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DEVELOPING A PREDICTION EQUATION FOR THE SIX-MINUTE WALK TEST IN HEALTHY AFRICAN-AMERICAN ADULTS

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DEDICATION

First and foremost, I am very thankful and grateful to my God for all the guidance, blessings, and support throughout this thesis and throughout my life. Most importantly, none of this could have happened without the one person who always stays by my side: my beloved mom. I dedicate this thesis to my mom, who offered her encouragement, support, prayers. I always call her whenever I feel down, and always I get motivated when I hear her voice praying and supporting me. This thesis stands as a testament to your unconditional love and encouragement. Thank you, mom for everything. Also, to my family and friends for supporting me throughout my thesis, especially my beloved wife and my adorable daughter for supporting me by listening, worrying, encouraging, caring, and celebrating with me throughout my achievements.

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Developing a prediction equation for the six-minute walk test in healthy African-American adults

By

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ABSTRACT

The six-minute walk test (6MWT) measures the total distance that an individual walks in a time frame of six minutes. It is a rough estimate of the functional exercise capacity of a patient and can be a predictor of mortality and morbidity. The goal of the 6MWT is to walk as fast as possible to cover as much ground as possible in six minutes. Currently, there are about 24 studies that has developed prediction equations to estimate the 6MWT distance in an individual, but only ~10% of the subject pool were black. As such, this study aimed to establish a prediction equation for six-minute walk distance (6 MWD) in healthy black adults. A total of 60 healthy black adults (28 male, 32 female) aged between 18 to 67 years old and a body mass index ranging from 17.2 to 32.3 kg/m^2 performed 6 MWT using American Thoracic Society guidelines for the 6MWT. Heart rate (HR) at rest was 80 (SD 10) beats/min and the mean HR for the full 6MWT was 137 (20) beats/min (72% of predicted HR_{max}). Males walked for a total distance of 709 (68) m (range of 603 to 841 m) while females walked for a total of 627 (55) m (range of 498 to 764 m). The first multiple regression model for healthy black adults was: Distance covered in six minutes = 78.39·(sex) + 2.02·(mean HR) + 2.03·(height in cm) + 8.0, Adjusted $R^2 = 0.58$, SEE = 47.5 m, $p < 0.001$. The second model was: Distance covered (m) = 61.5·(sex) + 1.24 · (height in cm) + 424.8, adjusted $R^2 = 0.27$, and the SEE = 62.5 m, $p < 0.001$. In conclusion, this regression model best predicts distance walked in black subjects < 40 years of age.

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CHAPTER I

INTRODUCTION

The six-minute walk test (6MWT) measures the total distance that an individual can walk as fast as possible along a 30 m corridor in six minutes. An individual undertaking the test is allowed to rest or self-space as required as they walk. It is a rough estimate of functional capacity assessed in a clinical environment that complements the measurement of peak oxygen uptake [1]. Developed by Balke in 1963 [2], clinicians today use the 6MWT to assist them on the prognosis, severity of disease, and response to treatment [3]. For example, clinicians can use the 6MWT to predict medical and surgical complications postoperatively [4]. The 6MWT is also a predictor of morbidity and mortality in heart failure [5] those with chronic obstructive pulmonary disease (COPD)[6]. It has been widely adopted as it has proved to be reliable, safe, inexpensive and easy to administer [7].

The use of a prediction equation to estimate the distance walked in a normal, healthy individuals is attractive to practitioners as it allows for the calculation of a metric for exercise performance in patients with cardiopulmonary diseases efficiently. However, there are a variety of prediction equations in literature which makes it difficult to establish which ones should be used. In fact, there are about 24 studies which developed prediction equations for the 6MWT [3, 7-30]. However, the prediction equations are only useful for the population studied as there are racial differences in the 6MWT [8]. Despite the large number of studies published on predicting the 6MWT, only a small number of studies cross-validate these equations [9]. Comparing prediction equations derived from one population is important in refining prediction equations [9].

Statement of the problem

Existing prediction equations for the 6MWT have been based on a multiple linear regression model. Age, weight, height, and sex are the usual predictors for the 6MWT. To our knowledge, no studies incorporating 6WMT have been conducted on a healthy adult African-American population. There have been prediction equations for the 6MWT developed for the Nigerian population [10], but that is only about 10% of the total sample size of all the studies to date (Tables 1-2). Since vital capacity (i.e. lung volume) is about 15% lower in blacks compared to age, height and sex-matched whites [31, 32], and the diffusing capacity is also lower in blacks compared to matched whites [32, 33], then specific equations should be made for the 6MWT in the black population. There is also ~6% larger hemoglobin concentration in whites compared to blacks [33], so arterial oxygen content and total oxygen transport would also be lower compared to whites. A reduction in total oxygen transport reduces functional capacity, and so the distance traveled over six minutes could also be lower in blacks compared to the white population. Several studies show that when matched for age and height and sex, the distance traveled over 6 minutes in the Nigerian population (i.e. black population) [10] is 30% less compared to whites [16, 18, 25]. This suggests that there may be racial differences between the distance traveled over 6 minutes between the two different populations.

Studies performed on healthy subjects have recorded significant differences in the mean distance walked given a person's age, height, sex, and sometimes weight (Tables 1-2). Among other factors, differences in study populations and methodology could influence the results. Additionally, most of the available predictive equations reveal a high variability in the distance walked over six minutes, signifying that others factors often not considered in test performance could play a significant role in the distance walked. For example, the difference in the predicted 6MWT results vary by 301 to 430 m (Table 3), demonstrating huge inter-study differences.

