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Normative reference values and regression equations to predict the 6-minute walk distance in the Asian adult population aged 21–80 years

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Summary at a glance: The 6-min walk test (6MWT) is a widely used field walking test. This study reports the normative reference values (NRV) of distance walked during 6MWT (6MWD) in healthy Singaporeans (aged 21–80) and updates the 6MWD reference equations. This information may facilitate the interpretation of the 6MWD in clinical populations.
Ethics approval: The Singapore Institute of Technology-Institutional Review Board (SIT-IRB Project Number: 2019099) approved this study to be carried out from June 2019 to January 2021. All participants gave written informed consent before data collection began.

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Background: The six-minute walk test (6MWT) is a widely adopted submaximal field-walking test to evaluate functional exercise capacity. This validated test is a reliable, safe, inexpensive, and straightforward assessment tool commonly used as an outcome measure, using the distance walked (6MWD) as the primary outcome. An earlier study has established the normative reference values (NRV) and equation in healthy Singaporeans — however, the small sample size and narrow age range curb adequate representation of the adult population profile.
Objectives: This study aims to update the NRV and reference equations to predict the distance walked during 6MWT (6MWD) for healthy Singaporeans aged 21–80.
Methods: This cross-sectional study recruited community-dwelling healthy subjects aged 21–80 via convenience sampling. Each subject completed two trials of 6MWT according to the standard protocol. Primary outcome measures included 6MWD, pre-and post-test heart rate (HR), oxygen saturation, and blood pressure (BP).
Results: 172 healthy Singaporeans (females = 90, males = 82) participated. The overall mean 6MWD was 578.00 ± 75.38 metres. The age-stratified mean 6MWD ranged from 601.3 ± 71.79 metres (aged 21–39) to 519.02 ± 55.42 metres (aged 60–80). Age, gender, and percentage maximum HR predicted (%PredHRmax) were the most significant variables ($p < 0.001$). 6MWD reference equation = 288.282 (height, m) + 27.463 × Gender (male = 1; female = 0) + 4.349 (%predHRmax) + 1.191 (HR reserve, bpm) −185.431 − 1.343 (age, years) − 1.614 (weight, kg), $R^2 = 58\%$. Applying equations from other studies to the Singaporean population resulted in an overestimation of the 6MWD.
Conclusion: This study updated the NRV and reference equations of 6MWD for healthy Singaporeans aged between 21–80 years. This update revises the local benchmarks of 6MWD in Singapore, a widely adopted outcome measure.

Keywords: 6-Minute walk test; exercise test; exercise capacity; outcome measures; reference values and equations.

Introduction

The six-minute walk test (6MWT) is a widely-used submaximal field walking test to evaluate functional exercise capacity.[1–5] The 6MWT is a safe, inexpensive, and straightforward test commonly used for assessment and as an outcome measure, using the distance walked (6MWD) as the primary outcome. It is valid and reliable in young and adult, healthy and diseased populations such as chronic obstructive pulmonary disease, pulmonary fibrosis, heart failure, and amputees.[6–11] As the test is self-paced and rests are allowed, it is considered an appropriate assessment of exercise capacity for individuals suffering from respiratory-related symptoms and the general geriatric population.[12–14] Thus, it has an advantage over other comprehensive cardiopulmonary exercise tests (CPET) in the clinical setting.

Judgement of the individual walking performance should be compared with that of a relevant population, and it requires the availability of normative references (norms) for the particular population.[1,15] Several studies have derived the normative reference values (NRV) and reference equations to estimate 6MWD specific to the respective local populations.[16–26] Factors, such as demographic and anthropometric profiles, clinical and physiological characteristics, have been reported as variables affecting the 6MWD.[3,4,8,16–19,21–24,27–31] Poh *et al.* further confirmed that the reference equations derived from the Caucasian population would overestimate the 6MWD in healthy Singaporeans.[22] Till date, the study by Poh *et al.* remains the only attempt to report the NRV and reference equation for healthy Singaporeans despite tremendous changes in the Singaporean population profile in the last 15 years.[32] Additionally, the small sample size ($n = 35$) and age range of 45–85 years in their study lacked representation of the healthy adult Singaporean population. Furthermore, the use of a 45 metres (m) corridor is uncommon in the land-scarce city-state. Thus, there is a need to update the NRV and derive reference equations that could be applicable to a broader age range.

Therefore, this study aims to do the following: (1) establish the NRV of 6MWD in the healthy

Singaporean population aged 21–80 years; (2) determine the correlations of variables that could influence the 6MWD; (3) establish the 6MWD reference equation applicable to healthy adult Singaporeans; (4) evaluate the age-matched comparisons of the Singapore data with published studies.

Methods

Study design

This cross-sectional study was conducted via convenience sampling at various community centres in Singapore from June 2019 to January 2021. Approval of the study was obtained from the University Institutional Review Board (Project number: 2019099). Personal particulars and written informed consent were obtained from every subject before the commencement of the study.

