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Protocol

Effects of home-based strength training with different intensities on muscle strength and physical functions in patients with Duchenne muscular dystrophy: Study protocol for an exploratory pilot randomized controlled trial

Wenzhu Li[a,*], Zhen Huang[a,*], Xueying Li[b], Ninghua Wang[a], Rongli Wang[a]

[a] Department of Rehabilitation Medicine, Peking University First Hospital, Beijing 100034, China
[b] Department of Biostatistics, Peking University First Hospital, Beijing 100034, China

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ABSTRACT

Background: Regular submaximal strengthening exercises are recommended for patients with Duchenne muscular dystrophy (DMD); however, evidence regarding the optimal intensity is limited.
Objective: To evaluate the effects of a 12-month home-based strength training program at different intensities on muscle strength and physical function in boys with DMD and inform the design of a future definitive randomized controlled trial (RCT).
Study design: Single-site, parallel-group, exploratory pilot RCT.
Methods: Sixty boys aged 5–10 years with DMD will be randomized in a 1:1:1 ratio to non-resistance, low-resistance, or moderate-resistance strength training groups. All groups will perform a standardized exercise regimen thrice weekly for 12 months at home, including warm-up, static stretching, and strengthening exercises. Training will be initiated through a face-to-face instructional session. Adherence and safety will be monitored using exercise logs and biweekly telephonic assessments. Primary and secondary outcomes will be assessed at baseline, 6 months, and 12 months by blinded outcome assessors.
Outcome measures: Primary outcome measures are muscle strength and the North Star Ambulatory Assessment. Secondary outcomes include the Motor Function Measure, timed function tests, range of motion, and Vignos and Brooke scales. The exploratory outcomes comprise feasibility (eligibility, recruitment rate, intervention adherence, and study completion rate), tolerability (nonadherence and withdrawal), and safety (adverse events, serum creatine kinase levels, and muscle pain).
Conclusions: This Chinese exploratory RCT will provide critical data on the preliminary effects and feasibility of home-based strength training at different intensities in DMD. These findings will guide sample size calculation and outcome selection for larger multicenter trials.

1. Introduction

Duchenne muscular dystrophy (DMD), an X-linked recessive disorder, has an estimated incidence ranging from 1 in 3800 to 1 in 6200 live male births.[1] DMD results from mutations in the dystrophin gene, leading to a complete or partial deficiency of the dystrophin protein. The lack or impaired function of dystrophin renders myofibers vulnerable to stretch-induced damage and necrosis.[2]

Clinically, DMD is characterized by delayed motor milestones, progressive muscle weakness, muscle contractures, loss of ambulation,

Abbreviations: 10RM, 10-repetition maximum; 6MWT, 6-minute walk test; AEs, Adverse events; ChiCTR, Chinese Clinical Trial Registry; CK, Creatine kinase; COVID-19, Coronavirus Disease 2019; CRF, Case report form; CTCAE, Common Terminology Criteria for Adverse Events; DMD, Duchenne muscular dystrophy; GCP, Good Clinical Practice; ID, identification number; ITT, Intention-to-treat; LVEF, Left ventricular ejection fraction; MFM, Motor Function Measure; NSAA, North Star Ambulatory Assessment; PROM, Passive range of motion; RCT, Randomized controlled trial; RM, Repetition maximum; SAEs, Serious adverse events; SPIRIT, Standard Protocol Items: Recommendations for Intervention Trials; VAS, visual analogue scale

* Correspondence to: Department of Rehabilitation Medicine, Peking University First Hospital, 8 Xishiku Street, Xicheng District, Beijing 100034, China.
E-mail addresses: bamboolna@pku.edu.cn (W. Li), huangzhen6313@163.com (Z. Huang), xyinglee@163.com (X. Li), wangninghua2003@163.com (N. Wang), wangrongli2004@163.com (R. Wang).

