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31 Abstract

32 **Purpose.** Muscular dystrophy (MD) is an umbrella term for muscle wasting conditions, for
33 which longitudinal changes in function and body composition are well established in children
34 with Duchenne (DMD), however changes in adults with DMD and Beckers (BMD),
35 respectively, remain poorly reported. This study aims to assess 12-month changes in lower-
36 limb strength, muscle size, body composition and physical activity in adults with Muscular
37 Dystrophy (MD).

38 **Methods.** Adult males with Duchenne MD (DMD; N = 15) and Beckers MD (BMD; N = 12)
39 were assessed at baseline and 12-months for body composition (Body fat and lean body mass
40 (LBM)), Isometric maximal voluntary contraction (Knee-Extension (KEMVC) and Plantar-
41 Flexion (PFMVC)) and physical activity (tri-axial accelerometry).

42 **Results.** 12-month change in strength was found as -19% (PFMVC) and -14% (KEMVC) in
43 DMD. 12-month change in strength in BMD, although non-significant, was explained by
44 physical activity ($R^2=.532-.585$). Changes in LBM (DMD) and body fat (BMD) were both
45 masked by non-significant changes in body mass.

46 **Discussion.** 12-month changes in adults with DMD appear consistent with paediatric
47 populations. Physical activity appears important for muscle function maintenance. Specific
48 monitoring of body composition, and potential co-morbidities, within adults with MD is
49 highlighted.

50 Keywords: Beckers; Duchenne; Dystrophy; Natural History; Physical Activity; Strength.

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52 Word Count: 3726

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Main Text:

Introduction

Duchenne (DMD) and Beckers (BMD) Muscular Dystrophy (MD) are two genetic conditions resulting in progressive muscle weakness and declining muscle mass [1]. Unlike many other forms of MD, which affect a variety of different proteins associated with the sarcolemma [2], DMD and BMD are unique in that they are both affected by impairment of the same protein, named Dystrophin [3, 4]. DMD results from an absent or non-functioning dystrophin protein, therefore is more progressive, with loss of ambulation by the age of 12 [5, 6]. BMD in comparison is caused by a partially functioning dystrophin protein, therefore a slower and more variable form of MD, with the loss of ambulation in adulthood [5, 6]. Despite the well acknowledged genetic understanding of these conditions [3, 4, 7-9], and a breadth of research assessing health and function in children with DMD [10-17], basic understanding of the progression of these conditions and impact on function and health measures remains minimal in adult populations [18].

Lower limb muscle strength has historically been a key outcome measure reported in MD [19-25], with assessment using direct measures (either objectively using dynamometers or through subjective assessments such as manual muscle testing (MMT)) or indirect measures, such as

81 sit-to-stand or 10m walk time [19, 22, 26-29]. Longitudinal strength change in BMD has only
82 been described through MMT assessment of knee extension strength (KEMVC) however,
83 showing annual declines of 1.2% [28]. More recently, the current authors demonstrated that in
84 adults with MD, variance in KEMVC and functional measures could be explained by
85 accelerometer determined physical activity (PA)[19]. It is therefore important to understand
86 the rate of strength decline in adults with BMD, but also to assess the impact of PA on strength.
87 Cross-sectional and natural history studies by comparison are more common within children
88 with DMD [20, 21, 23, 30, 31]. Indeed, muscle weakness is typically identified during
89 childhood in DMD, with impaired gait an early indicator of DMD [32, 33]. Subjective methods
90 of MMT or Medical research council scales (MRC%) have reported annual declines of
91 KEMVC as 4-5% and 1.2-2% in ambulant (5-13 years) and non-ambulant (13-24 years)
92 children with DMD, respectively [27, 34, 35]. Objective measures such as dynamometers
93 however have identified, annual declines of KEMVC as 15% in children with DMD (8-12
94 years) [36]. Despite lower limb muscle strength having limited clinical relevance in adults with
95 DMD, it remains essential that a comprehensive understanding of the progression of DMD in
96 this older, unreported age group is developed, in order to develop a life-long understanding of
97 condition progression, provide comparative norms using relevant and accessible methods, as
98 well as to provide comparisons for future longitudinal assessments of steroid or gene therapy
99 studies which may be relevant to this group [18, 37].

100 Strength and function have been associated with Lean Body Mass (LBM) in children with
101 DMD [38, 39]. While pseudohypertrophy (increased muscle size without relative increase in
102 strength) of the calves is well documented in children and adolescents with DMD [31, 40, 41],
103 recent research suggests it may not persist in adults with DMD however [19, 42]. Furthermore,
104 the pre-disposition of impaired muscular, respiratory and cardiac systems to ill health can be
105 placed under further pressure by increased sedentary behaviour [19], resulting in greater fat

106 mass, which has previously been cited as a common co-morbidity in adults with MD [43, 44],
107 and reported as higher in non-ambulant than ambulant adults with BMD [45]. Continual
108 assessment, and understanding, of body composition changes of both lean and fat mass is
109 essential, for not only their implications on function, but also the much broader impacts on
110 health and wellbeing [13, 46].

111 This study aims to: 1) Quantify changes, from a one year follow up, in body composition,
112 muscle strength, muscle size and physical activity levels in adults with DMD and BMD; and
113 2) Identify the impact of changes in physical activity on body composition and muscle strength.

114 The authors hypothesise that declines will be greater in DMD than BMD, although still evident
115 in both conditions, for lower limb strength, muscle size and LBM. In addition, PA may account
116 for some of the variance in lower limb strength change in BMD, but not DMD.

117 **Materials and Methods**

118 This study comprised of adult male volunteers with DMD (n= 15) and BMD (n= 12). All
119 participants were recruited from, and tested at, The Neuromuscular Centre (Winsford, UK). No
120 participants were habitually taking part in a structured training programme, however all were
121 receiving weekly, bi-weekly or monthly physiotherapy treatment, consisting of passive
122 stretching, along with access to low intensity cardiovascular exercise equipment (monthly
123 frequency of physiotherapy for DMD = 4 (1-4), BMD = 2 (1-2) expressed as Median (range).
124 Ethical approval was obtained through the Manchester Metropolitan University Ethics
125 Committee, and all participants signed informed consent forms prior to participation. All
126 procedures complied with the latest edition of the World Medical Association Declaration of
127 Helsinki [47].

128 All method protocols, data presentation and reliability, have been reported previously [19],
129 where they can be read in full. A brief overview of each method has been presented below.

