Review Article

The historical evolution of the six-minute walk test as a measure of functional exercise capacity: a narrative review

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Abstract: Chronic disorders are usually associated with impairment of functional capacity (ability to perform activities of daily living), hence, necessitating routine evaluation and monitoring of this impairment at baseline and in response to interventions as part of standard of care. The six-minute walk test (6MWT) is one of the most common modalities for the measurement, monitoring and prognostication of functional capacity. Since its development in the early 1980s, it has witnessed an increasing use as a valid and reliable tool for the objective quantification of the functional capacity of children, adolescents and adults with various chronic cardiopulmonary, haematologic, neuromuscular and metabolic disorders. It has become the most widely used tool for the evaluation of functional capacity by physicians, physical therapists, physiologists, rehabilitation specialists and nurse practitioners involved in the care of adults and children with these disorders. There exists a rich and growing body of literature on the evolution of this test from pre-existing measures of functional capacity, its measurement properties and utility in various adult and paediatric chronic disorders, as well as reference standards derived from healthy paediatric and adult populations. This review chronicles the landmark milestones in the evolution of this test and provides an up-to-date reference of important contributions to the development of the test for clinicians and researchers. Thus, it not only fills a need for the historical background of this test, but also provides a rich reference source of key works on different aspects of the test for the benefit of clinicians and researchers. The documentation of the historical background of clinical tests may also serve as inspiration for practitioners to be curious and innovative as they seek to optimise patients' care and functioning.

Keywords: Six-minute walk test (6MWT); history; development; utility

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Introduction

Functional capacity is the ability of a person to carry out daily activities of living such as walking, bathing or moving about, objectively quantified as the maximal oxygen consumption (VO_{2max}) during a maximal-effort cardiopulmonary exercise test (CPET) (1,2). In the literature, the term "functional capacity" has often been interchangeably used with closely related, but sometimes different, terms such as "functional exercise capacity" (3), "working capacity"(4), "physical fitness" (4,5), "physical

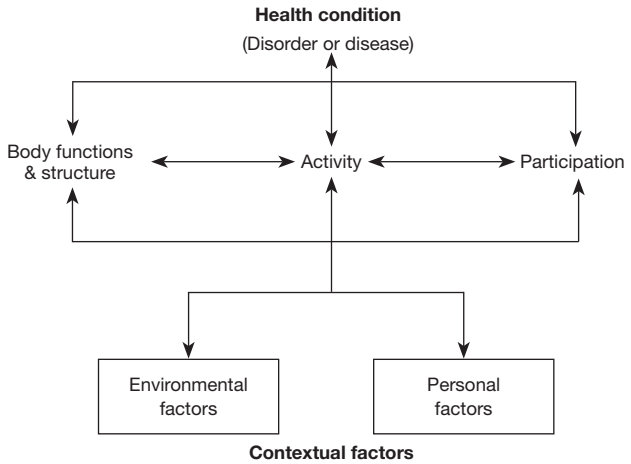

Figure 1 Biopsychosocial model of health in which a disease condition results in physiological or anatomical derangements, activity limitation and participation restriction in the context of environmental and personal factors. Reprinted from "Towards a common language for functioning, disability and health: ICF", WHO, page 9, Copyright [2002].

performance" (6), "cardiorespiratory performance" (6), "exercise tolerance" (7), "exercise capacity" (8), "cardiorespiratory fitness" (9,10), "functional status" (11,12), "walking capacity" (13), "aerobic fitness" (14), "aerobic power" (14), "ambulatory endurance" (15) and "cardiovascular fitness" (14).

The concept of evaluating a patient's functional capacity arose from a progressive understanding of the biopsychosocial model of health, in which diseases (or injuries) result, not only in derangements of normal bodily functions or structures, but also in *limitation* of the person's day-to-day activities and *restriction* of the person's participation in societal responsibilities (*Figure 1*) (16). Thus, the optimal care of such a person requires the measurement, evaluation and amelioration of these disease-associated activity limitation and participation restriction, in addition to the cure or amelioration of the underlying or primary physiological derangements (17).