Subjects

We recruited community-dwelling healthy Singaporean subjects aged 21–80 via convenience sampling from various districts in Singapore. A single mean and standard deviation (SD) method was used to determine the sample size. With reference to the previous study[21,26] that had reported the NRV of 6MWD, we predicted a small-medium effect size [Cohen's $d = 0.312$ [95% confidence interval (95%CI) 0.283–0.893]] with a minimum sample size of 142 subjects based on 95% confidence; expected population SD of 60 metres (m) and a precision of 10.[33] We allowed for a possible attrition rate of 20%, and thus a minimum of 170 subjects were needed to distribute across the age range. All subjects completed the Physical Activity Readiness Questionnaire for Everyone (PAR-Q$^+$).[34] before data collection to determine suitability. Inclusion criteria were: individuals between the ages of 21–80 years as of testing day; able to understand simple English; able to walk a minimum of six minutes independently; and clearance with the PAR-Q$^+$. Subjects were excluded if they had a history of chronic disease(s), such as cardiovascular, metabolic, respiratory, neuromuscular or musculoskeletal conditions that could affect the ability to perform physical exercises or cause changes to functional capacity; gait abnormality, such as the use of walking aid or leg length discrepancy ≥ 2 cm, measured from the anterior superior iliac spine to lateral malleolus, as such discrepancy is associated with prevalent, incident symptomatic, and progressive knee osteoarthritis;[35] current smoking history or any smoking history within the last 12 months; resting heart rate (HR) > 100 beats per minute (bpm) or < 50 bpm; resting systolic BP > 150 or < 90 mmHg, resting diastolic BP > 100 or < 50 mmHg; resting oxygen saturation (SpO_2) $< 95\%$, abnormal lung function, which is defined as forced expiratory volume in 1 second (FEV_1) $\leq 80\%$ or forced vital capacity (FVC) $\leq 80\%$ or $FEV_1/FVC \leq 70\%$.[36] These values were referenced from and kept consistent with other NRV reports on 6MWD for subsequent comparisons between the derived HR variables.[21,22,26]

Data collection

Researchers who were proficient in conducting the 6MWT performed the data collection. All subjects were instructed to wear comfortable clothes and walking shoes. The data obtained from subjects before undergoing 6MWT included PAR-Q$^+$, age, gender, height, weight, smoking history, medical history and medication use, HR, BP, SpO_2, dyspnoea score with the modified Borg's dyspnoea scale,[37] and Borg's rating of perceived exertion (RPE).[38] Body-mass index (BMI) calculation followed the standard formula.[39] The maximum predicted HR (PredHRmax) was calculated using $[208 \times (0.7 \times \text{Age})]$,[40] while heart rate reserve (HRR) was calculated with (PredHRmax – Resting HR). The percentage of maximum predicted HR (%predictHRmax) was derived using [(measured highest HR during 6MWT $\div$ PredHRmax) $\times 100\%$]. A calibrated standard portable spirometer (Spirolab, MIR) was used to measure lung functions. Each subject had to complete at least three measures according to the standard guidelines,[41] with the highest values of the FEV_1, FVC, and FEV_1/FVC considered for inclusion and exclusion criteria.

Six-minute walk test

The 6MWT was conducted along a 30-metre indoor walkway according to the guidelines of the American Thoracic Society (ATS).[1] Subjects walked back and forth and turned around two cones that marked the ends of the walkway. Subjects were instructed to "walk as far as possible in 6 minutes" and that they could slow down or rest if

necessary. At the end of every minute, the researchers gave standardised encouragement according to the ATS guidelines[1] and recorded heart rate and oxygen saturation with a portable pulse oximeter (Nellcor™ PM10N), dyspnoea and RPE scores.[37,38] At the end of 6 min, the 6 MWD was recorded. Two trials of 6 MWT were conducted on the same day to observe for learning effect,[11] with a minimum 30-minute rest interval between the two trials to ensure sufficient recovery and that HR, BP, and SpO_2 returned to baseline before the second trial. The longer distance walked between the two trials was used for all subsequent data analyses.

Statistical analysis

GraphPad Prism Version 8.4.3 (686) (GraphPad Software, San Diego, California, USA) was used to perform the statistical analysis. The level of significance was set at $p < 0.05$. Demographic and anthropometric data of subjects were examined for normal distribution using the Shapiro–Wilk test. Descriptive statistics were used to analyse central tendency, data spread, and the dataset's position via means, SD, 95% confidence interval (95%CI), percentage and percentiles accordingly. Chi-square Goodness of Fit test was used to compare the ethnicity ratio between the subject profiles and the Singaporean population.[42] Test–retest reliability was examined using the interclass correlation coefficient (ICC). Kruskal–Wallis test was used to analyse non-normal continuous variables by age groups, and Mann–Whitney U test to compare the variables by gender. Pearson's correlation coefficients assessed the correlation between variables. Linear regression was applied to establish the reference equation for 6MWD. To compare the age-matched Singapore data with the published reference equations, the measured 6MWD from this study was age-matched to each study and compared against the same age range of the calculated distance derived from the predictive regression formulae of the eleven identified reports.[16–26] The comparisons between measured and predicted 6MWD were analysed using paired *t*-tests.

RESULTS

Subject characteristics and 6MWD

One hundred and seventy-two subjects (82 males; 90 females) were included for data analysis from 175 subjects recruited, with three excluded based on exclusion criteria. Tables 1 and 2 present the demographics and characteristics of the subjects. The Chi-Square Goodness of Fit test showed a statistically significant difference ($p = 0.01$) in the subject ethnicity profile compared to the population profile of Singapore 2021,[42] with a higher percentage of Chinese subjects. The overall mean 6 MWD was 578.00 ± 75.38 m, where males walked an average of 600.32 ± 77.29 m while females averaged 557.62 ± 67.84 m ($p < 0.001$) (Table 1). The 6 MWD decreased progressively with age and ranged from 601.30 ± 71.79 m (age 21–39) to 519.02 ± 55.42 m (age 60–80) (Table 2). Test–retest reliability was excellent (ICC = 0.90). The highest HR achieved was 133.4 ± 21.48 bpm from the 21–39 year group; while the %PredHRmax ranged from $70.07 \pm 11.16\%$ (age 21–39) to 76.40 $\pm 11.76\%$ ($p = 0.008$) (Table 2).