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respiratory involvement, and cardiomyopathy. The initial functional limitations usually occur by the age of 5 years, presenting as clumsiness, frequent falls, and difficulties with jumping, running, stair climbing, or rising from the floor. Due to the loss of ambulation, most patients require wheelchair use between the ages of 10 and 15 years.[3] An early loss of gait and functional dependence often accelerate the progression of comorbidities such as contractures, scoliosis, respiratory insufficiency, and heart failure.[4] Most individuals die prematurely due to progressive cardiopulmonary failure, typically in the second or third decade of life.[5]

The diagnosis of DMD is typically established between 3 and 5 years of age through genetic testing and/or muscle biopsy. Till date, no curative treatment has been established for DMD.[6] The current therapeutic strategies, including glucocorticoid therapy, physical therapy, and emerging genetic and molecular interventions, such as ataluren and eteplirsen, have the potential to alleviate symptoms, modify disease progression, manage complications, and ultimately improve the quality of life and extend survival. Despite these advances, glucocorticoids and rehabilitation management remain the cornerstone interventions in DMD care, playing a key role in delaying muscle weakness and loss of ambulation, thereby prolonging survival.[4,6,7]

To preserve muscle function and prevent disuse atrophy and inactivity-related complications, the international guidelines recommend that all individuals with DMD engage in regular submaximal strengthening exercises with appropriate assistance, particularly during the early disease stages when the residual strength is relatively high. Given the risk of contraction-induced muscle damage, high-resistance training, eccentric exercise, and overexertion are unsuitable throughout the lifespan of patients with DMD.[4,8] However, most of these recommendations are extrapolated from preclinical studies in animal models of dystrophinopathy, and there is limited evidence regarding the optimal strength training parameters for patients with DMD.[9–12] Therefore, there arises a critical and urgent question on how to design a safe and effective strength training program with the appropriate intensity and to optimize the exercise prescription in DMD.

The primary objective of this exploratory randomized controlled trial (RCT) is to evaluate the effects of a 12-month home-based strength training program at different intensities (non-resistance, low-resistance, and moderate-resistance) on muscle strength and physical function in boys with DMD. The secondary objective is to explore the optimal exercise intensity by comparing the three intervention groups. Additionally, we will assess feasibility outcomes, including eligibility and recruitment rates, adherence, acceptability, study completion, and safety. The preliminary data will inform sample size calculations and power analyses for a future definitive RCT.

2. Methods

2.1. Study design and setting

This study is designed as a single-site, parallel-group, exploratory pilot RCT, and an overview of the study design is provided in Fig. 1. Patients will be recruited from the neuromuscular disease outpatient clinic at the Peking University First Hospital, where eligible individuals will be identified, screened, and provided with detailed study information. After enrolment, the participants will be randomly assigned to one of the three intervention arms: non-resistance strength training, low-resistance strength training, or moderate-resistance strength training. All outpatient assessments and rehabilitation intervention guidance will be conducted at the Department of Rehabilitation Medicine, Peking University First Hospital. Rehabilitation interventions, comprising strength training and conventional physical therapy, will be implemented in participants' homes. Comprehensive assessments will be performed at three time points: baseline, midpoint (6 months), and trial completion (12 months). These assessments will include evaluations of the muscle strength, ranges of motion, 6-minute walk test (6MWT), timed function tests, and scales evaluating motor function.[4,13] The protocol has been developed in accordance with the Standard Protocol Items: Recommendations for Intervention Trials (SPIRIT) guidelines.[14] A detailed schedule of enrolment, interventions, and assessments is presented in Table 1. The trial was registered with the Chinese Clinical Trial Registry (ChiCTR) on August 10, 2019 (Registration number: ChiCTR1900025075).

2.2. Eligibility criteria

Patients meeting all the inclusion criteria and none of the exclusion criteria are eligible for the study.

The inclusion criteria are as follows:

(1) Boys aged 5–10 years.
(2) Ability to walk more than 10 m continuously without assistive devices.
(3) Diagnosis of DMD established by genetic testing and/or muscle biopsy.[15,16]
(4) Receiving stable corticosteroid treatment (i.e., no change in type or dosage) for at least 6 months prior to enrolment.[7] The specific glucocorticoid type and dosage will be documented.
(5) No prior participation in a regular, structured strength training program.
(6) Willingness of the child and parents/guardians to provide written informed consent and adhere to the study protocol.

The exclusion criteria are as follows:

(1) Surgery within the preceding 90 days.
(2) Presence of other medical conditions that significantly impair mobility.
(3) Symptomatic cardiomyopathy or left ventricular ejection fraction (LVEF) $<$ 55% on echocardiogram.[17,18]
(4) Cognitive or attentional deficits that would preclude understanding and cooperation in assessments or training.
(5) Inability or unwillingness to comply with the study procedures.
(6) Concurrent participation in another interventional clinical trial.