130 ***Procedures***

131 All participants undertook Baseline and 12 \pm 1 month follow up testing. Testing involved
132 functional and morphological tests, which was followed by a 7-day PA assessment, using wrist-
133 worn three-dimensional accelerometers, worn 24 hours a day. The same equipment was used
134 for all participants and due to the high level of contractures present in some participants; all
135 participants were assessed in a seated position to ensure consistency.

136 ***Sample Size***

137 In order to determine the sample size required to provide a representative sample for 12 month
138 changes in adult populations of DMD, statistical *a Priori* power calculations were performed
139 using G*Power 3.1.9.2 software (Franz Faul, Universitat Kiel, Germany). For this calculation,
140 alpha was set a 0.05 and beta at 0.80. The DMD sample size was calculated to show a 10%
141 change in muscle strength score consistent with the natural history group previously reported
142 by Mendell et al. [34]. This method calculated an adequate adult DMD sample size of $n = 15$.
143 For BMD, due to the lack of extant data for *a Priori* calculation to be performed, it was deemed
144 that the power calculation for BMD participants in clinical trials ($n = 15$) by Bello et al. [7]
145 was appropriate.

146 ***Anthropometry***

147 All participants were weighed in a digital seated scales system (6875, Detecto, Webb City, Mo,
148 USA). Slings, shoes, splints etc. were weighed separately and subtracted from the gross weight.
149 All participants' height was calculated as point-to-point of arm span (index finger, elbow,
150 shoulder and across midline) to replicate the method used on non-ambulatory participants [45,
151 48].

152 ***Body Composition***

153 Body composition measures of body fat and LBM were measured using Bioelectrical
154 Impedance (BIA) in a fasted state following a 12 hour fast, with adhesive electrodes placed on

155 the right hand and foot. BIA has been promoted as a measure for change in fat and LBM over
156 time in a dystrophic population [16].

157 Lean Body Mass was determined by the following equation:

$$158 \quad LBM (Kg) = Body Mass (Kg) - Fat Mass (Kg)$$

159 Body Mass Index (BMI) was calculated using the following equation [49]:

$$160 \quad BMI \left(\frac{Kg}{m^2} \right) = Body Mass (Kg) \div Height^2 (m^2)$$

161 ***Muscle Strength***

162 Due to the high levels of contractures present in adults with DMD, strength testing protocols
163 were designed to be completed on the most mechanically limited participants, and replicated
164 on all others. Therefore, isometric plantar flexion maximal voluntary contraction (PFMVC)
165 and KEMVC force was recorded using a load cell, with all participants in a seated position
166 replicative of quantitative muscle testing [31]. The load cell was calibrated using a known load
167 of 500g-5kg, in 500g increments, prior to every strength testing session. MVC measures all
168 took place with the participant seated, with hip and knee angles maintained at 90°, for which
169 non-ambulant participants remained in their manual/power wheelchair. For KEMVC, a strap
170 was tightly fastened around the participant's ankle, and attached perpendicularly to the load
171 cell, which was fastened to a weighted support bar. For PFMVC the participants foot was
172 attached to a footplate, with the load cell attached underneath. PFMVC measures were taken
173 from 0° (neutral position), or as close to neutral as possible due to equinus deformity evident
174 in DMD [50]. For PFMVC the practitioner provided the resistive force to ensure an isometric
175 contraction, and all measures of force were normalised for gravity. Three trials were performed
176 for PFMVC and KEMVC respectively, with extended breaks of 1 minute between trials due to
177 the increased fatigue associated with MD [51]. Force (N) was converted to torque (N·m) by

178 multiplying the force measurement by the moment arm from the axis of rotation (knee or ankle)
179 to the point of force measurement (the strap height on the shin, or ball of the foot). PFMVC
180 and KEMVC measures have been presented as torque (N.m).

181 This method has been shown to be highly reliable for both PFMVC and KEMVC in adults with
182 DMD (Within Day ICC: 0.98 and 0.99; Between Day ICC: 0.98 and 0.99) and BMD (Within
183 Day ICC: 0.91 and 0.99; Between Day ICC: 0.83 and 0.99) [19].

184 *Muscle Size Assessment*

185 Gastrocnemius Medialis (GM) anatomical cross sectional area (ACSA) was measured using
186 transverse ultrasound scans (7.5-MHz linear array probe) at 50% of muscle length, consistent
187 with the muscle length at which the largest ACSA occurs [52]. Echoabsorptive tape (Transpore,
188 3M, USA) was used to project shadows on the ultrasound image during recording to provide a
189 positional reference. From which still images were captured then recreated into a single image
190 offline (Graphic Image Manipulation Program, GIMP Development) using the shadows from
191 echoabsorptive tape, muscle markers and aponeurosis of the muscle. The ACSA was then
192 measured using digitising software (ImageJ 1.45, National Institute of Health, USA). Further
193 details can be found in our previous reports of GM ACSA in MD [42, 45]. This method of
194 ACSA assessment has been reported previously as reliable (0.998) and valid (0.999) in
195 comparison to Magnetic Resonance Imaging (MRI) [53].

196 It is important to note that this method measures the area within the fascia of the muscle
197 boundaries only, it cannot differentiate muscle or fibrous tissue (more commonly recognised
198 as fat fraction) as seen in MRI [31, 54-56]. Therefore, GM ACSA is a method of assessing
199 psuedohypertrophy only, and not muscle quality or contractile capacity.

200 *10m Walk Time*

201 Nine ambulant BMD participants performed a 10m walk test, one participant however lost
202 ambulation during the one year follow up period, therefore data is presented of the 8
203 participants that completed both the Baseline and 12 months testing. The 10m walk was
204 performed on an even surface, and is a common measure of function within neuromuscular
205 conditions [36, 57]. All participants started in a standing position and were instructed to walk
206 as quickly and safely as they could, with the time recorded from the verbal instruction of “Go”
207 from the practitioner, to the point of crossing the finish line. Walking aids were permitted if
208 required. Participants 10m walk time were recorded as early in the day as possible to limit the
209 effect of fatigue, with the 12-month measure taking place at the same time.