Purpose of the study

The purpose of this study is to develop a prediction equation for 6MWT in healthy adult African-Americans (herein otherwise known as the black population). Prediction equations for the 6MWT in the black population are lacking. This study aims to fill this existing gap in the literature.

Research questions

1. What is the prediction equation for 6 MWT in healthy African-Americans?

2. How does this prediction equation compare to other prediction equations?

Significance of the study

The current study is important as the black population continues to have poor health outcomes compared to whites [34]. Prediction equations for the 6MWT is attractive to practitioners this test can estimate functional capacity in a cost-effective manner [9]. A range of factors such as age, height, and weight can influence the distance walked over six minutes. Furthermore; differences in lung volumes, pulmonary diffusing capacity, and hemoglobin concentration can differ between various racial groups. Thus, one could overestimate the predicted distance walked in blacks if using a prediction equation for the white population, which would incorrectly categorize a black individual as having a poor functional capacity.

Only one study to date focuses on the 6MWT in the healthy black population [10]. Thus, this investigation will add to the literature by recruiting from a healthy black population in Atlanta, GA.

Assumptions

There were various assumptions in this study. The first assumption was that the researcher followed the American Thoracic Society guidelines and conducted the 6MWT test appropriately. The second assumption was that the researcher coached and encouraged the subject appropriately during the test such that the subject gave a best effort. Third, the subject gave his or her best effort. And lastly, subjects of all adult ages would be recruited.

Limitations

One limitation was the ability to recruit healthy adult male and black female subjects of all ages. Specifically, it was difficult to recruit older subjects (>50 years old) as most of the subjects that attended Georgia State University are younger (< 29 years old). A second limitation was that the subjects were selected in only one geographical location (Atlanta, GA), and were mostly a part of the Georgia State University community. A third limitation was the difficulty in testing subjects during the weekends given the security issues of the Petit Science Center. The security guards did not allow for subject testing on the weekends, and this issue took a few weeks to correct.

Definition of Terms

ATS: American Thoracic Society.

BMI: Body mass index. It is kg divided by height in m^2 reported as kg/m^2

Prediction equation: A mathematical equation that predicts a value of the response variable for given values of factors [8].

6MWT: A test that measures the total distance that an individual can walk along a 30 m corridor to the best of his or her ability in a time frame of six minutes [16].

CHAPTER II

REVIEW OF THE LITERATURE

Introduction

The 6MWT is extensively used in clinical practice as well as in a laboratory setting to determine the aerobic endurance of an individual [27]. The test involves simple procedure whereby a patient walks as fast as possible back and forth a 30 m corridor. The reliability and validity of 6MWT has been established for clinical purpose in various population groups [27] including a systemic review of literature [35]. Although originally the test was developed for assessment of individuals in physically demanding activities by Balke in 1963 [2], over the years the research has set the utility of 6MWT in various disease conditions including heart failure [5] , COPD [6], obesity [36], cerebral palsy [37], amputation survivors [38], genetic disorders such as Down's syndrome [39], Alzheimer's disease [40], and fibromyalgia [41]. The utility of 6MWT is not limited to disease conditions and can be used for normal populations including extremes of age such as children [37], and older adults [42]. The data has been generated for various ethnic population groups including Arabs [11] Singaporeans [8], Brazilians [22], North Africans [13, 23, 24], Nigerians [10], Pakistanis [19], Indians [3], and Europeans [9].

The studies from different racial groups presented varying results that may suggests genetic and cultural differences. Studies from different racial groups showed differences in walking performance [35] thus indicating the importance of generating racially specific prediction equations. In the United States, there is much racial diversity, and thus it is important to provide the 6MWT predictions based on each racial group. For example, the African-American population in the United States is ~43 million (~13% of the total U.S.

population) [43], and it was our intent to recruit healthy volunteers from this ethnic group to fill the existing gap in the literature. As shown in Tables 1-2, the black population is under-represented in the development of prediction equations for the 6MWT. Thus, it was the objective to collect 6MWT data on black subjects from Atlanta.

Lung size and anthropometric differences between blacks and whites

The perceived difference of health parameters among blacks arises from multiple factors including anthropometric measurements. Over the years, number of studies have demonstrated that the lung size of black subjects is much smaller in comparison to their white counterparts [44-46]. The scaling factor of 0.85 to 0.88 has been advocated for accounting the lung size differences of the black population for appropriate equations [46, 47]. For example, vital capacity (i.e. lung volume) is about 15% lower in blacks compared to age, height, and sex matched whites [31, 32], and the diffusing capacity is also lower in blacks compared to matched whites [32, 33]. There is also ~6% larger hemoglobin concentration in whites compared to blacks [33], so arterial oxygen content and total oxygen transport is lower in the black poulation. A reduction in total oxygen transport could lower functional capacity, and so the distance traveled over six minutes could also be lower in blacks compared to the white population. Several studies show that when matched for age, height, and sex, the distance traveled over 6 minutes in the Nigerian population (i.e. black population) [10] is 30% less compared to whites [16, 18, 25]. This result suggests that there may be ethnic differences between the distance traveled over 6 minutes between the two different populations.

Furthermore, anthropometric characteristics differ between blacks and whites. Bone mineral content and bone mineral density, are larger in blacks compared to whites [48]. Limb mass is also larger in the black population [48]. This could reduce the distance traveled over six minutes. The studies from various ethnic groups for standardization of 6 MWT demonstrated that muscle mass and body mass index were factors accounting for observed differences in 6MWT performance among various groups [8, 49].

