Journal of NeuroEngineering and Rehabilitation

RESEARCH

Open Access

Longitudinal interaction between muscle impairments and gait pathology in growing children with Duchenne muscular dystrophy

Ines Vandekerckhove[1], Geert Molenberghs[2,3], Marleen Van den Hauwe[1,4], Nathalie Goemans[4,5], Liesbeth De Waele[4,5], Anja Van Campenhout[5,6], Friedl De Groote[7] and Kaat Desloovere[1,8*]

Abstract

Background Children with Duchenne muscular dystrophy (DMD) present with progressive gait pathology due to progressive muscle weakness and contractures. However, the associations between specific muscle impairments and specific gait features have never been quantified. Therefore, the aim of this longitudinal observational cohort study was to investigate the longitudinal interaction between progressive muscle impairments and progressive gait pathology in growing boys with DMD.

Methods Thirty-one boys with DMD (aged 4.6–16.4 years) were repeatedly measured between 2015 and 2022, resulting in a total dataset of 152 observations. Fixed dynamometry, goniometry and 3D gait analysis were used to assess lower limb muscle weakness, passive range of motion and gait. Joint random-effect models between gait and muscle outcomes were fitted. The correlation between the random intercepts (r_a) and random slopes (r_b) indicated the relationship between the initial values and progression rates over time of two outcomes, respectively.

Results Specific muscle impairments were related to specific gait features, both in terms of initial values (r_a=0.470–0.757; $p<0.029$) and progression rates (r_b=0.547–0.812; $p<0.024$). Decreased hip extension strength was associated with increased maximal posterior trunk angle (r_b=-0.588; $p=0.0004$), increased maximal anterior pelvic tilt angle (r_a=-0.543; $p=0.0040$ and r_b=-0.812; $p<0.0001$), and reduced maximal hip extension moment (r_a=0.536; $p=0.0289$). Decreased hip abduction strength was associated with increased step width (r_a=-0.549; $p=0.0021$) and increased maximal internal foot progression angle (r_b=-0.547; $p=0.0117$). Decreased knee extension strength was associated with reduced maximal knee extension moment (r_a=0.702; $p<0.0001$), reduced maximal knee power absorption (r_a=0.757; $p<0.0001$), and reduced dorsiflexion angle at initial contact (r_b=0.684; $p=0.0237$). Decreased dorsiflexion range of motion was associated with reduced dorsiflexion angle at initial contact (r_a=0.732; $p<0.0001$ and r_b=0.627; $p=0.0202$) and reduced maximal dorsiflexion angle in swing (r_a=0.663; $p<0.0001$).

Conclusion This is the first study that objectively quantified the longitudinal interaction between muscle impairments and gait features, providing valuable insights into the underlying mechanisms of pathological gait in DMD. The observed associations highlight the importance of targeted clinical assessments. These findings offer a

*Correspondence:
Kaat Desloovere
kaat.desloovere@kuleuven.be

Full list of author information is available at the end of the article

foundation for optimizing rehabilitation strategies, orthotic management, and orthopedic interventions, ultimately improving clinical decision-making and enhancing mobility outcomes in children with DMD.

Keywords Duchenne muscular dystrophy, Muscle weakness, Ankle range of motion, Gait, 3D gait analysis, Repeated multivariate analysis, Joint random-effect models, Longitudinal study

Background

Duchenne muscular dystrophy (DMD) is a severe X-linked neuromuscular disorder, affecting two per 10,000 newborn boys [1]. Disrupted dystrophin function due to mutations in the dystrophin gene causes progressive muscle degeneration with loss of contractile tissue and replacement by fat and fibrotic tissue [2]. Consequently, boys with DMD experience progressive muscle weakness and contractures that contribute to altered posture and gait [2, 3], eventually leading to loss of ambulation at a mean age of 12.7 years (range: 7.1 and 18.6 years of age) [4]. Delaying loss of ambulation is one of the treatment goals in DMD, in order to maintain a certain level of functionality and to postpone spinal deformities and contractures [2]. However, orthopedic and orthotic treatments that aim at optimizing gait performance indicated conflicting results on gait decline [5–9] and sensitive outcome measures are urgently needed to overcome the difficulties in the clinical development of promising novel treatments [10, 11]. An improved understanding of how the progression in underlying muscle impairments is associated with increasing gait pathology in DMD can improve clinical decision-making, lead to progress in rehabilitation, orthotic and orthopedic interventions, and reveal sensitive outcome measures to prove the efficacy of novel treatments in clinical trials.

Despite the clinical consensus that muscle impairments alter gait in DMD, insight in specific associations between muscle impairments and gait features is lacking. The relationship between underlying muscle impairments and clinical assessments, such as the 6-min walk test, the North Star Ambulatory Assessment, and timed tests has been extensively studied. However, these clinical assessments only measure global gross motor function, and are characterized by high variability in test outcomes [12]. Leveraging detailed 3D gait analysis to investigate these associations could provide novel and clinically relevant insights into the specific ways muscle impairments influence gait pathology in DMD. For example, it has been hypothesized that tiptoeing gait is a compensation mechanism for knee extension weakness, as it positions the ground reaction force near or in front of the knee joint center resulting in smaller knee extension moments [3, 7, 13, 14]. To date, only one study has investigated the relationship between muscle weakness and the gait pattern in DMD, but no meaningful associations were found [15]. However, the latter study was based on cross-sectional data of 15 boys with DMD. Due to the progressive and heterogeneous nature of DMD, these associations should be estimated from larger sample sizes and longitudinal data.

Linking the progression in muscle impairments to the progression in gait pathology in growing children with DMD may highlight the potential role of muscle impairments in gait deterioration. We recently established longitudinal trajectories of muscle impairments [16] and gait features [17] through an extensive 5–7 year follow-up. The muscle impairments were expressed as deficits in reference to typically developing (TD) peers, allowing the established trajectories to reflect pathological changes [16]. Muscle strength and ankle dorsiflexion range of motion followed a non-linear, piecewise trajectory [16]. At age 4.3–4.9 years, initial deficits were already present compared to TD peers, with the largest deficits around the hip, followed by the ankle and then the knee. The muscle outcomes remained stable or slightly improved until ages 6.6–9.4 years. After this period, steep declines in muscle strength and ankle dorsiflexion range of motion emerged. Weakness progressed in a proximal-to-distal pattern with hip strength declining at an earlier age, followed by knee strength and then ankle strength. The steepest declines were seen in knee extension and hip abduction strength. The progressive gait pathology evolved towards more anterior pelvic tilt, hip flexion, internal foot progression and less dorsiflexion at initial contact [17]. There was a high inter-subject variability in the longitudinal trajectories of both muscle impairments and gait features [16, 17], but it remains unclear which muscle impairments are related to which gait features and how their progression rates relate.

The aim of this study was to investigate the longitudinal interaction between progressive muscle impairments and progressive gait features in growing boys with DMD. Specifically, we aimed to determine whether the initial values of specific muscle impairments are related to the initial values of specific gait features and whether their progression rates are related. This is necessary to improve insights into the underlying mechanisms of pathological gait in DMD.

Methods

Participants

We conducted a prospective longitudinal cohort study, supplemented by a small retrospective component with additional data from the same participants. The study protocol consisted of multivariate repeated assessments

with a varying number of assessments among participants and varying time intervals between assessments. Typically, repeated assessments were scheduled at standardized 6-month intervals, except in cases involving retrospective data, disruptions due to COVID-19, or when a child's condition was too mild to warrant follow-up at 6 months.

Table 1 Overview of the selected gait features, the reasoning behind their selection, and the impairments believed to be related to these gait features

Selected gait features	Reason	Impairments postulated to be related to gait features
Maximal anterior pelvic tilt angle (°)	Previously reported significant longitudinal increase [17]	Hip extension weakness Knee extension weakness
Maximal hip extension moment during stance (Nm/kg)	Previously reported significant longitudinal decrease [17]	Hip extension weakness
Maximal posterior trunk angle (°)	Clinically relevant decrease in more severely affected gait patterns compared to the mildly affected gait pattern [18]	Hip extension weakness
Normalized step width (/)	Previously reported significant longitudinal increase as well as interaction effect between time and baseline age [17]	Hip abduction weakness
Maximal internal foot progression angle during stance (°)	Previously reported significant longitudinal increase [17]	Poorly understood
Lateral trunk range of motion (°)	Clinically relevant increase in more severely affected gait patterns compared to the mildly affected gait pattern [18]	Hip abduction weakness
Maximal knee extension moment during stance (Nm/kg)	Clinically relevant decrease in more severely affected gait patterns compared to the mildly affected gait pattern [18]	Knee extension weakness
Maximal knee power absorption during loading response (W/kg)	Clinically relevant decrease in more severely affected gait patterns compared to the mildly affected gait pattern [18]	Knee extension weakness
Dorsiflexion angle at initial contact (°)	Previously reported significant longitudinal decrease [17]	Knee extension weakness Dorsiflexion weakness Dorsiflexion range of motion deficit
Maximal dorsiflexion angle during swing (°)	Previously reported significant interaction effect between time and baseline age [17]	Dorsiflexion weakness Dorsiflexion range of motion deficit

kg = kilogram; Nm = Newton meter; W = Watt;

Boys with DMD were recruited via the Neuromuscular Reference Centre (NMRC) in the University Hospital Leuven between June 2018 and December 2022. The study included boys with a confirmed genetic diagnosis of DMD, who were between 3 and 16 years old at baseline, and able to walk at least 100 meters unaided and without assistive device. Exclusion criteria encompassed a clinical presentation of Becker muscular dystrophy, any history of muscle lengthening surgery, and cognitive or behavioral disorders that impeded accurate measurements. Corticosteroids intake and clinical trial participation with disease-modifying medication were allowed. NMRC implements a proactive and preventive approach to manage contractures, with early introduction of nighttime ankle foot orthoses (AFOs), often alongside the start of corticosteroids, before contracture development, and occasional serial casting if early losses in ankle dorsiflexion range of motion still appear. Retrospective data from the included children, collected between May 2015 and June 2018, was accessed from the University Hospital Leuven database to supplement the prospective data.