210 *Physical Activity*

211 Daily PA was monitored over a consecutive 7-day period using a wrist-worn tri-axial
212 accelerometer (GENEActiv, Kimbolton, Cambs, United Kingdom). Monitors were initiated to
213 collect data at 100 Hz, worn for 24 hours a day on the preferred wrist of participants and worn
214 continuously for 7 days [58]. Upon completion of 7-day monitoring, data is downloaded into
215 .bin files, converted to 60s epoch .csv files using the GENEActiv PC Software (Version 2.1).
216 60s epoch data files were then entered into an open source Excel macro (v2, Activinsights Ltd.)
217 [59]. GENEActiv monitors have shown high validity for the measurement of both PA and SB
218 (Pearon’s $r = 0.79-0.98$) [59, 60]. PA is presented as a percentage of time spent sedentary
219 (SB%) or total time spent physically active (TPA^{mins})[19].

220 *Functional Status*

221 All participants functional status was assessed by an experienced neuromuscular
222 physiotherapist using the Swinyard Severity Classification scale [61]. The Swinyard Severity
223 Classification grades function and ability to carry out activities of daily living from Stage 1
224 “mild abnormalities in gait, able to climb stairs without assistance”, to Stage 8 “Unable to sit

225 without considerable support, requires maximal assistance for activities of daily living”. The
226 Swinyard Severity Scale has been used extensively in MD research [62-64], and shown to be
227 highly correlated with fraction of lower limb muscle mass in DMD [54].

228 *Statistical Analyses*

229 All analyses were performed using IBM SPSS Statistics v21 software with a critical level of
230 statistical significance set at 5% and all data presented as mean (SD), except for Functional
231 Status which is presented as Median (Range). We have previously published between group
232 differences for baseline measures [19], with the present study interested in differences from
233 baseline-12 months, therefore statistical analysis has been performed on baseline to 12 month
234 changes only (within group), with baseline values presented for clarity. Test for parametricity
235 were performed upon all variables, for repeated measures in DMD, body mass, height, BMI,
236 Lean Mass and PFMVC were parametric, and all other variables were non-parametric. For
237 BMD height, body fat, Lean Mass, GM ACSA, PFMVC, SB% and TPA^{mins} were parametric,
238 all other variables were non-parametric. Respiratory, Gastrostomy and Ambulatory statuses are
239 presented as a characteristic and no statistical analysis was performed on it.

240 For repeated measures, Paired T-tests and Wilcoxon signed rank tests, for parametric and non-
241 parametric respectively, were used to identify changes, with a Bonferroni correction. Where
242 relevant, comparisons are presented with P values, the relative change (%) from baseline and
243 95% Confidence Intervals.

244 Stepwise Multiple Linear Regression was used to identify the best predictors of PFMVC
245 change from GM ACSA Change, LBM Change and Baseline PFMVC. Linear, Quadratic and
246 Cubic regressions are used to best model changes in body composition and muscle strength in
247 relation to age and changes in TPA^{mins}, with the best fit model presented.

248 **Results**

249 ***12 Month Changes***

250 ***DMD***

251 Compared to baseline, 12 month PFMVC and KEMVC decreased in DMD by 19% (P=0.002)
252 and 14% (P=0.003), respectively. Compared to baseline, 12 month LBM and GM ACSA
253 decreased by 5% (P=0.002) and 8% (P=0.012) respectively, in DMD. No other differences
254 were identified between baseline and 12 months for measures of anthropometrics, body
255 composition or muscle size for DMD (table 1, P>0.05).

256 **[Table 1 Here]**

257 ***BMD***

258 There was no difference in KEMVC or PFMVC compared to baseline in BMD (P>0.05).
259 Compared to baseline 10m walk time increased in ambulant BMD by 13% (P=0.005). No other
260 differences were identified between baseline and 12 months for any other measures (table 1).
261 Compared to baseline there was no significant change in GM ACSA or LBM in BMD (P>0.05).
262 In BMD, compared to baseline, Body Fat increased by 4% (P=0.009) after 12 months. One
263 BMD participant lost ambulation between baseline and 12 months. No other differences were
264 identified between baseline and 12 months for measures of anthropometric, body composition
265 or muscle size for BMD (table 2, P>0.05).

266 **[Table 2 Here]**

267 ***Regressions***

268 Stepwise Multiple Linear Regression identified a model containing Baseline PFMVC, GM
269 ACSA change and LBM Change best predicted PFMVC Change in DMD ($R^2=0.582$,
270 P=0.019).

271 No relationship was identified for DMD using any regression model for age or TPA^{mins} change
272 with change in PFMVC, KEMVC, LBM or body fat (P>0.05). No relationships were identified

273 for either DMD or BMD using any regression model for age with change in PFMVC, KEMVC,
274 LBM or body fat, or TPA^{mins} change with change in LBM or body fat (P>0.05).

275 In BMD quadratic polynomial regressions best identified relationships for TPA^{mins} change with
276 PFMVC change ($R^2=.585$, $P=0.019$, figure 1A) and KEMVC change ($R^2=0.532$, $P=0.033$,
277 figure 1B). No relationships were identified in DMD using any regression model for TPA^{mins}
278 PFMVC change or KEMVC change (P>0.05).

279 **[Figure 1 Here]**

280 **Discussion**

281 The present study reports 12 month changes in lower limb muscle strength, muscle size and
282 body composition in adults with BMD and DMD. 12-month changes in lower limb function
283 have been identified using objective measures of muscle strength in adults with DMD and
284 BMD. After 12 months, LBM, GM ACSA, PFMVC and KEMVC decreased in DMD, whereas
285 in BMD there was no change in any measure, other than body fat which increased. Although
286 there was no significant decrease in strength within BMD, the variance in the 12-month change
287 of PFMVC and KEMVC was partially attributable to the variance in physical activity change
288 over the same period.

289 The 14% decline in KEMVC in adults with DMD in the present study is consistent with the
290 15% decline previously reported over a similar timeframe in children with DMD [36]. These
291 declines in KEMVC are in contrast to the 2% and 1.2% declines reported in non-ambulant
292 children and adolescents with DMD, respectively [35, 36]. This discrepancy can be attributed
293 to the greater sensitivity of the methods used in the present study to quantify changes in
294 KEMVC, rather than subjective measures of MMT or MRC% [65, 66]. In adults with BMD
295 we observed no significant change in KEMVC or PFMVC, likely due to greater variance

296 associated with the condition, however the quantified declines of 14% KEMVC and 7%
297 PFMVC remain noteworthy.

