PREDICTION EQUATIONS FOR LUNG FUNCTION IN HEALTHY, LIFE TIME NEVER-SMOKING MALAYSIAN POPULATION

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Abstract. Several equations have been used to predict lung function standard results for different populations. It is important lung function evaluations use appropriate standards for the study population. The objective of this study was to develop a prediction equation for lung function test results for the Malaysian population. Spirometry was performed among 5,708 subjects and 1,483 healthy, lifetime never smoked subjects (386 males and 1,097 females). Prediction equations were derived for both men and women for FVC and FEV_1 results. The equations were validated on new subjects (n = 532, 222 males and 310 females) who met the same inclusion and exclusion criteria as the main cohort. There was a positive correlation between the measured values and the values derived from the new prediction equations (0.62 for FEV_1 and between 0.66 and 0.67 for FVC; both $p<0.05$) for both men and women with a smaller bias and limit of agreement compared to the published reference equations of ECCS, Knudson, Crapo and NHANES III . The reference equations derived from local spirometry data were more appropriate than generally used equations based on data from previous studies in different population.

Keywords: forced expiratory volume in 1 sec, Forced Vital Capacity, lung function, reference equation, spirometry

INTRODUCTION

The American Thoracic Society (ATS) recommends that pulmonary function laboratories use published reference equations (based on cross-sectional data) that most closely describe the populations tested in their laboratories (American Thoracic Society, 1991). Due to differences in study populations, procedures and methodologies, it is imperative to develop predictive equations specific for the population being tested.

Updated reference values are important to take into account birth cohort effects, such as changes in the distribution of lung function at a given age over time and new technical equipment. With outdated reference values, normal values may gradually lose their sensitivity for detecting abnormal lung function at an early stage.

One of the earliest studies of pulmonary function among Malaysians was

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carried out by Chan and Raman (1968) among 137 healthy subjects, aged 15 to 37 years. They observed a lower Forced Vital Capacity (FVC) than that of the western population and theorized these differences were accounted for by differences in physical attributes, such as body surface area, height and weight. In 1971, a study of respiratory function among Malaysian aboriginals was carried out among 43 subjects (Dugdale *et al*, 1971). This study found FVC was lower (mean 78%, SD 14%) than the predicted value calculated using the formula of Ferris *et al* (1965).

In 1993, a pilot study was carried out to establish normative lung function data for the Malaysian population among 1,999 subjects (1,385 males and 614 females) ranging in age from 13 to 69 years (Singh *et al*, 1993). In this study the authors found the predicted FVC value derived from equations based on other populations were considerably higher than the observed mean value found in the local population. The aim of our study was to develop gender specific predictive equations for Malaysian subjects.

MATERIALS AND METHODS

A total of 5,708 volunteers (2,542 males and 3,166 females) were screened for lung function parameters (FVC and FEV_1).

Of this cohort, 3,864 subjects (1,635 males and 2,229 females) met American Thoracic Society (ATS) acceptability and reproducibility criteria (Miller *et al*, 2005). Reduced lung function, as measured by forced expiratory volume at 1 second (FEV_1) and FVC, has been associated with chronic disease and has been shown to increase cardiovascular morbidity and mortality (Sin *et al*, 2005). In this study we recruited only life time never-smoking healthy subjects to exclude possible confounding factors that may affect lung function. Subjects with underlying chronic diseases, such as diabetes, hypertension, history of stroke and ischemic heart disease were excluded. Patients with chronic lung diseases or a history of smoking were also excluded. Altogether, 1,483 subjects (386 males and 1,097 females) "healthy" lifetime never-smokers were chosen for this study to develop the prediction equations.

To validate the newly developed prediction equation, subjects (n = 532; 222 males and 310 females) who met the same inclusion and exclusion criteria as the main cohort were freshly recruited.

The study was approved by the institutional ethical review board for human subjects. Prior to participation in this study all subjects gave written informed consent.

Anthropometry

For each subject, age, gender and height were recorded. Standing height was measured without shoes with the subjects' back to a vertical board. Both heels were placed together, touching the base of the vertical board. Height was measured from base of heel to the vertex.

Spiromtery

Flow volume spirometry was performed by two trained research staff-members, using a pneumotachographical open system at normal body temperature, stable atmospheric pressure and normal oxygen saturation (BPTS). The spirometer (Cosmed) met ATS requirements and was calibrated daily. Before testing, the required maneuvers were demonstrated by the trained operator. The FVC maneuver was performed in the sitting position without a nose clip and repeated for a maximum of 6 attempts until 3 FVC

values obtained varied no more than 100 ml or 5%, whichever was higher.