This study was approved under the Declaration of Helsinki by the local ethics committee (Ethical Committee UZ Leuven/KU Leuven; S61324). All methodology adhered to the relevant regulations and guidelines. Written informed consents were obtained from the parents or participants' caregivers, and participants aged 12 years or older provided informed assents.

Data collection and analysis

Anthropometric measures, i.e., body mass, height and lower limb segment lengths, were collected at each observation.

We made a selection of muscle impairments and gait features based on our previous longitudinal analyses (Table 1) [16–18]. Gait features were included based on two main criteria: (1) clinically relevant differences in gait features between severely affected and mildly affected gait patterns [18], or (2) significant longitudinal changes in gait features [17]. The selection of muscle impairments for the analyses was defined through clinical reasoning, where we focused on muscle impairments that were previously postulated [3, 7, 13, 14, 17, 19–23] as potential explanations for the gait features. This targeted approach was necessary to ensure feasibility and to identify clinically meaningful relationships.

Muscle weakness

Muscle strength was measured unilaterally. The weakest side, as determined by the manual muscle testing, was selected for assessment. If no weakest side could be identified, the assessed side was randomly selected by flipping a coin.

Hip extension, hip abduction, knee extension, and ankle dorsiflexion muscle strength were assessed with an instrumented strength assessment [24, 25]. Hereto, maximal voluntary isometric contractions (MVIC) were performed using a fixed dynamometer (MicroFet, Hogan Health Industries, West Jordan, UT United States) in a standardized test position. The mean maximal force over one to three representative MVIC trials was multiplied with its lever arm with respect to the joint to calculate the mean maximal joint torque per muscle group. Mean maximal joint torques were converted into unitless z-scores using anthropometric-related TD percentile curves for muscle strength ($n = 153$) [26]. As this accounts for the typical strength development, these z-scores reflect muscle strength deficits with respect to TD peers.

Contractures

Passive joint range of motion was measured bilaterally, but only the side corresponding to the strength assessment was further included for consistency.

Only the plantar flexion contractures were analyzed because our previous work [16] highlighted that this was the only contracture with a clear longitudinal trajectory. The passive range of motion of ankle dorsiflexion, with the knee extended and flexed at 90° [27], was measured in degrees using goniometry during a standardized clinical examination. Passive range of motion measures were converted into unit-less z-scores using the age-related normative reference values of Mudge et al. [27], as previously described [16]. As this accounts for the typical reduction in passive range of motion, these z-scores reflect range of motion deficits with respect to TD peers.

Gait

Gait was measured by 3D gait analysis according to a previously described protocol [17, 18]. The boys with DMD walked barefoot at self-selected speed on a 10-meter walkway. The Plug-In Gait Full-body reflective marker (diameter: 14 mm) model was applied. Marker trajectories were recorded with a 10–15 Vicon camera system (Vicon-UK, Oxford, UK; sampling frequency of 100 Hz; built-in Woltring filter with mode MSE and smoothing of 15 mm^2) and ground reaction forces were captured with two embedded force plates (AMTI, Watertown, MA, USA; sampling frequency: 1500 Hz). Kinetic data was obtained by combining marker trajectories with ground reaction forces. Initial contacts and toe offs were manually indicated, using force plate data when available, to define gait cycles (GCs) in the Nexus software (Nexus 2.10. Vicon-UK, Oxford, UK). Subsequently, trunk, pelvis and lower limb kinematic waveforms (expressed in degrees), and waveforms for lower limb internal joint moments (expressed in Newton meters per kilogram body mass), and power (expressed in Watt per kilogram body mass) were estimated. Ten GCs with kinematic data, of which three to five GCs with kinetic data, were collected bilaterally. We examined the quality of collected GCs in a custom-made software in MATLAB (The Mathworks Inc., Natick, M.A., 2016 and 2021b). Kinematic and kinetic waveforms were resampled to 101 data points per GC. Step width was normalized to leg length, as previously described [17, 18, 28]. Normalized step width, and the kinematic and kinetic waveforms of the selected GCs with good quality were averaged per observation separately for the right and left sides. Predefined gait features were obtained by calculating minima, maxima, range of motions, and values at specific events in the GC from the average continuous kinematic and kinetic waveforms. Only the gait features on the side corresponding to the strength assessment were further included.

Statistical analysis

Descriptive statistics were used to summarize subject characteristics as well as muscle and gait outcomes at the initial visit and across all observations. Medians, first quartiles (Q1), and third quartiles (Q3) were reported, as some parameters were not normally distributed, based on the Shapiro–Wilk test and visual inspection of distribution plots.

Joint random-effect models were applied to investigate the longitudinal correlation among multivariate outcomes. The outcome parameters were selected based on our previous results [16–18] and pairs of muscle impairments and gait features to jointly model were chosen based on clinical reasoning (Table 1). A mixed model was first fitted on each individual outcome, according to the previously documented workflow [17, 29]. Time course of the observations (starting from the initial visit and calculated by subtracting the age at the initial visit from the age at each observation) was selected as the fixed effect. A random intercept modelled the variability in starting point, while a random slope for time modelled the variability in trajectory among subjects. Then, joint models to estimate a gait outcome and muscle impairment outcome were created by linking the random effects of the two outcomes (Additional file 1) [30].

The estimates of the individual mixed models were used as starting values for the joint models, while unknown estimates were initiated at zero. Pearson correlation was estimated between random intercepts (r_a), which reflects the relationship between the initial values of the individual predicted trajectories for gait and muscle outcomes. Similarly, Pearson correlation (r_b) was estimated between random slopes, which reflects the relationship between their progression rates over time (Additional file 1) [30]. The data points of the patients with only one measurement contribute only to the correlation between the initial values.

Correlation coefficients were interpreted as negligible ($r < 0.300$), low ($r = 0.300$-0.499), moderate ($r = 0.500$-0.699), high ($r = 0.700$-0.899), or very high ($r \geq 0.900$) [31]. The significance threshold was set to $\alpha = 0.05$ and not corrected for multiple comparisons due to the explorative nature of the study. All analyses and visualizations were conducted in SAS® (version 9.4, Statistical Analysis Software, SAS Institute Inc., Cary, NC, USA).

Results

Thirty-one boys with DMD, aged between 4.6 and 16.4 years old, were repeatedly measured between 2015 and 2022 at multiple time points (median = 4; Q1-Q3 = 2–8; minimum (min) maximum (max) = 1–10) with a median time interval of 0.5 years (Q1-Q3 = 0.5-1.0 years; min-max = 0.4–3.5 years), covering a median follow-up time of 3.2 years (Q1-Q3 = 1.5–4.1 years; max = 6.6 years). In total, the included dataset consisted of 152 measurement sessions (Additional file 2). All patient characteristics are documented in Table 2. The flowchart in Additional file 3 provides an overview of the collected data, the excluded data after quality check, the missing data, and the included data.

Decreased hip extension strength was associated with increased maximal anterior pelvic tilt angle, both in terms of initial values and progression rates (Table 3; Fig. 1A-B). At initial values, decreased hip extension strength was also moderately associated with decreased maximal hip extension moment (Table 3; Fig. 1A-C). The rate of decrease in hip extension strength was moderately associated with the rate of increase in maximal posterior trunk angle (Table 3; Fig. 1A-D).

At initial values, decreased hip abduction strength was moderately associated with increased normalized step width (Table 4; Fig. 2A-B). Additionally, the rate of decrease in hip abduction strength was moderately associated with the rate of increase in maximal internal foot progression angle (Table 4; Fig. 2A-C). No significant correlations were found between hip abduction strength and lateral trunk range of motion, either at initial values or in their progression rates (Table 4; Fig. 2A-D).

At initial values, decreased knee extension strength was strongly associated with reduced maximal knee extension moment (Table 5; Fig. 3A-B) and with decreased maximal knee power absorption during loading response (Table 5; Fig. 3A-C). It was also weakly associated with increased maximal anterior pelvic tilt angle (Table 5; Fig. 3A-D). The rate of decrease in knee extension strength was moderately associated with the rate of decrease in dorsiflexion angle at initial contact (Table 5; Fig. 3A-E).

At initial values, decreased dorsiflexion strength was weakly associated with reduced dorsiflexion angle at initial contact (Table 6; Fig. 4A-B) and with decreased maximal dorsiflexion angle during swing (Table 6; Fig. 4A-C).

