

Research paper

Nemaline myopathy patient and caregiver perspectives: a multinational cross-sectional study

Stacy A. Cossette^a, Sanne A.J.H. van de Camp^b, Lucinda M. Lee^a, Matthias R. Lambert^c,
Laurent Servais^{d,e}, Nicol C Voermans^{a,b,*}

^a A Foundation Building Strength for Nemaline Myopathy 3825 El Camino Real Palo Alto, CA, 94306, USA

^b Department of Neurology, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Geert Grooteplein Zuid 10, Nijmegen, 6525, GA, the Netherlands

^c Independent researcher Boston, MA 02210, USA

^d Oxford Neuromuscular Centre, & NIHR, University of Oxford, UK

^e Neuromuscular Reference Center, Department of Pediatrics, University Hospital Liege & University of Liege, Belgium

ARTICLE INFO

Keywords:

Nemaline myopathy
Congenital myopathy
Patient perspectives
Cross-sectional international survey
Treatment outcome priorities

ABSTRACT

Nemaline myopathy (NM) is among the most common of the congenital myopathies, characterized by hypotonia and muscle weakness. Despite its prevalence and morbidity, NM remains underrepresented in studies of lived experience and the impact on patients and caregivers. To expand upon the current knowledge, we conducted an international cross-sectional survey to systematically characterize patient and caregiver perspectives, including daily challenges, medical complications across age groups, and priorities for future treatment development. All respondents reported facing daily challenges, regardless of disease severity. The most frequently cited challenges related to NM included mobility, fatigue, respiratory, and mental health. Our results indicated that children more frequently were reported as having severe phenotypes, and adults often present with milder forms, likely due to survival bias. While 7% of participants reported congenital-onset cardiac complications, 16% reported cardiac complications developing during childhood or adulthood. This study provides the first comprehensive assessment of NM patient and caregiver perspectives across age groups, severity levels, and 33 countries. By uncovering previously unreported insights, these findings establish a more complete understanding of NM that strengthens the patient-centered translational impact for future study and therapeutic development.

1. Introduction

Nemaline myopathy (NM) is one of the most common congenital myopathies and is broadly characterized by hypotonia and muscle weakness [1–3]. Weakness is often most pronounced in the axial and proximal muscles, leading to difficulties with feeding, speech, respiration, and mobility, along with bone malformations [1,4–8]. Diagnosis may be established through histopathologic detection of nemaline rods on muscle biopsy, but genetic testing has become the gold standard and is more often being used in the prenatal and neonatal periods [9]. To date, pathogenic variants in at least 12 genes have been identified as causative of NM [10]. Among these genes, *NEB*, which encodes nebulin, and *ACTA1*, which encodes skeletal α -actin, are the most commonly implicated [9,11–14]. Histopathologically, NM is defined by the presence of nemaline rods within muscle fibers, most readily identified by

electron microscopy and Modified Gomori Trichrome stain [1,9,15]. Rod burden varies across fibers and muscles and does not correlate with disease severity or prognosis, suggesting that rods represent a secondary manifestation of the disease process rather than a direct cause of muscle dysfunction [1,6,11,16].

NM is non-dystrophic and generally stable, with modest improvements in strength or function possible through physical therapy; although fluctuations in strength and function may occur due to changes in body size, physical activity, aging, comorbidities, and other factors [6, 7]. Patients with *ACTA1*, *NEB*, and *TPM3* subtypes are more likely to experience worsening respiratory function as adolescents or adults [4, 17]. Ventilatory failure is a common and often disproportionate complication resulting from diaphragmatic weakness and is the leading cause of morbidity and early mortality across all levels of NM severity [2,4,7,11,18–20]. Cardiac involvement is uncommon and usually a

* Corresponding author.

E-mail address: Nicol.Voermans@radboudumc.nl (N.C. Voermans).

<https://doi.org/10.1016/j.nmd.2026.107427>

Received 11 July 2026; Received in revised form 15 September 2026; Accepted 15 September 2026

Available online 16 September 2026

0960-8966/© 2026 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

sequela of untreated ventilatory failure [17]. Clinically, NM exhibits wide phenotypic variability, ranging from mild muscle weakness with preserved motor function to severe forms marked by akinesia and no ability to feed or breathe [1,6,19,20]. The degree of impairment can vary significantly within the same gene subtype, and even within the same genotype or extended family [11,21].

There is currently no curative treatment for NM; however, preclinical research is ongoing, and continued translation of these approaches may lead to future clinical trials [6,22–24]. Therefore, management of NM remains supportive, primarily addressing respiratory insufficiency, musculoskeletal weakness, feeding and swallowing impairment, GI dysfunction, orthopedic malformations, and communication difficulties [4]. Despite the condition's prevalence and substantial morbidity, the lived experience of NM from the perspectives of affected individuals and family caregivers has not been systematically studied. Understanding the patient's perspective is essential, as it provides insight into the aspects of the disease that have the greatest impact on daily life and therefore should be prioritized in current clinical care and future therapeutic development. Patient-reported experiences highlight the substantial, lifelong burden of the disease, extending beyond muscle weakness to encompass limitations in physical functioning, participation, independence, and psychosocial well-being. The present study addresses this unmet need by documenting patient and caregiver experiences and perspectives to optimize patient-centered care, guide supportive resource development, inform clinical trial design, and define the priorities most meaningful to the NM community. This is expected to help align future clinical care, advocacy efforts, and research initiatives with the priorities identified by the NM community.

2. Methods

2.1. Study team

The study team comprised academic researchers, advisory board members from A Foundation Building Strength for Nemaline Myopathy (AFBS), patient experts, and clinical researchers from Radboud University Medical Center (Radboudumc) and the University of Oxford.

The NM Perspectives and Priorities Survey was developed by our team members at AFBS using a professional version of a survey drafting and implementation platform called SurveyMonkey. The AFBS Scientific Advisory Board (SAB), a volunteer group consisting of scientists, clinicians, patients, and family caregivers, was invited to provide feedback on the draft survey. The draft then underwent review by the AFBS Community Engagement Committee, a volunteer group tasked with ensuring community relevance. Subsequently, the AFBS Community Advisory Board (CAB), comprising seven members representing a diverse range of severity levels of nemaline myopathy, patient and caregiver perspectives, genders, and national backgrounds, completed a pilot test of the survey. Feedback from the CAB informed refinements to question wording and response options, thereby improving survey accessibility and validity.

2.2. Survey purpose and design

The study was conducted as an English-language survey led by AFBS. The survey was conceived and designed in 2025 with the purpose of documenting patient and caregiver experiences and perspectives to optimize patient-centered care, guide supportive resource development, inform clinical trial design, and define the priorities most meaningful to the NM community. This project was launched by AFBS operating under internal organizational ethical guidelines for non-clinical research, which did not require formal institutional review board approval. To ensure the ethical treatment of all human subjects, protocols were designed to maintain participant anonymity and data privacy throughout the analysis.

