# LONGITUDINAL COMMUNITY WALKING ACTIVITY IN DUCHENNE MUSCULAR DYSTROPHY

EILEEN G. FOWLER, PhD, PT,[1] LORETTA A. STAUDT, MS, PT,[1] KENT R. HEBERER, PhD,[1] SUSAN E. SIENKO, PhD,[2] CATHLEEN E. BUCKON, MS,[2] ANITA M. BAGLEY, PhD, MPH,[3] MICHAEL D. SUSSMAN, MD,[2] and CRAIG M. MCDONALD, MD[3,4]

[1] Department of Orthopaedic Surgery, University of California Los Angeles, 22-70 Rehab Center, 1000 Veteran Avenue, Los Angeles, California 90095-1795, USA

[2] Shriners Hospitals for Children Portland, Portland, Oregon, USA

[3] Shriners Hospitals for Children Northern California, Sacramento, California, USA

[4] University of California Davis Medical Center, Sacramento, California, USA

*Accepted 7 July 2017*

ABSTRACT: *Introduction:* Natural history studies for Duchenne muscular dystrophy (DMD) have not included measures of community ambulation. *Methods:* Step activity (SA) monitors quantified community ambulation in 42 boys (ages 4–16 years) with DMD with serial enrollment up to 5 years by using a repeated-measures mixed model. Additionally, data were compared with 10-meter walk/run (10mWR) speed to determine validity and sensitivity. *Results:* There were significant declines in average strides/day and percent strides at moderate, high and pediatric high rates as a function of age ($P < 0.05$). Significant correlations for 10mWR versus high and low stride rates were found at baseline ($P < 0.05$). SA outcomes were sensitive to change over 1 year, but the direction and parameter differed by age group (younger vs. older). Changes in strides/day and percentages of high frequency and low frequency strides correlated significantly with changes in 10mWR speed ($P < 0.05$). *Discussion:* Community ambulation data provide valid and sensitive real-world measures that may inform clinical trials.

*Muscle Nerve* **57**: 401–406, 2018

Duchenne muscular dystrophy (DMD) is an x-linked recessive muscle disease with an estimated worldwide incidence of 1 in 3,500–5,500 male births.[1,2] DMD disrupts the manufacture of the dystrophin protein. Steroid treatment protocols have slowed the rate of functional decline associated with DMD.[3–5] Currently, gains in lower extremity function are expected up to 6–8 years of age, followed by a gradual decline until the loss of ambulation.[6–8] Natural history studies[8–11] are important to identify sensitive outcome measures for the assessment of recently developed DMD novel therapeutics[12–16]; however, community mobility has not been included.

Objective measurement provided by step activity (SA) monitors seems ideally suited for quantification of walking activity, a key marker of disease progression in DMD.[17] SA data can be collected without voluntary effort or cooperation of the participant other than agreeing to wear the monitor. Because it is not a physical performance test, factors such as age, intellectual ability, motivation, anxiety, and fatigue do not interfere with collection of quality data. Additionally, SA monitors may expand enrollment by enabling data collection from remote or widespread geographical areas.

Various pedometers and accelerometers have been used to track daily SA.[17–24] A large longitudinal study of SA reported that children without disability take 10,056 steps (5,028 strides)/day but found no relationship with age.[18] In contrast, McDonald *et al.*[20] reported significantly more strides/day for boys 6–10 years old ($7{,}001 \pm 580$ strides/day) compared with older boys ($5{,}354 \pm 566$ strides/day for 11–15 years and $5{,}394 \pm 480$ strides/day for 16–20 years). Approximately 6,500 strides/day are recommended for boys without disability to achieve health benefits.[25]

There are few studies of SA in boys with DMD. McDonald *et al.*[17] found significantly lower values for 5–13-year-old boys with DMD compared with control participants ($4{,}456 \pm 513$ vs. $6{,}311 \pm 493$ strides/day, respectively). Time spent at moderate (16–30 strides/min) and higher (>30 strides/min) cadences was significantly lower for the DMD group. Validity of SA data in this population was supported by strong correlations between the 6-minute walk distance (6MWD) and SA parameters in boys with DMD.[26] Little is known about responsiveness to intervention in DMD. Improved SA following 1 month of corticosteroids was reported, but only 5 boys were studied.[27] A recent study of ataluren showed positive trends in SA data favoring ataluren over a placebo.[16] Thus, accelerometry offers a valid measure of community based cadence that may be an informative outcome measure for determining therapeutic efficacy in clinical trials. This study examines longitudinal SA in boys with DMD as part of a broader natural history study. We hypothesize that SA outcomes will be sensitive to disease progression and correlate with