2.3. Participants and recruitment

The participants will be recruited from the neuromuscular disease outpatient clinic at Peking University First Hospital. The eligible patients and their parents/guardians will be provided with detailed study information by a rehabilitation physician. Written informed consent will be obtained from parents or guardians, and assent from children aged $\geq$ 8 years, before any study-specific procedures are performed. The principal investigator will document the reasons for ineligibility or refusal to participate.

2.4. Sample size

Consistent with the recommendations for exploratory pilot studies,[19] the sample size for this trial is based on the feasibility and practical considerations rather than a formal power calculation. According to our experience, approximately 200–400 patients with DMD attend the neuromuscular disease outpatient clinic at Peking University First Hospital annually. We anticipate that approximately 50% of the patients will meet the eligibility criteria. To account for a potential dropout rate of 10%, we aim to recruit 60 participants (20 per group) over an extended period. The recruitment period has been extended with funder approval owing to Coronavirus Disease 2019 (COVID-19)-related disruptions.

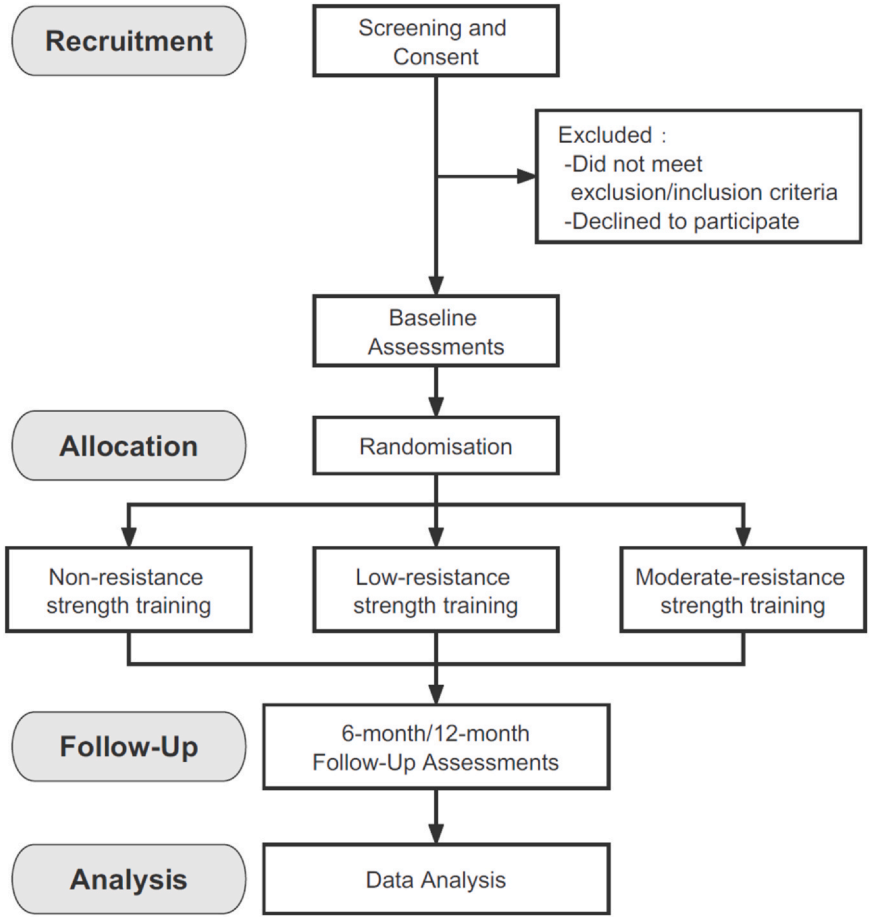

Fig. 1. Flow diagram of the study procedure.

Table 1
SPIRIT schedule of enrolment, interventions, and assessments.