Table 2 Group demographics

	Initial visit characteristics	Characteristics over all observations
	Frequency or median (Q1-Q3)	Frequency or median (Q1-Q3)
Subjects (n)	31	31
Observations (n)	31	152
Follow-up time (years)	0	3.2 (1.5–4.1)
Observations per participant (n)	1	4 (2–8)
Age (years)	8.7 (6.0–10.8)	10.2 (8.3–12.6)
Body mass (kg)	25.9 (19.2–34.7)	31.0 (24.2–42.5)
Height (m)	1.23 (1.08–1.31)	1.25 (1.17–1.33)
Body mass index (kg/m^2)	17.4 (16.6–21.2)	19.0 (16.6–23.1)
Corticosteroids		
Daily Deflazacort (% subjects)	87.10%	95.39%
Vamorolone (% subjects)	3.23%	1.32%
No steroids (% subjects)	9.68%	3.29%
Participation in clinical trial with disease modifying medication (% subjects)	25.81%	39.47%
Adherence nighttime ankle foot orthoses (% subjects)	80.65%	78.95%
Serial casting (% subjects)	3.23%	6.58%
Hip extension strength (Nm)	8.2 (6.5–10.7)	8.9 (5.5–12.7)
Hip extension strength (z-score)	-3.04 (-4.16– -2.44)	-3.34 (-4.80– -1.95)
Hip abduction strength (Nm)	10.8 (8.0–15.1)	12.1 (8.6–13.7)
Hip abduction strength (z-score)	-2.31 (-2.9– -2.02)	-2.78 (-3.67– -2.08)
Knee extension strength (Nm)	16.3 (11.2–20.7)	16.4 (11.3–19.5)
Knee extension strength (z-score)	-0.83 (-2.32– -0.56)	-1.95 (-3.17– -0.90)
Ankle dorsiflexion strength (Nm)	2.9 (1.9–4.7)	3.5 (2.4–4.6)
Ankle dorsiflexion strength (z-score)	-2.44 (-3.32– -1.58)	-3.07 (-3.51– -2.12)
Ankle dorsiflexion range of motion (°)	5.0 (0.0–10.0)	0 (-5–7.5)
Ankle dorsiflexion range of motion (z-score)	-3.13 (-4.24– -2.20)	-3.48 (-4.69– -2.67)
Maximal anterior pelvic tilt angle (°)	16.4 (14.3–19.1)	19.2 (14.5–22.7)
Maximal hip extension moment during stance (Nm/kg)	0.51 (0.37–0.69)	0.44 (0.27–0.57)
Maximal posterior trunk angle (°)	10.4 (6.0–15.5)	14.7 (7.2–20.1)
Normalized step width (/)	0.28 (0.25–0.31)	0.28 (0.26–0.33)
Maximal internal foot progression angle during stance (°)	-9.6 (-14.2– -3)	-3.5 (-12.0– -0.1)
Lateral trunk range of motion (°)	6.1 (2.9–7.4)	5.1 (3.0–7.4)
Maximal knee extension moment during stance (Nm/kg)	0.41 (0.34–0.50)	0.32 (0.24–0.53)
Maximal knee power absorption during loading response (W/kg)	0.66 (0.30–1.00)	0.37 (0.12–0.95)

Table 2 (continued)

	Initial visit characteristics	Characteristics over all observations
	Frequency or median (Q1-Q3)	Frequency or median (Q1-Q3)
Dorsiflexion angle at initial contact (°)	0.8 (-3.6–4.1)	-2.5 (-6.5–1.6)
Maximal dorsiflexion angle during swing (°)	4.8 (-1.0–6.9)	2.4 (-2.5–5.7)

kg = kilogram; m = meter ; Nm = Newton meter; W = Watt; n = number; Q1 = first quantile; Q3 = third quantile

Decreased dorsiflexion range of motion (with the knee extended) was associated with reduced dorsiflexion angle at initial contact, both in terms of initial values and progression rates (Table 6; Fig. 4B-D). At initial values, decreased dorsiflexion range of motion (with the knee extended) was also moderately associated with decreased maximal dorsiflexion angle during swing (Table 6; Fig. 4C-D).

Non-significant correlations are not described in the results section but are presented in the corresponding tables for completeness. To reduce redundancy, we chose to display the predicted trajectories of a given parameter only once across joint random-effect models presented in the same figure. However, because the predicted trajectories vary slightly between joint models, all individual predicted trajectories for each joint random-effect model are provided in Additional file 6. For each analyzed gait outcome, only timepoints with non-missing corresponding muscle strength data were included in the joint modelling. This explains the minor differences in sample size and trajectory shape across joint random-effect models. The influence of corticosteroid use, clinical trial participation and nighttime AFOs is explored in Additional files 7 and 8.

Discussion

This longitudinal observational cohort study aimed at investigating the longitudinal interaction between progressive muscle impairments and progressive gait features in growing boys with DMD. Several clinical hypotheses propose links between specific underlying muscle impairments and corresponding gait features, but these assumed relationships have largely remained theoretical and unquantified [15]. To date, only one prior study has examined these interactions, but it did not identify meaningful relationships [15]. In contrast, the current study revealed distinct associations between specific muscle impairments and specific gait features, both in terms of initial values and progression rates. A schematic overview of the key findings is provided in Fig. 5. By objectively quantifying these longitudinal interactions, the current study provides empirical support for clinical hypotheses and offers new insights into the mechanisms driving gait decline in boys with DMD.

Quantitative analyses revealed that hip extension weakness is associated with altered trunk and pelvic kinematics, as well as impaired hip kinetics in boys with DMD. Specifically, our results showed that increased hip extension weakness was associated with increased posterior trunk leaning over time, with increased anterior pelvic tilt both at initial values and as the weakness progressed, and with reduced hip extension moments at initial values. These findings support the clinical hypothesis of posterior trunk leaning as a successful compensation mechanism for hip extension weakness [3, 22, 23] and anterior pelvic tilt as the direct consequence of hip extension weakness [13, 14, 23]. It has been clinically hypothesized that boys with DMD lean their trunks posteriorly to compensate for hip extension weakness, as this posture shifts the ground reaction force more posteriorly to the hip joint center, thereby reducing the hip extension moment [3, 19, 20, 22]. Originally described by Sutherland et al. [3], this compensation mechanism is now quantitatively confirmed by our data, and importantly, we show that it becomes more pronounced as hip extension weakness progresses. Similarly, our findings confirm the clinical hypothesis that anterior pelvic tilt is a direct consequence of hip extension weakness [13, 14, 23], and that this tilt increases as hip extension weakness progresses. Interestingly, the association with anterior pelvic tilt was stronger than with posterior trunk lean, possibly because the pelvis is biomechanically closer and more directly affected by changes in hip extension strength. Our findings highlight the importance of preserving hip extension strength for as long as possible or designing assistive devices that provide support for hip extension. This may help minimize posterior trunk lean and reduce anterior pelvic tilt, which could postpone the onset of hip flexion contractures. However, more research is required to explore this further. Based on the current quantitative confirmation of clinical hypotheses, hip extension strength emerges as a key target for therapeutic interventions aimed at optimizing gait in boys with DMD.

Hip abduction weakness was quantitatively linked to changes in step width and foot kinematics in boys with DMD. Specifically, our findings indicated that increased hip abduction weakness was associated with increased step width at initial values and, as the weakness progressed, with increased internal foot progression. Therefore, the clinical hypothesis that boys with DMD increase their base of support to compensate for hip abduction weakness by shifting the ground reaction force more laterally to the hip joint [3, 17] is quantitatively supported

Table 3 Correlation between random intercepts (i.e., initial values of individual predicted trajectories) and random slopes (i.e., progression rates of individual predicted trajectories) of joint models between hip extension strength and gait features in boys with DMD

Muscle strength	Gait features	Correlation random intercepts r_a [CI] *p-value*	Correlation random slopes r_b [CI] *p-value*
Hip extension strength (z-score)	Maximal anterior pelvic tilt angle (°)	-0.543 [-0.771; -0.192] ***0.0040****	-0.812 [-0.922; -0.579] ***<0.0001****
Hip extension strength (z-score)	Maximal hip extension moment during stance (Nm/kg)	0.536 [0.061; 0.813] ***0.0289****	
Hip extension strength (z-score)	Maximal posterior trunk angle (°)	-0.369 [-0.711; 0.116] *0.1318*	-0.588 [-0.780; -0.294] ***0.0004****

p-values in bold indicate significance level at $p < 0.05$. The colors indicate the strength of the relationship: green, high; blue, moderate; yellow, low. For all parameters, a random intercept and slope model was selected, except for maximal hip extension moment during stance. For this parameter, a random intercept model was chosen based on the likelihood ratio test, which explains the absence of a random slope correlation in the joint model with hip extension strength. CI = 95% confidence interval; DMD = Duchenne muscular dystrophy; kg = kilogram; Nm = newton meter; r_a = Pearson correlation coefficient of random intercepts; r_b = Pearson correlation coefficient of random slopes.