Variable associations with 6MWD and regression equations

The relationships between 6MWD, demographics, anthropometric and physiological variables are presented in Table 3 and Fig. 1. These parameters are commonly collected before and during the 6MWT assessment as suggested by guidelines,[1] illustrating their readiness and potential usefulness in estimating and benchmarking the outcome measurement. 6MWD was significantly associated with age, gender, height, weight, average leg length, HRR and %PredHRmax (all $p < 0.05$). Notably, the correlation of average leg length ($r = 0.36$, $p < 0.001$) and height ($r = 0.38$, $p < 0.001$) to 6MWD was similar; also, a high correlation ($r = 0.83$, $p < 0.05$) was established between average leg length and height, thus only height was included in the linear regression analysis.

Stepwise linear regression analysis revealed that age, height, weight, gender, %PredHRmax, HRR were independent contributors to 6MWD (Table 4). Pre-6MWT available variables such as age and height, or age and gender alone explained 23–24% of the variance, respectively. The better reference equation was as follows: 6MWD (m) = 622.64 + 35.03 × Gender (male = 1; female = 0) −1.65 (age, years). However, with the addition of the post-test available variables, the percentage of the variance increased to 58%; and the reference equation was as follows: 6MWD (m) = 288.28 (height, m) + 27.46 × Gender (male = 1; female = 0) + 4.35 (%predHRmax) + 1.19

Table 1. Subjects' characteristics and measured variables during the 6MWT (by gender).

Characteristics	Total	Male	Female	*p*-value
Subjects, n	172	82	90	—
Age (years)	37.1 ± 18.5	34.7 ± 17.7	39.3 ± 19.0	0.10
Ethnicity, *n* (%)				0.01*
Chinese	158 (91.9)	77 (44.8)	81 (47.0)	—
Malay	5 (2.9)	3 (1.7)	2 (1.2)	—
Indian	9 (5.2)	2 (1.2)	7 (4.1)	—
Height (m)	1.66 ± 0.09	1.72 ± 0.07	1.60 ± 0.06	< 0.001
Weight (kg)	64.69 ± 13.90	72.44 ± 14.35	57.62 ± 8.82	< 0.001
BMI (kg/m^2)	23.46 ± 3.80	24.47 ± 3.85	22.54 ± 3.53	< 0.001
Average leg length (m)	0.87 ± 0.05	0.89 ± 0.05	0.84 ± 0.04	< 0.001
HR measurements				
Resting HR (bpm)	85.75 ± 14.49	82.87 ± 13.13	88.38 ± 15.22	< 0.001
HRR (bpm)	96.29 ± 18.29	100.87 ± 18.47	92.12 ± 17.19	< 0.001
Highest HR (bpm)	130.54 ± 20.58	129.35 ± 21.16	131.62 ± 20.09	0.472
HRchange (bpm)	44.79 ± 19.19	46.49 ± 19.87	43.24 ± 18.53	0.270
%PredHRmax	71.91 ± 11.32	70.62 ± 11.73	73.08 ± 10.85	0.154
6MWD (m)				
6MWD1	562.13 ± 74.74	586.21 ± 76.03	540.20 ± 66.72	< 0.001
95% CI	550.90 to 573.40	569.51 to 602.92	526.2 to 554.20	
6MWD2	570.33 ± 74.91	590.45 ± 77.22	552.00 ± 68.13	< 0.001
95% CI	559.1 to 581.60	573.48 to 607.41	537.70 to 566.30	
6MWD2 – 6MWD1	8.20 ± 32.90	4.24 ± 34.46	11.80 ± 31.17	0.13
95% CI	3.24 to 13.15	−3.34 to 11.08	5.28 to 18.33	
Best of 2 trials	578.00 ± 75.38	600.32 ± 77.29	557.62 ± 67.84	< 0.001
95% CI	566.60 to 589.30	583.3 to 617.3	543.4 to 571.8	

Notes: Values are expressed as *mean* ± *Standard Deviation* (*SD*),
$p < 0.05$ represents a significant value.
m: metres; **kg**: kilogram; **bpm**: beats per minute; **BMI**: Body mass index; **6MWT**: 6-minute walk test; **6MWD**: 6-minute walk distance; **HR**: Heart Rate; **Highest HR**: Highest heart rate achieved during 6MWT; **HRR**: heart rate reserve; **HRchange**: Difference between HighestHR heart rate and resting heart rate; **%PredHRmax**: peak HR achieved during 6MWD expressed as %predicted maximum HR with predicted HRmax as [208−(0.7×Age)]; **95% CI**: 95% Confidence Interval; **6MWD1**: 1st trial of 6MWD; **6MWD2**: 2nd trial of 6MWD; *subject ethnicity profile compared with Singapore population profile.

Table 2. Subjects' characteristics and measured variables during the 6MWT (by age).