Studies on the 6MWT in healthy subjects

To our knowledge, there are 24 studies that have developed prediction equations in healthy adults [3, 7-30] (Tables 1-2). There is a wide range of the estimated predicted distance covered over six minutes [3, 7-30]. The minimum and maximum predicted distances given an individual's height, age, and sex are listed in Table 3. There is a 301 to 430 m difference in the predicted distance covered for six minutes when standardizing to height, age, and sex. For example, Nigerians covers more distance than Arabs, but Nigerians covered less distance in compare to Brazilians, Americans, and Tunisians (Table 2).

Alameri *et al.* [11] recruited 238 young Saudi adults and reported that men walked longer in compare to women. The prediction equations from other populations overestimated the Arab 6 MWD by 109-340 meters. The regression analysis showed that age and height were most prominent variables for observed differences among Arab population.

To overcome the limitations of small sample size, Britto *et al.* [12] conducted a multicenter study with 617 participants. The authors also measured the physiological responses to test in addition to weight, height, and BMI. It was shown that age, sex, height, and change in HR during the 6MWT accounted for 62% of the variability in distance walked.

Bourahli *et al.* [13] recruited 200 young North African adults (16-40 years) and calculated the distance covered during 6MWT. The authors demonstrated that age, body mass index, gender, lean mass, forced expiratory volume in 1 second (FEV_1), and moderate intensity physical activity during the week predicted the distance traveled over six minutes. The multiple linear regression model explained 58% variability among test parameters. The reference equation was validated using second group of subjects comprising 39 individuals showing adequate agreement [11]. Another study from the same region recruited older adults (40-80 years) from Tunisia. The study observed that age, sex, height, and size accounted for 60% shared variance in distance walked for six minutes [23].

Hill *et al.* [14] recruited 77 healthy Canadians to describe the test performance for 6 MWT. The authors used robust methodological approach using ATS protocol [1] and presented cardiorespiratory data representing physiological response. The study revealed that 49% variance was attributed to age and gender. There was high correlation between the test performance and oxygen uptake at the test end thus underlying the importance of physiological parameters.

Fernandes *et al.* [3] recruited 174 western Indians (25-75 years old) and demonstrated that 6MWT performance correlated with age, height, and weight in univariate analysis. Stepwise multiple regression demonstrated age and sex as independent variables. The study results demonstrated that equations derived for whites, North Indians, South Indians overestimated the predicted value for western Indians. Another study from Asia selected 35 Singaporeans (45-85 years), which showed no significant differences in distance walked between males and females [8]. The stepwise multiple linear regression equation demonstrated that age, height, weight and percent predicted of maximum heart rate contributed to 78%

variance in the model. Like other studies from Asia, the distance traveled over six minutes was less compared to whites [16, 27].

Duncan *et al.* [9] used a novel approach to overcome the limitations of prediction equations using allometric equations. Allometric equations take the general form $Y = aM^b$, where Y is some biological variable, M is a measure of body size, and b is some scaling exponent. The authors recruited 125 adults, and the study demonstrated that all the available prediction equations showed relationships except those in the Arabic population [11] and every prediction equation demonstrated different results from actual except in subjects from Brazil [22]. The equations derived from Iwama *et al.* [23] demonstrated similar coefficient variation and bias. About 52% of the variability in the allometric model was attributed to BMI, age, and height.

In order to simplify the data, the predicted 6MWT distance is estimated based on 5542 subjects pooled from 24 studies (Tables 1-2). The mean predicted walk distance for 25 years old and 80 years old for both males and females of the same height is presented in Table 4. It is felt that the weighted average predicted distance based on 24 studies (Table 4) is currently the most accurate predicted distance given the huge variability between studies.

CHAPTER III

METHODOLOGY

This study was performed in conjunction with another study that examined differences in pulmonary diffusing capacity for nitric oxide between black and white subjects. This study was approved by the Georgia State University Ethics Board (IRB #H16120, Reference # 335588). Healthy non-smoking black men and women, mostly from Georgia State University, were recruited for one session of lung function tests and a 6MWT.

We aimed to recruit more than 100 healthy African-Americans in the age range of 18-90 years old. The participants were sub-grouped in five age groups in the age range of 18-29, 30-39, 40-49, 50-59, 60-69 years, 70-79 years of age, and ≥ 80 years old. We aimed to have 26 individuals (13 male and 13 female) in each age group to ensure adequate representation of all ages.

Inclusion criteria

- Apparently healthy, black, non-smoking and non-pregnant individuals' ≥ 18 years of age, with a body mass index (BMI) ranging from 17.0 to 34.9 kg/m^2. Non-smoking was defined as never smoked or quit smoking > 6 months previously.
- No cardiopulmonary disease or absent of major signs/symptoms suggestive of cardiopulmonary disease [50].

Exclusion criteria

- Individuals who were not 18 years of age or older, who are not black, or have a BMI < 17.0 or > 35.0 kg/m^2, or are currently smoking or ceased smoking within the previous six months, or are pregnant.
- Have cardiopulmonary disease or presence of major signs/symptoms suggestive of cardiopulmonary disease [50].
- Have chest or abdominal pain or any cause, stress incontinence, dementia or in a state of confusion [51].

