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- Expert Patient Capacity Building in Neuromuscular Disease Research (**Dr Kathryn Selby** with Dr Hanns Lochmüller)

GNE myopathy: a novel method for the estimation of disease prevalence using genomic databases

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GNE myopathy (GNEM), is a rare autosomal recessive disorder characterized by progressive skeletal muscle atrophy starting in early adulthood. The prevalence of GNEM is estimated to range between 1-9 in 1,000,000 individuals. However, this estimate may not fully capture the true extent of disease burden given the inherent difficulties in studying rare diseases and significant number of patients who may remain undiagnosed. We propose a more accurate prevalence estimate for GNEM which can be calculated using population allele frequency data. To do this EMBASE, MEDLINE, and SCOPUS were systematically searched to generate a list of published pathogenic GNE variants. Additionally, reported pathogenic/likely pathogenic GNE variants were collected from genomic databases: ClinVar, HGMD, and LOVD. The allele frequencies for these variants were pulled from the genomic aggregation database (GnomAD). All remaining variants on GnomAD of uncertain clinical significance were collected, filtered based on allele frequencies, in silico predictions, and domain specific hot spots to create a list of unreported likely pathogenic variants. These groups of variants were used in several combinations to calculate broad and stringent estimates for the prevalence of GNEM. Calculations used the sum of allele frequencies under the assumption of the Hardy-Weinberg equilibrium. More than 350 unique GNE variants were uncovered through these literature and genomic database searches and with the inclusion of the unreported likely pathogenic variants this number is increased even further. Based on these numbers it is estimated that the prevalence of GNEM is far greater than the previously reported 1-9 in 1,000,000 individuals.

Myoinflammation disrupts mitochondrial dynamics and function in a human myositis model

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Inclusion body myositis (IBM) exhibits a unique clinical and histologic phenotype among the spectrum of idiopathic inflammatory myopathy that can only be partially explained by the previously described pathomechanisms of inflammatory activity and degeneration. Especially, cell-autonomous mechanisms involving mitochondrial damage remain elusive. Mitochondria are dynamic intracellular networks, engaging in fusion- and fission-cycles, altering the mitochondrial network phenotype according to cell homeostasis. Our prior experiments showed increased mitochondrial fission in myoinflammation. In this work, we focused on the inflammation-induced change in mitochondrial dynamics and mitochondrial function.

In a cell culture model for myositis, human myotubes were exposed to pro-inflammatory cytokines (IL-1β, IFNγ), and subsequently, the influence on mitochondrial fusion (MFN2, OPA1) and fission proteins (DRP1) was evaluated (qPCR, WB, Life-Cell-Imaging). Mitochondrial phenotype and function (Confocal Microscopy, Seahorse XF Analysis) in the context of myoinflammation were evaluated in a in knock-down of MFN2 and DRP1 in myoblasts.

IL-1β and IFNγ resulted in a significant decreased expression of OPA1 (WB, $p = 0.016$). Knockdown of DRP1 reversed the observed fragmentation of the mitochondrial network. In DRP1-knockdown, Seahorse XF Analysis revealed an increased free respiratory capacity ($p = 0.077$) with reduced coupling efficiency ($p = 0.007$). MFN2-knockdown showed a massively fragmented mitochondrial network.

Mitochondrial dynamics are dysregulated in the cytokine-induced myogenic cell-culture model for myositis. DRP1-knockdown reverses mitochondrial fragmentation. Fission predates mitophagy for elimination of damaged mitochondria, therefore impaired mitochondrial dynamics might result in deficient mitochondrial quality control, consecutively accumulating damaged mitochondrial mass and influencing proper myofiber function.

Delayed diagnosis of the common single mtDNA deletion due to an atypical multisystem presentation

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We present the case of a 55-year-old woman with an atypical multisystem presentation associated with the common 5kb mtDNA deletion, and only mild clinical evidence of a myopathy. The patient presented with frequent migraines, chronic pain, depression, gastrointestinal symptoms, weight loss as well as progressive hearing loss, cataracts and ataxia. Moreover, she experienced one encephalopathic episode with amnesia and transient unresponsiveness.

