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# Relationships between muscle size, strength, and physical activity in adults with muscular dystrophy

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## Abstract

**Background** Muscular dystrophy (MD) is characterized by progressive muscle wasting and weakness, yet few comparisons to non-MD controls (CTRL) of muscle strength and size in this adult population exist. Physical activity (PA) is promoted to maintain health and muscle strength within MD; however, PA reporting in adults with MD is limited to recall data, and its impact on muscle strength is seldom explored.

**Methods** This study included 76 participants: 16 non-MD (CTRL, mean age 35.4), 15 Duchenne MD (DMD, mean age 24.2), 18 Becker's MD (BMD, mean age 42.4), 13 limb-girdle MD (LGMD, mean age 43.1), and 14 facioscapulohumeral MD (mean age 47.7). Body fat (%) and lean body mass (LBM) were measured using bioelectrical-impedance. Gastrocnemius medialis (GM) anatomical cross-sectional area (ACSA) was determined using B-mode ultrasound. Isometric maximal voluntary contraction (MVC) was assessed during plantar flexion (PFMVC) and knee extension (KEMVC). PA was measured for seven continuous days using triaxial accelerometry and was expressed as daily average minutes being physically active (TPA<sup>mins</sup>) or average daily percentage of waking hours being sedentary (sedentary behaviour). Additionally, 10 m walk time was assessed.

**Results** Muscular dystrophy groups had 34–46% higher body fat (%) than CTRL. DMD showed differences in LBM with 21–28% less LBM than all other groups. PFMVC and KEMVC were 36–75% and 24–92% lower, respectively, in MD groups than CTRL. GM ACSA was 47% and 39% larger in BMD and LGMD, respectively, compared with CTRL. PFMVC was associated with GM ACSA in DMD ( $P = 0.026$ ,  $R = 0.429$ ) and CTRL ( $P = 0.015$ ,  $R = 0.553$ ). MD groups were 14–38% more sedentary than CTRL groups, while DMD were more sedentary than BMD (14%), LGMD (8%), and facioscapulohumeral MD (14%). Sedentary behaviour was associated with LBM in DMD participants ( $P = 0.021$ ,  $R = -0.446$ ). TPA<sup>mins</sup> was associated with KEMVC ( $P = 0.020$ ,  $R = 0.540$ ) in BMD participants, while TPA<sup>mins</sup> was also the best predictor of 10 m walk time ( $P < 0.001$ ,  $R^2 = 0.540$ ) in ambulant MD, revealed by multiple linear regression.

**Conclusions** Quantified muscle weakness and impaired 10 m walking time is reported in adults with MD. Muscle weakness and 10 m walk time were associated with lower levels of TPA in adults with MD. Higher levels of sedentary behaviour were associated with reduced LBM in DMD. These findings suggest a need for investigations into patterns of PA behaviour, and relevant interventions to reduce sedentary behaviour and encourage PA in adults with MD regardless of impairment severity.

**Keywords** Muscular dystrophy; Strength; Lower limb; Muscle size; Physical activity

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## Introduction

Relationships between muscle size and strength have long been recognized and reported in healthy and clinical populations.<sup>1–3</sup> Similarly, the importance of physical activity (PA)

and exercise to maintain strength and health is commonly recognized<sup>4,5</sup>; however, these relationships have received little or no attention in adults with muscular dystrophy (MD). Where reported in children, the applicability to adults may be limited due to the degenerative/heterogeneous nature

of some classifications of MD. Despite an increasing volume of research supporting exercise interventions to maintain muscle function within this clinical population,<sup>6,7</sup> basic understanding of the relationship between muscle structure/function and habitual levels of PA in adults with MD remains largely unexplored.<sup>8</sup>

Muscular dystrophy is a broad group of neuromuscular conditions, characterized by muscle wasting and weakness and classified by absence or reduced expression of proteins associated with the sarcolemma.<sup>9</sup> Duchenne MD (DMD) is the most severe of the conditions, with symptom onset from early childhood and typical loss of ambulation from the age of 10 years, resultant from an absence of the dystrophin protein.<sup>10</sup> Becker's MD (BMD) is also a genetic condition resulting in an impaired or non-functional dystrophin protein but is considered a milder, yet more variable condition than DMD, with typical loss of ambulation from the age of 20 years.<sup>10</sup> Limb-girdle (LGMD) and facioscapulohumeral MD (FSHD) are both inherited neuromuscular conditions that in general present much later in life, with loss of ambulation mainly in the adult stage, and typically later than in BMD.<sup>11</sup> The nature of LGMD and FSHD results in great variance with various classifications within each condition, dependent upon the proteins affected.<sup>9</sup> Despite the well-established molecular and symptomatic differences between these MDs, direct comparisons between muscle strength and size between the conditions, and the potential influence of PA, have not been systematically addressed.<sup>12</sup>

Decreased muscle strength has long been recognized within MD and attributed to muscle wasting.<sup>13–15</sup> Lower limb strength comparisons between adults with MD and age-matched controls (CTRL) have been made in adults with BMD,<sup>12</sup> LGMD,<sup>12</sup> and FSHD.<sup>14,16</sup> Of these comparisons, lower isometric maximal voluntary contraction (MVC) strength was attributed to smaller lean mass in the knee extension (KEMVC) muscle group in FSHD.<sup>14</sup> While Løkken et al.<sup>12</sup> showed plantar flexors MVC (PFMVC) was associated with cross-sectional area in adults with LGMD2I. Decreased muscle strength has been shown within children and adolescents with DMD.<sup>17,13</sup> Within paediatric DMD populations, pseudohypertrophy is evident, due to the inflammatory process associated with muscle degradation resulting in apparent increased calf size compared with age-matched CTRL.<sup>18,19</sup> However, the relationship between cross-sectional area with muscle strength remains unexplored in adults with DMD, with Morse et al.<sup>20</sup> reporting decreased cross-sectional area in the *gastrocnemius medialis* (GM) compared with CTRL, suggesting an end of pseudohypertrophy in adulthood, with muscle size possibly becoming more representative of muscle strength.

Typically, in healthy adult populations, a combination of high habitual PA and medium intensity planned exercise sessions, is recommended in order to maintain and/or improve health and muscle strength.<sup>21,22</sup> Furthermore, within ageing

populations, where sarcopenia and muscular atrophy can become evident, PA measures have been positively associated with muscle strength and functional measures.<sup>23</sup> Similarly, Foong et al.<sup>24</sup> reported a positive association between PA intensity and both lower limb strength and lean mass in elderly participants. PA is promoted as a measure to maintain muscle mass and function within MD.<sup>25</sup> However, Jimenez-Moreno et al.<sup>8</sup> recently presented a systematic review of habitual PA within neuromuscular disorders, highlighting the distinct lack of PA data currently reported. Recall methods have been primarily used in MD research, namely, the bone and PA questionnaire (MD),<sup>26,27</sup> Baecke PA questionnaire (DMD),<sup>28</sup> and a self-developed PA questionnaire (DMD).<sup>29</sup> Quantitative measures of PA levels in DMD include step count activity,<sup>30,31</sup> accelerometry,<sup>32</sup> and doubly labelled water,<sup>33</sup> but have only been used with children. Thus, all current research has shown reduced PA levels in MD compared with healthy CTRL; however, only two of the aforementioned papers have measured PA in adults with MD, both of which used recall methods, which lack objectivity.<sup>27,26</sup> Recall methods have been shown previously to overestimate PA and underestimate sedentary behaviour (SB).<sup>34</sup>

In MD, PA may help to maintain muscle mass and strength, conversely, SB is likely to accelerate muscle atrophy through disuse, as well as promote other associated health risks such as increased fat mass, diabetes, and heart disease.<sup>35–38</sup> However, despite the lack of current knowledge and understanding of PA in MD, the importance of exercise and interventions is becoming more and more apparent within MD. Morse et al.<sup>26</sup> highlighted the strong associations between bone health and lifetime PA in MD. While MD populations have also shown physiological improvements following aerobic exercise interventions.<sup>6</sup> Janssen et al.<sup>39</sup> showed increased PA levels, through an aerobic training plan, decelerated muscle fat infiltration in adults with FSHD. Moreover, Jansen et al.<sup>40</sup> showed assisted bicycle training delays functional deterioration in boys with DMD. Further understanding of the habitual PA of adults with MD, along with its relationships with other functional measures, may enhance and specify future interventions.