The first page of the survey introduced the survey sponsor, purpose,

and provided directions for completing the survey. It was also explained that if there are two or more in that family with NM, the survey-taker may complete the survey separately for each person to provide the individual's experience and medical history. The first survey question (Q1) collected respondents' role and age range and also functioned as a screening item. One response option allowed individuals to indicate that neither they nor their relatives were affected by NM. Respondents selecting this option were not eligible to continue and were automatically redirected to the Foundation's website.

Page two of the survey began with a statement that informed respondents that the questionnaire was intended for NM patients and family caregivers and should be completed by someone 18 years of age or older. It then provided a brief statement regarding data privacy, expected completion time, and the number of questions. The AFBS Community Engagement Committee recommended breaking the survey into multiple pages instead of presenting one long list of questions, believing that showing smaller sets at a time would feel more comfortable to respondents. Accordingly, three additional page breaks were inserted, dividing the remaining question items into distinct sections.

The survey permitted multiple submissions from a single IP address, an option configurable within the survey platform. This feature was intentionally enabled given the occurrence of multiple affected individuals within some NM families.

Randomization was applied to the multiple-choice questions for which it was appropriate, helping to prevent order-related bias.

Some questions were presented as matrix items, which support weighted answer options. By assigning a numerical value to each response choice, the survey platform could convert qualitative selections into quantifiable data, making it possible to compute overall scores or weighted averages.

The survey, including the instructions provided to participants, is available in the Supplementary Materials Appendix.

2.3. Recruitment and implementation

Affected individuals with a clinical or genetic diagnosis of nemaline myopathy and family caregivers of patients living with the disorder anywhere in the world were eligible to take the survey. The survey was promoted through the Congenital Muscle Disease International Registry (CMDIR), the Dutch patient organization for muscle diseases (Spierziekten Nederland), the AFBS patient and family contact list, and NM-focused social media pages to invite patients and families to participate. The survey was open to respondents from April through October of 2025. Participants were directed to click a link to be brought to the online survey.

2.4. Data analysis

Data were analyzed using IBM SPSS Statistics software (version 28.0.0.0), developed by SPSS, Inc., Chicago, IL and SurveyMonkey, San Mateo, California, USA. For each analysis done, all subjects with available information were included. Descriptive statistics were predominantly used to analyze the patient's characteristics and perspectives. The group was divided based on age, <18 years old and ≥18 years old, ambulatory status (currently walks independently without support, never has walked independently at age-appropriate times, currently walks only short distances, such as within the house, currently walks long distances but may need mobility assistance sometimes, currently is too young to walk, used to walk but no longer does), self-reported severity, and gene subtype. The groups were compared using Chi Squared tests. Fig.s were made using R software.

The single open-ended question included in the survey, Q24 ("What aspects of your NM condition are poorly managed by your medical professionals?"), was analyzed separately using NVivo qualitative data analysis software. Responses (n = 156) were analyzed using an inductive thematic analysis approach following Virginia Braun and Victoria

Clarke's [25] method to identify, analyze, and interpret patterns within the data, which were then collated into overarching themes. Two respondents answered with non-words, so their responses could not be analyzed. Given the brevity of survey responses for Q24, the approach was adapted for this data. Themes were developed at a semantic level, focusing on patterns in respondents' explicit accounts. A full list of defined themes is provided in the supplemental materials.

Data cleaning occurred as needed, such as editing a response where the text that was typed into a comment box clearly corresponded to an existing multiple-choice option. Where appropriate and feasible, the study team contacted participants about their answers. Issues related to ascertainment bias were discussed among team members to mitigate any such effects.

3. Results

3.1. Study cohort

A total of 299 individuals initiated the survey. One hundred respondents exited the survey after the first question, which assessed age range, respondent role, and confirmation of nemaline myopathy within the family; therefore, no additional data were collected from these 100 cases. Responses were further excluded if respondents reported no affected family members with nemaline myopathy, living or deceased, including the respondent, or if an alternative (non-nemaline myopathy) genetic diagnosis was reported. Duplicate submissions from individuals reporting a single affected family member were also identified, and those respondents were notified by email that only their initial submission was retained for analysis. Original entries were preserved in a separate dataset for record-keeping purposes.

A total of 33 countries are represented in the dataset which were organized into geographic regions using standard international conventions Supplemental table 1. A large portion of the group (45%) were from the United States of America.

Respondents included affected adults and adolescents, as well as family caregivers of children or adults with nemaline myopathy. Eighty-five affected individuals were <18 years old, 86 were ≥18 years old, and 8 were no longer living, with the age at the time of death unknown. Patients with any genetic mutation resulting in a diagnosis of NM were invited to participate. The genes reported by respondents are depicted in Supplemental table 1.

Fifty percent of respondents reported a mild presentation (Fig. 1). A statistically significant difference was found between children and affected adults, with children being more severely affected and adults more mildly affected. No differences were found in reported severity for

the various genetic mutations.

3.2. Symptoms and challenges

When asked about their challenges, all respondents (100%) reported at least one or more challenges caused by NM. Participants most often reported being challenged in the areas 'mobility limitations related to NM', 'fatigue', and 'breathing limitations related to NM' (Fig. 2). In our cohort, 50% reported being challenged by mental health issues, but we found no statistically significant differences between ages, severity levels, and ambulation status. Challenges such as 'undependable nursing-level care at home', 'feeding limitations', 'speech limitations', and 'having time just to myself' were more frequently mentioned in relation to affected children. Among affected adults, the most frequently reported challenges were 'fatigue', 'pain', and 'finding romance'. Fatigue was reported consistently in affected adults, who tended to have milder presentations, and affected children, who tended to have more severe presentations of NM. When looking into differences between gene subtypes, *ACTA1* respondents more often reported feeding limitations related to NM (55%). In general, the participants reporting a worse ambulatory status more often report having additional challenges related to NM. However, among the additional challenges reported, we found no significant differences between 'having a fulfilling social life', 'able to find a job with flexibility', and 'fatigue', with regard to ambulation status.

Muscle involvement patterns differed markedly based on patient ambulatory status. Among the subgroup of patients who had never walked independently, diaphragm weakness was most pronounced, affecting 89% of cases. The most reported affected muscle groups were the proximal muscles (81%), followed by distal muscles (75%) and then the neck muscles (66%) (Fig. 3). However, for those too young to walk, proximal muscle weakness was reported in 50% and distal in 36%.

The majority of participants were able to walk at least a few steps, with 25% of participants able to walk without support (Table 1). Forty-six participants (29%) have never been able to walk, or used to walk but currently don't. A statistically significant difference was found between the different mutations for the ambulation status, with *ACTA1* having the largest group for 'never has walked independently', and *KBTBD13* having the largest group for 'currently walks independently'. Most of our participants (71%) reported using at least one form of mobility aid. In supplemental Fig. 1, the different mobility aids are presented.