Procedures

The study was conducted at Room 457 of Petit Science Center, of Georgia State University, and the procedures lasted approximately 1.75 hours per subject. Subjects signed an informed consent to participate in the study. Subjects filled out a questionnaire about their date of birth, sex, as well as a physical activity readiness questionnaire (PAR-Q) and a health questionnaire. Then selection anthropometric measurements were taken of selected participants including age, gender, height, weight, body mass index, waist size, and hip size. The average heart rate recorded via a POLAR A300 heart rate monitor (Polar Electro Oy, Kempele, Finland) during these lung function tests (i.e. 20-30 minutes) was used for data analyses. The ATS protocol [1] was used to explain the walk protocol to the participants. The subjects were instructed to walk as fast as possible for 6 minutes and take rest/slow down if necessary during the test time. Every participant walked alone back and forth along 30 m hallway. The participants were instructed to use loose clothing with comfortable footwear. Standardized phrases were used during the conduction of the test rather than individual statements. Laps were counted using a lap counter. Test termination criteria were explained to the participants before the test and participants were instructed to terminate the test if they suffered pain or breathlessness during test.

During exercise, a Polar heart rate monitor was used to measure the average heart rate, peak heart rate and recovery heart rate after one minute of completion of the test. The corridor was marked every 1.5 meters, and distance traveled during the test period were measured. Upon completion of test, study participants were asked to rate perceived exertion and fatigue on the Borg scale (range 6 to 20) with 6 = no exertion at all and 20 = maximal exertion [52].

All data were manually recorded on specially formatted collection sheets which was stored in a locked file cabinet in PSC 457. This lab was locked at all times with access granted only to the faculty advisor and student researchers. Electronic backup of information was provided by the investigators on excel spreadsheets on password protected computers, locked inside PSC 457. Subjects were paid $30 for their participation. The funding for this study was from the Jerome M. Sullivan Research Fund from the American Respiratory Care Foundation.

Statistical Analysis

Independent *t*-tests were used to compare the age and anthropometric parameters (height, BMI, waist circumference, hip circumference) between males and females. A repeated measures analysis of variance (ANOVA) was used to compare the mean heart rates measured over four different time points: At rest, over the full six-minute test, the peak heart rate during the test, and the heart rate at one-minute recovery.

A correlation between the distance traveled over six minutes, and age, age^2, sex, height, weight, mean heart rate over the full distance and peak heart rate measured during the test was examined first. From there, a stepwise multiple linear regression equation was developed with the variables that most correlated with the distance traveled over six minutes.

In prediction studies, the number of subjects should be sufficiently large. The larger the sample, the more likely it will be to represent the population. It is known that there is a direct relationship between the correlation and the ratio of the number of variables in the model (k) to the number of participants in the model (n), such that $(k - 1) \div (n - 1)$ [53]. For example, if a study has 40 participants and 30 variables, the R^2 would be 0.74 based on chance alone and the results would be meaningless. Thus, it is recommended that there be at least a 10:1 participant to variable ratio to avoid this error [53]. Another source suggests to use the formula $n \geq 50 + 8 \cdot k$ to predict how many subjects would be needed to develop a reliable equation [54]. According to this formula, studies where there are five potential predictors for the 6MWT (age, age^2, the interaction term $age \cdot age^2$, sex, weight, height), should include at least 60 to 98 subjects.

The lower limit of normal (LLN) was calculated by multiplying the standard error of the estimate by 2.0 and then subtracting that number from the prediction[1]. This value would represent the 2.5th percentile according to t-tables. Any patient that has a value below LLN was considered a reduction in functional capacity. The upper limit of normal (ULN) was calculated by multiplying the standard error of the estimate by 2.0 and adding it to the prediction[1]. This value would represent the 97.5th percentile according to t-tables. Any subject that has a value above the ULN would indicate a clinically meaningful increase in the distance traveled over six minutes above the predicted, which would signify superior functional capacity. A Type I

[1] When the Degrees of Freedom is 60, the z-score is not ± 1.96 for the 2.5th and 97.5th percentiles, it is ± 2.00.

probability level of 0.05 will be used. Statistical software utilized for this project was IBM SPSS Statistics Version 21.0, Chicago, IL.

CHAPTER IV

RESULTS

Subject characteristics

Between July to December of 2016, 60 subjects were recruited and all 60 completed the study. The anthropometric measurements of study subjects are shown in Table 5. The sample consisted of 32 females and 28 were males. The age of selected individuals ranged between 18 years and 67 years. The average weight was 73 ± 14 kg. Males were slightly heavier and taller (79 ±11 kg, 176 cm) than females (68 ± 14 kg, 163 cm). The BMI was not different between males and females. Heart rate measured at rest ranged from 59 to 105 beats/min (mean 80 ± 10 beats/min).

Six-minute walk distance and heart rates during the test

The average distance covered during test was 709 ± 68 meters for males and 627 ± 55 meters for females with average difference of 76 meters ($p < 0.001$) (Table 6). The average heart rate for the full six-minute test was 137 ± 20 beats/min which is about 72% of predicted maximum heart rate (Table 6). The peak heart rate was 151± 22 beats/min, which was 79% of predicted maximum heart rate. At one minute post-exercise, the heart rates dropped 109 ± 22 beats/min (57% of predicted maximum heart rate). The differences between these heart rates were statistically different (Figure 1).

6MWT prediction equation

The distance traveled over six minutes was significantly correlated to sex, height, the mean heart rate for the full test, and the peak heart rate during the test (Table 7). Sex, height, mean heart rate during the test, and peak heart rate achieved during the test we entered into the stepwise regression model. Sex had the largest shared variance in the model (31%), followed by the mean heart rate during the full test (24%), and followed by height (4%) for a total adjusted R^2 of 0.58 ($p < 0.001$).

Model 1:

Distance covered (m) = 78.39·(sex) + 2.02·(mean HR) + 2.03·(height in cm) + 8.0

Where males =1 and females = 0. The standard error of the estimate (SEE) was 47.5 m.