**Abbreviations:** 10mWR, 10-meter walk/run test; 6MWD, 6-minute walk distance; DMD, Duchenne muscular dystrophy; SA, step activity

**Key words:** accelerometry; community walking; Duchenne muscular dystrophy; gait; natural history; physical activity

**Funding**: Funding for this study was provided by Shriners Hospitals for Children (Grant No. 79115).

**Conflicts of Interest**: None of the authors have any conflicts of interest to disclose related to this work.

**Correspondence to:** E. G. Fowler; efowler@mednet.ucla.edu



Published online 10 July 2017 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/mus.25743

the 10-meter walk/run test (10mWR), a common clinical assessment of walking speed.

## MATERIALS AND METHODS

**Participants and Procedures.** Ambulatory boys with DMD, ages 4–16 years at enrollment, were recruited from clinics at 3 participating hospitals and from the community as part of a prospective longitudinal multicenter study. Institutional review board approval was obtained at each institution, and parental consent and child assent were obtained. Inclusion criteria were a diagnosis of DMD determined by clinical evaluation and either a blood DNA study or a muscle biopsy, the ability to walk independently, and the ability to understand directions for testing procedures. Data were collected at 6-month intervals over a 5-year period with continuous enrollment. Data were excluded from the natural history analysis if a participant was enrolled in an experimental drug treatment trial during the data collection period.

The StepWatch Activity Monitor (Modus Health LLC, Washington, DC) was used for this study. Good validity[20,21] and reliability[20,21,23] have been reported, and it was the most accurate of 3 devices studied in children with disability.[21] It is worn above 1 ankle, and, therefore, measures strides/min. Stride count accuracy was confirmed by correlating triggered LED light flashes with observed unilateral steps (strides). Parents and children were instructed in the correct orientation and placement of the SA monitor above the lateral malleolus of 1 lower limb and were provided with a calendar to denote time on/off, school attendance, typical versus atypical day, and reasons for activity variation or removal of the device (e.g., illness, weather, bathing, swimming). Data were collected in the boys' communities, including home and school. Participants were instructed to wear their monitor 3–5 weekdays and 2 weekend days following each laboratory evaluation. A postage paid envelope for return of the monitor and calendar was provided.

SA data were compared with the calendar to confirm accuracy. Days when the device was removed prematurely or that exhibited inconsistencies with the calendar were eliminated from further analysis. The SA monitor software provides a data summary including total strides/day and number of strides at varying activity levels. We examined stride count at the most commonly used default frequencies (high $>40$, moderate 16–40, and low 1–15 strides/min). A pediatric high cadence of $>60$ strides/min (pediatric high) was included in the analysis because a recent study of children with disability used this cutoff.[24] This higher value was based on a report of moderate to vigorous SA of typically developing children (10–12 years old).[28] Mean strides/day and the number of strides/day at each activity level were calculated. Percentage of pediatric high frequency, high frequency, moderate frequency, and low frequency strides was defined as the number of strides at each activity level divided by the total number of strides/day (multiplied by 100).

**Statistical Analysis.** *Validity.* We used the 10mWR test as the reference standard. Because data were confirmed as being normally distributed with the Shapiro-Wilk test, linear regression was used to examine the relationship of SA data (mean strides/day and percentage pediatric high frequency, high frequency, moderate frequency, and low frequency strides) with 10mWR at baseline. In addition, linear regressions of 1-year changes in SA versus 10mWR data were performed.

*Sensitivity to Change.* A two-way repeated-measure ANOVA was used to compare baseline and 1-year SA values for younger (4–7 years) and older ($\geq$8 years) groups for a subset of boys with at least 2 data collections obtained 1 year apart.

*Natural History Analysis.* SA data collected longitudinally over 6-month intervals were rounded to the closest age at the time of data collection. A repeated-measures mixed model was used to evaluate means across age group bins controlling for subject effect for average strides/day, percentage pediatric high frequency strides, percentage high frequency strides, percentage moderate frequency strides, percentage low frequency strides, and 10mWR speed. This design takes into account that the number of data points available for each participant may vary. The model takes advantage of the correlations among observations from subjects with multiple assessments over time and assumes that these correlations apply to all subjects.[29] Mean profiles and 1 SEM were plotted with the corresponding linear or quadratic best-fit trend curves. All statistics were calculated in JMP (SAS Institute, Cary, NC), with significance set at $P = 0.05$.