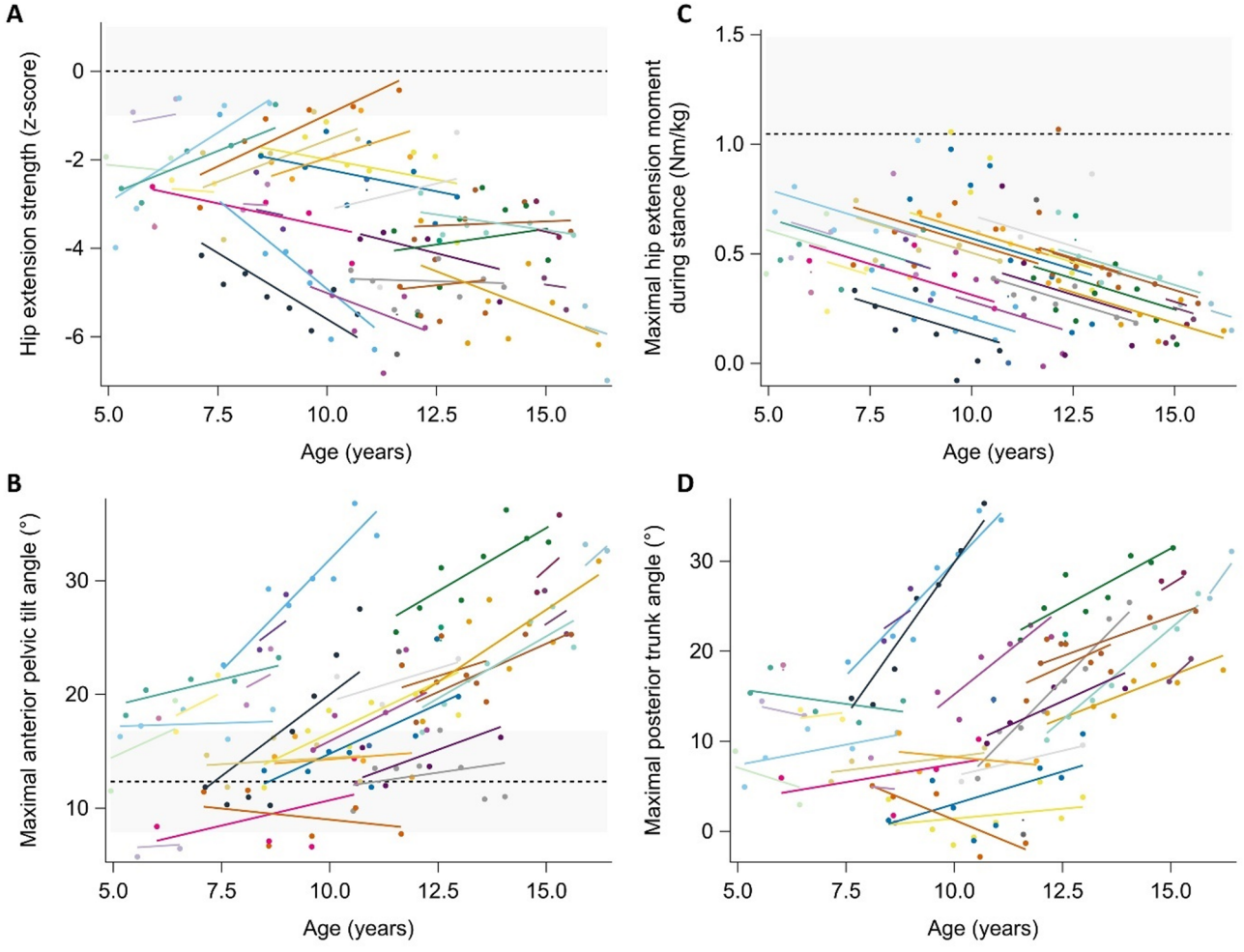

Fig. 1 Coupled predicted trajectories of hip extension strength and gait outcomes. Predicted individual trajectories (colored lines) and observed values (colored dot) for: **A** hip extension strength, **B** maximal anterior pelvic tilt angle, **C** maximal hip extension moment, and **D** maximal posterior trunk angle. Each color represents a different child with DMD. The dotted black line, with a surrounding gray band, shows the mean ± 1 standard deviation of values from TD children. Trunk data were not available for TD children. The plotted trajectories were derived from a joint random-effect model that links **A** hip extension strength and **B**,**C**,**D** a gait outcome over time. For all parameters, a random intercept and slope model was selected, except for maximal hip extension moment during stance. For this parameter, a random intercept model was chosen based on the likelihood ratio test, which explains why the predicted individual trajectories appear parallel. The relationships between the initial values (i.e., correlations between the random intercepts) and progression rates (i.e., correlations between the random slopes) for the paired outcomes are shown in Table 3. Full model estimates, including fixed effects and the random-effect covariance matrix, are provided in Additional files 4 and 5. DMD = Duchenne muscular dystrophy; kg = kilogram; Nm = Newton meter; TD = typically developing;

Table 4 Correlation between random intercepts (i.e., initial values of individual predicted trajectories) and random slopes (i.e., progression rates of individual predicted trajectories) of joint models between hip abduction strength and gait features in boys with DMD

Muscle strength	Gait features	Correlation random intercepts r_a [CI] *p-value*	Correlation random slopes r_b [CI] *p-value*
Hip abduction strength (z-score)	Normalized step width (/)	-0.549 [-0.766; -0.221] ***0.0021****	-0.403 [-0.766; 0.154] *0.1508*
Hip abduction strength (z-score)	Maximal internal foot progression angle during stance (°)	-0.291 [-0.539; 0.003] *0.0527*	-0.547 [-0.798; -0.136] ***0.0117****
Hip abduction strength (z-score)	Lateral trunk range of motion (°)	-0.196 [-0.493; 0.141] *0.252*	0.524 [-0.117; 0.856] *0.1029*

p-values in bold indicate significance level at $p < 0.05$. The colors indicate the strength of the relationship: green, high; blue, moderate; yellow, low. CI = 95% confidence interval; DMD = Duchenne muscular dystrophy; r_a = Pearson correlation coefficient of random intercepts; r_b = Pearson correlation coefficient of random slopes.

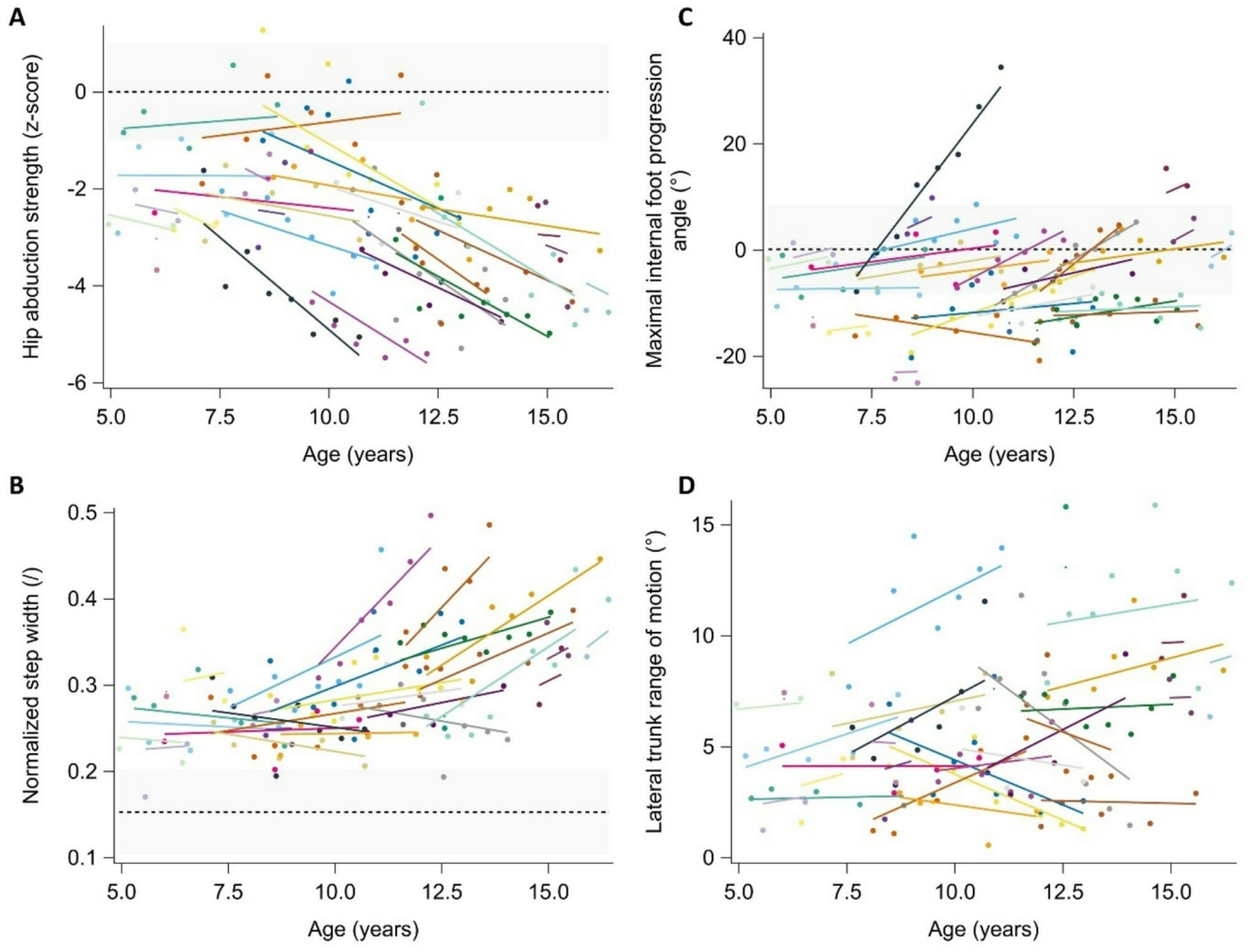

Fig. 2 Coupled predicted trajectories of hip abduction strength and gait outcomes. Predicted individual trajectories (colored lines) and observed values (colored dots) for: **A** hip abduction strength, **B** normalized step width, **C** maximal internal foot progression angle, and **D** lateral trunk range of motion. Each color represents a different child with DMD. The dotted black line, with a surrounding gray band, shows the mean ± 1 standard deviation of values from TD children. Trunk data were not available for TD children. The plotted trajectories were derived from a joint random-effect model that links **A** hip abduction muscle strength and **B**,**C**,**D** a gait outcome over time. The relationships between the initial values (i.e., correlations between the random intercepts) and progression rates (i.e., correlations between the random slopes) for the paired outcomes are shown in Table 4. Full model estimates, including fixed effects and the random-effect covariance matrix, are provided in Additional files 4 and 5. DMD = Duchenne muscular dystrophy; TD = typically developing;