	Enrolment	Allocation	Post-allocation	
Timepoint	***-t1***	***t0***	***t1 = 6 months***	***t2 = 12 months***
Enrolment:				
Eligibility screening	x			
Informed consent	x			
Allocation		x		
Interventions:				
Non-resistance strength training		x	x	x
Low-resistance strength training		x	x	x
Moderate-resistance strength training		x	x	x
Assessments:				
Isometric muscle strength		x	x	x
Ranges of motion		x	x	x
6-minute walk test		x	x	x
Time to walk/run 10 m		x	x	x
Time to ascend and descend four stairs		x	x	x
Time to stand from supine on the floor		x	x	x
North Star Ambulatory Assessment		x	x	x
Motor Function Measure		x	x	x
Vignos scale		x	x	x
Brooke scale		x	x	x

2.5. Randomization and blinding

Following the baseline assessments, the enrolled participants will be randomized in a 1:1:1 ratio to one of the three intervention groups. An independent statistician will generate a blocked randomization list using SAS V.9.4 with a fixed block size of 6. To ensure allocation concealment, an independent researcher not involved in recruitment, intervention, or assessment will prepare sequentially numbered, sealed, opaque envelopes containing group assignments. The researcher will assign the next available envelope upon participant enrolment. Allocation concealment will be maintained throughout the study. To prevent unblinding, outcome assessors will have no access to group assignment information, and participants will be instructed not to disclose their group allocation during assessments. Physiotherapists

delivering the intervention will be informed of the allocation; however, the outcome assessors will remain blinded to the group assignment throughout the study. The participants will not be completely blinded to the group assignment because it is apparent that a non-resistant or resistant group will be revealed once strength training starts.

2.6. Interventions

After randomization, the participants, together with their parents or guardians will receive a face-to-face standardized operating session delivered by an experienced physiotherapist. This session will provide comprehensive instructions for safely and correctly performing the prescribed 12-month home-based exercise program. During the session, they will receive structured training, including demonstration and return-demonstration of all exercises, and must demonstrate correct performance before starting the home program. The participants will receive a detailed intervention booklet, instructional videos, and necessary equipment (e.g., sandbags of specific weights). The program consists of three weekly sessions, each including warm-up, stretching, strength training, and cool-down sessions.

Each session will be initiated with a 15-minute warm-up on a stationary bicycle without resistance in a sitting position.[20] For participants with limited ankle dorsiflexion who are unable to maintain stable foot placement on the pedals, adjustable pedal straps or custom-fitted ankle-foot orthoses will be used to ensure secure foot positioning and optimize biomechanical alignment during cycling. Subsequently, a 10-minute passive stretching routine will target the major muscle groups prone to contracture: the gastrocnemius-soleus, hamstrings, and iliopsoas.[4] Each stretch will be held for 30 s and repeated thrice. Subsequently, the strength-training component will consist of four exercises: shoulder abduction, elbow flexion, hip flexion, and knee extension. These muscle groups were selected based on their functional relevance to daily activities (e.g., upper limb function for shoulder and elbow, and weight-bearing and ambulation for hip and knee), their well-documented susceptibility to disease progression in DMD, and their feasibility for home-based resistance training using sandbags. The exercises will be performed in a consistent order. During the first month, the participants will perform 1–2 sets of 10 repetitions per exercise. From the second month onwards, this will progress to three sets of 10 repetitions for each exercise, with a 2-minute rest between sets. Each session will end with a 10-minute cool-down of passive stretching.[21]

For the non-resistance group, strength training will consist of gravity-resisted limb movements only; for the low- and moderate-resistance groups, the training will incorporate sandbag loads equivalent to 30% and 60% of each participant's individually determined 10-repetition maximum (10RM), respectively.[21–23] It is important to clarify that the non-resistance group is not a true sedentary control, but rather an active comparator; the participants in this group will receive the same structured program using body weight resistance, enabling us to isolate the specific effect of added external load. The 10RM for each exercise will be assessed at baseline and 6 months by a certified physiotherapist using a standardized protocol to ensure reproducibility and safety. Following a brief warm-up of five submaximal repetitions, an initial submaximal load will be selected based on the participant's age and functional status. The load used and the number of repetitions successfully completed will be recorded and entered into a Brzycki prediction equation to estimate the 10RM.[24] A maximum of three attempts will be permitted, with a 2-minute rest interval between attempts, to prevent excessive fatigue. Throughout the testing, the physiotherapist will closely monitor for signs of overexertion such as compensatory movements or fatigue, and terminate the test immediately if any safety concerns arise. The details of the exercise training session and various weights of resistance-to-strength training are presented in Table 2.