298 The increase in body fat in BMD (+4%) in the present study appears consistent with our
299 previous research in which excess weight gain was identified as an issue in BMD, especially
300 in non-ambulant individuals [45]. The relative increase in body fat in BMD compared to DMD
301 may be due to the fact that BMD maintain a greater level of function and physical independence
302 [67], compared to DMD [48] who require assistance in the preparation and consumption of
303 food. Monitoring and management of food intake may be easier and more structured in DMD
304 [68], particularly given 4/15 participants in the current study consumed via PEG. The stable
305 body mass in both DMD and BMD did however mask changes in body composition, with
306 decreased LBM in DMD and increased body fat in BMD. Therefore reaffirming the need for
307 body composition monitoring in these conditions [16].

308 Adults with BMD that maintained or increased PA levels showed a relative increase or
309 maintenance of muscle strength compared to those that decreased PA levels. Increased PA has
310 previously been attributed to decelerating fatty infiltration of muscles in FSHD [69]. Based on
311 the present relationship between PA and declines in muscle strength, it seems reasonable to
312 suggest interventions that increase PA in adults with BMD may benefit muscle strength, while
313 potentially also alleviating some concerns around changes in fat mass identified in the present
314 study. Future work needs to investigate the benefits of increasing PA, and to further identify
315 psycho-somatic and/or social barriers and facilitators of PA and patterns of SB in this
316 population [70].

317 **Study Limitations**

318 The present study has two main limitations, the first being the sample size. Whilst the sample
319 size recruited is aligned with those identified during the *a Priori* power calculations (See
320 Methods [7, 34]), they are comparably small to some previous longitudinal studies [17, 71].

321 The present study however does report on longitudinal changes in function and health in a
322 previously unreported sample, adults with DMD [37], and utilises outcome measures that are
323 more sensitive to previous methods. Differences were identified within the present DMD
324 sample size of $n = 15$, while a Post Hoc calculation for adults with BMD using data from the
325 present study identifies $n = 15$ required for future studies monitoring lower limb muscle
326 strength. Whilst the recruited BMD sample size in the present study is slightly under-powered,
327 it is considerably larger than that reported previously in natural history studies on adults with
328 BMD [28], and contributes significantly to the currently limited longitudinal data in adults with
329 BMD.

330 Secondly, the present study is limited to 12 months monitoring only, which is comparably
331 shorter than some previous studies [28, 35], however consistent with many previous
332 longitudinal studies in children with DMD [25, 72-74]. The 12 month sample period was long
333 enough however to identify specific changes in LBM (DMD), body fat (BMD), GM ACSA
334 (DMD), PFMVC (DMD), KEMVC (DMD) and 10m walk time (BMD). Regardless, this
335 identification of differences in function and health within a 12 month time period is an
336 important finding itself, and further emphasises the need for continuous health and function
337 monitoring and management in these conditions.

338 All DMD participants will have received some form of steroid treatment through childhood
339 and adolescence. Whereby steroid treatment typically stops upon full-time wheelchair use.
340 Given the data collection from a non-NHS organisation, it is beyond the scope of the present
341 investigation to gain historical steroid treatment and dosage information. Therefore, all data
342 has been presented with the caveat that DMD participants will have historically received steroid
343 treatment, however it should be noted that none were currently receiving steroid treatment.

344 **Future Research**

345 Whilst it is important to further understand the progression of these conditions in what has been
346 previously described as an “unforeseen population” [37], further mechanistic insight is
347 required. Primarily, the reductions in strength in the current study are likely attributed to
348 progressive fat fraction within the muscle, synonymous with the condition [20]. Future research
349 should assess the progression of tissue changes in adults with DMD, however the reduction in
350 GM ACSA in the current study appears consistent with previous hypothesis’ that muscle size
351 becomes more representative of contractile tissue quantity in adulthood [42], with the end of
352 the inflammatory induced appearance of psuedohypertrophy. In addition, further understanding
353 of physical behaviours in adults with BMD is required, especially those who retain some form
354 of ambulation, given the present findings on body composition, and previous work
355 demonstrated positive effects of increased step count on contractile tissue in adults with
356 Fascioscapulohumeral MD [75]. More broadly, evidence based nutritional guidelines, with
357 specifics guidance for differing classifications and functional status are required to best manage
358 energy balance and reduce additional strains on health.

359 **Conclusion**

360 In conclusion, the present data describes natural history changes in body composition, strength
361 and physical activity in adults with DMD and BMD. Changes in DMD appear consistent with
362 the understanding of the condition, with 14-19% weaker PFMVC and KEMVC, consistent with
363 paediatric populations [16, 36, 42]. Change in DMD PFMVC was best explained by changes
364 in LBM, GM ACSA and Baseline PFMVC. Within BMD, 12 month changes in PFMVC and
365 KEMVC although not significant, were explained by change in minutes of physical activity.
366 Changes in LBM in DMD and body fat in BMD were both masked by non-significant changes
367 in body mass, furthering the need for specific monitoring of body composition to reduce the
368 development of potential co-morbidities.