Statistical analysis

Developing a new prediction equation. Multiple linear regression analysis was calculated for men and women separately to produce prediction equations for each lung function parameter (FVC and FEV_1) with independent variables (height and age) and a constant.

Validation of the new prediction equation. Comparisons were made between measured values of the subjects from the validation set and the predicted values obtained from the newly developed prediction equation, as well as from prediction equations from selected published references (Table 1) to ascertain the degree of over-estimation and/or under-estimation. The correlation coefficients (*r*) were computed. Bland-Altman plots were constructed to measure agreement between measured values and the predicted values, the bias and limits of agreement, since a high correlation co-efficient does not ensure the predicted and observed values are in agreement. All analysis was performed using SPSS version 16.1.

RESULTS

One thousand four hundred eighty-three subjects were included in the study (386 men, 1,097 women). Of these, 759 (184 males, 745 females) were from urban communities and 824 (202 males, 622 females) were from rural communities. A summary of the statistics of the anthropometric and lung function parameters is in Table 2.

A multiple linear regression analysis was performed to develop prediction equations for both FVC and FEV_1 using height and age as independent predictor

Table 1
Selected prediction equations.

Reference	Lung function	Equation		Study population
		Males	Females	
Quanjer *et al*, 1993 (ECCS)	FVC	0.0576H-0.0260A-4.340	0.0443H-0.0260A-2.890	European
	FEV	0.0430H-0.0290A-2.490	0.095H-0.025A-2.600	
Knudson *et al*, 1983	FVC	0.0844H-0.0298A-8.782	0.044H-0.0169A-3.195	European
	FEV_1	0.0665H-0.0292A-6.515	0.0665H-0.0292A-6.515	
Crapo *et al*, 1981	FVC	0.0600H-0.0214A-4.650	0.0491H-0.0216A-3.590	Asian (Middle-Eastern)
	FEV_1	0.0414H-0.0244A-2.190	0.0342H-0.0255A-1.578	
Hankinson *et al*, 1999 (NHANES)	FVC	-0.1933+0.0064A- 0.000269A2+0.000018642H2	-0.3560+0.01870*A- 0.000382A2+0.00014815H2	American (Caucasian)
	FEV_1	0.5536-0.01303A- 0.000172A2+0.0014098H2	0.4333-0.00361A- 0.000194A2+0.001196H2	

Table 2
Anthropometry and lung function parameters.

	Men (*n*=386)			Women (*n*=1,097)		
	Mean	SD	Range	Mean	SD	Range
Age (years)	53.1	10.9	22-92	48.5	10.3	20-89
Height (m)	1.6	0.1	1.3-1.8	1.5	0.06	1.1-2.0
FVC (l)	2.7	0.7	0.7-4.9	2.1	0.5	0.5-4.2
FEV_1 (l)	2.4	0.6	0.5-4.0	1.8	0.4	0.5-3.6

Table 3
Regression equation and residual standard deviation (RSD) for FVC and FEV_1 prediction equations.

Gender	Lung function	Equations	RSD
Men	FVC	-2.176-0.027A+3.889H	0.399
	FEV_1	-1.284-0.027A+3.167H	0.474
Women	FVC	-1.147-0.018A+2.695H	0.336
	FEV_1	-0.643-0.02A+2.265H	0.412

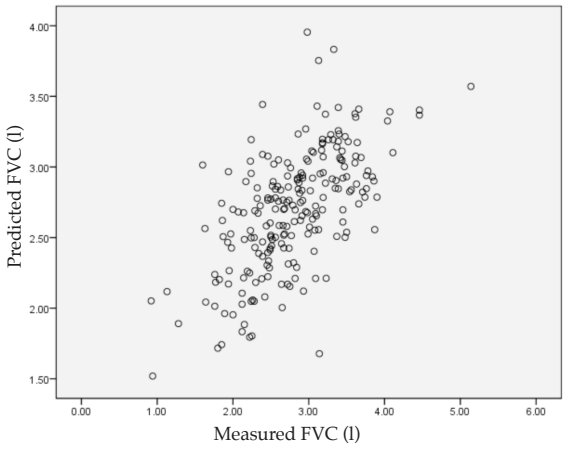
Table 4
Characteristics of test population.