This study aims to (i) investigate the relationship between muscle strength and size and (ii) establish the relationship between muscle size and strength with objective measures of PA, with implications for the maintenance of muscle function in MD.

## Methods

This study contains 76 adult male volunteers, only male volunteers were recruited to allow cross-condition comparisons with DMD and BMD, which are X-linked conditions.<sup>11</sup> MD participants were grouped by their dystrophic condition (DMD, BMD, LGMD, or FSHD). All MD participants were

recruited from and tested at The Neuromuscular Centre (Winsford, UK). CTRL participants were tested at Manchester Metropolitan University, Cheshire Campus (Crewe, UK). CTRL participants were self-reported as being recreationally active, however, were not undertaking any structured training programme. Similarly, no MD participants were taking part in a structured training programme; however, all were receiving weekly, biweekly, or monthly physiotherapy treatment, consisting of passive stretching, along with access to low intensity cardiovascular exercise equipment. Ethical approval was obtained through the Department of Exercise and Sport Science local Ethics Committee, and all participants signed informed consent forms prior to participation. All procedures complied with the World Medical Association Declaration of Helsinki.<sup>41</sup>

### Procedures

All participants were tested in a single testing session, subsequent from which 7 day PA was assessed using an accelerometer. The same equipment was used for all participants, with the exception of seated scales for body mass (BM) measures in non-ambulatory MD participants. Due to the high level of contractures present in some participants, all participants were assessed in a seated position to ensure consistency. Bio-electrical impedance (BIA) (Bodystat 1500, Bodystat Ltd., United Kingdom) and anthropometric measures were performed first, followed by B-mode ultrasound measures of the GM (MyLabGamma Portable Ultrasound, Esaote Biomedica, Genoa, Italy). Ultrasound recordings were taken of the participants' self-reported dominant leg. If a participant was unable to distinguish a dominant leg, the right leg was measured. Quantitative muscle strength was then taken from the self-reported dominant leg using a load cell (Zemic, Eten-Leur, Netherlands). Participants then performed a maximal handgrip strength test with their dominant hand. Upon completion of physical testing, a wrist-worn accelerometer was attached to the wrist of the self-reported dominant arm and worn for seven consecutive days (GENEActiv, Cambridge, United Kingdom).

### Anthropometry

Control participants' BM was measured by digital scales (Seca model 873, Seca, Germany). Alternatively, all MD participants were weighed in a digital seated scales system (6875, Detecto, Webb City, Mo, USA). Slings, shoes, splints, and so forth were weighed separately and subtracted from the gross weight. All participants' height was calculated as point-to-point of arm span (index finger, elbow, shoulder, and across midline) to replicate the method used on non-ambulatory participants. A correction of 3.5% was applied to the raw

data, consistent with regression data from Caucasian males in order to account for the known discrepancy between height and arm span measures.<sup>42</sup>

### Body composition

Body composition measures of fat and lean BM (LBM) were measured using BIA in a fasted state, with adhesive electrodes placed on the right hand and foot. Two distal electrodes were placed on the dorsal surfaces of the metatarsals and metacarpals, and two proximal electrodes were placed between the medial and lateral malleoli of the right ankle and between the styloid processes of the right ulna and radius. BIA has been commonly used as a quicker, cheaper, and more easily accessible alternative to other body composition measures, such as dual-energy X-ray absorptiometry (DEXA). BIA has been shown to be valid and reliable in comparison with DEXA in adults of healthy weight ( $R = 0.99$ )<sup>43</sup> and in overweight populations ( $R = 0.78$ ).<sup>44</sup> In addition, BIA has been promoted as a measure for change in fat and LBM over time in a dystrophic population.<sup>45</sup>

LBM was determined by the following equation:

$$\text{LBM (Kg)} = \text{Body Mass (Kg)} - \text{Fat Mass (Kg)}$$

Body mass index (BMI) was calculated using the following equation<sup>46</sup>:

$$\text{BMI} \left( \frac{\text{Kg}}{\text{m}^2} \right) = \text{Body Mass (Kg)} \div \text{Height}^2 (\text{m}^2)$$

### Strength

Due to the severe level of contractures and difficulties with body mechanics, all strength testing protocols were designed for the most severe participants and replicated across all conditions and participants. Isometric PFMVC and KEMVC force was recorded using a load cell with the participants in a seated position. The load cell was calibrated prior to every strength testing session. Three trials were performed, with extended breaks of 1 min between trials due to the increased fatigue associated with MD.<sup>47</sup> The highest measure of the three trials was used for analysis. The force produced was digitized using an analog-to-digital converter, displayed by a self-displayed and coded program using MyLabView (National Instruments, Berkshire, UK). Force (N) was converted to moment (N.m) by multiplying the force measurement by the moment arm from the axis of rotation (knee or ankle) to the point of force measurement (the strap height on the shin or ball of the foot). PFMVC and KEMVC measures have been presented as torque (N.m) and normalized to BM (N.m/kg), and presented as KEMVC/BM and PFMVC/BM, respectively,

while PFMVC is also normalised to GM ACSA ( $N.m/cm^2$ ) and presented as PFMVC/ACSA.

### Protocol

All MVC measures took place with the participant seated, with knee and hip angles maintained at 90°. Non-ambulant participants remained seated within their manual/power wheelchair. For knee extension, straps were used to limit hip flexion during contractions. A strap was securely fastened around ankle and attached perpendicularly to the load cell, which was securely fastened to a weighted support bar. The strap length was shortened until the strap was taut between the load cell and limb, while maintaining limb position. All participants were verbally encouraged throughout their maximal effort.

All participants' PFMVC was measured with ankle angle at 0° (neutral position); however, not all participants' ankles were able to be mechanically moved into a neutral position, with ankles typically in a plantar-flexed position due to contractures, and so measures were taken from as close to neutral position as possible. The participants' foot was attached to a footplate, with the load cell attached underneath. The practitioner produced the resistive force to ensure a static/isometric contraction occurred during MVC. Plantar-flexion forces were normalized for gravity.

### Reliability

Similar techniques to those used within this study have been common within neuromuscular research. The KEMVC protocol is similar to quantitative muscle testing and has been previously used within both clinical and non-clinical populations.<sup>48–50</sup> The plantar-flexion measures are restricted by the mechanical limitations previously mentioned within these conditions, namely, capacity that put the leg into full extension due to contractures and remain self-supported; however, similar techniques using a non-mechanical resistive force are common in dystrophic research.<sup>51,52</sup> Reliability testing was performed across all four dystrophic conditions, with within-day reliability performed with 1 min breaks between trials, while between-day reliability was performed over two separate days, separated by 1–4 weeks, to coincide with participants' physiotherapy appointment. Intraclass correlations (ICCs) (Table 1) showed strong reliability for between-day

and within-day reliability across all conditions for knee extension and plantar flexion and were in fact comparative or even stronger than ICCs in previous quantitative muscle assessment studies.<sup>53–55</sup>

### Ultrasound

GM anatomical cross-sectional area (ACSA) was measured using transverse ultrasound scans (7.5 MHz linear array probe) at 50% of muscle length, consistent with the muscle length at which the largest ACSA occurs.<sup>56</sup> Muscle length was measured with a tape measure over the skin surface, following identification of the visible origin of the GM at the posterior aspect of the femur to the distal formation of the myotendinous junction through ultrasonography.