Neuromuscular examination revealed a generally slim muscle profile with mild atrophy and distal weakness, as well as bilateral ophthalmoparesis with inability of upward and severe restriction of outward gaze. Previous laboratory results had intermittently shown elevated LDH and lactate. EMG examination of the vastus medialis found myopathic changes. Genetic testing of blood was normal (panel including mtDNA). A muscle biopsy showed a mitochondrial myopathy with ragged-red and COX-negative fibers, with mixed myopathic and neurogenic changes. Mitochondrial genome analysis of muscle tissue identified the common mtDNA deletion (m.8483_13459), with a heteroplasmy level of 10%. Under a treatment regimen with CoQ10 and levetiracetam, the patient was more alert with no further encephalopathic episodes. Nevertheless, various symptoms including bowel problems, ataxia and ophthalmoparesis remained unchanged.

In contrast, according to NAMDC-Registry data, 86.6% of patients with single large mtDNA deletions reported muscular symptoms beyond ophthalmoparesis (Barca et al, 2020). With PEO-plus phenotypes predominantly caused by nDNA mutations (Hirano & Pitceathly, 2023), this case broadens the known phenotype spectrum associated with m.8483_13459 mtDNA deletion. Moreover, diagnostic relevance of a skeletal muscle biopsy in suspected mitochondrial pathology, despite mild muscular symptoms, is emphasized.

Developing an optogenetic reference model for congenital myasthenic syndromes

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Congenital myasthenic syndromes (CMS) are caused by mutations in neuromuscular junction (NMJ)-related genes, ultimately causing defects affecting NMJ transmission. The zebrafish has been a successful organism for modelling several known CMS genes including transgenic lines for *CHRNG*, and morpholino models of *DOK7* and *SYT2*. We utilize the *syt2* morpholino model in an optogenetic zebrafish line expressing blue-light activated channelrhodopsin-2 (ChR2) in motor and Kolmer-Agduhr neurons. Action potentials triggered by optogenetic stimulation bypass peripheral sensory and brain neural circuitry, thus isolating stimulated behaviours to the NMJ signal transmission level. Optogenetic stimulation also facilitates collection of electrophysiological data from muscle fibres to assess NMJ function as compared to other, more technically challenging, paired motoneuron-muscle patch-clamping methods. Thus, muscle contractions triggered via blue light stimulation of motoneurons serve as a direct link between electrophysiological data and locomotor behaviours. We knocked down *syt2*, a synaptotagmin calcium sensor regulating fusion of synaptic vesicles, in this ChR2 line and performed electrophysiological measurements. At the NMJ we showed increased asynchronous release and decreases in quantal content and number of synaptic vesicle release sites. These results reflect other *syt2* morpholino knockdown studies using paired patch clamping methods. Upon blue light stimulation, optogenetic *syt2* knockdown fish showed significant decreases in distance travelled, velocity, and acceleration, pointing to a clear neuromuscular phenotype similar to that seen in CMS patients. This work represents a method suitable to assessing neuromuscular signal transmission defects and their resulting effects on locomotion.

Understanding the Role of GFPT1 and O-GlcNAcylation in Congenital Myasthenic Syndromes

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Congenital myasthenic syndromes (CMS) are a group of early-onset genetic neuromuscular disorders that result from mutations to genes involved in neuromuscular junction (NMJ) development, function, maintenance, and organization. Glutamine-fructose-6-phosphate transaminase 1(GFPT1) is the rate-limiting enzyme of the hexosamine biosynthetic pathway (HBP); a metabolic signalling pathway which produces UDP-GlcNAc, the precursor for N- and O-linked protein glycosylation. Biallelic mutations to GFPT1 reduces GFPT1 protein levels and enzymatic activity causing CMS, although the exact mechanism of how this happens is unknown.