Given that heart rates may not be easily measured clinically, another prediction equation was developed (Model 2) without the mean heart rate in the model. The LLN and ULN, respectively was ± 95 m of the predicted value. See Table 7.

Model 2:

If not able to use HR monitor:

Distance covered (m) = 61.5·(sex) + 1.24 · (height in cm) + 424.8

Where males =1 and females = 0. The adjusted R^2 = 0.27, and the SEE = 62.5 m, $p < 0.001$. The LLN and ULN, respectively was ± 125 m of the predicted value. See Table 8.

CHAPTER V

DISCUSSION

To our knowledge, this is one of the few studies that predict the distance walked over six minutes in a black population. We found that sex, mean heart rate during the walk, and height accounted for about 58% of the variance in the distance traveled between subjects. When mean heart rate was not included in the model, the model became less accurate but height and sex still accounted for 27% of the total variance.

As shown in Table 9, the current models (model 1 and model 2) are within about 4% of the weighted mean predicted distance of 24 studies, but only when young adults (< 29 years of age) are used. When older adults are used (i.e. 80 years of age), then the models do not predict distance walked adequately. In fact, there is a 25% higher predicted distance walked in subjects 80 years old when models 1 and 2 are used compared to the weighted mean of 24 studies [3, 7-30]. This discrepancy in distance walked in the older ages could be evident due to unequal number of subjects in the older age groups. About 67% of the subjects recruited were between 18 and 30 years old, and only 10% of the subjects were ≥ 46 years old. This presents a significant limitation in our findings.

The mean predicted distance walked in models 1 and 2 is similar to weighted mean predicted distance walked over 24 studies but only when the ages are between 18 and 30 years of age, and perhaps up to 40 years of age. Model 1 is a better model than Model 2 as the adjusted R^2 is better and the SEE is lower, but in a clinical setting, recording heart rates may not be possible. This study presented a model without the mean heart rates obtained for the walk.

Limitations

Our study was limited to 60 individuals. The small sample size resulted in obvious limitations as the study sample was not representative of all age groups. In addition, this single-center study limited representability of study participants to a general population of African-Americans. Although we employed inclusion and exclusion criteria to recruit participants, a convenience method of sampling was subject to bias in the sample selection. In order to overcome this limitation of biased sampling, forthcoming studies should be more inclusive with a larger sample size, using older adults, and the recruitment should be multi-centered.

Conclusions

Sex was the strongest predictor of the 6MWT in young adult black subjects < 40 years of age. Gender accounted for 30% of the total variance in the model. The mean heart rate achieved during the test explained 24% of the variance in the model. Height was the weakest predictor (4% of the model). Model 1 is accurate up to about 40 years of age.

The 6WMT helps clinicians to measure functional capacity in a clinical environment [3]. It has also been used to predict exercise intolerance for individuals with chronic diseases or healthy older adults [55]. The use of a prediction equation to estimate the distance walked in a normal, healthy individual, is attractive to practitioners as it allows for the calculation of a metric for exercise performance in patients with cardiopulmonary diseases efficiently [9]. Clinicians use the 6MWT to assist them on the prognosis, severity of disease, and response to treatment [3].

LIST OF TABLES

Table 1: Prediction equations for the 6MWT in subjects whose mean age is > 40 years old.

Study	**Prediction equation**	**ethnicity**	**Number of subjects**	**R^2**	**SEE**
Fernandes et al. (2016) (43 ± 12 yrs old) [range = 25 to 75 yrs old]	Females and Males 553.3 –2.11 · (age) + 45.32 · (sex) (where Females=0 & males=1)	Western Indians	89 ♀ 80 ♂	0.31	56.9
Duncan et al. (2015) (68 ± 5 yrs old) [range = 50 to 85 yrs old]	Females 260.3 · (height in $cm^{0.525}$) · (body mass in $kg^{-0.317}$) · exponential (-0.009 · age) Males 290.6 · (height in $cm^{0.525}$) · (body mass in $kg^{-0.317}$) · exponential(-0.009 · age)	Portuguese	172 ♀ 74 ♂	0.53	--
Ramadan & Chandrasekaran (2014) (46 ± 16 yrs old) [range = 21 to 67 years old]	Females -30.33 – 0.809 · (age) – 2.074 · (weight in kg) + 4.235 ·(height in cm) Males 61.02 – (2.51 · (age) + 1.51 · (weight in kg) – (0.06 · height in cm)	Indians	67 ♀ 58 ♂	0.27 0.29	76.9 62.4
Ngia et al. (2014) (69 ± 7 yrs old) [range = 55 to 5 years old]	Females and Males 941.8 – 5.77 · (age) + 44.71 · (sex)	Chinese	28 ♀ 25 ♂	0.52	65.8
Tveter et al. (2014) (55 ± 19) (> 50 yrs old) [range = 50 to 90 yrs old]	Female and Male 302.5 – 5.9 · (age in years) + 5.11 · (height in cm) - 2.89 · (weight in kg) + 31.01 · (sex) (where Females=0 & males=1)	Norwegian	113 ♀ 105 ♂	0.60	63
Britto et al. (2013) (52 yrs old)	Females and Males	Brazilians	321 ♀	0.46	--