Participants mostly reported 'dental and orthodontic' when asked about orthopedic and bone complications. This was followed by 'facial, jaw, and/or soft palate anomalies', and 'gait abnormalities' (Fig. 4). Table 1 shows the subdivision of heart problems, scoliosis, and feeding

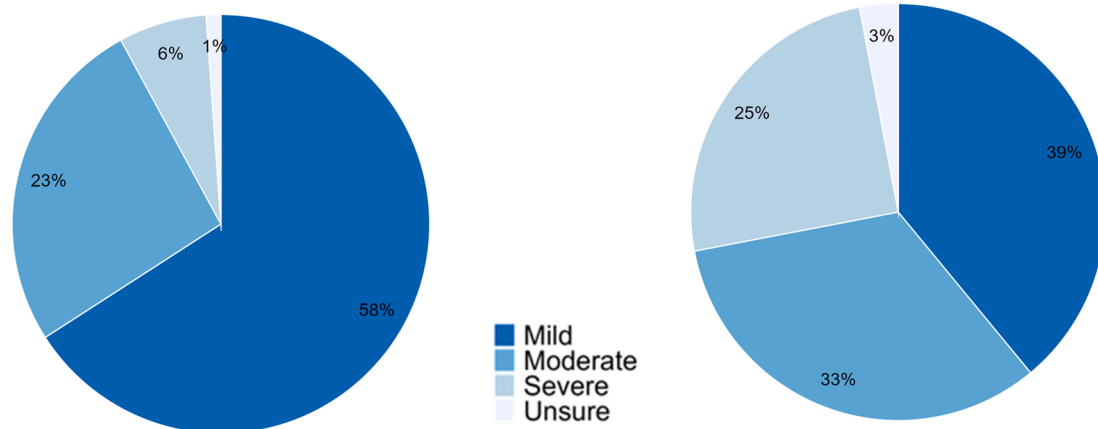


Fig. 1. Self-reported severity for A) adults and B) children. Mild: (independent movement of all body parts with some difficulty, independent walking attained at some point, independent breathing at least during waking hours, and able to safely swallow). Moderate: (a combination of the severe and mild signs, or something in between). Severe: (little or no independent movement, capacity to breathe, and ability to safely swallow).

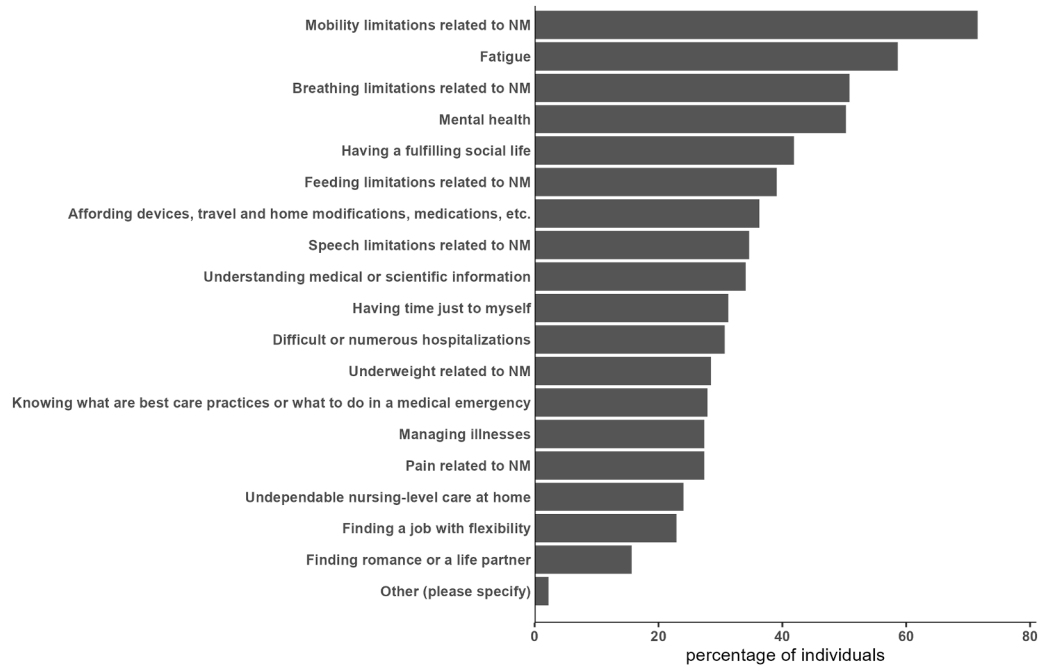


Fig. 2. Challenges. Participants selected which challenges from a list applied to their lives.

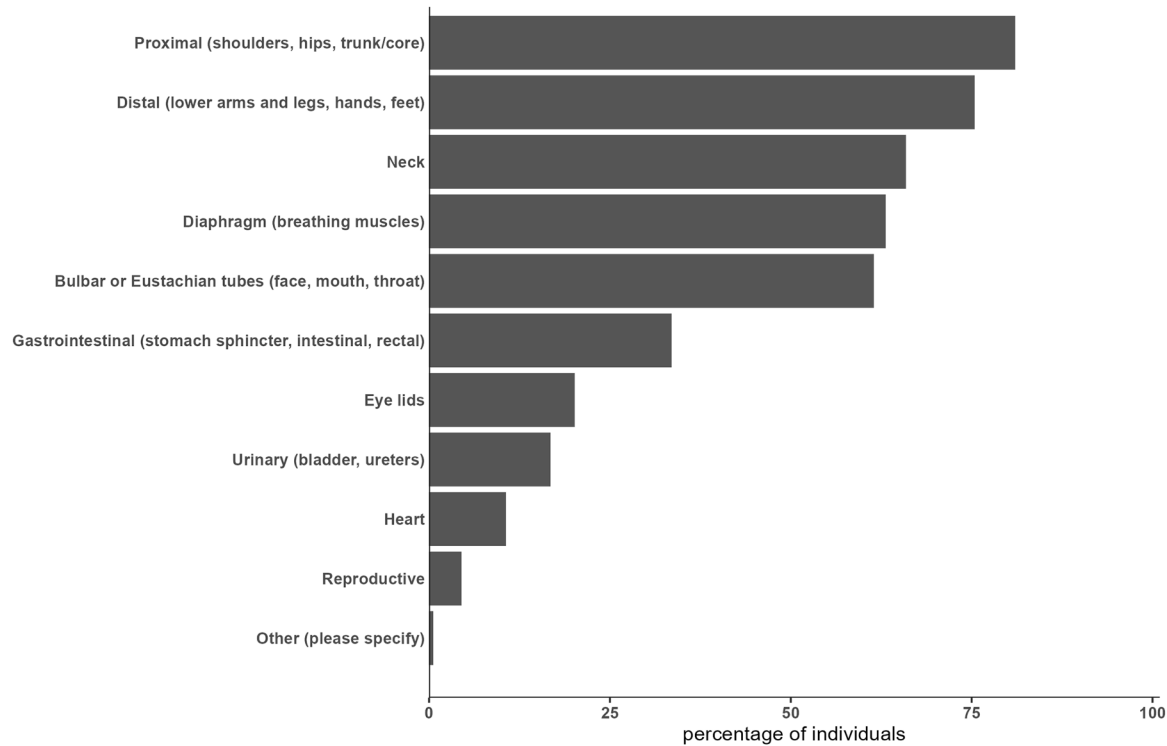


Fig. 3. Affected muscle groups. Participants selected which muscles experience weakness or dysfunction from a list of options.

