Supporting Information

Supplementary methods and results

This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors.

Appendix to: Collaro AJ, Foong R, Chang AB, et al. Which reference equation should we use for interpreting spirometry values for First Nations Australians? A cross-sectional study. *Med J Aust* 2024; doi: 10.5694/mja2.52036.

1. Generalised additive modelling for location, scale, and shape in Global Lung Function Initiative reference equations

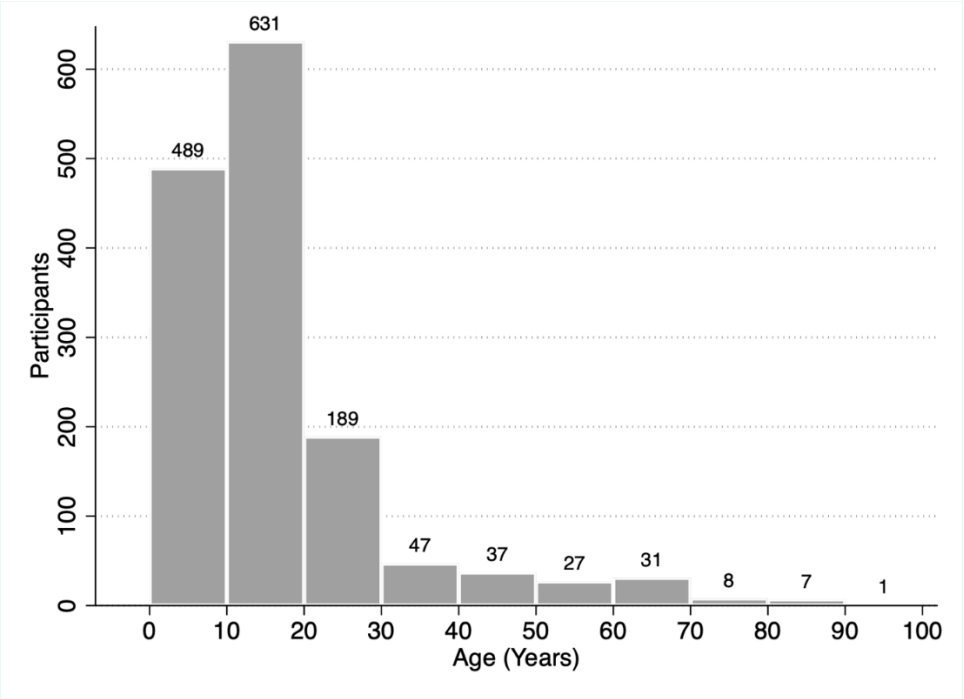
Generalised additive model for location, scale, and shape (GAMLSS)[1] is an approach recommended by the World Health Organization (WHO) Child Growth Standards for reference centile estimation[2] and has been used by the Global Lung Function Initiative (GLI) to develop reference values for spirometry[3] and by others for the fractional exhaled nitric oxide (FeNO) reference values.[4,5] The approach is thoroughly described in these five previous articles. Briefly, the mean or median (location), variability (scale) and skewness (shape) of the outcome distribution, conditioned by the required covariates, are each directly modelled using a flexible general additive approach that allows for non-linearity. GAMLSS results are similar to those of quantile regression.[6] They are both powerful and robust methods that provide an in-depth view of the association between predictors and the outcome. In some cases, GAMLSS may have greater statistical efficiency; that is, it provides more precise estimates.[7]

The approach used by the GLI is the LMS method, a subclass of GAMLSS. Age-specific L, M, and S coefficients are added to the generalised equation, in addition to an age-spline. The GLI-2012 generalised equation includes ethnicity-specific modifiers. The incorporation of the GLI-2022 Global equations into commercial lung function software is likely in the course of 2023, as providers routinely include additional GLI equations in routine software updates.