[range = 19 to 79 yrs old]	890.5 – 6.11 · (age) + 0.035 · (age^2) + 48.9 · (sex) – 4.87 · (BMI in kg/m^2)		296 ♂		
Soares & Pereira (2011) (95 subjects > 40 yrs old) [range = 20 to 80 yrs old]	Female and Male 511 + 0.0066 · (height in cm^2) - 0.030 · (age in $years^2$) - 0.068 · (BMI^2)	Brazilians	66 ♀ 66 ♂	0.55	54
Hill et al. (2011) (65 ± 11 yrs old) [range = 45 to 85 years old]	Females and Males 970.7 – 5.5·(age) + 56.3 · (sex) (where Females=0 & males=1)	Canadians	40 ♀ 37 ♂	0.49	--
Jenkins et al. (2009) (♀ 61 ± 9 yrs old) (♂ 64 ± 8 yrs old) [range = 45 to 85 yrs old]	Females 525 – 2.86 · (age) + 2.71 · (height in cm) – 6.22 · (BMI) Males 867 – 5.71 · (age) + 1.03 · (height in cm)	Australian Caucasians	61 ♀ 48 ♂	0.43 0.40	--
Masmoudi et al. (2008) (55 ± 11 yrs old) [range = 40 to 79 yrs old]	Female and Male 299.8 – 4.34 · (age in years) + 3.43 · (height in cm) - 1.46 · (weight in kg) + 62.5 · (sex) (where Females=0 & males=1)	Tunisians	75 ♀ 80 ♂	--	--
Ben Saad et al. (2009) ≥ 40 years of age (56 ± 10 yrs old)	Female and Male 160.3 · (sex) – 5.14 · (age in years) – 2.23 · (weight in kg) + 2.72 · (height in cm) + 720.5 (where Females = 0 & males = 1)	Tunisians	125 ♀ 104 ♂	0.77	122

Camarri et al. (2006) (65 ± 5 yrs old) [range = 55 to 75 yrs old]	Female and Male 216 + 4.12 · (height in cm) – 1.75 · (age in years) – 1.15 · (weight in kg) – 34.04 (where Females = 1 & Males = 0)	Caucasians	37 ♀ 33 ♂	0.29	--
Enright et al. (2003) (≥ 68 yrs old)	Female and Male 493 + 2.2 · (height in cm) – 0.93 · (weight in kg) – 5.3 · (age in years) + 17 · (sex) (where Females=0 & males=1)	Americans	437 ♀ 315 ♂	0.30	61.0
Gibbons et al. (2001) (45 ± 16 yrs) [range = 22 to 79 yrs old]	Females and Males 794 – 2.99 · (age in years) + 74 · (Sex) (where Females=0 & males=1)	Canadians	38 ♀ 41 ♂	0.41	--
Troosters et al. (1999) (65 ± 10 yrs old) [range = 50 to 85 yrs old]	Female and Male 218 + 5.14 · (height in cm) – 5.32 · (age in years) – 1.80 · (weight in kg) + 51.31 · (sex) (where Females=0 & males=1)	Belgium	22 ♀ 29 ♂	0.66	56.0
Enright & Sherrill (1998) (60 ± 8 yrs old) [range = 40 to 80 yrs old]	Females 667 + 2.11 · (height in cm) – 2.29 · (weight in kg) – 5.78 · (age in years) Males -309 + 7.57 · (height in cm) – 5.02 · (age in years) – 1.76 · (weight in kg)	Randomly chosen	173 ♀ 117 ♂	0.38 0.42	84.5 93.0

Table 2: Prediction equations for the 6MWT in subjects whose mean age is about 40 years old.

Study	**Prediction equation**	**Ethnicity**	**Number of subjects**	**R^2**	**SEE**
Bourahli et al. (2016) (28 ± 7 yrs old) [range = 16 to 40 yrs old]	Females and Males 800 + 64.71 · (Sex) – 10.23· (BMI in kg/m^2) – 1.63·(age) + 2.05 · (weight in kg)	North Africans	100 ♀ 100 ♂	0.59	22.6
Nusdwinuringtyas et al. (2015) (♀ 22 yrs old) (♂ 27 yrs old) [range = 18 to 50 yrs old]	Female and Males 586.3 + 0.62 · (body mass in kg) – 0.27 · (height in cm) + 63.34 · (sex) + 0.12 · (age in years) (where Females=0 & males=1)	Indonesians	65 ♀ 58 ♂	0.35	
Ajiboye et al. (2014) (36 ± 13 yrs old) [range = 21 to 67 yrs old]	Females 594.04 – 1.06 · (age) – 11.43 · (BMI in kg/m^2) + 3.32 · (weight in kg) Males 1.531 · (height in cm) – 1.60 · (age in years) + 336.6	Nigerians	198 ♀ 224 ♂	0.29 0.14	51.0 61.7
Tveter et al. (2014) (< 50 yrs old) [range = 18 to 49 yrs old]	Female and Male -224.28 + 5.91 · (height in cm) - 1.61 · (weight in kg)	Norwegian	79 ♀ 73 ♂	0.37	60
Kim et al. (2014) (37 ± 11 years old) [range = 22 to 59 yrs old]	Female and Males 105.7 +2.99 · (height in cm)	Koreans	164♀ 95 ♂	0.21	--
Roa et al. (2013) (37 ± 13 yrs) [range = 15 to 65 yrs old]	Females and Males 164.1 + 78.1 · (sex) - 1.9 · (age in years) + 1.95 · (height in cm) (where Females=0 & males=1)	Pakistanis	85 ♀ 211 ♂	0.33	--

Alameri et at. (2009) (29 ± 8 yrs old) [range = 16 to 50 yrs old]	Females and males combined 2.81·(height in cm) + 0.79 · (age in years) – 28.5	Arabs	111 ♀ 127 ♂	0.25	33.0
Iwama et al. (2009) (♀ 35 yrs old) (♂ 31 yrs old) [range = 13 to 84 yrs old]	Females and Males 622.5 – 1.85 · (age in years) + 61.5 · (Sex) (where Females=0 & males=1)	Brazilians	73 ♀ 61 ♂	0.30	71.0
Chetta et al. (2006) (♀ 33 ± 9 yrs old) (♂ 36 ± 8 yrs old) [range = 20 to 50 yrs old]	Females and males 518.9 + 1.25 · (height in cm) -2.81 · (age in years) – 39.1 · (Sex) (where Females=0 & males=1)	Italians	54 ♀ 48 ♂	0.42	--

Table 3: Difference in predicted 6MWT distance between the most disparate studies.