	Men (*n*= 222)			Women (*n*=310)		
	Mean	SD	Range	Mean	SD	Range
Age (years)	49.7	10.3	18-74	48.8	9.3	24-72
Height (m)	1.6	0.06	1.4-1.8	1.5	0.1	1.3-1.8
FVC (l)	2.8	0.6	0.9-5.1	2.2	0.47	0.9-3.6
FEV_1 (l)	2.4	0.7	0.7-4.2	1.9	0.4	0.8-3.2

variables for both sexes separately. Table 3 provides the newly developed prediction equations for FVC and FEV_1 for both sexes.

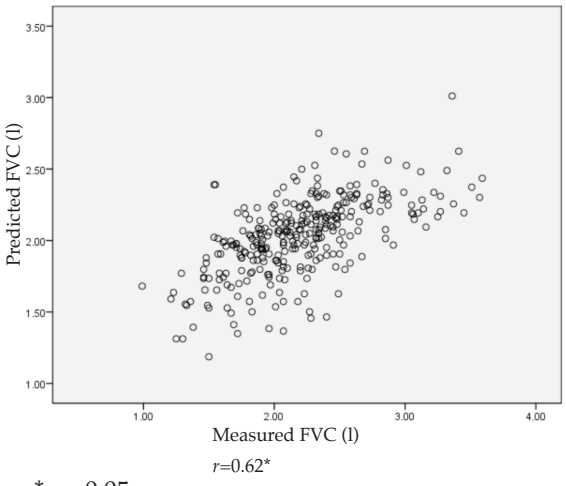
These newly developed prediction equations were tested on newly recruited subjects (test population). The test population characteristics are described in Table 4.

Using the newly developed prediction equations, the correlation coefficient of the measured against the predicted value for FVC was 0.62 (p<0.05) (Fig 1) and for FEV_1 was 0.66 (p<0.05) (Fig 2) for men. In women, the correlation coefficient of the measured *versus* the predicted FVC was 0.62 (p<0.05) (Fig 3) and the FEV_1 was 0.67 (p<0.05) (Fig 4).



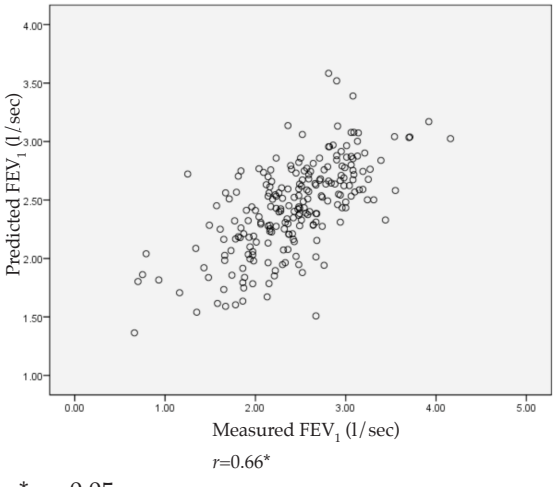
*$p < 0.05$

Fig 1–Correlation of measured FVC against the predicted FVC for men.



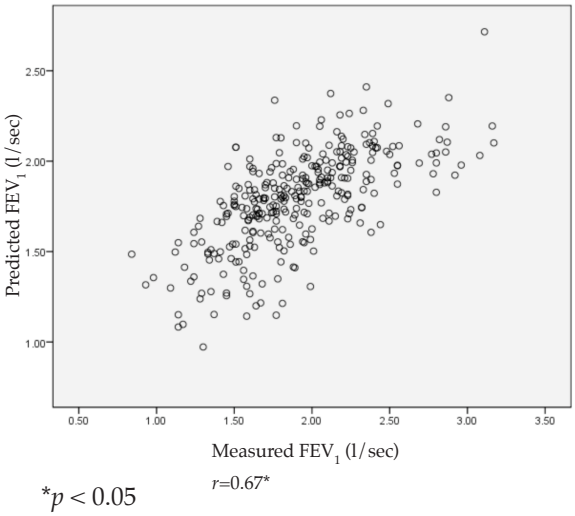
*$p < 0.05$

Fig 3–Correlation of measured FVC against the predicted FVC for women.



*$p < 0.05$

Fig 2–Correlation of measured FEV_1 against the predicted FEV_1 for men.



*$p < 0.05$

Fig 4–Correlation of measured FEV_1 against the predicted FEV_1 for women.

The lung function parameters of the test population were compared with selected published prediction equations derived from population based studies of different races. A moderately high correlation was found with all equations (Table 5). However, the correlation coefficients only show the strength of linear relationships, but not the agreement between the two values. Hence, Bland-Altman plots were created to assess agreement between measured values and the predicted values for the different selected published equations.