Echoabsorptive tape (Transpore, 3M, USA) was used to project shadows on the ultrasound image during recording to provide a positional reference. Strips of tape were placed longitudinally across the GM at 50% of muscle length, at approximately 3 cm intervals. The probe was moved in the transverse plane from the medial to the lateral borders of the muscle while digitally recording. Ultrasound transmission gel (Aquasonic 100, New Jersey, USA) was used to maximize image quality; minimal and consistent pressure was applied to avoid compression of the muscle. Ultrasound was recorded in real time (at 25 frames per second) and stored prior to digitizing. Ultrasound recordings were exported into video editing software (PowerDirector V6; Cyberlink Corporation, Tokyo, Japan), from which still images were captured. Images were captured at intervals consisting of two reference markers, as shown by shadows projected on the muscle from echoabsorptive tape. The entire GM ACSA was then recreated into a single image (Graphic Image Manipulation Program, GIMP Development) using the shadows from echoabsorptive tape, muscle markers, and aponeurosis of the muscle. The ACSA was then measured using digitizing software (ImageJ 1.45, National Institute of Health, USA). This method of ACSA measurement using ultrasound has been performed previously in dystrophic conditions<sup>20,27</sup> and previously reported as a valid (0.998) and reliable (0.999) measure in comparison with magnetic resonance imaging (MRI).<sup>57</sup>

**Table 1** Intraclass coefficients for muscle strength

Condition	n	Between-day ICC		Within-day ICC	
		Plantar flexion	Knee extension	Plantar flexion	Knee extension
DMD	15	0.984	0.987	0.985	0.991
BMD	18	0.832	0.991	0.911	0.992
LGMD	13	0.946	0.985	0.921	0.980
FSHD	14	0.921	0.956	0.934	0.973

Intraclass correlations (ICCs) for muscle strength in dystrophic conditions. BMD, Becker's muscular dystrophy; DMD, Duchenne muscular dystrophy; FSHD, facioscapulohumeral dystrophy; LGMD, limb-girdle muscular dystrophy.

## Handgrip

A digital handgrip dynamometer (Jamar plus, Patterson Medical, USA) was used to assess grip strength. Of the participants able to produce a measureable grip strength (three DMD participants produced 0 kg grip strength), three maximal attempts were performed. Measures were taken in a seated position for all participants, on their self-reported dominant hand, with the arm in an extended position to the side of the body. Extended 1 minute rest periods were allowed between trials due to the previously mentioned high fatigability of these conditions.

## 10 m walk test

A 10 m walk test was performed by 20 out of 24 ambulant participants (8 BMD, 2 LGMD, and 10 FSHD). The four participants to not perform the 10 m walk did so at their own request due to safety concerns. The 10 m walk was performed on an even, carpeted surface and is a common measure of function within neuromuscular conditions.<sup>52,58</sup> All participants started in a standing position and were instructed to walk as quickly and safely as they could, with the time recorded from the point of 'Go' from the practitioner to the point of crossing the finish line. Walking aids were permitted if required. Given the limited numbers, these participants were pooled for analysis upon 10 m walk time.

## Physical activity

Daily PA was monitored over a consecutive 7 day period using a wrist-worn triaxial accelerometer (GENEActiv, Kimbolton, Cambs, United Kingdom). Wrist-worn accelerometers have previously been recommended as the best location for accelerometers for wheelchair users,<sup>59</sup> as well as removing any issues of access and comfort that would be associated with other locations (such as mid-thigh or waist). Monitors were worn for 24 h a day on the preferred wrist of participants and worn continuously for 7 days.<sup>60</sup> Monitors were initialized to collect data at 100 Hz and acceleration values, recorded in g, and recorded continuously on each axis (x, y, and z). Recorded total activity time has been previously validated against doubly labelled water.<sup>61</sup> In addition, GENEActiv validation studies for both PA and SB have shown strong correlations (Pearson's  $r = 0.79-0.98$ ).<sup>62,63</sup>

Once wrist-worn monitors were returned post 7 day period, data were downloaded from monitors into .bin files and converted into 60s epoch .csv files using the GENEActiv PC Software (Version 2.1). 60s epoch data files were entered in an open source Excel macro (v2, Activinsights Ltd.),<sup>63</sup> which classified activity as sedentary (SB), light (LIPA), moderate (MIPA), or vigorous (VIPA) intensity. The PA intensity

thresholds used within the macro were not designed for adults with MD, therefore rather than incorrectly allocating PA to intensity domains, activity will be presented as time as sedentary or total time spent physically active (TPA). TPA, the sum of LIPA, MIPA, and VIPA time, is presented as average daily minutes (TPA<sup>mins</sup>), while SB is presented as percentage of waking hours (hereafter referred to as SB). Both SB and TPA<sup>mins</sup> will be used for comparisons, as well as correlations and regression analysis.

## Statistical analyses

All analyses were performed using IBM Statistics 21 software. The critical level of statistical significance was set at 5%. Tests for parametricity were performed upon all variables. All data, except for height and LBM, were non-parametric. Reliability of muscle strength measurements (KEMVC and PFMVC) within and between day was calculated using ICCs (absolute agreement) within the MD groups (Table 1). The Kruskal–Wallis test was used to compare between groups, with post hoc Mann–Whitney U (least significant difference or LSD) pairwise comparisons used where appropriate. Height and LBM was compared between groups using a one-way analysis of variance, and Tukey's used for post hoc comparison. Kendall Tau correlations were used to identify associations of anthropometric variables, muscle size, muscle strength, and PA. Significant associations with age were identified for KEMVC, KEMVC/BM, and PFMVC/BM, respectively, therefore analyses of covariance were performed to determine whether differences remained when age was controlled for. Bivariate linear regression was used to identify the best predictor of 10 m walk from muscle strength measures and TPA<sup>mins</sup>. Multiple linear regressions were used when two or more variables were associated. Post hoc effect size was determined by Phi, using PFMVC, KEMVC, and TPA<sup>mins</sup>, with moderate–strong effect sizes shown (Phi = 0.75–0.85). Where relevant, comparisons are presented with *P* values, and the relative difference (%) from a named experimental group.

## Results

### Demographic, anthropometric, and body composition measures

Duchenne MD participants were younger than those with BMD (43%,  $P < 0.001$ ), LGMD (44%,  $P < 0.001$ ), FSHD (49%,  $P < 0.001$ ), and CTRL (32%,  $P = 0.013$ ) (Table 2). Furthermore, CTRL were younger than FSHD (25%,  $P = 0.021$ ) (Table 2). No other differences were found between groups for age ( $P > 0.05$ ). As there were differences in age between participant groups, subgroup analysis was performed on the

**Table 2** Participant characteristics and anthropometrics

	DMD	BMD	LGMD	FSHD	CTRL
<i>n</i>	15	18	13	14	16
Ambulant	0/15	10/18	4/13	10/14	16/16
Age (years)	24.2 (6.1) <sup>a,b,c</sup>	42.4 (13.5)	43.1 (12.4)	47.1 (11.1) <sup>d</sup>	35.4 (12.7)
Mass (kg)	73.1 (14.6) <sup>a,b,c</sup>	86.5 (20.3)	96.9 (17.3) <sup>d</sup>	86.0 (11.2)	81.1 (18.2)
Stature (cm)	172.0 (4.3)	177.4 (6.0)	179.5 (6.9)	178.6 (8.1)	177.5 (9.3)
BMI (kg/m <sup>2</sup> )	25.5 (4.1)	27.3 (6.2)	29.5 (4.8)	26.6 (3.4)	25.5 (3.7)
Body fat (%)	33.3 (6.7) <sup>d</sup>	29.2 (10.0) <sup>d</sup>	33.7 (4.7) <sup>d</sup>	27.6 (7.3) <sup>d</sup>	18.2 (4.5)
Lean body mass (kg)	47.6 (7.7) <sup>a,b,c,d</sup>	60.0 (9.1)	64.1 (9.3)	61.0 (8.6)	66.0 (13.2)
GM ACSA (cm <sup>2</sup> )	23.3 (16.5)	27.9 (15.9) <sup>c,d</sup>	23.9 (11.0) <sup>d</sup>	16.6 (4.5)	14.7 (4.5)

Anthropometric measures. ACSA, anatomical cross-sectional area; BMD, Becker's muscular dystrophy; BMI, body mass index; CTRL, control; DMD, Duchenne muscular dystrophy; FSHD, facioscapulohumeral muscular dystrophy; GM, gastrocnemius medialis; LGMD, limb-girdle muscular dystrophy.