369 Acknowledgements

370 N/A

371 Conflict of Interest

372 No potential conflict of interest is reported by the authors

373 Data Availability

374 Data is available upon request to the Author.

375 References

- 376 1. Deconinck, N. and B. Dan, *Pathophysiology of duchenne muscular dystrophy: current*
377 *hypotheses*. Pediatric neurology, 2007. **36**(1): p. 1-7.
- 378 2. Huml, R.A., *Muscular Dystrophy: A Concise Guide*. 2015: Springer.
- 379 3. Bushby, K.M.D., et al., *The clinical, genetic and dystrophin characteristics of Becker muscular*
380 *dystrophy*. Journal of neurology, 1993. **240**(2): p. 105-112.
- 381 4. Hoffman, E.P., R.H. Brown, and L.M. Kunkel, *Dystrophin: the protein product of the Duchenne*
382 *muscular dystrophy locus*. Cell, 1987. **51**(6): p. 919-928.
- 383 5. Emery, A.E.H., *Population frequencies of inherited neuromuscular diseases—a world survey*.
384 *Neuromuscular disorders*, 1991. **1**(1): p. 19-29.
- 385 6. Emery, A.E.H., *The muscular dystrophies*. The Lancet, 2002. **359**(9307): p. 687-695.
- 386 7. Bello, L., et al., *Functional changes in Becker muscular dystrophy: implications for clinical*
387 *trials in dystrophinopathies*. Scientific reports, 2016. **6**: p. 32439.
- 388 8. Ervasti, J.M., et al., *Deficiency of a glycoprotein component of the dystrophin complex in*
389 *dystrophic muscle*. Nature, 1990. **345**(6273): p. 315-319.
- 390 9. Morandi, L., et al., *Dystrophin analysis in Duchenne and Becker muscular dystrophy carriers:*
391 *correlation with intracellular calcium and albumin*. Annals of neurology, 1990. **28**(5): p. 674-
392 679.
- 393 10. Inkley, S.R., F.C. Oldenburg, and P.J. Vignos, *Pulmonary function in Duchenne muscular*
394 *dystrophy related to stage of disease*. The American journal of medicine, 1974. **56**(3): p. 297-
395 306.
- 396 11. Brooke, M.H., et al., *Duchenne muscular dystrophy Patterns of clinical progression and*
397 *effects of supportive therapy*. Neurology, 1989. **39**(4): p. 475-475.
- 398 12. Bakker, J.P.J., et al., *Predictive factors of cessation of ambulation in patients with Duchenne*
399 *muscular dystrophy*. American journal of physical medicine & rehabilitation, 2002. **81**(12): p. 906-
400 912.
- 401 13. Davidson, Z.E. and H. Truby, *A review of nutrition in Duchenne muscular dystrophy*. Journal
402 *of human nutrition and dietetics*, 2009. **22**(5): p. 383-393.
- 403 14. Jones, D.A., et al., *Size and composition of the calf and quadriceps muscles in Duchenne*
404 *muscular dystrophy. A tomographic and histochemical study*. Journal of the neurological
405 *sciences*, 1983. **60**(2): p. 307-22.
- 406 15. Kohler, M., et al., *Quality of life, physical disability, and respiratory impairment in Duchenne*
407 *muscular dystrophy*. American journal of respiratory and critical care medicine, 2005. **172**(8):
408 p. 1032-1036.
- 409 16. Mok, E., et al., *Assessing change in body composition in children with Duchenne muscular*
410 *dystrophy: anthropometry and bioelectrical impedance analysis versus dual-energy X-ray*
411 *absorptiometry*. Clinical nutrition, 2010. **29**(5): p. 633-638.
- 412 17. Henricson, E., et al., *The 6-minute walk test and person-reported outcomes in boys with*
413 *duchenne muscular dystrophy and typically developing controls: longitudinal comparisons*
414 *and clinically-meaningful changes over one year*. PLoS currents, 2013. **5**.

- 415 18. Bettolo, C.M., et al., *Adult Duchenne population: A growing population*. Neuromuscular
416 Disorders, 2016. **26**: p. S126.
- 417 19. Jacques, M.F., et al., *Relationships between muscle size, strength, and physical activity in*
418 *adults with muscular dystrophy*. Journal of Cachexia, Sarcopenia and Muscle, 2018. **9**(6): p.
419 1042-1052.
- 420 20. Akima, H., et al., *Relationships of thigh muscle contractile and non-contractile tissue with*
421 *function, strength, and age in boys with Duchenne muscular dystrophy*. Neuromuscular
422 Disorders, 2012. **22**(1): p. 16-25.
- 423 21. Lerario, A., et al., *Quantitative muscle strength assessment in duchenne muscular dystrophy:*
424 *longitudinal study and correlation with functional measures*. BMC neurology, 2012. **12**(1): p.
425 91.
- 426 22. Alfano, L.N., et al., *Correlation of knee strength to functional outcomes in becker muscular*
427 *dystrophy*. Muscle & nerve, 2013. **47**(4): p. 550-554.
- 428 23. Bendixen, R.M., et al., *Participation in daily life activities and its relationship to strength and*
429 *functional measures in boys with Duchenne muscular dystrophy*. Disability and rehabilitation,
430 2014. **36**(22): p. 1918-1923.
- 431 24. Alemdaroğlu, I., et al., *Different types of upper extremity exercise training in Duchenne*
432 *muscular dystrophy: Effects on functional performance, strength, endurance, and*
433 *ambulation*. Muscle & nerve, 2015. **51**(5): p. 697-705.
- 434 25. Seferian, A.M., et al., *Upper limb strength and function changes during a one-year follow-up*
435 *in non-ambulant patients with Duchenne muscular dystrophy: an observational multicenter*
436 *trial*. PLoS One, 2015. **10**(2): p. e0113999.
- 437 26. Kilmer, D.D., R.T. Abresch, and J.W.M. Fowler, *Serial manual muscle testing in Duchenne*
438 *muscular dystrophy*. Archives of physical medicine and rehabilitation, 1993. **74**(11): p. 1168-
439 1171.
- 440 27. McDonald, C., et al., *Profiles of neuromuscular diseases: Duchenne muscular dystrophy*.
441 American journal of physical medicine & rehabilitation, 1995. **74**(5): p. S93.
- 442 28. McDonald, C.M., et al., *Profiles of neuromuscular diseases: Becker's muscular dystrophy*.
443 American journal of physical medicine & rehabilitation, 1995. **74**(5): p. S104.
- 444 29. McDonald, C.M., et al., *The 6-minute walk test and other clinical endpoints in duchenne*
445 *muscular dystrophy: Reliability, concurrent validity, and minimal clinically important*
446 *differences from a multicenter study*. Muscle & nerve, 2013. **48**(3): p. 357-368.
- 447 30. Batra, A., et al., *Two-Year Longitudinal Changes in Lower Limb Strength and Its Relation to*
448 *Loss in Function in a Large Cohort of Patients With Duchenne Muscular Dystrophy*. American
449 journal of physical medicine & rehabilitation, 2018. **97**(10): p. 734-740.
- 450 31. Wokke, B.H., et al., *Quantitative MRI and strength measurements in the assessment of*
451 *muscle quality in Duchenne muscular dystrophy*. Neuromuscular Disorders, 2014. **24**(5): p.
452 409-416.
- 453 32. D'Angelo, M.G., et al., *Gait pattern in Duchenne muscular dystrophy*. Gait & posture, 2009.
454 **29**(1): p. 36-41.
- 455 33. Hsu, J.D. and J. Furumasu, *Gait and posture changes in the Duchenne muscular dystrophy*
456 *child*. Clinical orthopaedics and related research, 1993. **288**: p. 122-125.
- 457 34. Mendell, J.R., et al., *Randomized, double-blind six-month trial of prednisone in Duchenne's*
458 *muscular dystrophy*. New England Journal of Medicine, 1989. **320**(24): p. 1592-1597.
- 459 35. Steffensen, B.F., et al., *Physical capacity in non-ambulatory people with Duchenne muscular*
460 *dystrophy or spinal muscular atrophy: a longitudinal study*. Developmental medicine and
461 child neurology, 2002. **44**(9): p. 623-632.
- 462 36. McDonald, C.M., et al., *THE 6-minute walk test and other endpoints in Duchenne muscular*
463 *dystrophy: Longitudinal natural history observations over 48 weeks from a multicenter study*.
464 Muscle & nerve, 2013. **48**(3): p. 343-356.

