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**Regression equations to predict 6-minute walk distance in Chinese adults aged  
55-85 years**

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Short Title: prediction of 6MWD in Chinese

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## ***Abstract***

**Objective:** 6-minute walk distance (6MWD) is used as a measure of functional exercise capacity in clinical populations and research. Reference equations to predict 6MWD in different populations have been established, however, available equations for Chinese are scarce. This study aimed to develop regression equations to predict 6MWD for Hong Kong Chinese.

**Design:** Cross-sectional study

**Subjects:** Healthy individuals aged 55 or above.

**Methods:** Subjects performed two 6-minute walk tests (6MWT) in accordance with a standard protocol. Heart rate (HR) was continuously monitored throughout the 6MWTs and the maximum HR was recorded. Measures recorded from the 6MWT that resulted in the highest 6MWD were used for regression analysis.

**Results:** Fifty-three subjects, aged  $69 \pm 7$  years, completed 6MWTs. The mean 6MWD was  $563 \pm 62$  m and was significantly correlated with age ( $r = -0.62$ ), height ( $r = 0.39$ ) and percentage of predicted maximal HR ( $\% \text{predHR}_{\text{max}}$ ) ( $r = 0.50$ ). A regression equation derived from the data showed that age, gender and  $\% \text{predHR}_{\text{max}}$  were independent contributors and together explained 65% of the variance in 6MWD. When HR was excluded, the equation explained 52% of the variance.

**Conclusions:** Regression equations were derived to estimate 6MWDs for Hong Kong Chinese. Application of these equations to Chinese living in different parts of China warrants further investigation.

**Keywords:** 6-minute walk distance, Chinese, exercise test, healthy individuals, regression equation

(Abstract: 200 words)

## **INTRODUCTION**

The 6-minute walk test (6MWT) is widely used to assess exercise capacity in older populations and in patients with chronic disease (1). The main outcome of the test is the distance walked (i.e. 6-minute walk distance, 6MWD). As the test is self-paced, and rests are allowed, it is considered to be an appropriate test for the assessment of walking capacity in daily life (1).

The 6MWD provides important information regarding survival in patients with chronic obstructive pulmonary disease (COPD) (2, 3), and idiopathic pulmonary fibrosis (4). In addition, 6MWD has been used to select patients for lung surgery (5, 6) and to evaluate interventions such as pulmonary rehabilitation (7), inhaled bronchodilators (8), the effects of supplemental oxygen therapy (9) and the use of a rollator (10).

When used as an outcome measure following an intervention, the difference in absolute 6MWD, percentage change in 6MWD, and change in percentage of the predicted 6MWD derived from equations developed in healthy individuals, have all been utilized (1). Several prediction equations to estimate 6MWD in healthy Caucasians have been reported (11-15). It appears that ethnicity (14) and variations in 6MWT protocol (15) may contribute to discrepancies between an individual's 6MWD and their predicted 6MWD. Lower 6MWDs in African-Americans compared to Caucasian Americans have

been reported (14) and equations published in Caucasian cohorts have been shown to over-estimate the distance walked by Asians (16). Geographic variations in 6MWD have also been reported with significant differences found in 6MWDs among healthy cohorts living in different countries and different regions of the same country (17). Hence, the published equation developed in Singaporeans (16), of whom most were Chinese (91%), may not be applicable for a population of Hong Kong Chinese.

Tsang (18) reported 6MWD reference values for healthy Hong Kong Chinese aged 21 to 70 years, of whom only four males were aged over 60 years. The walking course (15 m) was shorter than that recommended by published guidelines (30 m) (1) and their subjects were instructed to walk at a level of perceived exertion that ranged from 2 (weak/light) to 4 (somewhat strong) on the Borg RPE scale (19). The more frequent turns imposed by the short walking course, together with instructions pertaining to the required effort level, may have resulted in lower 6MWDs than may have been achieved using a protocol that did not attempt to standardise the effort level. The only other study that developed a regression equation in a Chinese population was reported by Poh et al (16). These authors studied 35 Singaporeans of whom 32 were Chinese. In their study, 78% of the variance in 6MWD could be explained by age, anthropometric data and the percentage of predicted heart rate (HR) maximum ( $\%predHR_{max}$ ) achieved during the 6MWT. However, there are some limitations to their equation. Specifically, the