Table 5 Correlation between random intercepts (i.e., initial values of individual predicted trajectories) and random slopes (i.e., progression rates of individual predicted trajectories) of joint models between knee extension strength and gait features in boys with DMD

Muscle strength	Gait features	Correlation random intercepts r_a [CI] *p-value*	Correlation random slopes r_b [CI] *p-value*
Knee extension strength (z-score)	Maximal knee extension moment during stance (Nm/kg)	0.702 [0.482; 0.838] ***<0.0001****	
Knee extension strength (z-score)	Maximal knee power absorption during loading response (W/kg)	0.757 [0.568 ; 0.870] ***<0.0001****	
Knee extension strength (z-score)	Maximal anterior pelvic tilt angle (°)	-0.470 [-0.693; -0.165] ***0.0036****	-0.524 [-0.835; 0.039] *0.0664*
Knee extension strength (z-score)	Dorsiflexion angle at initial contact (°)	0.200 [-0.188 ; 0.534] *0.3111*	0.684 [0.111; 0.916] ***0.0237****

p-values in bold indicate significance level at $p < 0.05$. The colors indicate the strength of the relationship: green, high; blue, moderate; yellow, low. For all parameters, a random intercept and slope model was selected, except for maximal knee extension moment during stance and maximal knee power absorption during loading response. For these parameters, a random intercept model was chosen based on the likelihood ratio test, which explains the absence of a random slope correlation in the joint model with knee extension strength. CI = 95% confidence interval; DMD = Duchenne muscular dystrophy; kg = kilogram; Nm = Newton meter; W = Watt; r_a = Pearson correlation coefficient of random intercepts; r_b = Pearson correlation coefficient of random slopes.

by our data. In contrast, although increased lateral trunk range of motion has also been reported as a compensatory mechanism [3, 19, 22], our findings did not support this hypothesis. Therefore, the current study suggests that increased step width, rather than lateral trunk range of motion, is the primary gait adaptation for hip abduction weakness in DMD. Additionally, progressive hip abduction weakness was also related to an increase in internal foot progression. This finding was unexpected, as internal foot progression directs the ground reaction force more medially to the hip joint. This result may be influenced by other co-occurring impairments, such as increasing stiffness or contractures of the tensor fascia latae or tibialis posterior [3, 17]. While our findings support the clinical hypothesis of increased step width as a compensatory strategy for hip abduction weakness, the underlying mechanisms of in-toeing gait remain poorly understood and warrant more investigation.

Knee extension weakness showed associations with deviations in pelvic and ankle kinematics, as well as knee joint kinetics in boys with DMD. Specifically, our results showed that increased knee extension weakness was associated with increased anterior pelvic tilt at initial values, with decreased dorsiflexion at initial contact over time as the weakness progressed, and with decreased knee extension moment and knee absorption during loading response at initial values. These findings support clinical hypotheses suggesting that increased anterior pelvic tilt [3] and tiptoeing gait [3, 7, 13, 14] compensate for knee extension weakness by positioning the ground reaction force closer to or in front of the knee joint center, resulting in reduced knee extension moment and knee power absorption during loading response [3, 7]. In TD gait, the quadriceps eccentrically contract to control knee flexion and absorb impact forces during loading response. By shifting the ground reaction force anteriorly to the knee joint, the external knee flexion moment is reduced, lowering the eccentric demand on the quadriceps, which is associated with less knee power absorption [7, 19]. The strong associations between knee extension weakness and knee extension moment and power absorption suggest that this compensation strategy for knee extension weakness is effective. Moreover, the association with dorsiflexion angle at initial contact was not only stronger but also evident over time, compared to the association with anterior pelvic tilt, indicating that tiptoeing gait is more important to compensate for knee extension weakness than tilting the pelvis more anteriorly. These findings highlight the importance of maintaining knee extension strength or developing assistive devices that support knee extension. This could help reduce the compensatory tiptoeing, which might postpone the development of plantar flexion contractures. However, this warrants further investigation in future research. Overall, our results quantitatively confirm clinical hypotheses and identify knee extension strength as a key target for optimizing gait in boys with DMD.

Ankle impairments were found to be quantitatively associated with alterations in ankle kinematics in boys with DMD. Specifically, increased dorsiflexion weakness was associated with reduced dorsiflexion at initial contact and during swing at initial values, while decreased dorsiflexion range of motion was associated with reduced dorsiflexion at initial contact both at initial values and as range of motion further declined, as well as with reduced dorsiflexion during swing at initial values. These findings support clinical hypotheses that dorsiflexion weakness contributes to drop foot during swing and that plantar flexion contractures lead to tiptoeing gait [3, 19, 21]. Interestingly, the association with reduced dorsiflexion range of motion was not only stronger but also evident over time, compared to the association with increased