- 465 37. Rahbek, J., et al., *Adult life with Duchenne muscular dystrophy: observations among an*
466 *emerging and unforeseen patient population*. *Pediatric Rehabilitation*, 2005. **8**(1): p. 17-28.
- 467 38. Palmieri, G.M.A., et al., *Assessment of whole body composition with dual energy X-ray*
468 *absorptiometry in Duchenne muscular dystrophy: Correlation of lean body mass with muscle*
469 *function*. *Muscle & Nerve: Official Journal of the American Association of Electrodiagnostic*
470 *Medicine*, 1996. **19**(6): p. 777-779.
- 471 39. Skalsky, A.J., et al., *Assessment of regional body composition with dual-energy X-ray*
472 *absorptiometry in Duchenne muscular dystrophy: Correlation of regional lean mass and*
473 *quantitative strength*. *Muscle & nerve*, 2009. **39**(5): p. 647-651.
- 474 40. Beenakker, E.A.C., et al., *Quantitative assessment of calf circumference in Duchenne*
475 *muscular dystrophy patients*. *Neuromuscular Disorders*, 2002. **12**(7): p. 639-642.
- 476 41. Vohra, R.S., et al., *Magnetic resonance assessment of hypertrophic and pseudo-hypertrophic*
477 *changes in lower leg muscles of boys with duchenne muscular dystrophy and their*
478 *relationship to functional measurements*. *PloS one*, 2015. **10**(6): p. e0128915.
- 479 42. Morse, C.I., et al., *Gastrocnemius medialis muscle architecture and physiological cross*
480 *sectional area in adult males with Duchenne muscular dystrophy*. *J Musculoskelet Neuronal*
481 *Interact*, 2015. **15**(2): p. 154-160.
- 482 43. Zanardi, M.C., et al., *Body composition and energy expenditure in Duchenne muscular*
483 *dystrophy*. *European journal of clinical nutrition*, 2003. **57**(2): p. 273-278.
- 484 44. Bostock, E.L., et al., *Impaired glucose tolerance in adults with duchenne and becker muscular*
485 *dystrophy*. *Nutrients*, 2018. **10**(12): p. 1947.
- 486 45. Jacques, M.F., et al., *Resting Energy Expenditure in Adults with Becker's Muscular Dystrophy*.
487 *PloS one*, 2017. **12**(1): p. e0169848.
- 488 46. Hogan, S.E., *Body composition and resting energy expenditure of individuals with Duchenne*
489 *and Becker muscular dystrophy*. *Canadian Journal of Dietetic Practice and Research*, 2008.
490 **69**(4): p. 208-212.
- 491 47. World Medical, A., *World Medical Association Declaration of Helsinki: ethical principles for*
492 *medical research involving human subjects*. *Jama*, 2013. **310**(20): p. 2191.
- 493 48. Morse, C.I., et al., *The cardiorespiratory response and physiological determinants of the*
494 *assisted 6-minute handbike cycle test in adult males with muscular dystrophy*. *Muscle &*
495 *nerve*, 2018. **58**(3): p. 427-433.
- 496 49. McCabe, M.P., L.A. Ricciardelli, and P. Parent, *BODY MASS INDEX*. *Eating Disorders: An*
497 *Encyclopedia of Causes, Treatment, and Prevention*, 2013. **34**: p. 90.
- 498 50. Williams, E.A., et al., *The management of equinus deformity in Duchenne muscular*
499 *dystrophy*. *The Journal of bone and joint surgery. British volume*, 1984. **66**(4): p. 546-550.
- 500 51. Sharma, K.R., M.A. Mynhier, and R.G. Miller, *Muscular fatigue in Duchenne muscular*
501 *dystrophy*. *Neurology*, 1995. **45**(2): p. 306-310.
- 502 52. Fukunaga, T., et al., *Physiological cross-sectional area of human leg muscles based on*
503 *magnetic resonance imaging*. *Journal of Orthopaedic Research*, 1992. **10**(6): p. 926-934.
- 504 53. Reeves, N.D., C.N. Maganaris, and M.V. Narici, *Ultrasonographic assessment of human*
505 *skeletal muscle size*. *European journal of applied physiology*, 2004. **91**(1): p. 116-118.
- 506 54. Liu, M., N. Chino, and T. Ishihara, *Muscle damage progression in Duchenne muscular*
507 *dystrophy evaluated by a new quantitative computed tomography method*. *Archives of*
508 *physical medicine and rehabilitation*, 1993. **74**(5): p. 507-514.
- 509 55. Løkken, N., et al., *Contractile properties are disrupted in Becker muscular dystrophy, but not*
510 *in limb girdle type 2I*. *Annals of Neurology*, 2016.
- 511 56. Willcocks, R.J., et al., *Longitudinal measurements of MRI-T2 in boys with Duchenne muscular*
512 *dystrophy: effects of age and disease progression*. *Neuromuscular Disorders*, 2014. **24**(5): p.
513 393-401.
- 514 57. Fowler, E.G., et al., *Longitudinal Community Walking Activity in Duchenne Muscular*
515 *Dystrophy*. *Muscle & Nerve*, 2017. **57**(3): p. 401-406.