Analysis with the Bland-Altman plot of the data for the men showed a mean

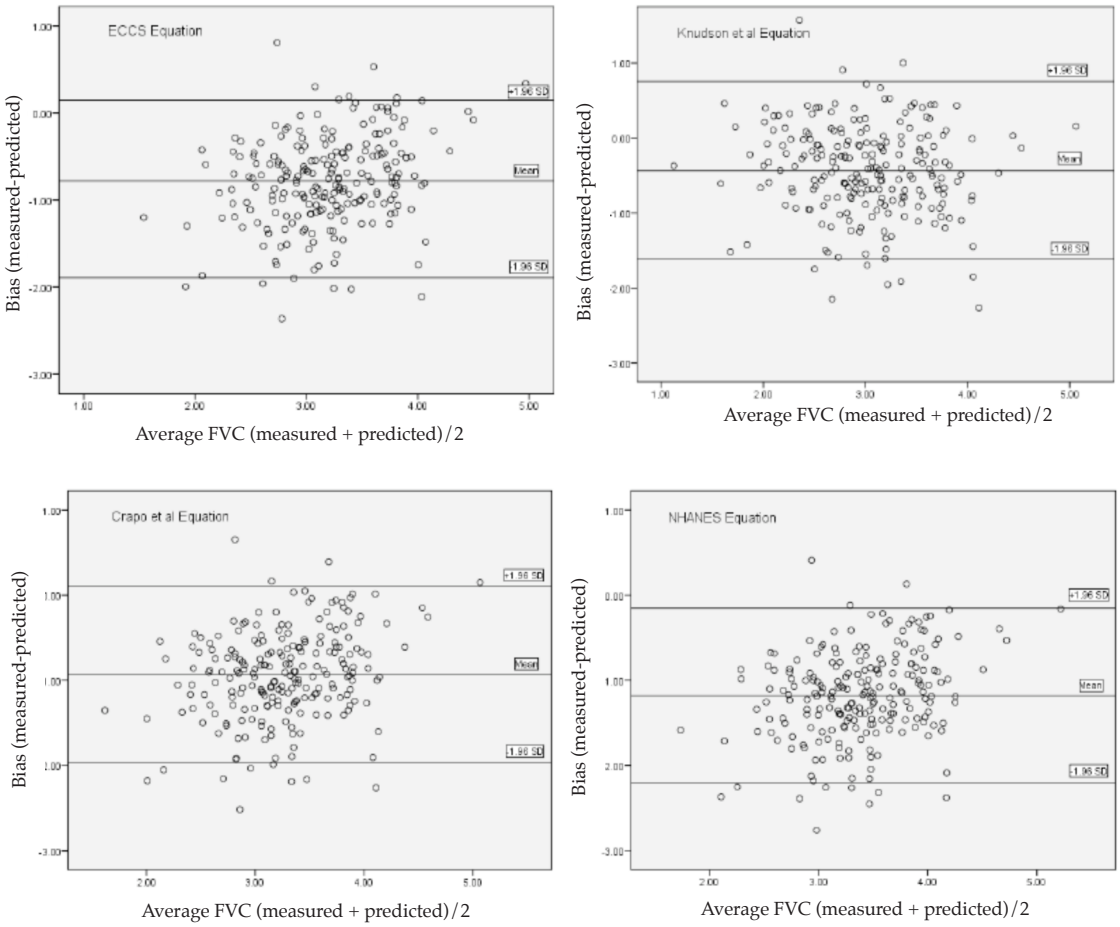
Table 5
Correlation of measured lung function parameters against selected published prediction equations.

Reference	Lung function	Correlation coefficients (*r*)	
		Males	Females
Quanjer *et al*, 1993 (ECCS)	FVC	0.607	0.621
	FEV_1	0.654	0.669
Knudson *et al*, 1983	FVC	0.594	0.619
	FEV_1	0.638	0.660
Crapo *et al*, 1981	FVC	0.602	0.621
	FEV_1	0.651	0.668
Hankinson *et al*, 1999 (NHANES)	FVC	0.609	0.609
	FEV_1	0.660	0.665

Table 6
Limits of agreement.

