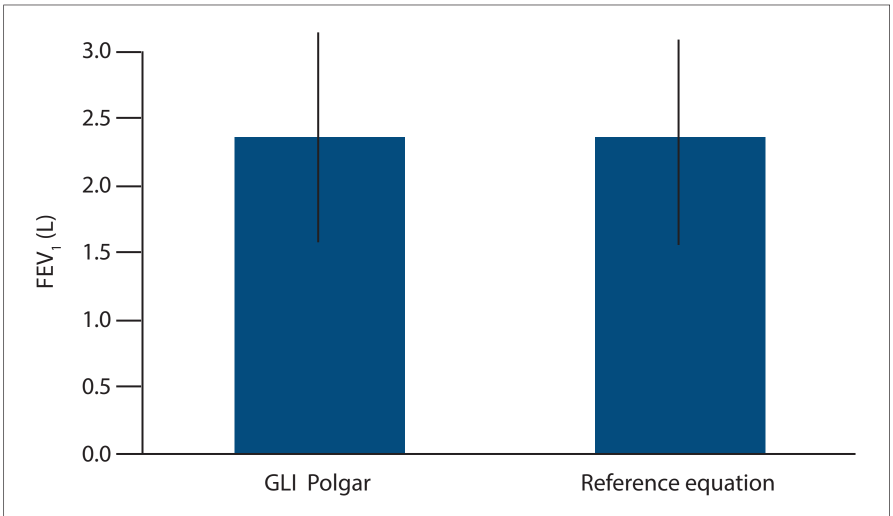

Fig. 1. Comparison of mean pre-bronchodilator FEV_1 for all children comparing the GLI_{2012} v. Polgar reference equations. (FEV_1 = forced expiratory volume in 1 second; GLI = Global Lung Initiative.)

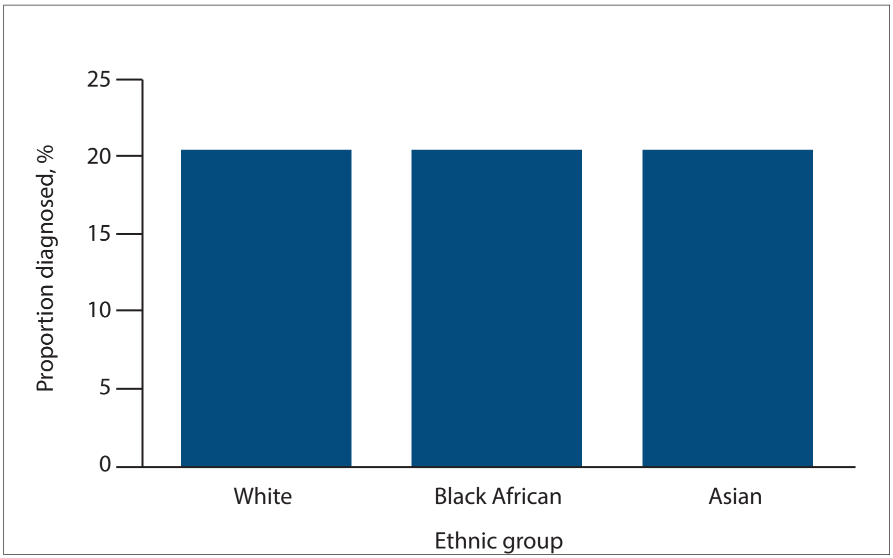

Fig. 2. Proportion of children diagnosed with any obstructive abnormality by ethnic group using the GLI_{2012} reference equation. (GLI = Global Lung Initiative.)

When comparing the proportion of children diagnosed with obstructive lung disease by ethnic group, we found no statistically significant differences in the proportion diagnosed using GLI_{2012} v. Polgar. The findings may be more representative for white children, owing to their larger sample size in this study. Overall, the aim of assessing whether ethnicity has any impact in the diagnosis of obstructive lung disease was not met because of the uneven distribution of ethnic groups. Of interest, we found differences in the proportion of children diagnosed with obstructive lung disease when comparing the two reference equations by age, although this did not reach significance and showed numerical differences only. It has been well described that lung function increases in the first few years of life through adolescence and plateaus in early adulthood.[16] A larger study is needed to assess whether age significantly influences interpretation.

These diagnostic discrepancies highlight the need for local validation to reduce misdiagnosis and improve clinical decision-making. By adopting standardised regional equations, healthcare providers in SA could achieve more accurate diagnostic outcomes, which would ultimately benefit paediatric patients and optimise resource allocation. With the recent recommendation of the GLI_{2022}, it would be of interest to assess whether this reference equation would yield different results in SA population.