problems. The degree of scoliosis was lowest among those with the *KBTD13* subtype, consistently a mild phenotype. Scoliosis was most severe among individuals with the *NEB* subtype and also among individuals who had never walked or who previously had independent ambulation but not at the time of the survey. Feeding difficulties were predominant in pediatric patients and reported more frequently in the *ACTA1* subtype, in which tube feeding was also more commonly required. When asked if they needed assistance with age-appropriate activities of daily living and self-care, 38% of the participants

responded that they need ‘a lot of assistance’, 39% that they need ‘some assistance’, and 23% require ‘no assistance’. The participants with an *ACTA1* mutation, and children, were reported as needing ‘a lot of assistance’ significantly more often than the other gene subtypes or the affected adults.

Fifty participants (32%) reported not using a respiratory device. Of those, 9 participants had received recommendations to use one or more respiratory devices by their clinicians but chose not to use any. The most used respiratory device was a bilevel positive airway pressure (BPAP)

Table 1
Information about current clinical condition.

Ambulation status (N(%)) (n=158)	
Currently is too young to walk (under 18 months of age)	14 (9%)
Currently walks independently without support	39 (25%)
Currently walks only short distances, such as within the house	35 (22%)
Currently walks long distances but may need mobility assistance sometimes	24 (15%)
Used to walk but no longer does	11 (7%)
Never has walked independently at age-appropriate times	35 (22%)
Heart problems (N(%)) (n=179)	
At birth	13 (7%)
Later in life	24 (16%)
Total	32 (18%)
Scoliosis (N(%)) (n=158)	
Sub-clinical: <10 degrees	79 (50%)
Mild: 10-30 degrees	22 (14%)
Moderate: 31-50 degrees	23 (15%)
Severe: ≥50 degrees	34 (22%)
Feeding issues (N(%)) (n=158)	
No	67 (37%)
Tube feedings were needed in the past	23 (13%)
Some foods need to be specially prepared	12 (7%)
Sometimes tube feeding along with oral nutrition	14 (8%)
Tube feedings are used for all meals	48 (27%)

device (39%), followed by a nebulizer (35%) and cough assistance device (34%) (Supplemental Fig. 2). Those who are able to walk independently and the affected adult respondents were least often reported to use any type of respiratory aid. However, independent of ambulatory status, respiratory aids are often used (Table 2).

Bulbar or Eustachian tube dysfunction was reported as a comorbidity by 61% of respondents. The gastrointestinal (GI) system, specifically the pyloric sphincter, intestinal motility, and rectum, was reported as adversely affected in 34% of respondents. The other body systems reported on are depicted in Supplemental Fig. 3. For children, GI system issues were followed in frequency by skin-related issues like bruising or eczema (25%) and immune problems (20%). In affected adults, GI symptoms were followed by hearing-related issues such as Eustachian tube dysfunction (38%) and vision difficulties (37%). No differences

Table 2
Use of a respiratory aid depicted per ambulatory status.

Ambulation status	N(%) Needing respiratory aid
Currently is too young to walk (under 18 months of age)	9 (64.3%)
Currently walks independently without support	16 (41%)
Currently walks long distances but may need mobility assistance sometimes	16 (66.7%)
Currently walks only short distances, such as within the house	27 (77.1%)
Never has walked independently at age-appropriate times	35 (100%)
Used to walk but no longer does	8 (72.7%)

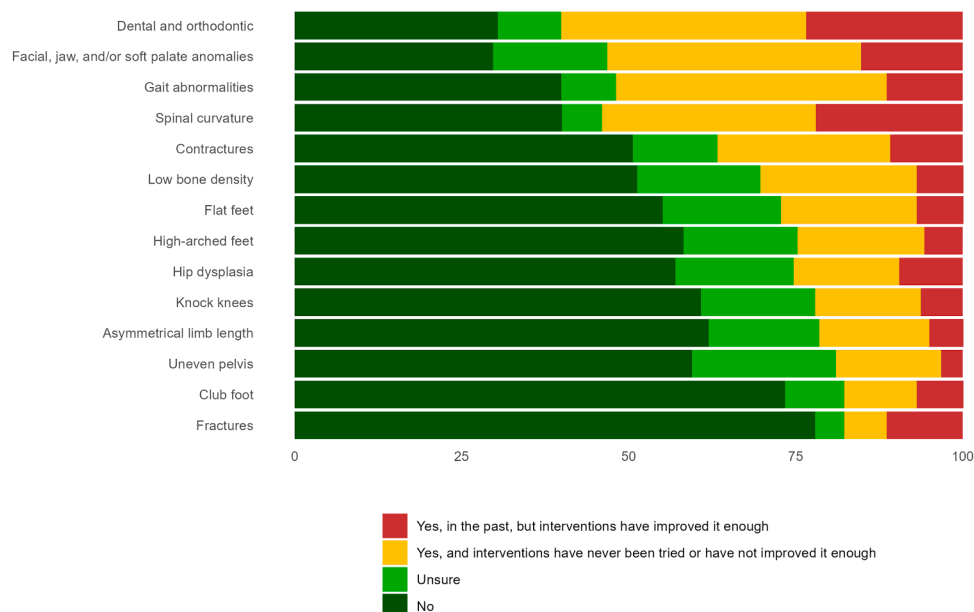


Fig. 4. Orthopedic and bone complications. Participants selected which complications affect their lives from a list of options.

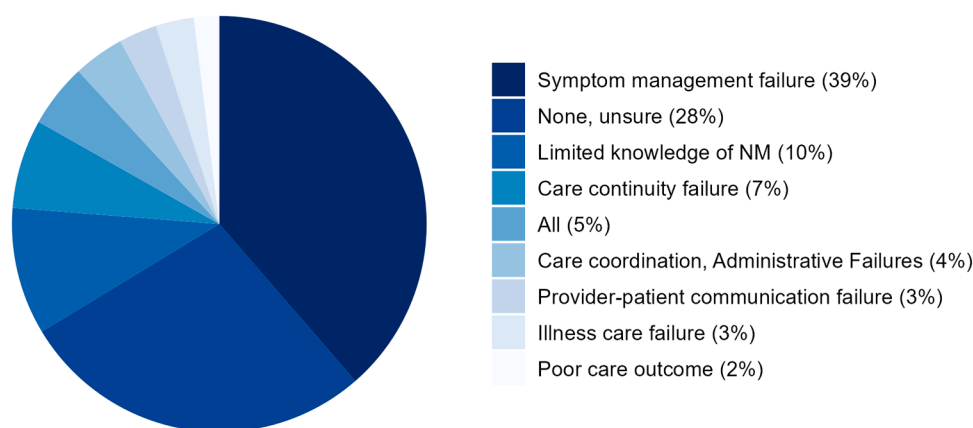


Fig. 5. Poorly managed aspects. Open-ended question for participants to describe the aspects of their condition that are mismanaged by their medical professionals.