	Age			
Characteristics	21–39 years	40–59 years	60–80 years	*p*-value
Subjects, *n*	115	20	37	
Ethnicity, *n* (%)				
Chinese	106 (61.6)	15 (8.7)	37 (21.5)	
Malay	5 (2.9)	0 (0)	0 (0)	
Indian	4 (2.4)	5 (2.9)	0 (0)	
Height (m)	1.68 ± 0.08	1.60 ± 0.08	1.60 ± 0.08	< 0.001
Weight (kg)	67.23 ± 14.80	58.33 ± 8.59	59.52 ± 10.27	0.003
BMI (kg/m^2)	23.64 ± 3.94	22.84 ± 2.65	23.20 ± 3.86	0.812
Average leg length (m)	0.88 ± 0.05	0.84 ± 0.03	0.83 ± 0.05	< 0.001
HR measurements				
Resting HR (bpm)	86.58 ± 14.51	85.00 ± 14.89	83.42 ± 14.35	0.740
HRR (bpm)	103.76 ± 14.46	85.98 ± 14.50	76.98 ± 14.42	< 0.001
Highest HR (bpm)	133.4 ± 21.48	130.3 ± 13.37	121.78 ± 18.73	< 0.001

Table 2. (*Continued*)

Characteristics	Age			*p*-value
	21–39 years	40–59 years	60–80 years	
HRchange (bpm)	46.88 ± 19.70	44.35 ± 13.03	38.53 ± 19.46	< 0.001
%PredHRmax	70.07 ± 11.16	74.97 ± 8.33	76.40 ± 11.76	0.008
6MWD (m)				
6MWD1	582.9 ± 73.91	538.60 ± 52.97	510.30 ± 57.57	< 0.001
95% CI	569.2 to 596.5	513.80 to 563.4	491.1 to 529.50	
6MWD2	593.1 ± 71.40	547.1 ± 62.03	512.00 ± 54.96	< 0.001
95% CI	579.90 to 606.30	518.00 to 576.10	493.70 to 530.30	
6MWD2 – 6MWD1	10.25 ± 36.06	8.45 ± 31.27	1.68 ± 21.23	0.116
95% CI	3.59 to 16.91	−6.185 to 23.08	−5.40 to 8.76	
Best of 2 trials	601.30 ± 71.79	553.00 ± 60.64	519.00 ± 55.42	< 0.001
95% CI	588.00 to 614.60	524.60 to 581.30	500.50 to 537.50	

Notes: Values are expressed as *mean* ± *Standard Deviation* (*SD*),
$p < 0.05$ represents a significant value.
m: metres; **kg**: kilogram; **bpm**: beats per minute; **BMI**: Body mass index; **6MWT**: 6-minute walk test; **6MWD**: 6-minute walk distance; **HR**: Heart Rate; **Highest HR**: Highest heart rate achieved during 6MWT; **HRR**: heart rate reserve; **HRchange**: Difference between HighestHR heart rate and resting heart rate; **%PredHRmax**: peak HR achieved during 6MWD expressed as %predicted maximum HR with predicted HRmax as [208−(0.7×Age)]; **95% CI**: 95% Confidence Interval; **6MWD1**: 1st trial of 6MWD;**6MWD2**: 2nd trial of 6MWD; *subject ethnicity profile compared with Singapore population profile.

Table 3. Univariate correlation coefficients (r) for 6MWD and subject variables ($n = 172$).

Variable	r	95% CI	*p*-value
Age (years)	−0.44	−0.5497 to −0.3063	< 0.001*
Gender	0.28	0.1400 to 0.4157	< 0.001*
Height (m)	0.38	0.2389 to 0.4969	< 0.001*
Weight (kg)	0.17	0.02043 to 0.3113	0.02*
BMI (kg/m²)	−0.44	−0.1925 to 0.1062	0.57
Average leg length (m)	0.36	0.2187 to 0.4806	< 0.001
Resting HR (bpm)	0.06	−0.09541 to 0.2030	0.47
HRR (bpm)	0.27	0.1207 to 0.3993	< 0.001*
%PredHRmax	0.36	0.2204 to 0.4821	< 0.001*

Notes: *$p < 0.05$ represents a significant value; CI 95%: 95% confidence intervnal; **m**: metres; **kg**: kilogram; Body mass index; **bpm**: beats per minute; **6MWD**: 6-minute walk distance; **HR**: Heart Rate; **HRR**: heart rate reserve; **%PredHRmax**: the percentage that highest HR achieved out of HRmax.

(HRR, bpm) −185.43−1.34 (age, years) −1.61 (weight, kg).

Comparisons with the 6MWD estimated using the previously published equations

Table 5 presents the age-matched measured data from this study compared to the age-matched 6MWD calculated using the predictive formulae from 11 previous similar studies.[16–26] The distance walked by the participants in this study was shorter than the calculated distances in 9 out of the 11 studies compared ($p < 0.001$), demonstrating the over-estimations with their predictive formulae,[16–18,20,22–26] with the exception of the study by Fernandes *et al.*[19] where our participants walked a significantly greater distance (91.06±

65.95) m, $p < 0.001$. The comparison made with Ngai *et al.* was statistically insignificant ($p = 0.22$).[21]

DISCUSSION

This study established an updated NRV and formulated the reference equations for 6MWD of healthy Singaporeans adults aged 21–80 years. This study reported that the overall mean 6MWD was 578.00 ± 75.38 m. Male subjects were found to walk a significantly longer distance than female subjects (600.32 ± 77.29 m versus 557.62 ± 67.84 m; $p < 0.001$), while the mean 6MWD decreased progressively with the advancement of age, from 601.30 ± 71.79 m (age 21–39 years) to 519.02 ± 55.42 m (age 60–80 years). The high ICC for repeated tests demonstrated good test–retest reliability and is consistent with previous studies.[21,24] The 6MWD is influenced by the learning effect[1,11,17,43] as the second test distance was consistently higher than the first test, but no more than 2%, which is well within the reported ranges for the healthy and diseased populations.[1,17,20,21,24,44] Two standardised tests were performed on the same day to avoid biases caused by the learning effect in this study, with the best of the two used in the analysis.