inclusion of  $\%predHR_{max}$  limits its application in individuals with symptoms such as dyspnoea that constrain their walking speed; and in those receiving medications that affect HR response to exercise. It has been well established that apart from age and gender, anthropometric measures are significant contributors to 6MWDs (11, 12, 15, 16). Deurenberg-Yap et al (20) demonstrated a difference in the body mass index (BMI) /body fat (BF) relationship among Asians, i.e. Chinese, Malays and Indians living in Singapore. Further, a difference in this relationship among Chinese living in the United States and China has been reported (21); suggesting different diet, lifestyle and subject demographics may contribute to variability in 6MWDs. Based on the above observations, it is possible that the equation reported by Poh (16) may not be applicable to Chinese individuals living in Hong Kong. Thus, there is a need to derive a regression equation that can predict the 6MWDs of middle-aged and older Chinese adults living in Hong Kong to also enable quantification of an individual's functional limitation and provide clinicians and patients with a more accurate and realistic expectation of improvements in 6MWD following interventions.

The objectives of this study were to 1) measure 6MWDs in healthy Hong Kong Chinese aged 55 to 85 years, and, 2) develop an equation to predict the 6MWD for this population.

## **METHODS**

### **Subjects**

Community-dwelling healthy individuals aged 55 to 85 years with no documented history of cardiopulmonary disease were recruited. Potential subjects were asked to undergo spirometry (Spirometer, Pony FX, Cosmed, Italy) that was carried out in accordance with recommended guidelines (22). Exclusion criteria comprised abnormal spirometry (i.e. Forced expiratory volume in one second (FEV<sub>1</sub>) <80% predicted or FEV<sub>1</sub>/ Forced vital capacity (FVC) <70%); hypertension (resting blood pressure >150/100 mmHg); neurological disorders (e.g. stroke); metabolic disease (e.g. diabetes mellitus); or presence of recent illness such as an upper respiratory tract infection in the previous 4 weeks. Individuals with severe musculoskeletal disorders likely to affect their walking performance were also excluded. Approval for the study was granted by the Ethics Committee of the involved University. All subjects gave written, informed consent prior to data collection.

### **Procedures**

Subjects were asked to refrain from caffeine, alcohol and consumption of a heavy meal for at least 2 hours prior to the testing session and to avoid strenuous physical exercise in the previous 24 hours.

### ***Anthropometric measurement***

Height and weight were measured and used to calculate BMI. Right and left leg length was measured from the greater trochanter to the lateral malleolus using a measuring tape (23). The mean leg length was used in the analyses.

### ***Level of physical activity***

Physical activities undertaken during the previous week were recorded and categorised based on the total duration spent performing moderate intensity activity: "inactive" (<30 minutes per week); "insufficiently active" (30-150 minutes per week) or "sufficiently active" (>150 minutes per week) (15).

### ***Six-minute walk test (6MWT)***

The 6MWT was performed in accordance with published guidelines along a 30m hallway (1). HR was continuously monitored throughout the test (Polar RS8000CX, Kempele Finland). Measurements of HR were recorded prior to and at the end of each minute throughout the test. Oxygen saturation (SpO<sub>2</sub>, pulse oximeter, Konica Minolta, Japan), blood pressure (measured using a sphygmomanometer), level of leg fatigue (19) (rated using Borg scale 0-10) were measured before and immediately upon test completion. The test was repeated twice separated by a minimum 20-minute rest or until HR has returned to within 10 beats of the previous resting value. The same

investigator (SN) supervised all tests.