- 516 58. Dillon, C.B., et al., *Number of days required to estimate habitual activity using wrist-worn*
517 *GENEActiv accelerometer: A cross-sectional study.* PloS one, 2016. **11**(5): p. e0109913.
- 518 59. Esliger, D.W., et al., *Validation of the GENEActiv Accelerometer.* Medicine and Science in Sports
519 and Exercise, 2011. **43**(6): p. 1085-1093.
- 520 60. Phillips, L.R.S., G. Parfitt, and A.V. Rowlands, *Calibration of the GENEActiv accelerometer for*
521 *assessment of physical activity intensity in children.* Journal of science and medicine in sport,
522 2013. **16**(2): p. 124-128.
- 523 61. Swinyard, C.A., G.G. Deaver, and L. Greenspan, *Gradients of functional ability of importance*
524 *in rehabilitation of patients with progressive muscular and neuromuscular diseases.* Archives
525 of physical medicine and rehabilitation, 1957. **38**(9): p. 574-579.
- 526 62. Melacini, P., et al., *Cardiac and respiratory involvement in advanced stage Duchenne*
527 *muscular dystrophy.* Neuromuscular disorders, 1996. **6**(5): p. 367-376.
- 528 63. Hunsaker, R.H., et al., *Cardiac function in Duchenne's muscular dystrophy: Results of 10-year*
529 *follow-up study and noninvasive tests.* The American journal of medicine, 1982. **73**(2): p.
530 235-238.
- 531 64. Yamada, Y., et al., *Long-term follow-up of dysphagia in adult patients with Duchenne*
532 *muscular dystrophy.* European Journal of Paediatric Neurology, 2018. **22**(5): p. 786-790.
- 533 65. Hogrel, J.-Y., et al., *Development of a French isometric strength normative database for*
534 *adults using quantitative muscle testing.* Archives of physical medicine and rehabilitation,
535 2007. **88**(10): p. 1289-1297.
- 536 66. Cuthbert, S.C. and G.J. Goodheart, *On the reliability and validity of manual muscle testing: a*
537 *literature review.* Chiropractic & osteopathy, 2007. **15**(1): p. 4.
- 538 67. Lue, Y.-J., et al., *Measurement of the functional status of patients with different types of*
539 *muscular dystrophy.* The Kaohsiung journal of medical sciences, 2009. **25**(6): p. 325-333.
- 540 68. Pane, M., et al., *Feeding problems and weight gain in Duchenne muscular dystrophy.*
541 *European journal of paediatric neurology,* 2006. **10**(5): p. 231-236.
- 542 69. Ferguson, M.R., et al., *Quantitative MRI reveals decelerated fatty infiltration in muscles of*
543 *active FSHD patients.* Neurology, 2016. **87**(16): p. 1746-1746.
- 544 70. Phillips, M., N. Flemming, and K. Tsintzas, *An exploratory study of physical activity and*
545 *perceived barriers to exercise in ambulant people with neuromuscular disease compared*
546 *with unaffected controls.* Clinical Rehabilitation, 2009. **23**(8): p. 746-755.
- 547 71. Pane, M., et al., *Long term natural history data in ambulant boys with Duchenne muscular*
548 *dystrophy: 36-month changes.* PLoS One, 2014. **9**(10): p. e108205.
- 549 72. Pane, M., et al., *6 Minute walk test in Duchenne MD patients with different mutations: 12*
550 *month changes.* PloS one, 2014. **9**(1): p. e83400.
- 551 73. Mazzone, E., et al., *Functional changes in Duchenne muscular dystrophy A 12-month*
552 *longitudinal cohort study.* Neurology, 2011. **77**(3): p. 250-256.
- 553 74. Bonati, U., et al., *Quantitative muscle MRI: a powerful surrogate outcome measure in*
554 *Duchenne muscular dystrophy.* Neuromuscular Disorders, 2015. **25**(9): p. 679-685.
- 555 75. Janssen, B., et al., *Quantitative MRI reveals decelerated fatty infiltration in muscles of active*
556 *FSHD patients.* Neurology, 2016. **86**(18): p. 1700-1707.

557 **Table 1.** 12 Month changes in body composition, muscle size, lower limb strength and
558 physical activity in Adults with DMD.

	DMD			
	Baseline	12-Months	%Change	95% CI
N			15	
Functional Status	8 (8-8)	8 (8-8)	-	-
Ambulatory Status				

No Walking Support	-	-	-	-
Walking Support	-	-	-	-
Manual Wheelchair	-	-	-	-
Electric Wheelchair	8/8	8/8	-	-
Respiratory Support	15/15	15/15	-	-
<i>Night-time only (%)</i>	13/15	13/15	-	-
<i>24/7 (%)</i>	2/15	2/15	-	-
PEG (%)	4/15	4/15	-	-
Age (years)	24.2 ±6.1	25.2 ±6.1	-	-
Stature (cm)	172.0 ±4.3	172.0 ±4.3	-	-
Body Mass (Kg)	73.1 ±14.6	71.4 ±14.5	-2%	-3.8; 2.8
BMI (Kg/m²)	25.5 ±4.1	24.5 ±7.5	-4%	-1.6; -0.2
Body Fat (Kg)	24.3 ±9.5	23.7 ±10.8	-3%	-7.3; 0.39
LBM (Kg)	47.6 ±7.7	45.0 ±6.4	-5%*	-3.99; -1.14
GM ACSA (cm²)	23.3 ±16.5	21.4 ±16.3	-8%*	-3.43; -0.49
PFMVC (N.m)	16.7 ±6.8	13.6 ±6.3	-19%*	-4.79; -1.49
KEMVC (N.m)	12.6 ±8.8	10.8 ±7.0	-14%*	-3.16; -0.31
SB%	96.4 ±4.5	98.5 ±0.02	2%	-0.32; 4.54
TPA^{mins}	13.5 ±16.1	7.17 ±8.9	-47%	-14; 1.7

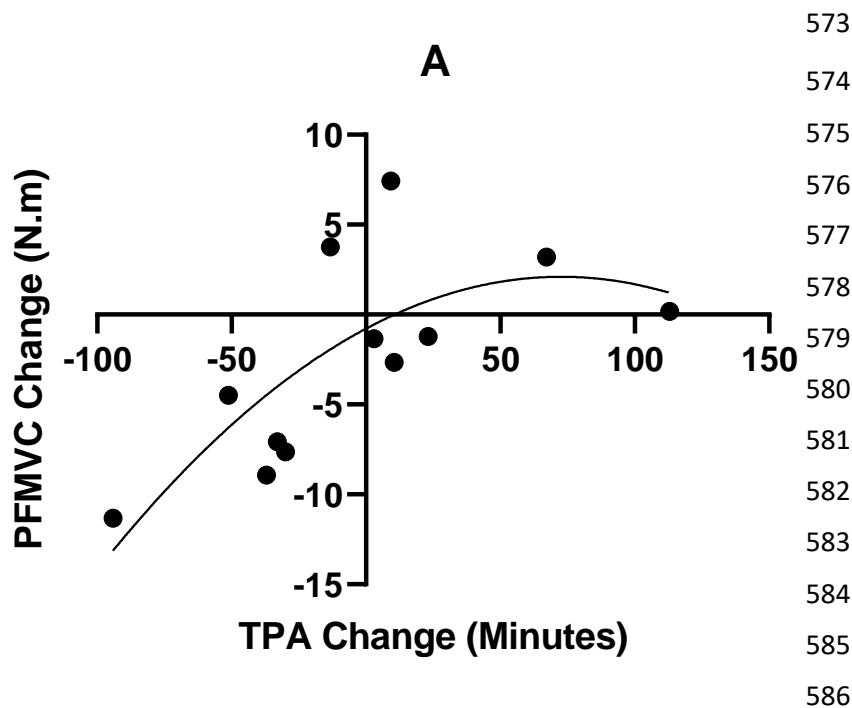
559 Table 1. One year changes in MD strength, physical activity and function. All data presented and Mean±SD, except for
560 Functional status which is presented as Median (Range), Respiratory Support, Ambulatory Status and PEG are presented as
561 absolute. DMD = Duchenne Muscular Dystrophy; 95% CI = 95% Confidence Intervals PEG = Percutaneous endoscopic
562 gastrostomy; PFMVC = Plantar-Flexion Maximum Voluntary Contraction; KEMVC = Knee Extension maximum Voluntary
563 Contraction; SB% = Sedentary Behaviour %; TPA^{mins} = Minutes of Total Physical Activity; m = metres; s = seconds; †
564 Ambulant BMD only (n=8); *denotes significant changes from baseline.