References

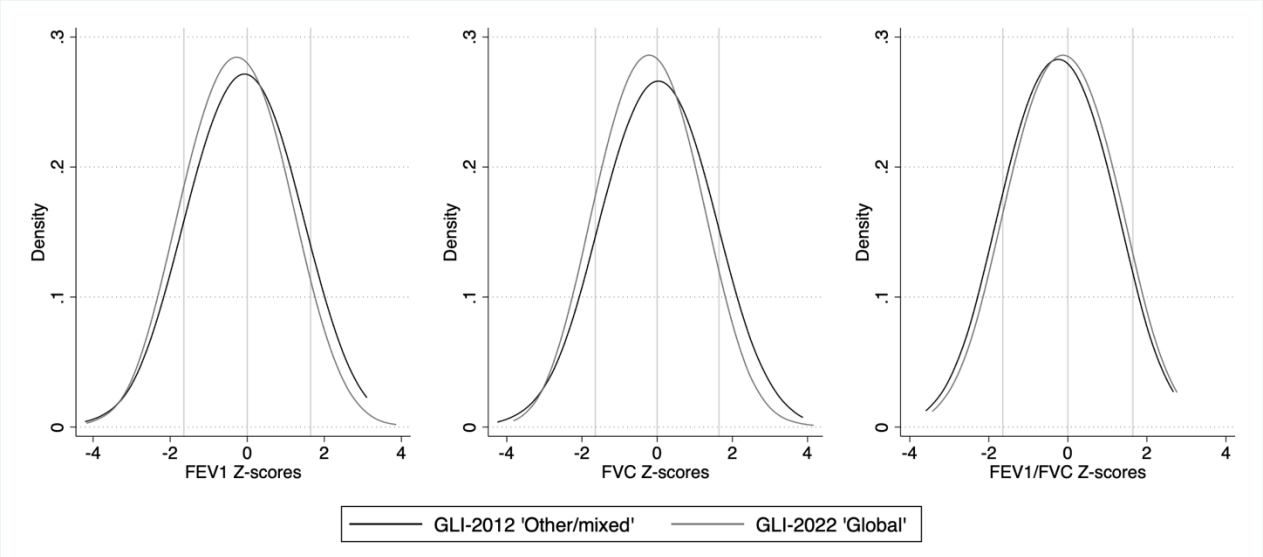
1. Stasinopoulos MD, Rigby RA, Heller GZ, et al. Flexible regression and smoothing. New York: Chapman and Hall/CRC, 2017.
2. World Health Organization. WHO child growth standards: methods and development. Geneva 2009. https://www.who.int/tools/child-growth-standards/publications (viewed Apr 2023).
3. Stanojevic S, Wade A, Stocks J, et al. Reference ranges for spirometry across all ages: a new approach. Am J Respir Crit Care Med 2008; 177: 253-260.
4. Jacinto T, Amaral R, Malinovschi A, et al. Exhaled NO reference limits in a large population-based sample using the Lambda-Mu-Sigma method. J Appl Physiol (1985) 2018; 125: 1620-1826.
5. Collaro AJ, Chang AB, Marchant JM, et al. Developing fractional exhaled nitric oxide predicted and upper limit of normal values for a disadvantaged population. Chest 2023; 163: 624-633.
6. Koenker R. Quantile regression: New York: Cambridge University Press, 2005.
7. Vicendese D, Te Marvelde L, McNair PD, et al. Predicting the whole distribution with methods for depth data analysis demonstrated on a colorectal cancer treatment study. Comm Com Inf Sc 2019; 1150: 162-182.

Figure 1. Distribution by age group of the 1467 healthy participants



Numbers above each bar are the number of participants within each 10-year age bracket.

Figure 2. Kernel density plots for FEV_1, FVC, and FEV_1/FVC Z-scores for 1467 healthy First Nations Australians, generated with the GLI-2012 other/mixed and GLI-2022 global reference equations



Vertical lines mark –1.64 and +1.64 Z-scores.

Table 1. Healthy group spirometry Z-scores generated with the GLI-2012 other/mixed and GLI-2022 global reference equations, by sex and ethnic group

	FEV_1			FVC			FEV_1/FVC		
Z-scores	**Aboriginal**	**Torres Strait Islander**	**Both**	**Aboriginal**	**Torres Strait Islander**	**Both**	**Aboriginal**	**Torres Strait Islander**	**Both**
GLI-2012 other/mixed									
Males	383	166	150	343	146	122	343	146	122
Mean	-0.15	0.06	-0.00	-0.07	0.05	0.20	-0.20	0.00	-0.34
SD	1.08	0.94	0.89	1.14	0.99	0.91	1.02	0.84	0.85
Proportion < 1.64 SDs	7%	3%	3%	8%	4%	3%	9%	3%	6%
Proportion > 1.64 SDs	3%	4%	3%	6%	6%	7%	3%	3%	1%
Females	416	188	164	385	163	135	385	163	135
Mean	-0.12	-0.01	-0.11	0.04	0.11	-0.07	-0.34	-0.35	-0.17
SD	1.10	0.98	0.89	1.15	0.99	0.96	0.89	0.74	0.85
Proportion < 1.64 SDs	8%	5%	3%	7%	4%	4%	8%	2%	4%
Proportion > 1.64 SDs	5%	5%	3%	6%	6%	6%	2%	1%	1%
GLI-2022 global									
Males	383	166	150	343	146	122	343	146	122
Mean	-0.34	-0.14	-0.27	-0.28	-0.19	-0.14	-0.08	0.12	-0.21
SD	0.97	0.90	0.79	0.96	0.90	0.76	0.98	0.79	0.81
Proportion < 1.64 SDs	7%	4%	4%	6%	4%	4%	6%	1%	4%
Proportion > 1.64 SDs	2%	2%	1%	3%	1%	2%	4%	3%	2%
Females	416	188	164	385	163	135	385	163	135
Mean	-0.27	-0.21	-0.34	-0.15	-0.15	-0.34	-0.22	-0.20	-0.02
SD	0.93	0.84	0.78	0.82	0.78	0.79	0.87	0.71	0.83
Proportion < 1.64 SDs	6%	5%	4%	4%	2%	3%	5%	1%	4%
Proportion > 1.64 SDs	3%	2%	1%	3%	1%	0%	2%	1%	2%

FEV_1 = Forced expiratory volume in the first second. FVC = Forced vital capacity. GLI = Global Lung Function Initiative. Both = Aboriginal and Torres Strait Islander.

Table 2. M and S ethnic coefficients for 'healthy' and 'not healthy' First Nations Australians generated using the GLI software.

		Healthy	Not healthy
Participants		1467	1233
FEV_1	M	-0.089	-0.2017
	S	0.0114	0.0114
FVC	M	-0.0854	-0.1791
	S	-0.0503	-0.0503
FEV_1/FVC	M	-0.0107	-0.0308
	S	-0.086	-0.086

FEV_1 = Forced expiratory volume in the first second. FVC = Forced vital capacity. GLI = Global Lung Function Initiative.