## RESULTS

For the validity and sensitivity to change analyses, baseline and 1-year data were available for a subset of 32 participants ranging in age from 4.1–11.3 years (mean $7.5 \pm 2.2$ years). Sixteen older boys ($\geq$8 years) and 16 younger boys (4–7 years) were included.

**Validity Analyses.** SA measures versus 10mWR at baseline are shown in Figure 1. Percentages of high frequency and low frequency strides were significantly correlated with 10mWR speed. Significant relationships were not found among mean strides/day, percentage moderate frequency, percentage pediatric high frequency, and 10mWR speed. Validity analyses for change over a 1-year period are shown in Figure 2. Significant positive relationships between changes in average strides/day and percentage high frequency strides versus 10mWR speed were found. In contrast, change in percentage of low frequency strides showed a significant negative correlation with change in 10mWR. Significant relationships between changes in percentage of moderate and pediatric high frequency strides versus 10mWR speed were not found.

**Sensitivity to Change Analyses.** Two-way repeated measures ANOVA over the 1-year period revealed significant differences by age for 10mWR speed and all SA parameters, with the exception of percentage moderate frequency ($P = 0.25$) and percentage pediatric high frequency strides ($P = 0.30$). For the older age group, significant reductions in average strides/day ($-1{,}624$ strides/day) and 10mWR speed ($-0.27$ m/s) as well as a significant increase in percentage low frequency strides ($+7\%$) were found.

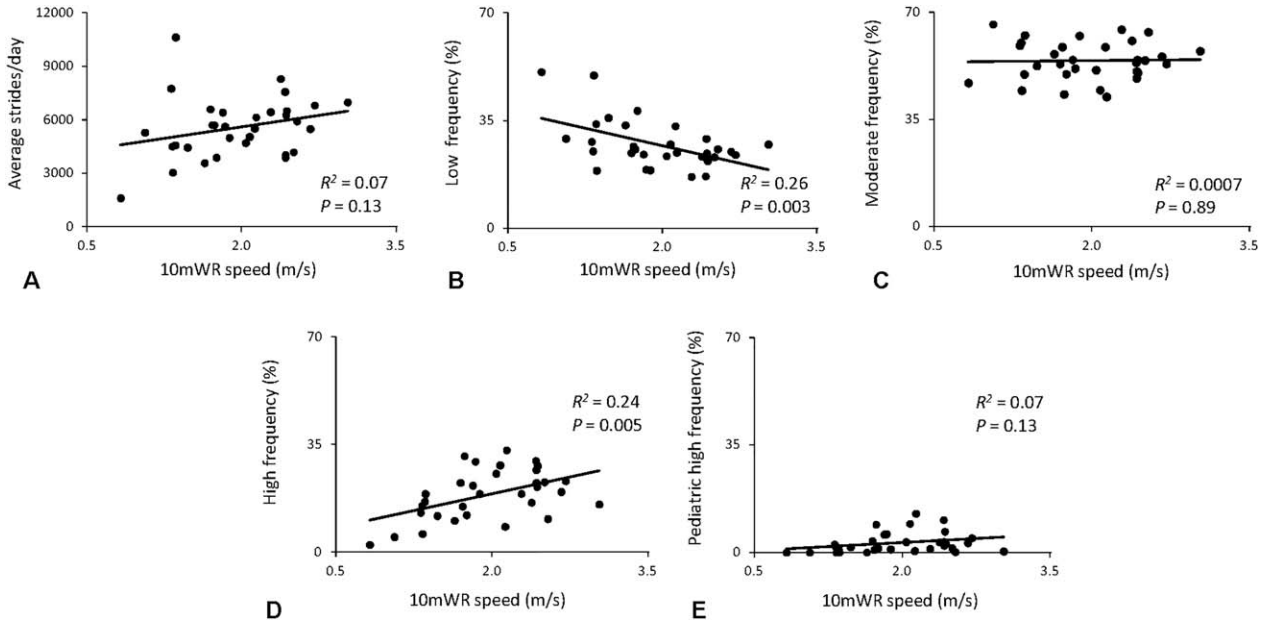


**FIGURE 1.** Correlations of average strides/day **(A)**, percentage low frequency strides **(B)**, percentage moderate frequency strides **(C)**, percentage high frequency strides **(D)**, and percentage pediatric high frequency strides **(E)** with 10-meter walk/run test (10mWR) speed at baseline.