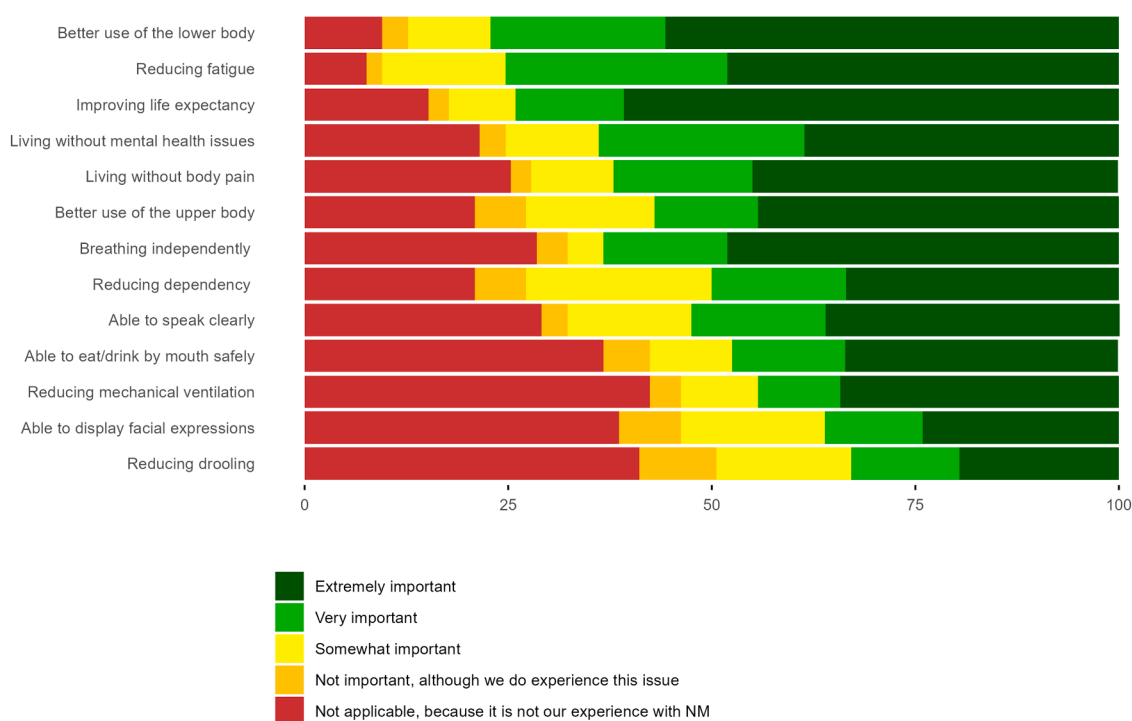


Fig. 6. Important treatment outcomes. Participants selected how important each treatment outcome would be in their lives using an ordinal scale.

were found between the various gene subtypes.

In an open-ended question, participants were asked to identify aspects of their condition they felt were inadequately managed by their clinical care teams. After categorizing the answers, the majority (69%) indicated at least one area of care being insufficient. The most commonly identified category was “symptom management failure” (44%), indicating that interventions were either lacking or did not meet appropriate standards of care. Fig. 5 presents a chart of all the identified categories. A description of the categories can be found in the supplemental material in Table S2.

3.3. Treatment outcomes

When asked to rate various treatment outcomes on importance, the most important outcome was ‘better use of the lower body for transitioning, standing, walking, climbing steps, etc.’, followed by reducing fatigue, and improving life expectancy (Fig. 6). No significant

differences were found for the top 3 important outcomes between children and adults. There were, however, significant differences when comparing the ambulatory status (Supplemental Fig. 4) and self-reported severity (Supplemental Fig. 5). In general, those with little to no ambulatory difficulty rate the treatment outcomes less important. Mild or moderately affected participants report ‘better use of the lower body’, ‘reducing fatigue’, and ‘improving life expectancy’ as most important. Severely affected participants, however, report ‘improving life expectancy’, ‘better use of the upper body’, and ‘reducing dependency’ as the top three. The respondents who reported relying upon assisted ventilation, either non-invasive or invasive, were more likely to rate reducing their dependency on mechanical ventilation as an important treatment outcome, with 43.2% reporting it as ‘extremely important’.

Most participants (92.4%) reported being ‘very’ or ‘somewhat’ willing to try new treatments, even in the presence of uncertainty or potential risk. No significant differences were observed between affected

adult respondents and caregivers of affected children.

All response data can be found in the Supplementary Materials appendix.

4. Discussion

This study included a broad international cohort of individuals with NM and family caregivers, with a relatively balanced distribution between affected children and affected adult patients. Participants represented 33 countries, although nearly half were from the United States, and most affected adults were reported to have mild presentations, which may influence the generalizability of findings. Most participants reported being willing to try new treatments, which may be an example of volunteer bias. We will discuss the main findings below.

Children were significantly more likely to be reported as having severe phenotypes, whereas adult patients more often reported having milder presentations of NM. This pattern most likely reflects survival bias and the fact that mild cases may not present to a physician until adulthood, but there also could be some nuances in perception of disease severity [26]. In our cohort, patient-reported severity varies, consistent with the broad range of clinical phenotypes observed both between and within genotypes of NM. Our results indicated that those with *ACTA1* subtypes tended to have more severe impairment than their self-reported classification suggested. As expected, the level of impairment influenced the reported priorities for treatment outcomes.

Ambulatory status differed significantly between those with *ACTA1* subtypes, which were associated with more severe motor impairment, and *KBTD13* subtypes, which were associated with better ambulation. As noted previously, *KBTD13* phenotypes tend to be milder [27] while *ACTA1* phenotypes can be experienced along a spectrum of mild to severe based on an individual's presentation. Joureau and colleagues found that *ACTA1* genotypes comprised up to 50% of the severe phenotypes reported [12]. Although *ACTA1* genotypes are more often reported as severe, Amburgey and colleagues found that there were no statistically significant differences between *ACTA1* and *NEB* patients in the number of supports needed in areas such as feeding, breathing, and ambulation [2]. It is important to note, however, that even those patients with the mildest forms of NM report daily functional difficulties that adversely impact their quality of life. Similar findings have been reported in other published studies [18,28].

All respondents (100%) noted challenges in daily life caused by NM. Affected children were more often reported as having challenges related to finding reliable nursing-level caregivers, feeding, communication, and limited personal time or respite for parents, whereas affected adults more frequently reported fatigue, pain, and difficulties finding romantic relationships. These differences are likely due to developmental life stages and different priorities in adulthood, in addition to the severity level of the disorder in affected children versus affected adults completing the survey, reflecting selective survival of individuals with milder forms of NM into adulthood.