To ensure intervention fidelity, the participants and caregivers will be asked to submit video recordings of exercise sessions monthly via WeChat or email; a physiotherapist will review these to verify technique and provide feedback within one week. Adherence will be monitored using exercise logs, and the percentage of correctly performed repetitions (based on video review) will be recorded as an objective fidelity metric. Throughout the 12-month program, research staff will conduct biweekly telephone calls using standardized questions to identify difficulties, reinforce proper technique, and provide support. The participants and their parents or guardians will also complete exercise diaries documenting start and finish times, completion status, and reasons for any deviations from the prescribed regimen.

2.7. Data collection, management, and monitoring

Data will be collected at baseline (within 2 weeks prior to randomization), 6 months (± 2 weeks), and 12 months (± 2 weeks) by trained and blinded assessors. The baseline data will include sociodemographic data (age, residential area, education level, and medical history) and anthropometric information (height, weight, and body mass index). All the participants will be assigned study-specific participant identification number (ID) numbers to ensure confidentiality. All data will be recorded on paper Case Report Forms (CRFs), identified only by a unique participant ID, and stored securely. These CRFs will be periodically scanned, and the data will be double-entered. This study will undergo monitoring and auditing in accordance with the policies of the Academic Research Office of Peking University First Hospital. All the collected data will be stored on a password-protected computer and backed up to an encrypted external hard drive, with the access restricted exclusively to authorized members of the research team.

2.8. Statistical analysis

Statistical analyses will be conducted using SPSS (version 26.0; IBM) for Windows. As this is an exploratory study, the primary focus will be on descriptive statistics and parameter estimation to inform future definitive trials rather than hypothesis testing. Dropout is defined as missing two consecutive scheduled follow-up assessments without formal study withdrawal or discontinuing the prescribed training intervention for more than 8 consecutive weeks without a medically approved reason. The participants meeting either criterion will be considered dropouts, and efforts will be made to contact them and document the reasons for their withdrawal. All analyses will follow the intention-to-treat (ITT) principle and the participants will be analyzed according to their original randomization. Missing data will be handled using multiple imputations where appropriate, and the patterns and reasons for missing data will be systematically reported.

For the feasibility outcomes, descriptive statistics, including counts, percentages, and rates with 95% confidence intervals will be presented. Regarding the clinical outcomes, the changes from baseline to 6 and 12 months will be calculated for continuous measures, such as muscle strength and 6MWT distance. To explore the group differences over time, mixed-effects models for repeated measures will be employed, which are particularly suitable because they account for within-subject correlations across time points and accommodate missing data. These models will include fixed effects for time (categorical), group, and time-by-group interaction, with adjustment for baseline value of the outcome measure and pre-specified covariates: age at enrolment, glucocorticoid therapy duration, and baseline muscle strength. Subject-specific random intercepts will account for within-subject correlation. The primary focus will be on the group-by-time interaction effect to assess differences in trajectory among the three groups. Between-group differences in change from baseline at each time point will be presented with 95% confidence intervals. For categorical outcomes such as changes in the Vignos or Brooke scale scores, chi-square or Fisher's exact tests will be applied. A two-tailed P-value < 0.05 will indicate statistical significance. Given the pilot nature of this trial, no adjustment for multiple comparisons will be made, all results will be

Table 2
Details of the exercise training session.

Exercise	Muscle groups	Intervention groups		
		Non-resistance	Low-resistance	Moderate-resistance
Bicycling	Lower limbs		15 min, non-resistance	
Stretching	Upper and lower limbs		10 min, moderate range of movement	
Strength training	Shoulder abduction	3 sets/10 repetitions/body weight	3 sets/10 repetitions/30% 10RM	3 sets/10 repetitions/60% 10RM
	Elbow flexion	3 sets/10 repetitions/body weight	3 sets/10 repetitions/30% 10RM	3 sets/10 repetitions/60% 10RM
	Hip flexion	3 sets/10 repetitions/body weight	3 sets/10 repetitions/30% 10RM	3 sets/10 repetitions/60% 10RM
	Knee extension	3 sets/10 repetitions/body weight	3 sets/10 repetitions/30% 10RM	3 sets/10 repetitions/60% 10RM
Stretching	Upper and lower limbs	10 min, moderate range of movement		

Abbreviation: RM, Repetition maximum.

interpreted with caution. Emphasis will be placed on the effect sizes and confidence intervals to guide the sample size calculations for future studies.

2.9. Patient and public involvement

Patients and the general public were not involved in the design of this study. A summary of the results will be provided to all the participating families upon completion of the study.