For the younger age group, a significant decrease in percentage low frequency strides (−5%) and a significant increase in percentage high frequency strides (+4%) were found.

**Natural History Analyses.** Demographics and baseline characteristics for 42 natural history participants are shown in Table 1. Baseline age ranged from 4 to 16 years. The number of data collections for each participant ranged from 1 to 7 (10 participants completed 7 data collections, 3 participants completed 6, 2 participants completed 5, 10 participants completed 4, 3 participants completed 3, 5 participants completed 2, and 9 participants completed 1). Average strides/day for the entire cohort at baseline was 4,881 (5,352 ± 1,899 for boys 4–7 years and 4,453 ± 2,255 for boys ≥ 8 years). Mean 10mWR speed at baseline was 1.71 m/s (1.8 ± 0.63 m/s for boys 4–7 years and 1.6 ± 0.71 m/s for boys ≥ 8 years). Longitudinal trends as a function of 25 age bins ranging from 4–16.5 years are shown in Figure 3. Data from at least 6 participants contributed to the means for age bins from 4.5 to 12.5 years, but fewer participants were included above

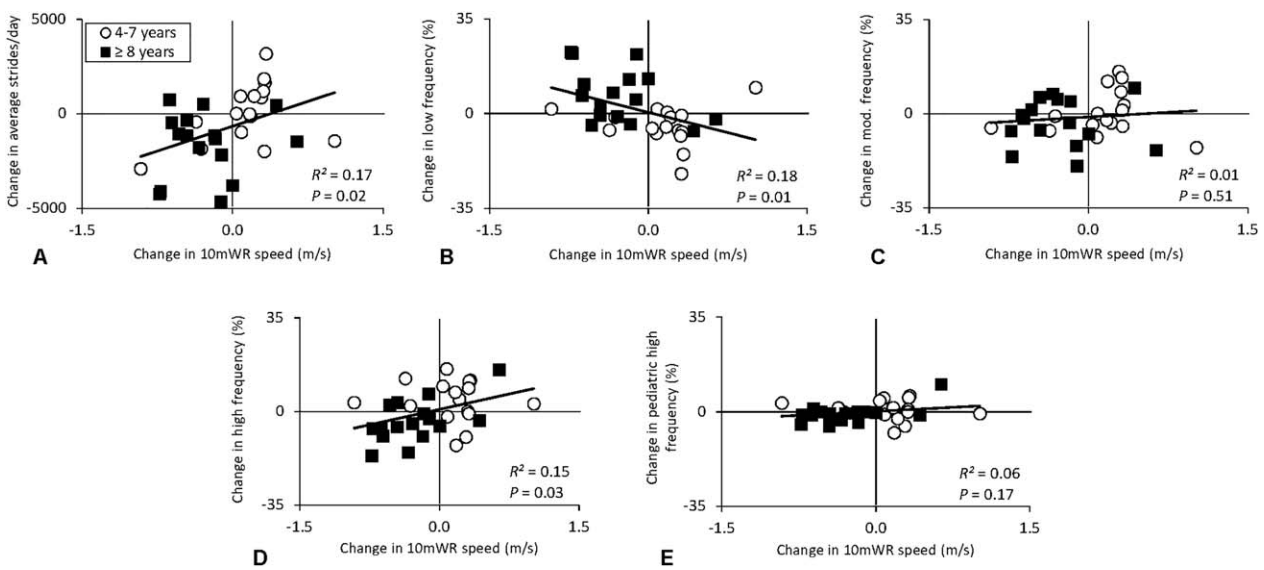


**FIGURE 2.** Correlations of change scores for average strides/day **(A)**, percentage low frequency strides **(B)**, percentage moderate (mod.) frequency strides **(C)**, percentage high frequency strides **(D)**, and percentage pediatric high frequency strides **(E)** with 10-meter walk/run test (10mWR) speed over 1 year.