Age, gender, height, weight, leg length, HRR and %predHRmax influenced the 6MWD significantly in this study (Table 3), while BMI and resting HR were found to be statistically insignificant. Our subjects achieved 71.91 ± 11.32 %PredHRmax during the 6MWT (Table 1), indicating moderate-intensity effort, consistent with previous studies.[17,22]

Age and gender accounted for 24% of the 6MWD variance, while the influence of %predictHRmax explained 25.4% of the variance. This suggests that

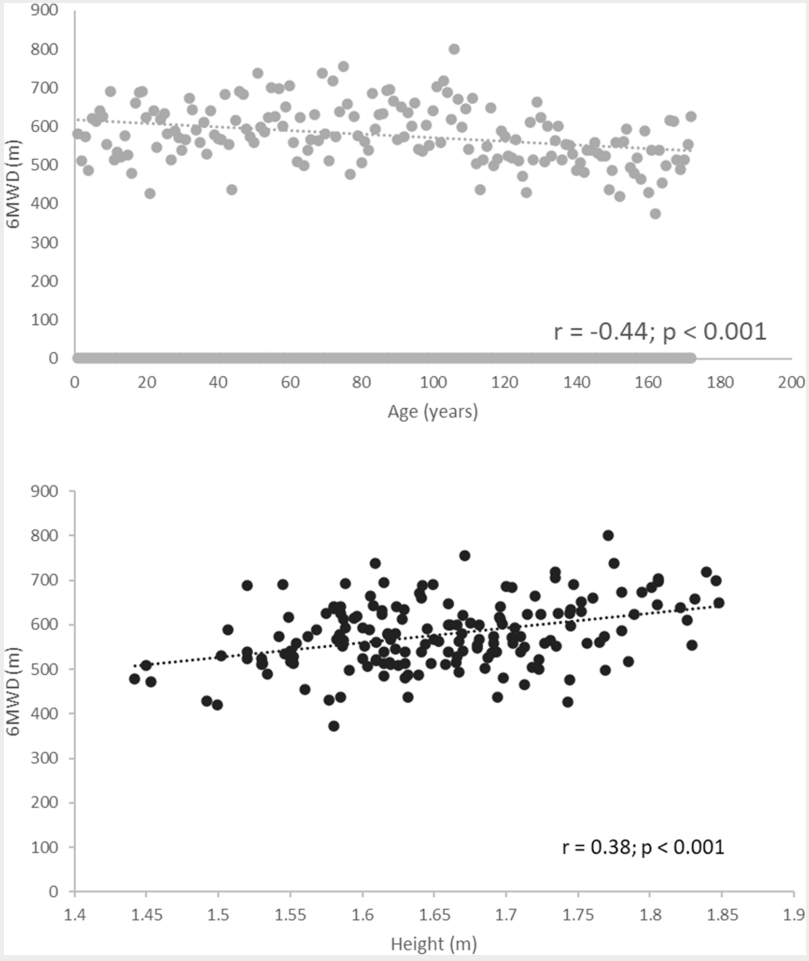
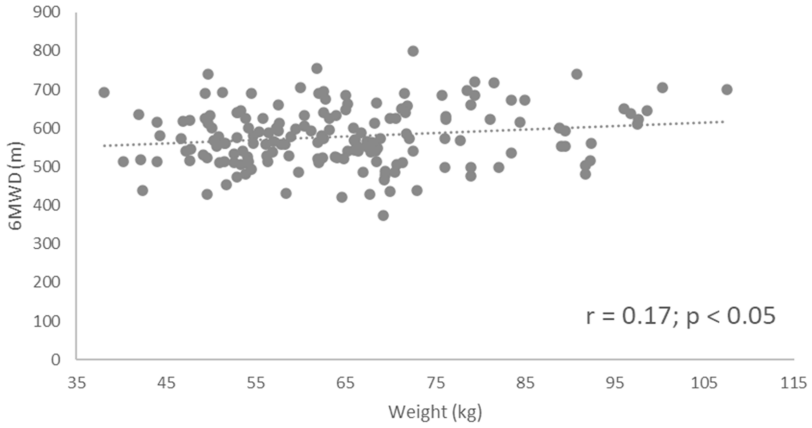
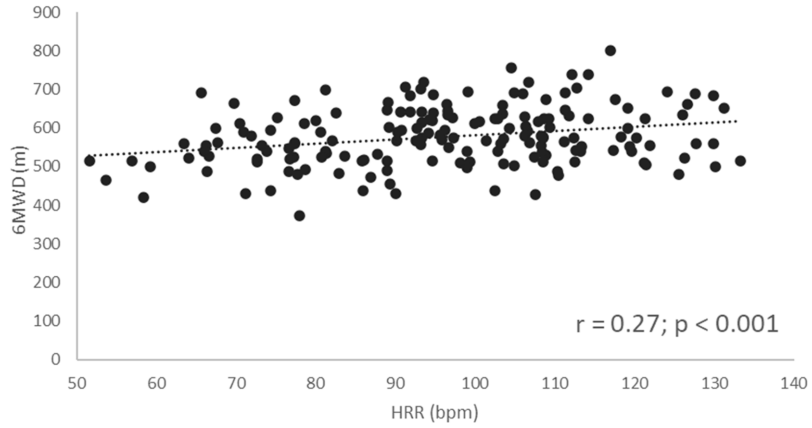


Fig. 1. The relationships between the 6MWD and Age, Height, Weight, HRR, and %PredHRmax; $p < 0.05$ represents the significance of an independent variable in predicting 6MWD.