We hypothesize that the impairment in GFPT1 causes a hypo-glycosylation environment at the NMJ resulting in dysfunction to proteins involved in neurotransmission and NMJ maintenance. We aimed to demonstrate this using a skeletal muscle-specific Gfpt1 knockout mouse model (Gfpt1tm1d/tm1d) and Gfpt1-deficient C2C12 cells. Both models demonstrated deficient Gfpt1 expression, a reduction in oligotransferase (Ogt) expression and a loss of protein O-GlcNAcylation. To examine the effects on the NMJ we performed western blots for AChRδ and showed an extra lower molecular weight species not present control samples. These species are sensitive to glycanase treatments, suggesting that AChRδ/CHRND is miss-glycosylated in GFPT1-CMS. We are currently examining the effects of mis-glycosylated AChRδ on overall AChR surface expression and AChR clustering. To see if we could bypass the defective HBP we supplemented the water of Gfpt1-deficient mice with 10%(w/v) D-galactose and saw a rescue in the mouse phenotype and a normalisation of the AChRδ glycosylation.

Investigating beta-2 adrenergic agonist treatment alternatives for congenital myasthenic syndromes

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Impaired function of the neuromuscular junction (NMJ) can cause congenital myasthenic syndromes (CMS), a group of rare genetic disorders characterized by fatigable skeletal muscle weakness. β2-adrenergic agonists, ephedrine and salbutamol, are used off-label for CMS treatment to stabilize the NMJ. Unfortunately, many CMS patients experience cardiac side effects with these treatments. Newer FDA-approved β2-adrenergic agonists, formoterol, olodaterol and indacaterol, have tighter binding to β2-receptors and longer half-lives. Downstream of β2-adrenergic agonists, the cyclic adenosine monophosphate (cAMP) signalling pathway is activated. Another promising treatment alternative is forskolin, an FDA-approved drug that acts directly on the cAMP signalling pathway, which was shown to improve NMJ morphology in a CMS zebrafish model. We hypothesize that formoterol, olodaterol, indacaterol and forskolin will be effective treatments for CMS. To test this hypothesis, we will first test these drugs in the C2C12 mouse muscle cell line and quantify cAMP and NMJ receptor levels. We will then administer the top performing drugs in a *ColQ*-CMS mouse model. We have chosen *ColQ* knockout (*ColQ*$^{-/-}$) mice, an established CMS model generated on a C57BL/6 background. *ColQ*$^{-/-}$ mice have abnormal NMJ morphology and reduced bodyweight, muscle fibre diameter and motor strength. Previously, salbutamol treatment was shown to significantly improve grip strength and NMJ morphology in *ColQ*$^{-/-}$ mice, thus making it a valid *in vivo* model to study alternatives for salbutamol. There is a strong incentive to find alternative treatment options for CMS, and my study will identify drugs that require lower and less frequent dosages.

Unraveling the pathophysiology of Bethlem Myopathy using a unique zebrafish model for the disease

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Bethlem myopathy (BM) is a muscle disease characterized by joint contractures and muscle weakness worsening with age. BM results from mutations in genes encoding one of the three collagen VI α-chains (COLVI), a component of the skeletal muscle extracellular matrix. How alteration in COLVI present outside muscle fibers induces dysfunction within muscle fibers in BM remains an unresolved issue. In the present study, using current- and voltage-clamp techniques combined with intracellular Ca^{2+} measurements, we explored properties of excitation-contraction coupling in isolated fast skeletal muscle fibers from 1-year-old zebrafish harboring an exon-skipping mutation (col6a1$^{\Delta ex14}$) the most frequently found in BM patients. Action potentials were found to be unchanged in col6a1$^{\Delta ex14}$ fish fibers. Density of charge movements produced by depolarization-induced activation of dihydropyridine receptors, that control sarcoplasmic reticulum (SR) Ca^{2+} release, was found to be reduced and their voltage-dependence shifted toward negative potentials in col6a1$^{\Delta ex14}$ fish. Voltage dependence of depolarization-evoked intracellular Ca^{2+} transients was also shifted toward negative voltages, promoting in this way an elevated pathogenic SR Ca^{2+} leak at resting membrane potentials. Higher frequency of unitary SR Ca^{2+} release events at rest in mutant fish confirmed the increased SR Ca^{2+} leak which, together with the observed reduced swimming performance in mutant fish, could explain muscle wasting observed in BM patient. In conclusion, our data contribute to identify the still elusive link that allows altered myomatrix in BM to transduce pathogenic signals within muscle and may provide tracks for treatment of this currently incurable disease.