Study strengths and limitations

The strengths of the current study are that we used lung function tests from a previously understudied cohort of children in SA, who had good-quality lung function tests performed by a single experienced lung function operator. This is the first study in SA to compare the GLI_{2012} with the Polgar reference equation, and as such adds to the body of work on this. Our study has several limitations, however. Owing to its retrospective nature, we do not have any clinical data on the participants. The

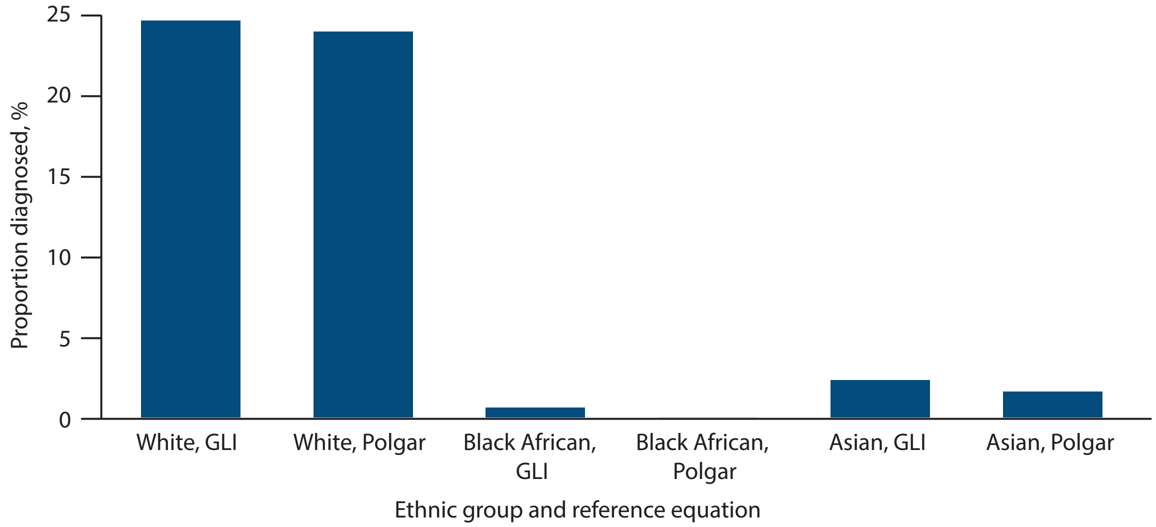

Fig. 3. Comparison of the proportion of children diagnosed with obstructive lung disease by ethnic group using the GLI_{2012} v. Polgar reference equations. (GLI = Global Lung Initiative.)

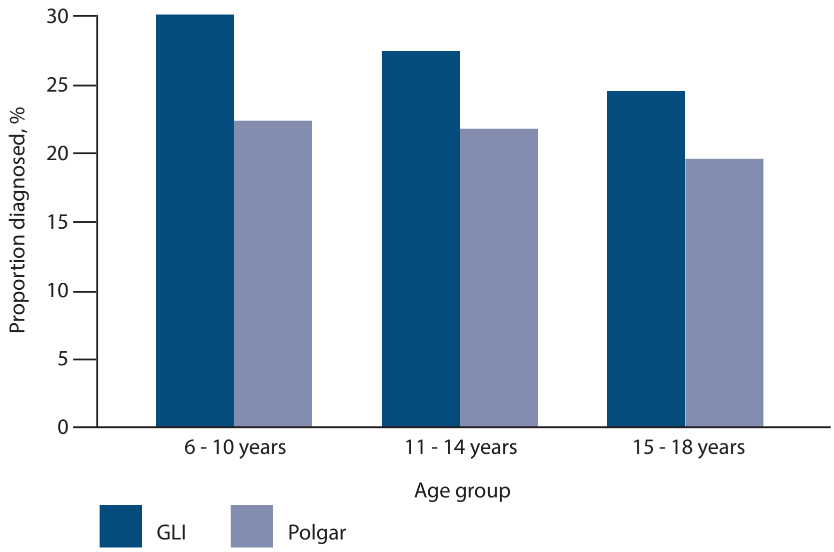

Fig. 4. Comparison of the proportion of children diagnosed with obstructive lung disease by age using the GLI_{2012} v. Polgar reference equations. (GLI = Global Lung Initiative.)

cohort was from a single clinical centre, which may limit generalisability to a broader SA population. The ethnic distribution of the sample was predominantly white, with smaller black African and Asian representation. Furthermore, while the Polgar and GLI_{2012} equations were rigorously compared, additional reference equations may yield differing diagnostic outcomes. One of these is the National Health and Nutrition Examination Survey (NHANES) reference equation, which has a reasonable proportion of children of African American origin, which may more closely reflect reference equations of black South African children. We also could not obtain any data regarding socioeconomic status, previous medical history, previous exposures including indoor and outdoor pollution, or other risk factors that are important for lung function interpretation.[14,17]

Future longitudinal studies to track lung function growth across ethnic and socioeconomic groups could provide further insight, ultimately enhancing diagnostic accuracy for paediatric respiratory conditions across the continent.

Conclusion

The present study highlights substantial variability in diagnosing paediatric obstructive lung disease across ethnic groups in SA, particularly when comparing the GLI_{2012} and Polgar reference equations. These findings highlight the limitations of applying non-region-specific standards, which may cause inconsistencies and misclassification in diagnosing lung disease in diverse populations. Addressing this gap by developing African-specific reference standards is imperative to provide accurate diagnoses and tailor effective clinical interventions.