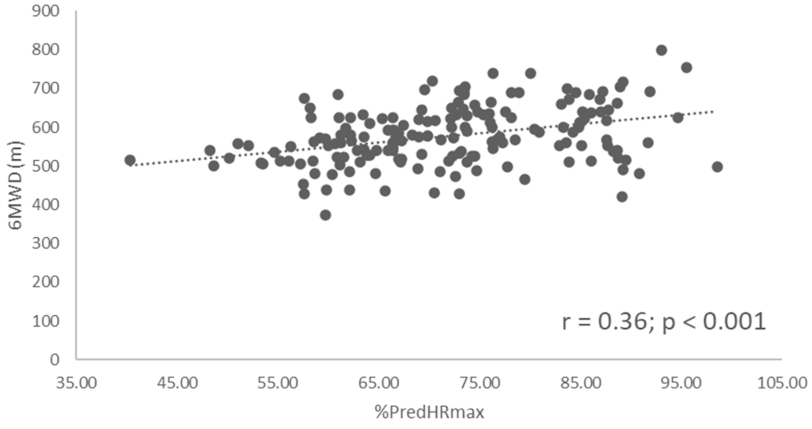


Fig. 1. (*Continued*)

age, gender, and %predictHRmax are the three most significant factors influencing the 6MWD. This report established two reference equations; one comprising simple pre-test variables with age and gender ($R^2 = 24\%$), indicating its predictive yet pragmatic application with obvious variables for any straightforward interpretation of the 6MWD. This simplified reference equation can also be particularly relevant to individuals on chronotropic agents, as such chronotropic effects may affect the regularity of the heart rate and rhythm, thus affecting the %predictHRmax. In contrast, the second reference equation comprised more variables and established a higher percentage of variance ($R^2 = 58\%$), which would be helpful for clinicians to benchmark the 6MWT performance of patients

Table 4. Linear regression models for predicting 6MWD.

Model	Independent variables	R^2	R^2 change	P (model)	Unstandardised coefficients		p (independent variables)
					B (95% CI)	SE	
	Pre-6MWT variables						
1	(Constant)	0.19	—	< 0.001	643.74 (620.77 to 666.70)	11.63	< 0.001
	Age				−1.77 (−2.33 to −1.22)	0.28	< 0.001
2	(Constant)	0.23	0.04	< 0.001	279.93 (255.79 to 304.07)	11.02	< 0.001
	Age				−1.39 (−1.94 to −0.87)	0.3	< 0.001
	Height				211.21 (62.55 to 359.88)	63.66	< 0.001
3	(Constant)	0.24	0.05	< 0.001	622.64 (597.31 to 647.96)	12.83	< 0.001
	Age				−1.65 (−2.2 to −1.11)	0.27	< 0.001
	Gender				35.03 (15.00 to 55.07)	10.15	< 0.001
	All 6MWT variables						
4	(Constant)	0.42	0.23	< 0.001	425.03 (368.83 to 481.24)	28.47	< 0.001
	Age				−2.27 (−2.75 to −1.78)	0.25	< 0.001
	%predHRmax				3.30 (2.50 to 4.09)	0.4	< 0.001
5	(Constant)	0.494	0.073	< 0.001	390.10 (335.59 to 444.60)	27.61	< 0.001
	Age				−2.15 (−2.61 to −1.69)	0.23	< 0.001
	%predHRmax				3.45 (2.70 to 4.20)	0.38	< 0.001
	Gender				41.24 (24.74 to 57.73)	8.36	< 0.001
6	(Constant)	0.524	0.03	< 0.001	233.08 (124.50 to 341.67)	55	< 0.001
	Age				−1.62 (−2.17 to −1.08)	0.28	< 0.001
	%predHRmax				4.01 (3.21 to 4.81)	0.41	< 0.001
	Gender				36.03 (19.69 to 52.38)	8.28	< 0.001
	HRR				1.03 (0.41 to 1.66)	0.32	< 0.001
7	(Constant)	0.542	0.018	< 0.001	274.38 (162.96 to 385.80)	56.43	< 0.001
	Age				−1.73 (−2.27 to −1.19)	0.28	< 0.001
	%predHRmax				4.17 (3.37 to 5.97)	0.4	< 0.001
	Gender				48.88 (30.01 to 67.75)	9.56	< 0.001
	HRR				1.06 (0.45 to 1.68)	0.31	0.001
	Weight				−0.89 (−1.58 to −0.21)	0.35	0.011
8	(Constant)	0.58	0.037	< 0.001	−185.43 (−445.62 to 74.76)	131.78	0.161
	Age				−1.34 (−1.90 to −0.78)	0.28	< 0.001
	%predHRmax				4.35 (3.58 to 5.12)	0.39	< 0.001
	Gender				27.46 (6.23 to 48.70)	10.75	0.012
	HRR				1.19 (0.60 to 1.78)	0.3	< 0.001
	Weight				−1.61 (−2.37 to −0.86)	0.38	< 0.001
	Height				288.28 (139.62 to 436.95)	75.3	< 0.001