Examples	**Height, weight, age, and BMI**	**Minimum Predicted Distance (m)**	**Maximum predicted Distance (m)**	**Difference (%)**
Example 1 (males)	Height = 170 cm Weight = 75 kg Age = 25 years BMI = 26	469 m Alameri *et al.* (2009)	899 m Jenkins *et al.* (2009)	430 m (48%)
Example 2 (females)	Height = 170 cm Weight = 75 kg Age = 25 years BMI = 26	448 m Roa *et al.* (2013)	833 m Hill *et al.* (2011)	385 m (46%)
Example 3 (males)	Height = 170 cm Weight = 75 kg Age = 80 years BMI = 26	390 m Enright *et al.* (2003)	691 m Camarri *et al.* (2006)	301 m (44%)
Example 4 (females)	Height = 170 cm Weight = 75 kg Age = 80 years BMI = 26	344 m Roa *et al.* (2013)	660 m Tveter *et al.* (2014)	316 m (48%)

Table 4. Weighted mean for the predicted 6MWT distance based on 24 studies.

Examples	**Height, weight, age, and BMI**	**Predicted Distance**	**LLN (5th percentile)**	**ULN (95th percentile)**
Example 1 (males)	Height = 170 cm Weight = 75 kg Age = 25 years BMI = 26	673 m	467 m	879 m
Example 2 (females)	Height = 170 cm Weight = 75 kg Age = 25 years BMI = 26	647m	463 m	831 m
Example 3 (males)	Height = 170 cm Weight = 75 kg Age = 80 years BMI = 26	513 m	378 m	647 m
Example 4 (females)	Height = 170 cm Weight = 75 kg Age = 80 years BMI = 26	474 m	336 m	612 m

Table 5. Anthropometric characteristics of the subjects including age.

	Males (n = 28)	**Females (n = 32)**	**Combined (n = 60)**
Age (years)	28 (9) [18-55]	32 (14) [20-67]	30 (12) [18-67]
Weight (kg)	78.5 (10.9) [61-102.4]	68.3 (13.9) [47.8-95.7]	73.1 (13.5) [47.8- 102.4]
Height (cm)	176 (7) [163-189]	163 (8) [140-180]	169 (10) [140-189]
Body mass index (kg/m^2)	25.3 (2.8) [18.8-30.6]	25.3 (4.4) [17.2-32.3]	25.3 (3.7) [17.2-32.3]
WHR	0.82 (0.04) [0.72-0.90]	0.8 (0.06) [0.69-0.96]	0.81 (0.05) [0.69-0.96]

Mean (SD). Brackets represent the range. Waist-hip ratio (WHR)

Table 6. Heart rate and distance covered over six minutes.

	Males (n = 28)	**Females (n = 32)**	**Combined (n = 60)**
6MWT distance (m)	709 (68) [603-841]	627 (55) [498-764]	664 (73) [498-841]
HR rest (bpm)	76 (8) [59-88]	84 (11) [61-105]	80 (10) [59-105]
HR peak (bpm)	145 (220 [109-185]	155 (20) [116-190]	151 (21) [109-190]
Mean HR for the full 6-minute test (bpm)	131 (20) [99-167]	142 (19) [110-177]	137 (20) [99-177]
HR recovery (bpm)	103 (23) [72-154]	144 (20) [70-148]	109 (22) [70-154]
RPE	11.8 (2) [7-16]	10.8 (2) [6-14]	11.3 (2.2) [6-16]

The parentheses represent the standard deviation. The brackets represent the range. The HR at rest was an average of 20-30 minutes sitting on a chair. The HR during recovery was the HR at 1-minute post-exercise.

Table 7. Correlations between the distance traveled over six minutes and several other variables (n = 60).

	6MWT (m)	Age (yrs)	Age^2	sex	Height (cm)	Weight (kg)	Mean HR for the full 6MWT (beats/min)	Peak HR during the 6MWT
6MWT (m)	--	- 0.16	-0.17	0.53**	0.45**	0.16	0.31*	0.34**

p<0.01; * p<0.05. As well, the correlation between height and weight was 0.524 and the correlation between height and sex was 0.66**. For sex, it was coded as 1 for males and 0 for females. There was no correlation between 6MWT distance and either resting or recovery heart rate at one-minute post-exercise.

Table 8. Coefficients in the stepwise multiple linear regression model (n = 59).

Model	**Unstandardized Coefficients**		**Standardized Coefficients**	***p*-value**	**95.0 % Confidence Interval for B**	
	B	**Std. Error**	**Beta**		**Lower Bound**	**Upper Bound**
Constant	8.03	153.7	--	0.96	-300	316
Sex (1 = males, 0 = females)	78.4	16.6	0.54	0.000	45.1	111.6
Mean heart rate over the full test	2.02	0.33	0.55	0.000	1.4	2.7
height (cm)	2.03	0.84	0.27	0.19	0.34	3.71

Multiple regression model for healthy black adults was: Distance covered (m) = 78.39·(sex) + 2.02·(mean HR) + 2.03·(height in cm) + 8.0, adjusted $R^2 = 0.58$, SEE = 47.5 m, $p < 0.001$

Table 9. Coefficients in the multiple linear regression model without the mean heart rate as a predictor (n = 59).