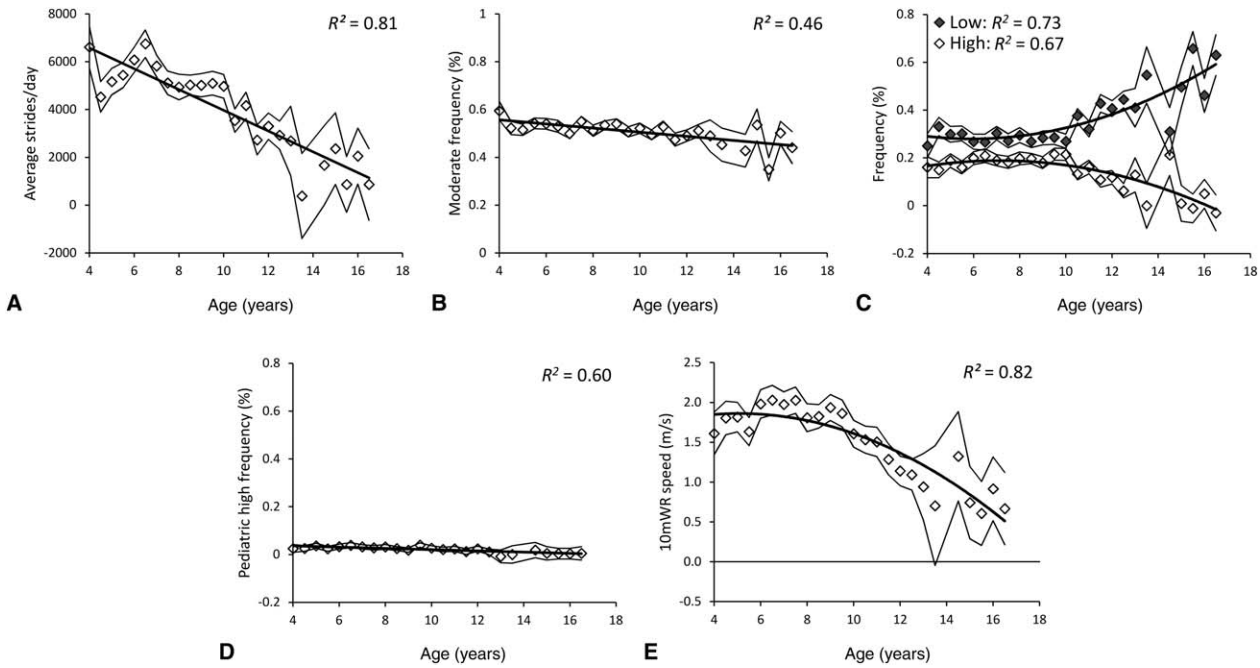


**FIGURE 3.** Longitudinal trends calculated from mean values ± 1 SEM for average strides/day **(A)**, percentage moderate frequency strides **(B)**, percentage low and high frequency strides **(C)**, percentage pediatric high frequency strides **(D)**, and 10-meter walk/run test (10mWR) speed **(E)** as a function of age. Average strides/day, percentage moderate frequency and pediatric high frequency strides were best fit with linear models. Percent low frequency and high frequency strides and 10mWR speed were best described by polynomial equations. All relationships were significant ($P < 0.001$).

and below this range (≤3). Significant relationships were found for all SA outcomes. Average strides/day initially increased for young boys (4–7 years), followed by a relative plateau at approximately 5,000 strides/day for boys 8–10 years, after which there was a decline as ambulation decreased and eventually ceased. Although these variations were observed, the curve was best fit with a linear equation. Although the percentage moderate frequency strides gradually declined with age in a linear fashion, trajectories of the mean trend for percentage high frequency and percentage low frequency strides followed diverging elliptical paths best fit with quadratic equations. Percentage high frequency strides initially increased but then declined with age, whereas percentage low frequency strides slightly decreased and then progressively increased with age. Similarly to percentage high frequency strides, 10mWR speeds decreased with age in a curvilinear fashion. Percentage pediatric high frequency stride data as a function of age were best fit by a linear equation. Although there was a significant decrease with age, the slope was close to 0. The maximum contribution was only 4% of the average number of strides compared with >20% for the other frequency cutoffs.