While the findings offer useful insights, it is important to note that the sample was largely dominated by one ethnic group. This imbalance limits the applicability of the results to the wider African demographic. Future research should aim for a more diverse ethnic representation in African populations to improve the robustness and applicability of findings.

Data availability. The datasets generated and analysed during the present study are available from the corresponding author (RM) on reasonable request.

Declaration. The research for this study was done in partial fulfilment of the requirements for TLM's MMed degree at the University of KwaZulu Natal. RM is a member of the editorial board

Acknowledgements. None.

Author contributions. TLM was responsible for the study design, data collection, analysis, and drafting of the manuscript. RM was responsible for the overall supervision of the study and assisted with the study concept, study design, data interpretation, and drafting and editing of the manuscript. LBZ assisted with the data collection and drafting and editing of the manuscript.

Funding. None.

Conflicts of interest. None.

1. Pellegrino GM, Gobbi A, Fantini M, Pellegrino R, Papa GFS. Lung function assessment in pediatric asthma: Selecting the optimal tests for clinical and research applications. Children (Basel) 2025;12(8):1073. https://doi.org/10.3390/children12081073
2. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: The Global Lung Function 2012 equations. Eur Respir J 2012;40(6):1324-1343. https://doi.org/10.1183/09031936.00080312
3. Pellegrino R, Viegi G, Brusasco V, et al. Interpretative strategies for lung function tests. Eur Respir J 2005;26(5):948-968. https://doi.org/10.1183/09031936.05.00035205
4. Arigliani M, Canciani MC, Mottini G, et al. Evaluation of the Global Lung Initiative 2012 reference values for spirometry in African children. Am J Respir Crit Care Med 2017;195(2):229-236. https://doi.org/10.1164/rccm.201604-0693OC
5. Hall GL, Thompson BR, Stanojevic S, et al. The Global Lung Initiative 2012 reference values reflect contemporary Australasian spirometry. Respirology 2012;17(7):1150-1151. https://doi.org/10.1111/j.1440-1843.2012.02232.x
6. Kirkby J, Welsh L, Lum S, et al. The EPICure study: Comparison of pediatric spirometry in community and laboratory settings. Pediatr Pulmonol 2008;43(12):1233-1241. https://doi.org/10.1002/ppul.20950
7. Masekela R, Hall GL, Stanojevic S, et al. An urgent need for African spirometry reference equations: The Paediatric and Adult African Spirometry study. Int J Tuberc Lung Dis 2019;23(8):952-958. https://doi.org/10.5588/ijtld.18.0442
8. Ndukwu CI, Ozoh OB, Ale BM, Ayuk AC, Elo-Ilo JC, Awokola BI. Spirometry abnormalities and its associated factors among primary school children in a Nigerian city. Clin Med Insights Pediatr 2021;15:11795565211001897. https://doi.org/10.1177/11795565211001897
9. Obaseki DO, Erhabor GE, Gnatiuc L, Adewole OO, Buist SA, Burney PG. Chronic airflow obstruction in a black African population: Results of BOLD study, Ile-Ife, Nigeria. COPD 2016;13(1):42-49. https://doi.org/10.3109/15412555.2015.1041102
10. Ben Saad H, El Attar MN, Hadj Mabrouk K, et al. The recent multi-ethnic global lung initiative 2012 (GLI_{2012}) reference values don't reflect contemporary adult's North African spirometry. Respir Med 2013;107(12):2000-2008. https://doi.org/10.1016/j.rmed.2013.10.015
11. Smith SJ, Gray DM, MacGinty RP, et al. Choosing the better Global Lung Initiative 2012 equation in South African population groups. Am J Respir Crit Care Med 2020;202(12):1724-1727. https://doi.org/10.1164/rccm.202005-2085LE
12. Bowerman C, Bhakta NR, Brazzale D, et al. A race-neutral approach to the interpretation of lung function measurements. Am J Respir Crit Care Med 2023;207(6):768-774. https://doi.org/10.1164/rccm.202205-0963OC
13. Brusasco V, Crapo R, Viegi G; American Thoracic Society; European Respiratory Society. Coming together: The ATS/ERS consensus on clinical pulmonary function testing. Eur Respir J 2005;26(1):1-2.https://doi.org/10.1183/09031936.05.00034205
14. Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med 1999;159(1):179-187. https://doi.org/10.1164/ajrccm.159.1.9712108
15. Polgar G, Promadhat V. Pulmonary Function Testing in Children: Techniques and Standards. Philadelphia: WB Saunders, 1971.
16. Agusti A, Faner R. Lung function trajectories in health and disease. Lancet Respir Med 2019;7(4):358-364. https://doi.org/10.1016/S2213-2600(18)30529-0
17. Bhakta NR, Bime C, Kaminsky DA, et al. Race and ethnicity in pulmonary function test interpretation: An official American Thoracic Society statement. Am J Respir Crit Care Med 2023;207(8):978-995. https://doi.org/10.1164/rccm.202302-0310ST

Received 27 February 2025. Accepted 15 September 2025. Published 19 December 2025.