<sup>a</sup>Denotes significance from BMD.

<sup>b</sup>Denotes significance from LGMD.

<sup>c</sup>Denotes significance from FSHD.

<sup>d</sup>Denotes significance from CTRL.

primary outcome measure (KEMVC), CTRL participants were split into Young (aged 18–30, *n* = 8) and Old (aged 31–55, *n* = 8) subgroups, so they matched with DMD and FSHD, respectively. As this approach provided the same statistical outcomes as a combined CTRL group, only comparisons for a combined CTRL are presented in the succeeding text. DMD participants were lighter than BMD (15%, *P* = 0.032), LGMD (25%, *P* < 0.001), and FSHD (15%, *P* = 0.029) participants, while LGMD participants were heavier than CTRL (19%, *P* = 0.012) (Table 2). There were no differences in stature between any groups (*P* > 0.05).

No differences were found between groups for BMI (*P* > 0.05, Table 2). DMD (45%, *P* < 0.001), BMD (38%, *P* < 0.001), LGMD (56%, *P* < 0.001), and FSHD (34%, *P* = 0.002) participants had higher body fat% than CTRL participants (Table 2). DMD participants had less LBM compared with BMD (21%, *P* = 0.001), LGMD (26%, *P* < 0.001), FSHD (22%, *P* = 0.002), and CTRL (28%, *P* < 0.001) participants (Table 2). No other differences were found between groups for LBM (*P* > 0.05).

Becker's MD participants' GM ACSA was larger than FSHD (40%, *P* = 0.039) and CTRL (47%, *P* = 0.001) participants, while

LGMD participants' GM ACSA was larger than CTRL (39%, *P* = 0.015) participants (Table 2). No other differences were found between groups for muscle size (*P* > 0.05).

### Muscle strength

Controls' KEMVC was significantly stronger than DMD (92%, *P* < 0.001), BMD (41%, *P* = 0.010), and LGMD (53%, *P* = 0.020) (Table 3). DMD participants had lower KEMVC than BMD (87%, *P* = 0.001), LGMD (87%, *P* = 0.002), and FSHD (90%, *P* < 0.001) (Table 3). No differences were found between other groups (*P* > 0.05). All differences between groups remained for KEMVC when age was controlled for by an analysis of covariance. DMD participants were also significantly weaker in KEMVC per BM than BMD (86%, *P* < 0.001), LGMD (82%, *P* = 0.001), FSHD (88%, *P* < 0.001), and CTRL (92%, *P* < 0.001), respectively (Table 3). While CTRL participants were stronger than BMD (40%, *P* = 0.009) and LGMD (53%, *P* = 0.003) participants in KEMVC/BM (Table 3). No other differences between groups were found for KEMVC/BM (*P* > 0.05). When age was controlled for, all differences

**Table 3** Muscle strength in adults with muscular dystrophy

	DMD	BMD	LGMD	FSHD	CTRL
KEMVC (N.m)	12.6 (8.8) <sup>a,b,c,d</sup>	96.6 (60.0) <sup>d</sup>	93.5 (56.6) <sup>d</sup>	123.6 (78.2)	164.6 (55.9)
KEMVC/BM (N.m/kg)	0.17 (0.1) <sup>a,b,c,d</sup>	1.23 (0.9) <sup>d</sup>	0.97 (0.6) <sup>c,d</sup>	1.41 (0.8)	2.04 (0.6)
PFMVC (N.m)	16.7 (6.8) <sup>a,c,d</sup>	32.7 (13.7) <sup>d</sup>	28.2 (15.4) <sup>d</sup>	43.8 (20.3)	67.0 (13.1)
PFMVC/BM (N.m/kg)	0.23 (0.1) <sup>a,b,c,d</sup>	0.40 (0.2) <sup>c,d</sup>	0.31 (0.2) <sup>c,d</sup>	0.51 (0.2) <sup>d</sup>	0.84 (0.1)
PFMVC/ACSA (N.m/cm <sup>2</sup> )	0.92 (0.5) <sup>c,d</sup>	1.46 (0.9) <sup>c,d</sup>	1.29 (0.8) <sup>c,d</sup>	2.75 (1.3) <sup>d</sup>	4.58 (0.7)
Handgrip (kg)	3.0 (3.1) <sup>a,b,c,d</sup>	19.5 (14.9) <sup>d</sup>	19.6 (9.5) <sup>d</sup>	24.1 (13.2) <sup>d</sup>	53.5 (10.0)

Strength measures. ACSA, anatomical cross-sectional area; BM, body mass; BMD, Becker's muscular dystrophy; CTRL, control; DMD, Duchenne muscular dystrophy; FSHD, facioscapulohumeral muscular dystrophy; KEMVC, knee extension maximal voluntary contraction; kg = kilograms; LGMD, limb-girdle muscular dystrophy, N.m, Newton metres; PFMVC, plantar flexion maximal voluntary contraction.

<sup>a</sup>Denotes significance from BMD.

<sup>b</sup>Denotes significance from LGMD.

<sup>c</sup>Denotes significance from FSHD.

<sup>d</sup>Denotes significance from CTRL.

remained, in addition FSHD were shown as stronger than LGMD (32%,  $P = 0.032$ ) (Table 3).

Control participants were significantly stronger in PFMVC than DMD (75%,  $P < 0.001$ ), BMD (51%,  $P < 0.001$ ), and LGMD (58%,  $P < 0.001$ ) participants, respectively (Table 3). FSHD (62%,  $P < 0.001$ ) and BMD (49%,  $P = 0.007$ ) participants were also stronger than DMD participants (Table 3). No other differences were found between conditions ( $P > 0.05$ ). PFMVC/BM in CTRL was significantly stronger than DMD (72%,  $P < 0.001$ ), BMD (53%,  $P < 0.001$ ), LGMD (63%,  $P < 0.001$ ), and FSHD (39%,  $P = 0.006$ ), respectively (Table 3). Similarly, FSHD were stronger than DMD (55%,  $P = 0.002$ ) and LGMD (39%,  $P = 0.042$ ) participants for PFMVC/BM. BMD participants had greater PFMVC/BM than DMD (42%,  $P = 0.017$ ) participants (Table 3). Once age had been controlled for statistically, all differences remained, in addition FSHD was stronger than BMD (23%,  $P = 0.048$ ) for PFMVC/BM (Table 3).

Control participants had significantly greater PFMVC/ACSA than DMD (80%,  $P < 0.001$ ), BMD (68%,  $P < 0.001$ ), LGMD (72%,  $P < 0.001$ ), and FSHD (40%,  $P = 0.049$ ) participants (Table 3). FSHD participants had greater PFMVC/ACSA than DMD (66%,  $P < 0.001$ ), BMD (47%,  $P = 0.009$ ), and LGMD (53%,  $P = 0.005$ ) participants, respectively (Table 3). No other differences were found between conditions ( $P > 0.05$ ).