The gold-standard test for the objective quantification of functional capacity—CPET—is a highly sophisticated laboratory-based test that requires special costly equipment and specially-trained personnel. Consequently, it is not readily accessible to patients especially in primary care, necessitating need for simpler but similarly valid and reliable field measures of functional capacity (4,17,18). Currently, the most widely studied valid and reliable field measure of functional capacity is the six-minute walk test (6MWT)—a simpler and cheaper test that quantifies functional capacity using the distance walked in six minutes [the six-minute walk distance (6MWD)] at a self-selected pace on a hard surface such a hospital corridor (1,2,19,20). Whereas the VO_{2max} measured during a CPET evaluates the physiological derangement domain of health, the 6MWD measured during a 6MWT predominantly evaluates the activity limitation domain (17). Hence, the 6MWT complements the CPET in the functional evaluation of patients but, occasionally, it may serve as an alternative where CPET is unavailable (21). Despite some limitations, the usefulness of the 6MWT has been demonstrated in numerous chronic adult and paediatric disorders, spanning the cardiopulmonary, musculoskeletal, neuromuscular, metabolic, endocrine and haematologic systems (1,22,23).

Although there exists a large and growing body of literature on various aspects of the 6MWT [for example, its measurement properties (2,15,22-29), clinical utility and methodology (1,15,19,27,30-33) and reference standards (20,34-40)], there has been limited attempts to present, in one paper, a detailed chronological record of important milestones in its evolution from pre-existing measures of functional capacity to its current status as the most widely used measure of functional capacity (41-44). Such a paper will provide a 'one-stop shop' and up-to-date reference of historical aspects of the test as well as key resources such as systematic reviews/meta-analyses of various aspects of the test for the benefit of clinical practitioners and researchers.

Methods & results

As part of a prior literature search for a project on the 6MWT of healthy Nigerian children (38), we conducted broad, unrestricted searches for papers related to 6MWT on multiple databases and search engines (PubMed, Google Scholar, Scopus, SciELO, Google, Yahoo and Bing) at various times from 2013 to August, 2018. The search terms used included "six-minute walk test" and its variations such as "6MWT", "6-minute walk test", "six-minute walking test" and also various forms of "functional capacity" such as "functional exercise capacity" or "exercise capacity". The term "history" was also included to search for specific articles that may have chronicled the historical aspects of the 6MWT.

There was no restriction on the papers selected in terms of date of publication, type of work (full-text journal article,

theses, conference abstracts or posters), geographical origin of work, subjects' age ranges or language of publication. English translations of non-English articles were requested from the authors and when this was not available or feasible, translation was done with the aid of Google Translate. With respect to this narrative review, no strict quality criteria were applied on the articles but only articles with information relevant to the construction of the chronological development of the 6MWT from pre-existing measures of functional capacity, its utilisation as a primary measure of functional capacity in disease and health and development of reference standards for its clinical use were included.

References of selected articles were further searched for additional relevant articles. Retrieved articles were stored in a database until needed. English translation to one of the selected articles originally written in Arabic was provided by the authors (45) while three other articles (46-48) in Spanish were translated to English using Google Translate.

Discussion

From the laboratory to the "field"

The 20th century witnessed the steady development of the laboratory-based CPET and the elaboration of sophisticated gas-measuring equipment (6,49,50). Following the invention of the cycle ergometer in the early 1920s, the maximal oxygen uptake (VO_{2max})—defined as the maximal amount of oxygen an exercising individual consumes during maximal CPET-became recognised as the gold-standard measure of functional capacity (5,6,10,50-52). Researchers such as Taylor and colleagues (6) and Mitchell and co-workers (51) published earlier protocols for the standardised performance of CPET. However, there were concerns that the CPET, apart from requiring sophisticated equipment, was relatively time-consuming as only one person could be tested at a time. Thus, the original search for field-based measures of functional capacity arose out of the need for valid and reliable tests that could be administered to a large number of healthy individuals (military personnel) at the same time using relatively simple equipment (4,18,53).