Reference	FVC (l)					
	Male			Female		
	+1.96 SD	-1.96 SD	Range	+1.96 SD	-1.96 SD	Range
Quanjer *et al*, 1993 (ECCS)	0.15	-1.89	2.04	0.45	-1.07	1.53
Knudson *et al*, 1983	0.75	-1.62	2.37	0.27	-1.21	1.48
Crapo *et al*, 1981	0.10	-1.96	2.07	0.21	-1.31	1.53
Hankinson *et al*, 1999 (NHANES)	-0.15	-2.19	2.04	0.01	-1.51	1.52
Our equation	0.96	-0.99	1.96	0.88	-0.56	1.45
Reference	FEV_1 (l/sec)					
	Male			Female		
	+1.96 SD	-1.96 SD	Range	+1.96 SD	-1.96 SD	Range
Quanjer *et al*, 1993 (ECCS)	0.34	-1.39	1.73	0.43	-0.87	1.29
Knudson *et al*, 1983	0.73	-1.22	1.94	0.67	-0.10	1.67
Crapo *et al*, 1981	0.05	-1.65	1.70	0.22	-1.05	1.27
Hankinson *et al*, 1999 (NHANES)	0.22	-1.53	1.75	0.15	-1.11	1.26
Our equation	0.84	-0.88	1.73	0.72	-0.50	1.22

bias that was negative, indicating an over-prediction of FVC by the selected published predictive equations (Fig 5). Similar results were obtained for FEV_1 (Fig 6). Data from the women also revealed an over-prediction of the measured values by the selected published predictive equations for both FVC and FEV_1 (Fig 7, 8).



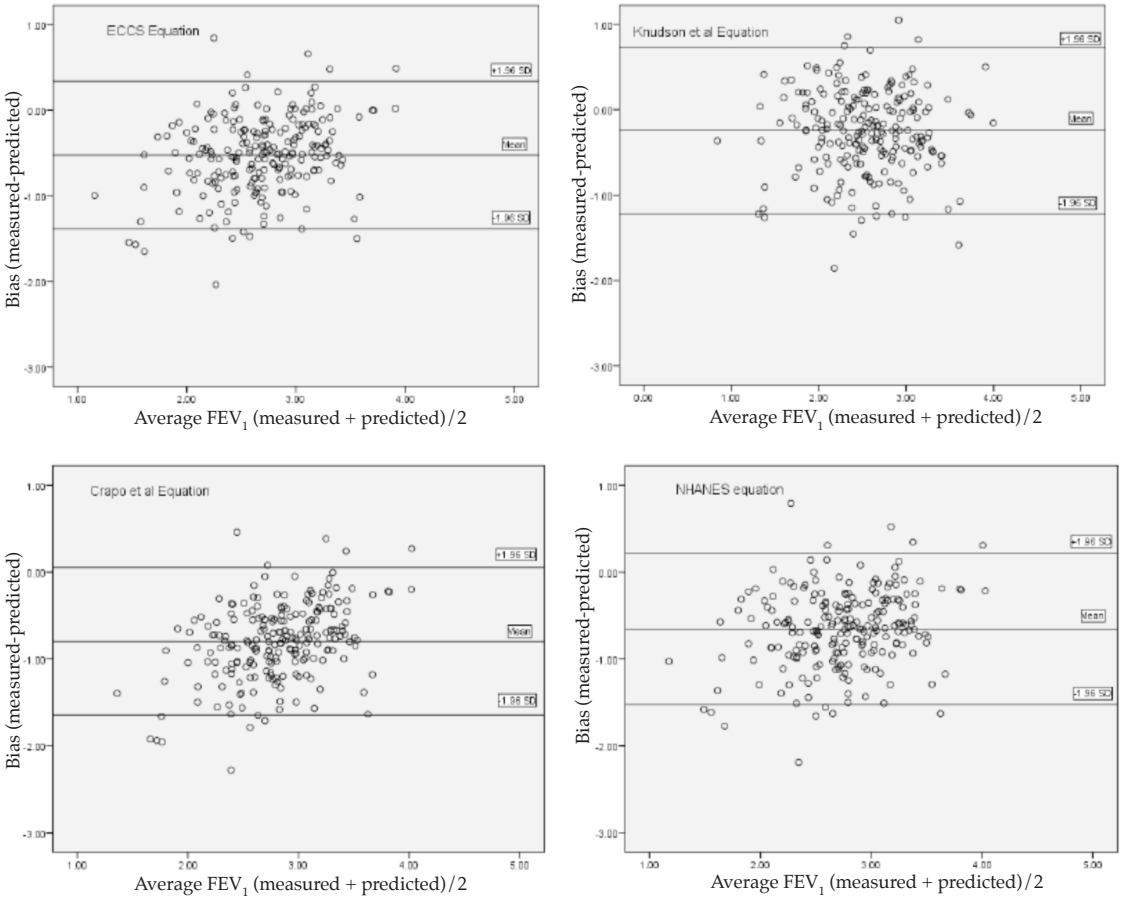
*$p < 0.05$

Fig 5–Bland-Altman plots for differences in mean FVC among males using selected published equations.