### Grip strength

Duchenne MD had significantly weaker handgrip strength than BMD (85%,  $P = 0.001$ ), LGMD (85%,  $P = 0.001$ ), FSHD (87%,  $P < 0.001$ ), and CTRL (94%,  $P < 0.001$ ) participants (Table 3). Compared with CTRL, grip strength was weaker in BMD (63%,  $P < 0.001$ ), LGMD (63%,  $P < 0.001$ ), and FSHD (55%,  $P = 0.003$ ) groups (Table 3). No other differences were found between groups ( $P > 0.05$ ).

### Physical activity

Participants with DMD displayed higher SB than BMD (14%,  $P < 0.001$ ), LGMD (8%,  $P = 0.016$ ), FSHD (14%,  $P < 0.001$ ),

and CTRL (39%,  $P < 0.001$ ) participants, respectively (Table 4). Conversely, CTRL had lower SB than BMD (29%,  $P < 0.001$ ), LGMD (33%,  $P < 0.001$ ), and FSHD (29%,  $P = 0.004$ ) participants, respectively (Table 4). No other differences were found between conditions for SB ( $P > 0.05$ ).

Duchenne MD participants had lower TPA<sup>mins</sup> than BMD (88%,  $P < 0.001$ ), LGMD (83%,  $P = 0.010$ ), FSHD (89%,  $P < 0.001$ ), and CTRL (96%,  $P < 0.001$ ) (Table 4). Furthermore, BMD (65%,  $P < 0.001$ ), LGMD (76%,  $P < 0.001$ ), and FSHD (64%,  $P = 0.001$ ) had lower TPA<sup>mins</sup> than CTRL (Table 4).

### Correlations

Age was shown to be significantly associated with measures of PFMVC/BM ( $R = -0.408$ ,  $P = 0.026$ ), KEMVC ( $R = -0.343$ ,  $P = 0.048$ ), and KEMVC/BM ( $R = -0.384$ ,  $P = 0.030$ ) in BMD participants.

Anthropometric associations with muscle strength revealed significant associations between GM ACSA and PFMVC in CTRL ( $R = 0.553$ ,  $P = 0.003$ ) and DMD ( $R = 0.429$ ,  $P = 0.026$ ) participants, respectively. Other conditions showed positive but non-significant associations between muscle size and PFMVC ( $P > 0.05$ ). No associations were identified between LBM and muscle strength measures in adults with MD ( $P > 0.05$ ).

Sedentary behaviour was negatively associated with LBM in participants with DMD ( $R = -0.446$ ,  $P = 0.021$ ), but no other groups. Furthermore, SB was negatively associated with KEMVC ( $R = -0.477$ ,  $P = 0.006$ ) and KEMVC/BM ( $R = -0.487$ ,  $P = 0.005$ ) in BMD, with other dystrophic groups showing no correlation. Furthermore, TPA<sup>mins</sup> was associated with KEMVC in BMD ( $R = 0.407$ ,  $P = 0.020$ ) participants.

Of the participants with the ability to ambulate, 20/24 recorded 10 m walk times. Strength measures associated with 10 m walk were KEMVC ( $R = 0.484$ ,  $P = 0.030$ ), KEMVC/BM ( $R = 0.514$ ,  $P = 0.020$ ), PFMVC ( $R = 0.502$ ,  $P = 0.024$ ), and PFMVC/BM ( $R = 0.472$ ,  $P = 0.001$ ). In addition, TPA<sup>mins</sup> was also associated with 10 m walk ( $R = 0.735$ ,  $P < 0.001$ ). Multiple linear regression identified TPA<sup>mins</sup> as the greatest predictor of 10 m walk time ( $R^2 = 0.540$ ,  $P < 0.001$ ), with all strength measures excluded.

**Table 4** Physical activity and 10 m walk time

	DMD	BMD	LGMD	FSHD	CTRL
TPA <sup>mins</sup>	13.5 (16.1) <sup>a,b,c,d</sup>	115.4 (63.1) <sup>d</sup>	80.3 (34.6) <sup>c,d</sup>	117.6 (58.2) <sup>d</sup>	329.1 (125.0)
Sedentary behaviour (%)	97.1 (3.3) <sup>a,b,c,d</sup>	83.8 (8.8) <sup>d</sup>	88.9 (5.4) <sup>d</sup>	83.1 (6.4) <sup>d</sup>	59.3 (15.2)
10 m walk (s) <sup>e</sup>	n/a		11.8 (4.5)		n/a

Physical activity and 10 m walk. BMD, Becker's muscular dystrophy; CTRL, control; DMD, Duchenne muscular dystrophy; FSHD, facioscapulohumeral muscular dystrophy; LGMD, limb-girdle muscular dystrophy; m, metre; s, second; TPA<sup>mins</sup>, total minutes being physically active.

<sup>a</sup>Denotes significance from BMD.

<sup>b</sup>Denotes significance from LGMD.

<sup>c</sup>Denotes significance from FSHD.

<sup>d</sup>Denotes significance from CTRL.

<sup>e</sup>Performed by 20/24 ambulant participants.



## Discussion

The present study showed cross-sectional findings of muscle weakness in adults across four MD classifications, with, as expected, a direct relationship between muscle strength and muscle size observed in adults with DMD. In addition, quantitative measures of PA show increased levels of SB in all dystrophic conditions in comparison with CTRL, particularly within DMD participants whom were more sedentary than BMD, LGMD, and FSHD participants. Furthermore, relationships were identified between muscle strength, specifically KEMVC, and TPA<sup>mins</sup> in adults with BMD. Moreover, relationships were also identified between TPA<sup>mins</sup> and 10 m walk times in the 20, cross-condition, participants that completed the functional task.

The present understanding of muscle strength in MD is primarily focussed in DMD paediatric populations.<sup>17</sup> Adults with DMD in the present study showed KEMVC 92% less than CTRL participants, reflective of the degenerative nature of the condition, with previous paediatric studies reporting KEMVC as 72–86% less than CTRL.<sup>13,64,17,15,65,66</sup> Similarly, the 75% lower PFMVC reported in the current study appears consistent with the progression of the condition, where previous studies have reported PFMVC in paediatric groups as 52–65% of age-matched CTRL.<sup>64,17,65,67</sup> More pronounced muscle weakness is predicted in adults with DMD; however, this is likely exacerbated into adulthood by a lack of PA. The relative maintenance of muscle strength of plantar flexors, compared with knee extensors, is consistent with the classical proximal-distal wasting<sup>11</sup>; however may also be influenced by the long-term impact of wheelchair use. There is currently a lack of quality natural history reports using quantitative measures of KE or PF MVC in adults with MD.<sup>52</sup>

Despite weakness being a clinical diagnostic tool,<sup>52,68</sup> there are limited quantitative measures of muscle strength in adults with MD compared with age-matched CTRL. Differences from CTRL in the present study, are similar to those reported previously. Of the other MDs measured (BMD, LGMD, FSHD), PFMVC in the present study was 42–49% less than CTRL, compared with 48–61% reported in adults with BMD and LGMD.<sup>12</sup> Additionally, KEMVC in the present study was 25% less than CTRL, compared with 55–58% in previous studies of FSHD.<sup>14,16</sup> The small differences between the present and previous research can be attributed to the heterogeneity of conditions,<sup>69</sup> participant sex differences (present study all male participants),<sup>12,16</sup> participants ages,<sup>14</sup> differences in strength assessment,<sup>12,14</sup> and condition severity in the participant groups [e.g. 47% non-ambulant (excluding DMD) in the current study], with previous research typically all ambulant.<sup>12,14</sup> The present data are particularly novel in the objective assessment of SB and PA as contributing factors to the differences between groups and participants with MD.