2.10. Ethics and dissemination

This study was approved by the Research Ethics Committee of Peking University First Hospital (Study ID: 2019–159; approval date: August 7, 2019). This study will be conducted in accordance with the international standards of Good Clinical Practice (GCP) and the ethical principles of the Declaration of Helsinki (2013 revision). Written informed consent will be obtained from the parents/guardians, assent will be obtained from children aged ≥ 8 years, who can withdraw at any time. Contact details will be provided to the parents or guardians for queries. The results will be disseminated through peer-reviewed publications and conference presentations.

3. Results

As this is an exploratory study, a priori outcome definition and accurate outcome assessment are needed to assess whether they can be collected for a full-scale RCT. Experienced physicians and physiotherapists will complete the following assessments in chronological order.

3.1. Primary clinical outcomes

3.1.1. Muscle strength

The maximum isometric muscle strength of the shoulder abductors, elbow flexors/extensors, hip flexors/extensors, and knee flexors/extensors will be measured bilaterally using a microFET3 handheld dynamometer (Hogan Health Industries, Salt Lake City, Utah, USA). For each muscle group, participants will perform three maximal voluntary contractions, holding each contraction against the dynamometer for 5 s. A 30-second rest period will be provided between trials, and the highest value of the three attempts will be recorded for analysis.[25]

3.1.2. North Star Ambulatory Assessment (NSAA)

The NSAA is a well-validated scale commonly used to assess the motor function in ambulatory boys with DMD. Recently, a revised version has been proposed for use in boys as young as 3 years of age.[26]

3.2. Secondary clinical outcomes

3.2.1. Ranges of motion

The passive range of motion (PROM) will be measured with a universal goniometer in standardized positions at the elbow (extension), hip (extension), knee (extension), and ankle (dorsiflexion).[27]

3.2.2. 6-minute walk test (6MWT)

The 6MWT has been established as a feasible, safe, and reproducible measure for assessing the functional capacity in ambulatory boys with DMD. In accordance with the ATS guidelines, the test will be conducted in a measured corridor. Under the supervision of trained study staff, the participants will be instructed to walk as quickly as possible and cover the greatest distance they can within 6 min.[28]

3.2.3. Timed function tests

The functional ability will also be assessed through a series of timed function tests, including the time taken to walk or run 10 m, ascend and descend four steps of stairs, and rise from a supine position on the floor. These tests are recognized as valid and reliable clinical tools for monitoring the changes in motor function in ambulant patients with DMD.[29] Each task will be performed up to three times barefoot, and the fastest time will be recorded.

3.2.4. Motor Function Measure (MFM)

The quantitative MFM scale is designed to assess the whole-body motor function and track disease progression in patients with neuromuscular disease.[30] The MFM was originally validated for patients aged 6–60 years, and its Chinese version has demonstrated strong reliability and validity in children with DMD aged ≥ 5 years.[31] This MFM scale comprises 32 items scored on a 4-point scale from 0 (cannot initiate the exercise) to 3 (completes the item with a standard pattern), covering three dimensions of motor performance: the standing and transfer function (D1 domain; 13 items), axial and proximal motor function (D2 domain; 12 items), and distal motor function (D3 domain; 7 items). For this study, the validated Chinese version of the MFM will be used.[31]

3.2.5. Vignos and brooke scale

Upper and lower extremity function will be graded using the Brooke and Vignos scales, respectively. These ordinal scales are widely used for patients with neuromuscular diseases. The Vignos scale grades the lower-limb function ranging from 1 to 10 points, whereas the Brooke scale grades the upper-limb function ranging from 1 to 6 points.[31]

3.3. Exploratory Outcomes

3.3.1. Eligibility rate

The eligibility rate refers to the proportion of screened patients who meet the eligibility criteria.

3.3.2. Recruitment rate

The recruitment rate refers to the proportion of eligible patients who provide informed consent.

3.3.3. Intervention adherence

The intervention adherence refers to the proportion of prescribed training sessions completed over a 12-month period. A session is considered fully completed if all prescribed components are performed as intended. Adherence will be assessed using three complementary methods: (1) daily exercise logs completed by caregivers, documenting session details, completion status, and reasons for any deviations; (2) monthly video submissions of at least one full training session, reviewed by a physiotherapist to verify technique and confirm fidelity to the prescribed protocol; and (3) biweekly telephone interviews incorporating a structured adherence check. The overall adherence rate for each participant will be calculated as: (number of fully completed sessions/total prescribed sessions) $\times$ 100%. Good adherence is predefined as completing $\geq$ 80% of prescribed sessions. For participants who discontinue the intervention but remain in the study, adherence will be calculated as zero for the period following discontinuation. Reasons for non-adherence (e.g., illness, fatigue, time constraints) will be systematically recorded and categorized.