The most cited earliest documented attempt at this was by Balke (4) in 1963. The author quantified the amount of oxygen consumed by a group of exercising subjects at increasing velocities while running on a treadmill in order to determine the VO_{2max}. Thereafter, the subjects ran on a 1-mile long course on a field for varying durations of time at the fastest possible pace and the velocities achieved were calculated. The author observed that oxygen consumption (VO_2) attained during the 12–20th minute of running was similar to VO_{2max} attained on a treadmill. It was thus concluded that a 15-minute run test (15MRT) was equivalent to a maximal-effort CPET. Subsequently, the test was applied in the evaluation of aviation staff, obese subjects and sick persons.

In 1968, Cooper (18) sought to modify Balke's 15MRT by studying 115 Airforce men who ran for 12 minutes at the fastest pace [12-minute run test (12MRT)]. The oxygen consumption calculated from the run test had an excellent correlation (r=0.897) with the VO_{2max} attained on a treadmill and thus the author concluded that the 12MRT was similar in performance to Balke's 15MRT. Thereafter, Cooper's 12MRT has been extensively used in the functional evaluation of military personnel and athletes. Cooper (54) subsequently published age- and sex-based nomograms for estimating VO_{2max} from distances attained during a 12MRT.

McGavin and colleagues (7), in 1976, argued that walking mimics daily activities better than running on a treadmill or cycling on an ergometer; hence, distances attained during a walk test would reflect daily functional impairments better than cycling or running. This argument was consequent to earlier studies such as that of Spiro and co-workers (55) who showed that maximal level of exertion (as may occur with running) was not required to assess functional capacity. Thus, McGavin *et al.* (7) modified Cooper's 12MRT to a 12-minute walk test (12MWT) and applied it on subjects with chronic obstructive pulmonary disease (COPD) along a hospital's indoor corridor. The 12-minute walk distance (12MWD) attained by the subjects correlated significantly with VO_{2max} attained during a CPET.

Similarly, in 1977, Mungall and Hainsworth (9) demonstrated the reproducibility of the 12MWT as a measure of functional capacity. These researchers also observed that the 12MWD was a better measure of the impairment of daily functioning compared to forced expiratory volume in one second (FEV_1). McGavin *et al.* (56) also later noted that the 12MWT was a better and more objective measure of functional capacity compared to subject-reported questionnaires. Thereafter, McGavin's 12MWT became common as an objective measure of functional capacity, including in clinical trials of adults with chronic lung diseases (56-62).

6MWT in adult subjects

McGavin's 12MWT continued as a commonly used field-based measure of functional capacity until in 1982 when Butland and co-workers (63) considered the 12MWT to be "*both time consuming for the investigator and exhausting for the patient*". This group thus tested the hypothesis that walk tests of shorter duration [two-minute walk test (2MWT) and 6MWT] would have similar performances to the 12MWT in the measurement of functional capacity. It was observed that the subjects attained the highest walk velocity within the first two minutes after which the distances attained at subsequent two-minute intervals stabilized. The correlations among the three tests were excellent (6MWD *vs.* 12MWD, r=0.955; 2MWD *vs.* 12MWD, r=0.864; and 6MWD *vs.* 2MWD, r=0.892; n=30) with the mean 12MWD being twice the mean 6MWD of the subjects and the mean 6MWD approximately thrice the mean 2MWD. The authors thus concluded that the 6MWT was a "sensible compromise" between a rather too-long 12MWT and a relatively poorly-discriminatory 2MWT.