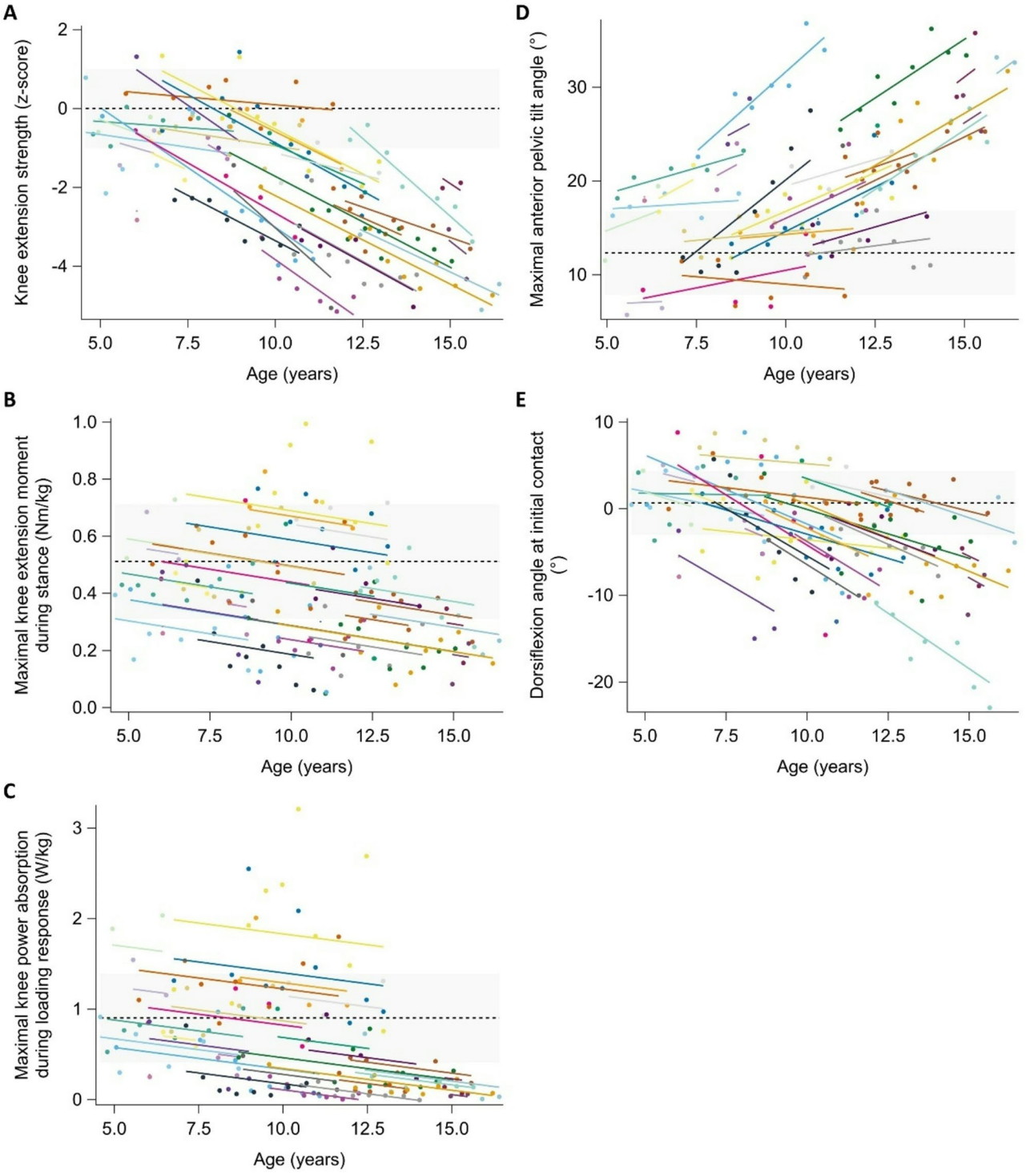

Fig. 3 Coupled predicted trajectories of knee extension strength and gait outcomes. Predicted individual trajectories (colored lines) and observed values (colored dots) for: **A** knee extension strength, **B** maximal knee extension moment, **C** maximal knee power absorption during loading response, **D** maximal anterior pelvic tilt angle, and **E** dorsiflexion angle at initial contact. Each color represents a different child with DMD. The dotted black line, with a surrounding gray band, shows the mean ± 1 standard deviation of values from TD children. The plotted trajectories were derived from a joint random-effect model that links **A** knee extension muscle strength and **B**,**C**,**D**,**E** a gait outcome over time. For all parameters, a random intercept and slope model was selected, except for maximal knee extension moment during stance and maximal knee power absorption during loading response. For these parameters, a random intercept model was chosen based on the likelihood ratio test, which explains why the predicted individual trajectories appear parallel. The relationships between the initial values (i.e., correlations between the random intercepts) and progression rates (i.e., correlations between the random slopes) for the paired outcomes are shown in Table 5. Full model estimates, including fixed effects and the random-effect covariance matrix, are provided in Additional files 4 and 5. DMD = Duchenne muscular dystrophy; kg = kilogram; Nm = Newton meter; TD = typically developing; W = Watt;

Table 6 Correlation between random intercepts (i.e., initial values of individual predicted trajectories) and random slopes (i.e., progression rates of individual predicted trajectories) of joint models between dorsiflexion strength as well as dorsiflexion range of motion and gait features in boys with DMD

Dorsiflexion strength and range of motion	Gait features	Correlation random intercepts r_a [CI] *p-value*	Correlation random slopes r_b [CI] *p-value*
Dorsiflexion strength (z-score)	Dorsiflexion angle at initial contact (°)	0.494 [0.122; 0.744] ***0.0113****	0.568 [-0.038; 0.868] *0.0643*
Dorsiflexion strength (z-score)	Maximal dorsiflexion angle during swing (°)	0.494 [0.189; 0.712] ***0.0024****	0.385 [-0.239; 0.784] *0.2210*
Dorsiflexion range of motion (z-score)	Dorsiflexion angle at initial contact (°)	0.732 [0.564; 0.841] ***<0.0001****	0.627 [0.114; 0.876] ***0.0202****
Dorsiflexion range of motion (z-score)	Maximal dorsiflexion angle during swing (°)	0.663 [0.402; 0.825] ***<0.0001****	0.409 [-0.185; 0.784] *0.1705*

p-values in bold indicate significance level at $p < 0.05$. The colors indicate the strength of the relationship: green, high; blue, moderate; yellow, low. CI = 95% confidence interval; DMD = Duchenne muscular dystrophy; r_a = Pearson correlation coefficient of random intercepts; r_b = Pearson correlation coefficient of random slopes.

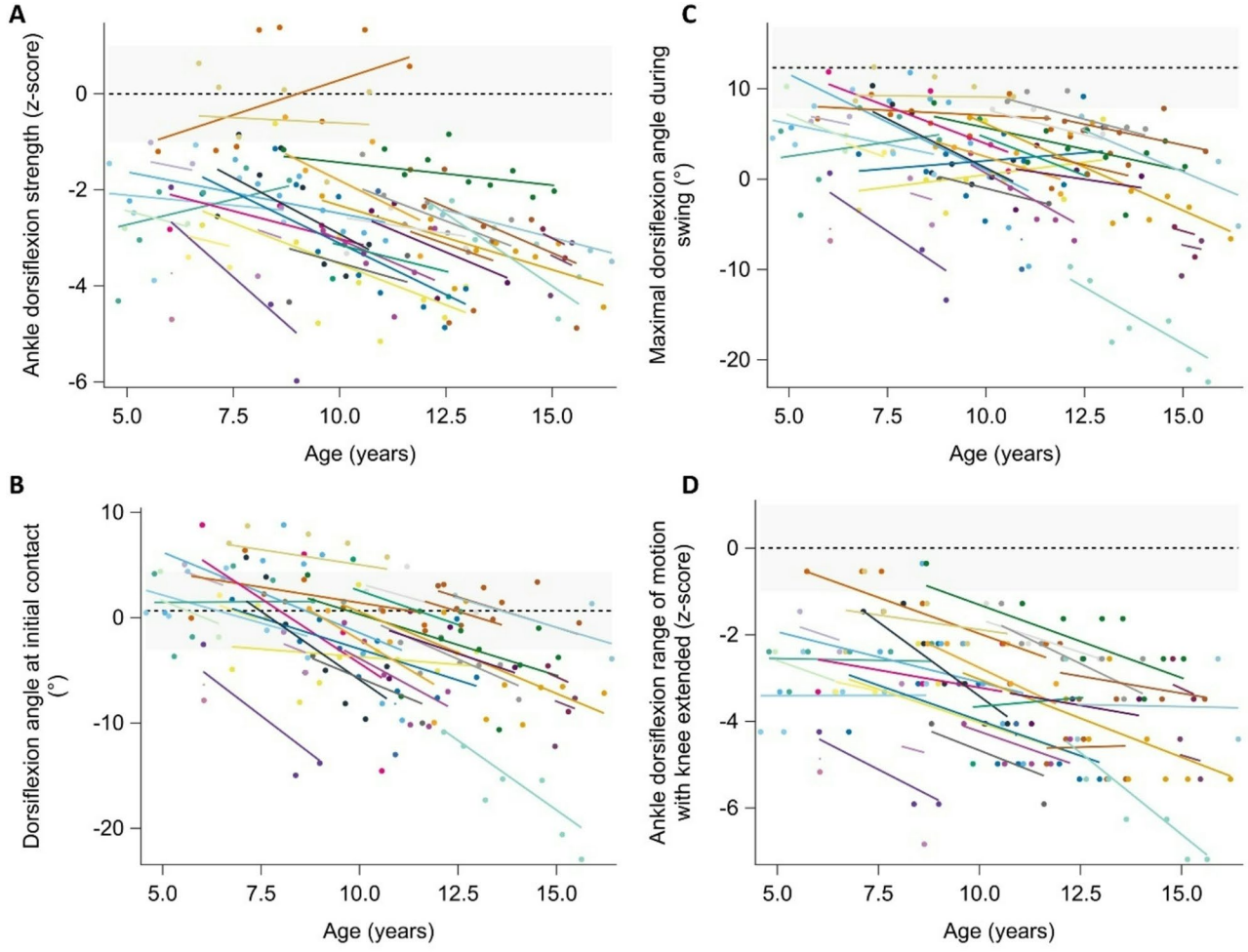

Fig. 4 Coupled predicted trajectories of dorsiflexion strength and range of motion, and gait outcomes. Predicted individual trajectories (colored lines) and observed values (colored dots) for: **A** ankle dorsiflexion strength, **B** dorsiflexion angle at initial contact, **C** maximal dorsiflexion angle during swing, and **D** ankle dorsiflexion range of motion. Each color represents a different child with DMD. The dotted black line, with a surrounding gray band, shows the mean ± 1 standard deviation of values from TD children. The plotted trajectories were derived from a joint random-effect model that links **A** ankle dorsiflexion muscle strength or **D** ankle dorsiflexion range of motion and **B,C** a gait outcome over time. The relationships between the initial values (i.e., correlations between the random intercepts) and progression rates (i.e., correlations between the random slopes) for the paired outcomes are shown in Table 6. Full model estimates, including fixed effects and the random-effect covariance matrix, are provided in Additional files 4 and 5. DMD = Duchenne muscular dystrophy; TD = typically developing;