Previous PA data from dystrophic conditions have almost exclusively been presented from paediatric DMD

populations.<sup>30,32,33</sup> The only PA comparisons from adults with dystrophic conditions to CTRL have been presented in the form of self-reported PA history from our previous papers.<sup>26,27</sup> The use of quantitative measures of PA through triaxial accelerometry allows for a much greater understanding PA. Understandably, adults with DMD had the highest SB; however, the ability of some DMD participants to participate in forms of PA, the negative association between SB and LBM, and previous evidence showing maintained function with the use of arm-cycle ergometers<sup>40</sup> suggest that PA should be encouraged through the use of adapted equipment and hydrotherapy.

The significant relationship between PA and KEMVC is a key finding from the current study. The relationships identified between TPA<sup>mins</sup> and KEMVC in BMD are furthered by the stronger relationship of TPA<sup>mins</sup> with 10 m walk time in ambulant MD participants and are consistent with those relationships identified within elderly populations<sup>24,70</sup> and paediatric DMD populations.<sup>58</sup> However, future work is required to quantify activity thresholds relative to separate conditions, and between ambulant and non-ambulant individuals, in order to quantify PA intensities, and the relative intensities relationships with functional outcomes.

### Study limitation and strengths

The authors acknowledge that a wide range of techniques have previously been used to describe changes in body composition and muscle size in clinical populations.<sup>71–73</sup> BIA, however, is necessary as an alternative to more stringent measures of body composition in MD where mobility is limited.<sup>45</sup> BIA has been used extensively in sarcopenia research<sup>74,75</sup> and shown as valid in obese and underweight individuals,<sup>76,44,77</sup> a degree of error is however likely to be introduced within MD given the fat infiltration of muscle tissue.<sup>44</sup> Based on previous validity data, BIA would underestimate the BF% in the present overweight MD participants and underestimate BF% in normal weight CTRL participants.<sup>44</sup> When corrected based on the values previously established, BF% would be 18% in CTRL (measured = 18.2%) and 33.8% in MD (measured = 30.8%). Therefore, despite the error associated with comparing BF% when using BIA, there is no meaningful impact on the conclusions drawn from the presented results. Similarly, the use of ultrasound for assessment of ACSA, although consistent with those previously reported, is likely to be overestimated in those individuals with high levels of muscle fat fraction (FF%).<sup>12</sup> Based on the work of Lokken et al.,<sup>12</sup> the actual GM contractile area of ambulant BMD participants is ~23% less than the measured ACSA; in contrast, the GM contractile area of the CTRL is 11% less than the measured ACSA. Based on this estimated value, the contractile area in ambulant BMD ( $n = 10$ ) is 15.7 cm<sup>2</sup> and CTRL is 13.0 cm<sup>2</sup> in the present study, consistent with the comparisons made by Lokken et al. It is

therefore likely that the present GM ACSA is higher in the BMD participants due to the presence of pseudohypertrophy.<sup>18</sup> Future work is required to determine whether the measurement of muscle area is meaningful within adults with MD as it may not reflect any functional measure due to the level of non-contractile material contained within the muscle compartment (as observed within the lack of correlation between ACSA and strength in the present study and previous<sup>12</sup>).

Although there are shortcomings to using BIA and ultrasound for assessing body composition and muscle mass, the use of transportable and adaptable equipment in the present study however has allowed for 60 adults with MD encompassing a wide range of functional ability to be assessed. Up to 60% of MD participants would have been unable to participate had DEXA or MRI been used for body composition and FF% assessment. The present authors suggest the use of adaptable equipment to encompass wide functional ranges in future studies, with the use of methods such as MRI to assess muscle FF% in sample subsets when possible and practical.

## Conclusions

The present study quantifies muscle weakness (PFMVC and KEMVC) across four MD classifications and can add to the

currently under-reported, yet clinically observed, physiological understanding of these conditions. Significant relationships were identified between muscle size and muscle strength of plantar flexors in DMD adults. Furthermore, cross-sectional findings of PA in dystrophic conditions are presented, with significant increases in SB in all MD conditions compared with CTRL. Relationships have been identified between SB and reduced LBM, minutes of being physically active and knee extension within BMD, as well as 10 m walk time in ambulant MD participants, suggesting PA should be encouraged. However, future work must quantify different PA intensities, as well as consider the safety and appropriateness of PA intensity relevant to MD classification.

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The authors certify that they comply with the ethical guidelines for authorship and publishing of the Journal of Cachexia, Sarcopenia and Muscle.<sup>78</sup>

## Conflict of interest

None declared.

## References

1. Fukunaga T, Miyatani M, Tachi M, Kouzaki M, Kawakami Y, Kanehisa H. Muscle volume is a major determinant of joint torque in humans. *Acta Physiol Scand* 2001;**172**:249–255.
2. Visser M, Deeg DJH, Lips P, Harris TB, Bouter LM. Skeletal muscle mass and muscle strength in relation to lower-extremity performance in older men and women. *J Am Geriatr Soc* 2000;**48**:381–386.
3. Hussain AW, Onambele GL, Williams AG, Morse CI. Muscle size, activation, and coactivation in adults with cerebral palsy. *Muscle Nerve* 2014;**49**:76–83.
4. Goodpaster BH, Park SW, Harris TB, Kritchevsky SB, Nevitt M, Schwartz AV, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci* 2006;**61**:1059–1064.
5. Lauretani F, Russo CR, Bandinelli S, Bartali B, Cavazzini C, Di Iorio A, et al. Age-associated changes in skeletal muscles and their effect on mobility: an operational diagnosis of sarcopenia. *J Appl Physiol* 2003;**95**:1851–1860.
6. Sveen ML, Jeppesen TD, Hauerslev S, Kober L, Krag TO, Vissing J. Endurance training improves fitness and strength in patients with Becker muscular dystrophy. *Brain* 2008;**131**:2824–2831.
7. Van der Kooij EL, Vogels OJM, van Asseldonk R, Lindeman E, Hendriks JCM, Wohlgemuth M, et al. Strength training and albuterol in facioscapulohumeral muscular dystrophy. *Neurology* 2004;**63**:702–708.
8. Jimenez-Moreno AC, Newman J, Charman SJ, Catt M, Trenell MI, Gorman GS, et al. Measuring habitual physical activity in neuromuscular disorders: a systematic review. *J Neuromuscul Dis* 2017;**4**:25–52.
9. Huml RA. *Muscular Dystrophy: A Concise Guide*. Cham: Springer; 2015.
10. Koenig M, Beggs AH, Moyer M, Scherpf S, Heindrich K, Bettecken T, et al. The molecular basis for Duchenne versus Becker muscular dystrophy: correlation of severity with type of deletion. *Am J Hum Genet* 1989;**45**:498–506.
11. Emery AEH. The muscular dystrophies. *Lancet* 2002;**359**:687–695.
12. Løkken N, Hedermann G, Thomsen C, Vissing J. Contractile properties are disrupted in Becker muscular dystrophy, but not in limb girdle type 2I. *Ann Neurol* 2016;**80**:466–471.
13. Akima H, Lott D, Senesac C, Deol J, Germain S, Arpan I, et al. Relationships of thigh muscle contractile and non-contractile tissue with function, strength, and age in boys with Duchenne muscular dystrophy. *Neuromuscul Disord* 2012;**22**:16–25.
14. Skalsky AJ, Abresch RT, Han JJ, Shin CS, McDonald CM. The relationship between regional body composition and quantitative strength in facioscapulohumeral muscular dystrophy (FSHD). *Neuromuscul Disord* 2008;**18**:873–880.
15. Skalsky AJ, Han JJ, Abresch RT, Shin CS, McDonald CM. Assessment of regional body composition with dual-energy X-ray absorptiometry in Duchenne muscular dystrophy: correlation of regional lean mass and quantitative strength. *Muscle Nerve* 2009;**39**:647–651.
16. Bachasson D, Temesi J, Bankole C, Lagrange E, Boutte C, Millet GY, et al. Assessment of quadriceps strength, endurance and fatigue in FSHD and CMT: benefits and limits