However values predicted by the newly developed equation had a mean bias of -0.019 l for FVC and -0.02 l/sec for FEV_1 for men (Fig 9) and 0.16 l for FVC and 0.11 l/sec for FEV_1 for women (Fig 10). From this data two observations can be made: 1) the plotted bias showed a lower variability using our newly developed prediction equation. Hence the limits of agreement (average difference ± 1.96 SD) between the measured and the average of the measured and the predicted values showed the smallest range for both the lung function parameters and for both genders (Table 6) indicating better agreement between the measured and predicted values; 2) the newly developed equation has a slightly negative bias for males, and a slightly positive bias for females, indicating an over-prediction in males and an under prediction in females.

DISCUSSION

The aim of our study was to develop prediction equations for FEV_1 and FVC

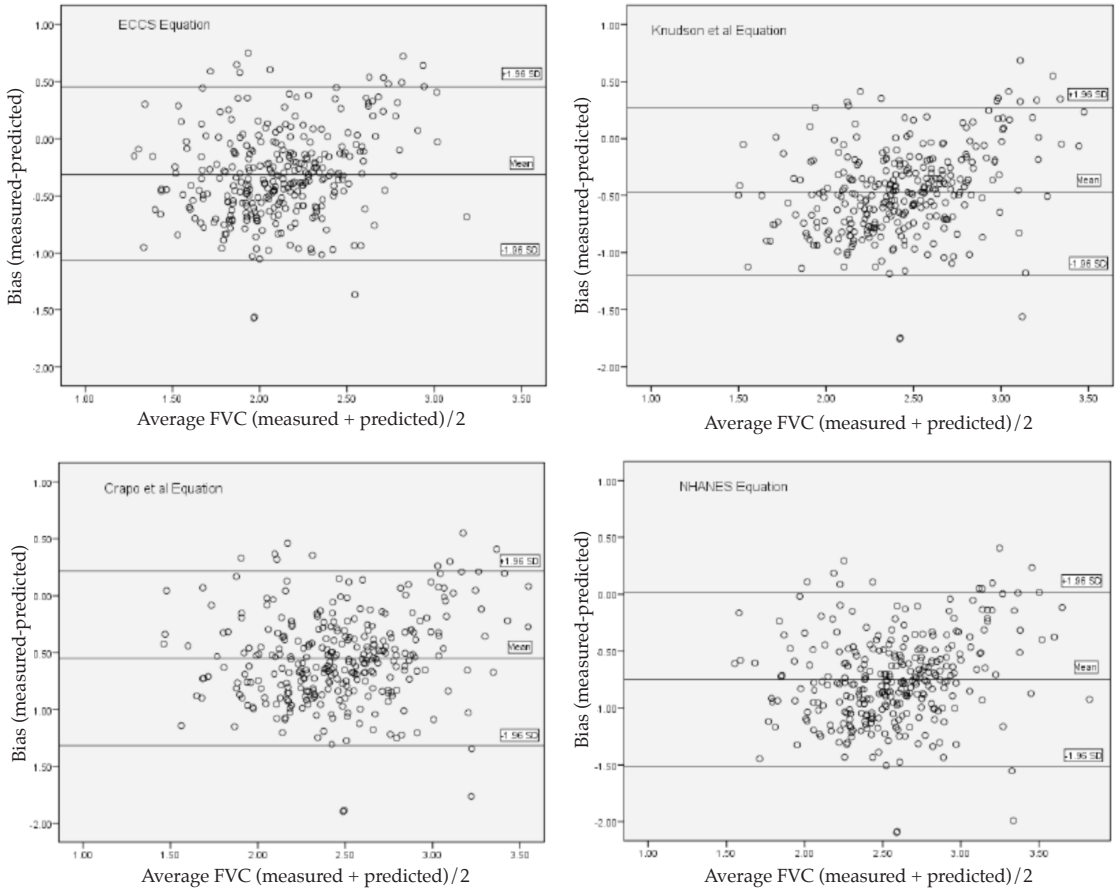


*$p < 0.05$

Fig 6–Bland-Altman plots for differences in mean FEV_1 among males using selected published equations.

for Malaysians. The mean FEV_1 and FVC values recorded from our study subjects were comparable with values reported from other studies of Malaysians and other Asian ethnic groups (Singh *et al*, 1993). However, they were lower than data reported from Europeans and North Americans. Differences in anthropometric characteristics among individuals of different racial and ethnic backgrounds may be the reason for this difference. The average height and height for age have been reported to be lower among Asian subjects (Korotzer *et al*, 2000). Muscle strength and parameters of aerobic capacity have also been shown to vary by ethnicity (Singh *et al*, 1995). These distinct anthropometric features along with lower FVC and FEV_1 warrant the development of specific prediction equations for Malaysians.