Two years after the 'birth' of Butland's 6MWT, Guyatt *et al.* (8) reported that the 6MWT, compared to the 2MWT, had better ability to detect clinically meaningful change in functional capacity. Thereafter, the 6MWT increasingly became the most used field test for the measurement of functional capacity in adults with chronic diseases (23). It was used mainly in adults with chronic airway diseases until in 1985 when Guyatt *et al.* (11,64,65) reported that the 6MWT correlated significantly with CPET and the New York Heart Association (NYHA) functional classification scores in adults with chronic heart failure. Similarly, in 1986, Lipkin *et al.* (66) found the 6MWT useful and less exerting than CPET in the measurement of the functional capacity of adults with chronic heart failure. Subsequently, its utility was extended beyond the cardiopulmonary domain to individuals with metabolic, haematologic, neuromuscular, rheumatologic, psychiatric, renal and chronic infectious disorders (1,20,23,24,30,67-69).

6MWT in paediatric subjects

The earliest reports of the use of 6MWT in paediatric subjects were in two separate studies of Dutch and American children by Gulmans *et al.* (70) and Nixon *et al.* (71), respectively, both in 1996. The authors demonstrated the validity and reliability of the 6MWT as a measure of the functional capacity of children with cystic fibrosis and end-stage cardiopulmonary disorders. Thereafter, the 6MWT was tested and utilised in other chronic disorders of childhood such as congenital heart diseases, end-stage renal disease, obesity, cerebral palsy and HIV infection (22,72-74).

Standardisation of the 6MWT

In 1984, Guyatt *et al.* (8) in a randomised interventional study of 43 adults with chronic cardiopulmonary disorders, observed that differential encouragements administered during a 6MWT significantly affected the distance achieved and thus recommended its standardisation. However, a comprehensive standardisation of the 6MWT was not available until in 2002 when the Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories of the American Thoracic Society (ATS) (1) published the first standard guidelines in order to harmonise its clinical application and enhance international comparison across studies. This statement provided guidelines on patient selection, equipment, indications and contraindications, standardised minute-by-minute encouragements and other aspects of the test in adult populations.

In two subsequent, long-overdue, reviews of the 2002 ATS guidelines, the ATS in conjunction with the European Respiratory Society (ERS) provided updates on the measurement properties (2) and "standard operating procedures" (30) of the 6MWT. The updates, in contrast to the 2002 guidelines, were more emphatic on the need for repeat testing when used for post-interventional evaluation in order to account for "learning effect". In 2015, the Polish Respiratory Society also issued consensus guidelines on the 6MWT (19).

Reference standards for the 6MWT in adults

Following the establishment of the validity and reliability of the 6MWT as a measure of functional capacity, the need for reference standards (reference values with or without predictive regression equations) became obvious in order to guide clinical interpretation of the test. The first reference standards and equations in adults were published by Enright and Sherill (75) in 1988 in a study of 290 healthy adults in USA. The 6MWD was independently predicted by height, weight, body mass index (BMI), age and sex. Thereafter, Troosters *et al.* (76) in 1999 and Gibbons *et al.* (77) in 2001 published reference equations derived from healthy Belgian and Canadian adults, respectively.