Comorbidities such as scoliosis, respiratory impairment, and feeding difficulties were frequently reported, in addition to the direct effects of skeletal muscle weakness that are most often thought of as associated with NM. These comorbidities can be more severe than the skeletal muscle weakness, yet may go unrecognized or improperly managed by treating physicians [10,20]. Respiratory muscle weakness is common among all severity levels of NM and it can present initially as nocturnal hypoventilation, then daytime hypoventilation, with hypoxia and hypercapnia commonplace [10,20,29]. If the breathing impairment is not properly treated using a bilevel positive airway pressure device with optimized settings via a mask interface, or tracheostomy in severe cases, the respiratory failure can progress to pulmonary hypertension and cor pulmonale [4,6,17,30,31]. Respiratory muscle weakness is the most life-threatening of the under-recognized or mismanaged comorbidities of NM. Interdisciplinary care with clinical specialists who understand how NM affects the various organ systems is critically important for

better outcomes.

The mental health implications of NM have been largely understudied, but our results show that it is a significant category of challenge for patients and family caregivers (50%). This aligns with previous studies which have shown that people with NM experience more emotional distress than healthy peers [10,18]. There is a general consensus that people with neuromuscular disease are more likely to experience psychological difficulties such as anxiety and depression, and having multiple comorbidities, as many of our participants indicated, has also been associated with higher levels of anxiety [32–35]. Physical limitations, stigma, and recurring medical complications that significantly disrupt daily life are frequently cited causes of significant stress for these patients [31,36]. The current study did not formally assess specific psychiatric comorbidities among participants, but our findings and comparative studies underscore that this warrants more sustained clinical and research attention, especially considering that many mental health symptoms are potentially treatable.

When considering treatment priorities, participants consistently ranked improvements in gross motor function as most important, followed by reducing fatigue, and increasing life expectancy. These priorities were consistently reported across age groups, although some variation was observed when stratified by ambulatory status, suggesting that functional motor level influences perceived treatment needs. Most respondents indicated a willingness to try new treatment options, suggesting a strong interest in clinical trial participation. No significant differences in willingness were observed across respondent age groups or respondent roles.

4.1. Limitations

The patients' medical histories were self-reported by the participants; therefore these data were not independently verified through a review of clinical medical records. However, in some cases where the respondent answered questions in contradictory ways, study staff contacted them for clarification.

Since the survey permitted multiple submissions from a single IP address, if a respondent forgot that they had already taken the survey and took it again, their new responses were recorded as new data from a new respondent at the same IP address. This feature was intentionally enabled given the known occurrence of multiple affected individuals within some NM families, but it had the effect of permitting duplicate responses from the same and only affected person within one NM family. In practice, almost none of the families with multiple affected members completed the survey more than once to provide additional clinical histories or perspectives. In hindsight, disabling the multiple-submission feature would have been preferred with this cohort.

Dividing the survey across multiple pages may have inadvertently created the impression for some respondents that the survey had concluded at earlier page breaks, causing the premature survey termination that was observed to occur precisely at page breaks following Q1 (N=179), Q11 (N=158), and Q24 (N=154). The attrition of participants after Q1 may be due to one of several different factors, depending on the individual. For some non-English-speaking participants, the translation burden may have discouraged continued participation after Q1. Others may have accessed the survey out of curiosity only, completing Q1 (the screening question) in order to access the questions on the following page without intending to answer them. Finally, related to initial and later attrition, some participants may not have perceived sufficient value in completing the entire survey. While this technical attrition reduced our sample size for the later questions, there is no indication that this drop-out was caused by participant fatigue or symptom severity, minimizing the risk of systemic selection bias.

Our study size was limited, and sampling bias is always a consideration. With a rare disease like NM, there are very limited means to identify and recruit affected individuals and their family caregivers to participate. Recruitment in this study relied heavily on patient advocacy

networks and community engagement, which may preferentially capture individuals who are more connected, engaged, or motivated to participate. As a result, the sample may not fully represent the broader NM population, including those with limited access to specialty care, lower health literacy, limited internet use, or differing socioeconomic and geographic backgrounds.

Because recruitment was conducted primarily in English, potential language and educational selection biases must be considered. In non-Anglophone nations, English literacy and access to translation resources heavily correlate with higher socioeconomic status and advanced education. Consequently, this demographic skew may limit the generalizability of our findings to the broader global NM population.

The study did not include a control group, by design. As such, all findings are intended to characterize the specific experiences, priorities, and perceptions of this NM population rather than establish comparative differences with a healthy population.

People who choose to participate in a survey may differ from those who do not choose to participate in their degree of general willingness to contribute.

4.2. Strengths

To our knowledge, this study provides the first comprehensive assessment of challenges and priorities across age groups, severity levels, and countries for individuals affected by NM. This study offers insights that are underrepresented in the clinical literature, including daily challenges, care gaps, and treatment priorities, thereby informing clinical care and trial design with a more complete understanding of the patient perspective. The mixed-methods approach enabled integrated qualitative and quantitative analyses, including subgroup comparisons.

Finally, our collaborative framework involving patients, caregivers, patient organizations, and researchers facilitated recruitment of a diverse cohort, improved contextual interpretation of findings, and supported the identification of clinically relevant priorities, strengthening scientific validity and translational relevance. Meaningful patient involvement throughout the research process ensured that the study addressed questions and outcomes that are most relevant to those living with NM. Such co-creation is increasingly recognized as an essential component of high-quality rare disease research, as it enhances the relevance, acceptability, and potential impact of study findings. By incorporating lived experience into study design, data interpretation, and prioritization of research objectives, patient participation helps bridge the gap between clinical research and real-world needs, ultimately supporting the development of patient-centered care and therapies that address outcomes of greatest importance to affected individuals and their families.

4.3. Future directions

Among the understudied factors associated with NM, gastrointestinal and mental health problems stood out as being commonly reported as part of the disease impact.

We show that GI complications, including those involving impaired motility and elimination, are common yet underreported features of the disease. Further study of this aspect is critical considering these symptoms are potentially treatable, especially when the underlying NM-related causes of these complications are properly addressed.

A clearer and more accurate understanding of the mental health landscape of NM can lead to better resource offerings targeted for this population. Proactive diagnosis is essential, since addressing potentially treatable psychological concerns can help mitigate the overall hardship these symptoms impose [35]. Evidence from clinical trials, observational studies, and lived experience supports the integration of tailored psychological interventions into routine multidisciplinary care for individuals with neuromuscular disorders and their families.

5. Conclusion

A comprehensive understanding of NM requires moving beyond the traditional medical model and adopting a patient-centered framework that recognizes caregiver and patient agency, priorities, and lived experience. As found in the Stinissen and colleagues [37] “Lessons Learned” study, integration of the patient perspective is essential to ensure that future study designs, including clinical trials, reflect outcomes that are impactful to those living with NM and caring for someone with NM. Utilizing qualitative methods, such as semi-structured interviews or focus groups, may provide a more nuanced understanding of the lived experience and perceived needs among patients and caregivers. Including patient and caregiver perspectives and priorities serves to improve research design, ensures that outcome measures reflect real-world needs, increases patient participation, and ultimately can improve health outcomes.