### ***Statistical analysis***

Data that did not conform to a normal distribution (assessed using the Shapiro-Wilks test) were transformed or analysed using non-parametric tests. Unpaired t-tests and Chi-squared test were used to compare data between genders. Variability in 6MWD between the two tests was calculated as the absolute (m) and percentage change in distance walked on the two tests. Test-retest reliability was examined using an intraclass correlation coefficient (ICC<sub>3,1</sub>). The maximum 6MWD achieved (better of the 2 tests) was used in the subsequent analyses. Relationships between the independent variables e.g. age, anthropometric data, lung function, %predHR<sub>max</sub> and 6MWD were examined using Pearson's correlation coefficients. Stepwise multiple regression analysis was performed on the variables that significantly ( $p < 0.1$ ) correlated with 6MWD in order to derive an equation to predict 6MWD. Measured 6MWDs were compared with predicted 6MWDs obtained from the equation derived by Poh et al (16) in Singaporean Asians by paired t-test. Data were analyzed using the statistical package (PASW, 17.0, SPSS Ltd, Chicago, IL, USA). A significant level of  $p < 0.05$  was used.

## **RESULTS**

### **Subject characteristics**

Seventy-four subjects enrolled in the study. Twenty-one were excluded due to the presence of cardiovascular disease (n=3), metabolic disease (n=4), pulmonary disease (n=2), musculoskeletal disorders (n=7) or abnormal spirometry (n=5). Fifty-three subjects (25 males) completed the study. Subject characteristics together with their 6MWDs are summarized in Table 1. Males were significantly taller, had greater leg length and were heavier (all  $p < 0.001$ ) (Table 1). Mean BMI was similar between males and females however more males were overweight or obese (68%) than females (40%) ( $p = 0.033$ ). Forty-seven percent of the subjects were considered to be "sufficiently active" for health benefits.

### **Six-minute walk distance**

The overall maximal 6MWD was  $563 \pm 62$  m, and was  $588 \pm 54$  m (478-702 m) for males and  $540 \pm 60$  m (402-632 m) for females ( $p = 0.004$ ). Test-retest reliability was good (ICC=0.85). Seventy percent of subjects walked further on their second test (mean increase  $26 \pm 33$  m,  $p < 0.001$ ) (Table 1). None of the subjects rested during the test and no adverse events were observed.

### **Heart rate, oxygen saturation and leg symptoms**

The peak HR achieved on the 6MWT was  $121 \pm 17$  bpm ( $80 \pm 10$  %predHR<sub>max</sub>). Twenty-one subjects exceeded 85% of their predHR<sub>max</sub>. There was a slight decrease in

SpO<sub>2</sub> (0.3±1.3%, *p*=0.07) at test end. Three subjects complained of leg fatigue (score > 0) at the end of the test.

### **Associations with six-minute walk distance**

6MWD was found to be significantly associated with age, height, %predHR<sub>max</sub>, FEV<sub>1</sub> and FVC (all *p*<0.01) and weight (*p*=0.073) but not with leg length, BMI nor level of physical activity (all *p*>0.05) (Table 2).

### **Predictors of six-minute walk distance**

Stepwise regression analysis revealed that age, gender and %predHR<sub>max</sub> were independent contributors to 6MWD (Table 3).

The model that included age and gender explained 52% of the total variance of 6MWDs (*F*=26.6, *p*<0.001). Age alone explained 38% while gender accounted for 14%.

The equation was as follow:

$$6MWD_{pred} (m) = 941.77 - (5.77 \times \text{age (years)}) + (44.71 \times \text{gender}) \text{ (where 1= male, 0=female).}$$

The inclusion of %predHR<sub>max</sub> in the model increased the amount of variance explained from 52% to 65%. In this model, age alone explained 38% while %predHR<sub>max</sub> and

gender contributed 14% and 13% of the variance respectively ( $F=29.8$ ,  $p<0.001$ ). The equation was as follow:

$$6MWD_{pred} \text{ (m)} = 722.35 - (5.11 \times \text{age (years)}) + (2.19 \times \%predHR_{max}) - (41.31 \times \text{gender})$$

(where 1= male, 0=female).