Table 1 Some* published prediction reference equations for adult populations

Author (country, year)	Prediction reference equation(s)
Rao *et al.* (Pakistan, 2011) (82)	6MWD =164.08+ (78.06× G) – (1.90× A) + (195× H); R^2 =0.330
Ajiboye *et al.* (Nigeria, 2014) (39)	6MWD = (419.83× H) – (1.02× A) – (1.03× W) –79.02; R^2 =0.303
Ngai *et al.* (China, 2014) (83)	6MWD =722.35– (5.11× A) + (2.19× *%predHRmax*) – (41.31× G); R^2 =0.650
Kim *et al.* (Korea, 2014) (84)	6MWD =105.7 + (299× H); R^2 =0.205
Ramanathan & Chandrasekaran (India, 2014) (85)	M: 6MWD =561.02– (2.51× A) + (1.51× W) – (5.50× H); R^2 =0.288
	F: 6MWD =30.325– (0.81× A) – (2.07× W) + (424× H); R^2 =0.272
Beekman *et al.* (Netherlands, 2014) (86)	M: 6MWD =1073– (6.03× A) – (5.79× BMI) + (1.86× HR_{diff}); R^2 =0.62
	F: 6MWD =878– (3.60× A) – (6.42× BMI) + (1.95× HR_{diff}); R^2 =0.71
Tveter *et al.* (Norway, 2014) (87)	6MWD = –224.28 + (591× H) – (1.61× W); R^2 =0.370
Nusdwinuringtyas *et al.* (Indonesia, 2014) (88)	6MWD =586.25+ (0.62× W) – (26.50× H) – (63.34× G) + (0.117× A); R^2 =0.367
Bourahli *et al.* (Algeria, 2015) (89)	6MWD =800.05 + (64.71× G) + (10.23× BMI) + (1.63× A) + (2.05× W); R^2 =0.587
Fernandes *et al.* (India, 2016) (90)	6MWD =553.29+ (–2.11× A) + (45.32× G); R^2 =0.307
Zou *et al.* (China, 2017) (91)	F: 6MWD =233.99– (1.82× A) + (263× H); R^2 =0.34
	M: 6MWD =141.33– (1.04× A) + (304× H); R^2 =0.28
Vaish *et al.* (India, 2017) (92)	F: 6MWD =856.55– (16.08× A); R^2 =0.350
	M: 6MWD =681.97– (19.99× A) + (206× H); R^2 =0.27
Padmavathy *et al.* (Malaysia, 2018) (93)	F: 6MWD =441.08+ (52.90× H) + (0.646× W) + (2.601× CE)
	M: 6MWD =60.06+ (236.70× H) + (0.780× W) + (18.04× CE)
Shrestha & Srivastava (Nepal, 2015) (94)	6MWD =395– (1.5× A) + (2.47× W) – (35.89× G)
Alqahtani (US African-Americans, 2017) (78)	6MWD =8.00+ (78.39× G) + (2.02× *PostHR*) + (203× H); R^2 =0.58

*, not included in previous systematic reviews (80). 6MWD, six-minute walk distance in meters; M, men; F, women; G, gender, where M =1, F =0, except for the Indonesian study where F =1 and M =0; A, age in years; H, height in meters; W, weight in kg; HR, heart rate in beats/min; HR_{diff}, heart rate difference; R^2, coefficient of determination; PostHR, post-exercise heart rate; %predHRmax, percentage predicted maximal heart rate; CE, chest expansion in cm.

These three studies were published before the 2002 ATS guidelines and so were characterized by wide variability in test protocols including course lengths and encouragements. Subsequent to the publication of the 2002 ATS guidelines, there was widespread development of reference standards and equations from various ethno-geographic regions of the world (20,39,78-81). Salbach *et al.* (80) in 2014 published a systematic review conducted on 20 studies that published prediction reference equations emanating from American, European, Asian and African adult populations. Additional equations that have been published after this Salbach's review are shown in *Table 1*.

6MWT reference standards in paediatric age groups

The publication of reference standards for the 6MWT in children lagged behind that of the adult population, arguably due to concerns about safety and validity. Also, because of lack of paediatric-specific guidelines on the 6MWT (till date), studies in both healthy and sick paediatric subjects have extrapolated the existing adult guidelines to children, frequently with methodological modifications such as use of shorter course lengths, incentive devices or "safety chasers" (22,34-36,38,95-98).