- of femoral nerve magnetic stimulation. *Clin Neurophysiol* 2014;**125**:396–405.
17. Mathur S, Lott DJ, Senesac C, Germain SA, Vohra RS, Sweeney HL, et al. Age-related differences in lower-limb muscle cross-sectional area and torque production in boys with Duchenne muscular dystrophy. *Arch Phys Med Rehabil* 2010;**91**:1051–1058.
  18. Jones DA, Round JM, Edwards RH, Grindwood SR, Tofts PS. Size and composition of the calf and quadriceps muscles in Duchenne muscular dystrophy. A tomographic and histochemical study. *J Neurol Sci* 1983;**60**:307–322.
  19. Deconinck N, Dan B. Pathophysiology of duchenne muscular dystrophy: current hypotheses. *Pediatr Neurol* 2007;**36**:1–7.
  20. Morse CI, Smith J, Denny A, Tweedale J, Searle ND. Gastrocnemius medialis muscle architecture and physiological cross sectional area in adult males with Duchenne muscular dystrophy. *J Musculoskelet Neuronal Interact* 2015;**15**:154–160.
  21. Warburton DER, Nicol CW, Bredin SSD. Health benefits of physical activity: the evidence. *Can Med Assoc J* 2006;**174**:801–809.
  22. Nelson ME, Rejeski WJ, Blair SN, Duncan PW, Judge JO, King AC, et al. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Circulation* 2007;**116**:1094–1105.
  23. Morie M, Reid KF, Miciak R, Lajevardi N, Choong K, Krasnoff JB, et al. Habitual physical activity levels are associated with performance in measures of physical function and mobility in older men. *J Am Geriatr Soc* 2010;**58**:1727–1733.
  24. Foong YC, Chherawala N, Aitken D, Scott D, Winzenberg T, Jones G. Accelerometer-determined physical activity, muscle mass, and leg strength in community-dwelling older adults. *J Cachexia Sarcopenia Muscle* 2015.
  25. Muscular Dystrophy Campaign U. Exercise advice for adults with muscle-wasting conditions 2014.
  26. Morse CI, Smith J, Denny A, Tweedale J, Searle ND, Winwood K, et al. Bone health measured using quantitative ultrasonography in adult males with muscular dystrophy. *J Musculoskelet Neuronal Interact* 2016;**16**:339–347.
  27. Jacques MF, Orme P, Smith J, Morse CI. Resting energy expenditure in adults with Becker's muscular dystrophy. *PLoS One* 2017;**12**:e0169848.
  28. Hawker GA, Ridout R, Harris VA, Chase CC, Fielding LJ, Biggar WD. Alendronate in the treatment of low bone mass in steroid-treated boys with Duchenne's muscular dystrophy. *Arch Phys Med Rehabil* 2005;**86**:284–288.
  29. Heutinck L, van Kampen N, Jansen M, de Groot I. Physical activity in boys with DMD is lower and less demanding compared to healthy boys. *Neuromuscul Disord* 2015;**25**:S303–S304.
  30. McDonald CM, Widman LM, Walsh DD, Walsh SA, Abresch RT. Use of step activity monitoring for continuous physical activity assessment in boys with Duchenne muscular dystrophy. *Arch Phys Med Rehabil* 2005;**86**:802–808.
  31. Davidson ZE, Ryan MM, Kornberg AJ, Walker KZ, Truby H. Strong correlation between the 6-minute walk test and accelerometry functional outcomes in boys with Duchenne muscular dystrophy. *J Child Neurol* 2015;**30**:357–363.
  32. Jeannot P-Y, Aminian K, Bloetzer C, Najafi B, Paraschiv-Ionescu A. Continuous monitoring and quantification of multiple parameters of daily physical activity in ambulatory Duchenne muscular dystrophy patients. *Eur J Paediatr Neurol* 2011;**15**:40–47.
  33. Elliott SA, Davidson ZE, Davies PSW, Truby H. Accuracy of parent-reported energy intake and physical activity levels in boys with Duchenne muscular dystrophy. *Nutr Clin Pract* 2015;**30**:297–304.
  34. Dyrstad SM, Hansen BH, Holme IM, Anderssen SA. Comparison of self-reported versus accelerometer-measured physical activity. *Med Sci Sports Exerc* 2014;**46**:99–106.
  35. Shields M, Tremblay MS. Sedentary behaviour and obesity. *Health Rep* 2008;**19**:19–30.
  36. Tremblay MS, Colley RC, Saunders TJ, Healy GN, Owen N. Physiological and health implications of a sedentary lifestyle. *Appl Physiol Nutr Metab* 2010;**35**:725–740.
  37. Dempsey PC, Owen N, Biddle SJH, Dunstan DW. Managing sedentary behavior to reduce the risk of diabetes and cardiovascular disease. *Curr Diab Rep* 2014;**14**:522.
  38. Wullems JA, Verschuere SMP, Degens H, Morse CI, Onambélé GL. A review of the assessment and prevalence of sedentarism in older adults, its physiology/health impact and non-exercise mobility countermeasures. *Biogerontology* 2016;**17**:547–565.
  39. Ferguson MR, Poliachik SL, Shaffer ML, Friedman SD, Voet N, Janssen B, et al. Quantitative MRI reveals decelerated fatty infiltration in muscles of active FSHD patients. *Neurology* 2016;**87**:1746.
  40. Jansen M, van Alfen N, Geurts ACH, de Groot IJM. Assisted bicycle training delays functional deterioration in boys with Duchenne muscular dystrophy: the randomized controlled trial "no use is disuse". *Neurorehabil Neural Repair* 2013;**27**:816–827.
  41. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 2013;**310**:2191.
  42. Reeves SL, Varakamin C, Henry CJ. The relationship between arm-span measurement and height with special reference to gender and ethnicity. *Eur J Clin Nutr* 1996;**50**:398–400.
  43. Okasora K, Takaya R, Tokuda M, Fukunaga Y, Oguni T, Tanaka H, et al. Comparison of bioelectrical impedance analysis and dual energy X-ray absorptiometry for assessment of body composition in children. *Pediatr Int* 1999;**41**:121–125.
  44. Sun G, French CR, Martin GR, Younghusband B, Green RC, Xie Y-g, et al. Comparison of multifrequency bioelectrical impedance analysis with dual-energy X-ray absorptiometry for assessment of percentage body fat in a large, healthy population. *Am J Clin Nutr* 2005;**81**:74–78.
  45. Mok E, Letellier G, Cuisset J-M, Denjean A, Gottrand F, Hankard R. Assessing change in body composition in children with Duchenne muscular dystrophy: anthropometry and bioelectrical impedance analysis versus dual-energy X-ray absorptiometry. *Clin Nutr* 2010;**29**:633–638.
  46. McCabe MP, Ricciardelli LA, Parent P. Body mass index. *Eat Disord* 2013;**34**:90.
  47. Sharma KR, Mynhier MA, Miller RG. Muscular fatigue in Duchenne muscular dystrophy. *Neurology* 1995;**45**:306–310.
  48. Brussock CM, Haley SM, Munsat TL, Bernhardt DB. Measurement of isometric force in children with and without Duchenne's muscular dystrophy. *Phys Ther* 1992;**72**:105–114.
  49. Hogrel J-Y, Payan CA, Ollivier G, Tanant V, Attarian S, Couillandre A, et al. Development of a French isometric strength normative database for adults using quantitative muscle testing. *Arch Phys Med Rehabil* 2007;**88**:1289–1297.
  50. Narici MV, Hoppeler H, Kayser B, Landoni L, Claassen H, Gavardi C, et al. Human quadriceps cross-sectional area, torque and neural activation during 6 months strength training. *Acta Physiol Scand* 1996;**157**:175–186.
  51. Willis TA, Hollingsworth KG, Coombs A, Sveen M-L, Andersen S, Stojkovic T, et al. Quantitative magnetic resonance imaging in limb-girdle muscular dystrophy 2I: a multinational cross-sectional study. *PLoS One* 2014;**9**:e90377.
  52. McDonald CM, Henricson EK, Abresch RT, Florence JM, Eagle M, Gappmaier E, et al. THE 6-minute walk test and other endpoints in Duchenne muscular dystrophy: longitudinal natural history observations over 48 weeks from a multicenter study. *Muscle Nerve* 2013;**48**:343–356.
  53. Personius KE, Pandya S, King WM, Tawil R, McDermott MP, Group FD. Facioscapulohumeral dystrophy natural history study: standardization of testing procedures and reliability of measurements. *Phys Ther* 1994;**74**:253–263.
  54. Escolar DM, Henricson EK, Mayhew J, Florence J, Leshner R, Patel KM, et al. Clinical evaluator reliability for quantitative and manual muscle testing measures of strength in children. *Muscle Nerve* 2001;**24**:787–793.
  55. Lewelt A, Krosschell KJ, Stoddard GJ, Weng C, Xue M, Marcus RL, et al. Resistance strength training exercise in children with spinal muscular atrophy. *Muscle Nerve* 2015;**52**:559–567.
  56. Fukunaga T, Roy RR, Shellock FG, Hodgson JA, Day MK, Lee PL, et al. Physiological