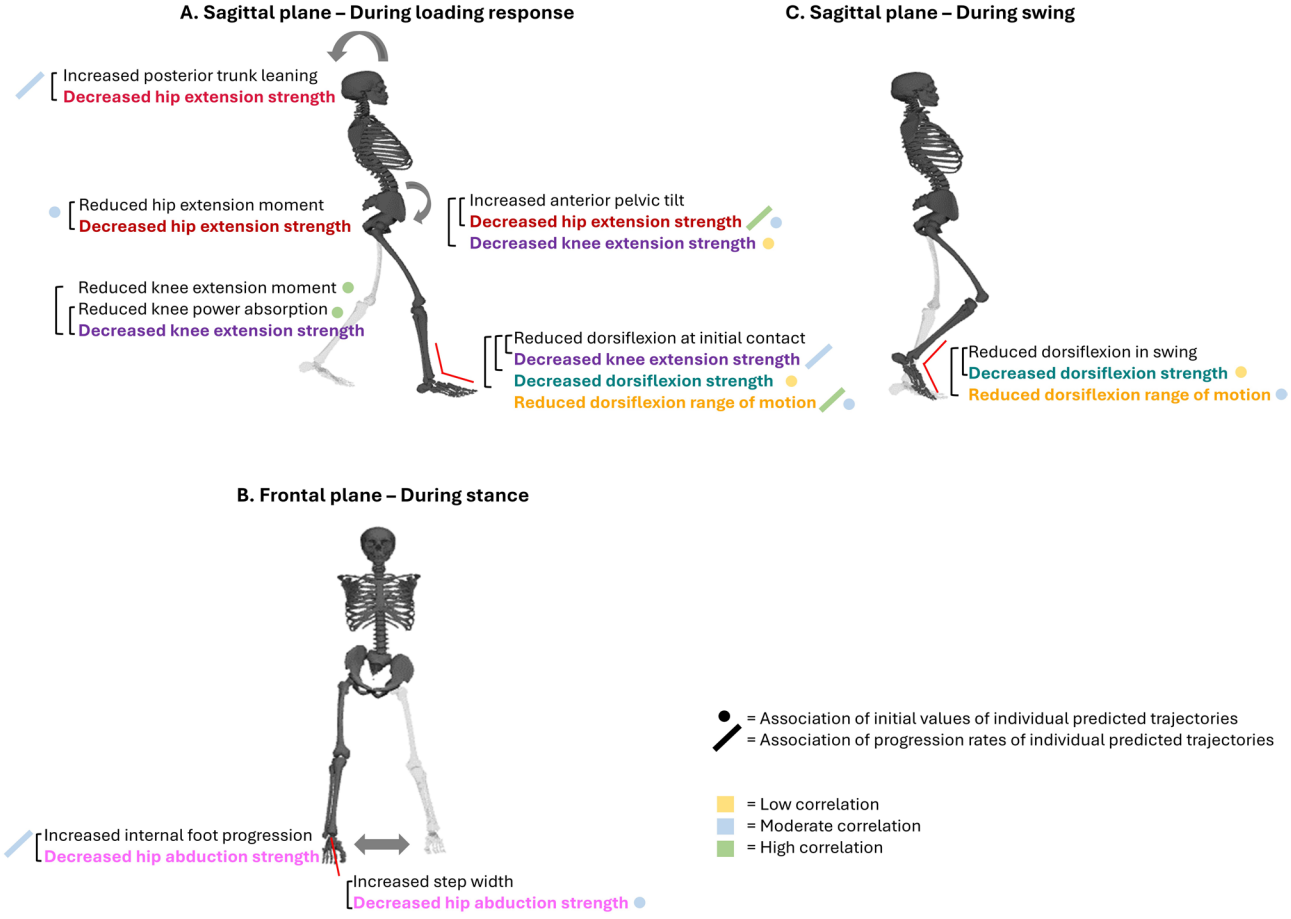

Fig. 5 Schematic overview of gait features related to underlying muscle impairments: key findings. Each joint random-effect model is indicated with a bracket. Correlations between initial values of individual predicted trajectories are indicated with dots and correlations between their progression rates with lines. The color of the dots and lines indicate the strength of the relationship.

dorsiflexion weakness, suggesting that plantar flexion contractures, more than dorsiflexion weakness, play a primary role in tiptoeing gait. This aligns with Sutherland et al. [3] who attributed the drop foot to dorsiflexion weakness in the early stage and to plantar flexion contractures in later stages. The findings highlight the importance of preserving dorsiflexion range of motion to mitigate tiptoeing. However, it remains unclear whether treating plantar flexion contractures would compromise compensatory strategies for weakened knee extensors (explained above) [7], as these impairments co-occur and decline simultaneously. Our results quantitatively support previous clinical hypotheses, but also underscore the need for further investigation to guide intervention strategies that balance ankle and knee function in DMD.

The current findings, based on quantified trajectories from integrated assessments of both muscle impairments and gait features over time, have important implications for the standard of care in patients. They offer precise, patient-specific insights into disease progression, which can improve communication with families and support timely, tailored rehabilitation strategies by identifying key factors affecting gait performance. Two clinical cases in Additional file 9 illustrate how this approach can inform targeted rehabilitation recommendations and personalized treatment strategies. This approach of longitudinal, integrated assessments may also be relevant for managing other neuromuscular disorders.

While the current findings reveal clear associations between specific muscle impairments and specific gait features, caution is needed in interpreting these as causal, given the presence of multiple co-occurring impairments and their simultaneous decline over time. Nonetheless, the current findings may inform future studies designed to better understand causation. Additionally, muscle impairments were assessed using stationary methods, while gait was evaluated through dynamic assessment. Due to fundamental differences in measurement context, associations between outcomes from stationary and dynamic assessments may not fully capture the influence of impairments during functional movement [32]. Stationary assessments of muscle impairments evaluate

isolated muscle groups in a controlled, mono-articular manner. Muscle strength is measured isometrically, and range of motion is assessed at a single joint while keeping other joints in standardized positions. In contrast, dynamic assessment of gait is highly complex, involving simultaneous changes in joint angles across multiple joints and planes, as well as changes in muscle lengths and contraction velocities. It is further influenced by interactions between multiple impairments and other factors such as intra- and inter-limb coordination and balance. Furthermore, both the number of repeated assessments and the time intervals between them varied across the participants. In some children with DMD, only a limited number of repeated measurements were obtained. The boys with DMD enrolled in the study at varying ages, resulting in a wide baseline age range. Moreover, there was an imbalance in the number of repeated assessments across the analyzed parameters, primarily due to missing data. The trunk marker model was not attached during assessments in very young children. In some cases, strength assessments could not be performed due to limited cooperation or understanding from the child. Hip muscle strength data were missing during the early phase of data collection, as the strength assessment had not yet been adapted to include hip muscles. Consequently, for each analyzed gait outcome, we decided to include only the timepoints with corresponding non-missing muscle strength data in the joint modelling, leading to variations in sample sizes and trajectory shape across the joint models. There was also inter-subject heterogeneity due to differences in medical and clinical histories, such as clinical trial participation, corticosteroid intake, gene mutation, adherence to nighttime AFOs, periods of serial casting, functional level, etc. This highlights the need for large-scale multicenter studies with larger sample sizes to account for such variability and improve generalizability of the results.

Conclusion

In conclusion, the initial values and progression rates of specific muscle impairments were associated with the initial values and progression rates of specific gait features in boys with DMD. This is the first study that objectively quantified these interactions, providing empirical evidence for previous clinical assumptions. 3D gait analysis emerges as a promising tool for evaluating the effects of therapeutic strategies and may complement existing outcome measures in future clinical trials. Moreover, the results provide insights into the underlying mechanisms of pathological gait in DMD. The observed associations highlight the importance of targeted clinical assessments. These findings offer a foundation for optimizing rehabilitation strategies, orthotic management, and orthopedic interventions, ultimately improving clinical decision-making and enhancing mobility outcomes in children with DMD.

Abbreviations

AFO	Ankle foot orthosis
DMD	Duchenne muscular dystrophy
GC	Gait cycle
MVIC	Maximal voluntary isometric contraction
NMRC	Neuromuscular Reference Centre
TD	Typically developing

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12984-025-01718-5.

Additional file 1. Details on statistical analysis.

Additional file 2. Overview of the collected longitudinal dataset.

Additional file 3. Flowchart of collected dataset, excluded data, missing data, and included dataset.

Additional file 4. Fixed effects of joint models between muscle and gait outcomes for the boys with DMD.

Additional file 5. Covariance matrix of random effects and measurement error of joint models between muscle and gait outcomes for the boys with DMD.

Additional file 6. All individual predicted trajectories for each joint random-effect model.

Additional file 7. Data exploration of the impact of no corticosteroids and clinical trial participation.

Additional file 8. Data exploration of the impact of poor nighttime ankle foot orthosis adherence.

Additional file 9. Two clinical cases.

Acknowledgements

The authors would like to thank all the boys and their parents who participated in this study. We also appreciate the colleagues of the University Hospital Leuven who assisted with recruitment. A special acknowledgment goes to Elze Stoop and Tijl Dewit for the support in data collection and processing.

Author contributions

The study was conceptualized and designed by IV and KD. Data collection was performed by IV and MVdH. Methodology was developed by IV and GM. Data analysis and visualizations were carried out by IV. IV, GM, MVdH, NG, LDW, AVC, FDG, and KD interpreted the results. The original draft was written by IV, while GM, MVdH, NG, LDW, AVC, FDG, and KD reviewed and edited the manuscript. All authors have read and approved the published version of the manuscript.

Funding

This research was funded by Duchenne Parent Project NL (17.011) and by the Research Foundation – Flanders (FWO-Vlaanderen) through a research fellowship to IV (1188923N). LDW is member of the European Reference Network for Rare Neuromuscular Diseases (ERN EURO-NMD).

Data availability

All data concerning this study is available within the manuscript. Detailed data is available upon reasonable request to the first author.