Notes: $*p < 0.05$ represents a significant value; **6MWD**: 6-minute walk distance; **B**: unstandardised regression coefficient; **95% CI**: 95% Confidence Interval; **SE**: standard error; **HR**: Heart Rate; **%PredHRmax**: peak HR achieved during 6MWD expressed as %predicted maximum HR with predicted HRmax as [208 − (0.7 × Age)]; Gender: (1 = male, 0 = female); **HRR**: heart rate reserve (beats per minute).

or clients. The influence of age and gender on 6MWD has been well reported in earlier studies about 6MWD reference equations.[15,17–19,23,24,28] The negative association of age with 6MWD could be due to a decline in physical fitness, as it has been found that ageing results in muscle loss, reduction in $VO_{2\,max}$,[45–47] decreased stride length, and altered gait. Similarly, it is well established that females generally have lower cardiovascular and muscular fitness than males.[48–53] The influence of %predictHRmax, as a measure of cardiac response during a submaximal self-paced field walking test accounts for a significant proportion of the variability in test performance, suggests that cardiac response can be used as a surrogate measure of the exercise effort during the test.[20] Although including %predHRmax

Table 5. Age-matched comparison between measured 6MWD from this study and predicted 6MWD from reference equations of published studies.

Study (Predictive Equation)	Country	Measured 6MWD (m) mean ± SD	Predicted 6MWD (m) mean ± SD	Difference (m) (Measured− Predicted) mean ± SD	*p*-value
Poh *et al.* (2006) 45–85 years 6MWD (m) = 5.50 (%predHRmax) +6.94 (height, cm)− 4.49 (age, year) − 3.51 (weight, kg) − 473.27	Singapore	527.73 ± 59.15	560.33 ± 74.17	−32.60 ± 69.42	< 0.001
Camarri *et al.* (2006) 55–75 years 6MWD (m) = 216.90 + 4.12 (height, cm) − 1.75 (age, years) −1.15 (weight, kg) − 34.04 (gender : males = 0; females = 1)	Australia	530.71 ± 59.66	675.17 ± 44.11	−144.46 ± 56.44	< 0.001
Chetta *et al.* (2006) 20–50 years 6MWD (m) = 518.85 + 1.25 (height, cm) − 2.82 (age, year) −39.07 (gender : males = 0; females = 1)	Italy	597.98 ± 18.63	636.52 ± 32.37	−38.54 ± 18.04	< 0.001
Jenkin *et al.* (2009) 45–85 years Males, 6MWD (m) = 748 − 6.32 (age, years) + 0.64 (height, cm) + 2.69 (%pred HRmax); Females, 6MWD (m) = 541 − 3.81 (age, years) + 1.80 (height, cm) − 6.92 (BMI) + 2.41 (%pred HRmax)	Western Australia	529.08 ± 19.99	618.24 ± 51.66	−87.90 ± 30.10	< 0.001
Ben Saad *et al.* (2009) 40–85 years 6MWD (m) = 720.50 − 160.27 × gender (gender: males = 0; females = 1) −5.14 × (age, years) − 2.23 × (weight, kg) +271.98 × (height, m)	North Africa	533.21 ± 22.98	601.36 ± 89.74	−68.26 ± 74.02	< 0.001
Casanova *et al.* (2011) 40–80 years 6MWD = 361 − 4 (age, years) + 2 (height, cm) + 3 (HRmax/HRmax % *pred*) −1.5 (weight, kg) − 30 (gender : males = 0; females = 1)	North & South America	535.95 ± 48.87	552.49 ± 46.65	−16.28 ± 21.12	< 0.001
Kim *et al.* (2014) 22–59 years 6MWD (m) = 105.7 + 2.99 × (height, cm)	Korea	592.04 ± 26.34	605.70 ± 25.31	−13.08 ± 46.80	< 0.001
Ngai *et al.* (2014) 55–85 years 6MWD (m) = 722.35 − 5.11 × (age, years) + 2.19 ×(%predHRmax) − 41.31 × gender (gender: males = 0; females = 1)	Hong Kong	527.75 ± 19.61	535.95 ± 40.87	−8.88 ± 44.49	= 0.22
Fernandes *et al.* (2016) 25–75 years 6MWD (m) = 553.289 − 2.11 × (age, years) + 45.323 ×gender (gender: male = 1, female = 0)	West India	566.53 ± 78.59	475.47 ± 48.91	91.06 ± 63.95	< 0.001
Zou *et al.* (2017) 18–30 years Female: 6MWD (m) = −0.458 + (difference in heart rate ×1.113) + 3.494 × (height, cm); Male: 6MWD (m) = −11.394 + (difference in heart rate ×0.692) + 3.659 × (height, cm)	China	594.13 ± 72.14	618.65 ± 29.82	−24.51 ± 68.54	< 0.001
Oliveira *et al.* (2019) 18–70 years 6MWD = 721.7 − 1.6 × (Age, years) − 4.0 × BMI +0.9 × ΔHR × 58.4 × gender (gender: male = 1; female = 0)	Portugal	581.01 ± 35.31	639.17 ± 48.14	−58.16 ± 28.74	< 0.001

Notes: Values expressed as *mean ± Standard Deviation (SD)*.
*$p < 0.05$ represents a significant difference between age-matched subjects measured vs predicted 6MWD. **6MWD**: 6-minute walk distance.

increases the variance of the reference equation, there are several limitations in the clinical setting as the magnitude of HR change could be influenced by external factors such as the use of chronotropic agents. As such, we consider it necessary to report both equations so that clinicians can choose to apply the appropriate equation to those who may experience chronotropic impairments during the test, e.g., patients who have heart failure or beta-blocker use.