- cross-sectional area of human leg muscles based on magnetic resonance imaging. *J Orthop Res* 1992;**10**:926–934.
57. Reeves ND, Maganaris CN, Narici MV. Ultrasonographic assessment of human skeletal muscle size. *Eur J Appl Physiol* 2004;**91**:116–118.
  58. Fowler EG, Staudt LA, Heberer KR, Sienko SE, Buckon CE, Bagley AM, et al. Longitudinal community walking activity in Duchenne muscular dystrophy. *Muscle Nerve* 2017; <https://doi.org/10.1002/mus.25743>.
  59. Nightingale TE, Walhin J-P, Thompson D, Bilzon JJ. Influence of accelerometer type and placement on physical activity energy expenditure prediction in manual wheelchair users. *PLoS One* 2015;**10**:e0126086.
  60. Dillon CB, Fitzgerald AP, Kearney PM, Perry IJ, Rennie KL, Kozarski R, et al. Number of days required to estimate habitual activity using wrist-worn GENEActiv accelerometer: a cross-sectional study. *PLoS One* 2016;**11**: e0109913.
  61. van Hees VT, Renström F, Wright A, Gradmark A, Catt M, Chen KY, et al. Estimation of daily energy expenditure in pregnant and non-pregnant women using a wrist-worn tri-axial accelerometer. *PLoS One* 2011;**6**:e22922.
  62. Phillips LRS, Parfitt G, Rowlands AV. Calibration of the GENEActiv accelerometer for assessment of physical activity intensity in children. *J Sci Med Sport* 2013;**16**:124–128.
  63. Eslinger DW, Rowlands AV, Hurst TL, Catt M, Murray P, Eston RG. Validation of the GENEActiv accelerometer. *Med Sci Sports Exerc* 2011;**43**:1085–1093.
  64. Lott DJ, Forbes SC, Mathur S, Germain SA, Senesac CR, Sweeney HL, et al. Assessment of intramuscular lipid and metabolites of the lower leg using magnetic resonance spectroscopy in boys with Duchenne muscular dystrophy. *Neuromuscul Disord* 2014;**24**:574–582.
  65. Wokke BH, Van Den Bergen JC, Versluis MJ, Niks EH, Milles J, Webb AG, et al. Quantitative MRI and strength measurements in the assessment of muscle quality in Duchenne muscular dystrophy. *Neuromuscul Disord* 2014;**24**:409–416.
  66. Lerario A, Bonfiglio S, Sormani M, Tettamanti A, Markt S, Napolitano S, et al. Quantitative muscle strength assessment in Duchenne muscular dystrophy: longitudinal study and correlation with functional measures. *BMC Neurol* 2012;**12**:91.
  67. Vohra RS, Lott D, Mathur S, Senesac C, Deol J, Germain S, et al. Magnetic resonance assessment of hypertrophic and pseudo-hypertrophic changes in lower leg muscles of boys with Duchenne muscular dystrophy and their relationship to functional measurements. *PLoS One* 2015;**10**: e0128915.
  68. Griggs RC, Moxley R, Mendell JR, Fenichel GM, Brooke MH, Pestronk A, et al. Duchenne dystrophy randomized, controlled trial of prednisone (18 months) and azathioprine (12 months). *Neurology* 1993;**43**:520–527.
  69. Wicklund MP, Kissel JT. The limb-girdle muscular dystrophies. *Neurol Clin* 2014;**32**:729–749.
  70. Santos DA, Silva AM, Baptista F, Santos R, Vale S, Mota J, et al. Sedentary behavior and physical activity are independently related to functional fitness in older adults. *Exp Gerontol* 2012;**47**:908–912.
  71. Martone AM, Bianchi L, Abete P, Bellelli G, Bo M, Cherubini A, et al. The incidence of sarcopenia among hospitalized older patients: results from the Glisten study. *J Cachexia Sarcopenia Muscle* 2017;**8**:907–914.
  72. Blauwhoff-Buskermolen S, Langius JAE, Becker A, Verheul HMW, de van der Schueren MAE. The influence of different muscle mass measurements on the diagnosis of cancer cachexia. *J Cachexia Sarcopenia Muscle* 2017;**8**:615–622.
  73. Yang M, Hu X, Wang H, Zhang L, Hao Q, Dong B. Sarcopenia predicts readmission and mortality in elderly patients in acute care wards: a prospective study. *J Cachexia Sarcopenia Muscle* 2017;**8**:251–258.
  74. Makizako H, Shimada H, Doi T, Tsutsumimoto K, Lee S, Lee SC, et al. Age-dependent changes in physical performance and body composition in community-dwelling Japanese older adults. *J Cachexia Sarcopenia Muscle* 2017;**8**:607–614.
  75. Heber D, Ingles S, Ashley JM, Maxwell MH, Lyons RF, Elashoff RM. Clinical detection of sarcopenic obesity by bioelectrical impedance analysis. *Am J Clin Nutr* 1996;**64**:472S–477S.
  76. Pateyjohns IR, Brinkworth GD, Buckley JD, Noakes M, Clifton PM. Comparison of three bioelectrical impedance methods with DXA in overweight and obese men. *Obesity* 2006;**14**:2064–2070.
  77. Lupoli L, Sergi G, Coin A, Perissinotto E, Volpato S, Busetto L, et al. Body composition in underweight elderly subjects: reliability of bioelectrical impedance analysis. *Clin Nutr* 2004;**23**:1371–1380.
  78. von Haehling S, Morley JE, Coats AJS, Anker SD. Ethical guidelines for publishing in the Journal of Cachexia, Sarcopenia and Muscle: update 2017. *J Cachexia Sarcopenia Muscle* 2017;**8**:1081–1083.