Investigating muscle specific kinase agonist antibody treatment for Agrn Congenital Myasthenia Syndromes

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When genetic mutations alter the neuromuscular junction (NMJ) development or function it can cause an inherited group of disorders called congenital myasthenia syndromes (CMS). Amongst the 35 known causative genes for CMS is Agrn which encodes for Agrin, a proteoglycan secreted by the presynaptic motor neuron. Its postsynaptic binding initiates signalling where muscle specific kinase (MuSK) phosphorylation promotes acetylcholine receptor (AChR) aggregation. While some treatments exist for Agrn-CMS, these can come with side effects, therefore there is a need to develop more therapies. A recent study demonstrated a beneficial effect of a MuSK agonist antibody (MAA) on a DOK7-CMS mouse model. We aimed to determine if the same MAA would show similar efficacy in a mouse model of Agrn-CMS. We hypothesized that the resultant MuSK phosphorylation independent of Agrin signaling would increase NMJ development and function. We bred mice with a mutation in the Agrn gene (Agrnnmf380) to recapitulate CMS phenotypes. Six Agrnnmf380 mice were injected with MAA, six were injected with a control antibody and six healthy WT mice were used for controls. We observed MAA impact on survival, bodyweight, muscle weight, and NMJ morphology. We also assessed the skeletal muscle strength with a neonatal tube test, grip strength, and inverted hanging wire. The MAA had a positive impact on Agrnnmf380 survival and improved body and muscle weight to WT levels. MAA also slightly improves muscle strength and NMJ morphology. We conclude that the MuSK agonist antibody is effective in rescuing prominent CMS phenotypes in our Agrn-CMS mouse model.

Exercise impact on insulin resistance in Myotonic Dystrophy Type 1

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Myotonic Dystrophy Type 1 (DM1) is a multisystemic neuromuscular disease that clinically presents with skeletal muscle weakness, atrophy, myotonia, gastrointestinal complications, and insulin resistance. While insulin resistance has been characterized particularly well within the context of type 2 diabetes, its pathomechanism in DM1 remains unclear. Insulin resistance limits skeletal muscle glucose uptake due to diminished insulin-dependent glucose transporter 4 (GLUT4) translocation to the plasma membrane. This project will examine the impact of exercise on GLUT4 translocation and how it affects insulin sensitivity in DM1 models and human DM1 tissue. The first aim will employ Qiagen's Ingenuity Pathway Analysis to analyze the proteomic profile of exercised and sedentary DM1 mice, thus identifying proteins implicated in exercise and insulin signaling. The second aim will examine molecular interactions impacting GLUT4 translocation in a DM1 cell model, including a glucose uptake assay to assess glucose uptake. The final aim will examine exercise's impact on GLUT4 translocation in DM1 tissue, utilizing RT-PCR, western blotting, and immunofluorescence to analyze relevant transcripts, proteins and GLUT4 translocation status in tissue sections. IPA's analysis determined that exercise significantly upregulates PGC-1α, a protein integral to metabolic regulation. This upregulation is correlated with an increase in transcription of *SLC2A4*, the gene encoding for GLUT4. Thus, I hypothesize that exercise regulates DM1 insulin sensitivity via PGC-1α-induced GLUT4 expression and translocation. Further work using the indicated molecular techniques are required to validate the

findings from IPA. Although preliminary, the data thus-far indicates that exercise can provide important benefits for DM1 patients.