Funding

This work was supported by A Foundation Building Strength for NemaLine Myopathy.

Data availability

The processed data supporting this work is available in the supplementary materials section and inquiries about the raw data can be sent to the corresponding author.

CRediT authorship contribution statement

Stacy A. Cossette: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Sanne A.J.H. van de Camp:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis. **Lucinda M. Lee:** Writing – original draft, Resources, Methodology, Investigation, Formal analysis, Conceptualization. **Matthias R. Lambert:** Writing – review & editing, Supervision. **Laurent Servais:** Writing – review & editing, Supervision. **Nicol C Voermans:** Writing – review & editing, Visualization, Validation, Supervision, Methodology, Conceptualization.

Declaration of competing interest

None.

Acknowledgements

The authors are sincerely grateful to the survey participants and to A Foundation Building Strength for providing the funding and support necessary for this work.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.nmd.2026.107427](https://doi.org/10.1016/j.nmd.2026.107427).

References

- [1] Sewry CA, Laitila JM, Wallgren-Pettersson C. NemaLine myopathies: a current view. *J Muscle Res Cell Motil* 2019;40(2):111–26. <https://doi.org/10.1007/s10974-019-09519-9>.
- [2] Amburgey K, Acker M, Saeed S, Amin R, Beggs AH, Bönnemann CG, et al. A cross-sectional study of nemaLine myopathy. *Neurology* 2021;96(10). <https://doi.org/10.1212/WNL.0000000000011458>.