### **Comparisons with published regression equation**

The mean 6MWD measured in this study was significantly greater than the 6MWDs predicted using the equation reported by Poh et al (16) by  $21 \pm 59$  m (95%CI, 5 to 37 m,  $p=0.013$ ) (Fig 1).

### **DISCUSSION**

This study demonstrated that the mean 6MWD for healthy Hong Kong Chinese aged 55-85 years was  $563 \pm 62$  m. The ICC was high for repeated tests demonstrating good test-retest reliability, consistent with other studies (16, 18, 24). The 6MWD on the second test was significantly greater than the first by 5%, which is within the reported range obtained for disease (0-17%) (1) and healthy populations (2-8%) (12, 13, 15, 17, 24).

The influence of age and gender on 6MWD is consistent with other studies (11-13, 15, 17). Muscle wasting and weakness occurs with ageing, with the average loss of muscle

strength by the 70's and 80's being 20-40% (25). The reduced muscle strength (26), decreased stride length and altered gait (27) due to ageing may account for the inverse relationship between age and gait speed (28) leading to a reduction in 6MWD with advancing age. Anthropometric measures (11, 12, 15-17) and FEV<sub>1</sub> (24) have been reported as contributors to the variance of 6MWD, however, the effect of these contributors was not apparent in this study. We postulate that this could be due to a difference in stature and the BMI/ BF relationship between Caucasians and Asians (29). This may also, in part, explain why Poh et al (16) demonstrated that the Caucasian prediction equations overestimated the actual distance walked by the Singaporean Chinese.

Our subjects achieved  $80 \pm 10$  %predHR<sub>max</sub> during the 6MWT indicating moderate to high intensity effort consistent with previous studies (12, 15-17). The addition of %predHR<sub>max</sub> into the regression model increased the percentage of variance explained from 52% to 65%, a finding in accordance with Jenkins et al (15), who, in a study of Australians, reported an increase of 40% to 61% and 43% to 58% when HR was included in male and female-specific equations (15). Although including %predHR<sub>max</sub> increases the amount of variance explained, there are several limitations in the clinical setting as the HR achieved could be influenced by external factors. Since subjects were allowed to walk at their own pace during the 6MWT, differences in effort level may

lead to variation in gait speed, and hence influence the peak HR achieved. Further, in the clinical setting, administration of medications that attenuate the HR response to exercise could also influence the peak HR achieved during the 6MWT. We therefore considered it necessary to provide regression models, with and without the inclusion of %predHR<sub>max</sub>, for the different clinical applications required.

A comparison of the 6MWDs measured in this study with reference 6MWDs for Hong Kong Chinese of a similar age (18) showed a marked discrepancy. Our subjects, irrespective of age group, walked further than that measured in Tsang's study, (males: 61-70 years 615±46 m vs 484±90 m,  $p=0.014$ ; females: 61-70 years 566±50 m vs 432±54 m,  $p<0.001$ ). Such discrepancies may be due to the small number of subjects in Tsang's study (18) that were over 60 years old, constraints imposed on the subject's effort level during the 6MWT, and the use of a shorter track (15 m) (18).

The 6MWDs measured in this study exceeded the predicted 6MWDs using Poh's equation by a mean of 21 m (16). Though the difference was statistically significant, the actual difference was small and may not be of clinical significance especially when considering the relatively small number of subjects in both studies. The pooled mean values for anthropometric measures, 6MWDs, and %predHR<sub>max</sub> in our subjects are similar to Poh's (16). However, in contrast to their findings, height and weight were not

independent predictors to 6MWD in our study. We postulate that this may be due to differences in the BMI/ BF relationship among Chinese living in different countries (21). Geographical variations in 6MWDs measured in Caucasians have also been reported (17). Habitual walking speed, lifestyle and psychosocial factors are hypothesized to be other possible contributors to this variability (17). During this study, we also collected 6MWDs in 26 healthy Chinese females residing in Macau, a Chinese city close to Hong Kong. The 6MWDs recorded in Macau were significantly lower ( $490\pm 61$  m vs  $541\pm 60$  m,  $p=0.003$ ) than those of our Hong Kong females despite subjects being of the same age and having similar anthropometric characteristics. Although the sample sizes were small, this may provide further evidence in support of geographical variations in 6MWDs. Further study in this area is warranted.