3.3.4. Study completion rate

The study completion rate refers to the proportion of enrolled participants who complete the 12-month follow-up assessment.

3.3.5. Tolerability and acceptability

The tolerability will be quantitatively assessed by the proportion of participants who require temporary suspension or modification of training due to adverse events (e.g., muscle pain, CK elevation), and the rate of withdrawal from the intervention that is potentially related to the study procedures. Acceptability will be evaluated through feedback from patients/parents or guardians during phone calls, and perceived burden of the program (completion time, equipment, et al.).

3.3.6. Safety

Safety involves the occurrence of any adverse events (AEs) related to the intervention or study procedure. These events will be documented in accordance with the GCP guidelines and will be graded for severity using the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. The study physician will assess each event for its relationship to the intervention. All serious adverse events (SAEs), defined as those resulting in death, life-threatening conditions, hospitalization, or significant disability, will be reported to the Research Ethics Committee within 24 h. Based on this assessment, the study physician will determine whether the intervention should be permanently discontinued or may be resumed after resolution.

To ensure participant safety, the serum creatine kinase (CK) levels and subjective muscle pain using numerical ratings on a visual analogue scale will be monitored every month. The parents will be instructed to document any unusual pain or fatigue in the provided exercise logs and to report these symptoms immediately during the bi-monthly phone calls. The predefined criteria for training modification or temporary suspension include: (1) evidence of muscle damage, defined as either an elevation in serum CK levels of $\geq$ 7000 U/L from baseline or an increase in the pain score of $\geq$ 4 points on the visual analogue scale (VAS); (2) a fall or injury directly associated with the training session.[32] In any such instance, the intervention will be halted, and the study physician will evaluate the situation. Any decision to adjust the intensity, temporarily pause, or permanently discontinue the intervention will be made on a case-by-case basis, with participant safety being the foremost priority. If training is temporarily suspended due to the above criteria, resumption will be permitted only after the participant's CK levels have returned to within 30% of baseline, the VAS pain score has been $\leq$ 2 for at least one week, and the study physician has provided approval. Upon resumption, the training will begin at 50% of the previous load and gradually progress to the full regimen under close monitoring.

To enhance safety and adherence in home settings, regular phone calls will be made for support and guidance, and participants will be encouraged to use instructional videos to maintain proper exercise techniques. The research team will also monitor the adherence to and safety of the home-based training program by collecting video recordings from the caregivers via WeChat or email.

4. Discussion

To the best of our knowledge, this is the first exploratory RCT in China to prospectively investigate the impact of a structured, home-based strength training program of varying intensities in children with DMD. The training intensities in this study (non-resistance, low-resistance, and moderate-resistance) were established based on the rehabilitation principles derived from the latest multidisciplinary management guidelines for DMD, which recommend submaximal strengthening.[4] Despite these recommendations, the evidence regarding the optimal level and intensity of strength training for children with DMD remains insufficient.[11]

This study directly addresses this critical gap in current evidence. We hypothesize that over a 12-month period, both low- and moderate-resistance training will be safe and feasible, and will result in better preservation of muscle strength and motor function compared to gravity-resisted (non-resistance) training. If the moderate-resistance (60% 10RM) group is found to be superior without raising safety concerns, this will provide a strong evidence-based foundation for future clinical recommendations. Conversely, if no significant difference is found, or if safety issues are identified, the results would suggest that lower-intensity regimens may be sufficient and would highlight the potential risks associated with higher-intensity overtraining. We anticipate that this exploratory study will demonstrate acceptable feasibility and will pave the way for the development of evidence-based exercise prescriptions with optimal strength training intensities for patients with DMD in China. Furthermore, the effect sizes derived from the exploratory clinical outcomes will be instrumental in powering sample size calculations for future definitive trials.