The data obtained from this study was fitted into a linear regression model, including height and age and was specific for each gender. The equations were then tested on data obtained from freshly recruited subjects. We obtained a good cor-



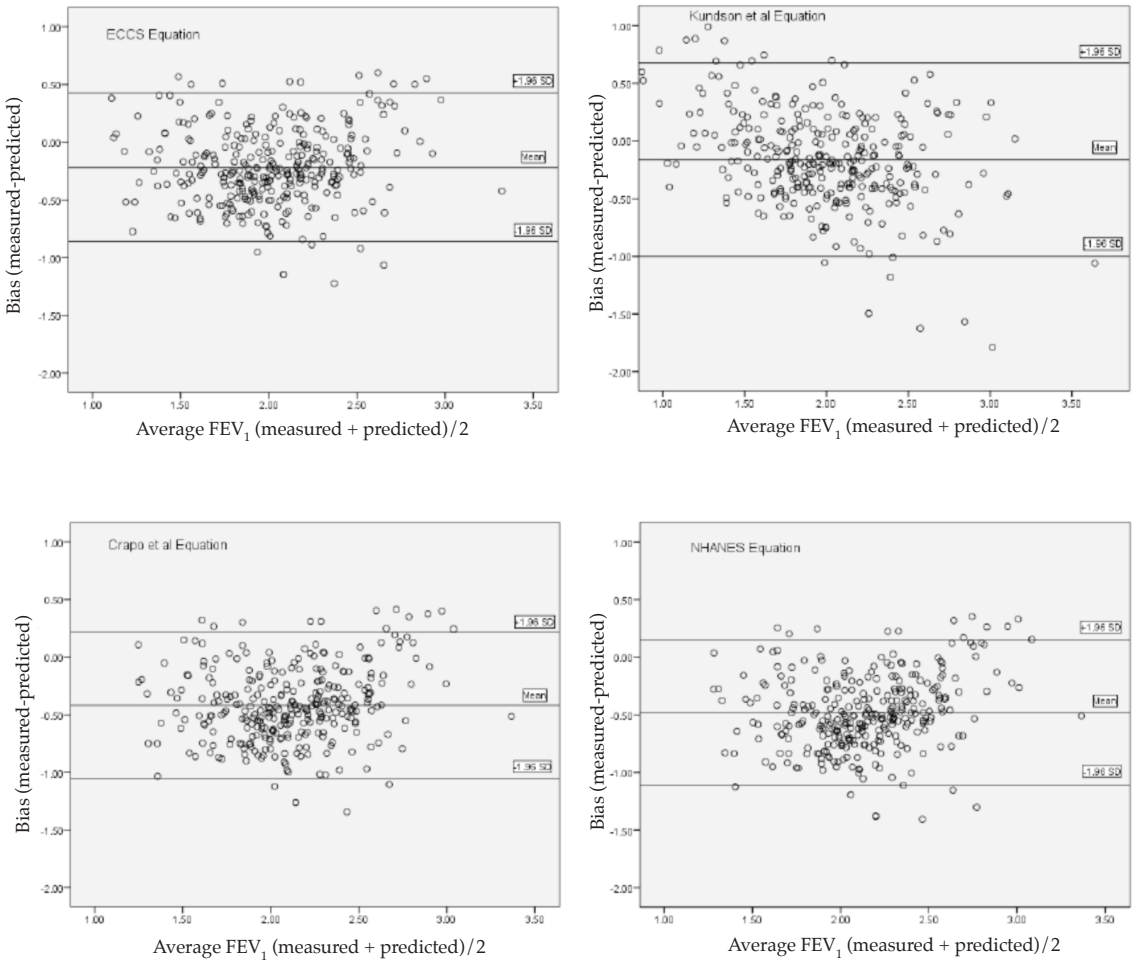
*$p < 0.05$

Fig 7–Bland-Altman plots for differences in mean FVC among females using selected published equations.

relation for both FVC and FEV_1 using the newly developed prediction equations.

Apart from testing the newly developed equations, the data were also compared with other existing reference values to determine if our equations were appropriate for Malaysians. The FVC and FEV_1 values measured were over predicted by the other reference values by wide limits of agreement. Although the limits of agreement were narrowest with our equation, there was a slight bias, with the male equation showing a negative bias and the female equation showing a positive bias. It is possible this difference may be due to the male:female ratio. We acknowledge this as a drawback of this study, but due to stringent inclusion and exclusion criteria, it was difficult to maintain an equal gender-ratio.