**Table 1.** Natural history demographics and baseline characteristics

| Characteristics | Data* |
|---|---|
| Number of participants | 42 |
| Mean age, years | 7.9 ± 2.9 |
| Age range, years | 4.1–16.1 |
| Mean height, cm | 118.5 ± 13.9 |
| Mean weight, kg | 27.1 ± 12.2 |
| Mean BMI, kg/m$^2$ | 18.5 ± 4.4 |
| Number taking steroids at baseline | 25 |
| Deflazacort | 13 |
| Prednisone | 12 |
| Median number of visits (min–max) | 4 (1–7) |
| Mean 10mWR speed, m/s | 1.71 ± 0.68 |
| Mean average strides/day | 4,881 ± 2,117 |
| Mean low frequency strides/day† | 1,345 ± 423 |
| Mean moderate frequency strides/day† | 2,665 ± 1,331 |
| Mean high frequency strides/day† | 871 ± 620 |
| Mean pediatric high frequency strides/day† | 144 ± 204 |

*10mWR, 10-meter walk/run test; BMI, body mass index.*

** ± SD as indicated.*

*†Low frequency, 1–15 strides/min; moderate frequency, 16–40 strides/min; high frequency, > 40 strides/min; pediatric high frequency, > 60 strides/min.*

## DISCUSSION

This long-term longitudinal study with follow-up of up to 5 years offers insight into the utility of community activity monitoring as an outcome measure. Examination of the natural history data in Figure 3 reveals that the decline in average strides/day as a function of age was similar to that of other functional metrics for DMD. As expected, average strides per day at baseline was lower than that reported for boys without disability.[17,18,20,23] Compared with a cross-sectional study of boys with DMD ages 5–13

years, our mean was slightly higher (4,881 vs. 4,456 strides/day).[17] The decline in walking speed as a function of age was similar to that reported in a previous 48-week longitudinal analysis of 10mWR in this population,[8] demonstrating little change from 4 to 7 years and a more predictable decline in speed for boys ≥8 years of age.

Additional insights into disease progression can be made by examining stride frequency relationships (see Fig. 3). With increasing age, percentage moderate frequency strides exhibited a modest gradual decline, whereas a major shift occurred from high frequency toward low frequency stride rates. These data support a decline in the time spent at high stride rates as a function of age found in a previous cross-sectional study of boys with DMD.[20] Decreased cadence occurs with increased leg length in typically developing children[30]; however, the effect of disease progression in boys with DMD certainly surpasses this maturational influence. The early age region of the high cadence curve corresponds to what has been referred to as the "honeymoon" period, when improvements in function are observed but at a rate below typically developing children.[6,7,31] Percentage high frequency strides decreased to zero prior to the cessation of walking in many participants, suggesting possible use of this measure as a prognostic indicator for loss of ambulation. The polynomial curve for 10mWR was most similar to the high stride rate curve, exhibiting an early plateau region followed by a steep decline above 10 years of age. The curve for percentage low frequency strides was virtually a mirror image of percentage high frequency strides. For the oldest boys who remained ambulatory, approximately 60% of strides/day were within this low cadence range.

Validity of community walking data was supported by the significant relationships between high and low stride rates and the 10mWR test at baseline (Fig. 1) and over a 1-year period (Fig. 2). It is logical that children who are capable of running would achieve higher speeds on the 10mWR test and also that they would walk at higher cadences during their daily activities. Therefore, the percentage of strides at high and low cadences was expected to have a stronger relationship with walking speed than those at moderate stride rates. Although baseline average strides/day did not exhibit a significant relationship with the 10mWR test, a previous study demonstrated a strong correlation between this measure and the 6MWD.[26] Therefore, average strides/day may be a better proxy for laboratory measures of walking endurance than for speed. The 6MWD became a standard clinical trial measure for DMD after the onset of the present study. The relationship for the percentage pediatric high frequency strides with the 10mWR was nonsignificant.

The relationship between SA and 10mWR data for 1-year change scores varied by age group. Significant correlations were found between 1-year change scores for SA measures and the 10mWR, with the exception of percentage moderate frequency and percentage pediatric high frequency strides, and data tended to cluster by age (see Fig. 2). Most data points for older boys were contained in quadrants that reflected a decrement in function (e.g., the lower left quadrant for average strides/day and percentage high frequency strides and the upper left for percentage low frequency strides). The reverse occurred for younger boys. These relationships emphasize the importance of examining stride rates in addition to average strides/day in boys with DMD. Although the correlations used to establish validity were in the correct direction and significant, the associated $R^2$ values suggest "low to medium" strength correlations, indicating that other factors contribute to walking speed. Stride length, in addition to cadence, is a primary determinate of walking speed in normal gait; however, these relationships are more complex in the presence of a progressive muscle disease.