Direct evidence for the safety and efficacy of specific resistance training intensities in DMD is limited, necessitating that our protocol design draws upon findings from other better-studied neuromuscular diseases with shared pathophysiological features such as Pompe disease, limb-girdle muscular dystrophy, and facioscapulohumeral muscular dystrophy.[21–23] In these populations, moderate-intensity resistance training, defined as 50%-70% of 10RM, has been consistently demonstrated to be both safe and beneficial.[21,23] Furthermore, van den Berg et al.[33] demonstrated that a 12-week program of standardized aerobic and resistance exercise at 70% of 4RM was safe and successfully completed by 92% (23/25) of participants with Pompe disease.

This study has several methodological strengths. Home-based design enhances the ecological validity and improves participant accessibility. By individualizing resistance according to each participant's 10RM and implementing rigorous safety monitoring, the protocol balances the therapeutic benefits with participant well-being. Furthermore, the selection of outcome measures in this study comprises a robust, clinically relevant battery sensitive to changes in DMD.[34] Dynamometer-quantified muscle strength has proven feasible and sensitive to variable rates of disease progression in both the upper and lower extremity muscle groups in DMD.[35] The 6MWT, NSAA, MFM, and timed function tests demonstrate high validity and reliability, with established correlations across time points, minimum clinically important differences, and a predictive capacity for functional motor changes.[34,36,37]

Recruitment is anticipated to be challenging. Based on our previous clinical experience, we estimated that approximately 60 patients could be recruited over a 6-month period. Recruitment for this exploratory

study was initiated in August 2019. However, the COVID-19 pandemic in Beijing led to a substantial decline in outpatient clinic visits among patients with DMD, significantly impacting trial enrolment. Although clinical services have gradually recovered, recruitment resumption has been slower than anticipated. With approval from the funder, the recruitment period was extended to achieve the target sample size of 60 participants. Recruitment for this trial was completed as of March 2026, with a total of 60 participants enrolled. The 12-month follow-up assessments are currently ongoing and will be finalized by December 2026.

5. Limitations

This study has several limitations. First, as an exploratory trial, the sample size of each training group is small, which may limit the statistical power and precision of the effect size estimates. However, given the rarity of DMD, a sample size of 20 participants per group is appropriate for this initial exploratory study. Second, the non-resistance group is not a true non-exercising control group, which means we cannot assess the absolute effect of exercise versus no exercise. This was a deliberate choice, as withholding all exercises was considered unethical, given the current guidelines. Finally, the supervision and implementation of home-based training largely depend on parents, whereas pragmatic training may introduce variability in the fidelity of intervention delivery.

6. Conclusions

This exploratory pilot RCT will evaluate the feasibility, tolerability, safety, and preliminary effects of a home-based strength-training program delivered at three distinct intensities among ambulatory boys with DMD. By systematically investigating a key parameter of exercise prescription, this study will generate critical data to inform the design and sample size estimation of a future definitive multicenter RCT. Ultimately, this study aims to establish a rigorous, generalizable evidence base to guide safe and effective strength-training recommendations, contributing to optimized, personalized rehabilitation strategies for individuals with DMD.

CRediT authorship contribution statement

Zhen Huang: Writing – review & editing, Supervision, Investigation, Conceptualization,Methodology. **Wenzhu Li:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization. **Rongli Wang:** Writing – review & editing, Conceptualization. **Ninghua Wang:** Writing – review & editing, Conceptualization. **Xueying Li:** Writing – review & editing, Software, Methodology, Conceptualization. All the authors have read and approved the final version of this manuscript.

Ethics approval

This study was approved by the Research Ethics Committee of Peking University First Hospital (Study ID: 2019–159). This study will be conducted in accordance with the international standards of Good Clinical Practice (GCP) and the ethical principles of the Declaration of Helsinki (2013 revision). Written informed consent will be obtained from the parents/guardians, assent will be obtained from children aged ≥ 8 years, who can withdraw at any time. Contact details will be provided to the parents or guardians for queries. The results will be disseminated through peer-reviewed publications and conference presentations.

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Data availability

The de-identified datasets generated and analyzed during this study will be available from the corresponding author upon reasonable request, subject to approval by the institutional ethics committee and compliance with data protection regulations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Declaration of Generative AI and AI-assisted technologies in the writing process

The authors declare that they did not use any generative AI or AI-assisted technologies in the conceptualization, design, or drafting of the manuscript. The authors take full responsibility for the integrity and originality of the work presented.

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