However, the prediction equations derived in this study are based on a large sample of healthy, never smoking individuals above the age of 18. The tests were performed in a standardized manner, using spirometers that conform to ATS



*$p < 0.05$

Fig 8–Bland-Altman plots for differences in mean FEV_1 among females using selected published equations.

recommendations (American Thoracic Society, 1991). Furthermore, validation studies involving large numbers of subjects selected in a similar manner as the study population and tested under identical circumstances were performed. These are the main strengths of our study design.

In conclusion, we developed prediction equations for adult never-smoked healthy Malaysians. The equations have been verified on a test population and have been found to describe the lung function of the test population adequately. Our equations represent an improvement in the standard of comparison over other equations developed on populations that are not comparable with ours. Our results support the development of prediction standards based on appropriate and comparable study samples.

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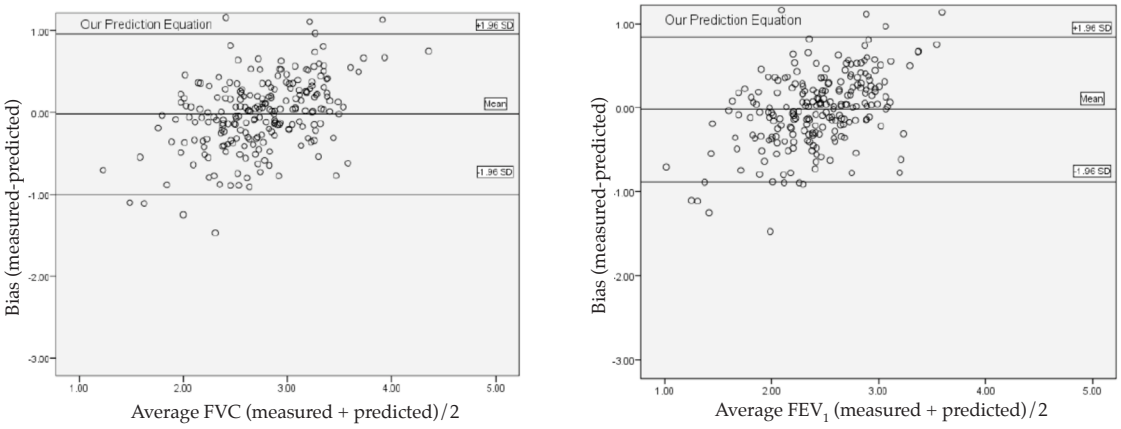
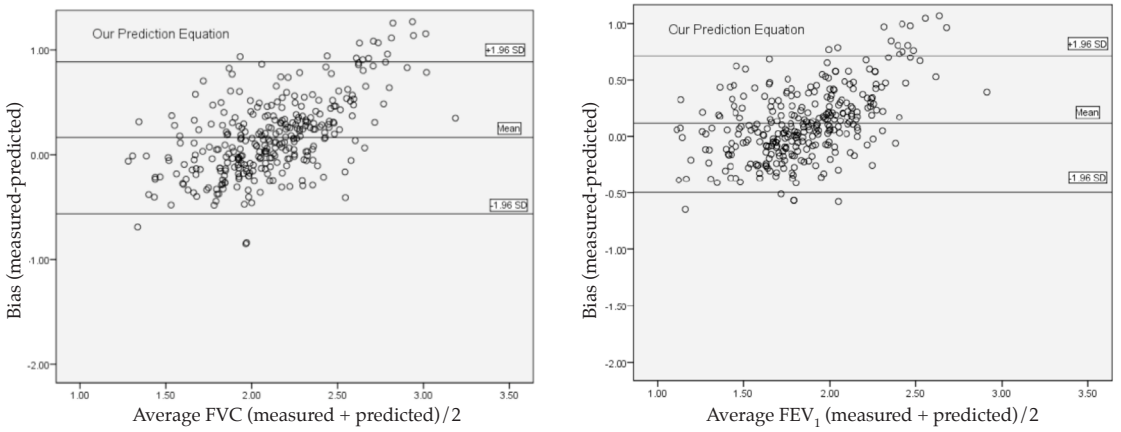


*$p < 0.05$

Fig 9–Bland-Altman plots for differences mean FVC and FEV_1 among males using the new prediction equation.



*$p < 0.05$

Fig 10–Bland-Altman plots for differences in mean FVC and FEV1 among females using the new prediction equation.

participated in this study and the research staff involved with data collection.

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