The reported 6MWD reference equations explained up to 58% of the variance, similar to other studies' findings,[15,17–19,23,24,28] despite the different age groups of the subjects. Eleven published studies (Table 4) were chosen to perform the age-matched comparison between measured 6MWD from this study and predicted 6MWD using their reference equations. Of the 11 studies being compared, nine overestimated the 6MWD[16–18,20,22–24] and one study underestimated the distance.[19] Only the 6MWD regression formula reported by Ngai *et al.* is not statistically significant compared to the Singaporean data.[21] The previously published reference equations did not reliably predict the 6MWD in our population. We found significant differences between measured 6MWD and 6MWD predicted from the published equations and could postulate two reasons. First, the published predictive formulae were derived from the NRV of the respective populations. Notably, Camarri *et al.*[6] reported that Australians covered a total of 655 ± 51 m (male: 685 ± 49 m; female: 628 ± 59 m) during the 6MWT; Ben Saad *et al.*[16] reported the average 6MWD for the West Africans was 624 ± 111 m (male: 711 ± 81 m; female: 511 ± 75 m), while the reference values for Western Indians were 483 ± 67.91 m (male: 512.38 ± 67.84 m; female 457.29 ± 56.75 m).[19] These reported values vary considerably from the NRV of our study. Naturally, the eventual calculated predictive 6MWD matched for the Singaporean anthropometric variables would differ significantly from the current findings, despite the consideration of age-matching. Second, the effect of %PredHRmax on 6MWD is well-established from previous studies.[19,21–26] and in this current report (25.4% of the variance). The range of %PredHRmax in the other studies differed substantially from $51.9 \pm 8.8\%$,[19] $63.0 \pm 10.5\%$,[26] $69.0 \pm 8.0\%$,[23] $80.0 \pm 10.0\%$,[21] and $87.0 \pm 13.0\%$[24]; however, this is congruent with the nature of a self-paced submaximal field walking test. Submaximal and self-paced testing relies heavily on self-perception, concepts which are reflected well in the variance in %PredHRmax among the different populations. Hence, we suggest this is a possible explanation as to why only the Ngai *et al.* predicted distance (total 6MWD: 563.0 ± 62.0 m; %PredHRmax: $80.0 \pm 10\%$) was statistically insignificant to our current results, while similar reports from China (total 6MWD: 502.0 ± 73.0 m; %PredHRmax: $69.0 \pm 8.0\%$)[23] and South Korean (total 6MWD: 598.5 ± 57.92 m; %PredHRmax: $63.0 \pm 10.48\%$)[26] were not. The implications of this, particularly in adults with chronic diseases, may include considerable errors regarding the level of disability and unrealistic expectations of the outcome measure. This justifies the use of our local specific reference equations and confirms the ATS recommendation to continue establishing updated regional reference equations.[1]

Some limitations in this study should be considered. First, the profile of existing subjects is statistically different from the overall Singaporean population profile despite presenting the three major ethnicities living in Singapore, with an over-representation of the Chinese ethnicity. Second, 67% of the subjects from this study were in the 21–39 age group, while the 40–59 and 60–80 age groups combined contributed to the remaining 33% of the overall sample size. This possibly skewed the results to the 20–39 age group with an over-representation of younger adults. Third, this study did not explicitly collect additional psychological data, such as depression, balance confidence, or fear of falling that might potentially influence the 6MWD, despite such information being screened via the PAR-Q$^+$. For example, the General Health Questions section of PAR-Q$^+$ screened for the loss of balance due to dizziness in the last 12 months in Question 3, while Question 6 from the Follow-up Questions section checked for mental health problems such as depression or anxiety.[34] Future studies should consider the inclusion of such information. Finally, there was also a 42% variance that could not be explained with the existing data. Future studies should establish missing variables that could account for the remaining variance.

Conclusions

This study updated the NRV and reference equations of 6MWD for healthy Singaporean adults aged 21–80 years. Age, gender, height, weight, HRR and %predHRmax were significantly correlated to 6MWD. Applying equations from other studies to the Singaporean population resulted in an overestimation of the 6MWD. The reference equation and NRV should be beneficial in establishing performance benchmarks to guide intervention and rehabilitation. Future follow-up studies should consider exploring reasons for the unexplained variance in our equation.

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Conflict of Interest

The authors declare no potential conflicts of interest for the research, authorship, and/or publication of this paper.

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Author Contributions

Meredith T. Yeung conceptualised and designed the study, analysed and interpreted the data, prepared and revised the manuscript critically for important intellectual content, and read and approved the final manuscript. Melissa Y. Chan and Katherin S. Huang conceptualised and designed the study and drafted and revised the manuscript critically for important intellectual content. Tian Jie Chen, Cyprian P. Chia, Meihiko M. Fong, Cherilyn S. Ho, Derek T. Koh, Mitchell J. Neo, and Mark Tan collected, analysed and interpreted the data. All authors approved the final manuscript.

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