The present study has some limitations including the relatively small sample size according to the suggested calculation of 10 subjects for each predictor (30). However, the anthropometric measurements of our subjects, stratified by gender, were within the reported median for the Hong Kong population (31) implying that our sample, albeit small, may still be applicable for population inference. Nevertheless, validation of our equation using a separate cohort of Hong Kong Chinese is necessary.

Predicted 6MWD values could assist in evaluation of intervention for patients with

impaired exercise capacity, such as patients with chronic diseases. This study demonstrated the 6MWD performance of Hong Kong Chinese aged 55 or above and developed prediction equations specifically for this population. Age, gender and %predHR<sub>max</sub> were found to be the major contributors accounting for 65% of the variability of the 6MWD. Discrepancies between the measured 6MWDs in this study and the predicted values derived in Singaporean Chinese may be due to geographic variations in 6MWD. Further study with a larger sample and the inclusion of Chinese subjects from different regions within Asia is warranted.

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Table 1 Characteristics of the 53 subjects and results of the 6MWTs

	Male (n=25)	Female (n=28)	Total (n=53)
<b>Age, years</b>	69.1±6.3	69.5±6.8	69.3±6.5
<b>Height, cm</b>	162.2±5.2***	152.0±5.8	156.8±7.5
	Range 154 to 171	Range 141 to 165	Range 141 to 171
<b>Leg length, cm</b>	78.9±3.7***	74.2±5.3	76.5±5.1
<b>Weight, kg</b>	62.7±7.2***	52.8±7.9	57.5±9.0
<b>BMI, kg/m<sup>2</sup></b>	23.8±2.3	22.8±2.8	23.3±2.6
<b>Weight Category<sup>32</sup></b>			
Underweight (<18.5)	0(0)*	0(0)	0(0)
Normal (18.5-22.9)	8(32)	17(61)	25(47)
Overweight (23-24.9)	10(40)	2(7)	12(23)
Obese I (25-29.9)	6(24)	8(29)	14(26)
Obese II (≥30)	1(4)	1(4)	2(4)
<b>Lung Function</b>			
FEV <sub>1</sub> , L	2.21±0.41***	1.70±0.35	1.94±0.46
FEV <sub>1</sub> , % predicted	89±8**	103±19	96±16

FVC, L	3.00±0.57***	2.19±0.42	2.57±0.64
FVC, % predicted	93±10**	107±19	100±17
FEV <sub>1</sub> /FVC, %	74±4**	78±4	76±4
<b>Level of Physical Activity</b>			
Sufficiently active	15(60)	10(36)	25(47)
Insufficiently active	10(40)	18(64)	28(53)
Inactive	0(0)	0(0)	0(0)
<b>Smoking History</b>			
Current smoker	4(16)***	0(0)	4(7)
Ex-smoker	9(36)	0(0)	9(17)
Non smoker	12(48)	28(100)	40(76)
<b>6MWT</b>			
6MWD test 1, m	557±59**	512±49	533±58
6MWD test 2, m	587±63**†	534±63†	560±64†
6MWD(better test),m	588±54**	540±60	563±62
	(478 to702)	(402 to 637)	(402 to 702)
Diff test 2-test, m (%)	29±27 (5±5%)†	24±39 (5±8%)†	26±33 (5±6%)†
95% CIs, m (%)	18 to 40 (3 to 7%)	9 to 39 (2 to 8%)	17 to 36 (3 to 7%)