The first published reference standards (mean 6MWD

Table 2 Some* published prediction reference equations for paediatric populations

Authors (country, year)	Prediction reference equation(s)
Acosta García *et al.* (Venezuela, 2012) (48)	6MWD =444.68+ (27.88× A); R^2 =0.46
Ubuane (Nigeria, 2017) (38)	6MWD =337.0+ (15.4× A) + (19.5× G) + (1.6× HR_{diff}) + (1.2× SBP_{diff}); R^2 =0.282
Vandoni *et al.* (Italy, 2018) (100)	6MWD = −160.16+ (93.35× A) − (4.05× A*2) + (7.34× G) + (2.12× W) − (250× H)
Jalili and Nazem (Iran, 2017) (45)	M: 6MWD =644.83+ (18.52× A) − (8.24× BMI); R^2 =0.627
de Assis Pereira Cacau *et al.* (Brazil, 2018) (35)	M: 6MWD = (16.86× A) + (1.89× HR_{diff}) − (0.80× W) + (336.91× R_1) + (360.91× R_2) F: 6MWD = (13.54× A) + (1.62× HR_{diff}) − (1.28× W) + (352.33× R_1) + (394.81× R_2)

*, not included in previous systematic reviews (34,36,40). 6MWD, six-minute walk distance in meters; M, boys; F, girls; G, gender, where M =1, F =0; A, age in years; H, height in meters; W, weight in kg; HR, heart rate in beats/min; HR_{diff}, heart rate difference; SBP_{diff}, systolic blood pressure difference; R^2, coefficient of determination; R_1 & R_2, geographical regions of residence in Brazil-North *vs.* South.

without equations) from healthy children was from a study of Chilean subjects by Escobar *et al.* (47) in 2001. Later in 2007, Li *et al.* (99) published the first predictive regression equations for the 6MWD of healthy Chinese children and adolescents (99). Subsequently, reference standards (with or without equations) were published from healthy European, American, Asian and African paediatric populations. Most of these reference standards and equations have been summarized in three separate systematic reviews by Cacau *et al.* (36), Mylius *et al.* (34) and Rodríguez-Núñez *et al.* (40). Reference equations that were not included or that were published after publication of these reviews are presented in *Table 2* (34,36,38).

In both adult and paediatric studies, the need for reference values and equations specific to each ethno-geographic region have been informed/justified by an observation of wide variation in the reference values (34,36,40,79,80). Thus, independent of differences in test methodologies and other influencing variables such as anthropometrics characteristics, race and ethnicity significantly influence subjects' performance on the 6MWT (34,36,40,101).

Novel approaches and innovations

The last decade has witnessed interesting innovations aimed at improving the efficiency of administering the 6MWT, as well as reducing the manpower required to conduct the test. For example, Du and colleagues (27,102) conceptualised the use of the 6MWT as a home-based "self-administered" measure of the functional capacity of community-dwelling patients with chronic heart failure (home-heart-walk test). This aimed to provide ambulatory patients with chronic heart disease with a self-monitoring tool (akin to self-monitoring with glucometer in diabetes care or hand-held spirometers in chronic lung diseases) that could help in the early detection and tracking of changes in their functional capacity while at home (27).

With the advent and widespread availability of smartphones, administration of the 6MWT has been further enhanced with the development and validation of smartphone applications that combine the functions of lap counter, stopwatch and calculator into a single application for use during a 6MWT at home or in clinic settings (103). Furthermore, applications that not only do the aforementioned but also use phone-based sensors such as gyroscopes to auto-derive the 6MWD (without counting the number of laps) and transmit the data remotely to clinicians have been developed (104). Thus, the 6MWT has come to stay as a relevant measure of functional capacity of patients with chronic diseases.

Conclusions

From its first documented use in the early 1980s, the 6MWT has become the most commonly used valid and reliable field-based objective measure of functional capacity in both adult and paediatric populations (23). A large and growing body of data exists on its development, utility, measurement properties and reference equations across various ethno-geographic populations. Apart from chronicling its evolution over the years, this review has highlighted prominent persons or groups who made contributions to its development. There is however need for paediatric-specific guidelines for use in children and

adolescents. Also, reference equations are needed in children from other ethnic groups such as North American and other sub-Saharan African regions.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jxym.2018.11.01). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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