Integration of a best practice advisory for myotonic dystrophy into an electronic healthcare record system - The Ottawa Hospital experience

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Myotonic Dystrophy (DM) is the most common form of muscular dystrophy in adults, classed as a rare genetic disease but with a relatively high prevalence in Eastern Canada. It is characterized by myotonia in the hands and legs, skeletal muscle weakness and wasting and involvement of the cardiac and respiratory system. DM is currently incurable, but standards of care have been published including the recommendation to avoid drugs that put patients at risk of complications including cardiac conduction delays and respiratory failure. However, this information is not readily available to prescribers at the point of care, leading to negative health outcomes. The Best Practice Advisory (BPA) is a programmed IT solution that has been implemented across the EPIC electronic medical record system at The Ottawa Hospital to provide reminders and suggestions, helping users make informed clinical decisions. Two BPAs for myotonic dystrophy have been created, notifying physicians of precautions, (i) when a DM diagnosis is entered, and (ii) when an offending agent is ordered. These alerts give users easy access to the standards of care of DM patients and prevent the erroneous prescription of harmful medications and anesthetics, classified as opioids, anxiolytics, succinylcholine, anticholinesterases and general anesthetics. Succeeding its activation in 2021, DM-BPA has been triggered 502 times. Its implementation across electronic healthcare systems in Canada would allow for improved medication safety administration for patients with DM, as well act as a starting point for potential future alert systems of rare diseases.

Is sensory neuropathy as a comorbid condition in Pompe disease?

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Introduction: Pompe disease is a glycogen storage disease involving mainly striated muscle. While cardiac, respiratory, and limb muscles are most severely affected and determine clinical outcomes, it should always be noted that with Enzyme Replacement Therapy (ERT), new phenotypes that can develop and involve the central and peripheral nervous systems should be considered. The aim of this study was evaluation the presence of concomitant small and large fiber neuropathy in Pompe patients.

Methods: In this case series study, nine Pompe patients were evaluated without any complaints of neuropathy. Three of them were disabled and the remaining six patients had problems in walking due to myopathy. Evaluation of small fiber neuropathy was based on the Small Fiber Neuropathy Screening List (SFNSL) and SUDOSCAN, sympathetic system evaluation on Sympathetic Skin Response (SSR), and large fiber neuropathy on electrodiagnostic findings.

Results: In this case series study, nine available Pompe patients (about 30% of all Pompe patients registered in Iran) were studied for sensory neuropathy. Seven patients had positive SFNSL and three patients (3/9, about 30%) had one positive electrophysiological test including SSR, SUDOSCAN, and NCS for neuropathy (these patients had a positive SFNSL too).

Discussion: Our study showed that sensory fiber neuropathy can be a comorbid condition. Due to ERT and the increase in life expectancy of these patients, timely screening using available methods such as questionnaires, physical exams or electrodiagnostic studies should be done to avoid potential debilitating conditions.

A novel recurrent intronic variant in Desmin (DES) causes a milder limb-girdle congenital myasthenic syndrome (LG-CMS) phenotype due to leaky splicing with intron retention.