- [3] Huang K, Bi FF, Yang H. A systematic review and meta-analysis of the prevalence of congenital myopathy. *front. neur.* 2021;12. doi:10.3389/fneur.2021.761636.
- [4] Wang CH, Dowling JJ, North K, Schroth MK, Sejersen T, Shapiro F, et al. Consensus statement on standard of care for congenital myopathies. *J Child Neurol* 2012;27(3):363–82. <https://doi.org/10.1177/0883073812436605>. PubMed PMID: 22431881; PubMed Central PMCID: PMC5234865.
- [5] Wallgren-Pettersson C, Pelin K, Nowak KJ, Munttoni F, Romero NB, Goebel HH, et al. Genotype-phenotype correlations in nemaline myopathy caused by mutations in the genes for nebulin and skeletal muscle alpha-actin. *Neuromuscul Disord* 2004;14(8–9):461–70. <https://doi.org/10.1016/j.nmd.2004.03.006>. PubMed PMID: 15336686.
- [6] Laitila J, Wallgren-Pettersson C. Recent advances in nemaline myopathy. *Neuromuscul Disord* 2021;31(10):955–67. <https://doi.org/10.1016/j.nmd.2021.07.012>. PubMed PMID: 34561123.
- [7] Konersman C, Cossette S, Foye SJ, Amburgey K, Rutkowski A, Lee L, et al. In: Welty S, editor. *The Care of Congenital Myopathy: A Guide for Families*; 2022. p. 222.
- [8] Haghighi A, Alvandi Z, Nilipour Y, Haghighi A, Kornreich R, Nafissi S, et al. Nemaline myopathy: reclassification of previously reported variants according to ACMG guidelines, and report of novel genetic variants. *Eur J Hum Genet* 2023;31(11):1237–50. <https://doi.org/10.1038/s41431-023-01378-w>. PubMed PMID: 37460656; PubMed Central PMCID: PMC10620380.
- [9] Hildebrandt C, Genetti CA, Logvinenko T, Win W, Barraza-Flores P, Hayes LH, et al. Retrospective cohort analysis of clinical, molecular, and histopathologic characteristics of 275 patients with nemaline myopathy. *Neurol Genet* 2025;11(4):e200277. <https://doi.org/10.1212/NXG.00000000000020277>.
- [10] Lehtokari VL, Similä M, Tammepuu M, Wallgren-Pettersson C, Strang-Karlsson S, Hiekkala S. Self-reported functioning among patients with ultra-rare nemaline myopathy or a related disorder in Finland: a pilot study. *Orphanet J Rare Dis* 2023;18:374. <https://doi.org/10.1186/s13023-023-02973-2>. PubMed PMID: 38037113; PubMed Central PMCID: PMC10691147.
- [11] Ogasawara M, Nishino I. A review of major causative genes in congenital myopathies. *J Hum Genet* 2023;68(3):215–25. <https://doi.org/10.1038/s10038-022-01045-w>. PubMed PMID: 35668205.
- [12] Joureau B, de Winter JM, Conijn S, Bogaards SJP, Kovacevic I, Kalganov A, et al. Dysfunctional sarcomere contractility contributes to muscle weakness in ACTA1-related nemaline myopathy (NEM3). *Ann Neurol* 2018;83(2):269–82. <https://doi.org/10.1002/ana.25144>. PubMed PMID: 29328520; PubMed Central PMCID: PMC5821533.
- [13] Pelin K, Hilpelä P, Donner K, Sewry C, Akkari PA, Wilton SD, et al. Mutations in the nebulin gene associated with autosomal recessive nemaline myopathy. *Proc Natl Acad Sci U S A* 1999;96(5):2305–10. <https://doi.org/10.1073/pnas.96.5.2305>. PubMed PMID: 10051637; PubMed Central PMCID: PMC26779.
- [14] Nowak KJ, Wattanasirichaigoon D, Goebel HH, Wilce M, Pelin K, Donner K, et al. Mutations in the skeletal muscle alpha-actin gene in patients with actin myopathy and nemaline myopathy. *Nat Genet* 1999;23(2):208–12. <https://doi.org/10.1038/13837>. PubMed PMID: 10508519.
- [15] Shy GM, Engel WK, Somers JE, Wanko TNEMALINE MYOPATHY. A NEW CONGENITAL MYOPATHY, 86. *Brain*; 1963. p. 793–810. <https://doi.org/10.1093/brain/86.4.793>. PubMed PMID: 14090530.
- [16] Lamont PJ, Thorburn DR, Fabian V, Vajsar J, Hawkins C, Saada Reisch A, et al. Nemaline rods and complex I deficiency in three infants with hypotonia, motor delay and failure to thrive. *Neuropediatrics* 2004;35(5):302–6. <https://doi.org/10.1055/s-2004-821243>. PubMed PMID: 15534765.
- [17] Coppens S. Congenital myopathies. *Management of Neuromuscular Disorders in Children: A Multidisciplinary Approach to Management*. London, UK: Mac Keith Press; 2019. p. 220–31.
- [18] van Kleef ESB, de Camp SAJH van, Groothuis JT, Erasmus CE, Gaytant MA, Vosse BAH, et al. A cross-sectional study in 18 patients with typical and mild forms of nemaline myopathy in the Netherlands. *Neuromuscul Disord* 2024;43:29–38. <https://doi.org/10.1016/j.nmd.2024.08.001>. PubMed PMID: 39180840.
- [19] Ryan MM, Schnell C, Strickland CD, Shield LK, Morgan G, Iannaccone ST, et al. Nemaline myopathy: a clinical study of 143 cases. *Ann Neurol* 2001;50(3):312–20. <https://doi.org/10.1002/ana.1080>. PubMed PMID: 11558787.
- [20] van Kleef ESB, van Doorn JLM, Gaytant MA, de Weerd W, Vosse BAH, Wallgren-Pettersson C, et al. Respiratory muscle function in patients with nemaline myopathy. *Neuromuscul Disord* 2022;32(8):654–63. <https://doi.org/10.1016/j.nmd.2022.06.009>.
- [21] Lehtokari VL, Pelin K, Sandbacka M, Ranta S, Donner K, Munttoni F, et al. Identification of 45 novel mutations in the nebulin gene associated with autosomal recessive nemaline myopathy. *Hum Mutat* 2006;27(9):946–56. <https://doi.org/10.1002/humu.20370>. PubMed PMID: 16917880.
- [22] de Winter JM, Gineste C, Minardi E, Brocca L, Rossi M, Borsboom T, et al. Acute and chronic tirasemtiv treatment improves in vivo and in vitro muscle performance in actin-based nemaline myopathy mice. *Hum Mol Genet* 2021;30(14):1305–20. <https://doi.org/10.1093/hmg/ddab112>. PubMed PMID: 33909041; PubMed Central PMCID: PMC8255131.
- [23] Fabian L, Karimi E, Farman GP, Gohlke J, Ottenheim CAC, Granzier HL, et al. Comprehensive phenotypic characterization of an allelic series of zebrafish models of NEB-related nemaline myopathy. *Hum Mol Genet* 2024;33(12):1036–54. <https://doi.org/10.1093/hmg/ddae033>. PubMed PMID: 38493359; PubMed Central PMCID: PMC11153343.
- [24] Fisher G, Mackels L, Markati T, Sarkozy A, Ochala J, Jungbluth H, et al. Early clinical and pre-clinical therapy development in Nemaline myopathy. *Expert Opin Ther Targets* 2022;26(10):853–67. <https://doi.org/10.1080/14728222.2022.2157258>. PubMed PMID: 36524401.
- [25] Braun V, Clarke V. Using thematic analysis in psychology. *Qualitat Res Psychol* 2006;3(2):77–101. <https://doi.org/10.1191/1478088706qp0630a>.
- [26] Bisciglia M, Severa G, Romero NB, Fardeau M, Rendu J, Stojkovic T, et al. Disease trajectories of a large french cohort of 142 congenital myopathy patients in adult age. *Eur J Neurol* 2025;32(4):e70109. <https://doi.org/10.1111/ene.70109>. PubMed PMID: 40159620; PubMed Central PMCID: PMC11955412.
- [27] van Kleef ESB, Bouman K, Molenaar JPF, Küsters B, Groothuis JT, Olivé M, et al. Nemaline myopathy type 6 caused by variants in the KBTBD13. *Gene Neurol Genet* 2024;10(6):e200214. <https://doi.org/10.1212/NXG.00000000000020214>. PubMed PMID: 39651462; PubMed Central PMCID: PMC11623396.
- [28] Jungbluth H, Sewry CA, Brown SC, Nowak KJ, Laing NG, Wallgren-Pettersson C, et al. Mild phenotype of nemaline myopathy with sleep hypoventilation due to a mutation in the skeletal muscle α -actin (ACTA1) gene. *Neuromuscul Disord* 2001;11(1):35–40. [https://doi.org/10.1016/S0960-8966\(00\)00167-X](https://doi.org/10.1016/S0960-8966(00)00167-X). PubMed PMID: 11166164.
- [29] Christophers B, Lopez MA, Gupta VA, Vogel H, Baylies M. Pediatric nemaline myopathy: a systematic review using individual patient data. *J Child Neurol* 2022;37(7):652–63. <https://doi.org/10.1177/08830738221096316>. PubMed PMID: 36960434; PubMed Central PMCID: PMC10032635.
- [30] Ohara M, Saito Y, Watanabe M, Mizutani S, Kobayashi M, Iida A, et al. An adult nemaline myopathy patient with respiratory and heart failure harboring a novel NEB variant. *eNeurologicalSci*. 2020;21:100268. doi:10.1016/j.ensci.2020.100268. PubMed PMID: 32399402; PubMed Central PMCID: PMC7479285.
- [31] Lee L. LIFE WITH CONGENITAL MYOPATHY: AN EXPLORATORY STUDY OF THE LIVED EXPERIENCE. University of North Carolina at Charlotte; 2026.
- [32] Vancampfort D, Koyanagi A, Hallgren M, Probst M, Stubbs B. The relationship between chronic physical conditions, multimorbidity and anxiety in the general population: A global perspective across 42 countries. *general hospital psychiatry*. 2017;45:1–6. doi:10.1016/j.genhosppsych.2016.11.002.
- [33] Rutkowski A, Cossette S, Lennox A, Schrooten A. Parent perspectives on neuromuscular disorders: from diagnosis, to parenting and living with, to advance care planning and preparing for death. *Neuromuscular Disorders in Children: A Multidisciplinary Approach to Management*. London, UK: Mac Keith Press; 2019. p. 2–21.
- [34] Cognitive Geuens S. Behavioral, and psychosocial aspects of growing up with a neuromuscular disease. *Management of Neuromuscular Disorders in Children: A Multidisciplinary Approach to Management* [Internet]. London, UK: Mac Keith Press; 2019. p. 406–16 [cited 2026 Jun 13]. Available from, <https://www.wiley.com/en-au/management-of-neuromuscular-disorders-in-children-a-multidisciplinary-approach-to-management-p-9781911612087>.
- [35] Pater R, Garmendia J, Gallais B, Graham C, Voet N, Angeard N, et al. 267th ENMC International workshop: psychological interventions for improving quality of life in slowly progressive neuromuscular disorders. *Neuromuscul Disord* 2023;33(7):562–9. <https://doi.org/10.1016/j.nmd.2023.03.012>. PubMed PMID: 37331200.
- [36] Jones KM, Bright C, O'Grady G, Rodrigues MJ, Ranta A, Roxburgh RH, et al. Coping in children and adolescents with a genetic muscle disorder—findings from a population-based study. *JND* 2021;8(6):1069–78. <https://doi.org/10.3233/JND-200564>.
- [37] Stinissen L, Böhm J, Bouma S, van Tienen J, Fischer H, Hughes Z, et al. Lessons learned from clinical studies in centronuclear myopathies: the patient perspective—a qualitative study. *Clin Therapeut* 2024;46(10):742–51. <https://doi.org/10.1016/j.clinthera.2024.03.008>. PubMed PMID: 38670885.