Declarations

Ethics approval and consent to participate

Data collection was approved by the local ethics committee (Ethical Committee UZ Leuven/KU Leuven; S61324) under the Declaration of Helsinki. The parents or participants' caregivers provided written informed

consents. Participants aged 12 years or older provided informed assents. All methodology adhered to the relevant regulations and guidelines.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Rehabilitation Sciences, KU Leuven, Leuven, Belgium
[2]Interuniversity Institute for Biostatistics and Statistical Bioinformatics (I-BioStat), KU Leuven, Leuven, Belgium
[3]Interuniversity Institute for Biostatistics and Statistical Bioinformatics (I-BioStat), Data Science Institute, Hasselt University, Hasselt, Belgium
[4]Department of Child Neurology, University Hospital Leuven, Leuven, Belgium
[5]Department of Development and Regeneration, KU Leuven, Leuven, Belgium
[6]Department of Orthopedics, University Hospital Leuven, Leuven, Belgium
[7]Department of Movement Sciences, KU Leuven, Leuven, Belgium
[8]Clinical Motion Analysis Laboratory, University Hospital Leuven, Pellenberg, Belgium

Received: 23 March 2025 / Accepted: 1 August 2025
Published online: 01 October 2025

References

1. Crisafulli S, Sultana J, Fontana A, Salvo F, Messina S, Messina S, et al. Global epidemiology of Duchenne muscular dystrophy: an updated systematic review and meta-analysis. Orphanet J Rare Dis. 2020;15:141. https://doi.org/10.1186/s13023-020-01430-8
2. Sussman M. Duchenne muscular dystrophy. J Am Acad Orthop Surg. 2002;10:138–51. https://doi.org/10.5435/00124635-200203000-00009
3. Sutherland DH, Olshen R, Cooper L, Wyatt M, Leach J, Mubarak S, et al. The pathomechanics of gait in Duchenne muscular dystrophy. Dev Med Child Neurol. 1981;23:3–22. https://doi.org/10.1111/j.1469-8749.1981.tb08442.x
4. Goemans N, Signorovitch J, McDonald C, Mercuri E, Niks E, Wong B, et al. Functional trajectories of upper limb and pulmonary function before and after loss of ambulation in Duchenne muscular dystrophy. Neuromuscul Disord. 2021;31:S47–162. https://doi.org/10.1016/j.nmd.2021.07.148
5. Rideau Y, Duport G, Delaubrier A, Guillou C, Renardel-Irani A, Bach J. Early treatment to preserve quality of locomotion for children with Duchenne muscular dystrophy. Semin Neurol. 1995;15:9–17. https://doi.org/10.1055/s-2008-1041001
6. Bakker JPJ, de Groot IJM, Beckerman H, de Jong BA, Lankhorst GJ. The effects of knee-ankle-foot orthoses in the treatment of Duchenne muscular dystrophy: review of the literature. Clin Rehabil. 2000;14:343–59. https://doi.org/10.1191/0269215500cr319oa
7. Khodadadeh S, McClelland MR, Patrick JH, Edwards RHT, Evans GA. Knee moments in Duchenne muscular dystrophy. Lancet. 1986;2:544–5.
8. de Souza MA, Figueiredo MML, de Baptista CRDJA, Aldaves RD, Mattiello-Sverzut AC. Beneficial effects of ankle-foot orthosis daytime use on the gait of Duchenne muscular dystrophy patients. Clin Biomech [Internet]. 2016;35:102–10. Available from: https://doi.org/10.1016/j.clinbiomech.2016.04.005
9. Eagle M. Report on the muscular dystrophy campaign workshop: exercise in neuromuscular diseases newcastle, January 2002. Neuromuscul Disord. 2002;12:975–83.
10. Markati T, Oskoui M, Farrar MA, Duong T, Goemans N, Servais L. Emerging therapies for Duchenne muscular dystrophy. Lancet Neurol [Internet]. 2022;21:814–29. Available from: https://doi.org/10.1016/S1474-4422(22)00125-9
11. Ricci G, Bello L, Torri F, Schirinzi E, Pegoraro E, Siciliano G. Therapeutic opportunities and clinical outcome measures in Duchenne muscular dystrophy. Neurol Sci [Internet]. 2022;43:625–33. Available from: https://doi.org/10.1007/s10072-022-06085-w
12. Goemans N, Van den Hauwe M, Signorovitch J, Swallow E, Song J. Colloborative trajectory analysis project (cTAP). Individualized prediction of changes in 6-minute walk distance for patients with Duchenne muscular dystrophy. PLoS ONE. 2016;11:e0164684. https://doi.org/10.1371/journal.pone.0164684
13. Doglio L, Pavan E, Pernigotti I, Petralia P, Frigo C, Minetti C. Early signs of gait deviation in Duchenne muscular dystrophy. Eur J Phys Rehabil Med [Internet]. 2011;47:587–94. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21912365
14. Romano A, Favetta M, Schirinzi T, Summa S, Minosse S, Catteruccia M et al. Evaluation of Gait in Duchenne Muscular Dystrophy: Relation of 3D Gait Analysis to Clinical Assessment. Neuromuscul Disord [Internet]. 2019;29:920–9. Available from: https://doi.org/10.1016/j.nmd.2019.10.007
15. Goudriaan M, Van den Hauwe M, Simon-Martinez C, Huenaerts C, Molenaers G, Goemans N et al. Gait deviations in Duchenne muscular dystrophy—Part 2. Statistical non-parametric mapping to analyze gait deviations in children with Duchenne muscular dystrophy. Gait Posture [Internet]. 2018;63:159–64. Available from: https://doi.org/10.1016/j.gaitpost.2018.04.038
16. Vandekerckhove I, Van den Hauwe M, Dewit T, Molenberghs G, Goemans N, De Waele L et al. Longitudinal trajectories of muscle impairments in growing boys with Duchenne muscular dystrophy. PLoS One [Internet]. 2025;20:e0307007. Available from: https://doi.org/10.1371/journal.pone.0307007
17. Vandekerckhove I, Van den Hauwe M, De Beukelaer N, Stoop E, Goudriaan M, Delporte M, et al. Longitudinal alterations in gait features in growing children with Duchenne muscular dystrophy. Front Hum Neurosci. 2022;16:861136. https://doi.org/10.3389/fnhum.2022.861136
18. Vandekerckhove I, Papageorgiou E, Hanssen B, De Beukelaer N, Van den Hauwe M, Goemans N, et al. Gait classification for growing children with Duchenne muscular dystrophy. Sci Rep. 2024;14:10828. https://doi.org/10.1038/s41598-024-61231-y
19. Gaudreault N, Gravel D, Nadeau S, Houde S, Gagnon D. Gait patterns comparison of children with Duchenne muscular dystrophy to those of control subjects considering the effect of gait velocity. Gait Posture. 2010;32:342–7. https://doi.org/10.1016/j.gaitpost.2010.06.003
20. Heberer K, Fowler E, Staudt L, Sienko S, Buckon CE, Bagley A et al. Hip kinetics during gait are clinically meaningful outcomes in young boys with Duchenne muscular dystrophy. Gait Posture [Internet]. 2016;48:159–64. Available from: https://doi.org/10.1016/j.gaitpost.2016.05.013
21. Goudriaan M, Van den Hauwe M, Dekeerle J, Verhelst L, Molenaers G, Goemans N et al. Gait deviations in Duchenne muscular dystrophy—Part 1. A systematic review. Gait Posture [Internet]. 2018;62:247–61. Available from: https://doi.org/10.1016/j.gaitpost.2018.03.020
22. Boccardi S, Gabardi C, Negrini A, Santambrogio GC. Locomotor and posture strategies in patients with Duchenne muscular dystrophy (DMD): part I. Gait analysis. EUR MED PHYS 1997;33:13-22.
23. D'Angelo MG, Berti M, Piccinini L, Romei M, Guglieri M, Bonato S, et al. Gait pattern in Duchenne muscular dystrophy. Gait Posture. 2009;29:36–41. https://doi.org/10.1016/j.gaitpost.2008.06.002
24. Goudriaan M, Nieuwenhuys A, Schless S, Goemans N, Molenaers G, Desloovere K. A new strength assessment to evaluate the association between muscle weakness and gait pathology in children with cerebral palsy. PLoS ONE. 2018;13:e0191097. https://doi.org/10.1371/journal.pone.0191097
25. Verreydt I, Vandekerckhove I, Stoop E, Peeters N, van Tittelboom V, Van de Walle P, et al. Instrumented strength assessment in typically developing children and children with a neural or neuromuscular disorder: A reliability, validity and responsiveness study. Front Physiol. 2022;13:855222. https://doi.org/10.3389/fphys.2022.855222
26. Vandekerckhove I, Hanssen B, Peeters N, Dewit T, De Beukelaer N, Van den Hauwe M et al. Anthropometric-related percentile curves for muscle size and strength of lower limb muscles of typically developing children. J Anat [Internet]. 2025;00:1–15. Available from: https://doi.org/10.1111/joa.14241

27. Mudge AJ, Bau KV, Purcell LN, Wu JC, Axt MW, Selber P, et al. Normative reference values for lower limb joint range, bone torsion, and alignment in children aged 4–16 years. J Pediatr Orthop Part B. 2014;23:15–25. https://doi.org/10.1097/BPB.0b013e328364220a
28. Hof AL. Scaling gait data to body size. Gait Posture. 1996;4:222–3.
29. Verbeke G, Molenberghs G. Linear mixed models for longitudinal data. Springer Series in Statistics, Springer-Verlag, New-York, 2000.
30. Molenberghs G, Verbeke G. Models for discrete longitudinal data. Springer Series in Statistics, Springer-Verlag, New-York, 2005.
31. Hinkle DE, Wiersma W, Jurs SG. Applied statistics for the behavioural sciences. Houghton Mifflin, Boston, MA,2003.
32. Desloovere K, Molenaers G, Feys H, Huenaerts C, Callewaert B, Van de Walle P. Do dynamic and static clinical measurements correlate with gait analysis parameters in children with cerebral palsy? Gait Posture. 2006;24:302–13. https://doi.org/10.1016/j.gaitpost.2005.10.008

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