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Desminopathies (DES) constitute a heterogenous spectrum of neuromuscular diseases involving cardiac and skeletal muscle. Dominant mutations are more common, typically manifesting as adult-onset myofibrillar myopathy with desmin aggregates in muscle. Rare recessive mutations typically cause severe early-onset myopathy due to desmin loss, also linked to neuromuscular junction dysfunction in mice and humans.
Three unrelated patients from southern India (2M,1F) aged 16, 21 and 22 years presented with childhood-onset gradually progressive fatigable limb-girdle weakness, ptosis, and speech and swallowing difficulties. Serum creatine kinase was elevated, and repetitive nerve stimulation showed decrement. Cardiac involvement was not reported. Clinically suspected as limb-girdle congenital myasthenic syndrome (LG-CMS), improvement was noted with pyridostigmine and salbutamol. All patients harbored a rare homozygous substitution in intron 5: DES(NM_001927.4):c.1023+5G>A. In-silico analysis predicted canonical donor splice site loss with activation of a deep intronic cryptic donor site. Muscle biopsy suggested myopathy with myofibrillar disarray, and immunohistochemistry showed partial desmin loss with absent staining in sarcoplasm and subsarcolemmal desmin-positive staining. RT-PCR of patient muscle RNA revealed two transcripts: a normal desmin transcript that was reduced compared to human myoblast control and an abnormally longer transcript suggesting leaky splicing at the intron 5 donor site. Sequencing of PCR products confirmed inclusion of intron 5 in the longer transcript, predicted to cause frameshift and premature stop codon leading to partial desmin loss.
This milder limb-girdle phenotype with associated neuromuscular junction features due to a recessive intronic mutation causing partial loss of desmin expands the known spectrum of desminopathies.

Treatabolome DB: linking treatments for rare diseases to genes and variants

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Although next-generation sequencing has dramatically improved diagnosis for rare disease (RD) patients, accessing information about the correct treatment for a diagnosed genetic defect

remains challenging for the treating clinician. The number of RDs (>7000) and their genetic heterogeneity impedes identification of existing treatments and means that patients often do not receive the appropriate treatment at diagnosis.

In a collaboration between disease experts and computational and genomics specialists, the Treatabolome group from the international Solve-RD consortium developed TreatabolomeDB, a database of RD-specific treatments designed to allow easy identification of variant, gene, and disease-specific therapies and the published evidence behind them.

TreatabolomeDB captures variant-to-treatment mappings from systematic literature reviews (SLRs) performed by disease experts. In neuromuscular disorders, eight SLRs have been completed to date covering congenital myasthenic syndromes, laminopathies, muscular channelopathies, mitochondrial disorders (Leigh syndromes), hereditary peripheral neuropathies, genetic forms of Parkinson's disease, and metabolic myopathies. Additional SLRs are welcomed.

TreatabolomeDB currently contains 3623 entries from 745 publications and is publicly accessible through programmatic interfaces and a web portal (treatabolome.org) supporting queries with standard terminologies including diagnostic (ORDO, OMIM, HPO), gene, variant, and treatment (ChEBI, UMLS, MeSH). It has been integrated into the RD-Connect Genome-Phenome Analysis Platform to enable identification of relevant treatments for RD patients at the time of diagnosis. Solve-RD analysis of actionability using TreatabolomeDB, IEMBase, ClinGen and treatment guidelines showed that 14.4% of cases diagnosed through the project were putatively treatable, underscoring the importance of genotype-to-treatment knowledgebases. Future developments include novel data collection methods through crowdsourcing with expert curation.

The Neuromuscular Disease Network for Canada (NMD4C): An interdisciplinary national collaboration to tackle unmet needs for NMD research and care