### HR and SpO<sub>2</sub> (better of 2 tests)

HR peak, bpm	122±18	119±17	121±17
%predHR <sub>max</sub> , %	81±10	79±10	80±10
95% CIs, %	77 to 85	75 to 83	77 to 83
SpO <sub>2</sub> end-test, %	97.7±1.4	98.1±1.4	97.9±1.4

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Data are mean ± SD (range) or number (percentages) unless otherwise stated; BMI= Body mass index; FEV<sub>1</sub>= Forced expiratory flow volume in one second; FVC = Forced vital capacity; Level of physical activity: "Sufficiently active"= participating more than 150 minutes of moderate-intensity physical activity in the previous week; "Insufficiently active"= participating 30-150 minutes of moderate-intensity physical activities in the previous week; "Inactive"= participating moderate-intensity of physical activities less than 30 minutes in the previous week (15); non smoker= subject who has never regularly smoked cigarettes; ex-smoker= subject who smoked regularly but had ceased to smoke prior to the study; 6MWT= 6-minute walk test; 6MWD= 6-minute walk distance; Diff test 2- test 1= difference between 6MWDs measured in test 2 and test 1; %predHR<sub>max</sub>=peak HR achieved during 6MWD expressed as %predicted maximum HR with predicted HR<sub>max</sub> as 220-age; SpO<sub>2</sub>= oxygen saturation. \**p*<0.05, \*\**p*<0.01, \*\*\**p*<0.001 for comparisons between males and females; †*p*<0.001

compared to test 1.

Table 2 Univariate correlation coefficients (r) for 6MWD and subject variables (n=53)

	Age (years)	Height (cm)	Leg length (cm)	Weight (kg)	BMI (kg/m <sup>2</sup> )	FEV <sub>1</sub> (L)	FVC (L)	%pred HR <sub>max</sub>
r	-0.62	0.39	0.05	0.25	0.04	0.58	0.59	0.50
p value	<0.001	0.004	NS	0.073	NS	<0.001	<0.001	<0.001

BMI= Body mass index; FEV<sub>1</sub>= Forced expiratory flow volume in one second; FVC = Forced vital capacity; %predHR<sub>max</sub>= peak HR achieved during 6MWD expressed as %predicted maximum HR with predicted HR<sub>max</sub> as 220-age; NS: not significant at  $p>0.1$ .

Table 3. Linear regression models for predicting 6MWD

Model	Independent variables	R <sup>2</sup>	R <sup>2</sup> change	F	P value (model)	Unstandardized coefficient		Standardized coefficient	P value (independent variables)
						B (95%CI)	SE		
1	(Constant)	0.38	-	31.5	<0.001	971.44 (824.76 to 111.13)	73.07		<0.001
	Age					-5.89 (-8.00 to -3.78)	1.05	-0.62	<0.001
2	(Constant)	0.52	0.14	26.6	<0.001	941.77 (809.55 to 1073.99)	65.83		<0.001
	Age					-5.77 (-7.65 to -3.88)	0.939	-0.61	<0.001
	Gender					44.71 (20.51 to 68.91)	12.05	0.37	0.001
3	(Constant)	0.65	0.13	29.8	<0.001	722.35 (567.95 to 876.76)	76.83		<0.001
	Age					-5.11 (-6.77 to -3.45)	0.83	-0.54	<0.001
	Gender					41.31 (20.33 to 62.28)	10.44	0.34	<0.001
	%HR <sub>max</sub>					2.19 (1.16 to 3.23)	0.52	0.37	<0.001

B=unstandardized regression coefficient; SE=standard error; % HR<sub>max</sub>= peak HR achieved during 6MWD expressed as % predicted maximum HR with predicted HR<sub>max</sub> as 220-age; Gender (1= Male, 0=Female)

## Figure Legend

Figure 1 Comparison of the measured 6MWD in this study and the predicted 6MWD determined from the equation derived in Poh's study (16). Line of identity is shown.

Footnote: \* referred to the longest distance walked in Test 1 and Test 2.