Sensitivity of outcome measures and variation with age are important factors to consider for DMD clinical trials, and 1 year is a common endpoint. Strides/day and cadence were sensitive measures, but the direction of change varied by age group. Blending age groups could certainly wash out the effects of a therapeutic intervention.

The SA software used for the present study provides multiple analyses that can be tailored to the population studied and the research questions. We examined the pediatric high in addition to the default stride rate cutoffs. Because there were insufficient strides at this cadence (see Fig. 1E), it does not appear to be a useful metric for this population. In contrast, all participants generated strides above 40 strides/min, supporting this cutoff as more meaningful for DMD studies. Another option is to study time spent at a particular stride rate.[17,24,26] Boys with DMD, however, are advised to limit physical activity and use a scooter or wheelchair for mobility at school and in the community, setting a limit on the number of steps they take each day but not their cadence when they do walk. In the present study, the average number of strides/day was analyzed, which is related to the time spent walking each day. The calculation of the percentage of these strides at different stride rates, however, was not related to the time spent walking and more relevant to a laboratory measure of walking speed capacity, which was a focus of this investigation.

This study has several limitations. A limitation of using rolling enrollment for natural history studies is variation in the number of participants within age bins. This study was not designed to evaluate the effect of steroids, which were the standard of care for all sites during data collection.[32] The age of diagnosis and steroid initiation varied, and some boys discontinued steroid use because of weight gain or behavioral changes. Steroid use was 78% at 6 years, increased to 100% at 8 years, and ranged from 80% to 100% between 8 and 13 years. All boys $\geq$ 13 years old that remained ambulatory, and therefore continued in the study, were taking steroids.

In summary, we found that SA monitors provide a valid measure of community ambulation in DMD and produce natural history data that can be used as a comparison for clinical trials. It is important to use technology that captures high and low stride rates because these are significantly correlated with walking speed and sensitive to both short-term and long-term disease progression.

Study data were presented to the American Academy of Cerebral Palsy and Developmental Medicine, September 2012, Toronto, Ontario, Canada. The authors thank the parents and children who participated in this study, Andy Vuong for his assistance with data analysis and manuscript preparation, and Jeff Gornbein for statistical consultation.

Ethical Publication Statement: We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## REFERENCES