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In 2020, the CIHR and MDC-funded NMD4C was launched with a mission to improve the care, research, and treatment of neuromuscular diseases (NMDs) for all Canadians. NMD4C has united >530 Canadian NMD stakeholders to share best practices, resources and expertise, build clinical and research capacity, and facilitate access to novel therapies.
To build capacity for researchers and physicians, NMD4C has held monthly continuing professional development (CPD)-accredited webinars, acquired Royal College approval of neuromuscular medicine as an Area of Focused Competency, launched a 41-week CPD-accredited online neuromuscular fellowship curriculum , and invited outstanding early-career (EC) researchers and physicians to present/chair webinars and integrate into working groups, published >40 EC blogs and profiles, and established annual EC awards and postdoctoral and clinical fellowship awards. We co-created online NMD patient-oriented research training modules. We have published a Canadian guidance on gene replacement therapy in spinal muscular atrophy, provided guidance on NMD respiratory care and vaccination during the COVID pandemic, developed infographics to disseminate Canadian clinical practice guidelines, identified gaps in multidisciplinary Duchenne muscular dystrophy standards of care in Canada, and submitted clinician group input on CADTH's draft reimbursement recommendations and treatments under review. To strengthen research resources and infrastructure, we developed a virtual NMD biobank catalogue, launched two new registry disease datasets, and established dedicated clinical trial support for bringing more NMD clinical trials to Canada.
With renewed funding until 2028, we will expand our collaborative community of NMD stakeholders to address emerging challenges for advancing care and research in Canada.

Compliance to Duchenne Muscular Dystrophy Care Considerations in Canada

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Background: Duchenne muscular dystrophy (DMD) is a neuromuscular disease resulting in progressive muscle degeneration. Without disease-modifying therapies and a cure, the implementation of multidisciplinary care has significantly impacted the progression of DMD. This study examined existing care practices for patients in Canada, evaluated the extent to which these practices adhere to international care guidelines, and sought to pinpoint aspects of care where current standards are not met.

Methods: A 175-question cross-sectional survey was sent to clinical professionals actively involved in the care of DMD patients in Canada. The survey focused on clinicians' familiarity with the guidelines and their experiences with evaluations, techniques, and interventions across ten domains of management: neuromuscular, respiratory, cardiac, endocrinology/corticosteroid usage, gastrointestinal/nutritional, bone health/osteoporosis, orthopedic/surgical, rehabilitation, psychosocial support, and transitions.

Results: A total of 94 expert clinicians completed the survey. 71% were highly familiar with the care considerations. Suboptimal adherence to care guidelines was noted in endocrine, gastrointestinal/nutritional, and psychosocial management for ambulatory-pediatric patients. Psychosocial as well as gastrointestinal/nutritional management remained problematic for non-ambulatory patients. Whereas, all domains, except for cardiac care and endocrinology, were sub-optimal for adult patients. This aligns with the gaps in the process of transitioning from pediatric to adult healthcare.

Conclusion: While specialized and multi-disciplinary care has positively contributed to outcomes for Canadians with DMD, disease experts felt that enhancing care coordination and refining the approach in certain areas can lead to better outcomes and support patients to live fulfilling lives well into adulthood.

Expert Patient Capacity Building in Neuromuscular Disease Research

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Background: The Strategy for Patient-Oriented Research (POR) emphasizes incorporating patient-partners on research teams to reorient and reprioritize research questions to match those of patients and to bring more effective and meaningful improvements in health outcomes and systems. This approach has gained traction in recent years and is promoted by scientific funding organizations. However, many patients and researchers struggle with how to operationalize research partnerships, both realistically and effectively. Training and resources on POR exist, but none are specific to theoretical and practical considerations related to neuromuscular disease (NMD), and lack content in inclusion, diversity, equity, and accessibility

(IDEA). This project examined existing training resources, evaluated the unique needs of patient-partners and sought to develop e-learning modules from a NMD perspective.

Methods: A literature search and landscaping of existing POR resources was conducted. Following formal assessment of resources, through participatory methods, patient-partners were involved in developing competencies, learning objectives, original content and activities on readiness, IDEA and relationship building. A backwards educational design process was employed.

Results: Available high-quality Canadian and international-POR resources and best practices were identified and published in a repository/resource catalogue, which has received 256 views-to-date. Three easy-to-use and accessible NMD e-training modules were developed in English and French in spring 2023, with 40 patient-partners and researchers successfully completing the training to date.

Conclusion: Incorporating patient engagement in the research process has been embraced, but adoption has been low. The 'importND' resources now equip NMD researchers and patients in Canada to meaningfully collaborate in the research process.