565 **Table 2.** 12 Month changes in body composition, muscle size, lower limb strength and physical
566 activity in Adults with BMD.

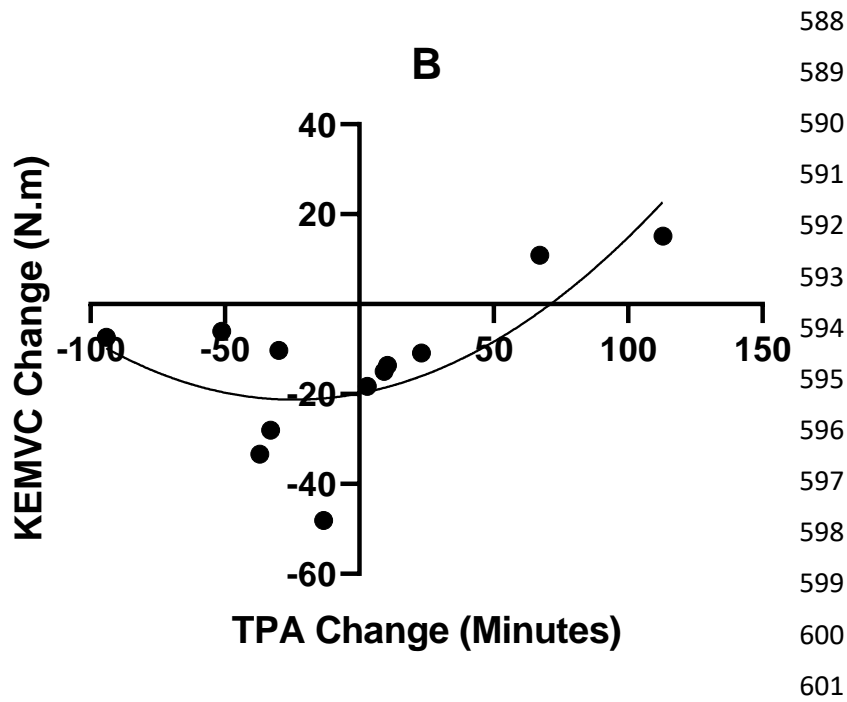
	BMD			
	Baseline	12 Months	% Change	95% CI
N			12	
Functional Status	3.5 (1-7)	3.5 (1-7)	-	-
Ambulatory Status				
No Walking Support	6	6	-	-
Walking Support	3	2	-	-
Manual Wheelchair	1	2	-	-
Electric Wheelchair	2	2	-	-
Respiratory Support	0/12	0/12	-	-
<i>Night-time only</i>	-	-	-	-
<i>24/7</i>	-	-	-	-
PEG	0/12	0/12	-	-
Age (years)	44.1 ±12.6	45.1 ±12.6	-	-
Stature (cm)	178.9 ±6.2	178.9 ±6.2	-	-
Body Mass (Kg)	84.4 ±15.1	85.1 ±16.4	0%	-1.22; 2.64
BMI (Kg/m²)	26.4 ±4.9	26.6 ±5.4	0%	-0.38; 0.84
Body Fat (Kg)	25.1 ±8.8	26.3 ±8.9	4%*	0.20; 2.19

LBM (Kg)	59.3 ±7.8	58.8 ±8.1	-1%	-2.05; 1.08
Ambulatory	9/12	8/12	-	-
GM ACSA (cm²)	29.7 ±18.4	26.6 ±14.4	-10%	-6.0; -0.11
PFMVC (N.m)	35.7 ±11.3	33.2 ±12.2	-7%	-6.01; 1.08
KEMVC (N.m)	97.7 ±64.3	83.9 ±56.2	14%	-24.8; -2.6
SB%	83.4 ±7.2	83.9 ±6.3	0%	-4; 5
TPA^{mins}	123.1 ±57.6	120.4 ±50.7	-2%	-17.2; 70.5
10m Walk (s)†	11.0 ±2.9	12.7 ±3.9	15%*	1.4; 3.4

567 Table 2. One year changes in MD strength, physical activity and function. All data presented and Mean±SD, except for
568 Functional status which is presented as Median (Range), Respiratory Support, Ambulatory Status and PEG which are presented
569 as absolute. BMD = Beckers Muscular Dystrophy; 95% CI = 95% Confidence Intervals; PEG = Percutaneous endoscopic
570 gastrostomy; PFMVC = Plantar-Flexion Maximum Voluntary Contraction; KEMVC = Knee Extension maximum Voluntary
571 Contraction; SB% = Sedentary Behaviour %; TPA^{mins} = Minutes of Total Physical Activity; m = metres; s = seconds; †
572 Ambulant BMD only (n=8); *denotes significant changes from baseline.



587



602 Figure 1. BMD strength change and physical activity change relationships A. PFMVC change and TPA^{mins} change in BMD B.
 603 KEMVC change and TPA^{mins} change in BMD. PFMVC = Plantar Flexion Maximal Voluntary Contraction, N.m = Newton
 604 Metres, TPA = Total Physical Activity, KEMVC = Knee Extension Maximal Voluntary Contraction.

605