1. Emery AE. Population frequencies of inherited neuromuscular diseases—a world survey. Neuromuscul Disord 1991;1:19–29.
2. Centers for Disease Control and Prevention (CDC). Prevalence of Duchenne/Becker muscular dystrophy among males aged 5–24 years—four states, 2007. MMWR Morb Mortal Wkly Rep 2009;58: 1119–1122.
3. Henricson EK, Abresch RT, Cnaan A, Hu F, Duong T, Arrieta A, *et al.* The cooperative international neuromuscular research group Duchenne natural history study: glucocorticoid treatment preserves clinically meaningful functional milestones and reduces rate of disease progression as measured by manual muscle testing and other commonly used clinical trial outcome measures. Muscle Nerve 2013; 48:55–67.
4. Balaban B, Matthews DJ, Clayton GH, Carry T. Corticosteroid treatment and functional improvement in Duchenne muscular dystrophy: long-term effect. Am J Phys Med Rehabil 2005;84:843–850.
5. Mendell JR, Moxley RT, Griggs RC, Brooke MH, Fenichel GM, Miller JP, *et al.* Randomized, double-blind six-month trial of prednisone in Duchenne's muscular dystrophy. N Engl J Med 1989;320:1592–1597.
6. McDonald CM, Henricson EK, Han JJ, Abresch RT, Nicorici A, Atkinson L, *et al.* The 6-minute walk test in Duchenne/Becker muscular dystrophy: longitudinal observations. Muscle Nerve 2010;42: 966–974.
7. Mazzone ES, Pane M, Sormani MP, Scalise R, Berardinelli A, Messina S, *et al.* 24 month longitudinal data in ambulant boys with Duchenne muscular dystrophy. PloS One 2013;8:e52512.
8. 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.
9. Pane M, Mazzone ES, Sivo S, Sormani MP, Messina S, D Amico A, *et al.* Long term natural history data in ambulant boys with Duchenne muscular dystrophy: 36 month changes. PloS One 2014;9: e108205.
10. Pizzato TM, Baptista CR, Souza MA, Benedicto MM, Martinez EZ, Mattiello-Sverzut AC. Longitudinal assessment of grip strength using bulb dynamometer in Duchenne muscular dystrophy. Braz J Phys Ther 2014;18:245–251.
11. Brehm M-A, Kempen JC, van der Kooi AJ, de Groot IJ, van den Bergen JC, Verschuuren JJ, *et al.* Age-related longitudinal changes in metabolic energy expenditure during walking in boys with Duchenne muscular dystrophy. PloS One 2014;9:e115200.
12. Goemans NM, Tulinius M, van den Akker JT, Burm BE, Ekhart PF, Heuvelmans N, *et al.* Systemic administration of PRO051 in Duchenne's muscular dystrophy. N Engl J Med 2011;364:1513–1522.
13. van Deutekom JC, Janson AA, Ginjaar IB, Frankhuizen WS, Aartsma-Rus A, Bremmer-Bout M, *et al.* Local dystrophin restoration with antisense oligonucleotide PRO051. N Engl J Med 2007;357:2677–2686.
14. Voit T, Topaloglu H, Straub V, Muntoni F, Deconinck N, Campion G, *et al.* Safety and efficacy of drisapersen for the treatment of Duchenne muscular dystrophy (DEMAND II): an exploratory, randomised, placebo-controlled phase 2 study. Lancet Neurol 2014;13:987–996.
15. Mendell JR, Goemans N, Lowes LP, Alfano LN, Berry K, Shao J, *et al.* Longitudinal effect of eteplirsen versus historical control on ambulation in Duchenne muscular dystrophy. Ann Neurol 2016;79:257–271.
16. Bushby K, Finkel R, Wong B, Barohn R, Campbell C, Comi GP, *et al.* Ataluren treatment of patients with nonsense mutation dystrophinopathy. Muscle Nerve 2014;50:477–487.
17. 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.
18. Telford RM, Telford RD, Cunningham RB, Cochrane T, Davey R, Waddington G. Longitudinal patterns of physical activity in children aged 8 to 12 years: the LOOK study. Int J Behav Nutr Phys Act 2013; 10:81-92.
19. Tudor-Locke C, Washington TL, Hart TL. Expected values for steps/day in special populations. Prev Med 2009;49:3-11.
20. McDonald CM, Widman L, Abresch RT, Walsh SA, Walsh DD. Utility of a step activity monitor for the measurement of daily ambulatory activity in children. Arch Phys Med Rehabil 2005;86:793–801.
21. Downs J, Leonard H, Jacoby P, Brisco L, Baikie G, Hill K. Rett syndrome: establishing a novel outcome measure for walking activity in an era of clinical trials for rare disorders. Disabil Rehabil 2014;37: 1992–1996.
22. Bjornson KF. Physical activity monitoring in children and youths. Pediatr Phys Ther 2005;17:37–45.
23. Song KM, Bjornson KF, Cappello T, Coleman K. Use of the StepWatch activity monitor for characterization of normal activity levels of children. J Pediatr Orthop 2006;26:245–249.
24. Bjornson KF, Zhou C, Stevenson R, Christakis D, Song K. Walking activity patterns in youth with cerebral palsy and youth developing typically. Disabil Rehabil 2014;36:1279–1284.
25. Tudor-Locke C, Bassett D Jr. How many steps/day are enough? Sports Med 2004;34:1–8.
26. 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.
27. Jeannet 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.
28. Graser SV, Vincent WJ, Pangrazi RP. Step it up: activity intensity using pedometers. J Phys Educ Recreat Dance 2009;80:22–24.
29. Verbeke G, Molenberghs G. Linear mixed models for longitudinal data. New York: Springer-Verlag; 2000. Chapters 7,8.
30. Lythgo N, Wilson C, Galea M. Basic gait and symmetry measures for primary school-aged children and young adults. II: Walking at slow, free, and fast speed. Gait Posture 2011;33:29–35.
31. Shieh PB. Duchenne muscular dystrophy: clinical trials and emerging tribulations. Curr Opin Neurol 2015;28:542–546.
32. Bushby K, Finkel R, Birnkrant DJ, Case LE, Clemens PR, Cripe L, *et al.* Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol 2010;9:77–93.