Model	**Unstandardized Coefficients**		**Standardized Coefficients**	***p*-value**	**95.0 % Confidence Interval for B**	
	B	**Std. Error**	**Beta**		**Lower Bound**	**Upper Bound**
Constant	424.8	176.9	--	0.20	70.5	779.2
Sex (1 = males, 0 = females)	61.5	21.4	0.42	0.006	18.6	104.4
height (cm)	1.24	1.08	0.17	0.258	-0.93	3.40

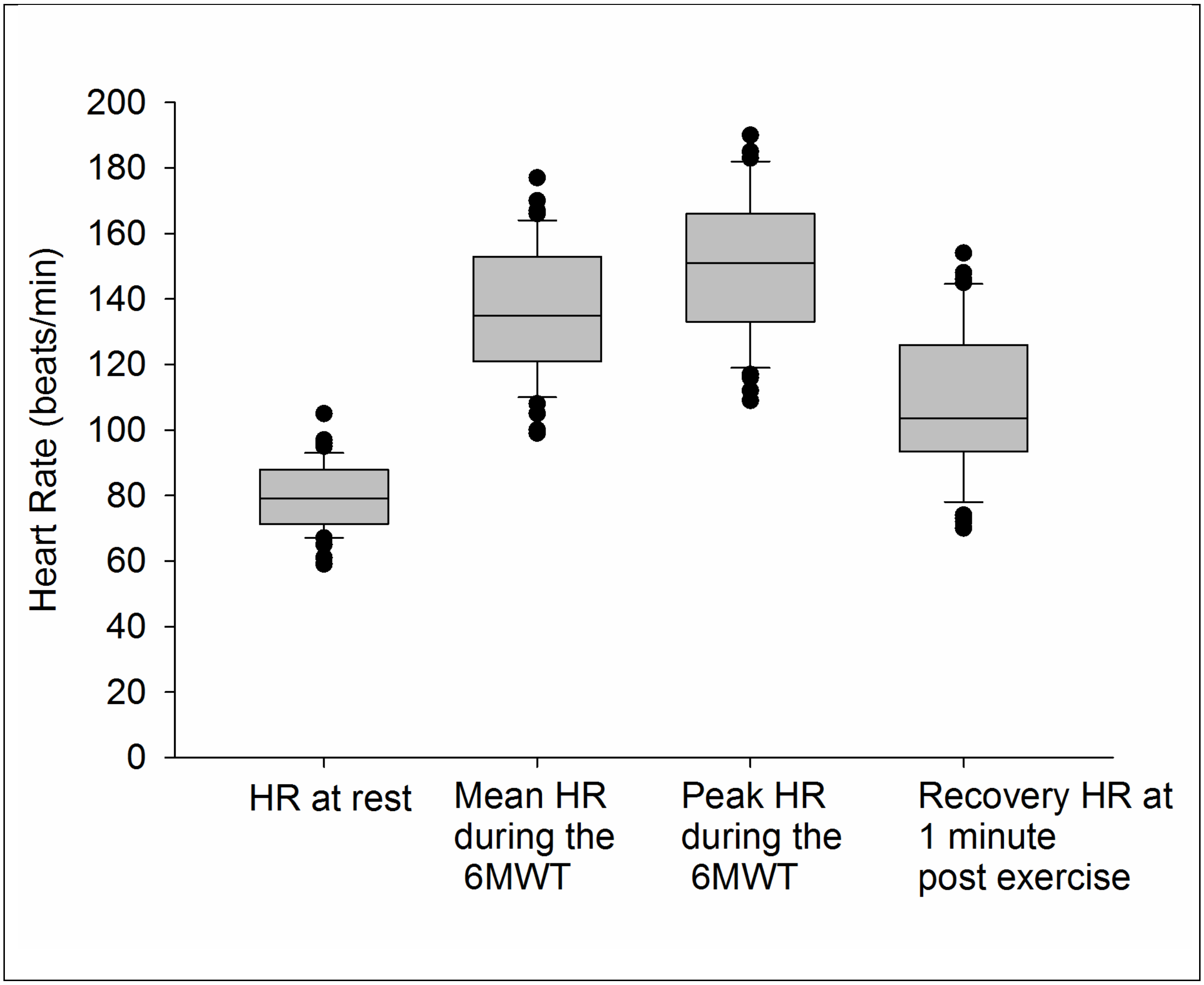
Multiple regression model for healthy black adults was: Distance covered (m) = 61.5·(sex) + 1.24 · (height in cm) + 424.8, adjusted $R^2 = 0.27$, SEE = 62.5 m, $p < 0.001$.

Table 10. Differences between the current models and the weighted mean based on 24 studies.

	Model 1 **(mean HR was 130 beats/min)**	**Model 2**	**Weighted mean based on 24 studies**	**Percent different between the two models compared to the weighted mean**
Males Height = 170 cm Weight = 75 kg Age = 25 years BMI = 26	694 m	697 m	673 m	~3%
Females Height = 170 cm Weight = 75 kg Age = 25 years BMI = 26	616 m	634 m	647 m	~4%
Males Height = 170 cm Weight = 75 kg Age = 80 years BMI = 26	694 m	697 m	513 m	~26%
Females Height = 170 cm Weight = 75 kg Age = 80 years BMI = 26	616 m	636 m	474 m	~24%

List of Figures

Figure 1. Heart Rates before, during, and one minute post-exercise (post-6MWT).



$p < 0.05$ for all pairwise comparisons.

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